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Supporting Information

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Second-Generation Total Synthesis of Spirastrellolide F Methyl Ester: The Alkyne Route**

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X-ray Crystal Structure Analysis of Compound 31

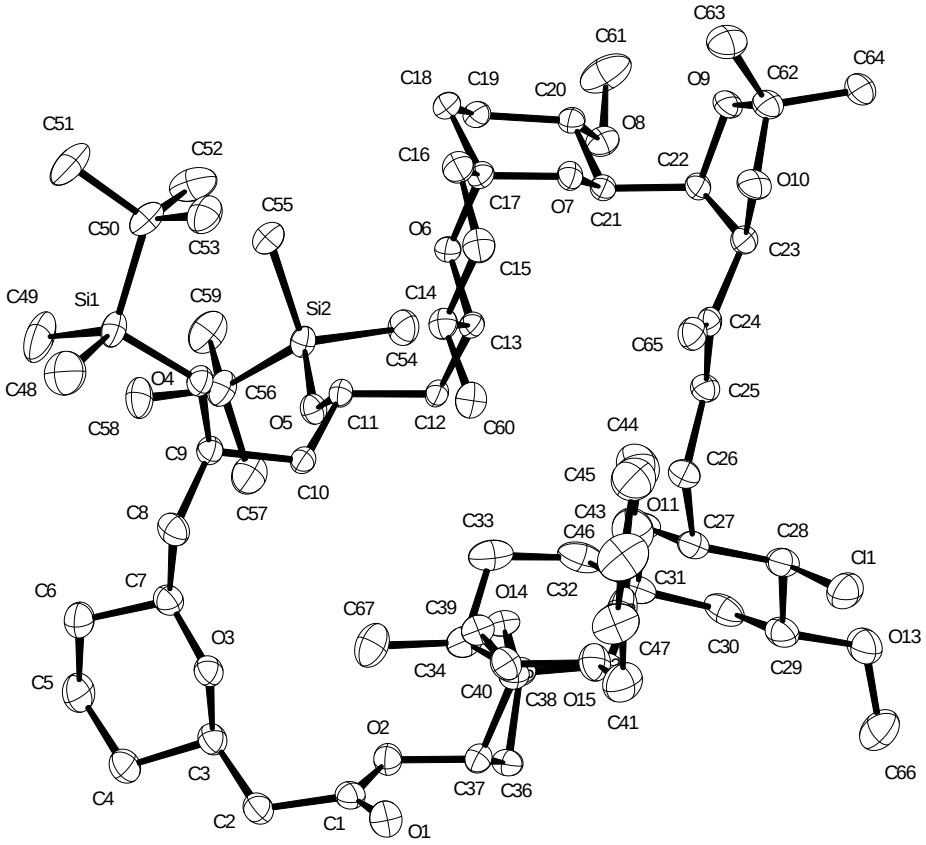
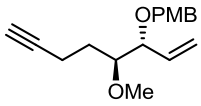


Figure S-1. Structure of compound **31** in the crystal. Hydrogen atoms omitted for clarity. Ellipsoids are shown at the 50 % probability level.

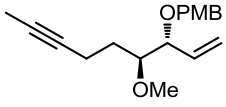
Crystal Data for 31: C_{67} H_{111} Cl O_{15} Si_2, M_r = 1248.19 g · mol^{-1}, colorless plate, crystal size 0.055 x 0.040 x 0.035 mm^3, orthorhombic, space group $P2_12_12$ [No. 18], a = 19.350(3) Å, 27.133(4) Å, c = 13.435(2) Å, V = 7053.8(16) Å^3, T = 100 K, Z = 4, D_{calc} = 1.175 g·cm^{-3}, λ = 0.71073 Å, μ(*Mo-K*$_\alpha$) = 0.149 mm^{-1}, Gaussian absorption correction (T_{min} = 0.9928, T_{max} = 0.9963), Bruker AXS Enraf-Nonius KappaCCD, 5.14 < θ < 36.58°, 262705 measured reflections, 33254 independent reflections (R_{int} = 0.137), 18504 reflections with $I > 2\sigma(I)$. Structure solved by direct methods and refined by full-matrix least-squares against F^2 to R_1 = 0.053 [$I > 2\sigma(I)$], wR_2 = 0.144 (all data), 782 parameters, H atoms riding, absolute structure parameter = 0.00(4), S = 1.011, residual electron density +0.8 / -0.5 e Å^{-3}. The highest maxima in the final difference Fourier map were in the region of the benzyl group indicating to a small degree that this group may adopt several conformations close to one another. CCDC 824552.

General. All reactions were carried out under Ar in flame-dried glassware. The solvents used were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O, 1,4-dioxane (Mg/anthracene), CH_2Cl_2, DME, MeCN (CaH_2), hexane, toluene (Na/K), MeOH (Mg). Flash chromatography: Merck silica gel 60 (230–400 mesh). NMR: Spectra were recorded on Bruker DPX 300, AMX 300, AV 400, or AVIII 600 spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: $\delta_C \equiv 77.0$ ppm; residual $CHCl_3$ in $CDCl_3$: $\delta_H \equiv 7.24$ ppm; CD_2Cl_2: $\delta_C \equiv 53.8$ ppm; residual ^1H: $\delta_H \equiv 5.32$ ppm; [D_8]-toluene: $\delta_C \equiv 20.4$ ppm; residual $D_5C_6CD_2H$: $\delta_H \equiv 2.09$ ppm; C_6D_6: $\delta_C \equiv 128.0$ ppm; residual C_6D_5H: $\delta_H \equiv 7.15$ ppm). IR: Spectrum One (Perkin-Elmer) spectrometer, wavenumbers ($\tilde{\nu}$) in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: ESQ3000 (Bruker), accurate mass determinations: Bruker APEX III FT-MS (7 T magnet) or Mat 95 (Finnigan). Unless stated otherwise, all commercially available compounds (Fluka, Lancaster, Aldrich) were used as received.

1-Methoxy-4-(((3*R*,4*S*)-4-methoxyoct-1-en-7-yn-3-yloxy)methyl)benzene (S-1). K_2CO_3 (4.88 g, 35.3 mmol) is added to a solution of TMS-alkyne **12** (3.06 g, 8.83 mmol) in MeOH (60 mL). The suspension is stirred for 1 h at room temperature before it was diluted with H_2O and ethyl acetate. The aqueous layer is extracted with ethyl acetate (3 x), the combined organic phases are washed with brine, dried over Na_2SO_4, filtered and evaporated, and the residue is purified by flash chromatography (hexane/ethyl acetate, 75:1 → 50:1) to afford the title compound as a pale yellow oil (2.15 g, 89%). $[\alpha]_D^{20} = -39.1$ (c = 1.0, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ =7.29 – 7.22 (m, 2H), 6.90 – 6.84 (m, 2H), 5.83 (ddd, J = 17.3, 10.3, 7.4 Hz, 1H), 5.34 (ddd, J = 10.4, 1.7, 0.8 Hz, 1H), 5.28 (ddd, J = 17.4, 1.8, 0.8 Hz, 1H), 4.57 (d, J = 11.6 Hz, 1H), 4.33 (d, J = 11.9 Hz, 1H), 3.84 – 3.77 (m, 1H), 3.80 (s, 3H), 3.42 (s, 3H), 3.38 (ddd, J = 6.4, 6.0, 4.1 Hz, 1H), 2.28 (td, J = 7.2, 2.6 Hz, 2H), 1.93 (t, J = 2.6 Hz, 1H), 1.77 – 1.68 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ= 159.3, 135.8, 130.8, 129.4 (2C), 119.0, 113.9 (2C), 84.5, 82.1, 81.5, 70.2, 68.5, 58.9, 55.4, 29.7, 14.8 ppm; IR (film) $\tilde{\nu}$ = 3295, 2934, 2866, 2835, 1612, 1586, 1512, 1464, 1442, 1301, 1245, 1172, 1107, 1068, 1033, 995, 928, 820 cm^{-1}; MS (EI): *m/z* (%): 274 [M^+] (<1), 121 (100), 97 (23), 45 (12). HRMS (ESI): *m/z* calcd. for $C_{17}H_{22}O_3Na$ [M^++Na]: 297.146117; found: 297.146025.

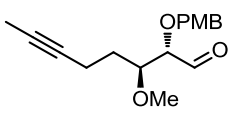


1-Methoxy-4-(((3*R*,4*S*)-4-methoxynon-1-en-7-yn-3-yloxy)methyl)benzene (13). *n*BuLi (5.30 mL, 8.44 mmol, 1.6 M in hexane) is added dropwise to a solution of the terminal alkyne **S-1** (1.93 g, 7.03 mmol) in THF (70 mL) at –78°C. The mixture is stirred for 15 min at that temperature before it is warmed to 0°C for 5 min and re-cooled to –78°C. After an additional 10 min, MeOTf (1.03 mL, 9.15 mmol) is added dropwise and stirring continued at this temperature for 30 min. The reaction is quenched with sat. aq. $NaHCO_3$, the mixture diluted with *tert*-butyl methyl ether and the aqueous layer extracted with *tert*-butyl methyl ether (3 x). The combined organic phases are washed with brine, dried over Na_2SO_4 and evaporated, and the residue is purified by flash chromatography (hexane/ethyl acetate, 10:1) to give alkyne **13** as a colorless oil (1.82 g, 80%). $[\alpha]_D^{20} = -23.9$ (c =



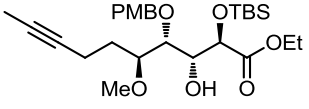
1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.34 – 7.30 (m, 2H), 6.95 – 6.92 (m, 2H), 5.94 – 5.84 (m, 1H), 5.39 – 5.36 (m, 2H), 4.59 (d, *J* = 11.4 Hz, 1H), 4.35 (d, *J* = 11.4 Hz, 1H), 3.89 – 3.83 (m, 1H), 3.85 (s, 3H), 3.44 (s, 3H), 3.43 – 3.38 (m, 1H), 2.28 – 2.21 (m, 2H), 1.82 (*br*.s, 3H), 1.72 – 1.65 ppm (m, 2H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 159.7, 136.5, 131.4, 129.7 (2C), 118.9, 114.1 (2C), 82.7, 82.4, 79.3, 76.0, 70.7, 59.0, 55.8, 30.7, 15.4, 3.7 ppm; IR (film) $\tilde{\nu}$ = 2920, 2861, 2835, 1612, 1512, 1301, 1246, 1172, 1106, 1068, 1033, 928, 821, 756 cm^{-1}; MS (EI): *m/z* (%): 121 (100), 111 (24), 91 (6), 53 (20); HRMS (ESI): *m/z* calcd. for $C_{18}H_{24}O_3Na$ [M^++Na]: 311.1619; found: 311.1618.

(2*S*,3*S*)-3-Methoxy-2-(4-methoxybenzyloxy)oct-6-ynal (14). K_2CO_3 (3.87 g, 28.0 mmol), $K_3[Fe(CN)_6]$ (9.22 g, 28.0 mmol) and OsO_4 (1.2 mL, 93 µmol, 2.5% in *t*BuOH, *w/w*) are added successively to a solution of $(DHQ)_2PYR$ (203 mg, 230 µmol) in *t*BuOH (50 mL) and H_2O (59 mL). The mixture is stirred for 20 min before a solution of alkene **13** (2.69 g, 9.33 mmol) in *t*BuOH (15 mL) is added at 0°C and stirring continued overnight. The reaction is quenched with aq. sat. Na_2SO_3 and the mixture stirred for 30 min. Sat. aq. $Na_2S_2O_3$ and ethyl acetate are added before the aqueous layer is separated and extracted with ethyl acetate (3 x). The combined extracts are washed with brine, dried over Na_2SO_4, filtered and evaporated, and the residue is purified by flash chromatography (hexane/ethyl acetate, 2:1 → 1:1) to give unreacted alkene **13** (860 mg) and the corresponding diol (1.33 g, 77% brsm, dr ≥ 9:1), which is directly used in the next step.



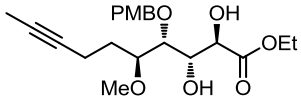
$Pb(OAc)_4$ (2.26 g, 4.58 mmol) is added in one portion to a solution of the diol (1.23 g, 3.82 mmol) in CH_2Cl_2 (38 mL). The mixture is stirred for 45 min before the reaction is carefully quenched with sat. aq. $NaHCO_3$. The mixture is diluted with ethyl acetate and the biphasic system filtered through Celite®. The aqueous layer is extracted with ethyl acetate (3 x), the combined organic phases are washed with brine, dried over Na_2SO_4, filtered and evaporated, and the residue is purified by flash chromatography (hexane/ethyl acetate, 10:1 → 4:1) to give aldehyde **14** (976 mg, 88%) as a colorless oil. ^{1}H NMR (400 MHz, C_6D_6): δ = 9.60 (d, *J* = 1.8 Hz, 1H), 7.16 – 7.12 (m, 2H), 6.77 – 6.73 (m, 2H), 4.40 (d, *J* = 11.6 Hz, 1H), 4.28 (d, *J* = 11.4, 1H), 3.67 – 3.62 (m, 2H), 3.28 (s, 3H), 3.14 (s, 3H), 2.30 – 2.14 (m, 2H), 1.96 – 1.87 (m, 1H), 1.68 – 1.60 (m, 1H), 1.52 ppm (t, *J* = 2.5 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 202.1, 160.0, 129.9, 129.8 (2C), 114.1 (2C), 84.5, 81.0, 78.7, 76.2, 72.6, 58.3, 54.8, 30.8, 15.2, 3.3 ppm. This aldehyde is unstable and should be used in the next step without delay.

Ester 16. A solution of silyl ketene acetal **15** (1.82 g, 6.64 mmol) in toluene (14 mL) and freshly prepared $MgBr_2$•OEt_2 (895 mg, 3.48 mmol) are successively added to a solution of aldehyde **14** (946 mg, 3.32 mmol) in toluene (26 mL) at –78°C. The mixture is stirred for 10 min before warming to room temperature over the course of 1 h. The reaction is quenched with sat. aq. $NaHCO_3$, the aqueous layer is extracted with ethyl acetate (3 x), the combined organic phases are dried over Na_2SO_4, filtered and evaporated, and the residue is purified by flash chromatography (hexanes/ethyl acetate, 20:1 → 5:1) to give ester **16** as a colorless oil (1.18 g, 70%, dr ≥ 10:1 (^{1}H NMR)). $[\alpha]_D^{20}$ = +10.1 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 – 7.27 (m, 2H), 6.90 – 6.86 (m, 2H), 4.70 (d, *J* = 10.9 Hz, 1H), 4.57 (d, *J* =

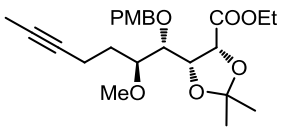


10.9 Hz, 1H), 4.26 (d, *J* = 6.8 Hz, 1H), 4.20 (dd, *J* = 14.4, 7.2 Hz, 2H), 3.90 (dt, *J* = 6.9, 2.1 Hz, 1H), 3.81 (s, 3H), 3.71 (dd, *J* = 3.8, 2.0 Hz, 1H), 3.52 (qi, *J* = 4.1 Hz, 1H), 3.42 (s, 3H), 3.14 (d, *J* = 7.1 Hz, 1H), 2.27 – 2.21 (m, 2H), 1.79 – 1.70 (m, 2H), 1.78 (t, *J* = 2.5 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.2, 159.3, 130.3, 129.3 (2C), 113.8 (2C), 81.4, 78.5, 76.6, 73.9, 73.1, 72.5, 60.9, 58.7, 55.3, 29.9, 25.7 (3C), 18.2, 15.0, 14.2, 3.5, –4.9, –5.2 (2C) ppm; IR (film) $\tilde{\nu}$ = 3496, 2930, 2857, 1747, 1613, 1514, 1463, 1248, 1173, 1103, 1033, 938, 836, 778 cm^{-1}; MS (EI): *m/z* (%): 451 (2), 281 (2), 218 (5), 121 (100), 111 (10), 75 (4), 73 (4); HRMS (ESI): *m/z* calcd. for $C_{27}H_{44}O_7SiNa$ [M^++Na]: 531.2746; found: 531.2749.

Diol S-2. TBAF (3.3 mL, 3.3 mmol, 1 M in THF) is added to a solution of compound **16** (1.12 g, 2.20 mmol) in THF (22 mL) at 0°C. After stirring for 30 min at 0°C and 60 min at ambient temperature, the reaction is quenched with sat. aq. NH_4Cl and the mixture diluted with ethyl acetate. The aqueous layer is extracted with ethyl acetate (3 x), the combined organic phases are washed with brine, dried over Na_2SO_4, filtered and evaporated, and the residue is purified by flash chromatography (hexanes/ethyl acetate, 2:1 → 0:1) to furnish diol **S-2** as a colorless oil (760 mg, 88%). $[\alpha]_D^{20}$ = –9.4 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 – 7.28 (m, 2H), 6.90 – 6.87 (m, 2H), 4.69 (d, *J* = 10.9 Hz, 1H), 4.56 (d, *J* = 10.6 Hz, 1H), 4.30 -4.21 (m, 3H), 3.89 (dt, *J* = 6.2, 2.8 Hz, 1H), 3.81 (s, 3H), 3.70 (dd, *J* = 4.6, 2.8 Hz, 1H), 3.60 (dt, *J* = 6.9, 4.9 Hz, 1H), 3.46 (s, 3H), 3.31 (d, *J* = 6.1 Hz, 1H), 2.98 (d, *J* = 7.8 Hz, 1H), 2.28 – 2.22 (m, 2H), 1.80 – 1.73 (m, 2H), 1.78 (t, *J* = 2.5 Hz, 3H), 1.30 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 159.5, 129.9, 129.8 (2C), 113.9 (2C), 80.8, 78.4, 77.8, 76.2, 73.4, 72.4, 72.3, 61.7, 59.0, 55.3, 30.2, 15.0, 14.2, 3.4 ppm; IR (film) $\tilde{\nu}$ = 3476, 2938, 2836, 1733, 1612, 1514, 1466, 1369, 1301, 1246, 1175, 1095, 1031, 822, 736 cm^{-1}; MS (EI): *m/z* (%): 394 [M^+] (<1), 273 (<1), 137 (8), 122 (12), 121 (100), 111 (24), 79 (4), 77 (4); HRMS (ESI): *m/z* calcd. for $C_{21}H_{30}O_7Na$ [M^++Na]: 417.1882; found: 417.1883.

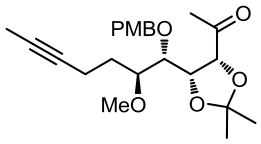


Acetal 17. 2,2-Dimethoxypropane (2.10 mL, 17.3 mmol) and camphorsulfonic acid (40 mg, 0.17 mmol) are added to a solution of diol **S-2** (681 mg, 1.72 mmol) in CH_2Cl_2 (17.2 mL) at 0°C. The mixture is stirred for 14 h at room temperature before the reaction is quenched with sat. aq. $NaHCO_3$. The aqueous layer is extracted with CH_2Cl_2 (3 x), the combined organic phases are dried over Na_2SO_4, filtered and evaporated, and the residue is purified by flash chromatography (hexanes/ethyl acetate, 4:1) to give acetal **17** as a colorless oil (650 mg, 87%). $[\alpha]_D^{20}$ = –18.1 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 – 7.28 (m, 2H), 6.88 – 6.84 (m, 2H), 4.67 (d, *J* = 11.1 Hz, 1H), 4.63 (d, *J* = 11.1 Hz, 1H), 4.53 (d, *J* = 6.6 Hz, 1H), 4.39 (t, *J* = 6.6 Hz, 1H), 4.12 – 4.03 (m, 2H), 3.89 (dd, *J* = 6.3, 5.0 Hz, 1H), 3.79 (s, 3H), 3.43 – 3.39 (m, 1H), 3.31 (s, 3H), 2.23 – 2.17 (m, 2H), 1.83 – 1.74 (m, 2H), 1.77 (t, *J* = 2.5 Hz, 3H), 1.60 (s, 3H), 1.40 (s, 3H), 1.22 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0, 159.0, 130.9, 129.3 (2C), 113.6 (2C), 110.4, 80.4, 79.8, 79.0, 76.3, 76.1, 75.7, 72.8, 60.9, 57.7, 55.2, 29.8, 26.6, 25.7, 14.5, 14.0, 3.4 ppm; IR (film) $\tilde{\nu}$ = 2983, 2937, 2836, 1743, 1613, 1514, 1463, 1380, 1370, 1246, 1185, 1100, 1077, 1034, 873, 820, 735, 702 cm^{-1}; MS (EI): *m/z* (%):



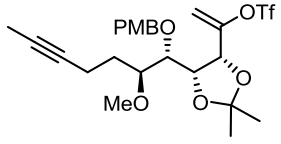
434 [M^+] (<1), 376 (<1), 173 (4), 135 (3), 121 (100), 111 (30), 83 (3), 77 (6); HRMS (ESI): *m/z* calcd. for $C_{24}H_{34}O_7Na$ [M^++Na]: 457.2200; found: 457.2197.

Ketone 19. *n*BuLi (470 µL, 750 µmol, 1.6 M in hexane) is added dropwise to a solution of methyl phenyl sulfone (141 mg, 90 µmol) in THF (3 mL) at –78°C. After stirring for 10 min, a solution of ester **17** (0.13 g, 0.30 mmol) in THF (2 x 1.5 mL) is slowly introduced and the mixture stirred for 15 min at that temperature and for 10 min at 0°C. The reaction is quenched with sat. aq. NH_4Cl and the mixture diluted with *tert*-butyl methyl ether. The aqueous layer is extracted with *tert*-butyl methyl ether (3 x) and the combined organic phases are washed with brine, dried over Na_2SO_4, filtered and evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate, 10:1) affords β-ketosulfone **18** as mixture with residual methyl phenyl sulfone, which is used in the next step without further purification.



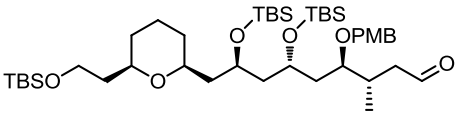
This crude material is dissolved in toluene (3 mL) in a J. YOUNG SCHLENK-flask before *n*Bu_3SnH (323 µL, 1.20 mmol) and AIBN (59 mg, 0.36 mmol) are successively added. The flask is stoppered and the mixture heated to 110°C for 3 h. After cooling to ambient temperature, the solvent is evaporated and the residue purified by flash chromatography (hexanes/ethyl acetate, 10:1) to afford ketone **19** as a colorless oil (96 mg, 79% over two steps). $[\alpha]_D^{20}$ = +13.1 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 – 7.21 (m, 2H), 6.85 – 6.82 (m, 2H), 4.72 (d, *J* = 11.1 Hz, 1H), 4.50 (dd, *J* = 8.2, 2.6 Hz, 1H), 4.34 (d, *J* = 8.1 Hz, 1H), 4.12 (d, *J* = 10.9 Hz, 1H), 3.79 (s, 3H), 3.73 (*br*. t, *J* = 2.9 Hz, 1H), 3.50 (dt, *J* = 9.2, 3.0 Hz, 1H), 3.41 (s, 3H), 2.36 – 2.20 (m, 2H), 2.06 – 1.94 (m, 1H), 2.00 (s, 3H), 1.81 – 1.68 (m, 1H), 1.78 (t, *J* = 2.4 Hz, 3H), 1.58 (s, 3H), 1.36 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 210.5, 158.9, 130.5, 128.9 (2C), 113.5 (2C), 110.0, 82.1, 81.0, 80.5, 79.0, 75.6, 75.4, 71.9, 58.2, 55.2, 30.3, 28.6, 26.5, 24.7, 15.3, 3.5 ppm; IR (film) $\tilde{\nu}$ = 2920, 1709, 1613, 1514, 1458, 1380, 1353, 1302, 1247, 1211, 1088, 1071, 1032, 869, 823 cm^{-1}; MS (EI): *m/z* (%): 404 [M^+] (<1), 346 (<1), 137 (3), 135 (4), 121 (100), 111 (30), 77 (6), 53 (10), 43 (17); HRMS (ESI): *m/z* calcd. for $C_{23}H_{32}O_6Na$ [M^++Na]: 427.2094; found: 427.2091.

Enol triflate 21. Freshly sublimed *p*-*t*$BuC_6H_4NTf_2$ (**20**, 45.0 mg, 109 µmol) is added to a solution of ketone **19** (20 mg, 49 µmol) in THF (1.2 mL). The mixture is cooled to –78°C before a solution of LiHMDS (89 µL, 89 µmol, 1 M in THF) is slowly introduced. After stirring for 10 min at this temperature, the solution is allowed to reach ambient temperature (10 min) before it is cooled again to –78°C. The reaction is then quenched with 10% aq. NaOH and the mixture diluted with hexanes. After reaching room temperature, the aqueous layer is extracted with hexanes (3 x), the combined organic phases are washed with brine, dried over Na_2SO_4 and evaporated, and the residue is purified by flash chromatography (hexanes/ethyl acetate, 10:1 → 4:1) to give product **21** as a pale yellow oil (15 mg, 57%). $[\alpha]_D^{20}$ = –16.9 (*c* = 0.7, CH_2Cl_2); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.38 – 7.34 (m, 2H), 6.84 – 6.80 (m, 2H), 5.06 (d, *J* = 3.8 Hz, 1H), 4.93 (d, *J* = 3.8 Hz, 1H), 4.81 (*br*. s, 2H), 4.41 (d, *J* = 6.6 Hz, 1H), 4.24 (t, *J* = 6.8 Hz, 1H), 3.86 (dd, *J* = 6.9, 4.7 Hz, 1H), 3.35 – 3.27 (m, 1H), 3.31 (s, 3H), 3.06 (s, 3H), 2.37 – 2.21 (m, 2H), 2.02 – 1.94 (m, 1H), 1.89 – 1.80 (m, 1H), 1.56 (s, 3H), 1.54 (t, *J* = 2.7 Hz, 3H), 1.17 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 159.7, 153.2, 131.2,



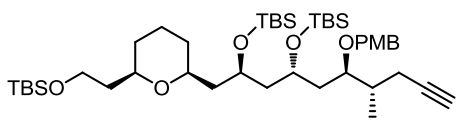
129.9 (2C), 119.3 (q, $J_{C\text{-}F}$ = 320 Hz), 113.9 (2C), 109.9, 106.5, 81.5, 80.0, 79.5, 77.0, 76.8, 75.8, 73.9, 57.2, 54.7, 29.9, 26.4, 24.8, 15.0, 3.3 ppm; IR (film) $\tilde{\nu}$ = 2987, 2938, 2840, 1613, 1514, 1421, 1384, 1248, 1208, 1139, 1100, 1074, 1035, 936, 874, 812, 698 cm^{-1}; MS (EI): *m/z* (%): 536 [M^+] (2), 478 (3), 403 (4), 345 (2), 313 (4), 273 (3), 246 (3), 155 (4), 135 (3), 121 (100), 111 (37); HRMS (ESI): *m/z* calcd. for $C_{24}H_{31}O_8SF_3Na$ [M^++Na]: 559.1587; found: 559.1584.

Aldehyde 7. *Catalyst preparation*: $[CpRu(CH_3CN)_3]PF_6$ (1 equiv.) and phosphine **10** (2 equivalents) are suspended a J. YOUNG SCHLENK-flask in carefully degassed CH_3CN (1 mL/24µmol [Ru]). The flask is tightly stoppered and the pale yellow mixture heated to 60°C for 7 h. After cooling to room temperature, the solvent is evaporated and the resulting yellow solid used in the hydration reaction without further purification.



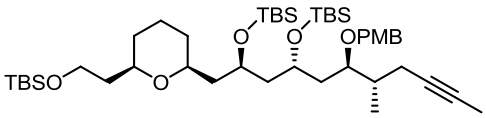
The ruthenium-complex $[RuL_2(CH_3CN)]PF_6$ (55 mg, 36 µmol) is added to a solution of alkyne **6** (600 mg, 772 µmol) in degassed acetone (7 mL) and H_2O (70 µL) and the resulting mixture is stirred for 14 h at 60°C in a sealed J. YOUNG SCHLENK-flask. At this point, additional H_2O (14 µL) and catalyst (25 mg, 16 µmol) are introduced and stirring continued for 7.5 h. For work up, the mixture is allowed to reach ambient temperature before it is adsorbed on Celite (ca. 2.5 g). Purification of the crude material by flash chromatography (hexanes/ethyl acetate, 1:0 → 9:1) furnishes aldehyde **7** as a colorless oil (540 mg, 88%), which is somewhat unstable and should be used in the next step without delay. $[\alpha]_D^{20}$ = +16.6 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, C_6D_6): δ = 9.45 (t, *J* = 1.6 Hz, 1H), 7.37 – 7.34 (m, 2H), 6.90 – 6.87 (m, 2H), 4.54 (d, *J* = 11.4 Hz, 1H), 4.45 (d, *J* = 11.4 Hz, 1H), 4.25 – 4.18 (m, 1H), 4.09 – 4.02 (m, 1H), 3.79 (t, *J* = 6.7 Hz, 2H), 3.61 – 3.50 (m, 2H), 3.48 – 3.42 (m, 1H), 3.34 (s, 3H), 2.50 – 2.40 (m, 1H), 2.20 (ddd, *J* = 17.2, 5.6, 1.5 Hz, 1H), 1.97 – 1.83 (m, 6H), 1.67 – 1.55 (m, 3H), 1.50 (ddd, *J* = 14.1, 8.8, 2.7 Hz, 1H), 1.28 – 1.14 (m, 3H), 1.21 – 1.09 (m, 2H), 1.04 (s, 9H), 1.00 (s, 9H), 0.99 (s, 9H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.24 (s, 3H), 0.22 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.07 ppm (s, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 200.1, 159.6, 131.7, 129.1 (2C), 114.1 (2C), 79.2, 74.6, 73.7, 70.5, 68.2, 66.9, 60.3, 54.8, 48.4, 47.4, 45.4, 40.5, 39.4, 32.7, 32.0, 30.5, 26.2 (9C), 24.1, 18.5, 18.3, 18.2, 15.3, –3.5, –3.7, –4.0 (2C), –5.1 (2C) ppm; IR (film) $\tilde{\nu}$ = 2929, 2856, 1728, 1614, 1514, 1471, 1386, 1248, 1069, 938, 832, 772, 663 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{43}H_{82}O_7Si_3Na$ [M^++Na]: 817.5264; found: 817.5261.

Alkyne S-3. Aldehyde **7** (170 mg, 21 µmol) is dissolved in MeOH (1.5 mL) before K_2CO_3 (58 mg, 42 µmol) and a solution of the Ohira-Bestmann reagent **11** (49 mg, 26 µmol) in MeOH (0.5 mL; additional 0.5 mL MeOH are used to rinse) are introduced. The mixture is stirred for 14 h before Et_2O (4.5 mL) and 5% aq. $NaHCO_3$ are added. The aqueous layer is extracted with Et_2O (3 x), the combined organic phases are washed with brine, dried over Na_2SO_4, filtered and evaporated, and the residue is purified by flash chromatography (hexanes/ethyl acetate, 20:1) to give alkyne **S-3** as a colorless oil (159 mg, 96%). $[\alpha]_D^{20}$ = +14.2 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.30 – 7.25 (m, 2H), 6.88 – 6.84 (m, 2H), 4.50 (d, *J* = 11.1 Hz, 1H), 4.40 (d, *J* = 10.9 Hz, 1H), 3.96 – 3.83 (m, 2H), 3.78 (s, 3H), 3.71 – 3.65 (m, 2H), 3.60 (ddd, *J* = 8.8, 5.1, 2.6



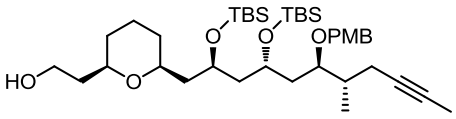
Hz, 1H), 3.44 – 3.33 (m, 2H), 2.26 – 2.12 (m, 2H), 2.12 – 2-01 (m, 1H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.83 – 1.76 (m, 1H), 1.73 – 1.31 (m, 11H), 1.20 – 1.09 (m, 2H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.88 (s, 18H), 0.87 (s, 9H), 0.08 (s, 6H), 0.06 (s, 3H), 0.03 (s, 3H), 0.02 ppm (s, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 159.6, 132.0, 129.4 (2C), 114.1 (2C), 84.0, 79.0, 75.0, 74.0, 70.9, 69.7, 68.2, 66.9, 60.7, 55.8, 48.3, 45.3, 40.6, 39.2, 36.0, 32.9, 26.4 (3C), 26.3 (6C), 24.4, 22.5, 18.5 (3C), 15.2, –3.2, –3.7, –3.8, –4.0, –5.0 (2C) ppm; IR (film) $\tilde{\nu}$ = 2951, 2929, 2856, 1614, 1514, 1471, 1462, 1248, 1080, 1004, 831, 772, 663 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{44}H_{82}O_6Si_3Na$ [M^++Na]: 813.5318; found: 813.5311.

Methylalkyne 8. *n*BuLi (195 µL, 310 µmol, 1.6 M in hexane) is added dropwise to a solution of



alkyne **S-3** (208 mg, 260 µmol) in THF (2 mL) at –78°C and the resulting mixture is stirred for 15 min at this temperature and for 10 min at 0°C, causing a color change to pale yellow. After re-cooling to –78°C, MeOTf (37 µL, 34 µmol) is added and the mixture stirred for 2 h before the reaction is quenched with sat. aq. $NaHCO_3$ and the mixture diluted with CH_2Cl_2. The aqueous phase is extracted with CH_2Cl_2 (3 x), the combined organic layers are washed with brine, dried over Na_2SO_4, filtered evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate, 50:1 → 20:1) affords product **8** as a colorless oil (194 mg, 93%). $[\alpha]_D^{20}$ = +11.5 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.30 – 7.26 (m, 2H), 6.88 – 6.84 (m, 2H), 4.50 (d, *J* = 10.9 Hz, 1H), 4.39 (d, *J* = 11.1 Hz, 1H), 3.96 – 3.83 (m, 2H), 3.79 (s, 3H), 3.72 – 3.65 (m, 2H), 3.62 (ddd, *J* = 9.2, 4.9, 2.2 Hz, 1H), 3.45 – 3.33 (m, 2H), 2.13 – 2.10 (m, 2H), 2.05 – 1.95 (m, 1H), 1.77 (t, *J* = 2.5 Hz, 3H), 1.81 – 1.74 (m, 1H), 1.72 – 1.31 (m, 11H), 1.20 – 1.09 (m, 2H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.08 (s, 6H), 0.06 (s, 3H), 0.03 (s, 3H), 0.02 ppm (s, 6H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 159.6, 132.2, 129.5 (2C), 114.1 (2C), 78.9, 78.3, 76.8, 75.0, 74.0, 70.7, 68.3, 66.9, 60.7, 55.8, 48.4, 45.3, 40.6, 39.0, 36.2, 32.8, 32.3, 26.3 (9C), 24.3, 23.0, 18.5 (3C), 15.2, 3.8, –3.2, –3.7, –3.9, –4.0, –5.0 (2C) ppm; IR (film) $\tilde{\nu}$ = 2929, 2856, 1514, 1471, 1462, 1386, 1247, 1078, 1004, 831, 772, 664 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{45}H_{84}O_6Si_3Na$ [M^++Na]: 827.5464; found: 827.5468.

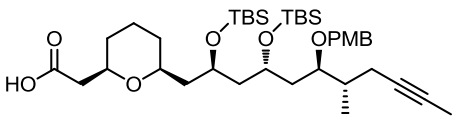
Alcohol S-4. This experiment was carried out in a Falcon^{TM}-tube (polyethylene). HF•pyridine



(1.8 mL, 1.0 g), pyridine (1.5 mL) and THF (6.5 mL) are added to a solution of compound **8** in THF (3.8 mL) at –10°C. After stirring for 14 h at this temperature, the mixture is diluted with ethyl acetate and the reaction carefully quenched with sat. aq. $NaHCO_3$, before the solution is allowed to reach ambient temperature. After the gas evolution has ceased, the aqueous phase is extracted with ethyl acetate (3 x), and the combined organic layers are washed with brine, dried over Na_2SO_4, filtered and evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate, 10:1 → 5:1) affords the primary alcohol **S-4** as a colorless oil (39 mg, 76%, 86% brsm). $[\alpha]_D^{20}$ = +20.9 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.29 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.52 (d, *J* = 11.4 Hz, 1H), 4.39 (d, *J* = 11.1 Hz, 1H), 3.91 – 3.83 (m, 2H), 3.79 (s, 3H), 3.74 – 3.66 (m, 2H), 3.65 – 3.59 (m, 1H), 3.53 – 3.44 (m, 2H), 2.40 (*br*. s, 1H), 2.14 – 2.08 (m, 2H), 2.05 – 1.96 (m, 1H), 1.84 – 1.74 (m, 1H), 1.77 (*br*. s, 3H), 1.71 – 1.11

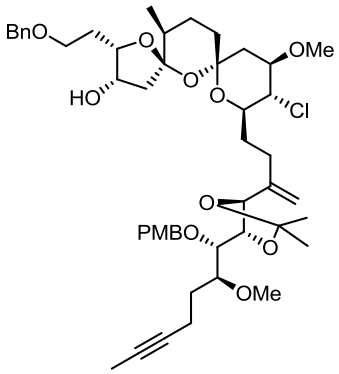
(m, 13H), 0.95 (d, J = 6.6 Hz, 3H), 0.89 (s, 18H), 0.09 (s, 6H), 0.07 (s, 3H), 0.04 ppm (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 159.6, 132.2, 129.5 (2C), 114.1 (2C), 79.0, 78.3, 78.2, 76.8, 74.4, 70.9, 68.1, 66.9, 61.6, 55.8, 48.2, 44.9, 39.2, 38.9, 36.1, 32.6, 32.2, 26.3 (6C), 24.2, 23.0, 18.5 (2C), 15.0, 3.8, -3.2, -3.7, -3.9, -4.2 ppm; IR (film) $\tilde{\nu}$ = 3517, 2929, 2856, 1613, 1513, 1471, 1386, 1247, 1060, 1039, 1004, 954, 833, 806, 772, 712 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{39}H_{70}O_6Si_2Na$ [M^++Na]: 713.4604; found: 713.4603.

Carboxylic acid 9. DESS-MARTIN periodinane is added to a solution of alcohol **S-4** (30 mg, 43 µmol) in un-distilled CH_2Cl_2 (2 mL) at 0°C and the resulting mixture is stirred for 2 h. The reaction is quenched by addition of a 1:1 (*v/v*) mixture of sat. aq. $NaHCO_3$ and sat. aq. $Na_2S_2O_3$. The mixture is diluted with CH_2Cl_2 and stirred until complete phase separation (~30 min) is reached. The aqueous layer is extracted with CH_2Cl_2 (3 x), the combinded organic phases are dried over Na_2SO_4, filtered and evaporated, and the residue used without further purification in the following step.



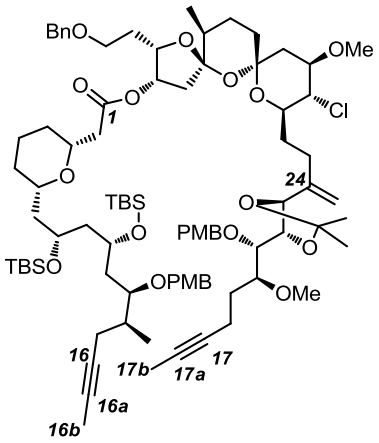
2-Methylbut-2-ene (38.0 µL, 361 µmol) and NaH_2PO_4 (11 mg, 95 µmol) are added to a solution of the crude aldehyde in *t*BuOH/H_2O (2 mL each). The resulting mixture is stirred for 5 min before $NaClO_2$ (23.0 mg, 258 µmol) is added. After stirring for 1 h, the reaction is quenched with sat. aq. NH_4Cl and the mixture diluted with ethyl acetate. The aqueous layer is separated and extracted with ethyl acetate (3 x), and the combined organic phases are washed with brine, dried over Na_2SO_4, filtered and evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate/AcOH, 4:1:0 → 2:1:0.01) affords carboxylic acid **9** as a pale yellow oil (28 mg, 92% over two steps).

Fragment 24. A solution of compound **22** (44 mg, 9.3 µmol) in THF (930 µL) is transferred *via* canula to a SCHLENK-flask containing 9-BBN (29.0 mg, 120 µmol) and the mixture is stirred for 5 h at room temperature. The solution of the formed alkylborane **23** is treated with carefully degassed aq. NaOH (1 M, 300 µL) and the mixture stirred for 1 h. The resulting borate-solution is transferred *via* canula to a SCHLENK-flask containing a solution of enol triflate **21** (40 mg, 7.5 µmol) in THF (750 µL) (additionally, 2 x 0.5 mL THF are used to rinse the flask). $AsPh_3$ (5.7 mg, 1.9 µmol) and $Pd(dppf)Cl_2$•CH_2Cl_2 (15.2 mg, 1.90 µmol) are added and the mixture is stirred at room temperature until TLC showed full conversion of the enol triflate. At this point, the solution is cooled to 0°C and aq. NaOH (1 M, 1.3 mL) and aq. H_2O_2 (0.1 mL, 30 % *w/w*) are added. After stirring for 30 min, the reaction is quenched with a solution of Na_2SO_3 (130 mg, 1.03 mmol) in H_2O (5.3 mL) and the resulting mixture allowed to reach ambient temperature. The aqueous layer is extracted with *tert*-butyl methyl ether (3 x) and the combined organic phases are washed with brine, dried over Na_2SO_4, filtered and evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate, 4:1 → 2:1) affords product **24** as a pale yellow oil (49 mg, 76%). $[\alpha]_D^{20}$ = –9.2 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, C_6D_6): δ = 7.49 – 7.45 (m, 2H), 7.13 – 7.03 (m, 5H), 6.85 – 6.81 (m, 2H), 5.27 (*br*. s, 1H), 5.08 (*br*. s, 1H), 4.94 (d, J = 10.9 Hz, 1H), 4.65 (d, J = 6.8 Hz, 1H), 4.44 (t, J = 7.0 Hz, 1H), 4.17 – 4.07 (m, 3H), 4.07 (d, J = 11.6 Hz, 1H), 4.03 (d, J = 11.6 Hz, 1H), 3.93 – 3.87 (m, 1H), 3.85 (dd, J = 7.0, 3.2

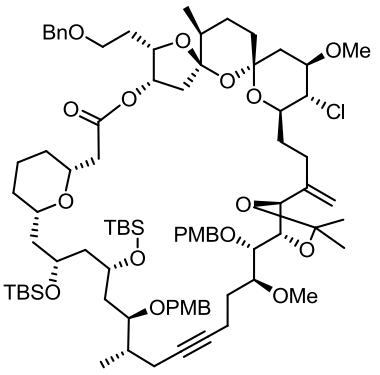


Hz, 1H), 3.70 (t, *J* = 9.8 Hz, 1H), 3.55 (dt, *J* = 9.1, 2.9 Hz, 1H), 3.29 (s, 3H), 3.22 (s, 3H), 3.25 – 3.18 (m, 1H), 3.20 (s, 3H), 3.10 – 3.02 (m, 2H), 2.76 – 2.59 (m, 2H), 2.51 – 2.31 (m, 4H), 2.25 – 2.00 (m, 6H), 1.94 – 1.78 (m, 2H), 1.75 (s, 3H), 1.73 – 1.65 (m, 1H), 1.58 – 1.49 (m, 1H), 1.55 (t, *J* = 2.5 Hz, 3H), 1.36 – 1.21 (m, 3H), 1.33 (s, 3H), 1.16 ppm (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ = 159.6, 147.6, 137.9, 131.9, 129.9 (2C), 128.7 (2C), 128.5 (2C), 128.3, 114.2 (2C), 114.0, 109.7, 109.0, 98.0, 84.7, 82.1, 81.3, 80.0, 79.9, 79.6, 77.5, 76.1, 74.5, 73.8, 73.4, 71.7, 67.6, 65.7, 57.7 (2C), 55.0, 48.8, 53.8, 38.7, 36.6, 32.8, 30.3, 29.6, 28.4, 27.6, 25.6, 24.5, 16.9, 15.8, 3.7 ppm; IR (film) $\tilde{\nu}$ = 3481, 2935, 1613, 1514, 1455, 1381, 1301, 1247, 1210, 1173, 1093, 1072, 1034, 977, 920, 824, 747, 698 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{48}H_{67}ClO_{11}Na$ [M^++Na]: 877.4257; found: 877.4264.

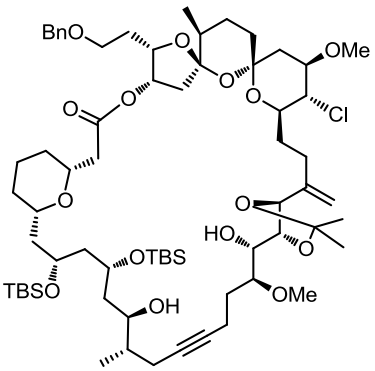
Diyne 25. Et_3N (66.0 µL, 473 µmol) and 2,4,6-trichlorobenzoyl chloride (18.0 µL, 113 µmol) are added to a solution of carboxylic acid **9** (40.0 mg, 56.7 µmol) in toluene (2 mL) at 0°C and the resulting mixture is stirred for 1 h at this temperature. A solution of alcohol **24** (40 mg, 47 µmol) and recrystallized DMAP (29.0 mg, 236 µmol) in toluene (1 mL) is added (the flask is rinsed with 2 x 0.5 mL of toluene), whereupon the mixture turns cloudy. The cooling bath is removed and the mixture stirred for 1.5 h at ambient temperature. The reaction is quenched with sat. aq. $NaHCO_3$ and ethyl acetate. The aqueous layer is extracted with ethyl acetate (3 x), the combined organic phases are washed with brine and dried over Na_2SO_4, filtered and evaporated, and the residue is purified by flash chromatography (hexanes/ethyl acetate, 15:1 → 5:1) to give diyne **25** as a colorless oil (62 mg, 85%). $[\alpha]_D^{20}$ = +3.3 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (600 MHz, C_6D_6): see Table S1; ^{13}C NMR (150 MHz, C_6D_6): see Table S1; IR (film) $\tilde{\nu}$ = 2931, 2857, 1737, 1613, 1514, 1461, 1381, 1301, 1247, 1173, 1068, 1038, 977, 929, 855, 774, 698 cm^{-1}; HRMS (ESI): calcd. for $C_{87}H_{133}O_{17}ClSi_2Na$ [M^++Na]: 1563.8659; found: 1563.8662.



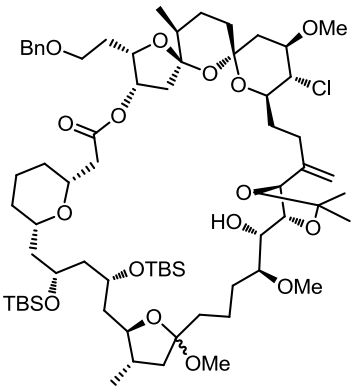
Cycloalkyne 26. A solution of diyne **25** (25.0 mg, 16.2 µmol) is transferred with toluene (14.1 mL) *via* canula to a flask containing molecular sieves (MS 5Å) (32 mg). A solution of the molybdenum complex **28** (1.75 mg, 1.30 µmol) in toluene (3.1 mL) is added to the resulting suspension stirred overnight. The mixtue is filtered through a short pad of silica, which is carefully rinsed with ethyl acetate. The combined filtrates are evaporated and the residue purified by flash chromatography (hexanes/ethyl acetate, 5:1) to yield product **26** as a white foam (21.0 mg, 87%). $[\alpha]_D^{20}$ = +5.8 (*c* = 0.9, CH_2Cl_2); ^{1}H NMR (600 MHz, C_6D_6): see Table S2; ^{13}C NMR (150 MHz, C_6D_6): see Table S2; IR (film) $\tilde{\nu}$ = 2930, 2856, 1738, 1613, 1514, 1247, 1087, 1066, 1038, 978, 834, 805, 774, 698 cm^{-1}; HRMS (ESI): calcd. for $C_{83}H_{127}O_{17}ClSi_2Na$ [M^++Na]: 1509.8205; found: 1509.8193.



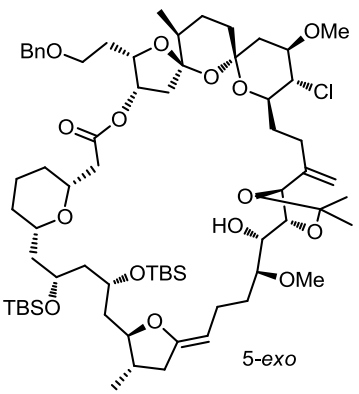
Diol 27. A solution of DDQ (11.4 mg, 50.4 μmol) in CH_2Cl_2 (0.9 mL) is added to a solution of cycloalkyne **26** (25.0 mg, 16.8 μmol) in undistilled CH_2Cl_2 (0.9 mL) at 0°C and the mixture is stirred at this temperature for 5 min before the cooling bath is removed. After 1 h the reaction is quenched with sat. aq. $NaHCO_3$. The solution is diluted with CH_2Cl_2 and stirred for 15 min, until the precipitate in the organic phase is dissolved. The aqueous layer is extracted with CH_2Cl_2, the combined extracts are dried over Na_2SO_4, filtered and evaporated, and the residue is purified by flash chromatography (hexanes/ethyl acetate, 20:1) to give diol **27** as a colorless oil (19.0 mg, 91%). $[\alpha]_D^{20}$ = +3.9 (*c* = 0.4, CH_2Cl_2); ^{1}H NMR (600 MHz, C_6D_6): see Table S3; ^{13}C NMR (150 MHz, C_6D_6): see Table S3; IR (film) $\tilde{\nu}$ = 3510, 2930, 2857, 1737, 1462, 1381, 1257, 1054, 978, 927, 835, 802, 775, 735, 698 cm^{-1}; HRMS (ESI): calcd. for $C_{67}H_{111}O_{15}ClSi_2Na$ [M^++Na]: 1269.7041; found: 1269.7042.

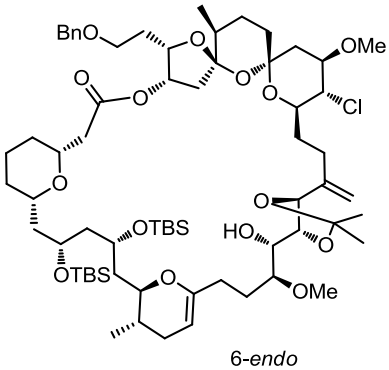


Furanosides 29. A solution of $AuCl{\cdot}SMe_2$ (44.9 μg in 10 μL CH_2Cl_2, 0.152 μmol) is added to a solution of diol **27** (1.90 mg, 1.52 μmol) in CH_2Cl_2 (200 μL). The mixture is stirred for 22.5 h before it is filtered through a pad of silica/Celite®. The pad is carefully rinsed with ethyl acetate and the combined filtrates are evaporated. The residue is dissolved in MeOH (250 μL) and a catalytic amount of pyridinium-*p*-toluenesulfonate is added. The mixture is stirred for 2 h before the reaction is quenched with sat. aq. $NaHCO_3$. The aqueous layer is extracted with ethyl acetate (3 x), the combined organic phases are dried over Na_2SO_4, filtered and evaporated, and the residue is purified by flash chromatography (hexanes/ethyl acetate, 20:1 → 5:1) to afford compound **29** as a colorless oil (0.7 mg, 36%, dr ~ 2.3:1 (^{1}H NMR)). ^{1}H NMR (600 MHz, C_6D_6): see Table S4; (major anomer) and Table S5 (minor anomer); ^{13}C NMR (150 MHz, C_6D_6): see Table S4 (major anomer) and Table S5 (minor anomer); HRMS (ESI): calcd. for $C_{68}H_{115}O_{16}ClSi_2Na$ [M^++Na]:1301.7310; found: 1301.7304.



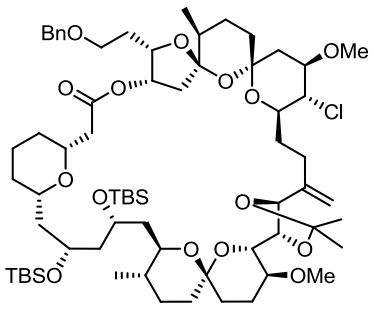
Enolethers 28 and 30. Diol **27** (5.0 mg, 4.0 μmol) and molecular sieves (MS 4Å, 15 mg) are suspended in CH_2Cl_2 (0.5 mL) and the mixture is stirred for 15 min before a solution of the gold complex **32** (40 μL, 0.40 μmol, 0.01 M in CH_2Cl_2) is added. Stirring is continued for 1 h before the reaction is quenched with Et_3N. After stirring for 5 min, the mixture is filtered through a short pad of SiO_2, which is carefully washed with Et_2O. The combined filtrates are evaporated and the residue purified by flash chromatography (hexanes/ethyl acetate, 10:1 → 4:1) to give compound **30** as the major product (admixed with enol ether **28**). Colorless oil (3.1 mg, 62%, **30**:**28** = 5:1).



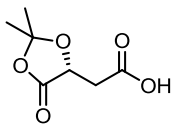


^{1}H NMR (600 MHz, C_6D_6): see Table S6 (**30**) and Table S7 (**28**); ^{13}C NMR (150 MHz, C_6D_6): see Table S6 (**30**) and Table S7 (**28**); HRMS (ESI): calcd. for $C_{67}H_{111}O_{15}ClSi_2Na$ [M^++Na]: 1269.7052; found.: 1269.7042.

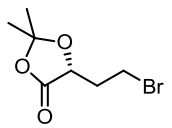
Macrolactone 31. A solution of pyridinium-*p*-toluenesulfonate (12 µL, 0.12 µmol, 0.01 M in CH_2Cl_2) is added to the mixture of enolethers **30** and **28** (5:1) (3.1 mg, 2.5 µmol) in toluene (0.5 mL) in a J. YOUNG SCHLENK-flask. The flask is carefully stoppered and the mixture heated to 80°C for 30 min. After cooling to room temperature, the solution is filtered through a pad of basic alumina, which is carefully washed with Et_2O. The combined filtrates are evaporated and the residue is purified by flash chromatography (hexanes/ethyl acetate, 10:1 → 4:1) to give 6,6-spiroketal **31** as a white foam (2.5 mg, 81%). The data are in full accord with those previously reported.[1]



(*R*)-(-)-2,2-Dimethyl-5-oxo-1,3-dioxolan-4-acetic acid (S-5). Pyridinium-*p*-toluenesulfonate (860 mg, 3.40 mmol) is added to a solution of D-(+)-malic acid **35** (5.00 g, 37.3 mmol) in 2,2-dimethoxypropane (20 mL). The mixture is stirred for 50 h before the solvent is evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate, 1:0 → 2:3) affords product **S-5** as a white solid (5.5 g, 84%). Mp = 113-114°C; $[\alpha]_D^{20}$ = –5.8 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, acetone-d_6): δ = 11.0 (*br*. s, 1H), 4.79 (dd, *J* = 5.7, 4.2 Hz, 1H), 2.89 (dd, *J* = 17.2, 4.3 Hz, 1H), 2.80 (dd, *J* = 17.1, 5.7 Hz, 1H), 1.57 (s, 3H), 1.55 (s, 3H); ^{13}C NMR (100 MHz, acetone-d_6): δ = 173.5, 171.5, 112.1, 72.3, 37.0, 27.7, 26.8; IR (film) $\tilde{\nu}$ = 3264, 1756, 1732, 1421, 1401, 1378, 1277, 1168, 1126, 998, 925, 839, 802, 667 cm^{-1}; MS (EI): *m/z* (%): 159 (18), 131 (11), 85 (12), 71 (20), 59 (28), 43 (100); HRMS (CI): *m/z* calcd. for $C_7H_{11}O_5$ [M^++H]: 175.0606; found: 175.0606. The analytical data are in agreement with the literature.[2]



(*R*)-5-(2-Bromoethyl)-2,2-dimethyl-1,3-dioxolan-4-one (S-6). A solution of BH_3·THF (4 mL, 4 mmol, 1 M in THF) is added over 30 min to a solution of carboxylic acid **S-5** (500 mg, 2.87 mmol) in THF (3 mL) at 0°C. The mixture is slowly warmed to ambient temperature and stirred for 6 h. After cooling to 0°C, MeOH (2 mL) is added and the solvent is evaporated (20°C bath temperature) to afford the desired alcohol, which is used in the next step without further purification.



A solution of the crude alcohol in CH_2Cl_2 (10 mL) is added dropwise to a solution of Ph_3PBr_2 (2.42 g, 5.74 mmol) and imidazole (1.18 g, 17.2 mmol) in CH_2Cl_2 (10 mL) at 0°C. The mixture is stirred overnight at ambient temperature before the reaction is quenched with brine. The

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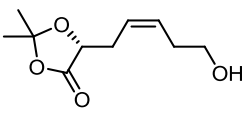
[1] See the Supporting Information of the following paper: S. Benson, M.-P. Collin, G. W. O'Neil, J. Ceccon, B. Fasching, M. D. B. Fenster, C. Godbout, K. Radkowski, R. Goddard, A. Fürstner, *Angew. Chem*. **2009**, *121*, 10130-10134; *Angew. Chem. Int. Ed*. **2009**, *48*, 9946-9950

[2] J. T. Kodra et al., *J. Med. Chem*. **2008**, *51*, 5387-5396.

aqueous layer is extracted with CH_2Cl_2 (3 x), the combined organic phases are dried over $MgSO_4$, filtered and evaporated (20°C bath temperature). Purification of the residue by flash chromatography (pentanes/Et_2O, 1:0 → 9:1) affords bromide **S-6** as a colorless oil (437 mg, 68% over two steps). $[\alpha]_D^{20}$ = +14.5 (*c* = 0.84, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.56 (dd, *J* = 8.2, 4.3 Hz, 1H), 3.59 – 3.44 (m, 2H), 2.43 – 2.33 (m, 1H), 2.28 – 2.17 (m, 1H), 1.60 (s, 3H), 1.60 ppm (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.5, 111.1, 72.0, 34.9, 27.9, 27.3, 25.8 ppm; IR (film) $\tilde{\nu}$ = 2993, 1788, 1437, 1382, 1327, 1292, 1255, 1241, 1218, 1163, 1114, 1048, 992, 946, 910, 883, 852, 764, 701 cm^{-1}; MS (EI): *m/z* (%): 207 (7), 137 (<1), 122 (1), 85 (14), 59 (21), 43 (100); HRMS (CI): *m/z* calcd. for $C_7H_{12}O_3Br$ [M^++H]: 222.9971; found: 222.9970.

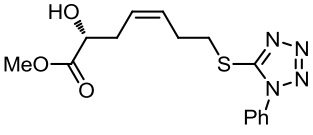
(*R*,*Z*)-5-(5-Hydroxypent-2-enyl)-2,2-dimethyl-1,3-dioxolan-4-one (38). A solution of bromide **S-6** (360 mg, 1.61 mmol) and PPh_3 (466 mg, 1.80 mmol) in CH_3CN (5 mL) is heated to 150°C in a microwave oven for 2.5 h. After cooling to room temperature, the solvent is evaporated, affording the corresponding phosphonium bromide **36** as a white foam, which is used in the next step without further purification.

A solution of phosphonium bromide **36** in THF (60 mL) and CH_2Cl_2 (30 mL) is cooled to –78°C before KHMDS (3.2 mL, 1.6 mmol, 0.5 M in toluene) and a solution aldehyde **37** (455 mg, 2.40 mmol) in THF (20 mL) are successively added. The mixture is warmed to 0°C and stirred for 1 h before the reaction is quenched with sat. aq. NH_4Cl. The aqueous layer is extracted with pentane (3 x), the combined extracts are dried over $MgSO_4$, filtered and evaporated (20°C bath temperature). Purification of the residue by flash chromatography (pentanes/Et_2O, 98:2 → 4:1) affords a mixture of the desired Z-alkene with unreacted aldehyde **37**, which is directly used in the following step.



To a solution of this crude product in THF (20 mL) are added NH_4F (72.0 mg, 1.93 mmol) and TBAF (1.93 mL, 1.93 mmol, 1 M in THF) at 0°C. The mixture is stirred overnight at ambient temperature before silica is added. The solvent is evaporated (20°C bath temperature) and the absorbed residue put on top of a silica gel column, which is eluated with pentanes/Et_2O (4:1 → 0:1) to give product **38** as a colorless oil (182 mg, 56% over three steps). $[\alpha]_D^{20}$ = +1.3 (*c* = 0.8, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.68 – 5.52 (m, 2H), 4.43 (dd, *J* = 6.3, 5.1 Hz, 1H), 3.65 (dd, *J* = 11.7, 5.8 Hz, 2H), 2.72 – 2.53 (m, 2H), 2.40 – 2.30 (m, 2H), 1.80 (t, *J* = 5.4 Hz, 1H), 1.60 (s, 3H), 1.53 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.8, 130.4, 125.6, 110.8, 74.0, 62.0, 31.1, 29.4, 27.1, 26.0 ppm; IR (film) $\tilde{\nu}$ = 3415, 2993, 2937, 2877, 1787, 1432, 1380, 1351, 1318, 1269, 1239, 1217, 1124, 1102, 1046, 988, 923, 897, 871, 840, 801, 741, 700 cm^{-1}; MS (EI): *m/z* (%): 200 [M^+] (<1), 170 (25), 116 (13), 112 (91), 97 (23), 70 (15), 67 (64), 59 (100), 43 (57), 31 (28); HRMS (ESI): *m/z* calcd. for $C_{10}H_{16}O_4Na$ [M^++Na]: 223.0940; found: 223.0941.

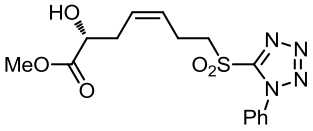
(*R*,*Z*)-Methyl 2-hydroxy-7-(1-phenyl-1*H*-tetrazol-5-ylthio)hept-4-enoate (39). 1-Phenyl-tetrazole-5-thiol (86.0 mg, 480 µmol), PPh_3 (126 mg, 480 µmol) und DIAD (95.0 µL, 480 µmol) are added to a solution of alcohol **38** (80 mg, 40 µmol) in THF (5 mL) at 0°C. The mixture is stirred at ambient temperature overnight before the solvent is evaporated



(20°C bath temperature). The resulting crude thioether is isolated as a colorless oil and used without further purification in the next step.

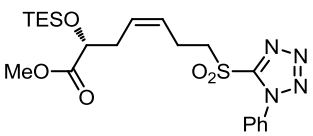
NaOMe (1.0 mg, 2 µmol) is added to a solution of the crude thioether in CH_2Cl_2 (4mL) and MeOH (1 mL) at 0°C. The mixture is stirred for 4 h at room temperature before the solvent is evaporated (20°C bath temperature). Purification of the residue by flash chromatography (pentanes/Et_2O, 4:1 → 1:1) affords product **39** as a colorless oil (115 mg, 86% over two steps). $[\alpha]_D^{20}$ = –16.2 (*c* = 0.6, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 – 7.50 (m, 5H), 5.67 – 5.51 (m, 2H), 4.28 – 4.23 (m, 1H), 3.78 (s, 3H), 3.50 – 3.32 (m, 2H), 2.96 (*br.* d, *J* = 4.7 Hz, 1H), 2.62 (*br.* dd, *J* = 14.9, 7.4 Hz, 2H), 2.62 – 2.53 (m, 1H), 2.52 – 2.43 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.7, 154.3, 133.6, 130.2, 129.8 (2C), 129.7, 126.5, 123.8 (2C), 70.0, 52.5, 32.8, 32.3, 27.1 ppm; IR (film) $\tilde{\nu}$ = 3460, 3017, 2952, 1737, 1596, 1499, 1438, 1412, 1387, 1278, 1242, 1213, 1101, 1074, 1015, 980, 917, 762, 694 cm^{-1}; MS (EI): *m/z* (%): 275 (7), 245 (100), 179 (20), 163 (11), 151 (16), 135 (21), 117 (22), 85 (10), 79 (11), 77 (28), 67 (54), 59 (8), 41 (21); HRMS (ESI): *m/z* calcd. for $C_{15}H_{18}N_4O_3SNa$ [M^++Na]: 357.0991; found: 357.0992.

(*R,Z*)-Methyl 2-hydroxy-7-(1-phenyl-1H-tetrazol-5-ylsulfonyl)hept-4-enoate (S-7).



$(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (16 mg, 13 µmol) and aq. H_2O_2 (200 µL, 30% *w/w*) are added to a solution of methyl ester **39** (21 mg, 62 µmol) in EtOH (0.5 mL) at 0°C. The mixture is warmed to 15°C over 5 min, before it is cooled to 5°C and stirred at this temperature for 5 h. For work up, the solution is diluted with EtOAc before the reaction is quenched by careful addition of a mixture (1:1, *v/v*) of sat. aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$. The mixture is allowed to reach room temperature, the aqueous layer is separated and extracted with EtOAc (3 x) the combined extracts are evaporated and the residue is purified by flash chromatography (hexanes/ethyl acetate, 9:1 → 1:1) to give sulfone **S-7** as a colorless oil (15 mg, 65%). $[\alpha]_D^{20}$ = –8.1 (*c* = 0.32, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 – 7.54 (m, 5H), 5.65 – 5.52 (m, 2H), 4.27 (*br.* dd, *J* = 5.8, 10.9 Hz, 1H), 3.81 – 3.74 (m, 2H), 3.79 (s, 3H), 2.91 (d, *J* = 5.5, 1H), 2,78 – 2.67 (m, 2H), 2.64 – 2.54 (m, 1H), 2.53 – 2.43 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.8, 153.5, 133.1, 131.6, 129.9 (2C), 127.7, 127.3, 125.2 (2C), 69.6, 55.6, 52.9, 32.2, 20.8 ppm; IR (film) $\tilde{\nu}$ = 3508, 2955, 1733, 1595, 1497, 1439, 1406, 1342, 1271, 1211, 1144, 1100, 1075, 1047, 1015, 979, 914, 762, 729, 687 cm^{-1}; MS (EI): *m/z* (%): 307 (9), 277 (61), 213 (10), 186 (21), 157 (19), 131 (18), 118 (79), 91 (18), 79 (64), 67 (100), 59 (17); HRMS (ESI): *m/z* calcd. for $C_{15}H_{18}N_4O_5SNa$ [M^++Na]: 389.0887; found: 389.0890.

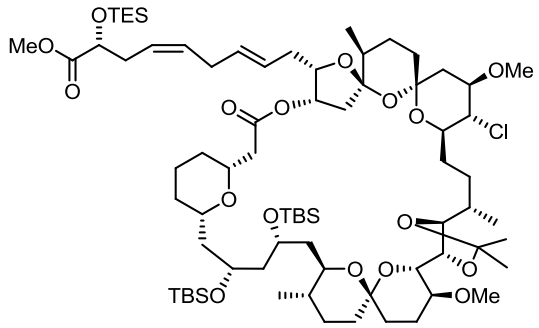
(*R,Z*)-Methyl 7-(1-phenyl-1*H*-tetrazol-5-ylsulfonyl)-2-(triethylsilyloxy)hept-4-enoate (40).



TESCl (12 µL, 70 µmol) and imidazole (6.3 mg, 93 µmol) are added to a solution of sulfone **S-7** (17 mg, 46 µmol) in CH_2Cl_2 (5 mL) at 0°C. The mixture is stirred overnight at ambient temperature before the solvent is evaporated. Purification of the residue by flash chromatography (hexanes/ethyl acetate, 95:5 → 4:1) affords compound **40** (20 mg, 90%) as a colorless oil. $[\alpha]_D^{20}$ = –4.6 (*c* = 0.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 – 7.55 (m, 5H), 5.66 – 5.47 (m, 2H), 4.27 (t, *J* = 5.7 Hz, 1H), 3.79 – 3.72 (m, 2H), 3.71 (s, 3H), 2.72 (*br.* dd, *J* = 15.6, 7.5 Hz, 2H), 2.51 (*br.* t, *J* = 6.2 Hz, 2H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.60 ppm (q, *J* =

7.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.5, 153.6, 133.2, 131.6, 129.9 (2C), 128.5, 126.5, 125.2 (2C), 71.5, 55.7, 52.1, 33.4, 20.7, 6.8 (3C), 4.7 (3C) ppm; IR (film) $\tilde{\nu}$ = 2969, 2954, 2915, 2877, 1738, 1595, 1498, 1459, 1436, 1415, 1347, 1280, 1230, 1216, 1203, 1114, 1126, 1014, 976, 943, 832, 760, 727, 687 cm^{-1}; MS (EI): *m/z* (%): 451 (18), 421 (7), 277 (12), 213 (20), 174 (35), 118 (19), 59 (20); HRMS (ESI): *m/z* calcd. for $C_{21}H_{32}N_4O_5SSiNa$ [M^++Na]: 503.1751; found: 503.1754.

Macrolactone 34. $Pd(OH)_2$ on carbon (Pearlman's catalyst, 2.6 mg, 20% Pd on carbon) is added to a solution of macrolactone **33a** (5.0 mg, 4.0 μmol) in ethyl acetate (1.5 mL). The suspension is stirred under H_2 (1 atm) for 2 h before it is filtered through a pad of Celite®. The filtrate is evaporated and the residue subjected to the next reaction without further purification.



DESS-MARTIN periodinane (3.4 mg, 8.0 μmol) is added to a solution of the crude alcohol in CH_2Cl_2 (500 μL) at 0°C. After stirring for 3 h at room temperature, additonal DESS-MARTIN periodinane (6.8 mg, 16 μmol) and $NaHCO_3$ (6.7 mg, 80 μmol) are added and stirring continued for 1 h. The reaction is quenched with a mixture (1:1, *v/v*) of sat. aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$. The emulsion is diluted with CH_2Cl_2 and stirred until complete phase separation is reached (~30 min). The aqueous layer is extracted with CH_2Cl_2 (3 x), the combined organic phases are washed with brine, dried over Na_2SO_4, filtered and evaporated, and the residue purified by flash chromatography (hexanes/ethyl acetate, 10:1 → 4:1) to give the corresponding aldehyde **33b** as a white foam (3.1 mg, 67% over two steps).

KHMDS (43 μL, 11 μmol, 0.25 M in THF) is added to a solution of sulfone **40** (6.5 mg, 13 μmol) in THF (100 μL) at –78°C. The reaction mixture is stirred at this temperature for 10 min and at –60°C for additional 2 h. The solution is then cooled to –78°C and added to a solution of aldehyde **33b** (3.1 mg, 2.7 μmol) in THF (100 μL) at –78°C via canula (the flask of the sulfone is rinsed with 100 μL of THF). The mixture is stirred at –65°C for 1.5 h before the reaction is quenched with sat. aq. NH_4Cl while cold. After reaching ambient temperature, the aqueous layer is extracted with Et_2O (5 x), the combined organic phases are evaporated and the residue is purified by flash chromatography (hexanes/ethyl acetate, 10:1 → 7:1) to yield product **34** as a white foam (2.9 mg, 76%). $[\alpha]_D^{20}$ = +6.9 (*c* = 0.65, CH_2Cl_2); ^{1}H NMR (600 MHz, C_6D_6): see Table S8; ^{13}C NMR (150 MHz, C_6D_6): see Table S8; IR (film) $\tilde{\nu}$ = 2930, 2878, 1739, 1461, 1376, 1250, 1193, 1081, 1005, 982, 835, 773, 745 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{74}H_{131}ClO_{17}Si_3Na$ [M^++Na]: 1433.8281; found: 1433.8275.

Table S1. NMR spectroscopic data of diyne **25**.

^{1}H[a)]	^{1}H NMR (600 MHz, C_6D_6)[b)]	^{13}C[a)]	^{13}C NMR (150 MHz, C_6D_6)[c)]
-	-	**1**	170.1
2a	2.60 dd (15.7, 6.6)	**2**	41.7
2b	2.23 dd (15.7, 6.5)		
3	3.83	**3**	73. 9
4a	1.44 *br.* d	**4**	31.4
4b	1.03		
5a	1.55	**5**	23.7
5b	1.31		
6a	1.36	**6**	32.1
6b	1.11		
7	3.62 m	**7**	74.2
8a	1.88	**8**	45.1
8b	1.61		
9	4.21 m	**9**	66.8
10a	1.96	**10**	48.2
10b			
11	4.16 m	**11**	68.4
12a	1.87	**12**	39.1
12b	1.67		
13	3.82	**13**	78.8
14	2.15	**14**	36.0
15a	2.30 m	**15**	23.0
15b			
-	-	**16**	78.2
-	-	**16a**	76.7
16b	1.64 t (2.5)	**16b**	3.6
-	-	**17**	79.7
-	-	**17a**	75.7
17b	1.55 t (2.6)	**17b**	3.4
18a	2.40	**18**	15.6
18b			
19a	2.10	**19**	30.0
19b	1.95		
20	3.56 dt (9.2, 3.0)	**20**	81.1
21	3.84	**21**	76.9
22	4.45 t (6.7)	**22**	79.6
23	4.65 d (6.8)	**23**	81.6
-	-	**24**	147.2
25a	2.56 m	**25**	27.4
25b			
26a	2.54	**26**	31.8
26b	2.01		
27	4.13 m	**27**	72.9
28	3.75 t (9.9)	**28**	64.4

29	3.87 ddd (11.1, 9.5, 4.9)	**29**	79.2
30a	2.11	**30**	43.5
30b	1.34		
-	-	**31**	97.9
32a	1.70	**32**	36.2
32b	1.34		
33a	2.13	**33**	24.0
33b	1.25 m		
34	1.53	**34**	38.1
-	-	**35**	108.7
36a	2.38 dd (15.1, 6.6)	**36**	47.0
36b	2.09 dd (15.2, 1.4)		
37	5.33 ddd (6.6, 3.9, 1.4)	**37**	73.8
38	4.44	**38**	79.9
39a	2.16	**39**	29.6
39b	2.01		
40a	3.52 t (6.4)	**40**	67.3
40b			
48	1.11 d (6.8)	**48**	15.1
49	3.21 s	**49**	57.5
50a	5.31 *br.* s	**50**	113.6
50b	5.09 *br.* s		
51	3.32 s	**51**	57.5
52	1.02 d (6.8)	**52**	16.6
Me (acetonide)	1.78 s	**Me (acetonide)**	27.2
Me (acetonide)	1.35 s	**Me (acetonide)**	25.5
-	-	**$(CH_3)_2C$**	108.8
***t*Bu**	1.05 s	***t*Bu**	26.2
***t*Bu**	1.04 s	***t*Bu**	26.2
MeSi	0.18	**MeSi**	-3.3
MeSi	0.24	**MeSi**	-3.9
MeSi	0.15	**MeSi**	-3.9
MeSi	0.28	**MeSi**	-4.2
-	-	**$(CH_3)_3C$Si**	18.3
-	-	**$(CH_3)_3C$Si**	18.3
-	-	***i*-Ph**	139.1
o-Ph	7.36 d	***o*-Ph**	127.7
m-Ph	7.24 t	***m*-Ph**	128.5
p-Ph	7.10 t	***p*-Ph**	127.6
PhCH_a	4.42 d (12.1)	**PhCH_2**	73.0
PhCH_b	4.37 d (12.0)		
***i*-Ph-OCH_3[(d)]**	-	***i*-Ph-OCH_3[(d)]**	131.8
***o*-Ph-OCH_3[(d)]**	7.36	***o*-Ph-OCH_3[(d)]**	129.1
***m*-Ph-OCH_3[(d)]**	6.88	***m*-Ph-OCH_3[(d)]**	114.0
***p*-Ph-OCH_3[(d)]**	-	***p*-Ph-OCH_3[(d)]**	159.5
Ph-OCH_3[(d)]	3.34 s	**Ph-OCH_3[(d)]**	54.7
CH_aPh-OCH_3[(d)]	4.58 d (11.2)	**CH_2Ph-OCH_3[(d)]**	70.7

C*H*$_b$Ph-OCH$_3$ $^{(d)}$	4.50 d (11.2)		
***i*-Ph-OCH$_3$**$^{(e)}$	-	***i*-Ph-OCH$_3$**$^{(e)}$	131.9
***o*-Ph-OCH$_3$**$^{(e)}$	7.48	***o*-Ph-OCH$_3$**$^{(e)}$	130.0
***m*-Ph-OCH$_3$**$^{(e)}$	6.84	***m*-Ph-OCH$_3$**$^{(e)}$	113.8
***p*-Ph-OCH$_3$**$^{(e)}$	-	***p*-Ph-OCH$_3$**$^{(e)}$	159.6
Ph-OC*H*$_3$ $^{(e)}$	3.33 s	**CH$_2$Ph-OC*H*$_3$**$^{(e)}$	54.7
C*H*$_a$Ph-OCH$_3$ $^{(e)}$	4.92 d (10.9)	***C*H$_2$Ph-OCH$_3$**$^{(e)}$	74.1
C*H*$_b$Ph-OCH$_3$ $^{(e)}$	4.86 d (10.9)		

[a] The numbering scheme of spirastrellolide F methyl ester (**1**) is used. [b] ^{1}H NMR; order of given values: chemical shift (δ_H in ppm), multiplicity, coupling constant (J in Hz). In cases in which only the chemical shift is given, the data are taken from 2D NMR experiments. [c] ^{13}C NMR: chemical shift (δ_C in ppm). [d] PMB-ether at C13.
[e] PMB-ether at C21.

Table S2. NMR spectroscopic data of cycloalkyne **26.**

$^{1}H^{a)}$	^{1}H NMR (600 MHz, C_6D_6)$^{b)}$	$^{13}C^{a)}$	^{13}C NMR (150 MHz, C_6D_6)$^{c)}$
-	-	**1**	170.4
2a	2.69 dd (16.8, 5.2)	**2**	41.7
2b	2.32 dd (16.8, 7.3)		
3	3.89 m	**3**	73.4
4a	1.65	**4**	31.6
4b	0.99		
5a	1.52	**5**	23.6
5b	1.31		
6a	1.29	**6**	32.1
6b	1.04		
7	3.60	**7**	73.7
8a	1.81 ddd	**8**	44.0
8b	1.50		
9	4.23	**9**	66.4
10a	2.02	**10**	47.3
10b			
11	4.22	**11**	67.4
12a	1.98	**12**	38.3
12b	1.59		
13	3.70 ddd (10.0, 4.0, 2.0)	**13**	79.1
14	2.18	**14**	37.3
15a	2.63 m	**15**	22.7
15b	2.18		
-	-	**16**	79.4
-	-	**17**	81.6
18a	2.51 m	**18**	15.2
18b			
19a	2.25	**19**	31.0
19b	2.11		
20	3.63 td (6.8, 3.3)	**20**	81.1
21	3.58 dd (6.4, 2.1)	**21**	78.7
22	4.69 dd (6.7, 2.1)	**22**	78.9
23	4.84 dt (6.7, n.r.)	**23**	79.3
-	-	**24**	145.4
25a	2.41	**25**	29.3
25b			
26a	2.41	**26**	32.4
26b	1.90		
27	4.02 m	**27**	73.0
28	3.60 t (9.9)	**28**	64.6
29	3.82 ddd (11.2, 9.5, 4.9)	**29**	79.2
30a	2.10	**30**	43.5
30b	1.31		
-	-	**31**	97.8

32a	1.69	**32**	36.4
32b	1.34		
33a	2.14	**33**	24.1
33b	1.29		
34	1.54	**34**	38.4
-		**35**	108.6
36a	2.42 dd (15.5, 6.1)	**36**	47.6
36b	2.19 d (15.5)		
37	5.13 dd (6.1, 3.5)	**37**	74.2
38	4.43 ddd (8.3, 5.2, 3.7)	**38**	79.9
39a	2.22	**39**	29.2
39b			
40a	3.47	**40**	67.0
40b	3.40		
48	1.30 d (6.1)	**48**	15.8
49	3.35 s	**49**	58.2
50a	5.77 t (n.r.)	**50**	111.7
50b	5.18 t (n.r.)		
51	3.31 s	**51**	57.6
52	1.12 d (6.7)	**52**	16.9
Me (acetonide)	1.72 s	**Me (acetonide)**	27.0
Me (acetonide)	1.40 s	**Me (acetonide)**	26.2
-	-	**$(CH_3)_2C$**	109.0
***t*Bu**	1.00 s	***t*Bu**	26.2
***t*Bu**	1.02 s	***t*Bu**	26.1
MeSi	0.14 s	**MeSi**	-3.7
MeSi	0.19 s	**MeSi**	-3.8
MeSi	0.12 s	**MeSi**	-4.2
MeSi	0.21 s	**MeSi**	-4.3
-	-	**$(CH_3)_3C$Si**	18.3
-	-	**$(CH_3)_3C$Si**	18.3
-	-	***i*-Ph**	138.8
o-Ph	7.28 d	***o*-Ph**	127.6
m-Ph	7.20 t	***m*-Ph**	128.6
p-Ph	7.06 t	***p*-Ph**	127.7
PhCH_a	4.32 d (12.0)	**PhCH_2**	73.0
PhCH_b	4.27 d (12.0)		
***i*-Ph-OCH_3[d]**	-	***i*-Ph-OCH_3[d]**	131.7
***o*-Ph-OCH_3[d]**	7.31	***o*-Ph-OCH_3[d]**	128.8
***m*-Ph-OCH_3[d]**	6.84	***m*-Ph-OCH_3[d]**	113.9
***p*-Ph-OCH_3[d]**	-	***p*-Ph-OCH_3[d]**	159.5
Ph-OCH_3[d]	3.30 s	**Ph-OCH_3[d]**	54.7
CH_aPh-OCH_3[d]	4.51 d (11.0)	**CH_2Ph-OCH_3[d]**	70.6
CH_bPh-OCH_3[d]	4.45 d (11.0)		
***i*-Ph-OCH_3[e]**	-	***i*-Ph-OCH_3[e]**	131.6
***o*-Ph-OCH_3[e]**	7.45	***o*-Ph-OCH_3[e]**	129.7
***m*-Ph-OCH_3[e]**	6.81	***m*-Ph-OCH_3[e]**	113.9

***p*-Ph-OCH$_3$$^{(e)}$**	-	***p*-Ph-OCH$_3$$^{(e)}$**	159.5
Ph-OC*H*$_3$$^{(e)}$	3.28 s	**CH$_2$Ph-OCH$_3$$^{(e)}$**	54.7
C*H*$_a$Ph-OCH$_3$$^{(e)}$	4.90 d (10.2)	***C*H$_2$Ph-OCH$_3$$^{(e)}$**	73.7
C*H*$_b$Ph-OCH$_3$$^{(e)}$	4.72 d (10.2)		

[a] The numbering scheme of spirastrellolide F methyl ester (**1**) is used. [b] ^{1}H NMR; order of given values: chemical shift (δ_H in ppm), multiplicity, coupling constant (*J* in Hz). In cases in which only the chemical shift is given, the data are taken from 2D NMR experiments. [c] ^{13}C NMR: chemical shift (δ_C in ppm). [d] PMB-ether at C13. [e] PMB-ether at C21. n.r. = not resolved.

Table S3. NMR spectroscopic data of compound **27**.

$^{1}H^{a)}$	^{1}H NMR (600 MHz, C_6D_6)$^{b)}$	$^{13}C^{a)}$	^{13}C NMR (150 MHz, C_6D_6)$^{c)}$
-	-	**1**	170.0
2a	2.88 dd (16.3, 3.3)	**2**	41.6
2b	2.52 dd (16.3, 10.2)		
3	3.84 ddt (10.3, 3.2, 2.0)	**3**	73.8
4a	2.05	**4**	31.7
4b	1.08		
5a	1.58	**5**	23.5
5b	1.36		
6a	1.29	**6**	32.2
6b	1.08		
7	3.63	**7**	73.7
8a	1.58	**8**	43.5
8b	1.43		
9	4.15 td (10.3, 4.1)	**9**	65.6
10a	2.28	**10**	44.1
10b	2.00 ddd (13.1, 11.3, 5.2)		
11	4.12	**11**	70.0
12a	1.80	**12**	37.2
12b	1.67		
13	4.08 dd (Σ 17.6)	**13**	71.9
14	1.91 m	**14**	40.1
15a	2.85	**15**	22.5
15b	2.46		
-	-	**16**	78.8
-	-	**17**	81.9
18a	2.57	**18**	14.0
18b	2.49		
19a	2.27	**19**	30.3
19b	2.20		
20	3.41	**20**	79.7
21	3.62 dd (9.0, 3.7)	**21**	71.1
22	4.63 d (7.0)	**22**	76.6
23	4.72 dt (7.0, n.r.)	**23**	78.4
-	-	**24**	146.7
25a	2.41	**25**	29.6
25b			
26a	2.31	**26**	32.4
26b	1.80		
27	3.97 ddd (10.3, 8.3, 2.2)	**27**	72.8
28	3.56 dd (Σ 19.8)	**28**	64.6
29	3.79 ddd (11.3, 9.6, 5.0)	**29**	79.3
30a	2.07 dd (12.8, 5.0)	**30**	43.5
30b	1.29		
-	-	**31**	97.7

32a	1.64	**32**	36.4
32b	1.28		
33a	2.13	**33**	24.0
33b	1.27		
34	1.47	**34**	38.4
-	-	**35**	108.6
36a	2.37 dd (15.5, 6.4)	**36**	47.6
36b	2.15 d (15.5)		
37	5.18 dd (6.3, 3.4)	**37**	74.2
38	4.41 ddd (8.3, 4.9, 3.5)	**38**	80.2
39a	2.15	**39**	28.9
39b			
40a	3.40	**40**	67.1
40b	3.38		
48	1.29 d (6.7)	**48**	16.3
49	3.30 s	**49**	57.7
50a	5.52 t (n.r.)	**50**	110.7
50b	5.07 t (n.r.)		
51	3.22 s	**51**	57.6
52	1.13 d (6.7)	**52**	16.8
Me (acetonide)	1.60 s	**Me (acetonide)**	26.7
Me (acetonide)	1.29 s	**Me (acetonide)**	25.5
-	-	**$(CH_3)_2C$**	108.6
***t*Bu**	1.02 s	***t*Bu**	26.1
***t*Bu**	0.89 s	***t*Bu**	25.8
MeSi	0.21 s	**MeSi**	-3.7
MeSi	0.01 s	**MeSi**	-4.6
MeSi	0.22 s	**MeSi**	-4.7
MeSi	0.01 s	**MeSi**	-5.1
-	-	**$(CH_3)_3C$Si**	18.2
-	-	**$(CH_3)_3C$Si**	18.0
-	-	***i*-Ph**	139.0
o-Ph	7.35 d	***o*-Ph**	127.7
m-Ph	7.25 t	***m*-Ph**	128.6
p-Ph	7.10 t	***p*-Ph**	127.7
PhCH_a	4.35 d (12.0)	**PhCH_2**	73.1
PhCH_b	4.30 d (12.0)		
OH-13	3.80 ~d	**-**	-
OH-21	2.23 d (4.0)	**-**	-

[a] The numbering scheme of spirastrellolide F methyl ester (**1**) is used. [b] ^{1}H NMR; order of given values: chemical shift (δ_H in ppm), multiplicity, coupling constant (J in Hz). In cases in which only the chemical shift is given, the data are taken from 2D NMR experiments. [c] ^{13}C NMR: chemical shift (δ_C in ppm). n.r. = not resolved; $\sum$ = if coupling constants were not clearly resolved, the sum of the coupling constants is given. It is also noteworthy that the chemical shift (δ_H) of residual H_2O in the spectrum is shifted to 0.45 ppm (normal shift in C_6D_6: 0.40 ppm).

Table S4. Spectroscopic data of compound **29** (major anomer).

$^{1}H^{a)}$	^{1}H NMR (600 MHz, C_6D_6)$^{b)}$	$^{13}C^{a)}$	^{13}C NMR (150 MHz, C_6D_6)$^{c)}$
-	-	**1**	169.8
2a	2.74 dd(16.7, 4.5)	**2**	41.0
2b	2.49 dd (16.8, 10.7)		
3	3.85	**3**	72.8
4a	2.05	**4**	30.5
4b	0.95		
5a	1.56	**5**	23.3
5b	1.34		
6a	1.31	**6**	32.5
6b	1.11		
7	3.65	**7**	73.0
8a	1.95	**8**	46.2
8b	1.59		
9	4.11 td (10.0, 3.0)	**9**	66.1
10a	2.04	**10**	49.7
10b			
11	4.02 td (10.0, 3.0)	**11**	68.3
12a	2.01	**12**	46.3
12b	1.80		
13	3.97 dd (Σ 18.0)	**13**	83.5
14	2.32	**14**	38.7
15a	2.19	**15**	46.1
15b	1.27		
-	-	**16**	109.7
17a	2.22	**17**	34.6
17b	1.48		
18a	1.84	**18**	20.4
18b	1.33		
19a	2.14	**19**	33.4
19b	1.66		
20	3.43	**20**	81.1
21	3.65 dd (9.0, 3.9)	**21**	73.5
22	4.78 d (7.0)	**22**	76.9
23	4.90 dt (7.0, n.r.)	**23**	77.9
-	-	**24**	146.3
25a	2.65 td (13.0, 2.5)	**25**	31.7
25b	2.52		
26a	2.41 td (13.5, 5.6)	**26**	33.8
26b	1.52		
27	3.86	**27**	73.3
28	3.51 dd (Σ 19.8)	**28**	65.2
29	3.77 ddd (11.4, 9.7, 5.0)	**29**	79.1
30a	2.06	**30**	43.4
30b	1.27		

-	-	**31**	97.6
32a	1.60	**32**	36.4
32b	1.25		
33a	2.15	**33**	23.6
33b	1.23		
34	1.39	**34**	38.6
-	-	**35**	108.7
36a	2.34 dd (15.8, 6.2)	**36**	47.9
36b	2.05 d (15.8)		
37	5.14 dd (6.1, 3.2)	**37**	73.7
38	4.40 dt (9.7, 3.5)	**38**	80.4
39a	2.19	**39**	28.8
39b			
40a	3.33	**40**	66.8
40b	3.29		
48	0.98 d (6.6)	**48**	17.2
49	3.47 s	**49**	59.1
50a	5.54 t (n.r.)	**50**	111.3
50b	5.07 t (n.r.)		
51	3.28 s	**51**	57.5
52	1.02	**52**	16.3
Me (acetonide)	1.66 s	**Me (acetonide)**	26.8
Me (acetonide)	1.30 s	**Me (acetonide)**	25.7
-	-	**$(CH_3)_2C$**	108.9
***t*Bu**	1.03 s	***t*Bu**	26.07
***t*Bu**	1.00 s	***t*Bu**	26.05
MeSi	0.17 s	**MeSi**	-3.8
MeSi	0.18 s	**MeSi**	-3.9
MeSi	0.21 s	**MeSi**	-4.5
MeSi	0.15 s	**MeSi**	-4.7
-	-	**$(CH_3)_3CSi$**	18.2
-	-	**$(CH_3)_3CSi$**	18.2
-	-	***i*-Ph**	138.8
o-Ph	7.31 d	***o*-Ph**	[d]
m-Ph	7.25 t	***m*-Ph**	128.6
p-Ph	7.12 t	***p*-Ph**	[d]
PhCH_a	4.31 d (12.3)	**PhCH_2**	73.1
PhCH_b	4.26 d (12.2)		
OH-21	2.24 d (3.6)	**-**	-
OMe-16	3.47 s	**OMe-16**	48.4

[a] The numbering scheme of spirastrellolide F methyl ester (**1**) is used. [b] ^{1}H NMR; order of given values: chemical shift (δ_H in ppm), multiplicity, coupling constant (J in Hz). In cases in which only the chemical shift is given, the data are taken from 2D NMR experiments. [c] ^{13}C NMR: chemical shift (δ_C in ppm). [d] ^{13}C NMR-signal overlaps with the solvent signal (C_6D_6). n.r. = not resolved; $\sum$ = if coupling constants were not clearly resolved, the sum of the coupling constants is given.

Table S5. NMR spectroscopic data of product **29** (minor anomer).

^{1}H[a)]	^{1}H NMR (600 MHz, C_6D_6)[b)]	^{13}C[a)]	^{13}C NMR (150 MHz, C_6D_6)[c)]
-	-	**1'**	169.8
2'a	2.91 dd (15.8, 4.5)	**2'**	41.6
2'b	2.53 dd (16.0, 10.4)		
3'	3.92	**3'**	73.2
4'a	1.85	**4'**	31.0
4'b	1.03		
5'a	1.54	**5'**	23.3
5'b	1.32		
6'a	1.31	**6'**	32.1
6'b	1.07		
7'	3.62	**7'**	73.3
8'a	1.91	**8'**	44.6
8'b	1.56		
9'	4.23	**9'**	66.2
10'a	2.09	**10'**	48.2
10'b	2.05		
11'	4.14	**11'**	68.3
12'a	1.89	**12'**	42.6
12'b	1.73		
13'	4.00 dd[d)]	**13'**	81.2
14'	1.61	**14'**	39.6
15'a	2.19	**15'**	45.3
15'b	1.79		
-	-	**16'**	109.5
17'a	2.17	**17'**	36.1
17'b	1.54		
18'a	1.85	**18'**	21.7
18'b	1.54		
19'a	2.30	**19'**	34.2
19'b	1.66		
20'	3.38	**20'**	81.8
21'	3.73 dd (9.1, 3.8)	**21'**	73.8
22'	4.71 d (7.1)	**22'**	76.7
23'	4.77	**23'**	78.2
-	-	**24'**	146.8
25'a	2.60	**25'**	30.5
25'b	2.57		
26'a	2.43	**26'**	32.9
26'b	1.62		
27'	3.94	**27'**	73.4
28'	3.55 dd (Σ 19.7)	**28'**	65.1
29'	3.79	**29'**	79.3
30'a	2.09	**30'**	43.5
30'b	1.30		

-	-	**31'**	97.7
32'a	1.65	**32'**	36.5
32'b	1.30		
33'a	2.17	**33'**	23.8
33'b	1.27		
34'	1.45	**34'**	38.6
-	-	**35'**	108.7
36'a	2.30 dd (15.5, 6.2)	**36'**	47.4
36'b	2.02		
37'	5.30 dd (6.2, 3.1)	**37'**	73.2
38'	4.46 dt (10.3, 3.2)	**38'**	80.4
39'a	2.35	**39'**	28.9
39'b	2.13		
40'a	3.43	**40'**	67.0
40'b			
48'	1.01	**48'**	17.2
49'	3.49 s	**49'**	59.9
50'a	5.60 t (n.r.)	**50'**	111.0
50'b	5.12 t (n.r.)		
51'	3.30 s	**51'**	57.6
52'	1.05 d (6.7)	**52'**	16.3
Me (acetonide)'	1.62 s	**Me (acetonide)'**	26.8
Me (acetonide)'	1.28 s	**Me (acetonide)'**	25.5
-	-	**$(CH_3)_2C$'**	108.5
***t*Bu'**	1.04 s	***t*Bu'**	26.1
***t*Bu'**	1.02 s	***t*Bu'**	26.1
MeSi'	0.20 s	**MeSi'**	-3.6
MeSi'	0.18 s	**MeSi'**	-3.9
MeSi'	0.24 s	**MeSi'**	-4.4
MeSi'	0.18 s	**MeSi'**	-4.6
-	-	**$(CH_3)_3C$Si'**	18.3
-	-	**$(CH_3)_3C$Si'**	18.2
-	-	***i*-Ph'**	138.9
o-Ph'	7.35 d	***o*-Ph'**	[e]
m-Ph'	7.25 t	***m*-Ph'**	128.6
p-Ph'	7.10 t	***p*-Ph'**	[e]
PhCH_a'	4.34 d (12.1)	**PhCH_2'**	73.1
PhCH_b'	4.29 d[d]		
OH-21'	2.24 d (3.7)	**-**	-
OMe-16'	3.18 s	**OMe-16'**	48.4

[a] The numbering scheme of spirastrellolide F methyl ester (**1**) is used. [b] ^{1}H NMR; order of given values: chemical shift (δ_H in ppm), multiplicity, coupling constant (J in Hz). In cases in which only the chemical shift is given, the data are taken from 2D NMR experiments. [c] ^{13}C NMR: chemical shift (δ_C in ppm). [d] signals are superimposed. [e] ^{13}C NMR-signal superimposed by the solvent signal (C_6D_6). n.r. = not resolved; $\sum$ = if coupling constants were not clearly measurable/ resolved, the sum of the coupling constants is given.

Table S6. NMR spectroscopic data of the 6-*endo*-product **30**.

^{1}H[a)]	^{1}H NMR (600 MHz, C_6D_6)[b)]	^{13}C[a)]	^{13}C NMR (150 MHz, C_6D_6)[c)]
-	-	**1**	169.8
2a	2.45 dd (14.5, 6.7)	**2**	42.2
2b	2.34		
3	3.61	**3**	74.4
4a	1.36	**4**	30.8
4b	1.28		
5a	1.62	**5**	23.7
5b	1.30		
6a	1.66	**6**	31.7
6b	1.16		
7	3.43 m	**7**	76.0
8a	2.07	**8**	45.2
8b	1.81		
9	4.07 qi (6.2)	**9**	67.7
10a	2.07	**10**	47.6
10b	1.93		
11	4.20 qi (6.1)	**11**	68.5
12a	1.95	**12**	43.0
12b			
13	3.72	**13**	77.4
14	1.59	**14**	32.1
15a	1.96	**15**	29.0
15b	1.63		
16	4.55	**16**	94.0
-		**17**	154.0
18a	2.45	**18**	28.7
18b	2.35		
19a	2.19	**19**	27.2
19b	2.14		
20	3.63	**20**	79.7
21	3.71	**21**	71.9
22	4.73 d (6.8)	**22**	77.0
23	4.83 dt (6.7, n.r.)	**23**	79.1
-		**24**	146.6
25a	2.50	**25**	29.7
25b	2.47		
26a	2.50	**26**	33.2
26b	1.58		
27	3.98 td (10.0, 1.0)	**27**	73.1
28	3.51 t (9.9)	**28**	65.2
29	3.82 ddd (11.2, 9.6, 5.0)	**29**	79.1
30a	2.08	**30**	43.4
30b	1.29		
-	-	**31**	97.5

32a	1.65	**32**	36.3
32b	1.30		
33a	2.10	**33**	23.9
33b	1.25		
34	1.48	**34**	37.8
-	-	**35**	108.2
36a	2.32	**36**	46.0
36b	2.10		
37	5.42 ddd (Σ 13.4)	**37**	73.5
38	4.69 ddd (8.0, 5.6, 4.5)	**38**	79.4
39a	2.23	**39**	29.3
39b			
40a	3.74	**40**	67.2
40b	3.62		
48	0.91 d (6.5)	**48**	18.1
49	3.35 s	**49**	57.4
50a	5.44 t (n.r.)	**50**	110.4
50b	4.93 (n.r.)		
51	3.29 s	**51**	57.5
52	1.04 d (6.7)	**52**	16.8
Me (acetonide)	1.66 s	**Me (acetonide)**	26.7
Me (acetonide)	1.30 s	**Me (acetonide)**	25.8
-		**$(CH_3)_2C$**	108.7
***t*Bu**	1.02 s	***t*Bu**	26.17
***t*Bu**	1.00 s	***t*Bu**	26.16
MeSi	0.15 s	**MeSi**	-3.6
MeSi	0.20 s	**MeSi**	-3.7
MeSi	0.21 s	**MeSi**	-3.8
MeSi	0.18 s	**MeSi**	-3.8
-	-	**$(CH_3)_3C$Si**	18.31
-	-	**$(CH_3)_3C$Si**	18.28
-	-	***i*-Ph**	139.1
o-Ph	7.44 d	***o*-Ph**	127.7
m-Ph	7.27 t	***m*-Ph**	128.6
p-Ph	7.10 t	***p*-Ph**	127.6
PhCH_a	4.55 d (11.8)	**PhCH_2**	73.2
PhCH_b	4.52 d (12.0)		
OH-21	2.33	**-**	-

[a] The numbering scheme of spirastrellolide F methyl ester (**1**) is used. [b] ^{1}H NMR; order of given values: chemical shift (δ_H in ppm), multiplicity, coupling constant (*J* in Hz). In cases in which only the chemical shift is given, the data are taken from 2D NMR experiments. [c] ^{13}C NMR: chemical shift (δ_C in ppm). n.r. = not resolved; ∑ = if coupling constants were not clearly resolved, the sum of the coupling constants is given.

Table S7. NMR spectroscopic data of the 5-*exo*-product **28**.

^{1}H[a)]	^{1}H NMR (600 MHz, C_6D_6)[b)]	^{13}C[a)]	^{13}C NMR (150 MHz, C_6D_6)[c)]
-	-	**1'**	169.7
2'a	2.61 dd (14.6, 6.4)	**2'**	42.6
2'b	2.40 dd (14.5, 6.2)		
3'	3.73	**3'**	74.1
4'a	1.48	**4'**	31.3
4'b	1.21		
5'a	1.62	**5'**	23.6
5'b	1.30		
6'a	1.67	**6'**	31.4
6'b	1.17		
7'	3.54	**7'**	75.4
8'a	2.09	**8'**	45.0
8'b	1.84		
9'	4.13 qi (6.2)	**9'**	67.4
10'a	2.15	**10'**	47.3
10'b	1.88		
11'	4.10 qi (6.1)	**11'**	69.4
12'a	1.81	**12'**	43.6
12'b			
13'	3.75	**13'**	84.9
14'	1.52	**14'**	39.0
15'a	2.26	**15'**	37.6
15'b	1.85		
-		**16'**	154.0
17'	4.25 dd (8.5, 5.5)	**17'**	96.1
18'a	2.75 m	**18'**	20.5
18'b	2.34		
19'a	2.20	**19'**	31.9
19'b	1.87		
20'	3.63	**20'**	79.7
21'	3.70	**21'**	73.1
22'	4.77 d (6.8)	**22'**	77.0
23'	4.80 dt (6.8, n.r.)	**23'**	79.7
-		**24'**	146.3
25'a	2.59	**25'**	29.5
25'b	2.47		
26'a	2.58	**26'**	32.4
26'b	1.59		
27'	3.99 td (10.0, 1.0)	**27'**	73.2
28'	3.53 t (9.9)	**28'**	65.4
29'	3.82 ddd[d)]	**29'**	79.0
30'a	2.08	**30'**	43.3
30'b	1.29		
-	-	**31'**	97.6

32'a	1.67	**32'**	36.3
32'b	1.30		
33'a	2.10	**33'**	24.1
33'b	1.25		
34'	1.48	**34'**	38.1
-	-	**35'**	108.4
36'a	2.37	**36'**	47.4
36'b	2.10		
37'	5.36 ddd (6.0, 3.5, 1.0)	**37'**	73.5
38'	4.66 ddd	**38'**	79.9
39'a	2.34	**39'**	29.3
39'b	2.28		
40'a	3.79	**40'**	67.2
40'b	3.61		
48'	0.75 d (6.5)	**48'**	16.1
49'	3.61 s	**49'**	58.8
50'a	5.55 dt (n.r.)	**50'**	109.4
50'b	4.98 t (n.r.)		
51'	3.30 s	**51'**	57.5
52'	1.02	**52'**	16.6
Me (acetonide)'	1.65 s	**Me (acetonide)'**	26.7
Me (acetonide)'	1.26 s	**Me (acetonide)'**	25.8
-	-	**$(CH_3)_2C$'**	108.6
***t*Bu'**	1.00 s	***t*Bu'**	26.13
***t*Bu'**	1.00 s	***t*Bu'**	26.11
MeSi'	0.17	**MeSi'**	-3.6
MeSi'	0.17	**MeSi'**	-3.8
MeSi'	0.14	**MeSi'**	-3.9
MeSi'	0.17	**MeSi'**	-4.0
-	-	**$(CH_3)_3C$Si'**	18.3
-	-	**$(CH_3)_3C$Si'**	18.2
-	-	***i*-Ph'**	139.2
o-Ph'	7.44 d	***o*-Ph'**	127.5
m-Ph'	7.27 t	***m*-Ph'**	128.6
p-Ph'	7.10 t	***p*-Ph'**	127.6
PhCH_a'	4.57 d (12.1)	**PhCH_2'**	73.1
PhCH_b'	4.47 d (12.0)		
OH-21'	2.27 d (3.3)	-	-

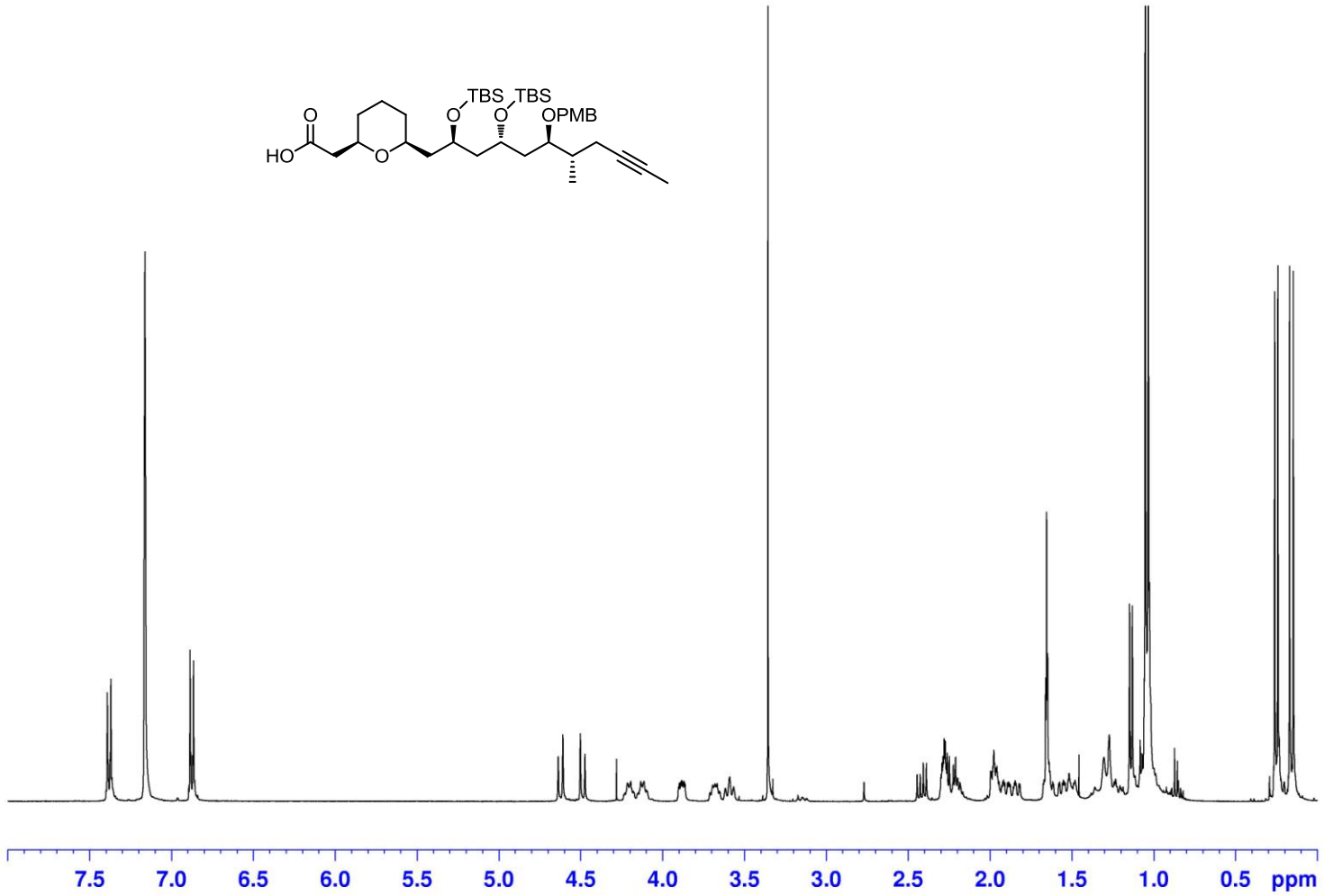
[a] The numbering scheme of spirastrellolide F methyl ester (**1**) is used. [b] ^{1}H NMR; order of given values: chemical shift (δ_H in ppm), multiplicity, coupling constant (J in Hz). In cases in which only the chemical shift is given, the data are taken from 2D NMR experiments. [c] ^{13}C NMR: chemical shift (δ_C in ppm). [d] signals superimposed. n.r. = not resolved.

Table S8. NMR spectroscopic data of compound **34**.

$^{1}H^{a)}$	^{1}H NMR (600 MHz, C_6D_6)$^{b)}$	$^{13}C^{a)}$	^{13}C NMR (150 MHz, C_6D_6)$^{c)}$
-	-	**1**	169.0
2a	2.48 dd (15.3, 8.9)	**2**	43.0
2b	2.24 dd (15.3, 2.6)		
3	3.77	**3**	74.7
4	1.16	**4**	31.2
5a	1.63	**5**	24.0
5b	1.38		
6a	1.71	**6**	32.5
6b	1.21		
7	3.38	**7**	76.1
8a	2.03	**8**	46.3
8b	1.81		
9	3.99	**9**	68.5
10a	2.00	**10**	49.8
10b	1.95		
11	4.36 m	**11**	66.4
12a	2.18	**12**	42.0
12b	2.15		
13	3.99	**13**	74.1
14	1.71	**14**	32.5
15a	1.84	**15**	29.1
15b	1.57		
16a	1.77	**16**	35.7
16b	1.52		
-	-	**17**	96.8
18a	1.85	**18**	34.5
18b	1.45		
19a	1.94	**19**	23.8
19b	1.82		
20	3.48 td (9.6, 4.6)	**20**	75.6
21	3.83 d (9.6)	**21**	70.8
22	4.72 d (6.0)	**22**	75.8
23	3.98 dd (10.3, 6.0)	**23**	81.9
24	2.30	**24**	33.8
25a	2.28	**25**	28.1
25b	1.57		
26a	2.28	**26**	29.1
26b	2.09		
27	3.98	**27**	73.3
28	3.74 t (9.9)	**28**	63.5
29	3.82	**29**	79.3
30a	2.11 dd (12.8, 4.9)	**30**	43.1
30b	1.30 dd (12.7, 11.2)		
-	-	**31**	97.8

32a	1.61	**32**	36.3
32b	1.32		
33a	2.10	**33**	24.3
33b	1.25		
34	1.50	**34**	38.4
-	-	**35**	108.3
36a	2.21 dd (15.4, 6.3)	**36**	47.8
36b	1.87 d (15.3)		
37	5.48 dd (6.2, 2.6)	**37**	72.1
38	4.13 ddd (10.7, 4.2, 2.6)	**38**	83.5
39a	2.64	**39**	32.0
39b	2.58		
40	5.51 dt (15.3, 7.4)	**40**	125.5
41	5.78 dt (15.3, 6.4)	**41**	133.2
42a	2.86 dt (16.3, 5.9)	**42**	31.0
42b	2.79 dt (16.3, 5.9)		
43	5.68	**43**	130.6
44	5.67	**44**	125.3
45	2.63 m	**45**	33.6
46	4.32 t (6.0)	**46**	72.4
47	-	**47**	173.1
48	1.06 d (6.2)	**48**	19.4
49	3.16 s	**49**	56.0
50	1.15 d (6.5)	**50**	16.9
51	3.31 s	**51**	57.5
52	1.05	**52**	16.9
53	3.41 s	**53**	51.3
Me (acetonide)	1.70 s	**Me (acetonide)**	26.9
Me (acetonide)	1.47 s	**Me (acetonide)**	26.5
-	-	**$(CH_3)_2C$**	108.5
***t*Bu**	1.05 s	***t*Bu**	26.5
***t*Bu**	1.03 s	***t*Bu**	26.1
$(CH_3CHa)_3Si$	0.67 dq (15.0, 7.8)	**$(CH_3CH_2)_3Si$**	5.1
$(CH_3CHb)_3Si$	0.64 dq (15.0, 8.2)		
$(CH_3CH_2)_3Si$	1.04 t (7.9)	**$(CH_3CH_2)_3Si$**	7.1
MeSi	0.33 s	**MeSi**	-2.9
MeSi	0.15 s	**MeSi**	-3.5
MeSi	0.19 s	**MeSi**	-4.08
MeSi	0.30 s	**MeSi**	-4.09
-	-	**$(CH_3)_3CSi$**	18.6
-	-	**$(CH_3)_3CSi$**	18.3

[a] The numbering scheme of spirastrellolide F methyl ester (**1**) is used. [b] ^{1}H NMR; order of given values: chemical shift (δ_H in ppm), multiplicity, coupling constant (J in Hz). In cases in which only the chemical shift is given, the data are taken from 2D NMR experiments. [c] ^{13}C NMR: chemical shift (δ_C in ppm).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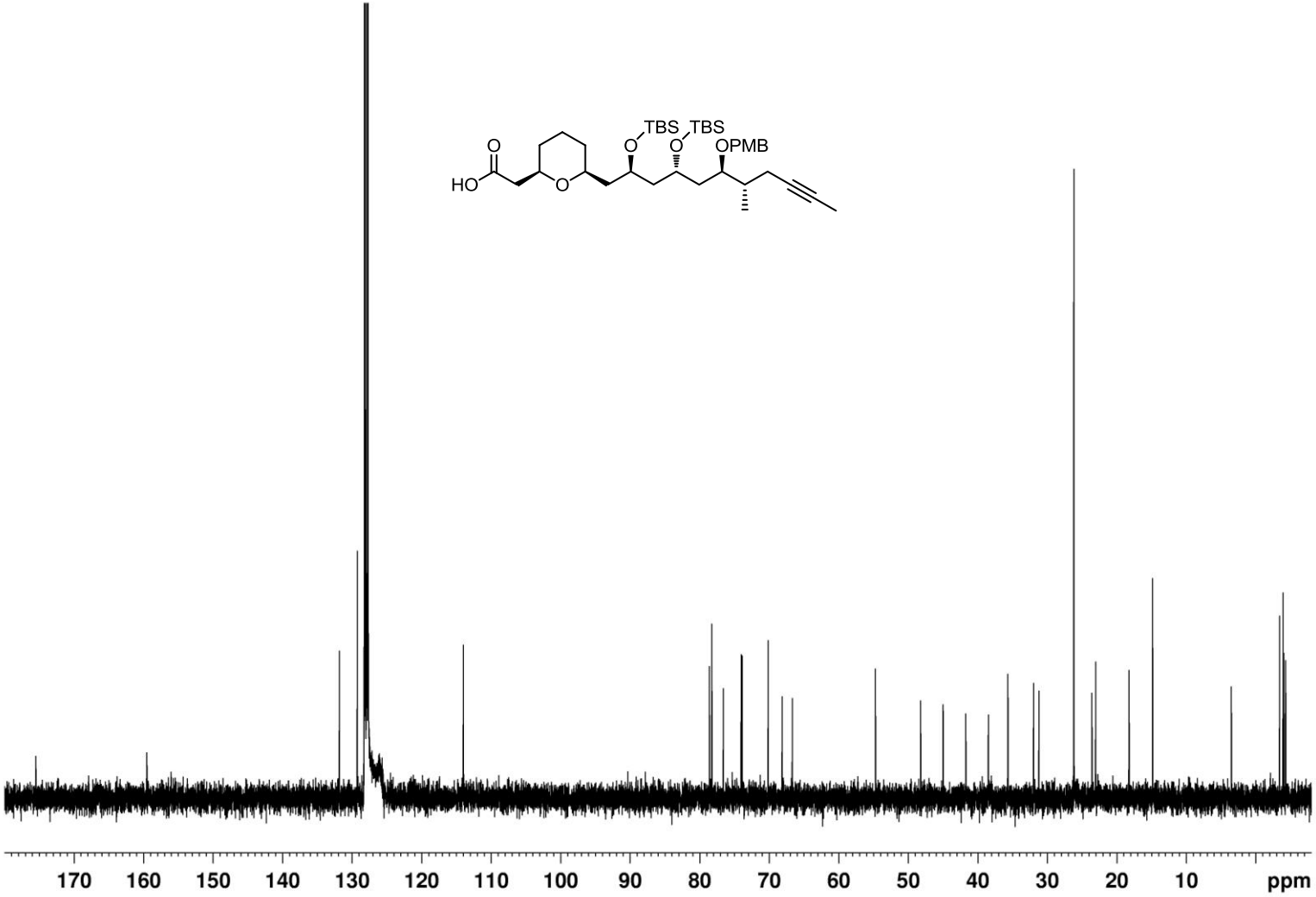
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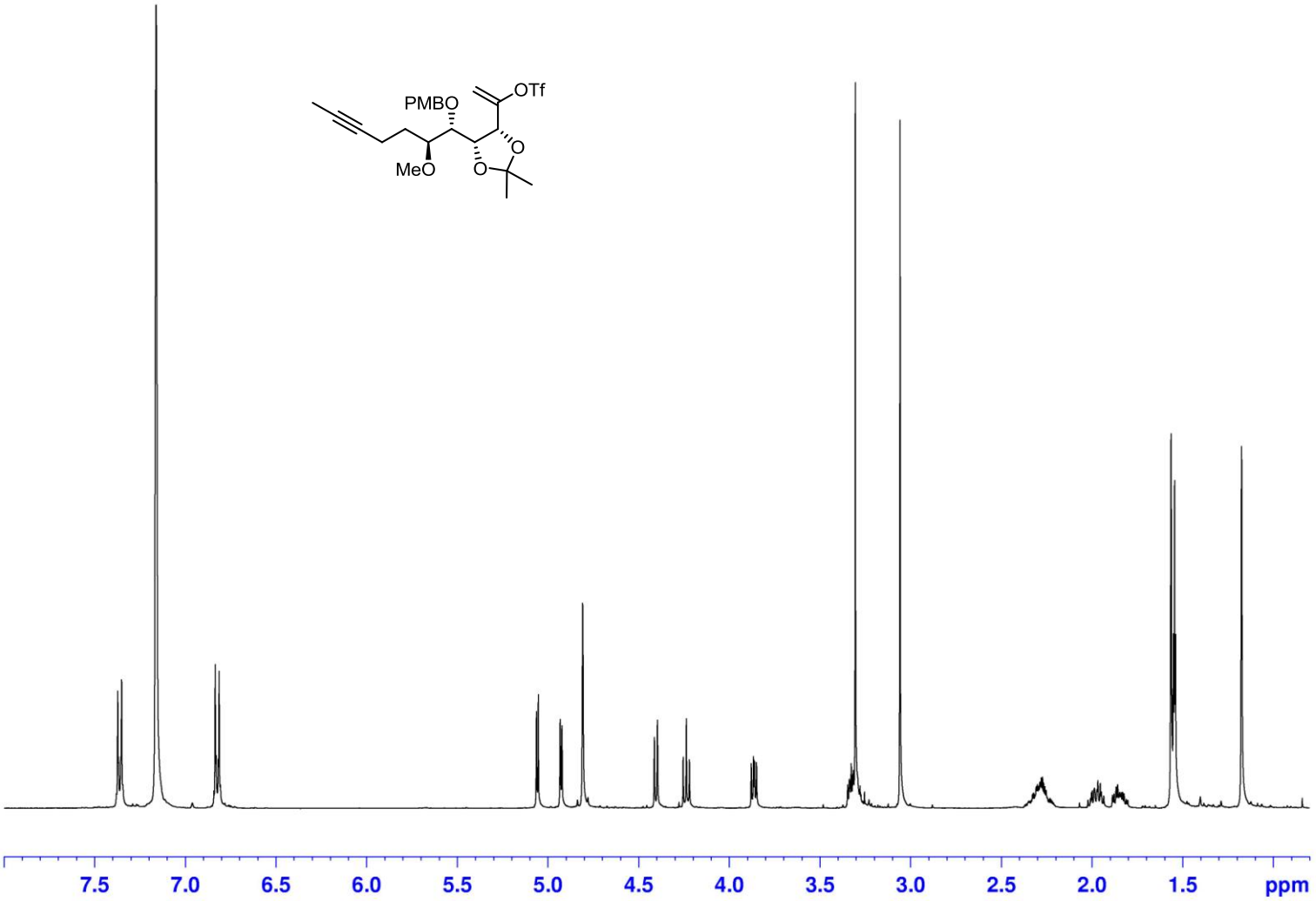
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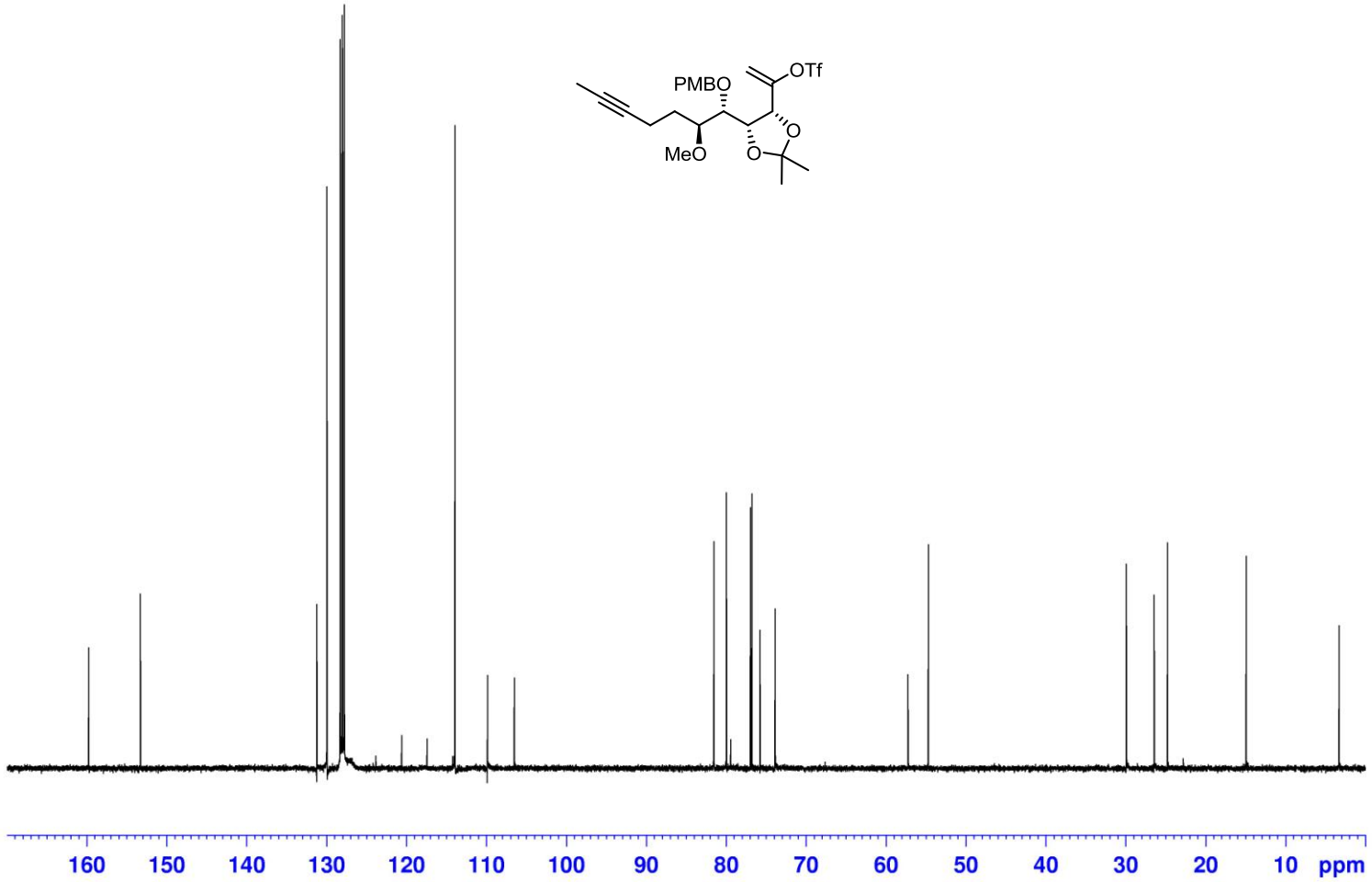
PMBO
OTf
MeO
O
O
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150
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100
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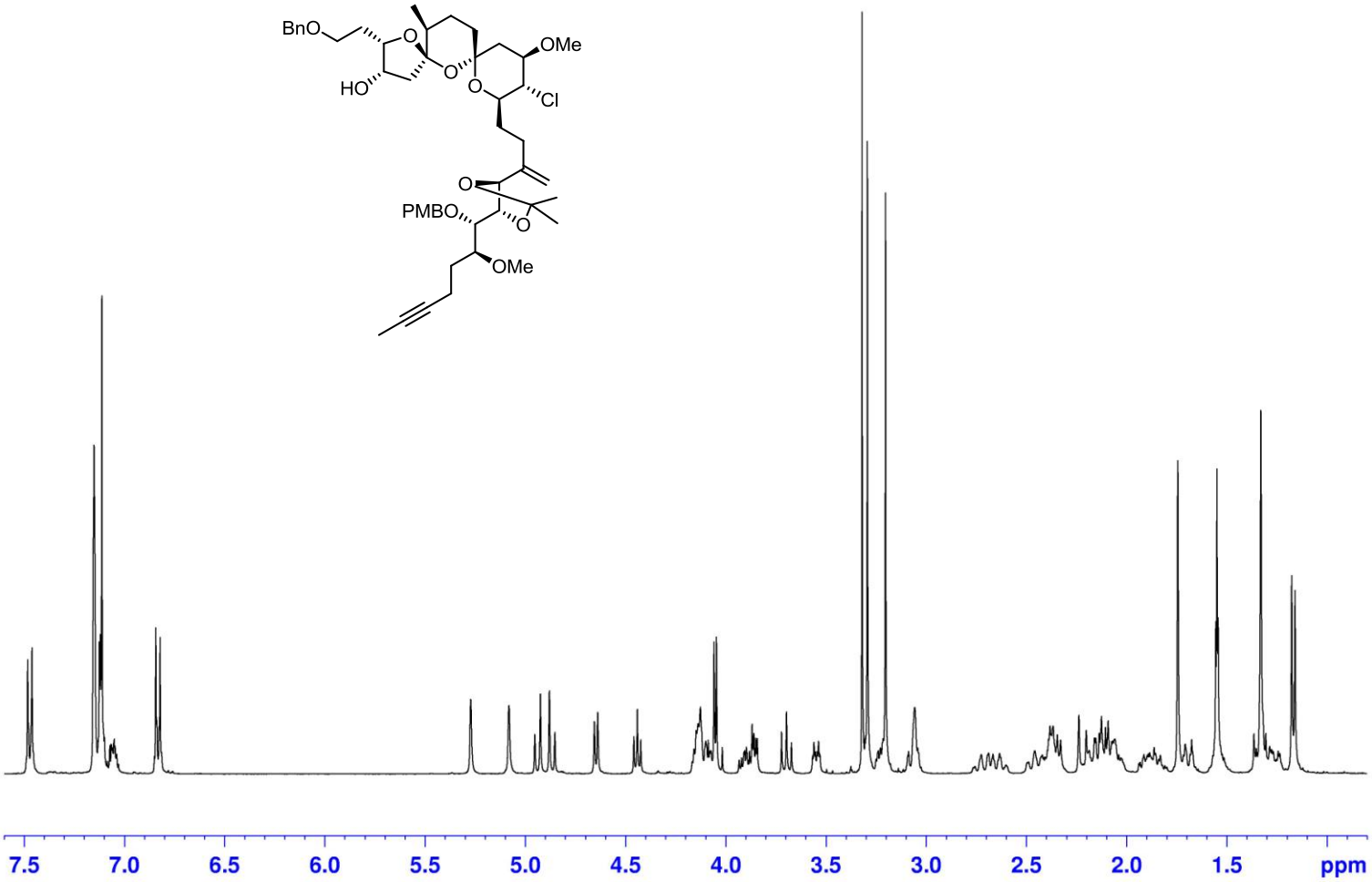
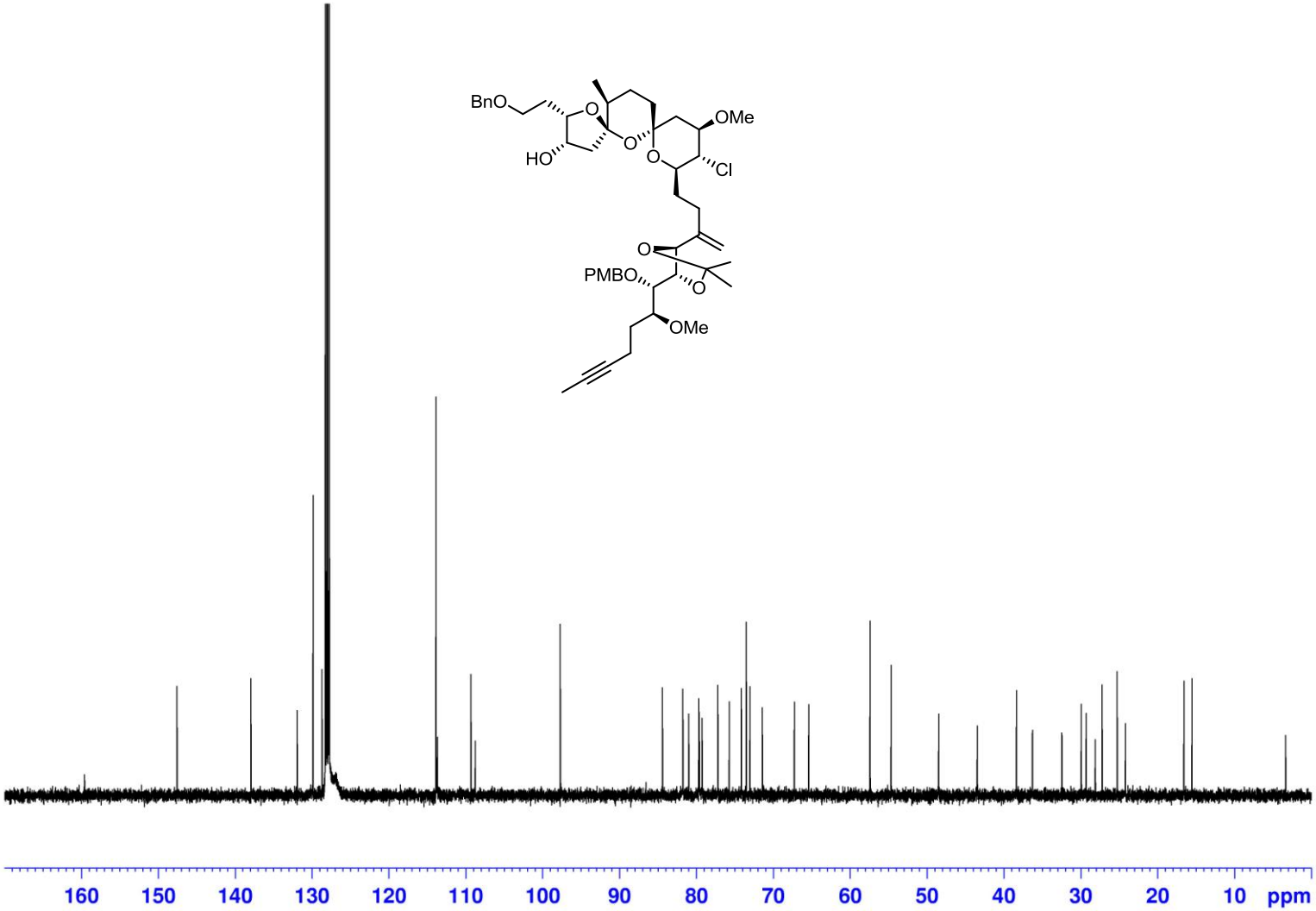
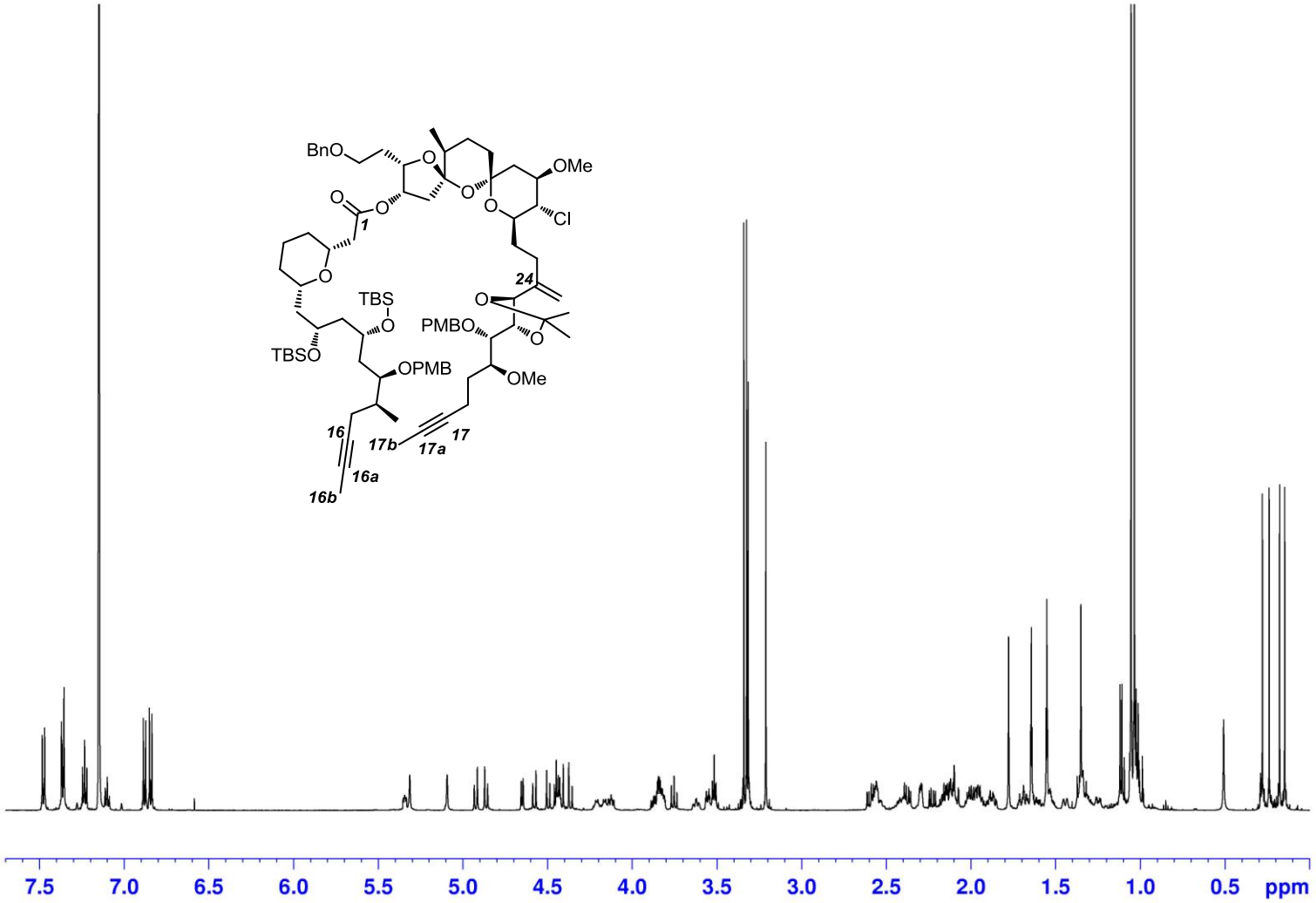
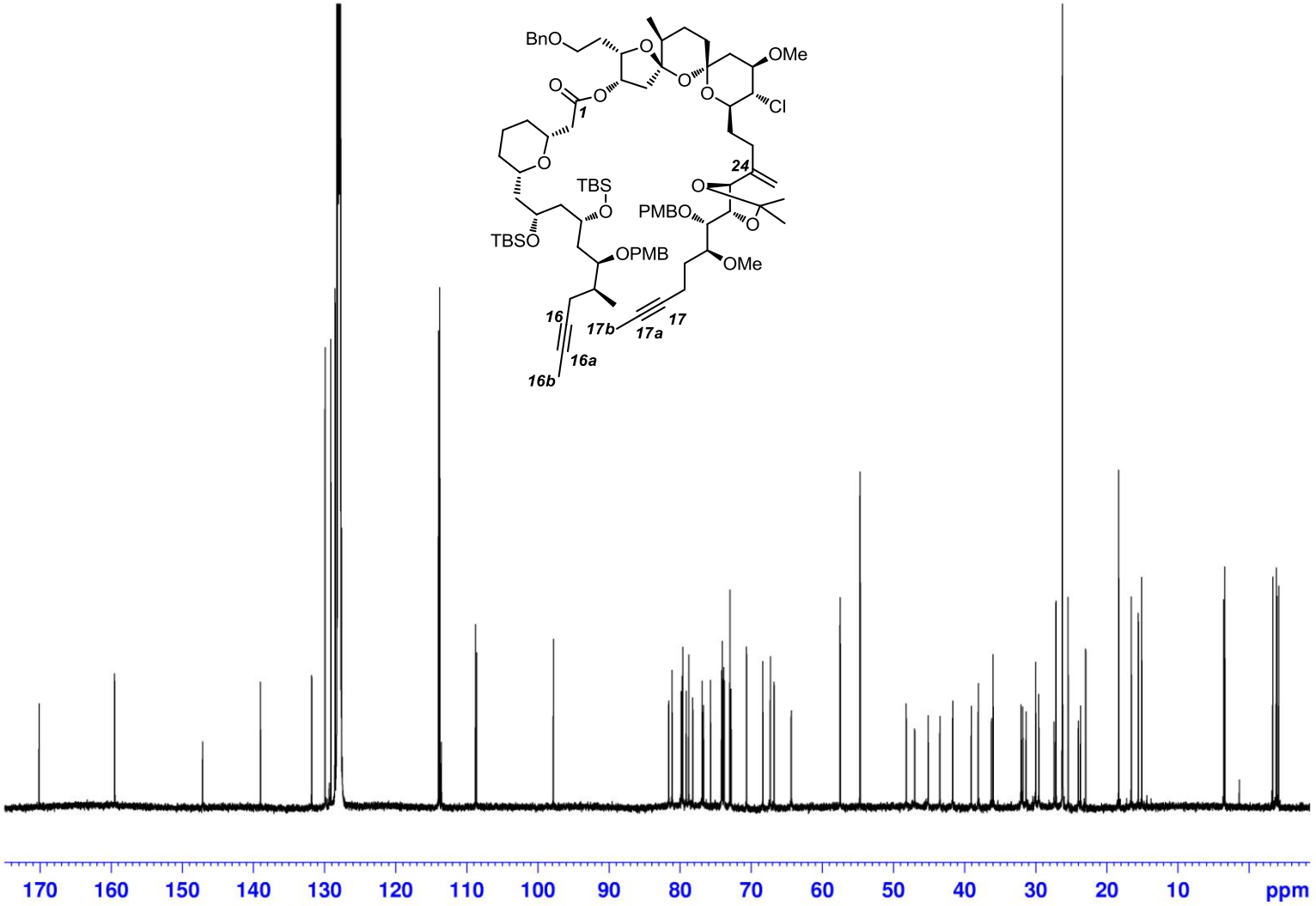
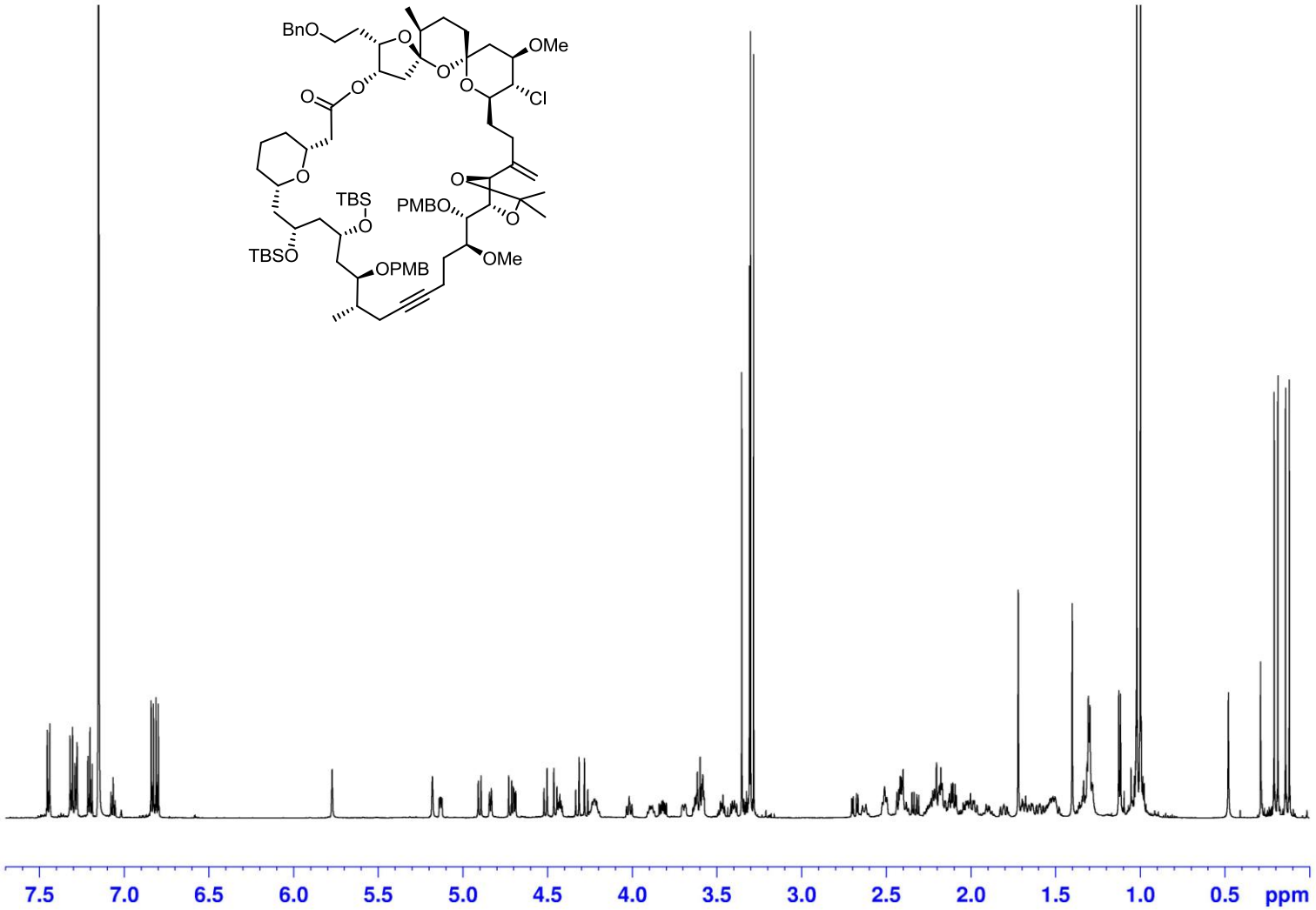
10
ppm

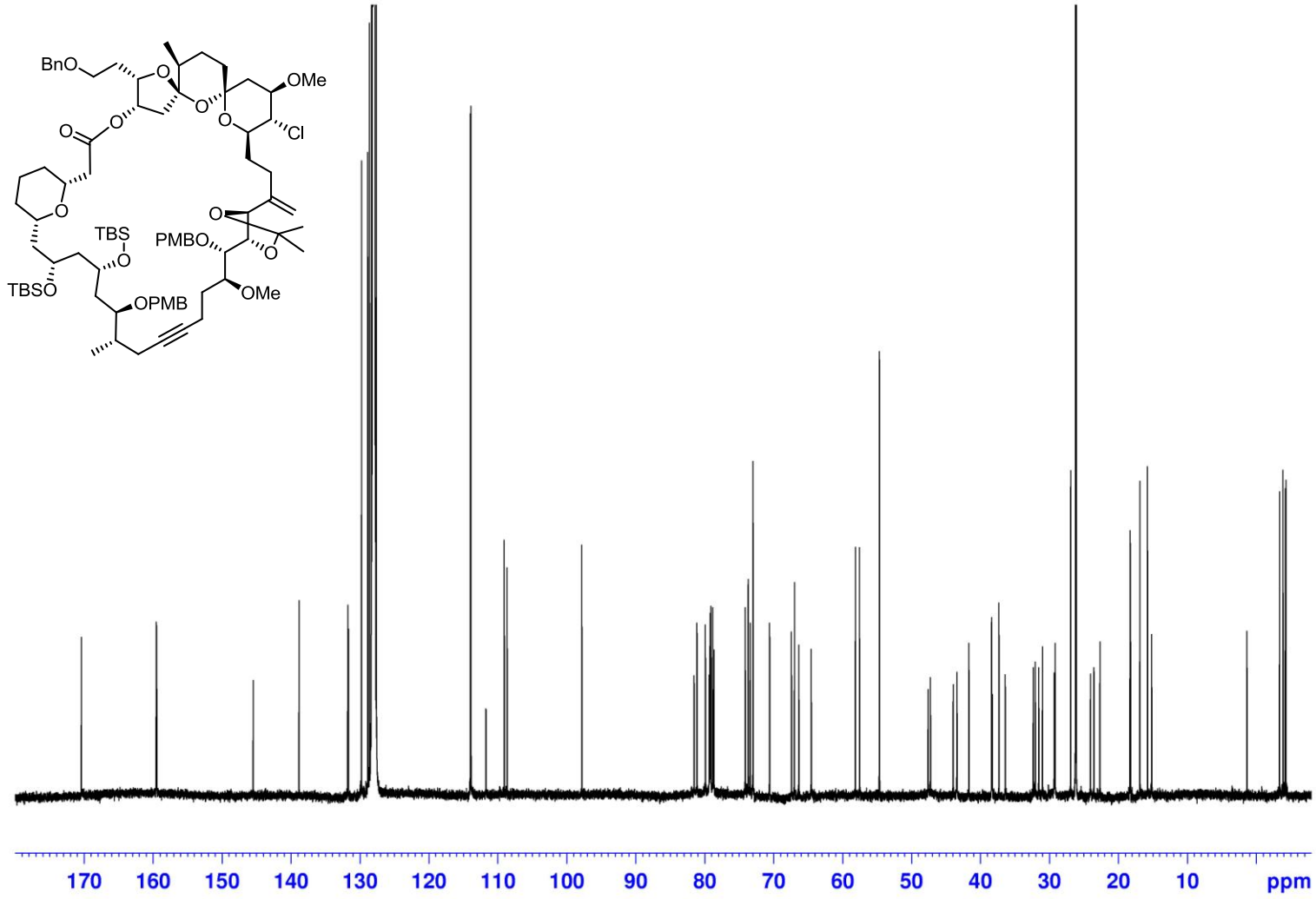

BnO
HO
OMe
Cl
PMBO
OMe
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm


BnO
HO
OMe
Cl
PMBO
OMe
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


BnO
OMe
Cl
1
24
TBS
TBSO
PMBO
OPMB
OMe
16
16a
16b
17b
17a
17
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
ppm


BnO
OMe
Cl
1
24
TBS
TBSO
PMBO
OPMB
OMe
16
16a
16b
17b
17a
17
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


BnO
O
O
O
O
O
OMe
Cl
O
TBS
O
TBSO
PMBO
O
OPMB
OMe
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
ppm


BnO
OMe
Cl
TBS
PMBO
TBSO
OPMB
OMe
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160
150
140
130
120
110
100
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70
60
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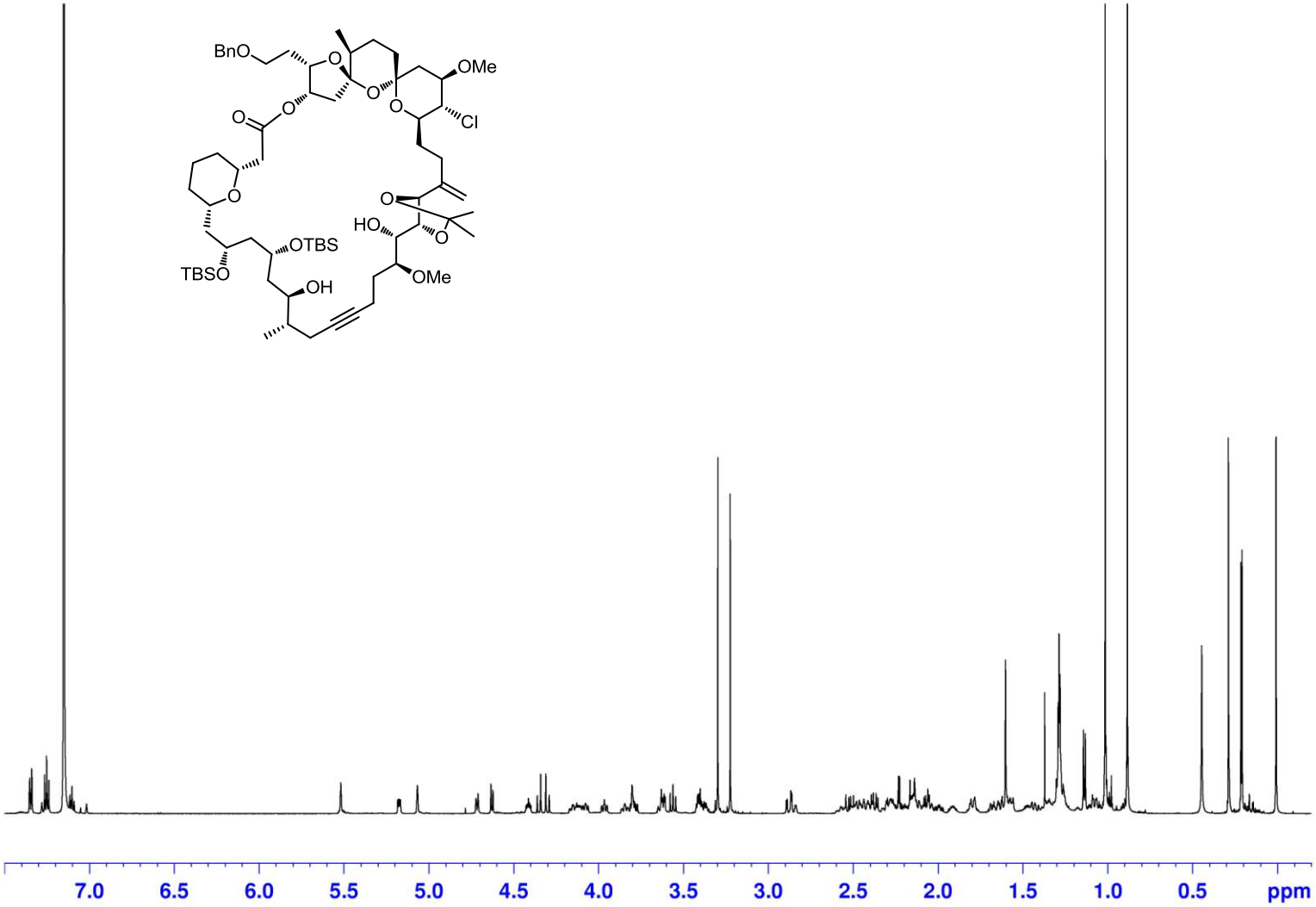
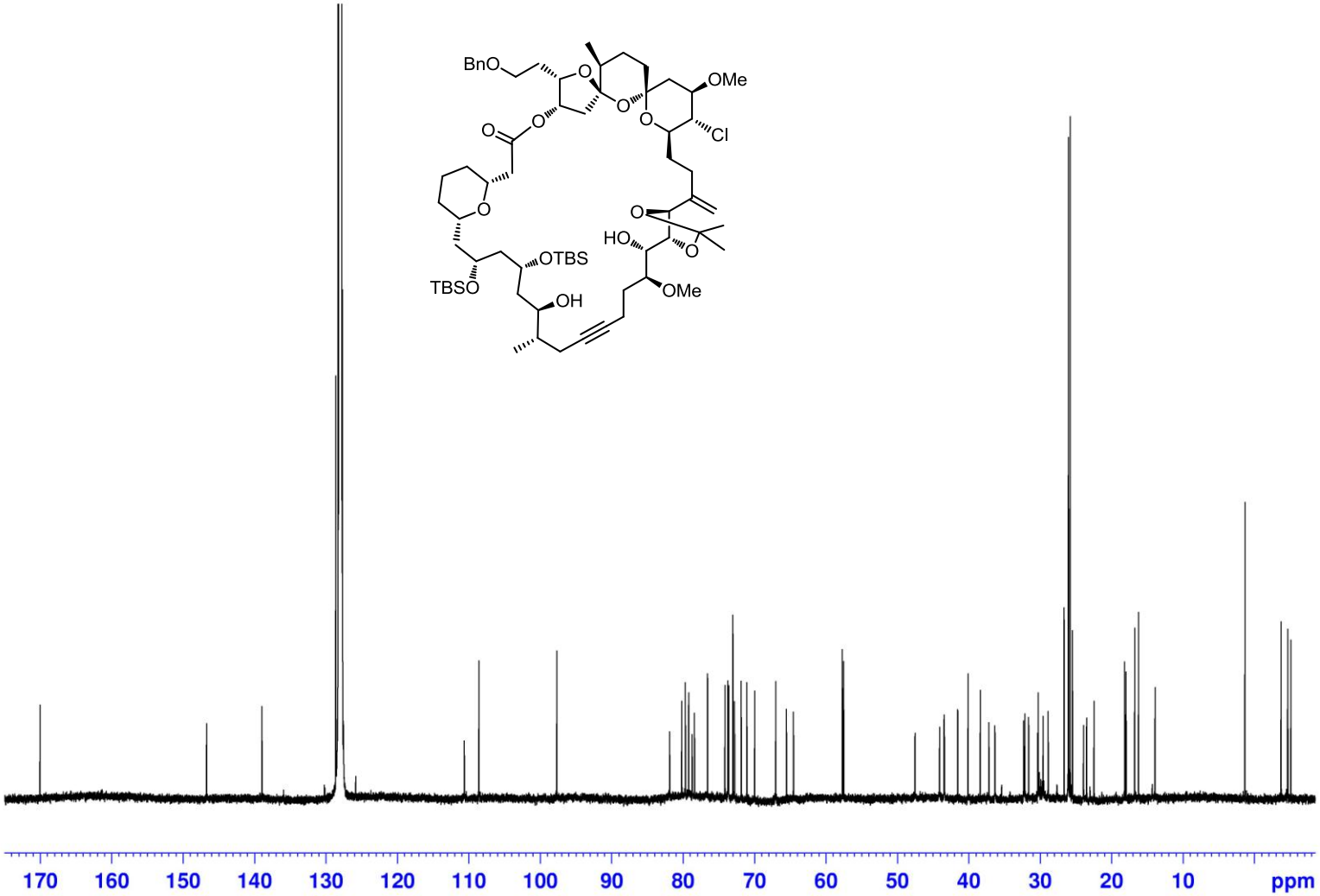
40
30
20
10
ppm


BnO
OMe
Cl
HO
OTBS
TBSO
OH
OMe
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
ppm


BnO
OMe
Cl
HO
OTBS
TBSO
OH
OMe
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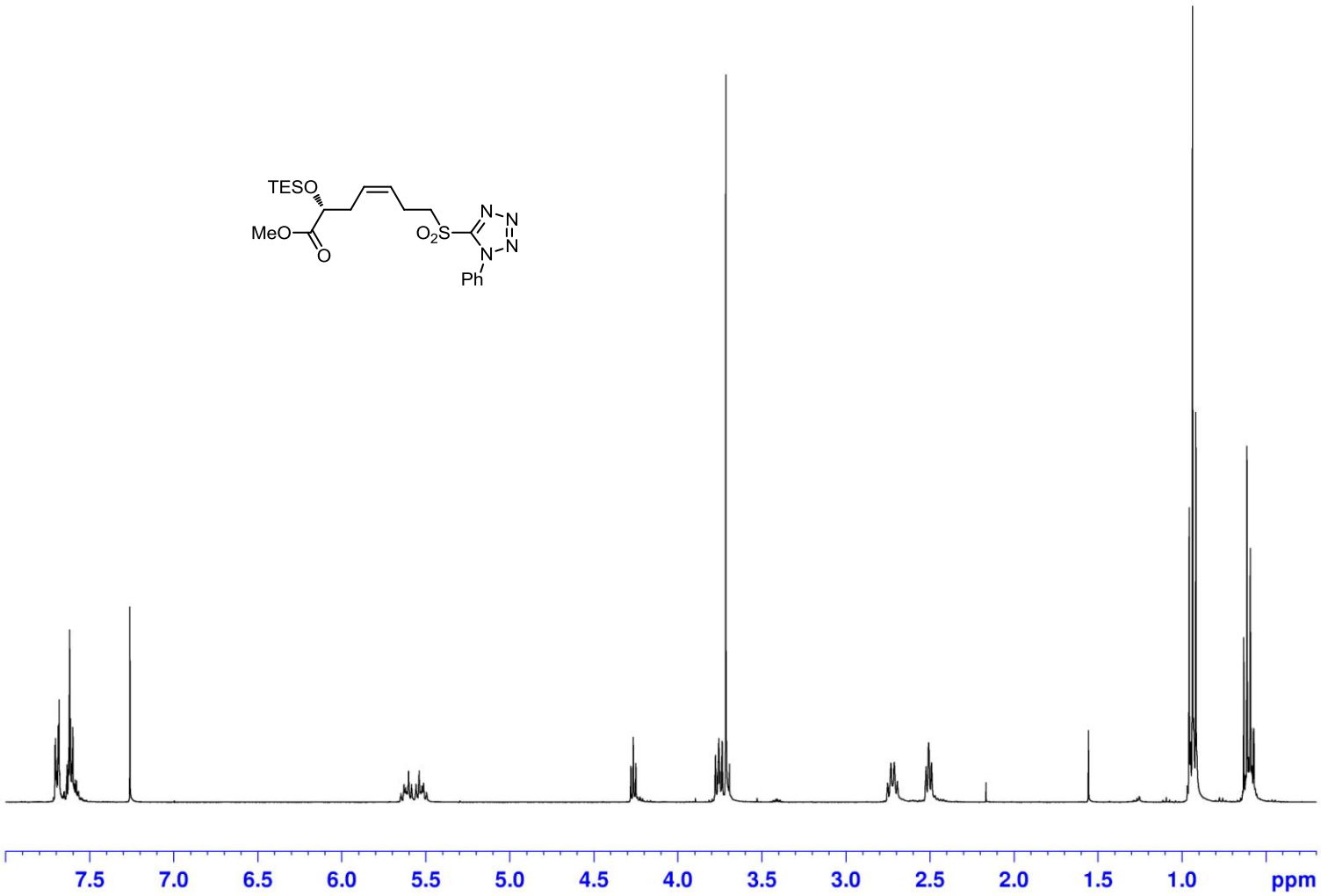
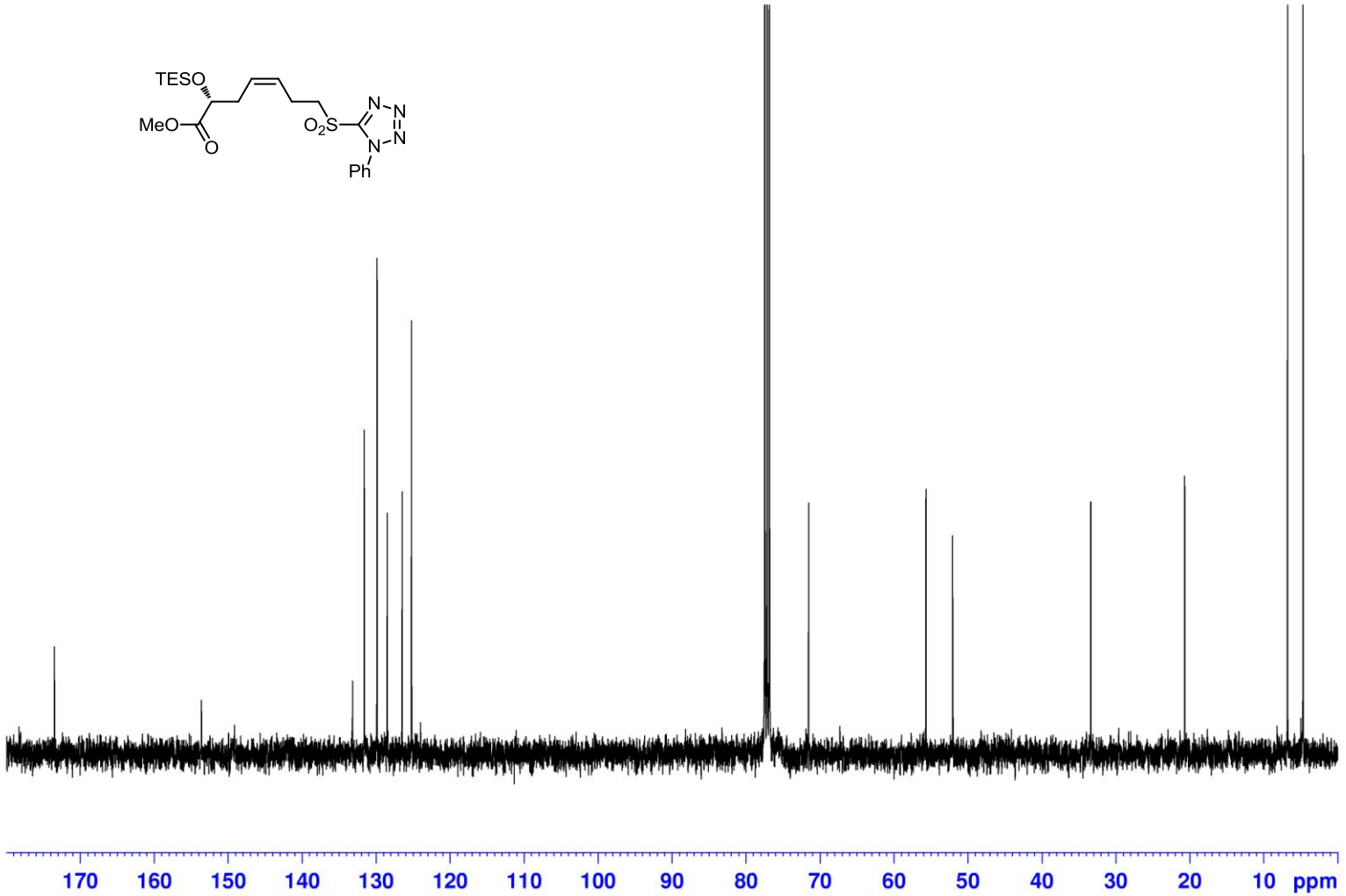
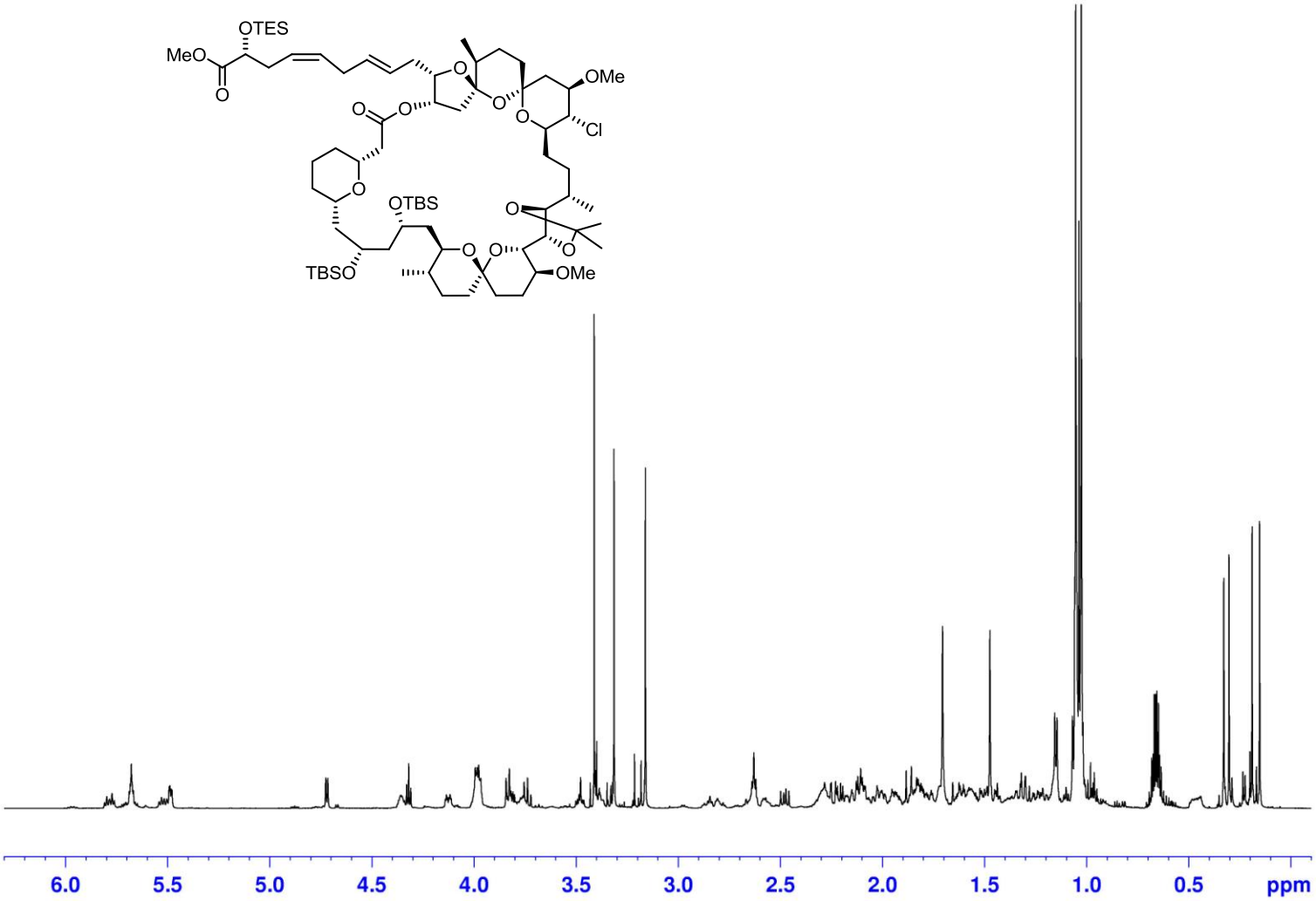
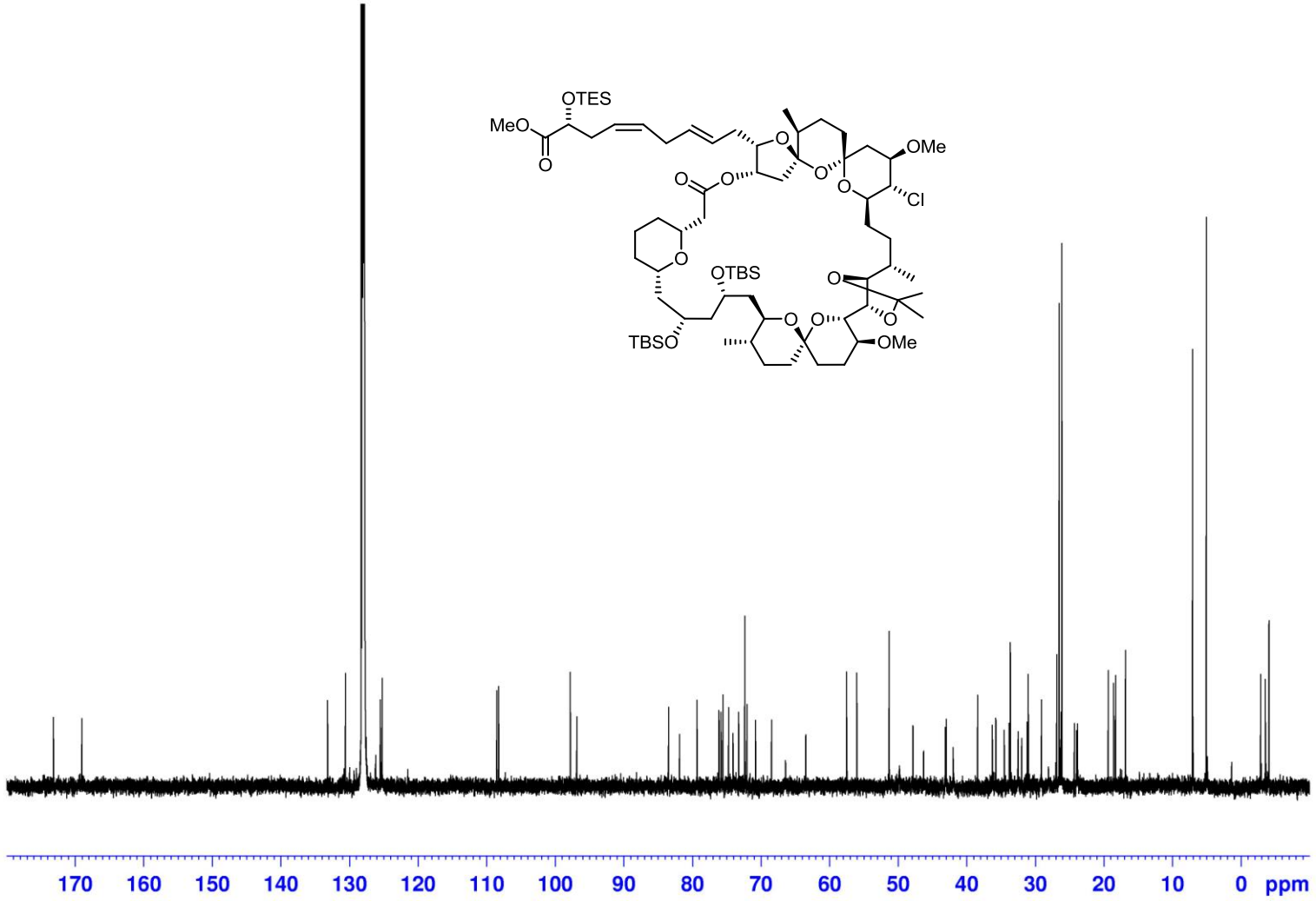
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


TESO
MeO
O
O2S
N
N
N
N
Ph
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
ppm


TESO
MeO
O
O2S
N
N
N
N
Ph
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


OTES
MeO
O
O
O
O
O
O
OMe
Cl
O
O
OTBS
TBSO
O
O
O
O
OMe
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


OTES
MeO
O
O
O
O
O
O
OMe
Cl
O
OTBS
O
O
O
O
TBSO
OMe
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm