

SUPPORTING INFORMATION

Catalysis-Based and Protecting Group-Free Total Syntheses of the Marine Oxylipins Hybridalactone and the Ecklonialactones A, B and C

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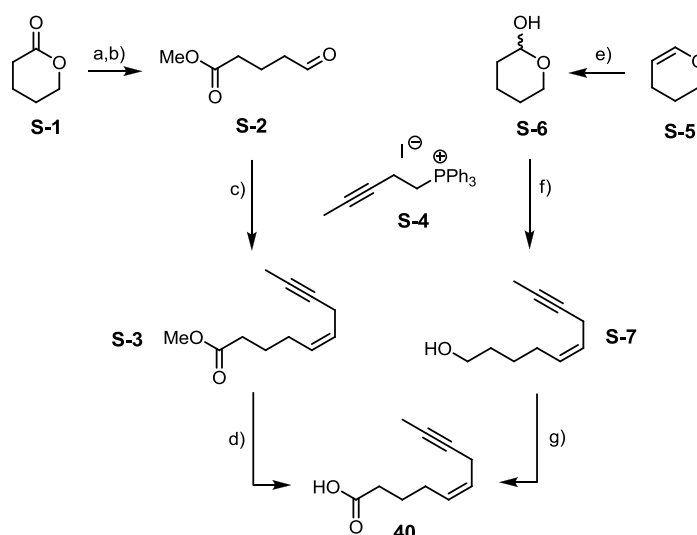
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X-ray Crystal Structure Analysis of Compound 20: $C_{16}H_{17}ClN_2O_6$, $M_r = 368.77 \text{ g} \cdot \text{mol}^{-1}$, colorless block, crystal size $0.24 \times 0.13 \times 0.08 \text{ mm}$, monoclinic, space group $C2$, $a = 16.4887(6) \text{ \AA}$, $b = 7.1507(3) \text{ \AA}$, $c = 14.5744(6) \text{ \AA}$, $\beta = 101.3360(10)^\circ$, $V = 1684.88(12) \text{ \AA}^3$, $T = 100 \text{ K}$, $Z = 4$, $D_{\text{calc}} = 1.454 \text{ g} \cdot \text{cm}^{-3}$, $\lambda = 1.54178 \text{ \AA}$, $\mu(\text{Cu-K}\alpha) = 2.341 \text{ mm}^{-1}$, Gaussian absorption correction ($T_{\text{min}} = 0.60$, $T_{\text{max}} = 0.83$), Nonius KappaCCD diffractometer, $3.09^\circ < \theta < 66.60^\circ$, 19135 measured reflections, 2577 independent reflections, 2469 reflections with $I > 2\sigma(I)$, Structure solved by direct methods and refined by full-matrix least-squares against F^2 to $R_1 = 0.027$ [$I > 2\sigma(I)$], $wR_2 = 0.060$, 288 parameters, H atoms riding, $S = 1.083$, absolute structure parameter $0.025(12)$, residual electron density $+0.2 / -0.2 \text{ e \AA}^{-3}$. **CCDC 821651** contains the supplementary crystallographic data, which can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

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 : $\delta_{\text{C}} \equiv 77.0 \text{ ppm}$; residual CHCl_3 in CDCl_3 : $\delta_{\text{H}} \equiv 7.24 \text{ ppm}$; CD_2Cl_2 : $\delta_{\text{C}} \equiv 53.8 \text{ ppm}$; residual ^1H : $\delta_{\text{H}} \equiv 5.32 \text{ ppm}$; $[\text{D}_8]\text{-toluene}$: $\delta_{\text{C}} \equiv 20.4 \text{ ppm}$; residual $\text{D}_5\text{C}_6\text{CD}_2\text{H}$: $\delta_{\text{H}} \equiv 2.09 \text{ ppm}$; C_6D_6 : $\delta_{\text{C}} \equiv 128.0 \text{ ppm}$; residual $\text{C}_6\text{D}_5\text{H}$: $\delta_{\text{H}} \equiv 7.15 \text{ ppm}$). 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.

Preparation of the Unsaturated Acid 40



Scheme S1. Reagents and conditions: a) MeOH, Dowex 50W-X8, reflux; b) PCC, MS $5\text{ \AA}$, CH_2Cl_2 , 82% (over both steps); c) **S-4**, NaHMDS, toluene/THF (1:4), $-90^\circ\text{C} \rightarrow \text{RT}$, 81%; d) KOH, MeOH, reflux, 93%; e) aq. HCl, 64%; f) **S-4**, NaH, DMF, 45%; g) (i) Dess-Martin periodinane, NaHCO_3 , CH_2Cl_2 ; (ii) NaClO_2 , NaH_2PO_4 , 2-methyl-2-butene, $t\text{BuOH}/\text{H}_2\text{O}$, 91%.

5-Iodopent-2-yne. PPh_3 (7.0 g, 26.8 mmol), imidazole (1.8 g, 26.8 mmol) and iodine (6.8 g, 26.8 mmol) were successively added to a solution of 3-pentyn-1-ol (1.5 g, 17.8 mmol) in MeCN (22 mL) and Et_2O (68 mL). The resulting mixture was stirred for 2 h before the reaction was quenched with aq. sat. NaHCO_3 (50 mL). The organic phase was washed with aq. sat. $\text{Na}_2\text{S}_2\text{O}_3$ (40 mL), dried over Na_2SO_4 and evaporated, and the residue passed through a short plug of silica (pentanes) to give, after careful evaporation, the title compound as a volatile liquid which was immediately used in the next step (3.45 g, quant.). ^1H NMR (400 MHz, CDCl_3): δ = 3.19 (t, J = 7.3 Hz, 2H), 2.71 (tq, J = 7.5, 2.5 Hz, 2H), 1.77 ppm (t, J = 2.5 Hz, 3 Hz); ^{13}C NMR (100 MHz, CDCl_3): δ = 77.9, 77.8, 24.1, 3.5, 2.6 ppm.

But-2-ynyl-5-triphenylphosphonium iodide (S-4). PPh_3 (4.67 g, 17.8 mmol) was added to a solution of 5-iodo-2-pentyne (3.45 g, 17.8 mmol) in toluene (15 mL) and the resulting mixture stirred at 80°C overnight. After reaching ambient temperature, the precipitate was filtered off, washed with toluene and dried in vacuo to give the title salt as a colorless solid (4.05 g, 50%). ^1H NMR (400 MHz, $[\text{D}_6]-\text{DMSO}$): δ = 7.92-7.75 (m, 15H), 3.84 (dt, J = 13.1, 7.2 Hz, 2H), 3.33 (s, 3H), 1.52 ppm (t, J = 2.3 Hz, 2H); ^{13}C NMR (100 MHz, $[\text{D}_6]-\text{DMSO}$): δ = 135.0 (d, J = 3 Hz), 133.7 (d, J = 10 Hz), 130.2 (d, J = 12 Hz), 118.1 (d, J = 87 Hz), 79.6, 76.3 (d, J = 14 Hz), 20.1 (d, J = 51 Hz), 12.3 (d, J = 4 Hz), 2.9 ppm; IR (film): $\tilde{\nu}$ = 3017 (w), 2903 (w), 1585 (w), 1434 (m), 1384 (w), 1341 (w), 1136 (w), 1110 (s), 995 (m), 843 (s), 733 (s), 719 (s), 685 (s) cm^{-1} ; MS (ESI): m/z : 329.2 [456-I]; HRMS (ESI): m/z : calcd. for $\text{C}_{23}\text{H}_{22}\text{P}$: 329.1454 [$\text{M}-\text{I}$] $^+$; found: 329.1452.

Methyl 5-Hydroxy-pentanoate.¹ Dowex 50W-X8 resin (100 mg) was added to a solution of δ -valerolactone (7.0 g, 70 mmol) in MeOH (365 mL) and the resulting suspension was stirred at reflux temperature for 4 h and at ambient temperature overnight. The resin was then filtered off and the solvent evaporated to give the title compound as a colorless liquid, which was used in the next step without further purification (8 g, quant.). ^1H NMR (400 MHz, CDCl_3): δ = 3.67 (s, 3H), 3.65 (t, J = 6.3 Hz, 2H), 2.36 (t, J = 7.2 Hz, 2H), 1.76-1.68 (m, 2H), 1.63-1.56 (m, 2H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 174.2, 66.1, 51.5, 33.6, 31.9, 21.0 ppm. HRMS (CI, *i*-butane): m/z : calcd. for $\text{C}_6\text{H}_{13}\text{O}_3$ 133.0865 [$\text{M}+\text{H}$] $^+$, found: 133.0865.

Aldehyde S-2.¹ Powdered MS 5 Å (100 mg) and PCC (6.5 g, 30 mmol) were added to a solution of methyl 5-hydroxy-pentanoate (2.0 g, 15 mmol) in CH_2Cl_2 (20 mL) and the resulting mixture was stirred overnight. For work-up, the mixture was diluted with Et_2O (50 mL), causing the formation of a black precipitate, which was filtered off through a pad of silica. After careful rising of the silica with ether, the combined filtrates were evaporated and the solvent removed in vacuo to give the desired aldehyde as a colorless oil, which was used in the next step without further purification (1.6 g, 82%). ^1H NMR (400 MHz, CDCl_3): δ = 9.76 (t, J = 1.3 Hz, 1H), 3.66 (s, 3H), 2.52 (dt, J = 7.2, 1.3 Hz, 2H), 2.36 (t, J = 7.2 Hz, 2H), 1.94 (qi, J = 7.2 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 201.5, 173.3, 51.6, 42.8, 32.9, 17.3 ppm; IR (film): $\tilde{\nu}$ = 2951, 1729, 1706, 1436, 1418, 1370, 1317, 1201, 1150, 1059, 1016, 993, 900, 864, 844, 799, 783, 703 cm^{-1} ; MS (EI): m/z (%): 131 (< 1) [M] $^+$, 111 (< 1), 102 (17), 99 (43), 87 (9), 74 (100), 71 (33), 59 (47), 55 (46), 43 (97), 39 (24), 39 (27); HRMS (CI, *i*-butane): m/z : calcd. for $\text{C}_6\text{H}_{11}\text{O}_3$ 131.0708 [$\text{M}+\text{H}$] $^+$, found: 131.0708.

¹ Enholm, E.; Joshi, A.; Wright, D. L. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5262.

Compound S-3. A solution of NaHMDS (0.39 g, 2.1 mmol) in THF (2 mL) was added to a suspension of phosphonium iodide **S-4** (0.91 g, 2.0 mmol) in THF (20 mL) and toluene (5 mL) at -30°C . The mixture was then stirred at ambient temperature for 1 h before it was cooled to -90°C . A solution of compound **S-2** (0.29 g, 2.2 mmol) in THF (2 mL) was added and the mixture allowed to slowly reach ambient temperature overnight. The reaction was quenched with aq. sat. NH_4Cl (4 mL) and water (1 mL), the aqueous phase was extracted with Et_2O , the combined organic layers were dried and evaporated, and the residue purified by flash chromatography (pentanes/ Et_2O , 2:1) to give the title compound as a colorless oil (0.29 g, 81%). ^1H NMR (400 MHz, CDCl_3): δ = 5.50-5.37 (m, 2H), 3.66 (s, 3H), 2.88-2.85 (m, 2H), 2.32 (t, J = 7.6 Hz, 2H), 2.08 (q, J = 7.2 Hz, 2H), 1.77 (t, J = 2.7 Hz, 3H), 1.70 (qi, J = 7.4 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 174.0, 129.9, 126.0, 77.2, 75.4, 51.5, 33.4, 26.4, 24.5, 17.1, 3.5 ppm; IR (film): $\tilde{\nu}$ = 3020, 2950, 1736, 1436, 1367, 1293, 1201, 1155, 1088, 1027, 861, 799, 689 cm^{-1} ; MS (EI): m/z (%): 180 (1) $[\text{M}]^+$, 165 (2), 149 (24), 140 (9), 120 (24), 106 (72), 91 (100), 77 (49), 66 (22), 53 (22), 39 (30), 27 (23); HRMS (EI): m/z : calcd. for $\text{C}_{11}\text{H}_{16}\text{O}_2$ 180.1150 $[\text{M}]^+$, found: 180.1150.

Compound S-6. 3,4-Dihydro-2*H*-pyran (4.6 g, 55 mmol) was added dropwise to aq. HCl (0.2 M, 20 mL) at 0°C and the resulting mixture was stirred at that temperature for 20 min before it was warmed to ambient temperature and stirred for additional 90 min. For work up, the mixture was carefully neutralized with aq. sat. NaHCO_3 and the product was extracted with CH_2Cl_2 . The combined extracts were dried over Na_2SO_4 , the solvent was evaporated, and the crude product purified by Kugelrohr distillation (ca. 130°C , 5 mbar) to give tetrahydro-2*H*-pyran-2-ol as a colorless oil (3.6 g, 35 mmol, 64%). The spectral data were identical with those of a commercial sample.

Compound S-7. Phosphonium iodide **S-4** (0.18 g, 0.40 mmol) was added to a suspension of NaH (9.6 mg, 0.40 mmol) in DMF (2 mL) and the resulting mixture was stirred at ambient temperature for 30 min. A solution of compound **S-6** (0.020 g, 0.20 mmol) in DMF (1 mL) was introduced and the resulting mixture stirred overnight. The reaction was quenched with aq. sat. NH_4Cl and the product extracted with a mixture of pentane and Et_2O . The combined organic layers were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (pentane/ Et_2O , 3 : 2) to give product **S-7** as a colorless oil (13.7 mg, 45%). ^1H NMR (400 MHz, CDCl_3): δ = 5.50-5.39 (m, 2H), 3.65 (t, J = 6.5 Hz, 2H), 2.93-2.83 (m, 2H), 2.08 (dt, J = 5.7, 7.2 Hz, 2H), 1.78 (t, J = 2.7 Hz, 3H), 1.63-1.54 (m, 2H), 1.50-1.40 (m, 2H), 1.26 (brs, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 130.9, 125.3, 77.4, 75.4, 62.8, 32.3, 26.8, 25.5, 17.1, 3.5 ppm; IR (film): $\tilde{\nu}$ = 3351, 3020, 2932, 2860, 1435, 1063, 689 cm^{-1} .

Acid 40. Method 1: KOH (0.13 g, 2.3 mmol) was added to a solution of compound **S-3** (0.27 g, 1.5 mmol) in MeOH (3 mL) and the resulting mixture stirred at reflux temperature for 2 h. For work-up, the mixture was diluted with water, acidified by aq. HCl until pH $\approx$ 2 was reached, and the aqueous layer extracted with Et_2O . The combined pentane phases were evaporated and the residue dried in vacuo. Colorless syrup (0.23 g, 93%).

Method 2: A solution of (*Z*)-5-decen-8-ynol **S-7** (13.7 mg, 0.090 mmol) in CH_2Cl_2 (1.5 mL) was added to a mixture of Dess-Martin periodinane (0.051 g, 0.12 mmol) and NaHCO_3 (0.038 g, 0.45 mmol) in CH_2Cl_2 (1.5 mL), and the resulting mixture was stirred at room temperature for 2 h. The reaction was quenched with aq. sat. $\text{Na}_2\text{S}_2\text{O}_3$ and the product extracted with Et_2O . The combined organic layer was dried over Na_2SO_4 and evaporated, and the resulting crude product used in the next step without further purification. 2-Methyl-2-butene (0.070 g, 1.0 mmol), NaH_2PO_4 (0.061 g, 0.51 mmol) and NaClO_2 were sequentially added to a solution of the crude aldehyde in a mixture of *t*BuOH (2 mL) and H_2O (2 mL). The resulting mixture was stirred for 20 min before the reaction was quenched with aq.

sat. NH_4Cl and the product extracted with a mixture of pentane and Et_2O . The combined extracts were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (pentane/ Et_2O , 3:2) to furnish acid **40** as a colorless oil (13.6 mg, 91%). ^1H NMR (400 MHz, CDCl_3): δ = 5.52-5.37 (m, 2H), 2.89-2.85 (m, 2H), 2.37 (t, J = 7.5 Hz, 2H), 2.12 (q, J = 7.2 Hz, 2H), 1.77 (t, J = 2.6 Hz, 3H), 1.72 (qi, J = 7.4 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 179.4, 129.7, 126.2, 77.2, 75.5, 33.2, 26.3, 24.2, 17.1, 3.5 ppm; IR (film): $\tilde{\nu}$ = 3020, 2920, 2861, 2667, 1705, 1413, 1292, 1239, 1156, 1086, 910, 798, 677 cm^{-1} ; MS (EI): m/z (%): 166 (1) $[\text{M}]^+$, 147 (1), 137 (6), 126 (15), 106 (66), 91 (100), 77 (63), 66 (38), 53 (24), 45 (13), 39 (35), 27 (29); HRMS (EI): m/z : calcd. for $\text{C}_{10}\text{H}_{14}\text{O}_2$ 166.0994 $[\text{M}]^+$, found: 166.0994.

Preparation of the Common Intermediate 22 – Auxiliary Based Route

Compound 13. Vinylmagnesium bromide (1 M in THF, 19.5 mL, 19.5 mmol) was added over 15 min to a suspension of CuI (3.71 g, 19.5 mmol) in THF (116 mL) at -78°C and the resulting mixture stirred for 30 min before a solution of compound **12** (2.9 g, 12 mmol)² in THF (30 mL) was added over the course of 1 h. Once the addition was complete, allyl iodide (4.08 g, 24.4 mmol) was introduced and the mixture warmed to -60°C , causing a color change to black and finally pale brown. After stirring for 30 min at -60°C , the mixture was allowed to reach ambient temperature. The reaction was quenched with aq. sat. NaHCO_3 , the aqueous layer extracted with *tert*-butyl methyl ether, the combined organic phases were dried and evaporated, and the residue purified by flash chromatography (hexanes/ EtOAc , 10:1) to give product **13** as a pale yellow syrup (3.12 g, 86%). $[\alpha]_D^{20}$ = -148 (c = 0.28, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ = 5.85-5.69 (m, 2H), 5.34 (d, J = 5.3 Hz, 1H), 5.24-5.23 (m, 1H), 5.20 (dt, J = 7.7, 1.1 Hz, 1H), 5.14-5.12 (m, 1H), 5.10-5.08 (m, 1H), 3.49 (td, J = 10.7, 4.2 Hz, 1H), 2.76-2.70 (m, 1H), 2.57-2.48 (m, 3H), 2.14 (dsept., J = 7.0, 2.7 Hz, 1H), 2.04-1.99 (m, 1H), 1.69-1.62 (m, 2H), 1.42-1.29 (m, 1H), 1.24 (ddt, J = 12.4, 10.5, 3.0 Hz, 1H), 1.08-0.94 (m, 1H), 0.92 (d, J = 6.6 Hz, 3H), 0.89 (d, J = 7.1 Hz, 3H), 0.87-0.81 (m, 2H), 0.79 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 175.8, 134.4, 134.1, 118.7, 118.1, 103.6, 78.6, 50.6, 47.6, 45.6, 40.1, 34.3, 33.3, 31.4, 25.3, 23.0, 22.2, 20.9, 15.6 ppm; IR (film): $\tilde{\nu}$ = 2951, 2921, 2856, 1775, 1453, 1413, 1370, 1317, 1239, 1165, 1102, 988, 915, 677 cm^{-1} ; MS (EI): m/z (%): 307 (<1) $[\text{M}+\text{H}]^+$, 291 (<1), 260 (<1), 221 (1), 168 (6), 151 (6), 139 (40), 122 (14), 109 (10), 94 (100), 83 (68), 79 (57), 69 (22), 55 (36), 41 (27); HRMS (ESI): m/z : calcd. for $\text{C}_{19}\text{H}_{30}\text{O}_3\text{Na}$ 329.2087 $[\text{M}+\text{Na}]^+$, found: 329.2085; elemental analysis calcd. (%) for: $\text{C}_{19}\text{H}_{30}\text{O}_3$ (306.44): C 74.47, H 9.87; found: C 74.35, H 9.78.

Compound 14. A solution of compound **13** (0.96 g, 3.1 mmol) in trifluoroacetic acid (80% in water, 10 mL) was stirred overnight before all volatile materials were pumped off in vacuo at 40 - 50°C bath temperature. The residue was purified by flash chromatography (hexanes/ EtOAc , 3:1) to give product **14** as a pale brown oil (502 mg, 95%). ^1H NMR (400 MHz, CDCl_3): δ = 5.91-5.69 (m, 4H), 5.71 (d, J = 5.1 Hz, 1H), 5.55 (d, J = 5.8 Hz, 1H), 5.27-5.09 (m, 8H), 2.93-2.87 (m, 1H), 2.82-2.73 (m, 2H), 2.64-2.43 (m, 4H), 2.39-2.31 (m, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 177.8, 176.0, 133.9, 133.7, 133.4, 132.9, 119.8, 119.3, 118.8, 118.5, 101.2, 97.5, 51.9, 49.2, 45.6, 41.7, 32.7, 31.2 ppm; IR (film): $\tilde{\nu}$ = 3378, 3082, 2984, 1749, 1643, 1437, 1359, 1316, 1167, 1113, 993, 917, 816, 730, 671 cm^{-1} ; MS (EI): m/z (%): 168 (2) $[\text{M}]^+$, 150 (7), 139 (1), 127 (2), 122 (7), 105 (2), 99 (18), 94 (51), 79 (100), 70 (35),

² Moradai, O. M.; Paquette, L. A. *Org. Synth.* **2003**, *80*, 66.

66 (24), 53 (18), 41 (23), 27 (17); HRMS (ESI): m/z : calcd. for $C_9H_{12}O_3Na$ 191.0679 $[M+Na]^+$, found: 191.0679.

Compound 15. $NaBH_4$ (1.21 g, 31.8 mmol) was added in portions to a solution of compound **14** (2.13 g, 12.7 mmol) in MeOH (53 mL). After stirring for 1 h at ambient temperature, additional $NaBH_4$ (242 mg, 6.40 mmol) was introduced and stirring continued for another 45 min. Next, the mixture was acidified upon addition of HCl in Et_2O (16 mL, 40 mmol, 2.5 M) and the resulting mixture stirred at reflux temperature for 1 h. After reaching ambient temperature, the mixture was carefully diluted with aq. sat. $NaHCO_3$ (75 mL), the aqueous phase was extracted with CH_2Cl_2 , the combined organic layers were dried and evaporated, and the residue purified by flash chromatography (pentanes/ Et_2O , 8:1) to give the title compound as a colorless oil (1.45 g, 75%). $[\alpha]_D^{20} = -1.2$ ($c = 0.37$, CH_2Cl_2); 1H NMR (400 MHz, $CDCl_3$): $\delta = 5.83$ -5.65 (m, 2H), 5.21-5.08 (m, 4H), 4.34 (dd, $J = 9.1, 8.1$ Hz, 1H), 3.89 (dd, $J = 9.2, 9.8$ Hz, 1H), 3.02-2.93 (m, 1H), 2.49-2.41 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 177.5, 135.1, 133.8, 118.7, 118.4, 70.0, 44.9, 44.6, 32.1$ ppm; IR (film): $\tilde{\nu} = 3081, 2985, 2907, 1771, 1642, 1479, 1437, 1347, 1322, 1235, 1197, 1162, 1096, 1065, 1014, 917, 741, 679$ cm^{-1} ; MS (EI): m/z (%): 152 (19) $[M]^+$, 137 (1), 123 (3), 111 (11), 107 (24), 93 (31), 79 (96), 67 (24), 54 (100), 39 (33), 27 (21); HRMS (CI, *i*-butane): m/z : calcd. for $C_9H_{13}O_2$ 153.0916 $[M+H]^+$, found: 153.0914.

Compound 18. Me_3Al (8.2 mL, 16 mmol, 2 M in heptane) was added at 0°C to a suspension of *N,O*-dimethylhydroxylamine hydrochloride (1.6 g, 16 mmol) in CH_2Cl_2 (16 mL) and the resulting mixture was stirred for 2 h at that temperature. Next, a solution of compound **15** (1.0 g, 6.6 mmol) in CH_2Cl_2 (16 mL) was introduced and stirring continued for 2 h. The reaction was quenched by careful, dropwise addition of aq. H_2SO_4 (10% w/w) and stirring continued until all precipitates had dissolved. The aqueous layer was extracted with CH_2Cl_2 , the combined organic layers were dried and evaporated, and the residue quickly passed through a pad of silica, eluting with hexanes/ $EtOAc$ (1:2). Evaporation of the filtrate gave Weinreb amide **16**, which had to be used in the next step without delay. Characteristic data: 1H NMR (400 MHz, $CDCl_3$): $\delta = 5.78$ -5.64 (m, 2H), 5.22-5.16 (m, 2H), 5.07-5.01 (m, 1H), 4.99-4.96 (m, 1H), 3.68 (s, 3H), 3.60-3.49 (m, 2H), 3.18 (s, 3H), 2.53-2.41 (m, 2H), 2.39-2.26 (m, 2H) ppm.

A solution of Weinreb amide **16** (1.3 g, 6.2 mmol) and complex **17** (228 mg, 0.25 mmol)³ in CH_2Cl_2 (36 mL) was stirred overnight before all volatile materials were evaporated. The residue was purified by flash chromatography (hexanes/ $EtOAc$, 1:2) to give product **18** as a syrup (0.85 g, 74% over both steps). $[\alpha]_D^{20} = -169$ ($c = 0.7$, CH_2Cl_2); 1H NMR (400 MHz, $CDCl_3$): $\delta = 5.57$ -5.53 (m, 1H), 5.57-5.54 (m, 1H), 3.71 (s, 3H), 3.69-3.65 (m, 1H), 5.38-3.54 (m, 1H), 3.28 (br t, $J = 6.1$ Hz, 2H), 3.20 (s, 3H), 2.74-2.66 (m, 1H), 2.59-2.51 (m, 1H), 2.02 ppm (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 176.6, 130.9, 129.9, 65.5, 61.3, 52.6, 42.4, 37.1, 32.5$ ppm; IR (film): $\tilde{\nu} = 3417$ (br, m), 3051 (w), 2934 (m), 1636 (s), 1444 (m), 1386 (s), 1324 (m), 1177 (m), 1116 (w), 1074 (m), 1030 (s), 1006 (s), 967 (m), 949 (w), 890 (w), 852 (w), 710 (s) cm^{-1} ; MS (EI): m/z (%): 185 (6) $[M]^+$, 167 (9), 154 (1), 136 (1), 125 (30), 108 (11), 97 (12), 79 (100), 67 (46), 61 (29), 55 (5), 41 (18), 31 (9); HRMS (ESI): m/z : calcd. for $C_9H_{15}NO_3Na$: 208.0944 $[M+Na]^+$; found: 208.0944.

Compound 19. $NaHCO_3$ (908 mg, 10.81 mmol) and Dess-Martin periodinane (688 mg, 1.61 mmol) were successively added to a solution of compound **18** (200 mg, 1.08 mmol) in CH_2Cl_2 (12 mL) and the resulting mixture was stirred for 1.5 h. The reaction was quenched at 0°C with aq. sat. $Na_2S_2O_3$,

³ Fürstner, A.; Guth, O.; Döffels, A.; Seidel, G.; Liebl, M.; Gabor, B.; Mynott, R. *Chem. Eur. J.* **2001**, *7*, 4811.

the aqueous phase was extracted with CH_2Cl_2 , and the combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (pentanes/ Et_2O , 1:1) to give aldehyde **19** as a pale yellow oil, which turned out to be rather unstable and was therefore used without delay in the next step (144 mg, 73%). $[\alpha]_D^{20} = -189.6$ ($c = 0.43$, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): $\delta = 9.69$ (s, 1H), 5.84-5.81-5.84 (m, 1H), 5.73-5.70 (m, 1H), 4.01 (br s, 1H), 3.81 (q, $J = 7.3$ Hz, 1H), 3.72 (br s, 3H), 3.20 (s, 3H), 2.78-2.62 ppm (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 199.7$, 174.8, 132.7, 124.6, 62.7, 61.3, 38.4, 35.5, 32.5 ppm; IR (film): $\tilde{\nu} = 2939$ (m), 2718 (w), 1720 (s), 1652 (s), 1443 (m), 1386 (s), 1342 (w), 1316 (w), 1176 (m), 1113 (m), 1003 (s), 964 (m), 948 (m), 843 (w), 704 (s) cm^{-1} ; MS (EI): m/z (%): 183 (16) $[\text{M}]^+$, 166 (1), 154 (6), 134 (1), 123 (27), 105 (3), 95 (12), 79 (8), 67 (100), 61 (32), 46 (4), 39 (20), 29 (4); HRMS (EI): m/z : calcd. for $\text{C}_9\text{H}_{13}\text{NO}_3$: 183.0895 $[\text{M}]^+$; found: 183.0893.

Compound 20. 2-Chloro-4-nitrobenzoyl chloride (50 mg, 0.23 mmol, 1.05 eq.) and catalytic amounts of DMAP were added to a solution of compound **18** (40 mg, 0.22 mmol) in CH_2Cl_2 (1 mL) and Et_3N (34 μL , 0.24 mmol). The mixture was stirred overnight before the reaction was quenched with aq. sat. NaHCO_3 . A standard extractive work-up followed by purification of the crude product by flash chromatography (hexanes/ EtOAc , 2:1) furnished product **20** as a white crystalline powder (53 mg, 65%). Crystals suitable for X-ray diffraction were grown by slowly diffusing pentane into a solution of **20** in Et_2O . $[\alpha]_D^{20} = -53$ ($c = 0.01$, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): $\delta = 8.30$ (d, $J = 2.2$ Hz, 1H), 8.14 (dd, $J = 8.6$, 2.2 Hz, 1H), 7.94 (d, $J = 8.6$ Hz, 1H), 5.77 (dq, $J = 5.6$, 2.3 Hz, 1H), 5.66 (dq, $J = 5.9$, 2.0 Hz, 1H), 4.43 (dd, $J = 10.9$, 6.3 Hz, 1H), 4.40 (dd, $J = 10.8$, 5.8 Hz, 1H), 3.67 (s, 3H), 3.66-3.61 (m, 1H), 3.36-3.30 (m, 1H), 3.18 (s, 3H), 2.77 (ddq, $J = 16.6$, 9.5, 2.4 Hz, 1H), 2.57 (ddq, $J = 16.6$, 7.0, 2.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3): $\delta = 175.7$ (br), 164.1, 149.4, 135.9, 134.7, 132.1, 130.9, 129.6, 126.0, 121.4, 68.6, 61.3, 48.8, 42.8, 37.2, 32.5 (br) ppm; IR (film): $\tilde{\nu} = 3096$, 3000, 2959, 2893, 1734, 1655, 1523, 1354, 1262, 1246, 1108, 1048, 1011, 773, 709 cm^{-1} ; MS (EI): m/z (%): 368 (3) $[\text{M}]^+$, 308 (14), 280 (3), 184 (26), 167 (15), 138 (13), 107 (29), 79 (100); HRMS (ESI): m/z : calcd. for $\text{C}_{16}\text{H}_{17}\text{N}_2\text{O}_6\text{NaCl}$ 391.0667 $[\text{M}+\text{Na}]^+$, found: 391.0670.

Compound 22. Compound **21** (227 mg, 1.18 mmol) and K_2CO_3 (217 mg, 1.57 mmol) were added to a solution of aldehyde **19** (144 mg, 0.79 mmol) in MeOH (10 mL) and the resulting mixture was stirred overnight. For work up, the mixture was partitioned between CH_2Cl_2 and brine, the combined organic layers were dried (Na_2SO_4) and evaporated, and the residue was purified by flash chromatography (pentanes/ Et_2O , 4:1) to give the corresponding terminal alkyne as a colorless oil (106 mg, 75%), which analyzed as follows: $[\alpha]_D^{20} = -165$ ($c = 0.22$, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): $\delta = 5.71$ -5.68 (m, 1H), 5.64-5.61 (m, 1H), 3.99-3.94 (m, 1H), 3.74 (s, 3H), 3.58 (br q, $J = 7.4$ Hz, 1H), 3.22 (s, 3H), 2.77 (ddq, $J = 16.4$, 9.5, 2.3 Hz, 1H), 2.49 (ddq, $J = 16.3$, 7.4, 2.4 Hz, 1H), 2.14 ppm (d, $J = 2.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 175.2$, 130.1, 129.6, 85.9, 69.3, 61.7, 47.0, 39.5, 36.9, 32.4 ppm; IR (film): $\tilde{\nu} = 3292$ (m), 2939 (m), 1652 (s), 1445 (m), 1423 (m), 1386 (s), 1340 (m), 1311 (w), 1163 (s), 1101 (m), 1008 (s), 975 (m), 937 (m), 814 (w), 767 (w) cm^{-1} ; MS (EI): m/z (%): 179 (5) $[\text{M}]^+$, 164 (< 1), 148 (16), 133 (< 1), 119 (25), 106 (2), 91 (100), 77 (2), 65 (29), 61 (8), 51 (5), 39 (12), 27 (2); HRMS (EI): m/z : calcd. for $\text{C}_{10}\text{H}_{13}\text{NO}_2$: 179.0946 $[\text{M}]^+$; found: 179.0946.

LiHMDS (177 mg, 1.06 mmol) was added to a solution of the terminal alkyne (150 mg, 0.84 mmol) in THF (5 mL) at -78°C . After stirring for 1.5 h, MeOTf (147 μL 1.3 mmol) was introduced and stirring continued at that temperature for 1 h. The reaction was quenched with aq. sat. NaHCO_3 while cold before the mixture was allowed to reach ambient temperature. A standard extractive work up

followed by flash chromatography of the crude material (pentanes/Et₂O, 4:1) gave product **22** as a colorless oil (130 mg, 80%). $[\alpha]_D^{20} = -307$ ($c = 0.4$, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): $\delta = 5.66$ -5.63 (m, 1H), 5.60-5.57 (m, 1H), 3.91-3.86 (m, 1H), 3.73 (s, 3H), 3.53-3.48 (m, 1H), 2.21 (s, 3H), 2.78-2.69 (m, 1H), 2.49-2.43 (m, 1H), 1.76 ppm (d, $J = 2.5$ Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 175.5$, 131.0, 128.8, 80.8, 76.8, 61.6, 47.2, 39.9, 36.8, 32.3, 3.5 ppm; IR (film): $\tilde{\nu} = 2941$ (w), 2919 (w), 1656 (s), 1443 (m), 1416 (m), 1384 (s), 1342 (m), 1310 (m), 1176 (m), 1102 (m), 1005 (s), 945 (m), 809 (w) cm⁻¹; MS (EI): m/z (%): 193 (7) [M]⁺, 178 (<1), 162 (23), 147 (1), 133 (30), 121 (3), 105 (100), 91 (2), 79 (41), 65 (6), 58 (6), 51 (10), 39 (11), 27 (9); HRMS (EI): m/z : calcd. for C₁₁H₁₅NO₂: 193.1102 [M]⁺; found: 193.1103.

Preparation of the Common Intermediate **22** – Catalytic Route

Pinacol Boronate 30c. Pinacol borane (16 mL, 110 mmol) was slowly added to phenylacetylene (12.8 mL, 122 mmol) and the resulting mixture was stirred at 140°C for 5 d. After reaching ambient temperature, the product was purified by distillation (72-74°C, 10⁻³ mbar) to give boronate **30c** as a colorless oil, which crystallized upon storage in the freezer (22.6 g, 89%). ¹H NMR (400 MHz, CDCl₃): $\delta = 7.48$ -7.50 (m, 2H), 7.40 (d, $J = 18.4$ Hz, 1H), 7.27-7.36 (m, 3H), 6.18 (d, $J = 18.4$ Hz, 1H), 1.32 ppm (s, 12H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 149.5$, 137.4, 128.9, 128.5, 127.0, 83.3, 24.8 ppm; ¹¹B NMR (128 MHz, CDCl₃): $\delta = 31.0$ ppm; IR (film): $\tilde{\nu} = 3022$ (w), 2977 (m), 2931 (w), 1620 (s), 1575 (m), 1494 (m), 1448 (m), 1385 (m), 1347 (s), 1319 (s), 1269 (w), 1208 (s), 1163 (w), 1140 (s), 1107 (w), 1072 (w), 996 (m), 968 (m), 849 (m), 746 (s), 690 (s) cm⁻¹; MS (EI): m/z (%): 230 (89) [M]⁺, 215 (31), 202 (1), 187 (10), 172 (10), 157 (11), 144 (100), 130 (91), 118 (14), 105 (22), 85 (8), 77 (13), 71 (2), 59 (6), 43 (16), 29 (3); HRMS (EI): m/z : calcd. for C₁₄H₁₉O₂B: 230.1478 [M]⁺; found: 230.1480.

Compound 31c. Diene **35** (15 mg, 57 μ mol)⁴ and aq. KOH (1.5 M, 570 μ L) were successively added to a solution of [Rh(C₂H₄)Cl]₂ (10 mg, 26 μ mol) in 1,4-dioxane (10 mL) and the resulting mixture was stirred for 15 min before pinacol boronate **30c** (790 mg, 3.4 mmol) and 2[5H]-furanone **29** (140 mg, 1.7 mmol) and a catalytic amount of SiO₂ were introduced. The mixture was stirred for 3 d at ambient temperature before all volatile materials were evaporated. The residue was purified by flash chromatography (pentanes/Et₂O, 1:1) to give compound **31c** as a colorless syrup, which solidified upon standing (170 mg, 52%, 80% *ee*, $[\alpha]_D^{20} = +19$ ($c = 0.1$, CH₂Cl₂)). Recrystallization from pentanes/CH₂Cl₂ increased the *ee* to 93% (140 mg) (GC: 25 m Hydrodex-B column, $\varnothing$ 0.25 mm, 230/200 50 min iso 8/min 230 5 min iso/350; 0.5 bar H₂, FID detector, $R_t = 43.9$ min, R_t (enantiomer) = 45.2 min). ¹H NMR (400 MHz, CDCl₃): $\delta = 7.24$ -7.37 (m, 5H), 6.53 (d, $J = 15.9$ Hz, 1H), 6.11 (dd, $J = 15.7$, 8.1 Hz, 1H), 4.51 (dd, $J = 8.8$, 7.8 Hz, 1H), 4.10 (dd, $J = 9.0$, 8.2 Hz, 1H), 3.35-3.46 (m, 1H), 2.76 (dd, $J = 17.4$, 8.3 Hz, 1H), 2.48 ppm (dd, $J = 17.4$, 9.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 176.4$, 136.1, 132.7, 128.7, 128.0, 126.9, 126.3, 72.5, 39.5, 34.7 ppm; IR (film): $\tilde{\nu} = 1773$ (s), 1760 (s), 1493 (w), 1478 (w), 1450 (w), 1417 (w), 1356 (w), 1273 (w), 1221 (w), 1178 (s), 1163 (m), 1042 (w), 1004 (m), 976 (m), 889 (w), 838 (w) cm⁻¹; MS (EI): m/z (%): 188 (50) [M]⁺, 141 (1), 130 (100), 115 (27), 104 (6), 91 (7), 77 (6), 71 (3), 64 (12), 51 (9), 39 (5), 27 (2); HRMS (EI): m/z : calcd. for C₁₂H₁₂O₂: 188.0837

⁴ Defieber, C.; Paquin, J.-F.; Serna, S.; Carreira, E. M. *Org. Lett.* **2004**, *6*, 3873.

[M]⁺; found: 188.0838. The enantiomer of this compound is known in the literature [*ent*-**31c**, *ee* = 91%, $[\alpha]_D^{23} = -33.9$ (*c* = 1.0, CHCl₃)].⁵

Compound 32. *n*BuLi (1.6 M in heptanes, 200 μ L, 0.32 mmol) was added to a solution of *i*Pr₂NH (49 μ L, 0.35 mmol) in THF (8 mL) at -78°C and the resulting mixture was stirred at 0°C for 30 min. After cooling to -78°C , a solution of compound **31c** (60 mg, 0.32 mmol) in THF (6 mL) was introduced and stirring continued at this temperature for 30 min prior to the addition of allyl iodide (35 μ L, 0.38 mmol). After an additional 45 min, the reaction was quenched with aq. sat. NaHCO₃ (5 mL), the aqueous phase was extracted with Et₂O, the combined organic layers were dried over Na₂SO₄ and evaporated, and the residue was purified by flash chromatography (pentanes/Et₂O, 10:1) to give product **32** as a colorless oil (63 mg, 87%). $[\alpha]_D^{20} = +56$ (*c* = 0.05, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 7.38-7.25 (m, 5H), 6.52 (d, *J* = 15.7 Hz, 1H), 6.03 (dd, *J* = 15.9, 8.6 Hz, 1H), 5.87-5.77 (m, 1H), 5.19-5.12 (m, 2H), 4.42 (dd, *J* = 9.1, 8.1 Hz, 1H), 3.99 (dd, *J* = 9.9, 9.1 Hz, 1H), 3.21-3.11 (m, 1H), 2.58-2.47 ppm (m, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 177.5, 136.1, 133.9, 133.8, 128.7, 128.1, 126.3, 126.2, 118.5, 70.2, 45.1, 44.6, 32.1 ppm; IR (film): $\tilde{\nu}$ = 3078 (w), 3027 (w), 2984 (w), 2907 (w), 1769 (s), 1641 (w), 1495 (w), 1352 (w), 1160 (m), 1013 (s), 966 (m), 748 (m) cm⁻¹; MS (EI): *m/z* (%): 228 (56) [M]⁺, 186 (85), 170 (28), 155 (28), 141 (99), 129 (100), 115 (54), 104 (57), 91 (62), 79 (42), 66 (14), 51 (15), 39 (23); HRMS (EI): *m/z*: calcd. for C₁₅H₁₆O₂ [M]⁺ 228.1150, found: 228.1152.

Compound 18. Me₃Al (2 M in heptanes, 329 μ L, 0.66 mmol) was added to a solution of *N,O*-dimethylhydroxylamine hydrochloride (64 mg, 0.66 mmol) in CH₂Cl₂ (2 mL) at 0°C and the resulting mixture was warmed to ambient temperature and stirred for 2 h. A solution of compound **32** (60 mg, 0.26 mmol) in CH₂Cl₂ (2 mL) was introduced at 0°C and stirring continued at this temperature for 2 h before the reaction was quenched by careful addition of aq. H₂SO₄ (3 mL, 10% v/v). The aqueous phase was washed with CH₂Cl₂ (3 x 4 mL), the combined organic layers were dried over Na₂SO₄ and evaporated. The residue was rapidly passed through a short pad of silica, eluting with hexanes/EtOAc (1:2). Product **33** thus obtained was immediately dissolved in CH₂Cl₂ (10 mL), the indenylidene metathesis catalyst **17** (19 mg, 0.02 mmol, 8 mol%) was added and the resulting mixture stirred overnight at ambient temperature. For work up, the solvent was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 1:2) to give product **18** as a yellow syrup (36 mg, 75% for two steps). The analytical and spectral data were identical to those reported above for the material derived from the auxiliary-based route.

Total Synthesis of Hybridalactone

2,3-Dibromopentanoic acid.⁶ Bromine (16.5 g, 103 mmol) was added at 0°C to a solution of 2E-pentenoic acid (10 g, 100 mmol) in CH₂Cl₂ (200 mL). Once the addition was complete, the mixture was stirred at ambient temperature for 3 h before all volatile materials were evaporated. The resulting product was used in the next step without further purification (25.5 g, 98%). ¹H NMR (400 MHz, CDCl₃): δ = 10.61 (br s, 1H), 4.45 (d, *J* = 11.1 Hz, 1H), 4.36 (ddd, *J* = 11.1, 8.2, 2.7 Hz, 1H), 2.31 (ddq, *J* = 14.6, 7.4, 2.6 Hz, 1H), 1.90 (ddq, *J* = 15.2, 7.4, 7.3 Hz, 1H), 1.11 (t, *J* = 7.2 Hz, 3H) ppm;

⁵ Kim, S.-G. *Tetrahedron Lett.* **2008**, 49, 6148.

⁶ Mori, K.; Brevet, J.-L. *Synthesis*, **1991**, 1125.

^{13}C NMR (100 MHz, CDCl_3): δ = 173.4, 53.3, 46.8, 28.3, 10.5 ppm; IR (film): $\tilde{\nu}$ = 3019, 2919, 1704, 1434, 1291, 1238, 1154, 909, 744, 694 cm^{-1} ; HRMS (CI, *i*-butane): m/z : calcd. for $\text{C}_5\text{H}_9\text{O}_2\text{Br}_2$ 258.8969 $[\text{M}+\text{H}]^+$, found: 258.8966.

Bromide 25.⁶ A solution of dibromopentanoic acid (18 g, 70 mmol) in DMF (15 mL) was added over the course of 1 h to a suspension of NaHCO_3 (10 g, 118 mmol, 1.7 eq.) in DMF (30 mL), which was stirred at 70°C under vacuum (ca. 130 mbar). Under these conditions, the volatile bromide **25** distilled off and was collected in a cold trap (−78°C). The collected material was washed with a minimum amount of water (ca. 150 μL /1 mL of product) and dried over Na_2SO_4 to give product **25** as a colorless liquid (8.2 g, 87%, *Z:E* > 96:4, GC). ^1H NMR (400 MHz, CDCl_3): δ = 6.13–6.06 (m, 2H), 2.25–2.17 (m, 2H), 1.02 (t, J = 7.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 136.4, 107.0, 23.2, 12.6 ppm; IR (film): $\tilde{\nu}$ = 2970, 2936, 1686, 1623, 1460, 1333, 1284, 1071, 886 cm^{-1} .

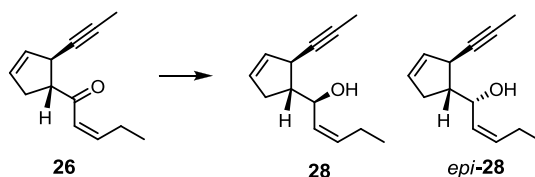
Compound 26. A solution of (*Z*)-1-bromo-1-butene (**25**, 1.35 g, 10 mmol) in Et_2O (4 mL) was added dropwise over 10 min to a suspension of lithium sand (0.31 g, 45 mmol) in Et_2O (8 mL) at −50°C. The resulting mixture was stirred at this temperature for 20 min before it was warmed to −40°C and stirred for additional 1 h. The mixture was then allowed to reach ambient temperature, before unreacted lithium was filtered off through a short pad of dried Celite and the resulting filtrate was immediately used in the next step.

A solution of (*Z*)-1-butenyllithium (ca. 0.8 M in Et_2O , 1.5 mL, 1.2 mmol) prepared as described above was slowly added to a solution of Weinreb amide **22** (0.19 g, 4.0 mmol) in Et_2O (4 mL) at 0°C and the resulting mixture stirred at 0°C for 1 h. The reaction was quenched with aq. sat. NH_4Cl and the product extracted with Et_2O . The combined organic layers were dried over Na_2SO_4 and evaporated. Purification of the residue by flash chromatography (hexane/ EtOAc , 40:1) provided product **26** as a pale yellow oil (0.16 g, 83%). $[\alpha]_D^{20}$ = −366 (c = 0.10, CH_2Cl_2); ^1H NMR (400 MHz, C_6D_6): δ = 6.02 (dt, J = 11.3, 1.7 Hz, 1H), 5.75 (dt, J = 11.4, 7.5 Hz, 1H), 5.54 (dq, J = 5.6, 2.3 Hz, 1H), 5.36 (dq, J = 5.5, 2.5 Hz, 1H), 4.03 (dqi, J = 9.5, 2.4 Hz, 1H), 3.29 (dt, J = 9.6, 6.9 Hz, 1H), 2.66 (dtd, J = 7.5, 7.5, 1.7 Hz, 2H), 2.59 (ddq, J = 16.7, 7.1, 2.4 Hz, 1H), 2.37 (ddq, J = 16.7, 9.8, 2.3 Hz, 1H), 1.51 (d, J = 2.3 Hz, 3H), 0.84 (t, J = 7.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 199.3, 150.8, 131.2, 129.0, 125.8, 81.5, 76.8, 58.8, 39.0, 34.9, 23.4, 13.7, 3.5 ppm; IR (film): $\tilde{\nu}$ = 3063, 3018, 2966, 2919, 2855, 1689, 1614, 1460, 1445, 1417, 1322, 1270, 1204, 1099, 1048, 1004, 943, 833, 811, 710 cm^{-1} ; MS (EI): m/z (%): 188 (13) $[\text{M}]^+$, 173 (21), 159 (27), 145 (17), 131 (47), 117 (13), 105 (21), 91 (16), 83 (100), 77 (20), 65 (6), 55 (29), 39 (12), 29 (11); HRMS (EI): m/z : calcd. for $\text{C}_{13}\text{H}_{16}\text{O}$: 188.1201 $[\text{M}]^+$; found: 188.1202.

Compound 28. EtOH (0.12 mL, 2.0 mmol) was added dropwise to a solution of LiAlH_4 (2.0 M in THF, 1.0 mL, 2.0 mmol) in THF (1 mL) and the resulting mixture was stirred for 10 min before a solution of (*R*)-1,1'-bi-2-naphthol (0.57 g, 2.0 mmol) in THF (3 mL) was added dropwise at 0°C. Stirring was continued for 30 min at room temperature before the solution was cooled to −78°C. This cold mixture was then added via canula to a cold (−78°C) solution of enone **26** (0.11 g, 0.60 mmol) in THF (4 mL). After stirring at −78°C for 72 h, MeOH was added and the mixture allowed to reach ambient temperature. Aq. sat. NH_4Cl and aq. HCl (1 M) were then added, the product was extracted with Et_2O , the combined organic layers were dried over Na_2SO_4 and evaporated. Purification of the residue by flash chromatography (hexane/ EtOAc , 10:1) afforded product **28** as a pale yellow oil (0.10 g, 90%, dr >10 : 1). $[\alpha]_D^{20}$ = −175 (c = 0.05, CH_2Cl_2); ^1H NMR (400 MHz, C_6D_6): δ = 5.68 (dq, J = 5.6, 2.1 Hz, 1H), 5.51 (dq, J = 5.5, 2.5 Hz, 1H), 5.37–5.29 (m, 2H), 4.33–4.28 (m, 1H), 3.65–3.59 (m, 1H), 2.64–2.54 (m, 1H), 2.36 (ddq, J = 16.5, 8.9, 2.3 Hz, 1H), 2.01 (ddq, J = 16.5, 6.8, 2.3 Hz, 1H), 1.96–1.83 (m, 2H), 1.54

(d, $J = 2.4$ Hz, 3H), 1.24 (br s, 1H), 0.81 (t, $J = 7.4$ Hz, 3H) ppm; ^{13}C NMR (100 MHz, C_6D_6): $\delta = 134.7$, 134.6, 132.2, 131.2, 82.5, 76.8, 70.3, 53.2, 39.3, 35.1, 21.7, 14.7, 3.8 ppm; IR (film): $\tilde{\nu} = 3363$, 3060, 3007, 2963, 2919, 2856, 1445, 1287, 1068, 1032, 937, 752, 716 cm^{-1} ; MS (EI): m/z (%): 189 (< 1), 172 (11), 157 (26), 143 (40), 128 (24), 115 (12), 104 (100), 91 (43), 85 (25), 77 (25), 67 (14), 57 (22), 41 (25), 19 (16); HRMS (CI, *i*-butane): calcd for $\text{C}_{13}\text{H}_{19}\text{O}$: 191.1436 $[\text{M}+\text{H}]^+$; found: 191.1437.

Table S1. Reduction of ketone **26** with various reducing agents.^[a]



Entry	Conditions	Yield	28 : epi-28
1	L-selectride, THF, -78°C	31%	1:0
2	K-selectride, THF, -78°C	[b]	
3	LiHBEt_3 , THF, -78°C	65%	5:1
4	$\text{BH}_3\cdot\text{THF}$, (<i>R</i>)-Me-CBS ^[c]	67%	1:7
5	$\text{BH}_3\cdot\text{THF}$, (<i>S</i>)-Me-CBS ^[c]	n.d.	1:2.5
6	Dibal-H, THF, -78°C	n.d.	1:1
7	Dibal-H, <i>n</i> -BuLi, THF/hexane, -78°C ^[d]	77%	4:1
8	Dibal-H, <i>sec</i> -BuLi, THF/hexane, -78°C	65%	5:1
9	Dibal-H, <i>tert</i> -BuLi, THF/hexane, -78°C	61%	5:1
10	Dibal-H, <i>tert</i> -BuOLi, THF, -78°C	n.d.	2:1
11	Red-Al, THF, -78°C	n.d.	3:1
12	LiAlH_4 , THF, -78°C	n.d.	2:1
13	LiAlH_4 , <i>S</i> -BINOL, EtOH, THF, -78°C	n.d.	2:1
14	LiAlH_4 , <i>R</i> -BINOL, EtOH, THF, -78°C	90%	>10:1

^[a] The use of *S*-Alpine hydride, *S*-Alpine borane, $\text{KHB}(\text{O}i\text{Pr})_3$, Luche conditions (NaBH_4 , CeCl_3) afforded only complex mixtures; ^[b] 1,4-reduction only; ^[c] Me-CBS refers to *B*-methyl oxazaborolidine derived from 1,1-diphenylpyrrolidinomethanol, cf. ref. 7; ^[d] see ref. 8

Compound 36. CH_2I_2 (32 μL , 0.40 mmol) was added dropwise to a solution of Et_2Zn (1.0 M in hexane, 0.20 mL, 0.20 mmol) in CH_2Cl_2 (1 mL) at -10°C . After stirring for 15 min, the mixture was cooled to -30°C and a solution of alcohol **28** (19.0 mg, 0.10 mmol) in CH_2Cl_2 (1 mL) was introduced. The resulting mixture was stirred at -20°C for 16 h before the reaction was quenched with aq. sat. NH_4Cl

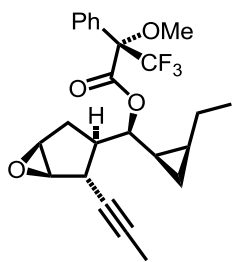
⁷ Corey, E. J.; Helal, C. J. *Angew. Chem., Int. Ed.* **1998**, 37, 1986.

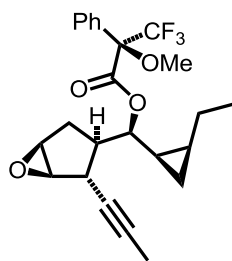
⁸ Kim, S.; Ahn, K. H. *J. Org. Chem.* **1984**, 49, 1717.

and the product extracted with Et₂O. The combined organic layers were dried over Na₂SO₄. Evaporation of the solvent followed by purification of the residue by flash chromatography (hexane/EtOAc, 10:1) provided product **36** as a colorless oil (13.3 mg, 65%). $[\alpha]_D^{20} = -141$ ($c = 0.27$, CH₂Cl₂); ¹H NMR (400 MHz, C₆D₆): $\delta = 5.73$ (dq, $J = 5.7, 2.2$ Hz, 1H), 5.59 (dq, $J = 5.7, 2.4$ Hz, 1H), 3.80 (m, 1H), 3.15 (dd, $J = 9.0, 4.9$ Hz, 1H), 2.69 (dtd, $J = 8.9, 7.5, 4.9$ Hz, 1H), 2.41 (ddq, $J = 16.3, 7.4, 2.5$ Hz, 1H), 2.31 (ddq, $J = 16.3, 7.5, 2.4$ Hz, 1H), 1.56 (d, $J = 2.4$ Hz, 3H), 1.48-1.38 (m, 1H), 1.15 (br s, 1H), 1.00 (tdd, $J = 8.7, 8.7, 5.6$ Hz, 1H), 0.94 (t, $J = 6.7$ Hz, 3H), 0.93-0.83 (m, 1H), 0.70-0.60 (m, 1H), 0.47 (td, $J = 8.4, 4.4$ Hz, 1H), -0.18 (dtd, $J = 5.5, 5.4, 1.3$ Hz, 1H) ppm; ¹³C NMR (100 MHz, C₆D₆): $\delta = 132.2, 130.2, 82.9, 76.1, 73.0, 53.3, 37.5, 35.3, 22.7, 22.3, 19.4, 14.5, 9.0, 3.5$ ppm; IR (film): $\tilde{\nu} = 3404, 2960, 2920, 2205, 2162, 2153, 2019, 1963, 1455, 1031, 714$ cm⁻¹; MS (EI): m/z (%): 203 (2), 186 (12), 171 (21), 157 (31), 143 (38), 129 (45), 117 (99.7), 104 (71), 99 (23), 91 (58), 77 (32), 65 (13), 57 (100), 41 (24), 29 (13); HRMS (CI, *i*-butane): calcd for C₁₄H₂₁O: 205.1592 [M+H]⁺; found: 205.1590.

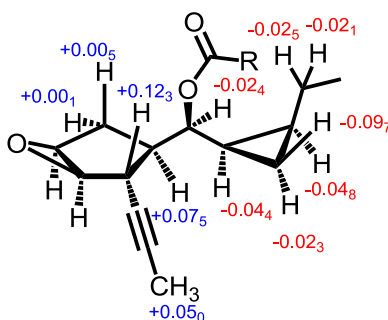
Compound 38. A solution of compound **36** (9.9 mg, 0.048 mmol) in CH₂Cl₂ (2 mL) was added to a reaction flask containing powdered activated MS 3Å. After stirring for 10 min, a stock solution of VO(acac)₂ (0.02 M in CH₂Cl₂, 0.24 mL, 4.8 μmol) was introduced and the resulting mixture stirred for 5 min before it was cooled to 0°C. A solution of *t*BuOOH (ca. 5.5 M in decane, 27 μL, 0.15 mmol) in CH₂Cl₂ (1 mL) was added dropwise and the resulting mixture stirred at ambient temperature for 2.5 h. At this point, a second portion of the stock solution of VO(acac)₂ (0.02 M in CH₂Cl₂, 0.12 mL, 2.4 μmol) was added and stirring continued at room temperature for another 2.5 h before the reaction was quenched with aq. sat. Na₂S₂O₃. Extraction with CH₂Cl₂, evaporation of the solvent and purification of the residue by flash chromatography (hexane/EtOAc, 5:1) furnished product **38** (7.4 mg, 69%) as a colorless oil. $[\alpha]_D^{20} = -97$ ($c = 0.16$, CH₂Cl₂); ¹H NMR (600 MHz, C₆D₆): $\delta = 3.53$ (dq, $J = \Sigma 4.4$ Hz, 1H), 3.38 (d, $J = 2.6$ Hz, 1H), 3.15 (dd, $J = 8.3, 5.9$ Hz, 1H), 3.06 (m, 1H), 2.57 (br s, 1H), 2.46 (dddd, $J = 9.0, 5.8, 3.1, 1.7$ Hz, 1H), 1.85 (ddd, $J = 14.8, 9.0, 1.4$ Hz, 1H), 1.82 (ddd, $J = 14.8, 3.1, -0.6$ Hz, 1H), 1.54 (m, 1H), 1.48 (d, $J = 2.6$ Hz, 3H), 1.02 (m, 1H), 0.95 (t, $J = 7.1$ Hz, 3H), 0.69 (qd, $J = 8.5, 5.5$ Hz, 1H), 0.57 (m, 1H), 0.52 (tdd, $J = 8.4, 4.2, 0.9$ Hz, 1H), 0.01 (td, $J = 5.5, 4.2$ Hz, 1H) ppm; ¹³C NMR (150 MHz, C₆D₆): $\delta = 79.1$ (s), 78.3 (s), 73.6 (d, ¹*J*_{CH} = 144 Hz), 61.2 (d, ¹*J*_{CH} = 188 Hz), 58.3 (d, ¹*J*_{CH} = 185 Hz), 52.1 (d, ¹*J*_{CH} = 134 Hz), 33.0 (d, ¹*J*_{CH} = 138 Hz), 30.8 (t, ¹*J*_{CH} = 130 Hz), 23.1 (d, ¹*J*_{CH} = 156 Hz), 22.8 (t, ¹*J*_{CH} = 126 Hz), 18.9 (d, ¹*J*_{CH} = 157 Hz), 14.6 (q, ¹*J*_{CH} = 126 Hz), 8.7 (t, ¹*J*_{CH} = 159 Hz), 3.4 ppm (q, ¹*J*_{CH} = 131 Hz); IR (film): $\tilde{\nu} = 3452, 2960, 2921, 2366, 2140, 2036, 1983, 1029, 840$ cm⁻¹; MS (EI): m/z (%): 220 (< 1) [M]⁺, 203 (3), 191 (2), 173 (2), 164 (10), 147 (4), 121 (13), 99 (57), 91 (27), 79 (40), 66 (10), 57 (100), 41 (23), 29 (12); HRMS (ESI): calcd for C₁₄H₂₀O₂Na: 243.1355 [M+Na]⁺; found: 243.1354.

(S)-Mosher ester derived from 38. ¹H NMR (600 MHz, C₆D₆): $\delta = 7.89$ (d, $J = 7.8$ Hz, 2H), 7.19 (m, 2H), 7.10 (t, $J = 7.4$ Hz, 1H), 5.05 (t, $J = 10.0$ Hz, 1H), 3.62 (q, $J_{\text{HF}} = 1.0$ Hz, 3H), 3.29 (d, $J = 2.5$ Hz, 1H), 3.03 (m, 1H), 3.02 (m, 1H), 2.52 (t, $J = 10.0$ Hz, 1H), 1.95 (d, $J = 15.0$ Hz, 1H), 1.69 (ddd, $J = 14.9, 10.0, 1.2$ Hz, 1H), 1.66 (m, 1H), 1.45 (d, $J = 2.5$ Hz, 3H), 1.15 (m, 1H), 0.92 (t, $J = 7.3$ Hz, 3H), 0.55 (m, 1H), 0.54 (m, 1H), 0.42 (tdd, $J = 8.4, 4.6, 0.7$ Hz, 1H), 0.19 (td, $J = 5.8, 4.6$ Hz, 1H) ppm; ¹³C NMR (150 MHz, C₆D₆): $\delta = 166.5, 133.2, 129.5, 128.5, 128.1, 124.4$ (q, $J_{\text{CF}} = 288.5$ Hz), 85.2 (q, $J_{\text{CF}} = 27.5$ Hz), 82.9, 78.9, 77.8, 60.0, 57.1, 55.5 (q, $J_{\text{CF}} = 1.1$ Hz), 49.5, 34.9, 28.8, 23.6, 21.0, 20.6, 14.3, 9.6, 3.3 ppm.





(R)-Mosher ester derived from 38. ^1H NMR (600 MHz, C_6D_6): δ = 7.85 (d, J = 7.7 Hz, 2H), 7.14 (m, 2H), 7.08 (t, J = 7.4 Hz, 1H), 5.08 (t, J = 10.1 Hz, 1H), 3.56 (q, J_{HF} = 1.0 Hz, 3H), 3.33 (d, J = 2.5 Hz, 1H), 3.05 (d, J = 2.2 Hz, 1H), 2.90 (m, 1H), 2.44 (t, J = 10.0 Hz, 1H), 1.95 (d, J = 14.9 Hz, 1H), 1.69 (ddd, J = 14.9, 10.0, 1.1 Hz, 1H), 1.68 (m, 1H), 1.40 (d, J = 2.5 Hz, 3H), 1.17 (m, 1H), 0.91 (t, J = 7.3 Hz, 3H), 0.60 (m, 1H), 0.59 (m, 1H), 0.44 (tdd, J = 8.4, 4.4, 0.7 Hz, 1H), 0.29 (td, J = 5.8, 4.4 Hz, 1H) ppm; ^{13}C NMR (150 MHz, C_6D_6): δ = 166.6, 133.4, 129.4, 128.5, 127.8, 124.4 (q, J_{CF} = 288.5 Hz), 84.9 (q, J_{CF} = 27.5 Hz), 82.4, 78.5, 77.6, 59.9, 57.1, 55.5 (q, J_{CF} = 1.2 Hz), 49.5, 34.5, 28.6, 23.6, 21.3, 20.9, 14.2, 9.7, 3.3 ppm.



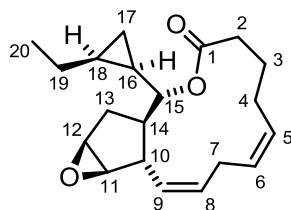
Scheme S2. Analysis [$\Delta\delta_{(S)-(R)}$] of the Mosher Esters derived from **38**.

Compound 41. Carbodiimide *p*-toluenesulfonate **39** (72.0 mg, 0.17 mmol) was added to a solution of (Z)-5-decen-8-ynoic acid **40** (23.3 mg, 0.14 mmol) in CH_2Cl_2 (0.5 mL) and the resulting mixture stirred for 1.5 h before a solution of compound **38** (9.8 mg, 0.044 mmol) in CH_2Cl_2 (0.5 mL) and a catalytic amount of DMAP were added. After stirring for 7 d, the precipitate was filtered off through a pad of silica, the filtrate was evaporated and the residue purified by flash chromatography (hexane/EtOAc, 10:1) to give product **41** (12.6 mg, 77%) as a colorless oil. $[\alpha]_D^{20}$ = -68 (c = 0.43, CH_2Cl_2); ^1H NMR (600 MHz, CDCl_3): δ = 5.47-5.36 (m, 2H), 4.57 (t, J = 9.8 Hz, 1H), 3.48 (m, 1H), 3.45 (d, J = 2.5 Hz, 1H), 2.87 (m, 2H), 2.75 (dq, J = Σ 4.5 Hz, 1H), 2.40 (tt, J = 9.7, 1.9 Hz, 1H), 2.32 (t, J = 7.5 Hz, 2H), 2.15 (dd, J = 14.9, 2.0 Hz, 1H), 2.09 (q, J = 7.1 Hz, 2H), 2.05 (ddd, J = 14.9, 9.8, 1.4 Hz, 1H), 1.77 (d, J = 2.5 Hz, 3H), 1.76 (t, J = 2.6 Hz, 3H), 1.70 (qi, J = 7.5 Hz, 2H), 1.66 (m, 1H), 1.09 (m, 1H), 0.99 (t, J = 7.2 Hz, 3H), 0.86 (m, 1H), 0.80 (dtd, J = 10.0, 8.6, 5.6 Hz, 1H), 0.56 (tdd, J = 8.5, 4.5, 0.6 Hz, 1H), 0.05 (td, J = 5.7, 4.7 Hz, 1H) ppm; ^{13}C NMR (150 MHz, CDCl_3): δ = 173.5 (s), 130.1 (d, $^1J_{\text{CH}}$ = 154 Hz), 125.8 (d, $^1J_{\text{CH}}$ = 155 Hz), 78.5 (s), 78.0 (d, $^1J_{\text{CH}}$ = 152 Hz), 77.9 (s), 77.4 (s), 75.4 (s), 60.5 (d, $^1J_{\text{CH}}$ = 189 Hz), 57.8 (d, $^1J_{\text{CH}}$ = 185 Hz), 50.0 (d, $^1J_{\text{CH}}$ = 135 Hz), 34.1 (t, $^1J_{\text{CH}}$ = 128 Hz), 33.8 (d, $^1J_{\text{CH}}$ = 138 Hz), 28.7 (t, $^1J_{\text{CH}}$ = 130 Hz), 26.5 (t, $^1J_{\text{CH}}$ = 126 Hz), 24.8 (t, $^1J_{\text{CH}}$ = 129 Hz), 23.1 (t, $^1J_{\text{CH}}$ = 125 Hz), 21.1 (d, $^1J_{\text{CH}}$ = 158 Hz), 20.2 (d, $^1J_{\text{CH}}$ = 157 Hz), 17.1 (t, $^1J_{\text{CH}}$ = 130 Hz), 14.2 (q, $^1J_{\text{CH}}$ = 125 Hz), 8.7 (t, $^1J_{\text{CH}}$ = 160 Hz), 3.6 (q, $^1J_{\text{CH}}$ = 131 Hz), 3.5 ppm (q, $^1J_{\text{CH}}$ = 131 Hz); IR (film): $\tilde{\nu}$ = 2923, 2358, 2337, 2178, 1728, 1155, 1035, 844 cm^{-1} ; MS (EI): m/z (%): 368 (< 1) $[\text{M}]^+$, 339 (< 1), 229 (1), 225 (< 1), 203 (15), 159 (6), 149 (18), 105 (100), 91 (22), 79 (26), 55 (19), 41 (12); HRMS (ESI): calcd for $\text{C}_{24}\text{H}_{32}\text{O}_3\text{Na}$: 391.2244 $[\text{M}+\text{Na}]^+$; found: 391.2246.

Compound 42. Diyne **41** (9.6 mg, 0.026 mmol) was dissolved in toluene (13 mL) and powdered, activated MS $5\text{\AA}$ (0.15 g) was added. The suspension was stirred for 15 min before a stock solution of complex **43b** (0.01 M in toluene, 0.39 mL, 3.9 μmol) was added and the resulting mixture stirred at

70°C for 24 h. After reaching ambient temperature, the suspension was filtered through a pad of silica, the filtrate was evaporated, and the residue purified by flash chromatography (hexanes/EtOAc, 10:1) to afford product **42** as a colorless oil (6.5 mg, 79%). $[\alpha]_D^{20} = -29$ ($c = 0.32$, CH_2Cl_2); ^1H NMR (600 MHz, C_6D_6): $\delta = 5.29$ (dddt, $J = 10.9, 6.0, 5.4, 1.4$ Hz, 1H), 5.24 (dddt, $J = 10.9, 7.9, 7.0, 1.4$ Hz, 1H), 4.42 (t, $J = 10.0$ Hz, 1H), 3.38 (d, $J = 2.5$ Hz, 1H), 3.23 (ddd, $J = 6.4, 2.8, 2.0$ Hz, 1H), 3.05 (t, $J = 2.4$ Hz, 1H), 3.03 (tt, $J = 10.3, 7.3$ Hz, 1H), 2.72 (ddd, $J = 18.7, 6.0, 3.1$ Hz, 1H), 2.64 (m, 1H), 2.62 (m, 1H), 2.36 (m, 1H), 2.30 (ddd, $J = 15.8, 8.8, 2.8$ Hz, 1H), 2.25 (ddd, $J = 15.8, 8.2, 2.8$ Hz, 1H), 1.71 (m, 1H), 1.65 (ddd, $J = 14.7, 10.2, 2.3$ Hz, 1H), 1.62 (dd, $J = 14.7, 7.7$ Hz, 1H), 1.61 (m, 1H), 1.45 (m, 1H), 0.90-0.82 (m, 5H), 0.57-0.49 (m, 2H), -0.04 (m, 1H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 172.4$ (s), 133.9 (d, $^1J_{\text{CH}} = 152$ Hz), 123.6 (d, $^1J_{\text{CH}} = 159$ Hz), 81.11 (s), 81.10 (s), 80.1 (d, $^1J_{\text{CH}} = 148$ Hz), 63.1 (d, $^1J_{\text{CH}} = 187$ Hz), 59.7 (d, $^1J_{\text{CH}} = 184$ Hz), 55.7 (d, $^1J_{\text{CH}} = 133$ Hz), 38.1 (d, $^1J_{\text{CH}} = 135$ Hz), 33.2 (d, $^1J_{\text{CH}} = 128$ Hz), 30.4 (t, $^1J_{\text{CH}} = 130$ Hz), 26.5 (t, $^1J_{\text{CH}} = 127$ Hz), 24.4 (t, $^1J_{\text{CH}} = 129$ Hz), 23.4 (t, $^1J_{\text{CH}} = 126$ Hz), 20.9 (d, $^1J_{\text{CH}} = 159$ Hz), 20.6 (d, $^1J_{\text{CH}} = 158$ Hz), 17.6 (t, $^1J_{\text{CH}} = 130$ Hz), 14.2 (q, $^1J_{\text{CH}} = 126$ Hz), 9.1 ppm (t, $^1J_{\text{CH}} = 160$ Hz); IR (film): $\tilde{\nu} = 2958, 2928, 2339, 2157, 2020, 1725, 1443, 1373, 1247, 1207, 1154, 1086, 1038, 938, 839, 798, 700$ cm^{-1} ; MS (EI): m/z (%): 314 (29) $[\text{M}]^+$, 299 (10), 285 (5), 267 (5), 245 (22), 227 (11), 216 (21), 198 (20), 155 (36), 143 (100), 129 (93), 105 (53), 91 (88), 79 (71), 67 (37), 55 (67), 41 (45); HRMS (ESI): calcd for $\text{C}_{20}\text{H}_{26}\text{O}_3\text{Na}$: 337.1774 $[\text{M}+\text{Na}]^+$; found: 337.1771.

Hybridalactone ((-)-1). $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ (84.6 mg, 0.34 mmol) was dissolved to EtOH (10 mL). NaBH_4 (12.7 mg, 0.34 mmol) and ethylenediamine (33 μL , 0.50 mmol) were sequentially added, and H_2 was bubbled through the resulting black suspension for 15 min. An aliquot of the suspension (0.12 mL, ca. 4.1 μmol) was added to a solution of cycloalkyne **42** (4.5 mg, 0.014 mmol) in EtOH (3 mL) and the resulting mixture was stirred under H_2 (1 atm) for 3 h. The catalyst was filtered off and the filtrate was evaporated. Purification of the residue by flash chromatography (hexane/EtOAc, 10:1) provided the title compound as colorless oil (3.8 mg, 84%). $[\alpha]_D^{20} = -52$ ($c = 0.19$, MeOH); IR (film): $\tilde{\nu} = 2962, 2352, 1724, 1260, 1214, 1022, 840, 800$ cm^{-1} ; MS (EI): m/z (%) = 316 (9) $[\text{M}]^+$, 247 (10), 234 (8), 218 (30), 178 (13), 161 (11), 145 (19), 131 (56), 117 (99), 105 (54), 91 (83), 79 (100), 67 (64), 55 (87), 41 (76); HRMS (ESI $^+$): calcd for $\text{C}_{20}\text{H}_{28}\text{O}_3\text{Na}$: 339.1931 $[\text{M}+\text{Na}]^+$, found: 339.1929.

Table S2. Comparison of the recorded ^1H NMR data (CDCl_3) of hybridalactone (**1**) with those reported in the literature.⁹

position	δ_{H} (lit., 360 MHz) (mult., J in Hz)	δ_{H} (exp., 600 MHz) (mult., J in Hz)	$\Delta\delta$
2	2.38 (m)	2.343	0.04
	2.27 (ddd, 3, 7, 15)	2.24 (ddd, 15.5, 7.1, 2.9)	0.03
3	2.00 (m)	1.92 (m)	0.08
	1.51 (m)	1.47 (m)	0.04
4	2.37 (ddd, 3, 7.5, 15)	2.340	0.03
	2.00 (m)	1.97	0.03
5	5.27 (dd, 2, 4, 11, 11)	5.23 (tddd, 10.8, 3.8, 2.3, 1.0)	0.04
6	5.48 (tdd, 0.7, 4, 11, 11)	5.46 (tddd, 10.9, 4.3, 1.9, 0.8)	0.02
7	3.38 (td, 11, 11, 14)	3.35 (dt, 14.6, 11.2)	0.03
8	5.53 (tdd, 0.7, 4, 5, 11, 11)	5.50 (dddd, 11.4, 10.8, 4.5, 1.0)	0.03
9	5.07 (td, 2, 11, 11)	5.05 (tdd, 10.7, 2.2, 0.7)	0.02
10	2.97 (d, 11)	2.93 (d, 10.7)	0.04
11	3.19 (d, 2.5)	3.15 (d, 2.5)	0.04
12	3.51 (dd, 1, 2.5)	3.49 (m)	0.02
13	2.25 (d, 14)	2.22 (d, 13.7)	0.03
	2.00 (m)	1.97 (ddd, 13.8, 10.2, 1.4)	0.03
14	2.00 (m)	2.02 (t, 10.1)	-0.02
15	4.72 (t, 10)	4.70 (t, 10.1)	0.02
16	0.76 (tdd, 5.5, 8, 8, 10)	0.73 (dtd, 10.1, 8.5, 5.6)	0.03
17	0.57 (td, 5.5, 8, 8)	0.54 (tdd, 8.5, 4.6, 0.8)	0.03
	0.05 (q, 5.5, 5.5, 5.5)	0.02 (dt, 4.7, 5.7)	0.03
18	0.91 (m, 2.5, 4.5, 5.5, 8, 8)	0.87 (m)	0.04
19	1.75 (ddq, 4, 7, 13)	1.71 (ddq, 13.9, 4.1, 7.0)	0.04
	1.17 (ddq, 2.5, 7, 13)	1.13 (ddq, 13.9, 10.2, 7.2)	0.04
20	1.03 (t, 7)	1.01 (t, 7.3)	0.02

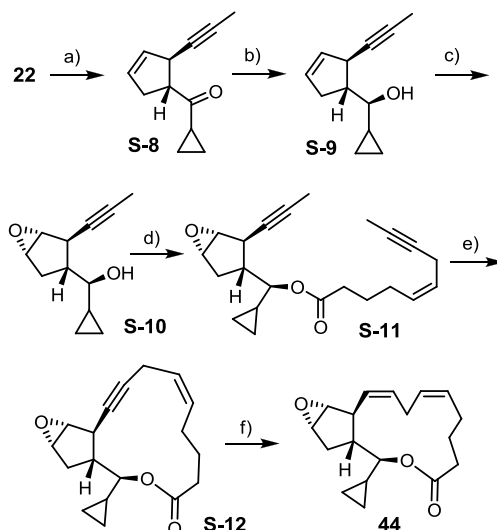
⁹ Higgs, M. D.; Mulheirn, L. J. *Tetrahedron* **1981**, 37, 4259.

Table S3. Comparison of the recorded ^{13}C NMR data (CDCl_3) of hybridalactone (**1**) with those reported in the literature.⁹

position	δ_{c} (lit., 90 MHz) (mult.)	δ_{c} (exp., 150 MHz) (mult., $^1J_{\text{CH}}$ in Hz)	$\Delta\delta$
1	176.1 (s)	173.2 (s)	2.9
2	32.7 (t)	32.7 (t, 128.5)	0.0
3	24.0 (t)	24.0 (t, 130)	0.0
4	25.7 (t)	25.7 (t, 126)	0.0
5	128.4 (d)	128.5 (d, 151)	-0.1
6	128.0 (d)	128.1 (d, 156)	-0.1
7	26.3 (t)	26.3 (t, 126.3)	0.0
8	128.9 (d)	129.0 (d, 154)	-0.1
9	126.9 (d)	127.0 (d, 153.5)	-0.1
10	41.6 (d)	41.5 (d, 132)	0.1
11	60.8 (d)	60.9 (d, 186)	-0.1
12	58.0 (d)	58.2 (d, 183.6)	-0.2
13	27.6 (t)	28.6 (dd, 133, 127)	-1.0
14	49.0 (d)	48.9 (d, 134)	0.1
15	78.8 (d)	78.9 (d, 152)	-0.1
16	21.1 (d)	21.2 (d, 156)	-0.1
17	8.4 (t)	8.5 (t, 156)	-0.1
18	20.4 (d)	20.4 (d, 156)	0.0
19	23.0 (t)	23.2 (t, 124)	-0.2
20	14.0 (q)	14.2 (q, 125)	-0.2

Synthesis of Des-Ethyl-Hybridalactone

Des-Ethyl-Hybridalactone. As an initial foray into the preparation of analogues, we targeted compound **44** differing from (–)-**1** only in the absence of the lateral ethyl substituent on the cyclopropyl unit. Whereas this formal deletion is thought to be a minor change in functional regard, it greatly simplifies the synthesis by avoiding the delicate stereoselective cyclopropanation (Scheme S3). Rather, it sufficed to react Weinreb amide **22** with cyclopropylmagnesium bromide and to reduce the resulting ketone **S-8** with L-selectride at low temperature to give the corresponding alcohol **S-9** as a single isomer. The rest of the synthesis follows the steps as outlined in the publication for hybridalactone itself. Although the steps were not optimized, the targeted compound **44** was obtained in respectable overall yield. Once again, the RCAM reaction was best performed with the modified catalyst **43b** endowed with tris-(*p*-methoxyphenyl)silanolate ligands.



Scheme S3. Reagents and conditions: a) cyclopropylmagnesium bromide, Et₂O/THF, 0°C, 90%; b) LiBH(*sec*-Bu)₃, THF, -78°C, 75%; c) *t*BuOOH, VO(acac)₂ (8 mol%), CH₂Cl₂, 0°C, 65%; d) acid **40**, **39**, DMAP cat., CH₂Cl₂, 68%; e) **43b** (4 mol%), MS 5Å, toluene, 72%; f) P2-Ni cat. [Ni(OAc)₂·4H₂O, NaBH₄, ethylenediamine], H₂ (1 atm), MeOH, 67%.

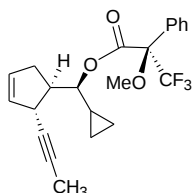
Compound S-8. Mg-turnings (530 mg, 22 mmol) were activated with a crystal of iodine before they were suspended in THF (35 mL). Cyclopropyl bromide (2.0 g, 17 mmol) was added at such a rate as to maintain gentle reflux. Once the reaction had ceased, the resulting solution of the Grignard reagent was syphoned off unreacted magnesium via canula.

An aliquot of this solution (~ 0.28 M in THF, 2 mL, 0.56 mmol) was then slowly added to a solution of compound **22** (108 mg, 0.56 mmol) in Et₂O (2 mL) at 0°C. After stirring for 1 h at this temperature, more of the Grignard solution was introduced (0.5 mL, 0.14 mmol) and stirring continued for another 30 min. The reaction was quenched with aq. sat. NaHCO₃, the resulting mixture was extracted with Et₂O, the combined ether layers were dried and evaporated, and the residue purified by flash chromatography (pentanes/Et₂O, 7:1) to give the title compound as a colorless oil (88 mg, 90%). $[\alpha]_D^{20} = -156$ (CH₂Cl₂, *c* = 1.4); ¹H NMR (400 MHz, CDCl₃): δ = 5.67 (dq, *J* = 5.5, 2.4 Hz, 1H), 5.57 (dq, *J* = 5.6, 2.2 Hz, 1H), 3.83-3.78 (m, 1H), 3.41 (dt, *J* = 9.6, 6.9 Hz, 1H), 2.73 (ddq, *J* = 16.7, 9.5, 2.4 Hz, 1H), 2.64 (ddq, *J* = 16.7, 7.1, 2.4 Hz, 1H), 2.07 (tt, *J* = 7.8, 4.6 Hz, 1H), 1.80 (d, *J* = 2.3 Hz, 3H), 1.08-1.04 (m, 2H), 0.94-0.89 (m, 2H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ = 210.4, 130.6, 129.1, 80.8, 76.8, 58.0, 38.5, 34.7, 19.6, 11.1, 11.0, 3.6 ppm; IR (film): $\tilde{\nu}$ = 3062, 3009, 2919, 2857, 1694, 1444, 1385, 1200, 1112, 1087, 1049, 937, 816, 713 cm⁻¹; MS (EI): *m/z* (%): 174 (7) [M]⁺, 159 (18), 146 (6), 131 (19), 117 (11), 105 (21), 91 (11), 77 (20), 69 (100), 51 (8), 41 (35), 39 (16); HRMS (EI): *m/z*: calcd. for C₁₂H₁₄O 174.1045 [M]⁺, found: 174.1046.

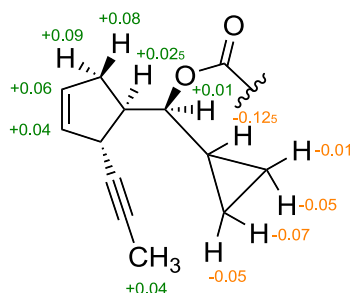
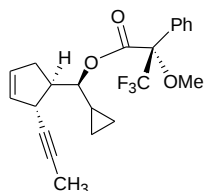
Compound S-9. L-Selectride (1 M in THF, 510 μL, 0.51 mmol) was slowly added to a solution of ketone **S-8** (80 mg, 0.46 mmol, 1.0 eq.) in THF (8 mL) at -78°C. After stirring for 1 h, more L-Selectride (230 μL, 0.5 eq.) was introduced and stirring continued for 30 min. The reaction was quenched with sat. aq. NH₄Cl while cold, the mixture allowed to reach ambient temperature, the aqueous layer was extracted with Et₂O, the combined ether layers were dried and evaporated, and the residue purified by flash chromatography (pentanes/Et₂O, 7:1) to give product **S-9** as a colorless oil (61 mg, 75%).

$[\alpha]_D^{20} = -124$ (CH_2Cl_2 , $c = 0.8$); ^1H NMR (400 MHz, CDCl_3): $\delta = 5.73$ (dddd, $J = 5.5, 2.6, 2.5$ Hz, 1H), 5.61 (dddd, $J = 3.9, 1.8$ Hz, 1H), 3.51-3.46 (m, 1H), 2.96 (dd, $J = 8.5, 6.4$ Hz, 1H), 2.59-2.49 (m, 2H), 2.30-2.20 (m, 1H), 1.80 (d, $J = 2.3$ Hz, 3H), 1.01 (dtt, $J = 8.3, 8.2, 5.0$ Hz, 1H), 0.60-0.48 (m, 2H), 0.32-0.30 (m, 2H) ppm; ^{13}C NMR (100 MHz, CDCl_3): $\delta = 131.6, 130.3, 81.8, 79.3, 77.2, 53.0, 38.5, 35.0, 16.5, 3.7, 3.4, 2.0$ ppm; IR (film): $\tilde{\nu} = 3418, 3064, 3004, 2918, 2856, 1620, 1429, 1348, 1303, 1264, 1086, 1026, 944, 824, 720$ cm^{-1} ; MS (ESI $^+$): 199 $[\text{M}+\text{Na}]^+$.

(R)-Mosher-Ester Derived from S-9. ^1H NMR (600 MHz, C_6D_6): $\delta = 7.77$ (d, $J = 7.7$ Hz, 2H), 7.08 (m, 2H), 7.03 (m, 1H), 5.55 (dq, $J = 5.7, 2.2$ Hz, 1H), 5.35 (dq, $J = 5.7, 2.4$ Hz, 1H), 4.60 (dd, $J = 9.9, 4.9$ Hz, 1H), 3.61 (m, 1H), 3.50 (s, 3H), 2.78 (ddt, $J = 9.2, 4.9, 7.7$ Hz, 1H), 2.21 (dddt, $J = 16.6, 9.2, 2.0, 2.5$ Hz, 1H), 1.97 (ddq, $J = 16.6, 7.7, 2.4$ Hz, 1H), 1.45 (d, $J = 2.5$ Hz, 3H), 1.00 (m, 1H), 0.43 (m, 1H), 0.29 (m, 1H), 0.28 (m, 1H), 0.10 (m, 1H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 166.5, 133.2, 131.7, 129.6, 129.5, 128.5, 127.8, 124.3$ ($J_{\text{CF}} = 288.4$ Hz), 85.0 ($J_{\text{CF}} = 27.3$ Hz), 83.2, 81.5, 76.7, 55.4 ($J_{\text{CF}} = 1.2$ Hz), 50.5, 38.4, 35.0, 14.1, 4.3, 4.0, 3.4 ppm.



(S)-Mosher-Ester Derived from S-9. ^1H NMR (600 MHz, C_6D_6): $\delta = 7.77$ (d, $J = 7.7$ Hz, 2H), 7.10 (m, 2H), 7.05 (m, 1H), 5.59 (dq, $J = 5.7, 2.2$ Hz, 1H), 5.41 (dq, $J = 5.7, 2.3$ Hz, 1H), 4.61 (dd, $J = 9.7, 5.0$ Hz, 1H), 3.66 (m, 1H), 3.46 (s, 3H), 2.81 (ddt, $J = 9.3, 5.0, 7.4$ Hz, 1H), 2.30 (dddt, $J = 16.8, 9.4, 2.0, 2.5$ Hz, 1H), 2.05 (ddq, $J = 16.8, 7.4, 2.4$ Hz, 1H), 1.49 (d, $J = 2.5$ Hz, 3H), 0.88 (m, 1H), 0.42 (m, 1H), 0.23 (m, 2H), 0.05 (m, 1H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 166.5, 133.1, 131.9, 129.6$ (2 C), 128.5, 128.0 ($J_{\text{CF}} = 0.6$ Hz), 124.3 ($J_{\text{CF}} = 288.4$ Hz), 85.3 ($J_{\text{CF}} = 27.4$ Hz), 83.3, 81.5, 76.9, 55.4 ($J_{\text{CF}} = 1.1$ Hz), 50.4, 38.6, 35.3, 14.0, 3.92, 3.88, 3.4 ppm.



Scheme S4. Analysis $[\Delta\delta_{(S)-(R)}]$ of the Mosher Esters derived from **S-9**.

Compound S-10. $\text{VO}(\text{acac})_2$ (13.2 mg, 50 μmol) and $t\text{BuOOH}$ (5.5 M in decane, 224 μL , 1.24 mmol) were added to a solution of alcohol **S-9** (55 mg, 0.31 mmol) in CH_2Cl_2 (6 mL) at 0°C and the mixture stirred at this temperature for 2 h. The reaction was quenched with aq. sat. $\text{Na}_2\text{S}_2\text{O}_3$, the aqueous phase extracted with CH_2Cl_2 , the combined extracts were dried over Na_2SO_4 and evaporated, and the residue was purified by flash chromatography (Et_2O /pentanes, 4:1) to give product **S-10** as a colorless oil (38.4 mg, 65%). $[\alpha]_D^{20} = -80$ ($c = 0.26$, CH_2Cl_2); ^1H NMR (600 MHz, C_6D_6): $\delta = 3.48$ (dq, $\Sigma J = 4.6$, 1H), 3.36 (d, $J = 2.7$ Hz, 1H), 3.04 (m, 1H), 2.84 (s, OH), 2.83 (m, 1H), 2.45 (m, 1H), 1.81 (ddd, $J = 15.0, 10.8, 1.8$ Hz, 1H), 1.79 (ddd, $J = 15.0, 1.3, -0.5$ Hz, 1H), 1.48 (d, $J = 2.6$ Hz, 3H), 0.65 (m, 1H), 0.30 (m, 2H),

0.27 (m, 1H), 0.19 (m, 1H) ppm; ^{13}C NMR (150 MHz, C_6D_6): δ = 79.0 (s), 78.3 (s), 77.3 (d, $^1J_{\text{CH}}$ = 144 Hz), 61.4 (d, $^1J_{\text{CH}}$ = 189 Hz), 58.5 (d, $^1J_{\text{CH}}$ = 185 Hz), 51.4 (d, $^1J_{\text{CH}}$ = 134 Hz), 32.9 (d, $^1J_{\text{CH}}$ = 138 Hz), 31.1 (t, $^1J_{\text{CH}}$ = 130 Hz), 17.2 (d, $^1J_{\text{CH}}$ = 158 Hz), 3.4 (q, $^1J_{\text{CH}}$ = 131 Hz), 2.7 (t, $^1J_{\text{CH}}$ = 162 Hz), 2.4 (t, $^1J_{\text{CH}}$ = 162 Hz) ppm; IR (film): $\tilde{\nu}$ = 3422, 3002, 2921, 2855, 1439, 1405, 1362, 1262, 1233, 1196, 1024, 984, 944, 914, 842, 693 cm^{-1} ; MS (EI): m/z (%): 192 (< 1) $[\text{M}]^+$, 175 (1), 159 (2), 145 (2), 131 (4), 121 (25), 104 (73), 91 (48), 79 (80), 71 (93), 53 (24), 43 (100); HRMS (CI, *i*-butane): m/z : calcd. for $\text{C}_{12}\text{H}_{17}\text{O}_2$ 193.1229 $[\text{M}+\text{H}]^+$, found: 193.1229.

Compound S-11. A solution of acid **40** and carbodiimide **39** in CH_2Cl_2 (1 mL) was stirred for 30 min before a solution of compound **S-10** (10 mg, 52 μmol) in CH_2Cl_2 (0.5 mL) and catalytic DMAP were introduced. Stirring was continued for 3 d before the precipitate was filtered off through a pad of silica and the filtrate was evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 15:1) to give the title compound as a colorless syrup (12 mg, 68%). $[\alpha]_D^{20}$ = -83 (c = 0.3, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ = 5.54 (dddt, J = 7.1, 10.4, 7.1, 1.6 Hz, 1H), 5.23 (dddt, J = 10.8, 7.2, 7.2, 1.7 Hz, 1H), 4.60 (t, J = 9.3 Hz, 1H), 3.40 (d, J = 2.5 Hz, 1H), 3.11-3.09 (m, 2H), 2.89-2.84 (m, 2H), 2.55 (tt, J = 9.7, 1.8 Hz, 1H), 2.16 (t, J = 7.5 Hz, 2H), 2.10 (dd, J = 14.9, 2.0 Hz, 1H), 1.89 (dd, J = 14.7, 7.3 Hz, 2H), 1.77 (ddd, J = 14.8, 9.8, 1.4 Hz, 1H), 1.62 (dd, J = 14.6, 7.3 Hz, 2H), 1.54 (t, J = 2.7 Hz, 3H), 1.48 (d, J = 2.5 Hz, 3H), 0.69-0.60 (m, 1H), 0.56-0.50 (m, 1H), 0.36-0.21 (m, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ = 172.9, 130.2, 126.5, 81.6, 78.8, 78.6, 77.9, 75.6, 60.8, 57.6, 50.5, 34.6, 34.1, 29.4, 26.7, 25.1, 17.6, 15.4, 5.3, 3.4, 2.5 ppm; IR (film): $\tilde{\nu}$ = 3018, 2920, 2858, 1725, 1439, 1405, 1370, 1288, 1259, 1240, 1193, 1154, 1085, 1051, 1027, 991, 968, 929, 842, 800, 693 cm^{-1} ; MS (EI): m/z (%): 340 (<1) $[\text{M}]^+$, 294 (1), 175 (9), 149 (8), 105 (100), 91 (19), 79 (18), 55 (12), 41 (10); HRMS (ESI): m/z : calcd. for $\text{C}_{22}\text{H}_{28}\text{O}_3\text{Na}$ 363.1931 $[\text{M}+\text{Na}]^+$, found: 363.1933.

Compound S-12. Molecular sieves (powder, 5 Å) were added to a solution of diyne **S-11** (5 mg, 15 μmol) in toluene (5 mL) and the suspension stirred for 20 min before a complex **43b** (1 mg, 4 mol%) was introduced. The mixture was stirred overnight before it was filtered through a plug of silica and the filtrate was evaporated. Purification of the residue by flash chromatography (hexanes/EtOAc, 15:1) gave cycloalkyne **S-12** as a colorless oil (3 mg, 72%). $[\alpha]_D^{20}$ = -16 (c = 0.18, CH_2Cl_2); ^1H NMR (600 MHz, C_6D_6): δ = 5.29 (dddt, J = 10.8, 6.5, 5.5, 1.5 Hz, 1H), 5.20 (dddt, J = 10.8, 8.3, 6.9, 1.3 Hz, 1H), 3.95 (dd, ΣJ = 19.9 Hz, 1H), 3.39 (m, 1H), 3.16 (ddd, J = 7.5, 3.0, 1.9 Hz, 1H), 3.03 (t, J = 2.6 Hz, 1H), 2.98 (tdd, J = 10.4, Σ 15.9 Hz, 1H), 2.70 (ddd, J = 18.6, 6.5, 3.1 Hz, 1H), 2.64 (ddd, J = 18.6, 5.4, 1.6 Hz, 1H), 2.63 (m, 1H), 2.30 (m, 1H), 2.29 (ddd, J = 16.3, 9.4, 2.4 Hz, 1H), 2.23 (ddd, J = 16.3, 8.8, 2.4 Hz, 1H), 1.74 (m, 1H), 1.60 (ddd, J = 14.6, 10.3, 2.7 Hz, 1H), 1.55 (m, 1H), 1.54 (dd, J = 14.7, 8.4 Hz, 1H), 0.78 (m, 1H), 0.19 (m, 2H), 0.18 (m, 1H), -0.07 (m, 1H) ppm; ^{13}C NMR (150 MHz, C_6D_6): δ = 172.4 (s), 133.9 (d, $^1J_{\text{CH}}$ = 153 Hz), 123.8 (d, $^1J_{\text{CH}}$ = 159 Hz), 83.9 (d, $^1J_{\text{CH}}$ = 148 Hz), 80.96 (s), 80.93 (s), 63.5 (d, $^1J_{\text{CH}}$ = 188 Hz), 59.6 (d, 183 Hz), 56.2 (d, $^1J_{\text{CH}}$ = 133 Hz), 38.1 (d, $^1J_{\text{CH}}$ = 135 Hz), 32.6 (t, $^1J_{\text{CH}}$ = 128 Hz), 30.9 (t, $^1J_{\text{CH}}$ = 131 Hz), 26.3 (t, $^1J_{\text{CH}}$ = 127 Hz), 24.1 (t, $^1J_{\text{CH}}$ = 129 Hz), 17.6 (t, $^1J_{\text{CH}}$ = 130 Hz), 14.9 (d, $^1J_{\text{CH}}$ = 162 Hz), 5.3 (dd, $^1J_{\text{CH}}$ = 161, 163 Hz), 2.2 (dd, $^1J_{\text{CH}}$ = 161, 162 Hz) ppm; IR (film): $\tilde{\nu}$ = 3083, 3012, 2926, 2855, 1724, 1436, 1373, 1244, 1206, 1155, 1100, 1024, 988, 943, 837, 718, 698 cm^{-1} ; MS (EI): m/z (%): 286 (< 1) $[\text{M}]^+$, 257 (2), 216 (13), 198 (14), 157 (32), 143 (91), 129 (79), 115 (47), 103 (26), 91 (100), 77 (59), 65 (41), 55 (61), 41 (77); HRMS (ESI): m/z : calcd. for $\text{C}_{18}\text{H}_{22}\text{O}_3\text{Na}$ 309.1461 $[\text{M}+\text{Na}]^+$, found: 309.1460.

Des-Ethyl-Hydrilactone (44). NaBH₄·4H₂O (9.6 mg, 0.25 mmol) und ethylendiamine (17 µL, 0.25 mmol) were added to a solution of Ni(OAc)₂·4H₂O (84 mg, 0.34 mmol) in MeOH (10 mL). Hydrogen gas was then bubbled through the stirred suspension for 15 min.

An aliquot of the resulting P2-Ni suspension (60 µL) was added to a solution of cycloalkyne **S-12** (3.0 mg, 10.5 µmol) in MeOH (2 mL) and the resulting mixture was stirred under an atmosphere of H₂ for 3 h. For work-up, the mixture was diluted with Et₂O (5 mL) and filtered through a pad of silica, the filtrate was evaporated, and the residue purified by HPLC [150 mm YMC-ODS-A 5 µm, Ø 20 mm, eluent: MeCN/H₂O (80:20), 10 mL/min, 308 K, R_t = 8.0] to give product **44** as a colorless oil (2 mg, 67%). $[\alpha]_D^{20} = -23$ (c = 0.1, CH₂Cl₂); ¹H NMR (600 MHz, C₆D₆): δ = 5.38 (m, 1H), 5.36 (dddd, J = 11.2, 10.8, 4.5, 0.9 Hz, 1H), 5.10 (tddd, J = 10.9, 4.0, 2.4, 0.9 Hz, 1H), 4.88 (tdd, J = 10.8, 2.3, 0.7 Hz, 1H), 4.76 (dd, J = 10.5, 9.2 Hz, 1H), 3.26 (dt, J = 14.8, 11.2 Hz, 1H), 3.11 (d, J = 10.7 Hz, 1H), 3.11 (dd, Σ J = 3.7 Hz, 1H), 3.03 (d, J = 2.5 Hz, 1H), 2.44 (m, 1H), 2.30 (ddd, J = 15.7, 11.3, 2.6 Hz, 1H), 2.15 (dd, J = 15.0, 1.7 Hz, 1H), 2.09(0) (m, 1H), 2.08(6) (m, 1H), 1.94 (m, 1H), 1.88 (m, 1H), 1.82 (m, 1H), 1.49 (ddd, J = 15.0, 10.0, 1.4 Hz, 1H), 1.23 (m, 1H), 0.55 (m, 1H), 0.54 (m, 1H), 0.41 (m, 1H), 0.35 (m, 1H), 0.23 (m, 1H) ppm; ¹H NMR (600 MHz, CDCl₃): δ = 5.50 (td, J = 11.0, 4.5 Hz, 1H), 5.46 (td, J = 10.9, 4.0 Hz, 1H), 5.24 (tdd, J = 10.9, Σ 5.6 Hz, 1H), 5.05 (td, J = 10.6, 1.9 Hz, 1H), 4.36 (dd, Σ J = 19.6 Hz, 1H), 3.50 (m, 1H), 3.34 (dt, J = 14.7, 11.1 Hz, 1H), 3.17 (d, J = 2.5 Hz, 1H), 2.93 (d, J = 10.7 Hz, 1H), 2.25 (ddd, J = 15.7, 7.1, 2.8 Hz, 1H), 2.38-2.30 (m, 2H), 2.35 (d, J = 14.6 Hz, 1H), 2.34 (ddd, J = 15.7, 11.3, 2.6 Hz, 1H), 2.25 (ddd, J = 15.7, 7.1, 2.8 Hz, 1H), 2.04 (t, J = 10.2 Hz, 1H), 1.99 (ddd, J = 14.6, 10.1, 1.2 Hz, 1H), 1.99-1.90 (m, 2H), 1.47 (m, 1H), 0.73 (m, 1H), 0.63 (m, 1H), 0.45 (m, 1H), 0.34 (m, 2H) ppm; ¹³C NMR (150 MHz, C₆D₆): δ = 172.5 (s), 128.9 (d, ¹J_{CH} = 153 Hz), 128.6 (d, ¹J_{CH} = 153 Hz), 128.4 (d, ¹J_{CH} = 153 Hz), 127.6 (d, ¹J_{CH} = 153 Hz), 82.6 (d, ¹J_{CH} = 151 Hz), 61.0 (d, ¹J_{CH} = 185 Hz), 57.9 (d, ¹J_{CH} = 183 Hz), 49.3 (d, ¹J_{CH} = 132 Hz), 42.1 (d, ¹J_{CH} = 132 Hz), 32.7 (t, ¹J_{CH} = 128 Hz), 29.0 (dd, ¹J_{CH} = 132, 126 Hz), 26.5 (t, ¹J_{CH} = 126 Hz), 26.0 (t, ¹J_{CH} = 127 Hz), 24.1 (t, ¹J_{CH} = 129 Hz), 15.4 (d, ¹J_{CH} = 158 Hz), 5.6 (t, ¹J_{CH} = 161 Hz), 2.2 (t, ¹J_{CH} = 161 Hz) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 173.1 (C), 129.1 (CH), 128.5 (CH), 127.2 (CH), 127.1 (CH), 82.4 (CH), 61.3 (CH), 58.4 (CH), 48.9 (CH), 41.6 (CH), 32.6 (CH₂), 28.9 (CH₂), 26.4 (CH₂), 25.7 (CH₂), 23.9 (CH₂), 14.9 (CH), 5.3 (CH₂), 1.7 (CH₂) ppm; IR (film): $\tilde{\nu}$ = 3017, 2956, 2931, 2911, 2855, 1716, 1443, 1421, 1400, 1375, 1213, 1163, 1026, 933, 842, 703 cm⁻¹; HRMS (EI): m/z: calcd. for C₁₈H₂₄O₃Na 311.1618 [M+Na]⁺, found: 311.1618.

Total Synthesis of the Ecklonialactones

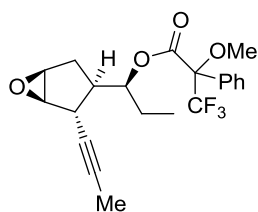
Ketone 23. EtMgBr (3 M in THF, 95 µL, 0.28 mmol) was added to a solution of Weinreb amide **22** (50 mg, 0.26 mmol) in THF (2 mL) at 0°C and the resulting mixture was stirred at that temperature for 30 min before the reaction was quenched with aq. sat. NH₄Cl (2 mL). The aqueous layer was extracted with Et₂O (3 x 2 mL), the combined organic phases were dried over Na₂SO₄ and evaporated, and the residue was purified by flash chromatography (pentanes/Et₂O, 7:1) to give ketone **23** as a colorless oil (39 mg, 93%). $[\alpha]_D^{20} = -394$ (c = 0.25, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃): δ = 5.53-5.49 (m, 1H), 5.43-5.39 (m, 1H), 3.59-3.52 (m, 1H), 3.13 (dt, J = 9.2, 7.6 Hz, 1H), 2.57-2.33 (m, 4H), 1.65 (d, J = 2.6 Hz, 3H), 0.95 ppm (t, J = 7.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ = 211.1, 130.6, 128.9, 80.6, 76.9, 57.3, 38.8, 35.4, 34.9, 7.8, 3.6 ppm; IR (film): $\tilde{\nu}$ = 3064 (w), 2977 (w), 2920 (w), 2857 (w), 1711 (s), 1446 (w), 1411 (w), 1362 (w), 1205 (w), 1118 (m), 1029 (w), 940 (w), 902 (w), 715 (m) cm⁻¹; MS (EI): m/z (%): 161 (3) [M-H]⁺, 147 (7), 133 (100), 119 (5), 105 (72), 91 (19), 79 (45), 65 (8), 57 (61), 51

(13), 39 (15), 29 (47); HRMS (CI, *iso*-butane): m/z : calcd. for $C_{11}H_{15}O$: 163.1123 $[M+H]^+$; found: 163.1122.

Alcohol 24. L-Selectride (1 M in THF, 660 μ L, 0.66 mmol) was added dropwise to a solution of ketone **23** (97 mg, 0.6 mmol) in THF (10 mL) at -78°C and the resulting mixture stirred at that temperature for 2 h before the reaction was quenched by careful addition of aq. sat. NH_4Cl (1 mL) to the cold mixture. After reaching ambient temperature, the mixture was diluted with aq. sat. NH_4Cl (6 mL), the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL), the combined organic phases were dried (Na_2SO_4) and evaporated, and the residue was purified by flash chromatography (pentanes/ Et_2O , 7:1) to give alcohol **24** as a colorless oil (68 mg, 69%). $[\alpha]_D^{20} = -232$ ($c = 0.2$, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): $\delta = 5.71$ - 5.68 (m, 1H), 5.59 - 5.56 (m, 1H), 3.58 - 3.53 (m, 1H), 3.43 - 3.38 (m, 1H), 2.51 - 2.44 (m, 1H), 2.37 (dq, $J = 8.3, 7.6$ Hz, 1H), 2.12 - 2.04 (m, 1H), 1.79 (d, $J = 2.3$ Hz, 3H), 1.67 - 1.57 (m, 1H), 1.52 - 1.40 (m, 1H), 0.99 ppm (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 131.7, 130.2, 81.8, 76.9, 76.8, 52.3, 38.5, 35.4, 28.6, 9.9, 3.6$ ppm; IR (film): $\tilde{\nu} = 3419$ (m, br), 3057 (w), 2961 (m), 2920 (s), 2855 (m), 1458 (m), 1378 (m), 1304 (m), 1123 (m), 1060 (m), 1029 (m), 970 (s), 943 (s), 892 (m), 718 (s), 679 (m) cm^{-1} ; MS (EI): m/z (%): $164 (< 1)$ $[M]^+$, 146 (28), 135 (27), 131 (14), 117 (100), 104 (19), 91 (64), 79 (24), 65 (10), 59 (9), 51 (9), 39 (13), 31 (10); HRMS (CI, *iso*-butane): m/z : calcd. for $C_{11}H_{17}O$: 165.1279 $[M+H]^+$; found: 165.1277.

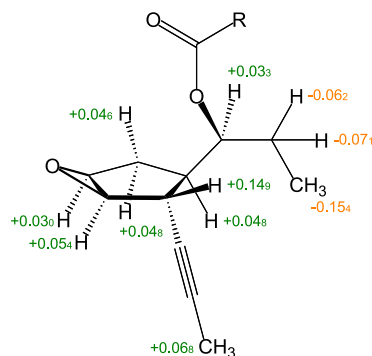
Compound 45. $\text{VO}(\text{acac})_2$ (7.8 mg, 0.03 mmol) was added to a solution of alcohol **24** (85 mg, 0.52 mmol) in CH_2Cl_2 (10 mL) prior to the slow addition of $t\text{BuOOH}$ (5.5 M in decane, 133 μ L, 0.73 mmol). After stirring for 2 h, additional $\text{VO}(\text{acac})_2$ (7.8 mg, 0.03 mmol) was introduced and stirring continued for 1 h. For work up, the mixture was poured into aq. sat. $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL), the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL), the combined organic phases were dried (Na_2SO_4) and evaporated, and the residue was purified by flash chromatography (pentanes/ Et_2O , 4:1) to give epoxide **45** as a colorless oil (90 mg, 94%). $[\alpha]_D^{20} = -97$ ($c = 0.14$, CH_2Cl_2); ^1H NMR (600 MHz, CDCl_3): $\delta = 3.57$ (dd, $\Sigma J = 4.2$ Hz, 1H), 3.53 (d, $J = 2.7$ Hz, 1H), 3.38 (d, $J = 2.7$ Hz, OH), 3.32 (ddt, $J = 7.6, 5.5, 3.0$ Hz, 1H), 3.16 (dq, $\Sigma J = 4.7$ Hz, 1H), 2.39 (ddt, $J = 10.7, 3.2, 1.7$ Hz, 1H), 2.31 (ddd, $J = 14.9, 10.8, 1.6$ Hz, 1H), 1.96 (dd, $J = 14.9, 1.7$ Hz, 1H), 1.78 (d, $J = 2.6$ Hz, 3H), 1.46 (dq, $J = 13.7, 7.5$ Hz, 1H), 1.41 (ddq, $J = 13.8, 7.4, 5.6$ Hz, 1H), 0.91 ppm (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 78.6$ (s), 77.9 (s), 75.2 (d, $J = 143$ Hz), 61.9 (d, $J_{\text{CH}} = 190$ Hz), 59.2 (d, $J_{\text{CH}} = 186$ Hz), 49.1 (d, $J_{\text{CH}} = 134$ Hz), 32.4 (t, $J_{\text{CH}} = 131$ Hz), 31.3 (d, $J_{\text{CH}} = 138$ Hz), 29.4 (t, $J_{\text{CH}} = 125$ Hz), 10.3 (q, $J_{\text{CH}} = 125$ Hz), 3.6 ppm (q, $J_{\text{CH}} = 131$ Hz); IR (film): $\tilde{\nu} = 3434$ (br), 2961 (m), 2922 (m), 2876 (m), 1439 (m), 1404 (m), 1263 (m), 1104 (m), 1054 (m), 975 (s), 940 (m), 840 (s), 693 (m) cm^{-1} ; MS (EI): m/z (%): $180 (< 1)$ $[M]^+$, $161 (< 1)$, 151 (22), 133 (7), 121 (18), 105 (100), 91 (29), 79 (64), 66 (15), 57 (15), 39 (22), 29 (18); HRMS (EI): m/z : calcd. for $C_{11}H_{16}O_2$: 180.1150 $[M]^+$; found: 180.1152.

(R)-Mosher-Ester derived from 45: ^1H NMR (600 MHz, CDCl_3): $\delta = 7.56$ (m, 2H), 7.40 (m, 3H), 4.96 (ddd, $J = 9.9, 6.2, 3.4$ Hz, 1H), 3.59 (q, $J_{\text{HF}} = 1.0$ Hz, 3H), 3.48 (m, 1H), 3.43 (d, $J = 2.5$ Hz, 1H), 2.66 (dq,



$J = 4.6$ Hz, 1H), 2.36 (tt, $J = 9.9, 1.9$ Hz, 1H), 2.03 (ddd, $J = 15.0, 9.9, 1.4$ Hz, 1H), 1.83 (dd, $J = 15.0, 2.0$ Hz, 1H), 1.77 (ddq, $J = 15.1, 3.4, 7.5$ Hz, 1H), 1.57 (ddq, $J = 15.0, 6.3, 7.5$ Hz, 1H), 1.70 (d, $J = 2.5$ Hz, 3H), 0.84 ppm (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 166.1, 132.1, 129.5, 128.4, 127.4, 123.4$ (q, $J_{\text{CF}} = 288.5$ Hz), 84.5 (q, $J_{\text{CF}} = 27.5$ Hz), $81.3, 78.5, 77.2, 60.8, 57.8, 55.4$ (q, $J_{\text{CF}} = 1.2$ Hz), $46.7, 33.8, 28.7, 24.5, 8.4, 3.5$ ppm.

(S)-Mosher-Ester derived from 45: ^1H NMR (600 MHz, CDCl_3): δ = 7.59 (m, 2H), 7.39 (m, 3H), 4.99 (ddd, J = 10.2, 6.4, 3.4, 1H), 3.59 (q, J_{HF} = 1.1 Hz, 3H), 3.51 (m, 1H), 3.49 (d, J = 2.5 Hz, 1H), 2.81 (dq, ΣJ = 4.4 Hz, 1H), 2.41 (tt, J = 9.9, 1.8 Hz, 1H), 2.08 (ddd, J = 15.0, 9.9, 1.3, 1H), 1.88 (dd, J = 15.0, 1.9 Hz, 1H), 1.77 (d, J = 2.5 Hz, 3H), 1.70 (ddq, J = 15.0, 3.4, 7.5 Hz, 1H), 1.50 (ddq, J = 15.0, 6.4, 7.4 Hz, 1H), 0.68 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ = 166.1, 132.3, 129.5, 128.4, 127.3, 123.9 (q, J_{CF} = 288.7 Hz), 84.4 (q, J_{CF} = 27.5 Hz), 81.5, 79.9, 77.3, 60.8, 57.9, 55.6 (q, J_{CF} = 1.3 Hz), 46.8, 34.3, 28.9, 24.4, 8.0, 3.6 ppm.



Scheme S5. Analysis [$\Delta\delta_{(S)-(R)}$] of the Mosher Esters derived from **45**.

Compound 46. Carbodiimide *p*-toluenesulfonate **39** (85 mg, 0.2 mmol) was added to a solution of 9-undecynoic acid (30 mg, 0.17 mmol) in CH_2Cl_2 (1.5 mL) and the resulting mixture was stirred for 1.5 h before a solution of alcohol **45** (20 mg, 0.11 mmol) in CH_2Cl_2 (1.5 mL) was introduced. DMAP (0.67 mg, 5.6 μmol) was then added and the resulting mixture stirred at ambient temperature overnight. For work up, all volatile materials were evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 15:1) to give ester **46** as a colorless oil (23 mg, 61%). $[\alpha]_D^{20}$ = -101 (c = 0.78, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ = 4.77 (ddd, J = 9.2, 7.5, 3.6 Hz, 1H), 3.49 (t, J = 1.9 Hz, 1H), 3.48 (t, J = 2.9 Hz, 1H), 2.83 (dt, J = 5.0, 2.5 Hz, 1H), 2.39 (tt, J = 2.9, 2.5 Hz, 1H), 2.32 (td, J = 7.5, 1.7 Hz, 2H), 2.14-2.06 (m, 3H), 1.87 (dd, J = 14.8, 2.7 Hz, 1H), 1.79 (d, J = 2.6 Hz, 3H), 1.78 (t, J = 2.6 Hz, 3H), 1.72-1.61 (m, 3H), 1.50-1.20 (m, 9H), 0.83 ppm (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 173.5, 79.3, 78.4, 78.2, 77.5, 75.4, 61.3, 58.2, 48.6, 34.6, 33.7, 29.3, 29.1, 29.0, 28.8, 28.7, 25.3, 25.1, 18.7, 9.0, 3.6, 3.5 ppm; IR (film): $\tilde{\nu}$ = 3017 (w), 2967 (m), 2932 (s), 2857 (m), 1731 (s), 1463 (m), 1441 (m), 1380 (m), 1244 (m), 1179 (m), 1091 (m), 1029 (w), 908 (s), 845 (s), 730 (s) cm^{-1} ; MS (EI): m/z (%): 344 (1) $[\text{M}]^+$, 329 (1), 315 (4), 222 (3), 197 (2), 179 (2), 162 (52), 147 (16), 119 (14), 105 (100), 91 (16), 81 (26), 67 (18), 55 (25), 41 (19); HRMS (ESI): m/z : calcd. for $\text{C}_{22}\text{H}_{32}\text{O}_3\text{Na}$: 367.2244 $[\text{M}+\text{Na}]^+$; found: 367.2247.

Compound 47. MS 5Å (powder, ca. 10 mg) was added to a solution of compound **46** (5.0 mg, 14.5 μmol) in toluene (1 mL) and the resulting mixture stirred for 20 min. In a second flask, complex **43a** (17.6 mg, 16.2 μmol) was dissolved in toluene (1 mL) and 45 μL (0.72 μmol , 4 mol%) of this stock solution were added to the suspension containing the diyne **46**. The mixture was stirred for 3 h at ambient temperature before it was filtered through a short plug of silica and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 15:1) to give product **47** as a colorless oil (3.4 mg, 80%). $[\alpha]_D^{20}$ = -52 (c = 0.05, CH_2Cl_2); ^1H NMR (600 MHz, CDCl_3): δ = 4.66 (ddd, J = 10.9, 7.8, 3.0 Hz, 1H), 3.51 (dd, ΣJ = 4.7 Hz, 1H), 3.48 (d, J = 2.5 Hz, 1H), 2.89 (tt, J = 4.6, 2.1 Hz, 1H), 2.57 (tt, J = 10.8,

4.8 Hz, 1H), 2.29 (t, J = 7.2 Hz, 2H), 2.17 (m, 2H), 2.10 (ddd, J = 14.9, 10.9, 2.2 Hz, 1H), 1.76 (m, 1H), 1.71 (dd, J = 14.8, 5.1 Hz, 1H), 1.70 (m, 1H), 1.66 (ddq, J = 14.5, 7.4, 3.1 Hz, 1H), 1.51-1.42 (m, 8H), 1.41 (dq, J = 14.5, 7.4 Hz, 1H), 0.82 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ = 173.8 (s), 83.3 (s), 80.5 (s), 79.6 (d), 62.6 (d), 60.0 (d), 52.1 (d), 36.5 (d), 33.9 (t), 30.0 (t), 26.7 (t), 26.1 (t), 25.6 (t), 25.50 (t), 25.49 (t), 23.9 (t), 18.2 (t), 8.9 (q) ppm; IR (film): $\tilde{\nu}$ = 3017 (w), 2962 (m), 2926 (m), 2855 (m), 1726 (s), 1456 (m), 1378 (m), 1266 (m), 1226 (m), 1089 (m), 1031 (w), 842 (m) cm^{-1} ; HRMS (ESI): m/z : calcd. for $\text{C}_{18}\text{H}_{26}\text{O}_3\text{Na}$: 313.1774 $[\text{M}+\text{Na}]^+$; found: 313.1751.

Ecklonialactone B (3). A mixture containing compound **47** (2.0 mg, 6.9 μmol) and commercial Lindlar catalyst (2.8 mg) in CH_2Cl_2 (4 mL) was stirred under an atmosphere of hydrogen (1 atm) for 2.5 h. The catalyst was filtered off and the filtrate evaporated to give product **3** as a colorless oil (1.8 mg, 90%).

$[\alpha]_D^{20}$ = -19 (c = 0.07, CH_2Cl_2); ^1H NMR (600 MHz, CDCl_3): δ = 5.47 (4d, J = 10.6, 8.4, 7.0, 1.2 Hz, 1H), 5.10 (ddt, J = 10.7, 9.6, 1.2 Hz, 1H), 4.95 (3d, J = 10.3, 7.6, 3.0 Hz, 1H), 3.49 (d, J = 2.6 Hz, 1H), 3.23 (d, J = 2.6 Hz, 1H), 3.00 (d, J = 9.7 Hz, 1H), 2.40 (3d, J = 15.2, 6.9, 3.8 Hz, 1H), 2.35 (3d, J = 15.2, 10.3, 3.2 Hz, 1H), 2.05 (m, 2H), 1.92 (m, 1H), 1.90 (m, 1H), 1.87 (m, 1H), 1.85 (m, 1H), 1.70 (ddq, J = 14.6, 3.1, 7.4 Hz, 1H), 1.55 (m, 1H), 1.42 (m, 2H), 1.38 (m, 2H), 1.37 (m, 1H), 1.35 (m, 3H), 1.29 (m, 1H), 0.79 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ = 174.1 (s), 131.9 (d, J_{CH} = 153 Hz), 128.3 (d, J_{CH} = 153), 78.7 (d, J_{CH} = 152 Hz), 61.1 (d, J_{CH} = 186 Hz), 57.2 (d, J_{CH} = 184 Hz), 46.4 (d, J_{CH} = 134 Hz), 40.0 (d, J_{CH} = 133 Hz), 33.5 (t, J_{CH} = 128 Hz), 28.8 (t, J_{CH} = 130 Hz), 26.79 (t), 26.75 (t), 26.3 (t), 25.4 (t), 25.3 (t), 25.2 (t), 24.2 (t, J_{CH} = 128 Hz), 8.8 (q, J_{CH} = 126 Hz) ppm; IR (film): $\tilde{\nu}$ = 2961 (m), 2931 (m), 2855 (w), 1732 (m), 1456 (w), 1260 (s), 1216 (w), 1175 (w), 1087 (s), 1018 (s), 862 (m), 799 (s) cm^{-1} ; HRMS (ESI): m/z : calcd. for $\text{C}_{18}\text{H}_{28}\text{O}_3\text{Na}$: 315.1931 $[\text{M}+\text{Na}]^+$; found: 315.1929.

Table S4. Comparison of the recorded ^{13}C NMR data of ecklonialactone B (**3**) with those reported in the literature.¹⁰

Position	δ_{c} (lit.)	multiplicity	δ_{c} (exp.)	multiplicity, $^1J_{\text{CH}}$	$\Delta\delta$
1	173.8	s	174.1	s	-0.3
2	33.5	t	33.5	t, 128 Hz	0
3	24.1	t	24.2	t, 128 Hz	-0.1
4	26.8	t	26.8	t	0
5	25.3	t	25.2	t	0.1
6	26.2	t	26.3	t	-0.1
7	26.8	t	26.8	t	0
8	25.3	t	25.3	t	0
9	131.8	d	131.9	d, 153 Hz	-0.1
10	128.2	d	128.3	d, 153 Hz	-0.1
11	40.0	d	40.0	d, 133 Hz	0
12	61.0	d	61.1	d, 186 Hz	-0.1
13	57.0	d	57.2	d, 184 Hz	-0.2
14	28.8	t	28.8	t, 130 Hz	0
15	46.3	d	46.4	d, 134 Hz	-0.1
16	78.6	d	78.7	d, 152 Hz	-0.1
17	25.3	t	25.4	t	-0.1
18	8.7	q	8.8	q, 126 Hz	-0.1

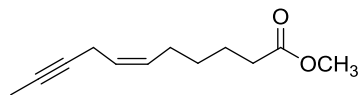
Methyl 6-Oxoheptanoate.¹¹ Ozone (ca. 40-50 mg/cm³) was bubbled through a mixture of cyclohexene (6.1 g, 74 mmol) and NaHCO₃ (2.0 g, 23.8 mmol) in CH₂Cl₂ (250 mL) and MeOH (50 mL) at -78°C until a pale blue color persisted. The mixture was then purged with Ar before it is allowed to reach ambient temperature. The mixture was filtered and the filtrate reduced to a volume of ca 50 mL. After dilution with CH₂Cl₂ (250 mL), NEt₃ (16 mL, 115 mmol) and Ac₂O (21.5 mL, 227 mmol) were introduced at 0°C and the resulting solution stirred overnight at ambient temperature. For work up, the mixture was successively washed with HCl (0.1 M, 150 mL), NaOH (10% w/w, 150 mL) and H₂O (150 mL), the organic layer (peroxide test must be negative at this point) was dried over Na₂SO₄ and evaporated. Distillation of the residue afforded the title compound as a colorless oil (5.7 g, 53%). ¹H NMR (400 MHz, CDCl₃): δ = 9.74 (t, J = 1.6 Hz, 1H), 3.64 (s, 3H), 2.46-2.41 (m, 2H), 2.34-2.29 (m, 2H), 1.68-1.59 ppm (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ = 202.0, 173.6, 51.5, 43.4, 33.6, 24.3, 21.4 ppm; IR (film): $\tilde{\nu}$ = 2951 (m), 2871 (w), 2723 (w), 1719 (s), 1436 (m), 1365 (m), 1196 (s), 1155 (s), 1093 (m), 1009 (m), 988 (m), 881 (w), 849 (w) 754 (w) cm⁻¹;

¹⁰ (a) Kurata, K.; Taniguchi, K.; Shiraishi, K.; Hayama, N.; Tanaka, I.; Suzuki, M. *Chem. Lett.* **1989**, 267; (b) Kurata, K.; Taniguchi, K.; Shiraishi, K.; Suzuki, M. *Phytochemistry* **1993**, 33, 155; (c) Todd, J. S.; Proteau, P. J.; Gerwick, W. H. *J. Nat. Prod.* **1994**, 57, 171.

¹¹ Claus, R. E.; Schreiber, S. L. *Org. Synth.* **1990**, Coll. Vol. 7, 168.

MS (EI): m/z (%): 144 (1) $[M-H]^+$, 126 (1), 116 (28), 113 (54), 101 (48), 95 (8), 87 (95), 84 (21), 74 (59), 70 (14), 67 (45), 59 (100), 55 (68), 43 (59), 39 (20), 29 (54), 27 (28); HRMS (CI, *iso*-butane): m/z : calcd. for $C_7H_{13}O_3$: 145.0865 $[M]^+$; found: 145.0863.

Undec-6Z-en-9-ynoic acid methyl ester. A solution of NaHMDS (210 mg, 1.15 mmol) in THF (2 mL)



was added at -30°C to a solution of but-2-ynyl-5-triphenylphosphonium iodide in THF (13 mL) and toluene (3 mL). The resulting mixture was allowed to reach ambient temperature and stirred until a clear yellow solution had formed

(ca. 1 h). At this point, the solution was cooled to -90°C before a solution of methyl 6-oxohexanoate (183 mg, 1.20 mmol) in THF (1 mL) was introduced. The resulting mixture was stirred overnight while reaching ambient temperature. Quenching of the reaction with aq. NH_4Cl (4 mL) followed by a standard extractive work up (Et_2O) and flash chromatography of the crude material (pentanes/ Et_2O , 1:1) furnished the title compound as a colorless oil (228 mg, 98%). ^1H NMR (400 MHz, CDCl_3): δ = 5.45-5.36 (m, 2H), 3.63 (s, 3H), 2.87-2.84 (m, 2H), 2.31 (t, J = 7.5 Hz, 2H), 2.07-2.02 (m, 2H), 1.76 (t, J = 2.6 Hz, 3H), 1.67-1.59 (m, 2H), 1.42-1.35 ppm (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ = 174.0, 130.6, 125.3, 75.3, 51.4, 33.9, 28.8, 26.7, 24.5, 17.1, 3.5 ppm; IR (film): $\tilde{\nu}$ = 3019 (w), 2922 (w), 2869 (w), 1734 (s), 1435 (m), 1361 (w), 1198 (m), 1171 (m), 1149 (m), 1095 (w), 1019 (w), 826 (w), 798 (w), 693 (w) cm^{-1} ; MS (EI): m/z (%): 194 (1) $[M]^+$, 179 (2), 163 (40), 147 (13), 134 (12), 120 (100), 105 (56), 91 (90), 74 (41), 66 (37), 59 (32), 41 (47), 27 (25); HRMS (EI): m/z : calcd. for $C_{12}H_{18}O_2$: 194.1307 $[M]^+$; found: 194.1307.

Undec-6Z-en-9-ynoic acid. KOH (100 mg, 1.78 mmol) was added to a solution of undec-6Z-en-9-ynoic acid methyl ester (228 mg, 1.18 mmol) in EtOH (2 mL) and the resulting mixture was stirred at reflux temperature for 1.5 h. After reaching ambient temperature, the solvent was evaporated, and the residue suspended in H_2O (5 mL). HCl (1 M) was added until a pH $\approx$ 2 was reached. The aqueous phase was extracted with pentanes (3 x 5 mL), the organic layer was evaporated and the residue dried in vacuo to give the title compound as a colorless syrup (155 mg, 73%). ^1H NMR (400 MHz, CDCl_3): δ = 1.45-1.38 (m, 2H), 1.69-1.61 (m, 2H), 1.77 (t, J = 2.5 Hz, 3H), 2.09-2.04 (m, 2H), 2.36 (t, J = 7.4 Hz, 2H), 2.88-2.85 (m, 2H), 5.47-5.38 ppm (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ = 180.0, 130.5, 125.4, 75.4, 33.9, 28.7, 26.6, 24.2, 17.1, 3.5 ppm; IR (film): $\tilde{\nu}$ = 3019 (m), 2921 (br m), 2861 (m), 1706 (s), 1413 (m), 1289 (m), 1233 (m), 909 (m), 799 (w), 732 (m) cm^{-1} ; MS (EI): m/z (%): 180 (4) $[M]^+$, 163 (2), 151 (16), 140 (17), 133 (3), 120 (38), 107 (41), 93 (100), 79 (83), 66 (47), 53 (27), 41 (43), 27 (27); HRMS (EI): m/z : calcd. for $C_{11}H_{16}O_2$: 180.1150 $[M]^+$; found: 180.1149.

Compound 51. Carbodiimide *p*-toluenesulfonate **39** (30 mg, 70 μmol) was added to a solution of undec-6Z-en-9-ynoic acid (11 mg, 58 μmol) in CH_2Cl_2 (0.5 mL) and the resulting mixture stirred for 1.5 h before a solution of alcohol **45** (7.0 mg, 39 μmol) in CH_2Cl_2 (0.5 mL) and DMAP (0.2 mg) were introduced. After stirring overnight, all volatile materials were evaporated and the residue purified by flash chromatography (hexanes/ EtOAc , 15:1) to give product **51** as a colorless oil (8.6 mg, 65%). $[\alpha]_D^{20}$ = -86 (CH_2Cl_2 , c = 0.43); ^1H NMR (400 MHz, CDCl_3): δ = 5.47-5.39 (m, 2H), 4.76 (ddd, J = 9.2, 7.4, 3.5 Hz, 1H), 3.50-3.47 (m, 2H), 2.88 (dq, J = 4.9, 2.5 Hz, 2H), 2.83 (dq, J = 2.4, 2.1 Hz, 1H), 2.40-2.31 (m, 3H), 2.40-2.11 (m, 3H), 1.85 (dd, J = 14.9, 2.5 Hz, 1H), 1.80 (d, J = 2.5 Hz, 3H), 1.78 (t, J = 2.5 Hz, 3H), 1.73-1.62 (m, 3H), 1.49-1.38 (m, 3H), 0.83 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ = 173.3, 130.7, 125.3, 78.4, 78.2, 77.6, 77.4, 75.3, 61.3, 58.2, 48.5, 34.5, 33.7, 29.3, 28.9, 26.8, 25.3, 24.7, 17.1, 8.9, 3.6, 3.5 ppm; IR (film): $\tilde{\nu}$ = 3020 (w), 2967 (m), 2921 (m), 2859 (w), 1729 (s), 1456

(m), 1441 (m), 1380 (m), 1256 (m), 1173 (s), 1144 (s), 1090 (s), 1030 (m), 953 (m), 928 (m); MS (EI): m/z (%): 342 (1) $[M]^+$, 313 (1), 289 (1), 274 (<1), 255 (<1), 235 (3), 197 (<1), 179 (1), 163 (15), 105 (100), 91 (21), 79 (18), 55 (9), 41 (12); HRMS (ESI): m/z : calcd. for $C_{22}H_{30}O_3Na$: 365.2078 $[M+Na]^+$; found: 365.2090.

Compound 52. Diyne **51** (3.9 mg, 11.4 μ mol) was dissolved in toluene (1 mL) and MS 5Å (powder, 10 mg) were added. After stirring for 20 min, 86 μ L of a stock solution of complex **43b** [7.2 mg (6.6 μ mol) in toluene (1 mL)] were added and the mixture stirred at ambient temperature for 7 h. For work up, the suspension was filtered through a cotton plug, the filtrate was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 15:1) to give compound **52** as a colorless liquid (3.5 mg, 90%). $[\alpha]_D^{20} = -84$ (CH_2Cl_2 , $c = 0.05$); 1H NMR (600 MHz, $CDCl_3$): $\delta = 5.56$ (dt, $J = 10.6$, 7.0 Hz, 1H), 5.51 (ddd, $J = 10.6$, 8.3, 6.8 Hz, 1H), 4.75 (ddd, $J = 10.7$, 8.4, 2.9 Hz, 1H), 3.50 (t, $J = 2.5$ Hz, 1H), 3.46 (d, $J = 2.5$ Hz, 1H), 2.92 (ddd, $J = 17.2$, 6.8, 2.0 Hz, 1H), 2.83 (dt, $J = 5.4$, 2.0 Hz, 1H), 2.75 (ddd, $J = 17.1$, 7.1, 2.6 Hz, 1H), 2.54 (tt, $J = 10.6$, 5.8 Hz, 1H), 2.41 (dt, $J = 15.2$, 7.2 Hz, 1H), 2.27 (dt, $J = 15.2$, 7.4 Hz, 2H), 2.21 (ddt, $J = 12.9$, 8.3, 7.7 Hz, 1H), 2.07 (ddd, $J = 14.8$, 10.6, 2.4 Hz, 1H), 1.99 (dq, $J = 13.0$, 6.8 Hz, 2H), 1.71 (m, 1H), 1.66 (dd, $J = 14.8$, 6.0 Hz, 1H), 1.61 (ddq, $J = 14.4$, 2.8, 7.4 Hz, 1H), 1.48 (qi., $J = 7.4$ Hz, 1H), 1.37 (ddq, $J = 14.4$, 8.4, 7.4 Hz, 1H), 0.82 ppm (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 173.2$ (s), 133.0 (d, $J_{CH} = 154$ Hz), 123.8 (d, $J_{CH} = 161$ Hz), 81.4 (s), 79.6 (s), 78.9 (d, $J_{CH} = 148$ Hz), 62.8 (d, $J_{CH} = 189$ Hz), 59.8 (d, $J_{CH} = 185$ Hz), 53.11 (d, $J_{CH} = 134$ Hz), 36.7 (d, $J_{CH} = 136$ Hz), 34.3 (t, $J_{CH} = 128$ Hz), 30.2 (t, $J_{CH} = 130$ Hz), 27.5 (t, $J_{CH} = 127$ Hz), 27.4 (t, $J_{CH} = 126$ Hz), 25.7 (t), 24.9 (t, $J_{CH} = 128$ Hz), 16.4 (t, $J_{CH} = 131$ Hz), 9.0 (q, $J_{CH} = 126$ Hz) ppm; IR (film): $\tilde{\nu} = 3021$ (w), 2962 (m), 2930 (m), 2855 (w), 1726 (s), 1459 (m), 1441 (w), 1380 (w), 1350 (w), 1330 (w), 1266 (m), 1251 (m), 1228 (m), 1211 (m), 1185 (m), 1165 (m), 1153 (m), 1091 (m), 1059 (w), 1032 (w), 1011 (w), 942 (w), 842 (s), 799 (w) cm^{-1} ; MS (EI): m/z (%): 288 (2) $[M]^+$, 270 (2), 259 (10), 241 (10), 213 (11), 201 (20), 187 (32), 157 (31), 143 (100), 129 (73), 115 (40), 103 (18), 91 (76), 79 (35), 65 (22), 55 (30), 41 (36); HRMS (ESI): m/z : calcd. for $C_{18}H_{24}O_3Na$: 311.1617 $[M+Na]^+$; found: 311.1618.

Ecklonialactone A (2). $NaBH_4$ (9.6 mg, 0.25 mmol) and ethylenediamine (17 μ L, 0.25 mmol) were successively added to a solution of $Ni(OAc)_2 \cdot 4H_2O$ (84 mg, 0.34 mmol) in EtOH (10 mL). H_2 was bubbled through the resulting black suspension for 15 min. An aliquot (200 μ L, ca. 7 μ mol) of this suspension was then added to a solution of cycloalkyne **52** (8.0 mg, 17 μ mol) in EtOH (2 mL) and the resulting mixture was stirred under H_2 (1 atm) for 2 h. The catalyst was filtered off, the filtrate was evaporated and the residue purified by preparative HPLC (150 mm YMC-ODS-A 5 μ m, MeCN/water 80:20, flow rate 15 mL/min, $t_r = 6.68$ min) to give ecklonialactone A (**2**) as a colorless solid (5.5 mg, 69%). $[\alpha]_D^{20} = -59$ (CH_2Cl_2 , $c = 0.025$); 1H NMR (600 MHz, $CDCl_3$): $\delta = 5.49$ (tdd, $J = 10.5$, 5.0, 1.3 Hz, 1H), 5.48 (dt, $J = 10.6$, 7.5, 1.5 Hz, 1H), 5.40 (m, 1H), 5.07 (dddd, $J = 10.7$, 9.8, 2.3, 0.9 Hz, 1H), 4.89 (dddd, $J = 8.9$, 7.3, 3.1, 1.5 Hz, 1H), 3.49 (d, $J = 2.6$ Hz, 1H), 3.21 (dd, $J = 2.6$, 0.5 Hz, 1H), 3.08 (ddd, $J = 15.5$, 10.5, 8.0 Hz, 1H), 3.06 (d, $J = 9.6$ Hz, 1H), 2.63 (ddd, $J = 15.5$, 5.9, 5.0 Hz, 1H), 2.41 (ddd, $J = 15.5$, 7.3, 5.2 Hz, 1H), 2.35 (ddd, $J = 15.0$, 8.9, 5.1 Hz, 1H), 2.04 (m, 1H), 1.99 (m, 1H), 1.93 (m, 2H), 1.87 (m, 1H), 1.75 (m, 1H), 1.72 (m, 1H), 1.69 (m, 1H), 1.43 (m, 2H), 1.39 (dq, $J = 14.6$, 7.3 Hz, 1H), 0.79 ppm (t, $J = 7.4$ Hz, 3H); 1H NMR (600 MHz, C_6D_6): $\delta = 5.42$ (m, 1H), 5.39 (m, 1H), 5.37 (tdd, $J = 10.5$, 5.0, 1.3 Hz, 1H), 5.27 (ddd, $J = 10.9$, 7.4, 3.2 Hz, 1H), 4.87 (4d, $J = 10.6$, 10.0, 3.2, 1.0 Hz, 1H), 3.19 (d, $J = 9.9$ Hz, 1H), 3.05 (m, 1H), 3.04 (ddt, $J = 2.6$, 0.5 Hz, 1H), 2.96 (m, 1H), 2.48 (m, 1H), 2.21 (ddd, $J = 14.9$, 6.9, 5.5 Hz, 1H), 2.17 (ddd, $J = 14.9$, 8.8, 5.1 Hz, 1H), 1.90 (m, 1H), 1.84 (m, 1H), 1.80 (t, $J = 10.0$ Hz, 1H), 1.68 (m, 1H), 1.62 (ddq, $J = 14.5$, 3.2, 7.4 Hz, 1H), 1.50 (ddt, $J = 14.9$, 1.2 Hz, 1H), 1.41 (m,

1H), 1.37 (ddd, $J = 15.0, 9.4, 1.3$ Hz, 1H), 1.30 (m, 2H), 1.24 (dqi., $J = 14.5, 7.4$ Hz, 1H), 0.77 ppm (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): $\delta = 173.7$ (s), 129.8 (d), 129.5 (d), 128.0 (d), 127.4 (d), 78.5 (d), 61.0 (d), 57.2 (d), 45.9 (d), 40.0 (d), 33.6 (t), 28.8 (t), 28.1 (t), 26.3 (t), 26.0 (t), 25.2 (t), 24.3 (t), 8.7 (q) ppm; IR (film): $\tilde{\nu} = 3007$ (m), 2962 (m), 2931 (m), 2855 (m), 1726 (s), 1456 (w), 1441 (w), 1398 (w), 1380 (w), 1342 (w), 1254 (m), 1218 (m), 1145 (m), 1105 (w), 1087 (w), 1051 (w), 1019 (w), 971 (w), 953 (w), 930 (w), 912 (w), 842 (m), 804 (w), 749 (w), 741 (w), 718 (w), 695 (w) cm^{-1} ; MS (ESI $^+$): 313 $[\text{M}+\text{Na}]^+$, 329 $[\text{M}+\text{K}]^+$, 603 $[2\text{M}+\text{Na}]^+$; HRMS (ESI): m/z : calcd. for $\text{C}_{18}\text{H}_{26}\text{O}_3\text{Na}$: 313.1774 $[\text{M}+\text{Na}]^+$; found: 313.1771.

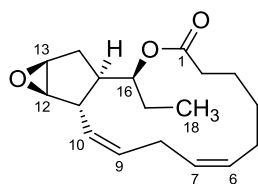


Table S5. Comparison of the recorded ^{13}C NMR data (CDCl_3) of ecklonialactone A (**2**) with those reported in the literature.¹⁰ Assignments marked * may be interchanged.

Position	δ_{C} (lit., 67.9 MHz), ppm	δ_{C} (exp., 150 MHz), ppm	$\Delta\delta$
1	173.6	173.7	0.1
2	33.6	33.6	0
3	24.3	24.3	0
4	28.1	28.1	0
5	26.0	26.0	0
6*	129.5	129.5	0
7	128.0	128.0	0
8	26.3	26.3	0
9*	129.8	129.8	0
10	127.5	127.4	-0.1
11	40.1	40.0	-0.1
12	61.0	61.0	0
13	57.2	57.2	0
14	28.8	28.8	0
15	46.0	45.9	-0.1
16	78.6	78.5	-0.1
17	25.3	25.2	-0.1
18	8.7	8.7	0

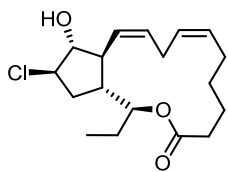


Table S6. Comparison of the recorded ^{13}C NMR data (ppm, CDCl_3) of eiseniachloride A (**7**) with those reported in the literature.¹²

Position	δ_{C} (lit., 125 MHz)	δ_{C} (exp., 150 MHz), multiplicity [$^1J_{\text{CH}}$]	$\Delta\delta$	
1	173.8	173.8	s	0.0
2	32.8	32.8	t	0.0
3	24.5	24.6	t	-0.1
4	27.7	27.7	t	0.0
5	25.6	25.6	t	0.0
6	130.0*	130.0	d	0.0
7	126.9*	126.7	d	0.2
8	26.7	26.7	t	0.0
9	130.9	131.0	d	-0.1
10	130.2	130.0	d	0.2
11	45.4	45.2	d [129.3]	0.2
12	85.5	85.4	d [147.9]	0.1
13	62.7	62.6	d [155.3]	0.1
14	36.5	36.4	t	0.1
15	41.8	41.5	d [129.3]	0.3
16	77.4	77.4	d [146.4]	0.0
17	25.6	25.5	t	0.1
18	9.9	9.9	q [126.4]	0.0

* The assignment of these two signals had to be interchanged relative to the assignment made in the original publication.

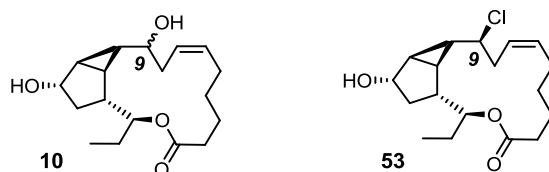
¹² Kousaka, K.; Ogi, N.; Akazawa, Y.; Fujieda, M.; Yamamoto, Y.; Takada, Y.; Kimura, J. *J. Nat. Prod.* **2003**, *66*, 1318.

Table S7. Comparison of the recorded ^1H NMR data (ppm, CDCl_3) of eiseniachloride A (**7**) with those reported in the literature.¹²

δ_{H} (lit., 500 MHz)			δ_{H} (exp., 600 MHz)		
H ₃ -18	0.82	t	H ₃ -18	0.81	t, $J = 7.4$ Hz
H-3	1.25	m	H-3	(1.71)	m
H-4	1.58*	m	H-4	(1.22)	m
H ₂ -17			H ₂ -17	(1.57)	m
H'-4	1.75*	m	H'-4	(1.57)	m
H'-3	1.80	m	H'-3	(1.77)	m
H-5			H-5	(1.79)	m
H-14	2.05	ddd	H-14	(2.04)	m
H'-14	2.13	ddd	H'-14	(2.10)	m
H-15	2.32	m	H-15	(2.31)	m
H-2	2.35	m	H-2	(2.31)	m
H'-5	2.45	m	H'-5	(2.40)	m
H-8	2.48	m	H-8	(2.47)	m
H'-2	2.50	m	H'-2	(2.47)	m
H-11	2.97	ddd	H-11	2.96	q, $J = 9.4$ Hz
H'-8	3.41	m	H'-8	3.40	ddd, $J = 15.1, 10.7, 8.6$ Hz
H-12	3.83	dd	H-12	3.81	dd, $J = 8.7, 6.7$ Hz
H-13	4.04	ddd	H-13	4.03	dt, $J = 9.0, 6.4$
H-16	4.73	dt	H-16	4.70	ddd, $J = 7.2, 6.4, 3.7$ Hz
H-10	5.35	dd	H-10	5.34	m
H-6	5.40	m	H-6	(5.38)	m
H-7	5.45	m	H-7	(5.40)	m
H-9	5.58	dt	H-9	5.57	tdd, $J = 10.9, 3.7, 0.8$ Hz

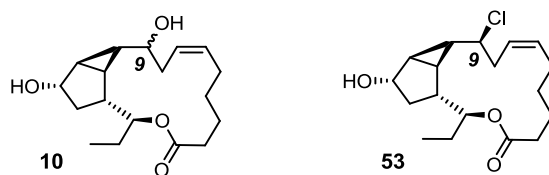
* supposedly erroneous assignment in the literature

Table S8. Comparison of the ^{13}C NMR spectra (ppm, CDCl_3) of oxylipin **10**¹² with its chlorinated analogue **53** derived from opening of **2** in non-purified CDCl_3 .

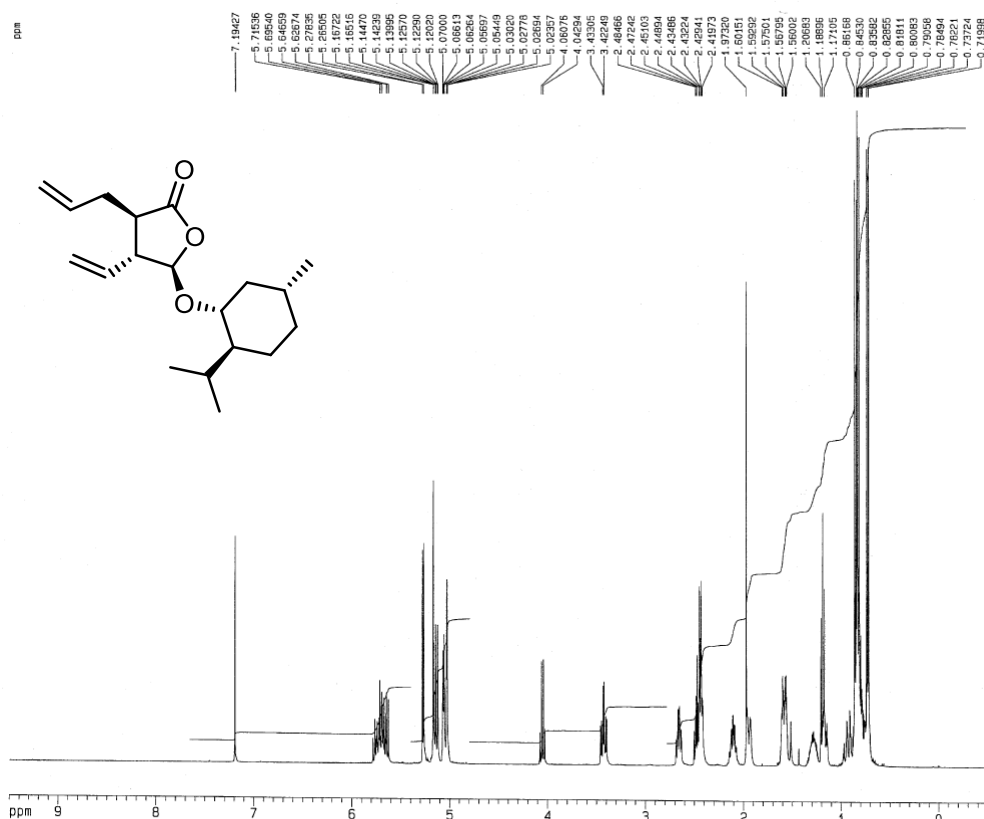


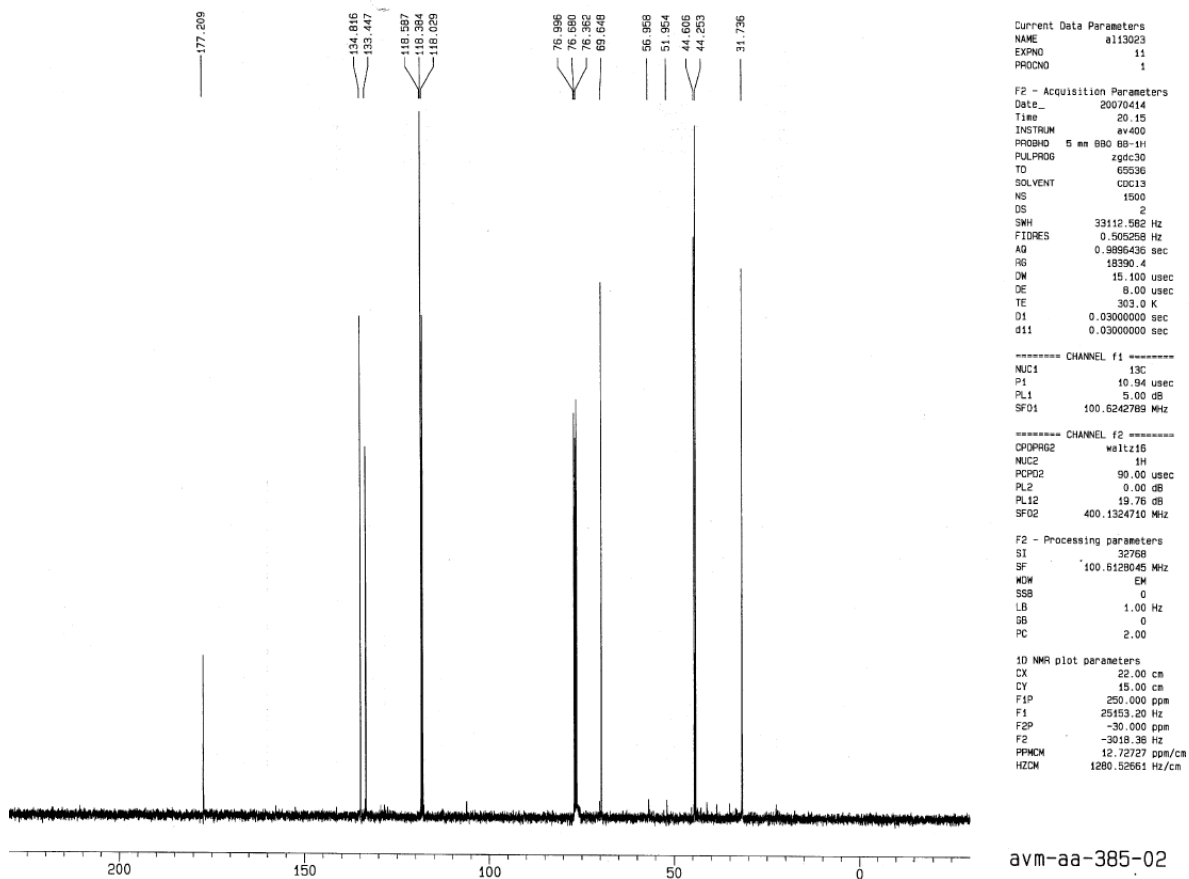
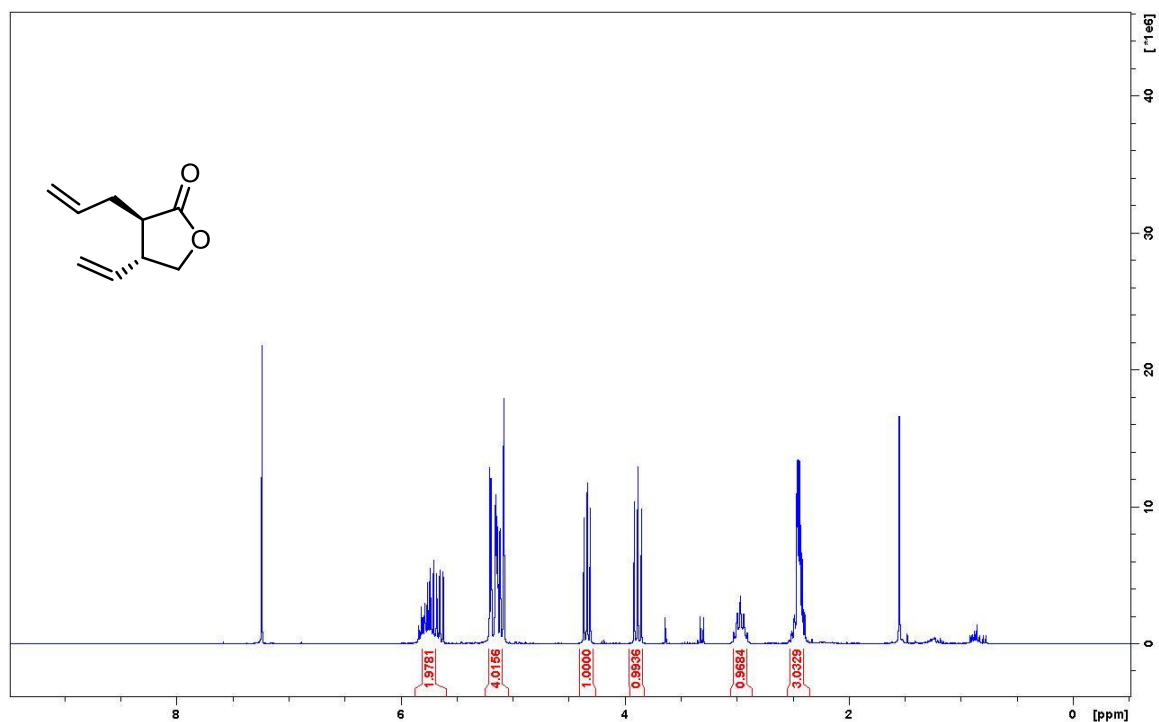
Position	δ_{C} (lit., 125 MHz)	δ_{C} (exp., 150 MHz); multiplicity [$^1J_{\text{CH}}$]		$\Delta\delta$
1	174.3	174.4	s	-0.1
2	34.5	34.4	t	0.1
3	24.0	23.7	t	0.3
4	27.4	27.2	t	0.2
5	26.1	25.9	t	0.2
6	130.3	129.6	d	0.7
7	126.6	127.0	d	-0.4
8	32.2	32.5	t	-0.3
9	68.3	60.8	d [152.1]	7.5
10	26.1	26.5	d [161.9]	-0.4
11	24.4	27.7	d [168.6]	-3.3
12	27.2	29.5	d [168.5]	-2.3
13	74.8	74.7	d [151.2]	0.1
14	37.1	36.7	t	0.4
15	43.8	43.6	d [134.1]	0.2
16	78.2	77.8	d [149.9]	0.4
17	26.6	26.8	t	-0.2
18	9.6	9.7	q [126.1]	-0.1

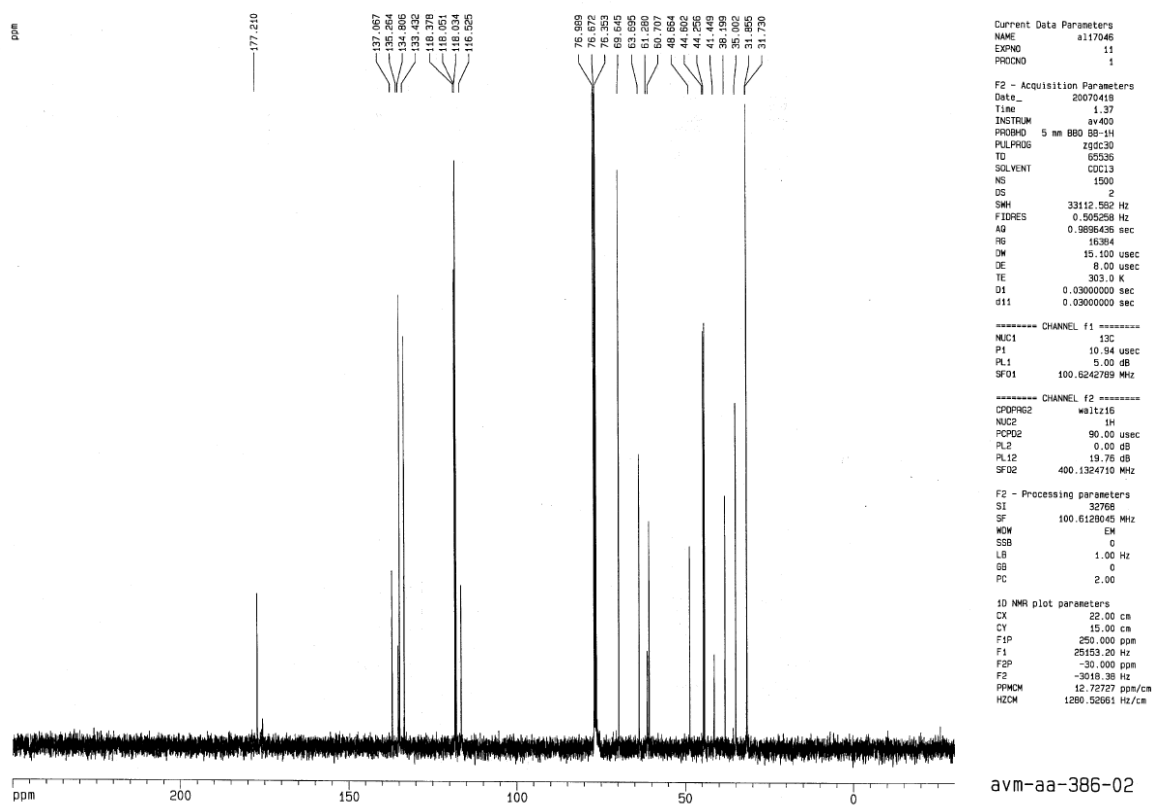
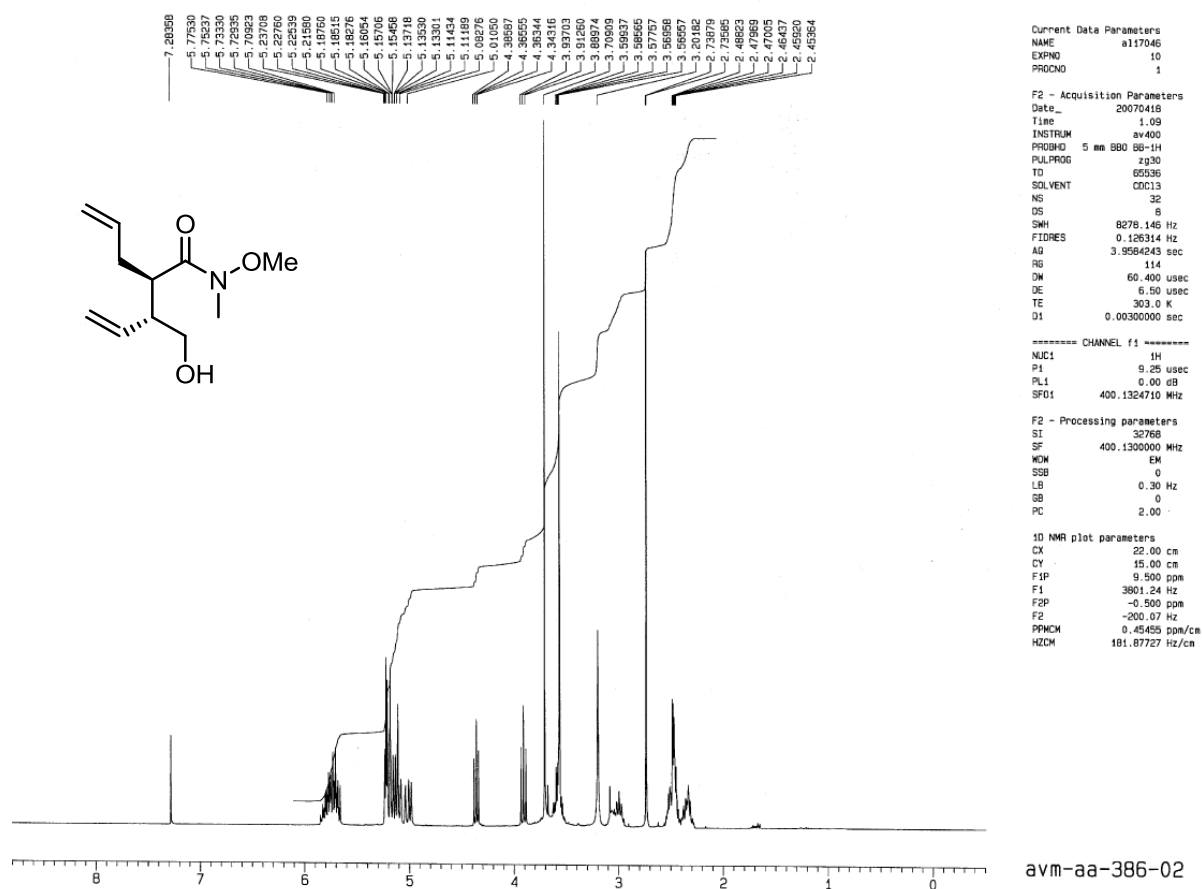
Table S8. Comparison of the ^1H NMR spectra (ppm, CDCl_3) of oxylipin **10**¹² with its chlorinated analogue **53** derived from opening of **2** in non-purified CDCl_3 .

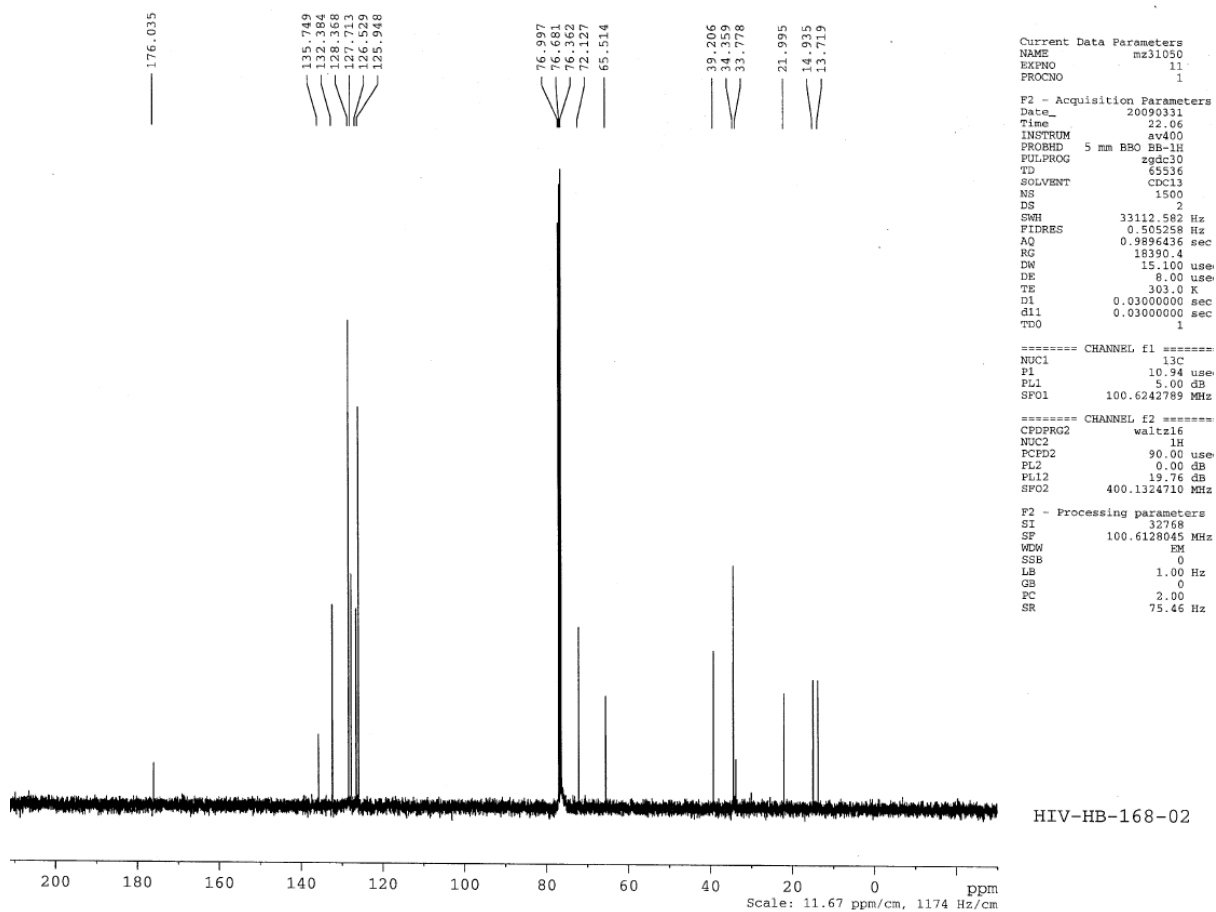
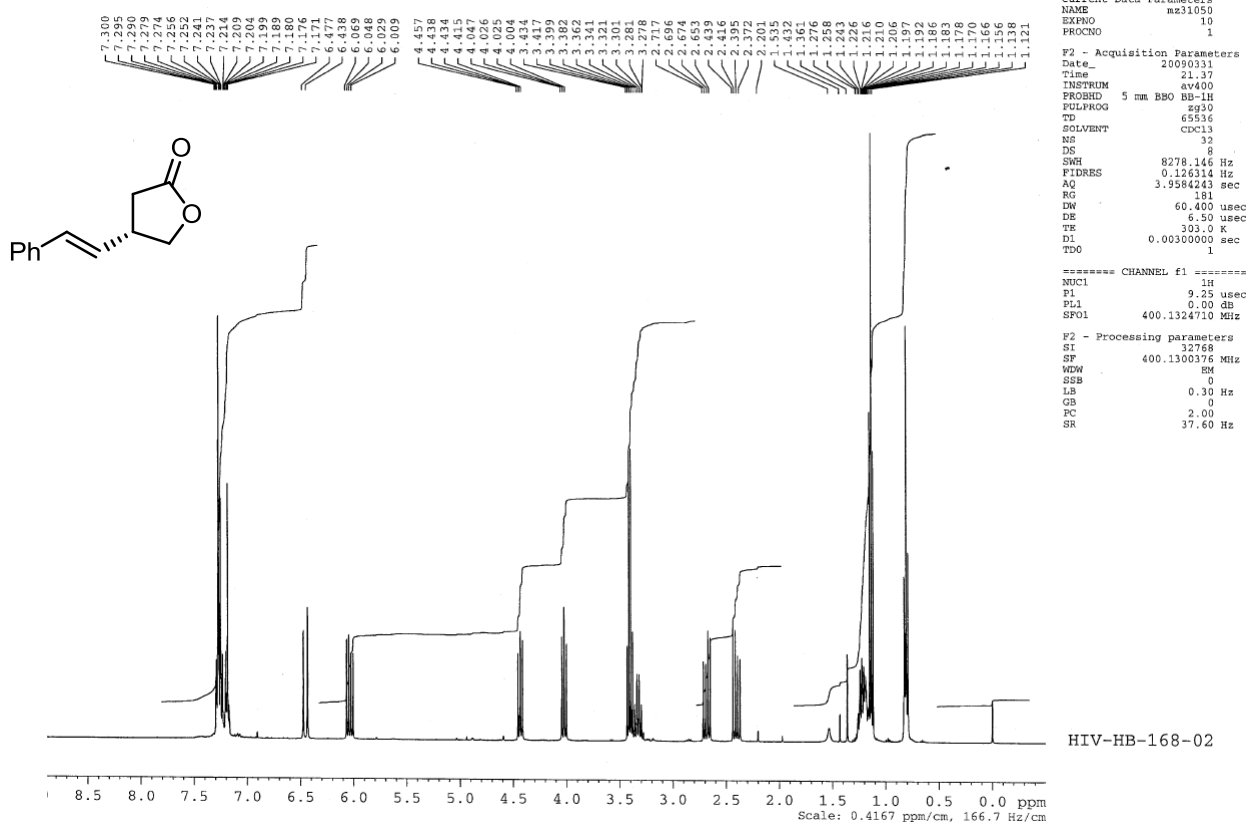


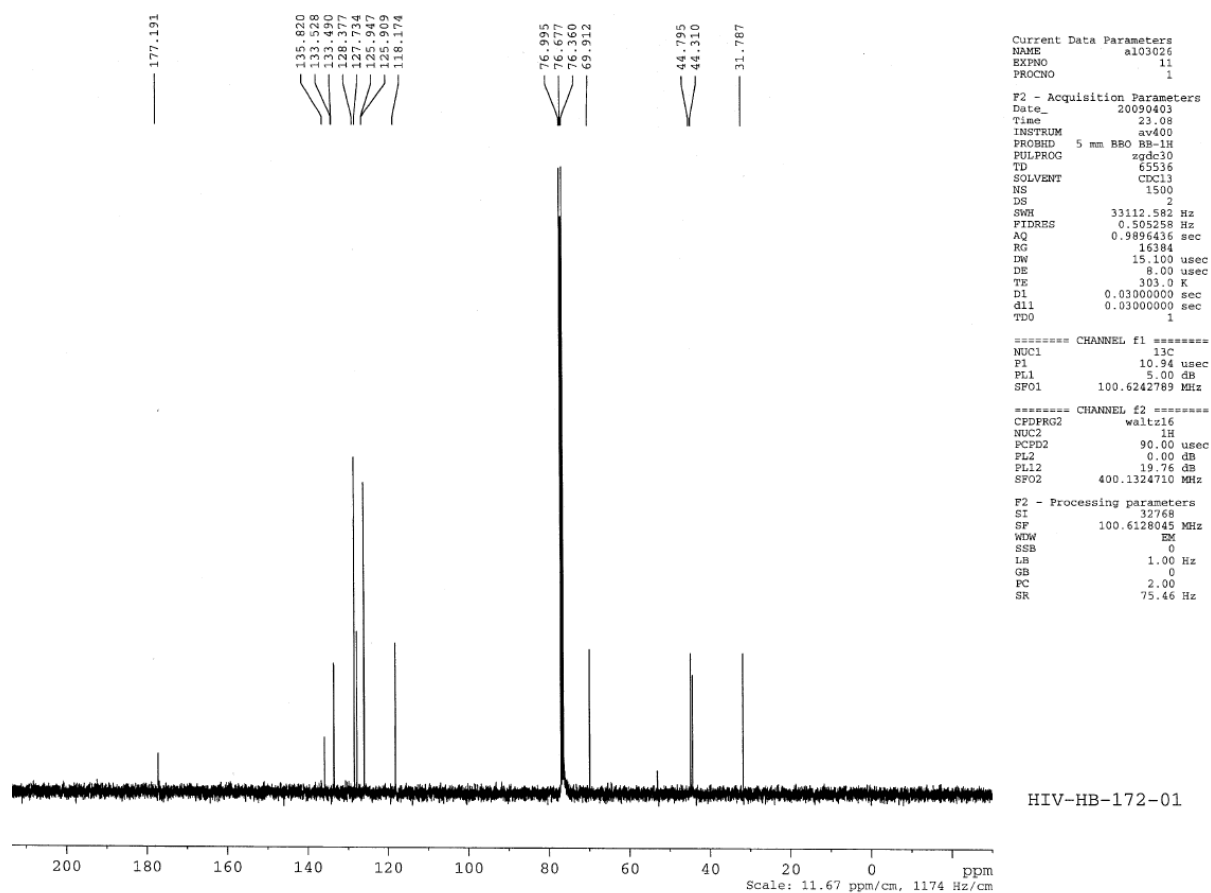
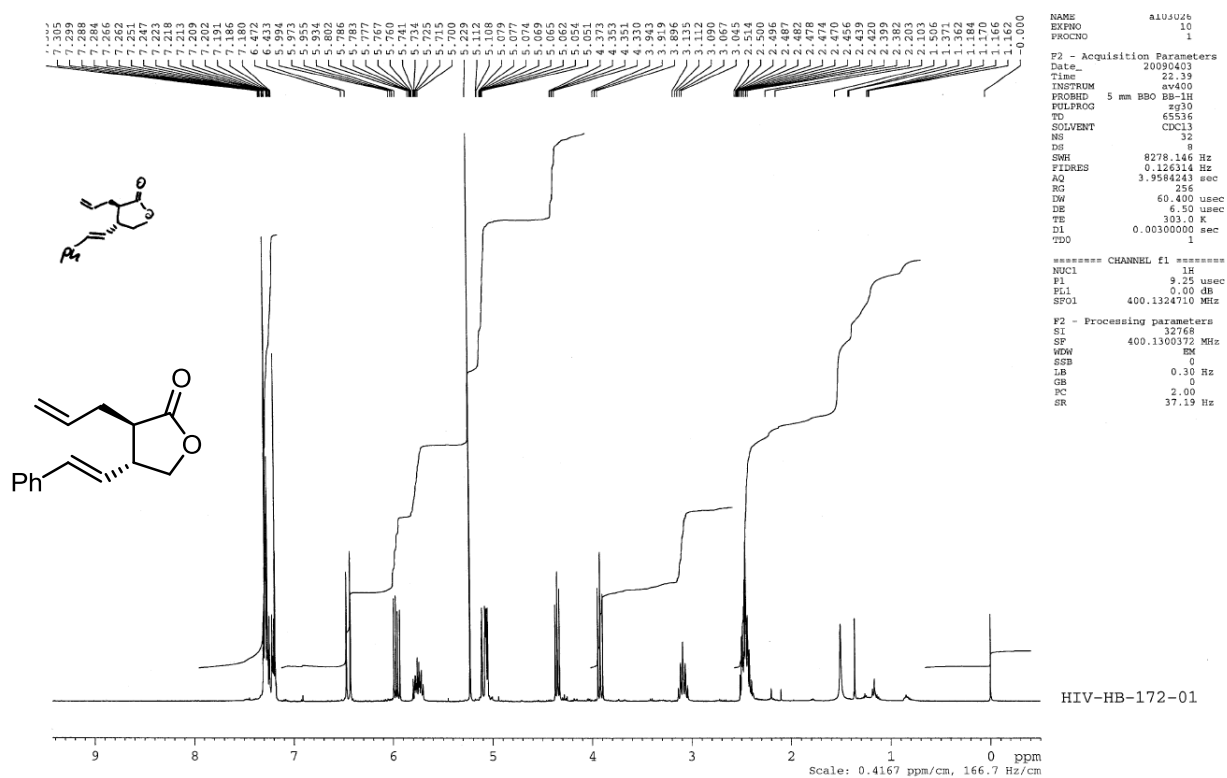
δ_{H} (lit., 500 MHz)			δ_{H} (exp., 600 MHz)		
H-10	0.79	dt, $J = 4.7, 3.6$ Hz	H-10	0.93	dt, $J = 5.6, 3.5$ Hz
H ₃ -18	0.86	t, $J = 7.3$ Hz	H ₃ -18	0.85	t, $J = 7.4$ Hz
H-17	1.48	m	H-17	(1.48)	m
H-14	1.50	m	H-14	(1.47)	m
H-11	1.53	dd, $J = 6.0, 3.6$ Hz	H-11	(1.71)	m
H-12 H ₂ -4	1.60	m	H-12	(1.70)	m
			H-4	(1.57)	m
			H'-4	(1.46)	m
H'-14	1.64	dd, $J = 7.8, 5.0$ Hz	H'-14	(1.57)	m
H-3	1.72	ddd, $J = 14.7, 7.8, 3.7$ Hz	H-3	(1.74)	m
H'-17	1.73	ddq, $J = 14.2, 7.3, 3.2$ Hz	H'-17	(1.69)	m
H'-3	1.80	m	H'-3	(1.78)	m
H-5	1.95	ddd, $J = 13.5, 8.2, 8.2$ Hz	H-5	(1.94)	m
H-15	2.05	m	H-15	(2.08)	m
H'-5	2.08	m	H'-5	(2.11)	m
H ₂ -8	2.15	m	H-8	(2.41)	m
			H'-8	(2.36)	m
H-2	2.33	dd, $J = 14.4, 10.1, 4.1$ Hz	H-2	(2.31)	m
H'-2	2.58	ddd, $J = 14.4, 7.8, 3.7$ Hz	H'-2	2.56	ddd, $J = 14.5, 7.6, 3.7$ Hz
H-9	4.18	ddd, $J = 8.2, 4.8, 4.7$ Hz	H-9	4.57	ddd, $J = 9.3, 5.6, 3.0$ Hz
H-13	4.22	d, $J = 5.0$ Hz	H-13	4.24	d, $J = 5.2$ Hz
H-16	4.85	ddd, $J = 9.9, 8.5, 3.2$ Hz	H-16	4.80	ddd, $J = 9.8, 8.2, 3.4$ Hz
H-7	5.32	dt, $J = 10.5, 6.8$ Hz	H-7	(5.34)	m
H-6	5.55	m	H-6	(5.49)	m

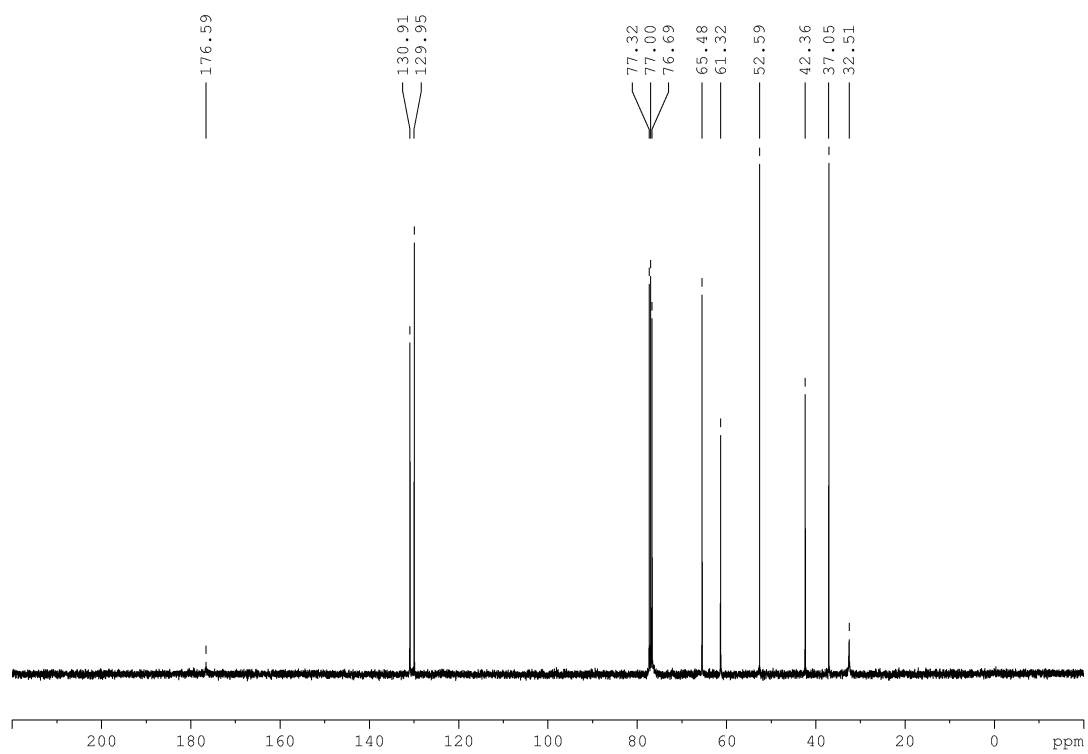
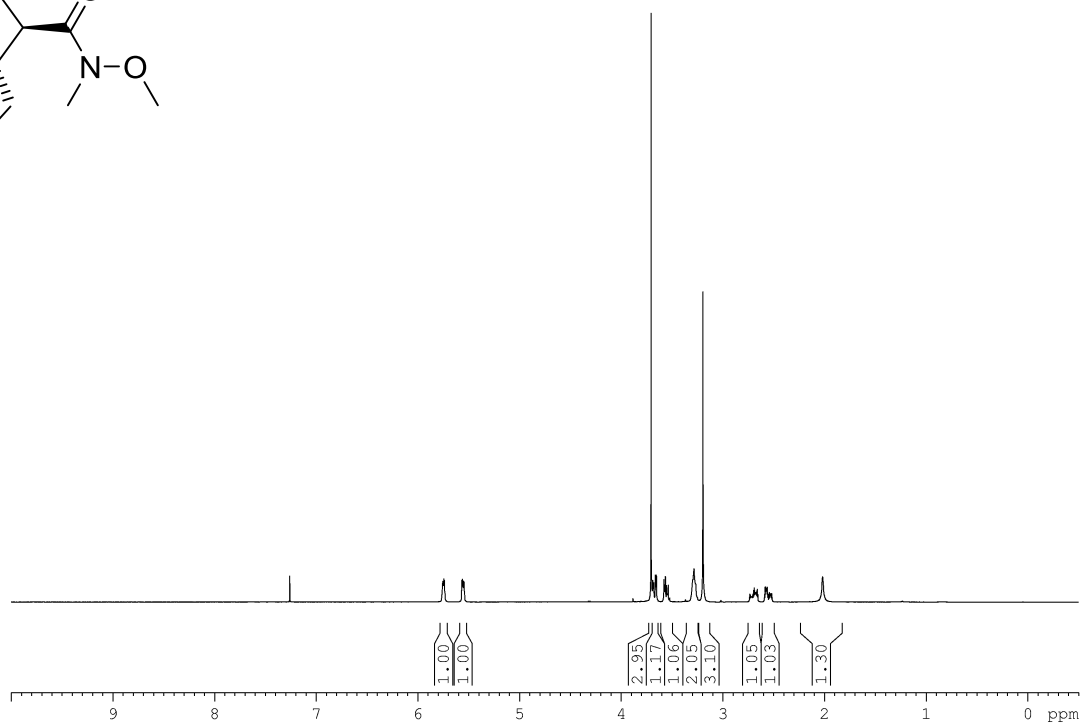
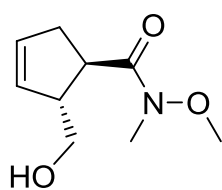


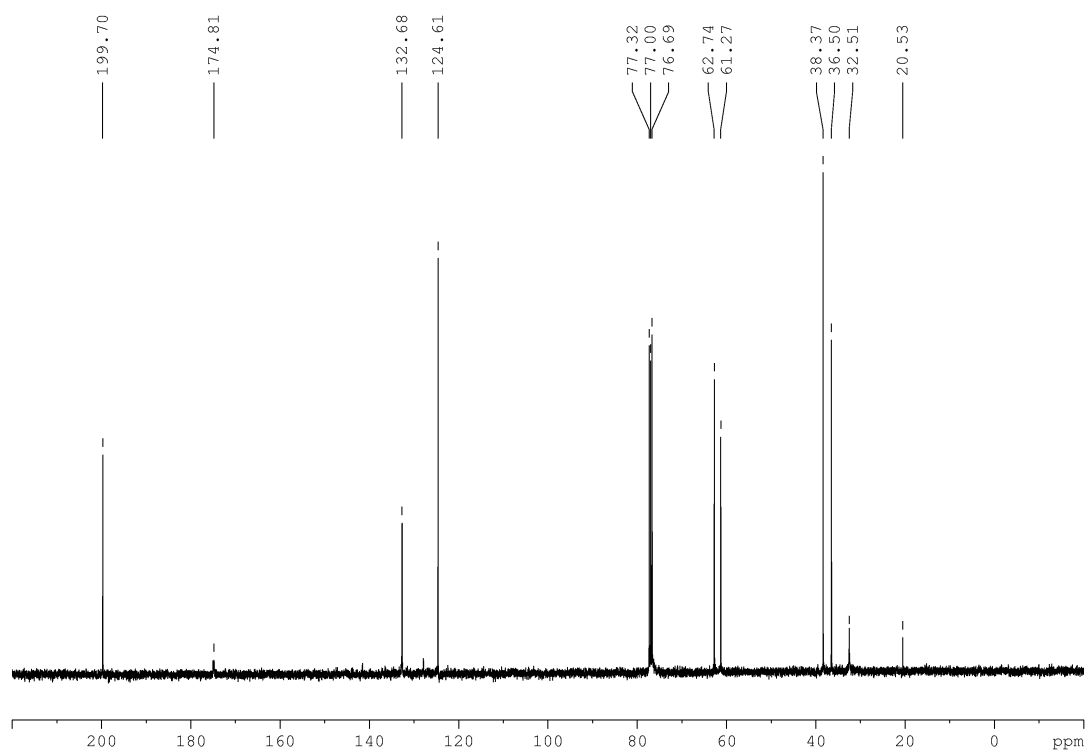
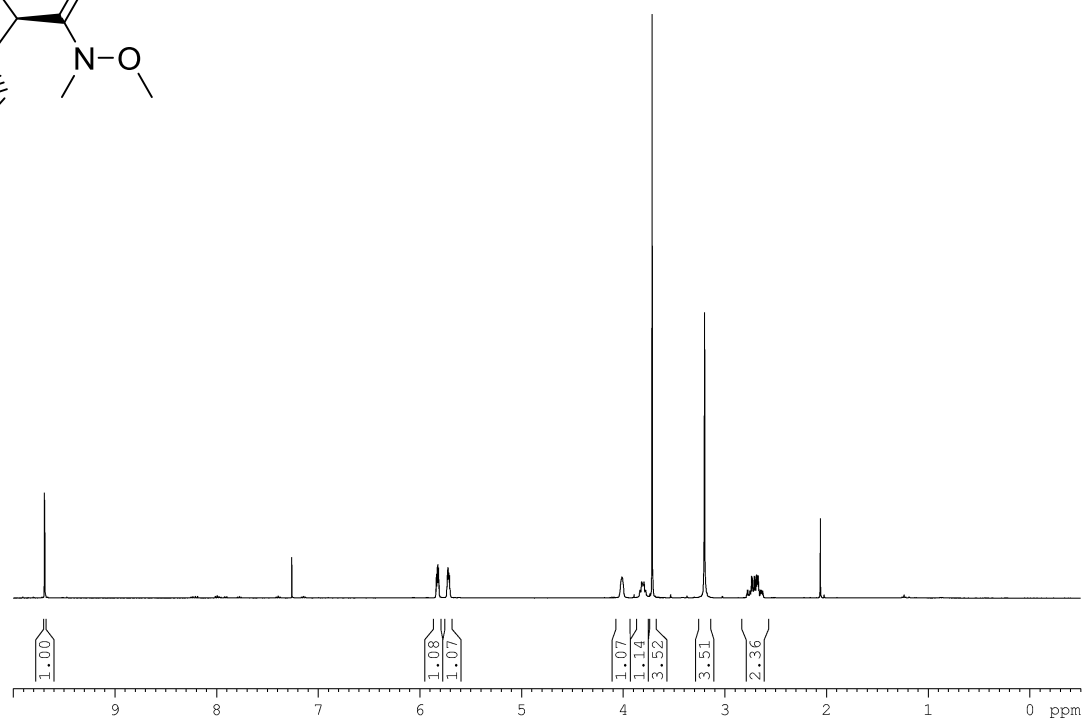
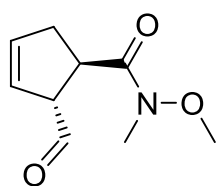


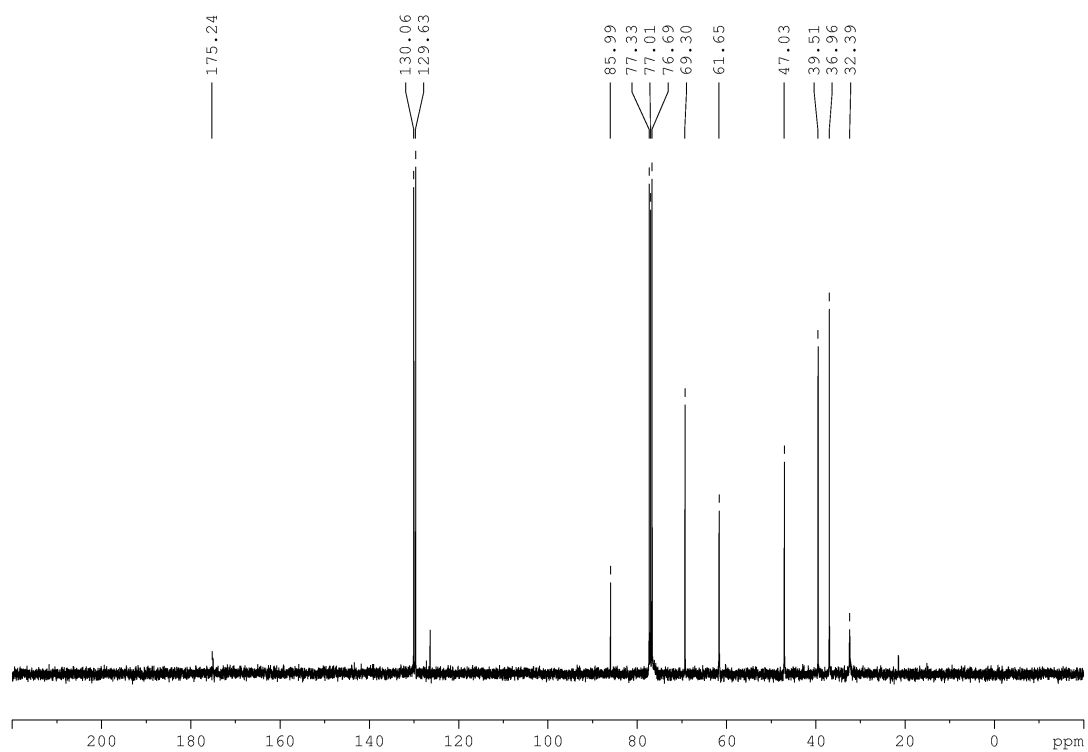
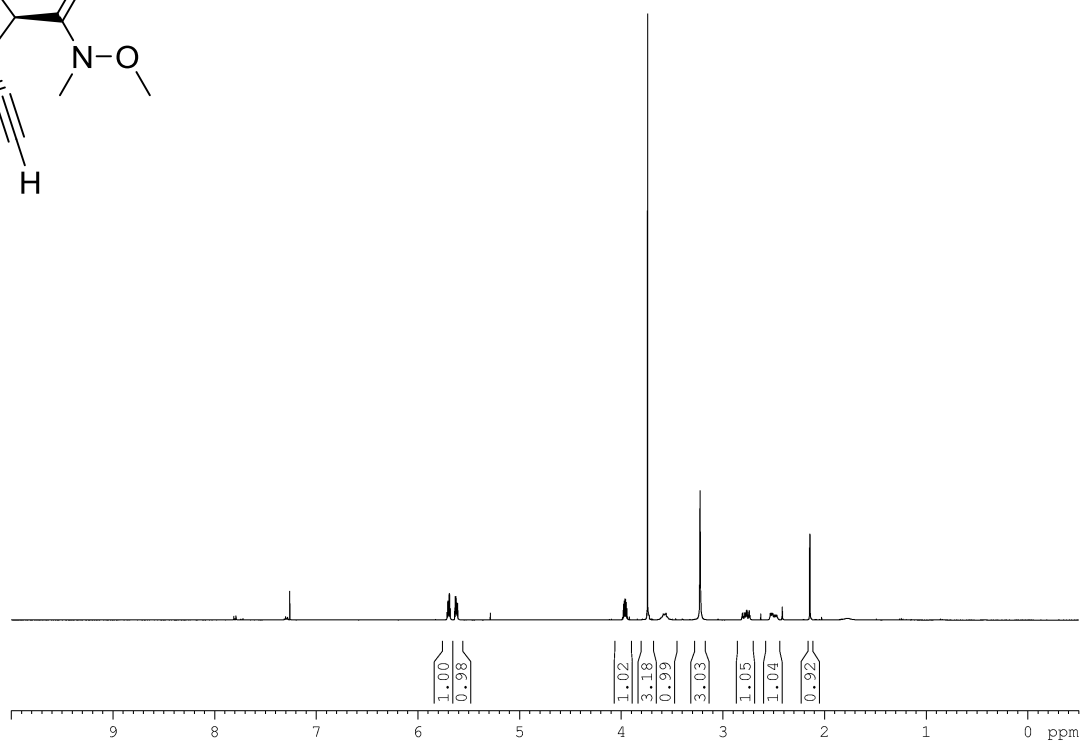
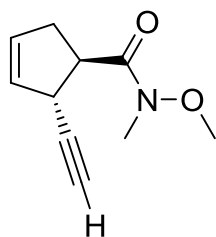


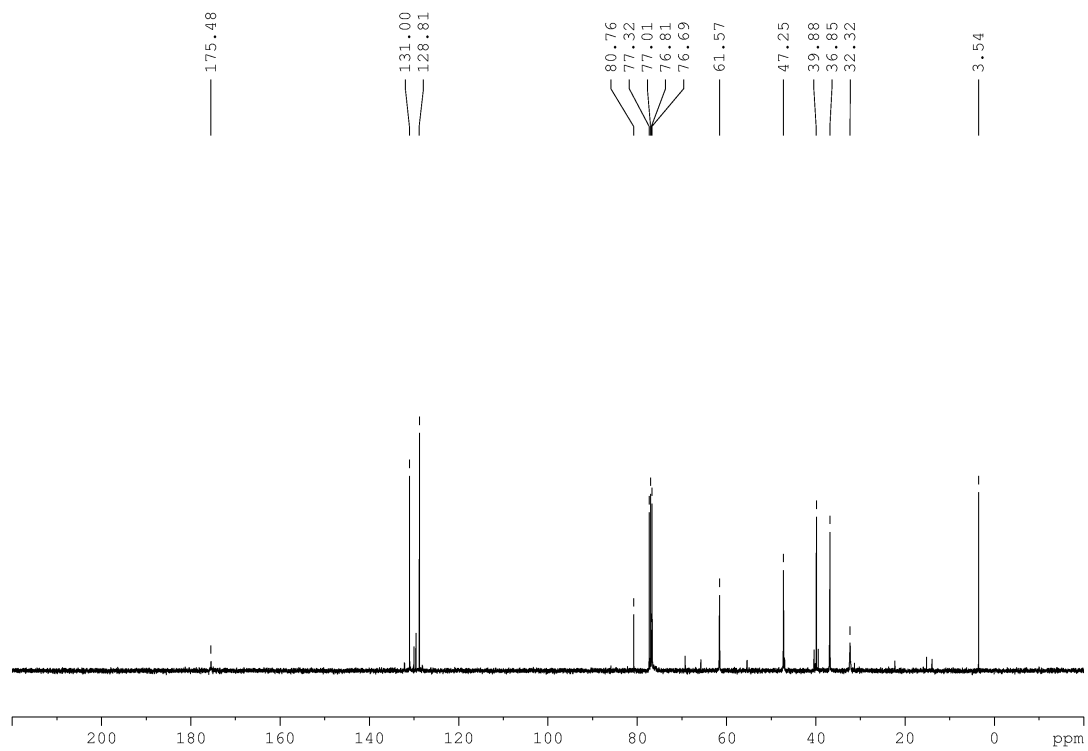
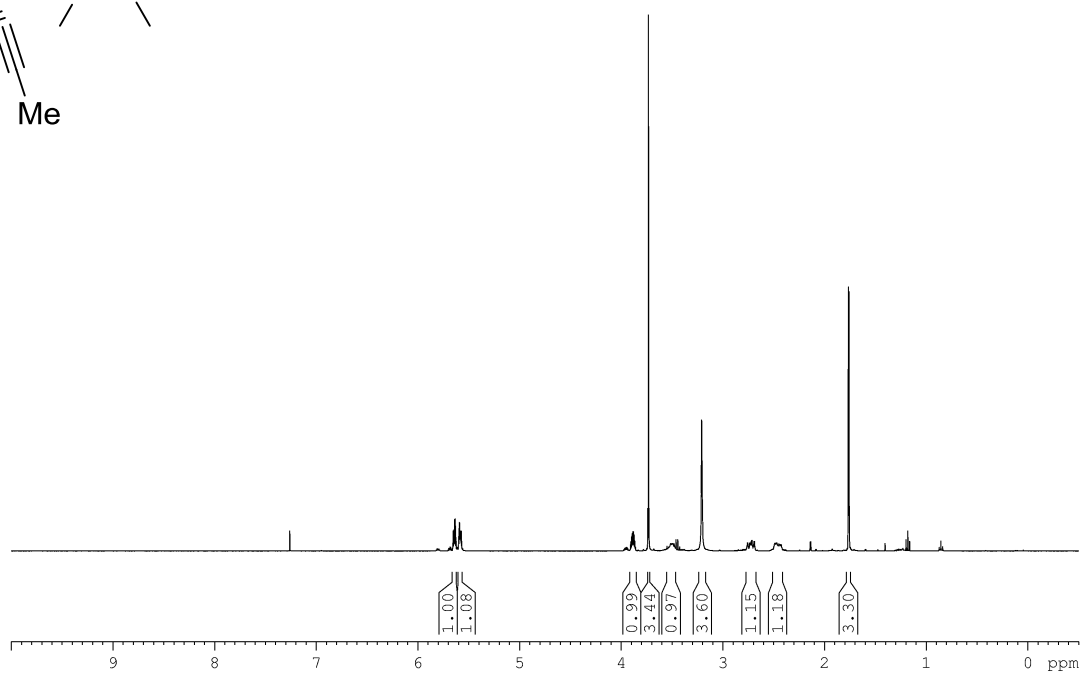
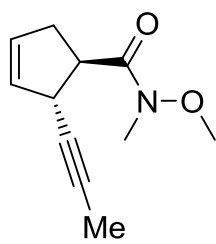


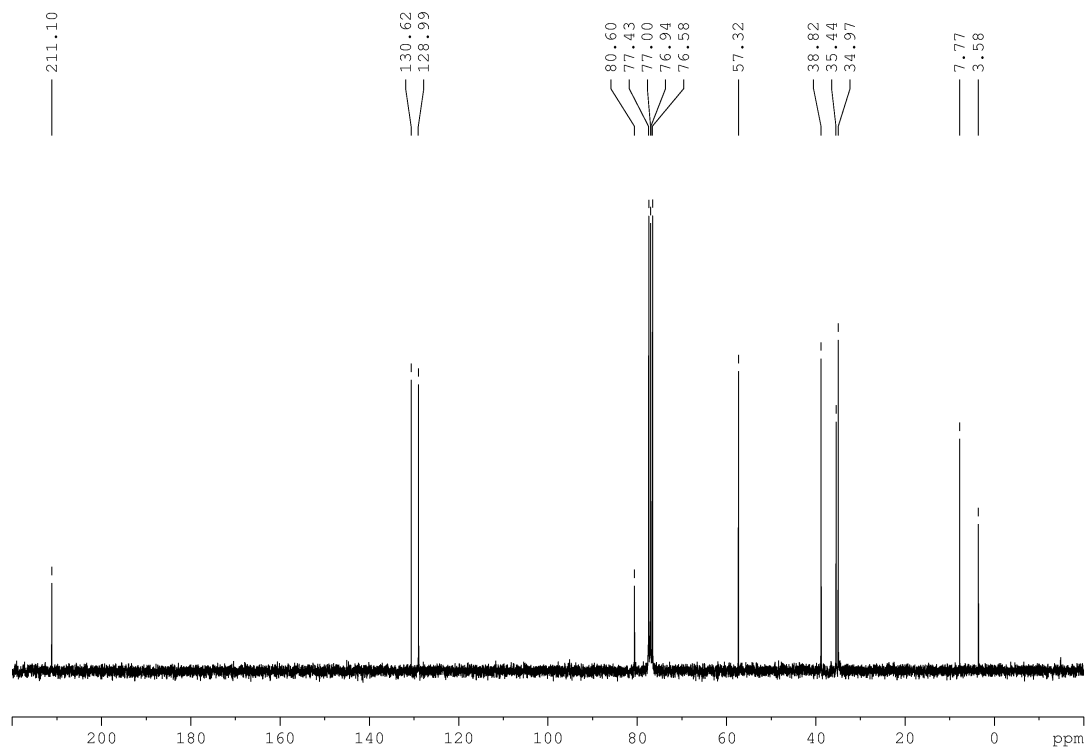
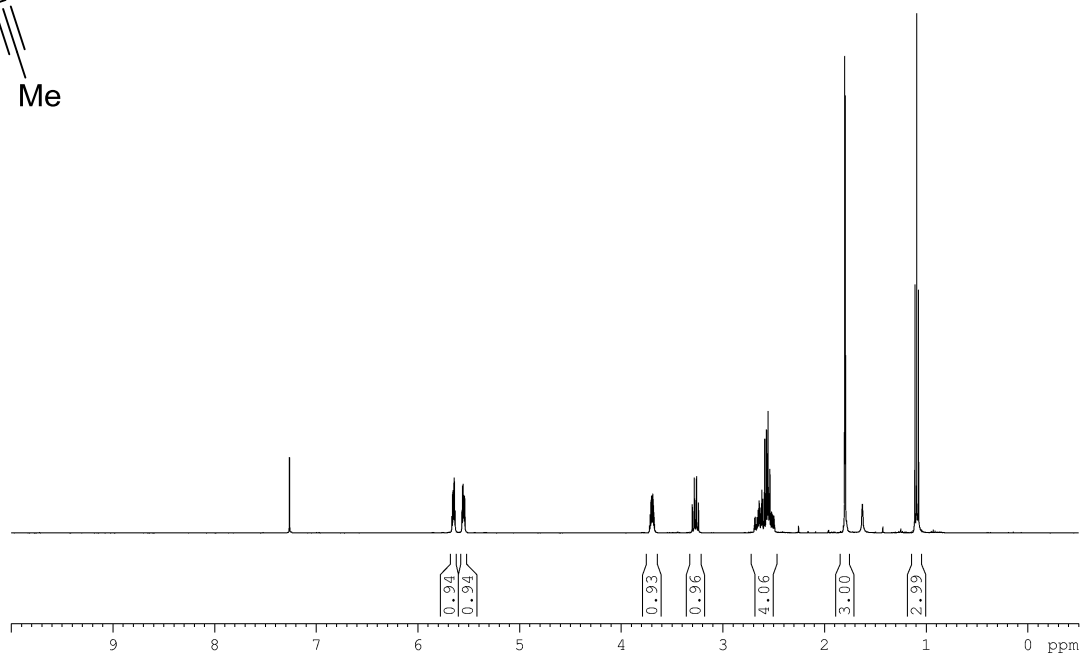
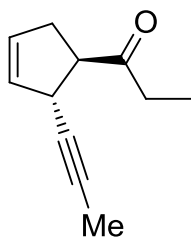


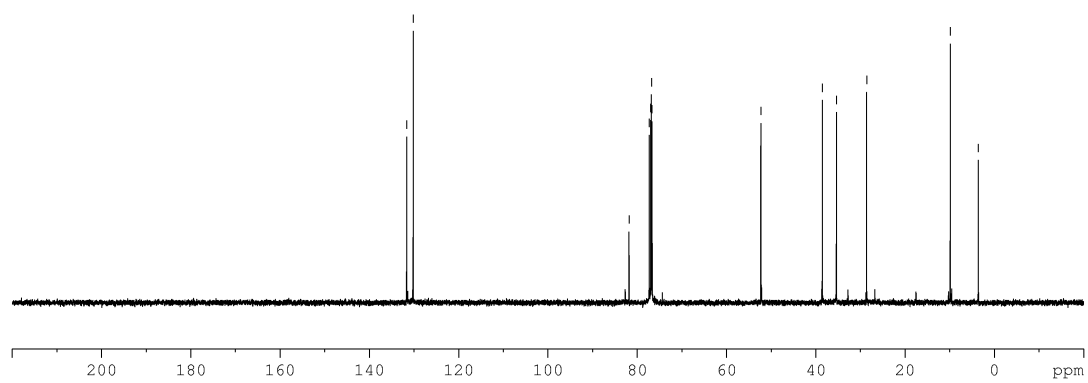
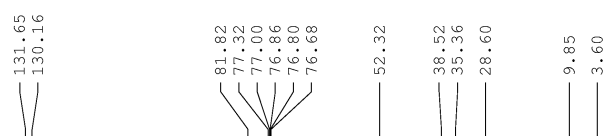
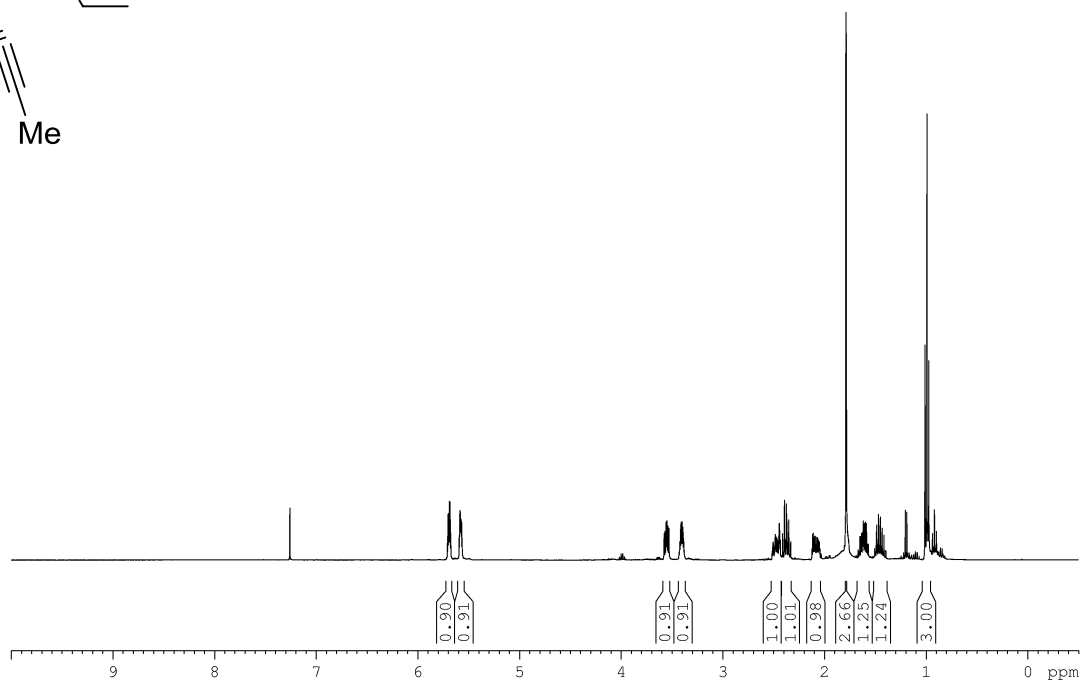
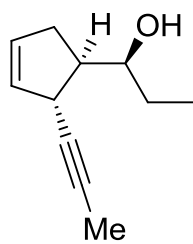


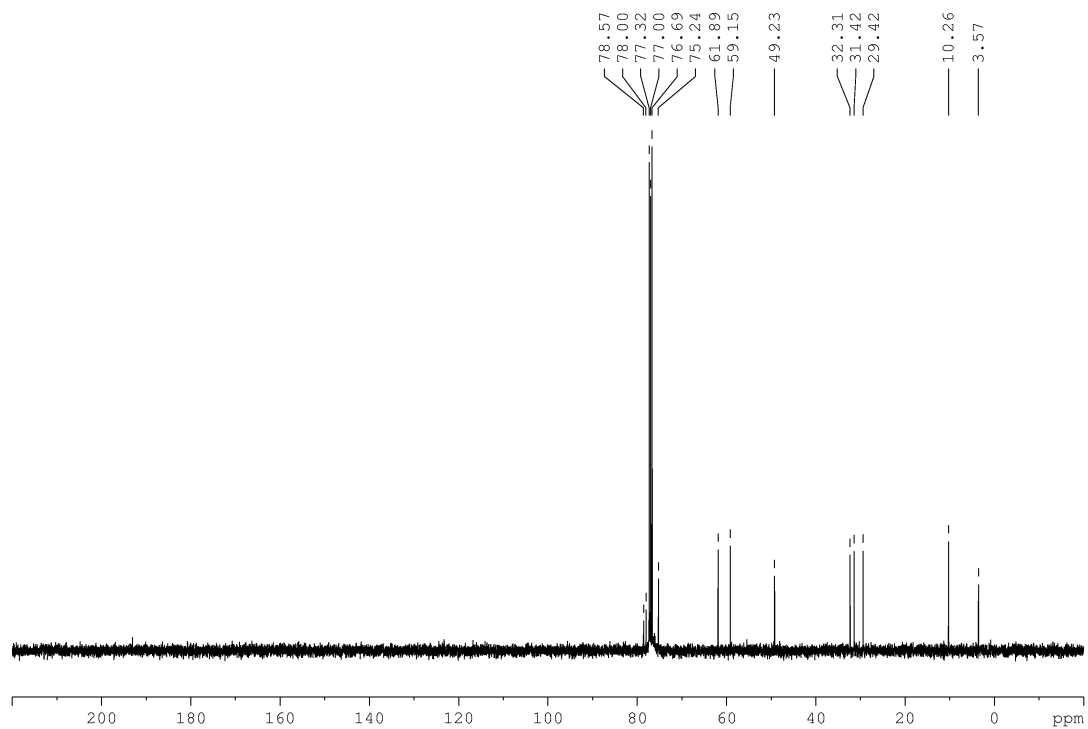
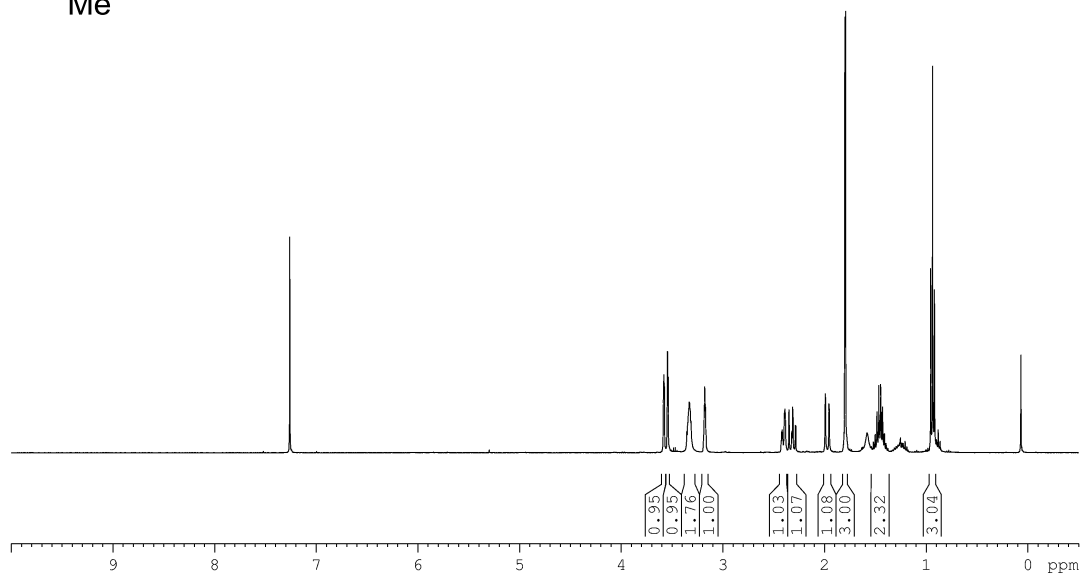
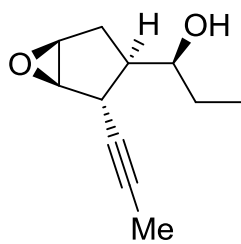


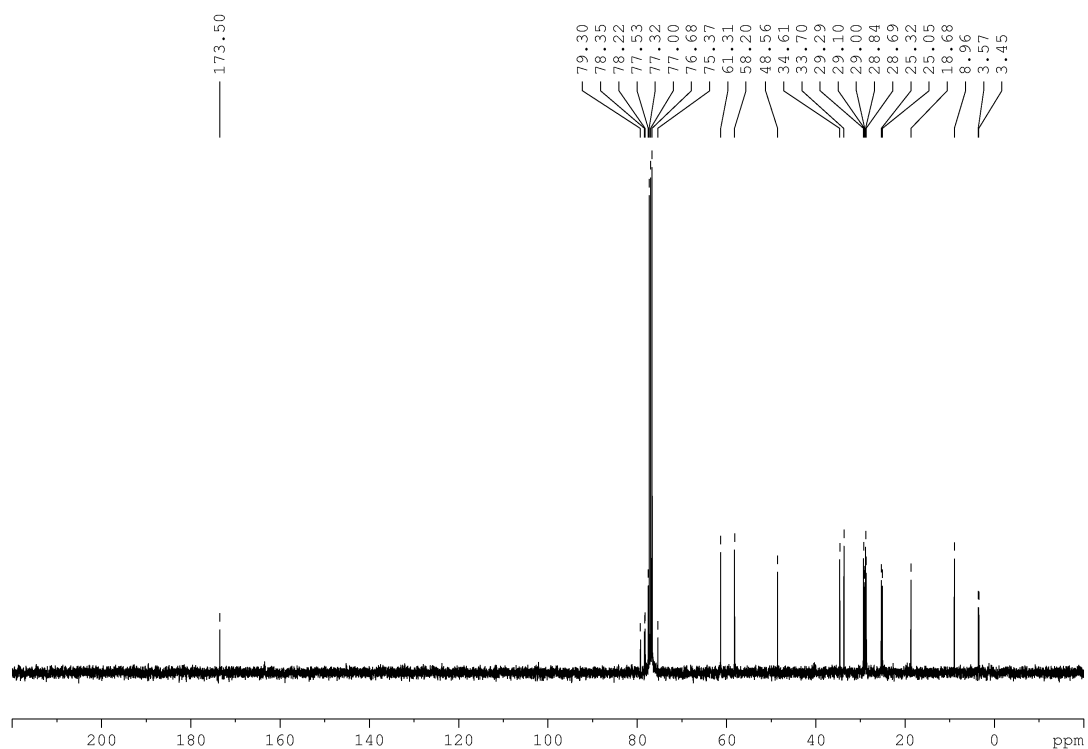
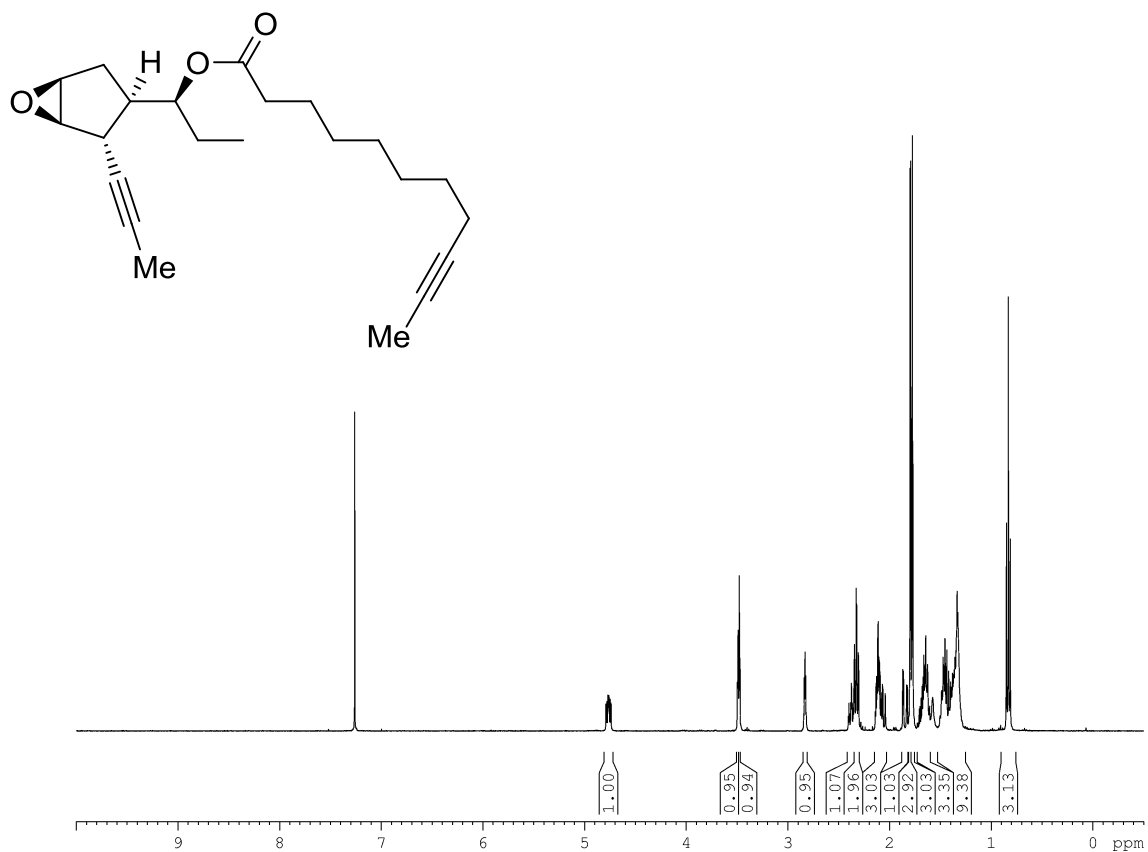


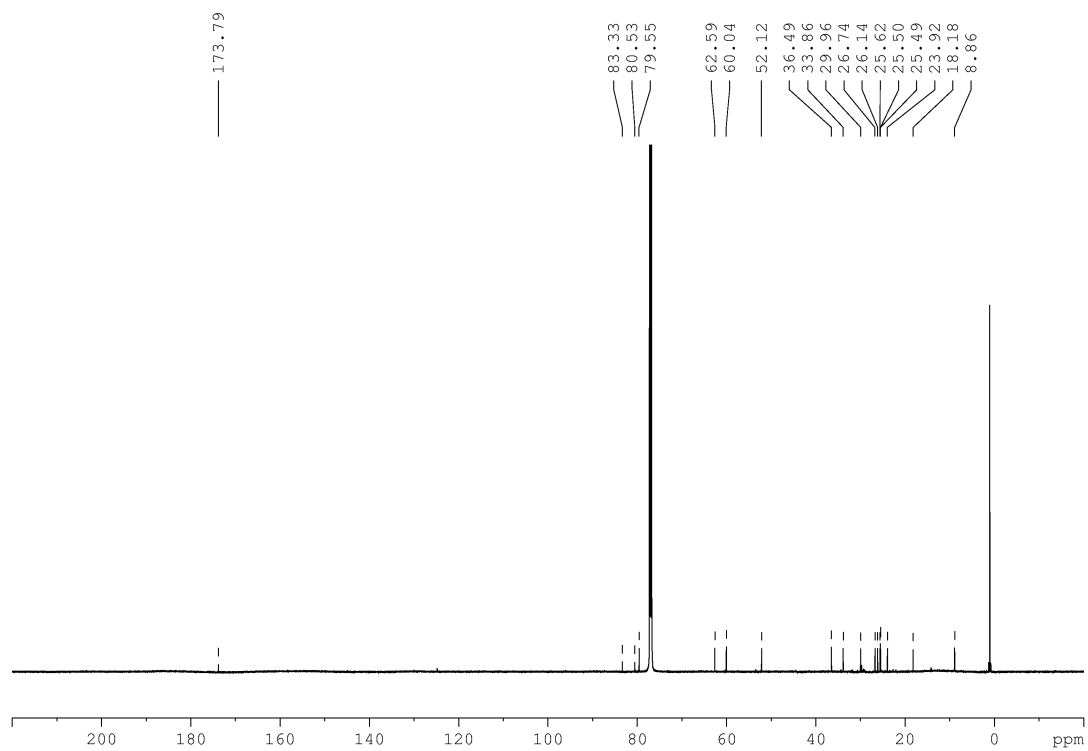
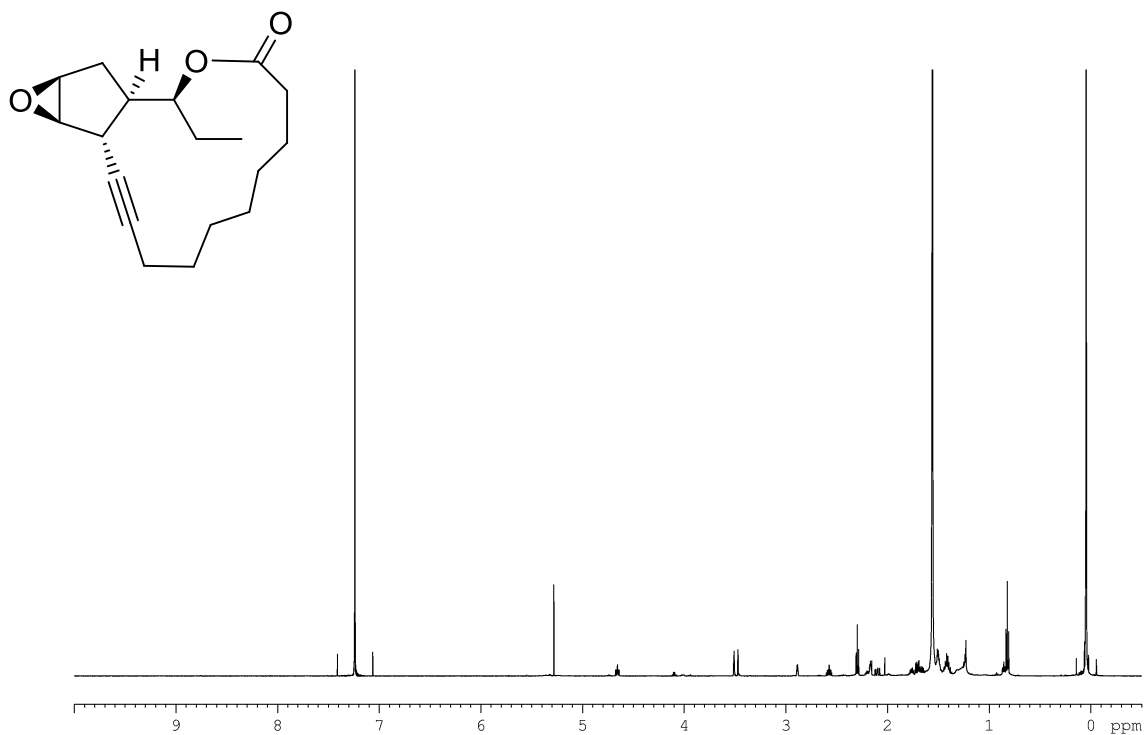


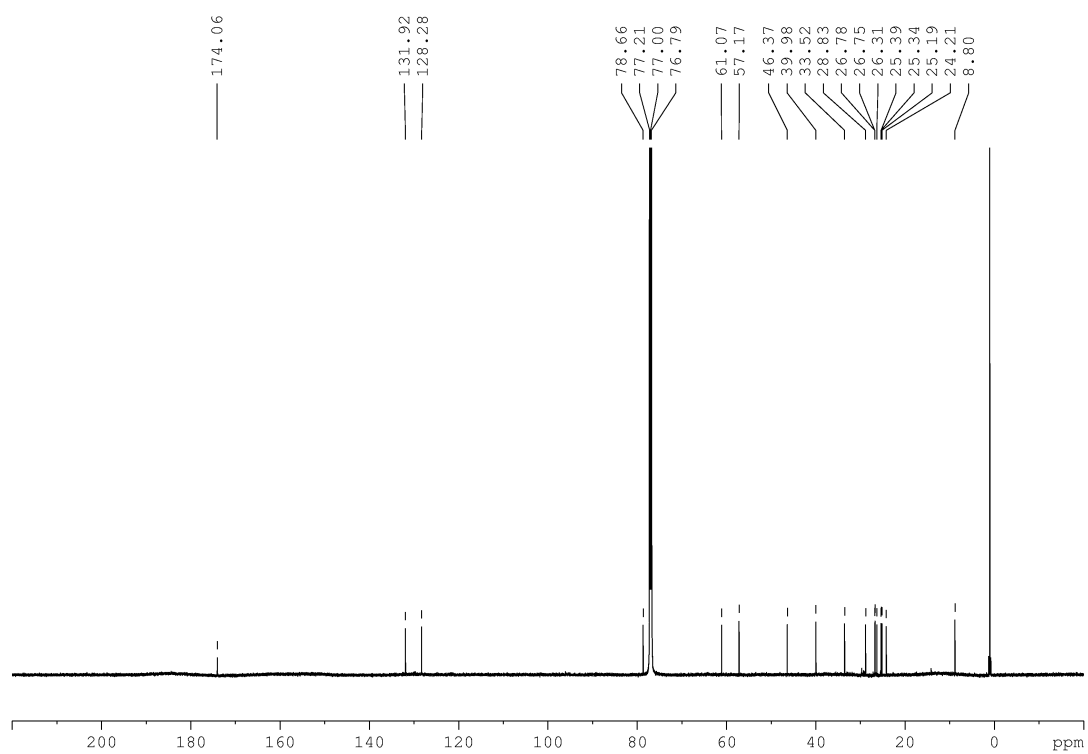
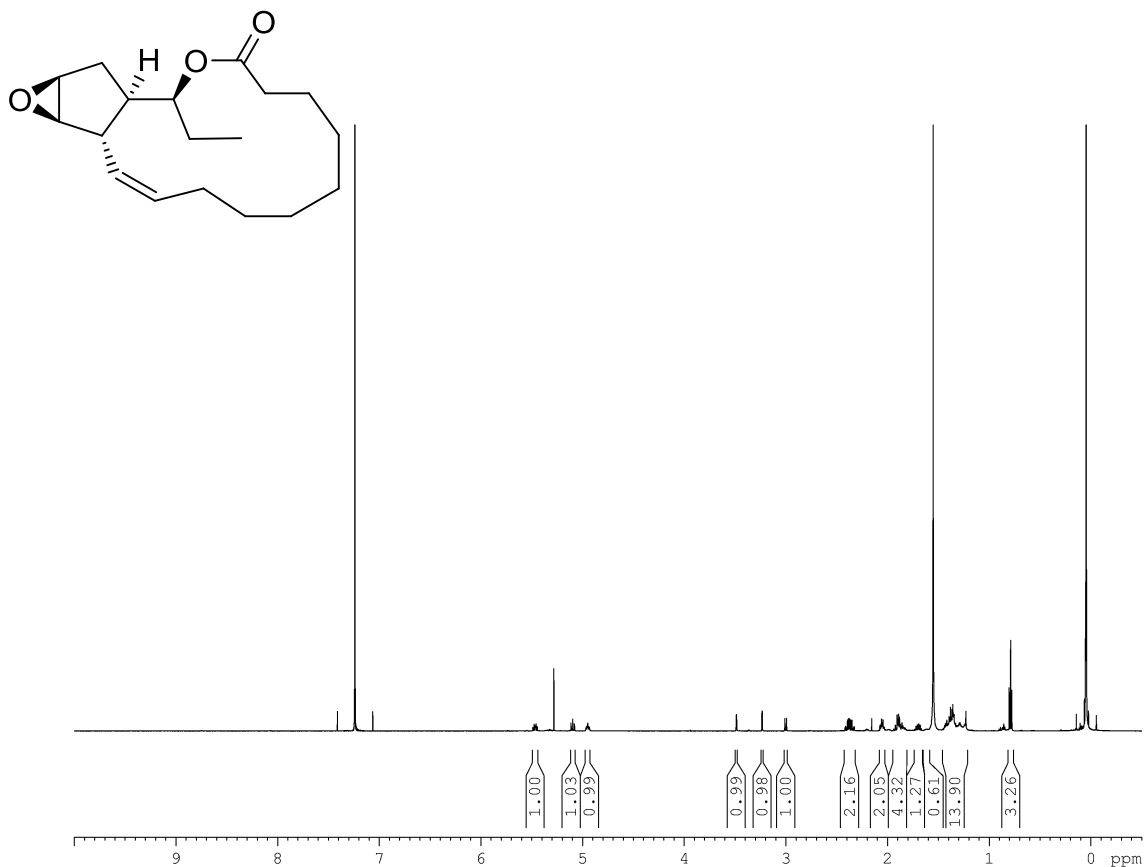


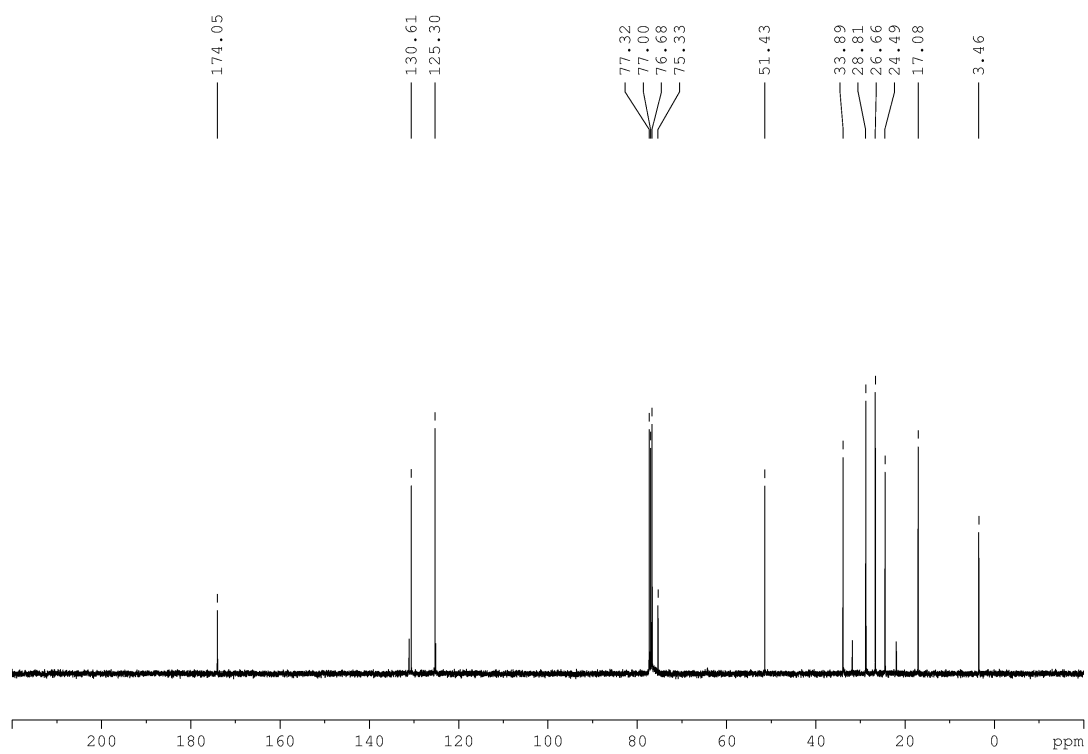
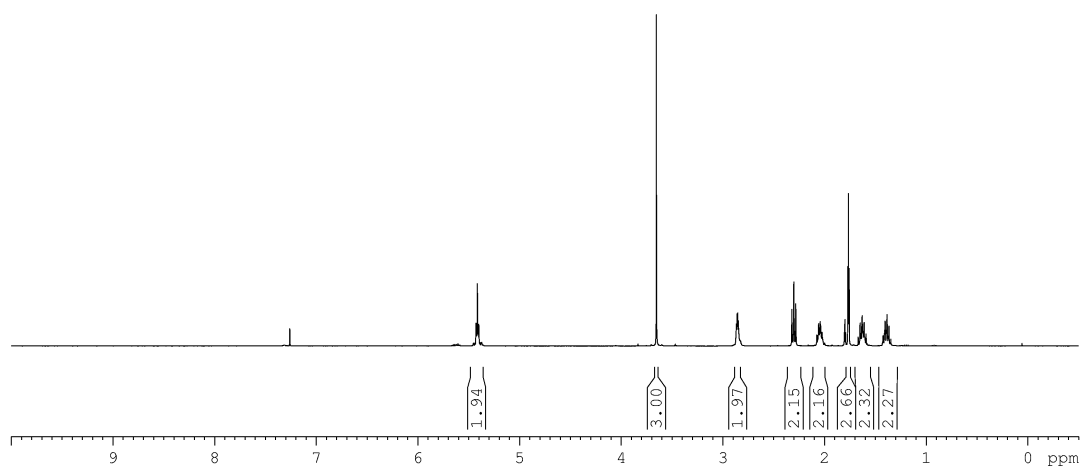
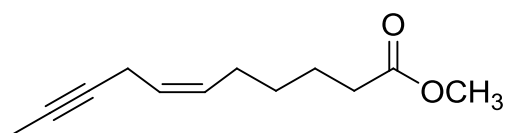


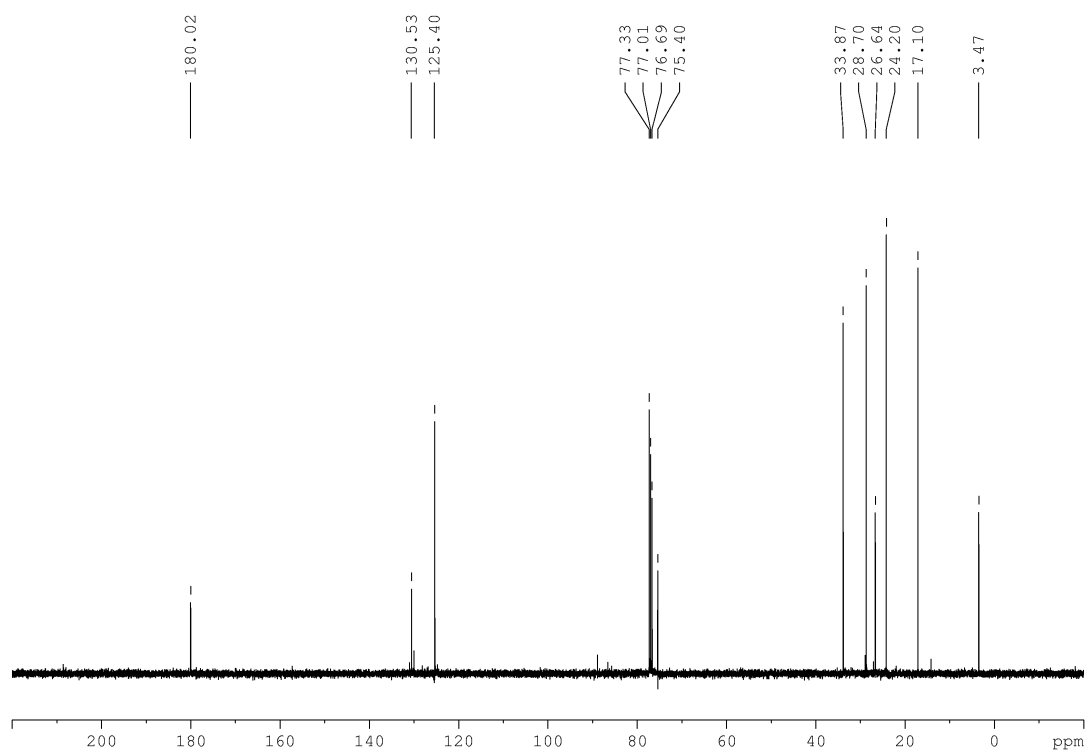
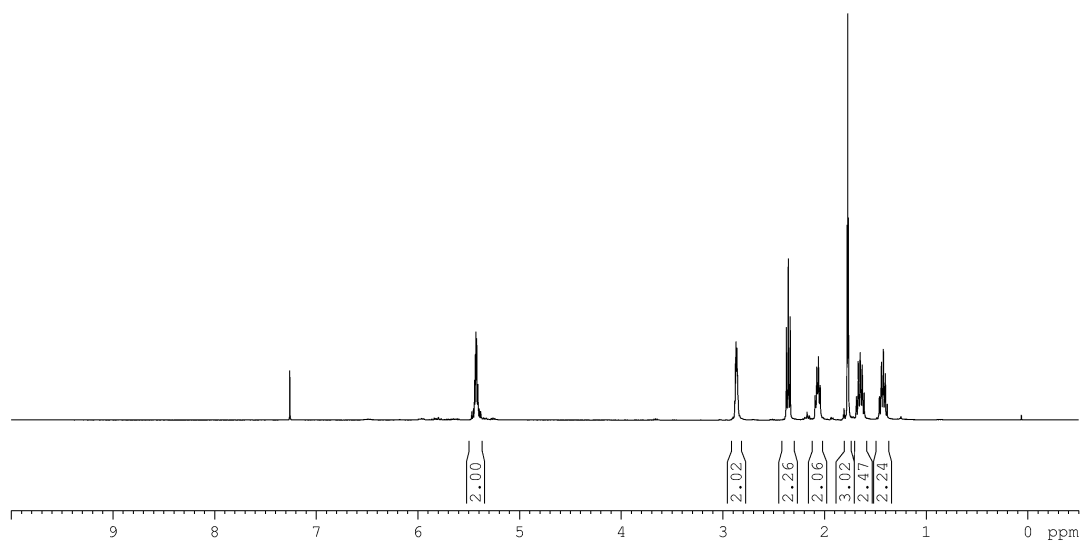
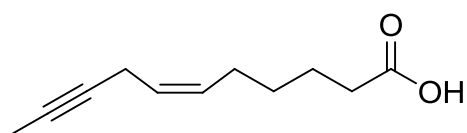


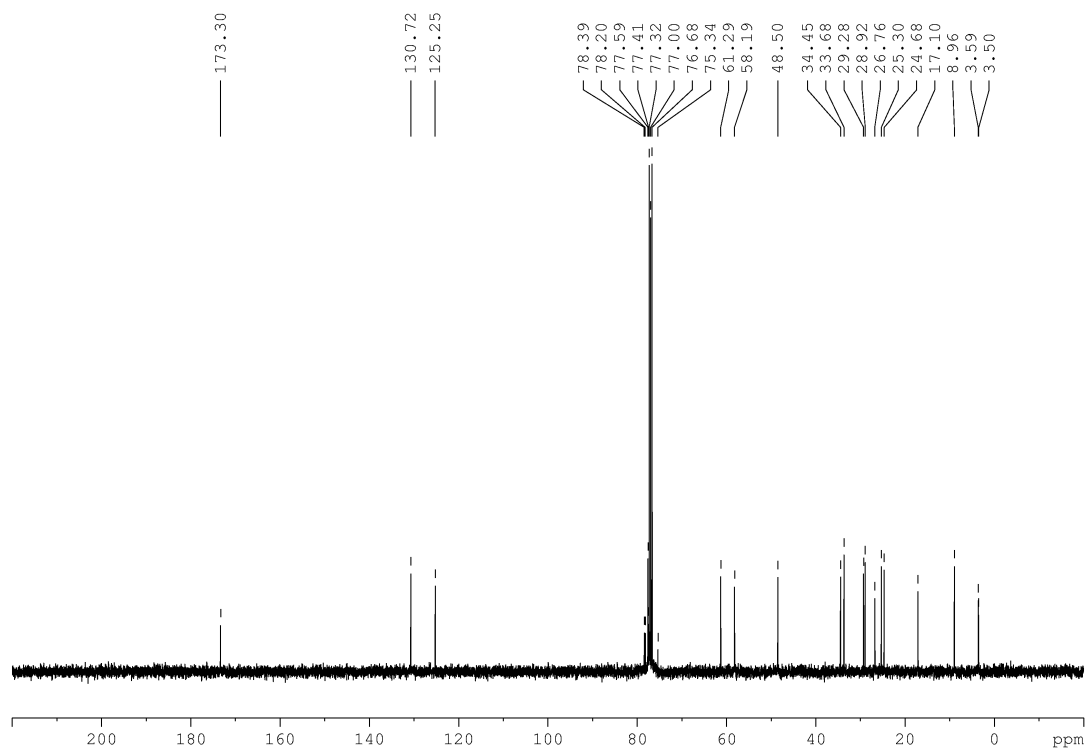
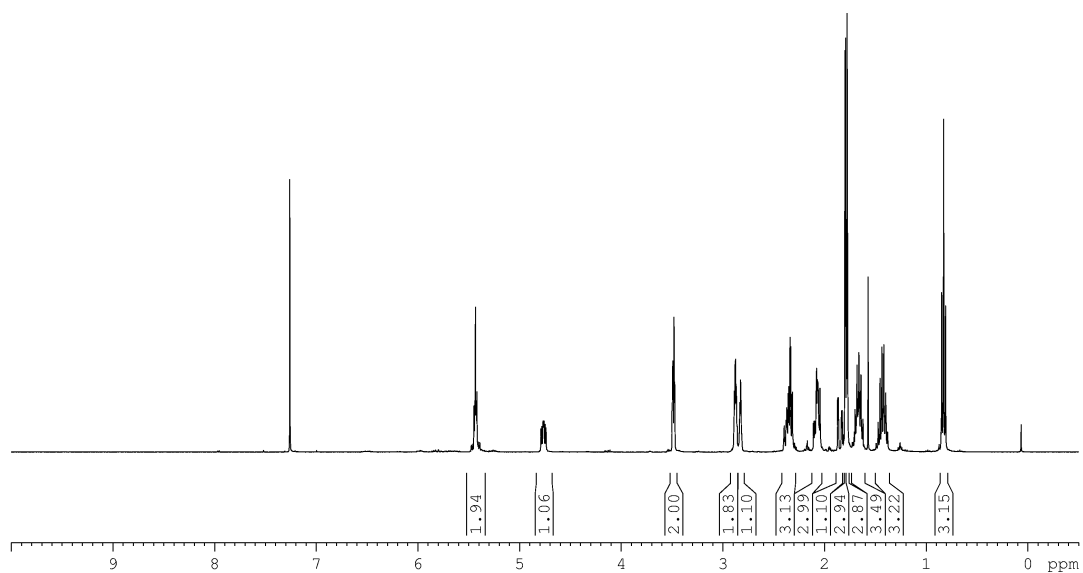
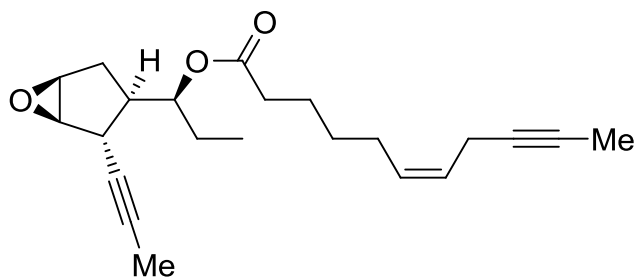


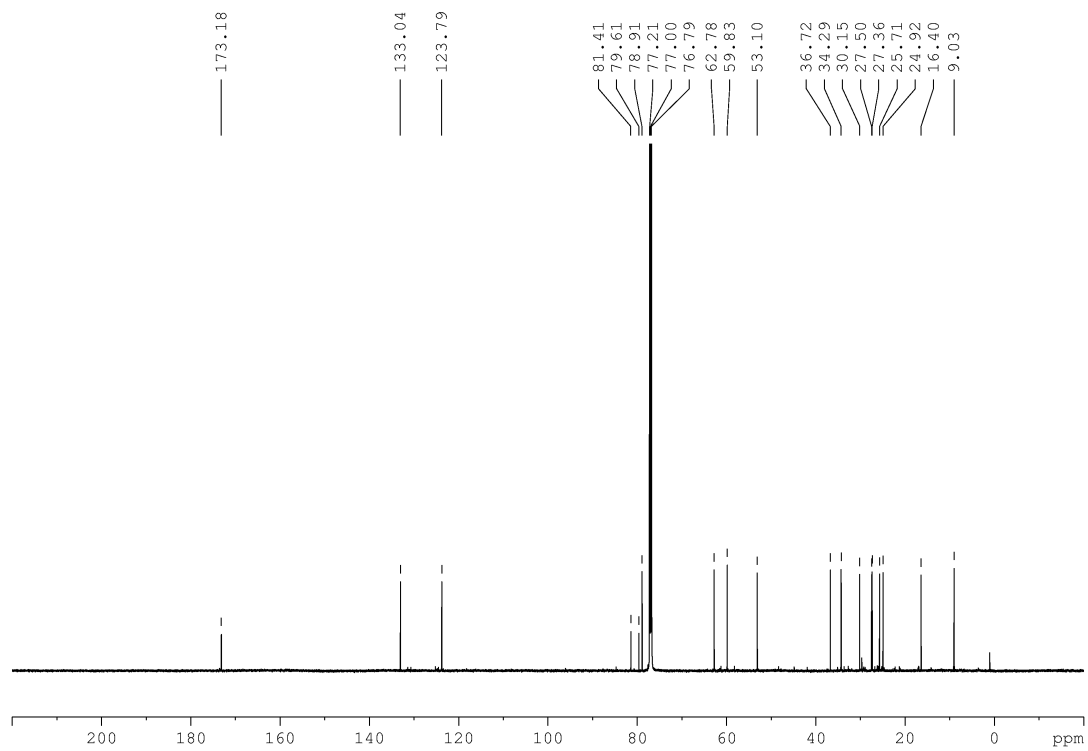
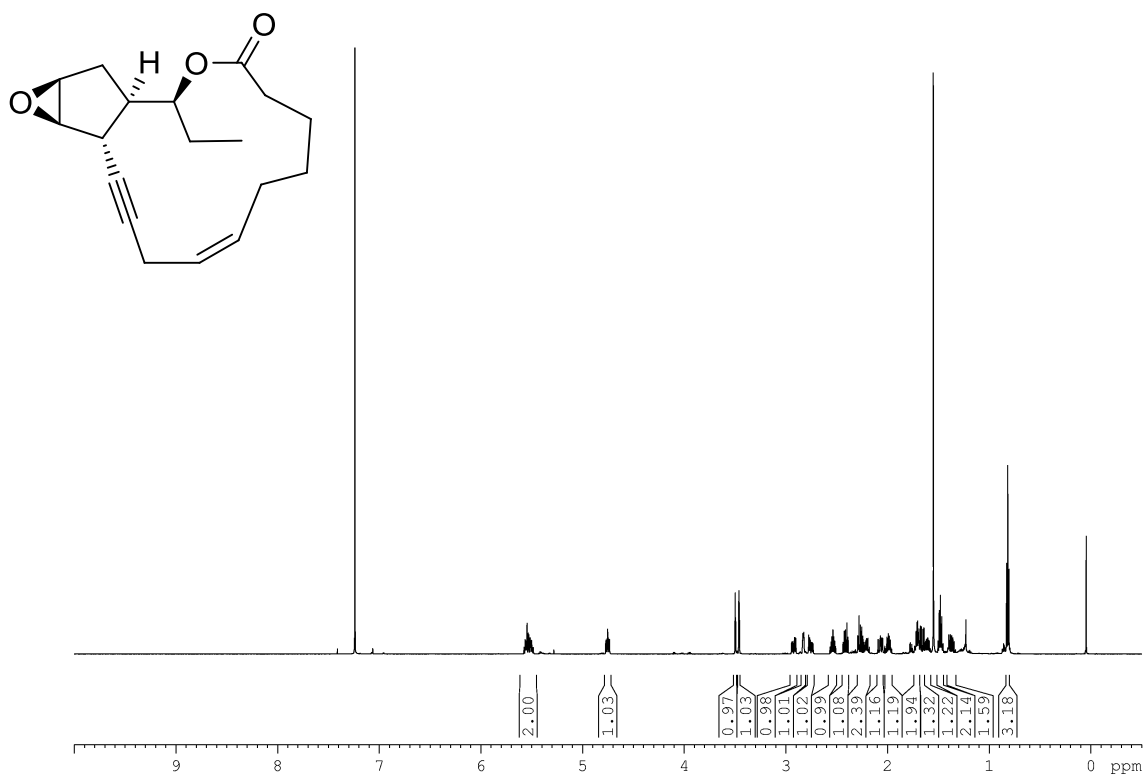


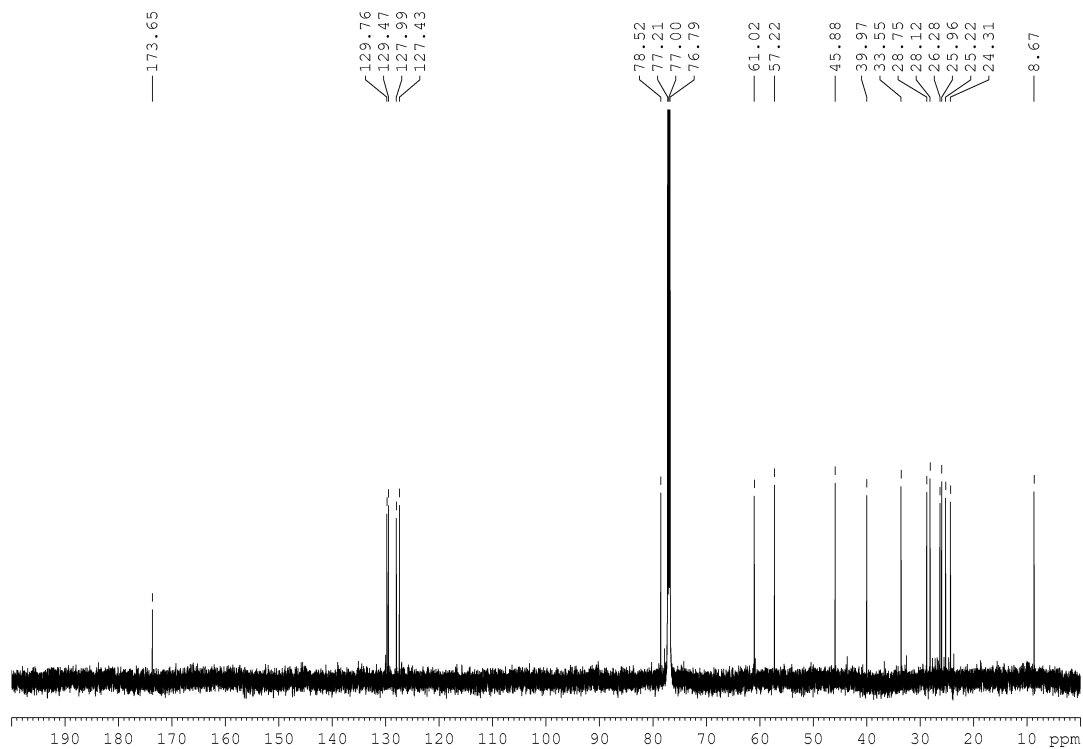
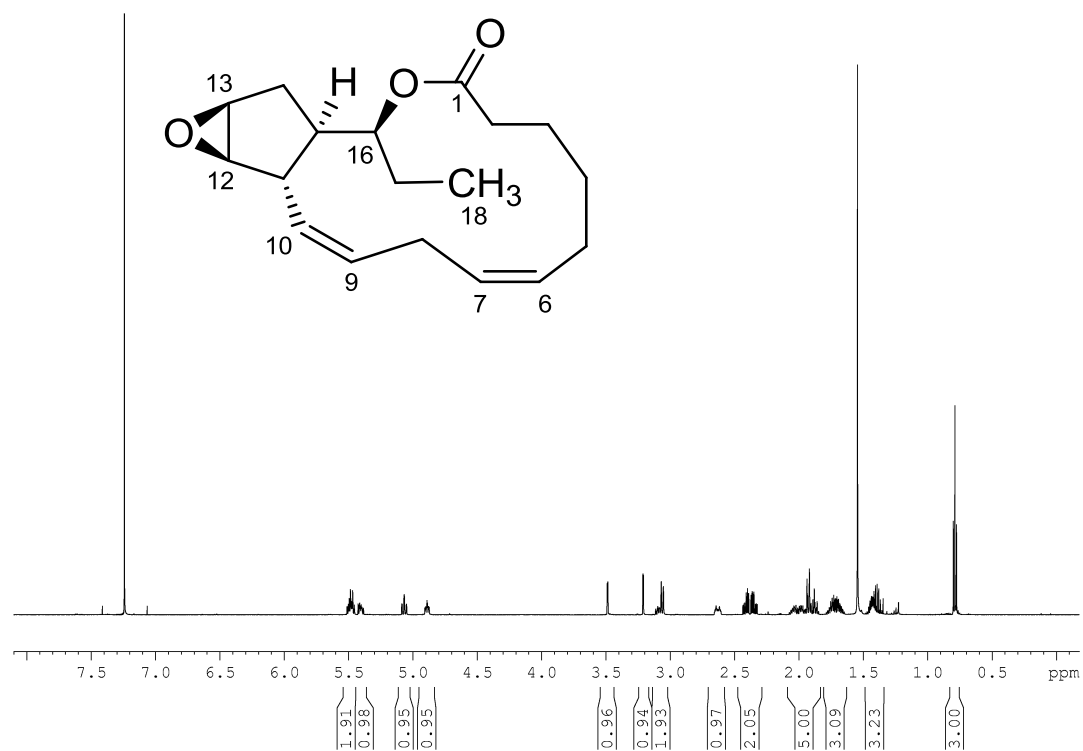


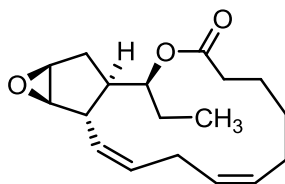
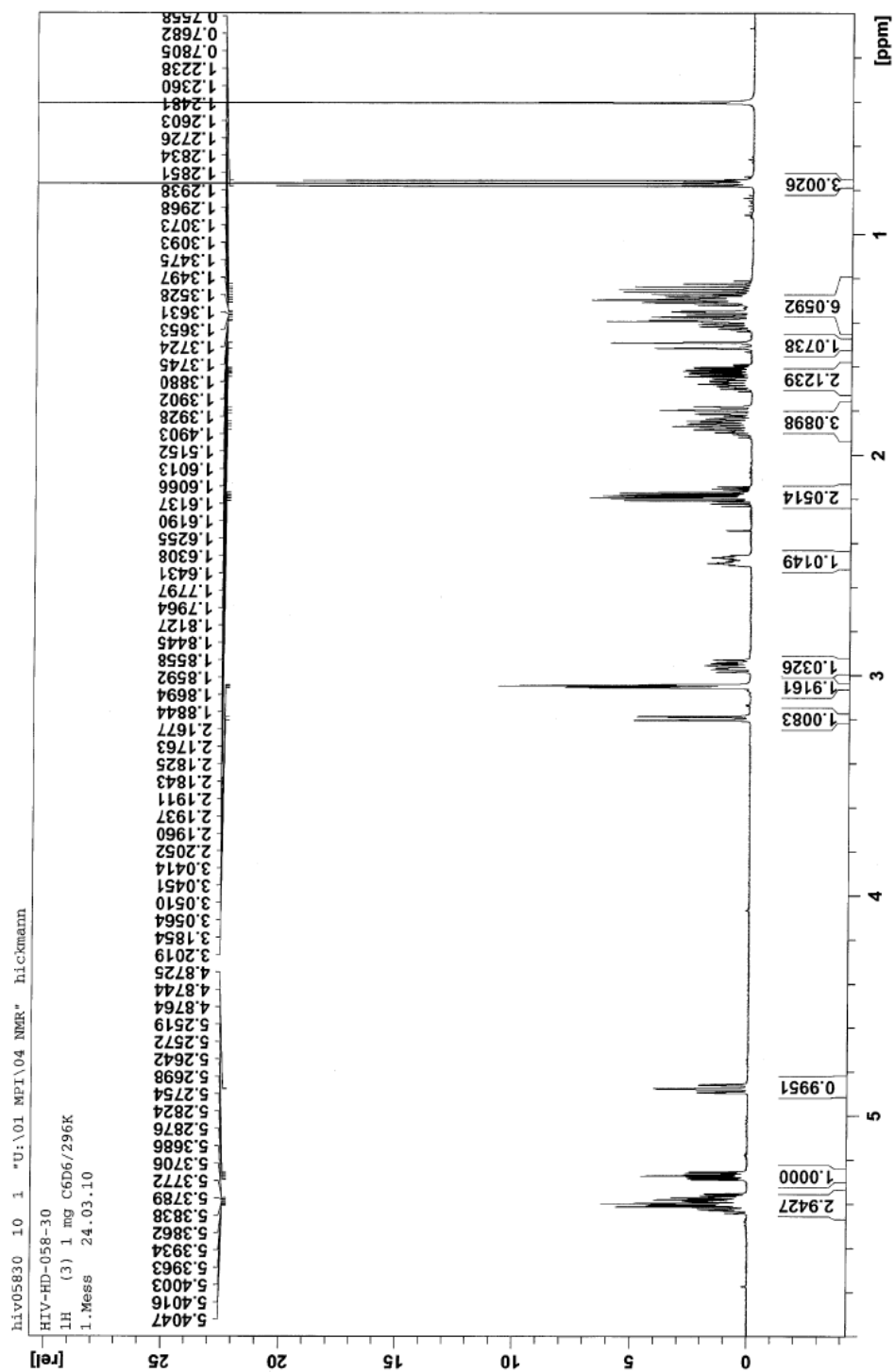


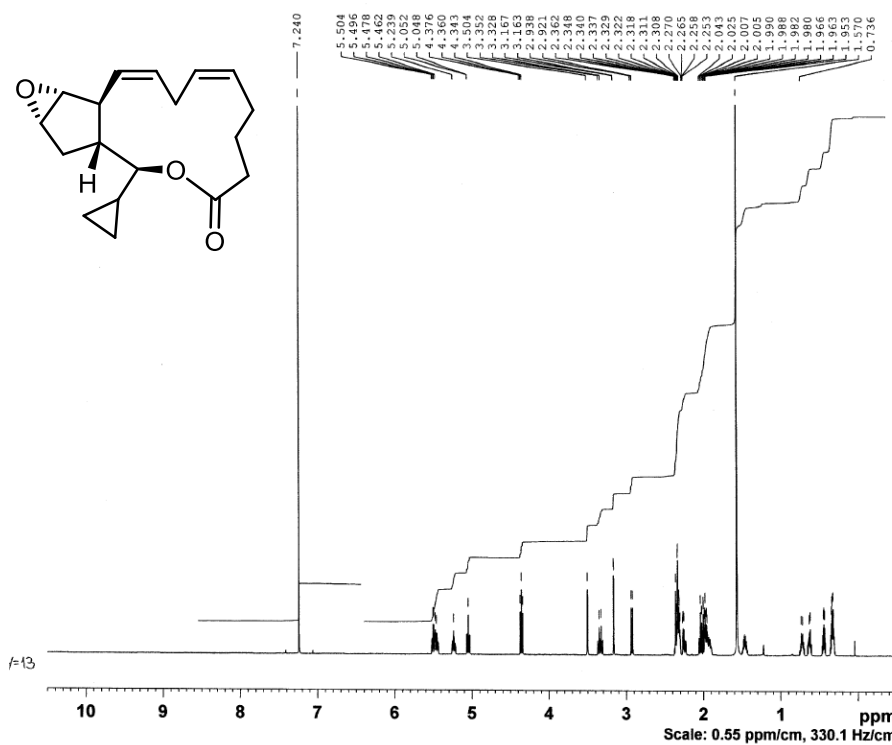








in C_6D_6 



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DE 10.00 usec
TE 290.5 K
D1 1.00000000 sec
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SP=24.87 2m

HIV-HD-156-31
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1.Mess 27.07.10

