

Biomimetic Synthesis of the Shimalactones

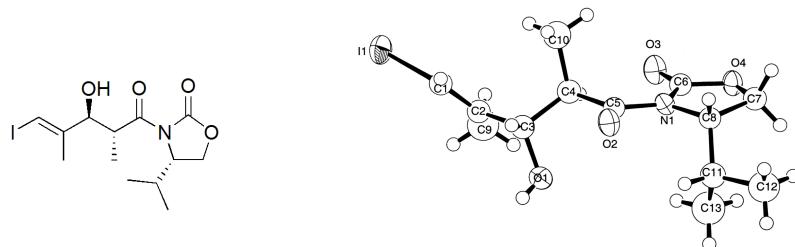
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Supporting Information

General Experimental Details: Flash column chromatography was carried out with EcoChrom ICN SiliTech 32-63 D 60Å silica gel. Reactions and chromatography fractions were monitored with Merck silica gel 60 F₂₅₄ TLC plates and visualized using charring solutions of potassium permanganate or 2,4-dinitrophenylhydrazine. Reactions were carried out under inert atmosphere in oven-dried glassware and were magnetically stirred. Ether, THF, toluene, and CH₂Cl₂ were purified by passage over activated alumina according to the procedure described by Bergman.^[13] Et₃N, *i*-Pr₂EtN, and benzene were distilled from CaH₂ immediately prior to use. All other reagents and solvents were used without further purification from commercial sources. Organic extracts were dried over MgSO₄ unless otherwise indicated.

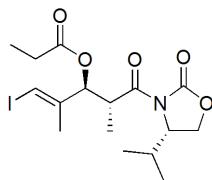
NMR spectra were measured using Varian AV-300, AVQ-400, AVB-400, AV-500, and Brüker DRX-500 spectrometers in CDCl₃ and calibrated from residual solvent signal. IR spectra were measured using a Genesis FT-IR spectrometer by evaporative thin film on a NaCl plate. Low and high resolution mass spectra as well as elemental analyses (LRMS, HRMS, and EA) were obtained using the Micro-Mass Facility operated by the College of Chemistry, University of California, Berkeley on a VG ProSpec Mass Spectrometer by either electron impact (EI) at 70 eV or with fast atom bombardment (FAB) as noted. Melting points were determined with an electrothermal apparatus and are uncorrected. Optical rotation was determined using a Perkin-Elmer 241 polarimeter equipped with mercury and 589 nm sodium lamps. Crystallographic analysis was performed at the Chexray Facility operated by the College of Chemistry, University of California, Berkeley using a Bruker SMART CCD (charge coupled device)-based diffractometer with graphite monochromated Mo-K α radiation.



(S)-3-((E)-(2*R*,3*S*)-3-Hydroxy-5-iodo-2,4-dimethylpent-4-enoyl)-4-isopropyl-oxazolidin-2-one (10). Activated manganese dioxide (1.22 g, 14.0 mmol) was added to a solution of (*E*)-3-iodo-2-methyl-prop-2-en-1-ol (200 mg, 1.01 mmol) in ether (4 mL) and the resulting suspension was stirred for 1 h. The reaction mixture was filtered through a Celite plug under argon and washed with dry ether (8 mL). The filtrate was dried over 3 Å molecular sieves (powder, 200 mg) for 30 min and cooled to -78 °C. In a separate

flask propionyloxazolidinone **8** (128 mg, 0.691 mmol) was dissolved in ether (2 mL) and cooled to 0 °C. *n*-Bu₂BOTf (0.35 mL, 1.40 mmol) was added dropwise to this solution followed by *i*-Pr₂EtN (0.14 mL, 0.804 mmol) and after stirring for 45 min the mixture was cooled to -78 °C. The solution containing the aldehyde was cannulated into this solution over 10 min and the resulting mixture was stirred for 6 h. The reaction mixture was then quenched with tartaric acid (0.52 g) and allowed to warm to rt overnight. Water (20 mL) was then added and the mixture was extracted with ether (3 x 20 mL). The combined organic phases were washed with saturated aqueous NaHCO₃ (2 x 20 mL) and cooled to 0 °C. A mixture of 5:1 MeOH:30% aqueous H₂O₂ (12 mL) was added and the mixture was stirred at rt for 30 min. It was then washed with saturated aqueous NaHCO₃ (20 mL), brine (20 mL), dried, and concentrated. The resulting biphasic mixture was pushed through a plug of silica using 20% EtOAc/hexanes. Purification by silica gel chromatography (20% EtOAc/hexanes) afforded **10** (208 mg, 79%) as a white solid along with propionyloxazolidinone **8** starting material (8.5 mg) as a colorless oil. Suitable crystals for the X-ray analysis were grown by evaporation from hexanes/ether (1:1) with trace MeOH (see the CIF file for experimental details).

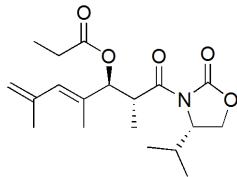
Data for **10**: R_f 0.33 (25% EtOAc/hexanes); IR 3473, 1781, 1693 cm⁻¹; ¹H NMR (500 MHz) δ 6.33 (s, 1H), 4.42 (m, 1H), 4.29 – 4.18 (m, 4H), 3.19 (d, 1H, *J* = 6.5 Hz), 2.34 (m, 1H), 1.85 (s, 3H), 1.08 (d, 3H, *J* = 6.5 Hz), 0.91 (d, 3H, *J* = 7.0 Hz), 0.87 (d, 3H, *J* = 7.0 Hz); ¹³C NMR (125 MHz) δ 176.2, 154.5, 147.7, 80.8, 79.9, 63.6, 59.0, 40.2, 28.6, 19.6, 18.1, 14.9, 14.8; HRMS not obtained (compound unstable under conditions); M.P. = 116.0 – 116.5 °C; [α]_D²³ = + 44.7° (c = 1.00, CHCl₃); anal. calcd for C₁₃H₂₀INO₄: C, 40.96; H, 5.29; N, 3.67, found: C, 41.25; H, 5.27; N, 3.80.



Propionic acid (E)-(S)-3-iodo-1-[(R)-2-((S)-4-isopropyl-2-oxooxazolidin-3-yl)-1-methyl-2-oxoethyl]-2-methylallyl ester (11). Propionic anhydride (1.80 mL, 14.0 mmol), Et₃N (1.80 mL, 13.0 mmol), and DMAP (360 mg, 2.94 mmol) were added to a solution of alcohol **25** (4.04 g, 10.6 mmol) in CH₂Cl₂ (100 mL) and the resulting solution was stirred for 1 h. The reaction mixture was then cooled to rt, diluted with CH₂Cl₂ (100 mL) and washed with 1 M HCl (50 mL), saturated aqueous NaHCO₃ (50 mL), and brine (50 mL). The solution was dried and concentrated. Purification by silica gel chromatography (20% EtOAc/hexanes) gave **11** (4.46 g, 96%) as a white solid.

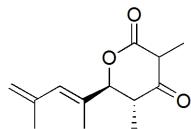
Data for **11**: R_f 0.38 (25% EtOAc/hexanes); IR 1778, 1738, 1703 cm⁻¹; ¹H NMR (400 MHz) δ 6.55 (s, 1H), 5.56 (d, 1H, *J* = 10.8 Hz), 4.45 – 4.19 (m, 4H), 2.33 – 2.15 (m, 3H), 1.82 (s, 3H), 1.07 (t, 3H, *J* = 7.6 Hz), 1.02 (d, 3H, *J* = 7.2 Hz), 0.89 (m, 6H); ¹³C NMR (100 MHz) δ 174.1, 172.8, 153.8, 143.2, 84.6, 79.2, 63.4, 58.7, 39.6, 28.5, 27.6, 19.4, 18.1, 14.8, 14.4, 9.1; HRMS (FAB) calculated for fragment C₁₃H₁₉NO₃I (M-EtCO₂⁺): 364.0410, found: 364.0419, M.P. = 125.5 – 126.5 °C; [α]_D²³ = + 9.9° (c = 1.00, CHCl₃);

anal. calcd for $C_{16}H_{24}INO_5$: C, 43.95; H, 5.53; N, 3.20, found: C, 44.18; H, 5.53; N, 3.35.



Propionic acid (E)-(S)-1-[(R)-2-((S)-4-isopropyl-2-oxo-oxazolidin-3-yl)-1-methyl-2-oxo-ethyl]-2,4-dimethyl-penta-2,4-dienyl ester (13). A solution of stannane **12** (454 mg, 1.37 mmol) and iodide **11** (500 mg, 1.14 mmol) in DMF (3 mL) was lyophilized three times. Then CuI (50 mg, 0.26 mmol), Pd(PPh₃)₄ (95 mg, 0.082 mmol), and CsF (350 mg, 2.3 mmol) were added. The reaction mixture was stirred at 45 °C for 6.5 h in the dark. It was then diluted with ether (30 mL) and water (40 mL), filtered through a plug of Celite, and washed with ether (100 mL). The phases were separated and the aqueous phase was extracted with ether (20 mL). The combined organic phases were washed with 10% aqueous NaCl (2 x 30 mL) and brine (30 mL), then dried and concentrated. Purification by silica gel chromatography (2% TEA, 25% EtOAc, 73% hexanes) afforded **13** (370 mg, 92%) as a light-yellow oil, which solidified upon storage at 0 °C.

Data for **13**: R_f 0.50 (25% EtOAc/hexanes); IR 2968, 1782, 1741, 1701 cm⁻¹; ¹H NMR (400 MHz) δ 6.06 (s, 1H), 5.40 (d, 1H, J = 10.4 Hz), 5.02 (s, 1H), 4.86 (s, 1H), 4.47 – 4.44 (m, 1H), 4.32 – 4.18 (m, 3H), 2.33 (m, 1H), 2.20 (m, 2H), 1.85 (s, 3H), 1.79 (d, 3H, J = 1.2 Hz), 1.09 – 1.04 (m, 6H), 0.91 – 0.88 (m, 6H); ¹³C NMR (100 MHz) δ 174.9, 173.0, 153.9, 141.1, 133.7, 131.8, 116.5, 82.0, 63.3, 58.7, 39.8, 28.5, 27.8, 23.6, 18.1, 14.8, 14.6, 13.3, 9.2, HRMS (FAB) calculated for $C_{13}H_{19}NO_3ILi$ ($M+Li^+$): 358.2206, found: 358.2202; M.P. = 48.0 – 51.0 °C; $[\alpha]_D^{23} = +79.9^\circ$ (c = 1.00, CHCl₃); anal. calcd for $C_{19}H_{29}NO_5$: C, 64.93; H, 8.32; N, 3.99, found: C, 65.02; H, 8.28; N, 3.91.



(5R,6S)-6-((E)-1,3-Dimethyl-buta-1,3-dienyl)-3,5-dimethyl-dihydro-pyran-2,4-dione (14). KHMDS (0.885 M in THF, 8.6 mL, 7.6 mmol) was added to a solution of propionate **13** (670 mg, 1.9 mmol) in THF (40 mL) at –78 °C and the reaction mixture was stirred for 2 h. It was then quenched at –78 °C with saturated aqueous NH₄Cl/MeOH/H₂O mixture (1:1:1, 60 mL) and warmed to rt. The mixture was acidified to pH 3 with 1 M HCl and extracted with EtOAc (4 x 30 mL). The combined organic extracts were washed with brine (30 mL), dried, and concentrated. Purification by silica gel chromatography (20% EtOAc/hexanes) afforded **14** (389 mg, 93%) as a white solid.

Data for **14**: R_f 0.28 (25% EtOAc/hexanes); IR 1746, 1715 cm⁻¹; ¹H NMR (400 MHz) δ 6.01 (s, 1H), 5.11 (t, 1H, J = 1.6 Hz), 4.91 (s, 1H), 4.71 (d, 1H, J = 10.8 Hz), 3.55 (q, 1H,

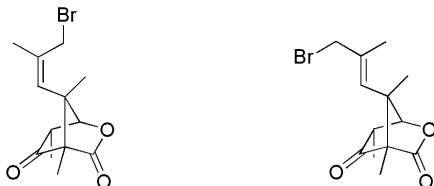
J = 6.8 Hz), 2.53 (m, 1H), 1.88 (s, 3H), 1.85 (d, 3H, *J* = 1.2 Hz), 1.38 (d, 3H, *J* = 6.8 Hz), 1.10 (d, 3H, *J* = 7.2 Hz); ¹³C NMR (100 MHz) δ 204.4, 169.7, 140.4, 134.6, 130.2, 117.2, 86.1, 50.2, 44.4, 23.2, 12.1, 11.8, 8.3; HRMS (FAB) calculated for C₁₃H₁₈O₃ (M⁺): 222.1256, found: 222.1255; M.P. = 83.0 – 84.0 °C; [α]_D²³ = –60.7° (c = 1.00, CHCl₃, 436 nm Hg); anal. calcd for C₁₃H₁₈O₃: C, 70.24; H, 8.16, found: C, 70.01; H, 8.30.



(1*S*,4*S*,6*R*)-4,6,7-Trimethyl-7-(2-methyl-propenyl)-2-oxa-bicyclo[2.2.1]heptane-3,5-dione (15a and 15b). To a solution of β -ketolactone **14** (501 mg, 2.25 mmol) in benzene (64 mL) was added 10-camphorsulfonic acid (522 mg, 2.25 mmol). The reaction tube was sealed and heated to 150 °C for 3.25 hr. The reaction mixture was then cooled to rt, partially concentrated, filtered through a plug of silica, and washed with 50% ether/hexane (15 mL). The resulting solution was concentrated. Purification by silica gel chromatography (8% EtOAc/hexanes) afforded **15a** (214 mg, 43%) as a light-yellow solid and its diastereomer **15b** (113 mg, 22%).

Data for **15a**: R_f 0.53 (25% EtOAc/hexanes); IR 1794, 1751 cm^{–1}; ¹H NMR (500 MHz) δ 5.10 (d, 1H, *J* = 2.5 Hz), 4.94 (s, 1H), 2.70 (qd, 1H, *J*_q = 7.5 Hz, *J*_d = 2.0 Hz), 1.74 (d, 3H, *J* = 0.5 Hz), 1.69 (d, 3H, *J* = 1.0 Hz), 1.34 (s, 3H), 1.21 (d, 3H, *J* = 7.0 Hz), 1.19, (s, 3H); ¹³C NMR (125 MHz) δ 208.3, 172.0, 138.4, 121.7, 85.4, 70.4, 57.7, 44.3, 26.9, 20.1, 17.1, 11.8, 4.9; HRMS (EI⁺) calculated for C₁₃H₁₈O₃ (M⁺): 222.1256, found: 222.1257; M.P. = 73.0 – 74.0 °C; [α]_D²³ = –77.9° (c = 1.03, CHCl₃); anal. calcd for C₁₃H₁₈O₃: C, 70.24; H, 8.16, found: C, 70.50; H, 7.98.

Data for **15b**: R_f 0.41 (25% EtOAc/hexanes); IR 1793, 1750 cm^{–1}; ¹H NMR (400 MHz) δ 5.15 (t, 1H, *J* = 1.4 Hz), 5.10 (d, 1H, *J* = 2.4 Hz), 2.67 (qd, 1H, *J*_q = 7.4 Hz, *J*_d = 2.2 Hz), 1.81 (d, 3H, *J* = 1.2 Hz), 1.76 (d, 3H, *J* = 1.2 Hz), 1.22 (d, 3H, *J* = 7.2 Hz), 1.19 (s, 3H), 1.17, (s, 3H); ¹³C NMR (125 MHz) δ 208.4, 172.3, 138.2, 121.3, 85.0, 70.1, 57.1, 43.3, 27.5, 20.1, 17.7, 11.6, 5.2; HRMS (EI⁺) calculated for C₁₃H₁₈O₃ (M⁺): 222.1256, found: 222.1257; M.P. = 63.0 – 64.0 °C; [α]_D²³ = +76.8° (c = 1.00, CHCl₃); anal. calcd for C₁₃H₁₈O₃: C, 70.24; H, 8.16, found: C, 70.11; H, 8.28.

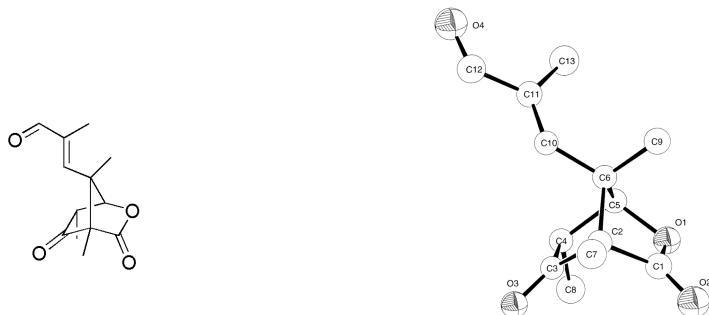


(1*S*,4*S*,6*R*)-7-((E)-3-Bromo-2-methyl-propenyl)-4,6,7-trimethyl-2-oxa-bicyclo[2.2.1]heptane-3,5-dione (16a and 16b). To a solution of bicyclic lactone **15a** (288 mg, 1.29 mmol) in carbon tetrachloride (5.0 mL) were added NBS (236 mg, 1.32 mg) and AIBN (21.0 mg, 0.128 mmol). The reaction mixture was heated to reflux for 1.5 hr, filtered

through a plug of silica, and washed with ether/hexanes (1:1, 15 mL). The resulting solution was concentrated. Purification by silica gel chromatography (gradient from 10% to 15% EtOAc/hexanes) afforded **16a** (182 mg, 47%) and **16b** (194 mg, 50%) as white solids.

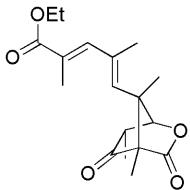
Data for 16a: R_f 0.55 (25% EtOAc/hexanes); IR 1787, 1753 cm^{-1} ; ^1H NMR (500 MHz) δ 5.15 (d, 1H, J = 1.5 Hz), 5.14 (d, 1H, J = 2.0 Hz), 4.08 (d, 1H, J = 10.0 Hz), 3.82 (d, 1H, J = 10.0 Hz), 2.83 (qd, 1H, J_q = 7.3 Hz, J_d = 2.3 Hz), 1.84 (d, 3H, J = 1.5 Hz), 1.37 (s, 3H), 1.18 (m, 6H); ^{13}C NMR (125 MHz) δ 207.8, 171.4, 137.7, 127.3, 85.0, 70.4, 57.6, 44.8, 31.6, 23.0, 17.9, 11.5, 4.9; HRMS (FAB) calculated for $\text{C}_{13}\text{H}_{17}\text{O}_3\text{Br}$ (M^+): 301.0439, found: 301.0442; M.P. = 117.0 – 118.0 $^{\circ}\text{C}$; $[\alpha]_D^{23} = +139.9^{\circ}$ (c = 1.04, CHCl_3); anal. calcd for $\text{C}_{13}\text{H}_{17}\text{O}_3\text{Br}$: C, 51.84; H, 5.69, found: C, 51.65; H, 5.92.

Data for **16b**: R_f 0.53 (25% EtOAc/hexanes); IR 1783, 1749 cm^{-1} ; ^1H NMR (500 MHz) δ 5.35 (s, 1H), 5.10 (d, 1H, J = 2.0 Hz), 3.83 (s, 2H), 2.61 (qd, 1H, J_q = 7.3 Hz, J_d = 2.3 Hz), 1.89 (d, 3H, J = 1.0 Hz), 1.34 (s, 3H), 1.18 (m, 6H); ^{13}C NMR (125 MHz) δ 207.5, 171.3, 138.2, 126.9, 84.8, 70.0, 57.5, 44.3, 40.0, 17.0, 16.5, 11.8, 4.9; HRMS (FAB) calculated for $\text{C}_{13}\text{H}_{17}\text{O}_3\text{Br} (\text{M}^+)$: 301.0439, found: 301.0444; M.P. = 82.0 – 83.0 $^{\circ}\text{C}$; $[\alpha]_D^{23} = -53.5^{\circ}$ (c = 1.07, CHCl_3); anal. calcd for $\text{C}_{13}\text{H}_{17}\text{O}_3\text{Br}$: C, 51.84; H, 5.69, found: C, 52.01; H, 5.81.



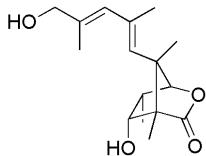
(E)-2-Methyl-3-((1*S*,4*S*,6*R*)-4,6,7-trimethyl-3,5-dioxo-2-oxa-bicyclo[2.2.1]hept-7-yl)-propenal (17). To a solution of *E*-allylic bromide **16b** (29.6 mg, 98.3 μ mol) in DMSO (0.5 mL) was added IBX (55.4 mg, 198 μ mol). The reaction mixture was heated to 50 $^{\circ}$ C for 1 hr, diluted with ether/hexanes (30 mL 1:1), and washed with saturated aqueous NaHCO₃ (10 mL), brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (20% EtOAc/hexanes) afforded **17** (19.6 mg, 84%) as a white solid. Suitable crystals for the X-ray analysis were grown by evaporation from EtOAc/ether (9:1) with trace MeOH (see the CIF file for experimental details).

Data for **17**: R_f 0.26 (25% EtOAc/hexanes); IR 1797, 1752, 1692 cm^{-1} ; ^1H NMR (500 MHz) δ 9.32 (s, 1H), 6.18 (d, 1H, J = 1.0 Hz), 5.20 (d, 1H, J = 2.0 Hz), 2.52 (qd, 1H, J_q = 7.3 Hz, J_d = 2.3 Hz), 1.88 (d, 3H, J = 1.5 Hz), 1.44 (s, 3H), 1.29 (s, 3H), 1.22 (d, 3H, J = 7.0 Hz); ^{13}C NMR (125 MHz) δ 206.6, 193.8, 170.5, 147.2, 142.3, 84.2, 69.7, 58.3, 44.8, 16.1, 11.8, 11.1, 4.9; HRMS (FAB) calculated for $\text{C}_{13}\text{H}_{17}\text{O}_4$ ($\text{M}+\text{H}^+$): 237.1127, found: 237.1124; M.P. = 139.5 – 140.5 $^{\circ}\text{C}$; $[\alpha]_D^{23} = -99.5^{\circ}$ (c = 1.00, CHCl_3); anal. calcd for $\text{C}_{13}\text{H}_{17}\text{O}_3\text{Br}$: C, 66.09, H, 6.83, found: C, 65.79, H, 6.90.



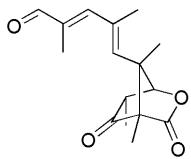
(2E,4E)-2,4-Dimethyl-5-((1S,4S,6R)-4,6,7-trimethyl-3,5-dioxo-2-oxabicyclo[2.2.1]hept-7-yl)-penta-2,4-dienoic acid ethyl ester (S1). Sodium hydride (60% in mineral oil, 32.2 mg, 0.805 mmol) was added to a solution of triethylphosphonopropionate (220 mg, 0.924 mmol) in THF (1.0 mL) at -30°C . After 15 min enal **17** (105 mg, 0.443 mmol) was added via a cannula as a solution in THF (1.0 mL) using THF (1.0 mL) to aid the transfer. The reaction was quenched with saturated aqueous NH_4Cl (3.0 mL) after 2 min. The mixture was extracted with ether (3 x 3 mL). The combined organic phases were washed with brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (15% EtOAc/hexanes) afforded **S1** (138 mg, 97%) as a colorless oil that solidified upon storage at 4°C .

Data for **S1**: R_f 0.37 (25% EtOAc/hexanes); IR 1797, 1753, 1709 cm^{-1} ; ^1H NMR (500 MHz) δ 6.95 (s, 1H), 5.25 (d, 1H, $J = 1.0$ Hz), 5.16 (d, 1H, $J = 2.5$ Hz), 4.18 (q, 2H, $J = 7.2$ Hz), 2.69 (qd, 1H, $J_q = 7.3$ Hz, $J_d = 2.0$ Hz), 1.92 (d, 3H, $J = 1.0$ Hz), 1.88 (d, 3H, $J = 1.0$ Hz), 1.40 (s, 3H), 1.28 (t, 3H, $J = 7.3$ Hz), 1.20 (d, 3H, $J = 7.5$ Hz), 1.18 (s, 3H); ^{13}C NMR (125 MHz) δ 207.5, 171.3, 168.4, 141.0, 137.5, 129.9, 128.6, 84.9, 70.2, 61.2, 58.2, 44.5, 18.7, 16.8, 14.4, 14.2, 11.8, 4.9; HRMS (FAB) calculated for $\text{C}_{18}\text{H}_{25}\text{O}_5$ ($\text{M}+\text{H}^+$): 321.1702, found: 321.1697; M.P. = $65.5 - 66.5^{\circ}\text{C}$; $[\alpha]_D^{23} = -29.6^{\circ}$ ($c = 0.90$, CHCl_3).



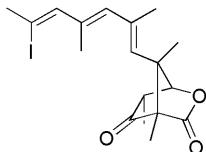
(1S,4S,5R,6S)-5-Hydroxy-7-((1E,3E)-5-hydroxy-2,4-dimethyl-penta-1,3-dienyl)-4,6,7-trimethyl-2-oxa-bicyclo[2.2.1]heptan-3-one (S2). LiEt₃BH (1.0 M in THF, 0.60 mL, 0.60 mmol) was added to a solution of ester **S1** (46.4 mg, 0.145 mmol) in THF (1.0 mL) at -78°C . The reaction was quenched with saturated aqueous NH_4Cl (3.0 mL) after 10 min. The mixture was extracted with ether (3 x 3 mL). The combined organic phases were washed with brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (50% EtOAc/hexanes) afforded **S2** (38.4 mg, 95%) as a colorless oil.

Data for **S2**: R_f 0.18 (50% EtOAc/hexanes); IR 3426, 1777, 1765 cm^{-1} ; ^1H NMR (500 MHz) δ 5.83 (s, 1H), 5.17 (s, 1H), 4.67 (s, 1H), 4.11 (d, 1H, $J = 9.5$ Hz), 4.04 (s, 2H), 2.54 (m, 1H), 2.11 (bs, 1H), 1.79 (bs, 1H), 1.75 (s, 6H), 1.19 (s, 3H), 1.15 (s, 3H), 1.02 (d, 3H, $J = 7.5$ Hz); ^{13}C NMR (100 MHz) δ 177.4, 136.03, 135.97, 128.7, 127.5, 86.9, 74.6, 68.8, 61.0, 54.4, 36.6, 18.7, 16.6, 15.5, 9.4, 8.0; HRMS (FAB) calculated for $\text{C}_{16}\text{H}_{24}\text{O}_4\text{Li}$ ($\text{M}+\text{Li}^+$): 287.1835, found: 287.1832; $[\alpha]_D^{23} = -12.5^{\circ}$ ($c = 1.05$, CHCl_3).



(2E,4E)-2,4-Dimethyl-5-((1S,4S,6R)-4,6,7-trimethyl-3,5-dioxo-2-oxabicyclo[2.2.1]hept-7-yl)-penta-2,4-dienal (18). Dess-Martin periodinane (422 mg, 0.995 mmol) was added to a solution of the diol **S2** (86.2 mg, 0.307 mmol) in CH_2Cl_2 (1.0 mL) at 0 °C. After 20 min the reaction was diluted with ether (5 mL) and quenched with a mixture of saturated aqueous NaHCO_3 and saturated aqueous Na_2SO_3 (5.0 mL, 1:1). After 15 min the phases were separated and the aqueous phase was extracted with ether (5 x 2 mL). The combined organic phases were washed with brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (20% EtOAc/hexanes) afforded **18** (73.7 mg, 87%) as a colorless oil that solidified upon storage at 4°C.

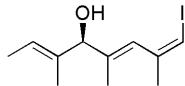
Data for **18**: R_f 0.19 (25% EtOAc/hexanes); IR 1797, 1753, 1678 cm^{-1} ; ^1H NMR (500 MHz) δ 9.38 (s, 1H), 6.61 (s, 1H), 5.50 (s, 1H), 5.20 (d, 1H, J = 2.0 Hz), 2.68 (qd, 1H, J_q = 7.3 Hz, J_d = 2.3 Hz), 2.07 (s, 3H), 1.87 (s, 3H), 1.43 (s, 3H), 1.22 (m, 6H); ^{13}C NMR (125 MHz) δ 207.5, 195.8, 171.3, 152.4, 138.5, 137.9, 133.7, 85.0, 70.4, 58.5, 44.9, 18.7, 16.8, 12.1, 11.3, 5.2; HRMS not obtained (compound unstable under conditions); M.P. = 118.5 – 120.0 °C; $[\alpha]_D^{23} = -41.6^\circ$ (c = 1.45, CHCl_3).



(1S,4S,6R)-7-((1E,3E,5Z)-6-Iodo-2,4-dimethyl-hepta-1,3,5-trienyl)-4,6,7-trimethyl-2-oxa-bicyclo[2.2.1]heptane-3,5-dione (19). $n\text{-BuLi}$ (2.5 M in hexanes, 0.10 mL, 0.25 mmol) was added to a solution of (ethyl)triphenylphosphonium iodide (98.5 mg, 0.235 mmol) in THF (1.0 mL) at rt. The mixture was stirred for 20 minutes and then transferred into a solution of I_2 (63.3 mg, 0.249 mmol) in THF (0.5 mL) at –78 °C. The reaction mixture became very viscous. The temperature was then elevated to –20 °C, and KHMDS (0.91 M in THF, 0.23 mL, 0.21 mmol) was added. The mixture turned a deep red color. Aldehyde **18** (31.6 mg, 0.114 mmol) in THF (1.0 mL) was added to the reaction mixture via a cannula using THF (1.0 mL) to aid the transfer. The reaction was quenched with saturated aqueous NH_4Cl (3.0 mL) after 10 min. The mixture was extracted with ether (3 x 3 mL). The combined organic phases were washed with brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (8% EtOAc/hexanes) afforded **19** (15.3 mg, 32%) as a light-yellow oil.

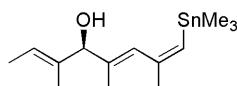
Data for **19**: R_f 0.21 (10% EtOAc/hexanes); IR 1797, 1751 cm^{-1} ; ^1H NMR (500 MHz) δ 5.96 (s, 1H), 5.80 (s, 1H), 5.16 (d, 1H, J = 2.0 Hz), 5.11 (s, 1H), 2.76 (qd, 1H, J_q = 7.3 Hz, J_d = 2.3 Hz), 2.56 (d, 3H, J = 1.5 Hz), 1.87 (d, 3H, J = 1.0 Hz), 1.78 (d, 3H, J = 0.5 Hz), 1.41 (s, 3H), 1.22 (d, 3H, J = 7.0 Hz), 1.20 (s, 3H); ^{13}C NMR (125 MHz) δ 207.9, 171.7, 137.97, 137.91, 136.1, 133.6, 126.2, 98.7, 85.2, 70.3, 58.3, 44.4, 35.2, 19.2, 18.0,

17.0, 11.9, 5.0; HRMS (FAB) calculated for $C_{18}H_{24}IO_3$ ($M+H^+$): 415.0770, found: 415.0758; $[\alpha]_D^{23} = +12.8^\circ$ ($c = 0.77$, $CHCl_3$).



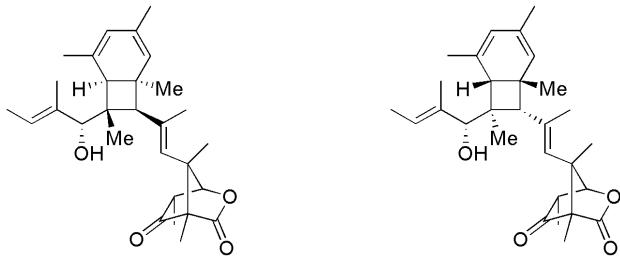
(2E,5E,7Z)-(R)-8-Iodo-3,5,7-trimethyl-octa-2,5,7-trien-4-ol (22). 2-Butyne (0.10 mL, 1.3 mmol) was added dropwise to a slurry of dicyclohexylborane (151 mg, 0.848 mmol) in toluene (0.5 mL) at rt and the reaction mixture became clear within 2 min. After 1 hr the reaction mixture was cooled to $-78^\circ C$ and Me_2Zn (2.0 M in toluene, 0.5 mL, 1.0 mmol). After 1 hr the ligand **21** (46.8 mg, 0.127 mmol) in toluene (1.5 mL) was added to the reaction mixture via a cannula. Then the temperature was increased to $-30^\circ C$ over a period of 0.5 h, the aldehyde **20** (0.5 mmol) was added, and the final mixture was allowed to stir for 10 h at $-30^\circ C$. The reaction was quenched with water (5.0 mL) and extracted with ether (3 x 3 mL). The combined organic phases were washed with brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (5% EtOAc/hexanes) afforded **22** (83.8 mg, 64%) as a light-yellow oil along with recovered **20** (34.7 mg).

Data for **22**: R_f 0.28 (10% EtOAc/hexanes); IR 3384 cm^{-1} ; 1H NMR (500 MHz) δ 6.04 (q, 1H, $J = 1.5$ Hz), 5.63 (s, 1H, $J = 6.5$ Hz), 4.44 (s, 1H), 1.98 (d, 3H, $J = 0.5$ Hz), 1.68 (bs, 1H), 1.66 (d, 3H, $J = 6.0$ Hz), 1.59 (s, 3H), 1.55 (d, 3H, $J = 1.0$ Hz); ^{13}C NMR (125 MHz) δ 145.2, 139.4, 135.7, 127.3, 122.2, 81.6, 77.1, 24.9, 14.7, 13.5, 12.0; HRMS (FAB) calculated for $C_{11}H_{16}I$ ($M-OH^+$): 275.0297, found: 275.0293; $[\alpha]_D^{23} = -23.8^\circ$ ($c = 1.03$, $CHCl_3$). Analysis of enantiomers by chiral HPLC (Chiralcel AD, flow rate 1.0 mL/min, 99:1 hexanes:ethanol, T_f minor 12.72, major 13.08 min) determined the e.e. to be 95%.



(2E,5E,7Z)-(R)-3,5,7-Trimethyl-8-trimethylstannanyl-octa-2,5,7-trien-4-ol (23). n -BuLi (2.19 M in hexanes, 2.70 mL, 5.91 mmol) was added to a solution of iodide **22** (832 mg, 2.85 mmol) in THF (6.0 mL) at $-78^\circ C$. After 10 min trimethyltin chloride (1.0 M in THF, 6.0 mL, 6.0 mmol) was added. The reaction was quenched with water (10 mL) after 10 min and extracted with ether (3 x 3 mL). The combined organic phases were washed with brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (5% EtOAc/hexanes) afforded **23** (212 mg, 23%) as a light-yellow oil.

Data for **23**: R_f 0.26 (10% EtOAc/hexanes); IR 3385 cm^{-1} ; 1H NMR (500 MHz) δ 6.16 (s, 1H), 5.80 (s, 1H, $^2J_{Sn} = 79.8$ Hz), 5.58 (q, 1H, $J = 5.5$ Hz), 4.36 (s, 1H); 2.02 (d, 3H, $J = 1.0$ Hz), 1.64 (d, 3H, $J = 6.5$ Hz), 1.60 (d, 3H, $J = 1.0$ Hz), 1.52 (s, 3H), 0.10 (s, 9H, $^2J_{119Sn} = 55.0$ Hz, $^2J_{117Sn} = 52.5$ Hz); ^{13}C NMR (125 MHz) δ 152.3, 137.1, 136.0, 130.5, 129.4, 121.6, 81.9, 27.7, 14.3, 13.4, 11.9, -8.74 ($^1J_{119Sn} = 348$ Hz, $^1J_{117Sn} = 331$ Hz); HRMS (FAB) calculated for $C_{14}H_{25}^{120}Sn$ ($M-OH^+$): 313.0978, found: 313.0981; $[\alpha]_D^{23} = -19.0^\circ$ ($c = 0.98$, $CHCl_3$).



Shimalactones A and B. To a solution of **23** (31.3 mg, 95.1 μ mol) and **19** (12.5 mg, 30.2 μ mol) in DMF (0.5 mL) was added tetrakis-triphenylphosphine palladium (5.0 mg, 4.3 μ mol) and copper(I) thiophene-2-carboxylate (10.2 mg, 53.5 μ mol). The reaction mixture was stirred at rt. After 1 hr it was diluted with a mixture of ether:hexane (4 mL 1:1), pushed through a plug of silica, and concentrated. Purification by silica gel chromatography (10% EtOAc/hexanes) afforded a mixture of shimalactone A and B (9.0 mg, 66%, 5:1 d.r.) as a colorless oil. While shimalactone A (3.0 mg) was purified by reverse phase HPLC (econocil C18, MeOH/H₂O), shimalactone B was characterized as a mixture with shimalactone A.

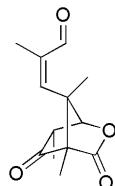
Data for shimalactone A: R_f 0.48 (25% EtOAc/hexanes); IR 3527, 2936, 1795, 1750 cm^{-1} ; HRMS (FAB) calculated for $C_{29}H_{40}O_4Li$ ($M+Li^+$): 459.3087, found: 459.3101; $[\alpha]_D^{23} = +10.9^\circ$ ($c = 0.58$, MeOH).

¹ H NMR isolation	¹ H NMR current (500 MHz)	¹³ C NMR isolation	¹³ C NMR current
5.49 (q, 1H, $J = 6.6$ Hz)	5.49 (q, 1H, $J = 6.5$ Hz)	207.6	207.6
5.46 (s, 1H)	5.46 (s, 1H)	171.8	171.7
5.27 (s, 1H)	5.27 (s, 1H)	138.2	138.2
5.10 (d, 1H, $J = 2.2$ Hz)	5.11 (d, 1H, $J = 2.5$ Hz)	136.5	136.5
4.83 (s, 1H)	4.83 (s, 1H)	132.5	132.6
3.84 (s, 1H)	3.85 (s, 1H)	129.4	129.4
2.68 (s, 1H)	2.68 (s, 1H)	123.9	123.85
2.60 (qd, 1H, $J = 7.2$ Hz, $J = 2.2$ Hz)	2.60 (qd, 1H, $J = 7.3$ Hz, $J = 2.3$ Hz)	123.8	123.80
2.39 (s, 1H)	2.40 (s, 1H)	123.5	123.5
1.71 (s, 3H)	1.71 (s, 3H)	122.5	122.5
1.65 (s, 6H)	1.66 (s, 6H)	86.3	86.3
1.60 (d, 3H, $J = 6.6$ Hz)	1.61 (d, 3H, $J = 7.0$ Hz)	85.2	85.1
1.55 (s, 3H)	1.55 (s, 3H)	70.1	70.1
1.34 (s, 3H)	1.34 (s, 3H)	60.7	60.7
1.19 (d, 3H, 7.2 Hz)	1.19 (d, 3H, 7.5 Hz)	58.3	58.2
1.15 (s, 3H)	1.16 (s, 3H)	51.7	51.7
1.10 (s, 3H)	1.10 (s, 3H)	49.6	49.6
1.01 (s, 3H)	1.01 (s, 3H)	44.0	44.0
		41.2	41.2
		31.9	31.9
		23.3	23.3

		22.1	22.0
		20.6	20.5
		16.8	16.8
		14.4	14.4
		13.2	13.2
		13.1	13.1
		11.6	11.6
		4.7	4.7

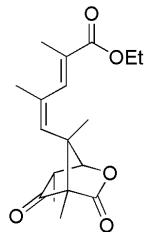
Data for shimalactone B: R_f 0.48 (25% EtOAc/hexanes). As shimalactone B was obtained as a mixture with shimalactone A and thus was not characterized beyond ^1H NMR.

^1H NMR isolation	^1H NMR current (500 MHz)
5.46 (s, 1H)	5.46 (s, 1H)
5.42 (q, 1H, J = 6.6 Hz)	5.41 (q, 1H, J = 6.5 Hz)
5.28 (s, 1H)	5.27 (s, 1H)
5.12 (d, 1H, J = 1.9 Hz)	5.13 (s, 1H)
4.76 (s, 1H)	4.75 (s, 1H)
3.66 (s, 1H)	3.66 (s, 1H)
3.03 (s, 1H)	3.03 (s, 1H)
2.77 (qd, 1H, J = 7.4 Hz, J = 1.9 Hz)	2.77 (qd, 1H, J = 7.3 Hz, J = 2.3 Hz)
2.68 (s, 1H)	2.68 (s, 1H)
1.77 (s, 3H)	1.77 (s, 3H)
1.66 (s, 3H)	1.66 (s, 3H)
1.58 (d, 3H), 1.57 (s, 3H)	1.57 (m, 6H)
1.50 (s, 3H)	1.49 (s, 3H)
1.32 (s, 3H)	1.32 (s, 3H)
1.21 (d, 3H, 7.4 Hz)	1.20 (d, 3H, 7.5 Hz)
1.15 (s, 3H)	1.16 (s, 3H)
1.13 (s, 3H)	1.13 (s, 3H)
0.98 (s, 3H)	0.97 (s, 3H)



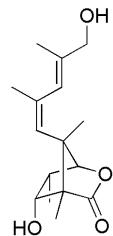
(Z)-2-Methyl-3-((1S,4S,6R)-4,6,7-trimethyl-3,5-dioxo-2-oxa-bicyclo[2.2.1]hept-7-yl)-propenal (S3). To a solution of Z-allylic bromide **16a** (97.6 mg, 0.324 mmol) in DMSO (1.0 mL) was added IBX (182 mg, 0.650 μmol). The reaction mixture was heated to 50 $^\circ\text{C}$ for 1 hr, diluted with ether/hexanes (30 mL 1:1), and washed with saturated aqueous NaHCO_3 (10 mL), brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (20% EtOAc/hexanes) afforded **S3** (67.4 mg, 88%) as a white solid.

Data for **S3**: R_f 0.38 (25% EtOAc/hexanes); IR 1797, 1753, 1681 cm^{-1} ; ^1H NMR (500 MHz) δ 10.08 (s, 1H), 6.07 (d, 1H, J = 1.0 Hz), 5.22 (d, 1H, J = 1.5 Hz), 2.65 (qd, 1H, J_q = 7.0 Hz, J_d = 2.0 Hz), 1.87 (d, 3H, J = 1.0 Hz), 1.51 (s, 3H), 1.26 (s, 3H), 1.21 (d, 3H, J = 7.5 Hz); ^{13}C NMR (125 MHz) δ 207.0, 190.6, 170.5, 141.1, 139.6, 86.3, 70.6, 58.0, 44.8, 19.6, 18.0, 11.8, 4.9; HRMS (FAB) calculated for $\text{C}_{13}\text{H}_{17}\text{O}_4$ ($\text{M}+\text{H}^+$): 237.1127, found: 237.1124; M.P. = 108.9 – 109.0 $^{\circ}\text{C}$; $[\alpha]_D^{23} = -61.0^\circ$ (c = 0.83, CHCl_3); anal. calcd for $\text{C}_{13}\text{H}_{17}\text{O}_3\text{Br}$: C, 66.09; H, 6.83, found: C, 66.14; H, 6.97.



(2E,4Z)-2,4-Dimethyl-5-((1S,4S,6R)-4,6,7-trimethyl-3,5-dioxo-2-oxabicyclo[2.2.1]hept-7-yl)-penta-2,4-dienoic acid ethyl ester (S4). Sodium hydride (60% in mineral oil, 124 mg, 3.10 mmol) was added to a solution of triethylphosphonopropionate (842 mg, 3.53 mmol) in THF (3.0 mL) at –10 $^{\circ}\text{C}$. After 15 min enal **S3** (419 mg, 1.77 mmol) was added via a cannula as a solution in THF (3.0 mL) using THF (2.0 mL) to aid the transfer. The reaction was quenched with saturated aqueous NH_4Cl (5.0 mL) after 2 min. The mixture was extracted with ether (3 x 10 mL). The combined organic phases were washed with brine (15 mL), dried, and concentrated. Purification by silica gel chromatography (10% EtOAc/hexanes) afforded **S4** (381 mg, 67%) as a colorless oil.

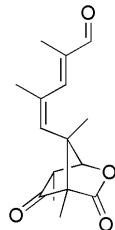
Data for **S4**: R_f 0.49 (25% EtOAc/hexanes); IR 1799, 1752, 1714 cm^{-1} ; ^1H NMR (500 MHz) δ 7.22 (s, 1H), 5.20 (d, 1H, J = 1.0 Hz), 4.94 (d, 1H, J = 2.0 Hz), 4.25 (q, 2H, J = 7.2 Hz), 2.65 (qd, 1H, J_q = 7.0 Hz, J_d = 2.0 Hz), 1.88 (d, 3H, J = 1.0 Hz), 1.84 (s, 3H), 1.33 (t, 3H, J = 7.0 Hz), 1.29 (s, 3H), 1.18 (s, 3H), 1.16 (d, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz) δ 207.9, 171.6, 167.6, 137.2, 137.1, 130.9, 126.8, 85.0, 70.1, 61.4, 58.0, 44.2, 24.0, 16.9, 14.4 (2C), 11.7, 4.8; HRMS (FAB) calculated for $\text{C}_{18}\text{H}_{25}\text{O}_5$ ($\text{M}+\text{H}^+$): 321.1702, found: 321.1700; $[\alpha]_D^{23} = -17.1^\circ$ (c = 1.46, CHCl_3).



(1S,4S,5R,6S)-5-Hydroxy-7-((1Z,3E)-5-hydroxy-2,4-dimethyl-penta-1,3-dienyl)-4,6,7-trimethyl-2-oxa-bicyclo[2.2.1]heptan-3-one (S5). LiEt_3BH (1.0 M in THF, 4.8 mL, 4.8 mmol) was added to a solution of ester **S4** (381 mg, 1.19 mmol) in THF (3.0 mL) at –78 $^{\circ}\text{C}$. The reaction was quenched with saturated aqueous NH_4Cl (3.0 mL) after 10 min. The mixture was extracted with ether (3 x 5 mL). The combined organic phases

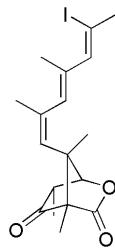
were washed with brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (50% EtOAc/hexanes) afforded **S5** (332 mg, 99.6%) as a colorless oil.

Data for **S5**: R_f 0.26 (50% EtOAc/hexanes); IR 3425, 1765 cm^{-1} ; ^1H NMR (400 MHz) δ 6.00 (s, 1H), 5.18 (s, 1H), 4.54 (s, 1H), 4.09 (d, 1H, J = 12.5 Hz), 4.05 (s, 2H), 2.51 (m, 1H), 2.27 (bm, 2H), 1.79 (s, 3H), 1.64 (s, 3H), 1.17 (s, 3H), 1.04 (s, 3H), 0.95 (d, 3H, J = 9.5 Hz); ^{13}C NMR (100 MHz) δ 178.1, 138.1, 136.4, 125.8, 122.9, 87.2, 74.5, 67.5, 60.9, 54.4, 36.1, 25.2, 16.4, 15.5, 9.3, 7.9; HRMS (FAB) calculated for $\text{C}_{16}\text{H}_{24}\text{O}_4\text{Li}$ ($\text{M}+\text{Li}^+$): 287.1835, found: 287.1829; $[\alpha]_D^{23} = +15.2^\circ$ (c = 1.52, CHCl_3).



(2E,4Z)-2,4-Dimethyl-5-((1S,4S,6R)-4,6,7-trimethyl-3,5-dioxo-2-oxabicyclo[2.2.1]hept-7-yl)-penta-2,4-dienal (S6). Dess-Martin periodinane (189 mg, 0.446 mmol) was added to a solution of the diol **S5** (38.4 mg, 0.137 mmol) in CH_2Cl_2 (1.0 mL) at 0 $^\circ\text{C}$. After 20 min the reaction was diluted with ether (5 mL) and quenched with a mixture of saturated aqueous NaHCO_3 and saturated aqueous Na_2SO_3 (5.0 mL, 1:1). After 15 min the phases were separated and the aqueous phase was extracted with ether (5 x 2 mL). The combined organic phases were washed with brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (20% EtOAc/hexanes) afforded **S6** (31.6 mg, 84%) as a white solid.

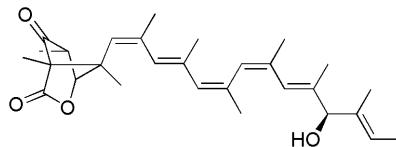
Data for **S6**: R_f 0.32 (25% EtOAc/hexanes); IR 1790, 1750, 1681 cm^{-1} ; ^1H NMR (500 MHz) δ 9.54 (s, 1H), 6.98 (s, 1H), 5.32 (s, 1H), 4.97 (d, 1H, J = 2.0 Hz), 2.66 (qd, 1H, J_q = 7.3 Hz, J_d = 2.3 Hz), 1.96 (d, 3H, J = 0.5 Hz), 1.86 (d, 3H, J = 1.0 Hz), 1.35 (s, 3H), 1.21 (s, 3H), 1.17 (d, 3H, J = 7.5 Hz); ^{13}C NMR (125 MHz) δ 207.5, 194.5, 171.2, 146.5, 140.8, 136.8, 129.4, 84.9, 70.3, 57.9, 44.3, 24.2, 17.1, 11.7, 11.3, 4.9; HRMS (FAB) calculated for $\text{C}_{16}\text{H}_{20}\text{O}_4\text{Li}$ ($\text{M}+\text{Li}^+$): 283.1522, found: 283.1524; M.P. = 95.5 – 97.0 $^\circ\text{C}$; $[\alpha]_D^{23} = -19.3^\circ$ (c = 1.02, CHCl_3).



(1S,4S,6R)-7-((1Z,3E,5Z)-6-Iodo-2,4-dimethyl-hepta-1,3,5-trienyl)-4,6,7-trimethyl-2-oxa-bicyclo[2.2.1]heptane-3,5-dione (24). $n\text{-BuLi}$ (2.5 M in hexanes, 0.52 mL, 1.3 mmol) was added to a solution of (ethyl)triphenylphosphonium iodide (549 mg, 1.31

mmol) in THF (2.0 mL) at rt. The mixture was stirred for 20 minutes and then transferred into a solution of I₂ (334 mg, 1.33 mmol) in THF (1.0 mL) at -78 °C. The reaction mixture became very viscous. The temperature was then elevated to -20 °C, and NaHMDS (2.0 M in THF, 0.61 mL, 1.22 mmol) was added. The mixture turned a deep red color. Aldehyde **S6** (181 mg, 0.655 mmol) in THF (1.0 mL) was added to the reaction mixture via a cannula using THF (1.0 mL) to aid the transfer. The reaction was quenched with saturated aqueous NH₄Cl (3.0 mL) after 6 min. The mixture was extracted with ether (3 x 5 mL). The combined organic phases were washed with brine (10 mL), dried, and concentrated. Purification by silica gel chromatography (8% EtOAc/hexanes) afforded **24** (77.3 mg, 29%, 47% b.o.r.s.m.) as a light-yellow oil along with the starting aldehyde (70.9 mg).

Data for **24**: R_f 0.43 (10% EtOAc/hexanes); IR 1793, 1751 cm⁻¹; ¹H NMR (500 MHz) δ 6.10 (s, 1H), 6.06 (s, 1H), 5.19 (s, 1H), 5.13 (s, 1H), 2.72 (q, 1H, J = 7.0 Hz), 2.62 (s, 3H), 1.85 (s, 3H), 1.80 (s, 3H), 1.33 (s, 3H), 1.17 (m, 6H); ¹³C NMR (125 MHz) δ 208.4, 172.1, 138.4, 137.9, 137.1, 128.5, 125.4, 99.2, 85.3, 70.3, 58.1, 44.2, 35.3, 25.2, 18.5, 16.9, 11.8, 4.9; HRMS (FAB) calculated for C₁₈H₂₄IO₃ (M+H⁺): 415.0770, found: 415.0763; [α]_D²³ = +4.6° (c = 0.61, CHCl₃).

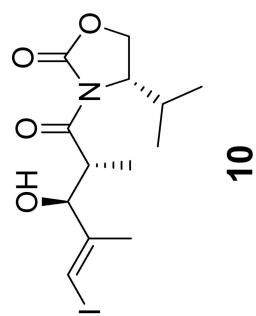
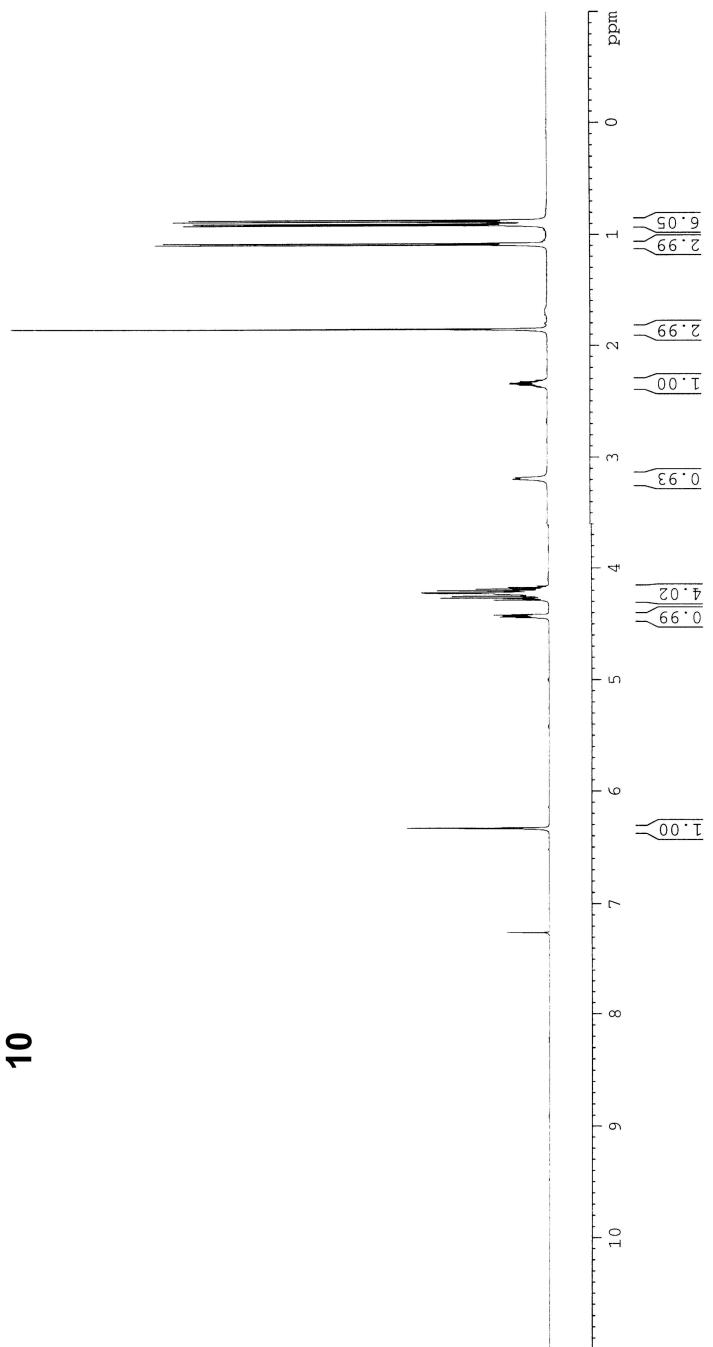


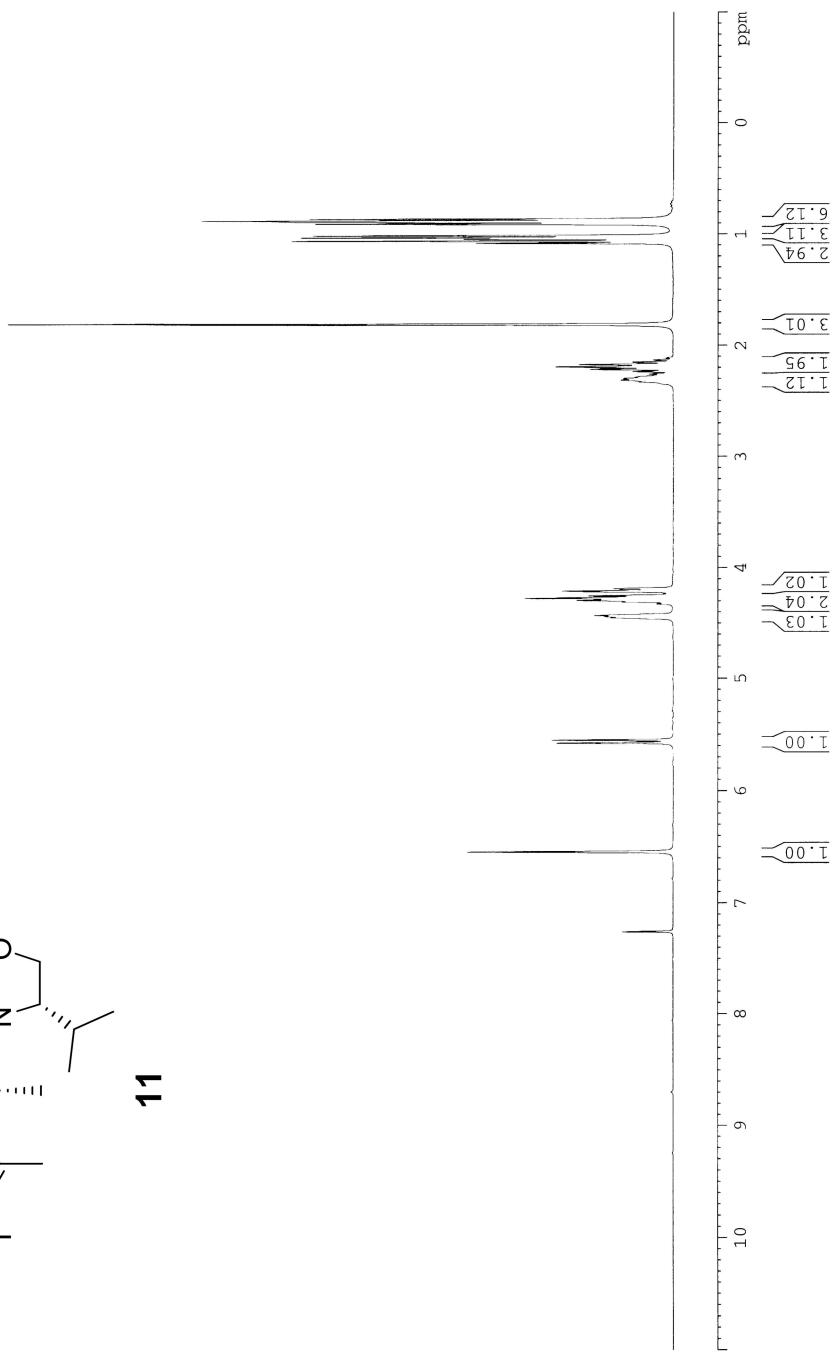
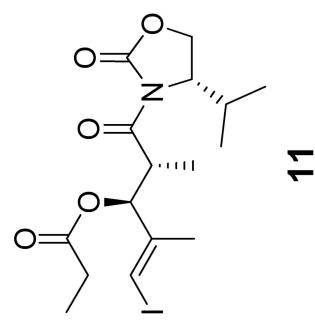
(1S,4S,6R)-7-((1Z,3E,5Z,7Z,9E,12E)-(R)-11-Hydroxy-2,4,6,8,10,12-hexamethyl-tetradeca-1,3,5,7,9,12-hexaenyl)-4,6,7-trimethyl-2-oxa-bicyclo[2.2.1]heptane-3,5-dione (25). To a solution of **24** (77.3 mg, 0.187 mmol) and **23** (103 mg, 0.313 μmol) in DMF (0.5 mL) was added tetrakis-triphenylphosphine palladium (10.6 mg, 9.17 μmol) and copper(I) thiophene-2-carboxylate (52.0 mg, 0.273 mmol). The reaction mixture was stirred at rt. After 1 hr it was diluted with a mixture of ether:hexane (4 mL 1:1), pushed through a plug of silica, and concentrated. Purification by silica gel chromatography (8% EtOAc/hexanes) afforded **25** (72.2 mg, 85%) as a light-yellow oil.

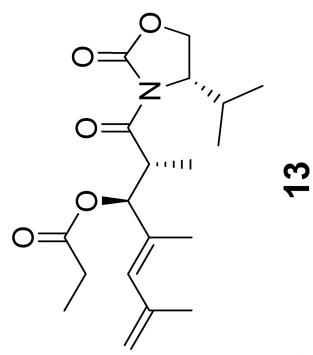
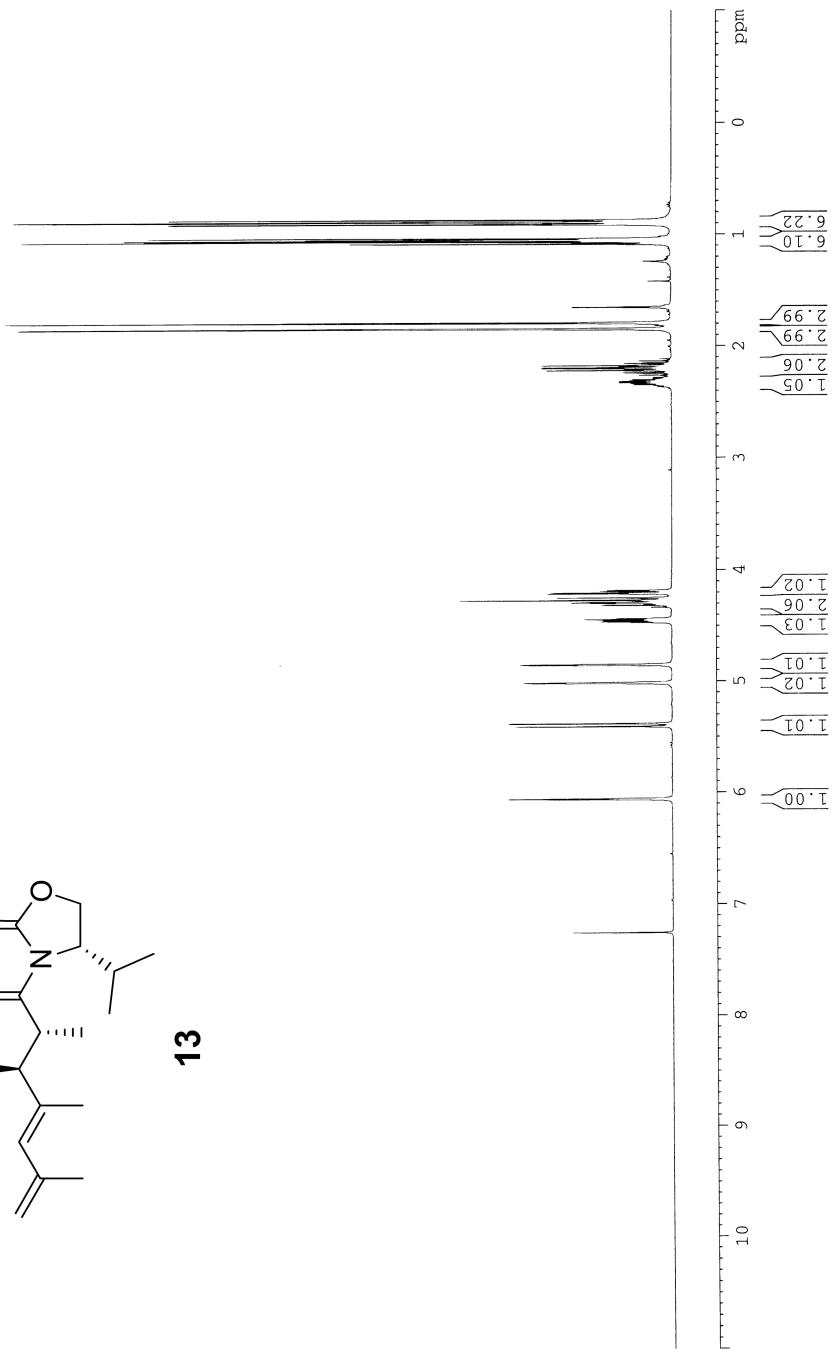
Data for **25**: R_f 0.43 (25% EtOAc/hexanes); IR 3535, 1797, 1751 cm⁻¹; ¹H NMR (500 MHz) δ 6.16 (s, 1H), 6.12 (s, 1H), 5.93 (s, 1H), 5.72 (s, 1H), 5.58 (q, 1H, J = 7.0 Hz), 5.06 (s, 1H), 5.01 (d, 1H, J = 2.0 Hz), 4.39 (s, 1H), 2.69 (qd, 1H, J_q = 7.5 Hz, J_d = 2.0 Hz), 1.89 (s, 3H), 1.85 (s, 3H), 1.83 (s, 3H), 1.76 (s, 3H), 1.64 (d, 3H, J = 6.5 Hz), 1.51 (s, 6H), 1.28 (s, 3H), 1.16 (s, 3H), 1.13 (d, 3H, J = 5.0 Hz); ¹³C NMR (125 MHz) δ 208.4, 172.1, 139.2, 137.6, 137.4, 136.3, 135.9, 135.6, 131.2, 128.7, 127.9, 125.8, 124.8, 121.9, 85.4, 81.8, 70.2, 58.1, 44.1, 25.5, 25.3, 24.5, 19.4, 16.7, 14.4, 13.4, 11.9, 11.7, 4.8; HRMS (FAB) calculated for C₂₉H₄₀O₄Li (M+Li⁺): 459.3087, found: 459.3078; [α]_D²³ = -14.9° (c = 1.24, CHCl₃).

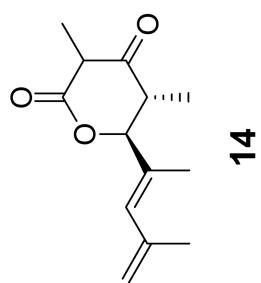
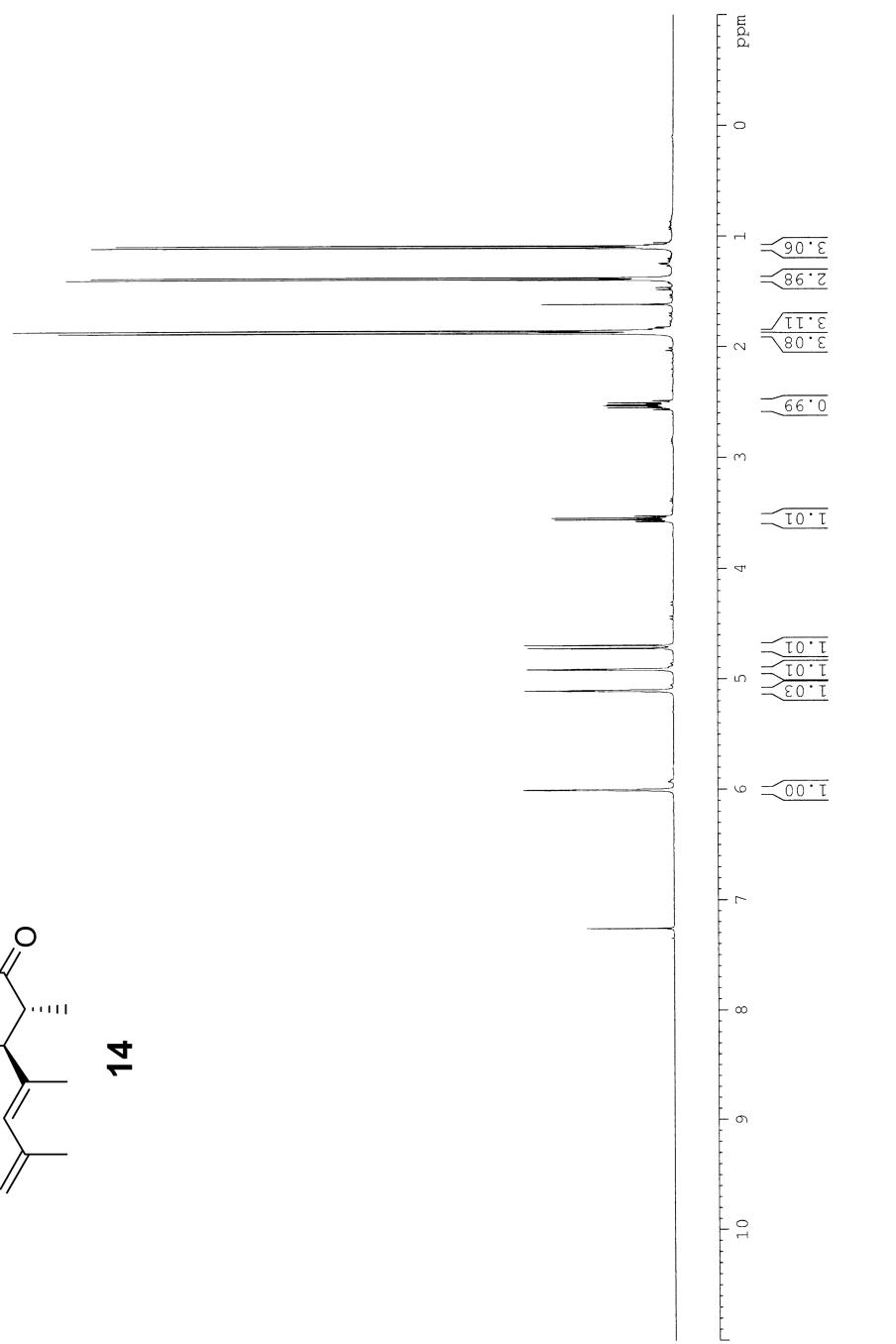
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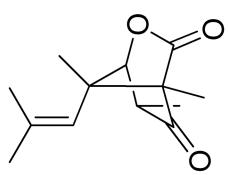
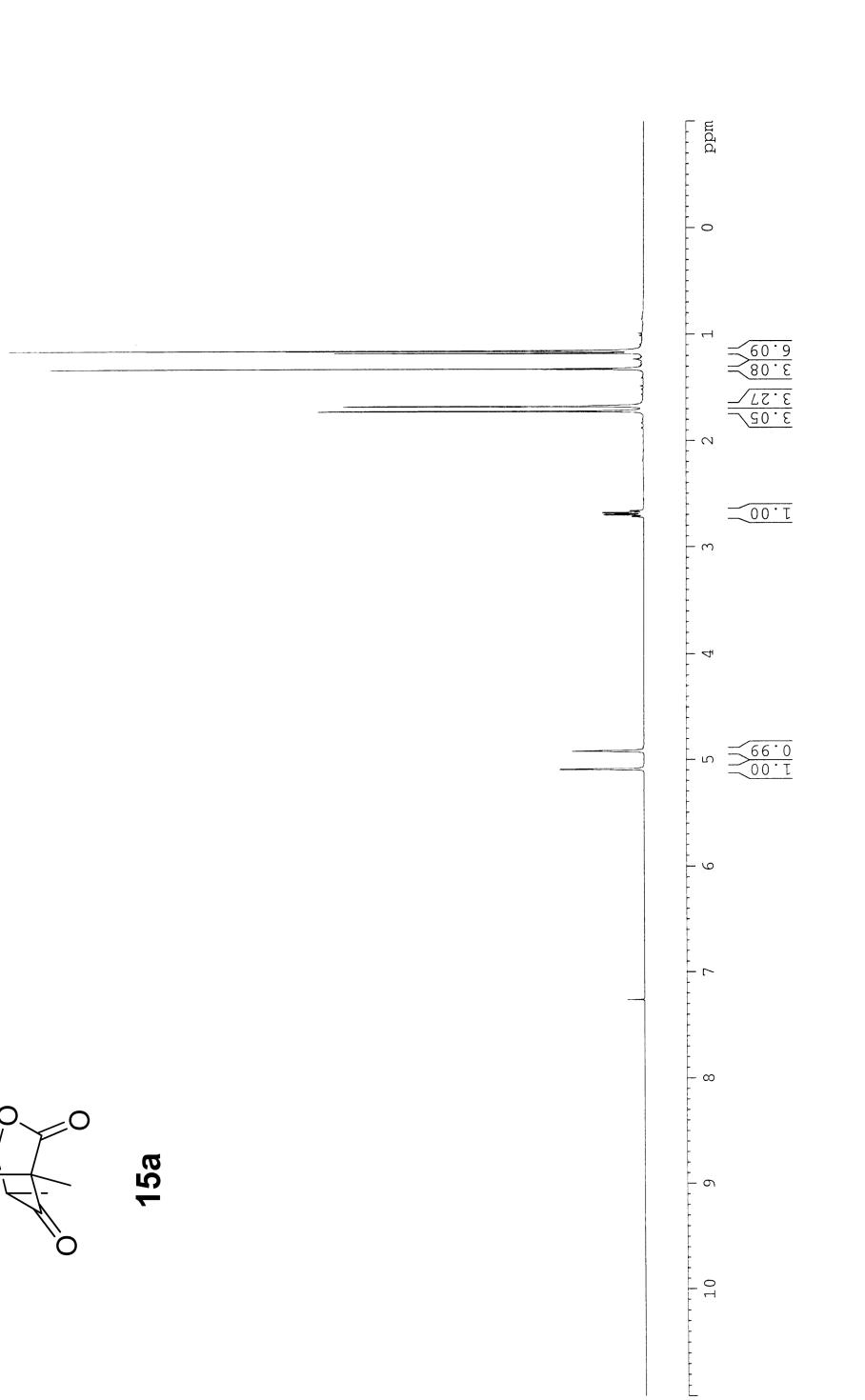
[13] P. J. Alaimo, D. W. Peters, J. Arnold, R. G. Bergman, *J. Chem. Ed.* **2001**, 78, 64.



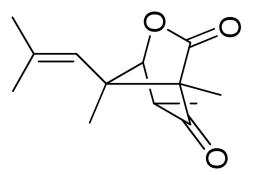




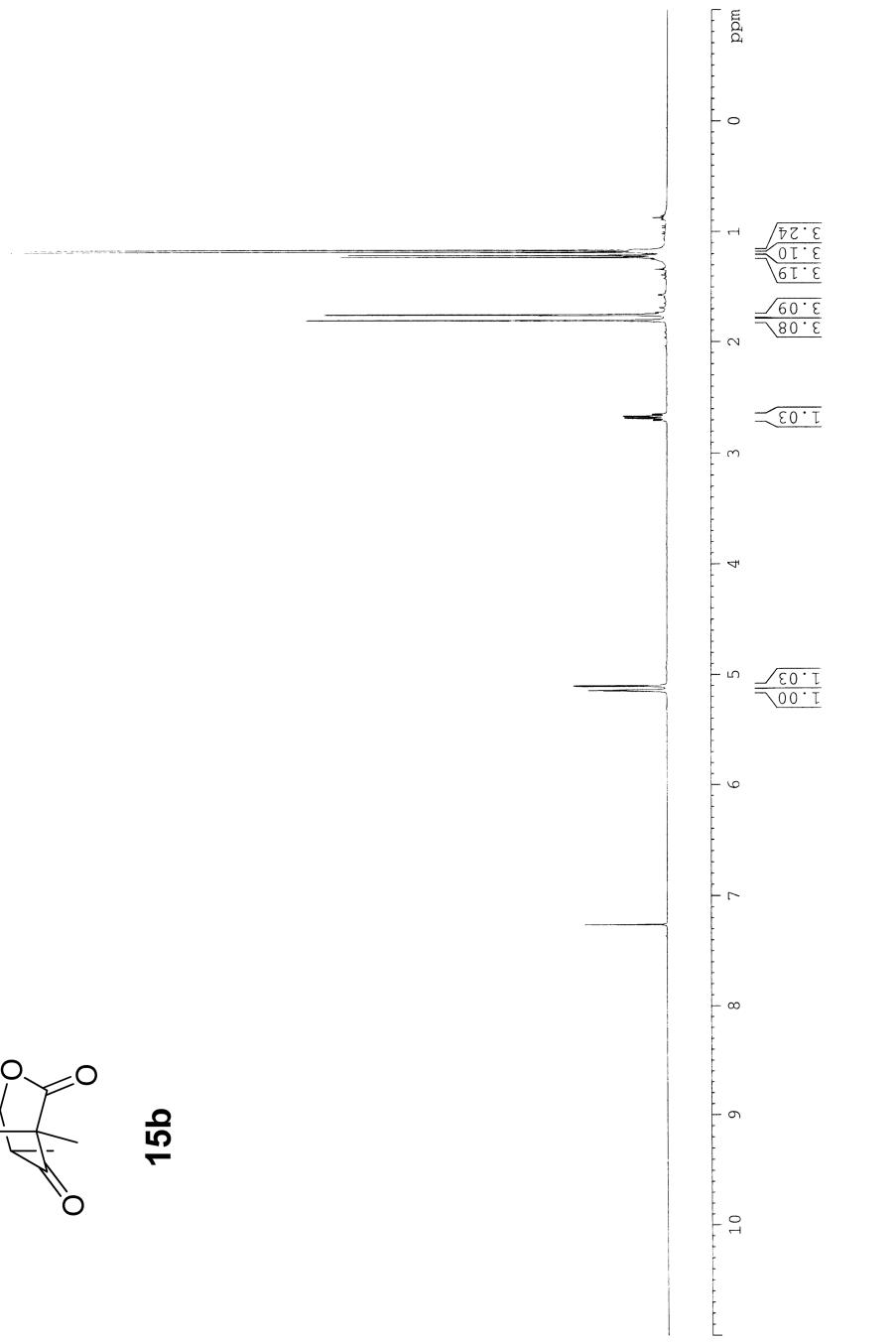


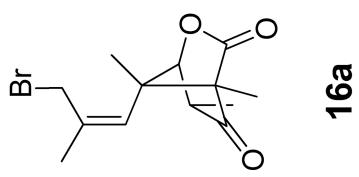
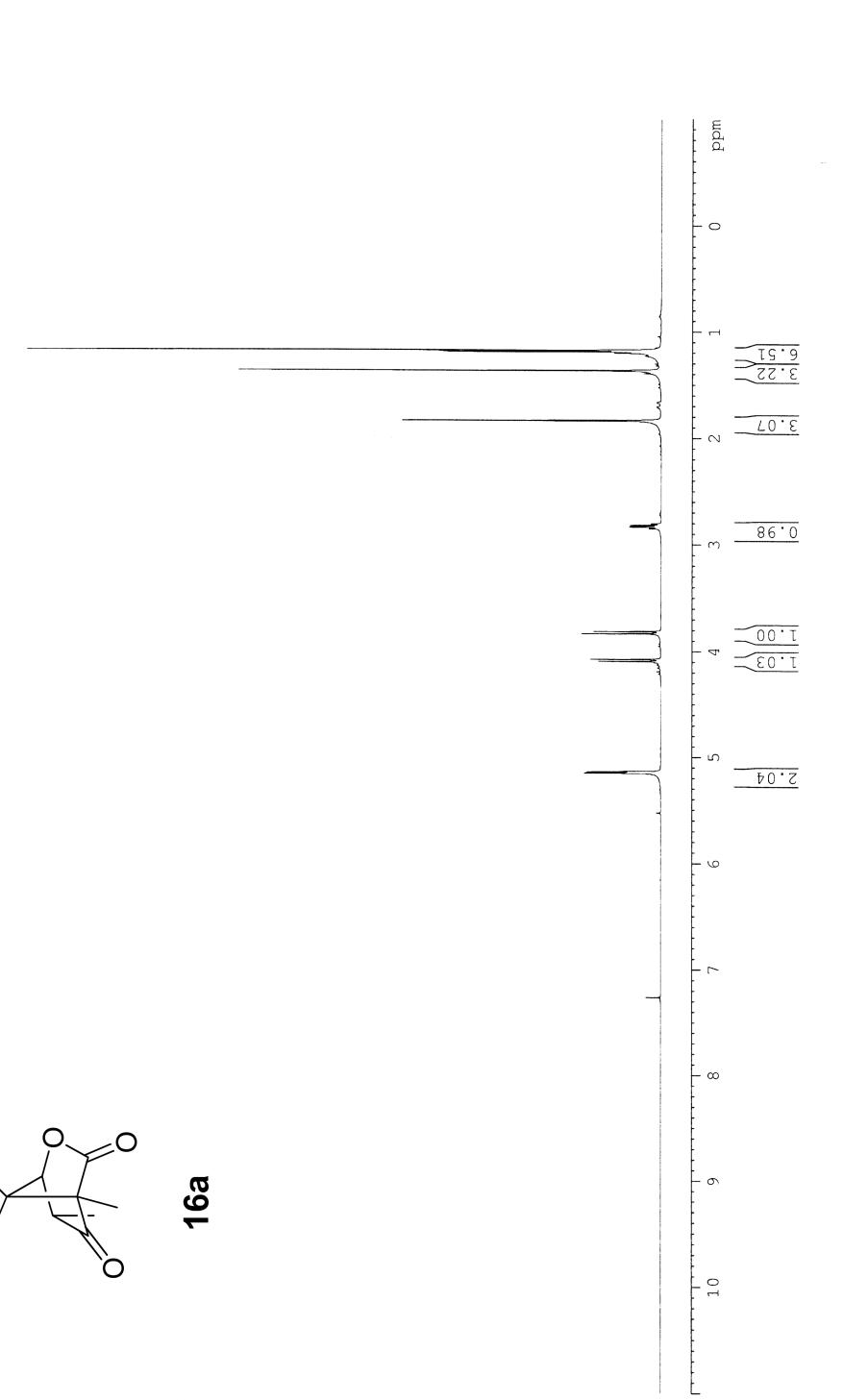


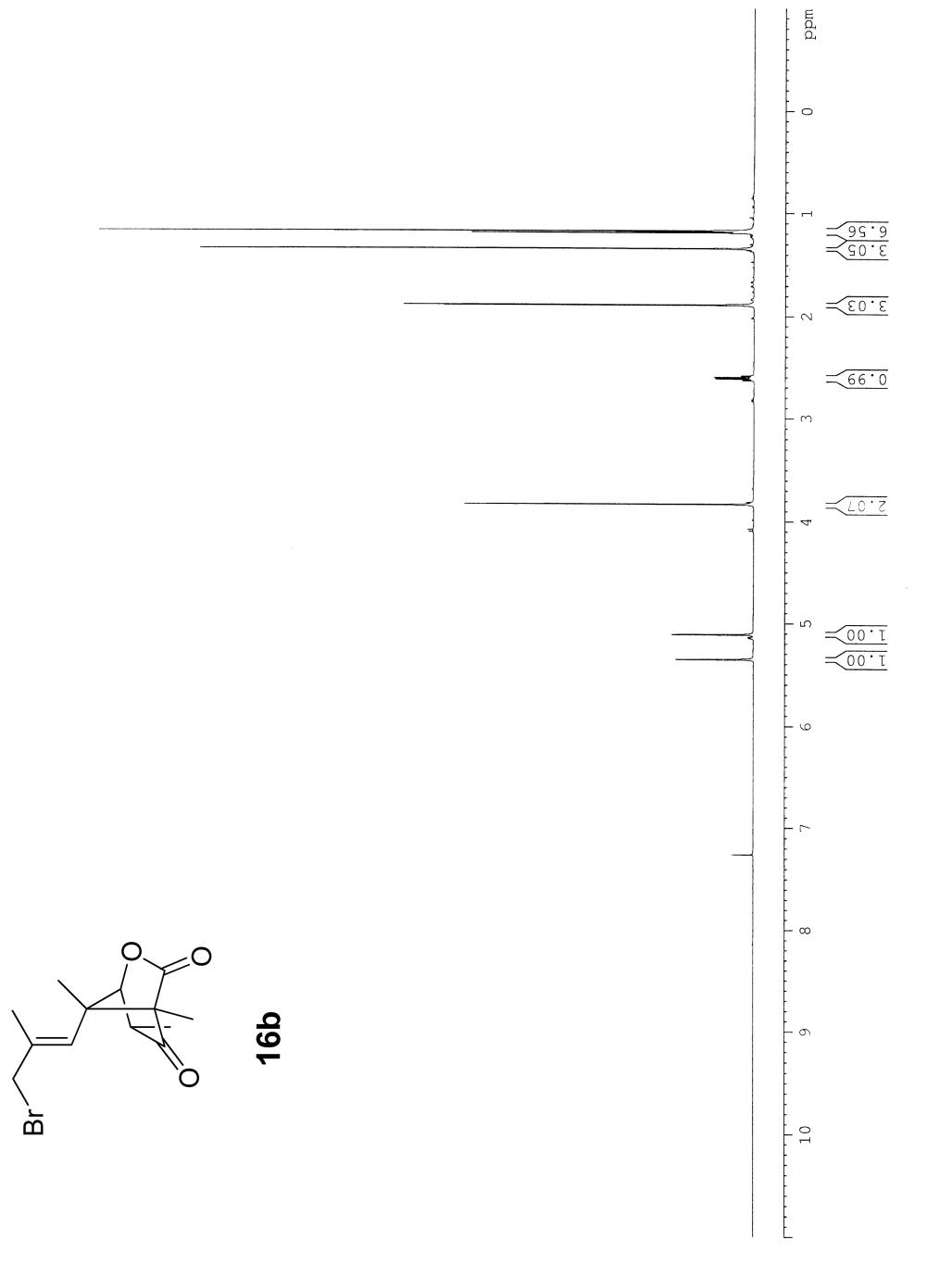
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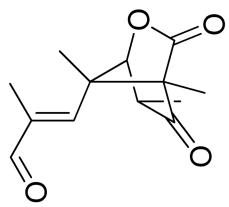
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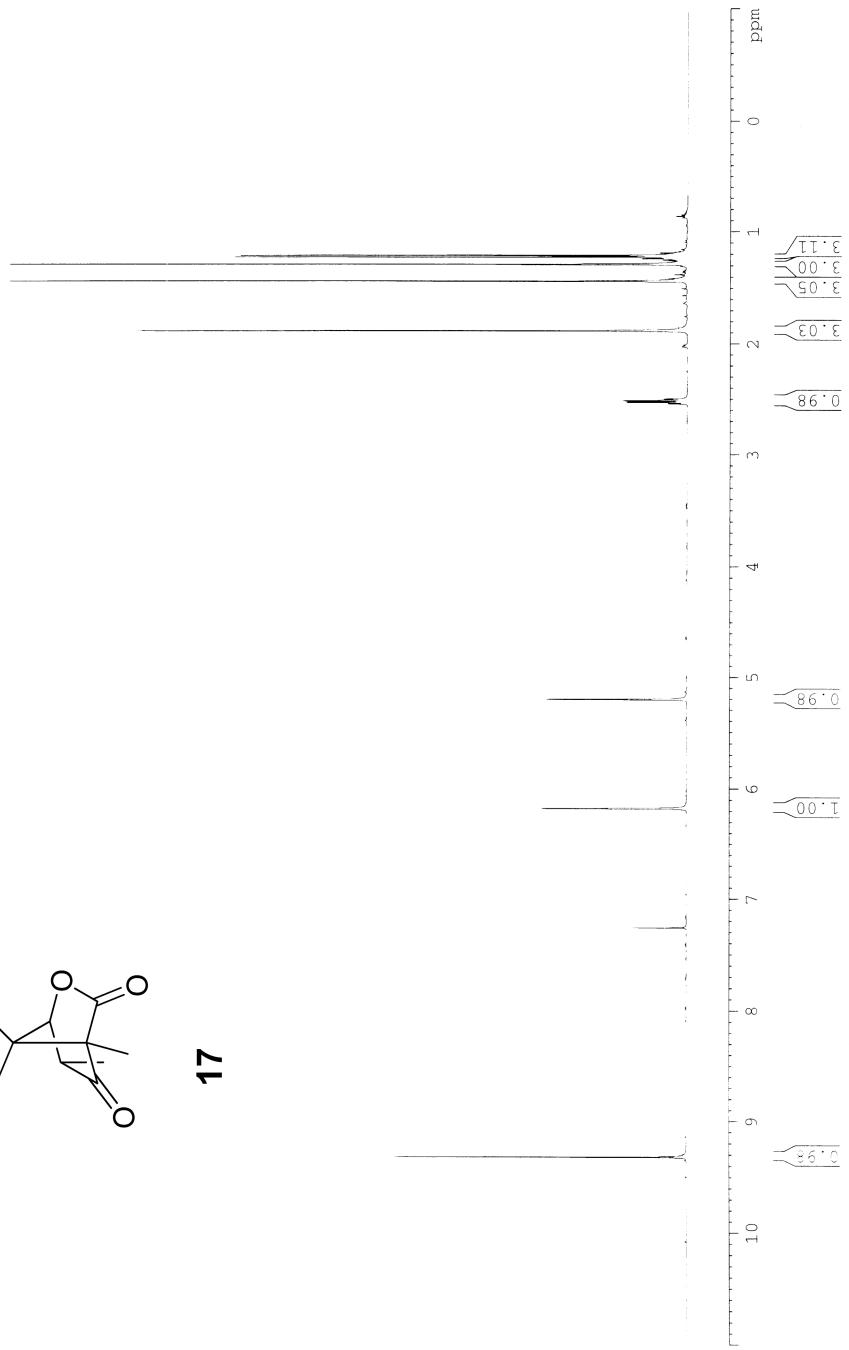


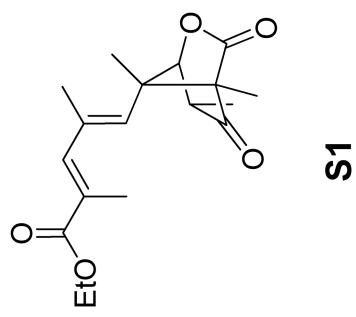
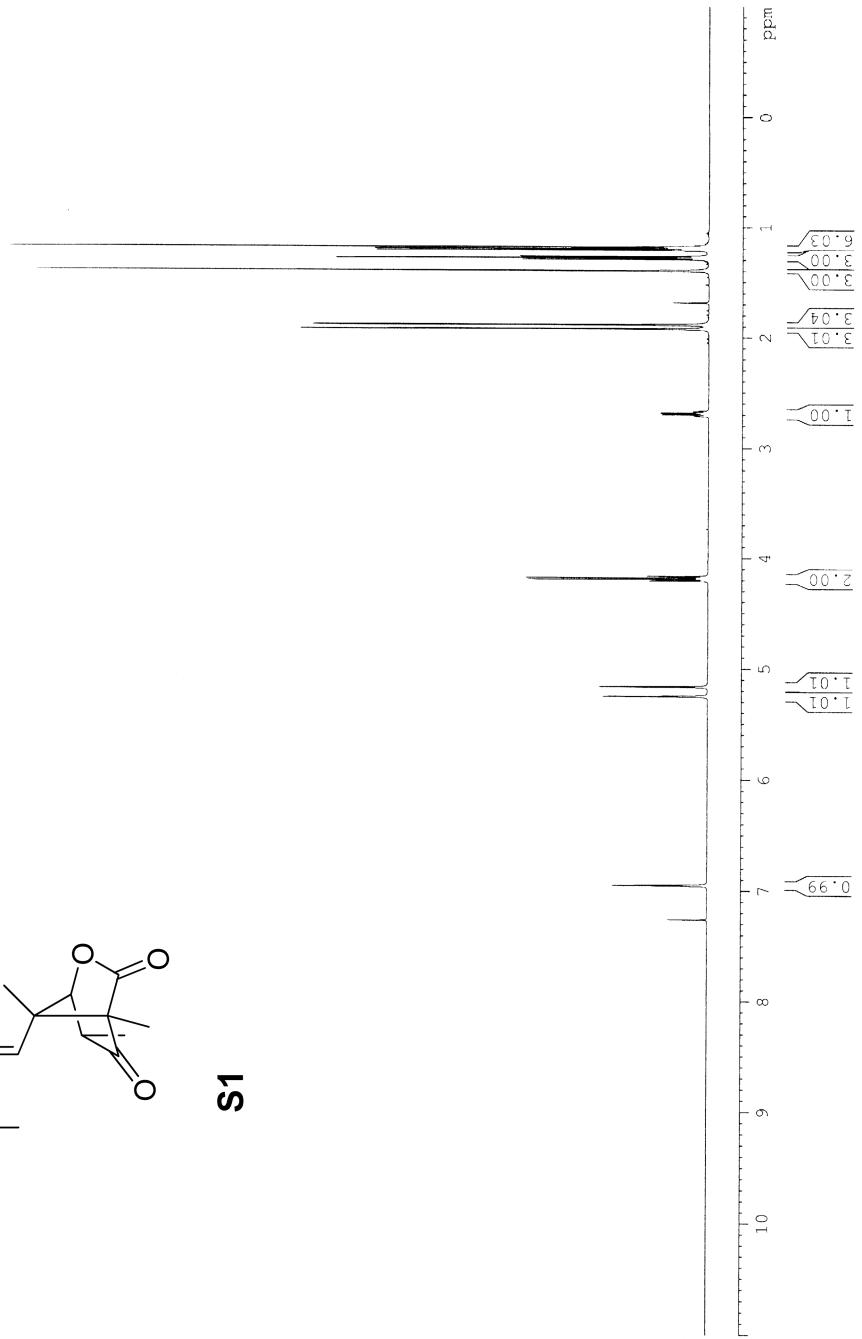


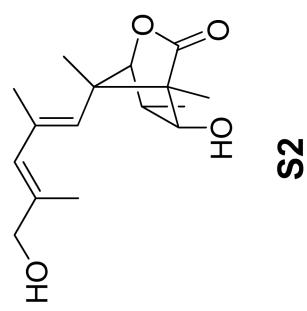
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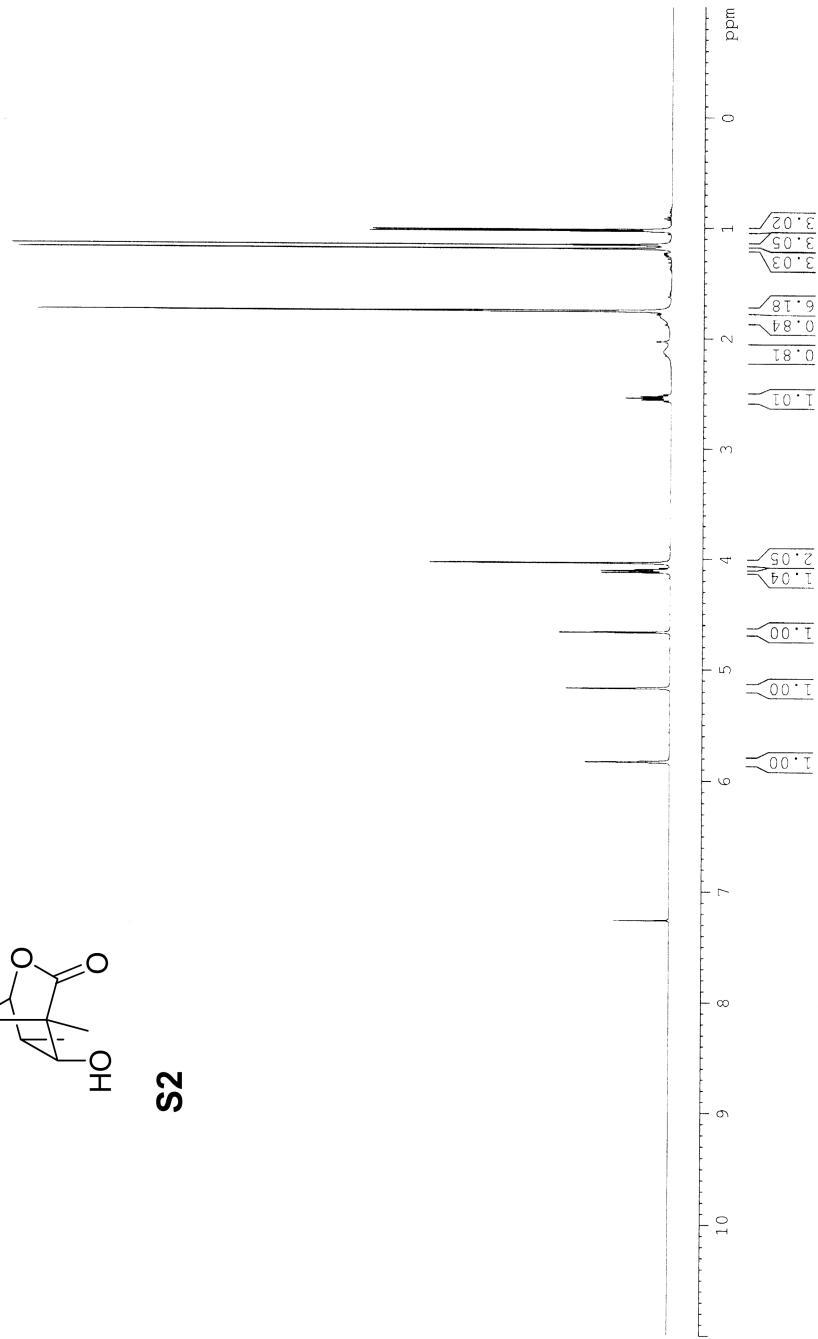
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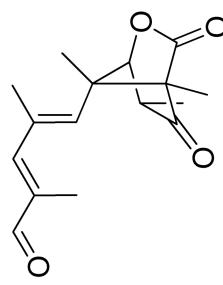




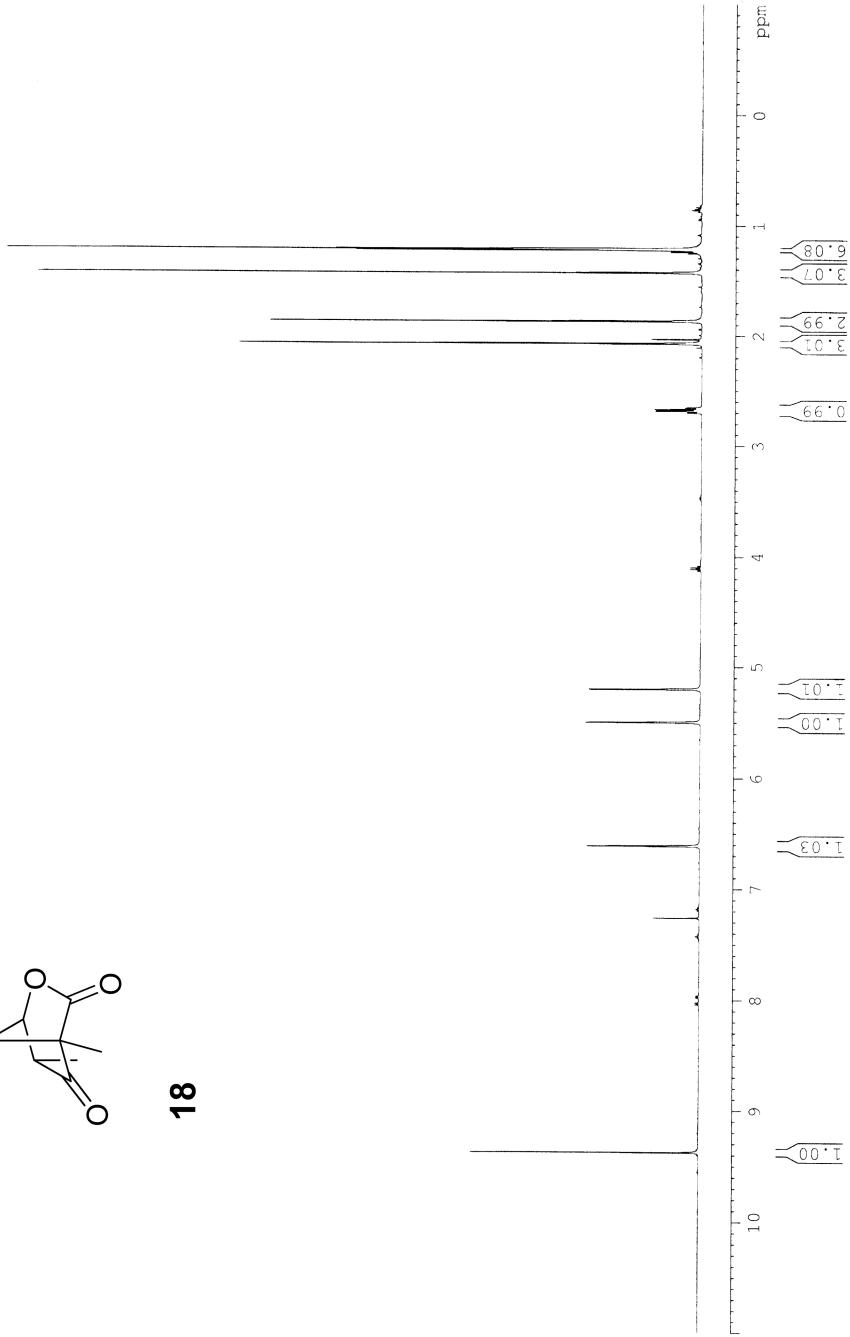


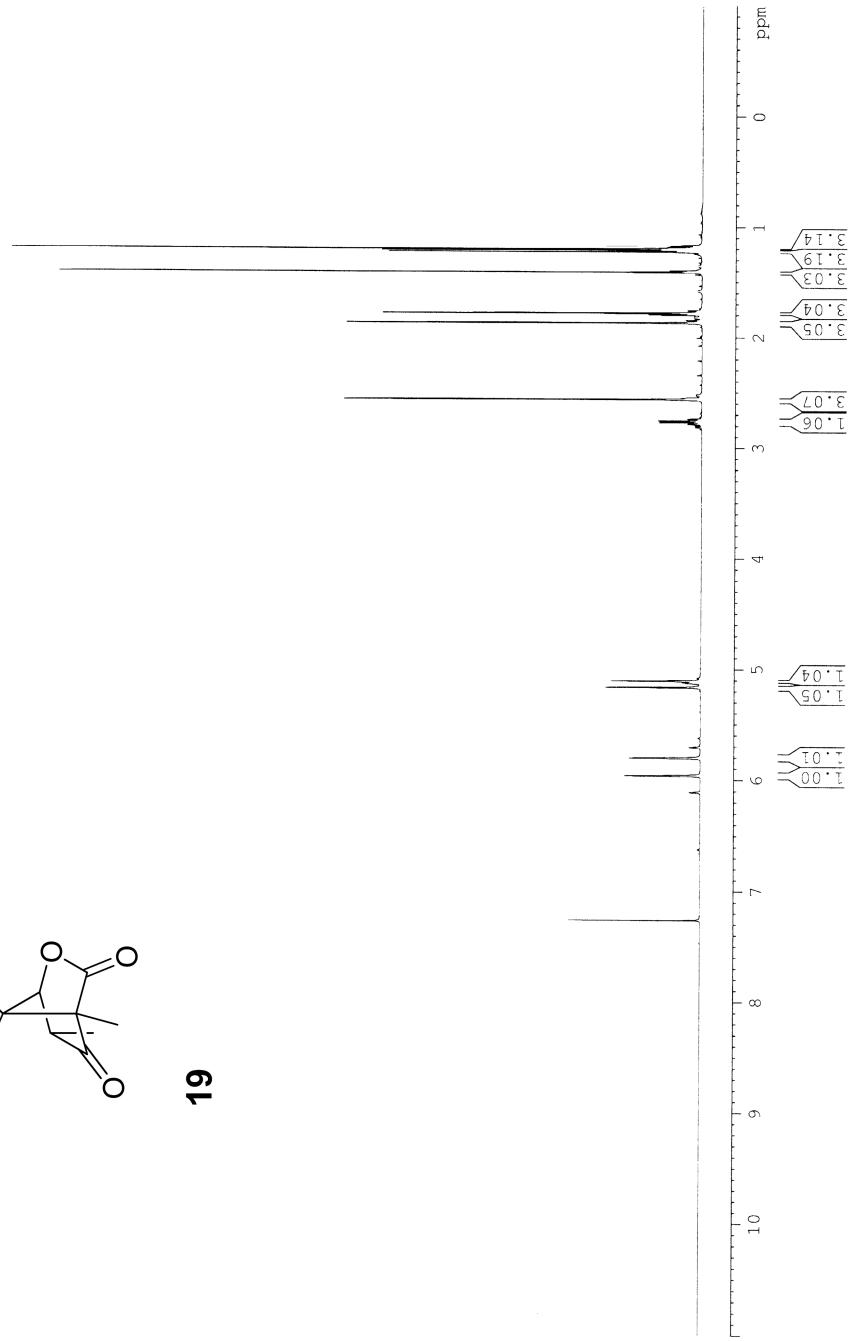
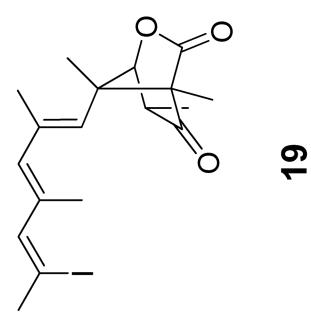
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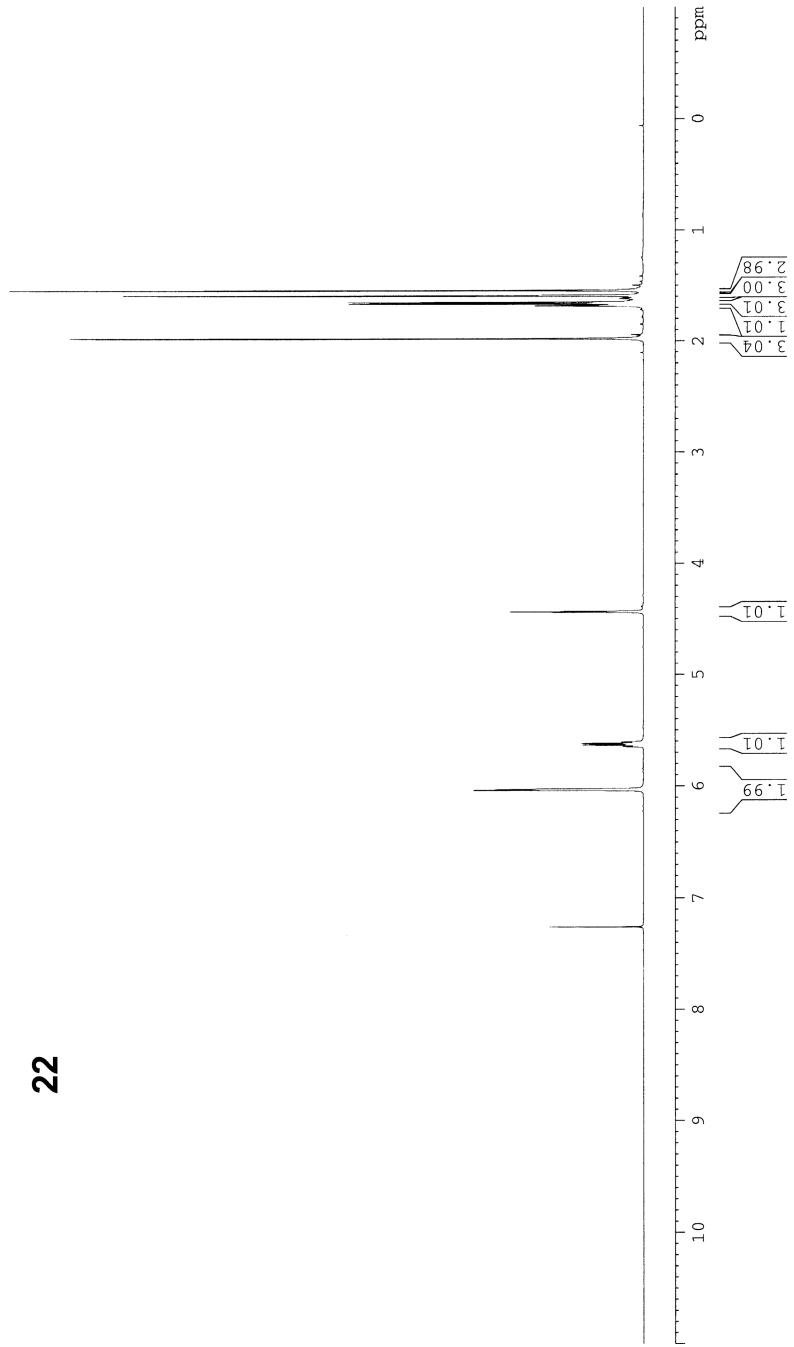
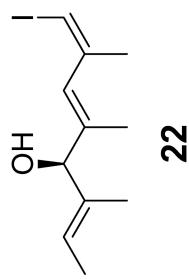


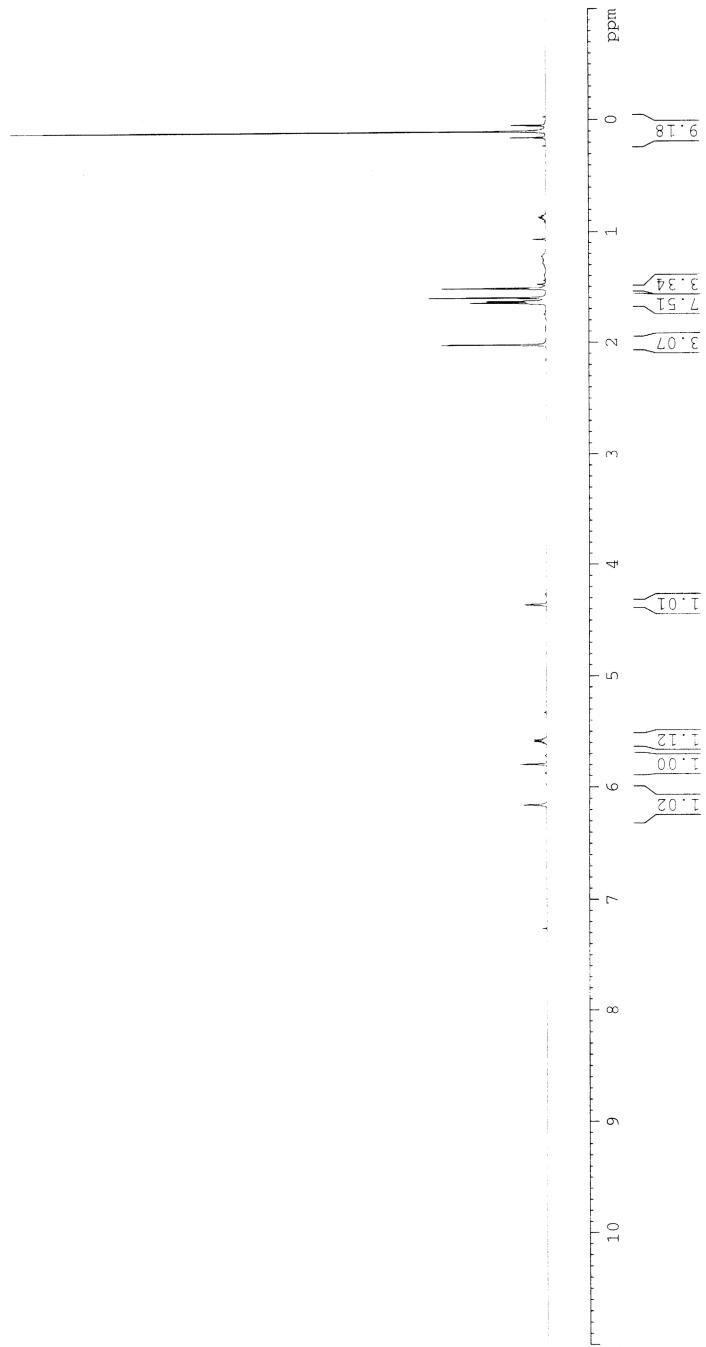
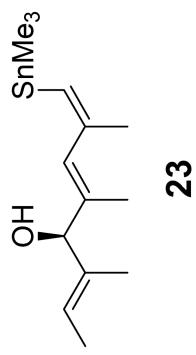


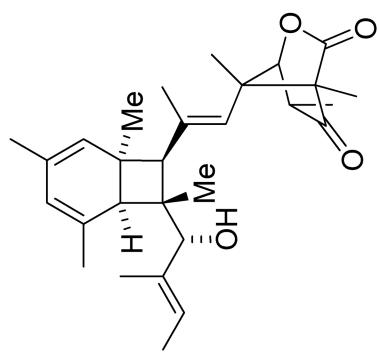
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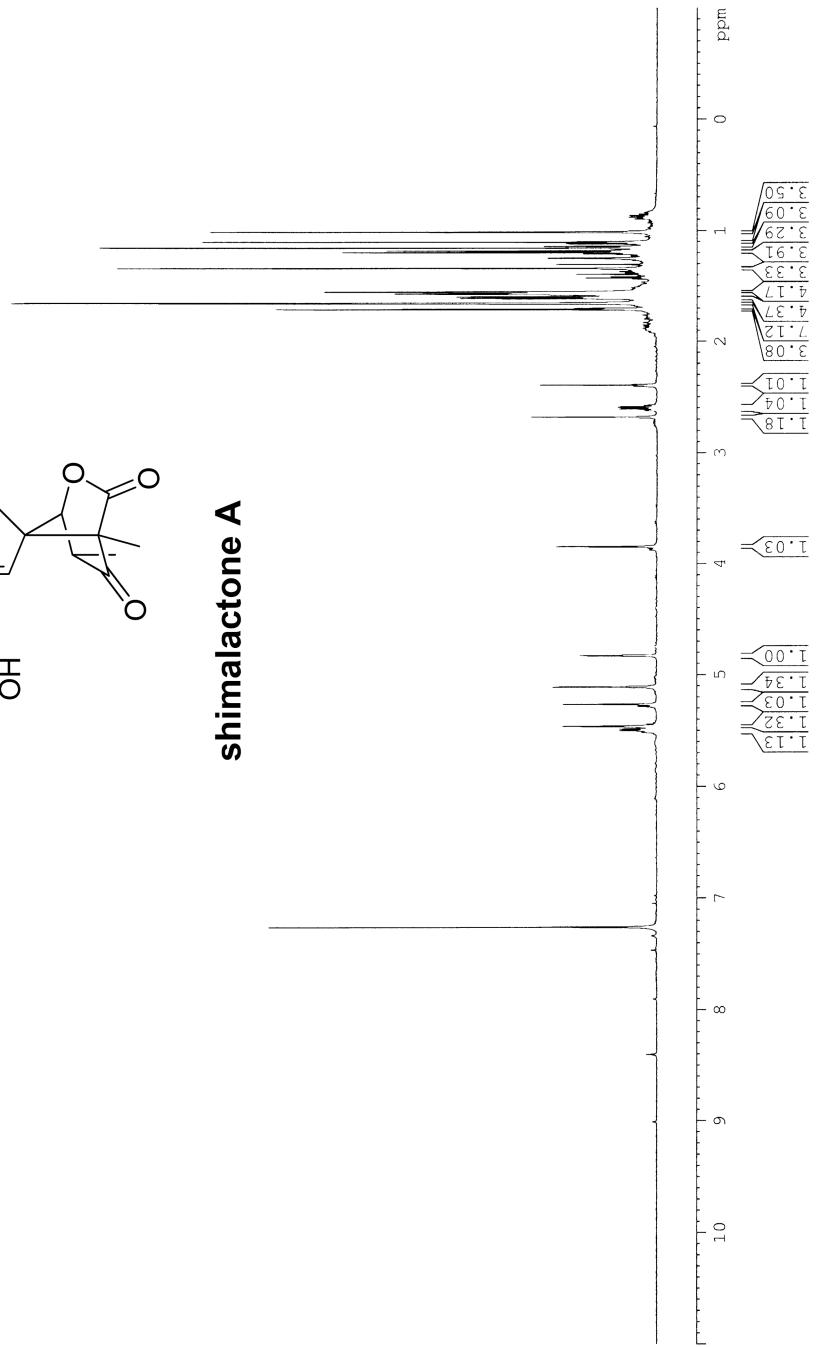


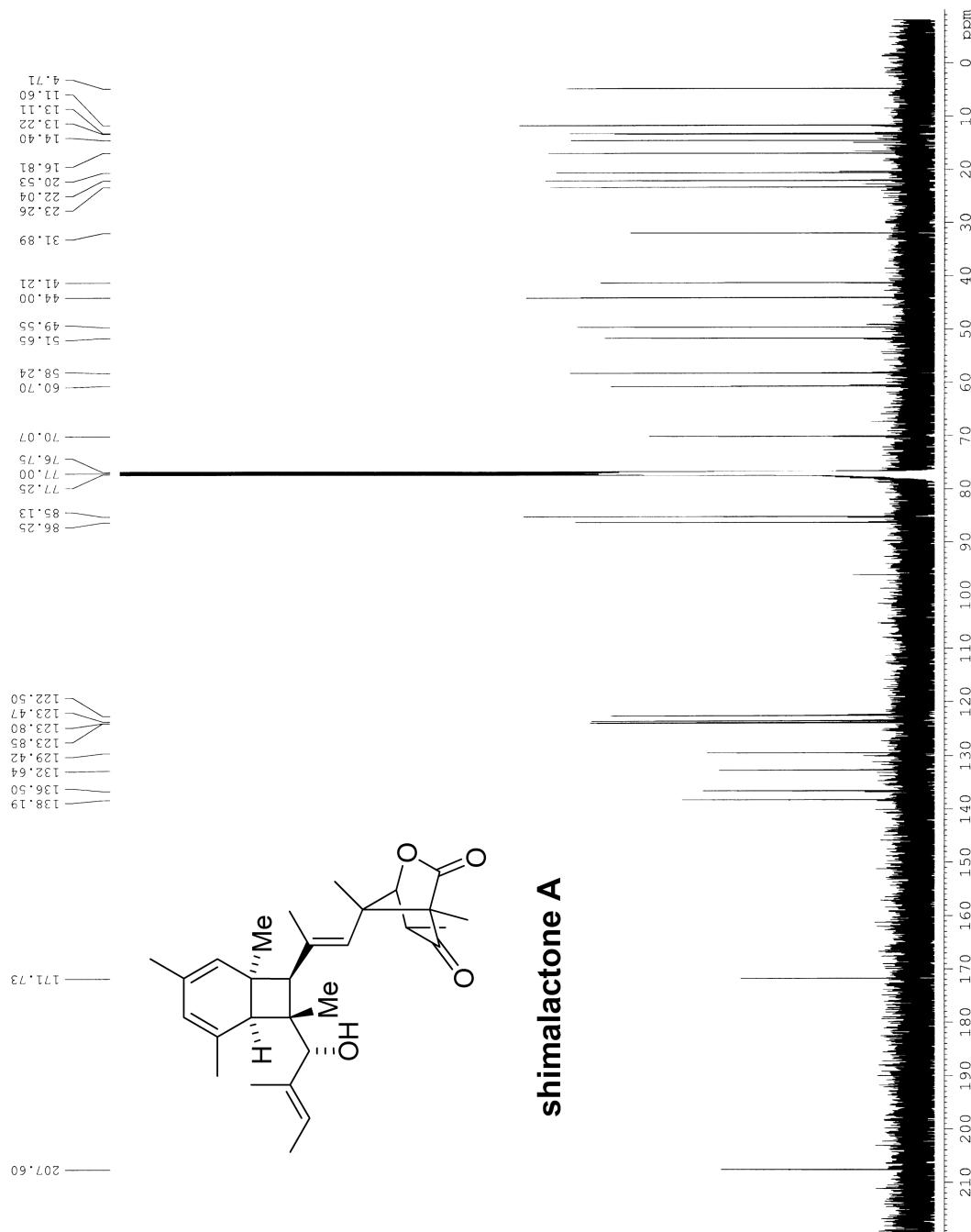


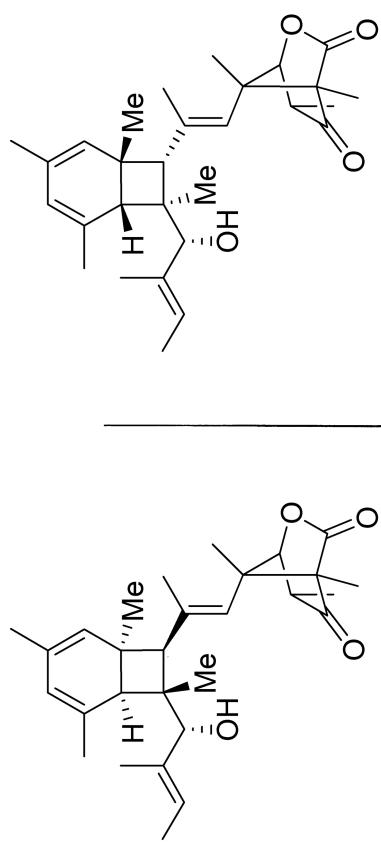




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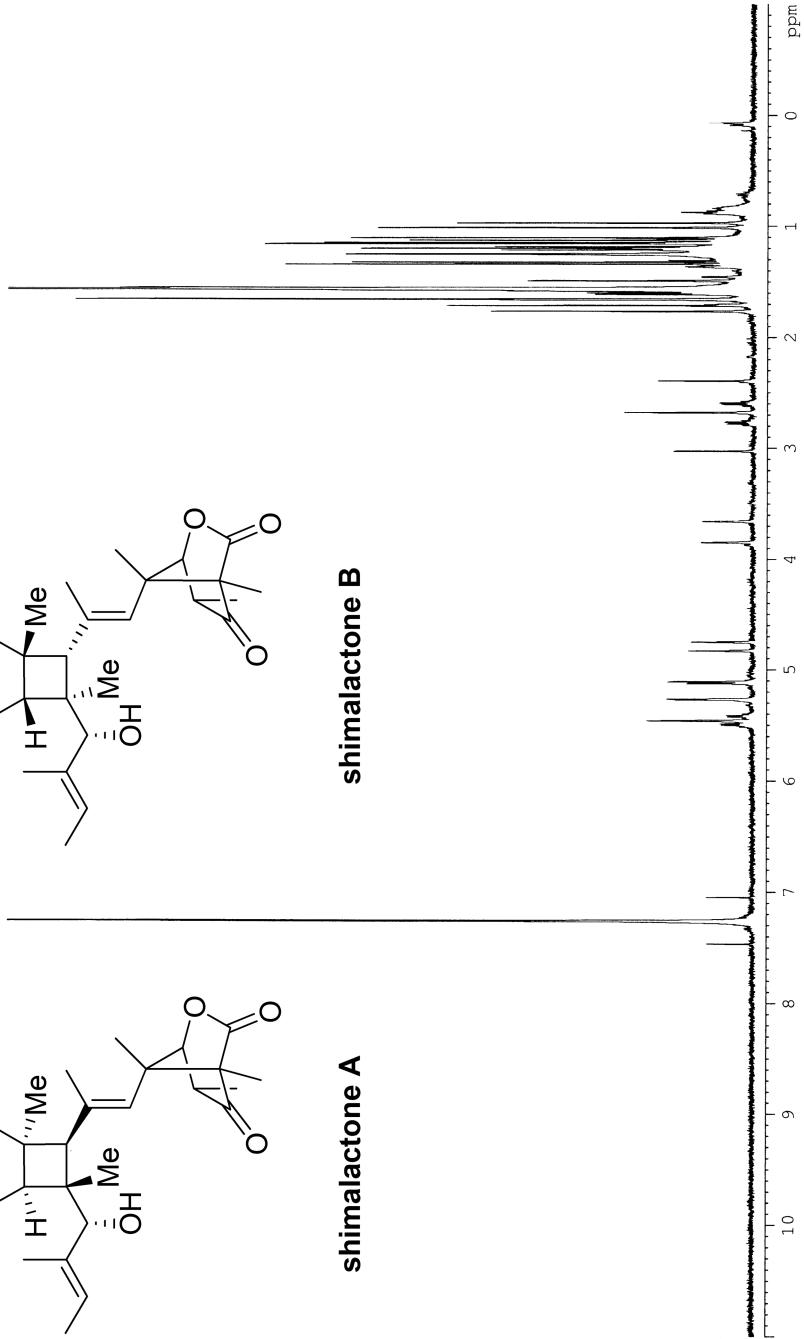


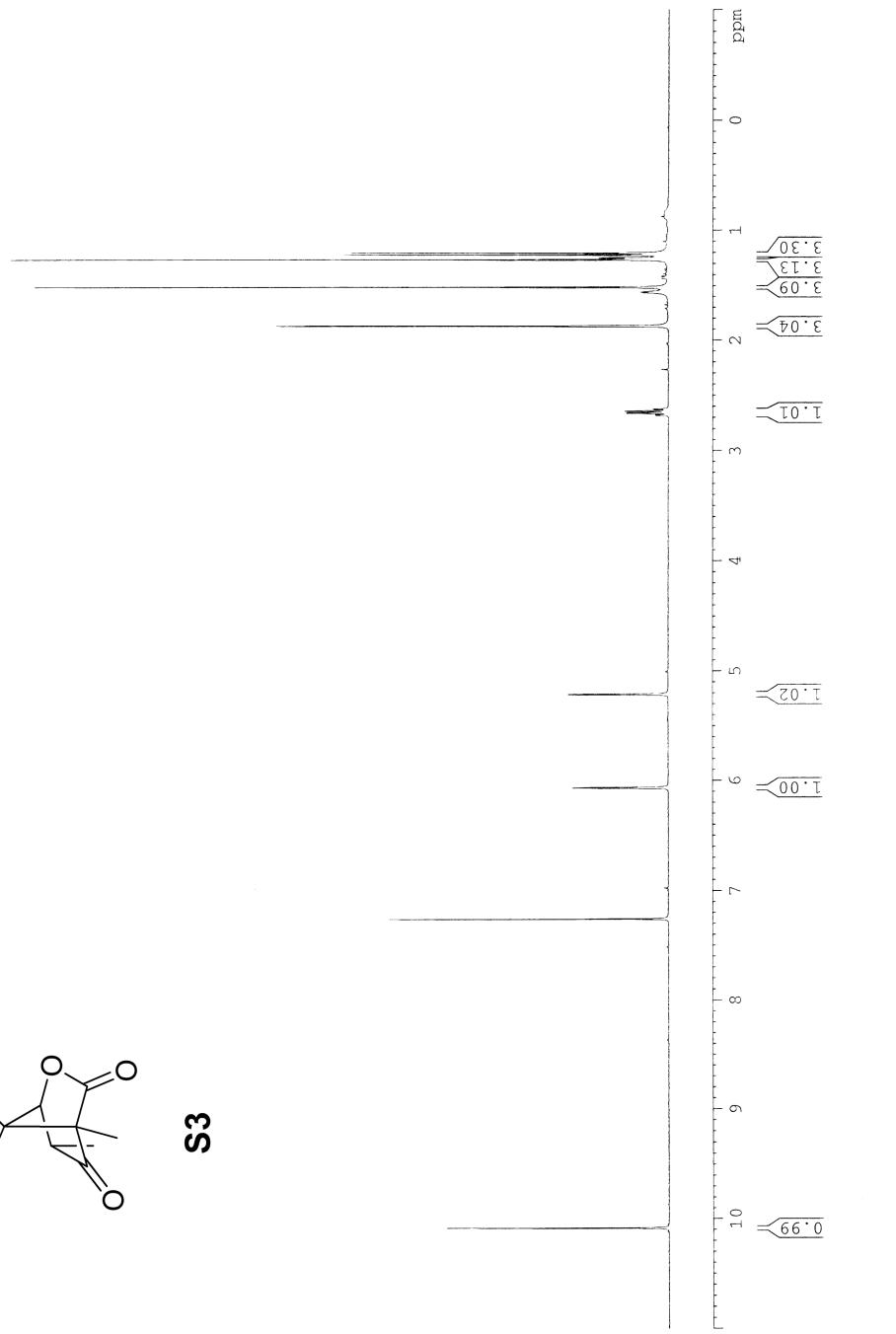
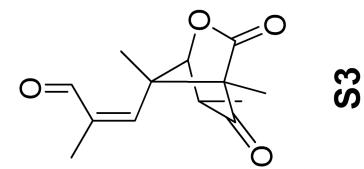


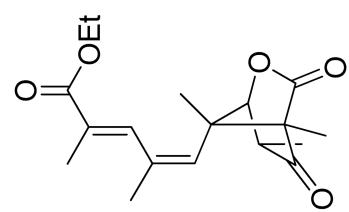
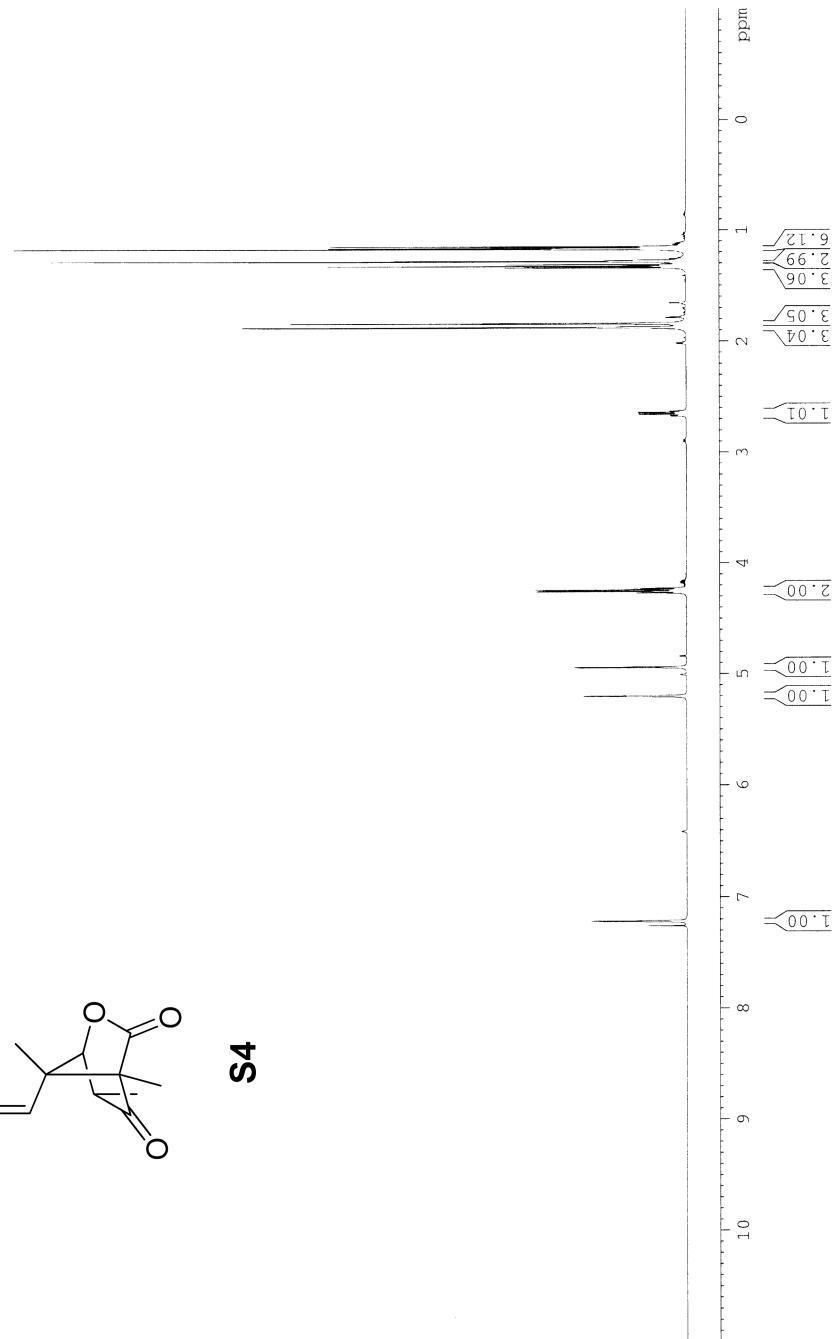


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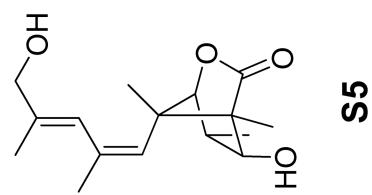
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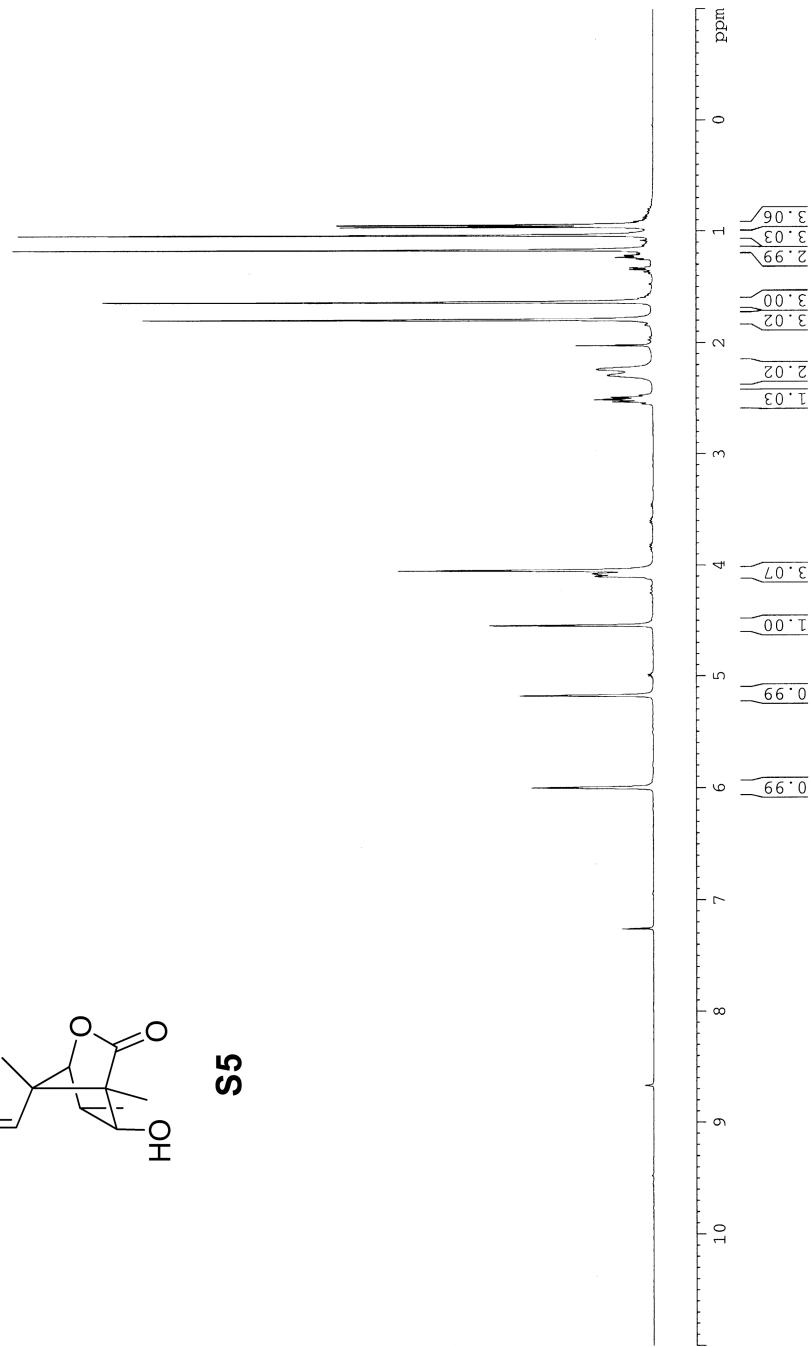


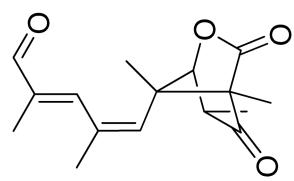


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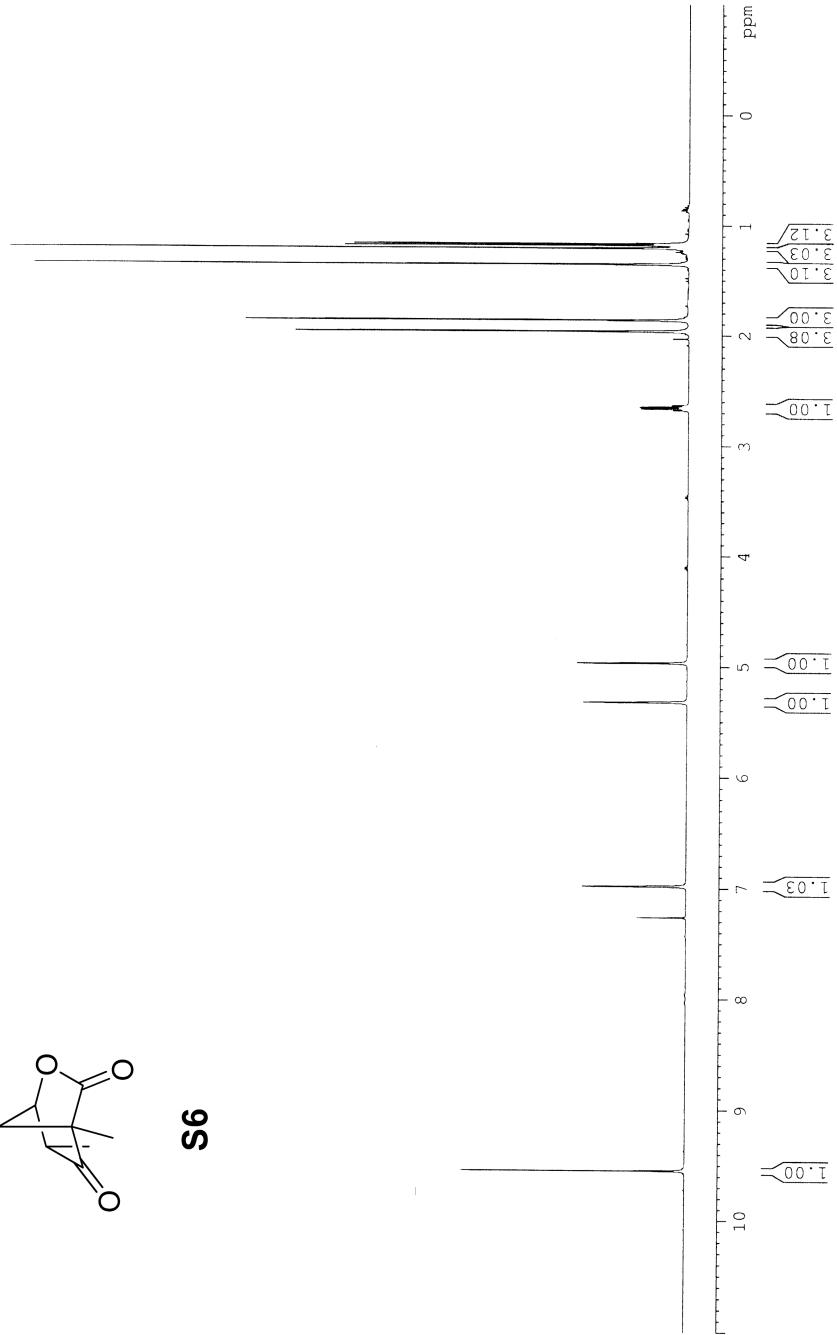


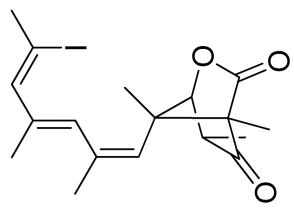
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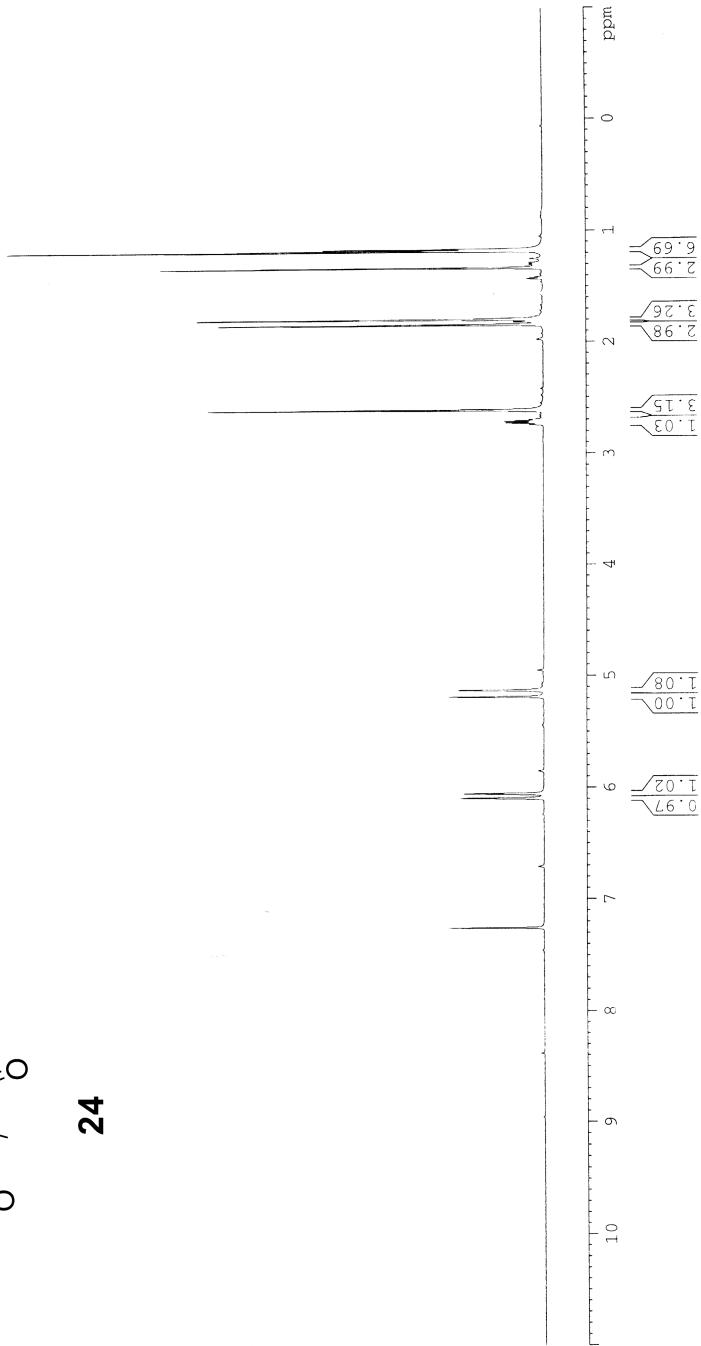


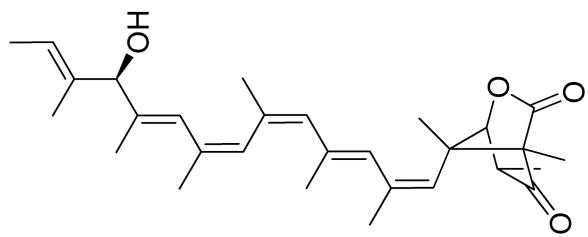
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