Evolution of the Total Synthesis of (-)-Okilactomycin Exploiting a Tandem Oxy-Cope Rearrangement/Oxidation, the Petasis-Ferrier Union/Rearrangement and Ring Closing Metathesis.

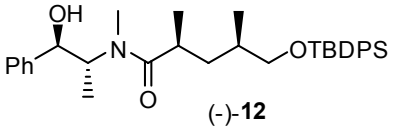
SUPPORTING INFORMATION

Amos, B. Smith, III,* Todd Bosanac, and Kallol Basu

Department of Chemistry, Laboratory for Research on the Structure of Matter, and Monell Chemical Senses Center, University of Pennsylvania, Philadelphia, Pennsylvania 19104

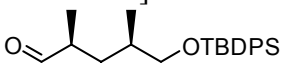
Experimental
Materials and Methods

Reactions were carried out in oven or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were freshly distilled and dried by standard techniques just before use. Diethyl ether and THF were distilled from sodium/benzophenone. Methylene chloride (CH_2Cl_2), benzene (PhH), and diisopropylamine were distilled from calcium hydride. Anhydrous pyridine (Pyr), triethylamine, diisopropylamine, *N,N*-dimethylformamide (DMF), acetonitrile (MeCN), and dimethyl sulfoxide (DMSO) were purchased from Aldrich and used without purification. *n*-Butylithium (*n*-BuLi) was purchased from Aldrich and titrated against *n*-benzylbenzamide prior to use. Trimethylsilyl trifluoromethanesulfonate (TMSOTf) was distilled from calcium hydride. Except as indicated otherwise, all other reagents were purchased from Aldrich, Acros, or Strem chemicals and used as received. Reactions were monitored by thin layer chromatography (TLC) with 0.25-mm E. Merck pre-coated silica gel plates (Kieselgel $60F_{254}$, Merck). Spots were detected by viewing under a UV light, putting into an iodine chamber, or colorizing with charring after dipping in an anisaldehyde solution composed of acetic acid, sulfuric acid, and methanol. Silica gel for flash chromatography (particle size 0.040-0.063 mm) was supplied by Silicycle and Sorbent Technologies. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. All melting points were obtained on a Thomas-Hoover apparatus. Infrared spectra were recorded on a Perkin-Elmer Model 283B spectrophotometer or a Jasco Model FT/IR-480 Plus spectrometer. Proton (^1H) and carbon (^{13}C) NMR spectra were recorded on a Bruker AMX-500 spectrometer. Chemical shifts are reported as δ values relative to chloroform (δ 7.27) or benzene (δ 7.16) for ^1H-NMR and chloroform (77) or benzene (δ 128.28) for ^{13}C-NMR. Optical rotations were measured on a Perkin-Elmer model 241 polarimeter in the solvent indicated. High-resolution mass spectra were measured at the University of Pennsylvania Mass Spectrometry Service on either a VG Micromass 70/70H or VG ZAB-E spectrometer.



(-)-**12**

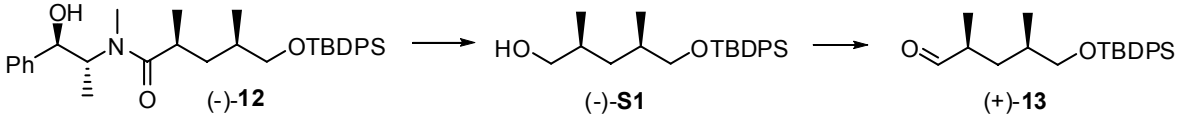
Amide (-)-**12**: To a cold (0 °C), stirred suspension of flame-dried LiCl (36.5 g, 860.3 mmol) and diisopropylamine (29.7 g, 41.1 mL, 293.6 mmol) in THF (270 mL) was added *n*-BuLi (109 mL of 2.5 M solution in hexanes, 273.1 mmol) dropwise *via* an addition funnel over 45 min. After the addition was complete, the mixture was stirred at 0 °C for an additional 15 min. The solution was then cooled to -78 °C and treated with a solution of amide (-)-**11** (31.7 g, 143.4 mmol) in THF (270 mL) *via* cannula. After being stirred at -78 °C for 30 min the mixture was warmed to room temperature and treated with a solution of the iodide (+)-**10** (30.0 g, 68.3 mmol) in THF (60 mL). The reaction mixture was stirred at room temperature for 24 h before being quenched with saturated aqueous solution of NH_4Cl (500 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 x 500 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a yellow residue, which was purified by column chromatography on silica gel (elution with 2:1 hexane:ethyl acetate) to afford amide (-)-**12** (34.5 g, 95%) as a colorless gum: $[\alpha]_D^{20}$ = -36.9 (*c* = 2.86, $CHCl_3$); IR (neat) 3371, 2930, 1618, 1472, 1428, 1112, 741, 701 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) (*-denotes signals from minor rotamer) δ *7.92 (m, 4 H), 7.87 (m, 4 H), 7.42 (d, *J* = 7.6 Hz, 2 H), 7.36-7.25 (m, 9 H), 5.25 (br s, 1 H), 4.64 (dd, *J* = 7.0, 7.0 Hz, 1 H), 4.30 (m, 1 H), *4.00 (m, 1 H), *3.89 (dd, *J* = 4.7, 9.5 Hz, 1 H), 3.66 (dd, *J* = 5.1, 9.8 Hz, 1 H), *3.07 (m, 1 H), *3.02 (s, 1 H), *2.88 (s, 3 H), 2.50 (m, 1 H), 2.40 (s, 3 H), *2.29 (m, 1 H), *2.09 (m, 1 H), 2.01 (m, 1 H), 1.79 (m, 1 H), *1.30 (s, 9 H), 1.27 (s, 9 H), 1.17-1.08 (m, 5 H), 1.03 (d, *J* = 6.7 Hz, 3 H), 0.92 (d, *J* = 6.6 Hz, 3 H), *0.76 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 179.1, *177.7, 142.8, *141.4, 135.81, 135.77, *134.3, *134.2, 134.03, 133.98, 129.72, 129.71, *129.6, *128.8, 128.4, 127.76, 127.72, 127.6, *127.0, 126.4, *77.4, *75.4, *69.6, 68.9, *58.0, *38.2, 37.7, 34.2, *33.7, 33.4, *33.3, 27.1, 19.5, *19.0, 17.9, *17.7, 17.5, *15.7, 14.5; high resolution mass spectra (ES+) m/z 554.3061 [$(M+Na)^+$; calcd for $C_{33}H_{45}NO_3SiNa^+$: 554.3066]



(+)-**13**

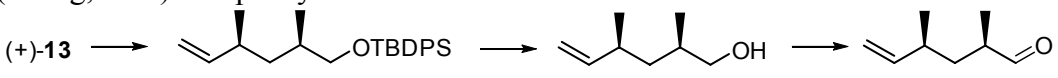
One Step Method: Aldehyde (+)-13: A suspension of LAH (1.9 g, 50.1 mmol) in hexanes (115.0 mL) was cooled to 0 °C and treated with ethyl acetate (distilled from CaH_2, 7.3 mL, 74.3 mmol) dropwise via syringe. After being stirred at 0 °C for 30 min the suspension was cooled to -78 °C when a solution of amide (-)-**12** (11.6 g, 21.8 mmol) in THF (75 mL) was introduced via cannula over 10 min. The resulting reaction mixture was warmed to 0 °C and stirred for 2 h then cannulated into a solution of 1 M aqueous solution of HCl (270 mL) and TFA (16.8 mL) over 5 min. The solution was stirred vigorously for 10 min then diluted with 1 M aqueous solution of HCl (450 mL). The layers were separated and the aqueous layer was extracted with 9:1 Hex:EtOAc (3 x 150 mL). The combined organic layers were carefully basified with a saturated aqueous solution of $NaHCO_3$ (250 mL), dried over Na_2SO_4, and filtered through a plug (3 cm) of SiO_2. The filtrate was concentrated to afford a yellow resiude which was purified by column chromatography on silica gel (elution with 9:1 hexane:ethyl acetate) to provide aldehyde (+)-**13** (5.5 g, 68%) as a pale yellow oil: $[\alpha]_D^{20}$ = +11.4 (*c* = 2.10, $CHCl_3$); IR (neat) 3071, 2960, 2857, 2708, 1729, 1473, 1429, 1390, 1112, 824, 701 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 9.27 (d, *J* = 1.3 Hz, 1 H), 7.76 (m, 4 H), 7.24 (m, 6 H), 3.43 (dd, *J* = 5.3, 10.0 Hz, 1 H), 3.37 (dd, *J* = 5.9, 10.0 Hz, 1 H), 1.99 (m, 1 H), 1.68-1.58 (m, 2 H), 1.17 (s, 9 H), 0.81 (d, *J* = 6.2 Hz, 3 H), 0.79

(m, 1 H), 0.73 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 203.2, 136.0, 134.1, 130.0, 128.1, 68.7, 43.9, 34.5, 33.4, 27.1, 19.5, 17.3, 14.0; high resolution mass spectra (ES+) m/z 391.2069 [$(M+Na)^+$; calcd for $C_{23}H_{32}O_2SiNa^+$: 391.2060].



Two Step Method: Aldehyde (+)-13: To a cold (0 °C), stirred solution of diisopropylamine (27.3 g, 38.0 mL, 269.3 mmol) in THF (270 mL) was added *n*-BuLi (100 mL of 2.5 M solution in hexanes, 250.1 mmol) dropwise *via* an addition funnel over 45 min. After the addition was complete, the mixture was stirred at 0 °C for an additional 15 min. Borane-ammonia complex (90%, 7.9 g, 256.5 mmol) was added in four portions over 15 min at 0 °C, and the suspension was stirred at 0 °C for 15 min. The mixture was then stirred at room temperature for 30 min before cooling back to 0 °C. A solution of amide (-)-**12** (34.1 g, 64.1 mmol) in THF (185 mL) was added dropwise via an addition funnel over 10 min. The reaction mixture was warmed to room temperature, held at this temperature for 2 h, and then cooled to 0 °C where excess hydride was quenched by careful addition of 3 N aqueous solution of HCl (650 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (4 x 600 mL). The combined organic layers were washed with 2 N aqueous solution of NaOH (125 mL) and brine (150 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a yellow oil, which was purified by column chromatography on silica gel (elution with 5:1 hexane:ethyl acetate) to afford alcohol (-)-**S1** (22.3 g, 94%) as a colorless oil: $[\alpha]_D^{20}$ = -1.2 (c = 0.6, $CHCl_3$); IR (neat) 3347, 2956, 2929, 2858, 1470, 1428, 1110, 823, 740, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67-7.65 (m, 4 H), 7.42-7.36 (m, 6 H), 3.53-3.41 (m, 3 H), 3.38-3.33 (m, 1 H), 1.77-1.72 (m, 1 H), 1.67-1.60 (m, 1 H), 1.54 (s, 1 H), 1.51-1.43 (m, 1 H), 1.06 (s, 9 H), 0.95 (d, J = 6.7 Hz, 3 H), 0.94-0.91 (m, 1 H), 0.89 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6 (4 C), 134.0 (2 C), 129.5 (2 C), 127.5 (4 C), 68.7, 68.2, 37.1, 33.1 (2 C), 26.8 (3 C), 19.2, 17.8, 17.4; high resolution mass spectra (ES+) m/z 393.2219 [$(M+Na)^+$; calcd for $C_{23}H_{34}O_2SiNa^+$: 393.2226].

To a cold (0 °C) solution of alcohol (-)-**S1** (30.2 g, 81.6 mmol) in CH_2Cl_2 (250 mL) and DMSO (116 mL) were added Et_3N (82.6 g, 113.8 mL, 816.2 mmol) followed by sulfur trioxide-pyridine complex (52 g, 326.5 mmol). After being stirred for 30 min at 0 °C, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ (600 mL) followed by H_2O (1 L). The aqueous layer was washed with Et_2O (3 x 1 L). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a yellow oil, which was purified by column chromatography on silica gel (elution with 25:1 hexane:ethyl acetate) to afford aldehyde (+)-**13** (27.0 g, 90%) as a pale yellow oil.

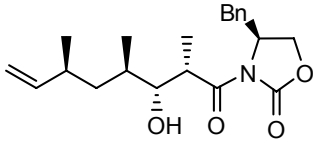


Aldehyde 14: To a cold (0 °C) suspension of bromomethyltriphenylphosphonium bromide (60.0 g, 168.0 mmol) in THF (340 mL) was added *n*-BuLi (64.0 mL of 2.5 M solution in hexanes, 160.4 mmol) dropwise *via* an addition funnel. The resulting yellow solution was stirred at 0 °C for 30 min, then a solution of the aldehyde (+)-**13** (28.1 g, 76.4 mmol) in THF (340 mL) was added dropwise over 1 h. After being stirred at 0 °C for 1.5 h, the reaction was quenched with a saturated aqueous solution of NH_4Cl (500 mL). The organic layer was separated and the aqueous layer was washed with Et_2O (3 x 500 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a yellow oil, which was purified by column

chromatography on silica gel (elution with 25:1 hexane:ethyl acetate) to afford alkene (+)-**S2** (26.8 g, 96%) as a colorless oil: $[\alpha]_D^{20}$ = +4.0 (*c* = 2.15, $CHCl_3$); IR (neat) 3072, 2959, 1473, 1429, 1112, 824, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (app dd, *J* = 1.3, 7.9 Hz, 4 H), 7.36 (m, 6 H), 5.62 (ddd, *J* = 8.0, 10.2, 17.7 Hz, 1 H), 4.98-4.89 (m, 2 H), 3.49 (dd, *J* = 5.8, 9.7 Hz, 1 H), 3.43 (dd, *J* = 6.4, 9.7 Hz, 1 H), 2.20 (m, 1 H), 1.72 (m, 1 H), 1.43 (ddd, *J* = 4.9, 9.3, 13.8 Hz, 1 H), 1.06 (s, 9 H), 1.03 (ddd, *J* = 5.4, 9.0, 13.8 Hz, 1 H), 0.97 (d, *J* = 6.7 Hz, 3 H), 0.91 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 135.9, 134.3, 129.7, 128.6, 127.8, 112.8, 69.5, 40.6, 35.7, 33.6, 27.1, 21.5, 19.6, 17.0; high resolution mass spectra (ES+) m/z 367.2471 [$(M)^+$; calcd for $C_{24}H_{34}OSi^+$: 367.2471].

To a cold (0 °C), stirred solution of silyl ether (+)-**S2** (26.8 g, 73.2 mmol) in THF (100 mL) was added TBAF (109.8 mL of 1.0 M solution in THF, 109.8 mmol) dropwise *via* an addition funnel. The orange mixture was stirred at room temperature for 5 h. The mixture was concentrated under vacuum (bath temperature less than 20 °C) to afford an orange residue, which was purified by column chromatography on silica gel (elution with 5:1 pentane:diethyl ether) to afford alcohol (+)-**S3** (9.1 g, 97%) as a colorless oil: $[\alpha]_D^{20}$ = +29.9 (*c* = 2.14, $CHCl_3$); IR (neat) 3349, 2957, 2924, 1643, 1419, 1376, 1035, 910 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.61 (ddd, *J* = 8.2, 10.2, 17.2 Hz, 1 H), 4.96 (ddd, *J* = 0.9, 0.9, 17.2 Hz, 1 H), 4.90 (dd, *J* = 1.9, 10.2 Hz, 1 H), 3.44 (dd, *J* = 5.8, 10.5 Hz, 1 H), 3.37 (dd, *J* = 6.5, 10.5 Hz, 1 H), 2.23 (m, 1 H), 1.96 (br s, 1 H), 1.64 (m, 1 H), 1.36 (ddd, = 4.6, 9.8, 13.9, Hz, 1 H), 1.04 (ddd, *J* = 4.9, 9.5, 13.9 Hz, 1 H), 0.99 (d, *J* = 6.7 Hz, 3 H), 0.88 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.5, 113.1, 68.7, 40.5, 35.7, 35.6, 21.6, 16.5; high resolution mass spectra (ES+) m/z 109.1020 [$(M\text{-}OH)^+$; calcd for $C_8H_{15}^+$: 109.1017]

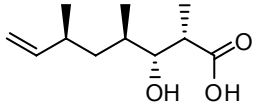
To a cold (0 °C) solution of alcohol (+)-**S3** (9.2 g, 71.8 mmol) in CH_2Cl_2 (250 mL) and DMSO (51 mL) were added Et_3N (36.3 g, 50.0 mL, 359.0 mmol) followed by sulfur trioxide-pyridine complex (45.7 g, 287.0 mmol). After being stirred at 0 °C for 30 min, the mixture was diluted with pentane (2 L), washed with saturated aqueous solution of $CuSO_4$ (4 x 1 L) followed by H_2O (2 x 1 L). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum (bath temeperature ~10 °C) to afford aldehyde **14** (8.4 g, 93%) as a pale yellow oil, which was directly used in the next step without further purification.



(+)-**16**

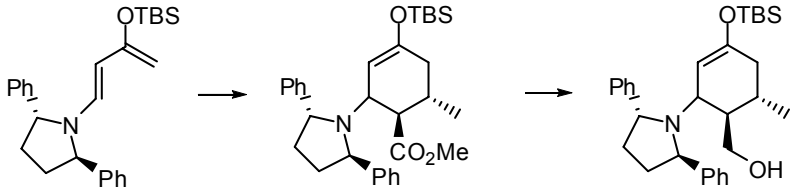
Aldol Adduct (+)-**16**: To a cold (0 °C), stirred solution of oxazolidinone (-)-**15** (15.3 g, 65.5 mmol) in CH_2Cl_2 (60 mL) were added Bu_2BOTf (77.4 mL of 1.0 M solution in CH_2Cl_2, 77.4 mmol) followed by Et_3N (7.8 g, 10.8 mL, 77.4 mmol). The mixture was stirred at 0 °C for 1 h before cooling to -78 °C. A solution of aldehyde **14** (7.5 g, 59.5 mmol) in CH_2Cl_2 (20 mL) *via* syringe over 5 min. After being stirred at -78 °C for 1.5 h, the mixture was warmed to 0 °C and stirring was continued for an additional 1 h at 0 °C. The reaction was treated with pH 7 buffer (74 mL) and MeOH (220 mL) followed by 2:1 mixture of MeOH and 30% aqueous solution of H_2O_2 (220 mL total). The mixture was vigorously stirred at room temperature for 1 h before being diluted with H_2O (100 mL). The mixture was extracted with Et_2O (3 x 350 mL) and the combined organic layers were washed with 5% saturated aqueous solution of $NaHCO_3$ (350 mL), brine (350 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to provide a yellow residue, which was purified by column chromatography on silica gel (elution

with 8:1 hexane:ethyl acetate) to afford aldol adduct (+)-**16** (19.8 g, 93%) as a white solid: $[\alpha]_D^{20}$ = +52.6 (*c* = 1.95, $CHCl_3$); IR (neat) 3522, 2963, 1781, 1700, 1696, 1457, 1388, 1210 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33 (m, 2 H), 7.29 (m, 1 H), 7.21 (d, *J* = 7.5 Hz, 2 H), 5.59 (ddd, *J* = 9.4, 9.4, 17.9 Hz, 1 H), 4.97 (app dt, *J* = 10.1, 0.7 Hz, 1 H), 4.87 (dddd, *J* = 3.1, 6.7, 6.7, 6.7 Hz, 1 H), 4.23-4.17 (m, 2 H), 3.98 (ddd, *J* = 3.2, 6.9, 6.9 Hz, 1 H), 3.60 (ddd, *J* = 3.5, 3.5, 7.4 Hz, 1 H), 3.25 (dd, *J* = 3.3, 13.3 Hz, 1 H), 2.82-2.77 (m, 2 H), 2.29-2.21 (m, 1 H), 1.74 (m, 1 H), 1.62-1.53 (m, 1 H), 1.23 (d, *J* = 7.0 Hz, 3 H), 1.04 (ddd, *J* = 3.5, 10.6, 13.8 Hz, 1 H), 1.02 (d, *J* = 6.4 Hz, 3 H), 0.88 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.8, 153.0, 144.4, 135.2, 129.6, 129.1, 127.6, 113.4, 76.1, 66.3, 55.3, 39.8, 39.7, 37.9, 36.0, 33.7, 22.3, 15.7, 10.6; high resolution mass spectra (ES+) m/z 359.2088 [M^+; calcd for $C_{21}H_{29}NO_4^+$: 359.2097].



(+)-**7**

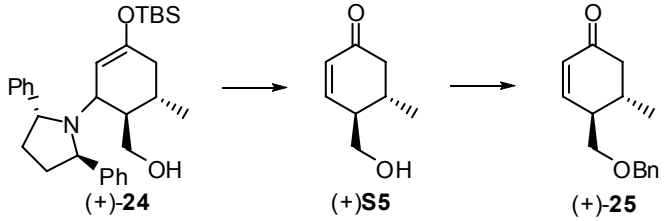
β-Hydroxy Carboxylic Acid (+)-**7**: To a cold (0 °C) solution of 30% H_2O_2 (22.0 mL) in water (26.0 mL) was added $LiOH{\cdot}H_2O$ (3.1 g, 73.0 mmol). The solution was stirred at 0 °C for 5 min before being treated with a solution of aldol adduct (+)-**16** (17.5 g, 48.7 mmol) in THF (140 mL) *via* cannula over 15 min. The reaction mixture was then stirred at room temperature for 1.5 h then carefully treated with a saturated aqueous solution of $Na_2S_2O_3$ (150 mL) followed by 2 M aqueous solution of HCl (150 mL). The mixture was extracted with EtOAc (3 x 500 mL), dried over Mg_2SO_4, and filtered. The filtrate was concentrated under vacuum to afford a residue which was purified by column chromatography on silica gel (elution with 3:1 hexane:ethyl acetate) to afford acid (+)-**7** (9.5 g, 97%) as an off-white crystalline solid: mp = 107-109 °C; $[\alpha]_D^{20}$ = +12.7 (*c* = 0.9, $CHCl_3$); IR (neat) 3500-2500, 3075, 2963, 2930, 1709, 1457, 1208, 978, 910 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 5.60 (ddd, *J* = 8.6, 10.2, 17.1 Hz, 1 H), 4.98 (ddd, *J* = 0.6, 2.0, 17.1 Hz, 1 H), 4.95 (dd, *J* = 2.0, 10.2 Hz, 1 H), 3.58 (dd, *J* = 4.1, 7.6 Hz, 1 H), 2.53 (dq, *J* = 4.1, 7.1 Hz, 1 H), 2.19-2.13 (m, 1 H), 1.73 (ddd, *J* = 2.7, 11.2, 13.6 Hz, 1 H), 1.63-1.55 (m, 1 H), 1.12 (d, *J* = 7.1 Hz, 3 H), 0.98 (d, *J* = 6.7 Hz, 3 H), 0.93 (ddd, *J* = 3.7, 10.5, 13.8 Hz, 1 H), 0.69 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 182.6, 144.8, 113.8, 76.7, 42.8, 39.7, 36.6, 34.3, 22.7, 16.0, 10.6; high resolution mass spectra (ES+) m/z 201.1497 [$(M+H)^+$; calcd for $C_{11}H_{21}O_3^+$: 201.1491].



Alcohol (+)-24: A mixture of diene (+)-**23** (29.6 g, 73.0 mmol) and methyl crotonate (9.5 g, 10.1 mL, 94.9 mmol) in toluene (75 mL) was heated at 90 °C for 24 h. The reaction mixture was cooled to room temeperature and concentrated under vacuum to afford an orange residue which was purified by column chromatography on silica gel (elution with 20:1 hexane:ethyl acetate with 2% Et_3N) to afford (+)-**S4** (32.6 g, 88%) as a 8:1 mixture of *endo* and *exo* cycloadducts as a yellow oil. The *endo* isomer was separated and characterized. **endo adduct**: $[\alpha]_D^{20}$ = +46.5 (*c* = 2.31, $CHCl_3$); IR (neat) 3028, 2956, 1733, 1663, 1601, 1491, 1433, 1370, 1252, 1170, 923, 838 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 (m, 8 H), 7.27-7.24 (m, 2 H), 4.47 (m, 2 H), 4.39 (dd, *J*

= 2.1, 2.1 Hz, 1 H), 4.01 (m, 1 H), 3.71 (s, 3 H), 2.59-2.51 (m, 2 H), 1.93-1.87 (m, 2 H), 1.71-1.60 (m, 2 H), 1.53 (dd, *J* = 10.7, 10.7 Hz, 1 H), 1.40-1.34 (m, 1 H), 0.90 (s, 9 H), 0.61 (d, *J* = 6.3 Hz, 3 H), 0.11 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4, 150.5, 146.3, 128.3, 128.2, 128.1, 127.0, 105.0, 64.5, 56.7, 53.8, 51.1, 38.1, 34.0, 31.8, 25.9, 19.4, 18.1, -4.1, -4.2; high resolution mass spectra (ES+) m/z 528.2884 [$(M+Na)^+$; calcd for $C_{31}H_{43}NO_3SiNa^+$: 528.2910].

To a cold (-78 °C) suspension of $LiAlH_4$ (4.9 g, 128.7 mmol) in Et_2O (140 mL) was added a solution of ester (+)-**S4** (32.6 g, 64.4 mmol) in Et_2O (70 mL) dropwise *via* an addition funnel. The reaction mixture was allowed to warm to room temperature slowly over 1.5 h then cooled to 0 °C and *carefully* treated with water (30 mL). The thick suspension was diluted with Et_2O (1 L), treated with $MgSO_4$, and filtered through a pad of celite. The filtrate was concentrated under vacuum to afford alcohol (+)-**24** as a mixture (8:1) of *endo* and *exo* alcohols as a yellow gum (29.8 g, 97%). The endo isomer was separated and characterized. **endo adduct**: $[\alpha]_D^{20}$ = +86.8 (*c* = 2.90, $CHCl_3$); IR (neat) 3407, 3029, 2955, 2857, 1665, 1472, 1372, 1251, 1204, 836, 778, 701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.34 (m, 8 H), 7.30-7.27 (m, 2 H), 6.27 (br s, 1 H), 4.44 (m, 2 H), 3.82-3.79 (m, 2 H), 3.67 (m, 1 H), 3.40 (dd, *J* = 9.8, 9.8 Hz, 1 H), 2.66-2.59 (m, 2 H), 2.18-2.12 (m, 2 H), 1.53 (dd, *J* = 1.2, 4.6, 16.5 Hz, 1 H), 1.30-1.23 (m, 1 H), 1.17-1.12 (m, 1 H), 0.86 (s, 9 H), 0.61-0.53 (m, 1 H), 0.54 (d, *J* = 6.5 Hz, 3 H), 0.05 (s, 3 H), -0.09 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.9, 143.7, 129.0, 128.5, 127.5, 102.4, 67.7, 64.9, 60.7, 42.8, 38.5, 33.2, 30.6, 25.7, 19.0, 18.0, -4.1, -4.5; high resolution mass spectra (ES+) m/z 478.3132 [$(M+H)^+$; calcd for $C_{30}H_{44}NO_2Si^+$: 478.3141].



(+)-**24** (+)**S5** (+)-**25**

Benzyl ether (+)-25: To a solution of the above silyl enol ether (+)-**24** (29.8 g, 62.4 mmol) in CH_3CN (120 mL) was added a 10% solution of HF in CH_3CN (120 mL). After being stirred at room temperature for 1 h, the mixture was directly poured on silica gel and purified by column chromatography (elution with 1:1 hexane:ethyl acetate to 1:2 hexane:ethyl acetate) to afford cyclohexenone (+)-**S5** (8.5 g, 97%) as a gold oil: $[\alpha]_D^{20}$ = +129.0 (*c* = 1.34, $CHCl_3$); IR (neat) 3407, 2960, 2931, 2880, 1664, 1394, 1078, 1043, 850 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (dd, *J* = 2.5, 10.1 Hz, 1 H), 6.54 (dd, *J* = 2.6, 10.1 Hz, 1 H), 3.94 (dd, *J* = 4.3, 10.6 Hz, 1 H), 3.74 (dd, *J* = 6.2, 10.6 Hz, 1 H), 2.49- 2.56 (m, 1 H), 2.25-2.30 (m, 1 H), 2.16-2.24 (m, 2 H), 1.57 (br s, 1 H), 1.12 (d, *J* = 6.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.8, 151.6, 130.5, 63.4, 46.2, 45.4, 31.3, 19.8; high resolution mass spectra (ES+) m/z 140.0843 [M^+; calcd for $C_8H_{12}O_2^+$: 140.0837].

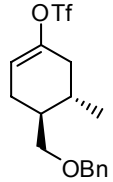
The chiral amine was eluted from the column with ethyl acetate:Et_3N (3:1) to give 12.00 g of recovered amine.

To a stirred solution of alcohol (+)-**S5** (5.6 g, 40.0 mmol) in benzyl bromide (300 mL) was added Ag_2O (25.0 g, 108 mmol). The suspension was stirred for 3 days at room temperature during which time additional Ag_2O (9.27 g, 40.0 mmol, 3 times) was added. Upon completion of the reaction, the suspension was diluted with Et_2O (500 mL), and filtered through a pad of celite. The filtrate was concentrated under vacuum. Excess benzyl bromide was removed by vacuum distillation at 60 °C and the residual oil was purified by column chromatography on silica gel

(elution with 9:1 hexane:ethyl acetate) to afford benzyl ether (+)-**25** (7.9 g, 85%) as a yellow oil: $[\alpha]_D^{20}$ = +109.9 (*c* = 1.58, $CHCl_3$); IR (neat) 3031, 2871, 1675, 1453, 1247, 1106, 736, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39-7.31 (m, 5 H), 6.97 (dd, *J* = 2.6, 10.2 Hz, 1 H), 6.05 (dd, *J* = 2.6, 9.9 Hz, 1 H), 4.59 (d, *J* = 12.1 Hz, 1 H), 4.54 (d, *J* = 12.1 Hz, 1 H), 3.69 (dd, *J* = 4.5, 9.2 Hz, 1 H), 3.51 (dd, *J* = 6.5, 9.2 Hz, 1 H), 2.50 (m, 1 H), 2.35 (m, 1 H), 2.21-2.15 (m, 2 H), 1.07 (d, *J* = 6.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.8, 152.2, 138.2, 129.9, 128.7, 128.0, 127.8, 73.6, 70.7, 45.5, 44.4, 31.8, 19.8; high resolution mass spectra (ES+) m/z 253.1202 $[(M+Na)^+$; calcd for $C_{15}H_{18}O_2Na^+$: 253.1205].

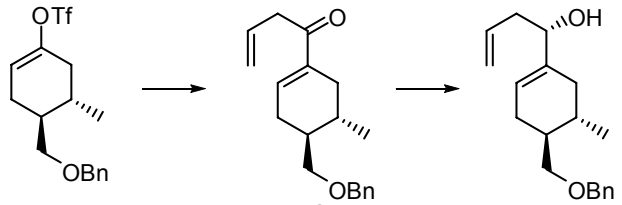
Modified Procedure for the Synthesis of (+)-25: To a cold (0 °C), stirred solution of alcohol (+)-**24** (18.9 g, 39.6 mmol) in THF (180 mL) was added NaHMDS (30 mL of 2.0 M solution in THF, 59.3 mmol). After the addition was complete the resulting mixture was stirred for additional 10 min at 0 °C. To this mixture were added benzyl bromide (10.2 g, 7.0 mL, 59.3 mmol) followed by tetrabutylammonium iodide (1.5 g, 4.0 mmol). The cold bath was removed and the mixture was stirred at room temperature for 1 h before being quenched with H_2O (400 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 x 150 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to afford the intermediate benzyl ether as yellow oil, which was directly used in the next step without further purification.

To a solution of above benzyl ether in MeCN (70 mL) was added a 10% HF-MeCN solution (90 mL). After being stirred at room temperature for 1 h, the mixture was directly poured on silica gel and purified by column chromatography (elution with 5:1 hexane:ethyl acetate) to afford (+)-**25** (8.2 g, 90% over two steps) as a yellow oil.



(-)-**26**

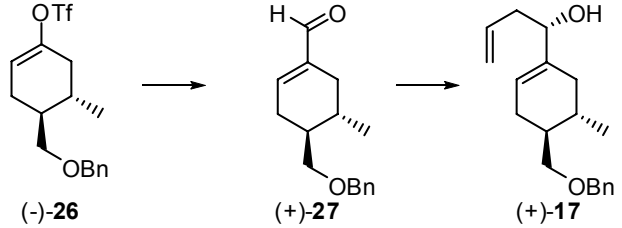
Vinyl triflate (-)-**26**: To a cold (-78 °C), stirred solution of cyclohexenone (+)-**25** (12.6 g, 54.8 mmol) in THF (250 mL) was added L-Selectride (60.3 mL of 1.0 M solution in THF, 60.3 mmol). The reaction mixture was stirred for 1 h at -78 °C then treated with solid *N*-phenyltriflimide (21.5 g, 60.3 mmol) and allowed to warm to rt over 2 h. Stirring continued at room temperature for an additional 4.5 h. The mixture was then diluted with pentane (800 mL), washed with water (500 mL), 1 M aqueous solution of NaOH (500 mL), and brine (750 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum to afford a residue which was purified by column chromatography on silica (elution with 40:1 hexane:ethyl acetate) to yield (-)-**26** (16.4 g, 82%) as a colorless oil: $[\alpha]_D^{20}$ = -36.8 (*c* = 1.2, $CHCl_3$); IR (neat) 2910, 1416, 1247, 1210, 1143, 1029, 877, 698, 610 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.30 (m, 5 H), 5.72 (br s, 1 H), 4.51 (ABq, *J* = 12.0 Hz, Δυ = 12.3 Hz, 2 H), 3.50 (dd, *J* = 4.6, 9.2 Hz, 1 H), 3.43 (dd, *J* = 6.5, 9.2 Hz, 1 H), 2.38-2.32 (m, 2 H), 2.21-2.16 (m, 1 H), 2.09-2.03 (m, 1 H), 2.03-1.95 (m, 1 H), 1.66-1.61 (m, 1 H), 1.02 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 138.6, 128.6, 127.9, 127.8, 117.5, 73.5, 71.7, 38.7, 34.9, 30.5, 26.8, 19.1; high resolution mass spectra (ES+) m/z 363.0878 $[(M-H)^+$; calcd for $C_{26}H_{18}O_4F_3S$ 363.0878].



(-)-**26** (+)-**S6** (+)-**17**

Alcohol (+)-17: A Parr bomb was charged with LiCl (95.3 mg, 2.249 mmol), $Pd(PPh_3)_4$ (50 mg, 0.043 mmol), followed by a solution of triflate (-)-**26** (315 mg, 0.865 mmol) and allyltrimethyl stannane (0.14 mL, 0.865 mmol) in THF (9 mL). The bomb was pressurized with carbon monoxide and vented three times before adjusting the pressure to 100 psi with carbon monoxide and stirred for 15 min. The bomb was vented and a solution of $ZnCl_2$ (0.5 M THF, 1.73 mL) was added. The bomb was pressurized to 100 psi with carbon monoxide and heated at 75 °C for 2.25 h then cooled to room temperature over 30 min. The solution was diluted with hexanes (50 mL), washed with water (2 x 25 mL), brine (2 x 25 mL), dried with $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to leave a residue which was purified by column chromatography on silica gel (elution with 10:1 hexane:ethyl acetate) to afford ketone (+)-**S6** (177 mg, 72%) as a colorless oil: $[\alpha]_D^{20}$ = +95.9 (*c* = 1.02, $CHCl_3$); IR (neat) 3029, 2954, 2894, 1669, 1642, 1496, 1453, 1191, 1113, 1094, 914, 737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5 H), 6.90 (br s, 1 H), 5.96 (dddd, *J* = 6.8, 6.8, 10.2, 17.1 Hz, 1 H), 5.16-5.09 (m, 2 H), 4.53 (d, *J* = 12.0 Hz, 1 H, 4.48 (d, *J* = 12.0 Hz, 1 H), 3.53 (dd, *J* = 4.2, 9.2 Hz, 1 H), 3.43 (app t, *J* = 1.4 Hz, 1 H), 3.41 (app t, *J* = 1.4 Hz, 1 H), 3.40 (dd, *J* = 6.8, 9.2 Hz, 1 H), 2.50-2.42 (m, 2 H), 2.27-2.21 (m, 1 H), 1.87-1.81 (m, 1 H), 1.69-1.59 (m, 2 H), 1.00 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.0, 139.8, 138.8, 138.2, 132.2, 128.6, 127.8, 127.7, 73.4, 72.6, 42.4, 39.3, 31.4, 29.7, 19.4; high resolution mass spectra (ES+) m/z 307.1665 [$(M+Na)^+$; calcd for $C_{19}H_{24}O_2Na^+$: 307.1674].

To a cold (-78 °C), stirred mixture of ketone (+)-**S6** (0.93 g, 3.27 mmol) and (*R*)-CBS-*B*-Me catalyst (0.33 mL of 1.0 M solution in toluene, 0.33 mmol) in toluene (6.5 mL) was added catecholborane (6.5 mL of 1.0 M solution in THF, 6.5 mmol) dropwise. The reaction mixture was stirred at -78 °C for 24 h before being quenched with 1 M aqueous solution of HCl (3 mL). The mixture was warmed to room temperature and extracted with Et_2O (100 mL). The organic layer was washed with water (50 mL), brine (50 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to leave a residue which was purified by column chromatography on silica gel (elution with 9:1 hexane:ethyl acetate) to afford allylic alcohol (+)-**17** (0.23 g, 81%) as a 5:1 mixture of diastereomers.

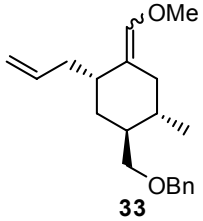


(-)-**26** (+)-**27** (+)-**17**

Modified Procedure for the Synthesis of (+)-**17**: A stirred solution of flame-dried LiCl (3.5 g, 82.8 mmol) and triflate (-)-**26** (11.6 g, 31.8 mmol) was purged with carbon monoxide for 20 min followed by addition of $Pd(PPh_3)_4$ (1.8 g, 1.6 mmol). The mixture was heated to 70 °C and treated with a solution of tributyltin hydride (11.1 g, 38.2 mmol) in THF (232 mL) *via* syringe pump over 5 h while bubbling carbon monoxide through the reaction mixture. After addition was complete, the mixture was cooled to room temperature, diluted with Et_2O (800 mL), washed with brine (3 x 400 mL), dried with $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to

leave a green residue which was purified by column chromatography on silica (elution with 15:1 hexane:ethyl acetate) to afford aldehyde (+)-**27** (6.8 g, 87%) as a pale yellow oil: $[\alpha]_D^{20}$ = +87.2 (*c* = 1.32, $CHCl_3$); IR (neat) 2894, 1684, 1646, 1094, 737, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.43 (s, 1 H), 7.58-7.27 (m, 5 H), 6.79 (br s, 1 H), 4.54 (d, *J* = 12.0 Hz, 1 H), 4.50 (d, *J* = 12.0 Hz, 1 H), 3.54 (dd, *J* = 4.0, 9.1 Hz, 1 H), 3.44 (dd, *J* = 6.5, 9.1 Hz, 1 H), 2.58-2.52 (m, 1 H), 2.43-2.39 (m, 1 H), 2.37-2.30 (m, 1 H), 1.85-1.79 (m, 1 H), 1.77-1.67 (m, 2 H), 1.01 (d, *J* = 6.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.2, 150.5, 140.9, 138.7, 128.6, 127.8, 127.76, 73.5, 72.4, 39.9, 29.9, 29.3, 29.2, 19.3; high resolution mass spectra (ES+) m/z 244.1455 [M^+; calcd for $C_{16}H_{20}O_2^+$: 244.1463].

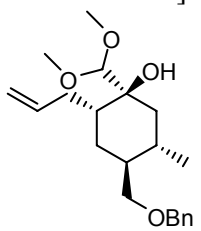
To a cold (0 °C) solution of bis-sulfonamide (+)-**28** (8.5 g, 16.3 mmol) in CH_2Cl_2 (75 mL) was added BBr_3 (16.3 mL of 1.0 M solution in CH_2Cl_2, 16.3 mmol). The solution was stirred for 30 min at 0 °C then the volatiles were removed under vacuum to afford a pale yellow solid which was redissolved in CH_2Cl_2 (75 mL) and treated with allyltributylstanane (5.4 g, 5.0 mL, 16.3 mmol) at 0 °C. After stirring for 1 h at room temperature, the solution was cooled to -78 °C, treated with a solution of aldehyde (+)-**27** (3.6 g, 14.8 mmol) in CH_2Cl_2 (31 mL), and stirred for 1 h at -78 °C. After 1 h the reaction mixture was warmed to room temperature, treated with pH 8 buffer solution (32 mL), and stirred for 15 min. The volatiles were removed under vacuum, the aqueous slurry was diluted with cold Et_2O (150 mL) and sulfonamide was filtered. The filtrate was washed with a 50% saturated aqueous solution of KF (3 x 50 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to give a crude residue that was purified by column chromatography on silica gel (elution with 10:1 hexane:ethyl acetate) to afford (+)-**17** (3.0 g, 71%) as a colorless oil: $[\alpha]_D^{20}$ = +39.2 (*c* = 1.60, $CHCl_3$); IR (neat) 3412, 2895, 1497, 1453, 1092, 1028, 910, 735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5 H), 5.77 (dddd, *J* = 7.2, 7.2, 10.1, 17.2 Hz, 1 H), 5.65 (br s, 1 H), 5.16-5.09 (m, 2 H), 4.53 (d, *J* = 12.0 Hz, 1 H), 4.49 (d, *J* = 12.0 Hz, 1 H), 4.03 (m, 1 H), 3.53 (dd, *J* = 4.6, 9.1 Hz, 1 H), 3.40 (dd, *J* = 6.8, 9.1 Hz, 1 H), 2.34-2.15 (m, 4 H), 2.03-1.98 (m, 1 H), 1.74-1.57 (m, 3 H), 1.56 (br s, 1 H), 0.99 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 138.5, 135.1, 128.5 (2 C), 127.73 (2 C), 127.65, 122.5, 117.8, 75.2, 73.3 (2 C), 73.2, 40.0, 32.0, 30.2, 28.5, 19.6; high resolution mass spectra (ES+) m/z 309.1819 [$(M+Na)^+$; calcd for $C_{19}H_{26}O_2Na^+$: 309.1831].



33

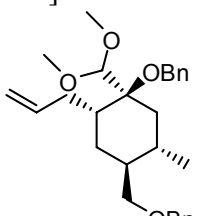
Enol Ether 33: To a cold (0 °C) suspension of KH (3.3 g, 82.8 mmol) in THF (80 mL) was added a solution of allylic alcohol (+)-**17** (4.7 g, 16.6 mmol) and 18-crown-6 (21.8 g, 82.8 mmol) in THF (85 mL). The reaction mixture was warmed to room temperature and stirred for 21 h. The mixture was cooled to 0 °C and treated with dimethylsulfate (4.7 mL, 49.7 mmol). After being stirred at 0 °C for 1 h, the mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (50 mL) followed by extraction with Et_2O (2 x 500 mL). The combined ethereal layers were washed with a saturated aqueous solution of $NaHCO_3$ (3 x 200 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to afford a brown residue that was purified by column chromatography on silica gel (elution with 30:1 hexane:ethyl acetate) to afford methyl enol ether **33** (4.8 g, 2:1 *E*:*Z* ratio of isomers, 96%) as a golden oil: IR (neat) 2926, 2852, 1682, 1638, 1454, 1364, 1198, 1125, 994 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.32

(m, 4 H), 7.29 (m, 1 H), 5.77 (d, *J* = 1.5 Hz, 1 H), 5.79-5.67 (m, 1 H), 5.01-4.94 (m, 2 H), 4.54 (d, *J* = 12.2 Hz, 1 H), 4.45 (d, *J* = 12.2 Hz, 1 H), 3.53 (s, 3 H), 3.51-3.46 (m, 1 H), 3.33 (dd, *J* = 6.5, 9.2 Hz, 1 H), 2.56 (dd, *J* = 4.2, 13.9 Hz, 1 H), 2.24-2.11 (m, 3 H), 1.87-1.73 (m, 2 H), 1.60-1.50 (m, 1 H), 1.45-1.26 (m, 2 H), 0.96 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) (* denotes signals corresponding to the *Z* isomer) δ 140.0, *139.8, 139.1, *138.1, 138.0, 128.4 (2 C), 127.5 (2 C) *119.7, 119.1, 115.3, 115.0, 73.8, 73.2, 59.5, *59.4, 39.6, *39.5, 38.5, 37.4, *36.5, 35.6, *35.5, 35.0, *34.4, *32.7, 30.1, 20.2, *20.1; high resolution mass spectra (ES+) m/z 323.1998 [$(M+Na)^+$; calcd for $C_{20}H_{28}O_2Na^+$: 323.1987].



(+)-**34**

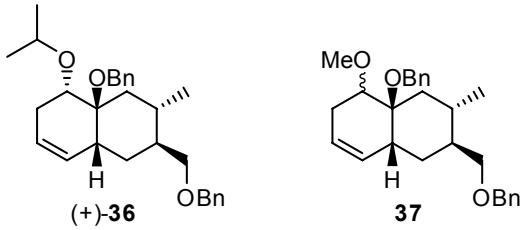
Alcohol (+)-34: To a cold (0 °C) solution of methyl enol-ether **33** (0.13 g, 0.42 mmol) in MeOH (4.1 mL) was added *m*CPBA (77%, 0.11 g, 0.46 mmol). After being stirred at 0 °C for 30 min, the mixture was quenched with a saturated aqueous solution of Na_2SO_3 (5 mL), followed by extraction with Et_2O (2 x 50 mL). The combined ethereal layers were washed with a saturated aqueous solution of $NaHCO_3$ (2 x 25 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to afford a residue that was purified by column chromatography on silica gel (elution with 8:1 hexane:ethyl acetate) to provide dimethyl acetal (+)-**34** (0.13 g, 91%) as a colorless oil: $[\alpha]_D^{20}$ = +11.5 (*c* = 2.8, $CHCl_3$); IR (neat) 3500, 2925, 1457, 1434, 1074, 910, 736, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (m, 4 H), 7.27 (m, 1 H), 5.81-5.74 (m, 1 H), 5.06-5.01 (m, 2 H), 4.52 (d, *J* = 12.1 Hz, 1 H), 4.44 (d, *J* = 12.1 Hz, 1 H), 4.07 (s, 1 H), 3.55 (s, 3 H), 3.29 (dd, *J* = 6.7, 9.2 Hz, 1 H), 3.51 (s, 3 H), 2.21-2.17 (m, 1 H), 2.05-1.98 (m, 1 H), 2.03 (s, 1 H), 1.89-1.86 (m, 1 H), 1.75-1.65 (m, 3 H), 1.56 (ddd, *J* = 1.5, 4.0, 13.8 Hz, 1 H), 1.41-1.35 (m, 1 H), 1.19 (dd, *J* = 13.6, 13.6 Hz, 1 H), 0.92 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 137.7, 128.2 (2 C), 127.3 (2 C), 127.2, 115.4, 107.9, 76.0, 73.8, 72.8, 58.2, 56.3, 39.6, 37.9, 37.7, 32.8, 29.0, 27.7, 20.0; high resolution mass spectra (ES+) m/z 371.2202 [$(M+Na)^+$; calcd for $C_{21}H_{32}O_4Na^+$: 371.2198].



(+)-**35**

α-Benzyloxy Dimethyl acetal (+)-35: To a cold (0 °C), stirred solution of alcohol (+)-**34** (0.57 g, 1.62 mmol) in DMF (5.4 mL) was added NaH (50 mg of 95% in oil, 2.11 mmol). The suspension was warmed to room temperature and stirred for 30 min prior to the additions of benzyl bromide (0.96 mL, 8.10 mmol) and *n*-tetrabutylammonium iodide (0.60 g, 1.62 mmol). The reaction mixture was stirred at room temperature for for 16 h before being quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL) and diluted with H_2O (20 mL). The mixture was extracted with Et_2O (50 mL), washed with water (2 x 25 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to leave a residue which was purified by column chromatography on silica gel (20:1 hexane:ethyl acetate) to afford α-benzyloxy dimethyl acetal (+)-**35** (0.67 g, 94%)

as a colorless oil: $[\alpha]_D^{20}$ = +8.0 (*c* = 1.05, $CHCl_3$); IR (neat) 3063, 3029, 2925, 2867, 1639, 1497, 1453, 1362, 1201, 1072, 734, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.1 Hz, 2 H), 7.36 (m, 4 H), 7.31-7.23 (m, 4 H), 5.81 (m, 1 H), 5.07 (m, 2 H), 5.03 (d, *J* =9.9 Hz, 1 H), 4.71 (d, *J* = 11.9 Hz, 1 H), 4.67 (d, *J* = 11.9 Hz, 1 H), 4.54 (d, *J* = 12.1 Hz, 1 H), 4.47 (d, *J* = 12.1 Hz, 1 H), 4.22 (s, 1 H), 3.57 (s, 3 H), 3.53 (s, 3 H), 3.52 (dd, *J* = 3.8, 9.3 Hz, 1 H), 3.39 (dd, *J* = 6.2 Hz, 9.3 Hz, 1 H), 2.36-2.30 (m, 2 H), 2.09 (ddd, *J* = 10.1, 10.1, 13.0 Hz, 1 H), 1.84-1.76 (m, 3 H), 1.49-1.42 (m, 1 H), 1.31 (dd, *J* = 12.2, 13.7 Hz, 1 H), 0.97 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 139.2, 138.3, 127.5, 127.4, 127.3, 126.9, 115.5, 110.3, 80.6, 74.1, 73.1, 64.7, 58.5, 57.5, 37.8, 36.1, 33.1, 29.1, 27.7, 20.3; high resolution mass spectra (ES+) m/z 461.2657 [$(M+Na)^+$; calcd for $C_{28}H_{38}O_4Na^+$: 461.2668].



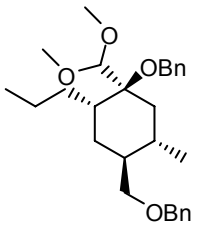
(+)-**36** **37**

Isopropyl Ether (+)-36 and Methyl Ether 37: To a cold (-78 °C), stirred mixture of acid (+)-**7** (26 mg, 0.13 mmol), acetal (+)-**35** (44 mg, 0.10 mmol), and *i*-PrOTMS (70 μL) in anhydrous CH_2Cl_2 (1 mL) was added TMSOTf (10 μL). The reaction mixture was stirred at -78 °C for 20 h then slowly allowed to warm to 0 °C over 10 h before being treated with triethylamine (0.1 mL). The mixture was stirred for 15 min at 0 °C prior to removal of solvent. The residue was purified by column chromatography on silica gel (elution with 20:1 hexane:ethyl acetate) to afford isopropyl ether (+)-**36** (13 mg, 30%) and methyl ether **37** as a 5:1 mixture of diastereomers (6 mg, 15%).

Data for (+)-**36**: $[\alpha]_D^{20}$ = +20.4 (*c* = 0.23, C_6H_6); IR (neat) 2924, 2865, 1453, 1365, 1086, 1028, 733, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (m, 2 H), 7.35-7.25 (m, 8 H), 5.55-5.51 (m, 1 H), 5.44-5.41 (m, 1 H), 4.80 (d, *J* = 11 .4 Hz, 1 H), 4.61 (d, *J* = 11.4 Hz, 1 H), 4.50 (d, *J* = 12.1 Hz, 1 H), 4.47 (d, *J* = 12.1 Hz, 1 H), 3.83 (dd, *J* = 6.5, 9.7 Hz, 1 H), 3.75 (septet, *J* = 6.1 Hz, 1 H), 3.55 (dd, *J* = 7.0, 9.2 Hz, 1 H), 2.65 (br s, 1 H), 2.60-2.54 (m, 1 H), 2.04-1.97 (m, 1 H), 2.00 (app dt, *J* = 12.7, 1.8 Hz, 1 H), 1.84 (ddd, *J* = 5.0, 13.0 Hz, 1 H), 1.69 (app dt, *J* = 13.2, 2.9 Hz, 1 H), 1.69-1.64 (m, 1 H), 1.36-1.29 (m, 1 H), 1.36-1.29 (m, 1 H), 1.24 (dd, *J* = 12.3, 14.3 Hz, 1 H), 1.18 (d, *J* = 6.1 Hz, 3 H), 1.17 (d, *J* = 6.1 Hz, 3 H), 0.94 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 139.2, 132.3, 128.5, 128.4, 127.6, 127.5, 127.3, 127.1, 124.4, 77.3, 77.2, 73.9, 73.2, 70.0, 64.1, 39.8, 39.7, 33.1, 32.8, 31.3, 29.2, 23.9, 22.6, 20.0; high resolution mass spectra (ES+) m/z 457.2715 [$(M+Na)^+$; calcd for $C_{29}H_{38}O_3Na^+$: 457.2719].

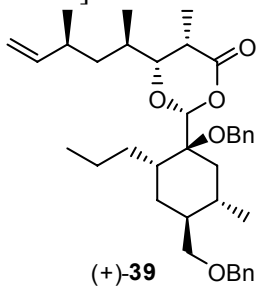
Data for **37**: IR (neat) 2923, 1497, 1453, 1365, 1097, 733, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) (* denotes minor diastereomer) δ 7.41 (m, 2 H), 7.35-7.23 (m, 8 H), *5.72 (m, 1 H), *5.65 (m, 1 H), 5.56 (m, 1 H), 5.45 (m, 1 H), 4.71 (d, *J* = 11.5 Hz, 1 H), 4.63 (s, 1 H), 4.58 (d, *J* = 11.5 Hz, 1 H), *4.54 (d, *J* = 12.1 Hz, 1 H), 4.53 (d, *J* = 12.1 Hz, 1 H), *4.49 (d, *J* = 12.1 Hz, 1 H), 4.48 (d, *J* = 12.1 Hz, 1 H), *4.04 (m, 1 H), 3.67 (dd, *J* = 6.5, 9.7 Hz, 1 H), 3.56 (dd, *J* = 3.7, 9.2 Hz, 1 H), 3.56 (dd, *J* = 3.7, 9.2 Hz, 1 H), *3.44 (s, 3 H), 3.41 (s, 3 H), 3.34 (dd, *J* = 7.1, 9.2 Hz, 1 H), 2.69 (m, 1 H), 2.00-1.90 (m, 2 H), 1.84 (app dt, *J* = 5.0, 12.9 Hz, 1 H), 1.77-1.69 (m, 2 H), 1.37-1.28 (m, 1 H), 1.25 (dd, *J* = 12.3, 14.2 Hz, 1 H), 1.15 (dd, *J* = 1.6, 6.1 Hz, 1 H), *0.95 (d, *J* = 6.5 Hz, 3 H), 0.90 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.3, 139.2, 132.4, 128.5, 128.4, 127.6, 127.5, 127.3, 127.1, 123.9, 80.7, 77.4, 73.9, 73.3, 63.9, 56.9, 39.8, 39.0, 33.2, 31.3, 31.2,

29.0, 20.0; high resolution mass spectra (ES+) m/z 429.2424 [$(M+Na)^+$; calcd for $C_{27}H_{34}O_3Na^+$: 429.2406].



(+)-**38**

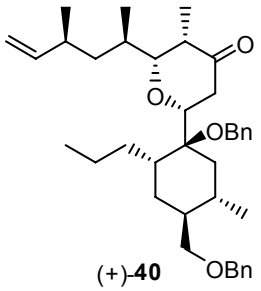
Saturated Acetal (+)-38: A mixture of alkene (+)-**35** (40 mg, 0.091 mmol) and Wilkinson's catalyst (17 mg, 0.018 mmol) in CH_2Cl_2 (0.5 mL) was stirred at room temperature under an atmosphere of hydrogen for 48 h. The volatile components from the reaction mixture were removed *in vacuo* and the residual solid was purified by column chromatography on silica gel (elution with 20:1 hexane:ethyl acetate) to afford alkane (+)-**38** (35 mg, 88%) as a colorless oil: $[\alpha]_D^{20}$ = +26.2 (*c* = 1.5, $CHCl_3$); IR (neat) 3029, 2954, 2924, 2869, 1453, 1363, 1201, 1093, 1074, 734, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.2 Hz, 2 H), 7.37-7.31 (m, 4 H), 7.30-7.20 (m, 4 H), 4.72 (d, *J* = 12.0 Hz, 1 H), 4.67 (d, *J* = 12.0 Hz, 1 H), 4.54 (d, *J* = 12.1 Hz, 1 H), 4.49 (d, *J* = 12.1 Hz, 1 H), 4.23 (s, 1 H), 3.57 (s, 3 H), 3.55 (dd, *J* = 5.4, 9.2 Hz, 1 H), 3.53 (s, 3 H), 3.36 (dd, *J* = 6.5, 9.2 Hz, 1 H), 2.19 (br m, 1 H), 1.89 (ddd, *J* = 1.4, 3.8, 14.0 Hz, 1 H), 1.79-1.70 (m, 3 H), 1.53-1.39 (m, 2 H), 1.36 (app q, *J* = 7.3 Hz, 2 H), 1.31-1.24 (m, 2 H), 0.95 (t, *J* = 7.3 Hz, 3 H), 0.94 (t, *J* = 6.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.7, 139.2, 128.5, 128.3, 127.6, 127.5, 127.3, 126.9, 110.3, 80.9, 74.4, 73.3, 64.8, 58.5, 57.3, 38.2, 36.4, 36.3, 30.2, 29.3, 27.6, 21.2, 20.4, 14.6; high resolution mass spectra (ES+) m/z 463.2827 [$(M+Na)^+$; calcd for $C_{28}H_{40}O_4Na^+$: 463.2824].



(+)-**39**

Dioxanone (+)-39: To a cold (-78 °C), stirred mixture of acid (+)-**7** (5.5 mg, 26.6 μmol), dimethyl acetal (+)-**38** (9 mg, 20.4 μmol), and isopropoxytrimethylsilane (15 μL, 81.6 μmol) in CH_2Cl_2 (0.25 mL) was added TMSOTf (1 drop, 0.5 eq). The reaction mixture was warmed to 0 °C and stirred for 1 h. The reaction was quenched with triethylamine (25 μL) and stirred for additional 15 min at 0 °C. The solution was extracted with Et_2O (15 mL), washed with a saturated aqueous solution of $NaHCO_3$ (2 x 10 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 9:1 to 4 :1 hexane:ethyl acetate) to afford dioxanone (+)-**39** as a colorless oil (6.0 mg, 51 %): $[\alpha]_D^{20}$ = +16.6 (*c* = 0.5, C_6H_6); IR (neat) 2956, 2929, 2870, 1748, 1496, 1453, 1248, 1099, 1070, 1028, 996, 734, 697 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.48 (d, *J* = 7.5 Hz, 2 H), 7.30 (d, *J* = 7.3 Hz, 2 H), 7.19 (ap d, J = 7.7 Hz, 4 H), 7.10 (appt, *J* = 7.4 Hz, 2 H), 5.52 (ddd, *J* = 8.5, 10.2, 17.2 Hz, 1 H), 4.98 (s, 1 H), 4.95 (ddd, *J* = 0.9, 1.8, 17.2 Hz, 1 H), 4.91 (dd, *J* = 1.8, 10.2 Hz, 1 H), 4.81 (d, *J* = 11.8 Hz, 1 H), 4.78 (d, *J* = 11.8 Hz, 1 H), 4.35 (d, *J* = 12.2 Hz, 1 H), 4.31 (d, *J* = 12.2 Hz, 1 H), 3.37 (dd, *J* = 3.6, 9.0 Hz, 1 H), 3.25 (dd, *J*

= 6.3, 9.0 Hz, 1 H), 2.90 (dd, *J* = 4.7, 8.0 Hz, 1 H), 2.52 (br d, *J* = 8.7 Hz, 1 H), 2.34 (dddd, *J* = 7.2, 7.2, 7.2, 10.0 Hz, 1 H), 2.15-2.08 (m, 1 H), 2.00-1.94 (m, 2 H), 1.89-1.86 (m, 2 H), 1.61-1.52 (m, 4 H), 1.44-1.28 (m, 4 H), 1.05 (d, *J* = 7.2 Hz, 3 H), 0.97 (t, *J* = 7.0 Hz, 3 H), 0.94 (d, *J* = 6.3 Hz, 3 H), 0.93 (d, *J* = 5.6 Hz, 3 H), 0.91 (m, 1 H), 0.56 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 171.0, 144.4, 140.7, 139.9, 128.9, 128.8, 128.0, 127.9, 127.7, 127.6, 113.9, 105.1, 82.3, 79.4, 74.2, 73.7, 65.4, 39.7, 39.0, 38.8, 36.9, 36.3, 35.9, 31.8, 30.6, 29.6, 28.0, 22.5, 21.6, 20.6, 15.2, 15.0, 11.9; high resolution mass spectra (ES+) m/z 599.3707 [$(M+Na)^+$; calcd for $C_{37}H_{52}O_5Na^+$: 599.3712].

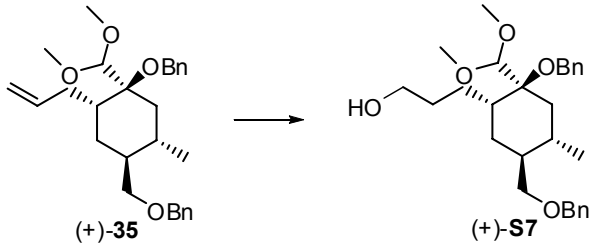


(+)-**40**

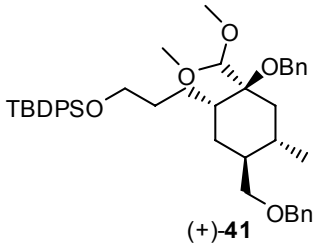
Tetrahydropyranone (+)-40: To a solution of dioxanone (+)-**39** (16.4 mg, 28.4 μmol) in THF (0.1 mL) was added Cp_2TiMe_2 (0.1 mL of 0.7 M solution in THF, 70 μmol) at room temperature. The reaction mixture was heated at reflux for 24 h under dark and during this time additional Cp_2TiMe_2 was added after 4 h (0.1 mL) and 17 h (0.1 mL). The mixture was cooled to room temperature, triturated with hexanes (5 mL), and stirred for 30 min. The resulting orange solid was filtered through a pad celite and the solid was washed with hexane. The filtrate was concentrated under vacuum to leave an orange solid which was purified by flash chromatography on silylated silica gel (eluant 20:1 hexane:ethyl acetate) to afford the intermediate enol acetal (0.27 g) as a colorless gum. The enol acetal was used in the next step without any delay.

To a suspension of Cs_2CO_3 (3.8 mg, 11.8 μmol) in CH_2Cl_2 (0.25 mL) was added Me_2AlCl (25 μL of 1.0 M solution in hexanes, 23.6 μmol) and stirred for 15 min at room temperature. This suspension was cooled to -78 °C and treated with a solution of enol ether prepared above (5.2 mg, 9.1 μmol) in CH_2Cl_2 (0.25 mL). After being stirred at -78 °C for 15 min, the mixture was warmed to room temperature and stirred at room temperature for 40 min. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (1 mL), extracted with CH_2Cl_2 (20 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by preparitive TLC (elution with 5:1 hexane:ethyl acetate) to afford tetrahydropyranone (+)-**40** (3.2 mg, 62%) as a colorless oil: $[\alpha]_D^{20}$ = +23.0 (*c* = 0.27, $CHCl_3$); IR (neat) 2927, 1714, 1455, 1094, 733, 697, 668 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.33 (m, 5 H), 7.32-7.24 (m, 5 H), 5.68 (ddd, *J* = 8.1, 10.3, 17.3 Hz, 1 H), 5.03 (ddd, *J* = 0.81, 1.8, 17.3 Hz, 1 H), 5.00 (d, *J* = 11.9 Hz, 1 H), 4.97 (dd, *J* = 1.8, 10.3 Hz, 1 H), 4.67 (d, *J* = 11.9 Hz, 1 H), 4.54 (d, *J* = 12.1 Hz, 1 H), 4.49 (d, *J* = 12.1 Hz, 1 H), 3.60 (dd, *J* = 2.6, 11.8 Hz, 1 H), 3.52 (dd, *J* = 3.7, 9.2 Hz, 1 H), 3.37 (dd, *J* = 6.3, 9.2 Hz, 1 H), 3.03 (dd, *J* = 2.3, 9.8 Hz, 1 H), 2.88 (dd, *J* = 11.8, 15.0 Hz, 1 H), 2.54 (dd, *J* = 2.2, 15.1 Hz, 1 H), 2.49 (appq, *J* = 7.1 Hz, 1 H), 2.33-2.25 (m, 1 H), 2.20 (dd, *J* = 1.6, 15.0 Hz, 1 H), 1.93-1.85 (m, 2 H), 1.83-1.77 (m, 1 H), 1.70 (ddd, *J* = 2.8, 2.8, 13.5 Hz, 1 H), 1.64-1.57 (m, 2 H), 1.49-1.30 (m, 4 H), 1.22-1.18 (m, 2 H), 1.08-1.05 (m, 1 H), 1.06 (d, *J* = 7.1 Hz, 3 H), 1.05 (d, *J* = 6.7 Hz, 3 H), 0.98 (d, *J* = 6.5 Hz, 3 H), 0.89 (t, *J* = 7.3 Hz, 3 H), 0.80 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.5, 144.7, 140.3, 139.2, 128.5, 127.58, 127.55, 127.29, 127.25, 113.3, 84.6, 83.0, 79.7, 74.2, 73.4, 65.9,

47.6, 41.1, 39.6, 38.2, 37.8, 36.1, 34.3, 32.6, 30.3, 30.0, 27.4, 22.3, 20.9, 20.5; high resolution mass spectra (ES+) m/z 597.3920 [$(M+Na)^+$; calcd for $C_{38}H_{54}O_4Na^+$: 597.3920].

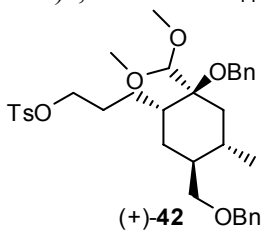


Alcohol (+)-S7: To a cold (0 °C), stirred solution of alkene (+)-**35** (107 mg, 0.24 mmol) in THF (0.75 mL) was added BH_3·THF (0.27 mL of a 1.0 M solution in THF, 0.27 mmol) dropwise via syringe. The cold bath was removed and the reaction mixture was warmed to room temperature. After being stirred at room temperature for 1.5 h the reaction was diluted CH_2CL_2 (5 mL) followed by treatment with H_2O_2 (7.5 mL of 30% aqueous solution) and NaOH (7.5 mL of 10% aqueous solution). The resulting mixture was stirred at room temperature for 45 min. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (20 mL), washed with brine (10 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 2:1 hexane:ethyl acetate) to afford the alcohol (+)-**S7** (92 mg, 83%) as a colorless oil: $[\alpha]_D^{20}$ = +35.3 (*c* = 1.84, C_6H_6); IR (neat) 3412, 3029, 2928, 2867, 1453, 1070, 1028, 734, 696, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (appd, *J* = 7.0 Hz, 2 H), 7.35 (appd, *J* = 4.3 Hz, 4 H), 7.32-7.21 (m, 4 H), 4.69 (d, *J* = 11.8 Hz, 1 H), 4.63 (d, *J* = 11.8 Hz, 1 H), 4.54 (d, *J* = 12.1 Hz, 1 H), 4.49 (d, *J* = 12.1 Hz 1 H), 4.28 (s, 1 H), 3.71-3.64 (m, 2 H), 3.56 (s, 3 H), 3.54 (dd, *J* = 5.5, 9.2 Hz, 1 H), 3.53 (s, 3 H), 3.37 (dd, *J* = 6.5, 9.2 Hz, 1 H), 2.17 (br d, *J* = 8.8 Hz, 1 H), 1.98 (br s, 1 H), 1.82-1.67 (m, 5 H), 1.65-1.58 (m, 1 H), 1.53-1.38 (m, 3 H), 1.31 (dd, *J* = 12.3, 13.9 Hz, 1 H), 0.95 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.3, 139.1, 128.5, 128.3, 127.6, 127.5, 127.3, 127.0, 110.2, 81.0, 74.2, 73.3, 64.6, 62.5, 58.5, 57.2, 38.2, 36.1, 35.7, 30.7, 29.1, 27.8, 23.2, 20.3; high resolution mass spectra (ES+) m/z 479.2765 [$(M+Na)^+$; calcd for $C_{28}H_{40}O_5Na^+$: 479.2773].



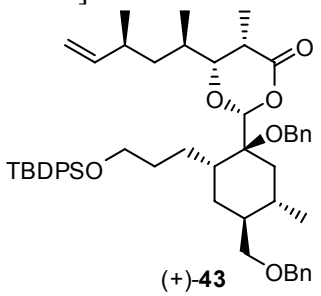
***tert*-Butyldiphenylsilyl Ether (+)-41**: To a stirred mixture of alcohol (+)-**S7** (90 mg, 0.20 mmol) and imidazole (15 mg, 0.22 mmol) in DMF (1 mL) was added *tert*-butyldiphenylsilyl chloride (55 μL, 0.22 mmol) at room temperature. The mixture was stirred at room temperature for 3 h before being quenched with H_2O (10 mL). The mixture was then extracted with Et_2O (30 mL), washed with a saturated aqueous solution of $NaHCO_3$ (15 mL) and water (2 x 15 mL). The organic layer was dried over $MgSO_4$ and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 20:1 hexane:ethyl acetate) to afford silyl ether (+)-**41** (130 mg, 95%) as a colorless oil: $[\alpha]_D^{20}$ = +18.3 (*c* = 1.0, C_6H_6); IR (neat) 3069, 2929, 2856, 1476, 1456, 1112, 1092, 735, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 1.5, 7.7 Hz, 4 H), 7.51-7.38 (m, 12 H), 7.36-7.32 (m, 3 H), 7.30-7.27 (m, 1 H), 4.79 (d, *J* = 12.0 Hz, 1 H), 4.76 (d, *J* = 12.0 Hz, 1 H), 4.61 (d, *J* = 12.1 Hz, 1

H), 4.56 (d, J = 12.1 Hz, 1 H), 4.28 (s, 1 H), 3.82 (appt, J = 6.1 Hz, 2 H), 3.61 (s, 3 H), 3.60 (dd, J = 3.7, 9.2 Hz, 1 H), 3.55 (s, 3 H), 3.45 (dd, J = 6.4, 9.2 Hz, 1 H), 2.26 (br d, J = 8.9 Hz, 1 H), 1.92-1.75 (m, 5 H), 1.66-1.59 (m, 2 H), 1.52-1.43 (m, 2 H), 1.34 (appt, J = 7.2 Hz, 1 H), 1.18 (s, 9 H), 1.02 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.6, 139.2, 135.8, 134.38, 134.36, 129.7, 128.5, 128.4, 128.2, 127.8, 127.5, 127.4, 127.3, 126.8, 110.3, 80.8, 74.2, 73.2, 64.8, 64.5, 58.5, 57.3, 38.1, 36.4, 36.2, 31.3, 29.2, 27.7, 27.1, 24.3, 20.3, 19.4; high resolution mass spectra (ES+) m/z 717.3920 [$(M+Na)^+$; calcd for $C_{44}H_{58}O_5SiNa^+$: 717.3951].

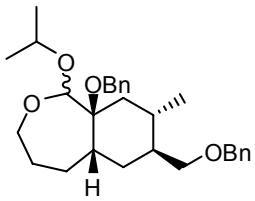


(+)-**42**

Tosylate (+)-42: To a stirred mixture of alcohol (+)-**S7** (0.24 g, 0.53 mmol), triethylamine (0.15 mL, 1.05 mmol), and DMAP (13 mg, 0.11 mmol) in CH_2Cl_2 (1.75 mL) was added TsCl (0.15 g, 0.79 mmol) at room temperature. The reaction mixture was stirred at room temperature for 1.5 h before being quenched with a saturated aqueous solution of $NaHCO_3$ (10 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (50 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 5:1 hexane:ethyl acetate) to afford tosylate (+)-**42** (0.13 g, 95%) as a colorless oil: $[\alpha]_D^{20}$ = +33.6 (c = 1.13, C_6H_6); IR (neat) 2926, 1496, 1453, 1361, 1189, 1177, 1096, 736, 697, 668 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.78 (d, J = 8.2 Hz, 2 H), 7.48 (d, J = 7.5 Hz, 2 H), 7.31 (d, J = 7.4 Hz, 2 H), 7.21-7.09 (m, 6 H), 6.71 (d, J = 8.2 Hz, 2 H), 4.77 (d, J = 11.7 Hz, 1 H), 4.71 (d, J = 11.7 Hz, 1 H), 4.34 (d, J = 12.2 Hz, 1 H), 4.31 (d, J = 12.2 Hz, 1 H), 4.02 (s, 1 H), 3.93 (appt, J = 5.8 Hz, 2 H), 3.55 (dd, J = 4.5, 9.1 Hz, 1 H), 3.35 (dd, J = 3.5, 8.9 Hz, 1 H), 3.25 (s, 3 H), 3.23 (m, 1 H), 3.22 (s, 3 H), 2.20 (br d, J = 8.6 Hz, 1 H), 2.01-1.88 (m, 5 H), 1.92 (s, 3 H), 1.56-1.47 (m, 1 H), 1.43-1.33 (m, 2 H), 1.31 (appt, J = 13.1 Hz, 1 H), 0.98 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 144.3, 141.3, 140.0, 130.1, 128.9, 128.8, 128.7, 110.4, 81.2, 74.3, 73.7, 71.1, 65.2, 57.9, 57.1, 38.8, 37.1, 36.7, 29.6, 28.5, 28.2, 24.3, 21.5, 20.6; high resolution mass spectra (ES+) m/z 633.2853 [$(M+Na)^+$; calcd for $C_{35}H_{46}O_7SNa^+$: 633.2862].



(+)-**43**



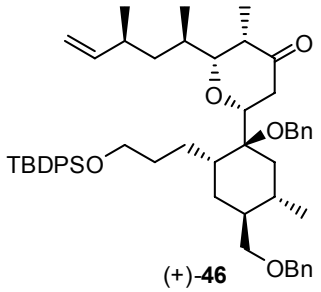
44

Dioxanone (+)-43 and Side Product 44: To a cold (-60 °C), stirred mixture of acid (+)-**7** (9.4 mg, 47 μmol), TBDPS-ether (+)-**41** (25 mg, 36 μmol), and isopropoxytrimethylsilane (30 μL, 144 μmol) in CH_2Cl_2 (0.36 mL) was added TMSOTf (2 drops, ~0.5 eq). After being stirred at -60 °C for 4.5 h, the reaction was warmed to -40 °C where it was stirred for 21 h. The reaction was quenched with triethylamine (50 μL) and the stirring was continued for additional 15 min at -40 °C. The reaction mixture was then warmed to room temperature and extracted with Et_2O (15 mL), washed with a saturated aqueous solution of $NaHCO_3$ (2 x 7.5 mL), dried over $MgSO_4$, and

filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 20:1 hexane:ethyl acetate) to afford dioxanone (+)-**43** (21.6 mg, 51%) as a colorless oil along with cyclic acetal **44** as a 2:1 mixture of diastereomers.

Data for (+)-43: $[\alpha]_D^{20}$ = +12.4 (*c* = 0.45, C_6H_6); IR (neat) 3070, 2955, 2929, 2858, 1751, 1456, 1428, 1250, 1111, 998, 736, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.85-7.82 (m, 4 H), 7.48 (d, *J* = 7.2 Hz, 2 H), 7.32-7.22 (m, 8 H), 7.21-7.18 (m, 4 H), 7.12-7.08 (m, 2 H), 5.52 (ddd, *J* = 8.4, 10.2, 17.1 Hz, 1 H), 5.02 (s, 1 H), 4.95 (ddd, *J* = 0.6, 1.8, 17.1 Hz, 1 H), 4.91 (dd, *J* = 1.8, 10.2 Hz, 1 H), 4.81 (s, 2 H), 4.36 (d, *J* = 12.2 Hz, 1 H), 4.32 (d, *J* = 12.2 Hz, 1 H), 3.80-3.75 (m, 2 H), 3.37 (dd, *J* = 3.6, 9.0 Hz, 1 H), 3.25 (dd, *J* = 6.2, 9.0 Hz, 1 H), 2.96 (dd, *J* = 4.8, 7.9 Hz, 1 H), 2.49 (br d, *J* = 7.7 Hz, 1 H), 2.37 (dddd, *J* = 5.0, 7.2, 7.2, 7.2 Hz, 1 H), 2.15-2.07 (m, 1 H), 2.02-1.93 (m, 2 H), 1.91-1.80 (m, 3 H), 1.67-1.43 (m, 6 H), 1.39 (dd, *J* = 12.6, 13.9 Hz, 1 H), 1.22 (s, 9 H), 1.03 (d, *J* = 7.2 Hz, 3 H), 0.95 (d, *J* = 6.3 Hz, 3 H), 0.92 (d, *J* = 6.7 Hz, 3 H), 0.92-0.87 (m, 1 H), 0.57 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) 171.0, 144.5, 140.7, 140.0, 136.4, 134.9, 130.32, 130.30, 128.9, 128.8, 128.7, 128.5, 128.3, 128.0, 127.9, 127.7, 127.6, 113.9, 104.5, 82.3, 79.4, 74.2, 73.7, 65.5, 65.0, 39.7, 39.0, 38.7, 36.9, 36.3, 36.0, 31.9, 31.7, 29.6, 28.2, 27.6, 25.0, 22.4, 20.6, 19.9, 15.2, 11.9; high resolution mass spectra (ES+) m/z 853.4835 [$(M+Na)^+$; calcd for $C_{53}H_{70}O_6SiNa^+$: 853.4839].

Data for Cyclic Acetal 44: IR (neat) 2928, 2864, 1496, 1453, 1377, 1095, 1060, 733, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ (* denotes minor diastereomer) *7.69 (d, *J* = 7.6 Hz, 1/3 H), 7.40-7.19 (18/3 H), *4.82 (d, *J* = 11.7 Hz, 2/3 H), 4.76 (d, *J* = 11.7 Hz, 1 H), 4.68 (d, *J* = 11.7 Hz, 1 H), 4.52 (d, *J* = 12.0 Hz, 1 H), 4.47 (d, *J* = 12.0 Hz, 1 H), 4.23 (dd, *J* = 5.7, 11.6 Hz, 2/3 H), 3.91 (septet, *J* = 6.2 Hz, 2/3 H), *3.87 (septet, *J* = 6.2 Hz, 1/3 H), 3.79 (dd, *J* = 4.6, 8.8 Hz, 2/3 H), 3.58-3.52 (m, 2 H), 3.46-3.39 (m, 1 H), 3.34-3.26 (m, 1 H), 2.32 (br s, 2/3 H), 2.02-1.47 (m, 10 H), 1.35 (m, 2 H), 1.27 (d, *J* = 6.2 Hz, 2 H), *1.25 (d, *J* = 6.2 Hz, 1 H), 1.17 (d, *J* = 6.0 Hz, 3 H), *0.95 (d, *J* = 5.8 Hz, 1 H), 0.90 (d, *J* = 6.5 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (* denotes minor diastereomer) 140.4, *140.1, *138.92, 138.89, 135.6, *129.4, 128.2, *128.1, *128.0, 127.9, *127.5, 127.4, 127.32, 127.26, 127.18, *127.06, 126.8, 126.7, *108.1, 103.4, 79.6, *74.0, 73.9, 73.0, *68.8, 68.7, *66.0, 64.5, *64.3, *42.8, *39.9, 39.3, *39.1, 37.1, 34.5, *34.3, *32.1, *30.7, 30.0; high resolution mass spectra (ES+) m/z 475.2815 [$(M+Na)^+$; calcd for $C_{29}H_{40}O_4Na^+$: 475.2824].

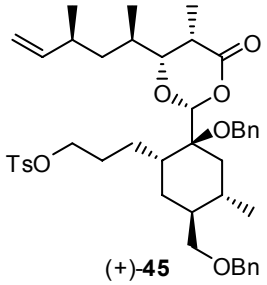


(+)-**46**

Tetrahydropyranone (+)-46: To a solution of dioxananone (+)-**43** (11 mg, 13.2 μmol) in THF (0.15 mL) was added Cp_2TiMe_2 (50 μL of 0.7 M solution in THF, 33.1 μmol). The reaction mixture was heated at reflux for 5 h under dark. It was then cooled to room temperature, triturated with hexanes (5 mL), and stirred for 30 min. The resulting orange solid was filtered through a pad of celite and the solid was washed with hexane. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel

(elution with 20:1 hexane:ethyl acetate) to afford the intermediate enol acetal (12.3 mg, quant). The enol acetal was used in the next step without further delay.

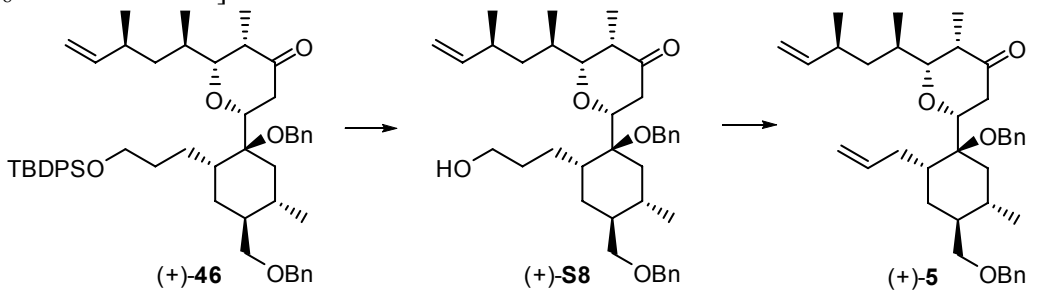
To a suspension of Cs_2CO_3 (5.6 mg, 17.2 μmol) in CH_2Cl_2 (0.35 mL) was added Me_2AlCl (34 μL of 1.0 M solution in hexanes, 34.0 μmol) at room temperature and stirred for 5 min. This suspension was cooled to -78 °C and treated with a solution of the enol acetal (12.3 mg, 13.2 μmol) prepared above in CH_2Cl_2 (0.45 mL followed by a 0.25 mL rinse). After being stirred at -78 °C for 5 min, the mixture was warmed to room temperature and stirred for 30 min. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (1 mL), extracted with CH_2Cl_2 (20 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified via preparative TLC (elution with 4:1 hexane:ethyl acetate) to afford tetrahydropyranone (+)-**46** (6.6 mg, 60%) as a colorless oil: $[\alpha]_D^{20}$ = +23.8 (*c* = 0.66, C_6H_6); IR (neat) 2929, 1713, 1496, 1453, 1428, 1094, 737, 700 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.81 (m, 4 H), 7.50 (d, *J* = 7.6 Hz, 2 H), 7.33-7.10 (m, 14 H), 5.73 (ddd, *J* = 8.0, 10.2, 17.2 Hz, 1 H), 5.17 (d, *J* = 11.9 Hz, 1 H), 5.04 (d, *J* = 17.2 Hz, 1 H), 4.99 (d, *J* = 10.2 Hz, 1 H), 4.79 (d, *J* = 11.9 Hz, 1 H), 4.38 (d, *J* = 12.2 Hz, 1 H), 4.34 (d, *J* = 12.2 Hz, 1 H), 3.65 (appt, *J* = 5.3 Hz, 2 H), 3.52 (dd, *J* = 3.4, 8.9 Hz, 1 H), 3.39 (dd, *J* = 3.4, 8.9 Hz, 1 H), 3.29 (dd, *J* = 6.2, 8.9 Hz, 1 H), 2.93 (dd, *J* = 11.9, 14.9 Hz, 1 H), 2.78 (dd, *J* = 2.1, 9.7 Hz, 1 H), 2.61 (br d, *J* = 14.6 Hz, 1 H), 2.45 (appq, *J* = 6.9 Hz, 1 H), 2.33 (d, *J* = 14.9 Hz, 1 H), 2.24-2.15 (m, 2 H), 1.91-1.88 (m, 1 H), 1.78-1.63 (m, 5 H), 1.42-1.26 (m, 4 H), 1.23 (s, 9 H), 1.14 (dd, *J* = 12.8, 14.8 Hz, 1 H), 1.06 (d, *J* = 6.6 Hz, 3 H), 0.99 (d, *J* = 6.4 Hz, 3 H), 0.97-0.92 (m, 1 H), 0.86 (d, *J* = 7.0 Hz, 3 H), 0.56 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 210.3, 145.1, 141.1, 139.9, 136.4, 134.9, 130.4, 129.01, 128.97, 128.5, 128.4, 128.0, 127.9, 127.7, 127.6, 113.6, 84.8, 83.4, 80.2, 74.2, 73.8, 66.4, 64.7, 47.9, 41.6, 40.3, 38.8, 38.1, 36.6, 34.9, 33.0, 31.4, 30.3, 28.2, 27.6, 25.1, 22.6, 20.9, 19.9, 15.2, 11.0; high resolution mass spectra (ES+) m/z 851.5078 [$(M+Na)^+$; calcd for $C_{54}H_{72}O_5SiNa^+$: 851.5047].



(+)-**45**

Dioxanone (+)-45: To a cold (-20 °C), stirred mixture of acid (+)-**7** (6.5 mg, 32.6 μmol), tosylate (+)-**42** (15.3 mg, 25.1 μmol), and isopropoxytrimethylsilane (18 μL, 100.3 μmol) in CH_2Cl_2 (0.25 mL) was added TMSOTf (2 drops, ~1.0 eq). After being stirred at -20 °C for 2 h, the reaction was quenched with triethylamine (25 μL) and stirred for 15 min at -20 °C. The mixture was extracted with Et_2O (15 mL), washed with a saturated aqueous solution of $NaHCO_3$ (2 x 7.5 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by preparative TLC (elution with 3:1 hexane:ethyl acetate) to afford dioxanone (+)-**45** (8.9 mg, 50%) as a colorless oil: $[\alpha]_D^{20}$ = +10.7 (*c* = 1.13, C_6H_6); IR (neat) 3064, 2955, 2869, 1743, 1454, 1361, 1189, 1177 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.85 (d, *J* = 8.3 Hz, 2 H), 7.47 (d, *J* = 7.8 Hz, 2 H), 7.30 (d, *J* = 7.8 Hz, 2 H), 7.21-7.16 (m, 5 H), 7.12-7.08 (m, 1 H), 6.81 (d, *J* = 8.3 Hz, 2 H), 5.55 (ddd, *J* = 8.4, 10.2, 17.3 Hz, 1 H), 4.98-4.92 (m, 2 H), 4.97 (s, 1 H), 4.78 (d, *J* = 11.8 Hz, 1 H), 4.75 (d, *J* = 11.8 Hz, 1 H), 4.34 (d, *J* = 12.2 Hz, 1 H), 4.30 (d, *J* = 12.2 Hz, 1 H), 3.93 (m, 1 H), 3.86 (m, 1 H), 3.32 (dd, *J* = 3.5, 9.0 Hz, 1 H), 3.19 (dd,

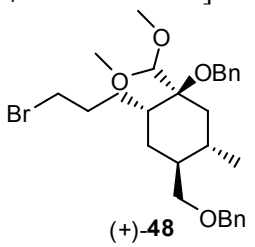
J = 6.5, 9.0 Hz, 1 H), 2.94 (dd, J = 4.6, 8.2 Hz, 1 H), 2.41 (app dq, J = 11.9, 7.3 Hz, 1 H), 2.39 (br d, 10.0 Hz, 1 H), 2.13 (m, 1 H), 1.95-1.81 (m, 3 H), 1.85 (s, 3 H), 1.64-1.57 (m, 4 H), 1.39-1.25 (m, 5 H), 1.10 (d, J = 7.2 Hz, 3 H), 0.96 (d, J = 6.7 Hz, 3 H), 0.91 (m, 1 H), 0.79 (d, J = 6.8 Hz, 3 H), 0.57 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 171.3, 144.6, 144.5, 140.1, 139.8, 134.8, 130.3, 128.94, 128.86, 128.7, 128.0, 127.96, 127.69, 127.66, 113.9, 104.9, 82.4, 79.2, 73.9, 73.7, 71.0, 65.5, 39.8, 39.0, 38.6, 36.4, 36.3, 36.0, 31.9, 29.4, 28.0, 24.5, 22.5, 21.5, 20.4, 15.1, 12.0; high resolution mass spectra (ES+) m/z 769.3761 [(M+Na)$^+$; calcd for $C_{44}H_{58}O_8SNa^+$: 769.3750].



Diene (+)-5: To a solution of silyl ether (+)-**46** (53.2 mg, 64.2 μmol) in THF (0.54 mL) was added TBAF (0.1 mL of a 1.0 M solution in THF, 100 μmol) at room temperature. The reaction mixture was stirred at room temperature for 15 h then diluted with Et_2O (15 mL), washed with a saturated aqueous solution of NH_4Cl (2 x 8 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by preparative TLC (elution with 1:1 hexane:ethyl acetate) to afford alcohol (+)-**S8** (32.4 mg, 85%) as a colorless oil: $[\alpha]_D^{20}$ = +44.0 (c = 1.08, $CHCl_3$); IR (neat) 3400, 2929, 2870, 1712, 1452, 1375, 1091, 1059, 734 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.24 (m, 10 H), 5.54 (ddd, J = 8.7, 10.2, 17.1 Hz, 1 H), 5.02 (ddd, J = 0.5, 1.9, 17.1 Hz, 1 H), 4.98 (dd, J = 12.0 Hz, 1 H), 4.65 (d, J = 12.0 Hz, 1 H), 4.54 (d, J = 12.2 Hz, 1 H), 4.49 (d, J = 12.2 Hz, 1 H), 4.36 (appt, J = 7.1 Hz, 1 H), 3.68 (dd, J = 2.4, 11.7 Hz, 1 H), 3.69-3.59 (m, 2 H), 3.53 (dd, J = 3.7, 9.2 Hz, 1 H), 3.37 (dd, J = 6.4, 9.2 Hz, 1 H), 3.05 (dd, J = 6.4, 9.2 Hz, 1 H), 2.69 (appt, J = 13.0 Hz, 1 H), 2.52-2.46 (m, 2 H), 2.40 (dd, J = 2.4, 14.3 Hz, 1 H), 2.31-2.23 (m, 1 H), 1.95 (ddd, J = 4.1, 13.2 Hz, 1 H), 1.78-1.58 (m, 6 H), 1.46-1.31 (m, 5 H), 1.16 (dd, J = 12.6, 15.1 Hz, 1 H), 1.09 (d, J = 6.8 Hz, 3 H), 1.07 (d, J = 6.7 Hz, 3 H), 0.98 (d, J = 6.5 Hz, 3 H), 0.93 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.0, 143.9, 140.3, 139.1, 128.5, 127.6, 127.5, 127.2, 127.0, 114.1, 88.0, 82.8, 79.7, 74.0, 73.3, 65.8, 63.1, 47.6, 41.6, 39.7, 38.2, 36.3, 36.0, 33.7, 32.2, 31.0, 29.8, 27.5, 24.2, 22.5, 20.4, 18.1, 9.0; high resolution mass spectra (ES+) m/z 613.3873 [(M+Na)$^+$; calcd for $C_{38}H_{54}O_5Na^+$: 613.3869].

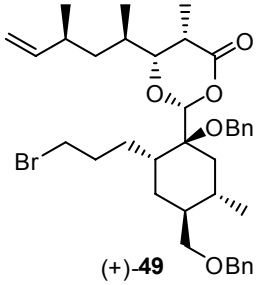
To a mixture of alcohol (+)-**S8** (24 mg, 40.7 μmol) and *o*-nitrophenylselenocyanate (29.6 mg, 130.2 μmol) in THF (0.25 mL) was added tributylphosphine (32 μL, 130.2 μmol) dropwise at room temperature. The dark solution was stirred at room temperature for 2 h before being treated with $NaHCO_3$ (105 mg) followed by H_2O_2 (0.15 mL of 30% aqueous solution). The reaction mixture was stirred at room temperature for an additional 4 h then treated with a saturated aqueous solution of $Na_2S_2O_3$ (1 mL). The mixture was extracted with Et_2O (20 mL), washed with water (2 x 10 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by preparative TLC (elution with 9:1 hexane:ethyl acetate) to afford tetrahydropyranone (+)-**5** (9 mg, 39%) as a colorless oil: $[\alpha]_D^{20}$ = +14.3 (c = 0.46, C_6H_6); IR (neat) 3065, 2927, 2869, 1713, 1640, 1497, 1453, 1097, 910, 733, 696 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.49 (d, J = 7.7 Hz, 2 H), 7.31 (d, J = 7.9 Hz, 2 H), 7.22-7.18 (m, 4 H), 7.14-7.09 (m, 2 H), 5.72 (ddd, J = 8.1, 10.3, 17.3 Hz, 1 H), 5.63-5.57 (m, 1 H), 5.13 (d,

J = 11.9 Hz, 1 H), 5.06-4.98 (m, 4 H), 4.76 (d, *J* = 11.9 Hz, 1 H), 4.35 (d, *J* = 12.2 Hz, 1 H), 4.29 (d, *J* = 12.2 Hz, 1 H), 3.40 (dd, *J* = 2.7, 11.9 Hz, 1 H), 3.34 (dd, *J* = 3.7, 9.1 Hz, 1 H), 3.30 (dd, *J* = 5.6, 9.1 Hz, 1 H), 2.95-2.89 (m, 1 H), 2.81-2.75 (m, 1 H), 2.61-2.57 (m, 1 H), 2.48-2.41 (m, 1 H), 2.30 (dd, *J* = 2.5, 14.9 Hz, 1 H), 2.20 (m, 1 H), 2.16 (dt, *J* = 4.3, 13.2 Hz, 1 H), 1.90-1.84 (m, 3 H), 1.80-1.68 (m, 3 H), 1.37-1.29 (m, 2 H), 1.06 (d, *J* = 6.7 Hz, 3 H), 1.06-1.00 (m, 1 H), 0.97 (d, *J* = 6.6 Hz, 3 H), 0.97-0.91 (m, 1 H), 0.85 (d, *J*= 7.1 Hz, 3 H), 0.56 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 210.3, 145.0, 141.0, 139.9, 137.6, 129.0, 128.9, 128.7, 128.3, 127.9, 127.7, 116.5, 113.7, 84.8, 83.2, 79.7, 74.0, 73.6, 66.4, 47.9, 41.5, 40.1, 38.6, 38.1, 36.6, 34.9, 33.8, 32.9, 30.6, 30.0, 28.5, 22.6, 20.8, 15.1, 11.0; high resolution mass spectra (ES+) m/z 595.3786 [$(M+Na)^+$; calcd for $C_{38}H_{52}O_4Na^+$: 595.3763].



(+)-**48**

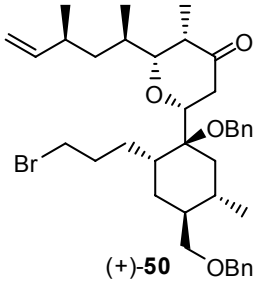
Bromide (+)-48: To a suspension of Schwartz' reagent (106 mg, 0.41 mmol) in CH_2Cl_2 (0.51 mL) was added a solution of alkene (+)-**35** (45 mg, 0.10 mmol) in CH_2Cl_2 (0.51 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h then cooled to 0 °C. The mixture was then treated with a solution of *N*-bromosuccinimide (91 mg, 0.51 mmol) in CH_2Cl_2 (1 mL). After being stirred at 0 °C for 20 min, the reaction was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (2 mL), extracted with Et_2O (30 mL). The organic layer was then washed with a saturated aqueous solution of $Na_2S_2O_3$ (15 mL), aqueous saturated solution of $NaHCO_3$ (2 x 15 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 9:1 hexane:ethyl acetate) to afford bromide (+)-**48** (47 mg, 90%) as a colorless oil: $[\alpha]_D^{20}$ = +36.8 (*c* = 0.03, benzene); IR (neat) 2925, 1456, 1363, 1073, 734 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.50 (d, *J* = 7.4 Hz, 2 H), 7.32 (d, *J* = 7.4 Hz, 2 H), 7.20 (app q, *J* = 7.4 Hz, 4 H), 7.11 (m, 2 H), 4.79 (d, *J* = 11.8 Hz, 1 H), 4.75 (d, *J* = 11.8 Hz, 1 H), 4.36 (d, *J* = 12.2 Hz, 1 H), 4.32 (d, *J* = 12.2 Hz, 1 H), 4.06 (s, 1 H), 3.38 (dd, *J* = 3.6, 9.0 Hz, 1 H), 3.26 (dd, *J* = 6.4, 9.0 Hz, 1 H), 3.25 (s, 3 H), 3.23 (s, 3 H), 3.07 (m, 2 H), 2.25 (br d, *J* = 9.7 Hz, 1 H), 1.96-1.80 (m, 4 H), 1.71-1.64 (m, 3 H), 1.41-1.30 (m, 2 H), 1.29 (dd, *J* = 12.4, 13.x, 1 H), 0.93 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 141.3, 140.0, 128.9, 128.8, 128.0, 127.89, 127.85, 127.5, 110.4, 81.3, 74.3, 73.7, 65.2, 57.9, 57.1, 39.0, 37.1, 36.6, 34.7, 32.2, 29.6, 28.6, 27.0, 20.7; high resolution mass spectra (ES+) m/z 541.1937 [$(M+Na)^+$; calcd for $C_{28}H_{39}BrO_4Na^+$: 541.1929].



(+)-**49**

Dioxanone (+)-49: To a cold (-20 °C), stirred mixture of acid (+)-**7** (90 mg, 0.45 mmol), bromide (+)-**48** (179 mg, 0.35 mmol), and isopropoxytrimethylsilane (0.25 mL, 1.38 mmol) in CH_2Cl_2 (2 mL) was added TMSOTf (30 μL, 0.17 mmol). The reaction mixture was warmed to 0

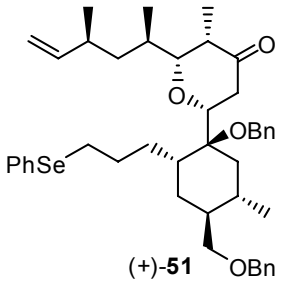
°C and stirred for 30 min at 0 °C before being quenched with triethylamine (25 μL) and stirred for an additional 15 min at 0 °C. The mixture was extracted with Et_2O (50 mL), washed with a saturated aqueous solution of $NaHCO_3$ (2 x 25 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 7:1 hexane:ethyl acetate) to afford dioxanone (+)-**49** (188 mg, 83%) as a colorless oil: $[\alpha]_D^{20}$ = +23.6 (*c* = 0.5, C_6H_6); IR (neat) 2928, 1751, 1457, 1246, 1097, 995, 736, 695, 668 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.56 (d, *J* = 7.4 Hz, 2 H), 7.39 (d, *J* = 7.4 Hz, 2 H), 7.28 (appt, *J* = 7.6 Hz, 4 H), 7.21-7.17 (m, 2 H), 5.62 (ddd, *J* = 8.4, 10.2, 17.2 Hz, 1 H), 5.06-5.00 (m, 2 H), 5.05 (s, 1 H), 4.88 (d, *J* = 11.7 Hz, 1 H), 4.85 (d, *J* = 11.7 Hz, 1 H), 4.43 (d, *J* = 12.2 Hz, 1 H), 4.39 (d, *J* = 12.2 Hz, 1 H), 3.42 (dd, *J* = 3.6, 9.0 Hz, 1 H), 3.30 (dd, *J* = 6.4, 9.0 Hz, 1 H), 3.16 (m, 2 H), 2.99 (dd, *J* = 4.7, 8.1 Hz, 1 H), 2.47-2.42 (m, 2 H), 2.21 (m, 1 H), 2.06-1.88 (m, 4 H), 1.76 (ddd, *J* = 3.0, 3.0, 13.9 Hz, 1 H), 1.71-1.64 (m, 3 H), 1.57-1.39 (m, 4 H), 1.14 (d, *J* = 7.2 Hz, 3 H), 1.04 (d, *J* = 6.7 Hz, 3 H), 1.03-0.98 (m, 1 H), 0.98 (d, *J* = 6.3 Hz, 3 H), 0.64 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 171.0, 144.4, 140.6, 139.8, 128.3, 128.0, 127.32, 127.30, 127.0, 113.9, 104.9, 82.4, 79.2, 73.9, 73.7, 65.5, 39.1, 38.4, 38.0, 35.9, 35.7, 35.1, 33.9, 31.2, 31.0, 28.8, 27.4, 26.4, 21.8, 19.8, 14.5, 11.3; high resolution mass spectra (ES+) m/z 677.2785 [$(M+Na)^+$; calcd for $C_{37}H_{51}BrO_5Na^+$: 677.2818].



(+)-**50** OBn

Tetrahydropyranone (+)-50: A mixture of dioxanone (+)-**49** (188 mg, 0.29 mmol) and Cp_2TiMe_2 (1 mL of 0.7 M solution in THF, 0.70 mmol) in THF (1 mL) was heated at reflux for 3 h under dark. The mixture was cooled to room temperature and triturated with hexanes (25 mL) followed by stirring for 30 min at room temperature. The resulting orange solid was filtered through a pad of celite and the solid was washed with hexane. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 9:1 hexane:ethyl acetate) to afford intermediate enol acetal (162 mg, 87%) as a colorless oil: $[\alpha]_D^{20}$ = +60.5 (*c* = 0.825, C_6H_6); IR (neat) 2932, 2868, 1657, 1455, 1374, 1268, 1096, 1003, 735, 696 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.57 (d, *J* = 8.1 Hz, 2 H), 7.31 (d, *J* = 7.5 Hz, 2 H), 7.25-7.17 (m, 4 H), 7.14-7.08 (m, 2 H), 5.66 (ddd, *J* = 8.2, 10.2, 17.2 Hz, 1 H), 5.04 (dq, *J* = 0.9, 17.2 Hz, 1 H), 4.99 (dd, *J* = 1.9, 10.2 Hz, 1 H), 4.97 (d, *J* = 11.7 Hz, 1 H), 4.83 (d, *J* = 11.7 Hz, 1 H), 4.64 (s, 1 H), 4.56 (s, 1 H), 4.34 (d, *J* = 12.2 Hz, 1 H), 4.30 (d, *J* = 12.2 Hz, 1 H), 4.16 (s, 1 H), 3.38 (dd, *J* = 3.6, 9.0 Hz, 1 H), 3.20 (dd, *J* = 6.7, 9.0 Hz, 1 H), 3.11-3.08 (m, 2 H), 3.07 (dd, *J* = 2.7, 10.1 Hz, 1 H), 2.41 (br d, *J* = 9.4 Hz, 1 H), 2.31-2.23 (m, 1 H), 2.14 (dq, *J* = 2.5, 6.9 Hz, 1 H), 2.03 (ddd, *J* = 1.4, 3.9, 14.0 Hz, 1 H), 1.97-1.66 (m, 6 H), 1.41-1.26 (m, 5 H), 1.08 (d, *J* = 6.9 Hz, 3 H), 1.03 (d, *J* = 6.7 Hz, 3 H), 0.91 (d, *J* = 6.5 Hz, 3 H), 0.90 (m, 1 H), 0.61 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 163.0, 144.2, 140.6, 139.3, 128.3, 128.1, 127.32, 127.26, 127.16, 126.8, 113.1, 106.0, 92.7, 84.6, 78.6, 73.6, 73.0, 64.8, 40.3, 38.2, 36.7, 35.8, 35.5, 35.1, 33.9, 31.8, 31.4, 28.9, 27.7, 26.2, 22.0, 20.0, 14.0, 13.4; high resolution mass spectra (ES+) m/z 675.3035 [$(M+Na)^+$; calcd for $C_{38}H_{53}BrO_4Na^+$: 675.3025].

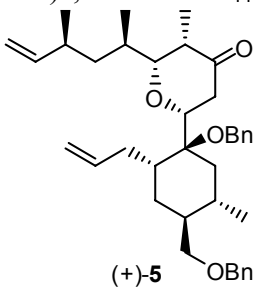
A suspension of Cs_2CO_3 (7.1 mg, 21.9 μmol) in CH_2Cl_2 (0.6 mL) was treated with Me_2AlCl (44 μL of 1.0 M solution in hexanes, 44.0 μmol) and stirred for 15 min at room temperature. This suspension was then cooled to -78 °C and treated with a solution of the above enol acetal (11 mg, 16.9 μmol) in CH_2Cl_2 (0.6 mL). The reaction mixture was stirred at -78 °C for 30 min then warmed to 23 °C and stirred for additional 30 min. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (2 mL) and extracted with Et_2O (15 mL). The organic layer was then washed with a saturated aqueous solution of $NaHCO_3$ (2 x 8 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by Prep TLC (elution with 4:1 hexane:ethyl acetate) to afford tetrahydropyranone (+)-**50** (10.0 mg, 91%) as a colorless oil: $[\alpha]_D^{20}$ = +39.0 (*c* = 0.40, C_6H_6); IR (neat) 2929, 1714, 1452, 1092, 733, 696 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.49 (d, *J* = 7.3 Hz, 2 H), 7.32 (d, *J* = 7.3 Hz, 2 H), 7.23-7.19 (m, 4 H), 7.16-7.10 (m, 2 H), 5.72 (ddd, *J* = 8.1, 10.3, 17.4 Hz, 1 H), 5.13 (d, *J* = 11.8 Hz, 1 H), 5.03 (d, *J* = 17.4 Hz, 1 H), 4.99 (dd, *J* = 1.8, 10.3 Hz, 1 H), 4.75 (d, *J* = 11.8 Hz, 1 H), 4.36 (d, *J* = 12.2 Hz, 1 H), 4.32 (d, *J* = 12.2 Hz, 1 H), 3.45 (dd, *J* = 2.6, 11.9 Hz, 1 H), 3.35 (d, *J* = 3.5, 9.0 Hz, 1 H), 3.24 (d, *J*= 6.3, 9.0 Hz, 1 H), 2.95-2.83 (m, 3 H), 2.72 (dd, *J* = 2.3, 9.8 Hz, 1 H), 2.57 (dd, *J* = 2.6, 15.1 Hz, 1 H), 2.45 (dq, *J* = 1.8, 7.0 Hz, 1 H), 2.32 (dd, *J* = 2.1, 14.9 Hz, 1 H), 2.20 (m, 1 H), 2.11 (dt, *J* = 3.9, 13.3 Hz, 1 H), 1.86 (m, 1 H), 1.75-1.62 (m, 3 H), 1.61-1.54 (m, 2 H), 1.38-1.26 (m, 4 H), 1.12 (m, 1 H), 1.06 (d, *J* = 6.7 Hz, 3 H), 0.94 (d, *J* = 6.5 Hz, 3 H), 0.92 (m, 1 H), 0.87 (d, *J* = 7.1 Hz, 3 H), 0.56 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 210.3, 145.0, 141.0, 139.8, 128.98, 128.95, 128.7, 128.0, 127.7, 113.6, 84.8, 83.3, 79.9, 74.0, 73.7, 66.5, 47.9, 41.5, 39.5, 38.7, 38.1, 36.6, 34.9, 34.2, 33.0, 31.1, 30.2, 27.8, 26.8, 22.6, 20.7, 15.2, 11.1; high resolution mass spectra (ES+) m/z 675.3020 [$(M+Na)^+$; calcd for $C_{38}H_{53}BrO_4Na^+$: 675.3025].



(+)-**51**

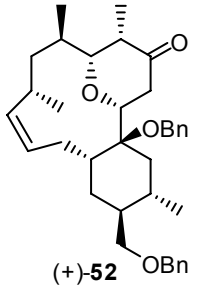
Selenide (+)-51: To a suspension of bromide (+)-**50** (2.19 g, 3.36 mmol) and Cs_2CO_3 (1.203 g, 4.36 mmol) in CH_3CN (35 mL) was added benzeneselenol (0.46 mL, 4.36 mmol) dropwise at room temperature. After being stirred at room temperature for 20 min, the reaction mixture was diluted with Et_2O (250 mL), washed with a saturated aqueous solution of $NaHCO_3$ (2 x 100 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 10:1 hexane:ethyl acetate) to afford selenide (+)-**51** (2.30 g, 94%) as a colorless oil: $[\alpha]_D^{20}$ = +40.0 (*c* = 0.10, C_6H_6); IR (neat) 2925, 1714, 1453, 1202, 1092, 911, 733, 665 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.53 (m, 2 H), 7.49 (d, *J* = 7.7 Hz, 2 H), 7.32 (d, *J* = 7.4 Hz, 2 H), 7.22-7.11 (m, 6 H), 7.05-7.02 (m, 2 H), 7.00-6.96 (m, 1 H), 5.72 (ddd, *J* = 8.0, 10.3, 17.3 Hz, 1 H), 5.14 (d, *J* = 11.9 Hz, 1 H), 5.04 (dq, *J* = 17.3, 0.9 Hz, 1 H), 4.99 (dd, *J* = 1.8, 10.3 Hz, 1 H), 4.76 (d, *J* = 11.9 Hz, 1 H), 4.35 (d, *J* = 12.2 Hz, 1 H), 4.31 (d, *J* = 12.2 Hz, 1 H), 3.46 (dd, *J* = 2.7, 11.9 Hz, 1 H), 3.32 (dd, *J* = 3.5, 9.0 Hz, 1 H), 3.24 (dd, *J* = 6.1, 9.0 Hz, 1 H), 2.90 (dd, *J* = 11.9, 14.9 Hz, 1 H), 2.75 (dd, *J* = 2.4, 9.8 Hz, 1 H), 2.69-2.56 (m, 3 H), 2.46 (dq, *J* = 2.0, 7.1 Hz, 1 H), 2.34 (dd, *J* = 1.9, 14.9 Hz, 1 H), 2.24-2.18 (m, 1 H), 2.10 (dt, *J* = 4.1, 13.3 Hz, 1 H), 1.88 (ddd, *J* = 2.9, 10.6, 13.1 Hz, 1 H),

1.75-1.67 (m, 3 H), 1.65 (tt, *J* = 2.8, 13.7 Hz, 1 H), 1.62-1.57 (m, 1 H), 1.45-1.39 (m, 1 H), 1.33-1.25 (m, 2 H), 1.23-1.19 (m, 1 H), 1.08 (dd, *J* = 12.7, 15.0 Hz, 1 H), 1.06 (d, *J* = 6.7 Hz, 3 H), 0.96 (d, *J* = 6.5 Hz, 3 H), 0.96-0.91 (m, 1 H), 0.86 (d, *J* = 7.1 Hz, 3 H), 0.57 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 210.5, 145.0, 141.1, 139.9, 133.6, 129.7, 128.9, 128.7, 128.5, 128.3, 128.0, 127.71, 127.66, 127.3, 113.6, 84.8, 83.4, 80.0, 74.1, 73.7, 66.4, 47.9, 41.6, 39.8, 38.8, 38.1, 36.6, 34.9, 33.0, 30.3, 28.4, 28.2, 28.1, 28.0, 22.6, 20.8, 15.2, 11.0; high resolution mass spectra (ES+) m/z 753.3377 [(M+Na)$^+$; calcd for $C_{44}H_{58}O_4SeNa^+$: 753.3398].



(+)-**5**

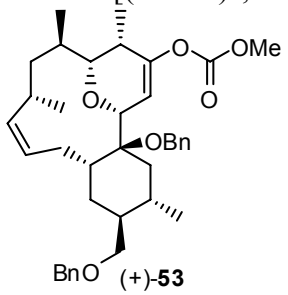
Bis-Alkene (+)-5: To a stirred mixture of selenide (+)-**51** (2.03 g, 3.15 mmol) and pyridine (1.3 mL, 15.75 mmol) in $CHCl_3$ (12 mL) was added Davis's oxaziridine (0.83 g, 3.15 mmol) at room temperature. The mixture was stirred at room temperature for 15 min prior to heating at 60 °C for 1 h. The mixture was cooled to room temperature and concentrated under vacuum to leave a yellow residue which was purified by column chromatography on silica gel (20:1 hexane:ethyl acetate) to afford bis alkene (+)-**5** (1.59 g, 94%) as a colorless oil: $[\alpha]_D^{20}$ = +14.3 (*c* = 0.46, C_6H_6); IR (neat) 3065, 2927, 2869, 1713, 1640, 1497, 1453, 1097, 910, 733, 696 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.49 (d, *J* = 7.7 Hz, 2 H), 7.31 (d, *J* = 7.9 Hz, 2 H), 7.22-7.18 (m, 4 H), 7.14-7.09 (m, 2 H), 5.72 (ddd, *J* = 8.1, 10.3, 17.3 Hz, 1 H), 5.63-5.57 (m, 1 H), 5.13 (d, *J* = 11.9 Hz, 1 H), 5.06-4.98 (m, 4 H), 4.76 (d, *J* = 11.9 Hz, 1 H), 4.35 (d, *J* = 12.2 Hz, 1 H), 4.29 (d, *J* = 12.2 Hz, 1 H), 3.40 (dd, *J* = 2.7, 11.9 Hz, 1 H), 3.34 (dd, *J* = 3.7, 9.1 Hz, 1 H), 3.30 (dd, *J* = 5.6, 9.1 Hz, 1 H), 2.30 (dd, *J* = 2.5, 14.9 Hz, 1 H), 2.20 (m, 1 H), 2.16 (dt, *J* = 4.3, 13.2 Hz, 1 H), 1.90-1.84 (m, 4 H), 1.80-1.68 (m, 5 H), 1.37-1.29 (m, 3 H), 1.06 (d, *J* = 6.7 Hz, 3 H), 1.06-1.00 (m, 1 H), 0.97 (d, *J* = 6.6 Hz, 3 H), 0.97-0.91 (m, 1 H), 0.85 (d, *J* = 7.1 Hz, 3 H), 0.56 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 210.3, 145.0, 141.0, 139.9, 137.6, 129.0, 128.9, 128.7, 128.3, 127.9, 127.7, 116.5, 113.7, 84.8, 83.2, 79.7, 74.0, 73.6, 66.4, 47.9, 41.5, 40.1, 38.6, 38.1, 36.6, 34.9, 33.8, 32.9, 30.6, 30.0, 28.5, 22.6, 20.8, 15.1, 11.0; high resolution mass spectra (ES+) m/z 595.3786 [(M+Na)$^+$; calcd for $C_{38}H_{52}O_4Na^+$: 595.3763].



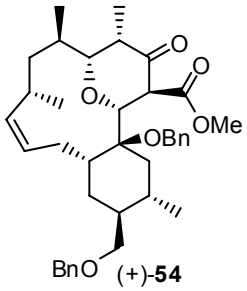
(+)-**52**

Macrocycle (+)-52: To a solution of diene (+)-**5** (168 mg, 0.29 mmol) in benzene (3860 mL) was added the Hoveyda-Grubbs 2nd gen. catalyst (55 mg, 0.088 mmol). The solution was heated at reflux for 6 h then concentrated *in vacuo* to leave a green residue which was purified by column chromatography on silica gel (elution with 9:1 hexane:ethyl acetate) to afford macrocycle (+)-**52** (299 mg, 89%) as a colorless foam: $[\alpha]_D^{20}$ = +14.3 (*c* = 0.46, C_6H_6); IR (neat) 2953, 2919, 2863, 1712, 1453, 1377, 1088, 1064, 734, 696 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ

7.37 (d, *J* = 7.8 Hz, 2 H), 7.33 (d, *J* = 7.5 Hz, 2 H), 7.20 (app dt, *J* = 3.0, 7.4 Hz, 4 H), 7.14-7.10 (m, 2 H), 5.17 (app dt, *J* = 2.5, 10.7 Hz, 1 H), 4.97 (app dt, *J* = 2.4, 10.7 Hz, 1 H), 4.37 (d, *J* = 12.1 Hz, 1 H), 4.34 (d, *J* = 11.2 Hz, 1 H), 4.33 (d, *J* = 12.1 Hz, 1 H), 3.82 (d, *J* = 11.2 Hz, 1 H), 3.63 (dd, *J* = 3.7, 11.4 Hz, 1 H), 3.45 (dd, *J* = 3.7, 9.0 Hz, 1 H), 3.23 (dd, *J* = 6.8, 8.9 Hz, 1 H), 2.92 (ddd, *J* = 10.6, 10.6, 14.7 Hz, 1 H), 2.87 (dd, *J* = 1.7, 8.5 Hz, 1 H), 2.68-2.62 (m, 1 H), 2.36 (app q, *J* = 6.8 Hz, 1 H), 2.22 (ddd, *J* = 0.7, 3.6, 14.9 Hz, 1 H), 2.05-1.96 (m, 2 H), 1.88 (dd, *J* = 12.4, 13.9 Hz, 1 H), 1.83-1.78 (m, 2 H), 1.65-1.59 (m, 3 H), 1.47-1.40 (m, 2 H), 1.34 (dd, *J* = 4.0, 14.0 Hz, 1 H), 0.97 (d, *J* = 6.5 Hz, 3 H), 0.97-0.93 (m, 1 H), 0.95 (d, *J* = 7.0 Hz, 3 H), 0.88 (d, *J* = 6.8 Hz, 3 H), 0.47 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 210.5, 139.3, 138.8, 136.2, 128.3, 128.2, 128.0, 127.6, 127.33, 127.26, 127.16, 82.6, 79.4, 78.4, 73.7, 73.0, 62.5, 48.3, 47.7, 39.3, 38.9, 38.5, 35.4, 35.0, 34.9, 31.3, 30.5, 29.1, 24.4, 20.0, 18.2, 10.3; high resolution mass spectra (ES+) m/z 567.3464 [(M+Na)$^+$; calcd for $C_{36}H_{48}O_4Na^+$: 567.3450].



(+)-**53**



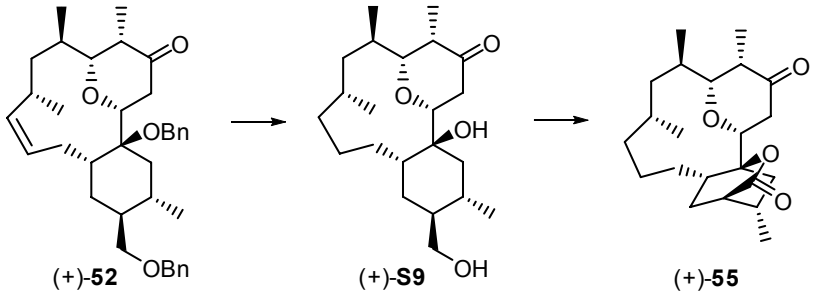
(+)-**54**

Vinyl Carbonate (+)-53 and β-Ketoester (+)-54: To a cold (-78 °C), stirred mixture of macrocycle (+)-**52** (18 mg, 32.8 μmol) and HMPA (vaccum distilled from CaH_2 prior to use, 6 μL) in THF (0.33 mL) was added LHMDS (36 μL of 1.0 M solution in THF, 36 μmol) dropwise via syringe. After being stirred for 30 min at -78 °C, Mander's reagent (purified by vaccum distillation from CaH_2 prior to use, 5 μL, 39.4 μmol) was added and the mixture was stirred at -78 °C for additional 30 min. The reaction was quenched with a saturated aqueous solution of NH_4Cl (1 mL). The solution was allowed to warm to room temperature then extracted with Et_2O (20 mL), washed with a saturated aqueous solution of NH_4Cl (2 x 10 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by preparative TLC (elution with 3:1 hexane:ethyl acetate) to afford vinyl carbonate (+)-**53** (10 mg, 43%) and β-Ketoester (+)-**54** (8 mg, 37%).

Spectral data for vinyl carbonate (+)-53: $[\alpha]_D^{20}$ = +30.3 (*c* = 0.3, $CHCl_3$); IR (neat) 2919, 2850, 1759, 1449, 1255, 1102, 734 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.41 (d, *J* = 7.4 Hz, 2 H), 7.32 (d, *J* = 7.2 Hz, 2 H), 7.20-7.06 (m, 6 H), 5.94 (d, *J* = 1.6 Hz, 1 H), 5.26 (app dt, *J* = 2.7, 10.6 Hz, 1 H), 5.14 (app dt, *J* = 2.3, 10.6 Hz, 1 H), 4.48 (d, *J* = 11.5 Hz, 1 H), 4.45 (dd, *J* = 1.6, 1.6 Hz, 1 H), 4.34 (d, *J* = 12.2 Hz, 1 H), 4.30 (d, *J* = 12.2 Hz, 1 H), 4.12 (d, *J* = 11.5 Hz, 1 H), 3.44 (dd, *J* = 3.7, 9.0 Hz, 1 H), 3.24 (s, 3 H), 3.21-3.17 (m, 2 H), 3.01 (ddd, *J* = 14.8, 10.3, 10.3 Hz, 1 H), 2.74-2.68 (m, 1 H), 2.32 (dq, *J* = 2.2, 6.7 Hz, 1 H), 2.16 (m, 1 H), 1.98-1.78 (m, 4 H), 1.68 (app dt, *J* = 13.1, 2.8 Hz, 1 H), 1.60-1.52 (m, 1 H), 1.46-1.29 (m, 3 H), 1.21-1.16 (m, 1 H), 1.15 (d, *J* = 6.7 Hz, 3 H), 1.01 (d, *J* = 7.0 Hz, 3 H), 0.92 (d, *J* = 6.5 Hz, 3 H), 0.60 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 154.8, 153.2, 140.1, 139.8, 137.3, 128.94, 128.87, 128.7, 128.0, 127.8, 127.7, 127.6, 113.2, 84.1, 80.7, 77.4, 74.4, 73.6, 62.7, 54.7, 48.6, 39.9, 39.8, 36.8, 36.3, 35.8, 34.7, 32.7, 30.9, 29.8, 25.4, 20.5, 19.2, 12.6; high resolution mass spectra (ES+) m/z 625.3527 [(M+Na)$^+$; calcd for $C_{38}H_{50}O_6Na^+$: 625.3505].

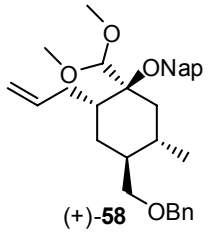
Spectral data for β-Ketoester (+)-54: $[\alpha]_D^{20}$ = +26.0 (*c* = 0.1, $CHCl_3$); IR (neat) 2921, 2854, 1742, 1712, 1451, 1262, 1079, 733, 695 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.48 (d, *J* = 7.4 Hz, 2

H), 7.29 (d, *J* = 7.4 Hz, 2 H), 7.20-7.05 (m, 6 H), 5.33 (app dt, *J* = 2.2, 10.5 Hz, 1 H), 5.01 (app dt, *J* = 2.1, 10.5 Hz, 1 H), 4.65 (d, *J* = 7.9 Hz, 1 H), 4.60 (d, *J* = 11.7 Hz, 1 H), 4.45 (d, *J* = 11.7 Hz, 1 H), 4.32 (d, *J* = 12.2 Hz, 1 H), 4.29 (d, *J* = 12.2 Hz, 1 H), 4.09 (d, *J* = 7.9 Hz, 1 H), 3.40 (dd, *J* = 3.7, 9.0 Hz, 1 H), 3.17 (dd, *J* = 6.6, 9.0 Hz, 1 H), 3.01 (s, 3 H), 2.99 (ddd, *J* = 14.9, 10.3, 10.3 Hz, 1 H), 2.60-2.53 (m, 1 H), 2.39 (dq, *J* = 1.7, 7.0 Hz, 1 H), 2.23 (br d, *J* = 8.5 Hz, 1 H), 2.03-1.97 (m, 1 H), 1.92 (dd, *J* = 12.5, 13.2 Hz, 1 H), 1.78-1.61 (m, 4 H), 1.44-1.26 (m, 3 H), 1.21 (d, *J* = 14.4 Hz, 1 H), 1.01-0.91 (m, 1 H), 0.95 (d, *J* = 6.4 Hz, 3 H), 0.94 (d, *J* = 6.9 Hz, 3 H), 0.94 (d, *J* = 6.9 Hz, 3 H), 0.40 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.1, 170.3, 140.1, 139.9, 136.4, 128.9, 128.7, 128.3, 127.95, 127.91, 127.3, 126.9, 82.6, 80.9, 80.8, 74.2, 73.7, 63.5, 54.4, 51.5, 48.0, 47.5, 40.1, 39.7, 36.70, 36.68, 36.0, 32.6, 31.2, 30.3, 24.8, 20.6, 19.1, 10.3; high resolution mass spectra (ES+) m/z 625.3487 [$(M+Na)^+$; calcd for $C_{38}H_{50}O_6Na^+$: 625.3505].



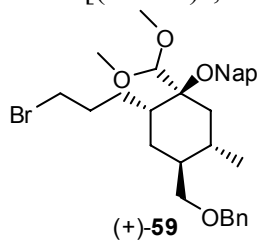
Bicyclic lactone (+)-55: A mixture of macrocycle (+)-**52** (35 mg, 0.064 mmol) and 20% $Pd(OH)_2$/C (10 mg) in EtOAc (1 mL) was stirred under an atmosphere of H_2 for 18 h at room temperature. The solution was then filtered through cotton and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 1:2 hexane:ethyl acetate) to addord diol (+)-**S9** (23 mg, quant) as a colorless oil: $[\alpha]_D^{20}$ = +67.0 (*c* = 0.97, $CHCl_3$); IR (neat) 3416, 2931, 1705, 1455, 1068, 755 cm^{-1}, ^{1}H NMR (500 MHz, C_6D_6) δ 3.58-3.52 (m, 3 H), 2.89 (dd, *J* = 9.5 Hz, 1 H), 2.69 (app d, *J* = 7.4 Hz, 2 H), 2.41 (dq, *J* = 1.8, 7.2 Hz, 1 H), 2.40-2.30 (br m, 2 H), 2.13 (ddd, *J* = 4.0, 13.0, 13.0 Hz, 1 H), 2.06 (ddd, *J* = 4.7, 12.4, 12.4 Hz, 1 H), 1.87-1.79 (m, 1 H), 1.64 (dd, *J* = 13.9, 12.6 Hz, 1 H), 1.58-1.49 (m, 5 H), 1.38-1.29 (m, 3 H), 1.21-1.08 (m, 4 H), 0.98-0.88 (m, 10 H), 0.57 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 213.6, 89.5, 85.2, 76.0, 66.0, 48.4, 47.0, 46.7, 41.6, 39.5, 38.8, 35.8, 35.2, 34.3, 31.8, 31.3, 28.5, 27.8, 24.7, 20.6, 20.0, 10.5; high resolution mass spectra (ES+) m/z 389.2663 [$(M+Na)^+$; calcd for $C_{22}H_{38}O_4Na^+$: 389.2668].

To a solution of diol (+)-**S9** (5 mg, 13.7 μmol) in CH_2Cl_2 (0.25 mL) was added PCC (9 mg, 41.0 μmol) at room temperature. After being stirred at room temperature for 1 h, the mixture was poured directly onto silica gel and purified by chromatography (elution with 4:1 hexane:ethyl acetate) to afford bicyclic lactone (+)-**55** (4 mg, 80%) as a crystalline solid: mp = 147-149 °C; $[\alpha]_D^{20}$ = +53.0 (*c* = 0.27, $CHCl_3$); IR (neat) 2950, 1764, 1713, 1456, 1265, 1080, 990, 949 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 3.41 (dd, *J* = 4.7, 10.2 Hz, 1 H), 2.56 (dd, *J* = 2.1, 9.6 Hz, 1 H), 2.54 (ddd, *J* = 16.5, 5.7, 1.0 Hz, 1 H), 2.27 (dd, *J* = 16.5, 10.2 Hz, 1 H), 2.24-2.21 (m, 1 H), 2.02-1.98 (m, 1 H), 1.69-1.45 (m, 5 H), 1.39-1.26 (m, 2 H), 1.22-1.17 (m, 1 H), 1.16 (dd, *J* = 6.7, 14.4 Hz, 1 H), 1.05-0.90 (m, 3 H), 0.88-0.72 (m, 4 H), 0.77 (d, *J* = 6.9 Hz, 3 H), 0.76 (d, *J* = 7.2 Hz, 3 H), 0.52 (d, *J* = 7.0 Hz, 3 H), 0.38 (d, *J* = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 213.6, 177.1, 85.9, 84.2, 76.9, 57.1, 42.9, 42.0, 38.9, 37.0, 33.6, 32.9, 29.1, 26.6, 25.4, 23.2, 22.4, 21.2, 20.0, 18.2, 13.1, 11.5, 3.2; high resolution mass spectra (ES+) m/z 362.2447 [$(M+Na)^+$; calcd for $C_{22}H_{34}O_4Na^+$: 362.2457].



(+)-**58**

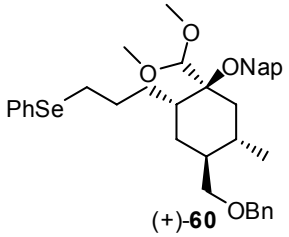
Napthyl Ether (+)-58: To a cold (0 °C) solution of alcohol (+)-**34** (5.44 g, 15.6 mmol) in DMF (55 mL) was added NaH (0.56 g of 95% in oil, 23.4 mmol) in portions. After being stirred at 0 °C for 45 min, 2-bromomethyl naphthalene (6.90 g, 31.2 mmol) and *n*-tetrabutylammonium iodide (5.77 g, 15.6 mmol) were added successively. The mixture was then warmed to room temperature and stirred for 36 h before being quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL) and H_2O (150 mL). The mixture was extracted with Et_2O (3 x 150 mL). The combined organic layers were then washed with brine (100 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a yellow oil which was purified by column chromatography on silica gel (elution with 20:1 hexane:ethyl acetate) to afford napthyl ether (+)-**58** (7.32 g, 96%) as a pale yellow oil: $[\alpha]_D^{20}$ = +14.0 (*c* = 0.3, $CHCl_3$); IR (neat) 3059, 2925, 2866, 1638, 1602, 1509, 1496, 1452, 1361, 1194, 1080, 909, 853, 814 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.91 (s, 1 H), 7.88-7.82 (m, 2 H), 7.78 (d, *J* = 8.5 Hz, 1 H), 7.59 (d, *J* = 8.4 Hz, 1 H), 7.51- 7.47 (m, 2 H), 7.41-7.31 (m, 5 H), 5.90 (m, 1 H), 5.16 (d, *J* = 17.3 Hz, 1 H), 5.11 (d, *J* = 10.2 Hz, 1 H), 4.92 (ABq, *J* = 12.1 Hz, $\Delta\upsilon_{AB}$ = 12.3 Hz, 2 H), 4.56 (ABq, *J* = 12.1 Hz, $\Delta\upsilon_{AB}$ = 34.7 Hz, 2 H), 4.31 (s, 1 H), 3.63 (s, 3 H), 3.60 (s, 3 H), 3.58 (dd, *J* = 3.7, 9.2 Hz, 1 H), 3.47 (dd, *J* = 6.2, 9.2 Hz, 1 H), 2.46 -2.39 (m, 2 H), 2.21-2.14 (m, 1 H), 1.96-1.80 (m, 4 H), 1.57-1.50 (m, 1 H), 1.40 (dd, *J* = 13.9, 13.9 Hz, 1 H), 1.04 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 138.3, 137.9, 133.6, 132.9, 128.4, 128.0, 127.9, 127.7, 127.5, 127.4, 125.9, 125.6, 125.5, 115.5, 110.3, 80.7, 74.0, 73.1, 64.9, 58.5, 57.4, 37.8, 36.4, 36.2, 33.1, 29.1, 27.8, 20.3; high resolution mass spectra (ES+) m/z 511.2812 [$(M+Na)^+$; calcd for $C_{32}H_{40}O_4Na^+$: 511.2824].



(+)-**59**

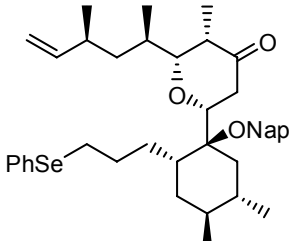
Bromide (+)-59: To a suspension of $Cp_2Zr(H)Cl$ (4.86 g, 18.8 mmol) in CH_2Cl_2 (25 mL) was added a solution of the alkene (+)-**58** (2.30 g, 4.71 mmol) in CH_2Cl_2 (25 mL). The cold bath was removed and the mixture was stirred at room temperature for 30 min. *N*-bromosuccinimide (4.51 g, 23.55 mmol) was added in one portion to the mixture and stirred for additional 10 min at room temperature. The reaction was diluted with Et_2O (800 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (3 x 100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 15:1 hexane:ethyl acetate) to afford bromide (+)-**59** (2.62 g, 98%) as a colorless gum: $[\alpha]_D^{20}$ = +37.1 (*c* = 0.65, $CHCl_3$); IR (neat) 2928, 1458, 1364, 1074, 814, 738 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 7.93 (s, 1 H), 7.70-7.62 (m, 4 H), 7.31 (app d, *J* = 7.6 Hz, 2 H), 7.27-7.24 (m, 2 H), 7.17-7.14 (m, 2 H), 7.09 (app t, *J* = 7.3 Hz, 1 H), 4.94 (d, *J* = 12.0 Hz, 1 H), 4.90 (d, *J* = 12.0 Hz, 1 H), 4.36 (d, *J* = 12.2 Hz, 1 H), 4.32 (d, *J* = 12.2 Hz, 1 H), 4.11 (s, 1 H), 3.39 (dd, *J* = 3.6, 9.0 Hz, 1 H), 3.28 (dd, *J* = 6.4, 9.0 Hz, 1 H), 3.27 (s, 3 H), 3.26 (s, 3 H), 2.31

(br d, J = 9.4 Hz, 1 H), 2.02 (ddd, J = 4.3, 13.3, 13.3 Hz, 1 H), 2.01-1.95 (m, 1 H), 1.91 (dd, J = 3.4, 14.1 Hz, 1 H), 1.87-1.80 (m, 1 H), 1.75-1.64 (m, 4 H), 1.44-1.35 (m, 3 H), 1.32 (dd, J = 12.8, 13.8 Hz, 1 H), 0.95 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (500 MHz, C_6D_6) δ 139.9, 138.9, 134.5, 133.7, 128.9, 128.7, 128.5, 128.0, 127.9, 126.49, 126.47, 126.2, 126.0, 81.4, 74.3, 73.7, 65.4, 58.0, 57.1, 39.0, 37.2, 36.7, 34.8, 32.3, 32.2, 29.6, 28.7, 27.0, 23.4, 20.7; high resolution mass spectra (ES+) m/z 591.2076 [$(M+Na)^+$; calcd for $C_{32}H_{41}BrO_4Na^+$: 591.2086].



(+)-**60**

Selenide (+)-60: To a stirred suspension of bromide (+)-**59** (0.31 g, 0.55 mmol) and Cs_2CO_3 (0.27 g, 0.82 mmol) was added benzene selenol (0.12 g, 0.76 mmol) dropwise via syringe at room temperature. After being stirred at room temperature for 1 h, the reaction was quenched with a saturated aqueous solution of NH_4Cl (20 mL) and H_2O (20 mL). The mixture was then extracted with Et_2O (3 x 70 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 15:1 hexane:ethyl acetate) to afford selenide (+)-**60** (0.33 g, 93%) as a colorless gum: $[\alpha]_D^{20}$ = +18.0 (c = 0.15, $CHCl_3$); IR (neat) 3055, 2930, 2866, 1453, 1362, 1197, 1076, 737, 695 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83-7.72 (m, 4 H), 7.69 (d, J = 8.6 Hz, 1 H), 7.53-7.46 (m, 3 H), 7.44-7.39 (m, 2 H), 7.34-7.20 (m, 7 H), 4.82 (d, J = 12.3 Hz, 1 H), 4.78 (d, J = 12.3 Hz, 1 H), 4.51 (d, J = 12.3 Hz, 1 H), 4.46 (d, J = 11.9 Hz, 1 H), 4.22 (s, 1 H), 3.56 (s, 3 H), 3.52-3.47 (m, 4 H), 3.33 (dd, J = 6.5, 9.1 Hz, 1 H), 3.07-2.90 (m, 2 H), 2.18 (bd, J = 10.1 Hz, 1 H), 1.90-1.82 (m, 2 H), 1.81-1.73 (m, 2 H), 1.72-1.62 (m, 2 H), 1.61-1.54 (m,1 H), 1.49-1.35 (m, 2 H), 1.29-1.22 (m, 1 H), 0.93 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 137.8, 133.4, 132.6, 132.5 (2 C), 130.6, 128.9 (2 C), 128.2 (2 C), 127.8, 127.7, 127.6, 127.4 (2 C), 127.3, 126.6, 125.6 (2 C), 125.4, 125.2, 80.7, 73.9, 73.1, 64.7, 58.5, 57.2, 38.0, 36.1, 36.0, 29.0, 28.4, 28.2, 27.8, 27.7, 27.5, 20.1; high resolution mass spectra (ES+) m/z 669.2483 [$(M+Na)^+$; calcd for $C_{38}H_{46}O_4SeNa^+$: 669.2561].

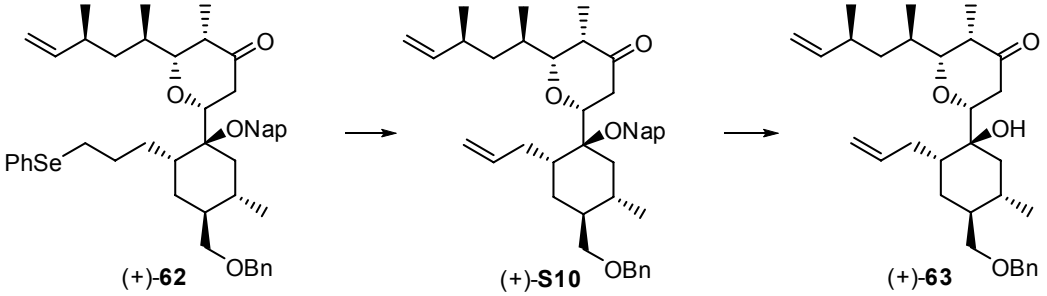


(+)-**62**

Tetrahydropyranone (+)-62: To a cold (0 °C) solution of acid (+)-**7** (0.14 g, 0.70 mmol) and acetal (+)-**60** (0.35 g, 0.54 mmol) in CH_2Cl_2 (4 mL) was added *i*-PrOTMS (0.29 g, 0.38 mL, 2.17 mmol) and TMSOTf (60 mg, 0.05 mL, 0.27 mmol). After being stirred for 30 min at 0 °C, the reaction was quenched with Et_3N (0.5 mL) and stirred for additional 5 min at 0 °C. The mixture was extracted with Et_2O (250 mL), washed with a saturated aqueous solution of $NaHCO_3$ (3 x 50 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to afford the intermediate dioxanone as a yellow gum which was used in the next step without further purification.

The dioxanone from the previous step was treated with a solution Cp_2TiMe_2 (3.30 mL of 0.5 M solution in THF, 1.62 mmol) and heated at 60 °C for 24 h in the dark. After cooling to room temperature, the mixture was diluted with hexane (200 mL), stirred for 1 h, and the resulting slurry was filtered through celite to remove the titanium salts. The filtrate was concentrated in *vacuo* to leave a yellow residue which was purified by flash chromatography on silylated silica gel (eluant 20:1 hexane:ethyl acetate) to afford unstable enol acetal (0.27 g) as a colorless gum.

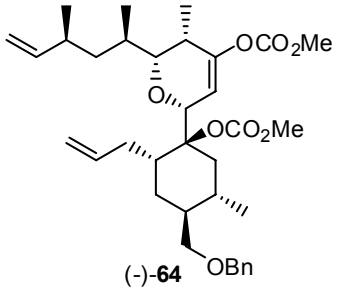
To a solution of the above enol acetal (0.27 g, 0.35 mmol) in CH_2Cl_2 (14 mL) was added Me_2AlCl (0.86 mL of 1.0 M solution in hexanes, 0.86 mmol) at room temperature. After being stirred at room temperature for 5 min, the mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL) and diluted with H_2O (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 10:1 hexane:ethyl acetate) to afford (+)-**62** (0.19 g, 42% over three steps) as a colorless gum: $[\alpha]_D^{20}$ = +42.6 (*c* = 1.0, $CHCl_3$); IR (neat) 2930, 1711, 1454, 1088, 736, 692 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.97 (s, 1 H), 7.72-7.61 (m, 4 H), 7.54-7.53 (m, 2 H), 7.31-7.25 (m, 4 H), 7.18-7.08 (m, 3 H), 7.06-7.02 (m, 2 H), 6.99-6.96 (m, 1 H), 5.83-5.74 (m, 1 H), 5.31 (d, *J* = 12.1 Hz, 1 H), 5.09-5.02 (m, 2 H), 4.93 (d, *J* = 12.1 Hz, 1 H), 4.34 (ABq, *J* = 12.2 Hz, Δυ = 19.2 Hz, 2 H), 3.50 (dd, *J* = 2.6, 11.9 Hz, 1 H), 3.33 (dd, *J* = 3.5, 9.0 Hz, 1 H), 3.26 (dd, *J* = 6.1, 9.0 Hz, 1 H), 2.97 (dd, *J* = 11.9, 14.9 Hz, 1 H), 2.78 (dd, *J* = 2.3, 9.8 Hz, 1 H), 2.68-2.59 (m, 3 H), 2.46 (dq, *J* = 1.9, 7.2 Hz, 1 H), 2.39 (dd, *J* = 1.9, 14.9 Hz, 1 H), 2.28-2.18 (m, 2 H), 1.92 (ddd, *J* = 2.3, 10.6, 13.1 Hz, 1 H), 1.79-1.65 (m, 5 H), 1.47-1.39 (m, 1 H), 1.36-1.27 (m, 2 H), 1.25-1.20 (m, 1 H), 1.13 (dd, *J* = 12.8, 15.1 Hz, 1 H), 1.08 (d, *J* = 6.7 Hz, 3 H), 0.98 (d, *J* = 6.5 Hz, 3 H), 0.98-0.94 (m, 1 H), 0.86 (d, *J* = 7.2 Hz, 3 H), 0.58 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 210.4, 145.1, 139.9, 138.6, 134.5, 133.6, 131.3, 129.7, 128.9, 128.74, 128.68, 128.5, 128.3, 128.0, 127.3, 126.6, 126.20, 126.16, 126.0, 113.7, 84.8, 83.4, 80.2, 74.0, 73.7, 66.6, 47.9, 41.6, 39.9, 38.8, 38.2, 36.6, 35.0, 33.0, 30.3, 28.4, 28.18, 28.16, 28.0, 22.7, 20.8, 15.2, 11.0; high resolution mass spectra (ES+) m/z 803.3576 [$(M+Na)^+$; calcd for $C_{48}H_{60}O_4SeNa^+$: 803.3555].



Alcohol (+)-63: To a solution of selenide (+)-**63** (444 mg, 0.569 mmol) in $CHCl_3$ (2 mL) and pyridine (0.225 mL, 2.845 mmol) was added Davis's oxaziridine (149 mg, 0.569 mmol). The reaction mixture was stirred at room temperature for 15 min then heated at 60 °C for 2 h. The mixture was cooled to room temperature and concentrated under vacuum to leave a yellow residue which was purified by column chromatography on silica gel (elution with 9:1 hexane:ethyl acetate) to afford diene (+)-**S10** (333 mg, 94%) as a colorless oil: $[\alpha]_D^{20}$ = +35.6 (*c* = 0.25, $CHCl_3$); IR (neat) 2927, 2868, 1712, 1458, 1375, 1261, 1096, 812, 737, 696 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.95 (s, 1 H), 7.71-7.60 (m, 4 H), 7.29-7.24 (m, 4 H), 7.16-7.12 (m, 2 H), 7.09-7.07 (m, 1 H), 5.76 (ddd, *J* = 8.0, 10.2, 17.3 Hz, 1 H), 5.61 (dddd, *J* = 7.5, 10.1, 14.1,

17.4 Hz, 1 H), 5.28 (d, *J* = 12.1 Hz, 1 H), 5.06 (d, *J* = 17.3 Hz, 1 H), 5.04-5.00 (m, 3 H), 4.91 (ABq, *J* = 12.2 Hz, Δυ = 25.9 Hz, 2 H), 3.44 (dd, *J* = 2.6, 11.8 Hz, 1 H), 3.34-3.30 (m, 2 H), 2.95 (dd, *J* = 11.9, 14.9 Hz, 1 H), 2.79 (dd, *J* = 2.3, 9.8 Hz, 1 H), 2.62 (dd, *J* = 2.8, 15.1 Hz, 1 H), 2.45 (dq, *J* = 2.3, 7.1 Hz, 1 H), 2.33 (dd, *J* = 1.9, 14.9 Hz, 1 H), 2.25-2.19 (m, 2 H), 1.94-1.88 (m, 3 H), 1.82-1.74 (m, 4 H), 1.38-1.32 (m, 1 H), 1.08 (d, *J* = 6.7 Hz, 3 H), 0.98 (d, *J* = 6.4 Hz, 3 H), 0.96 (ddd, *J* = 4.2, 9.4, 13.5 Hz, 1 H), 0.58 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 210.3, 145.1, 139.9, 138.6, 137.6, 134.5, 133.7, 128.9, 128.8, 128.7, 128.4, 127.91, 127.88, 126.6, 126.2, 126.1, 126.0, 116.6, 113.7, 84.9, 83.3, 79.9, 74.0, 73.6, 66.5, 47.9, 41.6, 40.2, 38.6, 38.2, 36.6, 35.0, 33.8, 33.0, 30.1, 28.6, 22.7, 20.8, 15.2, 11.0; high resolution mass spectra (ES+) m/z 645.3908 [$(M+Na)^+$; calcd for $C_{42}H_{54}O_4Na^+$: 645.3920].

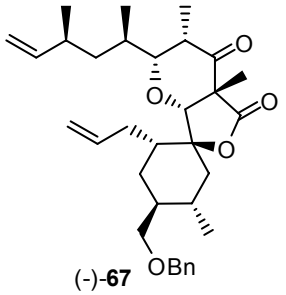
To a solution of napthyl ether (+)-**S10** (100 mg, 0.161 mmol) in CH_2Cl_2 (1.6 mL) and MeOH (0.19 mL) was added DDQ (73 mg, 0.321 mmol) in one portion at room temperature. After being stirred at room temperature for 1 h, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL) and H_2O (10 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 9:1 hexane:ethyl acetate) to afford alcohol (+)-**63** (65 mg, 84%) as a colorless oil: $[\alpha]_D^{20}$ = +9.6 (*c* = 0.125, $CHCl_3$); IR (neat) 3360, 2923, 2852, 1711, 1659, 1632, 1454, 1262, 1097, 912 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.33 (app d, *J* = 7.8 Hz, 2 H), 7.23-7.09 (m, 3 H), 5.68-5.52 (m, 2 H), 5.02-4.93 (m, 4 H), 4.34 (ABq, *J* = 12.2 Hz, Δυ = 26.7 Hz, 2 H), 3.41 (dd, *J* =3.8, 9.0 Hz, 1 H), 3.29 (dd, *J* = 6.3, 9.0 Hz, 1 H), 3.16 (dd, *J* = 2.6, 11.4 Hz, 1 H), 2.88-2.80 (m, 2 H), 2.46 (dq, *J* = 2.3, 7.2 Hz, 1 H), 2.24 (dd, *J* = 2.3, 14.8 Hz, 1 H), 2.18-2.14 (m, 1 H), 2.05 (ddd, *J* = 4.0, 13.3, 13.3 Hz, 1 H), 1.95 (dd, *J* = 3.9, 14.1 Hz, 1 H), 1.90-1.83 (m, 3 H), 1.78-1.70 (m, 3 H), 1.68-1.60 (m, 3 H), 1.01 (d, *J* = 6.7 Hz, 3 H), 0.97 (d, *J* = 6.5 Hz, 3 H), 0.90 (ddd, *J* = 5.7, 9.4, 13.6 Hz, 1 H), 0.84 (d, *J* = 7.2 Hz, 3 H), 0.54 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 210.2, 144.8, 140.0, 137.3, 128.9, 127.94, 127.89, 116.6, 113.7, 83.9, 81.3, 75.0, 74.2, 73.6, 47.8, 41.5, 40.8, 38.9, 38.8, 37.3, 36.5, 32.7, 30.0, 27.8, 22.6, 20.7, 14.9, 10.5; high resolution mass spectra (ES+) m/z 505.3290 [$(M+Na)^+$; calcd for $C_{31}H_{46}O_4Na^+$: 505.3294].



(-)-**64**

***Bis*-Carbonate** (-)-**64**: To a cold (-78 °C), stirred solution of alcohol (+)-**63** (61 mg, 0.13 mmol) in THF (1.2 mL) was added KHMDS (0.76 mL of 0.5 M solution in toluene, 0.38 mmol). The resulting yellow solution was stirred at -78 °C for 20 min before being treated with methyl chloroformate (0.12 g, 0.10 mL, 1.26 mmol). Stirring was continued at -78 °C for additional 30 min and subsequently at 0 °C for 15 min. The reaction was quenched with H_2O (20 mL) and the aqueous layer was extracted with ether (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 10:1 hexane:ethyl acetate with 1% Et_3N) to afford (-)-**64** (78 mg, 99%) as a colorless gum: $[\alpha]_D^{20}$ = -18.9 (*c* = 1.4, $CHCl_3$); IR (neat) 2956,

1762, 1740, 1439, 1253, 1115, 735, 698 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.28 (app d, *J* = 7.4 Hz, 2 H), 7.22-7.16 (m, 2 H), 7.09 (app t, *J* = 7.4 Hz, 1 H), 5.86 (d, *J* = 1.4 Hz, 1 H), 5.74-5.67 (m, 1 H), 5.66 (ddd, *J* = 8.5, 10.2, 17.3 Hz, 1 H), 5.25 (dd, *J* = 1.7, 1.7 Hz, 1 H), 5.11 (d, *J* = 17.0 Hz, 1 H), 5.01-4.97 (m, 2 H), 4.92 (dd, *J* = 2.0, 10.2 Hz, 1 H), 4.30 (d, *J* = 12.3 Hz, 1 H), 4.24 (d, *J* = 12.3 Hz, 1 H), 3.34-3.29 (m, 1 H), 3.32 (s, 3 H), 3.31 (s, 3 H), 3.18 (dd, *J* = 6.3, 9.1 Hz, 1 H), 3.13 (dd, *J* = 2.4, 10.1 Hz, 1 H), 2.99 (br d, *J* = 11.4 Hz, 1 H), 2.82 (br d, *J* = 14.2 Hz, 1 H) 2.40-2.37 (m, 1 H), 2.26 (dd, *J* = 2.5, 14.4 Hz, 1 H), 2.22-2.18 (m, 1 H), 2.10 (ddd, *J* = 3.3, 10.3, 10.3 Hz, 1 H), 1.98 (ddd, *J* = 3.1, 3.1, 13.8 Hz, 1 H), 1.94-1.84 (m, 3 H), 1.72-1.67 (m, 1 H), 1.56 (dd, *J* = 12.8, 14.1 Hz, 1 H), 1.48-1.40 (m, 1 H), 1.08 (d, *J* = 6.8 Hz, 3 H), 1.03 (d, *J* = 6.6 Hz, 3 H), 0.84 (d, *J* = 6.5 Hz, 3 H), 0.86-0.80 (m, 1 H), 0.61 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 154.8, 154.6, 153.6, 145.0 (2 C), 140.0, 138.0 (2 C), 128.8, 127.84, 127.80, 116.4, 113.6, 113.0, 89.3, 82.8, 77.8, 73.7, 73.6, 54.9, 54.2, 41.0, 38.8, 38.3, 36.4, 35.6, 34.4, 34.0, 32.3, 29.7, 28.7, 22.8, 20.3, 15.0, 11.9; high resolution mass spectra (ES+) m/z 621.3423 [$(M+Na)^+$; calcd for $C_{35}H_{50}O_8Na^+$: 621.3403].

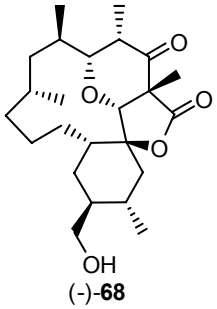


(-)-**67**

Diene (-)-67: To a cold (0 °C) solution of *bis*-carbonate (-)-**64** (98 mg, 0.17 mmol) in THF (15 mL) was added anhydrous NaOMe (36 mg, 0.66 mmol). After being stirred at 0 °C for 1 h, the mixture was quenched with a saturated aqueous solution of NH_4Cl (15 mL) and diluted with H_2O (10 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to leave a residue containing ß-ketolactone (-)-**66** as a colorless gum: $[\alpha]_D^{20}$ = -18.5 (*c* = 0.3, $CHCl_3$); IR (neat) 2928, 1779, 1714, 1556, 1455, 1196, 995 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.30 (d, *J* = 7.5 Hz, 2 H), 7.20 (dd, *J* = 7.4, 7.5 Hz, 2 H), 7.11 (app t, *J* = 7.4 Hz, 1 H), 5.65 (ddd, *J* = 7.9, 10.3, 17.3 Hz, 1 H), 5.42 (m, 1 H), 5.04-4.96 (m, 3 H), 4.90 (dd, *J* = 1.4, 17.0 Hz, 1 H), 4.35 (d, *J* = 12.3 Hz, 1 H), 4.28 (d, *J* = 12.3 Hz, 1 H), 3.74 (d, *J* = 4.5 Hz, 1 H), 3.34 (dd, *J* = 3.9, 9.0 Hz, 1 H), 3.21 (d, *J* = 4.5 Hz, 1 H), 3.09 (dd, *J* = 7.0, 9.0 Hz, 1 H), 2.56 (dd, *J* = 2.2, 9.8 Hz, 1 H), 2.39 (dq, *J* = 2.2, 7.3 Hz, 1 H), 2.24 (ddd, *J* = 1.5, 4.0, 14.6 Hz, 1 H), 2.18-2.12 (m, 1 H), 1.80-1.58 (m, 7 H), 1.34-1.27 (m, 2 H), 1.19 (dd, *J* = 12.5, 14.6 Hz, 1 H), 1.17-1.14 (m, 1 H), 1.00 (d, *J* = 7.3 Hz, 3 H), 0.99 (d, *J* = 6.6 Hz, 3 H), 0.82 (d, *J* = 6.4 Hz, 3 H), 0.45 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 201.5, 168.9, 144.6 (2 C), 139.8, 136.7 (2 C), 128.9, 128.7, 128.0, 117.1, 113.7, 90.3, 82.5, 79.0, 73.7, 73.5, 54.2, 47.1, 41.3, 39.4, 38.2, 36.3, 34.7, 34.2, 32.2, 30.6, 28.8, 22.4, 20.5, 14.9, 10.9; high resolution mass spectra (ES+) m/z 509.3242 [$(M+H)^+$; calcd for $C_{32}H_{45}O_5^+$: 509.3267].

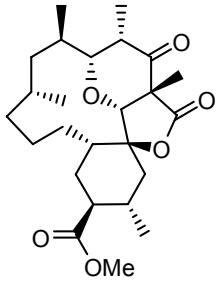
The unpurified lactone (-)-**66** from the previous step was dissolved in MeCN (3 mL). To this solution were added K_2CO_3 (91 mg, 0.66 mmol) and MeI (0.19 mL, 1.65 mmol). The mixture was then heated to 70 ^oC for 2 h before being cooled back to room temperature. The mixture was quenched with a saturated aqueous solution of NH_4Cl (10 mL) followed by extraction with EtOAc (4 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to leave a residue which was purified by column

chromatography on silica gel (elution with 10:1 hexane:ethyl acetate) to afford (-)-**67** (76 mg, 88% over two steps) as a colorless oil: $[\alpha]_D^{20}$ = -15.5 (*c* = 0.24, $CHCl_3$); IR (neat) 2923, 1776, 1714, 1454, 1373, 1203, 1095, 912 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.31 (d, *J* = 7.3 Hz, 2 H), 7.20 (dd, *J* = 7.3, 7.4 Hz, 2 H), 7.10 (appt, *J* = 7.4 Hz, 1 H), 5.63 (ddd, *J* = 7.9, 10.2, 17.3 Hz, 1 H), 5.61-5.51 (m, 1 H), 5.01-4.95 (m, 4 H), 4.35 (d, *J* = 12.3 Hz, 1 H), 4.29 (d, *J* = 12.3 Hz, 1 H), 3.83 (s, 1 H), 3.36 (dd, *J* = 4.0, 9.0 Hz, 1 H), 3.11 (dd, *J* = 7.0, 9.0 Hz, 1 H), 2.86 (dd, *J* = 2.5, 9.8 Hz, 1 H), 2.34 (dq, *J* = 2.5, 7.2 Hz, 1 H), 2.20-2.12 (m, 1 H), 2.09-1.97 (m, 2 H), 1.96 (ddd, *J* = 1.7, 3.9, 14.6 Hz, 1 H), 1.91 (ddd, *J* = 3.1, 3.1, 13.8 Hz, 1 H), 1.83 (dd, *J* = 4.3, 13.0 Hz, 1 H), 1.80-1.72 (m, 2 H), 1.67 (ddd, *J* = 3.0, 10.2, 13.2 Hz, 1 H), 1.63-1.56 (m, 1 H), 1.42-1.35 (m, 2 H), 1.38 (s, 3 H), 1.00 (d, *J* = 7.3 Hz, 3 H), 0.99 (d, *J* = 6.7 Hz, 3 H), 0.83 (ddd, *J* = 4.5, 9.3, 13.5 Hz, 1 H), 0.80 (d, *J* = 6.5 Hz, 3 H), 0.46 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 203.8, 171.7, 144.7 (2 C), 139.8, 137.1 (2 C), 128.92, 128.7, 128.0, 117.0, 113.7, 89.1, 85.3, 81.3, 73.8, 73.5, 55.3, 45.7, 42.5, 41.1, 38.2, 36.8, 36.3, 33.8, 32.3, 30.5, 29.1, 22.5, 22.4, 20.4, 15.2, 10.5; high resolution mass spectra (ES+) m/z 545.3269 [$(M+Na)^+$; calcd for $C_{33}H_{46}O_5Na^+$: 545.3243].



(-)-**68**

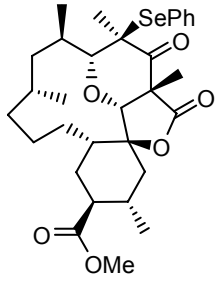
Alcohol (-)-68: A mixture of diene (-)-**67** (20 mg, 0.038 mmol) and Hoveyda-Grubbs 2nd generation catalyst (40 mg, 63 μmol) in benzene (600 mL) was purged with argon for 30 min, and sealed prior to heating at 80 °C for 24 h. The reaction was cooled to room temperature and exposed to air for 24 h. The solvent was removed under vacuum (bath temperature < 25 °C) to leave a dark green residue. The residue was dissolved in EtOAc (1 mL) and treated with 10% Pd/C (10 mg) and stirred under an atmosphere of hydrogen for 15 h. The reaction mixture was directly purified by column chromatography on silica (elution with 2:1 hexane:ethyl acetate) to afford alcohol (-)-**68** (13 mg, 84%) as a colorless gum: $[\alpha]_D^{20}$ = -5.4 (*c* = 0.35, $CHCl_3$); IR (neat) 3414, 2955, 2925, 1780, 1717, 1458, 1375, 1266, 1119, 755 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 3.91 (s, 1 H), 3.35 (ddd, *J* = 10.0, 10.0, 3.7 Hz, 1 H), 3.12 (dd, *J* = 4.0, 10.0 Hz, 1 H), 3.07 (ddd, *J* = 3.2, 6.5, 10.0 Hz, 1 H), 2.03 (dq, *J* = 4.0, 7.2 Hz, 1 H), 1.81 (ddd, *J* = 3.7, 12.9, 12.9 Hz, 1 H), 1.81-1.75 (m, 1 H), 1.68 (dd, *J* = 12.6, 13.7 Hz, 1 H), 1.62-1.58 (m, 3 H), 1.53 (ddd, *J* = 3.2, 3.2, 13.0 Hz, 1 H), 1.47 (m, 1 H), 1.40-1.35 (m, 1 H), 1.33-1.27 (m, 1 H), 1.25 (s, 3 H), 1.18-1.09 (m, 4 H), 1.07 (d, *J* = 7.2 Hz, 3 H), 1.07-1.00 (m, 2 H), 0.90 (d, *J* = 6.9 Hz, 3 H), 0.75 (dd, *J* = 7.4, 14.1 Hz, 1 H), 0.54 (d, *J* = 6.4 Hz, 3 H), 0.48 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 205.5, 171.5, 86.9, 86.3, 85.1, 65.6, 54.2, 45.0, 44.2, 42.2, 40.7, 38.3, 37.5, 34.8, 34.5, 32.2, 31.3, 29.1, 25.2, 25.1, 24.3, 19.9, 18.3, 10.4; high resolution mass spectra (ES+) m/z 429.2584 [$(M+Na)^+$; calcd for $C_{24}H_{38}O_5Na^+$: 429.2617].



(-)-**3**

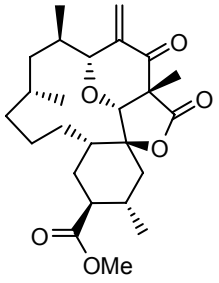
Methyl Ester (-)-3: To a solution of alcohol (-)-**68** (20 mg, 49.2 μmol) in CH_3CN (0.5 mL) and pH = 7 buffer (0.5 mL) was added $NaClO_2$ (17 mg, 123.0 μmol), TEMPO (1 mg, 4.0 μmol), and bleach (5% aqueous solution, 2 drops). After being stirred at room temperature for 5 h, the reaction was quenched with $Na_2S_2O_3$ (10 mg) and stirred for 5 min at room temperature. The solution was carefully treated with a 2 M aqueous HCl solution until pH 1 then extracted with EtOAc (3 x 10 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 2:1 ethyl acetate:hexane) to afford the carboxylic acid as a colorless oil: IR (neat) 3500-3000, 2924, 2854, 1790, 1711, 1456, 1375, 1262, 1118 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 3.84 (s, 1 H), 3.08 (dd, *J* = 3.4, 9.8 Hz, 1 H), 2.32-2.22 (m, 2 H), 2.07 (ddd, *J* = 3.1, 13.0, 14.1 Hz, 1 H), 2.02-1.98 (m, 1 H), 1.78-1.68 (m, 1 H), 1.60-1.55 (m, 2 H), 1.48-1.42 (m, 3 H), 1.40-1.27 (m, 4 H), 1.23 (s, 3 H), 1.16-1.05 (m, 4 H), 1.23 (s, 3 H), 1.16-1.05 (m, 4 H), 1.02 (d, *J* = 7.0 Hz, 3 H), 0.90 (d, *J* = 6.7 Hz, 3 H), 0.76-0.73 (m, 1 H), 0.60 (d, *J* = 6.4 Hz, 3 H), 0.47 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 205.2, 180.8, 171.1, 86.7, 85.4, 85.1, 54.0, 45.6, 44.9, 44.2, 41.2, 38.0, 36.1, 34.9, 34.5, 31.4, 31.2, 29.6, 25.2, 24.9, 24.2, 20.2, 18.3, 10.3.

To a solution of the above acid in benzene (3 mL) and MeOH (1 mL) was added $TMSCHN_2$ (0.3 mL of 2.0 M solution in Et_2O, 0.15 mmol) at 0 °C until yellow color persisted. The reaction mixture was concentrated *in vacuo* to leave a residue which was purified by column chromatography on silica gel (elution with 2:1 hexane:ethyl acetate) to afford methyl ester (-)-**3** (18 mg, 87% over two steps) as a colorless oil: $[\alpha]_D^{20}$ = -6.4 (*c* = 0.50, $CHCl_3$); IR (neat) 2955, 1787, 1736, 1454, 1373, 1160, 1117 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 3.87 (s, 1 H), 3.35 (s, 3 H), 3.11 (dd, *J* = 4.0, 10.0 Hz, 1 H), 2.33 (ddd, *J* = 3.5, 13.0, 13.0 Hz, 1 H), 2.31-2.26 (m, 1 H), 2.10 (ddd, *J* = 3.0, 13.0, 14.4 Hz, 1 H), 2.03 (dq, *J* = 4.0, 7.2 Hz, 1 H), 1.75-1.69 (m, 1 H), 1.62 (dd, *J* = 12.8, 14.3 Hz, 1 H), 1.53-1.41 (m, 2 H), 1.38-1.24 (m, 3 H), 1.25 (s, 3 H), 1.21-1.14 (m, 2 H), 1.12-0.96 (m, 4 H), 1.04 (d, *J* = 7.2 Hz, 3 H), 0.89 (d, *J* = 6.7 Hz, 3 H), 0.74 (dd, *J* = 7.4, 14.1 Hz, 1 H), 0.59 (d, *J* = 6.5 Hz, 3 H), 0.48 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 205.3, 175.3, 171.2, 86.7, 85.5, 85.1, 54.1, 51.4, 46.0, 44.9, 44.2, 41.4, 38.1, 36.3, 35.0, 34.5, 31.5, 31.2, 29.9, 25.2, 24.9, 24.2, 20.3, 18.3, 10.3; high resolution mass spectra (ES+) m/z 457.2585 [$(M+Na)^+$; calcd for $C_{25}H_{38}O_6Na^+$: 457.2566].



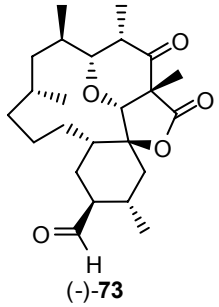
(-)-**71**

Selenide (-)-71: To a cold (-78 °C), stirred solution of methyl ester (-)-**3** (2.0 mg, 4.6 μmol) in THF (0.2 mL) was LHMDS (23 μL of 1.0 M solution in THF, 23.0 μmol) dropwise via syringe. After being stirred at -78 °C for 15 min the reaction mixture was warmed to 0 °C and stirred for an additional 15 min. To this solution was then added PhSeCl (9.0 mg, 46.0 μmol) and the reaction mixture was warmed to room temperature and stirred for 15 min at room temperature. The reaction was quenched with a saturated aqueous solution of NH_4Cl (1 mL), extracted with EtOAc (15 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 4:1 hexane:ethyl acetate) to afford selenide (-)-**71** (2.8 mg, 99%) as a colorless oil: $[\alpha]_D^{20}$ = -7.5 (*c* = 0.25, C_6H_6); IR (neat) 2925, 1786, 1733, 1451, 1375, 1246 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.50 (d, *J* = 7.1 Hz, 2 H), 7.05 (d, *J* = 7.4 Hz, 1 H), 6.99 (dd, *J* = 7.1, 7.4 Hz, 2 H), 3.99 (s, 1 H), 3.43 (d, *J* = 9.6 Hz, 1 H), 2.33 (ddd, *J* = 2.9, 12.9, 12.9 Hz, 1 H), 2.29-2.22 (m, 1 H), 2.09 (ddd, *J* = 3.0, 13.1, 13.1 Hz, 1 H), 1.90 (s, 3 H), 1.73-1.67 (m, 3 H), 1.58 (dd, *J* = 13.8, 13.8 Hz, 1 H), 1.51-1.44 (m, 4 H), 1.39-1.20 (m, 5 H), 1.33 (s, 3 H), 1.16-1.07 (m, 2 H), 1.13 (d, *J* = 7.0 Hz, 3 H), 0.99 (dd, *J* = 12.8, 13.3 Hz, 1 H), 0.92 (d, *J* = 6.7 Hz, 3 H), 0.72 (dd, *J* = 7.8, 14.1 Hz, 1 H), 0.56 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 175.2, 171.1, 138.9, 130.3, 129.5, 129.2, 126.7, 88.0, 86.5, 85.9, 54.3, 53.1, 51.4, 46.1, 45.9, 41.3, 37.8, 36.5, 36.1, 35.0, 32.0, 31.4, 30.5, 29.8, 28.7, 24.7, 23.9, 21.3, 20.3, 18.5; high resolution mass spectra (ES+) m/z 591.2234 [$(M+Na)^+$; calcd for $C_{31}H_{42}O_6SeNa^+$: 591.2225].



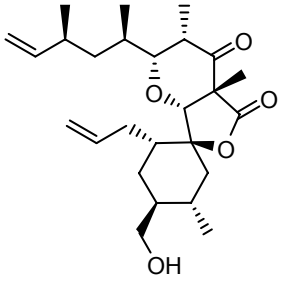
(-)-**72**

Methyl ester of Dihydro Okilactomycin (-)-72: To a cold (0 °C), stirred solution of selenide (-)-**71** (2.2 mg, 3.7 μmol) in $CHCl_3$ (0.37 mL) was added *m*-CPBA (77% max, 1.7 mg, 7.5 μmol). The reaction mixture was stirred at 0 °C for 15 min then treated with diisopropylethylamine (10 μL) and heated at reflux for 20 min. The reaction was cooled to room temperature and diluted with Et_2O (20 mL). The organic layer was washed with a saturated aqueous solution of $Na_2S_2O_3$ (10 mL), saturated aqueous solution of $NaHCO_3$ (3 x 10 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 4:1 hexane:ethyl acetate) to afford ester (-)-**72** (1.8 mg, 69%) as a colorless oil: $[\alpha]_D^{20}$ = -25.0 (*c* = 0.05, C_6H_6); IR (neat) 2955, 2925, 2855, 1788, 1733, 1710, 1626, 1455, 1264, 1027 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 6.25 (d, *J* = 0.9 Hz, 1 H), 5.04 (d, *J* = 1.5 Hz, 1 H), 3.86 (s, 1 H), 3.43 (d, *J* = 9.7 Hz, 1 H), 3.33 (s, 3 H), 2.35 (ddd, *J* = 3.6, 13.2, 13.2 Hz, 1 H), 2.33-2.27 (m, 1 H), 2.12 (ddd, *J* = 3.0, 13.0, 14.5 Hz, 1 H), 1.76-1.71 (m, 1 H), 1.68-1.61 (m, 2 H), 1.52-1.46 (m, 3 H), 1.39-1.20 (m, 5 H), 1.28 (s, 3 H), 1.13-1.08 (m, 2 H), 1.02-0.98 (m, 1 H), 0.90 (d, *J* = 6.9 Hz, 3 H), 0.70-0.67 (m, 1 H), 0.66 (d, *J* = 6.6 Hz, 3 H), 0.53 (d, *J* = 6.5 Hz, 3 H); high resolution mass spectra (ES+) m/z 455.2417 [$(M+Na)^+$; calcd for $C_{25}H_{36}O_6Na^+$: 455.2410].



(-)-**73**

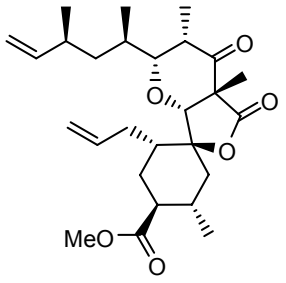
Aldehyde (-)-73: To a mixture of alcohol (-)-**68** (10 mg, 24.6 μmol) and pyridine (15 μL, 172.5 μmol) in CH_2Cl_2 (0.5 mL) was added Dess-Martin periodinane (21 mg, 49.2 μmol) at room temperature. The reaction was stirred at room temperature for 2 h then diluted with CH_2Cl_2 (20 mL), washed with a saturated aqueous solution of $NaHCO_3$ (10 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 4:1 hexane:ethyl acetate) to afford aldehyde (-)-**73** (9 mg, 90%) as a colorless oil: $[\alpha]_D^{20}$ = -11.4 (*c* = 0.10, C_6H_6); IR (neat) 2956, 2926, 1787, 1720, 1458, 1266, 1247, 1117, 984 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 9.15 (d, *J* = 3.8 Hz, 1 H), 3.84 (s, 1 H), 3.09 (dd, *J* = 4.0, 10.0 Hz, 1 H), 2.02 (dq, *J* = 4.0, 7.2 Hz, 1 H), 1.90-1.83 (m, 1 H), 1.84 (ddd, *J* = 3.8, 12.9, 12.9 Hz, 1 H), 1.73-1.67 (m, 2 H), 1.73-1.67 (m, 2 H), 1.53 (dd, *J* = 12.8 Hz, 14.3 Hz, 1 H), 1.47-1.36 (m, 3 H), 1.33-1.26 (m, 1 H), 1.23 (s, 3 H), 1.21-1.19 (m, 1 H), 1.15 (ddd, *J* = 2.9, 2.9, 12.8 Hz, 1 H), 1.12-1.07 (m, 3 H), 1.03 (d, *J* = 7.2 Hz, 3 H), 0.99-0.91 (m, 2 H), 0.89 (d, *J* = 6.9 Hz, 3 H), 0.74 (dd, *J* = 7.4, 14.1 Hz, 1 H), 0.48 (d, *J* = 6.9 Hz, 3 H), 0.45 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 205.3, 203.4, 171.2, 86.7, 85.4, 85.1, 54.1, 51.6, 44.9, 44.2, 40.9, 38.1, 36.0, 34.5, 31.5, 31.3, 31.1, 27.2, 25.1, 24.9, 24.2, 20.0, 18.3, 10.3; high resolution mass spectra (ES+) m/z 405.2629 [$(M+H)^+$; calcd for $C_{24}H_{37}O_5^+$: 405.2641].



(-)-**75**

Alcohol (-)-75: To a stirred solution of (-)-**67** (15 mg, 0.029 mmol) in CH_2Cl_2 (0.75 mL) and H_2O (30 μL) was added DDQ (196 mg, 0.862 mmol) at room temperature. After being stirred at room temperature for 24 h, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (10 mL) followed by H_2O (10 mL). The mixture was extracted with CH_2Cl_2 (3 x 10 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under vacuum to leave an orange residue which was purified by column chromatography on silica gel (elution with 2:1 hexane:ethyl acetate) to afford alcohol (-)-**75** (9 mg, 72%) as a colorless gum: $[\alpha]_D^{20}$ = -22.0 (*c* = 0.5, $CHCl_3$); IR (neat) 3415, 3075, 2928, 1773, 1712, 1456, 1127, 914, 671 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.79-5.71 (m, 1 H), 5.64-5.56 (m, 1 H), 5.12-5.06 (m, 2 H), 5.08-4.93 (m, 2 H), 4.18 (s, 1 H), 3.75 (dd, *J* = 3.6, 10.7 Hz, 1 H), 3.47 (dd, *J* = 6.9, 10.7 Hz, 1 H), 3.32 (dd, *J* = 2.5, 9.8 Hz, 1 H), 2.67-2.61 (m, 1 H), 2.29-2.22 (m, 2 H), 2.20-2.12 (m, 1 H), 1.92-1.88 (m, 1 H), 1.82-1.78 (m, 2 H), 1.77-1.65 (m, 4 H), 1.59 (s, 3 H), 1.48-1.44 (m, 2 H), 1.43-1.31 (m, 1 H), 1.10 (d, *J* = 7.3 Hz, 3 H), 1.02 (d, *J* = 6.7 Hz, 3 H), 0.98 (d, *J* = 6.5 Hz, 3 H),

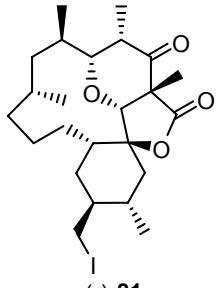
0.80 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.8, 172.0, 144.0, 136.0, 116.9, 113.1, 89.4, 84.6, 80.8, 65.5, 54.5, 45.0, 41.9, 40.4, 39.3, 35.7, 35.6, 33.0, 31.7, 29.0, 27.6, 22.8, 21.9, 19.8, 14.9, 10.4; high resolution mass spectra (ES+) m/z 455.2780 [$(M+Na)^+$; calcd for $C_{26}H_{40}O_5Na^+$: 455.2954].



(-)-**77**

Methyl Ester (-)-77: To a solution of alcohol (-)-**75** (5 mg, 11.6 μmol) in CH_3CN (0.12 mL) and pH 7 buffer (0.12 mL) was added $NaClO_2$ (2.6 mg, 29.0 μmol), TEMPO (~1 mg), and bleach (2 drops of 5% aqueous solution). After being stirred at room temperature for 7 h, the reaction was quenched with $Na_2S_2O_3$ (5 mg) and stirred for 5 min at room temperature. The solution was carefully treated with a 2 M aqueous HCl solution until pH 1 then extracted with EtOAc (3 x 5 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to afford the carboxylic acid as an orange gum which was was directly used in the next step without further purification.

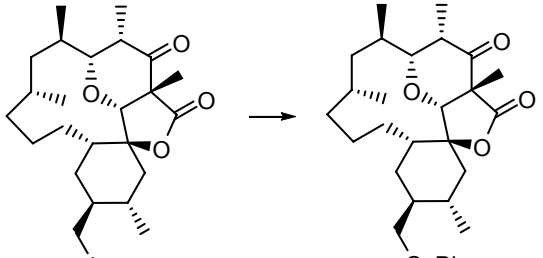
To a solution of acid from above in benzene (0.75 mL) and MeOH (0.25 mL) was added $TMSCHN_2$ (9 μL of 2.0 M solution in Et_2O, 17.4 μmol) at 0 °C until yellow color persisted. The reaction mixture was concentrated *in vacuo* to leave a residue which was purified by column chromatography on silica gel (elution with 5:1 hexane:ethyl acetate) to afford methyl ester (-)-**77** (4.3 mg, 80% over two steps) as a colorless oil: $[\alpha]_D^{20}$ = -23.0 (c = 0.2, $CHCl_3$); IR (neat) 2927, 1779, 1733, 1456, 1376, 1310, 994, 915 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80-5.69 (m, 1 H), 5.65-5.58 (m, 1 H), 5.18-5.11 (m, 2 H), 4.98-4.92 (m, 2 H), 4.18 (s, 1 H), 3.67 (s, 3 H), 3.32 (dd, J = 2.6, 9.9 Hz, 1 H), 2.68-2.62 (m, 1 H), 2.31-2.25 (m, 2 H), 2.21-2.11 (m, 2 H), 2.10-2.05 (m, 1 H), 2.91-2.81 (m, 3 H), 2.74-2.65 (m, 3 H), 1.60 (s, 3 H), 1.42-1.29 (m, 2 H), 1.13 (d, J = 7.2 Hz, 3 H), 1.04 (d, J = 6.8 Hz, 3 H), 0.94 (d, J = 6.5 Hz, 3 H), 0.84 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.6, 175.3, 171.7, 143.9, 135.3, 117.4, 113.1, 88.6, 84.5, 80.9, 54.3, 51.5, 44.9, 44.4, 41.3, 40.4, 35.6, 34.6, 32.5, 31.7, 29.5, 27.6, 22.7, 21.8, 20.2, 14.8, 10.3; high resolution mass spectra (ES+) m/z 483.2726 [$(M+Na)^+$; calcd for $C_{27}H_{40}O_6Na^+$: 483.2723].



(-)-**81**

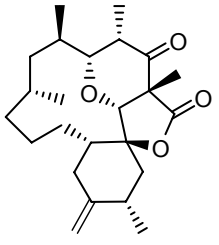
Iodide (-)-81: To a cold (0 °C), stirred solution of alcohol (-)-**68** (7 mg, 0.017 mmol) in THF (0.3 mL) were added PPh_3 (5.4 mg, 0.021 mmol), imidazole (2.3 mg, 0.034 mmol) and I_2 (5.7 mg, 0.022 mmol). The cold bath was removed and the mixture was stirred at room temperature for 30 min. The reaction was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (5 mL) and

extracted with CH_2Cl_2 (3 x 5 mL). The organic layers were combined, dried over $MgSO_4$, and filtered. The filtrate was concentrated under vacuum to leave a yellow residue which was purified by column chromatography on silica gel (elution with 5:1 hexane:ethyl acetate) to afford iodide (-)-**81** (8 mg, 90%) as a white solid: $[\alpha]_D^{20}$ = -21.4 (*c* = 0.85, $CHCl_3$); IR (neat) 2955, 2923, 1784, 1715, 1456, 1252, 1118 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 3.96 (s, 1 H), 3.09 (dd, *J* = 4.0, 10.0 Hz, 1 H), 2.99 (dd, *J* = 2.8, 9.8 Hz, 1 H), 2.51 (dd, *J* = 8.5, 9.8 Hz, 1 H), 2.0 (dq, *J* = 4.0, 14.4 Hz, 1 H), 1.77-1.1.65 (m, 2 H), 1.62-1.51 (m, 3 H), 1.50-1.40 (m, 3 H), 1.38-1.31 (m, 2 H), 1.28-1.22 (m, 1 H), 1.22 (s, 3 H), 1.15-1.07 (m, 3 H), 1.03-0.98 (m, 4 H), 0.89 (d, *J* = 6.8 Hz, 3 H), 0.78-0.71 (m, 2 H), 0.47 (d, *J* = 6.9 Hz, 3 H), 0.34 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 205.4, 171.3, 86.6, 86.2, 85.1, 54.2, 44.9, 44.2, 42.3, 39.9, 38.4, 38.2, 37.1, 34.5, 32.19, 32.16, 31.3, 25.1, 25.0, 24.2, 19.4, 18.3, 14.3, 10.3;high resolution mass spectra (ES+) m/z 539.1967 [$(M+Na)^+$; calcd for $C_{24}H_{37}IO_4Na^+$: 539.1972].



(-)-**81** (+)-**S11**

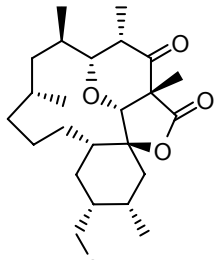
Selenide (+)-S11: To a stirred suspension of iodide (-)-**81** (5 mg, 9.7 μmol) and Cs_2CO_3 (4.1 mg, 13.0 μmol) in MeCN (0.2 mL) was added benzeneselenol (1.8 mg, 12.0 μmol) at room temperature. After being stirred at room temperature for 0.5 h, the reaction was poured directly on silica and purified by column chromatography on silica gel (elution with 5:1 hexane:ethyl acetate) to afford selenide (+)-**S11** (4.5 mg, 85%) as a colorless gum: $[\alpha]_D^{20}$ = +32.0 (*c* = 0.3, $CHCl_3$); IR (neat) 2923, 1785, 1457, 1094 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.56-7.52 (m, 2 H), 7.10-7.06 (m, 3 H), 3.96 (s, 1 H), 3.18 (dd, *J* = 4.1, 10.1 Hz, 1 H), 3.11 (dd, *J* = 2.8, 11.7 Hz, 1 H), 2.45 (dd, *J* = 9.9, 11.7 Hz, 1 H), 2.10 (dq, *J* = 4.1, 14.5 Hz, 1 H), 1.94-1.89 (m, 1 H), 1.87-1.79 (m, 2 H), 1.76-1.60 (m, 4 H), 1.53-1.25 (m, 3 H), 1.23-1.16 (m, 3 H), 1.14 (d, *J* = 7.1 Hz, 3 H), 1.10-0.97 (m, 6 H), 0.94 (d, *J* = 6.7 Hz, 3 H), 0.81 (dd, *J* = 7.3, 14.3 Hz, 1 H), 0.57 (d, *J* = 6.3 Hz, 3 H), 0.56 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 205.5, 171.4, 133.1 (2 C), 132.3, 129.6 (2 C), 127.1, 86.8, 86.2, 85.1, 54.2, 44.9, 44.2, 42.5, 39.5, 38.2, 37.6, 37.5, 34.5, 33.5, 32.5, 32.0, 31.3, 25.2, 25.1, 24.2, 19.8, 18.3, 10.4 ; high resolution mass spectra (ES+) m/z 569.1725 [$(M+Na)^+$; calcd for $C_{30}H_{42}O_4SeNa^+$: 569.1719].



(-)-**82**

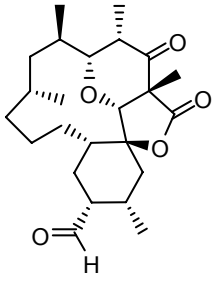
Alkene (-)-**82**: To a cold (0 °C) mixture of alcohol (-)-**68** (15 mg, 0.037 mmol), 2-nitrophenyl selenocyanate (59 mg, 0.258 mmol), and pyridine (44 mg, 45 μL, 0.554 mmol) in THF (1.5 mL) was added *n*-tributylphosphine (60 mg, 73 μL, 0.295 mmol) dropwise. The cold bath was removed and the dark brown mixture was stirred at room temperature overnight. The mixture

was cooled to 0 °C and H_2O_2 (0.5 mL of 30% solution in H_2O) was added dropwise. The mixture was warmed to room temperature and stirred for 1 h. The solution was diluted with H_2O (10 mL) and the organic layer was separated. The aqueous layer was extracted with EtOAc (4 x 10 mL). The combined organic layers were dried over Mg_2SO_4, filtered, and evaporated to leave a residue, which was dissolved in THF (2 mL) and heated to 45 °C for 3 h. The reaction mixture was concentrated under vacuum to leave a yellow residue which was purified by column chromatography on silica gel (elution with 15:1 to 10:1 hexane:ethyl acetate) to yield (-)-**82** (12.9 mg, 90%) as a light yellow crystalline solid: mp = 229-231 °C; $[\alpha]_D^{20}$ = -23.4 (*c* = 0.35, $CHCl_3$); IR (neat) 2965, 2929, 1784, 1716, 1456, 1253, 1116, 980, 728 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.68 (d, *J* = 1.86 Hz, 1 H), 4.64 (d, *J* = 1.49 Hz, 1 H), 4.30 (s, 1 H), 3.60 (dd, *J* = 4.1, 9.9 Hz, 1 H), 2.70-2.62 (m, 2 H), 2.45-2.36 (m, 1 H), 1.98 (dd, *J* = 2.2, 13.0 Hz, 1 H), 1.87-1.82 (m, 1 H), 1.76-1.64 (m, 5 H), 1.61-1.44 (m, 4 H), 1.41-1.23 (m, 5 H), 1.20 (d, *J* = 7.1 Hz, 3 H), 1.10-1.02 (m, 1 H), 1.00 (d, *J* = 6.3 Hz, 3 H), 0.94 (dd, *J* = 7.4, 14.0 Hz, 1 H), 0.88 (d, *J* = 6.7 Hz, 3 H), 0.85 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.1, 172.1, 148.0, 106.9, 87.1, 85.7, 84.7, 53.6, 44.4, 43.9, 42.7, 40.8, 38.1, 37.3, 33.9, 31.4, 31.2, 30.7, 25.1, 24.0, 23.6, 18.0, 17.6, 10.2; high resolution mass spectra (ES+) m/z 389.2698 $[(M+H)^+$; calcd for $C_{24}H_{38}O_4^+$: 389.2692].



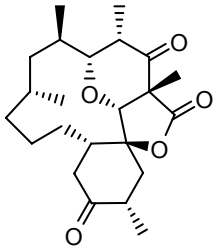
(-)-**83**

Alcohol (-)-83: To a cold (0 °C), stirred solution of alkene (-)-**82** (10 mg, 0.026 mmol) in THF (1.2 mL) was added BH_3·THF (0.08 mL of 1.0 M solution in THF, 0.077 mmol) dropwise via syringe. The cold bath was removed and the mixture was stirred at room temperature for 2 h. The reaction mixture was cooled to 0 °C and quenched with H_2O_2 (0.5 mL of 30% solution in H_2O) followed by a saturated aqueous solution of $NaHCO_3$ (0.5 mL). After being stirred at room temperature for 1 h, the mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 3:1 hexane:ethyl acetate) to afford alcohol (-)-**83** (10.0 mg, 95%) as a colorless oil: $[\alpha]_D^{20}$ = -29.0 (*c* = 0.3, $CHCl_3$); IR (neat) 3415, 2957, 2924, 1781, 1718, 1455, 1376, 1268, 1121, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.30 (s, 1 H), 3.78 (dd, *J* = 6.7, 10.7 Hz, 1 H), 3.60 (dd, *J* = 3.7, 9.9 Hz, 1 H), 3.53 (t, *J* = 11.1 Hz, 1 H), 2.65 (dq, *J* = 3.7, 14.6 Hz, 1 H), 2.26-2.20 (m, 1 H), 2.02-1.94 (m, 1 H), 1.88-1.81 (m, 1 H), 1.80-1.71 (m, 4 H), 1.67 (s, 3 H), 1.65-1.53 (m, 3 H), 1.50-1.45 (m, 2 H), 1.42-1.35 (m, 1 H), 1.26-1.23 (m, 1 H), 1.20-1.15 (m, 4 H), 1.08-1.01 (m, 1 H), 1.00-0.94 (m, 1 H), 0.93-0.87 (m, 6 H), 0.86 (d, *J* = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.2, 172.1, 87.1, 86.0, 85.0, 62.7, 53.4, 44.7, 44.0, 41.1, 40.0, 37.6, 34.0, 32.4, 32.1, 31.0, 30.6, 27.9, 25.4, 25.1, 23.8, 19.2, 18.1, 10.1; high resolution mass spectra (ES+) m/z 429.2583 $[(M+Na)^+$; calcd for $C_{24}H_{38}O_5Na^+$: 429.2617].



(-)-**86**

Aldehyde (-)-86: To a cold (0 ^{o}C) solution of alcohol (-)-**83** (5 mg, 0.012 mmol)) in CH_2Cl_2 (0.25 mL) and DMSO (0.25 mL) were added Et_3N (12.5 mg, 17 μL, 0.123 mmol) followed by sulfur trioxide-pyridine complex (10 mg, 0.062 mmol). After being stirred at 0 ^{o}C for 2 h, the mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL) followed by addition of H_2O (10 mL). The mixture was extracted with Et_2O (4 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a yellow residue which was purified by column chromatography on silica gel (elution with 5:1 hexane:ethyl acetate) to afford aldehyde (-)-**86** (4.6 mg, 93%) as a colorless oil: $[\alpha]_D^{20}$ = -7.3 (*c* = 0.26, $CHCl_3$); IR (neat) 2955, 2924, 2854, 1787, 1703, 1458, 1253, 986, 622 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (d, *J* = 1.1 Hz, 1 H), 4.30 (s, 1 H), 3.60 (dd, *J* = 3.7, 9.7 Hz, 1 H), 2.65 (dq, *J* = 3.7, 14.6 Hz, 1 H), 2.36-2.32 (m, 1 H), 2.25-2.13 (m, 3 H), 1.96-1.91 (m, 1 H), 1.84-1.78 (m, 1 H), 1.74-1.66 (m, 5 H), 1.62-1.52 (m, 2 H), 1.51-1.40 (m, 2 H), 1.39-1.32 (m, 2 H), 1.23 (d, *J* = 7.1 Hz, 3 H), 1.20-1.13 (m, 1 H), 1.11 (d, *J* = 6.7 Hz, 3 H), 1.03-0.93 (m, 2 H), 0.87 (d, *J* = 6.7 Hz, 3 H), 0.85 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.1, 205.0, 171.9, 86.4, 86.0, 85.0, 53.4, 49.8, 44.6, 44.0, 40.8, 37.3, 33.9, 33.1, 33.0, 32.1, 30.6, 26.9, 25.3, 24.7, 23.7, 18.7, 18.0, 10.1;

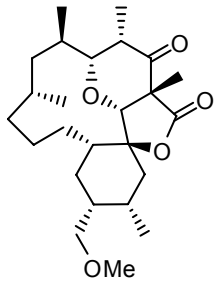


(-)-**85**

***Bis*-ketone (-)-85**: To a stirred solution of alkene (-)-**82** (12 mg, 0.031 mmol) in acetone (1.2 mL) and H_2O (0.3 mL) was added NMO (10.9 mg, 0.093 mmol) followed by OsO_4 (1 drop of 4% solution in H_2O) at room temperature. After being stirred at room temperature for 15 h the reaction was quenched with a saturated aqueous solution of Na_2SO_3 (6 mL) and stirred for additional 1 h. The mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a yellow residue which was purified by column chromatography on silica gel (elution with 1:1 hexane:ethyl acetate) to afford diol (12.5 mg, 96%) as a colorless gum: $[\alpha]_D^{20}$ = -9.1 (*c* = 0.28, $CHCl_3$); IR (neat) 3414, 2956, 2924, 1781, 1716, 1456, 1374, 629 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 4.02 (s, 1 H), 3.46 (d, *J* = 11.5 Hz, 1 H), 3.36 (d, *J* = 10.0 Hz, 1 H), 3.18 (dd, *J* = 4.1, 10.1 Hz, 1 H), 2.18-2.07 (m, 3 H), 1.89-1.81 (m, 1 H), 1.79-1.63 (m, 4 H), 1.54-1.38 (m, 2 H), 1.33 (s, 3 H), 1.31-1.25 (m, 1 H), 1.20-1.16 (m, 2 H), 1.14 (d, *J* = 7.1 Hz, 3 H), 1.08-0.98 (m, 3 H), 0.96 (d, *J* = 6.7 Hz, 3 H), 0.82 (dd, *J* = 7.4, 14.1 Hz, 1 H), 0.68 (d, *J* = 7.1 Hz, 3 H), 0.55 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 205.8, 171.5, 86.6, 86.0, 85.6, 74.1, 65.0, 54.5, 45.3, 44.4, 43.2,

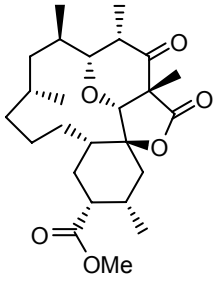
39.3, 38.3, 36.8, 34.9, 34.8, 31.33, 31.25, 25.8, 25.5, 24.5, 18.5, 14.9, 10.4; high resolution mass spectra (ES+) m/z 445.2578 [$(M+Na)^+$; calcd for $C_{24}H_{38}O_6Na^+$: 445.2566].

To a stirred solution of diol (12.5 mg, 0.030 mmol) in acetone (0.8 mL) and H_2O (0.2 mL) was added $NaIO_4$ (64 mg, 0.30 mmol) at room temperature. After being stirred at room temperature for 1 h, the mixture was diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 5:1 hexane:ethyl acetate) to afford *bis*-ketone (-)-**85** (11.1 mg, 95%) as a colorless oil: $[\alpha]_D^{20}$ = -24.8 (*c* = 0.13, $CHCl_3$); IR (neat) 2926, 1740, 1735, 1718, 1458, 1114, 611.3 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 3.95 (s, 1 H), 3.15 (dd, *J* = 4.1, 10.1 Hz, 1 H), 2.81 (dd, *J* = 5.6, 13.0 Hz, 1 H), 2.58-2.50 (m, 1 H), 2.11-2.00 (m, 4 H), 1.80-1.74 (m, 1 H), 1.70-1.62 (m, 1 H), 1.60-1.54 (m, 1 H), 1.51-1.37 (m, 2 H), 1.31 (s, 3 H), 1.27-1.18 (m, 1 H), 1.14-1.09 (m, 1 H), 1.08 (d, *J* = 7.5 Hz, 3 H), 1.04-0.94 (m, 3 H), 0.87 (d, *J* = 7.1 Hz, 3 H), 0.83 (d, *J* = 6.7 Hz, 3 H), 0.77 (dd, *J* = 7.3, 14.3 Hz, 1 H), 0.53 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 208.7, 205.3, 170.7, 86.1, 85.3 (2 C), 54.5, 47.0, 45.9, 45.0, 44.4, 40.0, 38.7, 37.9, 34.5, 32.0, 31.5, 25.1, 24.7, 24.2, 18.4, 14.5, 10.5; high resolution mass spectra (ES+) m/z 413.2307 [$(M+Na)^+$; calcd for $C_{23}H_{34}O_5Na^+$: 413.2304].



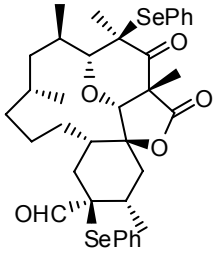
(-)-**88**

Methyl Ether (-)-88: To a stirred solution of alcohol (-)-**83** (7 mg, 0.017 mmol) in CH_2Cl_2 (1.5 mL) were added 2,6-di-*tert*-butyl-4-methylpyridine (17.7 mg, 0.086 mmol) and Me_3OBF_4 (12.7 mg, 0.086 mmol) at room temperature. After being stirred at room temperature for 1 h, the reaction was quenched with 1 N aqueous solution of $NaHSO_4$ (10 mL) and stirred for additional 10 min at room temperature. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 5:1 hexane:ethyl acetate) to afford methyl ether (-)-**88** (7.1 mg, 99%) as a colorless oil: $[\alpha]_D^{20}$ = -26.4 (*c* = 0.13, $CHCl_3$); IR (neat) 2924, 1785, 1717, 1457, 1258, 1115, 985 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.30 (s, 1 H), 3.59 (dd, *J* = 3.7, 10.0 Hz, 1 H), 3.37 (dd, *J* = 6.6, 9.6 Hz, 1 H), 3.31-3.22 (m, 4 H), 2.67 (dq, *J* = 4.3, 14.5 Hz, 1 H), 2.25-2.18 (m, 1 H), 1.98-1.92 (m, 2 H), 1.84-1.72 (m, 4 H), 1.68-1.65 (m, 4 H), 1.61-1.51 (m, 3 H), 1.48-1.42 (m, 2 H), 1.41-1.36 (m, 1 H), 1.29-1.25 (m, 2 H), 1.21 (d, *J* = 7.3 Hz, 3 H), 0.98-0.94 (m, 1 H), 0.91 (d, *J* = 6.8 Hz, 3 H), 0.88-0.84 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.2, 172.1, 87.2, 86.1, 84.9, 72.5, 58.2, 53.5, 44.6, 44.0, 41.1, 37.7, 36.6, 34.0, 32.4, 31.7, 31.1, 30.6, 27.9, 25.4, 25.0, 23.9, 19.0, 18.1, 10.1; high resolution mass spectra (ES+) m/z 421.2958 [$(M+H)^+$; calcd for $C_{25}H_{41}O_5^+$: 421.2954].



(-)-**80**

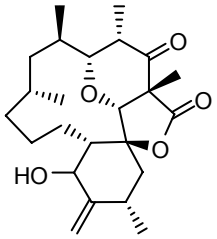
Methyl Ester (-)-80: To a stirred solution of methyl ether (-)-**88** (7.1 mg, 0.017 mmol) in CH_3CN (0.1 mL), CCl_4 (0.1 mL) and H_2O (0.1 mL) were added $NaIO_4$ (36 mg, 0.170 mmol) followed by $RuCl_3 \cdot xH_2O$ (one small crystal) at room temperature. After being stirred at room temperature for 5 h, the reaction was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (10 ml) and stirred for additional 1 h at room temperature. The mixture was extracted with CH_2Cl_2 (4 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 5:1 hexane:ethyl acetate) to afford methyl ester (-)-**80** (4.8 mg, 65%) as a colorless oil: $[\alpha]_D^{20}$ = -33.0 (*c* = 0.15, $CHCl_3$); IR (neat) 2955, 1787, 1736, 1454, 1373, 1160, 1117 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.26 (s, 1 H), 3.62 (s, 3 H), 3.59 (dd, *J* = 3.7, 9.9 Hz, 1 H), 2.67 (dq, *J* = 4.3, 14.5 Hz, 1 H), 2.48-2.44 (m, 1 H), 2.40 (t, *J* = 13.7 Hz, 1 H), 2.27-2.23 (m, 1 H), 2.10-2.04 (m, 1 H), 1.98-1.96 (m, 1 H), 1.81-1.76 (m, 2 H), 1.74-1.69 (m, 3 H), 1.67 (s, 3 H), 1.57-1.50 (m, 2 H), 1.49-1.42 (m, 1 H), 1.38-1.34 (m, 1 H), 1.23 (d, *J* = 7.3 Hz, 3 H), 1.19-1.10 (m, 2 H), 1.04 (d, *J* = 7.1 Hz, 3 H), 0.96-0.91 (m, 1 H), 0.88 (d, *J* = 6.8 Hz, 3 H), 0.85 (d, *J* = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.2, 175.3, 172.1, 87.2, 85.9, 84.9, 53.4, 50.9, 44.7, 44.0, 41.5, 40.9, 37.7, 34.2, 33.9, 32.4, 30.5, 27.5, 25.4, 24.7, 23.9, 18.8, 18.1, 14.1, 10.1; high resolution mass spectra (ES+) m/z 457.2550 [$(M+Na)^+$; calcd for $C_{25}H_{38}O_6Na^+$: 457.2566].



(-)-**90**

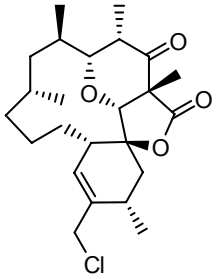
***Bis*-selenide (-)-90**: To a cold (-78 °C), stirred solution of aldehyde (-)-**86** (5 mg, 0.012 mmol) in THF (0.5 mL) was added NaHMDS (31 μL of 1.0 M solution in THF, 0.031 mmol) dropwise via syringe. After 10 min at -78 °C, a solution of PhSeCl (24 mg, 0.124 mmol) in THF (0.24 mL) was introduced to the stirred solution and the mixture was stirred for additional 30 min at -78 °C. The reaction was quenched with a saturated aqueous solution of NH_4Cl (5 mL) at -78 °C followed by warming up to room temperature. The mixture was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to leave a residue which was purified by Prep TLC (elution with 5:1 hexane:ethyl acetate) to afford *bis*-selenide (-)-**90** (5.9 mg, 65%) as a colorless oil: $[\alpha]_D^{20}$ = +12.0 (*c* = 0.3, $CHCl_3$); IR (neat) 2955, 2925, 1786, 1721, 1459, 1264, 1244, 1118, 986 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.39 (s, 1 H), 7.54-7.51 (m, 4 H), 7.45-7.39 (m, 2 H), 7.34-7.29 (m, 4 H), 4.33 (s, 1 H), 3.67 (d, *J* = 9.7 Hz, 1 H), 2.60-2.58 (m, 1 H), 2.28 (dd, *J* = 4.9, 13.8 Hz, 1 H), 2.09 (s, 3 H), 2.04-1.98 (m, 2 H), 1.84-1.79 (m, 2 H), 1.60-1.57 (m, 3 H), 1.45-1.41 (m, 4 H), 1.37-1.35 (m, 1 H), 1.29-1.21

(m, 5 H), 1.18 (d, J = 7.2 Hz, 3 H), 1.10-0.99 (m, 1 H), 0.94-0.79 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.5, 191.7, 171.7, 138.5 (2 C), 138.1 (2 C), 129.9 (2 C), 129.7 (2 C), 129.0, 128.9, 126.0, 124.8, 87.8, 86.4, 85.3, 59.2, 53.8, 52.9, 45.7, 42.7, 37.9, 36.8, 35.8, 35.2, 33.9, 31.2, 29.6, 28.3, 24.2, 23.3, 20.6, 17.9, 16.5; high resolution mass spectra (ES+) m/z 405.2629 [$(M+H)^+$; calcd for $C_{24}H_{44}O_5^+$: 405.2641].



(-)-**91**

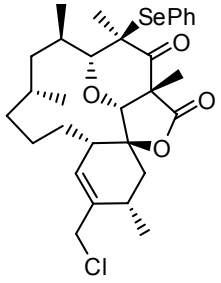
Alcohol (-)-91: To a stirred solution of alkene (-)-**82** (8 mg, 0.0206 mmol) in CH_2Cl_2 (0.8 mL) at 10 °C was added *t*-BuOOH (11 μL of 70% solution in H_2O, 0.0825 mmol) followed by SeO_2 (1.1 mg, 0.0103 mmol). After being stirred at 10 °C for 40 h, the mixture was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (0.2 mL) and diluted with H_2O (5 mL). The mixture was stirred at room temperature for 10 min before being extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 2:1 hexane:ethyl acetate) to afford secondary alcohol (-)-**91** (4.5 mg, 62% based on recovered starting material) as a colorless oil: $[\alpha]_D^{20}$ = -5.3 (c = 0.15, $CHCl_3$); IR (neat) 3418, 2925, 1786, 1717, 1458, 1256, 1120, 911, 731 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.96 (s, 1 H), 4.84 (s, 1 H), 4.37 (s, 1 H), 3.91 (d, J = 1.9 Hz, 1 H), 3.62 (dd, J = 3.7, 10.0 Hz, 1 H), 2.77-2.63 (m, 2 H), 2.10-2.03 (m, 1 H), 1.75-1.62 (m, 6 H), 1.55-1.48 (m, 2 H), 1.43-1.35 (m, 2 H), 1.30-1.23 (m, 2 H), 1.20 (d, J = 7.1 Hz, 3 H), 1.17-1.09 (m, 2 H), 1.06 (d, J = 6.7 Hz, 3 H), 0.96 (dd, J = 7.3, 14.0 Hz, 1 H), 0.88 (d, J = 6.7 Hz, 3 H), 0.86 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.5, 171.1, 148.6, 110.8, 87.6, 85.6, 84.9, 80.8, 52.0, 48.2, 44.3, 44.0, 37.8, 37.1, 33.9, 30.5, 29.0, 26.3, 25.1, 24.1, 23.6, 18.0, 17.3, 10.0; high resolution mass spectra (ES+) m/z 387.2548 [$(M-OH)^+$; calcd for $C_{24}H_{35}O_4^+$: 387.2536].



(-)-**93**

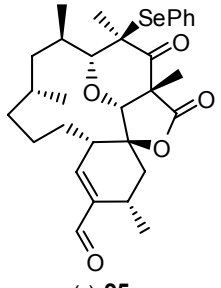
Allyl Chloride (-)-**93:** To a cold (0 °C), stirred solution of (-)-**91** (9 mg, 0.0223 mmol) in Et_2O (0.8 mL) and propylene oxide (0.2 mL) was added thionyl chloride (40 mg, 24 μL, 0.3340 mmol). After being stirred at 0 °C for 4 h, the mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (1 mL) and diluted with H_2O (10 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 7:1 hexane:ethyl acetate) to afford chloride (-)-**93** (7 mg, 74%) as a colorless gum: $[\alpha]_D^{20}$ = -2.0 (c = 0.17, $CHCl_3$); IR (neat) 2926, 1785,

1716, 1457, 1377, 1260, 1118 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.68 (d, *J* = 4.8 Hz, 1 H), 4.41 (s, 1 H), 4.11 (d, *J* = 11.9 Hz, 1 H), 3.90 (d, *J* = 11.5 Hz, 1 H), 3.64 (dd, *J* = 3.5, 9.7 Hz, 1 H), 2.67 (dq, *J* = 4.1, 14.7 Hz, 1 H), 2.63-2.55 (m, 1 H), 2.22-2.16 (m, 1 H), 1.83-1.66 (m, 5 H), 1.64-1.46 (m, 4 H), 1.43-1.31 (m, 2 H), 1.30-1.22 (m, 5 H), 1.06 (d, *J* = 7.1 Hz, 3 H), 1.04-0.96 (m, 2 H), 0.89 (d, *J* = 7.1 Hz, 3 H), 0.87 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.0, 171.7, 136.0, 129.5, 85.2, 85.1, 85.0, 53.3, 46.8, 44.6, 44.0, 42.2, 37.4, 33.8, 33.2, 30.5, 29.6, 27.8, 25.2, 23.8, 23.7, 18.3, 18.0, 10.1; high resolution mass spectra (ES+) m/z 445.2100 [$(M+Na)^+$; calcd for $C_{24}H_{35}ClO_4Na^+$: 445.2122].



(-)-**94**

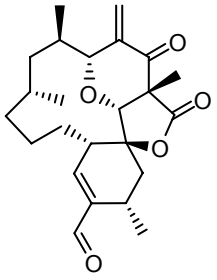
Selenide (-)-**94:** To a cold (-78 °C) solution of (-)-**93** (7 mg, 0.0166 mmol) in THF (1.2 mL) was added NaHMDS (0.13 mL of 0.25 M solution in THF, 0.0332 mmol) dropwise. After being stirred for 10 min at -78 °C, a solution of phenylselenenyl chloride (32 mg, 0.1660 mmol) in THF (0.32 mL) was added dropwise *via* syringe. The mixture was stirred at -78 °C for additional 20 min before being quenched with a saturated aqueous solution of NH_4Cl (1 mL) and slowly warmed to room temperature. The mixture was diluted with H_2O (10 mL) and extracted with Et_2O (4 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to leave an orange residue which was purified by column chromatography on silica gel (elution with 10:1 hexane:ethyl acetate) to afford (-)-**94** (8 mg, 83%) as a colorless gum: $[\alpha]_D^{20}$ = -7.5 (*c* = 0.28, $CHCl_3$); IR (neat) 2925, 1785, 1703, 1454, 1375, 1257, 969, 736 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.1 Hz, 2 H), 7.43 (t, *J* = 7.3 Hz, 1 H), 7.34 (t, *J* = 7.6 Hz, 2 H), 5.67 (d, *J* = 5.2 Hz, 1 H), 4.47 (s, 1 H), 4.09 (d, *J* = 12.3 Hz, 1 H), 3.87 (d, *J* = 11.5 Hz, 1 H), 3.74 (d, *J* = 9.7 Hz, 1 H), 2.56-2.46 (m, 1 H), 2.22-2.16 (m, 1 H), 2.10 (s, 3 H), 1.91-1.81 (m, 1 H), 1.77-1.69 (m, 1 H), 1.65-1.57 (m, 4 H), 1.56-1.48 (m, 3 H), 1.44 (s, 3 H), 1.31-1.15 (m, 5 H), 0.98 (d, *J* = 6.7 Hz, 3 H), 0.96-0.92 (m, 1 H), 0.91 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.7, 171.8, 138.2 (2 C), 135.9, 129.9, 129.5, 129.0 (2 C), 126.1, 87.9, 85.6, 84.9, 53.7, 52.9, 46.8, 45.8, 42.3, 37.1, 35.9, 33.6, 33.2, 31.3, 28.3, 28.0, 23.7, 23.4, 20.7, 18.4, 18.1; high resolution mass spectra (ES+) m/z 601.1598 [$(M+Na)^+$; calcd for $C_{30}H_{39}ClO_4SeNa^+$: 601.1600].



(-)-**95**

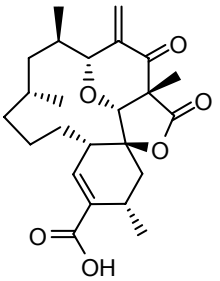
Aldehyde (-)-**95:** To a solution of chloride (-)-**94** (5.5 mg, 0.0095 mmol) in DMSO (0.5 mL) was added trimethylamine N-oxide (7.2 mg, 0.0950 mmol) at room temperature. After being stirred

at room temperature for 12 h, the mixture was quenched with a saturated aqueous solution of NaCl (10 mL) followed by extraction with Et_2O (5 x 8 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to leave a yellow residue which was purified by column chromatography on silica gel (elution with 3:1 hexane:ethyl acetate) to afford (-)-**95** (3.5 mg, 65%) as a colorless oil: $[\alpha]_D^{20}$ = -22.0 (*c* = 0.1, $CHCl_3$); IR (neat) 2925, 1787, 1686, 1456, 1255, 1107, 671 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.34 (s, 1 H), 7.55-7.51 (m, 2 H), 7.46-7.41 (m, 1 H), 7.37-7.32 (m, 2 H), 6.55 (dd, *J* = 1.9, 6.0 Hz, 1 H), 4.51 (s, 1 H), 3.76 (d, *J* = 9.7 Hz, 1 H), 2.66-2.58 (m, 1 H), 2.46-2.41 (m, 1 H), 2.11 (s, 3 H), 1.93-1.85 (m, 1 H), 1.76-1.59 (m, 5 H), 1.57-1.50 (m, 2 H), 1.45 (s, 3 H), 1.36-1.19 (m, 6 H), 1.08 (d, *J* = 7.1 Hz, 3 H), 0.98 (dd, *J* = 8.0, 14.3 Hz, 1 H), 0.93 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.3, 193.3, 171.5, 150.5, 143.1, 138.1 (2 C), 130.0, 129.1 (2 C), 125.9, 87.9, 85.0, 84.7, 53.7, 52.8, 45.7, 43.1, 37.0, 35.8, 33.4, 31.8, 31.4, 28.2, 25.9, 23.8, 23.3, 20.7, 19.2, 18.2; high resolution mass spectra (ES+) m/z 581.1757 [$(M+Na)^+$; calcd for $C_{30}H_{38}O_5SeNa^+$: 581.1782].



(-)-**96**

Aldehyde (-)-96: To a stirred solution of selenide (-)-**95** (4 mg, 0.0072 mmol) in THF (0.4 mL)/H_2O (0.1 mL) was added $NaIO_4$ (16 mg, 0.0771 mmol) in one portion at room temperature. After being stirred at room temperature for 5 h, the mixture was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (1 mL) and diluted with H_2O (5 mL). The solution was extracted with Et_2O (4 x 10 mL), dried over Mg_2SO_4, filtered, and concentrated under vacuum to leave a residue which was purified by column chromatography on silica gel (elution with 3:1 hexane:ethyl acetate) to afford (-)-**96** (2.6 mg, 90%) as a colorless gum: $[\alpha]_D^{20}$ = -24.0 (*c* = 0.1, $CHCl_3$); IR (neat) 2924, 1787, 1686, 1630, 1458, 1378, 1260, 1128, 1028, 972, 757 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.36 (s, 1 H), 6.57 (dd, *J* = 2.1, 6.3 Hz, 1 H), 6.45 (s, 1 H), 5.68 (d, *J* = 1.1 Hz, 1 H), 4.46 (s, 1 H), 3.93 (d, *J* = 8.9 Hz, 1 H), 2.75-2.67 (m, 1 H), 2.49-2.43 (m, 1 H), 2.03-1.95 (m, 1 H), 1.84-1.76 (m, 1 H), 1.73-1.64 (m, 3 H), 1.60-1.49 (m, 3 H), 1.39 (dd, *J* = 6.7, 15.3 Hz, 1 H), 1.34-1.23 (m, 5 H), 1.15 (d, *J* = 7.1 Hz, 3 H), 1.09 (d, *J* = 6.3 Hz, 3 H), 0.99 (dd, *J* = 7.6, 14.5 Hz, 1 H), 0.91 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.2, 191.7, 171.1, 150.4, 143.2, 141.9, 121.7, 84.8, 83.8, 82.4, 52.1, 45.0, 42.9, 37.5, 34.6, 33.6, 32.2, 30.1, 25.9, 25.7, 23.51, 23.46, 20.4, 19.2; high resolution mass spectra (ES+) m/z 423.2162 [$(M+Na)^+$; calcd for $C_{24}H_{32}O_5Na^+$: 423.2148].



(-)-Okilactomycin (**1**)

(-)-**Okilactomycin (1):** To a stirred mixture of aldehyde (-)-**96** (1.2 mg, 0.003 mmol) and 2-methyl-2-butene (7 mg, 11 μL, 0.100 mmol) in THF (0.15 mL) and *t*-BuOH (0.15 mL) was added an aqueous solution of $NaClO_2$ (1.4 mg, 0.015 mmol) and NaH_2PO_4 (1.8 mg, 0.015 mmol) in H_2O (0.05 mL) at room temperature. After being stirred at room temperature for 1 h, the mixture was quenched with an aqueous solution of 1 N HCl (0.25 mL) and diluted with H_2O (3 mL). The aqueous layer was extracted with EtOAc (5 x 5 mL), and the combined organic layers were dried over Mg_2SO_4, filtered, and evaporated to give a residue, which was purified by Prep TLC (elution with 80:1 $CHCl_3$:MeOH with 0.5% acetic acid) to afford (-)-**1** (1 mg, 80%) as a colorless gum: $[\alpha]_D^{20}$ = -37.0 (*c* = 0.03, $CHCl_3$); IR (neat) 2924, 2854, 1788, 1703, 1629, 1460, 1263, 1184, 972 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.84 (dd, *J* = 1.4, 5.9 Hz, 1 H), 6.44 (s, 1 H), 5.67 (s, 1 H), 4.44 (s, 1 H), 3.92 (d, *J* = 10.0 Hz, 1 H), 2.78-2.68 (m, 1 H), 2.38-2.30 (m, 1 H), 2.03-1.94 (m, 1 H), 1.82-1.76 (m, 2 H), 1.75-1.70 (m, 1 H), 1.69 (s, 3 H), 1.66-1.60 (m, 2 H), 1.55 (dd, *J* = 9.5, 14.1 Hz, 1 H), 1.41-1.34 (m, 1 H), 1.32-1.20 (m, 2 H), 1.12 (d, *J* = 6.7 Hz, 3 H), 1.08 (d, *J* = 6.3 Hz, 3 H), 1.07-1.02 (m, 1 H), 0.98 (dd, *J* = 7.3, 14.0 Hz, 1 H), 0.90 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.9, 171.2, 171.0, 142.0, 141.0, 133.0, 121.6, 85.0, 83.8, 82.4, 52.2, 45.0, 42.2, 37.6, 34.6, 33.7, 32.2, 30.1, 27.2, 25.7, 23.52, 23.41, 20.4, 20.1; high resolution mass spectra (ES+) m/z 415.2136 [$(M-H)^+$; calcd for $C_{24}H_{31}O_6^+$: 415.2120].