SUPPORTING INFORMATION

(+)-Sorangicin A: Evolution of a Viable Synthetic Strategy

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Experimental procedures for all compounds and NMR spectra of synthetic and natural (+)-sorangicin A.

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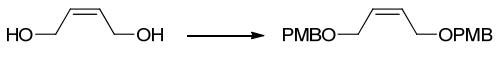
Experimental Section

Materials and Methods: Except as otherwise indicated, all reactions were carried out under an argon atmosphere in flame- or oven-dried glassware previously base-bathed in a KOH/2-propanol mixture overnight. The argon was sequentially dried and deoxygenated by passage through a Drierite tube and OXICLEAR™ filter from Aldrich, respectively. All azeotroping was performed from either HPLC grade benzene or toluene (stored over microwave activated 4 Å molecular sieves). Unless indicated otherwise, dry tetrahydrofuran (THF) and dichloromethane (CH_2Cl_2) were prepared via addition of microwave activated 4 Å molecular sieves to new HPLC grade solvent, sparging the solutions with argon, and sealing the bottles with Aldrich sure-seal caps. When noted, THF and diethyl ether were distilled from sodium/benzophenone. Toluene was distilled from calcium hydride. When noted, BF_3•OEt_2 was distilled over CaH_2 under aspirator pressure (bp ~50 ^oC, ~25 mmHg). Anhydrous dimethylformamide was purchased from Aldrich or Acros and used without purification. *n*-Butylithium (*n*-BuLi), *t*-butyllithium (*t*-BuLi) and methyllithium (MeLi) were purchased from Aldrich and titrated against *n*-benzylbenzamide prior to use.[1] 1,2,4,5-Di-*O*-isopropylidene-D-erythro-2,3-hexodiulo-2,6-pyranose (~5 g) was purchased from Aldrich, dissolved in hot hexanes (60 mL), and the solution decanted from a waxy yellow residue. The solution was then kept at ~0 ^oC for 8 h, and the resulting solid filtered, washed with cold hexanes, and dried under high vacuum to furnish ~5 g of recrystallized 1,2,4,5-Di-*O*-isopropylidene-D-erythro-2,3-hexodiulo-2,6-pyranose, mp = 97-98 ^oC. Acetylene was purchased from BOC gases, TMS-acetylene from GFS chemicals and *tert*-butyldiphenylsilyl chloride (BPSCl) from Gelest. Except as indicated otherwise, all other reagents were purchased from Aldrich, Acros, or Strem chemicals and used as received.

Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.25-mm E. Merck pre-coated silica gel plates. Silica gel for flash chromatography (particle size 0.040-0.063 mm) was supplied by Bodman, Silicycle and Sorbent Technologies. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated.

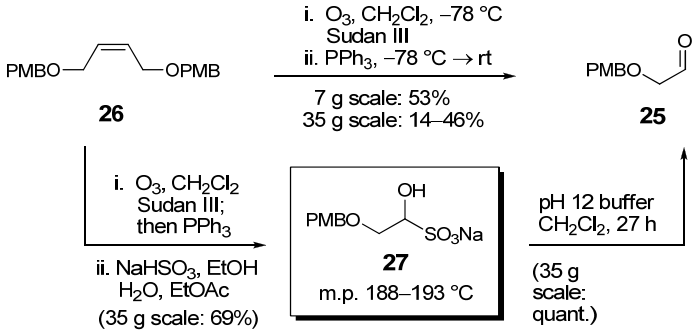
All melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were recorded on either a Perkin-Elmer Model 283B, Perkin-Elmer Model 1600 FTIR, or Jasco FTIR-480plus spectrometer. ^1H and ^{13}C spectra were recorded on a Bruker AMX-500 spectrometer. Chemical shifts are reported as δ values relative to internal chloroform (δ 7.26) benzene (δ 7.15) or DMSO (δ 2.50) for ^1H and either chloroform (δ 77.0) benzene (δ 128.0) or DMSO (δ 39.5) for ^{13}C. Optical rotations were obtained with a Perkin-Elmer model 241 polarimeter in the solvent

indicated. High resolution mass spectra were measured at the University of Pennsylvania Mass Spectrometry Center by Dr. Rakesh Kohli or Mr. John Dykins on either a VG Micromass 70/70H or VG ZAB-E spectrometer.



26

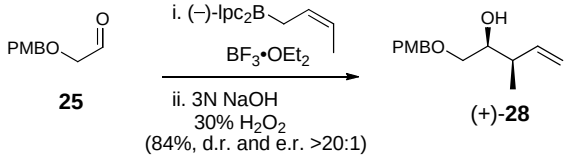
Bis-PMB ether 26. NaH (5.60 g, 60% wt., 139 mmol) was first washed with HPLC grade hexanes (3 x 30 mL) and dried under high vacuum. DMF (90.0 mL) was then added, and the white suspension was carefully treated with a solution of distilled *cis*-2-butene-1,4-diol (5.3 g, 60.4 mmol, bp = 103 ^{o}C, ~0.1 atm) in DMF (20 mL), followed by a 10 mL and 5 mL DMF rinse. Gas evolution! The pale brown solution was then warmed to 60 ^{o}C, and after 2 h, treated with tetrabutylammonium iodide (TBAI, 1.10 g, 3.02 139 mmol) and *p*-methoxybenzyl chloride (PMBCl, 18.8 mL, 139 mmol). Exotherm! After 2.5 h, the reaction was cooled to ambient temperature and diluted with diethyl ether (150 mL) and water (150 mL). The aqueous phase was then washed with diethyl ether (3 x 100 mL), and the combined organic layers were washed with water (2 x 50 mL), brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (6/1, hexanes/EtOAc, 10.0 cm diameter column, 5.0 in. SiO_2, flow rate 1.5 in./min.) gave 18.7 g (94% yield) of **26** as a colorless oil: R_f 0.13 (6/1, hexanes/EtOAc); IR (thin film, $CDCl_3$) 3000 (w), 2934 (w), 2836 (m), 1612 (s), 1586 (m), 1513 (s), 1464 (m), 1302 (m), 1248 (s), 1173 (m), 1081 (s), 1035 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.7 Hz, 4 H), 6.87 (d, *J* = 8.7 Hz, 4 H), 5.77 (m, 2 H), 4.42 (br s, 4 H), 4.04 (d, *J* = 3.7 Hz, 4 H), 3.80 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.24, 130.27, 129.50, 129.34, 113.80, 71.86, 65.46, 55.24; HRMS (ES+) m/z 351.1571 [$(M+Na)^+$; calcd for $C_{20}H_{24}O_4Na^+$: 351.1580].



Small-Scale Preparation of Aldehyde 25. On this small scale, HPLC grade CH_2Cl_2 was employed. A solution of bis-PMB ether **26** (7.00 g, 21.5 mmol) and a spatula tip of Sudan III in CH_2Cl_2 (215 mL) was cooled to –78 ^{o}C, and a stream of ozone was bubbled through the orangish/pink solution for 25 min.

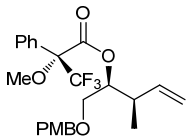
until a yellowish/brown color persisted. After purging the reaction with oxygen for 10 min., a solution of triphenylphosphine (8.40 g, 32.3 mmol) in CH_2Cl_2 (60.0 mL) was added dropwise over 15 min. The dry ice was then removed from the bath, and the solution slowly warmed to ambient temperature over 5.5 h. The orange solution was then concentrated *in vacuo* and purified via bulb to bulb distillation to afford 4.10 g (53% yield) of aldehyde **25** as an orange oil, bp ~135 ^oC (~5 mmHg): IR (thin film, $CDCl_3$) 3002 (w), 2837 (m), 2710 (w), 1733 (s), 1612 (s), 1586 (m), 1515 (s), 1465 (m), 1303 (m), 1249 (s), 1175 (m), 1109 (m), 1033 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.70 (br s, 1 H), 7.28 (d, J = 8.6 Hz, 2 H), 6.89 (d, J = 8.6 Hz, 2 H), 4.56 (br s, 2 H), 4.05 (br s, 2 H), 3.80 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.56, 159.65, 129.70, 128.89, 113.98, 75.00, 73.32, 55.25; HRMS (CI, NH_3) m/z 180.0786 [M^+; calcd for $C_{10}H_{12}O_3^+$: 180.0782].

Large-Scale Preparation of Aldehyde 25. On this large scale, HPLC grade CH_2Cl_2 was employed. A solution of bis-PMB ether **26** (35.0 g, 106 mmol) and a spatula tip of Sudan III in CH_2Cl_2 (190 mL) was cooled to –78 ^oC, and a stream of ozone was bubbled through the redish/pink solution for 1.5 h until an orange color persisted. After purging the reaction with oxygen for 15 min., a solution of triphenylphosphine (30.7 g, 117 mmol) in CH_2Cl_2 (220 mL) was added dropwise over 50 min. via addition funnel. The dry ice was then removed from the bath, and the solution slowly warmed to ambient temperature over 2 h. The orange solution was then concentrated *in vacuo* and the residue dissolved in absolute EtOH (90 mL), water (30 mL) and EtOAc (150 mL). The suspension was then heated to 45 ^oC for 1 h, cooled to 0 ^oC, and the resulting solid was filtered. After washing with cold EtOH (125 mL), the solid was dried under high vacuum to afford 39.4 g (69% yield) of bisulfite adduct **27** as a white powder, mp 188-193 ^oC: IR (KBr pellet) 3287 (br, s), 2926 (m), 2872 (m), 1613 (s), 1586 (w), 1515 (s), 1460 (m), 1409 (w), 1361 (m), 1304 (m), 1247 (s), 1189 (br, s), 1099 (s), 1038 (s) cm^{-1}; ^1H NMR (500 MHz, DMSO) δ 7.22 (d, J = 8.5 Hz, 2 H), 6.87 (d, J = 8.5 Hz, 2 H), 5.45 (dd, J = 5.7, 0.8 Hz, 1 H), 4.39 (d, J_{AB}= 11.6 Hz, 1 H), 4.36 (d, J_{AB}= 11.6 Hz, 1 H), 4.05 (ddd, J = 8.7, 5.7, 1.9 Hz, 1 H), 3.75 (m, 1 H), 3.72 (s, 3 H), 3.32 (dd, J = 10.6, 8.7 Hz, 1 H); ^{13}C NMR (125 MHz, DMSO) δ 158.58, 130.53, 129.14, 113.52, 82.46, 71.68, 71.14, 55.01; HRMS (ES+) m/z 307.0232 [$(M+Na)^+$; calcd for $C_{10}H_{13}O_6SNa_2^+$: 307.0331]. Using a continuous extractor, a solution of bisulfite adduct **27** (50.0 g, 175 mmol) in pH 12 aqueous solution (500 mL) was washed with CH_2Cl_2 brought to reflux. After 6 h, the pH of the aqueous layer had dropped to pH ~10 and solid K_2CO_3 was added to bring the pH back to ~11. After an additional 20 h, the CH_2Cl_2 in the collecting flask was concentrated to a reduced volume *in vacuo*, dried over $MgSO_4$ and reconcentrated to afford 31.6 g (100% yield) of aldehyde **25** as a pale green oil which was used without any further purification.



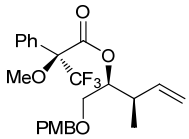
Alcohol (+)-28. Potassium *tert*-butoxide (~5.5 g) was heated at 100 °C under high vacuum overnight to dry. Some of this solid was then removed, and the flask containing the remaining KO*t*-Bu (4.20 g, 37.6 mmol) was equipped with a mechanical stir bar, charged with THF (16 mL), and cooled to –45 °C. *cis*-2-Butene (3.7 mL, 40.2 mmol) was then added via cannula, followed by *n*-BuLi (15.1 mL, 2.5 M in hexanes, 37.7 mmol) dropwise over 20 min. to produce an orange suspension. After an additional 5 min., the reaction was cooled to –78 °C and treated with 44.0 mL (13.5 g, 42.7 mmol) of a solution of (–)-methoxydiisocampheylborane (22.5 g, weighed out using a glove-bag) in THF (50 mL, overall volume = 73 mL) dropwise over 15 min. After an additional 30 min., the colorless slurry was sequentially treated with distilled BF_3•OEt_2 (6.40 mL, 50.2 mmol) dropwise over 10 min., azeotroped aldehyde **25** (4.5 g, 25.1 mmol) via syringe pump over 1.5 h, and 2 x 5 mL THF rinses. After an additional 3 h, the pale yellow slurry was charged with 3 N NaOH (45 mL) and allowed to slowly warm to ambient temperature. During this period, H_2O_2 (30% aq., 14.0 mL) was added in 1.5 mL portions to control bubbling, and after complete addition, the reaction was heated to reflux for 1 h. The biphasic solution was then cooled to ambient temperature, and after 12 h, diluted with water (50 mL). The aqueous phase was then washed with diethyl ether (3 x 50 mL) and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Distillation of the IPC-OH (bp ~60 °C, 0.15 mm Hg) left 6.2 g of a residue which was purified by flash chromatography (4/1, CH_2Cl_2/ether, 7.0 cm diameter column, 12.0 in. SiO_2, flow rate 1.0 in./min.) to afford 4.90 g (84% yield) of alcohol (+)-**28** as a pale yellow oil: R_f 0.60 (4/1, CH_2Cl_2/ether); $[\alpha]_D^{20}$ +18.2 (*c* 0.63, C_6H_6); IR (thin film, $CDCl_3$) 3457 (br, m), 3075 (w), 2959 (m), 2907 (m), 2865 (m), 2836 (m), 1639 (w), 1612 (m), 1586 (w), 1513 (s), 1462 (m), 1302 (m), 1248 (s), 1173 (m), 1098 (m), 1035 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.5 Hz, 2 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 5.73 (ddd, *J* = 17.5, 10.3, 7.9 Hz, 1 H), 5.03 (m, 2 H), 4.47 (br s, 2 H), 3.80 (s, 3 H), 3.62 (m, 1 H), 3.53 (dd, *J* = 9.5, 3.1 Hz, 1 H), 3.36 (dd, *J* = 9.5, 7.8 Hz, 1 H), 2.33 (m, 1 H), 1.07 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.21, 140.32, 130.04, 129.30, 114.97, 113.76, 73.33, 72.94, 72.39, 55.19, 41.03, 15.58; HRMS (CI, NH_3) m/z 236.1413 [M^+; calcd for $C_{14}H_{20}O_3^+$: 236.1412].

Determination of Absolute Stereochemistry of (+)-28.



(–)-**SI-1**

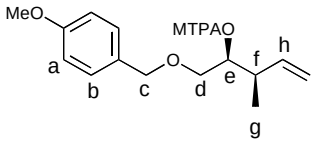
(*S*)-MTPA Ester (–)-SI-1. (*R*)-(-)-α-methoxy-α-trifluoromethylphenylacetyl chloride [(*R*)-MTPACl, 16.0 μL, 84.6 μmol) was added to a solution of (+)-**28** (10.0 mg, 42.3 μmol) and 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 20.6 mg, 169 μmol) in CH_2Cl_2 (500 μL) at ambient temperature. After 3 h, direct purification by Preparative-TLC (5/1, hexanes/EtOAc, 500 μm plate) afforded 18.0 mg (94% yield, >20:1 ratio of diastereomers) of ester (–)-**SI-1** as a colorless oil: R_f 0.42 (5/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –4.5 (*c* 0.71, C_6H_6); IR (thin film, $CDCl_3$) 3071 (w), 2953 (m), 2851 (w), 1749 (s), 1613 (m), 1514 (s), 1452 (m), 1249 (s), 1172 (s), 1123 (m), 1022 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, >20:1 mixture of diastereomers, *represents minor peaks) δ 7.60 (d, *J* = 7.8 Hz, 2 H), 7.35 (m, 1 H), 7.29 (m, 2 H), 7.21 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 5.66 (ddd, *J* = 17.5, 10.0, 7.6 Hz, 1 H), 5.26 (ddd, *J* = 7.1, 7.1, 3.2 Hz, 1 H), 5.15 (m, 2 H), 4.48 (d, J_{AB}= 11.4 Hz, 1 H), 4.41 (d, J_{AB}=11.4 Hz, 1 H), 3.80 (s, 3 H), 3.63 (dd, *J* = 10.9, 3.2 Hz, 1 H), 3.59 (dd, *J* = 10.9, 7.1 Hz, 1 H), 3.56 (s, 3 H), 2.55 (m, 1 H), *1.05 (d, *J* = 6.9 Hz, 3 H), 0.95 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.26, 159.28, 138.65, 132.56, 129.86, 129.42, 129.21, 128.20, 127.51, 124.59, 122.30, 116.04, 113.80, 77.85, 72.74, 69.36, 55.45, 55.27, 38.80, 15.13; HRMS (ES+) m/z 475.1728 [$(M+Na)^+$; calcd for $C_{24}H_{27}F_3O_5Na^+$: 475.1811].



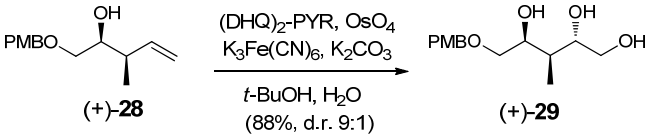
(+)-**SI-2**

(*R*)-MTPA Ester (+)-SI-2. In similar fashion, the (*R*)-MTPA ester of (+)-**28** was obtained in 94% yield as a colorless oil: R_f 0.42 (5/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +36.6 (*c* 0.85, C_6H_6); IR (thin film, $CDCl_3$) 3070 (w), 2952 (m), 2867 (w), 1747 (s), 1613 (m), 1513 (s), 1452 (m), 1250 (s), 1171 (s), 1121 (m), 1019 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, >20:1 mixture of diastereomers, *represents minor peaks) δ 7.56 (d, *J* = 7.6 Hz, 2 H), 7.39-7.31 (m, 3 H), 7.16 (d, *J* = 8.6 Hz, 2 H), 6.84 (d, *J* = 8.6 Hz, 2 H), 5.76 (ddd, *J* = 17.4, 10.4, 7.2 Hz, 1 H), 5.29 (ddd, *J* = 6.8, 6.8, 3.7 Hz, 1 H), 5.09 (m, 2 H), 4.39 (d, J_{AB}= 11.5 Hz, 1 H),

4.35 (d, J_{AB}= 11.5 Hz, 1 H) 3.80 (s, 3 H), 3.56 (dd, *J* = 10.8, 3.7 Hz, 1 H), 3.52 (dd, *J* = 10.8, 6.8 Hz, 1 H), 3.49 (s, 3 H), 2.62 (m, 1 H), 1.06 (d, *J* = 6.9 Hz, 3 H), *0.95 (d, *J* = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.26, 159.23, 138.95, 132.16, 129.94, 129.46, 129.17, 128.22, 127.81, 124.52, 122.23, 116.02, 113.75, 77.97, 72.77, 69.23, 55.44, 55.26, 38.55, 14.90; HRMS (ES+) m/z 475.1712 [$(M+Na)^+$; calcd for $C_{24}H_{27}F_3O_5^+$: 475.1811].



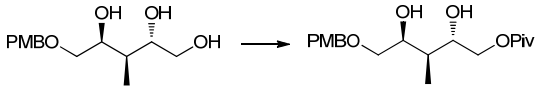
Proton	(*S*)-MTPA ester	(*R*)-MTPA ester	(*S*)-(*R*)
a	7.21	7.16	+0.05
b	6.86	6.84	+0.02
c1/c2	4.48/4.41	4.39/4.34	+0.09/+0.07
d1/d2	3.63/3.59	3.56/3.52	+0.07/+0.07
e	5.26	5.29	-0.03
f	2.55	2.62	-0.07
g	0.95	1.06	-0.11
h	5.66	5.76	-0.10



Triol (+)-29. A 0 ^{o}C suspension of $K_3Fe(CN)_6$ (895 mg, 2.72 mmol), K_2CO_3 (376 mg, 2.72 mmol) and $(DHQ)_2$-PYR (15.9 mg, 18.1 μmol) in *t*-BuOH:H_2O (1:1, 8.0 mL) was charged with OsO_4 (55.0 μL, 4% wt. in H_2O, 9.06 μmol) dropwise. After a few minutes, alcohol (+)-**28** (214 mg, 0.906 mmol) was added dropwise followed by 2 x 0.5 mL *t*-BuOH:H_2O rinses (1:1). After 16 h, the yellow suspension was *carefully* quenched by the portionwise addition of $NaHSO_3$ (1.50 g). Gas evolution! The brown suspension was then diluted with EtOAc (10 mL) and the aqueous phase was washed with EtOAc (3 x 5 mL). The combined organic layers were then washed with brine (5 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford a 9:1 mixture of diastereomers. Purification by flash chromatography (1/5, hexanes/EtOAc, 3.0 cm diameter column, 3.0 in. SiO_2, flow rate 2.0 in./min.) afforded 214 mg (88% yield, 9:1 mixture of diastereomers) of triol (+)-**29** as a pale yellow, viscous oil: R_f 0.24 (1/5, hexanes/EtOAc); $[\alpha]_D^{20}$ +3.0 (*c* 2.10, C_6H_6); IR (thin film, $CDCl_3$) 3388 (br, s), 2933 (m), 1612 (m), 1513 (s), 1457 (m), 1302 (m), 1248 (s), 1174 (m), 1079 (m), 1033 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 9:1 mixture of diastereomers, *represents minor peaks) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.89 (d, *J* = 8.6 Hz,

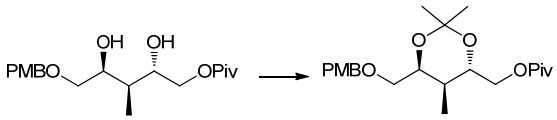
2 H), 4.51 (d, J_{AB}= 11.4 Hz, 1 H), 4.48 (d, J_{AB}= 11.4 Hz, 1 H), 4.08 (ddd, J = 7.3, 3.5, 3.5 Hz, 1 H), 3.81 (s, 3 H), 3.68 (m, 2 H), 3.54 (m, 3 H), 3.47 (m, 1 H), *2.99 (br s, 1 H), 2.87 (br s, 1 H), 2.10 (br, s, 1 H), 1.90 (m, 1 H), *1.76 (m, 1 H), 0.92 (d, J = 7.1 Hz, 3 H), *0.91 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.40, 129.78, 129.43, 113.92, 74.89, 73.18, 71.91, 71.72, 65.03, 55.26, 37.05, 11.47; HRMS (ES+) m/z 293.1354 [$(M+Na)^+$; calcd for $C_{14}H_{22}O_5Na^+$: 293.1467].

Determination of Absolute Stereochemistry from Dihydroxylation



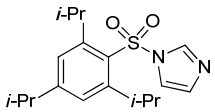
(+)-**29** (+)-**SI-3**

Diol (+)-SI-3. To a -78 °C solution of triol (+)-**29** (15.0 mg, 55.4 μmol) and 2,4,6-collidine (22.0 μL, 166 μmol) in CH_2Cl_2 (300 μL) was added trimethylacetyl chloride (PivCl, 10.0 μL, 83.1 μmol). After 30 min., the dry ice was removed from the bath, and the reaction was allowed to warm to 0 °C over 1.5 h. After 2 h, an additional 2.0 equiv. of 2,4,6-collidine and 1.0 equiv. PivCl were added sequentially. After an additional 45 min., the reaction was charged with a few crystals of 4-(*N*,*N*-dimethylamino)pyridine (DMAP). After 45 min., the reaction was diluted with water (3 mL) and CH_2Cl_2 (10 mL). The aqueous phase was then washed with CH_2Cl_2 (3 x 3 mL), and the combined organic layers were washed with 1 M $NaHSO_4$ (5 mL), sat. $NaHCO_3$ (5 mL), brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by Preparative-TLC (1/1, hexanes/EtOAc, 500 μm plate) afforded 4.3 mg (22% yield) of (+)-**SI-3** as a single diastereomer and 3.4 mg (23% recovery) of triol (+)-**29**. For (+)-**SI-3**: R_f 0.62 (1/5, hexanes/EtOAc); $[\alpha]_D^{20}$ +4.6 (*c* 0.21, CH_2Cl_2); IR (thin film, $CDCl_3$) 3437 (br, m), 2970 (m), 1727 (s), 1613 (m), 1513 (s), 1457 (m), 1286 (m), 1248 (s), 1171 (s), 1099 (m), 1034 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, J = 8.4 Hz, 2 H), 6.88 (d, J = 8.4 Hz, 2 H), 4.51 (d, J_{AB}= 11.4 Hz, 1 H), 4.47 (d, J_{AB}= 11.4 Hz, 1 H), 4.23 (dd, J = 11.5, 3.6 Hz, 1 H), 4.13 (m, 1 H), 4.10 (dd, J = 11.5, 6.5 Hz, 1 H), 3.82 (m, 1 H), 3.80 (s, 3 H), 3.50 (m, 2 H), 3.14 (d, J = 5.0 Hz, 1 H), 2.74 (d, J = 3.0 Hz, 1 H), 1.84 (m, 1 H), 1.21 (s, 9 H), 0.95 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.74, 159.40, 129.93, 129.37, 113.92, 73.25, 73.14, 72.06, 71.18, 67.17, 55.28, 38.87, 37.16, 27.19, 11.22; HRMS (ES+) m/z 377.1956 [$(M+Na)^+$; calcd for $C_{19}H_{30}O_6Na^+$: 377.2042].



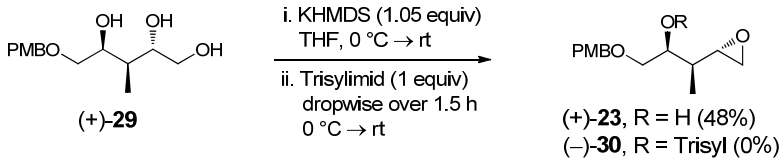
(+)-**SI-3** (+)-**SI-4**

Acetonide (+)-SI-4. To diol (+)-**SI-3** (4.30 mg, 12.1 μmol) and one crystal of *p*-toluenesulfonic acid monohydrate was added distilled 2,2-dimethoxypropane (2,2-DMP, 250 μL, bp 82 °C, 1 atm). After 1 h, the reaction was diluted with CH_2Cl_2 (5 mL) and sat. $NaHCO_3$ (3 mL). The aqueous layer was then washed with CH_2Cl_2 (3 x 3 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by Preparative-TLC (4/1, hexanes/EtOAc, 500 μm plate) afforded 5.3 mg (quant.) of (+)-**SI-4** as a pale yellow oil: R_f 0.43 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +5.3 (*c* 0.26, C_6H_6); IR (thin film, $CDCl_3$) 2981 (m), 2915 (m), 1729 (s), 1612 (m), 1513 (s), 1461 (m), 1379 (m), 1284 (m), 1247 (s), 1224 (s), 1171 (s), 1151 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 4.54 (d, J_{AB}= 11.6 Hz, 1 H), 4.42 (d, J_{AB}= 11.6 Hz, 1 H), 4.19 (dd, *J* = 11.6, 3.0 Hz, 1 H), 4.09 (m, 1 H), 4.02 (dd, *J* = 11.6, 7.3 Hz, 1 H), 3.85 (s, 3 H), 3.50 (m, 1 H), 3.44 (m, 2 H), 1.80 (m, 1 H), 1.37 (s, 3 H), 1.34 (s, 3 H), 1.20 (s, 9 H), 0.89 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.41, 159.25, 130.32, 129.28, 113.79, 100.88, 73.20, 73.03, 69.15, 67.98, 65.20, 55.27, 38.80, 34.67, 27.15, 24.83, 23.66, 11.53; HRMS (ES+) m/z 417.2238 [$(M+Na)^+$; calcd for $C_{22}H_{34}O_6Na^+$: 417.2355].



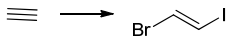
Trisylimidazole (**SI-5**)

2,4,6-Triisopropylbenzenesulfonyl imidazole (SI-5). To a solution of imidazole (15.3 g, 224 mmol) in HPLC grade chloroform (175 mL) was added 2,4,6-triisopropylbenzenesulfonyl chloride (34.0 g, 112 mmol) portionwise over 1-2 min. to afford a cloudy solution. After 1.5 h, the yellow suspension was filtered, and the eluent washed with sat. $NaHCO_3$ (100 mL) and water (2 x 100 mL). The organic layer was then dried over $MgSO_4$ and concentrated *in vacuo*. The white solid was then dissolved in hot benzene (100 mL), diluted with petroleum ether (100 mL) and cooled to 0 °C. After 14 h, the resulting solid was filtered, rinsed with cold petroleum ether, and dried under high vacuum to afford 27.8 g (74% yield) of **SI-5** as a white solid: mp 118-119 °C which matched that reported in the literature.[2]



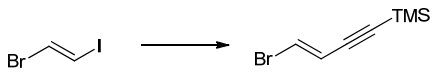
Epoxide (+)-23. To a 0 °C solution of triol (+)-**29** (18.5 mg, 68.4 μmol) in distilled THF (2.0 mL) was added KHMDS (0.5 M in toluene, 146 μL, 73.2 μmol) dropwise. After 10 min., the pale yellow solution was warmed to ambient temperature. Following an additional 20 min., the solution was cooled to –5 °C and treated with a solution of **SI-5** (Trisylimid., 22.8 mg, 68.4 μmol) in THF (300 μL) dropwise over 1.5 h. The homogeneous solution was then warmed to ambient temperature at which time the reaction became cloudy. After 1 h, the reaction was diluted with sat. NH_4Cl (5 mL) and hexanes/EtOAc (10 mL, 1/1). The aqueous phase was then washed with hexanes/EtOAc (3 x 5 mL, 1/1), and the combined organic layers were washed with sat. $NaHCO_3$ (3 x 5 mL), brine (5 mL), filtered through a pad of celite, dried over $MgSO_4$, and concentrated *in vacuo*. Careful purification by Preparative-TLC (9/1, hexanes/IPA, 500 μm plate) afforded 8.2 mg (48% yield) of (+)-**23** as a single diastereomer: R_f 0.41 (1/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +4.0 (*c* 0.40, $CHCl_3$); IR (thin film, $CDCl_3$) 3457 (br, m), 2963 (m), 2910 (m), 1612 (m), 1585 (w), 1513 (s), 1463 (m), 1302 (m), 1248 (s), 1174 (m), 1094 (m), 1033 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.6 Hz, 2 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 4.49 (br s, 2 H), 3.88 (m, 1 H), 3.80 (s, 3 H), 3.63 (dd, *J* = 9.6, 3.3 Hz, 1 H), 3.45 (dd, *J* = 9.6, 8.2 Hz, 1 H), 2.87 (ddd, *J* = 7.6, 4.1, 2.7 Hz, 1 H), 2.76 (dd, *J* = 4.9, 4.1 Hz, 1 H), 2.54 (d, *J* = 3.4 Hz, 1 H), 2.50 (dd, *J* = 4.9, 2.7 Hz, 1 H), 1.36 (m, 1 H), 1.02 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.26, 130.03, 129.37, 113.82, 73.01, 72.63, 72.20, 55.24, 54.30, 46.09, 39.35, 11.35; HRMS (CI, NH_3) m/z 252.1365 [M^+; calcd for $C_{14}H_{20}O_4^+$: 252.1361].

Epoxide (–)-30. R_f 0.39 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –3.6 (*c* 0.26, C_6H_6); IR (thin film, CH_2Cl_2) 2959 (s), 2869 (m), 1612 (m), 1600 (m), 1563 (w), 1513 (s), 1462 (m), 1425 (w), 1375 (m), 1341 (m), 1302 (w), 1248 (s), 1177 (s), 1105 (m), 1037 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (s, 2 H), 7.03 (d, *J* = 8.6 Hz, 2 H), 6.79 (d, *J* = 8.6 Hz, 2 H), 5.07 (m, 1 H), 4.22 (br s, 2 H), 4.17 (septet, *J* = 6.7 Hz, 2 H), 3.78 (s, 3 H), 3.55 (dd, *J* = 10.5, 5.3 Hz, 1 H), 3.49 (dd, *J* = 10.5, 6.0 Hz, 1 H), 2.89 (m, 1 H), 2.88 (m, 1 H), 2.72 (dd, *J* = 4.9, 4.0 Hz, 1 H), 2.49 (dd, *J* = 4.9, 2.6 Hz, 1 H), 1.77 (m, 1 H), 1.25 (d, *J* = 6.7 Hz, 18 H), 0.97 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.20, 153.20, 150.09, 131.80, 129.70, 129.18, 123.54, 113.71, 81.50, 72.73, 69.01, 55.24, 53.22, 45.93, 37.88, 34.21, 29.71, 24.68, 23.59, 10.23; HRMS (ES+) m/z 541.2600 [$(M+Na)^+$; calcd for $C_{29}H_{42}O_6SNa^+$: 541.2599].



SI-6

(*E*)-Iodobromoethylene (SI-6). Acetylene was bubbled through a 0 ^{o}C solution of IBr (47.4 g, 229 mmol) in 48% aqueous HBr (280 mL) with the venting gases directed into a 2 M NaOH solution. After about 1 h, a white precipitate began to form. After 18 h, acetylene bubbling was ceased, and the suspension was warmed to ambient temperature. The now redish/brown solution was then diluted with pentane (50 mL), and the aqueous phase was washed with additional pentane (2 x 25 mL). The combined organic layers were then washed with brine (3 x 25 mL) so the pH of the organic layer was neutral, and the brownish/purple organic phase was washed with sat. $Na_2S_2O_5$ (25 mL) to produce a colorless solution, brine (25 mL), dried over $MgSO_4$ and concentrated *in vacuo* without heating. Purificatiion via short-path distillation under aspirator pressure (25 mmHg, bp 50 ^{o}C) furnished 28.7 g (54% yield) of **SI-6** as a pink oil which solidified upon placing in refrigerator: IR (neat) 3069 (m), 1614 (m), 1559 (m), 1240 (w), 1139 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (d, *J* = 13.4 Hz, 1 H), 6.76 (d, *J* = 13.4 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 110.00, 76.70; HRMS (CI, NH_3) m/z 231.8386 [M^+; calcd for $C_2H_2BrI^+$: 231.8386].

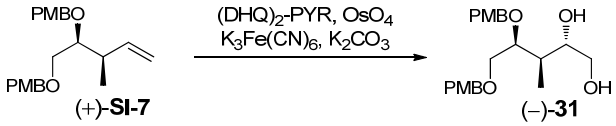


SI-6 **24**

Vinyl Bromide 24. To a solution of trimethylsilyl acetylene (2.50 mL, 17.4 mmol) in THF (25 mL) was added methylmagnesium bromide (7.00 mL, 3 M in diethyl ether, 20.9 mmol) dropwise over 5 min. Gas evolution! After 3 h, the pale brown solution was cannulated into a 0 ^{o}C suspension of flame-dried $ZnBr_2$ (5.10 g, 22.6 mmol) in THF (18.0 mL), followed by a 5 mL THF rinse. After 30 min., the white slurry was charged with a solution of **SI-6** (4.40 g, 19.1 mmol) and $Pd(PPh_3)_4$ (393 mg, 0.348 mmol) in THF (12.0 mL) via cannula, followed by a 1 mL THF rinse. The resulting slurry was then allowed to warm to ambient temperature, and after 17 h, was carefully quenched with sat. NH_4Cl (50 mL) and diluted with pentane (100 mL). The aqueous phase was then washed with pentane (2 x 20 mL), and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The resulting oil with solid material was then filtered, rinsing with pentane, and the eluent was concentrated *in vacuo* to afford an orange oil. Purification via Kugelror distillation (15 mmHg, bp <60 ^{o}C) initial produced material (~200 mg) that contained both **24** and recovered **SI-6**. This material was discarded, and upon heating the apparatus to >60 ^{o}C, 3.2 g of a pale yellow oil composed of a 14:1 mixture of **24**:**SI-6** was isolated. Redistillation of this material afforded 2.20 g (64% yield) of **24** as

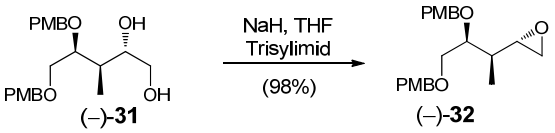
a >20:1 mixture with **SI-6**: bp 72 °C, 15 mmHg; IR (neat) 3073 (w), 2960 (m), 2899 (w), 2168 (m), 2111 (w), 2068 (w), 1694 (w), 1576 (w), 1408 (w), 1251 (s), 1198 (m), 1061 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.74 (d, *J* = 14.1 Hz, 1 H), 6.21 (d, *J* = 14.1 Hz, 1 H), 0.18 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.00, 117.62, 100.90, 97.41, -0.32; HRMS (CI, NH_3) m/z 186.9571 [$(M-CH_3)^+$; calcd for $C_6H_8BrSi^+$: 186.9578].

Bis-PMB ether (+)-SI-7. A suspension of NaH (723 mg, 95% wt., 28.5 mmol) and a spatula tip of tetrabutylammonium iodide (TBAI) in DMF (230 mL) was cooled to 0 °C, and treated with a solution of azeotroped alcohol (+)-**28** (4.50 g, 19.0 mmol) in DMF (10 mL) via cannula, followed by 2 x 5 mL DMF rinses. After 1 h, the orangish slurry was charged with *p*-methoxybenzyl chloride (PMBCl, 3.90 mL, 28.5 mmol) dropwise, and the reaction was allowed to warm to ambient temperature. After 14 h, the reaction mixture was diluted with water (200 mL) and hexanes/EtOAc (1/1, 200 mL). The aqueous phase was then washed with hexanes/EtOAc (1/1, 3 x 100 mL), and the combined organic layers were washed with brine (100 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (10/1, hexanes/EtOAc, 10.0 cm diameter column, 8.0 in. SiO_2, flow rate 1.5 in./min.) afforded 6.50 g (97% yield) of bis-PMB ether (+)-**SI-7** as a pale yellow oil: R_f 0.18 (10/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +6.1 (*c* 0.98, CH_2Cl_2); IR (thin film, $CDCl_3$) 2933 (w), 2904 (w), 2862 (w), 2835 (w), 1612 (m), 1513 (s), 1464 (w), 1301 (m), 1247 (s), 1172 (m), 1088 (m), 1035 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.7 Hz, 2 H), 7.26 (d, *J* = 8.7 Hz, 2 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 5.81 (ddd, *J* = 17.6, 10.3, 7.6 Hz, 1 H), 5.04 (m, 1 H), 4.99 (m, 1 H), 4.65 (d, J_{AB}= 11.2 Hz, 1 H), 4.51 (d, J_{AB}= 11.2 Hz, 1 H), 4.46 (br s, 2 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.58 (dd, *J* = 10.2, 3.7 Hz, 1 H), 3.50 (dd, *J* = 10.2, 6.1 Hz, 1 H), 3.44 (ddd, *J* = 6.1, 6.1, 3.7 Hz, 1 H), 2.48 (m, 1 H), 1.05 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.07, 159.00, 141.01, 131.07, 130.54, 129.31, 129.15, 114.39, 113.68, 113.60, 81.43, 72.91, 72.35, 71.20, 55.22, 39.94, 15.51; HRMS (ES+) m/z 379.1875 [$(M+Na)^+$; calcd for $C_{22}H_{28}O_4Na^+$: 379.1988].

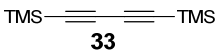


Small-Scale Preparation of Diol (–)-31. A 0 °C, mechanical stirred suspension of $K_3Fe(CN)_6$ (18.2 g, 55.2 mmol), K_2CO_3 (7.60 g, 55.2 mmol) and $(DHQ)_2$-PYR (325 mg, 0.368 mmol) in *t*-BuOH:H_2O (1:1, 150 mL) was charged with OsO_4 (1.10 mL, 4% wt. in H_2O, 0.184 mmol) dropwise. After a few minutes, bis-PMB ether (+)-**SI-7** (6.50 g, 18.4 mmol) was added dropwise followed by 3 x 12 mL *t*-BuOH:H_2O rinses (1:1). After 14 h, the orange suspension was *carefully* quenched by the portionwise addition of $NaHSO_3$ (31 g). Gas evolution! The brown suspension was then diluted with water (250 mL), EtOAc (250 mL), and the aqueous phase was washed with EtOAc (3 x 100 mL). The combined organic layers were then washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford an >7:1 mixture of diastereomers. Purification by flash chromatography (1/2, hexanes/EtOAc, 12.0 cm diameter column, 12.0 in. SiO_2, flow rate 1.0 in./min.) afforded 5.90 g (83% yield, single diastereomer) of diol (–)-**31**, and 885 mg (12% yield) of **31** as an ~2.5:1 mixture of diastereomers, as pale yellow, viscous oils. For (–)-**31**: R_f 0.32 (1/2, hexanes/EtOAc); $[\alpha]_D^{20}$ –14.1 (*c* 1.52, $CHCl_3$); IR (thin film, $CDCl_3$) 3418 (br, m), 2933 (m), 2836 (m), 1612 (m), 1514 (s), 1463 (m), 1302 (m), 1248 (s), 1173 (m), 1074 (m), 1034 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.5 Hz, 2 H), 7.25 (d, *J* = 8.5 Hz, 2 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 4.66 (d, J_{AB}= 11.3 Hz, 1 H), 4.54 (d, J_{AB}= 11.3 Hz, 1 H), 4.49 (d, J_{AB}= 11.5 Hz, 1 H), 4.46 (d, J_{AB}= 11.5 Hz, 1 H), 3.85 (m, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.68 (dd, *J* = 10.2, 6.1 Hz, 1 H), 3.64 (m, 1 H), 3.59 (app dd, *J* = 10.2, 4.1 Hz, 2 H), 3.47 (dd, *J* = 10.8, 5.8 Hz, 1 H), 1.99 (m, 1 H), 0.88 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.25, 159.20, 130.20, 130.04, 129.48, 129.22, 113.80, 113.78, 79.59, 74.14, 73.07, 72.01, 70.40, 65.00, 55.23, 36.91, 12.08; HRMS (ES+) m/z 413.1946 [$(M+Na)^+$; calcd for $C_{22}H_{30}O_6Na^+$: 413.2042].

Large-Scale Preparation of Diol (–)-11. On larger scales (i.e., 57.5 g olefin), only 0.01 equiv $(DHQ)_2$-PYR (1.4 g) was employed, and the ligand was recovered as follows: The combined organic layers were washed with 3% aqueous H_2SO_4 (450 mL) to produce an aqueous layer containing a precipitate. The organic layers were then washed with additional 3% aqueous H_2SO_4 (2 x 150 mL). The combined blue/green aqueous layers were then diluted with CH_2Cl_2 (200 mL) and basified with 3 N NaOH (300 mL) so the pH was ~14. The now brownish aqueous layer was then washed with CH_2Cl_2 (2 x 100 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated to afford a pale green foam. This material was then dissolved in EtOAc (7 mL), and placed in a refrigerator overnight. Filtration, rinsing with cold EtOAc, and two repetitive filtrations of the collected eluent afforded 710 mg (50% yield) of recovered $(DHQ)_2$-PYR. The ^1H NMR of this recovered material was identical to that of commercially available ligand.



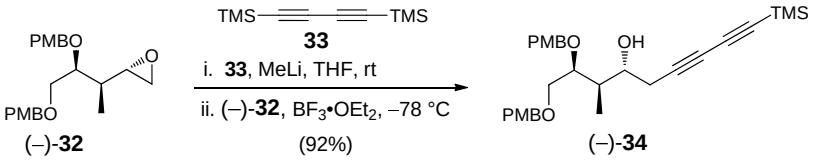
Epoxide (–)-32. On this large scale, HPLC grade THF was employed. To a mechanically stirred, 0 °C suspension of NaH (4.60 g, 95% wt, 183 mmol) in THF (1.1 L) was added a solution of diol (–)-**31** (23.8 g, 60.9 mmol) in THF (200 mL) via cannula, followed by 2 x 50 mL THF rinses. After 1 h, the white suspension was charged with a solution of **SI-5** (Trisylimid., 18.5 g, 55.4 mmol) in THF (200 mL) via syringe pump over 2.5 h. Following an additional 1 h, the white slurry was carefully quenched with sat. NH_4Cl (500 mL), and diluted with water (500 mL). The aqueous phase was then washed with diethyl ether (4 x 250 mL), and the combined organic layers were washed with sat. $NaHCO_3$ (2 x 250 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Purification by flash chromatography (4/1, hexanes/EtOAc → 100% EtOAc, 11.0 cm diameter column, 4.5 in. SiO_2, flow rate 1.5 in./min.) afforded 20.1 g (98% yield) of epoxide (–)-**32** as a pale yellow oil: R_f 0.17 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –14.4 (*c* 0.77, $CHCl_3$); IR (thin film, $CDCl_3$) 2995 (w), 2934 (w), 2907 (w), 2862 (w), 2835 (w), 1612 (m), 1585 (w), 1513 (s), 1463 (m), 1301 (m), 1247 (s), 1172 (m), 1085 (m), 1034 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.4 Hz, 2 H), 7.26 (d, *J* = 8.4 Hz, 2 H), 6.88 (d, *J* = 8.4 Hz, 2 H), 6.86 (d, *J* = 8.4 Hz, 2 H), 4.70 (d, J_{AB} = 11.2 Hz, 1 H), 4.55 (d, J_{AB} = 11.2 Hz, 1 H), 4.49 (d, J_{AB} = 11.5 Hz, 1 H), 4.45 (d, J_{AB} = 11.5 Hz, 1 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.78 (m, 1 H), 3.60 (app d, *J* = 5.7 Hz, 2 H), 2.92 (ddd, *J* = 6.9, 3.9, 2.7 Hz, 1 H), 2.76 (m, 1 H), 2.50 (dd, *J* = 5.1, 2.7 Hz, 1 H), 1.53 (m, 1 H), 0.95 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.05, 158.99, 130.95, 130.35, 129.24, 129.13, 113.65, 113.58, 78.96, 72.88, 72.78, 71.05, 55.15, 54.18, 46.42, 38.73, 10.33; HRMS (ES+) m/z 395.1835 [$(M+Na)^+$; calcd for $C_{22}H_{28}O_5Na^+$: 395.1834].



33

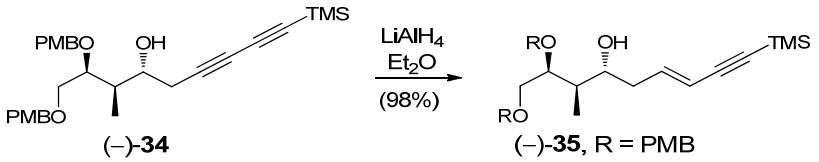
1,4-bis(trimethylsilyl)-1,3-butadiyne (33). Although commercially available, large quantities of **33** were prepared as follows. On this large scale, HPLC grade acetone was employed. A suspension of CuCl (10.0 g, 0.100 mmol) in acetone (180 mL) was purged with argon for 10 min., and charged with *N*, *N*, *N*', *N*'-tetramethylethylenediamine (TMEDA, 5.0 mL, 0.030 mmol). Stirring was stopped after 30 min., and the remaining solid allowed to settle, leaving a deep blue/green solution. A 2 L, four-neck flask, equipped with a mechanical stirrer, thermometer, dry-ice cold trap and O_2 gas inlet was then charged with acetone (600 mL) and (trimethylsilyl)acetylene (100 g, 1.00 mole). O_2 was then bubbled through the stirring solution (the venting O_2 was diluted with argon) and the CuCl/TMEDA solution was

added in 5 mL aliquots. During this time, the reaction turned blue/green and was slightly exothermic. If the reaction began to fade to an orange/brown color, simply increase the O_2 flow. Once the internal temperature reached 35 °C, the reaction was cooled with an ice-bath to bring the temperature down to ~25 °C. After complete addition of the CuCl/TMEDA solution, the reaction was kept between 25-30 °C using a warm water bath. After 2.5 h, O_2 bubbling was stopped, and the reaction was concentrated *in vacuo*. The solid residue was then diluted with pentane (300 mL) and washed with 3 N HCl (300 mL). The aqueous layer was then washed with pentane (3 x 200 mL), and the combined organic layers were washed with brine (100 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The orange/white residue was then charged with MeOH (800 mL), 3 N HCl (8 mL) and heated until complete dissolution occurred. Water was then added until the precipitate persisted, and the flask was allowed to cool to ambient temperature before placing in an ice bath. The solid was then filtered, rinsed with MeOH:H_2O (1:1, 100 mL), and dried under high vacuum to afford 99.0 g (100 % yield) of 1,4-bis(trimethylsilyl)-1,3-butadiyne (**33**) as a white/grey solid: mp 109-110 °C. The mp and NMR data matched those of the commercially available material and literature values.[3]



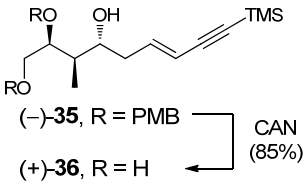
Diyne (–)-34. On this large scale, HPLC grade THF was employed. To a solution of **33** (21.0 g, 108 mmol) in THF (440 mL) was added MeLi (82 mL, 1.32 M in diethyl ether, 108 mmol) dropwise over 2-3 min. to afford a slightly cloudy yellow solution. A slight exotherm was observed on this larger scale! After 30 min., the reaction was cooled to –78 °C, and treated with a –78 °C solution of azeotroped epoxide (–)-**32** (21.0 g, 54.0 mmol) in THF (90 mL) via cannula, followed by 2 x 10 mL THF rinses. BF_3•OEt_2 (10.3 mL, 81.0 mmol) was then added dropwise over 2-3 min. After 30 min., the reaction was poured into stirring sat. NH_4Cl (500 mL), and diluted with diethyl ether (100 mL). The aqueous phase was then washed with CH_2Cl_2 (2 x 200 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (4/1, hexanes/EtOAc, 11.0 cm diameter column, 4.0 in. SiO_2, flow rate 1.5 in./min.) afforded 24.5 g (92% yield) of diyne (–)-**34** as a viscous yellow oil: R_f 0.40 (3/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –74.0 (*c* 1.82, C_6H_6); IR (thin film, CH_2Cl_2) 3446 (br, m), 2957 (m), 2909 (m), 2836 (m), 2224 (m), 2107 (m), 1612 (m), 1513 (s), 1464 (m), 1302 (m), 1249 (s), 1173 (m), 1035 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.6 Hz, 2 H), 7.24 (d, *J* = 8.6 Hz, 2 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 4.67 (d, J_{AB}= 11.2 Hz, 1 H), 4.54

(d, J_{AB}= 11.2 Hz, 1 H), 4.49 (d, J_{AB}= 11.5 Hz, 1 H), 4.46 (d, J_{AB}= 11.5 Hz, 1 H), 3.94 (m, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.67 (app dd, *J* = 10.2, 6.3 Hz, 2 H), 3.56 (dd, *J* = 10.2, 4.2 Hz, 1 H), 3.35 (d, *J* = 5.6 Hz, 1 H), 2.50 (dd, *J* = 17.4, 5.4 Hz, 1 H), 2.44 (dd, *J* = 17.4, 5.6 Hz, 1 H), 2.01 (m, 1 H), 0.90 (d, *J* = 7.1 Hz, 3 H), 0.18 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.24, 159.19, 130.19, 130.09, 129.59, 129.23, 113.78, 88.31, 83.49, 78.37, 76.46, 73.01, 72.52, 72.06, 71.10, 67.30, 55.21, 38.73, 26.17, 11.81, -0.40; HRMS (ES+) m/z 517.2372 [$(M+Na)^+$; calcd for $C_{29}H_{38}O_5SiNa^+$: 517.2489].

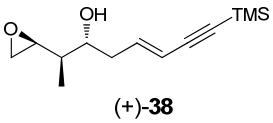


(–)-**34** (–)-**35**, R = PMB

Enyne (–)-35. On this large scale, anhydrous 20 L diethyl ether was employed. To a mechanically stirred suspension of lithium aluminum hydride (4.80 g, 95% wt., 121 mmol) in diethyl ether (1050 mL) was added a solution of diyne (–)-**34** (24.0 g, 48.5 mmol) in diethyl ether (100 mL) via cannula, followed by 2 x 50 mL diethyl ether rinses. Gas Evolution! The grey suspension was then heated to reflux for 5 h, cooled to ambient temperature, and carefully quenched by the portionwise addition of 2:1 Na_2SO_4•$10H_2O$:celite (170 g). Gas evolution! The suspension was then diluted with CH_2Cl_2 (250 mL). After 30 min., Na_2SO_4 (170 g) was added, and the suspension filtered, rinsing with CH_2Cl_2. The eluent was then concentrated *in vacuo* to afford 23.6 g (98% yield) of (–)-**35** as a yellow oil which was used without further purification: R_f 0.64 (2/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –14.5 (*c* 1.90, CH_2Cl_2); IR (thin film, $CDCl_3$) 3473 (br, m), 2956 (s), 2906 (s), 2171 (w), 2132 (m), 1935 (w), 1612 (s), 1585 (m), 1514 (s), 1302 (s), 1248 (s), 1173 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.6 Hz, 2 H), 7.24 (d, *J* = 8.6 Hz, 2 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 6.25 (ddd, *J* = 15.9, 7.3, 7.3 Hz, 1 H), 5.54 (d, *J* = 15.9 Hz, 1 H), 4.66 (d, J_{AB}= 11.3 Hz, 1 H), 4.53 (d, J_{AB}= 11.3 Hz, 1 H), 4.48 (d, J_{AB}= 11.6 Hz, 1 H), 4.45 (d, J_{AB}= 11.6 Hz, 1 H), 3.90 (m, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.67 (dd, *J* = 10.1, 6.3 Hz, 1 H), 3.56 (m, 1 H), 3.54 (dd, *J* = 10.1, 4.3 Hz, 1 H), 2.31 (m, 1 H), 2.17 (m, 1 H), 1.80 (m, 1 H), 0.88 (d, *J* = 7.1 Hz, 3 H), 0.18 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.25, 159.20, 147.27, 130.26, 130.14, 129.60, 129.23, 113.79, 111.97, 103.85, 93.06, 78.76, 73.42, 73.03, 71.98, 71.08, 55.24, 39.25, 38.92, 11.96, -0.06; HRMS (ES+) m/z 519.2525 [$(M+Na)^+$; calcd for $C_{29}H_{40}O_5SiNa^+$: 519.2645].

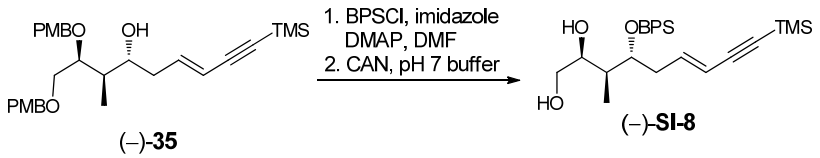


Triol (+)-36 To a 0 °C solution of enyne (–)-**35** (124 mg, 0.250 mmol) in HPLC grade acetonitrile (6.5 mL) and pH 7 buffer (650 μL) was added ammonium cerium(IV) nitrate (CAN, 824 mg, 1.50 mmol) in one portion. The ice bath was then removed, and the reaction was allowed to warm to ambient temperature. After 40 min., the orange suspension was quenched with sat. $NaHCO_3$ (10 mL). EtOAc (20 mL) and water (10 mL) were then added, and the aqueous phase was washed with EtOAc (4 x 5 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (100% EtOAc, prepared column with 1% Et_3N in 100% EtOAc, 1.5 cm diameter column, 4.0 in. SiO_2, flow rate 2.0 in./min.) afforded 54.8 mg (85% yield) of triol (+)-**36** as a yellow oil: R_f 0.33 (EtOAc); $[\alpha]_D^{20}$ +20.5 (*c* 0.36, C_6H_6); IR (thin film, $CDCl_3$) 3356 (br, s), 2958 (s), 2898 (s), 2171 (w), 2133 (m), 1421 (m), 1249 (s), 1082 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.21 (m, 1 H), 5.61 (d, *J* = 15.9 Hz, 1 H), 3.98 (br m, 1 H), 3.67 (br m, 2 H), 3.61 (br m, 1 H), 2.41 (m, 1 H), 2.29 (m, 1 H), 1.73 (m, 1 H), 0.94 (d, *J* = 7.0 Hz, 3 H), 0.18 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.03, 113.17, 103.27, 93.81, 74.21, 73.38, 64.44, 39.33, 39.20, 12.17, -0.15; HRMS (CI, NH_3) m/z 257.1575 [$(MH)^+$; calcd for $C_{13}H_{25}O_3Si^+$: 257.1573].



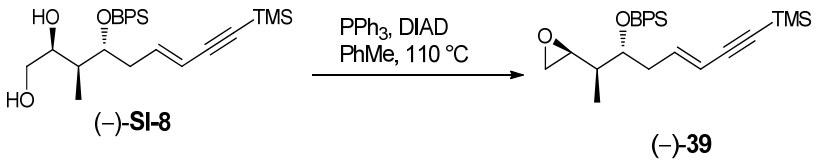
(+)-**38**

Epoxide (+)-38. Under a variety of conditions, yields ranged from 25-61%. This chemistry was not utilized to bring through large amounts of material, and as such an experimental procedure has not been provided. However, characterization data for (+)-**38** is as follows: R_f 0.26 (2/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +31.8 (*c* 0.66, C_6H_6); IR (thin film, C_6D_6) 3445 (br, s), 2962 (s), 2899 (m), 2172 (w), 2134 (m), 1409 (w), 1249 (s), 1082 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 6.20 (ddd, *J* = 15.9, 7.4, 7.4 Hz, 1 H), 5.52 (ddd, *J* = 15.9, 1.4, 1.4 Hz, 1 H), 3.05 (ddd, *J* = 11.9, 8.0, 4.1 Hz, 1 H), 2.58 (ddd, *J* = 6.5, 3.8, 2.8 Hz, 1 H), 2.29 (dd, *J* = 4.9, 3.8 Hz, 1 H), 2.17 (dd, *J* = 4.9, 2.8 Hz, 1 H), 1.92 (dddd, *J* = 14.4, 7.4, 4.1, 1.4 Hz, 1 H), 1.84 (m, 1 H), 1.40 (d, *J* = 4.1 Hz, 1 H), 1.13 (m, 1 H), 0.70 (d, *J* = 6.9 Hz, 3 H), 0.21 (s, 9 H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.18, 112.91, 104.60, 93.56, 72.92, 53.91, 46.06, 40.57, 38.61, 12.97, 0.04; HRMS (CI, NH_3) m/z 239.1461 [MH^+; calcd for $C_{13}H_{23}O_2Si^+$: 239.1466].



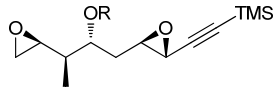
(–)-**35** (–)-**SI-8**

Diol (–)-SI-8. To a 60 °C solution of alcohol (–)-**35** (3.80 g, 7.80 mmol), imidazole (1.20 g, 18.7 mmol), and 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 47.6 mg, 0.390 mmol) in DMF (6.0 mL) was added BPSCl (2.40 mL, 9.36 mmol) dropwise. After 24 h, the reaction was diluted with water (100 mL) and diethyl ether (150 mL). The aqueous phase was then washed with diethyl ether (4 x 25 mL), and the combined organic layers were washed with water (6 x 25 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford an orange oil, which due to the difficulty in removing the generated BPSOH, was used without further purification. To a 0 °C solution of the crude BPS ether in HPLC grade CH_3CN (207 mL) and pH 7 buffer (20.7 mL) was added ammonium cerium(IV) nitrate (CAN, 25.7 g, 46.8 mmol) in one portion. After 1.5 h, the ice bath was removed, and the reaction was allowed to warm to ambient temperature. After an additional 1 h, the reaction was diluted with sat. $NaHCO_3$ (100 mL). Gas Evolution! The suspension was then diluted with water (300 mL) and EtOAc (200 mL), and the aqueous phase was washed with EtOAc (4 x 100 mL). The combined organic layers were then dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (4/1 → 2/1, hexanes/EtOAc, prepared column with 1% Et_3N in 4/1 hexanes/EtOAc, 7.0 cm diameter column, 8.0 in. SiO_2, flow rate 1.5 in./min.) afforded 2.80 g (73% yield, 2 steps) of diol (–)-**SI-8** as a yellow oil: R_f 0.20 (2/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –70.5 (*c* 0.56, C_6H_6); IR (thin film, $CDCl_3$) 3398 (br, m), 3071 (w), 2958 (m), 2931 (m), 2895 (m), 2858 (m), 2198 (w), 2134 (w), 1472 (m), 1427 (m), 1249 (m), 1111 (s), 1082 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.0, 1.4 Hz, 2 H), 7.66 (dd, *J* = 8.0, 1.4 Hz, 2 H), 7.45 (m, 3 H), 7.40 (m, 3 H), 5.78 (ddd, *J* = 15.9, 7.5, 7.5 Hz, 1 H), 5.25 (ddd, *J* = 15.9, 1.1, 1.1 Hz, 1 H), 4.11 (m, 1 H), 3.70 (m, 1 H), 3.59 (ddd, *J* = 11.5, 8.2, 3.7 Hz, 1 H), 3.43 (ddd, *J* = 11.5, 8.2, 3.9 Hz, 1 H), 3.20 (br s, 1 H), 2.45 (m, 1 H), 2.23 (m, 1 H), 1.88 (dd, *J* = 8.2, 3.7 Hz, 1 H), 1.60 (m, 1 H), 1.07 (s, 9 H), 0.98 (d, *J* = 7.0 Hz, 3 H), 0.15 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.40, 136.05, 135.91, 133.39, 132.26, 130.22, 129.96, 127.88, 127.69, 112.64, 103.37, 93.75, 78.45, 71.02, 65.50, 38.26, 37.14, 27.05, 19.40, 11.63, -0.11; HRMS (ESI) m/z 517.2545 [$(M+Na)^+$; calcd for $C_{29}H_{42}O_3Si_2Na^+$: 517.2672].



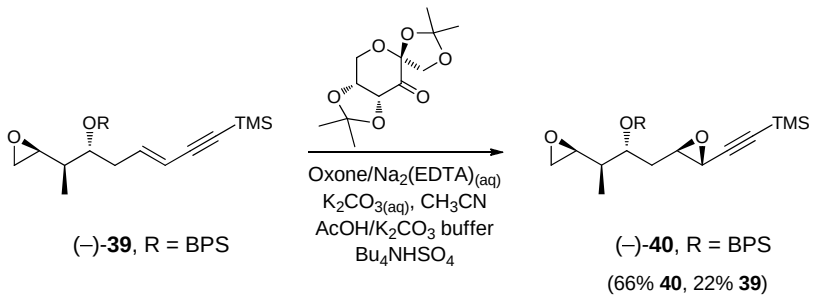
(–)-**SI-8** (–)-**39**

Epoxide (–)-39. On this large scale, HPLC grade toluene was employed. To a solution of diol (–)-**SI-8** (3.90 g, 7.90 mmol) and PPh_3 (10.3 g, 39.5 mmol) in toluene (106 mL) was added diisopropyl azodicarboxylate (DIAD, 7.7 mL, 39.5 mmol) dropwise to produce an orange solution. After 10 min., the reaction was heated to reflux and stirred for 29 h. The solution was then cooled to ambient temperature, concentrated *in vacuo*, and preabsorbed onto silica gel (100 mL). Purification by flash chromatography (50/1 → 20/1, hexanes/acetone, 7.0 cm diameter column, 7.0 in. SiO_2, flow rate 1.5 in./min.) afforded 3.40 g (91% yield) of epoxide (–)-**39** as a yellow oil: R_f 0.47 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –69.0 (*c* 0.51, C_6H_6); IR (thin film, $CDCl_3$) 3071 (w), 3047 (w), 2960 (s), 2931 (s), 2895 (s), 2857 (s), 2173 (w), 2135 (w), 1472 (m), 1427 (s), 1247 (s), 1111 (s), 1080 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (m, 4 H), 7.44 (m, 2 H), 7.38 (m, 4 H), 5.97 (ddd, *J* = 15.7, 7.4, 7.4 Hz, 1 H), 5.34 (d, *J* = 15.7 Hz, 1 H), 3.78 (m, 1 H), 2.81 (m, 1 H), 2.69 (m, 1 H), 2.39 (m, 1 H), 2.28 (m, 2 H), 1.39 (m, 1 H), 1.08 (s, 9 H), 1.03 (d, *J* = 6.8 Hz, 3 H), 0.18 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.47, 136.00, 135.97, 133.97, 133.48, 129.82, 129.70, 127.63, 127.55, 112.22, 103.62, 93.36, 75.41, 53.72, 47.29, 41.07, 38.07, 27.06, 19.45, 12.98, -0.07; HRMS (ESI) m/z 499.2467 [$(M+Na)^+$; calcd for $C_{29}H_{40}O_2Si_2Na^+$: 499.2567].



(+)-**10**, R = H

Bis-Epoxide (+)-10. Under a variety of conditions, yields for (+)-**10** were modest. This chemistry was not utilized to bring through large amounts of material, and as such an experimental procedure has not been provided. However, characterization data for (+)-**10** is as follows: R_f 0.21 (2/1, hexanes/EtOAc with 1% Et_3N); $[\alpha]_D^{20}$ +46.4 (*c* 0.95, C_6H_6); IR (thin film, $CDCl_3$) 3465 (m, br), 2963 (m), 2180 (w), 1250 (s), 844 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 3.27 (m, 2 H), 3.02 (d, *J* = 2.2 Hz, 1 H), 2.57 (ddd, *J* = 6.6, 3.9, 2.8 Hz, 1 H), 2.29 (dd, *J* = 4.9, 4.0 Hz, 1 H), 2.19 (dd, *J* = 4.9, 2.7 Hz, 1 H), 1.90 (d, *J* = 4.4 Hz, 1 H), 1.40 (ddd, *J* = 14.2, 10.0, 4.2 Hz, 1 H), 1.13 (m, 2 H), 0.68 (d, *J* = 6.9 Hz, 3 H), 0.13 (s, 9 H); ^{13}C NMR (125 MHz, C_6D_6) δ 103.19, 89.20, 70.97, 58.44, 53.81, 45.91, 45.84, 41.25, 36.71, 12.78, -0.30; HRMS (ES+) m/z 277.1224 [$(M+Na)^+$; calcd for $C_{13}H_{22}O_3SiNa^+$: 277.1234].

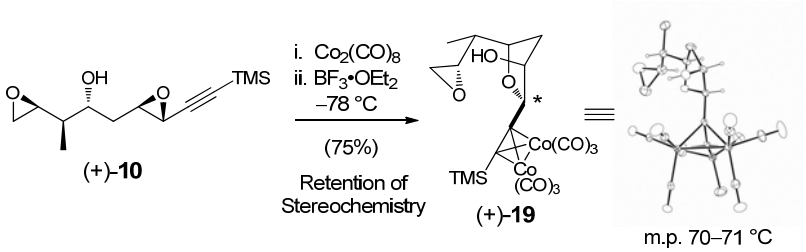


(–)-**39**, R = BPS

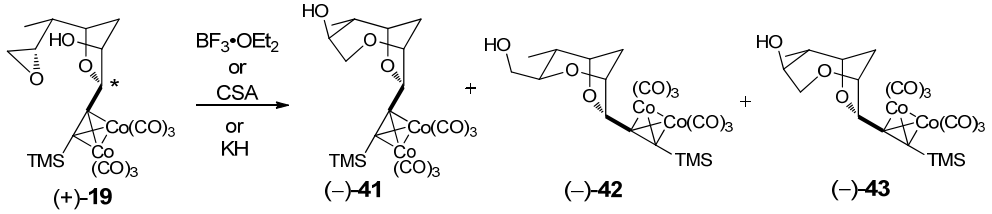
(–)-**40**, R = BPS

(66% **40**, 22% **39**)

Bis-epoxide (–)-40. IMPORTANT: Teflon tubing was used as the needles (no metal needles) for the K_2CO_3 and oxone solutions. To a solution of enyne (–)-**39** (506 mg, 1.06 mmol), 1,2,4,5-Di-*O*-isopropylidene-D-erythro-2,3-hexodiulo-2,6-pyranose (192 mg, 0.742 mmol) and Bu_4NHSO_4 (14.4 mg, 0.0424 mmol) in HPLC grade acetonitrile (39.0 mL) and buffer (10.0 mL, prepared by adding 0.5 mL AcOH to a 0.1 M $K_2CO_{2(aq)}$ solution), not under argon, was sequentially added a drop of the K_2CO_3 solution (1.28 g in 6.75 mL water, 9.22 mmol), followed by a drop of oxone solution [1.351 g in aqueous Na_2EDTA (6.75 mL, 4 x 10^{-4} M), 2.19 mmol] via a syringe pump over 6 h. The white suspension was then diluted with EtOAc (100 mL) and water (80 mL), and the aqueous phase was washed with EtOAc (3 x 100 mL). The combined organic layers were then dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (20/1 → 10/1, hexanes/EtOAc, 5.0 cm diameter column, 8.0 in. SiO_2, flow rate 1.5 in./min.) afforded 110 mg (22% yield) of recovered enyne (–)-**39**, and 332 mg (66% yield, >8:1 mixture of diastereomers) of bis-epoxide (–)-**40** as pale yellow oils. For (–)-**40**: R_f 0.43 (4/1, hexanes/acetone); $[\alpha]_D^{20}$ –24.6 (*c* 1.23, C_6H_6); IR (thin film, $CDCl_3$) 3071 (w), 3048 (w), 2960 (m), 2931 (m), 2895 (m), 2858 (m), 2180 (w), 1427 (m), 1250 (m), 1111 (s), 1060 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, >8:1 mixture of diastereomers, *represents minor peaks) δ 7.69 (m, 4 H), 7.44 (m, 2 H), 7.39 (m, 4 H), 3.96 (ddd, *J* = 6.7, 5.7, 3.5 Hz, 1 H), *3.17 (ddd, *J* = 5.7, 5.7, 2.1 Hz, 1 H), 3.00 (ddd, *J* = 6.7, 4.5, 2.1 Hz, 1 H), 2.95 (d, *J* = 2.1 Hz, 1 H), *2.88 (d, *J* = 2.1 Hz, 1 H), 2.69 (ddd, *J* = 9.7, 3.8, 2.7 Hz, 1 H), *2.62 (dd, *J* = 5.0, 3.9 Hz, 1 H), 2.60 (dd, *J* = 5.0, 3.8 Hz, 1 H), *2.34 (dd, *J* = 5.0, 2.8 Hz, 1 H), 2.30 (dd, *J* = 5.0, 2.7 Hz, 1 H), 1.82 (ddd, *J* = 14.4, 6.7, 4.5 Hz, 1 H), *1.75 (ddd, *J* = 14.6, 5.9, 5.9 Hz, 1 H), *1.63 (ddd, *J* = 14.6, 5.4, 5.4 Hz, 1 H), 1.57 (ddd, *J* = 14.4, 6.7, 5.7 Hz, 1 H), 1.46 (m, 1 H), 1.08 (s, 9 H), 1.01 (d, *J* = 6.9 Hz, 3 H), 0.16 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$, >8:1 mixture of diastereomers, *represents minor peaks) δ 135.96, 133.72, 133.39, 129.90, 129.82, 127.70, 127.65, 101.56, 89.42, 73.66, 58.12, *57.87, *53.80, 53.36, *46.78, 46.60, 45.83, *45.49, 41.36, 36.42, *35.95, 27.10, 19.44, *14.19, 11.72, -0.32; HRMS (ESI) m/z 515.2432 [$(M+Na)^+$; calcd for $C_{29}H_{40}O_3Si_2Na^+$: 515.2516].

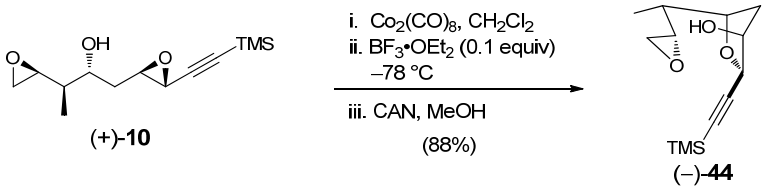


Cobalt Complex (+)-19. To a solution of $Co_2(CO)_8$ (39.2 mg, 0.114 mmol, weighed out using a glove bag) in CH_2Cl_2 (500 μL) was charged a solution of azeotroped bis-epoxide (+)-**10** (26.4 mg, 0.104 mmol) in CH_2Cl_2 (2.5 mL). After 1 h, the dark brown solution was cooled to –78 °C, and after 15 min., treated with 50 μL (0.0104 mmol) of a solution of distilled BF_3•OEt_2 (130 μL, distilled over CaH_2 under aspirator pressure) in CH_2Cl_2 (5.0 mL). After 10 min., the reaction was quenched with water (3 mL), warmed to ambient temperature, and the aqueous phase washed with CH_2Cl_2 (2 x 3 mL). The combined organic layers were then dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (5/1, hexanes/EtOAc, 1.5 cm diameter column, 3.0 in. SiO_2, flow rate 2.0 in./min.) afforded 42.0 mg (75% yield) of (+)-**19** as a brown oil: R_f 0.23 (5/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +45.0 (*c* 0.71, C_6H_6); IR (thin film, $CDCl_3$) 3446 (w), 2963 (w), 2086 (s), 2046 (s), 2016 (s), 1559 (w), 1456 (w), 1247 (w), 1047 (w), 839 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.79 (d, *J* = 3.8 Hz, 1 H), 4.35 (m, 1 H), 3.87 (ddd, *J* = 8.0, 8.0, 8.0 Hz, 1 H), 2.92 (m, 1 H), 2.74 (dd, *J* = 4.6, 4.2 Hz, 1 H), 2.63 (dd, *J* = 4.7, 2.7 Hz, 1 H), 2.52 (m, 1 H), 1.77 (ddd, *J* = 13.7, 7.4, 2.2 Hz, 1 H), 1.59 (d, *J* = 6.7 Hz, 1 H), 1.57 (m, 1 H), 1.03 (d, *J* = 6.8 Hz, 3 H), 0.31 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.17, 128.33, 102.15, 84.62, 79.90, 73.31, 54.68, 47.53, 41.77, 40.76, 13.02, 0.84; HRMS (FAB) m/z 427.9899 [$(M\text{-}4CO)^+$; calcd for $C_{15}H_{22}Co_2O_5Si^+$: 427.9697]. Vapor diffusion crystallization (EtOAc/heptane) afforded crystals suitable for X-ray analysis: mp 70-71 °C.



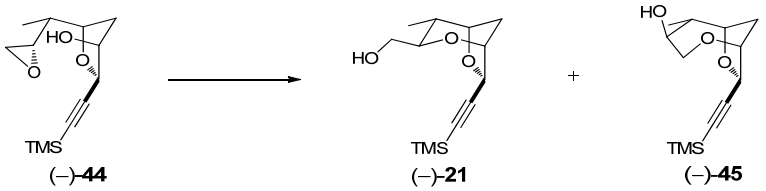
Cobalt Complexes (–)-41, (–)-42 and (–)-43. This chemistry was not utilized to bring through large amounts of material, and as such an experimental procedure has not been provided. However, characterization data is as follows: For (–)-**41:** R_f 0.38 (2/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –10.5 (*c* 0.10, C_6H_6); IR (thin film, C_6D_6) 3395 (br, w), 2960 (w), 2089 (m), 2045 (s), 2018 (s) cm^{-1}; ^1H NMR (500

MHz, C_6D_6) δ 4.63 (br d, *J* = 1.5 Hz, 1 H), 3.89 (br d, *J* = 2.1 Hz, 1 H), 3.84 (d, *J* = 9.4 Hz, 1 H), 3.59 (dd, *J* = 12.8, 2.6 Hz, 1 H), 3.50 (m, 1 H), 3.28 (m, 1 H), 1.71 (d, *J* = 14.5 Hz, 1 H), 1.35 (ddd, *J* = 14.5, 9.4, 3.7 Hz, 1 H), 1.17 (d, *J* = 6.7 Hz, 3 H), 0.86 (m, 1 H), 0.67 (br s, 1 H), 0.32 (s, 9 H); ^{13}C NMR (125 MHz, C_6D_6, unable to observe two carbons bound to cobalt) δ 200.85 (br), 86.30, 81.11, 77.34, 73.79, 68.35, 45.24, 32.88, 16.37, 0.82; HRMS (FAB) m/z 427.9899 [(M-4CO)$^+$; calcd for $C_{15}H_{22}Co_2O_5Si$: 427.9697]. For (–)-**42:** R_f 0.35 (2/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –41.6 (*c* 0.60, C_6H_6); IR (thin film, C_6D_6) 3397 (br, w), 2961 (w), 2089 (m), 2046 (s), 2018 (s) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 5.10 (br s, 1 H), 4.32 (dd, *J* = 4.3, 1.3 Hz, 1 H), 4.07 (ddd, *J* = 3.9, 1.9, 1.9 Hz, 1 H), 3.58 (dd, *J* = 12.6, 2.3 Hz, 1 H), 3.37 (dd, *J* = 12.6, 9.5 Hz, 1 H), 3.14 (m, 1 H), 1.84 (m, 2 H), 1.09 (d, *J* = 6.6 Hz, 3 H), 1.02 (m, 1 H), 0.73 (d, *J* = 5.1 Hz, 1 H), 0.23 (s, 9 H); ^{13}C NMR (125 MHz, C_6D_6, unable to observe two carbons bound to cobalt) δ 200.47, 89.43, 82.99, 82.75, 73.44, 69.19, 45.73, 31.57, 16.36, 0.55; HRMS (FAB) m/z 455.9765 [(M-3CO)$^+$; calcd for $C_{16}H_{22}Co_2O_6Si^+$: 455.9850]. For (–)-**43:** R_f 0.42 (2/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –35.2 (*c* 0.15, C_6H_6); IR (thin film, C_6D_6) 2960 (w), 2089 (m), 2047 (s), 2018 (s) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 5.30 (br s, 1 H), 4.35 (d, *J* = 2.2 Hz, 1 H), 3.96 (d, *J* = 6.4 Hz, 1 H), 3.53 (ddd, *J* = 11.5, 5.2, 2.4 Hz, 1 H), 3.34 (m, 1 H), 3.29 (m, 1 H), 1.89 (ddd, *J* = 11.6, 6.4, 3.0 Hz, 1 H), 1.56 (dd, *J* = 7.9, 5.3 Hz, 1 H), 1.40 (m, 1 H), 1.34 (dd, *J* = 11.6, 1.1 Hz, 1 H), 0.66 (d, *J* = 6.7 Hz, 3 H), 0.22 (s, 9 H); ^{13}C NMR (125 MHz, C_6D_6, unable to observe two carbons bound to cobalt) δ 200.47, 82.55, 80.61, 80.38, 78.19, 63.09, 36.76, 36.45, 15.23, 0.59; HRMS (FAB) m/z 456.0013 [(M-3CO)$^+$; calcd for $C_{16}H_{22}Co_2O_6Si^+$: 455.9850].



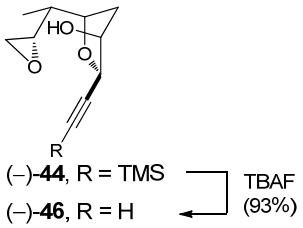
Epoxide (–)-44: One-Flask Preparation from Bis-Epoxide (+)-10. A solution of azeotroped (+)-**10** (21.3 mg, 83.7 μmol) in CH_2Cl_2 (2.7 mL) was treated with 145 μL (31.5 mg, 92.1 μmol) of a solution of Co_2CO_8 (283 mg, weighed out using a glove bag) in CH_2Cl_2 (1.3 mL). After 1 h, the brown solution was cooled to –78 °C, and treated with 50 μL (8.37 μmol) of a solution of distilled BF_3•OEt_2 (105 μL, distilled over CaH_2 under aspirator pressure) in CH_2Cl_2 (5.0 mL). After 10 min., 1.5 mL of a solution of ammonium cerium(IV) nitrate (CAN, 449 mg, 837 μmol) in HPLC grade MeOH was added (solution prepared with 1.8 g CAN and 5.9 mL HPLC grade MeOH). After an additional 10 min., the lighter

orange reaction was quenched with water (5 mL) and warmed to ambient temperature. The reaction was then diluted with water (5 mL) and CH_2Cl_2 (10 mL), and the aqueous phase was washed with CH_2Cl_2 (4 x 10 mL). The combined organic layers were then dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (2/1, hexanes/EtOAc, 1.0 cm diameter column, 4.0 in. SiO_2, flow rate 1.5 in./min.) afforded 18.9 mg (88% yield) of epoxide (–)-**44** as a pale yellow oil. R_f 0.23 (2/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –47.3 (*c* 0.55, C_6H_6); IR (thin film, $CDCl_3$) 3457 (m), 3053 (w), 2962 (s), 2928 (w), 2168 (w), 1326 (w), 1251 (s), 1086 (s), 1045 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.47 (d, *J* = 4.9 Hz, 1 H), 4.30 (dddd, *J* = 6.4, 4.9, 4.9, 4.9 Hz, 1 H), 3.81 (ddd, *J* = 7.7, 7.7, 7.7 Hz, 1 H), 2.89 (ddd, *J* = 6.8, 3.9, 2.7 Hz, 1 H), 2.82 (dd, *J* = 4.9, 4.0 Hz, 1 H), 2.67 (dd, *J* = 4.9, 2.7 Hz, 1 H), 2.31 (m, 1 H), 2.10 (d, *J* = 5.2 Hz, 1 H), 1.78 (ddd, *J* = 13.0, 7.7, 4.5 Hz, 1 H), 1.66 (m, 1 H), 0.98 (d, *J* = 6.9 Hz, 3 H), 0.20 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 100.11, 94.71, 80.79, 74.01, 72.13, 54.54, 47.47, 41.59, 37.76, 12.73, -0.22; HRMS (CI, NH_3) m/z 254.1326 [M^+; calcd for $C_{13}H_{22}O_3Si^+$: 254.1337].

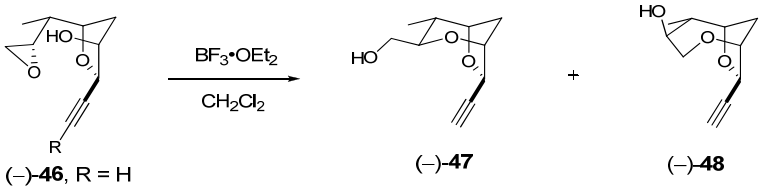


Bicycles (–)-21 and (–)-45. The chemistry utilized to access these compounds was not executed to bring through large amounts of material, and as such an experimental procedure has not been provided. However, characterization data is provided below: Purified via semi-prep HPLC (Waters Nova-Pak silica 6 □m, 19 x 300 mm column, flow rate 10 mL/min., 13% IPA in hexanes). For (–)-**21**: R_t~ 14 min.; R_f 0.26 (8/1, CH_2Cl_2/EtOAc); $[\alpha]_D^{20}$ –80.0 (*c* 0.13, C_6H_6); IR (thin film, C_6D_6) 3445 (br, m), 2960 (s), 2181 (w), 1457 (m), 1250 (m), 1076 (s), 842 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 4.37 (d, *J* = 2.7 Hz, 1 H), 4.33 (ddd, *J* = 9.7, 5.0, 2.7 Hz, 1 H), 3.96 (m, 1 H), 3.81 (dd, *J* = 6.2, 6.2 Hz, 1 H), 3.75 (ddd, *J* = 11.6, 6.2, 2.5 Hz, 1 H), 3.44 (ddd, *J* = 11.6, 6.4, 5.2 Hz, 1 H), 1.87 (dd, *J* = 6.5, 6.5 Hz, 1 H), 1.24 (m, 2 H), 1.18 (m, 1 H), 0.76 (d, *J* = 6.7 Hz, 3 H), 0.17 (s, 9 H); ^{13}C NMR (125 MHz, C_6D_6) δ 101.94, 92.61, 80.20, 78.27, 76.55, 71.76, 63.61, 38.31, 36.36, 15.32, -0.20; HRMS (ES+) m/z 277.1229 [$(M+Na)^+$; calcd for $C_{13}H_{22}O_3SiNa^+$: 277.1337]. For (–)–**45**: R_t~ 17 min.; R_f 0.16 (8/1, CH_2Cl_2/EtOAc); $[\alpha]_D^{20}$ –83.2 (*c* 0.13, C_6H_6); IR (thin film, C_6D_6) 3407 (br, m), 2958 (s), 2183 (w), 1457 (w), 1249 (m), 1077 (s), 842 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 4.31 (d, *J* = 3.2 Hz, 1 H), 3.97 (dd, *J* = 3.8, 3.8 Hz, 1 H), 3.93 (dd, *J* = 12.6, 2.1 Hz, 1 H), 3.78 (dd, *J* = 9.1, 1.7 Hz, 1 H), 3.57 (m, 1 H), 3.36 (dd, *J* = 12.6, 9.0

Hz, 1 H), 1.77 (d, *J* = 14.0 Hz, 1 H), 1.20 (ddd, *J* = 14.0, 9.1, 4.5 Hz, 1 H), 1.11 (d, *J* = 6.8 Hz, 3 H), 1.02 (m, 1 H), 0.85 (d, *J* = 6.1 Hz, 1 H), 0.18 (s, 9 H); ^{13}C NMR (125 MHz, C_6D_6) δ 102.37, 92.29, 81.34, 77.11, 75.62, 73.77, 68.65, 45.06, 32.96, 16.44, -0.01; HRMS (ES+) m/z 277.1239 [$(M+Na)^+$; calcd for $C_{13}H_{22}O_3SiNa^+$: 277.1337].

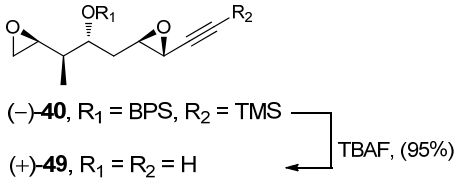


Epoxide (–)-46. A solution of (–)-**44** (18.9 mg, 74.2 μmol) in distilled THF (1.6 mL) was charged with tetrabutylammonium fluoride (TBAF, 82 μL, 1 M in THF, 81.6 μmol). After 1 h, the reaction was concentrated *in vacuo* and purified by flash chromatography (1/1, hexanes/EtOAc, 2.0 in. SiO_2 in a glass pipette) to afford 12.5 mg (93% yield) of epoxide (–)-**46** as a pale yellow oil: R_f 0.27 (1/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –43.7 (*c* 0.40 C_6H_6); IR (thin film, C_6D_6) 3418 (m), 3267 (m), 3054 (w), 2971 (m), 2928 (m), 2111 (w), 1457 (w), 1327 (w), 1261 (w), 1101 (m), 1042 (s) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 4.05 (dd, *J* = 4.9, 2.1 Hz, 1 H), 3.77 (m, 1 H), 3.33 (m, 1 H), 2.78 (ddd, *J* = 6.6, 3.9, 2.6 Hz, 1 H), 2.51 (dd, *J* = 5.1, 3.9 Hz, 1 H), 2.44 (dd, *J* = 5.1, 2.6 Hz, 1 H), 1.96 (d, *J* = 2.1 Hz, 1 H), 1.75 (d, *J* = 5.5 Hz, 1 H), 1.65 (m, 1 H), 1.49 (m, 2 H), 0.79 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 80.61, 79.69, 76.62, 73.32, 72.47, 54.14, 46.91, 41.77, 37.93, 12.67; HRMS (CI, NH_3) m/z 182.0942 [M^+; calcd for $C_{10}H_{14}O_3^+$: 182.0942].



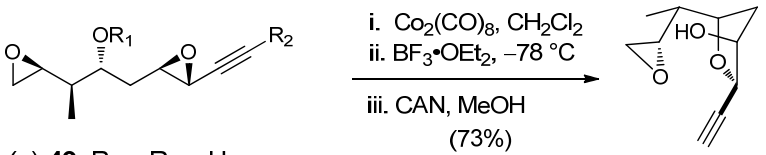
Bicycles (–)-47 and (–)-48. Representative procedure from entry 2 in Table 2. To a 40 °C solution of BF_3•OEt_2 (74 μL, 587 μmol) in CH_2Cl_2 (2.5 mL) was added a solution of azeotroped (–)-**46** (10.7 mg, 58.7 μmol) in CH_2Cl_2 (1.4 mL) dropwise over 5 min. The solution was then quenched with water (1.5 mL), cooled to ambient temperature, and diluted with CH_2Cl_2 (10 mL). The aqueous phase was then washed with CH_2Cl_2 (3 x 5 mL), and the combined organic layers were washed with brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford a 2.1:1 ratio of bicycles. Multiple purifications by

flash chromatography (3/1, CH_2Cl_2/diethyl ether, 1.5 cm diameter column, 6.0 in. SiO_2, flow rate 2.0 in./min.) afforded 7.2 mg (65% yield) of bicycle (–)-**47** and 3.5 mg (32% yield) of bicycle (–)-**48** as colorless oils. For bicycle (–)-**47**: R_f 0.25 (3/1, CH_2Cl_2/diethyl ether); $[\alpha]_D^{20}$ –120.0 (*c* 0.25, C_6H_6); IR (thin film, C_6D_6) 3432 (br, m), 3279 (br, m), 2959 (m), 2198 (s), 2876 (m), 2849 (m), 2119 (w), 1718 (w), 1149 (m), 1045 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 4.26 (dd, *J* = 2.5, 2.5 Hz, 1 H), 4.17 (ddd, *J* = 9.6, 4.4, 2.6 Hz, 1 H), 3.90 (m, 1 H), 3.80 (d, *J* = 6.2 Hz, 1 H), 3.68 (ddd, *J* = 11.6, 5.4, 2.6 Hz, 1 H), 3.38 (ddd, *J* = 11.6, 7.2, 4.4 Hz, 1 H), 2.15 (d, *J* = 2.4 Hz, 1 H), 1.72 (dd, *J* = 7.2, 5.4 Hz, 1 H), 1.31 (m, 1 H), 1.24 (dd, *J* = 11.6, 1.4 Hz, 1 H), 1.19 (ddd, *J* = 11.6, 6.2, 2.7 Hz, 1 H), 0.74 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 80.16, 79.53, 78.07, 76.38, 75.85, 71.10, 63.28, 38.14, 36.14, 15.28; HRMS (CI, NH_3) m/z 183.1018 [$(MH)^+$; calcd for $C_{10}H_{15}O_3^+$: 183.1020]. Vapor Diffusion crystallization (EtOAc/heptane) afforded crystals suitable for X-ray analysis: mp 71-73 °C. For bicycle (–)-**48**: R_f 0.15 (3/1, CH_2Cl_2/diethyl ether); $[\alpha]_D^{20}$ –33.0 (*c* 0.06, C_6H_6); IR (thin film, C_6D_6) 3401 (br, s), 3229 (s), 2917 (s), 2121 (w), 1462 (m), 1230 (m), 1158 (m), 1049 (s), 1028 (m) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 4.19 (dd, *J* = 3.0, 2.3 Hz, 1 H), 3.91 (m, 1 H), 3.83 (dd, *J* = 12.6, 2.2 Hz, 1 H), 3.77 (dd, *J* = 9.0, 1.7 Hz, 1 H), 3.50 (m, 1 H), 3.34 (dd, *J* = 12.6, 9.2 Hz, 1 H), 2.21 (d, *J* = 2.3 Hz, 1 H), 1.76 (d, *J* = 14.0 Hz, 1 H), 1.22 (ddd, *J* = 14.0, 9.0, 4.6 Hz, 1 H), 1.12 (d, *J* = 6.8 Hz, 3 H), 1.00 (m, 1 H), 0.83 (d, *J* = 5.1 Hz, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 81.45, 80.00, 76.98, 75.88, 75.08, 73.56, 68.86, 44.98, 32.67, 16.39; HRMS (CI, NH_3) m/z 182.0948 [M^+; calcd for $C_{10}H_{14}O_3^+$: 182.0942]. Vapor Diffusion crystallization (EtOAc/heptane) afforded crystals suitable for X-ray analysis: mp 135-140 °C.



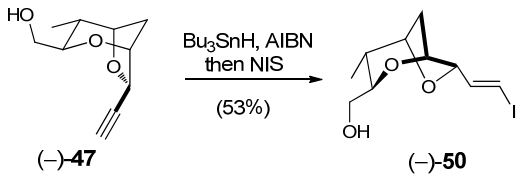
Bis-epoxide (+)-49. To a 0 °C solution of bis-epoxide (–)-**40** (1.30 g, 2.70 mmol) in distilled THF (32 mL) was added tetrabutylammonium fluoride (TBAF, 5.90 mL, 1 M in THF, 5.90 mmol). The ice bath was then removed, and the orange/brown solution was allowed to warm to ambient temperature. After 2 h, the reaction was diluted with water (50 mL) and EtOAc (50 mL). The aqueous phase was then washed with EtOAc (3 x 25 mL), and the combined organic layers were washed with brine (15 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (4/1 → 1/1, hexanes/EtOAc, prepared column with 1% Et_3N in 4/1, hexanes/EtOAc, 5.0 cm diameter column, 6.0 in. SiO_2, flow rate 1.5 in./min.) afforded 471 mg (95% yield, >8:1 mixture of diastereomers) of bis-epoxide

(+)-**49** as a pale yellow oil: R_f 0.33 (1/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +43.0 (*c* 0.46, C_6H_6); IR (neat) 3449 (br, s), 3283 (s), 2973 (m), 2366 (w), 1432 (m), 1332 (m), 1108 (m), 1043 (m), 969 (m), 880 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, >8:1 mixture of diastereomers, *represents minor peaks) δ 3.69 (m, 1 H), 3.28 (ddd, *J* = 6.6, 4.3, 2.2 Hz, 1 H), 3.15 (dd, *J* = 2.2, 1.6 Hz, 1 H), *3.11 (m, 1 H), 2.92 (ddd, *J* = 6.6, 4.0, 2.9 Hz, 1 H), 2.73 (dd, *J* = 4.7, 4.0 Hz, 1 H), *2.68 (m, 1 H), 2.63 (dd, *J* = 4.7, 2.9 Hz, 1 H), *2.59 (dd, *J* = 4.7, 2.9 Hz, 1 H), 2.52 (br s, 1 H), 2.25 (d, *J* = 1.6 Hz, 1 H), *1.85 (m, 1 H), 1.78 (ddd, *J* = 14.4, 9.9, 4.3 Hz, 1 H), 1.58 (m, 2 H), 0.90 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$, >8:1 mixture of diastereomers, *represents minor peaks) δ 80.25, 71.84, *71.59, 70.67, *57.03, 56.85, *53.17, 52.99, 44.26, *44.16, 43.32, 38.30, *37.93, 33.89, *33.75, 8.95; HRMS (CI, NH_3) m/z 183.1028 [$(MH)^+$; calcd for $C_{10}H_{15}O_3^+$: 183.1021].



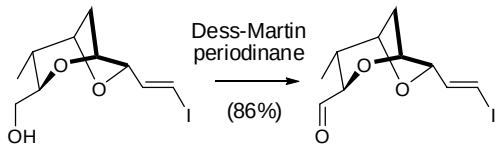
(+)-**49**, $R_1 = R_2 = H$ (–)-**46**

Epoxide (–)-46. A solution of azeotroped (+)-**49** (245 mg, 1.34 mmol) in CH_2Cl_2 (83.0 mL, CH_2Cl_2 was always sparged with argon for 15 min before use in this reaction) was treated with Co_2CO_8 (0.530 g, 1.54 mmol) in CH_2Cl_2 (5.0 mL). After 20 min., the dark brown solution was cooled to –78 °C, and treated with distilled BF_3•OEt_2 (17.0 μL, 0.134 mmol) in CH_2Cl_2 (0.10 mL). After an additional 15 min., this solution was added to a –78 °C suspension of ammonium cerium(IV) nitrate (CAN, 7.5 g, 13.4 mmol) in HPLC grade MeOH (25 mL, MeOH was always sparged with argon for 15 min before use in this reaction) via cannula, followed by 2 x 10 mL CH_2Cl_2 rinses. After 10 min., the reaction was cannulated to sat. $NaHCO_3$ (210 mL) and H_2O (90 mL), and warmed to ambient temperature. Water (200 mL) and CH_2Cl_2 (50 mL) were then added, and the layers separated. The aqueous layer was then washed with EtOAc (5 x 150 mL), and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (3/2 → 1/1, hexanes/EtOAc, 2.5 cm diameter column, 7.0 in. SiO_2, flow rate 1.5 in./min.) afforded 180 mg (73% yield) of epoxide (–)-**46** as a single diastereomer. Characterization data for epoxide (–)-**46** was reported above for the conversion of (–)-**44** to (–)-**46**.



(–)-**47** (–)-**50**

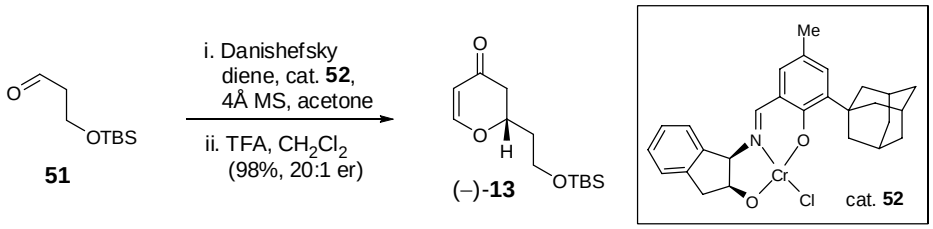
Vinyl Iodide (–)-50. To a solution of alkyne (–)-**47** (36.3 mg, 0.199 mmol) and AIBN (3.3 mg, 0.0199 mmol) in toluene (2.7 mL) was added Bu_3SnH (81.0 μL, 0.298 mmol). The solution was then warmed to 80 °C, and after 2 h, was cooled to ambient temperature and charged with *N*-iodosuccicimide (NIS, 89.6 mg, 0.398 mmol) in one portion to produce a deep red solution. After 10 min., the reaction was quenched with 1 M $Na_2S_2O_3$ (20 mL) and diluted with EtOAc (20 mL). The aqueous layer was then washed with EtOAc (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to afford a yellow oil. Purification by Preparative-TLC (1/1, hexanes/EtOAc, 1000 μm plate) afforded 32.6 mg (53% yield) of (–)-**50** as a yellow oil: R_f 0.17 (3/2, hexanes/EtOAc); $[\alpha]_D^{20}$ –30.7 (*c* 0.06, CH_2Cl_2); IR (thin film, $CDCl_3$) 3433 (br, s), 2960 (s), 2875 (s), 1711 (w), 1602 (w), 1458 (w), 1385 (w), 1344 (w), 1289 (w), 1217 (w), 1167 (w), 1148 (m), 1076 (s), 1048 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.81 (dd, *J* = 14.5, 5.2 Hz, 1 H), 6.56 (dd, *J* = 14.5, 1.7 Hz, 1 H), 4.38 (m, 1 H), 4.32 (m, 1 H), 4.27 (d, *J* = 6.6 Hz, 1 H), 3.70 (ddd, *J* = 11.7, 5.2, 2.5 Hz, 1 H), 3.63 (ddd, *J* = 9.6, 4.3, 2.5 Hz, 1 H), 3.49 (ddd, *J* = 11.7, 7.5, 4.3 Hz, 1 H), 2.00 (ddd, *J* = 11.7, 6.6, 2.8 Hz, 1 H), 1.89 (dd, *J* = 7.5, 5.2 Hz, 1 H), 1.83 (dd, *J* = 11.7, 1.5 Hz, 1 H), 1.67 (m, 1 H), 0.93 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.94, 83.51, 79.69, 79.42, 77.82, 75.71, 63.34, 38.30, 36.18, 15.49; HRMS (CI, NH_3) m/z 310.0052 [M^+; calcd for $C_{10}H_{15}IO_3^+$: 310.0065].



(–)-**50** (–)-**5**

Aldehyde (–)-5. To a 0 °C solution of alcohol (–)-**50** (10.2 mg, 32.8 μmol), and HPLC grade pyridine (13.0 μL, 164 μmol) in CH_2Cl_2 (1.9 mL) was added Dess-Martin periodinane (27.8 mg, 65.6 μmol). The reaction was then allowed to warm to ambient temperature, and after 2 h, was diluted with sat. $NaHCO_3$ (3 mL), water (10 mL) and CH_2Cl_2 (15 mL). The aqueous layer was then washed with CH_2Cl_2 (3 x 5 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (2/1, hexanes/EtOAc, 2.0 in. SiO_2 in a glass pipette) afforded 8.7 mg (86% yield) of aldehyde (–)-**5** as a pale yellow oil: R_f 0.19 (3/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –20.0 (*c*

0.05, $CHCl_3$); IR (thin film, C_6H_6) 3065 (w), 2963 (s), 2931 (s), 2875 (s), 2852 (s), 1735 (s), 1668 (w), 1603 (w), 1455 (m), 1378 (m), 1344 (w), 1290 (m), 1219 (m), 1167 (m), 1146 (m), 1073 (s), 1035 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 9.34 (d, *J* = 1.6 Hz, 1 H), 6.60 (dd, *J* = 14.5, 4.8 Hz, 1 H), 6.38 (dd, *J* = 14.5, 1.8 Hz, 1 H), 3.75 (dd, *J* = 10.0, 1.6 Hz, 1 H), 3.73 (m, 1 H), 3.68 (m, 2 H), 1.21 (ddd, *J* = 11.8, 6.5, 2.7 Hz, 1 H) 1.13 (dd, *J* = 11.8, 1.4 Hz, 1 H), 1.06 (m, 1 H), 0.82 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 199.59, 141.30, 83.31, 81.13, 79.15, 79.00, 75.31, 37.77, 36.77, 14.78; HRMS (CI, NH_3) m/z 308.9993 [$(MH)^+$; calcd for $C_{10}H_{14}IO_3^+$: 308.9987].



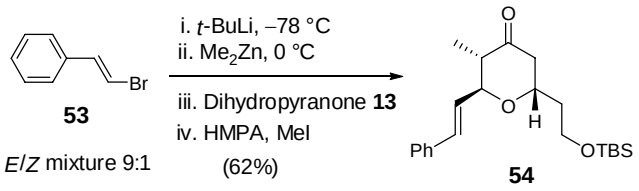
Dihydropyranone (–)-**13.** To a mixture of aldehyde **51** (11.3 g, 59.9 mmol), Cr(III) catalyst **52** (433 mg, 0.898 mmol) and powdered 4Å molecular sieves (11.9 g, oven-dried at >100 °C for 3 h and cooled under high vacuum) was added distilled acetone (11.9 mL). The reaction flask was then wrapped in Al foil, and the brown suspension was treated with Danishefsky's diene (17.5 mL, 89.8 mmol) dropwise. After 19 h, the reaction was diluted with CH_2Cl_2 (65 mL), cooled to 0 °C and charged with trifluoroacetic acid (6.90 mL, 89.8 mmol) dropwise. After 1 h, the suspension was filtered through celite, and the eluent washed with sat. $NaHCO_3$ (100 mL). The aqueous phase was then washed with CH_2Cl_2 (3 x 30 mL), and the combined organic layers were washed with brine (30 mL), dried over $MgSO_4$ and concentrated in vacuo to afford a dark orange oil. Purification by flash chromatography (6/1, hexanes/EtOAc) afforded 15.2 g (98% yield) of (–)-**13** as an orange oil: R_f 0.21 (6/1 hexanes/EtOAc); $[\alpha]_D^{20}$ –70.0 (c 1.00, CH_2Cl_2); IR (neat) 2955 (s), 2928 (s), 2884 (s), 2857 (s), 1686 (s), 1682 (s), 1598 (s), 1471 (m), 1463 (m), 1404 (s), 1361 (w), 1274 (s), 1213 (s), 1094 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 6.0 Hz, 1 H), 5.40 (dd, *J* = 6.0, 1.0 Hz, 1 H), 4.61 (m, 1 H), 3.79 (m, 2 H), 2.45-2.58 (m, 2 H), 2.04 (m, 1 H), 1.86 (m, 1 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.5, 163.0, 107.1, 76.5, 58.3, 42.0, 37.4, 25.9, 18.2, -5.3, -5.4; HRMS (CI, NH_3) m/z 257.1585 [MH+; calcd for $C_{13}H_{25}O_3Si^+$: 257.1572].

Determination of Enantiomeric Purity and Stereochemistry Verification of (–)-13.

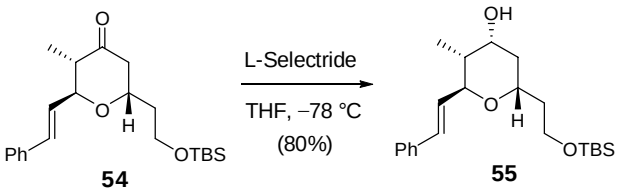
HPLC conditions: CHIRACEL-OD, 0.75 mL/min., 2% IPA in hexanes, 25 °C, λ=250 nm.

Compound	Retention Time (R_t)	% Area	Retention Time (R_t)	% Area
racemic	11.37 min.	49.9	12.48 min.	50.1
(–)-**13**	11.30 min.	5.0	12.16 min.	95.0

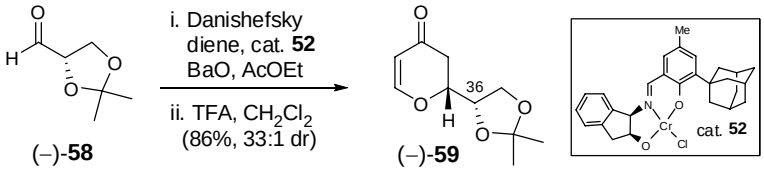
The retention times for (–)-**13** were identical to those previously reported for this compound[4] and thus verified the correct absolute stereochemistry.



Tetrahydropyranone 54. To a THF solution (1.2 mL) of *t*-BuLi (0.25 mL, 1.7 M in pentane, 0.429 mmol) at –78 °C was added a THF solution (0.8 mL) of β-bromostyrene (0.030 mL, 0.234 mmol). After 30 min at –78 °C Me_2Zn (0.12 mL, 2.0 M in toluene, 0.234 mmol) was introduced, and the reaction mixture was gradually warmed to 0 °C. After 15 min at 0 °C, the yellow mixture was recooled to –78 °C, and a THF solution (0.6 mL) of dihydropyranone (–)-**13** (50.0 mg, 0.195 mmol) was slowly added over 1 h via syringe pump. The resulting mixture was stirred for 30 min prior to the addition of HMPA (0.340 mL, 1.95 mmol). After another 10 min MeI (0.061 mL, 0.975 mmol) was added, and the resulting mixture was stirred at –20 °C for 19 h. The reaction mixture was quenched with saturated NH_4Cl solution (5 mL), and extracted with EtOAc (3×10 mL). The combined organic layers were dried over Na_2SO_4, filtered through a plug of silica gel on Celite to remove HMPA, and washed with copious EtOAc. The filtrate was concentrated in *vacuo* and the crude residue was purified by flash chromatography (3% to 10% EtOAc:hexanes) to afford tetrahydropyranone **54** (45.0 mg, 62%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.24 (series of m, 5H), 6.61 (d, J = 15.95 Hz, 1H), 6.24 (dd, J = 15.95, 6.75 Hz, 1H), 4.53-4.48 (m, 1H), 4.19 (t, J = 7.3 Hz, 1H), 3.77-3.67 (m, 2H), 2.71 (dd, J = 14.5, 5.65 Hz, 1H), 2.61-2.55 (m, 1H), 2.42 (dd, J = 14.5, 5.3 Hz, 1H), 1.91-1.84 (m, 1H), 1.71-1.64 (m, 1H), 1.11 (d, J = 6.75 Hz, 3H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.9, 136.2, 133.1, 128.5 (2C), 128.0, 127.8, 126.6 (2C), 78.6, 70.3, 59.1, 49.2, 45.6, 36.4, 25.8 (3C), 11.5 (2C), -5.4 (2C).

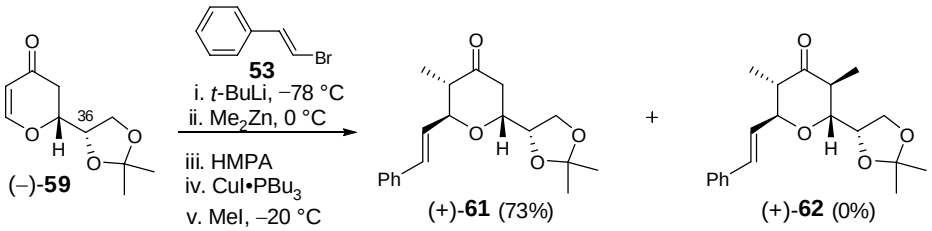


Hydroxyl 55. L-Selectride (0.040 mL, 1.0 M in THF, 0.040 mmol) was added to a THF solution (0.50 mL) of tetrahydropyranone **54** (10 mg, 0.027 mmol) at –78 °C. After 1 h, saturated NH_4Cl solution (5 mL) was added. After warming to rt, the aqueous layer was extracted with Et_2O (3×10 mL), and the combined extracts were washed with brine, dried over Na_2SO_4 and concentrated to give the crude residue, which was purified by flash chromatography (10% to 20% EtOAc:hexanes) to afford hydroxyl **55** (8.0 mg, 80%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.22 (series of m, 5H), 6.59 (dd, *J* = 16.2, 1.5 Hz, 1H), 6.28 (dd, *J* = 16.2, 5.5 Hz, 1H), 4.39-4.36 (m, 1H), 4.11-4.07 (m, 1H), 4.01-3.95 (m, 1H), 3.74 (dd, *J* = 6.8, 5.5 Hz, 2H), 2.04-2.00 (m, 1H), 1.97-1.90 (m, 1H), 1.84-1.77 (m, 2H), 1.70-1.62 (m, 1H), 1.09 (d, *J* = 7.0 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.8, 131.7, 129.3, 128.5 (2C), 127.5, 126.3 (2C), 67.6, 67.3, 59.7, 38.4, 38.2, 35.6, 25.9 (3C), .18.2, 12.1, -5.4 (2C).



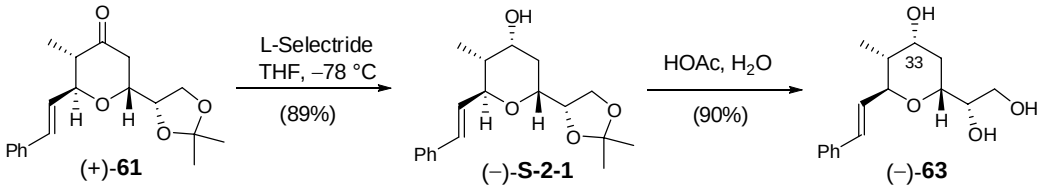
Dihydropyranone (–)-**59.** A 50 ml oven-dried round bottomed flask was charged with the Jacobsen catalyst (1*R*,2*S*)-**52** (482 mg, 0.990 mmol) and BaO (4.0 g), and purged with argon for 20 min. EtOAc (2.8 mL) was added, and the resulting mixture was stirred at rt for 1 h in the dark, after which freshly distilled aldehyde (–)-**58** (2.83 g, 21.8 mmol) was added to the flask followed by 3×0.2 mL EtOAc rinse. The reaction mixture was cooled to 0 °C and stirred for 20 min. The Danishefsky diene 1-methoxy-3-[(trimethylsilyl)oxy]butadiene (3.85 mL, 19.8 mmol) was added, and the reaction mixture was stirred at 4 °C for 24 h in the dark. The reaction mixture was then cooled to 0 °C and CH_2Cl_2 (32 mL) was added followed by twenty drops of TFA. The reaction mixture was stirred at rt for 10 min, and then filtered through a plug of silica gel on Celite, and washed with copious Et_2O. The filtrate was concentrated in *vacuo* and the crude residue was purified by careful flash chromatography (10% to 40% EtOAc:hexanes) to remove (*E*)-4-methoxybut-3-en-2-one and the minor diastereomer, and dihydropyranone (–)-**59** (3.30 g, 86%) was obtained as a brown oil. The crude NMR indicated a 33:1 dr. $[\alpha]_D^{24}$ –122.4 (*c* 1.05, MeOH),

literature data for dextrarotatory isomer: $[\alpha]_D^{20}$ +120.6 (*c* 0.5, MeOH);[5] IR (neat, cm^{-1}) 1680, 1597, 1481, 1457, 1406, 1373, 1276, 1224, 1066; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.33 (d, *J* = 5.8 Hz, 1H), 5.43 (d, *J* = 5.8 Hz, 1H), 4.35-4.26 (m, 2H), 4.14 (dd, *J* = 8.8, 5.9 Hz, 1H), 3.95 (dd, *J* = 8.8, 4.9 Hz, 1H), 2.67-2.59 (m, 2H), 1.43 (s, 3H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 191.8, 162.5, 110.4, 107.8, 79.4, 76.0, 66.2, 38.1, 26.6, 25.1.



Tetrahydropyranone (+)-**61.** To a THF solution (55.0 mL) of *t*-BuLi (23.0 mL, 1.4 M in pentane, 32.2 mmol) at –78 °C was added a THF solution (8.0 mL) of β-bromostyrene **53** (2.24 mL, 17.5 mmol) followed by 2×1 mL THF rinse. After 30 min at –78 °C Me_2Zn (9.7 mL, 1.8 M in toluene, 17.5 mmol) was introduced, and the reaction mixture was gradually warmed to 0 °C. After 15 min at 0 °C, the yellow mixture was recooled to –78 °C, and a THF solution (36 mL) of dihydropyrone (–)-**59** (2.66 g, 13.4 mmol) was slowly added over 1.5 h via syringe pump followed by 2×2 mL THF rinse. The resulting mixture was stirred for 30 min prior to the addition of HMPA (23.4 mL, 134.3 mmol). After another 10 min freshly prepared CuI•PBu_3 complex [by mixing Bu_3P (6.70 mL, 26.9 mmol) with CuI (2.04 g, 10.7 mmol) in THF (25.0 mL) at rt to generate a clear solution] was introduced. After 20 min, MeI (8.36 mL, 134 mmol) was added, and the resulting mixture was stirred at –20 °C for 2 days. The reaction mixture was quenched with saturated NH_4Cl solution (60 mL), and extracted with EtOAc (5×100 mL). The combined organic layers were dried over Na_2SO_4, filtered through a plug of silica gel on Celite to remove HMPA, and washed with copious EtOAc. The filtrate was concentrated in *vacuo* and the crude residue was purified by flash chromatography (5% to 20% EtOAc:hexanes) to afford tetrahydropyrone (+)-**61** (3.10 g, 73%) as a pale yellow oil. $[\alpha]_D^{25}$ +24.7 (*c* 1.00, $CHCl_3$); IR (neat, cm^{-1}) 1718, 1453, 1375, 1066; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.27 (d, *J* = 7.4 Hz, 1H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.20 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.41 (t, *J* = 6.8 Hz, 1H), 4.31 (dd, *J* = 11.8, 6.0 Hz, 1H), 4.18-4.12 (m, 2H), 3.76 (dd, *J* = 8.6, 6.0 Hz, 1H), 2.60 (d, *J* = 5.6 Hz, 2H), 2.53-2.48 (m, 1H), 1.40 (s, 3H), 1.34 (s, 3H), 1.15 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 136.1, 133.4, 128.6 (2C), 128.1, 127.7, 126.6 (2C), 110.4, 79.5, 77.6, 73.8, 66.8, 48.6, 40.4, 26.0, 25.0, 11.8; HRMS (ES) *m/z* $(M+H)^+$ calcd 317.1753, obsd 317.1758.

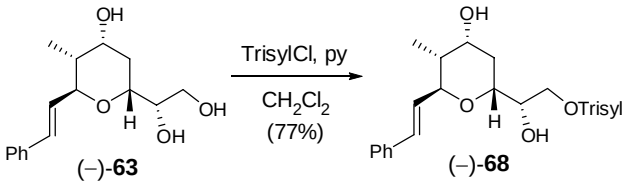
For bismethylation product (+)-**62**: $[\alpha]_D^{25}$ +37.7 (*c* 0.61, $CHCl_3$); IR (neat, cm^{-1}) 1715, 1377, 1211, 1067; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.27 (d, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 16.0 Hz, 1H), 6.22 (dd, *J* = 16.0, 7.0 Hz, 1H), 4.37-4.33 (m, 2H), 4.13 (dd, *J* = 8.4, 7.2 Hz, 1H), 3.83 (t, *J* = 4.4 Hz, 1H), 3.79 (dd, *J* = 8.2, 6.6 Hz, 1H), 2.66-2.54 (m, 2H), 1.40 (s, 3H), 1.34 (s, 3H), 1.32 (d, *J* = 7.2 Hz, 3H), 1.09 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.3, 136.3, 133.3, 128.7 (2C), 128.2, 128.0, 126.8 (2C), 110.6, 80.0, 79.8, 77.8, 67.1, 45.8, 44.6, 26.0, 25.3, 16.1, 11.4; HRMS (CI) *m/z* M^+ calcd 330.1831, obsd 330.1829.



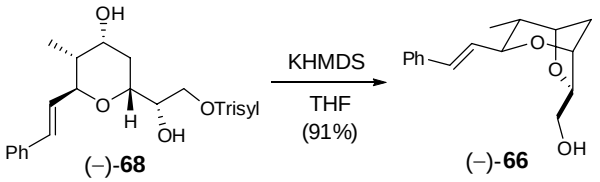
Hydroxyl (–)-S-2-1. L-Selectride (14.7 mL, 1.0 M in THF, 14.7 mmol) was added to a THF solution (210 mL) of tetrahydropyranone (+)-**61** (3.10 mg, 9.81 mmol) at –78 °C. After 2 h, saturated NH_4Cl solution (200 mL) was added. After warming to rt, the aqueous layer was extracted with Et_2O (3×200 mL), and the combined extracts were washed with brine, dried over Na_2SO_4 and concentrated to give the crude residue, which was purified by flash chromatography (10% to 40% EtOAc:hexanes) to afford hydroxyl (–)-**S-2-1** (2.77 g, 89%) as a colorless oil. $[\alpha]_D^{25}$ –33.1 (*c* 0.57, $CHCl_3$); IR (neat, cm^{-1}) 3449, 1452, 1374, 1215, 1065; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2 H), 7.25 (d, *J* = 7.4 Hz, 1H), 6.59 (dd, *J* = 16.1, 1.0 Hz, 1H), 6.21 (dd, *J* = 16.1, 5.7 Hz, 1H), 4.35 (t, *J* = 5.2 Hz, 1H), 4.31 (dd, *J* = 12.8, 6.4 Hz, 1H), 4.12 (dd, *J* = 8.4, 6.4 Hz, 1H), 4.08-4.05 (m, 1H), 3.86 (dd, *J* = 8.4, 5.9 Hz, 1H), 3.76-3.72 (m, 1H), 2.04-1.93 (m, 2H), 1.83-1.77 (m, 1H), 1.43 (s, 3H), 1.38 (s, 3H), 1.08 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.6, 132.2, 128.7, 128.5 (2C), 127.7, 126.4 (2C), 109.5, 77.5, 77.0, 71.7, 67.6, 66.7, 38.5, 31.9, 26.6, 25.2, 12.4**;** HRMS (ES) *m/z* $(M+Na)^+$ calcd 341.1729, obsd 341.1712.

Triol (–)-**63.** Alcohol (–)-**S-2-1** (1.15 g, 3.62 mmol) was treated with acetic acid (45.0 mL) in water (15.0 mL), and the reaction mixture was stirred at rt overnight. The reaction mixture was quenched with saturated $NaHCO_3$ solution and solid $NaHCO_3$, and extracted with EtOAc (6×100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated to leave a crude residue, which was purified by flash chromatography (3% to 7% MeOH:CH_2Cl_2) to afford triol (–)-**63** (0.91 g, 91%) as a white foam. $[\alpha]_D^{25}$ –34.3 (*c* 0.45, $CHCl_3$); IR (neat, cm^{-1}) 3389, 1650, 1070; ^1H NMR (500

MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 1H), 6.60 (dd, *J* = 16.1, 1.0 Hz, 1H), 6.20 (dd, *J* = 16.1, 5.8 Hz, 1H), 4.40 (t, *J* = 5.4 Hz, 1H), 4.10-4.07 (m, 1H), 3.98-3.94 (m, 1H), 3.89-3.86 (m, 1H), 3.78 (dd, *J* = 11.3, 3.6 Hz, 1H), 3.71 (dd, *J* = 11.3, 6.1 Hz, 1H), 2.00-1.96 (m, 1H), 1.93-1.81 (m, 2H), 1.06 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.5, 132.5, 128.5 (2C), 128.3, 127.8, 126.4 (2C), 76.4, 72.8, 71.8, 66.9, 64.1, 38.5, 31.1, 12.4; HRMS (ES) *m/z* $(M+Na)^+$ calcd 301.1416, obsd 301.1426.

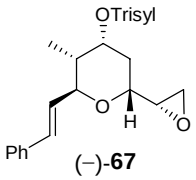


Sulfonate (–)-68. Triisopropylbenzenesulfonyl chloride (2.78 g, 9.17 mmol) was added to a solution of triol (–)-**63** (850 mg, 3.06 mmol) in pyridine (9.00 mL) and CH_2Cl_2 (14.0 mL) at 0 °C. The reaction mixture was stirred at rt for 18 h, and quenched with cold water (100 mL). The aqueous layer was extracted with EtOAc (3×100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (20% to 50% EtOAc:hexanes, silica gel was pretreated with 1% Et_3N) to afford sulfonate (–)-**68** (1.28 g, 77%) as a white foam. $[\alpha]_D^{25}$ -27.3 (*c* 0.67, $CHCl_3$); IR (neat, cm^{-1}) 3409, 1600, 1461, 1344, 1177; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.24 (d, *J* = 7.4 Hz, 1H), 7.18 (s, 2H), 6.56 (d, *J* = 16.1 Hz, 1H), 6.15 (dd, *J* = 16.1, 5.8 Hz, 1H), 4.34 (t, *J* = 5.8 Hz, 1H), 4.30 (dd, *J* = 10.5, 3.1 Hz, 1H), 4.23-4.21 (m, 1H), 4.16-4.06 (m, 5H), 3.81 (dd, *J* = 12.0, 6.8 Hz, 1H), 2.90 (sp, *J* = 7.0 Hz, 1H), 2.74 (br s, 1H), 1.96-1.86 (m, 3H), 1.25 (d, *J* = 6.7 Hz, 12H), 1.24 (d, *J* = 7.0 Hz, 6H), 1.03 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.8, 150.9 (2C), 136.5, 132.4, 129.0, 128.5 (2C), 128.3, 127.7, 126.4 (2C), 123.8 (2C), 76.7, 76.2, 70.9, 70.4, 66.9, 38.4, 34.2, 30.9, 29.6 (2C), 24.7 (4C), 23.4 (2C), 12.4; HRMS (ES) *m/z* $(M+H)^+$ calcd 545.2937, obsd 545.2919.



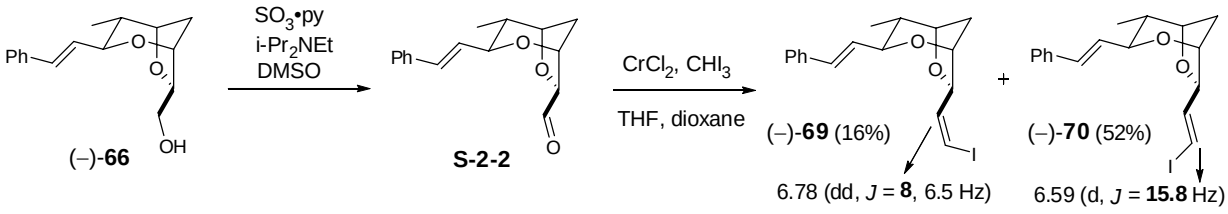
Alcohol (–)-66. To a THF solution (60.0 mL) of sulfonate (–)-**68** (1.07 g, 1.97 mmol) was added KHMDS (5.11 mL, 0.5 M in toluene, 2.56 mmol) at 0 °C. After 30 min, the ice bath was removed, and

the reaction mixture was stirred at rt for 3 h. The reaction mixture was quenched with saturated NH_4Cl solution (120 mL), and extracted with EtOAc (3×120 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (30% to 70% EtOAc:hexanes) to afford alcohol (–)-**66** (465 mg, 91%) as a colorless oil. $[\alpha]_D^{25}$ -52 (*c* 0.26, CH_2Cl_2); IR (neat, cm^{-1}) 3420, 1450, 1144, 1052, 967; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 15.8 Hz, 1H), 6.12 (dd, *J* = 15.8, 7.5 Hz, 1H), 4.45 (br s, 1H), 4.32 (d, *J* = 6.6 Hz, 1H), 4.10-4.04 (m, 3H), 3.98-3.93 (m, 1H), 2.64 (d, *J* = 9.3 Hz, 1H), 2.10-2.06 (m, 1H), 1.94 (dd, *J* = 11.7, 1.0 Hz, 1H), 1.54 (dq, *J* = 6.8, 6.8 Hz, 1H), 0.94 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.5, 132.5, 129.0, 128.5 (2C), 127.7, 126.5 (2C), 82.9, 79.7, 78.9, 74.4, 60.9, 41.6, 38.8, 15.2.



(–)-**67**

For oversulfonation product (–)-**67**: $[\alpha]_D^{29}$ –15 (*c* 1.00, $CHCl_3$); IR (neat, cm^{-1}) 1560, 1462, 1378, 1346, 1179, 1112, 860; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.25 (m, 5H), 7.18 (s, 2H), 6.52 (dd, *J* = 16.4, 2.0 Hz, 1H), 6.14 (dd, *J* = 16.4, 4.5 Hz, 1H), 5.04-5.00 (m, 1H), 4.47 (br t, *J* = 2.2 Hz, 1H), 4.18-4.12 (m, 2H), 3.71-3.67 (m, 1H), 3.05-3.02 (m, 1H), 2.94-2.89 (m, 1H), 2.78 (dd, *J* = 5.0, 4.0 Hz, 1H), 2.66 (dd, *J* = 5.0, 2.6 Hz, 1H), 2.45-2.35 (m, 1H), 1.97-1.91 (m, 1H), 1.85-1.82 (m, 1H), 1.26-1.20 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.7, 138.2, 136.0, 133.2 (2C), 130.8, 128.7 (2C), 128.2, 127.3, 126.6 (2C), 123.9 (2C), 78.6, 76.4, 70.1, 53.4, 45.1, 36.5, 34.4, 29.8 (4C), 29.7, 24.8 (2C), 23.7 (2C), 12.2; HRMS (ES) *m/z* $(M+Na)^+$ calcd 549.2651, obsd 549.2659.



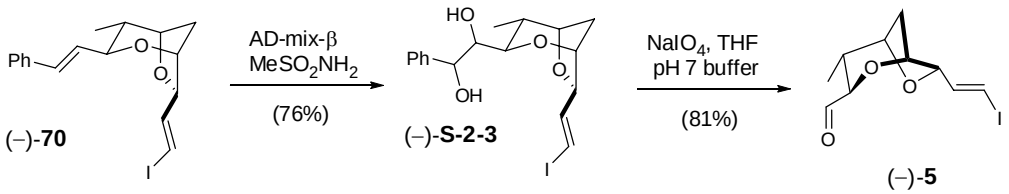
Aldehyde S-2-2. To a CH_2Cl_2 solution (6.20 mL) of alcohol (–)-**66** (310 mg, 1.19 mmol) was added *i*-Pr_2NEt (0.620 mL, 3.58 mmol) and DMSO (0.420 mL, 5.96 mmol). The mixture was cooled to 0 °C, and SO_3•Py was added in one portion. After 1 h, the reaction mixture was diluted with Et_2O (40 mL), washed sequentially with H_2O (40 mL), 1 M $KHSO_4$ (40 mL), H_2O (40 mL), and brine (40 mL). The

organic layer was dried over Na_2SO_4, and evaporated to yield crude aldehyde **S-2-2** (300 mg) as a colorless oil. ^{1}H NMR (500 MHz, C_6D_6) δ 9.81 (s, 1H), 7.20 (d, *J* = 7.3 Hz, 2H), 7.09 (t, *J* = 7.3 Hz, 2H), 7.03 (d, *J* = 7.3 Hz, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 6.05 (dd, *J* = 15.8, 6.8 Hz, 1H), 4.40 (br s, 1H), 3.94 (d, *J* = 6.4 Hz, 1H), 3.89 (br d, *J* = 2.8 Hz, 1H), 3.77 (dd, *J* = 9.0, 7.0 Hz, 1H), 1.44 (d, *J* = 11.6 Hz, 1H), 1.31-1.27 (m, 1H), 1.14-1.04 (m, 1H), 0.87 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 197.5, 137.1, 132.2, 128.8, 128.7, 128.6 (2C), 126.8 (2C), 87.5, 80.4, 80.0, 76.1, 41.7, 38.6, 15.0.

Vinyl iodide (–)-69. $CrCl_2$ (1.46 g, 11.9 mmol) was placed in 200 mL round bottom flask and was heated with heat gun under high vacuum before the flask was refilled with argon with cooling. The reaction flask was cooled to 0 °C, and degassed THF (10.0 mL) was added, then wrapped with aluminum foil. After 15 min, a dioxane solution (36.0 mL) of crude aldehyde **S-2-2** (300 mg) and CHI_3 (1.41 g, 3.58 mmol) was added slowly over 1 h via syringe pump, followed by 2×2 mL dioxane rinse. The resulting mixture was gradually warmed to rt and stirred overnight. The reaction mixture was quenched with brine (50 mL), and extracted with Et_2O (3×50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (5% to 15% EtOAc:hexanes, silica gel was pretreated with 1% Et_3N) to afford vinyl iodides (–)-**70** (230 mg, 52%) and (–)-**69** (70 mg, 16%) as white solids.

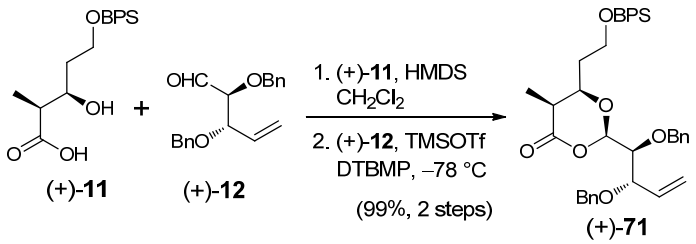
For (–)-**70**: $[\alpha]_D^{23}$ -25.1 (*c* 0.56, C_6H_6); IR (neat, cm^{-1}) 1604, 1450, 1140, 1068, 1040; ^{1}H NMR (500 MHz, C_6D_6) δ 7.21 (d, *J* = 7.2 Hz, 2H), 7.09 (t, *J* = 7.2 Hz, 2H), 7.03 (d, *J* = 7.2 Hz, 1H), 6.88 (dd, *J* = 14.6, 4.8 Hz, 1H), 6.59 (d, *J* = 15.8 Hz, 1H), 6.50 (dd, *J* = 14.6, 1.8 Hz, 1H), 6.09 (dd, *J* = 15.8, 6.9 Hz, 1H), 4.20-4.17 (m, 1H), 3.93-3.91 (m, 2H), 3.87-3.85 (m, 1H), 1.48-1.40 (m, 2H), 1.15-1.09 (m, 1H), 0.81 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 141.9, 137.2, 131.6, 129.6, 128.6 (2C), 127.6, 126.7 (2C), 83.5, 79.3, 78.9, 78.5, 75.5, 41.7, 38.6, 15.0; HRMS (ES) *m/z* $(M+H)^+$ calcd 383.0508, obsd 383.0525.

For (–)-**69**: $[\alpha]_D^{26}$ -136.6 (*c* 0.58, $CHCl_3$); IR (neat, cm^{-1}) 1608, 1449, 1270, 1142, 1070, 966; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.3 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 2H), 7.24 (d, *J* = 7.3 Hz, 1H), 6.78 (dd, *J* = 8.0, 6.5 Hz, 1H), 6.60-6.57 (m, 2H), 6.13 (dd, *J* = 16.0, 7.5 Hz, 1H), 4.66 (d, *J* = 1.5 Hz, 1H), 4.60 (dt, *J* = 6.5, 2.0 Hz, 1H), 4.34 (d, *J* = 6.5 Hz, 1H), 4.00 (dd, *J* = 9.0, 8.0 Hz, 1H), 2.14-2.10 (m, 1H), 2.00 (dd, *J* = 11.5, 1.5 Hz, 1H), 1.55 (dd, *J* = 7.0, 4.5 Hz, 1H), 0.97 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.8, 136.7, 132.7, 128.9, 128.7 (2C), 127.9, 126.7 (2C), 85.6, 84.3, 80.1, 79.7, 75.7, 41.8, 38.9, 15.3; HRMS (ES) *m/z* $(M+H)^+$ calcd 383.0508, obsd 383.0514.

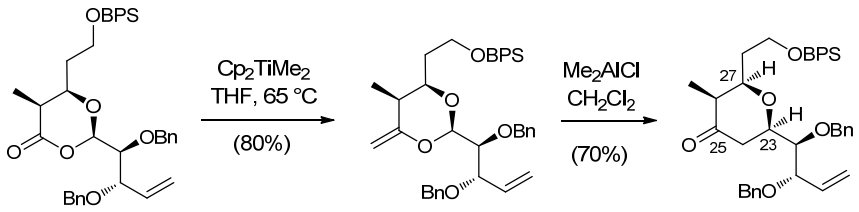


Diol (–)-**S-2-3.** Vinyl iodide (–)-**70** (126 mg, 0.330 mmol) was dissolved in *t*-BuOH (7.50 mL) and H_2O (7.50 mL), and treated with $MeSO_2NH_2$ (32.0 mg, 0.330 mmol) and AD-mix-β (462 mg) at 0 °C. After 1 h the reaction mixture was warmed to rt and stirred for 20 h. TLC indicated presence of starting material, and the reaction mixture was treated with additional $MeSO_2NH_2$ (32.0 mg, 0.330 mmol) and AD-mix-β (462 mg). After 8 h, Na_2SO_3 (2.00 g) was added, and the mixture was vigorously stirred for 1 h, diluted with brine (50 mL), and extracted with EtOAc (3×50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (20% to 60% EtOAc:hexanes) to afford diol (–)-**S-2-3** (104 mg, 76%) as a colorless oil. $[\alpha]_D^{25}$ -98.9 (*c* 1.86, C_6H_6); IR (neat, cm^{-1}) 3420, 1602, 1453, 1146, 1076, 1032; ^1H NMR (500 MHz, C_6D_6) δ 7.40 (d, *J* = 7.3 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 2H), 7.14 (d, *J* = 7.3 Hz, 1H), 6.73 (dd, *J* = 14.6, 5.2 Hz, 1H), 6.37 (dd, *J* = 14.6, 1.6 Hz, 1H), 4.88 (d, *J* = 2.5 Hz, 1H), 3.85 (dd, *J* = 9.8, 3.8 Hz, 1H), 3.77-3.74 (m, 2H), 3.67 (br d, *J* = 1.6 Hz, 1H), 3.58 (dd, *J* = 3.6, 2.8 Hz, 1H), 1.36-1.26 (m, 1H), 1.22 (dd, *J* = 11.6, 1.2 Hz, 1H), 1.13-1.10 (m, 1H), 0.79 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.4, 141.4, 128.4 (2C), 127.6, 126.8 (2C), 83.1, 80.6, 79.9, 79.4, 76.5, 75.4, 72.5, 38.1, 38.0, 16.1; HRMS (ES) *m/z* $(M+Na)^+$ calcd 439.0382, obsd 439.0406.

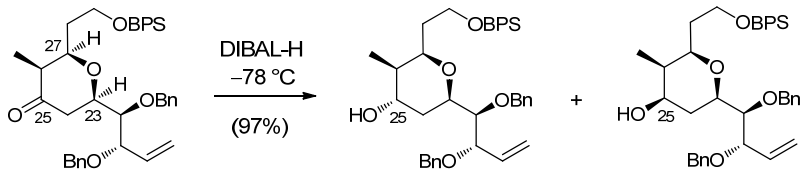
Bicycle (–)-5. A solution of diol (–)-**S-2-3** (100 mg, 0.24 mmol) in THF (16.6 mL) and pH 7 buffer (3.30 mL) was treated with $NaIO_4$ (333 mg, 1.56 mmol) in one portion. The resulting mixture was stirred for 4 h, diluted with brine (50 mL), and extracted with Et_2O (3×50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (10% to 50% EtOAc:hexanes) to afford bicycle (–)-**5** (60 mg, 81%) as a colorless oil. $[\alpha]_D^{24}$ -85.6 (c 1.04, C_6H_6); IR (neat, cm^{-1}) 1736, 1603, 1454, 1220, 1075; ^1H NMR (500 MHz, C_6D_6) δ 9.35 (d, *J* = 1.6 Hz, 1H), 6.61 (dd, *J* = 14.5, 4.8 Hz, 1H), 6.39 (dd, *J* = 14.5, 1.8 Hz, 1H), 3.77 (dd, *J* = 10.1, 1.5 Hz, 1H), 3.74 (br d, *J* = 1.5 Hz, 1H), 3.70-3.67 (m, 2H), 1.22 (ddd, *J* = 11.8, 6.5, 2.7 Hz, 1H), 1.13 (dd, *J* = 11.8, 1.3 Hz, 1H), 1.08-1.05 (m, 1H), 0.83 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 199.6, 141.2, 83.2, 81.0, 79.1, 78.9, 75.2, 37.7, 36.6, 14.7.



Dioxanone (+)-71. Aldehyde (+)-**12**[6] (0.370 g, 1.25 mmol) and the known bis-TMS compound[7] derived from (+)-**11** (0.730 g, 1.37 mmol) were combined in a flask and azeotroped with benzene (3 x 5 mL). The mixture was then dissolved in dichloromethane (4 mL) and cooled to –78 °C. In a separate flask were combined di-*t*-butylmethylpyridine (DTBMP, 104 mg), dichloromethane (2 mL), and TMSOTf (0.4 mL) sequentially. Using a syringe, the pre-mixed TMSOTf/DTBMP solution (0.75 mL) was added dropwise to the reaction flask and the resulting solution was allowed to mix at –78 °C for 11 h at which time it was then warmed to –50 °C for 15 min. Upon cooling back to –78 °C, the reaction was quenched by the rapid addition of triethylamine (1.70 mL, 12.5 mmol) and following removal of the ice bath, allowed to mix for 20 min. The contents of the flask were transferred to a separatory funnel containing dichloromethane (50 mL). The organics were washed with saturated sodium bicarbonate (2 x 20 mL) and the combined aqueous layers then washed with dichloromethane (30 mL). The combined organics were then dried over Na_2SO_4 and concentrated to provide a yellow oil. Purification was accomplished using column chromatography on silylated silica gel (20% EtOAc/Hexanes). The product containing fractions were then transferred to a separatory funnel and washed with a 3.6 M $NaHSO_3$ solution (30 mL), dried over Na_2SO_4, and concentrated to yield dioxonone (+)-**71** (0.830 g, 99% yield) as a yellow oil. The compound was immediately carried on to the next reaction: IR (neat) 2928, 1750, 1427, 1226, 1111 cm^{-1}; $[\alpha]_D^{20}$ +4.5 (c 1.10, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.61-7.53 (m, 3 H), 7.37-7.19 (m, 17 H), 5.87 (ddd, J = 17.7, 10.3, 7.7 Hz, 1 H), 5.58 (d, J = 3.0 Hz, 1 H), 5.38-5.31 (m, 2 H), 4.77 (d, J_{AB} = 11.4 Hz, 1H), 4.67 (d, J_{AB} = 11.3 Hz, 1 H), 4.61 (d, J_{AB} = 11.4 Hz, 1 H), 4.39 (d, J_{AB} = 11.5 Hz, 1 H), 4.27-4.21 (m, 1 H), 4.11 (dd, J = 7.5, 7.5 Hz, 1 H), 3.79-3.74 (m, 2 H), 3.63 (dd, J = 6.7, 3.0 Hz, 1 H), 2.71 (m, 1 H), 1.73 (dddd, J = 12.5, 6.2, 6.2, 6.2 Hz, 2 H), 1.21 (d, J = 7.3 Hz, 3 H), 0.99 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 138.2, 138.1, 135.5, 135.3, 133.5, 133.4, 129.8, 128.4, 128.3, 128.0, 127.9, 127.7, 127.6, 127.5, 119.6, 101.3, 80.5, 79.3, 75.0, 73.5, 70.6, 59.6, 39.5, 34.1, 30.1, 26.8, 11.9; HRMS (ES+) m/z 687.3100 [$(M+Na)^+$; calcd for $C_{41}H_{48}O_6SiNa^+$: 687.3220].

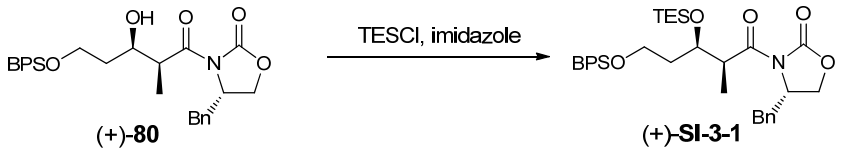


Tetrahydropyranone (+)-73. Dioxanone (+)-**71** (0.830 g, 1.25 mmol) was dissolved in a 0.7 M solution in THF of Tebbe reagent (14.0 mL) and the resulting solution was then heated to 62 °C for 8 h or until the reaction was judged complete by thin layer chromatography (thin layer chromatography sample was taken from the reaction mixture and diluted with hexanes prior to spotting on chromatography plates). Upon completion, the reaction was cooled to rt and 25 mL of hexanes was added and the resulting solution mixed for 20 min. Filtration through a pad of celite was then initiated followed by washing the celite pad with 50 mL of hexanes. Concentration of the filtrate was followed by first being passed through a plug of silylated silica gel using 10% EtOAc/Hexanes. The product containing fractions were concentrated and once again passed through a second plug of silylated silica using 10% EtOAc/Hexanes. The filtrate was concentrated to yield the crude enol ether (0.660 g, 80% yield) as a yellow oil which was carried as is into the rearrangement. The crude enol ether (0.660 g, 0.996 mmol) was dissolved in dichloromethane (20.0 mL) and cooled to –78 °C. $AlMe_2Cl$ (1.50 mL, 1.49 mmol) was then added dropwise and the resulting mixture stirred for 40 min. At this point the bath was removed and the mixture allowed to warm for 20 min and then re-cooled to –78 °C and quenched by rapid addition of 3 mL of sat. $NaHCO_3$. Contents were warmed to rt and then poured into a separatory funnel containing 25 mL of $NaHCO_3$ and 25 mL of dichloromethane. The organic layer was separated and the aqueous washed with 2 x 20 mL of dichloromethane. The collected organics were then dried ($MgSO_4$) and concentrated to provide an oil. Column chromatography (10% EtOAc/Hexanes) provided tetrahydropyranone (+)-**73** as a colorless oil (0.462 g, 70% yield): IR (neat) 2929, 2857, 1779, 1458, 1389, 1359, 1215, 1111 cm^{-1}; $[\alpha]_D^{20}$ +37.3 (c 1.65, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.64-7.60 (m, 3 H), 7.40-7.20 (m, 17 H), 5.80 (ddd, J = 17.5, 10.4, 7.8 Hz, 1 H), 5.32-5.20 (m, 2 H), 4.69 (app s, 2 H), 4.57 (d, J_{AB} = 11.9 Hz, 1 H), 4.26 (d, J_{AB} = 11.9 Hz, 1 H), 3.84-3.68 (m, 6 H), 2.61 (dd, J = 14.5, 11.5 Hz, 1 H), 2.30-2.16 (m, 2 H), 1.85-1.76 (m, 1 H), 1.62-1.52 (m, 1 H), 1.04 (d, J = 7.4 Hz, 3 H), 1.01 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.0, 138.4, 138.1, 135.5, 135.4, 133.7, 129.7, 128.4, 128.3, 128.2, 127.7, 127.6, 119.7, 82.4, 80.3, 75.5, 74.5, 70.4, 60.5, 49.2, 38.9, 35.0, 29.7, 26.8, 19.2, 10.9: HRMS (ES+) m/z 685.3307 [$(M+Na)^+$; calcd for $C_{42}H_{50}O_5SiNa^+$: 685.3428].



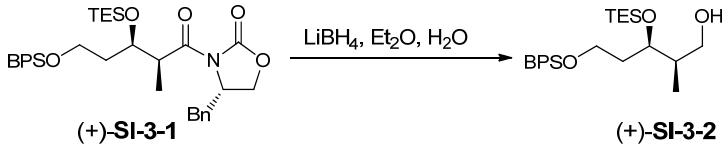
(+)-**73** **74β** **74α**

DIBAL Reduction. To a solution of (+)-**73** (0.110 g, 0.305 mmol) in dichloromethane (3.10 mL) cooled to –78 °C was added DIBAL (0.610 mL, 1.0 M solution in hexanes, 0.610 mmol). The reaction was maintained at –78 °C until complete consumption of starting material as judged by TLC analysis. The reaction was quenched by the addition of a 1:2 mixture of celite to $Na_2SO_4 \bullet 10H_2O$ and then allowed to warm to rt. Filtration and washing of the filter cake with 2 x 50 mL dichloromethane was followed by concentration to yield a 1.0 : 1.1 mixture of alcohols (by NMR) favoring the undesired equatorial alcohol as an oil. This mixture was separated using careful column chromatography (10% EtOAc/ Hexanes) to provide (+)-**74β** (desired) (0.093 g, 46% yield) and (+)-**74α** (undesired) (0.104 g, 50% yield). For (+)-**74β**: IR (neat) 3030, 2927, 1916, 1507, 1465, 1344, 1324, 1208, 1110, 1070, 1028 cm^{-1}; $[\alpha]_D^{20}$ +29.0 (c 1.80, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.59 (m, 3 H), 7.42-7.18 (m, 17 H), 5.84 (ddd, *J* =17.9, 10.1, 7.8 Hz, 1 H), 5.28-5.14 (m, 2 H), 4.74 (d, J_{AB} = 11.2 Hz, 1 H), 4.62 (d, J_{AB} = 11.2 Hz, 1 H), 4.56 (d, J_{AB} = 11.5 Hz, 1 H), 4.26 (d, J_{AB} = 11.5 Hz, 1 H), 3.93 (dd, *J* = 7.8, 4.5 Hz, 1 H), 3.80-3.66 (m, 3 H), 3.60 (dd, *J* = 6.0, 4.5 Hz, 1 H), 3.47-3.42 (m, 1 H), 3.41-3.34 (m, 1 H), 1.82-1.63 (m, 5 H), 1.03 (s, 9 H), 0.80 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.8, 138.7, 135.5, 135.3, 134.0, 129.6, 128.3, 128.2, 127.7, 127.6, 127.5, 127.4, 119.3, 82.8, 81.1, 75.8, 75.4, 74.5, 71.3, 70.4, 61.1, 38.4, 36.0, 30.5, 26.9, 19.2, 5.0; HRMS (ES+) m/z 687.3488 $[(M+Na)^+$; calcd for $C_{42}H_{52}O_5SiNa^+$: 687.3584]. For (+)-**74α**: IR (neat) 3030, 2980, 1959, 1496, 1465, 1362, 1330, 1208, 1110, 1070, 1028 cm^{-1}; $[\alpha]_D^{20}$ +16.0 (c 0.95, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.65-7.60 (m, 4 H), 7.40-7.20 (m, 16 H), 5.83 (ddd, *J* = 17.5, 10.4, 7.8 Hz, 1 H), 5.26-5.10 (m, 2 H), 4.73 (d, J_{AB} = 11.5 Hz, 1 H), 4.62 (d, J_{AB} = 11.5 Hz, 1 H), 4.53 (d, J_{AB} = 11.9 Hz, 1 H), 4.24 (d, J_{AB} = 11.9 Hz, 1 H), 3.95-3.82 (m, 3 H), 3.79-3.66 (m, 4 H), 3.54 (dd, *J* = 6.0, 4.5 Hz, 1 H), 1.80-1.63 (m, 2 H), 1.57-1.42 (m, 3 H), 1.03 (s, 9 H), 0.84 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 138.8, 135.6, 135.5, 135.3, 134.1, 134.0, 129.5, 128.3, 128.2, 128.1, 127.7, 127.6, 127.4, 119.3, 83.2, 81.1, 74.4, 72.0, 70.9, 70.6, 70.4, 61.5, 38.3, 36.0, 29.7, 26.9, 19.2, 11.1; HRMS (ES+) m/z 687.3483 $[(M+Na)^+$; calcd for $C_{42}H_{52}O_5SiNa^+$: 687.3584].



(+)-**80** (+)-**SI-3-1**

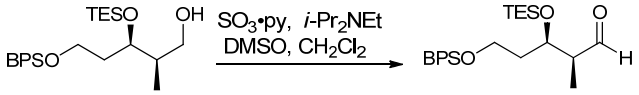
TES ether (+)-SI-3-1. To a flask containing (+)-**80** (10.1 g, 18.5 mmol) was added a 1:3 solution of THF/DMF (190 mL). Imidazole (3.20 g, 46.2 mmol) was then added followed by TESCl (4.0 mL, 24.0 mmol) and the resulting mixture was allowed to stir overnight at rt. Concentration and column chromatography of the crude reaction mixture (20% EtOAc/Hexanes) provided the desired TES protected alcohol (+)-**SI-3-1** (11.6 g, 95% yield) as a colorless oil: IR (neat) 2955, 2876, 1783, 1701, 1457, 1427, 1382, 1348, 1236, 1208, 1111 cm^{-1}; $[\alpha]_D^{20}$ +30.9 (c 0.45, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.73-7.66 (m, 3 H), 7.45-7.20 (m, 12 H), 4.58 (dddd, *J* = 9.6, 7.4, 2.9, 2.2 Hz, 1 H), 4.20 (ddd, *J* = 7.0, 4.8, 4.8 Hz, 1 H), 4.15 (dd, *J* = 9.3, 2.2 Hz, 1 H), 4.07 (dd, *J* = 9.3, 7.0 Hz, 1 H), 3.93 (dddd, *J* = 6.7, 6.7, 6.7, 5.2 Hz, 1 H), 3.78-3.73 (m, 2 H), 3.29 (dd, *J* = 13.4, 3.3 Hz, 1 H), 2.78 (dd, *J* = 13.4, 9.6 Hz, 1 H), 1.92-1.85 (m, 1 H), 1.82-1.74 (m, 1 H), 1.22 (d, *J* = 6.7 Hz, 3 H), 1.07 (s, 9 H), 0.92 (t, *J* = 7.8 Hz, 9 H), 0.57 (q, *J* = 7.8 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.1, 152.9, 135.6, 135.5, 133.9, 129.5, 129.4, 128.9, 128.3, 127.7, 127.6, 127.3, 70.3, 65.9, 60.5, 55.7, 43.4, 38.1, 37.7, 26.8, 19.1, 12.3, 6.9, 5.0; HRMS (ES+) m/z 682.3385 [$(M+Na)^+$; calcd for $C_{38}H_{53}NO_5Si_2Na^+$: 682.3462].



(+)-**SI-3-1** (+)-**SI-3-2**

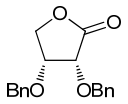
Alcohol (+)-SI-3-2. To a flask containing (+)-**SI-3-1** (11.2 g, 17.0 mmol) was added ether (60.0 mL) followed by water (0.40 mL). This solution was then cooled to 0 °C and a 2.0 M THF solution of $LiBH_4$ (10.2 mL, 20.4 mmol) was then added dropwise. The solution became cloudy white. The ice bath was then removed and the solution warmed to rt. Upon complete consumption of starting material as judged by TLC, the reaction was cooled back to 0 °C, and quenched by addition of a sat. $NaHCO_3$ solution (50 mL). This mixture was allowed to stir for 20 min before separating the layers. The aqueous layer was then washed with 2 x 100 mL of ether before washing the combined organics with 100 mL of brine. Drying of the organics ($MgSO_4$) was followed by concentration and column chromatography (10% EtOAc/Hexanes) to provide (+)-**SI-3-2** (8.10 g, 98% yield) as a colorless oil: IR (neat) 3448, 2955, 2875, 1785, 1701, 1458, 1427, 1388, 1238, 1111, 1007 cm^{-1}; $[\alpha]_D^{20}$ +0.67 (c 0.30, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.64 (m, 4 H), 7.46-7.35 (m, 6 H), 4.07 (ddd, *J* = 7.8, 4.8, 3.3 Hz, 1 H), 3.74 (dd, *J* = 6.3, 6.3 Hz, 2 H), 3.67 (dd, *J* = 9.6, 9.6 Hz, 1 H), 3.56-3.50 (m, 1 H), 2.74 (br s, 1 H), 1.99-1.91

(m, 1 H), 1.76-1.67 (m, 2 H), 1.07 (s, 9 H), 0.94 (t, J = 7.8 Hz, 9 H), 0.81 (d, J = 7.0 Hz, 3 H), 0.64-0.57 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.5, 135.1, 133.8, 129.6, 128.3, 127.6, 127.3, 72.7, 66.0, 60.1, 39.7, 35.1, 26.8, 19.1, 12.1, 6.8, 5.0; HRMS (ES+) m/z 509.2985 [$(M+Na)^+$; calcd for $C_{28}H_{46}O_3Si_2Na^+$: 509.2985].



(+)-**SI-3-2** (+)-**78**

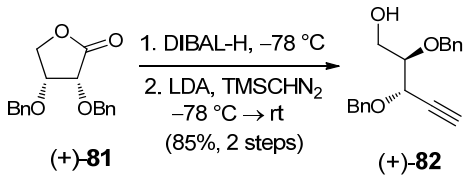
Aldehyde (+)-78. To a flask containing alcohol **(+)-SI-3-2** (1.71 g, 3.52 mmol) was added dichloromethane (35.0 mL) followed by dimethylsulfoxide (3.50 mL). To this solution was then added Hünigs' base (2.00 mL, 11.3 mmol) followed by SO_3•Py (1.68 g, 10.6 mmol). The resulting mixture was stirred at rt until the reaction was judged complete by TLC. Work-up was then performed as described previously to yield (+)-**78** as a yellow oil (1.67 g, 98% yield): IR (neat) 3071, 2955, 2876, 1707, 1460, 1427, 1389, 1237, 1111 cm^{-1}; $[\alpha]_D^{20}$ +8.70 (c 0.92, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75 (s, 1 H), 7.68-7.64 (m, 4 H), 7.46-7.36 (m, 6 H), 4.41 (ddd, J = 6.7, 6.7, 3.3 Hz, 1 H), 3.77-3.64 (m, 2 H), 2.44 (dddd, J = 6.7, 6.7, 6.7, 3.3 Hz, 1 H), 1.77-1.67 (m, 2 H), 1.06 (s, 9 H), 1.02 (d, J = 6.7 Hz, 3 H), 0.92 (t, J = 8.1 Hz, 9 H), 0.57 (q, J = 7.8 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.1, 135.5, 133.5, 129.7, 129.6, 127.6, 127.5, 69.0, 60.4, 51.3, 37.2, 26.8, 19.1, 7.6, 6.8, 5.0. Attempts at obtaining high resolution mass spectral data under either electrospray or chemical ionization were unsuccessful.



(+)-**81**

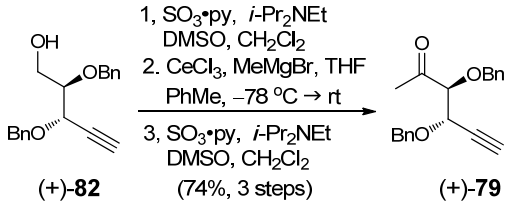
Lactone (+)-81. To a solution of D-erythronolactone (10.0 g, 84.7 mmol) in dry acetonitrile (500 mL) at room temperature was added benzyl bromide (75.0 mL). Anhydrous calcium sulfate (59.1 g, 423 mmol) was then added and the resulting mixture was stirred for 5 min at which time silver (I) oxide (39.2 g, 169 mmol) was added in three portions over 5 min. The resulting reaction flask was covered in aluminum foil and allowed to mix vigorously at room temperature for 12 h at which point a second portion of silver (I) oxide (39.2 g, 169 mmol) was added and the resulting mixture allowed to mix for 36 h. The reaction mixture was then filtered through a plug of celite to remove the solids, and the resulting filter cake was washed with 3 x 250 mL of acetonitrile. Concentration of the combined organics was followed by

column chromatography (30% EtOAc/Hexanes to 70 % EtOAc/Hexanes to 100% EtOAc) to yield (+)-**81** (22.9 g, 91% yield). The experimental data agreed with that present in the literature.[8]



(+)-**81** (+)-**82**

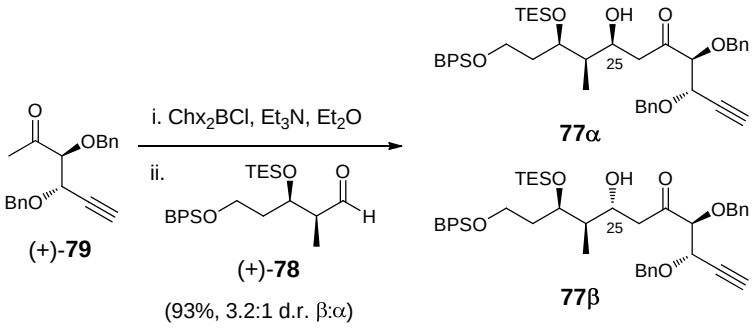
Alkyne (+)-82. To a solution of (+)-**81** (8.90 g, 29.9 mmol) in dichloromethane (300 mL) cooled to –78 °C was added DIBAL (39 mL, 1.0 M solution in hexanes, 39.0 mmol). The resulting solution was mixed at -78 °C for 1 h at which time it was quenched using a 2:1 mixture of Na_2SO_4•10 H_2O / Celite until mixing became difficult. At this time the cooling bath was removed and enough dichloromethane was added to afford a vigorously stirring solution. Stirring was then continued for 10 h at which time the solution was filtered and the filter cake was washed with 2 x 500 mL of ethyl acetate. Concentration of the organics afforded the crude lactol as an oil (8.77 g, 98% yield) which was used without further purification. To a flask containing THF (300 mL) was added a 2.0 M solution in hexanes of LDA (38 mL, 2.6 equiv.). The resulting solution was cooled to –78 °C at which time a solution of trimethylsilyldiazomethane (19 mL, 2.0 M in ether, 38.0 mmol) was added dropwise and the reaction stirred for 30 min. A solution of the crude lactol (8.80 g, 29.0 mmol) in THF (25.0 mL) was then added dropwise to the reaction flask, the bath was removed, and the reaction allowed to warm to rt. Upon warming the release of N_2 can be observed and care should be taken to have adequate ventilation. The reaction is monitored by TLC, and upon consumption of starting material, is quenched by the addition of sat. NH_4Cl (50 mL). Separation of the organic phase is followed by washing of the aqueous phase with 2 x 50 mL ether. The combined organics were dried ($MgSO_4$) and concentrated. The resulting yellow oil is purified by column chromatography eluting with 20% EtOAc/Hexanes. The product containing fractions were collected and concentrated to yield (+)-**82** (7.40 g, 87% yield) as a yellow oil: IR (neat) 3296, 3030, 2916, 1495, 1454, 1089 cm^{-1}; $[\alpha]_D^{20}$ +93.5 (c 0.97, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.43-7.28 (m, 10 H), 4.86 (d, J_{AB} = 11.7 Hz, 1 H), 4.81 (d, J_{AB} = 11.7 Hz, 1 H), 4.65 (d, J_{AB} = 11.7 Hz, 1 H), 4.55 (d, J_{AB} = 11.7 Hz, 1 H), 4.31 (dd, J = 5.3, 2.2 Hz, 1 H), 3.81-3.78 (m, 2 H), 3.72 (ddd, J = 5.3, 5.3, 4.7 Hz, 1 H), 2.56 (d, J = 2.2 Hz, 1 H), 2.09 (br s, 1 H); ^{13}C NMR (125 MHz, CDCl3) δ 141.5, 140.7, 131.6, 131.3, 131.0, 130.9, 130.6, 129.9, 80.9, 80.7, 75.4, 72.9, 70.6, 68.6, 61.0; HRMS (ES+) m/z 319.1317 [$(M+Na)^+$; calcd for $C_{19}H_{20}O_3Na^+$: 319.1412].



Ketone (+)-79. To a flask containing alcohol (+)-**82** (6.50 g, 22.0 mmol) was added dichloromethane (220 mL). Dimethylsulfoxide (50.0 mL), triethylamine (18.0 mL, 132 mmol), and SO_3•Py (10.4 g, 66.0 mmol) were then added sequentially. The reaction was then stirred at rt until judged complete by TLC. At this point the dichloromethane was removed under vacuum and the resulting syrup was taken up in 600 mL of pentane. The organic layer was then washed with 3 x 150 mL of a sat. $CuSO_4$ solution followed by 150 mL of water. The organic phase was then dried ($MgSO_4$) and concentrated to yield a pale yellow oil (6.3 g, 98% yield) of the desired aldehyde that was used without further purification.

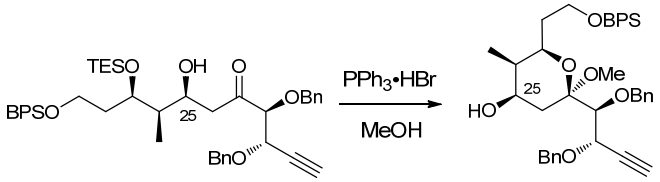
A 1.4 M solution of MeMgBr (23.8 mL, 33.3 mmol) in 3:1 PhMe/THF was added dropwise via syringe to a sonicated slurry of $CeCl_3$ (8.90 g, 37.4 mmol) in PhMe (170 mL) at -78 ^oC. The resulting grayish-lavender slurry was allowed to stir for a further 1h at -78 ^oC, and then was treated via cannula with a solution of the crude aldehyde in PhMe (40.0 mL) to afford a homogenous pale-yellow solution. After 1h at -78 ^oC, the reaction mixture was poured into 1N HCl (300 mL), extracted with Et_2O (3 X 200 mL), dried (Na_2SO_4), filtered through 100 g of SiO_2 with additional Et_2O (200 mL), and concentrated under reduced pressure to afford the crude mixture of alcohols (5.30 g, 78% yield) that were used in the next reaction without further purification.

The same oxidation and workup as for (+)-**82** was performed using the following amounts. The alcohol (5.30 g, 17 mmol) was dissolved in dichloromethane (170 mL). Dimethylsulfoxide (50.0 mL), triethylamine (14.0 mL, 102 mmol), and SO_3•Py (7.90 g, 51.0 mmol) were added sequentially and the reaction mixed until judged complete by TLC. The resulting ketone (+)-**82** was isolated as a yellow oil (4.90 g, 97% yield) after purification by column chromatography (20% EtOAc/Hexanes): IR (neat) 3283, 3031, 2869, 1720, 1496, 1454, 1354, 1208, 1092 cm^{-1}; $[\alpha]_D^{20}$ +72.2 (c 1.13, $CHCl_3$); ^1H NMR (500 MHz, CDCl3) δ 7.38-7.26 (m, 10 H), 4.82 (d, J_{AB} = 11.9 Hz, 1 H), 4.74 (d, J_{AB} = 11.9 Hz, 1 H), 4.68 (d, J_{AB} = 11.9 Hz, 1 H), 4.53 (d, J_{AB} = 11.9 Hz, 1 H), 4.46 (dd, J = 4.8, 2.2 Hz, 1 H), 4.05 (d, J = 4.8 Hz, 1 H), 2.58 (d, J = 2.2 Hz, 1 H), 2.19 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.1, 136.9, 128.4, 128.0, 127.9, 85.5, 79.1, 76.7, 76.1, 73.4, 70.9, 69.7, 27.2; HRMS (ES+) m/z 331.1324 [$(M+Na)^+$; calcd for $C_{20}H_{20}O_3Na^+$: 331.1412].



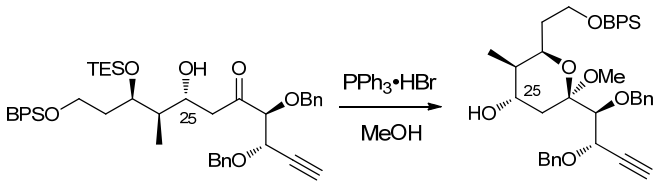
Alcohols (+)-77α and (+)-77β. To a flame-dried flask was added ether (8.00 mL) followed by dicyclohexylboron chloride (1.10 mL, 1.0 M in hexanes, 1.10 mmol) and the resulting solution was cooled to 0 °C. Triethylamine (0.15 mL, 1.10 mmol) was then added and the solution became cloudy. This was mixed for 20 min and cooled to –78 °C at which time a solution of ketone (+)-**79** (0.310 g, 1.0 mmol) in ether (2.00 mL) was added dropwise. The resulting solution was warmed to 0 °C and allowed to mix at 0 °C for 1.5 h before being recooled to –78 °C. A solution of aldehyde (+)-**78** (0.580 g, 1.20 mmol) in ether (2.00 mL) was then added dropwise and the resulting solution was mixed for 1 h and then warmed to –45 °C and quenched with a 1:1 MeOH/pH 7 buffer solution (50 mL), keeping the temperature below –35 °C. The contents were then poured into a flask containing 50 mL of ether at 0 °C. To the resulting mixture was slowly added a 1:1 solution of 30% H_2O_2/ pH 7 buffer (50 mL) making sure to keep the temperature below 5 °C. Upon complete addition, the resulting solution was mixed a further 1.5 h at 0 °C. The layers were separated and the resulting aqueous phase was washed with 3 x 50 mL ether. The combined organics were then dried with $MgSO_4$ and concentrated to provide a crude oil. Purification was accomplished using column chromatography (5% EtOAc/Hexanes to 10% EtOAc/Hexanes) to provide (+)-**17β** (0.550 g, 72% yield) and (+)-**17α** (0.180 g, 21% yield) as clear, colorless oils. For **17β**: IR (neat) 3448, 3287, 3096, 2955, 2876, 1724, 1471, 1389, 1240, 1111 cm^{-1}; $[\alpha]_D^{20}$ +47.3 (c 1.24, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.69-7.61 (m, 4 H), 7.45-7.21 (m, 16 H), 4.80 (d, J_{AB} = 11.9 Hz, 1 H), 4.75 (d, J_{AB} = 11.5 Hz, 1 H), 4.71 (d, J_{AB} = 11.5 Hz, 1 H), 4.45 (d, J_{AB} = 11.9 Hz, 1 H), 4.54-4.45 (m, 1 H), 4.30-4.24 (m, 1 H), 4.10 (d, *J* = 4.4 Hz, 1 H), 4.10-4.04 (m, 1 H), 3.67-3.56 (m, 1 H), 3.08 (br s, 1 H), 2.87 (dd, *J* = 17.8, 8.5 Hz, 1 H), 2.67 (dd, *J* = 18.2, 3.7 Hz, 1 H), 2.51 (d, *J* = 2.2 Hz, 1 H), 1.80-1.65 (m, 2 H), 1.58-1.45 (m, 2 H), 1.04 (s, 9 H), 0.92 (t, *J* = 7.8 Hz, 9 H), 0.82 (d, *J* = 7.0 Hz, 3 H), 0.57 (q, *J* = 7.8 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.1, 137.2, 137.0, 135.5, 133.8, 133.7, 129.6, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 85.2, 79.0, 76.2, 73.7, 73.4, 70.9, 70.0, 69.4, 60.7, 45.2, 41.0, 36.9, 26.8, 19.1, 7.5, 6.8, 5.2; HRMS (ES+) m/z 815.4159 [$(M+Na)^+$; calcd for $C_{48}H_{64}O_6Si_2Na^+$: 815.4241]. For **17α**: IR (neat) 3446, 3287, 3096, 2955, 2858, 1724, 1455, 1427, 1389,

1239, 1111 cm^{-1}; $[\alpha]_D^{20}$ +45.6 (c 0.68, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.68-7.62 (m, 4 H), 7.45-7.25 (m, 16 H), 4.83 (d, J_{AB} = 11.5 Hz, 1 H), 4.74 (d, J_{AB} = 11.9 Hz, 1 H), 4.70 (d, J_{AB} = 11.5 Hz, 1 H), 4.51 (d, J_{AB} = 11.9 Hz, 1 H), 4.50 (dd, J = 5.2, 2.6 Hz, 1 H), 4.21 (d, J = 4.8 Hz, 1 H), 4.15-4.09 (m, 1 H), 4.09-3.94 (m, 2 H), 3.72-3.64 (m, 2 H), 2.75 (dd, J = 16.3, 2.9 Hz, 1 H), 2.60 (dd, J = 16.3, 8.9 Hz, 1 H), 2.56 (d, J = 2.2 Hz, 1 H), 1.75-1.60 (m, 3 H), 1.05 (s, 9 H), 0.91 (t, J = 7.8 Hz, 9 H), 0.67 (d, J = 7.0 Hz, 3 H), 0.62-0.53 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.9, 137.3, 137.0, 135.5, 133.8, 133.7, 129.6, 129.5, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 85.2, 79.3, 76.1, 73.3, 72.1, 71.0, 70.1, 69.9, 60.7, 46.2, 42.8, 35.4, 26.8, 19.1, 12.1, 6.8, 4.9; HRMS (ES+) m/z 815.4135 [$(M+Na)^+$; calcd for $C_{48}H_{64}O_6Si_2Na^+$: 815.4241].



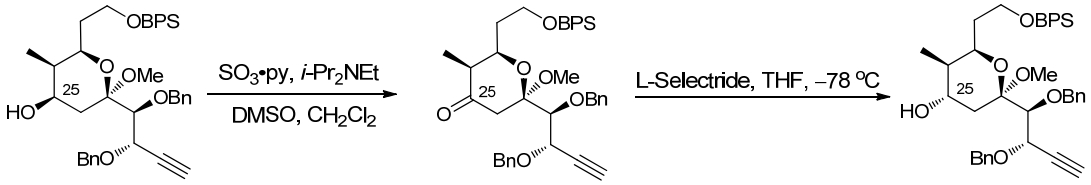
(+)-**77α** (+)-**83**

Alcohol (+)-83 (undesired). To a flask containing (+)-**77α** (2.59 g, 3.27 mmol) was added dry MeOH (33.0 mL) and THF (1.50 mL) and the solution cooled to 0 °C. A pre-made 0.01 M solution of PPh_3•HBr complex in dry MeOH (8.2 mL, 0.0817 mmol) was then added and the resulting mixture stirred at 0 °C for 7 h at which time the solution was poured into a flask containing 150 mL of ether and the resulting mixture extracted with 100 mL $NaHCO_3$, 100 mL water, and 100 mL brine. The organic layer was then dried ($MgSO_4$) and concentrated to yield a crude oil that was purified by column chromatography. Concentration of the product containing fractions then provided (+)-**83** (2.10 g, 92% yield) as a clear, colorless oil: IR (neat) 3447, 3284, 3068, 2930, 2857, 1782, 1471, 1427, 1360, 1209, 1111 cm^{-1}; $[\alpha]_D^{20}$ +55.6 (c 0.04, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.64 (m, 4 H), 7.46-7.21 (m, 16 H), 4.87 (d, J_{AB} = 11.9 Hz, 1 H), 4.87 (d, J_{AB} = 11.9 Hz, 1 H), 4.78 (d, J_{AB} = 11.9 Hz, 1 H), 4.52 (d, J_{AB} = 11.9 Hz, 1 H), 4.39 (dd, J = 2.2, 2.2 Hz, 1 H), 4.12-4.07 (m, 1 H), 3.89 (ddd, J = 8.9, 4.4, 2.2 Hz, 1 H), 3.85-3.73 (m, 3 H), 3.01 (s, 3 H), 2.57 (d, J = 2.2 Hz, 1 H), 2.07-2.01 (m, 2 H), 1.87-1.73 (m, 3 H), 1.67- 1.60 (m, 1 H), 1.06 (s, 9 H), 0.83 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.8, 137.7, 135.5, 133.9, 133.8, 129.6, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.1, 101.2, 81.8, 79.8, 74.4, 70.4, 69.4, 68.4, 67.8, 60.6, 47.8, 37.7, 35.7, 31.7, 26.8, 19.2, 4.0; HRMS (ES+) m/z 715.3533 [$(M+Na)^+$; calcd for $C_{43}H_{52}O_6SiNa^+$: 715.3444].



(+)-**77β** (+)-**75**

Alcohol (+)-75 (desired): The same procedure as used for alcohol (+)-**83** was performed using the following material: (+)-**77β** (5.18 g, 6.53 mmol) in MeOH (65.0 mL) and THF (3.00 mL) at 0 °C. Added PPh_3•HBr (16 mL, 0.01 M solution in MeOH, 0.160 mmol) and mixed at 0 °C for 7 h. Work-up as described above provided (+)-**75** (3.70 g, 82% yield) as a clear, colorless oil: IR (neat) 3529, 3287, 3030, 2930, 2857, 1496, 1454, 1427, 1359, 1217, 1111, 1064, 1028 cm^{-1}; $[\alpha]_D^{20}$ +66.1 (c 0.05, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.64 (m, 4 H), 7.46-7.21 (m, 16 H), 4.86 (d, J_{AB} = 12.2 Hz, 1 H), 4.84 (d, J_{AB} = 11.9 Hz, 1 H), 4.75 (d, J_{AB} = 11.9 Hz, 1 H), 4.50 (d, J_{AB} = 12.9 Hz, 1 H), 4.33 (dd, J = 2.2, 2.2 Hz, 1 H), 4.28-4.23 (m, 1 H), 3.84-3.74 (m, 4 H), 3.71 (d, J = 2.2 Hz, 1 H), 3.02 (s, 3 H), 2.57 (d, J = 2.2 Hz, 1 H), 2.31-2.26 (m, 1 H), 1.84-1.58 (m, 4 H), 1.05 (s, 9 H), 0.83 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6, 137.5, 135.5, 133.9, 133.8, 129.6, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 127.2, 101.7, 81.5, 79.7, 74.5, 70.4, 69.2, 63.4, 60.6, 47.7, 37.4, 35.7, 28.7, 26.8, 19.1, 10.6; HRMS (ES+) m/z 715.3449 [$(M+Na)^+$; calcd for $C_{43}H_{52}O_6SiNa^+$: 715.3533].

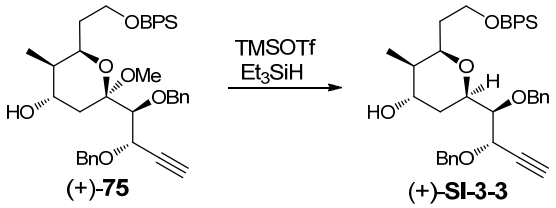


(+)-**83** (+)-**84** (+)-**75**

Ketone (+)-84. Alcohol (+)-**83** (0.420 g, 0.600 mmol) was dissolved in dichloromethane (60 mL) and to this solution was sequentially added dimethylsulfoxide (5.00 mL), triethylamine (0.42 mL, 3.00 mmol), and SO_3•Py (0.210 g, 1.32 mmol). The resulting solution was mixed at rt for several hours until starting material was consumed as judged by TLC. The usual work-up then provided a crude oil that was purified by column chromatography (10% EtOAc/Hexanes) to provide (+)-**84** (0.400 g, 95% yield) as a clear, colorless oil: IR (neat) 3281, 2929, 2857, 1779, 1719, 1458, 1389, 1359, 1215, 1111 cm^{-1}; $[\alpha]_D^{20}$ +54.2 (c 0.32, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.68-7.64 (m, 4 H), 7.46-7.24 (m, 16 H), 4.96 (d, J_{AB} = 11.9 Hz, 1 H), 4.88 (d, J_{AB} = 11.9 Hz, 1 H), 4.82 (d, J_{AB} = 11.9 Hz, 1 H), 4.51 (d, J_{AB} = 11.9 Hz, 1 H), 4.35 (dd, J = 2.2, 2.2 Hz, 1 H), 4.25-4.20 (m, 1 H), 3.94 (d, J = 2.2 Hz, 1 H), 3.85-3.74 (m, 2 H), 3.20 (d, J = 15.2 Hz, 1 H), 3.02 (s, 3 H), 2.59 (d, J = 1.8 Hz, 1 H), 2.40 (d, J = 15.2 Hz, 1 H), 2.31-2.25

(m, 1 H), 1.86 (dddd, J = 13.7, 9.3, 4.8, 4.8 Hz, 1 H), 1.68-1.58 (m, 1 H), 1.06 (d, J = 6.3 Hz, 3 H), 1.06 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.2, 138.5, 137.4, 135.5, 133.6, 129.7, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.4, 102.8, 81.4, 79.3, 76.7, 74.5, 70.5, 69.1, 68.0, 60.2, 48.2, 47.9, 42.0, 34.7, 26.8, 19.1, 10.3; HRMS (ES+) m/z 713.3296 [$(M+Na)^+$; calcd for $C_{43}H_{50}O_6SiNa^+$: 713.3377].

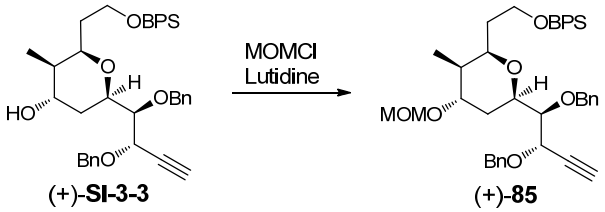
Alcohol (+)-75: To a flask containing ketone (+)-**84** (0.300 g, 0.430 mmol) was added THF (4.30 mL) and the resulting solution cooled to –78 °C. A 1.0 M solution of L-selectride in THF (0.600 mL, 0.600 mmol) was then added down the side of the flask and the reaction was allowed to stir overnight at –78 °C. The next morning the reaction was quenched by addition of 2 mL of saturated NH_4Cl and allowed to warm to rt. The layers were separated and the aqueous was washed with 2 x 10 mL of EtOAc. The combined organics were then dried ($MgSO_4$) and concentrated to yield a crude oil that was purified by column chromatography (20% EtOAc/Hexanes). The product containing fractions were collected and concentrated to provide alcohol (+)-**75** (0.280 g, 94% yield) as a clear, colorless oil.



(+)-**75** (+)-**SI-3-3**

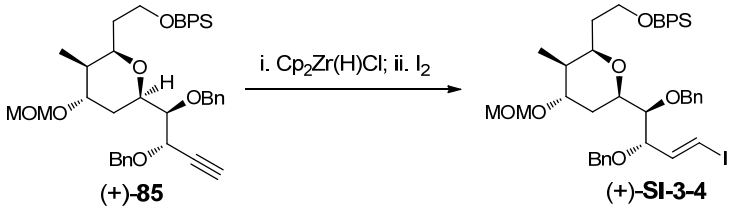
Alcohol (+)-SI-3-3: To a solution of (+)-**75** (0.312 g, 0.450 mmol) in dichloromethane (9.00 mL) cooled to –78 °C was added triethylsilane (1.50 mL, 9.00 mmol). At this time TMSOTf (1.40 mL, 1.0 M solution in dichloromethane, 1.40 mmol) was added dropwise and the reaction was immediately quenched by rapid injection of 5 mL of sat. NH_4Cl. The resulting mixture was allowed to warm to rt and an additional 5 mL of water was then added. Separation of the organic layer was followed by washing of the aqueous phase with 3 x 50 mL of dichloromethane. The combined organic layers were then dried ($MgSO_4$) and concentrated to yield a crude oil. Purification was then accomplished by column chromatography using 10% EtOAc/Hexanes to 30% EtOAc/Hexanes to provide (+)-**SI-3-3** (0.280 g, 93% yield) as a clear, colorless oil: IR (neat) 3030, 2956, 2880, 1959, 1496, 1455, 1390, 1350, 1208, 1110, 1070, 1028 cm^{-1}; $[\alpha]_D^{20}$ +56.4 (c 1.25, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78-7.71 (m, 4 H), 7.50-7.29 (m, 16 H), 4.92 (d, J_{AB} = 11.5 Hz, 1 H), 4.89 (d, J_{AB} = 11.9 Hz, 1 H), 4.73 (d, J_{AB} = 11.5 Hz, 1 H), 4.46 (d, J_{AB} = 11.5 Hz, 1 H), 4.41 (dd, J = 4.0, 2.2 Hz, 1 H), 4.10-4.06 (m, 1 H), 4.00-3.91 (m, 2 H), 3.81-3.75 (m, 2 H), 3.70 (dd, J = 6.7, 4.4 Hz, 1 H), 2.49 (d, J = 2.2 Hz, 1 H), 1.82-1.55 (m, 5 H), 1.11 (s, 9 H), 0.89 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6, 137.8, 135.5, 134.0, 129.5, 128.4,

128.3, 128.2, 128.1, 127.9, 127.7, 127.6, 127.4, 82.3, 80.1, 75.2, 74.3, 71.9, 71.0, 70.8, 70.4, 61.1, 38.3, 35.8, 29.7, 26.9, 19.2, 11.0; HRMS (ES+) m/z 685.3339 [$(M+Na)^+$; calcd for $C_{42}H_{50}O_5SiNa^+$: 685.3428].



(+)-**SI-3-3** (+)-**85**

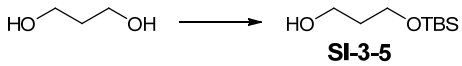
Alkyne (+)-85: To a solution of alcohol (+)-**SI-3-3** (0.312 g, 0.471 mmol) in acetonitrile (4.00 mL) was added 2,6-lutidine (0.220 mL, 1.88 mmol) followed by MOMCl (0.110 mL, 1.41 mmol). The resulting reaction mixture was then allowed to mix overnight at rt at which point it was quenched by the addition of 5 mL of sat. $NaHCO_3$ and 50 mL of EtOAc. The organic phase was then separated and the aqueous phase was washed by 2 x 50 mL of EtOAc. The combined organics were dried ($MgSO_4$) and concentrated to yield a crude oil. Purification was accomplished by column chromatography (10% EtOAc/Hexanes) to provide (+)-**85** (0.330 g, 100% yield) as a clear, colorless oil: IR (neat) 3288, 3030, 2929, 2884, 2113, 1958, 1588, 1496, 1469, 1428, 1349, 1308, 1209, 1109, 1039 cm^{-1}; $[\alpha]_D^{20}$ +42.4 (*c* 4.80, $CHCl_3$); ^1H NMR (500 MHz, CDCl3) δ 7.81-7.74 (m, 4 H), 7.52-7.28 (m, 16 H), 4.96 (d, J_{AB} = 11.5 Hz, 1 H), 4.93 (d, J_{AB} = 11.5 Hz, 1 H), 4.79 (d, J_{AB} = 11.5 Hz, 1 H), 4.73 (br s, 2 H), 4.51 (d, J_{AB} = 11.5 Hz, 1 H), 4.47 (dd, *J* = 4.0, 2.2 Hz, 1 H), 4.15-4.12 (m, 2 H), 4.05-3.99 (m, 1 H), 3.88-3.79 (m, 3 H), 3.75-3.73 (m, 1 H), 3.41 (s, 3 H), 2.53 (d, *J* = 2.2 Hz, 1 H), 1.86-1.74 (m, 2 H), 1.70-1.61 (m, 2 H), 1.15 (s, 9 H), 0.96 (d, *J* = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, CDC) δ 138.7, 137.9, 135.6, 134.2, 134.1, 129.5, 128.3, 128.2, 128.1, 127.9, 127.6, 127.5, 94.8, 82.5, 80.3, 75.5, 75.3, 74.4, 72.6, 71.4, 71.1, 71.0, 61.2, 55.3, 36.4, 36.0, 27.2, 26.9, 19.3, 11.1; HRMS (ES+) m/z 729.3573 [$(M+Na)^+$; calcd for $C_{44}H_{54}O_6SiNa^+$: 729.2690].



(+)-**85** (+)-**SI-3-4**

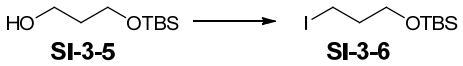
Vinyl Iodide (+)-SI-3-4. To a solution of alkyne (+)-**85** (0.320 g, 0.450 mmol) in dichloromethane (4.50 mL) was added Schwartz's reagent (0.580 g, 2.25 mmol) and the resulting cloudy white solution was allowed to mix at rt until a homogenous yellow solution was obtained (ca. 1 h). The resulting yellow

solution was allowed to mix for another 30 min at rt, slowly becoming orange in color, at which point solid I_2 (0.150 g, 0.585 mmol) was added. The resulting solution immediately turned yellow and eventually became deep red/brown in color. After 30 min, the reaction was quenched with 30 mL of sat. $NaHCO_3$ and the organic phase separated. The aqueous phase was then washed with 3 x 50 mL of dichloromethane and the combined organics were dried ($MgSO_4$) and concentrated to yield a crude yellow oil. Purification was accomplished by column chromatography (5% EtOAc/Hexanes to 20% EtOAc/Hexanes) to provide (+)-**SI-3-4** (0.380 g, 100% yield) as a clear yellow oil: IR (neat) 3067, 3030, 2929, 2883, 1603, 1454, 1427, 1358, 1108, 1071, 1039 cm^{-1}; $[\alpha]_D^{20}$ +25.4 (c 3.30, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.73-7.68 (m, 4 H), 7.46-7.26 (m, 16 H), 6.60 (dd, J = 14.8, 8.1 Hz, 1 H), 6.19 (d, J = 14.8 Hz, 1 H), 4.78 (d, J_{AB} = 11.5 Hz, 1 H), 4.67 (d, J_{AB} = 11.5 Hz, 1 H), 4.67 (br s, 2 H), 4.55 (d, J_{AB} = 11.9 Hz, 1 H), 4.29 (d, J_{AB} = 11.9 Hz, 1 H), 3.99-3.94 (m, 1 H), 3.93 (dd, J = 8.1, 4.0 Hz, 1 H), 3.81-3.70 (m, 4 H), 3.58 (dd, J = 6.3, 4.4 Hz, 1 H), 3.35 (s, 3 H), 1.85-1.55 (m, 5 H), 1.09 (s, 9 H), 0.91 (d, J = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 138.6, 138.1, 135.5, 135.4, 134.0, 133.9, 133.8, 129.6, 128.3, 128.2, 128.1, 127.7, 127.6, 127.5, 94.8, 82.5, 80.0, 75.5, 74.4, 72.5, 71.5, 70.8, 61.5, 55.3, 36.2, 36.0, 27.2, 26.9, 19.2, 11.1; HRMS (ES+) m/z 857.2717 [$(M+Na)^+$; calcd for $C_{44}H_{55}IO_6SiNa^+$: 857.2813].



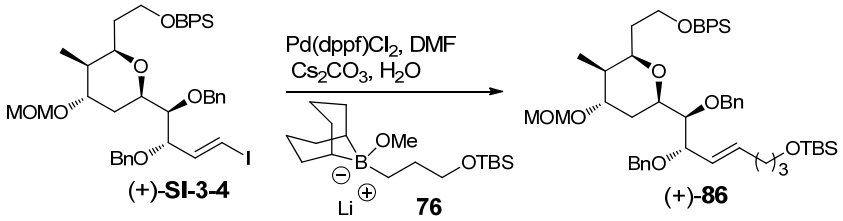
SI-3-5

Alcohol SI-3-5. To a 0 °C solution of distilled 1,3-propanediol (11.4 g, 150 mmol) in THF (335 mL) was added *n*-BuLi (59.9 mL, 2.5 M in hexanes, 150 mmol) dropwise via addition funnel. After 1 h, a solution of *tert*-butyldimethylsilyl chloride (20.9 g, 136 mmol) in THF (40.0 mL) was added via cannula and the reaction was allowed to warm to ambient temperature. After 15 h, the reaction was quenched with water (50 mL) and concentrated *in vacuo*. The residue was then extracted with CH_2Cl_2 (250 mL), and the aqueous phase was washed with CH_2Cl_2 (3 x 50 mL). The combined organic layers were then washed with brine (50 mL), dried over $MgSO_4$ and concentrated in vacuo to afford a yellow oil. Purification by flash chromatography (4/1 hexanes/EtOAc) afforded 25.0 g (97% yield) of **SI-3-5** as a pale yellow oil: R_f 0.26 (4/1 hexanes/EtOAc); IR (thin film, $CDCl_3$) 3355 (br, m), 2955 (s), 2928 (s), 2857 (s), 1472 (m), 1256 (s), 1097 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.82 (t, J = 5.6 Hz, 2 H), 3.78 (q, J = 5.4 Hz, 2 H), 2.59 (t, J = 5.3 Hz, 1 H), 1.76 (quint, J = 5.6 Hz, 2 H), 0.89 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.7, 62.2, 34.2, 25.8, 18.1, -5.5; HRMS (ES+) m/z 213.1280 [$(M+Na)^+$; calcd for $C_9H_{22}O_2SiNa^+$: 213.1388].



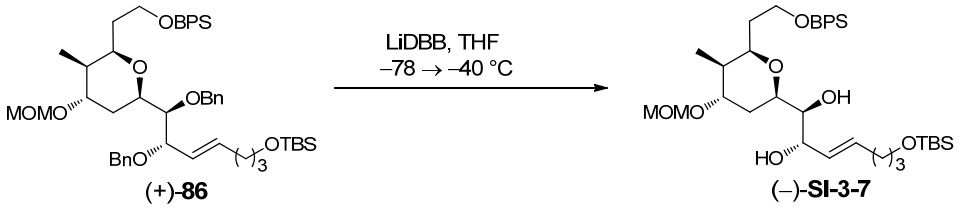
SI-3-5 **SI-3-6**

Iodide SI-3-6. To a flask containing alcohol **SI-3-5** (1.70 g, 8.76 mmol) was added dichloromethane (73.0 mL). The solution was cooled to 0 °C and triphenylphosphine (1.90 g, 7.30 mmol) followed by imidazole (0.750 g, 10.9 mmol) were added. Iodine (1.90 g, 7.66 mmol) was then added and the ice bath removed. The reaction was allowed to mix for 2 h at which time a 1:1 solution of 10% Na_2SO_3 : saturated $NaHCO_3$ (50 mL) was added. The organic layer was separated and the aqueous phase washed with 2 x 25 mL of dichloromethane. The combined organics were dried ($MgSO_4$) and concentrated to yield a crude oil which was purified by column chromatography (5% EtOAc/Hexanes) to provide **SI-3-6** as a clear, colorless oil. All spectra data matched that in the literature.[9]



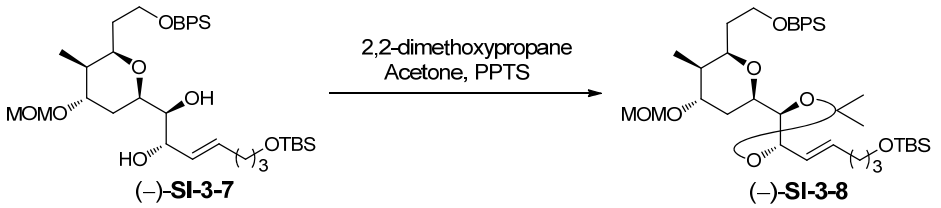
Suzuki-Miyaura coupling [(+)-86]. To a flask containing **SI-3-6** (0.400 g, 1.32 mmol) was added dry ether (4.90 mL) and the reaction flask was cooled to –78 °C. To this solution was added *t*-BuLi (1.80 mL, 1.5 M in pentane, 2.64 mmol) and the resulting anion was stirred for 10 min. at which point 9-BBN•OMe (2.70 mL, 1.0 M solution in hexanes, 2.70 mmol) was added and the reaction was stirred at –78 °C for 10 min before being warmed to rt and allowed to stir for 1 h. An aqueous solution of Cs_2CO_3 (0.440 mL, 3.0 M aq. Solution, 1.32 mmol) was then added followed by a solution of (+)-**SI-3-4** (0.370 g, 0.440 mmol) in DMF (4.90 mL). The $Pd(dppf)_2Cl_2$ (0.020 g, 0.022 mmol) was then added and the resulting mixture was allowed to stir at rt overnight. The reaction was quenched by addition of 10 mL of sat. $NaHCO_3$ and 20 mL of H_2O. The organic layer was separated and the aqueous layer washed with 2 x 25 mL of ether. The combined organic layers were washed with 50 mL of H_2O and 50 mL of brine then dried ($MgSO_4$) and concentrated to yield a crude oil. Purification was accomplished using careful column chromatography (5% EtOAc/Hexanes) to provide (+)-**86** (0.390 g, 100% yield) as a clear, colorless oil: IR (neat) 3378, 3067, 2927, 2857, 1451, 1411, 1361, 1300, 1253, 1106, 1039 cm^{-1}; $[\alpha]_D^{20}$ +12.2 (c 1.22, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.71-7.66 (m, 4 H), 7.43-7.22 (m, 16 H), 5.56 (ddd, J = 15.2, 6.3, 6.3 Hz, 1 H), 5.49 (dd, J = 15.2, 8.1 Hz, 1 H), 4.78 (d, J_{AB} = 11.5 Hz, 1 H), 4.69 (d, J_{AB} = 11.5 Hz, 1 H), 4.66 (d, J_{AB} = 7.0 Hz, 1 H), 4.64 (d, J_{AB} = 7.0 Hz, 1 H), 4.55 (d, J_{AB} = 11.9 Hz, 1

H), 4.26 (d, J_{AB} = 11.9 Hz, 1 H), 3.96-3.91 (m, 1 H), 3.88 (dd, *J* = 8.1, 4.4 Hz, 1 H), 3.84-3.71 (m, 3 H), 3.63-3.57 (m, 2 H), 3.33 (s, 3 H), 2.10 (ddd, *J* = 6.7, 6.7, 6.7 Hz, 2 H), 1.85-1.53 (m, 9 H), 1.07 (s, 9 H), 0.93 (s, 9 H), 0.92 (d, *J* = 5.9 Hz, 3 H), 0.06 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 142.7, 139.3, 139.0, 137.5, 132.6, 131.3, 131.2, 131.1, 130.6, 130.4, 130.3, 130.2, 130.1, 95.8, 83.8, 81.4, 76.7, 75.5, 74.2, 72.6, 71.1, 69.6, 61.8, 60.8, 54.0, 34.0, 33.7, 29.8, 26.0, 23.9, 23.0, 15.8, 14.9, 7.2, -10.1; HRMS (ES+) m/z 903,5050 [$(M+Na)^+$; calcd for $C_{53}H_{76}O_7Si_2Na^+$: 903.5130].



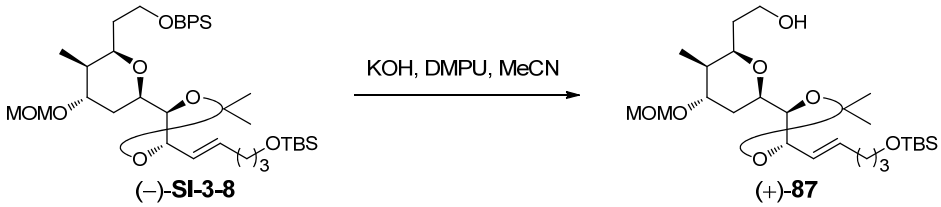
(+)-**86** (–)-**SI-3-7**

Diol (–)-SI-3-7. To a solution of (+)-**86** (0.0320 g, 0.0360 mmol) was added THF (0.700 mL) and the resulting solution was cooled to –78 °C. A pre-made 1.0 M solution of LiDBB in THF was then added dropwise until a deep blue color persisted at which time the reaction was allowed to warm to –40 °C. The reaction became red in color and more of the 1.0 M solution of LiDBB was added once again until a deep blue color persisted for 30 min. The reaction was then cooled back to –78 °C and quenched by the addition of 5 mL of sat. NH_4Cl and allowed to warm to rt. Purification was accomplished by column chromatography (20% EtOAc/Hexanes to 40% EtOAc/Hexanes) to provide (–)-**SI-3-7** (0.0220 g, 88% yield) as a clear, colorless oil: IR (neat) 3456, 2928, 2856, 1471, 1428, 1360, 1255, 1104, 1039 cm^{-1}; $[\alpha]_D^{20}$ –8.4 (c 0.35, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67-7.62 (m, 4 H), 7.42-7.31 (m, 6 H), 5.70 (ddd, *J* = 15.7, 6.8, 6.8 Hz, 1 H), 5.50 (dd, *J* = 15.7, 7.1 Hz, 1 H), 4.65 (br s, 2 H), 4.14-4.02 (m, 2 H), 3.77-3.66 (m, 4 H), 3.57 (app t, *J* = 6.6 Hz, 2 H), 3.42-3.36 (m, 1 H), 3.33 (s, 3 H), 2.72 (d, *J* = 2.5 Hz, 1 H), 2.07 (ddd, *J* = 6.9, 6.9, 6.9 Hz, 2 H), 1.94 (d, *J* = 3.6 Hz, 1 H), 1.85-1.80 (m, 1 H), 1.76-1.63 (m, 3 H), 1.60-1.52 (m, 3 H), 1.03 (s, 9 H), 0.87 (s, 9 H), 0.86 (d, *J* = 4.0 Hz, 3 H), -0.05 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 138.2, 138.1, 137.3, 132.7, 131.8, 130.6, 96.0, 75.2, 75.0, 74.6, 71.3, 61.6, 60.0, 54.1, 33.7, 33.4, 29.6, 25.9, 25.1, 23.9, 22.9, 15.8, 7.0, -10.1; HRMS (ES+) m/z 723.4086 [$(M+Na)^+$; calcd for $C_{39}H_{64}O_7Si_2Na^+$: 723.4191].



(–)-**SI-3-7** (–)-**SI-3-8**

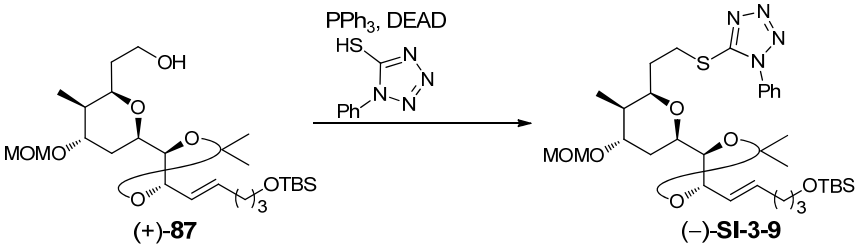
Acetonide (–)-SI-3-8. To a flask containing (–)-**SI-3-7** (0.144 g, 0.206 mmol) was added 2,2-dimethoxypropane (3.00 mL) followed by acetone (1.00 mL). A few crystals (< 2 mg) of PPTS were added and the resulting solution allowed to stir at rt overnight. The reaction mixture was then concentrated and the crude oil was purified by column chromatography (5% EtOAc/Hexanes) to provide (–)-**SI-3-8** (0.149 g, 98% yield) as a clear, colorless oil. IR (neat) 3048, 2930, 2856, 1472, 1379, 1250, 1103, 1039 cm^{-1}; $[\alpha]_D^{20}$ –4.7 (c 0.27, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.67-7.62 (m, 4 H), 7.42-7.31 (m, 6 H), 5.56 (ddd, *J* = 15.2, 6.6, 6.6 Hz, 1 H), 5.40 (dd, *J* = 15.2, 7.7 Hz, 1 H), 4.65 (br s, 2 H), 4.50 (dd, *J* = 7.1, 7.1 Hz, 1 H), 3.91-3.82 (m, 2 H), 3.78-3.61 (m, 4 H), 3.48 (app t, *J* = 6.4 Hz, 2 H), 3.32 (s, 3 H), 1.98-1.87 (m, 2 H), 1.81-1.43 (m, 7 H), 1.41 (s, 3 H), 1.32 (s, 3 H), 1.02 (s, 9 H), 0.89 (d, *J* = 7.0 Hz, 3 H), 0.88 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 137.4, 132.7, 130.6, 128.6, 127.6, 110.0, 95.7, 80.2, 79.0, 75.0, 71.1, 71.0, 61.7, 60.6, 54.0, 33.6, 33.5, 29.6, 25.8, 25.7, 24.8, 23.9, 22.9, 22.4, 15.7, 14.8, 7.1, - 10.1; HRMS (ES+) m/z 763.4412 [$(M+Na)^+$; calcd for $C_{42}H_{68}O_7Si_2Na^+$: 763.4504].



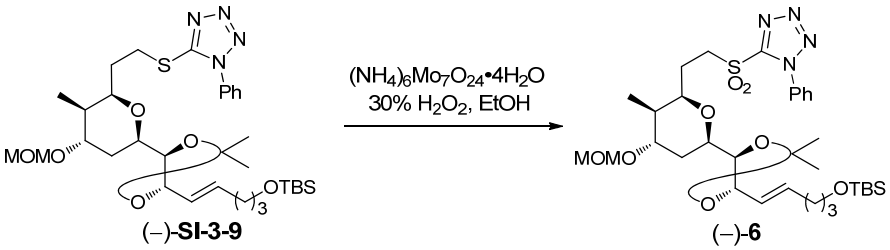
(–)-**SI-3-8** (+)-**87**

Alcohol (+)-87. To a flask containing (–)-**SI-3-8** (0.0220 g, 0.0290 mmol) was added DMPU (2.00 mL) followed by KOH (0.250 mL, 8.0 M aq. Solution, 2.00 mmol) and acetonitrile (2.00 mL) was then added. The resulting mixture was stirred at rt for 8 h at which time it was diluted with ether (50 mL) and washed with 2 x 25 mL of 10% HCl solution. The organic phase was then dried ($MgSO_4$) and concentrated to yield a crude oil. Purification was accomplished using column chromatography (10% to 40% EtOAc/Hexanes) to provide first recovered (–)-**SI-3-8** (0.006 g, 27% yield) and next (+)-**87** (0.010 g, 68% yield, 93% BORSM) as a yellow oil: IR (neat) 3488, 2929, 2856, 1734, 1670, 1471, 1380, 1255, 1099, 1039 cm^{-1}; $[\alpha]_D^{20}$ +8.8 (c 0.35, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.84 (ddd, *J* = 15.2, 6.6, 6.6 Hz, 1 H), 5.56 (dd, *J* = 15.2, 8.1 Hz, 1 H), 4.68 (br s, 2 H), 4.59 (dd, *J* = 8.5, 6.3 Hz, 1 H), 4.00-3.96 (m,

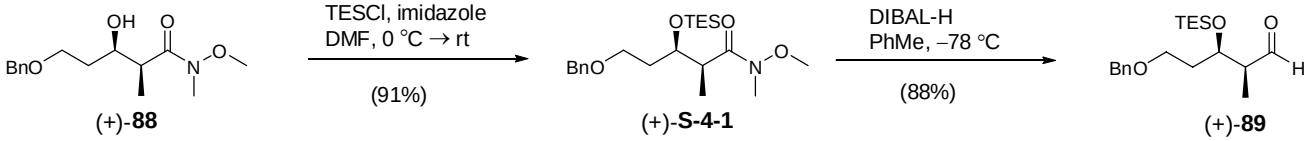
1 H), 3.94- 3.90 (m, 1 H), 3.86-3.80 (m, 1 H), 3.74-3.66 (m, 3 H), 3.64 (app t, *J* = 5.9 Hz, 2 H), 3.37 (s, 3 H), 2.15 (ddd, *J* = 8.5, 8.5, 8.5 Hz, 2 H), 1.84-1.73 (m, 2 H), 1.72-1.55 (m, 5 H), 1.44 (s, 3 H), 1.44-1.43 (m, 1 H), 1.34 (s, 3 H), 0.94 (d, *J* = 7.0 Hz, 3 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.3, 125.3, 108.0, 94.7, 79.7, 79.0, 74.9, 73.8, 71.2, 62.8, 61.0, 55.3, 36.5, 35.1, 31.9, 28.8, 28.3, 27.7, 25.9, 25.3, 18.3, 11.2, -5.4; HRMS (ES+) m/z 525,3214 [$(M+Na)^+$; calcd for $C_{26}H_{50}O_7SiNa^+$: 525.3326].



Thioether (–)-SI-3-9. To a flask containing (+)-**87** (0.0350 g, 0.0710 mmol) was added THF (1.00 mL). Triphenylphosphine (0.0220 g, 0.0852 mmol), 1-phenyl-1*H*-tetrazole-5-thiol (0.0250 g, 0.142 mmol), and diisopropylazadicarboxylate (0.020 mL, 0.0994 mmol) were sequentially added and the resulting yellow solution allowed to mix at rt for 20 min at which point TLC analysis showed consumption of starting material. The reaction was concentrated to approximately 0.5 mL and loaded on a 1000 micron prep plate using 20% EtOAc/Hexanes as eluent to provide 0.045 g (98% yield) of (–)-**SI-3-9** as a clear, colorless oil: IR (neat) 2924, 2854, 1734, 1598, 1500, 1380, 1256, 1098, 1064 cm^{-1}; $[\alpha]_D^{20}$ –1.8 (c 0.15, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61-7.52 (m, 5 H), 5.79 (ddd, *J* = 15.6, 6.7, 6.7 Hz, 1 H), 5.53 (dd, *J* = 15.6, 8.1 Hz, 1 H), 4.67 (br s, 2 H), 4.61 (dd, *J* = 7.4, 6.3 Hz, 1 H), 3.93 (dd, *J* = 8.1, 6.3 Hz, 1 H), 3.90 (ddd, *J* = 9.3, 2.9, 2.9 Hz, 1 H), 3.80-3.73 (m, 2 H), 3.57 (app t, *J* = 6.3 Hz, 2 H), 3.35 (s, 3 H), 2.14-2.06 (m, 3 H), 2.00-1.84 (m, 2 H), 1.83-1.76 (m, 2 H), 1.75-1.54 (m, 4 H), 1.43 (s, 3 H), 1.34 (s, 3 H), 0.90 (d, *J* = 7.0 Hz, 3 H), 0.85 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 135.1, 133.7, 130.0, 129.7, 125.5, 123.7, 108.1, 94.6, 79.9, 79.0, 74.8, 72.9, 71.3, 62.5, 55.3, 36.2, 32.8, 32.2, 30.3, 28.8, 28.4, 27.7, 25.9, 25.4, 18.2, 11.1, -5.4: HRMS (ES+) m/z 685.3427 [$(M+Na)^+$; calcd for $C_{33}H_{54}N_4O_6SSiNa^+$: 685.3533].



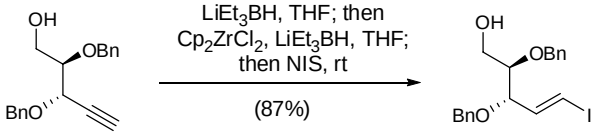
Sulfone (–)-6. To a flask containing (–)-**SI-3-9** (0.0290 g, 0.0440 mmol) was added EtOH (3.20 mL). The reaction flask was cooled to 0 °C and a pre-mixed solution of ammonium molybdate tetrahydrate (0.0210 g, 0.0176 mmol) and H_2O_2 (0.150 mL) was then added dropwise. The flask containing the pre-mixed solution was then washed with EtOH (1.00 mL) and this solution was added to the reaction flask. The resulting solution was then allowed to mix overnight slowly warming to rt. In the morning, the flask was diluted with 50 mL of ether and washed with 20 mL of sat. $NaHCO_3$. The aqueous phase was then washed with 10 mL of ether and the combined organics were dried ($MgSO_4$) and concentrated to yield a crude oil. Purification was accomplished using a 1000 micron prep-TLC plate with an eluent of 20% EtOAc/Hexanes to yield (–)-**6** (0.0290 g, 95% yield) as a clear, colorless oil: IR (neat) 2930, 2857, 1782, 1596, 1498, 1380, 1344, 1250, 1216, 1152, 1099, 1037 cm^{-1}; $[\alpha]_D^{20}$ –1.6 (c 1.05, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.72-7.55 (m, 5 H), 5.82 (ddd, *J* = 15.2, 6.7, 6.7 Hz, 1 H), 5.52 (dd, *J* = 15.2, 8.1 Hz, 1 H), 4.69 (d, J_{AB} = 7.0 Hz, 1 H), 4.67 (d, J_{AB} = 7.0 Hz, 1 H), 4.61 (dd, *J* = 8.9, 6.3 Hz, 1 H), 3.96 (dd, *J* = 7.4, 6.3 Hz, 1 H), 3.90-3.81 (m, 2 H), 3.80-3.66 (m, 3 H), 3.61 (app t, *J* = 6.7 Hz, 2 H), 3.38 (s, 3 H), 2.17- 2.05 (m, 3 H), 1.92-1.54 (m, 6 H), 1.44 (s, 3 H), 1.34 (s, 3 H), 0.93 (d, *J* = 7.0 Hz, 3 H), 0.87 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 135.3, 133.0, 131.4, 129.7, 125.5, 125.0, 108.2, 94.7, 79.7, 79.0, 74.7, 72.5, 71.4, 62.5, 55.4, 54.0, 36.3, 32.1, 28.7, 28.2, 27.7, 26.0, 25.9, 25.3, 18.3, 10.9, -5.3; HRMS (ES+) m/z 7173304 [$(M+Na)^+$; calcd for $C_{33}H_{54}N_4O_8SiNa^+$: 717.3432].



Amide (+)-S-4-1. A mixture of amide (+)-**88** (29.3 g, 104 mmol) and imidazole (23.0 g, 338 mmol) in DMF (520 mL) was treated with TESCl (28.0 mL, 169 mmol) at 0 °C. The mixture was allowed to gradually warm to rt over a period of 2.5 h, and then stirred for an additional 20 h. The reaction mixture was quenched by the slow addition of sat. aqueous $NaHCO_3$ (500 mL), and then diluted with Et_2O (200 mL). The resulting phases were separated and the aqueous phase was extracted with Et_2O (3 X 400 mL), washed with brine (400 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The

crude product was purified by flash chromatography (SiO_2) eluting with 2:1 hexanes/EtOAc to afford (+)-**S-4-1** (37.4 g, 91%) as a pale yellow to clear oil. The auxiliary could be recovered by flushing the flash column with 100% EtOAc. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.31 (d, *J* = 4.5 Hz, 3H), 7.28-7.24 (comp, 2H), 4.50-4.45 (comp, 2H), 4.07-4.03 (m, 1H), 3.60-3.51 (comp, 5H), 3.13 (s, 3H), 2.98 (br s, 1H), 1.87-1.78 (comp, 2H), 1.16-1.14 (d, *J* = 7.0 Hz, 3H), 0.98-0.93 (t, *J* = 8.0 Hz, 9H), 0.63-0.58 (comp, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 128.2, 127.7, 127.4, 125.4, 72.8, 71.6, 66.6, 61.2, 41.5, 35.7, 32.0, 31.9, 30.3, 29.6, 14.4, 6.9, 5.3, 5.1; IR (thin film) 2954, 2876, 1661, 1455, 1415, 1383, 1240, 1103, 1048, 999, 845, 737, 698 cm^{-1}; HRMS (ESI +) *m/z* 396.2585 $(M)^+$ [$C_{21}H_{37}NO_4Si^+$ requires 396.2570]; $[\alpha]_D^{24}$ +0.33 (c 0.92, $CHCl_3$).

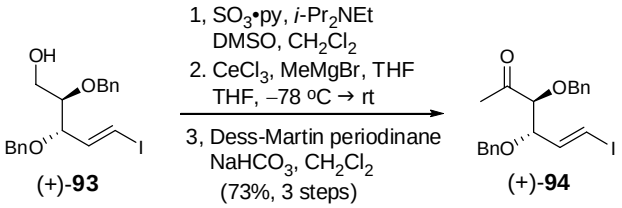
Aldehyde (+)-89: A 1.5 M solution of DIBAL-H in PhMe (91.0 mL, 136 mmol) was added dropwise via additional funnel to a solution of amide (+)-**S-4-1** (44.9 g, 114 mmol) in THF (810 mL) at -78 °C. After 2 h, the reaction mixture was quenched at -78 °C by the addition of a solution of 50% sat. aqueous Rochelle's salt solution (1 L), followed by dilution with EtOAc (500 mL). The resulting mixture was vigorously stirred at rt for 1.5 h, whereupon the phases were separated and the aqueous layer was extracted with Et_2O (3 X 500 mL). The combined organics extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to provide a crude pale yellow oil that was purified by flash chromatography (SiO_2) eluting with 9:1 hexanes/EtOAc to afford aldehyde (+)-**89** (33.7 g, 88%) as a clear to pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.39-7.30 (comp, 5H), 4.56-4.49 (comp, 2H), 4.41-4.36 (m, 1H), 3.59-3.54 (comp, 2H), 2.53-2.48 (m, 1H), 1.92-1.76 (comp, 2H), 1.11-1.09 (d, *J* = 7.0 Hz, 3H), 1.00-0.96 (t, J = 8.0 Hz, 9H), 0.65-0.60 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.0, 138.3, 128.4, 127.7, 127.6, 73.0, 69.4, 66.6, 51.7, 34.7, 7.9, 6.8, 5.1; IR (thin film) 2954, 2876, 1725, 1456, 1363, 1240, 1102, 1009, 811, 736, 696 cm^{-1}; $[\alpha]_D^{24}$ +53.8 (c 0.40, $CHCl_3$).



(+)-**82** (+)-**93**

Alcohol (+)-93: A 1 M solution of $LiEt_3BH$ in THF (9.00 mL, 8.96 mmol) was added dropwise to a solution of **(+)-82** (2.53 g, 8.53 mmol) in THF (17.0 mL) at 0 °C. The resulting solution was maintained at 0 °C for 1 h. In a separate flask, a 1 M solution of $LiEt_3BH$ in THF (17.1 mL, 17.1 mmol) was added dropwise to a solution of recrystallized Cp_2ZrCl_2 (4.99 g, 17.1 mmol) in THF (114 mL) at rt to afford a milky white solution of $Cp_2Zr(H)Cl$. The vessel containing the $Cp_2Zr(H)Cl$ was wrapped in foil to

exclude light and stirred at rt for 1 h, at which time the 0 °C solution of alkoxide was added rapidly via cannula to produce a transparent yellow solution. After 10 min, the mixture was treated in one portion with recrystallized NIS (4.80 g, 21.3 mmol) and allowed to stir at rt for 10 min before being quenched by the addition of sat. aqueous $NaHCO_3$ (50 mL). The resulting layers were separated and the aqueous phase was extracted with EtOAc (3 X 30 mL). The combined organic extracts were dried (Na_2SO_4), filtered through a pad of SiO_2 (50 g) with additional EtOAc (100 mL) and concentrated under reduced pressure. The crude dark yellow oil was purified by flash chromatography (SiO_2) eluting with hexanes/EtOAc (1:1) to afford **(+)-93** (3.15 g, 87%) as a yellow oil that solidified as a white solid (mp 58-59 °C) upon slow evaporation from CH_2Cl_2. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.23 (comp, 10H), 6.57-6.52 (dd, *J* = 14.6, 7.7 Hz, 1H), 6.43-6.40 (d, *J* = 14.6 Hz, 1H), 4.68-4.57 (comp, 4H), 4.39-4.37 (d, *J* = 11.7 Hz, 1H), 3.93-3.89 (t, *J* = 6.9 Hz, 1H), 3.72-3.67 (comp, 2H), 3.54-3.45 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 137.7, 137.5, 128.5, 128.1, 127.9, 127.8, 127.7, 81.4, 80.3 (2C), 72.9, 71.1, 61.6; IR (thin film) 3447, 3030, 2870, 1453, 1091, 950, 736, 697 cm^{-1}; HRMS (ESI +) *m/z* 447.0445 (M + Na)$^+$ [$C_{19}H_{21}IO_3Na^+$ requires 447.0398]; $[\alpha]_D^{24}$ +62.1 (c 0.28, $CHCl_3$).

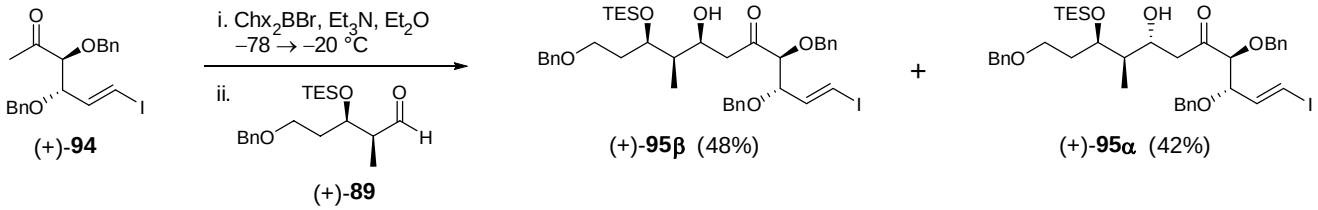


Ketone (+)-94: A slurry of SO_3·Py (970 mg, 6.09 mmol), DMSO (865 μL, 12.2 mmol) and pyridine (495 μL, 6.09 mmol) was added via large gauge syringe to a solution of **(+)-93** (861 mg, 2.03 mmol), DMSO (865 μL, 12.2 mmol) and Et*i*Pr$_2$ (2.2 mL, 12.2 mmol) in CH_2Cl_2 (7.00 mL) at -10 °C. The resulting mixture was allowed to warm to -5 °C over the course of 1 h and then poured into 1 N $NaHSO_4$ solution. The layers were separated and the aqueous phase was extracted with Et_2O (1 X 15 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure to provide a crude yellow oil that was resuspended in hexanes/Et_2O (1:1) (10 mL) and washed with additional 1 N $NaHSO_4$ (2 X 15 mL). The organics were again dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude oil obtained was azeotroped with PhMe (2 X 5 mL) and used without further purification.

A 1.4 M solution of MeMgBr (2.20 mL, 3.04 mmol) in 3:1 PhMe/THF was added dropwise via syringe to a sonicated slurry of $CeCl_3$ (850 mg, 3.55 mmol) in PhMe (17.0 mL) at -78 °C. The resulting

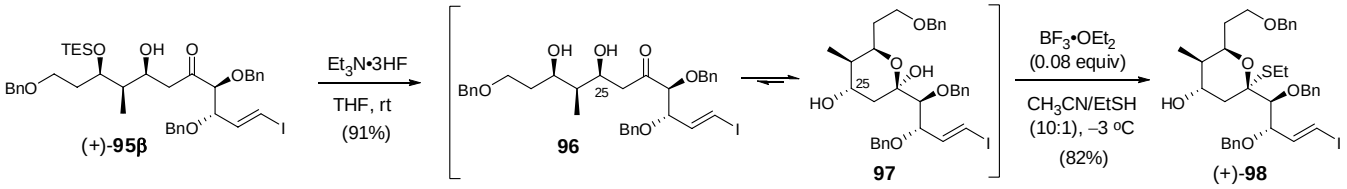
grayish-lavender slurry was allowed to stir for a further 1 h at -78 °C, and then was treated via cannula with a solution of the crude aldehyde in PhMe (4.00 mL) to afford a homogenous pale-yellow solution. After 1h at -78 °C, the reaction mixture was poured into 1 N HCl (30 mL), extracted with Et_2O (3 X 20 mL), dried (Na_2SO_4), filtered through 25 g of SiO_2 with additional Et_2O (20 mL), and concentrated under reduced pressure to afford the crude mixture of alcohols that were used in the next reaction without further purification.

Solid Dess-Martin periodinane (5.20 g, 12.2 mmol) was added in one portion to a rt slurry of the crude alcohols, $NaHCO_3$ (1.70 g, 20.3 mmol), and CH_2Cl_2 (12.0 mL) containing H_2O (24.0 μL). The mixture was stirred at rt in the absence of light for 17 h, and then quenched at rt upon addition of a mixture of 1:1 sat. $NaHCO_3$/sat. $Na_2S_2O_3$ (20 mL). Vigorous stirring was continued for a further 0.5 h, and then the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 X 10 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford a crude yellow oil that was purified by flash chromatography (SiO_2) eluting with 4:1 hexanes/EtOAc to afford ketone **(+)-94** (632 mg, 71% over 3 steps) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.26 (comp, 10H), 6.40-6.55 (dd, *J* = 14.5, 8.0 Hz, 1H), 6.46-6.43 (d, *J* = 14.5 Hz, 1H), 4.64-4.57 (comp, 3H), 4.39-4.36 (d, *J* = 12.0 Hz, 1H), 4.10-4.07 (dd, *J* = 7.5, 5.0 Hz, 1H), 3.89-3.87 (d, *J* = 5.5 Hz, 1H), 2.13 (s, 3H), ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.5, 142.5, 137.2, 137.1, 128.5, 128.4, 128.0, 127.9, 127.8, 85.5, 81.9, 81.2, 73.2, 70.9, 27.3; IR (thin film) 3031, 2869, 1718, 1604, 1496, 1454, 1353, 1093, 950, 737, 697 cm^{-1}; HRMS (ESI +) *m/z* 459.0443 $(M + Na)^+$ [$C_{20}H_{21}IO_3Na^+$ requires 459.0443]; $[\alpha]_D^{24}$ +48.8 (c 0.50, $CHCl_3$).

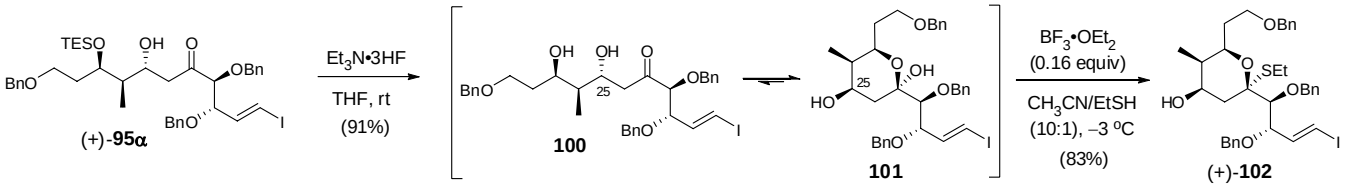


Aldol Adducts (+)-95α and (+)-95β: To a solution of Chx_2BBr (6.10 mL, 27.8 mmol) in Et_2O (107 mL) cooled to -78 °C was added Et_3N (7.00 mL, 50.6 mmol) via syringe. After 2 min, a solution of **(+)-94** (3.67 g, 8.43 mmol) in Et_2O (42.0 mL) was rapidly added via cannula. The reaction mixture was maintained at -78 °C for an additional 2.5 h, whereupon a solution of **(+)-89** (10.6 g, 31.3 mmol) in Et_2O (64.0 mL) was rapidly added via cannula. After 1 h, the reaction vessel was transferred to a -20 °C bath and stirring was continued for 18 h. The reaction was then quenched upon addition of pH 7 buffer (100 mL) and allowed to warm to rt. The resulting layers were separated and the aqueous phase was

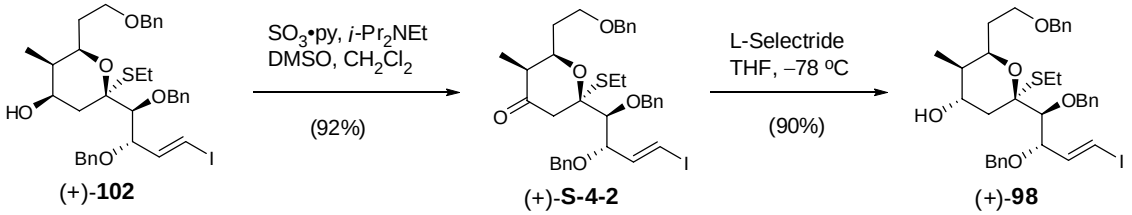
extracted with Et_2O (2 X 50 mL). The combined organics were concentrated under reduced pressure to afford a crude emulsion that was resuspended in a 3:1 mixture of MeOH/pH 7 buffer (200 mL) and cooled to 0 ^oC, whereupon 30% H_2O_2 (60 mL) was added. After 10 min, the resulting solution was removed from the cooling bath and allowed to stir at rt for 3 h before being poured into a mixture of H_2O (200 mL) and Et_2O (100 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 X 40 mL), washed with sat. aqueous $NaHCO_3$ (1 X 300 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a crude pale yellow oil that was purified by flash chromatography (SiO_2) using gradient elution (5% EtOAc/hexanes→10% EtOAc/hexanes→15% EtOAc/hexanes→20% EtOAc/hexanes→25% EtOAc/hexanes) to provide (+)-**95β** (3.08 g, 48%) and (+)-**95α** (2.74 g, 42%) both as pale-yellow oils. Data for **(+)-95β**: R_f = 0.35 in 3:1 hexanes/EtOAc), ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.25 (comp, 15H), 6.86-6.54 (dd, *J* = 14.0, 7.5 Hz, 1H), 6.40-6.37 (d, *J* = 14.5 Hz, 1H), 4.67-4.65 (d, *J* = 11.5 Hz, 1H), 4.59-4.56 (d, *J* = 12.0 Hz, 2H), 4.50-4.44 (comp, 2H), 4.37-4.343 (d, *J* = 12.0 Hz, 1H), 4.27-4.24 (m, 1H), 4.13-4.10 (dd, *J* = 8.0, 5.0 Hz, 1H), 4.02-3.98 (m, 1H), 3.93-3.92 (d, *J* = 4.5 Hz, 1H), 3.47-3.42 (comp, 2H), 3.02-3.01 (m, 1H), 2.87-2.82 (dd, *J* = 18.0, 10.0 Hz, 1H), 2.57-2.52 (dd, *J* = 17.5, 3.5 Hz, 1H), 1.88-1.76 (comp, 2H), 1.51-1.47 (m, 1H), 0.96-0.92 (t, *J* = 8.0 Hz, 9H), 0.87-0.85 (d, *J* = 7.0 Hz, 3H), 0.63-0.55 (comp, 6H);^{13}C NMR (125 MHz, $CDCl_3$) δ 210.3, 142.4, 138.4, 137.3, 137.2, 128.6, 128.5, 128.4, 128.3, 128.2, 128.17, 128.13, 128.0, 127.9, 127.7, 127.66, 127.60, 127.54, 85.2, 82.0, 81.1, 73.9, 73.3, 73.0, 70.9, 69.3, 67.0, 45.3, 41.3, 34.3, 7.8, 6.9, 5.2; IR (thin film) 3501, 3030, 2954, 2874, 1716, 1604, 1454, 1239, 1095, 1007, 736, 697 cm^{-1}; HRMS (ESI +) *m/z* 795.2554 $(M + Na)^+$ [$C_{39}H_{53}IO_6SiNa^+$ requires 795.2553]; $[\alpha]_D^{24}$ +12.5 (c 0.24, $CHCl_3$). Data for **(+)-95α**: R_f = 0.42 in 3:1 hexanes/EtOAc), ^1H NMR (500 MHz, $CDCl_3$) δ 7.34-7.22 (comp, 15H), 6.56-6.51 (dd, *J* = 14.5, 7.5 Hz, 1H), 6.42-6.39 (d, *J* = 14.5 Hz, 1H), 4.63-4.60 (d, *J* = 11.5 Hz, 1H), 4.57-4.54 (d, *J* = 12.0 Hz, 2H), 4.50-4.43 (comp, 2H), 4.36-4.33 (d, *J* = 12.0 Hz, 1H), 4.10-3.98 (comp, 5H), 3.50-3.47 (t, *J* = 6.5 Hz, 2H), 2.66-2.62 (dd, *J* = 16.0, 2.5 Hz, 1H), 2.55-2.49 (dd, *J* = 16.5, 9.0 Hz, 1H), 1.80-1.76 (comp, 2H), 1.68-1.63 (m, 1H), 0.94-0.91 (t, *J* = 8.0 Hz, 9H), 0.69-0.67 (d, *J* = 7.0 Hz, 3H), 0.63-0.54 (comp, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.4, 142.6, 138.4, 137.3, 137.2, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.6, 127.5, 85.0, 82.1, 81.0, 73.0, 72.9, 72.4, 71.1, 70.3, 67.0, 46.2, 42.9, 32.8, 12.1, 6.9, 5.0; IR (thin film) 3462, 3030, 2954, 2874, 1717, 1605, 1496, 1456, 1240, 1099, 1007, 841, 735, 698 cm^{-1}; HRMS (ESI +) *m/z* 795.2585 $(M + Na)^+$ [$C_{39}H_{53}IO_6SiNa^+$ requires 795.2553]; $[\alpha]_D^{24}$ +44.8 (c 0.29, $CHCl_3$).



Thioketal (+)-98: A rt solution of **(+)-95β** (5.03 g, 6.86 mmol) in THF (140 mL) (in a polyethylene bottle) was treated via syringe with $Et_3N{\cdot}3HF$ (5.60 mL, 34.3 mmol). The mixture was stirred 22 h in the absence of light, then diluted with Et_2O (100 mL) and concentrated under reduced pressure to afford a viscous yellow oil. The crude product mixture was purified by flash chromatography (SiO_2) eluting with 1:1 hexanes/EtOAc to afford diol **96** (4.07 g, 90%) that existed as a mixture of the acyclic 1,3-diol **96** and its cyclic hemiketal tautomer **97**. This material (4.07 g, 6.18 mmol) was dissolved in a 10:1 mixture of CH_3CN/EtSH (1.36 L) and cooled to an internal temperature of -2 °C. A 0.080 M solution of $BF_3{\cdot}OEt_2$ in MeCN (6.20 mL, 0.494 mmol) was added via syringe pump at a rate of 0.34 mL/h. After 17.5h, the mixture was quenched with sat. aqueous $NaHCO_3$ (25 mL) and allowed to warm to rt. The resulting solution was diluted with Et_2O (500 mL) and poured into brine (500 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 X 100 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure to provide a crude yellowish-brown oil that was purified by flash chromatography (SiO_2) eluting with 15% EtOAc/hexanes to afford **(+)-98** (3.57 g, 82%) as a pale-yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.24 (comp, 15H), 6.72-6.66 (dd, *J* = 14.5, 8.5 Hz, 1H), 6.37-6.34 (d, *J* = 14.5 Hz, 1H), 4.79-4.73 (comp, 2H), 4.60-4.57 (d, *J* = 12.5 Hz, 1H), 4.50-4.43 (comp, 4H), 4.38-4.34 (m, 1H), 4.32-4.29 (d, *J* = 12.5 Hz, 1H), 3.75-3.68 (comp, 2H), 3.55-3.52 (comp, 2H), 2.47-2.30 (comp, 3H), 1.89-1.81 (m, 1H), 1.74-1.63 (comp, 2H), 1.35-1.31 (d, *J* = 15.5 Hz, 1H), 1.04-1.01 (t, *J* = 7.5 Hz, 3H), 0.85-0.83 (d, *J* = 7.5Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 138.7, 138.3, 138.2, 128.4, 128.2, 128.1, 127.7, 127.6, 127.54, 127.46, 88.4, 86.5, 81.8, 81.0, 76.1, 73.0, 70.3, 69.8, 67.0, 64.1, 38.0, 33.1, 30.6, 21.1, 14.3, 10.8; IR (thin film) 3481, 3030, 2926, 2867, 1601, 1497, 1455, 1265, 1211, 1105, 1059, 960, 736, 698 cm^{-1}; HRMS (ESI +) *m/z* 725.1801 $(M + Na)^+$ [$C_{35}H_{43}IO_5SNa^+$ requires 725.1800]; $[\alpha]_D^{24}$ +79.4 (c 0.18, $CHCl_3$).



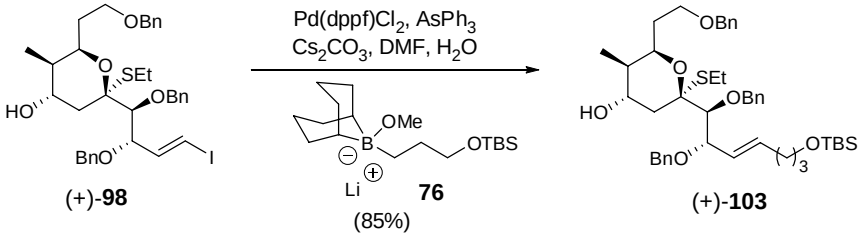
Thioketal (+)-102: A rt solution of **(+)-95α** (9.77 g, 12.6 mmol) in THF (250 mL) (in a polyethylene bottle) was treated via syringe with $Et_3N{\cdot}3HF$ (10.3 mL, 63.2 mmol). The mixture was stirred 21 h in the absence of light, then diluted with Et_2O (200 mL) and concentrated under reduced pressure to afford a viscous yellow oil. The crude product mixture was purified by flash chromatography (SiO_2) eluting with 1:1 hexanes/EtOAc to afford diol **100** (7.67 g, 92%) that existed as a mixture of the acyclic 1,3-diol **100** and its cyclic hemiketal tautomer **101**. A portion of this material (3.31 g, 5.03 mmol) was dissolved in a 10:1 mixture of CH_3CN/EtSH (1.10 L) and cooled to an internal temperature of -2 °C. A 0.080 M solution of $BF_3{\cdot}OEt_2$ in MeCN (10.0 mL, 0.805 mmol) was added via syringe pump at a rate of 0.5 mL/h. After 20 h, the mixture was quenched with sat. aqueous $NaHCO_3$ (25 mL) and allowed to warm to rt. The resulting solution was diluted with Et_2O (400 mL) and poured into brine (400 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 X 80 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure to provide a crude yellowish-brown oil that was purified by flash chromatography (SiO_2) eluting with 15% EtOAc/hexanes to afford (+)-**102** (2.94 g, 83%) as a pale-yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.24 (comp, 15H), 6.74-6.69 (dd, *J* = 15.0, 9.0 Hz, 1H), 6.38-6.34 (d, *J* = 14.5 Hz, 1H), 4.80-4.74 (comp, 2H), 4.59-4.57 (d, *J* = 12.0 Hz, 1H), 4.49-4.24 (comp, 4 H), 4.33-4.30 (d, *J* = 12.0 Hz, 1H), 4.19-4.15 (comp, 2H), 3.83 (m, 1H), 3.53-3.50 (comp, 2H), 2.29-2.21 (comp, 2H), 2.05-1.99 (t, *J* = 12.5 Hz, 1H), 1.90-1.78 (comp, 2H), 1.74-1.68 (m, 1H), 1.39-1.35 (dd, *J* = 13.5, 5.0 Hz, 1H), 1.03-0.99 (t, *J* = 7.5 Hz, 3H), 0.80-0.76 (d, *J* = 13.0 Hz, 3H);^{13}C NMR (125 MHz, $CDCl_3$) δ 142.9, 138.9, 138.27, 138.25, 128.3, 128.29, 128.1, 128.0, 127.7, 127.53, 127.50, 127.3, 89.8, 86.1, 81.8, 80.9, 76.1, 73.0, 70.0, 69.7, 69.2, 68.0, 67.1, 38.2, 33.0, 32.5, 20.3, 14.2, 4.4; IR (thin film) 3447, 3030, 2925, 2866, 1600, 1496, 1453, 1357, 1265, 1206, 1106, 1027, 959, 734, 697 cm^{-1}; HRMS (ESI +) *m/z* 725.1786 $(M + Na)^+$ [$C_{35}H_{43}IO_5SNa^+$ requires 725.1800]; $[\alpha]_D^{24}$ +113.5 (c 0.28, $CHCl_3$).



Pyranone (+)-S-4-2: Solid $SO_3{\cdot}Py$ (2.50 g, 15.8 mmol) was added in one portion to a mixture of **(+)-102** (3.70 g, 5.27 mmol), DMSO (1.10 mL, 15.8 mmol) and $EtN(i\text{-}Pr)_2$ (5.50 mL, 31.6 mmol) in CH_2Cl_2 (70.0 mL) cooled to an internal temperature of -17 °C. The resulting solution was allowed to warm to an internal temperature of 0 °C over a period of 1.5 h, and then was diluted with Et_2O (150 mL). The slurry

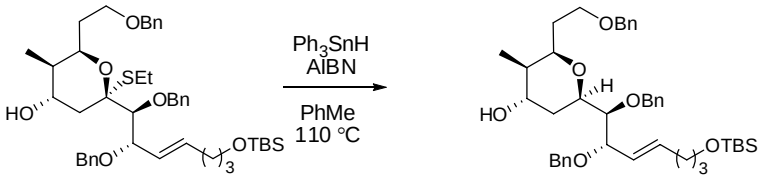
that formed was washed poured into 1 N $NaHSO_4$ (200 mL) and the aqueous phase was extracted with additional Et_2O (2 X 50 mL). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting crude yellow oil was purified by flash chromatography (SiO_2) eluting with 9:1 hexanes/EtOAc to afford pyranone (3.39 g, 92%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.24 (comp, 15H), 6.71-6.66 (dd, *J* = 14.8, 8.9 Hz, 1H), 6.43-6.40 (d, *J* = 14.8 Hz, 1H), 4.87 (s, 2H), 4.63-4.60 (d, *J* = 12.0 Hz, 1H), 4.55-4.51 (m, 1H), 4.50-4.43 (comp, 3H), 4.34-4.31 (d, *J* = 12.0 Hz, 1H), 3.97-3.96 (m, 1H), 3.56-3.53 (comp, 2H), 3.20-3.17 (d, *J* = 15.3 Hz, 1H), 2.36-2.24 (comp, 3H), 1.97-1.90 (comp, 2H), 1.79-1.72 (m, 1H), 1.07-1.05 (d, *J* = 7.5 Hz, 3H), 1.00-0.96 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.8, 142.3, 138.6, 138.1, 128.5, 128.4, 128.2, 128.1, 127.8, 127.68, 127.66, 127.62, 127.5, 90.5, 85.7, 81.7, 81.6, 76.3, 73.0, 69.8, 68.9, 66.6, 48.2, 42.0, 32.1, 29.7, 20.5, 13.9, 10.7; IR (thin film) 3030, 2923, 2854, 1719, 1602, 1497, 1454, 1097, 959, 734, 697 cm^{-1}; HRMS (ESI +) *m/z* 723.1365 $(M + Na)^+$ [$C_{35}H_{41}IO_5SNa^+$ requires 723.1617]; $[\alpha]_D^{24}$ +115.5 (c 0.51, $CHCl_3$).

Reduction of pyranone (+)-S-4-2 to (+)-98: A 1.0 M solution of L-Selectride in THF (1.10 mL, 1.10 mmol) was added dropwise via syringe to a solution of pyranone (+)-**S-4-2** (627 mg, 0.895 mmol) in THF (9.00 mL) cooled to -78 °C. The resulting mixture was maintained at -78 °C for 22 h, and then quenched upon the addition of H_2O (3 mL) and allowed to warm to rt over 3.5 h. The reaction mixture was then diluted with Et_2O (15 mL) and poured into a 25% w/v solution of aqueous NaOH (50 mL). The organic phase was washed with additional 25% w/v aqueous NaOH (2 X 30 mL), brine (1 X 50 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (SiO_2) eluting with 15% EtOAc/hexanes to afford (+)-**98** (567 mg, 90%) as a pale yellow oil.



Silyl ether (+)-103: A 1.7 M solution of *t*-BuLi in pentane (4.60 mL, 7.81 mmol) was rapidly added via syringe to a mixture of $I(CH_2)_3OTBS$ (1.10 g, 3.66 mmol) and 9-MeO-9-BBN (8.30 mL, 1 M in hexanes, 8.30 mmol) in Et_2O (41.0 mL) cooled to -78 °C. After 5 min, THF (41.0 mL) was rapidly added via syringe and the resulting solution was allowed to warm to rt for 1 h. In a separate flask, (+)-**98** (1.71 g,

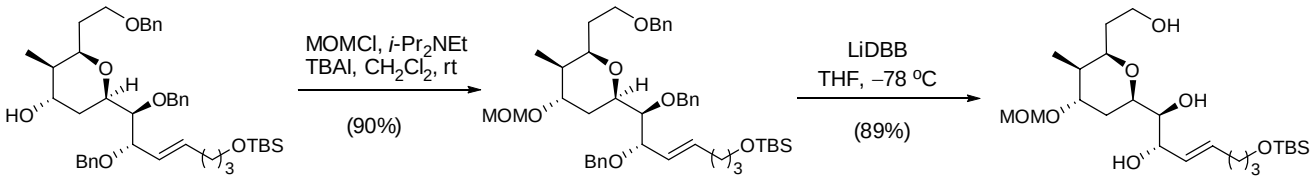
2.44 mmol), Pd(dppf)Cl_2 (996 mg, 1.22 mmol), $AsPh_3$ (112 mg, 0.366 mmol), Cs_2CO_3 (3.18 g, 9.76 mmol) and H_2O (1.00 mL, 59.0 mmol) were dissolved in DMF (41.0 mL) at rt. The ethereal boronate solution was then added rapidly to this mixture via cannula to provide a dark brown mixture that was stirred in the dark. After 16 h, the mixture was filtered through a pad of Celite using Et_2O (250 mL). The filtrate was washed with H_2O (400 mL), and the aqueous phase was extracted with Et_2O (3 X 70 mL). The combined organic phases were dried ($MgSO_4$), filtered through a pad of SiO_2 (400 g) with additional Et_2O (500 mL), and then concentrated under reduced pressure. The resulting crude amber oil was purified by flash chromatography (SiO_2) eluting with 9:1 hexanes/EtOAc to afford (+)-**103** (1.60 g, 88%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.26 (comp, 15H), 5.68-5.63 (comp, 2H), 4.84-4.80 (comp, 2H), 4.60-4.57 (d, *J* = 12.1 Hz, 1H), 4.53-4.46 (comp, 3H), 4.40-4.37 (m, 1H), 4.33-4.30 (d, *J* = 12.2 Hz, 1H), 3.81-3.76 (comp, 2H), 3.72-3.69 (m, 1H), 3.64-3.61 (t, *J* = 6.5 Hz, 2H), 3.57-3.55 (comp, 2H), 2.46-2.41 (comp, 2H), 2.38-2.34 (dd, *J* = 15.5, 4.0 Hz, 1H), 2.15-2.12 (comp, 2H), 1.93-1.85 (m, 1H), 1.77-1.60 (comp, 4H), 1.40-1.36 (d, *J* = 15.5 Hz, 1H), 1.09-1.05 (t, *J* = 7.5 Hz, 3H), 0.90 (s, 9H), 0.87-0.85 (d, *J* = 7.0 Hz, 3H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.3, 139.1, 138.4, 136.4, 128.4, 128.2, 128.0, 127.9, 127.6, 127.5, 127.2, 126.5, 88.8, 87.0, 80.8, 75.9, 73.0, 70.4, 68.9, 67.1, 63.9, 62.7, 38.0, 33.2, 32.3, 30.7, 28.9, 26.0, 14.4, 10.8, -5.3; IR (thin film) 3485, 3029, 2928, 2857, 1497, 1454, 1361, 1255, 1212, 1105, 1058, 977, 837, 776, 735, 698 cm^{-1}; HRMS (ESI +) *m/z* 771.4085 $(M + Na)^+$ [$C_{44}H_{64}O_6SiSNa^+$ requires 771.4090]; $[\alpha]_D^{24}$ +69.6 (c 0.58, $CHCl_3$).



(+)-**103** (+)-**105** (65%)

Tetrahydropyran (+)-105: To a rt solution of (+)-**103** (2.35 g, 3.13 mmol) and Ph_3SnH (8.00 mL, 32.0 mmol) was added solid AIBN (52.0 mg, 0.320 mmol). The resulting mixture was immersed in a preheated 115 ^{o}C oil bath, and stirred for 1.5 h. An additional portion of solid AIBN (52.0 mg, 0.320 mmol) was added, and the reaction was heated for another 45 min. The mixture was allowed to cool to rt and then filtered through a SiO_2 pad (75 g) with Et_2O (300 mL). The filtrate was concentrated under reduced pressure to provide a pale yellow slurry that was dissolved in a minimal volume of CH_2Cl_2 (5 mL) and purified by flash chromatography (SiO_2) using gradient elution [5% EtOAc/hex (to remove residual Ph_6Sn_2) → 10% EtOAc/hexanes → 15% EtOAc/hexanes → 20% EtOAc/hexanes → 25%

EtOAc/hexanes] to afford (+)-**105** (1.48 g, 68%) and the *trans*-2,6-disubstituted tetrahydropyran (230 mg, 11%) (undesired diastereomer is lower R_f). Data for **(+)-105**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.25 (comp, 15H), 5.67-5.63 (m, 1H), 5.53-5.48 (m, 1H), 4.81-4.78 (d, *J* = 11.4 Hz, 1H), 4.69-4.66 (d, *J* = 11.4Hz, 1H), 4.60-4.57 (d, *J* = 11.4 Hz; 1H), 4.52-4.47 (comp, 2H), 4.31-4.29 (d, *J* = 11.4 Hz, 1H), 3.92-3.88 (comp, 3H), 3.83-3.78 (m, 1H), 3.63-3.49 (comp, 6H), 2.14-2.11 (comp, 2H), 1.84-1.78 (m, 1H), 1.74-1.68 (m, 1H), 1.62-1.48 (comp, 5H), 0.94-0.86 (comp, 12H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 138.8, 138.5, 136.0, 128.3, 128.1, 128.0, 127.7, 127.6, 127.5, 127.31, 127.29, 127.1, 83.2, 80.6, 74.3, 72.9, 72.1, 71.1, 70.6, 69.9, 67.8, 62.6, 38.3, 33.2, 32.4, 29.6, 29.5, 29.3, 28.8, 25.9 (X2), 11.0, -5.3; IR (thin film) 3447, 3031, 2927, 2855, 1456, 1362, 1257, 1098, 972, 836, 776, 734, 697 cm^{-1}; HRMS (ESI +) *m/z* 711.4022 $(M + Na)^+$ [$C_{42}H_{60}O_6SiNa^+$ requires 771.4056]; $[\alpha]_D^{24}$ +30.8 (c 0.38, $CHCl_3$).

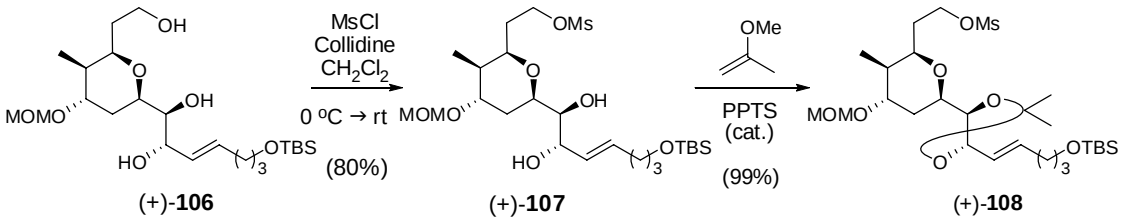


(+)-**105** (+)-**S-4-3** (+)-**106**

MOM-ether (+)-S-4-3: Solid TBAI (125 mg, 0.339 mmol) was added in one portion to a mixture of (+)-**105** (1.55 g, 2.25 mmol) and EtN(*i*-Pr)$_2$ (18.5 mL, 135 mmol) in CH_2Cl_2 at 0 °C. After 5 min of stirring, freshly distilled MOMCl (distilled from $CaCl_2$) (5.00 mL, 68.0 mmol) was added dropwise via syringe and the mixture was allowed to warm to rt. After 22 h, the mixture was diluted with Et_2O (25 mL) and poured into H_2O (50 mL). The layers were separated and the organic phase was washed with sat. aqueous NH_4Cl (3 X 50 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude yellow oil that was purified by flash chromatography (SiO_2) eluting with 15% EtOAc/hexanes to afford (+)-**S-4-3** (1.50 g, 90%) as a clear to pale yellow oil and recovered (+)-**105** (73 mg, 5%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.22 (comp, 15H), 5.65-5.59 (m, 1H), 5.57-5.46 (m, 1H), 4.79-4.77 (d, *J* = 11.5 Hz, 1H), 4.68-4.65 (d, *J* = 11.5 Hz, 1H), 4.63-4.59 (comp, 2H), 4.58-4.55 (d, *J* = 11.5 Hz, 1H), 4.51-4.45 (comp, 2H), 4.30-4.27 (d, *J* = 11.5 Hz, 1H), 3.93-3.90 (m, 1H), 3.88-3.84 (m, 1H), 3.72-3.70 (m, 1H), 3.61-3.45 (comp, 5H), 3.30 (s, 3H), 2.14-2.08 (comp, 2H), 1.83-1.74 (m, 1H), 1.73-1.52 (comp, 7H), 0.89-0.86 (comp, 12H), 0.03 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 138.9, 135.9, 128.3, 128.1, 128.0, 127.5, 127.4, 127.3, 127.2, 126.7, 95.6, 83.3, 81.0, 75.3, 74.3, 72.9, 72.8, 71.6, 69.9, 67.8, 62.6, 55.2, 36.3, 33.2, 32.4, 29.6, 28.8, 26.9, 25.9, 11.1, -5.3; IR (thin film) 3030, 2928, 2857, 1454,

1362, 1255, 1101, 1039, 972, 836, 776, 734, 697 cm^{-1}; HRMS (ESI +) *m/z* 755.4310 $(M + Na)^+$ [$C_{44}H_{64}O_7SiNa^+$ requires 755.4319]; $[\alpha]_D^{24}$ +34.5 (c 0.62, $CHCl_3$).

Triol (+)-106: A 3-neck flask was charged with Li^o wire (453 mg, 65.3 mmol) and rinsed with dry pentane to remove oil. The wire was then cut into small pieces with a metal spatula and smashed into ribbons using a glass rod. Solid DBB (18.3 g, 68.5 mmol) was subsequently added to the Li^o and the flask was charged with freshly sparged THF (380 mL). The mixture was cooled to 0 ^oC and maintained at this temperature with vigorous stirring (glass coated stir-bar) for 5h to provide a dark bluish-green solution of LiDBB (ca 0.17 M). In a separate flask, a solution of (+)-**S-4-3** (1.19 g, 1.63 mmol) in sparged THF (14.0 mL) was cooled to -78 ^oC and treated via syringe with the LiDBB solution. The reaction required ca 130 mL of the LiDBB solution to reach completion as indicated by the persistence of the dark greenish-blue LiDBB color (color should not dissipate after 5-10 min). The reaction was then quenched at -78 ^oC by the addition of sat. aqueous NH_4Cl (20 mL) and warmed to rt by removal of the cooling bath. The mixture was subsequently diluted with Et_2O (100 mL), and the resulting phases were separated. The aqueous layer was extracted with CH_2Cl_2 (3 X 50 mL) and the combined organic extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The resulting slurry containing predominately DBB was redissolved in a minimal volume of CH_2Cl_2 to permit loading onto a SiO_2 column. Flash chromatography utilizing gradient elution (3:1 hexanes/EtOAc until DBB separated; then 1:3 hexanes/EtOAc → 100% EtOAc) afforded (+)-**106** (670 mg, 89%) as a pale yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 5.84-5.79 (m, 1H), 5.60-5.53 (m, 1H), 4.70-4.66 (comp, 2H), 4.19-4.15 (t, *J* = 6.6 Hz, 1H), 4.08-4.05 (m, 1H), 3.84-3.79 (m, 1H), 3.77-3.73 (comp, 3H), 3.63-3.60 (t, *J* = 6.4 Hz, 2H), 3.52-3.49 (m, 1H), 3.36 (s, 3H), 2.68 (br s, 1H), 2.16-2.11 (comp, 3H), 1.88-1.83 (comp, 2H), 1.74-1.68 (comp, 3H), 1.63-1.60 (comp, 2H), 1.50-1.46 (m, 1H), 0.95-0.93 (d, *J* = 7.5 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.1, 128.5, 94.9, 75.3, 75.1, 74.8, 74.5, 74.2, 62.5, 61.3, 55.4, 36.6, 35.2, 32.2, 28.8, 27.5, 25.9 (X3), 18.3, 11.1, -5.3; IR (thin film) 3419, 2929, 1472, 1386, 1256, 1101, 1040, 973, 919, 837, 776 cm^{-1}; HRMS (ESI +) *m/z* 485.2929 $(M + Na)^+$ [$C_{23}H_{46}O_7SiNa^+$ requires 485.2911]; $[\alpha]_D^{24}$ +5.4 (c 0.33, $CHCl_3$).

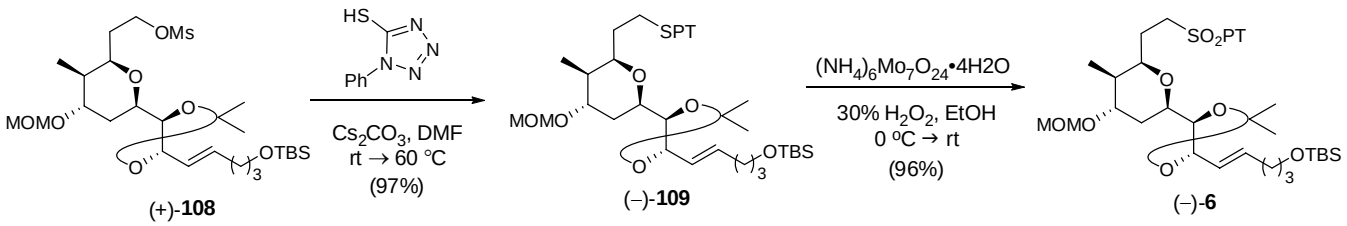


(+)-**106** (+)-**107** (+)-**108**

Mesylate (+)-107: Freshly distilled MsCl (dist. from P_2O_5) (70.0 μL, 0.910 mmol) was added via syringe to a mixture of (+)-**106** (350 mg, 0.756 mmol) and 2,4,6-collidine (1.00 mL, 7.60 mmol) in CH_2Cl_2 (13.0 mL) cooled to 0 ^oC. The mixture was allowed to slowly warm to rt and after 27 h, was poured into sat. aqueous NH_4Cl (25 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 X 10 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to provide a crude oil contaminated with excess collidine. Purification by flash chromatography (SiO_2) using gradient elution: 3:1 hexanes/EtOAc (to separate collidine) → 2:3 hexanes/EtOAc (to elute product) → 1:3 hexanes/EtOAc (to elute recovered (+)-**106**) → 100% EtOAc (to elute product with loss ofTBS) afforded (+)-**107** (322 mg, 81%) along with recovered (+)-**106** (21.0 mg, 6%) and 23.0 mg (7%) of product from which the TBS-ether has been cleaved. Data for (+)-**107**: ^1H NMR (500 MHz, $CDCl_3$) δ 5.67-5.53 (m, 1H), 5.57-5.52 (m, 1H), 4.68-4.64 (comp, 2H), 4.31-4.28 (comp, 2H), 4.19-4.16 (m, 1H), 4.02-3.99 (m, 1H), 3.82-3.76 (comp, 2H), 3.62-3.59 (t *J* = 6.0 Hz, 2H), 3.50-3.47 (m, 1H), 3.35 (s, 3H), 2.99 (s, 3H), 2.47-2.46 (d, *J* = 3.5 Hz, 1H), 2.16-2.10 (comp, 2H), 2.00-1.99 (d, *J* = 4.0 Hz, 1H), 1.94-1.81 (comp, 2H), 1.74-1.70 (comp, 3H), 1.62-1.58 (comp, 2H), 0.92-0.90 (d, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.0, 128.5, 94.9, 75.4, 75.0, 74.9, 74.3, 70.9, 67.2, 62.5, 55.5, 37.3, 36.3, 32.7, 32.2, 28.8, 27.5, 25.9 (X3), 10.9, -5.3; IR (thin film) 3446, 2930, 2857, 1669, 1471, 1360, 1257, 1176, 1101, 1038, 974, 922, 837, 778 cm^{-1}; HRMS (ESI +) *m/z* 563.2707 $(M + Na)^+$ [$C_{24}H_4O_9SSiNa^+$ requires 563.2686]; $[\alpha]_D^{24}$ +16.0 (c 0.13, $CHCl_3$).

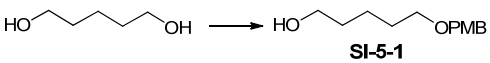
Acetonide (+)-108: Solid PPTS (5.00 mg, 22.0 μmol) was added in one portion to a rt mixture of (+)-**107** (227 mg, 0.433 mmol) and 2-methoxypropene (0.110 mL, 1.10 mmol) in CH_2Cl_2 (6 mL). After 7 h, the mixture was poured onto sat. aqueous $NaHCO_3$ (15 mL) and extracted with CH_2Cl_2 (3 X 10 mL). The combined organics were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting crude pale yellow oil was purified by flash chromatography (SiO_2) eluting with 3:1 hexanes/EtOAc to afford (+)-**108** (250 mg, 99%) as a clear to pale yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 5.99-5.76 (m, 1H), 5.53-5.51 (m, 1H), 4.66-4.65 (comp, 2H), 4.60-4.57 (t, *J* = 7.0 Hz, 1H), 4.31-4.28 (m, 1H), 4.23-4.21 (m, 1H), 3.95-3.92 (t, *J* = 7.5Hz, 1H), 3.89-3.86 (m, 1H), 3.75-3.72 (comp, 2H), 3.63-3.59 (t, *J* = 6.5 Hz, 2H), 3.35 (s, 3H), 2.97 (s, 3H), 2.15-2.10 (m, 2H), 1.93-1.85 (m, 1H), 1.74-1.57 (comp, 6H), 1.43 (s, 3H), 1.33 (s, 3H), 0.91-0.89 (d, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.1, 125.5, 94.8, 79.9, 78.9, 74.9, 71.5, 70.4 67.1, 62.7, 55.4, 37.5, 36.2, 32.9, 32.3, 28.8, 28.2, 27.6, 26.0 (3C), 25.3, 11.0, -5.3; IR (thin film) 2937, 2885, 1472, 1360,

1249, 1215, 1177, 1101, 1066, 1039, 965, 920, 837, 777 cm^{-1}; HRMS (ESI +) *m/z* 603.3024 $(M + Na)^+$ [$C_{27}H_{52}O_9SSiNa^+$ requires 603.2999]; $[\alpha]_D^{24}$ +24.6 (c 1.25, $CHCl_3$).



Thioether (–)-109: Solid Cs_2CO_3 (415 mg, 1.27 mmol) was added in one portion to a rt solution of (+)-**108** (148 mg, 0.255 mmol) and 1-phenyl-1*H*-tetrazole-5-thiol (136 mg, 0.764 mmol) in DMF (2.60 mL). The mixture was placed into a rt oil bath and heated to 60 °C for 4.5 h, and then cooled to rt. The resulting solution was diluted with Et_2O (10 mL) and washed with brine (15 mL). The aqueous phase was extracted with Et_2O (3 X 5 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting crude yellow oil was purified by flash chromatography (SiO_2) eluting with 15% EtOAc/hexanes to afford (–)-**109** (163 mg, 97%) as a yellow oil. All characterization data are in agreement with the previous one.

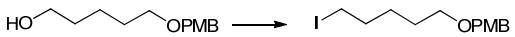
Sulphone (–)-6: A premixed solution of $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (75.0 mg, 60.0 μmol) and 30% H_2O_2 (0.370 mL, 3.60 mmol) were slowly added via glass pipette to a solution of (-)-**109** (160 mg, 0.241 mmol) in EtOH (24.0 mL) cooled to 0 °C. The mixture was allowed to slowly warm to rt and stirred for a total of 20 h, whereupon CH_2Cl_2 (50 mL) was added. The resulting solution was washed with a 1:1 mixture of sat. aqueous $NaHCO_3$/sat. aqueous Na_2SO_3 (100 mL). The aqueous phase was further extracted with CH_2Cl_2 (3 X 30 mL) and then the combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude oil thus obtained was purified by flash chromatography (SiO_2) eluting with 4:1 hexanes/EtOAc to afford (–)-**6** (151 mg, 96%). All characterization data are in agreement with the previous one.



SI-5-1

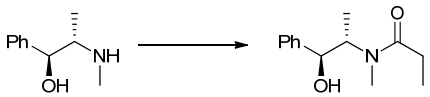
Alcohol SI-5-1. On this large scale, HPLC grade THF was employed. A mechanically stirred, 0 °C suspension of NaH (26.6 g, 95% wt., 1.05 mol) in THF (1.50 L) was charged with a solution of distilled 1,5-pentanediol (336 g, 3.20 mol, bp ~120 °C under high vacuum) in THF (500 mL) via cannula over 15 min. Gas Evolution! The suspension was then heated to reflux for 3 h before adding *p*-methoxybenzyl chloride (PMBCl, 65.0 mL, 478 mmol) and tetrabutylammonium iodide (TBAI, 8.80 g, 23.9 mmol)

sequentially. After 15 h, the reaction was quenched with water (500 mL) and concentrated *in vacuo*. The residue was then diluted with CH_2Cl_2 (1.0 L) and water (2.5 L). The aqueous phase was then washed with CH_2Cl_2 (3 x 250 mL), and the combined organic layers were washed with water (3 x 500 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (10/1 → 3/2, hexanes/EtOAc, 15.0 cm diameter column, 10.0 in. SiO_2, flow rate 0.5 in./min.) afforded 106 g (99% yield) of **SI-5-1** as a yellow oil: R_f 0.17 (2/1, hexanes/EtOAc); IR (neat) 3398 (br, m), 2936 (s), 2861 (s), 1612 (s), 1585 (w), 1512 (s), 1248 (s), 1173 (m), 1094 (s), 1035 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 4.43 (s, 2 H), 3.80 (s, 3 H), 3.63 (t, *J* = 6.5 Hz, 2 H), 3.45 (t, *J* = 6.5 Hz, 2 H), 1.60 (m, 4 H), 1.45 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.97, 130.47, 129.03, 113.61, 72.37, 69.87, 62.30, 55.07, 32.27, 29.25, 22.27; HRMS (CI, NH_3) m/z 224.1412 [M^+; calcd for $C_{13}H_{20}O_3^+$: 224.1412].



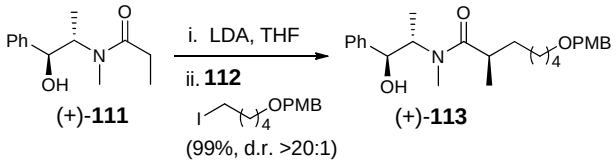
SI-5-1 **112**

Iodide 112. To a 0 °C solution of alcohol **SI-5-1** (18.1 g, 80.7 mmol) and imidazole (13.1 g, 194 mmol) in THF (340 mL), wrapped in Al foil, was sequentially added triphenylphosphine (25.4 g, 96.8 mmol) and THF (30.0 mL). After 10 min., iodine (24.5 g, 96.8 mmol) was added portionwise over 5 min., followed by rinsing the flask originally containing the iodine with THF (30.0 mL). After 15 min., the reaction was concentrated *in vacuo*. The resulting slurry was then diluted with EtOAc (300 mL), and washed with sat. $Na_2S_2O_3$ (2 x 100 mL), sat. $NaHCO_3$ (2 x 100 mL), dried over $MgSO_4$, concentrated *in vacuo* and preabsorbed onto 200 mL Si gel. Purification by flash chromatography (20/1 → 2/1, hexanes/EtOAc, 10.0 cm diameter column, 14.0 in. SiO_2, flow rate 2.0 in./min.) afforded 24.9 g (93% yield) of **112** as a yellow oil: R_f 0.33 (10/1, hexanes/EtOAc); IR (neat) 2934 (s), 2856 (s), 1612 (s), 1585 (m), 1512 (s), 1456 (s), 1360 (m), 1301 (s), 1247 (s), 1171 (s), 1099 (s), 1035 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 4.43 (s, 2 H), 3.81 (s, 3 H), 3.44 (t, *J* = 6.5 Hz, 2 H), 3.18 (t, *J* = 7.0 Hz, 2 H), 1.84 (m, 2 H), 1.62 (m, 2 H), 1.48 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ159.00, 130.50, 129.05, 113.64, 72.42, 69.53, 55.13, 33.20, 28.55, 27.13, 6.74; HRMS (CI, NH_3) m/z 335.0508 [MH^+; calcd for $C_{13}H_{20}IO_2^+$: 335.0507].



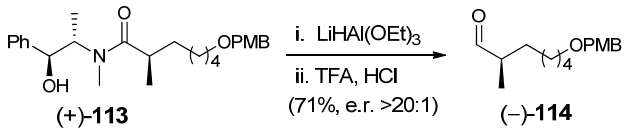
(+)-**111**

Amide (+)-111. On this large scale, HPLC grade CH_2Cl_2 was employed. A solution of (1S,2S)-(+)-pseudoephedrine (99.8 g, 604 mmol) in CH_2Cl_2 (1.00 L) was placed in an ambient temperature water bath and charged with triethylamine (102 mL, 725 mmol). Propionic anhydride (83.0 mL, 646 mmol) was then added in 5.0 mL aliquots over 10 min. Exotherm! After 1 h, water (200 mL) was added. The organic layer was then washed with 50% sat. $NaHCO_3$ (2 x 200 mL), 1 N HCl (2 x 200 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The solid was then recrystallized from hot toluene (400 mL) to afford 123 g (92% yield) of amide (+)-**111** as a white solid: mp 114-115 ^oC; R_f 0.40 (5/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +103.1 (*c* 0.66, MeOH); IR (neat) 3379 (br, m), 2979 (m), 2937 (m), 1623 (s), 1053 (s) cm^{-1}; ^1H NMR (500 MHz, C_6D_6, 3:1 mixture of rotamers, *represents minor peaks) δ 7.31 (d, *J* = 7.3 Hz, 2 H), 7.11 (m, 3 H), 4.77 (br s, 1 H), 4.51 (d, *J* = 7.3 Hz, 1 H), 4.20 (m, 1 H), *3.70 (m, 1 H), *2.80 (s, 3 H), *2.43 (m, 1 H), 2.12 (s, 3 H), 1.76 (m, 2 H), *1.21 (app t, *J* = 7.3 Hz, 3 H), 1.01 (app t, *J* = 7.4 Hz, 3 H), 0.95 (d, *J* = 7.0 Hz, 3 H), *0.57 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$, 3:1 mixture of rotamers, *represents minor peaks) δ 175.96, *174.87, 142.39, *141.44, *128.51, 128.21, *128.10, 127.49, *126.83, 126.36, 76.36, *75.29, 58.17, 32.38, 27.42, *26.69, *15.21, 14.31, *9.50, 9.08; HRMS (CI, NH_3) m/z 222.1486 [MH^+; calcd for $C_{13}H_{20}NO_2^+$: 222.1493].



Amide (+)-113. LiCl (9.60 g, 227 mmol) was first flame-dried under high vacuum and cooled under Ar. THF (88.0 mL), and $(i\text{-Pr})_2NH$ (18.0 mL, 128 mmol) were then added sequentially, and the suspension was cooled to -78 ^oC. *n*-BuLi (47.8 mL, 2.5 M in hexanes, 120 mmol) was then added via syringe over 3-4 min., followed by a 0 ^oC solution of amide (+)-**111** (13.8 g, 62.8 mmol) in THF (148 mL) via cannula, followed by a 30 mL THF rinse. After an additional 1 h, the suspension was warmed to 0 ^oC for 15 min., and then to ambient temperature for 5 min. The reaction was then re-cooled to 0 ^oC, and charged with a solution of azeotroped iodide **112** (10.0 g, 29.9 mmol) in THF (18.0 mL), followed by a 10 mL THF rinse. After an additional 2.5 h, the reaction was carefully quenched with sat. NH_4Cl (60 mL) and concentrated *in vacuo*. EtOAc (185 mL) and water (185 mL) were then added, and the aqueous layer was washed with EtOAc (2 x 40 mL). The combined organic layers were then dried over $MgSO_4$, concentrated *in vacuo* and preabsorbed onto 90 mL silica gel. Purification by flash chromatography (1/3, hexanes/EtOAc → 100% EtOAc, 10.0 cm diameter column, 9.0 in. SiO_2, flow rate 2.0 in./min.) afforded

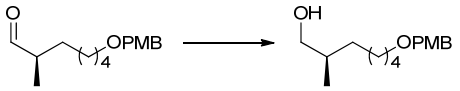
12.6 g (99% yield) of (+)-**113** as a yellow oil and 6.20 g (86% recovery) of (+)-**4-13**. For (+)-**4-14**: R_f 0.56 (1/5, hexanes/EtOAc); $[\alpha]_D^{20}$ +49.1 (*c* 0.77, $CHCl_3$); IR (neat) 3388 (br, s), 2933 (s), 2856 (s), 1616 (s), 1513 (s), 1464 (m), 1301 (m), 1247 (s), 1098 (s), 1035 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 5:1 mixture of rotamers, *represents minor peaks) δ 7.24 (m, 5 H), 7.15 (d, *J* = 8.6 Hz, 2 H), 6.77 (d, *J* = 8.6 Hz, 2 H), 4.51 (dd, *J* = 7.2, 7.2 Hz, 1 H), 4.43 (m, 1 H), 4.32 (br s, 2 H), *3.98 (m, 1 H), 3.69 (s, 3 H), 3.32 (app t, *J* = 6.5 Hz, 2 H), *2.79 (s, 3 H), 2.73 (s, 3 H), 2.47 (m, 1 H), 2.13 (d, *J* = 1.7 Hz, 1 H), *1.72 (m, 1 H), 1.48 (m, 2 H), 1.00-1.30 (m, 6 H), 1.03 (d, *J* = 6.9 Hz, 3 H), 0.97 (d, *J* = 6.7 Hz, 3 H), *0.90 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$, 5:1 mixture of rotamers, *represents minor peaks) δ 178.59, *177.51, 159.05, 142.65, *141.98, 130.70, 129.10, *128.45, *128.25, 128.11, *127.94, 127.32, *126.83, 126.27, 113.68, 76.07, 75.30, 72.34, *70.11, 69.93, 57.62, 55.13, 36.35, *35.59, 33.85, *29.64, 29.55, *27.25, 27.14, *26.27, 26.19, *18.04, 17.25, *15.52, 14.31; HRMS (ES+) m/z 450.2626 [$(M+Na)^+$; calcd for $C_{26}H_{37}NO_4Na^+$: 450.2619].



(+)-**113** (–)-**114**

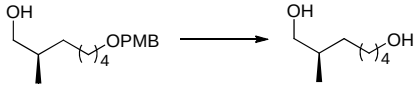
Aldehyde (–)-114. On this large scale, HPLC grade hexanes, EtOAc and THF were employed. A 0 °C suspension of lithium aluminum hydride (10.7 g, 95% wt., 267 mmol) and hexanes (758 mL) was charged with EtOAc (39.0 mL) over 2 min. After an additional 25 min., the reaction was cooled to -78 °C. A solution of azeotroped amide (+)-**113** (50.0 g, 116 mmol) in THF (404 mL) was then added via cannula over 25 min., followed by 2 x 50 mL THF rinses. Gas Evolution! The reaction was then warmed to 0 °C, and after 2 h, was cannulated into a solution of 1N HCl (1.4 L) and trifluoroacetic acid (TFA, 90 mL), followed by 3 x 20 mL THF rinses. After 10 min., the biphasic mixture was diluted with additional 1N HCl (600 mL), and the aqueous layer was washed with 7/1 hexanes/EtOAc (2 x 150 mL). The combined organic layers were then neutralized by the **CAREFUL** portionwise addition of sat. $NaHCO_3$ (1.5 L) until the pH of the organic layer was 7, and the pH of the aqueous layer was >7. The organic phase was then washed with brine, dried over $MgSO_4$, filtered through a 9.5 cm x 3.5 in. plug of Si gel (7/1, hexanes/EtOAc), and concentrated *in vacuo* to afford 21.8 g (71% yield) of (–)-**114** as a pale yellow oil: R_f 0.33 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –14.8 (*c* 0.53, $CHCl_3$); IR (neat) 2934 (s), 2857 (s), 2709 (w), 1724 (s), 1612 (m), 1585 (w), 1511 (s), 1464 (s), 1362 (m), 1301 (m), 1247 (s), 1172 (m), 1097 (s), 1035 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.60 (d, *J* = 2.0 Hz, 1 H), 7.25 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 4.42 (br s, 2 H), 3.80 (s, 3 H), 3.43 (app t, *J* = 6.5 Hz, 2 H), 2.31 (m, 1 H), 1.70 (m,

2 H), 1.60 (m, 2 H), 1.35 (m, 4 H), 1.08 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.17, 159.13, 130.72, 129.18, 113.75, 72.52, 69.89, 55.24, 46.22, 30.44, 29.67, 26.73, 26.23, 13.29; HRMS (CI, NH_3) m/z 264.1732 [M^+; calcd for $C_{16}H_{24}O_3^+$: 264.1725].



(–)-**114** (+)-**SI-5-2**

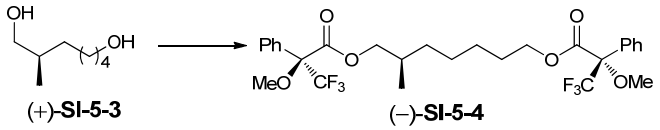
Alcohol (+)-SI-5-2. To a 0 °C solution of aldehyde (–)-**114** (79.0 mg, 0.299 mmol) in absolute EtOH (1.0 mL) was added sodium borohydride (22.6 mg, 2.0 equiv.). Some gas evolution. After 20 min., the reaction was diluted with sat. NH_4Cl (10 mL) and CH_2Cl_2 (10 mL). The aqueous layer was then washed with CH_2Cl_2 (2 x 3 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to afford 79.2 mg (quant.) of (+)-**SI-5-2** that was used without further purification: R_f 0.32 (2/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +6.1 (*c* 0.60, $CHCl_3$); IR (neat) 3419 (br, m), 2932 (s), 2856 (s), 1612 (s), 1586 (m), 1511 (s), 1464 (s), 1362 (m), 1302 (m), 1247 (s), 1172 (m), 1097 (s), 1035 (s) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.24 (d, J = 8.6 Hz, 2 H), 6.81 (d, J = 8.7 Hz, 2 H), 4.35 (s, 2 H), 3.35 (t, J = 6.5 Hz, 2 H), 3.31 (s, 3 H), 3.25 (dd, J = 5.8, 5.8, 1 H), 3.17 (dd, J = 6.5, 6.5 Hz, 1 H), 1.59 (m, 2 H), 1.33 (m, 5 H), 0.98 (m, 2 H), 0.83 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 159.66, 131.51, 129.32, 114.05, 72.73, 70.23, 68.03, 54.76, 36.04, 33.46, 30.24, 27.18, 26.97, 16.80; HRMS (ES+) m/z 289.1768 [$(M+Na)^+$; calcd for $C_{16}H_{26}O_3Na^+$: 289.1778].



(+)-**SI-5-2** (+)-**SI-5-3**

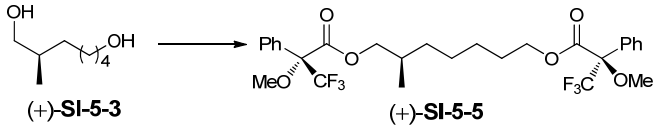
Diol (+)-SI-5-3. To a 0 °C solution of alcohol (+)-**SI-5-2** (79.2 mg, 0.297 mmol) in HPLC grade CH_3CN (7.70 mL) and pH 7 buffer (770 μL) was added ceric ammonium nitrate (CAN, 489 mg, 0.891 mmol) in one portion. The ice bath was then removed, and the reaction was allowed to warm to ambient temperature. After 1 h 15 min., the reaction was diluted with CH_2Cl_2 (20 mL), sat. $NaHCO_3$ (10 mL) and water (20 mL). The aqueous layer was then washed with CH_2Cl_2 (4 x 5 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo* (no high vacuum). Purification by flash chromatography (1/1 → 2/3, hexanes/EtOAc, 1.0 cm diameter column, 5.0 in. SiO_2, flow rate 2.0 in./min.) afforded 37 mg (85% yield) of (+)-**SI-5-3** as a pale yellow oil: R_f 0.15 (1/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +9.8 (*c* 0.56, CH_2Cl_2); IR (thin film, $CDCl_3$) 3324 (br, s), 2929 (s), 2857 (s), 1463 (m), 1378 (w),

1039 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.63 (app t, *J* = 6.6 Hz, 2 H), 3.49 (dd, *J* = 10.3, 5.9 Hz, 1 H), 3.42 (dd, *J* = 10.3, 6.5 Hz, 1 H), 1.58 (m, 3 H), 1.34 (m, 7 H), 1.12 (m, 1 H), 0.91 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 69.25, 62.91, 35.61, 33.01, 32.63, 26.65, 25.94, 16.49; HRMS (CI, NH_3) m/z 147.1378 [MH^+; calcd for $C_8H_{19}O_2^+$: 147.1385].



(+)-**SI-5-3** (–)-**SI-5-4**

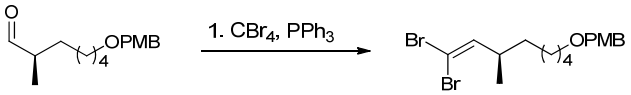
Bis-(*S*)-MTPA ester (–)-SI-5-4. To (*S*)-(–)-α-methoxy-α-trifluoromethylphenylacetic acid [(*S*)-MTPAOH, 72.0 mg, 3.0 equiv.], 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 113 mg, 9.0 equiv.) and 1-[3-(dimethylamino)propyl]3-ethyl-carbodiimide hydrochloride (EDC•HCl, 58.9 mg, 3.0 equiv.) was added a solution of (+)-**SI-5-3** in CH_2Cl_2 (400 μL), followed by a 100 μL CH_2Cl_2 rinse. After 2 h, the solution was diluted with sat. NH_4Cl (10 mL) and EtOAc (10 mL). The organic layer was then washed with sat. NH_4Cl (10 mL), sat. $NaHCO_3$ (2 x 5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by Preparative-TLC (2/1, hexanes/EtOAc, 1000 μm plate) afforded 5.1 mg (9% yield, >20:1 ratio of diastereomers) of (–)-**SI-5-4** as a colorless oil which was identical in all respects to the characterization data previously reported in the literature.[10] The remaining mass balance (12.3 mg) consisted of a mixture (~1:1) of monoesterified products. For (–)-**SI-5-4**: R_f 0.88 (1/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –43.9 (*c* 0.25, $CHCl_3$); IR (thin film, CH_2Cl_2) 2945 (m), 2851 (w), 1747 (s), 1451 (w), 1272 (m), 1168 (s), 1122 (m), 1081 (w), 1022 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (m, 4 H), 7.39 (m, 6 H), 4.31 (m, 1 H), 4.26 (m, 1 H), 4.16 (ddd, *J* = 10.7, 6.3, 1.1 Hz, 1 H), 4.11 (ddd, *J* = 10.7, 5.7, 1.1 Hz, 1 H), 3.54 (s, 6 H), 1.80 (m, 1 H), 1.65 (m, 2 H), 1.23-1.32 (m, 5 H), 1.13 (m, 1 H), 0.90 (d, *J* = 6.7 Hz, 3 H); HRMS (ES+) m/z 601.2027 [$(M+Na)^+$; calcd for $C_{28}H_{32}F_6O_6Na^+$: 601.2103].



(+)-**SI-5-3** (+)-**SI-5-5**

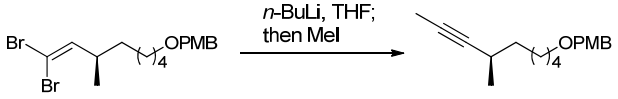
Bis-(*R*)-MTPA ester (+)-SI-5-5. To (*R*)-(+)-α-methoxy-α-trifluoromethylphenylacetic acid [(*R*)-MTPAOH, 72.0 mg, 3.0 equiv.], 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 113 mg, 9.0 equiv.) and 1-[3-(dimethylamino)propyl]3-ethyl-carbodiimide hydrochloride (EDC•HCl, 58.9 mg, 3.0 equiv.) was added a solution of (+)-**SI-5-3** in CH_2Cl_2 (400 μL), followed by a 100 μL CH_2Cl_2 rinse. After 2 h, the solution was diluted with sat. NH_4Cl (10 mL) and EtOAc (10 mL). The organic layer was then washed with sat.

NH_4Cl (10 mL), sat. $NaHCO_3$ (2 x 5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by Preparative-TLC (2/1, hexanes/EtOAc, 1000 μm plate) afforded 7.6 mg (13% yield, >20:1 ratio of diastereomers) of (+)-**SI-5-5** as a colorless oil, which was identical in all respects to the characterization data previously reported in the literature.[10] The remaining mass balance (13.5 mg) consisted of a mixture (~1:1) of monoesterified products. For (+)-**SI-5-5**: R_f 0.88 (1/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +39.5 (*c* 0.38, $CHCl_3$); IR (thin film, CH_2Cl_2) 2946 (m), 2852 (w), 1747 (s), 1451 (m), 1272 (s), 1169 (s), 1122 (m), 1081 (w), 1022 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (m, 4 H), 7.39 (m, 6 H), 4.32 (ddd, *J* = 10.8, 6.6, 6.6 Hz, 1 H), 4.27 (ddd, *J* = 10.8, 6.6, 6.6 Hz, 1 H), 4.20 (dd, *J* = 10.7, 5.8 Hz, 1 H), 4.06 (dd, *J* = 10.7, 6.5 Hz, 1 H), 3.54 (s, 6 H), 1.81 (m, 1 H), 1.66 (m, 2 H), 1.22-1.33 (m, 5 H), 1.13 (m, 1 H), 0.89 (d, *J* = 6.7 Hz, 3 H); HRMS (ES+) m/z 601.1983 [$(M+Na)^+$; calcd for $C_{28}H_{32}F_6O_6Na^+$: 601.2103].



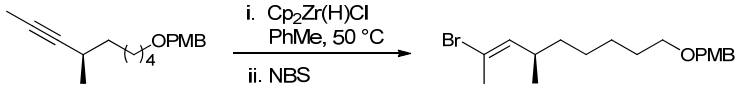
(–)-**114** (–)-**SI-5-6**

***Gem*-dibromide (–)-SI-5-6**. On this large scale, HPLC grade CH_2Cl_2 was employed. To a 0 °C solution of triphenylphosphine (72.2 g, 275 mmol) in CH_2Cl_2 (130 mL) was added a solution of carbon tetrabromide (45.6 g, 138 mmol) in CH_2Cl_2 (100 mL) via cannula over 4-5 min. The resulting orange solution then slowly formed an orange/white suspension, and after 30 min., was treated with a solution of azeotroped aldehyde (–)-**114** (18.2 g, 68.8 mmol) in CH_2Cl_2 (50.0 mL) via cannula, followed by 2 x 5 mL CH_2Cl_2 rinses. After 1.5 h, the reaction was triturated with the portionwise addition of pentane (600 mL), filtered through a 9.5 cm x 3.5 in. pad of Si gel (10/1, hexanes/EtOAc), and concentrated *in vacuo* to afford 32.2 g (112% yield) of crude (–)-**SI-5-6** which was used without further purification. On smaller scale, purification by flash chromatography (15/1 → 10/1, hexanes/EtOAc) afforded pure (–)-**SI-5-6** for characterization purposes: R_f 0.34 (10/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –5.6 (*c* 0.51, $CHCl_3$); IR (neat) 2931 (s), 2852 (s), 1612 (m), 1511 (s), 1464 (m), 1362 (w), 1301 (m), 1247 (s), 1172 (m), 1097 (s), 1037 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 6.15 (d, *J* = 9.4 Hz, 1 H), 4.43 (br s, 2 H), 3.80 (s, 3 H), 3.43 (app t, *J* = 6.5 Hz, 2 H), 2.44 (m, 1 H), 1.59 (m, 2 H), 1.32 (m, 6 H), 0.99 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.11, 144.38, 130.79, 129.18, 113.76, 87.21, 72.50, 70.03, 55.26, 38.25, 36.02, 29.63, 26.95, 26.21, 19.18; HRMS (CI, NH_3) m/z 418.0127 [M^+; calcd for $C_{17}H_{24}Br_2O_2^+$: 418.0142].



(–)-**SI-5-6** (–)-**115**

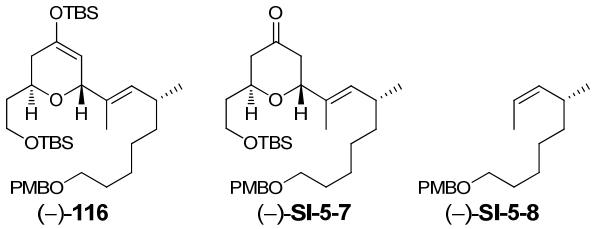
Alkyne (–)-115. On this large scale, HPLC grade THF was employed. To a -78 °C solution of crude azeotroped *gem*-dibromide (–)-**SI-5-6** (28.9 g, 68.8 mmol) in THF (360 mL) was added *n*-BuLi (76.8 mL, 2.5 equiv., 2.24 M in hexanes) dropwise over 10 min. After 1 h, the bright orange solution was charged with MeI (21.4 mL, 344 mmol), and after an additional 1 h, the resulting orange suspension was warmed to ambient temperature. Following an additional 2 h, the reaction was diluted with water (300 mL). The aqueous phase was then washed with Et_2O (2 x 100 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (25/1, hexanes/EtOAc, 11.0 cm diameter column, 4.5 in. SiO_2, flow rate 1.5 in./min.) afforded 18.4 g (98% yield, 2 steps from (–)-**114**) of (–)-**115** as a pale yellow oil: R_f 0.12 (20/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –21.9 (*c* 0.53, C_6D_6); IR (neat) 2932 (s), 2856 (s), 1612 (m), 1512 (s), 1456 (w), 1301 (w), 1247 (s), 1171 (m), 1096 (m), 1037 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 4.43 (br s, 2 H), 3.80 (s, 3 H), 3.44 (app t, *J* = 6.6 Hz, 2 H), 2.34 (m, 1 H), 1.78 (d, *J* = 2.3 Hz, 3 H), 1.61 (m, 2 H), 1.30-1.50 (m, 6 H), 1.11 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.09, 130.83, 129.15, 113.73, 83.94, 75.40, 72.48, 70.14, 55.23, 37.21, 29.71, 27.21, 26.05, 25.86, 21.39, 3.44; HRMS (ES+) m/z 297.1817 [$(M+Na)^+$; calcd for $C_{18}H_{26}O_2Na^+$: 297.1829].



(–)-**115** (87%, one isomer) (–)-**14**

Vinyl Bromide (–)-14. To a suspension of Cp_2ZrHCl (6.30 g, 23.4 mmol) in toluene (100 mL) was added a solution of azeotroped alkyne (–)-**115** (4.30 g, 15.6 mmol) in toluene (30.0 mL), followed by 2 x 10 mL toluene rinses. Gas Evolution! The suspension was then warmed to 50 °C, and after 1 h, was charged with *N*-bromosuccinimide (NBS, 4.60 g, 25.7 mmol) in one portion and cooled to ambient temperature. After 35 min., the reaction was triturated with 10/1 hexanes/EtOAc (100 mL), and filtered through celite, rinsing with 10/1 hexanes/EtOAc. The eluent was then washed with 1 M $Na_2S_2O_3$ (2 x 300 mL), 50% sat. $NaHCO_3$ (3 x 200 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (30/1 → 15/1, hexanes/EtOAc, 7.0 cm diameter column, 8.0 in. SiO_2, flow rate 1.5 in./min.) afforded 4.8 g (87% yield) of (–)-**14** as a pale yellow oil: R_f 0.19 (20/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –29.6 (*c* 0.55, C_6H_6); IR (neat) 2928 (s), 2854 (s), 1612 (m), 1512 (s), 1463 (m), 1302 (m), 1247

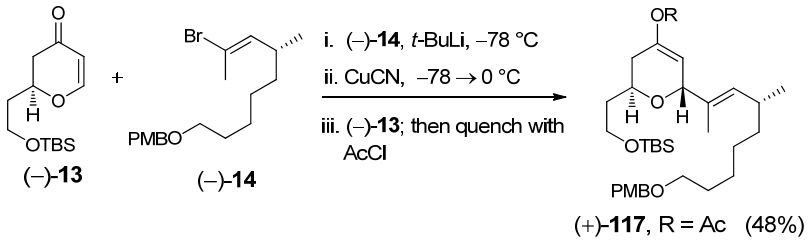
(s), 1172 (m), 1098 (m), 1037 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 5.61 (dd, *J* = 10.0, 1.2 Hz, 1 H), 4.43 (br s, 2 H), 3.80 (s, 3 H), 3.42 (app t, *J* = 6.5 Hz, 2 H), 2.30 (m, 1 H), 2.20 (s, 3 H), 1.59 (m, 2 H), 1.10-1.40 (m, 6 H), 0.96 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.11, 138.42, 130.80, 129.17, 118.07, 113.75, 72.49, 70.05, 55.25, 37.05, 34.75, 29.68, 27.15, 26.24, 23.40, 20.59; HRMS (CI, NH_3) m/z 355.1149 [M^+; calcd for $C_{18}H_{27}BrO_2^+$: 355.1193].



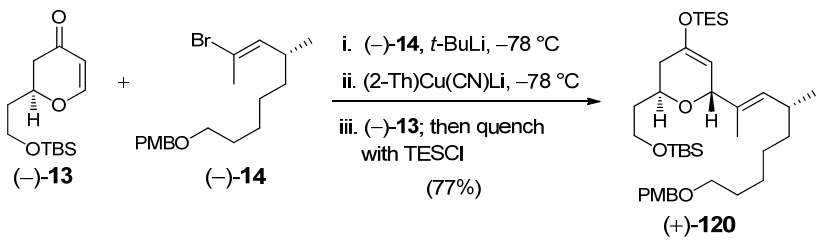
(–)-**116** (–)-**SI-5-7** (–)-**SI-5-8**

TBS-enol ether (–)-116, Ketone (–)-SI-5-7 and Olefin (–)-SI-5-8. *This was an unoptimized procedure*. To a -78 °C solution of *t*-BuLi (2.1 mL, 1.58 M in pentane, 3.42 mmol) in distilled THF (13.5 mL) was added a solution of azeotroped vinyl bromide (–)-**14** (551 mg, 1.55 mmol) in THF (2.00 mL) dropwise over 5 min., followed by 2 x 450 μL THF rinses. After 1 h, the yellow solution was added via cannula to a non-stirring, -78 °C suspension of CuCN (97.2 mg, 1.09 mmol) in THF (12.5 mL), followed by a 1.5 mL THF rinse. Stirring was then initiated, and the suspension was placed in a 0 °C bath for 5 min. The resulting yellow/orange solution was then re-cooled to -78 °C, and sequentially treated with 564 μL of a solution of azeotroped enone (–)-**13** (165 mg, 0.647 mmol) in THF, followed by *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf, 297 μL, 1.29 mmol). The enone/THF solution was prepared by dissolving 466 mg of enone (–)-**13** in THF to make a 1.6 mL solution. After 1 h, the reaction was quenched with triethylamine (900 μL), cannulated into sat. $NaHCO_3$ (30 mL) and rinsed with 3 x 3 mL CH_2Cl_2. The reaction was then diluted with water (25 mL) and CH_2Cl_2 (50 mL), and the aqueous phase was washed with CH_2Cl_2 (2 x 25 mL). The combined organic layers were then washed with sat. $NaHCO_3$ (25 mL), brine (25 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (40/1 → 4/1, hexanes/EtOAc, 5.0 cm diameter column, 10.0 in. SiO_2, flow rate 1.5 in./min., prepared column with 3% Et_3N in 40/1, hexanes/EtOAc) sequentially afforded 232 mg of olefin (–)-**SI-5-8**, 192 mg (46% yield) of TBS enol ether (–)-**116**, and 140 mg (41% yield) of ketone (–)-**SI-5-7** as pale yellow oils. For (–)-**116**: R_f 0.15 (20/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –6.0 (*c* 0.27, C_6H_6); IR (thin film, $CDCl_3$) 2929 (s), 2857 (s), 1674 (m), 1614 (w), 1513 (m), 1462 (m), 1361 (m), 1249 (s), 1203 (m), 1097 (s), 1038 (w), 909 (m), 836 (s), 778 (m) cm^{-1}; ^1H NMR (500 MHz,

$CDCl_3$) δ 7.25 (d, *J* = 8.7 Hz, 2 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 5.09 (d, *J* = 9.6 Hz, 1 H), 4.79 (d, *J* = 3.5 Hz, 1 H), 4.47 (br s, 1 H), 4.38 (br s, 2 H), 3.75 (s, 3 H), 3.70 (m, 2 H), 3.61 (m, 1 H), 3.37 (app t, *J* = 6.7 Hz, 2 H), 2.28 (m, 1 H), 1.96 (dd, *J* = 16.8, 9.2 Hz, 1 H), 1.87 (dd, *J* = 16.8, 4.1 Hz, 1 H), 1.71 (m, 1 H), 1.58 (m, 1 H), 1.50 (m, 2 H), 1.44 (s, 3 H), 1.18 (m, 6 H), 0.84 (s, 9 H), 0.82 (d, *J* = 6.7 Hz, 3 H), 0.78 (s, 9 H), 0.06 (s, 6 H), -0.06 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.98, 152.92, 139.44, 137.04, 134.05, 132.24, 115.94, 105.78, 76.35, 72.23, 69.84, 64.67, 59.12, 53.97, 36.30, 35.16, 33.79, 29.68, 27.03, 24.49, 23.39, 22.93, 22.66, 17.46, 14.78, 14.55, 10.78, -9.10, -9.14, -10.18; HRMS (ES+) m/z 669.4320 [$(M+Na)^+$; calcd for $C_{37}H_{66}O_5Si_2Na^+$: 669.4449]. For (–)-**SI-5-7**: R_f 0.32 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –12.0 (*c* 0.10, C_6H_6); IR (thin film, $CDCl_3$) 2927 (s), 2855 (s), 1718 (m), 1612 (w), 1513 (m), 1248 (s), 1095 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 5.10 (ddd, *J* = 9.5, 1.3, 1.3 Hz, 1 H), 4.48 (br dd, *J* = 5.0, 5.0 Hz, 1 H), 4.42 (br s, 2 H), 4.03 (dddd, *J* = 8.5, 8.5, 4.3, 4.3 Hz, 1 H), 3.80 (s, 3 H), 3.70 (m, 2 H), 3.41 (app t, *J* = 6.6 Hz, 2 H), 2.67 (ddd, *J* = 14.7, 4.5, 1.5 Hz, 1 H), 2.55 (ddd, *J* = 14.7, 5.7, 1.1 Hz, 1 H), 2.42 (ddd, *J* = 14.7, 4.1, 1.5 Hz, 1 H), 2.33, (m, 1 H), 2.24 (ddd, *J* = 1.1, 8.6, 14.7 Hz, 1 H), 1.81 (dddd, *J* = 19.3, 8.6, 5.3, 5.3 Hz, 1 H), 1.66 (s, 3 H), 1.65 (m, 1 H), 1.57 (m, 2 H), 1.30 (br m, 4 H), 1.18 (m, 2 H), 0.90 (d, *J* = 6.7 Hz, 3 H), 0.88 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 215.07, 163.95, 139.49, 135.22, 134.05, 132.23, 115.92, 76.49, 72.20, 69.76, 67.11, 58.02, 53.96, 45.54, 42.27, 36.00, 34.80, 29.78, 26.93, 24.39, 23.26, 22.87, 17.18, 14.73, 9.65, -10.25; HRMS (ES+) m/z 555.3479 [$(M+Na)^+$; calcd for $C_{31}H_{52}O_5SiNa^+$: 555.3584]. For (–)-**SI-5-8**: R_f 0.19 (20/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –1.2 (*c* 0.50, C_6H_6); IR (neat) 3004 (s), 2929 (br, s), 1613 (s), 1586 (m), 1512 (s), 1462 (s), 1362 (m), 1301 (m), 1246 (s), 1172 (s), 1099 (s), 1038 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.7 Hz, 2 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 5.34 (m, 1 H), 5.10 (m, 1 H), 4.38 (br s, 2 H), 3.75 (s, 3 H), 3.37 (app t, *J* = 6.7 Hz, 2 H), 2.36 (m, 1 H), 1.51 (dd, *J* = 6.8, 1.8 Hz, 3 H), 1.50 (m, 2 H), 1.20 (m, 6 H), 0.83 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.05, 137.27, 130.79, 129.14, 122.07, 113.69, 72.43, 70.15, 55.20, 37.42, 31.14, 29.72, 27.23, 26.32, 21.06, 12.92; HRMS (CI, NH_3) m/z 276.2088 [M^+; calcd for $C_{18}H_{28}O_2^+$: 276.2089].

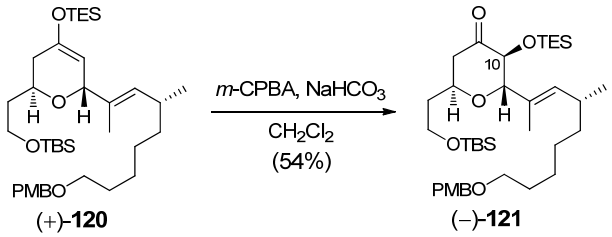


Enol acetate (+)-117. *This procedure was unoptimized.* To a -78 °C solution of *t*-BuLi (1.8 mL, 1.54 M in pentane, 2.81 mmol) in distilled THF (11.0 mL) was added a solution of azeotroped vinyl bromide (–)-**14** (454 mg, 1.28 mmol) in THF (1.50 mL) dropwise over 3 min., followed by 2 x 0.5 mL THF rinses. After 1 h, the yellow solution was added via cannula to a non-stirring, -78 °C suspension of CuCN (80.1 mg, 0.894 mmol) in THF (10.0 mL), followed by 2 x 1.0 mL THF rinses. Stirring was then initiated, and the suspension was placed in a 0 °C bath for 5 min. The resulting greenish solution was then re-cooled to -78 °C, and treated with 446 μL of a solution of azeotroped enone (–)-**13** (135 mg, 0.532 mmol) in THF. The enone/THF solution was prepared by dissolving 406 mg of (–)-**13** in THF to make a 1.30 mL solution. After 1 h, acetyl chloride (190 μL, 2.66 mmol) was added dropwise. After an additional 30 min., the reaction was allowed to warm to -50 °C, and then quenched with triethylamine (500 μL), followed by sat. $NaHCO_3$ (25 mL). The reaction was then diluted with water (25 mL) and CH_2Cl_2 (50 mL), and the aqueous phase was washed with CH_2Cl_2 (3 x 10 mL). The combined organic layers were then dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (10/1 → 3/1, hexanes/EtOAc, 5.0 cm diameter column, 10.0 in. SiO_2, flow rate 1.5 in./min., prepared column with 3% Et_3N in 10/1, hexanes/EtOAc) afforded 124 mg of olefin (–)-**SI-5-8** and 146 mg (48% yield) of (+)-**117** as pale yellow oils. For (+)-**117**: R_f 0.23 (7/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +18.5 (*c* 1.08, C_6H_6); IR (thin film, C_6D_6) 2930 (s), 2853 (s), 1758 (s), 1696 (w), 1609 (m), 1513 (m), 1460 (m), 1364 (m), 1249 (s), 1100 (s), 1037 (m) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.25 (d, *J* = 8.5 Hz, 2 H), 6.81 (d, *J* = 8.5 Hz, 2 H), 5.50 (br s, 1 H), 5.37 (d, *J* = 9.4 Hz, 1 H), 4.62 (br s, 1 H), 4.36 (br s, 2 H), 4.00 (dddd, *J* = 8.5, 8.5, 4.0, 4.0 Hz, 1 H), 3.76 (app t, *J* = 6.5 Hz, 2 H), 3.38 (app t, *J* = 6.5 Hz, 2 H), 3.32 (s, 3 H), 2.35 (m, 1 H), 2.25 (dddd, *J* = 16.4, 9.1, 2.2, 2.2 Hz, 1 H), 2.06 (dd, *J* = 16.4, 3.8 Hz, 1 H), 1.89 (dddd, *J* = 19.8, 8.3, 5.9, 5.9 Hz, 1 H), 1.74 (s, 3 H), 1.70 (m, 3 H), 1.65 (s, 3 H), 1.30 (m, 6 H), 0.96 (s, 9 H), 0.93 (d, *J* = 6.6 Hz, 3 H), 0.068 (s, 3 H), 0.062 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 168.15, 162.37, 146.66, 136.74, 133.42, 129.18, 128.28, 114.47, 114.03, 76.16, 72.71, 70.30, 65.33, 60.20, 54.74, 38.82, 37.80, 33.79, 32.78, 30.65, 27.80, 26.85, 26.16, 20.93, 20.46, 18.45, 14.80, -5.19; HRMS (ES+) m/z 597.3606 [$(M+Na)^+$; calcd for $C_{33}H_{54}O_6SiNa^+$: 597.3690].



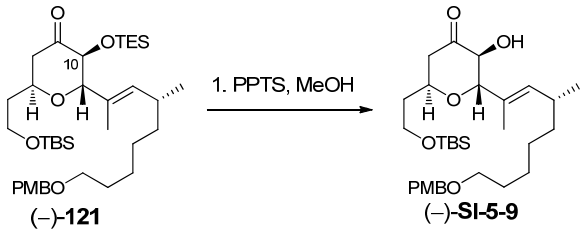
TES-enol ether (+)-120. Preparation of a 0.25 M (2-Th)Cu(CN)Li solution: A -78 °C solution of thiophene (1.90 mL, 23.8 mmol) in distilled THF (33.0 mL) was treated with *n*-BuLi (9.70 mL, 2.34 M in hexanes, 22.7 mmol) dropwise over 1-2 min. After 15 min. at -78 °C, the solution was warmed to -20 °C, and stirred an additional 30 min. The solution was then recooled to -78 oC, and cannulated into a non-stirring, -78 °C suspension of CuCN (2.00 g, 22.8 mmol) in THF (35.0 mL), followed by 2 x 5 mL THF rinses. Stirring was then initiated, and the suspension was warmed to -35 °C. After 15 min., the golden brown solution was cooled to -78 °C and diluted with THF (85 mL).

Concurrently, to a -78 °C solution of *t*-BuLi (25.1 mL, 1.66 M in pentane, 41.6 mmol) in distilled THF (430 mL) was added a solution of azeotroped vinyl bromide (–)-**14** (6.70 g, 18.9 mmol) in THF (30.0 mL) via cannula over 2-3 min., followed by 2 x 5 mL THF rinses. After 1 h, the yellow solution was added via cannula to the -78 °C (2-Th)Cu(CN)Li solution, followed by 2 x 10 mL THF rinses. After an additional 10 min., the orangish/brown solution was sequentially charged with 10.3 mL of a solution of azeotroped enone (–)-**13** (3.20 g, 12.6 mmol) in THF dropwise, followed by triethylsilyl chloride (TESCl, 5.30 mL, 31.5 mmol). The enone/THF solution was prepared by dissolving 4.50 g of (–)-**13** in THF to make a 14.5 mL solution. After 2 h, the reaction was poured into sat. $NaHCO_3$ (250 mL), rinsing with diethyl ether. Water (400 mL) was then added, and the aqueous phase was washed with CH_2Cl_2 (2 x 100 mL). The combined organic layers were then washed with water (250 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on activity III basic alumina (30/1 hexanes/diethyl ether → 100% diethyl ether, 10.0 cm diameter column, 10.0 in. SiO_2, flow rate 1.5 in./min.) sequentially afforded 1.60 g of olefin (–)-**SI-5-8**, and 6.30 g (77% yield) of TES-enol ether (+)-**120**, as pale yellow oils. For (+)-**120**: R_f 0.40 (10/1, hexanes/EtOAc); $[\alpha]_D^{20}$ +6.2 (*c* 0.45, C_6H_6); IR (thin film, $CDCl_3$) 2953 (s), 2927 (s), 2875 (s), 2855 (s), 1674 (m), 1603 (m), 1513 (m), 1463 (m), 1248 (s), 1202 (m), 1097 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 5.12 (d, *J* = 9.4 Hz, 1 H), 4.83 (d, *J* = 3.4 Hz, 1 H), 4.51 (br s, 1 H), 4.42 (br s, 2 H), 3.80 (s, 3 H), 3.73 (m, 2 H), 3.65 (m, 1 H), 3.42 (app t, *J* = 6.6 Hz, 2 H), 2.34 (m, 1 H), 2.03 (dd, *J* = 16.6, 8.4 Hz, 1 H), 1.95 (dd, *J* = 16.6, 3.9 Hz, 1 H), 1.79 (m, 1 H), 1.66 (m, 1 H), 1.65 (s, 3 H), 1.57 (m, 2 H), 1.17-1.38 (m, 6 H), 0.99 (t, *J* = 7.9 Hz, 9 H), 0.90 (d, *J* = 6.6 Hz, 3 H), 0.87 (s, 9 H), 0.69 (q, *J* = 7.9 Hz, 6 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.07, 148.56, 136.01, 133.67, 130.82, 129.14, 113.72, 103.58, 76.35, 72.48, 70.22, 65.25, 60.10, 55.24, 38.57, 37.49, 36.09, 32.32, 29.81, 27.43, 26.38, 25.94, 20.80, 18.25, 14.50, 6.66, 5.04, -5.32; HRMS (ES+) m/z 669.4321 [$(M+Na)^+$; calcd for $C_{37}H_{66}O_5Si_2Na^+$: 669.4449].



(+)-**120** (–)-**121**

TES-ether (–)-121. To a 0 °C suspension of TES-enol ether (+)-**120** (1.30 g, 2.10 mmol), and $NaHCO_3$ (495 mg, 5.88 mmol) in CH_2Cl_2 (58.0 mL) was added *m*-CPBA (1.30 g, 77% max., 2.10 mmol) in one portion. After 20 min., the ice bath was removed, and the reaction was allowed to warm to ambient temperature. After 1.5 h, the reaction was quenched with 1 M $Na_2S_2O_3$ (50 mL). The separated organic layer was then diluted with EtOAc (75 mL), washed with sat. $NaHCO_3$ (4 x 50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on activity I basic alumina (20/1 → 5/1, hexanes/diethyl ether, 5.5 cm diameter column, 6.0 in. SiO_2, flow rate 1.5 in./min.) afforded 108 mg (8% yield) of recovered TES enol ether (+)-**120**, and 748 mg (54% yield) of TES ether (–)-**121**, as pale yellow oils. For (–)-**121**: R_f 0.48 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –39.1 (*c* 0.92, C_6H_6); IR (neat) 2929 (br, s), 1728 (s), 1672 (w), 1613 (s), 1586 (m), 1512 (s), 1462 (s), 1413 (m), 1361 (s), 1300 (s), 1248 (s), 1173 (s), 1148 (s), 1097 (s), 1037 (s), 1008 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 5.22 (d, *J* = 8.8 Hz, 1 H), 4.42 (br s, 2 H), 4.36 (m, 1 H), 4.17 (d, *J* = 7.9 Hz, 1 H), 3.91 (d, *J* = 7.9 Hz, 1 H), 3.80 (s, 3 H), 3.64 (m, 2 H), 3.42 (app t, *J* = 6.6 Hz, 2 H), 2.71 (dd, *J* = 13.6, 6.4 Hz, 1 H), 2.43 (dd, *J* = 13.6, 3.3 Hz, 1 H), 2.36 (m, 1 H), 1.84 (m, 1 H), 1.69 (s, 3 H), 1.60 (m, 3 H), 1.28 (br m, 6 H), 0.92 (m, 12 H), 0.87 (s, 9 H), 0.60 (m, 6 H), 0.02 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.59, 159.09, 137.77, 130.84, 129.96, 129.17, 113.74, 82.88, 76.38, 72.47, 70.43, 70.21, 59.19, 55.26, 45.30, 37.16, 35.23, 32.27, 29.72, 27.25, 26.42, 25.93, 20.37, 18.30, 12.19, 6.84, 4.98, -5.42; HRMS (ES+) m/z 685.4293 [$(M+Na)^+$; calcd for $C_{37}H_{66}O_6Si_2Na^+$: 685.4398].

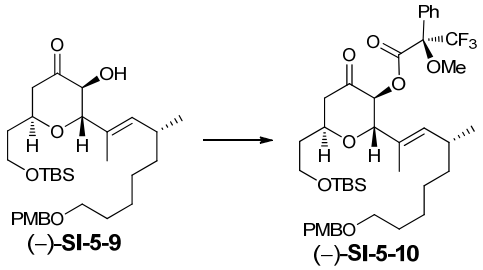


(–)-**121** (–)-**SI-5-9**

Alcohol (–)-SI-5-9. To a 0 °C solution of TES-ether (–)-**121** (1.30 g, 2.00 mmol) in MeOH (53.0 mL) was added pyridinium *p*-toluenesulfonate (PPTS, 101 mg, 0.40 mmol). After 4 h, the reaction was diluted with EtOAc (75 mL), sat. $NaHCO_3$ (20 mL) and water (100 mL). The aqueous layer was then washed with EtOAc (3 x 50 mL), and the combined organic layers were dried over $MgSO_4$, concentrated

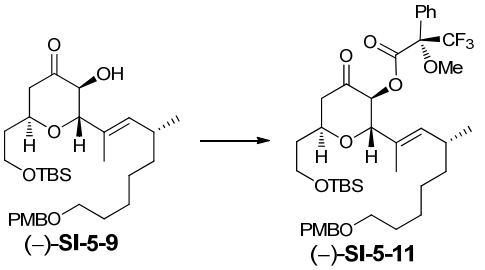
in vacuo, and placed under high vacuum overnight to afford 1.10 g (quant.) of (–)-**SI-5-9** as a colorless oil which was used without further purification: R_f 0.27 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –43.2 (*c* 0.43, C_6H_6); IR (neat) 3479 (br, m), 2929 (s), 2856 (s), 1717 (s), 1613 (m), 1586 (w), 1513 (s), 1462 (s), 1361 (m), 1301 (m), 1248 (s), 1172 (m), 1102 (br, s), 1036 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 5.25 (dd, *J* = 9.5, 1.0 Hz, 1 H), 4.55 (m, 1 H), 4.41 (br s, 2 H), 4.07 (dd, *J* = 9.4, 2.7 Hz, 1 H), 3.79 (s, 3 H), 3.72 (d, *J* = 9.4 Hz, 1 H), 3.64 (m, 2 H), 3.42 (m, 3 H), 2.91 (ddd, *J* = 13.7, 7.4, 1.3 Hz, 1 H), 2.49 (dd, *J* = 13.7, 1.5 Hz, 1 H), 2.41 (m, 1 H), 1.81 (dddd, *J* = 10.8, 9.1, 5.4, 5.4 Hz, 1 H), 1.73 (d, *J* = 1.0 Hz, 3 H), 1.59 (m, 4 H), 1.28 (m, 5 H), 0.95 (d, *J* = 6.6 Hz, 3 H), 0.88 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.00, 159.10, 137.86, 130.86, 129.71, 129.21, 113.75, 82.63, 74.85, 72.46, 71.38, 70.17, 59.18, 55.26, 44.34, 37.30, 34.45, 32.14, 29.69, 27.09, 26.21, 25.92, 20.66, 18.31, 11.54, -5.43; HRMS (ES+) m/z 571.3452 [$(M+Na)^+$; calcd for $C_{31}H_{52}O_6SiNa^+$: 571.3533].

Determination of Absolute Stereochemistry of (–)-SI-5-9.



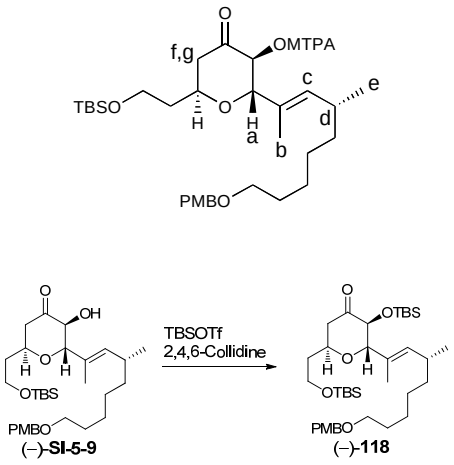
(*S*)-MTPA Ester (–)-SI-5-10. (*R*)-(–)-α-methoxy-α-trifluoromethylphenylacetyl chloride [(*R*)-MTPACl, 6.6 μL, 35.2 μmole) was added to a solution of azeotroped (–)-**SI-5-9** (9.70 mg, 17.6 μmole) and 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 8.60 mg, 70.4 μmole) in CH_2Cl_2 (250 μL) at ambient temperature. After 3 h, direct purification by preparative-TLC (4/1, hexanes/EtOAc, 500 μm plate) afforded 10.5 mg (78% yield, >20:1 ratio of diastereomers) of (–)-**SI-5-10** as a colorless oil: R_f 0.38 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –23.8 (*c* 0.50, C_6H_6); IR (thin film, $CDCl_3$) 2930 (s), 2855 (s), 1760 (s), 1734 (s), 1615 (w), 1513 (s), 1463 (m), 1361 (w), 1249 (s), 1171 (s), 1099 (s), 1035 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (m, 2 H), 7.39 (m, 3 H), 7.26 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 5.34 (d, *J* = 9.7 Hz, 1 H), 5.24 (d, *J* = 9.1 Hz, 1 H), 4.53 (m, 1 H), 4.43 (br s, 2 H), 4.12 (d, *J* = 9.7 Hz, 1 H), 3.80 (s, 3 H), 3.64 (m, 2 H), 3.59 (s, 3 H), 3.42 (app t, *J* = 6.6 Hz, 2 H), 2.99 (dd, *J* = 13.9, 7.2 Hz, 1 H), 2.51 (dd, *J* = 13.9, 1.7 Hz, 1 H), 2.24 (m, 1 H), 1.87 (dddd, *J* = 10.1, 10.1, 5.2, 5.2 Hz, 1 H), 1.66 (m, 1 H), 1.58 (s, 3 H), 1.56 (m, 2 H), 1.27 (m, 2 H), 1.16 (m, 2 H), 1.10 (m, 2 H), 0.87 (m, 12 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.21, 165.62, 159.09, 139.10, 131.83, 131.82, 129.64, 129.17,

128.60, 128.28, 127.73, 124.23, 121.93, 113.73, 78.81, 77.18, 72.47, 71.00, 70.15, 58.99, 55.53, 55.25, 45.43, 36.55, 34.44, 32.07, 29.67, 26.88, 26.30, 25.90, 19.88, 18.30, 11.79, -5.45; HRMS (ES+) m/z 787.3862 [$(M+Na)^+$; calcd for $C_{41}H_{59}F_3O_8SiNa^+$: 787.3931].



(–)-**SI-5-9** (–)-**SI-5-11**

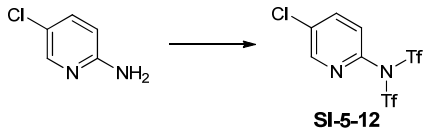
(*R*)-MTPA Ester (–)-SI-5-11. In similar fashion, (–)-**SI-5-11** was obtained in 57% yield (>20:1 mixture of diastereomers) as a colorless oil: R_f 0.38 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –12.5 (*c* 0.35, C_6H_6); IR (thin film, $CDCl_3$) 2930 (s), 2856 (s), 1759 (s), 1734 (s), 1612 (w), 1513 (m), 1464 (m), 1361 (m), 1249 (s), 1171 (s), 1099 (s), 1035 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (m, 2 H), 7.39 (m, 3 H), 7.25 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 5.33 (d, *J* = 9.6 Hz, 2 H), 4.54 (m, 1 H), 4.41 (br s, 2 H), 4.19 (d, *J* = 9.6 Hz, 1 H), 3.79 (s, 3 H), 3.64 (m, 2 H), 3.54 (s, 3 H), 3.40 (app t, *J* = 6.6 Hz, 2 H), 2.97 (dd, *J* = 13.9, 7.1 Hz, 1 H), 2.49 (dd, *J* = 13.9, 2.0 Hz, 1 H), 2.37 (m, 1 H), 1.86 (dddd, *J* = 9.6, 9.6, 5.1, 5.1 Hz, 1 H), 1.73 (s, 3 H), 1.65 (m, 1 H), 1.53 (m, 2 H), 1.25 (m, 6 H), 0.93 (d, *J* = 6.6 Hz, 3 H), 0.87 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$, one carbon overlapping with $CDCl_3$) δ 199.66, 165.55, 159.10, 139.32, 131.88, 130.86, 129.65, 129.18, 128.78, 128.25, 127.81, 124.27, 121.98, 113.74, 79.00, 72.44, 71.00, 70.15, 58.99, 55.54, 55.27, 45.34, 36.84, 34.52, 32.33, 29.60, 27.04, 26.35, 25.92, 20.13, 18.32, 11.76, -5.44; HRMS (ES+) m/z 787.3843 [$(M+Na)^+$; calcd for $C_{41}H_{59}F_3O_8SiNa^+$: 787.3931].



(–)-**SI-5-9** (–)-**118**

Proton	(*S*)-MTPA ester	(*R*)-MTPA ester	(*S*)-(*R*)
a	4.12	4.19	-0.07
b	1.58	1.73	-0.15
c	5.24	5.33	-0.09
d	2.24	2.37	-0.13
e	0.87	0.93	-0.06
f	2.99	2.97	+0.02
g	2.51	2.49	+0.02

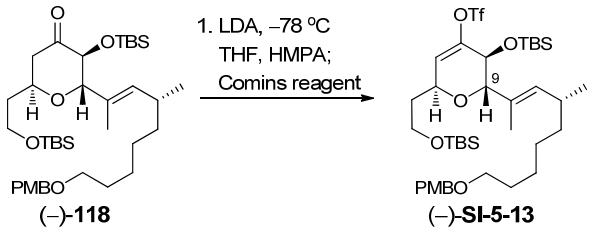
Bis-TBS ether (–)-118. To a -78 °C solution of (–)-**SI-5-9** (1.10 g, 2.10 mmol) and 2,4,6-collidine (838 μL, 6.30 mmol) was added TBSOTf (723 μL, 3.15 mmol). The reaction was then allowed to warm to -20 °C over 45 min., and after an additional 2 h, was diluted with sat. $NaHCO_3$ (15 mL), water (15 mL) and CH_2Cl_2 (15 mL). The aqueous layer was then washed with CH_2Cl_2 (3 x 10 mL), and the combined organic layers were washed with 1M $NaHSO_4$ (3 x 20 mL), brine (15 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford 1.30 g (95% yield) of (–)-**118** as a colorless oil which was used without further purification: R_f 0.61 (4/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –43.0 (*c* 0.89, C_6H_6); IR (neat) 2929 (s), 2856 (s), 1730 (s), 1613 (m), 1586 (w), 1513 (s), 1463 (s), 1388 (w), 1360 (m), 1301 (m), 1249 (s), 1172 (s), 1145 (s), 1097 (s), 1038 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 5.23 (d, *J* = 9.2 Hz, 1 H), 4.38 (br s, 2 H), 4.34 (m, 1 H), 4.11 (d, *J* = 8.3 Hz, 1 H), 3.86 (d, *J* = 8.3 Hz, 1 H), 3.75 (s, 3 H), 3.59 (m, 2 H), 3.37 (app t, *J* = 6.7 Hz, 2 H), 2.67 (dd, *J* = 13.8, 6.7 Hz, 1 H), 2.36 (dd, *J* = 13.8, 3.0 Hz, 1 H), 2.29 (m, 1 H), 1.77 (m, 1 H), 1.61 (s, 3 H), 1.51 (m, 4 H), 1.20 (m, 5 H), 0.84 (d, *J* = 6.7 Hz, 3 H), 0.786 (s, 9 H), 0.781 (s, 9 H), 0.01 (s, 3 H), -0.07 (s, 6 H), -0.11 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ214.17, 163.98, 141.57, 134.07, 133.14, 132.24, 115.94, 83.20, 76.57, 72.21, 70.15, 69.80, 58.18, 53.98, 43.48, 34.68, 32.59, 29.55, 26.92, 24.22, 23.43, 22.92, 22.70, 16.81, 14.94, 14.84, 8.29, -9.06, -10.16, -10.29; HRMS (ES+) m/z 685.4286 [$(M+Na)^+$; calcd for $C_{37}H_{66}O_6Si_2Na^+$: 685.4449].



SI-5-12

***N*-(5-chloro-2-pyridyl)triflimide (SI-5-12).** On this large scale, HPLC grade CH_2Cl_2 was employed. A mechanically stirred solution of 2-amino-5-chloropyridine (27.1 g, 211 mmol) in CH_2Cl_2 (800 mL) and pyridine (36.0 mL, 443 mmol) was cooled to -78 °C. The cloudy suspension was then charged with a solution of triflic anhydride (74.5 mL, 443 mmol) in CH_2Cl_2 (150 mL) dropwise via addition funnel over 2 h 15 min. After an additional 30 min., the bright yellow slurry was allowed to warm to ambient temperature. After 18 h, the bright orange solution was quenched with cold water (50 mL) and the layers were separated. The aqueous layer was then washed with CH_2Cl_2 (4 x 50 mL), and the combined organic layers were washed with cold 10% sat. NaOH (150 mL), cold water (100 mL), brine (100 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Be careful of bumping when placing under high vacuum! Purification via short path distillation (bp 80-90 °C, 0.01 mm Hg) containing a small vigreaux column in

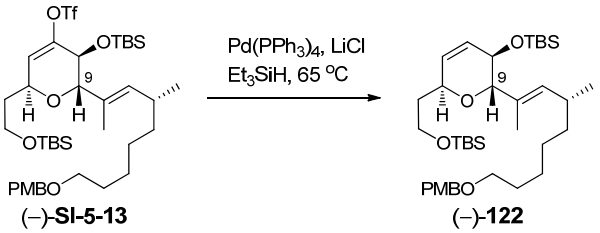
two batches furnished 51.6 g (62% yield) of **SI-5-12** as a white solid: mp 46-48 °C. Spectroscopic data matched that previously reported in the literature.[11]



(–)-**118** (–)-**SI-5-13**

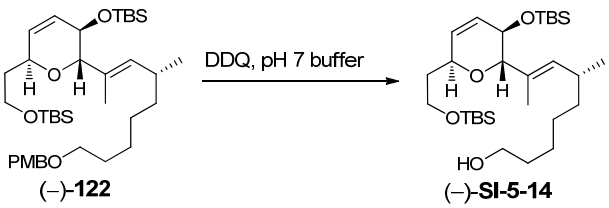
Enol Triflate (–)-SI-5-13. Preparation of a 0.5 M solution of lithium diisopropylamide (LDA): To a 0 °C solution of *n*-BuLi (4.30 mL, 2.28 M in hexanes, 10.0 mmol) in distilled THF (14.2 mL) was added (*i*-Pr)$_2$NH (1.40 mL, 10.1 mmol) dropwise. This solution was then allowed to stir for 15 min. before adding to the reaction.

To a -78 °C solution of azeotroped ketone (–)-**118** (2.10 g, 3.10 mmol) in distilled THF/HMPA (19/1, 112 mL) was added freshly prepared lithium diisopropyl amide (LDA, 9.50 mL, 0.5 M in THF, 4.75 mmol). After 30 min., 3.4 mL of a solution of azeotroped **SI-5-12** (1.80 g, 4.75 mmol) in THF/HMPA (19/1) was added dropwise. This solution was prepared by dissolving 3.00 g **SI-5-12** in THF to make a 5.50 mL solution. After 1.5 h, the resulting red/orange solution was quenched with sat. NH_4Cl (30 mL), and warmed to ambient temperature. After diluting with water (200 mL) and diethyl ether (200 mL), the aqueous phase was washed with diethyl ether (2 x 50 mL). The organic layer was then washed with water (3 x 50 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford 3.0 g (123 % yield) of the crude enol triflate that was used without further purification. On smaller scale, purification by flash chromatography (20/1, hexanes/EtOAc) afforded pure **SI-5-13** as a pale yellow oil: R_f 0.38 (10/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –35.2 (*c* 0.42, C_6H_6); IR (thin film, $CDCl_3$) 2930 (s), 2857 (s), 1614 (w), 1513 (m), 1462 (m), 1421 (m), 1362 (w), 1301 (w), 1248 (s), 1212 (s), 1143 (s), 1097 (s), 1039 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 5.89 (d, *J* = 2.1 Hz, 1 H), 5.17 (d, *J* = 9.2 Hz, 1 H), 4.41 (br s, 2 H), 4.37 (br s, 1 H), 4.23 (m, 1 H), 4.08 (d, *J* = 2.7 Hz, 1 H), 3.80 (s, 3 H), 3.73 (m, 2 H), 3.41 (app t, *J* = 6.7 Hz, 2 H), 2.36 (m, 1 H), 1.85 (m, 1 H), 1.80 (m, 1 H), 1.67 (s, 3 H), 1.58 (m, 2 H), 1.33-1.16 (m, 6 H), 0.92 (d, *J* = 6.8 Hz, 3 H), 0.89 (s, 9 H), 0.87 (s, 9 H), 0.12 (s, 3 H), 0.06 (s, 3 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ159.07, 146.49, 136.44, 130.77, 129.16, 128.60, 122.99, 113.72, 82.47, 72.47, 70.18, 66.32, 66.07, 59.04, 55.24, 36.94, 36.58, 32.47, 29.72, 27.35, 26.30, 25.87, 25.73, 20.36, 19.46, 18.21, 18.07, 14.19, -4.64, -5.46; HRMS (ES+) m/z 817.3773 [$(M+Na)^+$; calcd for $C_{38}H_{65}F_3O_8SSi_2Na^+$: 571.3533].



(–)-**SI-5-13** (–)-**122**

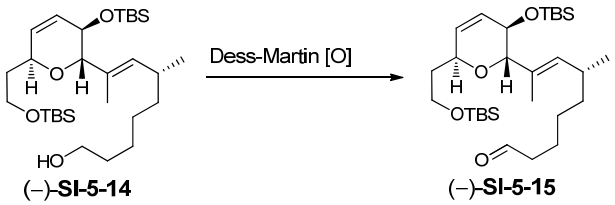
Diene (–)-122. To a solution of flame-dried LiCl (401 mg, 9.30 mmol) and $Pd(PPh_3)_4$ (182 mg, 0.155 mmol) in distilled THF (35.0 mL) was added a solution of the crude enol triflate (–)-**SI-5-13** (2.50 g, 3.10 mmol) in THF (16.0 mL), followed by 2 x 9 mL THF rinses. Triethylsilane (Et_3SiH, 1.50 mL, 9.30 mmol) was then added, and the reaction was heated to 65 °C. After 22 h, the reaction was cooled to ambient temperature and diluted with water (75 mL) and diethyl ether (75 mL). The aqueous phase was then washed with diethyl ether (3 x 20 mL), and the combined organic layers were then dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (20/1, hexanes/EtOAc, 5.0 cm diameter column, 8.5 in. SiO_2, flow rate 1.5 in./min.) afforded 1.50 g (77% yield, 2 steps from (–)-**118**) of (–)-**122** as a pale yellow oil: R_f 0.38 (10/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –74.5 (*c* 0.17, C_6H_6); IR (thin film, $CDCl_3$) 2929 (s), 2856 (s), 1720 (w), 1613 (w), 1512 (m), 1476 (m), 1360 (w), 1300 (w), 1249 (s), 1172 (w), 1099 (br, s), 1038 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 5.71 (br s, 2 H), 5.25 (d, *J* = 9.1 Hz, 1 H), 4.43 (br s, 2 H), 4.30 (dd, *J* = 9.4, 3.8 Hz, 1 H), 4.16 (dd, *J* = 7.7, 1.6 Hz, 1 H), 3.80 (s, 3 H), 3.71 (m, 2 H), 3.62 (d, *J* = 7.7 Hz, 1 H), 3.42 (app t, *J* = 6.6 Hz, 2 H), 2.37 (m, 1 H), 1.89 (m, 1 H), 1.69 (m, 1 H), 1.64 (s, 3 H), 1.59 (m, 2 H), 1.35-1.20 (m, 6 H), 0.93 (d, *J* = 6.7 Hz, 3 H), 0.88 (s, 9 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 6 H), 0.02 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.09, 136.46, 131.14, 130.86, 130.36, 130.00, 129.15, 113.74, 78.60, 72.45, 70.22, 69.78, 66.06, 60.21, 55.25, 37.23, 35.79, 32.01, 29.73, 27.22, 26.42, 25.96, 25.87, 20.40, 18.35, 18.10, 12.80, -4.25, -4.54, -5.36; HRMS (ES+) m/z 669.4372 [$(M+Na)^+$; calcd for $C_{37}H_{66}O_5Si_2Na^+$: 669.4346].



(–)-**122** (–)-**SI-5-14**

Alcohol (–)-SI-5-14. For this reaction, HPLC CH_2Cl_2 was employed. To a 0 °C solution of PMB ether (–)-**122** (40.0 mg, 61.8 μmol) in CH_2Cl_2 (2.0 mL) and pH 7 buffer (100 μL) was added 2,3-dichloro-5,6-

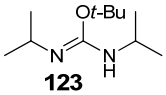
dicyano-1,4-benzoquinone (DDQ, 21.0 mg, 92.7 μmol) to produce a blue/green suspension. After 40 min., more DDQ (14.0 mg, 61.8 μmol) was added, and after an additional 30 min., the suspension was diluted with sat. $NaHCO_3$ (3 mL), water (10 mL) and CH_2Cl_2 (15 mL). The aqueous layer was then washed with CH_2Cl_2 (3 x 5 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by preparative-TLC (10/1, hexanes/EtOAc, 500 μm plate) afforded 33.6 mg of a mixture of (–)-**SI-5-14** and *p*-anisaldehyde which was used without further purification. In previous trials, further flash chromatography afforded pure (–)-**SI-5-14** for characterization purposes: R_f 0.13 (10/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –36.6 (*c* 0.62, $CDCl_3$); IR (thin film, $CDCl_3$) 3363 (br, w), 2929 (s), 2857 (s), 1471 (m), 1388 (w), 1361 (w), 1300 (w), 1254 (s), 1100 (br, s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.71 (br s, 2 H), 5.25 (dd, *J* = 9.2, 1.1 Hz, 1 H), 4.30 (m, 1 H), 4.16 (dd, *J* = 7.8, 2.0 Hz, 1 H), 3.72 (m, 2 H), 3.63 (app t, *J* = 6.6 Hz, 2 H), 3.62 (d, *J* = 7.8 Hz, 1 H), 2.38 (m, 1 H), 1.88 (m, 1 H), 1.68 (m, 1 H), 1.64 (d, *J* = 1.3 Hz, 3 H), 1.55 (m, 2 H), 1.30 (m, 6 H), 0.94 (d, *J* = 6.6 Hz, 3 H), 0.88 (s, 9 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 6 H), 0.02 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.30, 131.23, 130.34, 129.98, 78.54, 69.78, 66.10, 63.04, 60.20, 37.20, 35.78, 32.77, 32.00, 27.14, 25.95 (2), 25.86, 20.43, 18.33, 18.08, 12.88, -4.25, -4.53, -5.37; HRMS (ES+) m/z 549.3756 [$(M+Na)^+$; calcd for $C_{29}H_{58}O_4Si_2Na^+$: 549.3874].



(–)-**SI-5-14** (–)-**SI-5-15**

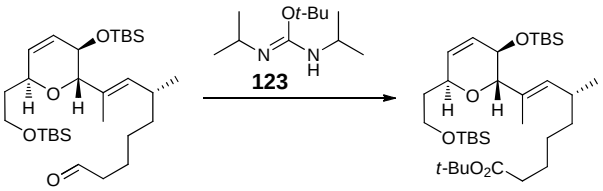
Aldehyde (–)-SI-15. To a 0 °C solution of the crude alcohol (–)-**SI-14** mixture (30.6 mg, 58.0 μmol) and pyridine (23.0 μL, 290 μmol) in CH_2Cl_2 (3.0 mL) was added Dess-Martin periodinane (49.2 mg, 116 μmol) in one portion. The ice bath was then removed, and the white suspension was allowed to warm to ambient temperature. After 1 h, the reaction was diluted with sat. $NaHCO_3$ (3 mL), water (10 mL), and CH_2Cl_2 (15 mL). The aqueous layer was then washed with CH_2Cl_2 (3 x 5 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (20/1, hexanes/EtOAc, 1.0 cm diameter column, 4.0 in. SiO_2, flow rate 2.0 in./min.) afforded 27.8 mg (86% yield, 2 steps from (–)-**122**) of (–)-**SI-5-15** as a pale yellow oil: R_f 0.26 (20/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –39.2 (*c* 1.66, $CDCl_3$); IR (thin film, $CDCl_3$) 2954 (s), 2856 (s), 2711 (w), 1728 (s), 1462 (s), 1388 (m), 1361 (m), 1252 (s), 1098 (br, s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.75 (app t,

J = 1.9 Hz, 1 H), 5.71 (br s, 2 H), 5.24 (d, J = 9.1 Hz, 1 H), 4.30 (dd, J = 9.3, 4.1 Hz, 1 H), 4.15 (dd, J = 7.8, 2.2 Hz, 1 H), 3.72 (m, 2 H), 3.61 (d, J = 7.8 Hz, 1 H), 2.40 (app dt, J = 7.8, 1.9 Hz, 2 H), 2.39 (m, 1 H), 1.88 (m, 1 H), 1.69 (m, 1 H), 1.64 (s, 3 H), 1.60 (m, 2 H), 1.38-1.20 (m, 4 H), 0.94 (d, J = 6.7 Hz, 3 H), 0.88 (s, 9 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 6 H), 0.02 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.64, 135.94, 131.58, 130.36, 129.97, 78.47, 69.80, 66.16, 60.18, 43.87, 36.95, 35.77, 31.91, 26.93, 25.95, 25.86, 22.27, 20.40, 18.34, 18.08, 12.92, -4.22, -4.53, -5.37; HRMS (ES+) m/z 547.3612 [$(M+Na)^+$; calcd for $C_{29}H_{56}O_4Si_2Na^+$: 524.3717].



123

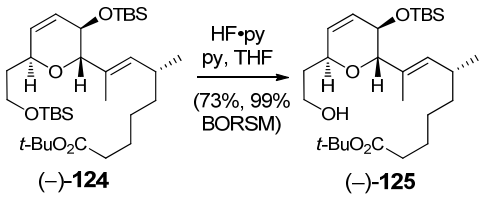
***N,N'*-Diisopropyl-*O*-*tert*-butylisourea (123).** To a solution of 1,3-diisopropylcarbodiimide (31.0 mL, 198 mmol) in *tert*-butanol (21.8 mL) was added CuCl (196 mg, 1.98 mmol). The resulting greenish/brown suspension was then wrapped in Al foil, and after 11 days, the reaction was diluted with hexanes (50 mL) and filtered through a plug of neutral alumina. The eluent was then concentrated *in vacuo* and purified via short-path distillation (bp ~70 °C, 10 mm Hg) to afford 24.9 g (63% yield) of **123** as a colorless oil. This characterization data matched that previously reported in the literature.[12]



(–)-**SI-5-15** (–)-**124**

Ester (–)-124. To a solution of aldehyde (–)-**SI-5-15** (162 mg, 308 μmol) in *tert*-butanol (6.10 mL) was added 2-methyl-2-butene (1.70 mL), followed by a solution of sodium chlorite (174 mg, 80% wt., 1.54 mmol) and sodium dihydrogenphosphate (370 mg, 3.08 mmol) in water (1.70 mL) dropwise. After 10 min., the reaction was diluted with sat. NH_4Cl (30 mL) and EtOAc (30 mL). The aqueous layer was then washed with EtOAc (4 x 10 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to afford the crude carboxylic acid that was used without further purification. To a solution of the crude carboxylic acid (167 mg, 308 μmol) in CH_2Cl_2 (19 mL) was added **123** (664 μL, 2.77 mmol). After 44 h, the white suspension was diluted with water (30 mL), and the layers were separated. The aqueous phase was then washed with CH_2Cl_2 (2 x 5 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (20/1,

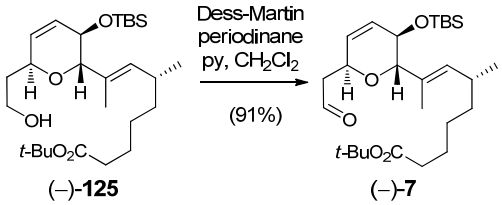
hexanes/EtOAc, 2.0 cm diameter column, 4.0 in. SiO_2, flow rate 1.5 in./min.) afforded 147 mg (80% yield, 2 steps from (–)-**SI-5-15**) of (–)-**124** as a pale yellow oil: R_f 0.25 (20/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –24.8 (*c* 1.49, $CDCl_3$); IR (thin film, CH_2Cl_2) 3031 (w), 2929 (s), 2857 (s), 1732 (s), 1604 (w), 1471 (m), 1462 (m), 1388 (m), 1366 (m), 1252 (s), 1134 (s), 1099 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.70 (br s, 2 H), 5.24 (dd, *J* = 9.2, 1.0 Hz, 1 H), 4.29 (dd, *J* = 9.5, 4.3 Hz, 1 H), 4.15 (dd, *J* = 7.8, 2.1 Hz, 1 H), 3.71 (m, 2 H), 3.61 (d, *J* = 7.8 Hz, 1 H), 2.37 (m, 1 H), 2.18 (app t, *J* = 7.6 Hz, 2 H), 1.88 (m, 1 H), 1.68 (m, 1 H), 1.64 (s, 3 H), 1.55 (m, 2 H), 1.43 (s, 9 H), 1.30-1.20 (m, 4 H), 0.93 (d, *J* = 6.7 Hz, 3 H), 0.88 (s, 9 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.03 (s, 6 H), 0.01 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.21, 136.19, 131.34, 130.34, 130.00, 79.84, 78.51, 69.79, 66.12, 60.19, 36.87, 35.78, 35.53, 31.90, 28.11, 26.83, 25.95, 25.85, 25.27, 20.33, 18.34, 18.08, 12.86, -4.24, -4.55, -5.37; HRMS (ES+) m/z 619.4201 [$(M+Na)^+$; calcd for $C_{33}H_{64}O_5Si_2Na^+$: 619.4292].



Scheme 36

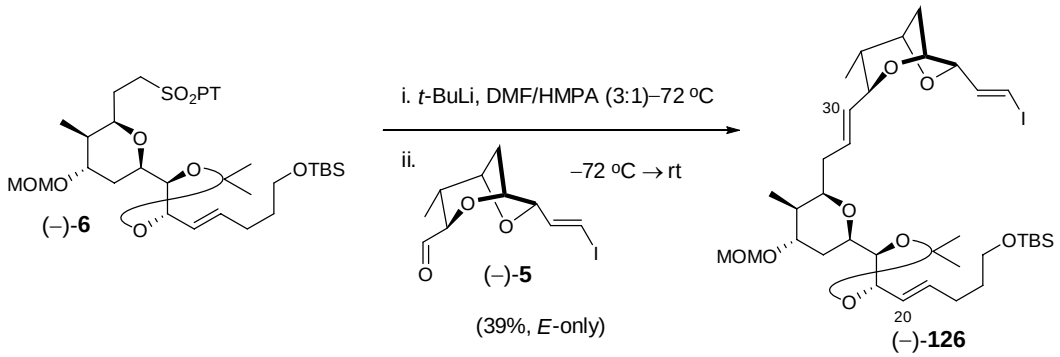
Alcohol (–)-125. To a solution of bis-TBS ether (–)-**124** (147 mg, 246 μmol) and distilled THF (10.2 mL) in a nalgene container was added 1.5 mL of a stock solution of HF•pyridine. The stock solution was prepared by adding pyridine (3.10 mL) portionwise to a solution of HF•pyridine (1.30 g) and THF (10.0 mL) in a nalgene container. After 24 h, the reaction was carefully diluted with sat. $NaHCO_3$ (10 mL) and diethyl ether (25 mL). The aqueous layer was then washed with diethyl ether (3 x 5 mL), and the combined organic layers were washed with sat. NH_4Cl (10 mL), sat $NaHCO_3$ (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (4/1 → 1/1, hexanes/EtOAc, 2.0 cm diameter column, 6.0 in. SiO_2, flow rate 1.5 in./min.) sequentially afforded 40.0 mg (27% yield) of recovered (–)-**124**, and 86.0 mg (77% yield) of (–)-**125**, as pale yellow oils. For (–)-**125**: R_f 0.20 (10/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –43.2 (*c* 0.55, $CDCl_3$); IR (thin film, CH_2Cl_2) 3446 (br, m), 3036 (w), 2930 (s), 2857 (s), 1731 (s), 1458 (m), 1389 (m), 1367 (m), 1252 (s), 1154 (s), 1122 (s), 1093 (s), 1068 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.76 (dd, *J* = 10.4, 0.8 Hz, 1 H), 5.66, (ddd, *J* = 10.4, 1.2, 1.2 Hz, 1 H), 5.29 (d, *J* = 9.0 Hz, 1 H), 4.34 (br d, *J* = 10.3 Hz, 1 H), 4.17 (d, *J* = 7.4 Hz, 1 H), 3.79 (m, 2 H), 3.75 (d, *J* = 7.4 Hz, 1 H), 2.72 (dd, *J* = 8.1, 3.2 Hz, 1 H), 2.37 (m, 1 H), 2.18 (app t, *J* = 7.4 Hz, 2 H), 2.02 (m, 1 H), 1.65 (s, 3 H), 1.63 (m, 1 H), 1.55 (m, 2 H), 1.44 (s, 9 H), 1.26 (m, 4 H), 0.93 (d, *J* = 6.7

Hz, 3 H), 0.87 (s, 9 H), 0.07 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.22, 137.17, 130.73, 130.15, 129.61, 79.87, 78.77, 73.41, 65.66, 61.93, 36.78, 35.53, 34.31, 31.99, 28.11, 26.87, 25.80, 25.23, 20.34, 18.04, 12.98, -4.26, -4.62; HRMS (ES+) m/z 505.3305 [$(M+Na)^+$; calcd for $C_{27}H_{50}O_5SiNa^+$: 505.3428].

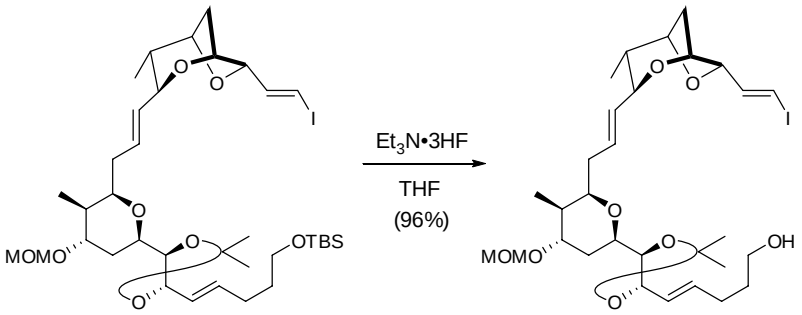


(–)-**125** (–)-**7**

Aldehyde (–)-7. To a 0 °C solution of alcohol (–)-**125** (11.4 mg, 23.6 μmol) and pyridine (9.50 μL, 118 μmol) in CH_2Cl_2 (1.50 mL) was added Dess-Martin periodinane (20.0 mg, 47.2 μmol) in one portion. The ice bath was then removed, and the reaction was allowed to warm to ambient temperature. After 1.5 h, the white suspension was diluted with sat. $NaHCO_3$ (3 mL), water (10 mL) and CH_2Cl_2 (15 mL). The aqueous layer was then washed with CH_2Cl_2 (3 x 5 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (7/1, hexanes/EtOAc, 1.0 cm diameter column, 3.0 in. SiO_2, flow rate 2.0 in./min.) afforded 10.3 mg (91% yield) of (–)-**7** as a pale yellow oil: R_f 0.11 (10/1, hexanes/EtOAc); $[\alpha]_D^{20}$ –37.8 (*c* 0.19, C_6D_6); IR (thin film, C_6H_6) 2931 (br, s), 2857 (m), 1727 (br, s), 1461 (w), 1369 (w), 1253 (w), 1153 (m), 1091 (m) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 9.32 (br s, 1 H), 5.73 (ddd, *J* = 10.3, 2.0, 2.0 Hz, 1 H), 5.39 (ddd, *J* = 10.3, 2.0, 2.0 Hz, 1 H), 5.36 (d, *J* = 9.5 Hz, 1 H), 4.49 (m, 1 H), 4.20 (dd, *J* = 7.5, 2.0 Hz, 1 H), 3.75 (d, *J* = 7.5 Hz, 1 H), 2.36 (ddd, *J* = 16.4, 8.4, 2.5 Hz, 1 H), 2.32 (m, 1 H), 2.17 (app t, *J* = 7.4 Hz, 2 H), 1.88 (ddd, *J* = 16.4, 5.4, 1.2 Hz, 1 H), 1.71 (s, 3 H), 1.61 (m, 2 H), 1.39 (s, 9 H), 1.26 (m, 4 H), 0.95 (s, 9 H), 0.91 (d, *J* = 6.7 Hz, 3 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 197.73, 171.45, 135.51, 130.57, 130.11, 128.07, 78.31, 78.26, 67.32, 65.08, 45.94, 36.29, 34.62, 31.27, 27.14, 26.19, 25.02, 24.65, 19.54, 17.19, 12.24, -5.14, -5.46; HRMS (ES+) m/z 503.3157 [$(M+Na)^+$; calcd for $C_{27}H_{48}O_5SiNa^+$: 503.3271].



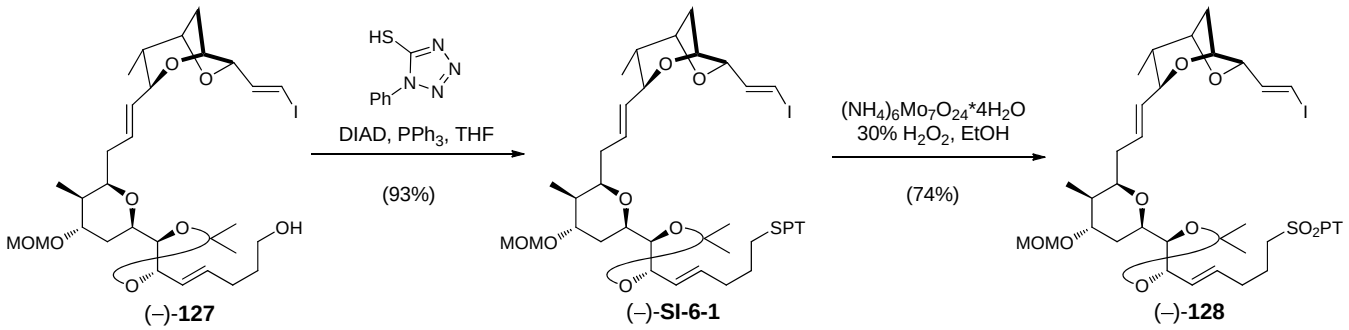
Triene (–)-126. At –72 °C, *t*-BuLi (1.7 M in pentane, 250 μL, 420 μmol) was added via syringe to a solution of sulfone (–)-**6** (292 mg, 420 μmol) in 3:1 DMF/HMPA (5.30 mL). After 2 min, a solution of aldehyde **(–)-5** (96 mg, 312 μmol) in 3:1 DMF/HMPA (3.9 mL) was rapidly added via cannula, and the resulting mixture was allowed to warm to rt over 2.5 h in the dark. A solution of saturated NH_4Cl solution (5 mL) was added to the reaction mixture, followed by H_2O (10 mL). The aqueous phase was extracted with Et_2O (3x10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The resulting crude oil was purified by preparatory TLC (SiO_2, 1 mm) eluting with hexanes/Et_2O (1:2) to afford triene (–)-**126** (94.0 mg, 39%) as a pale yellow oil, along with recovered (–)-**5** (12.0 mg, 13%) and (–)-**6** (113 mg, 39%). $[\alpha]_D^{20}$ –32.3 (*c* 0.55, C_6H_6); IR (neat, cm^{-1}) 1602, 1461, 1379, 1250, 1216, 1144, 1099, 1067, 1038; ^1H NMR (500 MHz, C_6D_6) δ 6.82 (dd, *J* = 14.5, 4.8 Hz, 1H), 6.43 (dd, *J* = 14.5, 1.5 Hz, 1H), 5.93 (ddd, *J* = 15.2, 6.7, 6.7 Hz, 1H), 5.82 (dd, *J* = 15.2, 6.3 Hz, 1H), 5.68 (m, 1H), 5.45 (dd, *J* = 15.2, 7.1 Hz, 1H), 4.76 (dd, *J* = 5.9, 5.9 Hz, 1H), 4.52 (d, J_{AB} = 6.7 Hz, 1H), 4.50 (d, J_{AB} = 6.7 Hz, 1H), 4.05 (m, 2H), 3.98 (m, 2H), 3.91 (d, *J* = 6.3 Hz, 1H), 3.88 (ddd, *J* = 2.6, 2.6, 2.6 Hz, 1H), 3.83 (ddd, *J* = 4.8, 2.2, 2.2 Hz, 1H), 3.66 (ddd, *J* = 2.9, 2.9, 2.9 Hz, 1H), 3.61 (app t, *J* = 6.3 Hz, 2H), 3.19 (s, 3H), 2.34 (ddd, *J* = 13.4, 6.7, 6.7 Hz, 1H), 2.22 (m, 2H), 2.05 (m, 1H), 2.02 (d, *J* = 14.5 Hz, 1H), 1.76-1.62 (m, 4H), 1.51 (s, 3H), 1.44 (d, *J* = 11.5 Hz, 1H), 1.40 (ddd, *J* = 11.5, 5.9, 2.6 Hz, 1H), 1.31 (s, 3H), 1.08 (dq, *J* = 9.3, 6.7 Hz, 1H), 1.00 (s, 9H), 0.81 (d, *J* = 7.1 Hz, 3H), 0.80 (d, *J* = 6.7 Hz, 3H), 0.09 (s, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.0, 132.7, 132.55, 129.2, 127.5, 108.3, 95.2, 83.5, 80.6, 79.4, 79.1, 78.9, 78.6, 75.8, 75.5, 73.9, 72.0, 62.7, 55.2, 41.8, 38.7, 36.3, 35.6, 323.0, 29.6, 29.1, 28.2, 26.2, 25.7, 18.5, 15.2, 10.8, -5.0; HRMS (ES) *m*/*z* $(M+Na)^+$ calcd for $C_{36}H_{61}IO_8SiNa^+$ 799.3078, obsd 799.3081.



(–)-**126** (–)-**127**

Alcohol (–)-127: TBS ether **(–)-126** (44.0 mg, 57.0 μmol) was dissolved in THF (1.10 mL) in a polyethylene vial. Neat $Et_3N{\cdot}3HF$ (65.0 μL, 0.390 mmol) was added via autopipetter and the resulting solution was stirred in the dark for 17 h. The reaction mixture was concentrated *in vacuo* and directly

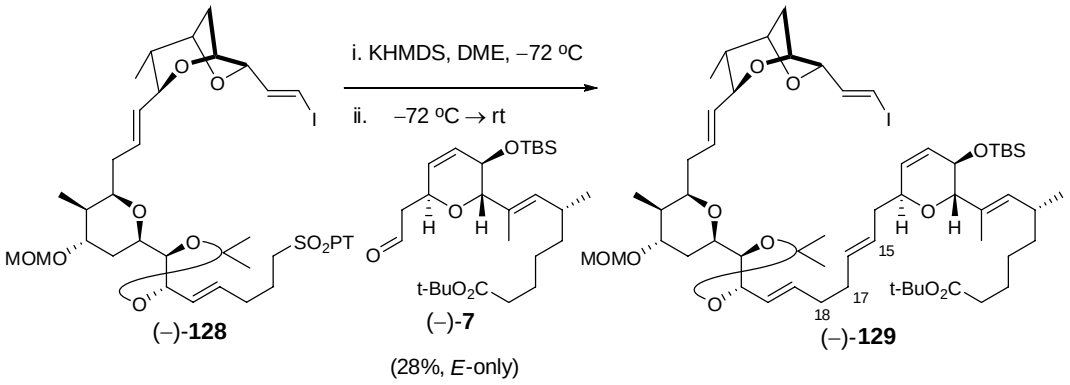
purified by flash chromatography (SiO_2) eluting with 2:3 hexanes/EtOAc to afford **(–)-127** (36.0 mg, 96%) as a pale yellow oil. $[\alpha]_D^{20}$ –26.2 (*c* 0.42, C_6H_6); IR (neat, cm^{-1}) 3480, 1670, 1602, 1455, 1379, 1247, 1216, 1144, 1097, 1066, 1037; ^1H NMR (500 MHz, C_6D_6) δ 6.82 (dd, *J* = 14.6, 4.9 Hz, 1H), 6.43 (dd, *J* = 14.6, 1.7 Hz, 1H), 5.89 (ddd, *J* = 15.3, 6.6, 6.6 Hz, 1H), 5.80 (ddd, *J* = 15.3, 6.2, 0.8 Hz, 1H), 5.70 (ddd, *J* = 15.3, 6.7, 6.7 Hz, 1H), 5.45 (dd, *J* = 15.3, 7.2 Hz, 1H), 4.76 (dd, *J* = 5.8, 5.8 Hz, 1H), 4.50 (br s, 2H), 4.06 (m, 2H), 4.00 (dd, *J* = 9.2, 7.6 Hz, 1H), 3.95 (ddd, *J* = 7.1, 7.1, 1.7 Hz, 1H), 3.89 (m, 2H), 3.81 (ddd, *J* = 4.5, 2.0, 2.0 Hz, 1H), 3.64 (ddd, *J* = 2.7, 2.7, 2.7 Hz, 1H), 3.47 (app t, *J* = 6.4 Hz, 2H), 3.19 (s, 3H), 2.31 (ddd, *J* = 14.1, 7.0, 7.0 Hz, 1H), 2.14 (ddd, *J* = 7.0, 7.0, 7.0 Hz, 2H), 2.02 (m, 2H), 1.73 (m, 1H), 1.68 (m, 1H), 1.58 (m, 2H), 1.50 (s, 3H), 1.44 (dd, *J* = 11.4, 1.4 Hz, 1H), 1.38 (ddd, *J* = 11.4, 6.2, 2.7 Hz, 1H), 1.31 (s, 3H), 1.07 (dq, *J* = 9.3, 6.8 Hz, 1H), 0.80 (d, *J* = 7.0 Hz, 3H), 0.79 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 141.94, 132.53, 132.40, 129.63, 127.66, 108.35, 95.29, 83.54, 80.55, 79.41, 79.08, 78.65, 76.03, 75.51, 74.13, 71.99, 62.07, 55.25, 41.74, 38.72, 36.37, 35.76, 32.82, 29.62, 29.13, 28.13, 25.62, 15.17, 10.85; HRMS (ES) *m*/*z* $(M+Na)^+$ calcd for $C_{30}H_{47}IO_8Na^+$ 685.2213, obsd 685.2204.



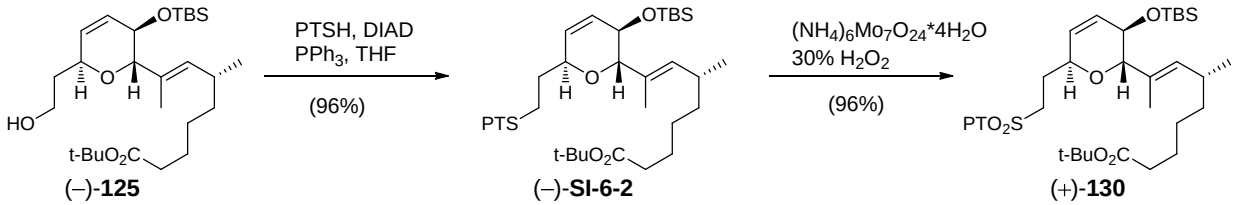
PTS Ether (–)-SI-6-1. To a solution of alcohol (–)-**127** (6.9 mg, 10.4 μmol), triphenylphosphine (4.4 mg, 16.6 μmol) and 1-phenyl-1H-tetrazole-5-thiol (5.0 mg, 28.1 μmol) in THF (1.3 mL) was added one drop of diisopropylazodicarboxylate (DIAD, ~5 μL, ~25 μmol). The resulting pale yellow solution gradually become colorless, and after 45 min, was concentrated *in vacuo* and purified via Preparative-TLC (1:1, hexanes/EtOAc on ½ of a 500 μm plate) to furnish PTS ether (–)-**SI-6-1** (7.9 mg, 93%) as a colorless oil. $[\alpha]_D^{20}$ –12.1 (*c* 0.45, C_6H_6); IR (neat, cm^{-1}) 1597, 1499, 1456, 1380, 1244, 1216, 1145, 1096, 1066, 1037; ^1H NMR (500 MHz, C_6D_6) δ 7.23 (m, 2H), 6.90-6.99 (m, 3H), 6.82 (dd, *J* = 14.5, 4.9 Hz, 1H), 6.43 (dd, *J* = 14.5, 1.7 Hz, 1H), 5.81 (m, 2H), 5.71 (ddd, *J* = 15.3, 7.0, 7.0 Hz, 1H), 5.45 (dd, *J* = 15.3, 6.9 Hz, 1H), 4.74 (m, 1H), 4.51 (br s, 2H), 4.02 (m, 3H), 3.95 (m, 1H), 3.90 (m, 2H), 3.86 (m, 1H), 3.65 (ddd, *J* = 2.6, 2.6, 2.6 Hz, 1H), 3.23 (m, 2H), 3.18 (s, 3H), 2.29 (ddd, *J* = 14.1, 7.0, 7.0 Hz,

1H), 2.12 (m, 2H), 2.00 (m, 2H), 1.84 (m, 2H), 1.72 (m, 1H), 1.64 (m, 1H), 1.50 (s, 3H), 1.43 (m, 2H), 1.30 (s, 3H), 1.09 (dq, *J* = 9.7, 6.7 Hz, 1H), 0.81 (d, *J* = 7.1 Hz, 3H), 0.80 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 154.27, 142.03, 134.37, 132.58, 130.91, 129.56, 129.27, 128.71, 124.00, 108.40, 95.19, 83.61, 80.54, 79.40, 79.06, 78.84, 78.49, 75.75, 75.57, 73.96, 71.94, 55.22, 41.82, 38.73, 36.44, 35.80, 32.94, 31.49, 30.16, 29.68, 29.10, 28.11, 25.56, 15.23, 10.84; HRMS (ES) *m*/*z* $(M+Na)^+$ calcd for $C_{37}H_{51}IN_4O_7SNa^+$ 845.2421, obsd 845.2408.

Sulfone (–)-128. To a 0 °C solution of PTS ether (–)-**SI-6-1** (10.1 mg, 12.2 μmol) in absolute EtOH (1.0 mL), not under argon, was added a pre-mixed solution of $(NH_4)_6Mo_7O_{24}•4H_2O$ (5.60 mg, 4.90 μmol) in H_2O_2 (30% aq., 40.0 μL) via a glass pipette, followed by 2x100 μL absolute EtOH rinses. The resulting yellow solution was then removed from the ice bath and allowed to warm to room temperature. After 8 h, the reaction mixture was diluted with diethyl ether (10 mL), saturated $NaHCO_3$ solution (5 mL) and water (10 mL). The aqueous layer was then extracted with diethyl ether (3x5 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purificaton via preparative-TLC (2:1, hexanes/EtOAc, 500 μM plate) furnished sulfone (–)-**128** (7.7 mg, 74%) as a colorless oil. $[\alpha]_D^{20}$ –20.3 (*c* 0.32, C_6H_6); IR (neat, cm^{-1}) 1598, 1498, 1479, 1461, 1343, 1247, 1216, 1153, 1097, 1066, 1037; ^{1}H NMR (500 MHz, C_6D_6) δ 7.36 (m, 2H), 6.90 (m, 3H), 6.82 (dd, *J* = 14.5, 5.0 Hz, 1H), 6.42 (dd, *J* = 14.5, 1.7 Hz, 1H), 5.79 (dd, *J* = 15.4, 5.9 Hz, 1H), 5.68-5.76 (m, 2H), 5.47 (dd, *J* = 15.3, 6.9 Hz, 1H), 4.71 (dd, *J* = 5.7, 5.7 Hz, 1H), 4.55 (br s, 2H), 4.01 (m, 3H), 3.96 (m, 1H), 3.89 (m, 2H), 3.84 (ddd, *J* = 5.0, 1.8, 1.8 Hz, 1H), 3.65 (ddd, *J* = 2.6, 2.6, 2.6 Hz, 1H), 3.53-3.43 (m, 2H), 3.21 (s, 3H), 2.29 (ddd, *J* = 14.1, 7.1, 7.1, 1H), 2.04-1.92 (m, 6H), 1.74 (m, 1H), 1.64 (m, 1H), 1.51 (s, 3H), 1.42 (m, 2H), 1.30 (s, 3H), 1.09 (dq, *J* = 9.3, 6.7 Hz, 1H), 0.81 (br d, *J* = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 154.17, 141.99, 133.60, 132.65, 130.89, 129.86, 129.58, 129.45, 129.35, 108.48, 95.21, 83.65, 80.48, 79.38, 79.20, 78.67, 78.48, 75.72, 75.58, 73.96, 71.89, 55.74, 55.24, 41.87, 38.72, 36.44, 35.84, 30.86, 29.68, 28.10, 25.54, 22.21, 15.22, 10.83; HRMS (ES) *m*/*z* $(M+Na)^+$ calcd for $C_{37}H_{51}IN_4O_9SNa^+$ 877.2319, obsd 877.2283.



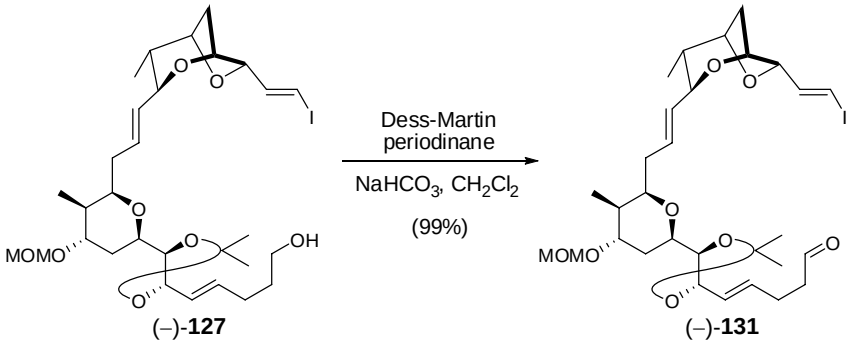
TBS Ether (–)-129. At –72 °C, KHMDS (0.5 M in PhMe, 23.0 μL, 11.5 μmol) was added via syringe to a solution of (–)-**128** (8.0 mg, 9.35 μmol) in DME (0.12 mL). After 10 min, the bright yellow mixture was treated via cannula with a solution of (–)-**7** (6.0 mg, 12.2 μmol) in DME (0.12 mL) and the mixture was allowed to warm to rt over 2 h. The reaction mixture was quenched with saturated NH_4Cl solution (2 mL). The aqueous phase was extracted with Et_2O (3x1 mL) and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude mixture was purified by flash chromatography (SiO_2) eluting with 3:1 hexanes/EtOAc to afford TBS ether (–)-**129** (2.9 mg, 28%) as a pale yellow oil, along with recovered sulfone (–)-**128** (4.0 mg, 50%) and aldehyde (–)-**7** (2.4 mg, 40%). $[\alpha]_D^{24}$ –34.9 (*c* 0.59, C_6H_6); IR (neat, cm^{-1}) 1730, 1459, 1368, 1251, 1150, 1066, 1038, 971, 837, 775; ^1H NMR (500 MHz, $CDCl_3$) δ 6.84-6.79 (dd, *J* = 14.5, 4.5 Hz, 1H), 6.56-6.52 (dd, *J* = 14.6, 1.7 Hz, 1H), 5.80-5.69 (m, 3H), 5.60-5.46 (m, 3H), 5.44-5.35 (m, 1H), 5.25-5.22 (d, *J* = 9.0 Hz, 1H), 4.67-4.59 (m, 3H), 4.35-4.33 (m, 1H), 4.31-4.28 (m, 1H), 4.24-4.22 (d, *J* = 6.4 Hz, 1H), 4.14-4.08 (m, 2H), 3.93-3.90 (m, 1H), 3.87-3.84 (t, *J* = 8.0 Hz, 1H), 3.77-3.69 (m, 3H), 3.67-3.65 (d, *J* = 7.8 Hz, 1H), 3.34 (s, 3H), 2.44-2.35 (m, 2H), 2.29-2.21 (m, 2H), 2.19-2.02 (m, 7H), 1.98-1.86 (m, 1H), 1.86-1.83 (m, 1H), 1.78-1.73 (m, 1H), 1.71-1.65 (m, 1H), 1.63-1.59 (m, 4H), 1.58-1.49 (m, 6H), 1.42 (s, 9H), 1.38-1.15 (m, 11H), 0.94-0.77 (m, 15H), 0.05-0.01 (d, *J* = 21.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 141.0, 136.6, 133.7, 132.4, 131.7, 131.1, 130.3, 130.1, 129.73, 129.66, 126.5, 125.9, 108.2, 94.9, 83.5, 79.9, 79.8, 79.4, 79.3, 78.9, 78.7, 77.8, 75.6, 75.3, 73.6, 73.2, 71.6, 65.8, 55.4, 41.3, 37.1, 37.0, 36.9, 35.8, 35.6, 35.1, 32.4, 32.3, 31.9, 29.7, 28.6, 28.1, 27.7, 26.8, 25.9, 25.4, 25.3, 22.7, 20.3, 18.1, 15.1, 14.1, 12.8, 10.6, -4.2, -4.5; HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{57}H_{93}IO_{11}SiNa^+$ 1131.5429, obsd 1131.5425.



PTS Ether (–)-SI-6-2. To a solution of alcohol (–)-**125** (13.0 mg, 26.0 μmol), triphenylphosphine (10.9 mg, 41.6 μmol) and 1-phenyl-1H-tetrazole-5-thiol (12.5 mg, 70.2 μmol) in THF (3.3 mL) was added one drop of diisopropylazodicarboxylate (DIAD, 10.0 μL, 49.0 μmol). The resulting pale yellow solution gradually become colorless, and after 45 min, was concentrated *in vacuo* and purified via Preparative-TLC (1:1, hexanes/EtOAc on ½ of a 500 μm plate) to furnish PTS ether (–)-**SI-6-2** (16.0 mg, 96%) as a colorless oil. $[\alpha]_D^{20}$ –43.2 (*c* 0.80, CH_2Cl_2); IR (thin film, CH_2Cl_2, cm^{-1}) 2954, 2928, 2856, 1728, 1597, 1500, 1462, 1388, 1366,1249, 1153, 1090; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58-7.51 (m, 5 H), 5.75 (ddd, *J* = 10.3, 1.9, 1.9 Hz, 1 H), 5.67 (ddd, *J* = 10.3, 2.2, 2.2 Hz, 1 H), 5.26 (d, *J* = 9.1 Hz, 1 H), 4.27 (m, 1 H), 4.15 (m, 1 H), 3.65 (d, *J* = 7.4 Hz, 1 H), 3.53 (ddd, *J* = 13.3, 8.1, 5.0 Hz, 1 H), 3.41 (ddd, *J* = 13.3, 7.6, 7.6 Hz, 1 H), 2.36 (m, 1 H), 2.20 (m, 1 H), 2.17 (t, *J* = 7.5 Hz, 2 H), 2.06 (m, 1 H), 1.64 (d, *J* = 1.0 Hz, 3 H), 1.52 (m, 2 H), 1.43 (s, 9 H), 1.27 (m, 4 H), 0.91 (d, *J* = 6.7 Hz, 3 H), 0.86 (s, 9 H), 0.06 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 173.18, 154.31, 136.59, 133.74, 133.88, 130.83, 130.03, 129.74, 128.96, 123.81, 79.86, 78.74, 71.22, 65.79, 36.81, 35.52, 32.30, 31.94, 30.19, 28.11, 26.82, 25.82, 25.24, 20.29, 18.05, 13.00, -4.25, -4.58; HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{34}H_{54}N_4O_4SSiNa^+$ 665.3532, obsd 665.3547.

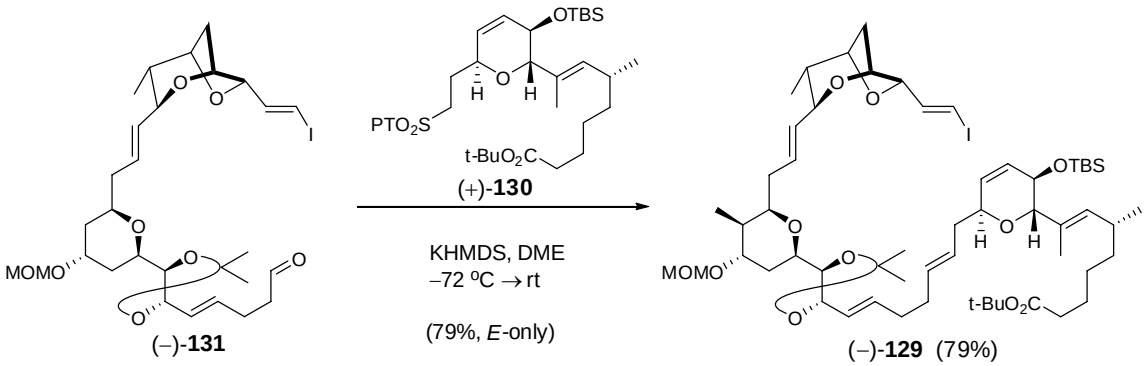
Sulfone (+)-130. To a 0 °C solution of PTS ether (–)-**SI-6-2** (16.0 mg, 24.8 μmol) in absolute EtOH (1.0 mL), not under argon, was added a pre-mixed solution of $(NH_4)_6Mo_7O_{24}•4H_2O$ (4.3 mg, 3.7 μmol) in H_2O_2 (30% aq., 40.0 μL) via a glass pipette, followed by 2x100 μL absolute EtOH rinses. The resulting yellow solution was then removed from the ice bath and allowed to warm to room temperature. After 12 h, the reaction mixture was diluted with diethyl ether (10 mL), saturated $NaHCO_3$ solution (5 mL) and water (10 mL). The aqueous layer was then extracted with diethyl ether (3x5 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purificaton via preparative-TLC (2:1, hexanes/EtOAc, 500 μm plate) furnished sulfone (+)-**130** (16.0 mg, 96%) as a colorless oil. $[\alpha]_D^{20}$ +10.5 (*c* 0.8, C_6H_6); IR (thin film, C_6H_6, cm^{-1}) 2955, 2929, 2857, 1728, 1596, 1498, 1461, 1391, 1340, 1251, 1156, 1115; ^1H NMR (500 MHz, C_6D_6) δ 7.69 (m, 2 H), 7.61 (m, 3 H), 5.82 (ddd, *J* = 10.3, 2.1, 2.1 Hz, 1 H), 5.66 (ddd, *J* = 10.3, 2.1, 2.1 Hz, 1 H), 5.29 (d, *J* = 9.3 Hz, 1 H), 4.24 (m, 1 H), 4.16 (m, 1 H), 3.93 (ddd, *J* = 15.1, 10.9, 4.5 Hz, 1 H), 3.79 (ddd, *J* = 15.1, 10.9, 5.2 Hz, 1 H),

3.69 (d, J = 7.1 Hz, 1 H), 2.40-2.28 (m, 2 H), 2.18 (t, J = 7.5 Hz, 2 H), 2.12 (m, 1 H), 1.65 (d, J = 0.9 Hz, 3 H), 1.60-1.50 (m, 2 H), 1.43 (s, 9 H), 1. 32-1.25 (m, 4 H), 0.93 (d, J = 6.6 Hz, 3 H), 0.87 (s,9 H), 0.06 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 173.20, 153.39, 137.10, 133.07, 131.59, 131.42, 130.38, 129.69, 128.10, 125.07, 79.87, 78.99, 70.25, 65.36, 53.54, 36.79, 35.54, 32.03, 28.12, 26.86, 25.95, 25.80, 25.24, 20.31, 18.03, 12.97, -4.25, -4.60; HRMS (ES) m/z $(M+Na)^+$ calcd for $C_{34}H_{54}IN_4O_6SSiNa^+$ 697.3430, obsd 697.3453.

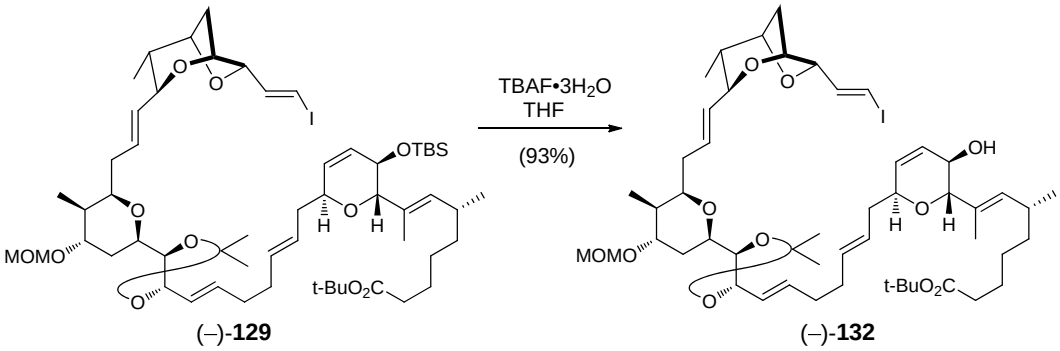


(–)-**127** (–)-**131**

Aldehyde (–)-131: At room temperature, solid Dess-Martin periodinane (35.0 mg, 82.0 μmol) was added in one portion to a slurry of (–)-**127** (18.0 mg, 27.0 μmol) and $NaHCO_3$ (27.0 mg, 0.330 mmol) in CH_2Cl_2 (1.4 mL). The mixture was stirred in the dark for 2 h and then diluted with Et_2O (1.5 mL), whereupon a 1:1:1 solution of saturated $NaHCO_3$/brine/$Na_2S_2O_3$ (3 mL) was added and stirring was continued until the aqueous layer became homogenous (20 min). The layers were separated and the aqueous phase was extracted with Et_2O (2x1 mL). The combined organic extracts were dried (Na_2SO_4), filtered through a pad of SiO_2 (5 g) with an Et_2O rinse (10 mL) and concentrated *in vacuo*. The crude residue was purified by flash chromatography (SiO_2) eluting with 1:1 hexanes/EtOAc to afford (–)-**131** (17.7 mg, 99%) as a pale yellow oil. $[\alpha]_D^{24}$ –31.9 (*c* 1.0, C_6H_6); IR (neat, cm^{-1}) 1724, 1457, 1378, 1216, 1144, 1101, 1066, 1036, 970, 941, 877, 799, 676; ^{1}H NMR (500 MHz, C_6D_6) δ 9.39-9.38 (m, 1H), 6.83-6.79 (dd, J = 14.5, 4.5 Hz, 1H), 6.46-6.42 (dd, J = 15.0, 2.0 Hz, 1H), 5.84-5.67 (m, 3H), 5.49-5.44 (dd, J = 15.5, 7.0 Hz, 1H), 4.73-4.70 (t, J = 6.0 Hz, 1H), 4.53 (s, 2H), 4.05-3.94 (m, 4H), 3.92-3.90 (d, J = 5.5 Hz, 1H), 3.98-3.87 (m, 1H), 3.85-3.82 (m, 1H), 3.67-3.65 (m, 1H), 3.21 (s, 3H), 2.33-2.20 (m, 2H), 2.08-1.97 (m, 4H), 1.77-1.71 (m, 1H), 1.68-1.62 (m, 1H), 1.51 (s, 3H), 1.43-1.27 (m, 6H), 1.11-1.05 (m, 1H), 0.87-0.75 (m, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 200.6, 142.4, 133.0, 131.1, 129.6, 108.8, 95.6, 84.0, 80.9, 79.8, 79.3, 79.2, 78.8, 76.2, 75.9, 74.4, 72.3, 55.6, 43.6, 42.2, 39.1, 36.8, 36.2, 30.5, 30.1, 28.5, 26.0, 25.6, 21.6, 15.6, 11.2; HRMS (ES) m/z $(M+Na)^+$ calcd for $C_{30}H_{45}IO_8Na^+$ 683.2057, obsd 683.2081.

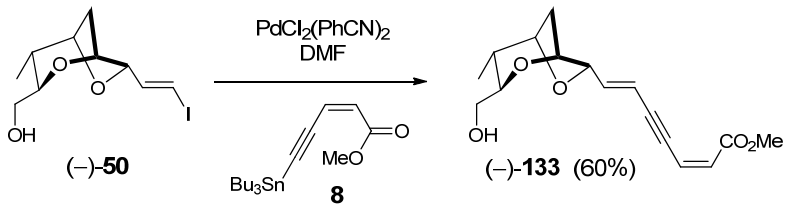


TBS Ether (–)**-129:** A 0.5 M solution of KHMDS in PhMe (107 μL, 54.0 μmol) was added via syringe to a solution of **(+)-130** (35.0 mg, 52.0 μmol) in DME (0.65 mL) cooled to -72 °C. After 10 min, the bright yellow mixture was treated via cannula with a rt solution of **(–)-131** (17.7 mg, 27.0 μmol) in DME (0.45 mL) and the mixture was allowed to warm to rt over 2 h. The reaction was quenched at rt upon addition of sat. aqueous NH_4Cl (2 mL) and Et_2O (1 mL). The resulting layers were separated and the aqueous phase was extracted with Et_2O (3 X 1 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product mixture was purified by flash chromatography (SiO_2) eluting with 3:1 hexanes/EtOAc to afford 23.5 mg of (–)**-129** (79%) as a pale yellow oil. (R_f = 0.47, 3:1 hexanes/EtOAc). All characterization data matched that obtained upon formation of (–)**-129** from (–)**-128** and (–)**-7**. .



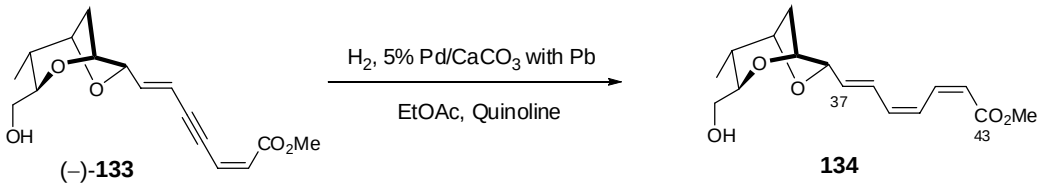
Alcohol (–)-132: Solid TBAF·$3H_2O$ (110 mg, 0.424 mmol) was added to a rt solution of **(–)-129** (23.5 mg, 21.1 μmol) in THF (0.42 mL). The mixture was stirred in the dark for 20 h, and then diluted with Et_2O (1 mL) and sat. aqueous NH_4Cl (2 mL). The layers were separated and the aqueous phase was extracted with Et_2O (4 X 1 mL). The combined organic extracts were dried (Na_2SO_4), filtered through a short plug of SiO_2 (5 g) with additional Et_2O (25 mL), and concentrated under reduced pressure. The resulting crude product was purified by flash chromatography (SiO_2) eluting with 1:1 hexanes/EtOAc to

afford (–)-**132** (19.6 mg, 93%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83-6.79 (dd, *J* = 14.5, 4.5 Hz, 1H), 6.56-6.52 (dd, *J* = 14.5, 1.8 Hz, 1H), 5.89-5.86 (m, 1H), 5.81-5.74 (m, 2H), 5.60-5.37 (m, 5H), 5.19-5.17 (d, *J* = 9.3 Hz, 1H), 4.66-4.59 (m, 3H), 4.35-4.33 (m, 1H), 4.30-4.28 (m, 1H), 4.24-4.22 (d, *J* = 6.4 Hz, 1H), 4.12-4.06 (m, 2H), 3.94-3.90 (m, 1H), 3.88-3.85 (m, 1H), 3.78-3.69 (m, 4H), 3.34 (s, 3H), 2.45-2.36 (m, 2H), 2.30-2.21 (m, 2H), 2.18-2.03 (m, 8H), 1.97-1.94 (m, 1H), 1.87-1.84 (m, 1H), 1.78-1.74 (m, 1H), 1.71-1.48 (m, 9H), 1.47-1.16 (m, 18H), 0.95-0.93 (d, *J* = 6.6 Hz, 3H), 0.89-0.87 (d, *J* = 6.6 Hz, 3H), 0.84-0.82 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 141.0, 136.5, 133.7, 132.6, 131.7, 130.8, 130.7, 130.3, 128.2, 126.3, 126.0, 108.2, 94.9, 83.5, 79.9, 79.8, 79.5, 79.4, 78.76, 78.73, 75.6, 75.3, 73.6, 72.4, 71.5, 63.7, 55.4, 41.3, 38.6, 37.3, 37.1, 35.8, 35.5, 35.1, 32.4, 32.3, 32.0, 29.7, 28.6, 28.1 (3C), 27.7, 27.1, 25.4, 25.0, 20.9, 15.1, 12.3, 10.6; IR (thin film) 3460, 2928, 1728, 1454, 1368, 1248, 1216, 1151, 1097, 1066, 1038, 971, 873, 730 cm^{-1}; MS (ESI +) *m/z* 1017.4587 (M + Na)$^+$ [$C_{51}H_{79}IO_{11}Na^+$ requires 1017.4564]; $[\alpha]_D^{24}$ –21.3 (*c* 0.44, $CHCl_3$).

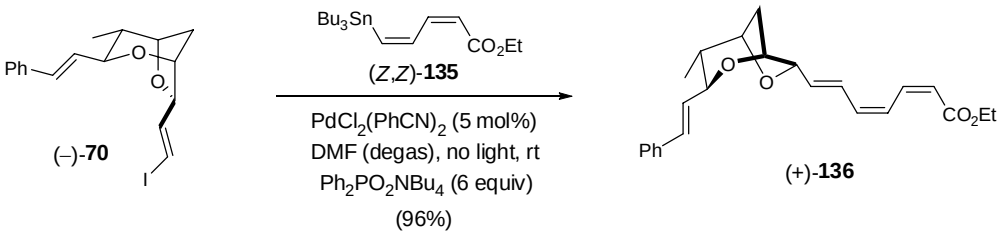


Ester (–)-133: The DMF was degassed with argon for 30 min. prior to use. Stock solutions were prepared by dissolving azeotroped stannane **8** (31.4 mg, 7.9 μmol) in DMF (1.0 mL), and $PdCl_2(PhCN)_2$ (2.5 mg, 0.007 μmol) in DMF (1.25 mL). To a solution of azeotroped vinyl iodide (–)-**50** (1.6 mg, 5.2 μmol) in DMF (1200 μL) was sequentially added 200 μL (~3 equiv.) of the stannane solution, followed by 100 μL (~0.1 equiv.) of the $PdCl_2(PhCN)_2$ solution. After 3 h, an additional 60 μL (~1 equiv.) of the stannane solution, and 100 μL (~0.1 equiv.) of the $PdCl_2(PhCN)_2$ solution were added. After an additional 2 h, the reaction was concentrated *in vacuo* and directly purified via preparative-TLC (1:1 hex/EtOAc, 500 μm plate, 4.5 in. x 4.5 in.) to furnish 0.9 mg (60% yield) of ester (–)-**133** as a pale yellow oil. For (–)-**133**: R_f 0.24 (1/2, hexanes/EtOAc); $[\alpha]_D^{20}$ –111.8 (*c* 0.70, EtOAc); IR (thin film, EtOAc) 3437 (br, m), 2955 (br, s), 2184 (m), 1722 (s), 1600 (m), 1439 (m), 1402 (w), 1289 (w), 1199 (br, s), 1109 (m), 1000 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.52 (dd, *J* = 15.9, 4.6 Hz, 1 H), 6.27 (dd, *J* = 11.3, 2.5 Hz, 1 H), 6.17 (ddd, *J* = 15.9, 2.3, 2.3 Hz, 1 H), 6.08 (d, *J* = 11.3 Hz, 1 H), 4.48 (m, 1 H), 4.41 (m, 1 H), 4.29 (d, *J* = 6.5 Hz, 1 H), 3.76 (s, 3 H), 3.70-3.62 (m, 2 H), 3.46 (m, 1 H), 2.04-1.98 (m, 2 H), 1.84 (dd, *J* = 11.7, 1.3 Hz, 1 H), 1.68 (m, 1 H), 0.93 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 165.16, 140.98, 127.47, 123.22, 111.82, 99.66, 87.24, 81.70, 79.83, 77.70, 76.21, 63.27, 51.47, 38.59, 36.16, 15.43; HRMS (ES+) m/z 315.0986 [$(M+Na)^+$; calcd for $C_{16}H_{20}O_5Na^+$: 315.1208].

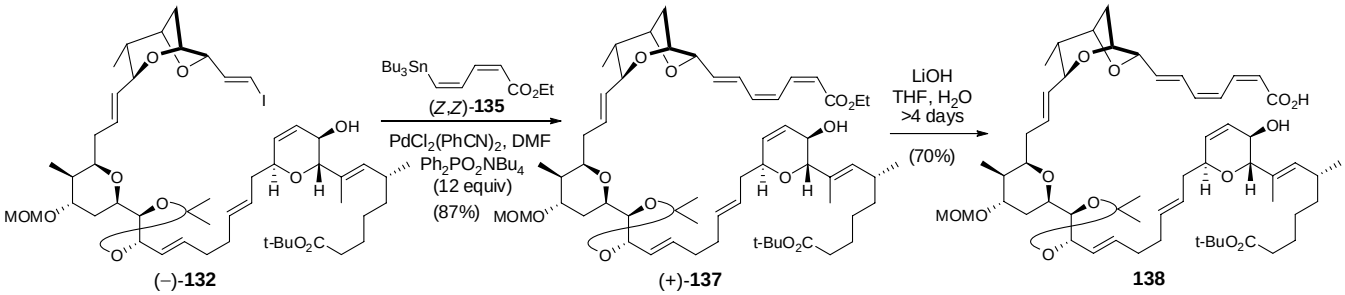


Trienoate 134: To 5% $Pd/CaCO_3$ poisoned with Pb (7.5 mg) under a hydrogen atmosphere was added a solution of ester (–)-**133** (5.0 mg, 17.1 μmol) and distilled quinoline (distilled over CaH_2 under high vacuum, 63.0 μL, 530 μmol) in distilled EtOAc (distilled over CaH_2 at 1 atm, 2 mL), followed by 2 x 500 μL EtOAc rinses. After 3 h, the suspension was filtered through Celite, rinsing with EtOAc, and concentrated *in vacuo* to afford an orange oil. Note: a significant amount of quinoline was also hydrogenated after 3 h, so the reaction is probably done much sooner. For **134**: R_f 0.24 (1/2, hexanes/EtOAc); diagnostic trienoate peaks in the ^1H NMR of the unpurified material (500 MHz, $CDCl_3$) δ 7.30 [dd, *J* = 11.5, 11.5 Hz, 1 H, C(40)], 7.09 [dd, *J* = 11.8, 11.8 Hz, 1 H, C(41)], 6.98 [m, 1 H, C(38)], 6.41 [dd, *J* = 11.1, 11.1 Hz, 1 H, C(39)], 6.16 [dd, *J* = 15.1, 5.3 Hz, 1 H, C(37)], 5.72 [d, *J* = 11.4 Hz, 1 H, C(42)]; HRMS (ES+) m/z 317.1379 [$(M+Na)^+$; calcd for $C_{16}H_{22}O_5Na^+$: 317.1364].



Trienoate (+)-136. A 15 mL round bottom flask was charged with dienoate **135** (9.7 mg, 23.3 μmol), vinyl iodide (–)-**70** (4.4 mg, 11.6 μmol), and $Ph_2PO_2NBu_4$ (32.0 mg, 69.9 μmol), and dissolved in degassed DMF (1.2 mL). $PdCl_2(PhCN)_2$ (0.22 mg, 0.58 μmol) was added and the reaction mixture was purged with argon for 5 min, and stirred at rt in the dark overnight. The reaction mixture was diluted with hexanes (4 mL), filtered through a Celite plug into brine (5 mL), and rinsed with Et_2O:hexanes (1:1, 20 mL). The mixture was extracted with Et_2O:hexanes (1:1, 3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give a crude residue, which was purified by flash chromatography (10% to 30% EtOAc:hexanes, silica gel was pretreated with 1% Et_3N) to afford trienoate (+)-**136** (4.2 mg, 96%) as a pale yellow oil. $[\alpha]_D^{28}$ +104.3 (*c* 0.14, $CHCl_3$); IR (neat, cm^{-1})

1712, 1612, 1448, 1219, 1183, 1038; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.21 (m, 6H), 7.13 (dt, *J* = 11.4, 0.8 Hz, 1H), 7.08-7.03 (m, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 6.46 (t, *J* = 11.0 Hz, 1H), 6.24 (dd, *J* = 15.1, 5.0 Hz, 1H), 6.10 (dd, *J* = 15.8, 7.5 Hz, 1H), 5.73 (d, *J* = 11.4 Hz, 1H), 4.57-4.55 (m, 1H), 4.47 (br d, *J* = 1.4 Hz, 1H), 4.35 (d, *J* = 6.4 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.12 (dd, *J* = 8.8, 8.0 Hz, 1H), 2.09 (ddd, *J* = 11.5, 6.4, 2.8 Hz, 1H), 1.99 (dd, *J* = 11.5, 1.4 Hz, 1H), 1.54-1.50 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 138.3, 136.7, 136.6, 133.4, 132.6, 129.0, 128.6 (2C), 127.8, 126.9, 126.7 (2C), 124.7, 118.3, 82.0, 79.7, 79.1, 76.6, 60.2, 41.7, 39.2, 15.2, 14.4; HRMS (ES) *m/z* $(M+Na)^+$ calcd 403.1885, obsd 403.1883.

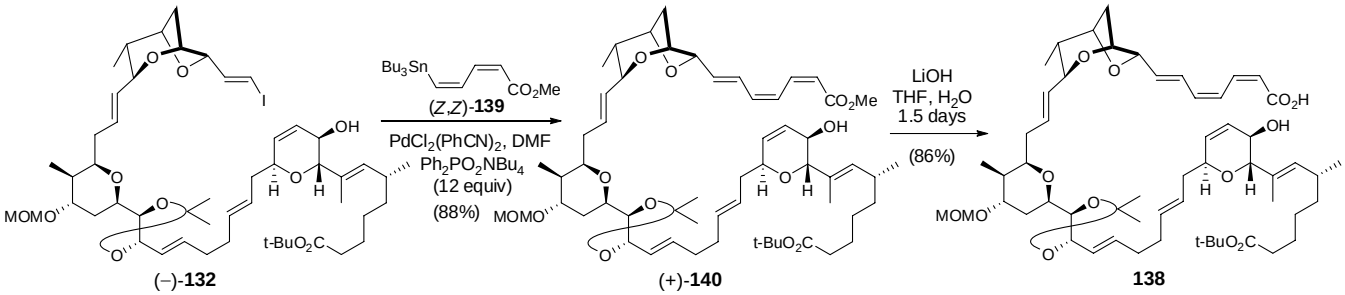


(–)-**132** (+)-**137** **138**

Trienoate (+)-137. A 15 mL round bottom flask was charged with stannane **135** (23.0 mg, 55.0 μmol), vinyl iodide (**–**)-**132** (4.6 mg, 4.6 μmol), $Ph_2PO_2NBu_4$ (25.0 mg, 55.0 μmol), and dissolved in degassed DMF (0.5 mL). To this was added $PdCl_2(PhCN)_2$ (0.1 mg, 0.30 μmol), and the reaction mixture was purged with argon for 5 min, and stirred at rt in the dark overnight. The reaction mixture was diluted with Et_2O/hexanes (1:1, 4 mL), filtered through a Celite plug into brine (5 mL), and rinsed with Et_2O/hexanes (1:1, 20 mL). The mixture was extracted using Et_2O/hexanes (1:1, 3×10 mL), and the combined organic layers were washed with brine, dried (Na_2SO_4) and concentrated *in vacuo* to give a crude residue, which was purified by flash chromatography (SiO_2, 0.2% to 1.5% MeOH/CH_2Cl_2, silica gel was pretreated with 0.5% Et_3N) to afford trienoate (+)-**137** (4.0 mg, 87%) as a yellow oil. $[\alpha]_D^{29}$ +6.8 (*c* 0.27, C_6H_6); IR (neat, cm^{-1}) 3447, 1714, 1611, 1448, 1368, 1217, 1180, 1066, 1037, 974; ^{1}H NMR (500 MHz, C_6D_6) δ 7.78 (dd, *J* = 11.6, 11.6 Hz, 1H), 7.05-6.99 (m, 1H), 6.89 (ddd, *J* = 11.6, 11.6, 0.8 Hz, 1H), 6.26 (dd, *J* = 11.6, 11.6 Hz, 1H), 6.09 (dd, *J* = 15.1, 4.9 Hz, 1H), 6.04 (ddd, *J* = 10.2, 2.2, 2.2 Hz, 1H), 5.91 (ddd, *J* = 15.6, 6.5, 6.5 Hz, 1H), 5.80 (dd, *J* = 15.6, 6.5 Hz, 1H), 5.75-5.66 (m, 3H), 5.54-5.38 (m, 3H), 5.28 (d, *J* = 9.7 Hz, 1H), 4.77 (dd, *J* = 5.4, 5.4 Hz, 1H), 4.52 (ABq, *J* = 6.5 Hz, Δν = 12.4 Hz, 2H), 4.24-4.20 (m, 3H), 4.11-3.96 (m, 10H), 3.66 (dd, *J* = 2.7, 2.7 Hz, 1H), 3.19 (s, 3H), 2.50-2.45 (m, 1H), 2.38-2.32 (m, 2H), 2.30-2.23 (m, 2H), 2.16-2.10 (m, 6H), 2.07-2.01 (m, 2H), 1.78 (d, *J* = 1.3 Hz, 3H), 1.75-1.64 (m, 2H), 1.58-1.54 (m, 2H), 1.52 (s, 3H), 1.49-1.43 (m, 1H), 1.39 (s, 9H), 1.33 (s,

3H), 1.26-1.10 (m, 6H), 0.98 (t, J = 7.2 Hz, 3H), 0.94 (d, J = 6.5 Hz, 3H), 0.93 (d, J = 6.5 Hz, 3H), 0.82 (d, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 172.9, 166.0, 138.4, 136.7, 135.9, 134.4, 132.6, 132.5, 132.3, 132.0, 130.5, 129.7, 129.0, 127.5, 127.0, 126.7, 124.9, 118.4, 108.3, 95.1, 81.9, 80.5, 80.1, 79.6, 79.4, 79.0, 78.5, 76.2, 75.8, 73.9, 72.9, 71.9, 64.3, 59.8, 55.1, 41.9, 39.2, 37.6, 37.4, 36.4, 35.7, 35.4, 32.8, 32.7, 32.1, 29.5, 28.1 (3C), 27.3, 25.6, 25.2, 21.2, 15.3, 14.2, 12.3, 10.8.

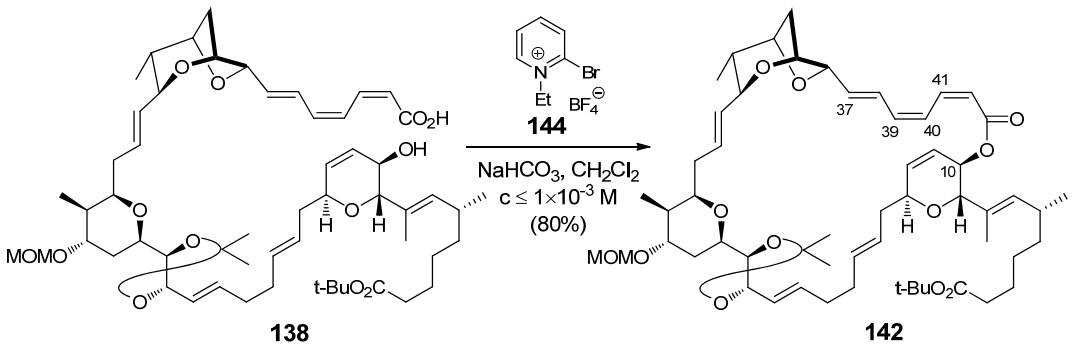
Seco Acid 138. A solution of trienoate (+)-**137** (3.0 mg, 3.0 μmol) in THF (0.6 mL) and H_2O (0.2 mL) was treated with 1 M LiOH solution (0.2 mL). The yellow reaction mixture was stirred for 4 days at rt in the dark. Brine (1 mL) was added and the pH value of the reaction mixture was adjusted to ca. 3 with 1 M $NaHSO_4$. The aqueous layer was extracted with EtOAc (4×2 mL), and the combined organic layers were washed with brine (2 mL), dried (Na_2SO_4) and concentrated *in vacuo* to give a crude residue, which was purified by flash chromatography (SiO_2, 0.5% to 5% MeOH/CH_2Cl_2) to afford seco acid **138** (2.0 mg, 70%) as a yellow oil. Seco acid **138** proved very unstable, and was carried on to the next step immediately after the ^{1}H NMR spectrum was taken. ^{1}H NMR (500 MHz, C_6D_6) δ 7.68 (dd, J = 11.6, 11.6 Hz, 1H), 7.05-7.00 (m, 1H), 6.89 (dd, J = 11.6, 11.6 Hz, 1H), 6.28 (dd, J = 11.6, 11.6 Hz, 1H), 6.07-6.02 (m, 2H), 5.93 (ddd, J = 15.2, 6.6, 6.6 Hz, 1H), 5.80 (dd, J = 15.2, 6.6 Hz, 1H), 5.72-5.62 (m, 3H), 5.56-5.42 (m, 3H), 5.37 (d, J = 9.4 Hz, 1H), 4.79 (dd, J = 5.6, 5.6 Hz, 1H), 4.52 (ABq, J = 6.9 Hz, Δν = 11.6 Hz, 2H), 4.28-4.21 (m, 3H), 4.14 (d, J = 7.5 Hz, 1H), 4.08-4.03 (m, 5H), 3.98-3.94 (m, 1H), 3.67 (d, J = 2.5 Hz, 1H), 3.19 (s, 3H), 2.55-2.50 (m, 1H), 2.42-2.30 (m, 3H), 2.16-2.09 (m, 6H), 2.06-1.98 (m, 2H), 1.80 (s, 3H), 1.76-1.64 (m, 3H), 1.53 (s, 3H), 1.50-1.43 (m, 1H), 1.38 (s, 9H), 1.33 (s, 3H), 1.27-1.12 (m, 7H), 0.94 (d, J = 6.7 Hz, 3H), 0.92 (d, J = 6.7 Hz, 3H), 0.83 (d, J = 6.9 Hz, 3H).



Trienoate (+)-140. A 15 mL round bottom flask was charged with stannane **139** (35.0 mg, 87.0 μmol), vinyl iodide (**–**)-**132** (7.2 mg, 7.2 μmol), $Ph_2PO_2NBu_4$ (40.0 mg, 87.0 μmol), and dissolved in degassed DMF (0.7 mL). To this was added $PdCl_2(PhCN)_2$ (0.14 mg, 0.36 μmol), and the reaction mixture was purged with argon for 5 min, and stirred at rt in the dark overnight. The reaction mixture was diluted with Et_2O/hexanes (1:1, 4 mL), filtered through a Celite plug into brine (5 mL), and rinsed with Et_2O/hexanes (1:1, 20 mL). The mixture was extracted using Et_2O/hexanes (1:1, 3×10 mL), and the

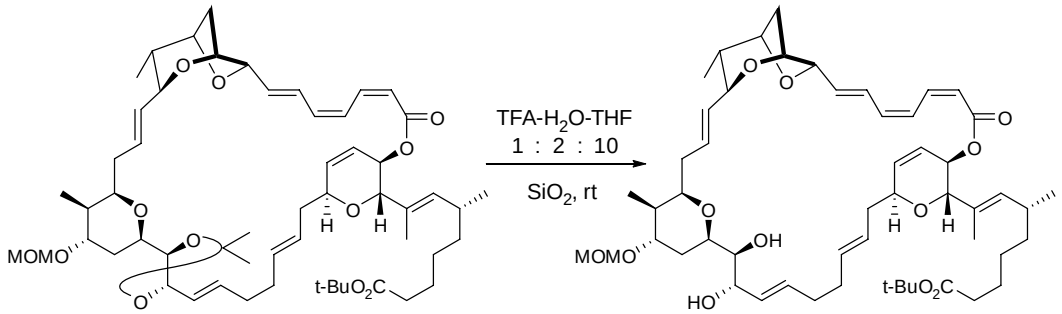
combined organic layers were washed with brine, dried (Na_2SO_4) and concentrated *in vacuo* to give a crude residue, which was purified by flash chromatography (SiO_2, 0.2% to 1.5% MeOH/CH_2Cl_2, silica gel was pretreated with 0.5% Et_3N) to afford trienoate (+)-**140** (6.2 mg, 88%) as a yellow oil. $[\alpha]_D^{29}$ +2.04 (*c* 0.24, C_6H_6); IR (neat, cm^{-1}) 3409, 1719, 1611, 1449, 1368, 1150, 1066; ^1H NMR (500 MHz, C_6D_6) δ 7.74 (dd, *J* = 11.2, 11.2 Hz, 1H), 7.05-6.99 (m, 1H), 6.88 (dd, *J* = 11.2, 11.2 Hz, 1H), 6.26 (dd, *J* = 11.2, 11.2 Hz, 1H), 6.09 (dd, *J* = 15.5, 4.6 Hz, 1H), 6.03 (d, *J* = 10.3 Hz, 1H), 5.91 (ddd, *J* = 15.5, 6.2, 6.2 Hz, 1H), 5.79 (dd, *J* = 15.5, 6.2 Hz, 1H), 5.75-5.69 (m, 2H), 5.64 (d, *J* = 11.8 Hz, 1H), 5.54-5.48 (m, 3H), 5.28 (d, *J* = 9.3 Hz, 1H), 4.77 (dd, *J* = 6.2, 6.2 Hz, 1H), 4.52 (ABq, *J* = 7.2 Hz, Δν = 13.4 Hz, 2H), 4.24-4.22 (m, 3H), 4.11-4.02 (m, 5H), 4.00-3.95 (m, 2H), 3.66 (d, *J* = 2.6 Hz, 1H), 3.39 (s, 3H), 3.19 (s, 3H), 2.50-2.45 (m, 1H), 2.38-2.32 (m, 2H), 2.30-2.25 (m, 1H), 2.16-2.10 (m, 7H), 2.07-2.02 (m, 2H), 1.78 (d, *J* = 1.0 Hz, 3H), 1.74-1.64 (m, 2H), 1.58-1.54 (m, 1H), 1.52 (s, 3H), 1.50-1.44 (m, 1H), 1.39 (s, 9H), 1.32 (s, 3H), 1.26-1.12 (m, 5H), 0.94 (d, *J* = 5.7 Hz, 6H), 0.82 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 173.0, 166.5, 138.7, 137.0, 136.0, 134.6, 132.7, 132.6, 132.4, 132.1, 130.6, 129.8, 129.1, 127.6, 127.1, 126.7, 124.9, 118.0, 108.4, 95.2, 82.0, 80.7, 80.2, 79.7, 79.5, 79.1, 78.6, 76.4, 75.9, 74.0, 73.0, 72.0, 64.4, 55.2, 50.8, 42.0, 39.3, 37.7, 37.5, 36.5, 35.8, 35.5, 35.1, 32.9, 32.8, 32.2, 30.7, 29.6, 28.2 (3C), 27.4, 25.7, 25.3, 21.3, 15.4, 12.4, 10.9.

Seco Acid 138. A solution of trienoate (+)-**140** (7.1 mg, 7.1 μmol) in THF (1.6 mL) and H_2O (0.4 mL) was treated with 1 M LiOH solution (0.4 mL). The yellow reaction mixture was stirred for 1.5 days at rt in the dark. Brine (1 mL) was added and the pH value of the reaction mixture was adjusted to ca. 3 with 1 M $NaHSO_4$. The aqueous layer was extracted with EtOAc (4×2 mL), and the combined organic layers were washed with brine (2 mL), dried (Na_2SO_4) and concentrated *in vacuo* to give a crude residue, which was purified by flash chromatography (SiO_2, 0.5% to 5% MeOH/CH_2Cl_2) to afford seco acid **138** (6.0 mg, 86%) as a yellow oil. Seco acid **138** proved very unstable, and was carried on to the next step immediately after the ^1H NMR spectrum was taken. Analytical data are identical to that prepared from (+)-**137**.



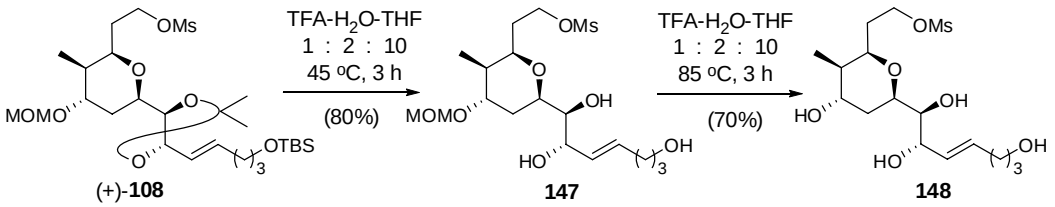
138 **142**

Macrolide 142. A slurry of seco acid **138** (2.0 mg, 2.0 μmol) and $NaHCO_3$ (85.0 mg, 1.00 mmol) in CH_2Cl_2 (2.1 mL) was treated with solid 2-bromo-1-ethylpyridinium tetrafluoroborate **144** (18.0 mg, 66 μmol) in one portion. The reaction mixture was vigorously stirred in the dark overnight, then transferred directly onto a silica gel column and purified by flash chromatography (0.2% to 1.6% MeOH/CH_2Cl_2) to afford macrolide **142** (1.6 mg, 80%) as a pale yellow foam. ^{1}H NMR (500 MHz, CD_3OD) δ 7.23-7.05 (m, 3H), 6.47 (dd, *J* = 11.2, 11.2 Hz, 1H), 6.24 (dd, *J* = 15.0, 4.6 Hz, 1H), 6.01-5.91 (m, 2H), 5.83-5.78 (m, 1H), 5.69 (d, *J* = 10.2 Hz, 1H), 5.58-5.52 (m, 3H), 5.43-5.35 (m, 3H), 5.11 (d, *J* = 9.3 Hz, 1H), 4.67 (ABq, *J* = 6.7 Hz, Δν = 10.5 Hz, 2H), 4.64-4.59 (m, 2H), 4.40 (br s, 1H), 4.31 (d, *J* = 6.4 Hz, 1H), 4.21-4.19 (m, 2H), 3.95-3.88 (m, 2H), 3.76-3.68 (m, 3H), 3.33 (s, 3H), 2.48-2.38 (m, 2H), 2.21-2.03 (m, 9H), 1.92 (d, *J* = 11.6 Hz, 1H), 1.75-1.60 (m, 5H), 1.69 (d, *J* = 1.0 Hz, 3H), 1.49-1.45 (m, 1H), 1.44 (s, 9H), 1.42 (s, 3H), 1.21-1.12 (m, 4H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 7.1 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H); HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{56}H_{82}O_{12}Na^+$ 969.5704, obsd 969.5681.



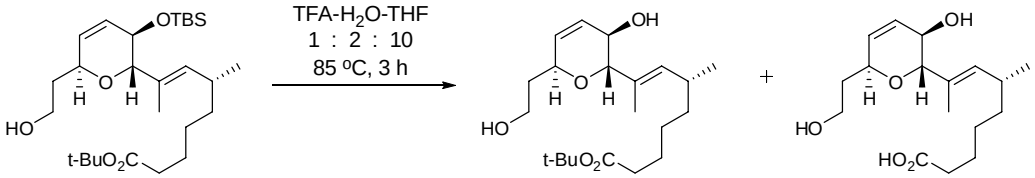
142 **146**

Diol 146. Macrolide **142** (1.0 mg, 1.0 μmol) was treated with TFA (6.0 μL) in THF (60 μL) and H_2O (12 μL). The reaction was monitored by TLC, and it was found the reaction rate leading to a new polar spot was accelerated by SiO_2 on TLC. After isolation of the new spot, ^{1}H NMR spectrum indicated the removal of acetonide protection, while the MOM and *t*-Butyl groups were still present, suggesting the structure of diol **146** (0.5 mg), further treatment with TFA-THF-H_2O at 85 ^oC led to complex mixtures.



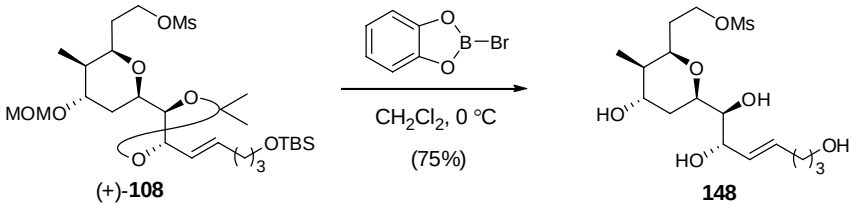
(+)-**108** **147** **148**

Mesylates 147 and 148. Acetonide (+)-**108** (2.3 mg, 4.0 μmol) was treated with TFA (25 μL) in THF (250 μL) and H_2O (50 μL) at 45 °C for 3 h. The reaction mixture was evaporated to dryness and purified by flash chromatography (1% to 5% MeOH/CH_2Cl_2) to afford mesylate **147** (1.3 mg, 80%) as a pale yellow oil, which was treated with the same condition under further heating (85 °C, 3 h) to give mesylate **148** (1.0 mg, 70%). For mesylate **147**: ^{1}H NMR (500 MHz, C_6D_6) δ 5.78-5.70 (m, 1H), 5.66 (dd, *J* = 15.5, 7 Hz, 1H), 4.68 (ABq, *J* = 7.0 Hz, Δν = 14.5 Hz, 2H), 4.60-4.50 (m, 1H), 4.19-3.80 (m, 5H), 3.59 (br s, 2H), 3.41 (t, *J* = 6.0 Hz, 2H), 3.18 (s, 3H), 2.21 (s, 3H), 2.20-1.95 (m, 4H), 1.60-1.10 (m, 7H), 0.65 (d, *J* = 7.5 Hz, 3H). For mesylate **148**: ^{1}H NMR (500 MHz, C_6D_6) δ 5.92-5.88 (m, 1H), 5.83-5.78 (m, 1H), 4.30-4.26 (m, 1H), 4.19-4.12 (m, 2H), 4.08-4.00 (m, 2H), 3.82-3.76 (m, 2H), 3.66-3.58 (m, 1H), 3.48 (br s, 1H), 2.26 (s, 3H), 1.78-1.24 (m, 9H), 1.12 (br s, 1H), 0.62 (d, *J* = 7.0 Hz, 3H).

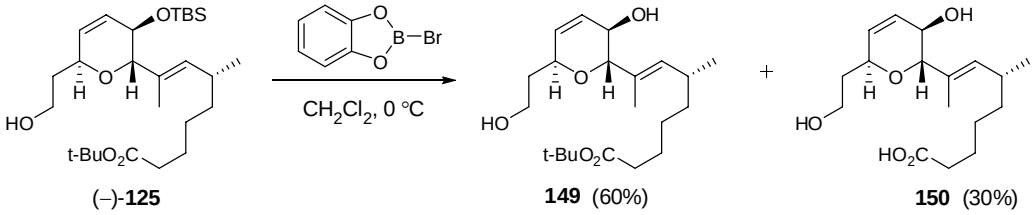


(–)-**125** **149** (40%) **150** (42%)

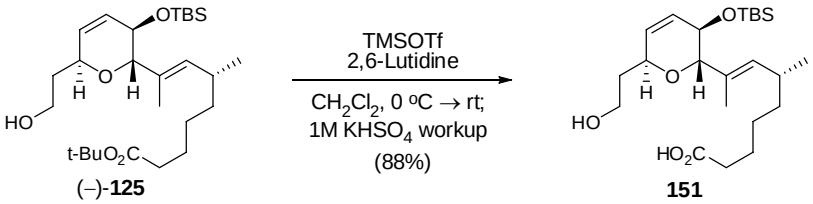
Diols 149 and 150. TBS ether (–)-**125** (3.0 mg, 6.2 μmol) was treated with TFA (35 μL) in THF (350 μL) and H_2O (70 μL) at 85 °C for 3 h. The reaction mixture was evaporated to dryness and purified by flash chromatography (1% to 5% MeOH/CH_2Cl_2) to afford diol **149** (1.0 mg, 40%) and diol **150** (1.0 mg, 42%). For diol **149**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91 (ddd, *J* = 10.3, 2.3, 2.3 Hz, 1H), 5.72 (ddd, *J* = 10.3, 2.3, 2.3 Hz, 1H), 5.23 (d, *J* = 9.6 Hz, 1H), 4.34-4.31 (m, 1H), 4.12-4.11 (m, 1H), 3.84-3.76 (m, 3H), 2.56 (br s, 1H), 2.45-2.39 (m, 1H), 2.21-2.13 (m, 3H), 1.98 (dddd, *J* = 14.6, 10.2, 7.9, 4.3 Hz, 1H), 1.67 (s, 3H), 1.56-1.48 (m, 2H), 1.43 (s, 9H), 1.36-1.16 (m, 4H), 0.94 (d, *J* = 6.6 Hz, 3H). For diol **150**: ^{1}H NMR (500 MHz, C_6D_6) δ 5.88 (dd, *J* = 10.5, 3.0 Hz, 1H), 5.45 (d, *J* = 10.0 Hz, 1H), 5.19 (d, *J* = 10.0 Hz, 1H), 4.19 (br s, 2H), 3.95 (d, *J* = 6.5 Hz, 1H), 3.68-3.64 (m, 1H), 3.58-3.55 (m, 1H), 2.34-2.32 (m, 1H), 2.13-2.08 (m, 2H), 1.86-1.76 (m, 1H), 1.73 (d, *J* = 1.0 Hz, 3H), 1.56-1.48 (m, 1H), 1.38-1.06 (m, 6H), 0.90 (d, *J* = 6.5 Hz, 3H).



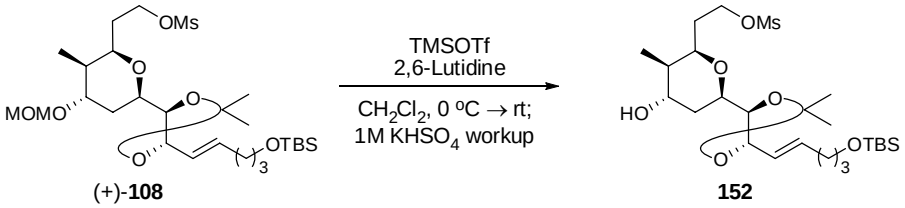
Mesylate 148. Acetonide (+)-**108** (2.4 mg, 4.0 μmol) in CH_2Cl_2 (1.0 mL) was treated with *B*-bromocatecholborane (124 μL, 25.0 μmol) at 0 °C for 2 h. The reaction mixture was quenched with sat. $NaHCO_3$, and neutralized with HCOOH. The aqueous layer was extracted with Et_2O (4×2 mL), and the combined organic layers were washed with brine (2 mL), dried (Na_2SO_4), filtered and evaporated to dryness and purified by flash chromatography (1% to 5% MeOH/CH_2Cl_2) to afford mesylate **148** (1.2 mg, 75%) as a pale yellow oil. Analytical data are same as for material prepared under TFA:H_2O:THF conditions.



Diols 149 and 150. Acetonide (–)-**125** (2.6 mg, 5.0 μmol) in CH_2Cl_2 (1.3 mL) was treated with *B*-bromocatecholborane (162 μL, 32.0 μmol) at 0 °C for 2 h. The reaction mixture was quenched with sat. $NaHCO_3$, and neutralized with HCOOH. The aqueous layer was extracted with Et_2O (4×2 mL), and the combined organic layers were washed with brine (2 mL), dried (Na_2SO_4), filtered and evaporated to dryness and purified by flash chromatography (1% to 7% MeOH/CH_2Cl_2) to afford diol **149** (1.2 mg, 60%) and diol **150** (0.5 mg, 30%). Analytical data are same as for material prepared under TFA:H_2O:THF conditions.

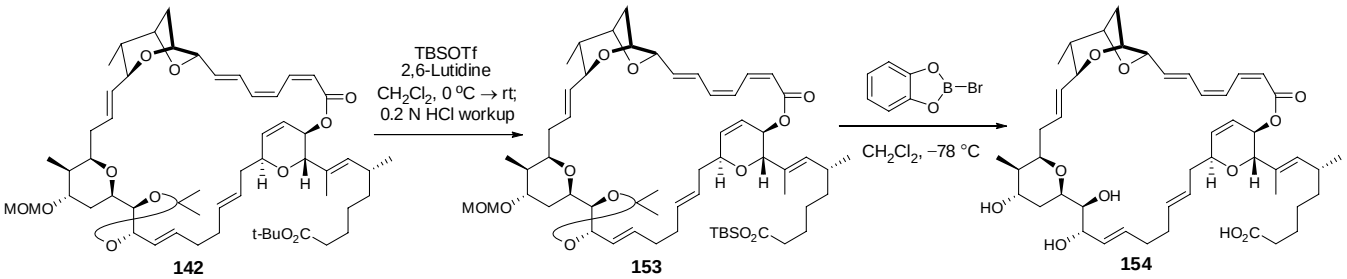


Acid 151. To a stirred solution of (–)-**125** (2.4 mg, 5.0 μmol) and 2,6-lutidine (6.7 μL, 57 μmol) in CH_2Cl_2 (500 μL) was added TMSOTf (6.7 μL, 37 μmol) at 0 °C. After 3 h at 0 °C, the reaction mixture was warmed to rt and stirred for 0.5 h before being quenched with 1M $KHSO_4$ (1 mL). The aqueous layer was extracted with Et_2O (4×2 mL), and the combined organic layers were washed with brine (2 mL), dried (Na_2SO_4), filtered and evaporated to give the crude product, which was purified by flash chromatography (1% to 5% MeOH/CH_2Cl_2) to afford acid **151** (1.8 mg, 88%). ^{1}H NMR (500 MHz, C_6D_6) δ 5.75 (d, *J* = 10.5 Hz, 1H), 5.41-5.38 (m, 2H), 4.25-4.23 (m, 2H), 3.91 (d, *J* = 7.0 Hz, 1H), 3.70-3.64 (m, 1H), 3.60-3.56 (m, 1H), 2.32-2.26 (m, 1H), 2.16 (t, *J* = 6.5 Hz, 2H), 1.82-1.74 (m, 1H), 1.77 (s, 3H), 1.58-1.46 (m, 2H), 1.30-1.12 (m, 6H), 0.97 (s, 9H), 0.9 (d, *J* = 6.5 Hz, 3H), 0.06 (s, 3H), 0.04 (s, 3H).



(+)-**108** **152**

Alcohol 152. To a stirred solution of (+)-**108** (2.2 mg, 3.8 μmol) and 2,6-lutidine (5.1 μL, 44 μmol) in CH_2Cl_2 (400 μL) was added TMSOTf (5.1 μL, 28 μmol) at 0 °C. After 3 h at 0 °C, the reaction mixture was warmed to rt and stirred for 0.5 h before being quenched with 1M $KHSO_4$ (1 mL). The aqueous layer was extracted with Et_2O (4×2 mL), and the combined organic layers were washed with brine (2 mL), dried (Na_2SO_4), filtered and evaporated to give the crude product, ^{1}H NMR of which showed removal of MOM protection, suggesting alcohol **152**.

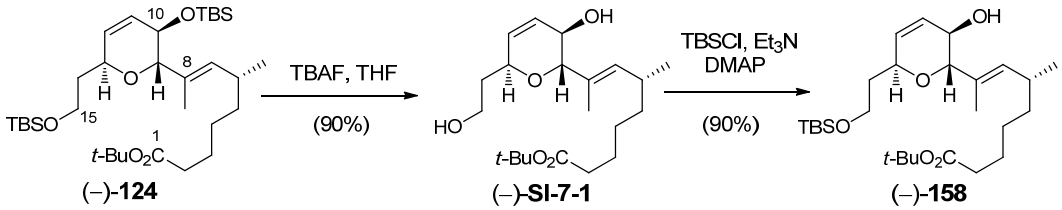


142 **153** **154**

Macrolide 154. To a stirred solution of macrolide **142** (1.0 mg, 1.0 μmol) and 2,6-lutidine (3.7 μL, 32 μmol) in CH_2Cl_2 (100 μL) was added TBSOTf (2.4 μL, 11 μmol) at 0 °C. After 30 min at 0 °C, the reaction mixture was warmed to rt and stirred for 3 h before being quenched with 0.2 N HCl (1 mL). The aqueous layer was extracted with Et_2O (4×2 mL), and the combined organic layers were washed

with brine (2 mL), dried (Na_2SO_4) and evaporated to give the crude TBS ester **153**. The ^{1}H NMR spectrum indicated conversion of the *t*-Butyl to the TBS ester.

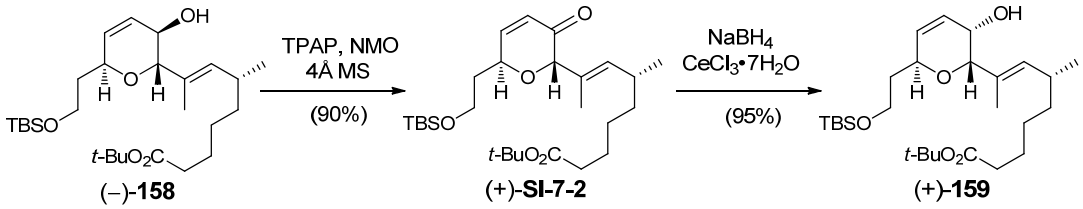
TBS ester **153** in CH_2Cl_2 (0.1 mL) was treated with *B*-bromocatecholborane (20 μL, 4.0 μmol) at –78 °C for 2 h. The reaction mixture was quenched with sat. $NaHCO_3$, and neutralized with HCOOH. The aqueous layer was extracted with Et_2O (4×2 mL), and the combined organic layers were washed with brine (2 mL), dried (Na_2SO_4), filtered and evaporated to dryness to give crude **154**. TLC comparison showed macrolide **154** was slightly more polar than natural sorangicin A (5% MeOH/CH_2Cl_2), while high resolution mass spectroscopy confirmed the molecular formular, and ^{1}H NMR spectrum indicated trienoate configuration was not affected by TBSOTf or *B*-bromocatecholborane conditions. HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{47}H_{66}O_{11}Na^+$ 829.4503, obsd 829.4503.



Diol (–)-**SI-7-1.** To a solution of (–)-**124** (72.0 mg, 0.120 mmol) in THF (3.4 mL) was added tetrabutylammonium fluoride (TBAF, 1 M in THF, 0.36 mL, 0.36 mmol). After being stirred overnight, the reaction mixture was diluted with water (5 mL) and EtOAc (5 mL). The aqueous phase was then washed with EtOAc (3x5 mL), and the combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash chromatography (20% to 70%, EtOAc/hexanes) afforded diol (–)-**SI-7-1** (40.0 mg, 90%) as a pale yellow oil: $[\alpha]_D^{29}$ –39.4 (*c* 1.06, $CHCl_3$); IR (neat, cm^{-1}) 3426 (br), 1728, 1454, 1391, 1367, 1156, 1061; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91 (ddd, *J* = 10.3, 2.3, 2.3 Hz, 1H), 5.72 (ddd, *J* = 10.3, 2.3, 2.3 Hz, 1H), 5.23 (d, *J* = 9.6 Hz, 1H), 4.34-4.31 (m, 1H), 4.12-4.11 (m, 1H), 3.84-3.76 (m, 3H), 2.56 (br s, 1H), 2.45-2.39 (m, 1H), 2.21-2.13 (m, 3H), 1.98 (dddd, *J* = 14.6, 10.2, 7.9, 4.3 Hz, 1H), 1.67 (s, 3H), 1.56-1.48 (m, 2H), 1.43 (s, 9H), 1.36-1.16 (m, 4H), 0.94 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6, 137.6, 130.8, 130.2, 128.5, 80.3, 79.9, 72.6, 63.6, 61.8, 37.1, 35.6, 34.9, 32.2, 28.3 (3C), 27.2, 25.0, 21.0, 12.4; HRMS (ES) m/z $(M+Na)^+$ calcd for $C_{21}H_{36}O_5Na^+$ 391.2460, obsd 391.2460.

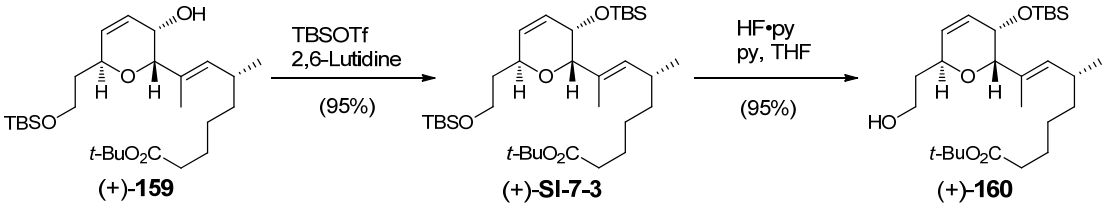
Allylic alcohol (–)-**158.** To a solution of diol (–)-**SI-7-1** (40.0 mg, 0.109 mmol) in CH_2Cl_2 (1.2 mL) was added DMAP (1.8 mg, 0.015 mmol) and Et_3N (25 μL, 0.18 mmol) followed by the addition of TBSCl

(26.5 mg, 0.180 mmol) in CH_2Cl_2 (1.2 mL). After 22 h the reaction mixture was quenched with saturated NH_4Cl solution (6 mL), and extracted with Et_2O (3×10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was purified by flash chromatography (2% to 30% EtOAc/hexanes) to afford allylic alcohol (–)-**158** (47.0 mg, 90%) as a pale yellow oil, along with (–)-**SI-7-1** (4.0 mg, 6%). $[\alpha]_D^{23}$ –38.8 (*c* 0.74, $CHCl_3$); IR (neat, cm^{-1}) 3440 (br), 1730, 1461, 1367, 1253, 1099, 837; ^1H NMR (500 MHz, $CDCl_3$) δ 5.87 (ddd, *J* = 10.3, 2.1, 2.1 Hz, 1H), 5.77 (ddd, *J* = 10.3, 2.1, 2.1 Hz, 1H), 5.19 (d, *J* = 9.5 Hz, 1H), 4.30-4.27 (m, 1H), 4.09 (br s, 1H), 3.78-3.70 (m, 2H), 3.69 (d, *J* = 7.1 Hz, 1H), 2.46-2.40 (m, 1H), 2.18 (dt, *J* = 7.4, 2.5 Hz, 2H), 2.01 (br d, *J* = 4.3 Hz, 1H), 1.89-1.82 (m, 1H), 1.75-1.68 (m, 1H), 1.67 (d, *J* = 1.0 Hz, 3H), 1.57-1.50 (m, 2H), 1.43 (s, 9H), 1.36-1.18 (m, 4H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 136.5, 131.6, 131.0, 128.0, 80.2, 79.6, 69.4, 64.0, 60.2, 37.2, 36.3, 35.6, 32.1, 28.3 (3C), 27.2, 26.1 (3C), 25.1, 21.0, 18.5, 12.3, -5.2 (2C); HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{27}H_{50}O_5SiNa^+$ 505.3325, obsd 505.3307.



Enone (–)-SI-7-2. A stirred solution of allylic alcohol (–)-**158** (52.0 mg, 0.108 mmol) and *N*-methylmorpholine *N*-oxide monohydrate (19.0 mg, 0.160 mmol) in CH_2Cl_2 (2.0 mL) was treated with 4 Å molecular sieves (54 mg). After 5 min, TPAP (3.8 mg, 0.011 mmol) was added, and the reaction mixture was stirred for a further 1 h before being passed through a pad of silica gel which was rinsed with ethyl acetate (20 mL). The solvent was evaporated under reduced pressure to yield enone (–)-**SI-7-2** (47.0 mg, 90%) as a yellow oil. $[\alpha]_D^{29}$ –43.9 (*c* 0.54, C_6H_6); IR (neat, cm^{-1}) 1730, 1693, 1462, 1254, 1155, 1093, 838; ^1H NMR (500 MHz, $CDCl_3$) δ 6.93 (dd, *J* = 10.3, 2.0 Hz, 1H), 6.04 (dd, *J* = 10.3, 2.4 Hz, 1H), 4.93 (d, *J* = 9.4 Hz, 1H), 4.44 (s, 1H), 4.39 (ddd, *J* = 6.5, 2.0, 2.0 Hz, 1H), 3.81-3.72 (m, 2H), 2.41-2.34 (m, 1H), 2.14 (t, *J* = 7.5 Hz, 2H), 1.86 (dd, *J* = 12.1, 6.2 Hz, 2H), 1.70 (d, *J* = 0.7 Hz, 3H), 1.54-1.48 (m, 2H), 1.42 (s, 9H), 1.29-1.11 (m, 4H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.1, 173.2, 151.9, 136.4, 128.1, 126.3, 82.6, 80.1, 66.3, 58.9, 37.04, 37.00, 35.6, 32.6, 28.2 (3C), 27.2, 26.0 (3C), 25.3, 20.5, 18.4, 14.4, -5.3 (2C)**;** HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{27}H_{48}O_5SiNa^+$ 503.3169, obsd 503.3175.

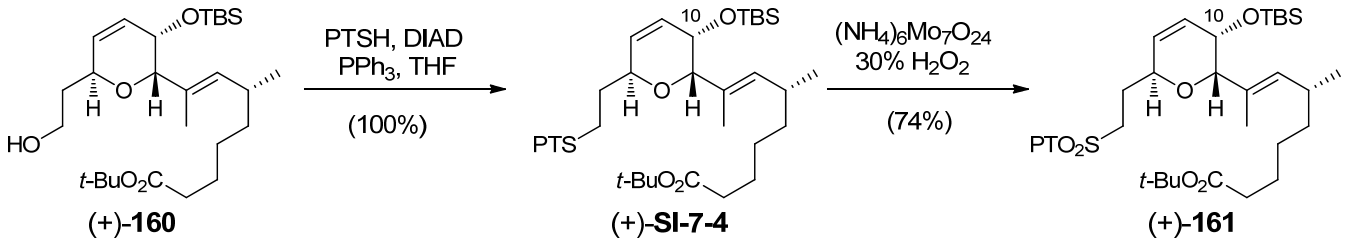
Allylic Alcohol (+)-**159.** To a solution of enone (–)-**SI-7-2** (36.0 mg, 0.075 mmol) in MeOH (3.0 mL) was added $CeCl_3 \bullet 7H_2O$ (279 mg, 0.750 mmol) at rt. After 5 min, $NaBH_4$ (5.7 mg, 0.15 mmol) was added at 0 °C. After 15 min, the reaction mixture was quenched with saturated NH_4Cl solution (15 mL), and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated to leave a crude residue, which was purified by flash chromatography (5% to 30% EtOAc/hexanes) to afford allylic alcohol (+)-**159** (34.2 mg, 95%) as a pale yellow oil. $[\alpha]_D^{30}$ +85.2 (*c* 0.54, $CHCl_3$); IR (neat, cm^{-1}) 3448, 1731, 1461, 1254, 1155, 1095, 837; ^1H NMR (500 MHz, $CDCl_3$) δ 6.05 (ddd, *J* = 10.1, 5.6, 2.0 Hz, 1H), 5.91 (dd, *J* = 10.1, 3.2 Hz, 1H), 5.43 (d, *J* = 9.6 Hz, 1H), 4.53-4.50 (m, 1H), 4.01 (s, 1H), 3.87 (t, *J* = 5.4 Hz, 1H), 3.78-3.73 (m, 1H), 3.71-3.67 (m, 1H), 2.48-2.41 (m, 1H), 2.19 (dt, *J* = 7.5, 1.5 Hz, 2H), 1.87-1.80 (m, 1H), 1.72 (d, *J* = 7.4 Hz, 1H), 1.65 (d, *J* = 0.5 Hz, 3H), 1.68-1.53 (m, 3H), 1.44 (s, 9H), 1.36-1.25 (m, 4H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 133.7, 132.8, 129.9, 126.3, 80.0, 73.7, 70.3, 62.5, 59.8, 37.4, 35.8, 34.4, 31.9, 28.3 (3C), 27.2, 26.1 (3C), 25.4, 21.4, 18.5, 14.2, -5.2 (2C); HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{27}H_{50}O_5SiNa^+$ 505.3325, obsd 505.3327.



Bis-TBS Ether (+)-SI-7-3. A stirred solution of (+)-**159** (45.0 mg, 0.0930 mmol) in anhydrous CH_2Cl_2 (2.2 mL) was cooled to –78 ºC and treated with 2,6-lutidine (43.0 μL, 0.373 mmol) and TBS triflate (43.0 μL, 0.187 mmol). After 1 h, the reaction mixture was quenched with saturated NH_4Cl solution (10 mL) and extracted with Et_2O (3x10 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield the crude product, which was purified by flash chromatography (2-10% EtOAc/hexanes) to yield (+)-**SI-7-3** (53.0 mg, 95%) as a pale yellow oil. $[\alpha]_D^{29}$ +59.0 (*c* 0.60, $CHCl_3$); IR (neat, cm^{-1}) 1733, 1463, 1365, 1253, 1100, 836; ^1H NMR (500 MHz, $CDCl_3$) δ 5.85 (ddd, *J* = 10.2, 4.6, 2.0 Hz, 1H), 5.78 (dd, *J* = 10.2, 1.7 Hz, 1H), 5.34 (d, *J* = 9.4 Hz, 1H), 4.38-4.36 (m, 1H), 4.09 (t, *J* = 3.7 Hz, 1H), 3.96 (s, 1H), 3.76-3.66 (m, 2H), 2.41-2.35 (m, 1H), 2.18 (t, *J* = 7.6 Hz, 2H), 1.83-1.76 (m, 1H), 1.65 (d, *J* = 0.8 Hz, 3H), 1.66-1.52 (m, 3H), 1.44 (s, 9H), 1.31-1.22 (m, 4H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.88 (s, 9H), 0.86 (s, 9H), 0.05 (s, 6H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 132.9, 132.4, 130.3, 127.2, 80.0, 76.1, 69.3, 65.4,

60.1, 37.4, 35.8, 35.4, 32.0, 28.3 (3C), 27.2, 26.11 (3C), 26.08 (3C), 25.5, 21.0, 18.5, 18.4, 14.3, -3.9, -4.3, -5.19, -5.24; HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{33}H_{64}O_5Si_2Na^+$ 619.4190, obsd 619.4211.

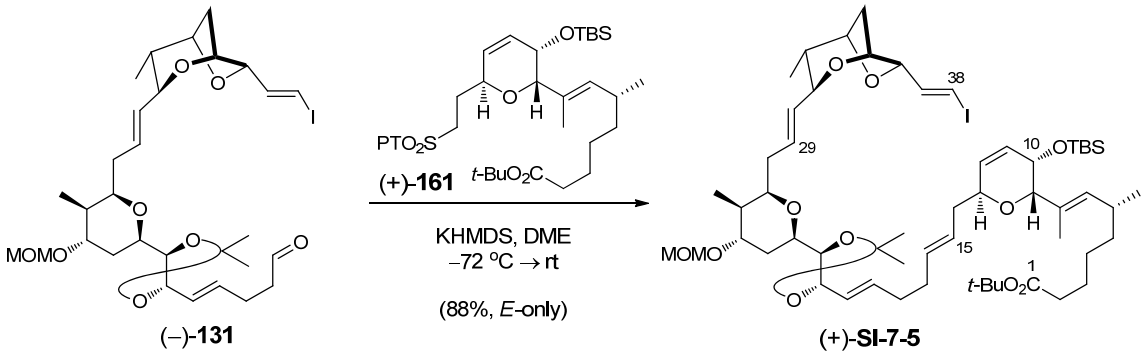
Alcohol (+)-160. To a solution of bis-TBS ether (+)-**SI-7-3** (53.0 mg, 0.0890 mmol) and THF (3.6 mL) in a nalgene container was added a stock solution of HF•pyridine (0.54 mL). The stock solution was prepared by adding pyridine (3.1 mL) portion wise to a solution of HF•pyridine (1.3 g) and THF (10 mL) in a nalgene container. After 18 h, additional HF•pyridine stock solution (0.2 mL) was added. After being stirred for an additional 8 h, the reaction was carefully diluted with saturated $NaHCO_3$ solution (10 mL) and diethyl ether (25 mL). The aqueous layer was then washed with diethyl ether (3x5 mL), and the combined organic layers were washed with saturated NH_4Cl solution (10 mL), saturated $NaHCO_3$ solution (10 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash chromatography (5% to 30% EtOAc/hexanes) afforded alcohol (+)-**160** (41.0 mg, 95%) as a pale yellow oil. $[\alpha]_D^{29}$ +84.6 (*c* 0.36, $CHCl_3$); IR (neat, cm^{-1}) 3450, 1730, 1460, 1366, 1252, 1114, 838; ^1H NMR (500 MHz, $CDCl_3$) δ 5.90 (ddd, *J* = 10.2, 4.8, 2.2 Hz, 1H), 5.73 (dd, *J* = 10.2, 2.4 Hz, 1H), 5.36 (d, *J* = 9.5 Hz, 1H), 4.46 (dd, *J* = 10.6, 2.5 Hz, 1H), 4.14-4.12 (m, 1H), 4.05 (s, 1H), 3.86-3.81 (m, 1H), 3.78-3.73 (m, 1H), 2.85 (dd, *J* = 8.3, 1.9 Hz, 1H), 2.41-2.36 (m, 1H), 2.18 (t, *J* = 7.6 Hz, 2H), 1.99-1.91 (m, 1H), 1.65 (d, *J* = 0.9 Hz, 3H), 1.61-1.51 (m, 3H), 1.43 (s, 9H), 1.32-1.21 (m, 4H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.85 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 133.3, 131.2, 129.6, 127.7, 80.0, 75.9, 73.5, 64.6, 62.1, 37.4, 35.8, 33.6, 32.0, 28.3 (3C), 27.1, 26.0 (3C), 25.4, 21.0, 18.3, 14.4, -3.9, -4.4; HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{27}H_{50}O_5SiNa^+$ 505.3325, obsd 505.3310.



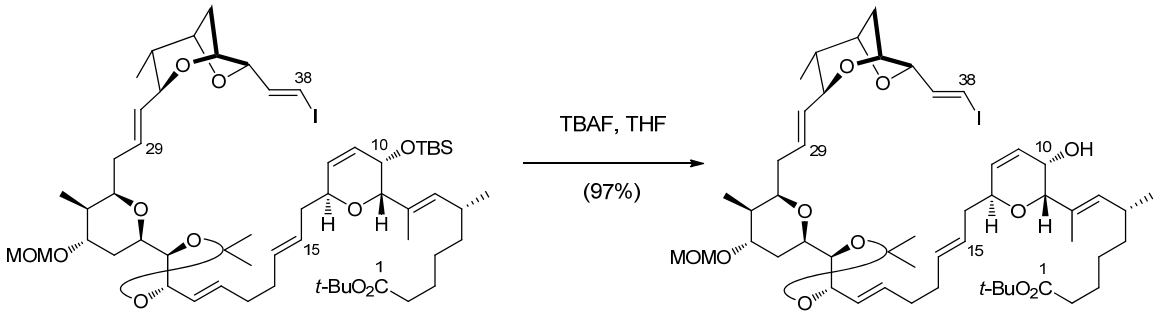
PTS Ether (+)-SI-7-4. To a solution of alcohol (+)-**160** (20.0 mg, 0.0410 mmol), triphenylphosphine (22.0 mg, 0.083 mmol) and 1-phenyl-1*H*-tetrazole-5-thiol (30.0 mg, 0.166 mmol) in THF (0.83 mL) was added diisopropylazodicarboxylate (DIAD, 33.0 μL, 0.166 mmol). After being stirred overnight, the reaction mixture was concentrated *in vacuo* and purified by flash chromatography (2% to 15% EtOAc/hexanes) to furnish (+)-**SI-7-4** (26.6 mg, 100%) as a pale yellow oil. $[\alpha]_D^{28}$ +62.2 (*c* 0.86, $CHCl_3$); IR (neat, cm^{-1}) 1728, 1597, 1499, 1388, 1366, 1250, 1154, 1110, 838; ^1H NMR (500 MHz, $CDCl_3$) δ

7.58-7.51 (m, 5H), 5.89 (ddd, *J* = 10.2, 4.6, 2.2 Hz, 1H), 5.73 (dd, *J* = 10.2, 2.8 Hz, 1H), 5.35 (d, *J* = 9.4 Hz, 1H), 4.38-4.36 (m, 1H), 4.12 (t, *J* = 3.6 Hz, 1H), 4.01 (s, 1H), 3.53 (ddd, *J* = 13.4, 7.8, 4.9 Hz, 1H), 3.40 (ddd, *J* = 13.4, 7.7, 7.7 Hz, 1H), 2.40-2.34 (m, 1H), 2.15 (t, *J* = 7.6 Hz, 2H), 2.12-2.01 (m, 2H), 1.66 (s, 3H), 1.55-1.50 (m, 2H), 1.42 (s, 9H), 1.31-1.20 (m, 4H), 0.91 (d, *J* = 6.7 Hz, 3H), 0.85 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 154.5, 133.9, 133.4, 130.6, 130.2, 129.9 (2C), 129.7, 128.4, 124.0 (2C), 80.0, 76.3, 70.7, 65.3, 37.3, 35.7, 32.0, 31.8, 30.0, 28.3 (3C), 27.1, 26.0 (3C), 25.4, 20.9, 18.3, 14.4, -4.0, -4.4; HRMS (ES) *m/z* $(M+H)^+$ calcd for $C_{34}H_{55}N_4O_4SiS^+$ 643.3713, obsd 643.3740.

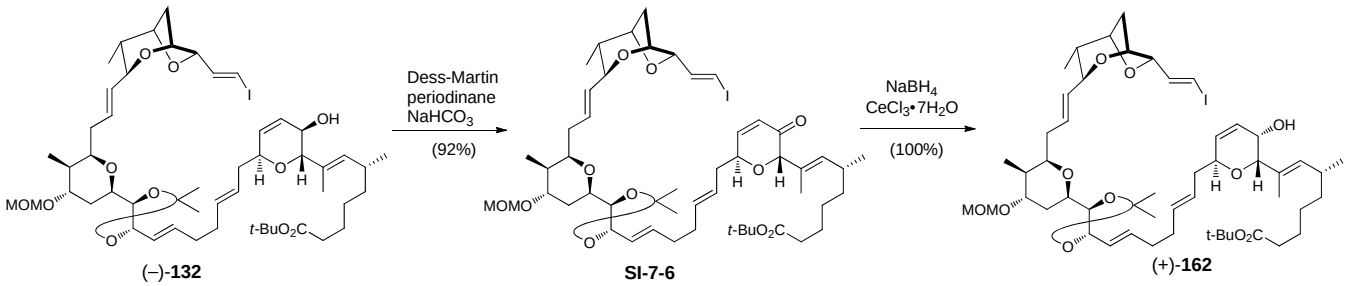
Sulfone (+)-161. To a 0 ^{o}C solution of PTS-ether (+)-**SI-7-4** (26.0 mg, 0.040 mmol) in absolute EtOH (4.0 mL) was added a pre-mixed solution of $(NH_4)_6Mo_7O_{24}•4H_2O$ (12.5 mg, 0.010 mmol) in H_2O_2 (30% aq., 0.060 mL, 0.60 mmol) via a glass pipette. The resulting yellow solution was then removed from the ice bath and allowed to warm to room temperature. After 18 h, the reaction mixture was diluted with diethyl ether (10 mL), saturated $NaHCO_3$ solution (5 mL) and water (10 mL). The aqueous layer was then extracted with diethyl ether (3x5 mL), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash chromatography (2% to 15% EtOAc/hexanes) furnished sulfone (+)-**161** (20.0 mg, 74%) as a pale yellow oil. $[\alpha]_D^{28}$ +78.5 (*c* 1.2, $CHCl_3$); IR (neat, cm^{-1}) 1728, 1460, 1342, 1154, 1111, 838; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.68 (m, 2H), 7.62-7.59 (m, 3H), 5.94 (ddd, *J* = 10.2, 4.3, 2.1 Hz, 1H), 5.70 (dd, *J* = 10.2, 1.8 Hz, 1H), 5.39 (d, *J* = 9.5 Hz, 1H), 4.32-4.30 (m, 1H), 4.17(t, *J* = 3.8 Hz, 1H), 4.04 (d, *J* = 2.9 Hz, 1H), 3.91 (ddd, *J* = 15.1, 11.1, 4.5 Hz, 1H), 3.79 (ddd, *J* = 15.1, 11.0, 5.1 Hz, 1H), 2.42-2.36 (m, 1H), 2.28-2.20 (m, 1H), 2.17-2.08 (m, 3H), 1.68 (d, *J* = 0.8 Hz, 3H), 1.56-1.50 (m, 2H), 1.43 (s, 9H), 1.32-1.22 (m, 4H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.86 (s, 9H), 0.06 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 153.5, 134.3, 133.2, 131.6, 130.0 (2C), 129.8, 129.2, 129.0, 125.2 (2C), 80.0, 76.7, 69.7, 65.2, 53.4, 37.3, 35.7, 32.1, 28.3 (3C), 27.2, 26.0 (3C), 25.7, 25.4, 20.9, 18.3, 14.4, -4.1, -4.4; HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{34}H_{54}N_4O_6SiSNa^+$ 697.3431, obsd 697.3405.



TBS Ether (+)-SI-7-5. At –72 °C, KHMDS (0.5 M in PhMe, 30.0 μL, 15.0 μmol) was added via syringe to a solution of (+)-**161** (10.2 mg, 15.0 μmol) in DME (0.16 mL). After 10 min, the bright yellow mixture was treated via cannula with a solution of (–)-**131** (5.0 mg, 7.6 μmol) in DME (0.16 mL) and the mixture was allowed to warm to rt over 2 h. The reaction mixture was quenched with saturated NH_4Cl solution (5 mL). The aqueous phase was extracted with Et_2O (3x5 mL) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The crude mixture was purified by flash chromatography (SiO_2, 5% to 30% EtOAc/hexanes, silica gel was pretreated with 0.5% Et_3N) to afford TBS ether (+)-**SI-7-5** (7.4 mg, 88%) as a pale yellow oil, along with recovered sulfone (+)-**161** (5.2 mg, 51%). $[\alpha]_D^{29}$ +26.0 (*c* 0.54, C_6H_6); IR (neat, cm^{-1}) 1730, 1457, 1367, 1251, 1099, 1066, 1038, 837, 775; ^1H NMR (500 MHz, C_6D_6) δ 6.84 (dd, *J* = 14.6, 4.8 Hz, 1H), 6.46 (dd, *J* = 14.6, 1.8 Hz, 1H), 5.96 (ddd, *J* = 15.2, 6.8, 6.8 Hz, 1H), 5.88 (ddd, *J* = 10.2, 4.7, 2.1 Hz, 1H), 5.83 (dd, *J* = 15.2, 6.4 Hz, 1H), 5.76 (dd, *J* = 10.2, 2.5 Hz, 1H), 5.71 (ddd, *J* = 15.2, 7.8, 7.8 Hz, 1H), 5.57-5.53 (m, 3H), 5.46 (dd, *J* = 15.2, 7.1 Hz, 1H), 4.79 (dd, *J* = 5.5, 5.5 Hz, 1H), 4.54 (ABq, *J* = 6.9 Hz, Δν = 10.1 Hz, 2H), 4.29-4.26 (m, 1H), 4.12 (s, 1H), 4.08-4.06 (m, 3H), 4.04-3.96 (m, 2H), 3.93 (d, *J* = 6.0 Hz, 1H), 3.91 (s, 1H), 3.87-3.85 (m, 1H), 3.69-3.67 (m, 1H), 3.21 (s, 3H), 2.45-2.40 (m, 2H), 2.37-2.31 (m, 1H), 2.27-2.18 (m, 7H), 2.06-2.00 (m, 2H), 1.84 (s, 3H), 1.74-1.62 (m, 4H), 1.54 (s, 3H), 1.48-1.40 (m, 2H), 1.42 (s, 9H), 1.34 (s, 3H), 1.31-1.27 (m, 4H), 1.12-1.06 (m, 1H), 1.04 (d, *J* = 6.6 Hz, 3H), 1.00 (s, 9H), 0.83 (d, *J* = 7.1 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H), 0.12 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 172.6, 142.1, 133.2, 132.65, 132.54, 132.47, 132.1, 131.3, 129.5, 127.64, 127.62, 127.0, 108.4, 95.2, 83.6, 80.7, 79.5, 79.4, 79.14, 79.05, 78.6, 76.8, 75.8, 75.5, 74.0, 72.8, 72.0, 66.1, 55.3, 41.8, 38.8, 37.8, 37.0, 36.5, 35.9, 35.8, 33.0, 32.9, 32.3, 29.7, 28.2 (4C), 27.5, 26.2 (3C), 25.8, 25.7, 21.3, 18.5, 15.3, 14.6, 10.9, -3.6, -4.1; HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{57}H_{93}IO_{11}SiNa^+$ 1131.5429, obsd 1131.5415.

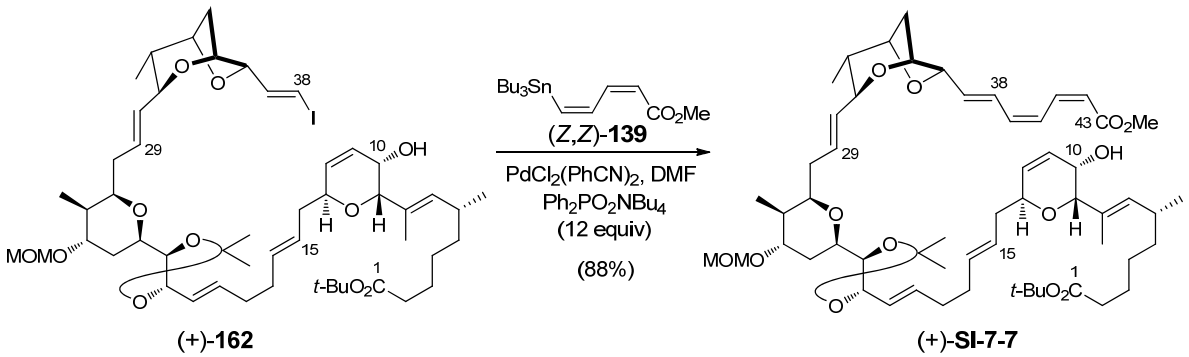


Vinyl Iodide (+)-162. Solid TBAF•3H_2O (33 mg, 0.126 mmol) was added to a solution of (+)-**SI-7-5** (7.0 mg, 6.3 μmol) in THF (0.15 mL) at rt. The reaction mixture was stirred in the dark for 20 h, and then diluted with Et_2O (2 mL) and saturated NH_4Cl solution (2 mL). The aqueous phase was extracted with Et_2O (4×2 mL). The combined organic extracts were dried (Na_2SO_4), filtered through a short plug of SiO_2, washed with additional Et_2O (25 mL), and concentrated *in vacuo*. The resulting crude product was purified by flash chromatography (SiO_2, 0.5% to 1.5% MeOH/CH_2Cl_2, silica gel was pretreated with 0.5% Et_3N) to afford vinyl iodide (+)-**162** (6.1 mg, 97%) as a pale yellow oil. $[\alpha]_D^{29}$ +26.9 (*c* 0.32, C_6H_6); IR (neat, cm^{-1}) 3436, 1729, 1456, 1367, 1217, 1149, 1066, 1038, 970; ^1H NMR (500 MHz, C_6D_6) δ 6.85 (dd, *J* = 14.6, 4.9 Hz, 1H), 6.46 (dd, *J* = 14.6, 1.8 Hz, 1H), 6.00 (ddd, *J* = 10.2, 5.6, 1.9 Hz, 1H), 5.96 (ddd, *J* = 15.2, 6.6, 6.6 Hz, 1H), 5.84 (dd, *J* = 15.2, 6.4 Hz, 1H), 5.75 (dd, *J* = 10.2, 3.3 Hz, 1H), 5.71 (ddd, *J* = 15.2, 8.5, 6.7 Hz, 1H), 5.60 (ddd, *J* = 9.7, 1.3, 1.3 Hz, 1H), 5.57-5.47 (m, 2H), 5.46 (dd, *J* = 15.2, 7.1 Hz, 1H), 4.80 (dd, *J* = 5.8, 5.8 Hz, 1H), 4.54 (ABq, *J* = 6.8 Hz, Δν = 9.7 Hz, 2H), 4.31-4.27 (m, 1H), 4.08-3.97 (m, 5H), 3.93 (d, *J* = 6.0 Hz, 1H), 3.91-3.90 (m, 1H), 3.86-3.84 (m, 1H), 3.78-3.77 (m, 1H), 3.69-3.67 (m, 1H), 3.21 (s, 3H), 2.45-2.32 (m, 3H), 2.23-2.15 (m, 7H), 2.07-2.01 (m, 2H), 1.72 (d, *J* = 0.8 Hz, 3H), 1.70-1.57 (m, 4H), 1.54 (s, 3H), 1.47-1.40 (m, 2H), 1.41 (s, 9H), 1.33 (s, 3H), 1.31-1.24 (m, 4H), 1.12-1.06 (m, 1H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.83 (d, *J* = 7.1 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 172.7, 142.1, 132.8, 132.6, 132.5, 132.4, 132.3, 131.3, 129.5, 127.7, 127.6, 126.9, 108.4, 95.2, 83.6, 80.7, 79.44, 79.36, 79.12, 79.08, 78.7, 76.8, 75.8, 75.5, 75.0, 74.1, 74.0, 72.0, 63.3, 55.3, 41.8, 38.8, 37.8, 36.5, 36.3, 35.84, 35.77, 33.0, 32.9, 32.2, 29.7, 28.2 (4C), 27.5, 25.72, 25.68, 21.6, 15.3, 14.3, 10.9; HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{51}H_{79}IO_{11}Na^+$ 1017.4565, obsd 1017.4566.

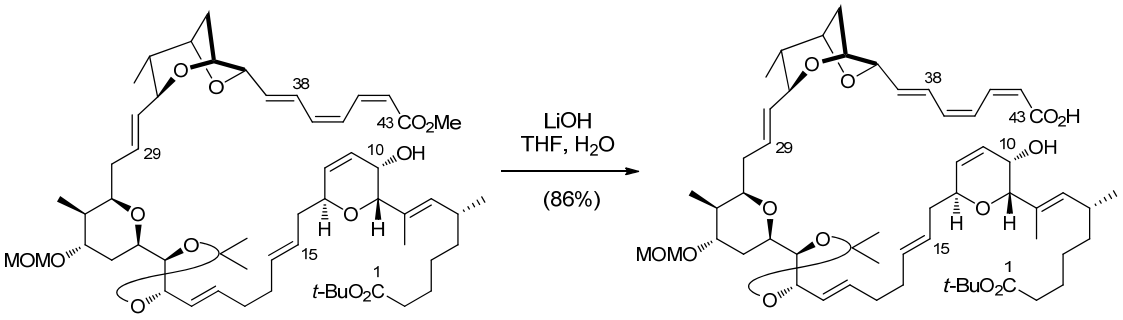


Enone SI-7-6. At room temperature, solid Dess-Martin periodinane (8.0 mg, 18 μmol) was added in one portion to a slurry of (–)-**132** (6.0 mg, 6.0 μmol) and $NaHCO_3$ (18 mg, 0.10 mmol) in CH_2Cl_2 (0.4 mL). The mixture was stirred in the dark for 2 h and then diluted with Et_2O (1.5 mL), whereupon a 1:1:1 solution of saturated $NaHCO_3$/brine/$Na_2S_2O_3$ (3 mL) was added and stirring was continued until the aqueous layer became homogeneous (20 min). The layers were separated and the aqueous phase was extracted with Et_2O (2x1 mL). The combined organic extracts were dried (Na_2SO_4), filtered through a pad of SiO_2 (5 g) with an Et_2O rinse (10 mL) and concentrated *in vacuo*. The crude residue was purified by flash chromatography (SiO_2) eluting with 1:1 hexanes/EtOAc to afford **SI-7-6** (5.5 mg, 92%) as a pale yellow oil. ^{1}H NMR (500 MHz, C_6D_6) δ 6.84 (dd, *J* = 14.5, 4.8 Hz, 1H), 6.51 (dd, *J* = 10.4, 2.0 Hz, 1H), 6.45 (dd, *J* = 14.5, 1.7 Hz, 1H), 6.06 (dd, *J* = 10.4, 2.3 Hz, 1H), 5.94 (ddd, *J* = 15.5, 6.7, 6.7 Hz, 1H), 5.83 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.70 (ddd, *J* = 15.0, 7.9, 6.4 Hz, 1H), 5.59-5.43 (m, 3H), 5.17 (d, *J* = 9.7 Hz, 1H), 4.78 (dd, *J* = 5.7, 5.7 Hz, 1H), 4.65 (s, 1H), 4.53 (ABq, *J* = 6.8 Hz, Δν = 10.6 Hz, 2H), 4.19 (dddd, *J* = 6.7, 6.7, 2.3, 2.3 Hz, 1H), 4.08-3.95 (m, 4H), 3.93-3.91 (m, 2H), 3.87-3.85 (m, 1H), 3.68-3.66 (m, 1H), 3.20 (s, 3H), 2.43-2.16 (m, 8H), 2.13 (t, *J* = 7.4 Hz, 2H), 2.06-2.00 (m, 2H), 1.73-1.63 (m, 2H), 1.71 (d, *J* = 1.0 Hz, 3H), 1.58-1.53 (m, 2H), 1.52 (s, 3H), 1.47-1.42 (m, 2H), 1.41 (s, 9H), 1.33 (s, 3H), 1.27-1.06 (m, 5H), 0.84 (d, *J* = 6.7 Hz, 3H), 0.83 (d, *J* = 7.1 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H).

Vinyl Iodide (+)-162. To a solution of enone **SI-7-6** (6.0 mg, 6.0 μmol) in MeOH (0.50 mL) was added $CeCl_3$•$7H_2O$ (45 mg, 0.12 mmol) at rt. After 10 min, $NaBH_4$ (1.0 mg, 24 μmol) was added at 0 °C. After 15 min, the reaction mixture was quenched with saturated NH_4Cl solution (5 mL), and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated to leave a crude residue, which was purified by flash chromatography (5% to 30% EtOAc/hexanes) to afford vinyl iodide (+)-**162** (6.0 mg, 100%) as a pale yellow oil. Analytical data matched that prepared from (–)-**131**.

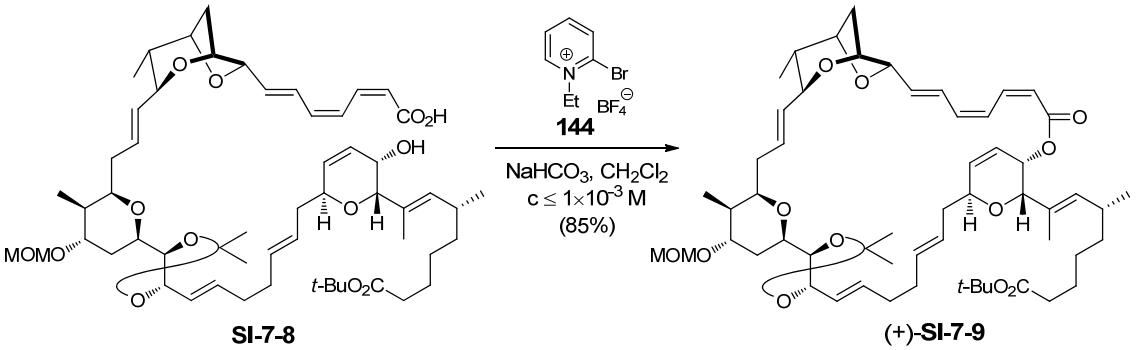


Trienoate (+)-SI-7-7. A 15 mL round bottom flask was charged with stannane **139** (16 mg, 40 μmol), vinyl iodide (+)-**162** (10 mg, 10 μmol), $Ph_2PO_2NBu_4$ (55.0 mg, 120 μmol), and dissolved in degassed DMF (1.1 mL). To this was added $PdCl_2(PhCN)_2$ (0.2 mg, 0.5 μmol), and the reaction mixture was purged with argon for 5 min, and stirred at rt in the dark overnight. The reaction mixture was diluted with Et_2O/hexanes (1:1, 4 mL), filtered through a Celite plug into brine (5 mL), and rinsed with Et_2O/hexanes (1:1, 20 mL). The mixture was extracted using Et_2O/hexanes (1:1, 3×10 mL), and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a crude residue, which was purified by flash chromatography (SiO_2, 0.2% to 1.5% MeOH/CH_2Cl_2, silica gel was pretreated with 0.5% Et_3N) to afford trienoate (+)-**SI-7-7** (8.6 mg, 88%) as a yellow oil. $[\alpha]_D^{29}$ +49.0 (*c* 0.26, C_6H_6); IR (neat, cm^{-1}) 3417, 1720, 1650, 1612, 1454, 1368, 1246, 1218, 1149, 1097, 1067, 1038, 974, 876; ^1H NMR (500 MHz, C_6D_6) δ 7.75 (dd, *J* = 11.5, 11.5 Hz, 1H), 7.05-7.00 (m, 1H), 6.88 (dd, *J* = 11.5, 11.5 Hz, 1H), 6.26 (dd, *J* = 11.5, 11.5 Hz, 1H), 6.10 (dd, *J* = 15.3, 4.9 Hz, 1H), 6.01 (ddd, *J* = 10.2, 5.6, 2.0 Hz, 1H), 5.93 (ddd, *J* = 15.4, 6.4, 6.4 Hz, 1H), 5.82 (dd, *J* = 15.4, 6.3 Hz, 1H), 5.74 (dd, *J* = 10.2, 3.2 Hz, 1H), 5.71 (ddd, *J* = 15.2, 7.6, 7.6 Hz, 1H), 5.64 (d, *J* = 11.5 Hz, 1H), 5.59 (d, *J* = 9.5 Hz, 1H), 5.54-5.43 (m, 3H), 4.78 (dd, *J* = 5.8, 5.8 Hz, 1H), 4.51 (ABq, *J* = 6.8 Hz, Δν = 11.0 Hz, 2H), 4.30-4.26 (m, 1H), 4.24-4.23 (m, 1H), 4.11-4.04 (m, 6H), 4.00-3.96 (m, 1H), 3.80-3.78 (m, 1H), 3.67-3.65 (m, 1H), 3.38 (s, 3H), 3.19 (s, 3H), 2.46-2.33 (m, 3H), 2.19-2.13 (m, 7H), 2.08-2.02 (m, 2H), 1.79-1.47 (m, 6H), 1.73 (s, 3H), 1.53 (s, 3H), 1.41 (s, 9H), 1.33 (s, 3H), 1.31-1.23 (m, 4H), 1.20-1.14 (m, 1H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 172.7, 166.5, 138.7, 136.9, 134.6, 132.8, 132.7, 132.5, 132.3 (2C), 131.4, 129.1, 127.7, 127.6, 126.9, 126.8, 125.0, 118.0, 108.4, 95.2, 82.0, 80.7, 79.5, 79.4, 79.1, 78.7, 76.4, 75.9, 75.0, 74.1, 74.0, 72.0, 63.4, 55.2, 50.8, 42.0, 39.3, 37.8, 36.5, 36.3, 35.83, 35.77, 33.0, 32.8, 32.2, 29.7, 28.2 (4C), 27.5, 25.7 (2C), 21.6, 15.4, 14.3, 10.9; HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{57}H_{86}O_{13}Na^+$ 1001.5966, obsd 1001.5975.



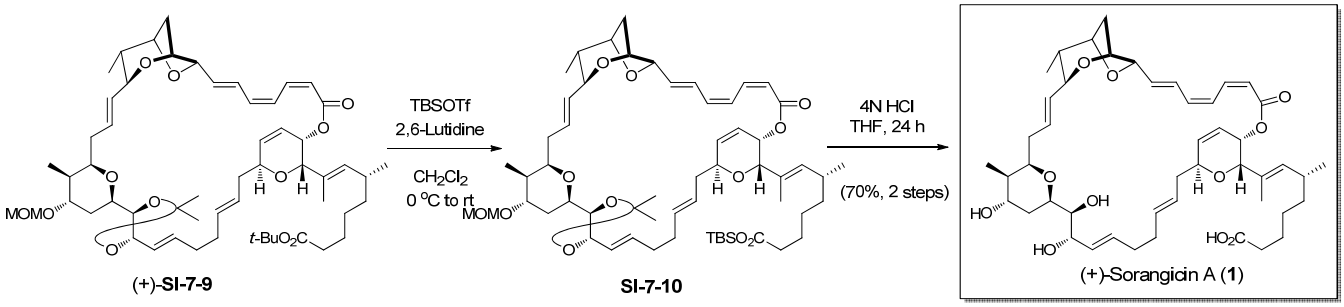
(+)-**SI-7-7** **SI-7-8**

Seco Acid SI-7-8. A solution of trienoate (+)-**SI-7-7** (6.6 mg, 6.7 μmol) in THF (1.6 mL) and H_2O (0.4 mL) was treated with 1 M LiOH solution (0.4 mL). The yellow reaction mixture was stirred for 1.5 days at rt in the dark. Brine (1 mL) was added and the pH value of the reaction mixture was adjusted to ca. 3 with 1 M $NaHSO_4$. The aqueous layer was extracted with EtOAc (4×2 mL), and the combined organic layers were washed with brine (2 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a crude residue, which was purified by flash chromatography (SiO_2, 0.5% to 5% MeOH/CH_2Cl_2) to afford seco acid **SI-7-8** (5.6 mg, 86%) as a yellow oil. Seco acid **SI-7-8** proved very unstable, and was carried on to the next step immediately after the ^{1}H NMR spectrum was taken. ^{1}H NMR (500 MHz, C_6D_6) δ 7.64 (dd, *J* = 11.5, 11.5 Hz, 1H), 7.03-6.97 (m, 1H), 6.89 (dd, *J* = 11.5, 11.5 Hz, 1H), 6.27 (dd, *J* = 11.5, 11.5 Hz, 1H), 6.08 (dd, *J* = 15.0, 4.7 Hz, 1H), 6.02 (ddd, *J* = 10.1, 5.8, 2.0 Hz, 1H), 5.93 (ddd, *J* = 15.4, 6.3, 6.3 Hz, 1H), 5.81 (dd, *J* = 15.4, 6.3 Hz, 1H), 5.74 (dd, *J* = 10.1, 3.1 Hz, 1H), 5.67-5.58 (m, 3H), 5.52-5.41 (m, 3H), 4.78 (dd, *J* = 5.5, 5.5 Hz, 1H), 4.53 (ABq, *J* = 6.9 Hz, Δν = 9.8 Hz, 2H), 4.33-4.28 (m, 1H), 4.24-4.23 (m, 1H), 4.09-4.04 (m, 6H), 3.98-3.95 (m, 1H), 3.82 (dd, *J* = 5.6, 2.0 Hz, 1H), 3.68-3.67 (m, 1H), 3.20 (s, 3H), 2.47-2.34 (m, 3H), 2.19-2.12 (m, 7H), 2.11-2.01 (m, 2H), 1.74 (d, *J* = 0.7 Hz, 3H), 1.72-1.47 (m, 6H), 1.53 (s, 3H), 1.41 (s, 9H), 1.33 (s, 3H), 1.31-1.24 (m, 4H), 1.18-1.12 (m, 1H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.83 (d, *J* = 7.1 Hz, 3H).



SI-7-8 (+)-**SI-7-9**

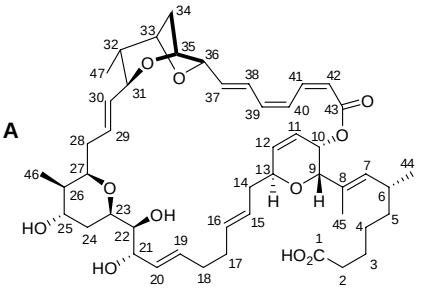
Macrolide (+)-SI-7-9. A slurry of seco acid **SI-7-8** (5.4 mg, 5.6 μmol) and $NaHCO_3$ (120 mg, 1.40 mmol) in CH_2Cl_2 (12 mL) was treated with solid 2-bromo-1-ethylpyridinium tetrafluoroborate **144** (31 mg, 0.11 mmol) in one portion. The reaction mixture was vigorously stirred in the dark overnight, then transferred directly onto a silica gel column and purified by flash chromatography (0.2% to 1.6% MeOH/CH_2Cl_2) to afford macrolide (+)-**SI-7-9** (4.7 mg, 85%) as a pale yellow foam. $[\alpha]_D^{28}$ +41.6 (*c* 0.36, MeOH); IR (neat, cm^{-1}) 1722, 1698, 1610, 1452, 1367, 1250, 1211, 1148, 1095, 1066, 1037, 971, 916, 871; ^1H NMR (500 MHz, CD_3OD) δ 7.16-7.06 (m, 2H), 7.04-6.99 (m, 1H), 6.44 (dd, *J* = 10.6, 10.6 Hz, 1H), 6.26 (dd, *J* = 15.4, 3.3 Hz, 1H), 6.14 (dd, *J* = 10.1, 3.1 Hz, 1H), 6.02 (ddd, *J* = 10.1, 5.9, 2.1 Hz, 1H), 5.73 (ddd, *J* = 15.1, 6.7, 6.7 Hz, 1H), 5.61 (d, *J* = 10.5 Hz, 1H), 5.56-5.52 (m, 3H), 5.38-5.34 (m, 3H), 5.26 (d, *J* = 10.1 Hz, 1H), 4.64 (ABq, *J* = 7.1 Hz, Δν = 17.6 Hz, 2H), 4.61-4.57 (m, 2H), 4.41-4.39 (m, 2H), 4.31 (d, *J* = 6.3 Hz, 1H), 4.21 (s, 1H), 3.94 (dd, *J* = 8.4, 6.3 Hz, 1H), 3.84 (dd, *J* = 9.6, 7.5 Hz, 1H), 3.77-3.68 (m, 3H), 3.32 (s, 3H), 2.42-2.33 (m, 2H), 2.23-2.01 (m, 9H), 1.92 (d, *J* = 10.5 Hz, 1H), 1.75 (d, *J* = 13.8 Hz, 1H), 1.69-1.62 (m, 2H), 1.61 (d, *J* = 0.8 Hz, 3H), 1.60-1.50 (m, 2H), 1.44 (s, 9H), 1.42 (s, 3H), 1.41-1.36 (m, 1H), 1.32 (s, 3H), 1.27-1.15 (m, 4H), 0.90 (d, *J* = 7.2 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 174.9, 167.8, 138.9, 137.7, 137.1, 135.7, 134.2, 133.9, 133.6 (2C), 131.24, 131.17, 128.0, 127.9, 127.6, 126.8, 123.7, 119.8, 109.8, 96.0, 81.9, 81.22 (2C), 81.18, 81.09, 80.1, 77.7, 76.6, 74.9, 74.4, 73.8, 73.3, 66.6, 55.8, 41.8, 39.6, 38.9, 36.7 (2C), 35.6, 35.1, 34.1, 33.1, 32.9, 30.8, 30.4, 28.5 (3C), 28.3, 28.2, 26.3, 25.7, 22.3, 15.3, 14.5, 10.8; HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{56}H_{82}O_{12}Na^+$ 969.5704, obsd 969.5670.



(+)-Sorangicin A (1). To a stirred solution of macrolide (+)-**SI-7-9** (3.5 mg, 3.7 μmol) and 2,6-lutidine (13 μL, 111 μmol) in CH_2Cl_2 (200 μL) was added TBSOTf (9 μL, 37 μmol) at 0 °C. After 30 min at 0 °C, the reaction mixture was warmed to rt and stirred for 3 h before being quenched with 0.2 N HCl (1 mL). The aqueous layer was extracted with Et_2O (4×2 mL), and the combined organic layers were washed with brine (2 mL), dried (Na_2SO_4), filtered and evaporated to give the crude TBS ester **SI-7-10**.

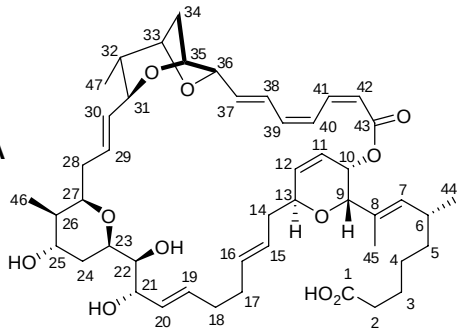
Without further purification, TBS ester **SI-7-10** was dissolved in THF (200 μL) and treated with 4 N HCl (200 μL) at 0 ^{o}C. The reaction mixture was warmed to rt and stirred for 24 h before being cooled to 0 ^{o}C and carefully neutralized with saturated $NaHCO_3$ solution (2 mL), and then acidified with HCOOH (0.5 mL, pH~3). The aqueous phase was extracted with CH_2Cl_2 (4×3 mL), and the combined organic layers were concentrated *in vacuo* to give a crude residue, which was purified by flash chromatography (SiO_2, 1% to 5% MeOH/CH_2Cl_2) to furnish (+)-sorangicin A (**1**) (2.1 mg, 70%, 2 steps) as an off-white solid. $[\alpha]_D^{20}$ +56 (*c* 0.06, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 7.22-7.12 (m, 2H, 40-H, 41-H), 6.99 (dd, *J* = 15.0, 11.0 Hz, 1H, 38-H), 6.44 (dd, *J* = 10.5, 10.5 Hz, 1H, 39-H), 6.22 (dd, *J* = 15.5, 4.5 Hz, 1H, 37-H), 6.13 (dd, *J* = 9.9, 3.0 Hz, 1H, 12-H), 6.01 (ddd, *J* = 9.9, 5.7, 2.0 Hz, 1H, 11-H), 5.75 (ddd, *J* = 15.4, 6.2, 6.2 Hz, 1H, 19-H), 5.62 (d, *J* = 10.6 Hz, 1H, 42-H), 5.60 (dd, *J* = 15.4, 7.4 Hz, 1H, 20-H), 5.55-5.53 (m, 2H, 15-H, 16-H), 5.52-5.48 (m, 1H, 29-H), 5.38 (ddd, *J* = 15.0, 8.4, 1.0 Hz, 1H, 30-H), 5.32-5.30 (m, 2H, 7-H, 10-H), 4.57 (br s, 1H, 36-H), 4.40-4.38 (m, 2H, 35-H, 13-H), 4.28 (d, *J* = 6.2 Hz, 1H, 33-H), 4.23 (s, 1H, 9-H), 4.15 (dd, *J* = 7.4, 4.5 Hz, 1H, 21-H), 3.88-3.82 (m, 3H, 27-H, 25-H, 31-H), 3.71 (ddd, *J* = 11.0, 7.3, 2.7 Hz, 1H, 23-H), 3.48 (dd, *J* = 7.3, 4.5 Hz, 1H, 22-H), 2.42-2.36 (m, 2H, 14-H_a, 6-H), 2.28-2.22 (m, 1H, 28-H_a), 2.23 (t, *J* = 7.5 Hz, 2H, 2-H), 2.19-2.09 (m, 6H, 17-H, 14-H_b, 28-H_b, 18-H), 2.05 (ddd, *J* = 11.5, 6.5, 2.6 Hz, 1H, 34-H_a), 1.93 (dd, *J* = 11.5, 1.5 Hz, 1H, 34-H_b), 1.74 (ddd, *J* = 14.0, 2.5, 2.5 Hz, 1H, 24-H_a), 1.66 (ddd, *J* = 14.0, 11.5, 2.6 Hz, 1H, 24-H_b), 1.63 (d, *J* = 0.7 Hz, 3H, 45-H), 1.61-1.53 (m, 3H, 3-H, 26-H), 1.42 (m, 1H, 32-H), 1.37-1.16 (m, 4H, 5-H, 4-H), 0.88 (d, *J* = 7.2 Hz, 3H, 46-H), 0.87 (d, *J* = 6.6 Hz, 3H, 44-H), 0.82 (d, *J* = 6.8 Hz, 3H, 47-H); ^{13}C NMR (125 MHz, CD_3OD) δ 179.18 (C-1), 167.66 (C-43), 139.16 (C-41), 137.77 (C-39), 136.95 (C-12), 134.94 (C-37), 134.61 (C-19), 134.10 (C-7), 133.69 (C-16), 132.98 (C-29), 132.79 (C-30), 131.09 (C-8), 129.96 (C-20), 128.25 (C-15), 127.74 (C-38), 126.96 (C-40), 123.71 (C-11), 119.55 (C-42), 82.08 (C-36), 81.20 (C-31), 80.98 (C-33), 77.76 (C-22), 77.49 (C-35), 75.23 (C-13), 74.85 (C-23), 74.67 (C-27), 74.37 (C-21), 74.17 (C-9), 71.01 (C-25), 66.68 (C-10), 42.06 (C-32), 39.80 (C-34), 38.69 (C-5), 38.28 (C-26), 37.14 (C-28), 36.23 (C-2), 35.34 (C-14), 34.20 (C-18), 33.51 (C-17), 32.96 (C-6), 30.89 (C-24), 28.40 (C-4), 26.64 (C-3), 21.85 (C-44), 15.39 (C-47), 14.39 (C-45), 10.85 (C-46); HRMS (ES) *m/z* $(M+Na)^+$ calcd for $C_{47}H_{66}O_{11}Na^+$ 829.4503, obsd 829.4507.

^{1}H NMR Chemical Shifts of (+)-Sorangicin A
δ (ppm in CD_3OD)



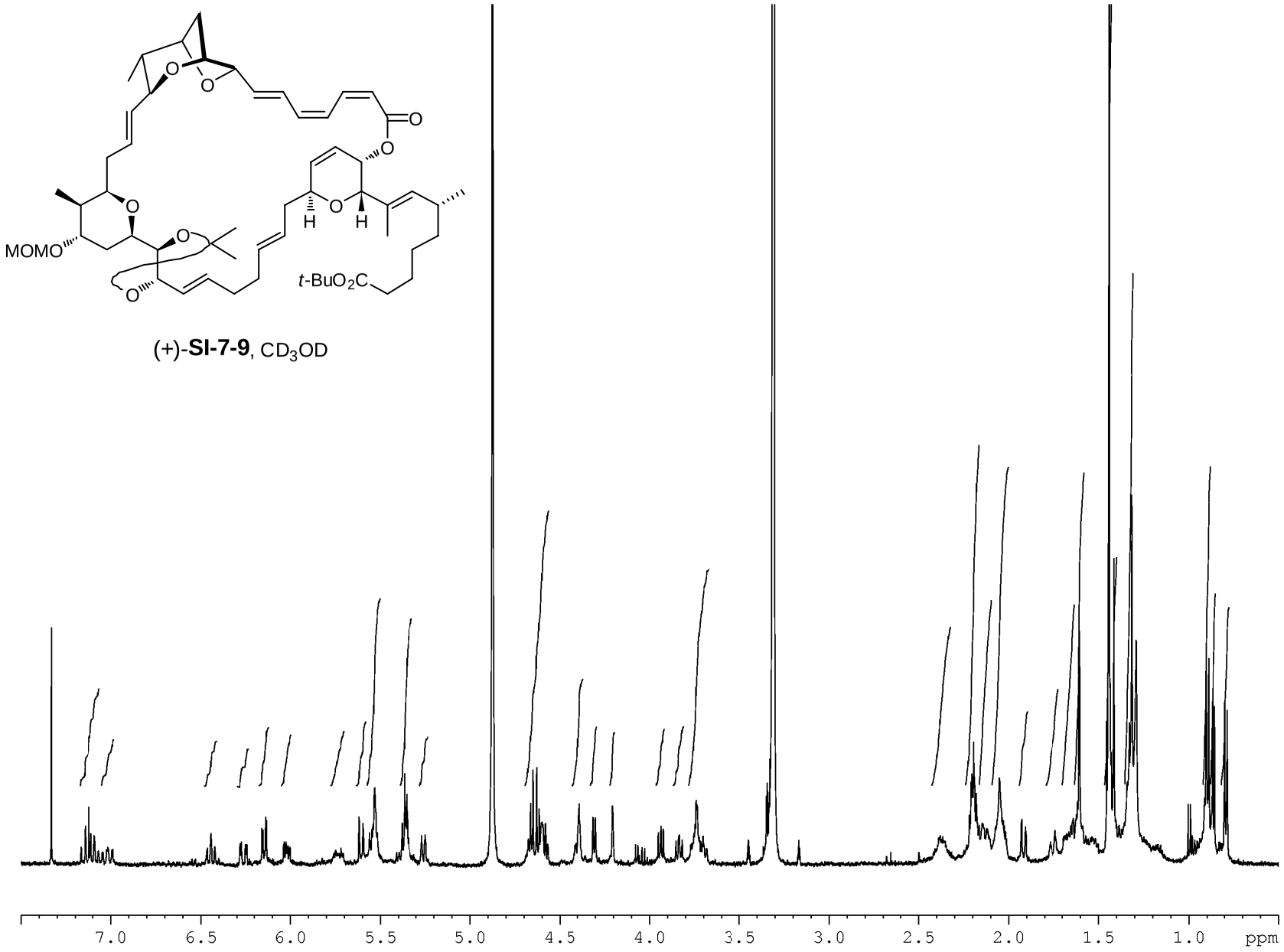
Proton Number	Synthetic (+)-Sorangicin A	Natural (+)-Sorangicin A
40-H, 41-H	7.22-7.12 (m, 2H)	7.22-7.12 (m, 2H)
38-H	6.99 (dd, *J* = 15.0, 11.0 Hz, 1H)	6.99 (dd, *J* = 14.9, 11.1 Hz, 1H)
39-H	6.44 (dd, *J* = 10.5, 10.5 Hz, 1H)	6.44 (dd, *J* = 10.6, 10.6 Hz, 1H)
37-H	6.22 (dd, *J* = 15.5, 4.5 Hz, 1H)	6.22 (dd, *J* = 15.4, 4.7 Hz, 1H)
12-H	6.13 (dd, *J* = 9.9, 3.0 Hz, 1H)	6.13 (dd, *J* = 10.0, 3.1 Hz, 1H)
11-H	6.01 (ddd, *J* = 9.9, 5.7, 2.0 Hz, 1H)	6.01 (ddd, *J* = 10.0, 5.8, 2.1 Hz, 1H)
19-H	5.75 (ddd, *J* = 15.4, 6.2, 6.2 Hz, 1H)	5.75 (ddd, *J* = 15.4, 6.2, 6.2 Hz, 1H)
42-H	5.62 (d, *J* = 10.6 Hz, 1H)	5.62 (d, *J* = 10.5 Hz, 1H)
20-H	5.60 (dd, *J* = 15.4, 7.4 Hz, 1H)	5.60 (dd, *J* = 15.5, 7.5 Hz, 1H)
15-H, 16-H	5.55-5.53 (m, 2H)	5.55-5.53 (m, 2H)
29-H	5.52-5.48 (m, 1H)	5.52-5.48 (m, 1H)
30-H	5.38 (ddd, *J* = 15.0, 8.4, 1.0 Hz, 1H)	5.38 (ddd, *J* = 15.0, 8.5, 1.0 Hz, 1H)
7-H, 10-H	5.32-5.30 (m, 2H)	5.32-5.30 (m, 2H)
36-H	4.57 (br s, 1H)	4.57 (br s, 1H)
35-H, 13-H	4.40-4.38 (m, 2H)	4.40-4.38 (m, 2H)
33-H	4.28 (d, *J* = 6.2 Hz, 1H)	4.28 (d, *J* = 6.4 Hz, 1H)
9-H	4.23 (s, 1H)	4.23 (s, 1H)
21-H	4.15 (dd, *J* = 7.4, 4.5 Hz, 1H)	4.15 (dd, *J* = 7.4, 4.6 Hz, 1H)
27-H, 25-H, 31-H	3.88-3.82 (m, 3H)	3.88-3.82 (m, 3H)
23-H	3.71 (ddd, *J* = 11.0, 7.3, 2.7 Hz, 1H)	3.71 (ddd, *J* = 11.0, 7.3, 2.7 Hz, 1H)
22-H	3.48 (dd, *J* = 7.3, 4.5 Hz, 1H)	3.48 (dd, *J* = 7.2, 4.6 Hz, 1H)
14-H_a, 6-H	2.42-2.36 (m, 2H)	2.42-2.36 (m, 2H)
28-H_a	2.28-2.22 (m, 1H)	2.28-2.23 (m, 1H)
2-H	2.23 (t, *J* = 7.5 Hz, 2H)	2.24 (t, *J* = 7.6 Hz, 2H)
17-H,14-H_b,28-H_b,18-H	2.19-2.09 (m, 6H)	2.19-2.09 (m, 6H)
34-H_a	2.05 (ddd, *J* = 11.5, 6.5, 2.6 Hz, 1H)	2.05 (ddd, *J* = 11.6, 6.5, 2.8 Hz, 1H)
34-H_b	1.93 (dd, *J* = 11.5, 1.5 Hz, 1H)	1.93 (dd, *J* = 11.6, 1.4 Hz, 1H)
24-H_a	1.74 (ddd, *J* = 14.0, 2.5, 2.5 Hz, 1H)	1.73 (ddd, *J* = 14.0, 2.5, 2.5 Hz, 1H)
24-H_b	1.66 (ddd, *J* = 14.0, 11.5, 2.6 Hz, 1H)	1.66 (ddd, *J* = 14.0, 11.6, 2.6 Hz, 1H)
45-H	1.63 (d, *J* = 0.7 Hz, 3H)	1.63 (d, *J* = 0.6 Hz, 3H)
3-H, 26-H	1.61-1.53 (m, 3H)	1.60-1.53 (m, 3H)
32-H	1.42 (m, 1H)	1.42 (m, 1H)
5-H, 4-H	1.37-1.16 (m, 4H)	1.38-1.16 (m, 4H)
46-H	0.88 (d, *J* = 7.2 Hz, 3H)	0.88 (d, *J* = 7.4 Hz, 3H)
44-H	0.87 (d, *J* = 6.6 Hz, 3H)	0.87 (d, *J* = 6.5 Hz, 3H)
47-H	0.82 (d, *J* = 6.8 Hz, 3H)	0.82 (d, *J* = 6.5 Hz, 3H)

^{13}C NMR Chemical Shifts of (+)-Sorangicin A
δ (ppm in CD_3OD)

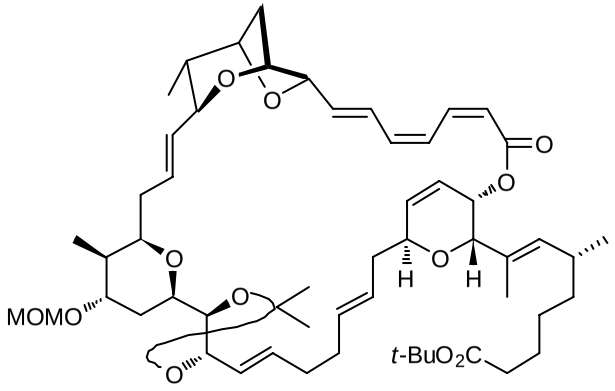


Carbon Number	Synthetic (+)-Sorangicin A	Natural (+)-Sorangicin A
C-1	179.18	178.61
C-43	167.66	167.66
C-41	139.16	139.19
C-39	137.77	137.78
C-12	136.95	136.96
C-37	134.94	134.93
C-19	134.61	134.63
C-7	134.10	134.10
C-16	133.69	133.70
C-29	132.98	132.97
C-30	132.79	132.80
C-8	131.09	131.17
C-20	129.96	129.95
C-15	128.25	128.25
C-38	127.74	127.74
C-40	126.96	126.96
C-11	123.71	123.70
C-42	119.55	119.55
C-36	82.08	82.09
C-31	81.20	81.21
C-33	80.98	80.99
C-22	77.76	77.76
C-35	77.49	77.49
C-13	75.23	75.22
C-23	74.85	74.85
C-27	74.67	74.67
C-21	74.37	74.36
C-9	74.17	74.19
C-25	71.01	71.01
C-10	66.68	66.73
C-32	42.06	42.05
C-34	39.80	39.81
C-5	38.69	38.64
C-26	38.28	38.30
C-28	37.14	37.14

Carbon Number	Synthetic (+)-Sorangicin A	Natural (+)-Sorangicin A
C-2	36.23	35.78
C-14	35.34	35.34
C-18	34.20	34.20
C-17	33.51	33.51
C-6	32.96	32.95
C-24	30.89	30.88
C-4	28.40	28.33
C-3	26.64	26.46
C-44	21.85	21.84
C-47	15.39	15.39
C-45	14.39	14.38
C-46	10.85	10.85

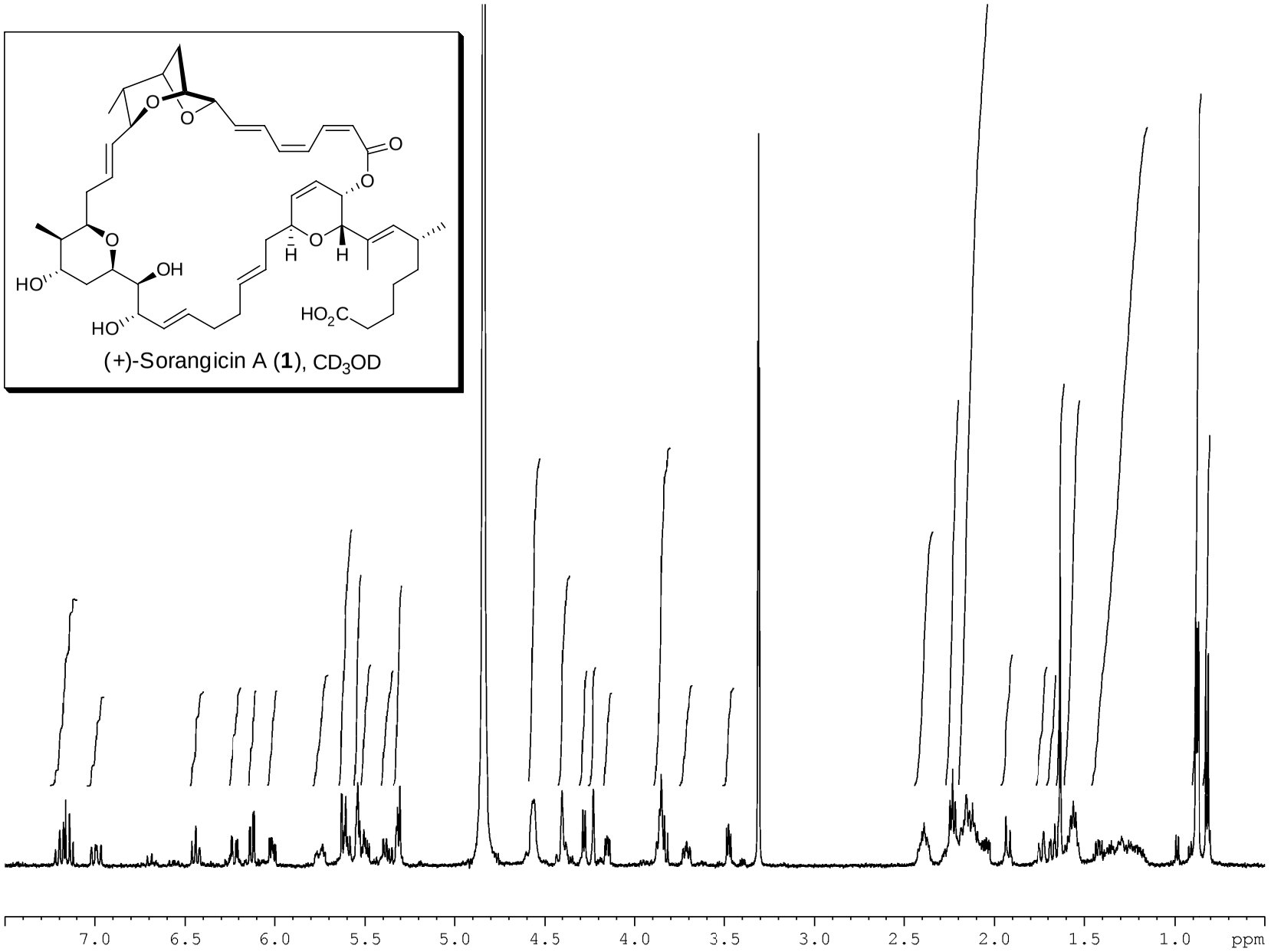


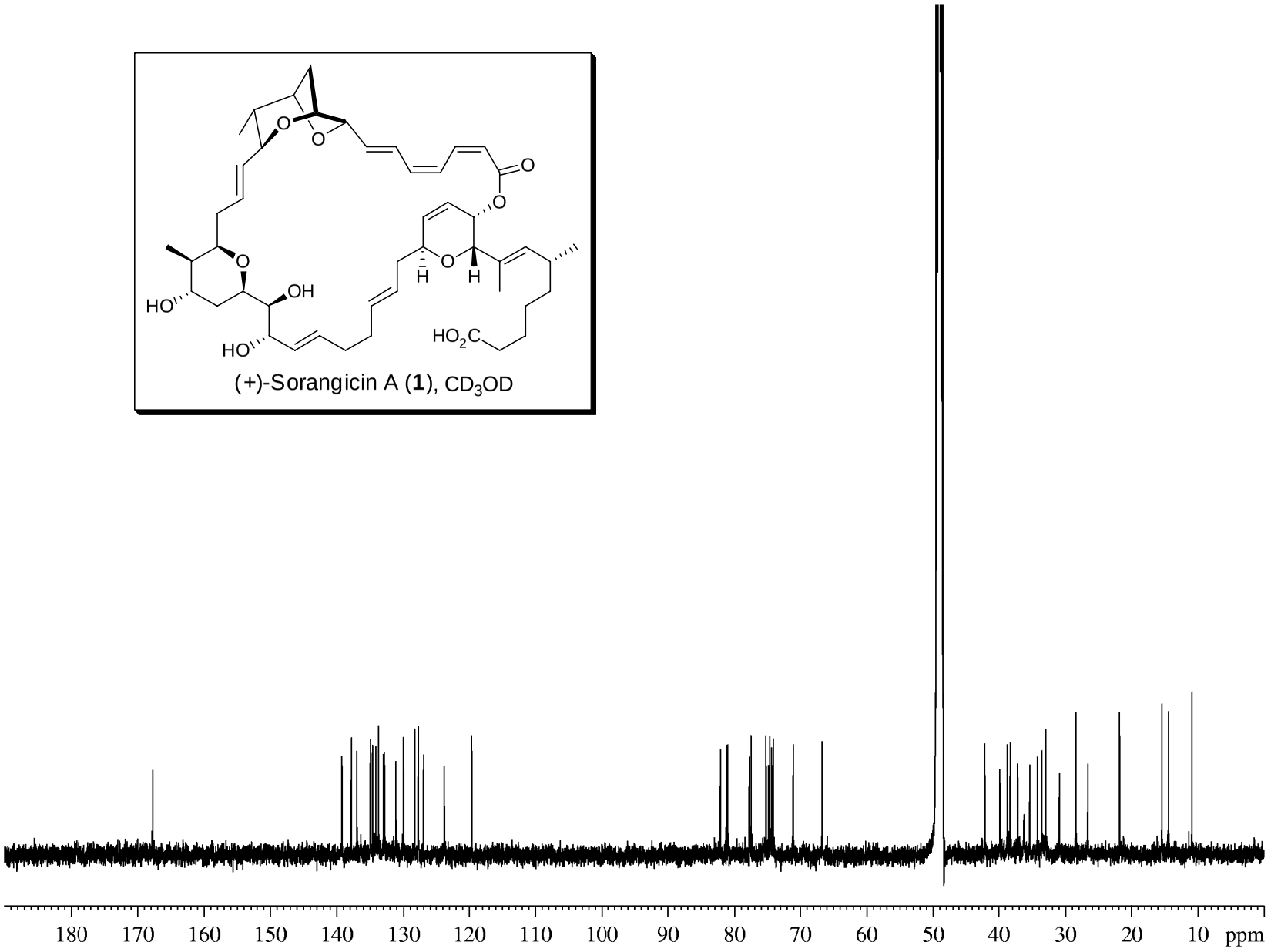
(+)-**SI-7-9**, CD_3OD


MOMO
t-BuO2C
H
H

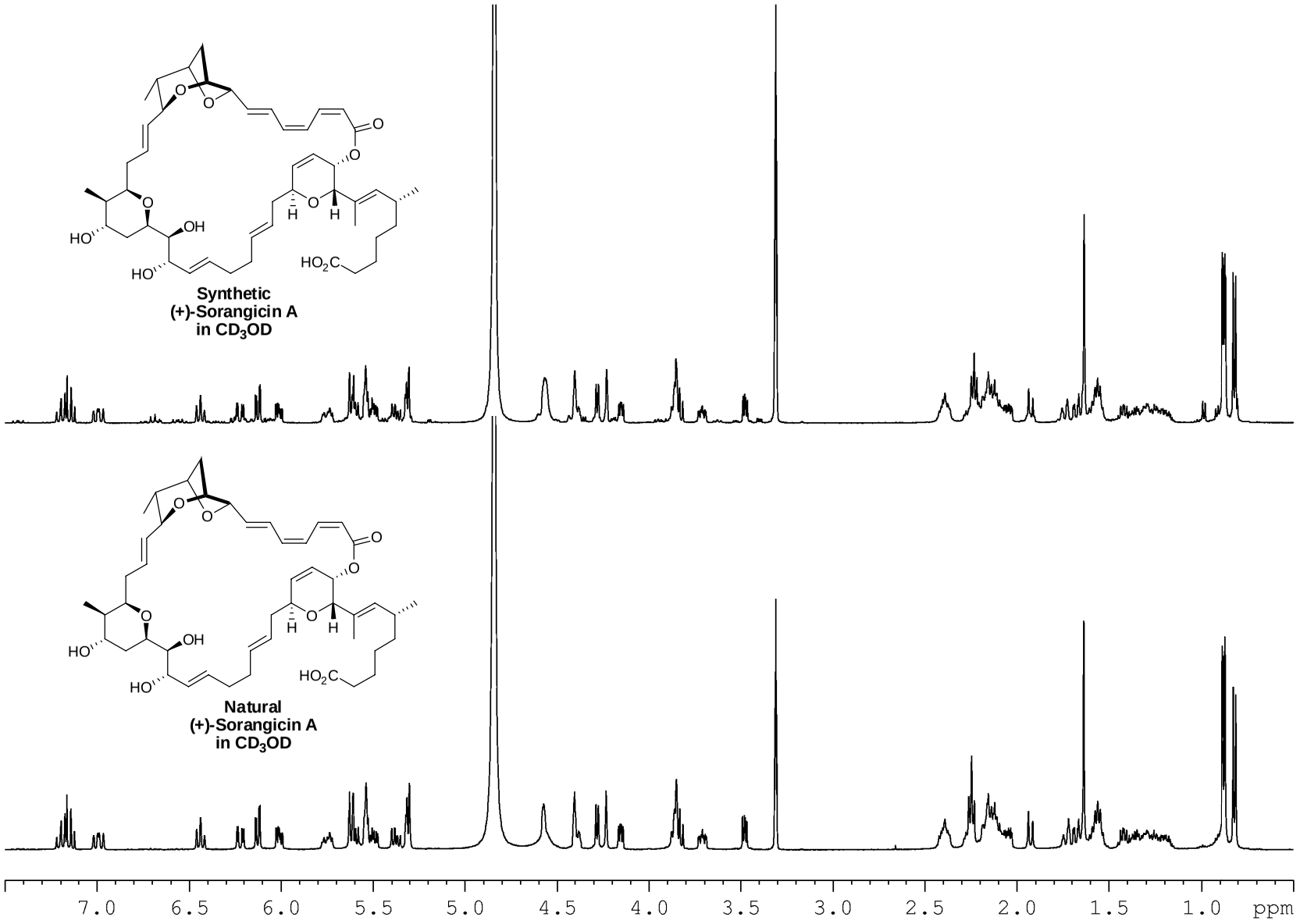
(+)-**SI-7-9**, CD_3OD

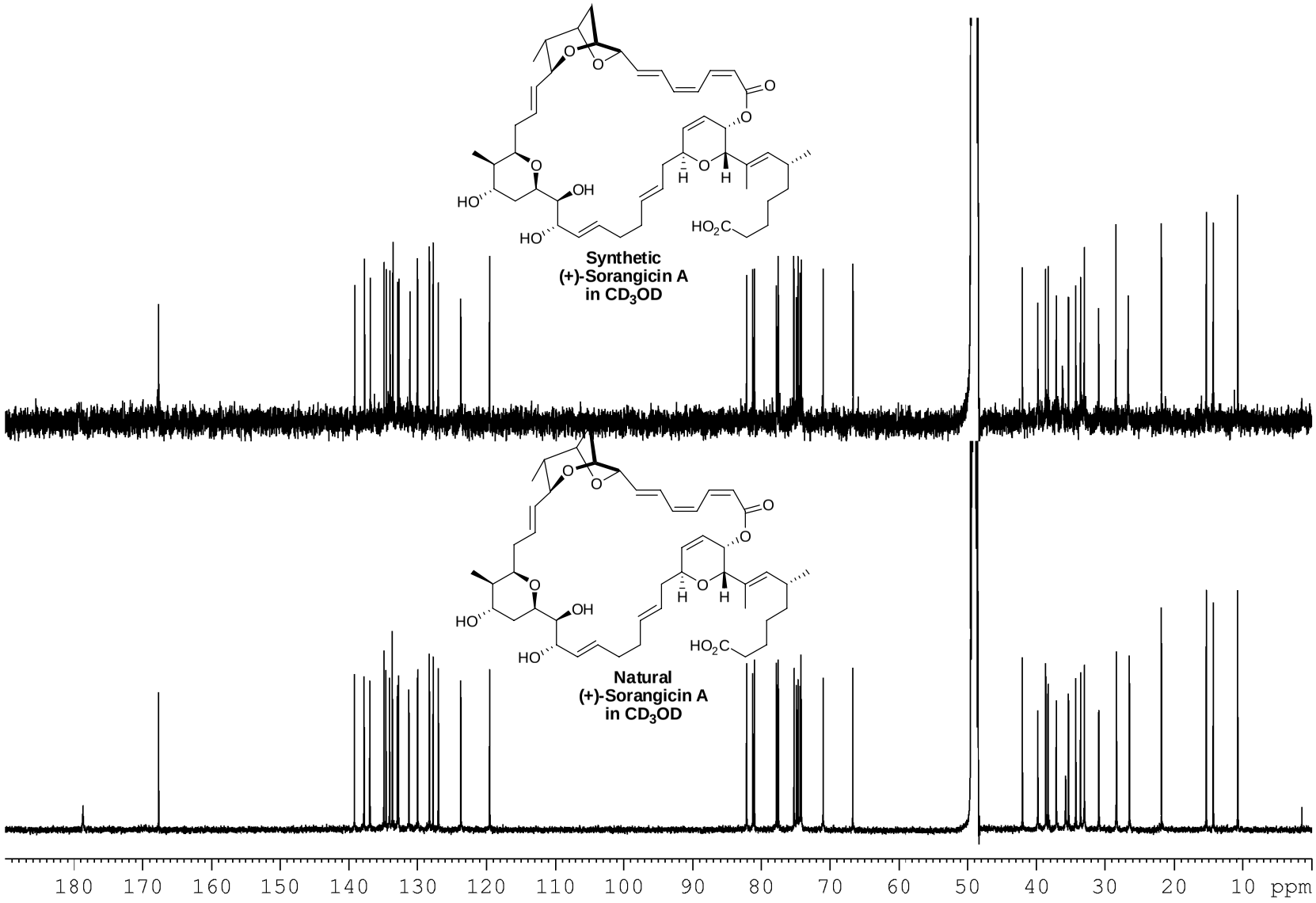
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


(+)-Sorangicin A (1), CD3OD
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm



(+)-Sorangicin A (**1**), CD_3OD


Synthetic
(+)-Sorangicin A
in CD3OD
Natural
(+)-Sorangicin A
in CD3OD
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm


Synthetic
(+)-Sorangicin A
in CD3OD
Natural
(+)-Sorangicin A
in CD3OD
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

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