SUPPLEMANTARY MATERIAL

for the
article
entitled

Studies on A Urea Directed Stork-Crabtree Hydrogenation. Synthesis of C1-C9 Subunit of (+)-Zincophorin.

authored by

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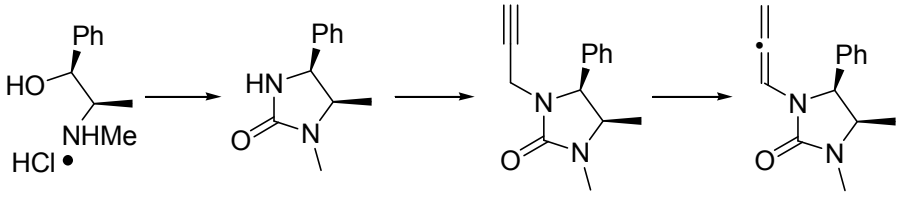
Contents of Supporting Information

EXPERIMENTAL SECTION

All reactions were performed in flame-dried glassware under a nitrogen atmosphere. Solvents were distilled prior to use. Reagents were used as purchased (Aldrich, Acros), except where noted. Chromatographic separations were performed using Bodman 60 Å SiO_2. ^1H and ^{13}C NMR spectra were obtained on Varian VI-300, VI-400, and VI-500 spectrometers using $CDCl_3$ (except where noted) with TMS or residual $CHCl_3$ in the solvent as standard. Melting points were determined using a Laboratory Devices MEL-TEMP and are uncorrected/calibrated. Infrared spectra were obtained using NaCl plates on a Bruker Equinox 55/S FT–IR Spectrophotometer, and relative intensities are expressed qualitatively as s (strong), m (medium), and w (weak). TLC analysis was performed using Aldrich 254 nm polyester-backed plates (60 Å, 250 μm) and visualized using UV and a suitable chemical stain. Low-resolution mass spectra were obtained using an Agilent-1100-HPLC/MSD and can be either APCI or ESI, or an IonSpec HiRes-MALDI FT-Mass Spectrometer. High-resolution mass spectral analyses were performed at University of Wisconsin Mass Spectrometry Laboratories. All spectral data obtained for new compounds are reported. X-Ray analyses were performed at the X-Ray facility in University of Minnesota.

Synthesis of Allenamide 9.



11 **12:** Close auxiliary **13** **9**

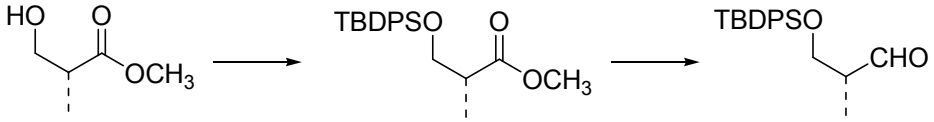
The (+)-ephedrine hydrochloride salt (17.0 g, 84.6 mmol) was mixed with urea (15.0 g, 253.8 mmol) and heated for 0.5 h at 170-175 ^oC followed by 1 h at 200-210 ^oC. The cooled mixture was treated with H_2O, and the somewhat oily solid precipitated was washed with 5% aq HCl and H_2O to get rid of the excess urea. Crystallization from 80% ethanol provided **12** (7.50 g, 48%) as a white solid.

To a solution of **12** (7.00 g, 36.8 mmol) in anhyd DMF (70 mL) was added NaH (60%w/w in mineral oil, 2.3 g, 55.2 mmol) in small portion at 0^oC. After stirring for 1 h under N_2 at rt, the mixture was cooled to 0^oC. Then propargyl bromide (6.5 mL, 73.6 mmol) was added dropwise over 30 min. After stirring for an additional 2 h, all the starting material **12** was consumed as evident by TLC analysis. Then the mixture was poured into ice water (40 mL) carefully, and extracted thoroughly with EtOAc (3 × 50 mL). The combined organic phases were washed with sat aq NaCl (3 × 30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 20-50% EtOAc in hexanes with 10% CH_2Cl_2) afforded pure propargyl amide **13** (8.20 g, 98%) of as a brown solid. **13:** R_f = 0.20 [33% EtOAc/hexanes]; mp 70-72 ^oC; $[\alpha]_D^{25}$ = + 123.1 ^{o} [*c* 2.0, CH_2Cl_2]; ^1H NMR (400 MHz, $CDCl_3$) δ 0.75 (d, 3H, *J* = 6.4 Hz), 2.14 (t, 1H, *J* = 2.4 Hz), 2.80 (s, 3H), 3.35 (dd, 1H, *J* = 2.4, 17.6 Hz), 3.80 (dq, 1H, *J* = 6.4, 8.8 Hz), 4.51 (dd, 1H, *J* = 2.4, 17.6 Hz), 7.18-7.20 (m, 3H), 7.30-7.38 (m, 3H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 14.7, 28.9, 32.3, 55.9, 61.3, 72.3, 78.5, 128.2, 128.5, 128.9, 135.5, 160.8; IR (neat) cm^{-1} 3226m, 2975m, 1697s, 1480m, 1437s, 1402s, 1365m; mass spectrum (APCI): m/e (% relative intensity) 229.2 (100) $(M+H)^+$, 191.2 (5); HRMS (MALDI) calcd for $C_{14}H_{17}ON$ $(M+H)^+$ 229.1335, found 229.1334.

To a solution of propargyl amide **13** (2.50 g, 11.0 mol) in anhyd THF (20 mL) was added *t*-BuOK (250.0 mg, 2.20 mmol) at 0 °C and the color of reaction turned into black. After stirring for 2 h under N_2 at rt, the mixture was filtered through a bed of Celite™ and diluted with EtOAc (50 mL). The mixture was washed with water (3 × 15 mL), dried over Na_2SO_4 and charcoal (to get rid of the color). Concentration under reduced pressure afforded **9** (2.40 g, 95%) as a yellow solid. **9:** R_f = 0.30 [33% EtOAc/hexanes]; mp 97-100 °C; $[\alpha]_D^{25}$ = + 105.2 ° [*c* 1.60, CH_2Cl_2]; ^1H NMR (500 MHz, $CDCl_3$) δ 0.78 (d, 3H, *J* = 7.0 Hz), 2.81 (s, 3H), 3.85 (dq, 1H, *J* = 6.5, 9.0 Hz), 4.70 (d, 1H, *J* = 9.0 Hz), 4.79 (dd, 1H, *J* = 6.0, 9.0 Hz), 5.08 (dd, 1H, *J* = 6.5, 9.0 Hz), 7.00 (dd, 1H, *J* = 6.5, 6.5 Hz), 7.10 (dd, 2H, *J* = 2.0, 9.0 Hz), 7.27-7.33 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.3, 29.1, 55.9, 61.2, 86.9, 96.7, 128.2, 128.5, 136.4, 158.2, 202.7; IR (neat) cm^{-1} 1689s, 1455m, 1420s, 1397s; mass spectrum (APCI): m/e (% relative intensity) 229.2 (100) $(M+H)^+$, 191.2 (15); HRMS (MALDI) calcd for $C_{14}H_{17}ON$ $(M+H)^+$ 229.1335, found 229.1333.

Synthesis of Aldehyde 15.



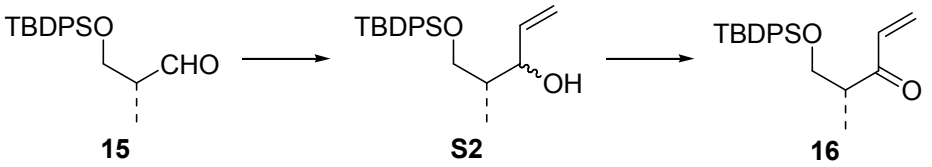
14 **S1** **15**

To a solution of **14** (5.00 g, 42.3 mmol) and imidazole (6.20 g, 91.8 mmol) in anhyd DMF (2 mL) was added TBDPSCl (12.2 g, 44.2 mol) at 0 °C. After stirring for 2 h under N_2 at rt, all the starting material **14** was consumed as evident via TLC analysis. Then the mixture was poured into water (40 mL), and extracted thoroughly with Et_2O (3 × 80 mL). The combined organic phases were washed with sat aq NaCl (2 × 40 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 5-10% EtOAc in hexanes) afforded pure silyl ether **S1** (14.1 g, 94%) of as a colorless oil. **S1:** R_f = 0.50 [10% EtOAc/hexanes]; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.17 (d, 3H, *J* = 7.0 Hz), 2.74 (ddq, 1H, *J* = 7.2, 7.2, 7.2 Hz), 3.70 (s, 3H), 3.74 (dd, 1H, *J* = 5.6, 10.0 Hz), 3.85 (dd, 1H, *J* = 7.2, 10.0 Hz), 7.37-7.46 (m, 6H), 7.67-7.69 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 19.2, 26.7, 42.4, 51.5, 65.9, 127.6, 129.6, 133.5, 133.7, 135.6, 175.3.

To a solution of silyl ether **S1** (3.00 g, 8.5 mmol) in anhyd CH_2Cl_2 (30 mL) was added DIBAL-H (1.0 *M* in Hexanes, 9 mL, 9.0 mmol) dropwise over 8 min at −78°C. After stirring for an additional 6 h at −78 °C, the reaction was quenched by adding MeOH (3 mL) via syringe pump dropwise to maintain the temperature below −70 °C. Then the resulting mixture was warmed up to rt

slowly and poured into sat aq potassium-sodium tartrate solution (30 mL). The mixture was vigorously stirred at rt until the phase separation occurred and the aqueous layer was extracted thoroughly with CH_2Cl_2 (3 × 25 mL). The combined organic phases were washed with sat aq NaCl (2 × 15 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 5-10% EtOAc in hexanes) afforded pure aldehyde **15** (2.7 g, 97%) as a colorless oil. **15:** R_f = 0.50 [10% EtOAc/hexanes]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (s, 9H), 1.09 (d, 3H, *J* = 6.8 Hz), 2.65 (m, 1H), 3.68 (s, 3H), 3.83 (dd, 1H, *J* = 6.0, 10.4 Hz), 3.90 (dd, 1H, *J* = 4.8, 10.4 Hz), 7.36-7.43 (m, 6H), 7.63-7.66 (m, 4H), 9.76 (dd, 1H, *J* = 1.6, 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.5, 19.5, 27.0, 49.1, 64.4, 128.0, 130.0, 133.4, 135.8, 204.6.

Synthesis of Chiral Enone 16.

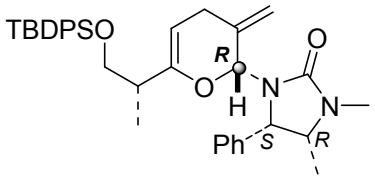


To a solution of vinyl magnesium bromide (1.0 *M*, 48.0 mL, 48.0 mmol) was added a solution of aldehyde **15** (12.0 g, 36.8 mmol) in anhyd THF (50 mL) dropwise over 15 min at −78 °C. After stirring for 5 min under N_2 at −78 °C, all the starting material **15** was consumed as evident by TLC analysis. Then the mixture was poured into sat aq NH_4Cl (100 mL), and extracted with Et_2O (2 × 100 mL). The combined organic phases were washed with sat aq NaCl (2 × 30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 5-20% EtOAc in hexanes) afforded allyl alcohol **S2** (10.8 g, 83%) of as a colorless oil.

To a solution of oxalyl chloride (2.80 mL, 30.8 mmol) in anhyd CH_2Cl_2 (70 mL) was added a solution of Me_2SO (4.6o mL, 61.6 mmol) in anhyd CH_2Cl_2 (15 mL) dropwise at −78 °C. The reaction mixture was stirred for 5 min at this temperature and a solution of the above allyl alcohol **S2** (10.0 g, 28.2 mmol) in anhyd CH_2Cl_2 (20 mL) was added over 10 min. After stirring for an additional 1 h, triethylamine (20.0 mL, 142.8 mmol) was added dropwise at −78 °C. The mixture was stirred for 10 min and then allowed to warm to around −20 °C. Then the mixture was poured into water, and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic phases were washed with sat aq NH_4Cl (3 × 50 mL) and water (2 × 50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 3-5% EtOAc in hexanes) afforded pure chiral enone **16** (8.00 g, 80%) as a colorless oil. **16:** R_f = 0.50 [10% EtOAc/hexanes]; $[\alpha]_D^{25} = -18.1^{o}$ [*c* 1.40, CH_2Cl_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (s, 9H), 1.08 (d, 3H, *J* = 6.8 Hz), 3.12 (ddq, 1H, *J* = 7.2, 7.2, 7.2 Hz), 3.67 (dd, 1H, *J* = 5.6, 10.0 Hz), 3.87 (dd, 1H, *J* = 7.2, 10.0 Hz), 5.76 (dd, 1H, *J* = 1.2, 10.6 Hz), 6.23 (dd, 1H, *J* = 1.2, 17.6 Hz), 6.44 (dd, 1H, *J* = 10.4, 17.5 Hz), 7.36-7.44 (m, 8H), 7.62-7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 19.5, 27.0,

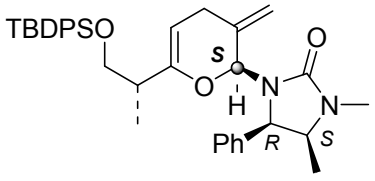
46.0, 66.3, 127.9, 128.3, 129.9, 133.6, 133.7, 135.8, 135.9, 136.1, 203.1; IR (neat) cm^{-1} 2931s, 1698s, 1679s, 1611m, 1472m, 1427s, 1361s; mass spectrum (APCI): m/e (% relative intensity) 275 (100) $(M\text{-}Ph+H)^+$, 229.2 (22); HRMS (MALDI) calcd for $C_{22}H_{28}O_2NaSi$ $(M+Na)^+$ 375.1751, found 375.1752.

The Hetero [4 + 2] Cycloadditions and Hydrogenations.



17

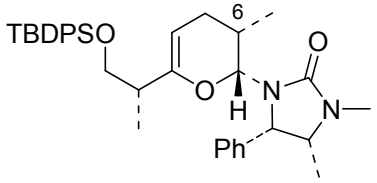
To a solution of chiral enone **16** (2.48 g, 7.03 mmol) in anhyd CH_3CN (50 mL) was added allenamide **9** (2.22 g, 9.72 mmol). This reaction mixture was sealed in sealed-tube equipped under N_2 and heated up to 90 ^oC for 2 d. Concentration under reduced pressure and purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-20% EtOAc in hexanes) afforded pure cycloadduct **17** (1.96 g, 58% based on recovery of 17% **16**) of as a colorless oil. **17:** R_f = 0.50 [33% EtOAc/hexanes]; $[\alpha]_D^{25}$ = – 100.4 ^{o} [*c* 1.00, CH_2Cl_2]; ^1H NMR (500 MHz, $CDCl_3$) δ 0.59 (d, 3H, *J* = 6.5 Hz), 1.11 (d, 3H, *J* = 6.5 Hz), 1.13 (s, 9H), 2.23 (dd, 1H, *J* = 2.5, 20.5 Hz), 2.39 (m, 1H), 2.51 (dd, 1H, *J* = 4.0, 20.0 Hz), 2.71 (s, 3H), 3.56-3.63 (m, 2H), 3.84 (dd, 1H, *J* = 6.5, 10.0 Hz), 4.52 (dd, 1H, *J* = 3.6, 4.0 Hz), 4.78 (s, 1H), 4.86 (d, 1H, *J* = 8.5 Hz), 5.03 (s, 1H), 6.26 (s, 1H), 7.09-7.10 (m, 2H), 7.24-7.28 (m, 3H), 7.42-7.52 (m, 6H), 7.71-7.74 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7, 14.8, 19.3, 26.9, 26.8, 28.6, 41.3, 56.7, 59.5, 66.5, 80.9, 94.4, 114.7, 127.59, 127.63, 127.68, 127.7, 129.50, 129.57, 133.8, 134.2, 135.46, 135.54, 135.59, 137.78, 137.98, 154.3, 161.4; IR (neat) cm^{-1} 2957s, 1710s, 1456m, 1396s, 1361s; mass spectrum (APCI): m/e (% relative intensity) 581.2 (25) $(M+H)^+$, 439.3 (100), 405.2 (80), 279.2 (50), 191.2 (75), 101.1 (75); HRMS (MALDI) calcd for $C_{36}H_{45}N_2O_3Si$ $(M+H)^+$ 581.3199, found 581.3761.



18

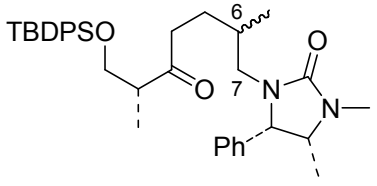
To a solution of enone **16** (248.0 mg, 0.70 mmol) in anhyd CH_3CN (5 mL) was added allenamide *ent*-**9** (221.0 mg, 0.97 mmol). This reaction mixture was sealed in sealed-tube equipped under N_2 and heated up to 90 ^oC for 2 d. Concentration under reduced pressure and purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-20% EtOAc in hexanes) afforded pure **18** (190.0 mg, 54% based on recovery of 13% **16**) of as a colorless oil (white solid can be recrystallized from Hexanes). **18:** R_f = 0.50 [33% EtOAc/hexanes]; mp 75-76 ^oC; $[\alpha]_D^{23}$ = + 72.6 ^{o} [*c* 2.35, CH_2Cl_2]; ^1H NMR (400 MHz, $CDCl_3$) δ 0.58 (d, 3H, *J* = 6.4 Hz), 1.05 (s, 9H), 1.09 (d, 3H, *J* =

6.8 Hz), 2.14 (dd, 1H, *J* = 2.8, 20.4 Hz), 2.39 (m, 1H), 2.47 (dd, 1H, *J* = 4.0, 20.4 Hz), 2.64 (s, 3H), 3.52 (dq, 1H, *J* = 8.4, 6.4 Hz), 3.58 (dd, 1H, *J* = 7.2, 9.6 Hz), 3.78 (dd, 1H, *J* = 6.0, 9.6 Hz), 4.46 (t, 1H, *J* = 3.6 Hz), 4.74 (t, 1H, *J* = 1.0 Hz), 4.75 (d, *J* = 8.4 Hz), 4.98 (s, 1H), 6.20 (s, 1H), 7.04-7.06 (m, 2H), 7.20-7.22 (m, 3H), 7.35-7.43 (m, 6H), 7.64-7.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 15.2, 19.6, 27.0, 27.2, 28.9, 41.2, 57.0, 59.9, 66.7, 81.1, 94.6, 115.0, 127.84, 127.86, 127.9, 128.1, 129.75, 129.80, 134.1, 134.4, 135.75, 135.84, 135.88, 138.0, 138.2, 154.7, 161.7; IR (neat) cm^{-1} 2930s, 2856s, 1708s, 1472m, 1425s, 907s; mass spectrum (APCI): m/e (% relative intensity) 581.3 (100) $(M+H)^+$, 567.1 (40), 201.3 (10), 101.2 (25); HRMS (ESI) calcd for $C_{36}H_{44}N_2O_3SiNa$ $(M+Na)^+$ 603.3019, found 603.3011.



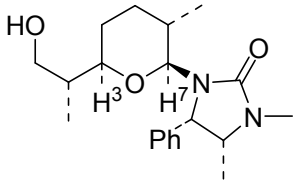
19

To a heterogeneous mixture of Pt/C (5%w/w, 1.40 g, 0.33 mmol) and cycloadduct **17** (3.80 g, 6.55 mmol) in MeOH (140 mL) was added $NaBH_4$ (800.0 mg, 21.0 mmol) in small portions at 0 ^oC carefully over 2 min. The mixture was hydrogenated with a H_2-balloon for 2 h at rt, and after which, the catalyst was filtered and washed with MeOH (50 mL). Removing MeOH under reduced pressure and the residue was diluted with Et_2O (100 mL). This mixture was washed with water (2 × 30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-17% EtOAc in hexanes) afforded pure **19** (2.40 g, 64%) as a colorless oil. **19:** R_f = 0.50 [33% EtOAc/hexanes]; $[\alpha]_D^{25}$ = – 29.9 ^{o} [*c* 1.45, CH_2Cl_2]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.67 (d, 3H, *J* = 6.5 Hz), 0.76 (d, 3H, *J* = 6.5 Hz), 1.14-1.16 (m, 12H), 1.22 (m, 1H), 1.94-2.04 (m, 2H), 2.43 (m, 1H), 2.75 (s, 3H), 3.63 (dd, 1H, *J* = 7.0, 9.5 Hz), 3.73 (dq, 1H, *J* = 6.5 Hz), 3.88 (dd, 1H, *J* = 6.5, 10.0 Hz), 4.49 (dd, 1H, *J* = 3.5, 4.0 Hz), 4.78 (s, 1H, *J* = 8.5 Hz), 5.83 (d, 1 H, *J* = 3.5 Hz), 7.33 (m, 4H), 7.43-7.52 (m, 7H), 7.75-7.76 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.9, 15.4, 15.6, 19.7, 27.2, 27.3, 29.0, 30.1, 41.5, 57.9, 58.8, 66.9, 83.0, 94.9, 127.89, 127.91, 127.93, 127.98, 129.84, 129.88, 134.26, 134.44, 135.87, 135.93, 139.22, 154.8, 163.5; IR (neat) cm^{-1} 2960s, 1710s, 1426s, 1393s, 1363m; mass spectrum (APCI): m/e (% relative intensity) 583.0 (20) $(M+H)^+$, 439.4 (100), 393.3 (50), 279.2 (30), 191.2 (20), 101.1 (75); HRMS (MALDI) calcd for $C_{36}H_{46}N_2O_3SiNa$ $(M+Na)^+$ 605.3170, found 605.3202.



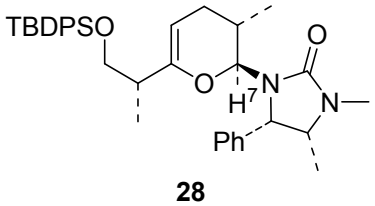
20

20: R_f = 0.30 [33% EtOAc/hexanes]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76 (d, 3H, *J* = 6.8 Hz), 0.77 (d, 3H, *J* = 6.8 Hz), 0.87 (d, 3H, *J* = 6.8 Hz), 0.96 (d, 3H, *J* = 6.8 Hz), 1.003 (d, 3H, *J* = 7.2 Hz), 1.007 (s, 9H), 1.02 (s, 9H), 1.03 (d, 3H, *J* = 6.8 Hz), 1.23-1.35 (m, 2H), 1.56-1.72 (m, 3H), 1.75-1.83 (m, 1H), 2.38-2.65 (m, 6H), 2.74 (s, 3H), 2.75 (s, 3H), 2.77-2.87 (m, 2H), 3.41-3.50 (m, 2H), 3.60-3.67 (m, 2H), 3.72-3.84 (m, 4H), 4.55 (d, 1H, *J* = 8.8 Hz), 4.66 (d, 1H, *J* = 8.8 Hz), 7.09-7.14 (m, 4H), 7.27-7.44 (m, 18H), 7.60-7.66 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3, 13.4, 15.05, 15.10, 17.56, 17.60, 19.41, 19.43, 27.02, 27.04, 27.17, 28.01, 29.41, 30.95, 31.78, 39.57, 40.33, 47.56, 47.75, 48.71, 48.75, 56.23, 62.44, 62.85, 66.48, 66.53, 127,96, 128.34, 128.44, 128.66, 128.73, 129.97, 133.46, 133.59, 135.75, 135.80, 136.09, 136.19, 162.31, 162.38, 213.54, 213.74; IR (neat) cm^{-1} 2932m, 2858m, 1698s, 1427s, 1384m; mass spectrum (APCI): m/e (% relative intensity) 585.3 (80) $(M+H)^+$, 329.1 (80); HRMS (MALDI) calcd for $C_{36}H_{48}N_2O_3SiNa$ $(M+Na)^+$ 607.3326, found 607.3336.



27

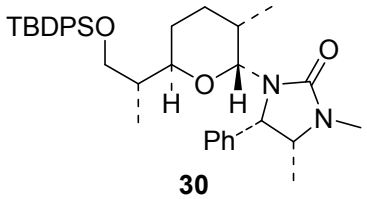
To a solution of **31** (40.0 mg, 0.068 mmol) in CH_3CN (1.2 mL) was added TBAF (1.0 *M* in THF, 136.0 μL, 0.136 mmol) at 0 ^oC. This mixture was stirred for 24 h at rt, all the starting material **31** was consumed as evident by TLC analysis. The reaction was quenched by adding water (5 mL), and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 20-100% EtOAc in hexanes) afforded pure **27** (18.0 mg, 78%) as a white solid. **27:** R_f = 0.20 [66% EtOAc/hexanes]; mp 141-143 ^oC $[\alpha]_D^{25}$ = + 98.8 ^{o} [*c* 0.60, CH_2Cl_2]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.57 (d, 3H, *J* = 7.5 Hz), 0.80 (d, 3H, *J* = 7.0 Hz), 0.96 (d, 3H, *J* = 6.0 Hz), 1.21-1.33 (m, 3H), 1.70 (m, 1H), 1.88-1.91 (m, 2H), 2.30 (s, 1H), 2.80 (s, 3H), 3.47 (d, 2H, *J* = 6.0 Hz), 3.55 (dd, 1H, *J* = 2.5, 10.5 Hz), 3.79 (dq, 1H, *J* = 7.0, 8.0 Hz), 4.66-4.67 (m, 2H), 7.27-7.37 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.2, 14.8, 17.5, 27.0, 28.9, 32.46, 32.48, 38.8, 56.8, 60.3, 66.5, 80.1, 87.9, 128.2, 128.3, 128.7, 137.8, 161.3; IR (neat) cm^{-1} 3417s, 2931s, 1687s, 1434s, 1402m, 1350m; mass spectrum (APCI): m/e (% relative intensity) 347.2 $(M+H)^+$ (100), 329.2 (20), 191.2 (10); HRMS (MALDI) calcd for $C_{20}H_{30}N_2O_3Na$ $(M+Na)^+$ 369.2149, found 369.2152.



28

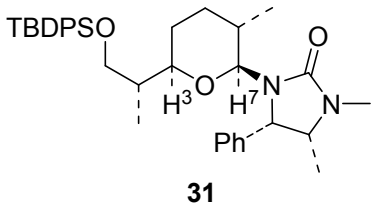
Crabtree's catalyst (2.50 mg, 0.0031 mmol) was dissolved in anhyd CH_2Cl_2 (1.2 mL). This mixture was stirred under 60 *psi* H_2 for 5-10 min at rt. To this solution of pre-activated Crabtree's

catalyst was added a solution of **19** (15.0 mg, 0.027 mmol) in CH_2Cl_2 (0.3 mL) under N_2. The mixture was stirred for 10 min and all the starting material **19** was consumed as evident by TLC analysis. Concentration under reduced pressure and purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-17% EtOAc in hexanes) afforded pure **28** (6.00 mg, 40%) as a colorless oil. **28:** R_f = 0.40 [33% EtOAc/hexanes]; $[\alpha]_D^{25}$ = + 43.3 ^{o} [*c* 0.40, $CHCl_3$]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.67 (d, 3H, *J* = 7.0 Hz), 0.73 (d, 3H, *J* = 7.0 Hz), 0.99 (d, 3H, *J* = 7.0 Hz), 1.01 (s, 9H), 1.74 (dd, 1H, *J* = 10.5, 16.5 Hz), 2.02 (ddd, 1H, *J* = 6.0, 6.0, 17.0 Hz), 2.11 (dd, 1H, *J* = 7.0, 13.5 Hz), 2.25 (m, 1H), 2.78 (s, 3H), 3.19 (dd, 1H, *J* = 7.5, 9.5 Hz), 3.49 (dd, 1H, *J* = 6.0, 9.5 Hz), 3.73 (m, 1H), 4.30 (d, 1H, *J* = 4.0 Hz), 4.65 (d, 1H, *J* = 8.5 Hz), 4.95 (d, 1H, *J* = 10.0 Hz), 7.10 (m, 4H), 7.36-7.43 (m, 7H), 7.60-7.70 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7, 14.8, 17.4, 19.5, 27.1, 28.9, 29.2, 30.1, 41.0, 56.6, 60.0, 66.6, 85.5, 94.6, 127.7, 127.8, 127.84, 127.9, 128.0, 128.5, 129.6, 129.7, 134.4, 134.6, 135.9, 135.91, 137.6, 155.3, 160.8; IR (neat) cm^{-1} 2930m, 2856m, 1712s, 1428s, 1389m; mass spectrum (APCI): m/e (% relative intensity) 583.2 (100) $(M+H)^+$, 327.2 (80), 231.2 (30); HRMS (MALDI) calcd for $C_{36}H_{46}N_2O_3SiNa$ $(M+Na)^+$ 605.3170, found 605.3168.



30

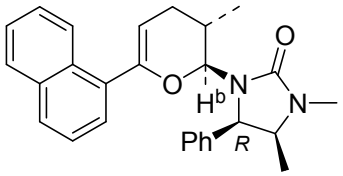
30: R_f = 0.50 [33% EtOAc/hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.63 (d, 3H, *J* = 6.0 Hz), 0.75 (d, 3H, *J* = 7.0 Hz), 0.93 (d, 3H, *J* = 6.5 Hz), 1.06 (m, 9H), 1.25-1.36 (m, 2H), 1.44-1.60 (m, 2H), 1.72-1.78 (m, 2H), 2.68 (s, 3H), 3.51 (dd, 1H, *J* = 6.0, 10.0 Hz), 3.68-3.73 (m, 2H), 4.11 (m, 1H), 4.75 (d, 1H, *J* = 9.0 Hz), 5.16 (d, 1H, *J* = 5.5 Hz), 7.33 (m, 4H), 7.43-7.52 (m, 7H), 7.75-7.76 (m, 4H); mass spectrum (APCI): m/e (% relative intensity) 585.3 $(M+H)^+$ (100), 507.3 (20), 329.2 (80).



31

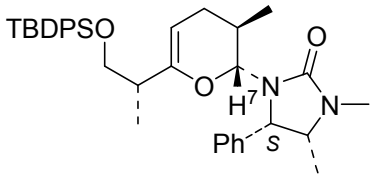
To a solution of **19** (54.0 mg, 0.093 mmol) in anhyd CH_2Cl_2 (3 mL) was added Crabtree's catalyst (7.50 mg, 0.0093 mmol). This mixture was hydrogenated under 60 *psi* for 2 h at rt. Concentration under reduced pressure and purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-13% EtOAc in hexanes) afforded pure **31** (40.0 mg, 74%) as a colorless liquid. **31**: R_f = 0.30 [20% EtOAc/hexanes]; $[\alpha]_D^{25}$ = + 15.2 ^{o} [*c* 0.60, $CHCl_3$]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.72 (d, 3H, *J* = 6.4 Hz), 0.89 (d, 3H, *J* = 6.8 Hz), 1.03 (s, 9H), 1.05 (d, 3H, *J* = 7.6 Hz), 1.13 (m, 1H), 1.28 (m, 1H), 1.48 (m, 1H), 1.74-1.80 (m, 2H), 1.97 (m, 1H), 2.76 (s, 3H), 3.28-3.32 (m, 2H), 3.45 (dd, 1H, *J* = 6.0, 10.0Hz Hz), 3.70 (dd, 1H, *J* = 6.4, 8.4 Hz), 4.46 (d, 1H, *J* =

8.4 Hz), 4.65 (d, 1H, *J* = 8.8 Hz), 7.14 (m, 4 H), 7.37-7.43 (m, 6H), 7.61-7.66 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.5, 14.7, 17.2, 19.3, 26.9, 28.5, 28.7, 32.35, 32.43, 40.6, 56.3, 59.9, 65.9, 77.6, 88.0, 127.4, 127.5, 127.53, 127.56, 127.60, 128.5, 129.40, 129.42, 133.9, 134.2, 135.6, 135.7, 137.7, 160.7. IR (neat) cm^{-1} 293m, 1706s, 1429m; mass spectrum (APCI): m/e (% relative intensity) 585.3 $(M+H)^+$ (100), 507.2 (15), 329.2 (20); HRMS (MALDI) calcd for $C_{36}H_{48}N_2O_3SiNa$ $(M+Na)^+$ 607.3326, found 607.3511.



39

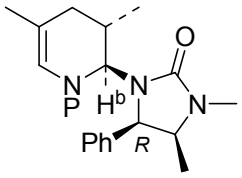
To a solution of **37** (20.0 mg, 0.050 mmol) in anhyd CH_2Cl_2 (1.5 mL) was added Crabtree's catalyst (4.00 mg, 0.005 mmol). This mixture was hydrogenated under 45 *psi* for 40 min at rt. Concentration under reduced pressure and purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-20% EtOAc in hexanes) afforded **39** (13.0 mg, 65%) as a colorless oil. **39:** R_f = 0.30 [33% EtOAc/hexanes]; $[\alpha]_D^{25}$ = - 64.1 ^{o} [*c* 1.10, $CHCl_3$]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.80 (d, 3H, *J* = 6.0 Hz), 0.81 (d, 3H, *J* = 6.0 Hz), 1.04 (m, 1H), 2.09 (ddd, 1H, *J* = 2.0, 10.5, 17.5 Hz), 2.77 (ddd, 1H, *J* = 5.5, 5.5, 17.5 Hz), 2.79 (s, 3H), 3.80 (dq, 1H, *J* = 6.5, 9.0 Hz), 4.94 (d, 1H, *J* = 9.0 Hz), 5.01 (dd, 1H, *J* = 2.5, 5.5 Hz), 5.65 (d, 1H, *J* = 10.0 Hz), 7.32-7.59 (m, 9H), 7.86 (d, 1H, *J* = 8.0 Hz), 7.89 (d, 1H, *J* = 8.0 Hz), 8.26 (d, 1H, *J* = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 17.5, 28.9, 29.9, 30.7, 57.1, 58.3, 87.0, 101.2, 125.4, 125.9, 126.2, 126.5, 126.8, 128.32, 128.35, 128.4, 128.87, 131.68, 133.86, 135.0, 138.7, 152.4, 162.8; IR (neat) cm^{-1} 2928m, 1711s, 1428m, 1395m; mass spectrum (APCI): m/e (% relative intensity) 413.2 (100) $(M+H)^+$, 213.2 (70); HRMS (MALDI) calcd for $C_{27}H_{27}N_2O_2$ $(M+H)^+$ 413.2229, found 413.2212.



40

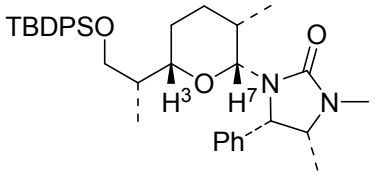
To a solution of **17** (20.0 mg, 0.035 mmol) in anhyd CH_2Cl_2 (1.2 mL) was added Crabtree's catalyst (2.80 mg, 0.0035 mmol). This mixture was hydrogenated under 60 *psi* for 1 h at rt. Concentration under reduced pressure and purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-17% EtOAc in hexanes) afforded pure **40** (10.0 mg, 50%) as a colorless oil. **40:** R_f = 0.50 [33% EtOAc/hexanes]; $[\alpha]_D^{25}$ = + 17.6 ^{o} [*c* 1.00, CH_2Cl_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.60 (d, 3H, *J* = 6.4 Hz), 0.74 (d, 3H, *J* = 6.4 Hz), 1.06 (d, 3H, *J* = 6.4 Hz), 1.07 (s, 9H), 1.47 (dq, 1H, *J* = 7.0, 10.4 Hz), 1.70 (dd, 1H, *J* = 12.0, 17.2 Hz), 1.89 (ddd, 1H, *J* = 5.6, 5.6, 16.4 Hz), 2.37 (m, 1H), 2.75 (s, 3H), 3.51 (dd, 1H, *J* = 3.6, 9.6 Hz), 3.68 (dq, 1H, *J* = 6.8, 9.2 Hz), 3.78 (d,

1H, J = 6.0, 9.6 Hz), 4.40 (dd, 1 H, J = 2.0, 5.6 Hz), 4.63 (d, 1H, J = 8.8 Hz), 5.15 (d, 1H, J = 10.4 Hz), 7.14-7.23 (m, 4H), 7.37-7.52 (m, 7H), 7.69 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 15.4, 17.4, 19.7, 27.2, 28.9, 29.6, 29.8, 41.1, 57.3, 58.3, 67.0, 86.3, 94.7, 127.87, 127.88, 128.1, 128.3, 128.8, 129.8, 134.3, 134.5, 135.9, 135.92, 138.6, 155.0, 162.8; IR (neat) cm^{-1} 2959s, 1712s, 1472m, 1427s, 1390m; mass spectrum (APCI): m/e (% relative intensity) 583.3 (100) $(M+H)^+$, 327.2 (80), 231.2 (60); HRMS (MALDI) calcd for $C_{36}H_{46}N_2O_3NaSi$ $(M+Na)^+$ 605.3170, found 605.3174.



43: P = SO_2Ph

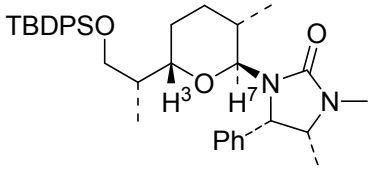
To a solution of **41** (15.0 mg, 0.034 mmol) in anhyd CH_2Cl_2 (1.5 mL) was added Crabtree's catalyst (3.00 mg, 0.0038 mmol). This mixture was hydrogenated under 60 *psi* for 24 h at rt. Concentration under reduced pressure and purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-20% EtOAc in hexanes) afforded pure **43** (5.60 mg, 37%) as a white solid. **43:** R_f = 0.40 [50% EtOAc/hexanes]; mp 148-151 ^{o}C; $[\alpha]_D^{25}$ = - 65.1^o [*c* 0.31, CH_2Cl_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.35 (d, 3H, J = 7.2 Hz), 0.71 (d, 3H, J = 6.4 Hz), 0.95 (m, 2H), 1.35 (d, 3H, J = 0.8 Hz), 1.70 (m, 1H), 2.74 (s, 3H), 3.76 (dd, 1H, J = 6.4, 8.8 Hz), 4.65 (d, 1H, J = 9.2 Hz), 5.36 (d, 1H, J = 3.6 Hz), 6.49 (d, 1H, J = 0.8 Hz), 7.20-7.29 (m, 5H), 7.49-7.60 (m, 3H), 7.86-7.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 18.4, 20.9, 29.1, 30.1, 32.2, 57.6, 58.9, 67.6, 115.5, 117.4, 127.5, 128.0, 129.3, 133.2, 138.7, 139.5, 162.9; IR (neat) cm^{-1} 2967m, 2918m, 2851m, 1697s, 1686s, 1478s, 1400s, 1367s, 1312s; mass spectrum (APCI): m/e (% relative intensity) 440.2 (100) $(M+H)^+$; HRMS (MALDI) calcd for $C_{24}H_{29}N_3O_3S$ $(M+H)^+$ 462.1827, found 462.1822.



26

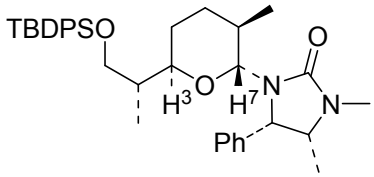
A heterogeneous mixture of Pt/Alumina (5%w/w, 80.0 mg, 0.020 mmol) and **19** (60.0 mg, 0.10 mmol) in hexanes (5 mL) was hydrogenated under 1500 *psi* in a high-pressure bomb at rt for 3 d. After which, the catalyst was filtered and washed with EtOAc (10 mL). Concentration under reduced pressure and purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-17% EtOAc in hexanes) afforded pure **26** (31.0 mg, 50%) as a colorless oil. **26:** R_f = 0.50 [33% EtOAc/hexanes]; $[\alpha]_D^{25}$ = + 49.8 ^{o} [*c* 1.00, CH_2Cl_2]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.62 (d, 3H, J = 6.5 Hz), 0.69 (d, 3H, J = 6.5 Hz), 0.96 (d, 3H, J = 7.0 Hz), 1.11 (s, 9H), 1.20-1.30 (m, 2H), 1.49 (ddd, 1H, J = 2.0, 6.0, 13.0 Hz), 1.71-1.80 (m, 2H), 1.93 (m, 1H), 2.70 (s, 3H), 3.50-3.60 (m, 3H), 3.75 (dd, 1H, J = 5.5, 10.0 Hz), 4.65 (d, 1H, J = 8.5 Hz), 5.15 (d, 1H, J = 2.0 Hz), 7.26-7.30 (m, 4 H),

7.42-7.48 (m, 7H), 7.26-7.30 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.6, 13.1, 15.5, 19.6, 22.3, 27.2, 28.9, 31.5, 31.6, 41.3, 57.8, 58.8, 66.1, 80.1, 86.5, 127.5, 127.8, 127.9, 129.8, 134.40, 134.44, 135.94, 135.95, 135.96, 136.00, 139.8, 168.2; IR (neat) cm^{-1} 2962s, 1708s, 1472m, 1427s, 1390s; mass spectrum (APCI): m/e (% relative intensity) 585.2 (100) $(M+H)^+$, 507.3 (30), 431.4 (20), 329.3 (80), 191.2 (30), 101.1 (90); HRMS (MALDI) calcd for $C_{36}H_{48}N_2O_3SiNa$ $(M+Na)^+$ 607.3332, found 607.3300.

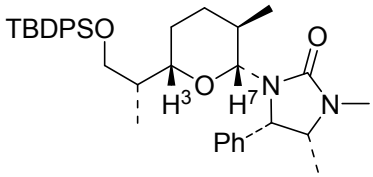


44

A heterogeneous mixture of Pt/Alumina (5%w/w, 6.00 mg, 0.0015 mmol) and **28** (9.0 mg, 0.015 mmol) in hexanes (1 mL) was hydrogenated under 1500 *psi* in a high-pressure bomb at rt for 6 d. After which, the catalyst was filtered and washed with EtOAc (10 mL). Concentration under reduced pressure and purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-17% EtOAc in hexanes) afforded pure **44** (89:11 at C3, 3.00 mg, 30%) as a colorless oil. **26:** R_f = 0.40 [33% EtOAc/hexanes]; $[\alpha]_D^{25}$ = + 65.3 ^{o} [*c* 0.40, $CHCl_3$]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.69 (d, 3H, *J* = 6.5 Hz), 0.93 (d, 3H, *J* = 6.5 Hz), 0.97 (d, 3H, *J* = 6.5 Hz), 1.13 (s, 9H), 1.16-1.23 (m, 1H), 1.57-1.62 (m, 1H), 1.68-1.80 (m, 2H), 1.87 (m, 1H), 2.80 (s, 3H), 3.00-3.06 (m, 1H), 3.55 (dq, 1H, *J* = 6.5, 6.5 Hz), 3.62 (dd, 1H, *J* = 3.5, 10.0 Hz), 3.73 (dd, 1H, *J* = 4.5, 10.0 Hz), 3.89 (ddd, 1H, *J* = 4.5, 4.5, 9.5 Hz), 4.17 (d, 1H, *J* = 8.0 Hz), 4.55 (d, 1H, *J* = 8.5 Hz), 7.22-7.27 (m, 3 H), 7.41-7.51 (m, 8H), 7.75 (d, 2H, *J* = 6.5 Hz), 7.79 (d, 2H, *J* = 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.8, 18.0, 19.6, 24.9, 27.1, 27.3, 28.6, 30.7, 35.4, 55.4, 61.5, 65.2, 73.3, 84.8, 127.8, 127.84, 128.0, 128.3, 129.7, 129.8, 134.2, 134.3, 136.0, 136.1, 136.6, 160.8; IR (neat) cm^{-1} 2979s, 1709s, 1472m, 1388s; mass spectrum (APCI): m/e (% relative intensity) 585.3 (80) $(M+H)^+$, 507.2 (20), 329.3 (100), 191.2 (20); HRMS (MALDI) calcd for $C_{36}H_{48}N_2O_3SiNa$ $(M+Na)^+$ 607.3326, found 607.3332.



45



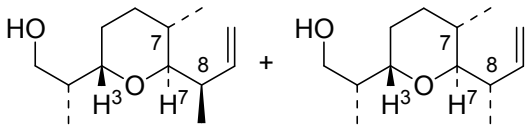
46

A heterogeneous mixture of Pt/Alumina (5%w/w, 67.0 mg, 0.017 mmol) and **40** (50.0 mg, 0.086 mmol) in hexanes (4 mL) was hydrogenated under 1500 *psi* in a high-pressure bomb at rt for 6 d. After which, the catalyst was filtered and washed with EtOAc (10 mL). Concentration under reduced pressure and purification of the crude residue via silica gel flash column chromatography (gradient eluent: 8-20% EtOAc in hexanes) afforded pure **46** (8.00 mg, 16%) and **45** (17. 0 mg, 34%) as colorless oil. **45:** R_f = 0.45 [33% EtOAc/hexanes]; $[\alpha]_D^{23}$ = + 5.10^o [*c* 0.35, CH_2Cl_2]; ^{1}H NMR (400

MHz, $CDCl_3$) δ 0.55 (d, 3H, *J* = 6.0 Hz), 0.73 (d, 3H, *J* = 6.8 Hz), 1.04 (s, 9H), 1.06 (d, 3H, *J* = 6.8 Hz), 1.10-1.28 (m, 2H), 1.38-1.43 (m, 1H), 1.53-1.60 (m, 2H), 2.10-2.17 (m, 1H), 2.75 (s, 3H), 3.47 (dd, 1H, *J* = 4.8, 10.4 Hz), 3.54 (dd, 1H, *J* = 4.4, 10.4 Hz), 3.75-3.79 (m, 1H), 3.82 (dq, 1H, *J* = 8.8, 6.4 Hz), 4.85 (d, 1H, *J* = 9.2 Hz), 4.95 (d, 1H, *J* = 10.0 Hz), 7.28 (m, 5H), 7.35-7.44 (m, 6H), 7.62-7.65 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 15.3, 17.7, 19.5, 26.2, 27.1, 27.6, 29.0, 32.8, 35.0, 57.2, 57.9, 66.8, 76.0, 82.4, 127.79, 127.85, 128.0, 128.2, 128.6, 129.8, 133.9, 135.83, 135.86, 135.93, 139.13, 162.95; IR (neat) cm^{-1} 2931s, 2858s, 1711s, 1427m, 1395s; mass spectrum (APCI): m/e (% relative intensity) 585.4 (55) $(M+H)^+$, 391.1 (40), 197.1 (70), 120.1 (75), 101.0 (100); HRMS (MALDI) calcd for $C_{36}H_{48}N_2O_3SiNa$ $(M+Na)^+$ 607.3326, found 602.3347.

46: R_f = 0.52 [33% EtOAc/hexanes]; $[\alpha]_D^{23}$ = + 31.0 ^{o} [*c* 0.12, CH_2Cl_2]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.54 (d, 3H, *J* = 6.4 Hz), 0.72 (d, 3H, *J* = 6.8 Hz), 0.95 (d, 3H, *J* = 6.8 Hz), 1.05 (s, 9H), 1.06-1.09 (m, 2H), 1.24 -1.27 (m, 1H), 1.43-1.46 (m, 1H), 1.60-1.63 (m, 1H), 1.84-1.94 (m, 1H), 2.68 (s, 3H), 3.35-3.39 (m, 1H), 3.48 (dd, 1H, *J* = 7.6, 10.0 Hz), 3.57 (dq, 1H, *J* = 9.2, 6.8 Hz), 3.75 (dd, 1H, *J* = 5.6, 10.0 Hz), 4.68 (d, 1H, *J* = 10.4 Hz), 4.72 (d, 1H, *J* = 9.2 Hz), 7.20-7.23 (m, 2H), 7.35-7.44 (m, 8H), 7.66-7.68 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.1, 15.3, 17.2, 19.6, 27.1, 27.3, 27.9, 29.0, 32.2, 33.7, 41.2, 57.3, 66.1, 78.6, 87.8, 127.8, 127.84, 128.0, 128.2, 128.7, 129.7, 134.2, 134.4, 135.9, 139.1, 162.9; IR (neat) cm^{-1} 2932s, 2858s, 1714s, 1429m, 1398s; mass spectrum (APCI): m/e (% relative intensity) 585.2 (100) $(M+H)^+$, 391.3 (30), 329.1 (65), 120.1 (75), 101.2 (80); HRMS (MALDI) calcd for $C_{36}H_{48}N_2O_3SiNa$ $(M+Na)^+$ 607.3327, found: 607.3333.

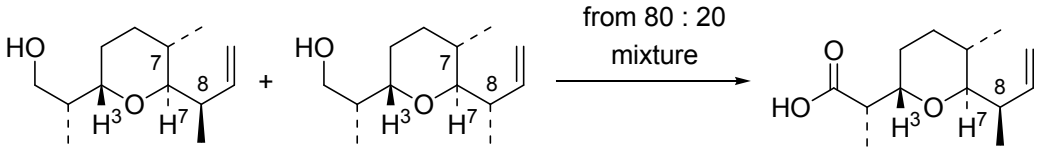
Crotylations and Oxidations.



50a **50b**

To a solution of **26** (340.0 mg, 0.58 mmol) and *Z*-crotylsilane (270.0 μL, 1.74 mmol) in CH_2Cl_2 (30 mL) was added $SnBr_4$ (1.13 g, 2.32 mmol) at −78 °C. Reaction was warmed to −35 °C slowly and stirred at this temperature for 24 h with exposure to the air. Then the mixture was quenched by adding sat aq $NaHCO_3$ (10 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were washed with sat aq NaCl (2 × 15 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 7-14% EtOAc in hexanes) afforded a mixture of **50a** and **50b** (1:3, 80.0 mg, 65%) as a colorless oil. **50b:** R_f = 0.30 [20% EtOAc/hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (d, 3H, *J* = 7.0 Hz), 1.04 (d, 3H, *J* = 7.0 Hz), 1.06 (d, 3H, *J* = 7.0 Hz), 1.35-1.40 (m, 1H), 1.48-1.63 (m, 2H), 1.70-1.88 (m, 3H), 2.71 (m, 1H), 3.19 (dd, 1H, *J* = 3.0, 9.0 Hz), 3.41 (bs, 1H), 3.47 (ddd, 1H, *J* = 3.5, 9.0, 9.0 Hz), 3.60 (m, 1 H), 5.00 (d, 1H, *J* = 10.5 Hz), 5.05 (d, 1H, *J* = 16.5 Hz), 5.64 (ddd, 1H, *J* = 8.0, 10.0, 17.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 16.1, 18.6, 24.9, 25.0, 28.4, 38.3, 39.1, 68.2, 76.5, 81.9, 114.9, 142.1. **50a:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.80 (d, 3H, *J* = 6.5 Hz), 0.99 (d, 3H, *J* = 7.0 Hz), 1.03 (d, 3H, *J* = 7.0 Hz), 1.36-1.41 (m, 1H), 1.50-1.60 (m, 2H), 1.69-1.78 (m, 2H), 1.81-1.87 (m,

1H), 2.65 (m, 1H), 3.06 (dd, 1H, J = 4.0, 8.0 Hz), 3.21 (dd, 1H, J = 4.0, 8.0 Hz), 3.48-3.55 (m, 1H), 3.57 (dd, 1 H, J = 4.0, 10.6 Hz), 3.57-3.64 (m, 1H), 5.05 (d, 1H, J = 10.0 Hz), 5.07 (d, 1H, J = 15.0 Hz), 5.84 (ddd, 1H, J = 8.5, 10.0, 15.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.47, 18.50, 25.2, 25.7, 29.1, 38.0, 38.9, 67.7, 76.1, 81.7, 114.6, 141.4; IR (neat) cm^{-1} 3439s, 2961s, 1640w, 1459s, 1376m; mass spectrum (APCI): m/e (% relative intensity) 213.3 (100) $(M+H)^+$, 195.2 (85), 177.2 (90), 157.2 (30), 139.2 (45); HRMS (ESI) calcd for $C_{13}H_{24}O_2Na$ $(M+Na)^+$ 235.1674, found 235.1673.



50a **50b** **51a**

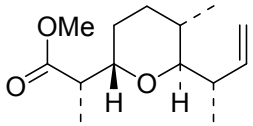
To a solution of a 4:1mixture of crotylation products **50a** and **50b** (7.00 mg, 0.033 mmol) in CH_2Cl_2 (0.5 mL) was added Dess-Martin Periodinane (15.0 mg, 0.035 mmol) at 0 °C. After stirring for 30 min, this mixture was quenched by adding sat aq $NaHCO_3$ (0.3 mL), sat aq $Na_2S_2O_3$ (0.3 mL), and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 5-10% EtOAc in hexanes) afforded the corresponding aldehyde intermediate (4:1, 6-7.0 mg, 96%) as a colorless oil.

To a solution of the aldehyde prepared above (12.0 mg, 0.057 mmol) and 2-Me-2-butene (20.0 μL) in *t*-BuOH (0.2 mL) and H_2O (0.1 mL) were added NaH_2PO_4 (17.0 mg, 0.123 mmol) and $NaClO_2$ (20.0 mg, 0.221 mol) at 0°C. After stirring for 5 min, this mixture was quenched by adding sat aq $NaHCO_3$ (0.3 mL), sat aq $Na_2S_2O_3$ (0.3 mL), and extracted with EtOAc (3 × 5 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-50% EtOAc in hexanes, then MeOH) afforded acids **51a** and **51b** (4:1, 11.0 mg, 85%) as a white solid. Crystallization in hexanes afforded pure acid **51a** (5.00 mg). **51a:** R_f = 0.40 [33% EtOAc/hexanes]; mp 88-90 °C; $[\alpha]_D^{25}$ = + 32.0 ° [*c* 0.40, CH_2Cl_2]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 (d, 3H, J = 6.5 Hz), 1.00 (d, 3H, J = 7.0 Hz), 1.14 (d, 3H, J = 7.0 Hz), 1.29-1.36 (m, 1H), 1.62-1.71 (m, 4H), 2.54 (ddq, 1 H, J = 6.0, 9.0, 7.0 Hz), 2.83 (dq, 1 H, J = 7.0, 10.0 Hz), 3.30 (dd, 1 H, J = 6.0, 6.0 Hz), 3.87 (ddd, 1H, J = 5.0, 5.0, 10.0 Hz), 5.00 (d, 1 H, J = 12.0 Hz), 5.01 (d, 1 H, J = 15.5 Hz), 5.81 (ddd, 1H, J = 9.0, 12.0, 15.0 Hz), 10.93 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 18.1, 18.13, 24.9, 26.1, 30.5, 39.1, 41.6, 73.6, 81.3, 114.9, 140.4, 178.9;IR (neat) cm^{-1} 2930s, 1711s, 1460s, 1378m; mass spectrum (APCI): m/e (% relative intensity) 227.2 (100) $(M+H)^+$, 209.2 (65), 153.2 (45). HRMS (ESI) calcd for $C_{13}H_{22}O_3Na$ $(M+Na)^+$ 249.1467, found 249.1467.

51b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.008 (d, 3H, J = 6.8 Hz), 1.02 (d, 3H, J = 6.0 Hz), 1.15 (d, 3H, J = 7.2 Hz), 1.32-1.41 (m, 1H), 1.54-1.59 (m, 2H), 1.61-1.66 (m, 1H), 1.73-1.81 (m, 1H), 2.63-2.71 (m, 2H), 3.25 (dd, 1 H, J = 3.6, 8.0 Hz), 3.77 (ddd, 1H, J = 6.8, 6.8, 6.8 Hz), 4.96 (d, 1 H, J = 10.4 Hz), 5.02 (d, 1 H, J = 16.0 Hz), 5.64 (ddd, 1 H, J = 8.0, 10.0, 17.2 Hz), 11.51 (brs, 1H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 13.8, 15.8, 18.5, 23.9, 25.2, 28.7, 38.5, 44.1, 72.5, 81.9, 114.5, 142.2, 180.4.

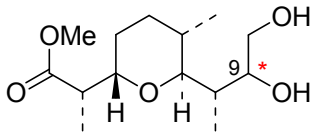
Esterification of 51a and 51b.



52

To a solution of a 1:3 mixture of acids **51a** and **51b** (36.0 mg, 0.16 mmol) in toluene (1 mL) and MeOH (0.5 mL) was added $TMSCHN_2$ (100.0 μL, 2.0 M in Et_2O, 0.19 mmol) at rt. After stirring for 30 min, this mixture was concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-13% EtOAc in hexanes) afforded ester **52** (1:3, 34.0 mg, 90%) as a colorless oil. **52:** R_f = 0.60 [20% EtOAc/hexanes]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, 3H, J = 6.4 Hz), 0.96 (d, 3H, J = 6.8 Hz), 0.97 (d, 3H, J = 6.4 Hz), 1.00 (d, 3H, J = 6.8 Hz), 1.07 (d, 3H, J = 7.2 Hz), 1.08 (d, 3H, J = 7.2 Hz), 1.20-1.78 (m, 10H), 2.41-2.49 (m, 1H), 2.62 (ddq, 1 H, J = 7.2, 7.2, 7.2 Hz), 2.83 (dq, 1 H, J = 7.2, 9.2 Hz), 2.98 (dq, 1 H, J = 6.8, 10.4 Hz), 3.19 (dd, 1 H, J = 4.4, 8.0 Hz), 3.21 (m, 1H), 3.68 (s, 6H), 3.76 (ddd, 1H, J = 4.4, 7.6, 9.2 Hz), 3.89-3.93 (m, 1H), 4.92-5.02 (m, 4H), 5.64 (ddd, 1H, J = 8.4, 10.4, 17.2 Hz), 5.83 (ddd, 1H, J = 10.0, 10.0, 18.0 Hz),; ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.5, 15.4, 17.9, 18.0, 18.5, 23.9, 24.9, 25.6, 27.0, 29.0, 31.8, 38.6, 39.4, 40.8, 43.9, 51.7, 51.8, 73.0, 74.6, 80.1, 81.3, 114.0, 114.6, 140.4, 142.7, 175.9, 176.1; IR (neat) cm^{-1} 2951s, 1739s, 1460m, 1376m; mass spectrum (APCI): m/e (% relative intensity) 241.2 (100) $(M+H)^+$, 223.2 (30), 209.2 (20). HRMS (ESI) calcd for $C_{14}H_{24}O_3Na$ $(M+Na)^+$ 263.1623, found 263.1620.

Dihydroxylation of 52.

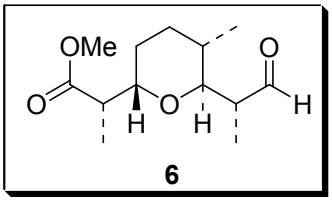


53 (8:1 at C9)

To a solution of the above ester **52** (34.0 mg, 0.14 mmol) and NMO (17.0 mg, 1.46 mmol) in acetone (0.8 mL) and water (80 μL) was added catalytic amount of OsO_4 at 0°C. After stirring for 2 h at rt, then the mixture was quenched with sat aq $Na_2S_2O_3$ (0.5 mL), and extracted with EtOAc (5 × 8 mL). The combined organic phases were dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 10-33% EtOAc in hexanes) afforded diol **53** (**major:** 8:1 at C9, 23.0 mg, 60%, **minor:** 7.00 mg, 20%) as colorless oil. **53:** R_f = 0.40 [50% EtOAc/hexanes]; $[\alpha]_D^{25}$ = + 48.9 ^{o} [c 0.80, $CHCl_3$]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 (d, 3H, J = 6.0 Hz), 0.81 (d, 3H, J = 5.2 Hz), 1.08 (d, 3H, J = 6.8 Hz), 1.22-1.30 (m, 1H), 1.54-1.64 (m, 3H), 1.54-1.64 (m, 4H), 2.46 (dd, 1 H, J = 2.8, 8.8 Hz), 3.18 (dq, 1 H, J = 6.8, 10.0 Hz), 3.42-3.53 (m, 2H), 3.63-3.71 (m, 2H), 3.73 (s, 3H), 3.95 (dd, 1H, J = 5.2, 11.2 Hz), 4.05 (d, 1H, J = 5.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.1, 14.3, 17.8, 25.5, 27.6, 31.8, 37.1, 40.3, 52.5, 65.3, 72.6, 75.0, 75.5, 177.3; IR (neat) cm^{-1} 3453s, 2951s, 1736s, 1459m, 1380m; mass spectrum (APCI):

m/e (% relative intensity) 275.2 (100) $(M+H)^+$, 257.2 (50), 239.2 (40); HRMS (MALDI) calcd for $C_{14}H_{26}O_5Na$ $(M+Na)^+$ 297.1673, found 297.1679.

Intercepting Cossy's Intermediate.



6

To a solution of diol **53** (15.0 mg, 0.055 mmol) in anhyd CH_2Cl_2 (2.0 mL) was added $Pb(OAc)_4$ (41.0 mg, 0.093 mmol) at − 20°C. After stirring for 5 min, then the mixture was quenched with sat aq $Na_2S_2O_3$ (0.5 mL) and sat aq $NaHCO_3$ (0.5 mL), and extracted with Et_2O (3 × 8 mL). The combined organic phases were dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 5-10% EtOAc in hexanes) afforded **6** (7.00 mg, 53%) as colorless oil. **6:** R_f = 0.50 [33% EtOAc/hexanes]; $[\alpha]_D^{25}$ = + 2.0 ° [*c* 0.40, $CHCl_3$]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, 3H, *J* = 6.4 Hz), 1.04 (d, 3H, *J* = 7.2 Hz), 1.06 (d, 3H, *J* = 7.2 Hz), 1.36 (m, 1H), 1.58-1.78 (m, 4H), 2.56 (qdd, *J* = 7.2, 4.0, 0.8 Hz, 1H), 3.04 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.66 (s, 3H), 3.86 (m, 1H), 3.90 (dd, *J* = 8.8, 4.0 Hz, 1H), 9.55 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 6.3, 14.2, 17.6, 24.7, 26.6, 31.1, 40.6, 47.8, 51.7, 75.0, 75.3, 175.4, 204.5; IR (neat) cm^{-1} 2953s, 1737s, 1461m, 1379m; mass spectrum (APCI): m/e (% relative intensity) 243.2 (10) $(M+H)^+$, 225.2 (100), 207.2 (50), 185.2 (80); HRMS (MALDI) calcd for $C_{13}H_{22}O_4Na$ $(M+Na)^+$ 265.1410, found 265.1410.

Matching of Our Aldehyde 6 with Cossy's Intermediate.

Cossy's Intermediate [ppm]	Ours	Δ - $[\alpha]^{25}_{D}$
$[\alpha]^{20}_{D}$ = + 7.0° (c 0.70, $CHCl_3$)	$[\alpha]^{25}_{D}$ = + 2.0° (c 0.40, $CHCl_3$)	+ 5°

^{1}H NMR

Cossy's Intermediate [ppm]	Ours [ppm]	Δδ
0.92 (d, *J* = 6.6 Hz, 3H)	0.91 (d, *J* = 6.4 Hz, 3H)	0.01 ppm; 0.2 Hz
1.05 (d, *J* = 7.0 Hz, 3H)	1.04 (d, *J* = 7.2 Hz, 3H)	0.01 ppm; 0.2 Hz
1.07 (d, *J* = 7.4Hz, 3H)	1.06 (d, *J* = 7.2Hz, 3H)	0.01 ppm; 0.2 Hz
1.32 (m, 1H)	1.36 (m, 1H)	0.04 ppm
1.55-1.79 (m, 4H)	1.58-1.78 (m, 4H)	0.01-0.03 ppm
2.56 (qdd, *J* = 7.0, 4.0, 1.1Hz, 1H)	2.56 (qdd, *J* = 7.2, 4.0, 0.8Hz, 1H)	0.00 ppm; 0.2 Hz, 0.0Hz
3.05 (dq, *J* = 10.7, 7.0 Hz, 1H)	3.04 (dq, *J* = 10.8, 7.2 Hz, 1H)	0.01 ppm; 0.1 Hz, 0.2 Hz
3.67 (s, 3H)	3.66 (s, 3H)	0.01 ppm
3.87 (m, 1H)	3.86 (m, 1H)	0.01 ppm
3.91 (dd, *J* = 8.8, 4.0 Hz, 1H)	3.90 (dd, *J* = 8.8, 4.0 Hz, 1H)	0.01 ppm; 0.0 Hz, 0.0 Hz
9.56 (d, *J* = 1.1 Hz, 1H)	9.55 (d, *J* = 0.8 Hz, 1H)	0.01 ppm; 0.3 Hz

^{13}C NMR

Cossy [ppm]	Ours [ppm]	Δδ [ppm]
6.30	6.30	0.00
14.2	14.2	0.00
17.6	17.6	0.00
24.7	24.7	0.00
26.6	26.6	0.00
31.1	31.1	0.00
40.6	40.6	0.00
47.8	47.8	0.00
51.7	51.7	0.00
75.0	75.0	0.00
75.3	75.3	0.00
175.4	175.4	0.00
204.4	204.5	0.10