Supporting Information

One-Pot Regio- and Stereoselective Cyclization of 1,2,n-Triols

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Experimental Details

Representative Experimental Procedures and Supplemental Data

General: Methylene chloride was dried over CaH₂ and freshly distilled prior to use. Tetrahydrofuran was freshly distilled from Na/benzophenone. Trimethyl orthoacetate was dried over Na and distilled and stored over 4 Å molecular sieves. BF₃•Et₂O was treated with a small quantity of ethyl ether, and then distilled under reduced pressure from CaH₂. All the other reagents were used as purchased from Aldrich or TCI. NMR spectra were obtained using either a 300 MHz Inova or 500 MHz Varian NMR spectrometer and referenced using deuterated chloroform or methanol. IR spectra were recorded on Nicolet IR/42 spectrometer using NaCl cells. Column chromatography was performed using Silicycle (40-60 µm) silica gel. Pre-coated silica gel 60 F₂₅₄ plates were used for analytical TLC.

Preparation of 1a.

To a solution of *cis*-4-decenal (1.0 mL, 4.44 mmol, 1.0 equiv) in anhydrous THF (10 mL) was added DIBAL (8.9 mL of a 1.0 M solution in hexane, 8.89 mmol, 2.0 equiv) at 0 °C. The reaction mixture was stirred at rt for 12 h. The reaction was quenched with 10% HCl. The mixture was stirred for 4 h at rt until the aqueous layer turned clear. The two layers were separated, and the aqueous layer was extracted with EtOAc (2x). The combined organic layers were washed with saturated NaHCO₃ and brine, and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the product was purified by column chromatography with 10% EtOAc/Hexane to yield 0.586 g (84.6%) of the desired alcohol. ¹H-NMR (300 MHz, CDCl₃) δ 0.85 (t, *J* = 6.9 Hz, 3H), 1.24 (m, 6H), 1.58 (p, *J* = 6.6 Hz, 2H), 1.89 (s, 1H), 2.00 (q, *J* = 6.3 Hz, 2H), 2.06 (q, *J* = 6.6 Hz, 2H), 3.60 (t, *J* = 6.3 Hz, 2H), 5.34 (m, 2H).

A round bottom flask was charged with the alcohol generated above (178.2 mg, 1.142 mmol, 1.0 equiv) and dissolved with acetone / H₂O (9:1, 10 mL). NMO (200.7 mg, 1.713 mmol, 1.5 equiv) was added to the reaction mixture. OsO₄ (1 mol%) was added, and the reaction mixture was stirred overnight at rt. The reaction was quenched by the addition of saturated sodium sulfite and extracted with EtOAc (3x). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated *in vacuo*. The crude product was dissolved in a minimum amount of acetone, and the solution was heated to reflux. Hexane was added dropwise to the solution until the solution became cloudy. Crystals were formed after the solution was cooled down to rt, yielding 0.127 mg (59%) of **1a**. ¹H-NMR (300 MHz, CDCl₃) δ 0.87 (t, *J* = 6.6 Hz, 3H), 1.29 (m, 5H), 1.44 (m, 4H), 1.62 (m, 1H), 1.70 (m, 2H), 2.27 (m, 3H), 3.66 (m, 4H).

Preparation of 2a.

The following procedure for substrate 2a is representative for all cyclization reactions with PPTS and BF₃•Et₂O.

Trimethyl orthoacetate (79 μL, 0.632 mmol, 1.2 equiv) was added to a mixture of triol **1a** (100 mg, 0.526 mmol, 1.0 equiv), PPTS (1.3 mg, 0.00526 mmol, 0.01 equiv) and CH₂Cl₂ (10 mL) at rt. The mixture was stirred for 15 min, and BF₃•Et₂O (6.7 μL, 0.0526 mmol, 0.1 equiv) was added at 0 °C. After TLC showed no orthoester remaining, the reaction was quenched with aqueous acetone. The solvent was removed under reduced pressure, and the product was purified via column chromatography (10% EtOAc in hexane) to yield compound **2a** in 81% (91 mg) yield. ¹H-NMR (500 MHz, CDCl₃) δ 0.83 (t, *J* = 7.0 Hz, 3H), 1.25 (m, 6H), 1.52 (m, 3H), 1.85 (m, 3H), 2.04 (s, 3H), 3.70 (m, 1H), 3.79 (m, 1H), 3.85 (m, 1H), 4.84

(m, 1H). ^{13}C -NMR (125 MHz, CDCl_3) δ 13.9, 21.1, 22.4, 24.9, 25.9, 27.8, 31.0, 31.6, 68.1, 75.2, 79.5, 170.9.¹

The following procedure for substrate **2a** is representative for all cyclization reactions with only $\text{BF}_3 \cdot \text{Et}_2\text{O}$.

Trimethyl orthoacetate (37 μL , 0.292 mmol, 1.2 equiv) was added to a solution of triol **1a** (46 mg, 0.244 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL), followed by the addition of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (3 μL , 0.024 mmol, 0.1 equiv) at 0 $^\circ\text{C}$. The reaction mixture was stirred at rt for 1 h, and quenched with aqueous acetone. The solvent was removed under reduced pressure, and the product was purified via column chromatography (10% EtOAc in hexane) to yield compound **2a** in 94% (49 mg) yield.

The *trans* stereochemistry of **2a** (result of inversion of stereochemistry) was verified through comparison with the product obtained independently as described below.

To a solution of *cis*-4-decenol (0.416 g, 2.67 mmol, 1.0 equiv) in CH_2Cl_2 (26 mL), mCPBA (0.72 g, 77%, 3.2 mmol, 1.2 equiv) was added at 0 $^\circ\text{C}$. The reaction mixture was stirred for 12 h and then washed with 10% aqueous NaHSO_3 , saturated Na_2CO_3 and brine. The organic phase was dried over NaSO_4 and concentrated *in vacuo*. The crude product was purified via column chromatography (20% EtOAc in Hexane) to yield 0.396 g of the desired product (86%). ^1H -NMR (300MHz, CDCl_3) δ 0.85 (t, J = 6.7 Hz, 3H), 1.1-1.7 (m, 9H), 1.88 (m, 3H), 2.40 (br, 1H), 3.35 (q, J = 5.5 Hz, 1H), 3.67 (q, J = 7.1 Hz, 1H), 3.77 (q, J = 6.6 Hz, 2H). Acetylation of the cyclized alcoholic product above (118 mg, 0.684 mmol, 1.0 equiv) in diethyl ether (10 mL) with acetic anhydride (0.13 mL, 1.37 mmol, 2.0 equiv) and pyridine

(0.11 mL, 1.37 mmol, 2.0 equiv) for 12 h yielded the acetylated THF. The NMR of this product was identical with **2a** generated through the one-pot cyclization of **1a**.

Preparation of 1b.

To a solution of LAH (0.337 g, 8.88 mmol, 1.0 equiv) in diethyl ether (10 mL) was added *trans*-4-decenoic acid ethyl ester (2.0 mL, 8.88 mmol, 1.0 equiv) dropwise at 0 °C. The reaction mixture was stirred at rt for 12 h. The reaction was quenched with 10% HCl, and the product was extracted with diethyl ether (3x). The combined organic layers were washed with saturated NaHCO₃ and brine, and dried over anhydrous Na₂SO₄. After removal of the solvent, the product was purified by flash chromatography (10% EtOAc in hexane) to yield the desired alcohol in 81% (1.122 g) yield. ¹H-NMR (300 MHz, CDCl₃) δ 0.84 (t, *J* = 7.1 Hz, 3H), 1.25 (m, 6H), 1.58 (p, *J* = 6.9 Hz, 2H), 1.87 (s, 1H), 1.94 (q, *J* = 7.1 Hz, 2H), 2.01 (q, *J* = 4.7 Hz, 2H), 3.59 (t, *J* = 6.6 Hz, 2H), 5.38 (m, 2H).

Dihydroxylation procedure identical to the preparation of **1a** with alcohol generated above gave the triol **1b** in 65% yield. ¹H-NMR (300 MHz, CDCl₃) δ 0.85 (t, *J* = 6.6 Hz, 3H), 1.26 (m, 5H), 1.42 (m, 4H), 1.63 (m, 3H), 3.34 (m, 2H), 3.61 (m, 2H), 4.12 (br, 3H).

Preparation of 2b.

Conversion of **1b** to **2b** under general cyclization conditions described for **2a** led to 74% product. ¹H-NMR (300 MHz, CDCl₃) δ 0.81 (t, 3H), 1.22 (m, 6H), 1.51 (m, 2H), 1.64 (m, 1H), 1.82 (m, 3H), 2.00 (s, 3H), 3.70 (m, 1H), 3.75 (m, 1H), 3.84 (m, 1H), 4.88 (dt, *J* = 8.0

Hz, 4.9 Hz, 1H). ^{13}C -NMR (75 MHz, CDCl_3) δ 13.9, 21.0, 22.4, 24.9, 25.6, 27.1, 30.5, 31.6, 68.5, 74.9, 79.8, 170.6. IR: 1024, 1074, 1240, 1371, 1462, 1743, 2862, 2932, 2957 cm^{-1} .¹

Preparation of 1c.

To a solution of *cis*-4-decenal (136.2 mg, 0.884 mmol, 1.0 equiv) in anhydrous THF (10 mL) at -78°C was added *n*BuLi (1.0 mL, 1.8 M solution in hexane, 1.769 mmol, 2.0 equiv). The reaction mixture was stirred at -78°C for 10 min and at rt for an additional 8 h. The reaction was quenched with saturated NH_4Cl , and extracted with EtOAc, followed by washing with brine, and was dried over anhydrous Na_2SO_4 . After evaporation of the solvent, the product was purified with column chromatography (10% EtOAc in Hexane) to yield the desired alcohol in 90% yield (168 mg). ^1H -NMR (300 MHz, CDCl_3) δ 0.85 (m, 6H), 1.20-1.51 (m, 14H), 1.56 (s, 1H), 1.95 (m, 2H), 2.05 (m, 2H), 3.57 (m, 1H), 5.40 (m, 2H). ^{13}C -NMR (75 MHz, CDCl_3) δ 14.0, 22.5, 22.7, 27.8, 28.9, 29.2, 31.4, 32.5, 37.1, 71.5, 129.7, 131.0.

Dihydroxylation procedure identical to the preparation of **1a** with alcohol generated above gave the triol **1c** in 62% yield (*dr* 1:1). ^1H -NMR (300 MHz, CD_3OD) δ 0.82 (m, 6H), 1.1-1.7 (m, 18H), 3.28 (m, 2H), 3.43 (s, 1H). ^{13}C -NMR (75 MHz, CD_3OD) δ 14.5, 23.7, 23.9, 26.8, 29.1, 29.1, 30.0, 30.3, 33.1, 33.9, 34.6, 34.9, 38.2, 38.2, 72.3, 72.7, 75.3, 75.4, 75.7.

Preparation of 2c.

Conversion of **1c** to **2c** under general cyclization conditions described for **2a** led to 82% product (*dr* 1:1). ^1H -NMR (500 MHz, CDCl_3) δ 0.85 (m, 6H), 1.18-1.60 (m, 15H), 1.70 (m,

1H), 1.80-2.00 (m, 2H), 2.02 (s, 3H), 3.78-3.98 (m, 2H), 4.50 (m, 1H). ¹³C-NMR (125 MHz, CDCl₃) δ 13.9, 14.0, 21.2, 22.5, 22.7, 25.0, 27.0, 27.7, 28.2, 28.3, 30.7, 30.8, 31.6, 31.7, 31.7, 35.4, 35.6, 75.1, 75.5, 79.4, 79.9, 80.0, 80.0, 170.7, 170.7.

Preparation of 1d.

1d

6-Methylhept-5-en-2-ol (1.0 g, 1 eq., 7.8 mmol) was dissolved in a 9:1 mixture of acetone/water (80 mL). NMO (1.6 g, 1.5 eq., 11.7 mmol) was added, followed by 0.5 mol% of osmium tetroxide. The brown solution was stirred overnight at rt, after which a light yellow solution resulted. The reaction was quenched with 1 mL of saturated sodium bisulfite solution and diluted with an equal volume of water. The aqueous was extracted 3x with portions of ethyl acetate. The combined organics were washed with brine, dried over sodium sulfate and the volatiles removed via rotary evaporation. The residue was purified by column chromatography (2:1 ethyl acetate/hexanes) to give the triol in 63% yield as a mixture of diastereomers. ¹H NMR (CDCl₃, 300 MHz) δ 3.8 (m, 1 H), 3.7 (m, 1H), 3.4 (s, 1H), 3.3 (m, 2H), 1.2-1.6 (m, 4H), 1.3 (s, 6H), 1.2 (d, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 78.8, 78.4, 73.2, 73.1, 68.3, 67.4, 36.6, 35.8, 28.5, 27.1, 26.3, 23.7, 23.3, 23.2.

Preparation of 2d.

2d

The triol **1d** (0.1 g, 1 eq., 0.62 mmol) and dry dichloromethane (10 mL) were combined at rt and trimethylorthoacetate (0.95 mL, 1.2 eq., 0.74 mmol) and a catalytic amount of PPTS (15.6 mg, 0.1 eq., 0.062 mmol) were added. The reaction was stirred at rt for 15 min, then cooled to 0 °C. Boron trifluoroetherate (7.8 μL, 0.1 eq., 0.062 mmol) was added and the reaction stirred at 0 °C for 30 min, warmed gradually to rt and quenched with saturated sodium bicarbonate. The reaction was diluted with more water and extracted 3x with portions of dichloromethane. The combined organics were washed with brine, dried over sodium sulfate

and the solvent was removed under reduced pressure. The residue was purified via column chromatography (hexanes/ethyl acetate gradient) to give the desired THF in 52% yield as a mixture of diastereomers. ^1H NMR (CDCl_3 , 300 MHz) δ 4.75 (m, 1H), 3.7 (m, 1H), 2.1 (s, 3H), 1.7 (m, 1H), 1.3-1.4 (overlapping m, 3H), 1.15 (s, 6H), 1.1 (d, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 171.4, 171.3, 80.0, 79.4, 72.3, 67.9, 67.3, 35.6, 35.2, 26.2, 26.1, 25.9, 25.3, 25.2, 25.1, 23.6, 21.0.

Preparation of 1e.

To a solution of *cis*-4-decenal (0.5 mL, 2.22 mmol, 1.0 equiv) in anhydrous THF (5 mL) at -78°C was added MeLi (1.9 mL, 1.4 M solution in diethyl ether, 2.67 mmol, 1.2 equiv). The reaction mixture was stirred at -78°C for 10 min and at rt for an additional 45 min. The reaction was quenched with saturated NH_4Cl , and extracted with EtOAc, followed by washing with brine, and was dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the product was used in the subsequent reaction without purification. ^1H -NMR (300 MHz, CDCl_3) δ 0.84 (t, $J = 6.6$ Hz, 3H), 1.14 (d, $J = 6.0$ Hz, 3H), 1.25 (m, 6H), 1.46 (m, 2H), 1.84 (s, 1H), 1.99 (m, 2H), 2.08 (m, 2H), 3.75 (m, 1H), 5.33 (m, 2H).

A solution of oxalyl chloride (0.23 mL, 2.66 mmol, 1.2 equiv) in anhydrous CH_2Cl_2 (5 mL) was cooled to -78°C , followed by the dropwise addition of a solution of DMSO (0.19 mL, 2.66 mmol, 1.2 equiv) in anhydrous CH_2Cl_2 (1 mL). The reaction mixture was stirred for 5 min. A solution of the alcohol generated above (2.22 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (4 mL) was then added to the reaction mixture at -78°C . After 5 min of stirring, Et_3N (1.55 mL, 11.1 mmol, 5.0 equiv) was added. The reaction mixture was warmed to ambient temperature, and was diluted with diethyl ether and water. The layers were separated, and the organic layers were washed with water, brine, and dried over anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure. The product was purified with column chromatography (10% EtOAc in Hexane) to yield the desired ketone in 97% yield (360 mg). ^1H -NMR (300

MHz, CDCl₃) δ 0.82 (t, J = 6.6 Hz, 3H), 1.23 (m, 6H), 1.97 (q, J = 6.6 Hz, 2H), 2.08 (s, 3H), 2.25 (q, J = 7.1 Hz, 2H), 2.42 (t, J = 7.4 Hz, 2H), 5.30 (m, 2H).²

To a solution of ketone generated above (360 mg, 2.14 mmol, 1.0 equiv) in anhydrous THF (5 mL) at -78 °C was added MeLi (1.84 mL, 1.4 M solution in diethyl ether, 2.57 mmol, 1.2 equiv). The reaction mixture was stirred at -78 °C for 10 min and at rt for an additional 45 min. The reaction was quenched with saturated NH₄Cl, and extracted with EtOAc, followed by washing with brine, and was dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the product was purified with column chromatography (10% EtOAc in hexane) to yield the desired alcohol in 71% yield (281 mg). ¹H-NMR (300 MHz, CDCl₃) δ 0.85 (t, J = 6.9 Hz, 3H), 1.19 (s, 6H), 1.25 (m, 6H), 1.50 (m, 2H), 2.00 (m, 4H), 5.33 (m, 2H).

1e

Dihydroxylation procedure identical to the preparation of **1a** with alcohol generated above gave the triol **1e** in 70% yield. ¹H-NMR (300 MHz, CDCl₃) δ 0.85 (t, J = 6.6 Hz, 3H), 1.19 (d, J = 8.0 Hz, 6H), 1.26 (m, 6H), 1.40 (m, 2H), 1.52 (m, 4H), 3.54 (m, 2H), 4.09 (s, 3H).

Preparation of **2e**.

2e

Conversion of **1e** to **2e** under general cyclization conditions described for **2a** led to 80% product. ¹H-NMR (300 MHz, CDCl₃) δ 0.84 (t, J = 6.6 Hz, 3H), 1.20 (d, J = 8.0 Hz, 6H), 1.25 (m, 6H), 1.52 (m, 2H), 1.68 (m, 2H), 2.00 (m, 2H), 2.06 (s, 3H), 4.00 (q, J = 5.2 Hz, 1H), 4.84 (q, J = 5.2 Hz, 1H). ¹³C-NMR (75 MHz, CDCl₃) δ 14.0, 21.2, 22.5, 25.1, 27.9, 28.2,

28.4, 30.9, 31.7, 38.2, 75.7, 79.0, 81.1. 170.9. IR: 1024, 1059, 1142, 1244, 1367, 1462, 1740, 2864, 2932, 2964 cm^{-1} . HRMS: $[\text{M}+\text{H}]^+$ (FAB) observed 243.1963, calc'd 243.1961.

Preparation of **1f**

Magnesium turnings (0.5 g, 20.6 mmol, 9.3 equiv) was added to a 100 mL round-bottom flask, which was equipped with a condenser. Benzyl bromide (2.25 mL, 21.3 mmol, 9.6 equiv) was dissolved in anhydrous diethyl ether (10 mL), and one third of it was added into the reaction flask. The reaction was initiated by warming the flask gradually, after which the rest of PhBr solution was added dropwise. The reaction was refluxed at 40 °C for 40 min. *cis*-4-Decenal dissolved in diethyl ether was then added dropwise at cold water bath temperature. The reaction was stirred for 30 min. The reaction was then quenched with saturated NH_4Cl aqueous solution. After complete disappearance of magnesium, the product was extracted with diethyl ether (3x). The combined organic layers were washed with brine, and dried over anhydrous Na_2SO_4 . The crude product was further purified by column chromatography with 10% EtOAc in hexane to yield the desired alcohol quantitatively (515 mg). ^1H -NMR (300 MHz, CDCl_3) δ 0.88 (t, J = 6.6 Hz, 3H), 1.27 (m, 6H), 1.83 (m, 2H), 2.05 (m, 5H), 4.65 (m, 1H), 5.38 (m, 2H), 7.32 (m, 5H).³

Dihydroxylation procedure identical to the preparation of **1a** with alcohol generated above gave the triol **1f** in 89% yield (mixture of diastereomer, *dr* 1:1). ^1H -NMR (300 MHz, CDCl_3) δ 0.85 (t, J = 5.8 Hz, 3H), 1.24 (m, 7H), 1.43 (m, 2H), 1.54 (m, 1H), 1.80 (m, 2H), 3.49 (m, 2H), 3.90 (br), 4.56 (dd, J = 8.8, 3.8 Hz, 0.5H), 4.68 (dd, J = 6.9, 4.9 Hz, 0.5H), 7.26 (m, 5H).

Preparation of 2f.

Conversion of **1f** to **2f** under general cyclization conditions described for **2a** led to 55% product **2f** (*dr* 1:1) along with 36% deacetylated product **2f'** (*dr* 1:1). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 0.87 (m, 3H), 1.3 (m, 6H), 1.7 (m, 5H), 2.18 (3H), 2.3 (1H), 4.12 (m, 0.5H), 4.23 (m, 0.5H), 4.95 (m, 2H), 7.3 (m, 5H).

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 0.88 (m, 3H), 1.3 (m, 4.5H), 1.45 (m, 3.5H), 1.9 (m, 3.5H), 2.3 (0.5H), 3.86 (1H), 3.98 (m, 0.5H), 4.14 (m, 0.5H), 4.84 (t, $J = 7.7$ Hz, 0.5H), 4.98 (dd, $J = 8.5, 6.3$ Hz, 0.5H), 7.31 (m, 5H).

Preparation of 1g.

1,4-Butanediol (1.0 mL, 11.3 mmol, 1.0 equiv) was added dropwise to a slurry of NaH (452 mg, 60 wt% in mineral oil, 11.3 mmol, 1.0 equiv) in anhydrous THF (40 mL) at 0 °C. PMBCl (1.53 mL, 11.3 mmol, 1.0 equiv) was then added dropwise followed by addition of Bu_4NI (459 mg, 1.24 mmol, 0.11 equiv). After stirring at rt for 1 h, the reaction was heated to 60 °C for 15 h. The reaction mixture was then poured into a solution of saturated NaHCO_3 and vigorously stirred. The two layers were separated, and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried over anhydrous Na_2SO_4 . The product was purified by column chromatography (40% EtOAc in hexane) to yield 94% of the desired product (2.225 g). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.54 (m, 4H), 3.36 (t, $J = 6.0$ Hz, 2H), 3.45 (t, $J = 5.8$ Hz, 2H), 3.61 (br, 1H), 3.64 (s, 3H), 4.32 (s, 2H), 6.76 (d, $J = 8.5$ Hz, 2H), 7.15 (d, $J = 8.8$ Hz, 2H).⁴

To a slurry of PCC (3.425 g, 15.9 mmol, 1.5 equiv) in CH_2Cl_2 (30 mL), a solution of alcohol generated above (2.225 g, 10.6 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added at rt under N_2 with vigorous stirring. After stirring for 4 h at rt, anhydrous diethyl ether was added, and the reaction mixture was filtered through celite. The filtrate was concentrated *in vacuo*, and the product was purified by column chromatography with 20% EtOAc in hexane to yield the desired aldehyde in 81% yield (1.789 g). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.79 (p, $J = 6.0$ Hz, 2H), 2.36 (td, $J = 7.1, 1.6$ Hz, 2H), 3.34 (t, $J = 6.0$ Hz, 2H), 3.64 (s, 3H), 4.29 (s, 2H), 6.76 (d, $J = 8.8$ Hz, 2H), 7.13 (d, $J = 8.8$ Hz, 2H) 9.60 (t, $J = 1.4$ Hz, 1H).⁵

To a solution of aldehyde generated above (1.789 g, 8.6 mmol, 1.0 equiv) in anhydrous THF (40 mL), $\text{Ph}_3\text{P=CH-CO}_2\text{Et}$ (4.49 g, 12.9 mmol, 1.5 equiv) was added, and the reaction mixture was refluxed for 19 h. The solvent was removed, the residue was dissolved in Et_2O / Hexane (10 : 90, 50 mL), and the insolubles were filtered. The filter cake was washed with the above mixed solvent. The filtrate was concentrated under reduced pressure and was subjected to column chromatography with 10% EtOAc in hexane to yield the desired alkene in 70% yield (1.669 g). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.23 (t, $J = 7.1$ Hz, 3H), 1.70 (p, $J = 7.7$ Hz, 2H), 2.24 (q, $J = 6.6$ Hz, 2H), 3.40 (t, $J = 6.3$ Hz, 2H), 3.74 (s, 3H), 4.12 (q, $J = 7.1$ Hz, 2H), 4.37 (s, 2H), 5.77 (dt, $J = 15.7, 1.4$ Hz, 1H), 6.82 (d, $J = 8.5$ Hz, 2H), 6.91 (dt, $J = 15.7, 6.9$ Hz, 1H), 7.20 (d, $J = 8.8$ Hz, 2H).

To a stirred solution of PMB protected alcohol generated above (0.770 g, 2.77 mmol, 1.0 equiv) in CH_2Cl_2 (27 mL) and water (3 mL) was added DDQ (0.754 g, 3.32 mmol, 1.2 equiv) and the reaction mixture was stirred at rt for 1 h. Saturated NaHCO_3 aqueous solution was added, and the mixture was extracted with CH_2Cl_2 (3x). The extract was washed with saturated NaHCO_3 and brine, and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column with 30% EtOAc in hexane to yield the desired alcohol in 98% yield (0.428 g). $^1\text{H-NMR}$ (300 MHz,

CCOC(=O)[C@H](O)[C@@H](O)CCO

1g

Preparation of 2g.

Preparation of 1h.

S13

phase, and the combined organic layers were washed with saturated NaHCO_3 and brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. The product was purified by column chromatography with 5% EtOAc in hexane to yield the desired cyanide in 26% yield (190 mg). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.51 (s, 6H), 2.09 (dd, $J = 14.0, 5.8$ Hz, 4H), 2.30 (4H), 5.05 (t, 1H).⁷

A solution of cyanide generated above (190 mg, 1.275 mmol, 1.0 equiv) and 25% aqueous sodium hydroxide (8.6 mL) in methanol (29 mL) was stirred at reflux for 16 h. The reaction mixture was cooled to rt. Water and EtOAc was added to the reaction mixture, and the two layers were separated. The pH of the aqueous layer was adjusted to 3 with 10% HCl, and the product was extracted with EtOAc (3x). The organic layer was washed with brine, and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure. The product was used for the next step without further purification. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.49 (s, 6H), 2.05 (m, 4H), 2.33 (m, 4H), 5.04 (t, 1H), 11.50 (br, 1H).⁸

LAH (54 mg, 1.41 mmol, 1.2 equiv) was suspended in dry diethyl ether and an ethereal solution of carboxylic acid generated above (197 mg, 1.17 mmol, 1.0 equiv) was added dropwise while cooling the reaction in an ice bath. The reaction mixture was stirred at rt for 3 h. 10% HCl was added to the reaction mixture to acidify the solution, and the mixture was stirred for 2 h. The two layers were separated and the aqueous layer was extracted with ether (3x). The combined organic layers were washed with saturated NaHCO_3 and brine, and dried over anhydrous MgSO_4 . After removal of the solvent under reduced pressure, the product was purified by column chromatography with 10% EtOAc in hexane to yield the desired alcohol in quantitative yield (180 mg). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.48 (m, 6H), 1.56 (m, 2H), 1.80 (s, 1H), 2.10 (m, 6H), 3.59 (t, $J = 6.6$ Hz, 2H), 5.05 (t, $J = 7.4$ Hz, 1H).⁹

Dihydroxylation procedure identical to the preparation of **1a** with alcohol generated above gave the triol **1h** in 65% yield. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.1-1.7 (m, 17H), 3.35 (d, J = 10.7 Hz, 1H), 3.68 (m, 2H).

Preparation of 2h.

Conversion of **1h** to **2h** under general cyclization conditions described for **2a** led to 50% product. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.1-1.9 (m, 12H), 2.01 (s, 3H), 2.20 (m, 2H), 3.76 (m, 2H), 4.57 (t, J = 6.9 Hz, 1H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 21.3, 21.5, 22.2, 25.5, 26.1, 26.2, 29.0, 30.1, 68.8, 80.8, 85.9, 170.5. IR: 1018, 1070, 1138, 1232, 1263, 1367, 1736, 2860, 2934 cm^{-1} . HRMS: (EI) M^+ observed 212.1413, calc'd 212.1412.

Preparation of 1i.

To a solution of *n*BuLi (9.9 mL of a 2.5 M solution in hexanes, 1.1 eq., 25 mmol) in 25 mL of dry THF cooled to 0 °C was added diisopropylamine (4.5 mL, 1.45 eq., 32 mmol). The solution was stirred for 15 min and cooled to -78 °C. Methylcyclohexane carboxylate (3.1 mL, 1.0 eq., 22 mmol) was added dropwise and the reaction stirred for an additional 30 min. Allyl iodide (2.2 mL, 1.1 eq., 25 mmol) dissolved in dry HMPA (4 mL) was added and the reaction was stirred another 10 min before warming to rt over 1 h. The reaction was quenched with water, extracted 3x with portions of diethyl ether, the combined organics were washed with brine, dried over sodium sulfate and the volatiles were removed via rotary evaporation. The crude material could be used directly in the next step. $^1\text{H NMR}$ (CDCl_3 ,

300 MHz) 5.6 (m, 1H), 4.9 (m, 2H), 3.6 (s, 3H), 2.1 (d, 2H) 1.5 (br m, 4H), 1.1-1.3 (br m, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) 176.7, 133.6, 117.4, 51.3, 47.3, 44.5, 33.6, 25.7, 23.0.

Half of the crude material from the previous reaction was reduced to the alcohol in THF at $-20\text{ }^{\circ}\text{C}$ using 2.2 eq. of DIBALH (as a 1.5 M solution in toluene). The reaction was quenched carefully with Rochelle's salt and glycerol (2 mL). The emulsion was stirred for 2 h, after which clean phase separation was observed. The layers were phase-separated and the aqueous was extracted with portions of diethyl ether (3x). The combined organics were washed with brine, dried over sodium sulfate and the volatiles were removed via rotary evaporation. The residue was purified using column chromatography (4:1 hexanes/ethyl acetate) to give the alcohol in 74% yield over the two steps. ^1H NMR (CDCl_3 , 300 MHz) δ 5.8 (m, 1H), 5.1 (m, 2H), 3.4 (d, 2H), 2.1 (d, 2H), 1.2-1.4 (br m's, 10H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 135.3, 117.0, 68.7, 39.9, 37.7, 32.2, 32.1, 26.3.

The alcohol generated above (2.0 g, 1.0 eq., 12.4 mmol) was dissolved in 100 mL of a 9:1 mixture of acetone/water. NMO (2.0 g, 1.2 eq., 14.9 mmol) and a catalytic amount of OsO_4 (0.05 mol%) were added and the reaction was stirred overnight at rt. An equal volume of water was added and the aqueous fraction was extracted with portions of ethyl acetate (3x). The combined organics were washed with brine, dried over sodium sulfate and the volatiles were removed via rotary evaporation. The residue was purified using column chromatography (2:1 hexanes/ethyl acetate) to give the triol in 89% yield. ^1H NMR (CDCl_3 , 300 MHz) δ 4.8 (br s, 1H), 4.4 (br s, 1H), 3.8 (br t, 1H), 3.5 (m, 2H), 3.3-3.4 (m, 2H), 1.1-1.5 (br m's, 10H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 69.5, 67.8, 67.7, 40.8, 36.7, 35.6, 31.1, 26.3, 21.5, 21.4.

Preparation of 2i.

The triol **1i** (0.2 g, 1.0 eq., 1.06 mmol) was dissolved in dry dichloromethane (30 mL). The solution was cooled to 0 °C and trimethylorthoacetate (0.16 mL, 1.2 eq., 1.28 mmol) and boron trifluoroetherate (12.5 μ L, 0.1 eq., 0.1 mmol) was added. The reaction was allowed to warm slowly to rt over 1 h, after which TLC indicated completion of the reaction. Sodium bicarbonate was used to quench the reaction and the aqueous layer was extracted with portions of dichloromethane (3x). The combined organics were washed with brine, dried over sodium sulfate and the volatiles were removed via rotary evaporation. The residue was purified using column chromatography (hexanes/ethyl acetate gradient) to give the desired THF in 87% yield. ^1H NMR (CDCl_3 , 300 MHz) δ 4.1 (m, 2H), 3.9 (m, 1H), 3.5 (s, 2H), 2.0 (s, 3H), 1.7 (m, 1H), 1.2-1.5 (overlapping m, 11H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 171.0, 78.4, 76.0, 66.8, 43.6, 40.3, 36.2, 35.1, 25.9, 23.9, 23.4, 20.8. GC/MS 152 (M-60, 8.8), 139 (100), 95 (68).

Preparation of 1j.

Dihydroxylation procedure identical to the preparation of **1a** with 2-allylphenol gave the triol **1j** in 99% yield. ^1H -NMR (300 MHz, CDCl_3) δ 2.71 (d, J = 5.8 Hz, 2H), 3.37 (dd, J = 11.5, 7.4 Hz, 1H), 3.55 (dd, J = 11.5, 2.5 Hz, 1H), 3.90 (m, 1H), 6.80 (m, 2H), 6.96 (m, 1H), 7.07 (m, 1H). ^{13}C -NMR (75 MHz, CDCl_3) δ 34.8, 65.8, 73.4, 116.7, 120.7, 124.4, 128.3, 131.5, 154.7.¹⁰

Preparation 2j.

Conversion of **1j** to **2j** under general cyclization conditions described for **2a** led to 84% product. ¹H-NMR (500 MHz, CDCl₃) δ 2.08 (s, 3H), 2.95 (dd, *J* = 15.7, 7.5 Hz, 1H), 3.29 (dd, *J* = 15.7, 9.5 Hz, 1H), 4.19 (dd, *J* = 11.7, 7.1 Hz, 1H), 4.32 (dd, *J* = 11.9, 3.5 Hz, 1H), 4.97 (m, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.84 (td, *J* = 7.3, 0.9 Hz, 1H), 7.10 (m, 1H), 7.15 (m, 1H). ¹³C-NMR (75 MHz, CDCl₃) δ 20.8, 31.9, 65.9, 79.9, 109.6, 120.7, 124.9, 125.7, 128.2, 159.1, 170.9. IR: 752, 1043, 1223, 1369, 1462, 1481, 1599, 1741, 2947 cm⁻¹.¹¹

Preparation of 1k.

To a slurry of PCC (1.474 g, 6.84 mmol, 1.0 equiv) in CH₂Cl₂ (30 mL), a solution of 1,5-cyclooctanediol (1.006 g, 6.84 mmol, 1.0 equiv) in CH₂Cl₂ (10 mL) was added at rt under N₂ with vigorous stirring. After stirring for 4 h at rt, anhydrous diethyl ether was added, and the reaction mixture was filtered through celite. The filtrate was concentrated *in vacuo*, and the product was purified by column chromatography with 40% EtOAc in hexane to yield 5-hydroxyl cyclooctanone in 76% yield (0.734 g). ¹H-NMR (300 MHz, CDCl₃) δ 1.50 (m, 2H), 1.70 (m, 4H), 1.89 (m, 4H), 2.06 (m, 2H), 2.89 (br, 1H), 4.30 (m, 1H).

To a stirred solution of 5-hydroxy cyclooctanone (734 mg, 5.17 mmol, 1.0 equiv) and DHP (0.47 mL, 5.17 mmol, 1.0 equiv) in CH₂Cl₂ (20 mL) at rt was added TsOH•H₂O (2 mg), and the mixture was stirred at rt for 3 h. The solution was diluted with diethyl ether, washed with saturated NaHCO₃, brine and water, and dried over anhydrous MgSO₄. After removal of the solvent under reduced pressure, the crude product was purified by column chromatography (20% EtOAc in hexane) to yield the desired ketone in 17% yield (197.2 mg). ¹H-NMR (300

MHz, CDCl₃) δ 1.40 (m, 4H), 1.5-2.0 (m, 10H), 2.25 (m, 2H), 2.43 (m, 2H), 3.35 (m, 1H), 3.50 (m, 1H), 3.75 (m, 1H), 4.48 (m, 1H).¹²

To a slurry of Ph₃PCH₃Br (0.468 g, 1.309 mmol, 1.5 equiv) in anhydrous THF (10 mL) was added KHMDS (2.62 mL, 0.5 M solution in toluene, 1.309 mmol, 1.5 equiv) at 0 °C under N₂ atmosphere. The reaction was warmed to rt stirred for 1 h and then cooled back to 0 °C. The ketone generated above (197 mg, 0.873 mmol, 1.0 equiv) in anhydrous THF (5 mL) was added, and the reaction was then stirred at rt for 3 h. The reaction was quenched with 10% HCl, the two layers were separated and the aqueous layer was extracted with diethyl ether (3x). The combined organic layers were washed with saturated NaHCO₃ and brine, and dried over anhydrous MgSO₄. After filtration, the solvent was removed under reduced pressure, and a 5% ether in hexane solution was added to the concentrated crude product to precipitate the byproduct. After filtration, the filtrate was concentrated *in vacuo* and purified by silica gel chromatography (5% ether in hexane) to yield 172 mg of the desired product (88%). ¹H-NMR (300 MHz, CDCl₃) δ 1.4-1.9 (m, 14H), 2.12 (m, 4H), 3.44 (m, 1H), 3.84 (m, 2H), 4.56 (m, 1H), 4.76 (m, 2H).

PTSA (7mg) was added to a solution of THP protected alcohol generated above (172 mg, 0.766 mmol, 1.0 equiv) in MeOH (10 mL). The mixture was stirred at rt for 2 h. The solvent was removed under reduced pressure. The product was purified by silica gel chromatography (20% EtOAc in hexane) to give 89 mg of the desired product (83%). ¹H-NMR (300 MHz, CDCl₃) δ 1.60 (m, 9H), 2.15 (m, 4H), 3.90 (m, 1H), 4.76 (s, 2H). ¹³C-NMR (75 MHz, CDCl₃) δ 24.0, 35.4, 35.6, 71.0, 112.8, 150.6.¹³

Dihydroxylation procedure identical to the preparation of **1a** with alcohol generated above gave the triol **1k** in 93% yield. $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 1.4-1.8 (m, 13H), 1.93 (m, 2H), 3.41 (s, 2H), 3.80 (tt, $J = 9.7, 2.7$ Hz, 1H). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ 19.1, 33.4, 38.0, 68.7, 72.0, 74.9.

Preparation of **2k**.

Conversion of **1k** to **2k** under general cyclization conditions described for **2a** led to 33% product **2k** along with 18% deacetylated product **2k'**. $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 1.48 (m, 4H), 1.64 (m, 4H), 1.91 (m, 2H), 2.02 (m, 2H), 2.08 (s, 3H), 3.82 (s, 2H), 4.10 (t, $J = 6.0$ Hz, 1H). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ 18.6, 21.0, 28.5, 30.4, 68.1, 69.5, 72.0, 171.2. IR: 1033, 1230, 1244, 1367, 1456, 1745, 2936 cm^{-1} . HRMS: $[\text{M}+\text{H}]^+$ (FAB) observed 199.1333, calc'd 199.1335.

$^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 1.40 (m, 2H), 1.50 (m, 2H), 1.63 (m, 2H), 1.72 (m, 2H), 1.88 (m, 2H), 2.03 (m, 3H), 3.27 (s, 2H), 4.07 (t, $J = 5.7$ Hz, 1H). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ 18.6, 28.8, 30.2, 68.1, 70.7, 71.6. IR: 800, 1028, 1452, 1466, 2858, 2926 cm^{-1} . HRMS: M^+ (EI) observed 156.1150, calc'd 156.1150.

Preparation of 1l.

To a slurry of $\text{Ph}_3\text{PCH}_2\text{CH}_2\text{CH}_2\text{CNCl}$ (1.798 g, 4.9 mmol, 1.0 equiv) in anhydrous THF (100 mL) was added KHMDS (10.8 mL, 0.5 M solution in toluene, 5.4 mmol, 1.1 equiv) at 0 °C under N_2 atmosphere. The reaction was warmed to rt, stirred for 1 h and cooled back to 0 °C. Benzaldehyde (1.0 mL, 9.8 mmol, 2.0 equiv) in anhydrous THF (15 mL) was added, and the reaction was then stirred at rt for 1 h. The reaction was quenched with 10% HCl, the two layers were separated and the aqueous layer was extracted with diethyl ether (3x). The combined organic layers were washed with saturated NaHCO_3 and brine, and dried over anhydrous MgSO_4 . After filtration, the solvent was removed under reduced pressure, and a 5% ether in hexane solution was added to the concentrated crude product to precipitate the byproduct. After filtration, the filtrate was concentrated *in vacuo* and purified by silica gel chromatography (10% ether in hexane) to yield 354 mg of the desired product (46%). ^1H -NMR (300 MHz, CDCl_3) δ 2.35 (t, J = 7.4 Hz, 2H), 2.61 (q, J = 6.9 Hz, 2H), 5.62 (dt, J = 11.5, 6.9 Hz, 1H), 6.60 (d, J = 11.5 Hz, 1H), 7.32 (m, 5H).

A solution of cyanide generated above (1.516 g, 9.66 mmol, 1.0 equiv) and 25% aqueous sodium hydroxide (65 mL) in methanol (219 mL) was stirred at reflux for 16 h. The reaction mixture was cooled to rt. Water and EtOAc was added to the reaction mixture, and the two layers were separated. The pH of the aqueous layer was adjusted to 3 with 10% HCl, and the product was extracted with EtOAc (3x). The organic layer was washed with brine, and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure. The product was used for the next step without further purification. ^1H -NMR (300 MHz, CDCl_3) δ 2.48 (t, J = 8.0 Hz, 2H), 2.65 (q, J = 7.1 Hz, 2H), 5.62 (dt, J = 11.8, 6.9 Hz, 1H), 6.47 (d, J = 11.5 Hz, 1H), 7.29 (m, 5H), 9.0 (br, 1H).

LAH (0.44 g, 11.6 mmol, 1.2 equiv) was suspended in dry diethyl ether (100 mL) and an ethereal solution of carboxylic acid generated above (9.66 mmol, 1.0 equiv) was added dropwise while cooling the reaction in an ice bath. The reaction mixture was stirred at rt for 3

h. 10% HCl was added to acidify the solution, and the mixture was stirred for 2 h. The two layers were separated and the aqueous layer was extracted with ether (3x). The combined organic layers were washed with saturated NaHCO₃ and brine, and dried over anhydrous MgSO₄. After removal of the solvent under reduced pressure, the product was purified by column chromatography with 20% EtOAc in hexane to yield the desired alcohol in 84 yield (1.317 g). ¹H-NMR (300 MHz, CDCl₃) δ 1.71 (p, *J* = 6.9 Hz, 2H), 2.44 (m, 3H), 3.62 (t, *J* = 6.6 Hz, 2H), 5.68 (dt, *J* = 11.8, 7.4 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 7.30 (m, 5H).¹⁴

Dihydroxylation procedure identical to the preparation of **1a** with alcohol generated above gave the triol **11** in 57% yield. ¹H-NMR (300 MHz, CDCl₃) δ 1.31 (m, 1H), 1.53 (m, 3H), 3.47 (m, 2H), 3.71 (m, 4H), 4.61 (d, *J* = 3.8 Hz, 1H), 7.27 (m, 5H).¹⁵

Preparation of **2l** and **5l**.

Conversion of **11** to **2l** under general cyclization conditions described for **2a** led to 48% product **2l** along with 24% product **5l**. ¹H-NMR (300 MHz, CDCl₃) δ 1.55 (m, 1H), 1.64 (m, 1H), 1.81 (m, 2H), 2.08 (s, 3H), 3.85 (m, 2H), 4.20 (q, *J* = 7.4 Hz, 1H), 5.60 (d, *J* = 7.7 Hz, 1H), 7.32 (m, 5H). ¹³C-NMR (125 MHz, CDCl₃) δ 21.2, 25.7, 28.3, 68.6, 78.0, 80.6, 127.4, 128.3, 128.4, 137.8, 170.2.¹⁶

¹H-NMR (500 MHz, CDCl₃) δ 1.48 (m, 1H), 1.85 (s, 3H), 1.91 (m, 1H), 2.00 (m, 1H), 2.10 (m, 1H), 3.66 (td, *J* = 11.5, 2.2 Hz, 1H), 4.21 (dt, *J* = 11.5, 2.4 Hz, 1H), 4.52 (s, 1H), 5.13 (s,

1H), 7.25 (m, 5H). ¹³C-NMR (125 MHz, CDCl₃) δ 20.4, 20.8, 28.2, 68.5, 69.6, 80.1, 126.0, 127.4, 128.0, 139.1, 170.2. IR: 704, 1022, 1093, 1240, 1373, 1452, 1736, 2851, 2955 cm⁻¹. The relative stereochemistry was confirmed as *cis* through measurement of the coupling constant for the protons at the site of substitution. The 0.9 Hz coupling is indicative of an axial-equatorial 1,2-proton interaction, which is expected from a 1,2-*cis*-disubstituted six member ring. HRMS: M⁺ (EI) observed 220.1100, calc'd 220.1099.

Preparation of 1m.

Pd(PPh₃)₄ (21 mg, 0.01 equiv) and CuI (7 mg, 0.02 equiv) were added to the solution of iodobenzene (0.48 mL, 4.3 mmol, 2.0 equiv) and 5-hydroxy pentyne (0.2 mL, 2.15 mmol, 1.0 equiv) in triethylamine (6.2 mL, 45 mmol, 10 equiv) and THF (1 mL) under N₂. The reaction mixture was stirred at rt for 12 h. The mixture was filtered and the filtrate was concentrated under reduced pressure. The product was purified by column chromatography (20% EtOAc in hexane) to yield the desired alcohol in 99% yield (340 mg).¹⁷ ¹H-NMR (300 MHz, CDCl₃) δ 1.82 (p, *J* = 7.1 Hz, 2H), 2.23 (s, 1H), 2.50 (t, *J* = 6.9 Hz, 2H), 3.77 (t, *J* = 6.0 Hz, 2H), 7.30 (m, 5H).

To a THF (20 mL) solution of LAH (0.408 g, 10.75 mmol, 5.0 equiv), the alcohol generated above (340 mg, 2.13 mmol, 1.0 equiv) was added at 0 °C under N₂. The reaction mixture was stirred at 0 °C for 30 min, and then it was refluxed for 48 h. The reaction was quenched with water and Na, K-tartrate. The product was extracted with diethyl ether (3x), and the combined organic layers were washed with brine, and dried over anhydrous Na₂SO₄. The concentrated crude product was further purified by column chromatography with 20% EtOAc in hexane to yield the desired alcohol in 90% yield (309 mg). ¹H-NMR (300 MHz, CDCl₃) δ 1.74 (p, *J* = 6.9 Hz, 2H), 2.31 (q, *J* = 6.9 Hz, 2H), 2.31 (s, 1H), 3.68 (t, *J* = 6.6 Hz, 2H), 6.23 (dt, *J* = 15.9, 6.9 Hz, 1H), 6.42 (d, *J* = 15.7 Hz, 1H), 7.30 (m, 5H).¹⁸

Dihydroxylation procedure identical to the preparation of **1a** with alcohol generated above gave the triol **1m** in 41% yield. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.32 (m, 2H), 1.51 (m, 2H), 3.45 (m, 2H), 3.58 (q, $J = 6.6$ Hz, 1H), 4.20 (br, 3H), 4.32 (d, $J = 7.4$ Hz, 1H), 7.25 (m, 5H).¹⁹

Preparation of **2m**.

Conversion of **1m** to **2m** under general cyclization conditions described for **2a** led to 83% product. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.60 (m, 1H), 1.74 (m, 1H), 1.79 (s, 3H), 1.86 (m, 1H), 2.24 (m, 1H), 3.51 (td, $J = 11.5, 2.5$ Hz, 1H), 4.05 (m, 1H), 4.15 (d, $J = 9.6$ Hz, 1H), 4.79 (m, 1H), 7.30 (m, 5H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 20.9, 25.2, 29.8, 68.2, 72.4, 82.3, 127.1, 128.1, 128.1, 138.9, 169.6. IR: 700, 758, 898, 956, 1039, 1089, 1238, 1263, 1307, 1439, 1454, 1495, 1743, 2856, 2949, 3034 cm^{-1} . The relative stereochemistry was confirmed as *trans* through measurement of the coupling constant for the protons at the site of substitution. The 9.3 Hz coupling is indicative of an axial-axial 1,2-proton interaction, which is expected from a 1,2-*trans*-disubstituted six member ring. HRMS: $[\text{M}+\text{H}]^+$ (FAB) observed 221.1177, calc'd 221.1179.

Preparation of **1n**.

To a slurry of $\text{Ph}_3\text{PCH}_2\text{CH}_2\text{CH}_2\text{CNCl}$ (1.50 g, 4.11 mmol, 1.0 equiv) in anhydrous THF (100 mL) was added KHMDS (9.1 mL, 0.5 M solution in toluene, 4.52 mmol, 1.1 equiv) at 0 °C under N_2 atmosphere. The reaction was warmed to rt, stirred for 1 h and cooled back to 0 °C. *p*-Anisaldehyde (1.0 mL, 8.22 mmol, 2.0 equiv) in anhydrous THF (15 mL) was added, and the reaction was then stirred at rt for 1 h. The reaction was quenched with 10% HCl, the two

layers were separated and the aqueous layer was extracted with diethyl ether (3x). The combined organic layers were washed with saturated NaHCO₃ and brine, and dried over anhydrous MgSO₄. After filtration, the solvent was removed under reduced pressure, and a 5% ether in hexane solution was added to the concentrated crude product to precipitate the byproduct. After filtration, the filtrate was concentrated *in vacuo* and purified by silica gel chromatography (5% EtOAc in hexane) to yield 439 mg of the desired product (57%). ¹H-NMR (300 MHz, CDCl₃) δ 2.41 (t, *J* = 7.1 Hz, 2H), 2.64 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 5.52 (dt, *J* = 11.5, 7.1 Hz, 1H), 6.50 (d, *J* = 11.3 Hz, 1H), 6.86 (d, *J* = 8.5 Hz, 2H), 7.15 (d, *J* = 8.8 Hz, 2H).

A solution of cyanide generated above (0.439 g, 2.35 mmol, 1.0 equiv) and 25% aqueous sodium hydroxide (15 mL) in methanol (53 mL) was stirred at reflux for 16 h. The reaction mixture was cooled to rt. Water and EtOAc was added to the reaction mixture, and the two layers were separated. The pH of the aqueous layer was adjusted to 3 with 10% HCl, and the product was extracted with EtOAc (3x). The organic layer was washed with brine, and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure. The product was used in the next step without further purification. ¹H-NMR (300 MHz, CDCl₃) δ 2.48 (t, *J* = 8.0 Hz, 2H), 2.65 (m, 2H), 3.79 (s, 3H), 5.53 (dt, *J* = 11.5, 6.9 Hz, 1H), 6.40 (d, *J* = 11.5 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 9.20 (br, 1H).

To a diethyl ether (10 mL) solution of LAH (0.105 g, 2.77 mmol, 1.2 equiv), the alcohol generated above (475 mg, 2.31 mmol, 1.0 equiv) was added at 0 °C under N₂. The reaction mixture was stirred at 0 °C for 30 min, and then it was refluxed for 48 h. The reaction was quenched with water and Na, K-tartrate. The product was extracted with diethyl ether (3x), and the combined organic layers were washed with brine, and dried over anhydrous Na₂SO₄. The concentrated crude product was further purified by column chromatography with 30% EtOAc in hexane to yield the desired alcohol in 90% yield (377 mg). ¹H-NMR (300 MHz,

CDCl₃) δ 1.67 (p, J = 7.1 Hz, 2H), 2.37 (q, J = 7.4 Hz, 2H), 2.57 (s, 1H), 3.59 (t, J = 6.6 Hz, 2H), 3.76 (s, 3H), 5.54 (dt, J = 11.5, 7.1 Hz, 1H), 6.35 (d, J = 11.5 Hz, 1H), 6.85 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 8.8 Hz, 2H).

Dihydroxylation procedure identical to the preparation of **1a** with alcohol generated above gave the triol **1n** in 35% yield. ¹H-NMR (300 MHz, CDCl₃) δ 1.65 (m, 4H), 2.6 (br, 3H), 3.60 (m, 3H), 3.78 (s, 3H), 4.59 (d, J = 4.7 Hz, 1H), 6.86 (d, J = 8.8 Hz, 2H), 7.26 (d, J = 8.8 Hz, 2H).

Preparation of **2n** and **5n**.

Conversion of **1n** to **2n** under general cyclization conditions described for **2a** led to 73% product **2n** along with 20% product **5n**. ¹H-NMR (300 MHz, CDCl₃) δ 1.58 (m, 1H), 1.76 (m, 1H), 1.80 (s, 3H), 1.85 (m, 1H), 2.23 (m, 1H), 3.50 (td, J = 11.5, 2.5 Hz, 1H), 3.76 (s, 3H), 4.03 (m, 1H), 4.10 (d, J = 9.6 Hz, 1H), 4.78 (td, J = 9.9, 4.7 Hz, 1H), 6.82 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 8.5 Hz, 2H). ¹³C-NMR (75 MHz, CDCl₃) δ 20.9, 25.3, 29.9, 55.2, 68.3, 72.4, 82.0, 113.5, 128.4, 131.1, 159.3, 169.7. IR: 829, 956, 1037, 1087, 1176, 1248, 1304, 1373, 1516, 1614, 1738, 2851, 2953 cm⁻¹. The relative stereochemistry was confirmed as *trans* through measurement of the coupling constant for the protons at the site of substitution. The 9.3 Hz coupling is indicative of an axial-axial 1,2-proton interaction, which is expected from a 1,2-*trans*-disubstituted six member ring. HRMS: [M+H]⁺ (FAB) observed 251.1285, calc'd 251.1285.

^1H -NMR (300 MHz, CDCl_3) δ 1.46 (m, 1H), 1.88 (s, 3H), 2.0 (m, 3H), 3.64 (t, J = 11.8 Hz, 1H), 3.75 (s, 3H), 4.18 (m, 1H), 4.46 (s, 1H), 5.05 (s, 1H), 6.81 (d, J = 6.9 Hz, 2H), 7.22 (d, J = 7.1 Hz, 2H). ^{13}C -NMR (125 MHz, CDCl_3) δ 20.4, 20.9, 28.1, 55.1, 68.6, 69.7, 79.8, 113.4, 127.2, 131.3, 158.8, 170.3. IR: 1024, 1091, 1248, 1373, 1516, 1738, 2856, 2957 cm^{-1} . The relative stereochemistry was confirmed as *cis* through measurement of the coupling constant for the protons at the site of substitution. The <0.3 Hz coupling is indicative of an axial-equatorial 1,2-proton interaction, which is expected from a 1,2-*cis*-disubstituted six member ring. HRMS: M^+ (EI) observed 250.1205, calc'd 250.1205.

Preparation of 1o.

To a slurry of $\text{Ph}_3\text{P}(\text{CH}_2)_4\text{OAcBr}$ (1.372 g, 3.0 mmol, 1.0 equiv) in anhydrous THF (20 mL) was added KHMDS (12 mL, 0.5 M solution in toluene, 6.0 mmol, 2.0 equiv) at 0 $^\circ\text{C}$ under N_2 atmosphere. The reaction was warmed to rt, stirred for 1 h and cooled back to 0 $^\circ\text{C}$. 4-Nitrobenzaldehyde (0.452 g, 3.0 mmol, 1.0 equiv) in anhydrous THF (15 mL) was added, and the reaction was then stirred at rt for 20 h. The reaction was quenched with 10% HCl, the two layers were separated and the aqueous layer was extracted with diethyl ether (3x). The combined organic layers were washed with saturated NaHCO_3 and brine, and dried over anhydrous MgSO_4 . After filtration, the solvent was removed under reduced pressure, and a 5% ether in hexane solution was added to the concentrated crude product to precipitate the byproduct. After filtration, the filtrate was concentrated *in vacuo* and purified by silica gel chromatography (10% EtOAc in hexane) to yield 60 mg of the desired product (8%). ^1H -NMR (300 MHz, CDCl_3) δ 1.77 (m, 2H), 1.96 (s, 3H), 2.37 (qd, J = 7.3, 1.9 Hz, 2H), 4.04 (t, J = 6.4 Hz, 2H), 5.81 (dt, J = 11.7, 7.5 Hz, 1H), 6.46 (d, J = 11.6 Hz, 1H), 7.36 (d, J = 8.6 Hz, 2H), 8.14 (d, J = 8.9 Hz, 2H). ^{13}C -NMR (75 MHz, CDCl_3) δ 20.8, 25.1, 28.4, 63.5, 123.4, 128.0, 129.3, 135.1, 144.0, 146.2, 170.9.

To a solution of the acetate generated above (60 mg, 0.242 mmol, 1.0 equiv) in methanol (10 mL) was added K_2CO_3 (1.0 g). The reaction mixture was stirred at rt for 2 h. Water and EtOAc were added and the two layers were separated. The aqueous layer was extracted with ethyl acetate (3x). The combined organic layers were dried over anhydrous Na_2SO_4 and filtered. After removal of the solvent under reduced pressure, the product was purified by flash chromatography with 30% EtOAc in hexane to yield the desired alcohol in 92% yield (46 mg). ^1H -NMR (500 MHz, CDCl_3) δ 1.58 (s, 1H), 1.71 (p, $J = 7.1$ Hz, 2H), 2.40 (qd, $J = 7.5$ Hz, 1.8 Hz, 2H), 3.65 (t, $J = 6.4$ Hz, 2H) 5.84 (dt, $J = 11.7$ Hz, 7.5 Hz, 1H), 6.45 (d, $J = 11.7$ Hz, 1H), 7.38 (d, $J = 8.8$ Hz, 2H), 8.13 (dd, $J = 6.8$ Hz, 2.0 Hz, 2H). ^{13}C -NMR (125 MHz, CDCl_3) δ 25.1, 32.4, 62.1, 123.5, 127.6, 129.3, 136.0, 144.2, 146.2.

Dihydroxylation procedure identical to the preparation of **1a** with alcohol generated above gave the triol **1o** in 86% yield. ^1H -NMR (500 MHz, CDCl_3) δ 1.40 (m, 1H), 1.56 (m, 1H), 1.70 (m, 2H), 3.63 (m, 1H), 3.74 (m, 1H), 3.90 (d, $J = 9.8$ Hz, 1H) 4.89 (d, $J = 3.9$ Hz, 1H), 7.57 (d, $J = 8.8$ Hz, 2H), 8.22 (d, $J = 8.8$ Hz, 2H).

Preparation of **2o**.

Conversion of **1o** to **2o** under general cyclization conditions described for **2a** led to 60% product **2o** along with 8% product **2o'**. ^1H -NMR (500 MHz, CDCl_3) δ 1.56 (dq, $J = 7.3$ Hz, 1H), 1.80 (m, 3H), 2.12 (s, 3H), 3.83 (m, 2H), 4.18 (q, $J = 6.6$ Hz, 1H), 5.71 (d, $J = 6.4$ Hz,

1H), 7.51 (d, J = 8.6 Hz, 2H), 8.18 (d, J = 8.8 Hz, 2H). ^{13}C -NMR (125 MHz, CDCl_3) δ 21.0, 25.7, 28.0, 68.8, 76.6, 80.0, 123.6, 128.1, 145.0, 147.6, 170.6. IR: 703, 839, 858, 1022, 1071, 1105, 1233, 1349, 1371, 1535, 1605, 1741, 2873, 2955, 2977, 3080, 3111 cm^{-1} . HRMS: $[\text{M}+\text{H}]^+$ (FAB) observed 266.1027, calc'd 266.1030.

^1H -NMR (500 MHz, CDCl_3) δ 1.51 (m, 1H), 1.83 (m, 3H), 2.64 (s, 1H), 3.81 (m, 1H), 3.92 (m, 1H), 4.08 (m, 1H), 5.04 (d, J = 3.8 Hz, 1H), 7.53 (d, J = 8.2 Hz, 2H), 8.19 (d, J = 8.8 Hz, 2H). ^{13}C -NMR (125 MHz, CDCl_3) δ 24.6, 26.0, 69.2, 73.2, 82.5, 123.5, 126.7, 147.2, 147.7. IR: 1047, 1242, 1373, 1741, 2849, 2916, 2984 cm^{-1} .

Preparation of **1p**.

Dihydroxylation procedure identical to the preparation of **1a** with *cis*-3-octen-1-ol gave the triol **1p** in 70% yield. ^1H -NMR (300 MHz, CDCl_3) δ 0.89 (t, J = 6.9 Hz, 3H), 1.35 (m, 6H), 1.70 (m, 2H), 2.3 (br, 2H), 3.0 (br, 1H), 3.63 (m, 1H), 3.89 (m, 3H). IR: 924, 964, 1010, 1045, 1069, 1074, 1315, 1441, 1468, 1481, 2856, 2914, 1939, 2953, 3221.

Preparation of **2p**.

Conversion of **1p** to **2p** under general cyclization conditions described for **2a** led to 71% product. ^1H -NMR (500 MHz, CDCl_3) δ 0.88 (t, J = 7.5 Hz, 3H), 1.2-1.6 (m, 6H), 1.94 (m, 1H), 2.06 (s, 3H), 2.27 (m, 1H), 3.68 (m, 1H), 3.75 (m, 1H), 3.99 (q, J = 7.5 Hz, 1H), 5.27 (m,

1H). ^{13}C -NMR (75 MHz, CDCl_3) δ 13.9, 21.0, 22.7, 28.5, 28.5, 33.5, 65.7, 74.6, 81.7, 162.8.²⁰

Preparation of 1q.

1,5-Pentandiol (1.0 mL, 9.16 mmol, 1.0 equiv) was added dropwise to a slurry of NaH (366 mg, 60 wt% in mineral oil, 9.16 mmol, 1.0 equiv) in anhydrous THF (40 mL) at 0 °C. PMBCl (1.24 mL, 9.16 mmol, 1.0 equiv) was then added dropwise followed by addition of *n*Bu₄NI (390 mg, 1.06 mmol, 0.11 equiv). After stirring at rt for 1 h, the reaction was heated to 60 °C for 15 h. The reaction mixture was then poured into a solution of saturated NaHCO₃ and vigorously stirred. The two layers were separated, and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried over anhydrous Na₂SO₄. The product was purified by column chromatography (30% EtOAc in hexane) to yield 70% of the desired product (1.436 g). ^1H -NMR (300 MHz, CDCl_3) δ 1.3-1.6 (m, 7H), 3.42 (t, *J* = 6.6 Hz, 2H), 3.59 (t, *J* = 6.3 Hz, 2H), 3.77 (s, 3H), 4.40 (s, 2H), 6.84 (d, 2H), 7.23 (d, 2H).

To a slurry of PCC (2.07 g, 9.61 mmol, 1.5 equiv) in CH_2Cl_2 (30 mL), a solution of alcohol generated above (1.436 g, 6.41 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added at rt under N₂ with vigorous stirring. After stirring for 4 h at rt, anhydrous diethyl ether was added, and the reaction mixture was filtered through celite. The filtrate was concentrated *in vacuo*, and the product was purified by column chromatography with 10% EtOAc in hexane to yield the desired aldehyde in 68% yield (0.966 g). ^1H -NMR (300 MHz, CDCl_3) δ 1.63 (m, 4H), 2.36 (t, 2H), 3.39 (t, 2H), 3.71 (s, 3H), 4.35 (s, 2H), 6.84 (d, 2H), 7.20 (d, 2H), 9.66 (s, 1H).

To a slurry of Ph₃P(CH₂)₃CH₃Br (0.416 g, 1.04 mmol, 1.0 equiv) in anhydrous THF (20 mL) was added KHMDS (2.29 mL, 0.5 M solution in toluene, 1.14 mmol, 1.1 equiv) at 0 °C under N₂ atmosphere. The reaction was warmed to rt, stirred for 1 h and cooled back to 0 °C. The aldehyde generated above (0.231 g, 1.04 mmol, 1.0 equiv) in anhydrous THF (5 mL) was added, and the reaction was then stirred at rt for 12 h. The reaction was quenched with 10%

HCl, the two layers were separated and the aqueous layer was extracted with diethyl ether (3x). The combined organic layers were washed with saturated NaHCO₃ and brine, and dried over anhydrous MgSO₄. After filtration, the solvent was removed under reduced pressure, and a 5% ether in hexane solution was added to the concentrated crude product to precipitate the byproduct. After filtration, the filtrate was concentrated *in vacuo* and purified by silica gel chromatography (5% EtOAc in hexane) to yield 179 mg of the desired product (66%). ¹H-NMR (300 MHz, CDCl₃) δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.36 (m, 4H), 1.61 (m, 2H), 1.99 (m, 4H), 3.43 (t, *J* = 6.3 Hz, 2H), 3.78 (s, 3H), 4.41 (s, 2H), 5.35 (m, 2H), 6.86 (d, 2H), 7.25 (d, 2H).

To a stirred solution of PMB protected alcohol generated above (0.179 g, 0.687 mmol, 1.0 equiv) in CH₂Cl₂ (9.5 mL) and water (0.5 mL) was added DDQ (0.187 g, 0.825 mmol, 1.2 equiv) and the reaction mixture was stirred at rt for 1 h. Saturated NaHCO₃ aqueous solution was added, and the mixture was extracted with CH₂Cl₂ (3x). The extract was washed with saturated NaHCO₃ and brine, and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column with 30% EtOAc in hexane to yield the desired alcohol in 80% yield (77 mg). ¹H-NMR (300 MHz, CDCl₃) δ 0.87 (t, *J* = 7.4 Hz, 3H), 1.35 (m, 4H), 1.53 (s, 1H), 1.55 (m, 2H), 2.03 (m, 4H), 3.61 (t, *J* = 6.6 Hz, 2H), 5.34 (m, 2H).

Dihydroxylation procedure identical to the preparation of **1a** with the alcohol generated above gave the triol **1q** in 50% yield. ¹H-NMR (300 MHz, CD₃OD) δ 0.94 (t, 3H), 1.36 (m, 4H), 1.56 (m, 6H), 3.36 (m, 2H), 3.56 (t, 2H). ¹³C-NMR (75 MHz, CD₃OD) δ 14.5, 20.1, 23.3, 33.3, 33.7, 35.9, 63.0, 75.7, 75.9.

Preparation of 2q.

Conversion of **1q** to **2q** under general cyclization conditions described for **2a** led to 78% product. $^1\text{H-NMR}$ (500 MHz, CDCl_3) δ 0.88 (t, 3H), 0.4-1.6 (m, 9H), 1.82 (m, 1H), 2.05 (s, 3H), 3.30 (m, 1H), 3.35 (m, 1H), 3.99 (m, 1H), 4.85 (m, 1H). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) δ 14.1, 18.9, 21.3, 23.5, 26.1, 27.7, 32.5, 69.2, 75.5, 78.3, 171.1. IR: 1091, 1242, 1371, 1738, 2855, 2939, 2959 cm^{-1} . HRMS: M^+ (EI) observed 200.1413, calc'd 200.1412.

Preparation of 1r.

To a diethyl ether (10 mL) solution of LAH (0.134 g, 3.54 mmol, 1.0 equiv), *cis*-octadec-6-enoic acid (1.0 g, 3.54 mmol, 1.0 equiv) was added at 0 °C under N_2 . The reaction mixture was stirred at 0 °C for 30 min, and kept for 12 h at rt. The reaction was quenched with water and Na, K-tartrate. The product was extracted with diethyl ether (3x), and the combined organic layers were washed with brine, and dried over anhydrous Na_2SO_4 . The concentrated crude product was further purified by column chromatography with 10% EtOAc in hexane to yield the desired alcohol in 92% yield (0.873 g). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 0.86 (t, J = 6.6 Hz, 3H), 1.2 (m, 22H), 1.56 (m, 2H), 2.00 (m, 4H), 3.63 (t, J = 6.6 Hz, 2H), 5.33 (m, 2H).

Dihydroxylation procedure identical to the preparation of **1a** with the alcohol generated above gave the triol **1r** in 63% yield. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 0.86 (t, J = 7.2 Hz, 3H), 1.2-1.6 (m, 28H), 3.64 (m, 4H).

Preparation of 2r.

Trimethyl orthoacetate (14 μ L, 0.110 mmol, 1.2 equiv) was added to a mixture of triol **1r** (28 mg, 0.0914 mmol, 1.0 equiv), PPTS (1 mg, 0.004 mmol, 0.04 equiv) and toluene (10 mL) at rt. The mixture was stirred for 15 min, and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (14 μ L, 0.110 mmol, 1.2 equiv) was added at 0 $^\circ\text{C}$. The reaction mixture was then refluxed for 10 h. The reaction was cooled to rt and quenched with aqueous acetone. The solvent was removed under reduced pressure, and the product was purified via column chromatography to yield compound **2r** in 47% (14 mg) yield. ^1H -NMR (300 MHz, CDCl_3) δ 0.85 (t, J = 6.3 Hz, 3H), 1.23 (s, 20H), 1.42-1.76 (m, 8H), 2.06 (s, 3H), 3.49 (m, 2H), 3.86 (m, 1H), 4.85 (m, 1H). ^{13}C -NMR (75 MHz, CDCl_3) δ 14.1, 21.1, 22.7, 25.5, 26.2, 26.6, 29.3, 29.5, 29.6, 30.5, 30.9, 31.7, 31.9, 69.4, 76.2, 79.5, 170.9. IR: 1024, 1116, 1240, 1371, 1466, 1740, 2855, 2926 cm^{-1} . HRMS: $[\text{M}+\text{H}]^+$ (FAB) observed 327.2901, calc'd 327.2900.

Preparation of (*S,S*)-1,4,5-decanetriol

To a THF (50 mL) solution of *trans*-4-decenol (321 mg, 2.06 mmol, 1.0 eq.), NaH (165 mg, 4.11 mmol, 2.0 eq.) was added at 0 $^\circ\text{C}$ under a N_2 atmosphere. The mixture was warmed to rt, stirred for 1 h and cooled back to 0 $^\circ\text{C}$. Benzyl bromide (0.488 mL, 4.11 mmol, 2.0 eq.) was then added dropwise, followed by addition of TBAI (76 mg, 0.206 mmol, 0.1 eq.). After stirring at rt for 10 h, the reaction mixture was poured into a solution of saturated NaHCO_3 and vigorously stirred. The layers were separated, and the aqueous layer was extracted with EtOAc (3x). The combined organics were dried with Na_2SO_4 , and the solvent was removed under reduced pressure. The product was purified by column chromatography to yield 241 mg (48%) of the desired product. ^1H -NMR (300 MHz, CDCl_3) δ 0.90 (t, J = 7.4 Hz, 3H), 1.30 (m, 6H), 1.69 (p, J = 7.4 Hz, 2H), 1.98 (m, 2H), 2.07 (m, 2H), 3.48 (t, J = 6.6 Hz, 2H), 4.50 (s, 2H), 5.41 (m, 2H), 7.34 (m, 5H). ^{13}C -NMR (75 MHz, CDCl_3) δ 14.0, 22.5, 29.1, 29.2, 29.6, 31.3, 32.5, 69.7, 72.8, 127.4, 127.6, 128.3, 129.3, 131.0, 138.6.

To a mixture of *t*BuOH (5 mL), water (5 mL) and AD-mix- α (1.4 g) was added MeSO₂NH₂ (95 mg). The mixture was stirred at rt until both phases were clear at which time it was cooled to 0 °C. The olefin generated above (241 mg, 0.98 mmol, 1.0 eq.) was added at 0 °C, and the heterogeneous slurry was stirred vigorously at 0 °C for 12 h. The reaction was quenched at 0 °C by addition of sodium sulfite (1.5 g) and then warmed to rt and stirred for 45 min. The reaction mixture was then extracted with EtOAc (3x), and the combined organics were washed with 2M KOH, then dried over MgSO₄ and concentrated. The product was purified with column chromatography (40% EtOAc in hexane) to yield 218 mg (80%) of the desired product. ¹H-NMR (300 MHz, CDCl₃) δ 0.87 (t, *J* = 6.1 Hz, 3H), 1.2-1.8 (m, 12H), 3.32 (m, 2H), 3.48 (t, *J* = 6.0 Hz, 2H), 4.48 (s, 2H), 7.30 (m, 5H); ¹³C-NMR (75 MHz, CDCl₃) δ 13.96, 22.52, 25.26, 25.93, 30.68, 31.79, 33.35, 70.29, 72.90, 73.95, 74.37, 127.55, 127.60, 128.28, 137.95.

The %*ee* for the diol generated above could not be determined since the enantiomers were not separable on a chiral HPLC column, nor could we achieve satisfactory separation utilizing chiral GC. There a small amount of the diol was converted to it the acetal pictured above to determine enantiomeric excess. The diol generated above (38 mg, 0.134 mmol, 1.0 eq.) was dissolved in a solution of acetone (1.5 mL) and 2,2-dimethoxypropane (0.5 mL, 4.0 mmol, 30 eq.). To this mixture was added *p*-toluenesulfonic acid (8 mg, 0.04 mmol, 0.3 eq.) and the reaction mixture was stirred at rt for 12 h. The pH of the solution was then adjusted to 7 with NH₄OH. Following this, the acetone was evaporated under vacuum. The residue was dissolved in EtOAc (10 mL), and the organics were washed with brine (3 x 2.5 mL). The combined organics were dried with Na₂SO₄ and the solvent was concentrated under vacuum to give a crude residue, which was purified by column chromatography to afford 30 mg (70%) of the desired product. The product was subjected to chiral HPLC analysis (ChiralCel OD with guard column, flushed with 1% *i*PrOH in hexane), yielding two separable enantiomers.

Based on HPLC results the diol is obtained with 91% *ee*. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 0.88 (t, $J = 6.9$ Hz, 3H), 1.29 (m, 4H), 1.36 (s, 6H), 1.48 (m, 4H), 1.66 (m, 4H), 3.50 (m, 2H), 3.59 (m, 2H), 4.49 (s, 2H), 7.28 (m, 5H).

To a solution of the chiral diol (91% *ee*) generated above (92 mg, 0.33 mmol, 1.0 eq.) in EtOH (10 mL) was added Pd/C (92 mg). The reaction mixture was stirred under H_2 atmosphere for 12 h. The mixture was filtered, and the solvent was removed under reduced pressure, and the product was purified by column chromatography (EtOAc) to yield 62 mg (98%) desired product. $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 0.85 (t, $J = 6.6$ Hz, 3H), 1.26 (m, 5H), 1.42 (m, 4H), 1.63 (m, 3H), 3.34 (m, 2H), 3.61 (m, 2H), 4.12 (br, 3H).

Conversion of above chiral triol under general cyclization conditions described for compound **2a** led to the desired product. Chiral GC analysis (Supelco β -DEX 325 column) indicates the product was obtained in 91% *ee*. All spectroscopic data match the authentic racemic product **2a**.

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1d

1d

2d

2h

2h

1i

1i

2i

2i

2j

2k

2k

2k'

2l

2l

1n

5n

S-100