SUPPORTING INFORMATION

Steroselective Heterocycle Synthesis through a Reversible Allylic Alcohol Transposition and Nucleophilic Addition Sequence

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General

$^1$H NMR and $^{13}$C NMR spectra were taken on a Bruker Avance 300 spectrometer at 300 MHz and 75 MHz respectively, a Bruker Avance 400 spectrometer at 400 MHz and 100 MHz, or a Bruker Avance 500 spectrometer at 500 MHz and 125 MHz, as specified. The chemical shifts are reported in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as a reference value, for $^1$H NMR: CDCl$_3$ = 7.27 ppm, CD$_2$Cl$_2$ = 5.31 ppm, CD$_3$OD = 5.06 ppm, for $^{13}$C NMR: CDCl$_3$ = 77.23, CD$_2$Cl$_2$ = 53.52, C$_6$D$_6$ = 128.37. Data are reported as follows: m = multiplet, s = singlet; d = doublet; t = triplet; q = quartet; p = pentet; dd = doublet of doublets; dt = doublet of triplets; br = broad. High resolution mass spectra were recorded on a Micromass UK Limited Q-Tof Ultima API or a Fissions VG Autospec spectrometer. Infrared (IR) spectra were taken on a Mattson Cygnus 100 spectrometer. Samples for IR were prepared as thin films on a NaCl plates by dissolving the corresponding compounds in CH$_2$Cl$_2$ followed by evaporation of the CH$_2$Cl$_2$. Methylene chloride was distilled under N$_2$ from CaH$_2$. Analytical TLC was performed on E. Merck pre-coated (25 mm) silica gel 60F-254 plates. Visualization was done under UV (254 nm). Flash chromatography was done using ICN SiliTech 32 Å silica gel. Reagent grade ethyl acetate, diethyl ether, pentane and hexanes (commercial mixture) were purchased from EM Science and used as is for chromatography. All reactions were performed in oven or flame-dried glassware under a positive pressure of N$_2$ with magnetic stirring unless otherwise noted.

General procedure for the Re$_2$O$_7$-mediated cyclization

To a solution of the substrate in CH$_2$Cl$_2$ (~0.05-0.10M) was added Re$_2$O$_7$ (0.05 equiv). The reaction mixture was stirred at rt (unless otherwise mentioned) until the starting was completely consumed as determined by TLC, then the reaction was quenched with a few drops of pyridine or triethylamine and the solvent was removed under vacuum. The final products were isolated after purification by flash chromatography or preparative TLC.

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\begin{array}{c}
\text{Reagents and conditions} \\
a) \text{DIBAL-H, THF,} -78^\circ \text{C, then I$_2$, 52\%. b) IBX, DMSO, 84\%. c) (MeO)$_2$CH, PPTs, MeOH, 88\%. d) BuLi, THF,} -78^\circ \text{C, then PhCHO, CH$_2$CHO, 60\%. e) HOAc, H$_2$O, 100\%.}
\end{array}
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$^1$H NMR (400 MHz, CD$_2$Cl$_2$) δ 9.73 (t, $J$ = 1.2 Hz, 1H), 7.26-7.29 (m, 2H), 7.15-7.21 (m, 3H), 5.65 (dt, $J$ = 0.4, 6.4, 15.6 Hz, 1H), 5.54 (t, $J$ = 1.2, 6.4, 15.6 Hz, 1H), 4.04 (app q, $J$ = 5.6 Hz, 1H), 2.59-2.73 (m, 2H), 2.51 (t, $J$ = 8.0 Hz, 2H), 2.35 (q, $J$ = 4.8 Hz, 2H), 1.70-1.87 (m, 2H); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) δ 202.3, 142.6, 134.7, 129.8, 128.8, 128.7, 126.1, 72.3, 43.5, 39.3, 32.1, 25.1; IR (neat) 3439, 3063, 3031, 2954, 2925, 2867, 1605, 1496, 1469, 1283, 1166.
1453, 1375, 1179, 1121, 1024 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{14}H_{18}O_2Na\) [M+Na]\(^+\) 241.1204, found 241.1211.

5-(4-phenylbut-1-en-1-yl)tetrahydrofuran-2-ol (5)

The general cyclization procedure was followed with 5 (50 mg, 0.23 mmol), Re\(_2\)O\(_7\) (5.5 mg, 0.011 mmol), and CH\(_2\)Cl\(_2\) (3 mL). The reaction was stirred at rt for 30 min and then was quenched with pyridine (25 \(\mu\)L). After evaporation of the solvent, the crude mixture was purified by flash chromatography (10-20% ethyl acetate in hexanes) to give the product (10 mg, 20%, dr = 1:2:1). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.24-7.28 (m, 2H), 7.14-7.19 (m, 3H), 5.70 (app q, \(J = 6.4\) Hz, 0.45H), 5.67 (app q, \(J = 6.4\) Hz, 0.55H), 5.54 (dt, \(J = 1.2, 7.6\) Hz, 0.45H), 5.49-5.52 (m, 0.55H), 5.44 (dt, \(J = 1.2, 7.2\) Hz 0.45H), 5.39-5.41 (m, 0.55H), 4.54 (q, \(J = 6.8\) Hz, 0.55H), 4.33 (q, \(J = 6.9, 0.45\)H), 2.65-2.72 (m, 2H), 2.57-2.63 (m, 1H), 2.30-2.43 (m, 2H), 1.82-2.16 (m, 2H), 1.70-1.82 (m, 1H), 1.46-1.55 (m, 0.6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 141.9, 133.0, 131.6, 131.4, 131.0, 128.4, 128.2, 125.7, 98.5, 98.4, 81.4, 78.8, 35.5, 34.2, 34.0, 33.8, 33.2, 30.4, 30.0; IR (neat) 3402, 3060, 3025, 2933, 2857, 1603, 1495, 1453, 1191, 1018; HRMS (ESI) calcd for C\(_{14}H_{18}O_2Na\) [M+Na]\(^+\) 241.1204, found 241.1228.

(E)-8,8-dimethoxy-1-phenyloct-4-en-3-ol (6)

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.28-7.32 (m, 2H), 7.18-7.22 (m, 3H), 5.68 (ddt, \(J = 0.4, 6.4\) Hz, 15.2, 1H), 5.55 (ddt, \(J = 1.2, 6.8, 15.2\) Hz, 1H), 4.40 (t, \(J = 5.6\) Hz, 1H), 4.09 (q, \(J = 5.7\) Hz, 2H), 3.34 (s, 6H), 2.64-2.77 (m, 2H), 2.10-2.15 (q, \(J = 7.1\) Hz, 2H), 1.77-1.94 (m, 2H), 1.74 (br, 1H), 1.70-1.70 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 142.0, 133.4, 131.2, 128.5, 128.4, 125.8, 103.9, 72.2, 52.76, 53.74, 38.8, 32.0, 31.8, 27.3; IR (neat) 3426, 3060, 3025, 2941, 2857, 2831, 1669, 1602, 1495, 1452, 1385, 1190, 1127, 1058 969, 913, 747 cm\(^{-1}\); HRMS (APCI) calcd for C\(_{16}H_{24}O_3Na\) [M+Na]\(^+\) 287.1623, found 287.1632.

2-methoxy-5-(4-phenylbut-1-en-1-yl)tetrahydrofuran (8)

The general cyclization procedure was followed with 6 (50 mg, 0.19 mmol), Re\(_2\)O\(_7\) (4.6 mg, 0.010 mmol), DCM (3 mL), the reaction was stirred at rt for 30 min, then was quenched with pyridine (25 \(\mu\)L). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (36 mg, 83%, dr = 6:4). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.28-7.25 (m, 2H), 7.18-7.25 (m, 3H), 5.69-5.84 (m, 1H), 5.43-5.65 (m, 1H), 5.08 (dd, \(J = 2.0, 5.2\) Hz, 0.6H), 4.99 (d, \(J = 4.4\) Hz, 0.4H), 4.50 (q, \(J = 7.1\) Hz, 0.6H), 4.45 (q, \(J = 7.7\) Hz, 0.4H), 3.39 (s, 1.8H), 3.37 (s, 1.2H), 2.62-2.82 (m, 2H), 2.26-2.53 (m, 2H), 1.70-2.20 (m, 3.4H), 1.50-1.62 (m, 0.6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 141.8, 132.8, 132.3, 131.8, 130.6, 128.5, 128.4, 128.32, 128.30, 125.9, 125.8, 105.3, 105.0, 81.5, 78.7, 54.9, 54.5, 35.53, 35.49, 34.1, 34.0, 33.5, 32.4, 30.3, 30.1; IR (neat) 3061, 3026, 2984, 2928, 2828, 1684, 1603, 1495, 1453, 1363, 1203, 1098, 1034, 966, 746 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{17}H_{20}O_3Na\) [M+Na]\(^+\) 255.1361, found 255.1374.

Reagents and conditions
a) HOAc, H\(_2\)O. b) TBDPSI, imidazole, DMAP, DMF. c) (EtO)\(_2\)P(O)(O)CH\(_2\)CH\(_3\), NaH, THF. d) H\(_2\)pyridine, THF.


(3E,8E)-10-hydroxydeca-3,8-dien-2-one (9)

\(^1\)H NMR (400 MHz, CH\(_2\)Cl\(_2\)) \(\delta\) 6.77 (dt, \(J = 7.2, 16.0\) Hz, 1H), 6.03 (dt, \(J = 1.4, 16.0\) Hz, 1H), 5.59-5.70 (m, 2H), 4.04 (d, \(J = 3.6\) Hz, 2H), 2.22 (dt, \(J = 1.4, 7.2\) Hz, 2H), 2.19 (s, 3H), 2.03-2.11 (m, 2H), 1.56 (p, \(J = 7.6\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CH\(_2\)Cl\(_2\)) \(\delta\) 198.3, 147.9, 131.7, 131.4, 130.1, 63.4, 31.8, 31.6, 27.6, 26.6; IR (neat) 3427, 3004, 2928, 2857, 1672, 1625, 1431, 1362, 1431, 1362, 1257, 1089, 972 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{10}H_{16}O_2Na\) [M+Na]\(^+\) 191.1048, found 191.1066.
1-((2S,6R)-6-vinyltetrahydro-2H-pyran-2-yl)propan-2-one (10)

The general rearrangement procedure was followed with 9 (14.2 mg, 0.084 mmol), Re₂O₇ (2.1 mg, 0.004 mmol), and CD₂Cl₂ (1.5 mL). The reaction was stirred at 20 °C for 10 min, after which the catalyst was removed through a small pad of Celite. ^1H NMR was taken directly to show a quantitative conversion. ^1H NMR (400 MHz, CD₂Cl₂) δ 5.90 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.16 (dt, J = 1.6, 17.2 Hz, 1H), 5.02 (dt, J = 1.6, 10.4 Hz, 1H), 3.75-3.85 (m, 2H), 2.63 (dd, J = 7.6, 15.6 Hz, 1H), 2.42 (dd, J = 5.2, 15.6 Hz, 1H), 2.13 (s, 3H), 1.79-1.87 (m, 1H), 1.51-1.65 (m, 3H), 1.13-1.29 (m, 2H); ^13C NMR (100 MHz, CD₂Cl₂) 207.1, 139.6, 113.7, 78.1, 74.1, 50.3, 31.19, 31.16, 30.6, 20.3; IR (neat) 2934, 2857, 1717, 1438, 1358, 1199, 1089, 1045, 989, 916 cm⁻¹; HRMS (EI) calcd for C₁₀H₁₅O₂ [M–H]⁺ 167.1072, found 167.1100.

Reagents and conditions
a) BuOCl, p-TsOH, Na₂SO₄, CH₂Cl₂, 64% (n = 1), 51% (n = 2), 52% (n = 3). b) Methyl acrylate, Grubbs-Hoveyda metathesis catalyst, CH₂Cl₂, reflux, 89% (n = 1), 97% (n = 2), 99% (n = 3). c) DiBAL-H, CH₂Cl₂, –78°C, 90% (n = 1), 89% (n = 2), 86% (n = 3).


(E)-6,6-bis(benzyloxy)hex-2-en-1-ol (11)

¹H NMR (400 MHz, CDCl₃) δ 7.34-7.45 (m, 10H), 5.62-5.76 (m, 2H), 4.83 (t, J = 6.0 Hz, 1H), 4.74 (d, J = 12.0 Hz, 2H), 4.64 (d, J = 12.0 Hz, 2H), 4.07 (d, J = 4.8 Hz, 2H), 2.40 (br, 1H), 2.24 (q, J = 7.0 Hz, 2H), 1.93 (q, J = 7.0 Hz, 2H); ^13C NMR (100 MHz, CDCl₃) δ 138.3, 131.6, 129.8, 128.6, 127.9, 127.8, 101.6, 67.4, 63.4, 32.8, 27.6; IR (neat) 3401, 3087, 3062, 3030, 2930-2868, 1670, 1605, 1496, 1453, 1385, 1353, 1208, 1124, 1023, 737 cm⁻¹; HRMS (APCI) calcd for C₂₀H₂₁O₃Na [M+Na]⁺ 355.1623, found 355.1608.

2-(Benzyloxy)-5-vinyltetrahydrofururan (12)

The general cyclization procedure was followed with 11 (100 mg, 0.32 mmol), Re₂O₇ (7.8 mg, 0.016 mmol), and CH₂Cl₂ (5 mL). The reaction was stirred at rt for 30 min and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (55 mg, 84%, dr = 6:4). ^1H NMR (400 MHz, CDCl₃) δ 7.28-7.40 (m, 5H), 5.95 (ddd, J = 7.2, 10.0, 17.2 Hz, 0.4H), 5.90 (ddd, J = 6.8, 10.4, 17.2 Hz, 0.6H), 5.23-5.33 (m, 2H), 5.13-5.18 (m, 1H), 4.82 (d, J = 12.0 Hz, 0.4H), 4.81 (d, J = 12.0 Hz, 0.6H), 4.81 (q, J = 6.8 Hz, 0.6H), 4.50-4.55 (m, 1.4H), 2.20-2.30 (m, 0.6H), 2.08-2.16 (m, 1.5H), 1.88-2.04 (m, 1.5H), 1.61-1.70 (m,0.8H); ^13C NMR (100 MHz, CDCl₃) 140.5, 138.5, 138.34, 138.32, 128.4, 127.94, 127.88, 127.5, 115.7, 115.6, 103.5, 103.2, 81.8, 78.9, 69.0, 68.6, 33.5, 32.1, 30.02, 30.0; IR (neat) 3064,3030, 2924, 2853, 1605, 1455,1273, 1205, 1025, 733 cm⁻¹; HRMS (APCI) calcd for C₁₃H₁₆O₂Na [M+Na]⁺ 227.1048, found 227.1049.

(E)-7,7-bis(benzyloxy)hept-2-en-1-ol (13)

¹H NMR (300 MHz, CDCl₃) 7.33-7.44 (m, 10H), 5.62-5.76 (m, 2H), 4.83 (t, J = 6.0 Hz, 1H), 4.75 (d, J = 11.7 Hz, 2H), 4.65 (d, J = 11.7 Hz, 2H), 2.14 (q, J = 6.5 Hz, 2H), 1.86 (q, J = 7.2 Hz, 2H), 1.95 (p, J = 7.6 Hz, 2H); ^13C NMR (75 MHz, CDCl₃) δ 138.4, 132.1, 129.8, 128.6, 127.9, 127.8, 102.1, 67.3,63.4, 32.9, 32.1, 24.4; IR 3403, 3062, 3030, 2932, 2865, 1669, 1605,1496, 1454,1384, 1351, 1208, 1124, 1023, 736 (neat) cm⁻¹; HRMS (ESI) calcd for C₂₁H₂₆O₃Na [M+Na]⁺ 349.1780, found 349.1754.

2-(benzyloxy)-6-vinyltetrahydro-2H-pyran (14)

The general rearrangement procedure was followed with 13 (100 mg, 0.31 mmol), Re₂O₇ (7.4 mg, 0.015 mmol), and DCM (5 mL). The reaction was stirred at rt for 30 min and then
was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (55 mg, 81%, dr = 7:3). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.28-7.41 (m, 5H), 5.95 (ddd, $J = 5.2, 10.4, 17.2$ Hz, 0.3H), 5.88 (ddd, $J = 6.0, 10.8, 17.2$ Hz, 0.7), 5.31 (dt, $J = 1.6, 17.2$ Hz, 0.3H), 5.26 (dt, $J = 1.6, 17.6$ Hz, 0.7H), 5.14 (dt, $J = 1.4, 10.8$ Hz, 0.3H), 5.13 (dt, $J = 1.4, 10.4$ Hz, 0.7H), 5.00 (d, $J = 1.6$ Hz, 0.3H), 4.95 (d, $J = 12.0$ Hz, 0.3H), 4.76 (d $J = 12.0$ Hz, 0.7H), 4.65 (d, $J = 12.0$ Hz, 0.3H), 4.55 (dd, $J = 2.0, 9.2$ Hz, 0.3H), 4.52 (d, $J = 12.0$ Hz, 0.7H), 4.31 (dddd, $J = 1.6, 1.6, 5.6, 10.4$ Hz, 0.7H), 3.93 (ddddd, $J = 1.2, 1.6, 2.4, 5.2, 11.2$ Hz, 0.3H), 1.25-2.05 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 139.3, 138.6, 138.4, 138.1, 128.4, 128.0, 127.8, 127.6, 127.5, 114.8, 114.6, 101.0, 96.7, 76.5, 69.8, 69.7, 68.5, 31.1, 31.0, 30.8, 29.5, 22.0, 18.0; IR (neat) 3065, 3030, 2940, 2867, 1646, 1604, 1496, 1454, 1357, 1261, 1205, 1121, 1023, 736 cm$^{-1}$; HRMS (APCI) calcd for C$_{14}$H$_{18}$O$_2$Na [M+Na]$^+$ 241.1204, found 241.1184.

$^{(E)}$-8,8-bis(benzyloxy)oct-2-en-1-ol (15)

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.34-7.46 (m, 10H), 5.64-5.76 (m, 2H), 4.83 (t, $J = 5.6$ Hz, 1H), 4.74 (d, $J = 12.0$ Hz, 2H), 4.65 (d, $J = 12.0$ Hz, 2H), 4.09 (d, $J = 4.8$ Hz, 2H), 2.64 (br, 1H), 2.12 (q, $J = 6.1$ Hz, 2H), 1.86 (q, $J = 6.8$ Hz, 2H), 1.41-1.58 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 138.4, 132.5, 129.5, 128.5, 127.9, 127.7, 102.2, 67.3, 63.4, 33.2, 32.2, 29.0, 24.3; IR (neat) 3406, 3062, 3030, 2923, 2861, 1669, 1605, 1494, 1454, 1384, 1351, 1205, 1125, 1022, 736 cm$^{-1}$; HRMS (APCI) calcd for C$_{22}$H$_{23}$O$_3$Na [M+Na]$^+$ 363.1936, found 363.1925.

2-(Benzyloxy)-7-vinlyoxepane (16)

The general rearrangement procedure was followed with 15 (100 mg, 0.29 mmol), Re$_2$O$_7$ (7.1 mg, 0.015 mmol), and CH$_2$Cl$_2$ (5 mL). The reaction was stirred at rt for 30 min and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (55 mg, 81%, dr = 9:1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.28-7.40 (m, 5H), 5.94 (ddd, $J = 5.2, 10.4, 17.2$ Hz, 1H), 5.34 (dt, $J = 1.6, 17.2$ Hz, 1H), 5.14 (dt, $J = 1.6, 10.4$ Hz, 0.1H), 5.13 (dt, $J = 1.6, 10.4$ Hz, 0.9H), 4.93 (dd, $J = 5.6, 8.8$ Hz, 0.9H), 4.88 (d, $J = 12.0$ Hz, 0.1H), 4.81 (d, $J = 11.6$ Hz, 0.9H), 4.70 (dd, $J = 3.6, 7.6$ Hz, 0.1H), 4.57 (d, $J = 12.0$ Hz, 0.1H), 4.52 (d, $J = 11.6$ Hz, 0.9H), 4.45 (dd, $J = 5.2, 9.6$ Hz, 0.9H), 4.01-4.04 (m, 0.1H), 2.13-2.22 (m, 1H), 1.88-1.98 (m, 1H), 1.65-1.87 (m, 3H), 1.36-1.60 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 140.3, 139.5, 138.4, 138.1, 128.4, 128.1, 128.0, 127.5, 113.6, 103.3, 100.3, 77.8, 71.1, 69.2, 69.1, 36.5, 35.9, 35.7, 35.4, 29.5, 24.7, 23.3, 22.5; IR (neat) 3064, 3030, 2931, 2856, 1645, 1605, 1496, 1452, 1356, 1206, 1131, 1055, 1024, 735 cm$^{-1}$; HRMS (APCI) calcd for C$_{15}$H$_{26}$O$_3$Na [M+Na]$^+$ 255.1361, found 255.1359.

Reagents and conditions

a) Penteny/l-magnesium bromide, THF, 0 °C, 89%. b) PCC, Celite, CH$_2$Cl$_2$, 96%. c) p-TsOH, (MeO)$_2$CH, MeOH, 50 °C, 93%. d) Ethyl acrylate, Grubbs-Hoveyda metathesis catalyst, CH$_2$Cl$_2$, reflux. e) DiBAL-H, CH$_2$Cl$_2$, −78 °C.


$^{(E)}$-7,7-Dimethoxy-9-phenylnon-2-en-1-ol (17)

$^1$H NMR (400 MHz, C$_6$D$_6$) δ 7.04-7.18 (m, 5H), 5.47-5.57 (m, 2H), 3.87 (br, 2H), 3.05 (s, 6H), 2.58-2.63 (m, 2H), 1.94 -2.01 (m, 2H), 1.89-1.93 (m, 2H), 1.66-1.71 (m, 2H), 1.40 (p, $J = 7.6$ Hz, 2H); $^{13}$C NMR (100 MHz, C$_6$D$_6$) δ 142.1, 131.1, 130.3, 128.4, 128.2, 125.8, 102.8, 63.1, 47.2, 34.7, 32.3, 32.2, 30.4, 23.5; IR (neat) 3400, 3025, 2949, 2829, 1669, 1603, 1495, 1454, 1368, 1181, 1054, 971, 743 cm$^{-1}$; HRMS (ESI) calcd for C$_{17}$H$_{26}$O$_3$Na [M+Na]$^+$ 301.1780, found 301.1811.
(±)-(2S, 6R)-2-methoxy-2-phenethyl-6-vinyltetrahydro-2H-pyran (18)

The general rearrangement cyclization procedure was followed with 17 (11 mg, 0.039 mmol), Re₂O₇ (2.0 mg, 0.004 mmol), and CD₂Cl₂ (1.0 mL). The reaction was stirred at 0 °C for 2 min, after which the cold bath was removed, and the reaction was stirred for another 8 min and then was quenched with pyridine (25 µL). Me₂(Bn)SiH (5 µL) was added as an internal standard and crude NMR was used to determine the yield of 85%. ¹H NMR (400 MHz, CDCl₃) δ 7.12-7.19 (m, 2H), 7.04-7.11 (m, 3H), 5.88 (ddd, J = 5.6, 9.8, 17.2 Hz, 1H), 5.29 (dt, J = 1.8, 17.2 Hz, 1H), 5.03 (dt, J = 1.6, 17.2 Hz, 1H), 4.08 (ddd, J = 1.2, 1.6, 2.4, 5.2, 11.6 Hz, 1H), 3.07 (s, 3H), 2.53-2.69 (m, 2H), 1.98-2.09 (m, 1H), 1.72 (ddd, J = 1.6, 1.6, 1.6, 12.8 Hz, 1H) 1.36-1.51 (m, 2H), 1.19-1.30 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 142.3, 139.8, 128.4, 128.3, 125.7, 113.3, 99.1, 70.7, 46.7, 38.4, 32.2, 31.0, 30.0 18.9; IR (neat) 3063, 3026, 2941, 2867, 1646, 1603, 1496, 1454, 1367, 1273, 1216, 1104, 1024, 924, 755, 738 cm⁻¹; HRMS (ESI) calc for C₁₆H₂₂O₂Na [M+Na]+ 269.1517, found 269.1548.

Scheme 5. Synthesis of substrate 19.

(S,E)-7,7-Bis(benzyloxy)-4-methylhept-2-en-1-ol (19)

¹H NMR (300 MHz, CDCl₃) δ 7.31-7.45 (m, 10H), 5.53-5.66 (m, 2H), 4.79 (t, J = 5.7 Hz, 1H), 4.73 (d, J = 11.7 Hz, 2H), 4.63 (d, J = 11.7 Hz, 2H), 4.10 (d, J = 4.2 Hz, 2H), 2.19 (heptet, J = 6.6 Hz, 1H), 1.94 (br, 1H), 1.74-1.88 (m, 2H), 1.40-1.54 (m, 2H), 1.06 (d, J = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 138.3, 138.1, 128.5, 127.9, 127.7, 102.3, 67.28, 67.26, 67.23, 63.6, 31.7, 31.1, 20.5; IR (neat) 3403, 3063, 3030, 2926, 2867, 1667, 1605, 1493, 1454, 1380, 1349, 1208, 1122, 1022, 756 cm⁻¹; HRMS (ESI) calc for C₂₂H₂₁O₃Na [M+Na]+ 363.1936, found 363.1973.

(2S,3S,6S)-6-(Benzyloxy)-3-methyl-2-vinyltetrahydro-2H-pyran (20)

The general rearrangement procedure was followed with 19 (50 mg, 0.16 mmol), Re₂O₇ (2 mg, 0.004 mmol), and CH₂Cl₂ (5 mL). The reaction was stirred at rt for 20 min and then was quenched with pyridine (25 µL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (33 mg, 100%, dr = 3:3:1:1).

¹H NMR (400 MHz, CDCl₃) δ 7.29-7.34 (m, 2H), 7.16-7.20 (m,2H), 7.07-7.12 (m, 1H), 5.74 (ddd, J = 4.8, 10.8, 17.2 Hz, 1H), 5.39 (dt, J = 2.0, 17.2 Hz, 1H), 5.10 (dt, J = 2.0, 10.8 Hz, 2H), 4.85 (d, J = 3.2 Hz, 1H), 4.70 (d, J = 12.0 Hz, 1H), 4.51 (ddd, J = 0.5, 1.4, 1.6, 2.4 Hz, 1H), 4.37 (d, J = 12.0 Hz, 1H), 2.13 (ddd, J = 4.6, 4.6, 13.6, 13.6 Hz, 1H), 1.68 (ddd, J = 4.4, 4.4, 14.0, 14.0 Hz, 1H), 1.54 (m, 1H), 1.45 (ddd, J = 1.2, 2.8, 4.4, 14.0 Hz, 1H), 1.21 (ddd, J = 2.4, 2.8, 5.2, 13.6 Hz, 1H), 0.93 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 138.7,138.4, 128.2, 127.8, 127.3, 113.6, 96.4, 70.8, 68.3, 31.3, 25.3, 24.2, 11.4; IR (neat) 3065, 3030, 2938, 2892, 1645, 1606, 1453, 1351, 1211, 1126, 1019, 729 cm⁻¹; HRMS (APCI) calc for C₁₅H₂₁O₂Na [M+Na]+ 255.1361, found 255.1372.

(2R, 3S, 6S)-6-(Benzyloxy)-3-methyl-2-vinyltetrahydro-2H-pyran and (2S, 3S, 6R)-(6-benzyloxy)-3-methyl-2-vinyltetrahydro-2H-pyran

¹H NMR (400 MHz, CDCl₃) δ 7.28-7.36 (m, 2H), 7.13-7.19 (m, 2H), 7.05-7.11 (m, 1H), 5.87 (ddd, J = 6.8, 10.4, 17.2 Hz, 0.75H), 5.81 (ddd, J = 5.2, 10.8, 17.2 Hz, 0.25H), 5.35 (dt, J = 2, 17.2 Hz, 0.25H), 5.27 (ddd, J = 0.8, 2.0, 17.2 Hz, 0.75H), 5.06-5.11 (m, 1H), 4.96 (d, J = 12.0 Hz, 0.25H), 4.89 (d, J = 3.2 Hz, 0.75H), 4.73 (d, J = 12.0 Hz, 0.75H), 4.53 (d, J = 12.0 Hz, 0.25H), 4.41 (dd, J = 2.8, 8.4 Hz, 0.25H), 4.40 (d, J = 12.0 Hz, 0.75H), 3.91 (dd, J = 7.2, 9.6 Hz, 0.75H), 3.84 (ddd, J = 1.6, 1.6, 3.8, 5.8 Hz, 0.25H), 1.45-1.85 (m, 3H), 1.25-1.45 (m, 2H), 0.87 (d, J = 6.4 Hz, 0.75H),
0.71 (d, J = 6.4 Hz, 2.25H); 13C NMR (100 MHz, C6D6) δ 138.8, 138.7, 138.2, 137.7, 128.21, 128.17, 127.8, 127.3, 116.0, 114.3, 100.9, 95.9, 69.3, 68.2, 35.1, 31.4, 30.2, 28.3, 26.8, 26.7, 17.7, 12.5; IR (neat) 3066, 3030, 2930, 2876, 1645, 1604, 1455, 1376, 1232, 1123, 1023, 923, 730 cm⁻¹; HRMS (APCI) calc'd for C13H26O2Na [M+Na]+ 255.1361, found 255.1377.

**Scheme 6. Synthesis of substrate 21.**

**(2R, 3S, 6R)-6-(Benzylxylo)-3-methyl-2-vinyltetrahydro-2H-pyrano**

1H NMR (400 MHz, C6D6) δ 7.33-7.37 (m, 2H), 7.13-7.20 (m, 2H), 7.06-7.12 (m, 2H), 5.89 (dd, J = 6.8, 10.4, 17.2 Hz, 1H), 5.29 (dd, J = 1.2, 2.0, 17.2 Hz, 1H), 5.09 (dd, J = 0.8, 2.0, 10.4 Hz, 1H), 4.98 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.37 (dd, J = 2.8, 8.8 Hz, 1H), 3.25 (dd, J = 2.8 Hz, 10), 1.60-1.75 (m, 2H), 1.41-1.48 (dt, J = 3.6, 13.6 Hz, 2H), 1.15-1.28 (m, 2H), 0.80-0.91 (m, 2H), 0.61 (d, J = 6.4 Hz, 3H); 13C NMR (100 MHz, C6D6) δ 138.8, 137.6, 128.2, 127.8, 127.3, 115.8, 100.7, 82.7, 69.5, 34.7, 31.7, 31.1, 16.8; IR (neat) 3065, 3029, 2952, 2929, 2873, 2853, 1645, 1606, 1496, 1362, 1146, 1055, 1091, 920, 736 cm⁻¹; HRMS (APCI) calc'd for C13H26O2Na [M+Na]+ 255.1361, found 255.1342.

**(5S,E)-8,8-Bis(benzyloxy)-5-methyloct-3-en-2-ol (21)**

1H NMR (400 MHz, CDCl3) δ 7.29-7.44 (m, 10H), 5.44-5.56 (m, 2H), 4.76 (t, J = 5.6 Hz, 1H), 4.69 (d, J = 12.0 Hz, 2H), 4.59 (d, J = 12.0 Hz, 2H), 4.26 (p, J = 5.6 Hz, 1H), 2.07-2.18 (m, 1H), 1.72-1.82 (m, 2H), 1.65 (br, 1H) 1.37-11.49 (m, 2H), 1.27 (d, J = 6.4 Hz, 3H), 1.02 (d, J = 6.8 Hz, 1H) 1.01 (d, J =6.8 Hz, 2H); 13C NMR (100 MHz, CDCl3) δ 138.3, 136.1, 136.0, 133.08, 133.04, 128.5, 127.8, 127.7, 102.27, 102.25, 68.9, 68.8, 67.24, 67.15, 67.13, 36.2, 36.1, 31.7, 31.6, 31.1, 23.6, 23.5, 20.6, 20.5 IR (neat) 3417, 3063, 3030, 2958, 2869, 1666, 1605, 1496, 1453, 1369, 1207, 1124, 1023, 972, 736 cm⁻¹; HRMS (ESI) calc'd for C23H30O3Na [M+Na]+ 377.2093, found 377.2063.

**Scheme 7. Synthesis of substrate 22.**

**(2R, 3S, 6S)-6-(Benzylxylo)-3-methyl-2-((E)-prop-1-en-1-yl)tetrahydro-2H-pyrano**

The general cyclization procedure was followed with 21 (50 mg, 0.14 mmol), Re2O5 (3 mg, 0.007 mmol), and CH2Cl2 (3 mL). The reaction was stirred at rt for 30 min and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (30 mg, 86%, dr = 3:1; trans: cis > 10:1 as determined by the 1H NMR spectrum of the crude mixture). 1H NMR (400 MHz, CD2Cl2) δ 7.24-7.36 (m, 5H), 6.66 (dq, J = 6.4, 15.2 Hz, 1H), 5.39 (ddq, J = 1.6, 8, 15.2 Hz, 1H), 4.88 (dd, J = 2.0, 2.4 Hz, 1H), 4.67 (d, J = 12.0 Hz, 1H), 4.42 (d, J = 12.0 Hz, 1H), 3.74 (dd, J = 8.8, 9.2 Hz, 1H) 1.66-1.75 (m, 2H), 1.70 (dd, J = 1.6, 6.4 Hz, 3H), 1.48-1.58 (m, 2H), 1.35-1.47 (m, 1H), 0.77 (d, J = 6.4 Hz, 3H); 13C NMR (100 MHz, CD2Cl2) δ 138.8, 131.2, 128.8, 128.2, 127.8, 127.3, 96.4, 76.4, 68.3, 35.0, 30.2, 26.7, 17.8, 17.5. IR (neat) 3063, 3030, 2929, 2876, 1676, 1604, 1454, 1376, 1230, 1049, 1022, 972, 920, 730 cm⁻¹; HRMS (ESI) calc'd for C16H22O2Na [M+Na]+ 269.1517, found 269.1558.

**Scheme 8. Synthesis of substrate 23.**

**(2S, 3S, 6R)-6-(Benzylxylo)-3-methyl-2-((E)-prop-1-en-1-yl)tetrahydro-2H-pyrano**

1H NMR (400 MHz, C6D6) δ 7.35-7.38 (m, 2H), 7.14-7.19 (m, 2H), 7.05-7.11 (m, 1H), 5.67 (ddq, J = 0.8, 6.0, 15.2 Hz, 1H), 5.58 (ddq, J = 1.6, 6.8, 15.2 Hz, 1H), 5.01 (d, J =12.0 Hz, 1H), 4.59 (d, J = 12.0 Hz, 1H), 4.40 (dd, J = 2.8, 8.8 Hz, 1H), 3.28 (dd, J = 6.8, 9.6 Hz, 1H), 1.63-1.79 (m, 2H), 1.59 (d, J = 6.4 Hz, 3H), 1.49 (dq, J = 3.6, 13.2 Hz, 1H), 1.19-1.33 (m, 1H), 0.83-0.95 (m, 1H), 0.65 (d, J = 6.8 Hz, 3H); 13C NMR (100 MHz, C6D6) δ 138.8, 131.3, 128.2, 127.8, 127.4, 127.2,
100.7, 82.6, 69.4, 34.9, 31.8, 31.2, 17.5, 17.1; IR (neat) 3030, 2950, 2929, 2853, 1676, 1606, 1454, 1365, 1146, 1102, 1078, 1031, 966, 735 cm⁻¹; HRMS (ESI) calcd for C₁₆H₂₅O₂Na [M+Na]⁺ 269.1517, found 269.1529.

Reagents and conditions
a) Vinyl oxirane, Grubbs-Hoveyda metathesis catalyst, CH₂Cl₂, reflux, 25%. b) Me₂CuCNLi, THF, -78 °C to rt, 60%

Scheme 7. Synthesis of substrate 23.

(±)-(2S, 5R, 6S)-2-Methoxy-5-methyl-2-phenethyl-6-vinyltetrahydro-2H-pyran (24)

The general rearrangement procedure was followed with 23 (50 mg, 0.17 mmol), Re₂O₇ (4 mg, 0.008 mmol), and CD₂Cl₂ (3.0 mL). The reaction was stirred at 0 °C for 30 min, after which the cold bath was removed, the reaction was stirred for another 10 min, then quenched with pyridine (25 μL). BnMe₂SiH (5 μL) was added as an internal standard, and a ¹H NMR spectrum was taken of the crude mixture to determine the yield (81%, dr = 10:1). ¹H NMR (500 MHz, CD₂Cl₂) δ 7.24-7.29 (m, 2H), 7.14-7.22 (m, 2H), 5.78 (ddd, J = 7.5, 10.0, 17.5 Hz, 1H), 5.23 (dd, J = 17.5, 2.0 Hz, 1H), 5.14 (dd, J = 10.0, 17.5 Hz, 1H), 3.60 (dd, J = 7.5, 10.0 Hz, 1H), 2.61 (m, 2H), 1.97 (ddd, J = 5.0, 12.0, 14.0 Hz, 2H), 1.81-1.85 (m, 1H), 1.76 (ddd, J = 4.5, 12.5, 14.0 Hz, 2H), 1.50-1.62 (m, 3H), 1.31-1.38 (m, 1H), 0.82 (d, J = 6.5 Hz, 3H); ¹³C NMR (125 MHz, CD₂Cl₂) δ 142.4, 138.1, 128.3, 128.2, 125.7, 116.5, 98.8, 78.1, 47.1, 38.0, 34.5, 32.9, 29.8, 27.6, 17.5; IR (neat) 3403, 3026, 2953, 2875, 1645, 1605, 1496, 1455, 1368, 1236, 1079, 1041, 932, 740 cm⁻¹; HRMS (APCI) calcd for C₁₇H₂₉O₃ [M+H⁺] 293.2117, found 293.2088.

Reagents and conditions
a) Diethyl phosphonopropionate, NaH, THF, 65%. b) DIBAL-H, CH₂Cl₂, -78 °C, 95%. c) IBX, DMSO, 100%. d) MeMgBr, THF, 0 °C, 100%, dr = 2:2:1.


(5S, Z)-8,8-Bis(benzoxyl)-3,5-dimethyloct-3-en-2-ol (25)

Major isomer: ¹H NMR (400 MHz, C₆D₆) δ 7.31-7.36 (m, 2H), 7.16-7.21 (m, 2H), 7.09-7.12 (m, 1H), 4.83 (d, J = 10.0 Hz, 1H), 4.71 (t, J = 5.6 Hz, 1H), 4.61 (dd, J = 4.8, 12.0 Hz, 2H), 4.52-4.58 (m, 1H), 4.49 (d, J = 12.0 Hz, 2H), 2.27-2.39 (m, 1H), 1.70-1.87 (m, 2H), 1.70 (d, J = 0.8 Hz, 3H), 1.38-1.46 (m, 1H), 1.22-1.34 (m, 1H), 1.13 (dd, J = 2.8, 6.4 Hz, 3H), 0.84 (d, J = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CD₂Cl₂) δ 138.62, 138.58, 137.2, 132.5, 128.3, 127.8, 127.9, 127.50, 127.49, 102.55, 67.4, 67.2, 65.6, 32.5, 31.4, 31.3, 21.52, 21.49, 16.8; IR (neat) 3439, 3063, 3030, 2954, 2867, 1605, 1496, 1453, 1375, 1121, 1024, 736 cm⁻¹; HRMS (ESI) calcd for C₂₄H₃₂O₃Na [M+Na⁺] 391.2249, found 391.2263. Minor isomer: ¹H NMR (400 MHz, C₆D₆) δ 7.29-7.35
The general cyclization procedure was followed with 25 (50 mg, 0.14 mmol), Re_2O_5 (3 mg, 0.007 mmol), and CH_2Cl_2 (1.5 mL), the reaction was stirred at rt for 30 min and then quenched with pyridine (25 µL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (32 mg, 91%, dr = 3:1). 

\[ ^1H \text{NMR (400 MHz, CD_3OD)} \delta 7.34-7.37 (m, 2H), 7.14-7.20 (m, 2H), 7.06-7.11 (m, 1H), 5.44 (q, J = 1.2, 6.8 Hz, 1H), 4.92 (d, J = 3.2 Hz, 1H), 4.79 (d, J = 12.4 Hz, 1H), 4.43 (d, J = 12.4 Hz, 1H), 3.92 (d, J = 10.4 Hz, 1H), 1.66-1.78 (m, 2H), 1.71 (d, J = 1.2 Hz, 3H), 1.52-1.63 (m, 2H), 1.53 (dq, J = 1.2, 6.4 Hz, 3H), 1.39-1.46 (m, 1H), 0.68 (d, J = 6.4 Hz, 3H); \]^13C NMR (100 MHz, CD_3OD) \delta 138.9, 135.2, 128.1, 127.8, 127.2, 122.4, 101.0, 88.5, 69.4, 31.9, 31.7, 31.2, 17.0, 12.7, 12.7, 11.1; IR (neat) 3030, 2950, 2927, 2888, 1731, 1602, 1454, 1308, 1285, 1174, 915, 779 cm\(^{-1}\); HRMS (APCI) calcd for C_{17}H_{26}O_3Na [M+Na]^+ 283.1674, found 283.1665.

\[ (2S,3S,6S)-6-(Benzyloxy)-2-((E)-but-2-en-2-yl)-3-methyltetrahydro-2H-pyran (26) \]

\[ (2S,3S,6R)-6-(Benzyloxy)-2-((E)-but-2-en-2-yl)-3-methyltetrahydro-2H-pyran \]

Reagents and conditions

a) O_3, CH_2Cl_2, -78 °C, then Me_2S, 33%. b) (MeO)_2CH, p-TsOH, MeOH, 50 °C, 52%. c) Methyl acrylate, Grubbs-Hoveyda second generation metathesis catalyst, CH_2Cl_2, reflux, 85%. d) DIBAL-H, CH_2Cl_2, -78 °C, 58%. e) HOAc, H_2O, 95%. 

\[ \text{HRMS (APCI) calcd for C}_{17}\text{H}_{26}\text{O}_3\text{Na [M+Na]^+} 283.1674, found 283.1685. \]

\[ \text{Scheme 9. Synthesis of substrate 27.} \]
3H), 1.77-1.82 (m, 1H), 1.60-1.65 (m, 1H), 1.17-1.36 (m, 3H), 0.78 (d, J = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, CH$_2$Cl$_2$) δ 207.0, 137.9, 116.2, 85.1, 73.7, 50.2, 34.9, 32.3, 31.8, 30.5, 17.4; IR (neat) 3079, 2927, 2873, 2851,1716, 1457, 1425, 1356, 1225, 1072, 1018, 991, 923 cm$^{-1}$; HRMS (ESI) calcd for C$_{11}$H$_{18}$O$_2$Na [M+Na]$^+$ 205.1204, found 205.1224.

Reagents and conditions

a) Methyl vinyl ketone, Grubbs-Hoveyda second generation metathesis catalyst, CH$_2$Cl$_2$, reflux, 85%. b) DiBAL-H, CH$_2$Cl$_2$, $-78$ °C, 48%, two steps. c) HOAc, H$_2$O, 82%.
d) (EtO)$_2$P(O)(CH$_2$CH$_2$)OH, Na, THF, 82%.

Scheme 10. Synthesis of substrate 29.

(3E,7S,8E)-10-hydroxy-7-methylundeca-3,8-dien-2-one (29)

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) δ 6.76 (dt, J = 6.9, 15.9 Hz, 1H), 6.03 (dd, J = 1.2, 15.9 Hz, 1H), 5.38-5.52 (m, 2H), 4.26 (q, J = 6.0 Hz, 2H), 2.21 (s, 3H), 2.04-2.21 (m, 3H), 1.38-1.47 (m, 2H), 1.23 (d, J = 6.3 Hz, 3H), 0.98 (d, J = 6.6 Hz, 1.5H), 0.97 (d, J = 6.6 Hz, 1.5H); $^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) δ 198.8, 148.47, 148.42, 135.4, 135.3, 133.5, 131.2, 68.7, 68.6, 35.89, 35.87, 35.0, 30.2, 26.9, 23.6, 23.56, 20.4; IR (neat) 3431, 2966, 2925, 2870, 1672, 1625, 1453, 1364, 1255, 1140, 1059, 975 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{20}$O$_2$Na [M+Na]$^+$ 219.1361, found 219.1392.

1-((2R,5S,6S)-5-methyl-6-((E)-prop-1-en-1-yl)tetrahydro-2H-pyran-2-yl)propan-2-one (30)

The general rearrangement procedure was followed with 29 (20.0 mg, 0.102 mmol), Re$_2$O$_7$ (2.5 mg, 0.005 mmol), and CH$_2$Cl$_2$ (1.5 mL). The reaction was stirred at rt for 50 min and then was quenched with pyridine (25 µL). Me$_2$(Bn)SiH (5 µl) was added as an internal standard. Crude $^1$H NMR was used to determine the yield of 90%. $^1$H NMR (400 MHz, CH$_2$Cl$_2$) δ 5.68 (ddq, J = 0.8, 6.4, 15.2 Hz, 1H), 5.40 (ddq, J = 1.6, 7.6, 15.2 Hz, 1H), 3.77 (dddd, J = 2.4, 2.4, 6.4, 10.8 Hz, 1H) 3.35 (dd, J = 8.4, 8.8 Hz, 1H), 2.74 (dd, J = 6.4, 15.6 Hz, 1H), 2.47 (dd, J = 6.0, 15.6 Hz, 1H), 2.17 (s, 3H), 1.78-1.84 (m, 1H), 1.70 (dd, J = 1.6, 6.4 Hz, 3H), 1.64-1.69 (m, 3H), 1.20-1.37 (m, 3H), 0.78 (d, J = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, CH$_2$Cl$_2$) δ 207.5, 130.9, 129.0, 85.1, 73.6, 50.3, 35.0, 32.3, 31.9, 31.0, 17.9, 17.8; IR (neat) 2925, 2872, 2852, 1716, 1676, 1453, 1357, 1224, 1186, 1169, 1151, 1069, 1014, 965 cm$^{-1}$; HRMS (APCI) calcd for C$_{12}$H$_{20}$O$_2$Na [M+Na]$^+$ 219.1361, found 219.1383.

Reagents and conditions

a) Butenediol bis((trehlyl) ether), Grubbs-Hoveyda metathesis catalyst, CH$_2$Cl$_2$, reflux, 42%. b) Bu$_4$NF, THF, 97%. c) HOAc, H$_2$O, 85%.

Scheme 11. Synthesis of substrate 38 and 46.

(E)-8,8-Dimethoxy-10-phenyldec-3-ene-1,2-diol (38)

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) δ 7.23-7.29 (m, 2H), 7.14-7.21 (m, 3H), 5.76 (ddt, J = 2.0, 7.0, 15.5 Hz, 1H), 5.47 (ddt, J = 1.2, 6.5, 5.0 Hz, 1H), 4.11-4.18 (m, 1H), 3.54-3.60 (m, 1H), 3.39-3.45 (m, 1H), 3.24 (s, 6H), 2.51-2.56 (m, 2H), 2.24 (br, 1H), 2.04-2.10 (q, J = 7.0 Hz, 2H), 2.04-2.10 (br, 1H), 1.81-1.86 (m, 2H), 1.59-1.64 (m, 2H), 1.34-1.41 (m, 2H); $^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) δ 142.2, 133.2, 129.4, 128.3, 128.2, 125.8, 102.8, 73.1, 66.6, 47.5, 34.2, 32.3, 31.8, 30.1, 23.2; IR (neat) 3399, 3061, 3025, 2949, 2828, 1669, 1603, 1495, 1454, 1303, 1182, 1072, 971, 742 cm$^{-1}$; HRMS (ESI) calcd for C$_{16}$H$_{20}$O$_3$Na [M+Na]$^+$ 331.1885, found 331.1889.
(E)-9,10-Dihydroxy-1-phenyldec-7-en-3-one (46)

$^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 7.23-7.30 (m, 2H), 7.14-7.20 (m, 3H), 5.69 (ddt, $J = 1.2, 6.8, 15.2$ Hz, 1H), 5.43 (ddt, $J = 1.4, 6.4, 15.2$ Hz, 1H), 4.09-4.17 (m, 1H), 3.56 (dd, $J = 2.0, 10.8$ Hz, 1H), 3.41 (dd, $J = 7.4, 11.2$ Hz, 1H), 2.85 (t, $J = 7.4$ Hz, 2H), 2.85 (br, 1H), 2.71 (t, $J = 7.4$ Hz, 2H), 2.71 (br, 1H), 2.38 (t, $J = 7.4$ Hz, 2H), 2.01 (q, $J = 7.4$ Hz, 2H), 1.62 (p, $J = 7.4$ Hz, 2H); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) $\delta$ 210.0, 141.4, 132.5, 129.6, 128.4, 128.3, 126.0, 73.0, 66.6, 44.1, 42.0, 31.6, 29.6, 23.0; HRMS (ESI) calcd for C$_{16}$H$_{22}$O$_3$Na [M+Na]$^+$ 285.1467, found 285.1470.

(±)-(1R, 5S, 7S)-5-Phenethyl-7-vinyl-6,8-dioxabicyclo[3.2.1]octane (40)

The general rearrangement procedure was followed with 38 (100 mg, 0.32 mmol), Re$_2$O$_7$ (8 mg, 0.02 mmol), and CH$_2$Cl$_2$ (5.0 mL). The reaction was stirred at rt for 21 h then was quenched by pyridine (25 µL). The crude material was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (39 mg, 49%, dr = 4:3, for substrate was quenched). $^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 7.22-7.29 (m, 2H), 7.18-7.22 (m, 2H), 7.12-7.18 (m, 1H), 6.05 (ddd, $J = 6.8, 10.4, 17.2$ Hz, 1H), 5.42 (dt, $J = 1.6, 17.2$ Hz, 1H), 5.29 (ddd, $J = 1.2, 1.6, 10.4$ Hz, 1H), 4.49 (ddq, $J = 1.2, 4.4, 6.8,$ 1H), 4.30 (t, $J = 4.0$), 2.73-2.79 (m, 2H), 1.94-2.00 (m, 2H), 1.90-2.00 (m, 1H), 1.72-1.83 (m, 1H), 1.63-1.79 (m, 2H), 1.53-1.63 (m, 2H); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) $\delta$ 142.7, 133.3, 128.34, 128.25, 125.6, 118.4, 108.7, 81.6, 77.7, 39.9, 33.4, 29.0, 24.6, 17.1; IR (neat) 3062, 2954, 2915, 1603, 1496, 1456, 1373, 1253, 1236, 1099, 1028, 988, 862,749 cm$^{-1}$; HRMS (APCI) calcd for C$_{16}$H$_{21}$O$_2$ [M+H]$^+$ 245.1442, found 245.1521.

(±)-(1R, 5S, 7R)-5-Phenethyl-7-vinyl-6,8-dioxabicyclo[3.2.1]octane (39)

$^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 7.23-7.28 (m, 2H), 7.13-7.21 (m, 3H), 5.88 (ddd, $J = 7.2, 10.0, 17.2$ Hz, 1H), 5.24 (ddd, $J = 1.2, 1.6, 17.2$ Hz, 1H), 5.10 (ddd, $J = 0.8, 1.6, 10.0$ Hz, 1H), 4.44 (ddd, $J = 0.4, 3.6$ Hz, 1H), 4.20 (br, 1H), 2.72-2.78 (m, 2H), 1.94-2.00 (m, 2H), 1.85-1.94 (m, 1H), 1.75-1.84 (m, 1H), 1.61-1.69 (m, 3H), 1.54-1.61 (m, 1H); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) $\delta$ 142.6, 139.0, 128.32, 128.27, 125.6, 115.3, 109.3, 80.8, 79.8, 39.6, 33.9, 29.4, 28.1, 17.1; IR (neat) 3062, 3026, 2925, 2871, 1728, 1607, 1496, 1457, 1374, 1343, 1278, 1234, 1179, 1111, 1085, 1032, 1004, 924, 750 cm$^{-1}$; HRMS (APCI) calcd for C$_{16}$H$_{21}$O$_2$ [M+H]$^+$ 245.1442, found 245.1581.

Reagents and conditions

a) AD-Mix β, CH$_3$SO$_2$NHz, iBuOH, H$_2$O, 0 °C. b) TESCl, imidazole, DMAP, DMF, 74% (two steps). c) Alkenyl ketal, Grubbs-Hoveyda metathesis catalyst, CH$_2$Cl$_2$, reflux, 27%. d) Bu$_2$NF, THF, 75%.

Scheme 12. Synthesis of 43.

(±)-9,10-Dimethoxy-11-phenylundec-4-ene-2,3-diol (43)

$^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 7.25-7.30 (m, 2H), 7.15-7.21 (m, 3H), 5.75 (ddt, $J = 0.8, 6.8, 15.2$ Hz, 1H), 5.46 (ddt, $J = 1.4, 7.2, 15.2$ Hz, 1H), 3.74 (t, $J = 6.8$ Hz, 1H), 3.60 (t, $J = 6.4$ Hz, 1H), 3.15 (s, 6H), 2.51-2.56 (m, 2H), 2.08 (q, $J = 6.8$ Hz, 2H), 1.82-1.88 (m, 2H), 1.60-1.65 (m, 2H), 1.35-1.43 (m, 2H), 1.12 (d, $J = 6.0$ Hz, 3H); $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) $\delta$ 142.2, 133.9, 130.0, 128.4, 128.2, 125.8, 102.9, 77.8, 70.8, 47.5, 34.2, 32.4, 31.9, 30.1, 23.2, 18.8; IR (neat) 3411, 3061, 3025, 2951, 2829, 1669, 1603, 1495, 1454, 1368, 1266, 1181, 1055, 972, 742 cm$^{-1}$; HRMS (EI) calcd for C$_{10}$H$_{30}$O$_4$Na [M+Na]$^+$ 345.2042, found 345.2051.
(1R, 5S, 7R)-5-Phenethyl-7-((E)-prop-1-en-1-yl)-6,8-dioxabicyclo[3.2.1]octane (44)

The general cyclization procedure was followed with 43 (50 mg, 0.16 mmol), \( \text{Re}_2\text{O}_7 \) (4 mg, 0.008 mmol), and \( \text{C}_2\text{H}_2\text{Cl}_2 \) (5.0 mL). The reaction was stirred at rt for 15 h and then was quenched with pyridine (25 µL). The crude mixture was purified by flash chromatography (1%–3% ethyl acetate in hexanes) to give the product (21 mg, 53%, dr = 7:5 : 1). \(^1\)H NMR (400 MHz, \( \text{CD}_2\text{Cl}_2 \)) \( \delta \) 7.23-7.29 (m, 2H), 7.18-7.22 (m, 2H), 7.12-7.18 (m, 1H), 5.67 (dtt, \( J = 0.4, 6.4, 15.2 \) Hz, 1H), 5.52 (dtt, \( J = 1.4, 8.0, 15.2 \) Hz, 1H), 4.40 (d, \( J = 8.0 \) Hz, 1H), 2.72-2.78 (m, 2H), 1.91-1.98 (m, 2H), 1.83-1.91 (m, 1H), 1.73-1.81 (m, 1H), 1.69 (dd, \( J = 1.6, 6.4, 3.6 \) Hz, 3H), 1.59-1.66 (m, 3H), 1.52-1.58 (m, 1H); \(^{13}\)C NMR (100 MHz, \( \text{CD}_2\text{Cl}_2 \)) \( \delta \) 142.7, 132.1, 128.33, 128.25, 127.3, 125.6, 108.9, 80.7, 79.9, 39.6, 34.0, 29.4, 28.1, 17.3, 17.1; IR (neat) 3061, 3026, 2950, 1671, 1603, 1496, 1453, 1373, 1344, 1175, 1067, 1024, 990, 906, 751 cm\(^{-1}\); HRMS (APCI) calcd for \( \text{C}_{17}\text{H}_{32}\text{O}_2 \) [M+H\(^+\)]\(^+\) 259.1698, found 259.1673.

Reagents and conditions
a) Pentenylmagnesium bromide, THF, 0 °C, 82%. b) PCC, Celite, \( \text{CH}_2\text{Cl}_2 \), 81%. c) (MeO)\(_2\)CH, \( \rho \)-TsOH, MeOH, 50 °C, 92%. d) Methyl acrylate, Grubbs-Hoveyda metathesis catalyst, \( \text{CH}_2\text{Cl}_2 \), reflux, 88%. e) DiBAL-H, \( \text{CH}_2\text{Cl}_2 \), −78 °C, 77%. f) HOAc, \( \text{H}_2\text{O} \), 84%.


\((2\text{E},11\text{E})\)-7,7-dimethoxytrideca-2,11-diene-1,13-diol (47)

\(^1\)H NMR (400 MHz, \( \text{CD}_2\text{D}_6 \)) \( \delta \) 5.53-5.75 (m, 4H), 4.06 (br, 4H), 3.22-3.38 (br, 2H), 3.07 (s, 6H), 2.00 (q, \( J = 3.2 \) Hz, 4H), 1.65-1.71 (m, 4H), 1.42 (p, \( J = 7.6 \) Hz, 4H); \(^{13}\)C NMR (100 MHz, \( \text{CD}_2\text{D}_6 \)) \( \delta \) 131.2, 130.3, 103.3, 62.9, 47.2, 32.3, 32.1, 23.5; IR (neat) 3384, 2946, 1710, 1670, 1457, 1369, 1314, 1180, 1088, 970 cm\(^{-1}\); HRMS (ESI) calcd for \( \text{C}_{13}\text{H}_{28}\text{O}_4\text{Na} \) [M+Na\(^+\)]\(^+\) 295.1885, found 295.1860.

\((2\text{E},11\text{E})\)-1,13-dihydroxytrideca-2,11-dien-7-one (50)

\(^1\)H NMR (400 MHz, \( \text{CD}_2\text{Cl}_2 \)) \( \delta \) 5.60-5.70 (m, 4H), 4.06 (br, 4H), 2.42 (t, \( J = 7.2 \) Hz, 4H), 2.25-2.35 (br, 2H), 2.02-2.09 (m, 4H), 1.66 (p, \( J = 7.2 \) Hz, 4H); \(^{13}\)C NMR (100 MHz, \( \text{CD}_2\text{Cl}_2 \)) \( \delta \) 211.0, 131.5, 130.1, 63.2, 41.8, 31.5, 23.1; IR (neat) 3250, 3052, 3011, 2933, 2865, 1698, 1457, 1415, 1371, 1266, 1088, 1016, 970 cm\(^{-1}\); HRMS (ESI) calcd for \( \text{C}_{13}\text{H}_{22}\text{O}_3\text{Na} \) [M+Na\(^+\)]\(^+\) 249.1467, found 249.1451.

\((\pm)-(2\text{R}, 6\text{R}, 8\text{R})\)-2,8-Divinyl-1,7-dioxaspiro[5.5]undecane (48)

The general rearrangement procedure was followed with 47 (14 mg, 0.051 mmol), \( \text{Re}_2\text{O}_7 \) (1.2 mg, 0.0025 mmol), and \( \text{C}_2\text{H}_2\text{Cl}_2 \) (1.0 mL). The reaction was stirred at rt for 30 min. \( \text{BnMe}_2\text{SiH} \) (5 µl) was added as an internal standard, and a \(^1\)H NMR spectrum was taken of the crude mixture to show an 88% yield and 1:1 ratio of two stereoisomers. Additional stirring (>12 h) resulted in the mixture giving essentially a single diastereomer (dr > 20:1) with a decrease in overall yield (60%). The general rearrangement cyclization procedure was also followed with 50 (50 mg, 0.221 mmol), \( \text{Re}_2\text{O}_7 \) (5.4 mg, 0.011 mmol), and \( \text{C}_2\text{H}_2\text{Cl}_2 \) (3.0 mL). The reaction was stirred at rt for 30 min. \( \text{BnMe}_2\text{SiH} \) (5 µl) was added as an internal standard, and a \(^1\)H NMR spectrum was taken of the crude mixture to show a 94% yield and 1:1 ratio of two stereoisomers. Additional stirring (48 h) with the addition of MeOH showed isomerization of the mixture to give essentially a single stereoisomer with a decrease in overall yield (61%). \(^1\)H NMR (400 MHz, \( \text{CD}_2\text{D}_6 \)) \( \delta \) 5.89 (ddd, \( J = 5.2, 10.4, 17.2 \) Hz, 2H), 5.30 (dt, \( J = 1.6, 17.2 \) Hz, 2H), 5.02 (dt, \( J = 1.6, 10.4 \) Hz, 2H), 4.17 (dddd, \( J = 1.2, 1.6, 2.4, 5.6, 11.2 \) Hz, 2H), 2.03 (dq, \( J = 4.0, 13.2 \) Hz, 2H), 1.63 (dddd, \( J = 1.6, 2.4, 4.0, 13.2 \) Hz, 2H), 1.41-1.49 (m, 2H), 1.34-1.41 (m, 2H), 1.17-1.34 (m, 4H); \(^{13}\)C NMR (100 MHz, \( \text{CD}_2\text{D}_6 \)) \( \delta \) 140.0 113.2, 95.9, 69.7, 35.2, 31.1, 18.8; IR 3012, 2927, 2854, 1646, 456, 1374, 1279, 1220, 981, 917 (neat) cm\(^{-1}\); HRMS (APCI) calcd for \( \text{C}_{13}\text{H}_{21}\text{O} \) [M+H\(^+\)]\(^+\) 209.1542, found 209.1567.

(5E, 12E)-8,8-dimethoxypentadeca-3,12-diene-2,14-diol (51)

\[
\text{H NMR (400 MHz, } \text{CDCl}_3\text{) } \delta 5.52-5.62 \text{ (m, 4H), 4.21 (p, } J = 5.2 \text{ Hz, 2H), } 3.07 \text{ (s, 6H), 2.89 (br, 2H), 1.94-2.0 (m, 4H), 1.65-1.70 \text{ (m, 4H), 1.37-1.45 (m, 4H), 1.25 (d, } J = 4.6 \text{ Hz, 6H); }^{13}\text{C NMR (100 MHz, } \text{CDCl}_3\text{) } \delta 135.5, 129.1, 103.2, 68.1, 47.1, 32.1, 32.0, 23.6, 23.5; \text{ IR (neat) } 3388, 2950, 1711, 1670, 1455, 1368, 1294, 1181, 1060, 969, 941, 864 \text{ cm}\(^{-1}\); HRMS (APCI) calcd for } C_{17}H_{32}O_4Na [M+Na]^{+} 323.2198, \text{ found } 323.2199.
\]

Scheme 15. Synthesis of substrate 53.

(S, E)-7,7-dimethoxypentadeca-2-en-1-11-diol (53)

\[
\text{H NMR (400 MHz, } \text{CDCl}_3\text{) } \delta 5.58-5.71 \text{ (m, 2H), 4.04 (br, 2H), 3.63-3.70 \text{ (m, 1H), } 3.09 \text{ (s, 3H), 3.08 (s, 3H), 1.95-2.05 \text{ (m, 2H), 1.62-1.76 \text{ (m, 4H), 1.28-1.60 \text{ (m, 6H), 1.12 (d, } J = 6.0 \text{ Hz, 3H); }^{13}\text{C NMR (100 MHz, } \text{CDCl}_3\text{) } \delta 131.1, 130.5, 103.4, 67.2, 62.9, 47.2, 39.4, 32.6, 32.1, 31.8, 23.6, 23.4, 20.1; \text{ IR (neat) } 3396, 2949, 2871, 1669, 1458, 1372, 1131, 1041, 971 \text{ cm}\(^{-1}\); HRMS (ESI) calcd for } C_{14}H_{20}O_2Na [M+Na]^{+} 283.1885, \text{ found } 283.1915; [\alpha]_D^{219} = +6.26 (c 0.91, CHCl_3); ee>99\% as determined by Mosher ester analysis.
\]

(2S, 6R, 8R)-2-methyl-8-vinyl-1,7-dioxaspiro[5.5]undecane (55)

The general rearrangement procedure was followed with 53 (50 mg, 0.19 mmol) and ReO\(_4\) (5 mg, 0.01 mmol) in CD\(_2\)Cl\(_2\) (3.0 mL), the reaction was stirred at rt for 24 h. BnMe\(_2\)SiH (5 μl) was added as an internal standard, and a 1H NMR spectrum was taken of the crude mixture to show a 61% yield. 1H NMR (400 MHz, CDCl\(_3\)) δ 5.88 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.26 (dt, J = 1.6, 17.2 Hz, 1H), 5.09 (dt, J = 1.6, 10.4 Hz, 1H), 4.08 (ddddd, J = 1.2, 1.6, 2.4, 5.2, 10.4 Hz, 1H), 3.72 (dddd, J = 2.0, 6.0, 6.0, 8.0 Hz, 1H), 1.86-2.02 (m, 2H), 1.49-1.70 (m, 6H), 1.35-1.46 (m 2H), 1.18-1.35 (m, 2H), 1.15 (d, J = 6.4, 3H); 13C NMR (100 MHz, CDCl\(_3\)) δ 139.8, 114.0, 96.3, 69.5, 65.2, 35.2, 35.1 32.7, 30.8, 21.9, 18.9, 18.8; IR (neat) 2924, 2853, 1658, 1459, 1377, 1224, 1087, 992 cm\(^{-1}\); HRMS (ESI) calcd for C\(_{12}\)H\(_{20}\)O\(_2\)Na [M+Na]\(^{+}\) 219.1361, found 219.1387.
[α]D = −43.2 (c 0.31, CHCl3); ee: 96% as determined by HPLC analysis using a Phenomenex Lux 5μ Cellulose-3 column (250 x 4.60 mm) with MeOH/H2O (60/40, v/v) as the mobile phase.

5-((2S, 6R)-6-vinyltetrahydro-2H-pyran-2-yl)pentan-2-one (57)

1H NMR (400 MHz, CD2Cl2) δ 5.82 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.18 (dt, J = 1.6, 17.2 Hz, 1H), 5.02 (dt, J = 1.6, 10.4 Hz, 1H), 3.77 (dddd, J = 1.2, 1.6, 2.4, 5.2, 10.8 Hz, 1H), 3.30 (ddd, J = 2.0, 5.2, 7.6, 10.8 Hz, 1H), 2.41 (t, J = 7.2 Hz, 2H), 2.08 (s, 3H), 1.78-1.85 (m, 2H), 1.35-1.70 (m, 6H), 1.08-1.27 (m, 4H); 13C NMR (100 MHz, CD2Cl2) δ 208.7, 140.0, 113.5, 78.0, 77.3, 43.5, 35.8, 31.6, 31.3, 29.6, 23.5, 20.0; IR 3080, 2933, 2857, 1715, 1647, 1440, 1410, 1364, 1201, 1167, 1090, 1046, 990,919 (neat) cm−1; HRMS (APCI) caled for C12H21O2 [M+H]+ 197.1542, found 197.1566.

1-methoxy-6-((2S,6S)-6-methyltetrahydro-2H-pyran-2-yl)hexan-3-one (58)

1H NMR (400 MHz, CD2Cl2) δ 3.58 (t, J = 6.4, 2H), 3.36 (dddd, J = 2.0, 6.0, 6.0, 6.0, 11.2, 1H), 3.22 (dddd, J = 2.0, 5.2, 7.2, 10.8, 1H), 1.72-1.81 (m, 1H), 1.58-1.78 (m, 1H), 1.47-1.58 (m, 4H), 1.27-1.47 (m, 3H), 1.09 (d, J = 6.4, 3H), 1.05-1.15 (m, 1H). 13C NMR (100 MHz, CD2Cl2) δ 209.0, 77.3, 73.6, 67.6, 58.5, 43.1, 42.7, 35.9, 33.4, 31.3, 23.7, 22.0, 19.8. IR (neat) 2967, 2930, 2860, 1714, 1452, 1387, 1373, 1322, 1202, 1118, 1083, 1041, 963 cm−1; HRMS (ESI) caled for C13H24O3Na [M+Na]+ 251.1623, found 251.1637.

Reagents and conditions
a) Methyl vinyl ketone, Grubbs-Hoveyda metathesis catalyst, CH2Cl2, reflux, 53%. b) DIBAL-H, CH2Cl2, −78 °C, 61%.


(E)-8,8-dimethoxytridec-3-ene-2,12-diol (54)

1H NMR (400 MHz, CD3OD) δ 5.48-5.64 (m, 2H), 4.20 (p, J = 6.0 Hz, 2H), 3.65 (q, J = 5.2 Hz, 1H), 3.091 (s, 3H), 3.087 (s, 3H), 2.79 (d, J = 14.8 Hz, 1H), 2.52 (d, J = 15.6 Hz, 1H), 1.95-2.02 (q, J = 7.2 Hz, 2H), 1.66-1.77 (m, 3H), 1.27-1.59 (m, 6H), 1.24 (d, J = 6.4 Hz, 3H), 1.10 (d, J = 6.4 Hz, 3H); 13C NMR (100 MHz, CD3OD) δ 135.73, 135.68, 129.1, 103.3, 68.12,68.09, 67.16, 67.10, 47.1, 39.4, 32.61, 32.59, 32.0, 31.8, 31.7, 23.7, 23.53, 23, 48, 23.44, 20.12, 20.08 IR (neat) 3391, 2952, 2830, 1170, 1670, 1457, 1370, 1313, 1126, 1064, 969, 941 cm−1; HRMS (ESI) caled for C13H20O4Na [M+Na]+ 297.2042, found 297.2065.

(2S, 6R, 8R)-2-methyl-8-((E)-prop-1-en-1-yl)-1,7-dioxaspiro[5.5]undecane (56)

The general cyclization procedure was followed with 54 (50 mg, 0.18 mmol) and ReO7 (4 mg, 0.009 mmol) in CDCl3 (3.0 mL). The mixture was stirred at rt for 30 min after which the reaction was quenched with pyridine (25 μL). BnMe2SiH (5 μL) was added as an internal standard, and a 1H NMR spectrum was taken of the crude mixture to show a 65% yield. 1H NMR (400 MHz, CDCl3) δ 5.69 (ddq, J = 1.2, 6.4, 15.2 Hz, 1H), 5.51 (ddq, J = 1.6, 6.0, 15.2 Hz, 1H), 4.02 (ddp, J = 1.2, 6.0, 11.6 Hz, 1H), 3.72 (ddq, J = 2.0, 6.4, 11.2 Hz, 1H), 1.85-1.99 (m, 2H), 1.71 (dd, J = 2.4, 6.4, 3H), 1.49-1.66 (m, 6H), 1.41 (ddd, J = 4.4, 8.4, 13.2, 2H), 1.28-1.36 (m, 1H), 1.18-1.28 (m, 1H), 1.15 (d, J = 6.4 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 132.8, 126.2, 96.3, 69.5, 65.1, 35.21., 35.16, 32.8, 31.0, 21.9, 18.9, 18.8, 17.9; IR (neat) 2936, 2869, 1676, 1440, 1383, 1280, 1224, 1204,1087, 991, 964 cm−1; HRMS (APCI) caled for C13H25O2 [M+H]+ 211.1698, found 211.1716.

S13
Scheme 17. Synthesis of substrate 61.

Spireotricycles 62 and 63

The general rearrangement procedure was followed with 61 (110 mg, 0.354 mmol), ReO₄ (8.6 mg, 0.018 mmol), and CH₂Cl₂ (3.0 mL). The reaction was stirred at 0 °C for 2 h and then was quenched with pyridine (25 μL). After evaporation of the solvent, the crude mixture was purified by flash chromatography (1%-3% ethyl acetate in hexanes) to give the product (87 mg, 84%, dr = 1:1, 62: 43 mg, 63: 44 mg).

Faster eluting major isomer 62: ¹H NMR (400 MHz, CDCl₃) δ 5.60 (ddq, J = 0.8, 6.4, 15.2 Hz, 2H), 5.40 (ddq, J = 1.6, 6.8, 15.2 Hz, 2H), 4.21 (dd, J = 7.2, 11.2 Hz, 2H), 1.85-1.98 (m, 4H), 1.79-1.83 (m, 2H), 1.65 (d, J = 6.4 Hz, 6H), 1.54-1.70 (m, 8H), 1.20-1.31 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 133.0, 125.8, 106.8, 71.4, 34.8, 31.2, 20.3, 17.5; IR (neat) 3023, 2981, 2937, 2864, 1731, 1676, 1452, 1439, 1375, 1314, 1266, 1231, 1072, 1028, 968, 874 cm⁻¹; HRMS (ESI) calcd for C₁₈H₃₀O₄Na [M+Na]⁺ 333.2042, found 333.2075.

Slower eluting minor isomer 63: ¹H NMR (400 MHz, CDCl₃) δ 5.58 (ddq, J = 0.8, 6.4, 15.6 Hz, 2H), 5.41 (ddq, J = 1.6, 6.8, 15.6 Hz, 2H), 4.28 (dd, J = 7.2, 10.8 Hz, 2H), 2.01-2.07 (m, 2H), 1.81-1.91 (m, 2H), 1.73-1.79 (m, 2H), 1.65 (d, J = 6.4 Hz, 6H), 1.48-1.63 (m, 8H), 1.22-1.33 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 133.0, 126.2, 107.2, 72.6, 37.4, 34.8, 31.1, 20.1, 17.5; IR (neat) 3022, 2936, 2864, 1676, 1453, 1439, 1377, 1301, 1233, 1165, 1073, 1028, 964, 866 cm⁻¹; HRMS (ESI) calcd for C₁₈H₂₆O₃Na [M+Na]⁺ 315.1936, found 315.1919. The stereochemical arrangement was established by HPLC analysis using a Phenomenex Lux 5μ Cellulose-3 column (250 x 4.60 mm) with MeOH/H₂O (Black line: 60/40 or Purple Line: 70/30, v/v) as the mobile phase.

The two stereoisomers were resubjected to the following isomerization condition: 7.2 mg ReO₄ (0.015 mmol) and 1.5 ml CDCl₂. After stirring at 0 °C for 4 h, the isomerizations were quenched with pyridine (25 μL). BnMe₂SiH (5 μL) was added as an internal standard to each isomerization mixture, and a ¹H NMR spectrum was taken of the crude mixture to show that the equilibration of 62 provided 51% of 60 and 27% of 63. The equilibration of 61 provided 52% of 62 and 29% of 63. Thus, after one cycle of isomerization: a total yield of 64% could be obtained for 62 and a total yield of 54% could be obtained for 63.
Figure 1. HPLC traces of 62 (pink) and 63 (black) using a chiral stationary phase.
Electronic Supplementary Material (ESI) for Chemical Science
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300 1H reduction of ester 100910

\[ \text{OH} \quad \text{OBn} \]

300 13C reduction of ester 160910
400B 1H CD2Cl2 NOESY Rearrangement Major Product 031011-3
400 MHz COSY CD2Cl2 Rearrangement Spot #1 033011
400R COSY CD2Cl2 Rearrangement Major Product 020111
### Electronic Supplementary Material (ESI) for Chemical Science

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