

Supplementary Information

A Novel Oxidative Cyclisation onto Vinyl Silanes

Timothy J. Donohoe,^{*a} Paul C. M. Winship,^a Ben S. Pilgrim,^a Daryl S. Walter^b and Cedric K. A. Callens^{†a}

^aDepartment of Chemistry, University of Oxford, Chemistry Research Laboratory, Mansfield Road, Oxford, OX1 3TA, UK. *timothy.donohoe@chem.ox.ac.uk*

^bGlaxoSmithKline, New Frontiers Science Park South, Harlow, Essex, CM19 5AW

* Author to whom correspondence should be addressed.

† Author to whom correspondence regarding X-ray crystallographic data should be addressed.

Table of Contents:

General methods	S2
Preparation and spectroscopic data for all compounds	S5
¹ H NMR and ¹³ C NMR of compounds 7 , 9 , 11 , 13 , 15 , 17 , 19 , 23 , 25 , 27 and 29	S24
Single-crystal X-ray diffraction report for compound 7	S35

General methods

^1H NMR and ^{13}C NMR spectra were recorded either on a 400 MHz or a 500 MHz spectrometer in CDCl_3 , $\text{DMSO-}d_6$, $\text{acetone-}d_6$ or $\text{MeOH-}d_4$ and referenced to residual solvent peaks or to SiMe_4 as an internal standard. Chemical shifts are quoted in ppm (parts per million) with signal splittings recorded as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), apparent (app.) and broad singlet (br. s). Coupling constants, J , are measured in Hz. ^1H and ^{13}C NMR spectra were recorded at room temperature unless otherwise stated. Flash column chromatography was performed using silica gel 60 (0.033-0.070mm, BDH). TLC analyses were performed on Merck Kiesegel 60 F₂₅₄ 0.25 mm precoated plates. Petrol refers to petroleum ether in the boiling range 40-60 °C. Product spots were visualised under UV light ($\lambda_{\text{max}} = 254 \text{ nm}$) and/or by staining with potassium permanganate or vanillin solutions. Reagents obtained from Acros, Aldrich, Avocado, Fluka and Lancaster fine chemicals suppliers were used directly as supplied. All anhydrous reactions were carried out in flame-dried glassware and under an inert atmosphere of argon. All solvents were distilled and properly dried, when necessary, prior to use.

General Procedure 1:

To a solution of diol (1 mmol) in acetonitrile (12 mL) and H_2O (8 mL) was added pyridine *N*-oxide (2 mmol), citric acid (0.75 mmol), potassium osmate dihydrate (0.01 mmol) and the metal trifluoromethanesulfonate (0.5 mmol). The resulting solution was warmed to 60 °C and the mixture left to stir until all starting material had reacted. Na_2SO_3 (5 mg) and H_2O (10 mL) were added and the reaction was cooled to room temperature. The mixture was extracted with EtOAc (3 × 50 mL) and the combined organic layers were washed with 2 M HCl (20 mL), 3 M NaOH (20 mL), brine (20 mL), dried over Na_2SO_4 , filtered and the solvent removed *in vacuo*. The crude product was purified as specified.

General Procedure 2:

To a solution of the alkene (1 mmol) and 4-methyl morpholine *N*-oxide (2 mmol) in $\text{H}_2\text{O}/\text{THF}/t\text{-BuOH}$ (1:10:8, 10 mL) was added osmium tetroxide (5.0 mol%) and the resulting

solution was stirred for 16 h at room temperature. Na₂SO₃ (200 mg) was added and the mixture was stirred for 30 min after which H₂O (40 mL) was added and the mixture extracted with EtOAc (3 × 40 mL). The combined organics were dried over Na₂SO₄, filtered and the solvent removed *in vacuo* to give the crude product which was purified as specified.

General Procedure 3:

To a mixture of the aldehyde (1 mmol), freshly purified Bestmann-Ohira reagent (1.2 mmol) and K₂CO₃ (2 mmol) was added MeOH (15 mL) and the reaction was stirred for 5 h at room temperature. Et₂O (40 mL) was added and the solution washed with H₂O (50 mL), 5% w/w aqueous NaHCO₃ (50 mL) and a further portion of H₂O (50 mL). The organic layer was dried over Na₂SO₄, filtered and the solvent removed *in vacuo* to give the crude product which was purified as specified.

General Procedure 4:

The alkyne (1 mmol) and the silane (1.2 mmol) were dissolved in CH₂Cl₂ (2 mL) and the solution was cooled to 0 °C and degassed with argon for 15 min. Pentamethylcyclopentadienyltris(acetonitrile) ruthenium (II) hexafluorophosphate (2 mol%) was added and the solution was warmed to room temperature and stirred for 16 h at this temperature. The solvent was removed *in vacuo* to give the crude product which was purified as specified.

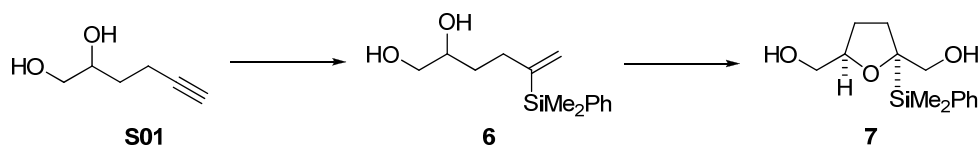
General Procedure 5:

To a solution of silylated-THF (1 mmol) in THF (5 mL) and DMF (1 mL) at 0 °C was added sodium hydride (4.0 mmol, 60% dispersion in mineral oil). The resultant mixture was stirred at 0 °C for 30 min before tetrabutylammonium iodide (0.1 mmol) and benzyl bromide (4.0 mmol) were added. The resulting solution was allowed to warm to room temperature and stirred for 20 h before a saturated solution of brine (15 mL) was added. The mixture was stirred for 30 min before being extracted with EtOAc (3 × 30 mL) and the combined organic

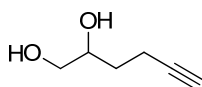
layers washed with H₂O (30 mL), brine (30 mL), dried over Na₂SO₄, filtered and the solvent removed *in vacuo* to give the crude product which was purified as specified.

General Procedure 6:

To a solution of benzyl-protected THF (1 mmol) in THF (10 mL) at 40 °C was added tetrabutylammonium fluoride (4.0 mL, 2.0 mmol, 0.5 M solution in THF) *via* syringe pump addition over 30 min. The resultant mixture was stirred at 40 °C for a further 30 min before MeOH (2.0 mL), potassium bicarbonate (3 mmol) and urea-hydrogen peroxide (5 mmol) were added. After stirring at 40 °C for 1 h, a saturated solution of sodium thiosulfate (15 mL) was added. The mixture was extracted with EtOAc (3 × 30 mL) and the combined organic layers washed with brine (30 mL), dried over Na₂SO₄, filtered and the solvent removed *in vacuo* to give the crude product which was purified as specified.

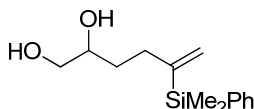


(±)-Hex-5-yn-1,2-diol, **S01**



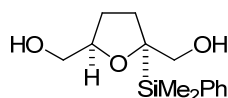
Pent-4-enal (841 mg, 10.0 mmol) was subjected to General Procedure 2. The crude aldehyde was then subjected to General Procedure 3. Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 1:1, then EtOAc], gave diol **S01** as a pale yellow oil (753 mg, 66% over two steps). ¹H NMR (400 MHz, MeOH-*d*₄) δ_H: 3.75-3.69 (1H, m), 3.51-3.43 (2H, m), 2.38-2.24 (2H, m), 2.22 (1H, s), 1.77-1.68 (1H, m), 1.61-1.52 (1H, m); ¹³C NMR (100 MHz, MeOH-*d*₄) δ_C: 83.7, 70.9, 68.6, 66.2, 32.5, 14.5.

(±)-5-(Dimethyl(phenyl)silyl)hex-5-ene-1,2-diol, **6**



Diol **S01** (161 mg, 1.41 mmol) was subjected to General Procedure 4 with dimethylphenylsilane (231 mg, 1.70 mmol). Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 3:1 then 1:1], gave vinyl silane **6** as an oil (305 mg, 86%). ¹H NMR (400 MHz, CDCl₃) δ_H: 7.56-7.50 (2H, m), 7.40-7.32 (3H, m), 5.72 (1H, m), 5.46 (1H, m), 3.62-3.56 (1H, m), 3.50 (1H, dd, *J* = 11.0, 2.2), 3.32 (1H, dd, *J* = 11.0, 7.7), 2.40 (1H, br. s), 2.36 (1H, br. s), 2.33-2.25 (1H, m), 2.20-2.12 (1H, m), 1.49-1.43 (2H, m), 0.40 (3H, s), 0.39 (3H, s); ¹³C NMR (100 MHz, CDCl₃) δ_C: 149.7, 138.1, 133.9, 129.1, 127.8, 126.3, 71.8, 66.6, 32.0, 31.7, -3.0, -3.1; IR ν_{max} (thin film)/cm⁻¹ 3316br., 2955, 1463, 1416, 1369, 1255, 1119, 1084, 1006, 835, 736; HRMS (ES⁺, *m/z*): Calculated 273.1281 (C₁₄H₂₂NaO₂Si); Found 273.1280.

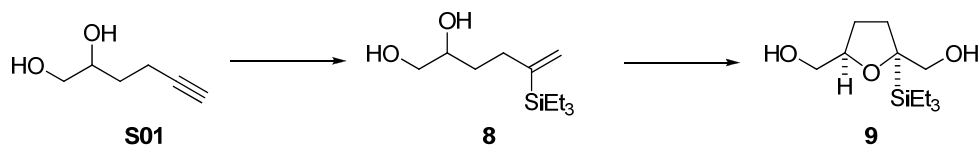
(±)-((2*R*,5*R*)-2-(Dimethyl(phenyl)silyl)tetrahydrofuran-2,5-diyl)dimethanol, 7



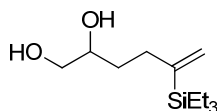
Method A: Vinyl silane **6** (180 mg, 0.718 mmol) was subjected to General Procedure 1 with potassium osmate dihydrate (2.5 mol%) at 60 °C for 16 h. Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 3:1 then 1:1], gave THF **7** as prisms (183 mg, 96%).

Method B: To a stirred solution of vinyl silane **6** (46.0 mg, 0.184 mmol), pyridine-*N*-oxide (34.9 mg, 0.367 mmol) and citric acid (26.5 mg, 0.138 mmol) in acetone/TFA/H₂O (9:5:1, 14 mL) was added potassium osmate dihydrate (3.4 mg, 5 mol%) and the solution stirred for 16 h at room temperature. Na₂SO₃ (100 mg) and saturated aqueous NaHCO₃ (20 mL) were added, the mixture was extracted with EtOAc (3 × 25 mL) and the combined organic layers were dried over Na₂SO₄, filtered and the solvent removed *in vacuo* to give the crude product which was purified by flash column chromatography, [SiO₂, petrol/EtOAc, 3:1 then 1:1], to give THF **7** as prisms (29 mg, 61%).

¹H NMR (400 MHz, CDCl₃) δ_H: 7.58 (2H, dd, *J* = 7.0, 1.7), 7.41-7.33 (3H, m), 3.91-3.86 (1H, m), 3.85 (1H, dd, *J* = 11.4, 4.6), 3.79 (1H, d, *J* = 11.6), 3.52 (1H, dd, *J* = 11.4, 3.6), 3.47 (1H, d, *J* = 11.6), 2.87 (2 H, br. s), 1.99-1.87 (3H, m), 1.72-1.62 (1H, m), 0.38 (3H, s), 0.37 (3H, s); **¹³C NMR** (100 MHz, CDCl₃) δ_C: 136.6, 134.4, 129.3, 127.8, 81.1, 80.6, 66.1, 64.6, 30.4, 28.1, -5.1, -5.2; **IR** (KBr disc)/cm⁻¹ 3346br., 3048, 2960, 1428, 1260, 1108, 1027, 816, 776; **HRMS** (ES⁺, *m/z*): Calculated 289.1230 (C₁₄H₂₂NaO₃Si); Found 289.1232. Data obtained for **7** were identical from both methods.

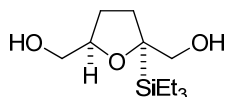


(±)-5-(Triethylsilyl)hex-5-ene-1,2-diol, 8

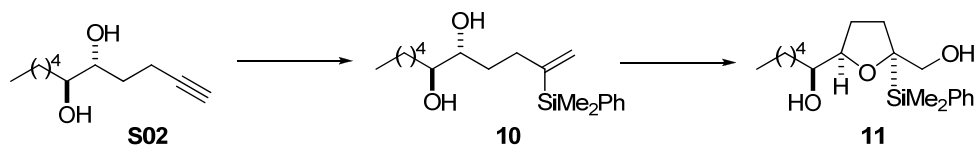


Diol **S01** (82.1 mg, 0.719 mmol) was subjected to General Procedure 4 with triethylsilane (100 mg, 0.861 mmol). Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 4:1 then 1:1], gave vinyl silane **8** as an oil (146 mg, 88%). ¹H NMR (400 MHz, CDCl₃) δ_H: 5.66 (1H, m), 5.33-5.32 (1H, m), 3.75-3.69 (1H, m), 3.66 (1H, dd, *J* = 11.0, 2.4), 3.46 (1H, dd, *J* = 11.0, 7.7), 2.69 (2H, br. s), 2.31-2.24 (1H, m), 2.17-2.09 (1H, m), 1.61-1.51 (2H, m), 0.92 (9H, t, *J* = 7.9), 0.61 (6H, q, *J* = 7.9); ¹³C NMR (100 MHz, CDCl₃) δ_C: 148.4, 125.5, 72.2, 66.8, 32.1, 31.9, 7.4, 2.9; IR (thin film)/cm⁻¹ 3361br., 2953, 2875, 1458, 1417, 1237, 1047, 922, 736; HRMS (ES⁺, *m/z*): Calculated 253.1594 (C₁₂H₂₆NaO₂Si); Found 253.1595.

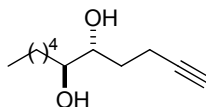
(±)-((2*R*,5*R*)-2-(Triethylsilyl)tetrahydrofuran-2,5-diyl)dimethanol, 9



Vinyl silane **8** (84.0 mg, 0.365 mmol) was subjected to General Procedure 1 with potassium osmate dihydrate (5.0 mol%) at 60 °C for 16 h. Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 4:1 then 1:1], gave THF **9** as an oil (83.0 mg, 92%). ¹H NMR (400 MHz, CDCl₃) δ_H: 4.02-3.97 (1H, m), 3.90 (1H, dd, *J* = 11.5, 2.6), 3.82 (1H, d, *J* = 11.5), 3.59 (1H, dd, *J* = 11.5, 3.2), 3.45 (1H, d, *J* = 11.5), 3.17 (2H, br. s), 2.10-1.97 (3H, m), 1.87-1.78 (1H, m), 0.98 (9H, t, *J* = 7.9), 0.63 (6H, q, *J* = 7.9); ¹³C NMR (100 MHz, CDCl₃) δ_C: 81.8, 80.7, 68.7, 64.4, 31.2, 28.1, 7.7, 2.0; IR (thin film)/cm⁻¹ 3356br., 2954, 1460, 1417, 1240, 1021, 932, 910, 863, 814, 751; HRMS (ES⁺, *m/z*): Calculated 269.1543 (C₁₂H₂₆NaO₃Si); Found 269.1541.

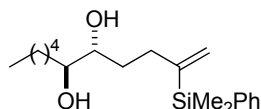


(±)-(5*R*,6*S*)-Undec-1-yne-5,6-diol, S02



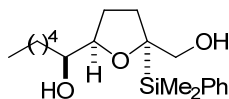
(*Z*)-Dec-4-enal (771 mg, 5.00 mmol) was subjected to General Procedure 2 to give the crude aldehyde which was then treated with General Procedure 3. Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 9:1 then 4:1], gave diol **S02** as prisms (581 mg, 63% over two steps). ¹H NMR (400 MHz, CDCl₃) δ_H: 3.75 (1H, ddd, *J* = 8.5, 4.3, 3.7), 3.65 (1H, ddd, *J* = 8.0, 4.6, 3.7), 2.44-2.30 (4H, m), 1.99 (1H, t, *J* = 2.7), 1.72-1.62 (2H, m), 1.55-1.25 (8H, m), 0.89 (3H, t, *J* = 6.7); ¹³C NMR (100 MHz, CDCl₃) δ_C: 84.2, 74.7, 73.4, 69.0, 31.8, 31.6, 29.5, 25.6, 22.6, 15.2, 14.1; IR (KBr disc)/cm⁻¹ 3307br., 2958, 2931, 2859, 1468, 1442, 1337, 1124, 1068, 1037, 867; HRMS (ES⁺, *m/z*): Calculated 207.1356 (C₁₁H₂₀NaO₂); Found 207.1360; m.p. 75-76 °C.

(±)-(5*R*,6*S*)-2-(Dimethyl(phenyl)silyl)undec-1-ene-5,6-diol, 10

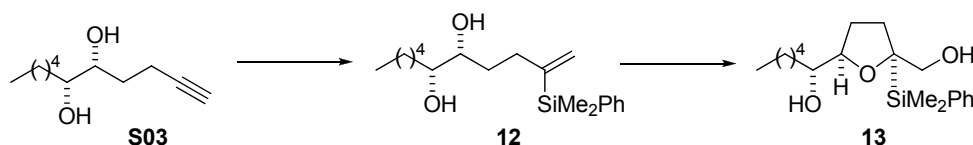


Diol **S02** (300 mg, 1.63 mmol) was subjected to General Procedure 4 with dimethylphenylsilane (266 mg, 1.96 mmol). Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 19:1 then 9:1 then 4:1], gave vinyl silane **10** as an oil (480 mg, 92%). ¹H NMR (400 MHz, CDCl₃) δ_H: 7.55-7.51 (2H, m), 7.38-7.34 (3H, m), 5.74 (1H, s), 5.47 (1H, s), 3.50-3.46 (2H, m), 2.37 (1H, ddd, *J* = 15.0, 7.5, 7.2), 2.15 (1H, ddd, *J* = 15.0, 8.0, 7.2), 1.85 (2H, br. s), 1.49-1.23 (10H, m), 0.91 (3H, t, *J* = 6.6), 0.40 (6H, s); ¹³C NMR (100 MHz, CDCl₃) δ_C: 150.0, 138.2, 133.9, 129.1, 127.8, 126.2, 74.6, 74.2, 32.2, 31.9, 31.2, 30.1, 25.7, 22.6, 14.1, -3.0, -3.1; IR (thin film)/cm⁻¹ 3386br., 2955, 2933, 2859, 1428, 1249, 1112, 1059, 926, 833, 818, 776, 732, 700; HRMS (ES⁺, *m/z*): Calculated 343.2064 (C₁₉H₃₂NaO₂Si); Found 343.2054.

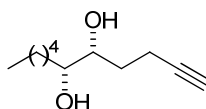
(±)-(S)-1-((2R,5R)-5-(Dimethyl(phenyl)silyl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)hexan-1-ol 11



Vinyl silane **10** (289 mg, 0.903 mmol) was subjected to General Procedure 1 with potassium osmate dihydrate (2.5 mol%) at 60 °C for 16 h. Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 9:1 then 3:1], gave THF **11** as an oil (277 mg, 91%). ¹H NMR (400 MHz, CDCl₃) δ_H: 7.59-7.56 (2H, m), 7.41-7.33 (3H, m), 3.94-3.90 (1H, m), 3.81 (1H, d, *J* = 11.5), 3.74-3.70 (1H, m), 3.46 (1H, d, *J* = 11.5), 3.03 (2H, br. s), 2.03-1.91 (3H, m), 1.62-1.54 (1H, m), 1.52-1.22 (8H, m), 0.89 (3H, t, *J* = 6.9), 0.36 (3H, s), 0.36 (3H, s); ¹³C NMR (100 MHz, CDCl₃) δ_C: 136.6, 134.4, 129.3, 127.8, 84.0, 80.2, 72.4, 68.0, 33.6, 31.8, 30.4, 25.7, 25.3, 22.6, 14.1, -5.2, -5.3; IR (thin film)/cm⁻¹ 3356br., 2931, 2861, 1428, 1249, 1110, 1056, 810, 735, 701; HRMS (ES⁺, *m/z*): Calculated 359.2013 (C₁₉H₃₂NaO₃Si); Found 359.2004.

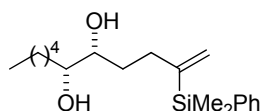


(±)-(5R,6R)-Undec-1-yne-5,6-diol, S03



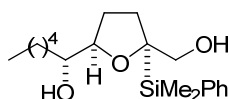
(*E*)-Dec-4-enal (771 mg, 5.00 mmol) was subjected to General Procedure 2 to give the crude aldehyde which was then treated with General Procedure 3. Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 9:1 then 4:1], gave diol **S03** as an oil (640 mg, 70% over two steps). ¹H NMR (400 MHz, CDCl₃) δ_H: 3.56 (1H, ddd, *J* = 9.0, 5.0, 4.1), 3.42 (1H, ddd, *J* = 9.0, 5.0, 3.8), 2.63 (2H, br. s), 2.38-2.33 (2H, m), 1.98 (1H, t, *J* = 2.7), 1.76-1.61 (2H, m), 1.53-1.23 (8H, m), 0.89 (3H, t, *J* = 6.8); ¹³C NMR (100 MHz, CDCl₃) δ_C: 84.1, 74.4, 73.1, 68.9, 33.5, 32.3, 31.9, 25.3, 22.6, 14.9, 14.1; IR (thin film)/cm⁻¹ 3311br., 2960, 2859, 2118, 1435, 1379, 1262, 1132, 1066, 941, 633; HRMS (ES⁺, *m/z*): Calculated 207.1356 (C₁₁H₂₀NaO₂); Found 207.1359.

(±)-(5*S*,6*S*)-2-(Dimethyl(phenyl)silyl)undec-1-ene-5,6-diol, **12**

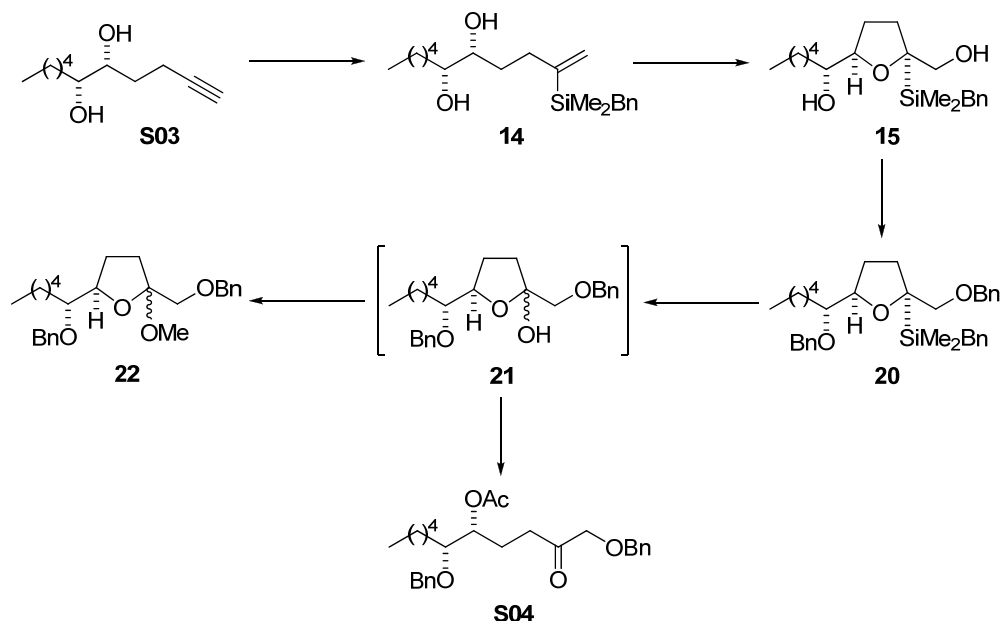


Diol **S03** (288 mg, 1.56 mmol) was subjected to General Procedure 4 with dimethylphenylsilane (255 mg, 1.87 mmol). Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 19:1 then 9:1 then 4:1], gave vinyl silane **12** as an oil (434 mg, 87%). ¹H NMR (400 MHz, CDCl₃) δ_H: 7.55-7.51 (2H, m), 7.37 (2H, d, *J* = 2.1), 7.35 (1H, d, *J* = 1.5), 5.73 (1H, ddd, *J* = 2.7, 1.5, 1.3), 5.47 (1H, d, *J* = 2.7), 3.32-3.26 (2H, m), 2.38-2.30 (1H, m), 2.23-2.15 (1H, m), 2.00 (2H, br. s), 1.57-1.22 (10H, m), 0.91 (3H, t, *J* = 7.0), 0.40 (3H, s), 0.40 (3H, s); ¹³C NMR (100 MHz, CDCl₃) δ_C: 150.0, 138.2, 133.9, 129.1, 127.8, 126.2, 74.5, 74.0, 33.5, 32.7, 31.9, 31.9, 25.3, 22.6, 14.1, -2.9, -3.1; IR (thin film)/cm⁻¹ 3384br., 2955, 2932, 1428, 1249, 1112, 1066, 926, 833, 818, 732, 700; HRMS (ES⁺, *m/z*): Calculated 343.2064 (C₁₉H₃₂NaO₂Si); Found 343.2059.

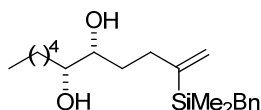
(±)-(R)-1-((2*R*,5*R*)-5-(dimethyl(phenyl)silyl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)hexan-1-ol **13**



Vinyl silane **12** (381 mg, 1.19 mmol) was subjected to General Procedure 1 with potassium osmate dihydrate (2.5 mol%) at 60 °C for 16 h. Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 9:1 then 3:1], gave THF **13** as an oil (354 mg, 88%). ¹H NMR (400 MHz, CDCl₃) δ_H: 7.60-7.56 (2H, m), 7.41-7.33 (3H, m), 3.72 (1H, d, *J* = 11.5), 3.61 (1H, ddd, *J* = 10.9, 6.2, 4.8), 3.48-3.42 (2H, m), 2.57 (2H, br. s), 2.20-1.89 (2H, m), 1.86-1.76 (1H, m), 1.72-1.65 (1H, m), 1.56-1.25 (8H, m), 0.91 (3H, t, *J* = 7.0), 0.40 (3H, s), 0.40 (3H, s); ¹³C NMR (100 MHz, CDCl₃) δ_C: 136.7, 134.4, 129.3, 127.8, 83.6, 80.4, 74.2, 68.2, 34.5, 31.9, 30.4, 29.2, 25.4, 22.7, 14.1, -5.0, -5.1; IR (thin film)/cm⁻¹ 3356br., 3069, 2956, 1462, 1428, 1249, 1192, 1055, 810, 775, 736, 701; HRMS (ES⁺, *m/z*): Calculated 359.2013 (C₁₉H₃₂NaO₃Si); Found 359.2008.

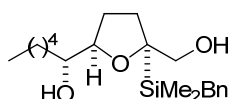


(±)-(5*S*,6*S*)-2-(Dimethyl(benzyl)silyl)undec-1-ene-5,6-diol, 14



Diol **S03** (200 mg, 1.09 mmol) was subjected to General Procedure 4 with benzyldimethylsilane (196 mg, 1.30 mmol). Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 19:1 then 9:1 then 4:1], gave vinyl silane **14** as an oil (294 mg, 81%). ¹H NMR (400 MHz, CDCl₃) δ_H: 7.28-7.18 (2H, m), 7.11-6.98 (3H, m), 5.67-5.64 (1H, m), 5.39-5.35 (1H, m), 3.44-3.37 (2H, m), 2.30 (1H, ddd, *J* = 14.8, 10.0, 5.4), 2.18 (2H, s), 2.17-2.10 (1H, m), 1.90 (2H, br. s), 1.65-1.25 (10H, m), 0.95-0.87 (3H, m), 0.08 (6H, s); ¹³C NMR (100 MHz, CDCl₃) δ_C: 150.2, 139.9, 128.3, 128.1, 125.3, 124.0, 74.5, 74.2, 33.6, 32.7, 31.9, 31.9, 25.5, 25.4, 22.6, 14.1, -3.4; IR (thin film)/cm⁻¹ 3384br., 3024, 2931, 1493, 1452, 1248, 1057, 831; HRMS (ES⁺, *m/z*): Calculated 357.2220 (C₂₀H₃₄NaO₂Si); Found 357.2220.

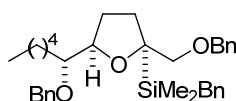
(±)-(R)-1-((2*R*,5*R*)-5-(dimethyl(benzyl)silyl)-5-(hydroxymethyl)tetrahydrofuran-2-yl)hexan-1-ol 15



Vinyl silane **14** (200 mg, 0.60 mmol) was subjected to General Procedure 1 with potassium osmate dihydrate (2.5 mol%) at 60 °C for 16 h. Purification by flash column chromatography,

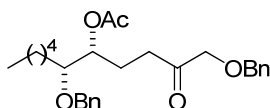
[SiO₂, petrol/EtOAc, 9:1 then 3:1], gave THF **15** as an oil (176 mg, 84%). ¹H NMR (400 MHz, CDCl₃) δ_H: 7.26-7.18 (2H, m), 7.13-7.00 (3H, m), 3.79-3.71 (2H, m), 3.52-3.42 (2H, m), 3.17 (2H, br. s), 2.24-2.14 (2H, m), 1.96-1.82 (4H, m), 1.59-1.26 (8H, m), 0.91 (3H, t, *J* = 6.6), 0.02 (3H, s), 0.01 (3H, s); ¹³C NMR (100 MHz, CDCl₃) δ_C: 139.6, 128.3, 128.2, 124.1, 83.8, 80.2, 74.3, 68.1, 34.5, 31.9, 30.4, 29.4, 25.5, 23.3, 22.7, 14.1, -5.4, -5.4; IR (thin film)/cm⁻¹ 3357 br., 2930, 1493, 1452, 1247, 1206, 1056, 818; HRMS (ES⁺, *m/z*): Calculated 373.2169 (C₂₀H₃₄NaO₃Si); Found 373.2162.

(±)-Benzyl((2*R*,5*R*)-5-((*R*)-1-(benzyloxy)hexyl)-2-(benzyloxymethyl)tetrahydrofuran-2-yl)dimethylsilane, **20**



THF **15** (450 mg, 1.29 mmol) was subjected to General Procedure 5. Purification by flash column chromatography, [SiO₂, petrol/EtOAc, 9:1], gave THF **20** as an oil (501 mg, 73%). ¹H NMR (400 MHz, CDCl₃) δ_H: 7.30-7.01 (10H, m), 7.22 (2H, app. t, *J* = 7.4), 7.09 (1H, t, *J* = 7.2), 7.04 (2H, d, *J* = 7.6), 4.88 (1H, d, *J* = 11.6), 4.66 (1H, d, *J* = 11.6), 4.48 (2H, s), 3.94-3.86 (1H, m), 3.47 (1H, d, *J* = 9.2), 3.45 (1H, d, *J* = 9.2), 3.39-3.32 (1H, m), 2.25 (2H, d, *J* = 1.6), 2.05-1.95 (1H, m), 1.90-1.80 (2H, m), 1.76-1.65 (1H, m), 1.60-1.21 (8H, m), 0.91 (3H, t, *J* = 7.2), 0.05 (3H, s), 0.04 (3H, s); ¹³C NMR (100 MHz, CDCl₃) δ_C: 140.3, 139.6, 138.7, 128.4, 128.3, 128.2, 128.1, 127.6, 127.5, 127.4, 84.6, 82.6, 78.2, 76.1, 73.5, 73.1, 32.0, 31.8, 30.8, 28.7, 25.4, 23.4, 22.7, 14.2, -5.4, -5.5; IR (thin film)/cm⁻¹ 2954, 2930, 2859, 1494, 1453, 1071, 1027, 818, 735; HRMS (ES⁺, *m/z*): Calculated 553.3108 (C₃₄H₄₆NaO₃Si); Found 553.3108.

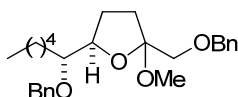
(±)-(5*R*,6*R*)-1,6-Bis(benzyloxy)-2-oxoundecan-5-yl acetate, **S04**



Benzylated THF **20** (150 mg, 0.28 mmol) was subjected to General Procedure 6. The resulting crude product was dissolved in pyridine (2 mL) and acetic anhydride (2 mL) and stirred at room temperature for 16 h before the solvent was removed *in vacuo*. Purification by flash column chromatography, [SiO₂, petrol/Et₂O, 4:1], gave ketone **S04** as an oil (91 mg, 73%). ¹H NMR (400 MHz, CDCl₃) δ_H: 7.39-7.25 (10H, m), 5.03 (1H, dt, *J* = 9.2, 4.2), 4.60

(2H, s), 4.58 (2H, s), 4.03 (2H, s), 3.42 (1H, dt, $J = 8.0, 4.2$), 2.46 (2H, t, $J = 7.2$), 2.04 (3H, s), 2.03-1.95 (1H, m), 1.91-1.80 (1H, m), 1.59-1.20 (8H, m), 0.88 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ_{C} : 207.8, 170.9, 138.4, 137.2, 128.5, 128.4, 128.0, 128.0, 127.9, 127.7, 79.2, 74.9, 73.4, 73.4, 72.4, 35.1, 31.9, 29.8, 25.3, 23.3, 22.6, 21.1, 14.1; IR (thin film)/ cm^{-1} 2926, 1736, 1453, 1374, 1239, 1070; HRMS (ES^+ , m/z): Calculated 463.2455 ($\text{C}_{27}\text{H}_{36}\text{NaO}_5$); Found 463.2456.

(±)-(5R)-5-((R)-1-(Benzyloxy)hexyl)-2-(benzyloxymethyl)-2-methoxytetrahydrofuran, 23



Benzylated THF **20** (76 mg, 0.14 mmol) was subjected to General Procedure 6. The resulting crude product was purified by flash column chromatography, [SiO_2 , petrol/EtOAc, 4:1], to afford lactol **21** as an oil (42 mg, 74%), as a complex mixture of isomers.

Lactol **21** (37 mg, 88 μmol) was dissolved in MeOH (1 mL) and CH_2Cl_2 (1 mL) under argon before pyridinium para-toluene sulfonate (4 mg, 18 μmol) was added. The resultant mixture was stirred at room temperature for 5 h before the solvent was removed *in vacuo*. Purification by flash column chromatography, [SiO_2 , petrol/EtOAc, 17:3], furnished lactol methyl ether **23** as an oil, and a (60:40) mixture of diastereomers (30 mg, 77%). ^1H NMR (400 MHz, CDCl_3) δ_{H} : (diastereomeric 60:40) 7.33-7.15 (10H, m), 4.75 (0.4H, d, $J = 11.6$), 4.65 (0.6H, d, $J = 11.6$), 4.75-4.47 (3H, m), 4.16-4.09 (0.6H, m), 4.07-3.99 (0.4H, m), 3.66-3.58 (1H, m), 3.33-3.23 (2H, m), 3.19 (3H, s), 2.04-1.51 (4H, m), 1.44-1.10 (8H, m), 0.84-0.76 (3H, m); ^{13}C NMR (100 MHz, CDCl_3) δ_{C} : (diastereomeric 60:40) 139.3, 139.2, 138.3(2), 128.4(2), 128.3(2), 127.9, 127.9, 127.9, 127.8, 127.7, 127.7, 127.4, 127.4, 108.2, 108.0, 84.6, 82.5, 81.8, 81.2, 73.5, 73.5, 72.9, 72.8, 70.7, 70.3, 49.0, 49.0, 34.7, 34.1, 32.1, 32.0, 31.1, 30.7, 27.5, 27.0, 25.4, 25.1, 22.7(2), 14.1(2); IR (thin film)/ cm^{-1} 2930, 2860, 1722, 1496, 1545, 1097, 1028, 736; HRMS (ES^+ , m/z): Calculated 435.2506 ($\text{C}_{26}\text{H}_{36}\text{NaO}_4$); Found 435.2490.

Protodesilylated **22**; ^1H NMR (400 MHz, CD_3Cl) δ_{H} : 7.37-7.23 (10H, m), 4.75 (1H, d, $J = 11.6$), 4.62-4.56 (3H, m), 4.17-4.10 (1H, m), 4.05-3.98 (1H, m), 3.51 (2H, qd, $J = 9.8, 5.2$), 3.39-3.33 (1H, m), 1.96-1.82 (2H, m), 1.76-1.62 (2H, m), 1.51-1.15 (8H, m), 0.87 (3H, t, $J = 7.0$); ^{13}C NMR (100 MHz, CDCl_3) δ_{C} : 139.3, 138.5, 128.3, 128.2, 128.0, 127.6, 127.5, 127.4, 82.4, 81.5, 78.4, 73.4, 73.0, 72.8, 32.0, 30.9, 28.2, 27.4, 25.4, 22.7, 14.1; IR (thin film)/ cm^{-1}

