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Stereoselective Synthesis of Protected L- and D-Dideoxysugars and Analogues via Prins Cyclisations

Ryan J. Beattie, Thomas W. Hornsby, Gemma Craig, M. Carmen Galan* and Christine L. Willis*

Supporting Information

1. General Information, 2
2. Preparation of Compounds, 3
3. Chiral SFC Data, 36
4. $^1$H and $^{13}$C NMR Spectra, 37
5. References, 75
General Procedures

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Anhydrous solvents were used which were dried using the Anhydrous Engineering Ltd. double alumina and alumina-copper catalysed drying columns. All moisture or air sensitive reactions were carried out in flame dried glassware under a positive pressure of N2 using standard syringe/septa techniques. Flash column chromatography was performed on silica gel (Merck Kieselgel 60, 230-400 mesh). Thin layer chromatography was carried out on Polygram 0.2 mm silica gel TLC plates visualising with 254 nm UV light and developing with either a KMnO4, phosphomolybdic acid or Vanillin dip, where appropriate. Optical rotations were determined with the sodium D line ($\lambda = 589$ nm) using a Perkin Elmer 241 MC polarimeter. $[\alpha]^{22}$ values are quoted in units $10^{-1}$ deg cm$^2$ g$^{-1}$. Infrared (IR) spectroscopy was recorded on a Perkin Elmer Spectrum 100 FT-IR spectrometer with an ATR diamond cell irradiating between 4000 cm$^{-1}$ and 600 cm$^{-1}$. Melting points were determined using an electrothermal melting point apparatus and are uncorrected. Electron impact (EI) and chemical ionisation (CI) mass spectra were recorded on a VG Analytical Autospec mass spectrometer. Methane was the ionization gas used for CI. Electrospray ionisation (ESI) mass spectra were recorded on a Micromass LCT mass spectrometer or a VG Quattro mass spectrometer. NMR spectra were recorded using either a Varian 400 MHz or JEOL ecp 400 MHz spectrometer. Chemical shifts ($\delta_H$) are quoted in parts per million (ppm), $J$ values are given in Hz and referenced to the appropriate residual solvent peak. Data reported as follows: chemical shift, integration, multiplicity ($s =$ singlet, br $s =$ broad singlet, $d =$ doublet, $t =$ triplet, $q =$ quartet, $qi =$ quintet, $sx =$ sextet, hept $=$ heptet, $m =$ multiplet, $dd =$ doublet of doublet, etc.), coupling constants, assignment. Chemical shifts ($\delta_C$) are quoted in parts per million (ppm), referenced to the appropriate residual solvent peak. DEPT$^{135}$, COSY and HMQC were used for all new compounds in assigning NMR spectra. Chiral SFC was performed using Diacel Chiralpak IA, IB and IC columns (4.6 x 250 mm x 5 $\mu$m) or a Whelk O-1 column (4.6 x 250 mm x 5 $\mu$m) on a WatersTharSFC system and monitored by DAD (Diode Array Detector).
Preparation of compounds

Benzyl(1,3-dithiane)dimethylsilane 4

\[
\begin{align*}
\text{S} & \quad \text{S} \\
\text{Bn} & \quad \text{Si} \\
\text{i)} & \quad n-\text{BuLi, THF, -20 °C} \\
\text{ii)} & \quad \text{BDMSCl, THF}
\end{align*}
\]

\(n\)-Butyllithium (14 mL, 1.57 M solution in hexanes, 22.0 mmol) was added dropwise to 1,3-dithiane (2.2 g, 18.3 mmol) in dry THF (60 mL) at -15 °C under \(\text{N}_2\). This was stirred for 6 h, warming to RT slowly. The solution was then added dropwise via cannula to a solution of benzyl(dimethyl)chlorosilane (3.7 mL, 20.2 mmol) in dry THF (30 mL) at 0 °C and the reaction allowed to warm to RT and stirred for 14 h. A saturated solution of ammonium chloride (25 mL) was added, the organic phase separated and aqueous layer extracted with \(\text{EtOAc}\) (3 x 20 mL). The combined organic phases were dried (MgSO\(_4\)) and concentrated \textit{in vacuo} to yield a dark brown oil. This was purified by column chromatography (Pet: \text{EtOAc}, 99:1) to afford a dark brown oil. Further purification by bulb to bulb distillation gave thioacetal 4 as a colourless oil (4.4 g, 89%); bp 235 °C at 8.0 mbar; \(\nu_{\text{max}}\) (neat)/cm\(^{-1}\) 3059 (ArCH), 2953 (CH), 1599 (ArC=C); \(\delta_H\) (400 MHz; CDCl\(_3\)) 0.14 (6H, s, 2 x SiCH\(_3\)), 1.99-2.18 (2H, m, CH\(_2\)), 2.27 (2H, s, CH\(_2\)Ph), 2.29 (2H, dt, \(J\ 14.3, 3.2, \text{SC}\text{H}_2\)), 2.78 (2H, td, \(J\ 14.3, 2.9, \text{SC}\text{H}_2\)), 3.72 (1H, s, SCH), 7.08-7.15 (3H, m, ArH), 7.23-7.25 (2H, m, ArH); \(\delta_C\) (100 MHz; CDCl\(_3\)) -5.2 (2 x SiCH\(_3\)), 23.1 (CH\(_2\)Ph), 26.2 (CH\(_2\)), 31.0 (2 x SC\text{H}2), 32.9 (CH), 124.3 (C-Ar), 128.1 (C-Ar), 128.3 (C-Ar), 138.9 (C-Ar); \(m/z\) (ESI) 291.0679 (MNa\(^+\), 100%, \(\text{C}_{13}\text{H}_{20}\text{NaS}_2\text{Si} \text{requires} \ 291.0668\)).

Benzyl(diethoxymethyl)dimethylsilane 5

\[
\begin{align*}
\text{Bn} & \quad \text{Si} \\
\text{S} & \quad \text{S} \\
\text{EtO} & \quad \text{Si} \\
\text{Bn} & \quad \text{EtO}
\end{align*}
\]

2-BDMS-1,3-dithiane 4 (6.35 g, 23.6 mmol) in dry ethanol (50 mL) was added to a two-neck round bottomed-flask equipped with a condenser and placed under \(\text{N}_2\). Mercury (II) chloride
(19.2 g, 70.8 mmol) and mercury (II) oxide (1.63 g, 47.2 mmol) were added and the resulting suspension was stirred vigorously at reflux for 3 h. The reaction mixture was filtered through Celite®, washing with Et₂O (3 x 10 mL) and concentrated in vacuo to yield a white oily residue. Purification by column chromatography (Pentane: Et₂O, 98:2) gave the silyl acetal 5 as a colourless oil (5.05 g, 85%); ν max (neat)/cm⁻¹ 3060 (ArCH), 2958 (CH), 1601 (C=C), 1056 (C-O); δH (400 MHz; CDCl₃) 0.06 (6H, s, 2 x SiC₃H₃), 1.22 (6H, t, J 7.1, CH₃), 2.20 (2H, s, CH₂Ph), 3.48 (2H, q, J 7.1, CH₂), 3.77 (2H, q, J 7.1, CH₂), 4.38 (1H, s, CH), 7.04-7.10 (3H, m, ArH), 7.21-7.25 (2H, m, ArH); δC (100 MHz; CDCl₃) -5.5 (SiC₃H₃), 15.6 (2 x C₃H₃), 23.3 (CH₂Ph), 65.7 (OCH₂), 106.5 (CH), 124.1 (C-Ar), 128.2 (C-Ar), 128.3 (C-Ar), 139.4 (C-Ar); m/z (ESI) 275.1427 (MNa⁺, 100%, C₁₄H₂₄O₂NaSi requires 275.1438).

(5E,3R)-1-Phenylhept-5-en-3-ol 6¹

Para-toluenesulfonic acid monohydrate (0.21 g, 1.1 mmol) was added to a solution of dihydrocinnamaldehyde (1.46 mL, 11.1 mmol) and alcohol (R)-SI-1¹ (2.32 g, 11.1 mmol) in dry CH₂Cl₂ (15 mL) under N₂. The mixture was stirred for 24 h at RT, then aqueous saturated sodium hydrogen carbonate (35 mL) was added. Triethylamine was added until the pH >7 and the mixture was stirred for 20 minutes. The resulting biphasic solution was separated and the aqueous layer extracted with CH₂Cl₂ (4 x 30 mL). The combined organic phases were washed with aqueous saturated NaHCO₃ (30 mL), dried (MgSO₄) and concentrated in vacuo. Purification using column chromatography (Pet: EtOAc, 95:5) gave alcohol 6 as a yellow oil (1.45 g, 69%); [α]²⁵ + 10.0 (c 1.05, CHCl₃), lit.¹ [α]²⁵ + 14.0 (c 1.00, CHCl₃); ν max (neat)/cm⁻¹ 3383 (OH), 3062 (ArCH), 3026 (C=CH), 2917 (C-H), 1603 (ArC=CH); δH (400 MHz; CDCl₃) 1.70 (3H, dd, J 6.2, 1.0, 7-H), 1.75-1.82 (2H, m, 2-H₂), 2.09 (1H, m, 4-HH), 2.25 (1H, m, 4-HH), 2.69 (1H, dd, J 13.9, 8.4, 1-HH), 2.82 (1H, dt, J 13.9, 7.7, 1-HH), 3.62 (1H, m, 3-H), 5.43 (1H, dt, J 15.2, 6.2, 1.5, 6-H), 5.57 (1H, tq, J 15.2, 6.2, 1.0, 5-H), 7.18-7.23 (3H, m, ArH), 7.28-7.32 (2H, m, ArH); δC (100 MHz; CDCl₃) 18.3 (C-H), 32.3 (C-2), 38.6 (C-1), 41.0 (C-4), 70.5 (C-3), 125.5 (C-Ar), 126.8 (C-6), 128.1 (C-Ar), 128.2 (C-Ar), 128.6 (C-5), 142.0 (ArC). Spectroscopic data were in accordance with the literature.¹
Trifluoroacetic acid (760 µl, 7.8 mmol) was added dropwise to a solution of alcohol 6 (99 mg, 0.52 mmol) and silyl acetal 5 (156 mg, 0.62 mmol) in dry CH₂Cl₂ (6 mL) at RT under N₂. The reaction was stirred for 6 h, then aqueous saturated NaHCO₃ (15 mL) was added carefully. The organic phase was separated and the aqueous phase extracted with CH₂Cl₂ (3 x 25 mL). The organic phases were combined, washed with aqueous saturated NaHCO₃ (10 mL) and then concentrated in vacuo. The resulting crude residue was redissolved in methanol (10 mL), to which K₂CO₃ (430 mg, 3.12 mmol) was added and stirred for 15 minutes. The methanol was removed under reduced pressure, water (10 mL) added and extracted with CH₂Cl₂ (3 x 20 mL). The combined organic phases were washed with brine (5 mL), dried (MgSO₄) and concentrated in vacuo to afford the crude residue. Which was purified by column chromatography (Pet: EtOAc, 85:5) to give alcohol 7 as a yellow oil (186 mg, 97%); [α]_D^{22} + 28.0 (c 1.01, CHCl₃); ν max (neat)/cm⁻¹ 3327 (OH), 3060 (ArCH), 3024 (ArCH), 2931 (CH), 1600 (ArC=C); δ_H (400 MHz; CDCl₃) 0.05 (3H, s, SiCH₃), 0.08 (3H, s, SiCH₃), 0.95 (3H, d, J 6.6, 2-CH₃), 1.29 (1H, app. q., J 11.3, 4-Hax), 1.52 (1H, m, 2-Hax), 1.73 (1H, m, 1'-HH), 1.87 (1H, m, 1'-HH), 1.94 (1H, ddd, J 11.3, 4.9, 2.0, 4-Heq), 2.21 (1H, d, J 13.7, SiCHH), 2.31 (1H, d, J 13.7, SiCHH), 2.68 (1H, m, 2'-HH), 2.74 (1H, d, J 11.0, 1-Hax), 2.81 (1H, m, 2'-HH), 3.23-3.29 (2H, m, 5-H and 3-H), 7.05-7.11 (3H, m, ArH), 7.17-7.31 (7H, m, ArH); δ_C (100 MHz; CDCl₃) -4.7 (SiCH₃), -3.6 (SiCH₃), 13.4 (2-CH₃), 23.9 (SiCH₂), 31.8 (C-2'), 38.0 (C-4), 41.2 (C-2), 41.5 (C-1'), 74.0 (C-1), 74.8 (C-3), 77.5 (C-5), 124.0 (C-Ar), 125.7 (C-Ar), 128.1 (C-Ar), 128.3 (C-Ar), 128.4 (C-Ar), 128.5 (C-Ar), 140.0 (C-Ar), 142.3 (C-Ar); m/z (ESI) 391.2051 (MNa⁺, 100%, C₂₃H₃₂O₂NaSi requires 391.2069).
(1S,3S,5R)-1-(Benzyldimethylsilane)-3-hydroxy-5-(2’-phenylethyl)-tetrahydropyran 9

[chemical structure]

Trifluoroacetic acid (3.32 mL, 34.1 mmol) was added dropwise to a solution of alcohol 8 (200 mg, 1.14 mmol) and silyl acetal 5 (315 mg, 1.25 mmol) in dry CH₂Cl₂ (12 mL) at RT under N₂. This was stirred for 3 h at RT, then aqueous saturated NaHCO₃ (15 mL) was added carefully. The organic phase was separated and the aqueous phase extracted with CH₂Cl₂ (3 x 25 mL). The organic phases were combined, washed with aqueous saturated NaHCO₃ (10 mL) and then concentrated in vacuo. The resulting crude residue was redissolved in methanol (10 mL), to which K₂CO₃ (1.13 g, 8.19 mmol) was added and left to stir for 30 minutes. The methanol was removed under reduced pressure, water (25 mL) added and extracted with CH₂Cl₂ (3 x 30 mL). The combined organic phases were dried (MgSO₄) and concentrated in vacuo to afford the crude residue. Which was purified by column chromatography (Pet: EtOAc, 85:5) to give alcohol 9 as a yellow oil (374 mg, 93%); [α]_D²⁰ + 34.0 (c 1.00, CHCl₃); νₘₐₓ (neat)/cm⁻¹ 3323 (OH), 3062 (ArCH), 3021 (ArCH), 2934 (CH), 1601 (ArC=CH), δₙ (400 MHz; CDCl₃) 0.02 (3H, s, SiCH₃), 0.05 (3H, s, SiCH₃), 1.20 (1H, app. q., J 11.0, 4-H⁰), 1.52 (1H, app. q, J 12.8, 2-H⁰), 1.51 (1H, br. s., OH), 1.71 (1H, m, 1’-HH), 1.79 (1H, m, 1’-HH), 1.88 (1H, m, 2-H⁰), 1.93 (1H, ddd, J 11.0, 5.0, 2.0, 4-H⁰), 2.17 (1H, d, J 13.6, SiCHH), 2.25 (1H, d, J 13.6, SiCHH), 2.71 (1H, m, 2’-HH), 2.81 (1H, m, 2’-HH), 3.04 (1H, dd, J 12.8, 2.0, 1-H), 3.23 (1H, tdd, J 11.0, 3.9, 2.0, 5-H), 3.71 (1H, br. ddt, J 12.8, 11.0, 5.0, 3-H), 7.04-7.11 (3H, m, ArH), 7.20-7.31 (7H, m, ArH); δ_C (100 MHz; CDCl₃) -6.0 (SiCH₃), -5.8 (SiCH₃), 23.0 (SiCH₃), 31.8 (C-2’), 36.4 (C-4), 38.0 (C-2), 41.8 (C-1’), 68.1 (C-1), 69.3 (C-3), 77.1 (C-5), 124.0 (C-Ar), 125.7 (C-Ar), 128.2 (C-Ar), 128.2 (C-Ar), 128.5 (C-Ar), 128.8 (C-Ar) 139.8 (C-Ar), 142.3 (C-Ar); m/z (ESI) 377.1907 (MNa⁺, 100%, C₂₂H₃₀O₂NaSi requires 377.1913).
Lithium tetrafluoroborate (58 mg, 0.62 mmol) was added in one portion to silyl acetal 5 (142 mg, 0.56 mmol) and allyltributylstannane (350 μl, 1.13 mmol) in MeCN (2.8 ml) with H₂O (20 μl) at -15 °C. This was left to slowly warm to RT over 2 h. Saturated aqueous NaHCO₃ (5 ml) was then added and the organics were extracted with EtOAc (3 x 10 ml). The combined organic phases were then dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (Pet: Et₂O, 91:9) afforded the title compound 10 as a colorless oil (75 mg, 61%); νmax (neat)/cm⁻¹: 3319 (OH), 3061 (ArCH), 3032 (ArCH), 1601 (ArC=C); δH (400 MHz; CDCl₃) 0.01 (SiC₃H₇), 0.06 (SiC₃H₇), 2.15 (1H, m, SiC₄H₇Ph), 2.18 (1H, d, J 13.6, SiCH₃Ph), 2.25 (1H, m, 2-HH), 2.34 (1H, m, 2-HH), 3.32 (1H, dd, J 11.2, 3.1, 1-H), 5.11–5.19 (2H, m, 4-H₂), 5.77 (1H, m, 3-H), 7.04–7.26 (5H, m, Ar-H); δC (100 MHz; CDCl₃) -6.0 (SiC₃H₇), -5.7 (SiC₃H₇), 23.2 (SiC₄H₇Ph), 38.0 (C-2), 62.3 (C-1), 118.1 (C-4), 124.1 (C-Ar), 128.2 (2 x C-Ar), 128.3 (2 x C-Ar), 135.8 (C-3), 139.6 (C-Ar); m/z (ESI) 243.1253 (MNa⁺, 100%, C₁₃H₂₀ONaSi requires 243.1283).

(1S*,3S*,5R*)-1-(Benzyl(dimethyl)silyl)-3-hydroxy-5-methyl-tetrahydropyran 11

Trifluoroacetic acid (185 μl, 1.91 mmol) was added dropwise to a solution of alcohol 10 (21 mg, 0.10 mmol) and acetaldehyde (32 μl, 0.60 mmol) in dry CH₂Cl₂ (1 ml) at room temperature. This was stirred for 50 minutes at room temperature, then aqueous saturated NaHCO₃ (3 ml) and triethylamine was added until pH >7. The organic phase was separated and the aqueous phase extracted with CH₂Cl₂ (3 x 5 ml). The combined organic phase was then concentrated in vacuo and the resulting crude residue was redissolved in methanol (4 ml), to which K₂CO₃ (80 mg, 0.6 mmol) was added and left to stir for 30 minutes. The methanol was removed under reduced pressure, water (5 ml) added and extracted with CH₂Cl₂ (3 x 5 ml). The combined organic phases were dried (MgSO₄) and concentrated in vacuo to afford the crude residue. This was further
purified by column chromatography (Pet: EtOAc, 80:20) to afford alcohol **11** as a colorless oil (22 mg, 89%); \( \nu_{\text{max}} \) (neat)/\( \text{cm}^{-1} \) 3321 (OH), 3063 (ArCH), 2934 (CH), 1600 (ArC=C); \( \delta H \) (400 MHz; CDCl\(_3\)) -0.04 (3H, s, SiC\(_3\)H\(_3\)), 0.02 (3H, s, SiC\(_3\)H\(_3\)), 1.14 (1H, app. q, \( J \) 11.0, 4-H\(_{\text{ax}}\)), 1.20 (3H, d, \( J \) 6.1, 1'-H\(_3\)), 1.30 (1H, app. q, \( J \) 11.0, 2-H\(_{\text{ax}}\)), 1.58 (1H, br. s, OH), 1.76 (1H, ddd, \( J \) 11.0, 6.6, 2.0, 2-H\(_{\text{eq}}\)), 1.94 (1H, ddd, \( J \) 11.0, 6.6, 2.0, 4-H\(_{\text{ax}}\)), 2.12 (1H, d, \( J \) 13.5, SiCHHPh), 2.23 (1H, d, \( J \) 13.5, SiCHHPh), 3.01 (1H, dd, \( J \) 11.0, 6.6, 2-H\(_{\text{ax}}\)), 3.33 (1H, app. sext. of d., \( J \) 6.6, 2.0, 5-H\(_{\text{ax}}\)), 3.71 (1H, ttd, \( J \) 11.0, 6.6, 2.0, 3-H\(_{\text{ax}}\)), 7.02 -7.10 (3H, m, Ar-H), 7.19- 7.23 (2H, m, Ar-H); \( \delta C \) (100 MHz; CDCl\(_3\)) -6.1 (SiC\(_3\)H\(_3\)), -5.9 (SiC\(_3\)H\(_3\)), 22.1 (C-1'), 23.0 (SiC\(_2\)Ph), 36.1 (C-2), 43.5 (C-4), 68.0 (C-1), 69.3 (C-3), 74.4 (C-5), 124.0 (C-Ar), 128.1 (2 x C-Ar), 128.2 (2 x C-Ar), 139.9 (C-Ar); \( m/z \) (ESI) 287.1439 (MNa\(^+\), 100%, C\(_{15}\)H\(_{24}\)O\(_2\)Na requires 287.1438).

(1S*,3S*,5R*)-1-(Benzyl(dimethyl)silyl)-3-hydroxy-5-(2'-(benzyloxy)ethyl)-tetrahydropyran **12**

Trifluoroacetic acid (0.56 mL, 7.26 mmol) was added dropwise to a solution of alcohol **10** (80 mg, 0.36 mmol) and 3-benzyloxypropanal (120 mg, 0.73 mmol) in dry CH\(_2\)Cl\(_2\) (5 ml) at RT. This was stirred for 50 minutes then aqueous saturated NaHCO\(_3\) (3 ml) and triethylamine was added until pH >7. The organic phase was separated and the aqueous phase extracted with CH\(_2\)Cl\(_2\) (3 x 10 mL). The combined organic phases were concentrated in vacuo and the resulting crude residue was redissolved in methanol (12 mL), to which K\(_2\)CO\(_3\) (100 mg, 0.73 mmol) was added and left to stir for 30 minutes. The methanol was removed under reduced pressure, water (10 mL) added and extracted with CH\(_2\)Cl\(_2\) (3 x 10 mL). The combined organic phases were dried (MgSO\(_4\)) and concentrated in vacuo to afford the crude residue which was purified by column chromatography (Pet: EtOAc, 90:10) to afford alcohol **12** as a colorless oil (114 mg, 82%); \( \nu_{\text{max}} \) (neat)/\( \text{cm}^{-1} \) 3370 (OH), 3065 (ArCH), 2927 (CH), 1600 (ArC=C), 1028 (C-O); \( \delta H \) (400 MHz; CDCl\(_3\)) -6.0 (3H, s, SiC\(_3\)H\(_3\)), 0.03 (3H, s, SiC\(_3\)H\(_3\)), 1.19 (1H, app. q., \( J \) 12.0, 2-H\(_{\text{ax}}\)), 1.43 (1H, app. td, \( J \) 12.5, 10.5, 4-H\(_{\text{ax}}\)), 1.74-1.85 (3H, m, 1'-H\(_2\) and 4-H\(_{\text{eq}}\)), 1.97 (1H, ddd, \( J \) 12.0, 4.5, 2.0, 2-H\(_{\text{eq}}\)), 2.12 (1H, d, \( J \) 13.5, SiCHH), 2.22 (1H, d, \( J \) 13.5, SiCHH), 3.11 (1H, dd, \( J \) 13.0, 2.0, 1-H), 3.43 (1H, dddd, \( J \) 10.5, 8.5, 4.5, 2.0, 5-H), 3.59-3.75 (3H, m, 2'-H\(_2\) and 3-H), 4.54 (2H, s, CH\(_2\)Ph), 7.04 (2H, \( J \) 7.5, Ar-H), 7.09 (1H, t, \( J \) 7.5, Ar-H), 7.21 (2H, t, \( J \) 7.5, Ar-H) 7.30 (1H, m, ArH), 7.34-7.37 (4H, m,
ArH; δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>) -6.1 (SiCH<sub>3</sub>), -5.8 (SiCH<sub>3</sub>), 23.1 (SiCH<sub>3</sub>), 36.4 (C-4), 36.7 (C-1'), 42.0 (C-2), 67.0 (C-2'), 68.0 (C-1), 69.3 (C-3), 73.1 (CH<sub>2</sub>Ph), 75.2 (C-Ar), 124.1 (C-Ar), 127.6 (C-Ar), 127.7 (2 x C-Ar), 128.3 (2 x C-Ar), 128.4 (2 x C-Ar), 139.9 (C-Ar); m/z (ESI) 407.1994 (MNa<sup>+</sup>, 100%, C<sub>23</sub>H<sub>32</sub>O<sub>3</sub>Na requires 407.2018).

(1S*,3S*,5R*)-3-O-Acetyl-1-(benzyldimethylsilyl)-5-methyl-tetrahydropyran 13

\[
\begin{align*}
\text{BnMe}_2\text{Si} & \text{OH} \quad \text{TMSOAc, AcOH} \\
& \text{TESOTf, CH}_2\text{Cl}_2 \\
\text{AcO} & \rightarrow \text{O} \quad \text{SiMe}_2\text{Bn} \\
\text{10} & \text{13}
\end{align*}
\]

To a solution of alcohol 10 (80 mg, 0.36 mmol), acetaldehyde (41 µL, 0.73 mmol) and trimethylsilyl acetate (54 µl, 0.36 mmol) in acetic acid (0.35 mL) was added triethylsilyl trifluoromethanesulfonate (246 µl, 1.09 mmol). This was stirred for 5 minutes, then the reaction mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and saturated aqueous solution of NaHCO<sub>3</sub> (15 mL) added. The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 10 mL), combined, washed with saturated aqueous solution of NaHCO<sub>3</sub> (15 mL), dried (MgSO<sub>4</sub>) and concentrated in vacuo. The crude residue was then purified by column chromatography (Pet: Et<sub>2</sub>O, 90:10) to give acetate 13 as a yellow oil (81 mg, 73%); ν<sub>max</sub> (neat)/cm<sup>-1</sup> 3065 (ArCH), 3020 (ArCH), 2937 (CH), 1739 (C=O), 1600 (ArC=C), 1027 (C-O); δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>) -0.05 (3H, s, SiCH<sub>3</sub>), 0.02 (3H, s, SiCH<sub>3</sub>), 1.19 (3H, d, J 6.3, 1'-H<sub>3</sub>), 1.26 (1H, app. q, J 11.5, 4-H<sub>ax</sub>), 1.41 (1H, app. q, J 12.5, 2-H<sub>eq</sub>), 1.80 (1H, ddd, J 12.5, 4.5, 2-H<sub>eq</sub>), 1.95 (1H, ddd, J 11.5, 4.5, 2.0, 4-H<sub>eq</sub>), 2.03 (3H, s, C(O)CH<sub>3</sub>), 2.12 (1H, d, J 13.5, SiCH<sub>2</sub>Ph), 2.23 (1H, d, J 13.5, SiCH<sub>2</sub>Ph), 3.01 (1H, dd, J 12.5, 2.0, 1-H<sub>ax</sub>), 3.40 (1H, app. sext. of d., J 6.3, 2.0, 5-H<sub>ax</sub>), 4.82 (1H, tt, J 11.0, 5.0, 3-H<sub>ax</sub>), 7.02 (2H, J 8.0, Ar-H), 7.07 (1H, t, J 7.5, Ar-H), 7.02 (2H, t, J 7.5, Ar-H); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>) -6.1 (SiCH<sub>3</sub>), -5.7 (SiCH<sub>3</sub>), 21.5 (COCH<sub>3</sub>), 22.1 (C-1'), 23.1 (SiCH<sub>2</sub>Ph), 32.5 (C-2), 39.7 (C-4), 68.1 (C-1), 71.8 (C-3), 74.5 (C-5), 124.2 (C-Ar), 128.3 (2 x C-Ar), 128.4 (2 x C-Ar), 139.8 (C-Ar), 170.7 (CO); m/z (ESI) 329.1543 (MNa<sup>+</sup>, 100%, C<sub>17</sub>H<sub>26</sub>O<sub>3</sub>NaSi requires 329.1549).
To a solution of alcohol 10 (80 mg, 0.36 mmol), 3-benzyloxypropanal (120 mg, 0.73 mmol) and trimethylsilyl acetate (54 µl, 0.36 mmol) in acetic acid (0.35 mL) was added triethylsilyl trifluoromethanesulfonate (246 µl, 1.09 mmol). This was stirred for 5 minutes, then the reaction mixture was diluted with CH₂Cl₂ (10 mL) and saturated aqueous solution of NaHCO₃ (15 mL) added. The aqueous phase was extracted with CH₂Cl₂ (3 x 10 mL), combined, washed with saturated aqueous solution of NaHCO₃ (15 mL), dried (MgSO₄) and concentrated in vacuo. The crude residue was then purified by column chromatography (Pet: Et₂O, 90:10) to give acetate 14 as a yellow oil (110 mg, 71%); v_max (neat)/cm⁻¹ 3059 (CH), 2951 (CH), 1738 (C=O), 1599 (C=C), 1026 (C-O); δ_H (400 MHz; CDCl₃) -0.06 (3H, s, SiC₃H₃), 0.01 (3H, s, SiC₃H₃), 1.32 (1H, app. q., J 12.0, 2-Hax), 1.43 (1H, app. q., J 12.0, 4-Hax), 1.75-1.83 (2H, m, 1'-H₂), 1.83 (1H, m, 4-Heq), 1.97 (1H, ddt, J 12.0, 4.5, 2.0, 2-Heq), 2.04 (3H, s, C(O)CH₃), 2.10 (1H, d, J 13.5, SiCHH), 2.20 (1H, d, J 13.5, SiCHH), 3.11 (1H, dd, J 12.0, 1.5, 1-H), 3.49 (1H, m, 5-H), 3.55-3.68 (2H, m, 2'-H₂), 4.52 (2H, s, CH₂Ph), 4.85 (1H, app. tt, J 11.0, 4.7, 3-H), 7.02 (2H, J 7.5, Ar-H), 7.07 (1H, t, J 7.5, Ar-H), 7.02 (2H, t, J 7.5, Ar-H) 7.29 (1H, m, ArH), 7.32-7.37 (4H, m, ArH); δ_C (100 MHz; CDCl₃) -6.1 (SiCH₃), -5.9 (SiCH₃), 21.5 (COCH₃), 23.0 (SiCH₂), 32.7 (C-4), 36.7 (C-1'), 38.1 (C-2), 66.8 (C-2'), 67.9 (C-1), 71.7 (C-3), 73.1 (CH₂Ph), 75.2 (C-5), 124.2 (C-Ar), 127.6 (2 x C-Ar), 127.7 (2 x C-Ar), 128.3 (2 x C-Ar), 128.5 (2 x C-Ar), 138.6 (C-Ar), 139.9 (C-Ar), 170.6 (CO); m/z (ESI) 449.2116 (MNa⁺, 100%, C₂₅H₃₄O₄NaSi requires 449.2124).
(1S,2R,3S,5R)-3-O-Acetyl-1-(Benzylidimethylsilane)-2-methyl-5-(2'-phenylethyl)-tetrahydropyran 18

![Chemical Structure](image)

Acetic anhydride (1.52 mL, 2.28 mmol), triethylamine (1.52 mL, 3.80 mmol) and a single crystal of DMAP were added to a solution of alcohol 7 (270 mg, 0.73 mmol) in dry CH$_2$Cl$_2$ (8 mL) and stirred at RT under N$_2$ for 1 h. The reaction was diluted with water (10 mL) and extracted with CH$_2$Cl$_2$ (3 x 10 mL). The combined organic phases were washed with saturated aqueous NaHCO$_3$ solution (1 x 10 mL), dried (MgSO$_4$) and concentrated in vacuo. Purification by column chromatography (Pet: EtOAc, 98:2) gave acetate 18 as a colourless oil (298 mg, 99%); [α]$^\text{D}_{20} +17.6$ (c 0.97, CHCl$_3$); $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3061 (ArCH), 3025 (ArCH), 2928 (CH), 1731 (C=O), 1600 (ArC=C), 1238 (C-O); $\delta_{\text{H}}$ (400 MHz; CDCl$_3$) 0.05 (3H, s, SiCH$_3$), 0.08 (3H, s, SiCH$_3$), 0.83 (3H, d, J 6.6, 2-CH$_3$), 1.27-1.31 (1H, m, 1'-HH), 1.32 (1H, app. q., J 11.2, 4-H$_{ax}$), 1.67-1.89 (2H, m, 2-H$_{ax}$ and 1'-HH), 2.01 (1H, ddd, J 11.2, 4.6, 1.7, 4-H$_{eq}$), 2.07 (3H, s, C(O)CH$_3$), 2.22 (1H, d, J 13.6, SiCHCH), 2.30 (1H, d, J 13.6, SiCHCH), 2.67 (1H, m, 2'-HH), 2.80 (1H, m, 2'-HH), 2.83 (1H, d, J 11.4, 1-H), 3.30 (1H, tdd, J 11.2, 4.0, 1.7, 5-H), 4.54 (1H, td, J 11.2, 4.6, 3-H), 7.04-7.32 (10H, m, ArH); $\delta_{\text{C}}$ (100 MHz; CDCl$_3$) -4.8 (SiCH$_3$), -3.7 (SiCH$_3$), 13.5 (2-CH$_3$), 21.2 (C(O)CH$_3$), 23.8 (SiCH$_3$), 31.8 (C-2'), 37.8 (C-4), 37.9 (C-2), 38.0 (C-1'), 74.1 (C-1), 76.9 (C-3), 77.1 (C-5), 124.1 (C-Ar), 125.7 (C-Ar), 128.2 (C-Ar), 128.3 (C-Ar), 128.4 (C-Ar), 128.5 (C-Ar), 139.8 (C-Ar), 142.2 (C-Ar), 170.9 (CO); $m/z$ (ESI) 433.2170 (MNa$^+$, 100%, C$_{25}$H$_{34}$NaSiO$_3$ requires 433.2169).

(1S,3S,5R)-3-O-Acetyl-1-(Benzylidimethylsilane)-5-(2'-phenylethyl)-tetrahydropyran 19

![Chemical Structure](image)

Acetic anhydride (507 µl, 0.76 mmol), triethylamine (605 µl, 1.25 mmol) and a single crystal of DMAP were added to a solution of alcohol 9 (90 mg, 0.25 mmol) in dry CH$_2$Cl$_2$ (2 mL) and stirred...
at RT under N₂ for 1 h. The reaction was diluted with water (5 mL) and extracted with CH₂Cl₂ (3 x 10 mL). The combined organic phases were washed with saturated aqueous NaHCO₃ solution (1 x 10 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (Pet: EtOAc, 95:5) gave acetate 19 as a colourless oil (96 mg, 97%); [α]ᵡ⁺ 19 (c 1.00, CHCl₃); νₑₓₘ (neat)/cm⁻¹ 3061 (ArCH), 2923 (CH), 1728 (C=O), 1601 (ArC=C), 1238 (C-O); δₓ (400 MHz; CDCl₃) 0.00 (3H, s, SiC₃H₃), 0.06 (3H, s, SiC₃H₃), 1.33 (1H, app. q., J 11.3, 4-Hₐx), 1.47 (1H, app. q., J 11.3, 2-Hₐx), 1.72 (1H, m, 1'⁻-HH), 1.82-1.90 (2H, m, 2⁻-Hₑq and 1'⁻-HH), 1.96 (1H, ddd, J 11.3, 6.4, 2.0, 4-Hₑq), 2.05 (3H, s, C(O)C₃H₃), 2.17 (1H, d, J 13.7, SiCHH), 2.25 (1H, d, J 13.7, SiCHH), 2.71 (1H, m, 2⁻-HH), 2.82 (1H, m, 2⁻-HH), 3.11 (1H, dd, J 11.3, 2.0, 1⁻-H), 3.28 (1H, ddd, J 11.3, 3.9, 2.0, 5⁻-H), 4.83 (1H, app. tt, J 11.3, 4.9, 3⁻-H), 7.04-7.11 (3H, m, ArH), 7.19-7.5 (7H, m, ArH); δₓ (100 MHz; CDCl₃) -6.1 (SiC₃H₃), -5.9 (SiC₃H₃), 21.4 (C(O)CH₃), 22.9 (SiCH₂), 31.7 (C-2'), 32.7 (C-1') 37.9 (C-4), 37.9 (C-2), 68.0 (C-1), 71.7 (C-3), 77.1 (C-5), 124.1 (C-Ar), 125.7 (C-Ar), 128.2 (2 x C-Ar), 128.2 (2 x C-Ar), 128.3 (2 x C-Ar), 128.4 (2 x C-Ar), 142.2 (2 x C-Ar), 170.5 (CO); m/z (ESI) 419.2000 (MNa⁺, 100%, C₂₅H₃₄NaSiO requires 419.2013).

(1S,2R,3S,5R)-3-O-Benzyl-1-(Benzyldimethylsilane)-2-methyl-5-(2'-phenylethyl)-tetrahydropyran 20

NaH (36 mg, 60% dispersion in oil, 0.88 mmol) was added to a solution of alcohol 7 (80 mg, 0.22 mmol) in dry THF (2 mL), cooled to 0 °C and stirred for 30 minutes under N₂. To the resulting suspension, TBAI (8 mg, 0.02 mmol) and benzyl bromide (150 mg, 0.88 mmol) were added and the reaction was allowed to warm to RT slowly. After stirring for 6 h, NH₄Cl solution (5 mL) was added and the reaction mixture diluted with CH₂Cl₂ (5 mL), separated and the aqueous layer extracted with CH₂Cl₂ (3 x 10 mL). The organic phases were combined and washed with brine (5 mL), dried (MgSO₄) and concentrated in vacuo to give a crude residue. Purification by column chromatography (EtOAc:Pet, 1:99) gave benzyl ether 20 as a yellow oil (99 mg, 99%); [α]ᵡ⁺ 29 (c 1.00 , CHCl₃); δₓ (400 MHz; CDCl₃) 0.05 (3H, s, SiCH₃), 0.08 (3H, s, SiCH₃), 0.96 (3H, d, J 6.4, 2-
(1S,3S,5R)-3-O-Benzyl-1-(Benzylimethylsilane)-5-ethyl-(2′-phenylethyl)-tetrahydropyran 21

NaH (41 mg, 60% dispersion in oil, 1.02 mmol) was added to a solution of alcohol 9 (90 mg, 0.22 mmol) in dry THF (2.5 mL), cooled to 0 °C and stirred for 30 minutes under N₂. To the resulting suspension, TBAI (9 mg, 0.03 mmol) and benzyl bromide (174 mg, 1.02 mmol) were added and the reaction was allowed to warm to RT slowly. After stirring for 12 h, NH₄Cl solution (10 mL) was added and the reaction mixture diluted with CH₂Cl₂ (10 mL), separated and the aqueous layers extracted with CH₂Cl₂ (3 x 10 mL). The organic phases were combined and washed with brine (10 mL), dried (MgSO₄) and concentrated in vacuo to give a crude residue. Further purification by column chromatography (EtOAc:Pet, 2:98) gave benzyl ether 21 as yellow oil (110 mg, 97%); δH (400 MHz; CDCl₃) - 0.01 (3H, s, SiCH₃), 0.06 (3H, s, SiCH₃), 1.28 (1H, app. q., J 11.0, 4-Hax), 1.42 (1H, app. q., J 12.7, 2-Hax), 1.72 (1H, m, 1′-HH), 1.83-1.91 (2H, m, 1′-HH and 2-Heq), 2.02 (1H, ddd, J 11.0, 4.7, 2.2, 4-Heq), 2.17 (1H, d, J 13.7, SiCHH), 2.26 (1H, d, J 13.7, SiCHH) 2.70 (1H, m, 2′-HH), 2.82 (1H, m, 2′-HH), 3.01 (1H, dd, J 12.7, 1.7, 1-Hax), 3.18 (1H, tdd, J 11.0, 4.2, 2.2, 5-H), 3.48 (1H, dtt, J 12.7, 11.0, 4.7, 3-Hax), 4.55 (2H, s, OCH₂Ph), 7.04-7.10 (3H, m, ArH), 7.19-7.39 (12H, m, ArH); δC (100 MHz; CDCl₃) - 6.0 (SiCH₃), -5.8 (SiCH₃), 23.1 (SiCH₃), 31.8 (C-2′), 33.4 (C-2), 38.1 (C-4), 38.8 (C-1′), 68.1 (C-1), 69.4 (OCH₂Ph), 75.8 (C-3), 77.2 (C-5), 124.0 (C-Ar), 125.7 (C-Ar), 127.5 (C-Ar), 127.6 (2 x C-Ar), 127.8 (2 x C-Ar), 128.2 (2 x C-Ar), 128.3 (2 x C-Ar), 128.4 (2 x
C-Ar), 128.5 (2 x C-Ar), 138.7 (C-Ar), 142.4 (C-Ar); m/z (ESI) 467.2361 (MNa⁺, 100%, C₂₅H₃₄NaSiO requires 467.2377).

General procedure for the oxidation of 1-silyl tetrahydropyrans

TBAF (1.5 eq, 0.25 M solution in THF) was added dropwise over 30 minutes to a solution of 1-silyl tetrahydropyran (0.1 mmol, 1 eq) in dry THF (1.5 mL) at 0 °C under N₂. Upon warming slowly to 15 °C, disappearance of 1-silyl tetrahydropyran was monitored by TLC. Urea hydrogen peroxide (5 eq), potassium hydrogen carbonate (3 eq) and dry methanol (0.25 mL) were added. This was left to warm to RT for 1 hour, monitored by TLC using phosphomolybdic acid staining, with the lactol visualized as a green spot. On completion aqueous saturated sodium thiosulfate solution (2 mL) was added, the organic phases separated and aqueous layer extracted with CH₂Cl₂ (3 x 5 mL). The crude reaction mixture was concentrated in vacuo then taken up in dry CH₂Cl₂ (1.5 mL). The solution was then cooled to 0 °C and triethylamine (5 eq), acetic anhydride (3 eq) and a crystal of DMAP was added. The reaction was stirred for 1h and on completion water (6 mL) was added and the organic phase separated. The aqueous phase was washed with CH₂Cl₂ (3 x 6 mL), the combined organic phases dried (MgSO₄) and concentrated in vacuo. The residue was then purified by column chromatography (Pet:EtOAc) to yield 1-O-acetates as a mixture of α/β anomers, inseparable by column chromatography. Selected data is reported below.

(2R,3S,5R)-1,3-O-Acetyl-2-methyl-5-(2′-phenylethyl)-tetrahydropyran 17 (from 18)

Yellow oil (80 %, α:β 51:49); δₜ (400 MHz; CDCl₃) 0.89 (3H, d, J 6.8, β-2-CH₃), 0.92 (3H, d, J 6.6, α-2-CH₃), 1.30-1.45 (2H, app. q., J 11.0, 2 x 4-Hax), 2.05 (β C(O)CH₃), 2.07 (α C(O)CH₃), 2.08 (β C(O)CH₃), 2.18 (α C(O)CH₃), 5.36 (1H, d, J 9.0, β 1-Hax), 6.13 (1H, d, J 3.5, α 1-Heq); δC (100 MHz; CDCl₃) 94.7 (C-1), 96.0 (C-1); m/z (ESI) 343.1530 (MNa⁺, 100%, C₁₈H₂₄O₃Na requires 343.1515).
(3S,5R)-1,3-O-Acetyl-5-(2’-phenylethyl)-tetrahydropyran 22 (from 19)

Colorless oil (64 %, α:β 29:71); \(\delta_H\) (400 MHz; CDCl\(_3\)) 2.05 (3H, s, 4-C(O)CH\(_3\)), 2.15 (3H, s, α-C(O)CH\(_3\)), 5.67 (1H, dd, \(J = 10.3, 2.5\), \(\beta\) 1-H\(_{ax}\)), 6.31 (1H, br. d, \(J = 2.7\), \(\alpha\) 1-H\(_{eq}\)) ; \(\delta_C\) (100 MHz; CDCl\(_3\)) 92.0 (C-1), 92.1 (C-1); \(m/z\) (ESI) 329.1345 (MNa\(^+\), 100%, \(C_{17}H_{22}O_5\)Na requires 329.1359).

(2R,3S,5R)-1-O-Acetyl-3-O-Benzyl-2-methyl-5-(2’-phenylethyl)-tetrahydropyran 23 (from 20)

Clear oil (73%, α:β 32:68); \(\delta_H\) (400 MHz; CDCl\(_3\)) 2.06 (3H, s, \(\alpha\) C(O)CH\(_3\)), 2.17 (3H, s, \(\beta\) C(O)CH\(_3\)), 5.32 (1H, d, \(J = 9.2\), \(\alpha\) 1-H\(_{ax}\)), 6.13 (1H, d, \(J = 3.5\), \(\beta\) 1-H\(_{eq}\)); \(\delta_C\) (100 MHz; CDCl\(_3\)) 95.2 (C-1), 96.4 (C-1); \(m/z\) (ESI) 391.1889 (MNa\(^+\), 100%, \(C_{23}H_{31}ONaClSi\) requires 391.1879).

(3S,5R)-1-O-Acetyl-3-O-Benzyl-5-(2’-phenylethyl)-tetrahydropyran 24 (from 21)

Colorless oil (71 % α:β 37:43); 2.04 (3H, s, \(\alpha\)-C(O)CH\(_3\)), 2.16 (3H, s, \(\beta\)-C(O)CH\(_3\)), 5.61 (1H, dd, \(J = 10.0, 2.2\), 1-H\(_{ax}\)), 6.33 (1H, br. d, \(J = 2.5\), 1-H\(_{eq}\)); \(\delta_C\) (100 MHz; CDCl\(_3\)) 92.6 (C-1), 92.7 (C-1); \(m/z\) (ESI) 377.17171 (MNa\(^+\), 100%, \(C_{22}H_{26}O_4\)Na requires 377.1723).
(2R)-1,2-Epoxy-3-O-(tert-butyldiphenylsilyl)-propane 25²

\[
\begin{align*}
\text{HO} & \quad \text{O} \\
& \quad \text{i) } n\text{-BuLi, THF,} \\
& \quad \text{\quad } -78 \, ^\circ \text{C} \\
& \quad \text{ii) TBDPSCI,} \\
& \quad \text{\quad } -78 \, ^\circ \text{C} \rightarrow \text{RT} \\
& \quad \text{TBDPSO} \\
\end{align*}
\]

\( n\text{-BuLi (1.48 M in hexanes, 4.56 mL, 6.78 mmol) was added dropwise to a solution of (S)-glycidol (0.45 mL, 6.75 mmol) in THF (14.0 mL) at } -78 \, ^\circ \text{C under an atmosphere of N}_2. \) After 20 min, TBDPSCI (1.86 g, 6.75 mmol) was added dropwise. After 5 min, the reaction mixture was warmed to RT and stirred for 72 h. A saturated aqueous solution of NH\(_4\)Cl (20 mL) was added and the reaction mixture was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine (20 mL), dried over MgSO\(_4\) and concentrated in vacuo. The residue was purified by column chromatography (Pet:EtOAc, 90:10) gave silyl ether 25 as a colourless oil (2.11 g, 99%); \([\alpha]^{22}_D + 1.0 (c \quad 1.00, \text{CHCl}_3), \) lit.¹ [\([\alpha]^{25}_D + 2.3 (c \quad 2.00, \text{CHCl}_3); \) \( \delta_H (400 \, \text{MHz; CDCl}_3) 1.10 \) (9H, s, (CH\(_3\))\(_3\)), 2.64 (1H, dd, \( J \quad 5.1, 2.7, 1\text{-HH})), 2.77 (1H, dd, \( J \quad 5.1, 4.2, 1\text{-HH})), 3.18 (1H, m, 2-H), 3.75 (1H, m, 3-HH), 3.89 (1H, m, 3-HH), 7.32-7.53 (6H, m, ArH), 7.62-7.84 (4H, m, ArH); \( \delta_C (100 \, \text{MHz; CDCl}_3) 19.3 \) (C(CH\(_3\))\(_3\)), 26.8 (C(CH\(_3\))\(_3\)), 44.5 (C-1), 52.3 (C-2), 64.3 (C-3), 127.7 (2 x C-Ar), 129.8 (2 x C-Ar), 133.3 (2 x C-Ar), 134.8 (2 x C-Ar), 135.6 (2 x C-Ar). Spectroscopic data in agreement with literature.²

(2R)-1-O-(tert-Butyldiphenylsilyl)-4-penten-1,2-diol 26²

Vinylmagnesium bromide (1.0 M in THF, 7.36 mL, 7.36 mmol) was added dropwise to a solution of CuCN (0.33 g, 3.68 mmol) in Et\(_2\)O (5 mL) at -78 °C under an atmosphere of N\(_2\). The reaction mixture was warmed to -60 °C until the CuCN had dissolved. The reaction mixture was cooled to -78 °C and a solution of epoxide 25 (500 mg, 1.60 mmol) in Et\(_2\)O (5 mL) added dropwise. The reaction mixture was slowly warmed to -60 °C and stirred for 3 h. The reaction mixture was quenched with a saturated aqueous solution of NH\(_4\)Cl (10 mL) and stirred for 25 mins. Et\(_2\)O (30
mL) and water (30 mL) were added and the organic phase was separated. The aqueous layer was extracted with Et<sub>2</sub>O (2 x 20 mL). The combined organic extracts were washed with brine (40 mL), dried over MgSO<sub>4</sub> and concentrated in vacuo. Purification by column chromatography (Pet: EtOAc, 90:10) gave alcohol 26 as a colourless oil (482 mg, 89%); [α]<sup>25</sup> + 2.5 (c 1.0, CHCl<sub>3</sub>), lit. [α]<sup>25</sup> + 3.0 (c 0.99, CHCl<sub>3</sub>); δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>) 1.10 (9H, s, (C<sub>H</sub>3)<sub>3</sub>), 2.21-2.29 (2H, m, 3-H), 3.56 (2H, m, 5-H), 5.03-5.13 (2H, s, 5-H), 5.74-5.87 (1H, d, J 4.7, 3-H), 7.36-7.50 (6H, m, ArH), 7.64-7.72 (4H, m, ArH); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; 18.9 (C(CH<sub>3</sub>)<sub>3</sub>), 26.5 (C(CH<sub>3</sub>)<sub>3</sub>), 37.2 (C-3), 67.0 (C-1), 70.9 (C-2), 117.1 (C-5), 127.4 (2 x C-Ar), 129.5 (2 x C-Ar), 134.0 (C-4), 134.5 (2 x C-Ar), 135.2 (2 x C-Ar). Spectroscopic data in agreement with the literature.<sup>2</sup>

(15,35,55)-3-O-Acetyl-5-acetoxyethyl-1-(benzyldimethylsilyl)-tetrahydropyran 27

![Chemical structure](image)

To a solution of homoallylic alcohol 26 (46 mg, 0.14 mmol), silyl acetal 5 (68 mg, 0.27 mmol) and trimethylsilyl acetate (20 µl, 0.14 mmol) in acetic acid (1 mL) was added triethylsilyl trifluoromethanesulphonate (TESOTf) (122 µl, 0.54 mmol). This was stirred for 5 minutes, then the reaction mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (3 mL) and saturated aqueous solution of NaHCO<sub>3</sub> (5 mL) added. The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 5 mL), combined, washed with saturated aqueous solution of NaHCO<sub>3</sub> (5 mL), dried (MgSO<sub>4</sub>) and concentrated in vacuo. The crude residue was then purified by column chromatography (Pet: EtO, 85:15) to give diacetate 27 as a yellow oil (32 mg, 65%); [α]<sup>23</sup> + 37 (c 1.00, CHCl<sub>3</sub>; ν<sub>max</sub> (neat)/cm<sup>-1</sup> 3059 (CH), 2955 (CH), 1737 (C=O), 1600 (C=O); δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>) 0.01 (3H, s, Si(CH<sub>3</sub>)<sub>3</sub>), 0.09 (3H, s, Si(CH<sub>3</sub>)<sub>3</sub>), 1.39 (1H, app. q., J 11.8, 2-H<sub>eq</sub>), 1.51 (1H, app. q., J 12.5, 4-H<sub>eq</sub>), 1.87 (1H, ddd, J 12.5, 4.7, 2.5, 4-H<sub>eq</sub>), 2.03 (1H, ddt, J 11.8, 4.7, 2.5, 2-H<sub>eq</sub>), 2.09 (3H, s, C(O)CH<sub>3</sub>), 2.15 (3H, s, C(O)CH<sub>3</sub>), 2.17 (1H, d, J 13.5, SiCHH), 2.29 (1H, d, J 13.5, SiCHH), 3.14 (1H, dd, J 11.8, 2.5, 1-H), 3.60 (1H, m, 5-H), 4.07 (1H, dd, J 11.5, 3.9, 1'-H<sub>eq</sub>), 4.19 (1H, dd, J 11.5, 6.9, 1'-H<sub>eq</sub>), 4.90 (1H, app. tt, J 11.8, 4.7, 3-H), 7.02-7.09 (3H, m, ArH), 7.18-7.22 (2H, m, ArH); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>) -6.3 (Si(CH<sub>3</sub>)<sub>3</sub>), -6.0 (Si(CH<sub>3</sub>)<sub>3</sub>), 20.8 (COCH<sub>3</sub>), 21.2 (COCH<sub>3</sub>), 22.3 (SiCH<sub>2</sub>), 32.3 (C-4), 34.0 (C-2), 66.8 (C-1'), 67.9 (C-1), 71.0 (C-3),
75.8 (C-5), 124.1 (C-Ar), 128.1 (2 x C-Ar), 128.2 (2 x C-Ar), 139.5 (C-Ar), 170.4 (CO), 170.8 (CO);

\[ m/z \text{ (ESI)} \ 387.1601 \ (MNa^+ \ 100\%, \ C_{19}H_{28}NO_5Na \text{ requires } 387.1604). \]

2,4-Dideoxy-gluc-3,5-diacetate hexopyranose 28

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\begin{align*}
\text{O} & \quad \text{O} \quad \text{SiMe}_2\text{Bn} \\
\text{AcO} & \quad \text{AcO} \quad 27 \\
\end{align*}
\]

TBAF (1 mL, 0.50 mmol, 0.5 M solution in THF) was added dropwise over 15 minutes to a solution of 1-silyl tetrahydropyran 27 (60 mg, 0.16 mmol, 1 eq) in dry THF (4 mL) at 0 °C under N₂. The reaction was warmed slowly to RT until disappearance of 1-silyl tetrahydropyran 27 by TLC. Urea hydrogen peroxide (78 mg, 0.82 mmol), potassium hydrogen carbonate (50 mg, 0.50 mmol) and dry methanol (1 mL) was added. The reaction was warmed to 40 °C and left to stir for 12 h and upon completion aqueous saturated sodium thiosulphate solution (3 mL) was added, the organic phases separated and aqueous layer extracted with CH₂Cl₂ (3 x 10 mL). The crude reaction mixture was concentrated in vacuo then taken up in dry CH₂Cl₂ (5 mL). The solution was then cooled to 0 °C and triethylamine (230 µl, 1.64 mmol), a crystal of DMAP then acetic anhydride (78 µl, 0.82 mmol) was added. The reaction was warmed to RT and left to stir for 1 h and on completion water (12 mL) was added and the organic phase separated. The aqueous phase was washed with CH₂Cl₂ (3 x 15 mL), the combined organic phases dried (MgSO₄) and concentrated in vacuo. The residue was then purified by column chromatography (Pet:Et₂O, 50:50) to yield 28 as a yellow oil, as a mixture of α/β anomers (26 mg, 57%, α:β 31:69); δH (400 MHz; CDCl₃) 1.67 (1H, m, 1 x 2-HH or 4-HH), 1.73-1.83 (4H, m, 4 x 2-HH or 4-HH), 1.94-2.04 (3H, m, 3 x 2-HH or 4-HH), 2.08-2.11 (9H, br. m, 3 x C(O)CH₃), 2.12-2.18 (3H, m, C(O)CH₃), 4.09-4.15 (4H, 2 x br. s, 2 x 1’-H₂), 4.18 (1H, m, β 5-Hₓ), 4.38 (1H, m, α 5-Hₓ), 5.16 (1H, br. m, α-3-Hₓ), 5.32 (1H, br. m, β 3-Hₓ), 6.01 (1H, dd, J 9.8, 2.0, β 1-Hₓ), 6.20 (1H, d, J 3.9, α 1-Hₑq); δC (100 MHz; CDCl₃) 20.8 (br. C(O)CH₃), 21.2 (br. C(O)CH₃), 29.7, 30.6, 30.9, 31.1, 34.0, 64.2 (α C-3), 65.0 (α C-5), 66.0 (C-1’), 66.2 (C-1’), 67.2 (β C-3), 70.0 (β C-5), 91.0 (β C-1), 91.1 (α C-1), 169.2 (CO), 169.4 (CO), 170.0 (CO), 170.2 (CO), 170.8 (CO), 170.9 (CO); m/z (ESI) 297.0940 (MNa⁺, 100%, C₁₂H₁₆O₇Na requires 297.0945).
(1S,3S,5S)-1-(Benzyldimethylsilyl)-3-ethoxy-5-((tert-butyldiphenylsilyloxy)methyl) – tetrahydropyran 29

Trifluoroacetic acid (580 µl, 5.96 mmol) was added dropwise to a solution of alcohol 26 (101 mg, 0.30 mmol) and silyl acetal 5 (90 mg, 0.36 mmol) in dry CH2Cl2 (4 mL) at RT under N2 and stirred for 5 mins. Aqueous saturated NaHCO3 (10 mL) was added, the organic phase was separated and the aqueous phase extracted with CH2Cl2 (3 x 10 mL). The combined organic phases were dried (MgSO4), then concentrated in vacuo to afford the crude residue. This was further purified by column chromatography (Pet: Et2O, 96:4) gave ethyl ether 29 as a colourless oil (58 mg, 74%); [α]D + 22 (c 0.45, CHCl3; νmax (neat)/cm−1 2937 (C-H), 1596 (C=C), 1090 (C-O), 1070 (C-O), 1003 (C-O); δH (400 MHz; CDCl3) -0.03 (3H, s, SiC6H3), 0.07 (3H, s, SiC6H3), 1.07 (9H, br. s., (CH3)3), 1.22 (3H, t, J 7.1, OCH2CH3), 1.27 (1H, app. q., J 11.3, 4-Hax), 1.36 (1H, app. q., J 11.5, 2-Hax), 1.83 (1H, ddd, J 11.5, 3.9, 2.0, 2-Heq), 2.04 (1H, ddd, J 11.3, 4.4, 2.0, 4-Heq), 2.13 (1H, d, J 13.5, SiCHH), 2.28 (1H, d, J 13.5, SiCHH), 3.06 (1H, dd, J 11.5, 2.0, 1-H), 3.42 (2H, m, 3-H and 5-H), 3.53 (2H, q, J 7.1, OCH2CH3), 3.63 (1H, dd, J 10.5, 4.2, 1'–HH), 3.72 (1H, dd, J 10.5, 5.6, 1’–HH), 7.04-7.22 (5H, m, ArH), 7.37-7.76 (10H, m, ArH); δC (100 MHz; CDCl3) -62.2 (SiCH3) -6.0 (SiC6H3) 14.1 (OCH2CH3), 26.8 ((CH3)3), 28.9 (C(CH3)3), 33.4 (C-2), 35.0 (C-4), 62.7 (OCH2CH3), 67.3 (C-1’), 68.0 (C-1), 76.2 (C-3), 79.2 (C-5), 123.9 (3 x C-Ar), 127.6 (2 x C-Ar), 128.1 (C-Ar), 128.3 (2 x C-Ar), 129.5 (2 x C-Ar), 129.6 (2 x C-Ar), 133.8 (C-Ar), 135.6 (2 x C-Ar), 135.7 (2 x C-Ar), 139.9 (C-Ar); m/z (ESI) 569.2891 (MNa+, 100%, C33H46NaSi3O3 requires 569.2883).

(2R)-1,2-Epoxy-3-O-(benzyl)-propane Si-2
To a solution of (S)-glycidol (896 µl, 1.0 g, 13.5 mmol) in THF (130 mL) was added NaH (2.15 g, 60% dispersion in oil, 54.0 mmol) at 0 °C under N₂. The resulting mixture was stirred for 30 minutes, after which benzyl bromide (6.41 mL, 54.0 mmol) and tert-butylammonium iodide (498 mg, 1.35 mmol) were added. The reaction mixture was allowed to warm to RT and stirred overnight. Saturated aqueous solution of NH₄Cl (130 mL) was then added. The organic phases were extracted with EtOAc (3 x 100 mL), combined, dried (MgSO₄) and concentrated in vacuo. The crude residue was then purified by column chromatography (Pet: Et₂O, 86: 14) to give epoxide SI-2 an colourless oil (2.09 g, 94%); [α]D²⁵ = -5.0 (c 0.97, CHCl₃), lit.⁴ [α]D²⁵ = -6.8 (c 1.0, CHCl₃); δH (400 MHz; CDCl₃) 2.54 (1H, dd, J 2.7, 5.4, 1-HH), 2.72 (1H, d, J 4.9, 1-HH), 3.11 (1H, m, 2-H), 3.37 (1H, dd, J 11.5, 5.9, 3-HH), 3.69 (1H, dd, J 11.5, 2.9, 3-HH), 4.48 (1H, d, J 12.0, CH₂Ph), 4.54 (1H, d, J 12.0, CH₂Ph), 7.18-7.29 (5H, m, ArH); δC (100 MHz; CDCl₃) 44.2 (C-1), 50.8 (C-2), 70.8 (CH₂Ph), 73.3 (C-3), 127.7 (C-Ar), 128.4 (C-Ar), 137.8 (C-Ar). Data in accordance with literature.⁵

(2R)-1-O-(Benzyl)-4-pentene-1,2-diol SI-3

To a solution of epoxide SI-2 (1.4 g, 9.74 mmol) in Et₂O (100 mL) and copper (I) iodide (185 mg, 0.97 mmol) at -78 °C under N₂ was added vinyl magnesium bromide (10.7 mL of 1M solution in THF, 10.7 mmol) dropwise over 5 minutes. The resulting mixture was allowed to stir for 4 h, after which saturated aqueous solution of NH₄Cl (50 mL) was added. The organics were separated and the aqueous layer extracted with Et₂O (3 x 50 mL), combined, then dried (MgSO₄) and concentrated in vacuo. The crude residue was then purified by column chromatography (85:15, Hexanes: Et₂O) to give alcohol SI-3 an colourless oil (1.85 g, 99%); [α]D²⁵ = 6.0 (c 1.5, CHCl₃), lit.⁶ [α]D²⁵ = 4.98 (c 1.0, CHCl₃); δH (400 MHz; CDCl₃) 2.19 (2H, m, 3-H₂), 3.31 (1H, dd, J 9.5, 7.4, 1-HH), 3.44 (1H, J 9.5 1.7, 1-HH), 3.81 (1H, m, OH), 3.94 (1H, m, 2-H). 4.49 (2H, s, CH₂Ph), 5.02 (1H, dd, J 10.1, 1.9, 5-HH), 5.05 (1H, dd, J 17.2, 1.9, 5-HH), 5.75 (1H, m, 4-H), 7.20-7.31 (5H, m, ArH); δC (100 MHz; CDCl₃) 37.9 (C-3), 69.7 (C-2), 73.3 (CH₂Ph), 73.8 (C-1), 117.7 (C-5), 127.6
(C-Ar), 127.7 (C-Ar), 128.4 (C-Ar), 134.2 (C-4), 137.9 (C-Ar). Data in accordance with the literature.⁷
To a solution of alcohol SI-3 (46 mg, 0.14 mmol) and silyl acetal 5 (68 mg, 0.27 mmol) and trimethylsilyl acetate (20 µl, 0.14 mmol) in acetic acid (1 mL) was added triethylsilyl trifluoromethanesulfonate (TESOTf) (122 µl, 0.54 mmol). This was stirred for 5 minutes, then the reaction mixture was diluted with CH$_2$Cl$_2$ (3 mL) and saturated aqueous solution of NaHCO$_3$ (5 mL) was carefully added. The aqueous phase was extracted with CH$_2$Cl$_2$ (3 x 5 mL), combined, washed with saturated aqueous solution of NaHCO$_3$ (5 mL), dried (MgSO$_4$) and concentrated in vacuo. The crude residue was then purified by column chromatography (91: 9, Hexanes: Et$_2$O) to give acetate 30 as yellow oil (42 mg, 72%); [$\alpha$]$^\circ_{23}$ + 28.3 (c 1.27, CHCl$_3$); $\nu_{max}$ (neat)/cm$^{-1}$ 3061 (CH), 2856 (CH), 1738 (C=O), 1600 (C=C), 1026 (C-O); $\delta_H$ (500 MHz; CDCl$_3$) -0.03 (3H, s, SiCH$_3$), 0.04 (3H, s, SiCH$_3$), 1.38 (1H, app. q., J 12.5, 4-H$_{ax}$), 1.46 (1H, app. q., J 12.5, 2-H$_{ax}$), 1.83 (1H, ddt, J 12.5, 6.6, 2.0, 2-H$_{eq}$), 2.01 (1H, ddt, J 12.5, 6.6, 2.2, 4-H$_{eq}$), 2.04 (3H, s, C(O)CH$_3$), 2.14 (1H, d, J 13.8, SiCHH), 2.24 (1H, d, J 13.8, SiCHH), 3.14 (1H, dd, J 12.5, 2.2, 1-H), 3.47 (1H, dd, J 13.3, 6.9, 1'-HH), 3.53-3.60 (2H, m, 1'-HH and 5-H), 4.61 (2H, s, CH$_2$Ph), 4.81 (1H, app. tt, J 12.5, 6.6, 3-H), 7.03-7.11 (3H, m, ArH), 7.19-7.23 (2H, m, ArH), 7.28-7.38 (5H, m, ArH); $\delta_C$ (100 MHz; CDCl$_3$) -6.2 (SiCH$_3$), -5.9 (SiCH$_3$), 21.3 (C(O)CH$_3$), 22.9 (SiCH$_3$), 32.6 (C-2), 34.4 (C-4), 68.1 (C-1), 71.5 (C-1'), 73.3 (OCH$_3$Ph), 73.3 (C-5), 77.9 (C-3), 124.1 (2 x C-Ar), 127.5 (2 x C-Ar), 128.2 (2 x C-Ar), 128.3 (2 x C-Ar), 128.4 (2 x C-Ar), 138.5 (C-Ar), 139.5 (C-Ar), 170.6 (CO); m/z (ESI) 435.1842 (MNa$^+$, 100%, C$_{24}$H$_{32}$O$_4$NaSi requires 435.1962).
**TBAF (2.1 mL, 1.04 mmol, 0.5 M solution in THF) was added dropwise over 15 minutes to a solution of 1-silyl tetrahydropyran 30 (143 mg, 0.35 mmol, 1 eq) in dry THF (2 mL) at 0 °C under N₂. The reaction was warmed slowly to room temperature until disappearance of 1-silyl tetrahydropyran 30 by TLC. Urea hydrogen peroxide (163 mg, 1.74 mmol), potassium hydrogen carbonate (104 mg, 1.04 mmol) and dry methanol (0.7 mL) was added. This was left to stir at RT for 12 h and upon completion aqueous saturated sodium thiosulphate solution (3 mL) was added, the organic phase separated and aqueous layer extracted with CH₂Cl₂ (3 x 5 mL). The crude reaction mixture was concentrated in vacuo then taken up in dry CH₂Cl₂ (3 mL). The solution was then cooled to 0 °C and triethylamine (420 μl, 3.00 mmol), a crystal of DMAP and acetic anhydride (190 μl, 2.00 mmol) was added. The reaction was warmed to RT and left to stir for 1 h and on completion water (6 mL) was added and the organic phase separated. The aqueous phase was washed with CH₂Cl₂ (3 x 10 mL), the combined organic phases dried (MgSO₄) and concentrated in vacuo. The residue was then purified by column chromatography (Pet:Et₂O, 75:25) to yield 31 as a colourless oil, as mixture of α/β anomers; (77 mg, 67% α: β 39:69); δ_H (400 MHz; CDCl₃) 1.67-1.88 (6H, m, 2 x 2-HH and 2 x 4-H₂), 1.94-2.04 (2H, m, 2 x 2-HH), 2.06 (6H, br. s., 2 x C(O)CH₃), 2.10 (3H, s, α C(O)CH₃), 2.11 (3H, s, β C(O)CH₃), 3.48-3.62 (4H, m, 2 x 1'-H₂), 4.11 (1H, m, β 5-H₄), 4.35 (1H, m, α 5-H₄), 4.54-4.60 (4H, m, 2 x CH₃Ph), 5.15 (1H, dd, J 6.4, 4.8, α 3-H₆), 5.21 (1H, dd, J 7.7, 4.4, β 3-H₆), 5.71 (1H, dd, J 9.9, 2.1, β 1-Hα), 6.33 (1H, d, J 2.8, α 1-Heq), 7.17-7.35 (10H, m, ArH); δ_C (100 MHz; CDCl₃) {21.1, 21.1, 21.2, 21.3} (C(O)CH₃), (33.0, 33.0, 32.4, 35.8) (C-2 and C-4), 69.2 (C-1'), 71.9 (C-1'), 72.1 (C-5), 72.1 (C-5), 72.3 (C-3), 73.4 (C-3), 92.1 (α C-1), 92.4 (β C-1), 127.7 (C-Ar), 128.3 (C-Ar), 129.7 (C-Ar), 137.9 (C-Ar), 168.9 (2 x CO), 170.1 (2 x CO); m/z (ESI) 345.1305 (MNa⁺, 100%, C₁₇H₂₂O₆Na requires 345.1309).
(1R,3S,5S)-3-O-Acetyl-1-O-cyclohexyl-5-(1’-(benzyloxy)methyl)-tetrahydropyran 32

BF₃·OEt₂ (37 µL, 0.30 mmol) was added dropwise to a solution of acetate 31 (65 mg, 0.20 mmol), cyclohexanol (32 µL, 0.30 mmol) and 4 Å molecular sieves (50 mg) in dry CH₂Cl₂ (5 mL) under N₂. The reaction was stirred for 4 h when a saturated aqueous solution of NaHCO₃ (15 mL) was added. The aqueous phase was extracted with CH₂Cl₂ (3 x 10 mL), combined, washed with saturated aqueous solution of NaHCO₃ (15 mL), dried (MgSO₄) and concentrated in vacuo. The crude residue was then purified by column chromatography (Pet: Et₂O, 90:10) to give acetate 31 as a colourless oil, as the α anomer (52 mg, 72%); νₘₐₓ (neat)/cm⁻¹ 2930 (CH), 2856 (CH), 1740 (C=O), 1452 (C-C), 1025 (C-O); δₓ (400 MHz; CDCl₃) 1.15-1.31 (4H, m, 4 x CyHex CH) 1.35 (1H, m, CyHex CH), 1.46 (1H, app. q, J 12.0, 4-H₃ax), 1.52 (1H, m, CyHex CH), 1.66 (1H, app. dt, J 11.5, 3.5, 2-H₃eq), 1.67-1.77 (2H, m, 2 x CyHex CH), 1.81-1.91 (2H, m, 2 x CyHex CH), 1.97-2.06 (5H, m, 2-H₃eq, 4-H₃eq and C(O)CH₃) 3.49 (1H, dd, J 10.5, 4.0, 1’-HH), 3.52 (1H, dd, J 10.5, 5.0, 1’-HH), 3.57 (1H, m, CyHex CH), 4.10 (1H, dtd, J 11.5, 4.5, 2.0, 5-H) 4.56 (1H, s, CHPh), 4.57 (1H, s, CHPh), 5.17 (1H, d, J 3.5, 1-H₃eq) 5.22 (1H, app. tt, J 11.5, 5.0, 3-H), 7.25-7.30 (1H, m, ArH), 7.31-7.36 (4H, m, ArH); δₓ (100 MHz; CDCl₃) 21.5 (C(O)CH₃), 24.1 (CH₂-CyHex), 24.4 (CH₂-CyHex), 25.8 (CH₂-CyHex), 31.6 (CH₂-CyHex), 33.6 (CH₂-CyHex), 33.9 (C-4), 36.2 (C-2), 66.9 (C-5), 67.4 (C-3), 73.0 (C-1’), 73.4 (OCH₂Ph), 74.6 (CH-CyHex), 95.7 (C-1), 127.6 (2 x C-Ar), 127.7 (C-Ar), 128.4 (2 x C-Ar), 138.4 (C-Ar), 170.5 (CO); m/z (ESI) 385.1986 (MNa⁺, 100%, C₂₁H₃₀O₅Na requires 385.1985).
(1R, 3R, 5R)-1-(Benzyldimethylsilyl)-5-(1’-benzyloxymethyl)-3-hydroxy-tetrahydropyran SI-4

Potassium carbonate (149 mg, 1.08 mmol) was added to a solution of acetate 30 (148 mg, 0.36 mmol) in methanol (4 mL) at RT. After stirring for 10 minutes, the methanol was removed under reduced pressure, water (5 mL) added and extracted with CH$_2$Cl$_2$ (3 x 5 mL). The combined organic phases were dried (MgSO$_4$) and concentrated in vacuo to give alcohol SI-4 as a colourless oil (130 mg, 98%); [α]$^23$$^0$ + 29 (c 1.00, CHCl$_3$); δ$_\mathrm{H}$ (400 MHz; CDCl$_3$) -0.02 (3H, s, SiCH$_3$), 0.05 (3H, s, SiCH$_3$), 1.25 (1H, app. q., J 12.2, 4-H$_{eq}$), 1.35 (1H, app. q., J 12.5, 2-H$_{eq}$), 1.79 (1H, ddd, J 12.5, 4.5, 2.0, 2-H$_{eq}$), 2.00 (1H, ddd, J 12.2, 4.5, 2.0, 4-H$_{eq}$), 2.14 (1H, d, J 13.7, SiCHH), 2.25 (1H, d, J 13.7, SiCHH), 3.08 (1H, dd, J 12.5, 2.0, 1-H), 3.45-3.51 (2H, m, 1’-H$_2$), 3.58 (1H, app. br. dtd, J 12.5, 5.7, 2.0, 5-H), 3.75 (1H, app. tt, J 12.5, 4.5, 3-H), 4.62 (2H, s, CH$_2$Ph), 7.04-7.09 (3H, m, ArH), 7.19-7.23 (2H, m, ArH), 7.28-7.39 (5H, m, ArH); δ$_\mathrm{C}$ (100 MHz; CDCl$_3$) -6.1 (SiCH$_3$), -5.9 (SiCH$_3$), 23.0 (SiCH$_2$), 36.3 (C-2), 38.4 (C-4), 68.3 (C-3), 69.1 (C-1), 73.4 (C-1’), 73.5 (OCH$_2$Ph), 78.0 (C-5), 124.0 (2 x C-Ar), 127.5 (2 x C-Ar), 127.5 (2 x C-Ar), 128.3 (2 x C-Ar), 128.4 (C-Ar), 128.5 (C-Ar), 138.7 (C-Ar), 139.8 (C-Ar); m/z (ESI) 393.1842 (MNa$^+$, 100%, C$_{22}$H$_{30}$O$_3$NaSi requires 493.1862).

(1R, 3S, 5R)-1-(Benzyldimethylsilyl)-5-(1’-benzyloxymethyl)-3-hydroxy-tetrahydropyran 33

Diethyl azodicarboxylate (94 µl, 0.60 mmol) was added dropwise to a solution of triphenylphosphine (157 mg, 0.60 mmol) and para-nitrobenzoic acid (100 mg, 0.60 mmol) in THF (2 mL) at 0 °C. Alcohol SI-4 (75 mg, 0.20 mmol) was added as a solution in THF (1 mL) dropwise and allowed to warm to RT over 1 h. The solvent was removed in vacuo and the resulting crude residue was filtered through a SiO$_2$ plug (Et$_2$O:Pet. 15:85). The solvent was removed in vacuo to afford a crude residue, which was taken up in methanol (3 mL) and potassium carbonate (55 mg,
0.4 mmol) added. After stirring for 10 minutes at RT, the methanol was removed under reduced pressure, water (5mL) added and extracted with CH$_2$Cl$_2$ (3 x 5 mL). The combined organic phases were dried (MgSO$_4$) and concentrated *in vacuo* to afford alcohol **33** as a colourless oil (64 mg, 87%); [α]$^{23}$ +22 (c 1.00, CHCl$_3$); δ$_H$ (400 MHz; CDCl$_3$) -0.03 (3H, s, SiC$_3$H$_3$), 0.03 (3H, s, SiC$_3$H$_3$), 1.46 (1H, ddd, J 13.2, 4.9, 2.2, 4-H$_{ax}$), 1.57-1.68 (2H, m, 2-H$_2$), 1.74 (1H, app. dd, J 13.2, 2.7, 4-H$_{eq}$), 2.14 (1H, d, J 13.5, SiCHH), 2.25 (1H, d, J 13.5, SiCHH), 3.45 (1H, dd, J 10.7, 4.4, 1’-HH), 3.52 (1H, J 10.7, 5.7, 1’-HH), 3.60 (1H, dd, J 13.2, 2.1, 1-H), 3.91 (1H, app. br. dtd, J 13.2, 5.7, 2.7, 5-H), 4.23 (1H, app. t, J 2.7, 3-H$_{eq}$), 4.62 (2H, s, CH$_2$Ph), 7.03-7.10 (3H, m, ArH), 7.17-7.24 (2H, m, ArH), 7.28-7.39 (5H, m, ArH); δ$_C$ (100 MHz; CDCl$_3$) -6.2 (SiC$_3$H$_3$), -5.7 (SiC$_3$H$_3$), 23.0 (SiC$_2$H$_3$), 33.6 (C-2), 35.6 (C-4), 63.6 (C-1), 63.7 (C-3), 72.5 (C-5), 73.3 (C-1’), 73.9 (OCH$_2$Ph), 124.0 (2 x C-Ar), 127.4 (2 x C-Ar), 127.5 (2 x C-Ar), 128.1 (2 x C-Ar), 128.3 (2 x C-Ar), 138.7 (C-Ar), 139.9 (C-Ar); m/z (ESI) 393.1842 (MNa$^+$, 100%, C$_{22}$H$_{30}$O$_3$NaSi requires 493.1862).

**(3S,5R)-1,3-O-Acetyl-5-(1'benzyloxymethyl)-tetrahydropyran 34**

TBAF (800 µl, 0.4 mmol, 0.5 M solution in THF) was added dropwise over 15 minutes to a solution of 1-silyl tetrahydropyran **33** (50 mg, 0.14 mmol, 1 eq) in dry THF (3 mL) at 0 °C under N$_2$. The reaction was warmed slowly to RT until disappearance of 1-silyl tetrahydropyran **33** by TLC. Urea hydrogen peroxide (64 mg, 0.68 mmol), potassium hydrogen carbonate (56 mg, 0.41 mmol) and dry methanol (1 mL) was added. This was left to stir at 40 °C for 12 h and upon completion aqueous saturated sodium thiosulphate solution (3 mL) was added, the organic phase separated and aqueous layer extracted with CH$_2$Cl$_2$ (3 x 5 mL). The crude reaction mixture was concentrated *in vacuo* then taken up in dry CH$_2$Cl$_2$ (5 mL). The solution was then cooled to 0 °C and triethylamine (189 µl, 1.4 mmol), a crystal of DMAP then acetic anhydride (65 µl, 0.68 mmol) was added. The reaction was warmed to RT and left to stir for 1 h and on completion water (5 mL) was added and the organic phase separated. The aqueous phase was washed with CH$_2$Cl$_2$ (3 x 10 mL), the combined organic phases dried (MgSO$_4$) and concentrated *in vacuo*. The residue was then purified by column chromatography (Pet:Et$_2$O, 75:25) to yield diacetate **34** as a
colourless oil and mixture of α/β anomers (33 mg, 75%, α:β 33:67); δH (400 MHz; CDCl3) 1.68-1.87 (6H, m, 2 x 2-H2 and 2 x 4-H2), 1.97-2.03 (2H, m, 2 x 2-H2), 2.04 (3H, s, α C(O)CH3), 2.08 (6H, br. s., 2 x C(O)CH3), 2.10 (3H, s, β C(O)CH3), 3.50-3.58 (4H, m, 2 x 1'-H2), 4.13 (1H, dqd, J 11.0, 3.4, β 5-Hax), 4.35 (1H, dqd, J 15.2, 4.7, 1.0, β 5-Hax), 4.54-4.60 (4H, m, 2 x CH2Ph), 5.15 (1H, q, J 3.2, α 3-Heq), 5.32 (1H, q, J 3.2, β 3-Heq), 6.01 (1H, dd, J 9.8, 2.5, β 1-Hax), 6.20 (1H, d, J 3.9, α 1-Heq), 7.28-7.37 (10H, m, ArH);

δC (100 MHz; CDCl3) {21.1, 21.2, 21.2, 21.3} (C(O)CH3), {31.0, 31.3, 31.4, 34.2} (C-4 and C-2), {65.3, 65.6, 67.6, 71.3, 72.1, 72.4, 73.4, 73.5} (C-1, C-1’, C-5 and C-3), 91.2 (β-C-1), 91.4 (α-C-1), 127.6 (2 x C-Ar), 127.7 (2 x C-Ar), 127.8 (2 x C-Ar), 128.4 (2 x C-Ar), 137.0 (2 x C-Ar), 169.2 (CO), 19.5 (CO), 170.1 (CO), 170.3 (CO); m/z (ESI) 345.1308 (MNa+, 100%, C17H22O6Na requires 345.1309).

(3R,4R)-3-Hydroxy-4-ethoxy-1-phenyl-hex-5-en 35

\[
\text{\begin{array}{c}
\text{OEt} \\
\text{OEt}
\end{array}} \quad \text{i) n-BuLi, TMEDA} \\
\text{ii) (ipc)2BOMe} \\
\text{iii) BF3•OEt2} \\
\text{iv) CHO(CH2)2Ph}
\]

To a solution of allyl ethyl ether (395 µl, 3.49 mmol) in THF (5 mL) and tetramethylethylenediamine (420 µl, 2.79 mmol) was added n-butyllithium (1.84 mL, 1.52 M solution in hexanes, 2.79 mmol) at -78 °C under N2. After stirring at -78 °C for 30 minutes, (+)-B-1-methoxydiisopinocampheylborane (881 mg, 2.79 mmol) in THF (1 mL) was added dropwise and the solution cleared. The reaction was stirred at -78 °C for 1 h, then BF3•OEt2 (570 µl, 4.64 mmol) was added and immediately followed by dihydrocinnamaldehyde (370 µl, 2.29 mmol). This was left to react for 4h at -78 °C, then saturated aqueous NaHCO3 (10 mL) was added and the organics were extracted with Et2O (3 x 10 mL). The combined organic phases were washed with 1M HCl (10 mL), dried (MgSO4) and concentrated in vacuo to afford the crude residue. Purification by column chromatography (Pet: Et2O, 93:7) gave alcohol 35 as a colourless oil (190 mg, 32%); [α]23D + 8.0 (c 0.56, CHCl3); δH (400 MHz; CDCl3) 1.21 (3H, t, J 6.9, CH3), 1.67-1.82 (2H, m, 2-H2), 2.67 (1H, dt, J 13.5, 8.3, 1-HH), 2.80-2.93 (2H, m, 3-H and 1-HH), 3.35 (1H, app p, J 8.9, 6.9, CHHCH3), 3.48 (1H, m, 4-H), 3.62 (1H, app p., J 6.9, CHHCH3), 5.26 (1H, dd, J 11.5, 1.8, 6-HH), 5.31 (1H, dd, J 8.8, 1.8, 6-HH), 5.62 (1H, ddd, J 11.5, 8.8, 1.8, 5-H); δC (100 MHz; CDCl3) 15.2
(CH₃), 31.8 (C-2), 34.3 (C-1), 64.1 (CH₂CH₃), 72.5 (C-3), 85.1 (C-4), 119.7 (C-6), 125.7 (C-5), 128.3 (C-Ar), 128.5 (C-Ar), 135.5 (C-Ar), 142.5 (C-Ar). Spectral data in accordance with the literature.⁸

\((1S,3R,4R)-1\text{-}(\text{Benzylidemethylsilyl})\text{-}4\text{-}(2'\text{-}\text{phenylethyl})\text{-}\text{tetrahydrofuran-3-al 36}\)

Trifluoroacetic acid (121 mg, 0.55 mmol) was added carefully dropwise to a solution of alcohol 35 (80 mg, 0.36 mmol) and silyl acetal 5 (110 mg, 0.44 mmol) in dry CH₂Cl₂ (3 mL) at 0 °C under N₂. This was stirred for 1 h whilst slowly warming to RT. Saturated aqueous NaHCO₃ (10 mL) was added and the organics were extracted with CH₂Cl₂ (3 x 10 mL). The combined organic phases were then dried (MgSO₄) and concentrated in vacuo to afford a brown residue. Purification by column chromatography (Pet: Et₂O, 93:7) gave aldehyde 36 as a colourless oil (59 mg, 46%); [α]²³ ¹⁰\( ^{(D)} + 14 \) (c 1.00, CHCl₃); \( \nu_{\text{max}} \) (neat)/cm⁻¹ 3082 (CH), 1600 (C=O), 1719 (C-O), 1029 (C-O); \( \delta \) (400 MHz; CDCl₃) 0.04 (3H, s, SiC₃H₃), 0.11 (3H, s, SiC₃H₃), 1.85 – 1.92 (2H, m, 1'-H₂), 2.00-2.07 (2H, m, 2-H₂), 2.21 (1H, d, J 12.7, SiCH₂), 2.26 (1H, d, J 12.7, SiCH₂), 2.70 (1H, m, 2'-HH), 2.85 (1H, m, 2'-HH), 2.95 (1H, ddd, J 14.7, 7.1, 4.4, 3-H), 3.35 (1H, dd, J 10.8, 7.4, 1-H), 3.89 (1H, td, J 8.2, 7.4, 4-H), 7.05-7.31 (10H, m, ArH), 9.6 (1H, d, J 4.4, CHO); \( \delta \) C (100 MHz; CDCl₃) -5.8 (SiCH₃), -5.8 (SiCH₃), 23.5 (SiC₃H₃Ph), 28.8 (C-2), 32.8 (C-2'), 33.1 (C-1'), 54.8 (C-3), 70.8 (C-1), 82.3 (C-4), 124.2 (C-Ar), 125.9 (C-Ar), 128.2 (2 x C-Ar), 128.3 (2 x C-Ar), 128.4 (2 x C-Ar), 128.5 (2 x C-Ar), 136.7 (C-Ar), 139.4 (C-Ar), 202.7 (CHO); \( m/z \) (ESI) 375.1747 (MNa⁺, 100%, C₂₂H₂₄O₂NaSi requires 375.1751).
(2S,3R)-1,2-Epoxy-3-hydroxy-pent-4-ene 43

Titanium tetraisopropoxide (1.40 mL, 4.73 mmol) followed by (R,R)-(−)-diisopropyl d-tartrate (1.32 mL, 6.31 mmol) was added to a solution of 4 Å molecular sieves (800 mg) in dry CH₂Cl₂ (48 mL) at -35 °C. This was stirred for 30 minutes then 1,4-pentadiene-3-ol (4.64 mL, 47.71 mmol) was added, followed by cumene hydroperoxide (18.09 mL, 122.39 mmol). The reaction was stirred for 36 h at – 35 °C then filtered through a SiO₂ plug, washing with CH₂Cl₂ (3 x 30 mL). Aqueous saturated sodium thiosulphate (20 mL) was added, the organic layer separated and the aqueous layer extracted with CH₂Cl₂ (3 x 10 mL). The organic layers were combined, dried (MgSO₄) and concentrated in vacuo to give yellow oil. This was purified by column chromatography (Pentane: Et₂O, 60:40) to remove excess cumene alcohol and cumene hydroperoxide. Kugelrohr distillation (120 °C, 30 mm/Hg) gave epoxide 43 as a colourless oil (2.62 g, 55%); [α]²³D -55 (c 1.00, CHCl₃), lit. [α]²⁵D -53 (C 0.73, CHCl₃); δH (400 MHz; CDCl₃) 2.17 (1H, br. s., O;H), 2.77 (1H, dd, J 5.0, 4.2, 1-HH), 2.81 (1H, dd, J 5.0, 2.8, 1-HH), 3.10 (1H, ddd, J 6.1, 4.2, 2.8, 2-H), 4.32 (1H, br. m, 3-H), 5.28 (1H, dd, J 10.5, 1.2, 5-HH), 5.39 (1H, dd, J 17.4, 2.7, 5-HH), 5.85 (1H, ddd, J 17.4, 10.5, 6.4, 4-H); δC (100 MHz; CDCl₃) 43.4 (C-1), 53.7 (C-2), 70.2 (C-3), 117.7 (C-5), 135.5 (C-4). All data in accordance with the literature.⁹

(2S,3S)-1,2-Epoxy-3-hydroxy-pent-4-en 37

(2S,3S)-1,2-Epoxy-3-hydroxy-pent-4-en 37
A round-bottomed flask was charged with triphenylphosphine (2.71 g, 10.35 mmol) and para-nitrobenzoic acid (1.72 g, 10.35 mmol) in THF (40 mL) and cooled to 0 °C. To the resulting solution, diethyl azodicarboxylate (1.63 mL, 10.35 mmol) was added dropwise and allowed to stir for 5 minutes at 0 °C. Epoxide 43 (986 mg, 9.86 mmol) in THF (10 mL) was added dropwise at 0 °C and then the reaction mixture was allowed to warm to RT with stirring over 1 h. Upon consumption of the starting material by TLC, the reaction mixture was concentrated and filtered through a plug of SiO$_2$ (Pet:Et$_2$O, 90:10 to 80:20) to obtain the para-nitrobenzoic acid adduct and other non-polar by-products. The filtrate was then concentrated in vacuo and taken up in methanol (10 mL). Potassium carbonate (1.43 g, 10.35 mmol) was added and the reaction mixture left to stir for 15 minutes, until disappearance of the para-nitrobenzoic acid adduct by TLC. Methanol was removed in vacuo and water (10 mL) and CH$_2$Cl$_2$ (10 mL) was added to the crude residue. The organic layer was separated and the aqueous layer extracted with CH$_2$Cl$_2$ (3 x 10 mL). The organic layers were combined, dried (MgSO$_4$) and concentrated in vacuo to give white oily residue. This was purified by column chromatography (Pentane: Et$_2$O, 60:40) to give alcohol 37 as a yellow oil (388 mg, 39%); [α]$^23$ -12 (c 1.0, CHCl$_3$), lit.$^{10}$ ent-37 [α]$^25$ +20.7 (c 1.8, CHCl$_3$); δ$_H$ (400 MHz; CDCl$_3$) 2.17 (1H, br. s., OH), 2.67 (1H, dd, J 5.0, 4.1, 1-HH), 2.76 (1H, dd, J 5.0, 2.8, 1-HH), 3.00 (1H, ddd, J 5.0, 4.1, 2.8, 2-H), 3.90 (1H, br. m, 3-H), 5.16 (1H, dd, J 10.4, 1.2, 5-HH), 5.31 (1H, dd, J 17.3, 2.8, 5-HH), 5.86 (1H, ddd, J 17.3, 10.4, 6.4, 4-H); δ$_C$ (100 MHz; CDCl$_3$) 44.7 (C-1), 54.8 (C-2), 72.6 (C-3), 116.7 (C-5), 136.1 (C-4). All data in accordance with the literature.$^{10}$

(2S)-1,2-Epoxy-3-O-(N,N-diisopropylcarbamate)-pent-4-en 39

\[
\begin{align*}
\text{O,} & \text{i) (Pr$_2$N)OC(O)Cl, NEt$_3$} \\
\text{O,} & \text{DMAP, CH$_2$Cl$_2$} \\
\text{O} & \text{ii) NaOH, THF, RT}
\end{align*}
\]

Syn-epoxide 37 (180 mg, 1.8 mmol) was added to a solution of triethylamine (275 µl, 1.98 mmol) and N,N-diisopropylcarbamoyl chloride (443 mg, 2.7 mmol) in dry CH$_2$Cl$_2$ (3 mL) and heated to reflux for 5 h under N$_2$. Upon disappearance of the starting epoxide by TLC, the
solvent was removed under reduced pressure to give the crude residue which was redissolved in Et₂O (10 mL) filtered through a plug of silica, washing with Et₂O (2 x 10 mL). The solvent was then removed under reduced pressure, giving a crude mixture of epoxide 39 and chlorohydrin 38. The crude residue was redissolved in THF (10 mL) and NaOH (72 mg, 1.8 mmol) was added. The reaction was left to stir for 10 minutes at RT, until chlorohydrin 38 was converted to epoxide 39, as monitored by TLC. The THF was removed under reduced pressure, water (10 mL) added and extracted with CH₂Cl₂ (3 x 5 mL). The combined organic phases were dried (MgSO₄) and concentrated in vacuo to afford the crude residue, which was further purified by column chromatography (Pet: Et₂O, 80:20) to give epoxide 39 as a colourless oil (282 mg, 69%); [α]²³ -20 (c 1.00, CHCl₃); δH (400 MHz; CDCl₃) 1.21 (6H, br. s., 2 x CH₃), 1.23 (6H, br. s., 2 x CH₃), 2.67 (1H, dd, J 4.5, 2.7, 1-HH), 2.82 (1H, app. td, J 4.5, 1.8, 1-HH), 3.16 (1H, ddd, J 9.8, 2.9, 1.8, 2-H), 3.83 (1H, br. s., NCH), 4.01 (1H, br. s., NCH), 5.13 (1H, app. tt., J 5.8, 1.5, 3-H), 5.27 (1H, dt, J 10.7, 2.5, 5-HH), 5.36 (1H, dt, J 17.1, 1.5, 5-HH), 5.88 (1H, ddd, J 17.1, 10.7, 1.5, 4-H); δC (100 MHz; CDCl₃) 20.4 (2 x CH₃), 21.4 (2 x CH₃), 44.4 (C-1), 45.9 (2 x br. NCH), 52.8 (C-2), 74.6 (C-3), 117.9 (C-5), 133.1 (C-4), 154.5 (CO); m/z (ESI) 250.1416 (MNa⁺, 100%, C₁₂H₂₁O₃NNa requires 250.1414).

(2S,3S)-2-Hydroxy-3-O-(N,N-diisopropylcarbamate)-pent-4-ene 40

Diisobutylaluminum hydride (1.84 mL, 1 M in hexanes, 1.84 mmol) was added dropwise to a stirring solution of epoxide 39 (139 mg, 0.61 mmol) in dry CH₂Cl₂ (6 mL) at -20 °C under N₂. The reaction was left to stir for 20 minutes at -20 °C, then 1 M HCl aqueous solution was added (5 mL). This was left to stir for a further 10 minutes, until the two phases separated. The organics were separated and the aqueous layer extracted with CH₂Cl₂ (3 x 5 mL). The combined organic phases dried (MgSO₄) and concentrated in vacuo to give alcohol 40 as a yellow oil (92 mg, 66%); [α]²³ -23 (c 1.00, CHCl₃); δH (400 MHz; CDCl₃) 1.18 (3H, d, J 6.4, 5-H₃), 1.22 (6H, br. s., (CH₃)₂), 1.23 (6H, br. d, (CH₃)₂), 2.30 (1H, br. s, OH), 3.80 (1H, br. s., NCH), 3.88 (1H, app. q., J 6.4, 4-H), 4.02 (1H, br. s., NCH), 5.09 (1H, t, J 6.1, 3-H), 5.27 (1H, d, J 10.0, 1.2, 1-HH), 5.33 (1H, dt, J 17.4,
1.5, 1-HH), 5.86 (1H, ddd, J 17.4, 10.0, 6.4, 2-H); δC (100 MHz; CDCl3) 19.0 (C-5), 20.6 (2 x br. CH3), 21.5 (2 x br. CH3), 46.1 (2 x br. NCH), 69.4 (C-4), 79.5 (C-3), 118.3 (C-2), 134.0 (C-1), 155.2 (CO); m/z (ESI) 252.1578 (MNa+; 100%, C12H23NO3NaSi requires 252.1570).

(1R,3S,4R,5S)-1-(Benzyldimethylsilyl)-4-O-(N,N-diisopropylcarbamate)-3-hydroxy-5-methyl-tetrahydropyran 41

Trifluoroacetic acid (900 µl, 7.20 mmol) was added dropwise to a solution of alcohol 40 (61 mg, 0.36 mmol) and silyl acetal 5 (118 mg, 0.47 mmol) in dry CH2Cl2 (4 mL) at 0 °C. This was stirred for 1 h at RT, then aqueous saturated NaHCO3 (15 mL) and triethylamine was added until pH >7. The organic phase was separated and the aqueous phase extracted with CH2Cl2 (3 x 15 mL). The combined organic phases were then concentrated in vacuo and the resulting crude residue was redissolved in methanol (15 mL), to which K2CO3 (298 mg, 2.16 mmol) was added and left to stir for 30 minutes. The methanol was removed under reduced pressure, water (20 mL) added and extracted with CH2Cl2 (3 x 20 mL). The combined organic phases were washed with brine (10 mL), dried (MgSO4) and concentrated in vacuo. Which was purified by column chromatography (Pet:Et2O, 75:25) to yield 41 as a yellow oil (105 mg, 72%); [α]23D +14 (c 1.00, CHCl3); δH (400 MHz; CDCl3) -0.04 (3H, s, SiC6H3), 0.03 (3H, s, SiCH3), 1.22 (3H, d, J 6.4, 5-Hβ), 1.24 (6H, br. s., (CH3)2), 1.32 (6H, br. s., (CH3)2), 1.66 (1H, td, J 12.2, 2.2, 2-Hax), 1.74 (1H, app. q., J 12.2, 2-Hax), 2.12 (1H, d, J 13.7, SiCHH), 2.24 (1H, d, J 13.7, SiCHH), 3.10 (1H, dd, J 12.2, 2.2, 1-Hax), 3.46 (1H, qd, J 6.4, 1.2, 5-Hax), 3.85 (2H, m, 3-H and NCH), 4.12 (1H, br. s., NCH), 4.96 (1H, dd, J 2.9, 1.2, 4-H), 7.00-7.10 (3H, m, ArH), 7.20-7.23 (2H, m, ArH); δC (100 MHz; CDCl3) -6.2 (SiCH3), -6.1 (SiCH3), 17.9 (C-5), 20.4 (2 x CH3), 21.6 (2 x CH3), 22.9 (SiCH2), 30.4 (C-2), 45.7 (NCH), 46.8 (NCH), 68.3 (C-
(3S,4S,5S)-1,3-O-Acetyl-4-O-(N,N-diisopropylcarbamate)-5-methyl-tetrahydropyran 42

TBAF (1.2 mL, 0.60 mmol, 0.5 M solution in THF) was added dropwise over 15 minutes to a solution of 1-silyl tetrahydropyran 41 (80 mg, 0.20 mmol, 1 eq) in dry THF (2 mL) at 0 °C under N₂. The reaction was warmed slowly to 30 °C and allowed to stir for 1 h until disappearance of 1-silyl tetrahydropyran 41 by TLC. Urea hydrogen peroxide (92 mg, 0.98 mmol), potassium hydrogen carbonate (60 mg, 0.6 mmol) and dry methanol (0.6 mL) was added. This was left to stir at RT for 12 h and upon completion aqueous saturated sodium thiosulphate solution (2 mL) was added, the organic phases separated and aqueous layer extracted with CH₂Cl₂ (3 x 5 mL). The crude reaction mixture was concentrated in vacuo then taken up in dry CH₂Cl₂ (3 mL). The solution was then cooled to 0 °C and triethylamine (420 µl, 3.00 mmol), a crystal of DMAP then acetic anhydride (190 µl, 2.00 mmol) was added. The reaction was warmed to RT and left to stir for 1 h and on completion water (6 mL) was added and the organic phase separated. The aqueous phase was washed with CH₂Cl₂ (3 x 10 mL), the combined organic phases dried (MgSO₄) and concentrated in vacuo. The residue was then purified by column chromatography (Pet:Et₂O, 60:40) to give 42 as a yellow oil, as a mixture of α/β anomers (54 mg, 77%, α:β 50:50); νₘₐₓ (neat)/cm⁻¹ 2969 (CH), 1748 (C=O acetate), 1690 (C=O carbamate), 1038 (C-O); δH (400 MHz; CDCl₃) 1.15 (1H, d, J 6.4, 6-H₃), 1.21 (1H, d, J 6.4, 6-H₃), 1.22-1.31 (24H, br. s., 4 x (CH₃)₂), 1.90
(4H, m, 4-H), 1.95 (2H, m, 2-HH), 2.00-2.01 (6H, br. s., 2 x 3-(O)CH₃), 2.10 (3H, s, β 1-(O)CH₃), 2.13 (3H, s, α 1-(O)CH₃), 2.16 (1H, m, 2-H), 3.82 (1H, m, 5-Hax), 3.86-4.07 (4H, br. s., 4 x NC(H), 2.00-2.01 (6H, br. s., 2 x 3-(O)CH₃), 2.10 (3H, s, β 1-(O)CH₃), 2.13 (1H, dd, J 3.4, 1.4, 4-H), 5.03 (1H, ddd, J 11.7, 5.5, 3.4, 3-Hax), 5.13 (1H, dd, J 3.4, 1.4, 4-H), 5.23 (1H, dd, J 2.7, 1.2, 4-H), 5.29 (1H, ddd, J 12.4, 5.3, 3.2, 3-Hax), 5.75 (1H, dd, J 9.4, 3.2, β 1-H), 6.30 (1H, dd, J 3.4, 0.4, α 1-H); δC (100 MHz; CDCl₃) 16.5 (C-6), 16.7 (C-6), 20.5 (4 x br. CH₃), 20.9 (3-(O)CH₃), 21.1 (3-(O)OCH₃), 21.4 (4 x br. CH₃), 29.4 (2-C), 31.1 (2-C), 45.8 (2 x br. NCH), 46.4 (2 x br. NCH), 66.4 (C-3), 67.9 (C-4), 68.2 (C-5), 68.8 (C-3), 69.2 (C-4), 71.0 (C-5), 91.9 (α C-1), 92.0 (β C-1), 154.7 (CO carbamate), 158.8 (CO carbamate), 169.0 (CO acetate), 169.5 (CO acetate), 169.9 (CO acetate); m/z (ESI) 382.1847 (MNa+, 100%, C₁₇H₂₉O₇NNa requires 382.1836).

(2S,3R)-1,2-Epoxy-3-O-(N,N-diisopropylcarbamate)-pent-4-ene SI-6

Anti-epoxide 44 (120 mg, 1.20 mmol) was added to a solution of triethylamine (183 µl, 1.32 mmol) and N,N-diisopropylcarbamoyl chloride (590 mg, 3.60 mmol) in dry CH₂Cl₂ (6 ml) and heated to reflux for 5 h. Upon disappearance of the epoxide solvent was removed under reduced pressure to yield the crude residue which was redissolved in Et₂O (10 ml) then passed through a plug of Celite®, washing with Et₂O (2 x 10 ml). The solvent was then removed under reduced pressure, giving a crude mixture of the protected epoxide compound SI-6 and chlorohydrin SI-5. The reaction was left to stir for 10 minutes at room temperature, until chlorohydrin SI-5 was converted to the title compound SI-6, as monitored by TLC. The THF was removed under reduced pressure, water (10 ml) added and extracted with CH₂Cl₂ (3 x 5 ml). The combined organic phases were dried (MgSO₄) and concentrated in vacuo to afford the crude residue, which was further purified by column chromatography (Pet: Et₂O, 80:20) to afford epoxide SI-6 as a colourless oil (161 mg, 59%); [α]²³ -32 (c 1.00, CHCl₃); δH (400 MHz; CDCl₃) 1.22 (6H, br. s, 2 x CH₃), 1.24 (6H, br. s, 2 x CH₃), 2.70 (1H, dd, J 5.1, 2.7, 1-HH), 2.80 (1H, dd, J 5.1, 4.2, 1-HH), 3.16 (1H, ddd, J 6.8, 4.2, 2.7, 2-H), 3.81 (1H, br. s, NCH), 4.02 (1H, br. s, NCH),
5.25 (1H, dd, J 6.8, 4.4, 3-H), 5.30 (1H, dd, J 10.6, 2.4, 5-HH), 5.39 (1H, dd, J 17.2, 2.4, 5-HH), 5.84 (1H, ddd, J 17.2, 10.6, 4.4-HH); δ\(_c\) (100 MHz; CDCl\(_3\)) 20.6 (2 x CH\(_3\)), 21.3 (2 x CH\(_3\)), 44.8 (C-1), 45.4 (br. NCH), 46.1 (br. NCH), 52.4 (C-2), 74.2 (C-3), 119.1 (C-5), 132.5 (C-4), 154.5 (CO); m/z (ESI) 250.1408 (MNa\(^+\), 100%, C\(_{12}\)H\(_{21}\)O\(_3\)NNa requires 250.1414).

Data for chlorohydrin SI-5; [\(\alpha\)]\(_{23}^D\) -23.5 (c 1.00, CHCl\(_3\)); δ\(_H\) (400 MHz; CDCl\(_3\)) 1.19-1.23 (6H, br. s, 2 x CH\(_3\)), 1.24-1.27 (6H, br. s, 2 x CH\(_3\)), 3.18 (1H, br. s, OH), 3.53 (1H, dd, J 11.3, 7.6, 1-HH), 2.80 (1H, dd., J 11.3, 3.9, 1-HH), 3.83 (1H, br. s., NCH), 4.01 (1H, br. s., 2-H), 4.07 (1H, br. s., NCH), 5.34 (1H, dd, J 10.7, 2.3, 5-HH), 5.35 (1H, m, 3-H), 5.39 (1H, d, J 17.4, 2.3, 5-HH), 5.95 (1H, ddd, J 17.4, 10.7, 6.9, 4-H); δ\(_c\) (100 MHz; CDCl\(_3\)) 20.2 (2 x br. CH\(_3\)), 21.5 (2 x br. CH\(_3\)), 45.8 (C-1), 45.4 (NCH), 46.1 (NCH), 73.6 (C-2), 76.8 (C-3), 119.0 (C-5), 132.9 (C-4), 154.9 (CO); m/z (ESI) 286.1194 (MNa\(^+\), 100%, C\(_{12}\)H\(_{22}\)O\(_3\)NClNa requires 286.1180).

(2S,3R)-4-hydroxy-3-O-(N,N-diisopropylcarbamate)-pent-1-ene 44

Diisobutylaluminum hydride (2.25 ml, 1 M in hexanes, 2.25 mmol) was added dropwise to a stirring solution of epoxide SI-6 (170 mg, 0.75 mmol) in dry CH\(_2\)Cl\(_2\) (8 ml) at -20 °C. The reaction was left to stir for 20 minutes at -20 °C, then 1 M HCl aqueous solution was added (5 ml). This was left to stir for 10 minutes, until the two phases separated. The organics were separated and the aqueous layer extracted with CH\(_2\)Cl\(_2\) (3 x 5 ml). The combined organic phases dried (MgSO\(_4\)) and concentrated in vacuo to afford alcohol 44 as a yellow oil (148 mg, 87%); [\(\alpha\)]\(_{23}^D\) -40 (c 1.00, CHCl\(_3\)); δ\(_H\) (400 MHz; CDCl\(_3\)) 1.17 (3H, d, J 6.4, 1-H3), 1.23 (12H, br. d, 2 x (CH\(_3\))\(_2\)), 3.84 (1H, br. s, NCH), 3.95 (1H, ddt, J 6.4, 3.4, 1.2, 2-H), 4.08 (1H, br. s, NCH), 5.21 (1H, dd, J 6.6, 1.2, 3-H), 5.29 (1H, dt, J 10.6, 1.4, 5-HH), 5.34 (1H, dt, J 17.4, 1.4, 5-HH), 5.88 (1H, ddd, J 17.4, 10.6, 6.6, 4-H); δ\(_c\) (100 MHz; CDCl\(_3\)) 17.8 (C-1), 20.4 (2 x br. CH\(_3\)), 21.4 (2 x br. CH\(_3\)), 46.2 (2 x br. NCH), 69.7 (C-2), 79.6 (C-3), 118.4 (C-4), 133.3 (C-5), 155.4 (CO); m/z (ESI) 286.1194 (MNa\(^+\), 100%, C\(_{12}\)H\(_{22}\)O\(_3\)NClNa requires 286.1180).
Trifluoroacetic acid (662 µl, 6.80 mmol) was added dropwise to a solution of alcohol 44 (77 mg, 0.34 mmol) and silyl acetal 5 (127 mg, 0.50 mmol) in dry CH₂Cl₂ (4 mL) at 0 °C. This was stirred for 1 h at RT, then aqueous saturated NaHCO₃ (15 mL) and triethylamine was added until pH >7. The organic phase was separated and the aqueous phase extracted with CH₂Cl₂ (3 x 10 mL). The combined organic phases were then concentrated in vacuo and the resulting crude residue was redissolved in methanol (10 ml), to which K₂CO₃ (139 mg, 1.01 mmol) was added and left to stir for 30 minutes. The methanol was removed under reduced pressure, water (20 mL) added and extracted with CH₂Cl₂ (3 x 20 mL). The combined organic phases were washed with brine (10 mL), dried (MgSO₄) and concentrated in vacuo to afford the crude residue. This residue was taken up in dry THF (6 mL) and cooled to 0 °C under a N₂ atmosphere. Lithium aluminium hydride (51 mg, 1.34 mmol) was added portion-wise and the mixture stirred for 5 minutes. The reaction mixture was then heated to reflux for 1 h, cooled to 0 °C and water (5 ml) carefully added dropwise. Ethyl acetate (5 ml) was added, the organics were separated and the aqueous layer further extracted using ethyl acetate (3 x 5 ml). The combined organics were combined, dried (MgSO₄) and concentrated in vacuo to afford the crude residue. This residue was further purified by column chromatography (Pet: Et₂O, 50:50) to afford the diol 45 as a yellow oil (54 mg, 57%); [α]²³ -15 (c 0.9, CHCl₃); δH (400 MHz; CDCl₃) -0.03 (3H, s, SiC₃H₃), 0.03 (3H, s, SiC₃H₃), 1.29 (3H, d, J 6.0, 1'-H₃), 1.53 (1H, app. q, J 12.8, 2'-H₃), 1.85 (1H, ddd, J 12.8, 5.1, 1.8, 2'-H₃), 2.12 (1H, d, J 13.7, SiCH₃), 2.22 (1H, d, J 13.7, SiCH₃), 2.26 (1H, br. s, OH), 3.04 (1H, m, 4-H or 5-H), 3.07 (1H, dd, J 12.8, 1.8, 1-H), 3.13 (1H, m, 4-H or 5-H), 3.54 (1H, ddd, J 12.8, 12.2, 5.1, 3-H), 6.99-7.24 (5H, m, ArH); δC (100 MHz; CDCl₃) -6.1 (SiCH₃), -5.8 (SiCH₃), 18.2 (C-1'), 23.0 (SiCH₂), 34.8 (C-2), 68.1 (C-1), 74.3 (C-3), 78.3 (C-4 or C-5), 78.7 (C-4 or C-5), 124.1 (C-Ar), 128.1 (C-Ar), 128.2 (C-Ar), 139.6 (C-Ar); m/z (ESI) 303.1377 (MNa⁺, 100%, C₁₅H₂₄O₃SiNa requires 303.1387).
Chiral SFC data

(Chiralpak IA, 125 bar, 40 C, 2 mL/min, MeOH); $t_R$ 6.08 min (minor enantiomer), 6.66 min (major enantiomer); $er = 97.5:2.5$
Peak Information

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NMR Spectra

Benzyl(1,3-dithiane)dimethylsilane 4

$^1$H NMR (CDCl$_3$, 400 MHz)

$^1$C NMR (CDCl$_3$, 100 MHz)
Benzyl(diethoxymethyl)dimethylsilane 5

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1S,2R,3S,5R)-1-(Dimethyl(benzyl)silyl)-2-methyl-3-hydroxy-5-(2'-phenylethyl)-tetrahydropyran 7

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1S,3S,5R)-1-(Dimethyl(benzyl)silyl)-3-hydroxy-5-(2’-phenylethyl)-tetrahydropyran 9

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
1-{Benzyl(dimethyl)silyl}-but-3-en-1-ol 10

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1R*,3R*,5S*)-1-(Benzyl(dimethyl)silyl)-3-hydroxy-5-methyl-tetrahydropyran 11

1H NMR (CDCl₃, 400 MHz)

13C NMR (CDCl₃, 100 MHz)
(1S*,3S*,5R*)-1-(Benzyldimethyl)silyl)-3-hydroxy-5-(2'-(benzyloxy)ethyl)-tetrahydropyran 12

$^1$H NMR (CDCl$_3$, 400 MHz)

$^1$C NMR (CDCl$_3$, 100 MHz)
(1S*,3S*,5R*)-3-O-Acetyl-1-(benzyldimethylsilyl)-5-methyl-tetrahydropyran 13

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)

AcO

SiMe$_2$Bn
(15S,3S,5S)-3-O-Acetyl-1-(benzylidemethylsilyl)-5-(2'-benzylethoxy)ethyl-tetrahydropyran 14

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(15,2R,35,5R)-3-O-Acetyl-1-(dimethyl(benzyl)silyl)-2-methyl-5-(2'-phenylethyl)-tetrahydropyran 18

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1S,3S,5R)-3-O-Acetyl-1-(dimethyl(benzyl)silyl)-5-(2'-phenylethyl)-tetrahydropyran 19

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1S,2R,3S,5R)-3-O-Benzyl-1-(dimethyl(benzyl)silyl)-2-methyl-5-(2’-phenylethyl)-tetrahydropyran 20

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1S,3S,5R)-3-O-Benzyl-1-(dimethyl(benzyl)silyl)-5-ethyl-(2'-phenylethyl)-tetrahydropyran

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(3S,5R)-1,3-O-Acetyl-2-methyl-5-(2'-phenylethyl)-tetrahydropyran 17

$^1H$ NMR (CDCl$_3$, 400 MHz)

$^{13}C$ NMR (CDCl$_3$, 100 MHz)
**(3S,5R)-1,3-O-Acetyl-5-(2’-phenylethyl)-tetrahydropyran 22**

**1H NMR (CDCl$_3$, 400 MHz)**

![H NMR spectrum](image1.png)

**13C NMR (CDCl$_3$, 100 MHz)**

![C NMR spectrum](image2.png)
(2R,3S,5R)-1-O-Acetyl-3-O-Benzyl-2-methyl-5-(2'-phenylethyl)-tetrahydropyran 23

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1S, 3S, 5S)-3-O-Acetyl-5-acetoxymethyl-1-(benzyldimethylsilyl)-tetrahydropyran 27

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
2,4-Dideoxy-gluc-3,5-diacetate hexopyranose 28

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (100MHz, CDCl$_3$)
(1S, 3S, 5S)-1-{Benzyldimethylsilyl}-3-ethoxy-5-{(tert-butyldiphenylsilyloxy)methyl} – tetrahydropyran 29

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1S,3S,5S)-3-O-Acetyl-1-(benzyldimethylsilyl)-5-(1'-{benzyloxy)methyl}-tetrahydropyran 30

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(3R, 5R)-1,3-O-Acteyl-5-(1'-benzyloxymethyl)-tetrahydropyran 31

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1R,3S,5S)-3-O-Acetyl-1-O-cyclohexyl-5-(1'-(benzyloxy)methyl)-tetrahydropyran 32

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1R, 3R, 5R)-1-(Benzyldimethylsilyl)-5-(1'-benzyloxymethyl)-3-hydroxy-tetrahydropyran SI-4

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1R, 3S, 5R)-1-(Benzyldimethylsilyl)-5-(1'-benzyloxymethyl)-3-hydroxy-tetrahydropyran 33

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(3S,5R)-1,3-O-Acetyl-5-(1’benzyloxymethyl)-tetrahydropyran 34

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(1S,3R,4R)-1-(Benzylidemethylsilyl)-4-(2'-phenylethyl)-tetrahydrofuran-3-al

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
NOESY 1D NMR (CDCl₃, 500 MHz)

1-H
3-H
2'-H₂
2-HH
4-H (irradiated)
(2S)-1,2-Epoxy-3-O-(N,N-diisopropylcarbamate)-pent-4-en 39

$^{1}$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(2S,3S)-2-Hydroxy-3-O-(N,N-diisopropylcarbamate)-pent-4-en 40

\[^1\text{H NMR (CDCl}_3, 400 \text{ MHz)}\]

\[^{13}\text{C NMR (CDCl}_3, 100 \text{ MHz)}\]
(1R,3S,4S,5S)-1-(Benzyldimethylsilyl)-4-O-(N,N-diisopropylcarbamate)-3-hydroxy-5-methyl-tetrahydropyran 41

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(3S,4S,5S)-1,3-O-Acetyl-4-O-(N,N-diisopropylcarbamate)5-methyl-tetrahydropyran 42

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
(2S,3R)-1,2-Epoxy-3-O-(N,N-diisopropylcarbamate)-pent-4-ene 44

$^{1}H$ NMR (CDCl$_3$, 400 MHz)

$^{13}C$ NMR (CDCl$_3$, 100 MHz)
(1R,3S,4R,5S)-1-(Benzyl(dimethyl)silane)-3,4-dihydroxy-5-methyl-tetrahydropyran 45

$^1$H NMR (CDCl$_3$, 400 MHz)

$^{13}$C NMR (CDCl$_3$, 100 MHz)
References