Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Stereocontrolled synthesis of the aconitine D ring from D-glucose

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General information

All chemicals were supplied by Sigma Aldrich, Tokyo Chemical Industry, Acros, Fisher Scientific and Fluorochem and were used as received. Dimethylformamide (DMF), toluene and benzene were purchased anhydrous. MeCN and MeOH were distilled from calcium hydride. Dichloromethane (DCM) and chloroform were distilled from calcium sulfate. All experiments were performed in oven-dry glassware under a protective atmosphere of nitrogen (dried by passage through anhydrous phosphorus pentoxide) as required.

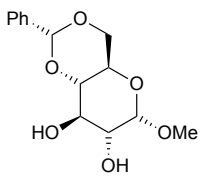
All column chromatography was performed using Fisher silica gel, 60 Å pore size, 230-400 mesh, 40-63 µm. 'Petrol' refers to petroleum ether, boiling range 40-60 ºC. All thin layer chromatography (TLC) analysis was performed using silica gel on Merck aluminium TLC silica gel plates, 60 with 254 nm fluorescent indicator, with visualisation by fluorescence quenching using 254 nm light or staining with potassium permanganate solution. All melting points (mp) were obtained using a Stuart SMP10 melting point instrument and are uncorrected.

Nuclear magnetic resonance (NMR) data were acquired using a Bruker Avance 400 MHz spectrometer with samples dissolved in an appropriate deuterated solvent. Chemical shifts (δ_H) for hydrogen are expressed in parts per million (ppm) relative to tetramethylsilane (0.0 ppm). Chemical shifts for carbon (δ_C) are reported in parts per million relative to the carbon resonances of the residual solvent peak. Carbon resonances were assigned by correlation with hydrogen resonance using HSQC and HMBC spectra. NMR results are reported as singlet (s), doublet (d), triplet (t), quartet (q) or combinations thereof, or multiplet (m). Coupling constants (J) are expressed in Hz and rounded to the nearest 0.1 Hz.

All Fourier transform infra-red (FTIR) data acquired as thin films using a Thermo Electron Corporation Nicolet 380 FTIR with Smart Orbit diamond window instrument with wavenumbers (ν_{max}) being reported in cm^{-1}.

Mass spectrum (MS) data exploiting electron impact ionization in the positive mode (EI^+) was acquired using an Agilent Technologies 7890A GC System (Agilent Technologies 30 m × 0.250 mm, 0.25 µm film) with on-line Agilent Technologies 5975B inert XL EI/CI MSD. MS data exploiting electrospray ionisation in the positive mode (ESI+) was acquired using a Bruker MicrOTOF-Q spectrometer or Thermo Scientific LTQ Orbitrap XL spectrometer with direct injection.

Methyl 4,6-O-benzylidene-α-D-glucopyranoside (α–7)[1]



To a solution of methyl α-D-glucopyranoside (10.02 g, 51.6 mmol) and benzaldehyde dimethyl acetal (10.8 mL) in chloroform (260 mL) was added (+)-camphorsulfonic acid (407 mg, 1.8 mmol). The mixture was heated at reflux in a soxhlet extractor containing powdered 4Å molecular sieves (17 g) for 72 h. Potassium carbonate

(2 g) was added and heating continued at reflux for a further 30 minutes, prior to filtering the hot reaction mixture and concentrating the filtrate *in vacuo*. The solid residue was washed with petrol (300 mL) and dried under vacuum to give the titled compound (13.89 g, 95 %) as a colourless solid.

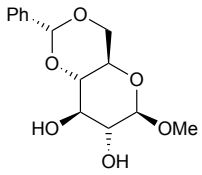
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.24 (1H, d, *J* = 9.7 Hz, 2-O*H*), 2.68 (1H, d, *J* = 1.7 Hz, 3-O*H*), 3.47 (3H, s, 1-OCH_3), 3.51 (1H, app. t, *J* = 9.6 Hz, 4-*H*), 3.64 (1H, app. td, *J* = 9.6 Hz, 3.8 Hz, 2-*H*), 3.76 (1H, app. t, *J* = 9.6 Hz, 6-H_{ax}), 3.79-3.85 (1H, m, 5-*H*), 3.94 (1H, app. t, *J* = 9.6 Hz, 3-*H*), 4.30 (1H, dd, *J* = 4.3 Hz, 9.6 Hz, 6-H_{eq}), 4.81 (1H, d, *J* = 3.8 Hz, 1-*H*), 5.54 (1H,s, PhC*H*), 7.35-7.40 (3H, m, Ar-*H*), 7.48-7.50 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 55.6, 62.4, 68.9, 71.9, 72.9, 80.9, 99.7, 102.0, 126.3, 128.3, 129.3, 137.0.

FTIR ν_{max} (solid, cm^{-1}): 1098, 3357.

HRMS *m/z* (ESI^+) calculated for $C_{14}H_{18}O_6$ $[M+H]^+$ 283.1176; found 283.1178 (error -0.3 ppm).

Methyl 4,6-*O*-benzylidene-β-D-glucopyranoside (β–7)[2]



To a stirred solution of methyl β-D-glucopyranoside (10.11 g, 56.1 mmol) and (+)-camphor-10-sulfonic acid (0.05 g, 0.2 mmol) in MeCN (400 mL) was added benzaldehyde dimethyl acetal (14.8 mL, 98.6 mmol) and stirred at room temperature for 27 h. Triethylamine (5 mL) was added and stirred for a further 1 h before the product was collected by filtration, washed with petrol (600 mL) and dried under vacuum to give the titled compound (14.92 g, 94 %) as a colourless solid.

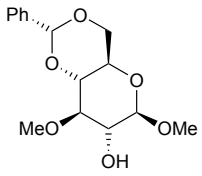
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.62 (1H, s, 2-O*H*), 2.75 (1H,s, 3-O*H*), 3.44-3.56 (3H, m, 2-*H*, 4-*H*, 5-*H*), 3.59 (3H, s, 1-OCH_3), 3.80 (1H, app. t, *J* = 10.2 Hz, 6-H_{ax}), 3.84 (1H, app. t, *J* = 9.0 Hz, 3-*H*), 4.34 (1H, d, *J* = 7.8 Hz, 1-*H*), 4.38 (1H, dd, *J* = 4.9 Hz, 10.2 Hz, 6-H_{eq}), 5.55 (1H, s, PhC*H*), 7.37-7.38 (3H, m, Ar-*H*), 7.49-7.51 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 57.6, 66.4, 68.7, 73.2, 74.6, 80.6, 102.0, 104.1, 126.3, 128.4, 129.3, 136.9.

FTIR ν_{max} (solid, cm^{-1}): 1082, 3100-3500.

HRMS *m/z* (ESI^+) calculated for $C_{14}H_{18}O_6$ $[M+Na]^+$: 305.0996, found 305.1008.

Methyl 4,6-*O*-benzylidene-3-O-methyl-β-D-glucopyranoside (β–9)[3]



To a stirred solution of methyl 4,6-*O*-benzylidene-β-D-glucopyranoside (**β–7**, 4.15 g, 14.7 mmol) in toluene (150 mL) was added dibutyltin oxide (3.97g, 15.9 mmol) and the mixture heated at reflux with azeotropic removal of water for 24 h. The reaction mixture was then cooled and concentrated *in vacuo* to give a residue,

which was dissolved in DMF (55 mL) and iodomethane (9 mL, 144.6 mmol) added. The mixture was stirred at 40 ºC for 25 h prior to concentrating *in vacuo* to give a yellow syrup. Purification by column chromatography, eluting toluene : ethyl acetate (50:50) gave the titled compound (3.25 g, 75 %) as an off-white solid.

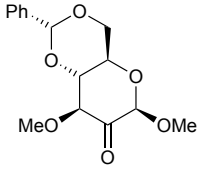
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.51 (1H, d, *J* = 1.9 Hz, 2-O*H*), 3.41-3.51 (3H, m, 2-*H*, 3-*H*, 5-*H*), 3.59 (3H, s, 1-OCH_3), 3.63 (1H, app. t, *J* = 9.1 Hz, 4-*H*), 3.68 (3H, s, 3-OCH_3), 3.80 (1H, app. t, *J* = 10.4 Hz, 6-H_{ax}), 4.35 (1H, d, *J* = 7.5 Hz, 1-*H*), 4.37 (1H, dd, *J* = 4.9 Hz, 10.4 Hz, 6-H_{eq}), 5.56 (1H, s, PhC*H*), 7.36-7.39 (3H, m, Ar-*H*), 7.48-7.50 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 57.5, 61.0, 66.3, 68.7, 74.1, 81.6, 82.2, 101.3, 126.0, 128.3, 129.0, 137.2.

FTIR ν_{max} (solid, cm^{-1}): 1094, 3200-3600.

HRMS m/z (ESI+) calculated for $C_{15}H_{20}O_6$ $[M+Na]^+$: 319.1152, found 319.1155.

Methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranosid-2-ulose (β–6)[4]



To a solution of methyl 4,6-*O*-benzylidene-3-O-methyl-β-D-glucopyranoside (**β–9**, 0.95 g, 3.2 mmol) in dimethyl sulfoxide (18 mL) was added acetic anhydride (8 mL) and stirred at room temperature for 24 h. The reaction was treated with saturated $NaHCO_3$ (50 mL) and extracted with EtOAc (2 x 25 mL). The combined organic extracts were washed sequentially with saturated $NaHCO_3$ (2 x 50 mL), water (50 mL) and brine (50 mL). The organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give a yellow oil. Purification by column chromatography, eluting acetone : petrol : water (40:59:1), gave the titled compound (645 mg, 69 %) as a colourless solid.

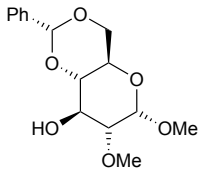
^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.42 (3H, s, 3-OCH_3), 3.44 (3H, s, 1-OCH_3), 3.80 (1H, dd, *J* = 1.6 Hz, 10.8 Hz, 6-H_{ax}), 3.82 (1H, dd, *J* = 1.0 Hz, 10.3 Hz, 5-*H*), 3.86-3.92 (1H, m, 4-*H*), 4.32-4.38 (2H, m, 3-*H*, 6-H_{eq}), 5.07 (1H, br s, 1-*H*), 5.67 (1H, s, PhC*H*), 7.39-7.45 (5H, m, Ar-*H*).

^{13}C NMR (DMSO-d_6, 100 MHz): δ_C 56.7, 59.0, 66.1, 68.1, 81.6, 84.6, 100.7, 101.5, 126.7, 128.6, 129.5, 137.7, 197.9.

FTIR ν_{max} (solid, cm^{-1}): 1064, 1081, 1752.

HRMS m/z (ESI+) calculated for $C_{15}H_{18}O_6$ $[M+H]^+$: 295.1176, found 295.1188.

Methyl 4,6-*O*-benzylidene-2-O-methyl-α-D-glucopyranoside (α–10)[1]



To a stirred solution of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**α–7**, 4.35 g, 15.4 mmol) in toluene (150 mL) was added dibutyltin oxide (4.23 g, 17.0 mmol) and the mixture heated at reflux with azeotropic removal of water for 22 h. The reaction mixture was then cooled and concentrated *in vacuo* to give a residue which was dissolved in DMF (55 mL), and iodomethane (9.6 mL, 154.2 mmol) was added. The mixture was stirred at 40 ºC for 71 h prior to concentrating *in vacuo* to give a yellow syrup. Purification by column chromatography, eluting toluene : EtOAc (50:50) gave the titled compound (3.81 g, 83 %) as an off-white solid.

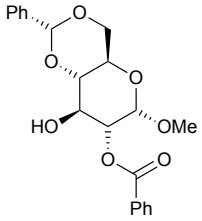
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.56 (1H, t, *J* = 1.5 Hz, 3-O*H*), 3.32 (1H,dd, *J* = 3.7 Hz, 9.3 Hz, 2-*H*), 3.47 (3H, s, 1-OCH_3), 3.53 (1H, app. t, *J* = 9.3 Hz, 4-*H*), 3.55 (3H, s, 2-OCH_3), 3.76 (1H, app. t, *J* = 10.2 Hz, 6-H_{ax}), 3.80-3.87 (1H, m, 5-*H*), 4.10 (1H, app. td, *J* = 2.0 Hz, 9.3 Hz, 3-*H*), 4.30 (1H, dd, *J* = 4.5 Hz, 10.2 Hz, 6-H_{eq}), 4.92 (1H, d, *J* = 3.7 Hz, 1-*H*), 5.55 (1H, s, PhC*H*), 7.35-7.39 (3H, m, Ar-*H*), 7.49-7.51 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 55.4, 58.8, 62.1, 69.0, 70.2, 81.2, 81.6, 97.8, 102.0, 126.3, 128.3, 129.3, 137.0.

FTIR ν_{max} (solid, cm^{-1}): 1087, 3273.

HRMS m/z (ESI+) calculated for $C_{15}H_{20}O_6$ $[M+H]^+$: 297.1333, found 297.1341.

Methyl 4,6-*O*-benzylidene-2-O-benzoyl-α-D-glucopyranoside[5]

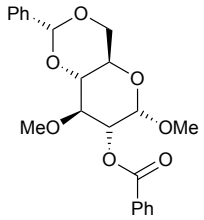


To a solution of methyl 4,6-O-benzylidene-α-D-glucopyranoside (**α–7**, 4.40 g, 15.6 mmol) in toluene:methanol (1:1 v/v) was added dibutyltin oxide (3.88 g, 15.6 mmol) and the mixture heated at reflux for 3 h, then concentrated *in vacuo* prior to addition of toluene (100 mL) and concentrating to dryness *in vacuo*. The mixture was then dissolved in toluene (55 mL), cooled to 0 ºC and treated with benzoyl chloride (1.81 mL, 15.6 mmol). The mixture was stirred for 30 minutes at 0 ºC prior to addition of methanol (10 mL) and stirring at room temperature for 22 h. The reaction mixture was then concentrated *in vacuo* and dissolved in 25 % EtOAc in hexane containing a small amount of DCM and passed through a silica plug. The filtrate was then concentrated *in vacuo* and the residue dispersed in 10 % EtOAc in hexane. The titled compound (1.00g, 2.59 mmol, 17 %) was collected by filtration as a colourless solid.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.45 (1H, d, *J* = 3.0 Hz, 3-O*H*), 3.41 (3H, s, 1-OCH_3), 3.65 (1H, app. t, *J* = 9.4 Hz, 4-*H*), 3.81 (1H, app. t, *J* = 10.2 Hz, 6-H_{ax}), 3.90-3.96 (1H, m, 5-*H*), 4.34 (1H, dd, *J* = 4.8 Hz, 10. Hz, 3-*H*), 4.42 (1H, dd, *J* = 10.2 Hz, 2.9 Hz, 6-H_{eq}), 5.05 (1H, dd, *J* = 3.8 Hz, 9.4 Hz, 2-*H*), 5.09 (1H, d, *J* = 3.8 Hz, 1-*H*), 5.59 (1H, s, PhC*H*), 7.37-7.42 (3H, m, Ar-H), 7.45-7.53 (4H, m, Ar-*H*), 7.57-7.62 (1H, m, Ar-*H*), 8.09-8.12 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 55.6, 62.0, 68.9, 69.0, 74.1, 81.5, 97.8, 102.1, 126.3, 128.4, 129.3, 129.5, 130.0, 133.4, 137.0, 166.2.

Methyl 4,6-*O*-benzylidene-2-O-benzoyl-3-O-methyl-α-D-glucopyranoside (α–11)[5]



To a solution of methyl 4,6-*O*-benzylidene-2-O-benzoyl-α-D-glucopyranoside (521 mg, 1.3 mmol) in DCM (30 mL) was added mercury cyanide (82.5 mg, 0.3 mmol), 2,6-di-tert-butyl pyridine (0.82 mL, 3.7 mmol) and methyl trifluoromethanesulfonate (0.62 mL, 5.5 mmol). The mixture was then heated at reflux for 42 h. The reaction mixture was then cooled and washed with saturated $NaHCO_3$ (2 x 50 mL). The organic extracts were then dried over sodium sulfate, filtered, and concentrated *in vacuo* to give a biphasic oil (1.53 g). Purification by column chromatography, eluting petrol : EtOAc (90:10) gave the titled compound (437 mg, 81 %) as a viscous yellow oil.

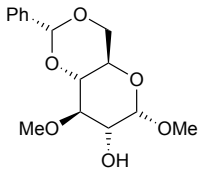
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 3.39 (3H, s, 1-OC*H*$_3$), 3.61 (3H, s, 3-OC*H*$_3$), 3.69 (1H, t, *J* = 9.4 Hz, 4-*H*), 3.81 (1H, t, *J* = 10.2 Hz, 6-*H*$_{ax}$), 3.90 (1H, dd, *J* = 4.6 Hz, 9.8 Hz, 5-*H*), 3.95 (1H, t, *J* = 9.4 Hz, 3-*H*), 4.33 (1H, dd, *J* = 4.7 Hz, 10.2 Hz, 6-*H*$_{eq}$), 5.02 (1H, dd, *J* = 3.8 Hz, 9.4 Hz, 2-*H*), 5.06 (1H, d, *J* = 3.8 Hz, 1-*H*), 5.60 (1H, s, PhC*H*), 7.36-7.40 (3H, m, Ar-*H*), 7.45-7.49 (2H, m, Ar-*H*), 7.50-7.60 (3H, m, Ar-*H*), 8.09-8.12 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 55.4, 61.1, 62.3, 69.0, 73.7, 77.8, 81.9, 97.9, 101.5, 126.1, 128.3, 128.5, 129.0, 129.7, 129.9, 133.3, 137.3, 166.0.

FTIR ν_{max} (solid, cm^{-1}): 1093, 1721.

HRMS *m/z* (ESI^+) calculated for $C_{22}H_{24}O_7$ $[M+H]^+$: 401.1595, found 401.1602.

Methyl 4,6-*O*-benzylidene-3-O-methyl-α-D-glucopyranoside (α–9)[5]



To a solution of methyl 4,6-O-benzylidene-2-O-benzoyl-3-O-methyl-α-D-glucopyranoside (**α–11**, 1.19 g, 3.0 mmol) in methanol (15 mL) was added a solution of sodium methoxide in methanol (25 wt%, 1.36 mL, 6.0 mmol) and stirred at room temperature for 2 h. The reaction mixture was then concentrated *in vacuo*, saturated ammonium chloride (50 mL) was added and extracted with EtOAc (2 x 50 mL). The combined organic extracts were dried over sodium carbonate, filtered, and concentrated *in vacuo* to give the titled compound as a colourless solid (0.95g).

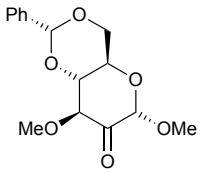
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.34 (1H, d, *J* = 7.6 Hz, 2-O*H*), 3.46 (3H, s, 1-OC*H*$_3$), 3.55-3.57 (2H, m, 3-*H*, 4-*H*), 3.63-3.65 (1H, m, 2-*H*), 3.67 (3H, s, 3-OC*H*$_3$), 3.70-3.90 (2H, m, 6-*H*$_{ax}$, 5-*H*), 4.29 (1H, dd, *J* = 4.2 Hz, 9.3 Hz, 6-*H*$_{eq}$), 4.80 (1H, d, *J* = 3.6, 1-*H*), 5.55 (1H, s, PhC*H*), 7.35-7.46 (5H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 55.5, 61.1, 62.5, 69.0, 72.3, 80.6, 82.0, 99.8, 101.3, 126.0, 128.3, 129.0, 137.3.

FTIR ν_{max} (solid, cm^{-1}): 1075, 3443.

HRMS *m/z* (ESI^+) calculated for $C_{15}H_{20}O_6$ $[M+H]^+$: 297.1333, found 297.1346.

Methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-glucopyranosid-2-ulose (α–6)[4]



To a solution of methyl 4,6-O-benzylidene-3-O-methyl-α-D-glucopyranoside (**α–9**, 0.95 g, 3.2 mmol) in dimethyl sulfoxide (18 mL) was added acetic anhydride (8 mL) and the reaction was stirred at room temperature for 24 h. The reaction mixture was treated with saturated $NaHCO_3$ (50 mL) and extracted with EtOAc (2 x 25 mL). The combined organic extracts were sequentially washed with saturated $NaHCO_3$ (2 x 50 mL), water (50 mL) and brine (50 mL) prior to drying over sodium sulfate, filtering, and concentrating *in vacuo* to give a yellow oil (2.46 g). Purification by column chromatography, eluting petrol: acetone: water (75:50:1) gave the titled compound (0.65 g, 69 % over 2 steps) as a colourless solid.

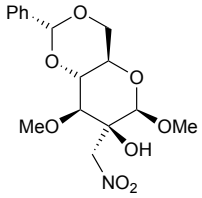
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 3.50 (3H, s, 1-OC*H*$_3$), 3.62 (3H, s, 3-OC*H*$_3$), 3.80 (1H, app. t, *J* = 10.5 Hz, 4-*H*), 3.81 (1H, app. t, *J* = 10.5 Hz, 6-*H*$_{ax}$), 4.23 (1H, app. td, *J* = 10.5 Hz, 5.0 Hz, 5-*H*), 4.36 (1H, d, *J* = 10.5 Hz, 3-*H*), 4.40 (1H, dd, *J* = 5.0 Hz, 10.5 Hz, 6-*H*$_{eq}$), 4.74 (1H, s, 1-*H*), 5.55 (1H, s, PhC*H*), 7.37-7.40 (3H, m, Ar-*H*), 7.49-7.52 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 55.8, 60.2, 63.2, 68.8, 82.8, 83.0, 101.4, 101.9, 126.2, 128.3, 129.2, 136.8, 197.3.

FTIR ν_{max} (solid, cm^{-1}): 1085, 1746.

HRMS *m/z* (ESI^+) calculated for $C_{15}H_{18}O_6$ $[M+H]^+$: 295.1176, found 295.1188.

Methyl 4,6-O-benzylidene-2-C-methylnitro-3-O-methyl-β-D-glucopyranoside (16)



To a solution of methyl 4,6-O-benzylidene-3-O-methyl-β-D-glucopyranosid-2-ulose (**β–6**, 312 mg, 1.1 mmol) in THF:nitromethane (1:1 v/v 5 mL) was added sodium methoxide (20.2 mg, 0.4 mmol) and stirred at room temperature. A second aliquot of sodium methoxide (18 mg, 0.3 mmol) was added after 4.5 h. After a total of 7 h the reaction was treated with acetic acid (70 %, 20 ml) and extracted with chloroform (2 x 20 mL). The combined organic extracts were washed with water (2 x 30 mL) dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Purification by column chromatography on silica gel, eluting toluene: EtOAc (50:50) gave the titled compound (281 mg, 75 %) as a colourless solid.

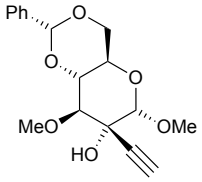
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.93 (1H, s, 2-O*H*), 3.39-3.43 (1H, m, 5-*H*), 3.58 (1H, d, *J* = 9.1 Hz, 3-*H*), 3.61 (3H, s, 1-OCH_3), 3.69 (3H, s, 3-OCH_3), 3.87 (1H, app. t, *J* = 10.4 Hz, 6-H_{ax}), 4.09-4.11 (1H, m, 4-*H*), 4.37 (1H, dd, *J* = 5.0 Hz, 10.4 Hz, 6-H_{eq}), 4.60 (1H, s, 1-*H*), 4.64 (1H, d, *J* = 11.1 Hz, CH_2NO_2), 4.81 (1H, d, *J* = 11.1 Hz, CH_2NO_2), 5.60 (1H, s, PhC*H*), 7.37-7.39 (3H, m, Ar-*H*), 7.46-7.49 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$,100 MHz): δ_C 57.8, 61.5, 66.3, 68.4, 75.1, 76.2, 78.5, 80.0, 100.8, 101.5, 125.9, 128.3, 129.1, 137.1.

FTIR ν_{max} (solid, cm^{-1}): 1087, 1372, 1542, 3414, 3518.

HRMS *m/z* (ESI$^+$) calculated for $C_{16}H_{21}NO_8$ $[M+Na]^+$: 378.1159, found 378.1162.

Methyl 4,6-O-benzylidene-2-C-ethynyl-3-O-methyl-α-D-glucopyranoside (**17**)



To a solution of methyl 4,6-O-benzylidene-3-O-methyl-α-D-glucopyranosid-2-ulose (**α–6**, 205 mg, 0.7 mmol) in THF (15 mL) at 0 ºC was added a solution of ethynylmagnesium bromide (0.5 M, 4 mL, 2 mmol). The reaction mixture was then stirred at room temperature. A further aliquot of ethynylmagnesium bromide solution was added (4 mL) after 7h and again after a further 16h. After a further 1h water (20 mL) was added. The reaction mixture was then filtered through a pad of celite washing with EtOAc (75 mL) and the filtrate was extracted with water (2 x 50 mL) and brine (2 x 50 mL) sequentially prior to drying over sodium sulfate, filtering and concentrating *in vacuo*. Purification by column chromatography on silica gel, eluting toluene: EtOAc (50:50) gave the titled compound (187 mg, 84 %) as a viscous colourless oil.

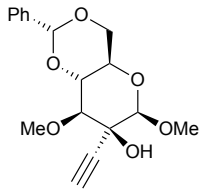
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.65 (1H, s, CC*H*), 2.94 (1H, s, 2-O*H*), 3.49 (3H, s, 1-OCH_3), 3.67 (1H, d, *J* = 9.2 Hz, 3-*H*), 3.72 (3H, s, 3-OCH_3), 3.85 (1H, app. t, *J* = 9.0 Hz, 6-H_{ax}), 3.82-3.96 (2H, m, 5-*H*, 4-*H*), 4.31 (1H, dd, *J* = 3.0 Hz, 9.0 Hz, 6-H_{eq}), 4.80 (1H, s, 1-*H*), 5.58 (1H, s, PhC*H*), 7.35-7.39 (3H, m, Ar-*H*), 7.47-7.50 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 55.8, 62.0, 63.5, 68.8, 73.1, 75.4, 81.2, 81.3, 81.8, 101.4, 102.2, 126.0, 128.3, 129.0, 137.2.

FTIR ν_{max} (solid, cm^{-1}): 1067, 3282, 3460.

HRMS *m/z* (ESI$^+$) calculated for $C_{17}H_{20}O_6$ $[M+H]^+$: 321.1333, found 321.1330.

Methyl 4,6-O-benzylidene-2-C-ethynyl-3-O-methyl-β-D-glucopyranoside (18)



To a solution of methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranosid-2-ulose (**β–6**, 296 mg, 1.0 mmol) in THF (15 mL) at 0 ºC was added a solution of ethynylmagnesium bromide (0.5 M, 4 mL, 2.0 mmol). The solution was warmed to room temperature. A second aliquot of ethynylmagnesium bromide (0.5 M, 4 mL, 2.0 mmol) was added after 6.5 h. After 24 h in total, water (10 mL) was added and the reaction mixture filtered through a pad of celite, washing with EtOAc (100 mL). The filtrate was washed with water (2 x 50 mL) and the combined aqueous extracts washed with EtOAc (2 x 50 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated *in vacuo*. Purification by column chromatography on silica gel, eluting toluene: EtOAc (50:50) gave the titled compound (298mg, 88 %) as a colourless solid.

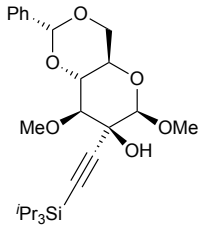
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.53 (1H, s, CC*H*), 2.98 (1H, br s, 2-O*H*), 3.43-3.47 (1H, m, 5-*H*), 3.52 (1H, d, *J* = 9.5 Hz, 3-*H*), 3.65 (3H, s, 1-OCH_3), 3.75 (3H, s, 3-OCH_3), 3.87 (1H, app. t, *J* = 10.5 Hz, 6-H_{ax}), 3.93 (1H, app. t, *J* = 9.5 Hz, 4-*H*), 4.36 (1H, dd, *J* = 5.0 Hz, 10.5 Hz, 6-H_{eq}), 4.50 (1H, s, 1-*H*), 5.57 (1H, s, PhC*H*), 7.35-7.39 (3H, m, Ar-*H*), 7.48-7.50 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 58.2, 62.1, 66.6, 68.4, 71.5, 73.4, 78.4, 82.4, 83.3, 101.5, 103.3, 126.0, 128.3, 129.0, 137.3.

FTIR ν_{max} (solid, cm^{-1}): 1091, 3276.

HRMS *m/z* (ESI$^+$) calculated for $C_{17}H_{20}O_6$ $[M+H]^+$: 321.1333, found 321.1337.

(2*R*,4a*R*,6*R*,7*S*,8*S*,8a*R*)-6,8-dimethoxy-2-phenyl-7-((triisopropylsilyl)ethynyl)hexahydropyrano[3,2-d][1,3]dioxin-7-ol (19)



Isopropylmagnesium chloride – lithium chloride complex in THF (1.3 M, 7.84 mL, 10.2 mmol) was added to a solution of (triisopropyl)acetylene (2.29 mL, 10.2 mmol) in THF (5 mL) at 0 ºC. The solution was stirred at this temperature for 20 minutes, allowed to warm to room temperature and stirred for 4 hours. The Grignard reagent prepared by this method was titrated and determined to be 0.79 M.

To a solution of methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranosid-2-ulose (**β–6**, 298 mg, 1.0 mmol) in THF (10 mL) at 0 ºC under an atmosphere of nitrogen was added Grignard solution prepared as above (2.6 mL). The reaction was allowed to warm to room temperature. Further aliquots of Grignard solution (2.6 mL) were added after 3 and 6 h. After 18 h the reaction was quenched by addition of water (10 mL) and the resulting mixture filtered through a pad of celite washing with EtOAc (60 mL). The filtrate was separated, and the organic phase washed sequentially with water (30 mL) and brine (40 mL) prior to drying over sodium sulfate, filtering,

and concentrating *in vacuo*. Purification by column chromatography on silica gel, eluting toluene: EtOAc (90:10), gave the titled compound (441 mg, 91 %) as a colourless oil.

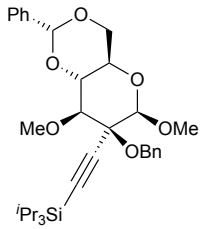
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.08 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$), 2.89 (1H, br s, 7-O*H*), 3.43-3.46 (1H, m, 4a-*H*), 3.52 (1H, d, *J* = 9.5 Hz, 8-*H*), 3.63 (3H, s, 6-OC*H*$_3$), 3.74 (3H, s, 8-OC*H*$_3$), 3.87 (1H, app. t, *J* = 10.5 Hz, 4-H_{ax}), 3.90 (1H, app. t, *J* = 9.5 Hz, 8a-*H*), 4.32 (1H, dd, *J* = 5.0 Hz, 10.5 Hz, 4-H_{eq}), 4.48 (1H, s, 6-*H*), 5.57 (1H, s, 2-*H*), 7.35-7.40 (3H, m, Ar-*H*), 7.48-7.50 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 11.1, 18.6, 58.4, 62.0, 66.6, 68.5, 71.8, 78.4, 83.9, 86.2, 101.5, 104.1, 106.2, 126.1, 128.2, 129.0, 137.4.

FTIR ν_{max} (solid, cm^{-1}): 1092.

HRMS *m/z* (ESI^+) calculated for $C_{26}H_{40}O_6Si$ $[M+H]^+$: 477.2667, found 477.2665.

(((2*R*,4a*R*,6*R*,7*S*,8*S*,8a*R*)-7-(benzyloxy)-6,8-dimethoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-7-yl)ethynyl)triisopropylsilane (20)



To an oil dispersion of sodium hydride (60 %wt, 231 mg, 5.8 mmol), washed with petrol (1 mL), was added THF (10 mL) and tetrabutylammonium iodide (43 mg, 0.12 mmol). A solution of (2*R*,4a*R*,6*R*,7*S*,8*S*,8a*R*)-6,8-dimethoxy-2-phenyl-7-((triisopropylsilyl)ethynyl)hexahydropyrano [3,2-d][1,3]dioxin-7-ol (**19**, 553 mg, 1.2 mmol) in THF (5 mL) was added, followed by benzyl bromide (1.4 mL, 11.6 mmol) and the reaction mixture was stirred for 15 h at room temperature. The reaction was quenched by careful addition of water (20 mL) and the mixture extracted with EtOAc (2 x 20 mL). The combined organic extracts were washed sequentially with saturated $NaHCO_3$ (30 mL) and brine (30 mL) prior to drying over sodium sulfate, filtering, and concentrating *in vacuo*. Purification by column chromatography on silica gel, eluting hexane: EtOAc (90:10), gave the titled compound (615 mg, 94 %) as a colourless oil.

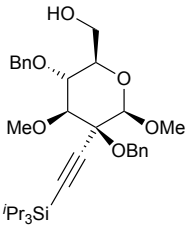
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.08 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$), 3.44-3.48 (1H, m, 4a-*H*), 3.54 (1H, d, *J* = 9.8 Hz, 8-*H*), 3.61 (3H, s, 6-OC*H*$_3$), 3.73 (3H, s, 8-OC*H*$_3$), 3.88 (1H, app. t, *J* = 10.4 Hz, 4-H_{ax}), 4.01 (1H, app. t, *J* = 9.8 Hz, 8a-*H*), 4.33 (1H, dd, *J* = 4.8 Hz, 10.4 Hz, 4-H_{eq}), 4.48 (1H, s, 6-*H*), 5.02 (1H, d, *J* = 12.2 Hz, C*H*$_2$Ph), 5.09 (1H, d, *J* = 12.2 Hz, C*H*$_2$Ph), 5.57 (1H, s, 2-*H*), 7.21-7.50 (10H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 11.1, 18.6, 58.7, 62.0, 67.7, 68.6, 70.7, 77.9, 85.5, 90.4, 101.4, 102.9, 106.4, 126.1, 126.9, 127.5, 127.9, 128.2, 128.9, 137.5, 139.9.

FTIR ν_{max} (solid, cm^{-1}): 1088.

HRMS *m/z* (ESI^+) calculated for $C_{33}H_{46}O_6Si$ $[M+NH_4]^+$: 584.3402, found 584.3403.

((2*R*,3*R*,4*S*,5*S*,6*R*)-3,5-bis(benzyloxy)-4,6-dimethoxy-5-((triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-2-yl)methanol (21)



To a solution of (((2*R*,4a*R*,6*R*,7*S*,8*S*,8a*R*)-7-(benzyloxy)-6,8-dimethoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-7-yl)ethynyl)triisopropylsilane (**20**, 476 mg, 0.84 mmol) in toluene (10 mL) was added a solution of diisobutylaluminum hydride (1M, 4.1 mL, 4.1 mmol) in hexane. The reaction mixture was stirred for 18 h at room temperature. The reaction mixture was then quenched by addition of methanol (5 mL) followed by sodium hydroxide solution (1M, 60 mL) and then extracted with EtOAc (2 x 30 mL). The combined extracts were washed sequentially with water (30 mL) and brine (30 mL) prior to drying over sodium sulfate, filtering, and concentrating *in vacuo* to give the titled compound (465 mg, 97 %) as a colourless oil that was used without further purification.

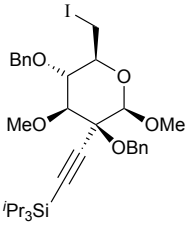
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.09 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$), 2.04 (1H, t, *J* = 6.7 Hz, 1-O*H*), 3.36-3.40 (1H, m, 2-*H*), 3.44 (1H, d, *J* = 9.4 Hz, 4-*H*), 3.56 (3H, s, 6-OC*H*$_3$), 3.68-3.74 (1H, m, 1-*H*$_a$), 3.76-3.81 (1H, m, 3-*H*), 3.78 (3H, s, 4-OC*H*$_3$), 3.84-3.91 (1H, m, 1-*H*$_b$), 4.39 (1H, s, 6-*H*), 4.61 (1H, d, *J* = 11.0 Hz, C*H*$_2$Ph), 4.87 (1H, d, *J* = 11.0 Hz, C*H*$_2$Ph), 5.04 (2H, d, *J* = 3.5 Hz, C*H*$_2$Ph), 7.20-7.42 (10H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 11.1, 18.5, 58.5, 61.9, 62.3, 70.2, 74.9, 75.2, 75.8, 77.0, 89.3, 90.5, 102.9, 105.5, 126.9, 127.4, 127.8, 127.9, 128.1, 128.5, 138.2, 139.9.

FTIR ν_{max} (solid, cm^{-1}): 1080.

HRMS *m/z* (ESI^+) calculated for $C_{33}H_{48}O_6Si$ $[M+NH_4]^+$: 586.3558, found 586.3563.

(((2*R*,3*S*,4*S*,5*S*,6*S*)-3,5-bis(benzyloxy)-6-(iodomethyl)-2,4-dimethoxytetrahydro-2H-pyran-3-yl)ethynyl)triisopropylsilane (22)



To a solution of ((2*R*,3*R*,4*S*,5*S*,6*R*)-3,5-bis(benzyloxy)-4,6-dimethoxy-5-((triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-2-yl)methanol (**21**, 497 mg, 0.87 mmol) in toluene (10 mL) at 60 ºC was added triphenylphosphine (346 mg, 1.3 mmol) and imidazole (205 mg, 3.0 mmol). Upon dissolution, iodine (382 mg, 1.5 mmol) was added and stirring continued at 60 ºC for 4 h. The reaction mixture was then cooled and EtOAc (30 mL) added. The mixture was then sequentially washed with saturated sodium thiosulfate (30 mL), water (30 mL), hydrochloric acid (1 M, 30 mL), water (30 mL), saturated sodium hydrogen carbonate (30 mL) and water (30 mL) prior to drying over sodium sulfate, filtering, and concentrating *in vacuo*. Purification by column

chromatography on silica gel, eluting Hexane:EtOAc (85:15), gave the titled compound (417.8 mg, 71 %) as a colourless oil.

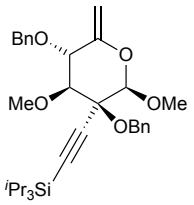
^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 1.08 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$), 3.21-3.30 (6-H, m, 2H, C*H*$_2$I), 3.42 (1H, d, *J* = 9.2 Hz, 4-*H*), 3.52-3.56 (1H, m, C*H*$_2$I), 3.58 (3H, s, 2-OC*H*$_3$), 3.58-3.63 (1H, m, 5-*H*), 3.77 (3H, s, 4-OC*H*$_3$), 4.39 (1H, s, 2-*H*), 4.63 (1H, d, *J* = 11.0 Hz, PhC*H*$_2$), 4.90 (1H, d, *J* = 11.0 Hz, PhC*H*$_2$), 5.01 (1H, d, *J* = 12.2 Hz, PhC*H*$_2$), 5.08 (1H, d, *J* = 12.2 Hz, PhC*H*$_2$), 7.23-7.46 (10H, m, Ar-*H*).

^{13}C NMR (100 MHz) δ_C 5.9, 11.1, 18.5, 58.3, 61.9, 70.2, 75.3, 75.4, 77.0, 78.6, 89.0, 90.6, 102.9, 105.4, 126.8, 127.5, 127.9, 128.0, 128.2, 128.5, 138.0, 139.9.

FTIR ν_{max} (solid, cm^{-1}): 1111.

HRMS *m/z* (ESI$^+$) calculated for $C_{33}H_{47}IO_5Si$ $[M+NH_4]^+$: 696.2576, found 696.2578.

(((2*R*,3*S*,4*S*,5*S*)-3,5-bis(benzyloxy)-2,4-dimethoxy-6-methylenetetrahydro-2H-pyran-3-yl)ethynyl)triisopropylsilane (5)



To a solution of (((2*R*,3*S*,4*S*,5*S*,6*S*)-3,5-bis(benzyloxy)-6-(iodomethyl)-2,4-dimethoxytetrahydro-2H-pyran-3-yl)ethynyl)triisopropylsilane (**22**, 3.18 g, 4.7 mmol) in DMF (30 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (1.4 mL, 9.4 mmol) and the mixture heated to 80 °C for 20 h. The reaction mixture was cooled, water (50 mL) added and extracted with EtOAc (4 x 20 mL). The combined organics were washed sequentially with hydrochloric acid (1 M, 2 x 30 mL), water, (30 mL) and brine (30 mL) prior to drying over sodium sulfate, filtering and concentrating in vacuo to give the titled compound as an orange oil (2.52 g, 98 %). An analytical sample was obtained by column chromatography (8:2, Petrol:EtOAc) as a colourless oil.

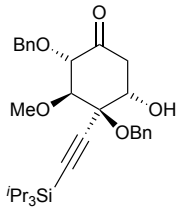
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.08 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$), 3.43 (1H, d, *J* = 9.3 Hz, 4-*H*), 3.60 (3H, s, 2-OC*H*$_3$), 3.73 (3H, s, 4-OC*H*$_3$), 4.23-4.27 (1H, m, 5-*H*), 4.47 (1H, s, 2-*H*), 4.72 (1H, d, *J* = 11.3 Hz, PhC*H*$_2$), 4.77 (1H, d, *J* = 11.3 Hz, PhC*H*$_2$), 4.79 (2H, app. dd, *J* = 1.5 Hz, 14.6 Hz, C=C*H*$_2$), 5.02 (2H, d, *J* = 2.0 Hz, PhC*H*$_2$), 7.20-7.42 (10H, m, Ar-*H*).

^{13}C NMR (100 MHz) δ_C 11.1, 18.5, 58.3, 62.0, 70.2, 74.3, 76.5, 77.0, 87.3, 90.5, 95.2, 102.6, 105.8, 126.9, 127.6, 127.7, 127.9, 128.0, 128.4, 138.2, 139.6, 154.9.

FTIR ν_{max} (solid, cm^{-1}): 1099.

HRMS *m/z* (ESI$^+$) calculated for $C_{33}H_{46}O_5Si$ $[M+Na]^+$: 573.3007, found 573.3018.

(2*S*,3*S*,4*R*,5*S*)-2,4-bis(benzyloxy)-5-hydroxy-3-methoxy-4-((triisopropylsilyl)ethynyl)cyclohexan-1-one (4)



To a solution of (((2*R*,3*S*,4*S*,5*S*)-3,5-bis(benzyloxy)-2,4-dimethoxy-6-methylenetetrahydro-2H-pyran-3-yl)ethynyl)triisopropylsilane (**5**, 85 mg, 0.15 mmol) in acetone/H_2O (2:1, 12 mL) was added mercury chloride (47 mg, 0.17 mmol) and the mixture heated to reflux for 26 h. The volatiles were removed *in vacuo* and the mixture extracted with DCM (2 x 30 mL). The combined organics were washed sequentially with water (2 x 30 mL) prior to drying over sodium sulfate, filtering and concentrating *in vacuo* to give the titled compound (82 mg, 98 %) as a yellow oil that solidified on standing. An analytical sample was obtained by column chromatography (80:20, Petrol:EtOAc) as a colourless solid.

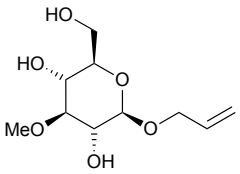
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.11 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$), 2.25 (1H, t, *J* = 2.2 Hz, 5-O*H*), 2.49 (1H, dd, *J* = 14.5 Hz, 2.8 Hz, 6-*H*$_a$), 2.85 (1H, dd, *J* = 14.5 Hz, 2.8 Hz, 6-*H*$_b$), 3.72 (3H, s, 3-OC*H*$_3$), 3.85 (1H, d, *J* = 12.0 Hz, 3-*H*), 4.10 (1H, t, *J* = 2.8 Hz, 5-*H*), 4.31 (1H, d, *J* = 12.0 Hz, 2-*H*), 4.61 (1H, d, *J* = 11.9 Hz, PhC*H*$_2$), 4.92 (1H, d, *J* = 11.9 Hz, PhC*H*$_2$), 4.95 (1H, d, *J* = 11.6 Hz, PhC*H*$_2$), 5.06 (1H, d, *J* = 11.6 Hz, PhC*H*$_2$), 7.28-7.37 (8H, m, Ar-*H*), 7.43-7.44 (2H, m, Ar-*H*).

^{13}C NMR (100 MHz): δ_C 11.1, 18.6, 41.9, 62.6, 70.2, 72.1, 73.7, 79.5, 84.0, 86.2, 91.7, 103.7, 127.6, 127.7, 127.8, 127.9, 128.3, 128.3, 138.0, 138.7, 204.8.

FTIR ν_{max} (solid, cm^{-1}): 1725.

HRMS *m/z* (ESI^+) calculated for $C_{32}H_{44}O_5Si$ $[M+NH_4]^+$: 554.3296, found 554.3297.

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-(allyloxy)-6-(hydroxymethyl)-4-methoxytetrahydro-2H-pyran-3,5-diol (28)[6]



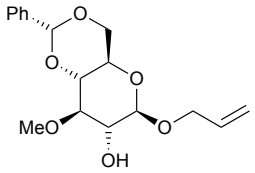
Hydrazine acetate (322.4 mg, 3.5 mmol) was added to a solution of (3*R*,4*S*,5*R*,6*R*)-6-(acetoxymethyl)-4-methoxytetrahydro-2H-pyran-2,3,5-triyl triacetate (**26**,[6] 1.01 g, 2.8 mmol) in DMF (10 ml) and heated to 50 ºC for 15 minutes. The reaction mixture was cooled and poured into brine (50 mL) and extracted with EtOAc (2 x 35 mL). The combined organic extracts were washed with brine (50 mL) and dried over sodium sulfate, filtered and concentrated *in vacuo*. The residue was dissolved in DCM (2.8 mL) and added to a mixture of sodium hydride (60% in mineral oil, washed with petrol prior to reaction, 169.7 mg, 4.2 mmol) and allyl bromide (2.4 mL, 27.7 mmol) at -20 ºC. The mixture was allowed to warm to room temperature over 2 h and stirred for a further 22 h. The reaction mixture was quenched by addition of glacial acetic acid (0.08 mL) and filtered, washing with DCM (25 mL) and concentrated *in vacuo*. Purification by column chromatography on silica gel, eluting petrol:EtOAc (50:50) gave (2*R*,3*R*,4*S*,5*R*,6*R*)-2-(acetoxymethyl)-6-(allyloxy)-4-methoxytetrahydro-2*H*-

pyran-3,5-diyl diacetate (445 mg, 44 %) as an orange oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 2.16 (1H, t, *J* = 6.3 Hz, CH_2OH), 2.49 (1H, d, *J* = 2.0 Hz, 3-O*H*), 2.75 (1H, d, *J* = 2.6 Hz, 5-O*H*), 3.20 (1H, t, *J* = 9.1 Hz, 4-*H*), 3.36-3.40 (1H, m, 6-*H*), 3.44–3.49 (1H, m, 3-*H*), 3.57 (1H, td, *J* = 9.1 Hz, 2.6 Hz, 5-*H*), 3.68 (3H, s, OCH_3), 3.78–3.85 (1H, m, CH_2OH), 3.89–3.94 (1H, m, CH_2OH), 4.14 (1H, dd, *J* = 6.4 Hz, 12.8 Hz, OCH_2CHCH_2), 4.36 (1H, d, *J* = 7.7 Hz, 2-*H*), 4.37 (1H, ddd, *J* = 1.4 Hz, 5.5 Hz, 12.8 Hz, OCH_2CHCH_2), 5.22–5.36 (2H, m, OCH_2CHCH_2), 5.89–5.99 (1H, m, OCH_2CHCH_2).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 60.8, 62.6, 70.2, 70.6, 74.2, 75.2, 85.3, 102.0, 118.2, 133.6.

(2*R*,4a*R*,6*R*,7*R*,8*R*,8a*R*)-6-(allyloxy)-8-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-7-ol (29)[7]



p-Toluenesulfonic acid (72.6 mg, 0.4 mmol) was added to a mixture of (2R,3R,4S,5R,6R)-2- (allyloxy)-6-(hydroxymethyl)-4-methoxytetrahydro-2H-pyran-3,5-diol (**28**, 8.59 g, 36.7 mmol) and benzaldehyde dimethylacetal (8.26 mL, 55.0 mmol) in DMF (56 mL). The mixture was heated to 50 ºC under vacuum for 2 h. Upon completion the reaction mixture was cooled and concentrated *in vacuo* to a volume of 15 mL. The solution was poured into saturated NaHCO3 (20 mL) and extracted with DCM (3 X 30 mL). The combined organic extracts were washed sequentially with saturated $NaHCO_3$ (20 mL), H_2O (20 mL) and brine (20 mL) prior to drying over sodium sulfate, filtering, and concentrating *in vacuo* to give an oily yellow solid (11.46 g). The crude was purified by column chromatography (75:25, petrol:EtOAc to 100 % EtOAc) to give (2*R*,4a*R*,6*R*,7*R*,8*R*,8a*R*)-6-(allyloxy)-8-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-7-ol (79) as a colourless solid (10.41 g, 88 %).

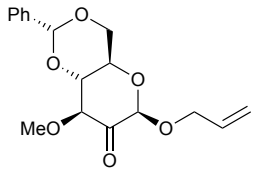
^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 2.54 (1H, br s, O*H*), 3.41-3.48 (2H, m, 7-H, 8-*H*), 3.51-3.55 (1H, m, 4a-*H*), 3.64 (1H, app. t, *J* = 9.2 Hz, 8a-*H*), 3.68 (3H, s, OCH_3), 3.80 (1H, app. t, *J* = 10.4 Hz, 4-H_{ax}), 4.10-4.20 (1H, m, OCH_2CHCH_2), 4.35 (1H, dd, *J* = 10.4 Hz, 4.9 Hz, 4-H_{eq}), 4.31-4.38 (1H, m, OCH_2CHCH_2), 4.47 (1H, d, *J* = 7.7 Hz, 6-*H*), 5.22-5.38 (2H, m, OCH_2CHCH_2), 5.56 (s, 1H, 2-H), 5.90-6.00 (1H, m, OCH_2CHCH_2), 7.33-7.40 (3H, m, Ar-*H*), 7.46-7.50 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 61.0, 66.4, 68.7, 70.6, 74.0, 81.5, 82.2, 101.2, 102.1, 118.3, 126.0, 128.2, 129.0, 133.4, 137.2.

IR ν_{max} (thin film, cm^{-1}): 3488, 3304, 2972, 2891.

HRMS: m/z (ESI+) calculated for $C_{17}H_{22}O_6$ $[M+H]^+$: 323.1489, found 323.1500.

(2*R*,4a*R*,8*S*,8a*R*)-6-(allyloxy)-8-methoxy-2-phenyltetrahydropyrano[3,2-d][1,3]dioxin-7(6H)-one



To a solution of (2*R*,4a*R*,6*R*,7*R*,8*R*,8a*R*)-6-(allyloxy)-8-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-7-ol (**29**, 8.86 g, 27.5 mmol) in DMSO (120 mL) was added acetic anhydride (60 mL). The reaction mixture was stirred at room temperature for 28 h prior to pouring into sat $NaHCO_3$ (500 mL) and extracting with EtOAc (3 x 150 mL). The combined organic extracts were washed sequentially with saturated $NaHCO_3$ (250 mL), H_2O (250 mL) and brine (250 mL) prior to drying over sodium sulfate, filtering and concentrating *in vacuo*. Purification by column chromatography on silica gel, eluting 50:50 to 60:40 EtOAc:Petrol gave the titled compound (5.49 g, 62 %) as a colourless solid.

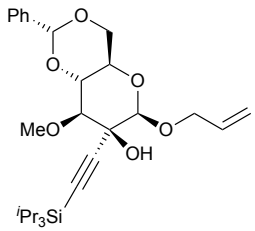
^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 3.64 (3H, s, OC*H*$_3$), 3.80-3.83 (1H, m, 4a-*H*), 3.85 (1H, t, *J* = 9.9 Hz, 4-*H*$_{ax}$), 3.90 (1H, t, *J* = 9.1 Hz, 8a-*H*), 4.08 (1H, d, *J* = 9.0 Hz, 8-*H*), 4.22 (1H, dd, *J* = 6.7 Hz, 12.6 Hz, OC*H*$_2$CHCH$_2$), 4.41 (1H, dd, *J* = 5.2 Hz, 12.6 Hz, OC*H*$_2$CHCH$_2$), 4.46 (1H, dd, *J* = 4.3 Hz, 9.9 Hz, 4-*H*$_{eq}$), 4.94 (1H, s, 6-*H*), 5.29 (1H, dd, *J* = 1.4 Hz, 10.4 Hz, OCH$_2$CHC*H*$_2$), 5.36 (1H, dd, *J* = 1.4 Hz, 17.2 Hz, OCH$_2$CHC*H*$_2$), 5.57 (1H, s, 2-*H*), 5.95 (1H, dddd *J* = 5.2 Hz, 6.7 Hz, 10.4 Hz, 17.2 Hz, OCH$_2$C*H*CH$_2$), 7.37-7.39 (3H, m, Ar-*H*), 7.49-7.52 (2H, m, Ar-*H*).

^{13}C NMR (100 MHz) δ_C 60.2, 68.6, 70.2, 80.3, 82.2, 84.9, 99.3, 101.4, 118.9, 126.2, 128.3, 129.0, 132.9, 136.6, 196.3.

FTIR ν_{max} (oil, cm^{-1}) 1755.

HRMS *m/z* (ESI$^+$) calculated for $C_{17}H_{20}O_6$ $[M+H]^+$: 321.1333, found 321.13334.

(2*R*,4a*R*,6*R*,7*S*,8*S*,8a*R*)-6-(allyloxy)-8-methoxy-2-phenyl-7-((triisopropylsilyl)ethynyl)hexahydropyrano [3,2-d][1,3]dioxin-7-ol (30)



iso-Propylmagnesium chloride lithium chloride complex solution (1.3 M in THF, 42.3 mL, 55 mmol) was added to (triisopropylsilyl)acetylene (12.3 mL, 55.0 mmol) in THF (55 mL) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 4 h. The solution was found to be 0.43 M by titration with salicylaldehyde phenylhydrazone and was used directly in the following step.

To a solution of (2*R*,4a*R*,8*S*,8a*R*)-6-(allyloxy)-8-methoxy-2-phenyltetrahydropyrano[3,2-d][1,3]dioxin-7(6H)-one (4.4 g, 13.7 mmol, 1 mmol) in dry THF (80 mL) at 0 °C was added stock Grignard solution (0.43 M, 63.7 ml, 27.4 mmol, 2 eq). The reaction mixture was then stirred at room temperature for 1.5 h. Saturated aqueous NH_4Cl (10 mL) was added, and the resulting mixture concentrated under reduced pressure to 50 mL). Saturated aqueous NH_4Cl (100 mL) was added, and the mixture was extracted with EtOAc (3 x 125 mL). The

combined organic layers were washed with brine (300 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel column chromatography on silica, eluting 92:8 to 80:20 toluene/EtOAc) gave the titled compound (6.5 g, 94%) as a colourless oil.

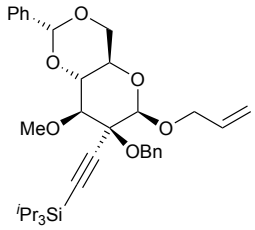
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.08 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$), 2.91 (1H, brs, 7-O*H*), 3.41-3.46 (1H, m, 4a-*H*), 3.51 (1H, d, *J* = 9.6 Hz, 8-*H*), 3.74 (3H, s, OC*H*$_3$), 3.87 (1H, app. t, *J* = 10.4 Hz, 4-*H*$_{ax}$), 3.91 (1H, app. t, *J* = 9.6 Hz, 8a-*H*), 4.19 (1H, dd, *J* = 6.6 Hz, 12.6 Hz, OC*H*$_2$CHCH$_2$), 4.39 (1H, dd, *J* = 4.9 Hz, 10.4 Hz, 4-*H*$_{eq}$), 4.42 (1H, dd, *J* = 5.2 Hz, 12.6 Hz, OC*H*$_2$CHCH$_2$), 4.61 (1H, s, 6-*H*), 5.22 (1H, dd, *J* = 1.4 Hz, 10.4 Hz, OCH$_2$CHC*H*$_2$), 5.35 (1H, dd, *J* = 1.4 Hz, 17.1 Hz, OCH$_2$CHC*H*$_2$), 5.57 (1H, s, PhC*H*), 5.94 (1H, dddd, *J* = 5.2 Hz, 6.6 Hz, 10.4 Hz, 17.1 Hz, OCH$_2$C*H*CH$_2$), 7.34-7.39 (3H, m, Ar-*H*), 7.47-7.50 (2H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 11.0, 18.5, 62.0, 66.5, 68.4, 71.0, 72.0, 78.4, 83.9, 86.2, 101.3, 101.4, 106.0, 118.4, 126.0, 128.2, 128.9, 133.3, 133.3.

IR ν_{max} (thin film, cm^{-1}) 1087.

HRMS *m/z* (ESI$^+$) calculated for $C_{28}H_{42}O_6Si$ $[M+H]^+$: 503.2823, found 503.2824.

(((2*R*,4a*R*,6*R*,7*S*,8*S*,8a*R*)-6-(allyloxy)-7-(benzyloxy)-8-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-7-yl)ethynyl)triisopropylsilane (31)



In a flame dried flask flushed with N_2, sodium hydride (60 % oil dispersion, 1.7 g, 43.3 mmol, 3.4 eq) washed with THF (15 mL) was suspended in dry distilled THF (15 mL). To this suspension stirring under N_2, was added tetrabutylammonium iodide (320 mg, 0.87 mmol, 0.07 eq), the mixture was cooled to 0 °C before adding a solution of (2*R*,4a*R*,6*R*,7*S*,8*S*,8a*R*)-6-(allyloxy)-8-methoxy-2-phenyl-7-((triisopropylsilyl)ethynyl)hexahydropyrano [3,2-d][1,3]dioxin-7-ol (**30**, 6.35 g, 12.63 mmol, 1 eq) in dry distilled THF (30 mL, prepared in a dry flask). After stirring for 5 min, benzyl bromide (5.1 mL, 43.3 mmol, 3.4 eq) was added and the reaction mixture stirred at room temperature for 20 h under N_2. The reaction was quenched by addition of saturated aqueous NH_4Cl (50 mL) and the mixture was extracted with EtOAc (3 X 150 mL). The combine organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure affording a yellow oil (12 g). Purification by column chromatography on silica, eluting 100:0 to 91:9 Petrol / EtOAc, gave the titled compound (6.77 g, 90%) as a colourless oil.

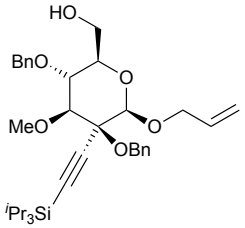
^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 1.07 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$), 3.43-3.47 (1H, m, 4a-*H*), 3.55 (1H, d, *J* = 9.7 Hz, 8-*H*), 3.72 (3H, s, OC*H*$_3$), 3.88 (1H, dd, *J* = 9.7 Hz, 10.4 Hz, 4-*H*$_{ax}$), 4.02 (1H, t, *J* = 9.7 Hz, 8a-*H*), 4.14 (1H, dd, *J* = 6.1 Hz, 12.8 Hz, OC*H*$_2$CHCH$_2$), 4.31 (1H, dd, *J* = 4.9 Hz, 10.4 Hz, 4-*H*$_{eq}$), 4.44 (1H, dd, *J* = 5.1 Hz, 12.8 Hz, OC*H*$_2$CHCH$_2$), 4.62 (1H, s, 6-*H*), 5.08 (2H, dd, *J* = 12.5 Hz, 15.2 Hz, C*H*$_2$Ph), 5.20 (1H, dd, *J* = 1.4 Hz, 10.4 Hz, OCH$_2$CHC*H*$_2$), 5.35 (1H, dd, *J* = 1.4 Hz, 17.3 Hz, OCH$_2$CHC*H*$_2$), 5.56 (1H, s, 2-*H*), 5.89-5.99 (1H, m, OCH$_2$C*H*CH$_2$), 7.18-7.23 (1H, m, Ar-*H*), 7.27-7.30 (2H, m, Ar-*H*), 7.33-7.37 (3H, m, Ar-*H*), 7.45-7.49 (4H, m, Ar-*H*).

^{13}C NMR (100 MHz) δ_C 11.1, 18.6, 62.0, 67.6, 68.6, 70.7, 71.2, 78.1, 78.5, 85.5, 90.4, 101.4, 102.8, 103.8, 117.5, 126.1, 126.8, 127.5, 127.9, 128.2, 128.9, 133.6, 137.5, 140.0.

IR ν_{max} (thin film, cm^{-1}): 2942, 2884, 1454.

HRMS *m/z* (ESI$^+$) calculated for $C_{35}H_{48}O_6Si$ $[M+H]^+$: 593.3293 found 593.3290.

((2*R*,3*R*,4*S*,5*S*,6*R*)-6-(allyloxy)-3,5-bis(benzyloxy)-4-methoxy-5-((triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-2-yl)methanol (32)



In a flame dried flask flushed with N_2, to a solution of (((2*R*,4a*R*,6*R*,7*S*,8*S*,8a*R*)-6-(allyloxy)-7-(benzyloxy)-8-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-7-yl)ethynyl)triisopropylsilane (**31**, 540 mg, 0.92 mmol, 1 eq) in toluene (8 mL) was added diisobutylaluminium hydride solution (1.0 M in hexanes, 2.5 mL, 2.5 mmol, 2.7 eq) dropwise over 10 mins. The mixture was stirred at room temperature for 23 h, then methanol (5 mL) and saturated Rochelle's salt solution (6 mL) were added sequentially. The mixture was stirred for 30 mins prior to extracting with EtOAc (3 x 15 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure to give the titled compound as a colourless oil (510 mg, 94 %).

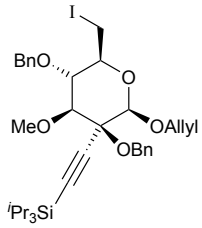
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.08 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$), 2.02 (1H, t, *J* = 6.8 Hz, 1-O*H*), 3.34-3.38 (1H, m, 2-*H*), 3.45 (1H, d, *J* = 9.4 Hz, 4-*H*), 3.71-3.88 (2H, m, 1-*H*$_2$), 3.78 (3H, s, 4-OC*H*$_3$), 4.10 (1H, dd, *J* = 5.9 Hz, 12.8 Hz, OC*H*$_2$CHCH$_2$), 4.38 (1H, dd, *J* = 5.1 Hz, 12.8 Hz, OC*H*$_2$CHCH$_2$), 4.53 (1H, s, 6-*H*), 4.60 (1H, d, *J* = 11.0 Hz, C*H*$_2$Ph), 4.87 (1H, d, *J* = 11.0 Hz, C*H*$_2$Ph), 5.03 (1H, d, *J* = 12.3 Hz, C*H*$_2$Ph), 5.10 (1H, d, *J* = 12.3 Hz, C*H*$_2$Ph), 5.18 (1H, dd, *J* = 1.4 Hz, 10.4 Hz, OCH$_2$CH=C*H*$_2$), 5.32 (1H, dd, *J* = 1.4 Hz, 17.3 Hz, OCH$_2$CH=C*H*$_2$), 5.88-5.92 (1H, m, OCH$_2$C*H*=CH$_2$), 7.22-7.24 (1H, m, Ar-*H*), 7.28-7.34 (7H, m, Ar-*H*), 7.42-7.44 (2H, m, Ar-*H*).

^{13}C NMR (100 MHz): δ_C 11.1, 18.6, 62.0, 62.3, 70.1, 71.2, 75.0, 75.1, 75.7, 77.2, 89.2, 90.6, 102.8, 103.0, 117.4, 126.9, 127.5, 127.8, 127.9, 128.1, 128.4, 133.7, 138.2, 139.9.

IR ν_{max} (oil, cm^{-1}) 1080, 1102.

m/z (ESI$^+$) calculated for $C_{35}H_{50}O_6Si$ $[M+NH_4]^+$: 612.3715 found 617.3266.

(((2R,3S,4S,5S,6S)-2-(allyloxy)-3,5-bis(benzyloxy)-6-(iodomethyl)-4-methoxytetrahydro-2H-pyran-3-yl)ethynyl)triisopropylsilane (33a)



To a solution of ((2R,3R,4S,5S,6R)-6-(allyloxy)-3,5-bis(benzyloxy)-4-methoxy-5- ((triisopropylsilyl) ethynyl)tetrahydro-2H-pyran-2-yl)methanol (**32**, 2.00 g, 3.4 mmol), triphenylphosphine (1.33 g, 5.1 mmol) and imidazole (785.6 mg, 11.5 mmol) in toluene (35 mL) at 70 °C was added iodine (1.04 g, 4.1 mmol). The mixture was stirred for 4 h prior to cooling, treating with H_2O (40 mL) and extracting with EtOAc (2 X 50 mL). The combined organics were washed sequentially with HCl (1 M, 100 mL), sat $NaHCO_3$ (100 mL) and brine (100 mL) prior to drying over sodium sulfate, filtering, and concentrating in vacuo to give a yellow oily solid (3.62 g). The crude was purified by column chromatography (9.5:0.5 Petrol:EtOAc) to give a colourless oil (1.94 g, 82 %).

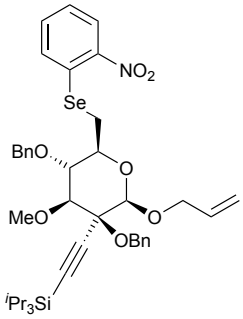
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.08 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$), 3.20 (1H, dd, *J* = 8.6 Hz, 10.2 Hz, C*H*$_a$I), 3.27-3.31 (1H, m, 6-*H*), 3.42 (1H, d, *J* 9.1 Hz, 4-*H*), 3.52 (1H, dd, *J* = 1.9 Hz, 10.2 Hz, C*H*$_b$I), 3.56 (1H, app. t, *J* = 9.0 Hz, 5-*H*), 3.77 (3H, s, 4-OC*H*$_3$), 4.15 (1H, ddt, *J* = 1.2 Hz, 6.4 Hz, 12.9 Hz, OC*H*$_2$CH=CH$_2$), 4.42 (1H, ddt, *J* = 1.4 Hz, 4.8 Hz, 12.9 Hz, OC*H*$_2$CH=CH$_2$), 4.52 (1H, s, 2-*H*), 4.62 (1H, d, *J* = 11.0 Hz, C*H*$_2$Ph), 4.90 (1H, d, *J* = 11.0 Hz, C*H*$_2$Ph), 5.02 (1H, d, *J* = 12.3 Hz, C*H*$_2$Ph), 5.12 (1H, d, *J* = 12.3 Hz, C*H*$_2$Ph), 5.19 (1H, dd, *J* = 1.5 Hz, 10.5 Hz, OCH$_2$CH=C*H*$_2$), 5.35 (1H, dd, *J* = 1.5 Hz, 17.3 Hz, OCH$_2$CH=C*H*$_2$), 5.88-5.98 (1H, m, OCH$_2$C*H*=CH$_2$), 7.20-7.23 (1H, m, Ar-*H*), 7.28-7.37 (7H, m, Ar-*H*), 7.46-7.47 (2H, m, Ar-*H*).

^{13}C NMR (100 MHz): δ_C 5.8, 11.1, 18.6, 62.0, 70.2, 70.7, 75.2, 75.5, 77.2, 78.6, 89.0, 90.6, 102.6, 102.7, 117.7, 126.8, 127.5, 127.8, 127.9, 128.1, 128.5, 133.7, 138.0, 139.9.

IR ν_{max} (thin film, cm^{-1}): 1071, 1108.

HRMS: *m/z* (ESI+): calculated for $C_{35}H_{49}O_5SiI$ $[M+NH_4]^+$; 722.2732, found 722.2735 (error -0.21).

(((2R,3S,4S,5S,6S)-2-(allyloxy)-3,5-bis(benzyloxy)-4-methoxy-6-(((2-nitrophenyl)selanyl)methyl) tetrahydro-2H-pyran-3-yl)ethynyl)triisopropylsilane (33b)



In a dry Schlenk flask, to a solution of ((2R,3R,4S,5S,6R)-6-(allyloxy)-3,5-bis(benzyloxy)-4-methoxy-5-((triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-2-yl)methanol (**32**, 490 mg, 0.82 mmol, 1 eq) and 2-nitrophenylselenocyanate (281 mg, 1.24 mmol, 1.5 eq) in dry THF (2 mL) stirring at 0 °C under N_2 was added dropwise PBu_3 (0.31 mL, 1.24 mmol, 1.5 eq). The mixture was then allowed to warm to room temperature, stirred for 17 h and concentrated *in vacuo*. Purification by chromatography on silica gel, eluting 15:1 to 10:1 petrol:EtOAc gave the titled compound (490 mg 76%) as a bright yellow oil.

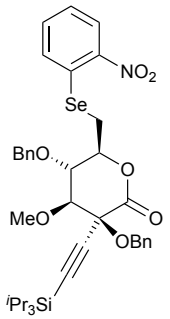
^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.07 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$)); 2.90 (1H, dd, *J* = 9.4 Hz, 12.8 Hz, C*H*$_2$Se), 3.27 (1H, dd, *J* = 1.5 Hz, 12.8 Hz, C*H*$_2$Se), 3.44 (1H, d, *J* = 9.0 Hz, 4-*H*), 3.50-3.53 (1H, m, 6-*H*), 3.68 (1H, app t, *J* = 9.0 Hz, 5-*H*), 3.81 (3H, s, OC*H*$_3$), 4.05 (1H, dd, *J* = 6.2 Hz, 12.9 Hz, OC*H*$_2$CHCH$_2$), 4.31 (1H, dd, *J* = 4.9 Hz, 12.9 Hz, OC*H*$_2$CH=CH$_2$), 4.49 (1H, s, 2-*H*), 4.66 (1H, d, *J* = 11.2 Hz, C*H*$_2$Ph), 4.98 (1H, d, *J* = 11.2 Hz, C*H*$_2$Ph), 5.01 (1H, d, *J* = 12.3 Hz, C*H*$_2$Ph), 5.12 (1H, d, *J* = 12.3 Hz, C*H*$_2$Ph), 5.15 (1H, dd, *J* = 1.1 Hz, 10.4 Hz, OCH$_2$CH=C*H*$_2$), 5.29 (1H, dd, *J* = 1.1 Hz, 17.2 Hz, OCH$_2$CH=C*H*$_2$), 5.81-5.91 (1H, m, OCH$_2$C*H*=CH$_2$), 7.22-7.26 (2H, m, Ar-*H*), 7.28-7.37 (8H, m, Ar-*H*), 7.47 (2H, d, *J* 7.4 Hz, Ar-*H*), 7.52 (1H, d, *J* 7.8 Hz, Ar-*H*), 8.27 (1H, dd, *J* 1.1 Hz, 8.0 Hz, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 11.1, 18.6, 28.1, 61.9, 70.2, 70.7, 75.2, 75.3, 77.2, 78.6, 89.2, 90.7, 102.7, 102.8, 117.6, 125.2, 126.3, 126.9, 127.5, 127.9, 128.0, 128.4, 128.5, 129.4, 133.49, 133.52, 134.0, 138.2, 140.0, 146.6.

IR ν_{max} (thin film, cm^{-1}): 3030, 2941, 2863, 1590, 1511.

HRMS: *m/z* (ESI+): calculated for $C_{41}H_{53}NO_7SeSi$ $[M+K]^+$: 818.2388, found 818.2382.

(3*S*,4*S*,5*S*,6*S*)-3,5-bis(benzyloxy)-4-methoxy-6-(((2-nitrophenyl)selanyl)methyl)-3-((triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-2-one (34b)



(((2*R*,3*S*,4*S*,5*S*,6*S*)-2-(allyloxy)-3,5-bis(benzyloxy)-4-methoxy-6-(((2-nitrophenyl)selanyl)methyl) tetrahydro-2H-pyran-3-yl)ethynyl)triisopropylsilane (**33b**, 475 mg, 0.61 mmol, 1 eq), $PdCl_2$ (22 mg, 0.12 mmol, 0.2 eq), dry methanol (8 mL), dry DCM (8 mL) were stirred vigorously at room temperature for 20 hours. Additional $PdCl_2$ (22 mg, 0.12 eq, 0.2 eq) was then added and the reaction was stirred for 24 hours. The reaction mixture was diluted with Et_2O (50 mL), filtered through celite and evaporated. DMSO (4 mL) and acetic anhydride (2 mL) were added sequentially, and the resulting solution was stirred at room temperature for 17 hours. The reaction mixture was poured in saturated aqueous $NaHCO_3$ (50 mL) and extracted with EtOAc (3 x 75 mL). The combined organic layers were washed with brine (2 x 30 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by chromatography on silica gel, eluting petrol : DCM 1:4 to 0:1 gave the titled compound (255 mg, 57% over two steps) as a bright yellow oil.

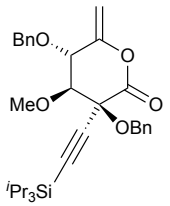
^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 0.97 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$)), 3.26 (1H, dd, *J* = 7.4 Hz, 13.3 Hz, C*H*$_2$Se), 3.36 (1H, dd, *J* = 3.7 Hz, 13.3 Hz, C*H*$_2$Se), 3.56 (3H, s, OC*H*$_3$), 3.80 (1H, d, *J* = 8.9 Hz, 4-*H*), 3.83-3.86 (1H, m, 5-*H*), 4.60 (1H, d, *J* = 11.2 Hz, C*H*$_2$Ph), 4.79 (1H, d, *J* = 11.2 Hz, C*H*$_2$Ph), 4.95 (1H, d, *J* = 11.1 Hz, C*H*$_2$Ph), 5.11 (1H, d, *J* = 11.1 Hz, C*H*$_2$Ph), 5.10-5.16 (1H, m, 6-*H*), 7.28-7.40 (10H, m, Ar-*H*), 7.43 (2H, d, *J* 7.4 Hz, Ar-*H*), 7.54 (1H, d, *J* 7.9 Hz, Ar-*H*), 8.29 (1H, d, *J* 8.1 Hz, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 11.0, 18.42, 18.44, 28.6, 61.0, 69.0, 72.6, 76.1, 77.8, 81.0, 84.6, 96.2, 96.7, 125.5, 126.4, 127.6, 128.0, 128.2, 128.4, 128.6, 128.8, 132.9, 133.7, 136.7, 138.1, 146.6, 166.0.

IR ν_{max} (thin film, cm^{-1}): 3031, 2941, 2864, 1772, 1590.

HRMS: m/z (ESI+) calculated for $C_{38}H_{47}NO_7SeSi$ $[M+Na]^+$: 760.2179, found 760.2180.

(3*S*,4*S*,5*S*)-3,5-bis(benzyloxy)-4-methoxy-6-methylene-3-((triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-2-one (23)



mCPBA (70%, 373 mg, 1.51 mmol, 1.2 eq) was added in one portion to a solution of (3*S*,4*S*,5*S*,6*S*)-3,5-bis(benzyloxy)-4-methoxy-6-(((2-nitrophenyl)selanyl)methyl)-3-((triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-2-one (**34b**, 930 mg, 1.26 mmol, 1 eq) in DCM (40 mL) at -78 °C with stirring. The reaction was warmed to 0 °C over 2.5 h, poured into ice cold saturated aqueous $NaHCO_3$ (100 mL) and extracted with DCM (3 x 150 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was dissolved in THF (40 mL), and $NaHCO_3$ (5.29 g, 50 eq) was added. The resulting mixture was then stirred at 65 °C for 3 h. Saturated aqueous $NaHCO_3$ (100 mL) was added, and the mixture was extracted with Et_2O (3 x 150 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by chromatography on silica gel, eluting 10:1 petroleum ether/EtOAc gave the titled compound (545 mg, 78%) as a yellow oil.

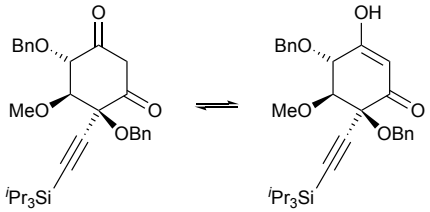
^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 1.09 (21H, s, Si((C*H*$_3$)$_2$C*H*)$_3$)), 3.60 (3H, s, OC*H*$_3$), 3.81 (1H, d, *J* = 4.1 Hz, 4-*H*), 4.29-4.31 (1H, m, 5-*H*), 4.64 (1H, d, *J* = 11.6 Hz, C*H*$_2$Ph), 4.71 (1H, d, *J* = 11.6 Hz, C*H*$_2$Ph), 4.77 (1H, d, *J* = 11.1 Hz, C*H*$_2$Ph), 4.80 (1H, app. t, *J* = 1.6 Hz, C*H*$_2$CO), 4.93 (1H, d, *J* = 11.1 Hz, C*H*$_2$Ph), 4.99 (1H, app. t, *J* = 1.6 Hz, C*H*$_2$CO), 7.28-7.37 (10H, m, Ar-*H*).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 11.1, 18.5, 61.0, 69.3, 72.0, 77.0, 77.2, 84.9, 94.6, 98.1, 98.4, 127.8, 127.97, 128.01, 128.18, 128.21, 128.5, 137.16, 137.22, 151.8, 164.0.

IR ν_{max} (thin film, cm^{-1}): 3032, 2942, 2865, 1786, 1665.

HRMS *m/z* (ESI+) calculated for $C_{32}H_{42}O_5Si$ $[M+K]^+$: 573.2433, found 573.2437.

(4*S*,5*S*,6*S*)-4,6-bis(benzyloxy)-5-methoxy-4-((triisopropylsilyl)ethynyl)cyclohexane-1,3-dione (3)



NaOMe (2.3 mg, 0.042 mmol, 1.5 eq) was suspended in dry DMSO (1 mL). A solution of (3*S*,4*S*,5*S*)-3,5-bis(benzyloxy)-4-methoxy-6-methylene-3-((triisopropylsilyl)ethynyl)tetrahydro-2H-pyran-2-one (**23**, 15 mg, 0.028 mmol, 1 eq) in dry DMSO (1 mL) was added dropwise over 2.5 h. The resulting solution was stirred for 30 min and then the mixture was diluted with water (5 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were extracted with water (10 mL). The combined aqueous layers were then acidified to pH 3 using HCl (1 M) and extracted with EtOAc (4 x 10 mL). The combined organic layers were then dried over $MgSO_4$ and evaporated. The original organic layers were also dried and evaporated. All crudes were combined and purified by silica gel column chromatography (3 g silica, toluene:acetone 10:1 to 3:1) affording the titled compound as a 1:1 mixture of diketone and enol ketone (10 mg, 67%). Starting material **26** (5 mg, 33%) was also recovered.

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.11 and 1.13 (21H (keto and enol), s, Si((C*H*$_3$)$_2$*CH*)$_3$)), 3.39 (1H, d, *J* = 16.6 Hz, keto 2-*H*$_2$), 3.60 (1H, d, *J* = 7.3 Hz, enol 5-*H*), 3.72 (1H, dd, *J* = 0.8 Hz, 16.6 Hz, keto 2-*H*$_2$), 3.62 (3H, s, OC*H*$_3$), 3.83 (1H, d, *J* = 8.7 Hz, keto 5-*H*), 3.84 (3H, s, OC*H*$_3$), 4.44 (1H, d, *J* = 7.3 Hz, enol 6-*H*), 4.52 (1H, d, *J* = 11.5 Hz, C*H*$_2$Ph), 4.69 (1H, d, *J* = 11.7 Hz, C*H*$_2$Ph), 4.70-4.71 (1H, m, keto 6-*H*), 4.72 (1H, d, *J* = 11.5 Hz, C*H*$_2$Ph), 4.77 (1H, d, *J* = 11.4 Hz, C*H*$_2$Ph), 4.89 (1H, d, *J* = 11.5 Hz, C*H*$_2$Ph), 4.92 (1H, d, *J* = 11.7 Hz, C*H*$_2$Ph), 4.96 (1H, d, *J* = 11.5 Hz, C*H*$_2$Ph), 5.11 (1H, d, *J* = 11.4 Hz, C*H*$_2$Ph), 5.45 (1H, d, *J* = 1.6 Hz, enol 2-*H*), 6.81 (1H, br s, enol O*H*), 7.26-7.42 (10H, m, Ar-H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 11.1, 11.2, 18.5, 18.58, 18.59, 52.9, 61.92, 61.96, 68.3, 69.4, 74.0, 75.1, 75.7, 80.2, 82.6, 83.2, 83.7, 87.4, 93.1, 96.2, 97.6, 100.7, 102.3, 127.5, 127.9, 127.96, 128.03, 128.11, 128.13, 128.2, 128.25, 128.3, 128.35, 128.4, 128.6, 129.0, 137.0, 137.1, 137.3, 137.9, 195.5, 198.4.

IR ν_{max} (thin film, cm^{-1}): 3032, 2941, 2864, 1602.

HRMS: *m/z* (ESI+): calculated for $C_{32}H_{42}O_5Si$ $[M+H]^+$: 535.2874, found 535.2888.

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