The Claisen rearrangement approach to fused bicyclic medium-ring oxacycles.

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Experimental

**General Information:** $^{1}$H-NMR spectra were recorded on Bruker DPX-250 (250 MHz), Bruker DRX-400 (400 MHz) and Bruker DRX-500 (500 MHz) spectrometers using deuterochloroform as an internal deuterium lock. The chemical shifts are quoted in ppm relative to tetramethylsilane ($\delta = 0.00$ ppm). The multiplicity of the signal is indicated as: s - singlet, d - doublet, t - triplet, q - quartet, qn - quintet, sp - septet, br - broad, m - multiplet, dd - doublet of doublets, dt - doublet of triplets etc. Coupling constants ($J$) are quoted in Hz. Two dimensional (2D) spectra were recorded on Bruker DRX-500 (500 MHz) spectrometers, fitted with gradient coils. Double Quantum Filtered (DQF) and magnitude COSY spectra were typically acquired with 256 slices in F$_1$ and 2048 points in F$_2$ (acquisition time approximately 20 min). Where useful, the FID was zero filled (128 K) and sine-bell shifted (SSB = 30) prior to Fourier Transformation in order to provide baseline resolved multiplets and, as a result, easily identifiable and measurable coupling constants. $^{13}$C-NMR spectra were recorded on Bruker DPX-250 (62.5 MHz), Bruker DRX-400 (100 MHz) and Bruker DRX-500 (125 MHz) instruments using an internal deuterium lock and proton decoupling. The chemical shift are quoted in ppm relative to tetramethylsilane ($\delta = 0.00$ ppm). The multiplicity of the signal was determined by attached proton tests (APT) or distortionless enhancement by polarisation transfer (DEPT) experiments and is indicated as C (s), CH (d), CH$_2$ (t) and CH$_3$ (q) groups where determined. Infrared spectra were recorded on Perkin-Elmer 1600 series FTIR (nujol, film, CHCl$_3$) and Perkin-Elmer Spectrum One ATR-FTIR (film) spectrometers. Mass spectra were recorded by the EPSRC Mass Spectrometry Service Centre, University of Swansea or the University of Cambridge. In Swansea, Electron Impact (EI) and Chemical Ionisation (CI) low resolution spectra were carried out on a VG model 12-253 under ACE conditions and a Quattro II low resolution triple quadrupole MS. Accurate mass measurements for EI and CI were performed on a +VG ZAB-E and Finnigan MAT 900 XLT instruments. In Cambridge, FAB, EI and CI low resolution and accurate mass spectra were performed on a Kratos MS-890 and on a Micromass Q-TOF instrument. Electrospray spectra were determined with an ES Bruker FTICR. All CI measurements were performed with NH$_3$ as the carrier gas. Microanalyses were carried out by the staff of the Microanalytical Service at the University of Cambridge. Melting Points were determined using a Köfler block melting point apparatus and are
uncorrected. Optical specific rotations were carried out using a Perkin-Elmer 241 polarimeter in a cell of path length 1 dm. The concentration \((c)\) is expressed in g/100 cm\(^3\). The specific rotation, denoted as \([\alpha]_D^T\), implies units of °cm\(^2\)g\(^-1\) (\(T = \text{temp } ^\circ\text{C}\)). Kugelrohr bulb-to-bulb distillations were carried out using a Büchi GKR-51 machine. Boiling points are the actual oven temperatures. Flash chromatography was carried out on silica gel [Merck 9385 Kieselgel 60 (230–400 ASTM)]. TLC was performed on 0.25 mm thick plates precoated with Merck Kieselgel 60 F\(_{254}\) silica gel. Non-aqueous reactions were carried out under an atmosphere of dry nitrogen or argon unless indicated to the contrary. Dry THF was distilled from potassium in a recycling still using benzophenone ketyl as indicator. Other solvents were purified by standard techniques. Ether refers to diethyl ether. Dioxane refers to 1,4-dioxane. Brine refers to a saturated solution of sodium chloride in water.

\((Z, \ 3S, \ 8S)-3-(\text{Benzyloxymethyl})oxy-2-methylene-8-triisopropylsilyloxyethyl-3,4,7,8-tetrahydro-2H-oxocine \textbf{10}\)

To a stirred solution of the lactone \textbf{7} (790 mg, 1.76 mmol) in toluene (60 mL) was added dimethyltitanocene (9.5 mL of a 50 mg/mL solution in toluene, 2.3 mmol) and the resulting orange solution was heated at reflux for 0.7 h. The resulting dark orange solution was allowed to cool and the solvent was removed \textit{in vacuo}. The residue was dissolved in DCM and deactivated basic alumina was added (6\% w/w water). The residue was preadsorbed onto alumina and purification by gravity chromatography (deactivated basic alumina, hexanee:ether, 20:1→10:1) provided the title compound \textbf{10} as a slightly yellow oil. Hexane was added and the yellow solution was allowed to stand overnight. Filtration through Celite\textsuperscript{™} followed by removal of the solvent \textit{in vacuo} provided the enol ether \textbf{10} as a clear and colourless oil (558 mg, 1.25 mmol, 71\%); (Found: C, 70.3; H, 9.6\%; C\(_{26}\)H\(_{42}\)O\(_4\)Si requires C, 69.9; H, 9.5\%); \([\alpha]_D^{21}\) -90.6 (c 0.805 in CHCl\(_3\)); IR (CDCl\(_3\)): \(\nu=1645\) (enol ether); \(^1\)H NMR (250 MHz, CDCl\(_3\)): \(\delta=7.37-7.26\) (5H, m, Ar), 5.83 (1H, dt, \(J\ (H, \ H)=10.9, \ 7.9\) Hz), 5.65 (1H, dt, \(J\ (H, \ H)=10.6, \ 7.4\) Hz), 4.88 (1H, d, \(J\ (H, \ H)=7.0\) Hz), 4.75 (1H, d, \(J\ (H, \ H)=7.0\) Hz), 4.72-4.72 (1H, d, \(J\ (H, \ H)=1.0\) Hz, OCH=CH\(_2\)), 4.68 (1H, d, \(J\ (H, \ H)=11.8\) Hz), 4.59 (1H, d, \(J\ (H, \ H)=1.0\), OCH=CH\(_2\)), 4.56 (1H, d, \(J\ (H, \ H)=11.8\) Hz), 4.22 (1H, dd, \(J\ (H,
H) = 10.7, 4.9 Hz), 3.97 (1H, dd, J (H, H) = 9.5, 5.6 Hz), 3.97 (1H, dd, J (H, H) = 9.5, 5.6 Hz), 3.86-3.77 (1H, m), 3.66 (1H dd, J (H, H) = 9.5, 7.0 Hz), 2.80 (1H, q, J (H, H) = 10.7 Hz, allylic), 2.45-2.18 (3H, m, allylic), 1.16-1.03 (21H, m, ((CH₃)₂CH)₃Si); ¹³C NMR (50 MHz, CDCl₃): δ = 162.0 (2-C), 138.0, 129.8, 129.0, 128.4, 128.0, 127.7, 102.7, 91.8, 86.1, 79.1, 69.6, 66.1 (CH₂OSi), 30.8, 30.2 (4-C, 7-C), 18.0 (((CH₃)₂CH)₃Si), 11.9 (((CH₃)₂CH)₃Si); MS (EI): m/z (%): 446 (M⁺, 8), 265 (100); Found 446.2852, C₂₆H₄₂O₄Si requires 446.2852.

(Z, 3S, 8S)-3-Hydroxy-2-methylene-8-triisopropylsilyloxyethyl-3,4,7,8-tetrahydro-2H-oxocine 11

To a stirred solution of the enol ether 10 (245 mg, 0.55 mmol) in THF (20 mL) at -78 °C was added freshly prepared LiDBB (2 mL of a solution prepared by sonicating di-tert-butylbiphenyl (1 g, 3.8 mmol) and lithium (26 mg, 3.8 mmol) in THF (4 mL) for 2 h). Stirring was continued for 1 min whereupon the green colour of the LiDBB had mainly discharged. Further LiDBB (1 mL) was added and stirring was continued for 2 min with the dark green colour of the LiDBB remaining. The reaction mixture was quenched at -78 °C by the addition of a saturated solution of NH₄Cl (20 mL) and the reaction mixture was allowed to reach room temperature. Ether (20 mL) was added and the organic phase was separated. The aqueous phase was further extracted with ether (2 × 20 mL) and dried (K₂CO₃). Purification by gravity chromatography (deactivated basic alumina, hexane:ether, 2:1) provided the title compound 11 as a clear and colourless oil (168 mg, 0.52 mmol, 94%); [α]D³⁺ = 5.9 (c 1.015 in CHCl₃); IR (CDCl₃): ν = 3500, 1649; ¹H NMR (250 MHz, CDCl₃): δ = 5.87-5.66 (m, 2H; 5-H, 6-H), 4.62 (d, J (H, H) = 1.4 Hz, 1H; OC=CH/H), 4.61 (d, J (H, H) = 1.4 Hz, 1H; OC=CH/H), 4.26-4.18 (m, 1H), 3.95-3.85 (m, 2H), 3.70-3.62 (m, 1H), 2.65 (dt, J (H, H) = 12.6, 9.1 Hz, 1H; allylic), 2.38-2.24 (m, 3H; allylic), 2.08 (d, J (H, H) = 8.0 Hz, 1H; OH), 1.16-1.01 (m, 21H; ((CH₃)₂CH)₃Si); ¹³C NMR (62.5 MHz, CDCl₃): δ = 164.2 (2-C), 129.4, 129.1 (5-C, 6-C), 99.5 (OC=CH₂), 84.4, 75.5 (3-C, 8-C), 65.3 (CH₂OSi), 33.0, 29.5 (4-C, 2-C), 18.0 (((CH₃)₂CH)₃Si), 11.9 (((CH₃)₂CH)₃Si); MS (CI, NH₃): m/z (%): 344 ((M+NH₄)⁺, 40), 327 ((M+H)⁺, 30), 77 (100); Found 327.2353, C₁₈H₃₅O₃Si requires 327.2353.
(Z, 3S, 8S)-3-Dimethylsilyloxy-2-methylene-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2H-oxocine 12

To a stirred solution of the enol ether 11 (114 mg, 0.35 mmol) in 1,1,3,3-tetramethyldisilazane (0.8 mL) was added solid NH₄Cl (ca. 2 mg) and the reaction mixture was heated to 60 °C and stirred at that temperature overnight. The reaction mixture was allowed to cool, dry hexane was added and filtration through a cotton wool plug followed by removal of the solvent in vacuo gave the required silane 12 (132 mg, 0.34 mmol, 99%) as an unstable oil; IR (CDCl₃): ν = 2118, 1646; ¹H NMR (250 MHz, CDCl₃): δ = 5.85-5.75 (m, 1H), 5.69-5.58 (m, 1H), 4.66 (sp, J (H, H) = 2.8 Hz, 1H; SiH), 4.59 (s, 1H; OC=CHH), 4.53 (s, 1H; OC=CHH), 4.17 (dd, J (H, H) = 10.7, 4.9 Hz, 1H), 3.98 (dd, J (H, H) = 9.4, 5.4 Hz, 1H), 3.82-3.77 (m, 1H; OC=C), 3.67 (dd, J (H, H) = 9.4, 7.0 Hz, 1H), 2.78 (q. J (H, H) = 10.8 Hz, 1H; allylic), 2.44-2.15 (m, 3H; allylic), 1.16-1.03 (m, 21H; ((CH₃)₂CH)₃Si), 0.22 (d, J (H, H) = 2.8 Hz, 6H; ((CH₃)₂SiH)); ¹³C NMR (62.5 MHz, CDCl₃): δ = 164.7 (2-C), 129.8, 129.1 (5-C, 6-C), 100.7 (OC=CH₂), 86.2, 77.9 (3-C, 8-C), 66.2 (CH₂OSi), 32.7, 30.9 (4-C, 7-C), 18.0 (((CH₃)₂CH)₃Si), 11.9 (((CH₃)₂CH)₃Si), -1.0 ((CH₃)₂Si); due to the instability of this compound satisfactory mass spectral data could not be obtained.

(Z, 2R, 3S, 8S)-3-Hydroxy-2-hydroxymethyl-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2H-oxocine 13

In a glove box a Schlenk tube was charged with (bicyclo(2.2.1)hepta-2,5-diene)(1,4-bis(diphenylphosphino)butane)rhodium(I) tetrafluoroborate (10 mg, 14.1 µmol). The Schlenk tube was removed form the glove box and the enol ether 11 (180 mg, 0.47 mmol) was added via cannula as a solution in THF (12 mL, 2 mL rinse). The resulting yellow solution was heated to 65 °C and stirred at that temperature over night. The reaction mixture was allowed to cool, ethylenediaminetetraacetic acid, disodium salt dihydrate (ca. 50 mg) was added and the resulting suspension was stirred for 1 h. The reaction mixture was diluted with hexane and filtered through a
pad of Celite™. The solvent was removed in vacuo to furnish a brown oil which was taken-up in THF / MeOH (1:1, 6 mL) to which a 15% solution of potassium hydroxide (0.73 mL) and 30% H₂O₂ (0.38 mL) were added. The reaction mixture was stirred for 1 h whereupon further potassium hydroxide solution (0.3 mL) and H₂O₂ (0.3 mL) were added. After 0.5 h the reaction was quenched by the addition of powdered sodium thiosulfate and stirring was continued overnight. The suspension was diluted with EtOAc (25 mL), dried (MgSO₄) and filtered through a pad of Celite™. The solvent was removed in vacuo and purification by flash chromatography (DCM:MeOH, 100:0→97:3) yielded the enol ether 11 (7 mg, 21 µmol, 5%). Further elution of the column furnished the title compound 13 (139 mg, 40 mmol, 86%) which was a slightly impure and proved difficult to purify further and hence was used in the next reaction without further purification. Characterisation is on the slightly impure compound; Rf 0.2 (DCM:MeOH, 95:5); IR (CHCl₃): υ=3621, 3441; ¹H NMR (250 MHz, CDCl₃): δ=5.92-5.70 (m, 2H; 5-H, 6-H), 3.95 (dd, J (H, H)=11.3, 9.4 Hz, 1H), 4.0-3.85 (br, 1H; OH), 3.84-3.49 (m, 6H), 2.45-2.02 (m, 5H; 4-H, 4'-H, 7-H, 7'-H, OH), 1.15-1.03 (21H, m, ((CH₃)₂CH)₃Si); ¹³C NMR (62.5 MHz, CDCl₃): δ=128.2, 128.0 (5-C, 6-C), 77.3, 76.5, 72.2, 64.9, 63.7, 35.4, 28.3, 17.9 (((CH₃)₂CH)₃Si), 11.9 (((CH₃)₂CH)₃Si); MS (CI, NH₃): m/z(%): 362 ((M+NH₄)⁺, 15%), 345 ((M+H)⁺, 100); Found 345.2460, C₁₈H₃₇O₄Si requires 345.2461.

\[(Z, 2R, 4aR, 6S, 10aS)-2-(4-Methoxy-phenyl)-6-triisopropylsilanyloxymethyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxa-benzocyclooctene\] 14

To a stirred solution of the slightly impure diol 13 (139 mg, 0.4 mmol) in benzene (12 mL) were added freshly distilled anisaldehyde (58 µl, 65 mg, 0.48 mmol) and PPTS (5 mg). The reaction mixture was heated at reflux with azeotropic removal of water (Dean-Stark apparatus) for 12 h and then allowed to cool. The solvent was removed in vacuo and the residue was preabsorbed onto silica. Purification by flash chromatography (hexane:ether, 5:1) yielded the title compound 14 (156 mg, 0.34 mmol, 85%) as a clear and colourless oil; Rf 0.3 (hexane:ether, 3:1); [α]D²⁸ -8.7 (c 0.195 in CHCl₃); IR (CHCl₃): υ=2944, 2866; ¹H NMR (500 MHz, CDCl₃): δ=7.40 (d, J (H, H)=8.6 Hz, 2H; Ar), 6.88 (d, J (H, H)=8.6 Hz, 2H; Ar), 6.88 (d, J (H, H)=8.6 Hz, 2H; Ar), 5.90 (dt, J (H, H)=10.3,
8.3 Hz, 1H; 9-H), 5.72 (dt, J (H, H)=10.3, 9.6 Hz, 1H; 8-H), 5.39 (s, 1H; 2-H), 4.17 (dd, 1H; J (H, H)=10.8, 5.3 Hz, 1H; 4-H), 3.89 (ddd, J (H, H)=10.8, 8.3, 5.3 Hz, 1H; 4a-H), 3.88 (dd, J (H, H)=10.5, 5.8 Hz, 1H; CH/HOSi), 3.81 (dd, J (H, H)=10.5, 5.1 Hz, 1H; CH/HOSi), 3.80 (s, 3H; CH$_3$O), 3.62-3.59 (m, 1H; 6-H), 3.57 (t, J (H, H)=10.8 Hz, 1H; 4-H'), 3.50 (ddd, J (H, H)=13.3, 8.5, 2.6 Hz, 1H; 10a-H), 2.55-2.47 (m, 2H; 7-H, 10-H), 2.40 (ddd, J (H, H)=13.3, 8.5, 2.6 Hz, 1H; 10-H'), 2.14 (ddd, J (H, H)=13.9, 6.9, 3.0 Hz, 1H; 7-H'), 1.16-1.05 (21H, m, ((CH$_3$)$_2$CH)$_3$Si); 13C NMR (62.5 MHz, CDCl$_3$): $\delta$=160.0, 130.5, 129.0, 127.4, 113.7, 100.8 (2-C), 80.5, 76.3, 70.3, 67.8 (4-C), 65.4 (CH$_2$OSi), 55.3 (CH$_3$O), 33.0, 28.3, 18.0 (((CH$_3$)$_2$CH)$_3$Si), 11.9 (((CH$_3$)$_2$CH)$_3$Si); MS (CI, NH$_3$): m/z (%) 463 ((M+H)$^+$, 45), 154 (100); Found 463.2876, C$_{26}$H$_{42}$O$_5$Si requires M, 463.2880.

(Z, 2R, 3S, 8, S)-2-Hydroxymethyl-3-(p-methoxybenzyloxy-8-triisopropylsilyloxyethyl-3,4,7,8-tetrahydro-2H-oxocine 15

To a stirred solution of the oxocane 14 (131 mg, 0.28 mmol) in toluene (4 mL) at -78 °C was added DIBAL-H (1.98 mL of a 1.0 M solution in DCM, 1.98 mmol). The resulting solution was stirred at -50 °C for 1 h and then at -30 °C for 1.5 h whereupon TLC analysis indicated that all the starting material had been consumed. The reaction mixture was recooled to -78 °C and quenched by the dropwise addition of MeOH (1.5 mL). The reaction mixture was allowed to warm to ambient temperature and a saturated solution of NH$_4$Cl (6 mL), 1 M sodium potassium tartrate (6 mL) and ether (10 mL) were added. The resulting gel was stirred until dissolution occurred (ca. 1 h). The organic phase was separated and the aqueous phase extracted with ether (10 mL). The organic phases were washed with brine (10 mL) and dried (MgSO$_4$) and the solvent was removed in vacuo. Purification by flash chromatography (hexane:ether, 1:1) gave the title compound 15 (104 mg, 0.22 mmol, 80%) as a white crystalline solid; mp 121-121.5 °C (from hexane); $[\alpha]_D^{21}+70.2$ (c 0.43 in CHCl$_3$); IR (CHCl$_3$): v=3451; $^1$H NMR (250 MHz, CDCl$_3$): $\delta$=7.23 (d, J (H, H)=8.6 Hz, 2H; Ar), 6.88 (d, J (H, H)=8.6 Hz, 2H; Ar), 5.90-5.70 (m, 2H; 5-H, 6-H), 4.56 (d, J (H, H)=11.0 Hz, 1H; ArCH/H), 4.34 (d, J (H, H)=11.0 Hz, 1H; ArCH/H), 3.96-3.76 (m, 8H), 3.79 (s, 3H; CH$_3$O), 3.59 (dd, J (H, H)=11.3, 3.1 Hz, 1H), 3.44 (ddd, J (H, H)=10.3, 8.2, 1.6 Hz,
1H), 3.27 (dt, \(J (H, H)=8.7, 2.8 \text{ Hz}, 1H\)), 2.53 (ddd, \(J (H, H)=13.5, 8.3, 2.8 \text{ Hz}, 1H\); allylic), 2.41-2.29 (m, 1H; allylic), 2.23-2.10 (m, 2H; allylic), 1.19-0.98 (21H, m, ((CH\(_3\))\(_2\)CH)\(_3\)Si); 13C NMR (62.5 MHz, CDCl\(_3\)): \(\delta=159.3, 130.0, 129.5, 128.7, 127.9, 113.9, 79.2, 75.6, 71.4, 64.8 \text{ (CH}_2\text{OSi}), 55.3 \text{ (CH}_3\text{O)}, 30.1, 28.5, 17.9 ((\text{CH}_3)\text{CH})\(_3\)Si), 11.9 ((\text{CH}_3)\text{CH})\(_3\)Si); MS (CI, NH\(_3\)): \(m/z\) (%) 482 ((M+NH\(_4\))\(^+\), 10), 465 ((M+H\(^+\), 40), 345 (100); Found 465.3041, C\(_{26}\)H\(_{45}\)O\(_5\)Si requires 465.3036.

\((Z, 2R, 3S, 8S)-2\text{-Carboxaldehyde-3-(4-methoxybenzyl)oxy-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2H-oxocine 16, (Z, 2R, 3S, 8S)-2-((S)-1-hydroxy-prop-2-eneyl)-3-(4-methoxybenzyl)oxy-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2H-oxocine 18, and (Z, 2R, 3S, 8S)-2-((R)-1-hydroxy-prop-2-eneyl)-3-(4-methoxybenzyl)oxy-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2H-oxocine 17}\)

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\text{To a stirred solution of the oxocane 15 (64 mg, 0.138 mmol) in DMSO (10 mL) at ambient temperature was added IBX (116 mg, 414 mmol). The resulting cloudy suspension became clear and colourless within 10 min and was stirred overnight. Water (20 mL) and ether (15 mL) were added and the organic phase was separated. The aqueous phase was extracted with ether (2 \times 15 mL) and the organic phases were washed with water (2 \times 20 mL), brine (20 mL) and dried (MgSO\(_4\)). The solvent was removed in vacuo to yield a semi-solid colourless residue 16 that was used in the next reaction without further purification; IR (CDCl\(_3\)): \(\nu=2857, 1734; ^1\text{H NMR (250 MHz, CDCl}_3\)): \(\delta=9.67 \text{ (d, J (H, H)=1.8 Hz, 1H; CHO)}, 7.23 \text{ (d, J (H, H)=8.8 Hz, 2H; Ar)}, 6.85 \text{ (d, J (H, H)=8.8 Hz, 2H; Ar)}, 5.90-5.70 \text{ (m, 2H; 5-H, 6-H)}, 4.58 \text{ (d, J (H, H)=11.1 Hz, 1H; ArCHH)}, 4.41 \text{ (d, J (H, H)=11.0 Hz, 1H; ArCHH)}, 4.19 \text{ (dd, J (H, H)=9.4, 1.7 Hz, 1H; 2-H)}, 3.99-3.95 \text{ (m, 5H)}, 3.79 \text{ (s, 3H; CH}_3\text{O)}, 2.59-2.30 \text{ (m,4H; allylic)}, 1.12-1.00 \text{ (m, 21H; ((CH}_3\text{)}_2\text{CH})_3\text{Si})}. \text{ The crude aldehyde 16 was coevaporated with toluene (3 \times 2 mL) and put under argon. In a glove box a Schlenk tube was charged with anhydrous cerium(III) chloride (190 mg, 0.772 mmol, ex-Aldrich). THF (3 mL) was added and the resulting granular suspension was sonicated for 2 h to yield a milky white suspension which was stirred overnight. The Schlenk}
flask was then cooled to -78 °C and vinylmagnesium bromide (0.69 mL of a 1.0 M solution in THF, 0.69 mmol) was added. The yellow reaction mixture was stirred for 2 h at -78 °C and the aldehyde 16 was added as solution in THF (1 mL, 2 × 0.5 mL) via cannula. The reaction mixture was stirred for 1 h at -78 °C and then at ambient temperature for 15 min. The reaction mixture was quenched by the addition of a saturated aqueous solution of NH₄Cl (15 mL) ether (15 mL) and enough 2 M hydrochloric acid to form a homogenous solution. The organic phase was separated and the aqueous phase was extracted with ether (2 × 15 mL). The organic phases were washed with brine (15 mL) and dried (MgSO₄). Purification by flash chromatography (CHCl₃:DCM, 1:1→1:0) gave 18 (10 mg, 20 µmol, 15%) as a clear and colourless oil and 17 (50 mg, 10.2 mmol, 74%) as a white crystalline solid.

Data for 18: Rf 0.2 (CHCl₃); [α]D²⁴ +2.1 (c 0.195 in CHCl₃); IR (CHCl₃): ν=3466; ¹H NMR (500 MHz, CDCl₃): δ=7.24 (d, J (H, H)=8.5 Hz, 2H; Ar), 6.87 (d, J (H, H)=8.5 Hz, 2H; Ar), 6.01 (ddd, J (H, H)=17.2, 10.5, 4.7 Hz, 1H; CH=CH₂), 5.85-5.77 (m, 2H; 5-H, 6-H), 5.33 (d, J (H, H)=17.3 Hz, 1H; CH=CHH-trans), 5.18 (d, J (H, H)=10.5 Hz, 1H; CH=CHH-cis), 4.54 (d, J (H, H)=10.5 Hz, 1H; ArCHH), 4.35 (d, J (H, H)=10.5 Hz, 1H; ArCHH), 4.30-4.25 (br, 1H; C=H=CH₂), 3.88 (dd, J (H, H)=10.1, 6.2 Hz, 1H; 5-H, 6-H), 3.74 (dd, J (H, H)=10.1, 6.2 Hz, 1H; 5-H, 6-H), 3.57 (dt, J (H, H)=8.8, 2.5 Hz, 1H; 7-H'), 3.21 (d, J (H, H)=9.1 Hz, 1H; OH), 2.57-2.52 (m, 1H; 4-H), 2.44-2.32 (m, 3H; 4-H', 7-H, 7-H'), 1.12-1.04 (21H, m, ((CH₃)₂CH)₃Si); ¹³C NMR (62.5 MHz, CDCl₃): δ=159.4, 139.0, 129.9, 129.7, 128.6, 128.6, 114.7, 113.0, 80.2, 76.0, 74.0, 71.2, 64.1 (CH₂OSi), 55.3 (CH₃O), 29.7, 28.8, 18.0 (((CH₃)₂CH)₃Si), 11.9 (((CH₃)₂CH)₃Si); MS (CI, NH₃): m/z(%): 508 ((M+NH₄)+, 20), 491 ((M+H)+, 100); Found 491.3191, C₂₈H₄₇O₅Si requires 491.3193.

Data for 17: mp 99-100 °C (from hexane); Rf 0.15 (CHCl₃); [α]D²⁴ +78.9 (c 0.175 in CHCl₃); IR (CHCl₃): v=3419; ¹H NMR (500 MHz, CDCl₃): δ=7.24 (d, J (H, H)=8.5 Hz, 2H; Ar), 6.86 (d, J (H, H)=8.5 Hz, 2H; Ar), 5.93 (ddd, J (H, H)=17.5, 10.4, 6.5 Hz, 1H; CH=CH₂), 5.86-5.81 (m, 1H; 5-H), 5.77-5.75 (m, 1H; 6-H), 5.22 (d, 1H; J (H, H)=17.5 Hz, 1H; CH=CHH-trans), 5.18 (d, 1H; J (H, H)=10.4 Hz, 1H; CH=CHH-cis), 4.62 (d, J (H, H)=11.46 Hz, 1H; OH), 4.58 (d, J (H, H)=10.9 Hz, 1H; ArCHH), 4.48 (brdd, J (H, H)=11.5, 4.5 Hz, 1H; CH=CH₂), 4.34 (d, J (H, H)=10.9 Hz, 1H; ArCHH), 4.01 (dd, J (H, H)=11.6, 10.5 Hz, 1H; CH=CHH(trans), 3.89 (dd, J (H, H)=9.3, 2.1 Hz, 1H;
2-H), 3.87-3.82 (brm, 1H; 8-H), 3.80 (s, 3H; CH3O), 3.56 (dd, J (H, H)=11.6, 2.5 Hz, 1H; CH2OSi), 3.35 (dt, J (H, H)=9.3, 2.5 Hz, 1H; 3-H), 2.56 (ddd, J (H, H)=13.7, 8.6, 2.6 Hz, 1H; 4-H), 2.34 (dt, J (H, H)=13.7, 7.7 Hz, 1H; 4-H'), 2.18-2.12 (m, 2H; 7-H), 1.18-1.04 (m, 21H; ((CH3)2CH)3Si); 13C NMR (62.5 MHz, CDCl3): δ=159.2, 137.2, 130.2, 129.1, 128.8, 127.7, 116.4 (CH2=CH), 113.8, 79.1, 77.8, 77.6, 72.7, 70.9, 63.5 (CH2OSi), 55.3 (CH3O), 29.7, 28.4, 17.9 (((CH3)2CH)3Si), 11.9 (((CH3)2CH)3Si); MS (Cl, NH3): m/z(%): 491 ((M+H)⁺, 10), 121 (100); Found 491.3184; C28H47O5Si requires 461.3193.

(Z, 2R, 3S, 8S)-2-(((R)-1-Hydroxy-prop-2-eneyl)-8-hydroxymethyl-3-(4-methoxybenzyl)oxy-3,4,7,8-tetrahydro-2H-oxocine 22

To a stirred solution of the oxocane 17 (4.8 mg, 10 µmol) in MeCN and water (3:1, 4 mL) was added CAN (32 mg, 59 µmol) and the resulting orange solution was stirred for 1 h at 0 °C. The reaction mixture was quenched by the addition of EtOAc (10 mL) and water (10 mL) and the organic phase was separated. The aqueous phase was extracted with EtOAc (10 mL) and the organic phases were washed with a saturated aqueous solution of Na2S2O3 and dried (MgSO4). Purification by flash chromatography (ether) provided the title compound 22 as a clear and colourless oil (2.8 mg, 8 µmol, 86%); Rf 0.1 (ether:hexane, 2:1); [α]D +72.9 (c 0.14 in CHCl3); IR (CHCl3): ν=3423; 1H NMR (250 MHz, CDCl3): δ=7.24 (d, J (H, H)=8.7 Hz, 2H; Ar), 6.89 (d, J (H, H)=8.7 Hz, 2H; Ar), 6.04 (ddd, J (H, H)=17.3, 10.4, 8.7 Hz, 1H; CH=CH2), 5.88-5.73 (m, 2H; 5-H, 6-H), 5.25 (ddd, J (H, H)=10.4, 1.8, 0.8 Hz, 1H; CH=CHH-cis), 5.18 (ddd, J (H, H)=17.3, 1.8, 1.0 Hz, 1H; CH=CHH-trans), 4.58 (d, J (H, H)=10.8 Hz, 1H; ArCH/H), 4.57-4.53 (m, 1H; CH=CH2COH), 4.30 (d, J (H, H)=10.8 Hz, 1H; ArCH/H), 3.96-3.88 (m, 2H), 3.81 (s, 3H; CH3O), 3.41 (d, J (H, H)=10.8 Hz, 1H), 3.37 (ddd, J (H, H)=12.2, 7.4, 2.8 Hz, 1H), 2.65-2.52 (m, 1H), 2.45-2.22 (m, 3H), 2.15-2.02 (m, 2H); 13C NMR (62.5 MHz, CDCl3): δ=159.4, 136.2, 130.1, 129.4, 128.6, 128.2, 118.3, 113.9, 79.6, 78.5, 74.1, 70.9, 61.6, 55.3, 31.9, 29.0; MS (Cl, NH3): m/z(%): 352 ((M+NH4)⁺, 100), 335 ((M+H)⁺, 75); Found 335.1861, C19H27O5 requires 335.1858.
(Z, 2S, 4R, 4aS, 6S, 10aS)-2-(4-Methoxy-phenyl)-6-triisopropylsilanyloxymethyl-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxa-benzocyclooctene 21

To a stirred solution of the allylic alcohol 17 (4 mg, 8 µmol) in DCM and water (18:1, 1 mL) was added DDQ (2.8 mg, 12 µmol) and the resulting green reaction mixture was stirred for 3 h. The reaction mixture was diluted with DCM, MgSO₄ was added and the mixture was filtered through a pad of silica with rinsing (DCM). Purification by flash chromatography (hexane:ether, 5:1) provided the title compound 21 as a clear and colourless oil (3 mg, 6 µmol, 78%); Rf 0.4 (hexane:ether, 1:1); [α]₀^19D ~4.0 (c 0.125 in CHCl₃); IR (CHCl₃): ν=2944; ¹H NMR (500 MHz, CDCl₃): δ=7.43 (d, J (H, H)=8.5 Hz, 2H; Ar), 6.88 (d, J (H, H)=8.5 Hz, 2H; Ar), 6.16 (ddd, J (H, H)=17.4, 10.7, 5.9 Hz, 1H; HC=CH₂), 5.34-5.89 (m, 1H; 9-H), 5.82-5.75 (m, 1H; 8-H), 5.53 (s, 1H; 2-H), 5.45 (d, J (H, H)=17.4 Hz, 1H; HC=CHH-trans), 5.25 (d, J (H, H)=10.7 Hz, 1H; HC=CHH-cis), 4.05-4.02 (m, 1H; 4-H), 3.89 (dd, J (H, H)=10.8, 5.0 Hz, 1H; CH₂OSi), 3.80 (s, 3H; CH₃O), 3.79 (dd, J (H, H)=10.0, 6.8 Hz, 1H; CH₂OSi), 3.65-3.58 (m, 1H; 6-H), 3.56-3.45 (m, 2H; 4a-H, 10a-H), 2.56-2.50 (m, 1H; 10-H), 2.47-2.38 (m, 2H; 10-H', 7-H), 2.30-2.23 (m, 1H; 7-H'), 1.10-1.06 (m, 21H; ((CH₃)₂CH)₃Si); ¹³C NMR (62.5 MHz, CDCl₃): δ=160.0, 136.6, 130.5, 129.2, 127.5, 127.3, 117.6, 113.6, 100.2, 81.3, 80.6, 77.3, 72.9, 65.6 (CH₂OSi), 55.3 (CH₃O), 32.8, 28.6, 18.0 (((CH₃)₂CH)₃Si), 11.9 (((CH₃)₂CH)₃Si); MS (Cl, NH₃): m/z(%): 489 ((M+H)+, 25), 137 (100); Found: 489.3031, C₂₈H₄₅O₅Si requires 489.3036.


TFA (0.71 mL) was added to a stirring solution of a mixture of allylic alcohols 17 and 18 (50 mg, 102 µmol) in DCM (3.6 mL) at -20 °C. After 5 min the initial yellow
solution became pink and TLC analysis indicated that no starting material remained. Stirring was continued for a further 5 min and then the reaction was quenched by the addition of a saturated solution of NaHCO₃ (10 mL) and DCM. The organic phase was separated and the aqueous phase was extracted with DCM (2 × 10 mL). The organic phases were dried (MgSO₄) and purification by flash chromatography (hexane:ether, 1:1) provided a mixture of 20 and 19 (34 mg, 92 µmol, 90%) as a clear and colourless oil.

Data for 20: Rf 0.2 (hexane:ether, 1:1); [α]D²³-33.8 (c 0.21 in CHCl₃); IR (CDCl₃): ν=3617, 3455; ¹H NMR (250 MHz, CDCl₃) δ=6.08 (ddd, J (H, H)=17.3, 10.5, 5.8 Hz, 1H; CH=CH₂), 5.92-5.73 (m, 2H; 5-H, 6-H), 5.40 (dt, J (H, H)=17.3, 1.6 Hz, 1H; CH=CHH-trans), 5.25 (dt, J (H, H)=10.5, 1.5 Hz, 1H; CH=CHH-cis), 4.25-4.29 (m, 1H), 3.94 (dd, J (H, H)=10.2, 6.8 Hz, 1H), 3.88-3.78 (m, 2H), 3.73-3.64 (m, 2H), 3.27 (d, J (H, H)=6.3 Hz, 1H; OH), 2.50 (ddd, J (H, H)=13.3, 8.3, 3.2 Hz, 1H; allylic), 2.40 (dd, J (H, H)=7.5, 6.4 Hz, 1H), 2.34-2.29 (m, 2H; allylic), 2.23 (d, J (H, H)=3.8 Hz, 1H; OH), 1.17-1.02 (m, 21H; ((CH₃)₂CH)₃Si); ¹³C NMR (62.5 MHz, CDCl₃): δ=138.4, 128.5, 128.5, 116.2, 77.4, 76.6, 75.2, 72.6, 64.1 (CH₂OSi), 34.1, 29.0, 18.0 (((CH₃)₂CH)₃Si), 11.9 (((CH₃)₂CH)₃Si); MS (CI, NH₃): m/z(%): 388 ((M+NH₄)+, 17), 371 ((M+H)+, 100); Found 371.2619, C₂₀H₃₉O₄Si requires 371.2617.

Data for 19: Rf 0.15 (hexane:ether, 1:1); [α]D²³+44.2 (c 0.38 in CHCl₃); IR (CHCl₃): ν=3611, 3428; ¹H NMR (250 MHz, CDCl₃): δ=6.04 (ddd, J (H, H)=17.3, 10.4, 6.6 Hz, 1H; CH=CH₂), 5.91-5.68 (m, 2H; 5-H, 6-H), 5.33 (ddd, J (H, H)=17.3, 1.9, 1.3 Hz, 1H; CH=CHH-trans), 5.23 (ddd, J (H, H)=10.4, 1.9, 1.2 Hz, 1H; CH=CHH-cis), 4.60 (d, J (H, H)=11.2 Hz, 1H; OH), 4.47-4.38 (m, 1H; 2-H), 3.99 (dd, J (H, H)=11.5, 10.1 Hz, 1H; CHHOSi), 3.85-3.73 (m, 2H), 3.59 (dd, J (H, H)=11.6, 2.8 Hz, 1H; CHHOSi), 3.65-3.50 (m, 1H), 3.59 (dd, J (H, H)=11.6, 2.8 Hz, 1H; CHHOSi), 2.41 (d, J (H, H)=7.7 Hz, 1H; allylic), 2.38 (dd, J (H, H)=8.4, 2.1 Hz, 1H; allylic), 2.19 (dd, J (H, H)=14.0, 10.3, 8.4 Hz, 1H; allylic), 2.02 (ddd, J (H, H)=14.0, 6.8, 3.4 Hz, 1H; allylic), 1.56 (d, J (H, H)=5.5 Hz, 1H; OH), 1.13-1.06 (m, 21H; ((CH₃)₂CH)₃Si); ¹³C NMR (62.5 MHz, CDCl₃): δ=137.1, 128.6, 127.9, 116.4, 78.2, 77.5, 73.1, 71.7, 63.5 (CH₂OSi), 35.5, 28.0, 17.9 (((CH₃)₂CH)₃Si), 11.9 (((CH₃)₂CH)₃Si); MS (Cl, NH₃): m/z(%): 371 ((M+H)+, 100); Found 371.2621, C₂₀H₃₉O₄Si requires 371.2617.
To a stirred solution of the diol 19 (10 mg, 27 µmol) in toluene (2 mL) was added phenylselenoacetaldehyde diethylacetal (9 mg, 32 µmol) and PPTS (1 mg). The reaction mixture was brought to reflux and heated at that temperature for 2 h. After cooling the solvent was removed in vacuo and purification by flash chromatography (hexane:ether, 12:1) provided the title compound 23 as a slightly yellow oil (14 mg, 25 µmol, 94%) as an inseparable mixture of diastereomers at the acetal carbon. NMR data indicated that the product was a 13:1 mixture of diastereomers the major diastereomer being with the phenylselenomethylene group in the equatorial position; 1H NMR for the major diastereomer is given: 1H NMR (500 MHz, CDCl3): δ=7.55-7.52 (m, 2H Ar), 7.26-7.23 (m, 3H; Ar), 6.08 (ddd, J (H, H)=17.3, 10.6, 6.0 Hz, 1H; CΗ=CH2), 5.89-5.84 (m, 1H; 8-H), 5.78-5.73 (m, 1H; 9-H), 5.35 (d, J (H, H)=17.3 Hz, 1H; CH=CΗH-trans), 5.21 (d, J (H, H)=10.6 Hz, 1H; CH=CΗH-cis), 4.83 (t, J (H, H)=5.0 Hz, 1H; 2-H), 3.55 (d, J (H, H)=5.3 Hz, 1H), 3.83 (d, J (H, H)=5.0 Hz, 1H), 3.64 (dd, J (H, H)=9.8, 7.0 Hz, 1H), 3.66-3.52 (m, 1H), 3.39-3.32 (m, 2H), 3.10 (d, J (H, H)=5.0 Hz, 2H; CΗ2SeAr), 2.47-2.29 (m, 3H; allylic), 2.24 (ddd, J (H, H)=14.0, 7.2, 3.0 Hz, 1H; allylic), 1.14-1.06 (m, 21H; ((CH3)2CH)3Si); 13C NMR (62.5 MHz, CDCl3): δ=135.4, 135.3, 133.7, 132.6, 132.6, 130.5, 129.2, 129.1, 129.1, 129.0, 127.3, 127.3, 127.1, 126.9, 117.8, 117.6, 77.3, 77.2, 74.3, 73.6, 72.7, 72.6, 65.6, 65.5, 32.6, 32.5, 30.8, 28.5, 28.5, 26.9, 18.0 (((CH3)2CH)3Si), 11.9 (((CH3)2CH)3Si); MS (EI): m/z(%): 552 (M+, 100); Found 552.2167, C28H44O4SeSi requires 552.2174.

Selected 1H NMR data are given for the minor diastereomer; 5.27 (dd, J (H, H)=7.5, 5.7 Hz, 1H; 2-H), 3.48 (dd, J (H, H)=12.7, 7.5 Hz, 1H; CHHSeAr), 3.20 (dd, J (H, H)=12.8, 5.7 Hz, 1H; CH/SeAr.)
(Z, 2S, 4S, 4aS, 6S, 10aS)-2-Phenylselanyl methyl-6-triisopropylsilanyloxy-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxa-benzocyclooctene 24

The selenoacetal 24 was prepared in 60% yield starting from the diol 20 as described for the selenoacetal 23. The selenoacetal 20 was isolated as a single diastereomer as determined by \( ^1 \text{H NMR analysis; } \left[ \alpha \right]_{D}^{25} = -91.1 \) (c 0.18 in CHCl\(_3\)). \(^1\)H NMR (250 MHz, CDCl\(_3\)): \( \delta =7.55-7.50 \) (m, 2H; Ar), 7.27-7.22 (m, 3H; Ar), 6.18 (ddd, \( J (H, H)=17.7, 11.0, 4.1 \) Hz, 1H; \( CH=CH_2 \)), 5.89-5.73 (m, 2H; 9-H, 8-H), 5.44 (dt, \( J (H, H)=17.7, 2.0 \) Hz, 1H; \( CH=CHH-trans \)), 5.31 (dt, \( J (H, H)=11.0, 2.0 \) Hz, 1H; \( CH=CHH-cis \)), 5.13 (t, \( J (H, H)=5.0 \) Hz, 1H; 2-H), 4.60 (ddt, \( J (H, H)=6.4, 4.1, 2.1 \) Hz, 1H; 4-H), 3.98 (dd, \( J (H, H)=9.7, 6.4 \) Hz, 1H; 4a-H), 3.87 (dd, \( J (H, H)=10.7, 6.4 \) Hz, 1H; \( CHHOSi \)), 3.76 (dd, \( J (H, H)=10.7, 4.7 \) Hz, 1H; \( CHHOSi \)), 3.68-3.52 (m, 1H; 6-H), 3.50 (dt, \( J (H, H)=9.7, 4.9 \) Hz, 1H; 10a-H), 3.05 (d, \( J (H, H)=5.0 \) Hz, 2H; \( CH_2SeAr \)), 2.52-2.30 (m, 3H; 10-H, 10'-H, 7-H), 2.12 (ddd, \( J (H, H)=13.6, 6.3, 3.4 \) Hz, 1H; 7-H'), 1.11-1.04 (m, 21H; ((CH\(_3\))\(_2\)CH)\(_3\)Si); \(^{13}\)C NMR (62.5 MHz, CDCl\(_3\)): \( \delta =132.4, 132.2, 130.6, 129.0, 129.0, 127.3, 118.8, 94.2, 77.2, 76.3, 75.7, 69.5, 64.9, 32.8, 31.1, 28.3, 18.0 ((CH\(_3\))\(_2\)CH)\(_3\)Si), 11.9 ((CH\(_3\))\(_2\)CH)\(_3\)Si); MS (Cl, NH\(_3\)): \( m/z(\%) = 570 ((M+NH_4)^+, 8), 553 ((M+H)^+, 5), 52 (100); Found 570.2513, C\(_{28}\)H\(_{48}\)O\(_4\)SeSiN requires 570.2518.

(Z, 4R, 4aS, 6S, 10aS)-6-Triisopropylsilanyloxymethyl-4-vinyl-4,4a,6,7,10a-hexahydro-1,3,5-trioxa-benzocycloocten-2-one 25

To a stirred suspension of the oxocane 19 (8.7 mg, 24 \( \mu \)mol) and freshly activated 4 Å powdered molecular sieves in DCM (1 mL) were added pyridine (11.5 \( \mu \)L, 11.3 mg, 141 \( \mu \)mol) and TEA (33 \( \mu \)L, 24 mg, 24 \( \mu \)mol). The resulting solution was cooled to -78 °C and triphosgene (7 mg, 24 \( \mu \)mol) was added via cannula as a solution in DCM (0.5 mL). The resulting orange solution was stirred for 15 min and then allowed to warm to room temperature. The reaction mixture was quenched by the addition of a saturated solution of NH\(_4\)Cl (2 mL) and was extracted with DCM (4 \( \times \) 2 mL). The
organic phases were dried (MgSO₄) and purification by flash chromatography (hexane:ether, 1:1) provided the title compound 25 (8.3 mg, 21 µmol, 89%) as a clear and colourless oil; [α]D²⁵ -47.5 (c 0.4 in CHCl₃); IR (CHCl₃): ν=1752; ¹H NMR (400 MHz, CDCl₃): δ=6.04 (dd, J (H, H)=17.2, 10.6, 6.2 Hz, 1H; CH=CH₂), 5.90-5.78 (m, 2H; 8-H, 9-H), 5.52 (dt, J (H, H)=17.2, 1.2 Hz, 1H; CH=CHH-trans), 5.36 (dt, J (H, H)=10.6, 1.2 Hz, 1H; CH=CHH-cis), 4.58 (ddt, J (H, H)=9.2, 6.2, 1.2 Hz, 1H; 4-H), 4.10 (dt, J (H, H)=9.5, 3.8 Hz, 1H; 10a-H), 3.94 (dd, J (H, H)=9.5, 9.2 Hz, 1H; 4a-H), 3.83 (d, J (H, H)=4.9 Hz, 2H; CH₂OSi), 3.71-3.67 (m, 1H; 6-H), 2.62-2.49 (m, 3H; allylic), 2.27-2.20 (m, 1H; allylic), 1.10-1.05 (m, 21H; ((CH₃)₂CH)₃Si); ¹³C NMR (62.5 MHz, CDCl₃): δ=148.2 (2-C), 132.5, 125.4, 119.7, 81.6, 80.0, 70.6, 65.6 (CH₂OSi), 31.5, 28.5, 18.0 (((CH₃)₂CH)₃Si), 11.9 (((CH₃)₂CH)₃Si); MS (Cl, NH₃): m/z (%): 414 ((M+NH₄)+, 10), 397 ((M+H)+, 3), 75 (100).

(5Z, 6aR, 10Z, 12aS)-3,4,9,8,12,12a-Hexahydro-8-triisopropylsilyloxymethyl-oxano(3,2-b)oxocin-2-one 26

From the selenoacetal 23.
To a stirring suspension of the selenoacetal 23 (14 mg, 25 µmol) in DCM (0.2 mL), water (0.3 mL) and MeOH (1.3 mL) were added NaHCO₃ (2.3 mg, 28 µmol) and sodium periodate (18 mg, 84 µmol). The resulting suspension was stirred for 2 h and then diluted with DCM (5 mL) and water (5 mL). The organic phase was separated and the aqueous phase was extracted with DCM (2 × 5 mL). The organic phases were dried (MgSO₄) and the solvent removed in vacuo the resulting oil was coevaporated with toluene (2 × 2 mL) and xylene (4 mL) and DBU (11.4 µL, 11.6 mg, 76 µmol) were added. The resulting solution was heated at reflux for 18 h and then allowed to cool. The solvent was removed in vacuo and purification by flash chromatography (hexane:ether, 5:1) provided the title compound 26 as a clear and colourless oil (9 mg, 23 µmol, 90%); [α]D²⁵ +28.3 (c 0.425 in CHCl₃); IR (CHCl₃): ν=1742; ¹H (500 MHz, CDCl₃) 5.88-5.82 (m, 2H; 10-H, 11-H), 5.68-5.62 (m, 2H; 5-H, 6-H), 4.65 (dd, J (H, H)=9.2, 3.4 Hz, 1H; 6a-H), 4.56 (dt, J (H, H)=9.2, 3.2 Hz, 1H; 12a-H), 3.84 (dd, J (H, H)=10.6, 5.5 Hz, 1H; CHHOSi), 3.82 (dd, J (H, H)=10.6, 4.9 Hz, 1H; CHHOSi),
3.76-3.72 (m, 1H; 8-H), 2.74 (ddd, J (H, H)=13.8, 6.2, 2.0 Hz, 1H; allylic), 2.65-2.57 (m, 2H; allylic), 2.52-2.46 (m, 2H; allylic), 2.31-2.17 (m, 2H; allylic), 2.10-2.01 (m, 1H; allylic), 1.08-1.04 (m, 21H; ((CH₃)₂CH)₃Si); ¹³C NMR (62.5 MHz, CDCl₃): δ=175.2 (2-C), 137.3, 129.6, 129.1, 127.4, 78.9, 76.1, 72.8, 64.8 (CH₂OSi), 37.8, 31.2, 29.0, 25.5, 18.0 (((CH₃)₂CH)₃Si), 11.9 (((CH₃)₂CH)₃Si); MS (EI): m/z(%): 394 (M⁺, 10), 239 (100); Found 394.2538, C₂₂H₃₈O₄Si requires 394.2539.

Similarly the lactone 26 could be prepared in >90% yield by oxidation of the selenoacetal 24 followed by pyrolysis of the resulting selenoxides as with the selenoacetal 23.

The lactone 26 was also prepared from the carbonate 25 as described below.

To a stirred solution of the carbonate 25 (8 mg, 20 µmol) in toluene (1 mL) was added dimethyltitanocene (117 µL, of a 50 mg/mL solution in toluene, 28 µmol) and the resulting orange solution was heated at reflux for 1.5 h and then allowed to cool. The solvent was removed in vacuo and purification by flash chromatography (hexane:ether, 5:1) provided the title compound 26 identical to that previously reported (63% yield).

(Z, 3R, 4S, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-3-hydroxy-4-methyl-3,4,7,8-tetrahydro-oxocin-2-one 27

To a solution of KHMDS (9.02 mL of a 0.5 M solution in toluene, 4.51 mmol) in toluene (150 mL) at -78 °C was slowly added a solution of the lactone 8 (1.0 g, 3.47 mmol) in toluene (20 mL, 5 mL rinse). The solution was stirred for 20 min then (±)-2-(phenylsulfanyl)-3-phenyloxaziridine (1.18 g, 4.51 mmol) was added slowly as a solution in toluene (20 mL, 5 mL rinse). The solution was stirred at -78 °C for 1.25 h until consumption of starting material was complete. The reaction was quenched via addition of (±)-camphor-10-sulfonic acid (2 g) in THF (20 mL) at -78 °C, then allowed to warm slowly to ambient temperature. The mixture was poured into water (150 mL) and extracted with EtOAc (3 × 150 mL). The combined organic extracts were washed with brine, dried (MgSO₄) and concentrated. Flash chromatography (hexane:EtOAc, 20:3) afforded the hydroxylactone 27 as a white solid (0.96 g, 3.15 mmol, 91%); (Found: C, 70.7; H, 7.9%; C₁₈H₂₄O₄ requires C, 71.0; H, 8.0); mp 59-61
°C; [α]D25 +12.1 (c 0.755 in CHCl3); Rf 0.31 (PE:EtOAc, 20:1); IR (CHCl3): ν=3690, 3543, 1731; 1H NMR (250 MHz, CDCl3): δ=7.28-7.37 (m, 5H; Ar), 5.49-5.67 (m, 2H; 5-H, 6-H), 4.60 (ddd, J (H, H)=10.0, 6.0, 2.0 Hz, 1H; 8-H), 4.50 (d, J (H, H)=12.0 Hz, 2H; CH2Ar), 3.89 (dd, J (H, H)=10.0, 9.0 Hz, 1H; 3-H), 3.53 (dd, J (H, H)=9.0, 3.5 Hz, 1H; CHHOBn), 3.38 (dd, J (H, H)=9.0, 6.5 Hz, 1H; CHHOBn), 2.73 (d, J (H, H)=8.5 Hz, 1H; OH), 2.48-2.59 (ddd, J (H, H)=14.5, 8.5, 6.0 Hz, 1H; 7β–H), 2.30-2.42 (m, 1H; 4-H), 2.17-2.27 (m, 1H; 7α-H), 1.91-2.03 (m, 1H; 9-H), 1.28 (d, J (H, H)=7.0 Hz, 3H; 4-C-Me), 1.06 (d, J (H, H)=7.0 Hz, 3H; 8-C-CH3); 13C NMR (62.5 MHz, CDCl3): δ=10.8, 138.5, 136.6, 128.3, 127.5, 127.5, 125.2, 76.2, 74.3, 73.2, 71.8, 39.5, 35.5, 28.5, 18.6, 14.2; MS (CI, NH3): m/z(%) 322 ((M+NH4)+, 61), 305 ((M+H)+, 11); Found 305.1749, C18H25O4 requires 305.1753.

(Z, 3R, 4S, 8S)-8-((1R)-2-Benzxyloxy-1-methyl-ethyl)-4-methyl-3-trimethylsilyloxy-3,4,7,8-tetrahydro-oxocin-2-one 28

![Chemical Structure](image)

To a stirred solution of the hydroxylactone 27 (300 mg, 98.6 mmol) in ether (20 mL) was added dry Et3N (0.549 mL, 39.4 mmol) and TMSCl (0.495 mL, 39.4 mmol). The solution was stirred for 30 min, then poured into water (20 mL). The product was extracted with ether (3 × 40 mL), the extracts were washed with water (20 mL) and brine (20 mL), dried (MgSO4) and concentrated to give the title compound 28 as a pale yellow oil (360 mg, 95.6 mmol, 97%); [α]D25 +27.8 (c 1.08 in CDCl3); Rf 0.23 (hexane:EtOAc, 9:1); IR (film): ν=1753; 1H NMR (400 MHz, CDCl3): δ=7.24-7.36 (m, 5H; Ar), 5.51-5.62 (m, 2H; 5-H, 6-H), 4.61-4.65 (m, 1H; 8-H), 4.50 (d, J (H, H)=12.0 Hz, 2H; CH2Ar), 3.91 (d, J (H, H)=10.0 Hz, 1H; 3-H), 3.57 (dd, J (H, H)=4.0, 9.0 Hz, 1H; CHHOBn), 3.34 (dd, J (H, H)=7.0, 9.0 Hz, 1H; CHHOBn), 2.53-2.60 (m, 2H; 7-H, 4-H), 2.20 (ddd, J (H, H)=2.5, 6.5, 14.5 Hz, 1H; 7-H”), 1.94-2.01 (m, 1H; 8-C-CHCH3), 1.16 (d, J (H, H)=6.5 Hz, 3H; 4-C-Me), 1.05 (d, J (H, H)=6.5 Hz, 3H; 8-C-CHCH3), 0.15 (s, 9H; (CH3)3Si); 13C NMR (125 MHz, CDCl3): δ=177.6, 138.6, 136.2, 128.3, 127.5, 127.4, 125.4, 77.4, 73.4, 73.1, 72.0, 38.7, 35.9, 28.7, 19.0, 14.1, -0.3; MS (ES): m/z(%): 399 ((M+Na)+, 100), 377 ((M+H)+, 9); Found 399.1974, C21H32O4SiNa requires 399.1966.
(Z, 3R, 4S, 8S)-8-(((1R)-2-Benzyl-1-ethyl)-4-methyl-2-methylene-3-trimethylsilyl-3,4,7,8-tetrahydro-2H-oxocine 29 and (Z, 3R, 4S, 8S)-8-(((1R)-2-benzyl-1-ethyl)-3-hydroxy-4-methyl-2-methylene-3,4,7,8-tetrahydro-2H-oxocine 30

To a solution of the lactone 28 (350 mg, 0.93) in toluene (20 mL) was added dimethyltitanocene (4.12 mL of a 94 mg/mL solution in toluene, 1.86 mmol). The mixture was heated to reflux in the absence of light for 1.5 h, after which time a further equivalent of dimethyltitanocene solution (2.06 mL) was added. The mixture was refluxed for a further hour after which time all the starting material had been consumed. The solution was allowed to cool, concentrated, then redissolved in DCM and evaporated onto deactivated basic alumina (Brockman Grade III, 6% water). The trimethylsilyl-protected enol ether 29 was purified via flash chromatography using basic alumina (hexane:EtOAc, 25:1) to give a yellow oil containing some cyclopentadienyl impurities; the mixture could be further purified (alumina chromatography) for the purposes of characterisation giving pure 29; [α]_D^25 +29.2 (c 0.64 in CDCl₃); R_f 0.49 (hexane:EtOAc, 10:1); IR (CHCl₃): ν=1643; ^1H NMR (400 MHz, CDCl₃): δ=7.26-7.36 (m, 5H; Ar), 7.26-7.36 (m, 5H; Ar), 5.43-5.55 (m, 2H; 5-H, 6-H), 4.94 (s, 1H; OCH=CHCH₃), 4.53 (s, 1H; OCH=CHH), 4.52 (d, J (H, H)=12.0 Hz, 2H; CH₂Ar), 3.85 (dd, J (H, H)=5.0, 10.0 Hz, 1H; 8-H), 3.62 (dd, J (H, H)=3.5, 9.0 Hz, 1H; CHHOBn), 3.53 (d, J (H, H)=10.0 Hz, 1H; 3-H), 3.49 (dd, J (H, H)=6.0, 9.0 Hz, 1H; CHHOBn), 2.64-2.80 (m, 1H; 7-H), 2.30-2.45 (m, 1H; 4-H), 1.91-2.10 (m, 1H; 7-H'), 1.75-1.89 (m, 1H; 8-C-CHCH₃), 1.11 (d, J (H, H)=6.5 Hz, 3H; 4-C-Me), 1.04 (d, J (H, H)=7.0 Hz, 3H; 8-C-CHCH₃), 0.14 (s, 9H; (CH₃)₃Si); ^13C NMR (62.5 MHz, CDCl₃): δ=166.8, 139.0, 136.9, 128.3, 127.5, 127.5, 127.3, 124.3, 93.6, 78.4, 76.1, 73.1, 72.6, 40.1, 36.0, 27.0, 19.8, 14.5, 0; MS (ES⁺): m/z (%): 397 ((M+Na)^+, 100); Found 397.2163, C₂₂H₃₄O₃SiNa requires 397.2175. The mixture was dissolved in dry methanol (10 mL) and solid potassium carbonate (0.1 g) was added. The solution was stirred for 30 min at room temperature, then filtered, and concentrated. After redissolving in DCM the mixture was evaporated onto deactivated basic alumina and purified via flash chromatography using basic alumina (hexanes:EtOAc,
20:1→5:1) to give the deprotected enol ether 30 as a colourless oil (120 mg, 0.397 mmol, 68%); \([\alpha]_D^{25} = -2.5 (c 0.55 \text{ in CDCl}_3); R_f 0.4 \text{ (hexanes:EtOAc, 3:1); IR (CHCl}_3): \nu = 3604, 1642; 1^H \text{ NMR (400 MHz, CDCl}_3): \delta = 7.23-7.35 \text{ (m, 5H; Ar), 7.23-7.35 (m, 5H; Ar), 5.43-5.46 (m, 2H; 5-H, 6-H), 4.96 (br s, 1H; OC=CH\text{H}), 4.58 (d, J (H, H)=1.5 Hz, 1H; OC=CH\text{H}), 4.51 (d, J (H, H)=12.0 Hz, 2H; CH\text{H}_2\text{Ar}), 3.90 (ddd, J (H, H)=1.0, 5.5, 9.5 Hz, 1H; 8-H), 3.63 (br d, 1H; 3-H), 3.60 (dd, J (H, H)=3.5, 9.0 Hz, 1H; \text{CH\text{H}O}\text{Bn}), 3.50 (dd, J (H, H)=6.0, 9.0 Hz, 1H; CH\text{H\text{O}}\text{Bn}), 2.72 (ddd, J (H, H)=5.5, 9.0, 14.0 Hz, 1H; 7-H), 2.37-2.47 (m, 1H; 4-H), 2.05 (partially resolved dd, 1H; 5-H'), 1.80-1.90 (m, 1H; 8-C-CH\text{H}_3), 1.73 (br d, J (H, H)=3.0 Hz, 1H; OH), 1.20 (d, J (H, H)=6.5 Hz, 3H; 4-C-Me), 1.03 (d, J (H, H)=7.0 Hz, 3H; 8-C-CH\text{H}_2\text{H}_3); \text{13C NMR (125 MHz, CDCl}_3): \delta = 167.1, 138.9, 136.7, 128.3, 127.5, 127.4, 124.6, 93.4, 78.8, 75.9, 73.2, 72.5, 39.2, 36.0, 27.2, 19.1, 14.5; MS (ES): \text{m/z(%)=325 ((M+Na)}^+, 100); Found 325.1774, C_{19}H_{26}O_3Na requires 325.1755.

(Z, 3R, 4S, 8S)-8-((1R)-2-Benzoyloxy-1-methyl-ethyl)-3-dimethylsilanyloxy-4-methyl-2-methylene-3,4,7,8-tetrahydro-2H-oxocine 31

The hydroxyenol ether 30 (120 mg, 0.397.97 mmol) was dissolved in tetramethyldisilazane (2 mL) and NH\text{H}_4\text{Cl} (10 mg) was added. The mixture was stirred at 60 °C for 18 h then allowed to cool, diluted with hexane (2 mL), and the mixture was filtered and concentrated. The product was redissolved in toluene and concentrated (2 \times 5 \text{ mL}) to give the enol ether 31 as a colourless oil (140 mg, 0.3.88 mmol, 98%); \([\alpha]_D^{25} = +49.2 (c 0.88 \text{ in CHCl}_3); R_f \text{ decomposes on silica; IR (CDCl}_3): \nu = 3019, 1522, 1476, 1423, 1221; 1^H \text{ NMR (500 MHz, CDCl}_3): \delta = 7.23-7.35 \text{ (m, 5H; Ar), 5.45-5.53 (m, 2H; 5-H, 6-H), 4.93 (s, 1H; OC=CH\text{H}), 4.62-4.66 (m, 1H; SiH), 4.56 (s, 1H; OC=CH\text{H}), 4.55 (d, J (H, H)=12.0 Hz, 1H; CH\text{HAr}), 4.49 (d, J (H, H)=12.0 Hz, 1H; CH\text{HAr}), 3.85 (dd, J (H, H)=4.5, 10.0 Hz, 1H; 8-H), 3.61 (dd, J (H, H)=3.5, 9.0 Hz, 1H; \text{CH\text{H}O}\text{Bn}), 3.55 (d, J (H, H)=10 Hz, 1H; 3-H), 3.49 (dd, J (H, H)=6.5, 9.0 Hz, 1H; CH\text{H\text{O}}\text{Bn}), 2.66-2.75 (m, 1H; 7-H), 2.35-2.44 (m, 1H; 4-H), 2.00-2.07 (m, 1H; 7-H'), 1.78-1.89 (m, 1H; 8-C-CH\text{H}_3), 1.12 (d, J (H, H)=6.5 Hz, 3H; 4-C-Me), 1.04 (d, J (H, H)=7.0 Hz, 3H; 8-C-CH\text{H}_2\text{H}_3), 0.22 (apparent t, J (H,
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$=7.25-7.36 (m, 5H; Ar), 7.25-7.36 (m, 5H; Ar), 5.44-5.53 (m, 2H; 5-H, 6-H), 4.60 (d, $J$ (H, H)=12.0 Hz, 1H; CH\text{HAr}), 4.44 (d, $J$ (H, H)=12.0 Hz, 1H; CH\text{HAr}), 3.92 (dd, $J$ (H, H)=3.0, 11.0 Hz, 1H; CH\text{HOH}), 3.79 (dd, $J$ (H, H)=4.0, 9.0 Hz, 1H; CH\text{HOH}), 3.47-3.58 (m, 2H; 8-H, CH\text{HOH}), 3.36 (dt, $J$ (H, H)=3.5, 9.0 Hz, 1H; 2-H), 3.26 (dd, $J$ (H, H)=2.5, 9.0 Hz, 1H; CH\text{HOH}), 3.12 (t, $J$ (H, H)=9.5 Hz, 1H; 3-H), 2.53-2.60 (m, 1H; 7-H), 2.44-2.50 (m, 1H; 4-H), 2.17-2.22 (m, 1H; 7-H'), 1.61-1.72 (m, 1H; 8-C-CH\text{CH}_3), 1.16 (d, $J$ (H, H)=6.5 Hz, 3H; 4-C-Me), 1.01 (d, $J$ (H, H)=7.0 Hz, 3H; 8-C-CH\text{CH}_3); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$=138.0, 136.9, 128.3, 127.9,
And the cis-diol \textit{33} as a white solid (38.8 mg, 0.121 mmol, 24.5%); mp 102 °C; \([\alpha]_{D}^{25}=-23.7\) (c 2.17 in DCM); \(R_{f}\) 0.19 (LP:EtOAc, 1:1); IR (CHCl3): \(\nu=3300-3600;\) \(1\)H NMR (400 MHz, CDCl3): \(\delta=7.27-7.37\) (m, 5H; Ar), 5.73-5.80 (m, 1H; 6-H), 5.42-5.47 (m, 1H; 5-H), 4.51 (s, 2H; CH2Ar), 4.08 (dt, \(J(H, H)=1.0, 5.0\) Hz, 1H; 2-H), 4.01-4.06 (m, 1H; 8-H), 3.66 (dd, \(J(H, H)=5.0, 11.5\) Hz, 1H; CHHOH), 3.61 (dd, \(J(H, H)=5.0, 11.5\) Hz, 1H; CHHOH), 3.54 (dd, \(J(H, H)=1.0, 9.5\) Hz, 1H; CHHOBn), 3.34-3.43 (m, 2H; CHHOBn, 3-H), 2.72-2.82 (m, 1H; 4-H), 2.59 (dddd, \(J(H, H)=2.0, 3.5, 7.5, 16.0\) H, 1H; 7-H), 2.24 (dt, \(J(H, H)=6.0, 16.0\) Hz, 1H; 7-H'), 2.01-2.11 (m, 1H; 8-C-CHCH3), 1.19 (d, \(J(H, H)=6.5\) Hz, 3H; 4-C-Me), 1.00 (d, \(J(H, H)=7.0\) Hz, 1H; 8-C-CHCH3); \(^{13}\)C NMR (100 MHz, CDCl3): \(\delta=138.2, 136.0, 128.4, 128.3, 127.7, 127.7, 80.3, 78.7, 73.7, 73.3, 71.8, 64.9, 37.9, 35.5, 31.9, 18.0, 15.1;\) MS (CI, perfluorotributylamine): \(m/z(%)\): 328 ((M+NH4\(^+\), 42), 321 ((M+H\(^+\), 100); Found 321.2070, C\(_{10}\)H\(_{25}\)O\(_4\) requires 321.2066.

\((Z, 2S, 4aR, 6S, 10S, 10aR)-6-((1R)-2-Benzyloxy-1-methyl-ethyl))-2-(4-methoxyphenyl)-10-methyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxabenzocylooctene \textit{35}\)

To a solution of the cis-diol \textit{33} (8 mg, 25 \(\mu\)mol) in benzene (3 mL) was added \(p\)-anisaldehyde (4 \(\mu\)L, 30 \(\mu\)mol) and PPTS (1 mg). The solution was heated under reflux (Dean-Stark) for 18 h, allowed to cool, and concentrated. Flash chromatography (hexanes:ether, 3:1\(\rightarrow\)2:1) gave the acetal \textit{35} as a white solid (10 mg, 25 \(\mu\)mol, 100%); mp 80-82 °C; \([\alpha]_{D}^{25}=-34.3\) (c 1.07 in CHCl3); \(R_{f}\) 0.33 (PE:EtOAc, 4:1); IR (CHCl3): \(\nu=2933, 2849;\) \(1\)H NMR (400 MHz, CDCl3): \(\delta=7.47\) (d, \(J(H, H)=8.5\) Hz, 2H; Ar), 7.26-7.36 (m, 5H; Ar), 6.88 (d, \(J(H, H)=8.5\) Hz, 2H; Ar), 5.80-5.87 (m, 1H; 8-H), 5.47 (s, 1H; 2-H), 5.41-5.46 (m, 1H; 9-H), 4.53 (d, \(J(H, H)=12.0\) Hz, 1H; CHHAr), 4.47 (d, \(J(H, H)=12.0\) Hz, 1H; CHHAr), 4.08 (d, \(J(H, H)=12.0\) Hz, 1H; 4-H), 3.97-4.02 (m, 1H; 6-H), 3.87 (d, \(J(H, H)=12.0\) Hz, 1H; 4-H'), 3.80 (s, 3H; OCH3), 0.92 (s, 9H; OPMs).
(Z, 2S, 4aS, 6S, 10S, 10aR)-6-((1R)-2-Benzylxy-1-methyl-ethyl))-2-(4-methoxyphenyl)-10-methyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxabenzocylooctene

To a solution of 32 (11 mg, 34.3 µmol) in benzene (10 mL) was added p-anisaldehyde (13 µL, 0.107 mmol) and PPTS (2 mg). The solution was heated under reflux (Dean-Stark) for 18 h, allowed to cool and concentrated. Flash chromatography (hexanes:ether, 3:1→2:1) gave the acetal 34 as a colourless oil (15 mg, 34.3 µmol, 100%); \([\alpha]_{D}^{25}+23.4 (c 0.67 \text{ in DCM})\); \(R_f 0.31 (\text{hexane:EtOAc, 5:1})\); IR (thin film): \(\nu=2959, 2927, 2859\); \(^1\)H (400 MHz, CDCl\(_3\)): \(\delta=7.41 (d, J (H, H)=8.5 \text{ Hz, 2H; Ar}), 7.26-7.36 (m, 5H; Ar), 6.88 (d, J (H, H)=8.5 \text{ Hz, 2H; Ar}), 5.49-5.56 (m, 2H, 8-H, 9-H), 5.39 (s, 1H; 2-H), 4.51 (d, J (H, H)=12.0 Hz, 1H; CHHAr), 4.45 (d, J (H, H)=12.0 Hz, 1H; CHHAr), 4.04 (dd, J (H, H)=5.0, 11.0 Hz, 1H; 4-H), 3.80 (s, 3H; OCH\(_3\)), 3.40-3.58 (m, 5H; 4-H', 4a-H, 6-H, CH\(_2\)OBn), 3.22 (t, J (H, H)=9.5 Hz, 1H; 10a-H), 2.58-2.73 (m, 2H; 7-H, 10-H), 1.98-2.06 (unresolved dd, 1H; 7-H'), 1.65-1.79 (m, 1H; 8-C-CHCH\(_3\)), 1.19 (d, J (H, H)=6.5 Hz, 3H; 4-C-Me), 1.04 (d, J (H, H)=7.0 Hz, 3H; 8-C-CHCH\(_3\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta=159.8, 138.8, 136.7, 130.6, 128.3, 127.5, 127.5, 127.2, 124.2, 113.5, 100.6, 83.8, 79.0, 73.2, 73.1, 72.5, 69.6, 55.3, 36.5, 36.2, 28.1, 18.0, 14.9; MS (Cl, perfluorotributylamine): \(m/z(%)\): 439 ((M+H)\(^+\), 63%); Found 439.2489, C\(_{27}\)H\(_{35}\)O\(_5\) requires 439.2484.
(Z, 2S, 3R, 4S, 8S)-8-((1R)-2-Benzyl氧y-1-methyl-ethyl)-2-hydroxymethyl-3-(4-methoxy-benzyl氧y)-4-methyl-3,4,7,8-tetrahydro-2H-oxocine, 36

To a solution of the acetal 34 (16 mg, 36.5 µmol) in toluene (1 mL) at -78 °C was added DIBAL-H (255 µL, 0.255 mmol, of a 1.0 M solution in toluene) dropwise. The solution was stirred and gradually allowed to warm to -5 °C over 2 h. Starting material remained and the mixture was recooled to -50 °C and further DIBAL-H (125 µL) was added. The mixture was warmed to -5 °C over 1 h, at which point the reaction was virtually complete. The solution was allowed to warm to room temperature, then ether (3 mL), a saturated aqueous solution of NH4Cl (1.5 mL) and a saturated aqueous solution of sodium potassium tartrate (1.5 mL) were added. The mixture was stirred until heterogeneous (1 h) then extracted with ether (3 × 15 mL), and the organic extracts washed with brine (10 mL), dried (MgSO4) and concentrated. Flash chromatography (hexane:EtOAc, 3:1→5:2) gave the starting material 34 (1.8 mg, 4.10 µmol, 10%) and the alcohol 36 (14.5 mg, 32.9 µmol, 90%) as a white solid; mp 52 °C (ether); [α]D25 1.9 (c 0.7 in CHCl3); Rf 0.17 (hexane:EtOAc, 4:1); IR (CHCl3): ν=3350-3500; 1H NMR (400 MHz, CDCl3): δ=7.23-7.35 (m, 7H; Ar), 6.86 (d, J (H, H)=8.5 Hz, 2H; Ar), 5.55 (dd, J (H, H)=7.0, 11.0 Hz, 1H; 5-H), 5.43-5.51 (m, 1H; 6-H), 4.60 (d, J (H, H)=12.0 Hz, 1H; CHHAr), 4.49 (d, J (H, H)=10.0 Hz, 1H; CHHAr), 4.45 (d, J (H, H)=12.0 Hz, 1H; CHHAr), 4.40 (d, J (H, H)=10.0 Hz, 1H; CHHAr), 3.93 (dt, J (H, H)=2.5, 10.0 Hz, 1H; CHHOH), 3.82 (dd, J (H, H)=4.0, 9.0 Hz, 1H; CHHOBn), 3.80 (s, 3H; OCH3), 3.67 (dd, J (H, H)=3.0, 10.0 Hz, 1H; OH), 3.51-3.61 (m, 2H; 8-H, CHHOH), 3.47 (dt, J (H, H)=3.0, 9.0 Hz, 1H; 2-H), 3.26 (dd, J (H, H)=2.5, 9.0 Hz, 1H; CHHOBn), 2.96 (t, J (H, H)=10.0 Hz, 1H; 3-H), 2.60-2.66 (m, 1H; 4-H), 2.55 (ddd, J (H, H)=6.5, 9.0, 14.5 Hz, 1H; 7-H'), 2.17 (dd, J (H, H)=6.5, 14.0 Hz, 1H; 7-H'), 1.63-1.69 (m, 1H; 8-C-CHCH3), 1.22 (d, J (H, H)=6.5 Hz, 3H; 4-C-Me), 1.01 (d, J (H, H)=7.0 Hz, 3H; 8-C-CHCH3); 13C NMR (100 MHz, CDCl3): δ=159.4, 137.9, 137.2, 128.3, 127.9, 127.7, 123.3, 133.4, 82.9, 82.1, 78.6, 74.2, 73.6, 72.4, 65.0, 55.3, 38.0, 36.1, 28.0, 18.9, 15.4; MS (CI, perfluorotributylamine); m/z(%): 458 ((M+NH4)+, 20), 441 ((M+H)+, 100); Found 441.2635, C27H37O5 requires 441.2641.
(Z, 2R, 3R, 4S, 8S)-8-((1R)-2-Benzylxoy-1-methyl-ethyl)-2-carbaldehyde-3-(4-methoxy-benzyloxy)-4-methyl-3,4,7,8-tetrahydro-2H-oxocine, 37

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\begin{align*}
\text{PMBO}^+ \quad \text{O} \quad \text{OBn} \\
\end{align*}
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To a solution of the alcohol 36 (14 mg, 31.8 µmol) in dry DMSO (2.5 mL) was added IBX (27 mg, 95.3 µmol) in one portion. The solution was stirred at room temperature for 18 h, then water (5 mL) was added. The mixture was poured into ether (10 mL) and the organic layer was separated. The aqueous phase was extracted with further ether (2 × 10 mL), the combined organic layers were washed with brine (MgSO₄) and concentrated. The product was redissolved in toluene and the solution was concentrated (3 × 2 mL) to give the aldehyde 37 as a pale yellow oil (13 mg, 29.6 µmol, 90%); \([\alpha]^2_{D}^0 \ 0.5 \ (c \ 1.16 \ \text{in CHCl}_3); \ R_f \ 0.30 \ (30\% \ \text{EtOAc} / \ \text{hexane}); \ IR \ (\text{film}): \ \nu=1735; \ \text{H} \ NMR \ (400 \ \text{MHz, CDCl}_3): \ \delta=9.58 \ (d, \ J (H, H)=3.5 \ Hz, \ 1H; \ CHO) \ 7.24-7.35 \ (m, \ 5H; \ Ar), \ 7.21 \ (d, \ J (H, H)=8.5 \ Hz, \ 2H; \ Ar), \ 6.86 \ (d, \ J (H, H)=8.5 \ Hz, \ 2H; \ Ar), \ 5.48-5.53 \ (m, \ 2H; \ 5-H, \ 6-H), \ 4.41-4.51 \ (m, \ 4H; \ 2 \times \ \text{CH}_2\text{Ar}), \ 3.79 \ (s, \ 3H; \ \text{OCH}_3), \ 3.77-3.80 \ (m, \ 1H; \ 2-H), \ 3.56 \ (dd, \ J (H, H)=3.5, \ 9.0 \ Hz, \ 1H; \ \text{CH}_2\text{OBn}), \ 3.44-3.52 \ (m, \ 2H; \ \text{CH}_2\text{OBn}), \ 3.37 \ (t, \ J (H, H)=9.0 \ Hz, \ 1H; \ 3-H), \ 2.68-2.75 \ (m, \ 1H; \ 4-H), \ 2.50-2.58 \ (m, \ 1H; \ 7-H), \ 2.24 \ (dd, \ J (H, H)=5.0, \ 16.0 \ Hz, \ 1H; \ 7-H'), \ 1.76-1.83 \ (m, \ 1H; \ 8-C-\text{CHCl}_3), \ 1.23 \ (d, \ J (H, H)=7.0 \ Hz, \ 3H; \ 4-C-\text{Me}), \ 1.00 \ (d, \ J (H, H)=7.0 \ Hz, \ 3H; \ 8-C-\text{CH}_2\text{H}_3); \ \text{C}^{13} \ NMR \ (100 \ \text{MHz, CDCl}_3): \ \delta=199.0, \ 159.5, \ 138.7, \ 135.8, \ 129.8, \ 129.6, \ 128.3, \ 127.4, \ 124.0, \ 113.9, \ 85.4, \ 80.4, \ 79.6, 73.5, \ 73.2, \ 72.4, \ 55.3, \ 37.9, \ 37.2, \ 28.4, \ 18.5, \ 14.7; \ MS \ (ES^+): \ m/z(\%)\text{:} \ 461 \ ((M+Na)^+, \ 100); \ Found \ 461.2302, \ C_{27}H_{34}O_5Na \ requires \ 461.2304.

(Z, 2S, 3R, 4S, 8S)-8-((1R)-2-Benzylxoy-1-methyl-ethyl)-2-((R/S)-1-hydroxy-prop-2-encyl)-3-(4-methoxy-benzyloxy)-4-methyl-3,4,7,8-tetrahydro-2H-oxocine 38

\[
\begin{align*}
\text{PMBO}^+ \quad \text{O} \quad \text{Obn} \\
\end{align*}
\]

To a solution of the aldehyde 37 (13 mg, 29.5 µmol) in DMSO (2 mL) in a Schlenk tube under Ar was added CrCl₃/1 mol% NiCl₂ (35 mg, 29.5 µmol) rapidly in one portion. Vinyl iodide (22 µL, 29.5 µmol) was added and the green solution was
stirred at room temperature for 72 h. A saturated aqueous solution of NH₄Cl (2 mL) was added, and the solution was stirred vigourously for 30 min. The product was extracted with EtOAc (3 × 10 mL), the organic layers were washed with water (5 mL) then brine (5 mL), dried (MgSO₄) and concentrated. Flash chromatography (LP:EtOAc, 5:1) afforded the allylic alcohols 38 as a colourless oil (5.5 mg, 11.8 μmol, 2:1 mixture of inseparable diastereomers, 40%); Rf 0.20 (PE:EtOAc, 5:1); IR (CDCl₃): ν=3300-3600; ¹H NMR (500 MHz, CDCl₃): δ=7.23-7.36 (m, 7H), 6.88 (d, J (H, H)=8.5 Hz, 2H), 6.87 (d, J (H, H)=8.5 Hz, 2H), 6.11 (ddd, J (H, H)=6.5, 10.5, 17.0 Hz, 1H), 5.96 (ddd, J (H, H)=5.0, 10.5, 17.0 Hz, 1H), 5.42-5.57 (m, 2H), 5.38 (dt, J (H, H)=1.5, 12.0 Hz, 1H), 5.26-5.32 (m, 2H), 5.12 (dt, J (H, H)=1.5, 10.5 Hz, 1H), 4.67 (d, J (H, H)=12.0 Hz, 1H), 4.54 (d, J (H, H)=10.5 Hz, 1H), 4.52 (s, 2H), 4.48 (d, J (H, H)=10.5 Hz, 1H), 4.40-4.51 (m, 1H), 4.38 (d, J (H, H)=12.0 Hz, 1H), 4.21 (d, J (H, H)=11.5 Hz, 1H), 3.93 (dd, J (H, H)=3.5, 9.0 Hz, 1H), 3.79 (s, 3H), 3.63 (dd, J (H, H)=3.0, 9.5 Hz, 1H), 3.52-3.59 (m, 2H), 3.37 (dd, J (H, H)=1.5, 9.0 Hz, 1H), 3.34 (dd, J (H, H)=6.5, 9.0 Hz, 1H), 3.22 (dd, J (H, H)=2.5, 9.0 Hz, 1H), 3.07 (t, J (H, H)=10.0 Hz, 1H), 2.45-2.73 (m, 3H), 2.17 (dd, J (H, H)=6.5, 14.0 Hz, 1H), 1.75-1.83 (m, 1H), 1.57-1.65 (m, 1H), 1.27 (d, J (H, H)=6.5 Hz, 3H), 1.24 (d, J (H, H)=6.5 Hz, 3H), 1.02 (d, J (H, H)=7.0 Hz, 3H), 0.97 (d, J (H, H)=7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ=159.3, 159.3, 139.4, 138.6, 137.7, 137.5, 137.2, 136.9, 130.3, 130.2, 129.7, 129.2, 128.3, 128.0, 127.7, 127.6, 127.5, 123.4, 123.1, 117.4, 115.4, 113.9, 85.0, 83.1, 81.5, 80.7, 79.3, 78.9, 74.2, 73.6, 73.5, 73.0, 72.5, 72.4, 72.0, 55.3, 55.3, 38.3, 38.1, 36.9, 36.3, 28.0, 27.7, 19.2, 19.0, 15.5, 14.7; MS (CI, perfluorotributylamine): m/z(%):484 ((M+NH₄)+, 15), 467 ((M+H)+, 100); Found 467.2790, C₂₉H₃₉O₅ requires 467.2797.

(Z, 2S, 3R, 4S, 8S)-8-((1R)-2-Benzylhydroxy-1-methyl-ethyl)-3-hydroxy-2-((1R/S)-1-hydroxy-prop-2-eneyl)-4-methyl-3,4,7,8-tetrahydro-2H-oxocine

To a solution of the alcohols 38 (6.2 mg, 16.6 μmol) in DCM (2 mL) stirring at -20 °C was added TFA (0.5 mL). The mixture was stirred for 30 min during which time the solution became pale orange. The reaction was quenched at -20 °C by addition of
a saturated aqueous solution of NaHCO₃ (4 mL), stirred vigourously and allowed to
warm to room temperature. The product was extracted with DCM (3 × 5 mL), the
extracts being washed with water (5 mL), brine (5 mL), dried (MgSO₄) and
concentrated. Flash chromatography (PE:EtOAc, 1:1) gave the title compounds as a
colourless oil (4.3 mg, 12.4 µmol, 75%); Rf 0.35 (PE:EtOAc, 1:1); IR (CHCl₃):
v=3440; ¹H NMR (400 MHz, CDCl₃): δ=7.26-7.36 (m, 5H; Ar), 6.02 (ddd, J (H, H)=5.5, 10.5, 17.5 Hz, 1H; minor, CH=CH₂), 5.97 (ddd, J (H, H)=7.0, 10.5, 17.5 Hz, 1H; major, CH=CH₂), 5.43-5.54 (m, 2H; both, H-5, H-6), 5.29-5.34 (m, 1H; both, CH=CHH), 5.22 (ddd, J (H, H)=1.0, 2.0, 10.5 Hz, 1H; major, CH=CHH), 5.17 (dt, J (H, H)=1.5, 10.5 Hz, 1H; minor, CH=CHH), 4.68 (d, J (H, H)=12.0 Hz, 1H; major, CHHAr), 4.39-4.45 (m, 1H; both, CHCH=CH₂), 4.48 (d, J (H, H)=13.0 Hz, 1H; minor, CHHAr), 4.39 (d, J (H, H)=12.0 Hz, 1H; major, CHHAr), 4.27 (d, J (H, H)=12.0 Hz, 1H; minor, CHHAr), 3.90 (dd, J (H, H)=3.5, 9.0 Hz, 1H; major, CHHOBn), 3.77-3.83 (m, 1H; minor, CHHOBn), 3.58 (dd, J (H, H)=6.5, 10.5 Hz, 1H; major, 8-H), 3.28-3.50 (m, 4H; minor, CHO/CH=CH₂, 3-H, 8-H, CHHOBn, both, 2-H), 3.20 (dd, J (H, H)=2.0, 9.0 Hz, 1H; major, CHHOBn), 3.10-3.14 (m, 1H; major, 3-H), 2.92 (br d, J (H, H)=9.0 Hz, 1H major, CHO/CH=CH₂), 2.44-2.60 (m, 2H; both, 7-H', 4-H), 2.13-2.27 (m, 1H; both, H-7), 1.69-1.78 (m, 1H; both, 8-C-CHCH₃), 1.64 (br d, J (H, H)=6.0 Hz, 1H; both, 3-C OH), 1.17 (d, J (H, H)=7.0 Hz, 3H; minor, 4-C-Me), 1.16 (d, J (H, H)=6.5 Hz, 3H; major, 4-C-Me), 1.00 (d, J (H, H)=7.0 Hz 3H; major, 8-C-CHCH₃), 0.99 (d, J (H, H)=7.0 Hz, 3H; minor 8-C-CHCH₃); ¹³C NMR (400 MHz, CDCl₃): δ=138.5, 138.4, 137.7, 137.2, 137.2, 136.9, 128.4, 128.3, 128.0, 127.7, 127.5, 123.6, 123.4, 116.6, 115.9, 84.3, 82.8, 78.9, 78.8, 74.3, 74.1, 74.0, 73.9, 73.5, 73.0, 72.6, 71.8, 38.1, 38.0, 36.5, 35.9, 27.8, 27.5, 18.9, 18.6, 15.6, 14.9; MS (CI, perfluorotributylamine): m/z(%): 364 ((M+NH₄)⁺, 19), 347 ((M+H)⁺, 63); Found 347.2223, C₂₁H₃₁O₄ requires 347.2222.
(Z, 4R/S, 4aS, 6S, 10S, 10aR)-6-((1R)-2-Benzoxo-1-methyl-ethyl)-10-methyl-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxabenzocycloocten-2-one 39

To a mixture of (Z, 2S, 3R, 4S, 8S)-8-((1R)-2-benzyloxy-1-methyl-ethyl)-3-hydroxy-2-((1R/S)-1-hydroxy-prop-2-eneyl)-4-methyl-3,4,7,8-tetrahydro-2H-oxocine (5 mg, 14.4 µmol), triphosgene (2.5 mg, 8.44 µmol) and 4Å molecular sieves (spatula tip) at -78 °C under N2 was added DCM (2 mL). The solution was stirred at -78 °C, pyridine (7 µL, 86.4 µmol) and Et3N (12 µL, 86.4 µmol) were added, and the mixture was allowed to warm slowly to -10 °C (1.5 h) at which point no starting material remained. The reaction was quenched via addition of of a saturated aqueous solution of NH4Cl (3 mL) and allowed to warm to room temperature. The product was extracted with DCM (3 × 10 mL), the extracts were washed with brine (5 mL), and dried (MgSO4), and concentrated. Flash chromatography (PE:EtOAc, 3:1) provided the carbonates 39 as a colourless oil (4.8 mg, 12.9 µmol, 90%); Rf 0.61 (PE: EtOAc, 1:1); IR (CHCl3): ν=2927, 1750; 1H NMR (400 MHz, CDCl3): δ=7.25-7.36 (m, 5H; both, Ar), 5.89 (ddd, J (H, H)=5.5, 10.5, 17.0 Hz, 1H; major, CH=CH2), 5.84-5.94 (m, 1H; minor, CH=CH2), 5.52-5.63 (m, 1H; both, 5-H), 5.44 (dt, J (H, H)=1.5, 17.0 Hz, 1H; major, CH=CHH), 5.40-5.48 (m, 3H; major, 6-H, minor, 6-H, CH=CHH), 5.36-5.40 (m, 1H; minor, CH=CHH), 5.22 (dt, J (H, H)=1.5, 10.5 Hz, 1H; major, CH=CHH), 4.64 (m, 1H; minor, allylic H), 4.57 (ddt, J (H, H)=1.5, 5.5, 9.5 Hz, 1H; major, CHCH=CH2), 4.40-4.53 (m, 2H; both, CH2Ar), 3.86 (unresolved dd, 1H; minor, 3-H), 3.83 (dd, J (H, H)=9.5, 10.5 Hz, 1H; major, 3-H), 3.74 (dd, J (H, H)=5.5, 10.0 Hz, 1H; minor, 2-H), 3.62 (dd, J (H, H)=6.5, 9.5 Hz, 1H; minor, 8-H), 3.53 (dd, J (H, H)=6.0, 9.5 Hz, 1H; major, 8-H), 3.46 (dd, J (H, H)=3.5, 9.0 Hz, 1H; major, CHHOBn), 3.42-3.45 (m, 2H; minor, CH2OBn), 3.40 (dd, J (H, H)=6.0, 9.0 Hz, 1H; major, CHHOBn), 3.35 (t, J (H, H)=9.5 Hz, 1H; major, 2-H), 2.61-2.71 (m, 1H; both, 4-H), 2.52-2.57 (m, 1H; major, 7-H), 2.47-2.53 (m, 1H; minor, 7-H), 2.28 (dd, J (H, H)=6.5, 14.5 Hz, 1H; both, 7-H'), 1.70-1.81 (m, 1H; both, 8-C-CHCH3), 1.27 (d, J (H, H)=6.5 Hz, 3H; major, 4-C-Me), 1.23 (d, J (H, H)=6.5Hz, 3H; minor, 4-C-Me), 1.04 (d, J (H, H)=6.5 Hz, 3H; minor, 8-C-CHCH3), 1.02 (d, J (H, H)=7.0 Hz, 3H; major, 8-C-CHCH3); 13C NMR (100 MHz, CDCl3): δ=148.2, 147.9, 138.5, 138.4, 134.8, 134.6, 131.9, 131.2, 128.4, 128.3, 128.7,
127.6, 127.5, 127.4, 125.6, 125.4, 119.2, 118.8, 82.4, 80.4, 80.0, 79.6, 79.5, 77.1, 75.0, 73.2, 72.6, 72.1, 71.9, 36.6, 36.5, 36.1, 36.0, 28.0, 28.0, 18.1, 17.8, 14.8, 14.8; MS (CI, perfluorotributylamine): \( m/z \) (%): 373 ((M+NH\(_4\))\(^+\), 23), 373 ((M+H))\(^+\), 9); Found 373.2015, C\(_{22}\)H\(_{29}\)O\(_5\) requires 373.2015.

\((5Z, 10Z, 6aS, 8S, 12S, 12aR)-8-((1R)-2-Benzylxy-1-methyl-ethyl)-12-methyl-4,6a,8,9,12,12a-hexahydro-3H-1,7-dioxaoctalen-2-one\) 40

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\begin{align*}
\text{To a solution of carbonates 39 (4.8 mg, 12.9 \mu mol) in toluene (2 mL) was added dimethyltitanocene (37 \mu L of a 94 mg/mL solution in toluene, 16.8 \mu mol). The mixture was heated under reflux in the absence of light for 1.5 h at which point further dimethyltitanocene (15 \mu L, 6.45 \mu mol) was added. After a further 1.5 h under reflux, the mixture was allowed to cool, concentrated, and purified by flash chromatography (PE:EtOAc, 20:3) to yield the bicyclic lactone 40 as a colourless oil (2.2 mg, 5.93 \mu mol, 46%); } \\
\text{[\(\alpha\)]\(_D\)}^{21} = -9.1 (c 0.22 in CHCl\(_3\)); R\(_f\) 0.33 (PE:EtOAc, 20:3); IR (CHCl\(_3\)): \(\nu\) = 1747; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) = 7.25-7.35 (m, 5H; Ar), 5.63-5.71 (m, 1H; 5-H), 5.58 (dd, \(J\) (H, H)=5.0, 12.0 Hz, 1H; 6-H), 5.47-5.56 (m, 2H; 10-H, 11-H), 4.26 (d, \(J\) (H, H)=3.0 Hz, 2H; CH\(_2\)Ar), 4.18 (dd, \(J\) (H, H)=9.5, 10.5 Hz, 1H; 12a-H), 4.08 (ddd, \(J\) (H, H)=2.0, 5.0, 9.5 Hz, 1H; 6a-H), 3.52 (dd, \(J\) (H, H)=3.5, 9.0 Hz, 1H; C\(_H\)HOBn), 3.47 (ddd, \(J\) (H, H)=2.0, 7.0, 9.0 Hz, 1H; 8-H), 3.43 (dd, \(J\) (H, H)=6.0, 9.0 Hz, 1H; C\(_H\)HOBn), 2.77 (ddd, \(J\) (H, H)=2.0, 6.5, 14.0 Hz, 1H; 3-H), 2.67-2.73 (m, 1H; 12-H), 2.60-2.67 (m, 1H; 4-H), 2.51-2.59 (m, 1H; 9-H), 2.27 (ddd, \(J\) (H, H)=5.0, 12.0, 14.0 Hz, 1H; 3-H'), 2.22-2.28 (m, 1H; 9-H'), 2.08-2.15 (m, 1H; 4-H'), 1.66-1.77 (m, 1H; 8-C-CH\(_3\)CH\(_3\)), 1.15 (d, \(J\) (H, H)=6.5 Hz, 3H; 12-C-Me), 1.00 (d, \(J\) (H, H)=7.0 Hz, 3H; 8-C-CH\(_3\)CH\(_3\)); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) = 174.9, 128.8, 136.9, 135.1, 129.9, 128.2, 127.5, 127.4, 125.0, 81.4, 79.9, 78.8, 73.1, 72.6, 37.4, 37.3, 35.6, 28.9, 25.5, 19.2, 14.7; MS (CI, perfluorotributylamine): \(m/z\) (%): 388 ((M+NH\(_4\))\(^+\), 42), 371 ((M+H))\(^+\), 100); Found 371.2224, C\(_{23}\)H\(_{31}\)O\(_4\) requires 371.2222.}
(Z, 3R, 7R, 8S)-8-((1(R))-2-Benzylxy-1-methyl-ethyl)-3-hydroxy-5,7-dimethyl-3,4,7,8-tetrahydrooxocin-2-one 41

To a cooled solution (-78 °C) of KHMDS (4.8 mL, 0.5 M solution in toluene, 2.40 mmol) in toluene (7 mL) was added the lactone 9² (325 mg, 1.09 mmol) via cannula as a solution in toluene (4 mL, 1 mL rinse). The mixture was stirred for 20 min. (+)-2-(Phenylsulfonyl)-3-phenyloxaziridine (900 mg, 3.43 mmol) was added dropwise via cannula as a solution in toluene (4 mL, 2 mL rinse). The mixture was stirred at -78 °C for a further 1.5 h, and was quenched at this temperature with a solution of (+)-camphor-10-sulfonic acid (approx. 2.5 eq.) in THF (5 mL). The mixture was warmed to ambient temperature and water (20 mL) was added. The mixture was extracted with ether (3 × 40 mL) and the combined organics were washed with brine (40 mL), dried (MgSO₄) and evaporated in vacuo. Purification by flash chromatography (hexane:ether, 19:11) yielded the title compound 41 as an inseparable mixture of 3-C diastereomers (307 mg, 0.963 mmol, 88%) in a ratio determined by ¹H NMR to be 20:1; $R_f$ (DCM:ether, 100:3) 0.17; $[\alpha]^2_{D}$ -10.2 (c 0.65 in CHCl₃); mp 102-104 °C; IR (CHCl₃): $\nu$=3541, 1741; ¹H NMR (400 MHz, CDCl₃): $\delta$=7.40-7.24 (m, 5H; Ar), 5.48 (d, $J$ (H, H)=8.7 Hz, 1H; major, 6-H), 5.09 (br s, 1H; minor, 6-H), 4.60 (dd, $J$ (H, H)=8.0, 3.7 Hz, 1H; major, 3-H), 4.87 (dd, $J$ (H, H)=9.3, 3.9 Hz, 1H; minor, 6-H), 4.62-4.56 (m, 1H; minor, 8-H), 4.56-4.45 (m, 3H; major, $CH_2$Ar, major, 8-H), 4.47 (d, $J$ (H, H)=12.1 Hz, 1H; minor $CH_2$Ar), 4.44 (d, $J$ (H, H)=12.1 Hz, 1H; minor, $CH_2$Ar), 3.60 (dd, $J$ (H, H)=8.7, 4.1 Hz, 1H; minor $CHOBn$), 3.58 (dd, $J$ (H, H)=9.1, 3.6 Hz, 1H; major, $CHOBn$), 3.39 (dd, $J$ (H, H)=8.7, 2.3 Hz, 1H; minor $CHOBn$), 3.32 (dd, $J$ (H, H)=9.1, 7.3 Hz, 1H; major, $CHOBn$), 3.08-2.85 (m, 1H; OH), 2.95-2.72 (m, 1H; major 4-H), 2.63-2.45 (m, 1H; major, 7-H), 2.27 (d, $J$ (H, H)=14.8 Hz, 1H; minor 4-H), 2.25 (dd, $J$ (H, H)=13.4, 5.9 Hz, 1H; major 4-H'), 2.17-2.00 (m, 1H; 8-C-$CHCH_3$), 1.82 (d, $J$ (H, H)=1.4 Hz, 3H; major 5-C-$CH_3$), 1.77 (d, $J$ (H, H)=1.4 Hz, 3H; minor 5-C-$CH_3$), 1.14 (d, $J$ (H, H)=7.2 Hz, 3H; major, $CH_3$), 1.07 (d, $J$ (H, H)=6.9 Hz, 3H; minor, $CH_3$), 1.06 (d, $J$ (H, H)=7.3 Hz, 3H; minor $CH_3$), 1.05 (d, $J$ (H, H)=6.9 Hz, 3H; major $CH_3$); ¹³C NMR (100 MHz, CDCl₃): $\delta$=179.7, 138.5, 129.1, 128.5, 128.3, 127.6, 127.5, 81.4, 73.3, 73.0, 72.3, 39.9 (br), 35.6, 34.3
(Z, 3R, 7R, 8S)-8-(1(R)-2-Benzylxoy-1-methyl-ethyl)-5,7-dimethyl-3-trimethylsilanyloxy-3,4,7,8-tetrahydrooxocin-2-one 42

To a solution of the alcohol 41 in THF was added Et$_3$N (50 µL, 0.36 mmol). Et$_3$N (300 µL) and TMSCl (300 µL) were mixed together and centrifuged in a sealed vessel at 4000 r.p.m. for 3 min. Approximately 75% of the supernatant liquid was added to the reaction mixture dropwise via syringe. The mixture was stirred at room temperature for 40 min, was cooled to 0 °C and then quenched by the addition of pH 7 phosphate buffer (5 mL). The mixture was extracted with ether (3 × 15 mL) and the combined organics were dried (MgSO$_4$) and evaporated. Purification by flash chromatography (hexane:ether, 9:1) yielded the title compound 42 (84 mg, 0.215 mmol, 88%); $R_f$ (hexane:ether, 9:1) 0.27; $[\alpha]_D^{22}$ +5.6 (c 2.5 in CHCl$_3$); IR (CHCl$_3$): $\nu=$(CHCl$_3$) 1755; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$= 7.40-7.23 (m, 5H; Ar), 5.37 (d, $J (H, H)$=8.9 Hz, 1H; HC=CH), 4.57-4.43 (m, 4H; CH$_2$Ar, 3-H, 8-H), 3.61 (dd, $J (H, H)$=9.2, 3.8 Hz, 1H; CH/HOBN), 3.27 (t, $J (H, H)$=9.2 Hz, 1H; CH/HOBN), 2.82-2.45 (m, 2H; 4-H, 7-H), 2.40-2.21 (m, 1H; 4-H'), 2.19-2.00 (m, 1H; 8-C-CH$_3$), 1.82 (s, 3H; 5-C-CH$_3$), 1.09 (d, $J (H, H)$=7.0 Hz, 3H; CH$_3$), 1.06 (d, $J (H, H)$=6.8 Hz, 3H; CH$_3$), 0.18 (s, 9H; (CH$_3$)$_2$Si); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$= 177.8 (2-C), 138.7, 128.6, 128.3, 127.6, 127.5, 79.6 (8-C), 73.2 (CH$_2$Ar), 72. 4 (CH$_2$OBn), 41.0 (4-C), 35.4 (1'-C), 34.0 (7-C), 27.7 (vinyl CH$_3$), 15.3 (Me), 0.0 ((CH$_3$)$_2$Si); MS (EI): Found M$^+$, 390.2230, C$_{22}$H$_{34}$O$_4$Si requires 390.2226.

(Z, 3R, 7R, 8S)-8-((1R)-2-Benzylxoy-1-methyl-ethyl)-5,7-dimethyl-2-methylene-3-trimethylsilanyloxy-3,4,7,8-tetrahydro-2H-oxocine

To a solution of the lactone 42 (515 mg, 1.32 mmol) in toluene (20 mL) was added dimethyltitanocene (8.2 mL of a 50 mg/mL solution in toluene, 1.98 mmol) via
A condenser was fitted to the flask and the mixture was heated under reflux with the exclusion of light for 1 h. Additional dimethyltitanocene (3.0 mL, 0.72 mmol) was added and the mixture was stirred a further 20 min. Following cooling, the mixture was preadsorbed onto deactivated UG1 alumina (deactivated by the addition of 6% H2O (w/w). The resultant solid was loaded onto a column of deactivated UG1 alumina and purified by eluting under gravity (hexane:ether, 94:6), yielding the title compound (503 mg, 1.29 mmol, 98%) as an orange oil; $R_f$ (hexane:ether 19:1) 0.31; $\left[\alpha\right]_D^{21} +16.5$ (c 1.2, CDCl3); IR (CHCl3): $\nu = 1646$; $^1$H NMR (400 MHz, CDCl3): $\delta = 7.40-7.24$ (m, 5H; Ar), 5.91 (s, 1H; OC=C=CH2), 5.16 (d, 1H; $J$ (H, H)=8.6 Hz, 1H; 6-H), 4.84 (s, 1H; OC=CH2Ar), 3.99 (br t, $J$ (H, H)=6.3 Hz, 1H; 3-H), 3.70 (t, $J$ (H, H)=4.9 Hz, 1H; 8-H), 3.59 (dd, $J$ (H, H)=9.2, 4.8 Hz, 1H; CH3O), 3.29 (dd, $J$ (H, H)=9.2, 7.8 Hz, 1H; CH3O), 2.81-2.62 (m, 1H; 7-H), 2.37-2.25 (m, 2H; 2 × 4-H), 2.14-1.97 (m, 1H; 8-C-CH3), 1.76 (d, $J$ (H, H)=1.3 Hz, 3H; vinyl CH3), 1.15 (d, $J$ (H, H)=6.9 Hz, 3H; 1'-C-CH3), 1.02 (d, $J$ (H, H)=7.1 Hz, 3H; 7-C-CH3), 0.15 (m, 9H; (CH3)3Si); $^{13}$C NMR (100 MHz, CDCl3): $\delta = 167.8$ (2-C), 138.9 (5-C), 134.2, 128.3, 128.1, 127.5, 127.4, 112.6 (C-6), 92.1 (H2C=C), 86.5 (8-C), 73.0 (CH2Ar), 72.5 (CH2OBn), 71.8 (3-C), 42.7 (4-C), 34.4 (1'-C), 34.2 (7-C), 26.5 (vinyl CH3), 16.9 (1-C-CH3), 15.0 (7-C-CH3), -0.1 ((CH3)3Si); MS (EI): Found M+ 388.2445, C23H36O3Si, requires 388.2434.

$^{(Z, 3R, 7R, 8S)}$-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-5,7-dimethyl-3-hydroxy-2-methylene-3,4,7,8-tetrahydro-2H-oxocine 43

![Structure of 43](image)

To a cooled (0 °C) solution of $^{(Z, 3R, 7R, 8S)}$-8-((1R)-2-benzyloxy-1-methyl-ethyl)-5,7-dimethyl-2-methylene-3-trimethylsilyloxy-3,4,7,8-tetrahydro-2H-oxocene (15.5 mg, 39.8 µmol) in dry MeOH (1 mL) was added solid K2CO3 (10 mg, 72 µmol). The mixture was warmed to ambient temperature and stirred for 30 min. Filtration of the mixture (glass wool) was followed by purification by gravity pipette chromatography (ether:hexane, 1:1) using deactivated UG1 alumina to afford the title compound 43 (11.0 mg, 34.7 µmol, 87%) as a clear oil; $R_f$ (ether:hexane, 1:1) 0.33; $\left[\alpha\right]_D^{22} +8.8$ (c 0.5, CHCl3); IR (CHCl3): $\nu = 3598$, 1644; $^1$H NMR (400 MHz, CDCl3): $\delta = 7.37-7.25$ (m,
5H; Ar), 5.13 (d, J (H, H)=9.3 Hz, 1H; 6-H), 4.86 (t, J (H, H)=1.3 Hz, 1H; OC=CHH), 4.57 (d, J (H, H)=1.3 Hz, 1H; OC=CHH), 4.48 (s, 2H; CH2Ar), 4.01 (br dd, J (H, H)=9.3 Hz, 1H; 3-H), 3.72 (dd, J (H, H)=9.3 Hz, 1H; 7-H), 3.57 (dd, J (H, H)=9.3 Hz, 1H; 6-H), 4.86 (t, J (H, H)=1.3 Hz, 1H; 8-H), 3.57 (dd, J (H, H)=9.3 Hz, 1H; CHHOBn), 3.24 (dd, J (H, H)=9.3 Hz, 7.9 Hz, 1H; CHHOBn). 2.83-2.71 (m, 1H; 7-H), 2.35 (d, J (H, H)=6.5 Hz, 2H; 4-H, 4-H’), 2.17 (s, 1H; OH), 2.11-2.02 (m, 1H; 8-C=CHCH3), 1.76 (s, 3H; vinyl CH3), 1.15 (d, J (H, H)=6.9 Hz, 3H; 1’-C=CH3), 1.00 (d, J (H, H)=7.1 Hz, 3H; 7-C=CH3). 13C NMR (100 MHz, CDCl 3): δ=168.2 (C=CH2), 138.8 (5-C), 133.4 (ArC), 128.6, 128.3, 127.6, 127.4, 91.6 (H2C=C), 86.7 (8-C), 73.0 (CH2Ar), 72.3 (CH2OBn), 71.9 (CHOH), 41.3 (4-C), 34.3 (1’-C), 34.0 (7-C), 26.4 (vinyl CH3), 17.1 (9-C=CH2), 15.4 (7-C=CH3); MS (CI, NH3): m/z(%): 334 ((M+NH4)+, 18), 317 ((M+H)+, 100); Found 317.2117. C20H29O3 requires 317.2117.

(2Z, 3R, 7R, 8S)-8-((1R)-2-Benzyl-oxy-1-methyl-ethyl)-5,7-dimethyl-3-dimethylsilanyloxy-2-methylene-3,4,7,8-tetrahydro-2H-oxocine 44

To a solution of the enol ether 43 (292 mg, 0.923 mmol) in 1,1,3,3-tetramethyldisilazane (1.9 mL) was added solid NH4Cl (~10 mg). The mixture was heated to 60 °C for 9 h. Upon cooling to ambient temperature, dry hexane (5 mL) was added. The mixture was quickly filtered through a plug of cotton wool and was then evaporated to afford the title compound 44 (342 mg, 0.91 mmol, 99%) as a yellow oil which was stored under vacuum for 48 h and then used immediately; [α]12D +8.8 (c 0.5, CHCl3); IR (CDCl3): ν=2245, 2120, 1646, 1453; 1H NMR (400 MHz, CDCl3): δ=7.37-7.32 (m, 4H; Ar), 7.32-7.24 (m, 1H; Ar), 5.17 (d, J (H, H)=9.5 Hz, 1H; 6-H), 4.84 (t, J (H, H)=1.2 Hz, 1H; OC=CHH), 4.68 (sp, J (H, H)=2.8 Hz, 1H; SiH), 4.53 (s, 1H; OC=CHH), 4.50 (s, 1H; CHHAr), 4.49 (s, 1H; CHHAr), 3.99 (br t, J (H, H)=5.8 Hz, 1H; 3-H), 3.70 (t, J (H, H)=5.5 Hz, 1H; 8-H), 3.58 (dd, J (H, H)=9.3, 3.8 Hz, 1H; CHHOBn), 3.27 (dd, J (H, H)=9.3, 7.8 Hz, 1H; CHHOBn), 2.80-2.67 (m, 1H; 7-H), 2.40-2.30 (m, 2H; 4-H, 4-H’), 2.12-2.01 (m, 1H; 8-C=CHCH3), 1.76 (d, J (H, H)=1.3 Hz, 3H; 5-C=CH3), 1.15 (d, J (H, H)=6.9 Hz, 3H; 8-C=CHCH3), 1.01 (d, J (H, H)=7.1 Hz, 3H; 7-C=CH3), 0.25 (d, J (H, H)=2.8 Hz, 3H; SiCH3), 0.24 (d, J (H,
$^1$H NMR (100 MHz, CDCl$_3$): $\delta = 167.2$ (C=CH$_2$), 138.9 (5-C), 133.9, 128.3, 127.5, 127.4, 92.2 (H$_2$C=C), 85.5 (8-C), 73.3 (3-C), 73.0 (CH$_2$Ar), 72.5 (CH$_2$OBn), 42.3 (4-C), 34.4 (1'-C), 34.2 (7-C), 26.4 (5-C-CH$_3$), 16.9 (8-C-CH$_3$), 15.0 (7-C-CH$_3$), -1.2 (SiCH$_3$), -1.3 (SiCH$_3$). This compound was not suitable for analysis by mass spectrometry.

(Z, 2R, 3R, 7R, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-3-hydroxy-2-hydroxymethyl-7-methyl-3,4,7,8-tetrahydro-2H-oxocin 45, and (Z, 2S, 3R, 7R, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-3-hydroxy-2-hydroxymethyl-7-methyl-3,4,7,8-tetrahydro-2H-oxocin 46

To a dry Schlenk tube in a glove box was added (bicyclo(2.2.1)hepta-2,5-diene)(1,4-bis(diphenylphosphino)butane)rhodium(I)tetrafluoroborate (~20 mg, 28 µmol). The Schlenk tube was sealed and taken out of the glove box. It was placed on a dry Ar manifold and was flushed with Ar and evacuated 3 times, finally leaving the catalyst under a positive pressure of argon. The enol ether 44 (190 mg, 0.51 mmol) was charged to the Schlenk tube via cannula as a solution in dry and O$_2$-free THF (6 mL, 6 mL rinse). THF (4 mL) was added. The solution was stirred for 26 h at 62 °C and was then cooled to ambient temperature. Solid EDTANa$_2$•2H$_2$O (50 mg) was added to the mixture and stirring was continued for 1 h. The mixture was then diluted with dry hexane (30 mL) and filtered through a plug of Celite™ eluting with dry hexane. The resulting liquid was evaporated in vacuo and dissolved in THF:MeOH 1:1 (7 mL). To this solution was added KOH (1.0 mL, 0.15 M) and H$_2$O$_2$ (0.5 mL, 30%) and the mixture was stirred for 1 h. Additional KOH (0.4 mL, 0.15 M) and H$_2$O$_2$ (0.2 mL, 30%) were added and stirring was continued for 15 min. The reaction was quenched by the addition of 10% Na$_2$S$_2$O$_3$ (60 mL). The mixture was extracted with EtOAc (3 × 50 mL) and the combined organic layers were washed with brine (50 mL). Purification by flash chromatography (DCM:MeOH, 25:1→50:3) led to the isolation of the product diols 45 and 46 (104 mg, 0.31 mmol, 61%) as an inseparable mixture of diastereomers in a ratio of approx 6.4:1 as judged by $^1$H NMR; $R_f$ (DCM:MeOH, 20:1) 0.12; $[\alpha]_D^{19} +13.7$ (c 1.4, CHCl$_3$); IR (CHCl$_3$): $\nu =$3942, 3688; $^1$H NMR (400
MHz, CDCl3): δ=7.40-7.24 (m, 5H; Ar), 5.35 (d, J (H, H)=6.8 Hz, 1H; 6-H), 4.51 (s, 2H; CH2Ar), 4.15-4.03 (m, 1H; 8-H), 4.03-3.91 (m, 2H; 2-H, 3-H), 3.74-3.60 (m, 2H; H2C=C), 3.56 (dd, J (H, H)=8.8, 3.8 Hz, 1H; CHHOBn), 3.40 (t, J (H, H)=8.8 Hz, 1H; CHHOBn), 2.97-2.87 (m, 1H; 7-H), 2.84 (d, J (H, H)=6.8 Hz, 1H; OH), 2.80-2.69 (m, 2H; 4-H), 2.30 (dd, J (H, H)=13.1, 7.0 Hz, 1H; 4-H'), 2.15-2.05 (m, 1H; 8-C-CH3), 1.72 (s, 3H; 5-C-CH3), 1.05 (d, J (H, H)=6.9 Hz, 3H; CH3), 1.04 (d, J (H, H)=7.4 Hz, 3H; CH3), 13C NMR (100 MHz, CDCl3): δ=138.3, 133.0, 131.0, 128.4, 127.8, 127.7, 83.0, 81.7, 74.3, 73.3, 72.6, 72.3, 71.5, 65.0, 40.5, 39.3, 38.3, 35.8, 34.9, 26.8, 25.9, 17.1, 16.9, 15.8, 14.4; MS (Cl, NH3): m/z (%): 352 ((M + NH4)+, 2), 335 ( (M + H) +, 13), 106 (100); Found 335.2219, C20H31O4 requires 335.2222.

\((Z, 2S, 4aR, 6S, 7R, 10aR)-6-((1R)-2-Benzyl-1-methyl-ethyl))-7,9-dimethyl-2-(4-methoxyphenyl)-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxabenzocyclooctene 47

To a solution of the mixture of diols 45 and 46 (100 mg, 0.30 mmol) in benzene was added anisaldehyde (45 µL, 0.36 mmol) via syringe followed by solid PPTS (8 mg). The mixture was heated under reflux (Dean-Stark conditions) for 2.5 h. The mixture was evaporated and the residue was purified by flash chromatography (hexane:ether, 3:1→13:7) to afford the major product acetal 47 (110 mg, 0.243 mmol, 81%) as a clear colourless oil. The 1H NMR data at -30 °C and 55 °C are reported, Rf (hexane:ether, 3:1) 0.17; [\(\alpha\)]D24 - 8.1 (c 0.85, CHCl3); IR (CHCl3): ν=1614, 1518, 1454, 1260, 1105; 1H (400 MHz, -30 °C CDCl3): δ=7.48-7.42 (m, 2H; Ar), 7.39-7.26 (m, 6H; Ar), 6.86 (d, J (H, H)=8.4 Hz, 2H; Ar), 5.48 (s, 1H; 2-H), 5.35 (d, J (H, H)=8.6 Hz, 1H; 8-H), 4.51 (d, J (H, H)=11.8 Hz, 1H; CHHAr), 4.44 (d, J (H, H)=11.8 Hz, 1H; CHHAr), 4.12 (dd, J (H, H)=11.1, 6.1 Hz, 1H; 10a-H), 4.06 (d, J (H, H)=12.2 Hz, 1H; 4-H), 3.91 (d, J (H, H)=12.2 Hz, 1H; 4-H'), 3.85-3.76 (m, 4H; CH3O, 6-H), 3.69 (br d, J (H, H)=8.6 Hz, 1H; CHHOBn), 3.62 (br s, 1H; 4a-H), 3.23-3.11 (m, 1H; 7-H), 3.17 (br t, J (H, H)=8.6 Hz, 1H; CHHOBn), 2.92 (br t, J (H, H)=11.8 Hz, 1H; 10-H), 2.24-2.14 (m, 2H; 10-H', 6-C-CH3H), 1.75 (s, 3H; 9-C-CH3), 1.12 (d, J (H, H)=6.5 Hz, 3H; 6-C-CH3H), 1.05 (d, J (H, H)=7.2 Hz, 3H; 7-C-CH3); 1H NMR (400 MHz, 55 °C CDCl3): δ=7.44 (dt, J (H, H)=8.6, 2.4 Hz, 2H; Ar), 7.36-7.24 (m, 6H; Ar), 6.85 (dt,
J (H, H)=8.6, 2.4 Hz, 2H; Ar), 5.46 (s, 1H; 2-H), 5.39 (d, J (H, H)=7.7 Hz, 1H; 8-H), 4.52 (d, J (H, H)=12.1 Hz, 1H; CH/Ar), 4.48 (d, J (H, H)=12.1 Hz, 1H; CH/Ar), 4.14 (dd, J (H, H)=12.1, 1.6 Hz, 1H; 4-H), 4.06 (ddd, J (H, H)=12.4, 6.2, 1.6 Hz, 1H, 10a-H), 4.06-3.99 (m, 1H; 6-H), 3.89 (dd, J (H, H)=12.1 Hz, 1H; 10-H), 3.79 (s, 3H; CH3O), 3.73 (dd, J (H, H)=9.1, 3.2 Hz, 1H; CHOBn), 3.66 (br q, J (H, H)=1.6, Hz 1H; 4a-H), 3.32 (t, J (H, H)=9.1 Hz, 1H; CHOBn), 3.17-3.05 (m, 1H; 7-H), 3.03 (br t, J (H, H)=12.4 Hz, 1H; 10-H), 2.23 (dd, J (H, H)=12.4, 6.2 Hz, 1H; 10-H'), 2.19-2.11 (m, 1H; 6-C-CH3), 1.79 (s, 3H; 9-C-CH3), 1.11 (d, J (H, H)=6.8 Hz, 1H; 9-C-CH3), 1.06 (d, J (H, H)=7.4 Hz, 3H; 7-C-CH3); 13C NMR (100 MHz, -30 °C CDCl3): δ=158.5, 137.0 (ArC), 132.5 (9-C), 129.3 (ArC), 129.1 (8-C), 127.4 (ArC), 127.0 (ArC), 126.7 (ArC), 126.4 (ArC), 112.2 (ArC), 100.1 (2-C), 84.4 (6-C), 79.8 (10a-C), 72.7 (CH2OBn), 72.1, 72.0, 62.9 (4a-C), 54.2 (CH3O), 38.5 (7-C), 34.2 (10-C), 32.9, 23.3 (9-C-CH3), 18.4 (7-C-CH3), 15.2; MS (Cl, NH3): m/z(%): 470 ((M+NH4)+, 15), 453 ((M+H)+, 75), 137 (100); Found 453.2637, C28H37O5 requires 453.2641.

(Z, 2R, 3R, 7R, 8S)-8-((1R)-2-Benzzyloxy-1-methyl-ethyl)-7,9-dimethyl-2-hydroxymethyl-3-(4-methoxy-benzyloxy)-3,4,7,8-tetrahydro-2H-oxocine 48

To a cooled (-78 °C) solution of the acetal 47 (93 mg, 0.205 mmol) in toluene was added DIBAL-H (1.44 mL, 1 M solution on DCM, 1.44 mmol) dropwise via syringe down the side of the flask. The mixture was warmed to -30 °C and stirred for 1 h. Upon re-cooling to -78 °C, the mixture was quenched by the slow addition of dry MeOH (11 mL). The cooling bath was removed and NH4Cl:sodium potassium tartrate 1:1 (10 mL) was added slowly via syringe during warming to ambient temperature. The mixture was extracted with ether (4 × 15 mL), each fraction was washed with the same portion of brine (15 mL) and the combined organic layers were dried (MgSO4) and evaporated. Purification by flash chromatography (ether:hexane, 1:1) afforded the alcohol 48 (90 mg, 0.198 mmol, 97%) as a clear colourless oil; Rf (ether:hexane, 1:1) 0.18; [α]D23 +7.9 (c 0.43, CHCl3); IR (CHCl3): ν=1612, 1514, 1266, 1248; 1H (400 MHz, CDCl3): δ=7.35-7.23 (m, 8H; Ar), 6.87 (m, 2H; Ar), 5.34 (d, J (H, H)=7.2 Hz, 1H; 6-H), 4.65 (d, J (H, H)=11.6 Hz, 1H; CH/Ar), 4.49 (s, 2H;
$C_2H_2Ar$), 4.38 (d, $J$ (H, H)=11.6 Hz, 1H; CHHA), 4.02-3.94 (m, 2H; 8-H, 2-H), 3.80 (s, 3H; CH$_3$O), 3.69 (dd, $J$ (H, H)=10.8, 6.1, 2.3 Hz, 1H; 3-H), 3.68-3.63 (m, 1H; CHHOH), 3.61 (dd, $J$ (H, H)=8.9, 4.3 Hz, 1H; CHHOH), 3.33 (dd, $J$ (H, H)=8.9, 7.1 Hz, 1H; CHHOH), 3.08-2.97 (m, 1H; 7-H), 2.84 (br t, $J$ (H, H)=10.8 Hz, 1H; 4-H), 2.37 (dd, $J$ (H, H)=8.4, 4.3 Hz, 1H, OH), 2.33 (dd, $J$ (H, H)=12.5, 6.1 Hz, 1H; 4-H), 2.20-2.09 (m, 1H; 8-C-HCH$_3$), 1.71 (s, 3H; 5-C-HCH$_3$), 1.04 (d, $J$ (H, H)=7.4 Hz, 3H; CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$=159.3, 138.5, 133.5, 130.9, 130.3, 129.6, 128.3, 127.6, 127.5, 113.9, 79.2, 74.7, 73.2, 70.5, 64.1, 55.3, 38.8, 35.4, 34.5, 25.3, 17.7, 15.9; MS (CI, NH$_3$): $m/z$ (%): 472 ((M+NH$_4^+$), 20), 455 ((M+H)$^+$, 100); Found 455.2790, $C_{28}H_{39}O_5$ requires 455.2797.

$^{(Z, 2S, 3R, 7R, 8S)}$-8-((1$R$)-2-Benzoyloxy-1-methyl-ethyl)-2-carbaldehyde-3-(4-methoxy-benzyloxy)-7-methyl-3,4,7,8-tetrahydro-2$^H$-oxocine 49

To a solution of the alcohol 48 (90 mg, 0.198 mmol) in DMSO (10 mL) was added $o$-iodoxybenzoic acid (IBX) (140 mg). The mixture was stirred under Ar for a period of 16 h. The mixture was cooled to 0 °C and water (2 mL) was added slowly. Water (40 mL) was then added and the mixture was extracted with ether (3×40 mL). The combined organic layers were washed with brine (50 mL), dried (MgSO$_4$) and evaporated. The clean (by $^1$H NMR) aldehyde 49 (90 mg, 0.198 mmol, 100%) was isolated as a clear oil; $R_f$ (hexane:ether, 1:1) 0.40; $[\alpha]_{D}^{25}$ -15.0 (c 1.69, CHCl$_3$); IR (CHCl$_3$): $\nu$=1731; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$=7.35-7.25 (m, 5H; Ar), 7.17 (d, $J$ (H, H)=8.6 Hz, 2H; Ar), 6.84 (d, $J$ (H, H)=8.6 Hz, 2H; Ar), 5.29 (d, $J$ (H, H)=8.5 Hz, 1H; 6-H), 4.49 (d, $J$ (H, H)=11.3 Hz, 1H CHHA), 4.42 (s, 2H; CH$_2$Ar), 4.34 (d, $J$ (H, H)=11.3 Hz, 1H; CHHA), 4.17 (d, $J$ (H, H)=2.3 Hz, 1H; 2-H), 4.12 (ddd, $J$ (H, H)=11.8, 6.3, 2.3 Hz, 1H; 3-H), 4.01 (dd, $J$ (H, H)=9.3, 3.4 Hz, 1H; 8-H), 3.79 (s, 3H; CH$_3$O), 3.42 (dd, $J$ (H, H)=9.2, 3.4 Hz, 1H; CHHOH), 3.25-3.14 (m, 1H; 7-H), 3.19 (dd, $J$ (H, H)=9.2, 6.7 Hz, 1H; CHHOH), 2.83 (t, $J$ (H, H)=11.8 Hz, 1H; 4-H), 2.11-1.98 (m, 1H; 8-C-HCH$_3$), 1.72 (s, 3H; 5-C-HCH$_3$), 1.08 (d, $J$ (H, H)=6.8 Hz, 3H; CH$_3$), 1.08 (d, $J$ (H, H)=7.5 Hz, 3H; CH$_3$); $^{13}$C NMR (62.5 MHz, CDCl$_3$): $\delta$=205.8,
A suspension of CeCl₃ (145 mg, 0.59 mmol) (pre-weighed in a glove box) in dry THF (1.5 mL) in a Schlenk tube was sonicated under Ar for 2 h and stirred overnight at ambient temperature. The mixture was cooled to -78 °C and vinylmagnesium bromide (0.505 mL of a 1 M solution in THF, 0.505 mmol) was added dropwise via syringe and the mixture was stirred for 2 h. The aldehyde 40 (45 mg, 0.100 mmol) was added via cannula as a solution in THF (1.0 mL, 0.5 mL rinse). The mixture was stirred at -78 °C for 1 h after which the mixture was warmed to 0 °C and quenched by the addition of NH₄Cl (3 mL). DCM (3 mL) was added and the layers were separated. The aqueous layer was extracted with DCM (3 × 5 mL) and the combined organics were dried (MgSO₄) and concentrated. Purification by flash chromatography (ether:hexane, 1:1) afforded the product alcohols 50 (38 mg, 0.079 mmol, 80%) as an inseparable mixture of diastereomers at the newly created stereocentre in a ratio as determined by ¹H NMR of approximately 3:1. An attempt to present the ¹H NMR data for the major isomer has been made; all other data was acquired on the mixture.}

**Chemical Data**

- MS (CI): m/z (%): 470 ((M+NH₄)⁺, 20), 453 ((M+H)⁺, 6), 163 (100); Found 470.2903, C₂₈H₄₀O₅N requires 470.2906.

(Z, 2R, 3R, 7R, 8S)-8-((1R)-2-Benzylxoy-1-methyl-ethyl)2-((1R/S)-1-hydroxy-prop-2-eneyl)-3-(4-methoxy-benzyloxy)-7-methyl-3,4,7,8-tetrahydro-2H-oxocine 50

- Rf (ether:hexane, 1:1) 0.48; [α]D²⁺ +9.5 (c 1.85, CHCl₃); IR (CHCl₃): ν = 3471; ¹H NMR (250 MHz, CDCl₃): δ = 7.35-7.22 (m, 8H; Ar), 6.90-6.82 (m, 2H; Ar), 5.86 (dd, J (H, H) = 17.2, 10.6, 4.6 Hz, 1H; HC=CH₂), 5.45-5.24 (m, 2H; 6-H, JHHC=C), 5.13 (t, J (H, H) = 10.6, 1.7 Hz, 1H; HHC=C), 4.62 (d, J (H, H) = 11.0 Hz, 1H; CHHAr), 4.49 (2H, s, CH₂Ar), 4.34 (d, J (H, H) = 11.0 Hz, 1H; CHHAr), 4.33-4.22 (m, 1H; CHO), 4.08 (dd, J (H, H) = 8.2, 3.0 Hz, 1H; 8-H), 4.00-3.88 (m, 2H; 3-H, OH), 3.80 (s, 3H; CH₃O), 3.76 (dd, J (H, H) = 9.0, 3.0 Hz, 1H; 2-H), 3.60-3.43 (m, 1H; CHHOBn), 3.35 (br t, J (H, H) = 8.3, 1H; CHHOBn), 3.11-2.95 (m, 1H; 7-H), 2.93 (br t, J (H, H) = 11.6 Hz, 1H; 4-H), 2.36 (dd, J (H, H) = 11.6, 6.3 Hz, 1H; 4-H'), 2.19-1.98 (m, 1H; 8-C-
CHCH3), 1.71 (s, 3H; 5-C-CH3), 1.09 (d, J (H, H)=6.9 Hz, 3H; CH3), 1.04 (d, J (H, H)=7.4 Hz, 3H; CH3); 13C NMR (62.5 MHz, CDCl3): δ=138.9, 131.4, 129.8, 129.8, 128.3, 128.2, 127.6, 127.5, 127.4, 114.7, 113.9, 75.3, 74.3, 73.2, 70.6, 55.3, 35.8, 34.6, 15.9; MS (CI): m/z (%): 498 ((M+NH4)+, 3), 481 ((M+H)+, 18), 179 (100); Found 481.2949, C30H41O5 requires 481.2954.

(Z, 2R, 3R, 7R, 8S)-8-((1R)-2-Benzylxoy-1-methyl-ethyl)-3-hydroxy-2-((1R/S)-1-hydroxy-prop-2-eneyl)-7-methyl-3,4,7,8-tetrahydro-2H-oxocine 51

To a cooled (-15 °C) solution of the mixture of alcohols 50 (34 mg, 0.071 mmol) in DCM (2 mL) was added trifluoroacetic acid (0.5 mL) dropwise via syringe down the side of the flask. The colour changed from yellow to pink over a period of approximately 5 min. The reaction was stirred for a further 5 min and quenched by the slow addition of NaHCO3 (12 mL). The mixture was extracted with DCM (3 × 10 mL), washed with brine (10 mL) and dried (MgSO4). Purification by flash chromatography (ether:hexane, 2:1) afforded the diols 51 (22.0 mg, 0.061 mmol, 86%) as clear colourless oils. The stereochemistry of the epimers at C-9 was not assigned.

Data for the minor diastereomer: Rf (ether:hexane, 2:1) 0.25; [α]D26 +18.6 (c 0.4, CHCl3); 1H NMR (400 MHz, CDCl3): δ=7.38-7.25 (m, 5H; Ar), 5.87 (ddd, J (H, H)=17.1, 10.4, 6.5 Hz, 1H; HC=CH2), 5.45-5.35 (m, 1H; 6-H), 5.45-5.28 (m, 1H; HHC=C), 5.19 (br d, J (H, H)=10.4 Hz, 1H; HHC=C), 4.54 (m, 3H; CH2Ar, CHOHC=C), 4.28-4.17 (m, 1H; 8-H), 3.95-3.80 (m, 1H; 2-H), 3.84 (t, J (H, H)=6.0 Hz, 1H; CHHOBn), 3.57 (dd, J (H, H)=6.0, 3.7 Hz, 1H; CHHOBn), 3.65-3.51 (m, 1H; 3-H), 3.13 (d, J (H, H)=4.0 Hz, 1H; OH), 2.86 (br dd, J (H, H)=15.9, 10.3 Hz, 1H; 4-H), 2.72 (d, J (H, H)=7.5 Hz, 1H; OH), 2.80-2.60 (m, 1H; 7-H), 2.36 (dd, J (H, H)=15.9, 7.9 Hz, 1H; 4-H'), 2.08-1.92 (m, 1H; 8-C-CHCH3), 1.73 (br s, 3H; 5-C-CCH3), 1.03 (d, J (H, H)=7.4 Hz, 3H; CH3), 0.96 (d, J (H, H)=7.0 Hz, 3H; CH3).

Data for the major diastereomer: Rf (ether:hexane, 2:1) 0.21; [α]D26 +26.6 (c 0.8, CDCl3); IR (CHCl3): v=3502; 1H NMR (400 MHz, CDCl3): δ=7.38-7.25 (m, 5H; Ar), 5.86 (ddd, J (H, H)=17.2, 10.7, 4.9 Hz, 1H; HC=CH2), 5.35 (dt, J (H, H)=17.2, 1.7 Hz,
To a solution of phenylselenoacetaldehyde diethylacetal (5.6 mg, 20.6 µmol) and PPTS (~1 mg) in toluene (1 mL) was added the mixture of diols 51 (6.2 mg, 17.1 µmol) via cannula as a solution in toluene (0.3 mL, 0.4 mL rinse). The mixture was heated under reflux for a period of 40 min after which it was cooled and diluted with EtOAc. Water (4 mL) was added and the layers were separated. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the combined organic layers were washed with NaHCO₃ (10 mL) and dried (MgSO₄). Purification by flash chromatography (DCM:ether, 19:11) afforded the title compound 52 (9.0 mg, 16.6 µmol, 97%) as a mixture of 3 diastereomers. The major diastereomer was fully characterised and ¹H NMR data is also reported for the two minor diastereomers. Data for the major diastereomer; (6 mg, 11.0 µmol, 65%); Rf (DCM) 0.33; [α]D³⁶ +45.7 (c 0.47, CDCl₃); IR (CHCl₃): ν=1579; ¹H NMR (250 MHz, CDCl₃): δ=138.3, 136.8, 131.1, 128.4, 127.8, 127.6, 115.6, 81.3, 75.6, 74.1, 73.0, 71.1, 38.9, 37.7, 36.1, 26.3, 16.7, 15.8; MS (Cl, NH₃): m/z(%) 378 ((M+NH₄)⁺, 25), 361 ((M+H)⁺, 100); Found 361.2382, C₂₂H₃₃O₄ requires 361.2379.
$CH_2Ar)$, 4.37-4.24 (m, 1H; $HCO(C)=C$), 4.07 (br d, $J(H, H)$=5.5 Hz, 1H; $CHOC(O)$), 3.78 (br dd, $J(H, H)$=11.5, 8.2 Hz, 1H; $CHHOBn$), 3.67 (s, 1H; 4a-H), 3.42 (br t, $J(H, H)$=8.2 Hz, 1H; $CHHOBn$), 3.15 (d, $J(H, H)$=5.2 Hz, 2H; $CH_2Se$), 3.03 (br t, $J(H, H)$=13.0 Hz, 1H; 4-H), 2.90-2.72 (m, 1H; 7-H), 2.18 (dd, $J(H, H)$=13.0, 6.5 Hz, 1H; 4-H), 2.10-1.93 (m, 1H; 8-C-CH$_2$), 1.77 (t, $J(H, H)$=1.3 Hz, 3H; vinyl CH$_3$), 0.99 (d, $J(H, H)$=6.9 Hz, 3H; CH$_3$), 0.97 (d, $J(H, H)$=7.4 Hz, 3H; CH$_3$); $^{13}$C NMR (62.5 MHz, CDCl$_3$): $\delta$=139.0, 135.8, 132.5, 132.4, 130.7, 129.0, 128.3, 127.6, 127.3, 126.8, 116.9, 101.0, 81.8, 79.2, 74.3, 73.1, 68.2, 53.4, 37.3, 35.6, 31.0, 26.5, 15.3; MS (CI, NH$_3$): $m/z$ (%): 543 ((M+H)$^+$, 25), 196 (100); Found 543.2014, C$_{30}$H$_{39}$O$_4$Se requires 543.2013.

Data for the first minor diasteromer: (1 mg, 1.8 $\mu$mol, 11%); $R_f$ (DCM) 0.43; $^1$H (250 MHz, CDCl$_3$): $\delta$=7.58-7.51 (m, 2H; Ar), 7.36-7.20 (m, 8H; Ar), 5.83 (ddd, $J(H, H)$=17.3, 10.5, 5.9 Hz, 1H; $HC=CH_2$), 5.35 (br d, $J(H, H)$=17.3 Hz, 1H; $HHC=C$), 5.25 (br t, $J(H, H)$=4.6 Hz, 1H; $CHCH_2Se$), 5.28-5.25 (m, 1H; 6-H), 5.18 (br d, $J(H, H)$=10.5 Hz, 1H; $HHC=C$), 4.47 (m, 2H; $CH_2Ar$), 4.27-4.20 (m, 1H; $CHOC(O)$), 4.10-4.00 (m, 1H; 10a-H), 3.97-3.88 (m, 2H; 4a-H, $HCO(C)=C$), 3.54 (dd, $J(H, H)$=9.0, 3.1 Hz, 1H; $CHHOBn$), 3.23 (br t, $J(H, H)$=9.0 Hz, 1H; $CHHOBn$), 3.10 (d, $J(H, H)$=4.6 Hz, 2H; $CH_2Se$), 2.91 (br t, $J(H, H)$=12.5 Hz, 1H; 4-H), 2.07 (dd, $J(H, H)$=12.5, 4.8 Hz, 1H; 4-H$'$), 1.73 (s, 3H; vinyl CH$_3$), 1.05 (d, $J(H, H)$=6.6 Hz, 3H; CH$_3$), 1.03 (d, $J(H, H)$=7.3 Hz, 3H; CH$_3$).

Data for the second minor diasteromer: (2 mg, 3.6 $\mu$mol, 21%); $R_f$(DCM) 0.22; $^1$H NMR (250 MHz, CDCl$_3$): $\delta$=7.55-7.45 (m, 2H; Ar), 7.37-7.18 (m, 8H; Ar), 5.85-5.65 (m, 1H; $HC=CH_2$), 5.40-5.16 (m, 3H; 6-H, C=C$CH_2$), 5.07 (t, $J(H, H)$=5.4 Hz, 1H; $CHCH_2Se$), 4.62-4.53 (m, 1H), 4.47 (s, 2H; $CH_2Ar$), 4.04-3.87 (m, 2H), 3.71-3.57 (m, 2H), 3.26 (br t, $J(H, H)$=8.8 Hz, 1H; $CHHOBn$), 3.14 (d, $J(H, H)$=4.7 Hz, 2H; $CH_2Se$), 3.20-3.05 (m, 1H; 7-H), 2.89 (br t, $J(H, H)$=11.8 Hz, 1H; 10-H), 2.23-2.06 (m, 2H; 10-H$'$, 8-C-CH$_2$), 1.73 (s, 3H; vinyl CH$_3$), 1.13 (d, $J(H, H)$=6.8 Hz, 3H; CH$_3$), 1.05 (d, $J(H, H)$=7.4 Hz, 3H; CH$_3$).
(5Z, 10Z, 6aR, 8S, 9R, 12aR)-8-((1R)-2-Benzylxoy-1-methyl-ethyl)-9,11-dimethyl-4,6a,8,9,12,12a-hexahydro-3H-1,7-dioxaoctalen-2-one 54

To a solution of the seleno acetals 52 (8 mg, 14.7 µmol) in 15% aqueous MeOH (1.5 mL) was added solid NaHCO3 (~1.4 mg, 16.17 µmol) and NaIO4 (9.4 mg, 44.4 µmol) and the mixture was stirred vigorously for 1.5 h. The reaction was quenched by the addition of water (5 mL) and DCM (5 mL) was added. The layers were separated and the aqueous layer was extracted with DCM (3 × 5 mL). The combined organic layers were dried (MgSO4) and concentrated. The resultant selenoxide was dried azeotropically twice with toluene (2 × 1 mL) and dissolved in xylene (2 mL). DBU (6.6 µL, 44.1 µmol) was added and the mixture was heated to 130 °C for a period of 24 h. After cooling, aqueous NH4Cl (2 mL) was added and the layers were separated. The aqueous layer was extracted with ether (3 × 5 mL) and the combined organic layers were dried (MgSO4). Purification by flash chromatography (hexane:ether, 3:1) afforded the lactone 54 (3.4 mg, 8.84 µmol, 60%) as a clear colourless oil; $R_f$ (hexane:ether, 3:1) 0.27; [$\alpha$]D²⁰ -12.7 (c 0.22, CHCl₃); IR (film): ν=1747; ¹H (250 MHz, CDCl₃) 7.38-7.22 (m, 5H; Ar), 5.83-5.71 (m, 2H; 5-H, 6-H), 5.30 (d, J (H, H)=8.3 Hz, 1H; 10a-H), 4.80 (ddd, J (H, H)=11.4, 5.7, 2.4 Hz, 1H; 12a-H), 4.49 (d, J (H, H)=12.1 Hz, 1H; CΗHAr), 4.45 (d, J (H, H)=12.1 Hz, 1H; CHΗHAr), 4.37 (dd, J (H, H)=4.4, 2.4 Hz, 1H; 6a-H), 3.84 (dd, J (H, H)=7.6, 3.9 Hz, 1H; 8-H), 3.62 (dd, J (H, H)=9.1, 3.4 Hz, 1H; CΗΗOBn), 3.27 (dd, J (H, H)=9.1, 7.8 Hz, 1H; CHΗHOBn), 3.12-2.96 (m, 2H; 4-H, 9-H), 2.94 (br t, J (H, H)=12.5 Hz, 1H; 12-H), 2.70 (dt, J (H, H)=13.1, 10.6, 4.6 Hz, 1H; 3-H), 2.21 (dd, J (H, H)=12.5, 5.7 Hz, 1H; 4-H), 2.18-2.05 (m, 2H; 4-H, 8-C-CH(CH₃)₂), 1.78 (s, 3H; 11-C-CH₃), 1.08 (d, J (H, H)=6.4 Hz, 3H; CH₃), 1.07 (d, J (H, H)=7.1 Hz, 3H; CH₃); ¹³C NMR (62.5 MHz, CDCl₃): δ=177.0 (2-C), 138.9 (11-C), 133.7 (6-C), 130.8 (10-C), 130.4 (5-C), 128.2 (ArC), 127.5 (ArC), 127.4 (ArC), 83.5 (br, 8-C), 79.0 (12a-C), 73.4 (CH₂OBn), 73.1 (CH₂Ar), 70.7 (6a-C), 39.0 (9-C), 37.7 (3-C), 34.8 (12-C), 34.6, 30.6 (CHCH₂OBn), 25.8 (4-C), 24.6 (vinyl CH₃), 18.0 (CH₃), 16.2 (CH₃); MS (CI, NH₃): m/z(%): 402 ((M+NH₄)+, 60), 385 ((M+H)+, 58), 196 (100); Found 385.2380, C₂₄H₃₃O₄ requires 385.2379.
The bicyclic lactone 54, above was also prepared from the carbonate 53. To a solution of the carbonate 53 (9.0 mg, 23.2 µmol) in toluene (1 mL) was added dimethyltitanocene (0.14 mL, 50 mg cm⁻³ solution in toluene, 33.3 µmol). The mixture was excluded from light and heated at reflux for a period of 3 h. The toluene was removed and the residue was purified by flash chromatography (hexane:ether, 3:1) to afford the lactone 54 (4.2 mg, 10.9 µmol, 47%) as a clear colourless oil.

(Z, 4R/S, 4aS, 6S, 9R, 10aR)-6-((1R)-2-Benzyloxy-1-methyl-ethyl)-7,9-dimethyl-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxabenzocycloocten-2-one 53

To a cooled (-78 °C) solution of the mixture of diols 51 (13 mg, 36 µmol) in DCM (2 mL) was added pyridine (18 µL, 216 µmol) and Et₃N (50 µL, 360 µmol) and crushed 4Å molecular sieves (~ 50 mg). To this solution was added triphosgene (11 mg, 36 µmol) via cannula as a solution in DCM (0.5 mL, 0.2 mL rinse). The mixture was stirred for 20 min at this temperature and was quenched by the addition of aqueous NH₄Cl (3 mL). The mixture was allowed to warm to ambient temperature and was extracted with DCM (3 × 5 mL). The combined organic layers were dried (MgSO₄) and concentrated. Purification by flash chromatography (ether:hexane, 2:1) afforded the title compound 53 (11.2 mg, 28 µmol, 80%) as a clear colourless oil. Rₚ (ether:hexane, 2:1) 0.35; [α]D³⁰ +85.4 (c 0.5, CDCl₃); IR (film): ν=1760; ¹H NMR (250 MHz, CDCl₃): δ=7.38-7.25 (m, 5H; Ar), 5.58 (ddd, J (H, H)=17.1, 10.8, 3.7 Hz, 1H; H₂C=CH₂), 5.43 (d, J (H, H)=7.4 Hz, 1H; 6-H), 5.33 (dd, J (H, H)=17.1, 1.4 Hz, 1H; HHC=C), 5.27 (dd, J (H, H)=10.8, 1.4 Hz, 1H; HHC=C), 4.82 (s, 1H; 4-H), 4.55 (ddd, J (H, H)=11.2, 6.8, 1.8 Hz, 1H; 10a-H), 4.50 (d, J (H, H)=11.8 Hz, 1H; CHHAr), 4.45 (d, J (H, H)=11.8 Hz, 1H; CHHAr), 4.17-4.01 (m, 2H; 4a-H, 6-H), 3.58 (dd, J (H, H)=9.1, 3.3 Hz, 1H; CHHOBn), 3.35 (dd, J (H, H)=9.1, 6.4 Hz, 1H; CHHOBn), 3.10-2.94 (m, 2H; 10-H, 7-H), 2.34 (dd, J (H, H)=12.9, 6.8 Hz, 1H; 10-H’), 2.17-2.00 (m, 1H; 6-C-CH₃), 1.75 (s, 3H; 9-C-CH₃), 1.09 (d, J (H, H)=7.2 Hz, 3H; CH₃), 1.07 (d, J (H, H)=7.4 Hz, 3H; CH₃); ¹³C NMR (100 MHz, CDCl₃): δ=148.1 (2-C), 138.1, 132.9, 132.2, 127.9, 127.8, 118.2, 83.4, 73.5, 73.3, 65.5, 34.9, 15.9; MS (Cl, NH₃):
m/z(%): 404 ((M+NH₄)⁺, 97), 387 ((M+H)⁺, 70); Found 387.2171, C₂₃H₃₁O₅ requires 387.2171.

(Z, 8S, 9R)-8-tButyldiphenylsilyloxy-9-((S)-1-hydroxy-prop-2- eneyl)-4,7,8,9-tetrahydro-3H-oxonin-2-one 58 and (Z, 8S, 9R)-8-tbutyldiphenylsilyloxy-9-((R)-1-hydroxy-prop-2- eneyl)-4,7,8,9-tetrahydro-3H-oxonin-2-one 59

Vinylbromide (ca. 0.5 mL) was condensed into a cold Schlenk tube (-20 °C) and then allowed to diffuse into a solution of the aldehyde 57³ (50 mg, 118 µmol) in degassed DMSO (5 mL, freeze-thaw 3 cycles). To this solution was added CrCl₂ containing 1% NiCl₂ (145 mg, 1.18 mmol) and the resulting green solution was allowed to stir overnight under an atmosphere of oxygen-free argon. The reaction mixture was quenched by the addition of 0.1 M aqueous solution of sodium serinate (30 mL), hexane (15 mL) and EtOAc (15 mL). The organic phase was separated and the aqueous phase was extracted with a mixture of hexane and EtOAc (1:1, 3 × 30 mL). The organic phases were washed with water (30 mL), brine (30 mL) and dried (MgSO₄). Purification by flash chromatography (1:1, hexane:ether) provided the title compounds 58 and 59 as a 2:1 mixture of diastereomers as clear and colourless oils (33 mg, 73 µmol, 62%).

Data for 59: Rf 0.4 (7:3, ether:hexane); [α]D²¹ -16.0 (c 0.89 in CHCl₃); IR (CHCl₃): ν=3580, 1732; ¹H NMR (250 MHz, CDCl₃): δ=7.76-7.68 (m, 4H; Ar), 7.50-7.36 (m, 6H; Ar), 5.87 (ddd, J (H, H)=17.2, 10.5, 4.7 Hz, 1H; HC=CH₂), 5.54-5.44 (m, 1H), 5.34-5.26 (m, 1H), 5.25 (dt, J (H, H)=17.2, 1.5 Hz, 1H; HC=CH⁻trans), 5.15 (dt, J (H, H)=10.5, 1.5 Hz, 1H; HC=CH⁻cis), 4.90 (dd, J (H, H)=8.2, 1.6 Hz, 1H), 4.40-4.23 (m, 2H), 2.45-2.16 (m, 6H; 3-H, 3-H', 4-H, 4-H', 7-H, 7-H'), 1.56 (d, J (H, H)=8.4 Hz, 1H; OH), 1.08 (s, 9H; (CH₃)₃Si); ¹³C NMR (62.5 MHz, CDCl₃): δ=173.9 (2-C), 137.6, 135.9, 135.9, 133.7, 133.2, 130.0, 129.9, 129.4, 127.8, 127.7, 127.6, 115.6, 80.9, 72.2, 70.8, 34.1, 33.5, 27.0 ((CH₃)₃C), 23.8, 19.2 ((CH₃)₅C); MS (Cl, NH₃): m/z(%): 468 ((M+NH₄)⁺, 20), 451 ((M+H)⁺, 10), 373 (100); Found 468.2575, C₂₇H₃₈O₄SiN requires, 468.2570.
Data for 58: \( R_f 0.3 \) (7:3, ether:hexane); \( \left[ \alpha \right]_D^{11} +10.2 \) (c 1.61 in CHCl\(_3\)); IR (CHCl\(_3\)): \( \nu =3488, 1728 \); \( ^1\)H NMR (250 MHz, CDCl\(_3\)): \( \delta =7.75-7.64 \) (m, 4H; Ar), 7.50-7.35 (m, 6H; Ar), 5.65-5.51 (m, 3H; 5-H, 6-H, HC=CH\(_2\)), 5.02 (ddd, J (H, H)=10.4, 1.5, 1.0 Hz, 1H; CH=CHH-cis), 4.88 (dd, J (H, H)=10.6, 1.3 Hz, 1H; CH=CHH-trans), 4.83 (dd, J (H, H)=8.2, 2.4 Hz, 1H), 4.32-4.22 (m, 1H), 3.95 (ddd, J (H, H)=8.3, 5.5, 2.6 Hz, 1H), 2.86 (brd, J (H, H)=5.6 Hz, 1H; OH), 2.65-2.25 (m, 4H), 2.28-2.22 (m, 2H), 1.09 (s, 9H; (CH\(_3\)\(_3\))Si); \( ^{13}\)C NMR (62.5 MHz, CDCl\(_3\)): \( \delta =175.6 \) (2-C), 136.0, 135.9, 134.8, 133.6, 132.9, 130.1, 129.9, 128.8, 128.5, 127.7, 118.4, 82.6, 72.8, 72.7, 33.6, 32.5, 27.0 ((CH\(_3\)\(_3\))C), 23.1, 19.2 ((CH\(_3\)\(_3\))C); MS (Cl, NH\(_3\)): \( m/z(\%) \): 468 ((M+NH\(_4\))\(^+\), 50), 451 ((M+H\(^+\)), 60, 274 (100); Found 468.2566, C\(_{27}\)H\(_{38}\)O\(_4\)SiN requires 468.2570.

\((Z, 8S, 9R)-8\)-Hydroxy-9-\((R)-1\)-hydroxy-prop-2-eneyl)-4,7,8,9-tetrahydro-3H-oxonin-2-one 60

To a stirred solution of the allylic alcohol 58 (15.5 mg, 34 \( \mu \)mol) in THF (1.5 mL) and pyridine (0.7 mL) was added HF•pyridine (0.15 mL) and the resulting solution was stirred for 24 h and then quenched by the addition of water (10 mL) and ether (10 mL). The organic phase was separated and the aqueous phase was extracted with ether (2 \( \times \) 10 mL). The organic phases were washed with a saturated aqueous solution of CuSO\(_4\) (2 \( \times \) 10 mL) and dried (MgSO\(_4\)). Purification by flash chromatography (1:1, hexane:ether→0:1, hexane:ether) provided starting material 58 (2 mg, 4.4 \( \mu \)mol, 13%). Further elution of the column provided the title compound 60 as a clear and colourless oil (5 mg, 24 \( \mu \)mol, 71%); \( R_f 0.4 \) (ether); \( \left[ \alpha \right]_D^{11} -96.4 \) (c 1.05 in CHCl\(_3\)); IR (CDCl\(_3\)): \( \nu =3613, 1734 \); \( ^1\)H (250 MHz, CDCl\(_3\)): \( \delta =5.95 \) (ddd, J (H, H)=17.2, 10.4, 6.7 Hz, 1H; HC=CH\(_2\)), 5.79-5.57 (m, 2H; 5-H, 6-H), 5.38 (dt, J (H, H)=17.2, 1.4 Hz, 1H; HC=CHH-cis), 5.27 (d, J (H, H)=10.4, 1.3 Hz, 1H; HC=CHH-trans), 5.27 (d, J (H, H)=10.4, 1.3 Hz, 1H; HC=CHH-cis), 4.68 (dd, J (H, H)=8.1, 5.9 Hz, 1H; 9-H), 4.40-4.30 (m, 1H), 2.62-2.20 (m, 8H; 3-H, 3-H’, 4-H, 4-H’, 7-H, 7-H’, OH, OH); \( ^{13}\)C NMR (62.5 MHz, CDCl\(_3\)): \( \delta =174.4 \) (2-C), 136.3, 128.9, 128.5, 118.0, 80.0, 74.7, 72.6, 33.8, 32.8, 23.7; MS (Cl, NH\(_3\)): \( m/z(\%) \): 230 ((M+NH\(_4\))\(^+\), 100), 213 ((M+H\(^+\)), 20); Found 213.1125, C\(_{11}\)H\(_{17}\)O\(_4\)N requires 213.1127.
(Z, 8S, 9R, 10R)-8-Hydroxy-10-vinyl-4,7,8,9-tetrahydro-3H-oxecin-2-one 61

The ten-membered lactone 61 was isolated in varying quantities during optimisation of the desilylation of 58; mp 112-114 °C (from ether/hexane); [α]D20 +33.9 (c 0.065 in CHCl3); IR (CDCl3): v=3570, 1731; 1H NMR (250 MHz, CDCl3): δ=5.94 (ddd, J (H, H)=17.3, 10.6, 6.2 Hz, 1H; HC=CH2), 5.82-5.72 (m, 1H), 5.45-5.63 (m, 2H), 5.42 (dt, J (H, H)=17.3, 1.4 Hz, 1H; HC=CHH-trans), 5.35 (dt, J (H, H)=10.4, 1.3 Hz, 1H; HC=CHH-cis), 4.06 (dq, J (H, H)=6.8, 2.3 Hz, 1H; 8-H), 3.90 (ddd, J (H, H)=6.8, 5.5, 1.3 Hz, 1H; 9-H), 2.73-2.76 (m, 1H), 2.65-2.21 (m, 7H); 13C NMR (62.5 MHz, CDCl3): δ=172.0 (1-C), 132.6, 128.3, 128.0, 119.0, 74.2, 70.6, 34.7, 32.0, 22.0; MS (CI, NH3): m/z (%): 230 ((M+NH4)+, 100), 213 ((M+H)+, 20); Found 213.1125, C11H17O4N requires 213.1127.

(Z, 4R, 4aS, 11aS)-4-Vinyl-4,4a,7,8,11,11a-hexahydro-1,3,5-trioxa-benzocyclononene-2,6-dione 62

To a stirred suspension of the oxonane 60 (18.7 mg, 88 µmol) and freshly activated 4 Å powdered molecular sieves in DCM (1 mL) at -78 °C were added pyridine (43 µL, 42 mg, 530 µmol) and TEA (122 µL, 89 mg, 0.88 mmol). Triphosgene (26 mg, 88 µmol) was added via cannula as a solution in DCM (0.5 mL). The resulting orange solution was stirred for 15 min and then allowed to warm to room temperature. The reaction mixture was quenched by the addition of a saturated solution of NH4Cl (2 mL) and was extracted with DCM (3 × 10 mL). The organic phases were washed with a saturated aqueous solution of CuSO4 (10 mL) and dried (MgSO4). Purification by flash chromatography (hexane:ether, 1:1) provided the title compound 62 (16.2 mg, 69 µmol, 78%) as a white crystalline solid; mp 126-127 °C (from hexane); [α]D6 -181 (c 0.1 in CHCl3); IR (CDCl3): v=1761; 1H NMR (250 MHz, CDCl3): δ=5.96 (ddd, J (H, H)=17.1, 10.4, 6.4 Hz, 1H; HC=CH2), 5.80-5.65 (m, 2H; 9-H, 10-H), 5.51 (d, J (H, H)=17.1 Hz, 1H; HC=CHH-trans), 5.42 (d, J (H, H)=10.4 Hz, 1H; HC=CHH-cis),
4.90 (t, J (H, H)=9.4 Hz, 1H; 4a-H), 4.81 (dd, J (H, H)=9.9, 6.5 Hz, 1H; 4-H), 4.35 (ddd, J (H, H)=9.3, 7.8, 2.4 Hz, 1H; 11a-H), 2.62-2.25 (m, 6H; 7-H, 7-H', 8-H, 8-H'), 11-H, 11-H'); $^{13}$C NMR (62.5 MHz, CDCl$_3$) 174.3 (6-C), 147.7 (2-C), 131.5, 130.2, 127.1, 121.4, 81.6, 72.8, 33.9, 29.8, 24.6; MS (CI, NH$_3$): m/z (%): ((M+NH$_4$)$^+$, 18), 239 ((M+H)$^+$, 100); Found 239.016, C$_{12}$H$_{15}$O$_5$ requires 239.0919.

(5Z, 6aR, 12Z, 13aS)-3,4,9,10,13,13a-Hexahydro-oxino(3,2-b)oxocin-2,8-dione 62

![Structure 62](image)

To a stirred solution of the carbonate 62 (14 mg, 58 µmol) in toluene (2 mL) was added dimethyltitanocene (229 µL, of a 50 mg/mL solution in toluene, 70 µmol) and the resulting orange solution was heated at reflux for 1.5 h and then allowed to cool. The solvent was removed in vacuo and purification by flash chromatography (hexane:ether, 2:1) provided the title compound 63 as a white crystalline solid (4.2 mg, 18 µmol, 31%); mp 109-111 °C (from hexane); [α]$_D^{16}$ -26.6 (c 0.165 in CHCl$_3$); IR (CHCl$_3$): ν=1744, 1737; $^1$H NMR (800 MHz, CDCl$_3$): δ=5.88-5.82 (m, 1H), 5.78-5.70 (m, 2H), 5.70-5.62 (m, 1H; 6a-H), 4.65 (brt, J (H, H)=7.5 Hz, 1H; 13a-H), 2.55-2.86 (m, 1H), 2.56-2.47 (br, 2H), 2.46-2.36 (m, 3H), 2.35-2.2.6 (m, 2H), 2.22-2.20 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ=175.9, 174.7, 132.4, 131.6, 129.0, 128.3, 75.3 (6a-C), 37.6, 34.2, 30.9, 24.9, 24.3; MS (CI, NH$_3$): m/z(%): 254 ((M+NH$_4$)$^+$, 100); Found 254.1393, C$_{13}$H$_{20}$NO$_4$ requires 254.1392.

(5Z, 3S, 8S, 9R)-8-Benzylloxy-9-tbutyldiphenylsilyloxymethyl-3-hydroxy-4,7,8,9-tetrahydro-3H-oxonin-2-one 65

![Structure 65](image)

KHMDS (6.48 mL of a 0.5 M solution in toluene, 3.24 mmol) was added to toluene (40 mL) and the resulting solution was cooled to -78 °C. A solution of 64 (980 mg, 1.91 mmol) in toluene (5 mL, 2 × 2.5 mL rinse) was added dropwise via cannula and the resulting solution was stirred at -78 °C for 1 h. A solution of (±)-2-(phenylsulfonyl)-3-phenyloxaziridine (1.09 g, 4.19 mmol) in toluene (10 mL) was added via cannula and the resulting solution was stirred for 1 h at –78 °C. CSA (1.09
g, 4.19 mmol) as a solution in THF (7 mL) was added via cannula and the reaction mixture was allowed to warm to ambient temperature. A saturated aqueous solution of NaHCO₃ (50 mL) was added and the organic phase was separated. The aqueous phase was extracted with ether (2 × 50 mL) and the combined organic extracts were dried (MgSO₄). Purification by flash chromatography (hexane:ether, 7:3) provided the title compound 65 as a clear and colourless oil (811 mg, 1.53 mmol, 80%); R f 0.2 (hexane:ether, 7:3); [α]D 20° -1.7 (c 1.98 in CHCl₃); IR (CHCl₃): ν=3577, 1741; ¹H NMR (250 MHz, CDCl₃): δ=7.68-7.60 (m, 4H; Ar), 7.44- 7.20 (m, 11H; Ar), 5.83-5.70 (m, 1H), 5.61-5.48 (m, 1H), 5.08 (ddd, J (H, H)=9.1, 5.2, 2.3 Hz, 1H; 9-H), 4.62 (d, J (H, H)=11.6 Hz, 1H; OCHHAr), 4.40 (d, J (H, H)=11.6 Hz, 1H; OCHHAr), 4.37 (ddd, J (H, H)=10.6, 5.6, 3.2 Hz, 1H; 3-H), 4.05 (dd, J (H, H)=11.6, 5.1 Hz, 1H; CHHOSi), 3.88 (dd, J (H, H)=11.6, 2.4 Hz, 1H; CHHOSi), 3.86-3.79 (m, 1H; 8-H), 2.60-2.53 (m, 2H), 2.37-2.28 (m, 2H), 2.10 (d, J (H, H)=10.6 Hz, 1H; OH), 1.05 (s, 9H; (CH₃)₃C)Si); ¹³C NMR (62.5 MHz, CDCl₃): δ=173.1 (2-C), 137.6, 135.7, 133.3, 130.9, 128.7, 128.5, 127.9, 123.0, 79.4, 71.6, 70.9, 63.3, 32.4, 30.7, 26.8, 19.3; MS (Cl, NH₃): m/z (%): 548 ((M+NH₄)⁺, 100), 531 ((M+H)⁺, 20); Found 548.2843, C₃₂H₄₀NO₅Si requires 548.2832.

(Z, 3S, 8S, 9R)-Benzyloxy-9-tbutyldiphenylsilyloxyethyl-3-trimethylsilyloxy-4,7,8,9-tetrahydro-3H-oxonin-2-one 66

To a stirred solution of the lactone 65 (779, 1.46 mmol) in THF (44 mL) was added TEA (2.03 mL, 1.48 g, 14.6 mmol) and dropwise TMSCl (0.93 mL, 794 mg, 7.35 mmol). The resulting white slurry was stirred for 4 h and then poured onto ether (50 mL) and pH 7 buffer (50 mL). The organic layer was separated and the aqueous phase was extracted with ethr (2 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried (MgSO₄) and purification by flash chromatography (hexane:ether, 9:1) provided the title compound 66 as a clear and colourless oil (715 mg, 1.19 mmol, 81%); R f 0.4 (hexane:ether, 3:1); (Found: C, 69.77; H, 7.72%; C₃₅H₄₆O₅Si requires C, 69.72; H, 7.69); [α]D 20° +22.0 (c 2.425 in CHCl₃); IR (CHCl₃): ν=2932, 1740 (CO); ¹H NMR (250 MHz, CDCl₃): δ=7.74-7.64 (m, 4H; Ar), 7.45-
7.16 (m, 1H; Ar), 5.80-5.67 (m, 1H), 5.64-5.52 (m, 1H), 5.10-4.96 (brm, 1H; 9-H), 4.59 (d, J (H, H)=11.6 Hz, 1H; OCH/HAr), 4.38 (dd, J (H, H)=7.9, 4.3 Hz, 1H; 3-H), 4.34 (d, J (H, H)=11.6 Hz, 1H; OCH/HAr), 4.59 (d, J (H, H)=11.6 Hz, 1H; OCH/HAr), 4.38 (dd, J (H, H)=7.9, 4.3 Hz, 1H; 3-H), 4.34 (d, J (H, H)=11.6 Hz, 1H; OCH/HAr), 3.95 (dd, J (H, H)=11.4, 5.7 Hz, 1H; C/HOSi), 3.86 (dd, J (H, H)=11.4, 2.9 Hz, 1H; CH/HOSi), 3.90-3.80 (m, 1H; 8-H), 2.75-2.26 (m, 4H), 1.06 (s, 9H; (CH3)3C)Si); 13C NMR (62.5 MHz, CDCl3): δ=173.0 (2-C), 137.9, 135.7, 135.6, 133.6, 133.3, 130.4, 129.7, 129.6, 128.4, 127.7, 125.3, 78.0, 77.5, 72.5, 71.3, 63.9, 33.5, 28.8, 26.8, 19.3 , -0.1; MS (CI, NH3): m/z(%) 620 ((M + NH4)+, 100), 603 (30); Found 603.2967, C35H47O5Si requires 603.2962.

(Z, 3S, 8S, 9R)-Benzyloxy-9-tbutyldiphenylsilyloxyethyl-2-methylene-3-trimethylsilyloxy-4,7,8,9-tetrahydro-3H-oxonine 67 and

(Z, 3S, 8S, 9R)-benzyloxy-9-tbutyldiphenylsilyloxyethyl-3-hydroxy-2-methylene-4,7,8,9-tetrahydro-3H-oxonine 68

To a stirred solution of the silylether 66 (685 mg, 1.13 mmol) in toluene (46 mL) was added dimethyltitanocene (4.08 mL of an 87 mg/mL solution in toluene, 1.71 mmol) and the resulting solution was heated at reflux for 1 hr. Acetone (2 mL) was added and the mixture was heated at reflux for a further 0.5 h. The reaction mixture was allowed to cool and the solvent was removed in vacuo. Purification by gravity chromatography on deactivated basic alumina (6% w/w water) (hexane:ether, 9:1) provided the impure enol ether 67 which was used in the next reaction without further purification. An analytical sample of the enol ether 67 was obtained by further purification on deactivated basic alumina (hexane:ether, 20:1); Rf 0.3 (hexane:ether, 9:1); [α]D58 +13.1 (c 0.68 in CHCl3); IR (CHCl3): ν=2931, 1641 (enol ether); 1H NMR (250 MHz, CDCl3): δ=7.75-7.67 (m, 4H; Ar), 7.48-7.33 (m, 6H; Ar), 7.30-7.16 (m, 5H; Ar), 5.74 (dt, J (H, H)=10.9, 5.3 Hz, 1H), 5.53 (dt, J (H, H)=10.9, 5.4 Hz, 1H), 4.78 (brs, 1H; OC=CHH), 4.63 (d, J (H, H)=11.4 Hz, 1H; CH/HAr), 4.30 (d, J (H, H)=11.4 Hz, 1H; CH/HAr), 4.27 (dd, J (H, H)=9.7, 6.2 Hz, 1H), 4.22 (d, J (H, H)=1.3 Hz, 1H; OC=CHH), 3.94-3.79 (m, 3H), 3.67 (dt, J (H, H)=8.1, 3.1 Hz, 1H), 2.94-2.76 (m, 2H), 2.33 (dt, J (H, H)=14.2, 4.0 Hz, 1H), 2.25 (dq, J (H, H)=11.9, 6.1 Hz, 1H), 1.06 (s, 9H; (CH3)2C)Si), 0.22 (s, 9H; (CH3)2Si); 13C NMR (62.5 MHz, CDCl3): δ=166.1 (1-C), 138.1, 135.7, 133.3, 129.6, 128.3, 127.9, 127.8, 127.7, 127.6, 92.8
(OC=CH₂), 85.1, 79.6, 74.0, 71.3, 66.2, 33.2, 26.8, 19.2 , 0.4; MS (EI): m/z(%):600 (M⁺, 1), 91 (100); Found 600.3085, C₃₆H₄₈O₄Si₂ requires 600.3091.

The crude enol ether 67 was dissolved in MeOH (11 mL), anhydrous K₂CO₃ (57 mg, 0.41 mmol) was added and the reaction mixture was stirred for 1 h. The reaction mixture was filtered through a pad of Celite™ rinsing with ether and the solvent was removed in vacuo. Purification by gravity chromatography on deactivated basic alumina (6% w/w water) (hexane:ether, 2:1) provided the enol ether 68 (366 mg, 0.69 mmol, 61% from the lactone 66); Rf 0.1 (hexane:ether, 2:1); [α]D¹⁸ +5.5 (c 1.155 in CHCl₃); IR (CHCl₃): ν=3594 (OH), 2931, 1641 (enol ether); ¹H NMR (250 MHz, CDCl₃): δ=7.74-7.66 (m, 4H; Ar), 7.48-7.21 (m, 11H; Ar), 5.75 (dt, J (H, H)=10.5 , 6.5 Hz, 1H), 5.55 (dt, J (H, H)=10.5, 6.2 Ha, 1H), 4.65 (d, J (H, H)=11.5 Hz, 1H; OCHHAr), 4.55 (d, J (H, H)=1.6 Hz, 1H; OC=CHH), 4.37 (d, J (H, H)=11.5 Hz, 1H; OCHHAr), 4.24 (d, J (H, H)=1.6 Hz, 1H; OC=CHH), 4.25-4.16 (m, 1H), 3.97-3.90 (m, 2H), 3.81 (dd, J (H, H)=11.3, 6.4 Hz, 1H; CHHOSi), 3.75-3.67 (m, 1H), 2.76-2.62 (m, 2H), 2.46-2.34 (m, 2H), 1.85 (d, J (H, H)=7.1 Hz, 1H; OH) , 1.05 (s, 9H; (CH₃)₂CSi); ¹³C NMR (62.5 MHz, CDCl₃) 165.6 (2-C), 138.0, 135.7, 133.4, 133.3, 129.6, 128.9, 128.4, 127.9, 127.7, 126.7, 126.9, 91.4, 85.1, 78.6, 73.2, 71.4, 65.6, 32.6, 30.4, 26.9, 26.8, 19.2; MS (CI, NH₃): m/z(%):546 ((M+NH₄)⁺, 65), 529 ((M+H)⁺, 60), 91 (100); Found 529.2765, C₃₃H₃₃O₄Si requires M 529.2774.

(Z, 3S, 8S, 9R)-Benzyloxy-9-tbutyldiphenylsilyloxy methyl-3-dimethylsilyloxy-2-methylene-4,7,8,9-tetrahydro-3H-oxonine 69

To a stirred solution of the enol ether 68 (58 mg, 0.11 mmol) in tetramethyldisilazane (0.7 mL) was added anhydrous NH₄Cl (2 mg) and the resulting mixture was heated at 60 °C overnight. The reaction mixture was diluted with anhydrous hexane and was filtered through dry Celite™ in air washing with anhydrous hexane. The solvent was removed in vacuo and the residue was dried under vacuum (<5 mmHg) overnight to provide the silane 69 as an unstable clear and colourless oil (64 mg, 0.11 mmol, 100%); IR (CHCl₃): ν=2120, 1641; ¹H NMR (250 MHz, CDCl₃): δ=7.71-7.67 (m, 4H Ar), 7.46-7.15 (m, 11H; Ar), 5.72 (dt, J (H, H)=11.1, 5.3 Hz, 1H), 5.50 (dt, J (H, H)=11.0, 5.5 Hz, 1H), 4.74 (sp, J (H, H)=2.9 Hz, 1H; SiH), 4.76 (bss, 1H; OC=CHH),
4.61 (d, J (H, H)=11.4 Hz, 1H; OCH2Ar), 4.29 (d, J (H, H)=11.4 Hz, 1H; OCH2Ar),
4.28-4.22 (m, 1H), 4.23 (d, J (H, H)=1.5 Hz, 1H; OC=CH2), 3.92-3.79 (m, 3H), 3.65
(dt, J (H, H)=8.2, 3.1 Hz, 1H), 2.90-2.75 (m, 2H), 2.36-2.22 (m, 2H), 1.03 (s, 9H;
(CH3)3C)Si), 0.275 (d, J (H, H)=2.9 Hz, 3H; (CH3)2SiH) , 0.268 (d, J (H, H)=2.9 Hz,
3H; (CH3)2SiH); 13C NMR (62.5 MHz, CDCl3): δ=165.4 (1-C), 138.1, 135.7, 133.3,
129.6, 128.4, 128.1, 127.8, 127.6, 127.6, 93.3 (OC=CH2), 85.2, 79.5, 75.6, 71.3, 66.1,
32.8, 26.9, 26.8, 19.1, -0.8.

(Z, 2R, 3S, 9(S)-8-Benzyloxy-9-tbutyldiphenylsilyloxyethyl-3-hydroxy-2-
hydroxymethyl-2,3,4,7,8,9-hexahydro-oxonine 70

In a glove box a Schlenk tube was charged with (bicyclo(2.2.1)hepta-2,5-diene)(1,4-
bis(diphenylphosphino)butane)rhodium(I) tetrafluoroborate (11 mg, 15.5 µmol). The
Schlenk tube was placed on an argon manifold and the silane 69 (170 mg, 0.29 mmol)
was added as a solution in acetone (10 mL, 5 mL rinse) via cannula. The resulting
orange solution was freeze-thaw degassed (3 cycles) and heated at reflux for 18 h.
The solvent was removed in vacuo, the residue taken up in ether and filtered through
Fluorosil™ to remove the coloured material. The solvent was removed in vacuo, the
residue taken up in THF (3 mL) and MeOH (3 mL) and 30% hydrogen peroxide (0.7
mL) and 15% KOH (0.35 mL) were added. The reaction mixture was stirred for 1 hr
and then quenched by the addition of saturated aqueous Na2S2O3 (20 mL) and ether
(20 mL). The aqueous phase was separated and extracted with ether. The organic
phases were washed with brine and dried (MgSO4). Purification by flash
chromatography (ether:hexane, 1:1) provided the enol ether 68 (56 mg, 102 µmol,
35%) and the title compound 70 as colourless crystals (96 mg, 175 µmol, 61%); Rf 0.3;
mp 156-158 °C (from ether); [α]D +14.5 (c 0.255 in CHCl3); 1H NMR (250 MHz,
CDCl3): δ=7.75-7.63 (m, 4H; Ar), 7.48-7.33 (m, 6H; Ar), 7.25-7.16 (m, 3H; Ar),
7.00-6.94 (m, 2H; Ar), 5.77-5.62 (m, 2H; 5-H, 6-H), 4.48 (d, J (H, H)=11.5 Hz, 1H;
CH2Ar), 4.13 (d, J (H, H)=11.5 Hz, 1H; CH2Ar), 4.00-3.89 (m, 2H), 3.88-3.80 (m,
2H), 3.80-3.68 (m, 2H), 3.30 (dt, J (H, H)=9.3, 3.2 Hz, 1H), 3.22-3.16 (m, 1H), 3.07
(t, J (H, H)=6.6 Hz, 1H), 2.87-2.73 (m, 2H), 2.36-2.22 (m, 2H), 2.10 (brd, J (H,
H)=5.1 Hz, 1H; OH), 1.10 (s, 9H; (CH₃)₃CSi); ¹³C NMR (62.5 MHz, CDCl₃): δ=137.5, 135.7, 135.7, 133.0, 132.8, 129.9, 129.7, 128.3, 127.8, 127.7, 127.6, 126.2, 80.3, 77.2, 75.0, 70.7, 69.1, 84.5, 62.5, 30.8, 28.9, 26.9 , 19.2; MS (CI, NH₃): m/z(%): 564 ((M+NH₄)⁺, 100), 547 ((M+H)⁺, 55); Found (ES) 564.3137, C₃₃H₄₆ClNO₅Si requires 564.3145.

(Z, 2R, 3S, 8S, 9R)-2,9-Bis-hydroxymethyl-8-benzyloxyl-3-hydroxy-2,3,4,7,8,9-hexahydro-oxonine 71

HF•pyridine complex (0.1 mL) was added to stirring solution of the diol 70 (4.4 mg, 8 µmol) in THF (1 mL) and pyridine (0.3 mL) and the resulting solution was stirred for 2 h at ambient temperature. The reaction mixture was quenched by the addition of 2 M HCl and ether, the aqueous phase was separated and further extracted with ether. The organic extracts were washed with 2 M HCl, brine and dried (MgSO₄). Purification by flash chromatography provided the title compound 71 as a clear and colourless oil (2.4 mg, 7.8 µmol, 97%); Rf 0.1 (ether); [α]D²⁰ +70.7 (c 0.075 in CHCl₃); ¹H NMR (250 MHz, CDCl₃) 7.39-7.30 (m, 5H; Ar), 5.82-5.67 (m, 2H; 5-H, 6-H), 4.70 (d, J (H, H)=11.4 Hz, 1H; CH/Ar), 4.42 (d, J (H, H)=11.4 Hz, 1H; CH/Ar), 3.95-3.69 (m, 5H), 3.67-3.59 (m, 1H), 3.54-3.38 (m, 3H), 2.78-2.40 (m, 6H); ¹³C NMR (62.5 MHz, CDCl₃) 137.1, 128.6, 128.1, 128.0, 126.7, 78.1, 77.2, 76.4, 71.3, 69.7, 63.3, 63.1, 31.9, 28.2; MS (CI, NH₃): m/z(%): 326 ((M+NH₄)⁺, 10), 309 ((M+H)⁺, 5), 238 (100); Found 326.1966, C₁₇H₂₈NO₅ requires 326.1967.

2(R), 3(S), 8(S), 9(R)-2,9-Bis-hydroxymethyl-oxonane-3,8-diol 72

To solution of the triol 71 (2.4 mg, 7.8 µmol) in ethanol (0.5 mL) was added palladium on carbon and the reaction mixture was degassed and saturated with hydrogen (water-pump, 3 cycles). The resulting suspension was stirred for 18 h and then filtered through Celite™ whereupon tlc analysis indicated incomplete reaction. The solvent was removed in vacuo and the residue was resubmitted to the reaction
conditions. After stirring for 18 h and filtration through Celite™ the solvent was removed in vacuo and purification by flash chromatography (EtOAc:MeOH, 95:5) provided the title compound 72 as a clear and colourless oil (1.5 mg, 6.9 µmol, 88%); \(R_f\) 0.05 (EtOAc); \(\left[\alpha\right]_{D}^{20} +26\) (c 0.05 in EtOH); \(^1\)H NMR (250 MHz, D₂O): \(\delta=3.89-3.62\) (m, 8H), 1.93-1.75 (m, 2H), 1.75-1.45 (m, 6H); \(^{13}\)C NMR (100 MHz, D₂O): \(\delta=78.5, 68.5, 61.4, 32.0\), 22.0; MS (CI, NH₃): \(m/z\) (%) 238 ((M+NH₄)+, 100), 220 ((M+NH₄–H₂O)+, 20); Found (ES) 238.1650, C₁₀H₂₄NO₅ requires 238.1654.

2(R), 4a(R), 6(R), 7(S), 11a(S)-7-Benzyloxy-6-butyldimethylsilyloxymethyl-2-(4-methoxy-phenyl)-4a,6,7,8,11,11a-hexahydro-4H-1,3,5-trioxa-benzocyclononene 73

PPTS (ca. 2 mg) was added to a stirring solution of the diol 70 (72 mg, 132 µmol) and \(p\)-anisaldehyde (22 mg, 158 µmol) in benzene (5 mL) and the reaction mixture was heated at reflux for 18 h. The reaction mixture was allowed to cool, so the solvent was removed in vacuo and purification by preparative layer chromatography (ether:hexane, 2:1) provide the title compound 73 as a clear and colourless oil (70 mg, 105 µmol, 80%); \(\left[\alpha\right]_{D}^{18} +45.1\) (c 0.94 in CHCl₃); \(^1\)H NMR (250 MHz, CDCl₃): \(\delta=7.74-7.63\) (m, 4H; Ar), 7.48-7.32 (m, 8H; Ar), 7.28-7.20 (m, 3H; Ar), 7.11-7.02 (m, 2H; Ar), 6.94-6.86 (m, 2H; Ar), 5.83-5.67 (m, 2H; 9-H, 10-H), 5.43 (s, 1H; ArCHO₂), 4.57 (d, \(J(H, H)=11.5\) Hz, 1H; CHAr), 4.45 (dd, \(J(H, H)=10.5, 3.6\) Hz, 1H), 4.25 (d, \(J(H, H)=11.5\) Hz, 1H; CH/Ar), 3.86-3.68 (m, 5H), 3.81 (s, 3H; OCH₃), 3.60-3.50 (m, 1H), 3.45-3.34 (m, 1H), 3.00-2.80 (m, 2H), 2.45-2.21 (m, 2H), 1.12 (s, 9H; (CH₃)₃CSi); \(^{13}\)C NMR (62.5 MHz, CDCl₃): \(\delta=160.1, 137.6, 135.8, 135.7, 133.4, 133.3, 130.5, 129.7, 128.3, 127.8, 127.8, 127.7, 127.6, 127.5, 126.4, 113.7, 101.6, 79.7, 76.8, 71.6, 70.9, 64.2, 55.3, 28.8, 28.3, 27.0, 19.3; MS (CI, NH₃): \(m/z\) (%): 665 ((M+H)+, 90), 316 (100); Found 665.3306, C₄₁H₄₉O₆Si requires 665.3298.
(Z, 2R, 3S, 8S, 9R)-8-Benzyloxy-9-tbutyldiphenylsilyloxyethyl-2-hydroxymethyl-3-(4-methoxy-phenyl)-2,3,4,7,8,9-hexahydro-oxonine 74 and (Z, 2R, 3S, 8S, 9R)-8-benzyloxy-2-9-bis-hydroxymethyl-3-(4-methoxy-phenyl)-2,3,4,7,8,9-hexahydro-oxonine

To a stirring solution of the acetal 73 (36 mg, 54 µmol) in DCM (1.1 mL) at – 78 °C was added DIBAL-H (0.38 mL of a 1 M solution in DCM, 380 µmol) and the resulting solution was allowed to warm to –30 °C over a 2 h period and was held at that temperature for 1 h. The reaction mixture was recooled to –78 °C and quenched by the addition of EtOH (0.3 mL) and was allowed to come to ambient temperature. A solution of Rochelle’s salt and saturated aqueous NH₄Cl (1:1 mixture, 2 mL), was added and the resulting gel was stirred until dissolution was complete. The aqueous phase was separated and further extracted with DCM. Purification by preparative layer chromatography (ether:hexane, 1:1) provided the title compound 74 as a clear and colourless oil (16 mg, 24 µmol, 45%); Rᶠ 0.4 (ether, hexane, 1:1); [α]D²⁸ +52.6 (c 0.7 in CHCl₃); ¹H NMR (250 MHz, CDCl₃): δ=7.70-7.64 (m, 4H; Ar), 7.47-7.33 (m, 6H; Ar), 7.28-7.13 (m, 3H; Ar), 6.96-6.84 (m, 4H; Ar), 5.77-5.54 (m, 2H; 5-H, 6-H), 4.61 (d, J (H, H)=10.9 Hz, 1H), 4.44 (d, J (H, H)=11.4 Hz, 1H), 4.41 (d, J (H, H)=10.9 Hz, 1H), 4.09 (d, J (H, H)=11.4 Hz, 1H), 3.95-3.64 (m, 6H), 3.80 (s, 3H; CH₃O), 3.38 (dt, J (H, H)=9.6, 2.8 Hz, 1H), 3.20-3.03 (m, 2H), 2.84-2.62 (m, 2H), 2.51-2.40 (m, 1H), 2.33-2.23 (m, 1H), 1.09 (s, 9H; (CH₃)₃CSi); ¹³C NMR (62.5 MHz, CDCl₃): δ=159.3, 137.6, 137.5, 135.7, 135.7, 133.0, 132.8, 130.3, 129.8, 129.9, 129.5, 128.4, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 126.9, 113.9, 113.7, 80.0, 79.6, 76.0, 71.4, 70.7, 65.8, 64.4, 62.0, 55.3, 28.7, 26.9, 26.4, 19.2; MS (CI, NH₃): m/z(%): 684 ((M+NH₄)⁺, 50), 667 ((M+H)⁺, 80), 154 (100); Found (ES) 684.3727, C₄₁H₅₄NO₆Si requires 684.3720.

Also isolated was (Z, 2R, 3S, 8S, 9R)-8-benzyloxy-2-9-bis-hydroxymethyl-3-(4-methoxy-phenyl)-2,3,4,7,8,9-hexahydro-oxonine; Rᶠ 0.1 (ether, hexane, 1:1); ¹H NMR (250 MHz, CDCl₃): δ=7.37-7.21 (m, 7H; Ar), 6.92-6.87 (m, 2H; Ar), 5.74-5.61 (m, 2H; 5-H, 6-H), 4.68 (d, J (H, H)=11.4 Hz, 1H), 4.61 (d, J (H, H)=11.1 Hz, 1H), 4.42 (d, J (H, H)=10.4 Hz, 1H), 4.39 (d, J (H, H)=11.1 Hz, 1H), 3.90-3.81 (m, 2H), 3.80 (s, 3H, CH₃O), 3.38 (dt, J (H, H)=9.6, 2.8 Hz, 1H), 3.20-3.03 (m, 2H), 2.84-2.62 (m, 2H), 2.51-2.40 (m, 1H), 2.33-2.23 (m, 1H), 1.09 (s, 9H; (CH₃)₃CSi); ¹³C NMR (62.5 MHz, CDCl₃): δ=159.3, 137.6, 137.5, 135.7, 135.7, 133.0, 132.8, 130.3, 129.8, 129.7, 129.5, 128.4, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 126.9, 113.9, 113.7, 80.0, 79.6, 76.0, 71.4, 70.7, 65.8, 64.4, 62.0, 55.3, 28.7, 26.9, 26.4, 19.2; MS (CI, NH₃): m/z(%): 684 ((M+NH₄)⁺, 50), 667 ((M+H)⁺, 80), 154 (100); Found (ES) 684.3727, C₄₁H₅₄NO₆Si requires 684.3720.

Supplementary Material (ESI) for Organic and Biomolecular Chemistry
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3H; CH$_3$O), 3.76-3.66 (m, 2H); 3.60-3.40 (m, 4H), 2.70-2.41 (m, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$=129.4, 137.7, 129.7, 128.5, 128.1, 127.9, 127.8, 127.6, 113.9, 76.3, 75.9, 71.4, 70.9, 62.8, 62.7, 55.3, 27.6, 27.5; MS (CI, NH$_3$): m/z(%): 446 ([M+NH$_4$]$^+$, 95), 129 ([M+H]$^+$, 20), 154 (100); Found 446.2546, C$_{25}$H$_{36}$NO$_6$ requires 446.2543.

(Z, 2R, 3S, 8S, 9R)-8-Benzylxy-9-butylidiphenylsilyloxymethyl-2-carbaldehyde-3-(4-methoxy-phenyl)-2,3,4,7,8,9-hexahydro-oxonine 75

![Diagram of the compound 75](attachment:image.png)

To a stirring solution of the alcohol 74 (15 mg, 22.5 µmol) in DMSO (1.7 mL) was added IBX (12 mg, 45 µmol) and the resulting solution was stirred for 18 h at ambient temperature. Ether (5 mL) and water (5 mL) were added. The aqueous phase was separated and extracted with ether (2 × 10 mL). The organic phases were washed with water (2 × 10 mL), brine (10 mL) and dried (MgSO$_4$). The solvent was removed in vacuo to provide the title compound 75 as a clear and colourless oil (15 mg, 22.5 µmol, 100%); R$_f$ 0.3 (hexane:ether, 1:1); IR (CDCl$_3$): v=1734; $^1$H NMR (250 MHz, CDCl$_3$): $\delta$=9.76 (d, J (H, H)=2.6 Hz, 1H; CHO), 7.65-7.57 (m, 4H; Ar), 7.45-7.30 (m, 6H; Ar), 7.24-7.13 (m, 5H; Ar), 7.00-6.92 (m, 2H; Ar), 6.87 (d, J (H, H)=11.5 Hz, 1H; Ar), 5.72 (dt, J (H, H)=10.3, 7.0 Hz, 1H), 5.58 (dt, J (H, H)=10.3, 6.3 Hz, 1H), 4.56 (d, J (H, H)=11.3 Hz, 1H), 4.44 (d, J (H, H)=11.5 Hz, 1H), 4.37 (d, J (H, H)=11.3 Hz, 1H), 4.09 (d, J (H, H)=11.5 Hz, 1H), 3.81 (s, 3H; CH$_3$O), 3.80-3.60 (m, 5H), 3.27 (t, J (H, H)=8.1 Hz, 1H), 2.90-2.68 (m, 2H), 2.46-2.35 (m, 1H), 2.21-2.12 (m, 1H), 1.06 (s, 9H; (CH$_3$)$_3$CSi); Note due to the lability of the aldehyde satisfactory mass spectral data could not be obtained.
(Z, 2R, 3S, 8S, 9R)-8-Benzyloxy-9-butyldimethylsilyloxyethyl-2-(1-hydroxy-allyl)-3-(4-methoxy-phenyl)-2,3,4,7,8,9-hexahydro-oxonine 76

To a stirring solution of the aldehyde 75 (15 mg, 22.5 µmol) (previously dried by azeotropic distillation with toluene (2 × 1 mL)) in THF (1.5 mL) at 0 °C was added vinylmagnesium bromide (113 µL of a 1.0 M solution in THF, 113 µmol) and the resulting solution was stirred at 0 °C for 2 h. Saturated aqueous NH4Cl and ether were added to quench the reaction. The aqueous layer was separated and extracted with ether. The organic phases were washed with brine, dried (MgSO4) and purificatrion by preparative layer chromatography (hexane:ether, 1:1) provided the title compound 76 as an inseparable 6:1 mixture of diastereomers (14.6 mg, 21 µmol, 94%); Rf 0.4 (hexane:ether, 1:1); 1H NMR (500 MHz, CDCl3): δ=7.65-7.60 (m, 4H; Ar), 7.43-7.30 (m, 5H; Ar), 7.25-7.15 (m, 6H; Ar), 6.96 (d, J (H, H)=6.8 Hz, 1H; Ar), 6.86 (d, J (H, H)=11.6 Hz, 1H; Ar), 6.00 (ddd, J (H, H)=17.3, 10.5, 5.9 Hz, 1H; CH=CH2), 5.65-5.56 (m, 2H), 5.16 (dt, J (H, H)=17.3, 1.5 Hz, 1H; trans-CHH=CH), 5.04 (dt, J (H, H)=10.5, 1.5 Hz, 1H; cis-CHH=CH), 4.54-4.52 (br, 1H; CH=O), 4.50 (d, J (H, H)=10.7 Hz, 1H), 4.45 (d, J (H, H)=11.0 Hz, 1H), 4.31 (d, J (H, H)=10.7 Hz, 1H), 4.16 (d, J (H, H)=11.6 Hz, 1H), 3.93 (dt, J (H, H)=11.5, 2.6 Hz, 1H; CH/HOSi), 3.86 (dt, J (H, H)=8.0, 2.6 Hz, 1H; 9-H), 3.80 (s, 3H; CH3O), 3.81-3.79 (m, 1H; CH/HOSi), 3.70-3.67 (m, 1H; 3-H), 3.50 (dd, J (H, H)=9.0, 2.3 Hz, 1H; 2-H), 3.16 (t, J (H, H)=8.0 Hz, 1H; 8-H), 2.80-2.72 (m, 1H; 7-H), 2.69-2.63 (m, 1H; 4-H), 2.41-2.35 (m, 4-H'), 2.25-2.19 (m, 1H; 7-H'), 1.07 (s, 9H; (CH3)3CSi); 13C NMR (62.5 MHz, CDCl3): δ=152.9, 137.6, 137.3, 135.8, 132.9, 130.4, 129.8, 129.7, 128.3, 128.2, 127.7, 127.7, 127.5, 127.1, 113.8, 80.9, 76.8, 76.0, 73.7, 70.7, 64.0, 55.3, 29.1, 26.9, 26.2, 19.1; MS (CI, NH3): m/z(%): 710 ((M+NH4)+, 100), 693 ((M+H)+, 55); Found (ES) 693.3622, C43H53O6Si requires 693.3622.
(Z, 2R, 3S, 8S, 9R)-8-Benzyloxy-9-tbutyldimethylsilyloxymethyl-3-hydroxy-2-(1-hydroxy-allyl)-2,3,4,7,8,9-hexahydro-oxonine 77

TFA (0.26 mL) was added to a stirring solution of the oxonanes 76 (13.5 mg, 19.5 µmol) in DCM (1 mL) at –20 °C. Stirring was continued for 15 mins and the reaction was quenched by the addition of saturated aqueous NaHCO3 (3 mL) and DCM (3 mL). The aqueous phase was separated and extracted further with DCM. The combined organic extracts were dried (MgSO4) and purification by preparative layer chromatography (hexane:ether, 1:1) provided the title compounds 77.

The major diastereomer was isolated as a clear and colourless oil (9 mg, 15 µmol, 77%); Rf 0.1 (hexane:ether, 1:1); [α]D20 +13.3 (c 0.18 in CHCl3); IR (CDCl3): ν=3570; 1H NMR (250 MHz, CDCl3): δ=7.47-7.30 (m, 6H; Ar), 7.25-7.15 (m, 3H; Ar), 7.02-6.96 (m, 2H; Ar), 6.03 (ddd, J (H, H)=17.4, 10.4, 4.7 Hz, 1H; CHH=CH), 5.76-5.61 (m, 2H; 5-H, 6-H), 5.42 (dt, J (H, H)=17.4, 1.9 Hz, 1H; trans-CHH=CH), 5.16 (dt, J (H, H)=10.7, 1.9 Hz, 1H; cis-CHH=CH), 4.73-4.67 (br, 1H), 4.50 (d, J (H, H)=11.6 Hz, 1H; CHHAr), 4.19 (d, J (H, H)=11.6 Hz, 1H; CHHAr), 4.18-4.09 (br, 1H), 3.95 (dd, J (H, H)=11.1, 2.4 Hz, 1H; CHHOSi), 3.88 (dt, J (H, H)=8.4, 2.4 Hz, 1H; 9-H), 3.73 (dd, J (H, H)=11.1, 8.4 Hz, 1H; CHHOSi), 3.39 (dd, J (H, H)=8.8, 2.6 Hz, 1H), 3.33-3.25 (m, 1H), 3.20 (t, J (H, H)=7.3 Hz, 1H), 2.82-2.67 (m, 2H), 2.33-2.19 (m, 2H), 1.08 (s, 9H; (CH3)3CSi); 13C NMR (62.5 MHz, CDCl3): δ=137.6, 137.5, 135.7, 135.7, 132.8, 132.7, 129.9, 128.5, 128.3, 127.8, 127.8, 127.6, 126.9, 114.3, 81.0, 77.8, 76.7, 72.8, 70.7, 68.5, 64.3, 30.3, 28.9, 26.9, 19.1; MS (CI, NH3): m/z(%): 590 ((M+NH4)+, 40), 573 ((M+H)+, 25), 274 (100); Found, 573.3028, C35H45O5Si requires 573.3036.

The minor diastereomer was isolated as a clear and colourless oil (1.3 mg, 2 µmol, 11%); Rf 0.15 (hexane:ether); 1H NMR (250 MHz, CDCl3): δ=7.69-7.59 (m, 4H; Ar), 7.45-7.29 (m, 6H; Ar), 7.25-7.17 (m, 3H; Ar), 7.06-6.98 (m, 2H; Ar), 6.19 (ddd, J (H, H)=17.6, 10.5, 4.1 Hz, 1H; CH2=CH), 5.77-5.62 (m, 2H; 5-H, 6-H), 5.36 (dt, J (H, H)=17.6, 1.7 Hz, 1H; trans-CHH=CH), 5.23 (dt, J (H, H)=10.5, 1.7 Hz, 1H; cis-CHH=CH), 4.74-4.65 (br, 1H), 4.50 (d, J (H, H)=11.6 Hz, 1H; CHHAr), 4.18 (d, J (H, H)=11.6 Hz, 1H; CHHAr), 4.00-3.90 (br, 1H), 3.91-3.86 (m, 2H; CH2OSi), 3.84-3.73.
(m, 1H), 3.44 (dd, J (H, H)=9.0, 4.1 Hz, 1H), 3.33 (t, J (H, H)=7.9 Hz, 1H), 2.98-2.87 (br, 1H), 2.85-2.70 (m, 2H), 2.55-2.43 (br, 1H), 2.28-2.13 (br, 2H), 1.08 (s, 9H; (CH₃)₃CSi); MS (CI, NH₃): m/z (%): 590 ((M+NH₄)⁺, 100), 573 ((M+H)⁺, 30); Found 590.3316, C₃₅H₄₉NO₅Si requires 590.3302.

(5Z, 6aR, 8R, 9R, 11Z, 13aS)-9-Benzylxoxy-8-tert-butyldimethylsilyloxyethyl-3,4,6a,8,9,10,13,13a-octahydro-1,7-dioxacyclooctacyclononen-2-one 79

To a solution of the major diastereomer of 77 (2.3 mg, 3.8 µmol) in toluene (1 mL) was added phenylselanylacetal diethyl acetal (1.3 mg, 4.6 µmol) and a small quantity of PPTS. The solution was heated under reflux for 2 h, allowed to cool and purified by preparative layer chromatography to give the corresponding selenides 78 (2.6 mg, 3.4 µmol, 91%). To a stirring solution of the selenides prepared above (2.6 mg, 3.4 µmol) in DCM (0.2 mL), MeOH (1.3 mL) and water (0.3 mL) was added NaHCO₃ (0.3 mg, 4 µmol) and NaIO₄ (2.9 mg, 12.9 µmol) and the resulting suspension was stirred at ambient temperature for 2 h. Water (5 mL) and DCM (5 mL) were added, the aqueous phase was separated and further extracted with DCM (4 × 5 mL). The organic phases were washed with brine (5 mL) and dried (MgSO₄). The solvent was removed in vacuo and the resultant selenoxides were dried under high vacuum for 18 h. Toluene (1 mL) and DBU (2 µL) were added and the resulting solution was heated at reflux for 18 h and then allowed to cool. The solvent was removed in vacuo and purification by flash chromatography (hexane:ether, 5:1) provided the title compound 79 (1.5 mg, 2.5 µmol, 74%) as a clear and colourless oil; Rf 0.2 (hexane:ether, 5:1); [α]ᵣ°+19.3 (c 0.073 in CHCl₃); IR (CHCl₃): v=1742; ¹H (500 MHz, CDCl₃): δ=7.66-7.63 (m, 4H; Ar), 7.42-7.37 (m, 2H; Ar), 7.34-7.28 (m, 6H; Ar), 7.23-7.17 (m, 3H; Ar), 7.00 (d, J (H, H)=6.7 Hz, 2H; Ar), 6.14 (dd, J (H, H)=11, 5 Hz, 1H; 6-H), 5.76 (dt, J (H, H)=10.5, 7.2 Hz, 1H), 5.61-5.53 (m, 2H), 4.67 (dt, J (H, H)=9.3, 3.3 Hz, 1H; 13a-H), 4.51 (d, J (H, H)=11.5 Hz, 1H; CHHAr), 4.19 (d, J (H, H)=11.5 Hz, 1H; CHHAr), 4.09-4.03 (m, 1H), 3.86-3.78 (m, 2H), 3.74 (dd, J (H, H)=11.9, 9.1 Hz, 1H), 3.17 (t, J (H, H)=8.8 Hz, 1H), 3.04 (t, J (H, H)=11.9 Hz, 1H), 2.95-2.86 (m, 1H), 2.74 (ddd, J (H, H)=13.6, 6.1, 1.6 Hz, 1H), 2.63-2.54 (m, 1H), 2.26 (ddd, J (H, H)=13.6,
12.5, 5.0 Hz. 1H), 2.34-2.25 (m, 1H), 2.17 (dd, J (H, H)=13.6, 7.6 Hz, 1H), 2.06-2.00 (m, 1H), 1.05 (s, 9H; (CH₃)₃Si); ¹³C NMR (62.5 MHz, CDCl₃) Note, one of the resonances of a carbon adjacent to oxygen is missing: δ=175.9, 138.6, 137.6, 135.7, 133.6, 133.4, 130.5, 129.6, 128.6, 128.3, 127.7, 127.62, 127.55, 125.1, 82.7, 76.8, 70.9, 62.3, 32.6, 37.7, 29.5, 27.9, 25.4, 19.2; MS (Cl, NH₃): m/z (%): 614 ((M+NH₄)⁺, 60), 597 ((M+H)⁺, 15), 274 (100); Found (ES) 597.3031, C₃₇H₄₂O₅Si requires 597.3036.
X-ray Crystal Structures.

X-ray Crystallographic Structure Determination of 15: Crystal data: C_{26}H_{44}O_{5}Si, \(M_\text{w}=464.70\), colourless block 0.10x0.10x0.10mm\(^3\), orthorhombic \(P2_12_12_1\) (No. 19), \(a=8.040(3), b=16.929(3), c=19.604(3)\AA\), \(V=2668(2)\AA^3\), \(Z=4\), \(T=180(2)\text{K}\), \(D_\text{X} = 1.157 \text{ g cm}^{-3}\), \(\lambda = 0.71073 \text{ Å}\), \(\mu = 0.120 \text{ mm}^{-1}\), Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 1.59° < \(\theta\) < 25.07°, 4732 independent reflections. The structure was solved by direct methods (SHELXS-97)\(^4\) and refined by least squares (SHELXL-97)\(^4\) using Chebyshev weights on \(F_\text{o}^2\) to \(R_1 = 0.046, wR_2 = 0.123\) \([I > 2\sigma(I)]\), 326 parameters, goodness-of-fit on \(F^2\) 1.246, residual electron density 0.54 e Å\(^{-3}\). The absolute structure was assigned from the known configuration of the starting material (Flack parameter: -0.2(2)). Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655148. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

X-ray Crystallographic Structure Determination of 17: Crystal data: C_{28}H_{46}O_{5}Si, \(M_\text{w}=490.74\), colourless block 0.25x0.25x0.25mm\(^3\), orthorhombic \(P2_12_12_1\) (No. 19), \(a=8.430 (1), b=16.304(1), c=20.801(1)\AA\), \(Z=4\), \(V=2858.9(4)\AA^3\), \(T=180(2)\text{K}\), \(D_\text{X} = 1.140 \text{ g cm}^{-3}\), \(\lambda = 0.71073 \text{ Å}\), \(\mu = 0.200 \text{ mm}^{-1}\), Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 3.11° < \(\theta\) < 25.03°, 4994 independent reflections. The structure was solved by direct methods (SHELXS-97)\(^4\) and refined by least squares (SHELXL-97)\(^4\) using Chebyshev weights on \(F_\text{o}^2\) to \(R_1 = 0.042, wR_2 = 0.098\) \([I > 2\sigma(I)]\), 312 parameters, goodness-of-fit on \(F^2\) 1.135, residual electron density 0.42 e Å\(^{-3}\). The absolute structure was assigned from the known configuration of the starting material (Flack parameter: 0.2(2)). Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655144. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].
X-ray Crystallographic Structure Determination of 61: Crystal data: C_{19}H_{26}O_{4}, \( M_e = 318.40 \), colourless block 0.30x0.20x0.10mm\(^3\), monoclinic \( P2_1 \) (No. 4), 
\( a = 10.8190(4), b = 5.3710(1), c = 15.6400(5) \text{\AA}, \beta = 102.809(2)^\circ, V = 886.21(5) \text{\AA}^3, Z = 2, \)
\( T = 180(2) \text{K}, D_X = 1.193 \text{ g cm}^{-3}, \lambda = 0.71073 \text{ \AA}, \mu = 0.082 \text{ mm}^{-1}, \) Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 
2.93\(^\circ\) \(< \theta < 25.02^\circ\), 19185 measured reflections, 1746 independent (\( R_{int} = 0.059 \)). The structure was solved by direct methods (SHELXS-97)\(^4\) and refined by least squares (SHELXL-97)\(^4\) using Chebyshev weights on \( F_o^2 \) to \( R_1 = 0.060, wR_2 = 0.161 \) \([I > 2\sigma(I)]\), 170 parameters, goodness-of-fit on \( F^2 \) 1.098, residual electron density 0.59 e Å\(^{-3}\). The –C\(_6\)H\(_5\) ring is disordered over two sites: common isotropic displacement parameters were assigned to the carbon atoms of this moiety. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655145. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

X-ray Crystallographic Structure Determination of 61: Crystal data: C\(_{11}\)H\(_{16}\)O\(_4\), \( M_e = 212.24 \), colourless block 0.14x0.04x0.02mm\(^3\), hexagonal \( P6_3 \) (No. 173), 
\( a = 14.343(7), c = 8.9246(4) \text{\AA}, V = 1590.0(2) \text{\AA}^3, Z = 6, \ T = 150(2) \text{K}, D_X = 1.330 \text{ g cm}^{-3}, \)
\( \lambda = 0.71073 \text{ \AA}, \mu = 0.200 \text{ mm}^{-1}, \) Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 2.72\(^\circ\) \(< \theta < 29.40^\circ\), 10627 measured reflections, 1632 independent (\( R_{int} = 0.027 \)). The structure was solved by direct methods (SHELXS-97)\(^4\) and refined by least squares (SHELXL-97)\(^4\) using Chebyshev weights on \( F_o^2 \) to \( R_1 = 0.033, wR_2 = 0.087 \) \([I > 2\sigma(I)]\), 138 parameters, goodness-of-fit on \( F^2 \) 1.191, residual electron density 0.30 e Å\(^{-3}\). Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655150. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].
X-ray Crystallographic Structure Determination of **62**: Crystal data: C_{12}H_{14}O_{5},

M_w=238.23, colourless block 0.06x0.04x0.04mm³, orthorhombic P2_12_12_1 (No. 19),

a=7.8054(5), b=10.1991(9), c=14.3886(6)Å, V=1145.5(1)Å³, Z=4, T = 150(2)K, \( D_X = 1.381 \text{ g cm}^{-3}, \lambda = 0.71073 \text{ Å}, \mu = 0.108 \text{ mm}^{-1} \),

Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 2.74° < θ < 29.43°, 8116 measured reflections, 1870 independent \( [R_{int} =0.022] \). The structure was solved by direct methods (SHELXS-97)⁴ and refined by least squares (SHELXL-97)⁴ using Chebyshev weights on \( F_0^2 \) to \( R1 = 0.044, wR2 = 0.108 \ [I > 2\sigma(I)] \), 190 parameters, goodness-of-fit on \( F^2 = 1.143 \), residual electron density 0.27 e Å⁻³. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655146. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

X-ray Crystallographic Structure Determination of **63**: Crystal data: C_{13}H_{16}O_{4},

M_w=236.26, colourless block 0.10x0.08x0.06mm³, monoclinic P2_1 (No. 4),

a=7.720(4), b=6.415(3), c=12.126(5)Å, β=96.62(1)°, V=596.6(5)Å³, Z=2, \( T = 150(2)K, D_X = 1.315 \text{ g cm}^{-3}, \lambda = 0.71073 \text{ Å}, \mu = 0.097 \text{ mm}^{-1} \),

Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 2.89° < θ < 29.63°, 4168 measured reflections, 1767 independent \( (R_{int}=0.055) \). The structure was solved by direct methods (SHELXS-97)⁴ and refined by least squares (SHELXL-97)⁴ using Chebyshev weights on \( F_0^2 \) to \( R1 = 0.046, wR2 = 0.118 \ [I > 2\sigma(I)] \), 154 parameters, goodness-of-fit on \( F^2 = 1.041 \), residual electron density 0.32 e Å⁻³. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655149. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].
References

1. We have previously reported the preparation of a lactone analogous to 7 but carrying a TBDPS instead of a TIPS protecting group and the lactone 7 was prepared analogously see: J. W. Burton, J. S. Clark, S. Derrer, T. C. Stork, J. G. Bendall and A. B. Holmes, *J. Am. Chem. Soc.*, 1997, **119**, 7483.


1H NMR (250 MHz; CDCl3)

13C NMR (62.5 MHz; CDCl3)
1H NMR (400 MHz; CDCl3)

13C NMR (100 MHz; CDCl3)
Variable Temperature 1H NMR (400 MHz; CDCl3)

Supplementary Material (ESI) for Organic and Biomolecular Chemistry
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$^{13}$C NMR (400 MHz; CDCl$_3$; 52 °C)

$^1$H NMR (400 MHz; CDCl$_3$)
$^{13}$C NMR (100 MHz; CDCl$_3$)

1H NMR (500 MHz; CDCl$_3$)
13C NMR (62.5 MHz; CDCl3)
Inset shows an expansion of the solvent resonance. The peak at 77.2 is CHCl3 in CDCl3.