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Supporting Information

A Synthesis of (+)-Obtusenyne

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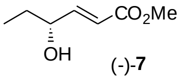
Experimental procedures and characterisation data for the following compounds are reported:
ent-(**4**), **(-)-7**, (±)-**15**, (±)-**16**, (±)-**19**, (±)-**20**, (±)-**21**, (±)-**22**, (±)-**23**, (±)-**28**, (±)-**29**, (±)-**30**, the secondary alcohol derived from (±)-**30**, (-)-**38**, (-)-**39**, (-)-**40**, **41**, (-)-**42,** (-)-**43, 46,** the lactols derived from **47, 48**, **49**, (-)-**50**, (-)-**51**, (-)-**52**, (-)-**53**, (-)-**54**, (-)-**56**, (-)-**57**, (-)-**58**, (+)-**59**, (-)-**60**, (-)-**61**, (-)-**62**, (-)-**63**, (-)-**65**, (-)-**66**, the fully protected oxonene derived from (-)-**66**, (-)-**67**, the fully protected oxonene derived from (-)-**68**, (-)-**69**, (-)-**70**, (-)-**71**, (-)-**72**, (-)-**73**, (-)-**74**, (-)-**75**, (-)-**76**, (-)-**83**, the fully reduced oxonane derived from (-)-**83**.

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 (δ = 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 shifts are quoted in ppm relative to tetramethylsilane (? = 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 [?]$_D^T$, implies units of ^{o}cm^{2}g^{-1} (T = temp °C). Microwave reactions were conducted in a fully automated coherent Emrys Liberator microwave system. This was purchased from Personal Chemistry: Hamnesplanaden 5, 75319 Uppsala, Sweden; http://www.personalchemistry.com. We thank Merck, Sharp and Dohme at Terlings Park for access to this equipment. 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 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.

(E, 4R)-Methyl 4-hydroxyhex-2-enoate (-)-7

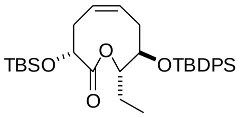


(-)-**7**

DBU (0.04 mL, 0.27 mmol) was added to a suspension of the epoxy ester (+)-**6** (200 mg, 1.39 mmol) in DCM (1.5 mL) and the resulting mixture was stirred for 1.5 h. The solvent was removed *in vacuo* and the residue purified by flash chromatography (ether:hexane, 1:1) to give the title compound (-)-**7** as a clear and colourless liquid

(172 mg, 86%); R_f 0.2 (ether:hexane, 1:1); $[a]^{21}_{\mathrm{D}}$ -25.8 (*c* 2.9, $CHCl_3$); lit.{Burgess, 1990 #109} $[a]^{25}_{\mathrm{D}}$ +23.5 (*c* 3, $CHCl_3$); IR (film): ν=3620, 3500, 1745; ^{1}H NMR (80 MHz, $CDCl_3$) δ=6.95 (dd, *J*(H, H)=4.8, 15.7 Hz, 1H; 3-H), 6.03 (dd, *J*(H, H)=1.6, 15.7 Hz, 1H; 2-H), 4.24 (m, 1H; 4-H), 3.74 (s, 3H; CH_3O), 1.82-1.45 (m, 3H; CH_2, OH), 0.96 (t, 3H, *J*(H, H)=7.0 Hz, CH_3); MS (CI, NH_3): *m/z* (%): Found $(M+NH_4)^+$ 162.1130 (100), $C_7H_{16}NO_3$ requires 162.1130.

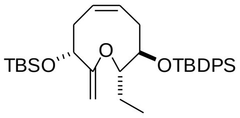
(Z, 3R, 8R*, 9S*)-3-tButyldimethylsilyloxy-8-tbutyldiphenylsilanyloxy-9-ethyl-4,7,8,9-tetrahydro-3H-oxonin-2-one, (±)-15*



(±)-**15**

The hydroxy lactone (±)-**12** (595 mg, 1.36 mmol), *t*butylchlorodimethylsilane (310 mg, 2.06 mmol) and imidazole (370 mg, 5.43 mmol) were stirred at 60 °C in DMF (5 mL) overnight. The reaction mixture was allowed to cool, poured into water (50 mL) and extracted with ether (3 × 100 mL). The extracts were washed with brine (25 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product. Purification by flash chromatography (hexane:ether, 20:1) furnished the TBS-ether **(±)-15** (734 mg, 98%) as a clear and colourless oil; (Found C, 69.3; H, 8.9%; $C_{32}H_{48}O_4Si_2$ requires C, 69.5; H, 8.8); R_f 0.35 (hexane:ether, 20:1); IR (film): ν=1730; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.66 (m, 4H; Ar), 7.40 (m, 6H; Ar), 5.38 (m, 2H; $C\mathit{H}{=}CH$), 4.88 (m, 1H; OCH), 4.31 (m, 1H; OCH), 3.75 (m, 1H; OCH), 2.07-2.52 (m, 4H; allylic CH_2), 1.78 (m, 1H; $C\mathit{H}HCH_3$), 1.46 (m, 1H; $CH\mathit{H}CH_3$), 1.04 (s, 9H; $C(C\mathit{H}_3)_3$), 0.84 (s, 9H; $C(C\mathit{H}_3)_3$), 0.82 (t, *J*(H, H)=7 Hz, 3H; $CH_2C\mathit{H}_3$), 0.04 (s, 3H; $SiCH_3$), 0.03 (s, 3H; $SiCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=173.9 (2-C), 135.9, 135.8, 133.8, 133.2, 130.4, 129.8, 129.7, 127.7, 127.6, 124.2, 80.8 (OCH), 76.0 (OCH), 72.6 (OCH), 33.2 (CH_2), 26.9 ($SiC(\mathit{C}H_3)_3$), 25.6 ($SiC(\mathit{C}H_3)_3$), 25.5 ($Si\mathit{C}(CH_3)_3$), 19.2 ($Si\mathit{C}(CH_3)_3$), 18.1, 9.6 ($CH_2\mathit{C}H_3$), -5.1 ($Si(CH_3)_2$), -5.2 ($Si(CH_3)_2$); MS (CI, NH_3): *m/z* (%): 570 ($(M+NH_4)^+$, 100), 553 ($(M+H)^+$, 30).

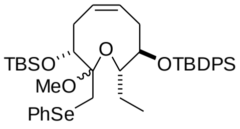
(Z, 3R, 8R*, 9S*) 3-tButyldimethylsilanyloxy-8-tbutyldiphenylsilanyloxy-9-ethyl-2-methylene-2,3,4,7,8,9-hexahydro-oxonine, (±)-16*



(±)-**16**

The *bis*-silylether **(±)-15** (475 mg, 0.859 mmol) and DMAP (116 mg, 0.949 mmol) were dissolved in THF (10 mL). The solution was freeze-thaw degassed (3 cycles) and cooled to -45 ºC. The Tebbe reagent (2.4 mL of a 0.45 M solution in toluene, 1.1 mmol) was then added to this mixture and the resulting dark red solution was stirred at -40 ºC for 0.5 h and then warmed to room temperature and stirred for a further 45 min. The reaction mixture was re-cooled to -15 ºC and a 3 M aqueous solution of NaOH (0.36 mL) was added to quench the reaction. The reaction mixture was then warmed to room temperature and poured into ether (100 mL) over anhydrous sodium sulphate. The supernatant was filtered through a short plug of Celite™ and the filtrate was concentrated *in vacuo* to give the crude product. Purification by chromatography on grade III neutral alumina (hexane) furnished the enol ether **(±)-16** (446 mg, 94%) as a clear and colourless oil; (Found C, 72.1; H, 9.1%; $C_{33}H_{50}O_3Si_2$ requires C, 71.9; H, 9.2); R_f 0.4 (hexane:DCM, 2:1); IR (film): ν=1630; ^{1}H NMR (500 MHz, C_6D_6): δ=7.73 (m, 4H; Ar), 7.19 (m, 6H; Ar), 5.93 (m, 1H; C*H*=CH), 5.54 (m, 1H; CH=C*H*), 4.22 (brs, 1H; OC=C*H*H), 4.06 (1H, brs, OC=CH*H*), 3.89-4.16 (m, 3H; 3 × OCH), 2.66-2.89 (m, 2H; allylic CH_2), 2.05-2.25 (m, 2H; allylic CH_2), 1.89-1.53 (m, 2H; CH_2CH_3), 1.14 (s, 9H; $C(CH_3)_3$), 0.98 (s, 9H; $C(CH_3)_3$), 0.83 (t, *J*(H, H)=7 Hz, 3H; CH_2CH_3), 0.13 (s, 3H; $SiCH_3$), 0.12 (s, 3H; $SiCH_3$); ^{13}C NMR (100 MHz, C_6D_6): δ=166.7 (9-C), 136.3, 136.3, 134.4, 134.0, 130.1, 128.7, 128.1, 89.3 ($OCH=CH_2$), 85.7 (OCH), 76.2 (OCH), 74.7 (OCH), 33.9 (($SiC(CH_3)_3$, 2 × coincident allylic CH_2), 27.3, 26.1, 19.5, 18.4, 8.8, -4.5, -4.3; MS (EI): *m/z* (%): 550 (M^+, 100).

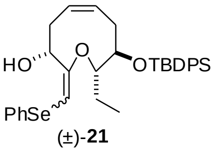
*(Z, 2S*R*, 3R*, 8R*, 9S*) 3-tButyldimethylsilanyloxy-8-tbutyldiphenylsilanyloxy-9-ethyl-2-methoxy-2-phenylselenomethyl-2,3,4,7,8,9-hexahydro-oxonine, (±)-19*



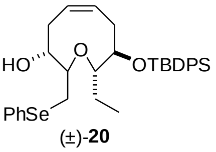
(±)-**19**

Phenylselenyl chloride (195 mg, 1.02 mmol) in dry DCM (1 mL) was added to a solution of the enol ether **(±)-16** (265 mg, 0.482 mmol) and DIPEA (0.18 mL, 1.03 mmol) in dry DCM (2 mL) and MeOH (0.5 mL) at room temperature. After stirring for 2 h more DIPEA (0.16 mL) and phenylselenyl chloride (181 mg, 0.95 mmol) in dry DCM (1 mL) were added. The solution was stirred for a further 3 h and then poured onto saturated aqueous $NaHCO_3$ (10 mL) and extracted with DCM (3 × 25 mL). The combined organic extracts were dried, the solvent removed and the residue purified by chromatography on grade III neutral alumina (hexane:DCM, 20:1) to give the title compound **(±)-19** (194 mg, 55%) as a clear yellow oil; R_f 0.6 (hexane:DCM, 20:1); IR (film): ν=2960; ^1H NMR (400 MHz, C_6D_6): δ=7.80 (m, 4H; Ar), 7.47 (m, 2H; Ar), 7.21 (m, 6H; Ar), 6.91 (m, 3H; Ar), 5.83-6.01 (m, 2H; CH=CH), 3.93-4.02 (m, 3H; 3 × OCH), 3.52 (d, *J*(H, H)=13.5 Hz, 1H; C*H*HSePh), 3.35 (d, *J*(H, H)=13.5 Hz, 1H; CH*H*SePh), 3.31 (s, 3H; OCH_3), 2.89-2.97 (m, 1H; CH_2), 2.48 (brt, *J*(H, H)=11 Hz, 1H; CH_2), 2.02-2.17 (m, 4H; 2 × CH_2), 1.17 (s, 9H; $C(CH_3)_3$), 1.00 (s, 9H, $C(CH_3)_3$), 0.88 (t, *J*(H, H)=7 Hz, 3H; CH_2CH_3), 0.14 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$); ^{13}C NMR (100 MHz, C_6D_6): δ=136.5, 136.4, 134.6, 133.9, 133.4, 132.7, 130.1, 129.7, 129.4, 127.9, 127.0, 126.6, 105.2, 77.0 (OCH), 73.1 (OCH), 71.2 (OCH), 50.7 (OCH_3), 33.4, 307, 30.1, 27.4, 26.1, 23.0, 19.7, 18.4, -4.4, -4.6; MS (FAB): *m/z* (%): 739 ($(M+H)^+$, 4), 429 (100); Found 739.3120, $C_{40}H_{59}O_4{}^{80}SeSi_2$ requires 739.3117.

(Z, 3R*, 8R*, 9S*)-8-tButyldiphenylsilanyloxy-9-ethyl-3-hydroxy2-phenylselanylmethyl-2,3,4,7,8,9-hexahydro-oxonine, (±)-20* and *(Z, 3R*, 8R*, 9S*)-8-tbutyldiphenylsilanyloxy-9-ethyl-3-hydroxy-2-phenylseleanylmethylene-2,3,4,7,8,9-hexahydro-oxonine, (±)-21



(±)-**21**



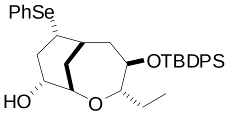
(±)-**20**

DIBAL (0.73 mL of a 1.0 M solution in hexanes, 0.73 mmol) was added dropwise to a solution of the acetal **(±)-19** (90 mg, 0.122 mmol) in dry DCM (2 mL) at 0 °C. The solution was stirred at 0 °C for 1 h then at room temperature for 17 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl (5 mL). The mixture was poured onto 5% HCl (10 mL) and was extracted with ether (3 × 40 mL). The extracts were combined, washed with water (10 mL), brine (10 mL), dried and evaporated. The products were separated by preparative layer chromatography (DCM:hexane, 3:1). The enol ether **(±)-21** was isolated as an oil as a 1:1 mixture of (*E*) and (*Z*) isomers (17 mg, 24%); R_f 0.3 (DCM:hexane, 3:1); IR (film): ν=3600; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.69-7.66 (m, 4H; Ar), 7.50-7.34 (m, 8H; Ar), 7.30-7.18 (m, 3H; Ar), 5.76 (s, 0.5H; C=CHSePh), 5.73 (s, 0.5H; C=CHSePh), 5.66-5.34 (m, 2H; CH=CH), 2.5-1.5 (m, 7H; OCH), 1.06 (s, 9H; $C(CH_3)_3$), 0.86 (t, 1.5H; *J*(H, H)=7 Hz, CH_2CH_3), 0.83 (t, *J*(H, H)=7 Hz, 1.5H; CH_2CH_3); MS (EI): *m/z* (%): 592 (M^+, 2); Found 592.1912, $C_{33}H_{40}O_3{}^{80}SeSi$ requires 592.1912.

The selenide **(±)-20** was isolated as a clear yellow oil (14 mg, 20%); R_f 0.3 (hexane:ether, 2:1); IR (film): ν=3580; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.63 (m, 3H; Ar), 7.52 (m, 2H; Ar), 7.37 (m, 6H; Ar), 7.25 (m, 3H; Ar), 5.50 (m, 2H; HC=CH), 3.98 (m, 1H; OCH), 3.82-3.75 (m, 2H; 2 × OCH), 3.22 (m, 1H; OCH), 3.18 (d, *J*(H, H)=12 Hz, 1H; C*H*HSePh), 3.06 (dd, *J*(H, H)=12, 4 Hz, 1H; CH*H*SePh), 2.55 (m, 2H; allylic CH_2), 2.28 (m, 1H; allylic CH_2), 2.08 (m, 1H; allylic CH_2), 1.52-1.24 (m, 2H; CH_2CH_3), 1.04 (s, 9H; $C(CH_3)_3$), 0.6 (t, *J*(H, H)=7 Hz, 3H; CH_2CH_3); MS (CI, NH_3): *m/z* (%): 595 ($(M+H)^+$, 2), 249 (100); Found 595.2147, $C_{33}H_{43}O_3{}^{80}SeSi$ requires 595.2147.

The racemic enol ether (±)-**18** (6.5 mg, 12%) was also isolated as a colourless oil.

(1S, 3S*, 4R*, 6S*, 7S*, 9R*)-4-tButyldiphenylsilanyloxy-3-ethyl-9-hydroxy-7-phenylselanyl-2-oxabicyclo(4.3.1)decane (±)-23*



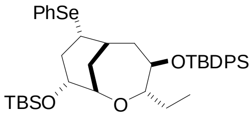
(±)-**23**

To a solution of the acetal **(±)-19** (50 mg, 69 μmol) in dry DCM (0.5 mL) cooled to -78 °C was added dropwise triethylsilane (16 μL, 0.10 mmol) followed by $TiCl_4$ (0.08 mL of a 1.0 M solution in DCM, 80 μmol). The resultant red solution was stirred at -78 °C for 20 min and then the reaction was quenched with MeOH (0.1 mL). The mixture was allowed to warm to room temperature, poured into saturated $NaHCO_3$ (5 mL) and extracted with ether (3 × 25 mL). The extracts were combined, washed with water (5 mL), brine (5 mL), dried and evaporated. Purification of the residue by flash chromatography (DCM:hexane, 1:1) gave the bicyclic ether **(±)-23** (24 mg, 59%) as an oil which crystallised on storage; (Found C, 66.5; H, 7.2%. $C_{33}H_{42}O_3SeSi$ requires C, 66.8; H, 7.1); mp 131-132 °C (ether/hexane); R_f 0.3 (hexane:ether, 1:1); IR (CCl_4): ν=3590; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.64-7.22 (m, 15H; Ar), 3.94 (m, 1H), 3.81

(q, *J*(H, H)=3 Hz, 1H,), 3.52-3.38 (m, 3H), 3.0 (apparent dt, 1H), 2.26-1.98 (m, 4H), 1.61 (brdd, *J*(H, H)=9, 3 Hz, 2H), 1.30 (m, 1H), 1.08 (m, 2H), 1.01 (s, 9H; $C(CH_3)_3$), 0.70 (t, *J*(H, H)=7 Hz, 3H; CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=135.9, 135.8, 134.8, 134.0, 133.8, 129.8, 129.7, 129.0, 128.9, 127.6, 127.6, 82.4 (OCH), 78.0 (OCH), 75.7 (OCH), 72.5 (OCH), 45.8 (*C*HSePh), 33.8 (CH_2), 31.8 (CH_2), 31.0, 28.7, 27.0, 19.2, 10.2; MS (CI, NH_3): *m/z* (%): 595 ($(M+H)^+$, 24), 339 (100).

The title compound could also be prepared by treatment of the TBS ether (±)-**22** with TBAF.

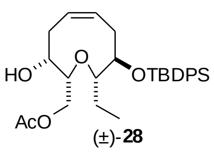
(1S*, 3S*, 4R*, 6S*, 7S*, 9R*)-9-tButyldimethylsilanyloxy-4-tbutyldiphenylsilanyloxy-3-ethyl-7-phenylselanyl-2-oxabicyclo(4.3.1)decane (±)-22



(±)-**22**

To a solution of the acetal **(±)-19** (39 mg, 53 µmol) in dry DCM (0.5 mL) cooled to -78 °C was added dropwise triethylsilane (17 µL, 0.11 mmol) followed by $TiCl_4$ (0.06 mL of a 1.0 M solution in DCM, 60 µmol). The resultant red solution was stirred at -78 °C for 20 min and then the reaction was quenched with saturated aqueous NH_4Cl (1 mL). The mixture was allowed to warm to room temperature, poured into water (5 mL) and extracted with DCM (3 × 20 mL). The extracts were combined, dried (Na_2SO_4) and evaporated. Purification of the residue by flash chromatography (hexane:ether, 19:1) gave the bicyclic ether **(±)-22** (29 mg, 79%) as an oil; R_f 0.4 (hexane:ether, 19:1); IR (CCl_4): ν=2970; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.67-7.24 (m, 15H; Ar), 3.80 (m, 2H), 3.60 (m, 1H), 3.35-3.47 (m, 2H), 2.95 (apparent dt, 1H), 2.24-2.15 (m, 2H), 1.88 (dt, *J*(H, H)=12.5, 4 Hz, 1H), 1.65 (m, 2H), 1.26-1.08 (m, 3H), 1.00 (s, 9H; $C(CH_3)_3$), 0.85 (s, 9H; $C(CH_3)_3$), 0.73 (t, *J*(H, H)=7 Hz, 3H; CH_2CH_3), 0.03 (s, 6H; 2 × $SiCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=135.9, 135.8, 134.7, 134.1, 133.9, 129.7, 129.6, 129.2, 128.9, 127.6, 127.5, 127.4, 82.7 (OCH), 78.3 (OCH), 76.9 (OCH), 74.3 (OCH), 46.4 (*C*HSePh), 33.3 (2 × CH_2), 31.9 (CH_2), 31.4 (CH), 31.2, 28.9, 27.0, 25.9, 19.2, 18.3, 10.7, -4.46, -4.53; MS (CI, NH_3): *m/z* (%): 709 ($(M+H)^+$, 100); Found 709.3010, $C_{39}H_{57}O_3{}^{80}SeSi_2$ requires 709.3012.

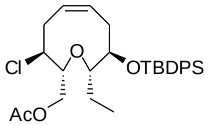
((Z, 2**R*****, 3*****R*****, 8*****R*****, 9*****S*****)-8-(*****t*****Butyldiphenylsilyloxy)-9-ethyl-3-hydroxy-2,3,4,7,8,9-hexahydrooxonin-2-yl)methyl acetate, (±)-28***



(±)-**28**

Acetic anhydride (5.0 µL, 53 µmol) was added to a solution of the diol (±)-**27** (22 mg, 48.8 µmol) and DMAP (7.7 mg, 63 µmol) in DCM (0.5 mL). The solution was stirred at ambient temperature for 4 h and then the solvent was removed *in vacuo*. Purification of the residue by flask chromatography (ether:hexane, 2:1) gave the title compound (±)-**28** as a clear and colourless oil (18.9 mg, 38 µmol, 72%);); $[a]_{\mathrm{D}}^{26}$ -44.3 (*c* 0.1, $CHCl_3$), R_f 0.3 (ether:hexane, 2:1); IR (film): ν=3422, 1740; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.70-7.63 (m, 4H; Ar), 7.46-7.34 (m, 6H; Ar), 5.70 (ddd, *J*(H, H)=12.0, 10.0, 6.0 Hz, 1H; 5-H), 5.54 (td, *J*(H, H)=10.0, 6.0 Hz, 1H; 6-H), 4.23 (dd, *J*(H, H)=11.0, 7.0 Hz, 1H; C*H*HO), 4.17 (dd, *J*(H, H)=11.0, 5.0 Hz, 1H; CH*H*O), 3.89 (m, 1H; 3-H), 3.86 (ddd, *J* (H, H)=7.0, 5.0, 2.0 Hz, 1H; 2-H), 3.78 (ddd, *J* (H, H)=10.0, 5.0, 2.0 Hz; 8-H), 3.38 (q, *J* (H, H)=2 Hz, 1H; 9-H), 2.62 (dt, *J* (H, H)=12.0, 10.0 Hz, 1H; 7-H), 2.58 (td, *J* (H, H)=13.0, 9.0 Hz, 1H; 4-H), 2.32 (dt, *J*(H, H)=13.0, 6.0 Hz, 1H; 4-H’), 2.06 (s, 3H; CH_3COO), 2.15-2.05 (m, 1H; 7-H’) 1.50-1.30 (m, 2H; CH_2CH_3), 1.25 (s, 1H; OH), 1.06 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=171.0, 135.9, 135.8, 134.0, 133.5, 130.4, 129.8, 129.7, 127.7, 127.6, 125.7, 86.0, 79.1, 74.5, 69.8, 63.5, 32.3, 27.0, 25.6, 20.9, 19.2, 8.6; MS (CI, NH_3): *m/z* (%): 514 ($(M+NH_4)^+$, 24), 497 ($(M+H)^+$, 44),); Found 514.2989, $C_{29}H_{44}NO_5Si$ requires 514.2989.

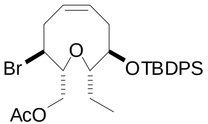
((Z, 2**R**, 3*****S**, 8*****R**, 9*****S**)-3-Chloro-8-(*****t*****butyldiphenylsilyloxy)-9-ethyl-2,3,4,7,8,9-hexahydrooxonin-2-yl)methyl acetate, (±)-*****29**



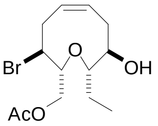
(±)-**29**

To a stirred suspension of the alcohol (±)-**28** (27 mg, 54 µmol) and 4 Å molecular sieves in DCM (1 mL) at 0 °C was added propylene oxide (50 µL) followed by $Me_2C{=}CCl(NMe_2)$ (12 µL, *ca.* 85 µmol). The reaction mixture was at 0 °C for 1 h and then at room temperature for 18 h. The solvent was removed *in vacuo* and purification by flash chromatography (ether:hexane, 1:4) gave the title compound (±)-**29** as a clear and colourless oil (20 mg, 38 μmol, 71%); R_f 0.5 (ether:hexane, 1:2); IR ($CHCl_3$): ν=1740; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.70-7.61 (m, 4H; Ar), 7.46-7.35 (m, 6H; Ar), 6.91-5.78 (m, 2H; 5-H, 6-H), 4.38 (dd, *J*(H, H)=11.0, 1.9 Hz, 1H; C*H*HOAc), 4.19 (dd, *J*(H, H)=11.0, 2.6 Hz, 1H; CH*H*OAc), 4.15 (dt, *J* (H, H)=12.5, 3.4 Hz, 1H; 3-H), 3.92-3.88 (m, 1H), 3.77 (dt, *J* (H, H)=8.4, 2.9 Hz, 1H), 3.39 (q, *J* (H, H)=4.0 Hz, 1H), 3.18 (ddd, *J* (H, H)=13.2, 9.6, 3.6 Hz, 1H; allylic CH), 2.50 (ddd, *J* (H, H)=12.0, 9.6, 2.4 Hz, 1H; allylic CH), 2.30 (ddd, *J* (H, H)=13.2, 4.6, 2.4, 1H; allylic CH), 2.09-2.01 (m, 1H; allylic CH), 2.05 (s, 3H; CH_3COO), 1.50-1.30 (m, 2H; C*H*$_2$CH$_3$), 1.06 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.9, 135.9, 135.8, 134.0, 133.5, 130.5, 129.9, 129.8, 127.8, 127.6, 125.3, 86.2, 81.1, 73.7, 63.5, 58.6, 31.3, 29.9, 27.1, 24.7, 20.9, 19.3, 7.9; MS (CI, NH_3): *m/z* (%): 515 ($(M+H)^+$, 30), 437 (44); Found 515.2384, $C_{32}H_{40}{}^{35}ClO_4Si$ requires 515.2384.

((Z, 2R, 3S*, 8R*, 9S*)-3-Bromo-8-(tbutyldiphenylsilyloxy)-9-ethyl-2,3,4,7,8,9-hexahydrooxonin-2-yl)methyl acetate, (±)-30* **and** *((2R*, 3S*, 8R*, 9S*, Z)-3-bromo-9-ethyl-8-hydroxy-2,3,4,7,8,9-hexahydrooxonin-2-yl)methyl acetate*

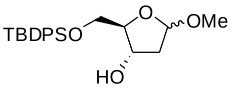


(±)-**30**



Following essentially the same procedure as that described for (±)-**29** above, the alcohol (±)-**28** was converted to the bromide (±)-**30** (45%) which was readily deprotected with TBAF to give the silghtly impure alcohol ((2*R**, 3*S**, 8*R**, 9*S**, *Z*)-3-bromo-9-ethyl-8-hydroxy-2,3,4,7,8,9-hexahydrooxonin-2-yl)methyl acetate, obtained as a colourless oil; R_f 0.15 (ether:hexane, 1:1); IR ($CHCl_3$): ν=3452, 1742; ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.95-5.85 (m, 2H; 5-H, 6-H), 4.42 (dd, *J*(H, H)=12.0, 2.0 Hz, 1H; C*H*HOAc), 4.28 (dd, *J*(H, H)=12.0, 4.0 Hz, 1H; CH*H*OAc), 4.32-4.26 (m, 1H; 3-H), 3.91 (dt, *J*(H, H)=8.0, 4.0 Hz, 1H; 9-H), 3.68 (ddd, *J* (H, H)=10.0, 4.0, 2.0 Hz, 1H; 2-H), 3.28 (ddd, *J* (H, H)=8.0, 5.0, 3.0 Hz, 1H; 8-H), 2.60-2.15 (m, 4H; 4-H, 4-H’, 7-H, 7-H’), 2.11 (s, 3H; CH_3COO), 1.80-1.65 (m, 2H; C*H*$_2$CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.8, 128.7, 127.5, 86.7, 83.7, 71.5, 64.7, 51.2, 32.2, 32.1, 24.6, 20.9, 7.4; MS (ES): *m/z* (%): 340 ($(M+NH_4)^+$, 30), 338 ($(M+NH_4)^+$, 30), 323 ($(M+H)^+$, 20), 321 ($(M+H)^+$, 20); Found 321.0710, $C_{13}H_{22}{}^{79}BrO_4$ requires 321.0710.

(2*R*, 3*S*, 5*R/S*)-2-tButyldiphenylsilanyloxymethyl-3-hydroxy-5-methoxy-tetrahydrofuran, 46



46

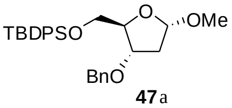
To a stirred solution of 2-deoxy-D-ribose **45** (3.0 g, 22.4 mmol) in dry MeOH (115 mL) was added a solution of HCl (8.08 mL of a 1.0 M solution in ether, 8.08 mmol). The resulting solution was stirred for 1 h. Pyridine (57 mL) was added and the solvents were removed *in vacuo*. The residue was dissolved in fresh pyridine (50 mL) and evaporated. The residue was dried under high vacuum for 1 h and then pyridine (23 mL) and *t*butylchlorodiphenylsilane (5.86 mL, 6.19 g, 22.5 mmol) were added and the mixture was stirred for 20 h at room temperature. The solvent was removed *in vacuo* and the residue was partitioned between water (100 mL) and EtOAc (100 mL). The aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic extracts were washed with a saturated aqueous solution of $CuSO_4$ (2 × 100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the mono-protected furanosides **46**. Purification by flash chromatography (hexane:ether, 7:3) provided the title compounds as clear and colourless oils; (Found C, 68.2; H, 7.6%; $C_{22}H_{30}O_4Si$ requires C, 68.4; H, 7.81); IR (film): ν=3460; MS (CI, NH_3): *m/z*(%): 404 ($(M+NH_4)^+$, 25), 372 (100); Found 404.2257 $C_{22}H_{34}NO_4Si$ requires 404.2257.

α-anomer **46**a less polar (3.65 g, 9.46 mmol, 42%); R_f 0.39 (petroleum ether 40-60:ether, 1:1); $[a]_{\mathrm{D}}^{24}$ +67.3 (*c* 0.98 in MeOH); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.71-7.62 (m, 4H; Ar), 7.47-7.34 (m, 6H; Ar), 5.11 (bd, *J*(H, H)=4.5 Hz, 1H; 1-H), 4.30 (bdd, *J*(H, H)=10.1, 5.6 Hz, 1H; 2-H), 4.16 (m, 1H; 4-H), 3.76 (dd, *J*(H, H)=10.9, 3.6 Hz, 1H; C*H*HOSi), 3.61 (dd, *J*(H, H)=10.9, 4.9 Hz, 1H; CH*H*OSi), 3.38 (s, 3H; OCH_3), 2.81 (bd, *J*(H, H)=10.7 Hz, 1H; OH), 2.26-2.13 (m, 1H; 2-H), 2.01 (bd, *J*(H, H)=13.5 Hz, 1H; 2-H'), 1.05 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=135.60, 135.55, 133.2, 133.1 129.8, 129.7, 127.74, 127.71, 105.6 (C-5), 87.7, 73.3, 64.4 (CH_2), 54.8 (OCH_3), 41.1, 26.8 ($C(CH_3)_3$), 19.2 ($C(CH_3)_3$).

β-anomer **46**b more polar (3.07 g, 7.94 mmol, 36%); $[a]_{\mathrm{D}}^{29}$ -29.3 (*c* 0.64 in MeOH); R_f 0.26 (petroleum ether 40-60:ether, 1:1); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.72-7.65 (m, 4H; Ar), 7.46-7.34 (m, 6H; Ar), 5.05 (dd, *J*(H, H)=5.1, 1.9 Hz, 1H; 1-H), 4.57-

4.47 (m, 1H; 3-H), 3.94 (dt, *J*(H, H)=7.5. 4.8 Hz, 1H; 4-H), 3.82 (dd, *J*(H, H)=10.1, 4.8 Hz, 1H; C*H*HOSi), 3.66 (dd, *J*(H, H)=10.1, 7.5 Hz, 1H; CH*H*OSi), 3.27 (s, 3H; OCH_3), 2.21 (ddd, *J*(H, H)=13.3, 6.9, 1.9 Hz, 1H; 2-H), 2.12-2.00 (m, 1H; 2-H'), 1.80 (brd, *J*(H, H)=4.1 Hz, 1H; OH), 1.08 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=135.5, 133.2, 129.8, 127.8, 105.0 (C-5), 85.7, 73.3, 65.4 (CH_2), 55.0 (OCH_3), 41.0 (CH_2), 26.8 ($C(CH_3)_3$), 19.2 ($C(CH_3)_3$).

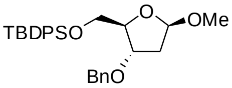
*(2***R***, 3***S***, 5***S***)-2-***t***Butyldiphenylsilanyloxymethyl-3-benzyloxy-5-methoxy-tetrahydrofuran, 47*a



47a

A 60% dispersion of sodium hydride in mineral oil (294 mg, 176 mg of NaH, 73.5 mmol) was washed with hexane (2 × 3 mL) and dried under high vacuum. THF (10 mL) was added and the resultant slurry was cooled to 0 °C. A solution of the furanoside **46**a (2.0 g, 5.2 mmol) in THF (10 mL, 2 × 10 mL rinse) was added *via* cannula and the reaction mixture was stirred at room temperature for 1 h. Benzyl bromide (0.8 mL, 1.16 g, 6.76 mmol) and TBAI (3.83 mg, 1.04 mmol) were added and the reaction mixture was stirred for 18 h. The reaction was then quenched by the addition of water (50 mL) and ether (50 mL). The aqueous layer was extracted with ether (2 × 50 mL) and the combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product. Purification by flash chromatography (petroleum ether 40-60:ether, 6:1); furnished the furanoside **47**a as a clear and colourless oil (2.3 g, 4.85 mmol, 93%); (Found C, 73.0; H, 7.9%; $C_{29}H_{36}O_4Si$ requires C, 73.07; H, 7.61); $[a]_D^{20}$ +56.8 (*c* 0.57, $CHCl_3$), R_f 0.66 (petroleum ether 40-60:ether, 3:1); IR (film): ν=3080; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.68-7.60 (m, 4H; Ar), 7.42-7.28 (m, 11H; Ar), 5.08 (dd, *J*(H, H)=5.3, 1.4 Hz, 1H; 5-H), 4.56 (d, *J*(H, H)=12.5 Hz, 1H; OC*H*HPh), 4.52 (d, *J*(H, H)=12.5 Hz, 1H; OCH*H*Ph), 4.22 (q, *J*(H, H)=4.1 Hz, 1H; 2-H), 4.10 (ddd, *J*(H, H)=7.4, 3.4, 2.4 Hz, 1H; 3-H), 3.72 (dd, *J*(H, H)=11.4, 4.0 Hz, 1H; C*H*HOSi), 3.67 (dd, *J*(H, H)=11.4, 4.4 Hz, 1H; CH*H*OSi), 3.41 (s, 3H; OCH_3), 2.21 (ddd, *J*(H, H)=14.0, 7.4, 5.3 Hz, 1H; 5-H), 2.07 (ddd, *J*(H, H)=14.0, 2.4, 1.4 Hz, 1H; 5-H'), 1.04 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=138.2, 135.61, 135.56, 133.3, 129.7, 128.3, 127.7, 127.5, 105.4, 84.2, 78.6, 71.4 (CH_2), 64.3, 55.1 (OCH_3), 38.9 (CH_2), 26.8 ($C(CH_3)_3$), 19.2 ($C(CH_3)_3$); MS (CI, NH_3): *m/z* (%): (($(M+NH_4)^+$, 4), 91 (100); Found 494.2727, $C_{29}H_{40}NO_4Si$ requires 494.2727.

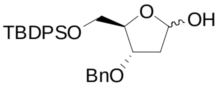
(2R, 3S, 5R)-2-tButyldiphenylsilanyloxymethyl-3-benzyloxy-5-methoxy-tetrahydrofuran, 47b



47b

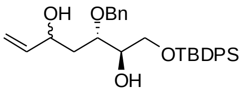
Following essentially the same procedure as described for **47**a above, **46**b was converted to the title compound **47**b (89%) as a clear and colourless oil; $[a]_D^{16}$ -39.7 (*c* 0.33, $CHCl_3$); R_f 0.64 (petroleum ether 40-60:ether, 3:1); ^1H NMR (250 MHz, $CDCl_3$): δ=7.72-7.64 (m, 4H; Ar), 7.44-7.27 (m, 11H; Ar), 5.10 (t, *J*(H, H)=4.1 Hz, 1H; 5-H), 4.55 (d, *J*(H, H)=12.0 Hz, 1H; OC*H*HPh), 4.48 (d, *J*(H, H)=12.0 Hz, 1H; OCH*H*Ph), 4.28-4.16 (m, 2H; 2-H, 3-H), 3.74 (dd, *J*(H, H)=10.9, 5.4 Hz, 1H; C*H*HOSi), 3.65 (dd, *J*(H, H)=10.9, 7.1 Hz, 1H; CH*H*OSi), 3.26 (s, 3H; OCH_3), 2.16 (dd, *J*(H, H)=5.8, 3.8 Hz, 2H; 4-H, 4-H'), 1.07 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=138.1, 135.8, 135.6, 133.5, 133.4, 129.7, 129.7, 128.4, 127.7, 127.6, 127.6, 105.5 (2-C), 84.5, 79.9, 71.5, 65.0, 55.0, 39.2, 26.9, 19.2; MS (ES): *m/z*(%): 494 (($(M+NH_4)^+$, 100); Found 494.2731, $C_{29}H_{40}NO_4Si$ requires 494.2727.

(2R/S, 3S, 5R)-4-Benzyloxy-5-tbutyldiphenylsilanyloxymethyl-2-hydroxy-tetrahydrofuran



To a stirred solution of a mixture of the furanosides **47** (12.1 g, 25.3 mmol) in ether (300 mL) at room temperature, was added a solution of BCl_3•SMe_2 (25 mL of a 2.0 M solution in DCM, 50 mmol). The reaction mixture was stirred for 10 mins and was then poured into a saturated solution of aqueous Na_2CO_3 (200 mL) followed immediately by the addition of THF (150 mL). The resultant mixture was then vigorously stirred for 1.5 h. The aqueous layer was extracted with ether (3 × 100 mL). The combined organic layers were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product. *Note*: it is essential to purify the crude product immediately to give a good yield. Purification by flash chromatography (petroleum ether 40-60:ether, 6:4→9:11) furnished the lactols as a clear and colourless oil (9.62 g, 86%); (Found C, 72.7; H, 7.5%; $C_{28}H_{34}O_4Si$ requires C, 72.7; H, 7.4); $[a]^{24}_{\mathrm{D}}$ +20.6 (*c* 1.85 in MeOH); R_f 0.29 and 0.21 (petroleum ether 40-60:ether, 1:1); IR (CCl_4): ν=3590, 3520; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.61-7.65 (m, 4H; Ar), 7.31-7.43 (m, 11H; Ar), 5.54-5.58 (m, 1H), 5.43 (dd, *J*(H, H)=11.0, 4.2 Hz, 1H; 1-H), 4.61 (d, *J*(H, H)=11.9 Hz, 1H; OC*H*HPh), 4.58 (d, *J*(H, H)=11.9 Hz, 1H; OCH*H*Ph), 4.43-4.48 (m, 2H), 4.29-4.35 (m, 1H), 4.16-4.22 (m, 1H), 3.78-3.82 (m, 1H), 3.59-3.72 (m, 2H), 3.45-3.49 (m, 1H), 3.28 (d, *J*(H, H)=7.3 Hz, 1H), 2.18-2.25 (m, 2H), 2.04-2.13 (m, 2H), 1.07 (s, 9H; $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=137.5, 135.7, 135.6, 135.5, 133.0, 130.0, 129.9, 129.8, 128.54, 128.45, 127.9, 127.79, 127.76, 127.7, 99.5, 99.2, 84.6, 84.0, 80.2, 79.1, 71.5, 71.3, 65.1, 64.1, 41.5, 39.0, 26.9, 26.8, 19.2; MS (CI, NH_3): *m/z*(%): 463 ($(M+H)^+$, 5), 196 (100); Found $(M+NH_4-H_2O)^+$ 462.2479, $C_{28}H_{36}NO_3Si$ requires 462.2464.

(2R, 3R, 5R/S)-3-Benzyloxy-1-tbutyldiphenylsilanyloxy-2,5-dihydroxy-hept-6-ene, 48



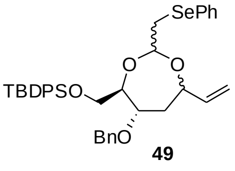
48

The lactols were azeotroped with toluene (3 × 20 mL) and then dried under high vacuum. To a stirred solution of the lactols, prepared above, (9.62 g, 21.7 mmol) in THF (50 mL) at 0 °C was slowly added a solution of vinylmagnesium bromide (45 mL of a 1.0 M solution in THF, 45.0 mmol). The reaction mixture was warmed to room temperature and stirred for 3 h, then quenched by the addition of a saturated solution of aqueous NH_4Cl (10 mL) and ether (10 mL). The aqueous phase was extracted with ether (3 × 50 mL). The combined organic extracts were washed with brine (150 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product. Purification by flash chromatography (petroleum ether 40-60:ether, 1:1→1:3) furnished the diols **48** as clear, colourless oils (8.09 g, 76%). The diols could be separated by radial chromatography (hexane:ether, 2:1). The most mobile band afforded the minor diastereomer as a colourless oil; (Found C, 73.3; H, 7.8%; $C_{30}H_{38}O_4Si$ requires C, 73.4; H, 7.8); $[a]^{24}_{\mathrm{D}}$ -10.9 (*c* 1.85 in MeOH); IR (CCl_4):

ν=3660-3400; R_f 0.15 (petroleum ether 40-60:ether, 1:1); ^{1}H NMR (250 MHz, CDCl$_3$): δ=7.67-7.63 (m, 4H; Ar), 7.47-7.35 (m, 6H; Ar), 7.30-7.18 (m, 5H; Ar), 5.86 (ddd, *J*(H, H)=17.3, 10.5, 5.3 Hz, 1H; C*H*=CH$_2$), 5.25 (ddd, *J*(H, H)=17.3, 1.5, 1.5 Hz, 1H; *trans* C*H*H=CH), 5.09 (ddd, *J*(H, H)=10.5, 1.5, 1.5 Hz, 1H; *cis* CH*H*=CH), 4.56 (d, *J*(H, H)=11.3 Hz, 1H; OC*H*HPh), 4.50 (d, *J*(H, H)=11.3 Hz, 1H; OCH*H*Ph), 4.37-4.34 (m, 1H), 3.90-3.71 (m, 4H), 1.86 (ddd, *J*(H, H)=14.8, 7.5, 3.0 Hz, 1H), 1.69 (ddd, *J*(H, H)=9.0, 4.8, 3.5 Hz, 1H), 1.07 (s, 9H; C(C*H*$_3$)$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ=141.0, 137.8, 135.6, 133.0, 129.9, 128.5, 128.1, 127.91, 127.85, 114.0, 77.0, 72.8, 72.4, 69.8, 64.6, 36.9, 26.9, 19.2; MS (CI, NH$_3$): *m/z*(%): 508 ((M+NH$_4$)$^+$, 1), 91 (100).

The least mobile band afforded the major diastereomer; (Found C, 73.5; H, 7.8%; $C_{30}H_{38}O_4Si$ requires C, 73.4; H, 7.8); $[a]_{\mathrm{D}}^{22}$ -28.0 (*c* 2.65 in MeOH); IR (CCl$_4$): ν=3660-3400; R_f 0.15 (petroleum ether 40-60:ether, 1:1); ^{1}H NMR (250 MHz, CDCl$_3$): δ=7.66-7.63 (m, 4H; Ar), 7.47-7.33 (m, 6H; Ar), 7.34-7.19 (m, 5H; Ar), 5.81 (ddd, *J*(H, H)=17.3, 10.5, 6.0 Hz, 1H; C*H*=CH$_2$), 5.21 (ddd, *J*(H, H)=17.3, 1.5, 1.5 Hz, 1H; *trans* C*H*H=CH), 5.08 (ddd, *J*(H, H)=10.5, 1.5, 1.5 Hz, 1H; *cis* CH*H*=CH), 4.56 (d, *J*(H, H)=11.3 Hz. 1H; OC*H*HPh), 4.50 (d, *J*(H, H)=11.3 Hz, 1H; OCH*H*Ph), 4.36-4.29 (m, 1H), 3.93-3.72 (m, 4H), 1.88-1.72 (m, 2H; CH$_2$), 1.06 (s, 9H; C(C*H*$_3$)$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ=140.7, 137.7, 135.6, 132.97, 132.96, 129.93, 129.92, 128.5, 128.1, 127.91, 127.85, 114.5, 78.1, 72.8, 71.9, 70.8, 64.4, 37.0, 26.9, 19.2; MS (CI, NH$_3$): *m/z*(%): 508 ((M+NH$_4$)$^+$, <1), 91 (100).

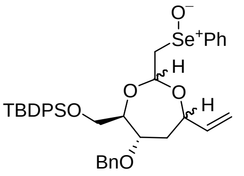
(2R/S, 4R, 5S, 7R/S)-tButyldiphenylsilanyloxymethyl-2-phenylselanylmethyl-7-vinyl-1,3-dioxepane 49



49

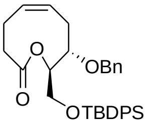
To a stirred solution of the diols **48** (8.09 g, 16.5 mmol) in toluene (300 mL), was added PPTS (0.21 g, 0.8 mmol) and 2-phenylselenoacetaldehyde diethylacetal (5.41 g, 19.8 mmol). The mixture was heated at reflux for 1.5 h under Dean-Stark conditions and then allowed to cool to room temperature. The reaction was quenched by the addition of water (75 mL). The aqueous layer was extracted with ether (2 × 100 mL) and the combined organic extracts were washed with brine (75 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product. Purification by flash chromatography (petroleum ether 40-60:ether, 25:1) furnished a diastereomeric mixture of the selenoacetals **49** as a pale yellow oil (8.73 g, 79%); (Found C, 67.8; H, 6.5 %; $C_{38}H_{44}O_4SiSe$ requires C, 67.9; H, 6.6); R_f 0.18 and 0.13 (petroleum ether 40-60:ether, 25:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.23-7.73 (m, 20H; Ar), 5.91 (ddd, J(H, H)=17.1, 10.4, 5.0 Hz, 1H; CH=CHH), 5.33-5.37 (m, 1H; CH=CHH), 5.18-5.21 (m, 2H; CH=CHH, CH(CH_2SePh)), 4.55-4.64 (m, 3H), 4.09-4.16 (m, 2H), 3.80-3.84 (m, 1H), 3.67-3.72 (m, 2H), 3.26 (d, J(H, H)=6.0 Hz, 2H; CH_2), 2.13-2.18 (m, 1H), 1.24 (s, 9H; C(CH_3)$_3$); MS (CI, NH_3): m/z(%): 690 (($M+NH_4)^+$, 1), 190 (100); Found M^+ 672.2170, $C_{38}H_{44}O_4SiSe$ requires 672.2174.

*(2***R***/***S***, 4***R***, 5***S***, 7***R***/***S***)-2-Phenylselanoxymethyl-4-tbutyldiphenylsilanyloxymethyl-5-benzyloxy-7-vinyl-1,3-dioxepane*



The selenoacetals **49** (8.73 g, 13.0 mmol) were dissolved in DCM (220 mL) and MeOH (510 mL). Water (*ca*. 25 mL) was added until the material started to come out of solution. NaHCO$_3$ (1.25 g, 14.3 mmol) and NaIO$_4$ (9.17 g, 42.9 mmol) were added and the cloudy mixture rapidly became a creamy white suspension. The reaction mixture was stirred for 3 h at room temperature, whereupon water (100 mL) was added. The aqueous layer was extracted with DCM (3 × 100 mL) and the combined organic extracts were washed with brine (100 mL) and dried (MgSO$_4$). The solvent was removed *in vacuo* to furnish what was presumed to be the selenoxides as a white foam (8.36 g, 93%); TLC analysis (petroleum ether 40-60:ether, 10:1) showed only base-line material.

*(***Z***, 8***S***, 9***R***)-8-Benzyloxy-9-tbutyldiphenylsilanyloxymethyl-4,7,8,9-tetrahydro-3H-oxonin-2-one(-)-43*

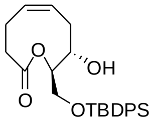


(-)-**43**

To a stirred solution of the selenoxides (8.36 g, 12.2 mmol) in toluene (1.2 L) was added DBU (12.1 mL, 80.9 mmol). The solution was heated at reflux under Dean-Stark conditions for 24 h and then allowed to cool to room temperature. The solvent was removed *in vacuo* to give the crude product. Purification by flash chromatography (petroleum ether 40-60:ether, 6:1) furnished the lactone (-)-**43** as a clear and colourless oil (4.53 g, 73%); $[a]_{\mathrm{D}}^{16}$ -5.8 (*c* 1.8 in MeOH); R_f 0.27 (petroleum ether 40-60:ether, 6:1); IR (film): ν=1745; ^{1}H NMR (400 MHz, CDCl$_3$) 7.76-7.80 (m, 4H; Ar), 7.36-7.52 (m, 11H; Ar), 5.72-5.78 (m, 2H; 5-H, 6-H), 4.90 (br s, 1H; 9-H), 4.73 (d, *J*(H, H)=11.7 Hz, 1H; OC*H*HPh), 4.51 (d, *J*(H, H)=11.7 Hz, 1H; OCH*H*Ph), 3.97-4.08 (m, 3H; C*H*$_2$OSi, 8-H), 2.31-2.66 (m, 6H; ring C*H*$_2$), 1.18 (s, 9H; C(C*H*$_3$)$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ=174.0, 138.0, 135.8, 135.7, 135.6, 133.6, 133.3, 129.7, 129.2, 128.4, 128.3, 127.7, 127.6, 77.7, 71.4, 63.8, 34.0, 28.8, 26.9, 23.9, 19.4;

MS (CI, NH_3): *m/z*(%): 532 ($(M+NH_4)^+$, 2), 515 ($(M+H)^+$, 10), 91 (100); Found 514.2540, $C_{32}H_{38}O_4Si$ requires 514.2539.

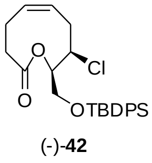
*(Z, 8S, 9R)-9-tButyldiphenylsilyloxymethyl-8-hydroxy-4,7,8,9-tetrahydro-3H-oxonin-2-one (-)-***50**



(-)-50

To a stirred solution of the lactone (-)-**43** (500 mg, 0.97 mmol) in DCM (25 mL) was added $BCl_3 \cdot SMe_2$ (2.43 mL of a 2.0 M solution in DCM, 4.86 mmol) and the resulting solution was stirred for 3 days. The reaction mixture was quenched by the addition of a saturated solution of sodium bicarbonate (25 mL). The aqueous phase was extracted with DCM (2 × 25 mL). The extracts were combined, washed with brine (25 mL), dried ($MgSO_4$) and evaporated. Purification of the residue by flash chromatography (hexane:ether, 3:2) provided the title compound (-)-**50** (267 mg, 0.63 mmol, 65%) as a clear and colourless oil; R_f 0.29 (hexane:ether, 1:1); $[a]_D^{19}$ -60.8 (*c* 0.5 in $CHCl_3$); IR (film): ν=3480, 1740; ^1H NMR (250 MHz, $CDCl_3$): δ=7.70-7.65 (m, 4H; ArH), 7.48-7.36 (m, 6H; ArH), 5.78-5.57 (m, 2H; 5-H, 6-H), 4.88-4.80 (m, 1H; 9-H), 4.18-4.09 (m, 1H; 8-H), 3.94 (dd, *J*(H, H)=10.5, 4.9 Hz, 1H; C*H*HOSi), 3.78 (dd, *J*(H, H)=10.5. 6.4 Hz, 1H; CH*H*OSi), 2.59 (d, *J*(H, H)=4.7 Hz, 1H; OH), 2.57-2.19 (m, 6H), 1.08 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=174.3 (1-C), 135.6, 132.8, 130.0, 129.1, 128.5, 127.8, 77.8, 75.3, 65.0, 33.9, 32.5, 26.8, 24.0, 19.2; MS (CI, NH_3): *m/z*(%): 442 ($(M+NH_4)^+$, 7), 425 ($(M+H)^+$, 27); Found 425.2148, $C_{25}H_{33}O_4Si$ requires 425.2148.

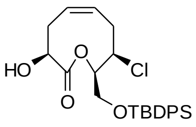
*(Z, 8R, 9R)-9-tButyldiphenylsilyloxymethyl-8-chloro-4,7,8,9-tetrahydro-3H-oxonin-2-one (-)-***42**



(-)-**42**

To a Schlenk tube pre-flushed with argon was added phosgene iminium chloride (2.56 g, 15.7 mmol), DCM (55 mL) and pyridine (1.86 mL, 23.5 mmol) and the resultant slurry was cooled to 0 °C. The alcohol (-)-**50** (2.01 g, 4.7 mmol) in DCM (10 mL, 2 × 1 mL rinse) was added *via* cannula and the mixture was allowed to warm to room temperature and was stirred for 1 h. The reaction mixture was quenched with a saturated solution of aqueous $NaHCO_3$ (60 mL) to provide a yellow biphasic mixture. The aqueous phase was extracted with DCM (3 × 60 mL). The extracts were combined and washed sequentially with a saturated solution of $CuSO_4$ (2 × 50 mL) and brine (50 mL) then dried ($MgSO_4$). Removal of the solvent *in vacuo* and purification of the residue by flash chromatography (hexane:ether, 3:1) gave the lactone (-)-**42** as a clear and colourless oil (2.06 g, 98%); (Found C, 67.8; H, 7.1%; $C_{25}H_{31}ClO_3Si$ requires C, 67.77; H, 7.05); R_f 0.6 (hexane:DCM, 1:1), $[a]_D^{17}$ -61.2 (*c* 0.94, $CHCl_3$); IR ($CHCl_3$): ν=1742; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.74-7.66 (m, 4H; Ar), 7.47-7.35 (m, 6H; Ar), 5.67 (m, 2H; 5-H, 6-H), 4.97-4.90 (m, 1H; 9-H), 4.52 (dd, *J*(H, H)=9.9, 4.3 Hz, 1H; 8-H), 4.01-3.89 (m, 2H; CH_2OSi), 3.07-2.94 (m, 1H), 2.88-2.72 (m, 1H), 2.61-2.46 (m. 2H), 2.32 (ddd, *J*(H, H)=13.3, 10.9, 4.9 Hz, 1H), 2.20-2.08 (m, 1H), 1.07 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=174.3 (1-C), 135.7, 135.5, 133.1, 130.5, 129.8, 129.7, 128.3, 127.7, 76.1, 62.8, 60.2, 34.1, 33.2, 26.7, 23.7, 19.2; MS (CI, NH_3): *m/z*(%): 460 ($(M+NH_4)^+$, 100), 443 ($(M+H)^+$, 70); Found 460.2084, $C_{25}H_{34}ClNO_3Si$ requires 460.2075.

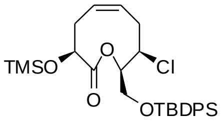
*(Z, 3*S*, 8*R*, 9*R*)-9-tButyldiphenylsilyloxymethyl-8-chloro-2-hydroxy-4,7,8,9-tetrahydro-3*H*-oxonin-2-one (-)-*51



(-)-**51**

A solution of the lactone (-)-**42** (950 mg, 2.14 mmol) in THF (20 mL, 2 × 2 mL rinse) was added *via* cannula to a stirring solution of KHMDS (6.6 mL of a 0.5 M solution in toluene, 3.3 mmol) in THF (20 mL) at -78 °C and the resulting solution was stirred for 1 h at -78 °C. (±)-*trans*-2-Phenylsulfonyl-3-phenyloxaziridine (1.18 g, 4.56 mmol) was added *via* cannula as a solution in THF (8 mL) and the resulting solution was stirred for 1 h before being quenched by the addition of CSA (1.18 g, 5.1 mmol) as a solution in THF (8 mL). The reaction mixture was allowed to warm to ambient temperature and ether and saturated aqueous $NaHCO_3$ were added. The aqueous phase was extracted twice with ether. The organic phases were combined, washed sequentially with 2 M aqueous hydrochloric acid and saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and evaporated. Purification of the residue twice by flash chromatography (DCM then hexane:ether, 3:1) provided the title compound (-)-**51** (662 mg, 1.44 mmol, 67%) as a clear and colourless oil; (Found C, 65.3; H, 6.9; Cl, 7.9%; $C_{25}H_{31}ClO_4Si$ requires C, 65.4; H, 6.8; Cl, 7.7); R_f 0.2 (hexane:ether, 3:1); $[a]_D^{18}$ -32.3 (*c* 0.48, $CHCl_3$); IR ($CHCl_3$): ν=3573, 2932, 1743; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.72-7.63 (m, 4H; Ar), 7.45-7.36 (m, 6H; Ar), 5.98-5.85 (m, 1H), 5.69-5.55 (m, 1H), 5.40-5.28 (br, 1H; 9-H), 4.50 (ddd, *J*(H, H)=9.0, 3.6, 3.0 Hz, 1H), 4.34 (ddd, *J*(H, H)=10.3, 8.1, 3.0 Hz, 1H; 8-H), 3.97 (dd, *J*(H, H)=10.7, 6.2 Hz, 1H; C*H*HOSi), 3.90 (dd, *J*(H, H)=10.7, 6.4 Hz, 1H; CH*H*OSi), 2.80-2.64 (m, 2H), 2.56-2.33 (m, 2H), 2.26 (d, *J*(H, H)=10.5 Hz, 1H; OH), 1.06 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (62.5, MHz, $CDCl_3$): δ=173.3 (1-C), 135.6, 135.6, 133.0, 132.3, 129.9, 129.8, 127.8, 124.6, 77.4, 70.8, 63.0, 60.5, 33.4, 32.0, 26.7, 19.2; MS (CI, NH_3): *m/z*(%): 476 ($(M+NH_4)^+$, 100); (ES) Found: 476.2022, $C_{25}H_{35}{}^{35}ClNO_4Si$ requires 476.2024.

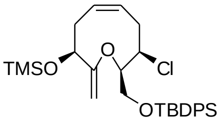
***(Z, 3S, 8*R*, 9*R*)-9-tButyldiphenylsilyloxymethyl-8-chloro-3-trimethylsilyloxyl-4,7,8,9-tetrahydro-3*H*-oxonin-2-one (-)-*52**



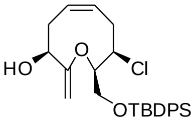
(-)-**52**

To a stirred solution of the alcohol (-)-**51** (484 mg, 1.05 mmol) in THF (25 mL) was added TEA (0.74 mL, 537 mg, 5.3 mmol) and TMSCl (0.33 mL, 288 mg, 2.68 mmol) and the resulting white suspension was stirred for 3 h before being quenched by the addition of pH 7 buffer (50 mL) and ether (50 mL). The aqueous phase was separated and extracted with ether. The organic phases were combined, washed with brine, dried and evaporated. The residue was purified by flash chromatography (hexane:ether, 9:1) to provide the title compound (-)-**52** as a clear and colourless oil (524 mg, 0.99 mmol, 94%); (Found C, 63.5; H, 7.3; Cl, 6.6%; $C_{28}H_{39}ClO_4Si_2$ requires C, 63.3; H, 7.4; Cl, 6.7); R_f 0.7 (hexane:ether, 95:5); $[a]_D^{20}$ -20.9 (*c* 1.14, $CHCl_3$); IR ($CDCl_3$): ν=1742; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.80-7.70 (m, 4H; Ar), 7.50-7.32 (m, 6H; Ar), 5.70 (dt, *J*(H, H)=10.8, 6.1 Hz, 1H), 5.57 (dt, *J*(H, H)=10.8, 6.1 Hz, 1H), 5.02 (brq, *J*(H, H)=4.8 Hz, 1H; 9-H), 4.49 (dt, *J*(H, H)=9.9, 4.7 Hz, 1H; 8-H), 4.30 (dd, *J*(H, H)=9.3, 5.8 Hz, 1H; 3-H), 4.06 (dd, *J*(H, H)=10.8, 6.3 Hz, 1H; *CH*HOSi), 4.00 (dd, *J*(H, H)=10.8, 6.4 Hz, 1H; CH*H*OSi), 3.25-3.04 (m, 1H), 2.94-2.73 (m, 1H), 2.52 (dt, *J*(H, H)=13.6, 5.3 Hz, 1H), 2.39 (dt, *J*(H, H)=12.4, 5.9 Hz, 1H), 1.09 (s, 9H; $(CH_3)_3C$), 0.16 (s, 9H; $(CH_3)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=173.0 (2-C), 135.7, 135.6, 133.2, 133.1, 129.9, 129.8, 127.7, 127.8, 127.0, 76.1, 73.2, 63.0, 59.2, 34.2, 27.0, 26.8, 19.2, -0.2; MS (CI, NH_3): *m/z*(%): 548 ($(M+NH_4)^+$, 100), 531 ($(M+H)^+$, 10); (ES) Found 531.2165, $C_{28}H_{40}ClO_4Si_2$ requires 531.2153.

(Z, 3**S*****, 8*****R*****, 9*****R*****)-9-tButyldiphenylsilyloxymethyl-8-chloro-2-methylene-3-trimethylsilyloxyl-2,3,4,7,8,9-hexahydro-oxonine (-)*-53** and ***(Z, 3*****S*****, 8*****R*****, 9*****R*****)-9-tbutyldiphenylsilyloxymethyl-8-chloro-3-hydroxy-2-methylene-2,3,4,7,8,9-hexahydro-oxonine* (-)-54**



(-)-**53**

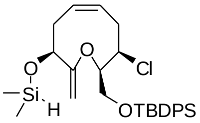


(-)-**54**

A solution of the lactone (-)-**52** (535 mg, 1.01 mmol) and DMAP (166 mg, 1.36 mmol) in THF (30 mL) was freeze-thaw degassed (3 cycles) and cooled to –50 °C. The Tebbe reagent (2.72 mL, of a 0.5 M solution in toluene, 1.36 mmol) was added and the resulting orange solution was allowed to warm to ambient temperature over 1.5 h before being re-cooled to –20 °C. Aqueous NaOH (1.6 mL of a 0.98 M solution, 1.57 mmol) was added dropwise and the reaction mixture was allowed to come to room temperature over 1 h. The quenched reaction mixture was poured into ether over anhydrous Na_2SO_4 and then filtered through Celite™. Purification by gravity chromatography on deactivated basic alumina (6% w/w water) (hexane:ether, 20:1) provided the impure enol ether (-)-**53** (457 mg) which was used in the next reaction without further purification. Further purification could be achieved on neutral alumina to provide analytically pure material; R_f 0.5 (hexane:ether, 10:1); $[a]_{\mathrm{D}}^{17}$ -35.0 (*c* 0.84, $CHCl_3$); IR ($CDCl_3$): ν=1640; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.74-7.62 (m, 4H; Ar), 7.49-7.33 (m, 6H; Ar), 5.57-5.42 (m, 2H; 5-H, 6-H), 4.45 (ddd, *J*(H, H)=10.7, 6.2, 3.2 Hz, 1H), 4.26 (d, *J*(H, H)=1.9 Hz, 1H; OC=C*H*H), 4.17 (dd, *J*(H, H)=10.1, 6.2 Hz, 1H; *CH*HOSi), 4.12 (d, *J*(H, H)=1.9 Hz, 1H; OC=*C*H*H*), 4.02-4.00 (m, 1H), 3.88-3.82 (m, 2H), 3.31-3.16 (m, 1H), 3.01-2.87 (m, 1H), 2.52 (ddd, *J*(H, H)=13.1, 6.2, 4.1 Hz, 1H), 2.19-2.08 (m, 1H), 1.06 (s, 9H; $(CH_3)_3C$), 0.11 (s, 9H; $(CH_3)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=166.1 (2-C), 135.6, 135.6, 133.3, 133.0, 129.8, 129.8, 129.4, 127.8, 127.1, 93.1 (OC=*C*H_2), 83.4, 74.4, 64.1, 61.2, 33.8, 33.2, 26.8, 19.2, 0.3; MS (CI, NH_3): *m/z*(%): 546 ($(M+NH_4)^+$, 100), 539 ($(M+H)^+$, 25); Found 546.2643, $C_{29}H_{45}ClNO_3Si_2$ requires 546.2627.

The impure enol ether (-)-**53** was dissolved in MeOH (16 mL) and anhydrous K_2CO_3 (10 mg, 72 μmol) was added. The reaction mixture was vigorously stirred for 1 h and the filtered through Celite™ rinsing with ether. The solvent was removed *in vacuo* and purification by gravity chromatography on deactivated basic alumina (6% w/w water) (hexane:ether, 3:1→1:1) provided the enol ether (-)-**54** as a clear and colourless oil (330 mg, 0.72 mmol, 71% from the lactone (-)-**52**) which occasionally crystallised; mp 48-50 °C (from ether); (Found C, 68.3; H, 7.1%; $C_{26}H_{33}ClO_3Si$ requires C, 68.3; H, 7.3); R_f 0.2 (hexane:ether, 3:1); $[a]_{\mathrm{D}}^{19}$ -39.2 (*c* 0.25, $CHCl_3$); IR ($CDCl_3$): ν=3593, 1643; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.73-7.65 (m, 4H; Ar), 7.47-7.37 (m, 6H; Ar), 5.58-5.50 (m, 2H; 5-H, 6-H), 4.46 (ddd, *J*(H, H)=10.7, 6.0, 3.0 Hz, 1H), 4.29 (d, *J*(H, H)=1.7 Hz, 1H; OC=C*H*H), 4.20 (d, *J*(H, H)=1.7 Hz, 1H; OC=CH*H*), 4.19-4.13 (m, 1H), 4.04 (dd, *J*(H, H)=12.4, 9.8 Hz, 1H), 3.96-3.91 (m, 2H), 3.20-3.12 (m, 1H), 2.85-2.77 (m, 1H), 2.56 (dt, *J*(H, H)=13.6, 4.7 Hz, 1H), 2.35 (dt, *J*(H, H)=13.2, 5.1 Hz, 1H), 1.95 (brd, *J*(H, H)=6.4 Hz, 1H; OH), 1.07 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=165.7 (2-C), 135.6, 135.5, 133.2, 132.9, 129.9, 129.8, 129.0, 127.8, 127.3, 93.0 (OC=*C*H_2), 83.7, 73.8, 64.2, 61.0, 33.7, 32.6, 26.8, 19.2; MS (CI, NH_3): *m/z*(%): 474 ($(M+NH_4)^+$, 100), 457 ($(M+H)^+$, 20); (ES) Found: 474.2240, $C_{26}H_{37}ClNO_3Si$ requires 474.2232.

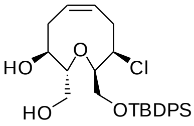
*(Z, 3*S*, 8*R*, 9*R*)-9-*t*Butyldiphenylsilyloxymethyl-8-chloro-3-dimethylsilyl-2-methylene-2,3,4,7,8,9-hexahydro-oxonine* **41**



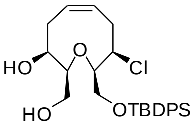
41

To a stirred solution of the alcohol (-)-**54** (105 mg, 0.23 mmol) in tetramethyldisilazane (1 mL) was added NH_4Cl (*ca.* 1 mg) and the resulting suspension was heated at 60 °C for 18 h. Dry hexane was added and the reaction mixture was filtered through Celite™. The solvent was removed *in vacuo* and the residue was dried under high vacuum for 12 h to provide the unstable title compound **41** as a clear and colourless oil (111 mg, 0.22 mmol, 94%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.72-7.65 (m, 4H; Ar), 7.47-7.36 (m, 6H; Ar), 5.54-5.45 (m, 2H; 5-H, 6-H), 4.62 (sp, *J*(H, H)=3.0 Hz, 1H; SiH), 4.45 (ddd, *J*(H, H)=11.1, 6.8, 3.4 Hz, 1H), 4.31 (d, *J*(H, H)=1.7 Hz, 1H; OC=C*H*H), 4.17 (dd, *J*(H, H)=9.8, 6.0 Hz. 1H), 4.16 (d, *J*(H, H)=1.7 Hz, 1H; OC=CH*H*), 4.04 (dd, *J*(H, H)=10.2, 7.3 Hz, 1H), 3.93 (dd, *J*(H, H)=10.2, 5.5 Hz, 1H), 3.90-3.86 (m, 1H), 3.27-3.18 (m, 1H), 2.98-2.91 (m, 1H), 2.56-2.50 (m, 1H), 2.23-2.17 (m, 1H), 1.05 (s, 9H; $(CH_3)_3C$), 0.21 (d, *J*(H, H)=3.0 Hz, 3H; $(CH_3)_2Si$), 0.19 (d, *J*(H, H)=3.0 Hz, 3H; $(CH_3)_2Si$).

*(Z, 2R, 3S, 8R, 9R)-9-tButyldimethylsilyloxymethyl-8-chloro-3-hydroxy-2-hydroxymethyl-2,3,4,7,8,9-hexahydro-oxonine (-)-***40** and *(Z, 2S, 3S, 8R, 9R)-9-tbutyldimethylsilyloxymethyl-8-chloro-3-hydroxy-2-hydroxymethyl-2,3,4,7,8,9-hexahydro-oxonine* **(-)-58**



(-)-**40**



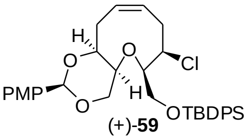
(-)-**58**

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 (3 mg, 4.2 μmol). The Schlenk tube was placed on an argon manifold and the silane **41** (50 mg, 97 μmol) was added as a solution in THF (2 mL, 1 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 Florisil™ to remove the coloured material. The solvent was removed *in vacuo*, the residue taken-up in THF (1 mL) and MeOH (1 mL) and 30% hydrogen peroxide (0.2 mL) and 15% KOH (0.1 mL) were added. The reaction mixture was stirred for 1 h and then quenched by the addition of saturated aqueous $Na_2S_2O_3$ and ether. The aqueous phase was extracted with ether (2 × 5 mL). The organic phases were combined, washed with brine (5 mL), dried ($MgSO_4$) and evaporated. Purification of the residue by preparative layer chromatography (DCM:MeOH, 95:5) provided the title compounds (-)-**40** and (-)-**58** and the enol ether (-)-**54** (9 mg, 19 μmol, 20%).

The more polar diastereomer (-)-**40** was isolated as a clear and colourless oil (23 mg, 48 μmol, 50%); R_f 0.3 (DCM:MeOH, 95:5); $[a]_{\mathrm{D}}^{20}$ -30.5 (*c* 0.52, $CHCl_3$); IR ($CDCl_3$): ν=3400 (OH); ^1H NMR (250 MHz, $CDCl_3$): δ=7.68-7.63 (m, 4H; Ar), 7.47-7.37 (m, 6H; Ar), 5.57 (dt, *J*(H, H)=10.5, 7.8 Hz, 1H), 5.48-4.42 (m, 1H), 4.10-4.07 (m, 1H), 3.89 (dd, *J*(H, H)=10.5, 7.4 Hz, 1H; *CH*HOSi), 3.79 (dd, *J*(H, H)=10.5, 5.0 Hz, 1H; C*HH*OSi), 3.68-3.60 (m, 3H), 3.60-3.57 (m, 2H), 3.05 (q, *J*(H, H)=11.6 Hz, 1H), 2.98-2.91 (m, 1H), 2.44-2.40 (m, 1H), 2.14-2.06 (m, 2H), 1.05 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=135.6, 133.1, 132.7, 130.5, 130.0, 127.9, 126.1, 81.9, 73.2, 70.2, 65.2, 64.4, 60.3, 33.5, 32.3, 26.8, 19.1; MS (CI, NH_3): *m/z*(%): 492 ($(M+NH_4)^+$, 40), 475 ($(M+H)^+$, 10), 274 (100); (ES) Found 492.2334. $C_{26}H_{39}ClNO_4Si$ requires 492.2337.

The less polar diastereomer (-)-**58** was isolated as a clear and colourless oil (8 mg, 17 μmol, 17%); R_f 0.4 (DCM:MeOH, 95:5); $[a]_{\mathrm{D}}^{19}$ -21.0 (*c* 0.24, $CHCl_3$); IR ($CDCl_3$): ν=3400 (OH); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.71-7.62 (m, 4H; Ar), 7.48-7.37 (m, 6H; Ar), 5.63 (dt, *J*(H, H)=11.1, 5.9 Hz, 1H), 5.53 (dt, *J*(H, H)=11.1, 5.5 Hz, 1H), 4.24 (ddd, *J*(H, H)=10.7, 6.4, 2.6 Hz, 1H), 4.03 (ddd, *J*(H, H)=10.2, 6.0, 2.7 Hz, 1H), 3.87-3.71 (m, 5H), 3.46-3.42 (m, 1H), 3.22-3.11 (m, 2H), 2.84 (q, *J*(H, H)=10.7 Hz, 1H), 2.53 (dt, *J*(H, H)=13.2, 5.5 Hz, 1H), 2.35 (dt, *J*(H, H)=12.8, 5.5 Hz, 1H), 1.06 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=135.6, 135.5, 133.1, 132.9, 129.9, 129.9, 128.9, 127.8, 127.7, 85.4, 85.0, 73.2, 65.5, 64.1, 61.0, 33.6, 32.6, 26.8, 19.1, 15.2; MS (CI, NH_3): *m/z*(%): 492 ($(M+NH_4)^+$, 60), 475 ($(M+H)^+$, 8), 274 (100); (ES) Found 492.2323, $C_{26}H_{39}ClNO_4Si$ requires 492.2337.

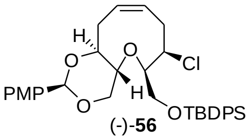
(Z, 2*R*, 4a*S*, 6*R*, 7*R*, 11a*S*)-6-tButyldimethylsilyloxymethyl-7-chloro-2-(4-methoxy-phenyl)-4a,6,7,8,11,11a-hexahydro-4H-1,3,5-trioxa-benzocyclononene (+)-59



(+)-**59**

PPTS (*ca.* 1 mg) was added to a stirred solution of the diol (-)-**58** (7.3 mg, 15.4 μmol) and *p*-anisaldehyde (3 mg) in benzene (1.5 mL) and the reaction mixture was heated at reflux for 18 h. The reaction mixture was allowed to cool, the solvent was removed *in vacuo* and purification of the residue by preparative layer chromatography (ether:hexane, 2:1) provided the title compound (+)-**59** as a clear and colourless oil (7 mg, 11.8 μmol, 77%); R_f 0.6 (ether:hexane, 2:1); $[a]_{\mathrm{D}}^{19}$ +54.7 (*c* 0.3, $CHCl_3$); IR ($CDCl_3$): ν=2931; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.65 (d, *J*(H, H)=7.6 Hz, 4H; Ar), 7.45-7.37 (m, 8H; Ar), 6.88 (d, *J*(H, H)=8.6 Hz, 2H; Ar), 5.61 (dt, *J*(H, H)=11.0, 5.0 Hz, 1H; 10-H), 5.54 (dt, *J*(H, H)=11.0, 5.0 Hz, 1H; 9-H), 5.43 (s, 1H; ArC*H*O_2), 4.43 (d, *J*(H, H)=12.6 Hz, 1H; 4-H), 4.14-4.09 (m, 2H; 7-H, 11a-H), 3.94 (dd, *J*(H, H)=12.7, 1.9 Hz, 1H; 4-H'), 3.91 (dd, *J*(H, H)=11.0, 5.7 Hz, 1H; C*H*HOSi), 3.84 (dd, *J*(H, H)=11.0, 5.7 Hz, 1H; CH*H*OSi), 3.79 (s, 3H; OCH_3), 3.33 (dt, *J*(H, H)=5.7, 3.1 Hz, 1H; 6-H), 3.28 (dt, *J*(H, H)=12.2, 11.0 Hz, 1H; 8β-H), 3.09 (dt, *J*(H, H)=11.3, 11.0 Hz, 1H; 11β-H), 2.89-2.87 (m, 1H; 4a-H), 2.47 (dt, *J*(H, H)=12.2, 5.0 Hz, 1H; 8α-H), 2.29 (dt, *J*(H, H)=11.3, 5.0 Hz, 1H; 11α-H), 1.06 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=160.0, 135.6, 135.5, 133.3, 133.1, 130.9, 129.9, 129.8, 128.9, 127.9, 127.8, 127.6, 113.6, 100.8 (2-C), 86.4, 78.6, 77.9, 72.2, 66.1, 60.6, 55.3, 33.8, 29.7, 26.9, 19.1; MS (CI, NH_3): *m/z*(%): 610 ($(M+NH_4)^+$, 96), 593 ($(M+H)^+$, 100); Found 610.2756, $C_{34}H_{45}ClNO_5Si$ requires 610.2756.

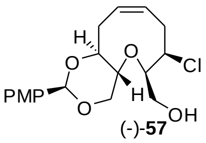
*(Z, 2*R*, 4a*R*, 6*R*, 7*R*, 11a*S*)-6-tButyldimethylsilyloxymethyl-7-chloro-2-(4-methoxy-phenyl)-4a,6,7,8,11,11a-hexahydro-4H-1,3,5-trioxa-benzocyclononene (-)-*56



(-)-**56**

Following the same procedure as that described for (+)-**59** above, (-)-**40** was converted to title compound (-)-**56** (91%), obtained as a clear and colourless oil; R_f 0.7 (ether:hexane, 2:1); $[a]_{\mathrm{D}}^{18}$ -52.5 (*c* 0.16, $\mathrm{CHCl_3}$); IR ($\mathrm{CDCl_3}$): ν=2931; ^{1}H NMR (500 MHz, $\mathrm{CDCl_3}$): δ=7.71-7.65 (m, 4H; Ar), 7.51-7.41 (m, 6H; Ar), 7.34 (d, *J*(H, H)=8.7 Hz, 2H; Ar), 6.88 (d, *J*(H, H)=8.7 Hz, 2H; Ar), 5.91 (m, 1H; 10-H), 5.52 (dt, *J*(H, H)=10.7, 6.2 Hz, 1H; 9-H), 5.03 (s, 1H; ArC*H*$\mathrm{O_2}$), 4.22 (ddd, *J*(H, H)=12.2, 4.1, 1.3 Hz, 1H; 7-H), 3.69 (dd, *J*(H, H)=10.2, 8.8 Hz, 1H; *CH*HOSi), 3.84 (dd, *J*(H, H)=10.0, 4.3 Hz, 1H; 4-H), 3.78 (s, 3H; $\mathrm{OCH_3}$), 3.73 (dt, *J*(H, H)=10.0, 4.3 Hz, 1H; 4a-H), 3.55-3.51 (m, 1H; 6-H), 3.47 (dd, *J*(H, H)=10.2, 4.7 Hz, 1H; CH*H*OSi), 3.33 (dd, *J*(H, H)=10.0, 7.5 Hz, 1H; 11a-H), 3.17-3.10 (m, 1H; 8-H), 3.12 (t, *J*(H, H)=10.0 Hz, 1H; 4-H'), 2.91-2.83 (m, 1H; 11-H), 2.46 (dt, *J*(H, H)=10.7, 5.3 Hz, 1H; 8-H'), 2.20-2.14 (m, 1H; 11-H'), 1.07 (s, 9H; $\mathrm{(CH_3)_3C}$); ^{13}C NMR (62.5 MHz, $\mathrm{CDCl_3}$): δ=160.1, 135.8, 135.6, 135.6, 132.8, 130.3, 130.1, 130.0, 129.8, 128.1, 128.0, 127.4, 126.7, 113.7, 101.3, 78.9, 75.6, 72.1, 70.3, 64.5, 59.5, 55.3, 32.4, 30.9, 26.9, 19.2; MS (CI, $\mathrm{NH_3}$); *m/z*(%): 610 ($\mathrm{(M+NH_4)^+}$, 2), 593 ($\mathrm{(M+H)^+}$,100); Found 593.2487, $\mathrm{C_{34}H_{42}ClO_5Si}$ requires 593.2490.

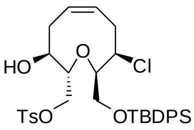
*(Z, 2*R*, 4a*R*, 6*R*, 7*R*, 11a*S*)-7-chloro-6-hydroxymethyl-2-(4-methoxy-phenyl)-4a,6,7,8,11,11a-hexahydro-4H-1,3,5-trioxa-benzocyclononene(-)-*57



(-)-**57**

To a stirred solution of the silylether (-)-**56** (71 mg, 120 μmol) in THF (2.5 mL), was added pyridine (0.62 mL, 7.8 mmol) and HF•pyridine (270 μL) and the resulting solution was stirred for 4 h. The reaction was quenched by the addition of a saturated solution of $\mathrm{NaHCO_3}$ (2.5 mL) and ether (2.5 mL). The aqueous phase was extracted with ether. The combined organic extracts were dried ($\mathrm{MgSO_4}$) and concentrated *in vacuo*. Purification of the residue by flash chromatography (ether:hexane, 2:1) gave the title compound (-)-**57** as a white solid (40 mg, 94%); R_f 0.15 (ether:hexane, 2:1); mp 121-124 °C (from ether); $[a]_D^{25}$ -16.3 (*c* 0.44, $CHCl_3$); IR ($CDCl_3$): ν=3462; ^1H NMR (500 MHz, $CDCl_3$): δ=7.37 (d, *J*(H, H)=8.5 Hz, 2H; Ar), 6.87 (m, 2H; Ar), 5.94 (dt, *J*(H, H)=10.5, 8.0 Hz, 1H; C*H*=CH), 5.53 (dt, *J*(H, H)=10.5, 8.0 Hz, 1H; CH=C*H*), 5.37 (s, 1H; ArC*H*O_2), 4.15 (ddd, *J*(H, H)=10.0, 4.0 Hz, 1H; 7-H), 4.12 (dd, *J*(H, H)=10.5, 3.5 Hz, 1H), 3.93 (ddd, *J*(H, H)=10.5, 9.5, 4.0 Hz, 1H), 3.86-3.77 (m, 4H), 3.79 (s, 3H; OCH_3), 3.68-3.60 (m, 1H), 3.17 (brq, *J*(H, H)=12.0 Hz, 1H; 8-H), 2.96-2.88 (m, 1H), 2.46 (ddd, *J*(H, H)=12.0, 6.0, 4.0 Hz, 1H), 2.30-2.27 (m, 1H), 1.76 (brs, 1H; OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=160.1, 130.3, 129.8, 127.5, 126.7, 113.7, 101.6, 79.1, 70.7, 64.3, 55.3, 32.9, 31.0; MS (ES): *m/z*(%): Found ($(M+H)^+$, 100) 355.1312, $C_{18}H_{24}{}^{35}ClO_5$ requires 355.1314.

*(Z, 2R, 3S, 8R, 9R)-9-tButyldiphenylsilyloxymethyl-8-chloro-3-hydroxy-2-*p-*tolunenesulfonyloxymethyl-2,3,4,7,8,9-hexahydro-oxonine* (-)-60

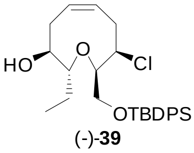


(-)-**60**

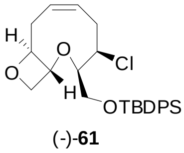
To a stirred solution of the diol (-)-**40** (12 mg, 25 μmol) in DCM (2 mL) at 0 °C was added triethylamine (10 μL, 7.6 mg, 75 μmol), DMAP (6.2 mg, 36 μmol) and *p*-toluenesulfonyl chloride (6.7 mg, 36 μmol), and the resulting solution was stirred at 0 °C for 3 h. The reaction mixture was quenched by the addition of 2 M aqueous hydrochloric acid (1 mL) and extracted with DCM (3 × 2 mL). The organic extracts were combined, dried ($MgSO_4$) and evaporated. Purification of the residue by preparative layer chromatography (ether:hexane, 2:1) provided the title compound (-)-**60** as a clear and colourless oil (8.2 mg, 13 μmol, 51%); R_f 0.2 (ether:hexane, 2:1); $[a]^{18}_{\mathrm{D}}$ -34.3 (*c* 0.105, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.72-7.60 (m, 4H; Ar), 7.50 (d, *J*(H, H)=8.4 Hz, 2H), 7.46-7.36 (m, 6H; Ar), 7.17 (d, *J*(H, H)=8.4 Hz, 2H), 5.84 (dt, *J*(H, H)=10.3, 7.7 Hz, 1H), 5.47 (dt, *J*(H, H)=10.3, 6.2 Hz, 1H), 4.26 (ddd, *J*(H, H)=11.8, 4.5, 1.7 Hz, 1H), 4.11 (dd, *J*(H, H)=11.5, 5.1 Hz, 1H), 3.89 (dd, *J*(H, H)=11.5, 1.7 Hz, 1H), 3.87-3.78 (m, 2H), 3.75-3.60 (m, 3H), 3.02 (q, *J*(H, H)=12.0 Hz, 1H), 2.98-2.86 (m, 1H), 2.50-2.42 (m, 1H), 2.40 (s, 3H; CH_3Ar), 2.33-2.26 (br, 1H; OH), 2.19-2.09 (m, 1H), 1.03 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=145.0, 135.7, 135.6, 133.5, 132.5, 130.1, 129.9, 129.8, 127.9, 127.8, 127.8, 126.4, 80.2, 73.2, 67.8, 63.0, 59.6, 33.2, 32.1, 26.9, 21.6, 19.2, 18.0; MS (CI, NH_3): *m/z*(%): 646 ($(M+NH_4)^+$, 10), 108 (100); Found 646.2423, $C_{33}H_{45}ClNO_6SSi$ requires 646.2425.

Starting material (-)-**40** (2.9 mg, 6.3 μmol, 25%) was also isolated.

(Z, 2R, 3S, 8R, 9R)-9-tButyldiphenylsilyloxymethyl-8-chloro-2-ethyl-3-hydroxy-2,3,4,7,8,9-hexahydro-oxonine (-)-39 and *(Z, 1R, 2S, 3R, 4R)-3-tbutyldimethylsilyloxymethyl-4-chloro-2,10-dioxa-bicyclo(7.2.0)undec-6-ene (-)*-61



(-)-**39**

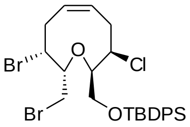


(-)-**61**

A Schlenk tube was charged with CuCN (11.3 mg, 0.127 mmol) which was dried by heating under vacuum (3 times with argon quench). The Schlenk tube was allowed to cool and ether (1 mL) was added. The slurry was cooled to – 78 °C. Methyllithium (158 µL of a 1.6 M solution in ether, 0.253 mmol) was added and the vigorously stirred mixture was warmed to 0 °C and stirred for 3 mins to provide a grey suspension. The cuprate was re-cooled to –78 °C and the tosylate (-)-**60** (8 mg, 13 µmol) was added as a solution in ether (1 mL, 0.5 mL rinse) *via* cannula. The reaction mixture was allowed to come to 0 °C and was stirred at that temperature for 1 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl (2 mL) and was stirred until complete dissolution. The aqueous layer was extracted with ether (4 × 2 mL). The combined organic phases were dried ($MgSO_4$) and evaporated. Purification of the residue by preparative layer chromatography (hexane:ether, 1:2) provided the oxetane (-)-**61** as a clear and colourless oil (4.4 mg, 9.6 µmol, 70%); R_f 0.6 (ether:hexane, 2:1); $[a]_{\mathrm{D}}^{20}$ -34.5 (*c* 0.055, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.65-7.62 (m, 4H; Ar), 7.46-7.36 (m, 6H; Ar), 5.87-5.81 (m, 1H; 7-H), 5.58 (ddt, *J*(H, H)=1.7, 6.0, 11.1 Hz, 1H; 6-H), 4.88 (q, *J*(H, H)=6.8 Hz, 1H; 1-H), 4.40-4.25 (m, 1H; 9-H), 4.18 (t, *J*(H, H)=6.8 Hz, 1H; 11β-H), 4.23 (dd, *J*(H, H)=6.4, 12.8 Hz, 1H; 4-H), 4.22 (t, *J*(H, H)=6.8 Hz, 1H; 11α-H), 3.76-3.66 (m, 3H; 3-H, CH_2OSi), 2.86 (q, *J*(H, H)=12.8 Hz, 1H; 5β–H), 2.77 (dt, *J*(H, H)=6.4, 12.8 Hz, 1H; 5α-H), 2.56 (dt, *J*(H, H)=6.8, 12.8 Hz, 1H; 8β-H), 2.33 (ddd, *J*(H, H)=2.1, 9.0, 12.8 Hz, 1H; 5α-H), 1.06 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=135.6, 133.3, 133.1, 129.9, 129.8, 129.6, 128.5, 127.8, 85.4, 77.2, 75.8, 73.3, 63.2, 58.4, 37.8, 32.7, 26.9, 19.2; MS (CI, NH_3): *m/z*(%): 474 ($(M + NH_4)^+$ 100); Found 474.2226, $C_{26}H_{37}{}^{35}ClNO_3Si$ requires 474.2231.

Also isolated was the hexahydrooxonine, (-)-**39** (2 mg, 4 µmol, 30%) as a clear and colourless oil that proved difficult to purify. The identity of (-)-**39** was secured by independent synthesis (*vide infra*);

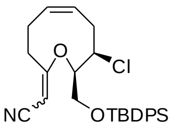
***(Z, 2*R*, 3*R*, 8*R*, 9*R*)-9-tButyldimethylsilyloxymethyl-8-chloro-3-bromo-2-bromomethyl-2,3,4,7,8,9-hexahydro-oxonine (-)-*62**



(-)-**62**

To a solution of the diol (-)-**40** (15 mg, 32 μmol) and freshly purified carbon tetrabromide (76 mg, 0.23 μmol) in toluene (1.5 mL) was added freshly distilled trioctylphosphane (204 μL, 170 mg, 0.46 μmol). The resulting solution was stirred for 0.5 h at ambient temperature and then heated at 70 °C for 18 h. The solvent was removed *in vacuo*. Purification of the residue by flash chromatography (hexane:DCM, 2:1) provided the title compound (-)-**62** as a clear and colourless oil (17.3 mg, 29 μmol, 90%); R_f 0.1 (hexane:DCM, 4:1); $[a]_D^{20}$ -37.6 (*c* 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, 50 °C; $CDCl_3$): δ=7.71-7.63 (m, 4H; Ar), 7.46-7.36 (m, 6H; Ar), 5.78-5.67 (m, 2H; 5-H, 6-H), 4.61 (brdt, *J*(H, H)=11.0, 2.4 Hz, 1H; 3-H), 4.46 (brd, *J*(H, H)=10.8 Hz, 1H; 8-H), 4.37-4.32 (m, 1H; 9-H), 4.23 (ddd, *J*(H, H)=9.1, 4.2, 3.9 Hz, 1H; 2-H), 3.90 (dd, *J*(H, H)=10.3, 7.8, 1H), 3.80 (dd, *J*(H, H)=10.3, 5.9 Hz, 1H), 3.46 (t, *J*(H, H)=9.7 Hz, 1H), 3.33 (dd, *J*(H, H)=10.1, 4.9 Hz, 1H), 3.01-2.84 (m, 2H), 2.80-2.65 (m, 2H), 1.07 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=135.6, 135.5, 132.8, 130.0, 129.9, 129.8, 129.7, 127.8, 127.8, 127.8, 127.7, 63.8, 63.7, 60.5, 53.5, 33.4, 26.9, 26.8, 26.8, 19.2; MS (CI, NH_3): *m/z*(%): 616 ($(M+NH_4)^+$, 30); Found 616.0649 $C_{26}H_{37}{}^{79}Br_2{}^{35}ClNO_2Si$ requires 616.0649, isotope pattern in agreement with proposed structure.

(Z, 8R, 9R)-(9-tButyldiphenylsilanyloxymethyl-8-chloro-4,7,8,9-tetrahydro-3H-oxonin-2-ylidene)-acetonitrile (-)-65 *Note: the a,b-unsaturated nitrile was formed as a single gemometric isomer whose configuration was not determined.*

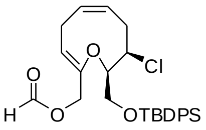


(-)-**65**

To the dibromide (-)-**62** (6 mg, 9.9 μmol) was added a solution of NaCN (9.8 mg, 0.22 mmol) in HMPA (0.5 mL) and the reaction mixture was stirred at room temperature for 20 min. The reaction was quenched by the addition of water (2 mL) and ether (2 mL). The aqueous phase was extracted with ether. The combined organic extracts were washed with water (2 × 5 mL) and dried ($MgSO_4$). Removal of the solvent *in vacuo* and purification of the residue by preparative layer chromatography (hexane:DCM, 1:1) gave the title compound (-)-**65** as a clear and colourless oil (3 mg, 6.4 μmol, 65%); R_f 0.2 (hexane:DCM, 1:1); $[a]_D^{25}$ -36.1 (*c* 0.21,

$CHCl_3$); IR ($CDCl_3$): ν=2217; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.65-7.59 (m, 4H; Ar), 7.48-7.37 (m, 6H; Ar), 5.72 (dt, *J*(H, H)=10.5, 6.5 Hz, 1H; 5-H), 5.48 (dt, *J*(H, H)=10.5, 5.5 Hz, 1H; 6-H), 4.91 (s, 1H; 1-H), 4.17 (ddd, *J*(H, H)=11.0, 5.5, 3.0 Hz, 1H; 8-H), 4.09 (dt, *J*(H, H)=6.0, 3.0 Hz, 1H; 9-H), 3.88 (d, *J*(H, H)=6.0 Hz, 2H; CH_2OSi), 2.95 (brq, *J*(H, H)=11.0 Hz, 1H; 7-H), 2.73-2.60 (m, 3H), 2.48 (dt, *J*(H, H)=13.0, 5.5 Hz, 1H), 2.17-2.10 (m, 1H), 1.07 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=179.9, 135.5, 135.5, 132.5, 132.0, 130.6, 130.1, 130.1, 127.9, 126.4, 117.9, 83.5, 79.1, 74.9, 64.7, 59.9, 33.6, 30.3, 26.8, 23.0, 21.4, 19.0; MS (CI, NH_3): *m/z*(%): Found 483.2227 $(M+NH_4)^+$, $C_{27}H_{36}{}^{35}ClN_2O_2Si$ requires 483.2235.

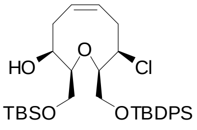
((Z, Z, 8R, 9R)-9-tButyldiphenylsilanyloxymethyl-8-chloro-4,7,8,9-tetrahydro-3H-oxonin-2-yl)methyl formate (-)-63



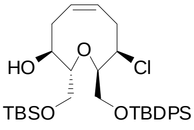
(-)-**63**

To a stirred solution of the dibromide (-)-**62** (19 mg, 31.6 mmol) in DMF (0.8 mL) was added caesium trifluoroacetate (40 mg, 0.16 mmol) and the reaction mixture heated overnight at 100 °C. Removal of the solvent *in vacuo* and purification of the residue by preparative layer chromatography (hexane:DCM, 2:1) gave the title compound (-)-**63** as a clear and colourless oil (12 mg, 24.7 μmol, 78%); R_f 0.1 (hexane:DCM, 2:1); $[a]_D^{25}$ -19.6 (*c* 0.53, $CHCl_3$); IR ($CDCl_3$): ν=1728; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.68-7.60 (m, 4H; Ar), 7.63 (s, 1H; CHO), 7.46-7.35 (m, 6H; Ar), 5.72 (dt, *J*(H, H)=10.5, 7.0 Hz, 1H; 5-H), 5.48 (dt, *J*(H, H)=10.5, 6.0 Hz, 1H; 6-H), 5.35 (t, *J*(H, H)=7.5 Hz, 1H; 3-H), 4.43 (d, *J*(H, H)=13.0 Hz, 1H; C*H*HOCHO), 4.40 (ddd, *J*(H, H)=11.0, 5.5, 2.0,1 H; 8-H), 4.24 (d, *J*(H, H)=13.0 Hz, 1H; C*H*HOCHO), 3.69-3.86 (m, 3H; CH_2OSi, 9-H), 3.49-3.39 (m, 2H; allylic CH_2), 2.56 (dt, *J*(H, H)=13.0, 6.5 Hz, 1H; allylic CH_2), 2.27 (dt, *J*(H, H)=13.0, 7.0 Hz, 1H; allylic CH_2), 1.04 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=160.2, 153.1, 135.6, 135.5, 133.2, 131.6, 129.9, 127.8, 124.8, 118.0, 82.2, 64.8, 63.5, 60.9, 32.9, 29.0, 26.8, 19.1; MS (CI, NH_3): *m/z*(%): Found 502.2177 $(M+NH_4)^+$, $C_{27}H_{37}{}^{35}ClNO_4Si$ requires 502.2180.

(Z, 2R, 3S, 8R, 9R)-2-tButyldimethylsilanyloxymethy)-9-tbutyldiphenylsilanyloxymethyl-8-chloro3-hydroxy-2,3,4,7,8,9-hexahydro-oxonine (-)-66, **and** *(Z, 2S, 3S, 8R, 9R)-2-tbutyldimethylsilanyloxymethy)-9-tbutyldiphenylsilanyloxymethyl-8-chloro3-hydroxy-2,3,4,7,8,9-hexahydro-oxonine (-)-68*



(-)-**66**



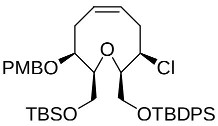
(-)-**68**

To a stirred solution of a mixture of the *cis*/*trans*-diols (-)-**40** and (-)-**58** (0.236 g, 0.498 mmol) in DCM (6 mL) at -78 ºC was added 2,6-lutidine (0.10 mL, 0.861 mmol) and *t*butyldimethylsilyl triflate (0.12 mL, 0.523 mmol). The resulting solution was stirred for 30 min at - 78 ºC and then allowed to warm to room temperature before being quenched by the additions of a saturated solution of $NaHCO_3$ (4 mL) and water (4 mL). The aqueous phase was extracted with DCM (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product. Purification by column chromatography (hexane:ether, 3:1) furnished the readily separable *trans*-silyl ether (-)-**68** and *cis*-silyl ether (-)-**66**.

The *trans*-silyl ether (-)-**68** (0.224 g, 77%) was isolated as a clear and colourless oil; R_f 0.60 (hexane:ether, 1:1); $[a]_{\mathrm{D}}^{25}$ -45.3 (*c* 0.71, $CHCl_3$); IR ($CDCl_3$): ν=3483; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.64-7.69 (m, 4H; Ar), 7.40-7.47 (m, 6H; Ar), 5.89 (dt, *J*(H, H)=10.5, 7.5 Hz, 1H; C*H*=CH), 5.47 (dt, *J*(H, H)=10.5, 6.4 Hz, 1H; CH=C*H*), 4.25 (ddd, *J*(H, H)=12.1, 4.6, 1.6 Hz, 1H; 8-H), 3.90 (dd, *J*(H, H)=9.0, 1.8 Hz, 1H; C*H*HOSi), 3.49-3.62 (m, 5H; 3 × OCH, CH*H*OSi, C*H*'H'OSi), 3.40 (t, *J*(H, H)=9.0 Hz, 1H; CH'*H*'OSi), 3.13 (q, *J*(H, H)=11.5 Hz, 1H; ring C*H*H), 2.97 (ddd, *J*(H, H)=13.8, 10.5, 6.8 Hz, 1H; ring CH*H*), 2.47 (dt, *J*(H, H)=11.5, 5.5 Hz, 1H; ring C*H*H), 2.03 (dd, *J*(H, H)=13.8, 7.3 Hz, 1H; ring CH*H*), 1.06 (s, 9H; $C(CH_3)_3$), 0.82 (s, 9H; $C(CH_3')_3$), 0.12 (s, 3H; $Si(CH_3)$), -0.04 (s, 3H; $Si(CH_3')$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=135.6, 135.4, 133.4, 133.0, 129.8, 129.8, 127.8, 127.7, 127.6, 64.5, 63.4, 60.8, 33.5, 32.0, 30.3, 26.8, 25.8, 19.1, 18.1, -5.6, -5.6; MS (CI, NH_3): *m/z*(%): 606 ($(M + NH_4)^+$,100); (ES) Found 606.3188, $C_{32}H_{53}{}^{35}ClNO_5Si$ requires 606.3202.

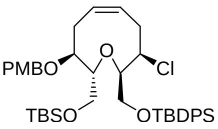
The *cis*-silyl ether (-)-**66** (47.3 mg, 16%) was isolated as a clear and colourless oil; R_f 0.72 (hexane:ether, 1:1); $[a]_{D}^{25}$ -5.7 (*c* 0.18, $CHCl_3$); IR ($CHCl_3$ film): ν=3433; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.65-7.71 (m, 4H; Ar), 7.39-7.47 (m, 6H; Ar), 5.67 (dt, *J*(H, H)=10.9, 5.8 Hz, 1H; C*H*=CH), 5.57 (dt, *J*(H, H)=10.9, 5.5 Hz, 1H; CH=C*H*), 4.36 (ddd, *J*(H, H)=10.7, 6.1, 2.6 Hz, 1H; 8-H), 4.04-4.09 (m, 1H), 3.85 (dd, *J*(H, H)=10.1, 8.0 Hz, 1H; C*H*HOSi), 3.76 (dd, *J*(H, H)=10.1, 5.4 Hz, 1H; C*H*'H'OSi), 3.72 (dd, *J*(H, H)=10.1, 8.0 Hz, 1H; CH*H*OSi), 3.63 (dd, *J*(H, H)=10.1, 5.4 Hz, 1H; CH'*H*'OSi), 3.44-3.48 (m, 1H), 3.18-3.25 (m, 2H; OCH, ring C*H*H), 2.86 (q, *J*(H, H)=11.6 Hz, 1H; ring CH*H*), 2.57 (dt, *J*(H, H)=12.1, 5.5 Hz, 1H; ring C*H*H), 2.42 (d, *J*(H, H)=5.0 Hz, 1H; CHO*H*), 2.36 (dt, *J*(H, H)=12.1, 5.5 Hz, 1H; ring CH*H*), 1.09 (s, 9H; $C(CH_3)_3$), 0.84 (s, 9H; $C(CH_3')_3$), -0.02 (s, 3H; $Si(CH_3)$), -0.05 (s, 3H; $Si(CH_3')$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=135.6, 135.4, 133.4, 132.9, 129.8, 129.7, 129.2, 127.8, 127.7, 127.6 (2 alkene, 8 Ar), 85.0 (2-C or 3-C or 9-C), 84.4 (2-C or 3-C or 9-C), 71.6 (2-C or 3-C or 9-C), 60.8 (8-C), 64.5 (1-C or 10-C), 63.4 (1-C or 10-C), 33.4 (ring CH_2), 31.9 (ring CH_2), 26.8 ($C(\mathit{C}H_3)_3$), 25.8 ($C(\mathit{C}H_3)_3$), 19.1 ($\mathit{C}(CH_3)_3$), 18.1 ($\mathit{C}(CH_3')_3$), -5.5 ($Si(C\mathit{H}_3)$), -5.6 ($Si(\mathit{C}H_3')$); MS (CI, NH_3): *m/z*(%): 589 ($(M+H)^+$, 10); (ES) Found 589.2940, $C_{32}H_{50}O_4Si_2{}^{35}Cl$ requires 589.2940.

(Z, 2S, 3S, 8R, 9R)-2-tButyldimethylsilanyloxymethyl-9-tbutyldiphenylsianlyloxymethyl-8-chloro-3-(4-methoxybenzyloxy)-2,3,4,7,8,9-hexahydro-oxonine



To a stirred solution of the TBS-protected hexahydrooxonine (-)-**66**, described above, (47 mg, 0.093 mmol) and $Sc(OTf)_3$ (1.4 mg, 3 mol%) in toluene (1.5 mL) was added freshly distilled *p*-methoxybenzyltrichloroacetimidate (67 mg, 0.237 mmol). The reaction mixture was stirred for 30 min and the solvent removed *in vacuo*. Purification of the residue by flash column chromatography (hexane:ether, 4:1) furnished the title compound (50 mg, 88%) as a clear and colourless oil; R_f 0.47 (hexane:ether, 3:1); $[a]_{D}^{25}$ +8.4 (*c* 0.25, $CHCl_3$); IR ($CHCl_3$ film): ν=2930, 2857; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.65-7.71 (m, 4H; Ar), 7.38-7.44 (m, 6H; Ar), 7.10-7.12 (m, 2H; Ar), 6.84-6.87 (m, 2H; Ar), 5.53-5.63 (m, 2H; C*H*=C*H*), 4.53 (d, *J*(H, H)=11.5 Hz, 1H; OC*H*HAr), 4.43 (d, *J*(H, H)=11.5 Hz, 1H; OCH*H*Ar), 4.46 (ddd, *J*(H, H)=10.9, 6.2, 2.5 Hz, 1H; 8-H), 3.81-3.90 (m, 3H), 3.81 (s, 3H; $\mathrm{OCH_3}$), 3.76 (ddd, *J*(H, H)=9.5, 5.8, 3.3 Hz, 1H), 3.71 (dd, *J*(H, H)=9.5, 7.8 Hz, 1H; OC*H*HSi), 3.44-3.50 (m, 2H), 3.20-3.30 (m, 2H; OCH, ring C*H*H), 2.90-2.96 (m, 1H; ring CH*H*), 2.57 (dt, *J*(H, H)=12.1, 5.4 Hz, 1H; ring C*H*H), 2.29 (dt, *J*(H, H)=11.6, 5.4 Hz, 1H; ring CH*H*), 1.07 (s, 9H; $\mathrm{C(CH_3)_3}$), 0.82 (s, 9H; $\mathrm{C(CH_3')_3}$), -0.08 (s, 3H; $\mathrm{Si(CH_3)}$), -0.12 (s, 3H; $\mathrm{Si(CH_3')}$); ^{13}C NMR (125 MHz, $\mathrm{CDCl_3}$): δ=159.0, 135.7, 135.4, 133.7, 133.0, 130.8, 129.8, 129.7, 129.6, 129.1, 127.5, 127.6, 113.8, 113.6, 86.1, 83.7, 71.5 (O*C*$\mathrm{H_2}$Ar), 63.8 (O*C*$\mathrm{H_2}$Si), 62.9 (O*C*$\mathrm{H_2}$'Si), 60.9 (8-C), 33.4 (ring $\mathrm{CH_2}$), 29.0 (ring $\mathrm{CH_2}$), 26.8 (C(*C*$\mathrm{H_3})_3$), 25.9 (C(*C*$\mathrm{H_3'})_3$), 19.2 (*C*$\mathrm{(CH_3)_3}$) 18.2 (*C*$\mathrm{(CH_3')_3}$), -5.51 (Si(*C*$\mathrm{H_3}$)), -5.54 (Si(*C*$\mathrm{H_3}$')) *Note* Owing to the conformational flexibility of the title compound one of the carbons adjacent to oxygen is broadened to the baseline; MS (CI, $\mathrm{NH_3}$): *m/z*(%): 726 ($\mathrm{(M+NH_4)^+}$, 20), 709 ($\mathrm{(M+H)^+}$, 5); (ES) Found 726.3777, $\mathrm{C_{40}H_{61}O_5NSi_2{}^{35}Cl}$ requires 726.3771.

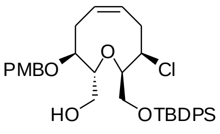
(Z, 2R, 3S, 8R, 9R)-2-tButyldimethylsilanyloxymethyl-9-tbutyldiphenylsianlyloxymethyl-8-chloro-3-(4-methoxybenzyloxy)-2,3,4,7,8,9-hexahydro-oxonine



To a stirred solution of mono-protected hexahydrooxonine (-)-**68** (54.6 mg, 0.093 mmol) and $\mathrm{Sc(OTf)_3}$ (1.4 mg, 3 mol%) in toluene (1.6 mL) was added freshly distilled *p*-methoxybenzyltrichloroacetimidate (77 mg, 0.273 mmol). The reaction mixture was stirred for 30 min and the solvent was removed *in vacuo*. Purification of the residue by flash column chromatography (hexane:ether, 4:1) furnished the PMB ether (58.0 mg, 88%) as a colourless oil; R_f 0.68 (hexane:ether, 2:1); $[a]_{\mathrm{D}}^{25}$ -59.4 (*c* 0.51, $\mathrm{CHCl_3}$); IR ($\mathrm{CHCl_3}$ film): ν=2930, 2857; ^{1}H NMR (500 MHz, $\mathrm{CDCl_3}$): δ=7.62-7.69 (m, 4H; Ar), 7.34-7.43 (m, 6H; Ar), 7.20-7.22 (m, 2H; Ar), 6.90-6.92 (m, 2H; Ar), 5.72 (dt, *J*(H, H)=10.5, 7.1 Hz, 1H; C*H*=CH), 5.48 (dt, *J*(H, H)=10.5, 6.5 Hz, 1H; CH=C*H*), 4.53 (d, *J*(H, H)=11.2 Hz, 1H; OC*H*HAr), 4.36 (ddd, *J*(H, H)=12.1, 4.6, 1.7 Hz, 1H; 8-H), 4.26 (d, *J*(H, H)=11.2 Hz, 1H; OCH*H*Ar), 3.96-3.98 (m, 2H), 3.84 (s, 3H; $\mathrm{OCH_3}$), 3.63 (dt, *J*(H, H)=9.1, 2.8 Hz, 1H), 3.57 (dd, *J*(H, H)=11.9, 2.8 Hz, 1H; C*H*HOSi), 3.47 (dt, *J*(H, H)=7.7, 2.0 Hz, 1H), 3.19 (q, *J*(H, H)=12.0 Hz, 1H; ring

C*H*H), 2.98-3.06 (m, 2H; ring CH*H*, C*H*'H'OSi), 2.94 (t, *J*(H, H)=9.0 Hz, 1H; CH'*H*'OSi), 2.47 (dt, *J*(H, H)=12.0, 5.4 Hz, 1H; ring C*H*H), 2.11 (dd, *J*(H, H)=13.7, 7.1 Hz, 1H; ring CH*H*), 1.06 (s, 9H; $C(CH_3)_3$), 0.71 (s, 9H; $C(CH_3')_3$), -0.16 (s, 3H; $Si(CH_3)$), -0.22 (s, 3H; $Si(CH_3')$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=159.4, 135.6, 134.2, 133.1, 131.1, 129.8, 129.7, 129.7, 129.5, 127.7, 125.9, 113.8, 81.8, 76.5, 71.5, 70.6, 63.4, 62.2, 59.9, 55.3, 32.4, 29.2, 26.9, 25.8, 19.2, 18.0, -5.5, -5.6; MS (CI, NH_3): *m/z*(%): 726 ($(M+NH_4)^+$, 50), 121 (100); (ES) Found 726.3772, $C_{40}H_{61}O_5NSi_2{}^{35}Cl$ requires 726.3777.

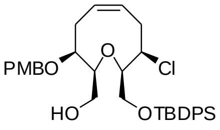
(Z, 2*R*, 3*S*, 8*R*, 9*R*)-9-tButyldiphenylsilanyloxymethyl-8-chloro-2-hydroxymethyl-3-(4-methoxybenzyloxy)-2,3,4,7,8,9-hexahydro-oxonine, (-)-69



(-)-**69**

To a stirred solution of the PMB ether prepared above (105.5 mg, 0.148 mmol) in MeOH (4 mL) was added PPTS (37.2 mg, 0.147 mmol). The resulting solution was stirred for 3 days. The reaction was then quenched by the addition of a saturated solution of aqueous $NaHCO_3$ (5 mL) and ether (5 mL). The aqueous phase was extracted with ether (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give the crude product. Purification by flash column chromatography (hexane:ether, 3:1) furnished the alcohol (-)-**69** (56.4 mg, 64%) as a clear and colourless oil along with some unreacted starting material (21.0 mg, 20%); R_f 0.19 (hexane:ether, 3:1); $[a]_D^{21}$ -23.1 (*c* 0.385, $CHCl_3$); IR ($CDCl_3$): ν=3591; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.64-7.68 (m, 4H; Ar), 7.41-7.46 (m, 6H; Ar), 7.24-7.26 (m, 2H; Ar), 6.91-6.92 (m, 2H; Ar), 5.78 (dt, *J*(H, H)=10.4, 7.4 Hz, 1H; C*H*=CH), 5.48 (dt, *J*(H, H)=10.4, 6.4 Hz, 1H; CH=C*H*), 4.59 (d, *J*(H, H)=11.0 Hz, 1H; OC*H*HAr), 4.33 (d, *J*(H, H)=11.0 Hz, 1H; OCH*H*Ar), 4.19 (ddd, *J*(H, H)=12.0, 4.4, 2.0 Hz, 1H; 8-H), 3.87-3.94 (m, 2H), 3.82 (s, 3H; OCH_3), 3.71 (ddd, *J*(H, H)=9.8, 5.9, 3.8 Hz, 1H; C*H*HOH), 3.56-3.61 (m, 2H), 3.40 (dt, *J*(H, H)=12.0, 6.1 Hz, 1H), 3.29 (dd, *J*(H, H)=9.7, 7.2 Hz, 1H; C*H*HOSi), 3.10 (q, *J*(H, H)=11.3 Hz, 1H; ring C*H*H), 2.94 (ddd, *J*(H, H)=14.3, 10.6, 7.5 Hz, 1H; ring CH*H*), 2.43-2.48 (m, 1H; ring C*H*H), 2.21 (dd, *J*(H, H)=14.3, 7.5 Hz, 1H; ring CH*H*), 1.91 (t, *J*(H, H)=5.9 Hz, 1H; CH_2O*H*), 1.06 (s, 9H; $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=159.5, 135.6, 134.8, 133.34, 132.8, 131.0, 129.9, 129.6, 129.5, 127.8, 127.7, 126.1, 114.0, 81.1, 76.3, 72.6, 71.0, 64.3, 63.5, 60.1, 55.3, 32.2, 29.7, 26.8, 26.5, 19.1; MS (CI, NH_3): *m/z*(%): 612 ($(M+NH_4)^+$, 1), 595 ($(M+H)^+$, 1), 121 (100); Found 595.2648, $C_{34}H_{44}ClO_5Si$ requires 595.2646.

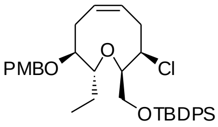
*(Z, 2*S*, 3*S*, 8*R*, 9*R*)-9-t*Butyldiphenylsilanyloxymethyl-8-chloro-2-hydroxymethyl-3-(4-methoxybenzyloxy)-2,3,4,7,8,9-hexahydro-oxonine, (-)-67*



(-)-**67**

To a stirred solution of the PMB ether prepared above (50 mg, 0.070 mmol) in MeOH (4 mL) was added PPTS (18 mg, 0.071 mmol). The resulting solution was stirred for 3 days. The reaction was then quenched by the addition of a saturated solution of aqueous $NaHCO_3$ (5 mL) and ether (5 mL). The aqueous phase was extracted with ether (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product. Purification by flash column chromatography (hexane:ether, 3:1) gave the alcohol (-)-**67** (28 mg, 67%) as a clear and colourless oil; R_f 0.10 (hexane: ether, 3:1); $[a]_{D}^{25}$ -4.1 (*c* 0.27, $CHCl_3$); IR ($CHCl_3$ film): ν=3448; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.66-7.69 (m, 4H; Ar), 7.39-7.47 (m, 6H; Ar), 7.24-7.25 (m, 2H; Ar), 6.88-6.90 (m, 2H; Ar), 5.63 (dt, *J*(H, H)=11.0, 6.0 Hz, 1H; C*H*=CH), 5.49 (dt, *J*(H, H)=11.0, 5.5 Hz, 1H; CH=C*H*), 4.61 (d, *J*(H, H)=11.6 Hz, 1H; OC*H*HAr), 4.36 (d, *J*(H, H)=11.6 Hz, 1H; OCH*H*Ar), 4.17 (ddd, *J*(H, H)=11.1, 5.7, 2.6 Hz, 1H; 8-H), 3.93 (dd, *J*(H, H)=10.5, 5.7 Hz, 1H; C*H*HOSi), 3.85 (dd, *J*(H, H)=10.5, 6.5 Hz, 1H; CH*H*OSi), 3.81 (s, 3H; OCH_3), 3.67-3.73 (m, 3H), 3.43-3.48 (m, 2H), 3.19 (q, *J*(H, H)=11.7 Hz, 1H; ring C*H*H), 2.93-3.00 (q, *J*(H, H)=11.7 Hz, 1H; ring CH*H*), 2.48 (dt, *J*(H, H)=12.2, 5.8 Hz, 1H; ring C*H*H), 2.44 (t, *J*(H, H)=6.4 Hz, 1H; CH_2OH), 2.28 (dt, *J*(H, H)=12.2, 5.0 Hz, 1H; ring CH*H*), 1.07 (s, 9H; $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=159.4, 135.6, 135.5, 133.2, 132.9, 129.9, 129.82, 129.80, 129.53, 129.47, 127.8, 127.0, 113.9, 83.3 (2-C or 3-C or 9-C), 82.0 (2-C or 3-C or 9-C), 78.0 (2-C or 3-C or 9-C), 70.8 (OCH_2Ar), 65.3 (1-C or 10-C), 63.4 (1-C or 10-C), 33.4 (ring CH_2), 27.9 (ring CH_2), 26.8 ($C(CH_3)_3$), 19.1 ($C(CH_3)_3$); MS (CI, NH_3): *m/z*(%): 612 ($(M+NH_4)^+$, 10); (ES) Found 612.2909, $C_{34}H_{47}O_5NSi^{35}Cl$ requires 612.2912.

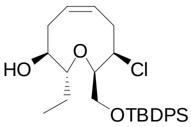
*(Z, 2*R*, 3*S*, 8*R*, 9*R*)-9-t*Butyldiphenylsilyloxymethyl-8-chloro-2-ethyl-3-(4-methoxy)benzyloxy-2,3,4,7,8,9-hexahydro-oxonine* (-)-70



(-)-**70**

To a stirred solution of the alcohol (-)-**69** (15 mg, 25 µmol) and pyridine (120 µl, 117 mg, 1.48 mmol) in DCM (2 mL) at –13 °C was added Tf_2O (15 µL, 25 mg, 88 µmol). The resulting solution was stirred for 10 min before being quenched by the addition of saturated aqueous $NaHCO_3$ (2 mL). DCM (5 mL) and saturated aqueous $NaHCO_3$ (5 mL) were added and the aqueous phase was extracted with DCM (3 × 5 mL). The organic extracts were combined, washed with 2 M aqueous hydrochloric acid, saturated aqueous $NaHCO_3$ (10 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude triflate was dried by azeotropic co-evaporation with anhydrous toluene (3 × 1 mL). A Schlenk tube was charged with CuI (24 mg, 0.126 mmol) which was then flushed with argon (3 times vacuum purge). Ether (1 mL) was added and the slurry was cooled to –78 °C. Methyl lithium (168 µL of a 1.5 M solution in ether, 0.25 mmol) was added dropwise and the vigorously stirred mixture was warmed to 0 °C and stirred for 3 mins to provide a grey suspension. The cuprate was re-cooled to –78 °C and the crude triflate was added as a solution in ether (1 mL, 0.5 mL rinse) *via* cannula. The reaction mixture was allowed to come to 0 °C and was stirred at that temperature for 1 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl (2 mL) and was stirred until complete dissolution. The aqueous layer was extracted with ether (4 × 2 mL). The organic phases were combined, dried ($MgSO_4$) and evaporated. Purification of the residue by preparative layer chromatography (DCM) provided the hexahydroxonine (-)-**70** as a clear and colourless oil (8 mg, 15 µmol, 62%); R_f 0.7 (DCM); $[a]_{\mathrm{D}}^{19}$ -21.4 (*c* 0.47, $CHCl_3$); IR ($CHCl_3$ film): ν=2931; ^1H NMR (500 MHz, $CDCl_3$): δ=7.65-7.60 (m, 4H; Ar), 7.45-7.34 (m, 6H; Ar), 7.23-7.20 (m, 2H; Ar), 6.90-6.87 (m, 2H; Ar), 5.73 (dt, *J*(H, H)=10.6, 7.1 Hz, 1H; 5-H), 5.44 (dt, *J*(H, H)=10.6, 6.3 Hz, 1H; 6-H), 4.51 (d, *J*(H, H)=10.9 Hz, 1H; C*H*HAr), 4.32 (ddd, *J*(H, H)=12.2, 4.7, 1.7 Hz, 1H; 8-H), 4.27 (d, *J*(H, H)=10.9 Hz, 1H; CH*H*Ar), 3.94 (t, *J*(H, H)=9.6 Hz, 1H; C*H*HOSi), 3.80 (s, 3H; CH_3O), 3.70 (dd, *J*(H, H)=9.6, 4.5 Hz, 1H; CH*H*OSi), 3.41 (ddd, *J*(H, H)=9.6, 4.5, 1.7 Hz, 1H; 9-H), 3.37 (dd, *J*(H, H)=9.1, 2.5 Hz, 1H; 2-H), 3.15 (q, *J*(H, H)=12.2 Hz, 1H; 7-H), 2.95 (ddd, *J*(H, H)=13.9, 10.6, 7.1 Hz, 1H; 4-H), 2.88 (dd, *J*(H, H)=9.1, 7.1 Hz, 1H; 3-H), 2.43 (dt, *J*(H, H)=12.2, 5.7 Hz, 1H; 7-H), 2.09 (dd, *J*(H, H)=13.9, 7.1 Hz, 1H; 4-H), 1.65 (ddq, *J*(H, H)=14.7, 7.3, 2.5 Hz, 1H; C*H*HCH$_3$), 1.04 (s, 9H; (CH$_3$)$_3$C), 0.84-0.73 (m, 1H; CH*H*CH$_3$), 0.69 (t, *J*(H, H)=7.3 Hz, 3H; CH$_2$C*H*$_3$); ^{13}C NMR (125 MHz, CDCl$_3$): δ=159.3, 135.5, 135.5, 133.7, 133.1, 131.6, 129.8, 129.8, 129.6, 127.8, 129.6, 127.8, 125.6, 113.8, 83.5, 79.7, 71.4, 71.1, 63.6, 60.1, 55.3, 32.3, 30.2, 26.8, 24.8, 19.2, 10.5; MS (CI, NH$_3$): *m/z*(%): 610 ((M+NH$_4$)$^+$, 2), 121 (100); Found 610.3127, C$_{35}$H$_{49}$ClNO$_4$Si requires 610.3119.

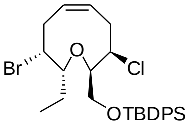
*(Z, 2*R*, 3*S*, 8*R*, 9*R*)-9-tButyldiphenylsilyloxymethyl-8-chloro-2-ethyl-3-hydroxy-2,3,4,7,8,9-hexahydro-oxonine* **(-)-*39***



(-)-**39**

To a stirred solution of the oxonene (-)-**70** (8.4 mg, 14 µmol) in DCM (1 mL) was added BCl$_3$•SMe$_2$ (35 µL, of a 2.0 M solution in DCM, 70 µmol) and the resulting solution was stirred for 10 min before being quenched by the addition of saturated aqueous NaHCO$_3$ (1 mL). DCM (5 mL) and water (5 mL) were added and the aqueous phase was extracted with DCM (2 × 5 mL). The combined organic extracts were dried (MgSO$_4$) and evaporated. Purification of the residue by preparative layer chromatography (hexane:ether, 2:1) provided the title compound (-)-**39** as a clear and colourless oil (6.4 mg, 13.6 µmol, 97%); *R$_f$* 0.4 (hexane:ether, 2:1); $[a]_{\mathrm{D}}^{19}$ -20.0 (*c* 0.28, CHCl$_3$); IR (CHCl$_3$ film): ν=3446; ^{1}H NMR (500 MHz, CDCl$_3$): δ=7.66-7.61 (m, 4H; Ar), 7.44-7.36 (m, 6H; Ar), 5.82 (dt, *J*(H, H)=10.5, 7.3 Hz, 1H; 5-H), 5.45 (dt, *J*(H, H)=10.5, 6.3 Hz, 1H; 6-H), 4.32 (ddd, *J*(H, H)=12.2, 4.7, 1.8 Hz, 1H; 8-H), 3.93 (dd, *J*(H, H)=9.7, 9.5 Hz, 1H; C*H*HOSi), 3.70 (dd, *J*(H, H)=9.7, 4.7 Hz, 1H; CH*H*OSi), 3.46 (ddd, *J*(H, H)=9.5, 4.7, 1.8 Hz, 1H; 9-H), 3.27 (dt, *J*(H, H)=9.2, 2.7 Hz, 1H; 2-H), 3.21 (brt, *J*(H, H)=12.2 Hz, 1H), 3.12 (q, *J*(H, H)=12.2 Hz, 1H; 7-H), 3.03 (ddd, *J*(H, H)=13.5, 10.7, 7.2 Hz, 1H; 4-H), 2.44 (dt, *J*(H, H)=12.2, 5.0 Hz, 1H; 7-H’), 1.98 (dd, *J*(H, H)=13.5, 7.3 Hz, 1H; 4-H’), 1.61 (ddq, *J*(H, H)=15.0, 7.3, 2.7 Hz, 1H; C*H*HCH$_3$), 1.04 (s, 9H; (CH$_3$)$_3$C), 0.95-0.87 (m, 1H; CH*H*CH$_3$), 0.73 (t, *J*(H, H)=7.3 Hz, 3H; CH$_2$C*H*$_3$); ^{13}C NMR (125 MHz, CDCl$_3$): δ=135.5, 135.5, 133.5, 133.0, 130.6, 129.8, 129.8, 127.8, 127.7, 125.8, 85.2, 72.6, 71.7, 63.6, 60.1, 34.1, 32.3, 26.8, 25.0, 19.1, 10.5; MS (CI, NH$_3$): *m/z*(%): 490 ((M+NH$_4$)$^+$, 33), 274 (100); Found 490.2540, C$_{27}$H$_{41}$ClNO$_3$Si requires 490.2544.

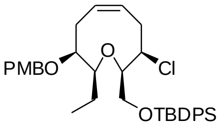
*(Z, 2*R*, 3*R*, 8*R*, 9*R*)-9-tButyldiphenylsilyloxymethyl-3-bromo-8-chloro-2-ethyl-2,3,4,7,8,9-hexahydro-oxonine* (-)-38



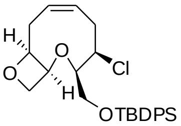
(-)-**38**

A Schlenk tube was charged with freshly purified CBr_4 (25 mg, 74 µmol) and was vacuum purged (3 times with argon). The alcohol prepared above (5 mg, 10.6 µmol) was added *via* cannula as a solution in toluene (0.5 mL, 0.5 mL rinse). Freshly distilled trioctylphosphane (66 µL, 55 g, 149 µmol) was added *via* syringe over 4 min and the resulting solution was stirred for 0.5 h at ambient temperature and then overnight at 75 °C. The solvent was removed *in vacuo* and purification of the residue by preparative layer chromatography (DCM:hexane, 2:1) provided the hexahydrooxonine (-)-**38** as a white crystalline solid (3.7 mg, 7 µmol, 65%); R_f 0.3 (DCM:hexane, 2:1); mp 118-120 °C (from hexane); $[a]_{\mathrm{D}}^{21}$ -36.5 (*c* 0.23, $CHCl_3$); IR ($CHCl_3$ film): ν=2927; ^{1}H NMR (400 MHz, 50 °C; $CDCl_3$): δ=7.71-7.65 (m, 4H; Ar), 7.45-7.35 (m, 6H; Ar), 5.78-5.67 (m, 2H; 5-H, 6-H), 4.54-4.49 (brm, *J*(H, H)=10.8 Hz, 1H), 4.34-4.30 (brm, 1H), 3.89 (t, *J*(H, H)=9.6 Hz, 1H; C*H*HOSi), 3.82-3.78 (brm, 1H), 3.81 (dd, *J*(H, H)=9.6, 5.4 Hz, 1H; CH*H*OSi), 3.04 (brq, *J*(H, H)=10.8 Hz, 1H), 2.89-2.78 (brm, 2H), 2.66-2.59 (brm, 1H), 1.58-1.49 (m, 2H; CH_2CH_3), 1.06 (s, 9H; $(CH_3)_3C$), 0.78 (t, *J*(H, H)=7.3 Hz, 3H; CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=135.5, 135.5, 133.2, 133.2, 129.7, 127.7, 127.7, 63.5, 31.7, 31.0, 29.0, 28.7, 26.7, 22.6, 21.4, 19.2, 14.1; MS (CI, NH_3): *m/z*(%): 552 ($(M+NH_4)^+$, 21), 165 (100); Found 552.1705, $C_{27}H_{40}{}^{79}Br^{35}ClNO_2Si$ requires 552.1700.

*(Z, 2*S*, 3*S*, 8*R*, 9*R*)-9-tButyldiphenylsilanyloxymethyl-8-chloro-2-ethyl-3-(4-methoxybenzyloxy)-2,3,4,7,8,9-hexahydro-oxonine, (-)-71* and *(Z, 1*S*, 3*R*, 4*R*, 9*S*)-3-tbutyldiphenylsilanyloxymethyl-4-chloro-2,10-dioxa-bicyclo(7.2.0)undec-6-ene, (-)-72*



(-)-**71**



(-)-**72**

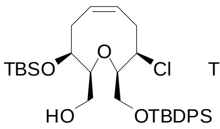
To a stirred solution of the alcohol (-)-**67** (16.0 mg, 0.027 mmol) and pyridine (0.12 mL, 1.484 mmol) in DCM (1.5 mL) at -20 ºC was added trifluoromethanesulfonic anhydride (15 µL, 0.089 mmol). The resulting solution was stirred at this temperature for 15 min before being quenched by the addition of a saturated solution of aqueous $NaHCO_3$ (2 mL) and DCM (5 mL). The aqueous phase was extracted with DCM (3 × 5 mL). The combined organic extracts were washed sequentially with a 2.0 M aqueous solution of HCl (10 mL) and saturated solution of aqueous $NaHCO_3$ (10 mL). The resulting organic solution was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude triflate as a pale yellow oil.

A Schlenk tube pre-flushed with argon was charged with finely-ground CuI (51 mg, 0.268 mmol) and then flushed with argon (3 × vacuum purge). Ether (1.0 mL) was added and the resulting suspension was vigorously stirred at -78 ºC, followed by the dropwise addition of methyllithium (0.36 mL of a 1.5 M solution in ether, 0.54 mmol). The mixture was allowed to warm to 0 ºC for 5 min to provide a colourless solution. The cuprate solution was re-cooled to -78 ºC and the previously prepared triflate was added dropwise as a solution in ether (1.0 mL). The reaction mixture was allowed to warm to 0 ºC and stirring was continued at this temperature for another 1.5 h. The reaction was quenched by the addition of a saturated solution of aqueous NH_4Cl (2 mL) and the mixture was stirred until the aqueous layer turned blue. The aqueous phase was extracted with ether (3 × 5 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product. Purification by column chromatography (hexane:ether, 4:1) furnished the desired ethyl substituted oxonene (-)-**71** (5.5 mg, 34%) and the oxetane (-)-**72** (4.3 mg, 34%).

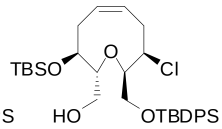
Data for the ethyl substituted oxonene (-)-**71**: R_f 0.54 (hexane:ether, 3:1); $[a]_D^{25}$ -5.5 (*c* 0.28, $CHCl_3$); IR ($CHCl_3$ film): ν=2931, 2858; ^{1}H NMR (500 MHz, $CDCl_3$) 7.66-7.69 (m, 4H; Ar), 7.38-7.46 (m, 6H; Ar), 7.24-7.26 (m, 2H; Ar), 6.86-6.88 (m, 2H; Ar), 5.64 (dt, *J*(H, H)=10.7, 5.8 Hz, 1H; C*H*=CH), 5.48 (dt, *J*(H, H)=10.7, 5.8 Hz, 1H; CH=C*H*), 4.57 (d, *J*(H, H)=11.5 Hz, 1H; OC*H*HAr), 4.35 (d, *J*(H, H)=11.5 Hz, 1H; OCH*H*Ar), 4.25 (ddd, *J*(H, H)=11.3, 5.6, 2.6 Hz, 1H; 8-H), 3.81-3.90 (m, 2H), 3.81 (s, 3H; OCH_3), 3.58 (dt, *J*(H, H)=8.6, 4.1 Hz, 1H), 3.41-3.44 (m, 1H), 3.17-3.24 (m, 2H; OC*H*, ring C*H*H), 2.94 (q, *J*(H, H)=11.4 Hz, 1H; ring CH*H*), 2.47 (dt, *J*(H, H)=12.0, 5.8 Hz, 1H; ring C*H*H), 2.22 (dt, *J*(H, H)=11.4, 5.4 Hz, 1H; ring CH*H*), 1.80 (dqn, *J*(H, H)=14.9, 7.5 Hz, 1H; C*H*HCH_3), 1.41-1.49 (m, 1H; CH*H*CH_3), 0.72 (t, *J*(H, H)=7.4 Hz, 3H; CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=159.1, 135.6, 135.5, 133.5, 133.1, 130.5, 130.4, 129.8, 129.7, 129.3, 127.8, 127.7, 126.6, 113.6, 84.8 (OCH), 80.9 (OCH), 70.8 (OCH_2Ar), 64.7 (OCH_2Si), 60.9 (3-C), 55.2 (OCH_3), 33.4 (allylic CH_2), 28.2 (allylic CH_2), 26.8 ($C(CH_3)_3$), 23.8 (CH_2CH_3), 19.1 ($C(CH_3)_3$), 10.2 (CH_2CH_3); MS (CI, NH_3): *m/z*(%): 610 ($(M+NH_4)^+$, 10); (ES) Found 610.3106, $C_{35}H_{49}O_4NSi^{35}Cl$ requires 610.3110.

Data for the oxetane (-)-**72**: R_f 0.28 (hexane: ether, 3:1); $[a]_D^{25}$ -20.5 (*c* 0.22, $CHCl_3$); IR ($CHCl_3$ film): ν=2930, 2857; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.64-7.68 (m, 4H; Ar), 7.40-7.48 (m, 6H; Ar), 5.57 (dt, *J*(H, H)=10.7, 5.9 Hz, 1H; C*H*=CH), 5.48 (dt, *J*(H, H)=10.7, 5.8 Hz, 1H; CH=C*H*), 4.56-4.84 (m, 3H), 4.10 (ddd, *J*(H, H)=11.8, 5.3, 2.3 Hz, 1H; 4-H), 3.77-3.85 (m, 3H), 3.26-3.40 (m, 3H; OC*H*, ring CH_2), 2.54 (dt, *J*(H, H)=11.3, 5.3 Hz, 1H; ring C*H*H), 2.10-2.14 (m, 1H; ring CH*H*), 1.07 (s, 9H; $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=136.5, 135.5, 133.1, 132.9, 129.90, 128.88, 128.3, 127.8, 127.7, 127.6, 86.9, 77.4 (1-C or 3-C or 9-C), 72.7 (1-C or 3-C or 9-C), 75.4 (OCH_2Ar), 63.8, 58.1 (4-C), 33.4 (ring CH_2), 29.1 (ring CH_2), 26.8 ($C(CH_3)_3$), 19.1 ($C(CH_3)_3$); MS (CI, NH_3): *m/z*(%): 474 ($(M+NH_4)^+$, 100), 457 ($(M+H)^+$, 15); (ES) Found 474.2230, $C_{26}H_{37}O_3NSi^{35}Cl$ requires 474.2231.

(Z, 2*S*, 3*S*, 8*R*, 9*R*)-3-tButyldimethylsilanyloxy-9-tbutyldiphenylsilanyloxymethyl-8-chloro-2-hydroxymethyl-2,3,4,7,8,9-hexahydro-oxonine, (-)-73* and *(Z, 2*R*, 3*S*, 8*R*, 9*R*)-3-tbutyldimethylsilanyloxy-9-tbutyldiphenylsilanyloxymethyl-8-chloro-2-hydroxymethyl-2,3,4,7,8,9-hexahydro-oxonine, (-)-75



(-)-**73**



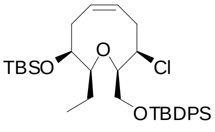
(-)-**75**

To a stirred solution of a mixture of the corresponding of the *bis*-silyl ethers (167.8 mg, 0.238 mmol) in MeOH (8 mL) was added PPTS (60.0 mg, 0.239 mmol). The resulting solution was stirred for 3 days. The reaction was then quenched by the addition of saturated solution of aqueous $NaHCO_3$ (10 mL) and ether (10 mL). The aqueous phase was extracted with ether (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give the crude product. Purification by flash column chromatography (DCM) gave the 2,9-*trans* alcohol (-)-**75** (50.8 mg, 36%); R_f 0.49 (DCM); $[a]_D^{25}$ -21.3 (*c* 0.32, $CHCl_3$); IR ($CHCl_3$ film):

ν=3476; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.66-7.75 (m, 4H; Ar), 7.40-7.48 (m, 6H; Ar), 5.83 (dt, *J*(H, H)=10.4, 7.8 Hz, 1H; C*H*=CH), 5.48 (dt, *J*(H, H)=10.4, 6.5 Hz, 1H; CH=C*H*), 4.20 (ddd, *J*(H, H)=12.0, 4.2, 2.1 Hz, 1H; 8-H), 3.93-3.94 (m, 2H), 3.62-3.66 (m, 3H), 3.51-3.54 (m, 1H), 3.32-3.36 (m, 1H), 3.08 (q, *J*(H, H)=11.8 Hz, 1H; ring C*H*H), 2.92-2.98 (m, 1H; ring CH*H*), 2.44-2.49 (m, 1H; ring C*H*H), 2.04-2.09 (m, 1H; ring CH*H*), 1.85 (br s, 1H; CH$_2$O*H*), 1.08 (s, 9H; C(C*H*$_3$)$_3$), 0.89 (s, 9H; C(C*H*$_3$’)$_3$), 0.15 (s, 3H; Si(CH$_3$)), 0.06 (s, 3H; Si(CH$_3$’)); ^{13}C NMR (125 MHz, $CDCl_3$): δ=135.6, 135.5, 133.3, 132.9, 130.3, 129.92, 129.91, 127.81, 127.79, 126.1, 82.8 (2-C or 3-C or 9-C), 72.6 (2-C or 3-C or 9-C), 69.6 (2-C or 3-C or 9-C), 64.4 (1-C or 10-C), 62.9 (1-C or 10-C), 33.8 (ring CH$_2$), 32.1 (ring CH$_2$), 26.8 (C(*C*H$_3$)$_3$), 25.7 (C(*C*H$_3$’)$_3$), 19.1 (*C*(CH$_3$)$_3$), 17.7 (*C*(CH$_3$’)$_3$), -4.3 (Si(*C*H$_3$)), -4.9 (Si(*C*H$_3$’)); MS (CI, NH_3): *m/z*(%): 606 ((M+NH$_4$)$^+$, 100), 589 ((M+H)$^+$, 20); (ES) Found 606.3197, $C_{32}H_{53}O_4NSi_2{}^{35}Cl$ requires 606.3202.

And the 2,9-*cis* alcohol (-)-**73** (13.7 mg, 10%); R_f 0.69 (DCM); $[a]^{25}_{\mathrm{D}}$ -18.6 (*c* 0.27, $CHCl_3$); IR ($CHCl_3$ film): ν=3464; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.67-7.70 (m, 4H; Ar), 7.39-7.47 (m, 6H; Ar), 5.70 (dt, *J*(H, H)=10.8, 6.1 Hz, 1H; C*H*=CH), 5.47 (dt, *J*(H, H)=10.8, 5.6 Hz, 1H; CH=C*H*), 4.14 (ddd, *J*(H, H)=11.6, 5.6, 2.6 Hz, 1H; 8-H), 4.00-4.04 (m, 1H), 3.96 (dd, *J*(H, H)=10.6, 5.8 Hz, 1H; C*H*HOSi), 3.84 (dd, *J*(H, H)=10.6, 6.5 Hz, 1H; CH*H*OSi), 3.67-3.76 (m, 2H), 3.54-3.57 (m, 2H), 3.19 (q, *J*(H, H)=11.7 Hz, 1H; ring C*H*H), 3.03 (q, *J*(H, H)=12.0 Hz, 1H; ring CH*H*), 2.42-2.49 (m, 2H; ring C*H*H, CH$_2$OH), 1.96-2.01 (m, 1H; ring CH*H*), 1.08 (s, 9H; C(CH$_3$)$_3$), 0.90 (s, 9H; C(CH$_3$’)$_3$), 0.11 (s, 3H; Si(CH$_3$)), 0.07 (s, 3H; Si(CH$_3$’)); ^{13}C NMR (125 MHz, $CDCl_3$): δ=135.6, 135.5, 133.1, 132.9, 130.1, 129.9, 129.8, 127.8, 126.5, 82.8 (2-C or 3-C or 9-C), 79.9 (2-C or 3-C or 9-C), 72.8 (2-C or 3-C or 9-C), 65.1 (1-C or 10-C), 63.2 (1-C or 10-C), 60.4 (8-C), 33.3 (ring CH$_2$), 3.19 (ring CH$_2$), 26.8 (C(*C*H$_3$)$_3$), 25.9 (C(*C*H$_3$’)$_3$), 19.1 (*C*(CH$_3$)$_3$), 18.0 (*C*(CH$_3$’)$_3$), -4.4 (Si(*C*H$_3$)) -5.0 (Si(*C*H$_3$’)); MS (CI, NH_3): *m/z*(%): 606 ((M+NH$_4$)$^+$, 100), 589 ((M+H)$^+$, 10); (ES) Found 606.3193, $C_{32}H_{53}O_4NSi_2{}^{35}Cl$ requires 606.3202.

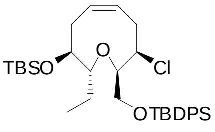
(Z, 2S, 3S, 8R, 9R)-3-tButyldimethylsilanyloxy-9-tbutyldiphenylsilanyloxymethyl-8-chloro-2-ethyl-2,3,4,7,8,9-hexahydro-oxonine, (-)-74



(-)-**74**

Following essentially the same procedure as that described for (-)-**71**/(-)-**72** above, the 2,9-*cis* alcohol (-)-**73** was converted to the ethyl substituted oxonene (-)-**74** (73%), obtained as a colourless oil; R_f 0.76 (hexane:ether, 9:1); $[\alpha]_D^{25}$ -15.9 (*c* 0.22, $CHCl_3$); IR ($CHCl_3$ film): ν=2928, 2856; ^1H NMR (500 MHz, $CDCl_3$): δ=7.66-7.71 (m, 4H; Ar), 7.39-7.47 (m, 6H; Ar), 5.71 (dt, *J*(H, H)=10.9, 6.2 Hz, 1H; C*H*=CH), 5.47 (dt, *J*(H, H)=10.9, 5.8 Hz, 1H; CH=C*H*), 4.26 (ddd, *J*(H, H)=11.4, 5.4, 2.6 Hz, 1H; 8-H), 3.90-3.94 (m, 1H), 3.85-3.87 (m, 2H), 3.54 (dt, *J*(H, H)=6.2, 2.7 Hz, 1H), 3.17-3.24 (m, 2H; OCH, ring, C*H*H), 2.97 (q, *J*(H, H)=11.5 Hz, 1H; ring CH*H*), 2.44 (dt, *J*(H, H)=11.5, 5.4 Hz, 1H; ring C*H*H), 1.94-1.98 (m, 1H; ring CH*H*), 1.79 (dqn, *J*(H, H)=14.7, 7.4, 1H; C*H*HCH_3), 1.39 (dqn, *J*(H, H)=14.7, 7.4 Hz, 1H; CH*H*CH_3), 1.07 (s, 9H; $C(CH_3)_3$), 0.90 (s, 9H, $C(CH_3')_3$), 0.80 (t, *J*(H, H)=7.4 Hz, 3H; CH_2CH_3), 0.09 (s, 3H; $Si(CH_3)$), 0.04 (s, 3H; $Si(CH_3')$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=135.5, 135.4, 133.5, 133.1, 130.6, 129.7, 127.7, 126.2, 125.5, 84.7 (2-C or 3-C or 9-C), 79.2 (2-C or 3-C or 9-C), 71.5 (2-C or 3-C or 9-C), 60.8 (8-C), 64.4 (10-C), 33.2 (ring CH_2), 32.0 (ring CH_2), 26.8 ($C(CH_3)_3$), 25.9 ($C(CH_3')_3$), 23.2 (CH_2CH_3), 19.1 ($C(CH_3)_3$), 18.0 ($C(CH_3')_3$), 10.5 (CH_2CH_3) -4.2 ($Si(CH_3)$), -4.9 ($Si(CH_3')$); MS (CI, NH_3): *m/z*(%): 604 ($(M+NH_4)^+$, 100); (ES) Found 604.3399, $C_{33}H_{55}O_3NSi_2{}^{35}Cl$ requires 604.3409.

(Z, 2*R*, 3*S*, 8*R*, 9*R*)-3-tButyldimethylsilanyloxy-9-tbutyldiphenylsilanyloxymethyl-8-chloro-2-ethyl-2,3,4,7,8,9-hexahydro-oxonine, (-)-76

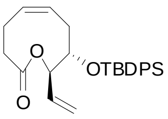


(-)-**76**

Following essentially the same procedure as that described for (-)-**71**/(-)-**72** above, except using CuCN instead of CuI, the 2,9-*trans* alcohol (-)-**75** was converted to the ethyl substituted oxonene (-)-**76** (36%), obtained as a colourless oil; R_f 0.76 (hexane:ether, 9:1); $[\alpha]_D^{25}$ -17.2 (*c* 0.14, $CHCl_3$); IR ($CHCl_3$ film): ν=2929, 2856; ^1H NMR (500 MHz, $CDCl_3$): δ=7.64-7.69 (m, 4H; Ar), 7.38-7.47 (m, 6H; Ar), 5.79-5.85

(m, 1H; C*H*=CH), 5.44-5.49 (m, 1H; CH=C*H*), 4.34 (ddd, *J*(H, H)=12.3, 4.6, 1.8 Hz, 1H; 8-H), 3.97 (t, *J*(H, H)=9.7 Hz, 1H; C*H*HOSi), 3.75 (dd, *J*(H, H)=9.7, 4.6 Hz, 1H; CH*H*OSi), 3.49-3.52 (m, 1H), 3.13-3.31 (m, 3H; 2 × OC*H*, ring C*H*H), 3.05 (ddd, *J*(H, H)=14.0, 11.2, 7.2 Hz, 1H; ring CH*H*), 2.45 (dt, *J*(H, H)=11.2, 5.4 Hz, 1H; ring C*H*H), 1.93 (dd, *J*(H, H)=14.0, 6.9 Hz, 1H; ring CH*H*), 1.63 (dqn, *J*(H, H)=14.9, 7.4 Hz, 1H; CH*H*CH_3), 1.07 (s, 9H; $C(CH_3)_3$), 0.98 (s, 9H; $C(CH_3')_3$), 0.78-0.86 (m, 1H; C*H*HCH_3), 0.73 (t, *J*(H, H)=7.2 Hz, 3H; CH_2CH_3), 0.11 (s, 3H; $Si(CH_3)$), 0.03 (s, 3H; $Si(CH_3')$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=135.6, 135.5, 135.4, 133.6, 133.1, 130.9, 129.9, 129.8, 127.8, 125.6, 85.4 (2-C or 3-C or 9-C), 72.9 (2-C or 3-C or 9=C), 71.4 (2-C or 3-C or 9-C), 63.7 (*C*H_2OSi), 34.3 (ring CH_2), 32.4 (ring CH_2), 26.8 ($C(CH_3)_3$), 25.7 ($C(CH_3')_3$), 24.8 (CH_2CH_3), 19.1 ($C(CH_3)_3$), 17.8 ($C(CH_3')_3$), 10.6 (CH_2CH_3), -4.2 ($Si(CH_3)$), -4.7 ($Si(CH_3')$); MS (ES): *m/z*(%): 609 ($(M+Na)^+$, 100); Found 609.2975, $C_{33}H_{51}O_3NaSi_2{}^{35}Cl$ requires 609.2963.

(Z, 8*S*, 9*R*)-8-*t*Butyldiphenylsilanyloxy-9-vinyl-2,3,4,7,8,9-hexahydro-oxonin-2-one, (-)-83

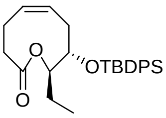


(-)-**83**

To a stirred solution of CH_3PPh_3Br (870 mg, 2.44 mmol) in THF (15 mL) at -78 °C was slowly added KHMDS (4.1 mL of a 0.5 M solution in toluene, 2.05 mmol). The resultant yellow solution was allowed to warm to room temperature and stirred for 30 min. To a stirred solution of the aldehyde (+)-**82**{Congreve, 1993 #173} (516 mg, 1.22 mmol) in THF (10 mL) at -78 °C, was added the preformed ylide solution. The reaction was then allowed to warm to room temperature and stirred for 30 min, before being quenched by the addition of a saturated solution of aqueous NH_4Cl (5 mL) and water (10 mL). The aqueous layer was extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude product. Purification by flash chromatography (petroleum ether 40-60:EtOAc, 10:1) afforded the vinyl substituted lactone (-)-**83** (503 mg, 98%) as a clear and colourless oil; (Found C, 74.3; H, 7.6%; $C_{26}H_{32}O_3Si$ requires C, 74.24; H, 7.67); R_f 0.29 (petroleum ether 40-60:ether, 9:1); $[a]_D^{25}$ -5.5 (*c* 1.78, $CHCl_3$); IR (CH_3Cl film): ν=1736; ^{1}H NMR (500 MHz, $CDCl_3$):

δ=7.70-7.71 (m, 4H; Ar), 7.39-7.48 (m, 6H; Ar), 5.90 (ddd, *J*(H, H)=17.2, 10.6, 5.7 Hz, 1H; C*H*=CHH), 5.51-5.54 (m, 1H; CH=C*H*), 5.37-5.39 (m, 1H; C*H*=CH), 5.29 (d, *J*(H, H)=17.2 Hz, 1H; *trans* CH=CH*H*), 5.25-5.27 (m, 1H; 9-H), 5.17 (d, *J*(H, H)=10.6 Hz, 1H; *cis* CH=C*H*H), 3.86-3.89 (m, 1H; 8-H), 2.12-2.47 (m, 6H; 3 × ring CH_2), 1.08 (s, 9H; $C(CH_3)$); ^{13}C NMR (62.5MHz, $CDCl_3$): δ=174.0 (2-C), 136.1, 135.9, 135.2, 134.8, 133.9, 133.6, 135.1, 128.8, 128.7, 128.7, 128.4, 127.8, 127.6, 117.1, 79.4 (8-C or 9-C), 76.2 (8-C or 9-C), 34.0, 33.6, 26.9, 23.7, 19.3; MS (ES): *m/z*(%): 438 ($(M+Na)^+$, 100), 421 ($(M+H)^+$, 60); Found 421.2196, $C_{26}H_{33}O_3Si$ requires 421.2199.

(Z, 8*S*, 9*R*)-8-*t*Butyldiphenylsilanyloxy-9-ethyl-3,4,8,9-tetrahydro-3*H*-oxonin-2-one, ent-4 *according to the procedure of Hoffmann:*{Kruger, 1997 #20}

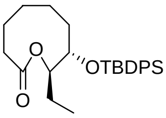


ent-**4**

To a stirred solution of the lactone (-)-**83** (17.8 mg, 0.042 mmol) in MeOH (4 mL) was added palladium on charcoal (10% Pd content) (4.9 mg). The resultant suspension was then flushed with hydrogen (3 × hydrogen balloon) and the solution was stirred under an atmosphere of hydrogen (hydrogen balloon) for 20 min. The reaction mixture was then filtered through a short pad of Celite™ and the resultant filtrate was concentrated *in vacuo* to give the crude product. Purification by column chromatography (hexane:ether, 10:1) furnished the ethyl substituted lactone *ent*-**4** (12.0 mg, 67%) as a colourless oil; R_f 0.30 (hexane:ether, 9:1); (Found C, 74.1; H, 8.3%; $C_{26}H_{34}O_3Si$ requires C, 73.9; H, 8.1); $[a]_D^{24}$ +14.5 (*c* 0.35, $CHCl_3$), lit. enantiomer $[a]_D^{24}$ -11.6 (*c* 1.00, $CHCl_3$) for **4**; IR (CH_3Cl film): ν=1733; ^1H NMR (500 MHz, $CDCl_3$): δ=7.68-7.71 (m, 4H; Ar), 7.39-7.46 (m, 6H; Ar), 5.47-5.52 (m, 1H; C*H*=CH), 5.30-5.35 (m, 1H; CH=C*H*), 4.87 (dt, *J*(H, H)=8.7, 2.7 Hz, 1H; 8-H), 3.70-3.74 (m, 1H; 9-H), 2.31-2.41 (m, 2H; ring CH_2), 2.16-2.23 (m, 4H; 2 × ring CH_2), 1.82 (dq, *J*(H, H)=14.8, 7.4 Hz, 1H; C*H*HCH$_3$), 1.33 (dqn, *J*(H, H)=14.8, 7.4 Hz, 1H; CH*H*CH$_3$), 1.07 (s, 9H; $C(CH_3)_3$), 0.83 (t, *J*(H, H)=7.4 Hz, 3H; CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=174.7 (2-C), 135.9, 135.8, 133.8, 133.3, 129.8, 129.7, 129.6, 127.7, 127.6, 127.3, 90.7 (8-C or 9-C), 76.1 (8-C or 9-C), 34.1 (ring CH_2), 33.8 (ring CH_2), 26.9 ($C(CH_3)_3$), 19.3 ($C(CH_3)_3$), 25.7 (ring CH_2 or CH_2CH_3), 23.9 (ring CH_2 or

*C*H$_2$CH$_3$), 9.4 (CH$_2$*C*H$_3$); MS (ES): *m/z*(%): 445 ((M+Na)$^+$, 100), 423 ((M+H)$^+$, 50); Found 445.2177, $C_{26}H_{34}O_3SiNa$ requires 445.2175.

*(8*S*, 9*R*)-8-(tButyldiphenylsilanyloxy)-9-ethyl-oxonan-2-one*



To a stirred solution of the lactone (-)-**83** (8.2 mg, 0.020 mmol) in MeOH (4 mL) was added palladium on charcoal (10% Pd content) (4.4 mg). The resultant suspension was then flushed with hydrogen (3 × hydrogen balloon) and the solution was stirred under an atmosphere of hydrogen (hydrogen balloon) for 1 h. The reaction mixture was then filtered through a short pad of Celite™ and the resultant filtrate was concentrated *in vacuo* to give the crude product. Purification by column chromatography (hexane:ether, 10:1) furnished the title compound (4.4 mg, 54%) as a colourless oil; R_f 0.34 (hexane:ether, 9:1); $[a]_{\mathrm{D}}^{24}$ +3.2 (*c* 0.22, $CHCl_3$); IR (film): ν=1737; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.66-7.70 (m, 4H; Ar), 7.38-7.46 (m, 6H; Ar), 4.89 (ddd, *J*(H, H)=9.6, 7.2, 3.0 Hz, 1H), 3.65 (ddd, *J*(H, H)=7.2, 5.6, 3.0 Hz, 1H), 2.34 (ddd, *J*(H, H)=13.5, 8.9, 4.9 Hz, 1H; 2-H), 2.26 (ddd, *J*(H, H)=13.5, 8.1, 3.3 Hz, 1H; 2-H'), 1.90-1.97 (m, 1H; ring CH_2), 1.76 (dq, *J*(H, H)=14.9, 7.5 Hz, 1H; $C\mathit{H}HCH_3$), 1.36-1.54 (m, 6H; 5 ring CH_2, $CH\mathit{H}CH_3$), 1.13-1.28 (m, 2H; ring CH_2), 1.06 (s, 9H; $C(CH)_3$), 0.85 (t, *J*(H, H)=7.4 Hz, 3H; $CH_2C\mathit{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=175.4 (2-C), 135.9, 135.8, 134.2, 133.6, 129.7, 129.6, 127.6, 127.5, 79.6 (8-C or 9-C), 76.5 (8-C or 9-C), 35.5 (2-C or 3-C), 31.7 (2-C or 3-C), 25.9, 25.6, 24.2, 23.6, 26.9 ($C(\mathit{C}H_3)_3$), 19.3 ($\mathit{C}(CH_3)_3$), 9.6 ($CH_2\mathit{C}H_3$); MS (ES): *m/z*(%): 447 ($(M+Na)^+$, 80), 425 ($(M+H)^+$, 100); Found 425.2521, $C_{26}H_{37}O_3Si$ requires 425.2512.

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