Supplementary Material (ESI) for Organic and Biomolecular Chemistry

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

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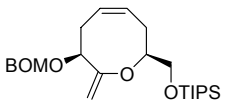
Experimental

General Information: ^{1}H-NMR spectra were recorded on Bruker DPX-250 (250 MHz), Bruker DRX-400 (400 MHz) and Bruker DRX-500 (500 MHz) spectrometers using deuterochloroform as an internal deuterium lock. The chemical shifts are quoted in ppm relative to tetramethylsilane (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 shift are quoted in ppm relative to tetramethylsilane (δ = 0.00 ppm). The multiplicity of the signal was determined by attached proton tests (APT) or distortionless enhancement by polarisation transfer (DEPT) experiments and is indicated as C (s), CH (d), CH_2 (t) and CH_3 (q) groups where determined. Infrared spectra were recorded on Perkin-Elmer 1600 series FTIR (nujol, film, $CHCl_3$) and Perkin-Elmer Spectrum One ATR-FTIR (film) spectrometers. Mass spectra were recorded by the EPSRC Mass Spectrometry Service Centre, University of Swansea or the University of Cambridge. In Swansea, Electron Impact (EI) and Chemical Ionisation (CI) low resolution spectra were carried out on a VG model 12-253 under ACE conditions and a Quattro II low resolution triple quadrupole MS. Accurate mass measurements for EI and CI were performed on a +VG ZAB-E and Finnigan MAT 900 XLT instruments. In Cambridge, FAB, EI and CI low resolution and accurate mass spectra were performed on a Kratos MS-890 and on a Micromass Q-TOF instrument. Electrospray spectra were determined with an ES Bruker FTICR. All CI measurements were performed with NH_3 as the carrier gas. Microanalyses were carried out by the staff of the Microanalytical Service at the University of Cambridge. Melting Points were determined using a Köfler block melting point apparatus and are

uncorrected. Optical specific rotations were carried out using a Perkin-Elmer 241 polarimeter in a cell of path length 1 dm. The concentration (*c*) is expressed in g/100 cm^3. The specific rotation, denoted as $[\alpha]_D^T$, implies units of $^{o}cm^2g^{-1}$ (T = temp ºC). 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.

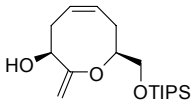
***(Z, 3S, 8S)-3-(Benzyloxymethyl)oxy-2-methylene-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2H-oxocine* 10**



To a stirred solution of the lactone **7**[1] (790 mg, 1.76 mmol) in toluene (60 mL) was added dimethyltitanocene (9.5 mL of a 50 mg/mL solution in toluene, 2.3 mmol) and the resulting orange solution was heated at reflux for 0.7 h. The resulting dark orange solution was allowed to cool and the solvent was removed *in vacuo*. The residue was dissolved in DCM and deactivated basic alumina was added (6% w/w water). The residue was preadsorbed onto alumina and purification by gravity chromatography (deactivated basic alumina, heaxane:ether, 20:1→10:1) provided the title compound **10** as a slightly yellow oil. Hexane was added and the yellow solution was allowed to stand overnight. Filtration through Celite™ followed by removal of the solvent *in vacuo* provided the enol ether **10** as a clear and colourless oil (558 mg, 1.25 mmol, 71%); (Found: C, 70.3; H, 9.6%; $C_{26}H_{42}O_4Si$ requires C, 69.9; H, 9.5%); $[\alpha]_D^{21}$ -90.6 (*c* 0.805 in $CHCl_3$); IR ($CDCl_3$): ν=1645 (enol ether); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.37-7.26 (5H, m, Ar), 5.83 (1H, dt, *J* (H, H)=10.9, 7.9 Hz), 5.65 (1H, dt, *J* (H, H)=10.6, 7.4 Hz), 4.88 (1H, d, *J* (H, H)=7.0 Hz), 4.75 (1H, d, *J* (H, H)=7.0 Hz), 4.72-4.72 (1H, d, *J* (H, H)=1.0 Hz, OCH=C*H*H), 4.68 (1H, d, *J* (H, H)=11.8 Hz), 4.59 (1H, d, *J* (H, H)=1.0, OCH=CH*H*), 4.56 (1H, d, *J* (H, H)=11.8 Hz), 4.22 (1H, dd, *J* (H,

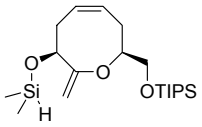
H)=10.7, 4.9 Hz), 3.97 (1H, dd, *J* (H, H)=9.5, 5.6 Hz), 3.97 (1H, dd, *J* (H, H)=9.5, 5.6 Hz), 3.86-3.77 (1H, m), 3.66 (1H dd, *J* (H, H)=9.5, 7.0 Hz), 2.80 (1H, q, *J* (H, H)=10.7 Hz, allylic), 2.45-2.18 (3H, m, allylic), 1.16-1.03 (21H, m, $((CH_3)_2CH)_3Si$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=162.0 (2-C), 138.0, 129.8, 129.0, 128.4, 128.0, 127.7, 102.7, 91.8, 86.1, 79.1, 69.6, 66.1 (CH_2OSi), 30.8, 30.2 (4-C, 7-C), 18.0 ($((\mathit{C}H_3)_2CH)_3Si$), 11.9 ($(((CH_3)_2\mathit{C}H)_3Si$); MS (EI): *m/z*(%): 446 (M^+, 8), 265 (100); Found 446.2852, $C_{26}H_{42}O_4Si$ requires 446.2852).

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



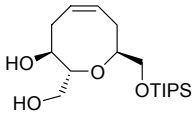
To a stirred solution of the enol ether **10** (245 mg, 0.55 mmol) in THF (20 mL) at -78 °C was added freshly prepared LiDBB (2 mL of a solution prepared by sonicating di-*tert*-butylbiphenyl (1 g, 3.8 mmol) and lithium (26 mg, 3.8 mmol) in THF (4 mL) for 2 h). Stirring was continued for 1 min whereupon the green colour of the LiDBB had mainly discharged. Further LiDBB (1 mL) was added and stirring was continued for 2 min with the dark green colour of the LiDBB remaining. The reaction mixture was quenched at -78 °C by the addition of a saturated solution of NH_4Cl (20 mL) and the reaction mixture was allowed to reach room temperature. Ether (20 mL) was added and the organic phase was separated. The aqueous phase was further extracted with ether (2 × 20 mL) and dried (K_2CO_3). Purification by gravity chromatography (deactivated basic alumina, hexane:ether, 2:1) provided the title compound **11** as a clear and colourless oil (168 mg, 0.52 mmol, 94%); $[\alpha]_D^{21}$ +5.9 (*c* 1.015 in $CHCl_3$); IR ($CDCl_3$): ν=3500, 1649; ^1H NMR (250 MHz, $CDCl_3$): δ=5.87-5.66 (m, 2H; 5-H, 6-H), 4.62 (d, *J* (H, H)=1.4 Hz, 1H; OC=C*H*H), 4.61 (d, *J* (H, H)=1.4 Hz, 1H; OC=CH*H*), 4.26-4.18 (m, 1H), 3.95-3.85 (m, 2H), 3.70-3.62 (m, 1H), 2.65 (dt, *J* (H, H)=12.6, 9.1 Hz, 1H; allylic), 2.38-2.24 (m, 3H; allylic), 2.08 (d, *J* (H, H)=8.0 Hz, 1H; OH), 1.16-1.01 (m, 21H; $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=164.2 (2-C), 129.4, 129.1 (5-C, 6-C), 99.5 (OC=$\mathit{C}H_2$), 84.4, 75.5 (3-C, 8-C), 65.3 (CH_2OSi), 33.0, 29.5 (4-C, 2-C), 18.0 ($((\mathit{C}H_3)_2CH)_3Si$), 11.9 ($(((CH_3)_2\mathit{C}H)_3Si$); MS (CI, NH_3): *m/z*(%): 344 ($(M+NH_4)^+$, 40), 327 ($(M+H)^+$, 30), 77 (100); Found 327.2353, $C_{18}H_{35}O_3Si$ requires 327.2353.

***(Z, 3S, 8S)-3-Dimethylsilyloxy-2-methylene-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2H-oxocine* 12**



To a stirred solution of the enol ether **11** (114 mg, 0.35 mmol) in 1,1,3,3-tetramethyldisilazane (0.8 mL) was added solid NH_4Cl (*ca*. 2 mg) and the reaction mixture was heated to 60 °C and stirred at that temperature overnight. The reaction mixture was allowed to cool, dry hexane was added and filtration through a cotton wool plug followed by removal of the solvent *in vacuo* gave the required silane **12** (132 mg, 0.34 mmol, 99%) as an unstable oil; IR ($CDCl_3$): ν=2118, 1646; ^{1}H NMR (250 MHz, $CDCl_3$): δ=5.85-5.75 (m, 1H), 5.69-5.58 (m, 1H), 4.66 (sp, *J* (H, H)=2.8 Hz, 1H; SiH), 4.59 (s, 1H; OC=C*H*H), 4.53 (s, 1H; OC=CH*H*), 4.17 (dd, *J* (H, H)=10.7, 4.9 Hz, 1H), 3.98 (dd, *J* (H, H)=9.4, 5.4 Hz, 1H), 3.82-3.77 (m, 1H; 8-H), 3.67 (dd, *J* (H, H)=9.4, 7.0 Hz, 1H), 2.78 (q, *J* (H, H)=10.8 Hz, 1H; allylic), 2.44-2.15 (m, 3H; allylic), 1.16-1.03 (m, 21H; $((CH_3)_2CH)_3Si$), 0.22 (d, *J* (H, H)=2.8 Hz, 6H; $(CH_3)_2SiH$)); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=164.7 (2-C), 129.8, 129.1 (5-C, 6-C), 100.7 (OC=*C*H_2), 86.2, 77.9 (3-C, 8-C), 66.2 (CH_2OSi), 32.7, 30.9 (4-C, 7-C), 18.0 ($((CH_3)_2CH)_3Si$), 11.9 ($(((CH_3)_2CH)_3Si$), -1.0 ($((CH_3)_2Si$); due to the instability of this compound satisfactory mass spectral data could not be obtained.

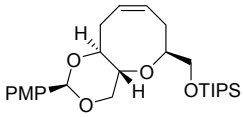
***(Z, 2R, 3S, 8S)-3-Hydroxy-2-hydroxymethyl-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2H-oxocine* 13**



In a glove box a Schlenk tube was charged with (bicyclo(2.2.1)hepta-2,5-diene)(1,4-bis(diphenylphosphino)butane)rhodium(I) tetrafluoroborate (10 mg, 14.1 μmol). The Schlenk tube was removed form the glove box and the enol ether **11** (180 mg, 0.47 mmol) was added *via* cannula as a solution in THF (12 mL, 2 mL rinse). The resulting yellow solution was heated to 65 °C and stirred at that temperature over night. The reaction mixture was allowed to cool, ethylenediaminetetraacetic acid, disodium salt dihydrate (*ca.* 50 mg) was added and the resulting suspension was stirred for 1 h. The reaction mixture was diluted with hexane and filtered through a

pad of Celite™. The solvent was removed *in vacuo* to furnish a brown oil which was taken-up in THF / MeOH (1:1, 6 mL) to which a 15% solution of potassium hydroxide (0.73 mL) and 30% H_2O_2 (0.38 mL) were added. The reaction mixture was stirred for 1 h whereupon further potassium hydroxide solution (0.3 mL) and H_2O_2 (0.3 mL) were added. After 0.5 h the reaction was quenched by the addition of powdered sodium thiosulfate and stirring was continued overnight. The suspension was diluted with EtOAc (25 mL), dried ($MgSO_4$) and filtered through a pad of Celite™. The solvent was removed *in vacuo* and purification by flash chromatography (DCM:MeOH, 100:0→97:3) yielded the enol ether **11** (7 mg, 21 μmol, 5%). Further elution of the column furnished the title compound **13** (139 mg, 40 mmol, 86%) which was a slightly impure and proved difficult to purify further and hence was used in the next reaction without further purification. Characterisation is on the slightly impure compound; R_f 0.2 (DCM:MeOH, 95:5); IR ($CHCl_3$): ν=3621, 3441; ^{1}H NMR (250 MHz, $CDCl_3$): δ=5.92-5.70 (m, 2H; 5-H, 6-H), 3.95 (dd, *J* (H, H)=11.3, 9.4 Hz, 1H), 4.0-3.85 (br, 1H; OH), 3.84-3.49 (m, 6H), 2.45-2.02 (m, 5H; 4-H, 4-H', 7-H, 7-H', OH), 1.15-1.03 (21H, m, $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=128.2, 128.0 (5-C, 6-C), 77.3, 76.5, 72.2, 64.9, 63.7, 35.4, 28.3, 17.9 $(((CH_3)_2CH)_3Si)$, 11.9 $(((CH_3)_2CH)_3Si)$; MS (CI, NH_3): *m/z*(%): 362 $((M+NH_4)^+$, 15%), 345 $((M+H)^+$, 100); Found 345.2460, $C_{18}H_{37}O_4Si$ requires 345.2461.

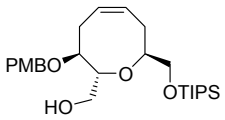
***(Z, 2*R*, 4a*R*, 6*S*, 10a*S*)-2-(4-Methoxy-phenyl)-6-triisopropylsilanyloxymethyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxa-benzocyclooctene* 14**



To a stirred solution of the slightly impure diol **13** (139 mg, 0.4 mmol) in benzene (12 mL) were added freshly distilled anisaldehyde (58 μl, 65 mg, 0.48 mmol) and PPTS (5 mg). The reaction mixture was heated at reflux with azeotropic removal of water (Dean-Stark apparatus) for 12 h and then allowed to cool. The solvent was removed *in vacuo* and the residue was preabsorbed onto silica. Purification by flash chromatography (hexane:ether, 5:1) yielded the title compound **14** (156 mg, 0.34 mmol, 85%) as a clear and colourless oil; R_f 0.3 (hexane:ether, 3:1); $[\alpha]_D^{18}$ -8.7 (*c* 0.195 in $CHCl_3$); IR ($CHCl_3$): ν=2944, 2866; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.40 (d, *J* (H, H)=8.6 Hz, 2H; Ar), 6.88 (d, *J* (H, H)=8.6 Hz, 2H; Ar), 5.90 (dt, *J* (H, H)=10.3,

8.3 Hz, 1H; 9-H), 5.72 (dt, *J* (H, H)=10.3, 9.6 Hz, 1H; 8-H), 5.39 (s, 1H; 2-H), 4.17 (dd, 1H; *J* (H, H)=10.8, 5.3 Hz, 1H; 4-H), 3.89 (ddd, *J* (H, H)=10.8, 8.3, 5.3 Hz, 1H; 4a-H), 3.88 (dd, *J* (H, H)=10.5, 5.8 Hz, 1H; C*H*HOSi), 3.81 (dd, *J* (H, H)=10.5, 5.1 Hz, 1H; CH*H*OSi), 3.80 (s, 3H; CH_3O), 3.62-3.59 (m, 1H; 6-H), 3.57 (t, *J* (H, H)=10.8 Hz, 1H; 4-H'), 3.50 (ddd, *J* (H, H)=13.3, 8.5, 2.6 Hz, 1H; 10a-H), 2.55-2.47 (m, 2H; 7-H, 10-H), 2.40 (ddd, *J* (H, H)=13.3, 8.5, 2.6 Hz, 1H; 10-H'), 2.14 (ddd, *J* (H, H)=13.9, 6.9, 3.0 Hz, 1H; 7-H'), 1.16-1.05 (21H, m, $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=160.0, 130.5, 129.0, 127.4, 113.7, 100.8 (2-C), 80.5, 76.3, 70.3, 67.8 (4-C), 65.4 (CH_2OSi), 55.3 (CH_3O), 33.0, 28.3, 18.0 ($((CH_3)_2CH)_3Si$), 11.9 ($((CH_3)_2CH)_3Si$); MS (CI, NH_3): *m/z*(%): 463 ($(M+H)^+$, 45), 154 (100); Found 463.2876, $C_{26}H_{42}O_5Si$ requires *M*, 463.2880.

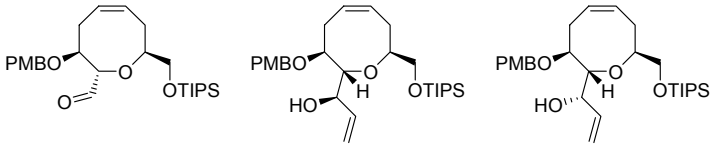
***(Z, 2*R*, 3*S*, 8,S)-2-Hydroxymethyl-3-(p-methoxybenzyloxy-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2*H*-oxocine* 15**



To a stirred solution of the oxocane **14** (131 mg, 0.28 mmol) in toluene (4 mL) at -78 °C was added DIBAL-H (1.98 mL of a 1.0 M solution in DCM, 1.98 mmol). The resulting solution was stirred at -50 °C for 1 h and then at -30 °C for 1.5 h whereupon TLC analysis indicated that all the starting material had been consumed. The reaction mixture was recooled to -78 °C and quenched by the dropwise addition of MeOH (1.5 mL). The reaction mixture was allowed to warm to ambient temperature and a saturated solution of NH_4Cl (6 mL), 1 M sodium potassium tartrate (6 mL) and ether (10 mL) were added. The resulting gel was stirred until dissolution occurred (*ca.* 1 h). The organic phase was separated and the aqueous phase extracted with ether (10 mL). The organic phases were washed with brine (10 mL) and dried ($MgSO_4$) and the solvent was removed *in vacuo*. Purification by flash chromatography (hexane:ether, 1:1) gave the title compound **15** (104 mg, 0.22 mmol, 80%) as a white crystalline solid; mp 121-121.5 °C (from hexane); $[\alpha]_D^{21}$ +70.2 (*c* 0.43 in $CHCl_3$); IR ($CHCl_3$): ν=3451; ^1H NMR (250 MHz, $CDCl_3$): δ=7.23 (d, *J* (H, H)=8.6 Hz, 2H; Ar), 6.88 (d, *J* (H, H)=8.6 Hz, 2H; Ar), 5.90-5.70 (m, 2H; 5-H, 6-H), 4.56 (d, *J* (H, H)=11.0 Hz, 1H; ArC*H*H), 4.34 (d, *J* (H, H)=11.0 Hz, 1H; ArCH*H*), 3.96-3.76 (m, 8H), 3.79 (s, 3H; CH_3O), 3.59 (dd,*J* (H, H)=11.3, 3.1 Hz, 1H), 3.44 (ddd, *J* (H, H)=10.3, 8.2, 1.6 Hz,

1H), 3.27 (dt, *J* (H, H)=8.7, 2.8 Hz, 1H), 2.53 (ddd, *J* (H, H)=13.5, 8.3, 2.8 Hz, 1H; allylic), 2.41-2.29 (m, 1H; allylic), 2.23-2.10 (m, 2H; allylic), 1.19-0.98 (21H, m, $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=159.3, 130.0, 129.5, 128.7, 127.9, 113.9, 79.2, 75.6, 71.4, 64.8 (CH_2OSi), 55.3 (CH_3O), 30.1, 28.5, 17.9 ($((CH_3)_2CH)_3Si$), 11.9 ($((CH_3)_2CH)_3Si$); MS (CI, NH_3): *m/z*(%): 482 $((M+NH_4)^+$, 10), 465 $((M+H)^+$, 40), 345 (100); Found 465.3041, $C_{26}H_{45}O_5Si$ requires 465.3036.

***(Z, 2*R*, *3*S, *8*S)-2-Carboxaldehyde-3-(4-methoxybenzyl)oxy-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2H-oxocine* 16**, ***(Z, 2*R*, *3*S, *8*S)-2-((S)-1-hydroxy-prop-2-eneyl)-3-(4-methoxybenzyl)oxy-8-(triisopropylsilyloxy)methyl-3,4,7,8-tetrahydro-2H-oxocine* 18**, and ***(Z, 2*R*, *3*S, *8*S)-2-((R)-1-hydroxy-prop-2-eneyl)-3-(4-methoxybenzyl)oxy-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2H-oxocine* 17**



To a stirred solution of the oxocane **15** (64 mg, 0.138 mmol) in DMSO (10 mL) at ambient temperature was added IBX (116 mg, 414 mmol). The resulting cloudy suspension became clear and colourless within 10 min and was stirred overnight. Water (20 mL) and ether (15 mL) were added and the organic phase was separated. The aqueous phase was extracted with ether (2 × 15 mL) and the organic phases were washed with water (2 × 20 mL), brine (20 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to yield a semi-solid colourless residue **16** that was used in the next reaction without further purification; IR ($CDCl_3$): ν=2857, 1734; ^1H NMR (250 MHz, $CDCl_3$): δ=9.67 (d, *J* (H, H)=1.8 Hz, 1H; CHO), 7.23 (d, *J* (H, H)=8.8 Hz, 2H; Ar), 6.85 (d, *J* (H, H)=8.8 Hz, 2H; Ar), 5.90-5.70 (m, 2H; 5-H, 6-H), 4.58 (d, *J* (H, H)=11.1 Hz, 1H; ArC*H*H), 4.41 (d, *J* (H, H)=11.0 Hz, 1H; ArCH*H*), 4.19 (dd, *J* (H, H)=9.4, 1.7 Hz, 1H; 2-H), 3.99-3.95 (m, 5H), 3.79 (s, 3H; CH_3O), 2.59-2.30 (m,4H; allylic), 1.12-1.00 (m, 21H; $((CH_3)_2CH)_3Si$). The crude aldehyde **16** was coevaporated with toluene (3 × 2 mL) and put under argon. In a glove box a Schlenk tube was charged with anhydrous cerium(III) chloride (190 mg, 0.772 mmol, ex-Aldrich). THF (3 mL) was added and the resulting granular suspension was sonicated for 2 h to yield a milky white suspension which was stirred overnight. The Schlenk

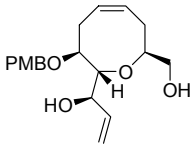
flask was then cooled to -78 °C and vinylmagnesium bromide (0.69 mL of a 1.0 M solution in THF, 0.69 mmol) was added. The yellow reaction mixture was stirred for 2 h at -78 °C and the aldehyde **16** was added as solution in THF (1 mL, 2 × 0.5 mL) *via* cannula. The reaction mixture was stirred for 1 h at -78 °C and then at ambient temperature for 15 min. The reaction mixture was quenched by the addition of a saturated aqueous solution of NH_4Cl (15 mL) ether (15 mL) and enough 2 M hydrochloric acid to form a homogenous solution. The organic phase was separated and the aqueous phase was extracted with ether (2 × 15 mL). The organic phases were washed with brine (15 mL) and dried ($MgSO_4$). Purification by flash chromatography ($CHCl_3$:DCM, 1:1→1:0) gave **18** (10 mg, 20 μmol, 15%) as a clear and colourless oil and **17** (50 mg, 10.2 mmol, 74%) as a white crystalline solid.

Data for **18**: R_f 0.2 ($CHCl_3$); $[\alpha]_D^{14}$ +2.1 (*c* 0.195 in $CHCl_3$); IR ($CHCl_3$): ν=3466; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.24 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 6.87 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 6.01 (ddd, *J* (H, H)=17.2, 10.5, 4.7 Hz, 1H; C*H*=CH_2), 5.85-5.77 (m, 2H; 5-H, 6-H), 5.33 (d, *J* (H, H)=17.3 Hz, 1H; CH=C*H*H-*trans*), 5.18 (d, *J* (H, H)=10.5 Hz, 1H; CH=CH*H*-*cis*), 4.54 (d, *J* (H, H)=10.5 Hz, 1H; ArC*H*H), 4.35 (d, *J* (H, H)=10.5 Hz, 1H; ArCH*H*), 4.30-4.25 (br, 1H; C*H*OH), 3.88 (dd, *J* (H, H)=10.1, 6.2 Hz, 1H; C*H*HOSi), 3.80 (s, 3H; CH_3O), 3.80-3.75 (m, 1H; 8-H), 3.74 (dd, *J* (H, H)=8.8, 3.1 Hz, 1H; 2-H), 3.67 (dd, *J* (H, H)=10.1, 6.2 Hz, 1H; CH*H*OSi), 3.57 (dt, *J* (H, H)=8.8, 2.5 Hz, 1H; 3-H), 3.21 (d, *J* (H, H)=9.1 Hz, 1H; OH), 2.57-2.52 (m, 1H; 4-H), 2.44-2.32 (m, 3H; 4-H', 7-H, 7-H'), 1.12-1.04 (21H, m, $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=159.4, 139.0, 129.9, 129.7, 128.6, 128.6, 114.7, 113.0, 80.2, 76.0, 74.0, 71.2, 64.1 (CH_2OSi), 55.3 (CH_3O), 29.7, 28.8, 18.0 ($((CH_3)_2CH)_3Si$), 11.9 ($((CH_3)_2CH)_3Si$); MS (CI, NH_3): *m/z*(%): 508 ($(M+NH_4)^+$, 20), 491 ($(M+H)^+$, 100); Found 491.3191, $C_{28}H_{47}O_5Si$ requires 461.3193.

Data for **17**: mp 99-100 °C (from hexane); R_f 0.15 ($CHCl_3$); $[\alpha]_D^{24}$ +78.9 (*c* 0.175 in $CHCl_3$); IR ($CHCl_3$): ν=3419; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.24 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 6.86 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 5.93 (ddd, *J* (H, H)=17.5, 10.4, 6.5 Hz, 1H; C*H*=CH_2), 5.86-5.81 (m, 1H; 5-H), 5.77-5.75 (m, 1H; 6-H), 5.22 (d, 1H; *J* (H, H)=17.5 Hz, 1H; CH=C*H*H-*trans*), 5.18 (d, 1H; *J* (H, H)=10.4 Hz, 1H; CH=CH*H*-*cis*), 4.62 (d, *J* (H, H)=11.46 Hz, 1H; OH), 4.58 (d, *J* (H, H)=10.9 Hz, 1H; ArC*H*H), 4.48 (brdd, *J* (H, H)=11.5, 4.5 Hz, 1H; C*H*OH), 4.34 (d, *J* (H, H)=10.9 Hz, 1H; ArCH*H*), 4.01 (dd, *J* (H, H)=11.6, 10.5 Hz, 1H; C*H*HOSi), 3.89 (dd, *J* (H, H)=9.3, 2.1 Hz, 1H;

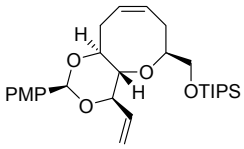
2-H), 3.87-3.82 (brm, 1H; 8-H), 3.80 (s, 3H; CH_3O), 3.56 (dd, *J* (H, H)=11.6, 2.5 Hz, 1H; CH*H*OSi), 3.35 (dt, *J* (H, H)=9.3, 2.5 Hz, 1H; 3-H), 2.56 (ddd, *J* (H, H)=13.7, 8.6, 2.6 Hz, 1H; 4-H), 2.34 (dt, *J* (H, H)=13.7, 7.7 Hz, 1H; 4-H'), 2.18-2.12 (m, 2H; 7-H), 1.18-1.04 (m, 21H; $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=159.2, 137.2, 130.2, 129.1, 128.8, 127.7, 116.4 (CH_2=CH), 113.8, 79.1, 77.8, 77.6, 72.7, 70.9, 63.5 (CH_2OSi), 55.3 (CH_3O), 29.7, 28.4, 17.9 ($((CH_3)_2CH)_3Si$), 11.9 ($((CH_3)_2CH)_3Si$); MS (CI, NH_3): *m/z*(%): 491 ($(M+H)^+$, 10), 121 (100); Found 491.3184; $C_{28}H_{47}O_5Si$ requires 461.3193.

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



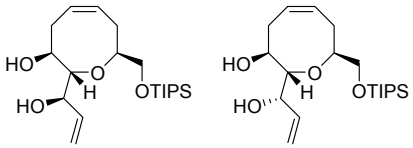
To a stirred solution of the oxocane **17** (4.8 mg, 10 μmol) in MeCN and water (3:1, 4 mL) was added CAN (32 mg, 59 μmol) and the resulting orange solution was stirred for 1 h at 0 °C. The reaction mixture was quenched by the addition of EtOAc (10 mL) and water (10 mL) and the organic phase was separated. The aqueous phase was extracted with EtOAc (10 mL) and the organic phases were washed with a saturated aqueous solution of $Na_2S_2O_3$ and dried ($MgSO_4$). Purification by flash chromatography (ether) provided the title compound **22** as a clear and colourless oil (2.8 mg, 8 μmol, 86%); R_f 0.1 (ether:hexane, 2:1); $[\alpha]_D^{19}$ +72.9 (*c* 0.14 in $CHCl_3$); IR ($CHCl_3$): ν=3423; ^1H NMR (250 MHz, $CDCl_3$): δ=7.24 (d, *J* (H, H)=8.7 Hz, 2H; Ar), 6.89 (d, *J* (H, H)=8.7 Hz, 2H; Ar), 6.04 (ddd, *J* (H, H)=17.3, 10.4, 8.7 Hz, 1H; C*H*=CH_2), 5.88-5.73 (m, 2H; 5-H. 6-H), 5.25 (ddd, *J* (H, H)=10.4, 1.8, 0.8 Hz, 1H; CH=C*H*H-*cis*), 5.18 (ddd, *J* (H, H)=17.3, 1.8, 1.0 Hz, 1H: CH=CH*H*-*trans*), 4.58 (d, *J* (H, H)=10.8 Hz, 1H; ArC*H*H), 4.57-4.53 (m, 1H; CH=CH_2CO*H*), 4.30 (d, *J* (H, H)=10.8 Hz, 1H; ArCH*H*), 3.96-3.88 (m, 2H), 3.81 (s, 3H; CH_3O), 3.41 (d, *J* (H, H)=10.8 Hz, 1H), 3.37 (ddd, *J* (H, H)=12.2, 7.4, 2.8 Hz, 1H), 2.65-2.52 (m, 1H), 2.45-2.22 (m, 3H), 2.15-2.02 (m, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=159.4, 136.2, 130.1, 129.4, 128.6, 128.2, 118.3, 113.9, 79.6, 78.5, 74.1, 70.9, 61.6, 55.3, 31.9, 29.0; MS (CI, NH_3): *m/z*(%): 352 ($(M+NH_4)^+$, 100), 335 ($(M+H)^+$, 75); Found 335.1861, $C_{19}H_{27}O_5$ requires 335.1858.

***(Z, 2*S*, 4*R*, 4a*S*, 6*S*, 10a*S*)-2-(4-Methoxy-phenyl)-6-triisopropylsilanyloxymethyl-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxa-benzocyclooctene* 21**



To a stirred solution of the allylic alcohol **17** (4 mg, 8 μmol) in DCM and water (18:1, 1 mL) was added DDQ (2.8 mg, 12 μmol) and the resulting green reaction mixture was stirred for 3 h. The reaction mixture was diluted with DCM, $MgSO_4$ was added and the mixture was filtered through a pad of silica with rinsing (DCM). Purification by flash chromatography (hexane:ether, 5:1) provided the title compound **21** as a clear and colourless oil (3 mg, 6 μmol, 78%); R_f 0.4 (hexane:ether, 1:1); $[\alpha]_D^{19}$ -4.0 (*c* 0.125 in $CHCl_3$); IR ($CHCl_3$): ν=2944; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.43 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 6.88 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 6.16 (ddd, *J* (H, H)=17.4, 10.7, 5.9 Hz, 1H; *H*C=CH_2), 5.34-5.89 (m, 1H; 9-H), 5.82-5.75 (m, 1H; 8-H), 5.53 (s, 1H; 2-H), 5.45 (d, *J* (H, H)=17.4 Hz, 1H; HC=C*H*H-*trans*), 5.25 (d, *J* (H, H)=10.7 Hz, 1H; HC=CH*H*-*cis*), 4.05-4.02 (m, 1H; 4-H), 3.89 (dd, *J* (H, H)=10.8, 5.0 Hz, 1H; C*H*HOSi), 3.80 (s, 3H; CH_3O), 3.70 (dd, *J* (H, H)=10.0, 6.8 Hz, 1H; CH*H*OSi), 3.65-3.58 (m, 1H; 6-H), 3.56-3.45 (m, 2H; 4a-H, 10a-H), 2.56-2.50 (m, 1H; 10-H), 2.47-2.38 (m, 2H; 10-H', 7-H), 2.30-2.23 (m, 1H; 7-H'), 1.10-1.06 (m, 21H; $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=160.0, 136.6, 130.5, 129.2, 127.5, 127.3, 117.6, 113.6, 100.2, 81.3, 80.6, 77.3, 72.9, 65.6 (CH_2OSi), 55.3 (CH_3O), 32.8, 28.6, 18.0 ($((CH_3)_2CH)_3Si$), 11.9 ($((CH_3)_2CH)_3Si$); MS (CI, NH_3): *m/z*(%): 489 ($(M+H)^+$, 25), 137 (100); Found: 489.3031, $C_{28}H_{45}O_5Si$ requires 489.3036.

***(Z, 2*R*, 3*S*, 8*S*)-3-Hydroxy-2-((*S*)-1-hydroxy-prop-2-eneyl)-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2*H*-oxocine* 20**, and ***(Z, 2*R*, 3*S*, 8*S*)--2-((*R*)-1-hydroxy-prop-2-eneyl)-8-triisopropylsilyloxymethyl-3,4,7,8-tetrahydro-2*H*-oxocine* 19**



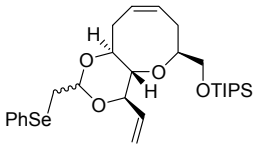
TFA (0.71 mL) was added to a stirring solution of a mixture of allylic alcohols **17** and **18** (50 mg, 102 μmol) in DCM (3.6 mL) at -20 °C. After 5 min the initial yellow

solution became pink and TLC analysis indicated that no starting material remained. Stirring was continued for a further 5 min and then the reaction was quenched by the addition of a saturated solution of $NaHCO_3$ (10 mL) and DCM. The organic phase was separated and the aqueous phase was extracted with DCM (2 × 10 mL). The organic phases were dried ($MgSO_4$) and purification by flash chromatography (hexane:ether, 1:1) provided a mixture of **20** and **19** (34 mg, 92 μmol, 90%) as a clear and colourless oil.

Data for **20**: R_f 0.2 (hexane:ether, 1:1); $[\alpha]_D^{23}$ -33.8 (*c* 0.21 in $CHCl_3$); IR ($CDCl_3$): ν=3617, 3455; ^{1}H NMR (250 MHz, $CDCl_3$) δ=6.08 (ddd, *J* (H, H)=17.3, 10.5, 5.8 Hz, 1H; C*H*=CH_2), 5.92-5.73 (m, 2H; 5-H, 6-H), 5.40 (dt, *J* (H, H)=17.3, 1.6 Hz, 1H; CH=C*H*H-*trans*), 5.25 (dt, *J* (H, H)=10.5, 1.5 Hz, 1H; CH=CH*H-cis*), 4.25-4.29 (m, 1H), 3.94 (dd, *J* (H, H)=10.2, 6.8 Hz, 1H), 3.88-3.78 (m, 2H), 3.73-3.64 (m, 2H), 3.27 (d, *J* (H, H)=6.3 Hz, 1H; OH), 2.50 (ddd, *J* (H, H)=13.3, 8.3, 3.2 Hz, 1H; allylic), 2.40 (dd, *J* (H, H)=7.5, 6.4 Hz, 1H), 2.34-2.29 (m, 2H; allylic), 2.23 (d, *J* (H, H)=3.8 Hz, 1H; OH), 1.17-1.02 (m, 21H; $((CH_3)_2CH)_3Si$); ^{13}C (62.5 MHz, $CDCl_3$) 138.4, 128.5, 128.5, 116.2, 77.4, 76.6, 75.2, 72.6, 64.1 (CH_2OSi), 34.1, 29.0, 18.0 ($(((CH_3)_2CH)_3Si$), 11.9 ($(((CH_3)_2CH)_3Si$); MS (CI, NH_3): *m/z*(%): 388 ($(M+NH_4)^+$, 17), 371 ($(M+H)^+$, 100); Found 371.2619, $C_{20}H_{39}O_4Si$ requires 371.2617.

Data for **19**: R_f 0.15 (hexane:ether, 1:1); $[\alpha]_D^{23}$ +44.2 (*c* 0.38 in $CHCl_3$); IR ($CHCl_3$): ν=3611, 3428; ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.04 (ddd, *J* (H, H)=17.3, 10.4, 6.6 Hz, 1H; C*H*=CH_2), 5.91-5.68 (m, 2H; 5-H, 6-H), 5.33 (ddd, *J* (H, H)=17.3, 1.9, 1.3 Hz, 1H; CH=C*H*H-*trans*), 5.23 (ddd, *J* (H, H)=10.4, 1.9, 1.2 Hz, 1H; CH=CH*H-cis*), 4.60 (d, *J* (H, H)=11.2 Hz, 1H; OH), 4.47-4.38 (m, 1H; 2-H), 3.99 (dd, *J* (H, H)=11.5, 10.1 Hz, 1H; C*H*HOSi), 3.85-3.73 (m, 2H), 3.59 (dd, *J* (H, H)=11.6, 2.8 Hz, 1H; CH*H*OSi), 3.65-3.50 (m, 1H), 3.59 (dd, *J* (H, H)=11.6, 2.8 Hz, 1H; C*H*HOSi), 2.41 (d, *J* (H, H)=7.7 Hz, 1H; allylic), 2.38 (dd, *J* (H, H)=8.4, 2.1 Hz, 1H; allylic), 2.19 (dd, *J* (H, H)=14.0, 10.3, 8.4 Hz, 1H; allylic), 2.02 (ddd, *J* (H, H)=14.0, 6.8, 3.4 Hz, 1H; allylic), 1.56 (d, *J* (H, H)=5.5 Hz, 1H; OH), 1.13-1.06 (m, 21H; $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=137.1, 128.6, 127.9, 116.4, 78.2, 77.5, 73.1, 71.7, 63.5 (CH_2OSi), 35.5, 28.0, 17.9 ($(((CH_3)_2CH)_3Si$), 11.9 ($(((CH_3)_2CH)_3Si$); MS (CI, NH_3): *m/z*(%): 371 ($(M+H)^+$, 100); Found 371.2621, $C_{20}H_{39}O_4Si$ requires 371.2617.

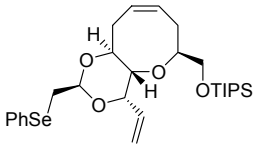
***(Z, 2*R/S*, 4*R*, 4a*S*, 6*S*, 10a*S*)-2-Phenylselanylmethyl-6-triisoproylsilanyloxy-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxa-benzocyclooctene* 23**



To a stirred solution of the diol **19** (10 mg, 27 μmol) in toluene (2 mL) was added phenylselenoacetaldehyde diethylacetal (9 mg, 32 μmol) and PPTS (1 mg). The reaction mixture was brought to reflux and heated at that temperature for 2 h. After cooling the solvent was removed *in vacuo* and purification by flash chromatography (hexane:ether, 12:1) provided the title compound **23** as a slightly yellow oil (14 mg, 25 μmol, 94%) as an inseparable mixture of diastereomers at the acetal carbon. NMR data indicated that the product was a 13:1 mixture of diastereomers the major diastereomer being with the phenylselenomethylene group in the equatorial position; ^{1}H NMR for the major diastereomer is given ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.55-7.52 (m, 2H Ar), 7.26-7.23 (m, 3H; Ar), 6.08 (ddd, *J* (H, H)=17.3, 10.6, 6.0 Hz, 1H; C*H*=CH_2), 5.89-5.84 (m, 1H; 8-H), 5.78-5.73 (m, 1H; 9-H), 5.35 (d, *J* (H, H)=17.3 Hz, 1H; CH=C*H*H-*trans*), 5.21 (d, *J* (H, H)=10.6 Hz, 1H; CH=CH*H*-*cis*), 4.83 (t, *J* (H, H)=5.0 Hz, 1H; 2-H), 3.55 (d, *J* (H, H)=5.3 Hz, 1H), 3.83 (d, *J* (H, H)=5.0 Hz, 1H), 3.64 (dd, *J* (H, H)=9.8, 7.0 Hz, 1H), 3.66-3.52 (m, 1H), 3.39-3.32 (m, 2H), 3.10 (d, *J* (H, H)=5.0 Hz, 2H; CH_2SeAr), 2.47-2.29 (m, 3H; allylic), 2.24 (ddd, *J* (H, H)=14.0, 7.2, 3.0 Hz, 1H; allylic), 1.14-1.06 (m, 21H; $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=135.4, 135.3, 133.7, 132.6, 132.6, 130.5, 129.2, 129.1, 129.1, 129.0, 127.3, 127.3, 127.1, 126.9, 117.8, 117.6, 77.3, 77.2, 74.3, 73.6, 72.7, 72.6, 65.6, 65.5, 32.6, 32.5, 30.8, 28.5, 28.5, 26.9, 18.0 ($((CH_3)_2CH)_3Si$), 11.9 ($((CH_3)_2CH)_3Si$); MS (EI): *m/z*(%): 552 (M^+, 100); Found 552.2167, $C_{28}H_{44}O_4SeSi$ requires 552.2174.

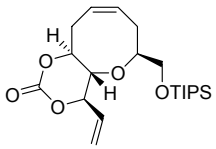
Selected ^{1}H NMR data are given for the minor diastereomer; 5.27 (dd, *J* (H, H)=7.5, 5.7 Hz, 1H; 2-H), 3.48 (dd, *J* (H, H)=12.7, 7.5 Hz, 1H; C*H*HSeAr), 3.20 (dd, *J* (H, H)=12.8, 5.7 Hz, 1H; CH*H*SeAr.

***(Z, 2S, 4S, 4aS, 6S, 10aS)-2-Phenylselanylmethyl-6-triisoproylsilanyloxy-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxa-benzocyclooctene* 24**



The selenoacetal **24** was prepared in 60% yield starting from the diol **20** as described for the selenoacetal **23**. The selenoacetal **20** was isolated as a single diastereomer as determined by ^{1}H NMR analysis; $[\alpha]_D^{25}$ -91.1 (*c* 0.18 in $CHCl_3$);^{1}H NMR (250 MHz, $CDCl_3$): δ=7.55-7.50 (m, 2H; Ar), 7.27-7.22 (m, 3H; Ar), 6.18 (ddd, *J* (H, H)=17.7, 11.0, 4.1 Hz, 1H; C*H*=CH_2), 5.89-5.73 (m, 2H; 9-H, 8-H), 5.44 (dt, *J* (H, H)=17.7, 2.0 Hz, 1H; CH=C*H*H-*trans*), 5.31 (dt, *J* (H, H)=11.0, 2.0 Hz, 1H; CH=CH*H*-*cis*), 5.13 (t, *J* (H, H)=5.0 Hz, 1H; 2-H), 4.60 (ddt, *J* (H, H)=6.4, 4.1, 2.1 Hz, 1H; 4-H), 3.98 (dd, *J* (H, H)=9.7, 6.4 Hz, 1H; 4a-H), 3.87 (dd, *J* (H, H)=10.7, 6.4 Hz, 1H; C*H*HOSi), 3.76 (dd, *J* (H, H)=10.7, 4.7 Hz, 1H; CH*H*OSi), 3.68-3.52 (m, 1H; 6-H), 3.50 (dt, *J* (H, H)=9.7, 4.9 Hz, 1H; 10a-H), 3.05 (d, *J* (H, H)=5.0 Hz, 2H; CH_2SeAr), 2.52-2.30 (m, 3H; 10-H, 10-H', 7-H), 2.12 (ddd, *J* (H, H)=13.6, 6.3, 3.4 Hz, 1H; 7-H'), 1.11-1.04 (m, 21H; $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=132.4, 132.2, 130.6, 129.0, 129.0, 127.3, 118.8, 94.2, 77.2, 76.3, 75.7, 69.5, 64.9, 32.8, 31.1, 28.3, 18.0 ($(C H_3)_2CH)_3Si$), 11.9 ($((CH_3)_2C H)_3Si$); MS (CI, NH_3): *m/z*(%): 570 ($(M+NH_4)^+$, 8), 553 ($(M+H)^+$, 5), 52 (100); Found 570.2513, $C_{28}H_{48}O_4SeSiN$ requires 570.2518.

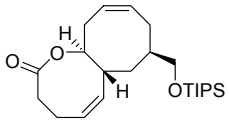
***(Z, 4R, 4aS, 6S, 10aS)-6-Triisopropylsilanyloxymethyl-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxa-benzocycloocten-2-one* 25**



To a stirred suspension of the oxocane **19** (8.7 mg, 24 μmol) and freshly activated 4 Å powdered molecular sieves in DCM (1 mL) were added pyridine (11.5 μL, 11.3 mg, 141 μmol) and TEA (33 μL, 24 mg, 24 μmol). The resulting solution was cooled to -78 °C and triphosgene (7 mg, 24 μmol) was added *via* cannula as a solution in DCM (0.5 mL). The resulting orange solution was stirred for 15 min and then allowed to warm to room temperature. The reaction mixture was quenched by the addition of a saturated solution of NH_4Cl (2 mL) and was extracted with DCM (4 × 2 mL). The

organic phases were dried ($MgSO_4$) and purification by flash chromatography (hexane:ether, 1:1) provided the title compound **25** (8.3 mg, 21 μmol, 89%) as a clear and colourless oil; $[\alpha]_D^{25}$ -47.5 (*c* 0.4 in $CHCl_3$); IR ($CHCl_3$): ν=1752; ^{1}H NMR (400 MHz, $CDCl_3$): δ=6.04 (ddd, *J* (H, H)=17.2, 10.6, 6.2 Hz, 1H; C*H*=CH_2), 5.90-5.78 (m, 2H; 8-H, 9-H), 5.52 (dt, *J* (H, H)=17.2, 1.2 Hz, 1H; CH=C*H*H-*trans*), 5.36 (dt, *J* (H, H)=10.6, 1.2 Hz, 1H; CH=CH*H-cis*), 4.58 (ddt, *J* (H, H)=9.2, 6.2, 1.2 Hz, 1H; 4-H), 4.10 (dt, *J* (H, H)=9.5, 3.8 Hz, 1H; 10a-H), 3.94 (dd, *J* (H, H)=9.5, 9.2 Hz, 1H; 4a-H), 3.83 (d, *J* (H, H)=4.9 Hz, 2H; CH_2OSi), 3.71-3.67 (m, 1H; 6-H), 2.62-2.49 (m, 3H; allylic), 2.27-2.20 (m, 1H; allylic), 1.10-1.05 (m, 21H; $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=148.2 (2-C), 132.5, 125.4, 119.7, 81.6, 80.0, 70.6, 65.6 (CH_2OSi), 31.5, 28.5, 18.0 ($((CH_3)_2CH)_3Si$), 11.9 ($(((CH_3)_2CH)_3Si$); MS (CI, NH_3): *m/z*(%): 414 ($(M+NH_4)^+$, 10), 397 ($(M+H)^+$, 3), 75 (100).

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



From the selenoacetal **23**.

To a stirring suspension of the selenoacetal **23** (14 mg, 25 μmol) in DCM (0.2 mL), water (0.3 mL) and MeOH (1.3 mL) were added $NaHCO_3$ (2.3 mg, 28 μmol) and sodium periodate (18 mg, 84 μmol). The resulting suspension was stirred for 2 h and then diluted with DCM (5 mL) and water (5 mL). The organic phase was separated and the aqueous phase was extracted with DCM (2 × 5 mL). The organic phases were dried ($MgSO_4$) and the solvent removed *in vacuo* the resulting oil was coevaporated with toluene (2 × 2 mL) and xylene (4 mL) and DBU (11.4 μL, 11.6 mg, 76 μmol) were added. The resulting solution was heated at reflux for 18 h and then allowed to cool. The solvent was removed *in vacuo* and purification by flash chromatography (hexane:ether, 5:1) provided the title compound **26** as a clear and colourless oil (9 mg, 23 μmol, 90%); $[\alpha]_D^{25}$ +28.3 (*c* 0.425 in $CHCl_3$); IR ($CHCl_3$): ν=1742; ^{1}H (500 MHz, $CDCl_3$) 5.88-5.82 (m, 2H; 10-H, 11-H), 5.68-5.62 (m, 2H; 5-H, 6-H), 4.65 (dd, *J* (H, H)=9.2, 3.4 Hz, 1H; 6a-H), 4.56 (dt, *J* (H, H)=9.2, 3.2 Hz, 1H; 12a-H), 3.84 (dd, *J* (H, H)=10.6, 5.5 Hz, 1H; C*H*HOSi), 3.82 (dd, *J* (H, H)=10.6, 4.9 Hz, 1H; CH*H*OSi),

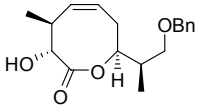
3.76-3.72 (m, 1H; 8-H), 2.74 (ddd, *J* (H, H)=13.8, 6.2, 2.0 Hz, 1H; allylic), 2.65-2.57 (m, 2H; allylic), 2.52-2.46 (m, 2H; allylic), 2.31-2.17 (m, 2H; allylic), 2.10-2.01 (m, 1H; allylic), 1.08-1.04 (m, 21H; $((CH_3)_2CH)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=175.2 (2-C), 137.3, 129.6, 129.1, 127.4, 78.9, 76.1, 72.8, 64.8 (CH_2OSi), 37.8, 31.2, 29.0, 25.5, 18.0 ($((CH_3)_2CH)_3Si$), 11.9 ($((CH_3)_2CH)_3Si$); MS (EI): *m/z*(%): 394 (M^+, 10), 239 (100); Found 394.2538, $C_{22}H_{38}O_4Si$ requires 394.2539.

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

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

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

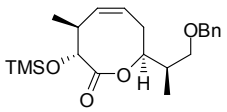
***(Z, 3*R*, 4*S*, 8*S*)-8-((1*R*)-2-Benzyloxy-1-methyl-ethyl)-3-hydroxy-4-methyl-3,4,7,8-tetrahydro-oxocin-2-one* 27**



To a solution of KHMDS (9.02 mL of a 0.5 M solution in toluene, 4.51 mmol) in toluene (150 mL) at -78 °C was slowly added a solution of the lactone **8**[2] (1.0 g, 3.47 mmol) in toluene (20 mL, 5 mL rinse). The solution was stirred for 20 min then (±)-2-(phenylslfonyl)-3-phenyloxaziridine (1.18 g, 4.51 mmol) was added slowly as a solution in toluene (20 mL, 5 mL rinse). The solution was stirred at -78 °C for 1.25 h until consumption of starting material was complete. The reaction was quenched *via* addition of (±)-camphor-10-sulfonic acid (2 g) in THF (20 mL) at -78 °C, then allowed to warm slowly to ambient temperature. The mixture was poured into water (150 mL) and extracted with EtOAc (3 × 150 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated. Flash chromatography (hexane:EtOAc, 20:3) afforded the hydroxylactone **27** as a white solid (0.96 g, 3.15 mmol, 91%); (Found: C, 70.7; H, 7.9%; $C_{18}H_{24}O_4$ requires C, 71.0; H, 8.0); mp 59-61

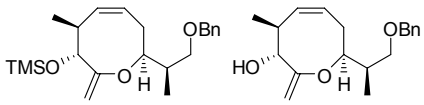
°C; $[\alpha]_D^{25}$ -12.1 (*c* 0.755 in $CHCl_3$); R_f 0.31 (PE:EtOAc, 20:1); IR ($CHCl_3$): ν=3690, 3543, 1731; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.28-7.37 (m, 5H; Ar), 5.49-5.67 (m, 2H; 5-H, 6-H), 4.60 (ddd, *J* (H, H)=10.0, 6.0, 2.0 Hz, 1H; 8-H), 4.50 (d, *J* (H, H)=12.0 Hz, 2H; C*H*$_2$Ar), 3.89 (dd, *J* (H, H)=10.0, 9.0 Hz, 1H; 3-H), 3.53 (dd, *J* (H, H)=9.0, 3.5 Hz, 1H; C*H*HOBn), 3.38 (dd, *J* (H, H)=9.0, 6.5 Hz, 1H; CH*H*OBn), 2.73 (d, *J* (H, H)=8.5 Hz, 1H; OH), 2.48-2.59 (ddd, *J* (H, H)=14.5, 8.5, 6.0 Hz, 1H; 7β–H), 2.30-2.42 (m, 1H; 4-H), 2.17-2.27 (m, 1H; 7α-H),1.91-2.03 (m, 1H; 9-H), 1.28 (d, *J* (H, H)=7.0 Hz, 3H; 4-C-Me), 1.06 (d, *J* (H, H)=7.0 Hz, 3H; 8-C-CHC*H*$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=10.8, 138.5, 136.6, 128.3, 127.5, 127.5, 125.2, 76.2, 74.3, 73.2, 71.8, 39.5, 35.5, 28.5, 18.6, 14.2; MS (CI, NH_3): *m/z*(%) 322 ($(M+NH_4)^+$, 61), 305 ($(M+H)^+$, 11); Found 305.1749, $C_{18}H_{25}O_4$ requires 305.1753.

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



To a stirred solution of the hydroxylactone **27** (300 mg, 98.6 mmol) in ether (20 mL) was added dry Et_3N (0.549 mL, 39.4 mmol) and TMSCl (0.495 mL, 39.4 mmol). The solution was stirred for 30 min, then poured into water (20 mL). The product was extracted with ether (3 × 40 mL), the extracts were washed with water (20 mL) and brine (20 mL), dried ($MgSO_4$) and concentrated to give the title compound **28** as a pale yellow oil (360 mg, 95.6 mmol, 97%); $[\alpha]_D^{25}$ +27.8 (*c* 1.08 in $CDCl_3$); R_f 0.23 (hexane:EtOAc, 9:1); IR (film): ν=1753; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.24-7.36 (m, 5H; Ar), 5.51-5.62 (m, 2H; 5-H, 6-H), 4.61-4.65 (m, 1H; 8-H), 4.50 (d, *J* (H, H)=12.0 Hz, 2H; C*H*$_2$Ar), 3.91 (d, *J* (H, H)=10.0 Hz, 1H; 3-H), 3.57 (dd, *J* (H, H)=4.0, 9.0 Hz, 1H; C*H*HOBn), 3.34 (dd, *J* (H, H)=7.0, 9.0 Hz, 1H; CH*H*OBn), 2.53-2.60 (m, 2H; 7-H, 4-H), 2.20 (ddd, *J* (H, H)=2.5, 6.5, 14.5 Hz, 1H; 7-H'), 1.94-2.01 (m, 1H; 8-C-C*H*CH_3), 1.16 (d, *J* (H, H)=6.5 Hz, 3H; 4-C-Me), 1.05 (d, *J* (H, H)=6.5 Hz, 3H; 8-C-CHC*H*$_3$), 0.15 (s, 9H; $(CH_3)_3Si$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=177.6, 138.6, 136.2, 128.3, 127.5, 127.4, 125.4, 77.4, 73.4, 73.1, 72.0, 38.7, 35.9, 28.7, 19.0, 14.1, -0.3; MS (ES): *m/z*(%): 399 ($(M+Na)^+$, 100), 377 ($(M+H)^+$, 9); Found 399.1974, $C_{21}H_{32}O_4SiNa$ requires 399.1966.

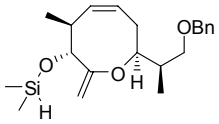
***(Z, 3*R*, 4*S*, 8*S*)-8-((1*R*)-2-Benzyloxy-1-methyl-ethyl)-4-methyl-2-methylene-3-trimethylsilanyloxy-3,4,7,8-tetrahydro-2*H*-oxocine* 29** and ***(Z, 3*R*, 4*S*, 8*S*)-8-((1*R*)-2-benzyloxy-1-methyl-ethyl)-3-hydroxy-4-methyl-2-methylene-3,4,7,8-tetrahydro-2*H*-oxocine* 30**



To a solution of the lactone **28** (350 mg, 0.93) in toluene (20 mL) was added dimethyltitanocene (4.12 mL of a 94 mg/mL solution in toluene, 1.86 mmol). The mixture was heated to reflux in the absence of light for 1.5 h, after which time a further equivalent of dimethyltitanocene solution (2.06 mL) was added. The mixture was refluxed for a further hour after which time all the starting material had been consumed. The solution was allowed to cool, concentrated, then redissolved in DCM and evaporated onto deactivated basic alumina (Brockman Grade III, 6% water). The trimethylsilyl-protected enol ether **29** was purified *via* flash chromatography using basic alumina (hexane:EtOAc, 25:1) to give a yellow oil containing some cyclopentadienyl impurities; the mixture could be further purified (alumina chromatography) for the purposes of characterisation giving pure **29**; $[\alpha]_D^{25}$ +29.2 (*c* 0.64 in $CDCl_3$); R_f 0.49 (hexane:EtOAc, 10:1); IR ($CHCl_3$): ν=1643; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.26-7.36 (m, 5H; Ar), 7.26-7.36 (m, 5H; Ar), 5.43-5.55 (m, 2H; 5-H, 6-H), 4.94 (s, 1H; OCH=C*H*H), 4.53 (s, 1H; OCH=CH*H*), 4.52 (d, *J* (H, H)=12.0 Hz, 2H; CH_2Ar), 3.85 (dd, *J* (H, H)=5.0, 10.0 Hz, 1H; 8-H), 3.62 (dd, *J* (H, H)=3.5, 9.0 Hz, 1H; C*H*HOBn), 3.53 (d, *J* (H, H)=10.0 Hz, 1H; 3-H), 3.49 (dd, *J* (H, H)=6.0, 9.0 Hz,1H; CH*H*OBn), 2.64-2.80 (m, 1H; 7-H), 2.30-2.45 (m, 1H; 4-H), 1.91-2.10 (m, 1H; 7-H'), 1.75-1.89 (m, 1H; 8-C-C*H*CH_3), 1.11 (d, *J* (H, H)=6.5 Hz, 3H; 4-C-Me), 1.04 (d, *J* (H, H)=7.0 Hz, 3H; 8-C-CHCH_3), 0.14 (s, 9H; $(CH_3)_3$Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=166.8, 139.0, 136.9, 128.3, 127.5, 127.5, 127.3, 124.3, 93.6, 78.4, 76.1, 73.1, 72.6, 40.1, 36.0, 27.0, 19.8, 14.5, 0; MS (ES^+): *m/z*(%): 397 ($(M+Na)^+$, 100); Found 397.2163, $C_{22}H_{34}O_3SiNa$ requires 397.2175. The mixture was dissolved in dry methanol (10 mL) and solid potassium carbonate (0.1 g) was added. The solution was stirred for 30 min at room temperature, then filtered, and concentrated. After redissolving in DCM the mixture was evaporated onto deactivated basic alumina and purified *via* flash chromatography using basic alumina (hexanes:EtOAc,

20:1→5:1) to give the deprotected enol ether **30** as a colourless oil (120 mg, 0.397 mmol, 68%); $[\alpha]_D^{25}$ -2.5 (*c* 0.55 in $CDCl_3$); R_f 0.4 (hexanes:EtOAC, 3:1); IR ($CHCl_3$): ν=3604, 1642; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.23-7.35 (m, 5H; Ar), 7.23-7.35 (m, 5H; Ar), 5.43-5.46 (m, 2H; 5-H, 6-H), 4.96 (br s, 1H; OC=C*H*H), 4.58 (d, *J* (H, H)=1.5 Hz, 1H; OC=CH*H*), 4.51 (d, *J* (H, H)=12.0 Hz, 2H; CH_2Ar), 3.90 (ddd, *J* (H, H)=1.0, 5.5, 9.5 Hz, 1H; 8-H), 3.63 (br d, 1H; 3-H), 3.60 (dd, *J* (H, H)=3.5, 9.0 Hz, 1H; C*H*HOBn), 3.50 (dd, *J* (H, H)=6.0, 9.0 Hz, 1H; CH*H*OBn), 2.72 (ddd, *J* (H, H)=5.5, 9.0, 14.0 Hz, 1H; 7-H), 2.37-2.47 (m, 1H; 4-H), 2.05 (partially resolved dd, 1H; 5-H'), 1.80-1.90 (m, 1H; 8-C-C*H*CH_3), 1.73 (br d, *J* (H, H)=3.0 Hz, 1H; OH), 1.20 (d, *J* (H, H)=6.5 Hz, 3H; 4-C-Me), 1.03 (d, *J* (H, H)=7.0 Hz, 3H; 8-C-CHCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=167.1, 138.9, 136.7, 128.3, 127.5, 127.4, 124.6, 93.4, 78.8, 75.9, 73.2, 72.5, 39.2, 36.0, 27.2, 19.1, 14.5; MS (ES): *m/z*(%):325 ($(M+Na)^+$, 100); Found 325.1774, $C_{19}H_{26}O_3Na$ requires 325.1755.

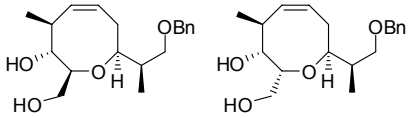
***(Z, 3*R*, 4*S*, 8*S*)-8-((1*R*)-2-Benzyloxy-1-methyl-ethyl)-3-dimethylsilanyloxy-4-methyl-2-methylene-3,4,7,8-tetrahydro-2*H*-oxocine* 31**



The hydroxyenol ether **30** (120 mg, 0.397.97 mmol) was dissolved in tetramethyldisilazane (2 mL) and NH_4Cl (10 mg) was added. The mixture was stirred at 60 °C for 18 h then allowed to cool, diluted with hexane (2 mL), and the mixture was filtered and concentrated. The product was redissolved in toluene and concentrated (2 × 5 mL) to give the enol ether **31** as a colourless oil (140 mg, 0.3.88 mmol, 98%); $[\alpha]_D^{25}$ +49.2 (*c* 0.88 in $CHCl_3$); R_f decomposes on silica; IR ($CDCl_3$): ν=3019, 1522, 1476, 1423, 1221; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.23-7.35 (m, 5H; Ar), 5.45-5.53 (m, 2H; 5-H, 6-H), 4.93 (s, 1H; OC=C*H*H), 4.62-4.66 (m, 1H; SiH), 4.56 (s, 1H; OC=CH*H*), 4.55 (d, *J* (H, H)=12.0 Hz, 1H; C*H*HAr), 4.49 (d, *J* (H, H)=12.0 Hz, 1H; CH*H*Ar), 3.85 (dd, *J* (H, H)=4.5, 10.0 Hz, 1H; 8-H), 3.61 (dd, *J* (H, H)=3.5, 9.0 Hz, 1H; C*H*HOBn), 3.55 (d, *J* (H, H)=10 Hz, 1H; 3-H), 3.49 (dd, *J* (H, H)=6.5, 9.0 Hz, 1H; CH*H*OBn), 2.66-2.75 (m, 1H; 7-H), 2.35-2.44 (m, 1H; 4-H), 2.00-2.07 (m, 1H; 7-H'), 1.78-1.89 (m, 1H; 8-C-C*H*CH_3), 1.12 (d, *J* (H, H)=6.5 Hz, 3H; 4-C-Me), 1.04 (d, *J* (H, H)=7.0 Hz, 3H; 8-C-CHCH_3), 0.22 (apparent t, *J* (H,

H)=3.0 Hz, 6H; $Si(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=166.2, 138.9, 136.7, 128.3, 127.3, 124.4, 93.8, 78.5, 77.6, 73.1, 72.6, 40.0, 36.0, 27.1, 19.6, 14.5, -1.2, -1.4; MS (ES): *m/z*(%): 383 ($(M+Na)^+$, 100); Found 383.1985, $C_{21}H_{32}O_3SiNa$ requires 383.2013.

***(Z, 2S, 3R, 4S, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-3-hydroxy-2-hydroxymethyl-4-methyl-3,4,7,8-tetrahydro-2H-oxocine* 32,** and ***(Z, 2R, 3R, 4S, 8S)-8-((1R)-2-benzyloxy-1-methyl-ethyl)-3-hydroxy-2-hydroxymethyl-4-methyl-3,4,7,8-tetrahydro-2H-oxocine* 33**

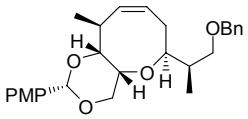


To (bicyclo(2.2.1)hepta-2,5-diene)(1,4-bis-(diphenylphosphino)butane) rhodium(I) tetrafluoroborate (20 mg, 29.6 μmol) was added a solution of the enol ether **31** (178 mg, 0.494 mmol) in THF (20 mL, 5 mL rinse). The solution was stirred at 50 °C for 2 days under N_2. After this time the mixture was cooled to room temperature and EDTA (10 mg) was added, and the solution was stirred for 30 min. The mixture was diluted with hexane (25 mL), filtered and concentrated. The residue was redissolved in methanol and THF (6 mL of a 1:1 solution) and aqueous solution of H_2O_2 (30%) and potassium hydroxide (15%) (4 mL of a 1:1 solution) was added and stirring was continued for 1.5 h. A saturated aqueous solution of $Na_2S_2O_3$ (5 mL) was added slowly and the mixture stirred for a further 30 min. The product was extracted with EtOAc (3 × 50 mL), the organic layers being washed with brine, combined, dried ($MgSO_4$) and concentrated. Flash chromatography (hexane:EtOAc, 5:2) gave the *trans*-diol **32** as a colourless oil (51.9 mg, 10.162 mmol, 32.8%); $[\alpha]_D^{25}$ 3.4 (*c* 0.77 in $CDCl_3$); R_f 0.25 (PE:EtOAc, 1:1); IR ($CHCl_3$): ν=3300-3600; ^1H NMR (400 MHz, $CDCl_3$): δ=7.25-7.36 (m, 5H; Ar), 7.25-7.36 (m, 5H; Ar), 5.44-5.53 (m, 2H; 5-H, 6-H), 4.60 (d, *J* (H, H)=12.0 Hz, 1H; C*H*HAr), 4.44 (d, *J* (H, H)=12.0 Hz, 1H; CH*H*Ar), 3.92 (dd, *J* (H, H)=3.0, 11.0 Hz, 1H; C*H*HOH), 3.79 (dd, *J* (H, H)=4.0, 9.0 Hz, 1H; C*H*HOBn), 3.47-3.58 (m, 2H; 8-H, CH*H*OH), 3.36 (dt, *J* (H, H)=3.5, 9.0 Hz, 1H; 2-H), 3.26 (dd, *J* (H, H)=2.5, 9.0 Hz, 1H; C*H*HOBn), 3.12 (t, *J* (H, H)=9.5 Hz, 1H; 3-H), 2.53-2.60 (m, 1H; 7-H), 2.44-2.50 (m, 1H; 4-H), 2.17-2.22 (m, 1H; 7-H'), 1.61-1.72 (m, 1H; 8-C-C*H*CH_3), 1.16 (d, *J* (H, H)=6.5 Hz, 3H; 4-C-Me), 1.01 (d, *J* (H, H)=7.0 Hz, 3H; 8-C-CHC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=138.0, 136.9, 128.3, 127.9,

127.7, 123.6, 82.7, 78.7, 75.1, 73.5, 72.3, 65.4, 38.2, 36.0, 27.9, 18.6, 15.4; MS (CI, perfluorotributylamine): *m/z*(%): Found ($(M+NH_4)^+$, 33), 321 ($(M+H)^+$, 98); Found 321.2069, $C_{19}H_{29}O_4$ requires 321.2066.

And the cis-*diol* **33** as a white solid (38.8 mg, 0.121 mmol, 24.5%); mp 102 °C; $[\alpha]_D^{25}$ -23.7 (*c* 2.17 in DCM); R_f 0.19 (LP:EtOAc, 1:1); IR ($CHCl_3$): ν=3300-3600; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.27-7.37 (m, 5H; Ar), 5.73-5.80 (m, 1H; 6-H), 5.42-5.47 (m, 1H; 5-H), 4.51 (s, 2H; CH_2Ar), 4.08 (dt, *J* (H, H)=1.0, 5.0 Hz, 1H; 2-H), 4.01-4.06 (m, 1H; 8-H), 3.66 (dd, *J* (H, H)=5.0, 11.5 Hz, 1H; C*H*HOH), 3.61 (dd, *J* (H, H)=5.0, 11.5 Hz, 1H; CH*H*OH), 3.54 (dd, *J* (H, H)=1.0, 9.5 Hz, 1H; C*H*HOBn), 3.34-3.43 (m, 2H; CH*H*OBn, 3-H), 2.72-2.82 (m, 1H; 4-H), 2.59 (dddd, *J* (H, H)=2.0, 3.5, 7.5, 16.0 H, 1H; 7-H), 2.24 (dt, *J* (H, H)=6.0, 16.0 Hz, 1H; 7-H'), 2.01-2.11 (m, 1H; 8-C-C*H*CH_3), 1.19 (d, *J* (H, H)=6.5 Hz, 3H; 4-C-Me), 1.00 (d, *J* (H, H)=7.0 Hz, 1H; 8-C-CHC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=138.2, 136.0, 128.4, 128.3, 127.7, 127.7, 80.3, 78.7, 73.7, 73.3, 71.8, 64.9, 37.9, 35.5, 31.9, 18.0, 15.1; MS (CI, perfluorotributylamine): *m/z*(%): 328 ($(M+NH_4)^+$, 42), 321 ($(M+H)^+$, 100); Found 321.2070, $C_{19}H_{29}O_4$ requires 321.2066.

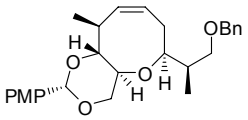
(Z, 2S, 4aR, 6S, 10S, 10aR)-6-((1R)-2-Benzyloxy-1-methyl-ethyl))-2-(4-methoxyphenyl)-10-methyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxabenzocyclooctene **35**



To a solution of the *cis*-diol **33** (8 mg, 25 μmol) in benzene (3 mL) was added *p*-anisaldehyde (4 μL, 30 μmol) and PPTS (1 mg). The solution was heated under reflux (Dean-Stark) for 18 h, allowed to cool, and concentrated. Flash chromatography (hexanes:ether, 3:1→2:1) gave the acetal **35** as a white solid (10 mg, 25 μmol, 100%); mp 80-82 °C; $[\alpha]_D^{25}$ -34.3 (*c* 1.07 in $CHCl_3$); R_f 0.33 (PE:EtOAc, 4:1); IR ($CHCl_3$): ν=2933, 2849; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.47 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 7.26-7.36 (m, 5H; Ar), 6.88 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 5.80-5.87 (m, 1H; 8-H), 5.47 (s, 1H; 2-H), 5.41-5.46 (m, 1H; 9-H), 4.53 (d, *J* (H, H)=12.0 Hz, 1H; CH*H*Ar), 4.47 (d, *J* (H, H)=12.0 Hz, 1H; CH*H*Ar), 4.08 (d, *J* (H, H)=12.0 Hz, 1H; 4-H), 3.97-4.02 (m, 1H; 6-H), 3.87 (d, *J* (H, H)=12.0 Hz, 1H; 4-H'), 3.80 (s, 3H; OCH_3),

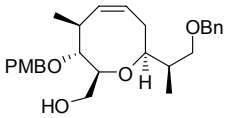
3.72-3.77 (m, 2H; 4a-H, C*H*HOBn), 3.49 (dd, *J* (H, H)=10.5, 1.5 Hz, 1H; 3-H), 3.25 (t, *J* (H, H)=8.5 Hz, 1H; CH*H*OBn), 3.03-3.11 (m, 1H; 10-H), 2.72-2.77 (m, 1H; 7-H), 2.20-2.27 (m, 1H; 7-H'), 2.08-2.17 (m, 1H; 8-C-C*H*CH_3), 1.21 (d, *J* (H, H)=6.5 Hz, 3H; 4-C-Me), 1.05 (d, 3H; *J* (H, H)=6.5 Hz, 3H; 8-C-CHC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.7, 138.5, 135.6, 131.0, 128.4, 127.9, 127.6, 127.4, 113.3, 101.0, 86.7, 79.4, 73.4, 73.2, 72.9, 64.4, 55.3, 34.4, 33.7, 31.4, 17.4, 15.6; MS (ES, polyethylenimine): *m/z*(%):456 ($(M+NH_4)^+$, 100), 439 ($(M+H)^+$, 27); Found 439.2492, $C_{27}H_{35}O_5$ requires 439.2484.

(Z, 2S, 4aS, 6S, 10S, 10aR)-6-((1R)-2-Benzyloxy-1-methyl-ethyl))-2-(4-methoxyphenyl)-10-methyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxabenzocyclooctene **34**



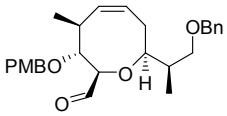
To a solution of **32** (11 mg, 34.3 μmol) in benzene (10 mL) was added *p*-anisaldehyde (13 μL, 0.107 mmol) and PPTS (2 mg). The solution was heated under reflux (Dean-Stark) for 18 h, allowed to cool and concentrated. Flash chromatography (hexanes:ether, 3:1→2:1) gave the acetal **34** as a colourless oil (15 mg, 34.3 μmol, 100%); $[\alpha]_D^{25}$ +23.4 (*c* 0.67 in DCM); R_f 0.31 (hexane:EtOAc, 5:1); IR (thin film): ν=2959, 2927, 2859; ^{1}H (400 MHz, $CDCl_3$): δ=7.41 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 7.26-7.36 (m, 5H; Ar), 6.88 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 5.49-5.56 (m, 2H; 8-H, 9-H), 5.39 (s, 1H; 2-H), 4.51 (d, *J* (H, H)=12.0 Hz, 1H; C*H*HAr), 4.45 (d, *J* (H, H)=12.0 Hz, 1H; CH*H*Ar), 4.04 (dd, *J* (H, H)=5.0, 11.0 Hz, 1H; 4-H), 3.80 (s, 3H; OCH_3), 3.40-3.58 (m, 5H; 4-H', 4a-H, 6-H, CH_2OBn), 3.22 (t, *J* (H, H)=9.5 Hz, 1H; 10a-H), 2.58-2.73 (m, 2H; 7-H, 10-H), 1.98-2.06 (unresolved dd, 1H; 7-H'), 1.65-1.79 (m, 1H; 8-C-C*H*CH_3), 1.19 (d, *J* (H, H)=6.5 Hz, 3H; 4-C-Me), 1.04 (d, *J* (H, H)=7.0 Hz, 3H; 8-C-CHC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.8, 138.8, 136.7, 130.6, 128.3, 127.5, 127.5, 127.2, 124.2, 113.5, 100.6, 83.8, 79.0, 73.2, 73.1, 72.5, 69.6, 55.3, 36.5, 36.2, 28.1, 18.0, 14.9; MS (CI, perfluorotributylamine): *m/z*(%): 439 ($(M+H)^+$, 63%); Found 439.2489, $C_{27}H_{35}O_5$ requires 439.2484.

***(Z, 2S, 3R, 4S, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-2-hydroxymethyl-3-(4-methoxy-benzyloxy)-4-methyl-3,4,7,8-tetrahydro-2H-oxocine,* 36**



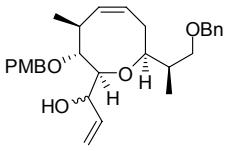
To a solution of the acetal **34** (16 mg, 36.5 μmol) in toluene (1 mL) at -78 °C was added DIBAL-H (255 μL, 0.255 mmol, of a 1.0 M solution in toluene) dropwise. The solution was stirred and gradually allowed to warm to -5 °C over 2 h. Starting material remained and the mixture was recooled to -50 °C and further DIBAL-H (125 μL) was added. The mixture was warmed to -5 °C over 1 h, at which point the reaction was virtually complete. The solution was allowed to warm to room temperature, then ether (3 mL), a saturated aqueous solution of NH_4Cl (1.5 mL) and a saturated aqueous solution of sodium potassium tartrate (1.5 mL) were added. The mixture was stirred until heterogeneous (1 h) then extracted with ether (3 × 15 mL), and the organic extracts washed with brine (10 mL), dried ($MgSO_4$) and concentrated. Flash chromatography (hexane:EtOAc, 3:1→5:2) gave the starting material **34** (1.8 mg, 4.10 μmol, 10%) and the alcohol **36** (14.5 mg, 32.9 μ mol, 90%) as a white solid; mp 52 °C (ether); $[\alpha]_D^{25}$ 1.9 (*c* 0.7 in $CHCl_3$); R_f 0.17 (hexane:EtOAc, 4:1); IR ($CHCl_3$): ν=3350-3500; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.23-7.35 (m, 7H; Ar), 6.86 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 5.55 (dd, *J* (H, H)=7.0, 11.0 Hz, 1H; 5-H), 5.43-5.51 (m, 1H; 6-H), 4.60 (d, *J* (H, H)=12.0 Hz, 1H; C*H*HAr), 4.49 (d, *J* (H, H)=10.0 Hz, 1H; C*H*HAr), 4.45 (d, *J* (H, H)=12.0 Hz, 1H; CH*H*Ar), 4.40 (d, *J* (H, H)=10.0 Hz, 1H; CH*H*Ar), 3.93 (dt, *J* (H, H)=2.5, 10.0 Hz, 1H; C*H*HOH), 3.82 (dd, *J* (H, H)=4.0, 9.0 Hz, 1H; C*H*HOBn), 3.80 (s, 3H; OCH_3), 3.67 (dd, *J* (H, H)=3.0, 10.0 Hz, 1H; OH), 3.51-3.61 (m, 2H; 8-H, CH*H*OH), 3.47 (dt, *J* (H, H)=3.0, 9.0 Hz, 1H; 2-H), 3.26 (dd, *J* (H, H)=2.5, 9.0 Hz, 1H; CH*H*OBn), 2.96 (t, *J* (H, H)=10.0 Hz, 1H; 3-H), 2.60-2.66 (m, 1H; 4-H), 2.55 (ddd, *J* (H, H)=6.5, 9.0, 14.5 Hz, 1H; 7-H), 2.17 (dd, *J* (H, H)=6.5, 14.0 Hz, 1H; 7-H'), 1.63-1.69 (m, 1H; 8-C-C*H*CH_3), 1.22 (d, *J* (H, H)=6.5 Hz, 3H; 4-C-Me), 1.01 (d, *J* (H, H)=7.0 Hz, 3H; 8-C-CHC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.4, 137.9, 137.2, 128.3, 127.9, 127.7, 123.3, 133.4, 82.9, 82.1, 78.6, 74.2, 73.6, 72.4, 65.0, 55.3, 38.0, 36.1, 28.0, 18.9, 15.4; MS (CI, perfluorotributylamine); *m/z*(%):458 ($(M+NH_4)^+$, 20), 441 ($(M+H)^+$, 100); Found 441.2635, $C_{27}H_{37}O_5$ requires 441.2641.

***(Z, 2R, 3R, 4S, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-2-carbaldehyde-3-(4-methoxy-benzyloxy)-4-methyl-3,4,7,8-tetrahydro-2H-oxocine,* 37**



To a solution of the alcohol **36** (14 mg, 31.8 μmol) in dry DMSO (2.5 mL) was added IBX (27 mg, 95.3 μmol) in one portion. The solution was stirred at room temperature for 18 h, then water (5 mL) was added. The mixture was poured into ether (10 mL) and the organic layer was separated. The aqueous phase was extracted with further ether (2 × 10 mL), the combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated. The product was redissolved in toluene and the solution was concentrated (3 × 2 mL) to give the aldehyde **37** as a pale yellow oil (13 mg, 29.6 μmol, 90%); $[\alpha]_D^{25}$ 0.5 (*c* 1.16 in $CHCl_3$); R_f 0.30 (30% EtOAc / hexane); IR (film): ν=1735; ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.58 (d, *J* (H, H)=3.5 Hz, 1H; CHO) 7.24-7.35 (m, 5H; Ar), 7.21 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 6.86 (d, *J* (H, H)=8.5 Hz, 2H; Ar), 5.48-5.53 (m, 2H; 5-H, 6-H), 4.41-4.51 (m, 4H; 2 × CH_2Ar), 3.79 (s, 3H; OCH_3), 3.77-3.80 (m, 1H; 2-H), 3.56 (dd, *J* (H, H)=3.5, 9.0 Hz, 1H; C*H*HOBn), 3.44-3.52 (m, 2H; CH*H*OBn, 8-H), 3.37 (t, *J* (H, H)=9.0 Hz, 1H; 3-H), 2.68-2.75 (m, 1H; 4-H), 2.50-2.58 (m, 1H; 7-H), 2.24 (dd, *J* (H, H)=5.0, 16.0 Hz, 1H; 7-H'), 1.76-1.83 (m, 1H; 8-C-C*H*CH_3), 1.23 (d, *J* (H, H)=7.0 Hz, 3H; 4-C-Me), 1.00 (d, *J* (H, H)=7.0 Hz, 3H; 8-C-CHC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=199.0, 159.5, 138.7, 135.8, 129.8, 129.6, 128.3 ,127.4, 124.0, 113.9, 85.4, 80.4, 79.6, 73.5, 73.2, 72.4, 55.3, 37.9, 37.2, 28.4, 18.5, 14.7; MS (ES^+): *m/z*(%):461 ($(M+Na)^+$, 100); Found 461.2302, $C_{27}H_{34}O_5Na$ requires 461.2304.

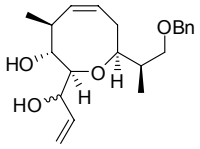
***(Z, 2S, 3R, 4S, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-2-((R/S)-1-hydroxy-prop-2-eneyl)-3-(4-methoxy-benzyloxy)-4-methyl-3,4,7,8-tetrahydro-2H-oxocine* 38**



To a solution of the aldehyde **37** (13 mg, 29.5 μmol) in DMSO (2 mL) in a Schlenk tube under Ar was added $CrCl_2$/1 mol% $NiCl_2$ (35 mg, 29.5 μmol) rapidly in one portion. Vinyl iodide (22 μL, 29.5 μmol) was added and the green solution was

stirred at room temperature for 72 h. A saturated aqueous solution of NH_4Cl (2 mL) was added, and the solution was stirred vigourously for 30 min. The product was extracted with EtOAc (3 × 10 mL), the organic layers were washed with water (5 mL) then brine (5 mL), dried ($MgSO_4$) and concentrated. Flash chromatography (LP:EtOAc, 5:1) afforded the allylic alcohols **38** as a colourless oil (5.5 mg, 11.8 μmol, 2:1 mixture of inseparable diastereomers, 40%); R_f 0.20 (PE:EtOAc, 5:1); IR ($CDCl_3$): ν=3300-3600; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.23-7.36 (m, 7H), 6.88 (d, *J* (H, H)=8.5 Hz, 2H), 6.87 (d, *J* (H, H)=8.5 Hz, 2H), 6.11 (ddd, *J* (H, H)=6.5, 10.5, 17.0 Hz, 1H), 5.96 (ddd, *J* (H, H)=5.0, 10.5, 17.0 Hz, 1H), 5.42-5.57 (m, 2H), 5.38 (dt, *J* (H, H)=1.5, 12.0 Hz, 1H), 5.26-5.32 (m, 2H), 5.12 (dt, *J* (H, H)=1.5, 10.5 Hz, 1H), 4.67 (d, *J* (H, H)=12.0 Hz, 1H), 4.54 (d, *J* (H, H)=10.5 Hz, 1H), 4.52 (s, 2H), 4.48 (d, *J* (H, H)=10.5 Hz, 1H), 4.40-4.51 (m, 1H), 4.38 (d, *J* (H, H)=12.0 Hz, 1H), 4.21 (d, *J* (H, H)=11.5 Hz, 1H), 3.93 (dd, *J* (H, H)=3.5, 9.0 Hz, 1H), 3.79 (s, 3H), 3.63 (dd, *J* (H, H)=3.0, 9.5 Hz, 1H), 3.52-3.59 (m, 2H), 3.37 (dd, *J* (H, H)=1.5, 9.0 Hz, 1H), 3.34 (dd, *J* (H, H)=6.5, 9.0 Hz, 1H), 3.22 (dd, *J* (H, H)=2.5, 9.0 Hz, 1H), 3.07 (t, *J* (H, H)=10.0 Hz, 1H), 2.45-2.73 (m, 3H), 2.17 (dd, *J* (H, H)=6.5, 14.0 Hz, 1H), 1.75-1.83 (m, 1H), 1.57-1.65 (m, 1H), 1.27 (d, *J* (H, H)=6.5 Hz, 3H), 1.24 (d, *J* (H, H)=6.5 Hz, 3H), 1.02 (d, *J* (H, H)=7.0 Hz, 3H), 0.97 (d, *J* (H, H)=7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.3, 159.3, 139.4, 138.6, 137.7, 137.5, 137.2, 136.9, 130.3, 130.2, 129.7, 129.2, 128.3, 128.3, 128.0, 127.7, 127.6, 127.5, 123.4, 123.1, 117.4, 115.4, 113.9, 85.0, 83.1, 81.5, 80.7, 79.3, 78.9, 74.2, 73.6, 73.5, 73.0, 72.5, 72.4, 72.0, 55.3, 55.3, 38.3, 38.1, 36.9, 36.3, 28.0, 27.7, 19.2, 19.0, 15.5, 14.7; MS (CI, perfluorotributylamine): *m/z*(%):484 ($(M+NH_4)^+$, 15), 467 ($(M+H)^+$, 100); Found 467.2790, $C_{29}H_{39}O_5$ requires 467.2797.

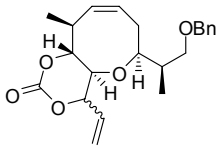
(Z, 2*S*, 3*R*, 4*S*, 8*S*)-8-((1*R*)-2-Benzyloxy-1-methyl-ethyl)-3-hydroxy-2-((1*R*/*S*)-1-hydroxy-prop-2-eneyl)-4-methyl-3,4,7,8-tetrahydro-2*H*-oxocine



To a solution of the alcohols **38** (6.2 mg, 16.6 μmol) in DCM (2 mL) stirring at -20 °C was added TFA (0.5 mL). The mixture was stirred for 30 min during which time the solution became pale orange. The reaction was quenched at -20 °C by addition of

a saturated aqueous solution of $NaHCO_3$ (4 mL), stirred vigourously and allowed to warm to room temperature. The product was extracted with DCM (3 × 5 mL), the extracts being washed with water (5 mL), brine (5 mL), dried ($MgSO_4$) and concentrated. Flash chromatography (PE:EtOAc, 1:1) gave the title compounds as a colourless oil (4.3 mg, 12.4 μmol, 75%); R_f 0.35 (PE:EtOAc, 1:1); IR ($CHCl_3$): ν=3440; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.26-7.36 (m, 5H; Ar), 6.02 (ddd, *J* (H, H)=5.5, 10.5, 17.5 Hz, 1H; minor, C*H*=CH_2), 5.97 (ddd, *J* (H, H)=7.0, 10.5, 17.5 Hz, 1H; major, C*H*=CH_2), 5.43-5.54 (m, 2H; both, H-5, H-6), 5.29-5.34 (m, 1H; both, CH=C*H*H), 5.22 (ddd, *J* (H, H)=1.0, 2.0, 10.5 Hz, 1H; major, CH=CH*H*), 5.17 (dt, *J* (H, H)=1.5, 10.5 Hz, 1H; minor, CH=CH*H*), 4.68 (d, *J* (H, H)=12.0 Hz, 1H; major, C*H*HAr), 4.39-4.45 (m, 1H; both, C*H*CH=CH_2), 4.48 (d, *J* (H, H)=13.0 Hz, 1H; minor, C*H*HAr), 4.39 (d, *J* (H, H)=12.0 Hz, 1H; major, CH*H*Ar), 4.27 (d, *J* (H, H)=12.0 Hz, 1H; minor, CH*H*Ar), 3.90 (dd, *J* (H, H)=3.5, 9.0 Hz, 1H; major, C*H*HOBn), 3.77-3.83 (m, 1H; minor, C*H*HOBn), 3.58 (dd, *J* (H, H)=6.5, 10.5 Hz, 1H; major, 8-H), 3.28-3.50 (m, 4H; minor, CHO*H*CH=CH_2, 3-H, 8-H, CH*H*OBn, both, 2-H), 3.20 (dd, *J* (H, H)=2.0, 9.0 Hz, 1H; major, CH*H*OBn), 3.10-3.14 (m, 1H; major, 3-H), 2.92 (br d, *J* (H, H)=9.0 Hz, 1H major, CHO*H*CH=CH_2), 2.44-2.60 (m, 2H; both, 7-H', 4-H), 2.13-2.27 (m, 1H; both, H-7), 1.69-1.78 (m, 1H; both, 8-C-C*H*CH_3), 1.64 (br d, *J* (H, H)=6.0 Hz, 1H; both, 3-C OH), 1.17 (d, *J* (H, H)=7.0 Hz, 3H; minor, 4-C-Me), 1.16 (d, *J* (H, H)=6.5 Hz, 3H; major, 4-C-Me), 1.00 (d, *J* (H, H)=7.0 Hz 3H; major, 8-C-CHC*H*$_3$), 0.99 (d, *J* (H, H)=7.0 Hz, 3H; minor 8-C-CHC*H*$_3$); ^{13}C NMR (400 MHz, $CDCl_3$): δ=138.5, 138.4, 137.7, 137.2, 137.2, 136.9, 128.4, 128.3, 128.0, 127.7, 127.6, 127.5, 123.6, 123.4, 116.6, 115.9, 84.3, 82.8, 78.9, 78.8, 74.3, 74.1, 74.0, 73.9, 73.5, 73.0, 72.6, 71.8, 38.1, 38.0, 36.5, 35.9, 27.8, 27.5, 18.9, 18.6, 15.6, 14.9; MS (CI, perfluorotributylamine): *m/z*(%): 364 ($(M+NH_4)^+$, 19), 347 ($(M+H)^+$, 63); Found 347.2223, $C_{21}H_{31}O_4$ requires 347.2222.

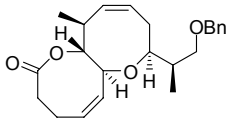
***(Z, 4R/S, 4aS, 6S, 10S, 10aR)-6-((1R)-2-Benzyloxy-1-methyl-ethyl)-10-methyl-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxabenzocycloocten-2-one* 39**



To a mixture of (*Z*, 2*S*, 3*R*, 4*S*, 8*S*)-8-((1*R*)-2-benzyloxy-1-methyl-ethyl)-3-hydroxy-2-((1*R*/*S*)-1-hydroxy-prop-2-eneyl)-4-methyl-3,4,7,8-tetrahydro-2*H*-oxocine (5 mg, 14.4 μmol), triphosgene (2.5 mg, 8.44 μmol) and 4Å molecular sieves (spatula tip) at -78 °C under N_2 was added DCM (2 mL). The solution was stirred at -78 °C, pyridine (7 μL, 86.4 μmol) and Et_3N (12 μL, 86.4 μmol) were added, and the mixture was allowed to warm slowly to -10 °C (1.5 h) at which point no starting material remained. The reaction was quenched *via* addition of of a saturated aqueous solution of NH_4Cl (3 mL) and allowed to warm to room temperature. The product was extracted with DCM (3 × 10 mL), the extracts were washed with brine (5 mL), and dried ($MgSO_4$), and concentrated. Flash chromatography (PE:EtOAc, 3:1) provided the carbonates **39** as a colourless oil (4.8 mg, 12.9 μmol, 90%); R_f 0.61 (PE: EtOAc, 1:1); IR ($CHCl_3$): ν=2927, 1750; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.25-7.36 (m, 5H; both, Ar), 5.89 (ddd, *J* (H, H)=5.5, 10.5, 17.0 Hz, 1H; major, C*H*=CH_2), 5.84-5.94 (m, 1H; minor, C*H*=CH_2), 5.52-5.63 (m, 1H; both, 5-H), 5.44 (dt, *J* (H, H)=1.5, 17.0 Hz, 1H; major, CH=C*H*H), 5.40-5.48 (m, 3H; major, 6-H, minor, 6-H, CH=C*H*H), 5.36-5.40 (m, 1H; minor, CH=CH*H*), 5.22 (dt, *J* (H, H)=1.5, 10.5 Hz, 1H; major, CH=CH*H*), 4.64 (m, 1H; minor, allylic H), 4.57 (ddt, *J* (H, H)=1.5, 5.5, 9.5 Hz, 1H; major, C*H*CH=CH_2), 4.40-4.53 (m, 2H; both, CH_2Ar), 3.86 (unresolved dd, 1H; minor, 3-H), 3.83 (dd, *J* (H, H)=9.5, 10.5 Hz, 1H; major, 3-H), 3.74 (dd, *J* (H, H)=5.5, 10.0 Hz, 1H; minor, 2-H), 3.62 (dd, *J* (H, H)=6.5, 9.5 Hz, 1H; minor, 8-H), 3.53 (dd, *J* (H, H)=6.0, 9.5 Hz, 1H; major, 8-H), 3.46 (dd, *J* (H, H)=3.5, 9.0 Hz, 1H; major, C*H*HOBn), 3.42-3.45 (m, 2H; minor, CH_2OBn), 3.40 (dd, *J* (H, H)=6.0, 9.0 Hz, 1H; major, CH*H*OBn), 3.35 (t, *J* (H, H)=9.5 Hz, 1H; major, 2-H), 2.61-2.71 (m, 1H; both, 4-H), 2.52-2.57 (m, 1H; major, 7-H), 2.47-2.53 (m, 1H; minor, 7-H), 2.28 (dd, *J* (H, H)=6.5, 14.5 Hz, 1H; both, 7-H'), 1.70-1.81 (m, 1H; both, 8-C-C*H*CH_3), 1.27 (d, *J* (H, H)=6.5 Hz, 3H; major, 4-C-Me), 1.23 (d, *J* (H, H)=6.5Hz, 3H; minor, 4-C-Me), 1.04 (d, *J* (H, H)=6.5 Hz, 3H; minor, 8-C-CHCH_3), 1.02 (d, *J* (H, H)=7.0 Hz, 3H; major, 8-C-CHCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=148.2, 147.9, 138.5, 138.4, 134.8, 134.6, 131.9, 131.2, 128.4, 128.3, 127.7,

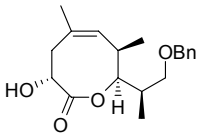
127.6, 127.5, 127.4, 125.6, 125.4, 119.2, 118.8, 82.4, 80.4, 80.0, 79.6, 79.5, 77.1, 75.0, 73.2, 72.6, 72.1, 71.9, 36.6, 36.5, 36.1, 36.0, 28.0, 28.0, 18.1, 17.8, 14.8, 14.8; MS (CI, perfluorotributylamine): *m/z*(%):373 ($(M+NH_4)^+$, 23), 373 ($(M+H)^+$, 9); Found 373.2015, $C_{22}H_{29}O_5$ requires 373.2015.

***(5Z, 10Z, 6a*S*, 8*S*, 12*S*, 12a*R*)-8-((1*R*)-2-Benzyloxy-1-methyl-ethyl)-12-methyl-4,6a,8,9,12,12a-hexahydro-3*H*-1,7-dioxa-octalen-2-one* 40**



To a solution of carbonates **39** (4.8 mg, 12.9 μmol) in toluene (2 mL) was added dimethyltitanocene (37 μL of a 94 mg/mL solution in toluene, 16.8 μmol). The mixture was heated under reflux in the absence of light for 1.5 h at which point further dimethyltitanocene (15 μL, 6.45 μmol) was added. After a further 1.5 h under reflux, the mixture was allowed to cool, concentrated, and purified by flash chromatography (PE:EtOAc, 20:3) to yield the bicyclic lactone **40** as a colourless oil (2.2 mg, 5.93 μ mol, 46%); $[\alpha]_D^{21}$ -9.1 (*c* 0.22 in $CHCl_3$); R_f 0.33 (PE:EtOAc, 20:3); IR ($CHCl_3$): ν=1747; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.25-7.35 (m, 5H; Ar), 5.63-5.71 (m, 1H; 5-H), 5.58 (dd, *J* (H, H)=5.0, 12.0 Hz, 1H; 6-H), 5.47-5.56 (m, 2H; 10-H, 11-H), 4.26 (d, *J* (H, H)=3.0 Hz, 2H; C*H*$_2$Ar), 4.18 (dd, *J* (H, H)=9.5, 10.5 Hz, 1H; 12a-H), 4.08 (ddd, *J* (H, H)=2.0, 5.0, 9.5 Hz, 1H; 6a-H), 3.52 (dd, *J* (H, H)=3.5, 9.0 Hz, 1H; C*H*HOBn), 3.47 (ddd, *J* (H, H)=2.0, 7.0, 9.0 Hz, 1H; 8-H), 3.43 (dd, *J* (H, H)=6.0, 9.0 Hz, 1H; CH*H*OBn), 2.77 (ddd, *J* (H, H)=2.0, 6.5, 14.0 Hz, 1H; 3-H), 2.67-2.73 (m, 1H; 12-H), 2.60-2.67 (m, 1H; 4-H), 2.51-2.59 (m, 1H; 9-H), 2.27 (ddd, *J* (H, H)=5.0, 12.0, 14.0 Hz, 1H; 3-H'), 2.22-2.28 (m, 1H; 9-H'), 2.08-2.15 (m, 1H; 4-H'), 1.66-1.77 (m, 1H; 8-C-C*H*CH$_3$), 1.15 (d, *J* (H, H)=6.5 Hz, 3H; 12-C-Me), 1.00 (d, *J* (H, H)=7.0 Hz, 3H; 8-C-CHC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=174.9, 128.8, 136.9, 135.1, 129.9, 128.2, 127.5, 127.4, 125.0, 81.4, 79.9, 78.8, 73.1, 72.6, 37.4, 37.3, 35.6, 28.9, 25.5, 19.2, 14.7; MS (CI, perfluorotributylamine): *m/z*(%): 388 ($(M+NH_4)^+$, 42), 371 ($(M+H)^+$, 100); Found 371.2224, $C_{23}H_{31}O_4$ requires 371.2222.

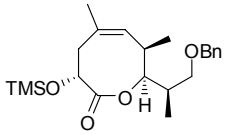
***(Z, 3R, 7R, 8S)-8-(1(R)-2-Benzyloxy-1-methyl-ethyl)-3-hydroxy-5,7-dimethyl-3,4,7,8-tetrahydrooxocin-2-one* 41**



To a cooled solution (-78 °C) of KHMDS (4.8 mL, 0.5 M solution in toluene, 2.40 mmol) in toluene (7 mL) was added the lactone **9**[2] (325 mg, 1.09 mmol) *via* cannula as a solution in toluene (4 mL, 1 mL rinse). The mixture was stirred for 20 min. (±)-2-(Phenylsulfonyl)-3-phenyloxaziridine (900 mg, 3.43 mmol) was added dropwise *via* cannula as a solution in toluene (4 mL, 2 mL rinse). The mixture was stirred at -78 °C for a further 1.5 h, and was quenched at this temperature with a solution of (±)-camphor-10-sulfonic acid (approx. 2.5 eq.) in THF (5 mL). The mixture was warmed to ambient temperature and water (20 mL) was added. The mixture was extracted with ether (3 × 40 mL) and the combined organics were washed with brine (40 mL), dried ($MgSO_4$) and evaporated *in vacuo*. Purification by flash chromatography (hexane:ether, 19:11) yielded the title compound **41** as a an inseparable mixture of 3-C diastereomers (307 mg, 0.963 mmol, 88%) in a ratio determined by ^{1}H NMR to be 20:1; R_f(DCM:ether, 100:3) 0.17; $[\alpha]_D^{23}$ -10.2 (*c* 0.65 in $CHCl_3$); mp 102-104 °C; IR ($CHCl_3$): ν=3541, 1741; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.40-7.24 (m, 5H; Ar), 5.48 (d, *J* (H, H)=8.7 Hz, 1H; major, 6-H), 5.09 (br s, 1H; minor, 6-H), 4.60 (dd, *J* (H, H)=8.0, 3.7 Hz, 1H; major, 3-H), 4.87 (dd, *J* (H, H)=9.3, 3.9 Hz, 1H; minor, 6-H), 4.62-4.56 (m, 1H; minor, 8-H), 4.56-4.45 (m, 3H; major, C*H*$_2$Ar, major, 8-H), 4.47 (d, *J* (H, H)=12.1 Hz, 1H; minor C*H*HAr), 4.44 (d, *J* (H, H)=12.1 Hz, 1H; minor, CH*H*Ar), 3.60 (dd, *J* (H, H)=8.7, 4.1 Hz, 1H; minor C*H*HOBn), 3.58 (dd, *J* (H, H)=9.1, 3.6 Hz, 1H; major, C*H*HOBn), 3.39 (dd, *J* (H, H)=8.7, 2.3 Hz, 1H; minor CH*H*OBn), 3.32 (dd, *J* (H, H)=9.1, 7.3 Hz, 1H; major, CH*H*OBn), 3.08-2.85 (m, 1H; OH), 2.95-2.72 (m, 1H; major 4-H), 2.63-2.45 (m, 1H; major, 7-H), 2.27 (d, *J* (H, H)=14.8 Hz, 1H; minor 4-H), 2.25 (dd, *J* (H, H)=13.4, 5.9 Hz, 1H; major 4-H'), 2.17-2.00 (m, 1H; 8-C-C*H*CH$_3$), 1.82 (d, *J* (H, H)=1.4 Hz, 3H; major 5-C-CH$_3$), 1.77 (d, *J* (H, H)=1.4 Hz, 3H; minor 5-C-CH$_3$) 1.14 (d, *J* (H, H)=7.2 Hz, 3H; major, CH$_3$), 1.07 (d, *J* (H, H)=6.9 Hz, 3H; minor, CH$_3$), 1.06 (d, *J* (H, H)=7.3 Hz, 3H; minor CH$_3$), 1.05 (d, *J* (H, H)=6.9 Hz, 3H; major CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=179.7, 138.5, 129.1, 128.5, 128.3, 127.6, 127.5, 81.4, 73.3, 73.0, 72.3, 39.9 (br), 35.6, 34.3

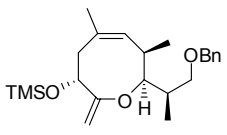
(br), 28.3 (br), 14.1 (br), 12.5 (br); MS (CI, NH_3): *m/z*(%) 336 ($(M+NH_4)^+$, 100), 319 ($(M+H)^+$, 35); Found 319.1902, $C_{19}H_{27}O_4$ requires 319.1909.

***(Z, 3R, 7R, 8S)-8-(1(R)-2-Benzyloxy-1-methyl-ethyl)-5,7-dimethyl-3-trimethylsilanyloxy-3,4,7,8-tetrahydrooxocin-2-one* 42**



To a solution of the alcohol **41** in THF was added Et_3N (50 μL, 0.36 mmol). Et_3N (300 μL) and TMSCl (300 μL) were mixed together and centrifuged in a sealed vessel at 4000 r.p.m. for 3 min. Approximately 75% of the supernatant liquid was added to the reaction mixture dropwise *via* syringe. The mixture was stirred at room temperature for 40 min, was cooled to 0 °C and then quenched by the addition of pH 7 phosphate buffer (5 mL). The mixture was extracted with ether (3 × 15 mL) and the combined organics were dried ($MgSO_4$) and evaporated. Purification by flash chromatography (hexane:ether, 9:1) yielded the title compound **42** (84 mg, 0.215 mmol, 88%); R_f (hexane:ether, 9:1) 0.27; $[\alpha]_D^{22}$ +5.6 (*c* 2.5 in $CHCl_3$); IR ($CHCl_3$): ν=($CHCl_3$) 1755; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.40-7.23 (m, 5H; Ar), 5.37 (d, *J* (H, H)=8.9 Hz, 1H; *H*C=C), 4.57-4.43 (m, 4H; C*H*$_2$Ar, 3-H, 8-H), 3.61 (dd, *J* (H, H)=9.2, 3.8 Hz, 1H; C*H*HOBn), 3.27 (t, *J* (H, H)=9.2 Hz, 1H; C*H*HOBn), 2.82-2.45 (m, 2H; 4-H, 7-H), 2.40-2.21 (m, 1H; 4-H'), 2.19-2.00 (m, 1H; 8-C-C*H*CH_3), 1.82 (s, 3H; 5-C-CH_3), 1.09 (d, *J* (H, H)=7.0 Hz, 3H; CH_3), 1.06 (d, *J* (H, H)=6.8 Hz, 3H; CH_3), 0.18 (s, 9H; $(CH_3)_3Si$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=177.8 (2-C), 138.7, 128.6, 128.3, 127.6, 127.5, 79.6 (8-C), 73.2 (*C*H_2Ar), 72. 4 (*C*H_2OBn), 41.0 (4-C), 35.4 (1'-C), 34.0 (7-C), 27.7 (vinyl CH_3), 15.3 (Me), 0.0 ($(CH_3)_3Si$); MS (EI): Found M^+, 390.2230, $C_{22}H_{34}O_4Si$ requires 390.2226.

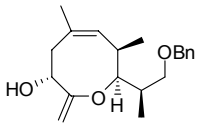
(Z, 3R, 7R, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-5,7-dimethyl-2-methylene-3-trimethylsilanyloxy-3,4,7,8-tetrahydro-2H-oxocine



To a solution of the lactone **42** (515 mg, 1.32 mmol) in toluene (20 mL) was added dimethyltitanocene (8.2 mL of a 50 mg/mL solution in toluene, 1.98 mmol.) *via*

syringe. A condenser was fitted to the flask and the mixture was heated under reflux with the exclusion of light for 1 h. Additional dimethyltitanocene (3.0 mL, 0.72 mmol) was added and the mixture was stirred a further 20 min. Following cooling, the mixture was preadsorbed onto deactivated UG1 alumina (deactivated by the addition of 6% H_2O (w/w). The resultant solid was loaded onto a column of deactivated UG1 alumina and purified by eluting under gravity (hexane:ether, 94:6), yielding the title compound (503 mg, 1.29 mmol, 98%) as an orange oil; R_f (hexane:ether 19:1) 0.31; $[\alpha]_D^{21}$ +16.5 (*c* 1.2, $CDCl_3$); IR ($CHCl_3$): ν=1646; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.40-7.24 (m, 5H; Ar), 5.91 (s, 1H; OC=C*H*H), 5.16 (d, 1H; *J* (H, H)=8.6 Hz, 1H; 6-H), 4.84 (s, 1H; OC=CH*H*), 4.51 (s, 2H; CH_2Ar), 3.99 (br t, *J* (H, H)=6.3 Hz, 1H; 3-H), 3.70 (t, *J* (H, H)=4.9 Hz, 1H; 8-H), 3.59 (dd, *J* (H, H)=9.2, 4.8 Hz, 1H; C*H*HOBn), 3.29 (dd, *J* (H, H)=9.2, 7.8 Hz, 1H; CH*H*OBn), 2.81-2.62 (m, 1H; 7-H), 2.37-2.25 (m, 2H; 2 × 4-H), 2.14-1.97 (m, 1H; 8-C-C*H*CH_3), 1.76 (d, *J* (H, H)=1.3 Hz, 3H; vinyl CH_3), 1.15 (d, *J* (H, H)=6.9 Hz, 3H; 1'-C-CH_3), 1.02 (d, *J* (H, H)=7.1 Hz, 3H; 7-C-CH_3), 0.15 (m, 9H; $(CH_3)_3$Si); ^{13}C NMR (100 MHz, $CDCl_3$): δ=167.8 (2-C), 138.9 (5-C), 134.2, 128.3, 128.1, 127.5, 127.4, 112.6 (C-6), 92.1 (H_2C=C), 86.5 (8-C), 73.0 (*C*H_2Ar), 72.5 (*C*H_2OBn), 71.8 (3-C), 42.7 (4-C), 34.4 (1'-C), 34.2 (7-C), 26.5 (vinyl CH_3), 16.9 (1-C-*C*H_3), 15.0 (7-C-*C*H_3), -0.1 ($(CH_3)_3$Si); MS (EI): Found M^+ 388.2445, $C_{23}H_{36}O_3Si$, requires 388.2434.

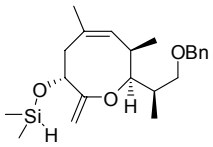
***(Z, 3*R*, 7*R*, 8*S*)-8-((1*R*)-2-Benzyloxy-1-methyl-ethyl)-5,7-dimethyl-3-hydroxy-2-methylene-3,4,7,8-tetrahydro-2*H*-oxocine* 43**



To a cooled (0 °C) solution of (*Z*, 3*R*, 7*R*, 8*S*)-8-((1*R*)-2-benzyloxy-1-methyl-ethyl)-5,7-dimethyl-2-methylene-3-trimethylsilanyloxy-3,4,7,8-tetrahydro-2*H*-oxocine (15.5 mg, 39.8 μmol) in dry MeOH (1 mL) was added solid K_2CO_3 (10 mg, 72 μmol). The mixture was warmed to ambient temperature and stirred for 30 min. Filtration of the mixture (glass wool) was followed by purification by gravity pipette chromatography (ether:hexane, 1:1) using deactivated UG1 alumina to afford the title compound **43** (11.0 mg, 34.7 μmol, 87%) as a clear oil; R_f (ether:hexane, 1:1) 0.33; $[\alpha]_D^{22}$ +8.8 (*c* 0.5, $CHCl_3$); IR ($CHCl_3$): ν=3598, 1644; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.37-7.25 (m,

5H; Ar), 5.13 (d, *J* (H, H)=9.3 Hz, 1H; 6-H), 4.86 (t, *J* (H, H)=1.3 Hz, 1H; OC=C*H*H), 4.57 (d, *J* (H, H)=1.3 Hz, 1H; OC=CH*H*), 4.48 (s, 2H; CH_2Ar), 4.01 (br dd, *J* (H, H)=10.3, 6.5 Hz, 1H; 3-H), 3.72 (dd, *J* (H, H)=5.0, 4.3 Hz, 1H; 8-H), 3.57 (dd, *J* (H, H)=9.3, 3.8 Hz, 1H; C*H*HOBn), 3.24 (dd, *J* (H, H)=9.3, 7.9 Hz, 1H; CH*H*OBn), 2.83-2.71 (m, 1H; 7-H), 2.35 (d, *J* (H, H)=6.5 Hz, 2H; 4-H, 4-H'), 2.17 (s, 1H; OH), 2.11-2.02 (m, 1H; 8-C-C*H*CH_3), 1.76 (s, 3H; vinyl CH_3), 1.15 (d, *J* (H, H)=6.9 Hz, 3H; 1'-C-CH_3), 1.00 (d, *J* (H, H)=7.1 Hz, 3H; 7-C-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=168.2 (*C*=CH_2), 138.8 (5-C), 133.4 (ArC), 128.6, 128.3, 127.6, 127.4, 91.6 (H_2C=C), 86.7 (8-C), 73.0 (*C*H_2Ar), 72.3 (*C*H_2OBn), 71.9 (*C*HOH), 41.3 (4-C), 34.3 (1'-C), 34.0 (7-C), 26.4 (vinyl CH_3), 17.1 (9-C-*C*H_3), 15.4 (7-C-*C*H_3); MS (CI, NH_3): *m/z*(%): 334 ((M+NH_4)$^+$, 18), 317 ((M+H)$^+$, 100); Found 317.2117. $C_20H_{29}O_3$ requires 317.2117.

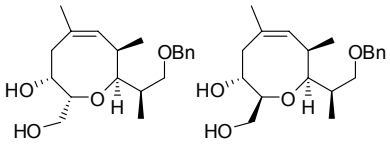
***(Z, 3R, 7R, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-5,7-dimethyl-3-dimethylsilanyloxy-2-methylene- -3,4,7,8-tetrahydro-2H-oxocine* 44**



To a solution of the enol ether **43** (292 mg, 0.923 mmol) in 1,1,3,3-tetramethyldisilazane (1.9 mL) was added solid NH_4Cl (~10 mg). The mixture was heated to 60 °C for 9 h. Upon cooling to ambient temperature, dry hexane (5 mL) was added. The mixture was quickly filtered through a plug of cotton wool and was then evaporated to afford the title compound **44** (342 mg, 0.91 mmol, 99%) as a yellow oil which was stored under vacuum for 48 h and then used immediately; $[\alpha]_D^{22}$ +8.8 (*c* 0.5, $CHCl_3$); IR ($CDCl_3$): ν=2245, 2120, 1646, 1453; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.37-7.32 (m, 4H; Ar), 7.32-7.24 (m, 1H; Ar), 5.17 (d, *J* (H, H)=9.5 Hz; 1H; 6-H), 4.84 (t, *J* (H, H)=1.2 Hz, 1H; OC=C*H*H), 4.68 (sp, *J* (H, H)=2.8 Hz, 1H; Si-H), 4.53 (s, 1H; OC=CH*H*), 4.50 (s, 1H; C*H*HAr), 4.49 (s, 1H; CH*H*Ar), 3.99 (br t, *J* (H, H)=5.8 Hz, 1H; 3-H), 3.70 (t, *J* (H, H)=5.5 Hz, 1H; 8-H), 3.58 (dd, *J* (H, H)=9.3, 3.8 Hz, 1H; C*H*HOBn), 3.27 (dd, *J* (H, H)=9.3, 7.8 Hz, 1H; CH*H*OBn), 2.80-2.67 (m, 1H; 7-H), 2.40-2.30 (m, 2H; 4-H, 4-H'), 2.12-2.01 (m, 1H; 8-C-C*H*CH_3), 1.76 (d, *J* (H, H)=1.3 Hz, 3H; 5-C-CH_3), 1.15 (d, *J* (H, H)=6.9 Hz, 3H; 8-C-CHC*H*$_3$), 1.01 (d, *J* (H, H)=7.1 Hz, 3H; 7-C-CH_3), 0.25 (d, *J* (H, H)=2.8 Hz, 3H; SiCH_3), 0.24 (d, *J* (H,

H)=2.8 Hz, 3H; $SiCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=167.2 (*C*=CH_2), 138.9 (5-C), 133.9, 128.3, 127.5, 127.4, 92.2 (H_2C=C), 85.5 (8-C), 73.3 (3-C), 73.0 (CH_2Ar), 72.5 (CH_2OBn), 42.3 (4-C), 34.4 (1'-C), 34.2 (7-C), 26.4 (5-C-CH_3), 16.9 (8-C-CHCH_3), 15.0 (7-C-CH_3), -1.2 ($SiCH_3$), -1.3 ($SiCH_3$). This compound was not suitable for analysis by mass spectrometry.

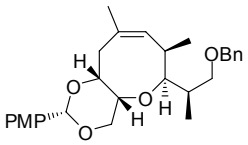
***(Z, 2R, 3R, 7R, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-3-hydroxy-2-hydroxymethyl-7-methyl-3,4,7,8-tetrahydro-2H-oxocin* 45, *and (Z, 2S, 3R, 7R, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-3-hydroxy-2-hydroxymethyl-7-methyl-3,4,7,8-tetrahydro-2H-oxocin* 46**



To a dry Schlenk tube in a glove box was added (bicyclo(2.2.1)hepta-2,5-diene)(1,4-bis(diphenylphosphino)butane)rhodium(I)tetrafluoroborate (~20 mg, 28 μmol). The Schlenk tube was sealed and taken out of the glove box. It was placed on a dry Ar manifold and was flushed with Ar and evacuated 3 times, finally leaving the catalyst under a positive pressure of argon. The enol ether **44** (190 mg, 0.51 mmol) was charged to the Schlenk tube *via* cannula as a solution in dry and O_2-free THF (6 mL, 6 mL rinse). THF (4 mL) was added. The solution was stirred for 26 h at 62 °C and was then cooled to ambient temperature. Solid $EDTANa_2 \bullet 2H_2O$ (50 mg) was added to the mixture and stirring was continued for 1 h. The mixture was then diluted with dry hexane (30 mL) and filtered through a plug of Celite™ eluting with dry hexane. The resulting liquid was evaporated *in vacuo* and dissolved in THF:MeOH 1:1 (7 mL). To this solution was added KOH (1.0 mL, 0.15 M) and H_2O_2 (0.5 mL, 30%) and the mixture was stirred for 1 h. Additional KOH (0.4 mL, 0.15 M) and H_2O_2 (0.2 mL, 30%) were added and stirring was continued for 15 min. The reaction was quenched by the addition of 10% $Na_2S_2O_3$ (60 mL). The mixture was extracted with EtOAc (3 × 50 mL) and the combined organic layers were washed with brine (50 mL). Purification by flash chromatography (DCM:MeOH, 25:1→50:3) led to the isolation of the product diols **45** and **46** (104 mg, 0.31 mmol, 61%) as an inseparable mixture of diastereomers in a ratio of approx 6.4:1 as judged by ^1H NMR; R_f (DCM:MeOH, 20:1) 0.12; $[\alpha]_D^{24}$ +13.7 (*c* 1.4, $CHCl_3$); IR ($CHCl_3$): ν=3942, 3688; ^1H NMR (400

MHz, $CDCl_3$): δ=7.40-7.24 (m, 5H; Ar), 5.35 (d, *J* (H, H)=6.8 Hz, 1H; 6-H), 4.51 (s, 2H; C*H*$_2$Ar), 4.15-4.03 (m, 1H; 8-H), 4.03-3.91 (m, 2H; 2-H, 3-H), 3.74-3.60 (m, 2H; *H*$_2$C=C), 3.56 (dd, *J* (H, H)=8.8, 3.8 Hz, 1H; C*H*HOBn), 3.40 (t, *J* (H, H)=8.8 Hz, 1H; CH*H*OBn), 2.97-2.87 (m, 1H; 7-H), 2.84 (d, *J* (H, H)=6.8 Hz, 1H; OH), 2.80-2.69 (m, 2H; 4-H), 2.30 (dd, *J* (H, H)=13.1, 7.0 Hz, 1H; 4-H'), 2.15-2.05 (m, 1H; 8-C-C*H*CH_3), 1.72 (s, 3H; 5-C-CH_3), 1.05 (d, *J* (H, H)=6.9 Hz, 3H; CH_3), 1.04 (d, *J* (H, H)=7.4 Hz, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=138.3, 133.0, 131.0, 128.4, 127.8, 127.7, 83.0, 81.7, 74.3, 73.3, 72.6, 72.3, 71.5, 65.0, 40.5, 39.3, 38.3, 35.8, 34.9, 26.8, 25.9, 17.1, 16.9, 15.8, 14.4; MS (CI, NH_3): *m/z*(%): 352 ((M + NH_4)$^+$, 2), 335 ((M + H)$^+$, 13), 106 (100); Found 335.2219, $C_{20}H_{31}O_4$ requires 335.2222.

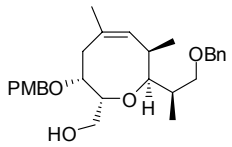
***(Z, 2*S*, 4a*R*, 6*S*, 7*R*, 10a*R*)-6-((1*R*)-2-Benzyloxy-1-methyl-ethyl))-7,9-dimethyl-2-(4-methoxyphenyl)-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxabenzocyclooctene* 47**



To a solution of the mixture of diols **45** and **46** (100 mg, 0.30 mmol) in benzene was added anisaldehyde (45 μL, 0.36 mmol) *via* syringe followed by solid PPTS (8 mg). The mixture was heated under reflux (Dean-Stark conditions) for 2.5 h. The mixture was evaporated and the residue was purified by flash chromatography (hexane ether, 3:1→13:7) to afford the major product acetal **47** (110 mg, 0.243 mmol, 81%) as a clear colourless oil. The ^{1}H NMR data at -30 °C and 55 °C are reported, R_f (hexane:ether, 3:1) 0.17; $[\alpha]_D^{24}$ - 8.1 (*c* 0.85, $CHCl_3$); IR ($CHCl_3$): ν=1614, 1518, 1454, 1260, 1105; ^{1}H (400 MHz, -30 °C $CDCl_3$): δ=7.48-7.42 (m, 2H; Ar), 7.39-7.26 (m, 6H; Ar), 6.86 (d, *J* (H, H)=8.4 Hz, 2H; Ar), 5.48 (s, 1H; 2-H), 5.35 (d, *J* (H, H)=8.6 Hz, 1H; 8-H), 4.51 (d, *J* (H, H)=11.8 Hz, 1H; C*H*HAr), 4.44 (d, *J* (H, H)=11.8 Hz, 1H; CH*H*Ar), 4.12 (dd, *J* (H, H)=11.1, 6.1 Hz, 1H; 10a-H), 4.06 (d, *J* (H, H)=12.2 Hz, 1H; 4-H), 3.91 (d, *J* (H, H)=12.2 Hz, 1H; 4-H'), 3.85-3.76 (m, 4H; CH_3O, 6-H), 3.69 (br d, *J* (H, H)=8.6 Hz, 1H; C*H*HOBn), 3.62 (br s, 1H; 4a-H), 3.23-3.11 (m, 1H; 7-H), 3.17 (br t, *J* (H, H)=8.6 Hz, 1H; CH*H*OBn), 2.92 (br t, *J* (H, H)=11.8 Hz, 1H; 10-H), 2.24-2.14 (m, 2H; 10-H', 6-C-C*H*CH_3), 1.75 (s, 3H; 9-C-CH_3), 1.12 (d, *J* (H, H)=6.5 Hz, 3H; 6-C-CHC*H*$_3$), 1.05 (d, *J* (H, H)=7.2 Hz, 3H; 7-C-CH_3); ^{1}H NMR (400 MHz, 55 °C $CDCl_3$): δ=7.44 (dt, *J* (H, H)=8.6, 2.4 Hz, 2H; Ar), 7.36-7.24 (m, 6H; Ar), 6.85 (dt,

J (H, H)=8.6, 2.4 Hz, 2H; Ar), 5.46 (s, 1H; 2-H), 5.39 (d, *J* (H, H)=7.7 Hz, 1H; 8-H), 4.52 (d, *J* (H, H)=12.1 Hz, 1H; C*H*HAr), 4.48 (d, *J* (H, H)=12.1 Hz, 1H; CH*H*Ar), 4.14 (dd, *J* (H, H)=12.1, 1.6 Hz, 1H; 4-H), 4.06 (ddd, *J* (H, H)=12.4, 6.2, 1.6 Hz, 1H, 10a-H), 4.06-3.99 (m, 1H; 6-H), 3.89 (dd. *J* (H, H)=12.1, 1.6 Hz, 1H; 4-H'), 3.79 (s, 3H; CH_3O), 3.73 (dd, *J* (H, H)=9.1, 3.2 Hz, 1H; C*H*HOBn), 3.66 (br q, *J* (H, H)=1.6, Hz 1H; 4a-H), 3.32 (t, *J* (H, H)=9.1 Hz, 1H; CH*H*OBn), 3.17-3.05 (m, 1H; 7-H), 3.03 (br t, *J* (H, H)=12.4 Hz, 1H; 10-H), 2.23 (dd, *J* (H, H)=12.4, 6.2 Hz, 1H; 10-H'), 2.19-2.11 (m, 1H; 6-C-C*H*CH_3), 1.79 (s, 3H; 9-C-CH_3), 1.11 (d, *J* (H, H)=6.8 Hz, 1H; 9-C-CH_3), 1.06 (d, *J* (H, H)=7.4 Hz, 3H; 7-C-CH_3); ^{13}C NMR (100 MHz, -30 °C $CDCl_3$): δ=158.5, 137.0 (ArC), 132.5 (9-C), 129.3 (ArC), 129.1 (8-C), 127.4 (ArC), 127.0 (ArC), 126.7 (ArC), 126.4 (ArC), 112.2 (ArC), 100.1 (2-C), 84.4 (6-C), 79.8 (10a-C), 72.7 (*C*H_2OBn), 72.1, 72.0, 62.9 (4a-C), 54.2 (CH_3O), 38.5 (7-C), 34.2 (10-C), 32.9, 23.3 (9-C-*C*H_3), 18.4 (7-C-*C*H_3), 15.2; MS (CI, NH_3): *m/z*(%): 470 ($(M+NH_4)^+$, 15), 453 ($(M+H)^+$, 75), 137 (100); Found 453.2637, $C_{28}H_{37}O_5$ requires 453.2641.

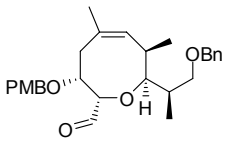
***(Z, 2*R*, 3*R*, 7*R*, 8*S*)-8-((1*R*)-2-Benzyloxy-1-methyl-ethyl)-7,9-dimethyl-2-hydroxymethyl-3-(4-methoxy-benzyloxy)-3,4,7,8-tetrahydro-2*H*-oxocine* 48**



To a cooled (-78 °C) solution of the acetal **47** (93 mg, 0.205 mmol) in toluene was added DIBAL-H (1.44 mL, 1 M solution on DCM, 1.44 mmol) dropwise *via* syringe down the side of the flask. The mixture was warmed to -30 °C and stirred for 1 h. Upon re-cooling to -78 °C, the mixture was quenched by the slow addition of dry MeOH (11 mL). The cooling bath was removed and NH_4Cl:sodium potassium tartrate 1:1 (10 mL) was added slowly *via* syringe during warming to ambient temperature. The mixture was extracted with ether (4 × 15 mL), each fraction was washed with the same portion of brine (15 mL) and the combined organic layers were dried ($MgSO_4$) and evaporated. Purification by flash chromatography (ether:hexane, 1:1) afforded the alcohol **48** (90 mg, 0.198 mmol, 97%) as a clear colourless oil; R_f (ether:hexane, 1:1) 0.18; $[\alpha]_D^{23}$ +7.9 (*c* 0.43, $CHCl_3$); IR ($CHCl_3$): ν=1612, 1514, 1266, 1248; ^{1}H (400 MHz, $CDCl_3$): δ=7.35-7.23 (m, 8H; Ar), 6.87 (m, 2H; Ar), 5.34 (d, *J* (H, H)=7.2 Hz, 1H; 6-H), 4.65 (d, *J* (H, H)=11.6 Hz, 1H; C*H*HAr), 4.49 (s, 2H;

C*H*$_2$Ar), 4.38 (d, *J* (H, H)=11.6 Hz, 1H; CH*H*Ar), 4.02-3.94 (m, 2H; 8-H, 2-H), 3.80 (s, 3H; CH_3O), 3.69 (ddd, *J* (H, H)=10.8, 6.1, 2.3 Hz, 1H; 3-H), 3.68-3.63 (m, 1H; C*H*HOH), 3.61 (dd, *J* (H, H)=8.9, 4.3 Hz, 1H; C*H*HOBn), 3.58-3.52 (m, 1H; CH*H*OH), 3.33 (dd, *J* (H, H)=8.9, 7.1 Hz, 1H; CH*H*OBn), 3.08-2.97 (m, 1H; 7-H), 2.84 (br t, *J* (H, H)=10.8 Hz, 1H; 4-H), 2.37 (dd, *J* (H, H)=8.4, 4.3 Hz, 1H, OH), 2.33 (dd, *J* (H, H)=12.5, 6.1 Hz, 1H; 4-H), 2.20-2.09 (m, 1H; 8-C-C*H*CH_3), 1.71 (s, 3H; 5-C-CH_3), 1.06 (d, *J* (H, H)=7.1 Hz, 3H; CH_3), 1.04 (d, *J* (H, H)=7.4 Hz, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=159.3, 138.5, 133.5, 130.9, 130.3, 129.6, 128.3, 127.6, 127.5, 113.9, 79.2, 74.7, 73.2, 70.5, 64.1, 55.3, 38.8, 35.4, 34.5, 25.3, 17.7, 15.9; MS (CI, NH_3): *m/z*(%): 472 ($(M+NH_4)^+$, 20), 455 ($(M+H)^+$, 100); Found 455.2790, $C_{28}H_{39}O_5$ requires 455.2797.

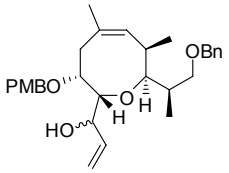
***(Z, 2S, 3R, 7R, 8S)-8-((1R)-2-Benzyloxy-1-methyl-ethyl)-2-carbaldehyde-3-(4-methoxy-benzyloxy)-7-methyl-3,4,7,8-tetrahydro-2H-oxocine* 49**



To a solution of the alcohol **48** (90 mg, 0.198 mmol) in DMSO (10 mL) was added *o*-iodoxybenzoic acid (IBX) (140 mg). The mixture was stirred under Ar for a period of 16 h. The mixture was cooled to 0 °C and water (2 mL) was added slowly. Water (40 mL) was then added and the mixture was extracted with ether (3 × 40 mL). The combined organic layers were washed with brine (50 mL), dried ($MgSO_4$) and evaporated. The clean (by ^{1}H NMR) aldehyde **49** (90 mg, 0.198 mmol, 100%) was isolated as a clear oil; R_f (hexane:ether, 1:1) 0.40; $[\alpha]_D^{25}$ -15.0 (*c* 1.69, $CHCl_3$); IR ($CHCl_3$): ν=1731; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.35-7.25 (m, 5H; Ar), 7.17 (d, *J* (H, H)=8.6 Hz, 2H; Ar), 6.84 (d, *J* (H, H)=8.6 Hz, 2H; Ar), 5.29 (d, *J* (H, H)=8.5 Hz, 1H; 6-H), 4.49 (d, *J* (H, H)=11.3 Hz, 1H C*H*HAr), 4.42 (s, 2H; C*H*$_2$Ar), 4.34 (d, *J* (H, H)=11.3 Hz, 1H; CH*H*Ar), 4.17 (d, *J* (H, H)=2.3 Hz, 1H; 2-H), 4.12 (ddd, *J* (H, H)=11.8, 6.3, 2.3 Hz, 1H; 3-H), 4.01 (dd, *J* (H, H)=9.3, 3.4 Hz, 1H; 8-H), 3.79 (s, 3H; CH_3O), 3.42 (dd, *J* (H, H)=9.2, 3.4 Hz, 1H; C*H*HOBn), 3.25-3.14 (m, 1H; 7-H), 3.19 (dd, *J* (H, H)=9.2, 6.7 Hz, 1H; CH*H*OBn), 2.83 (t, *J* (H, H)=11.8 Hz, 1H; 4-H), 2.11-1.98 (m, 1H; 8-C-C*H*CH_3), 1.72 (s, 3H; 5-C-CH_3), 1.08 (d, *J* (H, H)=6.8 Hz, 3H; CH_3), 1.08 (d, *J* (H, H)=7.5 Hz, 3H; CH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=205.8,

159.3, 138.3, 135.3, 130.2, 129.8, 129.6, 128.3, 127.7, 127.6, 113.7, 85.4, 81.9, 78.5, 73.2, 73.2, 71.4, 55.3, 39.5, 34.6, 33.6, 24.5, 19.0, 15.8; MS (CI): *m/z*(%): 470 ($(M+NH_4)^+$, 20), 453 ($(M+H)^+$, 6), 163 (100); Found 470.2903, $C_{28}H_{40}O_5N$ requires 470.2906.

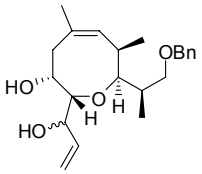
***(Z, 2*R*, *3*R*, *7*R*, *8*S)-8-((1*R*)-2-Benzyloxy-1-methyl-ethyl)2-((1*R/*S*)-1-hydroxy-prop-2-eneyl)-3-(4-methoxy-benzyloxy)-7-methyl-3,4,7,8-tetrahydro-2*H*-oxocine* 50**



A suspension of $CeCl_3$ (145 mg, 0.59 mmol) (pre-weighed in a glove box) in dry THF (1.5 mL) in a Schlenk tube was sonicated under Ar for 2 h and stirred overnight at ambient temperature. The mixture was cooled to -78 °C and vinylmagnesium bromide (0.505 mL of a 1 M solution in THF, 0.505 mmol) was added dropwise *via* syringe and the mixture was stirred for 2 h. The aldehyde **40** (45 mg, 0.100 mmol) was added *via* cannula as a solution in THF (1.0 mL, 0.5 mL rinse). The mixture was stirred at -78 °C for 1 h after which the mixture was warmed to 0 °C and quenched by the addition of NH_4Cl (3 mL). DCM (3 mL) was added and the layers were separated. The aqueous layer was extracted with DCM (3 × 5 mL) and the combined organics were dried ($MgSO_4$) and concentrated. Purification by flash chromatography (ether:hexane, 1:1) afforded the product alcohols **50** (38 mg, 0.079 mmol, 80%) as an inseparable mixture of diastereomers at the newly created stereocentre in a ratio as determined by ^{1}H NMR of approximately 3:1. An attempt to present the ^{1}H NMR data for the major isomer has been made; all other data was acquired on the mixture. R_f (ether:hexane, 1:1) 0.48; $[\alpha]_D^{22}$ +9.5 (*c* 1.85, $CHCl_3$); IR ($CHCl_3$): ν=3471; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.35-7.22 (m, 8H; Ar), 6.90-6.82 (m, 2H; Ar), 5.86 (ddd, *J* (H, H)=17.2, 10.6, 4.6 Hz, 1H; *H*C=CH_2), 5.45-5.24 (m, 2H; 6-H, *H*HC=C), 5.13 (t, *J* (H, H)=10.6, 1.7 Hz, 1H; H*H*C=C), 4.62 (d, *J* (H, H)=11.0 Hz, 1H; C*H*HAr), 4.49 (2H, s, CH_2Ar), 4.34 (d, *J* (H, H)=11.0 Hz, 1H; CH*H*Ar), 4.33-4.22 (m, 1H; C*H*OH), 4.08 (dd, *J* (H, H)=8.2, 3.0 Hz, 1H; 8-H), 4.00-3.88 (m, 2H; 3-H, OH), 3.80 (s, 3H; CH_3O), 3.76 (dd, *J* (H, H)=9.0, 3.0 Hz, 1H; 2-H), 3.60-3.43 (m, 1H; C*H*HOBn), 3.35 (br t, *J* (H, H)=8.3, 1H; CH*H*OBn), 3.11-2.95 (m, 1H; 7-H), 2.93 (br t, *J* (H, H)=11.6 Hz, 1H; 4-H), 2.36 (dd, *J* (H, H)=11.6, 6.3 Hz, 1H; 4-H'), 2.19-1.98 (m, 1H; 8-C-

C*H*CH_3), 1.71 (s, 3H; 5-C-CH_3), 1.09 (d, *J* (H, H)=6.9 Hz, 3H; CH_3), 1.04 (d, *J* (H, H)=7.4 Hz, 3H; CH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=138.9, 131.4, 129.8, 129.8, 128.3, 128.2, 127.6, 127.5, 127.4, 114.7, 113.9, 75.3, 74.3, 73.2, 70.6, 55.3, 35.8, 34.6, 15.9; MS (CI): *m/z*(%): 498 ($(M+NH_4)^+$, 3), 481 ($(M+H)^+$, 18), 179 (100); Found 481.2949, $C_{30}H_{41}O_5$ requires 481.2954.

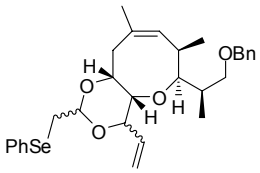
***(Z, 2*R*, 3*R*, 7*R*, 8*S*)-8-((1*R*)-2-Benzyloxy-1-methyl-ethyl)-3-hydroxy-2-((1*R*/*S*)-1-hydroxy-prop-2-eneyl)-7-methyl-3,4,7,8-tetrahydro-2*H*-oxocine* 51**



To a cooled (-15 °C) solution of the mixture of alcohols **50** (34 mg, 0.071 mmol) in DCM (2 mL) was added trifluoroacetic acid (0.5 mL) dropwise *via* syringe down the side of the flask. The colour changed from yellow to pink over a period of approximately 5 min. The reaction was stirred for a further 5 min and quenched by the slow addition of $NaHCO_3$ (12 mL). The mixture was extracted with DCM (3 × 10 mL), washed with brine (10 mL) and dried ($MgSO_4$). Purification by flash chromatography (ether:hexane, 2:1) afforded the diols **51** (22.0 mg, 0.061 mmol, 86%) as clear colourless oils. The stereochemistry of the epimers at C-9 was not assigned. Data for the minor diastereomer: R_f (ether:hexane, 2:1) 0.25; $[\alpha]_D^{26}$ +18.6 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38-7.25 (m, 5H; Ar), 5.87 (ddd, *J* (H, H)=17.1, 10.4, 6.5 Hz, 1H; *H*C=CH_2), 5.45-5.35 (m, 1H; 6-H), 5.45-5.28 (m, 1H; *H*HC=C), 5.19 (br d, *J* (H, H)=10.4 Hz, 1H; H*H*C=C), 4.54 (m, 3H; CH_2Ar, C*H*OHC=C), 4.28-4.17 (m, 1H; 8-H), 3.95-3.80 (m, 1H; 2-H), 3.84 (t, *J* (H, H)=6.0 Hz, 1H; C*H*HOBn), 3.57 (dd, *J* (H, H)=6.0, 3.7 Hz, 1H; CH*H*OBn), 3.65-3.51 (m, 1H; 3-H), 3.13 (d, *J* (H, H)=4.0 Hz, 1H; OH), 2.86 (br dd, *J* (H, H)=15.9, 10.3 Hz, 1H; 4-H), 2.72 (d, *J* (H, H)=7.5 Hz, 1H; OH), 2.80-2.60 (m, 1H; 7-H), 2.36 (dd, *J* (H, H)=15.9, 7.9 Hz, 1H; 4-H'), 2.08-1.92 (m, 1H; 8-C-C*H*CH_3), 1.73 (br s, 3H; 5-C-CCH_3), 1.03 (d, *J* (H, H)=7.4 Hz, 3H; CH_3), 0.96 (d, *J* (H, H)=7.0 Hz, 3H; CH_3). Data for the major diastereomer: R_f (ether:hexane, 2:1) 0.21; $[\alpha]_D^{26}$ +26.6 (*c* 0.8, $CDCl_3$); IR ($CHCl_3$): ν=3502; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38-7.25 (m, 5H; Ar), 5.86 (ddd, *J* (H, H)=17.2, 10.7, 4.9 Hz, 1H; *H*C=CH_2), 5.35 (dt, *J* (H, H)=17.2, 1.7 Hz,

1H; *H*HC=CH), 5.34 (d, *J* (H, H)=7.8 Hz, 1H; 6-H), 5.19 (dt, *J* (H, H)=10.7, 1.7 Hz, 1H; H*H*C=CH), 4.51 (s, 2H; CH_2Ar), 4.36-4.31 (m, 1H; C*H*OHC=C), 4.20 (br d, *J* (H, H)=6.3 Hz, 1H), 4.16-4.08 (m, 1H; 3-H), 3.82 (dd, *J* (H, H)=4.2, 1.3 Hz, 1H; 2-H), 3.63 (dd, *J* (H, H)=8.8, 3.5 Hz, 1H; C*H*HOBn), 3.42 (dd, *J* (H, H)=8.8, 6.6 Hz, 1H; CH*H*OBn), 3.21 (d, *J* (H, H)=4.3 Hz, 1H; 3-C-OH), 3.15 (d, *J* (H, H)=4.1 Hz, 1H; CHO*H*C=C), 2.95-2.85 (m, 1H; 7-H), 2.80 (br t, *J* (H, H)=13.0 Hz, 1H; 4-H), 2.28 (dd, *J* (H, H)=13.0, 7.3 Hz, 1H; 4-H'), 2.10-1.98 (m, 1H; 8-C-C*H*CH_3), 1.70 (s, 3H; 5-C-CH_3), 1.04 (d, *J* (H, H)=6.5 Hz, 3H; CH_3), 1.03 (d, *J* (H, H)=7.4 Hz, 3H; CH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=138.3, 136.8, 131.1, 128.4, 127.8, 127.6, 115.6, 81.3, 75.6, 74.1, 73.0, 71.1, 38.9, 37.7, 36.1, 26.3, 16.7, 15.8; MS (CI, NH_3): *m/z*(%) 378 ($(M+NH_4)^+$, 25), 361 ($(M+H)^+$, 100); Found 361.2382, $C_{22}H_{33}O_4$ requires 361.2379.

***(Z, 4a*S*, 6*S*, 7*R*, 10a*R*)-6-[(R)-1-(benzyloxy)propan-2-yl)]-7,9-dimtheyl-2-phenylselanylmethyl-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxa-benzocyclooctene* 52**



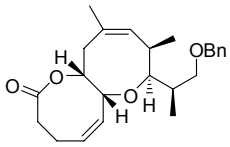
To a solution of phenylselenoacetaldehyde diethylacetal (5.6 mg, 20.6 μmol) and PPTS (~1 mg) in toluene (1 mL) was added the mixture of diols **51** (6.2 mg, 17.1 μmol) *via* cannula as a solution in toluene (0.3 mL, 0.4 mL rinse). The mixture was heated under reflux for a period of 40 min after which it was cooled and diluted with EtOAc. Water (4 mL) was added and the layers were separated. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the combined organic layers were washed with $NaHCO_3$ (10 mL) and dried ($MgSO_4$). Purification by flash chromatography (DCM:ether, 19:11) afforded the title compound **52** (9.0 mg, 16.6 μmol, 97%) as a mixture of 3 diastereomers. The major diastereomer was fully characterised and ^{1}H NMR data is also reported for the two minor diastereomers. Data for the major diastereomer; (6 mg, 11.0 μmol, 65%); R_f (DCM) 0.33; $[\alpha]_D^{26}$ +45.7 (*c* 0.47, $CDCl_3$); IR ($CHCl_3$): ν=1579; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.56-7.49 (m, 2H; Ar), 7.39-7.20 (m, 8H; Ar), 6.00 (ddd, *J* (H, H)=17.2, 10.6, 6.5 Hz, 1H; *H*C=CH_2), 5.41 (d, *J* (H, H)=5.5 Hz, 1H; 8-H), 5.27 (br d, *J* (H, H)=17.2 Hz, 1H; *H*HC=C), 5.17 (br d, *J* (H, H)=10.6 Hz, 1H; H*H*C=C), 4.87 (t, *J* (H, H)=5.2 Hz, 1H; C*H*CH_2Se), 4.53 (s, 2H;

C*H*$_2$Ar), 4.37-4.24 (m, 1H; *H*C(O)C=C), 4.07 (br d, *J* (H, H)=5.5 Hz, 1H; C*H*OC(O)), 3.78 (br dd, *J* (H, H)=11.5, 8.2 Hz, 1H; C*H*HOBn), 3.67 (s, 1H; 4a-H), 3.42 (br t, *J* (H, H)=8.2 Hz, 1H; CH*H*OBn), 3.15 (d, *J* (H, H)=5.2 Hz, 2H; CH_2Se), 3.03 (br t, *J* (H, H)=13.0 Hz, 1H; 4-H), 2.90-2.72 (m, 1H; 7-H), 2.18 (dd, *J* (H, H)=13.0, 6.5 Hz, 1H; 4-H), 2.10-1.93 (m, 1H; 8-C-C*H*CH_3), 1.77 (t, *J* (H, H)=1.3 Hz, 3H; vinyl CH_3), 0.99 (d, *J* (H, H)=6.9 Hz, 3H; CH_3), 0.97 (d, *J* (H, H)=7.4 Hz, 3H; CH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=139.0, 135.8, 132.5, 132.4, 130.7, 129.0, 128.3, 127.6, 127.3, 126.8, 116.9, 101.0, 81.8, 79.2, 74.3, 73.1, 68.2, 53.4, 37.3, 35.6, 31.0, 26.5, 15.3; MS (CI, NH_3): *m/z*(%): 543 ($(M+H)^+$, 25), 196 (100); Found 543.2014, $C_{30}H_{39}O_4Se$ requires 543.2013.

Data for the first minor diastereromer: (1 mg, 1.8 μmol, 11%); R_f (DCM) 0.43; ^{1}H (250 MHz, $CDCl_3$): δ=7.58-7.51 (m, 2H; Ar), 7.36-7.20 (m, 8H; Ar), 5.83 (ddd, *J* (H, H)=17.3, 10.5, 5.9 Hz, 1H; *H*C=CH_2), 5.35 (br d, *J* (H, H)=17.3 Hz, 1H; *H*HC=C), 5.25 (br t, *J* (H, H)=4.6 Hz, 1H; C*H*CH_2Se), 5.28-5.25 (m, 1H; 6-H), 5.18 (br d, *J* (H, H)=10.5 Hz, 1H; H*H*C=C), 4.47 (m, 2H; C*H*$_2$Ar), 4.27-4.20 (m, 1H; C*H*OC(O)), 4.10-4.00 (m, 1H; 10a-H), 3.97-3.88 (m, 2H; 4a-H, *H*C(O)C=C), 3.54 (dd, *J* (H, H)=9.0, 3.1 Hz, 1H; C*H*HOBn), 3.23 (br t, *J* (H, H)=9.0 Hz, 1H; CH*H*OBn), 3.10 (d, *J* (H, H)=4.6 Hz, 2H; CH_2Se), 2.91 (br t, *J* (H, H)=12.5 Hz, 1H; 4-H), 2.07 (dd, *J* (H, H)=12.5, 4.8 Hz, 1H; 4-H'), 1.73 (s, 3H; vinyl CH_3), 1.05 (d, *J* (H, H)=6.6 Hz, 3H; CH_3), 1.03 (d, *J* (H, H)=7.3 Hz, 3H; CH_3).

Data for the second minor diastereromer; (2 mg, 3.6 μmol, 21%); R_f(DCM) 0.22; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.55-7.45 (m, 2H; Ar), 7.37-7.18 (m, 8H; Ar), 5.85-5.65 (m, 1H; *H*C=CH_2), 5.40-5.16 (m, 3H; 6-H, C=C*H*$_2$), 5.07 (t, *J* (H, H)=5.4 Hz, 1H; C*H*CH_2Se), 4.62-4.53 (m, 1H), 4.47 (s, 2H; C*H*$_2$Ar), 4.04-3.87 (m, 2H), 3.71-3.57 (m, 2H), 3.26 (br t, *J* (H, H)=8.8 Hz, 1H; C*H*HOBn), 3.14 (d, *J* (H, H)=4.7 Hz, 2H; CH_2Se), 3.20-3.05 (m, 1H; 7-H), 2.89 (br t, *J* (H, H)=11.8 Hz, 1H; 10-H), 2.23-2.06 (m, 2H; 10-H', 8-C-C*H*CH_3), 1.73 (s, 3H; vinyl CH_3), 1.13 (d, *J* (H, H)=6.8 Hz, 3H; CH_3), 1.05 (d, *J* (H, H)=7.4 Hz, 3H; CH_3).

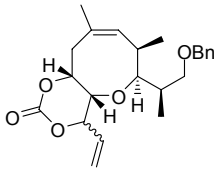
***(5Z, 10Z, 6a*R*, 8*S*, 9*R*, 12a*R*)-8-((1*R*)-2-Benzyloxy-1-methyl-ethyl)-9,11-dimethyl-4,6a,8,9,12,12a-hexahydro-3*H*-1,7-dioxa-octalen-2-one* 54**



To a solution of the seleno acetals **52** (8 mg, 14.7 μmol) in 15% aqueous MeOH (1.5 mL) was added solid $NaHCO_3$ (~1.4 mg, 16.17 μmol) and $NaIO_4$ (9.4 mg, 44.4 μmol) and the mixture was stirred vigorously for 1.5 h. The reaction was quenched by the addition of water (5 mL) and DCM (5 mL) was added. The layers were separated and the aqueous layer was extracted with DCM (3 × 5mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The resultant selenoxide was dried azeotropically twice with toluene (2 × 1 mL) and dissolved in xylene (2 mL). DBU (6.6 μL, 44.1 μmol) was added and the mixture was heated to 130 °C for a period of 24 h. After cooling, aqueous NH_4Cl (2 mL) was added and the layers were separated. The aqueous layer was extracted with ether (3 × 5 mL) and the combined organic layers were dried ($MgSO_4$). Purification by flash chromatography (hexane:ether, 3:1) afforded the lactone **54** (3.4 mg, 8.84 μmol, 60%) as a clear colourless oil; R_f (hexane:ether, 3:1) 0.27; $[\alpha]_D^{20}$ -12.7 (*c* 0.22, $CHCl_3$); IR (film): ν=1747; ^{1}H (250 MHz, $CDCl_3$) 7.38-7.22 (m, 5H; Ar), 5.83-5.71 (m, 2H; 5-H, 6-H), 5.30 (d, *J* (H, H)=8.3 Hz, 1H; 10a-H), 4.80 (ddd, *J* (H, H)=11.4, 5.7, 2.4 Hz, 1H; 12a-H), 4.49 (d, *J* (H, H)=12.1 Hz, 1H; C*H*HAr), 4.45 (d, *J* (H, H)=12.1 Hz, 1H; CH*H*Ar), 4.37 (dd, *J* (H, H)=4.4, 2.4 Hz, 1H; 6a-H), 3.84 (dd, *J* (H, H)=7.6, 3.9 Hz, 1H; 8-H), 3.62 (dd, *J* (H, H)=9.1, 3.4 Hz, 1H; C*H*HOBn), 3.27 (dd, *J* (H, H)=9.1, 7.8 Hz, 1H; CH*H*OBn), 3.12-2.96 (m, 2H; 4-H, 9-H), 2.94 (br t, *J* (H, H)=12.5 Hz, 1H; 12-H), 2.70 (dt, *J* (H, H)=13.1, 5.4 Hz, 1H; 3-H), 2.31 (ddd, *J* (H, H)=13.1, 10.6, 4.6 Hz, 1H; 3-H), 2.21 (dd, *J* (H, H)=12.5, 5.7 Hz, 1H; 4-H), 2.18-2.05 (m, 2H; 4-H, 8-C-C*H*CH_3), 1.78 (s, 3H; 11-C-CH_3), 1.08 (d, *J* (H, H)=6.4 Hz, 3H; CH_3), 1.07 (d, *J* (H, H)=7.1 Hz, 3H; CH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=177.0 (2-C), 138.9 (11-C), 133.7 (6-C), 130.8 (10-C), 130.4 (5-C), 128.2 (ArC), 127.5 (ArC), 127.4 (ArC), 83.5 (br, 8-C), 79.0 (12a-C), 73.4 (*C*H_2OBn), 73.1 (*C*H_2Ar), 70.7 (6a-C), 39.0 (9-C), 37.7 (3-C), 34.8 (12-C), 34.6, 30.6 (*C*HCH$_2$OBn), 25.8 (4-C), 24.6 (vinyl CH_3), 18.0 (CH_3), 16.2 (CH_3); MS (CI, NH_3): *m/z*(%): 402 ((M+NH_4)$^+$, 60), 385 ((M+H)$^+$, 58), 196 (100); Found 385.2380, $C_{24}H_{33}O_4$ requires 385.2379.

The bicyclic lactone **54**, above was also prepared from the carbonate **53**. To a solution of the carbonate **53** (9.0 mg, 23.2 μmol) in toluene (1 mL) was added dimethyltitanocene (0.14 mL, 50 mg cm^{-3} solution in toluene, 33.3 μmol). The mixture was excluded from light and heated at reflux for a period of 3 h. The toluene was removed and the residue was purified by flash chromatography (hexane:ether, 3:1) to afford the lactone **54** (4.2 mg, 10.9 μmol, 47%) as a clear colourless oil.

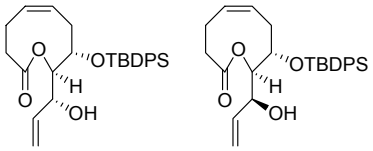
***(Z, 4*R/S*, 4a*S*, 6*S*, 9R, 10a*R*)-6-((1*R*)-2-Benzyloxy-1-methyl-ethyl)-7,9-dimethyl-4-vinyl-4,4a,6,7,10,10a-hexahydro-1,3,5-trioxabenzocycloocten-2-one* 53**



To a cooled (-78 °C) solution of the mixture of diols **51** (13 mg, 36 μmol) in DCM (2 mL) was added pyridine (18 μL, 216 μmol) and Et_3N (50 μL, 360 μmol) and crushed 4Å molecular sieves (~ 50 mg). To this solution was added triphosgene (11 mg, 36μmol) *via* cannula as a solution in DCM (0.5 mL, 0.2 mL rinse). The mixture was stirred for 20 min at this temperature and was quenched by the addition of aqueous NH_4Cl (3 mL). The mixture was allowed to warm to ambient temperature and was extracted with DCM (3 × 5 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. Purification by flash chromatography (ether:hexane, 2:1) afforded the title compound **53** (11.2 mg, 28 μmol, 80%) as a clear colourless oil. R_f (ether:hexane, 2:1) 0.35; $[\alpha]_D^{20}$ +85.4 (*c* 0.5, $CDCl_3$); IR (film): ν=1760; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.38-7.25 (m, 5H; Ar), 5.58 (ddd, *J* (H, H)=17.1, 10.8, 3.7 Hz, 1H; *H*C=CH_2), 5.43 (d, *J* (H, H)=7.4 Hz, 1H; 6-H), 5.33 (dd, *J* (H, H)=17.1, 1.4 Hz, 1H; *H*HC=C), 5.27 (dd, *J* (H, H)=10.8, 1.4 Hz, 1H; H*H*C=C), 4.82 (s, 1H; 4-H), 4.55 (ddd, *J* (H, H)=11.2, 6.8, 1.8 Hz, 1H; 10a-H), 4.50 (d, *J* (H, H)=11.8 Hz, 1H; C*H*HAr), 4.45 (d, *J* (H, H)=11.8 Hz, 1H; CH*H*Ar), 4.17-4.01 (m, 2H; 4a-H, 6-H), 3.58 (dd, *J* (H, H)=9.1, 3.3 Hz, 1H; C*H*HOBn), 3.35 (dd, *J* (H, H)=9.1, 6.4 Hz, 1H; CH*H*OBn), 3.10-2.94 (m, 2H; 10-H, 7-H), 2.34 (dd, *J* (H, H)=12.9, 6.8 Hz, 1H; 10-H'), 2.17-2.00 (m, 1H; 6-C-C*H*CH_3), 1.75 (s, 3H; 9-C-CH_3), 1.09 (d, *J* (H, H)=7.2 Hz, 3H; CH_3), 1.07 (d, *J* (H, H)=7.4 Hz, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=148.1 (2-C), 138.1, 132.9, 132.2, 127.9, 127.8, 118.2, 83.4, 73.5, 73.3, 65.5, 34.9, 15.9; MS (CI, NH_3):

m/z(%): 404 ((M+NH_4)$^+$, 97), 387 ((M+H)$^+$, 70); Found 387.2171, $C_{23}H_{31}O_5$ requires 387.2171.

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

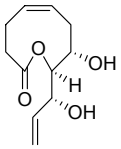


Vinylbromide (*ca.* 0.5 mL) was condensed into a cold Schlenk tube (-20 °C) and then allowed to diffuse into a solution of the aldehyde **57**[3] (50 mg, 118 μmol) in degassed DMSO (5 mL, freeze-thaw 3 cycles). To this solution was added $CrCl_2$ containing 1% $NiCl_2$ (145 mg, 1.18 mmol) and the resulting green solution was allowed to stir overnight under an atmosphere of oxygen-free argon. The reaction mixture was quenched by the addition of 0.1 M aqueous solution of sodium serinate (30 mL), hexane (15 mL) and EtOAc (15 mL). The organic phase was separated and the aqueous phase was extracted with a mixture of hexane and EtOAc (1:1, 3 × 30 mL). The organic phases were washed with water (30 mL), brine (30 mL) and dried ($MgSO_4$). Purification by flash chromatography (1:1, hexane:ether) provided the title compounds **58** and **59** as a 2:1 mixture of diastereomers as clear and colourless oils (33 mg, 73 μmol, 62%).

Data for **59**:R_f 0.4 (7:3, ether:hexane); $[\alpha]_D^{21}$ -16.0 (*c* 0.89 in $CHCl_3$); IR ($CHCl_3$): ν=3580, 1732; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.76-7.68 (m, 4H; Ar), 7.50-7.36 (m, 6H; Ar), 5.87 (ddd, *J* (H, H)=17.2, 10.5, 4.7 Hz, 1H; *H*C=CH_2), 5.54-5.44 (m, 1H), 5.34-5.26 (m, 1H), 5.25 (dt, *J* (H, H)=17.2, 1.5 Hz, 1H; HC=C*H*H-*trans*), 5.15 (dt, *J* (H, H)=10.5, 1.5 Hz, 1H; HC=CH*H-cis*), 4.90 (dd, *J* (H, H)=8.2, 1.6 Hz, 1H), 4.40-4.23 (m, 2H), 2.45-2.16 (m, 6H; 3-H, 3-H', 4-H, 4-H', 7-H, 7-H'), 1.56 (d, *J* (H, H)=8.4 Hz, 1H; OH), 1.08 (s, 9H; $(CH_3)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=173.9 (2-C), 137.6, 135.9, 135.9, 133.7, 133.2, 130.0, 129.9, 129.4, 127.8, 127.7, 127.6, 115.6, 80.9, 72.2, 70.8, 34.1, 33.5, 27.0 ((*C*H_3)$_3$C), 23.8, 19.2 ((CH$_3$)$_3$*C*); MS (CI, NH_3): *m/z*(%): 468 ((M+NH_4)$^+$, 20), 451 ((M+H)$^+$, 10), 373 (100); Found 468.2575, $C_{27}H_{38}O_4SiN$ requires, 468.2570.

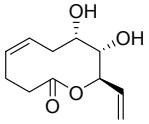
Data for **58**: R_f 0.3 (7:3, ether:hexane); $[\alpha]_D^{21}$ +10.2 (*c* 1.61 in $CHCl_3$); IR ($CHCl_3$): ν=3488, 1728; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.75-7.64 (m, 4H; Ar), 7.50-7.35 (m, 6H; Ar), 5.65-5.51 (m, 3H; 5-H, 6-H, *H*C=CH_2), 5.02 (ddd, *J* (H, H)=10.4, 1.5, 1.0 Hz, 1H; CH=C*H*H-*cis*), 4.88 (dd, *J* (H, H)=10.6, 1.3 Hz, 1H; CH=CH*H-trans*), 4.83 (dd, *J* (H, H)=8.2, 2.4 Hz, 1H), 4.32-4.22 (m, 1H), 3.95 (ddd, *J* (H, H)=8.3, 5.5, 2.6 Hz, 1H), 2.86 (brd, *J* (H, H)=5.6 Hz, 1H; OH), 2.65-2.25 (m, 4H), 2.28-2.22 (m, 2H), 1.09 (s, 9H; $(CH_3)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=175.6 (2-C), 136.0, 135.9, 134.8, 133.6, 132.9, 130.1, 129.9, 128.8, 128.5, 127.7, 118.4, 82.6, 72.8, 72.7, 33.6, 32.5, 27.0 ((*C*$H_3)_3$C), 23.1, 19.2 (($CH_3)_3$*C*); MS (CI, NH_3): *m/z*(%): 468 ($(M+NH_4)^+$, 50), 451 ($(M+H)^+$, 30), 274 (100); Found 468.2566, $C_{27}H_{38}O_4SiN$ requires 468.2570.

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



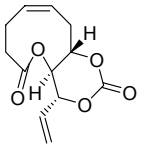
To a stirred solution of the allylic alcohol **58** (15.5 mg, 34 μmol) in THF (1.5 mL) and pyridine (0.7 mL) was added HF•pyridine (0.15 mL) and the resulting solution was stirred for 24 h and then quenched by the addition of water (10 mL) and ether (10 mL). The organic phase was separated and the aqueous phase was extracted with ether (2 × 10 mL). The organic phases were washed with a saturated aqueous solution of $CuSO_4$ (2 × 10 mL) and dried ($MgSO_4$). Purification by flash chromatography (1:1, hexane:ether→0:1, hexane:ether) provided starting material **58** (2 mg, 4.4 μmol, 13%). Further elution of the column provided the title compound **60** as a clear and colourless oil (5 mg, 24 μmol, 71%); R_f 0.4 (ether); $[\alpha]_D^{21}$ -96.4 (*c* 1.05 in $CHCl_3$); IR ($CDCl_3$): ν=3613, 1734; ^{1}H (250 MHz, $CDCl_3$): δ=5.95 (ddd, *J* (H, H)=17.2, 10.4, 6.7 Hz, 1H; *H*C=CH_2), 5.79-5.57 (m, 2H; 5-H, 6-H), 5.38 (dt, *J* (H, H)=17.2, 1.4 Hz, 1H; HC=C*H*H-*trans*), 5.27 (d, *J* (H, H)=10.4, 1.3 Hz, 1H; HC=CH*H-cis*), 4.68 (dd, *J* (H, H)=8.1, 5.9 Hz, 1H; 9-H), 4.40-4.30 (m, 1H), 2.62-2.20 (m, 8H; 3-H, 3-H', 4-H. 4-H', 7-H, 7-H', OH, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=174.4 (2-C), 136.3, 128.9, 128.5, 118.0, 80.0, 74.7, 72.6, 33.8, 32.8, 23.7; MS (CI, NH_3): *m/z*(%): 230 ($(M+NH_4)^+$, 100), 213 ($(M+H)^+$, 20); Found 213.1125, $C_{11}H_{17}O_4N$ requires 213.1127.

***(Z, 8*S*, 9*R*, 10*R*)-8-Hydroxy-10-vinyl-4,7,8,9-tetrahydro-3*H*-oxecin-2-one* 61**



The ten-membered lactone **61** was isolated in varying quantites during optimisation of the desilylation of **58**; mp 112-114 °C (from ether/hexane); $[\alpha]_D^{20}$ +33.9 (*c* 0.065 in $CHCl_3$); IR ($CDCl_3$): ν=3570, 1731; ^{1}H NMR (250 MHz, $CDCl_3$): δ=5.94 (ddd, *J* (H, H)=17.3, 10.6, 6.2 Hz, 1H; *H*C=CH_2), 5.82-5.72 (m, 1H), 5.45-5.63 (m, 2H), 5.42 (dt, *J* (H, H)=17.3, 1.4 Hz, 1H; HC=C*H*H-*trans*), 5.35 (dt, *J* (H, H)=10.4, 1.3 Hz, 1H; HC=CH*H-cis*), 4.06 (dq, *J* (H, H)=6.8, 2.3 Hz, 1H; 8-H), 3.90 (ddd, *J* (H, H)=6.8, 5.5, 1.3 Hz, 1H; 9-H), 2.73-2.76 (m, 1H), 2.65-2.21 (m, 7H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=172.0 (1-C), 132.6, 128.3, 128.0, 119.0, 74.2, 70.6, 34.7, 32.0, 22.0; MS (CI, NH_3): *m/z*(%): 230 ($(M+NH_4)^+$, 100), 213 ($(M+H)^+$, 20); Found 213.1125, $C_{11}H_{17}O_4N$ requires 213.1127.

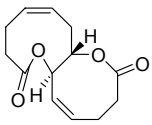
***(Z, 4*R*, 4a*S*, 11a*S)-4-Vinyl-4,4a,7,8,11,11a-hexahydro-1,3,5-trioxa-benzocyclononene-2,6-dione* 62**



To a stirred suspension of the oxonane **60** (18.7 mg, 88 μmol) and freshly activated 4 Å powdered molecular sieves in DCM (1 mL) at -78 °C were added pyridine (43 μL, 42 mg, 530 μmol) and TEA (122 μL, 89 mg, 0.88 mmol). Triphosgene (26 mg, 88 μmol) was added *via* cannula as a solution in DCM (0.5 mL). The resulting orange solution was stirred for 15 min and then allowed to warm to room temperature. The reaction mixture was quenched by the addition of a saturated solution of NH_4Cl (2 mL) and was extracted with DCM (3 × 10 mL). The organic phases were washed with a saturated aqueous solution of $CuSO_4$ (10 mL) and dried ($MgSO_4$). Purification by flash chromatography (hexane:ether, 1:1) provided the title compound **62** (16.2 mg, 69 μmol, 78%) as a white crystalline solid; mp 126-127 °C (from hexane); $[\alpha]_D^{16}$ -181 (*c* 0.1 in $CHCl_3$); IR ($CDCl_3$): ν=1761; ^{1}H NMR (250 MHz, $CDCl_3$): δ=5.96 (ddd, *J* (H, H)=17.1, 10.4, 6.4 Hz, 1H; *H*C=CH_2), 5.80-5.65 (m, 2H; 9-H, 10-H), 5.51 (d, *J* (H, H)=17.1 Hz, 1H; HC=C*H*H-*trans*), 5.42 (d, *J* (H, H)=10.4 Hz, 1H; HC=CH*H-cis*),

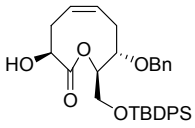
4.90 (t, *J* (H, H)=9.4 Hz, 1H; 4a-H), 4.81 (dd, *J* (H, H)=9.9, 6.5 Hz, 1H; 4-H), 4.35 (ddd, *J* (H, H)=9.3, 7.8, 2.4 Hz, 1H; 11a-H), 2.62-2.25 (m, 6H; 7-H, 7-H', 8-H. 8-H', 11-H, 11-H'); ^{13}C NMR (62.5 MHz, $CDCl_3$) 174.3 (6-C), 147.7 (2-C), 131.5, 130.2, 127.1, 121.4, 81.6, 72.8, 33.9, 29.8, 24.6; MS (CI, NH_3): *m/z*(%): $((M+NH_4)^+$, 18), 239 $((M+H)^+$, 100); Found 239.016, $C_{12}H_{15}O_5$ requires 239.0919.

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



To a stirred solution of the carbonate **62** (14 mg, 58 μmol) in toluene (2 mL) was added dimethyltitanocene (229 μL, of a 50 mg/mL solution in toluene, 70 μmol) and the resulting orange solution was heated at reflux for 1.5 h and then allowed to cool. The solvent was removed *in vacuo* and purification by flash chromatography (hexane:ether, 2:1) provided the title compound **63** as a white crystalline solid (4.2 mg, 18 μmol, 31%); mp 109-111 °C (from hexane); $[\alpha]_D^{16}$ -26.6 (*c* 0.165 in $CHCl_3$); IR ($CHCl_3$): ν=1744, 1737; ^{1}H NMR (800 MHz, $CDCl_3$): δ=5.88-5.82 (m, 1H), 5.78-5.70 (m, 2H), 5.70-5.62 (m, 1H; 6a-H), 4.65 (brt, *J* (H, H)=7.5 Hz, 1H; 13a-H), 2.55-2.86 (m, 1H), 2.56-2.47 (br, 2H), 2.46-2.36 (m, 3H), 2.35-2.2.6 (m, 2H), 2.22-2.20 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=175.9, 174.7, 132.4, 131.6, 129.0, 128.3, 75,3 (6a-C), 37.6, 34.2, 30.9, 24.9, 24.3; MS (CI, NH_3): *m/z*(%): 254 $((M+NH_4)^+$, 100)); Found 254.1393, $C_{13}H_{20}NO_4$ requires 254.1392.

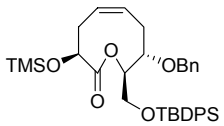
***(Z, 3*S*, 8*S*, 9*R*)-8-Benzyloxy-9-t*butyldiphenylsilyloxymethyl-3-hydroxy-4,7,8,9-tetrahydro-3*H*-oxonin-2-one* 65**



KHMDS (6.48 mL of a 0.5 M solution in toluene, 3.24 mmol) was added to toluene (40 mL) and the resulting solution was cooled to -78 °C. A solution of **64** (980 mg, 1.91 mmol) in toluene (5 mL, 2 × 2.5 mL rinse) was added dropwise *via* cannula and the resulting solution was stirred at -78 °C for 1 h. A solution of (±)-2-(phenylsulfonyl)-3-phenyloxaziridine (1.09 g, 4.19 mmol) in tolune (10 mL) was added *via* cannula and the resulting solution was stirred for 1 h at –78 °C. CSA (1.09

g, 4.19 mmol) as a solution in THF (7 mL) was added *via* cannula and the reaction mixture was allowed to warm to ambient temperature. A saturated aqueous solution of $NaHCO_3$ (50 mL) was added and the organic phase was separated. The aqueous phase was extracted with ether (2 × 50 mL) and the combined organic extracts were dried ($MgSO_4$). Purification by flash chromatography (hexane:ether, 7:3) provided the title compound **65** as a clear and colourless oil (811 mg, 1.53 mmol, 80%); R_f 0.2 (hexane:ether, 7:3); $[\alpha]_D^{17}$ -1.7 (*c* 1.98 in $CHCl_3$); IR ($CHCl_3$): ν=3577, 1741; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.68-7.60 (m, 4H; Ar), 7.44-7.20 (m, 11H; Ar), 5.83-5.70 (m, 1H), 5.61-5.48 (m, 1H), 5.08 (ddd, *J* (H, H)=9.1, 5.2, 2.3 Hz, 1H; 9-H), 4.62 (d, *J* (H, H)=11.6 Hz, 1H; OC*H*HAr), 4.40 (d, *J* (H, H)=11.6 Hz, 1H; OCH*H*Ar), 4.37 (ddd, *J* (H, H)=10.6, 5.6, 3.2 Hz, 1H; 3-H), 4.05 (dd, *J* (H, H)=11.6, 5.1 Hz, 1H; C*H*HOSi), 3.88 (dd, *J* (H, H)=11.6, 2.4 Hz, 1H; CH*H*OSi), 3.86-3.79 (m, 1H; 8-H), 2.60-2.53 (m, 2H), 2.37-2.28 (m, 2H), 2.10 (d, *J* (H, H)=10.6 Hz, 1H; OH), 1.05 (s, 9H; $(CH_3)_3$C)Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=173.1 (2-C), 137.6, 135.7, 133.3, 130.9, 128.7, 128.5, 127.9, 123.0, 79.4, 71.6, 70.9, 63.3, 32.4, 30.7, 26.8, 19.3; MS (CI, NH_3): *m/z*(%): 548 ($(M+NH_4)^+$, 100), 531 ($(M+H)^+$, 20); Found 548.2843, $C_{32}H_{42}NO_5Si$ requires 548.2832.

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

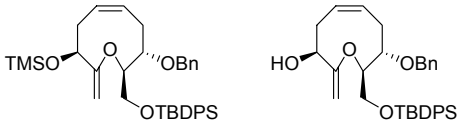


To a stirred solution of the lactone **65** (779, 1.46 mmol) in THF (44 mL) was added TEA (2.03 mL, 1.48 g, 14.6 mmol) and dropwise TMSCl (0.93 mL, 794 mg, 7.35 mmol). The resulting white slurry was stirred for 4 h and then poured onto ether (50 mL) and pH 7 buffer (50 mL). The organic layer was separated and the aqueous phase was extracted with ethr (2 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$) and purification by flash chromatography (hexane:ether, 9:1) provided the title compound **66** as a clear and colourless oil (715 mg, 1.19 mmol, 81%); R_f 0.4 (hexane:ether, 3:1); (Found: C, 69.77; H, 7.72%; $C_{35}H_{46}O_5Si$ requires C, 69.72; H, 7.69); $[\alpha]_D^{18}$ +22.0 (*c* 2.425 in $CHCl_3$); IR ($CHCl_3$): ν=2932, 1740 (CO); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.74-7.64 (m, 4H; Ar), 7.45-

7.16 (m, 11H; Ar), 5.80-5.67 (m, 1H), 5.64-5.52 (m, 1H), 5.10-4.96 (brm, 1H; 9-H), 4.59 (d, *J* (H, H)=11.6 Hz, 1H; OC*H*HAr), 4.38 (dd, *J* (H, H)=7.9, 4.3 Hz, 1H; 3-H), 4.34 (d, *J* (H, H)=11.6 Hz, 1H; OCH*H*Ar), 3.95 (dd, *J* (H, H)=11.4, 5.7 Hz, 1H; C*H*HOSi), 3.86 (dd, *J* (H, H)=11.4, 2.9 Hz, 1H; CH*H*OSi), 3.90-3.80 (m, 1H; 8-H), 2.75-2.26 (m, 4H) , 1.06 (s, 9H; $(CH_3)_3C$)Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=173.0 (2-C), 137.9, 135.7, 135.6, 133.6, 133.3, 130.4, 129.7, 129.6, 128.4, 127.7, 125.3, 78.0, 77.5, 72.5, 71.3, 63.9, 33.5, 28.8, 26.8, 19.3 , -0.1; MS (CI, NH_3): *m/z*(%) 620 ($(M + NH_4)^+$, 100), 603 (30); Found 603.2967, $C_{35}H_{47}O_5Si$ requires 603.2962.

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

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

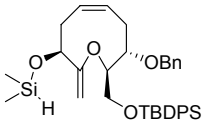


To a stirred solution of the silylether **66** (685 mg, 1.13 mmol) in toluene (46 mL) was added dimethyltitanocene (4.08 mL of an 87 mg/mL solution in toluene, 1.71 mmol) and the resulting solution was heated at reflux for 1 hr. Acetone (2 mL) was added and the mixture was heated at reflux for a further 0.5 h. The reaction mixture was allowed to cool and the solvent was removed *in vacuo*. Purification by gravity chromatography on deactivated basic alumina (6% w/w water) (hexane:ether, 9:1) provided the impure enol ether **67** which was used in the next reaction without further purificaiton. An analytical sample of the enol ether **67** was obatined by further purification on deactivated basic alumina (hexane:ether, 20;1); R_f 0.3 (hexane:ether, 9:1); $[\alpha]_D^{18}$ +13.1 (*c* 0.68 in $CHCl_3$); IR ($CHCl_3$): ν=2931, 1641 (enol ether); ^1H NMR (250 MHz, $CDCl_3$): δ=7.75-7.67 (m, 4H; Ar), 7.48-7.33 (m, 6H; Ar), 7.30-7.16 (m, 5H; Ar), 5.74 (dt, *J* (H, H)=10.9, 5.3 Hz, 1H), 5.53 (dt, *J* (H, H)=10.9, 5.4 Hz, 1H), 4.78 (brs, 1H; OC=C*H*H), 4.63 (d, *J* (H, H)=11.4 Hz, 1H; C*H*HAr), 4.30 (d, *J* (H, H)=11.4 Hz, 1H; CH*H*Ar), 4.27 (dd, *J* (H, H)=9.7, 6.2 Hz, 1H), 4.22 (d, *J* (H, H)=1.3 Hz, 1H; OC=CH*H*), 3.94-3.79 (m, 3H), 3.67 (dt, *J* (H, H)=8.1, 3.1 Hz, 1H), 2.94-2.76 (m, 2H), 2.33 (dt, *J* (H, H)=14.2, 4.0 Hz, 1H), 2.25 (dq, *J* (H, H)=11.9, 6.1 Hz, 1H), 1.06 (s, 9H; $(CH_3)_3C$)Si) , 0.22 (s, 9H; $(CH_3)_3Si$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=166.1 (1-C), 138.1, 135.7, 133.3, 129.6, 128.3, 127.9, 127.8, 127.7, 127.6, 92.8

(OC=*C*H_2), 85.1, 79.6, 74.0, 71.3, 66.2, 33.2, 26.8, 19.2 , 0.4; MS (EI): *m/z*(%):600 (M^+, 1), 91 (100); Found 600.3085, $C_{36}H_{48}O_4Si_2$ requires 600.3091.

The crude enol ether **67** was dissolved in MeOH (11 mL), anhydrous K_2CO_3 (57 mg, 0.41 mmol) was added and the reaction mixture was stirred for 1 h. The reaction mixture was filtered through a pad of Celite™ rinsing with ether and the solvent was removed *in vacuo*. Purification by gravity chromatography on deactivated basic alumina (6% w/w water) (hexane:ether, 2:1) provided the enol ether **68** (366 mg, 0.69 mmol, 61% from the lactone **66**); R_f 0.1 (hexane:ether, 2:1); $[\alpha]_D^{18}$ +5.5 (*c* 1.155 in $CHCl_3$); IR ($CHCl_3$): ν=3594 (OH), 2931, 1641 (enol ether); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.74-7.66 (m, 4H; Ar), 7.48-7.21 (m, 11H; Ar), 5.75 (dt, *J* (H, H)=10.5 , 6.5 Hz, 1H), 5.55 (dt, *J* (H, H)=10.5, 6.2 Ha, 1H), 4.65 (d, *J* (H, H)=11.5 Hz, 1H; OC*H*HAr), 4.55 (d, *J* (H, H)=1.6 Hz, 1H; OC=C*H*H), 4.37 (d, *J* (H, H)=11.5 Hz, 1H; OCH*H*Ar), 4.24 (d, *J* (H, H)=1.6 Hz, 1H; OC=CH*H*), 4.25-4.16 (m, 1H), 3.97-3.90 (m, 2H), 3.81 (dd, *J* (H, H)=11.3, 6.4 Hz, 1H; C*H*HOSi), 3.75-3.67 (m, 1H), 2.76-2.62 (m, 2H), 2.46-2.34 (m, 2H), 1.85 (d, *J* (H, H)=7.1 Hz, 1H; OH) , 1.05 (s, 9H; $(CH_3)_3$C)Si); ^{13}C NMR (62.5 MHz, $CDCl_3$) 165.6 (2-C), 138.0, 135.7, 133.4, 133.3, 129.6, 128.9, 128.4, 127.9, 127.7, 127.7, 126.9, 91.4, 85.1, 78.6, 73.2, 71.4, 65.6, 32.6, 30.4, 26.9, 26.8, 19.2; MS (CI, NH_3): *m/z*(%):546 ($(M+NH_4)^+$, 65), 529 ($(M+H)^+$, 60), 91 (100); Found 529.2765, $C_{33}H_{33}O_4Si$ requires *M* 529.2774.

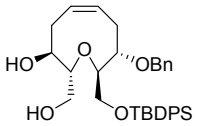
***(Z, 3*S*, 8*S*, 9*R*)-Benzyloxy-9-tbutyldiphenylsilyloxymethyl-3-dimethylsilyloxy-2-methylene-4,7,8,9-tetrahydro-3*H*-oxonine* 69**



To a stirred solution of the enol ether **68** (58 mg, 0.11 mmol) in tetramethyldisilazane (0.7 mL) was added anhydrous NH_4Cl (2 mg) and the resulting mixture was heated at 60 °C overnight. The reaction mixture was diluted with anhydrous hexane and was filtered through dry Celite™ in air washing with anhydrous hexane. The solvent was removed *in vacuo* and the residue was dried under vacuum (<5 mmHg) overight to provide the silane **69** as an unstable clear and colourless oil (64 mg, 0.11 mmol, 100%); IR ($CHCl_3$): ν=2120, 1641; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.71-7.67 (m, 4H Ar), 7.46-7.15 (m, 11H; Ar), 5.72 (dt, *J* (H, H)=11.1, 5.3 Hz, 1H), 5.50 (dt, *J* (H, H)=11.0, 5.5 Hz, 1H), 4.74 (sp, *J* (H, H)=2.9 Hz, 1H; SiH), 4.76 (brs, 1H; OC=C*H*H),

4.61 (d, *J* (H, H)=11.4 Hz, 1H; OC*H*HAr), 4.29 (d, *J* (H, H)=11.4 Hz, 1H; OCH*H*Ar), 4.28-4.22 (m, 1H), 4.23 (d, *J* (H, H)=1.5 Hz, 1H; OC=CH*H*), 3.92-3.79 (m, 3H), 3.65 (dt, *J* (H, H)=8.2, 3.1 Hz, 1H), 2.90-2.75 (m, 2H), 2.36-2.22 (m, 2H), 1.03 (s, 9H; $(CH_3)_3C$)Si), 0.275 (d, *J* (H, H)=2.9 Hz, 3H; $(CH_3)_2$SiH) , 0.268 (d, *J* (H, H)=2.9 Hz, 3H; $(CH_3)_2$SiH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=165.4 (1-C), 138.1, 135.7, 133.3, 129.6, 128.4, 128.1, 127.8, 127.6, 127.6, 93.3 (OC=*C*H_2), 85.2, 79.5, 75.6, 71.3, 66.1, 32.8, 26.9, 26.8, 19.1, -0.8.

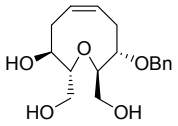
***(Z, 2*R*, 3*S*, 8*S*, 9(*R*)-8-Benzyloxy-9-t*butyldiphenylsilyloxymethyl-3-hydroxy-2-hydroxymethyl-2,3,4,7,8,9-hexahydro-oxonine* 70**



In a glove box a Schlenk tube was charged with (bicyclo(2.2.1)hepta-2,5-diene)(1,4-bis(diphenylphosphino)butane)rhodium(I) tetrafluoroborate (11 mg, 15.5 μmol). The Schlenk tube was placed on an argon manifold and the silane **69** (170 mg, 0.29 mmol) was added as a solution in acetone (10 mL, 5 mL rinse) *via* cannula. The resulting orange solution was freeze-thaw degassed (3 cycles) and heated at reflux for 18 h. The solvent was removed *in vacuo*, the residue taken-up in ether and filtered through Fluorosil™ to remove the coloured material. The solvent was removed *in vacuo*, the residue taken-up in THF (3 mL) and MeOH (3 mL) and 30% hydrogen peroxide (0.7 mL) and 15% KOH (0.35 mL) were added. The reaction mixture was stirred for 1 hr and then quenched by the addition of saturated aqueous $Na_2S_2O_3$ (20 mL) and ether (20 mL). The aqueous phase was separated and extracted with ether. The organic phases were washed with brine and dried ($MgSO_4$). Purification by flash chromatography (ether:hexane, 1:1) provided the enol ether **68** (56 mg, 102 μmol, 35%) and the title compound **70** as colourless crystals (96 mg, 175 μmol, 61%); R_f 0.3; mp 156-158 °C (from ether); $[\alpha]_D^{17}$ +14.5 (*c* 0.255 in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.75-7.63 (m, 4H; Ar), 7.48-7.33 (m, 6H; Ar), 7.25-7.16 (m, 3H; Ar), 7.00-6.94 (m, 2H; Ar), 5.77-5.62 (m, 2H; 5-H, 6-H), 4.48 (d, *J* (H, H)=11.5 Hz, 1H; C*H*HAr), 4.13 (d, *J* (H, H)=11.5 Hz, 1H; CH*H*Ar), 4.00-3.89 (m, 2H), 3.88-3.80 (m, 2H), 3.80-3.68 (m, 2H), 3.30 (dt, *J* (H, H)=9.3, 3.2 Hz, 1H), 3.22-3.16 (m, 1H), 3.07 (t, *J* (H, H)=6.6 Hz, 1H), 2.87-2.73 (m, 2H), 2.36-2.22 (m, 2H), 2.10 (brd, *J* (H,

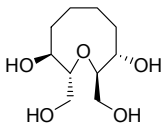
H)=5.1 Hz, 1H; OH), 1.10 (s, 9H; $(CH_3)_3CSi$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=137.5, 135.7, 135.7, 133.0, 132.8, 129.9, 129.7, 128.3, 127.8, 127.7, 127.6, 126.2, 80.3, 77.2, 75.0, 70.7, 69.1, 84.5, 62.5, 30.8, 28.9, 26.9 , 19.2; MS (CI, NH_3): *m/z*(%): 564 ($(M+NH_4)^+$, 100), 547 ($(M+H)^+$, 55); Found (ES) 564.3137, $C_{33}H_{46}ClNO_5Si$ requires 564.3145.

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



HF•pyridine complex (0.1 mL) was added to stirring solution of the diol **70** (4.4 mg, 8 μmol) in THF (1 mL) and pyridine (0.3 mL) and the resulting solution was stirred for 2 h at ambient temperature. The reaction mixture was quenched by the addition of 2 M HCl and ether, the aqueous phase was separated and further extracted with ether. The organic extracts were washed with 2 M HCl, brine and dried ($MgSO_4$). Purification by flash chromatography provided the title compound **71** as a clear and colourless oil (2.4 mg, 7.8 μmol, 97%); R_f 0.1 (ether); $[\alpha]_D^{20}$ +70.7 (*c* 0.075 in $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) 7.39-7.30 (m, 5H; Ar), 5.82-5.67 (m, 2H; 5-H, 6-H), 4.70 (d, *J* (H, H)=11.4 Hz, 1H; C*H*HAr), 4.42 (d, *J* (H, H)=11.4 Hz, 1H; CH*H*Ar), 3.95-3.69 (m, 5H), 3.67-3.59 (m, 1H), 3.54-3.38 (m, 3H), 2.78-2.40 (m, 6H); ^{13}C NMR (62.5 MHz, $CDCl_3$) 137.1, 128.6, 128.1, 128.0, 126.7, 78.1, 77.2, 76.4, 71.3, 69.7, 63.3, 63.1, 31.9, 28.2; MS (CI, NH_3): *m/z*(%): 326 ($(M+NH_4)^+$, 10), 309 ($(M+H)^+$, 2), 238 (100); Found 326.1966, $C_{17}H_{28}NO_5$ requires 326.1967.

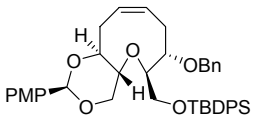
***2(*R*), 3(*S*), 8(*S*), 9(*R*)-2,9-Bis-hydroxymethyl-oxonane-3,8-diol* 72**



To solution of the triol **71** (2.4 mg, 7.8 μmol) in ethanol (0.5 mL) was added palladium on carbon and the reaction mixture was degassed and saturated with hydrogen (water-pump, 3 cycles). The resulting suspension was stirred for 18 h and then filtered through Celite™ whereupon tlc analysis indicated incomplete reaction. The solvent was removed *in vacuo* and the residue was resubmitted to the reaction

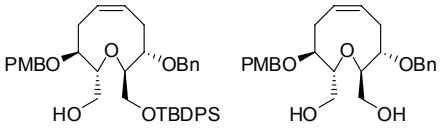
conditions. After stirring for 18 h and filtration through Celite™ the solvent was removed *in vacuo* and purification by flash chromatography (EtOAc:MeOH, 95:5) provided the title compound **72** as a clear and colourless oil (1.5 mg, 6.9 μmol, 88%); R_f 0.05 (EtOAc); $[\alpha]_D^{20}$ +26 (*c* 0.05 in EtOH); ^{1}H NMR (250 MHz, D_2O): δ=3.89-3.62 (m, 8H), 1.93-1.75 (m, 2H), 1.75-1.45 (m, 6H); ^{13}C NMR (100 MHz, D_2O): δ=78.5, 68.5, 61.4, 32.0 , 22.0; MS (CI, NH_3): *m/z*(%) 238 ($(M+NH_4)^+$, 100), 220 ($(M+NH_4-H_2O)^+$, 20); Found (ES) 238.1650, $C_{10}H_{24}NO_5$ requires 238.1654.

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



PPTS (*ca.* 2 mg) was added to a stirring solution of the diol **70** (72 mg, 132 μmol) and *p*-anisaldehyde (22 mg, 158 μmol) in benzene (5 mL) and the reaction mixture was heated at reflux for 18 h. The reaction mixture was allowed to cool, the solvent was removed *in vacuo* and purification by preparative layer chromatography (ether:hexane, 2:1) provide the title compound **73** as a clear and colourless oil (70 mg, 105 μmol, 80%); $[\alpha]_D^{18}$ +45.1 (*c* 0.94 in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.74-7.63 (m, 4H; Ar), 7.48-7.32 (m, 8H; Ar), 7.28-7.20 (m, 3H; Ar), 7.11-7.02 (m, 2H; Ar), 6.94-6.86 (m, 2H; Ar), 5.83-5.67 (m, 2H; 9-H, 10-H), 5.43 (s, 1H; Ar*CH*O_2), 4.57 (d, *J* (H, H)=11.5 Hz, 1H; *CH*HAr), 4.45 (dd, *J* (H, H)=10.5, 3.6 Hz, 1H), 4.25 (d, *J* (H, H)=11.5 Hz, 1H; CH*H*Ar), 3.86-3.68 (m, 5H), 3.81 (s, 3H; OCH_3), 3.60-3.50 (m, 1H), 3.45-3.34 (m, 1H), 3.00-2.80 (m, 2H), 2.45-2.21 (m, 2H), 1.12 (s, 9H; $(CH_3)_3$CSi); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=160.1, 137.6, 135.8, 135.7, 133.4, 133.3, 130.5, 129.7, 128.3, 127.8, 127.8, 127.7, 127.6, 127.5, 126.4, 113.7, 101.6, 79.7, 76.8, 71.6, 70.9, 64.2, 55.3, 28.8, 28.3, 27.0, 19.3; MS (CI, NH_3): *m/z*(%): 665 ($(M+H)^+$, 90), 316 (100); Found 665.3306, $C_{41}H_{49}O_6Si$ requires 665.3298.

(Z, 2*R*, 3*S*, 8*S*, 9*R*)-8-Benzyloxy-9-tbutyldiphenylsilyloxymethyl-2-hydroxymethyl-3-(4-methoxy-phenyl)-2,3,4,7,8,9-hexahydro-oxonine* 74** and ***(Z, 2*R*, 3*S*, 8*S*, 9*R*)-8-benzyloxy-2-9-bis-hydroxymethyl-3-(4-methoxy-phenyl)-2,3,4,7,8,9-hexahydro-oxonine

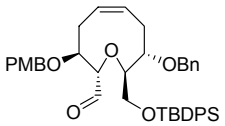


To a stirring solution of the acetal **73** (36 mg, 54 μmol) in DCM (1.1 mL) at – 78 °C was added DIBAL-H (0.38 mL of a 1 M solution in DCM, 380 μmol) and the resulting solution was allowed to warm to –30 °C over a 2 h period and was held at that temperature for 1 h. The reaction mixture was recooled to –78 °C and quenched by the addition of EtOH (0.3 mL) and was allowed to come to ambient temperature. A solution of Rochelle's salt and saturated aqueous NH_4Cl (1:1 mixture, 2 mL), was added and the resulting gel was stirred until dissolution was complete. The aqueous phase was separated and further extracted with DCM. Purification by preparative layer chromatography (ether:hexane, 1:1) provided the title compound **74** as a clear and colourless oil (16 mg, 24 μmol, 45%); R_f 0.4 (ether, hexane, 1:1); $[\alpha]_D^{18}$ +52.6 (*c* 0.7 in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.70-7.64 (m, 4H; Ar), 7.47-7.33 (m, 6H; Ar), 7.28-7.13 (m, 3H; Ar), 6.96-6.84 (m, 4H; Ar), 5.77-5.54 (m, 2H; 5-H, 6-H), 4.61 (d, *J* (H, H)=10.9 Hz, 1H), 4.44 (d, *J* (H, H)=11.4 Hz, 1H), 4.41 (d, *J* (H, H)=10.9 Hz, 1H), 4.09 (d, *J* (H, H)=11.4 Hz, 1H), 3.95-3.64 (m, 6H), 3.80 (s, 3H; CH_3O), 3.38 (dt, *J* (H, H)=9.6, 2.8 Hz, 1H), 3.20-3.03 (m, 2H), 2.84-2.62 (m, 2H), 2.51-2.40 (m, 1H), 2.33-2.23 (m, 1H) , 1.09 (s, 9H; $(CH_3)_3CSi$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=159.3, 137.6, 137.5, 135.7, 135.7, 133.0, 132.8, 130.3, 129.8, 129.7, 129.5, 128.4, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 126.9, 113.9, 113.7, 80.0, 79.6, 76.0, 71.4, 70.7, 65.8, 64.4, 62.0, 55.3, 28.7, 26.9, 26.4, 19.2; MS (CI, NH_3): *m/z*(%): 684 ($(M+NH_4)^+$, 50), 667 ($(M+H)^+$, 80), 154 (100); Found (ES) 684.3727, $C_{41}H_{54}NO_6Si$ requires 684.3720.

Also isolated was (*Z*, 2*R*, 3*S*, 8*S*, 9*R*)-8-benzyloxy-2-9-bis-hydroxymethyl-3-(4-methoxy-phenyl)-2,3,4,7,8,9-hexahydro-oxonine; R_f 0.1 (ether, hexane, 1:1); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.37-7.21 (m, 7H; Ar), 6.92-6.87 (m, 2H; Ar), 5.74-5.61 (m, 2H; 5-H, 6-H), 4.68 (d, *J* (H, H)=11.4 Hz, 1H), 4.61 (d, *J* (H, H)=11.1 Hz, 1H), 4.42 (d, *J* (H, H)=10.4 Hz, 1H), 4.39 (d, *J* (H, H)=11.1 Hz, 1H), 3.90-3.81 (m, 2H), 3.80 (s,

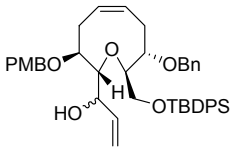
3H; CH_3O), 3.76-3.66 (m, 2H); 3.60-3.40 (m, 4H), 2.70-2.41 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=129.4, 137.7, 129.7, 128.5, 128.1, 127.9, 127.8, 127.6, 113.9, 76.3, 75.9, 71.4, 70.9, 62.8, 62.7, 55.3, 27.6, 27.5; MS (CI, NH_3): *m/z*(%): 446 ($(M+NH_4)^+$, 95), 129 ($(M+H)^+$, 20), 154 (100); Found 446.2546, $C_{25}H_{36}NO_6$ requires 446.2543.

***(Z, 2*R*, *3*S*, *8*S*, *9*R)-8-Benzyloxy-9-t*butyldiphenylsilyloxymethyl-2-carbaldehyde-3-(4-methoxy-phenyl)-2,3,4,7,8,9-hexahydro-oxonine* 75**



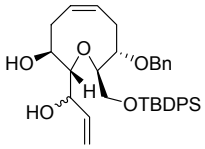
To a stirring solution of the alcohol **74** (15 mg, 22.5 μmol) in DMSO (1.7 mL) was added IBX (12 mg, 45 μmol) and the resulting solution was stirred for 18 h at ambient temperature. Ether (5 mL) and water (5 mL) were added. The aqueous phase was separated and extracted with ether (2 × 10 mL). The organic phases were washed with water (2 × 10 mL), brine (10 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to provide the title compound **75** as a clear and colourless oil (15 mg, 22.5 μmol, 100%); R_f 0.3 (hexane:ether, 1:1); IR ($CDCl_3$): ν=1734; ^1H NMR (250 MHz, $CDCl_3$): δ=9.76 (d, *J* (H, H)=2.6 Hz, 1H; CHO), 7.65-7.57 (m, 4H; Ar), 7.45-7.30 (m, 6H; Ar), 7.24-7.13 (m, 5H; Ar), 7.00-6.92 (m, 2H; Ar), 6.87 (d, *J* (H, H)=11.5 Hz, 1H; Ar), 5.72 (dt, *J* (H, H)=10.3, 7.0 Hz, 1H), 5.58 (dt, *J* (H, H)=10.3, 6.3 Hz, 1H), 4.56 (d, *J* (H, H)=11.3 Hz, 1H), 4.44 (d, *J* (H, H)=11.5 Hz, 1H), 4.37 (d, *J* (H, H)=11.3 Hz, 1H), 4.09 (d, *J* (H, H)=11.5 Hz, 1H), 3.81 (s, 3H; CH_3O), 3.80-3.60 (m, 5H), 3.27 (t, *J* (H, H)=8.1 Hz, 1H), 2.90-2.68 (m, 2H), 2.46-2.35 (m, 1H), 2.21-2.12 (m, 1H), 1.06 (s, 9H; $(CH_3)_3CSi$); *Note* due to the lability of the aldehyde satisfactory mass spectral data could not be obtained.

***(Z, 2*R*, 3*S*, 8*S*, 9*R*)-8-Benzyloxy-9-tbutyldimethylsilyloxymethyl-2-(1-hydroxy-allyl)-3-(4-methoxy-phenyl)-2,3,4,7,8,9-hexahydro-oxonine* 76**



To a stirring solution of the aldehyde **75** (15 mg, 22.5 μmol) (previously dried by azeotropic distillation with toluene (2 × 1 mL)) in THF (1.5 mL) at 0 °C was added vinylmagnesium bromide (113 μL of a 1.0 M solution in THF, 113 μmol) and the resulting solution was stirred at 0 °C for 2 h. Saturated aqueous NH_4Cl and ether were added to quench the reaction. The aqueous layer was separated and extracted with ether. The organic phases were washed with brine, dried ($MgSO_4$) and purificatrion by preparative layer chromatography (hexane:ether, 1:1) provided the title compound **76** as an inseparable 6:1 mixture of diastereomers (14.6 mg, 21 μmol, 94%); R_f 0.4 (hexane:ether, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.65-7.60 (m, 4H; Ar), 7.43-7.30 (m, 5H; Ar), 7.25-7.15 (m, 6H; Ar), 6.96 (d, *J* (H, H)=6.8 Hz, 1H; Ar), 6.86 (d, *J* (H, H)=11.6 Hz, 1H; Ar), 6.00 (ddd, *J* (H, H)=17.3, 10.5, 5.9 Hz, 1H; CH_2=C*H*), 5.65-5.56 (m, 2H), 5.16 (dt, *J* (H, H)=17,3, 1.5 Hz, 1H; *trans*-C*H*H=CH), 5.04 (dt, *J* (H, H)=10.5, 1.5 Hz, 1H; *cis*-CH*H*=CH), 4.54-4.52 (br, 1H; C*H*OH), 4.50 (d, *J* (H, H)=10.7 Hz, 1H), 4.45 (d, *J* (H, H)=11.0 Hz, 1H), 4.31 (d, *J* (H, H)=10.7 Hz, 1H), 4.16 (d, *J* (H, H)=11.6 Hz, 1H), 3.93 (dt, *J* (H, H)=11.5, 2.6 Hz, 1H; C*H*HOSi), 3.86 (dt, *J* (H, H)=8.0, 2.6 Hz, 1H; 9-H), 3.80 (s, 3H; CH_3O), 3.81-3.79 (m, 1H; CH*H*OSi), 3.70-3.67 (m, 1H; 3-H), 3.50 (dd, *J* (H, H)=9.0, 2.3 Hz, 1H; 2-H), 3.16 (t, *J* (H, H)=8.0 Hz, 1H; 8-H), 2.80-2.72 (m, 1H; 7-H), 2.69-2.63 (m, 1H; 4-H), 2.41-2.35 (m, 4-H'), 2.25-2.19 (m, 1H; 7-H'), 1.07 (s, 9H; $(CH_3)_3$CSi); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=152.9, 137.6, 137.3, 135.8, 132.9, 130.4, 129.8, 129.7, 128.3, 128.2, 127.7, 127.7, 127.5, 127.1, 113.8, 80.9, 76.8, 76.0, 73.7, 70.7, 64.0, 55.3, 29.1, 26.9, 26.2, 19.1; MS (CI, NH_3): *m/z*(%): 710 ($(M+NH_4)^+$, 100) , 693 ($(M+H)^+$, 55); Found (ES) 693.3622, $C_{43}H_{53}O_6Si$ requires 693.3622.

***(Z, 2R, 3S, 8S, 9R)-8-Benzyloxy-9-tbutyldimethylsilyloxymethyl-3-hydroxy-2-(1-hydroxy-allyl)-2,3,4,7,8,9-hexahydro-oxonine* 77**



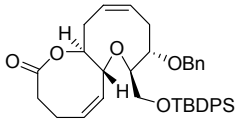
TFA (0.26 mL) was added to a stirring solution of the oxonanes **76** (13.5 mg, 19.5 μmol) in DCM (1 mL) at –20 °C. Stirring was continued for 15 mins and the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (3 mL) and DCM (3 mL). The aqueous phase wsa separated and extracted further with DCM. The combined organic extracts were dried ($MgSO_4$) and purificaition by preparative layer chromatography (hexane:ether, 1:1) provided the title compounds **77**.

The major diastereomer was isolated as a clear and colourless oil (9 mg, 15 μmol, 77%); R_f 0.1 (hexane:ether, 1:1); $[\alpha]_D^{20}$ +13.3 (*c* 0.18 in $CHCl_3$); IR ($CDCl_3$): ν=3570; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.47-7.30 (m, 6H; Ar), 7.25-7.15 (m, 3H; Ar), 7.02-6.96 (m, 2H; Ar), 6.03 (ddd, *J* (H, H)=17.4, 10.4, 4.7 Hz, 1H; CHH=C*H*), 5.76-5.61 (m, 2H; 5-H, 6-H), 5.42 (dt, *J* (H, H)=17.4, 1.9 Hz, 1H; *trans*-C*H*H=CH), 5.16 (dt, *J* (H, H)=10.7, 1.9 Hz, 1H; *cis*-CH*H*=CH), 4.73-4.67 (br, 1H), 4.50 (d, *J* (H, H)=11.6 Hz, 1H; C*H*HAr), 4.19 (d, *J* (H, H)=11.6 Hz, 1H; CH*H*Ar), 4.18-4.09 (br, 1H), 3.95 (dd, *J* (H, H)=11.1, 2.4 Hz, 1H; C*H*HOSi), 3.88 (dt, *J* (H, H)=8.4, 2.4 Hz, 1H; 9-H), 3.73 (dd, *J* (H, H)=11.1, 8.4 Hz, 1H; CH*H*OSi), 3.39 (dd, *J* (H, H)=8.8, 2.6 Hz, 1H), 3.33-3.25 (m, 1H), 3.20 (t, *J* (H, H)=7.3 Hz, 1H), 2.82-2.67 (m, 2H), 2.33-2.19 (m, 2H), 1.08 (s, 9H; $(CH_3)_3CSi$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=137.6, 137.5, 135.7, 135.7, 132.8, 132.7, 129.9, 128.5, 128.3, 127.8, 127.8, 127.6, 126.9, 114.3, 81.0, 77.8, 76.7, 72.8, 70.7, 68.5, 64.3, 30.3, 28.9, 26.9, 19.1; MS (CI, NH_3): *m/z*(%): 590 ($(M+NH_4)^+$, 40), 573 ($(M+H)^+$, 25), 274 (100); Found, 573.3028, $C_{35}H_{45}O_5Si$ requires 573.3036.

The minor diastereomer was isolated as a clear and colourless oil (1.3 mg, 2 μmol, 11%); R_f 0.15 (hexane:ether); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.69-7.59 (m, 4H; Ar), 7.45-7.29 (m, 6H; Ar), 7.25-7.17 (m, 3H; Ar), 7.06-6.98 (m, 2H; Ar), 6.19 (ddd, *J* (H, H)=17.6, 10.5, 4.1 Hz, 1H; CH_2=C*H*), 5.77-5.62 (m, 2H; 5-H, 6-H), 5.36 (dt, *J* (H, H)=17.6, 1.7 Hz, 1H; *trans*-C*H*H=CH), 5.23 (dt, *J* (H, H)=10.5, 1.7 Hz, 1H; *cis*-CH*H*=CH), 4.74-4.65 (br, 1H), 4.50 (d, *J* (H, H)=11.6 Hz, 1H; C*H*HAr), 4.18 (d, *J* (H, H)=11.6 Hz, 1H; CH*H*Ar), 4.00-3.90 (br, 1H), 3.91-3.86 (m, 2H; CH_2OSi), 3.84-3.73

(m, 1H), 3.44 (dd, *J* (H, H)=9.0, 4.1 Hz, 1H), 3.33 (t, *J* (H, H)=7.9 Hz, 1H), 2.98-2.87 (br, 1H), 2.85-2.70 (m, 2H), 2.55-.2.43 (br, 1H), 2.28-2.13 (br, 2H), 1.08 (s, 9H; $(CH_3)_3CSi$); MS (CI, NH_3): *m/z*(%): 590 ($(M+NH_4)^+$, 100), 573 ($(M+H)^+$, 30); Found 590.3316, $C_{35}H_{49}NO_5Si$ requires 590.3302.

(5Z, 6a*R, *8*R, *9*R, *11*Z, *13a*S)-9-Benzyloxy-8-*tert*-butyldimethylsilyloxymethyl-3,4,6a,8,9,10,13,13a-octahydro-1,7-dioxa-cyclooctacyclononen-2-one 79



To a solution of the major diastereomer of **77** (2.3 mg, 3.8 μmol) in toluene (1 mL) was added phenylselanylacetal diethyl acetal (1.3 mg, 4.6 μmol) and a small quantity of PPTS. The solution was heated under reflux for 2 h, allowed to cool and purified by preparative layer chromatography to give the corresponding selenides **78** (2.6 mg, 3.4 μmol, 91%). To a stirring solution of the selenides prepared above (2.6 mg, 3.4 μmol) in DCM (0.2 mL), MeOH (1.3 mL) and water (0.3 mL) was added $NaHCO_3$ (0.3 mg, 4 μmol) and $NaIO_4$ (2.9 mg, 12.9 μmol) and the resulting suspension was stirred at ambient temperature for 2 h. Water (5 mL) and DCM (5 mL) were added, the aqueous phase was separated and further extracted with DCM (4 × 5 mL). The organic phases were washed with brine (5 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* and the resultant selenoxides were dried under high vacuum for 18 h. Toluene (1 mL) and DBU (2 μL) were added and the resulting solution was heated at reflux for 18 h and then allowed to cool. The solvent was removed *in vacuo* and purification by flash chromatography (hexane:ether, 5:1) provided the title compound **79** (1.5 mg, 2.5 μmol, 74%) as a clear and colourless oil; R_f 0.2 (hexane:ether, 5:1); $[\alpha]_D^{19}$ +19.3 (*c* 0.073 in $CHCl_3$); IR ($CHCl_3$): ν=1742; ^1H (500 MHz, $CDCl_3$): δ=7.66-7.63 (m, 4H; Ar), 7.42-7.37 (m, 2H; Ar), 7.34-7.28 (m, 6H; Ar), 7.23-7.17 (m, 3H; Ar), 7.00 (d, *J* (H, H)=6.7 Hz, 2H; Ar), 6.14 (dd, *J* (H, H)=11, 5 Hz, 1H; 6-H), 5.76 (dt, *J* (H, H)=10.5, 7.2 Hz, 1H), 5.61-5.53 (m, 2H), 4.67 (dt, *J* (H, H)=9.3, 3.3 Hz, 1H; 13a-H), 4.51 (d, *J* (H, H)=11.5 Hz, 1H; C*H*HAr), 4.19 (d, *J* (H, H)=11.5 Hz, 1H; CH*H*Ar), 4.09-4.03 (m, 1H), 3.86-3.78 (m, 2H), 3.74 (dd, *J* (H, H)=11.9, 9.1 Hz, 1H), 3.17 (t, *J* (H, H)=8.8 Hz, 1H), 3.04 (t, *J* (H, H)=11.9 Hz, 1H), 2.95-2.86 (m, 1H), 2.74 (ddd, *J* (H, H)=13.6, 6.1, 1.6 Hz, 1H), 2.63-2.54 (m, 1H), 2.26 (ddd, *J* (H, H)=13.6,

12.5, 5.0 Hz. 1H), 2.34-2.25 (m, 1H), 2.17 (dd, *J* (H, H)=13.6, 7.6 Hz, 1H), 2.06-2.00 (m, 1H), 1.05 (s, 9H; $(CH_3)_3CSi$)); ^{13}C NMR (62.5 MHz, $CDCl_3$) *Note, one of the resonances of a carbon adjacent to oxygen is missing*: δ=175.9, 138.6, 137.6, 135.7, 133.6, 133.4, 130.5, 129.6, 128.6, 128.3, 127.7, 127.62, 127.55, 125.1, 82.7, 76.8, 70.9, 62.3, 32.6, 37.7, 29.5, 27.9, 25.4, 19.2; MS (CI, NH_3): *m/z*(%): 614 ($(M+NH_4)^+$, 60) , 597 ($(M+H)^+$, 15), 274 (100); Found (ES) 597.3031, $C_{37}H_{45}O_5Si$ requires 597.3036.

X-ray Crystal Structures.

X-ray Crystallographic Structure Determination of **15:** Crystal data: $C_{26}H_{44}O_5Si$, M_w=464.70, colourless block 0.10x0.10x0.10mm^3, orthorhombic $P2_12_12_1$ (No. 19), a=8.040(3), b=16.929(3), c=19.604(3)Å, V=2668(2)Å^3, Z=4, T = 180(2)K, D_X = 1.157 g cm^{-3}, λ = 0.71073 Å, μ 0.120 mm^{-1}, Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 1.59° < θ < 25.07°, 4732 independent reflections. The structure was solved by direct methods (*SHELXS*-97)[4] and refined by least squares (*SHELXL*-97)[4] using Chebyshev weights on F_o^2 to $R1$ = 0.046, $wR2$ = 0.123 [$I > 2\sigma(I)$], 326 parameters, goodness-of-fit on F^2 1.246, residual electron density 0.54 e Å^{-3}. The absolute structure was assigned from the known configuration of the starting material (Flack parameter: -0.2(2)). Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655148. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

X-ray Crystallographic Structure Determination of **17:** Crystal data: $C_{28}H_{46}O_5Si$, M_w=490.74, colourless block 0.25x0.25x0.25mm^3, orthorhombic $P2_12_12_1$ (No. 19), a=8.430 (1), b=16.304(1), c=20.801(1)Å, Z=4, V=2858.9(4)Å^3, T = 180(2)K, D_X = 1.140 g cm^{-3}, λ = 0.71073 Å, μ 0.200 mm^{-1}, Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 3.11° < θ < 25.03°, 4994 independent reflections. The structure was solved by direct methods (*SHELXS*-97)[4] and refined by least squares (*SHELXL*-97)[4] using Chebyshev weights on F_o^2 to $R1$ = 0.042, $wR2$ = 0.098 [$I > 2\sigma(I)$], 312 parameters, goodness-of-fit on F^2 1.135, residual electron density 0.42 e Å^{-3}. The absolute structure was assigned from the known configuration of the starting material (Flack parameter: 0.2(2)). Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655144. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

X-ray Crystallographic Structure Determination of **41**: Crystal data: $C_{19}H_{26}O_4$, M_w=318.40, colourless block 0.30x0.20x0.10mm^3, monoclinic $P2_1$ (No. 4), a=10.8190(4), b=5.3710(1), c=15.6400(5)Å, β=102.809(2)°, V=886.21(5)Å^3, Z=2, T = 180(2)K, D_X = 1.193 g cm^{-3}, λ = 0.71073 Å, μ 0.082 mm^{-1}, Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 2.93° < θ < 25.02°, 19185 measured reflections, 1746 independent (R_{int}=0.059). The structure was solved by direct methods (*SHELXS*-97)[4] and refined by least squares (*SHELXL*-97)[4] using Chebyshev weights on F_o^2 to $R1$ = 0.060, $wR2$ = 0.161 [$I > 2\sigma(I)$], 170 parameters, goodness-of-fit on F^2 1.098, residual electron density 0.59 e Å^{-3}. The $-C_6H_5$ ring is disordered over two sites: common isotropic displacement parameters were assigned to the carbon atoms of this moiety. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655145. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

X-ray Crystallographic Structure Determination of **61**: Crystal data: $C_{11}H_{16}O_4$, M_w=212.24, colourless block 0.14x0.04x0.02mm^3, hexagonal $P6_3$ (No. 173), a=14.343(7), c=8.9246(4)Å, V=1590.0(2)Å^3, Z=6, T = 150(2)K, D_X = 1.330 g cm^{-3}, λ = 0.71073 Å, μ 0.200 mm^{-1}, Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 2.72° < θ < 29.40°, 10627 measured reflections, 1632 independent (R_{int}=0.027). The structure was solved by direct methods (*SHELXS*-97)[4] and refined by least squares (*SHELXL*-97)[4] using Chebyshev weights on F_o^2 to $R1$ = 0.033, $wR2$ = 0.087 [$I > 2\sigma(I)$], 138 parameters, goodness-of-fit on F^2 1.191, residual electron density 0.30 e Å^{-3}. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655150. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

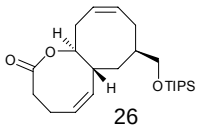
X-ray Crystallographic Structure Determination of **62**: Crystal data: $C_{12}H_{14}O_5$, M_w=238.23, colourless block 0.06x0.04x0.04mm^3, orthorhombic $P2_12_12_1$ (No. 19), a=7.8054(5), b=10.1991(9), c=14.3886(6)Å, V=1145.5(1)Å^3, Z=4, T = 150(2)K, D_X = 1.381 g cm^{-3}, λ = 0.71073 Å, μ 0.108 mm^{-1}, Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 2.74° < θ < 29.43°, 8116 measured reflections, 1870 independent [$R_{(int}$ =0.022]. The structure was solved by direct methods (*SHELXS*-97)[4] and refined by least squares (*SHELXL*-97)[4] using Chebyshev weights on F_o^2 to $R1$ = 0.044, $wR2$ = 0.108 [$I > 2\sigma(I)$], 190 parameters, goodness-of-fit on F^2 1.143, residual electron density 0.27 e Å^{-3}. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655146. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

X-ray Crystallographic Structure Determination of **63**: Crystal data: $C_{13}H_{16}O_4$, M_w=236.26, colourless block 0.10x0.08x0.06mm^3, monoclinic $P2_1$ (No. 4), a=7.720(4), b=6.415(3), c=12.126(5)Å, β=96.62(1)°, V=596.6(5)Å^3, Z=2, T = 150(2)K, D_X = 1.315 g cm^{-3}, λ = 0.71073 Å, μ 0.097 mm^{-1}, Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems Cryostream cooling apparatus, 2.89° < θ < 29.63°, 4168 measured reflections, 1767 independent (R_{int}=0.055). The structure was solved by direct methods (*SHELXS*-97)[4] and refined by least squares (*SHELXL*-97)[4] using Chebyshev weights on F_o^2 to $R1$ = 0.046, $wR2$ = 0.118 [$I > 2\sigma(I)$], 154 parameters, goodness-of-fit on F^2 1.041, residual electron density 0.32 e Å^{-3}. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-655149. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

References

1. We have previously reported the preparation of a lactone analogous to **7** but carrying a TBDPS instead of a TIPS protecting group and the lactone **7** was prepared analogously see: J. W. Burton, J. S. Clark, S. Derrer, T. C. Stork, J. G. Bendall and A. B. Holmes, *J. Am. Chem. Soc*., 1997, **119**, 7483.
2. E. A. Anderson, J. E. P. Davidson, J. R. Harrison, P. T. O'Sullivan, J. W. Burton, I. Collins and A. B. Holmes, *Tetrahedron*, 2002, **58**, 1943.
3. M. S. Congreve, A. B. Holmes, A. B. Hughes and M. G. Looney, *J. Am. Chem. Soc.*, 1993, **115**, 5815.
4. G. M. Sheldrick (**1997**). *SHELXS-97 / SHELXL-97*. University of Göttingen, Germany.

1H NMR (250 MHz; CDCl3)



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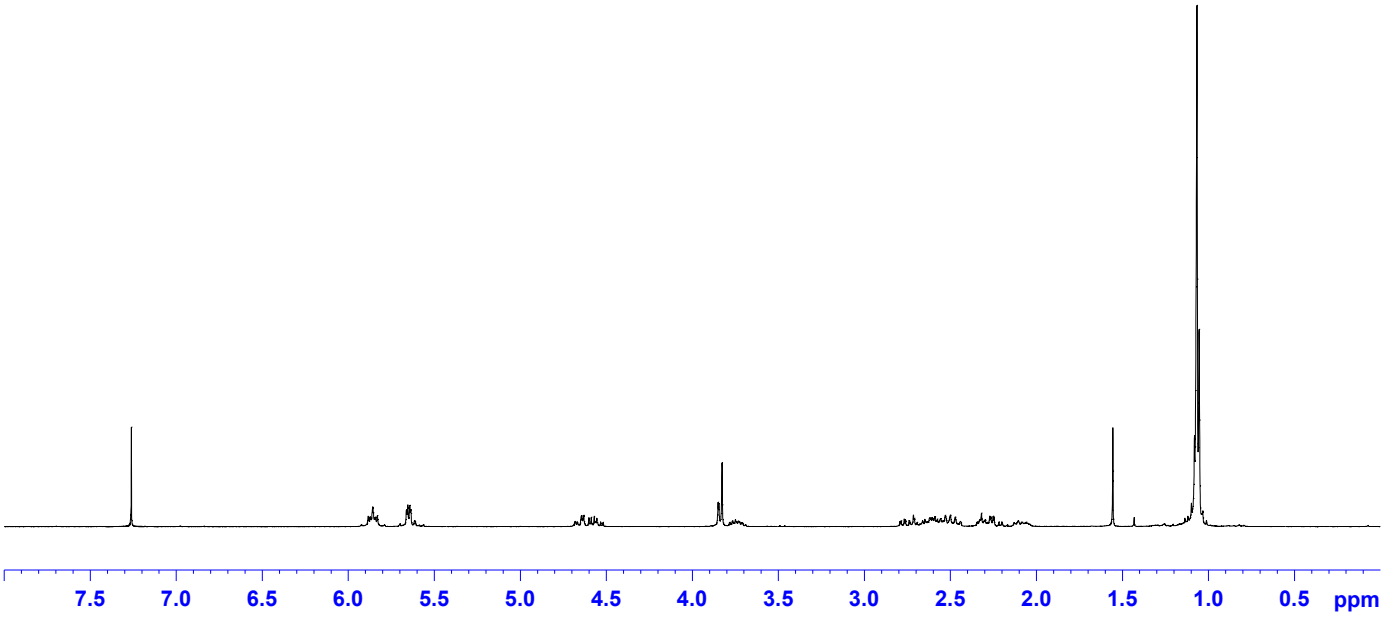
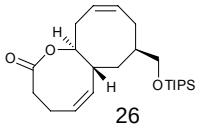
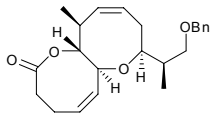


13C NMR (62.5 MHz,; CDCl3)



26

1H NMR (400 MHz; CDCl3)



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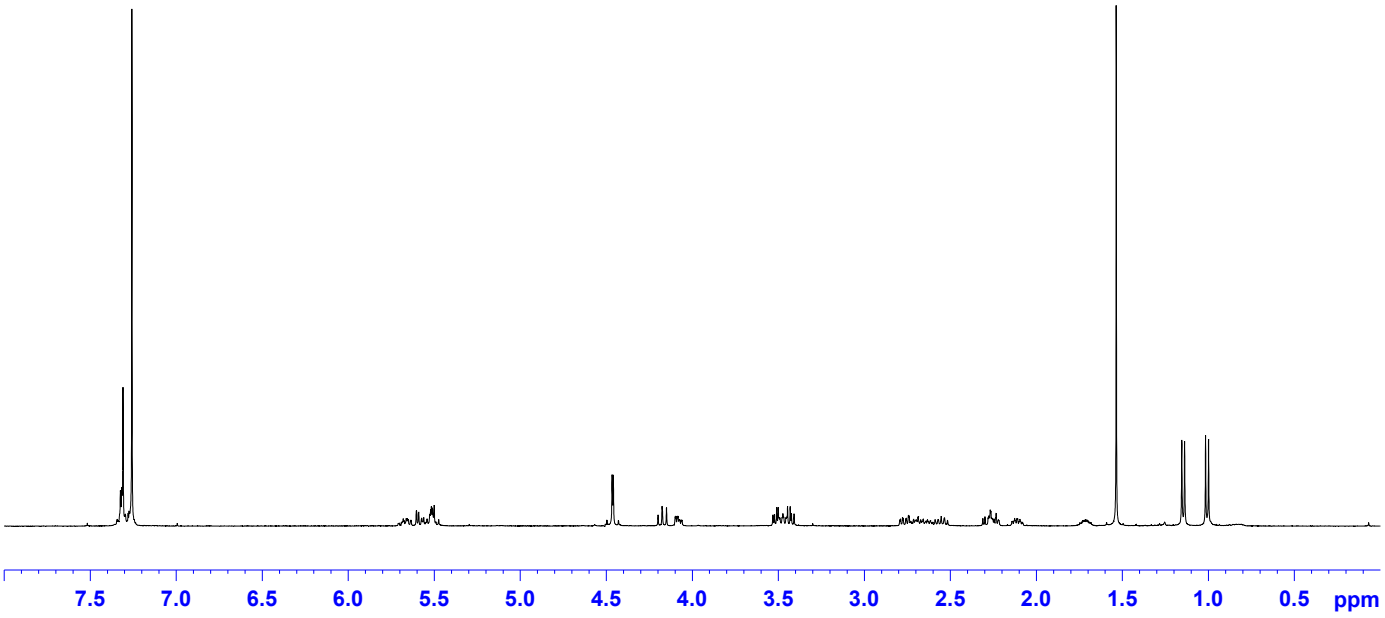

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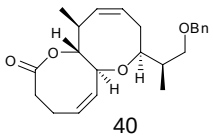

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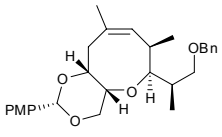
Variable Temperature 1H NMR (400 MHz; CDCl3)



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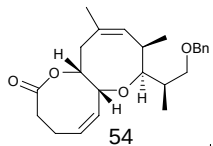

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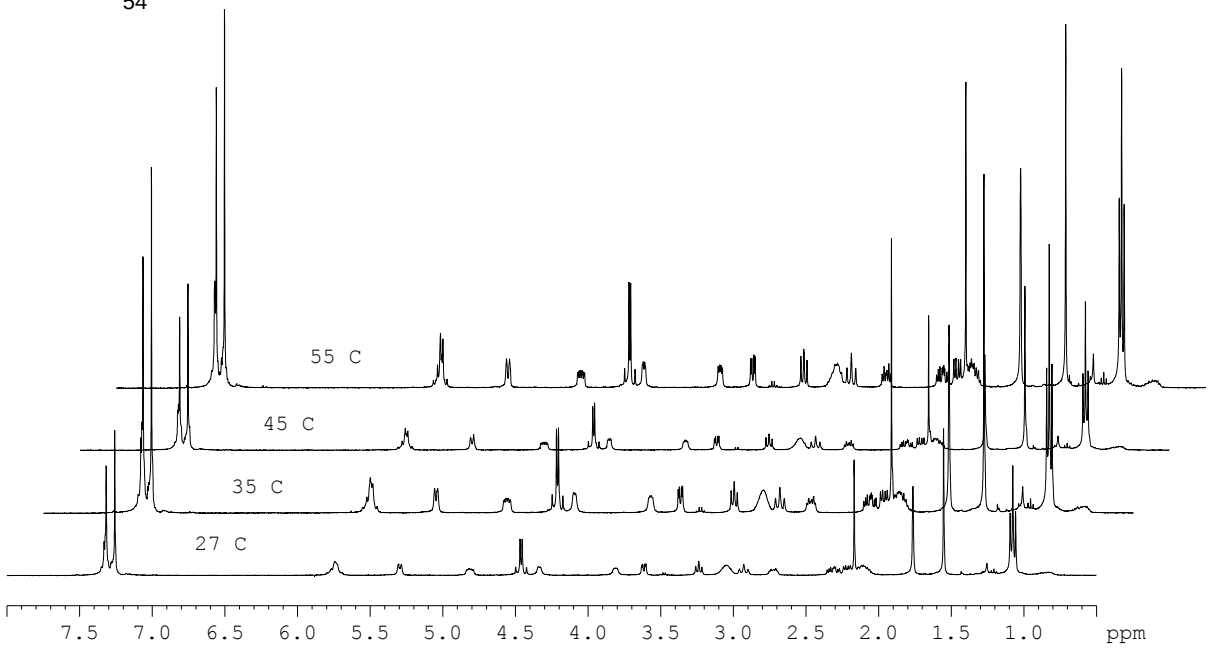
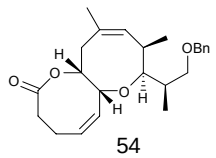
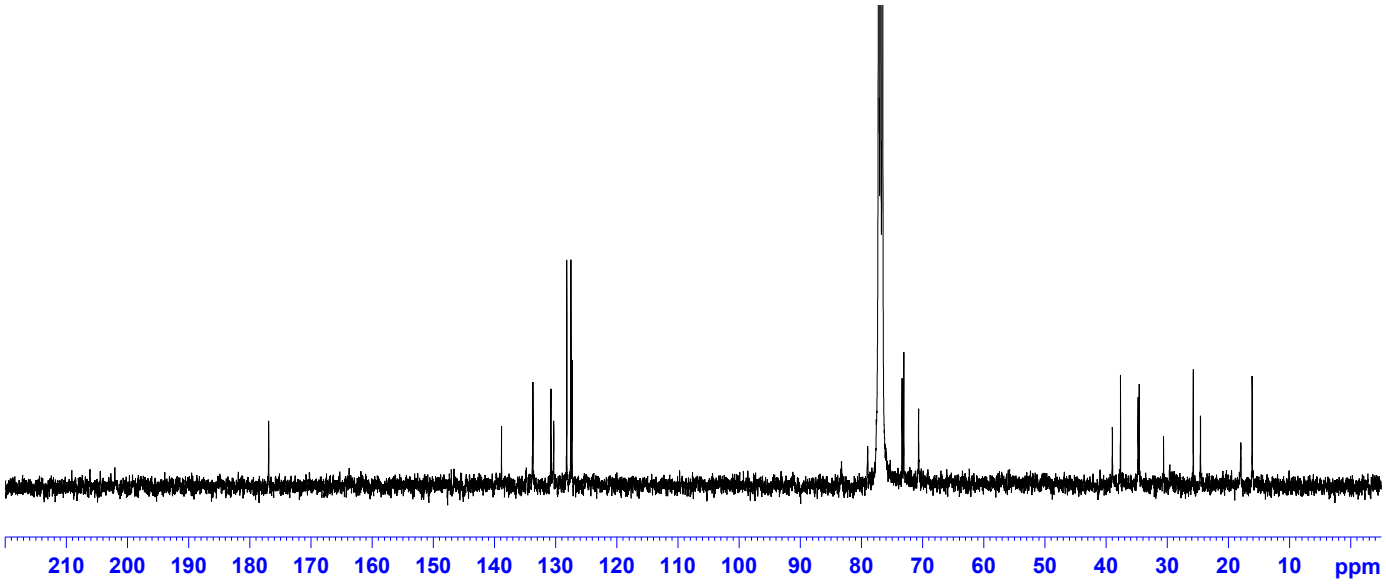


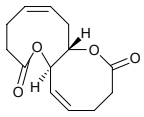
13C NMR (400 MHz; CDCl3; 32 C)



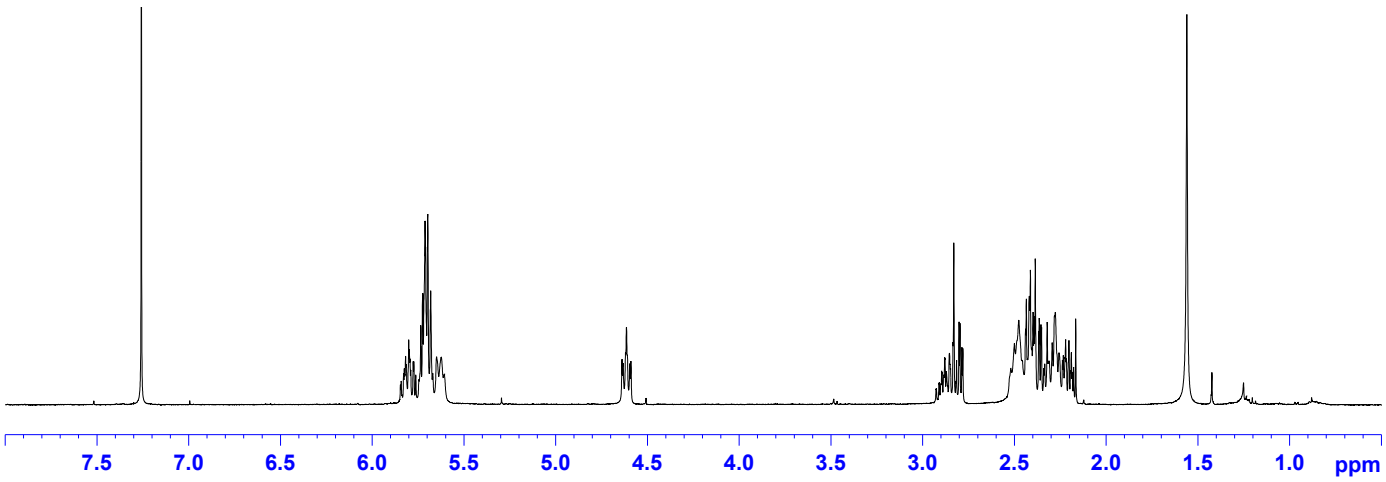
54



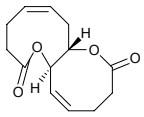
1H NMR (400 MHz; CDCl3)



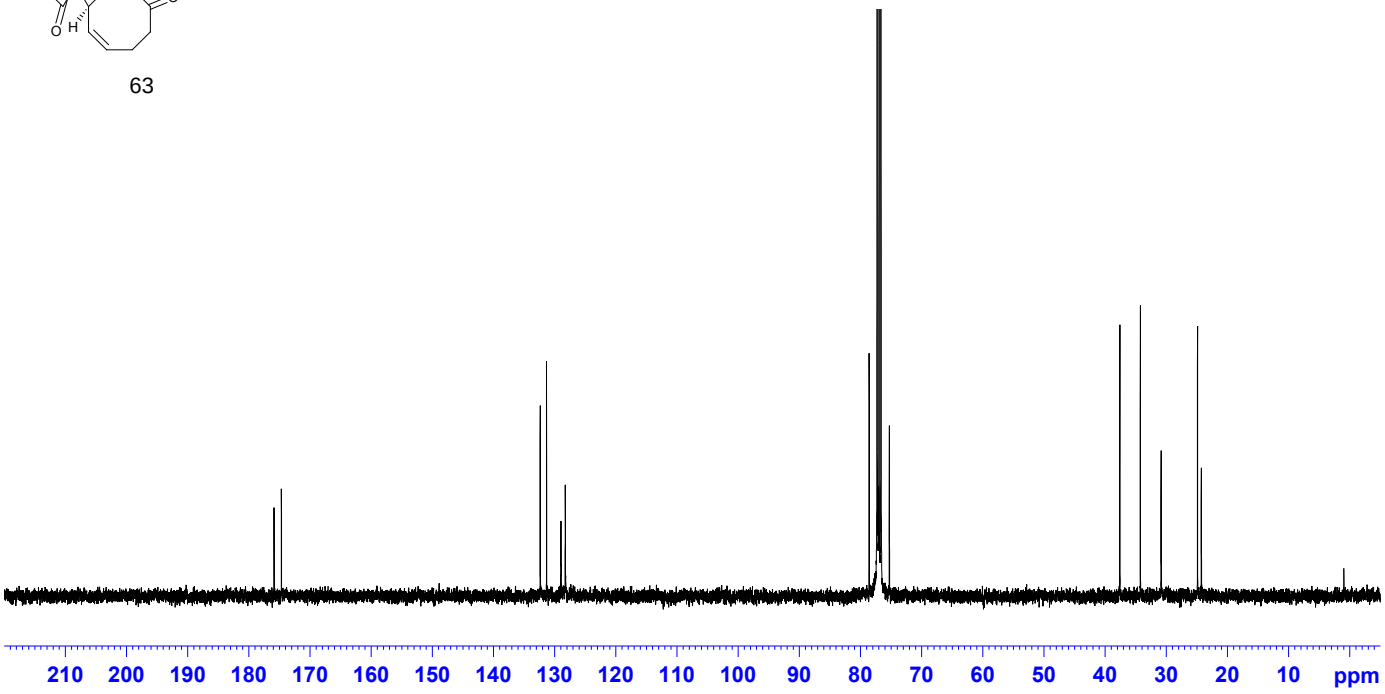
63



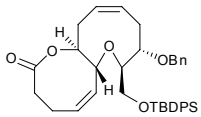
13C NMR (100 MHz; CDCl3)



63



1H NMR (500 MHz; CDCl3)



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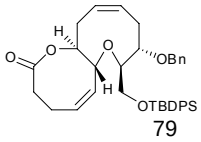
13C NMR (62.5 MHz, CDCl3)
Inset shows an expansion of the solvent resonance.
The peak at 77.2 is CHCl3 in CDCl3.



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