Electronic Supplementary Material for Organic & Biomolecular Chemistry

Electronic Supplementary Information

The Stereocontrolled Total Synthesis of Altohyrtin A/Spongistatin 1. Part 1: The AB-Spiroacetal Segment

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General Experimental Details

^{1}H nuclear magnetic resonance (NMR) spectra were recorded at either 250, 400 500 or 800 MHz on Bruker DPX 250, DPX 400, DRX 500 or DRX 800 spectrometers at ambient temperature using an internal deuterium lock. The following internal references were used for the residual protons in the following solvents: $CDCl_3$ (δ_H 7.26), C_6D_6 (δ_H 7.16) and CD_3CN (δ_H 1.94). Data are presented as follows: chemical shift (in ppm on the δ scale relative to tetramethylsilane $\delta_{TMS} = 0$), integration, multiplicity, coupling constant and interpretation XX-C<u>H</u> where XX refers to the carbon no. to which the proton in question is attached. Where reasonable, this numbering is based on the spongistatin skeleton. The following abbreviations for splitting patterns are used: s, singlet; d, doublet; t, triplet; q, quartet; quin., quintet; m, multiplet; br, broad. When the multiplet is derived from couplings to non-equivalent protons with coincidentally the same coupling constants then the multiplet is referred to as app, apparent. Assignments were determined either on the basis of unambiguous chemical shift or coupling pattern, COSY experiments or by analogy to fully interpreted spectra for related compounds. ^{13}C nuclear magnetic resonance (NMR) spectra were recorded at 100.6 MHz or 62.5 MHz on Bruker AM 400 or DPX 250 spectrometers respectively at ambient temperature using an internal deuterium lock, and all chemical shift values are reported in parts per million (δ) downfield relative to tetramethylsilane (TMS, $\delta_{TMS} = 0$). An internal reference was used for $CDCl_3$ (δ_C 77.16) and C_6D_6 (δ_C 128.06).

Infra-red spectra were recorded on Perkin-Elmer 1620 (FT-IR) spectrometers using 0.5 cm sodium chloride plates. Absorbance bands are reported in wavenumbers (cm^{-1}) relative to polystyrene as the calibrant, and the following abbreviations are used to describe their appearance: w, weak; s, strong; br, broad. Only the most significant bands are reported.

High and low resolution mass spectra were acquired using positive chemical ionisation using NH_4^+ (+CI, NH_3) by the EPSRC National Mass Spectrometry Service Centre, Swansea, UK and the Departmental Mass Spectrometry Service, University Chemical Laboratory, Cambridge, using electron impact (EI), electrospray (+ESI), chemical ionisation (+CI) or fast atom bombardment (+FAB) ionisation techniques. The parent ion $[M]^+$ or $[MH]^+$ or $[M + NH_4]^+$ is quoted, followed by significant fragments with their relative intensities.

Optical rotations were recorded on a Perkin Elmer 241 polarimeter at the sodium D line (589 nm) and are reported as follows: $[\alpha]_D^{20}$, concentration (*c* in g/100 mL) and solvent (all the rotations were measured at a temperature of 20 °C). Melting points were recorded on a Kofler hot-stage and are uncorrected.

Analytical thin layer chromatography (TLC) was carried out using Merck Kieselgel 60 F_{254} plates with visualisation either by ultra violet light (254 nm), anisaldehyde or Goofy's dips. Flash column chromatography was carried out using Merck Kieselgel 60 (230-400 mesh) under a positive

pressure using distilled solvents and in this thesis the term implies subsequent removal of the solvents *in vacuo* unless otherwise stated. High Performance Liquid Chromatography (HPLC) was carried out using a Rainin Instrument Co. Inc. DYNAMAX Macro-HPLC column (internal diameter: 21.4 mm), prepacked with 8 micron irregular silica particles, and equipped with a Gilson refractive index detector (Model 131) or a Gilson UV detector (Model 111B) at a wavelength of 254 nm. A flow rate of 10 mL min^{-1} was used and all solvents were vacuum-filtered and degassed prior to use.

Reagents and solvents were prepared using standard means.[1] Anhydrous CH_2Cl_2, MeOH and hexane were distilled from CaH_2 and stored under argon; ether was distilled from sodium metal/benzophenone ketyl and stored under an argon atmosphere; THF was distilled from either $LiAlH_4$ or potassium metal/benzophenone ketyl and stored under an argon atmosphere. Triethylamine (Et_3N), *i*-Pr_2NEt, pyridine and 2,6-lutidine were distilled from and stored over CaH_2. Acetic acid (AcOH) was distilled from CrO_3 and Ac_2O and stored under an argon atmosphere. Simple aldehydes were distilled from calcium chloride immediately prior to use. All other reagents were used as received except where noted in the experimental procedure.

All experiments were performed under anhydrous conditions, utilising anhydrous solvents, under an atmosphere of argon, except where stated, using oven-dried glassware and employing standard techniques in handling air-sensitive materials. All reactants added *via* cannula were added using a positive pressure of argon. Where a reaction temperature is not specified the reaction was performed at room temperature. Where a compound has been published in the literature, all spectroscopic and physical properties matched those reported.

Experimental Procedures and Product Characterisation Data

(*R*)-6-Benzyloxy-4-(triethylsiloxy)-1-hexene (11)

To a cold (–78 °C), stirred solution of alcohol **10** (3.85 g, 18.7 mmol) in dry CH_2Cl_2 (80 mL) was added 2,6-lutidine (6.5 mL, 56 mmol, 3 equiv.) followed by TESOTf (6.3 mL, 28 mmol, 1.5 equiv.). The resultant solution was stirred at –78 °C for 2 h and then EtOH (5 mL) was added to quench the excess TESOTf. Saturated aqueous NH_4Cl (50 mL) was added and the reaction was allowed to warm to rt. The layers were separated and the aqueous phase was extracted with Et_2O (4 x 150 mL). The combined organic extracts were washed with pH 7 buffer (2 x 100 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude oil was flash chromatographed (5:95 Et_2O/hexanes) to yield the TES ether **11** (5.88 g, 98%), as a colourless oil: $\mathbf{R_f}$ 0.40 (5:95 Et_2O/hexanes); $[\alpha]_D^{20}$ –17.5 (*c* 1.86, $CHCl_3$); **IR** (liquid film) 3074, 3030, 1641 cm^{-1}; **^{1}H NMR** δ (250 MHz, $CDCl_3$) 7.29–7.35 (5H, m, Ar), 5.74–5.90 (1H, m, H_5), 5.01–5.07 (2H, m, -CH=CH_2), 4.45, 4.53 (2H, AB_q, J = 11.9 Hz, -OCH_2Ph), 3.91 (1H, qn, J = 7.2 Hz, H_3), 3.52–3.62 (2H, m, H_{1A} and H_{1B}), 2.24 (2H, t, J = 6.7 Hz, H_{4A} and H_{4B}), 1.69–1.82 (2H, m, H_{2A} and H_{2B}), 0.95 (9H, t, J = 8.0 Hz, -OSi(CH_2CH_3)$_3$), 0.60 (6H, q, J = 8.0 Hz, -OSi(CH_2CH_3)$_3$); **^{13}C NMR** δ (62.5 MHz, $CDCl_3$) 138.6, 134.9, 128.3, 127.7, 127.5, 117.0, 73.0, 69.0, 67.1, 42.4, 36.8, 5.9, 5.1; **HRMS** (CI, NH_3) calcd. for $C_{19}H_{33}O_2Si$ (MH^+) 321.2251, found 321.2250.

(*S*)-5-Benzyloxy-3-(triethylsiloxy)pentanal (12)

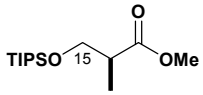
To a cold (–78 °C), stirred solution of the TES ether **11** (194 mg, 0.605 mmol) in dry CH_2Cl_2 (40 mL) was added a spatula tip of $NaHCO_3$ to help suppress hydrolysis of the TES ether. A stream of O_3 was then bubbled through this mixture until the solution became blue in colour (*ca*. 1 min), indicating an excess of O_3. N_2 was bubbled through the mixture until the blue colour dissipated. Triphenylphosphine (317 mg, 1.21 mmol, 2.0 equiv.) was added and the mixture was warmed to rt and stirred for 3.5 h when TLC analysis indicated that the ozonide was completely converted to the aldehyde **12**. The reaction was concentrated *in vacuo* and the residue was flash chromatographed (neat hexanes → 50:50 CH_2Cl_2/hexanes → neat CH_2Cl_2) to yield the aldehyde **12** (185 mg, 95%), as

[1] D. A. Perrin and W. L. F. Armarego, *Purification of Laboratory Chemicals*, Pergamon Press, Oxford, 1988.

a colourless oil: $\mathbf{R_f}$ 0.35 (CH_2Cl_2); $[\alpha]_D^{20}$ –4.8 (*c* 2.06, $CHCl_3$); **IR** (liquid film) 1725, 1603, 1455 cm^{-1}; **^{1}H NMR** δ (250 MHz, $CDCl_3$) 9.80 (1H, t, *J* = 2.0 Hz, $\underline{H}_5$), 7.28–7.35 (5H, m, Ar), 4.45, 4.51 (2H, AB_q, *J* = 12.0 Hz, -OC$\underline{H}_2$Ph), 4.41 (1H, qn, *J* = 6.0 Hz, $\underline{H}_3$), 3.55 (2H, t, *J* = 6.0 Hz, $\underline{H}_{1A}$ and $\underline{H}_{1B}$), 2.48–2.68 (2H, m, $\underline{H}_{4A}$ and $\underline{H}_{4B}$), 1.76–1.93 (2H, m, $\underline{H}_{2A}$ and $\underline{H}_{2B}$), 0.95 (9H, t, *J* = 7.9 Hz, -OSi($CH_2C\underline{H}_3$)$_3$), 0.60 (6H, q, *J* = 7.9 Hz, -OSi($C\underline{H}_2CH_3$)$_3$); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 202.1, 138.2, 128.4, 127.7, 127.6, 73.0, 66.3, 65.5, 51.2, 37.7, 6.8, 4.9; **HRMS** (+FAB) calcd. for $C_{18}H_{31}O_3Si$ (MH^+) 323.2042, found 323.2055.

(4*S*,6*S*)-8-Benzyloxy-4-(*tert*-butyldimethylsiloxy)-6-(triethylsiloxy)-2-octanone (7)
Imidazole (1.54 g, 22.64 mmol) and TBSCl (2.05 g, 13.58 mmol) were added to a stirred solution of aldol product **14** (4.30 g, 11.32 mmol) in DMF (30 mL) and the reaction was stirred overnight at RT. The reaction mixture was then partitioned between CH_2Cl_2 (100 mL) and pH 7 buffer (100 mL) and the organic layer was washed with water (3 x 100 mL) before being dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (10:90 Et_2O/hexanes) afforded the desired TBS ether **7** (5.44 g, 97%) as a colourless oil: $\mathbf{R_f}$ 0.30 (10:90 Et_2O/hexanes); $[\alpha]_D^{20}$ –0.4 (*c* 2.08, $CHCl_3$); **IR** (liquid film) 3030, 1718 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.25–7.36 (5H, m, Ar), 4.47, 4.50 (2H, AB_q, *J* = 11.9 Hz, -OC$\underline{H}_2$Ph), 4.25 (1H, qn, *J* = 6.0 Hz, $\underline{H}_3$ or $\underline{H}_5$), 3.95 (1H, qn, *J* = 5.7 Hz, $\underline{H}_3$ or $\underline{H}_5$), 3.54 (2H, t, *J* = 6.6 Hz, $\underline{H}_{1A}$ and $\underline{H}_{1B}$), 2.57 (2H, d, *J* = 5.9 Hz, $\underline{H}_{6A}$ and $\underline{H}_{6B}$), 2.13 (3H, s, C_7-C$\underline{H}_3$), 1.57–1.88 (4H, m, $\underline{H}_{2A}$, $\underline{H}_{2B}$, $\underline{H}_{4A}$ and $\underline{H}_{4B}$), 0.95 (9H, t, *J* = 7.9 Hz, -OSi($CH_2C\underline{H}_3$)$_3$), 0.85 (9H, s, -OSiMe$_2^{t}\underline{Bu}$), 0.59 (6H, q, *J* = 7.9 Hz, -OSi($C\underline{H}_2CH_3$)$_3$), 0.02, 0.05 (6H, s, s, -OSi$\underline{Me}_2$^{t}Bu); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 207.5, 138.2, 128.2, 127.6, 127.4, 73.0, 66.8, 66.7, 66.4, 51.3, 45.4, 37.2, 31.6, 25.8, 17.9, 6.9, 5.1, –4.5, –4.7; **HRMS** (+FAB) calcd. for $C_{27}H_{50}O_4Si_2$ (MH^+) 495.3326, found 495.3355.

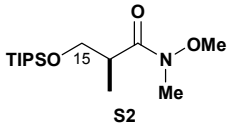
Methyl (*S*)-2-methyl-3-(triisopropylsiloxy)-propionate (S1)



S1

To a cooled (0 ºC) solution of methyl (*S*)-3-hydroxy-2-methylpropionate **15** (40 g, 0.34 mol) in CH_2Cl_2 (170 mL) was added imidazole (27.7 g, 0.407 mol, 1.2 equiv.) and DMAP (414 mg, 3.39 mmol, 1 mol%). TIPSCl (76.2 mL, 0.356 mol, 1.05 equiv.) was added slowly over a 15 min period. The resultant solution was allowed to warm to RT overnight. Sat. NH_4Cl (200 mL) and H_2O (100 mL) were added and the layers were separated. The aqueous phase was extracted with Et_2O (4 x 100 mL) and the combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$) and concentrated *in vacuo* to yield silyl ether **S1** (91.7 g, 99%) as a colourless oil: $\mathbf{R_f}$ 0.80 (5:95 EtOAc/hexanes); **^{1}H NMR** δ (400 MHz, $CDCl_3$) 3.85 (1H, dd, *J* = 9.4, 6.7 Hz, 15-C$\underline{H}_a$H$_b$), 3.75 (1H, dd, *J* = 9.4, 6.0 Hz, 15-CH$_a$$\underline{H}_b$), 3.66 (3H, s, OC$\underline{H}_3$), 2.66 (1H, sextet, *J* = 6.7 Hz, 14-C$\underline{H}$), 1.15 (3H, d, *J* = 7.0 Hz, 14-CHC$\underline{H}_3$), 1.01–1.09 (21H, m, Si(C$\underline{H}$(C$\underline{H}_3$)$_2$)$_3$).

(*S*)-*N*-Methoxy-2,*N*-dimethyl-3-(triisopropylsiloxy)-propionamide (S2)



S2

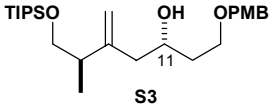
i-PrMgCl (2.0 M in THF, 425 mL, 0.850 mol, 2.6 equiv.) was added dropwise over a 3 h period to a cooled (–20 ºC) mixture of ester **S1** (90.0 g, 0.328 mol) and MeONHMe•HCl (43.2 g, 0.443 mol, 1.35 equiv.) in THF (200 mL) whilst carefully maintaining the temperature ≤ –10 ºC. The reaction was stirred at –20 ºC for a further 1 h then quenched by the cautious addition of sat. NH_4Cl (150 mL). The cooling bath was removed, H_2O (200 mL), 1 M HCl (100 mL) and Et_2O (200 mL) were added and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 100 mL). The combined organic extracts were washed with sat. NH_4Cl (100 mL) and brine (100 mL), dried

($MgSO_4$) and concentrated *in vacuo*. The resultant crude oil of **S2** (99.5 g, 100%) was carried through to the next reaction without further purification: $\mathbf{R_f}$ 0.50 (15:85 EtOAc/hexanes); $[\alpha]_D^{20}$ +17.2 (*c* 2.95, $CHCl_3$); **^{1}H NMR** δ (400 MHz, $CDCl_3$) 3.92 (1H, t, *J* = 9.0 Hz, 15-C$\underline{H}_a$H$_b$), 3.70 (3H, s, OC$\underline{H}_3$), 3.60 (1H, dd, *J* = 9.0, 6.3 Hz, 15-CH$_a\underline{H}_b$), 3.18 (4H, m, NC$\underline{H}_3$ + 14-C$\underline{H}$), 1.03–1.09 (24H, m, 14-CHC$\underline{H}_3$ + Si(C$\underline{H}$(C$\underline{H}_3$)$_2$)$_3$).

(*S*)-3-Methyl-4-(triisopropylsiloxy)-butan-2-one (16)

To a cold (–78 ºC) solution of Weinreb amide (**S2**, from above procedure) (99.5 g, 0.328 mol) in THF (250 mL) was added MeMgBr (3.0 M in Et_2O, 150 mL, 0.450 mol, 1.37 equiv.) *via* cannula. The solution was warmed to 0 ºC and stirred at this temperature for 3 h. The reaction was quenched by pouring the solution into a conical containing sat. NH_4Cl (150 mL) whilst vigorously stirring. 1 M HCl (50 mL) was added and the layers were separated. The aqueous phase was extracted with Et_2O (4 x 100 mL). The combined organic extracts were washed with sat. NH_4Cl (150 mL) and brine (150 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The resultant crude material was purified by distillation through a 15 cm packed column at reduced pressure to afford ketone **16** (63.4 g, 75%) as a colourless oil: **b. pt.** 68–69 ºC (0.08 mm Hg); $\mathbf{R_f}$ 0.20 (5:95 Et_2O/hexanes); $[\alpha]_D^{20}$ +27.6 (*c* 2.72, $CHCl_3$); **IR** (liquid film) 1719, 1463 cm^{-1}; **^{1}H NMR** δ (500 MHz, $CDCl_3$) 3.83 (1H, dd, *J* = 9.7, 7.3 Hz, 15-C$\underline{H}_a$H$_b$), 3.76 (1H, dd, *J* = 9.7, 5.5 Hz, 15-CH$_a\underline{H}_b$), 2.76 (1H, br sextet, *J* = 7.0 Hz, 14-C$\underline{H}$), 2.20 (3H, s, 12-C$\underline{H}_3$), 1.02–1.10 (24H, m, 14-CHC$\underline{H}_3$ + Si(C$\underline{H}$(C$\underline{H}_3$)$_2$)$_3$); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 211.9, 65.9, 49.4, 29.5, 17.9, 12.9, 11.8.

(3*S*)-1-(*p*-Methoxybenzyloxy)-5-[1-(triisopropylsiloxy)-prop-2-(*R*)-yl]-hex-5-en-3-ol (S3)



S3

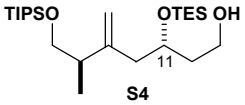
To a solution of *p*-nitrobenzoate **21** (14.9 g, 0.950 mmol) in MeOH (100 mL) was added K_2CO_3 (3.40 g, 24.8 mmol, 1 equiv.) and the mixture was stirred at RT for 16 h. The reaction was concentrated *in vacuo* and the resultant oil was dissolved in Et_2O (200 mL), brine (100 mL) was added and the layers were separated. The aqueous phase was extracted with EtOAc (3 x 100 mL) and the combined organic extracts were washed with brine (100 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash chromatography (3:97 → 20:80 EtOAc/hexanes) gave **S3** (10.9 g, 97%), as a colourless oil: $\mathbf{R_f}$ 0.35 (30:70 Et_2O/hexanes); $[\alpha]_D^{20}$ +6.4 (*c* 1.99, $CHCl_3$); **IR** (liquid film) 3458, 1641, 1613, 1586, 1463 cm^{-1}; **^{1}H NMR** δ (500 MHz, $CDCl_3$) 7.25 (2H, d, *J* = 8.5 Hz, Ar$\underline{H}$), 6.87 (2H, d, *J* = 8.5 Hz, Ar$\underline{H}$), 4.92 (1H, s, C=C$\underline{H}_a$H$_b$), 4.90 (1H, s, C=CH$_a\underline{H}_b$), 4.45 (2H, s, OC$\underline{H}_2$Ar), 3.91–3.95 (1H, m, 11-C$\underline{H}$), 3.80 (3H, s, OC$\underline{H}_3$), 3.59–3.69 (3H, m, 9-C$\underline{H}_2$ + 15-C$\underline{H}_a$H$_b$), 3.53 (1H, dd, *J* = 9.5, 6.9 Hz, 15-CH$_a\underline{H}_b$), 2.86 (1H, d, *J* = 1.5 Hz, O$\underline{H}$), 2.36 (1H, sextet, *J* = 6.8 Hz, 14-C$\underline{H}$), 2.26 (1H, dd, *J* = 13.9, 4.2 Hz, 12-C$\underline{H}_a$H$_b$), 2.17 (1H, dd, *J* = 13.9, 8.7 Hz, 12-CH$_a\underline{H}_b$), 1.71–1.82 (2H, m, 10-C$\underline{H}_2$), 1.04–1.11 (24H, m, 14-CHC$\underline{H}_3$ + Si(C$\underline{H}$(C$\underline{H}_3$)$_2$)$_3$); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 159.2, 149.2, 130.3, 129.2, 113.8, 112.1, 72.9, 68.6, 68.2, 68.1, 55.2, 44.2, 42.1, 36.6, 18.0, 16.9, 12.0; **HRMS** (+FAB) Calc. for $C_{26}H_{47}O_4Si$ $[MH]^+$: 451.3243, found: 451.3243.

(4*S*)-2-[1-(Triisopropylsiloxy)-prop-2-(*R*)-yl]-6-(*p*-methoxybenzyloxy)-4-(triethylsiloxy)-hex-1-ene (22)

To a cold (0 °C) solution of alcohol **S3** (12.5 g, 27.8 mmol) and imidazole (2.83 g, 41.6 mmol, 1.5 equiv.) in DMF (50 mL) was added TESCl (5.57 mL, 33.2 mmol, 1.2 equiv.). The reaction mixture was allowed to warm to RT and stirred for further 16 h. The reaction mixture was cooled to 0 °C and MeOH (2 mL) was added. The mixture was poured into 2% aq. $NaHCO_3$ (200 mL) and Et_2O (200 mL) was added. The layers were separated and the aqueous phase was extracted with Et_2O (4 x 100 mL). The combined organics were washed with brine (100 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (2.5:97.5 → 25:75 Et_2O/light petroleum) afforded

TES ether **22** (15.2 g, 97%) as a colourless oil: $\mathbf{R_f}$ 0.30 (5:95 Et_2O/hexanes); $[\alpha]_D^{20}$ +14.1 (*c* 2.14, $CHCl_3$); **IR** (liquid film) 1640, 1613, 1586, 1513, 1463 cm^{-1}; **^{1}H NMR** δ (500 MHz, $CDCl_3$) 7.24 (2H, d, *J* = 8.6 Hz, ArH), 6.86 (2H, d, *J* = 8.6 Hz, ArH), 4.82 (1H, s, C=CH_aH_b), 4.80 (1H, s, C=CH_aH_b), 4.40 (2H, AB_q, *J* = 11.6 Hz, OCH_2Ar), 3.97 (1H, m, 11-CH), 3.80 (3H, s, OCH_3), 3.70 (1H, dd, *J* = 9.4, 5.2 Hz, 15-CH_aH_b), 3.52 (2H, t, *J* = 6.7 Hz, 9-CH_2), 3.44 (1H, dd, *J* = 9.4, 8.0 Hz, 15-CH_aH_b), 2.28 (1H, dd, *J* = 14.0, 5.1 Hz, 12-CH_aH_b), 2.26 (1H, m, 14-CH), 2.15 (1H, dd, *J* = 14.0, 7.6 Hz, 12-CH_aH_b), 1.86 (1H, m, 10-CH_aH_b), 1.63 (1H, m, 10-CH_aH_b), 1.03–1.10 (24H, m, 14-CHCH_3 + Si(CH(CH_3)$_2$)$_3$), 0.94 (9H, t, *J* = 7.9 Hz, Si($CH_2C H_3$)$_3$), 0.58 (6H, q, *J* = 7.9 Hz, Si(CH_2CH$_3$)$_3$); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 159.0, 148.6, 130.7, 129.2, 113.8, 111.4, 72.5, 68.6, 67.7, 66.9, 55.2, 44.5, 42.3, 36.7, 18.0, 16.7, 11.9, 6.9, 5.0; **HRMS** (+FAB) Calc. for $C_{32}H_{59}O_4Si_2$ $[M - H]^+$: 563.3952, found: 563.3936.

(3*S*)-5-[1-(Triisopropylsiloxy)-prop-2-(*R*)-yl]-3-(triethylsiloxy)-hex-5-en-1-ol (S4)



S4

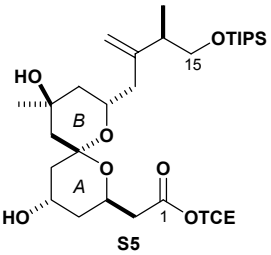
To a cold (0 °C), stirred solution of the PMB ether **22** (71 mg, 0.126 mmol, 1.0 equiv.) in a 10:1 mixture of CH_2Cl_2 (1.1 mL) and pH 7 buffer (100 μL) was added DDQ (43 mg, 0.19 mmol, 1.5 equiv.). The resultant orange/brown suspension was stirred at 0 °C for 15 min at which point a further aliquot of DDQ (43 mg, 0.19 mmol, 1.5 equiv.) was added. The mixture was stirred at 0 °C for 30 min at which point TLC analysis indicated complete consumption of the starting material **22**. Saturated aqueous $NaHCO_3$ (3 mL) was added and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. The crude oil was flash chromatographed to yield the desired primary alcohol **S4** (53 mg, 95%), as a colourless oil: $\mathbf{R_f}$ 0.55 (20:80 EtOAc/hexanes); $[\alpha]_D^{20}$ +20.2 (*c* 1.65, $CHCl_3$); **IR** (liquid film) 3387, 3080, 1641, 1462 cm^{-1}; **^{1}H NMR** δ (500 MHz, $CDCl_3$) 4.84 (1H, s, C=CH_aH_b), 4.80 (1H, s, C=CH_aH_b), 4.08–4.12 (1H, m, 11-CH), 3.84 (1H, m, 9-CH_aH_b), 3.72 (1H, m, 9-CH_aH_b), 3.70 (1H, m, 15-CH_aH_b), 3.49 (1H, dd, *J* = 9.4, 7.5 Hz, 15-CH_aH_b), 2.53 (1H, t, *J* = 5.2 Hz, OH), 2.37 (1H, dd, *J* = 14.0, 4.7 Hz, 12-CH_aH_b), 2.19–2.28 (2H, m, 12-CH_aH_b + 14-CH), 1.87 (1H, m, 10-CH_aH_b), 1.63 (1H, m, 10-CH_aH_b), 1.03–1.10 (24H, m, 14-CHCH_3 + Si(CH(CH_3)$_2$)$_3$), 0.98 (9H, t, *J* = 8.0 Hz, Si($CH_2C H_3$)$_3$), 0.64 (6H, q, *J* = 8.0 Hz, Si(CH_2CH$_3$)$_3$); **^{13}C NMR** δ (62.5 MHz, $CDCl_3$) 148.5, 111.5, 71.3, 67.6, 60.4, 43.6, 42.4, 37.4, 18.0, 16.9, 12.0, 6.8, 5.0; **HRMS** (+FAB) Calc. for $C_{24}H_{53}O_3Si_2$ $[MH]^+$: 445.3533, found: 445.3552.

(3*S*)-5-[1-(Triisopropylsiloxy)-prop-2-(*R*)-yl]-3-(triethylsiloxy)-hex-5-enal (8)

To a suspension of Dess–Martin periodinane (5.34 g, 12.6 mmol, 2 equiv.) in CH_2Cl_2 (30 mL) was added pyridine (5.09 mL, 62.9 mmol, 10 equiv.) at RT. The resultant mixture was stirred at RT for further 15 min before a solution of alcohol **S4** (2.80 g, 6.29 mmol) in CH_2Cl_2 (10 mL + 2 x 10 mL washings) was added. The reaction was stirred at RT for further 30 min and poured into sat. aq. $Na_2S_2O_3$/$NaHCO_3$ (1:1, 50 mL). The biphasic mixture was stirred for 15 min, the layers were separated and aqueous phase was extracted with Et_2O (3 x 50 mL). The combined organics were washed with brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (5:95 → 10:90 Et_2O/light petroleum) afforded aldehyde **8** (2.55 g, 91%) as a colourless oil: $\mathbf{R_f}$ 0.50 (10:90 Et_2O/hexanes); $[\alpha]_D^{20}$ +17.4 (*c* 2.14, $CHCl_3$); **IR** (liquid film) 1727, 1640, 1461 cm^{-1}; **^{1}H NMR** δ (500 MHz, $CDCl_3$) 9.80 (1H, m, 9-CHO), 4.88 (1H, s, C=CH_aH_b), 4.82 (1H, s, C=CH_aH_b), 4.35–4.40 (1H, m, 11-CH), 3.69 (1H, dd, *J* = 9.4, 5.9 Hz, 15-CH_aH_b), 3.50 (1H, dd, *J* = 9.4, 7.3 Hz, 15-CH_aH_b), 2.60 (1H, ddd, *J* = 15.9, 4.0, 1.5 Hz, 10-CH_aH_b), 2.49 (1H, dd, *J* = 15.9, 6.9, 2.8 Hz, 10-CH_aH_b), 2.40 (1H, dd, *J* = 14.0, 4.9 Hz, 12-CH_aH_b), 2.21–2.30 (2H, m, 12-CH_aH_b + 14-CH), 1.04–1.12 (24H, m, 14-CHCH_3 + Si(CH(CH_3)$_2$)$_3$), 0.95 (9H, t, *J* = 7.9 Hz, Si($CH_2C H_3$)$_3$), 0.62 (6H, q, *J* = 7.9 Hz, Si(CH_2CH$_3$)$_3$); **^{13}C NMR** δ (62.5 MHz, $CDCl_3$) 202.0, 148.1, 112.2, 67.6, 67.3, 50.4, 44.2,

42.4, 18.0, 16.7, 12.0, 6.8, 4.9; **HRMS** (+FAB) Calc. for $C_{24}H_{49}O_3Si_2$ $[M–H]^+$: 441.3220, found: 441.3216.

2,2,2-Trichloroethyl (2*R*,4*S*,6*S*,8*S*,10*S*)-(4,10-dihydroxy-10-methyl-8-{2-[1-(triisopropylsiloxy)-prop-2-(*R*)-yl]-allyl}-1,7-dioxaspiro[5.5]undec-2-yl)-acetate (S5)



S5

To a solution of **26** (3.19 g, 4.20 mmol) in MeCN (100 mL) was added HF (40% aq., 12.2 mL) and the mixture was stirred for 2 h at RT. The reaction mixture was cooled to 0 °C and quenched by the cautious addition of sat. aq. $NaHCO_3$ (300 mL) followed by EtOAc (300 mL). The layers were separated and the aqueous phase was extracted with EtOAc (4 x 300 mL), combined organics were dried ($MgSO_4$) and concentrated *in vacuo*. The crude triol was used in the following reaction without purification.

To a solution of the crude triol (max. of 4.20 mmol), imidazole (1.14 g, 16.8 mmol, 4 equiv.) and DMAP (cat.) in CH_2Cl_2 (60 mL) was added TIPSCl (2.45 mL, 8.40 mmol, 2 equiv.). The reaction mixture was stirred at RT for 6 h then quenched with sat. aq. $NaHCO_3$ (100 mL). Et_2O (100 mL) was added and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 80 mL) and the combined organics were washed with brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (10:90 → 50:50 Et_2O/light petroleum) afforded diol **S5** (2.57 g, 95% over two steps from **26**) as a colourless oil: $\mathbf{R_f}$ 0.38 (40:60 EtOAc/hexanes); $[\alpha]_D^{20}$ –10.4 (*c* 1.71, $CHCl_3$); **IR** (liquid film) 3497 (br), 1758 cm^{-1}; **^{1}H NMR** δ (500 MHz, $CDCl_3$) 4.98 (1H, s, C=C$\underline{H}_a$H$_b$), 4.95 (1H, s, C=CH$_a\underline{H}_b$), 4.84 (1H, d, *J* = 12.0 Hz, OC$\underline{H}_a$H$_b$CCl$_3$), 4.71 (1H, d, *J* = 12.0 Hz, OCH$_a\underline{H}_b$CCl$_3$), 4.42 (1H, m, 11-C$\underline{H}$), 4.35 (1H, m, 3-C$\underline{H}$), 4.19 (1H, br s, O$\underline{H}$), 4.09 (1H, d, *J* = 10.5 Hz, O$\underline{H}$), 4.03 (1H, m, 5-C$\underline{H}$), 3.65 (1H, dd, *J* = 9.4, 5.4 Hz, 15-C$\underline{H}_a$H$_b$), 3.49 (1H, dd, *J* = 9.4, 6.8 Hz, 15-CH$_a\underline{H}_b$), 2.70 (1H, dd, *J* = 16.9, 9.9 Hz, 2-C$\underline{H}_a$H$_b$), 2.64 (1H, dd, *J* = 16.9, 3.1 Hz, 2-CH$_a\underline{H}_b$), 2.50 (1H, app sextet, *J* = 6.4 Hz, 14-C$\underline{H}$), 2.37 (1H, dd, *J* = 14.0, 2.2 Hz, 12-C$\underline{H}_a$H$_b$), 2.25 (1H, dd, *J* = 14.0, 9.9 Hz, 12-CH$_a\underline{H}_b$), 1.86 (1H, br d, *J* = 14.1 Hz, 6-C$\underline{H}_a$H$_b$), 1.80 (1H, br d, *J* = 14.7 Hz, 4-C$\underline{H}_a$H$_b$), 1.74 (2H, app t, *J* = 15.1 Hz, 10-C$\underline{H}_2$), 1.65 (1H, dd, *J* = 14.1, 3.4 Hz, 4-CH$_a\underline{H}_b$), 1.48–1.54 (3H, m, 6-CH$_a\underline{H}_b$ + 8-C$\underline{H}_2$), 1.35 (1H, app t, *J* = 12.5 Hz, 10-CH$_a\underline{H}_b$), 1.18 (3H, s, 9-CC$\underline{H}_3$), 1.10 (3H, d, *J* = 6.8 Hz, 14-CHC$\underline{H}_3$), 1.04–1.07 (21H, m, Si(C$\underline{H}$(C$\underline{H}_3$)$_2$)$_3$); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 169.4, 148.9, 112.2, 100.3, 94.7, 73.9, 68.7, 67.6, 64.9, 64.1, 61.4, 45.3, 44.0, 43.2, 40.3, 39.5, 39.4, 37.5, 29.8, 18.1, 16.3, 11.9; **HRMS** (+CI, NH_3) Calc. for $C_{29}H_{52}O_7Cl_3Si$ $[MH]^+$: 645.2548, found: 645.2549; **m/z** (+CI, NH_3) 662 ($[M + NH_4]^+$, 11), 645 ($[MH]^+$, 10), 629 (26), 627 (24), 593 (20), 453 (29), 358 (53), 343 (55), 327 (46), 325 (100).

2,2,2-Trichloroethyl (2*R*,4*S*,6*S*,8*S*,10*S*)-(4-acetoxy-10-hydroxy-10-methyl-8-{2-[1-(triisopropylsiloxy)-prop-2-(*R*)-yl]-allyl}-1,7-dioxaspiro[5.5]undec-2-yl)-acetate (27)

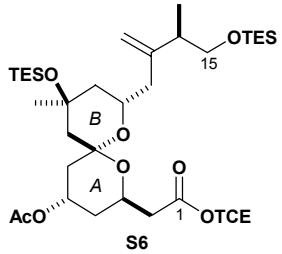
To a solution of diol **S5** (1.94 g, 3.01 mmol) and DMAP (735 mg, 6.02 mmol, 2 equiv.) in CH_2Cl_2 (20 mL) was added Ac_2O (20 mL) and the resulting mixture was stirred at RT for 3 h. The reaction was quenched by slow addition to a stirred solution of sat. aq. $NaHCO_3$ (100 mL) and then vigorously stirred for 1 h. The mixture was diluted with H_2O (50 mL) and Et_2O (100 mL) and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 100 mL), combined organics were washed with sat. aq. $NaHCO_3$ (50 mL), brine (50 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Flash chromatography (5:95 → 50:50 Et_2O/light petroleum) afforded acetate **27** (2.00 g, 97%) as a colourless oil: $\mathbf{R_f}$ 0.30 (30:70 EtOAc/hexanes); $[\alpha]_D^{20}$ –28.8 (*c* 0.60, $CHCl_3$); **IR** (liquid film) 3523 (m, OH), 1756, 1730 (s, C=O), 1643 (w, C=C); **^{1}H NMR** δ (500 MHz,

$CDCl_3$) 5.06 (1H, m, 5-C$\underline{H}$), 5.00 (1H, s, C=C$\underline{H}_a$H$_b$), 4.89 (1H, s, C=CH$_a\underline{H}_b$), 4.81 (1H, d, J = 12.0 Hz, OC$\underline{H}_a$H$_b$), 4.72 (1H, d, J = 12.0 Hz, OCH$_a\underline{H}_b$CCl$_3$), 4.48 (1H, m, 3-C$\underline{H}$), 4.29 (1H, m, 11-C$\underline{H}$), 4.11 (1H, s, O$\underline{H}$), 3.70 (1H, dd, J = 9.4, 5.2 Hz, 15-C$\underline{H}_a$H$_b$), 3.48 (1H, dd, J = 9.4, 7.3 Hz, 15-CH$_a\underline{H}_b$), 2.61–2.69 (2H, m, 2-C$\underline{H}_2$), 2.41 (1H, m, 14-C$\underline{H}$), 2.38 (1H, dd, J = 14.5, 6.8 Hz, 12-C$\underline{H}_a$H$_b$), 2.02 (1H, dd, J = 14.7, 5.6 Hz, 12-CH$_a\underline{H}_b$), 2.05 (3H, s, COC$\underline{H}_3$), 2.03 (1H, m, 6-C$\underline{H}_a$H$_b$), 1.83 (1H, m, 10-C$\underline{H}_a$H$_b$), 1.68–1.75 (2H, m, 4-C$\underline{H}_2$), 1.64 (1H, dd, J = 7.6, 4.1 Hz, 6-CH$_a\underline{H}_b$), 1.53 (1H, d, J = 14.1 Hz, 8-C$\underline{H}_a$H$_b$), 1.44 (1H, d, J = 14.1 Hz, 8-CH$_a\underline{H}_b$), 1.25 (1H, dd, J = 13.3, 11.9 Hz, 10-CH$_a\underline{H}_b$), 1.15 (3H, s, 9-CC$\underline{H}_3$), 1.08 (3H, d, J = 6.8 Hz, 14-CHC$\underline{H}_3$), 1.02–1.05 (21H, m, Si(C$\underline{H}$(C$\underline{H}_3$)$_2$)$_3$); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 170.7, 169.2, 148.2, 111.4, 98.4, 94.7, 73.9, 68.1, 67.9, 65.9, 65.0, 61.4, 60.3, 45.9, 43.3, 42.0, 41.8, 39.6, 37.3, 34.1, 29.9, 21.4, 18.0, 16.5, 11.9; **HRMS** (+CI, NH_3) Calc. for $C_{31}H_{53}O_8Cl_3SiNa$ $[MH]^+$: 709.2473, found: 709.2497; **m/z** (+FAB) 709 ($[M + Na]^+$, 50), 671 (10), 645 (10), 629 (20), 609 (30), 327 (50), 287 (55).

2,2,2-Trichloroethyl (2*R*,4*S*,6*S*,8*S*,10*S*)-(4-acetoxy-10-hydroxy-8-{2-[1-hydroxy-prop-2-(*R*)-yl]-allyl}-10-methyl-1,7-dioxaspiro[5.5]undec-2-yl)-acetate (28)

To a solution of TIPS ether **27** (2.01 g, 2.93 mmol) in MeCN (60 mL) at RT was added HF (40% aq., 7.4 mL). The reaction mixture was stirred at RT for 45 min and then cautiously quenched with sat. aq. $NaHCO_3$ (200 mL). Et_2O (100 mL) was added and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 100 mL) and the combined organics were washed with brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (5:95 → 50:50 Et_2O/light petroleum) afforded diol **28** (1.24 g, 80%) as a colourless oil: **R_f** 0.15 (40:60 EtOAc/hexanes); **^{1}H NMR** δ (500 MHz, $CDCl_3$) 5.12 (1H, s, C=C$\underline{H}_a$H$_b$), 5.07 (1H, m, 5-C$\underline{H}$), 4.95 (1H, s, C=CH$_a\underline{H}_b$), 4.86 (1H, d, J = 12.0 Hz, OC$\underline{H}_a$H$_b$CCl$_3$), 4.70 (1H, d, J = 12.0 Hz, OCH$_a\underline{H}_b$CCl$_3$), 4.51 (1H, m, 3-C$\underline{H}$), 4.30 (1H, m, 11-C$\underline{H}$), 4.06 (1H, s, 9-CO$\underline{H}$), 3.59 (1H, m, 15-C$\underline{H}_a$H$_b$), 3.51 (1H, m, 15-CH$_a\underline{H}_b$), 2.66–2.68 (2H, m, 2-C$\underline{H}_2$), 2.50 (1H, br sextet, J = 6.8 Hz, 14-C$\underline{H}$), 2.34 (1H, dd, J = 14.1, 7.3 Hz, 12-C$\underline{H}_a$H$_b$), 2.21 (1H, dd, J = 14.1, 6.0 Hz, 12-CH$_a\underline{H}_b$), 2.06 (3H, s, COC$\underline{H}_3$), 2.00 (1H, m, 4-C$\underline{H}_a$H$_b$), 1.84 (1H, dd, J = 14.2, 1.7 Hz, 6-C$\underline{H}_a$H$_b$), 1.70-1.76 (3H, m, 4-CH$_a\underline{H}_b$ + 6-CH$_a\underline{H}_b$ + 8-C$\underline{H}_a$H$_b$), 1.66 (1H, dd, J = 13.3, 4.2Hz, 10-C$\underline{H}_a$H$_b$), 1.61 (1H, br t, J = 3.0 Hz, O$\underline{H}$), 1.45 (1H, d, J = 14.1 Hz, 8-CH$_a\underline{H}_b$), 1.26 (1H, dd, J = 13.3, 12.1 Hz, 10-CH$_a\underline{H}_b$), 1.16 (3H, s, 9-CC$\underline{H}_3$), 1.09 (3H, d, J = 6.9 Hz, 14-CHC$\underline{H}_3$).

2,2,2-Trichloroethyl (2*R*,4*S*,6*S*,8*S*,10*S*)-(4-acetoxy-8-{2-[1-triethylsiloxy-prop-2-(*R*)-yl]-allyl}-10-methyl-10-(triethylsiloxy)-1,7-dioxaspiro[5.5]undec-2-yl)-acetate (S6)



S6

To a cold (–78 °C) solution of diol **28** (1.65 g, 3.11 mmol) in CH_2Cl_2 (40 mL) was added 2,6-lutidine (2.18 mL, 18.7 mmol, 6 equiv.), followed by TESOTf (2.82 mL, 12.5 mmol, 4 equiv.). The reaction mixture was stirred at –78 °C for 2 h then warmed to 0 °C and stirred for further 1 h. The reaction was quenched by the addition of sat. aq. $NaHCO_3$ (50 mL) and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 30 mL), the combined organics were washed with brine (30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (5:95 → 25:75 Et_2O/light petroleum) afforded bis-TES ether **S6** (2.22 g, 94%) as a colourless oil: **R_f** 0.43 (30:70 Et_2O/hexanes); $[\alpha]_D^{20}$ –47.1 (*c* 2.05, $CHCl_3$); **IR** (liquid film) 2954, 1762, 1736 (s, C=O), 1458; **^{1}H NMR** δ (500 MHz, $CDCl_3$) 5.05 (1H, m, 5-C$\underline{H}$), 4.95 (1H, s, C=C$\underline{H}_a$H$_b$), 4.85 (1H, s, C=CH$_a\underline{H}_b$), 4.76 (1H, d, J = 12.0 Hz, OC$\underline{H}_a$H$_b$CCl$_3$), 4.71 (1H, d, J = 12.0 Hz, OCH$_a\underline{H}_b$CCl$_3$), 4.49 (1H, m, 3-C$\underline{H}$), 4.25 (1H, m, 11-C$\underline{H}$), 3.64 (1H, dd, J = 9.7, 5.2 Hz, 15-C$\underline{H}_a$H$_b$), 3.37 (1H, dd, J =

9.7, 8.2 Hz, 15-$CH_a\underline{H}_b$), 2.77 (1H, dd, *J* = 16.2, 5.5 Hz, 2-$C\underline{H}_aH_b$), 2.53 (1H, dd, *J* = 16.2, 7.9 Hz, 2-$CH_a\underline{H}_b$), 2.34 (2H, m, 14-C$\underline{H}$ + 12-$C\underline{H}_aH_b$), 2.10 (1H, dd, *J* = 14.2, 6.3 Hz, 12-$CH_a\underline{H}_b$), 2.03 (3H, s, $COC\underline{H}_3$), 1.88 (2H, m, 4-$C\underline{H}_aH_b$ + 6-$C\underline{H}_aH_b$), 1.76 (1H, d, *J* = 14.2 Hz, 8-$C\underline{H}_aH_b$), 1.59 (3H, m, 4-$CH_a\underline{H}_b$ + 6-$CH_a\underline{H}_b$ + 10-$C\underline{H}_aH_b$), 1.28 (1H, d, *J* = 14.2 Hz, 8-$CH_a\underline{H}_b$), 1.20 (3H, s, 9-$CC\underline{H}_3$), 1.17 (1H, m, 10-$CH_a\underline{H}_b$), 1.08 (3H, d, *J* = 6.8 Hz, 14-$CHC\underline{H}_3$), 0.95 (18H, m, 2 x $Si(CH_2C\underline{H}_3)_3$), 0.55 (12H, m, 2 x $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 171.9, 170.0, 149.4, 112.2, 98.0, 95.8, 74.8, 71.2, 68.4, 67.8, 65.8, 61.6, 48.4, 45.5, 43.0, 42.7, 41.0, 39.3, 34.8, 32.9, 31.2, 22.4, 17.5, 8.2, 7.7, 5.3; **HRMS** (+CI, NH_3) Calc. for $C_{34}H_{61}O_8Cl_3Si_2Na$ $[M + Na]^+$: 781.2868, found: 781.2882.

Trichloroethyl (2*R*,4*S*,6*S*,8*S*,10*S*)-(4-acetoxy-8-{2-[1-hydroxy-prop-2-(*R*)-yl]-allyl}-10-methyl-10-(triethylsiloxy)-1,7-dioxaspiro[5.5]undec-2-yl)-acetate (29)

To a cold (0 °C) solution of bis-TES ether **S6** (2.29 g, 3.02 mmol) in CH_2Cl_2/MeOH (4:1, 37.5 mL) was added PPTS (cat.). The reaction mixture was stirred at 0 °C for 1 h then quenched by the addition of Et_3N (few drops) to neutralise the PPTS. The mixture was concentrated *in vacuo* and flash chromatography (10:90 → 60:40 Et_2O/light petroleum) afforded 1° alcohol **29** (1.83 g, 94%) as a colourless oil: $\mathbf{R_f}$ 0.40 (40:60 EtOAc/hexanes); $[\alpha]_D^{20}$ –59.3 (*c* 1.75, $CHCl_3$); **IR** (liquid film) 3523 (m, OH), 1759, 1734 (s, C=O), 1639 (w, C=C); **^{1}H NMR** δ (500 MHz, $CDCl_3$) 5.08 (1H, s, C=$C\underline{H}_aH_b$), 5.06 (1H, m, 5-C$\underline{H}$), 4.85 (1H, s, C=$CH_a\underline{H}_b$), 4.82 (1H, d, *J* = 12.0 Hz, $OC\underline{H}_aH_bCCl_3$), 4.65 (1H, d, *J* = 12.0 Hz, $OCH_a\underline{H}_bCCl_3$), 4.51 (1H, m, 3-C$\underline{H}$), 4.25 (1H, m, 11-C$\underline{H}$), 3.59 (1H, m, 15-$C\underline{H}_aH_b$), 3.51 (1H, m, 15-$CH_a\underline{H}_b$), 2.77 (1H, dd, *J* = 16.4, 6.8 Hz, 2-$C\underline{H}_aH_b$), 2.53 (1H, dd, *J* = 16.4, 7.0 Hz, 2-$CH_a\underline{H}_b$), 2.48 (1H, m, 14-C$\underline{H}$), 2.33 (1H, dd, *J* = 14.4, 6.8 Hz, 12-$C\underline{H}_aH_b$), 2.14 (1H, dd, *J* = 14.4, 6.0 Hz, 12-$CH_a\underline{H}_b$), 2.05 (3H, s, $COC\underline{H}_3$), 1.83–1.90 (2H, m, 4-$C\underline{H}_aH_b$ + 6-$C\underline{H}_aH_b$), 1.79 (1H, dd, *J* = 14.4, 1.8 Hz, 8-$C\underline{H}_aH_b$), 1.72 (1H, br t, *J* = 6.1 Hz, O$\underline{H}$), 1.54–1.66 (3H, m, 4-$CH_a\underline{H}_b$ + 6-$CH_a\underline{H}_b$ +10-$C\underline{H}_aH_b$), 1.30 (1H, d, *J* = 14.2 Hz, 8-$CH_a\underline{H}_b$), 1.21–1.25 (4H, m, 10-$CH_a\underline{H}_b$ + 9-$CC\underline{H}_3$), 1.08 (3H, d, *J* = 6.9 Hz, 14-$CHC\underline{H}_3$), 0.94 (9H, m, $Si(CH_2C\underline{H}_3)_3$), 0.59 (6H, m, $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 172.4, 170.9, 149.4, 113.9, 98.6, 96.3, 75.4, 71.7, 68.3, 67.5, 66.5, 62.1, 49.0, 46.2, 43.8, 42.6, 41.5, 39.8, 35.4, 33.5, 31.8, 22.9, 17.8, 8.5, 8.2; **HRMS** (+CI, NH_3) Calc. for $C_{28}H_{48}O_8Cl_3Si$ $[M + H]^+$: 645.2184, found: 645.2184; **m/z** (+FAB) 662 ($[M + Na]^+$, 80) 645 (100), 585 (40), 513 (60), 435 (100).