Electronic Supporting Information

Synthesis of the DEF-*bis*-Spiroacetal of Spirastrellolide A Exploiting a Double Asymmetric Dihydroxylation / Spiroacetalisation Strategy

Ian Paterson,* Edward A. Anderson, Stephen M. Dalby, Jong Ho Lim, Philip Maltas and Christian Moessner

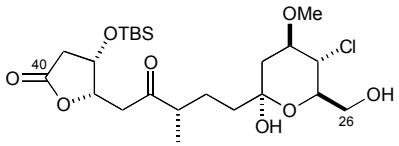
University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK.

General Experimental Details

Thin layer chromatography was carried out on commercial glass backed silica gel 60 F254 plates. Visualization of chromatograms was accomplished using ultraviolet light (254 nm) and/or heating the plate after staining with either a solution of 20% ceric ammonium molybdate w/v in H_2O or 20% potassium permanganate w/v in H_2O. Melting points were measured on a Shandon melting point apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 241 polarimeter at 589 nm (sodium D line) and concentrations (c) are reported in g/100 mL. Infrared (IR) spectra were recorded on a Perkin-Elmer 1620 FT-IR spectrophotometer with internal calibration. Only selected, characteristic IR absorption data are provided for each compound. NMR spectra were recorded using deuterochloroform ($CDCl_3$), deuterobenzene (C_6D_6) or deuteromethanol (CD_3OD) as the solvent. Chemical shifts (δ) are given in parts per million (ppm) from tetramethylsilane ($\delta = 0$) and were measured relative to the signal of the solvent in which the sample was analysed ($CDCl_3$: δ 7.26, ^{1}H NMR; δ 77.0, ^{13}C NMR. C_6D_6: δ 7.15, ^{1}H NMR; δ 128.8, ^{13}C NMR; CD_3OD: δ 3.31, ^{1}H NMR; δ 49.0, ^{13}C NMR). Coupling constants (*J* values) are given in Hertz (Hz) and are reported to the nearest 0.1 Hz. ^{1}H NMR spectral data are tabulated in the order: number of protons, multiplicity (br, broad; s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; m, multiplet), coupling constant and proton assignment where applicable

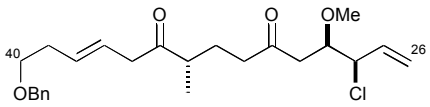
Characterisation data

(4*S*,5*S*)-4-(*tert*-butyldimethylsilyloxy)-5-((*S*)-5-((2*S*,4*R*,5*S*,6*R*)-5-chloro-2-hydroxy-6-(hydroxymethyl)-4-methoxy-tetrahydro-pyran-2-yl)-3-methyl-2-oxopentyl)-dihydrofuran-2-one **13**



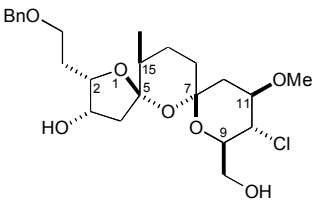
R$_f$ 0.31 (1:2 40-60 petroleum ether / ethyl acetate); $[\alpha]_D^{22}$ –4.9 (c 1.66, $CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3422, 2932, 2859, 1779, 1709, 1463, 1382, 1256, 1157, 1091, 989, 959, 838, 779; **^{1}H NMR** (500MHz, $CDCl_3$) δ_H 4.85-4.81 (1H, m, H37), 4.56 (1H, app t, *J* = 4.4 Hz, H38), 4.01-3.96 (1H, m, H27), 3.87 (1H, br d, *J* = 11.9 Hz, H26a), 3.78 (1H, br dd, *J* = 11.9, 5.0 Hz, H26b), 3.69 (1H, dt, *J* = 10.2, 4.8 Hz, H29), 3.64 (1H, t, *J* 9.8 Hz), 3.45 (3H, s, MeO), 3.28 (1H, br s, OH), 3.05 (1H, dd, *J* = 17.5, 6.7 Hz, H36a), 2.81 (1H, dd, *J* = 17.5, 6.1 Hz, H36b), 2.76 (1H, dd, *J* = 17.6, 5.5 Hz, H39a), 2.68-2.60 (1H, m, H34), 2.42 (1H, d, *J* = 17.4 Hz, H39b), 2.38 (1H, br s, OH), 2.30 (1H, dd, *J* = 12.8, 4.7 Hz, H30a), 1.79-1.72 (1H, m, H33), 1.62-1.56 (3H, m, 2 x H32, H33), 1.36 (1H, br t, *J* = 11.9 Hz, H30b), 1.11 (3H, d, *J* = 7.0 Hz, Me), 0.87 (9H, s, Si*t*-Bu), 0.07 (3H, s, SiMe), 0.02 (3H, s, SiMe); **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ_C = 211.2, 175.1, 98.1, 80.9, 78.8, 73.4, 69.5, 62.5, 59.5, 57.7, 46.2, 40.1, 39.4, 38.9, 38.9, 25.8, 25.6, 18.0, 16.0, -4.7, -5.1; **HRMS** (ES+) calcd for $C_{23}H_{41}ClO_8SiNa$ $[M+Na]^+$ 531.2151, found 531.2157.

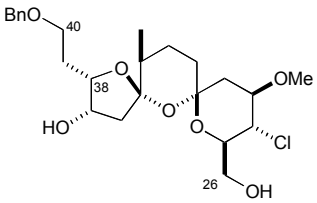
(7*R*,12*R*,13*R*)-1-Benzyloxy-13-chloro-12-methoxy-7-methyl-pentadeca-(3*E*),14-diene-6,10-dione, **16**.



R$_f$ 0.29 (1:1 Et_2O / hexane); $[\alpha]_D^{22}$ +29.5 (c 2.1, $CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2933, 1712; **^{1}H NMR** (500MHz, $CDCl_3$) δ_H 7.36-7.29 (5H, m, Ph), 5.95 (1H, ddd, *J* = 16.9, 10.2, 7.6 Hz, H27), 5.63 (1H, m, H37), 5.59 (1H, m, H38), 5.40 (1H, d, *J* = 16.9 Hz, H26a), 5.23 (1H, d, *J* = 10.2 Hz, H26b), 4.53 (2H, s, C$\underline{H}_2$Ph), 4.52 (1H, obs m, H28), 3.96 (1H, dt, *J* = 7.3, 4.4, H29), 3.53 (2H, t, *J* = 6.8 Hz, H40), 3.44 (3H, s, OMe), 3.19 (1H, d, *J* = 6.1 Hz, H36a), 3.18 (1H, t, *J* = 4.7 Hz, H36b), 2.68 (1H, d, *J* = 4.4 Hz, H30a), 2.66 (1H d, *J* = 7.3 Hz, H30b), 2.62 (1H, m, H34), 2.41 (2H, obs m, H32), 2.41 (2H, obs m, H39), 1.93 (1H, ddt, *J* = 14.1, 7.8, 7.7 Hz, H31a), 1.65 (1H, ddt, *J* = 14.1, 8.4, 6.2 Hz, H31b), 1.10 (3H, d, *J* = 7.1 Hz, Me); **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ_C = 211.9, 207.8, 138.5, 134.2, 131.3, 128.4, 127.6, 127.5, 123.9, 118.9, 79.6, 72.9, 69.8, 62.6, 58.9, 45.0, 44.6, 43.7, 41.0, 33.0, 26.0, 16.4; **HRMS** (ES+) calcd for $C_{24}H_{33}ClO_4Na$ $[M+Na]^+$ 443.1965, found 443.1963.

(2*S*,3*S*,5*R*,7*R*,9*R*,10*R*,11*R*,15*S*)-2-(2-Benzyloxyethyl)-10-chloro-9-hydroxymethyl-11-methoxy-15-methyl-1,6,8-trioxa-dispiro[4.1.5.3]pentadecan-3-ol, 15.

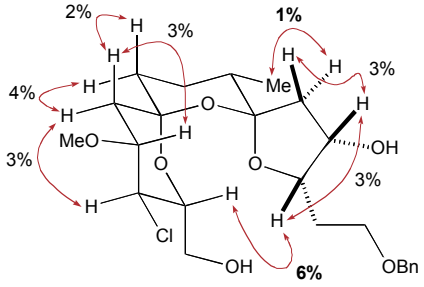


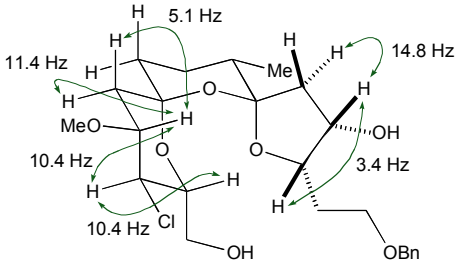


(Name numbering) (Spirastrellolide numbering)

Rf = 0.27 (1:1 EtOAc / 40-60 petroleum ether); $[\alpha]_D^{22}$ –16.6 (c 0.8, $CDCl_3$); **IR** (thin film, ν_{max}/cm^{-1}): 3461, 2929; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 7.39-7.31 (5H, m, PhH), 4.55 (2H, d, *J* = 11.6 CH_aH_bPh), 4.52 (2H, d, *J* = 11.6 CH_aH_bPh), 4.31 (1H, br dd, *J* = 3.7, H37), 4.17 (1H, dt, *J* = 3.7, 8.5, H38), 3.99 (1H, ddd, *J* = 10.8, 8.4, 2.4 Hz, H26a), 3.88 (1H, ddd, *J* = 10.4, 8.4, 2.4 Hz, H27), 3.70 (1H, dt, *J* = 3.8, 9.9 Hz, H40), 3.59 (1H, obs m, H26b), 3.63 (1H, m, H29), 3.56 (1H, m, H40b), 3.50 (1H, t, *J* = 10.4 Hz, H28), 3.47 (3H, s, OMe), 3.35 (1H, br s, OH-37), 2.44 (1H, dd, *J* = 8.4, 2.4 Hz, OH-26), 2.36 (1H, dd, *J* = 6.9, 14.8 Hz, H36a), 2.23 (1H, dd, *J* = 12.9, 5.1 Hz, H30a), 2.17 (1H, t, *J* = 14.8 Hz, H36b), 2.08 (2H, m, 2 x H39), 1.88 (1H, dq, *J* = 3.3, 13.3 Hz, H33a), 1.80 (1H, dt, *J* = 13.3, 3.3 Hz, H32a), 1.72 (1H, m, H34), 1.63 (1H, dt, *J* = 4.1, 13.3 H32b), 1.45 (1H, m, H33b), 1.41 (1H dd, *J* = 12.9, 11.4 Hz, H30b), 1.01 (3H, d, *J* = 6.7 Hz, Me); **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ_C = 137.3, 128.6, 128.0, 127.8, 109.5, 97.9, 84.3, 78.9, 73.7, 73.2, 71.2, 67.2, 63.1, 60.3, 57.6, 47.5, 42.9, 37.7, 35.8, 28.3, 23.8, 16.3; **HRMS** (ES+) calcd for $C_{24}H_{35}ClO_7Na$ $[M+Na]^+$ 493.1969, found 493.1954.

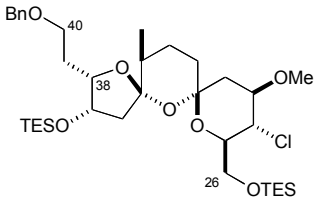
NOE data / coupling constant data for **15**:





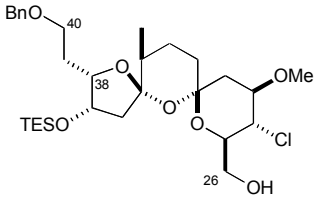
Selected ^{1}H NMR NOE enhancements **Selected ^{1}H NMR coupling constants**

(2*S*,3*S*,5*R*,7*R*,9*R*,10*R*,11*R*,15*S*)-2-(2-Benzyloxyethyl)-10-chloro-9-triethylsilyloxymethyl-11-methoxy-15-methyl-1,6,8-trioxa-dispiro[4.1.5.3]pentadecan-3-ol triethylsilyl ether, **22**.



R$_f$ 0.17 (20:1 40-60 petroleum ether / ethyl acetate); $[\alpha]_D^{22}$ –0.5 (c 1.16 in $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 2955, 2877, 1457, 1380, 1239, 1133, 1070, 992, 926, 733; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37-7.27 (5H, m, Ph), 4.56 (1H, d, *J* = 11.9 Hz, C$\underline{H}_a$H$_b$Ph), 4.51 (1H, d, *J* = 11.9 Hz, CH$_a\underline{H}_b$Ph), 4.36-4.32 (1H, m, H37), 4.13 (1H, dt, *J* = 8.4, 4.4 Hz, H38), 4.06 (1H, dd, *J* = 11.4, 2.0 Hz, H26), 3.96 (1H, t, *J* = 10.0 Hz, H28), 3.76 (1H, dd, 11.3, 1.2 Hz, H26), 3.71-3.65 (2H, m, H27, H29), 3.62-3.53 (2H, m, 2 x H40), 3.47 (3H, s, MeO), 2.24 (1H, dd, *J* = 14.1, 6.4 Hz, H36), 2.13 (1H, dd, *J* = 12.7, 5.0 Hz, H30), 2.00 (1H, dd, *J* = 14.0, 2.7 Hz, H36), 1.99-1.77 (5H, m, H32, H33, H39, 2 x H40), 1.71-1.62 (1H, m, H34), 1.54 (1H, dt, *J* = 13.4, 4.0 Hz, H32), 1.41-1.31 (2H, m, H30, H33), 1.00-0.93 (21H, m, 6 x SiCH$_2$C$\underline{H}_3$ and Me), 0.64-0.56 (12H, m, 6 x SiC$\underline{H}_2$CH$_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 138.6, 128.3, 127.5, 108.7, 97.8, 80.4, 79.2, 73.9, 72.8, 72.1, 68.0, 61.8, 59.0, 57.3, 48.6, 42.6, 37.6, 35.7, 29.6, 23.7, 16.4, 6.8, 4.8, 4.6; **HRMS** calc. for $C_{36}H_{67}NClO_7Si_2[M+NH_4]^+$ 716.4139, found 716.4142.

(2*S*,3*S*,5*R*,7*R*,9*R*,10*R*,11*R*,15*S*)-2-(2-Benzyloxyethyl)-10-chloro-9-hydroxymethyl-11-methoxy-15-methyl-1,6,8-trioxa-dispiro[4.1.5.3]pentadecan-3-ol triethylsilyl ether, **4**.



R$_f$ 0.12 (4:1 40-60 petroleum ether / ethyl acetate); $[\alpha]_D^{22}$ +6.8 (c 1.0 in $CHCl_3$); **IR** (thin film, ν_{max}/cm^{-1}) 3508, 2934, 2876, 1455, 1380, 1240, 1191, 1168, 1075, 985, 926, 861, 737; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37-7.27 (5H, m, Ph), 4.56 (1H, d, *J* = 11.9 Hz, C$\underline{H}_a$H$_b$Ph), 4.47 (1H, d, *J* = 11.9 Hz, CH$_a\underline{H}_b$Ph), 4.43-4.38 (1H, m, H37), 4.26-4.21 (1H, m, H38), 3.95-3.90 (1H, m, H26), 3.85-3.80 (1H, m, H27), 3.68-3.55 (5H, m, H26, H28, H29, 2 x H40), 3.45 (3H, MeO), 2.25-2.14 (3H, m, OH, H30, H36), 2.01 (1H, dd, *J* = 13.9, 3.6 Hz, H36), 1.92-1.85 (3H, m, H33, 2 x H39), 1.78 (1H, app. dt, *J* = 13.4, 2.7 Hz, H32), 1.71-1.63 (1H, m, H34), 1.61-1.54 (1H, m, H32), 1.44-1.34 (2H, m, H30, H33), 0.98-0.91 (12H, m, 3 x SiCH$_2$C$\underline{H}_3$ and Me), 0.61-0.54 (6H, m, 3 x SiC$\underline{H}_2$CH$_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 138.6, 128.3, 127.7, 127.4, 108.8, 97.7, 80.5, 79.0, 73.3, 72.7, 71.6,

67.5, 62.8, 59.9, 57.5, 47.8, 42.8, 37.2, 35.6, 29.1, 23.6, 16.4, 6.8, 4.8; **HRMS** calc. for $C_{30}H_{53}NClO_7Si$ $[M+NH_4]^+$ 602.3274, found 602.3274.