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Supporting Information

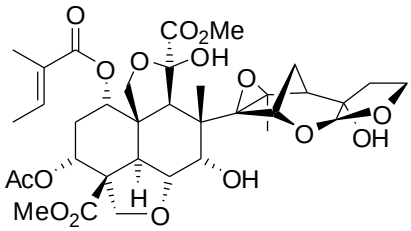
The Synthesis of Azadirachtin: A Potent Insect Antifeedant

Steven V. Ley,[a]* Antonio Abad-Somovilla,[b] James C. Anderson,[b] Carles Ayats,[a] Rolf Bänteli,[a] Edith Beckmann,[a] Alistair Boyer,[a] Maria G. Brasca,[b] Abigail Brice,[a] Howard B. Broughton,[b] Brenda J. Burke,[a] Ed Cleator,[a] Donald Craig,[b] Alastair A. Denholm,[a] Thomas Durand-Reville,[a] Luca B. Gobbi,[a] Michael Göbel,[a] Brian Lawrence Gray,[a] Robert B. Grossmann,[a] Claire E. Gutteridge,[a] Norbert Hahn,[a] Sarah L. Harding,[a] David C. Jennens,[a] Lynn Jennens,[a] Peter J. Lovell,[b] Helen J. Lovell,[a] Mary L. de la Puente,[a] Hartmuth C. Kolb,[b] Win-Jan Koot,[a] Sarah L. Maslen,[a] Catherine F. McCusker,[a] Amos Mattes,[a] Andrew R. Pape,[a] Andrea Pinto,[a] Dinos Santafianos,[b] James S. Scott,[a] Steven C. Smith,[b] Andrew Q. Somers,[a] Christopher D. Spilling,[a] Frank Stelzer,[a] Peter L. Toogood,[b] Richard M. Turner,[a] Gemma E. Veitch,[a] Anthony Wood,[b] Cornelia Zumbrunn[a]

[a] Department of Chemistry,University of Cambridge,Lensfied Road, Cambridge, CB2 1EW, UK.

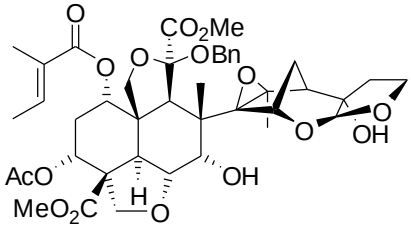
[b] Department of Chemistry, Imperial College London, Exhibition Road, London SW7 2AZ.

22,23-dihydroazadirachtin 5



Azadirachtin **1** was obtained in pure form following flash column chromatography (Biotage 40 + M, 60 to 80% ethyl acetate in petrol) of crude Neem Oil, enriched to 42% azadirachtin content purchased from Knightel Ltd, UK. A solution of azadirachtin **1** (10 g, 13.87 mmol) in MeOH (175 mL) was added to a suspension of Pd/C (4.56 g, 10 wt% Pd) in MeOH (10 mL) under an atmosphere of argon. The reaction vessel was placed under an atmosphere of hydrogen and the reaction mixture was stirred vigorously for 80 min. The hydrogen was vented, then the crude reaction mixture was filtered through a pad of Celite and Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (60-70% ethyl acetate in petrol) to give 22,23-dihydroazadirachtin **5** (51.6 g, 69%) as a white solid. m.p. 157-160 °C; $[a]_D^{20}$ = - 27.8 (*c* = 0.37 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 6.87 (qd, *J* = 7.0, 1.4 Hz, 1H; H3'), 5.47 (t, *J* = 2.7 Hz, 1H; H3), 5.25 (s, 1H; H21), 5.06 (s, 1H; OH), 4.72 (t, *J* = 2.7 Hz, 1H; H1), 4.70 (d, *J* = 2.6 Hz, 1H; H7); 4.64 (d, *J* = 3.3 Hz, 1H; H15), 4.56 (dd, *J* = 12.5, 2.6 Hz, 1H; H6), 4.12 (d, *J* = 9.7 Hz, 1H; H1), 4.05 (d, *J* = 9.0 Hz, 1H; H28), 4.03-3.96 (m, 1H; H23), 3.92-3.86 (m, 1H; H23), 3.77 (s, 3H; CO_2Me), 3.72 (d, *J* = 9.0 Hz, 1H; H28), 3.66 (s, 3H; CO_2Me), 3.60 (d, *J* = 9.7 Hz, 1H; H19), 3.29 (s, 1H; OH), 3.25 (d, *J* = 12.5 Hz, 1H; H5), 3.17 (s, 1H; H9), 2.68 (s, 1H; OH), 2.44 (d, *J* = 5.2 Hz, 1H; H17), 2.29 (dt, *J* = 16.9, 2.4 Hz, 1H; H2), 2.20 (dt, *J* = 16.9, 3.1 Hz, 1H; H2), 2.18-2.08 (m, 1H; H22), 2.04-1.96 (m, 1H; H22), 1.99 (s, 3H; H18), 1.93 (s, 3H; OAc), 1.82 (br s, 3H; 5'Me), 1.76 (d, *J* = 7.0 Hz, 1H; 4'Me), 1.72 (s, 3H; 30Me), 1.65 (m, 1H; H16), 1.51 (d, *J* = 13.0 Hz, 1H; H16); IR (film) $?_{max}/cm^{-1}$ 3432, 2954, 2910, 1733, 1703, 1646.

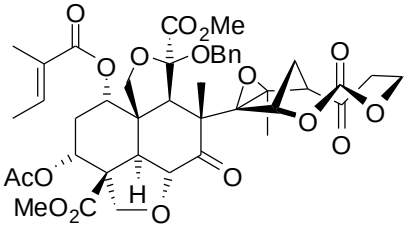
22,23-dihydro-11-benzyloxyazadirachtin 17



Freshly prepared Ag_2O (104 g, 449 mmol) was added to a solution of 22,23-dihydroazadirachtin **5** (51.5 g, 71.2 mmol) in DMF (1.5 L). The mixture was heated to 40 °C and benzyl bromide (81 mL, 1.71 mol) was added. The reaction was stopped after 20 min by filtering the reaction mixture through a pad of Celite

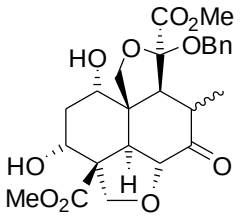
(eluting with 2.5 L diethyl ether). The filtrate was concentrated *in vacuo*, filtered through Celite to afford a cloudy viscous yellow oil residue. This oil was filtered again through Celite (eluting with 2.5 L chloroform) and concentrated *in vacuo* and purified by flash column chromatography (ethyl acetate : chloroform : petrol (2:2:1)) to give the benzyl ether **17** (36.1 g, 62%) as a white solid. m.p. 153-154 °C; $[a]_D^{20}$ = +0.9 (*c* = 1.06 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.38-7.18 (m, 5H; Ph), 6.84 (qd, *J* = 7.1, 1.3 Hz, 1H; H3'), 5.49 (t, *J* = 2.7 Hz, 1H; H3), 5.15 (s, 1H; H2l), 4.74 (t, *J* = 3.0 Hz, 1H; H1), 4.73 (d, *J* = 11.3 Hz, 1H; C*H*HPh), 2.58 (dd, *J* = 12.4, 2.8 Hz, 1H; H6), 4.53 (d, *J* = 2.8 Hz, 1H; H7), 4.48 (d, *J* = 11.3 Hz, 1H; CH*H*Ph), 4.37 (d, *J* = 3.4 Hz, 1H; H5), 4.14 (d, *J* = 9.4 Hz, 1H; H19), 4.06 (d, *J* = 8.9 Hz, 1H; H28), 3.98 (td, *J* = 8.4, 4.5 Hz, 1H; H23), 3.87 (d, *J* = 8.4 Hz, 1H; H23), 3.78 (s, 3H; OMe), 3.42 (s, 1H; OH), 3.27 (s, 1H; H9), 3.21 (d, *J* = 12.4 Hz, 1H; H5), 2.78 (s, 1H; OH), 2.38 (d, *J* = 5.2 Hz, 1H; H17), 2.27 (br, 2H; 2 × H2), 2.17-2.07 (m, 1H; H22), 2.03-1.97 (m, 1H; H22) 1.95 (s, 3H; 18Me), 1.92 (s, 3H; OAc), 1.83 (br s, 3H; 5'Me), 1.77 (d, *J* = 7.0 Hz, 3H; 4'Me), 1.75-1.67 (m, 1H; H16), 1.59 (s, 3H; 30Me), 1.47 (d, *J* = 12.8 Hz, 1H; H16); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 173.3 (s), 169.6 (s), 169.5 (s), 166.4 (s), 137.5 (s), 137.4 (d), 128.67 (s), 128.1 (2 × d), 127.4 (d), 127.4 (2 × d), 107.6 (d), 107.2 (s), 81.3 (s), 76.9 (d), 75.2 (d), 73.7 (d), 73.1 (t), 70.3 (d), 69.3 (t), 68.4 (s), 66.9 (d), 66.6 (t), 65.0 (t), 64.6 (s), 53.0 (q), 52.8 (q), 52.5 (s), 49.6 (d), 49.4 (s), 46.3 (d), 44.7 (s), 41.1 (t), 37.26 (d), 30.0 (t), 24.4 (t), 21.4 (q), 21.0 (q), 19.1 (q), 14.3 (q), 12.0 (q); IR (film) $?_{max}$/cm^{-1} 3452, 2953, 1742, 1436, 1376, 1267, 1219, 1135, 1043.

Cyclic carbonate 18



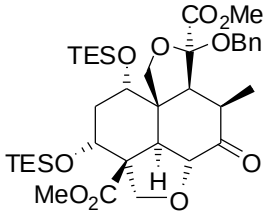
To a solution of 22,23-dihydro-11-benzyloxyazadirachtin **17** (25 g, 30.8 mmol) in CH_2Cl_2 (6.3 L) was added PCC (75 g) and powdered activated 4? molecular sieves (75 g). The mixture was heated to 40°C for 90 min, then cooled to room temperature and ethyl acetate (6.3 L) was added. After a further 30 min of stirring, the mixture was filtered through a pad of Florisil and concentrated *in vacuo*. Purification by chromatography (ethyl acetate : chloroform : petrol (2:2:1)) gave the carbonate **18** (14.0 g, 39%) as a colourless solid. m.p. 149-150 °C; $[a]_D$ = +30.4 (*c* = 1.01 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.33-7.26 (m, 5H; Ph), 6.68 (qd, *J* = 7.1, 1.3 Hz, 1H; H3'), 5.49 (t, *J* = 2.8 Hz, 1H; H3), 5.19 (d, *J* = 14.2 Hz, 1H; H6), 4.82 (t, *J* = 2.4Hz, 1H; H1), 4.76 (br s, 1H; H15), 4.70 (d, *J* = 10.8 Hz, 1H; C*H*HPh), 4.57-4.50 (m, 1H; H23), 4.48 (d, *J* = 10.0 Hz, 1H; H19), 4.42 (d, *J* = 10.8 Hz, 1H; CH*H*Ph), 4.21 (dd, *J* = 11.5, 9.5 Hz, 1H; H23), 4.06 (d, *J* = 9.0 Hz, 1H; H28), 3.80 (d, *J* = 10.0 Hz, 1H; H19), 3.78 (s, 3H; CO_2Me), 3.75 (d, *J* = 9.0 Hz, 1H; H28), 3.70 (s, 1H; H9), 3.67 (s, 3H; CO_2Me), 2.87 (t, *J* = 3.6 Hz, 1H; H17), 2.85 (m, 1H; H22), 2.76 (d, *J* = 14.2 Hz, 1H; H5), 2.60 (dd, *J* = 14.4, 8.7 Hz, 1H; H22), 2.30 (dt, *J* = 16.9, 2.3 Hz, 1H; H2), 2.19 (dt, *J* = 16.9, 3.2 Hz, 1H; H2), 1.90 (s, 3H; OAc), 1.80 (br s, 3H; 5'Me), 1.79 (s, 3H; 18Me), 1.74 (m, 5H; 4'Me, 2 × H16), 1.64 (s, 3H; 30Me); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 208.3 (s), 201.6 (s), 172.3 (s), 169.6 (s), 169.2 (s), 166.2 (s), 152.2 (s), 137.6 (d), 136.4 (s), 128.7 (s), 128.5 (d), 128.4 (d), 128.3 (d), 128.1 (2 × d), 106.8 (s), 82.3 (d), 75.6 (d), 73.1 (t), 70.2 (d), 70.0 (t), 67.6 (s or t), 67.5 (s or t), 67.1 (s or t), 66.9 (s or t), 66.3 (d), 54.9 (d), 53.3 (d or q), 53.2 (s), 53.1 (d or q), 52.6 (s), 48.3 (s), 45.1 (d), 42.3 (t), 30.8 (t), 30.0 (t), 21.1 (q), 20.8 (q), 16.9 (q), 14.2 (q), 12.2 (q); IR (film) $?_{max}$/cm^{-1} 2956, 1743, 1455, 1436, 1394, 1267, 1217, 1043.

Diol 16



Sodium methoxide (149 mg, 2.8 mmol) was added to a stirred solution of the carbonate **18** (100 mg, 0.12 mmol) in MeOH (8 mL). After stirring for 2 h the reaction was quenched by the addition of saturated NH_4Cl solution (2 mL) and diluted with water (5 mL). The product was extracted with chloroform (2 × 10 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. Flash column chromatography (75% ethyl acetate in chloroform) gave an inseparable 2:1 a:ß mixture of diols **16** and 8-epi-**16** (36 mg, 60%) as a colourless oil; Data for **16**: ^{1}H NMR (400 MHz, $CDCl_3$): d = 7.42-7.25 (m, 5H; Ph), 4.83 (d, *J* = 11.5 Hz, 1H; C*H*HPh), 4.47 (m, 1H; H3), 4.42 (d, *J* = 11.5 Hz, 1H; CH*H*Ph), 4.10 (d, *J* = 13.8 Hz, 1H; H6), 4.07 (d, *J* = 8.3 Hz, 1H; H28), 4.03 (dt, *J* = 3.0, 1.2 Hz, 1H; H1), 3.96 (d, *J* = 8.3 Hz, 1H; H28), 3.81 (s, 3H; CO_2Me), 3.60 (2 × d, *J* = 9.6 Hz, 2H; 2 × H19), 3.50 (s, 3H; CO_2Me), 3.18 (d, *J* = 3.3 Hz, 1H; OH), 3.14 (d, *J* = 6.4 Hz, 1H; H9), 3.02 (d, *J* = 13.8 Hz, 1H; H5), 2.96 (d, *J* = 6.9 Hz, 1H; OH), 2.75 (quintet, *J* = 6.6 Hz, 1H; H8), 2.32-2.29 (m, 2H; 2 × H2), 1.25 (d, *J* = 7.0 Hz, 3H; 30Me). 8-*epi*-**16**: ^{1}H NMR (400 MHz, $CDCl_3$): *d* = 7.42-7.25 (m, 5H; Ph), 4.74 (d, *J* = 14.1 Hz, 1H; H6), 4.72 (d, *J* = 11.5 Hz, 1H; C*H*HPh), 4.56 (d, *J* = 11.5 Hz, 1H; CH*H*Ph), 4.47 (dt, *J* = 7.3, 2.8 Hz, 1H; H3), 4.19-4.16 (m, 2H; H1, H19), 4.13 (d, *J* = 8.6 Hz, 1H; H28), 4.03 (d, *J* = 8.6 Hz, 1H; H28), 3.81 (s, 3H; CO_2Me), 3.71 (s, 3H; CO_2Me), 3.61 (d, *J* = 9.6 Hz, 1H; H19) 3.33 (d, *J* = 7.5 Hz, 1H; OH), 3.17-3.13 (m, 1H; H8), 3.09 (d, *J* = 6.6 Hz, 1H; OH), 2.92 (d, *J* = 8.3 Hz, 1H; H9), 2.71 (d, *J* = 14.3 Hz, 1H; H5), 2.29 (dt, *J* = 15.6, 2.9 Hz, 1H; H2), 1.96 (dt, *J* = 15.6, 2.9 Hz, 1H; H2), 1.30 (d, *J* = 6.8 Hz, 3H; 30Me).

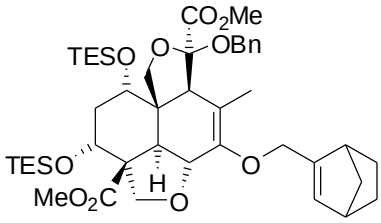
Bis silyl ether 21



iPr_2NEt (288 µL, 1.7mmol) and TES-OTf (293 µL, 1.3 mmol) were added to a solution of the diol **16** (82 mg, 0.17 mmol) in CH_2Cl_2 at - 60 $^?$C. After 30 min the reaction was warmed to 0 $^?$C and stirred for a further 2 h. The reaction was diluted with saturated $NaHCO_3$ solution (5 mL) and the product was extracted into chloroform (3 × 10 mL). The organic extracts were dried ($MgSO_4$) and the solvent removed *in vacuo.* Flash chromatography (30% ethyl acetate in petrol) afforded 8-*epi*-**21** and **21** (85 mg, 71%) as a colourless oil. Data for **21**: ^{1}H NMR (400 MHz, $CDCl_3$): *d* = 7.33-7.21 (m, 5H; Ph), 4.82 (d, *J* = 11.6 Hz, 1H; C*H*HPh), 4.40 (d, *J* = 11.6 Hz, 1H; CH*H*Ph), 4.32 (s, 1H; H1), 4.13 (d, *J* = 14.1 Hz, 1H; H6), 3.97 (d, *J* = 8.0 Hz, 1H; H28), 3.92 (s, 1H; H3), 3.90 (d, *J* = 8.0 Hz, 1H; H28), 3.79 (s, 3H; CO_2Me), 3.61 (d, *J* = 9.5 Hz, 1H; H19), 3.48 (s, 3H; CO_2Me), 3.44 (d, *J* = 9.5 Hz, 1H; H19), 3.16 (d, *J* = 14.2 Hz, 1H; H5), 3.02 (d, *J* = 6.3 Hz, 1H; H9), 2.67 (m, 1H; H8), 2.29 (app. dt, *J* = 15.6, 3.4 Hz, 1H; H2), 1.98 (d, *J* = 15.6 Hz, 1H; H2), 1.20 (d, *J* = 6.9 Hz, 3H; 30Me), 0.99 (t, *J* = 8.0 Hz, 9H; $SiCH_2C\mathit{H}_3$), 0.90 (m, 9H; $SiCH_2C\mathit{H}_3$), 0.66 (m, 6H; $SiC\mathit{H}_2CH_3$), 0.56 (m, 6H; $SiC\mathit{H}_2CH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 208.3 (s), 174.8 (s), 169.0 (s), 137.0 (s), 128.5 (2 × d), 127.8 (d), 127.7 (2 × d), 105.6 (s), 76.2 (d), 73.4 (t), 72.9

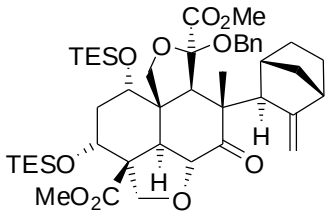
(d), 68.8 (t), 66.5 (t), 66.5 (d), 66.1 (t), 56.3 (d), 53.3 (s), 52.5 (q), 51.9 (q), 47.5 (s), 43.3 (d), 41.4 (d), 37.9 (t), 11.32 (q), 7.0 (3 × q), 6.9 (3 × q), 5.0 (3 × t), 4.7 (3 × t).

Allylic enol ether 25



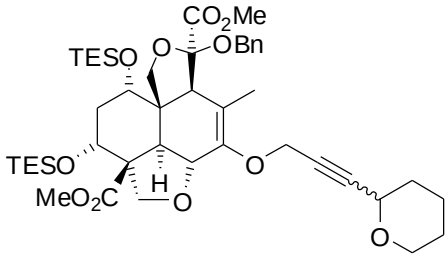
Sodium hydride (60 wt% dispersion in mineral oil, 8.3 mg, 0.21 mmol) was washed with petrol (5 × 2 cm^3), dried *in vacuo* and then suspended in degassed THF (2 mL) under an atmosphere of argon and cooled to 0 °C. A solution of ketone **21** (20.0 mg, 0.028 mmol) in THF (1 mL) was added dropwise and then the mixture was stirred at 0 °C for 15 min. 15-crown-5 (0.015 mL, 0.075 mmol) was added and the mixture was stirred for a further 10 min before a solution of allyl bromide **24** (100 mg, 0.54 mmol) was added dropwise. The mixture was stirred at 0 °C for 2 h then quenched by the addition of saturated aqueous NH_4Cl (2 mL). The mixture was extracted with ethyl acetate (3 × 10 mL), dried ($MgSO_4$) and the solvent was removed *in vacuo* to leave a yellow oil. The crude product was purified by flash column chromatography (33% diethyl ether in petrol) to give a 1:1.2 diastereoisomeric mixture of enol ethers **25** (22 mg, 96%) as a white foam. IR (film) $?_{max}/cm^{-1}$ 2954, 2935, 2878, 1747, 1724, 1656, 1132, 1126, 1066; HRMS 847.4241 ($[M+Na]^+$ $C_{45}H_{68}O_{10}Si_2Na$ requires 847.4249). Major Isomer: ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.32-7.28 (m, 5H; Ar), 5.82 (br s, 1H; H14), 4.52-4.46 (m, 4H; H6, 2 × H18, C*H*HPh), 4.43-4.41 (m, 1H; H1), 4.15 (d, *J* = 12.6 Hz, 1H; OCH*H*Ph), 4.23 (d, *J* = 7.9 Hz, 1H; H28), 3.97 (d, *J* = 7.9 Hz, 1H; H28), 3.87-3.85 (m, 1H; H3), 3.79 (s, 3H; CO_2Me), 3.57 (s, 3H; CO_2Me), 3.59-3.56 (m, 2H; 2 × H19), 3.26 (m, 1H; H9), 2.92 (br s, 1H; H17), 2.91 (d, *J* = 11.7 Hz, 1H; H5), 2.77 (br s, 1H; H15), 2.24 (dt, *J* = 15.5, 3.0 Hz, 1H; H2), 1.94 (dt, *J* = 15.5, 1.4 Hz, 1H; H2), 1.73 (s, 3H; 30Me), 1.64-1.54 (m, 2H; H20, H21), 1.44-1.39 (m, 1H; H16), 1.09-0.95 (m, 3H; H16, H20, H21), 0.98-0.97 (m, 18H; $SiCH_2C\mathit{H}_3$), 0.67-0.52 (m, 12H; $SiC\mathit{H}_2CH_3$); ^{13}C NMR (150 MHz, $CDC1_3$): *d* = 175.3 (s), 169.8 (s), 153.2 (s), 146.0 (s), 138.4 (s), 130.8 (d), 128.1 (2 × d), 127.3 (d), 127.2 (2 × d), 113.0 (s), 105.8 (s), 73.3 (t), 70.8 (d), 70.7 (d), 68.2 (t), 68.0 (t), 66.7, (d), 65.4 (t), 58.0 (d), 54.3 (s), 52.4 (q), 52.0 (q), 48.1 (t), 47.7 (s), 45.7 (d), 42.8 (d) 42.2 (d), 37.5 (t), 26.2 (t), 24.4(t), 15.0 (q), 7.0 (3 × q), 6.9 (3 × q), 4.9 (2 × t), 4.7 (3 × t). Minor Isomer: ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.32-7.28 (m, 5H; Ar), 5.82 (br s, 1H; H14), 4.52-4.46 (m, 4H; H6, 2 × H18, OC*H*HPh), 4.43-4.41 (m, 1H; H1), 4.24 (d, *J* = 12.8 Hz, 1H; OCH*H*Ph), 4.23 (d, *J* = 7.9 Hz, 1H; H28), 3.98 (d, *J* = 7.9 Hz, 1H; H28), 3.87-3.85 (m, 1H; H3), 3.77 (s, 3H; CO_2Me), 3.58 (s, 3H; CO_2Me), 3.59-3.56 (m, 2H; 2 × H19), 3.26 (m, 1H; H9), 2.91 (d, *J* = 11.7 Hz, 1H; H5), 2.87 (br s, 1H; H17), 2.69 (br s, 1H; H15), 2.24 (dt, *J* = 15.5, 3.0 Hz, 1H; H2), 1.94 (dt, *J* = 15.5, 1.4 Hz, 1H; H2), 1.73 (s, 3H; 30Me), 1.64-1.54 (m, 2H; H20, H21), 1.44-1.39 (m, 1H; H16), 1.09-0.95 (m, 3H; H16, H20, H21), 0.98-0.97 (m, 18H; $SiCH_2C\mathit{H}_3$), 0.67-0.52 (m, 12H; $SiC\mathit{H}_2CH_3$); ^{13}C NMR (150 MHz, CDCl3): *d* = 175.3 (s), 169.9 (s), 153.4 (s), 146.1 (s), 138.4 (s), 130.9 (s), 128.1 (2 × d), 127.3 (d), 127.2 (2 × d), 112.6 (s), 105.9 (s), 73.3 (t), 70.8 (d), 70.7 (d), 68.2 (t), 68.0 (t), 66.7 (d), 65.5 (t), 58.0 (d), 54.3 (s), 52.4 (q), 52.0 (q), 48.1 (t), 48.0 (s), 45.7 (d), 43.0 (d), 42.2 (d), 37.5 (t), 26.1 (t), 24.6 (t), 15.1 (q), 7.0 (q), 6.9 (q), 4.9 (t), 4.7 (t).

Claisen rearrangement product 26



All glassware was washed (5 × $NaHCO_3$, 5 × H_2O) and oven dried before use. A diastereomeric mixture of enol ethers **25** (12.0 mg, 0.015 mmol) was dissolved in 1,2-dichlorobenzene (0.3 mL). The mixture was degassed and then heated to 167 °C for 16 h in a sealed tube. The crude product was purified by flash column chromatography (petrol to remove the solvent followed by 33% diethyl ether in petrol) to give the ketone **26** (2.0 mg, 42%; 83% based on conversion of one diastereomer) as a white foam. ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.35-7.29 (m, 3H; Ar), 7.21 (d, *J* = 7.4 Hz, 2H; Ar), 5.05 (s, 1H; H18), 4.90 (d, *J* = 11.9 Hz, 1H; C*H*HPh), 4.44 (s, 1H; H18), 4.42 (d, *J* = 11.9 Hz, 1H; CH*H*Ph), 4.36-4.34 (m, 1H; H1), 4.07 (d, *J* = 14.8 Hz, 1H; H6), 3.95-3.92 (m, 1H; H3), 3.89-3.85 (m, 2H; H28), 3.80 (s, 3H; CO_2Me), 3.59 (d, *J* = 14.8 Hz, 1H; H5), 3.57 (d, *J* = 9.1 Hz, 1H; H19), 3.49 (s, 1H; H9), 3.42 (d, *J* = 9.1 Hz, 1H; H19), 3.39 (s, 3H; CO_2Me), 2.76 (br s, 1H; H14), 2.62 (br s, 1H; H17), 2.44 (dt, *J* = 15.6, 4.1 Hz, 1H; H2), 2.35 (br s, 1H; H15), 2.00 (dt, *J* = 15.6, 2.8 Hz, 1H; H2), 1.71 (d, *J* = 10.4 Hz, 1H; H16), 1.60-1.55 (m, 2H; H20, H21), 1.27-1.24 (m, 2H; H20, H21), 1.23 (s, 3H; 30Me), 1.07 (t, *J* = 8.0 Hz, 9H; $SiCH_2CH_3$), 1.05 (d, *J* = 10.4 Hz, 1H; H16), 0.92 (t, *J* = 8.1 Hz, 9H; $SiCH_2CH_3$), 0.86-0.77 (m, 6H; $SiCH_2CH_3$), 0.62-0.50 (m, 6H; $SiCH_2CH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 206.7 (s), 174.7 (s), 168.8 (s), 153.9 (s), 137.2 (s), 128.4 (2 × d), 127.6 (d), 127.4 (2 × d), 109.3 (t), 106.0 (s), 75.6 (d), 74.4 (d), 72.9 (t), 71.1 (t), 66.4 (d), 65.5 (t), 58.0 (d), 55.9 (s), 53.2 (s), 53.0 (q), 52.5 (d), 51.8 (q), 47.6 (s), 46.4 (d), 41.0 (d), 39.6 (d), 39.2 (t), 37.6 (t), 31.1 (t), 31.0 (t), 18.0 (q), 7.4 (3 × q), 7.0 (3 × q), 5.5 (3 × t), 4.9 (3 × t); IR (film) $?_{max}$/cm^{-1} 2955, 2913, 2878, 1754, 1723, 1128, 1093, 1072; HRMS (ESI) 847.4269 ($[M+Na]^+$ $C_{45}H_{68}O_{10}Si_2Na$ requires 847.4249).

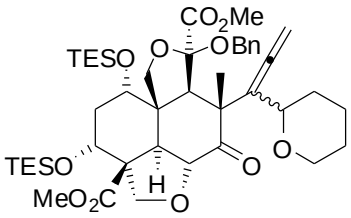
Propargyl enol ether 30



Sodium hydride (60% in mineral oil, 27 mg, 0.68 mmol) was washed with pentane (5 × 1 mL) and dried *in vacuo*. THF (degassed, 0.5 mL) was added and the mixture was cooled to 0 °C. A solution of **21** (49 mg, 0.068 mmol) in THF (degassed, 0.5 mL + 2 × 0.2 mL rinses) was added *via* cannula. After stirring for 15 min at 0 °C, 15-crown-5 (36 ml, 0.18 mmol) was added and the resulting mixture was stirred 10 min more at the same temperature. A solution of **29** (30 mg, 0.14 mmol) in THF (degassed, 0.5 mL + 2 × 0.2 mL rinses) was then transferred *via* cannula and it was stirred for 2 h at 0 °C. After addition of saturated aqueous NH_4Cl (1 mL) and dilution with ethyl acetate (10 mL), the organic layer was washed with saturated aqueous NH_4Cl (10 mL), brine (10 mL) and water (10 mL). Drying (Na_2SO_4), evaporation of the solvent and chromatography (Biotage 12S, 33% diethyl ether in petrol) afforded a diastereomeric mixture of enol ethers **25** (37 mg, 66%) as a colourless oil. ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.23-7.33

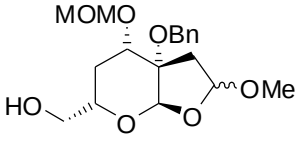
(m, 5H; Bn), 4.54-4.59 (m, 2H; C*H*HPh, H18), 4.47-4.51 (m, 2H; H6, H18), 4.44 (d, *J* = 15.1 Hz, 1H; CH*H*Ph), 4.35 (s, 1H; H1), 4.22-4.27 (m, 1H; H15), 4.10 (d, *J* = 8.0 Hz, 1H; H28), 3.96 (d, *J* = 8.0 Hz, 1H; H28), 3.94-3.98 (m, 1H; H21), 3.87 (s, 1H; H3), 3.80 (s, 3H; CO_2Me), 3.54 (s, 3H; CO_2Me), 3.45-3.52 (m, 1H; H21), 3.46 (d, *J* = 9.5 Hz, 1H; H19), 3.42 (d, *J* = 9.3 Hz, 1H; H19), 3.26 (s, 1H; H9), 2.90 (d, *J* = 11.8, 1H; H5), 2.23-2.26 (m, 1H; H2), 1.95 (d, *J* = 15.6 Hz, 1H; H2), 1.82-1.86 (m, 1H; H16), 1.75-1.80 (m, 1H; H16), 1.75 (s, 3H; 30Me), 1.63-1.68 (m, 1H; H16), 1.48-1.59 (m, 3H; 2 × H20, H16), 0.95 (t, *J* = 8.1 Hz, 9 H; $SiCH_2CH_3$), 0.93 (t, *J* = 8.1 Hz, 9H; $SiCH_2CH_3$), 0.55-0.68 (m, 12H; $SiCH_2CH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 175.18 (s), 169.67 (s), 152.56 (s), 152.47 (s'), 138.44 (s), 138.42 (s'), 128.23 (d), 128.22 (d), 127.27 (d), 127.17 (d), 127.12 (d), 115.71 (s), 115.59 (s'), 105.65 (s), 105.63 (s'), 85.07 (s), 85.04 (s'), 81.43 (s), 81.41 (s'), 73.78 (t), 70.79 (d), 70.77 (d'), 70.67 (d), 70.55 (d'), 67.67 (t), 66.85 (d), 66.63 (d), 66.21 (t), 65.41 (t), 65.37 (t'), 58.57 (t), 58.42 (t'), 58.06 (d), 58.04 (d'), 54.25 (s), 52.43 (q), 51.96 (q'), 47.64 (s), 46.06 (d), 45.97 (d'), 37.52 (t), 31.78 (t), 31.72 (t'), 25.64 (t), 25.57 (t'), 21.54 (t), 15.27 (q), 6.97 (3 × q), 6.96 (3 × q), 4.71 (3 × t), 4.94 (3 × t); IR (CH_2Cl_2) ν_{max}/cm^{-1} 2955, 2876, 1748, 1722, 1606, 1456, 1382, 1132, 1111, 1081, 1005; HRMS 863.4217 ($[M+Na]^+$ $C_{45}H_{68}O_{11}Si_2Na$ requires 836.4192). ' denotes signals in the ^{13}C NMR spectrum which have been resolved for the separate diastereoisomers.

Allene 31



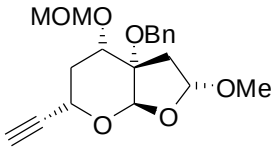
The reaction vial was washed with saturated aqueous K_2CO_3 and oven-dried. A degassed solution of **30** (16 mg, 0.019 mmol) in 1,2-dichlorobenzene (1 ml) was heated with pulsed microwave irradiation (2 × 15 min, 180 °C; 15 min, 220 °C). The 1,2-dichlorobenzene was removed by filtration through silica (petrol for 1,2-dichlorobenzene then diethyl ether). The crude product was purified by flash column chromatography (*Biotage* 12S, 25% diethyl ether in petrol) to give a diastereomeric mixture of allenes **31** (8.5 mg, 53%). Data reported for a single diastereoisomer: $[a]_D^{30}$ = - 20.8 (*c* = 1.00 in $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): *d* = 7.25-7.35 (m, 5H; Ph), 5.00 (dd, *J* = 10.0, 2.0 Hz, 1H; 18H), 4.88 (d, *J* = 10.5 Hz, 1H; 18H), 4.82 (d, *J* = 11.5 Hz, 1H; C*H*HPh), 4.45 (m, 1H; H1), 4.39 (d, *J* = 11.5 Hz, 1H; CH*H*Ph), 4.12 (d, *J* = 15.0 Hz, 1H; H6), 3.98 (s, 1H; H3), 3.79 (s, 3H; CO_2Me), 3.76-4.01 (m, 4H; 2 × H28 or 2 × H19, H21, H15), 3.55 (d, *J* = 9.4 Hz, 1H; H19 or H28), 3.51 (d, *J* = 9.4 Hz, 1H; H19 or H28), 3.47 (s, 1H; H9), 3.45 (s, 3H; CO_2Me), 3.42-3.49 (m, 1H; H5), 3.36 (dd, *J* = 10.9, 10.9 Hz, 1H; H21), 2.22-2.24 (m, 1H; H2), 1.82-1.94 (m, 3H; H2, 2 × H16 or 2 × H17), 1.60 (s, 3H; 30Me), 1.43-1.62 (m, 4H; 2 × H20, 2 × H16 or 2 × H17), 1.03 (t, *J* = 7.9 Hz, 9H; $SiCH_2CH_3$), 0.92 (t, *J* = 7.9 Hz, 9H; $SiCH_2CH_3$), 0.79 (q, *J* = 7.9 Hz, 6H; $SiCH_2CH_3$), 0.55-0.59 (m, 6H; $SiCH_2CH_3$); IR (film) ν_{max}/cm^{-1} 2954, 2877, 1754, 1722, 1456, 1435, 1239, 1077; HRMS 863.4162 ($[M+Na]^+$ $C_{45}H_{68}O_{11}Si_2Na$ requires 863.4192).

Methyl acetals 50



A solution of lactol (3.75 g, 8.25 mmol), anhydrous trimethylorthoformate (25 mL, 228 mmol) and CSA (190 mg, 0.83 mmol) in MeOH (abs., 250 mL) was stirred at room temperature for 1 h. The reaction was quenched by the addition of solid $NaHCO_3$ (400 mg) and the solvent was removed *in vacuo*. The residue was purified by flash chromatography (25%-50% ethyl acetate in petrol) to yield a diastereomeric mixture of methyl acetals **50** as colourless oil (2.40 g, 82%). Repeated column chromatography (25%-50% ethyl acetate in petrol) allowed the separation of the diastereomers yielding the pure less-polar a-isomer 23*epi*-**50** (600 mg, 21%) followed by the more-polar 23ß-isomer **50** (1.44 g, 50%) and the remainder was a mixture of 23epimers (194 mg, 7%). 23*epi*-**50**: $[a]_D$ = +51.7 (c = 2.00 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.35-7.23 (m, 5H; Ph), 5.40 (s, 1H; H21), 5.03 (dd, *J* = 5.5, 1.5 Hz, 1H; H23), 4.93 (d, *J* = 11.5 Hz, 1H; C*H*HPh), 4.80 (d, *J* = 6.8 Hz, 1H; OC*H*HO), 4.77 (d, *J* = 6.8 Hz, 1H; OCH*H*O), 4.61 (d, *J* = 11.5 Hz, 1H; CH*H*Ph), 4.35 (dd, *J* = 11.5, 4.4 Hz 1H; H17), 4.01-4.04 (m, 1H; H15), 3.71 (dd, *J* = 11.5, 3.3 Hz, 1H; H14), 3.65 (dd, *J* = 11.5, 6.0 Hz, 1H; H14), 3.41 (s, 3H; OMe), 3.39 (s, 3H; OMe), 2.31-2.39 (m, 2H; H22), 2.19 (br s, 1H; OH), 1.96 (m, 1H; H16), 1.85 (m, 1H; H16). **50**: $[a]_D$ = - 12.9 (*c* = 2.00 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.35-7.23 (m, 5H; Ph), 5.45 (s, 1H; H23), 5.00 (dd, *J* = 6.0, 4.7 Hz, 1H; H23), 4.93 (d, *J* = 11.5 Hz, 1H; C*H*HPh), 4.79 (d, *J* = 7.2 Hz, 1H; OC*H*HO), 4.69 (d, *J* = 6.6 Hz, 1H; OCH*H*O), 4.59 (d, *J* = 12.1, 1H; CH*H*Ph), 4.01 (m, 1H; H15), 3.75 (dd, *J* = 11.8, 3.0 Hz, 1H; H17), 3.69 (dd, *J* = 11.8, 3.0 Hz, 1H; H14), 3.61 (dd, *J* = 11.8, 5.8 Hz, 1H; H14), 3.43 (s, 6H; 2 × OMe), 2.70 (dd, *J* = 13.7, 6.0 Hz, 1H; H22), 2.17 (br s, 1H; OH), 2.10 (dd, *J* = 13.5, 4.7 Hz, 1H; H22), 2.00 (m, 1H; H16), 1.76 (m, 1H; H16).

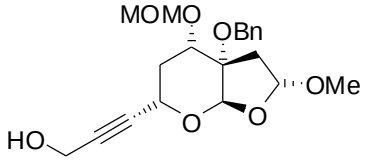
Alkyne 51



DMSO (1.44 ml, 20.4 mmol) was added dropwise to a solution of oxalyl chloride (710 µL, 8.14 mmol) in CH_2Cl_2 (50 mL) at - 78 °C. After 20 min a solution of alcohol **50** (1.44 g, 4.07 mmol) in CH_2Cl_2 (15 mL) was added and the resulting mixture was stirred at - 78 °C for 3 h. NEt_3 (2.27 ml, 16.3 mmol) was added and after 10 min stirring was continued at room temperature for further 15 min, then the reaction was quenched by the addition of saturated aqueous NH_4Cl. After extraction with diethyl ether and drying of the combined organic layers ($MgSO_4$), the solvent was removed *in vacuo*. The resulting crude product **50a** (1.53 g) was used withough further purification. To a solution of dimethyl-(1-diazo-2-oxopropyl)-phosphonate (1.56 g, 8.14 mmol) in MeOH (abs., 30 mL) was added anhydrous K_2CO_3 (1.97 g, 14.2 mmol) and the resulting suspension was stirred for 15 min. Crude aldehyde **50a** (*ca*. 4.07 mmol) in MeOH (abs., 10 mL) was added and stirring continued for 16 h. The solvent was removed *in vacuo* and the residue partitioned between saturated aqueous $NaHCO_3$ and diethyl ether. After extraction with diethyl ether, drying of the combined organic layers ($MgSO_4$), and removal of the solvent *in vacuo,* the residue was purified by flash chromatography (25-50% ethyl acetate in petrol) to yield the alkyne **51** (1.1 g, 77% over two steps) as colourless oil. $[a]_D$ = - 13.8 (*c* = 2.00 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.39-7.23 (m, 5H; Ph), 5.46 (s, 1H; H23), 5.00 (dd, *J* = 6.0, 4.9 Hz, 1H; H23), 4.92 (d, *J* = 11.5 Hz, 1H; C*H*HPh), 4.79 (d, *J* = 6.6 Hz, 1H; OC*H*HO), 4.69 (d, *J* = 7.1 Hz, 1H; OCH*H*O), 4.67 (m, 1H; H15), 4.61 (d, *J* = 12.1 Hz, 1H; CH*H*Ph), 3.69 (dd, *J* = 12.1, 3.8 Hz, 1H; H17), 3.44 (s, 3H; OMe), 3.43 (s, 3H; OMe), 2.65 (dd, *J* = 13.4, 6.3 Hz, 1H; H22), 2.47 (d, *J* = 2.2 Hz, 1H; H13), 2.26 (ddd, *J* = 12.1, 12.1, 12.1 Hz, 1H; H16), 2.12-2.06 (m, 2H; H16, H22); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 139.1 (s), 128.2 (2 × d), 127.3 (d), 127.0 (2 × d), 102.4 (d), 101.0 (d), 95.7 (t), 81.3 (s), 78.0 (s), 76.9 (d), 73.3 (d), 69.1 (t), 61.7 (d), 55.9 (q), 55.8 (q), 36.9 (t), 32.5 (t); IR (film) $?_{max}$/cm^{-1} 3277, 2933, 1453, 1371, 1316,

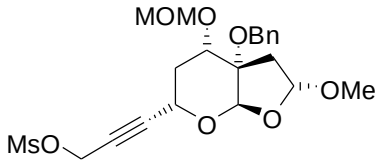
1262, 1213, 1146, 1108, 1040, 981, 954, 739, 698; HRMS 371.1482 ($[M+Na]^+$ $C_{19}H_{24}O_6Na$ requires 371.1465).

Propargyl alcohol 52



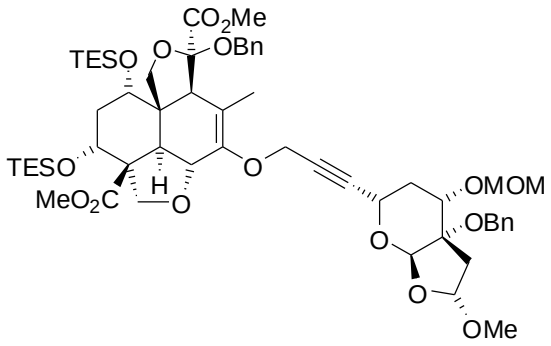
To a solution of alkyne **51** (1.10 g, 3.14 mmol) in THF (30 mL) was added isopropylmagnesium chloride (2 M in THF, 7.85 mL, 15.7 mmol) at room temperature. The reaction mixture was heated to 45 °C and after 90 min paraformaldehyde (pre-dried, 753 mg, 25.1 mmol) was added and stirring continued for further 2.5 h at 45 °C. Addition of saturated aqueous NH_4Cl was followed by extraction with ethyl acetate. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (20-50% ethyl acetate in petrol) to yield the propargyl alcohol **52** as colourless oil (1.05 g, 89%). $[a]_D$ = - 16.2 (*c* = 2.00 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.39-7.23 (m, 5H; Ph), 5.44 (s, 1H; H21), 4.99 (dd, *J* = 6.3, 4.7 Hz, 1H; H23), 4.91 (d, *J* = 12.1 Hz, 1H; C*H*HPh), 4.78 (d, *J* = 7.1 Hz, 1H; OC*H*HO), 4.71 (d, *J* = 13.2 Hz, 1H; H15), 4.69 (d, *J* = 7.1 Hz, 1H; OCH*H*O), 4.60 (d, *J* = 11.5 Hz, CH*H*Ph), 4.27 (d, *J* = 1.6 Hz, 2H; H18), 3.68 (dd, *J* = 12.1, 3.8 Hz, 1H; H17), 3.44 (s, 3H; OMe), 3.43 (s, 3H; OMe), 2.64 (dd, *J* = 13.5, 6.3 Hz, 1H; H22), 2.24 (ddd, *J* = 12.2, 12.2, 11.8 Hz, 1H; H16), 2.09 (dd, *J* = 13.5, 4.9 Hz, 1H; H22), 2.06 (m, 1H; H16), 1.89 (br s, 1H; OH); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 139.0 (s), 128.2 (2 × d), 127.3 (d), 127.1 (2 × d), 102.4 (d), 101.0 (d), 95.7 (t), 83.6 (s), 83.2 (s), 78.0 (s), 76.9 (d), 69.1 (t), 61.9 (d), 55.9 (q), 55.8 (q), 51.0 (t), 36.8 (t), 32.4 (t); IR (film) $?_{max}$/cm^{-1} 2936, 2342, 1371, 1211, 1145, 1107, 1032, 978, 953, 743; HRMS 401.1577 ($[M+Na]^+$ $C_{20}H_{26}O_7Na$ requires 401.1576).

Mesylate 37



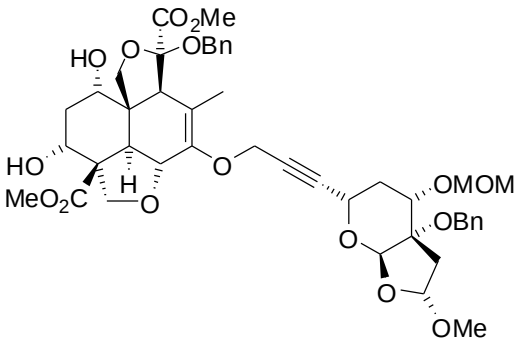
To a solution of propargyl alcohol **36** (1.05 g, 2.79 mmol) in CH_2Cl_2 (30 mL) was added *i*Pr_2NEt (850 µl, 4.88 mmol) followed by Ms_2O (729 mg, 4.19 mmol) at 0 °C. After 90 min the solvent was removed *in vacuo* and the residue was purified by flash column chromatography (20-50% ethyl acetate in petrol) to yield the mesylate **37** as colourless oil (1.15 g, 89%). $[a]_D$ = - 9.3 (*c* = 1.00 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.39-7.23 (m, 5H; Ph), 5.42 (s, 1H; H21), 5.00 (dd, *J* = 6.3, 4.6 Hz, 1H; H23), 4.91 (d, *J* = 12.1 Hz, 1H; C*H*HPh), 4.88 (d, *J* = 1.6 Hz, 2H; H18), 4.79 (d, *J* = 6.6 Hz, 1H; OC*H*HO), 4.74 (dd, *J* = 10.7, 0.8 Hz, 1H; H15) 4.70 (d, *J* = 6.6 Hz, 1H; OCH*H*O), 4.60 (d, *J* = 11.5 Hz, 1H; CH*H*Ph), 3.69 (dd, *J* = 12.1, 3.8 Hz, 1H; H17), 3.44 (s, 3H; OMe), 3.43 (s, 3H; OMe), 3.10 (s, 3H; SMe), 2.64 (dd, *J* = 13.4 Hz, 6.3 Hz, 1H; H22), 2.24 (ddd, *J* = 12.1, 12.1, 12.1 Hz, 1H; H16), 2.10 (dd, *J* = 13.4, 4.6 Hz, 1H; H22), 2.06 (ddd, *J* = 12.7, 3.8, 2.5 Hz, 1H; H16); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 139.0 (s), 128.3 (2 × d), 127.4 (d), 127.1 (2 × d), 102.5 (d), 101.1 (d), 95.8 (t), 87.4, (s), 78.0 (s), 77.3 (s), 76.9 (d), 69.3 (t), 61.7 (d), 57.5 (t), 55.9 (q), 55.8 (q), 39.1 (q), 36.8 (t), 32.1 (t); IR (film) $?_{max}$/cm^{-1} 2936, 2342, 1359, 1211, 1175, 1107, 1040, 978, 946; HRMS 479.1344 ($[M+Na]^+$ $C_{21}H_{28}O_9NaS$ requires 479.1352).

Propargyl enol ether 53



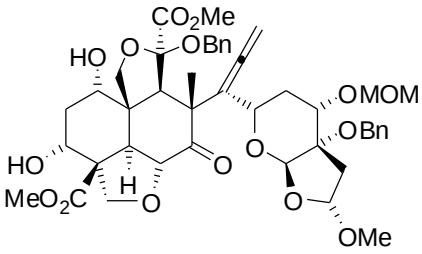
A suspension of sodium hydride (60 wt% in mineral oil, 450 mg, 11.3 mmol) in THF (4 mL) was cooled to 0 °C. A precooled (0 °C) solution of the decalin moiety **21** (202 mg, 282 µmol) in THF (3 mL + 1 mL rinse) added *via* cannula. After 20 min 15-crown-5 (168 µl, 844 µmol) was added and stirring continued for further 20 min. A precooled (0 °C) solution of propargyl mesylate **37** (642 mg, 1.41 mmol) in THF (4 mL + 2 × 0.75 mL rinses) was then transferred *via* cannula to the reaction mixture and the colour of the reaction solution changed from pale yellow to reddish brown. After stirring for 6 h at 0 °C the reaction was quenched by the addition of saturated aqueous NH_4Cl (5 ml) and water (10 mL). After extraction with CH_2Cl_2, the combined organic layers were dried ($MgSO_4$), concentrated *in vacuo* and purified by flash column chromatography (10-50% diethyl ether in petrol, followed by ether) afforded the propargyl enol ether **53** (195 mg, 65%) as colourless oil followed by un-reacted propargyl mesylate **37** (443 mg, 88%). $[a]_D$ = +6.8 (*c* = 0.40 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.39-7.19 (m, 10H; Ph), 5.43 (s, 1H; H21), 4.96 (dd, *J* = 6.0, 5.4 Hz, 1H; H23), 4.90 (d, *J* = 12.1 Hz, 1H; C*H*HPh), 4.78 (d, *J* = 6.6 Hz, 1H; OC*H*HO), 4.67 (d, *J* = 7.1 Hz, 1H; OCH*H*O), 4.60 (d, *J* = 12.1, 1H; C*H*HPh), 4.57-4.47 (m, 5H; H18, H15, H6, CH*H*Ph), 4.43 (d, *J* = 15.9 Hz, 1H; CH*H*Ph), 4.33 (s, 1H; H1), 4.10 (d, *J* = 7.9 Hz, 1H; H28), 3.96 (d, *J* = 7.9 Hz, 1H; H28), 3.86 (s, 1H; H3), 3.79 (s, 3H; CO_2Me), 3.61 (dd, *J* = 12.1, 3.8 Hz, 1H; H17), 3.53 (s, 3H; CO_2Me), 3.46 (d, *J* = 11.0 Hz, 1H; H19), 3.43 (s, 3H; OMe), 3.43 (d, *J* = 8.8 Hz, 1H; H19), 3.41 (s, 3H; OMe), 3.25 (s, 1H; H9), 2.90 (d, *J* = 11.5 Hz, 1H; H5), 2.63 (dd, *J* = 13.7, 6.0 Hz, 1H; H22), 2.30-2.15 (m, 1H; H16, H2), 2.09-2.01 (m, 2H; H22, H16), 1.94 (d, *J* = 15.4 Hz, 1H; H2), 1.74 (s, 3H; 30Me), 0.93 (m, 18H; $SiCH_2C\mathit{H}_3$), 0.58 (m, 12H; $SiC\mathit{H}_2CH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 175.2 (s), 169.7 (s), 152.4 (s), 139.1 (s), 138.3 (s), 128.3 (d), 128.2 (d), 127.4 (d), 127.2 (d), 127.1 (d), 127.0 (d), 126.9 (d), 115.7 (s), 105.6 (s), 102.4 (d), 100.8 (d), 95.4 (t), 83.6 (s), 81.4 (s), 77.9 (s), 76.8 (d), 73.7 (t), 70.7 (d), 70.4 (d), 69.1 (t), 67.6 (t), 66.6 (d), 65.4 (t), 61.9 (d), 58.3 (t), 58.0 (d), 55.9 (q), 55.8 (q), 54.2 (s), 52.5 (q), 52.0 (q), 47.6 (s), 46.1 (d), 37.5 (t), 36.9 (t), 32.2 (t), 15.3 (q), 7.0 (q), 6.9 (q), 4.9 (t), 4.7 (t); IR (film) $?_{max}$/cm^{-1} 2952, 2877, 1750, 1721, 1497, 1454, 1372, 1315, 1216, 1131, 1107, 1074, 1035, 1002, 955, 872, 840, 809, 784, 729, 697; HRMS 1101.5052 ($[M+Na]^+$ $C_{57}H_{82}O_{16}Si_2Na$ requires 1101.5034).

Propargylic enol ether diol 54



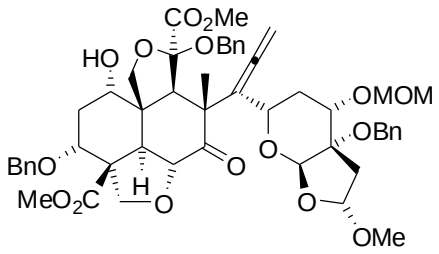
To a solution of propargyl enol ether **53** (195 mg, 181 μmol) in THF (10 mL) was added TBAF (1 M in THF, 540μl, 540 μmol) at 0 °C. The reaction mixture was allowed to reach room temperature over 16 h. Following removal of the solvent *in vacuo*, flash column chromatography (25-75% ethyl acetate in petrol) afforded the diol **54** (141 mg, 92%) as colourless oil. $[a]_D$ = +1.6 (*c* = 1.00 in $CHCl_3$); HRMS 873.3334 ($[M+Na]^+$ $C_{45}H_{54}O_{16}Na$ requires 873.3310).

Allene diol 55



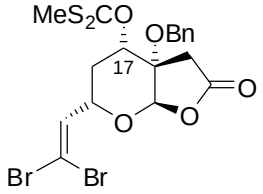
All glassware was washed with saturated aqueous Na_2CO_3 solution (3 ×), water (3 ×), distilled acetone (3 ×) and dried at 200 °C for 16 h before use. The diol **54** (133 mg, 156 μmol) was dissolved in degassed nitrobenzene (6 mL) and transferred into two microwave flasks. Each reaction mixture was heated under microwave irradiation (3 × 5 min at 185 °C). Direct flash column chromatography of the crude reaction mixture (pure petrol to remove nitrobenzene then 10-75% ethyl acetate in petrol) yielded the allene **55** (133 mg, quantitative) as colourless oil. $[a]_D$ = - 11.5 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *d* = 7.39-7.19 (m, 10 H; Ph), 5.38 (s, 1H; H21), 5.01 (dd, *J* = 6.1, 4.7 Hz, 1H; H23), 4.97 (d, *J* = 11.5 Hz, 1H; C*H*HPh), 4.93 (m, 2H; H18), 4.91 (d, *J* = 11.5 Hz, 1H; C*H*HPh), 4.77 (d, *J* = 6.6 Hz; 1H; OC*H*HO), 4.66 (d, *J* = 6.6 Hz, 1H; OCH*H*O), 4.57 (d, *J* = 11.5 Hz, 1H; CH*H*Ph), 4.52 (m, 1H; H15), 4.48 (d, *J* = 11.5 Hz, 1H; CH*H*Ph), 4.36 (s, 1H; H1), 4.25 (d, *J* = 14.3 Hz, 1H; H6), 4.04 (d, *J* = 7.6, 1H; H28), 3.99 (m, 1H; H3), 3.92 (d, *J* = 8.2 Hz, 1H; H28), 3.76 (s, 1H; H9), 3.71 (m, 1H; H17, H19), 3.63 (s, 3H; CO_2Me), 3.54 (m, 2H; H5, H19), 3.45 (s, 3H; CO_2Me), 3.43 (s, 3H; OMe), 3.42 (s, 3H; OMe), 2.67 (dd, *J* = 13.2, 6.1 Hz, 1H; H22), 2.29-2.15 (m, 5H; 2 × H2, H16, 2 × OH), 2.06 (dd, *J* = 13.4, 4.7 Hz, 1H; H22), 1.84 (d, *J* = 12.1 Hz, 1H; H16), 1.56 (s, 3H; 30Me); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 207.1 (s), 206.6 (s), 174.4 (s), 168.9 (s), 139.1 (s), 136.9 (s), 128.5 (d), 128.2 (2 × d), 127.8 (d), 127.3 (d), 127.1 (d), 127.0 (d), 105.9 (s), 105.7 (s), 102.8 (d), 101.3 (d), 95.5 (t), 80.6 (t), 78.1 (s), 77.8 (d), 75.7 (d), 73.4 (d), 73.0 (t), 69.3 (t), 69.1 (t), 67.1 (d), 65.9 (t), 57.6 (d), 55.9 (2 × q), 55.2 (s), 53.5 (s), 52.6 (q), 51.9 (q), 48.5 (s), 38.3 (d), 37.1 (t), 34.8 (t), 32.4 (t), 22.5 (q), 1 × d not observed; IR (film) $?_{max}$/cm^{-1} 2951, 1754, 1725, 1437, 1241, 1093, 1046, 1241; HRMS 873.3325 ($[M+Na]^+$; $C_{45}H_{54}O_{16}Na$ requires 873.3310).

Benzyl ether 56



To a solution of diol **55** were added benzyl bromide (55 µl, 468 µmol), *n*Bu_4NI (0.1 eq.) and finally sodium hydride (60 wt% in mineral oil, 19 mg, 468 µmol) at room temperature and the resulting reaction mixture was stirrred for 16 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl, and the reaction mixture was extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product which was purified by flash column chromatography (10-80% ethyl acetate in petrol) to give the product **56** (111 mg, 76%) as colourless oil. $[a]_D$ = - 8.0 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.39-7.19 (m, 15H; Ph), 5.34 (s, 1H; H21), 5.03 (m, 1H; H23), 4.99 (d, *J* = 11.5 Hz, 1H; C*H*HPh), 4.87 (d, *J* = 11.1 Hz, 1H; C*H*HPh), 4.76 (d, *J* = 6.8 Hz, 1H; OC*H*HO), 4.67 (d, *J* = 6.8 Hz, 1H; OCH*H*O), 4.76-4.60 (m, 2H; H18), 4.59 (d, *J* = 11.1 Hz, 1H; CH*H*Ph), 4.48 (d, *J* = 12.1 Hz, 1H; CH*H*Ph), 4.41 (m, 2H; H1, H15), 4.20 (m, 1H; H3), 4.16 (d, *J* = 14.3 Hz, 1H; H6), 3.88 (d, *J* = 7.1 Hz, 1H; H28), 3.83 (s, 3H; CO_2Me), 3.79 (d, *J* = 7.1 Hz, 1H; H28), 3.78 (m, 1H; H17), 3.62 (d, *J* = 9.3 Hz, 1H; H19), 3.49 (d, *J* = 9.3 Hz, 1H; H19), 3.45 (s, 3H; CO_2Me), 3.43 (d, *J* = 12.1 Hz, 1H; CH*H*Ph), 3.40 (m, 7H; 2 × OMe, H9), 3.35 (d, *J* = 12.6 Hz, 1H; H5) 3.20 (br s, 1H; OH), 2.61 (dd, *J* = 13.4, 6.3 Hz, 1H; H22), 2.36 (m, 1H; H16), 2.08 (m, 2H; H16, H22), 1.87 (m, 1H; H2), 1.58 (m, 1H; H2), 1.51 (s, 3H; 30Me); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 207.1 (s), 206.6 (s), 173.9 (s), 168.8 (s), 139.4 (s), 137.0 (s), 136.2 (s), 128.8 (d), 128.5 (d), 128.3 (d), 128.1 (d), 127.8 (d), 127.3 (d), 127.1 (d), 127.0 (d), 109.0 (s), 105.7 (s), 102.9 (d), 101.4 (d), 95.0 (d), 80.2 (t), 78.4 (s), 77.5 (d), 75.6 (d), 74.9 (d), 73.7 (t), 72.7 (d), 72.6 (t), 68.9 (t), 68.6 (t), 67.4 (d), 65.8 (t), 56.7 (s), 55.9 (q), 55.6 (q), 55.2 (d), 52.9 (s), 52.7 (q), 60.0 (q), 48.2 (s), 38.8 (d), 37.2 (t), 32.2 (t), 31.7 (t), 22.6 (q), 1 × t not observed; IR (film) $?_{max}$/cm^{-1} 2952, 1754, 1725, 1437, 1242, 1092, 1045, 733, 701; HRMS 963.3782 ($[M+Na]^+$; $C_{52}H_{60}O_{16}Na$ requires 963.3774).

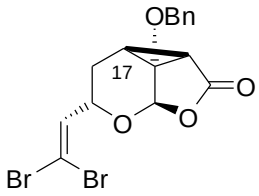
C17 xanthate ester 64

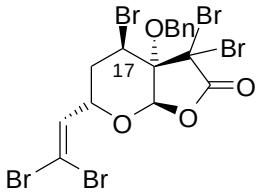


To a solution of alcohol **57** (5 mg, 0.011 mmol) in THF (0.5 mL) at - 78 °C was added carbon disulfide (0.002 mL, 0.034 mmol). After stirring for 30 min NaHMDS (2 M in THF, 0.0065 mL, 0.013 mmol) was added. After a further 30 min at - 78 °C methyl iodide was added (2 M in *tert*-butyl methyl ether (0.0275 mL, 0.055 mmol). The reaction was then stirred at - 78 °C for 1 h before quenching with saturated aqueous NH_4Cl solution (0.1 mL) and warming to room temperature. The reaction was partitioned between ethyl acetate (5 mL) and saturated aqueous $NaHCO_3$ solution (5 mL), the organic layer separated, dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography (20% ethyl acetate in hexanes) afforded the title compound **64** as a yellow oil (5 mg, 85%); $[a]_D$ = - 32.4 (*c* = 0.37 in $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.43-7.35 (m, 5H; Ph), 6.57 (d, *J* = 7.4 Hz, 1H; H14), 6.04 (dd, *J* = 6.6, 4.1 Hz, 1H; H17), 5.76 (s, 1H; H21), 4.82 (d, *J* = 13.8 Hz, 1H; C*H*HPh), 4.68-4.66 (m, 1H; H15), 4.57 (d, *J* = 13.8 Hz, 1H; CH*H*Ph), 2.96 (d, *J* = 13.9 Hz, 1H; H23), 2.88 (d, *J* = 13.9 Hz, 1H; H23), 2.64 (s, 3H; SMe), 2.28 (app. dt, *J* = 15.4, 6.6 Hz, 1H; H16), 2.17 (dd, *J* = 15.4, 4.1 Hz, 1H; H16); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 215.5 (s), 169.2 (s), 137.2 (s), 135.8 (d), 128.6 (2 × d), 128.8 (d), 127.4 (2 × d), 104.0 (d), 93.7 (s), 78.0 (d), 77.2 (s), 72.0 (d), 69.5 (t), 37.2 (t), 29.0 (t), 19.6 (q); IR (film) ν_{max}/cm^{-1} 2923, 1795, 1454, 1379, 1166, 1097; HRMS 536.9098 [(M+H)$^+$ $C_{18}H_{19}Br_2O_5S_2$ requires 536.9041] ? = 10.3 ppm.

Cyclopropane 66 and pentabromo derivative 67

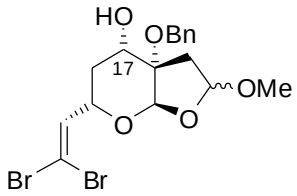




To a solution of alcohol **57** (10 mg, 0.022 mmol) in CH_2Cl_2 (0.2 mL) at 0 °C was added carbon tetrabromide (34 mg, 0.10 mmol). The reaction was stirred at 0 °C for 5 min before triphenylphosphine (26 mg, 0.10 mmol) was added. After stirring at room temperature for 24 h the reaction was partitioned between CH_2Cl_2 (5 mL) and saturated aqueous $NaHCO_3$ solution (5 mL), the organic layer was separated, dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography (5-25% ethyl acetate in petrol) afforded the cyclopropane **66** as a colourless oil (3 mg, 32%), pentabromo derivative **67** as a colourless oil (4.5 mg, 31%) and starting alcohol **57** (2.5 mg, 25%).

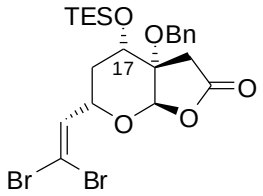
Cyclopropane **66**: $[a]_D$ = - 8.0 (*c* = 0.13 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.43-7.31 (m, 5H; Ph), 6.57 (d, *J* = 7.7 Hz, 1H; H14), 5.99 (s, 1H; H21), 4.70 (d, *J* = 11.6 Hz, 1H; C*H*HPh), 4.67 (d, *J* = 11.6 Hz, 1H; CH*H*Ph), 4.47 (dd, *J* = 13.1, 7.1 Hz, 1H; H15), 2.43 (d, *J* = 9.6 Hz, 1H; H23), 2.18-2.17 (m, 1H; H17), 2.06 (app. td, *J* = 15.2, 7.3 Hz, H16), 2.00 (app. dt, *J* = 15.2, 1.8 Hz, 1H; H16); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 170.1 (s), 137.1 (d), 136.1 (s), 128.8 (2 × d), 128.7 (d), 128.0 (2 × d), 97.7 (d), 92.9 (s), 70.0 (t), 68.9 (s), 67.7 (d), 29.3 (d), 25.2 (d), 22.8 (t); IR (film) ν_{max}/cm^{-1} 2924, 2328, 1787, 1456, 1277, 1172, 1115; HRMS 450.9151 [(M+Na)$^+$ $C_{16}H_{14}BrO_4Na$ requires 450.9156] ? = 0.5 ppm. Pentabromo derivitive **67**: $[a]_D$ = - 16.0 (*c* = 0.25 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.43-7.37 (m, 5H; Ph), 6.49 (d, *J* = 7.3 Hz, 1H; H14), 6.10 (s, 1H; H21), 4.98 (d, *J* = 11.1 Hz, 1H; C*H*HPh), 4.54 (d, *J* = 11.1 Hz, 1H; CH*H*Ph), 4.45 (app. q, *J* = 7.3 Hz, 1H; H15), 2.48 (ddd, *J* = 7.4, 3.2, 1.6 Hz, 1H; H17), 2.08 (ddd, *J* = 15.4, 5.6, 3.2 Hz, 1H; H16), 1.99-1.98 (m, 1H; H16); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 168.3 (s), 136.5 (d), 135.7 (s), 128.8 (3 × d), 128.1 (2 × d), 96.6 (d), 96.3 (s), 72.0 (t), 69.1 (s), 66.9 (d), 34.5 (d), 22.2 (t); IR (film) ν_{max}/cm^{-1} 2925, 1795, 1453, 1379, 1166, 1097; HRMS 530.8443 [(M+Na)$^+$ $C_{16}H_{14}Br_3O_4Na$ requires 530.8418] ? = 4.6 ppm.

C17-hydroxyl C23-methyl acetal 68



To a solution of lactone **57** (0.10 g, 0.22 mmol) in CH_2Cl_2 (6 mL) at - 78 °C was added DIBAL-H (1 M in CH_2Cl_2, 0.55 mL, 0.55 mmol) and the reaction stirred for 2.5 h. TLC analysis indicated that the reaction was incomplete and therefore further DIBAL-H was added (0.55 mL, 0.55 mmol) and the reaction stirred for 1 h before quenching with MeOH (4 mL). The reaction was then allowed to warm to room temperature and saturated aqueous sodum potassium tartrate solution added, after which stirring was continued for 14 h. The product was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic extracts dried ($MgSO_4$) and concentrated *in vacuo* to afford the corresponding lactol as a colourless oil that was used without purification in the subsequent step. To a solution of the lactol (*ca.* 0.22 mmol) in acetonitrile (12 mL) was added 3? molecular sieves (320 mg), Amberlyst-15 (60 mg) and MeOH (2.8 mL). The reaction was stirred for 24 h at room temperature, filtered through Celite and then concentrated *in vacuo*. Column chromatography (20% ethyl acetate in petrol) afforded an epimeric mixture of acetals (58 mg, 57% over 2 steps) with a significant amount of unknown contaminant aldehyde. IR (film) $?_{max}/cm^{-1}$ 3446, 2923, 1455, 1378, 1091; HRMS (ESI) 484.9573 [$(M+Na)^+$ $C_{17}H_{20}O_5Br_2Na$ requires 484.9570] ? = 0.6 ppm. **23a-68**: ^{1}H NMR (500 MHz, $CDCl_3$): ?*d* = 7.37–7.28 (m, 5H; Ph), 6.55 (d, *J* = 7.6 Hz, 1H; H14), 5.58 (s, 1H; H21), 5.00 (dd, *J* = 6.3, 4.0 Hz, 1H; H23), 4.64–4.57 (m, 3H; CH_2Ph, H15), 3.69 (app. td, *J* = 9.0, 4.3 Hz, 1H; H17), 3.44 (s, 3H; OMe), 2.57 (dd, *J* = 14.1, 6.3 Hz, 1H; H22), 2.46 (d, *J* = 9.0 Hz, 1H; OH), 2.16 (dd, *J* = 14.1, 4.0 Hz, 1H; H22), 1.91 (ddd, *J* = 12.8, 4.2, 2.7 Hz, 1H; H16), 1.77-1.75 (m, 1H; H16); ^{13}C NMR (125 MHz, $CDCl_3$): *d* = ?137.7 (s), 137.6 (d), 128.5 (2 × d), 127.9 (d), 127.3 (2 × d), 100.5 (d), 98.2 (d), 91.6 (s), 77.9 (s), 71.6 (d), 70.0 (d), 66.2 (t), 55.8 (q), 34.7 (d), 32.9 (d). **23ß-68**: ^{1}H NMR (500 MHz, $CDCl_3$): *d* = 7.38–7.29 (m, 5H; Ph), 6.66 (d, *J* = 7.9 Hz, 1H; H14), 5.49 (s, 1H; H21), 5.10 (dd, *J* = 6.4, 1.8 Hz, 1H; H23), 4.62-4.60 (m, 1H; H15), 4.60-4.58 (m, 2H; CH_2Ph), 4.33 (ddd, *J* = 9.3, 8.1, 5.9 Hz, 1H; H17), 3.43 (s, 3H; OMe), 2.56 (d, *J* = 5.9 Hz, 1H; OH), 2.49 (dd, *J* = 14.0, 6.4 Hz, 1H; H22), 2.22 (dd, *J* = 14.0, 1.8 Hz, 1H; H22), 2.02 (app. dt, *J* = 13.2, 4.0 Hz, 1H; H16), 1.79 (app. dt, *J* = 13.3, 9.9 Hz, 1H; H16); ^{13}C NMR (125 MHz, $CDCl_3$): *d* = ?137.6 (d), 137.6 (s), 128.6 (2 × d), 128.0 (d), 127.3 (2 × d), 102.7 (d), 102.1 (d), 92.0 (s), 78.8 (s), 70.8 (d), 68.7 (d) 66.3 (t), 55.7 (q), 36.0 (t), 32.9 (t).

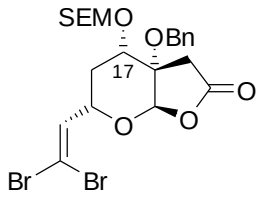
C17 TES ether 70



To a solution of alcohol **57** (10 mg, 0.022 mmol) in CH_2Cl_2 (0.5 mL) was added *i*Pr_2NEt (0.021 mL, 0.12 mmol) followed by TES-OTf (0.018 mL, 0.08 mmol). After stirring at room temperature for 24 h the reaction was partitioned between CH_2Cl_2 (5 mL) and saturated aqueous $NaHCO_3$ solution (5 mL), the organic layer separated, dried ($MgSO_4$) and concentrated *in vacuo* to afford the silyl ether **70** as a colourless oil (12 mg, 98%). $[a]_D$ = - 84.0 (*c* = 0.40 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.29-7.26 (m, 5H; Ph), 6.54 (d, *J* = 7.3 Hz, 1H; H14), 5.67 (s, 1H; H21), 5.06 (d, *J* = 11.6 Hz, 1H; C*H*HPh),

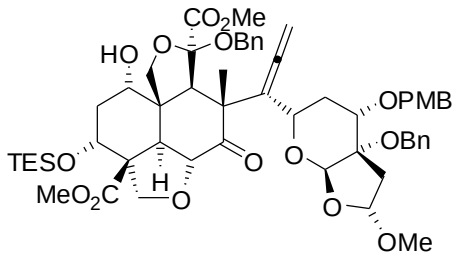
4.58 (d, *J* = 11.6 Hz, 1H; CH*H*Ph), 4.53-4.52 (m, 1H; H15), 3.90 (dd, *J* = 11.7, 3.6 Hz, H17), 3.03 (d, *J* = 16.4 Hz, 1H; H23), 2.81 (d, *J* = 16.4 Hz, 1H; H23), 2.09 (app. dt, *J* =12.8 Hz, t not resolved, 1H; H16), 1.86 (d, *J* = 12.8 Hz, 1H; H16), 0.96 (t, *J* = 8.0 Hz, 9H; $SiCH_2CH_3$), 0.65 (q, *J* = 8.0 Hz, 6H; $SiCH_2CH_3$); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 169.7 (s), 138.4 (s), 136.5 (d), 128.5 (2 × d), 127.8 (d), 127.2 (2 × d), 104.5 (d), 73.6 (d), 71.4 (d), 71.0 (t), 38.2 (t), 33.0 (t), 6.8 (3 × q), 5.9 (3 × t); IR (film) ν_{max}/cm^{-1} 2958, 1793, 1265, 1169, 950; HRMS 583.0117 [$(M+Na)^+$ $C_{22}H_{30}O_5SiBr_2Na$ requires 583.0121] ? = 0.8 ppm.

C17 SEM ether 73



To a solution of alcohol **57** (10 mg, 0.022 mmol) in CH_2Cl_2 (0.25 mL) at 0 °C was added *i*Pr_2NEt (0.058 mL, 0.32 mmol), chloromethyltrimethylsilylethyl ether (0.028 mL, 0.16 mmol) and DMAP (2 crystals). The ice bath was then removed and the reaction allowed to stir for 48 h at room temperature. The reaction was then partitioned between CH_2Cl_2 (5 mL) and saturated aqueous $NaHCO_3$ solution (5 mL), the organic layer separated, dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography (0-10% ethyl acetate in petrol) afforded **73** as a colurless oil (10.5 mg, 83%). $[a]_D$ = - 25.7 (*c* = 0.18 in $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$,): *d* = 7.34-7.26 (m, 5H; Ph), 6.56 (d, *J* = 6.6 Hz, 1H; H14), 5.71 (s, 1H; H21), 4.98 (d, *J* = 11.7 Hz, 1H; C*H*HPh), 4.83 (d, *J* = 7.1 Hz, 1H; OC*H*HO), 4.77 (d, *J* = 7.1 Hz, 1H; OCH*H*O), 4.60 (d, *J* = 11.7 Hz, 1H; CH*H*Ph), 4.59-4.58 (m, 1H; H15), 3.83 (dd, *J* = 11.5, 4.7 Hz, 1H; H17), 3.71-3.64 (m, 2H; $OCH_2CH_2SiMe_3$), 3.04 (d, *J* = 16.5 Hz, 1H; H23), 2.83 (d, *J* = 16.5 Hz, 1H; H23), 2.05-2.01 (m, 2H; 2 × H16), 0.99-0.96 (m, 2H; $OCH_2CH_2SiMe_3$), 0.04 (s, 9H; $SiMe_3$); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 169.6 (s), 138.1 (s), 136.3 (d), 128.5 (2 × d), 127.8 (d), 127.1 (2 × d), 104.4 (d), 93.7 (t), 93.0 (s), 77.2 (s), 75.1 (d), 73.1 (d), 70.2 (t), 66.0 (t), 38.0 (t), 31.9 (t), 14.1 (t), –1.5 (3 × q); IR (film) ν_{max}/cm^{-1} 2921, 2320, 1789, 1456, 1277; HRMS 599.0082 [$(M+Na)^+$ $C_{22}H_{30}O_6SiBr_2Na$ requires 599.0090] ? = 1.4 ppm.

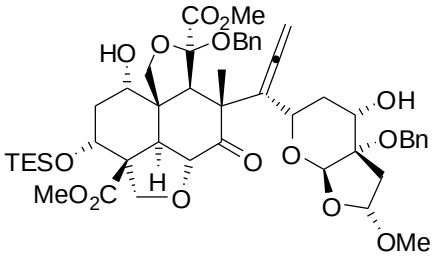
C3-TES ether allene 84



To diol **82** (10 mg, 0.01 mmol) in CH_2Cl_2 (1 mL) at - 78 °C was added *i*Pr_2NEt (0.022 mL, 0.12 mmol) followed by TES-OTf (0.018 mL, 0.08 mmol). After stirring at - 78 °C for 30 min, the reaction was quenched *via* addition of saturated aqueous NH_4Cl solution (0.1 mL) and then allowed to warm to room temperature. The reaction was then partitioned between saturated aqueous $NaHCO_3$ solution (5 mL) and CH_2Cl_2 (5 mL), the organic layer separated, dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography (25-50% ethyl acetate in hexanes) provided silyl ether **84** as a colourless oil (10.5 mg, >98%). $[a]_D$ = - 9.4 (*c* = 0.09 in $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): *d* = 7.37-7.19 (m, 12H; Ar), 6.90 (d, *J* = 8.5 Hz, 2H; Ar), 5.38 (br s, 1H; H21), 5.00 (m, 2H; OH, H18), 4.90 (d, *J* = 12.3 Hz, 1H; C*H*HPh), 4.82 (d, *J* = 11.2 Hz, 1H; H18), 4.75 (app.t, *J* = 5.0 Hz, 1H; H23), 4.70 (d, *J* = 11.4 Hz, 1H; C*H*HAr),

4.60 (d, *J* = 12.3 Hz, 1H; CH*H*Ph), 4.55-4.40 (m, 3H; H1, C*H*$_2$Ph), 4.35 (d, *J* = 11.4 Hz, 1H; CH*H*Ar), 4.18 (d, *J* = 14.2 Hz, 1H; H6), 3.95-3.88 (m, 9H; CO_2Me, OMe, 2 × H28, H15), 3.62-3.61 (m, 1H; H15), 3.58 (m, 1H; H17), 3.56-3.54 (m, 2H; H9, H19), 3.45-3.38 (m, 6H; H3, H5, H19, CO_2Me), 3.35 (s, 3H; OMe), 2.42 (dd, *J* = 13.5, 6.2 Hz, 1H; H22), 2.20 (d, *J* = 15.0 Hz, 1H; H2), 2.12 (d, *J* = 15.6 Hz, 1H; H2), 2.05-1.90 (m, 3H; H22, 2 × H16), 1.50 (s, 3H; 30Me), 0.96 (t, *J* = 8.0 Hz, 9H; SiCH$_2$C*H*$_3$), 0.65 (q, *J* = 8.0 Hz, 6H; SiC*H*$_2$CH$_3$); ^{13}C NMR (150 MHz, $CDCl_3$): *d* = 206.5 (s), 206.3 (s), 174.0 (s), 168.7 (s), 159.2 (s), 139.6 (s), 137.1 (s), 130.3 (s), 129.4 (4 × d), 128.5 (2 × d), 128.0 (2 × d), 127.7 (d), 127.6 (2 × d), 127.0 (d), 113.8 (2 × d), 109.2 (s), 105.9 (s), 103.3 (d), 101.2 (d), 78.5 (d), 77.2 (t), 75.5 (d), 73.1 (d), 73.0 (t), 70.2 (t), 69.0 (t), 69.0 (s), 68.5 (d), 67.7 (d), 65.8 (t), 55.5 (q), 55.3 (q), 53.1 (s), 52.6 (q), 52.0 (q), 48.3 (s), 45.2 (d), 38.0 (d), 37.2 (t), 35.5 (t), 32.1 (t), 22.6 (q), (3 × q), 4.5 (3 x t), 1 × s, 1 × t not observed; IR (film) ν_{max}/cm^{-1} 3645, 2961, 2923, 2335, 1731, 1260, 1017; HRMS 1063.4488 [(M+Na)$^+$ $C_{57}H_{72}O_{16}Na$ requires 1063.4487] ? = 0.1 ppm.

C3-Silyl ether diol 84a



To a stirred solution of PMB ether **84** (15 mg, 0.015 mmol) in CH_2Cl_2 (0.6 mL) and H_2O (0.03 mL) was added DDQ (13.5 mg, 0.051 mmol). The reaction was allowed to stir at room temperature for 1.5 h before partitioning between saturated aqueous $NaHCO_3$ solution (5 mL) and CH_2Cl_2 (5 mL). The organic layer was then separated, dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography (25-100% ethyl acetate in hexanes) provided the product as a colourless oil (12 mg, 87%); $[a]_D$ = - 8.4 (*c* = 0.13 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *d* = 7.38-7.25 (m, 10H; Ph), 5.57 (s, 1H; H21), 5.03 (dd, *J* = 6.0, 4.0 Hz, 1H; H23), 5.02 (d, *J* = 12.0 Hz, 1H; C*H*HPh), 4.98 (d, *J* = 11.2 Hz, 1H; H18), 4.80 (d, *J* = 11.2 Hz, 1H; H18), 4.63 (d, *J* = 11.5 Hz, 1H; C*H*HPh), 4.60 (d, *J* = 11.5 Hz, 1H; CH*H*Ph), 4.53-4.52 (m, 1H; H1), 4.51 (d, *J* = 11.9 Hz, 1H; CH*H*Ph), 4.49 (br s, 1H; H15), 4.17 (d, *J* = 14.2 Hz, 1H; H6), 3.90-3.72 (m, 6H; CO_2Me, 2 × H28, H3, H17), 3.60 (d, *J* = 9.4 Hz, H19), 3.52-3.45 (m, 2H; H19, H9), 3.43 (s, 3H; CO_2Me), 3.41 (s, 3H; OMe), 3.39 (s, 1H; H9), 2.50 (dd, *J* = 14.0, 6.2 Hz, 1H; H22), 2.40 (d, *J* = 10.5 Hz, 1H; OH), 2.25-2.05 (m, 3H; H22, 2 × H2), 1.82 (q, *J* = 12.0 Hz, 1H; H16), 1.72-1.70 (m, 1H; H16), 1.57 (s, 3H; 30Me), 0.96 (t, *J* = 8.0 Hz, 9H; SiCH$_2$C*H*$_3$), 0.65 (q, *J* = 8.0, 6H; SiC*H*$_2$CH$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): *d* = 206.6 (s), 206.3 (s), 174.0 (s), 168.7 (s), 138.1 (s), 137.1 (s), 128.5 (2 × d), 128.4 (2 × d), 127.8 (d), 127.7 (3 × d), 127.3 (2 × d), 109.3 (s), 105.8 (s), 101.3 (d), 99.6 (d), 78.6 (s), 76.7 (t), 75.5 (d), 73.0 (d), 71.1 (d), 68.9 (t), 68.5 (d), 66.5 (d), 66.0 (t), 65.8 (t), 55.5 (q), 53.1 (s), 52.6 (q), 52.0 (q), 52.0 (s), 48.2 (s), 38.0 (d), 37.3 (d), 35.5 (t), 35.3 (t), 34.0 (t), 22.6 (q), 6.7 (3 × q), 4.5 (3 × t), 1 × t not observed; IR (film) ν_{max}/cm^{-1} 2923, 2851, 1728, 1464, 1071; HRMS 943.3894 [(M+Na)$^+$ $C_{49}H_{64}O_{15}SiNa$ requires 944.1132] ? = 1.9 ppm.