SUPPORTING INFORMATION

Alkene protection against acid using a bromide substituent: application in a total synthesis of (−)-6,7-dideoxsqualestatin H5

Hasanain A. A. Almohseni, Hamad H. Al Mamari, Anne Valade, Herman O. Sintim and David M. Hodgson*

Department of Chemistry, Chemistry Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA, United Kingdom
david.hodgson@chem.ox.ac.uk
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1. General techniques

All reactions requiring anhydrous conditions were carried out in flame–dried glassware under an atmosphere of nitrogen (or argon), the later having been passed through a column of calcium chloride and silica gel. THF, CH₂Cl₂ and DMF were obtained from drying stills.¹ Methanol was dried over activated 4 Å MS under argon. Diisopropylamine, triethylamine and 2,6-lutidine were distilled under nitrogen from CaH₂. A fresh batch of MoOPH was prepared following a slightly modified procedure using molybdic acid² instead of molybdenum(VI) oxide,³ and dried overnight under high vacuum prior use. n-BuLi in hexanes was titrated by adding a solution of 2-propanol (1.0 M in toluene with 0.2% of 1,10-phenanthroline) slowly to a solution of n-BuLi in toluene until a change of colour from clear to red then yellow. MeLi in ether was titrated by adding slowly MeLi to a solution of N-benzylbenzamide (100 mg in 5 ml THF) at –20 °C; the end-point was marked by a colour change from clear to blue. Commercial starting materials were used without further purification, unless otherwise stated. Petrol (petroleum ether) 40–60 °C was used in flash column chromatography, which was carried out using silica gel (VWR chemicals, BDH), and monitored by TLC (Merck 60 F254) plates. TLC plates were viewed using ultraviolet light (λmax = 254/365 nm) and by immersion in KMnO₄ or anisaldehyde stains, followed by heating. Infrared spectra were obtained using a PerkinElmer FT–IR spectrometer (Universal ATR Sampling Accessory) with absorption maxima quoted in wavenumbers (cm⁻¹). Peaks are described as broad (br), weak (w), medium (m) and strong (s). Nuclear magnetic resonance (¹H NMR, ¹³C NMR and ¹⁹F NMR) spectra were recorded on Bruker Avance UltraShield AVC 500, AVX 500 and AVF 400, in CDCl₃ and CD₃OD, referenced to solvent peaks. Chemical shifts are quoted in parts per million (ppm). The splittings are quoted as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), multiplet (m) and pseudo (p). Proton coupling constants (J) are reported to the nearest 0.5 Hz. E/Z Assignments and stereochemistry of cycloadduct 12 were based on NOE studies. [α]D²⁵ values are given in 10⁻¹ deg cm² g⁻¹. Concentrations (c) are given in g/cm³. Low resolution mass spectra were obtained using electrospray ionisation (ESI). High resolution mass spectra were obtained by ESI using tetraoctylammonium bromide or sodium dodecyl sulfate as the lock mass; values are quoted as ratio of mass to charge (m/z) in Daltons.
2. Experimental procedures

(a) Model studies and methylation cross-coupling optimisation

2,4-Dimethyl-5-phenyl-2-pentene (10)

\[
\text{Ph}
\]

\[\text{CH}_2=\text{C}-(\text{CH}_3)_2\]

\[n\text{-BuLi (1.3 mL, 2.5 M in hexanes, 3.3 mmol) was added dropwise to a solution of isopropyltriphenylphosphonium iodide (1.6 g, 3.7 mmol) in THF (8 mL) at } -78 \degree \text{C. The mixture was warmed to rt, stirred for 30 min, then the dark red solution was re-cooled to } -78 \degree \text{C and a solution of aldehyde rac-17}^4 \text{ (0.25 g, 1.69 mmol) in THF (4 mL) was added dropwise. After stirring at rt for 4 h, the mixture was quenched with water (30 mL), extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with brine (30 mL), dried (MgSO}_4) \text{, and evaporated under reduced pressure. Purification of the residue by column chromatography (20% Et}_2\text{O in petrol) gave alkene 10}^5 \text{ (175 mg, 60%), as a colourless liquid; } R_f = 0.71 \text{ (20% Et}_2\text{O in petrol).}^1 \text{H NMR (400 MHz; CDCl}_3) \delta 7.30-7.13 \text{ (5H, m, ArH), 4.99 (1H, dquint, } J = 9, 1.5, \text{CH}=\text{C}-(\text{CH}_3)_2), 2.69-2.48 \text{ (3H, m, CH}_2\text{Ph), 1.67 (3H, d, } J = 1.5, \text{one CH}_3 \text{ of } =\text{C}-(\text{CH}_3)_2), 1.46 (3H, d, } J = 1.5, \text{second CH}_3 \text{ of } =\text{C}-(\text{CH}_3)_2), 0.95 (3H, d, } J = 6.5, \text{CHCH}_3);^13 \text{C NMR (100 MHz; CDCl}_3) \delta 141.4 \text{ (ArC), 130.6 (C}=-\text{CH), 130.5 (C}=-\text{CH), 129.4 (ArCH) 128.1 (ArCH), 125.7 (ArCH), 44.2 (CH}_2\text{Ph), 34.8 (CHCH}_3), 25.9 (CH}_3), 20.9 (CHCH}_3), 17.9 (CH}_3).\]

1,1,3-Trimethyl-1,2,3,4-tetrahydronaphthalene (11)

\[
\text{CH}_3
\]

\[\text{CH}_3
\]

\[\text{CH}_3
\]

To a solution of alkene 10 (100 mg, 0.57 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (4.2 mL) was added TFA (2.1 mL) and H\textsubscript{2}O (210 μL). The reaction mixture was heated at 40 °C for 48 h, then cooled to rt, sat. aq. NaHCO\textsubscript{3} (5 mL) added and extracted with Et\textsubscript{2}O (2 x 15 mL). The combined organic layers were washed with brine (10 mL), dried (K\textsubscript{2}CO\textsubscript{3}) and evaporated under reduced pressure to give tetralin 11\textsuperscript{6} (94 mg, 95%) as a colourless liquid; \textit{Rf} = 0.71 (0.5% Et\textsubscript{2}O in petrol); \textit{\textsuperscript{1}H NMR (400 MHz; CDCl\textsubscript{3})} \delta 7.33 (1H, d, } J = 7.5, \text{ArH), 7.19–7.02 (3H, m, ArH), 2.84–2.74 (1H, m, CHHAr), 2.44–2.34 (1H, m, CHHAr), 2.04–1.91 (1H, m, CHCH\textsubscript{3}), 1.67–1.59 (1H, m, C(CH\textsubscript{3})\textsubscript{2}CHH), 1.42–1.32 (4H, m, C(CH\textsubscript{3})\textsubscript{2}CHH and CH\textsubscript{3}), 1.25 (3H, s, CH\textsubscript{3}), 1.05 (3H, d, } J = 6.5, \text{CHCH}_3);^13 \text{C NMR (100 MHz; CDCl}_3) \delta 145.6 (ArC), 136.3 (ArC), 129.0 (ArCH) 126.7
(ArCH), 126.0 (ArCH), 125.4 (ArCH), 48.5 (C(CH\(_3\)_2CH\(_2\)), 39.9 (CH\(_2\)Ar), 35.1 (C(CH\(_3\)_2)), 32.9 (CH\(_3\)), 31.9 (CH\(_3\)), 25.9 (CHCH\(_3\)), 22.6 (CHCH\(_3\)).

**(Z)**-6-Bromo-8-methyl-9-phenylnon-6-ene-1,3-diyI bis(2,2,2-trifluoroacetate) (25)

\[
\begin{align*}
\text{F}_3\text{CO}_2^- & \quad \text{F}_3\text{CO}_2^- \\
\text{Br} & \quad \text{Ph}
\end{align*}
\]

To a solution of 1,3-diol 22 (100 mg, 0.30 mmol) in CH\(_2\)Cl\(_2\) (2.20 mL) were added TFA (1.10 mL) and H\(_2\)O (110 \(\mu\)L). The reaction mixture was heated at 40 \(^\circ\)C for 48 h. The mixture was then concentrated under reduced pressure to give bistrifluoroacetate 25 (156 mg, quant), as a yellow oil, a 1:1 diastereomeric mixture; \(R_f = 0.35\) (4% EtOAc in petrol); \(\nu_{\text{max}}/\text{cm}^{-1}/(\text{film}) 3027\) w, 1784 s, 1454 w, 1220 s, 775 m, 731 m, 700 m; \(^1\)H NMR (400 MHz; CDCl\(_3\)) \(\delta\) 7.30–7.14 (5H, m, ArH), 5.54–5.49 (1H, m, CH=CBr), 5.15–5.04 (1H, m, CHOCOCF\(_3\)), 4.41–4.33 (2H, m, CH\(_2\)OCOCF\(_3\)), 2.94–2.83 (1H, m, CH\(_2\)CH\(_3\)), 2.71–2.64 (1H, m, CH/Ph), 2.59–2.51 (1H, m, CH/Ph), 2.50–2.40 (2H, m, CH\(_2\)CBr), 2.12 (2H, q, \(J = 6\), OCH\(_2\)CH\(_2\)CHO), 2.01–1.89 (2H, m, CH\(_2\)CH\(_2\)CBr), 0.97 (3H, d, \(J = 6.5\), CHCH\(_3\)); \(^{13}\)C NMR (100 MHz; CDCl\(_3\)) \(\delta\) 157.3 (2 x q, \(J_{\text{C-F}} = 42\), C=O), 140.0, 140.0 (ArC), 136.2, 136.1 (C=CBr), 129.4, 129.3 (ArCH) 128.3, 128.3 (ArCH), 126.2, 126.1 (ArCH), 124.5, 124.4 (C=CBr), 114.7 (2 x Q, \(J_{\text{C-F}} = 286\), CF\(_3\)), 74.9, 74.7 (CHOCOCF\(_3\)), 61.6 (CH\(_2\)OCOCF\(_3\)), 42.5 (CH\(_2\)Ph), 38.1, 38.0 (CHCH\(_3\)), 37.0, 36.9 (CH\(_2\)CH\(_2\)CBr), 32.5, 32.3, 32.2 (CH\(_2\)CH\(_2\)CBr and OCH\(_2\)CH\(_2\)CHO), 19.1 (CHCH\(_3\)); \(^{19}\)F NMR (377 MHz) \(\delta\) –75.1; HRMS \(m/z\) (M+Na\(^+\)) found: 541.0421. C\(_{20}\)H\(_{21}\)O\(_4\)BrF\(_6\)Na requires 541.0419.

**(Z)**-6-Bromo-1-((tert-butyltrimethylsilyl)oxy)-8-methyl-9-phenylnon-6-en-3-ol (23)

\[
\begin{align*}
\text{TBSO} & \quad \text{HO} \\
& \quad \text{Br} \\
\text{Ph} & \quad \text{Br}
\end{align*}
\]

To a solution of 1,3-diol 22 (0.97 mg, 3.05 mmol) and imidazole (477 mg, 7.01 mmol) in DMF (8 mL) at 0 \(^\circ\)C was added TBSCl (480 mg, 3.2 mmol) in DMF (8 mL). The mixture was stirred for 6 h at 0 \(^\circ\)C, then water (5 mL) was added, extracted with Et\(_2\)O (2 x 10 mL), washed with brine (5 mL), and dried (Na\(_2\)SO\(_4\)). Evaporation under reduced pressure followed by column chromatography (20% Et\(_2\)O in petrol) gave TBS ether 23 (1.15 g, 86%), as a colourless oil, a 1:1 diastereomeric mixture; \(R_f = 0.34\) (20% Et\(_2\)O in petrol); \(\nu_{\text{max}}/\text{cm}^{-1}/(\text{film}) 3448\) br, 2967 m, 2928 m, 2856 m, 1466 m, 1079 s, 885 m, 625 s; \(^1\)H NMR (400 MHz; CDCl\(_3\))
δ 7.29–7.13 (5H, m, ArH), 5.53 (1H, d, J = 8.5, CH=CBr), 3.92–3.85 (1H, m, CH(OH)), 3.83–3.66 (2H, m, CH₂OTBS), 3.47 and 3.42 (1H, 2 x s, CH(OH)), 2.95–2.82 (1H, m, CHCH₃), 2.73–2.64 (1H, m, CHPh), 2.61–2.42 (3H, m, CH₂ and CHHPh), 1.71–1.56 (4H, m, 2 x CH₂), 0.96 (3H, pdd, J = 6.5, 4, CHCH₃), 0.89 (9H, s, OSiMe₃), 0.08 (6H, s, OSi(CH₃)₂); ¹³C NMR (100 MHz; CDCl₃) δ 140.3, 140.2 (ArC), 134.2, 134.1 (C=CBr), 129.4, 129.3 (ArCH) 128.2 (ArCH), 127.2 (C=CBr), 126.0 (ArCH) 71.1, 70.9 (CH(OH)), 63.0 (CH₂OTBS), 42.7, 42.6 (CH₂Ph), 38.4, 38.3, 38.0, 37.9, 37.8, 37.7, (all CH₂), 36.1, 35.9 (CHCH₃), 26.0 (SiCMe₃) 19.3, 19.2 (CHCH₃), 18.2 (SiCMe₃), -5.4 (OSi(CH₃)₂), -5.4 (OSi(CH₃)₂); HRMS m/z (M+H⁺) found: 441.1822. C₂₂H₃₈O₂⁷⁹Br²⁸Si requires 441.1819.

(E)-1-((tert-Butyldimethylsilyl)oxy)-6,8-dimethyl-9-phenylnon-6-en-3-ol (27)

MeLi (112 μL, 1.6 M in Et₂O, 0.18 mmol) was added to a solution of 9-OMe-9BBN (180 μL, 1 M in hexanes, 0.18 mmol) in THF (1 mL). After 10 min, PdCl₂(dppf) (11 mg, 10 mol%) and NaOMe (12 mg, 0.22 mmol) were added, followed by a solution of TBS ether 23 (66 mg, 0.15 mmol) in THF (0.5 mL) dropwise. After refluxing for 48 h, the mixture was cooled to rt, added water (1 mL), extracted with Et₂O (2 × 5 mL), washed with brine (2 mL) and dried (MgSO₄). Evaporation under reduced pressure followed by column chromatography (5% EtOAc in petrol) gave E-alkene 27 (42 mg, 75%), as a colourless oil, a 1:1 diastereomeric mixture; R₉ = 0.33 (5% EtOAc in petrol); νmax/cm⁻¹(film) 3386 br, 2955 m, 2925 m, 2856 s, 1495 m, 1254 m, 1083 s, 834 s, 776 s, 698 m, 663 s; ¹H NMR (400 MHz; CDCl₃) δ 7.28–7.10 (5H, m, ArH), 5.00 (1H, d, J = 9, CH=CCH₃), 3.92–3.85 (1H, m, CH(OH)), 3.83–3.69 (2H, m, CH₂OTBS), 3.37 and 3.35 (1H, 2 x d, J = 2.5, CHOH), 2.67–2.56 (1H, m, CHCH₃), 2.55–2.49 (2H, m, CH₂Ph), 2.13–1.91 (2H, m, CH₂), 1.67–1.44 (4H, m, 2 x CH₂), 1.42 (3H, s, =CCH₃), 0.94 (3H, 2 x d, J = 6.5, CHCH₃), 0.90 (9H, s, OSiCMe₃), 0.08 (6H, s, OSi(CH₃)₂); ¹³C NMR (100 MHz; CDCl₃) δ 141.3, 141.3 (ArC), 134.1 (C=CCH₃), 130.5, 130.5 (C=CCH₃), 129.4 (ArCH) 128.1, 128.1 (ArCH), 125.7 (ArCH) 72.0, 71.9 (CH(OH)), 63.0 (CH₂OTBS), 42.1 (CH₂Ph), 38.4, 38.3, 35.9, 35.8, 35.6, (all CH₂), 34.7 (CHCH₃), 26.0 (SiCMe₃), 21.0, 20.9 (CHCH₃), 18.2 (SiCMe₃), 16.2, 16.2 (=CCH₃), -5.4 (one CH₃ of OSi(CH₃)₂), -5.4 (another CH₃ of OSi(CH₃)₂). HRMS m/z (M+H⁺) found: 377.2876. C₂₃H₄₁O₂Si requires 377.2873.
(Z)-5-(3-Bromo-5-methyl-6-phenylhex-3-en-1-yl)-2,2,3,3,9,9,10,10-octamethyl-4,8-dioxa-3,9-disilaundecane (24)

![Chemical structure](image)

To a solution of TBS ether 23 (50.0 mg, 0.11 mmol) in CH$_2$Cl$_2$ (1.5 mL) at 0 °C was added 2,6-lutidine (40 μL, 0.3 mmol) followed by TBSOTf (47 μL, 0.20 mmol). The mixture was stirred for 2 h at 0 °C, then sat. aq. NaHCO$_3$ (2 mL) added, extracted with EtOAc (2 × 5 mL) and the combined organic layers dried (MgSO$_4$) and evaporated under reduced pressure. Purification the residue by column chromatography (5% Et$_2$O in petrol) gave bis-TBS ether 24 (59 mg, 94%) as a colourless oil, a 1:1 diastereomeric mixture; $R_f = 0.65$ (5% Et$_2$O in petrol); $\nu_{max}$/cm$^{-1}$ (film) 3064 w, 2955 s, 2359 w, 1658 w, 1603 m, 1496 m, 1472 m, 1361 m, 1256 s, 1036 m, 1006 m, 836 s, 775 s; $^1$H NMR (400 MHz; CDCl$_3$) δ 7.31–7.16 (5H, m, ArH), 5.49 (1H, d, $J = 8.5$, CH=CBr), 3.87–3.79 (1H, m, CHOTBS), 3.71–3.64 (2H, m, CH$_2$OTBS), 2.95–2.84 (1H, m, CHCH$_3$), 2.72 (1H, dd, $J = 13.5$, $J = 6$ ,CH/Ph), 2.25 (1H, dd, $J = 13.5$, $J = 8$ ,CH/Ph), 2.48–1.41 (2H, m, CH$_2$CBr), 1.76–1.59 (4H, m, CH$_2$CH(OTBS)CH$_2$), 0.97 (3H, d, $J = 6.5$, CHCH$_3$), 0.91 (18H, s, 2 x OSiCMe$_3$), 0.06 (12H, s, 2 x OSi(CH$_3$)$_2$); $^{13}$C NMR (100 MHz; CDCl$_3$) δ 140.2 (ArC), 133.7, (C=CBr), 129.4 (ArCH), 128.3 (ArCH), 127.7, 127.6 (C=CBr), 126.1 (ArCH) 68.5 (CHOTBS), 60.0, 60.0 (CH$_2$OTBS), 42.7 (CH$_2$Ph), 40.1, 38.0 (2 x CH$_2$), 37.5, 37.5 (CHCH$_3$), 26.3, 36.2 (CH$_2$), 26.1, 26.1 (SiCMe$_3$), 19.2 (CHCH$_3$), 18.4, 18.3 (SiCMe$_3$), -4.3, -4.4 (one CH$_3$ of OSi(CH$_3$)$_2$), -5.1, -4.4 (another CH$_3$ of OSi(CH$_3$)$_2$); HRMS $m/z$ (M+H$^+$) found: 555.2672. C$_{28}$H$_{52}$BrO$_2$Si$_2$ requires 555.2684.

Following the procedure to 27 above, but using bis-TBS ether 24 (55 mg, 0.1 mmol), gave after column chromatography (petrol) bis-TBS E-alkene 28 (37 mg, 76%), as a colourless oil, a 1:1 diastereomeric mixture; $R_f = 0.63$ (0.5% Et$_2$O in petrol); $\nu_{max}$/cm$^{-1}$ (film) 2977s, 2931s, 2861s, 1644 m, 1444 s, 1382s, 1350 s, 1298 m, 1257 m, 1125 br, 1043 m, 837 s, 775 m; $^1$H NMR

(E)-5-(3,5-Dimethyl-6-phenylhex-3-en-1-yl)-2,2,3,3,9,9,10,10-octamethyl-4,8-dioxa-3,9-disilaundecane (28)

![Chemical structure](image)

Following the procedure to 27 above, but using bis-TBS ether 24 (55 mg, 0.1 mmol), gave after column chromatography (petrol) bis-TBS E-alkene 28 (37 mg, 76%), as a colourless oil, a 1:1 diastereomeric mixture; $R_f = 0.63$ (0.5% Et$_2$O in petrol); $\nu_{max}$/cm$^{-1}$ (film) 2977s, 2931s, 2861s, 1644 m, 1444 s, 1382 s, 1350 s, 1298 m, 1257 m, 1125 br, 1043 m, 837 s, 775 m; $^1$H NMR
(400 MHz; CDCl$_3$) $\delta$ 7.28–7.11 (5H, m, ArH), 4.98 (1H, d, $J$ = 9, CH=CCH$_3$), 3.82–3.74 (1H, m, CHOTBS), 3.72–3.63 (2H, m, CH$_2$OTBS), 2.67–2.56 (1H, m, CHCH$_3$), 2.55–2.48 (2H, m, CH$_2$Ph), 2.04–1.87 (2H, m, CH$_2$CCH$_3$), 1.66 (2H, q, $J$ = 6.5, CH$_2$CH$_2$OTBS), 1.55–1.46 (2H, m, CH$_2$CH$_2$CCH$_3$), 1.42 (3H, d, $J$ = 1, =CCH$_3$), 0.95 (3H, d, $J$ = 6.5, CHCH$_3$), 0.91 (18H, s, 2 x OSiCMe$_3$), 0.06 (12H, s, 2 x OSi(CH$_3$)$_2$); $^{13}$C NMR (100 MHz; CDCl$_3$) $\delta$ 141.3 (ArC), 134.4, 134.4 (C=CCH$_3$), 130.2, 130.2 (C=CCH$_3$), 129.4, 129.4 (ArCH) 128.1 (ArCH), 125.7 (ArCH) 69.4 (CHOTBS), 60.2, 60.2 (CH$_2$OTBS), 44.2, 44.2 (CH$_2$Ph), 40.2, 40.2, 36.2, 36.1, 35.4, 35.4 (all CH$_2$), 34.7 (CHCH$_3$), 26.1, 26.1 (SiCMe$_3$), 20.9, 20.9 (CHCH$_3$), 18.5, 18.3 (SiCMe$_3$), 16.3 (=CCH$_3$), -4.2, -4.4 (one CH$_3$ of OSi(CH$_3$)$_2$), -5.1 (another CH$_3$ of OSi(CH$_3$)$_2$); HRMS $m/z$ (M+H$^+$) found: 491.3734. C$_{29}$H$_{55}$O$_2$^{28}Si$_2$ requires 491.3735.

**Dimethyl (4$R$,5$R$)-4-((E)-6,8-dimethyl-9-phenyl-3-((triethylsilyloxy)non-6-en-1-yl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (SI-1)**

![Dimethyl (4R,5R)-4-((E)-6,8-dimethyl-9-phenyl-3-((triethylsilyloxy)non-6-en-1-yl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (SI-1)](attachment:attachment)

To a solution of B-OMe-9BBN (93 μL, 1 M in hexane, 0.093 mmol) in THF (400 μL) was added MeLi (78 μL, 1.2 M in Et$_2$O, 0.093 mmol). Meanwhile, a mixture of PdCl$_2$(dpdf) (3 mg, 10 mol%), aq. Cs$_2$CO$_3$ (45 mg, 3 M, 0.138 mmol), AsPh$_3$ (4 mg, 30 mol%) and alkylated tartrate 14 (from rac-17) (30 mg, 0.046 mmol) was prepared in DMF (400 μL) at rt. To the mixture containing 14 and the catalyst system, the borinate complex solution was added dropwise and then the mixture stirred at rt for 40 h. The reaction mixture was then quenched with water (1 mL), extracted with Et$_2$O (3 × 2 mL), washed with brine (2 mL) and dried (MgSO$_4$). Evaporation under reduced pressure followed by column chromatography (10–30% EtOAc in petrol) gave E-alkene tartrate SI-1 (20 mg, 75%), as a colourless oil, a mixture of 4 diastereoisomers. $R_f$ = 0.53 (20% EtOAc in petrol); $\nu_{\text{max/cm}}^{-1}$ (film) 3019 s, 2956 s, 2876 m, 1750 m, 1453 m, 1384 m; $^1$H NMR (500 MHz; CDCl$_3$) $\delta$ 7.27–7.10 (5H, m, ArH), 4.93 (2H, d, $J$ = 8, CH=CCH$_3$ and CHCO$_2$Me), 3.81 (3H, s, OMe), 3.79 (3H, s, OMe), 3.62–3.53 (1H, m, CHOTES), 2.63–2.54 (1H, m, CHCH$_3$), 2.51 (1H, pd, $J$ = 7, CH$_2$Ph), 2.00–1.74 (4H, m, 2 x CH$_2$), 1.68–1.59 (5H, m, CH$_2$ and one Me of CMe$_2$), 1.47–1.41 (5H, m, CH$_2$ and second Me of CMe$_2$), 1.38 (3H, s, =CCH$_3$), 0.94 (12H, pq, $J$ = 7.5, OSi(CH$_2$CH$_3$)$_3$ and CHCH$_3$), 0.57 (6H, q, $J$ = 7.5, OSi(CH$_2$CH$_3$)$_3$); $^{13}$C NMR (125 MHz; CDCl$_3$) $\delta$ 172.6, 172.5 (CO$_2$Me), 169.0, 168.8
(CO$_2$Me), 141.3 (ArC), 134.0, 134.0 (C=CCH$_3$), 130.4, 130.4 (C=CCH$_3$), 129.4 (ArCH) 128.1, 128.1 (ArCH), 125.7 (ArCH), 112.8, 112.7 (CMe$_2$), 86.1, 85.8 (quat. C), 80.3, 80.2 (CHCO$_2$Me), 71.9, 71.9 (CHOTES), 53.0 (OMe), 52.5, 52.4 (OMe), 44.2, 42.1 (CH$_2$Ph), 36.0, 35.9, 35.5, 35.4 (all CH$_2$), 34.7, 34.7 (CHCH$_3$), 31.4, 31.1, 30.7, 30.2 (all CH$_2$), 27.9, 27.8, 26.2, 26.1 (C(CH$_3$)$_2$), 20.9, 20.9 (CHCH$_3$), 16.2, 16.2 (=CCH$_3$), 7.1 (OSi(CH$_2$CH$_3$)$_3$), 5.2, 5.2 (OSi(CH$_2$CH$_3$)$_3$); HRMS m/z (M+Na$^+$) found: 599.3371. C$_{32}$H$_{52}$O$_7$Si requires 599.3374. [$^1$H and $^{13}$C NMR spectra of alkylated tartrate 14 (from rac-17) are also provided in Section 5 below.]

Table S1: Optimisation of the conditions for methylation cross–coupling with alkylated tartrate 14.a

<table>
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<th>Entry</th>
<th>Base</th>
<th>Ligand (Pd:L; 1:4)</th>
<th>Solvent (5:5:1)</th>
<th>Temp. (°C)</th>
<th>Time (h)</th>
<th>14:SI-1b</th>
<th>Yield (%)c</th>
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<td>48</td>
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<td>-</td>
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<td>rt</td>
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<td>THF</td>
<td>50</td>
<td>48</td>
<td>70:30</td>
<td>-</td>
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<td>-</td>
<td>THF/DMF</td>
<td>rt</td>
<td>48</td>
<td>25:75</td>
<td>-</td>
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<td>-</td>
<td>THF/DMF/H$_2$O</td>
<td>rt</td>
<td>48</td>
<td>Trace 14</td>
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<td>-</td>
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<td>48</td>
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<td>Ph$_3$As</td>
<td>THF/DMF/H$_2$O</td>
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<td>75</td>
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<tr>
<td>8</td>
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<td>Ph$_3$As</td>
<td>THF/DMF/MeOH</td>
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<td>8</td>
<td>0</td>
<td>68</td>
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</tbody>
</table>

a Reaction conditions: alkylated tartrate 14 (1 equiv.), B-MeO-9BBN (2 equiv.), MeLi (2 equiv.), PdCl$_2$(dppf) (10 mol%).
b Ratio by integration of crude $^1$H NMR spectra. c Isolated yield of SI-1.

(b) Total synthesis of (−)-6,7-dideoxysqualenetatin H5

(−)-(R,E)-Ethyl 4-methyl-5-phenylpent-2-enoate (18)

A mixture of ethyl (triphenylphosphoranylidene)acetate (9.5 g, 27 mmol) and (R)-2-methyl-3-phenylpropanal 17 (3.7 g, 25 mmol) in CH$_2$Cl$_2$ (23 mL) was stirred for 48 h at rt. The solution was then diluted with hexane (15 mL), filtered through Celite$^e$ and evaporated under reduced pressure. The residue was purified by column chromatography (10% EtOAc in petrol) to give E-enoate 18 (5.23 g, 96%) as a colourless oil; $R_t = 0.78$ (10% EtOAc in petrol); [$\alpha$]$_D^{25} = -52$ (c=1.0, CHCl$_3$); $\nu_{max}$/cm$^{-1}$(film) 3027 w, 2976 s, 2928 m, 1715 s, 1650 m, 1454 m, 1367 w, 1267 m, 1204 w, 1174 s, 1040 m, 745 m, 699 m; $^1$H NMR (400 MHz; CDCl$_3$) δ 7.25–7.03 (5H,
m, ArH), 6.88 (1H, dd, J = 15.5, 6.5, CH=CHCO₂), 5.68 (1H, d, J = 15.5, CH=CHCO₂), 4.10 (2H, q, J = 7, OCH₂CH₃), 2.69 (1H, dd, J = 12, 5, CHHPh), 2.60–2.46 (2H, m, CHHPh and CHCH₃), 1.20 (3H, t, J = 7, OCH₂CH₃), 0.97 (3H, d, J = 6.5, CHCH₃); ¹³C NMR (100 MHz; CDCl₃) δ 166.9 (CO₂Et), 153.6 (CH=CHCO₂), 139.7 (ArC), 129.2 (ArCH), 128.4 (ArCH), 126.3 (ArCH), 120.0 (CH=CHCO₂), 60.3 (CO₂CH₂CH₃), 42.5 (CH₂Ph), 38.3 (CHCH₃), 18.8 (CHCH₃), 14.4 (CO₂CH₂CH₃); HRMS m/z (M+H⁺) found: 219.1380. C₁₄H₁₉O₂ requires 219.1379.

(−)-(R,Z)-Ethyl 2-bromo-4-methyl-5-phenylpent-2-enoate (19)

Bromine (1.65 mL, 32.2 mmol) was added dropwise to a stirred solution of E-enoate 18 (5.20 g, 23.8 mmol) in CH₂Cl₂ (46 mL) at 0 °C. After 2 h, the solution was diluted with sat. aq. Na₂S₂O₃ (20 mL), extracted with Et₂O (2×30 mL), dried (MgSO₄) and concentrated under reduced pressure. Et₃N (16.5 mL, 119 mmol) was added to a stirred solution of the residue in CH₂Cl₂ (46 mL) at rt. After 12 h, the heterogeneous mixture was concentrated under reduced pressure followed by column chromatography (5% EtOAc in petrol) to give Z-α-bromoenoate 19 (6.43 g, 91%) as a pale yellow oil; Rf = 0.48 (5% EtOAc in petrol); [α]₂⁰D = −7.6 (c=1.0, CHCl₃); νₘₐₓ/cm⁻¹(film) 3028 w, 2961 s, 2872 m, 2360 w, 1731 s, 1538 m, 1454 m, 1367 w, 1249 s, 1094 w, 1035 m, 749 m, 700 m;¹H NMR (400 MHz; CDCl₃) δ 7.32–7.14 (6H, m, ArH and CH=CBr), 4.27 (2H, q, J = 7, OCH₂CH₃), 3.11–3.00 (1H, m, CHCH₃), 2.81 (1H, dd, J = 13.5, 6.5, CHHPh), 2.62 (1H, dd, J = 13.5, 8, CHHPh), 1.33 (3H, t, J = 7, OCH₂CH₃), 1.06 (3H, d, J = 6.5, CHCH₃), ¹³C NMR (100 MHz; CDCl₃) δ 162.6 (CO₂Et), 150.4 (CH=CBr), 139.1 (ArC), 129.2 (ArCH), 128.5 (ArCH), 126.4 (ArCH), 115.5 (CH=CBr), 62.6 (OCH₂CH₃), 41.7 (CH₂Ph), 38.7 (CHCH₃), 18.3 (CHCH₃), 14.3 (OCH₂CH₃); HRMS m/z (M+NH₄⁺) found: 314.0752. C₁₄H₂₁⁷⁹BrNO₂ requires 314.0750.

(−)-(R,Z)-2-Bromo-4-methyl-5-phenylpent-2-en-1-ol (SI-2)

DIBAL–H (60 mL, 1.0 M in hexanes, 62.2 mmol) was added dropwise to a solution of Z-α-bromoenoate 19 (6.16 g, 20.7 mmol) in CH₂Cl₂ (180 mL) at −78 °C. After stirring at −78 °C for 2 h, the mixture was diluted with ether and warmed to 0 °C. Water (2.4 mL) was added dropwise, followed by 15% aq. NaOH (2.4 mL), and then further of water (6 mL). The mixture
was stirred for 15 min, dried (MgSO$_4$), and filtered. Evaporation under reduced pressure followed by column chromatography (10% EtOAc in petrol) gave allylic alcohol **SI-2** (4.29 g, 81%), as a yellow oil; $R_f = 0.16$ (10% EtOAc in petrol); $[\alpha]_D^{23} = -8.0 (c=1.0, \text{CHCl}_3)$; $\nu_{\text{max}}/\text{cm}^{-1} (\text{film})$ 3605 s, 3480 br, 3028 s, 2927 s, 2253 s, 1494 m, 1453 s, 1378 s, 1262 m, 1100 m, 907 s; $^1$H NMR (400 MHz; CDCl$_3$) $\delta$ 7.30–7.20 (5H, m, ArH), 5.86 (1H, d, $J = 9, \text{CH}=$CBr), 4.13 (2H, s, CH$_2$OH), 2.92–2.80 (1H, m, $CHCH_3$), 2.66 (1H, d, $J = 13.5, 6.5, \text{CH}=$HPh), 2.49 (1H, dd, $J = 13.5, 8, \text{CH}=$HPh), 1.79 (1H, br, OH), 0.93 (3H, d, $J = 6.5, \text{CH}=$H$_3$); $^{13}$C NMR (100 MHz; CDCl$_3$) $\delta$ 139.8 (ArC), 135.3 (C=CBr), 129.3 (ArCH) 128.3 (ArCH), 126.2 (ArCH), 125.8 (C=CBr), 68.5 (CH$_2$OH), 42.4 (CH$_2$Ph), 37.5 (CHCH$_3$), 19.0 (CH$_3$); HRMS $m/z$ (M+NH$_4^+$) found: 272.0642. C$_{12}$H$_8^{79}$BrNO requires 272.0645.

**(-)-(R,Z)-(4,5-Dibromo-2-methylpent-3-ethyl)benzene (20)**

![Diagram](image)

To a stirred solution of allylic alcohol **SI-2** (6.32 g, 24.8 mmol) and Ph$_3$P (24.3 g, 92.6 mmol) in MeCN (400 mL) was added CBr$_4$ (30.9 g, 93.2 mmol) at 0 °C. After 1 h at 0 °C, the reaction mixture was allowed to warm to rt, and then passed through a short silica gel column using 20% ether in petrol. Evaporation under reduced pressure followed by column chromatography (petrol) gave allylic bromide **20** (8.98 g, quant), as a yellow oil; $R_f = 0.47$ (petrol); $[\alpha]_D^{23} = -3.8 (c=1.0, \text{CHCl}_3)$; $\nu_{\text{max}}/\text{cm}^{-1} (\text{film})$ 3028 m, 2964 m, 2252 s, 1495 m, 1453 s, 1214 s, 908 s; $^1$H NMR (400 MHz; CDCl$_3$) $\delta$ 7.31–7.15 (5H, m, ArH), 5.96 (1H, d, $J = 9, \text{CH}=$CBr), 4.21 (2H, s, CH$_2$Br), 2.95–2.83 (1H, m, $CHCH_3$), 2.73 (1H, dd, $J = 13.5, 6.5, \text{CH}=$HPh), 2.57 (1H, dd, $J = 13.5, 7.5, \text{CH}=$HPh), 1.00 (3H, d, $J = 6.5, \text{CH}=$H$_3$); $^{13}$C NMR (100 MHz; CDCl$_3$) $\delta$ 139.4 (ArC), 139.4 (C=CBr), 129.4 (ArCH) 128.4 (ArCH), 126.3 (ArCH), 121.6 (C=CBr), 41.1 (CH$_2$Ph), 39.0 (CH$_2$Br), 38.2 (CHCH$_3$), 18.7 (CH$_3$); HRMS $m/z$ (M$^+$) found: 315.9465. C$_{12}$H$_8^{79}$Br$_2$ requires 315.9457.

**(-)-(R,Z)-Ethyl 6-bromo-8-methyl-3-oxo-9-phenylnon-6-enoate (21)**

![Diagram](image)

The procedure of Huckin and Weiler$^9$ was followed with slight modifications. Ethyl acetoacetate (4.20 mL, 33.4 mmol) was added dropwise to a suspension of NaH (1.48 g, 60%
in mineral oil, 37.0 mmol) in THF (250 mL) at 0 °C. The resulting mixture was stirred for 10 min until the solution became clear. n-BuLi (13.8 mL, 2.5 M in hexanes, 34.6 mmol) was added dropwise over 30 min and the reaction mixture was stirred at 0 °C for 10 min. A solution of allylic bromide 20 (3.8 g, 11.9 mmol) in THF (20 mL) at 0 °C was then added via cannula over 5 min. The reaction mixture was then stirred at 0 °C for 30 min, then at rt for 10 min and quenched with HCl (20 mL, 2M). The mixture was extracted with Et₂O (2 x 100 mL). The combined organic layers were washed with water until pH was neutralised (2 x 50 mL), dried (MgSO₄) and concentrated under reduced pressure. Purification of the residue by column chromatography (0–20% Et₂O in petrol) gave β-ketoester 21 (3.44 g, 79%), as a pale yellow oil; Rf = 0.2 (10% Et₂O in petrol); [α]D²₃ = −11.4 (c=1.0, CHCl₃); νmax/cm⁻¹(film) 2962 m, 2927 m, 1746 s, 1716 s, 1651 m, 1454 m, 1368 m, 1317 s, 1033 s, 746 s, 700 s; ¹H NMR (400 MHz; CDCl₃) δ (discernable) of major keto-tautomer: 7.22–7.06 (5H, m, ArH), 5.49 (1H, d, J = 8.5, CH=CBr), 4.13 (2H, q, J = 7, OCH₂CH₃), 3.34 (2H, s, CH₂(CO)₂), 2.83–2.72 (1H, m, CHCH₃), 2.71–2.56 (5H, m, CH₂CH₂CO and CHHPh), 2.46 (1H, dd, J = 13.5, 7.5, CHHPh), 1.29 (3H, t, J = 7, OCH₂CH₃), 0.89 (3H, d, J = 6.5, CHCH₃); ¹³C NMR (100 MHz; CDCl₃) δ (discernable) of major keto-tautomer: 201.3 (CH₂COCH₂), 167.1 (CO₂Et), 140.0 (ArC), 135.4 (C=CBr), 129.4 (ArCH) 128.2 (ArCH), 126.1 (ArCH), 125.0 (C=CBr), 61.6 (OCH₂CH₃), 49.6 (COCH₂CO), 42.5 (CH₂Ph), 41.8 and 38.0 (CH₂CH₂CO), 35.5 (CHCH₃), 19.2 (CHCH₃), 14.3 (OCH₂CH₃); ¹H NMR (400 MHz; CDCl₃) δ (discernable) of minor enol-tautomer: 12.00 (0.1H, s, CH=COH), 4.91 (0.1H, s, CH=COH); ¹³C NMR (100 MHz; CDCl₃) δ (discernable) of minor enol-tautomer: 135.45 (C=CBr), 129.3 (ArCH), 90.2 (CH=COH), 60.2 (OCH₂CH₃), 42.5 (CH₂Ph), 39.0 and 38.3 (CH₂CH₂CO), 34.1 (CHCH₃), 19.1 (CHCH₃), 14.4 (OCH₂CH₃); HRMS m/z (M+NH₄⁺) found: 384.1168. C₁₈H₂₇⁷⁹BrNO₃ requires 384.1169.

(−)-(8R,Z)-6-Bromo-8-methyl-9-phenylnon-6-ene-1,3-diol (8R-22)

A solution of β-ketoester 21 (3.20 g, 8.71 mmol) in THF (30 mL) was added to a suspension of NaBH₄ (1.21 g, 32.0 mmol) in THF (100 mL). The reaction mixture was heated to reflux. MeOH (12 mL) was added dropwise to the refluxing mixture over 10 min and then reflux continued for 1 h. The mixture was then allowed to cool to rt and water (50 mL) was added. The mixture was extracted with Et₂O (3 x 100 mL) and the combined organic layers dried (MgSO₄). Evaporation under reduced pressure followed by column chromatography (20%
petrol in Et$_2$O) gave 1,3-diol 8R-22 (2.60 g, 91%), as a yellow oil, a 1:1 epimeric mixture at C–3; $R_f$=0.19 (20% petrol in Et$_2$O); [α]$^23_{D}$ = -8.1 (c=1.0, CHCl$_3$); $\nu_{\text{max}}$/cm$^{-1}$(film) 3351 br, 3027 m, 2925 s, 1654 w, 1602 w, 1495 m, 1453 s, 1059 s, 744 s, 700 s; $^1$H NMR (400 MHz; CDCl$_3$) δ 7.30–7.15 (5H, m, ArH), 5.53 (1H, d, J = 8.5, CH=CHBr), 3.89–3.60 (3H, m, CH$_2$OH and CHOH), 3.01–2.84 (3H, m, CHCH$_3$ and 2 x OH), 2.72–2.41 (4H, m, CH$_2$CH$_2$CBr and CH$_2$Ph), 1.73–1.58 (4H, m, CH$_2$CH(OH)CH$_2$), 0.98 (3H, pt, J = 6.5, CHCH$_3$); $^{13}$C NMR (100 MHz; CDCl$_3$) δ 140.3, 140.1 (ArC), 134.4, 134.3 (C=CHBr), 129.3, 129.2 (ArCH) 128.2 (ArCH), 126.8 (C=CHBr), 126.1, 126.0 (ArCH) 70.9, 70.5 (CHOH), 61.6 (CH$_2$OH), 42.6, 42.5 (CH$_2$Ph), 38.4, 38.3, 37.9, 37.8, 37.6 (CH$_2$CH$_2$CH(OH)CH$_2$), 36.2, 35.8 (CHCH$_3$), 19.4, 19.2 (CH$_3$); HRMS m/z (M+H$^+$) found: 344.1222. C$_{16}$H$_{27}$BrNO$_2$ requires 344.1220.

(−)-(8R,Z)-6-Bromo-1-iodo-8-methyl-9-phenylnon-6-en-3-ol (SI-3)

A solution of Ph$_3$P (2.0 g, 7.6 mmol), imidazole (0.9 g, 13 mmol) and I$_2$ (1.0 g, 3.9 mmol) in CH$_2$Cl$_2$ (75 mL) was added dropwise via cannula over 30 min to a stirred solution of 1,3-diol 8R-22 (2.2 g, 6.7 mmol) in CH$_2$Cl$_2$ (25 mL) at 0 ºC. After a further 1 h at 0 ºC, the solution was warmed to rt and stirred overnight. The solution was then re-cooled to 0 ºC, and I$_2$ (1.0 g, 3.9 mmol) was added portionwise over 5 min. The suspension was then stirred for 30 min at 0 ºC, then filtered through Celite®, washed through with CH$_2$Cl$_2$ (30 mL) and concentrated under reduced pressure. Purification of the residue by column chromatography (3% acetone in petrol) gave iodo alcohol SI-3 (2.04 g, 70%), as a yellow oil, a 1:1 epimeric mixture at C–3; $R_f$ = 0.24 (3% acetone in petrol); [α]$^23_{D}$ = -32.2 (c=1.0, CHCl$_3$); $\nu_{\text{max}}$/cm$^{-1}$ (film) 3424 br, 2925 w, 1651 m, 1494 w, 1453 w; $^1$H NMR (400 MHz; CDCl$_3$) δ 7.31–7.15 (5H, m, ArH), 5.56–5.50 (1H, m, CH=CHBr), 3.71–3.63 (0.5H, m, CHOH), 3.47–3.39 (0.5H, m, CHOH), 3.33–3.16 (2H, m, CH$_2$I), 2.99–2.85 (1H, m, CHCH$_3$), 2.72–2.47 (4H, m, CH$_2$ and CH$_2$Ph), 1.99–1.82 (2H, m, CH$_2$), 1.75–1.59 (2H, m, CH$_2$), 1.41 (0.5H, d, J = 5.5, CHOH), 1.28 (0.5H, d, J = 5.5, CHOH), 1.03–0.97 (3H, m, CHCH$_3$); $^{13}$C NMR (100 MHz; CDCl$_3$) δ 140.4, 140.1 (ArC), 134.8, 134.6 (C=CHBr), 129.3, 129.3 (ArCH) 128.3, 128.3 (ArCH), 126.6, 126.6 (C=CHBr), 126.1, 126.1 (ArCH), 70.6, 70.2 (CHOH), 42.7, 42.6 (CH$_2$Ph), 41.2, 40.7, 38.0, 37.9, 37.9, 37.5 (all CH$_2$), 35.6, 34.9 (CHCH$_3$), 19.6, 19.3 (CH$_3$), 2.6, 3.0 (CH$_2$I); HRMS m/z (M+H$^+$) found: 454.0240. C$_{16}$H$_{26}$BrNO requires 454.0237.
(--)([(8R,Z)-6-Bromo-1-iodo-8-methyl-9-phenylnon-6-en-3-yl)oxy]triethylsilane (16)

2,6-Lutidine (1.8 mL, 16 mmol) and TESOTf (1.8 mL, 8.2 mmol) were added to a stirred solution of iodo alcohol SI-3 (2.0 g, 4.5 mmol) in CH₂Cl₂ (140 mL) at −78 °C. After 2 h, the mixture was diluted with sat. aq. NaHCO₃ (50 mL) and extracted with CH₂Cl₂ (2 × 100 mL). The combined organic layers were washed with HCl (50 mL, 0.1 M), water (2 × 50 mL), brine (2 × 50 mL), dried (MgSO₄) and evaporated under reduced pressure. Purification of the residue by column chromatography (10% Et₂O in petrol) gave iodide 16 (2.3 g, 93%), as a colourless oil, a 1:1 epimeric mixture at C–3; [α]₀²⁺ = 0.69 (10% Et₂O in petrol); [α]₀²⁺ = −26.1 (c=1.0, CHCl₃); νₘₐₓ/cm⁻¹ (film) 2952 w, 2866 m, 1495 w, 1451 w; ¹H NMR (400 MHz; CDCl₃) δ 7.30–7.15 (5H, m, ArH), 5.50 (1H, d, J = 8.5, CH=CBr), 3.78–3.69 (1H, m, CHOTES), 3.24–3.14 (2H, m, CH₂I), 2.93–2.83 (1H, m, CHCH₃), 2.71 (1H, dd, J = 13.5, 6.5, CHHPh), 2.53 (1H, dd, J = 13.5, 8, CHHPh), 2.41 (2H, t, J = 7.5, CH₂CBr), 1.98–1.91 (2H, m, CH₂), 1.76–1.59 (2H, m, CH₂), 1.01–0.94 (12H, m, OSi(CH₂CH₃)₃ and CHCH₃), 0.63 (6H, q, J = 7.5, OSi(CH₂CH₃)₃); ¹³C NMR (100 MHz; CDCl₃) δ 140.1 (ArC), 134.2 (C=CBr), 129.4 (ArCH) 128.3, 128.3 (ArCH), 126.9 (C=CBr), 126.0 (ArCH), 71.2, 71.2 (CHOTES), 42.6, 42.6 (CH₂Ph), 40.9, 40.8 (CH₂), 38.0 (CHCH₃), 37.3, 35.6, 35.5 (all CH₂), 19.2, 19.2 (CHCH₃), 7.1 (OSi(CH₂CH₃)₃), 5.3 (OSi(CH₂CH₃)₃), 3.0, 2.9 (CH₂I); HRMS m/z (M+NH₄⁺) found: 568.1097. C₂₂H₄⁰⁷⁹BrINOSi requires 568.1102.

(--)-Dimethyl (4R,5R)-4-((8R,Z)-6-bromo-8-methyl-9-phenyl-3-((triethylsilyl)oxy)non-6-en-1-yl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (8'R-14)

A solution of LDA [prepared from i-Pr₂NH (300 μL, 2.14 mmol) and n-BuLi (1.10 mL, 1.6 M in hexanes, 1.76 mmol)] in THF (10 mL) at −78 °C, was added dropwise over 3 h to a mixture of dimethyl-2,3-O-isopropylidene-L-tartrate (13) (0.25 mL, 1.36 mmol) and iodide 16 (645 mg, 1.17 mmol) in THF (20 mL) and HMPA (4 mL) at −78 °C. After 72 h at −78 °C, the mixture was quenched with sat. aq. NH₄Cl (10 mL) and extracted with Et₂O (3 × 10 mL). The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure. Purification of
the residue by column chromatography (10% Et₂O in petrol) gave alkylation tartrate 8'R-14 (531 mg, 71%), as a yellow oil, an ~1:1 epimeric mixture at C–3'; $\beta = 0.18$ (5% Et₂O in petrol); $[\alpha]^{23}_D = -42.1$ (c=1.0, CHCl₃); ν max/cm⁻¹ (film) 3059 s, 2956 s, 1756 s, 1655 m, 1495 m, 1455 m, 1375 m, 1265 s, 1104 m, 807 s, 743 s, 739 s; ¹H NMR (500 MHz; CDC₁₃) δ 7.29–7.14 (5H, m, ArH), 5.47 (1H, d, J = 8.5, CH=CHBr), 4.94 and 4.92 (1H, 2 x s, CH(CO₂Me)), 3.82 (3H, s, OMe), 3.80 (3H, s, OMe), 3.65–3.57 (1H, m, CHOTES), 2.91–2.82 (1H, m, CHCHOH), 2.72–2.67 (1H, m, CHHPh), 2.54–2.48 (1H, m, CHHPh), 2.42–2.34 (2H, m, CH₂CBr), 1.97–1.89 (1H, m, C(CO₂Me)CH₃CH₂CH₂CHOTES), 1.81–1.70 (1H, m, C(CO₂Me)CH₃CH₂CH₂CHOTES), 1.64–1.58 (7H, m, C(CO₂Me)CH₃CH₂CH₂CHOTES, CH₂CH₂CBr and one Me of CMe₂), 1.44 (3H, s, one Me of CMe₂), 0.97–0.92 (12H, m, OSi(CH₂CH₃)₃ and CHCH₃), 0.60–0.54 (6H, m, OSi(CH₂CH₃)₃); ¹³C NMR (125 MHz; CDCl₃) δ 172.6, 172.4 (CO₂Me), 169.0, 168.7 (CO₂Me), 140.2, 140.2 (ArC), 134.0, 133.9 (C=CHBr), 129.4 (ArCH) 128.3, 128.3 (ArCH), 127.2 (C=CHBr), 126.1 (ArCH), 112.9, 112.7 (CMe₂), 86.1, 85.7 (quat. C), 80.3, 80.3 (CHCO₂Me), 71.0, 70.9 (CHOTES), 53.0 (OMe), 52.47, 52.45 (OMe), 42.6, 42.6 (CH₂Ph), 38.0, 37.5 (CHCH₃), 36.1, 36.0, 31.2, 30.9, 30.5, 30.2, 27.9, 27.8 (all CH₂), 26.2, 26.1 (C(CH₃)₃), 19.2 (CHCH₃), 7.1 (OSi(CH₂CH₃)₃), 5.2 (OSi(CH₂CH₃)₃); HRMS m/z (M+NH₄⁺) found: 658.2766, C₃₁H₅₃⁷⁹BrNO₇Si requires 658.2769.

(–)-Dimethyl (4R)-4-((8R,Z)-6-bromo-8-methyl-9-phenyl-3-((triethylsilyl)oxy)non-6-en-1-yl)-5-hydroxy-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (29)

Alkylation tartrate 8'R-14 (1.0 g, 1.55 mmol) in THF (8 mL) at −78 °C was added over 30 min to a stirred solution of LDA [prepared from i-Pr₂NH (0.3 mL, 2.0 mmol) and n-BuLi (0.8 mL, 2.5 M in hexanes, 2.0 mmol)] in THF (6 mL) at −78 °C. After 15 min, MoOPH₂⁺ (1.6 g, 3.8 mmol) was added via a solid addition tube over 5 min at −78 °C. The reaction mixture was stirred for additional 30 min, then warmed to −40 °C. The mixture was stirred at −40 °C overnight, then warmed to −20 °C for 1 h before sat. aq. Na₂SO₃ (10 mL) was added. The mixture was then allowed to warm to rt over 1 h, extracted with Et₂O (3 × 20 mL), and the combined organic layers washed with sat. aq. CuSO₄ (10 mL), dried (MgSO₄) and concentrated under reduced pressure. Purification of the residue by column chromatography (0–50% Et₂O
in petrol) gave hydroxy acetonide 29 (726 mg, 71%), as a yellow oil, a mixture of 4 diastereomers; \( R_f = 0.13 \) (40% Et\(_2\)O in petrol); \([\alpha]_D^{23} = -20.1 \) (c=1.0, CHCl\(_3\)); \( \nu_{\text{max}}/\text{cm}^{-1}(\text{film}) \) 3426 br, 2963 s, 2086 w, 1752 s, 1644 m, 1421 m, 1264 s, 806 s, 738 s; \(^1\)H NMR (500 MHz; CDCl\(_3\)) \( \delta \) 7.29–7.14 (5H, m, ArH), 5.48–5.43 (1H, m, CH=CBr), 4.06, 4.58, 4.51 and 4.50 (1H, 4 x s, OH), 3.89, 3.80, 3.78 and 3.70 (6H, 4 x s, 2 x OMe), 3.69–3.58 (1H, m, CHOTES), 2.90–2.81 (1H, m, CHCH\(_3\)), 2.72–2.66 (1H, m, CH/HPh), 2.54–2.47 (1H, m, CH/HPh), 2.43–2.35 (2H, m, CH\(_2\)Br), 2.15–1.81 (2H, m, C(CO\(_2\)Me)\(\text{CH}_2\)\(\text{CH}_2\)), 1.78–1.53 (10H, m, CH\(_2\)CH\(_2\)Br, C(CO\(_2\)Me)\(\text{CH}_2\)\(\text{CH}_2\) and CMe\(_2\)), 0.98–0.92 (12H, m, OSi(CH\(_2\)CH\(_3\))\(_3\) and CHCH\(_3\)), 0.61–0.53 (6H, m, OSi(CH\(_2\)CH\(_3\))\(_3\)); \(^{13}\)C NMR (125 MHz; CDCl\(_3\)) \( \delta \) 171.7, 170.3, 170.2, 170.1, 169.3, 169.2 (CO\(_2\)Me), 140.1, 140.1 (ArC), 134.0, 133.9, 133.8, 133.7 (C=CBr), 129.3, 129.3 (ArCH) 128.2, 128.2 (ArCH), 127.3, 127.2, 127.2, 127.1 (C=CBr), 126.0, 126.0, 126.0 (ArCH), 114.3, 114.3, 113.6, 113.5 (CMe\(_2\)), 102.2, 102.0, 101.9, 101.8 (COH), 92.9, 92.7, 91.7, 91.1 (quat. C), 70.9, 70.8, 70.7, 70.6 (CHOTES), 54.1, 54.1, 54.0, 52.7, 52.5 (OMe), 42.6, 42.6, 42.6, 42.6 (CH\(_2\)Ph), 38.0, 38.0, 37.9, 37.9 , 37.9, 37.7, 37.5, 37.4, 37.2, 36.0, 35.9, 35.7, 31.9, 31.9, 31.4, 31.3, 31.3, 31.2, 31.2, 30.9 29.3, 29.2, 28.7, 28.7, 28.6, 28.4, 28.3, 27.5, 27.5, then 19.1, 19.1 (CHCH\(_3\)), 7.1 (OSi(CH\(_2\)CH\(_3\))\(_3\)), 5.2, 5.2, 5.2, 5.1 (OSi(CH\(_2\)CH\(_3\))\(_3\)); HRMS \( m/z \) (M+H\(^+\)) found: 657.2454. C\(_{31}\)H\(_{50}\)\(^{79}\)BrO\(_8\)Si requires 657.2453.

\((-\))Dimethyl (2\(R\))-2-((8\(R\),\(Z\))-bromo-8-methyl-9-phenyl-3-((triethylsilyl)oxy)non-6-en-1-yl)-3-oxo-2-((triethylsilyl)oxy)succinate (30)

A mixture of hydroxy acetonide 29 (302 mg, 0.46 mmol) and H\(_2\)SO\(_4\) (40 mL, 0.1 M in MeOH) was stirred at rt. After 24 h, pyridine (1.0 mL, 12.4 mmol) was added, the mixture was concentrated under reduced pressure and the residue was diluted with Et\(_2\)O (30 mL) and filtered. The filtrate was concentrated under reduced pressure to give the corresponding lactol which was used in the next step without further purification. To the crude lactol in dry DMF (2 mL) at \(-10 \, ^\circ\text{C}\) was added TESCl (0.50 mL, 2.98 mmol) and imidazole (272 mg, 4.0 mmol). The reaction mixture was stirred at \(-10 \, ^\circ\text{C}\) for 24 h, and then at rt for 24 h. The mixture was then concentrated under reduced pressured and purified by chromatography (florisil\(^\circledR\), 0–20% Et\(_2\)O in petrol) to give bis-TES ether 30 (313 mg, 95%), as a colourless oil, an \( \sim 1:1 \) epimeric
mixture at C–3'; $R_f= 0.7$ (60% Et$_2$O in petrol); $[\alpha]^23_D=-18.6$ (c=1.0, CHCl$_3$); $\nu_{max}$/cm$^{-1}$(film) 3055 m, 2957 s, 2877 m, 1741 s, 1455 m, 1266 s, 1092 m, 1015 m, 739 s; $^1$H NMR (400 MHz; CDCl$_3$) $\delta$ 7.29–7.15 (5H, m, ArH), 5.49 (1H, d, $J = 8.5$, CH=CBr), 3.84 (3H, s, OMe), 3.77 (3H, s, OMe), 3.70–3.63 (1H, m, CHOTES), 2.94–2.83 (1H, m, CHCH$_3$), 2.75–2.66 (1H, m, CHHPh), 2.57–2.49 (1H, m, CHHPh), 2.41 (2H, t, $J = 7.5$, CH$_2$CBr), 2.24–1.92 (2H, m, C(O$_2$Me)$_2$CH$_2$CH$_2$), 1.72–1.45 (4H, m, CH$_2$CH$_2$CBr and C(O$_2$Me)$_2$CH$_2$CH$_2$), 1.00–0.91 (21H, m, 2 x OSi(CH$_2$CH$_3$)$_3$ and CHCH$_3$), 0.73–0.56 (12H, m, 2 x OSi(CH$_2$CH$_3$)$_3$); $^{13}$C NMR (100 MHz; CDCl$_3$) $\delta$ 190.8 (C=O), 170.0 (CO$_2$Me), 162.9 (CO$_2$Me), 140.0 (ArC), 133.8 (C=CBr), 129.2 (ArCH), 128.1 (ArCH), 127.1 (C=CBr), 125.9 (ArCH), 84.0, 84.0 (quat C), 77.6, 70.5 (CHOTES), 52.8, 52.6, 52.6 (2 x OMe), 42.5, 42.5 (CH$_2$Ph), 37.9, 37.8 (CHCH$_3$), 37.4, 37.2, 35.5, 35.3, 32.5, 32.2, 30.1, 29.7 (all CH$_2$), 19.0, 19.0 (CHCH$_3$), 6.9, 6.8, 6.7, 6.6 (OSi(CH$_2$CH$_3$)$_3$), 5.8, 5.7, 5.1, 5.0 (OSi(CH$_2$CH$_3$)$_3$); HRMS m/z (M+NH$_4^+$) found: 730.3168. C$_{34}$H$_{61}$BrNO$_7$Si$_2$ requires 730.3164.

$(-)$-Dimethyl (Z)-2-((8R,Z)-6-bromo-8-methyl-9-phenyl-3-(((triethylsilyl)oxy)non-6-en-1-yl)-3-(2-(p-tolyl)hydrazineylidene)-2-(((triethylsilyl)oxy)succinate (SI-4)

A mixture of bis-TES ether 30 (90 mg, 0.126 mmol) and TsNHNH$_2$ (35 mg, 0.19 mmol) in THF (1.5 mL) was refluxed for 20 h. The mixture was concentrated under reduced pressure and purified by column chromatography (0–60% Et$_2$O in petrol) to give Z$^{10}$-hydrazone SI-4 (52 mg, 47% (58% brsm)), as a pale yellow oil, an ~1:1 epimeric mixture at C–3'; $R_f= 0.61$ (60% Et$_2$O in petrol); $[\alpha]^23_D=-21.5$ (c=1.0, CHCl$_3$); $\nu_{max}$/cm$^{-1}$(film) 3180 br, 2956 m, 2932 m, 1752 s, 1704 s, 1496 m, 1053 m; $^1$H NMR (400 MHz; CDCl$_3$) $\delta$ 11.72, 11.69 (1H, 2 x s, NH), 7.84 (2H, d, $J = 8.5$, 2 x ArCH), 7.32–7.23 (4H, m, 4 x ArCH), 7.30–7.14 (3H, m, 3 x ArCH), 5.52 (1H, d, $J = 8.5$, CH=CBr), 3.75 (3H, s, OMe), 3.67 (3H, s, OMe), 3.65–3.59 (1H, m, CHOTES), 2.94–2.83 (1H, m, CHCH$_3$), 2.72 (1H, dd, $J = 13.5$, 6, CHHPh), 2.54–2.47 (1H, m, CHHPh), 2.45–2.36 (3H, s, Ar–Me and 2H, m, CH$_2$CBr), 2.08–1.82 (2H, m, C(O$_2$Me)$_2$CH$_2$CH$_2$CHOTES), 1.71–1.59 (2H, m, CH$_2$), 1.50–1.37 (1H, m, CHH), 1.35–1.24 (1H, m, CHH), 1.00–0.93 (12H, m, OSi(CH$_2$CH$_3$)$_3$ and CHCH$_3$), 0.80–0.74 (9H, m, OSi(CH$_2$CH$_3$)$_3$), 0.64–0.56 (6H, m, OSi(CH$_2$CH$_3$)$_3$), 0.42–0.33 (6H, m, OSi(CH$_2$CH$_3$)$_3$); $^{13}$C NMR (100 MHz; CDCl$_3$) $\delta$ 172.4, 172.4 (CO$_2$Me), 162.0 (NCCO$_2$Me), 144.6, 140.1 (ArC), 137.1, 137.0
(C=Br), 135.6 (ArCH), 126.9, 126.8 (C=CBr), 126.0 (ArCH), 80.9, 80.7 (quat. C), 71.3, 71.1 (CHOTES), 52.4, 52.3 (OMe), 42.6, 42.6 (CH2Ph), 38.0, 38.0, 37.6, 37.3, 36.2, 35.9, 33.7, 33.1, 31.1, 31.0, then 21.7 (Ar–Me), 19.1, 19.1 (CHCH3), 7.1, 7.1, (OSi(CH2CH3)3), 7.0 (OSi(CH2CH3)3), 6.3 (OSi(CH2CH3)3), 5.3, 5.2 (OSi(CH2CH3)3); HRMS m/z (M+NH4+\(^+\)) found: 898.3526. C\(_{41}\)H\(_{69}\)BrN\(_3\)O\(_8\)Si\(_2\) requires 898.3522.

(−)-Dimethyl 2-(((8R,Z)-6-bromo-3-hydroxy-8-methyl-9-phenylnon-6-en-1-yl)-3-diazo-2-((triethylsilyl)oxy)succinate (SI-5)

To the Z-hydrazone SI-4 (66 mg, 0.075 mmol) in CH\(_2\)Cl\(_2\) (200 µL) was added Et\(_3\)N (50 µL, 0.36 mmol) dropwise at rt. After 2 h, the mixture was concentrated to give a (6:4) mixture of diazo bis−TES ether and diazo alcohol SI-5; to this mixture in THF (300 µL) was added AcOH (150 µL) and water (150 µL). After 5 h stirring at rt, the mixture was quenched with aq. sat. NaHCO\(_3\) (2 mL), extracted with EtOAc (2 x 5 mL), dried (MgSO\(_4\)) and concentrated under reduced pressure. Purification of the residue by column chromatography (10–30% Et\(_2\)O in petrol) gave diazo alcohol SI-5 (42 mg, 92%, from SI-4), as a yellow oil, an 1:1 epimeric mixture at C−3; \(R_f = 0.34\) (30% Et\(_2\)O in petrol); \([\alpha]_{D}^{23} = −23.4\) (c=1.0, CHCl\(_3\)); \(\nu_{\text{max}}/\text{cm}^{-1}\) (film) 3518 m, 3027 w, 2955 s, 2877 s, 2098 s, 1747 s, 1707 s, 1495 m, 1437 s, 1315 s, 1141 m, 742 s; \(^1\)H NMR (400 MHz; CDCl\(_3\)) \(\delta\) 7.29–7.14 (5H, m, ArH), 5.53–5.45 (1H, m, CH=CBr), 3.71–3.71 (6H, m, 2 x OMe), 3.70–3.61 and 3.57–3.49 (1H, m, CHOH), 2.98–2.82 (1H, m, CHCH\(_3\)), 2.73–2.34 (4H, m, CH2Ph, and CH2CBr), 2.18–1.84 (2H, m, C(CO\(_2\)Me)CH\(_2\)CH\(_2\)), 1.73–1.34 (4H, m, CH\(_2\)CH(OH)CH\(_2\)), 1.02–0.91 (12 H, m, OSi(CH\(_2\)CH\(_3\))\(_3\) and CHCH\(_3\)), 0.66–0.55 (6H, m, OSi(CH\(_2\)CH\(_3\))\(_3\)); \(^1\)C NMR (100 MHz; CDCl\(_3\)) \(\delta\) 171.9, 171.8 (CO\(_2\)Me), 165.3 (NCCO\(_2\)Me), 140.4, 140.1 (ArC), 134.5, 134.3 (C=CBr), 129.3, 129.3 (ArCH) 128.3, 128.2 (ArCH), 126.9, 126.8 (C=CBr), 126.2, 126.0 (ArCH), 76.2, 176.0 (quat. C), 70.4, 69.6 (CHOH), 64.9 (C=N2), 52.9, 52.8 (OMe), 52.0, 51.9 (OMe), 42.8, 42.6 (CH2Ph), 37.9, 37.6 (CHCH\(_3\)), 63.1, 35.3, 34.6, 31.5, 29.8 (all CH2), then 19.5, 19.3 (CHCH\(_3\)), 7.0, 6.7 (OSi(CH\(_2\)CH\(_3\))\(_3\)), 5.9, 5.2 (OSi(CH\(_2\)CH\(_3\))\(_3\)); HRMS m/z (M+NH4+) found: 628.2414. C\(_{28}\)H\(_{47}\)BrN\(_3\)O\(_6\)Si requires 628.2412.
(−)-Dimethyl 2-((R,Z)-6-bromo-8-methyl-3-oxo-9-phenylnon-6-en-1-yl)-3-diazo-2-((triethylsilyl)oxy)succinate (13)

To diazo alcohol SI-5 (54 mg, 0.088 mmol) in CH₂Cl₂ (2 mL) at rt was added Dess−Martin periodinane (88 mg, 0.21 mmol). After 3 h, the mixture was filtered through Celite® and then purified by column chromatography (10−40% Et₂O in petrol) to give ketone 13 (51 mg, 95%), as a yellow oil; \( R_f = 0.57 \) (60% Et₂O in petrol); \( [\alpha]_D^{23} = -24.9 \) (c=1.0, CHCl₃); \( \nu_{\max} / \text{cm}^{-1} \) (film) 2956 s, 2877 s, 2098 s, 1711 s, 1437 s, 1260 s, 1138 m, 738 s; \(^1\)H NMR (500 MHz; CDCl₃) \( \delta \) 7.28−7.12 (5H, m, ArH), 5.53 (1H, d, \( J = 8.5, \) CH=CBr), 3.75 (3H, s, OMe), 3.73 (3H, s, OMe), 2.89−2.79 (1H, m, CHCH₃), 2.70−2.49 (7H, m, CH₂Ph, CHH and 2 x CH₂), 2.44−2.37 (1H, m, CHH) 2.29−2.18 (2H, m, CH₂), 0.97−0.90 (12H, m, OSi(CH₂CH₃)₃ and CHCH₃), 0.65−0.55 (6H, m, OSi(CH₂CH₃)₃); \(^{13}\)C NMR (125 MHz; CDCl₃) \( \delta \) 207.7 (C=O), 171.5 (CO₂Me), 165.2 (NCCO₂Me), 140.0 (ArC), 135.1 (C=CBr), 129.4 (ArCH) 128.2 (ArCH), 126.1 (ArCH), 125.5 (C=CBr), 75.5 (quat. C), 64.8 (C=N₂), 53.0 (OMe), 52.1 (OMe), 42.5 (CH₂Ph), 41.7 (CH₂), 38.0 (CHCH₃), 37.4 (CH₂), 35.7 (CH₂), 32.3 (CH₂), 19.1 (CHCH₃), 7.0 (OSi(CH₂CH₃)₃), 5.8 (OSi(CH₂CH₃)₃); HRMS \( m/z \) (M+NH₄⁺) found: 626.2246. C₂₅H₄₅BrN₅O₆Si requires 626.2256.

(−)-Trimethyl (1S,2R,5R,7S)-5-((R,Z)-3-bromo-5-methyl-6-phenylhex-3-en-1-yl)-2-((triethylsilyl)oxy)-6,8-dioxabicyclo[3.2.1]octane-1,2,7-tricarboxylate (12)

A mixture of ketone 13 (26 mg, 0.043 mmol), freshly distilled methyl glyoxylate\(^{11} \) (25 mg, 0.28 mmol) and Rh₂(OAc)₄ (~1 mg, cat) in toluene (1.5 mL) was refluxed at 110 °C for 2 h. The mixture was then concentrated under reduced pressure and purified by column chromatography (0−20% EtOAc in petrol) to give cycloadduct 12 (19 mg, 66%), as a colourless oil; \( R_f = 0.39 \) (60% Et₂O in petrol); \( [\alpha]_D^{23} = -13.7 \) (c=1.0, CHCl₃); \( \nu_{\max} / \text{cm}^{-1} \) (film) 2955 s, 2876 s, 1840 s, 1755 s, 1495 s, 1438 s, 1375 m, 1264 s, 1197 m, 1013 s, 738 s; \(^1\)H NMR (500 MHz; CDCl₃) \( \delta \) 7.26−7.15 (5H, m, ArH), 5.59 (1H, d, \( J = 8.5, \) CH=CBr), 5.55 (1H, s, CHCO₂Me), 3.81 (3H, s, OMe), 3.70 (3H, s, OMe), 3.69 (3H, s, OMe), 2.92−2.83 (1H, m, CHCH₃), 2.75−2.65 (3H, m, CH₂CH₂CBr and CHHPh), 2.5 (1H, ddd, \( J = 13.5, \) 8, CHHPh), 2.40 (1H, S20
dd, J = 14, 12.5, 6, 1Hendo of TESOC(CO₂Me)CHHCH₂), 2.17–2.06 (2H, m, CH₂CBr), 1.87 (1H, td, J = 13, 5.5, 1Hendo of TESOC(CO₂Me)CH₂CHH), 1.76 (1H, pdd, J = 14, 5, TESOC(CO₂Me)CHHCH₂), 1.66 (1H, pdd, J= 13, 5.5, TESOC(CO₂Me)CH₂CHH), 0.97–0.91 (12H, m, OSi(CH₂CH₃)₃ and CHCH₃), 0.69–0.59 (6H, m, OSi(CH₂CH₃)₃); ¹³C NMR (125 MHz; CDCl₃) δ 173.4 (CO₂Me), 169.4 (CO₂Me), 166.8 (CO₂Me), 140.2 (ArC), 134.1 (C=CBr), 129.4 (ArCH) 128.2 (ArCH), 126.7 (C=CBr), 126.0 (ArCH), 111.1 (O=C=O), 90.3 (TESOCOCO₂Me), 77.5 (CHCO₂Me), 77.3 (TESOCOCO₂Me), 52.7 (OMe), 52.6 (OMe), 52.5 (OMe), 42.6 (CH₂Ph), 38.0 (CHCH₃), 35.9, 35.1, 29.9, 29.8 (4 x CH₂), 19.1 (CHCH₃), 7.2 (OSi(CH₂CH₃)₃), 6.7 (OSi(CH₂CH₃)₃); HRMS m/z (M+NH₄⁺) found: 686.2351. C₃₁H₄₉⁷⁹BrNO₉Si requires 686.2354.

(−)-Trimethyl (1S,2R,5R,7S)-5-((R,Z)-3-bromo-5-methyl-6-phenylhex-3-en-1-yl)-2-hydroxy-6,8-dioxabicyclo[3.2.1]octane-1,2,7-tricarboxylate (31) and (−)-Trimethyl (1R,3S,4S,5R)-1-((R,Z)-3-bromo-5-methyl-6-phenylhex-3-en-1-yl)-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (32)

To a solution of cycloadduct 12 (19 mg, 0.028 mmol) in CH₂Cl₂ (210 μL) were added TFA (105 μL) and H₂O (10.5 μL). The reaction mixture was heated at 40 °C for 48 h. The mixture was then concentrated under reduced pressure and purified by column chromatography (5–30% EtOAc in petrol). First eluted, cycloadduct alcohol 31 (3 mg, 19%), as a colourless oil; Rf = 0.48 (100% Et₂O in petrol); [α]D²³ = −8.2 (c=1.0, CHCl₃); νmax/cm⁻¹ (film) 3462 br, 2925 s, 1736 s, 1456 s, 1260 s, 1092 m, 796 s, 737 s; ¹H NMR (500 MHz; CDCl₃) δ 7.26–7.14 (5H, m, ArH), 5.58 (1H, d, J = 8.5, CH=CBr), 5.47 (1H, s, CHCO₂Me), 3.92 (3H, s, OMe), 3.75 (3H, s, OMe), 3.71 (3H, s, OMe), 2.94–2.83 (1H, m, CHCH₃), 2.82–2.55 (3H, m, CH₂CH₂Br and CHHPh), 2.51 (1H, dd, J = 13.5, 8, CHHPh), 2.36–2.27 (1H, m, TESOC(CO₂Me)CHHCH₂), 2.25–1.92 (4H, m, CH₂CBr, TESOC(CO₂Me)CHHCH₂ and TESOC(CO₂Me)CH₂CHH), 1.81–1.73 (1H, m, TESOC(CO₂Me)CH₂CHH), 0.95 (3H, m, CH₂CH₃); ¹³C NMR (125 MHz; CDCl₃) δ 173.8 (CO₂Me), 169.1 (CO₂Me), 166.9 (CO₂Me), 140.2 (ArC), 134.3 (C=CBr), 129.4 (ArCH) 128.3 (ArCH), 126.7 (C=CBr), 126.0 (ArCH), 111.8 (O=C=O), 89.4 (TESOCOCO₂Me), 77.7 (CHCO₂Me), 74.1 (TESOCOCO₂Me), 52.9 (OMe), 53.2 (OMe), 52.7 (OMe), 42.6 (CH₂Ph), 38.0 (CHCH₃), 35.8, 34.9, 29.9, 29.5 (4 x
CH₂), 19.1 (CHCH₃); HRMS m/z (M+NH₄⁺) found: 572.1491. C₂₃H₃₅⁷⁹BrNO₉ requires 572.1490.

Second eluted, alkenyl bromide 32 (5.5 mg, 35%) as a colourless oil; Rf = 0.40 (100% Et₂O in petrol); [α]D²³ = −7.3 (c=1.0, CHCl₃); νmax/cm⁻¹ (film) 3452 br, 2923 s, 1731 s, 1456 s, 1261 s, 1093 m, 795 s, 731 s; ¹H NMR (500 MHz; CDCl₃) δ 7.29–7.14 (5H, m, ArH), 5.58 (1H, d, J = 8.5, CH=CBr), 4.79 (1H, s, CH₂CO₂Me), 3.89 (3H, s, OMe), 3.77 (6H, s, 2 x OMe), 3.65 (1H, s, OH), 3.06–2.98 (1H, m, Hendo of C(CH₂Me)CH=CH₂), 2.95–2.85 (1H, m, CHCH₃), 2.71–2.55 (4H, m, CH₂Ph and CH₂), 2.26–2.14 (2H, m, CH₂), 2.05–1.93 (2H, m, CH₂), 1.90–1.82 (1H, m, Hexo of C(CH₂Me)CH=CH₂), 0.98 (3H, d, J = 6.5, CHCH₃); ¹³C NMR (125 MHz; CDCl₃) δ 170.0 (CO₂Me), 168.8 (CO₂Me), 167.5 (CO₂Me), 140.3 (ArC), 134.8 (C=CBr), 129.3 (ArCH) 128.3 (ArCH), 126.4 (C=CBr), 126.2 (ArCH), 108.5 (O−C−O), 88.0 (CO₂Me), 75.2 (COH), 74.9 (CHCO₂Me), 53.5 (OMe), 53.0 (OMe), 52.8 (OMe), 42.7 (CH₂Ph), 38.0 (CHCH₃), 36.0, 35.4, 31.4, 29.3 (4 x CH₂), 19.5 (CHCH₃); HRMS m/z (M + NH₄⁺) found: 572.1490. C₂₅H₃₇⁷⁹BrNO₉ requires 572.1490.

(−)-Trimethyl (1S,3S,4S,5R)-1-((R,E)-3,5-dimethyl-6-phenylhex-3-en-1-yl)-4-hydroxy-2,8-Dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (33)

To a solution of 9-MeO-9-BBN (7 μL, 1.0 M in hexane, 0.007 mmol) in THF (30 μL) was added MeLi (6 μL, 1.2 M in Et₂O, 0.007 mmol) and stirred for 5 min at rt. Meanwhile, a mixture of PdCl₂(dpdp) (0.4 mg, 15 mol%), Cs₂CO₃ (3.5 μL, 3 M in MeOH), Ph₃As (0.4 mg, 40 mol%) and alkenyl bromide 32 (3 mg, 0.0036 mmol) in DMF (30 μL) was prepared at rt. To the mixture containing 32 and the catalyst system, the borinate complex solution was added dropwise and then the reaction mixture was stirred at 40 °C for 6 h. The reaction mixture was then quenched with water (1 mL), extracted with EtOAc (3 × 4 mL), and the combined organic layers washed with brine (2 mL) and dried (MgSO₄). Evaporation under reduced pressured followed by column chromatography (0–40% EtOAc in petrol) gave 6,7-dideoxyisqualestatin H5 trimethyl ester 33 (0.8 mg, 45%) as a colourless oil, Rf = 0.15 (40% EtOAc in petrol); [α]D²⁵ = −37.9 (c= 0.53, CHCl₃); νmax/cm⁻¹ (film) 3078 br, 2956 s, 2925 s, 2854 s, 1768 s, 1739 s, 1439 s, 1266 s; ¹H NMR (500 MHz; CDCl₃) δ 7.24–7.11 (5H, m, ArCH), 5.02 (1H, d, J = 9, CH=CH₃), 4.86 (1H, s, CH₂CO₂Me), 3.89 (3H, s, OMe), 3.77 (3H, s, OMe), 3.76 (3H, s, OMe), 3.16–3.05 (1H, m, Hendo of C(CH₂Me)CH=CH₂), 2.67–2.58 (1H, m, CHCH₃), 2.54–
2.48 (2H, m, CH₂Ph), 2.21–1.95 (8H, m, H₆exo of C(CO₂Me)CHHCH₂, C(CO₂Me)CH₂CH₂, CH₂CH₂CMe and OH), 1.46 (3H, d, J = 1.5, =CCH₃), 0.93 (3H, d, J = 6.5, CHCH₃);¹³C NMR (125 MHz; CDCl₃) δ 170.1 (CO₂Me), 168.9 (CO₂Me), 167.7 (CO₂Me), 141.3 (C=CH), 133.2 (ArC), 130.8 (C=CH), 129.4 (ArCH), 128.2 (ArCH), 125.8 (ArCH), 109.3 (O−C−O), 88.2 (CO₂Me), 75.3 (COH), 75.0 (CHCO₂Me), 53.5 (OMe), 53.0 (OMe), 52.8 (OMe), 44.1 (CH₂Ph), 35.2 (CHCH₃), 34.7, 33.5, 31.3, 29.3 (4 x CH₂), 21.0 (CHCH₃), 16.3 (=CCH₃); HRMS m/z (M+Na⁺) found 513.2094, C₂₆H₃₄O₆Na requires 513.2095.

(−)-(15,3S,4S,5R)-1-((R,E)-3,5-Dimethyl-6-phenylhex-3-en-1-yl)-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylic acid (6,7-dideoxysqualestatin H5) (5)

To a mixture of 6,7-dideoxysqualestatin H5 trimethyl ester 33 (2.0 mg, 0.0041 mmol) and KOt-Bu (5.0 mg, 0.045 mmol) was added 1,4-dioxane (0.25 mL) and H₂O (0.36 mL) at 0 °C, and then slowly warmed to rt over 1 h and left to stir for 2 h. The reaction mixture was then refluxed at 110 °C overnight. The solvent was evaporated, and H₂O (2.5 mL) added. The mixture was washed with Et₂O (2 x 2.5 mL), acidified with HCl (1 mL, 0.1 M), extracted with EtOAc (3 x 5 mL) and the combined organic layers washed with brine (2.5 mL). The combined organic layers were evaporated under reduced pressure to give 1.6 mg of material that was re-dissolved in MeOH (0.5 mL). The solution was extracted with n-hexane (2 x 0.5 mL), and the methanolic layer was concentrated under reduced pressure to give 6,7-dideoxysqualestatin H5 (5) (1.4 mg 78%); [α]D²⁵ = −12.9 (c= 0.09, MeOH); νmax/cm⁻¹(film) 3437 br, 2956 w, 2530 br, 1730 s, 1452 w, 1050 s, 880 s;¹H NMR (500 MHz; CD₂OD) δ 7.23 (2H, t, J = 7.5, ArCH), 7.16–7.11 (3H, m, ArCH), 5.04 (1H, d, J = 9, CH=CCH₃), 4.84 (1H, s, CHCO₂Me), 3.79 (1H, s, OH), 3.23–3.15 (1H, m, Hendo of C(CO₂Me)CHHCH₂), 2.70–2.62 (1H, m, CHCH₃), 2.59 (1H, dd, J = 13, 6, CHHPh), 2.48 (1H, dd, J = 13, 8, CHHPh), 2.22–2.10 (2H, m, C(CO₂Me)CH₂CH₂), 2.08–1.94 (4H, m, CH₂CH₂CHCH₃), 1.90–1.84 (1H, m, 1Hexo of C(CO₂Me)CHHCH₂), 1.43 (3H, d, J = 1, CCH₃), 0.96 (3H, d, J = 6.5, CHCH₃);¹³C NMR (125 MHz; CD₂OD) δ 173.5 (CO₂H), 172.5 (CO₂H), 171.2 (CO₂H), 142.4 (ArC), 135.0 (C=CH), 131.7 (C=CH), 130.3 (ArCH), 129.0 (ArCH), 126.7 (ArCH), 109.8 (O−C−O), 89.5 (CO₂Me), 76.2 (COH), 75.9 (CHCO₂Me), 45.1 (CH₂Ph), 36.5 (CHCH₃), 35.9 (C(CO₂Me)CH₂CH₂), 34.7 (C(CO₂Me)CH₂CH₂), 32.2 (CH₂CH₂CCH₃), 30.3 (CH₂CH₂CCH₃), 21.4 (CHCH₃), 16.1 (CCH₃); HRMS m/z (M+Na⁺) found: 471.1625, C₂₃H₂₈O₉Na requires 471.1626.
3. NMR data comparison of synthetic 6,7-dideoxysqualestatin H5 (5) with natural isolate\textsuperscript{12}

![Chemical Structure](image)

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*\textsuperscript{12}NMR spectra of the natural isolate were recorded on a Bruker AM500, while the synthetic spectra were recorded on a Bruker AVC500 (\( ^1H\) NMR–500 MHz and \( ^13C\) NMR–125 MHz, CD\textsubscript{3}OD).
4. References


5. $^1$H and $^{13}$C NMR Spectra
$^{13}$C (100 MHz, CDCl$_3$)
1H (400 MHz, CDCl₃)
$^{13}$C (100 MHz, CDCl$_3$)
$^1$H (400 MHz, CDCl$_3$)
$^{13}$C (100 MHz, CDCl$_3$)
$^1$H (400 MHz, CDCl$_3$)
$^{13}$C (100 MHz, CDCl$_3$)
$^{1}H$ (400 MHz, CDCl$_3$)
\[^{13}C\ (100\ \text{MHz, CDCl}_3)\]
$^1$H (400 MHz, CDCl$_3$)
$^1^3$C (100 MHz, CDCl$_3$)
TBSO
TBSO
TBSO

28

$^1$H (400 MHz, CDCl$_3$)
$^{13}$C (100 MHz, CDCl$_3$)
\[ ^1H (500 \text{ MHz}, \text{CDCl}_3) \]
$^{13}$C (125 MHz, CDCl$_3$)
SI-1

$^1$H (500 MHz, CDCl$_3$)
SI-1

$^{13}$C (125 MHz, CDCl$_3$)
$^{13}$C (100 MHz, CDCl$_3$)
$^{1}H$ (400 MHz, CDCl$_3$)
$^1{\text{H}}$ (100 MHz, CDCl$_3$)
SI-2

$^1$H (400 MHz, CDCl$_3$)
$^{13}$C (100 MHz, CDCl$_3$)
$^1$H (400 MHz, CDCl$_3$)
$^{13}$C (100 MHz, CDCl$_3$)
$^1$H (400 MHz, CDCl$_3$)
$^{13}$C (100 MHz, CDCl$_3$)
8R-22

$^1$H (400 MHz, CDCl$_3$)
$\text{HO}$

$\text{HO}$

$\text{Br}$

$\text{Ph}$

$8R-22$

$^{13}C$ (100 MHz, CDCl$_3$)
SI-3

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$^1$H (100 MHz, CDCl₃)
$^1$H (400 MHz, CDCl$_3$)
$^{13}\text{C} (100 \text{ MHz, CDCl}_3)$
$^{1}H$ (500 MHz, CDCl$_3$)
$8'R$-14

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$^1$H (500 MHz, CDCl$_3$)
$^{13}$C (125 MHz, CDCl$_3$)
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$^{13}$C (100 MHz, CDCl$_3$)
SI-5

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$^1$H (500 MHz, CDCl$_3$)
$^{13}$C (125 MHz, CDCl$_3$)
$^{1}H$ (500 MHz, CDCl$_3$)
$^{13}$C (125 MHz, CDCl$_3$)
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$^1$H (500 MHz, CDCl$_3$)
$^{13}$C (125 MHz, CDCl$_3$)
$^{1}H$ (500 MHz, CDCl$_3$)
$^{13}$C (125 MHz, CDCl$_3$)

33

\[
\text{MeO}_2\text{C} - \text{O} - \text{H} - \text{CO}_2\text{Me}
\]

\[
\text{MeO}_2\text{C} - \text{O} - \text{Ph}
\]
$^1$H (500 MHz, CD$_3$OD)
$^{13}$C (125 MHz, CD$_3$OD)