Supporting Information

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I) General Experimental

All experiments were performed in oven-dried glassware (anhydrous conditions) and under an argon atmosphere unless otherwise stated.

**Solvents and reagents:** Solvents were distilled under argon prior to use; CH$_2$Cl$_2$, MeOH, MeCN and PhMe from calcium hydride; Et$_2$O and THF from calcium hydride and LiAlH$_4$, with triphenyl methane indicator for THF. All solvents were dry reagent grade unless otherwise stated. All chemical reagents used were commercially available from Fisher and Sigma Aldrich in the highest available purity. Commercial nBuLi (in hexanes) and tBuLi were titrated prior to use using 2,6-di-tert-butyl-4-methylphenol in Et$_2$O with 1,10-phenanthroline as an indicator.

**Chromatography:** Thin layer chromatography (TLC) was performed on pre-coated glass-backed Merck Kieselgel 60 F$_{254}$ plates with visualisation effected with ultra-violet irradiation ($\lambda$ = 254 nm) and/or staining using potassium permanganate, vanillin or ninhydrin solutions. Flash column chromatography with Merck Kieselgel (230–400 mesh) silica gel performed according to the method employed by W. C. Still et al.$^\dagger$ All solvents used for chromatographic purification were distilled prior to use with the exception of Et$_2$O and HPLC grade n-hexane, which were used as supplied.

**Atom labeling:** Labeling is in accord with the natural product numbering system and is indicated on the relevant diagram.

**NMR spectroscopy:** $^1$H NMR spectra recorded on Bruker DPX-400 or Bruker Avance 500 (with dual cryoprobe) operating at 400 and 500 MHz respectively, with deuterated solvent acting as an internal deuterium lock. Data is reported in the following manner: chemical shift [in parts per million (ppm)] relative to tetramethylsilane (external standard), number of protons and assignment, chemical, multiplicity and coupling constant $J$ (measured in Hz to the nearest 0.1 Hz). The multiplicity of a signal is indicated as: s-singlet, d-doublet, t-triplet, m-multiplet, br-

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broad, appar-apparent or combinations of these. $^{13}$C NMR spectra recorded on the same DPX-400 or Bruker Avance 500 (with dual cryoprobe) operating at 100 and 126 Hz respectively with broadband proton decoupling and the deuterium solvent as an internal lock. $^{19}$F NMR spectra were recorded on a Bruker Avance 400 (376 MHz) QNP Ultrashield spectrometer with broadband proton decoupling using the deuterated solvent as internal deuterium lock. Chemical shift data are given in parts per million relative to CFCl$_3$ (external standard).

Residual protic solvent also acted as an internal reference (CDCl$_3$; $^1$H NMR = 7.26 ppm, $^{13}$C = 77.1 ppm, (CD$_3$)$_2$SO; $^1$H NMR 2.50 ppm, $^{13}$C = 39.5 ppm, CD$_3$OD; $^1$H NMR 4.88, 3.34 ppm, $^{13}$C = 49.0 ppm; C$_6$D$_6$; $^1$H NMR 7.16 ppm, $^{13}$C = 128.06 ppm)

Structural assignments were made with the aid of DEPT 135, HMQC, HSQC, HMBC, COSY, NOESY and individual nOe experiments in the assignment of signals in $^1$H and $^{13}$C NMR spectra.

**Infrared Spectroscopy**: Spectra were recorded on a Perkin-Elmer Spectrum One FT-IR ATR (Attenuated Total Reflectance) Spectrometer as a thin film deposited on the ATR. Only selected characteristic peaks are recorded.

**Optical rotations**: Measured on Perkin Elmer 343 polarimeter and [α]$_D$ values quoted in 10$^{-1}$deg cm$^2$g$^{-1}$ with concentration (c) quoted in g(100 mL)$^{-1}$.

**Mass Spectroscopy (EI, ESI)**: High resolution mass spectra (HRMS) recorded on Waters Micromass LCT spectrometer using time of flight with positive electrospray ionisation (ESI$^+$) or negative electrospray ionisation (ESI$^{-}$), an ABI/MDS Sciex Q-STAR Pulsar with ESI$^+$, or a Bruker BioApex II 4.7e FTICR utilising either ESI$^+$ or a positive electron ionisation (EI$^+$) source equipped with a direct insertion probe. The mass reported is that containing the most abundant isotopes ($^{35}$Cl and $^{79}$Br). This was performed at the Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, with each value obtained within 5 ppm of the calculated mass.
Melting points: Determined using an SRS Optimelt MPA 100 automated melting point system, with range quoted to the nearest whole number.

X-ray crystallography: Recorded by Dr John E. Davies at the Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge using a Nonius Kappa CCD detector. Crystal structure images presented in this thesis were produced using ORTEP-3 for windows.† All crystallographic data has been deposited on the Cambridge Structural Database compiled by the Cambridge Crystallographic Data Centre (CCDC). The corresponding CCDC number for each compound is listed by the relevant structure.

Elemental Analysis: Performed by Alan Dickerson at the Microanalytical Laboratories, Department of Chemistry, University of Cambridge. All reported values are within ±0.5% of the calculated value.

Naming of compounds: Carried out using the computer programme ACD/Name. This software generates the systematic name of chemical structures according to the guidelines specified by the International Union of Pure and Applied Chemistry (IUPAC). As a result the numbering system used in these names does not follow that of the natural product. In order to allow for the straightforward comparison of data, the NMR assignments given follow the natural product numbering system which is shown on the chemical structure.

Structures not shown in the manuscript that have been described in the Supporting Information are numbered with the form S#.

II) Experimental Procedures

(2S)-Methanesulfonic acid-1-methyl-prop-2-ynyl ester 9

To a stirring solution of (2S)-3-butyn-2-ol (1.0 g, 14.3 mmol) in CH₂Cl₂ (25 mL) at −78 °C was added Et₃N (8.0 mL, 57.1 mmol) followed by methanesulfonyl chloride (3.3 mL, 42.9 mmol) over 30 mins, resulting in the formation of a yellow precipitate. The mixture was stirred for 1 h at −78 °C, quenched by the addition of sat. aq. NaHCO₃ (25 mL), and the layers separated. The aqueous layer was further extracted with CH₂Cl₂ (2 × 25 mL), and the combined organic layers dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography [SiO₂, petroleum ether (40:60): Et₂O, 8:2] gave the title compound 9 as a colourless oil (1.97 g, 93%).

Rₛ = 0.05 [petroleum ether (40:60): Et₂O, 9:1]; [α]D²⁵ = −106.4 (c = 0.42, CHCl₃); IR (film) νmax/cm⁻¹ 3281, 3031, 2999, 2943, 1353, 1332, 1172, 1123, 1089, 1016; ¹H NMR (CDCl₃, 400 MHz) δ = 5.27 (1H, qd, J = 6.7, 2.1 Hz, C3H), 3.10 (3H, s, SO₂CH₃), 2.70 (1H, d, J = 2.1 Hz, C1H), 1.65 (3H, d, J = 6.7 Hz, C4H₃); ¹³C NMR (CDCl₃, 100 MHz) δ = 80.2 (C2), 76.3 (C1H), 67.5 (C3H), 39.2 (SO₂CH₃), 22.5 (C4H₃); HRMS (ESI) found 171.0095 ([M+Na]⁺ C₅H₈O₃SNa requires 171.0086). All spectroscopic data in agreement with that previously published.¹

(2R,3R,4R)-1-(tert-Butyl-dimethyl-silanyloxy)-2,4-dimethyl-hex-5-yn-3-ol 10a

To a stirring solution of Pd(OAc)₂ (440 mg, 1.96 mmol) in THF (250 mL) at −78 °C was added PPh₃ (520 mg, 1.98 mmol). The resulting yellow solution was stirred for 10 mins at which point 9 (4.77 g, 30.9 mmol) and 8a (4.46 g, 20.1 mmol)² were added dropwise sequentially. After
stirring for 5 mins ZnEt$_2$ (1 M in hexanes, 66.0 mL, 66.0 mmol) was added to the mixture over a period of 1 h. The reaction mixture was stirred for 30 mins at −78 °C before being slowly warmed to −20 °C and maintained at this temperature for a further 24 h. The reaction was quenched by the addition of sat. aq. NH$_4$Cl (80 mL), diluted with Et$_2$O (80 mL) and warmed to RT. The layers were separated and the aqueous layer further extracted with Et$_2$O (3 × 80 mL), and the combined organic layers dried (MgSO$_4$), and concentrated in vacuo. Purification by column chromatography [SiO$_2$, petroleum ether (40–60):Et$_2$O:Et$_3$N, 90:9:1→80:19:1] gave the title compound 10a (1.41 g, 70%). as a pale yellow oil as the major diastereomer (dr = 94:6).

$R_f = 0.10$ [petroleum ether (40–60):Et$_2$O, 9:1]; [$\alpha$]$^{25.0}_D$ = +6.3 (c = 0.34, CHCl$_3$); IR (film) $v_{\text{max}}$/cm$^{-1}$ 3600, 3312, 2956, 2930, 2858, 1472, 1463, 1388, 1361, 1251, 1086; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 3.67$ (2H, d, $J = 6.6$ Hz, CH$_A$H$_B$OSi), 3.59–3.56 (1H, m, C$_7$H), 2.70–2.65 (1H, m, C$_6$H), 2.63 (1H, d, $J = 4.5$ Hz, C$_7$HOH), 2.13 (1H, d, $J = 2.3$ Hz, C$_4$H), 1.83–1.75 (1H, m, C$_8$H), 1.20 (3H, d, $J = 7.0$ Hz, C$_{25}$H$_3$), 0.96 (3H, d, $J = 7.0$ Hz, C$_{24}$H$_3$), 0.90 (9H, s, C(CH$_3$)$_3$ of tBu), 0.06 (6H, s, Si(CH$_3$)$_2$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 86.4$ (C5), 76.2 (C7H), 70.2 (C4H), 67.2 (C9H$_2$), 37.5 (C8H), 30.5 (C6H), 25.8 (3C, C(CH$_3$)$_3$ of tBu), 18.2 (C(CH$_3$)$_3$ of tBu), 17.6 (C$_{25}$H$_3$) 10.3 (C$_{24}$H$_3$), −5.5 (2C, Si(CH$_3$)$_2$); HRMS (+ESI) Found [M+H]$^+$ = 257.1940; C$_{14}$H$_{29}$O$_2$Si requires 257.1937, Δ 1.17 ppm.

tert-Butyl-((2R,3R,4R)-3-(4-methoxy-benzyloxy)-2,4-dimethyl-hex-5-ynyloxy)-dimethylsilane S1

To a solution of 10a (932 mg, 4.01 mmol) in DMF (6 mL) and THF (6 mL) at 0 °C was added NaH (60% in mineral oil, 193 mg, 4.83 mmol). The reaction mixture was stirred for 45 mins at RT. Then PMBBr (705 μL, 4.82 mmol) was added dropwise and the reaction stirred for 2 h at RT. The reaction was quenched using sat. aq. NH$_4$Cl (20 mL) and diluted with Et$_2$O (20 mL). The aqueous layer was separated and extracted with Et$_2$O (2 × 20 mL). The combined organics were washed with sat. aq. LiCl (50 mL), dried (MgSO$_4$) and concentrated in vacuo to give a pale
yellow oil. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 95:5→9:1] gave the title compound S1 (1.16 g, 82%) as a colourless oil.

\[ R_f = 0.46 \] [petroleum ether (40–60):Et₂O, 9:1]; \[ \alpha \]D\text{25.0} = −23.8 (c = 0.51, CHCl₃); IR (film) \( \nu_{\text{max}}/\text{cm}^{-1} \): 3310, 2954, 2929, 2857, 1613, 1514, 1463, 1247, 1083, 1036; \(^1\)H NMR (CDCl₃, 400 MHz) \( \delta = \) 7.30 (2H, d, \( J = 8.6 \) Hz, Ar), 6.86 (2H, d, \( J = 8.6 \) Hz, Ar), 4.76 (1H, d, \( J = 10.8 \) Hz, CH₂Ar), 4.54 (1H, d, \( J = 10.8 \) Hz, CH₂Ar), 3.80 (3H, s, OCH₃), 3.58–3.42 (3H, m, C₇H and C₉H₂), 2.81–2.72 (1H, m, C₆H), 2.07 (1H, d, \( J = 2.4 \) Hz, C₄H), 1.98–1.92 (1H, m, C₈H), 1.20 (3H, d, \( J = 7.0 \) Hz, C₂₅H₃), 0.94–0.88 (12H, m, C₂₄H₃ and C(CH₃)₃ of tBu), 0.04 (6H, s, Si(CH₃)₂); \(^{13}\)C NMR (CDCl₃, 100 MHz) \( \delta = \) 159.1 (Ar), 131.3 (2C, Ar), 129.4 (2C, Ar), 113.6 (Ar), 87.5 (C₅), 81.5 (C₇H), 74.3 (OCH₂Ar), 69.2 (C₄H), 65.5 (C₉H₂), 55.2 (OCH₃), 38.3 (C₈H), 29.5 (C₆H), 25.9 (3C, C(CH₃)₃ of tBu), 18.2 (C(CH₃)₃ of tBu), 17.9 (C₂₅H₃), 11.2 (C₂₄H₃), −5.4 (2C, Si(CH₃)₂); HRMS (+ESI) Found [M+H]^+ = 377.2498; C₂₂H₃₇O₃Si requires 377.2512, Δ 3.71 ppm.

\((4R,5R,6R)-7-(\text{tert}-\text{Butyl-dimethyl-silanyloxy})-5-(4\text{-methoxy-benzyloxy})-4,6\text{-dimethylhept-2-ynoic acid ethyl ester S2}\)

To a solution of S1 (3.54 g, 9.40 mmol) in THF (145 mL) at −78 °C was added nBuLi (1.5 M in hexanes, 6.90 mL, 10.3 mmol) dropwise. The reaction was stirred for 1 h, after which ethyl chloroformate (1.35 mL, 14.1 mmol) was added and the reaction allowed to warm to RT over 18 h. The reaction was quenched by the addition of sat. aq. NH₄Cl (140 mL) and diluted with Et₂O (150 mL). The aqueous layer was separated and extracted with Et₂O (2 × 120 mL). The combined organic layers were dried (MgSO₄), filtered and concentrated \textit{in vacuo} to afford a pale yellow oil. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 98:2→9:1] gave the title compound S2 (4.02 g, 95%) as a pale yellow oil.
$R_f = 0.18$ [petroleum ether (40–60):Et$_2$O, 9:1]; $[\alpha]_D^{25.0} = +3.2$ (c = 0.575, CHCl$_3$); IR (film) $\nu_{\text{max}}$/cm$^{-1}$: 2955, 2930, 2858, 2239, 1709, 1613, 1463, 1244, 1086, 1035; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta =$ 7.32 (2H, d, $J = 8.6$ Hz, Ar), 6.87 (2H, d, $J = 8.6$ Hz, Ar), 4.75 (1H, d, $J = 10.5$ Hz, OCH$_A$H$_B$Ar), 4.54 (1H, d, $J = 10.5$ Hz, OCH$_A$H$_B$Ar), 4.22 (2H, q, $J = 7.1$ Hz, OCH$_2$CH$_3$), 3.80 (3H, s, OCH$_3$), 3.61–3.48 (3H, m, C$_7$H and C$_9$H$_A$H$_B$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta =$ 159.2 (Ar), 154.2 (C$_3$), 130.9 (2C, Ar), 129.6 (2C, Ar), 113.7 (Ar), 92.0 (C$_5$), 80.9 (C$_7$H), 74.5 (OCH$_2$Ar), 73.7 (C$_4$), 65.3 (C$_9$H$_2$), 61.6 (OCH$_2$CH$_3$), 55.2 (OCH$_3$), 38.2 (C$_8$H), 29.9 (C$_6$H), 25.9 (3C, C(CH$_3$)$_3$ of tBu), 18.2 (C(CH$_3$)$_3$ of tBu), 16.8 (C$_{25}$H$_3$), 14.0 (OCH$_2$CH$_3$), 10.7 (C$_{24}$H$_3$), −5.4 (2C, Si(CH$_3$)$_2$); HRMS (+ESI) Found [M+H]$^+$ = 449.2739; C$_{25}$H$_{41}$O$_5$Si requires 449.2723, $\Delta$ 3.56 ppm.

$^{(7R,9S,10S)}$-9-$((R)$)-2-(tert-Butyl-dimethyl-silyloxy)-1-methyl-ethyl)-7-hydroxy-10-methyl-8-oxa-1,4-dithia-spiro[4.5]dec-7-yl)-acetic acid methyl ester 13a

The first step of the following procedure was conducted in 6 parallel batches that were combined for purification.

To a solution of $i$Pr$_2$NH (690 $\mu$L, 4.90 mmol) in THF (9 mL) at −78 °C was added nBuLi (1.5 M in hexanes, 3.26 mL, 4.90 mmol) dropwise. The solution was allowed to warm to 0 °C, stirred for 10 min and then re-cooled to −78 °C. Methyl acetate (410 $\mu$L, 5.11 mmol) was added dropwise and the reaction stirred for 1 h. This solution of the preformed anion was then cannulated quickly to a solution of S2 (1.00 g, 2.22 mmol) in THF (9 mL) at −78 °C. The reaction was then warmed to RT over 18 h. TLC [petroleum ether (40–60):Et$_2$O, 7:3] showed conversion to a major product. The reaction was quenched with sat. aq. NH$_4$Cl (10 mL), the aqueous layer separated and extracted with Et$_2$O (3 × 15 mL). The combined organic layers of 6
batches were dried (MgSO₄) and concentrated in vacuo to give 11a (6.35 g, 6 batches, 13.32 mmol, assumed quant.) as a pale yellow oil which was used directly in the next step.

To a solution of 11a (13.32 mmol) in MeOH (150 mL) and CH₂Cl₂ (150 mL) at −10 °C was added 1,2-ethanedithiol (1.25 mL, 14.9 mmol), followed by NaOMe (795 mg, 13.98 mmol). The reaction was allowed to warm to RT and stirred for 18 h. The reaction was quenched by the addition of sat. aq. NH₄Cl (250 mL). The aqueous layer was extracted with Et₂O (3 × 200 mL). The organic phases were dried (MgSO₄) and concentrated in vacuo.

The resulting pale yellow oil (12a) was dissolved in CH₂Cl₂ (800 mL) and pH 7 phosphate buffer (80 mL) at RT. DDQ (4.54 g, 20.0 mmol) was then added and the reaction mixture stirred for 3 h. The reaction was quenched by the addition of sat. aq. NH₄Cl (500 mL) and the phases separated. The aqueous layer was extracted with CH₂Cl₂ (2 × 250 mL) and Et₂O (150 mL). The combined organic layers were washed with H₂O (400 mL), dried (MgSO₄) and concentrated in vacuo to give a dark brown oil. The crude product was dissolved in CH₂Cl₂ and stirred with aminoethyl polystyrene quadra gel (6 g) overnight. Filtration, evaporation and purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 8:2 → 7:3] gave the title compound 13a (4.12 g, 68% over 3 steps) as a white crystalline solid.

**R⁷** = 0.32 [petroleum ether (40–60):Et₂O, 7:3]; **m.p.** = 45–46 °C; [α]D²⁵ = −15.9 (c = 0.50, CHCl₃); **IR** (film) νmax/cm⁻¹ 3508, 2957, 2928, 2890, 2854, 1723, 1437, 1410, 1253, 1162, 1143, 1074, 1002; **¹H NMR** (CDCl₃, 400 MHz) δ = 4.89 (1H, d, J = 1.4 Hz, OH), 3.86 (1H, dd, J = 10.1, 2.0 Hz, C7H), 3.71 (3H, s, C1O₂CH₃), 3.53 (1H, dd, J = 9.6, 6.9 Hz, C9H₂H₈B), 3.37 (1H, dd, J = 9.5, 7.4 Hz, C9H₂H₈B), 3.30–3.20 (4H, m, SCH₂CH₂S), 2.60 (1H, d, J = 14.0 Hz, C₄H₂H₈B), 2.57 (2H, s, C₂H₄H₈B), 2.32 (1H, dd, J = 14.0, 1.4 Hz, C₄H₂H₈B), 1.95–1.85 (2H, m, C₆H and C₈H), 1.09 (3H, d, J = 6.6 Hz, C₂₅H₃), 0.92 (9H, s, C(CH₃)₃ of tBu), 0.81 (3H, d, J = 6.9 Hz, C₂₄H₃), 0.06 (3H, s, Si(CH₃)₂), 0.05 (3H, s, Si(CH₃)₂); **¹³C NMR** (CDCl₃, 100 MHz) δ = 171.9 (C₁O₂CH₃), 95.4 (C₃), 73.6 (C₇H), 70.5 (C₅), 66.4 (C₉H₂), 52.1 (C₁O₂CH₃), 52.0 (C₄H₂), 45.7 (C₂H₂), 43.4 (C₆H), 41.4 (SCH₂CH₂S), 39.1 (SCH₂CH₂S), 37.4 (C₈H), 26.4 (3C, C(CH₃)₃ of tBu), 18.7 (C(CH₃)₃ of tBu), 12.4 (C₂₅H₃), 9.4 (C₂₄H₃), −5.0 (2C, Si(CH₃)₂); **HRMS** (+ESI) Found [M+Na]+ = 473.1836; C₂₀H₃₈O₅SiS₂Na requires 473.1828, Δ 1.69 ppm.
((7R,9S,10S)-9-((R)-2-Hydroxy-1-methyl-ethyl)-7-methoxy-10-methyl-8-oxa-1,4-dithiaspiro[4.5]dec-7-yl)-acetic acid methyl ester S3

To a solution of 13a (2.88 g, 6.40 mmol) in MeOH (60 mL) at RT was added trimethylorthoformate (10.5 mL, 96.0 mmol) and pyridinium p-toluenesulphonate (3.22 g, 12.8 mmol) sequentially. The reaction was stirred for 18 h at RT after which it was quenched by the addition of sat. aq. NH₄Cl (250 mL). The resulting mixture was extracted with Et₂O (3 × 200 mL) and the combined organic layers dried (MgSO₄) and concentrated in vacuo to give a white solid. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 1:1] gave the title compound S3 (2.06 g, 92%) as white needles.

R_f = 0.21 [Et₂O:p petroleum ether (40–60), 7:3]; m.p. = 90–91 °C; [α]D²⁵.₀ = −45.7 (c = 0.67, CHCl₃); IR (film) ν_max/cm⁻¹ 3311, 2967, 2940, 2920, 2891, 1737, 1437, 1354, 1330, 1266, 1222, 1163, 1135, 1103, 1046, 1025; ¹H NMR (CDCl₃, 400 MHz) δ = 3.78–3.71 (2H, m, C7H and C9H₂), 3.69 (3H, s, C1O₂CH₃), 3.70–3.67 (1H, m, C9HAH_B), 3.28 (3H, s, C3OCH₃), 3.28–3.16 (4H, m, SCH₂CH₂S), 2.69–2.66 (3H, m, C2H_AH_B and C4H_AH_B), 2.56 (1H, d, J = 13.5 Hz, C4H_AH_B), 2.17 (1H, bs, CH₂OH), 1.98–1.90 (1H, m, C8H), 1.88–1.80 (1H, m, C6H), 1.07 (3H, d, J = 6.6 Hz, C25H₃), 0.93 (3H, d, J = 7.0 Hz, C24H₃); ¹³C NMR (CDCl₃, 100 MHz) δ = 163.9 (C1O₂CH₃), 98.1 (C3), 76.7 (C7H), 69.3 (C5), 67.1 (C9H₂), 51.8 (C1O₂CH₃), 50.5 (C2H₂), 47.8 (C3OCH₃), 43.4 (C6H), 41.7 (C4H₂), 41.7 (SCH₂CH₂S), 38.6 (SCH₂CH₂S), 35.9 (C8H), 11.9 (C25H₃), 8.8 (C24H₃); HRMS (+ESI) Found [M+Na]⁺ = 373.1122; C₁₅H₂₆O₅S₂Na requires 373.1119, Δ 0.80 ppm. Elemental Analysis found C, 51.41; H, 7.37. C₁₅H₂₆O₅S₂ requires C, 51.40; H, 7.48%.

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((2S,5S,6S)-6-((R)-2-Hydroxy-1-methyl-ethyl)-2-methoxy-5-methyl-4-oxo-tetrahydropyran-2-yl)-acetic acid methyl ester 14a

To a solution of S3 (1.06 g, 3.04 mmol) in MeCN (50 mL) and H2O (6.7 mL) at 0 °C was added a freshly prepared solution of BTI (0.067 M in MeCN, 90.0 mL, 6.03 mmol) dropwise. The reaction mixture was stirred at 0 °C for 2 h after which it was quenched by the addition of a mixture of sat. aq. Na2SO3 (50 mL) and sat. aq. NaHCO3 (50 mL) (1:1). The reaction was diluted with EtOAc (150 mL) and the phases separated. The aqueous layer was extracted with EtOAc (2 × 80 mL) and the combined organic layers dried (MgSO4) and concentrated in vacuo. Purification by column chromatography [SiO2, Et2O:pentaneether (40–60), 7:3] gave the title compound 14a (674 mg, 86%) as a pale yellow oil.

RF = 0.20 [Et2O:pentaneether (40–60), 7:3]; [α]D25.0 = –96.3 (c = 0.50, CHCl3); IR (film) νmax/cm⁻¹ 3426, 2971, 2883, 1717, 1439, 1321, 1245, 1195, 1166, 1139, 1099, 1048, 1000; ¹H NMR (CDCl3, 400 MHz) δ = 3.81 (1H, dd, J = 10.6, 2.1 Hz, C7H), 3.76–3.72 (2H, m, C9H₂H₃), 3.72 (3H, s, C1O₂CH₃), 3.26 (3H, s, C3OCH₃), 2.94 (1H, d, J = 14.0 Hz, C4H₂H₃B), 2.88 (1H, d, J = 13.8 Hz, C2H₂H₃B), 2.64 (1H, d, J = 14.0 Hz, C4H₂H₃B), 2.63 (1H, d, J = 13.8 Hz, C2H₂H₃B), 2.49–2.41 (1H, m, C6H), 1.98–1.80 (1H, m, C8H), 1.71 (1H, bs, CH₂OH), 1.01 (3H, d, J = 7.1 Hz, C24H₃), 0.99 (3H, d, J = 6.7 Hz, C25H₃); ¹³C NMR (CDCl3, 100 MHz) δ = 206.2 (C5O), 169.2 (C1O₂CH₃), 101.1 (C3), 76.6 (C7H), 66.3 (C9H₂), 52.0 (C1O₂CH₃), 49.5 (C4H₂), 48.4 (C3OCH₃), 45.7 (C6H), 41.1 (C2H₂), 36.2 (C8H), 8.7 (C25H₃), 8.6 (C24H₃); HRMS (+ESI) Found [M+Na]⁺ = 297.1319; C₁₃H₂₂O₆Na requires 297.1314, Δ 1.68 ppm.
To a solution of 14a (1.19 g, 4.34 mmol) in CH$_2$Cl$_2$ (110 mL) at –10 °C was added TfOH (460 μL, 5.21 mmol) dropwise. After approximately 1 min the reaction was quenched by the addition of sat. aq. NaHCO$_3$ (30 mL) and extracted with CH$_2$Cl$_2$ (2 × 50 mL) and Et$_2$O (2 × 50 mL). The combined organic extracts were dried (MgSO$_4$) and concentrated in vacuo to give a pale yellow oil. The crude product was then re-dissolved in CH$_2$Cl$_2$ (115 mL) and cooled to 0 °C. To this was added imidazole (740 mg, 10.85 mmol) followed by TBSCl (850 mg, 5.64 mmol) portionwise and the reaction mixture stirred at RT for 2 h. The reaction was quenched by the addition of sat. aq. NH$_4$Cl (100 mL) and the phases separated. The aqueous layer was extracted with Et$_2$O (2 × 80 mL) and the combined organic layers dried (MgSO$_4$) and concentrated in vacuo to give a yellow oil. Purification by column chromatography [SiO$_2$, petroleum ether (40–60):Et$_2$O, 7:3 → 6:4] gave the title compound 17a (1.27 g, 83% over 2 steps) as a pale yellow oil.

$R_f = 0.29$ [petroleum ether (40–60):Et$_2$O, 6:4]; $[\alpha]_D^{25.0} = -115.0$ (c = 0.70, CHCl$_3$); *IR* (film) $\nu_{\text{max}}$/cm$^{-1}$ 2954, 2930, 2883, 2857, 2336, 1747, 1674, 1622, 1461, 1398, 1343, 1252, 1200, 1151, 1084, 1006; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 5.39$ (1H, s, C$_4$H), 4.31 (1H, dd, $J = 12.8, 2.3$ Hz, C$_7$H), 3.73 (3H, s, C$_1$O$_2$CH$_3$), 3.66–3.58 (1H, m, C$_9$H$_A$H$_B$), 3.54 (1H, dd, $J = 9.8, 5.9$ Hz, C$_9$H$_A$H$_B$), 3.73 (3H, s, C$_1$O$_2$CH$_3$), 3.66–3.58 (1H, m, C$_9$H$_A$H$_B$), 3.54 (1H, dd, $J = 9.8, 5.9$ Hz, C$_9$H$_A$H$_B$), 3.25 (2H, d, $J = 1.8$ Hz, C$_2$H$_A$H$_B$), 2.56–2.48 (1H, m, C$_6$H), 2.04–1.96 (1H, m, C$_8$H), 1.08 (3H, d, $J = 7.0$ Hz, C$_{25}$H$_3$), 0.92 (3H, d, $J = 6.7$ Hz, C$_{24}$H$_3$), 0.88 (9H, s, C(CH$_3)_3$ of tBu), 0.05 (3H, s, Si(CH$_3)_2$), 0.04 (3H, s, Si(CH$_3)_2$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 195.3$ (C$_5$O), 168.1 (C$_1$O$_2$CH$_3$), 167.8 (C$_3$), 105.3 (C$_4$H), 83.2 (C$_7$H), 64.3 (C$_9$H$_2$), 52.4 (C$_1$O$_2$CH$_3$), 40.4 (C$_2$H$_2$), 40.2 (C$_6$H), 36.9 (C$_8$H), 25.8 (3C, C(CH$_3)_3$ of tBu), 18.2 (C(CH$_3)_3$ of tBu), 9.8 (C$_{25}$H$_3$), 9.5 (C$_{24}$H$_3$), –5.5 (2C, Si(CH$_3)_2$); HRMS (+ESI) Found [M+H]$^+$ = 357.2106; C$_{18}$H$_{33}$O$_5$Si requires 357.2097, Δ 2.52 ppm.
(4R,5S,6S)-4-(tert-Butyl-dimethyl-silanyloxy)-6-((R)-2-(tert-butyl-dimethyl-silanyloxy)-1-methyl-ethyl)-5-methyl-5,6-dihydro-4\(H\)-pyran-2-yl)-acetic acid methyl ester 19a

To a solution of 17a (396 mg, 1.11 mmol) in MeOH (14 mL) at RT was added CeCl\(_3\)•7H\(_2\)O (560 mg, 1.50 mmol) and the solution stirred for 30 min. The reaction mixture was then cooled to \(-78 °C\) and NaBH\(_4\) (126 mg, 1.34 mmol) added in one portion. After 1.5 h at \(-78 °C\), TLC analysis [Et\(_2\)O:petroleum ether (40–60), 8:2] showed no remaining starting material and so the reaction was diluted with Et\(_2\)O (25 mL) and quenched by the addition of sat. aq. NaHCO\(_3\) (20 mL). The aqueous layer was separated and extracted with Et\(_2\)O (2 × 25 mL). The combined organic layers were dried (MgSO\(_4\)) and concentrated \textit{in vacuo} to give a pale yellow oil (394 mg) which was used directly in the next step.

The crude product was then re-dissolved in CH\(_2\)Cl\(_2\) (40 mL) and cooled to 0 °C. To this was added imidazole (375 mg, 5.51 mmol), TBSCl (415 mg, 2.75 mmol), and DMAP (67 mg, 0.55 mmol) and the reaction mixture stirred at RT for 18 h. The reaction was quenched by the addition of sat. aq. NH\(_4\)Cl (50 mL) and the phases separated. The aqueous layer was extracted with Et\(_2\)O (2 × 50 mL) and the combined organic layers dried (MgSO\(_4\)) and concentrated \textit{in vacuo} to give a yellow residue. Purification by column chromatography [SiO\(_2\), petroleum ether (40–60):Et\(_2\)O, 96:4] gave the title compound 19a (470 mg, 90% over 2 steps) as a colourless oil which crystallised at low temperature.

\(R_f = 0.35\) [petroleum ether (40–60):Et\(_2\)O, 94:6]; \([\alpha]_D^{25.0} = +13.9\) (c = 0.50, CHCl\(_3\)); \textbf{IR} (film) \(\nu_{\text{max}}/\text{cm}^{-1}\) 2954, 2929, 2857, 1747, 1682, 1469, 1405, 1358, 1334, 1249, 1205, 1165, 1098, 1066, 1040, 1007; \textbf{\(^1\)H NMR} (CDCl\(_3\), 400 MHz) \(\delta = 4.59\) (1H, d, \(J = 1.7 \text{ Hz}, \text{C}4\text{H}\)), 3.96 (1H, d, \(J = 8.0 \text{ Hz}, \text{C}5\text{H}\)), 3.81 (1H, dd, \(J = 10.1, 2.7 \text{ Hz}, \text{C}7\text{H}\)), 3.68 (3H, s, ClO\(_2\)CH\(_3\)), 3.60 (1H, dd, \(J = 9.7, 7.5 \text{ Hz}, \text{C}9\text{H}A\text{H}B\)), 3.48 (1H, dd, \(J = 9.7, 6.2 \text{ Hz}, \text{C}9\text{H}A\text{H}B\)), 3.04 (1H, d, \(J = 15.4 \text{ Hz}, \text{C}2\text{H}A\text{H}B\)), 2.99 (1H, d, \(J = 15.4 \text{ Hz}, \text{C}2\text{H}A\text{H}B\)), 2.00–1.92 (1H, m, C8H), 1.80–1.72 (1H, m,
C6H), 0.94–0.89 (12H, m, C(CH3)3 of tBu and C25H3), 0.89 (9H, s, C(CH3)3 of tBu), 0.84 (3H, d, J = 6.9 Hz, C24H3), 0.09 (3H, s, Si(CH3)2), 0.08 (3H, s, Si(CH3)2), 0.03 (6H, s, Si(CH3)2); 13C NMR (CDCl3, 100 MHz) δ = 170.4 (C1O2CH3), 148.1 (C3), 103.5 (C4H), 78.8 (C7H), 70.7 (C5H), 65.3 (C9H2), 51.8 (C1O2CH3), 39.8 (C2H2), 36.6 (C6H), 36.3 (C8H), 25.9 (6C, C(CH3)3 of tBu), 18.3 (C(CH3)3 of tBu), 18.1 (C(CH3)3 of tBu), 13.9 (C25H3), 9.4 (C24H3), -4.1 (Si(CH3)2), -4.6 (Si(CH3)2), -5.4 (2C, Si(CH3)2); HRMS (+ESI) Found [M+Na]+ = 495.2927; C24H48O5Si2Na requires 495.2938, Δ 2.22 ppm.

((2S,4S,5S,6S)-4-(tert-Butyl-dimethyl-silanyloxy)-6-((R)-2-(tert-butyl-dimethylsilanyloxy)-1-methyl-ethyl)-2-methoxy-5-methyl-tetrahydro-pyran-2-yl)-acetic acid methyl ester 20a

To a solution of 19a (156 mg, 0.33 mmol) in CH2Cl2 (10 mL) was added MeOH (330 μL) and (±)-CSA (8 mg, 0.033 mmol) sequentially at RT. The mixture was stirred for 2 h, after which the reaction was quenched by the addition of sat. aq. NaHCO3 (10 mL). The phases were separated and the aqueous layer extracted with CH2Cl2 (3 × 10 mL). The combined organic layers were dried (MgSO4) and concentrated in vacuo. Purification by column chromatography [SiO2, petroleum ether (40–60):Et2O, 95:5→9:1] gave the title compound 20a (113 mg, 68%) as a colourless oil.†

*RF = 0.66 [petroleum ether (40–60):Et2O, 85:15]; [α]D25.0 = –48.1 (c = 0.51, CHCl3); IR (film) νmax/cm−1 2954, 2929, 2858, 1746, 1472, 1437, 1382, 1360, 1314, 1251, 1220, 1148, 1128, 1067, 1034, 1005; 1H NMR (CDCl3, 400 MHz) δ = 3.67 (3H, s, C1O2CH3), 3.66–3.54 (2H, m, C5H and C9H(A)H(B)), 3.48–3.41 (2H, m, C7H and C9H(A)H(B)), 3.19 (3H, s, C3OCH3), 2.61 (2H, s, C2H(A)H(B)), 2.12 (1H, dd, J = 12.9, 4.7 Hz, equatorial C4H(A)H(B)), 1.88–1.80 (1H, m, C8H), 1.67

† Despite performing this reaction under identical reaction conditions, this procedure was found to be unreliable, giving yields ranging between 20–68%.
(1H, dd, J = 12.7, 11.0 Hz, axial C4H2H6), 1.47–1.38 (1H, m, C6H), 0.89 (9H, s, C(CH3)3 of tBu), 0.88 (9H, s, C(CH3)3 of tBu), 0.85 (3H, d, J = 6.5 Hz, C25H3), 0.77 (3H, d, J = 6.9 Hz, C24H3), 0.07 (6H, s, Si(CH2)3), 0.04 (3H, s, Si(CH2)3), 0.02 (3H, s, Si(CH2)3); 13C NMR (CDCl3, 100 MHz) δ = 169.9 (C1O2CH3), 98.7 (C3), 72.5 (C7H), 70.7 (C5H), 65.6 (C9H2), 51.5 (C1O2CH3), 47.7 (C3OCH3), 43.1 (C4H2), 41.9 (C2H2), 39.7 (C6H), 36.6 (C8H), 25.9 (6C, C(CH3)3 of tBu), 18.2 (C(CH3)3 of tBu), 18.0 (C(CH3)3 of tBu), 12.5 (C25H3), 8.9 (C24H3), −4.0 (Si(CH3)2), −4.7 (Si(CH3)2), −5.3 (Si(CH3)2), −5.4 (Si(CH3)2); HRMS (+ESI) Found [M+Na]+ = 527.3198; C25H42O6Si2Na requires 527.3200, Δ 0.38 ppm.

(2R,3R,4R)-1-(Benzyloxy)-2,4-dimethylhex-5-yn-3-ol 10b

![Chemical Structure](image)

To a stirring solution of Pd(OAc)2 (150 mg, 0.67 mmol) in THF (80 mL) at −78 °C was added PPh3 (170 mg, 0.67 mmol). The resulting yellow solution was stirred for 10 mins at which point 9 (1.73 g, 11.7 mmol) and 8b (1.54 g, 8.36 mmol) were added dropwise sequentially. After stirring for 5 mins ZnEt2 (1 M in hexanes, 25.0 mL, 25.0 mmol) was added to the mixture over a period of 1 h. The reaction mixture was stirred for 30 mins at −78 °C before being slowly warmed to −25 °C and maintained at this temperature for a further 24 h. The reaction was quenched by the addition of sat. aq. NH4Cl (160 mL), diluted with Et2O (200 mL) and warmed to RT. The layers were separated and the aqueous layer further extracted with Et2O (3 × 150 mL), and the combined organic layers dried (MgSO4), and concentrated in vacuo. Purification by column chromatography [SiO2, petroleum ether (40–60):Et2O:Et3N, 98:1:1→95:4:1] gave the title compound 10b (4.01 g, 71%) as a pale yellow oil as the major diastereomer (dr = 94:6).

Diastereomeric ratio ascertained by 1H NMR spectroscopy of the crude mixture; δH 0.99 (3H, d, J = 7.0 Hz, C24H3 major), 0.93 (3H, d, J = 6.9 Hz, C24H3 minor).

\[ R_t = 0.10 \text{ [petroleum ether (40–60):Et2O, 9:1]; } \ [\alpha]_D^{25.0} = +10.9 \ (c = 0.73, \ CHCl_3); \ \text{IR (film) } \nu_{\text{max}}/\text{cm}^{-1} \ 3500, 3294, 2972, 2875, 1454, 1363, 1207, 1095, 1028; \ 1H \ NMR (CDCl3, 400 MHz) \delta \]
= 7.38–7.28 (5H, m, Ph), 4.51 (2H, s, OCH₂Ph), 3.58–3.53 (2H, m, C7H and C9H₃H₃), 3.48 (1H, dd, J = 9.2, 5.1 Hz, C9H₃H₃), 2.69–2.62 (1H, m, C6H), 2.35 (1H, d, J = 5.3 Hz, CHOH), 2.13 (1H, d, J = 2.4 Hz, C4H), 2.05–1.95 (1H, m, C8H), 1.21 (3H, d, J = 7.0 Hz, C25H₃), 1.20 (3H, d, J = 7.0 Hz, C24H₃);

\(^{13}C\) NMR (CDCl₃, 100 MHz) δ = 138.3 (ipso Ph), 128.4 (2C, ortho Ph), 127.6 (2C, meta Ph), 127.5 (para Ph), 86.2 (C5), 75.7 (C7H), 73.9 (C9H₂), 73.3 (OCH₂Ph), 70.5 (C₄H), 36.3 (C₈H), 30.5 (C₆H), 17.7 (C₂₅H₃), 10.9 (C₂₄H₃); HRMS (+ESI) Found [M+Na]⁺ = 255.1353; C₁₅H₂₀O₂Na requires 255.1361, Δ3.14 ppm.

1-((1R,2R)-1-((R)-2-Benzylxy-1-methyl-ethyl)-2-methyl-but-3ynyloxymethyl)-4-methoxy-benzene S₄

To a solution of 10b (13.2 g, 51.5 mmol) in DMF (180 mL) and THF (180 mL) at 0 °C was added NaH (60% in mineral oil, 2.47 g, 61.8 mmol). The mixture was stirred for 45 min at RT, after which PMBBr (9.00 mL, 61.5 mmol) was added dropwise and the reaction stirred for 2 h at RT. The reaction was quenched by the addition of sat. aq. NH₄Cl (200 mL) and diluted with Et₂O (200 mL). The phases were separated and the aqueous layer extracted with Et₂O (2 × 150 mL). The combined organics were washed with sat. aq. LiCl (200 mL), dried (MgSO₄) and concentrated in vacuo to give a pale yellow oil. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O:Et₃N, 94:5:1→90:9:1] gave the title compound S₄ (16.8 g, 86%) as a colourless oil.

\( R_f = 0.29 \) [petroleum ether (40–60):Et₂O, 9:1]; \([\alpha]_D^{25.0} = \) –34.7 (c = 0.73, CHCl₃); IR (film) \( \nu_{\text{max}}/\text{cm}^{-1} \) 3293, 2971, 2932, 2906, 2859, 1612, 1514, 1454, 1362, 1301, 1246, 1172, 1073, 1036; \(^1H\) NMR (CDCl₃, 400 MHz) δ = 7.36–7.30 (4H, m, Ph), 7.28–7.24 (3H, m, Ph and (CH)₂COCH₃ of PMB), 6.85 (2H, d, J = 8.6 Hz, C(CH)₂ of PMB), 4.77 (1H, d, J = 10.8 Hz, OCH₃H₃Ph), 4.50–4.42 (3H, m, OCH₃H₃Ph and OCH₃H₃Ph(OCH₃)), 3.80 (3H, s, OCH₃), 3.54 (1H, dd, J = 7.0, 4.1 Hz, C₇H), 3.46 (1H, dd, J = 9.1, 7.5 Hz, C₉H₃H₃), 3.37 (1H, dd, J = 9.1, 5.7 Hz, C₉H₃H₃), 2.80–2.72 (1H, m, C₆H), 2.17–2.10 (1H, m, C₈H), 2.08 (1H, d, J = 2.4 Hz, C₄H), 1.20 (3H, d, J
= 7.1 Hz, C25H3), 0.94 (3H, d, J = 6.9 Hz, C24H3);

\[ ^{13}C \text{ NMR} \ (\text{CDCl}_3, \ 100 \text{ MHz}) \ \delta = 159.1 \ (\text{Ar}), 138.5 \ (\text{ipso Ph}), 131.2 \ (2\text{C, Ar}), 129.4 \ (2\text{C, Ar}), 128.3 \ (2\text{C, ortho Ph}), 127.7 \ (2\text{C, meta Ph}), 127.5 \ (\text{para Ph}), 113.6 \ (\text{Ar}), 87.4 \ (C5), 81.6 \ (C7H), 74.3 \ (\text{OCH}_2\text{Ar}), 73.0 \ (2\text{C, C9H}_2 \ \text{and OCH}_2\text{Ph}), 69.3 \ (C4), 55.3 \ (\text{OCH}_3), 36.0 \ (\text{C8H}), 29.5 \ (\text{C6H}), 17.9 \ (\text{C25H}_3), 11.4 \ (\text{C24H}_3); \]

HRMS (+ESI) Found [M+H]^+ = 353.2112; C23H29O3 requires 353.2117, Δ 1.42 ppm.

\((4R,5R,6R)-7-\text{Benzyloxy-5-(4-methoxy-benzyloxy)-4,6-dimethyl-hept-2-ynoic acid ethyl ester S5}\)

To a solution of S4 (1.53 g, 4.34 mmol) in THF (65 mL) at −78 °C was added nBuLi (1.47 M in hexanes, 3.25 mL, 4.78 mmol) dropwise. The reaction was stirred for 1 h, after which ethyl chloroformate (625 μL, 6.51 mmol) was added and the reaction allowed to warm to RT over 18 h. The reaction was quenched by the addition of sat. aq. NH4Cl (80 mL) and diluted with Et2O (80 mL). The aqueous layer was separated and extracted with Et2O (2 × 80 mL). The combined organic layers were dried (MgSO4), filtered and concentrated in vacuo to afford a pale yellow oil. Purification by column chromatography [SiO2, petroleum ether (40–60):Et2O, 8:2] gave the title compound S5 (1.74 g, 95%) as a pale yellow oil.

\[ R_f = 0.23 \] [petroleum ether (40–60):Et2O, 8:2]; \[ [\alpha]_{D}^{25.0} = -4.1 \ (c = 0.815, \ \text{CHCl}_3); \]

IR (film) \[ \nu_{\text{max}}/\text{cm}^{-1} = 2973, 2938, 2921, 2240, 1706, 1613, 1514, 1454, 1365, 1301, 1243, 1173, 1033; \]

\[ ^{1}H \text{ NMR} \ (\text{CDCl}_3, \ 400 \text{ MHz}) \ \delta = 7.37–7.30 \ (4\text{H, m, Ph}), 7.29–7.25 \ (3\text{H, m, Ph and (C(CH)\text{2COCH}_3} \text{ of PMB}), 6.85 \ (2\text{H, d, J = 8.6 Hz, C(CH)\text{2 of PMB}}), 4.76 \ (1\text{H, d, J = 10.5 Hz, OCH}_4\text{H}_3\text{Ph}), 4.50–

4.42 \ (3\text{H, m, OCH}_3\text{H}_3\text{Ph and OCH}_3\text{Ph(OCH}_3\text{))}, 4.21 \ (2\text{H, q, J = 7.1 Hz, OCH}_2\text{CH}_3), 3.80 \ (3\text{H, s, OCH}_3), 3.63 \ (1\text{H, dd, J = 7.6, 3.6 Hz, C7H}), 3.47 \ (1\text{H, dd, J = 9.0, 8.0 Hz, C9H}_4\text{H}_3\text{)), 3.37 \ (1\text{H, dd, J = 9.1, 5.4 Hz, C9H}_4\text{H}_3\text{)), 2.88 \ (1\text{H, quint, J = 7.2 Hz, C6H}), 2.12–2.05 \ (1\text{H, m, C8H}), 1.29 \ (3\text{H, t, J = 7.1 Hz, OCH}_2\text{CH}_3), 1.22 \ (3\text{H, d, J = 7.1 Hz, C25H}_3), 0.91 \ (3\text{H, d, J = 6.9 Hz, C24H}_3); \]

\[ ^{13}C \text{ NMR} \ (\text{CDCl}_3, \ 100 \text{ MHz}) \ \delta = 159.2 \ (\text{Ar}), 153.8 \ (C3), 138.4 \ (\text{ipso Ph}), 130.8 \ (2\text{C, Ar}), 129.6 \ (2\text{C, Ar}), 128.4 \ (2\text{C, ortho Ph}), 127.7 \ (2\text{C, meta Ph}), 127.6 \ (\text{para Ph}), 113.7 \ (\text{Ar}), 91.9 \ (C5), 81.0 \]
(C7H), 74.6 (OCH₂Ar), 74.1 (C4), 73.1 (OCH₂Ph), 72.7 (C9H₂), 61.7 (OCH₂CH₃), 55.3 (OCH₃), 35.8 (C8H), 29.9 (C6H), 16.8 (C25H₃), 14.0 (OCH₂CH₃), 10.9 (C24H₃); HRMS (+ESI) Found [M+Na]⁺ = 447.2151; C₂₆H₃₂O₅Na requires 447.2147, Δ 0.89 ppm.

(7R,9S,10S)-9-((R)-2-Benzylxoy-1-methyl-ethyl)-7-hydroxy-10-methyl-8-oxa-1,4-dithiaspiro[4.5]dec-7-yl)-acetic acid methyl ester 13b

To a solution of iPr₂NH (440 µL, 3.12 mmol) in THF (5 mL) at –78 °C was added nBuLi (1.5 N in hexanes, 2.08 mL, 3.12 mmol) dropwise. The solution was allowed to warm to 0 °C, stirred for 10 min and then re-cooled to –78 °C. Methyl acetate (260 µL, 3.25 mmol) was added dropwise and the reaction stirred for 1 h. This solution of the preformed anion was then cannulated quickly to a solution of S₅ (575 mg, 1.35 mmol) in THF (6 mL) at –78 °C. The reaction was then warmed to RT over 18 h. The reaction was quenched with sat. aq. NH₄Cl (10 mL), the aqueous layer separated and extracted with Et₂O (3 × 15 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo to give 11b (3.12 mmol, assumed quant.) as a pale yellow oil which was used directly in the next step.

To a solution of 11b (3.12 mmol, assumed quant.) in MeOH (18 mL) and CH₂Cl₂ (18 mL) at –10 °C was added 1,2-ethanedithiol (125 µL, 1.49 mmol), followed by NaOMe (80 mg, 1.49 mmol). The reaction was allowed to warm to RT and stirred for 18 h. The reaction was quenched by the addition of sat. aq. NH₄Cl (25 mL). The aqueous layer was extracted with Et₂O (3 × 20 mL). The organic phases were dried (MgSO₄) and concentrated in vacuo. The resulting pale yellow oil (12b) was dissolved in CH₂Cl₂ (80 mL) and pH 7 phosphate buffer (8 mL) at RT. DDQ (340 mg, 1.49 mmol) was then added and the reaction mixture stirred for 3 h. The reaction was quenched by the addition of sat. aq. NH₄Cl (50 mL) and the phases separated. The aqueous layer was extracted with CH₂Cl₂ (2 × 25 mL) and Et₂O (15 mL). The combined organic layers
were washed with H₂O (60 mL), dried (MgSO₄) and concentrated in vacuo to give a dark brown oil. The crude product was dissolved in CH₂Cl₂ and stirred with aminoethyl polystyrene quadra gel (1.0 g) overnight. Filtration, evaporation and purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 7:3] gave the title compound 13b (345 mg, 60% over 3 steps) as a colourless oil.

**Rf** = 0.31 [petroleum ether (40–60):Et₂O, 6:4]; [α]D = −9.9 (c = 0.91, CHCl₃); **IR** (film) v_{max}/cm⁻¹ 3456, 2969, 2924, 2875, 1717, 1453, 1437, 1347, 1170, 1092, 1002; **¹H NMR** (CDCl₃, 400 MHz) δ = 7.37–7.29 (4H, m, Ph), 7.28–7.23 (1H, m, Ph), 4.86 (1H, d, J = 1.5 Hz, OH), 4.55 (1H, d, J = 12.0 Hz, OCH₂Ph), 4.46 (1H, d, J = 12.0 Hz, OCH₂Ph), 3.93 (1H, dd, J = 10.1, 2.1 Hz, C₇H), 3.65 (3H, s, C₁O₂CH₃), 3.40 (1H, dd, J = 9.0, 6.9 Hz, C₉H₁₈), 3.31–3.23 (5H, m, C₉H₁₈ and SCH₂CH₂S), 2.60 (1H, d, J = 13.8 Hz, C₂H₂H₂B), 2.56 (2H, s, C₄H₂H₂B), 2.31 (1H, dd, J = 13.8, 1.5 Hz, C₂H₂H₂B), 2.13–2.07 (1H, m, C₈H), 1.91–1.87 (1H, m, C₆H), 1.09 (3H, d, J = 6.6 Hz, C₂₅H₃), 0.84 (3H, d, J = 6.9 Hz, C₂₄H₃); **¹³C NMR** (CDCl₃, 100 MHz) δ = 171.6 (C₁O₂CH₃), 138.8 (ipso Ph), 128.3 (2C, ortho Ph), 127.6 (2C, meta Ph), 127.4 (para Ph), 95.0 (C₃), 73.6 (C₉H₂), 73.3 (C₇H), 73.2 (OCH₂Ph), 70.0 (C₅), 51.7 (C₁O₂CH₃), 51.6 (C₂H₂), 45.3 (C₄H₂), 43.3 (C₆H), 41.2 (SCH₂CH₂S), 38.8 (SCH₂CH₂S), 34.7 (C₈H), 12.0 (C₂₅H₃), 9.6 (C₂₄H₃); **HRMS** (+ESI) Found [M+Na]^+ = 449.1439; C_{2₁}H_{₃₀}O₅S₂Na requires 449.1432, Δ 1.56 ppm.

((7R,9S,10S)-9-((R)-2-Benzoyloxy-1-methyl-ethyl)-7-methoxy-10-methyl-8-oxa-1,4-dithiaspiro[4.5]dec-7-yl)-acetic acid methyl ester S6

To a solution of 13b (275 mg, 0.64 mmol) in MeOH (6 mL) at RT was added trimethylorthoformate (1.05 mL, 9.67 mmol) and pyridinium p-toluenesulphonate (325 mg, 1.29 mmol) sequentially. The reaction was stirred for 18 h at RT after which it was quenched by the addition of sat. aq. NH₄Cl (25 mL). The resulting mixture was extracted with Et₂O (3 ×
20 mL) and the combined organic layers dried (MgSO₄) and concentrated *in vacuo* to give a white solid. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 7:3] gave the title compound S6 (230 mg, 81%) as a colourless oil.

\[ R_f = 0.36 \text{ [petroleum ether (40–60):Et₂O, 7:3]; } [\alpha]_D^{25.0} = -28.9 \text{ (c = 0.425, CHCl₃); IR (film) } \nu_{\text{max}}/\text{cm}^{-1} \text{ 2969, 2926, 2881, 1737, 1454, 1436, 1319, 1230, 1191, 1096, 1025; } ^1\text{H NMR (CDCl₃, 400 MHz) } \delta = 7.37–7.29 \text{ (4H, m, Ph), 7.28–7.26 (1H, m, Ph), 4.51 (1H, d, } J = 11.9 \text{ Hz, OCH₃Ph), 4.46 (1H, d, } J = 11.9 \text{ Hz, OCH₃Ph), 3.73 (1H, dd, } J = 10.1, 1.9 \text{ Hz, C7H), 3.66 (3H, s, C1O₂CH₃), 3.57 (1H, t, } J = 8.6 \text{ Hz, C9H₂B), 3.33 (1H, dd, } J = 8.6, 6.5 \text{ Hz, C9H₂B), 3.25 (3H, s, C3OCH₃), 3.25–3.16 (4H, m, SCH₂CH₂S), 2.66 (2H, s, C2H₂B), 2.60 (2H, s, C4H₂), 2.18–2.10 (1H, m, C8H), 1.87–1.82 (1H, m, C6H), 1.07 (3H, d, } J = 6.6 \text{ Hz, C25H₃), 0.84 (3H, d, } J = 6.9 \text{ Hz, C24H₃); } ^13\text{C NMR (CDCl₃, 100 MHz) } \delta = 169.5 \text{ (C1O₂CH₃), 138.5 (ipso Ph), 128.3 (2C, ortho Ph), 127.6 (2C, meta Ph), 127.5 (para Ph), 97.8 (C3), 73.3 (C7H), 73.2 (C9H₂), 73.0 (OCH₂Ph), 69.7 (C5), 51.7 (C1O₂CH₃), 50.7 (C2H₂), 47.5 (C3OCH₃), 43.3 (C6H), 41.9 (C4H₂), 41.7 (SCH₂CH₂S), 38.6 (SCH₂CH₂S), 34.5 (C8H), 11.9 (C25H₃), 9.4 (C24H₃); HRMS (+ESI) Found [M+Na]^+ = 463.1567; C₂₂H₃₀O₅S₂Na requires 463.1589, Δ 4.75 ppm.\]

\((2S,5S,6S)-6-((R)-2-Benzylxoy-1-methyl-ethyl)-2-methoxy-5-methyl-4-oxo-tetrahydropyran-2-yl)-acetic acid methyl ester 14b

To a solution of S6 (513 mg, 1.16 mmol) in MeCN (20 mL) and H₂O (2.6 mL) at 0 °C was added a freshly prepared solution of BTI (0.033 M in MeCN, 70.0 mL, 2.33 mmol) dropwise. The reaction mixture was stirred at 0 °C for 2 h after which it was quenched by the addition of a mixture of sat. aq. Na₂SO₃ (50 mL) and sat. aq. NaHCO₃ (50 mL) (1:1). The reaction was diluted with EtOAc (70 mL) and the phases separated. The aqueous layer was extracted with EtOAc (2 × 70 mL) and the combined organic layers dried (MgSO₄) and concentrated *in vacuo*. Purification
by column chromatography [SiO$_2$, Et$_2$O:petroleum ether (40–60), 8:2] gave the title compound 14b (368 mg, 87%) as a pale yellow oil.

$R_f = 0.25$ [petroleum ether (40–60):Et$_2$O, 7:3]; $[\alpha]_D^{25.0} = -68.0$ (c = 0.57, CHCl$_3$); IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 2973, 2937, 2880, 1720, 1437, 1315, 1244, 1195, 1166, 1139, 1096, 1047, 1016; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 7.40–7.26$ (5H, m, Ph), 4.49 (2H, s, OCH$_A$H$_B$Ph), 3.81 (1H, dd, $J = 10.7$, 1.7 Hz, C7H), 3.69 (3H, s, C1O$_2$CH$_3$), 3.61 (1H, t, $J = 8.8$ Hz, C9H$_A$H$_B$), 3.41 (1H, dd, $J = 8.9$, 5.9 Hz, C9H$_A$H$_B$), 3.17 (3H, s, C3OCH$_3$), 3.15 (1H, dd, $J = 10.7$, 1.7 Hz, C7H), 3.03 (1H, t, $J = 8.9$ Hz, C9H$_A$H$_B$), 2.98 (1H, m, C6H), 2.15–2.08 (1H, m, C8H), 0.98 (3H, d, $J = 6.6$ Hz, C25H$_3$), 0.93 (3H, d, $J = 7.0$ Hz, C24H$_3$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 206.9$ (C5O), 169.3 (C1O$_2$CH$_3$), 138.3 (ipso Ph), 128.4 (2C, ortho Ph), 127.6 (2C, meta Ph), 127.5 (para Ph), 100.8 (C3), 74.0 (C7H), 73.0 (OCH$_2$Ph), 72.6 (C9H$_2$), 51.8 (C1O$_2$CH$_3$), 49.7 (C4H$_2$), 48.2 (C3OCH$_3$), 45.6 (C6H), 41.0 (C2H$_2$), 34.5 (C8H), 9.0 (C24H$_3$), 8.7 (C25H$_3$); HRMS (+ESI) Found [M+Na]$^+$ = 387.1777; C$_{20}$H$_{28}$O$_6$Na requires 387.1784, $\Delta$ 0.18 ppm.

((5S,6S)-6-((R)-2-Benzylxoy-1-methyl-ethyl)-5-methyl-4-oxo-5,6-dihydro-4H-pyran-2-y1)-acetic acid methyl ester 17b

To a solution of 14b (285 mg, 0.78 mmol) in CH$_2$Cl$_2$ (20 mL) at -10 °C was added TfOH (85 μL, 0.94 mmol) dropwise. After approximately 2 mins the reaction was quenched by the addition of sat. aq. NaHCO$_3$ (5 mL) and extracted with CH$_2$Cl$_2$ (2 × 20 mL) and Et$_2$O (2 × 20 mL). The combined organic extracts were dried (MgSO$_4$) and concentrated in vacuo to give a colourless oil. Purification by column chromatography [SiO$_2$, Et$_2$O:petroleum ether (40–60), 1:1] gave the title compound 17b (228 mg, 88%) as a colourless oil.
\( R_t = 0.14 \) [petroleum ether (40–60):Et₂O, 1:1]; \( [\alpha]_D^{25.0} = -96.1 \) (c = 0.71, CHCl₃); IR (film) \( \nu_{\max}/\text{cm}^{-1} \): 2971, 2938, 2904, 2882, 1743, 1671, 1619, 1455, 1397, 1343, 1256, 1200, 1152, 1086, 1012; H NMR (CDCl₃, 400 MHz) \( \delta = 7.36–7.25 \) (5H, m, Ph), 5.39 (1H, s, C4H), 4.51 (2H, s, OCH₃), 4.34 (1H, dd, \( J = 13.0, 2.3 \) Hz, C7H), 3.69 (3H, s, C1O₂CH₃), 3.54 (1H, t, \( J = 8.9, 8.6 \) Hz, C9H₂), 3.43 (1H, dd, \( J = 9.1, 5.9 \) Hz, C9H₂), 3.25 (1H, d, \( J = 15.9 \) Hz, C2H₂), 3.19 (1H, d, \( J = 6.9 \) Hz, C2H₂), 0.96 (3H, d, \( J = 7.0 \) Hz, C2H₂); C NMR (CDCl₃, 100 MHz) \( \delta = 195.2 \) (C5O), 168.2 (C1O₂CH₃), 167.9 (C3), 138.3 (ipsos Ph), 128.4 (2C, ortho Ph), 127.6 (2C, meta Ph), 127.5 (para Ph), 105.4 (C4H), 83.6 (C7H), 73.2 (OCH₃), 71.7 (C9H₂), 52.3 (C1O₂CH₃), 40.3 (C2H₂), 40.3 (C6H), 34.9 (C8H), 9.7 (C2H₂), 9.6 (C2H₂); HRMS (+ESI) Found [M+H]⁺ = 333.1695; C₁₉H₂₅O₅ requires 333.1702, \( \Delta 2.10 \) ppm.

\((4R,5S,6S)-6-((R)-2-Benzyloxy-1-methyl-ethyl)-4-(tert-butyl-dimethyl-silanyloxy)-5-methyl-5,6-dihydro-4H-pyran-2-yl-acetic acid methyl ester 19b\)

To a solution of 17b (223 mg, 0.67 mmol) in MeOH (8 mL) at RT was added CeCl₃•7H₂O (338 mg, 0.91 mmol) and the solution stirred for 30 min. The reaction mixture was then cooled to \( -78 \) °C and NaBH₄ (76 mg, 2.01 mmol) added in one portion. After 1.5 h at \( -78 \) °C, TLC analysis [Et₂O:petroleum ether (40–60), 7:3] showed no remaining starting material and so the reaction was diluted with Et₂O (10 mL) and quenched by the addition of sat. aq. NaHCO₃ (10 mL). The aqueous layer was separated and extracted with Et₂O (2 \( \times \) 10 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo to give a pale yellow oil (195 mg) which was used directly in the next step.

The crude product was then re-dissolved in CH₂Cl₂ (15 mL) and cooled to 0 °C. To this was added imidazole (250 mg, 3.36 mmol), TBSCl (253 mg, 1.68 mmol), and DMAP (40 mg, 0.33 mmol) and the reaction mixture stirred at RT for 18 h. The reaction was quenched by the
addition of sat. aq. NH₄Cl (25 mL) and the phases separated. The aqueous layer was extracted with Et₂O (2 × 25 mL) and the combined organic layers dried (MgSO₄) and concentrated in vacuo to give a yellow residue. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 9:1→8:2] gave the title compound 19b (292 mg, 97% over 2 steps) as a colourless oil.

**Rf = 0.54 [petroleum ether (40–60):Et₂O, 7:3]; [α]D²⁵.⁰ = +16.4 (c = 0.50, CHCl₃); IR (film) v_max/cm⁻¹ 2956, 2930, 2884, 2856, 1746, 1681, 1358, 1251, 1189, 1151, 1072, 1048, 1007;**

**¹H NMR (CDCl₃, 400 MHz) δ = 7.37–7.29 (4H, m, Ph), 7.28–7.26 (1H, m, Ph), 4.59 (1H, d, J = 1.6 Hz, C4H), 4.52 (1H, d, J = 12.0 Hz, OCH₃H₂BPh), 4.47 (1H, d, J = 12.0 Hz, OCH₃H₂BPh), 3.99 (1H, d, J = 8.2 Hz, C5H), 3.87 (1H, dd, J = 10.3, 2.5 Hz, C7H), 3.63 (3H, s, C1O₂CH₃), 3.50 (1H, t, J = 8.9, 7.8 Hz, C9H₂A), 3.37 (1H, dd, J = 9.0, 6.3 Hz, C9H₂B), 3.05 (1H, d, J = 15.4 Hz, C2H₂B), 2.98 (1H, d, J = 15.4 Hz, C2H₂B), 2.15–2.08 (1H, m, C8H), 1.80–1.70 (1H, m, C6H), 0.95–0.84 (15H, m, C(C(CH₃)₃ of tBu), C24H₃ and C25H₃), 0.06 (6H, s, Si(CH₃)₂);**

**¹³C NMR (CDCl₃, 100 MHz) δ = 170.4 (C₁O₂CH₃), 148.1 (C₃), 138.7 (ipso Ph), 128.3 (2C, ortho Ph), 127.5 (2C, meta Ph), 127.4 (para Ph), 103.8 (C₄H), 79.1 (C₇H), 73.2 (OCH₃Ph), 72.9 (C₉H₂), 70.8 (C₅H), 51.8 (C₁O₂CH₃), 39.8 (C₂H₂), 36.7 (C₈H), 31.9 (C₆H), 25.9 (3C, C(CH₃)₃ of tBu), 18.3 (C(CH₃)₃ of tBu), 13.6 (C₂₅H₃), 9.4 (C₂₄H₃), –4.5 (Si(CH₃)₂), –4.1 (Si(CH₃)₂);**

**HRMS (+ESI) Found [M+Na]⁺ = 471.2545; C₂₅H₄₀O₅SiNa requires 471.2543, Δ 0.42 ppm.**

(2R,3R,4R)-1-(enzyloxy)-2,4-dimethylhex-5-en-3-ol 22⁴

**Procedure 1**

To a 3-necked flask containing THF (150 mL) at –78 °C was condensed trans-but-2-ene (8.50 mL, 94.8 mmol). The resulting solution was stirred for 5 min, after which KOtBu (1 M in THF, 36.4 mL, 36.4 mmol) and nBuLi (2.5 M in hexanes, 14.6 mL, 36.4 mmol) were added dropwise sequentially via cannula ensuring that the internal temperature did not exceed –70 °C.
The resulting bright yellow solution was warmed to –50 °C and maintained at this temperature for a further 30 min after which it was re-cooled to –78 °C. A solution of (+)-Ipc₂BOMe (13.9 g, 44.0 mmol) in Et₂O (54 mL) was then added dropwise, again ensuring that the temperature did not rise above –70 °C. The colourless mixture was stirred for 45 min at –78 °C and BF₃•OEt₂ (6.30 mL, 51.0 mmol) added slowly. After stirring for a further 5 min, 8b (5.22 g, 29.3 mmol) in Et₂O (100 mL) was added dropwise. The solution was stirred at –78 °C for 4 h and then treated with 3 M NaOH (21 mL) followed by H₂O₂ (30%, 9 mL) and warmed to RT slowly over 12 h. The reaction mixture was diluted with H₂O (75 mL) and Et₂O (75 mL) and the layers separated. The aqueous layer was further extracted with Et₂O (3 × 100 mL), and the combined organic layers washed with brine (150 mL), dried (MgSO₄), and concentrated in vacuo. Purification firstly by sublimation of (+)-isopinocampheol (3 days), followed by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 9:1] gave the title compound 22 (2.54 g, 37%, dr = 86:14) as a yellow oil.

Diastereomeric ratio ascertained by ¹H NMR spectroscopy of the crude mixture; δH 5.90 (1H, ddd, J = 16.5, 11.2, 8.5 Hz, C5H minor), 5.80 (1H, ddd, J = 16.2, 10.0, 8.4 Hz, C5H major).

Procedure 2

To a solution of (S,S)-Diisopropyl tartrate (E)-crotylboronate 21† (17.0 g, 57.0 mmol) in PhMe (160 mL) at RT was added 4 Å MS (6.0 g). The mixture was cooled to –78 °C, at which point a solution of 8b (8.5 g, 47.5 mmol) in PhMe (15 mL) was added via cannula over 30 min. The reaction was stirred at –78 °C for 16 h, warmed to –10 °C and 2 N NaOH (130 mL) added dropwise over 15 mins. The mixture was stirred for a further 1 h 30 mins, and then filtered through a pad of Celite® under suction using PhMe (5 × 50 mL). The layers were separated and the aqueous layer further extracted with Et₂O (2 × 200 mL). The combined organic layers were washed with sat. aq. NaHCO₃ (200 mL), brine (200 mL), dried (MgSO₄) and concentrated in vacuo.

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†(S,S)-Diisopropyl tartrate (E)-crotylboronate 21 prepared according to the procedure detailed by Roush. This reagent was obtained as a 0.4:0.6 mixture of unbound (S,S)-diisopropyltartrate: (S,S)-Diisopropyl tartrate (E)-crotylboronate, and as such was scaled in order to compensate for this ratio.
vacuo. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 7:3] gave the title compound 22 (11.4 g, 70%, dr = 88:12) as a yellow oil.

Diastereomeric ratio ascertained by ¹H NMR spectroscopy of the crude mixture; δH 5.90 (1H, ddd, J = 16.5, 11.2, 8.5 Hz, C5H minor), 5.80 (1H, ddd, J = 16.2, 10.0, 8.4 Hz, C5H major).

\[ R_f = 0.21 \text{ [petroleum ether (40–60):Et}_2\text{O, 8:2]; } [\alpha]_{\text{D}}^{25.0} = -6.4 \text{ (c = 0.713, CHCl}_3\text{); } \text{IR (film)} \nu_{\text{max}}/\text{cm}^{-1} 3468, 3067, 3031, 2971, 2933, 2869, 1639, 1494, 1454, 1364, 1306, 1209, 1094, 1029; \] ²H NMR (CDCl₃, 400 MHz) δ = 7.36–7.26 (5H, m, Ph), 5.80 (1H, ddd, J = 16.2, 10.0, 8.4 Hz, C5H), 5.15–5.08 (2 × 1H, 2 × dd, broad unresolved, C4HₐHₐ), 4.52 (2H, s, OCH₂Ph), 3.57 (1H, dd, J = 9.0, 6.0 Hz, C9HₐHₐ), 3.50 (1H, dd, J = 9.2, 5.4 Hz, C9HₐHₐ), 3.49–3.45 (1H, m, C7H), 2.28–2.23 (1H, m, C6H), 2.15–2.02 (1H, br s, OH), 1.97–1.93 (1H, m, C8H), 0.98 (3H, d, J = 6.7 Hz, C25H₃), 0.97 (3H, d, J = 6.9 Hz, C24H₃); ¹³C NMR (CDCl₃, 100 MHz) δ = 141.9 (C5H), 138.4 (ipso Ph), 128.5 (2C, ortho Ph), 127.8 (para Ph), 127.6 (2C, meta Ph), 115.7 (C₄H₂), 75.4 (C₇H), 74.8 (C₉H₂), 73.6 (OCH₂Ph), 41.1 (C₆H), 35.1 (C₈H), 17.7 (C₂₅H₃), 14.0 (C₂₄H₃); HRMS (+ESI) Found [M+Na]⁺ = 257.1513; C₁₅H₂₂O₂Na requires 257.1512, Δ 0.39 ppm.

(2R,3R,4R)-1-(Benzylxy)-2,4-dimethylhex-5-en-3-yl (2S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate S7

To a solution of 22 (16.6 mg, 70.8 μmol) in CH₂Cl₂ (1.1 mL) at RT was added (S)-(−)-α-methyl-α-(trifluoromethyl)phenylacetic acid (51.5 mg, 0.220 mmol) followed by DCC (45.4 mg, 0.220 mmol) and DMAP (26.9 mg, 0.220 mmol). After 20 h the resulting white precipitate was
removed by filtration and the solvent removed in vacuo. Purification by column chromatography (SiO\textsubscript{2}, hexane:Et\textsubscript{2}O, 98:2→95:5) gave the title compound S7 (22.3 mg, 70%) as a colourless oil.\textsuperscript{†}

\[ R_f = 0.53 \text{(hexane:Et}_2\text{O, 7:3); } [\alpha]_D^{27.4} = -25.6 \text{ (c = 1.32, CHCl}_3); \ IR \text{ (film) } \nu_{\text{max}}/\text{cm}^{-1} \text{ 3063, 2974, 2937, 2857, 1743, 1497, 1453, 1380, 1364, 1255, 1166, 1105, 1081, 1015, 994; } ^1\text{H NMR} \text{ (CDCl}_3, 400 MHz) \delta = 7.58 \text{ (2H, d, } J = 6.9 \text{ Hz, ortho Ph), 7.40–7.27 \text{ (8H, m, Ph), 5.73 \text{ (1H, ddd, } J = 16.8, 10.6, 8.8 \text{ Hz, C5H}), 5.30–5.26 \text{ (1H, m, C7H), 5.01–4.95 \text{ (} 2 \times 1\text{H, } 2 \times \text{dd, broad unresolved, C4H}_A\text{H}_B), 4.46 \text{ (1H, d, } J = 12.0 \text{ Hz, OCH}_A\text{H}_B\text{Ph), 4.37 \text{ (1H, d, } J = 12.0 \text{ Hz, OCH}_A\text{H}_B\text{Ph), 3.53 \text{ (3H, s, OCH}_3\text{), 3.19 \text{ (2H, d, } J = 6.6 \text{ Hz, C9H}_A\text{H}_B\text{), 2.58–2.48 \text{ (1H, m, C6H), 2.17–2.10 \text{ (1H, m, C8H), 1.02 \text{ (3H, d, } J = 6.9 \text{ Hz, C25H}), 0.87 \text{ (3H, d, } J = 6.9 \text{ Hz, C24H); } ^{13}\text{C NMR} \text{ (CDCl}_3, 100 MHz) \delta = 166.1 \text{ (C=O), 140.1 \text{ (C5H), 138.3 \text{ (ipso benzyl Ph), 132.2 \text{ (Ph), 129.5 \text{ (Ph), 128.4 \text{ (2C, ortho benzyl Ph), 128.2 \text{ (2C, Ph), 127.8 \text{ (para benzyl Ph), 127.7 \text{ (2C, Ph), 127.6 \text{ (2C, meta benzyl Ph), 123.5 \text{ (q, } J = 288.5 \text{ Hz, CF}_3\text{), 116.0 \text{ (C4H}_2\text{), 84.5 \text{ (q, } J = 27.6 \text{ Hz, CCF}_3\text{), 79.9 \text{ (C7H), 73.2 \text{ (OCH}_2\text{Ph), 72.3 \text{ (C9H}_2\text{), 55.5 \text{ (OCH}_3\text{), 40.8 \text{ (C6H), 35.2 \text{ (C8H), 17.6 \text{ (C25H), 11.2 \text{ (C24H); } } ^{19}\text{F} \text{ (CDCl}_3, 400 MHz) \delta = -71.21; } \text{HRMS (} +\text{ESI) Found [M+H]}^+ = 451.2085; \text{C}_{25}\text{H}_{30}\text{O}_4\text{F}_3 \text{ requires 451.2091, } \Delta 1.33 \text{ ppm.}}

\begin{align*}
(2R,3S,4R)-1-(Benzyloxy)-2,4-dimethylhex-5-en-3-yl (2R)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate S8
\end{align*}

\begin{figure}
\centering
\includegraphics[width=0.2\textwidth]{structure.png}
\caption{Structure of S8}
\end{figure}

To a solution of 22 (18.8 mg, 80 μmol) in CH\textsubscript{2}Cl\textsubscript{2} (1.25 mL) at RT was added (R)-(+)\textendash{}α-methyl-α-(trifluoromethyl)phenylacetic acid (93.7 mg, 0.40 mmol) followed by DCC (82.5 mg, 0.40 mmol) and DMAP (48.9 mg, 0.40 mmol). After 20 h the resulting white precipitate was

\textsuperscript{†} The minor diastereomer obtained from 22 could not be removed from the reaction at this stage.
removed by filtration and the solvent removed \textit{in vacuo}. Purification by column chromatography (SiO$_2$, hexane:Et$_2$O, 98:2→95:5) gave the title compound S\textit{8} (26.6 mg, 74\%) as a colourless oil.\footnote{The minor diastereomer obtained from 22 could not be removed from the reaction at this stage.}

$R_f = 0.63$ (hexane:Et$_2$O, 7:3); $[\alpha]_{D}^{27.5} = -7.8$ (c = 1.39, CHCl$_3$); \textbf{IR} (film) $\nu_{\text{max}}$/cm$^{-1}$ 3071, 2975, 2944, 2853, 1742, 1497, 1453, 1380, 1364, 1254, 1166, 1105, 1082, 1014, 994, 920; \textbf{H NMR} (CDCl$_3$, 400 MHz) $\delta = 7.57$ (2H, d, $J = 6.9$ Hz, \textit{ortho} Ph), 7.40–7.28 (8H, m, Ph), 5.67 (1H, ddd, $J = 17.2$, 10.0, 8.8 Hz, C5H), 5.28–5.24 (1H, m, C7H), 4.97–4.89 (2 × 1H, 2 × dd, broad unresolved, C4H$_{A,B}$), 4.48 (1H, d, $J = 11.9$ Hz, OCH$_A$H$_B$Ph), 4.39 (1H, d, $J = 11.9$ Hz, OCH$_A$H$_B$Ph), 3.48 (3H, s, OCH$_3$), 3.26 (2H, d, $J = 6.1$ Hz, C9H$_{A,B}$), 2.55–2.45 (1H, m, C6H), 2.19–2.11 (1H, m, C8H), 0.99 (3H, d, $J = 6.9$ Hz, C25H$_3$), 0.93 (3H, d, $J = 6.9$ Hz, C24H$_3$); \textbf{C NMR} $\delta =$ (CDCl$_3$, 100 MHz) 166.1 (C=O), 139.7 (C5H), 138.3 (ipso benzyl Ph), 132.0 (Ph), 129.5 (2C, Ph), 128.4 (2C, \textit{ortho} benzyl Ph), 128.3 (2C, Ph), 127.9 (\textit{para} benzyl Ph), 127.8 (Ph), 127.6 (2C, \textit{meta} benzyl Ph), 123.5 (q, $J = 288.4$ Hz, CF$_3$) 116.0 (C4H$_2$), 84.7 (q, $J = 27.8$ Hz, CCF$_3$), 79.9 (C7H), 73.3 (OCH$_2$Ph), 72.4 (C9H$_2$), 55.3 (OCH$_3$), 40.7 (C6H), 35.2 (C8H), 17.3 (C25H$_3$), 11.5 (C24H$_3$); \textbf{F} (CDCl$_3$, 400 MHz) $\delta = -71.24$; \textbf{HRMS} (+ESI) Found [M+H]$^+$ = 451.2091; C$_{25}$H$_{30}$O$_4$F$_3$ requires 451.2091, \Delta 0.00 ppm.
Based on the model proposed by Mosher, the alcohol was assigned the \((R)\)-configuration.

**5-O-Benzyl-2,4-dideoxy-2,4-dimethyl-d-lyxose S9**

To a solution of 22 (3.40 g, 14.5 mmol) in acetone (242 mL) and H₂O (121 mL) (2:1) at RT was added NMO (2.30 g, 19.6 mmol) and OsO₄ [2.5% (w/w) in tBuOH (9.20 mL, 0.725 mmol]. The reaction mixture was stirred for 16 h after which it was quenched with sodium sulfite (5.0 g) and stirred for a further 2 h. The mixture was diluted with H₂O (150 mL) and the layers separated. The aqueous layer was further extracted with CH₂Cl₂ (2 × 150 mL) and the combined organic layers dried (MgSO₄) and concentrated in vacuo. The isolated triol (3.89 g, 14.5 mmol) was used immediately in the next step of the reaction without further purification.
To a solution of the crude triol (3.89 g, 14.5 mmol) in THF (153 mL) and H₂O (15.3 mL) (10:1) at 0 °C was added NaIO₄ (9.30 g, 43.5 mmol). The reaction mixture was warmed to RT over 45 min and then diluted with Et₂O (100 mL) and H₂O (100 mL). The layers were separated and the aqueous layer further extracted with Et₂O (2 × 100 mL). The combined organic layers were washed with H₂O (300 mL) and brine (300 mL) before being dried (MgSO₄) and concentrated in vacuo to give the title compound S9. The relatively clean (> 90% by ¹H NMR) aldehyde (3.43 g, quant.) was carried through to the next step in the synthesis without further purification.

\[ R_f = 0.19 \text{ [petroleum ether (40–60):Et}_2\text{O, 7:3]; } [\alpha]_D^{25.0} = +1.4 \text{ (c = 0.68, CHCl}_3); \text{ IR (film) } \nu_{\text{max}}/\text{cm}^{-1} 3452, 2972, 2940, 2877, 1721, 1455, 1381, 1366, 1195, 1148, 1097, 1031; \text{ } \text{¹H NMR (CDCl}_3, 400 MHz) } \delta = 9.79 (1H, d, J = 2.2 Hz, C5HO), 7.38–7.30 (5H, m, Ph), 4.52 (2H, d, J = 1.8 Hz, OCH₂Ph), 4.01 (1H, dd, J = 8.9, 2.3 Hz, C7H), 3.59–3.55 (2 × 1H, 2 × dd, broad unresolved, C9H₂H₂), 2.53–2.49 (1H, m, C6H), 1.93–1.89 (1H, m, C8H), 1.04 (3H, d, J = 7.2 Hz, C25H₂), 0.99 (3H, d, J = 7.1 Hz, C24H₃); \text{¹³C NMR (CDCl}_3, 100 MHz) } \delta = 205.7 \text{ (C5HO), 137.9 (ipso Ph), 128.6 (2C, ortho Ph), 127.8 (para Ph), 127.7 (2C, meta Ph), 74.7 (C9H₂), 74.3 (C7H), 73.5 (OCH₂Ph), 49.4 (C6H), 35.1 (C8H), 10.7 (C25H₃), 9.8 (C24H₃); HRMS (+ESI) Found [M+Na]⁺ = 259.1306; C₁₄H₂₀O₃Na requires 259.1305, Δ 0.39 ppm.}

\( (2R,3S,4R,5S)-1-(Benzyloxy)-2,4-dimethyloct-7-yn-3,5-diol 23 \)

To a suspension of freshly activated Zn† (5.49 g, 84.0 mmol) in THF (43 mL) at 0 °C was added propargyl bromide (80% in PhMe, 12.67 mL, 117.54 mmol) dropwise. The mixture was cooled to −100 °C and freshly prepared S9 (3.96 g, 16.8 mmol) was added dropwise via cannula as a solution in THF (43 mL), ensuring that the internal temperature did not rise above −95 °C. The reaction was maintained at −100 °C for 2 h and then diluted with 0.1 N HCl (800 mL) and

† Zn activated by stirring in 1 N HCl for 1 h, washing with H₂O (2 × 100 mL) and dried under vacuum at 150 °C. The resulting powder was then ground using a mortar and pestle.
allowed to warm to RT. The layers were separated and the aqueous layer extracted with EtOAc (2 × 1 L), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:EtOAc, 7:3) gave the title compound 23 (2.90 g, 72% over 3 steps, dr = 85:15) as an inseparable mixture of diastereomers.⁷

Diastereomeric ratio ascertained by ¹H NMR spectroscopy of the crude mixture; δ_H 0.84 (3H, d, J = 7.1 Hz, C25H₃ major), 0.80 (3H, d, J = 6.9 Hz, C25H₃, minor).

R_f = 0.20 [petroleum ether (40–60):Et₂O, 1:1]; [α]D²⁵.₀ = −7.7 (c = 0.73, CHCl₃); IR (film) ν_max/cm⁻¹ 3397, 3296, 2964, 2924, 2873, 1455, 1383, 1366, 1255, 1207, 1102; ¹H NMR (CDCl₃, 500 MHz) δ = 7.36–7.28 (5H, m, Ph), 4.52 (1H, d, J = 12.0 Hz, OCH₂A₃H₅Ph), 4.48 (1H, d, J = 12.0 Hz, OCH₂A₃H₅Ph), 4.07 (1H, ddd, J = 8.0, 5.5, 2.4 Hz, C5H), 3.82 (1H, dd, J = 8.8, 2.6 Hz, C7H), 3.60 (1H, dd, J = 9.0, 3.9 Hz, C9H₂₄H₅), 3.54 (1H, dd, J = 9.0, 4.6 Hz, C9H₂₄H₅), 2.49 (1H, ddd, J = 17.0, 8.5, 2.7 Hz, C4H₂₄H₅B), 2.35 (1H, ddd, J = 16.5, 5.3, 2.7 Hz, C4H₂₄H₅B), 2.00 (1H, t, J = 2.7 Hz, C2H), 1.96–1.90 (1H, m, C6H), 1.89–1.83 (1H, m, C8H), 1.02 (3H, d, J = 7.1 Hz, C24H₃), 0.84 (3H, d, J = 7.1 Hz, C25H₃); ¹³C NMR (CDCl₃, 126 MHz) δ = 137.8 (ipsoph, Ph), 128.5 (2C, ortho Ph), 127.8 (para Ph), 127.6 (2C, meta Ph), 82.0 (C3) 76.6 (C7H), 75.6 (C9H₂), 73.5 (OCH₃Ph), 72.2 (C5H), 69.9 (C2H), 38.9 (C6H), 35.3 (C8H), 23.5 (C4H₂), 11.7 (C25H₃), 10.0 (C24H₃); HRMS (+ESI) Found [M+Na]+ = 299.1610; C₁₇H₂₄O₃Na requires 299.1618, Δ 2.67 ppm.

(5S)-1-O-Benzyl-2,4-dideoxy-2,4-dimethyl-3,5-O-(1-methylethylidene)-5-C-prop-2-yn-1-yl-D-arabinitol S10

To a solution of 23 (1.89 g, 6.85 mmol) in acetone (33 mL) at RT was added 2,2-dimethoxypropane (6.74 mL, 54.8 mmol) and (±)-CSA (0.16 g, 0.685 mmol). The reaction mixture was stirred for 1 h and then diluted with sat. aq. NaHCO₃ (20 mL). The layers were
separated and the aqueous layer further extracted with Et₂O (4 × 30 mL), dried (MgSO₄) and concentrated in vacuo to give a yellow oil. The crude title compound S10 (assumed quant.) was used directly.

A small amount of the title compound S10 was purified by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 9:1] for full characterisation as a colourless oil.

\[ R_f = 0.29 \text{ [petroleum ether (40:60):Et}_2\text{O, 9:1]}; \quad [\alpha]_{D}^{25.0} = -2.0 \quad (c = 0.30, \text{CHCl}_3); \quad \text{IR (film)} \nu_{\text{max}}/\text{cm}^{-1} \quad 3302, 2980, 2918, 2873, 1455, 1364, 1227, 1201, 1173, 1140, 1097; \quad \text{IR (film)} \nu_{\text{max}}/\text{cm}^{-1} \quad 3302, 2980, 2918, 2873, 1455, 1382, 1364, 1227, 1201, 1173, 1140, 1097, 1060, 1022; \]

\[ ^1\text{H NMR (CDCl}_3, 500 \text{MHz}) \delta = 7.33–7.26 (5H, m, Ph), 4.51 (1H, d, \quad J = 11.7 \text{ Hz, OCH}_2\text{H}_2\text{Ph}), 4.48 (1H, d, \quad J = 12.0 \text{ Hz, OCH}_2\text{H}_2\text{Ph}), 3.96 (1H, td, \quad J = 7.2, 4.8 \text{ Hz, C5H}), 3.48–3.46 (1H, m, C7H), 3.33 (1H, dd, \quad J = 9.1, 5.9 \text{ Hz, C9H}_2\text{H}_2\text{B}), 2.35 (1H, dd, \quad J = 7.1, 2.6 \text{ Hz, C4H}_2\text{H}_2\text{B}), 2.26 (1H, dd, \quad J = 8.1, 2.7 \text{ Hz, C4H}_2\text{H}_2\text{B}), 1.95 (1H, t, \quad J = 2.6 \text{ Hz, C2H}), 1.92–1.88 (1H, m, C8H), 1.30 (3H, s, acetonide CH₃), 1.28 (3H, s, acetonide CH₃), 0.93 (3H, d, \quad J = 6.9 \text{ Hz, C24H}_3), 0.86 (3H, d, \quad J = 6.8 \text{ Hz, C25H}_3); \]

\[ ^{13}\text{C NMR (CDCl}_3, 126 \text{MHz}) \delta = 138.6 (ipso Ph), 128.3 (2C, ortho Ph), 127.6 (para Ph), 127.4 (2C, meta Ph), 100.6 (C(CH)_3_2, trans acetonide), 81.0 (C3), 73.8 (C7H), 73.1 (OCH_2Ph), 72.8 (C9H_2), 69.3 (C2H), 68.2 (C5H), 36.3 (C8H), 35.4 (C6H), 25.1 (one of C(CH)_3_2 trans acetonide), 23.5 (one of C(CH)_3_2 trans acetonide), 21.0 (C4H_2), 11.4 (C25H_3), 11.1 (C24H_3); \]

HRMS (+ESI) Found [M+Na]^+ = 339.1937; C_{20}H_{28}O_{3}Na requires 339.1931, Δ 1.77 ppm.

(5S)-1-O-Benzyl-2,4-dideoxy-5-C-(4-methoxy-4-oxobut-2-yn-1-yl)-2,4-dimethyl-3,5-O-(1-methylethylidene)-D-arabinitol 24

\[ \text{To a solution of S10 (assumed quant., 6.85 mmol) in THF (68 mL) at } -40 ^\circ\text{C was added } n\text{BuLi (2.08 M in hexanes, 3.95 mL, 8.22 mmol) dropwise. The resulting yellow solution was cooled to} \]
–78 °C and stirred for 15 min after which methyl chloroformate (1.59 mL, 20.6 mmol) was added dropwise. The now colourless solution was stirred at –78 °C for 30 min and then warmed to RT slowly over 90 mins. The reaction mixture was quenched with sat. aq. NH₄Cl (50 mL) and diluted with Et₂O (50 mL). The layers were separated and the aqueous layer further extracted with Et₂O (3 × 75 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O:Et₃N, 9:0.9:0.1] gave the title compound 24 (1.87 g, 73% over 2 steps) as a white solid and as a single diastereomer.

**Rf** = 0.62 [petroleum ether (40–60):Et₂O, 7:3]; **m.p.** = 60–63 °C; [α]D²⁵.⁰ = –3.8 (c = 0.79, CHCl₃); **IR** (film) νmax/cm⁻¹ 2984, 2936, 2873, 2241, 1715, 1455, 1435, 1382, 1362, 1252, 1226, 1171, 1141, 1088, 1072, 1057, 1019; **¹H NMR** (CDCl₃, 500 MHz) δ = 7.35–7.25 (5H, m, Ph), 4.49 (1H, d, J = 12.1 Hz, OCH₄H₂Ph), 4.47 (1H, d, J = 12.0 Hz, OCH₄H₂Ph), 4.01 (1H, td, J = 7.5, 4.9 Hz, C5H), 3.75 (3H, s, C1O₂CH₃), 3.46 (1H, dd, J = 8.1, 2.9 Hz, C7H), 3.42 (1H, dd, J = 9.0, 7.8 Hz, C9H4H₃), 3.32 (1H, dd, J = 9.0, 5.8 Hz, C9H₄H₃), 2.49 (1H, dd, J = 17.0, 7.3 Hz, C4H₄H₃), 2.39 (1H, dd, J = 17.0, 7.7 Hz, C4H₄H₃), 1.99–1.95 (1H, m, C6H), 1.90–1.86 (1H, m, C8H), 1.30 (3H, s, acetonide CH₃), 1.27 (3H, s, acetonide CH₃), 0.92 (3H, d, J = 6.9 Hz, C24H₃), 0.85 (3H, d, J = 6.8 Hz, C25H₃); **¹³C NMR** (CDCl₃, 126 MHz) δ = 154.0 (C1O₂CH₃), 138.6 (ipso Ph), 128.3 (2C, ortho Ph), 127.6 (para Ph), 127.5 (2C, meta Ph), 100.9 (C(CH₃)₂, trans acetonide), 86.2 (C3), 73.7 (C7H), 73.6 (C2), 73.1 (OCH₂Ph), 72.7 (C9H₂), 67.6 (C5H), 52.6 (C1O₂CH₃), 36.2 (C6H), 35.6 (C8H), 25.0 (one of C(CH₃)₂ trans acetonide), 23.3 (one of C(CH₃)₂ trans acetonide), 21.3 (C4H₂), 11.5 (C25H₃), 11.0 (C24H₃); **HRMS** (+ESI) Found [M+H]+ = 375.2176; C₂₂H₃₁O₅ requires 375.2171, Δ 1.33 ppm; **Elemental Analysis** found C, 70.60; H, 8.17. C₂₂H₃₀O₅ requires C, 70.56; H, 8.07%.

The structure and relative stereochemistry was confirmed by X-ray crystallographic analysis after crystallisation from analytical grade EtOH.
CCDC 882400 contains the supplementary crystallographic data for this thesis. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
Methyl (5S,6R,7S,8R)-9-(benzyloxy)-5,7-dihydroxy-6,8-dimethylnon-2-ynoate 25

To a solution of 24 (733 mg, 1.96 mmol) in MeOH (24 mL) at RT was added QP-SA resin (1.12 g, 3.5 mmol/g, 3.92 mmol). The reaction was stirred at RT until TLC analysis indicated that the starting material had been consumed. The QP-SA resin was removed by filtration and the reaction mixture concentrated in vacuo. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 1:1] gave the title compound 25 (619 mg, 95%) as a colourless oil.

\( R_f = 0.26 \) [petroleum ether (40–60):Et₂O, 1:1]; \( [\alpha]_D^{25.0} = -9.8 \) (c = 0.56, CHCl₃); \( \text{IR (film)} \)
\( \nu_{\text{max}}/\text{cm}^{-1} 3409, 2918, 2964, 2861, 2240, 1714, 1453, 1436, 1363, 1258, 1102, 1074, 1029; \)
\( \text{¹H NMR (CDCl₃, 500 MHz)} \) δ = 7.37–7.27 (5H, m, Ph), 4.53 (1H, d, \( J = 11.9 \) Hz, OCH₃Ph), 4.48 (1H, d, \( J = 11.9 \) Hz, OCH₃Ph), 4.08 (1H, ddd, \( J = 7.8, 5.4, 2.2 \) Hz, C₅H), 3.83 (1H, dd, \( J = 9.0, 2.3 \) Hz, C₇H), 3.73 (3H, s, C₁O₂CH₃), 3.62 (1H, dd, \( J = 9.0, 3.5 \) Hz, C₉H₃H₃), 3.54 (1H, dd, \( J = 9.0, 4.4 \) Hz, C₉H₃H₃), 3.07–2.93 (2H, br s, 2 × OH), 2.63 (1H, dd, \( J = 17.1, 8.1 \) Hz, C₄H₄H₄), 2.51 (1H, dd, \( J = 17.1, 5.4 \) Hz, C₄H₄H₄), 1.98–1.94 (1H, m, C₆H), 1.87–1.83 (1H, m, C₈H), 1.02 (3H, d, \( J = 7.1 \) Hz, C₂₄H₃), 0.84 (3H, d, \( J = 7.1 \) Hz, C₂₅H₃); \( \text{¹³C NMR (CDCl₃, 126 MHz)} \) δ = 154.1 (C₁O₂CH₃), 137.7 (ipso Ph), 128.5 (2C, ortho Ph), 127.9 (para Ph), 127.6 (2C, meta Ph), 87.6 (C₃), 77.2 (C₇H), 75.8 (C₉H₂), 74.0 (C₂), 73.6 (OCH₂Ph), 72.2 (C₅H), 52.6 (C₁O₂CH₃), 39.2 (C₆H), 35.2 (C₈H), 23.6 (C₄H₂), 12.2 (C₂₅H₃), 9.9 (C₂₄H₃); \( \text{HRMS (+ESI)} \) Found [M+H]⁺ = 335.1873; C₁₉H₂₇O₅ requires 335.1858, Δ 4.48 ppm.
To substrate 25 (1.42 g, 4.25 mmol) was added AuCl₃ (25.8 mg, 85 μmol) in MeOH (0.01 M, 8.5 mL) at RT. After 45 min the reaction mixture was diluted with EtOAc and petroleum ether (30–40) (1:1, 100 mL), and quenched with sat. aq. NaHCO₃ (100 mL). The layers were separated and the organic layer washed with H₂O (2 × 50 mL) and brine (2 × 50 mL) before being dried (MgSO₄) and concentrated in vacuo. The residue was filtered through a pad of Celite® under suction using EtOAc (3 × 30 mL), and concentrated in vacuo to give the title compound 26 (1.49 g, 96%) as a colourless oil.

Rᵥ = 0.33 (hexane:EtOAc, 1:1); [α]D²⁵ ; ⁰ = −48.1 (c = 0.59, CHCl₃); IR (film) νₚₐₓ/cm⁻¹ 3466, 2968, 2932, 2885, 1738, 1454, 1438, 1378, 1362, 1313, 1221, 1093, 1072, 1054, 1017; ¹H NMR (CDCl₃, 500 MHz) δ = 7.34–7.22 (5H, m, Ph), 4.48 (1H, d, J = 11.9 Hz, OCH₂BPh), 4.43 (1H, d, J = 11.9 Hz, OCH₃BPh), 3.65 (3H, s, C1O₂CH₃), 3.66–3.62 (1H, m, C5H), 3.54 (1H, dd, J = 8.7, 8.6 Hz, C9HₓAₓBₓ), 3.48 (1H, dd, J = 10.9, 1.3 Hz, C7H), 3.32 (1H, dd, J = 8.7, 6.2 Hz, C9HₓAₓBₓ), 3.14 (3H, s, C3OCH₃), 2.66 (1H, d, J = 13.7 Hz, C2HₓAₓBₓ), 2.58 (1H, d, J = 13.6 Hz, C2HₓAₓBₓ), 2.23 (1H, dd, J = 12.7, 4.7 Hz, equatorial C4HₓAₓBₓ), 2.11–2.07 (1H, m, C8H), 1.63 (1H, dd, J = 12.3, 11.5 Hz, axial C4HₓAₓBₓ), 1.43–1.39 (1H, m, C6H), 1.39 (1H, d, J = 5.6 Hz, C5HOH), 0.92 (3H, d, J = 6.5 Hz, C25H₃), 0.81 (3H, d, J = 6.9 Hz, C24H₃); ¹³C NMR (CDCl₃, 126 MHz) δ = 169.7 (C1O₂CH₃), 138.4 (ipso Ph), 128.3 (2C, ortho Ph), 127.6 (para Ph), 127.5 (2C, meta Ph), 98.7 (C3), 73.1 (C9H₂), 73.0 (OCH₂Ph), 72.7 (C7H), 70.0 (C1O₂CH₃), 51.7 (C5H), 47.8 (C3OCH₃), 42.7 (C4H₂), 41.7 (C2H₂), 39.6 (C6H), 33.7 (C8H), 12.0 (C25H₃), 9.3 (C24H₃); HRMS (+ESI) Found [M+Na]⁺ = 389.1948; C₂₀H₃₀O₆Na requires 389.1940, Δ 2.06 ppm; Elemental Analysis found C, 66.05; H, 8.29. C₂₀H₃₀O₆ requires C, 65.55; H, 8.25%.
**Dimethyl 9-O-benzyl-5-O-(tert-butyl(dimethyl)silyl)-2,4,6,8-tetradeoxy-6,8-dimethyl-β-D-galacto-non-3-ulopyranosidonate 20a**

![Chemical structure diagram]

**Procedure 1**

To a solution of 26 (1.49 g, 4.07 mmol) in CH$_2$Cl$_2$ (41 mL) at −78 °C was added 2,6-lutidine (1.04 mL, 8.95 mmol) and TBSOTf (1.03 mL, 4.48 mmol) sequentially. The reaction mixture was stirred for 2 h at −78 °C and then allowed to warm to 0 °C after which CH$_2$Cl$_2$ (120 mL) and H$_2$O (120 mL) were added. The layers were separated and the aqueous layer further extracted with CH$_2$Cl$_2$ (4 × 100 mL). The combined organic layers were washed sequentially with a cooled solution (0 °C) of 1 N HCl (150 mL), sat. aq. NaHCO$_3$ (150 mL), H$_2$O (150 mL) and brine (150 mL) before being dried (MgSO$_4$) and concentrated in vacuo. Purification by column chromatography [SiO$_2$, hexane→hexane:Et$_2$O, 1:1] gave the title compound 20a (1.78 g, 91%) as a colourless oil.

**Procedure 2**

To a solution of 19b (226 mg, 0.50 mmol) in CH$_2$Cl$_2$ (11 mL) was added MeOH (500 μL) and (±)-CSA (12 mg, 0.05 mmol) sequentially at RT. The mixture was stirred for 2 h, after which the reaction was quenched by the addition of sat. aq. NaHCO$_3$ (10 mL). The phases were separated and the aqueous layer extracted with CH$_2$Cl$_2$ (3 × 10 mL). The combined organic layers were dried (MgSO$_4$) and concentrated in vacuo. Purification by column chromatography [SiO$_2$, petroleum ether (40–60):Et$_2$O, 95:5→9:1] gave the title compound 20a (178 mg, 74%) as a colourless oil.$^\dagger$

$^\dagger$ Despite performing this reaction under identical reaction conditions, this procedure was found to be unreliable, giving yields ranging between 20–74%.
\(R_f = 0.42\) [petroleum ether (40–60):Et\(_2\)O, 8:2]; \([\alpha]_{D}^{25.0} = -31.5\) \(c = 0.83, \text{CHCl}_3\); \(\text{IR (film)}\) \(v_{\text{max}}/\text{cm}^{-1}\): 2964, 2930, 2856, 1743, 1455, 1437, 1378, 1361, 1315, 1250, 1220, 1069, 1029, 1005; \(^1\text{H NMR (CDCl}_3, 500 \text{MHz)} \delta = 7.37–7.29\) (4H, m, Ph), 7.28–7.26 (1H, m, Ph), 4.50 (1H, d, \(J = 11.9\) Hz, OCH\(_A\)H\(_B\)Ph), 4.46 (1H, d, \(J = 11.9\) Hz, OCH\(_A\)H\(_B\)Ph), 3.67 (3H, s, C1O\(_2\)CH\(_3\)), 3.64 (1H, m, C5H), 3.56 (1H, dd, \(J = 8.6, 8.5\) Hz, C9H\(_A\)H\(_B\)), 3.48 (1H, dd, \(J = 10.6, 1.6\) Hz, C7H), 3.34 (1H, dd, \(J = 8.8, 6.2\) Hz, C9H\(_A\)H\(_B\)), 3.17 (3H, s, C3OCH\(_3\)), 2.62 (1H, d, \(J = 13.6\) Hz, C2H\(_A\)H\(_B\)), 2.58 (1H, d, \(J = 13.5\) Hz, C2H\(_A\)H\(_B\)), 2.14–2.07 (2H, m, equatorial C4H and C8H), 1.67 (1H, dd, \(J = 12.8, 10.9\) Hz, axial C4H), 1.48–1.39 (1H, m, C6H), 0.89 (9H, s, C(CH\(_3\))\(_3\) of tBu), 0.87 (3H, d, \(J = 6.6\) Hz, C25H\(_3\)), 0.84 (3H, d, \(J = 6.9\) Hz, C24H\(_3\)), 0.06 (6H, s, Si(CH\(_3\))\(_2\)); \(^{13}\text{C NMR (CDCl}_3, 126 \text{MHz)} \delta = 169.8\) (C1O\(_2\)CH\(_3\)), 138.5 (ipso Ph), 128.3 (2C, ortho Ph), 127.6 (para Ph), 127.5 (2C, meta Ph), 98.8 (C3), 73.2 (C9H\(_2\)), 73.0 (OCH\(_2\)Ph), 72.8 (C7H), 70.6 (C1O\(_2\)CH\(_3\)), 51.6 (C5H), 47.6 (C3OCH\(_3\)), 43.1 (C4H\(_2\)), 41.8 (C2H\(_2\)), 39.8 (C6H), 33.9 (C8H), 25.8 (3C, C(CH\(_3\))\(_3\) of tBu), 18.0 (C(CH\(_3\))\(_3\) of tBu), 12.4 (C25H\(_3\)), 9.3 (C24H\(_3\)), −4.1 (Si(CH\(_3\))\(_2\)), −4.7 (Si(CH\(_3\))\(_2\)); \(\text{HRMS (+ESI)}\) Found [M+Na]\(^+\) = 503.2805; C\(_{26}\)H\(_{44}\)O\(_6\)SiNa requires 503.2806, Δ 0.20 ppm.

**Dimethyl 2,4,6,8-tetra(deoxy)-6,8-dimethyl-\(\beta\)-\(D\)-galacto-non-3-ulopyranosidonate S11**

![Dimethyl 2,4,6,8-tetra(deoxy)-6,8-dimethyl-\(\beta\)-\(D\)-galacto-non-3-ulopyranosidonate S11](image)

**Procedure 1**

To a solution of 20b (642 mg, 1.34 mmol) in EtOAc (40 mL) at RT was added 10% Pd/C (164 mg). The resulting suspension was evacuated and back filled with hydrogen (× 3) and left to stir under a hydrogen atmosphere for 48 h. The mixture was then filtered through a pad of Celite\(^\circledR\) under suction using PhMe (3 × 50 mL) and concentrated in vacuo to give the title compound S11 (502 mg, 96%) as a colourless oil.\(^9\)
Procedure 2

To a solution of 20a (113 mg, 0.224 mmol) in THF (5 mL) at RT was added TBAF (1.0 M in THF, 225 μL, 0.225 mmol) dropwise. After 1 h, TLC showed partial conversion to a new product. A further equivalent of TBAF (225 μL, 0.225 mmol) was added and the reaction mixture stirred for an additional 1 h. The reaction was quenched by the addition of sat. aq. NaHCO₃ (10 mL) and the phases separated. The aqueous layer was extracted with Et₂O (3 × 10 mL) and the combined organic layers dried (MgSO₄) and concentrat ed in vacuo. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 9:1→6:4] gave the title compound S11 (58 mg, 67%) as a colourless oil as well as starting unreacted 20a (17 mg, 11%).

R_f = 0.10 (hexane:Et₂O, 3:2); [α]D^25.0 = −39.4 (c = 1.12, CHCl₃), [lit.]^7 [α]D^25 −38 (c = 1.0, CHCl₃); IR (film) ν_{max}/cm⁻¹ 3479, 2956, 2931, 2858, 1743, 1463, 1438, 1378, 1362, 1315, 1250, 1223, 1073, 1033, 1003; ^1H NMR (CDCl₃, 500 MHz) δ = 3.72 (1H, d, J = 10.7, 3.6 Hz, C9H_AH_B), 3.66 (3H, s, C1O₂CH₃), 3.67–3.58 (2H, m, C5H and C9H_AH_B), 3.48 (1H, dd, J = 10.6, 2.3 Hz, C7H), 3.20 (3H, s, C3OCH₃), 2.67 (1H, d, J = 13.4 Hz, C2H_AH_B), 2.54 (1H, d, J = 13.4 Hz, C2H_AH_B), 2.33 (1H, br s, C9H_AH_BOH), 2.07 (1H, dd, J = 13.0, 4.7 Hz, equatorial C4H_AH_B), 1.88–1.84 (1H, m, C8H), 1.68 (1H, dd, J = 12.8, 13.0 Hz, axial C4H_AH_B), 1.46–1.39 (1H, m, C6H), 0.91 (3H, d, J = 7.1 Hz, C25H₃), 0.86 (9H, s, C(CH₃)₃ of tBu), 0.84 (3H, d, J = 6.6 Hz, C24H₃), 0.04 (6H, s, Si(CH₃)₂); ^13C NMR (CDCl₃, 126 MHz) δ = 169.6 (C1O₂CH₃), 99.2 (C3), 77.2 (C7H), 70.2 (C5H), 67.4 (C9H₂), 51.7 (C1O₂CH₃), 47.8 (C3OCH₃), 42.9 (C4H₂), 41.8 (C2H₂), 39.9 (C6H), 35.2 (C8H), 25.8 (3C, C(CH₃)₃ of tBu), 18.0 (C(CH₃)₃ of tBu), 12.4 (C24H₃), 8.8 (C25H₃), −4.1 (Si(CH₃)₂), −4.8 (Si(CH₃)₂); HRMS (+ESI) Found [M+Na]^+ = 413.2335; C₁₉H₃₈O₆SiNa requires 413.2329, Δ 1.45 ppm.
Dimethyl (7S)-2,4,6,8-tetradeoxy-2,4-dimethyl-L-galacto-non-7-ulopyranosiduronate 5

To a solution of S11 (652 mg, 1.67 mmol) in CH₂Cl₂ (84 mL) at RT was added K₂CO₃ (3.23 g, 23.4 mmol) and freshly prepared Dess–Martin periodinane (2.12 g, 5.00 mmol) sequentially. The cloudy reaction mixture was stirred for 90 min after which hexane (100 mL) was added, resulting in precipitation. The solids were removed by filtration and the liquor partially concentrated in vacuo before being re-filtered and concentrated to dryness. Purification by column chromatography (SiO₂, hexane:Et₂O, 4:1) gave the title compound 5 (564 mg, 87%) as a colourless oil.

Rᵥ = 0.16 (hexane:Et₂O, 4:1); [α]D²⁷.⁶ = −21.9 (c = 0.95, CHCl₃); IR (film) νmax/cm⁻¹ 2952, 2932, 2858, 1736, 1463, 1438, 1377, 1360, 1251, 1221, 1148, 1073, 1031, 1004; ¹H NMR (CDCl₃, 400 MHz) δ = 9.71 (1H, s, C9HO), 3.89 (1H, dd, J = 10.6, 2.3 Hz, C7H), 3.74–3.67 (1H, m, C5H), 3.66 (3H, s, C1O₂CH₃), 3.16 (3H, s, C3OCH₃), 3.02 (1H, d, J = 13.9 Hz, C2H₄H₈), 2.54 (1H, d, J = 13.9 Hz, C2H₄H₈), 2.50 (1H, qd, J = 6.9, 2.3 Hz, C8H), 2.16 (1H, dd, J = 13.0, 4.7 Hz, equatorial C4H₄H₈), 1.67 (1H, dd, J = 13.0, 10.9 Hz, axial C4H₄H₈), 1.53–1.46 (1H, m, C6H), 1.12 (3H, d, J = 7.0 Hz, C24H₃), 0.91 (3H, d, J = 6.7 Hz, C25H₃), 0.89 (9H, s, C(CH₃)₃ of tBu), 0.07 (6H, s, Si(CH₃)₂); ¹³C NMR (CDCl₃, 100 MHz) δ = 204.2 (C9HO), 169.5 (C1O₂CH₃), 99.3 (C3), 73.2 (C7H), 70.1 (C5H), 51.7 (C1O₂CH₃), 48.1 (C3OCH₃), 47.2 (C8H), 43.0 (C4H₂), 41.5 (C2H₂), 39.6 (C6H), 25.7 (3C, C(CH₃)₃ of tBu), 18.0 (C(CH₃)₃ of tBu), 12.6 (C24H₃), 6.2 (C25H₃), −4.0 (Si(CH₃)₂), −4.8 (Si(CH₃)₂); HRMS (+ESI) Found [M+Na]⁺ = 411.2194; C₁₉H₃₆O₆SiNa requires 411.2179, Δ 3.65 ppm; Elemental Analysis found C, 58.81; H, 9.19. C₁₉H₃₆O₆Si requires C, 58.73; H, 9.34%. 


To a slurry of Cp$_2$ZrCl$_2$ (3.48 g, 11.9 mmol) in CH$_2$Cl$_2$ (100 mL) at RT was added Me$_3$Al (17.2 mL, 179.0 mmol) dropwise. The reaction was stirred for 30 mins at RT and then cooled to –10 °C, at which point a solution of 4-pentyn-1-ol (5.0 g, 59.5 mmol) in CH$_2$Cl$_2$ (25 mL) was added dropwise via syringe over 10 mins. The mixture was warmed to RT and stirred for 18 h, with the reaction progress monitored by removal of an aliquot and integration of the resulting C10CH$_2$ methylene group by $^1$H NMR. When complete, the reaction mixture was cooled to –30 °C and a solution of I$_2$ (19.6 g, 77.4 mmol) in THF (50 mL) was added dropwise over 1 h. The mixture was allowed to warm to RT slowly over a period of 5 h, after which it was re-cooled to –30 °C and quenched by slowly pouring onto a mixture of hexane (500 mL) and Rochelle’s salt (100 mL). The mixture was diluted with Et$_2$O (500 mL) and the layers separated. The aqueous layer was further extracted with Et$_2$O (2 × 500 mL) and the combined organics dried (MgSO$_4$) and concentrated in vacuo. Purification by column chromatography [SiO$_2$, petroleum ether (30:40):Et$_2$O, 9:1] gave the title compound S12 (10.7 g, 84%) as a pale yellow oil.

$R_f$ = 0.25 [petroleum ether (30:40):Et$_2$O, 9:1]; IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 3324, 2940, 2874, 1617, 1438, 1376, 1267, 1142, 1059; $^1$H NMR (CDCl$_3$, 400 MHz) δ = 5.93 (1H, s, C10H), 3.66 (2H, t, $J$ = 6.2 Hz, C14H$_2$), 2.30 (2H, dd, $J$ = 7.7, 7.5 Hz, C12H$_2$), 1.85 (3H, s, C23H$_3$), 1.77–1.69 (2H, m, C13H$_2$); $^{13}$C NMR (CDCl$_3$, 150 MHz) δ = 147.4 (C11), 74.9 (C10H), 62.0 (C14H$_2$), 35.7 (C12H$_2$), 30.5 (C13H$_2$), 23.8 (C23H$_3$); HRMS (+El) Found [M]$^+$ = 225.9854; C$_6$H$_{11}$IO requires 225.9855, Δ 0.44 ppm. All spectroscopic data in agreement with that previously published.
5-Iodo-4-methyl-pent-4-enal 31

To a stirring solution of oxalyl chloride (3.63 mL, 33 mmol) in CH$_2$Cl$_2$ (30 mL) at −78 °C was added DMSO (4.68 mL, 66.0 mmol) dropwise. The reaction mixture was stirred for 10 min at −78 °C and a solution of S12 (5.00 g, 22.0 mmol) in CH$_2$Cl$_2$ (30 mL) was added slowly resulting in the formation of a white precipitate. The mixture was stirred for 20 min at −78 °C at which point Et$_3$N (15.3 mL, 110.0 mmol) was added dropwise. The suspension was allowed to warm to RT over 30 min after which sat. aq. NH$_4$Cl (50 mL) was added and the layers separated. The organic layer was washed with sat. aq. NH$_4$Cl (3 × 20 mL), brine (100 mL), dried (MgSO$_4$), and concentrated in vacuo to give the title compound 31 (3.96 g, 80%) as a pale yellow oil.

$R_f = 0.13$ [petroleum ether (40–60):Et$_2$O, 9:1]; IR (film) $v_{\text{max}}$/cm$^{-1}$ 2913, 2823, 2724, 1721, 1442, 1376, 1269, 1128, 1069; $^1$H NMR (CDCl$_3$, 600 MHz) $\delta =$ 9.78 (1H, s, C14HO), 5.98 (1H, s, C10H), 2.60–2.58 (2H, m, C13H$_2$), 2.55–2.52 (2H, m, C12H$_2$), 1.86 (3H, s, C23H$_3$); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta =$ 200.7 (C14HO), 145.8 (C11), 75.9 (C10H), 41.8 (C13H$_2$), 31.5 (C12H$_2$), 24.0 (C23H$_3$); HRMS (+EI) Found [M]$^+$ = 223.9695; C$_6$H$_9$IO requires 223.9698, Δ 1.34 ppm.

Ethyl (R,2E,6E)-7-iodo-6-methyl-4-((phenylamino)oxy)hepta-2,6-dienoate 35

To a solution of 31 (87.0 mg, 0.380 mmol) in DMSO (2 mL) at RT was added L-Proline (7.3 mg, 63.0 μmol) and nitrosobenzene (33.9 mg, 0.316 mmol) sequentially to give a green solution. The initial green solution turned yellow after 20 minutes, and after an additional 40 mins, THF (2 ml) was added, followed by phosphorane 34 (165 mg, 0.474 mmol) in one portion. The reaction was stirred for 3 h at RT, after which sat. aq. NH$_4$Cl (10 mL) was added and the mixture extracted with Et$_2$O (2 × 10 mL). The combined organic layers were dried (MgSO$_4$) and concentrated in vacuo to give the title compound 35 (3.80 g, 80%) as a pale yellow oil.
Vacuo. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 9:1→8:2] gave the title compound 35 [84.0 mg, 66% (based on PhNO)] as a clear oil.

*Rf* = 0.21 (hexane:EtOAc, 9:1); [α]$_D^{28.7}$ = +22.4 (c = 1.0, CHCl₃); IR (film) ν$_{max}$/cm⁻¹ 3291, 3053, 2980, 2923, 2853, 1713, 1657, 1600, 1493, 1444, 1369, 1304, 1274, 1165, 1095, 1028, 980; ¹H NMR (CDCl₃, 600 MHz) δ = 6.28–6.24 (2H, obscured dd, meta-Ph-H), 7.00 (1H, br s, NH), 6.97 (2H, t, J = 7.2 Hz, para-Ph-H), 6.93–6.87 (3H, m, ortho-Ph-H and C₁₄H), 6.12 (1H, s, C₁₀H), 6.06 (1H, d, J = 15.8 Hz, C₁₅H), 4.52 (1H, q, J = 6.6 Hz, C₁₃H), 4.22 (2H, q, J = 7.1 Hz, CH₂CH₃), 2.27 (1H, dd, J = 14.0, 8.0 Hz, C₁₂H₄H₆B), 2.49 (1H, dd, J = 14.1, 5.3 Hz, C₁₂H₄H₆B), 1.93 (3H, s, C₂₃H₃), 1.31 (3H, t, J = 7.1 Hz, CH₃CH₂CH₃); ¹³C NMR (CDCl₃, 150 MHz) δ = 166.3 (CO₂CH₂CH₃), 148.5 (IPSO Ph), 146.2 (C₁₄H), 143.4 (C₁₁), 129.5 (2C, meta Ph), 123.6 (para Ph), 122.8 (C₁₅H), 114.9 (2C, ortho Ph), 81.4 (C₁₃H), 79.2 (C₁₀H), 61.1 (CH₂CH₃), 43.6 (C₁₂H₂), 24.9 (C₂₃H₃), 14.6 (CH₂CH₃); HRMS (+ESI) Found [M+H]$^+$ = 402.0578; C₁₆H₂₀INO₃ requires 402.0566, Δ 2.90 ppm.

(R,2E,6E)-Ethyl 4-hydroxy-7-iodo-6-methylhepta-2,6-dienoate S13

To a solution of 35 (300 mg, 0.747 mmol) in iPrOH (2 mL) and THF (0.2 mL) at RT was added CuSO₄ (239 mg, 149.0 mmol) in one portion. The reaction was heated to 40°C for 4 days, after which it was quenched by the addition of sat. aq. NH₄Cl (2 mL) and the mixture extracted with Et₂O (3 × 5 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography [SiO₂, petroleum ether (40–60):Et₂O, 65:35] gave the title compound S13 (121 mg, 52%) as a colourless oil.

*Rf* = 0.32 (hexane:Et₂O, 1:1); [α]$_D^{25.0}$ = +17.1 (c = 0.70, CHCl₃); IR (film) ν$_{max}$/cm⁻¹ 3442, 2981, 1699, 1657; ¹H NMR (CDCl₃, 600 MHz) δ = 6.91 (1H, dd, J = 15.6, 4.6 Hz, C₁₄H), 6.10–6.07 (2H, m overlapped, C₁₀H and C₁₅H), 4.46–4.43 (1H, m, C₁₃H), 4.21 (2H, q, J = 7.1 Hz, OCH₂CH₃), 2.51 (1H, dd, J = 13.9, 4.1 Hz, C₁₂H₄H₆B), 2.43 (1H, dd, J = 13.9, 8.9 Hz,
C12H4A1H2, 1.90 (3H, s, C23H3), 1.29 (3H, t, J = 7.1 Hz, OCH2CH3); 13C NMR (CDCl3, 150 MHz) δ = 166.3 (C=O), 148.3 (C14H), 143.4 (C11), 120.9 (C15H), 78.7 (C10H), 68.4 (C13H), 60.5 (OCH2CH3), 46.6 (C12H2), 24.0 (C23H3), 14.2 (OCH2CH3); HRMS (+ESI) Found [M+Na]+ = 332.9972; C10H15INO3 requires 332.9958, Δ 4.20 ppm.

(R,2E,6E)-Ethyl 4-(tert-butyldimethylsilyloxy)-7-iodo-6-methylhepta-2,6-dienoate 36

To a solution of S13 (797 mg, 2.57 mmol) in CH2Cl2 (25 mL) at −78 °C was added 2,6-lutidine (1.2 mL, 10.3 mmol) followed by TBSOTf (1.18 mL, 5.14 mmol). The reaction was stirred at −78 °C for 3.5 h after which the mixture quenched with sat. aq. NaHCO3 (15 mL), diluted with CH2Cl2 (15 mL) and allowed to warm to RT. The organic layers were separated and the aqueous phase further extracted with CH2Cl2 (10 mL). The combined organic layers were washed with 1 M HCl (10 mL), brine (10 mL), dried (MgSO4) and concentrated in vacuo. Purification by column chromatography [SiO2, petroleum ether (40–60):Et2O, 99:1 → 9:1] gave the title compound 36 (1.01 g, 93%) as a colourless oil.

Rf = 0.31 (hexane:Et2O, 95:5); [α]D25.0 = +29.0 (c = 0.40, CHCl3); IR (film) νmax/cm−1 2955, 2930, 2857, 1718, 1660; 1H NMR (CDCl3, 600 MHz) δ = 6.89 (1H, dd, J = 15.5, 4.7 Hz, C14H), 5.99–5.97 (2H, m overlapped, C10H and C15H), 4.39–4.35 (1H, m, C13H), 4.22–4.18 (2H, m, OCH2CH3), 2.44–2.37 (2H, m, C12H4A1H2), 1.86 (3H, s, C23H3), 1.30 (3H, t, J = 7.1 Hz, OCH2CH3), 0.90 (9H, s, C(CH3)3 of tBu), 0.03 (3H, s, Si(CH3)2), 0.01 (3H, s, Si(CH3)2); 13C NMR (CDCl3, 150 MHz) δ = 166.5 (C=O), 149.8 (C14H), 143.3 (C11), 120.3 (C15H), 78.7 (C10H), 69.8 (C13H), 60.4 (OCH2CH3), 47.3 (C12H2), 25.8 (3C, C(CH3)3 of tBu), 24.5 (C23H3), 18.1 (C(CH3)3 of tBu), 14.2 (OCH2CH3), −4.7 (Si(CH3)2), −4.9 (Si(CH3)2); HRMS (+ESI) Found [M+Na]+ = 447.0828; C16H29O3SiNa requires 447.0828, Δ 0.00 ppm.
(\(R,2E,6E\))-4-(tert-Butyldimethylsilyloxy)-7-iodo-6-methylhepta-2,6-dien-1-ol 37

To a stirred solution of 36 (1.01 g, 2.39 mmol) in THF (25 mL) at \(-78^\circ\text{C}\) was added DIBAL (1 M in hexanes; 5.98 mL, 5.98 mmol), and the reaction was stirred for 3.5 h whilst allowing to warm to 0 °C. The reaction was quenched with Rochelle’s salt (15 mL), diluted with Et\(_2\)O (40 mL) and stirred overnight. The layers were separated and the aqueous phase extracted with Et\(_2\)O (2 \times 10 mL). The combined organic layers were dried (MgSO\(_4\)) and concentrated \textit{in vacuo} to yield 37 (913 mg, quant.) as a colourless oil:

\(R_I = 0.17\) (hexane:Et\(_2\)O, 8:2); [\(\alpha\)]\(_D\)\(^{25.0}\) = \(-12.5\) (c = 0.58, CHCl\(_3\)); \textbf{IR} (film) \(\nu_{\text{max}}/\text{cm}^{-1}: 3348, 2927, 2857\); \(\textbf{H NMR}\) (CDCl\(_3\), 600 MHz) \(\delta = 5.92\) (1H, s, C10H), 5.78 (1H, dt, \(J = 15.4, 5.4\) Hz, C15H), 5.66 (1H, dd, \(J = 15.4, 6.0\) Hz, C14H), 4.25–4.22 (1H, m, C13H), 4.14 (2H, d, \(J = 5.4\) Hz, C16H\(_2\)), 2.41 (1H, dd, \(J = 13.4, 7.8\) Hz, C12H\(_A\)H\(_B\)), 2.33 (1H, d, \(J = 13.4, 4.8\) Hz, C12H\(_A\)H\(_B\)), 1.85 (3H, s, C23H), 1.49 (1H, br s, OH), 0.88 (9H, s, C(CH\(_3\))\(_3\) of tBu), 0.02 (3H, s, Si(CH\(_3\))\(_2\)), 0.01 (3H, s, Si(CH\(_3\))\(_2\))\); \(\textbf{C NMR}\) (CDCl\(_3\), 150 MHz) \(\delta = 144.2\) (C11), 134.2 (C14H), 128.9 (C15H), 77.9 (C10H), 70.8 (C13H), 63.0 (C16H\(_2\)), 48.2 (C12H\(_2\)), 25.8 (3C, C(CH\(_3\))\(_3\) of tBu), 24.5 (C23H), 18.1 (C(CH\(_3\))\(_3\) of tBu), 0.4 (Si(CH\(_3\))\(_2\)), 0.4 (Si(CH\(_3\))\(_2\)); \textbf{HRMS} (+ESI) Found [M+Na]\(^+\) = 405.0708; \(\text{C}_{14}\text{H}_{27}\text{IO}_{2}\text{SiNa}\) requires 405.0717, \(\Delta 2.22\) ppm.

((\(R,1E,5E\))-7-Bromo-1-iodo-2-methylhepta-1,5-dien-4-yloxy)(tertbutyl) dimethylsilane 38

To a solution of 37 (90.2 mg, 0.236 mmol) in CH\(_2\)Cl\(_2\) (0.5 mL) at \(-40^\circ\text{C}\) was added PPh\(_3\) (68.0 mg, 0.260 mmol) and CBr\(_4\) (86.0 mg, 0.260 mmol) in CH\(_2\)Cl\(_2\) (2 mL) and the mixture was stirred for 3 h. Further PPh\(_3\) (34.0 mg, 0.130 mmol) and CBr\(_4\) (43 mg, 0.130 mmol) in CH\(_2\)Cl\(_2\) (0.4 mL) were added and the mixture was stirred for a further 1.5 h. The reaction was quenched
with sat. aq. NaHCO₃ (2 mL), removed from the cold bath and diluted with CH₂Cl₂ (2 mL). After warming to RT, the layers were separated, and the aqueous phase extracted with CH₂Cl₂ (2 × 2 mL). The combined organic layers were washed with brine (4 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:Et₂O, 96:4) gave the title compound 38 (40.0 mg, 0.090 mmol) with a minor impurity (15%). The corresponding signals for 38 are reported for characterisation:

\[ R_f = 0.45 \text{ (hexane:Et}_2\text{O, 95:5); IR (film) } \nu_{\text{max}}/\text{cm}^{-1} 2954, 2929, 2856, 1617; ^1\text{H NMR} \text{ (CDCl}_3, 600 \text{ MHz}) \delta = 5.93 \text{ (1H, s, C10H), 5.87–5.82 (1H, m, C15H), 5.71 (1H, dd, } J = 15.2, 5.8 \text{ Hz, C14H), 4.24–4.21 (1H, m, C13H), 3.94 (2H, d, } J = 7.5 \text{ Hz, C16H}_2, 2.40 \text{ (1H, dd, } J = 13.4, 7.7 \text{ Hz, C12}H_AH_B), 2.32 \text{ (1H, dd, } J = 13.4, 4.8 \text{ Hz, C12}H_AH_B), 1.85 \text{ (3H, s, C23}H, 0.88 \text{ (9H, s, C(CH}_3)_3 \text{ of } t\text{Bu), 0.02 (3H, s, Si(C(CH}_3)_2), 0.02 (3H, s, Si(C(CH}_3)_2); ^13\text{C NMR} \text{ (CDCl}_3, 150 \text{ MHz}) } \delta = 143.8 \text{ (C11), 137.7 (C14H), 126.1 (C15H), 78.2 (C10H), 70.4 (C13H), 47.9 (C12H}_2, 32.1 \text{ (C16H}_2), 25.8 \text{ (3C, C(CH}_3)_3 \text{ of } t\text{Bu), 24.6 (C23}H, 18.1 \text{ (C(CH}_3)_3 \text{ of } t\text{Bu), } -4.4 \text{ (Si(CH}_3)_2), -4.9 \text{ (Si(CH}_3)_2); HRMS (+ESI) Found } [M+Na]^+ = 466.9864; C_{14}H_{26}BrI\text{OSiNa requires 466.9873, } \Delta 1.93 \text{ ppm.} \]

**Diethyl (R,2E,6E)-4-(tert-butyldimethylsilyloxy)-7-iodo-6-methylhepta-2,6-dienylphosphonate 39**

To 38 (40.0 mg, 0.090 mmol) was added freshly distilled P(OEt)₃ (100 μL). The mixture was heated at 100 °C for 4 h, after which the remaining P(OEt)₃ was removed under vacuum (100 °C). Purification by column chromatography (SiO₂, EtOAc:hexane, 8:2→9:1) gave the title compound 39 (40.0 mg, 80% over 2 steps) as a colourless oil.

\[ R_f = 0.33 \text{ (EtOAc:hexane, 8:2); } [\alpha]_{D}^{25.0} = +15.0 \text{ (c = 0.90, CHCl}_3); \text{ IR (film) } \nu_{\text{max}}/\text{cm}^{-1} 2929, 2857, 1618, 1250, 1024; ^1\text{H NMR} \text{ (CDCl}_3, 600 \text{ MHz}) \delta = 5.92 \text{ (1H, s, C10H), 5.59–5.57 (2H, m, C14H and C15H), 4.21–4.19 (1H, m, C13H), 4.12–4.07 (4H, m, P(OCH}_2CH}_3)_2, 2.58–2.54 (2H,
m, C16H2), 2.39 (1H, dd, J = 13.4, 7.7 Hz, C12H₈H₈), 2.31 (1H, dd, J = 13.4, 4.8 Hz, C12H₂H₂), 1.55 (3H, s, C2H₃), 1.32 (6H, t, J = 7.0 Hz, P(OCH₃CH₃)₂), 0.88 (9H, s, C(CH₃)₃ of tBu), 0.02 (3H, s, Si(CH₂)₂), 0.01 (3H, s, Si(CH₂)₂); ¹³C NMR (CDCl₃, 150 MHz) δ = 144.2 (C11), 137.8 (d, J = 13.5 Hz, C15H), 119.3 (d, J = 10.5 Hz, C14H), 77.9 (C10H), 71.1 (C13H), 61.8 (d, J = 7.5 Hz, POCH₂), 61.7 (d, J = 6.0 Hz, POCH₂), 48.2 (C12H₂), 30.1 (d, J = 138 Hz, C16H₂), 25.8 (3C, C(CH₃)₃ of tBu), 24.6 (C23H₃), 18.1 (C(CH₃)₃ of tBu), 16.5–16.4 (m, P(OCH₂CH₂)₂), −4.5 (Si(CH₂)₂), −4.9 (Si(CH₂)₂); HRMS (+ESI) Found [M+Na]⁺ = 525.1061; C₁₈H₃₆I₄O₄PSiNa requires 525.1063, Δ 0.38 ppm.

1-tert-Butyl-5-((R,2E,6E)-4-(tert-butyldimethylsilyloxy)-7-iodo-6-methylhepta-2,6-dienylthio)-1H-tetrazole 40a

To a solution of 37 (74.0 mg, 0.194 mmol), 1-tert-butyl-1H-tetrazole-5-thiol (46.0 mg, 0.290 mmol) and PPh₃ (76.0 mg, 0.290 mmol) in THF (3 mL) at RT was added DIAD (69 μL, 0.350 mmol) dropwise, resulting in a yellow-orange solution. After 10 min, the solution was concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:Et₂O, 9:1→7:3) gave the title compound 40a (86.0 mg, 85%) as a colourless oil.

ᵣᵣ = 0.33 (hexane:Et₂O, 7:3); [α]D⁵⁺ = +7.3 (c = 1.10, CHCl₃); IR (film) νmax/cm⁻¹ 2928, 2856; ¹H NMR (CDCl₃, 600 MHz) δ = 5.89 (1H, s, C10H), 5.79–5.78 (2H, m overlapped, C14H and C15H), 4.19–4.17 (1H, m, C13H), 4.00–3.98 (2H, m, C16H₂), 2.36 (1H, dd, J = 13.4, 7.6 Hz, C12H₂H₂), 2.29 (1H, dd, J = 13.4, 4.9 Hz, C12H₂H₂), 1.81 (3H, s, C23H₃), 1.71 (9H, s, NC(CH₃)₃), 0.84 (9H, s, C(CH₃)₃ of tBu), −0.02 (3H, s, Si(CH₂)₂), −0.07 (3H, s, Si(CH₂)₂); ¹³C NMR (CDCl₃, 150 MHz) δ = 152.0 (S(CN)N), 143.9 (C11), 138.4 (C14H or C15H), 123.3 (C14H or C15H), 78.0 (C10H), 70.6 (C13H), 61.0 (NC(CH₃)₃), 48.0 (C12H₂), 35.3 (C16H₂), 28.8 (3C, NC(CH₃)₃), 25.8 (3C, C(CH₃)₃ of tBu), 24.5 (C23H₃), 18.1 (C(CH₃)₃ of tBu), −4.5 (Si(CH₂)₂), −4.9 (Si(CH₂)₂); HRMS (+ESI) Found [M+Na]⁺ = 545.1255; C₁₉H₃₅IN₄OSSiNa requires 545.1243, Δ 2.20 ppm.
1-tert-Butyl-5-((2E,6E)-(tert-butyldimethylsilyloxy)-7-iodo-6-methylhepta-2,6-dienylsulfonyl)-1H-tetrazole 41a

To a stirred solution of 40a (63.0 mg, 0.121 mmol) in EtOH (2 mL) at 0 °C was added ammonium molybdate tetrahydrate (149 mg, 0.121 mmol) in H₂O₂ (100 volumes, 500 μL) dropwise. After 1 h, the ice-bath was removed then the reaction stirred for a further 2 h after which it was quenched with sat. aq. NH₄Cl (3 mL) and diluted with Et₂O (10 mL). The layers were separated then the organic layer was washed with brine (5 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:Et₂O, 9:1→8:2) gave the title compound 41a (51.0 mg, 76%) as a colourless oil.

*Rf* = 0.27 (hexane:Et₂O, 8:2); [α]D²⁵.⁰ = +28.3 (c = 0.40, CHCl₃); **IR** (film) ν_max/cm⁻¹: 2929, 2857, 1340, 1162; **¹H NMR** (CDCl₃, 600 MHz) δ = 6.04 (1H, dd, *J* = 15.4, 5.2 Hz, C₁₄H), 5.93 (1H, s, C₁₁H), 5.81–5.76 (1H, m, C₁₅H), 4.53 (1H, dd, *J* = 14.2, 7.1 Hz, C₁₆H₁₆H₂B), 4.48 (1H, dd, *J* = 14.2, 7.8 Hz, C₁₆H₁₆H₂B), 4.26–4.23 (1H, m, C₁₃H), 2.38–2.30 (2H, m, C₁₂H₂), 1.84–1.83 (12H, m overlapped, C₂₃CH₃ and NC(CH₃)₃), 0.84 (9H, s, C(CH₃)₃ of tBu), −0.03 (3H, s, Si(CH₃)₂), −0.11 (3H, s, Si(CH₃)₂); **¹³C NMR** (CDCl₃, 150 MHz) δ = 153.7 (S(CN)N), 145.7 (C₁₄H), 143.5 (C₁₁), 113.7 (C₁₅H), 78.5 (C₁₁H), 70.3 (C₁₃H), 65.4 (NC(CH₃)₃), 59.7 (C₁₆H₂), 47.7 (C₁₂H₂), 29.7 (NC(CH₃)₃), 25.7 (3C, C(CH₃)₃ of tBu), 24.5 (C₂₃H₃), 18.0 (C(CH₃)₃ of tBu), −4.8 (Si(CH₃)₂), −5.0 (Si(CH₃)₂); **HRMS (+ESI)** Found [M+Na]⁺ = 577.1146; C₁₉H₂₅IN₄O₅SSiNa requires 577.1142, Δ 0.69 ppm.
5-((R,2E,6E)-4-(tert-Butyldimethylsilyloxy)-7-iodo-6-methylhepta-2,6-dienylthio)-1-phenyl-1H-tetrazole 40b

To a solution of 37 (189 mg, 0.495 mmol), 1-phenyl-1H-tetrazole-5-thiol (132 mg, 0.743 mmol) and PPh₃ (195 mg, 0.743 mmol) in THF (6 mL) at RT was added DIAD (175 µL, 0.891 mmol) dropwise, resulting in a yellow-orange solution. After 10 min, the solution was concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:Et₂O, 95:5 → 7:3) gave the title compound 40b (258 mg, 96%) as a colourless oil.

R₁ = 0.21 (hexane:Et₂O, 8:2); [α]D²⁵ = +11.1 (c = 0.95, CHCl₃); IR (film) νmax/cm⁻¹ 2928, 2855, 1597; ¹H NMR (CDCl₃, 600 MHz) δ = 7.58–7.53 (5H, m, Ar), 5.89 (1H, s, C₁₀H), 5.81–5.79 (2H, m, C₁₄H and C₁₅H), 4.20–4.17 (1H, m, C₁₃H), 4.01 (2H, d, J = 5.8 Hz, C₁₆H₂), 2.36 (1H, dd, J = 13.4, 6.8 Hz, C₁₂H₄H₅), 2.29 (1H, dd, J = 13.4, 5.0 Hz, C₁₂H₅H₆), 1.82 (3H, s, C₂₃H₃), 0.84 (9H, s, C(CH₃)₃ of tBu), −0.02 (3H, s, Si(CH₃)₂), −0.07 (3H, s, Si(CH₃)₂); ¹³C NMR (CDCl₃, 150 MHz) δ = 153.7 (S(CH₃)₂ of tBu), 143.8 (C₁₁), 138.7 (C₁₄H or C₁₅H), 133.7 (ipso-Ar-C), 130.1 (para-Ar-C), 129.8 (2C, ortho-Ar-C or meta-Ar-C), 123.8 (2C, ortho-Ar-C or meta-Ar-C), 123.0 (C₁₄H or C₁₅H), 78.1 (C₁₀H), 70.5 (C₁₃H), 48.0 (C₁₂H₂), 34.7 (C₁₆H₂), 25.8 (3C, C(CH₃)₃ of tBu), 24.6 (C₂₃H₃), 18.1 (C(CH₃)₃ of tBu), −4.5 (Si(CH₃)₂), −4.9 (Si(CH₃)₂); HRMS (+ESI) Found [M+Na]^+ = 565.0950; C₂₁H₃₁N₄OSSiNa requires 565.0930, Δ 3.54 ppm.

5-((R,2E,6E)-4-(tert-Butyldimethylsilyloxy)-7-iodo-6-methylhepta-2,6-dienylsulfonyl)-1-phenyl-1H-tetrazole 41b

To a stirred solution of 40b (85.0 mg, 0.157 mmol) in EtOH (3 mL) at 0 °C was added ammonium moylbdate tetrahydrate (387 mg, 0.313 mmol) in H₂O₂ (100 volumes, 1 mL)
dropwise. The reaction mixture became yellow solution and a white precipitate formed. The ice-bath was removed, the reaction stirred for a further 2 h at RT after which it was quenched by the addition of sat. aq. NH₄Cl (4 mL) and diluted with Et₂O (15 mL). The layers were separated and the organic layer washed with brine (2 × 5 mL), dried (Na₂SO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:Et₂O, 9:1→8:2) gave the title compound 41b (74.0 mg, 82%) as a colourless oil.

**R** = 0.21 (hexane:Et₂O, 8:2); [α]D²⁵⁰ = +13.4 (c = 1.05, CHCl₃); **IR** (film) νmax/cm⁻¹ 2952, 2929, 2857, 1596, 1148; **¹H NMR** (CDCl₃, 600 MHz) δ = 7.67–7.59 (5H, m, Ar), 6.02 (1H, dd, J = 15.3, 5.0 Hz, C14H), 5.91 (1H, s, C10H), 5.78–5.74 (1H, m, C15H), 4.46 (1H, dd, J = 14.4, 7.1 Hz, C16H₄H₉B), 4.40 (1H, dd, J = 14.4, 7.7 Hz, C16H₄H₉B) 4.25–4.22 (1H, m, C13H), 2.36–2.28 (2H, m, C12H₃H₉B), 1.82 (3H, s, C23CH₃), 0.84 (9H, s, C(CH₃)₃ of tBu), −0.03 (3H, s, Si(CH₃)₂), −0.11 (3H, s, Si(CH₃)₂); **¹³C NMR** (CDCl₃, 150 MHz) δ = 153.1 (S(CN)N), 146.1 (C14H), 143.4 (C11), 133.0 (ipso-Ar-C), 131.5 (para-Ar-C), 129.7 (2C, ortho-Ar-C or meta-Ar-C), 125.1 (2C, ortho-Ar-C or meta-Ar-C), 112.9 (C15H), 78.6 (C10H), 70.2 (C13H), 59.1 (C16H₂), 47.6 (C12H₂), 25.7 (3C, C(CH₃)₃ of tBu), 24.5 (C23H₃), 18.0 (C(CH₃)₃ of tBu), −4.8 (Si(CH₃)₂), −5.0 (Si(CH₃)₂); **HRMS** (+ESI) Found [M+Na]⁺ = 597.0829; C₂₁H₂₁IN₄O₃SSiNa requires 597.0829, Δ 0.00 ppm.

**2-((R,2E,6E)-4-(tert-Butyldimethylsilyloxy)-7-iodo-6-methylhepta-2,6-dienylthio)benzo[d]thiazole 40c**

To a solution of 37 (90.2 mg, 0.236 mmol), mercaptobenzothiazole (59.0 mg, 0.354 mmol) and PPh₃ (93.0 mg, 0.354 mmol) in THF (4 mL) at RT was added DIAD (86 μL, 0.425 mmol) dropwise, resulting in a yellow-orange solution. After 10 min, the solution was concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:Et₂O, 95:5) gave the title compound 40c (131.0 mg, quant.) as a colourless oil.
$R_f = 0.18$ (hexane:Et₂O, 95:5); $[\alpha]_D^{25.0} = +12.4$ (c = 0.75, CHCl₃); IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 2954, 2927, 2855, 1618; $^1H$ NMR (CDCl₃, 600 MHz) $\delta$ = 7.87 (1H, d, $J$ = 7.9 Hz, Ar), 7.76 (1H, d, $J$ = 7.9 Hz, Ar), 7.42 (1H, t, $J$ = 7.9 Hz, Ar), 7.30 (1H, t, $J$ = 7.9 Hz, Ar), 5.87 (1H, s, C10H), 5.81–5.78 (2H, m, C14H and C15H), 4.20–4.18 (1H, m, C13H), 3.97 (2H, d, $J$ = 5.6 Hz, C16H₂), 2.37 (1H, dd, $J$ = 13.5, 7.7 Hz, C12H₄ArB), 2.28 (1H, dd, $J$ = 13.5, 4.6 Hz, C12H₄ArB₂), 1.82 (3H, s, C23CH₃), 0.83 (9H, s, C(CH₃)₃ of tBu), −0.02 (3H, s, Si(CH₃)₂), −0.06 (3H, s, Si(CH₃)₂); $^{13}C$ NMR (CDCl₃, 150 MHz) $\delta$ = 165.1 (Ar), 153.2 (Ar), 144.0 (C11), 137.6 (C14H or C15H), 135.3 (Ar), 126.0 (Ar), 126.4 (Ar), 124.0 (C14H or C15H), 121.6 (Ar), 121.0 (Ar), 78.0 (C10H), 70.8 (C13H), 48.1 (C12H₂), 35.0 (C16H), 25.8 (3C, C(CH₃)₃ of tBu), 24.6 (C23H₃), 18.1 (C(CH₃)₃ of tBu), −4.5 (Si(CH₃)₂), −4.9 (Si(CH₃)₂); HRMS (+ESI) Found [M+H]$^+$ = 532.0684; C₂₁H₂₁NO₂Si requires 532.0661, $\Delta$ 4.32 ppm.

2-((R,2E,6E)-4-(tert-Butyldimethylsilyloxy)-7-iodo-6-methylhepta-2,6-dienylthio)benzo[d]thiazole 41c

To a stirred solution of 40c (48.0 mg, 0.090 mmol) in EtOH (3 mL) at 0 °C was added ammonium molybdate tetrahydrate (167 mg, 0.135 mmol) in H₂O₂ (100 volumes, 500 μL). The reaction mixture became a yellow solution and a white precipitate formed. The ice-bath was removed, the reaction stirred at RT for 2 h then quenched with sat. aq. NH₄Cl (4 mL) and diluted with Et₂O (15 mL). The layers were separated and the organic layer washed with brine (3 × 5 mL), dried (Na₂SO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:Et₂O, 9:1→8:2) gave the title compound 41c (43.0 mg, 85%) as a colourless oil.

$R_f = 0.49$ (hexane:Et₂O, 1:1); $[\alpha]_D^{25.0} = +10.3$ (c = 1.05, CHCl₃); IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 2953, 2928, 2856, 1555, 1332, 1142; $^1H$ NMR (CDCl₃, 600 MHz) $\delta$ = 8.22 (1H, d, $J$ = 8.1 Hz, Ar), 8.01 (1H, d, $J$ = 8.1 Hz, Ar), 7.65 (1H, dd, $J$ = 8.1, 7.5 Hz, Ar), 7.60 (1H, dd, $J$ = 8.1, 7.5 Hz, Ar), 5.78 (1H, s, C10H), 5.75–5.67 (2H, m, C14H and C15H), 4.27–4.19 (2H, m, C16H₂), 4.17–4.14 (1H, m, C13H), 2.22 (1H, dd, $J$ = 13.4, 7.7 Hz, C12H₄ArB), 2.14 (1H, dd, $J$ = 13.4, 4.8 Hz, C12H₄ArB₂).
1.76 (3H, s, C23H3), 0.79 (9H, s, C(CH3)3 of tBu), −0.05 (3H, s, Si(CH3)2), −0.12 (3H, s, Si(CH3)2); 13C NMR (CDCl3, 150 MHz) δ = 165.4 (Ar), 152.6 (Ar), 144.4 (C14H or C15H), 143.5 (C11), 136.7 (Ar), 128.1 (Ar), 127.7 (Ar), 125.5 (Ar), 122.3 (Ar), 114.3 (C14H or C15H), 78.3 (C10H), 70.2 (C13H), 57.7 (C16H2), 47.7 (C12H2), 25.7 (3C, C(CH3)3 of tBu), 24.5 (C23H3), 18.0 (C(CH3)3 of tBu), −4.8 (Si(CH3)2), −5.0 (Si(CH3)2); HRMS (+ESI) Found [M+Na]+ = 586.0385; C21H30INO3S2SiNa requires 586.0379, Δ 1.02 ppm.

(1S,2R)-2-Benzoyl-cyclopropanecarboxylic acid diethylamide 45

To a vigorously stirred slurry of Cs2CO3 (19.0 g, 58.3 mmol) and 44 (3.27 g, 9.64 mmol) in MeCN (60 mL) at 80 °C was added a solution of 1-phenyl-propenone 43 (7.70 g, 58.3 mmol) and 2-bromo-N,N-diethyl-acetamide 42 (9.38 g, 48.6 mmol) in MeCN (250 mL) dropwise over 24 h. Following the addition, the reaction was stirred for an additional 12 h at 80 °C after which it was cooled to RT and diluted with Et2O (200 mL). The mixture was washed with 1 N HCl (150 mL) and the layers separated. The aqueous layer was further extracted with Et2O (200 mL) and the combined organics dried (MgSO4) and concentrated in vacuo. Purification by column chromatography [SiO2, petroleum ether (30–40):Et2O, 1:1] gave the title compound 45 (10.4 g, 82%) as a pale yellow oil.

Rf = 0.38 [petroleum ether (30–40):Et2O, 1:1]; [α]D25.0 = −121.2 (c = 0.90, CHCl3); IR (film) νmax/cm−1 2976, 2935, 1671, 1620, 1448, 1385, 1331, 1259, 1220, 1142; 1H NMR (CDCl3, 600 MHz) δ = 8.04 (2H, d, J = 7.3 Hz, ortho-Ar-H), 7.58 (1H, t, J = 7.3 Hz, para-Ar-H), 7.48 (2H, t, J = 7.3 Hz, meta-Ar-H), 3.48–3.43 (2H, m, NCH2CH3), 3.41 (2H, q, J = 7.1 Hz, NCH2CH3'), 3.25 (1H, ddd, J = 8.4, 5.4, 3.9 Hz, C21H), 2.53 (1H, ddd, J = 8.6, 5.9, 3.9 Hz, C20H), 1.63 (1H, ddd, J = 8.6, 5.9, 2.9 Hz, C22H3H8), 1.55 (1H, ddd, J = 8.4, 5.5, 2.9 Hz, C22H3H8), 1.21 (3H, t, J = 7.2 Hz, NCH2CH3), 1.21 (3H, t, J = 7.1 Hz, NCH2CH3'); 13C NMR (CDCl3, 150 MHz) δ = 198.5 (C=O), 169.7 (C19), 137.2 (ipso-Ar-C), 133.3 (para-Ar-C), 128.6 (2C, meta-Ar-C), 128.4 (2C, ortho-Ar-C), 42.3 (NCH2CH3), 41.1 (NCH2CH3'), 25.9 (C21H),
23.7 (C20H), 18.2 (C22H), 14.8 (NCH2CH3), 13.2 (NCH2CH3); **HRMS** (EI) Found [M]+ = 245.1417; C15H19NO2 requires 245.1416, Δ 0.41 ppm.

**HPLC**: Daicel Chiralpak AD-H. Hexane:iPrOH, 98:2, 1 mL/min, 254 nm: t<sub>R</sub> (major) = 26 min, t<sub>R</sub> (minor) = 20 min. er = 98.5:1.5. All spectroscopic data in agreement with that previously published.\(^\text{10}\)

\((lR,2S)-2\)-Diethylcarbamoyl-cyclopropanecarboxylic acid 46

![Chemical Structure](image)

To a solution of 45 (2.00 g, 8.15 mmol) and Urea•H2O2 (7.67 g, 81.6 mmol) in HFIP (20 mL) at 0 °C was added TFAA (2.88 mL, 20.4 mmol) dropwise (caution: exothermic) and the reaction mixture slowly warmed to RT. After 12 h stirring at RT additional TFAA (2.88 mL, 20.4 mmol) was added and the stirring continued for 12 h. At this point further TFAA (2.88 mL, 20.4 mmol) was added and the reaction stirred for a final supplementary period of 12 h. The reaction was diluted with Et2O (200 mL) and carefully poured onto a mixture of Na2S2O4 (100 mL) and sat. aq. NaHCO3 (100 mL). The layers were separated and the aqueous layer further extracted with Et2O (2 × 100 mL). The combined organic layers were dried (MgSO4) and concentrated in vacuo. Purification by column chromatography [SiO2, petroleum ether (30:40):Et2O, 1:1] gave a 2.4:1 (by \(^1\)H NMR) mixture (2.12 g) of the desired ester [Rf = 0.35 (petroleum ether:Et2O, 1:1)].and starting material S14. The mixture was used directly in the next step of the reaction sequence.

To a solution of S14 (2.12 g) in MeCN (5 mL) at RT was added a solution of NaOH (1.63 g, 40.8 mmol) in H2O (20 mL) dropwise. The reaction mixture was heated to 50 °C and maintained at this temperature for 4 h after which it was cooled to RT and diluted with Et2O (50 mL). The aqueous phase was neutralised by the dropwise addition of 3 N HCl and extracted with Et2O (2 × 100 mL). The aqueous layer was then further acidified to pH 1 by the addition of aqueous 3 N HCl, and re-extracted with EtOAc (5 × 100 mL). The combined organics were dried (MgSO4)
and concentrated in vacuo to give the title compound (46) contaminated with phenol. The phenol was removed from the crude reaction mixture by evaporation under vacuum (<10 mmHg) and high temperature (55 °C) to provide the title compound 46 (731 mg, 48% over 2 steps) as a yellow oil, which crystallised as needles on storage.

m.p. = 68–70 °C; [α]D$^{25}$0 = +179.8 ($c = 0.40$, CHCl$_3$); IR (film) ν$_{max}$/cm$^{-1}$ 2982, 2938, 1725, 1585, 1493, 1430, 1404, 1364, 1316, 1265, 1179, 1147, 1081; $^1$H NMR (CDCl$_3$, 600 MHz) δ = 3.48 (2H, q, $J = 7.2$ Hz, NCH$_2$CH$_3$), 3.45–3.38 (2H, m, NCH$_2$CH$_3$'), 2.38–2.32 (1H, m, C21H), 2.26–2.21 (1H, m, C20H), 1.59–1.53 (1H, m, C22H$_A$H$_B$), 1.45–1.39 (1H, m, C22H$_A$H$_B$), 1.25 (3H, t, $J = 7.2$ Hz, NCH$_2$CH$_3$), 1.11 (3H, t, $J = 7.1$ Hz, NCH$_2$CH$_3$'); $^{13}$C NMR (CDCl$_3$, 150 MHz) δ = 177.8 (C=O), 169.1 (C19), 42.4 (NCH$_2$CH$_3$), 41.2 (NCH$_2$CH$_3$), 21.7 (C21H), 21.5 (C20H), 15.8 (C22H$_2$), 14.8 (NCH$_2$CH$_3$), 13.1 (NCH$_2$CH$_3$'); An accurate mass could not be obtained for this compound.

(1R,2S)-2-Diethylcarbamoyl-cyclopropanecarbonyl chloride S15

![Diagram](attachment:diagram.png)

To S14 (100 mg, 0.541 mmol) was added thionyl chloride (5 mL) and the reaction mixture stirred at RT for 12 h. The mixture was then concentrated in vacuo to give the title compound S15 (108 mg, 98%) as a yellow oil which was used directly in the next step of the reaction sequence.

(1S,2R)-2-Chloro-cyclopropanecarboxylic acid diethylamide 47

![Diagram](attachment:diagram.png)

To a solution of S15 (108 mg, 0.512 mmol) in CCl$_4$ (25.6 mL) was added 2-mercaptopyridine $N$-oxide sodium salt (92 mg, 0.615 mmol), DMAP (13 mg, 0.102 mmol) and TBAI (38 mg,
0.102 mmol). The reaction was stirred in the absence of light for 1 h after which TLC analysis indicated the formation of a major product \( R_f = 0.16 \) (petroleum ether (30–40):EtO, 4:1). At this point AIBN (4 mg, 0.256 mmol) was added and the reaction heated to 80 °C for 5 h in the absence of light. The reaction mixture was cooled to RT and the volatiles removed \textit{in vacuo} to leave a dark brown residue. Purification by column chromatography [SiO\(_2\), petroleum ether (30–40):EtO, 15:1 \( \rightarrow \) 4:1] gave the title compound 47 (51 mg, 57%) as a colourless oil.

\( R_f = 0.34 \) [petroleum ether (30–40):EtO, 1:1]; \( \left[ \alpha \right]_D^{25.0} = -80.0 \) (c = 0.75, CHCl\(_3\)); \( \text{IR} \) (film) \( \nu_{\text{max}}/\text{cm}^{-1} \) 2974, 1630, 1449, 1362, 1271, 1244, 1142, 1076; \( ^1\text{H NMR} \) (CDCl\(_3\), 600 MHz) \( \delta = 3.51 \text{–} 3.46 \) (2H, m, NC\(_H_2\)CH\(_3\)), 3.41 – 3.36 (3H, m, NC\(_H_2\)'CH\(_3\)' and C\(_{21}\)H), 2.11 – 2.05 (1H, m, C\(_{20}\)H), 1.64 – 1.58 (1H, m, C\(_{22}\)H\(_A\)H\(_B\)), 1.29 – 1.24 (4H, m, NCH\(_2\)C\(_H_3\) and C\(_{22}\)H\(_A\)H\(_B\)), 1.11 (3H, t, \( J = 7.2 \text{ Hz, NCH}_2'CH_3\)'); \( ^{13}\text{C NMR} \) (CDCl\(_3\), 150 MHz) \( \delta = 169.1 \) (C\(_{19}\)), 42.3 (N\(_C\)H\(_2\)CH\(_3\)), 41.0 (N\(_C\)H\(_2\)'CH\(_3\)'), 33.7 (C\(_{21}\)H), 22.6 (C\(_{20}\)H), 17.6 (C\(_{22}\)H\(_2\)), 14.9 (NCH\(_2\)CH\(_3\)), 13.2 (NCH\(_2\)'CH\(_3\)'); \( \text{HRMS} \) (ESI) Found \([\text{M}+\text{H}]^+ = 176.0837\); C\(_8\)H\(_{15}\)ClNO requires 176.0842, \( \Delta 2.84 \) ppm.

\( (4S,5S)-2\text{-Butyl-}N,N,N',N'-\text{tetramethyl-1,3,2-dioxaborolane-4,5-dicarboxamide 51}^{11} \)

To a solution of \((-\text{)}-N,N,N',N'-\text{tetramethyl-D-tartaric acid} (20 g, 97.9 mmol) in PhMe (65 mL) was added 1-butaneboronic acid (11.98 g, 117.5 mmol) in one portion. The mixture was heated at reflux under Dean–Stark conditions until \( ca. 3.5 \text{ mL of H}_2\text{O was collected. The reaction was cooled to RT and the PhMe removed \textit{in vacuo}. The mixture was suspended in CH}_2\text{Cl}_2 (35 mL), filtered through a pad of Celite\textsuperscript{®} under suction using CH\(_2\)Cl\(_2\) (3 \times 100 mL). The mixture was once again concentrated \textit{in vacuo} to give the title compound 51 (24.6 g, 93%) as a colourless oil.

\[ \left[ \alpha \right]_D^{25.0} = +99.0 \) (c = 1.0, CHCl\(_3\)), [lit.\textsuperscript{14} \( \left[ \alpha \right]_D^{20} = +106 \) (c = 1.00, CHCl\(_3\))]; \( \text{IR} \) (film) \( \nu_{\text{max}}/\text{cm}^{-1} \) 3433, 2928, 2872, 1644, 1501, 1466, 1401, 1380, 1254, 1218, 1153, 1059, 1025, 971; \( ^1\text{H NMR} \) (CDCl\(_3\), 400 MHz) \( \delta = 5.52 \) (2H, s, \( 2 \times CHCON(CH_3)_2\), 3.20 (6H, s, N(CH\(_3\))\(_2\)). 2.98 (6H, s,
N(CH$_3$)$_2$), 1.44–1.34 (2H, m, CH$_2$ of Bu), 1.34–1.26 (2H, m, CH$_2$ of Bu), 0.89–0.83 (5H, m, BCH$_2$ and CH$_3$ of Bu); $^1^3$C NMR (CDCl$_3$, 100 MHz) δ = 168.5 (2 × CHCON(CH$_3$)$_2$), 75.8 (2 × CHCON(CH$_3$)$_2$), 37.2 (2C, N(CH$_3$)$_2$), 36.0 (2C, N(CH$_3$)$_2$), 25.9 (CH$_3$CH$_2$), 25.2 (BCH$_2$CH$_2$), 13.8 (CH$_3$CH$_2$)$_2$; HRMS (+ESI) Found [M+Na]$^+$ = 293.1631; C$_{12}$H$_{23}$O$_4$N$_2$BNa requires 293.1643, Δ 4.09 ppm. All spectroscopic data in agreement with that previously published.

((1$S$,2$R$)-2-Chlorocyclopropyl)methanol 52$^1^2$

To a solution of ZnEt$_2$ (7.31 mL, 71.3 mmol) in CH$_2$Cl$_2$ (71 mL) cooled to 0 °C (internal) was added CH$_2$I$_2$ (11.5 mL, 142.6 mmol) dropwise over 90 min.† Once the addition was complete a pre-mixed solution of (E)-3-chloroprop-2-en-1-ol (50)$^{1^3}$ (1 g, 10.8 mmol), (4$S$,5$S$)-2-butyl-N,N,N′,N′-tetramethyl-1,3,2-dioxaborolane-4,5-dicarboxamide 51 (3.21 g, 11.9 mmol) in CH$_2$Cl$_2$ (79 mL) was added rapidly via cannula over 5 min ensuring that the internal temperature did not exceed 10 °C. The reaction mixture was allowed to warm to RT slowly over 16 h. The reaction was quenched with sat. aq. NH$_4$Cl (10 mL) and 3 N HCl (36 mL) added and stirred for 10 min. After this time, 5 M KOH (140 mL) was added to the entire mixture at RT and stirred for 4 h. The combined layers were separated and the aqueous layer further extracted with Et$_2$O (3 × 100 mL). The combined organic layers were dried (MgSO$_4$) and concentrated in vacuo. Purification by column chromatography [SiO$_2$, petroleum ether (30–40):Et$_2$O, 3:2] gave the title compound 52 (848 mg, 74%) as a colourless oil.

$R_f$ = 0.37 [petroleum ether (30–40):Et$_2$O, 1:1]; [$\alpha$]$_D$,$^{26.9}$ = –60.5 (c = 0.97, CHCl$_3$), [lit.$^{1^5}$ [$\alpha$]$_D$,$^{20}$ = –54.5 (c = 0.56, CHCl$_3$)]; IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 3323, 2925, 2875, 1442, 1399, 1368, 1318, 1271, 1086, 1025; $^1$H NMR (CDCl$_3$, 400 MHz) δ = 3.63–3.56 (1H, m, C19H$_A$H$_B$), 3.54–3.47 (1H, m, C19H$_A$H$_B$), 2.94–2.89 (1H, m, C21H), 1.54–1.48 (2H, m, C20H and OH), 1.05–0.99 (1H, m, C22H$_A$H$_B$), 0.91 (1H, m, C22H$_A$H$_B$); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ = 63.9 (C19H$_2$), 30.8 (C21H), 24.5 (C20H), 13.6 (C22H$_2$); HRMS (+ESI) Found [M+Na]$^+$ = 129.0082; C$_4$H$_7$OClNa

† Due to the long relaxation time the reported broad chemical shift of 9.9 ppm for BCH$_2$ could not be accounted for.

† Note - ‘violent explosions’ have been reported during this addition in excess of an 8 mmol scale.$^{1^1}$
requires 129.0077, Δ 3.88 ppm. All spectroscopic data in agreement with that previously published.\textsuperscript{12}

GC analysis of \textbf{52} was performed using a 6890N Network GC system (Agilent Technologies Inc., Palo Alto, CA, USA), equipped with a Varian CP7502, CHIRASIL DEX CB (25.0 m × 250 μm × 0.25 μ nominal) capillary column. The GC analyses were carried out in split mode (ratio 50:1) using helium as a carrier gas at a flow rate of 134 mL/min 25.00 psig). The injection port temperature was 250 °C the oven was maintained at an initial temperature of 100 °C, programmed at 0.5 °C/min to reach a temperature of 120 °C where it was held, post-run, for 1 min. The FID detector was at 250 °C, using H\textsubscript{2} flow at 40.00 mL/min, air at 450 mL/min and helium makeup flow at 45.0 mL/min. The two enantiomers eluted at 6.0 and 6.3 min respectively. Cyclopropane \textbf{52} was shown to have er = 97.5:2.5.
(1R,2S)-1-Chloro-2-(2,2-dibromoethenyl)cyclopropane 48\(^{12}\)

![Diagram](attachment:image.png)

**Procedure from compound 52**

To a solution of 52 (848 mg, 7.96 mmol) in CH\(_2\)Cl\(_2\) (57 mL) at RT was added Celite\(^{®}\) (3.43 g) followed by PCC (3.43 g, 15.92 mmol) in one portion and the brown mixture stirred for 12 h. The reaction was diluted with Et\(_2\)O (50 mL) and filtered through a pad of silica. The solvent was carefully removed by distillation at 65 °C using a vigreux column and the crude aldehyde (53) (assumed quant.) used directly in the next step.

A solution of PPh\(_3\) (8.35 g, 31.8 mmol) in CH\(_2\)Cl\(_2\) (34 mL) was cooled to 0 °C and CBr\(_4\) (5.28 g, 15.9 mmol) added in one portion, resulting in a bright yellow solution. This solution was stirred for 10 min, after which a solution of crude aldehyde 53 (assumed quant., 7.96 mmol) in CH\(_2\)Cl\(_2\) (10 mL) was added dropwise via cannula. The resulting brown mixture was allowed to warm to RT slowly over 22 h. The reaction mixture was transferred to a conical flask and pentane (100 mL) added resulting in precipitation. The mixture was stirred vigorously for 1 min, and the liquor filtered through a sinter funnel. The remaining brown residue was re-suspended in CH\(_2\)Cl\(_2\) (15 mL) and pentane (50 mL) added. Once again, the mixture was stirred vigorously and the liquor decanted off. This process was repeated once more, and the combined organics concentrated in vacuo (400 mbar, RT). Purification by column chromatography (SiO\(_2\), pentane) gave the title compound 48 (1.44 g, 70% over 2 steps) as a colourless oil.

\[ R_f = 0.58 \text{ (pentane): } [\alpha]_D^{26.1} = -75.7 \ (c = 1.03, \text{CHCl}_3), \ [\text{lit.}]^{12} [\alpha]_D^{20} = -70.9 \ (c = 0.65, \text{CHCl}_3); \]

\[ \text{IR (film) } \nu_{\max}/\text{cm}^{-1} \ 3022, 1609, 1432, 1360, 1279, 1241, 1197, 1162, 1086, 1066, 1042; \]

\[ \text{H NMR (CDCl}_3, 400 \text{ MHz}) \ \delta = 5.84 \ (1\text{H, d, } J = 8.9 \text{ Hz, C19H}), 3.08–3.03 \ (1\text{H, m, C21H}), 2.07–1.99 \ (1\text{H, m, C20H}), 1.40–1.34 \ (1\text{H, m, C22H}_A\text{H}_B), 1.18–1.12 \ (1\text{H, m, C22H}_A\text{H}_B); \]

\[ \text{C NMR (CDCl}_3, 100 \text{ MHz}) \ \delta = 137.2 \ (\text{C19H}), 89.8 \ (\text{C18Br}_2), 33.0 \ (\text{C21H}), 26.0 \ (\text{C20H}), 17.5 \ (\text{C22H}_2); \]

\[ \text{HRMS (+EI) Found } [\text{M}]^+ = 257.8445; \text{ C}_5\text{H}_5\text{ClBr}_2 \text{ requires } 257.8441, \Delta 1.55 \text{ ppm. All spectroscopic data in agreement with that previously published.}^{12} \]
3-((1S,2R)-2-Chlorocyclopropyl)prop-2-yn-1-ol 57

To a solution of 48 (177 mg, 0.680 mmol) in THF (14 mL) at −78 °C was added nBuLi (1.6 M in hexane; 850 μL, 1.36 mmol) dropwise, and the resulting solution stirred for 30 min. To this solution was added paraformaldehyde (38.0 mg, 1.36 mmol) in one portion and the reaction stirred for 10 min. The cold bath was removed and the reaction stirred for a further 30 min before quenching with sat. aq. NH₄Cl (5 mL). The resulting layers were separated, the aqueous phase was extracted with Et₂O (5 mL), the combined organic layers dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:Et₂O, 75:25→65:35) gave the title compound 57 (63.0 mg, 71%) as a colourless oil.

Rᵣ = 0.14 (hexane:Et₂O, 7:3); [α]₂⁰⁺ = −166.5 (c = 0.95, CHCl₃); IR (film) νₒ/cm⁻¹ 3326, 2932, 2869; ¹H NMR (CDCl₃, 600 MHz) δ = 4.22 (2H, dd, J = 6.1, 1.8 Hz, C₁₇H₂), 3.17–3.14 (1H, m, C₂₁H), 1.71–1.68 (1H, m, C₂₀H), 1.46 (1H, t, J = 6.1 Hz, OH), 1.27–1.24 (2H, m, C₂₂H₂); ¹³C NMR (CDCl₃, 150 MHz) δ = 85.1 (C₁₉), 76.5 (C₁₈), 51.2 (C₁₇H₂), 33.8 (C₂₁H), 18.8 (C₂₂H₂), 11.2 (C₂₀H); HRMS (+ESI) Found [M+Na]⁺ = 153.0077; C₆H₇ClONa requires 153.0083, Δ 3.92 ppm.

5-((3-((1S,2R)-2-Chlorocyclopropyl)prop-2-yn-1-yl)thio)-1-phenyl-1H-tetrazole 59

To a solution of 57 (25.0 mg, 0.192 mmol) in THF (1.5 mL) at RT was added PPh₃ (75.0 mg, 0.288 mmol), 1-phenyl-1H-tetrazole-5-thiol (68.0 mg, 0.384 mmol) and DIAD (68.0 μL, 0.345 mmol) sequentially. After stirring for 10 mins, the solvent was removed in vacuo. Purification by column chromatography (SiO₂, hexane:Et₂O, 4:1) gave the title compound 59 (50.0 mg, 89%) as a colourless oil.
$R_f = 0.25$ (hexane:Et$_2$O, 4:1), $[\alpha]_D^{25.0} = -75.0 \, (c = 1.00, \text{CHCl}_3)$, IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 1598, 1498, 1462, 1235, 1090, 1074, 1049, 1014, 994, 919; $^1$H NMR (CDCl$_3$, 600 MHz) $\delta =$ 7.57 (5H, br s, Ph), 4.13 (2H, $d$, $J = 1.8$ Hz, C17H$_2$), 3.13–3.10 (1H, m, C21H), 1.67–1.62 (1H, m, C20H), 1.24–1.20 (2H, m, C22H$_2$); $^{13}$C NMR (CDCl$_3$, 125 MHz) 153.0 (S(CN)N), 133.5 (ipso-Ar-C), 130.3, para-Ar-C), 129.9 (2C, ortho-Ar-C or meta-Ar-C), 123.8 (2C, ortho-Ar-C or meta-Ar-C), 84.3 (C19), 71.5 (C18), 33.8 (C21H), 22.6 (C17H$_2$), 18.8 (C22H$_2$), 11.2 (C20H); HRMS (+ESI) Found [M+H]$^+$ = 291.0484; C$_{13}$H$_{12}$N$_4$SCl requires 291.0471, $\Delta$ 4.47 ppm

**tert-Butyl(((1$E$,4$R$,5$E$,7$E$)-10-((1$S$,2$R$)-2-chlorocyclopropyl)-1-iodo-2-methyldeca-1,5,7,-trien-9-yn-4-yl)oxy)dimethylsilane 55**

**Procedure 1**

To a stirred solution of 57 (63 mg, 0.482 mmol) in CH$_2$Cl$_2$ (5 mL) at RT was added MnO$_2$ (419 mg, 4.82 mmol) portionwise over 2 h until TLC analysis (hexane:Et$_2$O, 3:2) indicated the reaction was complete (compound 27). The reaction mixture was filtered through oven dried SiO$_2$ and washed with CH$_2$Cl$_2$ (10 mL). The filtrate was partially concentrated $\text{in vacuo}$ (400 mbar, 30 °C)$^\dagger$ to a volume of ca. 3 mL then DMF (1 mL) was added and the solution was further concentrated $\text{in vacuo}$ (400 mbar, 30 °C) to remove the remaining CH$_2$Cl$_2$. The resulting aldehyde 28 solution in DMF was then dried over 4 Å molecular sieves.

In a separate flask 41b (185 mg, 0.321 mmol) was dissolved in DMPU (2 mL) at RT and oven dried Cs$_2$CO$_3$ (209 mg, 0.642 mmol) added. The aldehyde 28 solution was immediately cannulated into the reaction and rinsed through the cannula with additional DMPU (0.5 mL). After stirring for 15 h, the reaction was quenched with sat. aq. NH$_4$Cl (5 mL) and diluted with Et$_2$O (10 mL). The layers were separated and the aqueous phase extracted with Et$_2$O (10 mL). The combined organic layers were washed with sat. aq. LiCl (4 × 5 mL), brine (5 mL), dried (Na$_2$SO$_4$) and concentrated $\text{in vacuo}$. Purification by column chromatography (SiO$_2$, ...)
hexane:Et₂O, 99:1→95:5) gave the title compound 41b (79.6 mg, 52%) as a colourless oil [1:1 mixture of E:Z isomers at C16/C17].

**Procedure 2**

To a stirring solution of oxalyl chloride (0.26 mL, 3.0 mmol) in CH₂Cl₂ (10 mL) at −78 °C was added DMSO (0.43 mL, 6.0 mmol) dropwise. The reaction mixture was stirred for 10 min at −78 °C and a solution of 63 (0.71 g, 2.0 mmol) in CH₂Cl₂ (5 mL + 1 mL rinse) was added dropwise. The mixture was stirred for 20 min at −78 °C at which point Et₃N (1.4 mL, 10.0 mmol) was added dropwise. The suspension was allowed to warm to RT over 30 min after which sat. aq. NH₄Cl (20 mL) was added and the layers separated. The organic layer was washed with sat. aq. NH₄Cl (3 × 20 mL), brine (30 mL), dried (MgSO₄), and concentrated *in vacuo* to give crude aldehyde 64 (0.71 g, assumed quant.) as a colourless oil.

To a stirring solution of phosphonate 66 (0.55 g, 2.0 mmol) in THF (8 mL) at −78 °C was added LiHMDS (1 M in THF, 2.1 mL, 2.1 mmol) dropwise. The solution was stirred for 1 h at −78 °C before a solution of aldehyde 64 (0.71 g) was added as solution in THF (3 mL + 1 mL rinse). After stirring for 3 h, the reaction was warmed to RT, diluted with EtOAc (35 mL) and quenched by the addition of NH₄Cl (20 mL). The aqueous layer was separated and extracted with EtOAc (2 × 20 mL). The combined organic layers were dried (MgSO₄), filtered and concentrated *in vacuo* to afford a pale yellow oil. Purification by column chromatography (SiO₂, hexane) gave the title compound 55 (0.76 g, 80%) as a colourless oil [4:1 mixture of E:Z isomers at C14/C15].

**Procedure 3**

To a solution of vinyl silane 67 (347 mg, 0.82 mmol) in MeCN (51 mL) at RT was added NIS (277 mg, 1.23 mmol) in one portion. The reaction mixture was stirred in the absence of light for 90 min, after which it was quenched by the addition of sat. aq. Na₂S₂O₃ (50 mL) and diluted with pentane (100 mL) to give a triphasic system. The top layer was collected and the remaining other layers further extracted with pentane (3 × 120 mL). The combined top layers were dried (MgSO₄) and concentrated *in vacuo*. Purification by column chromatography (SiO₂, hexane) gave the title compound 55 (330 mg, 84%) as a colourless oil.
$R_f = 0.23$ (pentane:Et$_2$O, 99:1); $[\alpha]_D^{25.9} = -88.9$ (c = 1.08, CHCl$_3$); IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2955, 2928, 2856, 1472, 1463, 1361, 1255, 1143, 1107, 1070, 983, 925, 834; $^1$H NMR (CDCl$_3$, 500 MHz) $\delta =$ 6.47 (1H, dd, $J = 15.5$, 10.9 Hz, C16H), 6.15 (1H, dd, $J = 15.2$, 10.9 Hz, C15H), 5.90 (1H, s, C10H), 5.68 (1H, dd, $J = 15.2$, 6.2 Hz, C14H), 5.50 (1H, dd, $J = 15.6$, 1.8 Hz, C17H), 4.25–4.20 (1H, m, C13H), 3.18–3.14 (1H, m, C21H), 2.39 (1H, dd, $J = 13.4$, 7.7 Hz, C12H$_A$H$_B$), 2.30 (1H, dd, $J = 13.4$, 4.8 Hz, C12H$_A$H$_B$), 1.82 (3H, s, C23H$_3$), 1.81–1.76 (1H, m, C20H), 1.29–1.25 (2H, m, C22H$_A$H$_B$), 0.86 (9H, s, C(CH$_3)_3$ of tBu), 0.00 (3H, s, Si(CH$_3)_2$), $-$0.03 (3H, s, Si(CH$_3)_2$); $^{13}$C NMR (CDCl$_3$, 126 MHz) $\delta =$ 143.9 (C11), 140.9 (C16H), 138.4 (C14H), 128.7 (C15H), 110.8 (C17H), 91.5 (C19), 78.0 (C10H), 77.7 (C18), 71.0 (C13H), 48.1 (C12H$_2$), 34.3 (C21H), 25.8 (3C, C(CH$_3)_3$ of tBu), 24.5 (C23H$_3$), 19.3 (C22H$_2$), 18.1 (C(CH$_3)_3$ of tBu), 12.1 (C20H), $-$4.5 (Si(CH$_3)_2$), $-$4.9 (Si(CH$_3)_2$); An accurate mass could not be obtained for this compound.

Key nOe observation:

No observed nOe suggests that TMS-iodine exchange has occurred with retention of configuration.

(R,E)-2-((tert-Butyldimethylsilyl)oxy)-5-ido-4-methylpent-4-en-1-ol 63

To a solution of 62$^{14}$ (1.21 g, 5.0 mmol) in pyridine (10 mL) at 0 °C was added pivaloyl chloride (0.62 mL, 5.3 mmol) dropwise. The reaction was stirred for 30 min, diluted with Et$_2$O (30 mL), and quenched with 2 M HCl (30 mL). The aqueous layer was separated and extracted with Et$_2$O (2 × 20 mL). The combined organic layers were dried (MgSO$_4$), filtered and concentrated in vacuo to afford a colourless oil. The crude alcohol was then dissolved in CH$_2$Cl$_2$ (10 mL), 2,6-lutidine added (1.16 mL, 10.0 mmol) and cooled to $-$78 °C. TBSOTf (1.22 mL, 5.30 mmol) was
then added dropwise and the reaction was stirred for 1 h. The reaction was quenched with 1 M HCl (20 mL), diluted with CH₂Cl₂ (15 mL) and warmed to RT. The aqueous layer was separated and extracted with CH₂Cl₂ (2 × 15 mL). The combined organic layers were dried (MgSO₄), filtered and concentrated in vacuo to afford a colourless oil. The crude was then dissolved in CH₂Cl₂ (30 mL), cooled to −78 °C and diisobutylaluminium hydride (1 M in CH₂Cl₂, 10.0 mL, 10.0 mmol) added dropwise. After 1 hr the reaction was quenched by the addition of MeOH (5 mL) and warmed to RT. The reaction was diluted with CH₂Cl₂ (20 mL) and sat. aq. Rochelles salt added (50 mL). After stirring for 2 h, the aqueous layer was separated and extracted with CH₂Cl₂ (2 × 20 mL). The combined organic layers were dried (MgSO₄), filtered and concentrated in vacuo to afford a colourless oil. Purification by column chromatography [SiO₂, petroleum ether (40–60):EtOAc, 9:1] gave the title compound 63 (1.43 g, 80% over 3 steps) as a colourless oil.

\[ R_f = 0.23 \text{ [petroleum ether (40–60):EtOAc, 9:1]; } \left[ \alpha \right]_D^{25.0} = -3.0 \left( c = 1.20, \text{CHCl}_3 \right); \text{ IR (film) } \nu_{\text{max}}/\text{cm}^{-1} 3403, 2928, 2857, 2342, 1471, 1361, 1252, 1104, 1042, 960, 834; \text{ } ^1\text{H NMR (CDCl}_3, 400 \text{ MHz} ) \delta = 5.97–5.96 \left( 1\text{H, m, C10H}\right), 3.87–3.82 \left( 1\text{H, m, C13H}\right), 3.53 \left( 1\text{H, dd, } J = 11.0 \text{ Hz, } 4.0 \text{ Hz, C14H}_A\text{H}_B\right), 3.42 \left( 1\text{H, dd, } J = 11.0 \text{ Hz, } 4.0 \text{ Hz, C14H}_A\text{H}_B\right), 2.41 \left( 2\text{H, d, } J = 8.0 \text{ Hz, C12H}_2\right), 1.85 \left( 3\text{H, m, C23H}_3\right), 0.91 \left( 9\text{H, s, C(CH}_3)_3 \text{ of tBu}\right), 0.07 \left( 3\text{H, s, Si(CH}_3)_3\right), 0.06 \left( 3\text{H, s, Si(CH}_3)_3\right); \text{ } ^{13}\text{C NMR (CDCl}_3, 100 \text{ MHz} ) \delta = 144.0 \left( C11\right), 78.0 \left( C10H\right), 70.6 \left( C13H\right), 65.9 \left( C14H_2\right), 44.0 \left( C12H_2\right), 25.9 \left( 3\text{C, C(CH}_3)_3 \text{ of tBu}\right), 24.4 \left( C23H_3\right) 18.0 \left( C(CH}_3)_3 \text{ of tBu}\right), -4.6 \left( 2\text{C, Si(CH}_3)_2\right); \text{ HRMS (+ESI) Found } [M–H]^+ = 355.0603; \text{ } C_{12}H_{24}O_2Si \text{ requires 355.596, } \Delta 2.10 \text{ ppm.} \]
Diethyl (\((E)\)-5-((1R,2S)-2-chlorocyclopropyl)pent-2-en-4-yn-1-yl)phosphonate 66

To a 50 mL round-bottomed flask was added 48 (1.17 g, 4.5 mmol), DMF (5 mL) and TBAF (1 M in THF, 12.5 mL, 12.5 mmol). The reaction vessel was sealed, and the mixture heated at 65 °C for 90 min. The reaction mixture was cooled to RT after which brine (7 mL) was added and the mixture extracted with pentane (5 \times 20 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo (400 mbar, RT) to give the crude alkynyl bromide (86) (assumed quant.). The crude was dissolved in THF (12 mL) and stannane 65¹⁵ (2.10 g, 4.5 mmol), AsPh₃ (98.0 mg, 0.32 mmol) and Pd₂dba₃ (73.3 mg, 0.08 mmol) were added. After stirring for 16 hr at RT, the reaction was concentrated in vacuo. Purification by column chromatography [SiO₂, EtOAc:petroleum ether (40–60), 7:3] gave the title compound 66 (0.70 g, 56% over 2 steps) as a clear oil.

\[ R_f = 0.15 \] [petroleum ether (40–60):EtOAc, 3:7]; \[ [\alpha]D^{25.0} = -83.0 \] (c = 1.70, CHCl₃); \textbf{IR} (film) \( \nu_{max}/\text{cm}^{-1} \) 2932, 2246, 1393, 1252, 1026, 957, 904; \textbf{¹H NMR} (CDCl₃, 400 MHz) \( \delta = 5.99 \) (1H, dt, \( J = 15.7 \text{ Hz}, 7.7 \text{ Hz}, \text{C16H} \)), 5.56 (1H, dd, \( J = 15.7 \text{ Hz}, 5.5 \text{ Hz}, \text{C17H} \)), 4.15–4.07 (4H, m, 2 \times OCH₂CH₃), 3.18–3.15 (1H, m, C21H), 2.66 (1H, dd, \( J = 7.9 \text{Hz}, 1.3 \text{ Hz}, \text{C15H₃H₅} \)), 2.60 (1H, dd, \( J = 7.9 \text{Hz}, 1.3 \text{ Hz}, \text{C15H₃H₅} \)), 1.34–1.25 (8H, m, 2 \times OCH₂CH₃ and C22H₃H₆), \textbf{¹³C NMR} (CDCl₃, 100 MHz) \( \delta = 132.2 \) (d, \( J = 12.7 \text{ Hz}, \text{C16H} \)), 114.2 (d, \( J = 16.0 \text{ Hz}, \text{C17H} \)), 89.0 (C19), 76.4 (d, \( J = 5.5 \text{Hz}, \text{C18} \)), 62.1 (d, \( J = 6.6 \text{ Hz}, \text{OCH₂CH₃} \)), 34.1 (C15H₂), 31.8 (C21H), 19.1 (C22H₂), 16.4 (d, \( J = 6.0 \text{ Hz}, \text{OCH₂CH₃} \)), 11.8 (C20H); \textbf{HRMS} (+ESI) Found [M+H]^+ = 277.0774; \textbf{C₁₂H₁₅ClO₃P} requires 277.0760, \( \Delta 4.60 \text{ ppm} \).
((1E)-2-Iodoprop-1-en-1-yl)(trimethyl)silane $73^{16}$

To a solution of catalyst $71^{17}$ (4.18 g, 11.8 mmol) in THF (233 mL) at RT was added 1-(trimethylsilyl)-1-propyne (35.9 mL, 242.6 mmol) followed by the dropwise addition of $\text{Bu}_3\text{SnH}$ (63.3 mL, 235.5 mmol). The dark reaction mixture was stirred for 40 min after which the mixture was concentrated in vacuo. Purification by column chromatography (SiO$_2$, hexane) gave the desired hydrostannylated product as well as $\text{Bu}_3\text{SnH}$ as an inseparable mixture (83.3 g). The crude mixture was separated into 2 batches (40 g and 43.3 g) and used directly in the next step in the reaction sequence.

To a solution of the crude mixture (40 g) in CH$_2$Cl$_2$ (300 mL) at 0 °C was added a solution of I$_2$ in CH$_2$Cl$_2$ (0.0262 M, 119.1 mmol) via cannula dropwise until a dark purple colour persisted. The mixture was immediately quenched with 20% aq. Na$_2$S$_2$O$_3$ (60 mL) and warmed to RT. The layers were separated and the aqueous layer further extracted with CH$_2$Cl$_2$ (250 mL). The combined organic layers were dried (MgSO$_4$) and concentrated in vacuo. Purification by column chromatography (SiO$_2$, hexane) gave the title compound $73$ (17.5 g, 62% over 2 steps) as a colourless oil.$^\dagger$

$R_f = 0.56$ (hexane); IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 2921, 2955, 2921, 2901, 2853, 1592, 1430, 1409, 1373, 1248, 1050, 955, 835; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 6.20$ (1H, s, C10H), 2.54 (3H, s, C23H$_3$), 0.15 (9H, s, C10HSi(CH$_3$)$_3$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 144.3$ (C10H), 110.0 (C11), 34.7 (C23H$_3$), −0.2 (3C, C10HSi(CH$_3$)$_3$); An accurate mass could not be obtained for this compound. All spectroscopic data in agreement with that previously published.

$^\dagger$ Purification often had to be repeated due to the similar $R_f$ of vinyl iodide $73$ and the tin byproducts.
(2R,4E)-4-Methyl-5(trimethylsilyl)pent-4-ene-1,2-diol 75

To a solution of thiophene (0.33 mL, 4.16 mmol) in THF (4.9 mL) at −78 °C was added nBuLi (2.33 M in hexanes, 1.79 mL, 4.16 mmol) dropwise and the pale yellow solution stirred for 40 min. The resulting thienyllithium solution was added to a suspension of CuCN (0.37 g, 4.16 mmol) in THF (4.9 mL) at −40 °C via cannula providing a bright yellow solution of Li(2-Th)CuCN. In the meantime, tBuLi (1.6 M in pentane, 4.68 mL, 7.49 mmol) was added to a solution of vinyl iodide 73† (1.0 g, 4.16 mmol) in Et₂O (18 mL) at −90 °C and the pale yellow solution stirred for 40 min. After this time the Li(2-Th)CuCN solution (−40 °C) was added to the vinyllithium solution (−90 °C) dropwise via cannula and then warmed to −40 °C. After 1 h at −40 °C a solution of (S)-glycidol (61) (55 μL, 0.832 mmol) in Et₂O (8.3 mL) was added, followed immediately by BF₃•OEt₂ (0.15 mL, 1.25 mmol). The mixture was stirred for 90 min ensuring that the temperature did not rise above −25 °C, and then quenched by the addition of NH₄Cl–NH₃ (2:1, 25 mL) and allowed to warm to RT. The layers were separated and the aqueous layer further extracted with EtOAc (4 × 50 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, EtOAc:hexane, 7:3) gave the title compound 75 (113 mg, 72%) as a colourless oil.

\[ R_f = 0.47 \text{ (EtOAc)}; \ [\alpha]_D^{27.6} = +4.2 \ (c = 0.78, \text{ CHCl}_3); \ IR \text{ (film)} \nu_{\text{max}} / \text{cm}^{-1} \ 3361, 2953, 2901, 1617, 1437, 1409, 1378, 1247, 1147, 1091, 1037; ^1\text{H NMR} \ (\text{CDCl}_3, 400 \text{ MHz}) \delta = 5.34 \ (1\text{H, s, C10H}), 3.91–3.84 \ (1\text{H, m, C13H}), 3.71–3.64 \ (1\text{H, m, C14H}_2\text{H}_B), 3.52–3.45 \ (1\text{H, m, C14H}_A\text{H}_B), 2.27–2.22 \ (2\text{H, m, C12H}_A\text{H}_B), 2.00 \ (1\text{H, d, } J = 3.0 \text{ Hz, C13HOH}), 1.90 \ (1\text{H, t, } J = 5.9 \text{ Hz, C14H}_2\text{OH}), 1.83 \ (3\text{H, s, C23H}_3), 0.2 \ (9\text{H, s, C10HSi(CH}_3)_3); ^{13}\text{C NMR} \ (\text{CDCl}_3, 100 \text{ MHz}) \delta = 150.9 \ (C11), 128.1 \ (C10H), 69.5 \ (C13HOH), 66.6 \ (C14H)_2, 46.7 \ (C12H)_2, 21.8 \ (C23H)_3, –0.1 \ (3\text{C, C10HSi(CH}_3)_3); \ HRMS \ (+ESI) \text{ Found} \ [\text{M+Na}]^+ = 211.1129; \text{ C}_9\text{H}_{20}\text{O}_2\text{SiNa requires 211.1125, } \Delta 1.89 \text{ ppm.}

† The volatile vinyl iodide was dried by stirring with 4 Å MS for 1 h in Et₂O, and then separated by filtration under inert atmosphere directly before use.
Variable amounts of by-product 77 (colourless oil) were isolated from the previous procedure (for 75) when less than 5.0 equiv of vinyl iodide 73 were used.

\[ R_f = 0.74 \text{ (Et}_2\text{O:hexane, 1:1)}, \quad [\alpha]^{25.9}_D = +20.0 \quad (c = 0.20, \text{CHCl}_3); \quad \text{IR (film)} \nu_{\text{max}}/\text{cm}^{-1} \quad 3347, \quad 2952, \quad 2869, \quad 1467, \quad 1415, \quad 1395, \quad 1365, \quad 1248, \quad 1199, \quad 1171, \quad 1087, \quad 1039, \quad 1012; \quad ^1\text{H NMR (CDCl}_3, \quad 400 \text{ MHz)} \delta = 3.88–3.81 (1H, m, C13H), \quad 3.60–3.54 (1H, m, C14H\textsubscript{A}H\textsubscript{B}), \quad 3.42–3.35 (1H, m, C14H\textsubscript{A}H\textsubscript{B}), \quad 2.02–1.98 (2H, m, 2 × OH), \quad 1.36 (1H, dd, \quad J = 14.6, \quad 7.7 \text{ Hz, C12H}_A\textsubscript{H}_B), \quad 1.27 (1H, dd, \quad J = 14.6, \quad 2.9 \text{ Hz, C12H}_A\textsubscript{H}_B), \quad 0.98 \quad (9H, s, \quad C(CH)_3 \text{ of tBu}); \quad ^{13}\text{C NMR (CDCl}_3, \quad 100 \text{ MHz)} \delta = 69.9 \quad (C13H), \quad 68.1 \quad (C14H_2), \quad 46.9 \quad (C12H_2), \quad 30.1 \quad (C(CH)_3 \text{ of tBu}), \quad 30.0 \quad (3C, \quad C(CH)_3 \text{ of tBu}); \quad \text{HRMS (+ESI) Found [M+Na]^+ = 155.1049; C}_7\text{H}_{16}\text{O}_2\text{Na requires 155.1043, } \Delta 3.87 \text{ ppm.}

(2\text{R})-4,4-\text{Dimethylpentane-1,2-diy}l \text{ bis(4-bromobenzoate)} \text{ S16}

The structure by by-product 77 was confirmed by conversion to the above compound (S16).

To a solution of 77 (36.1 mg, 0.27 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (3 mL) at RT was added Et\textsubscript{3}N (0.11 mL, 0.79 mmol) followed by DMAP (2 crystals) and 4-bromobenzoil chloride (70.0 mg, 0.320 mmol). The reaction mixture was stirred for 3 h, before more Et\textsubscript{3}N (0.11 mL, 0.79 mmol), DMAP (2 small crystals) and 4-bromobenzoil chloride (70 mg, 0.320 mmol) were added. After a further 16 h and quenched by the addition of sat. aq. NH\textsubscript{4}Cl (5 mL). The layers were separated and the aqueous layer further extracted with EtOAc (3 × 10 mL) and the combined organic layers
washed with brine (20 mL), dried (MgSO₄), and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:EtOAc, 9:1) gave the title compound S16 (104 mg, 77%) as a white solid.

\[ R_f = 0.85 \text{ (EtOAc:hexane, 7:3); } m.p. = 101–104 \, ^\circ\text{C}; [\alpha]_{D}^{28.5} = -31.1 \text{ (c = 0.75, CHCl₃); } \text{IR (film)} \nu_{\text{max}}/\text{cm}^{-1} 2952, 2869, 1713, 1590, 1483, 1398, 1367, 1301, 1266, 1206, 1172, 1137, 1116, 1101, 1013, 995; \text{^1H NMR (CDCl}_3, 400 MHz) } \delta = 7.88 \text{ (2H, d, } J = 8.5 \text{ Hz, Ar), 7.82 \text{ (2H, d, } J = 8.5 \text{ Hz, Ar), 7.57 \text{ (2H, d, } J = 8.5 \text{ Hz, Ar), 7.55 \text{ (2H, d, } J = 8.5 \text{ Hz, Ar), 5.68–5.61 \text{ (1H, m, C13H), 4.49 \text{ (1H, dd, } J = 11.7, 3.6 \text{ Hz, C14H}_A\text{H}_B), 4.34 \text{ (1H, dd, } J = 11.7, 7.2 \text{ Hz, C14H}_A\text{H}_B), 1.83 \text{ (1H, dd, } J = 14.9, 8.6 \text{ Hz, C12H}_A\text{H}_B), 1.59 \text{ (1H, dd, } J = 14.8, 2.7 \text{ Hz, C12H}_A\text{H}_B), 0.98 \text{ (9H, C(CH}_3)_3 \text{ of } t\text{Bu); } \text{^13C NMR (CDCl}_3, 100 MHz) } \delta = 165.5 \text{ (C=O), 165.3 \text{ (C=O), 131.8 \text{ (2C, CH of Ar), 131.8 \text{ (2C, CH of Ar), 131.1 \text{ (2C, CH of Ar), 131.1 \text{ (2C, CH of Ar), 129.1 \text{ (quaternary Ar), 128.7 \text{ (quaternary Ar), 128.3 \text{ (quaternary Ar), 128.3 \text{ (quaternary Ar), 70.1 \text{ (C13H), 67.1 \text{ (C14H}_2), 44.2 \text{ (C12H}_2), 30.1 \text{ (C(CH}_3)_3 \text{ of } t\text{Bu), 29.8 \text{ (3C, C(CH}_3)_3 \text{ of } t\text{Bu); HRMS (+ESI)} \text{ Found } [\text{M+Na}]^+ = 518.9784; C_{21}H_{23}O_4\text{Br}_2\text{Na requires 518.9777}, \Delta 1.35 \text{ ppm.}}}

The structure and absolute stereochemistry was confirmed by X-ray crystallographic analysis after crystallisation from analytical grade Et₂O.

CCDC 882398 contains the supplementary crystallographic data for this thesis. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
To a suspension of NaH (60% in mineral oil, 8.92 g, 223 mmol) in DMF (260 mL) cooled to 0 °C was added \( p \)-methoxybenzyl chloride (30.2 mL, 223 mmol) dropwise over 25 min. The mixture was stirred for 25 min at 0 °C after which (S)-glycidol (15.0 g, 202.5 mmol) was added dropwise over 25 min via syringe. The mixture was then allowed to RT slowly over 16 h after which it was poured into a separating funnel containing \( \text{NH}_4 \text{Cl} \) (400 mL) and EtOAc (700 mL). The layers were separated and the organic layer washed with 10% aq. NaHCO\(_3\) (400 mL) and H\(_2\)O (400 mL). The combined aqueous layers were then further extracted with EtOAc (500 mL) and the combined organic layers dried (MgSO\(_4\)) and concentrated in vacuo.

Purification by column chromatography (SiO\(_2\), hexane:EtOAc, 9:1→3:2) gave the title compound 74 (38.7 g, 98%) as a colourless oil.

\( R_f = 0.18 \) (hexane:EtOAc, 4:1); \( [\alpha]_D^{24.1} = +3.5 \) (\( c = 0.86 \), CHCl\(_3\)), [lit.\(^{22}\) \( [\alpha]_D^{23} = +3.5 \) (\( c = 1.00 \), CHCl\(_3\))]; IR (film) \( \nu_{\text{max}}/\text{cm}^{-1} \) 3000, 1905, 2837, 1612, 1586, 1512, 1464, 1443, 1384, 1335, 1302, 1244, 1174, 1086, 1032; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \( \delta = 7.27 \) (2H, d, \( J = 10.1 \) Hz, (\( \text{CH}_2\text{COCH}_3\) of PMB), 6.88 (2H, d, \( J = 8.6 \) Hz, C(CH\(_2\) of PMB), 4.55 (1H, d, \( J = 11.5 \) Hz, OCH\(_A\)H\(_B\)Ph(OCH\(_3\))), 4.49 (1H, d, \( J = 11.5 \) Hz, OCH\(_A\)H\(_B\)Ph(OCH\(_3\))), 3.81 (3H, s, OCH\(_3\)), 3.73 (1H, dd, \( J = 11.4 \), 3.1 Hz, C14H\(_A\)H\(_B\)), 3.42 (1H, dd, \( J = 11.4 \), 5.8 Hz, C14H\(_A\)H\(_B\)), 3.20–3.15 (1H, m, C13H), 2.79 (1H, t, \( J = 4.7 \) Hz, C12H\(_A\)H\(_B\)), 2.61 (1H, dd, \( J = 5.0 \), 2.7 Hz, C12H\(_A\)H\(_B\)); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \( \delta = 159.3 \) (C(OCH\(_3\)) of PMB), 130.0 (CCH\(_2\text{CH}_2\text{C(OCH}_3\) of PMB), 129.5 (2C, CCH\(_2\text{CH}_2\text{C(OCH}_3\) of PMB), 113.9 (2C, CCH\(_2\text{CH}_2\text{C(OCH}_3\) of PMB), 73.0 (OCH\(_2\)), 70.6 (C14H\(_2\)), 55.3 (OCH\(_3\) of PMB), 50.9 (C13H), 44.4 (C12H\(_2\)); HRMS (+ESI) Found [M+Na]\(^+\) = 217.0843; C\(_{11}\)H\(_{14}\)O\(_3\)Na requires 217.0835, \( \Delta 3.69 \) ppm.
**tert-Butyl(((2R,4E)-1-((4-methoxybenzyl)oxy)-4-methyl-5-(trimethylsilyl)pent-4-en-2-yl)dimethylsilane S17**

To a solution of vinyl iodide 73† (12.7 g, 53.0 mmol) in PhMe (530 mL) at −78 °C was added tBuLi (1.28 M in pentane, 82.8 mL, 105.9 mmol) dropwise and the pale yellow solution stirred for 45 min. After cooling to −85 °C (internal), a solution of epoxide 74 (25.7 g, 132.4 mmol) in PhMe (150 mL) was added dropwise to the vinyl lithium solution via cannula, followed immediately by BF$_3$•OEt$_2$ (16.3 mL, 132.4 mmol) ensuring that the temperature did not exceed −70 °C. The reaction was maintained at −78 °C for 2 h and then quenched with sat. aq. NaHCO$_3$ (450 mL), diluted with EtOAc (450 mL) and slowly warmed to RT. The layers were separated and the aqueous layer further extracted with EtOAc (3 × 400 mL). The combined organic layers were dried (MgSO$_4$) and concentrated *in vacuo*. Purification by column chromatography (SiO$_2$, dry load, hexane:EtOAc, 8:2) gave the desired alcohol (76) (9.71 g, 31.5 mmol) which was used directly in the next step of the reaction sequence.

To a solution of alcohol 76 (9.71 g, 31.5 mmol) in CH$_2$Cl$_2$ (315 mL) at −78 °C was added 2,6-lutidine (8.1 mL, 69.4 mmol) and TBSOTf (8.0 mL, 34.7 mmol) sequentially. The reaction mixture was stirred for 90 min at −78 °C and H$_2$O (200 mL) added. The layers were separated and the aqueous layer further extracted with CH$_2$Cl$_2$ (4 × 150 mL). The combined organic layers were dried (MgSO$_4$) and concentrated *in vacuo*. Purification by column chromatography (SiO$_2$, hexane→hexane:EtOAc, 95:5) gave the title compound S17 (11.8 g, 53% over 2 steps) as a colourless oil.

\[ R_f = 0.48 \text{ (hexane:EtOAc, 95:5); } \left[ \alpha \right]_{D}^{26.8} = +5.8 \ (c = 1.19, \text{ CHCl}_3); \text{ IR (film) } \nu_{\text{max/cm}^{-1}} \text{ 2953, 2929, 2856, 1615, 1513, 1464, 1362, 1302, 1246, 1172, 1087, 1038, 1005, 971; } \text{ ^1H NMR (CDCl}_3, 400 MHz) } \delta = 7.25 \ (2\ H, \text{ d, } J = 10.1 \text{ Hz, } (CH)_2\text{COCH}_3 \text{ of PMB), 6.87 \ (2 \ H, \text{ d, } J = } \]

† The vinyl iodide was used directly without any drying techniques due to its volatility.

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8.6 Hz, C(CH)2 of PMB), 5.25 (1H, s, C10H), 4.45 (2H, s, OCH2Ar(OCH3)), 3.99–3.93 (1H, m, C13H), 3.81 (3H, s, OCH3), 3.36 (1H, dd, J = 9.2, 5.2 Hz, C14H_AH_B), 3.32 (1H, dd, J = 9.5, 5.3 Hz, C14H_AH_B), 2.33 (1H, dd, J = 13.2, 4.8 Hz, C12H_AH_B), 2.17 (1H, dd, J = 13.4, 7.5 Hz, C12H_AH_B), 1.79 (3H, s, C23H3), 0.87 (9H, s, C(CH3)3 of tBu), 0.08 (9H, s, C10HSi(CH3)3), 0.04 (3H, s, Si(CH3)2), 0.03 (3H, s, Si(CH3)2); 13C NMR (CDCl3, 100 MHz) δ = 159.1 (C(OCH3) of PMB), 151.9 (C11), 130.6 (CCH2CH2C(OCH3) of PMB), 129.2 (CCH2CH2C(OCH3) of PMB), 126.8 (C10H), 113.7 (CCH2CH2C(OCH3) of PMB), 74.5 (C14H2), 73.0 (OCH2Ph(OCH3)), 70.6 (C13H), 55.3 (OCH3 of PMB), 48.3 (C12H2), 25.9 (3C, C(CH3)3 of tBu), 22.3 (C23H3), 18.2 (C(CH3)3 of tBu), 0.1 (3C, C10HSi(CH3)3), –4.3 (Si(CH3)2), –4.7 (Si(CH3)2); HRMS (+ESI) Found [M+H]+ = 423.2759; C23H43O3Si2 requires 423.2751, Δ 1.89 ppm and [M+Na]+ = 445.2581; C23H45O3Si2Na requires 445.2570, Δ 2.47 ppm.
(2R,4E)-2-((tert-Butyl(dimethyl)silyl)oxy)-4-methyl-5-(trimethylsilyl)pent-4-en-1-ol 79

To a solution of S17 (11.8 g, 28.0 mmol) in CH₂Cl₂ (340 mL) at 0 °C was added pH 7 phosphate buffer (35 mL) followed by DDQ (8.89 g, 39.2 mmol). The reaction mixture was stirred for 40 min, after which another portion of DDQ (3.18 g, 14.0 mmol) was added. After an additional 40 min at 0 °C the mixture allowed to warm to RT, diluted with CH₂Cl₂ (150 mL) and sat. aq. NaHCO₃ (400 mL) added. The layers were separated and the organic layer further washed with H₂O (400 mL), dried (MgSO₄) and filtered. To the resulting filtrate was added BZA resin (30.5 g, 5.5 mmol/g, 167.9 mmol) and the mixture stirred for 90 min. The resin was removed by filtration and the reaction mixture concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:Et₂O, 9:1) gave the title compound 79 (7.50 g, 89%) as a colourless oil.

\[ R_f = 0.28 \text{ (hexane:Et}_2\text{O, 9:1); } [\alpha]_{D28.6} = -6.8 \text{ (c = 0.83, CHCl}_3); \text{ IR (film) } \nu_{\text{max}}/\text{cm}^{-1} 3381, 2954, 2930, 2858, 1618, 1473, 1463, 1439, 1387, 1378, 1362, 1248, 1105, 1072, 1043, 1005; \text{ }^1\text{H NMR (CDCl}_3, 400 \text{ MHz) } \delta = 5.27 \text{ (1H, s, C}_10\text{H)}, 3.93–3.87 \text{ (1H, m, C}_13\text{H}), 3.60–3.53 \text{ (1H, m, C}_14\text{H}_2\text{O)}, 1.86 \text{ (1H, t, } J = 6.4 \text{ Hz, C}_14\text{H}_2\text{O}), 1.80 \text{ (3H, s, C}_23\text{H}_3), 0.90 \text{ (9H, s, C(CH}_3)_3 \text{ of tBu), 0.10–0.09 \text{ (15H, br s, Si(CH}_3)_2 \text{ and CHSi(CH}_3)_3); } \text{ }^{13}\text{C NMR (CDCl}_3, 100 \text{ MHz) } \delta = 151.1 \text{ (C11), 127.4 (C10H), 71.6 (C13H), 66.3 (C14H}_2), 47.7 (C12H}_2), 25.9 (3C, C(CH}_3)_3 \text{ of tBu), 22.3 (C23H}_3), 18.1 (C(CH}_3)_3 \text{ of tBu), 0.0 (3C, C10HSi(CH}_3)_3), -4.4 (Si(CH}_3)_2), -4.5 (Si(CH}_3)_2); \text{ HRMS (+ESI) Found [M+Na]}^+ = 325.2005; \text{ C}_{15}\text{H}_{34}\text{O}_2\text{Si}_2\text{Na requires 325.1995, } \Delta 3.08 \text{ ppm; Elemental Analysis found C, 59.59; H, 11.32. C}_{15}\text{H}_{34}\text{O}_2\text{Si}_2 \text{ requires C, 59.54; H, 11.33%}.\]
**tert-Butyl(((3R,5E)-1,1-dibromo-5-methyl-6-(trimethylsilyl)hexa-1,5-dien-3-yl)oxy)dimethylsilane 81**

To a solution of 79 (3.77 g, 12.5 mmol) and Et$_3$N (17.4 mL, 124.7 mmol) in CH$_2$Cl$_2$ (80 mL) at 0 °C was added a solution of SO$_3$•pyr (9.9 g, 62.4 mmol) in DMSO (67 mL) dropwise via syringe over 15 min. The reaction mixture was stirred at 0 °C for 30 min, after which it was warmed to RT slowly over 1 h and diluted with EtOAc:hexane (1:1, 566 mL). The mixture was washed with 1 N HCl (2 × 75 mL), sat. aq. NaHCO$_3$ (150 mL), brine (150 mL), dried (MgSO$_4$) and concentrated *in vacuo* to give aldehyde 80 (3.74 g, 99%). The aldehyde was carried through to the next step in the synthesis without further purification.

A solution of PPh$_3$ (13.08 g, 49.9 mmol) in CH$_2$Cl$_2$ (290 mL) was cooled to 0 °C and CBr$_4$ (8.27 g, 24.9 mmol) added in one portion. The resulting bright yellow solution was stirred for 15 min, during which time a separate solution of crude aldehyde 80 (3.74 g, 12.5 mmol) in CH$_2$Cl$_2$ (290 mL) was also cooled to 0 °C and 2,6-lutidine (2.92 mL, 25.1 mmol) added. The aldehyde solution was then transferred to the ylide dropwise over 20 min via cannula, and the mixture maintained at 0 °C for 1 h. The solution was quenched with sat. aq. NH$_4$Cl (290 mL), further diluted with CH$_2$Cl$_2$ (290 mL) and then warmed to RT. The layers were separated, and the aqueous layer further extracted with CH$_2$Cl$_2$ (300 mL). The combined organic layers were dried (MgSO$_4$) and concentrated *in vacuo*. Purification by column chromatography (SiO$_2$, dry load, hexane) gave the title compound 81 (5.03 g, 89% over 2 steps) as a colourless oil.

$R_f = 0.50$ (pentane); $[\alpha]_{D}^{26.2} = -11.8$ (c = 1.00, CHCl$_3$); IR (film) $\nu_{max}$/cm$^{-1}$ 2955, 2928, 2856, 1618 (C=CBr$_2$), 1475, 1463, 1362, 1248, 1078, 1022; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ = 6.36 (1H, d, J = 8.1 Hz, C14H), 5.26 (1H, s, C10H), 4.45–4.39 (1H, m, C13H), 2.27 (1H, dd, J = 13.0, 7.8 Hz, C12H$_A$H$_B$), 2.20 (1H, dd, J = 13.0, 5.3 Hz, C12H$_A$H$_B$), 1.82 (3H, s, C23H), 0.87 (9H, s, C(CH$_3$)$_3$ of tBu), 0.10 (9H, s, C10HSi(CH$_3$)$_3$), 0.06 (3H, s, Si(CH$_3$)$_2$), 0.05 (3H, s, Si(CH$_3$)$_2$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ = 150.0 (C11), 142.0 (C14H), 128.1 (C10H), 88.2 (C15Br$_2$), 72.8
tert-Butyl(dimethyl)(((3R,5E)-5-methyl-6-(trimethylsilyl)hex-5-en-1-yn-3-yl)oxy)silane 82

To a solution of 81 (8.10 g, 17.8 mmol) in THF (310 mL) at −78 °C was added nBuLi (2.21 M in hexanes, 16.9 mL, 37.4 mmol) dropwise resulting in the formation of a red-brown solution. After 40 min at −78 °C, the dry-ice/acetone bath was removed and the solution allowed to warm to RT over 1 h, during which time the solution once again became bright yellow. The reaction mixture was quenched with H₂O (300 mL) and diluted with pentane (400 mL). The layers were separated and the aqueous layer further extracted with pentane (2 × 300 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane) gave the title compound 82 (4.48 g, 85%) as a colourless oil.

\[ R_f = 0.38 \text{ (pentane); } \alpha_D^{28.5} = +34.2 \text{ (c = 0.75, CHCl}_3); \]
\[ \text{IR (film) } \nu_{\text{max}}/\text{cm}^{-1} = 3313, 2955, 2930, 1858, 1619, 1475, 1464, 1377, 1362, 1342, 1249, 1088, 1005; \]
\[ ^1\text{H NMR (CDCl}_3, 400 \text{ MHz) } \delta = 5.31 \text{ (1H, s, C10H), 4.47 \text{ (1H, ddd, } J = 7.7, 5.5, 2.0 \text{ Hz, C13H), 2.49–2.40 \text{ (2H, m, C12H}_2\text{H}_3), 2.38 \text{ (1H, d, } J = 2.0 \text{ Hz, C15H), 1.81 \text{ (3H, s, C23H}_3), 0.89 \text{ (9H, s, C(CH}_3)_3 \text{ of tBu), 0.13 \text{ (3H, s, Si(CH}_3)_2), 0.09 \text{ (12H, br s, Si(CH}_3)_2 \text{ and C10HSi(CH}_3)_3); } \]
\[ ^{13}\text{C NMR (CDCl}_3, 100 \text{ MHz) } \delta = 150.3 \text{ (C11), 127.5 \text{ (C10H), 85.6 \text{ (C14), 72.1 \text{ (C15H), 62.0 \text{ (C13H), 51.5 \text{ (C12H}_2), 25.8 \text{ (3C, C(CH}_3)_3 \text{ of tBu), 22.2 \text{ (C23H}_3), 18.2 \text{ (C(CH}_3)_3 \text{ of tBu), 0.0 \text{ (3C, C10HSi(CH}_3)_3), –4.6 \text{ (Si(CH}_3)_2), –5.1 \text{ (Si(CH}_3)_2); HRMS (+ESI) Found [M+Na]^+ = 319.1877; C_{16}H_{32}OSi_{2}Na requires 319.1884, } \]
\[ = 1.89 \text{ ppm.} \]
**tert-Butyl(dimethyl)(((1E,3R,5E)-5-methyl-1-(tributylstannanyl)-6-(trimethylsilyl)hex-1,5-dien-3-yl)oxy)silane 83**

To a solution of 82 (52 mg, 0.176 mmol) in THF (5.9 mL) at 0 °C was added Pd(PPh\(_3\))\(_2\)Cl\(_2\) (3.7 mg, 5.28 μmol) in one portion, followed by the dropwise addition of Bu\(_3\)SnH (56 μL, 0.21 mmol) via syringe. The dark yellow solution was stirred at 0 °C for 2 h, after which it was allowed to warm to RT and the solvent removed in vacuo. Purification by column chromatography (SiO\(_2\), hexane) gave the title compound 83 (57.8 mg, 56%) as a colourless oil.

\( R_f = 0.28 \) (hexane); \([\alpha]_D^{25.2} = +10.3 \) (c = 0.94, CHCl\(_3\)); IR (film) \( \nu_{\text{max}}/\text{cm}^{-1} \) 2956, 2927, 2856, 1617, 1463, 1376, 1361, 1248, 1090, 1068; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \( \delta = 6.04 \) (1H, d, \( J = 19.0 \) Hz, C15H), 5.93 (1H, dd, \( J = 19.0, 5.4 \) Hz, C14H), 5.24 (1H, s, C10H), 4.21–4.15 (1H, m, C13H), 2.27 (1H, dd, \( J = 13.0, 7.6 \) Hz, C12H\(_A\)H\(_B\)), 2.18 (1H, dd, \( J = 13.0, 5.5 \) Hz, C12H\(_A\)H\(_B\)), 1.80 (3H, s, C23H\(_3\)), 1.52–1.44 (6H, m, CH\(_2\) of SnBu\(_3\)), 1.35–1.25 (6H, m, CH\(_2\) of SnBu\(_3\)), 0.91–0.86 (24H, m, CH\(_2\) of SnBu\(_3\), CH\(_3\) of SnBu\(_3\) and C(CH\(_3\))\(_3\) of tBu), 0.09 (9H, s, C10HSi(CH\(_3\))\(_3\)), 0.03 (3H, s, Si(CH\(_3\))\(_2\)), 0.02 (3H, s, Si(CH\(_3\))\(_2\)); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \( \delta = 151.9 \) (C11), 151.5 (C15H), 126.7 (C10H), 126.3 (C14H), 75.8 (C13H), 51.8 (C12H\(_2\)), 29.1 (3C, Bu), 27.3 (3C, Bu), 26.0 (3C, C(CH\(_3\))\(_3\) of tBu), 22.5 (C23H\(_3\)), 18.4 (C(CH\(_3\))\(_3\) of tBu), 13.7 (3C, Bu), 9.5 (3C, Bu), 0.1 (3C, C10HSi(CH\(_3\))\(_3\)), −4.3 (Si(CH\(_3\))\(_2\)), −4.8 (Si(CH\(_3\))\(_2\)); An accurate mass could not be obtained for this compound, but a mass corresponding to the loss of butane was obtained HRMS (+EI) Found [M−C\(_4\)H\(_9\)]\(^+\) = 531.2516; C\(_{24}\)H\(_{51}\)OSi\(_2\)Sn requires 531.2495, \( \Delta 3.95 \) ppm.
**tert-Butyl(((1E,3R,5E)-1-iodo-5-methyl-6-(trimethylsilyl)hexa-1,5-dien-3-yl)oxy)dimethylsilane 84**

To a solution of 82 (4.48 g, 15.1 mmol) in THF (500 mL) at 0 °C was added (PPh₃)₂PdCl₂ (318 mg, 0.45 mmol) in one portion, followed by the dropwise addition of Bu₃SnH (10.2 mL, 37.8 mmol) via syringe. The dark yellow solution was stirred at 0 °C for 2 h, after which it was allowed to warm to RT and the solvent removed *in vacuo* to leave a dark residue.

The residue was re-dissolved in CH₂Cl₂ (250 mL) and cooled to −78 °C. A solution of I₂ in CH₂Cl₂ (0.079 M, 37.8 mmol) was added via cannula dropwise until a dark purple colour persisted. The mixture was immediately quenched with 20% aq. Na₂S₂O₃ (500 mL) and warmed to RT. The layers were separated and the aqueous layer further extracted with CH₂Cl₂ (3 × 500 mL). The combined organic layers were washed with 20% aq. Na₂S₂O₃ (500 mL), brine (500 mL), dried (MgSO₄) and concentrated *in vacuo* to give an orange oil. Purification by column chromatography (SiO₂, hexane) gave the title compound 84 (3.16 g, 49% over 2 steps) as a colourless oil.

**Physical Data**

- R<sub>f</sub> = 0.38 (hexane); [α]<sub>D</sub><sup>25.3</sup> = +14.0 (c = 1.06, CHCl₃);
- IR (film) v<sub>max</sub>/cm<sup>−1</sup> = 2954, 2929, 2857, 1616, 1472, 1463, 1361, 1248, 1206, 1160, 1094, 1074, 1006, 940;
- <sup>1</sup>H NMR (CDCl₃, 400 MHz) δ = 6.51 (1H, dd, J = 14.4, 6.0 Hz, C₁₁H), 6.19 (1H, dd, J = 14.4, 0.8 Hz, C₁₁H), 5.24 (1H, s, C₁₁H), 4.24–4.18 (1H, m, C₁₂H) 2.26 (1H, dd, J = 13.1, 7.3 Hz, C₁₂H₁₂H₈), 2.18 (1H, dd, J = 13.1, 5.6 Hz, C₁₁H₂₁H₈), 1.78 (3H, s, C₂₃H₂₃), 0.88 (9H, s, C(CH₃)₃ of tBu), 0.10 (9H, s, C₁₁HSi(CH₃)₃), 0.04 (3H, s, Si(CH₃)₂), 0.03 (3H, s, Si(CH₃)₂);
- <sup>13</sup>C NMR (CDCl₃, 100 MHz) δ = 150.5 (C₁₁), 149.0 (C₁₁H), 127.9 (C₁₁H), 75.5 (C₁₁H), 74.5 (C₁₁H), 51.0 (C₁₂H₂), 25.9 (3C, C(CH₃)₃ of tBu), 22.5 (C₂₃H₂₃), 18.2 (C(CH₃)₃ of tBu), 0.0 (3C, C₁₀HSi(CH₃)₃), −4.5 (Si(CH₃)₂), −4.9 (Si(CH₃)₂);
- HRMS (+ESI) Found [M+Na]<sup>+</sup> = 447.1028; C₁₆H₃₃IOSi₂Na requires 447.1007, Δ 4.70 ppm;
- **Elemental Analysis** found C, 45.31; H, 7.75. C₁₆H₃₃IOSi₂Na requires C, 45.27; H, 7.84%.
((E)-2-Iodoethenyl)(trimethyl)silane 91

To stannane 87\(^{19}\) (308 mg, 0.79 mmol) in CH\(_2\)Cl\(_2\) (2.4 mL) at 0 °C was added a solution of I\(_2\) in CH\(_2\)Cl\(_2\) (0.0787 M, 0.947 mmol) via cannula dropwise until a dark purple colour persisted. The mixture was immediately quenched with sat. aq. Na\(_2\)S\(_2\)O\(_3\) (5 mL) and warmed to RT. The resulting dark mixture was extracted with CH\(_2\)Cl\(_2\) (2 × 20 mL) and the combined organic layers dried (MgSO\(_4\)) and carefully concentrated in vacuo (400 mbar, RT). Purification by column chromatography (SiO\(_2\), pentane) gave the title compound 91 (70.4 mg, 40%) as a colourless oil.

\(R_f = 0.58\) (pentane); IR (film) \(\nu_{\text{max}}/\text{cm}^{-1}\) 2956, 2898, 1542, 1412, 1247, 1146, 953, 835, 767; \(^{1}\)H NMR (CDCl\(_3\), 400 MHz) \(\delta = 7.08\) (1H, d, \(J = 16.2\) Hz, C16H), 6.68 (1H, d, \(J = 16.1\) Hz, C17H), 0.09 (9H, s, Si(CH\(_3\))\(_3\)) ; \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta = 150.5\) (C16H), 89.5 (C17H), –1.5 (3C, Si(CH\(_3\))\(_3\)); HRMS (+EI) Found [M]+ = 225.9660; C\(_5\)H\(_{11}\)ISi requires 225.9669, \(\Delta\) 3.98 ppm.

((1\(E\)-4-((1\(S\),2\(R\))-2-Chlorocyclopropyl)but-1-en-3-yn-1-yl)(trimethyl)silane 88

To a solution of dibromide 48 (417 mg, 1.60 mmol) in Et\(_2\)O at −78 °C was added \(n\)BuLi (2.16 M in hexanes, 1.76 mmol) dropwise, resulting in the formation of a yellow solution. The mixture was stirred for 15 min at this temperature after which it was warmed to 0 °C, stirred for a further 10 min and then re-cooled to –78 °C. Additional \(n\)BuLi (2.16 M in hexanes, 1.76 mmol) was added dropwise to the reaction mixture at −78 °C, stirred for 15 min and then once again warmed to 0 °C and stirred for 30 min. The now dark yellow solution was again re-cooled to −78 °C whereupon H\(_2\)O (20 mL) was added. The reaction was warmed to RT, extracted with Et\(_2\)O (3 × 50 mL) and the combined extracts washed with brine (50 mL) and dried (MgSO\(_4\)). The solvent was carefully removed by distillation at 65 °C using a vigreux column and the crude alkyne (90) (assumed quant.) used directly in the next step without further purification.
To a solution of crude alkyne 90 (assumed quant., 1.60 mmol), vinyl iodide 91 (145 mg, 0.64 mmol) in MeCN (12.8 mL) at RT was added (PPh\textsubscript{3})\textsubscript{2}PdCl\textsubscript{2} (31.4 mg, 45 μmol) and CuI (25.6 mg, 0.134 mmol) sequentially. The mixture was cooled to 0 °C and Et\textsubscript{3}N (0.39 mL, 2.82 mmol) added dropwise. The reaction was maintained at 0 °C for 1 h in the absence of light and then warmed to RT, diluted with pentane (10 mL) and quenched with pH 7 phosphate buffer (10 mL). The mixture was extracted with pentane (3 × 20 mL) and the combined organics washed with H\textsubscript{2}O (30 mL), brine (30 mL), dried (MgSO\textsubscript{4}) and carefully concentrated \textit{in vacuo} (400 mbar, RT). Purification by column chromatography (SiO\textsubscript{2}, pentane) gave the title compound 88 (104 mg, 82% from vinyl iodide 91) as a colourless oil.

\(R_f = 0.48\) [petroleum ether (30–40)]; [\(\alpha\)]\textsubscript{D}\textsuperscript{26.6} = −162.4 (c = 1.33, CHCl\textsubscript{3}); IR (film) \(\nu_{\text{max}}/\text{cm}^{-1}\) 2956, 2929, 1572, 1465, 1432, 1306, 1248, 1209, 1096, 1060, 1044, 999, 975; \(^1\)H NMR (CDCl\textsubscript{3}, 500 MHz) \(\delta = 6.35\) (1H, d, \(J = 19.2\) Hz, C16H), 5.86 (1H, dd, \(J = 19.2, 1.8\) Hz, C17H), 3.17–3.14 (1H, m, C21H), 1.80–1.74 (1H, m, C20H), 1.28–1.24 (2H, m, C22H\textsubscript{2}H\textsubscript{3}), 0.06 (9H, s, Si(CH\textsubscript{3})\textsubscript{3}); \(^{13}\)C NMR (CDCl\textsubscript{3}, 126 MHz) \(\delta = 145.4\) (C16H), 123.0 (C17H), 89.3 (C19), 78.9 (C18), 34.2 (C21H), 19.2 (C22H\textsubscript{2}), 11.9 (C20H), −1.7 (3C, Si(CH\textsubscript{3})\textsubscript{3}); HRMS (+EI) Found [M]\textsuperscript{+} = 198.0634; C\textsubscript{10}H\textsubscript{15}ClSi requires 198.0626, Δ 4.04 ppm.

\((1R,2S)-1\)-Chloro-2-((3Z)-4-iodobut-3-en-1-yn-1-yl)cyclopropane S18

To a solution of 88 (9.70 mg, 48.8 μmol) in MeCN (1 mL) at RT was added NIS (16.5 mg, 73.2 μmol) in one portion and the reaction stirred in the absence of light for 16 h. The mixture was quenched by the addition of sat. aq. Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3} (1 mL) and diluted with pentane (2 mL). The layers were separated and the aqueous layer extracted with pentane (3 × 2 mL), dried (MgSO\textsubscript{4}) and carefully concentrated \textit{in vacuo} (400 mbar, RT) to give the title compound S18 as well as E-isomer 89 in a 3:1 mixture. Purification by column chromatography (SiO\textsubscript{2}, pentane) provided a sample of the title compound S18 (2.5 mg, 20%) for full characterisation as a colourless oil.
**R** = 0.53 (pentane); [α]_D^{27.6} = −90.0 (c = 0.07, CHCl_3) **IR** (film) ν_{max}/cm^{-1} 2956, 2924, 2213, 1574, 1457, 1429, 1297, 1257, 1058, 1041, 989; **^1^H NMR** (CDCl_3, 500 MHz) δ = 6.69 (1H, d, J = 8.2 Hz, C16H), 6.53 (1H, dd, J = 8.3, 2.0 Hz, C17H), 6.28–3.24 (1H, m, C21H), 1.85–1.80 (1H, m, C20H), 1.41–1.32 (2H, m, C22H_AH_B); **^13^C NMR** (CDCl_3, 126 MHz) δ = 122.4 (C17H), 96.9 (C19), 91.9 (C16H), 78.1 (C18), 34.3 (C21H), 19.5 (C22H_2), 12.2 (C20H); **HRMS** (+EI) Found [M]^+ = 251.9201; C_7H_6ClI requires 251.9197, Δ 0.00 ppm.

(1R,2S)-1-Chloro-2-((3E)-4-iodobut-3-en-1-yn-1-yl)cyclopropane 89

![Image](image.png)

To a solution of IPy_2BF_4 (48.7 mg, 0.131 mmol) in CH_2Cl_2 (0.4 mL) at RT was added HBF_4•OEt_2 (36 μL, 0.262 mmol) dropwise resulting in a dark red solution. The mixture was cooled to 0 °C after which 88 (13 mg, 65.4 μmol) in CH_2Cl_2 (0.4 mL) was added dropwise. The reaction was maintained at 0 °C for 30 min† and then diluted with CH_2Cl_2 (2 mL) followed by the addition of sat. aq. NaHCO_3 (1 mL) and L-ascorbic acid (20% w/w, 2 mL). The resulting yellow solution was allowed to warm to RT over 30 min. The layers were separated and the aqueous layer further extracted with CH_2Cl_2 (3 × 5 mL), dried (MgSO_4) and concentrated in vacuo. Purification by column chromatography (Florisil, pentane) gave the title compound 89 (15.9 mg, 96%) as a colourless oil.

**R** = 0.48 [petroleum ether (30–40)]; [α]_D^{27.8} = −152.7 (c = 1.18, CHCl_3); **IR** (film) ν_{max}/cm^{-1} 3058, 2924, 2218, 1686, 1564, 1430, 1358, 1256, 1177, 1096, 1060, 1045, 997, 923; **^1^H NMR** (CDCl_3, 400 MHz) δ = 6.73 (1H, d, J = 15.0 Hz, C16H), 6.44 (1H, dd, J = 15.0, 1.9 Hz, C17H), 3.20–3.15 (1H, m, C21H), 1.75–1.69 (1H, m, C20H), 1.32–1.27 (2H, m, C22H_AH_B); **^13^C NMR** (CDCl_3, 100 MHz) δ = 124.7 (C17H), 90.8 (C19), 89.7 (C16H), 77.7 (C18), 34.0 (C21H), 19.2 (C22H_2), 11.9 (C20H); **HRMS** (+EI) Found [M]^+ = 251.9197; C_7H_6ClI requires 251.9197, Δ 0.00 ppm.

† The starting material 88 and product 89 were co-polar. On several occasions the reaction was not complete after 30 min, but re-submission of the crude material to the above conditions gave comparable yields.
**Tributyl((1E)-4-((1S,2R)-2-chlorocyclopropyl)but-1-en-3-yn-1-yl)stannane 93**

![Chemical structure](image)

To a 50 mL round-bottomed flask was added 48 (2.56 g, 9.85 mmol), DMF (9.9 mL) and TBAF (1 M in THF, 24.6 mL, 24.6 mmol). The reaction vessel was sealed, and the mixture heated at 65 °C for 90 min, after which TLC analysis showed formation of a single product. The reaction mixture was cooled to RT after which brine (12 mL) was added and the mixture extracted with pentane (5 × 40 mL). The combined organic layers were dried (MgSO₄) and concentrated *in vacuo* (400 mbar, RT) to give the crude alkynyl bromide 86 (assumed quant.) which was used directly in the next step ([*R*<sub>f</sub> = 0.83 (hexane)].

To a solution of crude alkynyl bromide 86 (assumed quant., 9.85 mmol) in THF (25 mL) at RT was added Pd₂dba₃ (901 mg, 0.985 mmol) and AsPh₃ (1.21 g, 3.94 mmol) sequentially and stirred for 10 min. This was followed by the addition of Ag₂CO₃ (2.72 g, 9.85 mmol) in one portion and stirred for a further 10 min. The reaction mixture was then cooled to −10 °C and a solution of (E)-ethene-1,2-diylbis(tributylstannane) 92<sup>20</sup> (10.5 mL, 19.7 mmol) in THF (25 mL) added in one portion *via* syringe. The reaction was maintained at −10 °C for 40 h, after which it was warmed to RT and the solvent removed *in vacuo*. Purification by column chromatography (SiO₂, pentane) gave the title compound 93 (1.83 g, 45% over 2 steps) as a colourless oil.

[*R*<sub>f</sub> = 0.73 (hexane); [α]<sub>D</sub><sup>25.0</sup> = −73.7 (c = 1.14, CHCl₃); IR (film) ν<sub>max</sub>/cm⁻¹ 2956, 2923, 2872, 2853, 1556, 1464, 1417, 1377, 1356, 1340, 1292, 1255, 1184, 1152, 1072, 1043; <sup>1</sup>HNMR (CDCl₃, 400 MHz) δ = 6.78 (1H, d, J = 19.7 Hz, C₁₆H), 5.89 (1H, dd, J = 19.7, 1.7 Hz, C₁₇H), 3.20–3.15 (1H, m, C₂₁H), 1.82–1.75 (1H, m, C₂₀H), 1.54–1.44 (6H, m, CH₂ of SnBu₃), 1.33–1.25 (8H, m, C₂₂H₄H₈ and CH₂ of SnBu₃), 0.93–0.86 (15H, m, CH₂ of SnBu₃ and CH₃ of SnBu₃); <sup>13</sup>C NMR (CDCl₃, 100 MHz) δ = 146.7 (C₁₆H), 125.4 (C₁₇H), 87.3 (C₁₉), 79.1 (C₁₈), 34.3 (C₂₁H), 28.9 (3C, Bu), 27.5 (3C, Bu), 19.2 (C₂₂H₂), 13.7 (3C, Bu), 11.4 (C₂₀H), 9.6 (3C, Bu); An accurate mass could not be obtained for this compound, but a mass corresponding to the loss of butane was obtained HRMS (+EI) Found [M–C₄H₉]⁺ = 359.0589; C₁₅H₂₃ClSn requires
359.0583, $\Delta$ 1.67 ppm; **Elemental Analysis** found C, 55.37; H, 8.01; Cl, 8.28. C$_{19}$H$_{33}$ClSn requires C, 54.91; H, 8.00; Cl, 8.53%.

**tert-Butyl(((1E,4R,5E,7E)-10-((1S,2R)-2-chlorocyclopropyl)-2-methyl-1-trimethylsilyl)deca-1,5,7-trien-9-yn-4-yl)oxy)dimethylsilane 67**

To a solution of vinyl iodide 84 (555 mg, 1.31 mmol) and stannane 93 (707 mg, 1.70 mmol) in DMF (28 mL) at RT was added freshly prepared Pd(PFur$_3$)$_2$Cl$_2$ 121 (126 mg, 0.197 mmol) in one portion resulting in an orange solution. The reaction was stirred in the absence of light for 22 h, after which brine (28 mL) was added. The mixture was extracted with pentane ($5 \times 40$ mL) and the combined organic layers dried (MgSO$_4$) and concentrated *in vacuo*. Purification by column chromatography (SiO$_2$, hexane) gave the title compound 67 (347 mg, 63%) as a pale yellow oil.

$R_f = 0.16$ (pentane); $[\alpha]_D^{27.0} = -97.4$ (c = 0.59, CHCl$_3$); **IR** (film) $\nu_{\text{max}}$cm$^{-1}$ 2955, 2929, 2857, 1617, 1472, 1465, 1431, 1362, 1249, 1108, 1098, 1069, 983, 939, 926, 836; **$^1$H NMR** (CDCl$_3$, 400 MHz) $\delta =$ 6.49 (1H, dd, J = 15.5, 10.9 Hz, C16H), 6.14 (1H, dd, J = 15.2, 10.9 Hz, C15H), 5.73 (1H, dd, J = 15.2, 6.1 Hz, C14H), 5.49 (1H, d, J = 15.5 Hz, C17H), 5.22 (1H, s, C10H), 4.31–4.25 (1H, m, C13H), 3.19–3.14 (1H, m, C21H), 2.27 (1H, dd, J = 13.0, 7.5 Hz, C12H$_2$H$_B$), 2.17 (1H, dd, J = 13.0, 5.4 Hz, C12H$_A$H$_B$), 1.83–1.78 (1H, m, C20H), 1.78 (3H, s, C23H), 1.30–1.25 (2H, m, C22H$_A$H$_B$), 0.88 (9H, s, C(CH$_3$)$_3$ of tBu), 0.08 (9H, s, C10HSi(CH$_3$)$_3$), 0.02 (3H, s, Si(CH$_3$)$_2$), 0.00 (3H, s, Si(CH$_3$)$_2$); **$^{13}$C NMR** (CDCl$_3$, 100 MHz) $\delta =$ 151.1 (C11), 141.3 (C16H), 139.5 (C14H), 128.1 (C15H), 127.3 (C10H), 110.2 (C17H), 91.1 (C19), 77.9 (C18), 72.1 (C13H), 51.6 (C12H$_2$), 34.3 (C21H), 25.9 (3C, C(CH$_3$)$_3$ of tBu), 22.5 (C23H), 19.3 (C(CH$_3$)$_3$ of tBu), 18.3 (C22H$_2$), 12.1 (C20H), 0.0 (3C, C10HSi(CH$_3$)$_3$), −4.6 (Si(CH$_3$)$_2$), −4.8 (Si(CH$_3$)$_2$); An accurate mass could not be obtained for this compound.
(1S,2R,1′R,2′R)-1,1′-(3E,5E)-Octa-3,5-diene-1,7-diyne-1,8-diylbis(2-chlorocyclopropane)

S19

A small amount of homocoupled material S19 (26.5 mg) was isolated from the previous procedure (for compound 67) for full characterisation as an off-white solid.

$R_f = 0.18$ (hexane); m.p. = 54–56 °C; $[\alpha]_{D}^{25.8} = -399.8$ (c = 1.12, CHCl$_3$); IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 2925, 2854, 2209, 1465, 1430, 1358, 1254, 1097, 1067, 1047, 975; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 6.53$–6.45 (2 × 1H, m, C17H), 5.63–5.53 (2 × 1H, m, C16H), 3.20–3.15 (2 × 1H, C21H), 1.84–1.78 (2 × 1H, m, C20H), 1.32–1.25 (2 × 2H, m, C22H$_{A}$H$_{B}$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 140.4$ (2C, C16H), 113.0 (2C, C17H), 93.4 (2C, C19), 77.8 (2C, C18), 34.3 (2C, C21H), 19.4 (2C, C22H$_2$), 12.2 (2C, C20H); HRMS (+EI) Found [M]$^+$ = 250.0305; $C_{14}H_{12}Cl_2$ requires 250.0311, Δ 2.40 ppm.
Dimethyl (7S)-5-O-(tert-butyl(dimethyl)silyl)-7-((2R,3R,4E,7R,8E,10E)-7-((tert-butyl(dimethyl)silyl)oxy)-13-((1S,2R)-2-chlorocyclopropyl)-3-hydroxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl)-2,4,6-trideoxy-6-methyl-a-L-threo-hept-3-ulopyranosidonate S20

To a solution of vinyl iodide 55† (202.5 mg, 0.425 mmol) in Et₂O (2 mL) at −78 °C was added tBuLi (1.61 M, 0.57 mL, 0.916 mmol) dropwise resulting in the formation of a dark red solution. The mixture was stirred for 10 min after which a freshly prepared ethereal ZnBr₂ solution‡ (0.9 M, 0.49 mL, 0.441 mmol) was added dropwise. The resulting bright yellow solution was immediately warmed to 0 °C and maintained at this temperature for 1 h. In the meantime, a stock solution of (1S,2R)-(+)~N-methylephedrine (129 mg, 0.720 mmol) in PhMe (3.6 mL) was made, and dried by stirring with CaH₂ for 45 min. The stock solution was then cooled to 0 °C and nBuLi (2.25 M, 0.32 mL, 0.720 mmol) added dropwise and stirred for a further 15 min. Following this 1.96 mL (0.360 mmol) of this stock solution was then added to the organozinc solution and the reaction maintained at 0 °C for a further 1 h. After this time, aldehyde 5† (127.2 mg, 0.327 mmol) was added as a solution in PhMe (0.70 mL) with further rinsing with PhMe (2×1 mL). The reaction was stirred for a further 1 h at 0 °C after which it was quenched by the addition of sat. aq. NH₄Cl (1.5 mL) and H₂O (0.5 mL) and warmed to RT. The layers were separated and the aqueous layer further extracted with Et₂O (3×10 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:Et₂O, 4:1→2:1→1:1) gave the title compound S20 (116 mg, 48%) as a pale yellow oil.

† Azeotroped with PhMe (×3) prior to use.
‡ Prepared by heating ZnBr₂ at 250 °C under vacuum for 3 days, then dissolved in freshly distilled Et₂O.
$R_f = 0.38$ (hexane:Et$_2$O, 1:1); [$\alpha$]$_D^{26.2} = -70.3$ (c = 1.00, CHCl$_3$); IR (film) $\nu_{\max}$/cm$^{-1}$ 2954, 2930, 2857, 1742, 1463, 1438, 1378, 1361, 1253, 1223, 1146, 1074, 1039, 985; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ = 6.47 (1H, dd, $J = 15.5, 10.8$ Hz, C16H), 6.13 (1H, dd, $J = 15.1, 11.1$ Hz, C15H), 5.72 (1H, dd, $J = 15.1, 6.2$ Hz, C14H), 5.48 (1H, d, $J = 15.6$ Hz, C17H), 5.24 (1H, d, $J = 8.6$ Hz, C10H), 4.36–4.27 (2H, m, C9H and C13H), 3.77 (1H, d, $J = 10.6$ Hz, C7H), 3.67 (3H, s, C1O$_2$CH$_3$), 3.70–3.63 (1H, m, C5H), 3.28 (3H, s, C3OCH$_3$), 3.18–3.14 (1H, m, C21H), 2.69 (1H, d, $J = 13.4$ Hz, C2H$_A$H$_B$), 2.61 (1H, d, $J = 13.5$ Hz, C2H$_A$H$_B$), 2.29 (1H, dd, $J = 13.4, 6.1$ Hz, C12H$_A$H$_B$), 2.17 (1H, dd, $J = 13.2, 6.6$ Hz, C12H$_A$H$_B$), 2.12 (1H, dd, $J = 13.2, 4.8$ Hz, equatorial C4H$_A$H$_B$), 1.91 (1H, d, $J = 5.2$ Hz, C9H(OH)), 1.82–1.76 (1H, m, C20H), 1.74–1.65 (2H, m, axial C4H$_A$H$_B$ and C8H), 1.70 (3H, s, C23H$_3$), 1.50–1.40 (1H, m, C6H), 1.30–1.25 (2H, m, C22H$_A$H$_B$), 0.90 (9H, s, C(CH$_3)_3$ of tBu), 0.88 (9H, s, C(CH$_3)_3$ of tBu), 0.84 (3H, d, $J = 6.5$ Hz, C25H$_3$), 0.81 (3H, d, $J = 7.0$ Hz, C24H$_3$), 0.07 (6H, s, Si(CH$_3)_2$), 0.04 (3H, s, Si(CH$_3)_2$), 0.01 (3H, s, Si(CH$_3)_2$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ = 169.8 (C1O$_2$CH$_3$), 141.1 (C16H), 139.0 (C14H), 135.1 (C11), 131.0 (C10H), 128.5 (C15H), 110.6 (C17H), 99.2 (C3), 91.3 (C19), 77.8 (C18), 72.9 (C7H), 72.1 (one of C9H or C13H), 70.4 (one of C9H or C13H), 70.2 (C5H), 51.7 (C1O$_2$CH$_3$), 48.5 (C12H$_2$), 48.4 (C3OCH$_3$), 43.1 (C4H$_2$), 42.0 (C2H$_2$), 40.0 (C6H), 39.3 (C8H), 34.3 (C21H), 25.9 (6C, C(CH$_3)_3$ of tBu), 19.3 (C22H$_2$), 18.2 (C(CH$_3)_3$ of tBu), 18.1 (C(CH$_3)_3$ of tBu), 17.8 (C23H$_3$), 12.5 (C20H), 12.1 (C25H$_3$), 9.7 (C24H$_3$), 4.0 (Si(CH$_3)_2$), 4.4 (Si(CH$_3)_2$), 4.6 (Si(CH$_3)_2$), 4.7 (Si(CH$_3)_2$); HRMS (+ESI) Found [M+Na]$^+$ = 761.3987; C$_{39}$H$_{67}$O$_7$ClSi$_2$Na requires 761.4006, $\Delta$ 2.50 ppm.$^\dagger$

$^\dagger$ Note: Pyran 5 is completely consumed in this reaction.
Deiodinated by-product S21 (92.8 mg) was isolated from the previous procedure (for compound S20) for full characterisation as a colourless oil.

$R_f = 0.86$ (hexane:Et$_2$O, 1:1); $[\alpha]^{25.7}_D = -110.2$ (c = 1.02, CHCl$_3$); \(\text{IR (film)}\) $\nu_{\text{max}}$/cm$^{-1}$ 2954, 2930, 2857, 1648, 1472, 1463, 1431, 1391, 1362, 1255, 1107, 1096, 1068, 983; \(\text{\textsuperscript{1}H NMR (CDCl}_3, 400$ MHz) $\delta = 6.50$ (1H, dd, $J = 15.5, 10.8$ Hz, C16H), 6.16 (1H, dd, $J = 15.1, 10.9$ Hz, C15H), 5.75 (1H, dd, $J = 15.2, 6.1$ Hz, C14H), 5.49 (1H, d, $J = 15.6$, C17H), 4.78 (1H, s, C10H$_A$H$_B$), 4.69 (1H, s, C10H$_A$H$_B$), 4.31–4.25 (1H, m, C13H), 3.19–3.14 (1H, m, C21H), 2.26 (1H, dd, $J = 13.3, 6.4$ Hz, C12H$_A$H$_B$), 2.15 (1H, dd, $J = 13.4, 6.2$ Hz, C12H$_A$H$_B$), 1.83–1.77 (1H, m, C20H), 1.73 (3H, s, C23H$_3$), 1.30–1.25 (2H, m, C22H$_A$H$_B$), 0.88 (9H, s, C(CH$_3$)$_3$ of tBu), 0.04 (3H, s, Si(CH$_3$)$_2$), 0.01 (3H, s, Si(CH$_3$)$_2$); \(\text{\textsuperscript{13}C NMR (CDCl}_3, 100$ MHz) $\delta = 141.9$ (C11), 141.3 (C16H), 139.3 (C14H), 128.3 (C10H$_2$), 113.4 (C15H), 110.3 (C17H), 91.2 (C19), 77.9 (C18), 71.7 (C13H), 46.9 (C12H$_2$), 34.3 (C21H), 25.9 (3C, C(CH$_3$)$_3$ of tBu), 23.1 (C23H$_3$), 19.3 (C22H$_2$), 18.3 (C(CH$_3$)$_3$ of tBu), 12.1 (C20H), −4.4 (Si(CH$_3$)$_2$), −4.8 (Si(CH$_3$)$_2$); An accurate mass could not be obtained for this compound.
Dimethyl (7S)-5-O-(tert-butyl(dimethyl)silyl)-7-((2R,3R,4E,7R,8E,10E)-7-(((tert-butyl(dimethyl)silyl)oxy)-13-((1S,2R)-2-chlorocyclopropyl)-3-methoxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl)-2,4,6-trideoxy-6-methyl-α-L-threo-hept-3-ulopyranosidonate 95

To a solution of S20 (102.0 mg, 0.138 mmol) in CH₂Cl₂ (6.9 mL) at RT was added 2,6-di-tert-butylpyridine (0.62 mL, 2.76 mmol) and MeOTf (0.15 mL, 1.38 mmol) sequentially. The reaction was stirred at RT for 21 h after which it was quenched by the addition of MeOH (2.5 mL) and poured onto sat. aq. NaHCO₃ (30 mL). The reaction mixture was extracted with CH₂Cl₂ (3 × 30 mL) and the combined organic layers dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:Et₂O, 20:1→10:1) gave the title compound 95 (75.7 mg, 73%) as a colourless oil.

Rᵣ = 0.58 (hexane:Et₂O, 7:3); [α]D²⁶.o = −84.8 (c = 1.07, CHCl₃), [lit.⁷ [α]D²³ = −76.58 (c = 1.45, CHCl₃)]; IR (film) νmax/cm⁻¹ 2952, 2929, 2857, 1743, 1471, 1463, 1376, 1361, 1315, 1255, 1223, 1188, 1146, 1079, 1041, 984; ¹H NMR (CDCl₃, 400 MHz) δ = 6.46 (1H, dd, J = 15.5, 10.9 Hz, C₁₆H), 6.12 (1H, dd, J = 15.2, 10.9 Hz, C₁₅H), 5.72 (1H, dd, J = 15.1, 6.5 Hz, C₁₄H), 5.46 (1H, d, J = 15.5 Hz, C₁₇H), 4.93 (1H, d, J = 9.6 Hz, C₁₀H), 4.36–4.30 (1H, m, C₁₃H), 3.86 (1H, t, J = 9.7 Hz, C₉H), 3.72 (1H, m, C₅H), 3.69–3.66 (1H, m, C₇H), 3.66 (3H, s, C₁O₂CH₃), 3.23 (3H, s, C₃OCH₃), 3.20–3.14 (1H, m, C₂₁H), 3.11 (3H, s, C₉H(OCH₃)), 2.66 (1H, d, J = 13.5 Hz, C₂H₄A₁H₄B), 2.62 (1H, d, J = 13.5 Hz, C₂H₄A₁H₄B), 2.38 (1H, dd, J = 13.2, 5.3 Hz, C₁₂H₄A₁H₂B), 2.23 (1H, dd, J = 13.3, 7.5 Hz, C₁₂H₄A₁H₂B), 2.12 (1H, dd, J = 12.8, 4.6 Hz, equatorial C₄H₄A₁H₂B), 1.83–1.76 (1H, m, C₂₀H), 1.69 (3H, s, C₂₃H₃), 1.72–1.65 (2H, m, axial C₄H₄A₁H₂B and C₈H), 1.44–1.36 (1H, m, C₆H), 1.30–1.25 (2H, m, C₂₂H₄A₁H₂B), 0.89 (9H, s, C(CH₃)₃ of tBu), 0.88 (9H, s, C(CH₃)₃ of tBu), 0.84 (3H, d, J = 6.5 Hz, C₂₅H₃), 0.68 (3H, d, J = 7.0 Hz, C₂₄H₃), 0.07 (6H, s, Si(CH₃)₂), 0.05 (3H, s, Si(CH₃)₂), 0.03 (3H, s, Si(CH₃)₂); ¹³C NMR (CDCl₃, 100 MHz) δ = 170.0 (C₁O₂CH₃), 141.1 (C₁₆H), 138.9 (C₁₄H), 136.9 (C₁₁), 129.0 (C₁₀H), 128.7
(C15H), 110.5 (C17H), 98.9 (C3), 91.3 (C19), 77.8 (C9H), 77.3 (C18), 72.3 (C13H), 71.8 (C5H), 70.7 (C7H), 55.3 (C9H(OCH3)), 51.6 (C1O2CH3), 48.8 (C12H2), 47.7 (C3OCH3), 43.4 (C4H2), 42.1 (C2H2), 39.9 (C6H), 38.6 (C8H), 34.3 (C21H), 25.9 (6C, C(CH3)3 of tBu), 19.3 (C22H2), 18.1 (2C, C(CH3)3 of tBu), 18.0 (C23H3), 12.4 (C20H), 12.1 (C25H3), 8.7 (C24H3), –4.0 (Si(CH3)2), –4.3 (Si(CH3)2), –4.6 (Si(CH3)2), –4.7 (Si(CH3)2); HRMS (+ESI) Found [M+Na]+ = 775.4148; C40H69O7ClSi2Na requires 775.4163, Δ 1.93 ppm; Elemental Analysis found C, 63.80; H, 9.24; Cl, 4.68. C40H69O7ClSi2 requires C, 63.75; H, 9.23; Cl, 4.70%.
Dimethyl (7S)-5-O-(tert-butyl(dimethyl)silyl)-7-((2R,3R,4E,7R,8E,10E)-13-((1S,2R)-2-chlorocyclopropyl)-7-hydroxy-3-methoxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl)-2,4,6-trideoxy-6-methyl-a-1-threo-hept-3-ulopyranosidonate 99

To a solution of 95 (75.7 mg, 0.10 mmol) in THF (3 mL) at RT was added TBAF (1 M in THF, 0.60 mL, 0.60 mmol) dropwise. The reaction mixture was stirred at RT for 30 min at which point TLC analysis indicated complete consumption of starting material. The reaction was quenched by the addition of sat. aq. NH₄Cl (1.2 mL) and EtOAc (10 mL) added. The layers were separated and the aqueous layer further extracted with EtOAc (3 × 10 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:Et₂O, 4:1→2:1→1:1) gave the title compound 99 (47.1 mg, 74%) as an off-white foam/gum.

Rₛ = 0.20 (hexane:Et₂O, 1:1); [α]₂₆.₀ = -71.6 (c = 0.86, CHCl₃), [lit.⁷ [α]₂₃ = -68.33 (c = 1.10, CHCl₃)]; IR (film) νmax/cm⁻¹ 3434, 2956, 2930, 2857, 1741, 1465, 1437, 1381, 1316, 1255, 1223, 1189, 1146, 1123, 1078, 1034, 984; ¹H NMR (CDCl₃, 400 MHz) δ = 6.49 (1H, dd, J = 15.4, 10.9 Hz, C₁₆H), 6.26 (1H, dd, J = 15.1, 10.9 Hz, C₁₅H), 5.77 (1H, dd, J = 15.2, 6.2 Hz, C₁₄H), 5.52 (1H, d, J = 15.5 Hz, C₁₇H), 5.03 (1H, d, J = 9.5 Hz, C₁₀H), 4.36–4.29 (1H, m, C₁₃H), 3.90 (1H, d, J = 15.5 Hz, C₁₇H), 5.03 (1H, d, J = 9.5 Hz, C₁₀H), 4.36–4.29 (1H, m, C₁₃H), 3.90 (1H, t, J = 9.7 Hz, C₉H), 3.73 (1H, m, C₅H), 3.71–3.63 (1H, m, C₇H), 3.66 (3H, s, C₁O₂CH₃), 3.23 (3H, s, C₃OCH₃), 3.20–3.15 (1H, m, C₂₁H), 3.13 (3H, s, C₉H(OCH₃)), 2.66 (1H, d, J = 13.5 Hz, C₂H₄H₃B), 2.62 (1H, d, J = 13.2 Hz, C₂H₄H₃B), 2.31 (2H, appar. d, J = 6.8 Hz, C₁₂H₄H₃B), 2.12 (1H, dd, J = 12.8, 4.6 Hz, equatorial C₄H₄H₃B), 1.82–1.76 (1H, m, C₂₀H), 1.73 (3H, s, C₂₃H₃), 1.71–1.65 (2H, m, axial C₄H₄H₃B and C₈H), 1.46–1.35 (1H, m, C₆H), 1.30–1.26 (2H, m, C₂₂H₄H₃B), 0.89 (9H, s, C(CH₃)₃ of tBu), 0.84 (3H, d, J = 6.5 Hz, C₂₅H₃), 0.70 (3H, d, J = 7.0 Hz, C₂₄H₃), 0.06 (6H, s, Si(CH₃)₂); ¹³C NMR (CDCl₃, 100 MHz) δ = 169.9 (C₁O₂CH₃), 140.7 (C₁₆H), 137.7 (C₁₄H), 136.7 (C₁₁), 129.7 (C₁₀H), 129.5 (C₁₅H), 111.4 (C₁₇H), 98.9
(C3), 91.7 (C19), 77.7 (C9H), 77.3 (C18), 71.8 (C7H), 70.7 (C13H), 55.4 (C9H(OCH3)), 51.6 (C1O2CH3), 48.0 (C12H2), 47.8 (C3OCH3), 43.4 (C4H2), 42.1 (C2H2), 39.9 (C6H), 38.5 (C8H), 34.3 (C21H), 25.9 (3C, C(tBu)), 19.3 (C22H2), 18.1 (3C, C(CH3)3 of tBu), 17.2 (C23H3), 12.4 (C25H3), 8.9 (C24H3), –4.0 (Si(CH3)2), –4.6 (Si(CH3)2); 

HRMS (+ESI) Found [M+Na]+ = 661.3299; C34H55O7ClSiNa requires 661.3298, Δ 0.15 ppm. All spectroscopic data in agreement with that previously published.7

Methyl (7S)-5-O-(tert-butyl(dimethyl)silyl)-7-((2R,3R,4E,7R,8E,10E)-13-((1S,2R)-2-chlorocyclopropyl)-7-hydroxy-3-methoxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl)-2,4,6-trideoxy-6-methyl-α-L-threo-hept-3-ulopyranosidonic acid 1007

To a solution of 99 (47.1 mg, 73.7 μmol) in MeOH (2.5 mL) at RT was added Ba(OH)2•8H2O (349 mg, 1.105 mmol) in one portion and stirred for 18 h. The reaction was poured onto EtOAc (20 mL) and H2O (10 mL) (2:1) and stirred vigorously, with 0.05 M HCl added slowly dropwise until the pH of the aqueous layer reached 1 (approximately 100 mL of 0.05 M HCl). The layers were separated and the aqueous layer further extracted with EtOAc (50 mL). The combined organic layers were dried (MgSO4) and concentrated in vacuo to give the title compound 100 (50.0 mg, quant.) as an off-white foam/gum.

Rf = 0.13 (hexane:Et2O, 1:1); [α]D25.9 = –66.3 (c = 1.25, CHCl3), [lit.7 [α]D23 = –98.41 (c = 0.57, CHCl3)]; IR (film) νmax/cm–1 2927, 2853, 1712, 1463, 1437, 1383, 1315, 1256, 1221, 1189, 1147, 1124, 1078, 1031, 984; 1H NMR (C6D6, 400 MHz) δ = 6.66 (1H, dd, J = 15.4, 10.9 Hz, C16H), 6.23 (1H, dd, J = 15.0, 11.1 Hz, C15H), 5.69–5.62 (2H, m, C14H and C17H), 5.13 (1H, d, J = 9.4 Hz, C10H), 4.22–4.16 (2H, m, C7H and C13H), 4.13 (1H, t, J = 9.7 Hz, C9H), 4.01 (1H, td, J = 10.2, 4.4 Hz, C5H), 3.35 (3H, s, C3OCH3), 3.20 (3H, s, C9H(OCH3)), 3.02–2.97 (1H, m, C21H), 2.72 (1H, d, J = 13.9 Hz, C2H3Hb), 2.68 (1H, d, J = 13.8 Hz, C2H3Hb), 2.56 (1H, dd, J =
= 12.9, 12.7, 4.5, 4.3 Hz, equatorial C4H_A(H_B), 2.30–2.16 (2H, m, 2 × C12H_A(H_B), 2.07–1.92 (2H, m, axial C4H_A(H_B) and C8H), 1.73 (3H, s, C23H), 1.75–1.68 (2H, m, C6H and C20H), 1.09 (9H, s, C(CH3)_3 of tBu), 1.04 (3H, d, J = 6.4 Hz, C25H), 0.95 (3H, d, J = 6.9 Hz, C24H), 0.93–0.90 (2H, m, C22H_A(H_B), 0.23 (3H, s, Si(CH3)_2), 0.17 (3H, s, Si(CH3)_2); ¹³C NMR (C_6D_6, 100 MHz)  δ = 174.2 (C1O2H), 141.1 (C16H), 138.5 (C14H), 136.9 (C11), 129.5 (C10H), 129.2 (C15H), 111.5 (C17H), 99.1 (C3), 91.9 (C19), 78.2 (C18), 77.5 (C9H), 72.4 (one of C7H or C13H), 70.9 (C5H), 70.0 (one of C7H or C13H), 55.0 (C9H(OCH3)), 47.8 (C12H2), 47.8 (C3OCH3), 43.8 (C4H2), 42.1 (C2H2), 40.2 (C6H), 38.9 (C8H), 34.2 (C21H), 25.9 (3C, C(CH3)_3 of tBu), 18.9 (C22H2), 18.1 (C(CH3)_3 of tBu), 17.1 (C23H3), 12.5 (C20H), 12.2 (C25H3), 8.9 (C24H3), −4.1 (Si(CH3)_2), −4.8 (Si(CH3)_2); HRMS (+ESI) Found [M+Na]^+ = 647.3146; C_{33}H_{53}O_7ClSiNa requires 647.3141, Δ 0.77 ppm.

(1R,6R,8E,10R,11R,12R,13R,14S)-6-((1E,3E)-6-((1S,2R)-2-Chlorocyclopropyl)hexa-1,3-dien-5-yn-1-yl)-1,14-dihydroxy-10-methoxy-8,11,13-trimethyl-5,16-dioxabicyclo[10.3.1]hexadec-8-en-4-one ²²

To a solution of 100 (62.9 mg, 0.10 mmol) in PhMe (7.4 mL) at RT was added Et3N (83.6 μL, 0.60 mmol) and freshly distilled 2,4,6-trichlorobenzoyl chloride (78.1 μL, 0.50 mmol) sequentially dropwise. The reaction mixture was stirred for 30 min at RT after which it was further diluted with PhMe (29 mL). This solution was then added via syringe pump to a solution of DMAP (61.1 mg, 0.50 mmol) in PhMe (74 mL) at 80 °C over 8.5 h. Following addition, the reaction mixture was stirred for a further 30 min at 80 °C before being cooled to RT and quenched by the addition of MeOH (10 mL) and sat. aq. NaHCO₃ (34 mL). The layers were separated and the aqueous layer further extracted with EtOAc (3 × 60 mL) and the combined organic layers washed with brine (120 mL), dried (MgSO₄), and concentrated in vacuo.
Purification by column chromatography (SiO₂, hexane:EtOAc, 9:1) gave a mixture (assumed quant.) of TBS-protected aglycon and C3-eliminated material.

To the semi-pure mixture (assumed quant., 0.10 mmol) dissolved in THF (15 mL) at RT was added H₂O (3 mL) (5:1) followed by TFA (0.82 mL, 10.7 mmol) dropwise. The reaction was stirred at RT for 12 h after which it was quenched by the addition of sat. aq. NaHCO₃ (27 mL). The mixture was extracted with EtOAc (3 × 30 mL) and the combined organic extracts dried (MgSO₄), and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:EtOAc, 7:3→1:1) gave the title compound 4 (27.6 mg, 58% over 2 steps) as an off-white foam/gum.

Rf = 0.17 (hexane:EtOAc, 7:3); [α]D²⁵.⁶ = −44.6 (c = 0.75, CHCl₃), [lit.²² [α]D²⁰ = −33.4 (c = 0.53, CHCl₃)]; IR (film) νmax/cm⁻¹ 3442, 2964, 2925, 2873, 1702, 1431, 1415, 1348, 1323, 1256, 1225, 1178, 1151, 1080, 1023, 999, 978; ¹H NMR (CDCl₃, 400 MHz) δ = 6.48 (1H, dd, J = 15.5, 10.9 Hz, C16H), 6.27 (1H, dd, J = 14.9, 10.9 Hz, C15H), 5.86–5.80 (1H, m, C13H), 5.76 (1H, dd, J = 15.5, 15.5 Hz, C17H), 5.57 (1H, dd, J = 14.9, 6.4 Hz, C14H), 5.31 (1H, d, J = 9.4 Hz, C10H), 5.02 (1H, d, J = 2.2 Hz, C3OH), 3.80 (1H, dd, J = 9.7, 2.0 Hz, C9H), 3.79–3.75 (1H, m, C5H), 3.61 (1H, dd, J = 10.2, 2.4 Hz, C7H), 3.23 (3H, s, C9H(OCH₃)), 3.20–3.16 (1H, m, C21H), 2.55 (1H, d, J = 12.9 Hz, C2HₐHₖ), 2.44 (1H, d, J = 12.9 Hz, C2HₐHₖ), 2.31–2.28 (2H, m, 2 × C12HₐHₖ), 2.25–2.18 (1H, m, C8H), 2.10 (1H, dd, J = 11.9, 4.6 Hz, equatorial C4HₐHₖ), 1.84–1.76 (1H, m, C20H), 1.73 (3H, s, C23H₃), 1.59–1.52 (1H, br s, C5OH), 1.43–1.35 (1H, m, C6H), 1.31–1.25 (3H, m, C22HₐHₖ and axial C4HₐHₖ), 0.98 (6H, d, J = 6.7 Hz, C24H₃ and C25H₃); ¹³C NMR (CDCl₃, 100 MHz) δ = 171.7 (C1O₂), 140.2 (C16H) 132.7 (C14H), 132.3 (C11), 131.0 (C15H), 127.9 (C10H), 112.6 (C17H), 95.4 (C3), 92.3 (C19), 79.8 (C9H), 77.3 (C18), 75.0 (C7H), 71.5 (C13H), 69.6 (C5H), 55.3 (C9H(OCH₃)), 47.0 (C12H₂), 44.8 (C2H₂), 43.8 (C4H₂), 40.1 (C6H), 36.9 (C8H), 34.3 (C21H), 19.4 (C22H₂), 16.1 (C23H₃), 12.1 (C20H), 12.1 (C25H₃), 6.6 (C24H₃); HRMS (+ESI) Found [M+Na]+ = 501.2009; C₂₆H₃₅O₆ClNa requires 501.2014, Δ 1.00 ppm. All spectroscopic data in agreement with that previously published.²²
1,5-Anhydro-2,6-dideoxy-L-arabino-hex-1-enitol S22

To a solution of 3,4-di-O-acetyl-6-deoxy-L-glucal† 107 (5.0 g, 23.3 mmol) in MeOH (110 mL) at RT was added PS-Na$_2$CO$_3$ (3.21 mmol/g, 7.56 g, 24.3 mmol) and the mixture shaken for 4 h. The reaction mixture was filtered and the beads washed with CH$_2$Cl$_2$ (2 × 30 mL), and MeOH (2 × 30 mL). The combined washings were concentrated in vacuo to give the title compound S22 as a white solid (3.31 g, quant.) which was used without further purification.

$R_f = 0.10$ (hexane:Et$_2$O, 6:4); m.p. = 67–70 °C; $[\alpha]_D^{25.0} = +12.6$ (c = 0.44, CHCl$_3$); IR (film) $\nu_{max}/cm^{-1}$ 3262, 3002, 2932, 2889, 1643, 1449, 1412, 1389, 1358, 1263, 1226, 1149, 1112, 1044, 1025; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 6.32$ (1H, d, $J = 6.1$ Hz, C1′H), 4.71 (1H, dd, $J = 6.0, 1.9$ Hz, C2′H), 4.21 (1H, tt, $J = 6.9, 1.7$ Hz, C3′H), 3.90–3.83 (1H, m, C5′H), 3.43–3.39 (1H, m, C4′H), 2.29–2.27 (1H, br s, C3′HOH), 1.77–1.75 (1H, br s, C4′HOH), 1.39 (3H, d, $J = 6.3$ Hz, C6′H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 144.9$ (C1′H), 102.7 (C2′H), 75.7 (C4′H), 74.4 (C5′H), 70.4 (C3′H), 17.1 (C6′H$_3$); HRMS (+EI) Found [M]$^+$ = 130.0624; C$_6$H$_{10}$O$_3$ requires 130.0624, $\Delta$ 0.00 ppm; Elemental Analysis found C, 55.29; H, 7.86. C$_6$H$_{10}$O$_3$ requires C, 55.37; H, 7.74%.

1,5-Anhydro-2,6-dideoxy-L-erythro-hex-1-en-3-ulose 106

To a vigorously stirring solution of S22 (3.31 g, 25.5 mmol) in CH$_2$Cl$_2$ (255 mL) at RT was added MnO$_2$ (13.3 g, 152.8 mmol). The mixture was stirred at RT until TLC analysis indicated that the starting material had been consumed. The MnO$_2$ was removed by filtration through a pad of silica under suction. The silica pad was washed with Et$_2$O (2 × 30 mL) and CH$_2$Cl$_2$ (2 × 30 mL) and the combined washings concentrated in vacuo to give the title compound 106 (2.2 g, 74% over 2 steps) as a white solid.

† er = 98.5:1.5
$R_f = 0.19$ (hexane:Et$_2$O, 6:4); m.p. = 93–94 °C; $[\alpha]_{D}^{25.0} = -154.0$ (c = 1.04, CHCl$_3$); IR (film) $\nu_{\text{max}}$ cm$^{-1}$: 3399, 3106, 2986, 2915, 1661, 1592, 1466, 1406, 1379, 1325, 1253, 1203, 1126, 1051, 1030; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ = 7.39 (1H, d, $J = 5.8$ Hz, C1′H), 5.46 (1H, d, $J = 5.8$ Hz, C2′H), 4.24–4.16 (1H, m, C5′H), 3.97 (1H, dd, $J = 13.1$, 1.7 Hz, C4′H), 3.51 (1H, d, $J = 1.7$ Hz, C4′HOH), 1.59 (3H, d, $J = 6.2$ Hz, C6′H$_3$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ = 194.1 (C3′), 164.7 (C1′H), 103.5 (C2′H), 72.8 (C4′H), 18.0 (C6′H$_3$); An accurate mass could not be obtained for this compound, but a low resolution mass could be obtained; HRMS (+ESI): 129.17 [M+H]$^+$, 126.98 [M–H]$^+$.

1,5-Anhydro-2,6-dideoxy-4-O-((4-nitrophenyl)sulfonyl)-L-erythro-hex-1-en-3-ulose S23$^{23}$

![Chemical structure](image)

To a solution of S22 (820 mg, 6.41 mmol) in CH$_2$Cl$_2$ (30 mL) at 0 °C was added pyridine (0.78 mL, 9.61 mmol) followed by nosyl chloride (1.70 g, 7.69 mmol) and the mixture slowly warmed to RT. After 48 h stirring at RT additional pyridine (2.85 mL, 35.26 mmol) and nosyl chloride (3.98 g, 17.95 mmol) were added and stirring continued for a further 24 h. The mixture was cooled to 0 °C, H$_2$O (10 mL) added and stirred at this temperature for 30 min, after which more H$_2$O (50 mL) was added. The layers were separated and the aqueous layer further extracted with CH$_2$Cl$_2$ (3 × 50 mL) and the combined organic layers washed with brine, dried (MgSO$_4$) and concentrated in vacuo. Purification by column chromatography (SiO$_2$, hexane:EtOAc, 85:15) gave the title compound S23 (1.89 g, 95%) as a yellow solid.

$R_f = 0.53$ [petroleum ether (40–60):EtOAc, 1:1]; m.p. = 92–93 °C (lit$^{23}$ = 93 °C); $[\alpha]_{D}^{25.0} = -128.3$ (c = 0.71, CHCl$_3$); IR (film) $\nu_{\text{max}}$ cm$^{-1}$: 3107, 2988, 1693, 1595, 1530, 1450, 1405, 1378, 1349, 1314, 1254, 1184, 1094, 1043, 1023; $^1$H NMR (CDCl$_3$, 500 MHz) $\delta = 8.38$ (2H, d, $J = 9.1$ Hz, Ar, ortho to NO$_2$), 8.17 (2H, d, $J = 9.1$ Hz, Ar, ortho to SO$_2$), 7.33 (1H, d, $J = 5.8$ Hz, C1′H), 5.35 (1H, d, $J = 5.8$ Hz, C2′H), 4.99 (1H, d, $J = 11.6$ Hz, C4′H), 4.54–4.50 (1H, m, C5′H), 1.60 (3H, d, $J = 6.4$ Hz, C6′H$_3$); $^{13}$C NMR (CDCl$_3$, 126 MHz) $\delta = 186.1$ (C3′), 163.6 (C1′H), 150.8 (Ar, ipso to NO$_2$), 142.0 (Ar, ipso to SO$_2$), 129.7 (2C, Ar, ortho to NO$_2$), 124.1 (2C, Ar, ortho to SO$_2$), 105.0 (C2′H), 79.6 (C4′H), 77.4 (C5′H), 17.4 (C6′H); HRMS (+ESI)
Found [M+H]^+ = 314.0349; C_{12}H_{12}NO_7S requires 314.0334, Δ 4.78 ppm; **Elemental Analysis** found C, 46.14; H, 3.53; N, 4.31. C_{12}H_{11}NO_7S requires C, 46.01; H, 3.54; N, 4.47%. All physical data in agreement with enantiomeric compound published by Nicolaou.\textsuperscript{23}

1,5-Anhydro-4-azido2,4,6-trideoxy-L-threo-hex-1-en-3-ulose 108\textsuperscript{23}

![Chemical Structure](image)

To a solution of S\textsuperscript{23} (1.67 g, 5.33 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (33 mL) at 0 °C was added a solution of nBu\textsubscript{4}NN\textsubscript{3} (4.28 g, 15.0 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (30 mL, cooled to 0 °C) via cannula. The reaction mixture was stirred at 0 °C for 1 h and then warmed to RT slowly over the course of 2 h. The reaction was quenched by the addition of H\textsubscript{2}O (50 mL) and the layers separated. The aqueous layer was further extracted using CH\textsubscript{2}Cl\textsubscript{2} (2 × 100 mL) and the combined organic layers washed with brine (150 mL), dried (MgSO\textsubscript{4}) and concentrated *in vacuo* to give an orange oil. Purification by column chromatography (SiO\textsubscript{2}, hexane:Et\textsubscript{2}O, 2:1) gave the title compound 108 (586 mg, 72%) as a yellow oil.

\[ R_f = 0.21 \text{ (hexane:EtOAc, 4:1); } [\alpha]^{28,4}_{D} = +48.1 \text{ (c = 0.73, CHCl}_3) \]; **IR** (film) \( \nu_{\text{max}}/\text{cm}^{-1} \): 2991, 2101, 1668, 1589, 1453, 1410, 1384, 1273, 1224, 1192, 1153, 1049; **\textsuperscript{1}H NMR** (CDCl\textsubscript{3}, 500 MHz) \( \delta = 7.37 \text{ (1H, d, } J = 7.5 \text{ Hz, } C1'H), 5.48 \text{ (1H, dd, } J = 7.5, 1.0 \text{ Hz, } C2'H), 4.55-4.51 \text{ (1H, m, } C5'H), 3.80 \text{ (1H, dd, } J = 4.0, 1.5 \text{ Hz, } C4'H), 1.48 \text{ (3H, d, } J = 8.0 \text{ Hz, } C6'H_3); **\textsuperscript{13}C NMR** (CDCl\textsubscript{3}, 126 MHz) \( \delta = 187.3 \text{ (C3'), 163.6 (C1'H), 104.9 (C2'H), 77.3 (C5'H), 63.9 (C4'H), 15.3 (C6'H_3); **HRMS** (+ESI) Found [M+H]^+ = 176.0430; C\textsubscript{6}H\textsubscript{7}N\textsubscript{3}O\textsubscript{2}Na requires 176.0429, Δ 0.57 ppm. All physical data in agreement with enantiomeric compound published by Nicolaou.\textsuperscript{23}

nOe experiments performed to reveal the stereochemical relationship gave inconclusive results.
2,6-Anhydro-3-azido-1,3,5-trideoxy-4-C-methyl-L-arabinohex-5-enitol 104

To a solution of 108 (2.6 g, 17.0 mmol) in THF (154 mL) cooled to –100 °C was added MeLi (1.6 M in Et₂O, 21.2 mL, 34.0 mmol) dropwise. After 2 h at –100 °C, the reaction was quenched with sat. aq. NH₄Cl (120 mL), diluted with EtOAc (120 mL) and allowed to warm to RT. The layers were separated and the aqueous layer further extracted with EtOAc (3 × 120 mL). The combined organic layers were washed with brine, dried (MgSO₄) and concentrated in vacuo to give a yellow oil. Purification by column chromatography (SiO₂, hexane:Et₂O, 8:2) gave the title compound 104 (2.27 g, 79%) as a yellow oil and single diastereomer.

\[ R_f = 0.62 \text{ [petroleum ether (40–60):EtOAc, 1:1]} \]
\[ [\alpha]_{D}^{25.0} = -51.1 \text{ (c = 1.31, CHCl₃)} \]
\[ \text{IR (film) } v_{\text{max}}/\text{cm}^{-1} \text{ 3423, 2986, 2937, 2913, 2107, 1645, 1449, 1385, 1342, 1312, 1278, 1233, 1157, 1136, 1076, 1054} \]
\[ \text{H NMR (CDCl₃, 400 MHz) } \delta = 6.27 \text{ (1H, d, } J = 6.3 \text{ Hz, C1'H)}, 4.69 \text{ (1H, dd, } J = 6.3, 1.8 \text{ Hz, C2'H)}, 4.19 \text{ (1H, q, } J = 6.5 \text{ Hz, C5'H)}, 3.34–3.32 \text{ (1H, br s, C4'H)}, 1.45 \text{ (3H, d, } J = 6.5 \text{ Hz, C6'H₃)}, 1.43 \text{ (3H, s, C8'H₃)} \]
\[ \text{C NMR (CDCl₃, 100 MHz) } \delta = 143.6 \text{ (C1'H), 106.8 (C2'H), 72.2 (C5'H), 68.9 (C4'H), 68.4 (C3'), 29.6 (C8'H₃), 18.0 (C6'H₃)} \]
An accurate mass could not be obtained for this compound. All physical data in agreement with enantiomeric compound published by Nicolaou.²³
Methyl 4-azido-4,6-dideoxy-3-C-methyl-α-L-talopyranoside 109

To a suspension of 104 (327 mg, 1.93 mmol) and NaHCO₃ (0.49 g, 5.79 mmol) in MeOH (7.4 mL) at 0 °C was added m-CPBA (70%, 0.57 g, 2.32 mmol). The mixture was stirred at 0 °C for 5 min and then warmed to RT. After 1 h the reaction was quenched with H₂O (25 mL), the layers separated and the aqueous layer further extracted with EtOAc (3 × 25 mL). The combined organic layers were partially concentrated in vacuo and the resulting bilayer re-dissolved in EtOAc (10 mL). The layers were again separated and the aqueous layer further extracted with EtOAc (3 × 25 mL). The combined organics were dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (Florisil, hexane:Et₂O, 7:3) gave the title compound 109 (218 mg, 52%) as a colourless oil.

Rᵋ = 0.34 (hexane:EtOAc, 1:1); [α]D²⁸.⁴ = −104.2 (c = 0.48, CHCl₃); IR (film) νmax/cm⁻¹ 3448, 2983, 2938, 2105, 1449, 1385, 1341, 1259, 1128, 1066, 1050, 999, 976, 943, 909; ¹H NMR (CDCl₃, 400 MHz) δ = 4.77 (1H, s, C1′H), 4.03 (1H, q, J = 6.4 Hz, C5′H), 3.58 (1H, s, C3′OH), 3.37 (3H, s, C1′HOCH₃), 3.31 (1H, d, J = 12.0 Hz, C2′H), 3.25 (1H, s, C4′H), 2.67 (1H, d, J = 12.0 Hz, C2′HOH), 1.39 (3H, s, C8′H₃), 1.35 (3H, d, J = 6.4 Hz, C6′H₃); ¹³C NMR (CDCl₃, 100 MHz) δ = 102.1 (C1′H), 73.3 (C2′H), 71.2 (C4′H), 70.0 (C3′), 64.3 (C5′H), 55.5 (C1′HOCH₃), 23.6 (C8′H₃), 18.1 (C6′H₃); HRMS (+ESI) Found [M+Na]+ = 240.0955; C₈H₁₅N₃O₄Na requires 240.0962, Δ 2.92 ppm. All physical data in agreement with enantiomeric compound published by Nicolaou.²³

Key selected observed nOe’s:

No nOe was observed between C1′H and C5′H, suggesting a trans-arrangement.
Methyl 4-azido-4,6-dideoxy-3-C-methyl-2-O-methyl-α-L-talopyranoside 110

To a mixture of freshly sublimed KOrBu (299 mg, 2.66 mmol) in THF (6.8 mL) at 0 °C was added a solution of 109 (551 mg, 2.54 mmol) in THF (8.3 mL) dropwise. The reaction mixture was stirred for 40 min at 0 °C after which MeI (0.19 mL, 3.05 mmol) was added dropwise to the bright yellow solution and stirred for 4 h. After this time, further KOrBu (71.2 mg, 0.636 mmol) and MeI (31.6 μL, 0.508 mmol) were added and the reaction maintained at 0 °C until TLC analysis indicated full conversion of the starting material. The reaction was quenched with H2O (18 mL), diluted with CH2Cl2 (30 mL) and warmed to RT. The layers were separated, the aqueous layer further extracted with CH2Cl2 (3 × 30 mL), and the combined organics dried (MgSO4) and concentrated in vacuo. Purification by column chromatography (Florisil, hexane:Et2O, 7:3→Et2O) gave the title compound 110 (446 mg, 79%) as a colourless oil.

Rf = 0.28 (hexane:Et2O, 7:3); [α]D27.0 = −49.2 (c = 1.03, CHCl3); IR (film) νmax/cm−1 3516, 2984, 2944, 2913, 2833, 2104, 1463, 1445, 1383, 1348, 1280, 1263, 1179, 1134, 1104, 1060, 1023; 1H NMR (CDCl3, 500 MHz) δ = 4.77 (1H, s C1′H), 3.98 (1H, dq, J = 6.5, 1.4 Hz, C5′H), 3.68 (1H, s, C3′OH), 3.47 (3H, s, OCH3), 3.34 (3H, s, C1′HOCH3), 3.09 (1H, br s, C4′H), 2.88 (1H, s, C2′H), 1.38 (3H, s, C8′H3), 1.34 (3H, d, J = 6.5 Hz, C6′H3); 13C NMR (CDCl3, 126 MHz) δ = 98.4 (C1′H), 81.9 (C2′H), 70.1 (C4′H), 69.6 (C3′), 64.2 (C5′H), 59.8 (OCH3), 55.2 (C1′HOCH3), 24.5 (C8′H3), 17.9 (C6′H3); HRMS (+ESI) Found [M+Na]+ = 254.1122; C9H17N3O4Na requires 254.1111, Δ 4.33 ppm. All physical data in agreement with enantiomeric compound published by Nicolaou.

The corresponding D-configured enantiomer was synthesised and found to have the following optical rotation: [α]D26.0 = +54.6 (c = 1.17, CHCl3).
(3aR,4S,6R,7R,7aR)-6,7-Dimethoxy-4,7a-dimethyltetrahydro-4H-pyrano[3,4-d]oxazolo[2(3H)]-one 101

To a solution of 110 (156 mg, 0.675 mmol) in EtOAc (68 mL) at RT was added Pd(OH)_2/C (26 mg). The flask was then evacuated and backfilled with hydrogen (× 3) and left to stir at RT for 4 h 30 min. The mixture was filtered through a pad of Celite® under suction using EtOAc (3 × 80 mL) and concentrated in vacuo. The isolated amine (S24) (120 mg, 87%) was used immediately in the next step of the reaction without further purification.

To a solution of amine (S24) (120 mg, 0.585 mmol) in CH_2Cl_2 (9.8 mL) at –78 °C was added pyridine (0.85 mL, 10.5 mmol) followed by a solution of triphosgene (189.5 mg, 0.702 mmol) in CH_2Cl_2 (5.1 mL) via syringe. The resulting bright orange solution was stirred at –78 °C for 20 min after which it was warmed to RT over 1 h. The solution was quenched with 1 N HCl (5 mL) and the layers separated. The aqueous layer was further extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layers washed with sat. aq. NaHCO_3 (20 mL), brine (20 mL), dried (MgSO_4) and concentrated in vacuo. Purification by column chromatography (SiO_2, EtOAc:hexane, 4:1) gave the title compound 101 (97 mg, 72%) as a white solid.

**R_f** = 0.26 [EtOAc:petroleum ether (40–60), 4:1]; **m.p.** = 145–147 °C (lit\(^{23}\) = 147–148 °C); [\(_{D}^{23}\)] = –87.3 (c = 1.01, CHCl_3); **IR** (film) \(\nu_{\text{max}}/\text{cm}^{-1}\) 3298, 2913, 1744, 1719, 1425, 1374, 1320, 1273, 1202, 1105, 1061, 1027, 999; \(^{1}H\) **NMR** (CDCl_3, 400 MHz) \(\delta = 5.17\) (1H, br s, NH), 4.63 (1H, d, \(J = 5.5\) Hz, C1'H), 3.91 (1H, qd, \(J = 6.4, 1.4\) Hz, C5'H), 3.55 (3H, s, OCH_3), 3.43 (3H, s, C1'HOC_H_3), 3.35 (1H, br s, C4'H), 3.19 (1H, d, \(J = 5.5\) Hz, C2'H), 1.53 (3H, s, C8'H_3), 1.17 (3H, d, \(J = 6.5\) Hz, C6'H_3); \(^{13}C\) **NMR** (CDCl_3, 100 MHz) \(\delta = 158.0\) (NH7'O), 101.6 (C1'H), 81.8 (C3'), 81.1 (C2'H), 63.3 (C5'H), 61.1 (C4'H), 60.7 (OCH_3), 55.0 (C1'HOCH_3), 23.3 (C8'H_3), 15.7 (C6'H_3); **HRMS** (+ESI) Found [M+Na]^+ = 232.1189; C_{10}H_{18}NO_5 requires 232.1185, \(\Delta = 1.72\) ppm; **Elemental Analysis** found C, 51.85; H, 7.30; N, 5.83. C_{10}H_{18}NO_5 requires C, 51.94; H, 7.41; N, 6.06%.
(3aR,4S,6R,7R,7aR)-6,7-Dimethoxy-4,7a-dimethyl-3-(tripropan-2-ylsilyl)tetrahydro-4H-pyrano[3,4-d][1,3]oxazol-2(3H)-one 111

To a solution of 101 (130 mg, 0.563 mmol) in CH₂Cl₂ (13 mL) at RT was added 2,6-lutidine (0.26 mL, 2.25 mmol) followed by TIPSOTf (0.30 mL, 1.13 mmol) and the reaction stirred for 14 h. The reaction was diluted with CH₂Cl₂ (20 mL) and quenched with sat. aq. NH₄Cl (20 mL). The layers were separated and the aqueous layer further extracted with CH₂Cl₂ (3 × 50 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (Florisil, hexane→hexane:Et₂O, 1:1→EtOAc) gave the title compound 111 (211 mg, 97%) as a white solid.

Rₛ = 0.22 (Et₂O:hexane, 1:1); m.p. = 154–156 °C; [α]ᴰ²⁷.₁ = -79.6 (c = 0.96, CHCl₃); IR (film) νₓₓₓ/ν cm⁻¹ 2973, 2948, 2870, 1731, 1363, 1318, 1284, 1248, 1207, 1195, 1138, 1103, 1055, 1026; ¹H NMR (CDCl₃, 400 MHz) δ = 4.60 (1H, d, J = 5.8 Hz, C1'H), (1H, qd, J = 6.3, 2.2 Hz, C5'H), 3.53 (3H, s, OCH₃), 3.43 (1H, br s, C4'H), 3.42 (3H, s, C1'HOCH₃), 3.23 (1H, d, J = 5.8 Hz, C2'H), 1.53 (3H, s, C8'H₃), 1.41 (3H, septet, J = 7.5 Hz, Si(CH(CH₃)₂)₃), 1.24–1.16 (21H, m, Si(CH(CH₃)₂)₃ and C6'H₃); ¹³C NMR (CDCl₃, 100 MHz) δ = 161.2 (C7'O₂), 102.1 (C1'H), 82.1 (C3'), 81.6 (C2'H), 65.6 (C5'H), 65.2 (C4'H), 60.3 (OCH₃), 54.9 (C1'HOCH₃), 22.5 (C8'H₃), 19.1 (3C, Si(CH(CH₃)₂)₃), 19.1 (3C, Si(CH(CH₃)₂)₃), 17.0 (C6'H₃), 13.2 (3C, Si(CH(CH₃)₂)₃); HRMS (+ESI) Found [M+H]⁺ = 388.2519; C₁₉H₃₈NO₅Si requires 388.2524, Δ 1.29 ppm and [M+Na]⁺ = 410.2339; C₁₉H₃₇NO₅SiNa requires 410.2347, Δ 1.95 ppm; Elemental Analysis found C, 58.94; H, 9.59; N, 3.55. C₁₉H₃₇NO₅Si requires C, 58.88; H, 9.62; N, 3.61%.
(3aR,4S,6S,7R,7aR)-7-Methoxy-4,7a-dimethyl-6-(phenylthio)-3-tripropan-2-ylsilyl)tetrahydro-4H-pyrano[3,4-d][1,3]oxazol-2(3H)-one 112

To a solution of 111 (121 mg, 0.313 mmol) in CH$_2$Cl$_2$ (3.2 mL) at 0 °C was added thiophenol (0.32 mL, 3.13 mmol) followed by BF$_3$•OEt$_2$ (0.58 mL, 4.70 mmol) and the mixture allowed to warm to RT slowly over 16 h. The reaction was quenched by the addition of sat. aq. NaHCO$_3$ (3 mL). The layers were separated and the aqueous layer further extracted with CH$_2$Cl$_2$ (3 × 10 mL). The combined organic layers were dried (MgSO$_4$) and concentrated in vacuo. Purification by column chromatography (Florisil, dry load, hexane→hexane:Et$_2$O, 9:1→7:3→EtOAc) gave the title compound 112 (116 mg, 80%) as a white solid.

$R_f = 0.28$ (hexane:Et$_2$O, 7:3); m.p. = 127–130 °C; $[\alpha]_D^{28.3} = -75.0$ (c = 0.82, CHCl$_3$); IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 3690, 3677, 2969, 2905, 1722, 1469, 1455, 1443, 1395, 1385, 1365, 1318, 1249, 1211, 1126, 1104, 1083, 1057, 1025; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 7.52$ (2H, d, $J = 6.9$ Hz, ortho Ph), 7.32–7.24 (3H, m, meta and para Ph), 5.31 (1H, d, $J = 7.9$ Hz, C1'H), 4.06 (1H, qd, $J = 6.5, 2.4$ Hz, C5'H), 3.66 (3H, s, OCH$_3$), 3.49 (1H, d, $J = 2.5$ Hz, C4'H), 3.30 (1H, d, $J = 8.2$ Hz, C2'H), 1.59 (3H, s, C8'H$_3$), 1.44–1.34 (3H, m, Si(CH(CH$_3$)$_2$)$_3$), 1.22–1.16 (21H, m, Si(CH(CH$_3$)$_2$)$_3$ and C6'H$_3$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 161.1$ (C7'O$_2$), 134.1 (ipso Ph), 131.7 (2C, ortho Ph), 128.9 (2C, meta Ph), 127.4 (para Ph), 86.7 (C1'H), 82.6 (C2'H), 81.5 (C3'), 66.4 (C5'H), 64.6 (C4'H), 61.8 (OCH$_3$), 22.8 (C8'H$_3$), 19.0 (3C, Si(CH(CH$_3$)$_2$)$_3$), 19.0 (3C, Si(CH(CH$_3$)$_2$)$_3$), 17.0 (C6'H$_3$), 13.1 (3C, Si(CH(CH$_3$)$_2$)$_3$); HRMS (+ESI) Found [M+H]$^+$ = 466.2462; C$_{24}$H$_{40}$NO$_4$SiS requires 466.2447, $\Delta$ 3.22 ppm; Elemental Analysis found C, 62.01; H, 8.37; N, 2.87. C$_{24}$H$_{39}$NO$_4$SiS requires C, 61.90; H, 8.44; N, 3.01%.

The structure and absolute stereochemistry was confirmed by X-ray crystallographic analysis after crystallisation from analytical grade Et$_2$O.
CCDC 882399 contains the supplementary crystallographic data for this thesis. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
Methyl 4,6-dideoxy-4-(formylamino)-3-C-methyl-2-O-methyl-α-L-talopyranoside 102

To a solution of 110 (212 mg, 0.918 mmol) in EtOAc (92 mL) at RT was added Pd(OH)$_2$/C (35 mg). The flask was then evacuated and backfilled with hydrogen (× 3) and left to stir at RT for 4 h 30 min. The mixture was filtered through a pad of Celite® under suction using EtOAc (3 × 100 mL) and concentrated in vacuo. The isolated amine (S24) (assumed quant.) was used immediately in the next step of the reaction without further purification.

To a solution of the crude amine (S24) (assumed quant., 0.91 mmol) in CHCl$_3$ (9.1 mL) was added freshly prepared 113$^{24}$ (0.23 mL, 1.82 mmol). The reaction was stirred at RT for 1 h, and then concentrated in vacuo. Purification by column chromatography (SiO$_2$, CH$_2$Cl$_2$:MeOH, 9:1) gave the title compound 102 (160 mg, 75% over 2 steps) as an off-white gum consisting of 2 rotamers (3.2:1 by $^1$H NMR).

Rotameric ratio ascertained by $^1$H NMR spectroscopy of the purified mixture; $\delta_H$ 8.16 (1H, d, $J = 1.7$ Hz, NHC7′H0 major), 7.81 (1H, d, $J = 11.9$ Hz, NHC7′H0 minor).

$R_f = 0.28$ (minor), 0.23 (major) (CH$_2$Cl$_2$:MeOH, 9:1); [$\alpha$]$^D_{27.6} = -72.7$ (c = 0.94, CHCl$_3$); IR (film) $v_{\text{max}}$/cm$^{-1}$ 3397, 2984, 2940, 2911, 2832, 1681, 1643, 1513, 1464, 1449, 1385, 1356, 1344, 1311, 1185, 1131, 1058, 1024; $^1$H NMR (d$_6$-DMSO, 500 MHz) $\delta = 8.16$ (1H, d, $J = 1.7$ Hz, NHC7′H0 major rotamer), 7.81 (1H, d, $J = 11.9$ Hz, NHC7′H0 minor rotamer), 7.08 (1H, d, $J = 9.9$ Hz, NHC7′H0 major rotamer), 6.19 (1H, t, $J = 11.3$ Hz, NHC7′H0 minor rotamer), 4.72 (1H, d, $J = 1.5$ Hz, C1′H minor rotamer), 4.71 (1H, d, $J = 2.2$ Hz, C1′H major rotamer), 4.64 (1H, s, C3′OH minor rotamer), 4.43 (1H, s, C3′OH major rotamer), 3.94–3.90 (2 × 1H, qd, $J = 6.2$, 2.3 Hz, C5′H major and minor rotamers), 3.70 (1H, dd, $J = 9.8$, 2.1 Hz, C4′H major rotamer), 3.40 (3H, s, OCH$_3$ major rotamer), 3.39 (3H, s, OCH$_3$ minor rotamer), 3.29 (6H, s, C1′HOCH$_3$ major and minor rotamers), 3.13 (1H, dd, $J = 12.4$, 1.5 Hz, C4′H minor rotamer), 2.87 (1H, s, C2′H minor rotamer), 2.85 (1H, s, C2′H major rotamer), 1.28 (3H, s, C8′H$_3$ minor...
rotamer), 1.26 (3H, s, C8′H3 major rotamer), 1.05 (3H, d, J = 6.4 Hz, C6′H3 minor rotamer), 1.01 (3H, d, J = 6.5 Hz, C6′H3 major rotamer); \(^{13}\)C NMR (d\(^6\)-DMSO, 126 MHz) δ = 164.7 (NHC7′HO minor rotamer), 162.0 (NHC7′HO major rotamer), 98.7 (C1′H major and minor rotamers\(^\dagger\)), 82.7 (C2′H major rotamer), 82.4 (C2′H minor rotamer), 68.5 (C3′ major rotamer), 68.0 (C3′ minor rotamer), 64.9 (C5′H major rotamer), 64.3 (C5′H minor rotamer), 59.5 (OCH\(_3\) major and minor rotamers\(^\dagger\)), 54.8 (C1′HOCH\(_3\) major and minor rotamers\(^\dagger\)), 54.5 (C4′H major and minor rotamers\(^\dagger\)), 24.8 (C8′H3 major and minor rotamers\(^\dagger\)), 17.4 (C6′H3 minor rotamer), 17.0 (C6′H3 major rotamer); HRMS (+ESI) Found [M+H]+ = 234.1341; C\(_{10}\)H\(_{20}\)NO\(_5\) requires 234.1342, Δ 0.43 ppm and [M+Na]+ = 256.1161; C\(_{10}\)H\(_{19}\)NO\(_5\)Na requires 256.1160, Δ 0.39 ppm.

The structure and relative stereochemistry was confirmed by X-ray crystallographic analysis after crystallisation from analytical grade Et\(_2\)O.

\[\text{CCDC 882397 contains the supplementary crystallographic data for this thesis. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via}\]

\[\text{www.ccdc.cam.ac.uk/data_request/cif.}\]

\(^\dagger\) minor rotamer cannot be distinguished.
Variable Temperature $^1$H NMR of 102 (formyl region shown for clarity)
Phenyl 4-azido-4,6-dideoxy-3-C-methyl-2-O-methyl-1-thio-3-O-(trimethylsilyl)-α-L-talopyranoside 115

To a 20 mL Biotage® microwave vial was added 110 (103.4 mg, 0.448 mmol), 1,2-dichloroethane (5.8 mL), ZnI₂ (429 mg, 1.34 mmol), Bu₄NI (253 mg, 0.685 mmol), and TMSSPh (0.42 mL, 2.24 mmol). The reaction was heated to 65 °C and maintained at this temperature for 1 h, after which it was cooled to RT. The reaction was quenched with sat. aq. Ba(OH)₂•8H₂O (8 mL). The mixture was extracted with CH₂Cl₂ (3 × 15 mL) and the combined organic layers washed with brine (20 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, dry load, hexane→hexane:Et₂O, 99:1→98:2) gave the title compound 115 (102.5 mg, 60%) as a colourless oil.

Rᵣ = 0.56 (hexane:Et₂O, 4:1); [α]ᵣ²⁸.⁹ = −40.2 (c = 1.24, CHCl₃); IR (film) νmax/cm⁻¹ 2938, 2976, 2901, 2102, 1584, 1478, 1440, 1382, 1364, 1337, 1249, 1155, 1112, 1096, 1070, 1010, 984; ¹H NMR (CDCl₃, 400 MHz) δ = 7.50 (2H, d, J = 7.2 Hz, ortho Ph), 7.33–7.23 (3H, m, meta and para Ph), 5.39 (1H, d, J = 5.5 Hz, C1’H), 4.33–4.26 (1H, m, C5’H), 3.54 (3H, s, OCH₃), 3.17 (1H, d, J = 4.0 Hz, C4’H), 3.05 (1H, d, J = 5.5 Hz, C2’H), 1.53 (3H, s, C8’H₃), 1.38 (3H, d, J = 6.7 Hz, C6’H₃), 0.19 (9H, s, Si(CH₃)₃); ¹³C NMR (CDCl₃, 100 MHz) δ = 135.0 (ipso Ph), 130.8 (2C, ortho Ph), 129.0 (2C, meta Ph), 127.2 (para Ph), 84.5 (C2’H), 82.6 (C1’H), 77.1 (C3’), 69.0 (C5’H), 66.7 (C4’H), 60.4 (OCH₃), 25.5 (C8’H₃), 16.1 (C6’H₃), 2.7 (3C, Si(CH₃)₃); HRMS (+ESI) Found [M+Na]⁺ = 404.1435; C₁₇H₂₇N₃O₃SiSNa requires 404.1435, Δ 0.00 ppm.
Key selected observed nOe’s:

- An nOe was observed between C1’H and C6’H₃ suggesting that 
  conformers 1 and 3 are disfavoured.
- An nOe was observed between C5’H and C8’H₃ suggesting that 
  conformer 2 is disfavoured.
- \( \alpha \)-conformer 4 accounts for all observed nOe interactions indicating that C1’H is 
  equatorial.

The corresponding D-configured enantiomer was synthesised and found to have the following 
optical rotation: \([\alpha]_D^{25.1} = +41.1 \ (c = 1.10, \text{CHCl}_3)\).
(2S,3S,4S)-2,4-Dimethyl-3,4-dihydro-2H-pyran-3,4-diol 116

To a stirred solution of 106 (100 mg, 0.78 mmol) in Et₂O (8 mL) at −78 °C was added MeLi•LiBr (1.5 M in Et₂O; 1.56 mL, 2.34 mmol) dropwise. After stirring for 1 h, the reaction was removed from the cold bath then immediately quenched with sat. aq. NH₄Cl (3 mL) and warmed to RT. The resulting layers were separated and the aqueous phase extracted with EtOAc (3 × 5 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo to give the title compound 116 (113 mg, 78%, dr > 95:5) as a white crystalline solid:

R_f = 0.17 (hexane:EtOAc, 1:1); m.p. = 98–99 °C (from EtOAc) (lit. 25 101 °C); [α]D²⁵ = −78.0 (c = 0.20, CHCl₃); IR (film) ν_max/cm⁻¹ 3374 (br, OH), 2997, 2934, 2907, 1645 (C=C); ¹H NMR (CDCl₃, 600 MHz) δ = 6.20 (1H, d, J = 6.0 Hz, C1'H), 4.71 (1H, d, J = 6.0 Hz, C2'H), 3.87–3.92 (1H, m, C5'H), 3.63 (1H, dd, J = 9.9, 4.1 Hz, C4'H), 2.09 (1H, d, J = 4.1 Hz, C4'OH), 1.39 (3H, d, J = 6.3 Hz, C6'H₃), 1.33 (s, 3H, C7'H₃); ¹³C NMR (CDCl₃, 150 MHz) δ = 143.0 (C1'H), 107.6 (C2'H), 78.1 (C5'H), 73.6 (C4'H), 70.9 (C3'), 23.8 (C7'H₃), 17.7 (C6'H₃); HRMS (+ESI) Found [M+Na]⁺ = 167.0679; C₇H₁₂O₃Na requires 167.0679, Δ 0.0 ppm; Elemental Analysis found C, 58.30; H, 8.40. C₇H₁₂O₃ requires C, 58.30; H, 8.40%.

(2S,3S,4S)-3-(tert-Butyldimethylsilyloxy)-2,4-dimethyl-3,4-dihydro-2Hpyran-4-ol S25

To a stirred solution of 116 (50.0 mg, 0.35 mmol) and 2,6-lutidine (163 μL, 1.40 mmol) in DMF (4 mL) at RT was added TBSOTf (122 μL, 0.53 mmol). After 1 h, additional 2,6-lutidine (163 μL, 1.40 mmol) and TBSOTf (122 μL, 0.53 mmol) were added, the reaction stirred for a further 1.5 h then quenched with sat. aq. NH₄Cl (10 mL) and diluted with EtOAc (10 mL). The
layers were separated and the aqueous phase extracted with EtOAc (10 mL). The combined organic layers were washed with sat. aq. LiCl (2 × 5 mL), dried (Na₂SO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:Et₂O, 8:2) gave the title compound S25 (43.0 mg, 48%) as a colourless oil:

\[ R_f = 0.14 \] (hexane:Et₂O, 8:2); \([\alpha]_D^{25.0} -65.4 \) (c = 1.30, CHCl₃); \textbf{IR} (film) \( \nu_{\text{max/cm}} = 3479 \) (br, OH), 2956, 2931, 2891, 2858, 1649 (C=C); \textbf{¹H NMR} (CDCl₃, 600 MHz) \( \delta = 6.19 \) (1H, d, \( J = 6.0 \) Hz, C1'H), 4.67 (1H, d, \( J = 6.0 \) Hz, C2'H), 3.83–3.78 (1H, m, C5'H), 3.61 (1H, d, \( J = 10.2 \) Hz, C4'H), 1.36 (1H, s, C3'OH), 1.31 (3H, d, \( J = 6.0 \) Hz, C6'H₃), 1.29 (3H, s, C7'H₃), 0.93 (9H, s, C(CH₃)₃ of tBu), 0.17 (3H, s, Si(CH₃)₃), 0.12 (3H, s, Si(CH₃)₃); \textbf{¹³C NMR} (CDCl₃, 150 MHz) \( \delta = 142.7 \) (C1'H), 108.4 (C2'H), 79.1 (C4'H), 74.6 (C5'H), 71.6 (C3'), 26.0 (3C, C(CH₃)₃ of tBu), 24.4 (C7'H₃), 18.4 (C6'H₃ or C(CH₃)₃ of tBu), 18.3 (C6'H₃ or C(CH₃)₃ of tBu), −3.7 (Si(CH₃)₂), −4.7 (Si(CH₃)₂); \textbf{HRMS} (+ESI) Found [M+Na]+ = 281.1533; C₁₃H₂₆O₂SiNa requires 281.1543, \( \Delta 3.56 \) ppm.

\( (2S,3S,4S)-3,4-\text{Di(tert-butyltrimethylsilyloxy)-2,4-dimethyl-3,4-dihydro-2Hpyran-4-ol S26} \)

Isolated from the previous reaction as a colourless oil (61.0 mg, 47%).

\[ R_f = 0.78 \] (hexane:Et₂O, 8:2); \([\alpha]_D^{25.0} +12.8 \) (c = 1.00, CHCl₃); \textbf{IR} (film) \( \nu_{\text{max/cm}} = 2956, 2930, 2858, 2889, 1652 \) (C=C); \textbf{¹H NMR} (CDCl₃, 600 MHz) \( \delta = 6.17 \) (1H, d, \( J = 6.1 \) Hz, C1'H), 4.73 (1H, d, \( J = 6.1 \) Hz, C2'H), 3.76–3.73 (1H, m, C5'H), 3.63 (1H, d, \( J = 13.4 \) Hz, C4'H), 1.30 (3H, d, \( J = 6.4 \) Hz, C6'H₃), 1.29 (3H, s, C7'H₃), 0.91 (9H, s, C(CH₃)₃ of tBu), 0.88 (9H, s, C(CH₃)₃ of tBu), 0.16 (3H, s, Si(CH₃)₃), 0.15 (3H, s, Si(CH₃)₃), 0.10 (3H, s, Si(CH₃)₃), 0.10 (3H, s, Si(CH₃)₃); \textbf{¹³C NMR} (CDCl₃, 150 MHz) \( \delta = 142.0 \) (C1'H), 109.0 (C2'H), 79.6 (C4'H), 75.0 (C5'H), 74.2 (C3'), 26.3 (3C, C(CH₃)₃ of tBu), 26.1 (3C, C(CH₃)₃ of tBu), 26.0 (C7'H₃), 18.6 (C6'H₃), 18.4 (C(CH₃)₃ of tBu), 18.4 (C(CH₃)₃ of tBu), −1.6 (Si(CH₃)₂), −1.7 (Si(CH₃)₂), −3.4
(Si(CH$_3$)$_2$)$_2$, $-4.7$ (Si(CH$_3$)$_2$); **HRMS (+ESI)** Found [M+Na]$^+$ = 395.2413; C$_{19}$H$_{40}$O$_3$Si$_2$Na requires 395.2408, Δ 1.27 ppm.

$(2R,3R,4S,5S,6S)$-5-(tert-Butyldimethylsilyloxy)-2-methoxy-4,6-dimethyltetrahydro-$2H$-pyran-3,4-diol 117

To a stirred solution of S25 (355 mg, 1.37 mmol) in MeOH (14 mL) at RT was added NaHCO$_3$ (575 mg, 6.85 mmol). The resulting suspension was cooled to 0 °C and magnesium monoperoxyphthalate hexahydrate (80%; 1.02 g, 1.65 mmol) was added. After 2 h, the reaction was quenched with sat. aq. NaHCO$_3$ (5 mL) and diluted with EtOAc (10 mL). The layers were separated, the aqueous phase extracted with EtOAc (3 $\times$ 5 mL) and the combined organic layers partially concentrated in vacuo to remove MeOH. The resulting bilayer oil was redissolved in EtOAc (10 mL), the layers separated, the organic layer dried (Na$_2$SO$_4$) and concentrated in vacuo to give 117 as a white solid, which was used without further purification.

An analytical quantity was purified for characterisation by column chromatography (SiO$_2$, hexane:Et$_2$O, 1:1→2:3).

$R_f$ = 0.38 (Et$_2$O:hexane, 7:3); **m.p.** = 57–63 °C (from Et$_2$O); [α]$^D_{25.0}$ $-81.0$ (c = 0.50, CHCl$_3$); **IR** (film) $\nu_{\text{max}}$/cm$^{-1}$ 3495 (br, OH), 2930, 2857; **$^1$H NMR** (CDCl$_3$, 600 MHz) δ = 4.67 (1H, s, C1’H), 3.60–3.57 (2H, m overlap, C5’H and C2’H), 3.48 (1H, d, $J = 9.3$ Hz, C4’H), 3.36 (3H, s, OCH$_3$), 2.73 (1H, d, $J = 3.5$ Hz, C2’OH), 1.29 (3H, s, C7’H$_3$), 1.25 (3H, d, $J = 6.1$ Hz, C6’H$_3$), 0.91 (9H, s, C(CH$_3$)$_3$ of tBu), 0.14 (3H, s, Si(CH$_3$)$_3$), 0.10 (3H, s, Si(CH$_3$)$_3$); **$^{13}$C NMR** (CDCl$_3$, 150 MHz) δ = 101.0 (C1’H), 76.6 (C4’H), 75.4 (C2’H), 73.4 (C3’), 67.6 (C5’H), 55.1 (OCH$_3$), 26.0 (3C, C(CH$_3$)$_3$ of tBu), 19.5 (C7’H$_3$), 18.5 (C6’H$_3$), 18.3 (C(CH$_3$)$_3$ of tBu), $-3.8$ (Si(CH$_3$)$_2$), $-4.6$ (Si(CH$_3$)$_2$); **HRMS (+ESI)** Found [M+Na]$^+$ = 329.1766; C$_{14}$H$_{30}$O$_5$SiNa requires 329.1760, Δ 1.82 ppm. **Elemental Analysis** found C, 54.60; H, 9.70. C$_7$H$_{12}$O$_3$ requires C, 54.90; H, 9.90%.
(2S,3S,4S,5R,6R)-3-(tert-Butyldimethylsilyloxy)-5,6-dimethoxy-2,4-dimethyltetrahydro-2H-pyran-4-ol 118

![Chemical Structure](image)

To a stirred solution of 117 (167.0 mg, 0.545 mmol) in DMF (5 mL) was added MeI (85 μL, 1.36 mmol) followed by freshly prepared Ag₂O (315 mg, 1.36 mmol) and the reaction was stirred in the absence of light. After 4.5 h, the suspension was filtered through a pad of Celite® and the residue washed with Et₂O. The filtrate was washed with sat. aq. LiCl (4 × 5 mL) and brine (5 mL), dried (Na₂SO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane:Et₂O, 85:15 → 3:2) gave the title compound 118 (139.0 mg, 80% over 2 steps) as a colourless oil.

Rᵣ = 0.18 (hexane:Et₂O, 7:3); [α]₂⁰⁺⁰⁻⁴⁴.⁵ (c = 0.90, CHCl₃); IR (film) ν<sub>max</sub>/cm⁻¹ 3548 (OH), 2932, 2900, 2857; ¹H NMR (CDCl₃, 600 MHz) δ = 4.71 (1H, s, C¹'H), 3.56–3.54 (1H, m, C⁵'H), 3.46 (3H, s, C²'OCH₃), 3.36 (3H, s, C¹'OCH₃), 3.30 (1H, d, J = 9.3 Hz, C⁴'H), 3.08 (1H, s, C²'H), 2.82 (1H, s, C³'OH), 1.25 (3H, s, C⁷'H₃), 1.24 (3H, d, J = 6.3 Hz, C⁶'H₃), 0.90 (9H, s, C(CH₃)₃ of tBu), 0.14 (3H, s, Si(CH₃)₃), 0.07 (3H, s, Si(CH₃)₃); ¹³C NMR (CDCl₃, 150 MHz) δ = 98.0 (C¹'H), 85.2 (C²'H), 77.8 (C⁴'H), 72.5 (C³'), 67.6 (C⁵'H), 59.2 (C²'OCH₃), 54.9 (C¹'OCH₃), 26.0 (3C, C(CH₃)₃ of tBu), 18.5 (C⁶'H₃), 18.4 (C⁷'H₃ or C(CH₃)₃ of tBu)), 18.4 (C⁷'H₃ or C(CH₃)₃ of tBu), −3.8 (Si(CH₃)₃), −4.8 (Si(CH₃)₃); HRMS (+ESI) Found [M+Na]⁺ = 343.1908; C₁₅H₃₂O₅SiNa requires 343.1917, Δ 2.62 ppm.

Phenyl 4-O-(tert-butyl(dimethyl)silyl)-6-deoxy-3-C-methyl-2-O-methyl-1-thio-3-O-(trimethylsilyl)-α-L-mannopyranoside 119

![Chemical Structure](image)

To a 20 mL Biotage® microwave vial was added 118 (103.7 mg, 0.324 mmol), 1,2-dichloroethane (4.2 mL), ZnI₂ (310 mg, 0.972 mmol), Bu₄NI (183 mg, 0.496 mmol), and
TMSSPh (0.307 mL, 1.62 mmol). The reaction was heated to 65 °C and maintained at this temperature for 1 h, after which it was cooled to RT. The reaction was quenched with sat. aq. Ba(OH)$_2$•8H$_2$O (8 mL). The mixture was extracted with CH$_2$Cl$_2$ (3 × 15 mL) and the combined organic layers washed with brine (20 mL), dried (MgSO$_4$) and concentrated in vacuo. Purification by column chromatography (SiO$_2$, dry load, hexane→hexane:Et$_2$O, 99:1→98:2) gave the title compound 119 (98 mg, 64%) as a white solid.

$R_f = 0.31$ (hexane:Et$_2$O, 95:5); m.p. = 59–62 °C (CH$_2$Cl$_2$); $[\alpha]^2_{D} = -76.6 \ (c = 1.03, \text{CHCl}_3)$; IR (film) $\nu_{\text{max}}$ cm$^{-1}$: 2955, 2931, 2857, 1585, 1473, 1463, 1439, 1382, 1361, 1248, 1172, 1097, 1086, 1011; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 7.53$ (2H, d, $J = 7.2$ Hz, ortho Ph), 7.31–7.21 (3H, m, meta and para Ph), 5.40 (1H, d, $J = 4.4$ Hz, C1′H), 3.98 (1H, m, appar. quintet $J = 6.5$ Hz, C5′H), 3.50 (1H, d, $J = 6.4$ Hz, C4′H), 3.42 (3H, s, OCH$_3$), 3.38 (1H, d, $J = 4.4$ Hz, C2′H), 1.42 (3H, s, C7′H$_3$), 1.32 (3H, d, $J = 6.6$ Hz, C6′H$_3$), 0.92 (9H, s, C(CH$_3$)$_3$ of tBu), 0.15 (9H, s, Si(CH$_3$)$_3$), 0.12 (3H, s, Si(CH)$_3$_2), 0.09 (3H, s, Si(CH)$_3$_2); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 136.0$ (ipso Ph), 130.9 (2C, ortho Ph), 128.9 (2C, meta Ph), 126.9 (para Ph), 84.5 (C2′H), 83.0 (C1′H), 77.8 (C4′H), 77.6 (C3′), 71.8 (C5′H), 58.7 (OCH$_3$), 26.0 (3C, C(CH$_3$)$_3$ of tBu), 22.4 (C7′H$_3$), 18.6 (C(CH$_3$)$_3$ of tBu), 18.2 (C6′H$_3$), 2.7 (3C, Si(CH$_3$)$_3$), -3.7 (Si(CH)$_3$_2), -4.3 (Si(CH$_3$)$_2$); HRMS (+ESI) Found [M+Na]$^+$ = 493.2216; C$_{23}$H$_{42}$O$_4$Si$_2$Na requires 493.2235, $\Delta$ 3.85 ppm; Elemental Analysis found C, 58.77; H, 9.04. C$_{23}$H$_{42}$O$_4$Si$_2$S requires C, 58.67; H, 8.99%.
The structure and absolute stereochemistry was confirmed by X-ray crystallographic analysis after crystallisation from analytical grade CH$_2$Cl$_2$.

**Phenyl 6--deoxy-3-C-methyl-2-O-methyl-1-thio-α-L-mannopyranoside 122**

To a solution of 119 (70.1 mg, 0.15 mmol) in THF (2.7 mL) at RT was added TBAF (1 M in THF, 0.60 mL, 0.60 mmol) dropwise. The reaction mixture was stirred for 6 h, and additional TBAF (1 M in THF, 0.20 mL, 0.20 mmol) was added. After a further 12 h TLC analysis indicated that the starting material had been consumed and the reaction mixture was concentrated in vacuo. Purification by column chromatography (SiO$_2$, hexane→hexane:EtOAc, 1:1→EtOAc) gave the title compound 122 (38 mg, 89%) as a white solid.

$R_f = 0.29$ (hexane:EtOAc, 1:1); **m.p.** = 102–106 °C; $[α]_{D}^{25.0} = –120.3$ (c = 1.02, CHCl$_3$); **IR** (film) $\nu_{max}$/cm$^{-1}$ 3492, 3407, 2972, 2924, 2897, 2853, 1478, 1453, 1439, 1405, 1373, 1256, 1177,
1157, 1111, 1086, 1064, 1027; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 7.50$ (2H, d, $J = 7.1$ Hz, ortho Ph), 7.35–7.27 (3H, m, meta and para Ph), 5.57 (1H, s, C1'H), 4.11–4.03 (1H, m, C5'H), 3.49 (1H, s, C4'H), 3.47 (3H, s, OCH$_3$), 3.44 (1H, s, C2'H), 3.10–3.03 (1H, br s, C3'OH), 2.43–2.31 (1H, br s, C4'OH), 1.46 (3H, s, C7'H$_3$), 1.34 (3H, d, $J = 6.2$ Hz, C6'H$_3$); An accurate mass could not be obtained for this compound.

Phenyl 6--deoxy-3-C-methyl-2-O-methyl-1-thio-4-O-(triethylsilyl)-α-L-mannopyranoside

S27

To a solution of 122 (21.8 mg, 0.767 mmol) in pyridine (0.5 mL) at RT was added DMAP (3.75 mg, 39.7 μmol) and TESCl (54 μL, 0.324 mmol) sequentially. After 1 h 45 min at RT the reaction was diluted with CH$_2$Cl$_2$ (20 mL) and washed with sat. aq. NaHCO$_3$ (10 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (10 mL) and the combined organic layers dried (MgSO$_4$) and concentrated in vacuo. Azeotropic removal of pyridine with hexane (3 × 10 mL) followed by purification by column chromatography (SiO$_2$, hexane→hex:EtOAc, 4:1) gave the title compound S27 (26.1 mg, 85%) as a colourless oil.

$R_f = 0.63$ (hexane:EtOAc, 4:1); $[\alpha]_D^{25.8} = -109.1$ (c = 1.25, CHCl$_3$); IR (film) $\nu_{max}$/cm$^{-1}$ 3545, 2934, 2876, 1728, 1584, 1479, 1457, 1440, 1415, 1397, 1397, 1332, 1294, 1265, 1240, 1175, 1162, 1162, 1105, 1085, 1007; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 7.50$ (2H, d, $J = 7.1$ Hz, ortho Ph), 7.34–7.27 (3H, m, meta and para Ph), 5.54 (1H, s, C1'H), 4.05–3.97 (1H, m, C5'H), 3.46 (3H, s, OCH$_3$), 3.44 (1H, d, $J = 9.5$ Hz, C4'H), 3.40 (1H, d, $J = 1.1$ Hz, C2'H), 2.94 (1H, s, C3'OH), 1.38 (3H, s, C7'H$_3$), 1.28 (3H, d, $J = 6.2$ Hz, C6'H$_3$), 0.99 (9H, t, $J = 7.9$ Hz, Si(CH$_2$CH$_3$)$_3$), 0.73–0.65 (6H, m, Si(CH$_2$CH$_3$)$_3$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 136.0$ (ipso Ph), 131.0 (2C, ortho Ph), 129.0 (2C, meta Ph), 127.3 (para Ph), 87.4 (C2'H), 84.4 (C1'H), 78.2
(C\(^4\)H), 72.8 (C\(^3\)\(^\prime\)H), 69.2 (C\(^5\)\(^\prime\)H), 58.6 (OCH\(_3\)), 19.0 (C\(^7\)H\(_3\)), 18.2 (C\(^6\)H\(_3\)), 7.0 (3C, Si(CH\(_2\)CH\(_3\))\(_3\)), 5.2 (3C, Si(CH\(_2\)CH\(_3\))\(_3\)); HRMS (+ESI) Found [M+Na]\(^+\) = 421.1836; C\(_{20}\)H\(_{34}\)O\(_4\)SiNa requires 421.1839, Δ 0.71 ppm.

**Phenyl 6-deoxy-4-O-(diethyl(propyl)silyl)-3-C-methyl-2-O-methyl-1-thio-3-O-(trimethylsilyl)-α-L-mannopyranoside 123**

![Chemical structure](image)

**Procedure 1**

To a solution of S27 (8.3 mg, 20.8 μmol) in CH\(_2\)Cl\(_2\) (0.70 mL) at −78 °C was added 2,6-lutidine (7 μL, 62.4 μmol) and TMSOTf (6 μL, 30.6 μmol) sequentially. The reaction mixture was stirred for 30 min at −78 °C after which pH 7 phosphate buffer (1 mL) was added and the reaction warmed to RT and diluted with CH\(_2\)Cl\(_2\) (10 mL). The layers were separated and the organic layer washed with brine (5 mL). The aqueous layer was then further extracted with EtOAc (10 mL) and the combined organic layers dried (MgSO\(_4\)) and concentrated *in vacuo*. Purification by column chromatography (SiO\(_2\), hexane→hexane:EtOAc, 4:1) gave the title compound 123 (8.3 mg, 85%) as a colourless oil.

**Procedure 2**

To a 20 mL Biotage® microwave vial was added 125 (102.8 mg, 0.321 mmol), 1,2-dichloroethane (4.2 mL), ZnI\(_2\) (307.4 mg, 0.963 mmol), Bu\(_4\)NI (181.4 mg, 0.491 mmol), and TMSSPh (0.30 mL, 1.60 mmol). The reaction was heated to 65 °C and maintained at this temperature for 2 h 40 min, after which it was cooled to RT. The reaction was quenched with sat. aq. Ba(OH)\(_2\)•8H\(_2\)O (8 mL). The mixture was extracted with CH\(_2\)Cl\(_2\) (3 × 15 mL) and the combined organic layers washed with brine (20 mL), dried (MgSO\(_4\)) and concentrated *in vacuo*. Purification by column chromatography (SiO\(_2\), dry load, hexane→hexane:Et\(_2\)O, 99:1→98:2) gave the title compound 123 (130.2 mg, 86%) as a colourless oil.
**R**\textsubscript{f} = 0.80 (hexane:EtOAc, 4:1); [\textit{\alpha}]\textsubscript{D}\textsuperscript{25.1} = −38.2 (c = 0.83, CHCl\textsubscript{3}); \textbf{IR} (film) \textit{v}_{\text{max}}/\text{cm}^{-1} 2954, 2925, 2876, 1733, 1585, 1479, 1457, 1441, 1414, 1380, 1300, 1248, 1168, 1099, 1011; \textbf{\textit{\textsuperscript{1}H NMR}} (CDCl\textsubscript{3}, 400 MHz) \(\delta = 7.52\) (2H, d, \(J = 7.2\) Hz, \textit{ortho} Ph), 7.32–7.20 (3H, m, \textit{meta} and \textit{para} Ph), 5.40 (1H, d, \(J = 4.4\) Hz, C1’H), 3.97 (1H, m, appar. quintet \(J = 6.6\) Hz, C5’H), 3.53 (1H, d, \(J = 6.6\) Hz, C4’H), 3.42 (3H, s, \textit{OCH\textsubscript{3}}), 3.39 (1H, d, \(J = 4.4\) Hz, C2’H), 1.41 (3H, s, C7’H\textsubscript{3}), 1.31 (3H, d, \(J = 6.6\) Hz, C6’H\textsubscript{3}), 0.99 (9H, t, \(J = 8.0\) Hz, Si(CH\textsubscript{2}CH\textsubscript{3})\textsubscript{3}), 0.65 (6H, q, \(J = 7.8\) Hz, Si(CH\textsubscript{2}CH\textsubscript{3})\textsubscript{3}); \textbf{\textit{\textsuperscript{13}C NMR}} (CDCl\textsubscript{3}, 100 MHz) \(\delta = 136.1\) (ipso Ph), 130.8 (2C, \textit{ortho} Ph), 128.9 (2C, \textit{meta} Ph), 126.9 (\textit{para} Ph), 84.6 (C2’H), 83.0 (C1’H), 78.0 (C4’H), 77.6 (C3’), 71.8 (C5’H), 58.6 (OCH\textsubscript{3}), 22.3 (C7’H\textsubscript{3}), 18.3 (C6’H\textsubscript{3}), 7.0 (3C, Si(CH\textsubscript{2}CH\textsubscript{3})\textsubscript{3}), 5.3 (3C, Si(CH\textsubscript{2}CH\textsubscript{3})\textsubscript{3}), 2.7 (3C, Si(CH\textsubscript{3})\textsubscript{3}); \textbf{HRMS (+ESI)} Found [M+Na]\textsuperscript{+} = 493.2229; C\textsubscript{23}H\textsubscript{42}O\textsubscript{4}Si\textsubscript{2}SNa requires 493.2235, \(\Delta 1.22\) ppm.

**Methyl 6-deoxy-4-\textit{O}-(diethyl(propyl)silyl)-3-C-methyl-\textit{\alpha}-\textit{L}-mannopyranoside 124**

![Chemical Structure](image)

To a solution of 116 (565 mg, 3.92 mmol) in pyridine (27.6 mL) at RT was added DMAP (192 mg, 1.57 mmol) and TESCl (2.10 mL, 12.5 mmol) sequentially. After 1 h at RT the reaction was diluted with CH\textsubscript{2}Cl\textsubscript{2} (100 mL) and washed with sat. aq. NaHCO\textsubscript{3} (80 mL). The aqueous layer was extracted with CH\textsubscript{2}Cl\textsubscript{2} (100 mL) and the combined organic layers dried (MgSO\textsubscript{4}) and concentrated \textit{in vacuo}. Azeotropic removal of pyridine with hexane (3 \(\times\) 10 mL) followed by column chromatography (SiO\textsubscript{2}, hexane\rightarrow hexane:EtOAc, 9:1) gave the desired semi-pure mono-protected sugar (assumed quant.). The mixture was used directly in the next step in the reaction sequence.

To a suspension of the mono-protected sugar (assumed quant., 3.92 mmol) and NaHCO\textsubscript{3} (0.988 g, 11.76 mmol) in MeOH (15.1 mL) at 0 °C was added \textit{m}-CPBA (70\%, 1.16 g, 4.70 mmol). The mixture was maintained at 0 °C for 5 min and then warmed to RT. After 1 h the reaction was quenched with H\textsubscript{2}O (60 mL), the layers separated and the aqueous layer further extracted with EtOAc (3 \(\times\) 100 mL). The combined organic layers were dried (MgSO\textsubscript{4}) and...
concentrated in vacuo. Purification by column chromatography (SiO$_2$, hexane:Et$_2$O, 7:3) gave the title compound **124** (540 mg, 45% over 2 steps) as a white solid.

$R_f = 0.20$ (hexane:Et$_2$O, 1:1); m.p. = 99–102 °C; $[\alpha]_D^{26.5} = -72.8$ (c = 0.85, CHCl$_3$); IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 3247, 2956, 2898, 2878, 1448, 1416, 1386, 1352, 1340, 1309, 1284, 1263, 1242, 1195, 1163, 1133, 1116, 1093, 1051, 1018, 1000, 963; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 4.68$ (1H, s, C1'H), 3.63–3.53 (2H, m, C2'H and C5'H), 3.51 (1H, d, $J = 9.4$ Hz, C4'H), 3.36 (3H, s, C1'HOCH$_3$), 2.60 (1H, d, $J = 3.8$ Hz, C2'HOH), 2.11 (1H, s, C3'OH), 1.30 (3H, s, C7'H$_3$), 1.26 (3H, d, $J = 6.1$ Hz, C6'H$_3$), 0.98 (9H, t, $J = 7.9$ Hz, Si(CH$_2$CH$_3$)$_3$), 0.67 (6H, q, $J = 7.9$ Hz, Si(CH$_2$CH$_3$)$_3$); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 101.0$ (C1'H), 77.3 (C4'H), 75.5 (C2'H), 73.5 (C3'), 67.7 (C5'H), 55.1 (C1'HOCH$_3$), 19.5 (C7'H$_3$), 18.3 (C6'H$_3$), 7.0 (3C, Si(CH$_2$CH$_3$)$_3$), 5.2 (3C, Si(CH$_2$CH$_3$)$_3$); HRMS (+ESI) Found [M+Na]$^+$ = 329.1747; C$_{14}$H$_{30}$O$_5$SiNa requires 329.1755, $\Delta$ 2.43 ppm; **Elemental Analysis** found C, 55.06; H, 9.85. C$_{14}$H$_{30}$O$_5$ requires C, 54.87; H, 9.87%.

The structure and relative stereochemistry was confirmed by X-ray crystallographic analysis after crystallisation from analytical grade CHCl$_3$.

CCDC 882402 contains the supplementary crystallographic data for this thesis. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
Methyl 6-deoxy-4-O-(diethyl(propyl)silyl)-3-C-methyl-2-O-methyl-α-L-mannopyranoside 125

To a mixture of freshly sublimed KOtBu (178.4 mg, 1.59 mmol) in THF (4.2 mL) at 0 °C was added a solution of 124 (440 mg, 1.44 mmol) in THF (5 mL) dropwise. The reaction mixture was stirred for 40 min at 0 °C after which MeI (0.11 mL, 1.73 mmol) was added dropwise to the pale yellow solution and stirred for 1 h. After this time, further KOtBu (16.2 mg, 0.144 mmol) and MeI (18.0 μL, 0.289 mmol) were added and the reaction maintained at 0 °C until TLC analysis indicated full conversion of the starting material. The reaction was quenched with H2O (9 mL), diluted with CH2Cl2 (20 mL) and warmed to RT. The layers were separated, the aqueous layer further extracted with CH2Cl2 (3 × 20 mL), and the combined organics dried (MgSO4) and concentrated in vacuo. Purification by column chromatography (Florisil, hexane:Et2O, 7:3) gave the title compound 125 (373 mg, 81%) as a colourless oil.

\[ R_f = 0.52 \text{(hexane:Et}_2\text{O, 1:1); } [\alpha]_{D}^{25.9} = -37.1 \text{ (c = 1.16, CHCl}_3); \text{ IR (film) } \nu_{\text{max}}/\text{cm}^{-1} = 3549, 2952, 2909, 2877, 2830, 1458, 1415, 1389, 1358, 1340, 1308, 1261, 1237, 1182, 1142, 1118, 1099, 1061, 1007; \text{ } ^1{H} \text{ NMR (CDCl}_3, 400 MHz) } \delta = 4.71 \text{ (1H, s C1'H), 3.60–3.50 (1H, m, C5'H), 3.47 (3H, s, OCH}_3), 3.36 \text{ (3H, s, C1'HOCH}_3), 3.34 \text{ (1H, d, J = 9.4 Hz C4'H), 3.09 (1H, d, J = 0.8 Hz, C2'H), 2.84 (1H, s, C3'OH), 1.25 (3H, s, C7'H}_3), 1.24 \text{ (3H, d, J = 6.3 Hz, C6'H}_3); } \text{ } ^{13}{C} \text{ NMR (CDCl}_3, 100 MHz) } \delta = 98.0 \text{ (C1'H), 85.2 (C2'H), 77.9 (C4'H), 72.5 (C3'), 67.7 (C5'H), 59.2 (OCH}_3), 54.9 \text{ (C1'HOCH}_3), 18.4 \text{ (C7'H}_3), 18.3 \text{ (C6'H}_3), 7.0 \text{ (3C, Si(CH}_2\text{CH}_3)_3); } \text{ HRMS (+ESI) Found } [M+Na]^+ \text{ = 343.1903; C}_{15}\text{H}_{32}\text{O}_8\text{SiNa requires 343.1911, } \Delta \text{ 2.33 ppm.} \]
Callipeltoside A (1)

To a solution of aglycon 4 (6.7 mg, 14 μmol) and thioglycoside 112 (13.0 mg, 28 μmol) in CH₂Cl₂ (3.3 mL) at RT was added 4 Å MS followed by DTBMP (7.3 mg, 35.6 μmol) and the mixture stirred for 50 min.† The reaction was cooled to −15 °C and NIS (6.3 mg, 28 μmol) and TfOH [(47 μL, 5.3 μmol) of a stock solution of TfOH in CH₂Cl₂ (0.1 mL, 1.125 mmol in 10 mL CH₂Cl₂)] added sequentially. The resulting light pink solution was allowed to warm to RT slowly over 16 h. The reaction was quenched by the addition of sat. aq. NaHCO₃ (12 mL) and diluted with EtOAc (10 mL). The layers were separated and the aqueous layer further extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with sat. aq. Na₂S₂O₃ (30 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:EtOAc, 7:3) gave TIPS-protected callipeltoside A (assumed quant.) as an off-white foam/gum [Rᵣ = 0.20 (hexane:EtOAc, 7:3)].²⁶

To a solution of TIPS-protected callipeltoside A (assumed quant., 14 μmol) in THF (0.88 mL) at RT was added TBAF (1 M in THF, 0.88 mL, 27 μmol). After 10 min, TLC analysis indicated that the reaction was complete and the solvent removed in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:EtOAc, 2:3→EtOAc) gave the title compound callipeltoside A 1 (7.9 mg, 83% over 2 steps) as an off-white gum.²⁷ The sample was further purified using HPLC (see below).

† The aglycon 4 and thioglycoside 112 were azeotroped with PhMe (× 3) prior to use.
$R_f = 0.30$ (EtOAc); $[\alpha]_D^{25.3} = -17.5$ (c = 0.33, MeOH), [lit. $^{22}$ $[\alpha]_D^{20} = -17.6$ (c = 0.04, MeOH)];

**IR** (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 3361, 2923, 2854, 1744, 1701, 1633, 1615, 1606, 1456, 1419, 1375, 1321, 1261, 1227, 1181, 1154, 1095, 1058, 1025, 980; **$^1$H NMR** (CD$_3$OD, 500 MHz) $\delta = 6.53$ (1H, dd, $J = 15.4$, 10.8 Hz, C16H), 6.36 (1H, dd, $J = 14.4$, 10.8 Hz, C15H), 5.86 (1H, m overlapped, C14H), 5.85 (1H, m overlapped, C13H), 5.68 (1H, dd, $J = 15.5$, 1.9 Hz, C17H), 5.30 (1H, d, $J = 9.8$ Hz, C10H), 4.74 (1H, d, $J = 6.2$ Hz, C1'H), 3.98 (1H, qd, $J = 6.5$, 1.7 Hz, C5'H), 3.91 (1H, dd, $J = 9.6$, 2.4 Hz, C9H), 3.75 (1H, dt, $J = 10.7$, 4.7 Hz, C5H), 3.68 (1H, d, $J = 10.4$, 2.4 Hz, C7H), 3.62 (3H, s, OCH$_3$), 3.47 (1H, d, $J = 1.9$ Hz, C4'H), 3.45 (1H, d, $J = 6.2$ Hz, C2'H), 3.28 (1H, m, C21H), 3.24 (3H, s, C9H(OCH$_3$)), 2.56 (1H, d, $J = 12.9$ Hz, C2HA$_B$), 2.49 (1H, d, $J = 12.9$ Hz, C2HA$_B$), 2.37 (1H, m overlapped, C12HA$_B$), 2.30 (1H, m overlapped, C12HA$_B$), 2.25 (1H, m overlapped, C8H), 2.25 (1H, m overlapped, equatorial C4HA$_B$), 1.85 (1H, m, C20H), 1.77 (3H, s, C23H$_3$), 1.56 (1H, m, C6H), 1.53 (3H, s, C8'H$_3$), 1.43 (1H, t, $J = 11.7$ Hz, axial C4HA$_B$), 1.30 (2H, m, C22HA$_B$), 1.12 (3H, d, $J = 6.5$ Hz, C6'H$_3$), 1.02 (3H, d, $J = 6.5$ Hz, C25H$_3$), 0.99 (3H, d, $J = 7.0$ Hz, C24H$_3$); **$^{13}$C NMR** (CD$_3$OD, 126 MHz) $\delta = 172.9$ (C1O$_2$), 161.1 (C7'O$_2$), 141.6 (C16H), 134.4 (C14H), 134.3 (C11), 132.0 (C15H), 128.4 (C10H), 113.5 (C17H), 103.6 (C1'H), 96.6 (C3), 92.8 (C19), 83.9 (C3'), 83.1 (C2'H), 81.4 (C9H), 78.8 (C5H), 78.4 (C18), 76.4 (C7H), 72.7 (C13H), 65.3 (C5'H), 62.7 (C4'H), 62.0 (OCH$_3$), 55.4 (C9H(OCH$_3$)), 47.8 (C12H$_2$), 46.1 (C2H$_2$), 44.5 (C4H$_2$), 39.9 (C6H), 38.2 (C8H), 35.1 (C21H)*, 23.0 (C8'H$_3$), 19.8 (C22H$_3$), 16.3 (C23H$_3$), 15.9 (C6'H$_3$), 12.8 (C20H)*, 12.8 (C25H$_3$), 6.8 (C24H$_3$); **HRMS** (+ESI) Found [M+Na]$^+$ = 700.2853; C$_{35}$H$_{48}$O$_{10}$NClNa requires 700.2859, $\Delta$ 0.86 ppm.$^\dagger$

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$^\dagger$ The data is assigned in the same style as originally reported for the natural product.
### H NMR comparison between synthetic and natural callipeltoside A (CD$_3$OD)

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$^{13}$C NMR comparison between synthetic and natural callipeltoside A (CD$_3$OD)

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*Carbons C20 and C21 have been reassigned following work conducted by Paterson.$^{28}$
A further NMR experiment was conducted in order to elucidate the configuration at the anomeric carbon. Measurement of the $^1J_{C-H}$ value from a HSQC (Heteronuclear Single Quantum Coherence) experiment without $^{13}$C decoupling is known to be diagnostic of the configuration of the glycosidic linkage. A value of ~170 Hz suggests an equatorial proton at C1′H, whilst ~160 Hz indicates an axial proton. The measurement gave $^1J_{C-H} = 174.2$ Hz, indicating an **equatorial proton** at the anomeric carbon.  

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HPLC conditions

Preparative HPLC purification was performed on an Agilent HP 1100 series chromatograph equipped with a Waters μBondapak C18 column (column length 150 mm, internal diameter of column 3.9 mm, particle size 10 μm, temperature 25 °C). Elution was carried out at a flow rate of 1.0 mL/min using MeOH:H₂O (75:25) and detection was with diode array detection (λ= 250, 272 and 286). The sample was made up to a concentration of 0.015mg/μL with purification carried out using 25 μL injections which saturated the detector at λ= 250, 272 and 286. $t_R = 11.8$ min.
To a solution of aglycon 4 (6.1 mg, 12.7 μmol) and thioglycoside 115 (9.7 mg, 25.4 μmol) in CH₂Cl₂ (3.2 mL) at RT was added 4 Å MS followed by DTBMP (6.62 mg, 32.3 μmol) and the mixture stirred for 50 min.† The reaction was cooled to −15 °C and NIS (5.6 mg, 25.4 μmol) and TfOH [(43 μL, 4.8 μmol) of a stock solution of TfOH in CH₂Cl₂ (0.1 mL, 1.125 mmol in 10 mL CH₂Cl₂)] added sequentially. The resulting light pink solution was allowed to warm to RT slowly over 16 h. The reaction was quenched by the addition of sat. aq. NaHCO₃ (8 mL) and diluted with EtOAc (15 mL). The layers were separated and the aqueous layer further extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with sat. aq. Na₂S₂O₃ (40 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:EtOAc, 9:1→4:1→1:1) gave title compound 126 (5.3 mg, 56%) as a pale yellow oil [Rf = 0.37 (hexane:EtOAc, 4:1)].²⁶

The 5.3 mg of product was divided into 2 portions and processed using the following 3 step procedure. After this, the 2 batches were combined and purified by column chromatography. The yield (of 2) quoted is based on the 5.3 mg isolated from the aforementioned glycosidation step.

† The aglycon 4 and thioglycoside 115 were azeotroped with PhMe (× 3) prior to use.
Callipeltoside B (2)

To a solution of 126 (2.2 mg, 2.9 μmol) in pyridine (95 μL) and H₂O (9.5 μL) (10:1) at RT was added Et₃N (5.9 μL) and 1,3-propanedithiol (5.9 μL, 58.7 μmol) sequentially. The reaction was stirred for 2 h 30 min and further Et₃N (5.9 μL) and 1,3-propanedithiol (5.9 μL, 58.7 μmol) added. After 90 min TLC analysis indicated complete consumption of the starting material. Azeotropic removal of the solvents with PhMe (3 × 10 mL) gave the requisite amine (assumed quant.) as an off-white residue. The isolated amine was used immediately in the next step of the reaction without further purification.

To a solution of crude amine (assumed quant., 2.9 μmol) in CHCl₃ (0.2 mL) was added freshly prepared 113 (31.1 mg, 0.147 mmol). The reaction was stirred at RT for 30 min and additional 113 (31.1 mg, 0.147 mmol) was added and stirred for 30 min after which the mixture was concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:EtOAc, 9:1→4:1→7:3→3:2→1:1→2:3→EtOAc) gave TMS-protected callipeltoside B (assumed quant.) as a clear oil \([R_f = 0.45 \text{ (hexane:EtOAc, 1:1)}]\). The isolated TMS-protected callipeltoside B was used immediately in the next step of the reaction without characterisation.

To a solution of TMS-protected callipeltoside B (assumed quant., 2.9 μmol) in DMF (0.5 mL) at RT was added TASF (4 mg, 14.5 μmol) and the mixture heated to 40 °C. After 30 min the reaction was cooled to RT, quenched by the addition of pH 7 phosphate buffer (1 mL) and diluted with EtOAc (2 mL). The layers were separated and the aqueous layer further extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with 10% aq. LiCl (2 × 8 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂,
hexane→hexane:EtOAc, 7:3→1:1→3:7→EtOAc→CH₂Cl₂:MeOH, 9:1) gave the title compound callipeltoside B 2 (2.5 mg, 52% over 3 steps) as an off-white gum consisting of 2 rotamers (4:1 by ¹H NMR).³⁰ The sample was further purified by HPLC (see below).

Rotameric ratio ascertained by ¹H NMR spectroscopy of the purified mixture; δ₂ (CDCl₃, 500 MHz) 8.36 (1H, d, J = 1.4 Hz, NHC7’HO major), 7.93 (1H, d, J = 11.9 Hz, NHC7’HO minor).

₉₁ = 0.18 (minor), 0.14 (major) (EtOAc); [α]₂⁶₂ = –21.0 (c = 0.10, CDCl₃); IR (film) ν₂₉/ cm⁻¹ 3433, 2976, 2925, 2857, 1675, 1512, 1457, 1416, 1380, 1347, 1324, 1310, 1255, 1226, 1179, 1098, 1086, 1058, 1023, 980.

Callipeltoside B ¹H and ¹³C NMR in CDCl₃

¹H NMR (CDCl₃, 500 MHz)† δ = 8.36 (1H, d, J = 1.4 Hz, NHC7’HO major rotamer), 7.93 (1H, d, J = 11.9 Hz, NHC7’HO minor rotamer), 6.48 (1H, dd, J = 15.4, 10.6 Hz, C16H), 6.31 (1H, d, J = 10.4 Hz, NHC7’HO major rotamer), 6.26 (1H, dd, J = 15.2, 10.9 Hz, C15H), 6.13 (1H, t, J = 11.4 Hz, NHC7’HO minor rotamer), 5.82 (1H, m, C13H), 5.76 (1H, dd, J = 15.2, 6.7 Hz, C14H), 5.57 (1H, dd, J = 15.5, 1.8 Hz, C17H), 5.29 (1H, d, J = 9.4 Hz, C10H), 5.03 (1H, d, J = 2.3 Hz, C3OH), 4.97 (1H, s, C1’H), 4.11 (1H, qd, J = 6.6, 1.4 Hz, C5’H major and minor rotamers), 3.97 (1H, d, J = 10.4 Hz, C4’H major rotamer), 3.81 (1H, dd, J = 9.4, 2.2 Hz, C9H), 3.71 (1H, td, J = 10.9, 4.5 Hz, C5H), 3.65 (1H, dd, J = 10.4, 2.3 Hz, C7H), 3.47 (3H, s, OCH₃ major rotamer), 3.43 (3H, s, OCH₃ minor rotamer), 3.28 (1H, d, J = 0.7 Hz, C3’OH minor rotamer), 3.23 (3H, s, C9H(OCH₃)), 3.18 (1H, m, C21H)*, 3.08 (1H, d, J = 0.8 Hz, C3’OH major rotamer), 2.97 (1H, br s, C2’H major rotamer), 2.96 (1H, br s, C2’H minor rotamer), 2.96 (1H, d overlapped, C4’H minor rotamer), 2.55 (1H, appar. dd, J = 12.9, 3.9 Hz, C2HₐHₐ), 2.43 (1H, d, J = 13.0 Hz, C2HₐHₐ), 2.30 (1H, appar. d, J = 3.7 Hz, C12HₐHₐ), 2.29 (1H, m overlapped, C12HₐHₐ)*, 2.21 (1H, dd, J = 11.5, 4.7 Hz, equatorial C4HₐHₐ), 2.20 (1H, m overlapped, C8H), 1.80 (1H, m, C20H), 1.73 (3H, s, C23H₃), 1.47 (1H, m, C6H), 1.45 (3H, d, J = 0.7 Hz, C8’H₃ major rotamer), 1.43 (3H, d, J = 0.9 Hz, C8’H₃ minor rotamer), 1.36 (1H, td, J = 11.7, 2.5 Hz, axial C4HₐHₐ),

† Only the rotameric peaks attributed to the sugar are distinguishable in the ¹H NMR.
1.29 (2H, m, C22H$_2$B)°, 1.14 (3H, d, $J = 6.4$ Hz, C6′H$_3$ minor rotamer), 1.12 (3H, d, $J = 6.4$ Hz, C6′H$_3$ major rotamer), 0.98 (3H, d, $J = 7.0$ Hz, C24H$_3$), 0.93 (3H, d, $J = 6.5$ Hz, C25H$_3$); $^{13}$C NMR (CDCl$_3$, 126 MHz) δ = 171.7 (C1O$_2$), 164.8 (NHC'7HO minor rotamer), 161.5 (NHC'7HO major rotamer), 140.1 (C16H), 132.6 (C14H), 132.4 (C11), 131.0 (C15H), 127.7 (C10H), 112.6 (C17H), 99.2 (C1'H major rotamer), 98.8 (C1'H minor rotamer), 95.2 (C3), 92.3 (C19), 83.4 (C2'H major rotamer), 82.7 (C2'H minor rotamer), 79.7 (C9H), 79.6 (C5H), 77.4 (C18), 74.8 (C7H), 71.6 (C13H), 68.0 (C3′ major rotamer), 68.0 (C3′ minor rotamer), 64.9 (C5′H major rotamer), 64.4 (C5′H minor rotamer), 61.0 (C4'H major rotamer), 59.3 (OCH$_3$ major rotamer), 59.0 (OCH$_3$ minor rotamer), 55.5 (C4'H major rotamer), 55.2 (C9H(OCH$_3$)), 46.9 (C12H$_2$), 44.7 (C2H$_2$), 42.4 (C4H$_2$), 38.4 (C6H), 37.0 (C8H), 34.3 (C21H), 23.8 (C8′H$_3$ major rotamer), 23.5 (C8′H$_3$ minor rotamer), 19.3 (C22H$_2$), 17.7 (C6′H$_3$ minor rotamer), 17.3 (C6′H$_3$ major rotamer), 16.1 (C23H$_3$), 12.4 (C20H), 12.1 (C25H$_3$), 6.5 (C24H$_3$).

Callipeltoside B $^1$H and $^{13}$C NMR in CD$_3$OD

$^1$H NMR (CD$_3$OD, 500 MHz) δ = 8.24 (1H, s, NHC7'HO major rotamer), 7.90 (1H, s, NHC7'HO minor rotamer), 6.53 (1H, dd, $J = 15.4$, 10.9 Hz, C16H), 6.36 (1H, dd, $J = 14.3$, 11.0 Hz, C15H), 5.86 (1H, m overlapped, C14H), 5.84 (1H, m overlapped, C13H), 5.67 (1H, dd, $J = 15.4$, 1.9 Hz, C17H), 5.30 (1H, d, $J = 9.7$ Hz, C10H), 5.0 (1H, d, $J = 1.1$ Hz, C1'H), 4.16 (1H, qd, $J = 6.5$, 1.7 Hz, C5'H), 3.90 (1H, dd, $J = 9.7$, 2.4 Hz, C9H), 3.86 (1H, s, C4'H), 3.73 (1H, td, $J = 10.6$, 4.6 Hz, C5H), 3.68 (1H, dd, $J = 10.4$, 2.5 Hz, C7H), 3.49 (3H, s, OCH$_3$ major rotamer), 3.49 (3H, s, OCH$_3$ minor rotamer), 3.27 (1H, m, C21H), 3.24 (3H, s, C9H(OCH$_3$)), 3.04 (1H, t, $J = 1.1$ Hz, C2'H minor rotamer), 3.01 (1H, t, $J = 1.1$ Hz, C2'H major rotamer), 2.58 (1H, d, $J = 13.0$ Hz, C2H$_4$B), 2.50 (1H, d, $J = 12.9$ Hz, C2H$_4$B), 2.37 (1H, m overlapped, C12H$_4$B), 2.30 (1H, m overlapped, C12H$_4$B), 2.24 (1H, m overlapped, C8H), 2.24 (1H, m overlapped, equatorial C4H$_2$B), 1.83 (1H, m, C20H), 1.77 (3H, s, C23H$_3$), 1.51 (1H, m, C6H), 1.46 (1H, t, $J = 11.4$ Hz, axial C4H$_2$B), 1.44 (3H, s, C8′H$_3$), 1.30 (2H, m, C22H$_2$B), 1.13 (3H, d, $J = 6.3$ Hz, C6′H$_3$ minor rotamer), 1.10 (3H, d, $J = 6.4$ Hz, C6′H$_3$ major rotamer), 0.99 (6H, appar. d, $J = 6.5$ Hz, C24H$_3$ and C25H$_3$); $^{13}$C NMR (CD$_3$OD, 126 MHz) δ = 172.9 (C1O$_2$), 164.6 (NHC'7HO), 141.6 (C16H), 134.4 (C11), 134.2 (C14H), 132.1 (C15H), 128.3 (C10H), 113.5 (C17H), 101.2 (C1'H), 96.6 (C3), 92.8 (C19), 84.5 (C2'H), 81.3 (C9H), 80.8 (C5H), 78.4
(C18), 76.3 (C7H), 72.7 (C13H), 69.7 (C3’), 66.2 (C5‘H), 59.8 (OCH₃), 57.1 (C4’H), 55.4 (C9H(OCH₃)), 47.8 (C12H₂), 45.9 (C2H₂), 43.8 (C4H₂), 39.8 (C6H), 38.3 (C8H), 35.1 (C21H), 24.8 (C8’H₃), 19.8 (C22H₂), 17.6 (C6’H₃), 16.3 (C23H₃), 12.8 (C20H), 12.7 (C25H₃), 6.8 (C24H₃); **HRMS** (+ESI) Found [M+Na]⁺ = 702.3018; C₃₅H₅₀O₁₀NClNa requires 702.3015, Δ 0.30 ppm.†

* Protons and carbons reassigned based on 2D COSY, HSQC and HMBC data recorded for the synthetic sample.

† Following a personal communication with Professor Zampella, a ¹³C NMR (CD₃OD) derived from the HSQC/HMBC was provided. Hence, the data was also recorded in CD₃OD and found to match the data provided for the natural isolate.
### 1H NMR comparison between synthetic and natural callipeltoside B (CDCl₃)

<table>
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<th>Atom</th>
<th>Natural callipeltoside B[^10]</th>
<th>Synthetic callipeltoside B</th>
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<td>δ in ppm (500 MHz)</td>
<td>δ in ppm (500 MHz)</td>
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<tr>
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<tr>
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<td>2.53 (d, 13.5), 2.43 (d, 13.5)</td>
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<tr>
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<td>1.46 (m)</td>
<td>5.29 (br dd, 9.1)</td>
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<td>5.57 (dd, 15.5, 1.8)</td>
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<td>8</td>
<td>2.20 (m)</td>
<td>2.20 (m, overlapped)</td>
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<td>2.30 (appar. d, 3.7)</td>
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<td>16</td>
<td>[1.29 (m)][^*]</td>
<td>4.97 (br s)</td>
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<td>4.11 (qd, 6.6, 1.4)</td>
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<td>1.14 (d, 6.4), 1.12 (d, 6.4)</td>
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<td>27</td>
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<td>8.36 (d, 1.4), 7.93 (d, 11.9)</td>
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<td>3.47 (s), 3.43 (s)</td>
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<td>30</td>
<td>6.32[^†] (d, 10.5), 6.13 (t, 10.5)</td>
<td>7.93 (d, 11.9), 6.13 (t, 11.4)</td>
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<tr>
<td>31</td>
<td>3.28 (d, 0.7), 3.08 (d, 0.8)</td>
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</tr>
</tbody>
</table>

[^†]: The tabulated data differs from the spectrum supplied by Professor Zampella. We attribute this to a typographical error.
A further NMR experiment (CDCl₃) was conducted in order to elucidate the configuration at the anomeric carbon. Measurement of the $^1J_{C-H}$ value from a HSQC (Heteronuclear Single Quantum Coherence) experiment without $^{13}C$ decoupling is known to be diagnostic of the configuration of the glycosidic linkage. A value of ~170 Hz suggests an equatorial proton at C1′H, whilst ~160 Hz indicates an axial proton. The measurement gave $^1J_{C-H} = 165.6$ Hz, giving an inconclusive result.²⁹

Key selected observed nOe’s from NOESY (CDCl₃)

- An nOe was observed between C1′H and C2′H suggesting that conformer 2 is disfavoured.
- An nOe was observed between C1′H and OMe suggesting that conformer 3 is disfavoured.
- An nOe between C6′H₃ and C4′H suggesting that conformers 1 and 2 are disfavoured.
- $\alpha$-conformer 4 accounts for all observed nOe interactions indicating that C1′H is equatorial.
• An nOe (CDCl$_3$) was observed between the formyl and NH protons of the major rotamer suggesting that the predominant form is cis.

• As expected, no nOe (CDCl$_3$) between the formyl and NH protons was observed for the trans (minor) rotamer.
**HPLC conditions**

Preparative HPLC purification was performed on an Agilent HP 1100 series chromatograph equipped with a Waters μBondapak C18 column (column length 150 mm, internal diameter of column 3.9 mm, particle size 10 μm, temperature 25 °C). Elution was carried out at a flow rate of 2.0 mL/min using MeOH:H₂O (80:20) and detection was with diode array detection (λ= 250, 272 and 286). The sample was made up to a concentration of 0.003 mg/μL with purification carried out using 30 μL injections which saturated the detector at λ= 250, 272 and 286. $t_R = 3.6$ min.
(1S,5R,7E,9R,10R,11R,12R,13S)-5-[(1E,3E)-6-[(1S,2R)-2-chlorocyclopropyl]hexa-1,3-dien-5-yn-1-yl]-1-hydroxy-9-methoxy-7,10,12-trimethyl-3-oxo-4,15-dioxabicyclo[9.3.1]pentadec-7-en-13-yl 4-azido-4,6-dideoxy-3-C-methyl-2-O-methyl-3-O-(trimethylsilyl)-α-D-talopyranoside 127

To a solution of aglycon 4 (4.5 mg, 9.4 μmol) and thioglycoside ent-115 (7.2 mg, 18.8 μmol) in CH₂Cl₂ (2.4 mL) at RT was added 4 Å MS followed by DTBMP (4.9 mg, 23.9 μmol) and the mixture stirred for 50 min.† The reaction was cooled to −15 °C and NIS (4.2 mg, 18.8 μmol) and TfOH [(32 μL, 3.6 μmol) of a stock solution of TfOH in CH₂Cl₂ (0.1 mL, 1.125 mmol in 10 mL CH₂Cl₂)] added sequentially. The resulting light pink solution was allowed to warm to RT slowly over 16 h. The reaction was quenched by the addition of sat. aq. NaHCO₃ (6 mL) and diluted with EtOAc (10 mL). The layers were separated and the aqueous layer further extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with sat. aq. Na₂S₂O₃ (30 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:EtOAc, 9:1→4:1→1:1) gave title compound 127 (2.9 mg, 41%) as a pale yellow oil [Rᶠ= 0.39 (hexane:EtOAc, 4:1)].²⁶

† The aglycon 4 and thioglycoside ent-115 were azeotroped with PhMe (× 3) prior to use.
Callipeltoside B diastereomer 128

To a solution of 127 (2.9 mg, 3.9 μmol) in pyridine (95 μL) and H₂O (9.5 μL) (10:1) at RT was added Et₃N (7.8 μL) and 1,3-propanedithiol (7.8 μL, 77.0 μmol) sequentially. The reaction was stirred for 2 h 30 min and further Et₃N (7.8 μL) and 1,3-propanedithiol (7.8 μL, 77.0 μmol) added. After 90 min TLC analysis indicated complete consumption of the starting material. Azeotropic removal of the solvents with PhMe (3 × 10 mL) gave the requisite amine (assumed quant.) as an off-white residue. The isolated amine was used immediately in the next step of the reaction without further purification.

To a solution of crude amine (assumed quant. 3.9 μmol) in CHCl₃ (0.2 mL) was added freshly prepared 113²⁻ (164 mg, 0.77 mmol). The reaction was stirred at RT for 1 h after which the mixture was concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:EtOAc, 9:1→4:1→7:3→3:2→1:1→2:3→EtOAc) gave TMS-protected callipeltoside B (assumed quant.) as a clear oil [R_f = 0.34 (hexane:EtOAc, 1:1)]. The isolated TMS-protected callipeltoside B was used immediately in the next step of the reaction without characterisation.

To a solution of TMS-protected callipeltoside B (assumed quant., 3.9 μmol) in DMF (0.5 mL) at RT was added TASF (5.3 mg, 19.5 μmol) and the mixture heated to 40 °C. After 30 min the reaction was cooled to RT, quenched by the addition of pH 7 phosphate buffer (1 mL) and diluted with EtOAc (2 mL). The layers were separated and the aqueous layer further extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with 10% aq. LiCl (2 × 8 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂,
hexane→hexane:EtOAc, 7:3→1:1→3:7→EtOAc→CH₂Cl₂:MeOH, 9:1) gave the title compound 128 (1.5 mg, 57% over 3 steps) as an off-white gum consisting of 2 rotamers (4:1 by ¹H NMR). The sample was further purified by HPLC (see below).

Rotameric ratio ascertained by ¹H NMR spectroscopy of the purified mixture; δₜ (CDCl₃, 500 MHz) 8.36 (1H, d, J = 1.4 Hz, NHC₇’Hₐ major), 7.93 (1H, d, J = 11.9 Hz, NHC₇’HO minor).

Rᵣ = 0.18 (minor), 0.14 (major) (EtOAc); [α]ᵥ⁺ = +3.0 (c = 0.10, CDCl₃); IR (film) νmax/cm⁻¹ 3404, 2962, 2917, 2849, 1693, 1463, 1441, 1415, 1386, 1346, 1325, 1310, 1260, 1174, 1175, 1094, 1084, 1045, 1018, 983; ¹H NMR (CDCl₃, 500 MHz) † δ = 8.37 (1H, d, J = 1.4 Hz, NHC₇’HO major rotamer), 7.94 (1H, d, J = 11.7 Hz, NHC₇’HO minor rotamer), 6.48 (1H, dd, J = 15.8, 10.9 Hz, C₁₆H), 6.30 (1H, d, J = 9.5 Hz, NHC₇’HO major rotamer), 6.27 (1H, dd, J = 15.5, 11.0 Hz, C₁₅H), 6.14 (1H, t, J = 11.7 Hz, NHC₇’HO minor rotamer), 5.83 (1H, m, C₁₃H), 5.76 (1H, dd, J = 15.2, 6.4 Hz, C₁₄H), 5.58 (1H, d, J = 14.0 Hz, C₁₇H), 5.30 (1H, d, J = 8.3 Hz, C₁₀H), 5.06 (1H, dd, J = 7.0, 2.0 Hz, C₃OH), 5.01 (1H, s, C₁’H), 4.16 (1H, m, C₅’H major and minor rotamers), 4.00 (1H, d, J = 10.5 Hz, C₄’H major rotamer), 3.85 (1H, td, J = 10.7, 4.5 Hz, C₅H), 3.81 (1H, dd, J = 9.7, 2.2 Hz, C₉H), 3.66 (1H, dd, J = 10.4, 2.2 Hz, C₇H), 3.47 (3H, s, OCH₃ major rotamer), 3.43 (3H, s, OCH₃ minor rotamer), 3.29 (1H, s, C₃’OH minor rotamer), 3.24 (3H, s, C₉H(OCH₃)), 3.18 (1H, m, C₂₁H), 3.09 (1H, s, C₃’OH major rotamer), 2.99 (1H, d, J = 10.5 Hz, C₄’H minor rotamer), 2.89 (1H, s, C₂’H major rotamer), 2.88 (1H, s, C₂’H minor rotamer), 2.54 (1H, d, J = 12.9 Hz, C₂₉HₐH₉B), 2.44 (1H, appar. dd, J = 12.9, 2.8 Hz, C₂HₐH₉B), 2.31 (1H, appar. d, J = 4.3 Hz, C₁₂HₐH₉B), 2.30 (1H, m overlapped, C₁₂HₐH₉B), 2.24 (1H, m, C₈H), 2.19 (1H, dd, J = 11.7, 4.4 Hz, equatorial C₄H₉H₉B), 1.80 (1H, m, C₂₀H), 1.73 (3H, s, C₂₃H₃), 1.54 (1H, m overlapped, C₆H), 1.47 (3H, s, C₈’H₃ major rotamer), 1.45 (3H, s, C₈’H₃ minor rotamer), 1.40 (1H, m overlapped, axial C₄H₉H₉B), 1.30 (2H, m, C₂₂HₐH₉B), 1.17 (3H, d, J = 6.4 Hz, C₆’H₃ minor rotamer), 1.14 (3H, d, J = 6.4 Hz, C₆’H₃ major rotamer), 0.99 (3H, d, J = 7.0 Hz, C₂₄H₉), 0.96 (3H, d, J = 6.4 Hz, C₂₅H₉); ¹³C NMR (CDCl₃, 126 MHz) † δ =

† Only the rotameric peaks attributed to the sugar are distinguishable in the ¹H NMR.

† The ¹³C NMR peaks corresponding to the minor rotamer could not be observed due to the small amount of sample isolated.
171.7 (C1O₂), 161.5 (NHC'O7HO), 140.1 (C16H), 132.5 (C14H), 132.4 (C11), 131.0 (C15H), 127.7 (C10H), 112.6 (C17H), 95.2 (C3), 93.7 (C1'H), 92.4 (C19), 83.8 (C2'H), 79.7 (C9H), 77.4 (C18 overlapped), 75.0 (C7H), 74.7 (C5H), 71.7 (C13H), 68.1 (C3'), 65.2 (C5'H), 59.4 (OCH₃), 55.5 (C4'H), 55.2 (C9H(OCH₃)), 46.9 (C12H₂), 44.8 (C2H₂), 39.6 (C4H₂), 37.7 (C6H), 37.0 (C8H), 34.3 (C21H), 23.7 (C8'H₃), 19.3 (C22H₂), 17.3 (C6'H₃), 16.1 (C23H₃), 12.7 (C20H), 12.1 (C25H₃), 6.5 (C24H₃); **HRMS** (+ESI) Found [M+Na]^+ = 702.3004; C₃₅H₅₀O₁₀NClNa requires 702.3015, Δ 1.58 ppm.
A further NMR experiment was conducted in order to elucidate the configuration at the anomeric carbon. Measurement of the $^1J_{C-H}$ value from a HSQC (Heteronuclear Single Quantum Coherence) experiment without $^{13}$C decoupling is known to be diagnostic of the configuration of the glycosidic linkage. A value of $\sim$170 Hz suggests an equatorial proton at C1'H, whilst $\sim$160 Hz indicates an axial proton. The measurement gave $^1J_{C-H} = 166.3$ Hz, giving an inconclusive result.$^{29}$

Key selected observed nOe’s from NOESY

- An nOe was observed between C1'H and C2'H suggesting that conformers 3 and 4 are disfavoured.
- An nOe was observed between C1'H and OMe suggesting that conformer 2 is disfavoured.
- $\alpha$-conformer 1 accounts for all observed nOe interactions indicating that C1'H is equatorial.
As in the case for the natural product, an nOe was observed between the formyl and NH protons of the major rotamer suggesting that the predominant form is cis.

As expected, no nOe between the formyl and NH protons was observed for the trans (minor) rotamer.
HPLC conditions
Preparative HPLC purification was performed on an Agilent HP 1100 series chromatograph equipped with a Waters μBondapak C18 column (column length 150 mm, internal diameter of column 3.9 mm, particle size 10 μm, temperature 25 °C). Elution was carried out at a flow rate of 2.0 mL/min using MeOH:H₂O (80:20) and detection was with diode array detection (λ= 250, 272 and 286). The sample was made up to a concentration of 0.003 mg/μL with purification carried out using 20 μL injections which saturated the detector at λ= 250, 272 and 286. t<sub>R</sub> = 3.0 min.
Callipeltoside C (3)

To a solution of aglycon 4 (6.4 mg, 13.4 μmol) and thioglycoside 123 (12.6 mg, 26.7 μmol) in CH₂Cl₂ (3.4 mL) at RT was added 4 Å MS followed by DTBMP (7.0 mg, 34 μmol) and the mixture stirred for 50 min. The reaction was cooled to −15 °C and NIS (6.0 mg, 26.7 μmol) and TfOH [(45 μL, 5.1 μmol) of a stock solution of TfOH in CH₂Cl₂ (0.1 mL, 1.125 mmol in 10 mL CH₂Cl₂)] added sequentially resulting in the formation of a light pink colour. The reaction was allowed to warm to RT slowly over 16 h. The reaction was quenched by the addition of sat. aq. NaHCO₃ (10 mL) and diluted with EtOAc (15 mL). The layers were separated and the aqueous layer further extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with sat. aq. Na₂S₂O₃ (30 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:EtOAc, 9:1→4:1→1:1) gave bis-protected callipeltoside C (assumed quant.) as a pale yellow oil/foam [Rᶠ = 0.37 (hexane:EtOAc, 4:1)].

To a solution of bis-protected callipeltoside C (assumed quant., 13.4 μmol) in DMF (1.8 mL) at RT was added TASF (23.3 mg, 85 μmol) and the mixture heated to 40 °C. After 1 h, further TASF (14.6 mg, 53 μmol) was added, and the reaction maintained at 40 °C for an additional 1 h. The reaction was cooled to RT, quenched by the addition of pH 7 phosphate buffer (10 mL) and diluted with EtOAc (10 mL). The layers were separated and the aqueous layer further extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with 10% aq. LiCl (2 × 15 mL), dried (MgSO₄) and concentrated in vacuo. Purification by column chromatography (SiO₂, hexane→hexane:EtOAc, 4:1→1:1→EtOAc) gave the title compound callipeltoside C 3.

† The aglycon 4 and thioglycoside 123 were azeotroped with PhMe (× 3) prior to use.
(5.0 mg, 57% over 2 steps) as an off-white gum. The sample was further purified using HPLC (see below).

$R_f = 0.13$ (hexane:EtOAc, 1:1); $[\alpha]_{D}^{25.0} = -32.0$ ($c = 0.30$, CDCl$_3$), $[\alpha]_{D}^{23} = -23.1$ ($c = 0.18$, CDCl$_3$); IR (film) $\nu_{\text{max}}$/cm$^{-1}$ 3360, 3187, 2923, 2852, 1703, 1660, 1632, 1468, 1423, 1411, 1378, 1342, 1319, 1260, 1226, 1180, 1154, 1136, 1086, 1052, 1023, 979; $^1$H NMR (CDCl$_3$, 500 MHz) $\delta =$ 6.48 (1H, dd, $J = 15.4$, 10.9 Hz, C16H), 6.27 (1H, dd, $J = 15.1$, 10.9 Hz, C15H), 5.82 (1H, m, C13H), 5.76 (1H, dd, $J = 15.1$, 6.4 Hz, C14H), 5.58 (1H, dd, $J = 15.3$, 1.7 Hz, C17H), 5.30 (1H, d, $J = 9.2$ Hz, C10H), 4.99 (1H, d, $J = 2.3$ Hz, C3OH), 4.94 (1H, s, C1'H), 3.81 (1H, dd, $J = 9.5$, 2.4 Hz, C9H), 3.70 (1H, td, $J = 10.3$, 4.5 Hz, C5H), 3.65 (1H, m overlapped, C7H), 3.65 (1H, dq overlapped, C5'H), 3.47 (3H, s, OCH$_3$), 3.36 (1H, dd, $J = 9.6$, 2.3 Hz, C4'H), 3.23 (3H, s, C9H(OCH$_3$)), 3.18 (1H, m, C21H)$^*$, 3.12 (1H, d, $J = 1.0$ Hz, C2'H), 2.88 (1H, s, C3'O'H)$^*$, 2.52 (1H, d, $J = 12.9$ Hz, C2H$_A$H$_B$), 2.43 (1H, d, $J = 12.9$ Hz, C2H$_A$H$_B$), 2.30 (1H, appar. d, $J = 4.0$ Hz, C12H$_A$H$_B$), 2.28 (1H, m overlapped, C12H$_A$H$_B$)$^*$, 2.25 (1H, m overlapped, equatorial C4H$_A$H$_B$), 2.20 (1H, m overlapped, C8H)$^*$, 2.03 (1H, s, C4'H'O'H)$^*$, 1.80 (1H, m, C20H), 1.74 (3H, d, $J = 0.9$ Hz, C23H$_3$), 1.47 (1H, m, C6H), 1.35 (1H, td, $J = 11.2$, 2.0 Hz, axial C4H$_A$H$_B$), 1.31 (3H, s, C7'H$_3$), 1.29 (2H, m, C22H$_A$H$_B$)$^*$, 1.26 (3H, d, $J = 6.1$ Hz, C6'H$_3$), 0.98 (3H, d, $J = 7.0$ Hz, C24H$_3$), 0.92 (3H, d, $J = 6.5$ Hz, C25H$_3$); $^{13}$C NMR (CDCl$_3$, 126 MHz) $\delta =$ 171.8 (C1O$_2$), 140.1 (C16H), 132.7 (C14H), 132.4 (C11), 130.9 (C15H), 127.7 (C10H), 112.5 (C17H), 98.7 (C1'H), 95.2 (C3), 92.3 (C19), 84.7 (C2'H), 79.7 (C9H), 79.1 (C5H), 77.5 (C18), 76.7 (C4'H), 74.8 (C7H), 72.3 (C3'), 71.5 (C13H), 67.0 (C5'H), 59.0 (OCH$_3$), 55.2 (C9H(OCH$_3$)), 46.9 (C12H$_2$), 44.7 (C2H$_2$), 42.4 (C4H$_2$), 38.5 (C6H), 37.0 (C8H), 34.3 (C21H)$^*$, 19.3 (C22H$_2$), 17.8 (C6'H$_3$), 17.8 (C7'H$_3$), 16.1 (C23H$_3$), 12.4 (C20H)$^*$, 12.1 (C25H$_3$), 6.5 (C24H$_3$); HRMS (+ESI) Found [M+Na]$^+$ = 675.2904; C$_{34}$H$_{49}$O$_{10}$ClNa requires 675.2906, $\Delta$ 0.35 ppm.$^\dagger$

* Protons and carbons reassigned based on 2D COSY, HSQC and HMBC data recorded for the synthetic sample.

$^\dagger$ The data is assigned in the same style as originally reported for the natural product.
**$^1$H NMR comparison between synthetic, natural and previously synthesised callipeltoside C (CDCl$_3$)**

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<th>MacMillan callipeltoside C$_7$</th>
<th>Synthetic callipeltoside C</th>
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**13C NMR comparison between synthetic, natural and previously synthesised callipeltoside C (CDCl₃)**

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† Due to the small sample of natural product, the carbon signals were detected in the HMQC spectrum.
*Protons and carbons reassigned based on COSY, HSQC and HMBC data recorded for the synthetic sample.

A further NMR experiment was conducted in order to elucidate the configuration at the anomeric carbon. Measurement of the $J_{C-H}$ value from a HSQC (Heteronuclear Single Quantum Coherence) experiment without $^{13}$C decoupling is known to be diagnostic of the configuration of the glycosidic linkage. A value of ~170 Hz suggests an equatorial proton at C1'H, whilst ~160 Hz indicates an axial proton. The measurement gave $J_{C-H} = 166.5$ Hz, giving an inconclusive result.29

Key selected observed nOe’s from NOESY

- An nOe was observed between C1'H and C2'H suggesting that conformer 2 is disfavoured.
- An nOe was observed between C1'H and OMe suggesting that conformer 3 is disfavoured.
- An nOe between C4'H and C5'H suggesting that conformers 3 and 4 are disfavoured.
- $\beta$-conformer 1 accounts for all observed nOe interactions indicating that C1'H is equatorial.
HPLC conditions
Preparative HPLC purification was performed on an Agilent HP 1100 series chromatograph equipped with a Waters μBondapak C18 column (column length 150 mm, internal diameter of column 3.9 mm, particle size 10 μm, temperature 25 °C). Elution was carried out at a flow rate of 2.0 mL/min using MeOH:H₂O (70:30) and detection was with diode array detection (λ= 250, 272 and 286). The sample was made up to a concentration of 0.015 mg/μL with purification carried out using 25 μL injections which saturated the detector at λ= 250, 272 and 286. \( t_R = 6.1 \) min.
III) Selected NMR Spectra

$^1$H NMR: Dimethyl (7$S$)-5-O-(tert-butyl(dimethyl)silyl)-7-((2R,3$R$,4$E$,7$R$,8$E$,10$E$)-7-((tert-butyl(dimethyl)silyl)oxy)-13-((1$S$,2$R$)-2-chlorocyclopropyl)-3-hydroxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl)-2,4,6-trideoxy-6-methyl-$\alpha$-L-threo-hept-3-ulopyranosidonate S20
$^{13}$C NMR: Dimethyl (7S)-5-O-(tert-butyl(dimethyl)silyl)-7-((2R,3R,4E,7R,8E,10E)-7-(tert-butyl(dimethyl)silyloxy)-13-((1S,2R)-2-chlorocyclopropyl)-3-hydroxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl)-2,4,6-trideoxy-6-methyl-$a$-$L$-$threo$-$hept$-$3-ulopyranosidonate S20
$^1$H NMR: Dimethyl \((7S)-5-O-(\text{tert}-\text{butyl}(\text{dimethyl})silyl)-7-((2R,3R,4E,7R,8E,10E)-7-(\text{tert}-\text{butyl}(\text{dimethyl})silyl)oxy)-13-((1S,2R)-2\text{-chlorocyclopropyl})-3\text{-methoxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl})-2,4,6\text{-trideoxy-6-methyl-\(\alpha\)-L-threo-hept-3-ulopyranosid}onate \ 95
$^{13}$C NMR: Dimethyl (7$S$)-5-O-(tert-butyl(dimethyl)silyl)-7-((2$R$,3$R$,4$E$,7$R$,8$E$,10$E$)-(tert-butyl(dimethyl)silyl)oxy)-13-((1$S$,2$R$)-2-chlorocyclopropyl)-3-methoxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl)-2,4,6-trideoxy-6-methyl-$\alpha$-L-threo-hept-3-ulopyranosidonate 95
$^1$H NMR: Dimethyl (7S)-5-O-(tert-butyl(dimethyl)silyl)-7-((2R,3R,4E,7R,8E,10E)-13-((1S,2R)-2-chlorocyclopropyl)-7-hydroxy-3-methoxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl)-2,4,6-trideoxy-6-methyl-α-L-threo-hept-3-ulopyranosidonate 99
$^{13}$C NMR: Dimethyl (7$S$)-5-O-(tert-butyl(dimethyl)silyl)-7-((2$R$,3$R$,4$E$,7$R$,8$E$,10$E$)-13-((1$S$,2$R$)-2-chlorocyclopropyl)-7-hydroxy-3-methoxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl)-2,4,6-trideoxy-6-methyl-$\alpha$-L-threo-hept-3-ulopyranosidonate 99
$^1$H NMR: Methyl (7$S$)-5-\((tert\text{-}\text{butyl(dimethyl)silyl})\)-7-\(((2R,3R,4E,7R,8E,10E)-(1S,2R)-2\text{-}\text{chlorocyclopropyl})\)-7\text{-}\text{hydroxy}-3\text{-}\text{methoxy}-5\text{-}\text{methyltrideca-4,8,10-trien-12-yn-2-yl})\)-2,4,6\text{-}\text{trideoxy-6-methyl-\text{\textalpha}{-L-threo-hept-3-ulopyranosidonic acid}} 100
$^{13}$C NMR: Methyl (7$S$)-5-$O$-(tert-butyl(dimethyl)silyl)-7-((2$R$,3$R$,4$E$,7$R$,8$E$,10$E$)-13-((1$S$,2$R$)-2-chlorocyclopropyl)-7-hydroxy-3-methoxy-5-methyltrideca-4,8,10-trien-12-yn-2-yl)-2,4,6-trideoxy-6-methyl-$\alpha$-L-threo-hept-3-ulopyranosidonic acid 100
$^1$H NMR: (1R,6R,8E,10R,11R,12R,13R,14S)-6-((1E,3E)-6-((1S,2R)-2-Chlorocyclopropyl)hexa-1,3-dien-5-yn-1-yl)-1,14-dihydroxy-10-methoxy-8,11,13-trimethyl-5,16-dioxabicyclo[10.3.1]hexadec-8-en-4-one 4
$^{13}$C NMR: $(1R,6R,8E,10R,11R,12R,13R,14S)-6-((1E,3E)-6-((1S,2R)-2-
 Chlorocyclopropyl)hexa-1,3-dien-5-yn-1-yl)-1,14-dihydroxy-10-methoxy-8,11,13-trimethyl-5,16-dioxabicyclo[10.3.1]hexadec-8-en-4-one 4
$^1$H NMR: Callipeltoside A (1)
$^{13}$C NMR: Callipeltoside A (1)
$^1$H NMR: Callipeltoside B (2), CDCl$_3$
$^{13}$C NMR: Callipeltoside B (2), CDCl$_3$
$^1$H NMR: Callipeltoside B (2), MeOD

![NMR Spectrogram for Callipeltoside B (2), MeOD](image_url)
$^{13}$C NMR: Callipeltoside B (2), MeOD
$^1$H NMR: Callipeltoside B diastereomer 128
$^{13}$C NMR: Callipeltoside B diastereomer 128
$^1$H NMR: Callipeltoside C (3)
$^{13}$C NMR: Callipeltoside C (3)
IV) References


