CHAPTER 6

EXPERIMENTAL

6.1 GENERAL

SOLVENTS

Acetone was dried over anhydrous K$_2$CO$_3$ for 24 hours. The salt was then filtered off and the solvent subsequently distilled over 3 Å molecular sieves and stored under N$_2$.

Benzene and toluene were dried by heating the respective solvent over sodium-benzophenone under a N$_2$ atmosphere until the solution turned a deep blue colour. The solvent was freshly distilled before use.

Diethyl ether and THF were pre-dried over freshly ground KOH. The KOH was then filtered off and the solvent dried from sodium-benzophenone. The solvents were distilled under N$_2$ prior to use.

Dichloromethane and dimethylformamide were respectively heated over CaH$_2$ under N$_2$ with subsequent distillation.

Ethanol and methanol were distilled from Mg/I$_2$ and stored over 3 Å molecular sieves.

Ethyl acetate was distilled from K$_2$CO$_3$ using a Vigreux distillation column.

Hexanes were distilled prior to use.

HMPA was heated over CaH$_2$ under an argon atmosphere for one week prior to its use. The solvent was only used if freshly distilled.
Pyridine was pre-dried over anhydrous CaCl₂ and then distilled from 3 Å molecular sieves.

**CHROMATOGRAPHY**

Thin layer chromatography (TLC) was conducted quantitatively on “Merck GF₂₅₄ pre-coated silica gel glass plates” (0.25 mm layer). Various solvent mixtures were used to elute the chromatograms with a mixture of hexanes and EtOAc usually being the eluent of choice. Aromatic derivatives were visualised by their fluorescence under UV light (254 nm) while carbohydrate substrates were detected after spraying the TLC plate with a chromic acid solution and then heating it over an open flame.

“Flash column chromatography” (FCC) refers to column chromatography under nitrogen pressure (ca. 50 kPa). The columns were loaded with Merck Kieselgel 60 (230-400 mesh) and eluted with appropriate solvent mixtures in a volume per volume ratio.

**CHARACTERISATION TECHNIQUES**

**Nuclear Magnetic Resonance Spectroscopy (NMR)**

NMR-spectra were recorded using a Varian Gemini 2000, 300 MHz spectrometer. The samples were usually made up in CDCl₃, unless otherwise stated. The ¹H-NMR data are listed in order: Chemical shift (δ), reported in ppm and referenced to the residual solvent peak of CHCl₃ [δ = 7.24]), the number of integrating protons, the multiplicity, the coupling constant J expressed in Hz, and finally the specific hydrogen allocation. Spin-decoupling experiments aided in the determination of the coupling constants and hydrogen allocation. The relative stereochemistry was determined after studying nuclear Overhauser effect spectra. ¹³C-NMR data are listed in the order: chemical shift (δ), reported in ppm referenced to the solvent peak of CDCl₃ [(δ = 77.0 ppm)] and the
specific carbon atom allocation. DEPT and HETCOR spectroscopy were used to assist in the allocation of difficult spectra where necessary.

nOe: Signal enhancement due to nOe is an example of cross-polarization, in which a polarization of the spin states in nucleus causes a polarization of the spin states in another nucleus. Although the hydrogens producing the nOe effect influence carbon atoms more distant than the ones to which they are attached, their effectiveness drop off rapidly with distance. The interaction of the spin-spin dipoles operates through space, not through bonds, and its magnitude decreases as a function of the inverse of $r^3$, where $r$ is the radial distance from the hydrogen of origin. The nuclei need to be very close together in order to exhibit the nOe effect. For difficult peak assignments, irradiation of a selected hydrogen or group of hydrogen leads to a greater enhancement in the signal of the closer of the carbons being considered.

HETCOR (heteronuclear chemical shift correlation): Protons and carbons interact in two different ways. First, they both have magnetic properties and can induce relaxation on one another and secondly, the two types of nuclei can be spin-coupled to each other. The latter interaction is useful because directly bonded protons and carbons have $J$ values that are at least 10 times larger than nuclei related by two-bond or three-bond couplings. This allows one to identify carbons and protons that are directly bonded to each other. HETCOR is a two-dimensional experiment in which the chemical shifts of the $^{13}$C atoms are plotted along one axis and the chemical shifts of the $^1$H atoms along the other. A spot of intensity within the two-dimensional spectrum indicates the existence of a C-H bond.

**Mass Spectrometry (EIMS / CIMS)**

The compilation of fragmentation and accurate mass determinations were recorded on a Finnigan Matt 8200 spectrometer at an electron impact of 70 eV. The data was listed with all major peak intensities being percentages of the base peak.
**Infrared Spectroscopy (IR)**

A Perkin-Elmer 881 spectrometer was used to record IR spectra using dry chloroform as the solvent. The data was listed with characteristic peaks indicated in wavenumber (cm\(^{-1}\)).

**Optical Rotation ([\(\alpha\)]\(_D\))**

A Jasco model DIP-730 spectropolarimeter having a cell with a 10 mm path length was used to determine optical rotations. The concentration \(c\). indicates the concentration of the sample in grams per 100 ml of solution.

**Melting Points (MP)**

Melting points were determined using a Reichert Thermopan microscope together with a Koffler hot-stage and are uncorrected.

**CHEMICAL METHODS**

All new compounds are fully characterised \(\text{i.e.} \) \(^1\)H, \(^13\)C NMR, IR, EIMS / CIMS / HRMS, [\(\alpha\)]\(_D\) etc.) while for known compounds only MP, \(^1\)H, \(^13\)C NMR IR and EIMS / CIMS / HRMS is given. The [\(\alpha\)]\(_D\) values for known carbohydrate derivatives were not determined. All eluents for flash chromatography are the same as those specified for TLC unless otherwise stated.

All reactions were performed in flamed out glass apparatus using dry solvents unless otherwise stated. All samarium diiodide reactions were carried out under argon using degassed solvents while standard chemistry was done under an atmosphere of nitrogen. Room temperature refers to a temperature ranging from 20-25 °C.
6.2 ARYL γ-KETOESTERS AS PRECURSORS FOR γ-BUTYROLACTONE DIMERS IN SAMARIUM(II) IODIDE-MEDIATED REACTIONS

6.2.1 The Stetter Reaction: Preparation of 1,4-Ketoesters

**Ethyl 4-Phenyl-4-oxobutanoate** (2.2a)

![Structural formula of Ethyl 4-Phenyl-4-oxobutanoate](image)

A solution of freshly distilled benzaldehyde (2.058 g, 20.0 mmol) and anhydrous DMF (8 mL) was added to a stirred mixture of NaCN (0.098 g, 2.0 mmol) and DMF (8 mL) at 20 °C. After one hour of stirring, a solution of ethyl acrylate (1.457 g, 15.0 mmol) and DMF (16 mL) was added dropwise over thirty minutes. After a further three hours of stirring twice the amount of water was added. After repeated extraction with chloroform, the combined extracts were washed with dilute HCl, a saturated NaHCO₃ solution and finally water. The mixture of products was passed through a 20 cm flash silica column using a 4:1 hexane-EtOAc mixture as the eluent. The resultant product was then distilled (b.p. 115 °C at 0.6 mm Hg) on the Kugelrohr affording the ester (1.20 g, 5.8 mmol, 39%) a colourless oil.

TLC: \( R_f \) 0.47 (4:1 hexanes-EtOAc)

**¹H NMR:** (300 MHz, CDCl₃) \( \delta_H \) 7.95-7.92 ((m, 2H, H2’ and H6’), 7.54-7.50 (m, 1H, H4’), 7.44-7.39 (m, 2H, H3’ and H5’), 4.12 (q, 2H, \( J = 7.2 \) Hz, H1’), 3.27 (t, 2H, \( J = 6.6 \) Hz, H3), 2.71 (t, 2H, \( J = 6.6 \) Hz, H2), 1.22 (t, 3H, \( J = 7.2 \) Hz, H2’).

**¹³C NMR:** (75 MHz, CDCl₃) \( \delta_C \) 197.9 (C4), 172.7 (C1), 136.4 (C1’), 133.0 (C4’), 128.4 (C3’ and C5’), 127.9 (C2’ and C6’), 60.5 (s, OCH₂), 33.3 (C3), 28.2 (C2), 14.2 (CH₂CH₃).
EIMS: 206 (M+, 10%), 161 (M+ - OCH₂CH₃, 25%), 105 (M+ - CH₂CH₂CO₂CH₂CH₃, 100%), 77 (M+ - COCH₂CH₂CO₂CH₂CH₃, 54%).

A HETCOR spectrum assisted in the ¹³C NMR peak assignments.

**n-Butyl 4-Phenyl-4-oxobutanoate (2.2b)**

![Chemical Structure of n-Butyl 4-Phenyl-4-oxobutanoate](image)

A solution of freshly distilled benzaldehyde (4.24 g, 40 mmol) and anhydrous DMF (16 mL) was added to a stirred mixture of NaCN (0.196 g, 0.4 mmol) and DMF (16 mL) at 20 °C. After one hour of stirring, a solution of butyl acrylate (3.84 g, 30 mmol) and DMF (16 mL) was added dropwise over thirty minutes. After a further three hours of stirring twice the amount of water was added. After repeated extraction with chloroform, the combined extracts were washed with dilute HCl, a saturated NaHCO₃ solution and finally water. After chromatography the ester was isolated (3.05 g, 0.013 mol, 43%).

**TLC:** Rf 0.48 (4:1 hexanes-EtOAc)

**¹H NMR:** (300 MHz, CDCl₃) δH 7.98-7.95 (m, 2H, H2' and H6'), 7.58-7.52 (m, 1H, H4'), 7.47-7.42 (m, 2H, H3' and H5'), 4.09 (t, 2H, J = 7.1 Hz, H1''), 3.30 (t, 2H, J = 6.6 Hz, H3), 2.75 (t, 2H, J = 6.6 Hz, H2), 1.59 (pentet, 2H, J = 7.1 Hz, H2''), 1.36 (sextet, 2H, J = 7.1 Hz, H3''), 0.91 (t, 3H, J = 7.1 Hz, H4'').

**¹³C NMR:** (75 MHz, CDCl₃) δC 198.0 (C4), 172.9 (C1), 136.5 (C1'), 133.1 (C4'), 128.5 (C3', C5'), 128.0 (C2', C6'), 64.6 (C1''), 33.4 (C3), 30.7 (C2''), 28.3 (C2), 19.2 (C3''), 13.8 (C4'').
EIMS: 234 (M⁺, 8%), 161 (M⁺ - OBu, 82%), 133 (M⁺ - COOBu, 31%), 105 (M⁺ - CH₂CH₂COOBu, 100%), 77 (COCH₂CH₂COOBu, 82%).

6.2.2 General procedure for the preparation of the following 1,4-ketoesters

A solution of para-Cl-benzaldehyde (3.51 g, 25 mmol) and anhydrous DMF (20 mL) was added to a stirred mixture of NaCN (0.24 g, 5 mmol) and DMF (20 mL) at 20 °C. After one hour of stirring, a solution of the electrophile (25 mmol) and DMF (10 mL) was added dropwise over thirty minutes. After a further three hours of stirring twice the amount of water was added. After repeated extraction with chloroform, the combined extracts were washed with dilute HCl, a saturated NaHCO₃ solution and finally water. After chromatography the ester was isolated.

Ethyl 4-(4-Chlorophenyl)-4-oxobutanoate (2.2c)

![Chemical structure](image)

Yield: 2.30 g, 0.010 mol, 51%
MP: 57-58 °C (Lit.¹ 58-59 °C)
TLC: Rᵋ 0.34 (5:1 hexanes-EtOAc)
¹H NMR: (300 MHz, CDCl₃) δH 7.92-7.89 (dm, 2H, J = 9.0 Hz, H2’ and H6’), 7.44-7.40 (dm, 2H, J = 9.0 Hz, H3’ and H5’), 4.14 (q, 2H, J = 7.2 Hz, OCH₂), 3.26 (t, 2H, J = 6.6 Hz, H3), 2.73 (t, 2H, J = 6.6 Hz, H2), 1.25 (t, 3H, J = 7.2 Hz, CH₂CH₃).
**13C NMR:** (75 MHz, CDCl$_3$) $\delta$C 197.0 (C4), 172.7 (C1), 139.6 (C-Cl), 134.8 (C1’), 129.4 (C3’ and C5’), 128.9 (C2’ and C6’), 60.7 (s, OCH$_2$), 33.4 (C3), 28.3 (C2), 14.3 (CH$_2$CH$_3$).

**EIMS:** 240 (M$^+$, 12%), 195 (M$^+$ - OEt +1, 22%), 167 (M$^+$ - COOEt + 1, 4%), 139 (M$^+$ - CH$_2$CH$_2$COOEt, 100%), 111 (M$^+$ - COCH$_2$CH$_2$COOEt, 29%).

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**n-Butyl 4-(4-Chlorophenyl)-4-oxobutanoate (2.2d)**

![Chemical Structure](image)

**Yield:** 3.053 g, 0.013 mol, 43%

**MP:** 32-34 °C

**TLC:** R$_f$ 0.44 (5:1 hexanes-EtOAc)

**$^1$H NMR:** (300 MHz, CDCl$_3$) $\delta$H 7.92-7.88 (dm, 2H, $J = 8.7$ Hz, H2’ and H6’), 7.44-7.40 (dm, 2H, $J = 8.7$ Hz, H3’ and H5’), 4.08 (t, 2H, $J = 7.1$ Hz, H1”’), 3.26 (t, 2H, $J = 6.6$ Hz, H3), 2.74 (t, 2H, $J = 6.6$ Hz, H2), 1.58 (pentet, 2H, $J = 7.1$ Hz, H2”’), 1.36 (sextet, 2H, $J = 7.1$ Hz, H3”’), 0.91 (t, 3H, $J = 7.1$ Hz, H4”’).

**$^{13}$C NMR:** (75 MHz, CDCl$_3$) $\delta$C 196.8 (C4), 172.7 (C1), 139.6 (C-Cl), 134.8 (C1’), 129.4 (C3’ and C5’), 128.9 (C2’ and C6’), 64.7 (C1”’), 33.4 (C3), 30.7 (C2”’), 28.2 (C2), 19.2 (C3”’), 13.8 (C4”’).

**EIMS:** 269 (M$^+$, 22%), 213 (M$^+$ - Bu +1, 54%), 195 (M$^+$ - OBu+1, 78%), 167 (M$^+$ - COOBu + 1, 21%), 139 (M$^+$ - CH$_2$CH$_2$COOBu, 100%), 111 (M$^+$ - COCH$_2$CH$_2$COOBu, 30%).
Methyl 4-(4-Chlorophenyl)-4-oxo-3-methylbutanoate (2.2e)

![Methyl 4-(4-Chlorophenyl)-4-oxo-3-methylbutanoate](image)

Yield: 1.600 g, 0.007 mol, 22%

TLC: Rf 0.20 (10:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 7.91-7.88 (dm, 2H, $J = 8.9$ Hz, H2’ and H6’), 7.43-7.40 (dm, 2H, $J = 8.9$ Hz, H3’ and H5’), 3.91-3.80 (m, 1H, H3), 3.61 (s, 3H, OCH$_3$), 2.93 (dd, 1H, $J = 16.8$ and $J = 8.7$ Hz, H2a), 2.43 (dd, 1H, $J = 16.8$ and $J = 5.6$ Hz, H2b), 1.18 (d, 3H, $J = 7.2$ Hz, CH$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 201.4 (C4), 172.6 (C1), 139.4 (C-Cl), 134.1 (C1’), 129.8 (C3’, C5’), 128.9 (C2’, C6’), 51.7 (OCH$_3$), 37.2 (C2 and C3), 17.8 (CH$_3$).

IR: $\nu_{max}$(CHCl$_3$)/cm$^{-1}$ 3039, 1737, 1694.

EIMS: 240 (M$^+$, 2%), 209 (M$^+$- OCH$_3$, 8%), 180 (M$^+$- COOCH$_3$, 8%), 154 (M$^+$- CHCH$_2$CH$_2$OCH$_3$, 9%), 139 (M$^+$- CH(CH$_3$)CH$_2$CH$_2$COOCH$_3$, 100%), 111 (M$^+$- COCH(CH$_3$)CH$_2$CH$_2$COOCH$_3$, 21%).

Methyl 4-(4-Chlorophenyl)-4-oxo-2-methylbutanoate (2.2f)

![Methyl 4-(4-Chlorophenyl)-4-oxo-2-methylbutanoate](image)

Yield: 0.818 g, 0.003 mol, 17%

TLC: Rf 0.20 (10:1 hexanes-EtOAc)
**Ethyl 4-(4-Methoxyphenyl)-4-oxobutanoate**

\[
\text{OEt} \quad \text{O} \\
\text{MeO} \\
\text{MeO}
\]

3-Benzyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazole (0.630 g, 2.5 mmol) and TEA (1.515 g, 0.015 mol) were added to ethyl acrylate (25 mL) at 80 °C. The \(p\)-methoxybenzaldehyde (3.404 g, 25 mmol) was then added dropwise. After stirring under a \(N_2\) atmosphere for 12 hours the ethyl acrylate was removed in vacuo. The residue was treated with dilute \(H_2SO_4\) and extracted with ether. After passing the crude mixture through a plug of silica the ketoester was isolated (2.040 g, 0.008 mol, 32 %).

MP: 48-50 °C

TLC: \(R_f\) 0.43 (5:1 hexanes-EtOAc)
$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 7.94-7.91 (dd, 2H, $J = 8.3$ Hz, H2’ and H6’), 6.91-6.88 (dd, 2H, $J = 8.3$ Hz, H3’ and H5’), 4.12 (q, 2H, $J = 7.2$ Hz, H1’), 3.23 (t, 2H, $J = 6.8$ Hz, H3), 2.71 (t, 2H, $J = 6.8$ Hz, H2), 1.23 (t, 3H, $J = 7.2$ Hz, H2’).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 196.4 (C4), 172.9 (C1), 163.4 (C4’), 130.2 (C2’, C6’), 129.6 (s, OCH$_2$CH$_3$), 113.6 (C3’, C5’), 60.5 (C1’), 55.4 (OCH$_3$), 33.0 (C3), 28.4 (C2), 14.2 (s, OCH$_2$CH$_3$).

EIMS: 236 (M$^+$, 10%), 191 (M$^+$ - OCH$_2$CH$_3$, 14%), 135 (M$^+$ - CH$_2$CH$_2$CO$_2$CH$_2$CH$_3$, 100%).

6.2.3 Lactonisation and Pinacol Coupling of γ-Ketoesters with SmI$_2$

To a solution of SmI$_2$ (2.4 equivalents, 0.096 mmol) in tetrahydrofuran (10 mL) under reflux (oil-bath temperature 75 °C) was added the γ-ketoester 2.2 (0.39 mmol) in tetrahydrofuran (2 mL). The resulting solution was heated under reflux for 8 hours, after which it was quenched with 0.2 mL of a 25% aqueous solution of NH$_4$Cl at room temperature. The volatile component of the mixture was removed in vacuo and the residue passed through a short filter column of silica. The crude products were finally purified by column chromatography.
Meso-2,2'-bis(2-phenyl-3,4-dihydro-5,(2H)-furanone) (2.6a)

Yield: 35% (total 79% from 2.2a)
35% (total 72% from 2.2b)

MP: 226-228 °C

TLC: $R_f$ 0.09 (DCM)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 7.56-7.52 (m, 4H), 7.41-7.37 (m, 6H), 2.81 (ddd, 2H, $J = 13.5, 10.6$ and 5.1 Hz), 2.37 (ddd, 2H, $J = 13.5, 7.6$ and 5.1 Hz), 2.11 (ddd, 2H, $J = 18.0, 10.6$ and 5.1 Hz), 1.31 (ddd, 2H, $J = 18.0, 10.6$ and 7.6 Hz).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 175.7, 139.3, 128.6, 128.5, 126.9, 88.8, 81.0, 28.1.

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3025, 1780, 1181.

HRMS: Found 323.1283. Calculated for C$_{20}$H$_{19}$O$_4$ 323.1283.

A HETCOR spectrum assisted the allocation of $^{13}$C NMR and $^1$H NMR peaks, while the APT experiment showed that C-5 was indeed a quaternary carbon.
**Rac-2,2'-bis(2-phenyl-3,4-dihydro-5(2H)-furanone (2.6a)**

![Image of molecular structure]

**Yield:** 44% (total 79% from 2.2a)
37% (total 72% from 2.2b)

**MP:** 176-178 °C

**TLC:** Rf 0.23 (DCM)

**1H NMR:** (300 MHz, CDCl$_3$) $\delta$H 7.32-7.20 (m, 6H), 6.98-6.96 (m, 4H), 3.05-2.96 (m, 2H), 2.80-2.70 (m, 2H), 2.42-2.19 (m, 4H).

**13C NMR:** (75 MHz, CDCl$_3$) $\delta$C 175.3, 137.7, 128.6, 127.5, 91.2, 30.0, 28.7.

**IR:** $\nu_{max}$ (CHCl$_3$)/cm$^{-1}$ 3024, 1795, 1180.

**HRMS:** Found 323.1283. Calculated for C$_{20}$H$_{19}$O$_4$ 323.1283.

**Meso-2,2'-bis[2-(4-chlorophenyl)-3,4-dihydro-5(2H)-furanone (2.6b)**

![Image of molecular structure]

**Yield:** 42% (total 87% from 2.2c)
45% (total 83% from 2.2d)

**MP:** 240-242 °C

**TLC:** Rf 0.45 (DCM)

**1H NMR:** (300 MHz, CDCl$_3$) $\delta$H 7.94 (d, 4H, $J = 8.9$ Hz), 7.38 (d, 4H, $J = 8.9$ Hz), 2.71 (ddd, 2H, $J = 13.4$, 10.7 and 5.9 Hz), 2.35 (ddd, 2H, $J = 13.4$, 10.6
and 6.9 Hz), 2.18 (ddd, 2H, $J = 17.9, 10.6$ and 5.9 Hz), 1.54 (ddd, 2H, $J = 17.9, 10.7$ and 6.9 Hz).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 175.0, 137.5, 135.1, 128.8, 128.4, 88.5, 31.0, 28.0.

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3019, 2935, 1793, 1636, 1201, 1069.

HRMS: Found 390.0426. Calculated for C$_{20}$H$_{16}$O$_4$Cl$_2$ 390.0425.

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*Rac-2,2’-bis[2-(4-chlorophenyl)-3,4-dihydro-5(2H)-furanone (2.6b)*

![Image of molecular structure]

Yield: 45% (total 87% from 2.2c)

38% (total 83% from 2.2d)

MP: 216-218 °C

TLC: $R_f$ 0.33 (DCM)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 7.22 (d, 4H, $J = 8.9$ Hz), 6.94 (d, 4H, $J = 8.9$ Hz), 2.93 (ddd, 2H, $J = 12.6, 9.8$ and 7.5 Hz), 2.76 (ddd, 2H, $J = 17.5, 9.8$ and 4.8 Hz), 2.37 (ddd, 2H, $J = 17.5, 9.8$ and 7.5 Hz), 2.22 (ddd, 2H, $J = 12.6, 9.8$ and 4.8 Hz).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 174.7, 136.2, 135.0, 128.7, 128.0, 90.4, 30.1, 28.5.

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3033, 2949, 1796, 1660, 1198, 1083.

HRMS: Found 390.0426. Calculated for C$_{20}$H$_{16}$O$_4$Cl$_2$ 390.0426.
Meso-2,2'-bis[2-(4-chlorophenyl)-4-hydro-3-methyl-5(2H)-furanone (2.6d)

Yield: 25% (total 55%)
MP: 198-200 °C
TLC: R_f 0.54 (5:1 hexanes-EtOAc)
^1H NMR: (300 MHz, CDCl_3) δ_H 7.56 (d, 4H, J = 8.4 Hz), 7.41 (d, 4H, J = 8.4 Hz), 2.66-2.58 (m, 2H), 1.87 (dd, 2H, J = 17.7 and 8.4 Hz), 1.76 (dd, 2H, J = 17.7 and 9.5 Hz), 0.95 (d, 6H, J = 6.9 Hz).
^13C NMR: (75 MHz, CDCl_3) δ_C 174.6, 135.1, 133.7, 128.7, 92.0, 36.7, 36.4, 17.8.
IR: ν_max (CHCl_3)/cm⁻¹ 3019, 1800, 1657, 1420, 1226, 1087.
HRMS: Found 419.0827. Calculated for C_{22}H_{20}O_4Cl_2 419.0817.

Rac-2,2'-bis[2-(4-chlorophenyl)-4-hydro-3-methyl-5(2H)-furanone (2.6d)

Yield: 30% (total 55%)
MP: waxy oil
TLC: R_f 0.41 (5:1 hexanes-EtOAc)
^1H NMR: (300 MHz, CDCl_3) δ_H 7.09 (s, 8H), 3.10-3.04 (m, 2H), 2.70 (dd, 2H, J = 17.7 and 8.6 Hz), 2.12 (dd, 2H, J = 17.7 and 12.6 Hz), 0.89 (d, 6H, J = 6.6 Hz).
$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$$_C$ 174.7, 134.8, 133.8, 128.0, 93.8, 36.7, 34.9, 17.7.
IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3436, 3026, 1800, 1659, 1424, 1191, 1087.
HRMS: Found 419.0821. Calculated for C$_{22}$H$_{20}$O$_4^{35}$Cl$_2$ 419.0817.

*Meso- and Rac-2,2'-bis[2-(4-methoxyphenyl)-3,4-dihydro-5(2H)-furanone(2.6e)*

Yield: 86% (2:1 Racemic:meso)
P: 204-206 °C
TLC: $R_f$ 0.52 (1:1 hexanes-EtOAc)
$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$$_H$ 7.41 (d, 4H, $J$ = 9.0 Hz), 6.89 (d, 8H, $J$ = 9.0 Hz), 6.74 (d, 4H, $J$ = 9.0 Hz), 3.78 (s, 3H), 3.76 (s, 3H), 2.94 (ddd, 2H, $J$ = 12.8, 9.7 and 7.6 Hz), 2.79-2.64 (m, 4H), 2.38-2.26 (m, 4H), 1.41 (ddd, 2H, $J$ = 18.0, 10.6 and 7.4 Hz).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$$_C$ 175.9, 175.5’, 159.5, 159.4’, 131.2, 129.6’, 128.9, 128.1’, 113.7, 112.8’, 91.1’, 88.9, 55.2, 55.2’, 31.0, 29.8’, 28.8’, 28.2.
HRMS: Found 383.1494. Calculated for C$_{22}$H$_{23}$O$_6$ 383.1495.
6.3 PINACOL COUPLING WITH SAMARIIUM DIODDE

6.3.1 OXIME STUDIES

2,3,5-tri-\(O\)-Benzyl-D-arabinose-\(O\)-methyl oxime (3.2)

\(\text{\textit{2,3,5-tri-}\(O\)-Benzyl-D-arabinofuranose (100 mg, 0.24 mmol) was dissolved in dry pyridine (1 mL) and stirring was initiated. To this solution was added }\(O\)-methyl hydroxylamine hydrochloride (26 mg, 0.31 mmol). The reaction was allowed to stir at room temperature for 6 hours. The desired oxime was obtained in 100\% yield (110 mg, 0.24 mmol, 100\%).}

TLC: \(R_f\) 0.70 (2:1 hexanes-EtOAc)

\(^1\text{H NMR:}\) (300 MHz, CDCl\(_3\)) \(\delta_H\) (major and \textit{minor} isomers) 7.44 (d, 1H, \(J = 7.8\) Hz, H1), 7.38-7.18 (m, 30H, 5H \(\times\) 3 aromatics, 5H \(\times\) 3 aromatics), 6.91 (d, 1H, \(J = 6.0\) Hz, H1), 4.93 (dd, 1H, \(J = 6.0\) and 3.0 Hz, H2), 4.66-4.39 (m, 14H, OCH\(_2\)Ph \(\times\) 3, OCH\(_2\)Ph \(\times\) 3, H2, H3), 4.27 (dd, 1H, \(J = 8.0\) and 3.8 Hz, H3), 4.03-3.99 (m, 2H, H4 and H4), 3.87 (s, 3H, OCH\(_3\)), 3.85 (s, 3H, OCH\(_3\)), 3.80 (dd, 1H, \(J = 7.2\) and 3.0 Hz, H5), 3.67 (dd, 1H, \(J = 7.2\) and 3.9 Hz, H5), 2.66 (d, 1H, \(J = 6.3\) Hz, OH), 2.58 (d, 1H, \(J = 6.6\) Hz, OH).

\(^{13}\text{C NMR:}\) (75 MHz, CDCl\(_3\)) \(\delta_C\) 151.2 (C1), 148.3 (C1), 138.6 (ipso), 137.8 (ipso), 137.6 (ipso), 137.2 (ipso), Aromatics - 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 80.1 (OCH\(_2\)Ph), 78.8 (OCH\(_2\)Ph), 76.5 (OCH\(_2\)Ph), 74.1 (OCH\(_2\)Ph), 74.0 (OCH\(_2\)Ph), 73.4 (OCH\(_2\)Ph), 73.4 (C3), 72.4 (C3),
2,3,5-tri-O-Benzyl-d-arabino-pentos-4-ulose-O-methyloxime (3,3)

![Chemical Structure](image)

To a solution of 2,3,5-tri-O-benzyl-d-arabinose-O-methyloxime (100 mg, 0.22 mmol) in dry DCM (1 mL) was added Dess-Martin Periodinane (122 mg, 0.288 mmol) the reaction mixture was allowed to stir at room temperature for approximately 30 minutes, monitoring by TLC to completion. The solvent was removed in vacuo and the residue was purified by chromatography to afford the title compound as a colourless oil (94 mg, 0.21 mmol, 96%).

**TLC:** \( R_f \) 0.35 (5:1 hexanes-EtOAc)

**\(^1\)H NMR:** (300 MHz, CDCl\(_3\)) \( \delta \)H (major and minor isomers) 7.38 (d, 1H, \( J = 7.5 \) Hz, H1), 7.36-7.20 (m, 30H, 5H × 3 aromatics, 5H × 3 aromatics), 6.84 (d, 1H, \( J = 5.4 \) Hz, H1), 4.97 (dd, 1H, \( J = 5.4 \) and 3.2 Hz, H2), 4.62-4.23 (m, 16H, OCH\(_2\)Ph × 3, H5, H2, OCH\(_2\)Ph × 3, H5, H3), 4.11 (d, 1H, \( J = 3.9 \) Hz, H3), 3.85 (s, 3H, OCH\(_3\)), 3.78 (s, 3H, OCH\(_3\)).

**\(^13\)C NMR:** (75 MHz, CDCl\(_3\)) \( \delta \)C 206.5 (C4), 206.2 (C4), 149.8 (C1), 146.8 (C1), 137.1 (ipso), 137.0 (ipso), 136.7 (ipso), 136.6(ipso), 136.4 (ipso), 136.3
(ipso), Aromatics - 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.6, 84.4 (OC\textsubscript{2}H\textsubscript{2}Ph), 83.1 (OC\textsubscript{2}H\textsubscript{2}Ph), 76.5 (OC\textsubscript{2}H\textsubscript{2}Ph), 74.5 (OC\textsubscript{2}H\textsubscript{2}Ph), 74.3 (OC\textsubscript{2}H\textsubscript{2}Ph), 74.2 (OC\textsubscript{2}H\textsubscript{2}Ph), 74.1 (C5), 73.2 (C5), 73.2 (C3), 73.2 (C3), 72.7 (C2), 71.4 (C2), 62.1 (OC\textsubscript{2}H\textsubscript{3}), 61.9 (OC\textsubscript{2}H\textsubscript{3}).

IR: $\nu_{\text{max}}$(CHCl\textsubscript{3})/cm$^{-1}$ 3026, 1160, 1427, 1208, 1083.

HRMS: Found 447.2046. Calculated for C\textsubscript{27}H\textsubscript{29}NO\textsubscript{5} 447.2045.

EIMS: 447 (M$^+$, 1%), 416 (M$^+$ - OCH\textsubscript{2}, 1%), 91 (C\textsubscript{7}H\textsubscript{7}, 100%).

2,3,5-tri-O-Benzyl-4-hydroxy-D-arabinose oxime (3,5)

The general procedure to form an oxime (3,2) was carried out using hydroxylamine hydrochloride as an oxime source and 2,3,5-tri-O-benzyl-D-arabinofuranose (100 mg, 0.24 mmol), the substrate onto which the oxime is going to be introduced. The desired oxime was obtained in 100% yield (105 mg, 0.24 mmol, 100%).

TLC: $R_f$ 0.70 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl\textsubscript{3}) $\delta$\textsubscript{H} (major and minor isomers) 9.69(s, 1H, N-OH), 9.41 (s, 1H, N-OH), 7.57 (d, 1H, $J = 7.9$ Hz, H1), 7.42-7.23 (m, 30H, 5H $\times$ 3 aromatics, 5H $\times$ 3 aromatics), 7.04 (d, 1H, $J = 6.2$ Hz, H1), 5.14 (dd, 1H, $J = 6.2$ and 3.1 Hz, H2), 4.68-4.42 (m, 14H, OCH\textsubscript{2}Ph $\times$ 3, OCH\textsubscript{2}Ph $\times$ 3, H2, H3), 4.35 (dd, 1H, $J = 7.9$ and 3.8 Hz, H3), 4.16-4.06 (m, 2H, H4 and H4), 3.93 (dd, 1H, $J = 7.5$ and 3.0 Hz, H5a), 3.76-3.64 (m, 3H, H5a and H5b), 3.42 (br s, 1H, OH), 3.14 (br s, 1H, OH).
13C NMR:  (75 MHz, CDCl$_3$) $\delta_{C}$ 151.6 (C1), 149.4 (C1), 137.4 (ipso), 137.3 (ipso), 137.2 (ipso), 137.1 (ipso), 136.9 (ipso and ipso), Aromatics - 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 127.4, 127.4, 127.3, 79.8 (OCH$_2$Ph), 78.7 (OCH$_2$Ph), 76.4 (OCH$_2$Ph), 76.3 (OCH$_2$Ph), 73.9 (OCH$_2$Ph), 73.1 (C3), 73.0 (OCH$_2$Ph), 72.1 (C3), 71.6 (C5), 71.0 (C5), 70.7 (C4), 70.6 (C4), 69.6 (C2), 69.5 (C2).

IR:  $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3570, 2935, 2866, 1657, 1400, 1345, 1222, 1156, 975.

HRMS:  Found 435.2050.  Calculated for C$_{26}$H$_{29}$NO$_5$ 435.2046.

2,3,5-tri-<i>O</i>-Benzyl-<i>D</i>-arabinose-<i>O</i>-(<i>tert</i>-butyldimethylsilyl)-oxime (3.6)

A solution of 2,3,5-tri-<i>O</i>-benzyl-<i>D</i>-arabinose oxime (100 mg, 0.238 mmol) and imidazole (10% m/m) in dry pyridine (1 mL) was cooled to 0 °C. To this solution was added <i>t</i>-butyldimethylsilylchloride (48 mg, 0.32 mmol), after which the solution was allowed to warm to room temperature. The reaction mixture was allowed to stir for a further 6 hours, after which the solvent was removed in vacuo, and the residue was purified by flash chromatography (5:1 hexanes-EtOAc) to afford the silyl ether (104 mg, 0.189 mmol, 88%).

TLC:  $R_f$ 0.70 (2:1 hexanes-EtOAc)

$^1$H NMR:  (300 MHz, CDCl$_3$) $\delta_{H}$ (major and <i>minor</i> isomers) 7.60 (d, 1H, $J$ = 7.8 Hz, H1), 7.38-7.22 (m, 30H, 5H × 3 aromatics, 5H × 3 aromatics), 7.15 (d, 1H, $J$ = 5.7 Hz, H1), 5.10 (dd, 1H, $J$ = 5.9 and 2.9 Hz, H2), 4.67-4.37 (m, 14H, OCH$_2$Ph × 3, OCH$_2$Ph × 3, H2, H3), 4.31 (dd, 1H, $J$ = 7.8 and 3.9 Hz, H3), 4.08-3.99 (m, 2H, H4 and H4), 3.88 (dd, 1H, $J$ = 7.5 and 2.7 Hz, H4).
H5a), 3.70 (dd, 1H, J = 7.5 and 2.7 Hz, H5a), 3.62-3.57 (m, 2H, H5b and H5b), 2.71 (d, 1H, J = 5.7 Hz, OH), 2.61 (d, 1H, J = 6.9 Hz, OH), 0.97 (s, 9H, C(CH$_3$)$_3$), 0.21 (s, 3H, SiC$_3$H$_3$), 0.20 (s, 3H, SiC$_3$H$_3$), 0.19 (s, 3H, SiC$_3$H$_3$), 0.18 (s, 3H, SiC$_3$H$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 156.0 (C1), 152.9 (C1), 137.8 (ipso), 137.7 (ipso), 137.6 (ipso and ipso), 136.9 (ipso and ipso), Aromatics - 128.3, 128.2, 128.2, 128.1, 128.7, 128.0, 127.8, 127.8, 127.7, 127.6, 127.5, 79.9 (OCH$_2$Ph), 78.9 (OCH$_2$Ph), 76.2 (OCH$_2$Ph), 74.0 (OCH$_2$Ph), 73.9 (OCH$_2$Ph), 73.3 (C3), 73.2 (OCH$_2$Ph), 72.4 (C3), 72.0 (C5), 71.0 (C5), 70.7 (C4), 70.6 (C4), 69.6 (C2), 69.7 (C2), 64.1 (C(CH$_3$)$_3$), 25.9 (C(CH$_3$)$_3$), 18.2 C(CH$_3$)$_3$, 17.9 C(CH$_3$)$_3$, -5.19 (SiC$_3$H$_3$), -5.26 (SiC$_3$H$_3$).

IR: $\nu_{max}$(CHCl$_3$)/cm$^{-1}$ 3575, 2935, 2866, 2824, 1657, 1345, 1222, 975.

HRMS: Found 550.2987. Calculated for C$_{32}$H$_{44}$NO$_5$Si 550.2989.

2,3,5-tri-O-Benzyl-D-arabino-pentos-4-ulose-O-(tert-butyldimethylsilyl)-oxime (3.7)

The general route for Dess-Martin oxidation (3.3) was carried out on 2,3,5-tri-O-benzyl-D-arabinose-O-(tert-butyldimethylsilyl)-oxime (100 mg, 0.182 mmol). The product was purified by column chromatography (5:1 hexanes-EtOAc) to afford the oxidised product (81 mg, 0.147 mmol, 81%).

TLC: $R_f$ 0.52 (5:1 hexanes-EtOAc)
\begin{align*}
\text{H NMR: } & \delta_H \text{ (300 MHz, CDCl}_3) \text{ H} 7.31-7.22 \ (m, \ 15H, \ 5H \times 3 \text{ aromatics}), \ 7.08 \ (d, \ 1H, \ J = 5.2 \ Hz, \ H1), \ 5.12 \ (dd, \ 1H, \ J = 5.2 \ and \ 2.9 \ Hz, \ H2), \ 4.56-4.19 \ (m, \ 9H, \ OCH}_3\text{Ph \times 3, \ H3, \ H5a, \ H5b), \ 0.91 \ (s, \ 9H, \ C(CH}_3)_3, \ 0.16 \ (s, \ 3H, \ SiC \text{H}_3), \ 0.14 \ (s, \ 3H, \ SiC \text{H}_3). \\
1^3C \text{ NMR: } & \delta_C \text{ (75 MHz, CDCl}_3) \text{ C} 206.3 \ (C4), \ 154.4 \ (C1), \ 137.1 \ (ipso), \ 136.5 \ (ipso), \ 136.4 \ (ipso), \text{ Aromatics} - 128.4, \ 128.3, \ 128.2, \ 128.1, \ 128.0, \ 127.9, \ 127.8, \ 127.7, \ 83.4 \ (C5), \ 74.3 \ (C3), \ 74.2 \ (C2), \ 73.2 \ (OCH}_2\text{Ph), \ 73.1 \ (OCH}_2\text{Ph), \ 72.7 \ (OCH}_2\text{Ph), \ 25.9 \ (C(CH}_3)_3, \ 18.0 \text{ (SiCCH}_3), -5.22 \ (\text{SiCCH}_3), -5.27 \ (\text{SiCCH}_3). \\
IR: & \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \ 3564, \ 2930, \ 2867, \ 1656, \ 1220, \ 869. \\
HRMS: & \text{Found} \ 550.2975. \ \text{Calculated for} \ C_{32}H_{44}NO_5Si \ 550.2989. \\
EIMS: & 549 (M+1, 25\%), \ 434 (M+1 - \text{TBDMS, 26\%}), \ 181 (100\%).
\end{align*}

$2,3,5$-tri-$O$-Benzyl-$d$-arabinose-$O$-(tert-butyldiphenylsilyl)-oxime ($3.9$)

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{structure.png}
\caption{$2,3,5$-tri-$O$-Benzyl-$d$-arabinose-$O$-(tert-butyldiphenylsilyl)-oxime ($3.9$)}
\end{figure}

A solution of $2,3,5$-tri-$O$-benzyl-$d$-arabinose oxime (500 mg, 1.188 mmol) and imidazole (10\% m/m) in dry pyridine (2 mL) was cooled to $0$ °C. To this solution was added $t$-butyldiphenylsilylchloride (0.37 mL, 1.46 mmol), after which the reaction mixture was allowed to warm to room temperature. The reaction mixture was allowed to stir for a further 6 hours. The solvent was removed in vacuo, and the residue was purified by flash chromatography (5:1 hexanes-EtOAc) to afford the silyl ether (630 mg, 0.936 mmol, 79\%).

\text{TLC: } \text{R}_f \ 0.39 \ (5:1 \text{ hexanes-EtOAc)}
\( ^1 \text{H NMR:} \) (300 MHz, CDCl_3) \( \delta \)H 7.76 (d, 1H, \( J = 8.1 \) Hz, H1), 7.34-7.44 and 7.41-7.14 (m, 25H, aromatics), 4.56-4.35 and 4.25-4.20 and 4.03-3.98 and 3.68-3.53 and 2.66-2.59 (m, 12H, OCH_2Ph \times 3, H2, H3, H4, H5a, H5b and OH), 1.39 (s, 9H, C(CH_3)_3).

\( ^{13} \text{C NMR:} \) (75 MHz, CDCl_3) \( \delta \)C 154.1 (C1), 138.6 (ipso \times 2), 136.9 (ipso), 135.4 (meta Si), 133.2 (ipso Si), 129.6 (ortho Si), Aromatics - 128.3, 128.1, 127.9, 127.8, 127.6, 127.5, 79.9 (C2), 75.8 (OCH_2Ph), 73.8 (OCH_2Ph), 73.3 (OCH_2Ph), 70.9 (C3), 70.6 (C4), 70.0 (C5), 27.1 (C(CH_3)_3), 19.3 (C(CH_3)_3).

IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3575, 2935, 2866, 2824, 1657, 1345, 1222, 975.

EIMS: 674 (M+1, 20%), 91 ([CH_2Ph]+, 100%)

2,3,5-tri-O-Benzyl-D-arabino-pentos-4-ulse-O-(tert-butyldiphenylsilyl)-oxime (3.10)

The general route for Dess-Martin oxidation (3.3) was carried out on 2,3,5-tri-O-benzyl-D-arabinose-O-(tert-butyldiphenylsilyl)-oxime (500 mg, 0.743 mmol). The product was purified by column chromatography (5:1 hexanes-EtOAc) to afford the oxidised product (498 mg, 0.743 mmol, 98%).

TLC: \( R_f 0.47 \) (5:1 hexanes-EtOAc)

\( ^1 \text{H NMR:} \) (300 MHz, CDCl_3) \( \delta \)H 7.77 (d, 1H, \( J = 7.5 \) Hz, H1), 7.69-7.63 and 7.41-7.19 and 7.09-7.06 (m, 25H, aromatics and TBDPS aromatics), 4.60 (t, 1H, \( J = 11.6 \) Hz, H2), 4.52-4.10 (m, 11H, OCH_2Ph \times 3, H3, H4, H5a, H5b and OH), 1.13 (s, 9H, C(CH_3)_3).
\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \(\delta\)C 206.1 (C4), 152.9 (C1), 137.0 (ipso), 136.5 (ipso), 136.4 (ipso), 135.4 (meta Si), 132.9 (ipso Si), 132.7 (ipso Si), 129.7 (ortho Si), Aromatics - 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5, 84.0 (C2), 75.3 (C3), 74.3 (OCH\(_2\)Ph), 74.0 (OCH\(_2\)Ph), 73.2 (OCH\(_2\)Ph), 71.0 (C5), 27.1 (C(CH\(_3\))\(_3\)), 19.2 (C(CH\(_3\))\(_3\)).

IR: \(\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}\) 3574, 2920, 2867, 1657, 1655, 1330, 975.

CIMS: 672 (M+1, 100%), 654 (M+1 - H\(_2\)O, 6%), 564 (M\(^+\) - OBn, 24%), 458 (M\(^+\) - 2OBn, 5%), 416 (M\(^+\) - OTBDPS, 29%).

6.3.2 STUDIES ON AN IMPROVED RADICAL ACCEPTOR

2,3,5-tri-\(O\)-Benzyl-\(N\)-phenyl-d-arabinofuranosylamine (3.12)

\[
\begin{array}{c}
\text{OBn} \\
\text{BnO} \\
\text{NHPh} \\
\text{OBn}
\end{array}
\]

2,3,5-tri-\(O\)-benzyl arabinofuranose (100 mg, 0.24 mmol) was dissolved in dry pyridine (1 mL) and stirring was initiated. To this solution was added analine (28 \(\mu\)L, 0.312 mmol). The reaction was allowed to stir at room temperature overnight hour. Leaving reaction for a further four days did not result in any of the desired imine forming. On chromatography (5:1 hexanes-EtOAc) the desired imine was not obtained, instead a cyclised product was obtained (98 mg, 0.197 mmol, 92%).

TLC: \(R_f\) 0.40 (5:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \(\delta\)H 7.50-7.31 (m, 30H, aromatics and aromatics), 7.26 (dd, 2H, \(J = 8.1\) and 7.8 Hz, \textit{para} NHPh and \textit{para} NHPh), 6.90-6.80 (m, 142
8H, ortho and meta aromatics and ortho and meta aromatics, 5.62 (d, 1H, J = 10.3 Hz, H1), 5.53 (dd, 1H, J = 8.9 and 4.2 Hz, H1), 5.03 (d, 1H, J = 8.9 Hz, NH), 4.86 (d, 1H, J = 10.3 Hz, NH), 4.69-4.53 (m, 13H, OCH$_2$Ph ×3, OCH$_2$Ph ×3, H4), 4.42-4.30 (m, 1H, H4), 4.22-4.10 (m, 4H, H2, H3, H2 and H3), 3.72-3.61 (m, 4H, H5a, H5b, H5a and H5b).

$^{13}$C NMR: (75 MHz, CDCl$_3$) δC (Mixture isomers) 145.2 (ipso NPh), 144.9(ipso NPh), 138.0 (ipso and ipso), 137.6 (ipso), 137.4 (ipso), 137.2 (ipso), 137.0 (ipso), Aromatics and meta NPh and meta NPh – 129.1, 128.4, 128.3, 128.2, 128.1, 127.9, 127.7, 127.6, 127.5, 127.4, 119.0 (para NPh), 118.8 (para NPh), 114.3 (ortho NPh × 2), 114.1 (ortho NPh × 2), 88.1 (C1), 86.3 (C4), 84.5 (C1), 83.3 (C3), 82.6 (C4), 82.4 (C3), 80.8 (C2), 79.9 (C2), 73.2 (C5 and C5), 72.1 (OCH$_2$Ph), 71.8 (OCH$_2$Ph), 71.7 (OCH$_2$Ph), 71.5 (OCH$_2$Ph), 70.7 (OCH$_2$Ph), 70.1 (OCH$_2$Ph).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3693, 2945, 1607, 1510, 1456, 1311, 1260, 1235, 1223, 738.

CIMS: 496 (M+1, 100%), 403 (M$^+$ - NPh, 1%), 388 (M$^+$ - OBn, 8%), 91 (Bn, 32%).

Methyl $\alpha,\beta$-d-ribofuranoside $^3$ (3.13)

D-Ribose (100 mg, 0.26 mmol) was dissolved in methanol (1 mL) and cooled to 0 °C. A catalytic amount of conc. H$_2$SO$_4$ (10 µL) was added to the cooled solution. The reaction mixture was allowed to stir for a further 10 minutes at 0 °C and then placed in the refrigerator overnight. The reaction mixture was neutralised with NaHCO$_3$ and the solvent removed in vacuo.
Due to the complexity of the spectra obtained the compound was characterised at the next step of the synthesis.

Methyl 2,3,5-tri-O-benzyl-α-D-ribofuranoside⁴ (3.14a)

To a stirred solution of methyl α,β-D-ribofuranoside (1.5g, 10 mmol Ribose) in DMF (14 mL) at 0 °C, was added sodium hydride (1.5 equivalents per hydroxide). The reaction mixture was allowed to stir at 0 °C until the evolution of hydrogen gas had ceased (approximately 30 minutes). Benzyl bromide (5 equivalents per hydroxide) was added dropwise over 30 minutes. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction was once again cooled to 0 °C. The excess sodium hydride was then quenched with MeOH (5 mL) and Et₃N (2 mL) was added to destroy the excess BnBr. After stirring for a further 4 hours, the reaction mixture was diluted with EtOAc (20 mL) and washed with water (3 × 15 mL). After drying over sodium sulfate the solvent was removed in vacuo and the residue was purified by column chromatography (10:1 hexanes-EtOAc) to afford the desired benzylated product in low yield (Major isomer (955 mg, 2.20 mmol, 22% over two steps).

TLC:  R₇ 0.43 (5:1 hexanes-EtOAc)

¹H NMR:  (300 MHz, CDCl₃) δH 7.37-7.30 (m, 15H, OCH₂Ph × 3 aromatics), 4.94 (s, 1H, H1), 4.71-4.46 (A series of overlapping d, 6H, OCH₃Ph × 3), 4.39-4.34 (m, 1H, H4), 4.04 (dd, 1H, J = 7.2 and 4.8 Hz, H3), 3.86 (d, 1H, J =
4.8 Hz, H2), 3.63 (dd, 1H, J = 10.5 and 3.6 Hz, H5a), 3.53 (dd, 1H, J = 10.5 and 6.0 Hz, H5b), 3.33 (s, 3H, OCH3).

13C NMR: (75 MHz, CDCl3) δC 138.2 (ipso), 137.7 (ipso × 2), Aromatics – 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 127.4, 106.2 (C1), 80.4 (C4), 79.6 (C3), 78.3 (C2), 73.1 (OCH2Ph), 72.3 (OCH2Ph), 72.2 (OCH2Ph), 71.3 (C5), 55.0 (OCH3).

IR: νmax(CHCl3)/cm⁻¹ 3022, 2869, 1702, 1499, 1224, 1212, 949, 776.

EIMS: 434 (M⁺, 5%), 402 (M⁺ - CH3OH, 10%), 91 (CH2Ph⁺, 100%).

Methyl 2,3,5-tri-O-benzyl-β-D-ribofuranoside (3.14b)

To a solution of methyl α,β-D-ribofuranoside (190 mg, 1.16 mmol) in benzyl bromide (1.5 mL) was added crushed potassium hydroxide (250 mg) and tetrabutylammonium bromide (25 mg). The reaction was allowed to stir at room temperature overnight. Diethyl ether was added and the reaction mixture decanted into a separating funnel. After washing with water, drying over sodium sulphate solvent was removed in vacuo. Column chromatography gave the desired benzylated product in low yields.

TLC: Rf 0.18 (10:1 hexanes-EtOAc)

1H NMR: (300 MHz, CDCl3) δH 7.36-7.26 (m, 15H, OCH2Ph × 3 aromatics), 5.10 (s, 1H, H1), 4.55-4.37 (A series of overlapping d, 6H, OCH2Ph × 3), 4.42-4.33 (m, 1H, H4), 4.09 (dd, 1H, J = 7.1 and 4.8 Hz, H3), 3.92 (d, 1H, J = 4.8 Hz, H2), 3.65 (dd, 1H, J = 10.7 and 3.6 Hz, H5a), 3.30 (s, 3H, OCH3) 3.54 (dd, 1H, J = 10.7 and 5.7 Hz, H5b).
$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 138.6 (ipso), 138.1 (ipso), 137.9 (ipso), Aromatics – 128.5, 128.2, 127.9, 127.8, 127.7, 127.5, 127.4, 104.3 (C1), 80.5 (C4), 79.6 (C3), 78.5 (C2), 73.1 (OCH$_2$Ph), 72.4 (OCH$_2$Ph), 72.1 (OCH$_2$Ph), 69.5 (C5), 55.8 (OCH$_3$).

IR: $\nu_{\text{max}}$(CHCl$_3$/cm$^{-1}$) 3023, 2870, 1702, 1499, 1224, 1212, 949, 777.

EIMS: 434 (M$^+$, 5%), 402 (M$^+$ - CH$_3$OH, 10%), 91 (Bn, 100%).
2,3,5-tri-O-Benzyl-d-ribofuranoside (3.15)

To a solution of the protected β-D-pentafuranoside (5.0 mmol) in dioxane (40 mL) was added 0.1 N hydrochloric acid (10 mL). The solution was boiled gently for 2 hours, with 10 mL of distillate being collected. The solution was made up to its original volume with dioxane and boiled gently for an additional hour, after which the excess acid was neutralised with Et₃N and the solvent removed in vacuo. The residue was dissolved in ethyl acetate (20 mL) and washed with water (3 × 10 mL) and dried over MgSO₄. Removal of the solvent followed by chromatography afforded the title compounds as colourless oils (α,β-mixtures, α-isomer: major product).

Yield: 350 mg, 0.828 mmol, 72% over two steps
TLC: Rₐ 0.48 (2:1 hexanes-EtOAc)

¹H NMR: (300 MHz, CDCl₃) δH (Major isomer) 7.37-7.23 (m, 15H, OCH₂Ph × 3 aromatics), 5.31 (d, 1H, J = 6.6 Hz, H1), 4.74-4.37 (A series of overlapping d, 6H, OCH₂Ph × 3), 4.25-4.18 (m, 1H, H4), 3.98 (m, 1H, H3), 3.86 (d, 1H, J = 4.5 Hz, H2), 3.67 (dd, 1H, J = 10.3 and 2.4 Hz, H5a), 3.47 (dd, 1H, J = 10.3 and 3.0 Hz, H5b), 3.39 (d, 1H, J = 6.6 Hz, OH).

¹³C NMR: (75 MHz, CDCl₃) δC 137.5 (ipso), 137.3 (ipso), 137.1 (ipso), Aromatics – 128.4, 128.3, 128.2, 127.9, 127.8, 127.6, 127.4, 100.3 (C1), 77.7 (C4), 77.6 (C3), 77.1 (C2), 73.4 (OCH₂Ph), 72.3 (OCH₂Ph), 72.2 (OCH₂Ph), 69.3 (C5).

IR: νmax(CHCl₃)/cm⁻¹ 3499, 3447, 3022, 2870, 1670, 1640, 1609, 913, 700.
CIMS: 421 (M+1, 1%), 403 (M+1 - H2O, 17%), 313 (M+ - OBN, 6%), 295 (M+ - OBN - H2O, 100%), 206 (M+ - 2OBN, 3%), 181 (C14H13, 78%), 91 (Bn, 71%).

\[ \text{N-(2,3,5-tri-O-benzyl-D-arabinofuranosyl)-para-toluenesulfonylhydrazine (3.16)} \]

2,3,5-tri-O-Benzyl arabinofuranose (100 mg, 0.24 mmol) was dissolved in dry pyridine (1 mL) and stirring was initiated. To this solution was added para-toluenesulfonylhydrazide (58 mg, 0.312 mmol). The reaction was allowed to stir at room temperature overnight hour. Leaving reaction for a further four days did not result in any of the desired oxime forming. The desired imine was not obtained after chromatography (2:1 hexanes-EtOAc), instead a cyclised product was obtained (111 mg, 0.189 mmol, 79%).

TLC: \( R_f 0.36 \) (2:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \( \delta_H 7.69 \) (d, 1H, \( J = 7.8 \) Hz, H1), 7.60 (d, 1H, \( J = 7.5 \) Hz, H1), 7.15-7.03 (m, 30H, aromatics), 6.82 (s, 2H, NH), 6.35 (s, 2H, NH), 4.47-4.01 (m, 13H, OCH\(_2\)Ph \times 3, OCH\(_2\)Ph \times 3 and H4), 3.83-3.76 (m, 1H, H4), 3.67-3.56 (m, 4H, H2, H3, H2 and H3), 3.40-3.22 (unresolved dd, 4H, H5a, H5b, H5a and H5b), 2.19 (s, 3H, PhCH\(_3\)), 1.88 (s, 3H, PhCH\(_3\)).

\(^1^3\)C NMR: (75 MHz, CDCl\(_3\)) \( \delta_C \) (Mixture isomers) 143.7 (ipso SO\(_2\)Ph), 143.4(ipso SO\(_2\)Ph), 137.5 (ipso), 137.4 (ipso), 137.3 (ipso and ipso), 137.2 (ipso), 135.3 (ipso PhMe), 135.2 (ipso PhMe), 129.3 (para and para), Aromatics
- 128.2, 127.8, 127.7, 127.6, 127.5, 94.2 (C1), 90.3 (C1), 83.8 (C4), 82.3 (C3), 81.8 (C4), 81.6 (C3), 80.3 (C2), 79.8 (C2), 73.3 (OCH₂Ph), 73.2 (OCH₂Ph), 71.8 (OCH₂Ph and OCH₂Ph), 71.7 (OCH₂Ph), 71.5 (OCH₂Ph), 70.5 (C5), 69.7 (C5).

IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3306, 3070, 2930, 2870, 1601, 1498, 1456, 1332, 1167, 911, 815.

EIMS: 588 (M⁺, 4%), 481 (M⁺ - OBn, 3%), 433 (M⁺ - SO₂PhCH₃, 17%), 405 (M+1 - NHNHSO₂PhCH₃, 100%).

2,3,5-tri-(Benzyloxy)-4-hydroxy-pentanenitrile (3.17) and
4-Acetoxy-2,3,5-tri-(benzyloxy)-pentanenitrile (3.18)

2,3,5-tri-O-Benzyl-4-O-hydroxy-D-arabinose oxime ether (3.5) (200 mg, 0.459 mmol) was dissolved acetic anhydride (1 mL) and stirring was initiated. The reaction was allowed to stir at room temperature for 1 hour. Removal of solvent in vacuo followed by column chromatography (4:1 hexanes-EtOAc) gave the desired nitrile (3.17) (15%) was obtained in low yield, in addition to the acetylated product (3.18) (10%).

(2S,3S)-2,3,5-tri-(Benzyloxy)-4-hydroxy-pentanenitrile (3.17)

TLC: \( R_f \) 0.40 (4:1 hexanes-EtOAc)

\(^1\text{H NMR:} \) (300 MHz, CDCl₃) \( \delta_H \) 7.33-7.28 (m, 15H, aromatics), 4.89 (d, 1H, \( J = 11.4 \text{ Hz, } \text{OCH}_2 \text{H}_6 \text{Ph} \)), 4.85 (d, 1H, \( J = 11.4 \text{ Hz, } \text{OCH}_2 \text{H}_6 \text{Ph} \)), 4.63-42 (m
of d, 4H, OCH$_2$Ph $\times$ 2), 4.51 (d, 1H, $J$ = 2.9 Hz, H2), 4.01-3.90 (m, 1H, H4), 3.78 (dd, 1H, $J$ = 8.1 and 2.9 Hz, H3), 3.61 (dd, 1H, $J$ = 9.6 and 3.8 Hz, H5a), 3.56 (dd, 1H, $J$ = 9.6 and 4.2 Hz, H5b), 2.37 (d, 1H, $J$ = 6.6 Hz, OH).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 137.3 (ipso), 136.9 (ipso), 135.4 (ipso), Aromatics - 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 117.3 (C1), 78.8 (C3), 74.6 (OCH$_2$Ph), 73.4 (OCH$_2$Ph), 72.8 (OCH$_2$Ph), 69.8 (C5), 68.9 (C4), 67.2 (C2).

IR: $\nu_{max}$(CHCl$_3$)/cm$^{-1}$ 3070, 3022, 2870, 1655, 1540, 1526, 804.

EIMS: 418 (M+1, 25%), 391 (M$^+$ - CN, 1%), 343 (M+1 - Bn, 22%), 311 (M+1 - OBn, 12%), 181 (C$_{14}$H$_{13}$, 98%), 91 (Bn, 100%).

(2S,3S)-4-Acetoxy-2,3,5-tri-(benzyloxy)-pentanenitrile (3.18)

TLC: $R_f$ 0.51 (4:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 7.32-7.27 (m, 15H, aromatics), 5.11 (dt, 1H, $J$ = 7.8 3.6 Hz, H4), 4.87 (d, 1H, $J$ = 11.7 Hz, OCH$_3$H$_3$Ph), 4.85 (d, 1H, $J$ = 10.7 Hz, OCH$_3$H$_3$Ph), 4.64 (d, 1H, $J$ = 11.7 Hz, OCH$_3$H$_3$Ph), 4.50 (d, 1H, $J$ = 10.7 Hz, OCH$_3$H$_3$Ph), 4.45 (s, 2H, OCH$_2$Ph), 4.26 (d, 1H, $J$ = 3.8 Hz, H2), 4.09 (dd, 2H, $J$ = 7.8 and 3.8Hz, H5a and H5b), 1.81 (s, 3H, OCCH$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 169.4 (OOCCH$_3$), 137.5 (ipso), 136.9 (ipso), 135.0 (ipso), Aromatics - 128.7, 128.6, 128.5, 128.3, 128.2, 128.0, 127.7, 127.6, 116.7 (C1), 76.7 (C3), 75.1 (OCH$_2$Ph), 73.2 (OCH$_2$Ph), 72.3 (OCH$_2$Ph), 70.6 (C5), 67.2 (C4), 66.8 (C2), 20.9 (OOCCH$_3$).
$\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3024, 293, 2876, 1745, 1615, 1562, 1220, 1213, 868, 790.

EIMS: 459 (M$^+$, 72%), 433 (M$^+$ - CN, 4%), 417 (M+1 - Ac, 13%), 343 (M+1 - CN - Bn, 53%), 235 (100%).

$(2S,3R)$-2,3,5-tri-(Benzyloxy)-4-oxopentanenitrile (3.19)

\[
\begin{align*}
\text{OBn} & \quad \text{CN} \\
\text{Bn} & \quad \text{OBn}
\end{align*}
\]

The general route for Dess-Martin oxidation (3.3) was carried out on 1-cyano-2,3,5-O-tris-phenylmethyl-4-O-hydroxy-D-arabinose (52 mg, 0.125 mmol). The product was purified by column chromatography (4:1 hexanes-EtOAc) (42 mg, 0.101 mmol, 82%).

TLC: $R_f$ 0.41 (4:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 7.45-7.10 (m, 15H, aromatics), 4.92-4.71 (m of d, 3H, OCH$_3$H$_3$Ph and OCH$_2$Ph), 4.63 (d, 1H, $J = 2.7$ Hz, H2), 4.58-4.34 (m of d, 3H, OCH$_3$H$_3$Ph and OCH$_2$Ph), 4.49 (d, 1H, $J = 3.0$ Hz, H3), 4.27 (d, 1H, $J = 4.7$ Hz, H5a), 4.25 (d, 1H, $J = 4.7$Hz, H5b).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 203.8 (C4), 136.7 (ipso), 136.6 (ipso), 134.6 (ipso), Aromatics - 128.7, 128.6, 128.5, 128.4, 128.0, 127.8, 127.7, 115.5 (C1), 81.6 (C3), 74.7 (OCH$_2$Ph), 74.0 (OCH$_2$Ph), 73.2 (OCH$_2$Ph), 72.8 (C5), 67.6 (C2).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3200, 1701, 1225, 1215, 787, 777, 760, 755, 744.

EIMS: 416 (M+1, 46%), 308 (M+1 - OBn, 36%), 202 (M+1 - 2OBn, 5%), 181 (C$_{14}$H$_{13}$, 43%), 107 (OBn, 24%), 91 (Bn, 100%).
6.3.3 1,4-DIKETONES AS PRECURSORS FOR CHIRAL CYCLOBUTANE-1,2-DIOLS

(2R,3S,4S)-1,3,4-tri-(benzyloxy)-nonane-2,5-diol (3.21)

Magnesium (173 mg, 7.13 mmol) was added to a flamed out two neck flask, fitted with a reflux condenser and a dropping funnel. A solution of butyl bromide (0.77 mL, 7.13 mmol) in THF (5 mL) was added dropwise to the magnesium with constant stirring. A small iodine crystal was added to initiate the reaction. An ice bath was used to cool the reaction and keep it at reflux temperature. After addition of all of the butyl bromide solution the reaction mixture was heated to 50 °C for 15 minutes.

Both Grignard reagent and substrate (300 mg, 0.71 mmol) in THF (3 mL) were cooled to 0 °C, the Grignard reagent was added dropwise to the sugar solution with constant stirring. The reaction was allowed to warm to room temperature. The solvent was removed in vacuo and the residue washed with NaHCO₃ and extracted with EtOAc. (Make an excess of Grignard and add until all starting material has been converted, monitor by TLC plates). The desired product was obtained in high yield as a colorless oil after column chromatography (3:1 hexanes-EtOAc) (326 mg, 0.168 mmol, 96%).

TLC: Rₜ 0.28 (3:1 hexanes-EtOAc)

¹H NMR: (300 MHz, CDCl₃) δH 7.38-7.31 (m, 15H, aromatics), 4.82-4.55 (m, 6H, OCH₂Ph), 4.16-4.11 (m, 1H, H2), 3.96-3.56 (m, 5H, H1a, H1b, H3, H4, H5), 3.40 (br s, OH), 3.35 (d, OH), 2.99 (d, OH, J = 5.4 Hz), 2.87 (br s, OH), 1.70-1.15 (m, 6H, (CH₂)₃CH₃), 0.94 (t, 3H, J = 7.1 Hz, (CH₂)₃CH₃).

¹³C NMR: (75 MHz, CDCl₃) δC (major and minor isomers) 137.8 (ipso), 137.7(ipso), 137.6 (ipso), 137.5 (ipso), 137.4 (ipso), Aromatics - 128.1, 128.0, 127.9,
127.8, 127.7, 127.6, 127.5, 127.4, 81.0 (C4), 80.4 (C4), 78.3 (C3), 77.8 (C3), 74.2 (C2), 73.5 (C5), 73.1 (C1 and C2), 73.0 (C5), 72.9 (C1), 71.0 (OCH₂Ph), 70.9 (OCH₂Ph), 70.7 (OCH₂Ph), 70.4 (OCH₂Ph), 70.1 (OCH₂Ph), 33.9 (C6), 33.3 (C6), 27.8 (C7), 27.7 (C7), 22.6 (C8), 22.5 (C8), 14.0 (C9), 13.9 (C9).

IR: \( \nu \text{max}(\text{CHCl}_3)/\text{cm}^{-1} \) 3582, 2956, 2880, 1396, 1368, 1142, 1100, 1027, 916.

HRMS: Found 479.2796. Calculated for C₃₀H₃₉O₅ 479.2797.

FAB: 479 (M+1)

(3R,4R)-1,3,4-tri-(benzyl oxy)-2,5-nonanedione \(^6\) (322)

A solution of TFAA (80 µL, 0.525 mmol) in CH₂Cl₂ (100 µL) was added dropwise to a solution of DMSO (37 µL, 0.525 mmol) in CH₂Cl₂ (0.5 mL) at -78 °C and stirred for 1 hour at the same temperature. To the stirring mixture was added dropwise a solution of 2,3,5-\textit{O}-\textit{tris}-phenylmethyl-1-butyl-D-arabinofuranose (50 mg, 0.105 mmol) in CH₂Cl₂ (320 µL) at -78 °C, and thereafter the reaction mixture was stirred for an additional 2 hours at the same temperature. A solution of Et₃N (126 µL, 0.840 mmol) in CH₂Cl₂ (210 µL) was added dropwise, and the stirring continued for 0.5 hours at -78 °C. The reaction mixture was removed from cooling bath and allowed to reach room temperature with stirring. The reaction was partitioned between CH₂Cl₂ and ice water. The product was purified further by column chromatography (5:1 hexanes-EtOAc) (72-98%).

MP: 64-66 °C

TLC: \( R_f \) 0.31 (5:1 hexanes-EtOAc)
\[ \text{1H NMR:} \ (300 \text{ MHz, CDCl}_3 \delta_H \ 7.42-7.16 \text{ (m, 15H, aromatics)}, 4.62-4.21 \text{ (m, 10H, OCH}_3\text{Ph} \times 3, \text{H1a, H1b, H3, H4)}, 2.56 \text{ (dt, 1H, } J = 18.3 \text{ and 7.5 Hz, H6a)}, 2.29 \text{ (dt, 1H, } J = 18.3 \text{ and 7.5 Hz, H6b)}, 1.49-1.39 \text{ (m, 2H, CH}_2\text{CH}_2\text{CH}_2\text{CH}_3), 1.30-1.15 \text{ (m, 2H, (CH}_2\text{)_2CH}_2\text{CH}_3)}, 0.84 \text{ (t, 3H, } J = 7.4 \text{ Hz, (CH}_2\text{)_3CH}_3). \]

\[ \text{13C NMR:} \ (75 \text{ MHz, CDCl}_3 \delta_C \ 210.0 \text{ (C2)}, 206.6 \text{ (C5), 136.9 (ipso), 136.4 (ipso), 136.1 (ipso), Aromatics - 128.5, 128.4, 128.3, 128.2, 127.8, 84.5 (C4), 83.7 (C3), 74.3 (OCH}_2\text{Ph} \times 2), 74.2 (OCH}_2\text{Ph), 73.3 (C1), 39.4 (C6), 24.9 (C7), 22.2 (C8), 13.8 (C9).} \]

IR: \[ \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \ 3081, 3026, 2993, 2880, 1793, 1740, 1695, 140, 1333 1100, 1034, 913. \]

HRMS: Found 475.2485. Calculated for C\text{30}H\text{35}O\text{5} 475.2484.

FAB: 475 (M+1)

3,4-Di(benzyloxy)-1-[(benzyloxy)methyl]-2-butyl-cyclobutane-1,2-diol \(^7\) (3,23)

(3R,4R)-1,3,4-tri-(benzyloxy)-2,5-nonanedione (67 mg, 0.21 mmol) was dissolved in degassed THF (5mL) and the solvent removed by vacuum distillation to ensure an oxygen-free system. The residue was dissolved in THF (6 mL) and added dropwise with stirring to a freshly prepared solution of SmI\(_2\) in THF (6 mL of 0.1 M solution, 0.63 mmol, 3.0 equiv.) at room temperature. The mixture was allowed to reflux, monitoring by TLC, after which it was diluted with EtOAc (20 mL) and filtered through a thin pad of silica gel. The solvent was removed in vacuo and the residue was purified by column chromatography (3:1 hexanes-EtOAc) (11 mg, 0.021 mmol, 14%).
TLC:  \( R_f \) 0.75 (3:1 hexanes-EtOAc)

\(^1\)H NMR:  (300 MHz, CDCl\(_3\)) \( \delta \) 7.32-7.24 (M, 15H, aromatics), 4.65-4.43 (M, 6H, OCH\(_2\)Ph \( \times \) 3), 3.83 (dd, 2H, \( J = 33.3 \) and 6.0 Hz), 3.65 (dd, 2H, \( J = 28.8 \) and 9.9 Hz), 2.85 (s, 1H, OH), 2.67 (s, 1H, OH), 1.41-1.24 (m, 6H, (CH\(_2\))\(_3\)CH\(_3\)), 0.87 (t, 3H, \( J = 6.9 \)Hz, (CH\(_2\))\(_3\)CH\(_3\)).

\(^{13}\)C NMR:  (75 MHz, CDCl\(_3\)) \( \delta \) C 138.0 (ipso), 137.7 (ipso), 137.4 (ipso), 128.4 (meta), 128.3 (meta), 128.3 (meta), 127.9 (ortho and para), 127.8 (ortho), 127.7 (para and ortho), 127.6 (para), 81.7 (C3), 80.2 (C4), 76.2 (C1), 75.8 (C2), 73.7 (CH\(_2\)OBn), 72.1 (OCH\(_2\)Ph), 72.0 (OCH\(_2\)Ph) 71.8 (OCH\(_2\)Ph), 34.0 (CH\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)), 25.5(CH\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)), 23.2 (CH\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)), 14.1 (CH\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)).

IR:  \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \). 3070, 3016, 2934, 2872, 1723, 1704, 1685, 1458, 1272, 1109, 1026, 913.

HRMS:  Found 476.2566. Calculated for C\(_{30}\)H\(_{36}\)O\(_5\) 476.2563.

EIMS:  477 (M+1, 46%), 368 (M\(^+\) - C\(_7\)H\(_8\)O, 16%), 296 (M\(^+\) - C\(_8\)H\(_{12}\)O - C\(_4\)H\(_9\), 58%), 85 (100%).

[\( \alpha \)]\(_D\):  -29.6 (c = 3.0, CHCl\(_3\)).

\((1R,2R,3S,5R)-2,3,5\)-tri-(Benzyloxy)-1-(2-thienyl)-pentane-1,4-diol (3.24)

![Chemical Structure](image)

To a solution of thiophene (0.2 mL, 2.50 mmol) in THF (8 mL) was added n-butyllithium (1.0 eq, 1.6 M hexane solution) dropwise at 0 °C. The solution was allowed to rise to room temperature and stirred for a further hour.
To a solution of 2,3,5-tri-O-benzyl arabinofuranose (289 mg, 0.687 mmol) in THF (3 mL) was added dropwise thienyllithium in THF solution (3.5 eq.) at 0 °C under stirring. After stirring at room temperature 3 hours, the reaction was quenched with H₂O. The solvent was removed \textit{in vacuo} and a CH₂Cl₂ / water extraction was carried out. Further purification was achieved by column chromatography (3:1 hexanes-EtOAc) (335 mg, 0.665 mmol, 96%).

TLC: \( R_f 0.33 \) (3:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl₃) \( \delta_H \) 7.40-7.23 (m, 30H, aromatics), 7.21-7.17 (m, 2H, \textit{thiophene} aromatics), 7.04-6.93 (m, 4H, \textit{thiophene} aromatics), 5.28 (br s, 1H), 5.23 (t, 1H, \( J = 5.5 \) Hz), 4.67-4.50 (m, 12H), 4.35 (dd, 2H, \( J = 34.8 \) and 11.1 Hz), 4.10-4.09 (m, 2H, H4), 3.98 (t, 1H, \( J = 4.1 \) Hz), 3.89 (d, 1H, \( J = 6.9 \) Hz), 3.73-3.59 (m, 4H), 3.45 (d, 1H, \( J = 4.5 \) Hz, OH), 2.95 (d, 1H, \( J = 5.7 \) Hz, OH), 1.80 (br s, OH × 2).

\(^13\)C NMR: (75 MHz, CDCl₃) \( \delta_C \) (major and minor isomers) 145.9 (C1’), 145.8 (C1’), 137.8 (ipso), 137.7 (ipso × 2), 137.6 (ipso), 137.5 (ipso), 137.4 (ipso), Aromatics - 128.3, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 126.6 (C3’), 126.5 (C3’), 124.7 (C2’), 124.6 (C2’), 124.2 (C4’), 124.2 (C4’), 83.3 (C3), 81.8 (C3), 78.5 (C2), 78.0 (C2), 73.7 (C4 and C4), 73.6 (C1), 73.5 (C1), 73.3 (C5 and C5), 70.9 (OCH₂Ph), 70.8 (OCH₂Ph), 70.7 (OCH₂Ph), 70.1 (OCH₂Ph), 69.9 (OCH₂Ph), 69.7 (OCH₂Ph).

IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3560, 2880, 1459, 1396, 1358, 1097, 1069, 1031, 920, 833.


FAB: 504 (M⁺)
(2R,3R)-2,3,5-tri-(Benzyloxy)-1-(2-thienyl)-1,4-pentanedione (3.25)

The general procedure to perform a Swern oxidation (3.22) was carried out to oxidise 3.24 (53 mg, 0.105 mmol). After column chromatography (5:1 hexanes-EtOAc) the title compound was isolated as an oil (34 mg, 0.104 mmol, 65%).

TLC: \( R_f \) 0.44 (3:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \( \delta \)H 7.89 (dd, 1H, \( J = 3.8 \) and 1.1 Hz, H3'), 7.66 (dd, 1H, \( J = 5.1 \) and 1.2 Hz, H2'), 7.35-6.94 (m, 16H, aromatics), 4.89 (d, 1H, \( J = 3.0 \) Hz), 4.72 (d, 1H, \( J = 11.4 \) Hz), 4.32 (t, 1H, \( J = 2.4 \) Hz), 4.66-4.22 (m, 7H).

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \( \delta \)C 205.9 (C4), 190.1 (C1), 141.1 (C1'), 136.9 (ipso), 136.5 (ipso), 135.9 (ipso), 134.8 (C2'), 134.1 (C4'), Aromatics - 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.6, 126.6 (C3'), 83.8 (C2), 83.3 (C3), 74.4 (OCH\(_2\)Ph), 74.1 (OCH\(_2\)Ph), 73.5 (OCH\(_2\)Ph), 73.3 (C5).

IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3074, 2873, 1733, 1692, 1688, 1660, 1500, 1413, 1358, 133, 1139, 1104, 1034, 920, 864.

2,3-Di-O-benzyl-1-(2-thienyl)-5-methoxybenzyl-1,4-dihydroxy-cyclobutane (3.26)

(2R,3R)-2,3,5-O-tris-Phenylmethyl-1-(2-thienyl)-1,4-pentanedione (69 mg, 0.21 mmol) was subjected to Hoffmann’s conditions in the same manner as 3.23. The residue was purified by column chromatography (4:1 hexanes-EtOAc) (21 mg, 0.042 mmol, 20%).

TLC: R_f 0.27 (4:1 hexanes-EtOAc)

^1^H NMR: (300 MHz, CDCl_3) δ_H 7.37-7.20 (m, 15H, aromatics), 7.05 (dd, 1H, J = 3.6 and 3.3 Hz, H3'), 7.01 (d, 1H, J = 3.6 Hz, H2'), 6.98 (d, 1H, J = 3.3 Hz, H4’), 4.75-4.49 (m, 6H, OCH_2Ph × 3), 4.43 (d, 1H, J = 6.6 Hz, H4), 4.04 (d, 1H, J = 6.6 Hz, H3), 3.71 (s, 2H, CH_2OBn), 3.41(s, 1H, OH), 2.89 (s, 1H, OH).

^1^3^C NMR: (75 MHz, CDCl_3) δ_C 138.6 (ipso), 137.9 (ipso), 137.5 (C1'), 137.0 (ipso),
Aromatics - 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 126.9, 126.8 (C4'), 125.1 (C2'), 124.6 (C3'), 83.4 (C4), 79.5 (C3), 75.0 (C2), 73.6 (C1), 72.6 (OCH_2Ph), 72.4 (OCH_2Ph × 2), 70.6 (CH_2OBn).

IR: \nu_{max}(CHCl_3)/cm^{-1} 3441, 3038, 2930, 2879, 1538, 1523 1458, 1263, 1099.


EIMS: 502 (M^+, 34%), 501 (M^+ - H, 100%), 484 (M^+ - H_2O, 35%), 347 (M+1 - Ph × 2, 1%).

[\alpha]_D: -11.1 (c = 0.5, CHCl_3).
Methyl 2,3-\textit{O}-isopropylidene-\textit{\beta}-\textit{D}-ribofuranoside (327)

To a solution of \textit{D}-ribose (3 g, 0.02 mol) in anhydrous acetone (12 mL) and anhydrous methanol (12 mL) was added a catalytic amount of concentrated HCl (300 µL). The reaction mixture was allowed to reflux for approximately 2 hours. Thereafter left to stir at room temperature overnight. The reaction was neutralised with triethyl amine. 30 mL of water was added and the solvent was removed \textit{in vacuo}. The product was purified by column chromatography (2:1 hexanes-EtOAc) (3.590 g, 0.018 mol, 88 %).

\textbf{TLC:} \quad R_f \ 0.67 \ (1:1 \ \text{hexanes-EtOAc})

\textbf{\textsuperscript{1}H NMR:} \quad (300 MHz, CDCl\textsubscript{3}) \ \delta_H \ 4.89 \ (s, \ 1H, H1), \ 4.74 \ (d, \ 1H, J = 6.0 \ Hz, H3), \ 4.50 \ (d, \ 1H, J = 6.0 \ Hz, H2), \ 4.33 \ (t, \ 1H, J = 3.3 \ Hz, H4), \ 3.63-3.48 \ (m, \ 2H, H5a \ and \ H5b), \ 3.34 \ (s, \ 3H, OCH\textsubscript{3}), \ 3.23 \ (dd, \ 1H, J = 9.3 \ and \ 3.6 \ Hz, \ OH \times 2), \ 1.40 \ (s, \ 3H, CH\textsubscript{3}-isopropylidene), \ 1.24 \ (s, \ 3H, CH\textsubscript{3}-isopropylidene).

\textbf{\textsuperscript{13}C NMR:} \quad (75 MHz, CDCl\textsubscript{3}) \ \delta_C \ 111.9 \ (acetal-C), \ 109.7 \ (C1), \ 88.1 \ (C3), \ 85.6 \ (C2), \ 81.3 \ (C4), \ 63.8 \ (C5), \ 55.3 \ (OCH\textsubscript{3}), \ 26.2 \ (CH\textsubscript{3}-isopropylidene), \ 24.6 \ (CH\textsubscript{3}-isopropylidene).

\textbf{EIMS:} \quad 189 (M\textsuperscript{+} - H\textsubscript{2}O, 14%), \ 173 \ (M+1 - OCH\textsubscript{3}, 48%), \ 143 \ (M\textsuperscript{+} - C\textsubscript{2}H\textsubscript{4}O\textsubscript{2}, 18%), \ 59 \ (86%), \ 43 \ (100%).

\textbf{HRMS:} \quad \text{Found} \ 207.0998. \ \text{Calculated} \ \text{for} \ C\textsubscript{9}H\textsubscript{16}O\textsubscript{5} \ 204.0998.
Methyl 2,3-\(O\)-isopropylidene-5-\(O\)-tosyl-\(\beta\)-\(D\)-ribofuranoside (3.28)

Methyl 2,3-\(O\)-isopropylidene-\(\beta\)-\(D\)-ribofuranoside (2.12 g, 0.010 mol) was dissolved in dry pyridine (6 mL) and cooled to 0 \(^\circ\)C. To the reaction mixture was added \(p\)-toluene sulfonyl chloride (3.3 g, 0.017 mol). The reaction was allowed to warm to room temperature and left to stir for 15 hours. 5 mL of water was added and the reaction was allowed to stir for a further 30 minutes. The reaction mixture was extracted with chloroform, washed with 0.05 M \(\text{H}_2\text{SO}_4\) (30 mL), 0.2 M \(\text{NaOH}\) (3×30 mL) and water (30 mL) respectively. The solvent was removed \textit{in vacuo} and the product purified by column chromatography (5:1 hexanes-EtOAc) (3.071 g, 8.578 mmol, 86%).

TLC: \(R_f\) 0.35 (5:1 hexanes-EtOAc)

\(^1\text{H} NMR:\) (300 MHz, CDCl\(_3\)) \(\delta_H\) 7.77 (d, 2H, \(J = 8.4\) Hz, Tosyl aromatics), 7.33 (d, 2H, \(J = 8.4\) Hz, Tosyl aromatics), 4.89 (s, 1H, H1), 4.57 (dd, 1H, \(J = 6.0\) and 0.9 Hz, H3), 4.50 (d, 1H, \(J = 6.0\) Hz, H2), 4.28 (td, 1H, \(J = 7.2\) and 0.9 Hz, H4), 3.99 (dd, 1H, \(J = 10.0\) and 7.2 Hz, H5a), 3.97 (dd, 1H, \(J = 10.0\) and 7.5 Hz, H5b), 3.20 (s, 3H, O\(\text{CH}_3\)), 2.42 (s, 3H, Ph\(\text{CH}_3\)), 1.41 (s, 3H, \(\text{CH}_3\)-isopropylidene), 1.25 (s, 3H, \(\text{CH}_3\)-isopropylidene).

\(^{13}\text{C} NMR:\) (75 MHz, CDCl\(_3\)) \(\delta_C\) 144.9 (C1‘), 132.6 (C4‘), 129.8 (C2‘), 127.9 (C3‘), 112.6 (acetal-C), 109.4 (C1), 84.8 (C2), 83.5 (C3), 81.3 (C4), 69.2 (C5), 55.0 (O\(\text{CH}_3\)), 26.3 (\(\text{CH}_3\)-isopropylidene), 24.9 (\(\text{CH}_3\)-isopropylidene), 21.6 (Ph–\(\text{CH}_3\)).

IR: \(\nu_{\text{max}}\) (CHCl\(_3\))/cm\(^{-1}\) 1668, 1656, 1375, 1311, 1179, 1162, 985, 963, 869, 816, 730, 669.

EIMS: 359 (M+1, 2\%), 327 (M\(^+\) - O\(\text{CH}_3\), %), 173 (M+1 - Tosyl - O\(\text{CH}_3\), 42\%).
Methyl 5-deoxy-2,3-\(\text{O}\)-isopropylidene-\(\beta\)-D-ribofuranoside \(^8\) (3.29)

\[
\text{Methyl 2,3-\(\text{O}\)-isopropylidene-5-\(\text{O}\)-tosyl-\(\beta\)-D-ribofuranoside (500 mg, 1.397 mol) was dissolved in dry THF (4 mL) and LiAlH}_4 (164 mg, 4.32 mmol) added in small amounts. The reaction was heated to reflux for 3 hours and allowed to cool to 0 °C. Ethanol was added carefully, followed by ice water. The solution was extracted with CHCl}_3. After drying over MgSO}_4, the crude product was chromatographed (10:1 hexanes-EtOAc) to give a clear oil (80-98%).}

TLC: \(R_f\) 0.52 (10:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \(\delta_H\) 4.82 (s, 1H, H1), 4.53 (d, 1H, \(J = 5.9\) Hz, H2), 4.39 (d, 1H, \(J = 5.9\) Hz, H3), 4.23 (q, 1H, \(J = 6.9\) Hz, H4), 3.22 (s, 3H, OC\(\text{H}_3\)), 1.37 (s, 3H, CH\(_3\)-isopropylidene), 1.20 (s, 3H, CH\(_3\)-isopropylidene), 1.68 (d, 3H, \(J = 6.9\) Hz, H5).

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \(\delta_C\) 111.9 (C1), 109.3 (acetal-C), 85.6 (C3), 85.0 (C2), 82.9 (C4), 54.0 (OCH\(_3\)), 26.3 (CH\(_3\)-isopropylidene), 24.8 (CH\(_3\)-isopropylidene), 20.8 (C5).

HRMS: Found 201.1002. Calculated for C\(_9\)H\(_{15}\)O\(_4\) 201.1001.

EIMS: 201 (M\(^+\), 3%), 154 (100%).
5-Deoxy-2,3-\textit{O}-isopropylidene-D-ribofuranose (3.30)

The 5-deoxy derivative (3.29, 1.124 g, 5.97 mol) was dissolved in MeOH (5.4 mL) and 0.2 M \( \text{H}_2\text{SO}_4 \) (2.3 mL) was added. The reaction mixture was heated to reflux for 2 hours after which the solvent was removed \textit{in vacuo} to approximately 1 mL. 0.2 M \( \text{H}_2\text{SO}_4 \) (5.4 mL) was added and the reaction reheated to reflux for 1.5 hours. The reaction was neutralised with TEA and all the solvent removed. The resulting oil was dried under vacuum overnight. Acetone (23 mL) was added to the residue together with 2 drops of conc. \( \text{H}_2\text{SO}_4 \). After 3 hours TEA was once again added to neutralise the reaction. After removal of the solvent the crude products were flushed through a silica column (1:1 hexanes-EtOAc) to obtain a mixture of anomers, as a clear oil (50-70% over two steps).

**TLC:** \( R_f \) 0.67 (1:1 hexanes-EtOAc)

**\(^1\)H NMR:** (300 MHz, CDCl\(_3\)) \( \delta_H \) 5.72 (d, 1H, \( J = 4.2 \) Hz, H1), 5.27 (d, 1H, \( J = 2.7 \) Hz, H1), 4.47 (dd, 1H, \( J = 9.0 \) and 4.2 Hz, H2), 4.52 (d, 1H, \( J = 5.7 \) Hz, H3), 4.43 (d, 1H, \( J = 2.7 \) Hz, H2), 4.36-4.32 (m, 1H, H4), 3.76 (dd, 1H, \( J = 9.0 \) and 6.2 Hz, H3), 3.44 (dq, 1H, \( J = 6.2 \) and 6.0 Hz, H4), 2.50 (br s, 2H, OH and OH), 1.49 (s, 3H, \( \text{CH}_3\)-isopropylidene), 1.33 (s, 3H, \( \text{CH}_3\)-isopropylidene), 1.29 (s, 3H, \( \text{CH}_3\)-isopropylidene), 1.28 (s, 3H, \( \text{CH}_3\)-isopropylidene), 1.27 (d, 3H, \( J = 6.9 \) Hz, H5a, b and c), 1.21 (d, 3H, \( J = 6.6 \) Hz, H5).

**\(^{13}\)C NMR:** (75 MHz, CDCl\(_3\)) \( \delta_C \) 112.1 (acetal-C), 112.2 (acetal-C), 103.5 (C1), 102.8 (C1), 86.1 (C3), 85.2 (C2), 82.9 (C4), 78.4 (C3), 77.0 (C2), 75.9 (C4), 26.4 (\( \text{CH}_3\)-isopropylidene), 26.3 (\( \text{CH}_3\)-isopropylidene), 26.2 (\( \text{CH}_3\)-isopropylidene), 24.7 (\( \text{CH}_3\)-isopropylidene), 21.4 (C5), 16.7 (C5).

**HRMS:** Found 174.0892. Calculated for C\(_6\)H\(_{14}\)O\(_4\) 174.0892.

**EIMS:** 174 (M\(^+\), 33%), 154 (100%).
2,3-Isopropylidene-1-phenyl-pentane-1,5-diol (3.31)

The general procedure to prepare a Grignard reagent (3.21) using bromobenzene was carried out followed by the Grignard reaction with 5-deoxy-2,3-\textit{O}-isopropylidene-\textit{D}-ribofuranose (50 mg, 0.287 mmol). The desired product was obtained as a colorless oil after chromatography (4:1 hexanes-EtOAc) (68 mg, 0.272 mmol, 95%).

**TLC:** \( R_f \) 0.23 (4:1 hexanes-EtOAc)

**\(^1\)H NMR:** (300 MHz, CDCl\(_3\)) \( \delta_H \) 7.26-7.21 (m, 5H, aromatics), 4.64 (d, 1H, \( J = 9.6 \) Hz, H1), 4.15 (br s, 1H, OH), 4.20 (dd, 1H, \( J = 9.6 \) and 5.3 Hz, H2), 4.03 (br s, 1H, OH), 4.00-4.11 (m, 1H, H4), 3.93 (dd, 1H, \( J = 9.3 \) and 5.3 Hz, H3), 1.35 (s, 3H, CH\(_3\)-isopropylidene), 1.31 (d, 3H, \( J = 6.0 \) Hz, H5a, b and c), 1.23 (s, 3H, CH\(_3\)-isopropylidene).

**\(^{13}\)C NMR:** (75 MHz, CDCl\(_3\)) \( \delta_C \) 141.3 (ipso), 128.2 (ortho), 128.1 (meta), 127.3 (para), 108.4 (acetal-C), 82.1 (C2), 80.2 (C3), 72.4 (C1), 65.6 (C4), 27.9 (CH\(_3\)-isopropylidene), 25.3 (CH\(_3\)-isopropylidene), 20.5 (C5).

**IR:** \( \nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1} \) 3367, 3023, 2997, 1703, 1424, 1384, 1375, 1247, 1071, 1773, 663.

**EIMS:** 253 (M+1, 1%), 237 (M\(^+\) - CH\(_3\), 3%), 177 (M+1 - C\(_6\)H\(_5\), 3%), 131 (M+1 - C\(_9\)H\(_{14}\), 33%), 59 (100%).
The general procedure to perform a Swern oxidation (3.22) was carried out to oxidise 3.31 (53 mg, 0.210 mmol). The reaction was partitioned between CH$_2$Cl$_2$ and ice water. The product was purified further by column chromatography (4:1 hexanes-EtOAc) (43 mg, 0.172 mmol, 82%).

TLC: R$_f$ 0.39 (4:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 7.97 (d, 2H, $J = 7.5$ Hz, ortho aromatics), 7.58 (t, 1H, $J = 7.2$ Hz, para aromatics), 7.46 (dd, 2H, $J = 7.5$ and 7.25 Hz, meta aromatics), 5.65 (d, 1H, $J = 6.6$ Hz, H2), 4.73 (d, 1H, $J = 6.6$ Hz, H3), 2.36 (s, 3H, H5a, b and c), 1.49 (s, 3H, CH$_3$-isopropylidene), 1.48 (s, 3H, CH$_3$-isopropylidene).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 206.8 (C4), 194.4 (C1), 134.9 (ipso), 133.7 (para), 129.1 (ortho), 128.6 (meta), 112.3 (acetal-C), 82.0 (C2), 80.1 (C3), 27.7 (C5), 27.0 (CH$_3$-isopropylidene), 25.8 (CH$_3$-isopropylidene).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 2671, 1735, 1706, 1700, 1602, 1520, 1498, 1453, 1099, 1027, 864.

EIMS: 249 (M+1, 0.02%), 122 (M$^+$ - C$_7$H$_9$O$_2$, 33%), 105 (M$^+$ - C$_7$H$_5$O, 100%).
5,5'-bis(7-hydroxy-2,2,7-trimethyl-5-phenyl-tetrahydrofuro[3,4-]1,3-dioxolane (3.34)

The diketone (69 mg, 0.28 mmol) in THF (12 mL) was added dropwise to a solution of SmI$_2$ (1.417 mmol, 3.0 eq) in THF (15 mL) at -78 °C under argon. The reaction was allowed to warm to rt over 24 hrs and then quenched by removing the argon. The mixture was filtered through a thin pad of silica and then chromatographed (7:1 hexanes-EtOAc). The product was isolated as an oil (20 mg, 0.039mmol, 14%).

TLC:  R$_f$ 0.29 (5:1 hexanes-EtOAc)

$^1$H NMR  (300 MHz, CDCl$_3$) $\delta$$_H$ 7.30-7.21 (m, 10H, aromatics and aromatics), 5.228 (d, 2H, $J$ = 6.5 Hz, H4 and H4), 4.86 (d, 2H, $J$ = 6.5 Hz, H8 and H8), 1.38 (s, 6H, CH$_3$-isopropylidene and CH$_3$-isopropylidene), 1.26 (s, 3H, CH$_3$-isopropylidene and CH$_3$-isopropylidene), 1.11 (s, 3H, CH$_3$ and CH$_3$).

$^{13}$C NMR:  (75 MHz, CDCl$_3$) $\delta$$_C$ 136.5 (ipso and ipso), 127.2 (para and para), 12.7 (ortho, meta, ortho and meta), 112.6 (acetal-C and acetal-C), 108.2 (C5 and C5), 92.7 (C7 and C7), 86.9 (C4 and C4), 81.8 (C8 and C8), 25.5 (CH$_3$ and CH$_3$), 25.5 (CH$_3$-isopropylidene and CH$_3$-isopropylidene), 24.9 (CH$_3$-isopropylidene and CH$_3$-isopropylidene).

IR:  $\nu$$_{max}$(CHCl$_3$)/cm$^{-1}$ 3021, 2946, 1450, 1385, 1225, 1218, 976, 881.

CIMS:  480 (M$^+$ - H$_2$O, 33%), 249 (C$_{14}$H$_{17}$O$_4$, 100%), 231 (C$_{14}$H$_{17}$O$_4$ - H$_2$O, 82%).
(1R,2S,3S,4S)-3,4-O-Isopropylidene-1-methyl-2-phenyl-cyclobutane-1,2-diol (3.33)

The diketone (60 mg, 0.242 mmol) in THF (4 mL) was added dropwise to a solution of SmI$_2$ (0.725 mmol, 3.0 equivalent) and HMPA (1 equivalent / Sm) in THF (9 mL) at -78 ºC under argon. The reaction was allowed to warm to room temperature over 24 hours and then quenched by removing the argon. The mixture was filtered through a thin pad of silica and then chromatographed. The desired product was obtained as an oil (6 mg, 0.024 mmol, 10 %).

TLC: R$_f$ 0.41 (3:1 hexanes-EtOAc)

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$H 7.52 (dd, 2H, $J = 8.4$ and 1.6 Hz, aromatics), 7.37-7.29 (m, 3H, aromatics), 4.73 (d, 1H, $J = 5.1$ Hz, H4), 4.54 (d, 1H, $J = 5.1$ Hz, H3), 2.73 (br. s, 1H, OH), 1.91 (br. s, 1H, OH), 1.51 (s, 3H, CH$_3$), 1.43 (s, 1H, 3H, CH$_3$-isopropylidene), 1.35 (s, 3H, CH$_3$-isopropylidene).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 136.7 (ipso) 128.6 (ortho), 128.2 (meta), 128.0 (para), 109.7 (acetal-C), 81.5 (C2), 77.5 (C4), 76.2 (C3), 66.6 (C1), 25.5 (CH$_3$-isopropylidene), 25.4 (CH$_3$-isopropylidene), 21.4 (CH$_3$).

IR: $\nu_{max}$(CHCl$_3$/cm$^{-1}$) 3610, 3454, 3450, 3030, 3032, 1700, 1660.

HRMS: Found 232.1096. Calculated for C$_{14}$H$_{16}$O$_3$ 232.1099.

CIMS: 251 (M+1, 24%), 250 (M$^+$, 4%), 233 (M+1 - H$_2$O, 2%), 175 (M+2 - Ph, 16%).

$[\alpha]$$_D$: -3.1 ($c = 1.0$, CHCl$_3$).
1-(2-Furyl)-2,3-O-isopropylidene-pentane-1,4-diol (3.35)

To a solution of furan (0.876 mL, 12.067 mmol) in THF (30 mL) was added η-butyllithium (1.0 eq, 1.6 M hexane solution) dropwise at 0 °C. The solution was allowed to rise to room temperature and stirred for a further hour.

To a solution of 5-deoxy-2,3-O-isopropylidene-D-ribofuranose (600 mg, 3.447 mmol) in THF (6 mL) was added dropwise furan-lithium in THF solution (3.5 eq.) at 0 °C under stirring. After stirring at room temperature overnight, the reaction was quenched with H₂O. The solvent was removed \textit{in vacuo} and a CH₂Cl₂ / water extraction was carried out. Further purification was achieved by column chromatography (4:1 hexanes-EtOAc) (334 mg, 1.379mmol, 40%).

**TLC:** \( R_f \) 0.12 (4:1 hexanes-EtOAc)

**\(^1\)H NMR:** (300 MHz, CDCl₃) \( \delta_H \) 7.38 (dd, 1H, \( J = 1.8 \) and 0.8 Hz, H2'), 6.33 (dd, 1H, \( J = 3.3 \) and 1.8 Hz, H3'), 6.29 (d, 1H, \( J = 3.3 \) Hz, H4'), 4.75 (dd, 1H, \( J = 9.6 \) and 3.0 Hz, H1), 4.45 (d, 1H, \( J = 3.3 \) Hz, OH), 4.39 (dd, 1H, \( J = 9.6 \) and 4.8 Hz, H2), 4.16 (d, 1H, \( J = 3.0 \) Hz, OH), 4.02-3.96 (m, 1H, H4), 3.91 (dd, 1H, \( J = 9.0 \) and 4.8 Hz, H3), 1.29 (s, 3H, CH₃-isopropylidene), 1.27 (d, 3H, \( J = 6.3 \) Hz, H5a, b and c), 1.26 (s, 3H, CH₃-isopropylidene).

**\(^1^C\) NMR:** (75 MHz, CDCl₃) \( \delta_C \) 153.7 (C1'), 142.2 (C4'), 110.1 (acetal-C), 108.6 (C3'), 108.1 (C2'), 81.7 (C3), 78.2 (C2), 65.7 (C4), 65.5 (C1), 27.9 (CH₃-isopropylidene), 25.4 (CH₃-isopropylidene), 20.4 (C5).

**IR:** \( \nu_{max}(\text{CHCl}_3)/\text{cm}^{-1} \) 3797, 3023, 1749, 1736, 1220, 1211, 1073, 1014.

**CIMS:** 242 (M⁺, 1%), 225 (M+1 - H₂O, 60%), 167 (M⁺ - CH₃ - isopropylidene - H₂O, 100%).
1-(2-Furyl)-2,3-O-isopropylidene-pentane-1,4-dione (3.36)

The general procedure to perform a Swern oxidation (3.22) was carried out to oxidise 3.35 (236 mg, 0.960 mmol). The reaction was partitioned between CH₂Cl₂ and ice water. The product was purified further by column chromatography (5:1 hexanes-EtOAc) and obtained as a mixture of isomers (119 mg, 0.499 mmol, 52%).

TLC: R_f 0.19 (5:1 hexanes-EtOAc)

H NMR: (300 MHz, CDCl₃) δH (major and minor isomers) 7.69 (dd, 1H, J = 1.7 and 0.6 Hz, H2’), 7.61 (dd, 1H, J = 1.7 and 0.6 Hz, H2’), 7.43 (dd, 1H, J = 3.6 and 0.9 Hz, H3’), 7.33 (dd, 1H, J = 3.6 and 0.9 Hz, H3’), 6.59 (dd, 1H, J = 3.6 and 1.7 Hz, H4’), 6.55 (dd, 1H, J = 3.6 and 1.8 Hz, H4’), 5.45 (d, 1H, J = 6.9 Hz, H2), 4.77 (d, 1H, J = 6.9 Hz, H3), 2.47 (s, 3H, H5a, b and c), 2.26 (s, 3H, H5a, b and c), 1.72 (s, 3H, CH₃-isopropylidene), 1.58 (s, 3H, CH₃-isopropylidene), 1.54 (s, 3H, CH₃-isopropylidene), 1.45 (s, 3H, CH₃-isopropylidene).

C NMR: (75 MHz, CDCl₃) δC 206.9 (C1), 183.1 (C4), 151.1 (C1’), 14.22 (C4’), 119.6 (C3’), 112.5 (C2’), 112.4 (acetal-C), 82.2 (C3), 79.4 (C2), 27.5 (C5), 26.8 (CH₃-isopropylidene), 25.5 (CH₃-isopropylidene).

IR: ν_max(CHCl₃)/cm⁻¹ 1724, 1720, 1715, 1529, 1522, 1072, 885.

CIMS: 239 (M+1, 100%), 221 (M+1 - H₂O, 9%), 171 (M+1 - furan, 1%).
3,4-\textit{O}-Isopropylidene-nonane-2,5-diol (3.37)

The general procedure to prepare a Grignard reagent (3.21) using bromobutane was carried out followed by the Grignard reaction with 5-deoxy-2,3-\textit{O}-isopropylidene-D-ribofuranose (450 mg, 2.586 mmol). The desired product was obtained as a colorless oil after chromatography (4:1 hexanes-EtOAc) (364mg, 1.569 mmol, 61%).

\textbf{TLC:} \quad R_f \ 0.28 \ (4:1 \ hexanes-EtOAc)

\textbf{\textsuperscript{1}H NMR:} \quad (300 MHz, CDCl\textsubscript{3}) \ \delta_H \ 4.48 \ (br \ s, \ 1H, \ OH), \ 4.34 \ (br \ s, \ 1H, \ OH), \ 3.97-3.73 \ (m, \ 4H, \ H2, \ H3, \ H4 \ and \ H5), \ 1.69 \ (t, \ 1H, \ J = 9.3 \ Hz, \ H6a), \ 1.46-1.08 \ (m, \ 5H, \ CH\textsubscript{2}(CH\textsubscript{2})\textsubscript{2}CH\textsubscript{3}, \ H6b), \ 1.26 \ (s, \ 3H, \ CH\textsubscript{3}-isopropylidene), \ 1.23 \ (s, \ 3H, \ CH\textsubscript{3}-isopropylidene), \ 1.19 \ (d, \ 3H, \ J = 5.7 \ Hz, \ H1a, \ b \ and \ c), \ 0.83 \ (t, \ 3H, \ J = 6.3 \ Hz, \ (CH\textsubscript{2})\textsubscript{3}CH\textsubscript{3}).

\textbf{\textsuperscript{13}C NMR:} \quad (75 MHz, CDCl\textsubscript{3}) \ \delta_C \ 107.9 \ (acetal-C), \ 81.6 \ (C4), \ 80.2 \ (C3), \ 69.2 \ (C2), \ 65.6 \ (C5), \ 33.6 \ (C6), \ 27.0 \ (C7), \ 25.4 \ (CH\textsubscript{3}-isopropylidene), \ 25.0 \ (CH\textsubscript{3}-isopropylidene), \ 22.6 \ (C8), \ 20.4 \ (C1), \ 13.9 \ (C9).

\textbf{IR:} \quad \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \ 3430, \ 1459, \ 1422, \ 1385, \ 1240, \ 1230, \ 1068, \ 903.

\textbf{CIMS:} \quad 233 \ (M+1, \ 56\%), \ 215 \ (M+1 - H\textsubscript{2}O, \ 35\%), \ 175 \ (M^+ - \text{butyl, } 100\%), \ 157 \ (M^+ - \text{butyl - H}_2\text{O, } 34\%), \ 139 \ (M^+ - \text{butyl - 2H}_2\text{O, } 16\%).
3,4-\textit{O}-Isopropylidene-nonane-2,5-dione (3.38)

The general procedure to perform a Swern oxidation (3.22) was carried out to oxidise 3.37 (100 mg, 0.431 mmol). The reaction was partitioned between CH\textsubscript{2}Cl\textsubscript{2} and ice water. The product was purified further by column chromatography (10:1 hexanes-EtOAc) (35 mg, 0.153 mmol, 33%).

TLC: \( R_f \) 0.42 (5:1 hexanes-EtOAc)

\textbf{\textsuperscript{1}H NMR:} (300 MHz, CDCl\textsubscript{3}) \( \delta \) H 4.71 (d, 1H, \( J = 7.5 \) Hz, H4), 4.66 (d, 1H, \( J = 7.5 \) Hz, H3), 2.53 (td, 2H, \( J = 7.5 \) and 4.2 Hz, H6a and b), 2.19 (s, 3H, H1a, b and c), 1.54 (s, 3H, CH\textsubscript{3}-isopropylidene), 1.53-1.01 (m, 4H, CH\textsubscript{2}(CH\textsubscript{2})\textsubscript{2}CH\textsubscript{3}), 1.37 (s, 3H, CH\textsubscript{3}-isopropylidene), 0.86 (t, 3H, \( J = 7.5 \) Hz, (CH\textsubscript{2})\textsubscript{3}CH\textsubscript{3}).

\textbf{\textsuperscript{13}C NMR:} (75 MHz, CDCl\textsubscript{3}) \( \delta \) C 207.6 (C2), 205.8 (C5), 111.8 (acetal-C), 82.0 (C4), 81.8 (C3), 39.9 (C6), 27.7 (C1), 26.7 (C7), 25.3 (CH\textsubscript{3}-isopropylidene), 24.9 (CH\textsubscript{3}-isopropylidene), 22.1 (C8), 13.8 (C9).

\textbf{IR:} \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 1766, 1759, 1745, 1727, 1658, 1640, 1241, 1081, 869.

\textbf{CIMS:} 229 (M+1, 100%), 211 (M+ - H\textsubscript{2}O, 8%), 199 (M\textsuperscript{+} - CH\textsubscript{2}CH\textsubscript{3}, 6%), 185 (M\textsuperscript{+} - CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{3}, 22%), 171 (M\textsuperscript{+} - butyl, 5%).
(1S,2S,3S,4R)-1,4-Dihydroxy-1-(butyl)-4-methyl-2,3-dioxy-methylethylidene-cyclobutane (3.39)

The diketone (35 mg, 0.151 mmol) was subjected to the same pinacol cyclisation reaction conditions as the phenyl analogue (3.33). The desired product was obtained as an oil (3 mg, 0.013 mmol, 12%).

TLC: \( R_f 0.42 \) (2:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \( \delta \) 4.32 (d, 1H, \( J = 5.5 \) Hz, H3), 4.18 (d, 1H, \( J = 5.5 \) Hz, H4), 2.81 (s, 1H, OH), 1.54 (s, 3H, CH\(_3\)), 1.35-1.23 (m, 6H, (CH\(_2\))\(_3\)CH\(_3\)), 1.29 (s, 1H, 3H, CH\(_3\)-isopropylidene), 1.24 (s, 3H, CH\(_3\)-isopropylidene), 0.90 (t, 3H, \( J = 6.6 \) Hz, (CH\(_2\))\(_3\)CH\(_3\)).

\(^1\)C NMR: (75 MHz, CDCl\(_3\)) \( \delta \) C 114.2 (acetal -C), 81.7 (C1), 79.6 (C4), 77.7 (C3), 72.2 (C2), 31.1 (CH\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)), 29.6 (CH\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)), 25.4 (CH\(_3\)-isopropylidene), 24.9 (CH\(_3\)-isopropylidene), 23.2 (CH\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)), 20.5 (CH\(_3\)), 14.0 (CH\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)).

IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3601, 3455, 3040, 3033, 1701, 1664.


CIMS: 231 (M+1, 11%), 230 (M\(^+\), 3%), 215 (M\(^+\) - CH\(_3\), 24%), 201 (M\(^+\) - CH\(_2\)CH\(_3\), 16%), 173 (M\(^+\) - Bu, 3%), 155 (M\(^+\) - Bu - H\(_2\)O, 18%).

\([\alpha]_D\): -14.7 \((c = 1.0, \text{CHCl}_3)\).
6.4 FOUR-EXO-TRIG CYCLISATIONS

6.4.1 ARABINOSE – Dithioacetal route

2,3-O-Isopropylidene-D-ribofuranose (4.7)

A catalytic amount of H$_2$SO$_4$ (10% m/m) was added to a slurry of D-ribose (100 mg, 0.66 mmol) in anhydrous acetone (1 mL). The reaction mixture, which became clear after 30 minutes, was allowed to stir overnight at room temperature. The pH of the solution was adjusted to pH 7 with Et$_3$N. The resulting slurry was filtered through a Celite pad and the clear filtrate evaporated in vacuo. The resulting crude syrup was chromatographed (EtOAc) to afford the protected ribose as a colourless viscous oil (90 mg, 0.47 mmol, 72%).

TLC: $R_f$ 0.78 (EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 5.30 (br s, 1H, H1), 4.82 (d, 1H, $J = 6.0$ Hz, H2), 4.59 (d, 1H, $J = 6.0$ Hz, H3), 4.39-4.37 (m, 1H, H4), 3.72-3.69 (m, 2H, H5), 1.46 (s, 3H, CH$_3$-isopropylidene), 1.30 (s, 3H, CH$_3$-isopropylidene).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 112.0 (s, acetal-C), 102.9 (s, C1), 87.8 and 86.9 (s, C3, C2), 81.7 (s, C4), 63.7 (s, C5), 26.4 (CH$_3$-isopropylidene), 24.8 (CH$_3$-isopropylidene).

EIMS: 175 (M$^+$ - CH$_3$, 92%), 157 (M$^+$ - CH$_3$ - H$_2$O, 28%), 59 (100%).

The data compared favourably with previously reported analytical data.$^8$
5-O-(Triphenylmethyl)-2,3-O-isopropylidene-D-ribofuranose (4.8)

To a solution of 2,3-O-isopropylidene-D-ribose (100 mg, 0.53 mmol) and imidazole (10% m/m) in dry pyridine (1 mL) was added tritylchloride (176 mg, 0.63 mmol). The reaction flask was stoppered and placed in a 100 °C oil bath and allowed to stir until all the reagents had dissolved. The reaction mixture was removed from the oil bath and left to stir overnight. The solvent was removed in vacuo, and the residue was purified by flash chromatography (4:1 hexanes-EtOAc) to afford the trityl ether (163 mg, 0.38 mmol, 72%).

TLC: \( R_f = 0.28 \) (4:1 hexanes-EtOAc)

\( ^1H \) NMR: (300 MHz, CDCl₃) \( \delta_H = 7.44-7.40 \) (m, 6H, ortho aromatics), 7.34-7.25 (m, 9H, aromatics), 5.34 (d, 1H, \( J = 8.4 \) Hz, H1), 4.78 (dd, 1H, \( J = 10.2 \) and 5.8 Hz, H3), 4.65 (d, 1H, \( J = 5.8 \) Hz, H2), 4.36 (m, 1H, Hz, H4), 4.02 (d, 1H, \( J = 8.4 \) Hz, OH), 3.42 (dd, 1H, \( J = 10.2 \) and 3.6 Hz, H5a), 3.34 (dd, 1H, \( J = 10.2 \) and 4.2 Hz, H5b), 1.49 (s, CH₃-isopropylidene), 1.35 (s, CH₃-isopropylidene).

\( ^13C \) NMR: (75 MHz, CDCl₃) \( \delta_C = 142.8 \) (ipso C(Ph)₃), Aromatics – 128.5, 128.4, 127.9, 127.7, 127.3, 126.9, 112.0 (acetal-C), 103.3 (C1), 87.8 (C(Ph)₃), 86.7 (C4), 82.0 (C3), 81.9 (C2), 79.2 (C5), 26.4 (CH₃-isopropylidene), 25.1 (CH₃-isopropylidene).

EIMS: 432 (M⁺, 4%), 417 (M⁺ - CH₃, 2%), 243 (100%).
5-O-(t-Butyldimethylsilyl)-2,3-O-isopropyldene-D-ribofuranose (4,9)

The general procedure for TBDMS primary protection (3,6) was carried out on 2,3-O-isopropyldene-D-ribofuranose (100 mg, 0.238 mmol). The residue was purified by flash chromatography (3:1 hexanes-EtOAc) to afford the silyl ether (60 mg, 0.20 mmol, 75%).

MP: 56-58 °C (Lit. 55-57 °C)

TLC: Rf 0.80 (3:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 5.26 (d, 1H, $J = 11.9$ Hz, H1), 4.76 (d, 1H, $J = 11.9$ Hz, H2), 4.67 (d, 1H, $J = 5.9$ Hz, H3), 4.48 (d, 1H, $J = 5.9$ Hz, H4), 4.33 (br s, 1H, OH), 3.76 (dd, 1H, $J = 11.1$ and 2.1 Hz, H5a), 3.71 (dd, 1H, $J = 11.1$ and 2.1 Hz, H5b), 1.46 (s, 3H, CH$_3$-isopropyldene), 1.30 (s, 3H, CH$_3$-isopropyldene), 0.91 (s, 9H, C(CH$_3$)$_3$), 0.12 (s, 6H, SiC H$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 111.9 (acetal-C), 103.4 (C1), 87.6 (C4), 86.9 (C3), 81.7 (C2), 64.7 (C5), 26.4 (CH$_3$-isopropyldene), 25.8 (C(CH$_3$)$_3$), 24.9 (CH$_3$-isopropyldene), 18.3 (C(CH$_3$)$_3$), -5.5 (Si(CH$_3$)$_2$).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3378, 3024, 2937, 1473, 1385, 1377, 1240, 1160, 1087, 1045, 872, 840.

EIMS: 289 (M$^+$ - CH$_3$, 15%), 247 (M$^+$ - C(CH$_3$)$_3$, 65%), 189 (M$^+$ - TBDMS, 65%), 75 (100%).
A solution of 2,3-O-isopropylidene-D-ribose (177 mg, 0.93 mmol) and DMAP (114 mg, 0.93 mmol) in dry pyridine (1 mL) was cooled to -10 °C. To this solution was slowly added pivaloyl chloride (137 µL, 1.20 mmol). After 2 hours, MeOH was added, and the reaction solution was allowed to warm to room temperature. Once the reaction was complete (TLC) all the solvent was removed in vacuo. EtOAc was added and the organic layer was washed with saturated aqueous NaHCO₃ solution, water and brine. Drying over MgSO₄ and evaporation of solvent in vacuo at or below 40 °C gave the crude product. This residue was purified by flash chromatography (4:1 hexanes-EtOAc) to afford the silyl ether (178 mg, 0.65 mmol, 70%).

**TLC:** Rf 0.35 (4:1 hexanes-EtOAc)

**¹H NMR:**

(300 MHz, CDCl₃) δH 5.44 (br. s, 1H, H1), 5.38 (dd, 1H, H1), 4.39-4.26 (m, 4H), 4.15 (dd, 1H, J = 12.0 and 3.6 Hz, H5a), 4.09 (dd, 1H, J = 12.0 and 3.6 Hz, H5b), 4.08-4.01 (m, 2H, H5a,b), 1.55 (s, 3H, CH₃-isopropylidene), 1.47 (s, 3H, CH₃-isopropylidene), 1.31 (s, 3H, CH₃-isopropylidene), 1.205 (s, 9H, C(CH₃)₃), 1.19 (s, 9H, C(CH₃)₃).

**¹³C NMR:**

(75 MHz, CDCl₃) δC 178.5 (C=O), 177.8 (C=O), 113.9 (acetal-C), 112.6 (acetal-C), 103.1 (C1), 97.5 (C1) 85.9, 85.0, 81.7, 81.5, 79.2, 78.5 (C2, C3, C4), 65.5 (C5), 65.3 (C5), 38.9 (C(CH₃)₃), 38.7 (C(CH₃)₃), 27.2 (C(CH₃)₃), 27.2 (C(CH₃)₃), 26.5 (CH₃-isopropylidene), 26.2 (CH₃-isopropylidene), 25.0 (CH₃-isopropylidene), 24.8 (CH₃-isopropylidene).

**EIMS:** 259 (M⁺ - CH₃, 40%), 159 (M⁺ - C₆H₁₁O₂, 9%), 114 (M⁺ - C₇H₁₁O₄, 32%).
Ethyl (2Z,4S,5S)-4,5-isopropylidene-7-[(2,2-dimethylpropyl)oxy]-6-oxo hept-2-enoate \(^{11}(4.11)\)

To a solution of 5-O-(2,2-dimethyl-propanoyl)-2,3-O-isopropylidene-D-ribose (100 mg, 0.37 mmol) in dry DCM (1.5 mL) was added [ethyl(triphenylphosphoranylidene)acetate] (157 mg, 0.45 mmol) and the reaction mixture stirred at room temperature. Upon completion (approximately 6 days, TLC), the mixture was diluted with DCM (1.5 mL), treated with Dess-Martin periodinane (191 mg, 0.45 mmol) and stirred at room temperature for 3 hours. The solvent was removed in vacuo and the residue was purified by chromatography (5:1 hexanes-EtOAc) to afford the title compound as a colourless oil (91 mg, 0.27 mmol, 72%).

TLC:
\[ R_f 0.5 \text{ (5:1 hexanes-EtOAc)} \]

\(^1\)H NMR:
\[ (300 \text{ MHz, CDCl}_3) \] \(\delta_H\) 6.20 (dd, 1H, \(J = 11.5 \text{ and } 7.7 \text{ Hz, H3}\)), 5.95 (dd, 1H, \(J = 11.5 \text{ and } 1.7 \text{ Hz, H2}\)), 5.90 (td, 1H, \(J = 7.7 \text{ and } 1.7 \text{ Hz, H4}\)), 4.84 (d, 1H, \(J = 18.2 \text{ Hz, H7a}\)), 4.83 (d, 1H, \(J = 7.7 \text{ Hz, H5}\)), 4.75 (d, 1H, \(J = 18.2 \text{, H7b}\)), 4.16 (qd, 2H, \(J = 7.2 \text{ and } 0.5 \text{ Hz, OCH}_2\text{CH}_3\)), 1.61 (s, 3H, \(\text{CH}_3\)-isopropylidene), 1.40 (s, 3H, \(\text{CH}_3\)-isopropylidene), 1.27 (t, 3H, \(J = 7.2 \text{ Hz, OCH}_2\text{CH}_3\)).

\(^{13}\)C NMR:
\[ (75 \text{ MHz, CDCl}_3) \] \(\delta_C\) 201.4 (C6), 177.6 (Piv-C=O), 165.4 (C1), 142.3 (C3), 123.2 (C2), 111.0 (acetal-C), 81.2 and 75.5 (C4, C5), 67.4 (C7), 60.6 (OCH\(_2\)CH\(_3\)), 38.7 (C(CH\(_3\))\(_3\)), 27.2 (C(CH\(_3\))\(_3\)), 26.6 (CH\(_3\)-isopropylidene), 24.6 (CH\(_3\)-isopropylidene), 14.2 (OCH\(_2\)CH\(_3\)).

IR:
\[ \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} 3040, 2960, 1740, 1715, 1490, 1384, 1220. \]

HRMS:
Found 343.1756. Calculated for C\(_{17}\)H\(_{27}\)O\(_7\) 343.1757.

\([\alpha]_D\):
+84.0 (c = 1.0 CHCl\(_3\)).
D-Arabinose dibenzyl dithioacetal (4.12)

A solution of D-arabinose (100 mg, 0.6 mmol) in conc. HCl (100 µL) was cooled to 0 °C. To this cooled solution was slowly added benzyl mercaptan (320 µL, 2.70 mmol). The reaction mixture was left to stir overnight. A thick paste formed overnight. This paste was dissolved in CHCl₃ extracted with water. The CHCl₃ was removed in vacuo in the fume hood, due to the terrible stench that accompanies this reaction. The crude product was purified by column chromatography (1:1 hexanes-EtOAc) and the desired product was obtained as a chunky white powder (112 mg, 0.29 mmol, 49%).

**MP:** 122-124 °C

**TLC:** $R_f$ 0.50 (EtOAc)

**¹H NMR:** (300 MHz, CDCl₃) $\delta_H$ 7.28-7.20 (m, 10H, aromatics), 3.96-3.86 (m, 3H, H2, H3, H4), 3.85-3.79 (m, 4H, $\text{CH}_2\text{Ph}$ and $\boxed{\text{CH}_2\text{Ph}}$), 3.78-3.70 (m, 1H, H1), 3.65-3.54 (m, 2H, H5a and H5b).

**¹³C NMR:** (75 MHz, CDCl₃) $\delta_C$ 139.6 (ipso), 139.4 (ipso), 130.2 (ortho and ortho), 129.4 (meta and meta), 127.9 (para), 127.8 (para), 73.1 (C4), 73.0 (C3), 72.1 (C2), 64.9 (C5), 55.7 (C1), 36.4 (C$\text{H}_2\text{Ph}$), 35.9 (C$\text{H}_2\text{Ph}$).

**EIMS:** 380 (M⁺, 9%), 259 (M+1 - C$_7$H$_6$S, 73%), 133 (M+1 - C$_{14}$H$_{16}$S$_2$, 63%), 91 (C$_7$H$_7$, 100%).
D-Arabinose diallyl dithioacetal (4.13)

The general procedure to introduce a dithioacetal protection using concentrated HCl (4.12) was carried out using allyl mercaptan (212 µL, 2.66 mmol) to protect D-arabinose (100 mg, 0.60 mmol) at the anomeric position. The crude product was purified by column chromatography (1:1 hexanes-EtOAc) and the desired product was obtained as a chunky white powder (144 mg, 0.51 mmol, 78%).

MP: 60-62 °C (waxy solid)
TLC: Rf 0.43 (EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 5.90-5.72 (m, 2H, CH$_2$CHCH$_2$ and CH$_2$CHCH$_2$), 5.24-5.08 (m, 4H, CH$_2$CHCH$_2$ and CH$_2$CHCH$_2$), 3.99 (d, 1H, $J = 8.4$ Hz, H1), 3.90-3.70 (m, 5H, H2, H3, H4, H5a and H5b), 3.40-3.24 (m, 4H, CH$_2$CHCH$_2$ and CH$_2$CHCH$_2$), 2.66 (v br s, 3H, OH × 3), 2.15 (br s, 1H, OH).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 133.7 (CH$_2$CHCH$_2$), 133.5 (CH$_2$CHCH$_2$), 118.4 (CH$_2$CHCH$_2$), 118.3 (CH$_2$CHCH$_2$), 72.6 (C4), 70.8 (C3), 70.7 (C2), 64.0 (C5), 54.3 (C1), 34.4 (CH$_2$CHCH$_2$), 32.8 (CH$_2$CHCH$_2$).

EIMS: 281 (M+1, 10%), 207 (M$^+$ - C$_3$H$_8$S, 16%), 189 (M$^+$ - C$_3$H$_5$S - H$_2$O, 17%), 133 (M$^+$ - C$_6$H$_{11}$S$_2$, 81%), 115 (100%), 73 (C$_3$H$_5$S, 77%).
5-O-(tert-Butyldiphenylsilyl)-D-arabinofuranose (4.14)

The general procedure for TBDPS primary protection (3.9) was carried out on D-arabinose (100 mg, 0.67 mmol). The residue was purified by flash chromatography (1:1 hexanes-EtOAc, followed by pure EtOAc) to afford the silyl ether (182 mg, 0.47 mmol, 72%).

TLC: Rf 0.11 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 7.70-7.63 (m, 4H, ortho aromatics), 7.45-7.33 (m, 6H, para and meta aromatics), 5.38 (br s, 1H), 5.26 (d, 1H, $J = 3.9$ Hz), 4.25-3.66 (a series of m, 5H, 5H, OH, OH), 1.05(s, 9H, C(CH$_3$)$_3$), 1.05(s, 9H, C(CH$_3$)$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 135.5 (ortho and ortho), 135.4 (ortho and ortho), 132.2 (ipso), 132.1 (ipso), 131.7 (ipso), 131.5 (ipso), 130.1 (para), 130.0 (para and para), 129.9 (para), 127.9 (meta and meta), 127.8 (meta and meta), 103.2 (C1), 96.5 (C1), 86.8 (C4), 82.8 (C4), 79.0 (C2), 77.9 (C3), 77.6 (C2), 76.2 (C3), 64.5 (C5), 64.0 (C5), 26.8 (C(CH$_3$)$_3$), 26.6 (C(CH$_3$)$_3$), 19.1 (C(CH$_3$)$_3$), 19.0 (C(CH$_3$)$_3$).
5-O-(tert-Butyldiphenylsilyl)-D-arabinose dibenzyl dithioacetal (4.15)

The general procedure to introduce a dithioacetal protection using conc. HCl (4.12) was carried out using benzyl mercaptan (197 mg i.e. 212 µL, 2.66 mmol) to protect 5-O-(tert-butyldiphenylsilyl)-D-arabinose (100 mg, 0.26 mmol) at the anomeric position. The crude product was purified by column chromatography (5:1 hexanes-EtOAc) and the desired product was obtained as a white powder (82 mg, 0.13 mmol, 51%).

TLC: \( R_f 0.16 \) (5:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \( \delta \) H 7.65-7.15 (m, 20H, aromatics), 3.93 (t, 1H, J = 7.8 Hz, H4), 3.87-3.70 (m, 8H, H1, H2, CH\(_2\)Ph and CH\(_2\)Ph), 3.67-3.59 (m, 1H, H3,), 3.03 (d, 1H, J = 2.1 Hz, OH), 2.57 (d, 1H, J = 7.2 Hz, H5a), 2.26 (d, 1H, J = 8.4 Hz, H5b), 1.05 (s, 9H, C(CH\(_3\))\(_3\)).

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \( \delta \) C 137.5 (ortho Si), 137.4 (ortho Si), 135.4 (ipso), 135.3 (ipso), 132.8 (ipso Si), 132.7 (ipso Si), 129.7 (para Si x 2), 128.9 (meta), 128.8 (meta), 128.5 (ortho), 128.4 (ortho), 127.6 (meta Si x 2), 127.4 (para), 127.2 (para), 71.9 (C3), 70.9 (C2), 70.1 (C4), 64.8 (C5), 54.7 (C1), 35.7 (CH\(_2\)Ph), 34.5 (CH\(_2\)Ph), 26.8 (C(CH\(_3\))\(_3\)), 19.2 (C(CH\(_3\))\(_3\)).

EIMS: 619 (M+1, 1%), 560 (M\(^+\) - C\(_4\)H\(_{10}\), 1%), 163 (C\(_3\)H\(_{10}\)O\(_4\)Si, 38%), 91 (C\(_3\)H\(_7\), 100%).
To a solution of 5-O-(tert-butyldiphenylsilyl)-D-arabinose dibenzyl dithioacetal (100 mg, 0.16 mmol) and CuSO$_4$ (73 mg, 0.45 mmol) in anhydrous acetone (1 mL) was added a catalytic amount of H$_2$SO$_4$ (10% m/m). The reaction took place within 5 minutes. The reaction mixture was neutralised with triethylamine and the solvent removed in vacuo. The crude product was purified by column chromatography (10:1 hexanes-EtOAc) to obtain the desired product (103 mg, 0.15 mmol, 98%) as an oil.

TLC: \[ R_f 0.33 \ (10:1 \text{ hexanes-EtOAc}), \ 0.81 \ (4:1 \text{ hexanes-EtOAc}) \]

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 7.72-7.10 (m, 20H, aromatics), 4.30 (dd, 1H, $J = 7.2$ and 2.4 Hz, H3), 3.93 (dd, 1H, $J = 8.4$ and 7.5 Hz, H2), 3.85 (d, 2H, $J = 1.5$ Hz, CH$_2$Ph), 3.79 (d, 1H, 2.7 Hz, H1), 3.77 (d, 2H, $J = 1.5$ Hz, CH$_2$Ph), 3.65 (dd, 2H, $J = 10.5$ and 1.7 Hz, H5 and H5b), 3.56-3.44 (m, 1H, H4), 1.37 (s, 3H, CH$_3$-isopropylidene), 1.25 (s, 3H, CH$_3$-isopropylidene), 1.07 (s, 9H, C(CH$_3$)$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 138.2 (ortho Si), 138.0 (ortho Si), 135.5 (ipso), 135.4 (ipso), 133.1 (ipso Si), 132.8 (ipso Si), 129.7 (para Si), 129.2 (meta), 129.0 (meta), 128.4 (ortho), 128.4 (ortho), 127.7 (meta Si), 127.6 (meta Si), 126.9 (para and para), 109.8 (acetal-C), 83.7 (C3), 73.4 (C4), 65.2 (C5), 52.1 (C1), 35.7 (CH$_2$Ph), 35.3 (CH$_2$Ph), 29.7 (CH$_3$-isopropylidene), 26.9 (C(CH$_3$)$_3$), 26.6 (CH$_3$-isopropylidene), 19.3 (C(CH$_3$)$_3$).

EIMS: 659 (M+1, 2%), 419 (M$^+$ - C$_{16}$H$_{19}$Si, 26%), 404 (M$^+$ - C$_{16}$H$_{19}$Osi, 1%), 241 (M$^+$ - C$_{30}$H$_{30}$Si, 70%), 91 (C$_7$H$_7$, 100%).
To a solution of D-arabinose dibenzyl dithioacetal (100 mg, 0.26 mmol) in anhydrous acetone (1 mL) was added a catalytic amount of H$_2$SO$_4$ (10% m/m). After 16 hours, P$_2$O$_5$ (50 mg) was added with cooling and stirring. The reaction was left to stir for 1 hour. The reaction mixture was filtered to remove the P$_2$O$_5$. After filtering and washing with acetone anhydrous, CuSO$_4$ (50 mg) was added and the reaction was left to react for a further 24 hours. After filtering, the solvent was removed *in vacuo* and the product purified by column chromatography (5:1 hexanes-EtOAc) (83 mg, 0.180 mmol, 68%) as a thick oil.

**TLC:** $R_f$ 0.80 (5:1 hexanes-EtOAc)

**$^1$H NMR:** (300 MHz, CDCl$_3$) $\delta$ 7.37-7.08 (m, 10H, aromatics), 4.32 (dd, 1H, $J = 6.9$ and 2.4 Hz), 4.05-3.75 (m, 9H, CH$_2$Ph $\times$ 2), 1.41 (s, 3H, CH$_3$-isopropylidene), 1.34 (s, 3H, CH$_3$-isopropylidene), 1.27 (s, 3H, CH$_3$-isopropylidene), 1.06 (s, 3H, CH$_3$-isopropylidene).

**$^{13}$C NMR:** (75 MHz, CDCl$_3$) $\delta$C 138.2 ($ipso$), 137.9 ($ipso$), 129.2 ($ortho$), 128.9 ($ortho$), 128.4 ($meta \times 2$), 126.9 ($para \times 2$), 110.2 (acetal-C), 109.6 (acetal-C), 83.6 (C4), 78.9 (C3), 77.2 (C2), 67.5 (C5), 51.6 (C1), 35.5 (CH$_2$Ph), 35.0 (CH$_2$Ph), 27.2 (CH$_3$-isopropylidene), 26.9 (CH$_3$-isopropylidene), 26.4 (CH$_3$-isopropylidene), 25.3 (CH$_3$-isopropylidene).

**IR:** $\nu_{max}$(CHCl$_3$)/cm$^{-1}$ 2949, 2866, 1278, 1229, 1160, 1093, 975.

**HRMS:** Found 460.1742. Calculated for C$_{25}$H$_{32}$S$_2$O$_4$ 460.1742.

**EIMS:** 461 (M+1, 7%), 460 (M+, 20%), 336 (M$^+$ - C$_7$H$_8$S, 10%), 91 (100%).
2,3-\textit{O-bis-DHP-\text-d-arabinose dibenzyl dithioacetal} $^{13}$ (4.29)

To a reaction mixture of 1-Benzyl dithioacetal-\text-d-arabinose (50 mg, 0.132 mmol) and \textit{para}-toluenesulphonic acid (10 mmol %) in chloroform (0.5 mL) was added 6,6’-bi(3,4-dihydro-2\textit{H}-pyran) (66 mg, 0.395 mmol). The reaction mixture was allowed to stir at reflux overnight. Chloroform was added and the reaction solution was allowed to stir for a further day, at room temperature. The chloroform was removed \textit{in vacuo} and a DCM / NaHCO$_3$ workup was carried out. Column chromatography (2:1 hexanes-EtOAc) yielded the desired product as a colourless oil (43 mg, 0.093mmol, 72%).

\textbf{TLC:} \hspace{1em} R$_f$ 0.86 (1:1 hexanes-EtOAc)

$^1$\textbf{H NMR:} \hspace{1em} (300 MHz, CDCl$_3$) $\delta$H 7.50-7.10 (m, 10H, aromatics), 4.18-3.50 (m, 13H, CH$_2$Ph $\times$ 2, OCH$_2$ of DHP$\times$ 2, H2, H3, H4, H5a and H5b), 2.93 (br s, OH), 2.12 (d, 1H, $J$ = 8.4 Hz, OH), 2.90-1.20 (m, 12H, CH$_2$ of DHP).

$^{13}$\textbf{C NMR:} \hspace{1em} (75 MHz, CDCl$_3$) $\delta$C 137.7 (ipso), 137.4 (ipso), Aromatics - 129.1, 128.9, 128.7, 128.6, 127.3, 96.3 (C1’A), 95.3 (C1’B), 70.9 (C3), 70.0 (C2), 66.3 (C4), 60.9 (C5’A), 60.8 (C5’B), 60.7 (C5), 54.8 (C1), 35.8 (CH$_2$Ph), 34.4 (CH$_2$Ph), 28.4 (C2’A and C2’B), 25.0 (C4’A and C4’B), 18.3 (C3’A), 18.1 (C3’B).

\textbf{IR:} \hspace{1em} $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3603, 2880, 1097, 1076, 1045.

\textbf{HRMS:} \hspace{1em} Found 463.2189. Calculated for C$_{22}$H$_{39}$S$_2$O$_6$ 463.2188.

\textbf{EIMS:} \hspace{1em} 463 (M+1, 30%), 154 (100%).
6.4.2 ARABINOSE – Wittig Route

6.4.2.1 ARABINOSE – Wittig Route – isopropylidene (TBDPS / TBDMS)

**Ethyl (2E,4S,5R)-7-O-(tert-butyldiphenylsilyl)-4,5,6-trihydroxyhept-2-enoate (4.31)**

![Chemical Structure](image)

To a solution of 5-O-(tert-butyldiphenylsilyl)-D-arabinose (300 mg, 0.773 mmol) in dry DCM (3 mL) was added [ethyl(triphenylphosphoranylidene)acetate] (323 mg, 0.928 mmol) and the reaction mixture stirred at room temperature. Upon completion (approximately 2 days, TLC), the solvent was removed in vacuo and the residue was purified by chromatography (2:1 hexanes-EtOAc) to afford the title compound as a colourless oil (214 mg, 0.464 mmol, 60%)

**TLC:** $R_f$ 0.63 (1:1 hexanes-EtOAc)

**$^1$H NMR:** (300 MHz, CDCl$_3$) $\delta$H 7.64-7.62 (m, 4H, ortho aromatics), 7.52-7.34 (m, 6H, meta and para aromatics), 6.97 (dd, 1H, $J = 15.6$ and 4.2 Hz, H3), 6.13 (dd, 1H, $J = 15.6$ and 2.1 Hz, H2), 4.57(dt, 1H, $J = 4.2$ and 2.1 Hz, H6), 4.18 (q, 2H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 3.85-3.74 (m, 3H, H4, H5 and H7a), 3.65 (dd, 1H, $J = 6.3$ and 2.1 Hz, H7b), 2.73 (br s, 1H, OH), 1.28 (t, 3H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 1.06 (s, 9H, C(CH$_3$)$_3$).

**$^{13}$C NMR:** (75 MHz, CDCl$_3$) $\delta$C 166.4 (C1), 147.7 (C3), 135.3 (ortho), 132.4 (ipso), 129.8 (meta), 127.7 (para), 121.4 (C2), 73.2 (C5), 71.5 (C6), 70.3 (C4), 64.9 (C7), 60.4 (s, OCH$_2$CH$_3$), 26.8 (C(CH$_3$)$_3$), 19.1 (C(CH$_3$)$_3$), 14.1 (OCH$_2$CH$_3$).
IR: \( \nu_{\text{max}} \text{(CHCl}_3)/\text{cm}^{-1} \): 3755, 3567, 3024, 2864, 1717, 1656, 1310, 1279, 1205, 1181, 982, 823, 741.

EIMS: 305 (M+1 - C\(_{12}\)H\(_{10}\), 41%), 259 (M\(^+\) - C\(_{14}\)H\(_{15}\)O, 31%), 241 (100%).

Ethyl (2\(E\),4\(S\),5\(R\))-7-\(O\)-(tert-butyldiphenylsilyl)-6-hydroxy-4,5-\(O\)-isopropylidene hept-2-enoate (4.32)

The general procedure to isopropylidene protect arabinose analogues, using anhydrous CuSO\(_4\), a catalytic amount of H\(_2\)SO\(_4\) and dry acetone, (4.18) was used to protect ethyl (2\(E\),4\(S\),5\(R\))-7-\(O\)-(tert-butyldiphenylsilyl)-4,5,6-trihydroxyhept-2-enoate (100 mg, 0.218 mmol). The reaction mixture was allowed to stir at room temperature for approximately 15 minutes. The reaction mixture was filtered and neutralised with triethyl amine. The solvent was removed in vacuo and the residue was purified by chromatography (5:1 hexanes-EtOAc) to afford the title compound as a colourless oil (90 mg, 0.181 mmol, 83%), along with 4.36 (15 mg, 0.031 mmol, 14%), and starting material.

TLC: \text{R}_f\ 0.54 (3:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \( \delta \text{H} \): 7.67-7.62 (m, 4H, ortho aromatics), 7.46-7.34 (m, 6H, meta and para aromatics), 7.03 (dd, 1H, \( J = 15.8 \) and 4.7 Hz, H3), 6.15 (dd, 1H, \( J = 15.8 \) and 1.8 Hz, H2), 4.60 (ddd, 1H, \( J = 6.9, 4.8 \) and 1.8 Hz, H4), 4.19 (q, 2H, \( J = 7.2 \) Hz, OCH\(_2\)CH\(_3\)), 3.83-3.74 (m, 4H, H5, H6, H7a and H7b), 2.62 (d, 1H, \( J = 3.0 \) Hz, OH), 1.38 (s, 3H, CH\(_3\)-isopropylidene), 1.37 (s, 3H, CH\(_3\)-isopropylidene), 1.28 (t, 3H, \( J = 7.2 \) Hz, OCH\(_2\)CH\(_3\)), 1.06 (s, 9H, C(CH\(_3\))\(_3\)).
$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 166.1 (C1), 145.3 (C3), 135.4 ($\text{ortho} \times 2$), 132.7 ($\text{ipso}$), 132.6 ($\text{ipso}$), 129.8 ($\text{meta}$), 129.7 ($\text{meta}$), 127.7 ($\text{para}$), 127.6 ($\text{para}$), 121.5 (C2), 109.9 (acetal-C), 79.8 (C5), 78.4 (C4), 72.9 (C6), 64.8 (C7), 60.4 (OCH$_2$CH$_3$), 26.9 (CH$_3$-$\text{isopropylidene}$), 26.8 (C(CH$_3$)$_3$), 26.6 (CH$_3$-$\text{isopropylidene}$), 19.2 (C(CH$_3$)$_3$), 14.3 (OCH$_2$CH$_3$).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3566, 3427, 2937, 2899, 1721, 1430, 1310, 1269, 1225, 1114, 983, 824.

EIMS: 483 (M$^+$ - CH$_3$, 63%), 441 (M$^+$ - C$_4$H$_9$, 79%), 383 (M$^+$ - C$_8$H$_{19}$, 100%).

**Ethyl (2E,4S,5R)-7-O-(tert-butyldiphenylsilyl)-5,6-O-isopropylidene)-4-hydroxy-hept-2-enoate (4.33)**

The title compound was obtained as a byproduct as a colourless oil (15 mg, 0.031 mmol, 14%), in the reaction to synthesis 4.32.

TLC: $R_f$ 0.34 (3:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 7.67-7.62 (m, 4H, ortho), 7.43-7.34 (m, 6H, meta and para), 7.04 (dd, 1H, $J = 15.6$ and 4.2 Hz, H3), 6.16 (dd, 1H, $J = 15.6$ and 1.8 Hz, H2), 4.69-4.61 (m, 1H, H4), 4.29-4.14 (m, 2H, H5 and H6), 3.99 (dd, 1H, $J = 10.9$ and 7.5 Hz, H7a), 4.18 (q, 2H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 3.77 (dd, 1H, $J = 10.9$ and 4.2 Hz, H7b), 3.05 (d, 1H, $J = 6.3$ Hz, OH), 1.43 (s, 3H, CH$_3$-$\text{isopropylidene}$), 1.32 (s, 3H, CH$_3$-$\text{isopropylidene}$), 1.27 (t, 3H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 1.05 (s, 9H, C(CH$_3$)$_3$).


**13C NMR:**

$(75 \text{ MHz, CDCl}_3) \delta_{C} 166.2 (C1), 146.8 (C3), 135.5 (ortho), 135.4 (ortho), 132.4 (ipso \times 2), 129.8 (meta \times 2), 127.8 (para), 127.7 (para), 121.8 (C2), 108.6 (acetal-C), 78.6 (C5), 76.8 (C6), 68.8 (C4), 62.3 (C7), 60.4 (OCH$_2$CH$_3$), 27.0 (CH$_3$-isopropylidene), 26.8 (C(CH$_3$)$_3$), 24.8 (CH$_3$-isopropylidene), 19.2 (C(CH$_3$)$_3$), 14.3 (OCH$_2$CH$_3$).

**IR:**

$\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$: 3565, 3427, 2930, 2898, 1721, 1430, 1311, 1269, 1110, 980, 824.

**EIMS:**

483 (M$^+$ - CH$_3$, 1%), 441 (M$^+$ - C$_4$H$_9$, 1%), 383 (M$^+$ - C$_8$H$_{19}$, 1%), 305 (M$^+$ - C$_{14}$H$_{24}$, 22%), 241 (M+1 - OTBDPS, 100%).

Ethyl \((2E,4S,5R)-7-O-(\text{tert-butyldiphenylsilyl})-4,5-O-isopropylidene-6-oxo\) hept-2-enoate (4.34)

The general route for Dess-Martin oxidation (3.3) was carried out on ethyl \((2E,4S,5R)-7-O-(\text{tert-butyldiphenylsilyl})-6-hydroxy-4,5-O-isopropylidene-hept-2-enoate\) (100 mg, 0.200 mmol) (4.32). The residue was purified by chromatography (5:1 hexanes-EtOAc) to afford the title compound as a colourless oil (99 mg, 0.200 mmol, 98%).

**TLC:**

$R_f$ 0.56 (5:1 hexanes-EtOAc)

$^1$H NMR:

$(300 \text{ MHz, CDCl}_3) \delta_{H}$ 7.67-7.64 (m, 4H, ortho aromatics), 7.42-7.33 (m, 6H, meta and para aromatics), 6.85 (dd, 1H, $J = 15.8$ and 5.1 Hz, H3), 6.06 (dd, 1H, $J = 15.8$ and 1.8 Hz, H2), 4.64 (d, 1H, $J = 19.2$ Hz, H7a), 4.55 (d, 1H, $J = 19.2$ Hz, H7b), 4.30 (ddd, 1H, $J = 7.8$, 4.8 and 1.5 Hz, H4), 4.19 (q, 2H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 4.08 (d, 1H, $J = 7.8$ Hz, H5),...
1.36 (s, 3H, CH₃-isopropylidene), 1.28 (t, 3H, J = 7.2 Hz, OCH₂CH₃), 1.21 (s, 3H, CH₃-isopropylidene), 1.09 (s, 9H, C(CH₃)₃).

**¹³C NMR:** (75 MHz, CDCl₃) δC 204.7 (C6), 165.4 (C1), 142.6 (C3), 135.3 (ortho), 135.2 (ortho), 132.4 (ipsa), 132.3 (ipsa), 129.7 (meta), 129.6 (meta), 127.5 (para), 127.4 (para), 122.4 (C2), 111.3 (acetal-C), 82.5 (C5), 76.4 (C4), 67.3 (C7), 60.3 (OCH₂CH₃), 26.5(C(CH₃)₃), 26.3 (CH₃-isopropylidene), 25.7 (CH₃-isopropylidene), 19.1 (C(CH₃)₃), 14.0 (OCH₂CH₃).

**IR:** νmax(CHCl₃)/cm⁻¹ 2900, 2863, 1793, 1723, 1707, 1657, 1387, 1269, 1225, 1218, 1113, 1036, 824.

**HRMS:** Found 497.2360. Calculated for C₂₈H₃₇O₆Si 497.2359.

**Ethyl (2E,4S, 5R)-7-O-(tert-butyldiphenylsilyl)-5,6-O-isopropylidene-4-oxohept-2-enoate (4.35)**

The general route for Dess-Martin oxidation (3.3) was carried out on 4.33 to obtain the title compound. After column chromatography (5:1 hexanes-EtOAc) the desired product was obtained as a colourless oil (91 mg, 0.184 mmol, 92%).

**TLC:** Rₜ 0.50 (5:1 hexanes-EtOAc)

**¹H NMR:** (300 MHz, CDCl₃) δH 7.64-7.56 (m, 4H, ortho aromatics), 7.53 (d, 1H, J = 15.9 Hz, H3), 7.39-7.31 (m, 6H, meta and para aromatics), 6.71 (d, 1H, J = 15.9 Hz, H2), 4.73 (d, 1H, J = 7.8 Hz, H5), 4.48 (ddd, 1H, J = 7.8, 5.1 and 3.6 Hz, H6), 4.21 (q, 2H, J = 7.2 Hz, OCH₂CH₃), 3.72 (dd, 1H, J = 11.4 and 5.0 Hz, H7a), 3.66 (dd, 1H, J = 11.4 and 3.6 Hz, H7b), 1.59 (s, 3H, CH₃-isopropylidene), 1.36 (s, 3H, CH₃-isopropylidene), 1.24 (t, 3H, J = 7.2 Hz, OCH₂CH₃), 0.95 (s, 9H, C(CH₃)₃).
$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 196.7 (C4), 165.2 (C1), 136.3 (C3), 135.5 (ortho), 135.4 (ortho), 132.7 (ipso), 132.6 (ipso), 130.8 (meta), 129.7 (meta), 129.6 (para), 127.6 (para), 127.5 (C2), 110.2 (acetal-C), 80.7 (C6), 78.9 (C5), 61.5 (OCH$_2$CH$_3$), 60.3 (C7), 26.8 (CH$_3$-isopropylidene), 26.7 (C(CH$_3$)$_3$), 24.7 (CH$_3$-isopropylidene), 19.1 (C(CH$_3$)$_3$), 14.2 (OCH$_2$CH$_3$).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 2899, 1793, 1720, 1700, 1387, 1380, 1230, 1210, 1035.

HRMS: Found 497.2359. Calculated for C$_{28}$H$_{37}$O$_6$Si 497.2359.

Ethyl (2$E$,4$S$,5$R$)-7-hydroxy-4,5-0-isopropylidene-6-oxohept-2-enoate$^{14}$ (4.36)

A solution of ethyl (2$E$,4$S$,5$R$)-7-0-(tert-butyldiphenylsilyl)-4,5-0-isopropylidene-6-oxohept-2-enoate (4.34) (50 mg, 0.101 mmol) in dry THF (2 mL) was cooled to 0 $^\circ$C and to the solution was added HF-pyridine (0.12 mL). The reaction mixture was allowed to stir at 0 $^\circ$C for approximately 30 minutes and thereafter left to stir at room temperature, monitoring by TLC to completion. The reaction mixture was diluted with ether (20 mL) and neutralised with NaHCO$_3$. The organic layer was dried over MgSO$_4$ and the solvent removed in vacuo. The residue was purified by chromatography to afford the title compound (52 mg, 0.101 mmol, 89%).

TLC: $R_f$ 0.46 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 6.94 (dd, 1H, $J = 15.6$ and 5.1 Hz, H3), 6.15 (d, 1H, $J = 15.6$ Hz, H2), 4.55 (d, 1H, $J = 14.8$ Hz, H7a), 4.27 (d, 1H, $J = 14.8$ Hz, H7b), 4.26 - 4.20 (m, 2H, H4 and H5), 4.20 (q, 2H, $J = 7.2$ Hz,
OCH₂CH₃), 1.46 (s, 3H, CH₃-isopropylidene), 1.45 (s, 3H, CH₃-isopropylidene), 1.29 (t, 3H, J = 7.2 Hz, OCH₂CH₃).

¹³C NMR: (75 MHz, CDCl₃) δC 207.9 (C6), 165.6 (C1), 142.4 (C3), 123.2 (C2), 11.9 (acetal-C), 82.9 (C5), 81.3 (C4), 66.2 (C7), 60.7 (OCH₂CH₃), 26.6 (CH₃-isopropylidene), 26.3 (CH₃-isopropylidene), 14.2 (OCH₂CH₃).

IR: νmax(CHCl₃)/cm⁻¹ 3455, 3034, 2995, 1740, 1722, 1702, 1374, 1215, 1204, 982, 668.

EIMS: 199 (M+1 - isopropylidene - H₂O, 48%), 60 (100%).

**Ethyl (2E,4S,5R)-7-O-(tert-butyldimethylsilyl)-4,5-O-isopropylidene-6-oxohept-2-enoate (4.37)**

The general procedure for TBDMS primary protection (3.6) was carried out on ethyl (2E,4S,5R)-7-hydroxy-4,5-O-isopropylidene-6-oxohept-2-enoate (200 mg, 0.78 mmol). The residue was purified by flash chromatography (7:1 hexanes-EtOAc) to afford the silyl ether (225 mg, 0.61 mmol, 60%).

TLC: Rf 0.49 (7:1 hexanes-EtOAc)

¹H NMR: (300 MHz, CDCl₃) δH 6.96 (dd, 1H, J = 15.6 and 4.8 Hz, H3), 6.15 (d, 1H, J = 15.6 Hz, H2), 4.65 (d, 1H, J = 19.2 Hz, H7a), 4.64 (ddd, 1H, J = 7.8, 4.8 and 1.2 Hz, H4), 4.53 (d, 1H, J = 19.2 Hz, H7b), 4.28 (d, 1H, J = 7.8 Hz, H5), 4.20 (q, 2H, J = 7.2 Hz, OCH₂CH₃), 1.46 (s, 3H, CH₃-isopropylidene x 2), 1.28 (t, 3H, J = 7.2 Hz, OCH₂CH₃), 0.92 (s, 9H, C(CH₃)₃), 0.10 (s, 3H, SiCH₃), 0.09 (s, 3H, SiCH₃).
$^{13}$C NMR: (75 MHz, CDCl$_3$) δ$_C$ 205.8 (C6), 165.7 (C1), 143.1 (C3), 122.8 (C2), 111.7 (acetal-C), 82.5 (C5), 76.9 (C4), 67.4 (C7), 60.6 (OCH$_2$CH$_3$), 26.7 (CH$_3$-isopropylidene), 26.3 (CH$_3$-isopropylidene), 25.8 (C(CH$_3$)$_3$), 18.5 (C(CH$_3$)$_3$), 14.2 (OCH$_2$CH$_3$), - 5.33 (SiCH$_3$), - 5.43 (SiCH$_3$).

IR: $\nu_{max}$(CHCl$_3$)/cm$^{-1}$ 3425, 2905, 1737, 1717, 1707, 1376, 1307, 1227, 1182, 1038, 840, 766, 733.

EIMS: 343 (M$^+$ - C$_2$H$_5$, 1%), 327 (M$^+$ - OEt, 2%), 257 (M$^+$ - TBDMS, 10%), 199 (M$^+$ - OTBDMS - isopropylidene, 2%), 43 (100%).

5-O-(tert-Butyldimethylsilyl)-d-arabinofuranose (4.38)

![Structure of 5-O-(tert-Butyldimethylsilyl)-d-arabinofuranose](image)

The general procedure for TBDMS primary protection (3.6) was carried out on d-arabinose (100 mg, 0.67 mmol). The residue was purified by flash chromatography (1:1 hexanes-EtOAc, followed by pure EtOAc) to afford the silyl ether (117 mg, 0.44 mmol, 66%).

TLC: R$_f$ 0.10 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) δ$_H$ 5.29 (s, 1H, H1), 5.25 (d, 1H, $J = 3.6$ Hz, H1), 4.28 (br s, 1H), 4.14-4.05 and 3.95-3.89 and 3.84-3.69 (a series of m, 5H, H2, H3, H4, H5a and H5b), 0.91 (s, 9H, C(CH$_3$)$_3$), 0.88 (s, 9H, C(CH$_3$)$_3$), 0.11 (s, 6H, SiCH$_3$ x 2), 0.09 (s, 6H, SiC$_3$H$_3$ x 2).

$^{13}$C NMR: (75 MHz, CDCl$_3$) δ$_C$ 103.4 (C1), 96.8 (C1), 87.0 (C4), 83.2 (C4), 78.8 (C2), 77.8 (C3), 77.7 (C2), 76.3 (C3), 63.8 (C5), 63.4 (C5), 25.9
(C(CH₃)₃), 25.8 (C(CH₃)₃), 18.5 (C(CH₃)₃), 18.4 (C(CH₃)₃), -5.5 (SiCH₃),
-5.4 (SiCH₃ and SiCH₃), -5.6 (SiCH₃).

EIMS: 265 (M+1, 1%), 247 (M+1 - H₂O, 15%), 207 (M⁺ - t-Bu, 4%), 148 (M⁺ -
TBDMS, 5%), 133 (M⁺ - OTBDMS, 18%).

Ethyl (2E,4S,5R)-7-O-(tert-butyldimethylsilyl)-4,5,6-trihydroxyhept-2-enoate (4.39)

The general procedure to perform a Wittig reaction with
[ethyl(triphenylphosphoranylidene)acetate] in DCM (4.31) was carried out on 5-O-(tert-
butyldimethylsilyl)-D-arabinofuranose (462 mg, 1.75 mmol). Upon completion
(approximately 2 days, TLC), the solvent was removed in vacuo and the residue was
purified by chromatography (2:1 hexanes-EtOAc) to afford the title compound as a
colourless oil (301 mg, 0.901 mmol, 51%).

TLC:  Rₕ 0.59 (1:1 hexanes-EtOAc)

¹H NMR:  (300 MHz, CDCl₃) δH  6.98 (dd, 1H, J = 15.6 and 4.2 Hz, H3), 6.15 (d,
1H, J = 15.6 Hz, H2), 4.60-4.56 (m, 1H, H6), 4.17 (q, 2H, J = 6.9 Hz,
OCH₂CH₃), 3.78-3.77 3.73-3.67 and 3.64-3.62 (m, 4H), 2.85 (br s, 1H,
OH), 1.27 (t, 3H, J = 6.9 Hz, OCH₂CH₃), 0.88 (s, 9H, C(CH₃)₃), 0.08 (s,
6H, SiCH₃ × 2).

¹³C NMR:  (75 MHz, CDCl₃) δC 166.4 (C1), 147.9 (C3), 121.4 (C2), 73.4 (C5), 71.1
(C6), 70.2 (C4), 64.1 (C7), 60.3 (s, OCH₂CH₃), 25.7 (C(CH₃)₃), 18.1
(C(CH₃)₃), 14.0 (OCH₂CH₃), -5.9 (SiCH₃ × 2).

IR: ν_max(CHCl₃)/cm⁻¹ 3450, 1717, 1664, 1393, 1372, 1216, 1098.
EIMS: 335 (M+1, 3%), 143 (CH$_2$OTBDMS, 22%), 117 (M+1 - CH$_2$OTBDMS - OEt, 100%).

**Ethyl (2E,4S,5R)-7-O-(tert-butyldimethylsilyl)-4,5-O-isopropylidene-6-hydroxy-hept-2-enoate (4.40)**

![Chemical Structure](image)

The general procedure to isopropylidene protect arabinose analogues, using anhydrous CuSO$_4$, a catalytic amount of H$_2$SO$_4$ and dry acetone, (4.18) was used to protect ethyl (2E,4S,5R)-7-O-(tert-butyldimethylsilyl)-4,5,6-trihydroxyhept-2-enoate (100 mg, 0.299 mmol). The residue was purified by chromatography (5:1 hexanes-EtOAc) to afford the title compound as a colourless oil, along with 4.43, starting material and a variety of decomposed forms of the varying substrate. Due to the very small yields and large amount of products obtained no yields were determined. Repeating the reaction failed to form any of the single isopropylidene protected products, but gave 4.44, as the single product (100%).

**TLC:** R$_f$ 0.31 (5:1 hexanes-EtOAc)

**$^1$H NMR:** (300 MHz, CDCl$_3$) $\delta$H 7.05 (dd, 1H, $J = 15.6$ and 3.6 Hz, H3), 6.17 (dd, 1H, $J = 15.6$ and 1.5 Hz, H2), 4.60 - 4.51 (m, 1H, H4), 4.20 (q, 2H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 4.24 - 4.12 (m, 2H, H5, H6), 3.92 (dd, 1H, $J = 10.7$ and 7.4 Hz, H7a), 3.75 (dd, 1H, $J = 10.7$ and 3.0 Hz, H7b), 3.29 (d, 1H, $J = 6.0$ Hz, OH), 1.47 (s, 3H, CH$_3$-isopropylidene), 1.34 (s, 3H, CH$_3$-isopropylidene), 1.25 (t, 3H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 0.89 (s, 9H, C(CH$_3$)$_3$), 0.09 (s, 3H, SiCH$_3$), 0.09 (s, 3H, SiC H$_3$).
The title compound was obtained as one of the by-products in the reaction to synthesise 4.40, as a colourless oil.

**Ethyl (2E,4S,5R)-7-O-(tert-butyldimethylsilyl)-4-hydroxy-5,6-O-isopropylidene-hept-2-enoate (4.41)**

![Ethyl (2E,4S,5R)-7-O-(tert-butyldimethylsilyl)-4-hydroxy-5,6-O-isopropylidene-hept-2-enoate (4.41)](image)

The title compound was obtained as one of the by-products in the reaction to synthesise 4.40, as a colourless oil.

**TLC:** \( R_f \) 0.28 (5:1 hexanes-EtOAc)

**\(^1\)H NMR:**

\[ \delta (300 \text{ MHz, CDCl}_3) \]

- 6.98 (dd, 1H, \( J = 15.8 \) and 4.1 Hz, H3)
- 6.16 (dd, 1H, \( J = 15.8 \) and 2.1 Hz, H2)
- 4.55 - 4.52 (m, 1H, H4)
- 4.18 (q, 2H, \( J = 7.2 \) Hz, OCH\(_2\)CH\(_3\))
- 3.97 - 3.89 (m, 1H, H6)
- 3.82 (dd, 1H, \( J = 9.9 \) and 5.1 Hz, H5)
- 3.2 - 3.59 (m, 2H, H7a and H7b)
- 2.07 (d, 1H, \( J = 4.8 \) Hz, OH)
- 1.42 (s, 3H, CH\(_3\)-isopropylidene)
- 1.32 (s, 3H, CH\(_3\)-isopropylidene)
- 1.27 (t, 3H, \( J = 7.2 \) Hz, OCH\(_2\)CH\(_3\))
- 0.88 (s, 9H, C(CH\(_3\))\(_3\))
- 0.07 (s, 3H, SiCH\(_3\))
- 0.06 (s, 3H, SiC H\(_3\))

**\(^{13}\)C NMR:**

\[ \delta (75 \text{ MHz, CDCl}_3) \]

- 166.0 (C1)
- 142.8 (C3)
- 122.3 (C2)
- 101.3 (acetal-C)
- 74.3(C5)
- 72.2 (C6)
- 70.6 (C4)
- 64.5 (C7)
- 60.4 (OCH\(_2\)CH\(_3\))
(C(CH₃)₃), 24.6 CH₃-isopropylidene), 24.0 CH₃-isopropylidene), 18.3 (C(CH₃)₃), 14.3 (OCH₂CH₃), - 5.28 (SiCH₃), - 5.32 (SiCH₃).

IR: \(\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3558, 2990, 2959, 1719, 1700, 1473, 1259, 1224, 1063, 1008, 980.

EIMS: 374 (M⁺, 2%), 359 (M⁺ - CH₃, 20%), 329 (M⁺ - OEt, 1%), 317 (M⁺ - C₄H₉, 17%), 259 (M⁺ - TBDMS, 29%), 117 (100%).

Ethyl (2E,4S,5R)-4,5:6,7-di-O-isopropylidene-hept-2-enoate \( (\text{4.42}) \)

\[
\text{\includegraphics[width=2cm]{structure.png}}
\]

The general procedure to isopropylidene protect arabinose analogues, using anhydrous CuSO₄, a catalytic amount H₂SO₄ and dry acetone, \( (\text{4.18}) \) was used to protect ethyl (2E,4S,5R)-7-O-(tert-butyldimethylsilyl)-4,5,6-trihydroxyhept-2-enoate (300 mg, 0.898 mmol). The residue was purified by chromatography (5:1 hexanes-EtOAc) to afford the title compound as a colourless oil (269 mg, 0.898 mmol, approx. 100%).

TLC: \( R_f \) 0.47 (5:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDC₃) \( \delta_H \) 6.93 (dd, 1H, \( J = 15.8 \) and 4.5 Hz, H3), 6.08 (dd, 1H, \( J = 15.8 \) and 1.3 Hz, H2), 4.52 (ddd, 1H, \( J = 6.3, 4.5 \) and 1.8 Hz, H4), 4.12 (q, 2H, \( J = 7.2 \) Hz, OCH₂CH₃), 4.07 - 4.01 (m, 2H, H5 and H6), 3.86 (dd, 1H, \( J = 10.8 \) and 6.9 Hz, H7a), 3.60 (dd, 1H, \( J = 10.8 \) and 7.5 Hz, H7b), 1.34 (s, 3H, CH₃-isopropylidene), 1.38 (s, 6H, CH₃-isopropylidene × 2), 1.27 (s, 3H, CH₃-isopropylidene), 1.21 (t, 3H, \( J = 7.2 \) Hz, OCH₂CH₃).
\(^{13}\)C NMR: \((75\text{ MHz, CDCl}_3)\) \(\delta_C\) 165.9 (C1), 144.3 (C3), 121.1 (C2), 110.0 (acetal-C), 109.6 (acetal-C), 80.9 (C5), 78.8 (C4), 76.8 (C6), 67.3 (C7), 60.2 (OCH\_2CH\_3), 26.8 (CH\_3-isopropylidene), 26.6 (CH\_3-isopropylidene \(\times 2\)), 25.0 (CH\_3-isopropylidene), 14.1 (OCH\_2CH\_3).

EIMS: 301 (M+1, 0.01%), 285 (M\(^+\) - CH\_3, 19%), 241 (M+1 - C\_4H\_10, 28%), 199 (M\(^+\) - C\_7H\_17, 12%), 101 (C\_7H\_17, 69%), 43 (C\_3H\_7, 100%).

Ethyl (2\(E\),4\(S\),5\(R\))-4,5-\(O\)-isopropylidene-6,7-dihydroxy-hept-2-enoate\(^{12}\) (4,43)

![Image of the compound](image)

To ethyl (2\(E\),4\(S\),5\(R\))-4,5:6,7-di-\(O\)-isopropylidene-hept-2-enoate (200 mg, 0.668 mmol) was added 80% acetic acid (2 mL). The reaction mixture was allowed to stir overnight at room temperature. The acetic acid was removed \textit{in vacuo} and the residue was purified by chromatography (2:1 hexanes-EtOAc) to afford the title compound (123 mg, 0.474 mmol, 71%).

TLC: \(R_f\) 0.11 (2:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \(\delta_H\) 7.00 (dd, 1H, \(J = 15.3\) and 3.9 Hz, H3), 6.16 (d, 1H, \(J = 15.3\) Hz, H2), 4.69-4.55 (m, 1H, H4), 4.19 (q, 2H, \(J = 7.2\) Hz, OCH\(_2\)CH\(_3\)), 3.89 – 3.62 (m, 4H, H5, H6, H7a and H7b), 2.87 (v br s, 2H, OH \(\times 2\)), 1.43 (s, 3H, CH\(_3\)-isopropylidene), 1.40 (s, 3H, CH\(_3\)-isopropylidene), 1.28 (t, 3H, \(J = 7.2\) Hz, OCH\(_2\)CH\(_3\)).

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \(\delta_C\) 166.4 (C1), 145.3 (C3), 121.7 (C2), 110.0 (acetal-C), 80.4 (C5), 77.8 (C4), 72.5 (C6), 63.5 (C7), 60.7 (OCH\_2CH\_3), 26.9 (CH\(_3\)-isopropylidene), 26.6 (CH\(_3\)-isopropylidene), 14.2 (OCH\_2CH\_3).

IR: \(\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}\) 3422, 2993, 1711, 1374, 1277, 1239, 1167, 983, 867.
EIMS: 259 (M⁺, 3%), 242 (M⁺ - H₂O, 2%), 213 (M⁺ - C₂H₆O, 8%), 43 (100%).

Ethyl (2E,4S,5R)-7-O-(tert-butyldimethylsilyl)-4,5-O-isopropylidene-6-oxo hept-2-enoate (4.40)

The general procedure for TBDMS primary protection (3.6) was carried out on ethyl (2E,4S,5R)-4,5-O-isopropylidene-6,7-dihydroxy-hept-2-enoate (50 mg, 0.192 mmol). The residue was purified by flash chromatography (7:1 hexanes-EtOAc) to afford the silyl ether (57 mg, 0.154 mmol, 80%).

TLC: Rf 0.49 (7:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl₃) δH 7.02 (dd, 1H, J = 15.6 and 4.5 Hz, H3), 6.16 (d, 1H, J = 15.6 Hz, H2), 4.63-4.59 (m, 1H, H4), 4.20 (q, 2H, J = 7.2 Hz, OCH₂CH₃), 3.79 – 3.69 (m, 4H, H5, H6, H7a and H7b), 2.57 (d, 1H, J = 2.7 Hz, OH), 1.42 (s, 3H, CH₃-isopropylidene), 1.31 (s, 3H, CH₃-isopropylidene), 1.28 (t, 3H, J = 7.2 Hz, OCH₂CH₃), 0.89 (s, 9H, C(CH₃)₃), 0.08 (s, 6H, SiCH₃ × 2).

$^{13}$C NMR: (75 MHz, CDCl₃) δC 166.2 (C1), 145.5 (C3), 121.3 (C2), 109.8 (acetal-C), 79.8 (C5), 78.5 (C4), 72.8 (C6), 63.9 (C7), 60.4 (OCH₂CH₃), 27.0 (CH₃-isopropylidene), 26.4 (CH₃-isopropylidene), 25.9 (C(CH₃)₃), 18.3 (C(CH₃)₃), 14.2 (OCH₂CH₃), - 5.30 (SiCH₃), - 5.4 (SiCH₃).

IR: $v_{max}$(CHCl₃)/cm⁻¹ 3559, 2992, 2959, 1719, 1706, 1473, 1385, 1259, 1223, 1063, 1008, 980, 767.

EIMS: 374 (M⁺, 1%), 359 (M⁺ - CH₃, 23%), 329 (M⁺ - OEt, 1%), 317 (M⁺ - C₄H₉, 7%), 259 (M⁺ - TBDMS, 19%), 117 (100%).
Ethyl (2E,4S,5R)-7-O-(tert-butyldimethylsilyl)-4,5-O-isopropylidene-6-oxohept-2-enoate (4.37)

The general route for Dess-Martin oxidation (3.3) was carried out on ethyl (2E,4S,5R)-7-O-(tert-butyldimethylsilyl)-4,5-O-isopropylidene-6-hydroxy-hept-2-enoate (100 mg, 0.267 mmol). The residue was purified by chromatography (7:1 hexanes-EtOAc) to afford the title compound as a colourless oil (89 mg, 0.240 mmol, 90%).

Product characterised above when carried out by a different synthetic route.

6.4.2.2 ARABINOSE – Wittig Route – bis-DHP (TBDPS)

Ethyl (2E,4S,5R)-7-O-(tert-butyldiphenylsilyl)-4,5-O-bis-DHP-6-hydroxy-hept-2-enoate (4.44)

The general route towards the protection using bis-DHP, in CHCl₃, in the presence of CSA (4.29) was used to protect ethyl (2E,4S,5R)-7-O-(tert-butyldiphenylsilyl)-4,5,6-trihydroxy-hept-2-enoate (500 mg, 1.092 mmol). Column chromatography (7:1 hexanes-
EtOAc) yielded the desired product as a colourless oil (218 mg, 0.349 mmol, 38%), along with the ethyl \((2E,4S,5R)-7-O-(\text{tert-butyl)diphenylsilyl})-5,6-O-bis-DHP-4-hydroxy-hept-2-enoate\) (12%) (total yield of the two products obtained therefore is 50%).

**TLC:**  \(R_f 0.25\) (7:1 hexanes-EtOAc)

**\(^1\)H NMR:** (300 MHz, CDCl\(_3\)) \(\delta_H\) (Mixture of isomers) 7.75-7.60 (m, 8H, ortho aromatics and ortho aromatics), 7.44-7.31 (m, 12H, meta and para aromatics and meta and para aromatics), 7.24 (dd, 1H, \(J = 15.6\) and 4.5 Hz, H3), 6.99 (dd, 1H, \(J = 15.6\) and 3.6 Hz, H3), 6.25 (dd, 1H, \(J = 15.6\) and 1.8 Hz, H2), 4.93 (ddd, 1H, \(J = 4.2\), 3.6 and 2.0 Hz, \(J = 3.6\) Hz, OCH\(_2\)CH\(_3\)), 4.19 (q, 2H, \(J = 7.2\) Hz, OCH\(_2\)CH\(_3\)), 3.67-3.46 (m, 8H, \(\text{OCH}_2\text{CH}_3\) \(\times\) 2 and \(\text{OCH}_2\text{CH}_3\) \(\times\) 2), 3.55 (dd, 1H, \(J = 12.0\) and 9.3 Hz, H5), 2.58 (d, 1H, \(J = 7.5\) Hz, OH), 2.53 (d, 1H, \(J = 6.3\) Hz, OH), 2.00-1.30 (m, 24H, CH\(_2\) of DHP \(\times\) 6 and CH\(_2\) of DHP \(\times\) 6), 1.04 (s, 9H, C(CH\(_3\))\(_3\)), 1.02 (s, 9H, C(CH\(_3\))\(_3\)).

**\(^{13}\)C NMR:** (75 MHz, CDCl\(_3\)) \(\delta_C\) 166.6 (C1), 166.5 (C1), 146.8 (C3), 143.7 (C3), 135.5 (ortho and ortho), 135.4 (ortho and ortho), 132.7 (ipso and ipso), 132.6 ipso and ipso, 129.8 para and para, 127.7 \(J\)meta and \(J\)meta, 121.4 (C2), 122.1 (C2), 102.1 (1’A), 101.6 (1’B), 96.0 (1’A), 95.8 (1’B), 73.8 (C5), 71.3 (C5), 71.2 (C6), 70.9 (C6), 69.3 (C4), 69.2 (C4), 66.4 (C7), 63.8 (C7), 62.1 (5’A), 61.7 (5’A), 60.9 (OCH\(_2\)CH\(_3\) and OCH\(_2\)CH\(_3\)), 60.3 (5’A and 5’B), 29.8 (2’A), 29.7 (2’B), 28.3 (2’A), 28.2 (2’B), 26.9 (C(CH\(_3\))\(_3\)), 26.8 (C(CH\(_3\))\(_3\)), 24.9 (4’A), 24.8 (4’B), 24.6 (4’A), 24.5 (4’B), 19.2 (C(CH\(_3\))\(_3\)), 19.1 (C(CH\(_3\))\(_3\)), 18.1 (3’A and 3’A), 18.0 (3’B and 3’B), 14.3 (OCH\(_2\)CH\(_3\) and OCH\(_2\)CH\(_3\)).

**IR:** \(\nu_{\text{max}}\) (CHCl\(_3\))/\(\text{cm}^{-1}\) 3377, 3022, 2947, 2862, 1444, 1393, 1275, 1221, 1114, 1050, 969, 778.

**EIMS:** 625 (M+1, 1%), 441 (M+ - DHP - CH\(_3\), 1%), 168 (DHP, 13%), 167 (100%).
Ethyl (2E,4S,5R)-7-O-(tert-butyldiphenylsilyl)-5,6-O-bis-DHP-4-hydroxy-hept-2-enoate (4.45)

This product was obtained as a byproduct (82 mg, 0.131 mmol, 12%) in the preparation of ethyl (2E,4S,5R)-7-O-(tert-butyldiphenylsilyl)-4,5-O-bis-DHP-6-hydroxy-hept-2-enoate (4.44).

TLC:  \( R_f \) 0.35 (7:1 hexanes-EtOAc)

\(^1\)H NMR:  (300 MHz, CDCl\(_3\)) \( \delta \)H 7.67-7.60 (m, 4H, ortho aromatics), 7.45-7.30 (m, 6H, meta and para aromatics), 7.10 (dd, 1H, \( J = 15.6 \) and 3.0 Hz, H3), 6.20 (dd, 1H, \( J = 15.6 \) and 2.4 Hz, H2), 4.77 (d, 1H, \( J = 9.6 \) Hz, OH), 4.40-4.03 (m, 2H, H4 and H6), 4.19 (q, 2H, \( J = 7.2 \) Hz, OCH\(_2\)CH\(_3\)), 3.98-3.78 (m, 2H, OCH\(_2\) of DHP \( \times 2 \)), 1.84-1.35 (m, 12H, CH\(_2\) of DHP \( \times 6 \)), 1.28 (t, 3H, \( J = 7.2 \) Hz, OCH\(_2\)CH\(_3\)), 1.02 (s, 9H, C(CH\(_3\))\(_3\)).

\(^{13}\)C NMR:  (75 MHz, CDCl\(_3\)) \( \delta \)C 166.5 (C1), 150.4 (C3), 135.5 (ortho), 135.4 (ortho), 133.0 (ipso), 129.8 (para), 127.7 (meta), 127.6 (meta), 121.9 (C2), 96.5 (1’A), 94.4 (1’B), 73.3(C6), 70.1 (C4), 66.5 (C5), 63.2 (C7), 62.9 (OCH\(_2\)CH\(_3\)), 60.6 (5’A), 60.3 (5’B), 29.7 (2’A), 28.6 (2’B), 26.7 (C(CH\(_3\))\(_3\)), 24.7 (4’A and 4’B), 19.2 (C(CH\(_3\))\(_3\)), 18.1 (3’A), 18.0 (3’B), 14.3 (OCH\(_2\)CH\(_3\)).

IR:  \( \nu \) max(CHCl\(_3\))/cm\(^{-1}\) 3678, 3021, 2947, 2862, 1444, 1431, 1222, 1213, 1114, 1075, 995, 787.

EIMS:  625 (M+1, 77%), 607 (M+1 - H\(_2\)O, 4%), 579 (M\(^+\) - OEt, 1%), 441 (M\(^+\) - DHP - CH\(_3\), 2%), 168 (DHP, 13%), 167 (100%).
Ethyl (2E,4S,5R)-7-O-(tert-butyldiphenylsilyl)-4,5-O-bis-DHP-6-oxo-hept-2-enoate (4.46)

The general route for Dess-Martin oxidation (3.3) was carried out on ethyl (2E,4S,5R)-7-O-(tert-butyldiphenylsilyl)-4,5-O-bis-DHP-6-hydroxy-hept-2-enoate (4.44) (500 mg, 0.801 mmol). The product was purified by column chromatography (7:1 hexanes-EtOAc) (439 mg, 0.705 mmol, 88%).

TLC: Rf 0.04 (7:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H (Mixture of isomers) 7.71-7.64 (m, 8H, ortho aromatics and ortho aromatics), 7.42-7.33 (m, 12H, meta and para aromatics and meta and para aromatics), 7.12 (dd, 1H, $J = 15.6$ and 4.5 Hz, H3), 6.93 (dd, 1H, $J = 15.6$ and 4.2 Hz, H3), 6.23 (dd, 1H, $J = 15.6$ and 1.9 Hz, H2), 6.17 (dd, 1H, $J = 15.6$ and 1.8 Hz, H2), 5.34 (dd, 1H, $J = 4.5$ and 1.8 Hz, H4), 4.66 (dd, 1H, $J = 4.2$ and 1.9 Hz, H5), 4.64 (d, 1H, $J = 4.5$ and 1.8 Hz, H7a), 4.55 (d, 1H, $J = 18.6$ Hz, H7a), 4.51 (q, 2H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 4.18 (q, 2H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 4.13-4.03 (m, 3H, H7a, H7b, H5), 4.01-3.92 and 3.72-3.28 (m, 8H, OCH$_2$ of DHP × 2, and OCH$_2$ of DHP × 2), 2.00-1.35 (m, 24H, CH$_2$ of DHP × 6 and CH$_2$ of DHP × 6), 1.29 (t, 3H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 1.28 (t, 3H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 1.09 (s, 9H, C(CH$_3$)$_3$), 1.01 (s, 9H, C(CH$_3$)$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 207.8 (C6), 203.5 (C6), 165.9 (C1), 165.7 (C1), 142.9 (C3), 141.7 (C3), 135.5 (ortho), 135.4 (ortho and ortho), 135.3 (ortho), 132.9 (ipso), 132.8 (ipso), 132.7 (ipso), 132.5 (ipso), 129.8 (para...
and para), 129.7 (para), 129.6 (meta), 127.6 (meta), 122.4 (C2), 122.1 (C2), 101.6 (1'A), 101.4 (1'B), 96.0 (1'A), 95.9 (1'B), 74.6 (C5), 73.9 (C5), 71.9 (C4), 67.6 (C7), 66.0 (C4), 64.8 (C7), 62.2 (5'A), 61.7 (5'B), 61.1 (5'A), 60.9 (5'B), 60.4 (OC\textsubscript{2}H\textsubscript{4}CH\textsubscript{3}), 60.3 (OC\textsubscript{2}H\textsubscript{4}CH\textsubscript{3}), 29.5 (2'A), 29.2 (2'B), 28.1 (2'A), 27.8 (2'B), 26.7 (C(CH\textsubscript{3})\textsubscript{3}), 26.6 (C(CH\textsubscript{3})\textsubscript{3}), 24.7 (4'A), 24.6 (4'B), 24.2 (4'A), 24.1 (4'B), 19.2 (C(CH\textsubscript{3})\textsubscript{3}), 19.0 (C(CH\textsubscript{3})\textsubscript{3}), 18.8 (3'A and 3'A), 18.2 (3'B and 3'B), 14.3 (OCH\textsubscript{2}CH\textsubscript{3}), 14.2 (OCH\textsubscript{2}CH\textsubscript{3}).

IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3022, 1769, 1561, 1393, 1276, 1217, 1167, 1112, 997.

CIMS: 623 (M+1, 2%), 605 (M+1 - H\textsubscript{2}O, 8%), 239 (TBDPS, 15%), 168 (DHP, 16%), 167 (100%).

Ethyl (2\(E\),4\(S\),5\(R\))-7-O-(\text{tert}-butyldiphenylsilyl)-5,6-O-bis-DHP-4-oxo-hept-2-enoate (4.47)

The general route for Dess-Martin oxidation (3.3) was carried out ethyl (2\(E\),4\(S\),5\(R\))-7-O-(\text{tert}-butyldiphenylsilyl)-5,6-O-bis-DHP-4-hydroxy-hept-2-enoate (4.45) (50 mg, 0.080 mmol). The product was purified by column chromatography (7:1 hexanes-EtOAc) (50 mg, 0.080 mmol, 100%).

TLC: \( R_f \) 0.58 (7:1 hexanes-EtOAc)

\( ^1\text{H} \) NMR: (300 MHz, CDCl\textsubscript{3}) \( \delta \text{H} \) 7.66-7.56 (m, 4H, ortho aromatics), 7.57 (d, 1H, \( J = 15.9 \) Hz, H3), 7.38-7.35 (m, 6H, meta and para aromatics), 6.65 (d, 1H, \( J = 15.9 \) Hz, H2), 4.46 (ddd, 1H, \( J = 6.9, 6.6 \) and 3.6 Hz, H6), 4.23 (d, 1H,
$J = 3.6$ Hz, H5), 4.22 (q, 2H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 4.00 (dd, 1H, $J = 10.8$ and 6.6 Hz, H7a), 3.84 (dd, 1H, $J = 10.8$ and 6.9 Hz, H7b), 3.78-3.60 and 3.50-3.32 (m, 4H, CH$_2$ of DHP × 2), 1.90-1.40 (m, 12H, CH$_2$ of DHP × 6), 1.28 (t, 3H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 0.97 (s, 9H, C(CH$_3$)$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$ C 195.8 (C4), 165.6 (C1), 138.8 (C2), 135.4 (C3, ortho), 132.9 (ipso), 127.6 (meta), 97.2 (1’A), 96.4 (1’B), 73.3(C5), 67.6 (C6), 62.9 (C7), 61.8 (OCH$_2$CH$_3$), 61.5 (5’A), 60.7 (5’B), 29.0 (2’A), 28.6 (2’B), 26.6 (C(CH$_3$)$_3$), 24.7 (4’A) 24.5 (4’B), 19.1 (C(CH$_3$)$_3$), 18.0 (3’A), 17.9 (3’B), 14.1 (OCH$_2$CH$_3$).  

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3021, 1769, 1562, 1393, 1276, 1218, 1110, 1109, 995.  

CIMS: 623 (M+1, 2%), 455 (M+1 - DHP, 1%), 256 (TBDPSOH, 13%), 168 (DHP, 4%), 167 (100%).

### 6.4.3 MANNOFURANOSE

Ethyl (2E,4S,5S)-4,5:7,8-di-(dioxy-isopropylidene)-6-oxo-oct-2-enoate

The general procedure to perform a Wittig reaction with [ethyl(triphenylphosphoranylidene)acetate] in DCM was carried out on 2,3:5,6-di-O-isopropylidene-D-mannofuranose (200 mg, 0.77 mmol) followed by in situ Dess-Martin oxidation (4.11). The residue was purified by chromatography (7:1 hexanes-EtOAc) to afford the cis and trans title compounds as colourless oils.
Ethyl (2Z,4S,5S,7R)-4,5:7,8-di-O-isopropylidene-6-oxo-oct-2-enoate (4.49)

Yield: 5% (total 68%)

TLC: Rf 0.82 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 6.17 (dd, 1H, $J = 11.4$ and 7.5 Hz, H3), 5.91 (dd, 1H, $J = 11.4$ and 1.5 Hz, H2), 5.86 (ddd, 1H, $J = 7.5$, 7.5 and 1.5 Hz, H4), 5.07 (d, 1H, $J = 7.5$ Hz, H5), 4.69 (dd, 1H, $J = 7.7$ and 5.8 Hz, H7), 4.20-4.12 (m, 3H, $\text{CH}_2\text{CH}_3$ and H8a), 3.95 (dd, 1H, $J = 8.9$ and 5.8 Hz, H8b), 1.54 (s, 3H, $\text{CH}_3$-isopropylidene), 1.41 (s, 3H, $\text{CH}_3$-isopropylidene), 1.39 (s, 3H, $\text{CH}_3$-isopropylidene), 1.35 (s, 3H, $\text{CH}_3$-isopropylidene), 1.27 (t, 3H, $J = 7.1$ Hz, OCH$_2$CH$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 203.9 (C6), 165.5 (C1), 143.7 (C3), 122.5 (C2), 111.1 (acetal-C), 110.9 (acetal-C), 79.9 (C5), 78.8 (C4), 74. (C7), 65.4 (C8), 60.6 (OCH$_2$CH$_3$), 26.8 ($\text{CH}_3$-isopropylidene), 25.8 ($\text{CH}_3$-isopropylidene), 25.3 ($\text{CH}_3$-isopropylidene), 24.9 ($\text{CH}_3$-isopropylidene), 14.2 (OCH$_2$CH$_3$).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3026, 1727, 1660.

HRMS: Found 329.1601. Calculated for C$_{16}$H$_{24}$O$_7$ 329.1600.

FAB: 329 (M+1)
Ethyl (2E,4S,5S,7R)-4,5:7,8-di-O-isopropylidene-6-oxo-oct-2-enoate (4.50)

Yield: 63% (total 68%)
TLC: Rf 0.67 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) δ$_H$ 6.76 (dd, 1H, $J = 15.2$ and 3.4 Hz, H3), 6.09 (d, 1H, $J = 15.2$ Hz, H2), 5.03 (s, 2H, H4 and H5), 4.71 (dd, 1H, $J = 8.1$ and 6.3 Hz, H7), 4.21-4.11 (m, 3H, OCH$_2$CH$_3$ and H8a), 3.87 (dd, 1H, $J = 8.7$ and 6.3 Hz, H8b), 1.59 (s, 3H, CH$_3$-isopropylidene), 1.42 (s, 3H, CH$_3$-isopropylidene), 1.39 (s, 3H, CH$_3$-isopropylidene), 1.35 (s, 3H, CH$_3$-isopropylidene), 1.23 (t, 3H, $J = 7.1$ Hz, CH$_2$CH$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) δ$_C$ 204.1 (C6), 165.2 (C1), 141.5 (C3), 123.3 (C2), 110.7 (acetal-C), 110.6 (acetal-C), 81.2 (C5), 75.6 (C4), 75.8 (C7), 64.9 (C8), 60.5 (OCH$_2$CH$_3$), 26.6 (CH$_3$-isopropylidene), 25.5 (CH$_3$-isopropylidene), 24.7 (CH$_3$-isopropylidene), 24.5 (CH$_3$-isopropylidene), 14.1 (OCH$_2$CH$_3$).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3026, 1723, 1664.

HRMS: Found 329.1600. Calculated for C$_{16}$H$_{24}$O$_7$ 329.1600.

FAB: 329 (M+1)
Mannofuranose Monomers

Ethyl (2E,4S,5S)-4,5:7,8-di-(dioxo-isopropylidene)-6-oxo-oct-2-enoate (69 mg, 0.21 mmol) was dissolved in degassed THF (5 mL) and the solvent removed by vacuum distillation to ensure an oxygen-free system. The residue was then dissolved in THF (20 mL) and added dropwise over 20 minutes with stirring to a freshly prepared solution of SmI$_2$ in THF (8.8 mL of a 0.1 M solution, 0.88 mmol, 4.2 equiv.) and HMPA (0.21 mL, 1.43 mmol, 6.8 equiv.) at –78 °C. The mixture was stirred at –78 °C for 2 hours, after which it was diluted with EtOAc (20 ml) and filtered through a thin pad of silica gel. The solvent was removed in vacuo and the residue was purified by flash column chromatography (3:1 hexanes-EtOAc). Three monomer isomers were obtained.

(1’R,5’R,6’R,7’R)-[7-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-7-hydroxy-3,3-dimethyl-2,4-dioxa-bicyclo[3.2.0]hepta-6-yl]-acetic acid ethyl ester (4.51)

Yield: 50% (total 83%).

TLC: $R_f$ 0.47 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 4.46 (t, 1H, $J = 6.9$ Hz, H4’’), 4.41 (s, 1H, H5’), 4.40 (s, 1H, H1’), 4.12 (q, 2H, $J = 7.1$ Hz, OCH$_2$CH$_3$), 3.99 (dd, 1H, $J = 8.4$ and 6.9 Hz, H5’’a), 3.75 (dd, 1H, $J = 8.4$ and 6.9 Hz, H5’’b), 2.61-2.48 (m, 2H, H1a and H1b), 2.53 (d, 1H, $J = 6.0$ Hz, OH), 2.47-2.38 (m, 1H, H6’), 1.56 (s, 3H, CH$_3$-isopropylidene), 1.42 (s, 3H, CH$_3$-
isopropylidene), 1.37 (s, 3H, CH$_3$-isopropylidene), 1.25 (s, 3H, CH$_3$-isopropylidene), 1.24 (t, 3H, $J = 7.1$ Hz, OCH$_2$CH$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 172.1 (C2), 114.9 (C3'), 109.3 (C2''), 81.0 (C5'), 76.2 (C7'), 75.9 (C4''), 71.9 (C1'), 63.9 (C8), 60.7 (OCH$_2$CH$_3$), 42.1 (C1), 31.5 (C6'), 26.5 (CH$_3$-isopropylidene), 26.3 (CH$_3$-isopropylidene), 25.6 (CH$_3$-isopropylidene), 24.9 (CH$_3$-isopropylidene), 14.2 (OCH$_2$CH$_3$).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3568, 2949, 1733, 1730, 1066.

HRMS: Found 331.1756. Calculated for C$_{16}$H$_{26}$O$_7$ 331.1757.

FAB: 331 (M+1)

$[^{\alpha}]_D$: +61.1 ($c = 1.0$ CHCl$_3$).

(1'S,5'S,6'R,7'R)-[7-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-7-hydroxy-3,3-dimethyl-2,4-dioxa-bicyclo[3.2.0]hepta-6-yl]-acetic acid ethyl ester (4.52)

Yield: 33% (total 83%).

TLC: R$_f$ 0.29 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 4.84 (dd, 1H, $J = 6.3$ and 5.4 Hz, H1'), 4.43 (t, 1H, $J = 7.2$ Hz, H4''), 4.38 (dd, 1H, $J = 5.4$ and 2.1 Hz, H5'), 4.13 (q, 2H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 3.92 (dd, 1H, $J = 7.5$ and 7.2 Hz, H5''a), 3.77 (dd, 1H, $J = 7.5$ and 7.2 Hz, H5''b), 2.77-2.66 (m, 1H, H6'), 2.55 (dd, 1H, $J = 16.2$ and 11.4 Hz, H1a), 2.55 (s, 1H, OH), 2.13 (dd, 1H, $J = 16.2$ and 5.9 Hz, H1b), 1.54 (s, 3H, CH$_3$-isopropylidene), 1.45 (s, 3H, CH$_3$-isopropylidene), 1.37 (s, 3H, CH$_3$-isopropylidene), 1.26 (s, 3H, CH$_3$-isopropylidene), 1.23 (t, 3H, $J = 7.2$ Hz, OCH$_2$CH$_3$).
$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 171.3 (C2), 113.9 (C3'), 108.9 (C2''), 81.2 (C5'), 75.9 (C7'), 74.5 (C4''), 71.3 (C1'), 63.9 (C5''), 60.7 (OCH$_2$CH$_3$), 39.5 (C1), 29.3 (C6'), 26.2 (CH$_3$-isopropylidene), 25.3 (CH$_3$-isopropylidene), 25.2 (CH$_3$-isopropylidene), 24.5 (CH$_3$-isopropylidene), 14.2 (OCH$_2$CH$_3$).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3429, 3033, 2935, 1735, 1222.

HRMS: Found 331.1757. Calculated for C$_{16}$H$_{26}$O$_7$ 331.1757.

FAB: 331 (M+1)

$[\alpha]_D$: +19.5 ($c = 0.5$ CHCl$_3$).

(1'S,5'S,6'R,7'S)-[7-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-7-hydroxy-3,3-dimethyl-2,4-dioxa-bicyclo[3.2.0]hepta-6-yl]-acetic acid ethyl ester (4.53)

Yield: 15% (total 45%; A - 30% and B - 19%).

TLC: $R_f$ 0.56 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 4.77 (dd, 1H, $J = 5.7$ and 5.4 Hz, H5'), 4.33 (dd, 1H, $J = 8.4$ and 6.6 Hz, H4''), 4.28-3.99 (m, 4H, H1', OCH$_2$CH$_3$, H5''a), 3.69 (t, 1H, $J = 8.6$ Hz, H5''b), 2.91 (dd, 1H, $J = 12.6$ and 6.6 Hz, H1'a), 2.27 (ddd, 1H, $J = 13.2$, 12.6 and 5.4 Hz, H6'), 2.09 (dd, 1H, $J = 13.2$ and 6.6 Hz, H1'b), 1.41 (s, 3H, CH$_3$-isopropylidene), 1.35 (s, 3H, CH$_3$-isopropylidene), 1.34 (s, 3H, CH$_3$-isopropylidene), 1.27 (t, 3H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 1.26 (s, 3H, CH$_3$-isopropylidene).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 174.5 (C2), 110.3 (C3'), 107.9 (C2''), 85.6 (C5'), 82.9 (C7'), 78.9 (C4''), 78.6 (C1'), 65.3 (C5''), 61.2 (OCH$_2$CH$_3$), 42.8 (C1), 35.3 (C6'), 26.0 (CH$_3$-isopropylidene), 25.9 (CH$_3$-isopropylidene), 25.3 (CH$_3$-isopropylidene), 23.7 (CH$_3$-isopropylidene), 14.0 (OCH$_2$CH$_3$).
IR: \( \nu_{\text{max}}(\text{CHCl}_3) / \text{cm}^{-1} \) 3400, 3026, 2942, 1702, 1045.

HRMS: Found 331.1757. Calculated for \( \text{C}_{16}\text{H}_{26}\text{O}_7 \) 331.1757.

FAB: 331 (M+1)

\([\alpha]_D: +19.4 \ (c = 0.5 \ \text{CHCl}_3)\).

The above monomer obtained is expected to be the cis monomer. The exact stereochemistry could not be assigned from NOE experiments due to the large overlap of NMR signals.

Carrying out the above mentioned reaction with Ethyl (2\(E\),4\(S\),5\(S\),7\(R\))-4,5:7,8-di-O-isopropylidene-6-oxo-oct-2-enoate, under the same conditions as discussed above gave Monomer 4.52 (20 mg, 0.06 mmol, 29%), with only trace amounts of Monomer 4.53 being detected.

6.4.4 LYXOSE

2,3-\(O\)-Isopropylidene-D-lyxofuranose (4.55)

The general procedure to isopropylidene protect sugar derivatives, using a catalytic amount \( \text{H}_2\text{SO}_4 \) and dry acetone, (4.7) was used to protect D-lyxose (100 mg, 0.66 mmol). The resulting slurry was filtered through a short filter column (EtOAc) and the solvent removed in vacuo. The resulting crude syrup was rinsed with dry pyridine twice and subjected to TBDMS protection.
5-\(O\)-(t-Butyldimethylsilyl)-2,3-\(O\)-isopropylidene-\(D\)-lyxofuranose (4.56)

The general procedure for TBDMS primary protection (3.6) was carried out on 2,3-\(O\)-isopropylidene-\(D\)-lyxofuranose (50 mg, 0.26 mmol). The residue was purified by flash chromatography (3:1 hexanes-EtOAc) to afford the silyl ether (57 mg, 0.19 mmol, 72%).

**TLC:** \(R_f\) 0.52 (EtOAc)

**\(\text{H NMR:}\)\ ((300 MHz, CDCl\textsubscript{3}) \(\delta_H\) 5.30 (d, 1H, \(J = 1.8\) Hz, H1), 4.66 (dd, 1H, \(J = 5.9\) and 3.8 Hz, H3), 4.49 (d, 1H, \(J = 6.0\) Hz, H2), 4.25 (br s, OH), 4.18-4.13 (m, 1H, H4), 3.84 (dd, 1H, \(J = 10.6\) and 4.9 Hz, H5a), 3.73 (dd, 1H, \(J = 10.6\) and 7.1 Hz, H5b), 1.36 (s, 3H, \(\text{CH}_3\)-isopropylidene), 1.22 (s, 3H, \(\text{CH}_3\)-isopropylidene \(3\)), 0.83 (s, 9H, C(\(\text{CH}_3\))\(3\)), 0.12 (s, 6H, Si\(\text{CH}_3\) \(\times 2\)).

**\(\text{C NMR:}\)\ ((75 MHz, CDCl\textsubscript{3}) \(\delta_C\) 112.2 (acetal-C), 100.9 (C1), 85.5 (C2), 80.5 (C3), 79.6 (C4), 61.4 (C5), 25.9 (\(\text{CH}_3\)-isopropylidene), 25.9 (C(\(\text{CH}_3\))\(3\)), 24.8 (\(\text{CH}_3\)-isopropylidene), 18.4 (C(\(\text{CH}_3\))\(3\)), -5.4 (Si\(\text{CH}_3\) \(\times 2\)).

IR: \(\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}\) 3603, 3033, 2803, 1340, 1320, 1167, 996, 972, 850.

HRMS: Found 305.1784. Calculated for C\(14\)H\(29\)SiO\(5\) 305.1784.

EIMS: 305 (M+1, 55%), 289 (M\(^+\) - CH\(_3\), 53%), 247 (M\(^+\) - C\(_4\)H\(_9\), 80%), 159 (M+1 - CH\(_2\)OTBDMS, 55%), 75 (100%).
Ethyl \((2E,4R,5R)-7-t\text{-butyldimethylsilyloxy}-4,5\text{-O-isopropylidene}-6\text{-oxo}\) hept-2-enoate \((4.57)\)

The general procedure to perform a Wittig reaction with [ethyl(triphenylphosphoranylidene)acetate] in DCM was carried out on protected lyxose derivative \((4.56)\) (1.050 mg, 3.44 mmol) followed by \textit{in situ} Dess-Martin oxidation \((4.11)\). The residue was purified by chromatography (7:1 hexanes-EtOAc) to afford the \(Z\) and \(E\) title compounds as colourless oils.

Ethyl \((2E,4R,5R)-7-O-(t\text{-butyldimethylsilyloxy})-4,5\text{-O-isopropylidene}-6\text{-oxo}\) hept-2-enoate

Yield: 749 mg, 2.10 mmol, 56% (total yield 73%).

TLC: \(R_f\) 0.57 (5:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \(\delta_H\) 6.73 (dd, 1H, \(J = 15.6\) and 4.5 Hz, H3), 6.07 (dd, 1H, \(J = 15.6\) and 1.7 Hz, H2), 5.02-4.94 (m, 2H, H4 and H5), 4.42 (d, 1H, \(J = 18.8\) Hz, H7a), 4.13 (d, 1H, \(J = 18.8\) Hz, H7b), 4.12 (q, 2H, \(J = 7.2\) Hz, OCH\(_2\)CH\(_3\)), 1.59 (s, 3H, CH\(_3\)-isopropylidene), 1.37 (s, 3H, CH\(_3\)-isopropylidene), 1.23 (t, 3H, \(J = 7.1\) Hz, OCH\(_2\)CH\(_3\)), 0.88 (s, 9H, C(C(CH\(_3\)))\(_3\)), 0.05 (s, 3H, SiCH\(_3\)), 0.03 (s, 3H, SiCH\(_3\)).

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \(\delta_C\) 205.7 (C6), 165.2 (C1), 140.9 (C3), 123.5 (C2), 110.8 (acetal-C), 81.6 (C4), 75.9 (C5), 68.3 (C7), 60. (OCH\(_2\)CH\(_3\)), 26.8 (CH\(_3\)-isopropylidene), 25.8 (C(CH\(_3\)))\(_3\)), 24.8 (CH\(_3\)-isopropylidene), 18.3 (C(CH\(_3\)))\(_3\)), 14.2 (OCH\(_2\)CH\(_3\)), -5.5 (SiCH\(_3\) \(\times\) 2).

IR: \(\nu_{\text{max}}\text{(CHCl}_3\text{)}/\text{cm}^{-1}\) 1723, 1386, 1313, 1267, 1191, 1111, 1080, 1034, 982, 847.
Ethyl (2E,4R,5R)-7-O-(t-butyldimethylsilyloxy)-4,5-O-isopropylidene-6-oxo-hept-2-enoate

Yield: 224 mg, 0.602 mmol, 17% (total yield 73%).

TLC: \( R_f 0.77 \) (5:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) 6.08 - 6.02 (m, 1H, H3), 5.88-5.82 (m, 2H, H2 and H4), 4.88 (d, 1H, \( J = 8.1 \) Hz, H5), 4.45 (d, 1H, \( J = 18.9 \) Hz, H7a), 4.23 (d, 1H, \( J = 18.9 \) Hz, H7b), 4.13 (qd, 2H, \( J = 6.9 \) and \( 1.4 \) Hz, OCH\(_2\)CH\(_3\)), 1.54 (s, 3H, CH\(_3\)-isopropylidene), 1.35 (s, 3H, CH\(_3\)-isopropylidene), 1.24 (t, 3H, \( J = 6.9 \) Hz, OCH\(_2\)CH\(_3\)), 0.84 (s, 9H, C(CH\(_3\))\(_3\)), 0.04 (s, 3H, SiCH\(_3\)), -0.02 (s, 3H, SiCH\(_3\))

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \( \delta\)C 205.4 (C6), 165.1 (C1), 142.8 (C3), 123.0 (C2), 110.7 (acetal-C), 80.6 (C4), 74.7 (C5), 68.5 (C7), 60.5 (OCH\(_2\)CH\(_3\)), 26.7 (CH\(_3\)-isopropylidene), 25.8 (C(CH\(_3\))\(_3\)), 24.7 (CH\(_3\)-isopropylidene), 18.4 (C(CH\(_3\))\(_3\)), 14.1 (OCH\(_2\)CH\(_3\)), -5.3 (SiCH\(_3\) \( \times \) 2)

IR: \( \nu_{\text{max}}\) (CHCl\(_3\))/cm\(^{-1}\) 1728, 1386, 1267, 1160, 1128, 1038, 986.

EIMS: 373 (M+1, 24%), 357 (M\(^+\) - CH\(_3\), 7%), 315 (M\(^+\) - C\(_4\)H\(_9\), 59%), 229 (M+1 - CH\(_2\)OTBDMS, 42%), 187 (100%).
Lyxose Monomers

General procedure to form monomers with SmI$_2$, in THF in the presence of HMPA via normal addition (4.51) was used to form monomers from ethyl (2E,4S,5S)-7-O-(t-butyldimethylsilyloxy)-4,5-O-isopropylidene-6-oxo-hept-2-enoate (78 mg, 0.21 mmol). The residue was purified by column chromatography (3:1 hexanes-EtOAc). Four monomer isomers were obtained.
(1'S,5'S,6'S,7'S)-[7-(tert-Butyl-dimethyl-silanyloxymethyl)-7-hydroxy-3,3-dimethyl-2,4-dioxa-bicyclo[3.2.0]hepta-6-yl]-acetic acid ethyl ester (4.58)

Yield: 4 mg, 5% (total yield: 55%)

TLC: Rf 0.56 (5:1 hexane-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 4.75 (t, 1H, $J = 5.6$ Hz, H5'), 4.21 (d, 1H, $J = 5.7$ Hz, H1'), 4.20-4.06 (m, 2H, OCH$_2$CH$_3$), 3.97 (s, 1H, OH), 3.80 (d, 2H, $J = 1.5$ Hz, CH$_2$OTBDMS), 2.80 (dd, 1H, $J = 12.5$ and 6.6 Hz, H1a), 2.26 (td, 1H, $J = 13.5$ and 5.1 Hz, H6'), 2.03 (dd, 1H, $J = 13.6$ and 6.6 Hz, H1b), 1.41 (s, 3H, CH$_3$-isopropylidene), 1.24 (s, 3H, CH$_3$-isopropylidene), 1.25 (t, 3H, $J = 6.9$ Hz, OCH$_2$CH$_3$), 0.87 (s, 9H, C(CH$_3$)$_3$), 0.05 (s, 3H, SiCH$_3$), 0.04 (s, 3H, SiCH$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 173.9 (C2), 110.0 (C3'), 85.4 (C1'), 83.1 (C7'), 78.9 (C5'), 66.1 (CH$_2$OTBDMS), 60.7 (OCH$_2$CH$_3$), 45.7 (C6'), 34.8 (C1), 26.2 (CH$_3$-isopropylidene), 25.9 (C(CH$_3$)$_3$), 23.8 (CH$_3$-isopropylidene), 18.4 (C(CH$_3$)$_3$), 14.1 (OCH$_2$CH$_3$), -5.40 (SiCH$_3$ × 2).

IR: $\nu_{\max}$ (CHCl$_3$/cm$^{-1}$) 3040, 2960, 2870, 1790, 1740, 1660, 1540, 1390, 1270.

HRMS: Found 375.2202. Calculated for C$_{18}$H$_{35}$O$_6$Si 375.4223.

EIMS: 375 (M+1, 4%), 359 (M$^+$ - CH$_3$, 31%), 329 (M$^+$ - OEt, 40%), 317 (M$^+$ - C$_4$H$_9$, 72%), 259 (M$^+$ - TBDMS, 53%), 28 (100%).

$[\alpha]_D$: -28.2 ($c = 2.0$ CHCl$_3$).
(1'R,5'R,6'R,7'S)-[7-(tert-Butyl-dimethyl-silanyloxy)methyl]-7-hydroxy-3,3-dimethyl-2,4-dioxa-bicyclo[3.2.0]hepta-6-yl]-acetic acid ethyl ester (4.59)

Yield: 18 mg, 20% (total yield: 55%)

TLC: $R_f$ 0.46 (5:1 hexane-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 4.37 (s, 1H, H1’), 4.36 (s, 1H, H5’), 4.10 (q, 2H, $J$ = 7.2 Hz, OCH$_2$CH$_3$), 3.84 (d, 1H, $J$ = 9.9 Hz, CH$_3$H$_6$OTBDMS), 3.51 (d, 1H, $J$ = 9.9 Hz, CH$_3$H$_6$OTBDMS), 3.02 (s, 1H, OH), 2.56 (dd, 1H, $J$ = 16.2 and 9.0 Hz, H1a), 2.44 (dd, 1H, $J$ = 16.2 and 6.9 Hz, H1b), 2.34 (ddd, 1H, $J$ = 9.0, 6.9 and 1.8 Hz, H6’), 1.50 (s, 3H, CH$_3$-isopropylidene), 1.22 (s, 3H, CH$_3$-isopropylidene), 1.22 (t, 3H, $J$ = 7.2 Hz, OCH$_2$CH$_3$), 0.87 (s, 9H, C(CH$_3$)$_3$), 0.06 (s, 3H, SiC$_2$H$_3$), 0.56 (s, 3H, SiCH$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 172.4 (C2), 114.4 (C3’), 80.7 (C1), 75.8 (C5’), 73.2 (C7’), 64.7 (CH$_3$OTBDMS), 60.4 (OCH$_2$CH$_3$), 43.2 (C6’), 31.7 (C1), 26.4 (CH$_3$-isopropylidene), 25.9 (C(CH$_3$)$_3$), 25.8 (CH$_3$-isopropylidene), 18.4 (C(CH$_3$)$_3$), 14.2 (OCH$_2$CH$_3$), -5.31 (SiC$_2$H$_3$), -5.33 (SiCH$_3$).

IR: $\nu_{max}$ (CHCl$_3$)/cm$^{-1}$ 3040, 2960, 2880, 1790, 1740, 1715, 1660, 1560, 1390, 1270, 1220

HRMS: Found 375.2203. Calculated for C$_{18}$H$_{35}$O$_6$Si 375.2203.

$[^{[\alpha]}]$D: -138.9 ($c$ = 16.0 CHCl$_3$).
(1’R,5’R,6’S,7’S)-[7-(tert-Butyl-dimethyl-silanyloxy methyl)-7-hydroxy-3,3-dimethyl-2,4-diox a-bicyclo[3.2.0]hepta-6-yl]-acetic acid ethyl ester (4.60)

Yield: 15 mg, 13% (total yield: 55%)

TLC: Rf 0.31 (5:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \(\delta\) 4.76 (t, 1H, \(J = 5.5\) Hz, H5’), 4.41 (dd, 1H, \(J = 5.5\) and 1.7 Hz, H1’), 4.11 (q, 2H, \(J = 7.2\) Hz, OCH\(_2\)CH\(_3\)), 3.71 (d, 1H, \(J = 10.2\) Hz, CH\(_3\)H\(_6\)OTBDMS), 3.57 (d, 1H, \(J = 10.2\) Hz, CH\(_3\)H\(_6\)OTBDMS), 3.18 (s, 1H, OH), 2.64-2.56 (m, 2H, H1a and H1b), 2.50 (dd, 1H, \(J = 5.7\) and 3.9 Hz, H6’), 1.47 (s, 3H, CH\(_3\)-isopropylidene), 1.24 (s, 3H, CH\(_3\)-isopropylidene), 1.23 (t, 3H, \(J = 6.9\) Hz, OCH\(_2\)CH\(_3\)), 0.88 (s, 9H, C(CH\(_3\))\(_3\)), 0.07 (s, 3H, SiCH\(_3\)), 0.05 (s, 3H, SiCH\(_3\)).

\(^13\)C NMR: (75 MHz, CDCl\(_3\)) \(\delta\)C 172.2 (s, C2), 113.6 (C3’), 80.5 (C1’, 76.8 (C7’), 71.9 (C5’), 63.1 (CH\(_2\)OTBDMS), 60.5 (OCH\(_2\)CH\(_3\)), 40.6 (C6’), 28.8 (C1), 25.9 (C(CH\(_3\))\(_3\)), 25.3 (CH\(_3\)-isopropylidene), 25.2 (CH\(_3\)-isopropylidene), 18.3 (C(CH\(_3\))\(_3\)), 14.2 (OCH\(_2\)CH\(_3\)), -5.4 (SiCH\(_3\) \(\times\) 2)

IR: \(v\)\(_{\text{max}}\) (CHCl\(_3\))/cm\(^{-1}\) 3040, 2960, 2880, 1780, 1740, 1715, 1660, 1390, 1272, 1230.

HRMS: Found 375.2212. Calculated for C\(_{18}\)H\(_{35}\)O\(_6\)Si 375.2203.

\([\alpha]_D\): +57.7 (c = 2.0 CHCl\(_3\)).
(1'R,5'R,6'S,7'R)-[7-(tert-Butyl-dimethyl-silanyloxy)methyl]-7-hydroxy-3,3-dimethyl-2,4-dioxa-bicyclo[3.2.0]hepta-6-yl-acetic acid ethyl ester (4.61)

Yield: 12 mg, 17% (total yield: 55%)

TLC: Rf 0.27 (4:1 hexane-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 4.58 (d, 1H, $J = 4.8$ Hz, H1'), 4.12 (q, 2H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 4.04 (t, 1H, $J = 4.8$ Hz, H5'), 3.64 (d, 1H, $J = 10.1$ Hz, CH$_3$H$_6$OTBDMS), 3.59 (d, 1H, $J = 10.1$ Hz, CH$_3$H$_6$OTBDMS), 2.92 (s, 1H, OH), 2.71-2.55 (m, 3H, H6', H1a and H1b), 1.58 (s, 3H, CH$_3$-isopropylidene), 1.31 (s, 3H, CH$_3$-isopropylidene), 1.23 (t, 3H, $J = 7.2$ Hz, OCH$_2$CH$_3$), 0.89 (s, 9H, C(CH$_3$)$_3$), 0.06 (s, 3H, SiCH$_3$), 0.05 (s, 3H, SiCH$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 172.4 (C2), 114.3 (C3'), 79.4 (C1'), 73.6 (C5'), 69.0 (C7'), 64.2 (CH$_2$OTBDMS), 60.5 (CH$_2$CH$_3$), 52.6 (C6'), 31.9 (C1), 27.4 (CH$_3$-isopropylidene), 26.4 (CH$_3$-isopropylidene), 25.8 (C(CH$_3$)$_3$), 18.2 (C(CH$_3$)$_3$), 14.2 (OCH$_2$CH$_3$), -5.6 (SiCH$_3$ x 2)

IR: $\nu_{\text{max}}$(CHCl$_3$/cm$^{-1}$) 3040, 2960, 2880, 1790, 1740, 1715, 1660, 1560, 1390, 1270, 1220.

HRMS: Found 375.2202. Calculated for C$_{18}$H$_{35}$O$_6$Si 3754.2203.

$[\alpha]_D$: +61.7 (c = 5.0 CHCl$_3$).
Ethyl \((2E,4S,5S)-7-O-\text{-}(t\text{-butyldimethylsilyloxy})\text{-}4,5\text{-}O\text{-}isopropylidene\text{-}6\text{-}oxo\text{-}hept\text{-}2\text{-}enoate\) (78 mg, 0.21 mmol) was dissolved in degassed THF (5 mL) and the solvent removed by vacuum distillation to ensure an oxygen-free system. The residue was dissolved in THF (2 mL) and cooled to -78 °C. A freshly prepared solution of SmI\(_2\) in THF (6.3 mL of 0.1 M solution, 0.63 mmol, 3.0 equiv.) and HMPA (0.21 mL, 1.43 mmol, 6.8 equiv.) was added dropwise over 3 hours minutes with stirring to at -78 °C. The mixture was stirred at -78 °C for 2 hours, after which it was diluted with EtOAc (20 mL) and filtered through a thin pad of silica gel. The solvent was removed \textit{in vacuo} and the residue was purified by column chromatography. A single dimer was obtained (34 mg, 13%).

**TLC:** \(R_f\) 0.32 (4:1 hexanes-EtOAc)

**\(^1\)H NMR:**

\(300\ \text{MHz, CDCl}_3\) \(\delta_H\) 4.81 (t, 1H, \(J = 5.6\ \text{Hz}, \ H3\)), 4.73 (t, 1H, \(J = 5.6\ \text{Hz}, \ H3'\)), 4.36 (d, 1H, \(J = 5.4\ \text{Hz}, \ H1'\)), 4.19 (d, 1H, \(J = 5.7\ \text{Hz}, \ H1\)), 4.16-4.10 (m, 2H, \(\text{OCH}_2\text{CH}_3\)), 3.88 (d, 1H, \(J = 9.6\ \text{Hz}, \ \text{CH}_3\text{OTBDMS}'\)), 3.75 (d, 1H, \(J = 9.6\ \text{Hz}, \ \text{CH}_2\text{OTBDMS}'\)), 3.46 (d, 2H, \(J = 1.2\ \text{Hz}, \ \text{CH}_2\text{OTBDMS}\)), 3.17 (s, 1H, \(\text{OH}'\)), 2.99 (d, 1H, \(J = 12.9\ \text{Hz}, \ H5'\)), 3.02-2.91 (m, 1H, \(H4\)), 2.73-2.64 (m, 1H, \(H4'\)), 2.68 (d, 1H, \(J = 12.0\ \text{Hz}, \ H5\)), 1.56 (s, 1H, \(\text{OH}\)), 1.52 (s, 3H, \(\text{CH}_3\text{-isopropylidene}'\)), 1.39 (s, 3H, \(\text{CH}_3\text{-isopropylidene}'\)), 1.35 (s, 3H, \(\text{CH}_3\text{-isopropylidene}'\)), 1.25 (s, 3H, \(\text{CH}_3\text{-isopropylidene}'\)), 1.26 (t, 3H, \(J = 6.6\ \text{Hz}, \ \text{OCH}_2\text{CH}_3\)), 1.24 (t, 3H, \(J = 6.8\ \text{Hz}, \ \text{OCH}_2\text{CH}_3\))
Hz, OCH$_2$CH$_3$'), 0.87 (s, 9H, C(CH$_3$)$_3$), 0.86 (s, 9H, C(CH$_3$)$_3$'), 0.05 (s, 6H, SiCH$_3$ and SiCH$_3$'), 0.04 (s, 6H, SiCH$_3$ and SiCH$_3$').

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 172.3 (C1''), 171.3 (C1'''), 110.3 (C2''), 109.6 (C2), 84.3 (C3), 82.6 (C3'), 80.5 (C1), 80.4 (C1), 80.3 (C4), 80.2 (C4'), 66.1 (CH$_2$OTBDMS), 63.8 (CH$_2$OTBDMS'), 60.6 (OCH$_2$CH$_3$), 60.5 (OCH$_2$CH$_3$'), 54.8 (C6), 50.5 (C6'), 42.4 (C5), 40.3 (C5'), 26.5 (CH$_3$-isopropylidene), 26.4 (CH$_3$-isopropylidene), 25.9 (C(CH$_3$)$_3$), 25.8 (C(CH$_3$)$_3$'), 24.8 (CH$_3$-isopropylidene'), 24.3 (CH$_3$-isopropylidene'), 18.4 (C(CH$_3$)$_3$), 18.3 (C(CH$_3$)$_3$'), 14.2 (OCH$_2$CH$_3$), 14.1 (OCH$_2$CH$_3$), -5.30 (SiCH$_3$), -5.37 (SiCH$_3$'), -5.52 (SiCH$_3$), -5.54 (SiCH$_3$).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3041, 2960, 1740, 1714, 1662, 1220, 1100.

HRMS: Found 747.4172. Calculated for C$_{36}$H$_{66}$O$_{12}$Si$_2$ 747.4171.

$[\alpha]_D$: +29.5 ($c = 0.5$ CHCl$_3$).
6.5 SAMARIUM DIIODIDE-MEDIATED CYCLISATION BETWEEN AN ALDEHYDE AND AN ACTIVATED ALKENE

6.5.1 Approaches using anomeric $O$-allyl groups

Methyl 2,3-$O$-Isopropylidene $\beta$-$D$-ribofuranoside (5.1) – see 3.27

Methyl 2,3-$O$-isopropylidene-5-$O$-(tosyl)- $\beta$-$D$-ribofuranoside (5.2a) – see 3.28

Methyl 5-iodo-5-deoxy-2,3-$O$-isopropylidene $D$-ribofuranoside $^{15}$ (5.2b)

To a solution of methyl 2,3-$O$-isopropylidene $\beta$-$D$-ribofuranoside (100 mg, 0.490 mmol, 3.29), triphenyl phosphine (193 mg, 0.735 mmol) and imidazole (10 mol %) dissolved in dry toluene (2 mL) was added iodine (174 mg, 0.686 mmol). The reaction mixture was allowed to heat under reflux. The reaction was monitored by TLC to completion, by which time the reaction mixture became clear. A saturated sodium hydrogen carbonate was added and the reaction mixture was allowed to stir for a further 5 minutes. The reaction mixture was diluted with EtOAc and washed with a 3% thiosulfate solution. The organic phase was dried over MgSO4 and the solvent removed in vacuo. The product was purified by column chromatography (153 mg, 0.490 mmol, 100%).

TLC: $R_f$ 0.79 (5:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 5.00 (s, 1H, H1), 4.72 (dd, 1H, $J = 5.7$ and 0.6 Hz, H3), 4.58 (d, 1H, $J = 5.9$ Hz, H2), 4.39 (ddd, 1H, $J = 9.9$, 6.0 and 0.6 Hz,
Methyl 5-C-Cyano-5-deoxy-2,3-O-isopropylidene β-D-ribofuranoside (5.3 via Route a)

To a solution of methyl 5-iodo-5-deoxy-2,3-O-isopropylidene β-D-ribofuranoside (50 mg, 0.159 mmol) and 18-crown-6 (4 mg, 0.013 mmol) dissolved in dry acetonitrile (100 µL) was added potassium cyanide (21 mg, 0.319 mmol). The reaction mixture was allowed to heat at the reflux temperature of the mixture for two days. The solvent was removed in vacuo and the product purified by column chromatography (13 mg, 0.061 mmol, 38%, on conversion 55%).

**MP:** 73-75 °C

**TLC:** Rf 0.28 (5:1 hexanes-EtOAc)

**1H NMR:** (300 MHz, CDCl₃) δH 4.98 (s, 1H, H1), 4.62 (dd, 1H, J = 9.2 and 6.2 Hz, H3), 4.61 (d, 1H, J = 9.2 Hz, H2), 4.44 (ddd, 1H, J = 8.1, 6.9 and 0.6 Hz, H4), 3.38 (s, 3H, OCH₃), 2.68 (dd, 1H, J = 16.4 and 8.1 Hz, H5a), 2.58
(dd, 1H, J = 16.4 and 8.1 Hz, H5b), 1.45 (s, 3H, CH3-isopropylidene), 1.29 (s, 3H, CH3-isopropylidene).

13C NMR: (75 MHz, CDCl3) δC 116.8 (C6), 113.0 (acetal-C), 110.0 (C1), 85.0 (C2), 83.1 (C3), 81.8 (C4), 55.4 (OCH3), 26.3 (CH3-isopropylidene), 24.9 (CH3-isopropylidene), 23.6 (C5).

IR: νmax(CHCl3)/cm⁻¹ 2943, 2841, 1562, 1540, 1382, 1107, 1051, 869, 669.


Methyl 5-C-Cyano-2,3-O-isopropylidene β-D-ribofuranoside (5.3 via Route b)

Triflic anhydride (0.11 mL), dissolved in DCM (0.18 mL) was added dropwise to a stirred, ice cold solution of the sugar (108 mg, 0.522 mmol) in pyridine (0.068 mL) in DCM (0.78 mL). After the reaction was left to stir for a further 5-10 minutes (monitor by TLC), it was worked up below 20 °C as follows: The mixture was quenched with ice and diluted with DCM. The organic layer was washed twice with ice water, once with 5% KHSO4 and once more with ice water. The aqueous washings were back extracted with DCM. The combined organic layers were dried over magnesium sulfate. The magnesium sulfate was filtered off and the solvent removed on a cold Buchi.

The residue was dissolved in dry acetonitrile (1 mL). 18-Crown-6 (21 mg) was added and stirring was initiated. Potassium cyanide (107 mg) was added. The reaction mixture was allowed to stir for approximately 2 hours (monitor by TLC). The solvent was removed in vacuo and an aqueous / DCM workup was carried out. After column chromatography (5:1 hexanes-EtOAc) afforded the desired product (42 mg, 0.20 mmol, 37%, on conversion 60%).
Product characterised above when introduction of the cyano functionality was carried out by displacement of the iodo group (5.3 via Route b).

Methyl 5-C-Cyano-2,3-O-isopropylidene α-D-ribofuranoside (5.3b)

Butyl lithium (1.29 mL, 1.2925 mmol, 1.2 equivalents) was added to 5 mL of THF at -78 °C. To this solution was added diisopropylamine (167 L, 1.175 mmol). The reaction mixture was allowed to stir at -78 °C for approximately 30 minutes.

Methyl 5-C-Cyano-2,3-O-isopropylidene D-ribofuranoside (50 mg, 0.235 mmol) was dissolved in THF (1 mL) and cooled to -78 °C. To this solution was added 1 mL from the bulk LDA solution. The reaction mixture was allowed to stir for a further hour at -78 °C, after which the reaction was allowed to warm to room temperature. The reaction mixture was left to stir at room temperature overnight. The solvent was removed in vacuo and the product purified by column chromatography (5:1 hexanes-EtOAc). NMR analysis of the product showed that the same compound had been recovered but that epimerisation had occurred.

TLC: \( R_f \) 0.26 (5:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\textsubscript{3}) \( \delta_H \) 4.89 (s, 1H, H1), 4.68 (dd, 1H, \( J = 5.8 \) and 3.6 Hz, H3), 4.57 (d, 1H, \( J = 5.8 \) Hz, H2), 4.19 (ddd, 1H, \( J = 6.8, 6.8 \) and 3.6 Hz, H4), 3.33 (s, 3H, OCH\textsubscript{3}), 2.72 (d, 1H, \( J = 6.8 \) Hz, H5a and H5b), 1.45 (s, 3H, CH\textsubscript{3}-isopropylidene), 1.29 (s, 3H, CH\textsubscript{3}-isopropylidene).
\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \(\delta\)C 117.2 (C6), 113.1 (acetal-C), 107.2 (C1), 84.9 (C2), 79.3 (C3), 75.1 (C4), 54.9 (O\(\text{CH}_3\)), 25.8 (CH\(_3\)-isopropylidene), 24.7 (CH\(_3\)-isopropylidene), 17.8 (C5).

2,3-O-Isopropylidene-D-ribofuranose (5.5) – see 4.7

5-O-(Triphenylmethyl)-2,3-O-isopropylidene-D-ribofuranose (5.6) – see 4.8

1-O-Acetyl-5-O-(triphenylmethyl)-2,3-O-isopropylidene-D-ribofuranose (5.7)

To a solution of 5-O-(triphenylmethyl)-2,3-O-isopropylidene-D-ribofuranose (400 mg, 0.925 mmol, 4.8) in dry pyridine (1.4 mL) was added distilled acetic anhydride (436 \(\mu\)L, 4.625 mmol). The reaction mixture was allowed to stir for 4 hours at room temperature. The solvent was removed \textit{in vacuo}, and the residue was purified by flash chromatography (4:1 hexanes-EtOAc) to afford the acetylated product (425mg, 0.897 mmol, 97%).

MP: 100-102 °C

TLC: \(R_f\) 0.45 (4:1 Hexane-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \(\delta\)H 7.48 (d, 6H, \(J = 6.9\) Hz, \textit{ortho} aromatics), 7.34-7.25 (m, 9H, \textit{meta} and \textit{para} aromatics), 6.24 (s, 1H, H1), 4.75 (d, 1H, \(J = 6.0\) Hz, H3), 4.71 (d, 1H, \(J = 6.0\) Hz, H2), 4.55 (dd, 1H, \(J = 6.3\) and 5.1 Hz, H4), 3.24 (dd, 1H, \(J = 9.9\) and 5.1 Hz, H5a), 3.19 (dd, 1H, \(J = 9.9\) and 6.3 Hz, H5b), 1.84 (s, 3H, O\(\text{CH}_3\)), 1.53 (s, 3H, CH\(_3\)-isopropylidene), 1.35 (s, 3H, CH\(_3\)-isopropylidene).
$^{13}$C NMR:  (75 MHz, CDCl$_3$) δC 169.2 (OCC$_3$), 143.5 (ipso), 128.4 (ortho), 127.6 (meta), 126.9 (para), 112.6 (acetal-C), 102.3 (C1), 87.1 (C2), 86.7 (C(Ph)$_3$), 85.1 (C3), 81.6 (C4), 64.2 (C5), 26.5 (CH$_3$-isopropylidene), 21.0 (OCCH$_3$).

IR:  ν$_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 1746, 1702, 1377, 1314, 1006, 966, 708.

HRMS:  Found 474.2023.  Calculated for C$_{29}$H$_{30}$O$_6$ 474.2044.

EIMS:  474 (M$^+$, 5%), 243 (M$^+$ - 3 × Ph, 68%), 165 (100%).

1-O-Acetyl-2,3-O-isopropylidene-ß-ribofuranose (5.8)

1-O-Acetyl-5-O-(triphenylmethyl)-2,3-O-isopropylidene-ß-ribofuranose (400 mg, 0.844 mmol) was dissolved in a mixture of formic acid and ether (3:1, 4.8 mL:1.6mL) and allowed to stir for 20 minutes. The reaction was diluted with ether and washed with sodium bicarbonate, until neutral. The solvent was removed in vacuo, and the residue was purified by flash chromatography (3:1 hexanes-EtOAc) to afford the hydroxy acetylated product (61 mg, 0.261 mmol, 31%, on conversion 53%). Due to the formation of a formate product (see text) the reaction can not be left to go to completion and appears to be low yielding.

TLC:  R$_f$ 0.08 (3:1 Hexane-EtOAc)

$^1$H NMR:  (300 MHz, CDCl$_3$) δ$_H$ 6.13 (s, 1H, H1), 4.68 (d, 1H, J = 6.0 Hz, H3), 4.62 (d, 1H, J = 6.0 Hz, H2), 4.30 (t, 1H, J = 5.7 Hz, H4), 3.65 (dd, 1H, J = 5.9 Hz, H5a), 3.58 (dd, 1H, J = 5.9 Hz, H5b), 2.62 (br s, 1H, OH), 1.99 (s, 3H, OH);
1-O-Acetyl-5-C-iodo-5-deoxy-2,3-O-isopropylidene-D-ribofuranose (5.9)

The general procedure to displace a free hydroxyl group with iodine, using I$_2$, PPh$_3$, Imidazole in DCM (5.2b), was carried out with 1-O-acetyl-5-hydroxy-2,3-O-isopropylidene-D-ribofuranose (100 mg, 0.431 mmol). The product was purified by column chromatography (3:1 hexanes-EtOAc) (147 mg, 0.431 mmol, 100%).

TLC: R$_f$ 0.54 (3:1 Hexane-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 6.23 (s, 1H, H1), 4.7 8 (dd, 1H, $J = 6.0$ and 0.9 Hz, H3), 4.68 (d, 1H, $J = 6.0$ Hz, H2), 4.46 (ddd, 1H, $J = 10.3$, 5.7 and 0.9 Hz, H4), 3.21 (dd, 1H, $J = 10.1$ and 5.7 Hz, H5a), 3.05 (dd, 1H, $J = 10.3$ and 10.1 Hz, H5b), 2.02 (s, 3H, OCCH$_3$), 1.44 (s, 3H, CH$_3$-isopropylidene), 1.29 (s, 3H, CH$_3$-isopropylidene).
The general route for the protection with a triflate group, using triflic anhydride and pyridine in DCM, followed by displacement with a nitrile functionality, using KCN, 18-crown-6 in acetonitrile (5.3 via Route b), was carried out on 1-O-acetyl-2,3-O-isopropylidene-D-ribofuranose (121 mg, 0.522 mmol). Column chromatography (5:1 hexanes-EtOAc) afforded the desired product (85 mg, 0.373 mmol, 73%).

1-O-Acetyl-5-C-cyano-5-deoxy-2,3-O-isopropylidene-D-ribofuranose (5.11)

\[
\text{\begin{center}
\begin{tikzpicture}
\node (1) at (0,0) {OAc};
\node (2) at (1,0) {O};
\node (3) at (2,0) {CN};
\node (4) at (2,2) {O};
\node (5) at (1,2) {O};
\node (6) at (0,2) {O};
\node (7) at (0,1.5) {OAc};
\node (8) at (1,1.5) {O};
\node (9) at (2,1.5) {CN};
\node (10) at (0,-1) {O};
\node (11) at (1,-1) {O};
\node (12) at (2,-1) {O};
\end{tikzpicture}
\end{center}}
\]

\[\text{O OAc CN O O} \]

\[\text{MP: 114-117 °C}\]
\[\text{TLC: } R_t 0.83 \text{ (2:1 hexanes-EtOAc)}\]
\[\text{\(^1\)H NMR: (300 MHz, CDCl}_3\) \(\delta_H 6.22 \text{ (s, 1H, H1)}, 4.75 \text{ (d, 1H, } J = 6.5 \text{ Hz, H2)},
\]
\[4.71 \text{ (d, 1H, } J = 6.5 \text{ Hz, H3)}, 4.98 \text{ (t, 1H, } J = 7.2 \text{ Hz, H4)}, 2.67 \text{ (dd, 1H, } J = 16.8 \text{ and 7.2 Hz, H5a)},
\]
\[2.62 \text{ (dd, 1H, } J = 16.8 \text{ and 7.2 Hz, H5b)}, 2.06 \text{ (s, 3H, OOCCH}_3\text{)}, 1.47 \text{ (s, 3H, CH}_3\text{-isopropylidene)},
\]
\[1.30 \text{ (s, 3H, CH}_3\text{-isopropylidene)}.\]

\[\text{\(^13\)C NMR: (75 MHz, CDCl}_3\) \(\delta_C 168.8 \text{ (OOCCH}_3\text{)}, 115.9 \text{ (C6)}, 113.6 \text{ (acetal-C)},
\]
\[102.0 \text{ (C1)}, 84.9 \text{ (C3)} 82.9 \text{ (C2)}, 82.8 \text{ (C4)}, 26.3 \text{ (CH}_3\text{-isopropylidene)},
\]
\[24.9 \text{ (CH}_3\text{-isopropylidene)}, 23.2 \text{ (C5)}, 21.2 \text{ (OOCCH}_3\text{)}.\]
IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3654, 1702, 1460, 1381, 1211, 970, 914, 868.

EIMS: 241 (M\(^+\), 1%), 198 (M\(^+\) - Ac, 1%), 182 (M\(^+\) - OAc, 100%).

5-\textit{O}-(Triphenylmethyl)-\textit{D}-ribofuranose (5.15)

\[
\begin{align*}
\text{O} & \quad \text{Trit} & \text{O} & \quad \text{OH} \\
\text{OH} & \quad & \text{HO} & \quad \text{OH}
\end{align*}
\]

The general procedure for trityl primary protection (4.8) was carried out on \textit{D}-ribose (1 g, 6.661 mmol). The residue was purified by flash chromatography (1:1 hexanes-EtOAc) to afford the silyl ether (2.30 g, 5.86 mmol, 88%).

TLC: \( R_f 0.17 \) (1:1 hexanes-EtOAc)

\(^1\text{H NMR:}\) (300 MHz, CDCl\(_3\)) \( \delta_H 7.45 - 7.38 \) (m, 6H and 6H, \textit{ortho}), 7.31 - 7.19 (m, 9H and 9H, \textit{meta} and \textit{para}), 5.41 (d, 1H, \( J = 3.9 \) Hz), 5.28 (s, 1H), 4.42 - 4.31 (m, \( \beta \) anomer), 4.26 - 4.19 (m), 4.07 - 4.02 (m), 3.40 (dd, 1H, \( J = 10.2 \) and 4.5 Hz, H5a), 3.39 (dd, 1H, \( J = 10.2 \) and 4.3 Hz, H5b), 3.31 (dd, 1H, \( J = 10.2 \) and 3.9 Hz, H5a), 3.13 (dd, 1H, \( J = 10.2 \) and 3.9 Hz, H5b).

\(^{13}\text{C NMR:}\) (75 MHz, CDCl\(_3\)) \( \delta_C 143.5 \) (\textit{ipso}), 143.4 (\textit{ipso}), 128.6 (\textit{ortho}), 128.5 (\textit{ortho}), 128.1 (\textit{meta}), 127.8 (\textit{para}), 127.1 (\textit{meta}), 127.0 (\textit{para}), 96.7 (C1\(^\text{\alpha}\)), 86.8 (C4), 82.8 (C(Ph)), 72.0 (C2), 71.6 (C3), 63.9 (C5).
To a solution of 5-O-(triphenylmethyl)-D-ribose (300 mg, 0.765 mmol) in dry pyridine (1.2 mL) was added distilled acetic anhydride (1.1 mL, 1.147 mmol). The reaction mixture was allowed to stir for 4 hours at room temperature. The solvent was removed in vacuo, and the residue was purified by flash chromatography to afford the triacetylated product (387 mg, 0.742 mmol, 97%).

**TLC:**  \( R_f \) 0.17 (4:1 hexanes-EtOAc)

**\(^1\)H NMR:** (300 MHz, CDCl\(_3\)) \( \delta \) \(_H\) 7.40 - 7.34 (m, 6H\(^\alpha\) and 6H\(^\beta\), ortho), 7.25 - 7.10 (m, 9H\(^\alpha\) and 9H\(^\beta\), meta and para), 6.49 (d, 1H\(^\beta\), \( J = 4.2 \) Hz), 6.15 (s, 1H\(^\alpha\)), 5.64 - 5.32 (m, 2H\(^\alpha\) and 2H\(^\beta\)), 4.33-4.24 (m, 1H\(^\alpha\) and 1H\(^\beta\)), 3.38 (dd, 1H\(^\beta\), \( J = 10.2 \) and 4.2 Hz, H5a\(^\beta\)), 3.15 (dd, 1H\(^\alpha\), \( J = 10.2 \) and 3.9 Hz, H5a\(^\alpha\)), 2.04 (s, 3H\(^\beta\), OCCH\(_3\)\(^\beta\)), 2.02 (s, 3H\(^\alpha\), OCCH\(_3\)\(^\alpha\)), 1.99 (s, 3H\(^\beta\), OCCH\(_3\)\(^\beta\)), 1.92 (s, 3H\(^\alpha\), OCCH\(_3\)\(^\alpha\)), 1.89 (s, 3H\(^\alpha\), OCCH\(_3\)\(^\alpha\)).

**\(^{13}\)C NMR:** (75 MHz, CDCl\(_3\)) \( \delta \) \(_C\) 174.2 (OCCH\(_3\)\(^\beta\)), 169.3 (OCCH\(_3\)\(^\beta\)), 169.2 (OCCH\(_3\)\(^\alpha\)), 169.1 (OCCH\(_3\)\(^\alpha\)), 168.9 (OCCH\(_3\)\(^\alpha\)), 143.3 (ipso\(^\alpha\)), 143.0 (ipso\(^\beta\)), 128.2 (ortho\(^\alpha\)), 128.0 (ortho\(^\beta\)), 127.5 (meta\(^\beta\)), 127.4 (meta\(^\alpha\)), 126.8 (para\(^\beta\)), 126.7 (para\(^\alpha\)), 97.9 (C1\(^\alpha\)), 94.9 (C1\(^\beta\)), 86.6 (C4\(^\beta\)), 86.5 (C4\(^\alpha\)), 83.0 (C(Ph)\(_3\)\(^\alpha\)), 80.5 (C(Ph)\(_3\)\(^\alpha\)), 73.9 (C2\(^\alpha\) and \(^\beta\)), 70.3 (C3\(^\alpha\)), 70.2 (C3\(^\beta\)), 62.8 (C5\(^\alpha\) and \(^\beta\)), 20.8 (OCCH\(_3\)\(^\beta\)), 20.7 (OCCH\(_3\)\(^\alpha\)), 20.3 (OCCH\(_3\)\(^\beta\)), 20.2 (OCCH\(_3\)\(^\alpha\)), 20.1 (OCCH\(_3\)\(^\alpha\)), 20.0 (OCCH\(_3\)\(^\beta\)).

**IR:** \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 1751, 1702, 1451, 1374, 1222, 1032, 968.
EIMS: 518 (M+, 1%), 458 (M+1 - OAc, 1%), 259 (M+ - OTrityl, 6%), 243 (Trityl, 100%).

1,2,3-Tri-O-acetyl-5-hydroxy-D-ribofuranose (5.17)

\[
\text{O} \quad \text{OAc} \\
\text{O} \quad \text{OAc} \\
\text{OH} \\
\text{AcO} \\
\text{OAc}
\]

The general procedure to remove a trityl group (5.8) using a mixture of formic acid and ether was used to deprotect 1,2,3-tri-O-acetyl-5-O-(triphenylmethyl)-D-ribofuranose (200 mg, 0.386 mmol). The residue was purified by flash chromatography to afford the hydroxy triacetylated product. Due to the formation of a formate product the reaction can not be left to go to completion and it is necessary to recover starting material and repeat the reaction to attain sufficient product to continue with the synthesis.

TLC: \( R_f 0.13 \) (2:1 hexanes-EtOAc)

\(^1\text{H NMR:} \) (300 MHz, CDCl\(_3\)) \( \delta_{H} \) 6.12 (s, 1H, H1), 5.37 (dd, 1H, \( J = 6.9 \) and \( 5.0 \) Hz, H3), 5.31 (d, 1H, \( J = 5.0 \) Hz, H2), 4.30 - 4.15 (m, 1H, H4), 3.82 (unresolved dd, 1H, \( J = 10.2 \) Hz, H5a), 3.62 (unresolved dd, 1H, \( J = 10.2 \) Hz, H5b), 3.00 (br s, 1H, OH), 2.10 (s, 3H, OCCH\(_3\)), 2.07 (s, 3H, OCCH\(_3\)), 2.04 (s, 3H, OCCH\(_3\)).

\(^{13}\text{C NMR:} \) (75 MHz, CDCl\(_3\)) \( \delta_{C} \) 169.8 (OCCCH\(_3\)), 169.3 (OCCH\(_3\)), 169.2 (OCCCH\(_3\)), 98.0 (C1), 82.3 (C4), 74.5 (C2), 69.7 (C3), 61.8 (C5), 21.1 (OCCH\(_3\)), 20.5 (OCCH\(_3\) \( \times 2 \)).

IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3024, 1475, 1457, 1452, 1220, 1209, 670.

EIMS: 276 (M+, 1%), 259 (M+1 - H\(_2\)O, 3%), 245 (M+1 - C\(_2\)H\(_6\), 8%), 217 (M+ - OAc, 100%).
1,2,3-Tri-\(O\)-acetyl-5-C-cyano-5-deoxy-D-ribofuranose (5.19)

The general route for the protection with a triflate group, using triflic anhydride and pyridine in DCM, followed by displacement with a nitrile functionality, using KCN, 18-crown-6 in acetonitrile (5.3 via Route b), was carried out on 5.17 (171 mg, 0.619 mmol). After column chromatography (2:1 hexanes-EtOAc) a mixture of isomers was obtained (85 mg, 0.373 mmol, 73%).

\begin{itemize}
  \item **TLC:** \(R_f\) 0.56 (1:1 hexanes-EtOAc)
  \item **\(^1\)H NMR:** (300 MHz, CDCl\(_3\)) \(\delta_H 6.10\) (s, 1H, H1), 5.35 (s, 1H, H2), 5.32 (d, 1H \(J = 4.8\) Hz, H3), 4.34 - 4.29 (m, 1H, H4), 2.85 (dd, 1H, \(J = 16.7\) and 5.1 Hz, H5a), 2.73 (dd, 1H, \(J = 16.7\) and 4.4 Hz, H5b), 2.12 (s, 3H, O\(\text{OCCH}_3\)), 2.11 (s, 3H, O\(\text{OCCH}_3\)), 2.07 (s, 3H, O\(\text{OCCH}_3\)).
  \item **\(^13\)C NMR:** (75 MHz, CDCl\(_3\)) \(\delta_C 169.6\) (O\(\text{OCCH}_3\)), 169.2 (O\(\text{OCCH}_3\)), 169.9 (O\(\text{OCCH}_3\)), 115.5 (C6), 97.5 (C1), 76.3 (C4), 73.9 (C3), 72.6 (C2), 22.8 (C5), 21.1 (O\(\text{OCCH}_3\)), 20.5 (O\(\text{OCCH}_3\)), 20.4 (O\(\text{OCCH}_3\)).
  \item **IR:** \(\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}\) 3025, 1754, 1703, 1223, 1213, 788, 776, 774.
  \item **EIMS:** 259 (M\(^+\) - CN, 1%), 226 (M\(^+\) - O\(\text{Ac}\), 1%), 216 (M\(^+\) - CN - Ac, 1%), 104 (M\(^+\) - C\(_6\)H\(_{13}\)O\(_6\), 17%), 43 (100%).
\end{itemize}

\begin{itemize}
  \item **TLC:** \(R_f\) 0.50 (1:1 hexanes-EtOAc)
  \item **\(^1\)H NMR:** (300 MHz, CDCl\(_3\)) \(\delta_H 6.45\) (d, 1H, \(J = 4.5\) Hz, H1), 5.23 (dd, 1H, \(J = 7.2\) and 4.5 Hz, H2), 5.08 (d, 1H, \(J = 7.2\) and 4.2 Hz, H3), 4.34 (td, 1H, \(J = 5.0\) and 4.2 Hz, H4), 2.84 (d, 2H, \(J = 5.0\) Hz, H5a and H5b), 2.12 (s, 3H, O\(\text{OCCH}_3\)), 2.11 (s, 3H, O\(\text{OCCH}_3\)), 2.09 (s, 3H, O\(\text{OCCH}_3\)).
  \item **\(^13\)C NMR:** (75 MHz, CDCl\(_3\)) \(\delta_C 170.2\) (O\(\text{OCCH}_3\)), 169.2 (O\(\text{OCCH}_3\)), 169.1
\end{itemize}
(OOCCH₃), 115.7 (C6), 93.9 (C1), 79.0 (C4), 71.4 (C3), 69.7 (C2), 22.1 (C5), 20.9 (OOCCH₃), 20.6 (OOCCH₃), 20.3 (OOCCH₃).

5-O-(tert-Butyldiphenylsilyl)-D-ribofuranose (5.20)

The general procedure for TBDPS primary protection (3.9) was carried out on D-ribose (500 mg, 3.33 mmol). The residue was purified by flash chromatography (1:1 hexanes-EtOAc followed by pure EtOAc) to afford the silyl ether (1.619 g, 4.172 mmol, 89%).

TLC: \[ R_f \ 0.27 \ (1:1 \text{ hexanes-EtOAc}) \]

\(^1\)H NMR: (300 MHz, CDCl₃) \( \delta_H \) 7.70-7.63 (m, 4H, \textit{ortho} aromatics), 7.43-7.38 (m, 6H, \textit{para} and \textit{meta} aromatics), 5.38 (br s), 5.25 (br s), 5.20 (br s), 4.09-4.03 (m), 4.87-3.70 (m), 1.04(s, 9H, C(CH₃)₃).

\(^1^3\)C NMR: (75 MHz, CDCl₃) \( \delta_C \) 135.5 (ipso), 135.3 (ipso), 132.9 (ortho), 132.6 (ortho), 129.6 (meta × 2), 127.6 (para), 127.5 (para), 96.7 (C1), 84.4 (C4), 71.9 (C2), 71.5 (C3), 63.9 (C5), 26.7 (C(CH₃)₃), 19.2 (C(CH₃)₃).
To a solution of 5-O-(tert-butyldiphenylsilyl)-D-ribose (633 mg, 1.63 mmol) in dry pyridine (2.5 mL) was added distilled acetic anhydride (2 mL, 4.89 mmol). The reaction mixture was allowed to stir for 4 hours at room temperature. The solvent was removed in vacuo, and the residue was purified by flash chromatography to afford the triacetylated product (799 mg, 1.532 mmol, 94%).

TLC: \( R_f 0.86 \) (1:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \( \delta_H \) 7.71-7.60 (m, 4H, ortho aromatics), 7.46-7.34 (m, 6H, para and meta aromatics), 6.18 (s, 1H, \( \alpha \) anommer), 5.89 (d, 1H, \( J = 6.9 \) Hz, \( \beta \) anommer), 5.57 (dd, 1H, \( J = 6.0 \) and 5.1 Hz, H3), 5.47(d, 1H, \( J = 5.1 \) Hz, H2), 4.29-4.23 (m, 1H, H4), 3.84 (dd, 1H, \( J = 11.4 \) and 3.6 Hz, H5a), 3.72 (dd, 1H, \( J = 11.4 \) and 3.5 Hz, H5b), 2.12 (s, 3H, OOCC\( \text{CH}_3 \)), 2.05 (s, 3H, OOCC\( \text{CH}_3 \)), 1.95 (s, 3H, OOCC\( \text{CH}_3 \)), 1.07 (s, 9H, C(CH\(_3\))\(_3 \)).

(5:1 \( \alpha:\beta \) anommer mixture obtained, main isomer characterised).

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \( \delta_C \) 169.6 (OOC\( \text{CH}_3 \)), 169.4 (OOC\( \text{CH}_3 \)), 169.3 (OOC\( \text{CH}_3 \)), 135.5 (\( \alpha \) ortho), 135.4 (\( \alpha \) ortho), 132.8 (ipso\(^\alpha\)), 132.6 (ipso\(^\alpha\)), 129.8 (para\(^\alpha\)), 129.7 (para\(^\alpha\)), 127.7 (meta\(^\alpha\)), 127.6 (meta\(^\alpha\)), 98.2 (C1), 82.3 (C4), 74.4 (C2), 70.6 (C3), 63.2 (C5), 26.7 (C(CH\(_3\))\(_3 \)), 21.0 (OOC\( \text{CH}_3 \)), 20.9 (OOC\( \text{CH}_3 \)), 20.6 (OOC\( \text{CH}_3 \)), 19.3 (C(CH\(_3\))\(_3 \)).

IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 2964, 2937, 1762, 1737, 1475, 1430, 1375, 1221, 1209, 1106, 1010.

EIMS: 515 (M+1, 1%), 457 (M\(^+\) - C\(_4\)H\(_9\), 28%), 395 (M\(^+\) - C\(_4\)H\(_8\)O\(_2\), 2%), 241 (M\(^+\) - OTBDPS, - H\(_2\)O, 25%).
1,2,3-Trι-O-acetyl-D-ribofuranose (5.17)

A solution of 1,2,3-trι-O-acetyl-5-O-(tert-butyldiphenylsilyl)-D-ribose (234 mg, 0.455 mmol) in dry THF (9 mL) was cooled to 0 °C and to the solution was added HF.pyridine (0.54 mL). The reaction mixture was allowed to stir at 0 °C for approximately 30 minutes and thereafter left to stir at room temperature, monitoring by TLC to completion. The reaction mixture was diluted with ether (50 mL) and neutralised with NaHCO₃. The organic layer was dried over MgSO₄ and the solvent removed in vacuo. The residue was purified by chromatography to afford the title compound (69 mg, 0.250 mmol, 50%).

Product characterised above when carried out by a different synthetic route.

Benzyl 2,3-di-O-benzyl-5-O-triphenylmethyl-D-ribofuranose (5.22a, isomer a) and Benzyl 2-O-benzyl-5-O-(triphenylmethyl)-D-ribofuranose

The general route for the benzylation of sugar derivatives (room temperature, benzyl bromide, KOH, minimal DMF to dissolve sugar) (3.15b) was used for the tribenzylation of 5-O-triphenylmethyl-D-ribose (1.0 g, 2.5 mmol). After column chromatography (10:1 hexanes-EtOAc) the desired product was obtained as the minor product (300mg, 0.453 mmol, 17%), along with 1,2-di-O-benzyl-3-hydroxy-5-O-triphenylmethyl-D-ribose (55%).
Benzyl 2,3-di-O-benzyl-5-O-(triphenylmethyl)-D-ribofuranose

TLC: \( R_f 0.28 \) (10:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\) \( \delta_H \) (Major isomer) 7.60-7.10 (m, 30H, aromatics), 5.19 (s, 1H, H1), 4.81-4.41 (m, 7H, OCH\(_2\)Ph \( \times 2 \) and H4), 4.27 (dd, 1H, J = 7.4 and 4.3 Hz, H3), 4.01 (d, 1H, J = 4.3 Hz, H2), 3.43 (dd, 1H, J = 9.9 and 3.6 Hz, H5a), 3.24 (dd, 1H, J = 9.9 and 4.8 Hz, H5b).

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\) \( \delta_C \) 143.8 (ipso C(Ph)\(_3\)), 137.7 (ipso), 137.6 (ipso), 137.3 (ipso), Aromatics – 130.1, 129.9, 128.6, 128.2, 128.1, 127.9, 127.8, 127.6, 126.8, 104.3 (C1), 86.3 (C4), 80.6 (C(Ph)\(_3\)), 79.7 (C3), 78.3 (C2), 72.3 (OCH\(_2\)Ph), 72.2 (OCH\(_2\)Ph), 69.3 (anomeric OCH\(_2\)Ph), 64.2 (C5).

IR: \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 2933, 2372, 1675, 1650, 1639, 1633, 901, 785, 773.

EIMS: 661 (M-1, 1%), 448 (M\(^+\) - OBn, 1%), 243 (Trityl, 100%), 91 (Bn, 11%).

**Major Product:**

Benzyl 2-O-benzyl-5-O-(triphenylmethyl)-D-ribofuranose

Yield: 800 mg, 1.39 mmol, 55%

TLC: \( R_f 0.28 \) (10:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\) \( \delta_H \) (Major isomer and minor isomer) 7.62-7.29 (m, 50H, aromatics and aromatics), 5.31 (d, 1H, J = 3.6 Hz, H1), 5.26 (d, 1H, J = 4.56 Hz, H1), 5.03-4.56 (m, 8H, OCH\(_2\)Ph \( \times 2 \) and OCH\(_2\)Ph \( \times 2 \)), 4.41-4.19 (m, 4H, H4, H4, H3 and H3), 4.10 (unresolved dd, 1H, J = 3.9 Hz,
H2), 3.96 (dd, 1H, J = 7.2 and 3.0 Hz, H2), 3.46 (dd, 1H, J = 10.2 and 3.6 Hz, H5a), 3.37 (dd, 1H, J = 10.2 and 4.5 Hz, H5b), 3.28-3.18 (m, 2H, H5a and H5b).

13C NMR: (75 MHz, CDCl3) δC 143.7 (ipso C(Ph)3), 143.5 (ipso C(Ph)3), 137.8 (ipso), 137.7 (ipso), 137.4 (ipso), 137.2 (ipso), Aromatics – 128.6, 128.4, 128.3, 128.2, 128.1, 127.7, 127.6, 127.5, 127.4, 127.3, 126.8, 126.7, 100.4 (C1), 100.1 (C1), 86.6 (C4), 86.5 (C4), 85.6 (C(Ph)3), 82.2 (C(Ph)3), 78.0 (C3 and C3), 76.9 (C2 and C2), 72.5 (OCH2Ph), 72.1 (OCH2Ph), 68.9 (anomeric OCH2Ph), 68.8 (anomeric OCH2Ph), 63.8 (C5), 63.7 (C5).

Confirmation of major product:

Benzyl 3-O-acetyl-2-O-benzyl-5-O-(triphenylmethyl)-D-ribofuranose

The general route towards acetylation using acetic anhydride and pyridine (5.7) was used to acetylate benzyl 2-O-benzyl-5-O-(triphenylmethyl)-D-ribofuranose (JC331.4). After column chromatography (10:1 hexanes-EtOAc) the product was isolated in good yield (89%).

TLC: Rf 0.28 (10:1 hexanes-EtOAc)

1H NMR: (300 MHz, CDCl3) δH 7.46-7.21 (m, 25H, aromatics), 5.22 (dd, 1H, J = 6.6 and 2.7 Hz, H3), 5.13 (d, 1H, J = 4.5 Hz, H1), 4.87 (d, 1H, J = 12.6 Hz, OCH3H8Ph), 4.74-4.58 (m, 3H, OCH3H8Ph and OCH2Ph), 4.19 (ddd, 1H, J = 6.6, 3.6 and 3.3 Hz, H4), 4.08 (dd, 1H, J = 6.6 and 4.5 Hz, H2), 3.34 (dd, 1H, J = 10.5 and 3.6 Hz, H5a), 3.19 (dd, 1H, J = 10.5 and 3.3 Hz, H5b), 2.12 (s, 3H, OOCCH3).
\textsuperscript{13}C NMR: (75 MHz, CDCl\textsubscript{3}) \delta_C 170.7 (OOC\textsubscript{CH\textsubscript{3}}), 143.6 (\textit{ipso} C(Ph)\textsubscript{3}), 137.9 (\textit{ipso}), 137.6 (\textit{ipso}), Aromatics – 128.5, 128.3, 128.1, 127.8, 127.7, 127.4, 126.9, 99.3 (C1), 86.6 (C4), 81.5 (C(Ph)\textsubscript{3}), 77.3 (C3), 73.0 (C2), 70.7 (OCH\textsubscript{2}Ph), 68.6 (anomeric OCH\textsubscript{2}Ph), 63.7 (C5), 21.2 (OOC\textsubscript{CH\textsubscript{3}}).

IR: \nu_{\text{max}}(\text{CHCl}\textsubscript{3})/\text{cm}\textsuperscript{-1} 2935, 2875, 1739, 1692, 1452, 1377, 1250, 1231, 1097, 1038, 901, 793.

CIMS: 615 (M+1, 1%), 243 (Trityl, 77%), 181 (C\textsubscript{14}H\textsubscript{13}, 23%), 107 (OBn, 27%), 89 (100%).

Benzyl 2,3-di-O-benzyl-5-O-(triphenylmethyl)-\textbeta-D-ribofuranose (\textbf{5.22a, isomer b})

\[
\text{OTrit} \\
\text{OBn} \\
\text{BnO} \\
\text{OBn}
\]

The general route for the benzylation of sugar derivatives (room temperature, benzyl bromide, KOH, minimal DMF to dissolve sugar) (\textbf{3.15b}) was used for the benzylation benzyl 2-O-benzyl-5-O-(triphenylmethyl-D-ribose) (700 mg, 1.22 mmol). After column chromatography (10:1 hexanes-EtOAc) the desired product was obtained (200 mg, 0.302 mmol, 25%).

TLC: \text{R}_f 0.28 (10:1 hexanes-EtOAc)

\textsuperscript{1}H NMR: (300 MHz, CDCl\textsubscript{3}) \delta_H 7.52-7.27 (m, 30H, aromatics), 5.15 (unresolved d, 1H, H1), 4.96 (d, 1H, J = 12.6 Hz, OCH\textsubscript{3}H\textsubscript{3}Ph), 4.79-4.58 (m, 5H, OCH\textsubscript{3}H\textsubscript{3}Ph and OCH\textsubscript{2}Ph \times 2), 4.32 (unresolved ddd, 1H, H4), 3.89 (br s, 2H, H2 and H3), 3.23 (ddd, 1H, J = 9.9 and 3.9 Hz, H5a), 3.04 (dd, 1H, J = 9.9 and 2.4 Hz, H5b).
\[ ^{13}\text{C NMR:} \quad (75 \text{ MHz, CDCl}_3) \delta C \, 143.6 \, (ipso \, C(\text{Ph})_3), \, 138.2 \, (ipso), \, 138.1 \, (ipso), \, 137.8 \, (ipso), \, \text{Aromatics} - 128.5, \, 128.2, \, 128.0, \, 127.9, \, 127.6, \, 127.5, \, 127.2, \, 126.8, \, 99.3 \, (C1), \, 86.5 \, (C4), \, 82.2 \, (C(\text{Ph})_3), \, 77.9 \, (C3), \, 75.6 \, (C2), \, 72.3 \, (\text{OCH}_2\text{Ph}), \, 72.1 \, (\text{OCH}_2\text{Ph}), \, 68.7 \, (\text{anomeric OCH}_2\text{Ph}), \, 63.9 \, (C5). \]

Benzyl 2,3-di-O-benzyl-5-O-(tert-butyldiphenylsilyl)-\(\alpha\)-D-ribofuranose (5.22b, isomer a)

The general route for the benzylation of sugar derivatives (0 °C, NaH, DMF, benzyl bromide) (3.15a) was used for the tribenzylation of 5-O-tert-butyldiphenylsilyl-D-ribofuranose (1 g, 2.6 mmol). After column chromatography (10:1 hexanes-EtOAc) the desired product was isolated in a yield of (513 mg, 0.78 mmol, 35%).

TLC: \( R_f \) 0.33 (5:1 hexanes-EtOAc)

\[ ^{1}\text{H NMR:} \quad (300 \text{ MHz, CDCl}_3) \delta H \, 7.70-7.55 \, (m, \, 4H \, ortho \, \text{aromatics of TBDPS}), \, 7.50-7.08 \, (m, \, 21H, \, \text{OCH}_2\text{Ph} \times 3 \, \text{aromatics and TBDPS aromatics}), \, 5.09 \, (d, \, 1H, \, J = 4.4 \, \text{Hz}, \, H1), \, 4.93 \, (d, \, 1H, \, J = 12.6, \, \text{OCH}_2\text{H}_3\text{Ph}), \, 4.78-4.61 \, (m, \, 5H, \, \text{OCH}_2\text{H}_3\text{Ph} \, \text{and OCH}_2\text{Ph} \times 2), \, 4.28-4.22 \, (m, \, 1H, \, H4), \, 4.04 \, (dd, \, 1H, \, J = 6.6 \, \text{and} \, 3.0 \, \text{Hz}, \, H3), \, 3.87 \, (dd, \, 1H, \, J = 6.6 \, \text{and} \, 4.4 \, \text{Hz}, \, H2), \, 3.66 \, (dd, \, 1H, \, J = 11.0 \, \text{and} \, 3.6 \, \text{Hz}, \, H5a), \, 3.57 \, (dd, \, 1H, \, J = 11.0 \, \text{and} \, 3.6 \, \text{Hz}, \, H5b), \, 1.02 \, (s, \, 9H, \, C(\text{CH}_3)_3). \]

\[ ^{13}\text{C NMR:} \quad (75 \text{ MHz, CDCl}_3) \delta C \, 138.3 \, (ipso), \, 138.1 \, (ipso), \, 137.8 \, (ipso), \, 135.5 \, (ortho \, \text{Si}), \, 135.4 \, (ortho \, \text{Si}), \, 133.1 \, (ipso \, \text{Si}), \, 133.0 \, (ipso \, \text{Si}), \, 129.6 \, (para \, \text{Si}), \, 129.5 \, (para \, \text{Si}), \, 128.2 \, (meta \, \text{Si}), \, 128.1 \, (meta \, \text{Si}), \, \text{Aromatics} - 127.9, \]
127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 99.4 (C1), 83.5 (C4), 78.1 (C3),
75.3 (C2), 72.3 (OCH₂Ph × 2), 68.6 (anomeric OCH₂Ph), 64.0 (C5), 26.7
(C(CH₃)₃), 19.1 (C(CH₃)₃).

IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 2932, 1701, 1687, 1222, 1214, 823, 788.

EIMS: 658 (M⁺, 1%), 579 (M+1 - Ph, 15%), 531 (M⁺ - OBn, 1%), 443 (M+1 -
2OBn, 35%), 353 (M⁺ - Bn - 2OBn, 4%), 239 (TBDPS, 1%), 91 (Bn, 100%).

Benzyl 2,3-di-O-benzyl-5-O-tert-butyldiphenylsilyl-\( \alpha \)-D-ribofuranose (5.22b isomer b)
and benzyl 2-O-benzyl-5-O-tert-butyldiphenylsilyl-\( \alpha \)-D-ribofuranose

The general route for the benzylaion of sugar derivatives (room temperature, benzyl
bromide, KOH, minimal DMF to dissolve sugar) (3.15b) was used for the tribenzylaion
of 5-O-(tert-butyldiphenylsilyl)-D-ribofuranose (450 mg, 1.16 mmol). The di-O-benzyl-
protected product and tri-O-benzyl product (5.22b, isomer b) were obtained, both in low
yield. It was further found that the di-protected product could be converted to the tri-
protected analogue by heating the reaction mixture under reflux.

Benzyl 2,3-di-O-benzyl-5-O-tert-butyldiphenylsilyl-\( \alpha \)-D-ribofuranose

Yield: 26% (From heating of di-protected product).

TLC: \( R_\text{f} \) 0.34 (20:1 hexanes-EtOAc)

\(^1\text{H NMR:} \) (300 MHz, CDCl₃) \( \delta \) 7.73-7.69 (m, 4H ortho aromatics of TBDPS), 7.42-
7.25 (m, 21H, OCH₂Ph × 3 aromatics and TBDPS aromatics), 5.12 (s, 1H, 
H1), 4.69 (d, 1H, \( J = 12.3 \), OCH₂H₃Ph), 4.64 (d, 1H, \( J = 12.3 \),
OCH₂H₃Ph), 4.57 (d, 1H, \( J = 12.3 \), OCH₂H₃Ph), 4.47 (d, 1H, \( J = 12.3 \),
OCH$_3$H$_2$Ph), 4.55 (d, 1H, $J = 11.7$, OCH$_3$H$_2$Ph), 4.45 (d, 1H, $J = 11.7$, OCH$_3$H$_2$Ph), 4.34-4.29 (m, 1H, H4), 4.19 (dd, 1H, $J = 6.6$ and 4.7 Hz, H3), 3.95 (d, 1H, $J = 4.7$ Hz, H2), 3.87 (dd, 1H, $J = 11.0$ and 3.9 Hz, H5a), 3.76 (dd, 1H, $J = 11.0$ and 4.5 Hz, H5b), 1.03 (s, 9H, C(CH$_3$)$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 137.8 (ipso), 137.7 (ipso), 137.4 (ipso), 135.4 (ortho Si × 2), 133.3 (ipso Si), 133.2 (ipso Si), 129.5 (para Si), 128.2 (meta Si), 128.2 (meta Si), Aromatics – 128.2, 128.5, 127.9, 127.8, 127.6, 127.5, 104.2 (C1), 82.1 (C4), 80.0 (C3), 78.0 (C2), 72.3 (OCH$_2$Ph), 72.2 (OCH$_2$Ph), 69.3 (anomeric OCH$_2$Ph), 64.2 (C5), 26.8 (C(CH$_3$)$_3$), 19.3 (C(CH$_3$)$_3$).

IR: $\nu_{max}$(CHCl$_3$/cm$^{-1}$) 2933, 1700, 1689, 1230, 1222, 1211, 824.

EIMS: 658 (M$^+$, 1%), 579 (M+1 - Ph, 15%), 531 (M$^+$ - OBn, 1%), 443 (M+1 - 2OBn, 35%), 353 (M$^+$ - Bn - 2OBn, 4%), 239 (TBDPS, 1%), 91 (Bn, 100%).

Benzyl 2-O-benzyl-5-O-tert-butyldiphenylsilyl-α-D-ribofuranose

TLC: $R_f$ 0.16 (10:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 7.80-7.67 (m, 4H ortho aromatics of TBDPS), 7.42-7.33 (m, 16H, OCH$_2$Ph × 2 aromatics and TBDPS aromatics), 5.16 (d, 1H, $J = 3.9$ Hz, H1), 4.89 (d, 1H, $J = 12.0$, OCH$_3$H$_2$Ph), 4.77 (d, 1H, $J = 12.0$, OCH$_3$H$_2$Ph), 4.67 (d, 1H, $J = 12.0$, OCH$_3$H$_2$Ph), 4.64 (d, 1H, $J = 12.0$, OCH$_3$H$_2$Ph), 4.32 (ddd, 1H, $J = 9.0$, 5.9 and 5.7 Hz, H3), 4.28 (m, 1H, H4), 4.07 (dd, 1H, $J = 5.9$ and 3.9 Hz, H2), 3.83 (dd, 1H, $J = 11.2$ and 3.0 Hz, H5a), 3.77 (dd, 1H, $J = 11.2$ and 3.3 Hz, H5b), 3.23 (d, 1H, $J = 9.0$ Hz, OH), 1.04 (s, 9H, C(CH$_3$)$_3$).
\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \(\delta\) 137.4 (\textit{ipso} CH\(_2\)Ph), 137.2 (\textit{ipso} CH\(_2\)Ph), 135.4 (\textit{ortho} Si), 135.3 (\textit{ortho} Si), 132.9 (\textit{ipso} Si), 132.8 (\textit{ipso} Si), 129.6 (\textit{para} Si), 129.5 (\textit{para} Si), 128.3 (\textit{meta} Si), 128.2 (\textit{meta} Si), Aromatics - 127.8, 127.7, 127.6, 127.5, 126.8, 126.7, 100.1 (C1), 86.8 (C4), 78.1 (C3), 72.0 (C2), 70.1 (OCH\(_2\)Ph), 68.9 (anomeric OCH\(_2\)Ph), 64.1 (C5), 26.7 (C(CH\(_3\))\(_3\)), 19.1 (C(CH\(_3\))\(_3\)).

IR: \(\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}\) 3025, 2930, 1711, 1688, 1223, 1211, 799.

EIMS: 421 (M+1, 1%), 403 (M+1 - H\(_2\)O, 64%), 313 (M+1 - OBn, 6%), 295 (M\(^+\) - OBn - H\(_2\)O, 45%), 206 (M\(^+\) - 2OBn, 3%), 181 (C\(_{14}\)H\(_{13}\), 6%), 91 (Bn, 100%).

Benzyl 2,3-di-O-benzyl-D-ribose (5.23b)

The general route for the removal of a TBDPS primary protection, using HF.Pyridine (4.38), was carried out to remove the primary protection of benzyl 2,3-di-O-benzyl-5-\textit{tert}-butyldiphenylsilyl-D-ribofuranose (200 mg, 0.304 mmol). After column chromatography the desired deprotected product was isolated (78 mg, 0.185 mmol, 61%).

TLC: \(R_f\) 0.29 (2:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \(\delta\) 7.32-7.24 (m, 15H, OCH\(_2\)Ph \(\times\) 3 aromatics), 5.08 (s, 1H, H1), 4.72 (d, 1H, \(J = 11.7\) Hz, OCH\(_3\)H\(_2\)Ph), 4.67-4.55 (m, 4H, OCH\(_3\)Ph \(\times\) 2), 4.41 (d, 1H, \(J = 11.7\) Hz, OCH\(_3\)H\(_2\)Ph), 4.26-4.19 (m, 1H, H4), 4.11 (dd, 1H, \(J = 8.6\) and 5.9 Hz, H3), 3.92 (d, 1H, \(J = 8.6\) Hz, H2),
3.68 (dd, 1H, \( J = 10.4 \) and 3.9 Hz, H5a), 3.55 (dd, 1H, \( J = 10.4 \) and 5.7 Hz, H5b), 2.56 (d, 1H, \( J = 9.3 \) Hz, OH).

\[ ^{13} \text{C NMR:} \] (75 MHz, CDCl\(_3\)) \( \delta \)C 138.0 (ipso), 137.1 (ipso), 137.0 (ipso), Aromatics – 128.5, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 103.8 (C1), 83.4 (C4), 82.0 (C2), 73.3 (C3), 72.8 (OCH\(_2\)Ph), 71.8 (OCH\(_2\)Ph), 71.5 (anomeric OCH\(_2\)Ph), 69.3 (C5)

IR: \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 3070, 3022, 2879, 1656, 1499, 1218, 1213, 915, 821.

EIMS: 421 (M+1, 13%), 403 (M+1 – H\(_2\)O, 5%), 313 (M+ - OBn, 40%), 295 (M+ - OBn – H\(_2\)O, 78%), 206 (M+ - 2OBn, 19%), 91 (Bn, 100%).

Benzyl 2,3-di-O-benzyl-D-ribofuranose (5.23b)

To a solution of benzyl 2,3-di-O-benzyl-5-O-triphenylmethyl-D-ribofuranose (210 mg, 0.317 mmol) in DCM (7 mL) was added a solution of BF\(_3\).(OEt)\(_2\) (0.14 mL) in MeOH (0.3 mL) at room temperature. The reaction mixture was allowed to stir overnight, thereafter poured over water, washed with NaHCO\(_3\) and dried over MgSO\(_4\). Column chromatography (7:1 hexanes-EtOAc) gave the desired deprotected product as a mixture of isomers (27mg, 0.063 mmol, 20%), in addition to 2,3-O-bis-phenylmethyl-1-hydroxy-5-O-methyl-D-ribose (5.23a).

Product characterised when deprotection of TBDPS analogue was carried out.
Methyl 2,3-dio-benzyl-5-O-methyl-D-ribofuranoside (5.23a)

TLC: $R_f$ 0.25 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 7.42-7.25 (m, 10H, aromatics), 4.90 (s, 1H, H1), 4.67-4.49 (m, 4H, OCH$_2$Ph $\times$ 2), 4.31-4.25 (m, 1H, H4), 4.13 (dd, 1H, $J = 9.0$ and 6.0 Hz, H3), 3.87 (d, 1H, $J = 6.0$ Hz, H2), 3.81 (unresolved dd, 1H, H5a), 3.58 (unresolved dd, 1H, H5b), 3.75 (s, 1H, OCH$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 137.5 ($ipso \times 2$), Aromatics – 128.3, 127.9, 127.8, 127.7, 106.7 (C1), 82.4 (C4), 80.1 (C2), 77.2 (C3), 72.6 (OCH$_2$Ph), 72.4 (OCH$_2$Ph), 62.7 (C5), 55.6 (OCH$_3$).

Benzyl 2,3-di-O-benzyl-5-C-cyano-5-deoxy-D-ribofuranoside (5.25b)

The general route for the protection with a triflate group, using triflic anhydride and pyridine in DCM, followed by displacement with a nitrile functionality, using KCN, 18-crown-6 in acetonitrile (5.3 via Route b), was carried out on benzyl 2,3-di-O-benzyl-D-ribofuranose (100 mg, 0.238 mmol). Column chromatography (5:1 hexanes-EtOAc) afforded the desired product (Major isomer 53 mg, 0.123 mmol, 52%, minor isomer 8 mg, 0.019 mmol, 8%, total yield 60%).
Major isomer:

TLC: $R_f$ 0.26 (5:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 7.41-7.33 (m, 15H, OCH$_2$Ph $\times$ 3 aromatics), 5.09 (d, 1H, $J = 3.9$ Hz, H1), 4.88-4.45 (A series of d, 6H, $J = 11.7$ Hz, OCH$_3$Ph $\times$ 3), 4.24 (ddd, 1H, $J = 5.1$, 4.8 and 4.8 Hz, H4), 3.88 (dd, 1H, $J = 6.6$ and 4.2 Hz, H2), 3.73 (dd, 1H, $J = 6.6$ and 5.1 Hz, H3), 2.53 (dd, 1H, $J = 16.8$ and 4.8 Hz, H5a), 2.30 (dd, 1H, $J = 16.8$ and 4.8 Hz, H5b).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 137.6 (ipso), 137.4 (ipso), 137.3 (ipso), Aromatics – 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 116.5 (C6), 100.0 (C1), 77.7 (C4), 76.8 (C3), 76.7 (C2), 72.9 (OCH$_2$Ph), 72.8 (OCH$_2$Ph), 69.6 (anomeric OCH$_2$Ph), 21.8 (C5).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3027, 1754, 1705, 1222, 1211, 1210, 788.

EIMS: 454 (M+1, 1%), 429 (M+2 - CN, 100%), 321 (M+1 - CN - OBn, 34%), 91 (Bn, 34%).

Minor isomer

TLC: $R_f$ 0.36 (5:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 7.43-7.30 (m, 15H, OCH$_2$Ph $\times$ 3 aromatics), 5.05 (s, 1H, H1), 4.78 (d, 1H, $J = 11.7$ Hz, OCH$_3$H$_3$Ph), 4.63-4.41 (A series of d, 5H, $J = 11.7$ Hz, OCH$_2$Ph $\times$ 2 and OCH$_3$H$_3$Ph), 4.32 (ddd, 1H, $J = 8.0$, 5.1 and 4.8 Hz, H4), 4.08 (dd, 1H, $J = 8.0$ and 4.4 Hz, H3), 3.94 (d, 1H, $J = 4.4$ Hz, H2), 2.72 (dd, 1H, $J = 17.0$ and 4.8 Hz, H5a), 2.54 (dd, 1H, $J = 17.0$ and 5.1 Hz, H5b).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 137.2 (ipso), 137.1 (ipso), 136.93 (ipso), Aromatics – 128.4, 128.3, 128.2, 128.0, 127.9, 116.6 (C6), 104.2 (C1), 80.8 (C4), 79.1 (C3), 76.1 (C2), 72.8 (OCH$_2$Ph), 72.4 (OCH$_2$Ph), 69.5 (anomeric OCH$_2$Ph), 22.8 (C5).
1-O-Methyl-2,3-di-O-benzyl-5-C-cyano-5-deoxy-D-ribofuranoside (5.25a)

The general route for the protection with a triflate group, using triflic anhydride and pyridine in DCM, followed by displacement with a nitrile functionality, using KCN, 18-crown-6 in acetonitrile (5.3 via Route b), was carried out on 2,3-di-O-benzyl-D-ribofuranoside (64 mg, 0.194 mmol). Column chromatography (5:1 hexanes-EtOAc) afforded the desired product (27 mg, 0.076 mmol, 39%).

**TLC:** \[ R_f 0.24 \text{(5:1 hexanes-EtOAc)} \]

**$^1$H NMR:**

(300 MHz, CDCl$_3$) $\delta_H$ 7.81-7.40 (m, 10H, aromatics), 4.87 (s, 1H, H1), 4.68-4.55 (m, 3H, OCH$_2$H$_2$Ph and OCH$_2$Ph), 4.44 (d, 1H, $J = 11.7$ Hz, OCH$_2$H$_2$Ph), 4.34-4.26 (m, 1H, H4), 4.02 (dd, 1H, $J = 7.2$ and 3.9 Hz, H3), 3.87 (d, 1H, $J = 3.9$ Hz, H2), 3.36 (s, 3H, OCH$_3$), 2.71 (dd, 1H, $J = 17.1$ and 4.5 Hz, H5a), 2.53 (dd, 1H, $J = 17.1$ and 4.9 Hz, H5b).

**$^{13}$C NMR:**

(75 MHz, CDCl$_3$) $\delta_C$ 137.2 ($ipso$), 137.0 ($ipso$), Aromatics – 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 116.5 (C6), 106.1 (C1), 80.6 (C4), 78.9 (C3), 75.9 (C2), 72.7 (OCH$_2$Ph), 72.3 (OCH$_2$Ph), 55.2 (OCH$_3$), 22.8 (C5).

**IR:** $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3073, 2933, 1737, 1542, 1521, 1500, 1416, 1064, 1029, 949.

**CIMS:** 353 (M$^+$, 55%), 321 (M$^+$ - OCH$_3$, 31%), 91 (Bn, 100%).
5-O-(tert-butyldiphenylsilyl)-3,4-bis-DHP-2-hydroxy-D-arabinofuranose (5.27)

The general route towards the protection using bis-DHP, in CHCl₃, in the presence of CSA (4.3) was used to protect 5-O-(tert-butyldiphenylsilyl)-D-arabinose (3.9) (500 mg, 1.289 mmol). Column chromatography (7:1 hexanes-EtOAc) afforded the bis-DHP-protected product (220 mg, 0.400 mmol, 32%).

TLC: Rᵣ 0.51 (5:1 hexanes-EtOAc)

¹H NMR: (300 MHz, CDCl₃) δH 7.68-7.66 (m, 4H, ortho aromatics), 7.37-7.34 (m, 6H, meta and para aromatics), 4.34 (d, 1H, J = 3.0 Hz, H1), 4.13-4.07 (m, 2H, H2 and H3), 3.96-3.67 (m, 7H, H4, H5a, H5b, OCH₂ of DHP × 2), 2.52 (br s, 1H, OH), 2.23 (dt, 2H, J = 16.5 and 4.5 Hz, CH₂ of DHP), 2.05-1.35 (m, 10H, CH₂ of DHP × 5), 1.06 (s, 9H, C(CH₃)₃).

¹³C NMR: (75 MHz, CDCl₃) δC 135.4 (ortho), 135.3 (ortho), 133.3 (ipso), 129.4 (para), 127.5 (meta), 127.4 (meta), 102.6 (1’A and 1’B), 94.0 (C4), 86.2 (C1), 78.8 (C2), 76.3 (C3), 66.4 (C5), 64.3 (5’A), 61.7 (5’B), 29.7 (2’A), 26.7 (C(CH₃)₃), 24.6 (2’B), 22.3 (4’A), 22.2 (4’B), 19.2 (3’A and 3’B), 18.0 (C(CH₃)₃).

IR: vmax(CHCl₃)/cm⁻¹ 3455, 2939, 2862, 1738, 1689, 1450, 1430, 1217, 1191, 1114, 823, 613.

EIMS: 555 (M+1, 1%), 537 (M+1 - H₂O, 100%).
5-O-(tert-butyldiphenylsilyl)-3,4-bis-DHP-2-O-acetyl-d-arabinose (5.28)

The general route towards acetylation using acetic anhydride and pyridine (5.7) was used to acetylate 5-O-(tert-butyldiphenylsilyl)-3,4-bis-DHP-2-hydroxy-d-arabinofuranose (100 mg, 0.181 mmol). After column chromatography (5:1 hexanes-EtOAc) the product was isolated in good yield (168 mg, 0.288 mmol, 84%).

TLC: R$_f$ 0.84 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 7.69-7.66 (m, 4H, ortho aromatics), 7.36-7.24 (m, 6H, meta and para aromatics), 5.23 (d, 1H, $J = 3.0$ Hz, H3), 4.20 (d, 1H, $J = 3.3$ Hz, H1), 4.14 (unresolved dd, 1H, H5a), 4.10 (d, 1H, $J = 3.0$ Hz, H2), 4.05-4.00 (m, 1H, H4), 3.95-3.64 (m, 4H, OCH$_2$ of DHP × 2), 3.78 (unresolved dd, 1H, H5b), 2.45 (dt, 2H, $J = 16.1$ and 4.8 Hz, CH$_2$ of DHP), 2.07 (s, 3H, OOCCH$_3$), 2.05-1.80 and 1.62-1.20 (m, 10H, CH$_2$ of DHP × 5), 1.04 (s, 9H, C(CH$_3$)$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 169.8 (OOCCH$_3$), 135.5 (ortho), 133.4 (ipso), 129.4 (para), 127.5 ($\eta$meta), 102.4 (1’A and 1’B), 94.3 (C4), 84.1 (C3), 79.7 (C1), 74.2 (C2), 66.6 (C5), 64.2 (5’A), 62.0 (5’B), 29.7 (2’A), 26.7 (C(\((\text{CH}_3)\))$_3$), 24.6 (2’B), 22.4 (4’A), 22.3 (4’B), 21.0 (OOCCH$_3$), 19.3 (3’A and 3’B), 18.0 (C(\((\text{CH}_3)\))$_3$).

IR: $\nu_{\max}$(CHCl$_3$)/cm$^{-1}$ 3017, 2941, 2884, 2862, 1742, 1471, 1449, 1431, 1369, 1244, 1229, 1151, 1111, 989, 937, 706, 647.

EIMS: 596 (M, 3%), 579 (M+ - H$_2$O, 100%), 537 (M$^+$ - OAc, 5%), 519 (M$^+$ - Ph, 65%), 429 (M+1 - DHP, 4%).
The general route for the removal of a TBDPS primary protection, using HF.Pyridine (4.38), was carried out to remove the primary protection on 3,4-\textit{bis}-DHP-5-\textit{O}-(\textit{tert}-butyldiphenylsilyl)-2-\textit{O}-acetyl-D-arabinose (150 mg, 0.252 mmol). Chromatography (2:1 hexanes-EtOAc) of the crude residue gave the deprotected product (49 mg, 0.131 mmol, 52%).

\textbf{TLC:} \textit{R} \textsubscript{f} 0.18 (2:1 hexanes-EtOAc)

\textbf{\textsuperscript{1}H NMR:} (300 MHz, CDCl\textsubscript{3}) \( \delta \text{H} 5.01 \) (d, 1H, \( J = 3.3 \) Hz, H3), 4.23 (d, 1H, \( J = 2.8 \) Hz, H1), 4.12 (dd, 1H, \( J = 10.8 \) and 4.5 Hz, H5a), 4.08 (d, 1H, \( J = 2.8 \) Hz, H2), 3.97-3.93 (m, 1H, H4), 3.91-3.75 and 3.72-3.64 (m, 5H, OCH\textsubscript{2} of DHP \( \times 2 \) and H5b), 2.06(s, 3H, OOCCH\textsubscript{3}), 2.12-1.80 and 1.69-1.44 (m, 12H, CH\textsubscript{2} of DHP \( \times 6 \)).

\textbf{\textsuperscript{13}C NMR:} (75 MHz, CDCl\textsubscript{3}) \( \delta \text{C} 170.1 \) (OOCCH\textsubscript{3}), 101.9 (1’A), 94.5 (1’B), 84.8 (C4), 79.5 (C3), 76.9 (C1), 74.0 (C2), 66.6 (C5), 62.9 (5’A), 62.0 (5’B), 29.9 (2’A), 24.5 (2’B), 22.5 (4’A), 22.2 (4’B), 20.9 (OOCCH\textsubscript{3}), 17.9 (3’A and 3’B).

\textbf{IR:} \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3455, 1738, 1694, 1689, 1450, 1432, 1220, 1218, 1217, 1192, 1114, 1014, 936, 777.

\textbf{EIMS:} 371 (M+1, 2%), 355 (M\textsuperscript{+} - CH\textsubscript{3}, 100%), 311 (M\textsuperscript{+} - OAc, 5%), 202 (M\textsuperscript{+} - DHP, 1%).
Methyl 5-\(O\)-(tert-butyldiphenylsilyl)-\(D\)-arabinoside \(^{16}(5.30)\)

\[
\text{\begin{tiny}
\begin{array}{c}
\text{OTBDPS}
\end{array}
\end{tiny}}
\]

NaCl (20.0 g) and an excess of \(\text{H}_2\text{SO}_4\) were allowed to react and the resultant HCl gas was bubbled through methanol (100 mL). After an increase in mass of 2 g the methanol was diluted with more methanol (100 mL). Arabinose (5.0 g, 33 mmol) was dissolved in the acidic methanol, taking approximately 2 hours for complete dissociation. After a further 4 hours pyridine (20 mL) was added and the solvents removed. After leaving the crude mixture under vacuum overnight the general procedure for TBDPS primary protection \(^{3.9}\) was carried out. Column chromatography (2:1 hexanes-EtOAc) yielded the desired product as a mixture of isomers (major isomer 638 mg, 1.587 mmol, 52%, minor isomer 200 mg, 0.498 mmol, 16%, total over two steps 68%).

**Major isomer(\(\alpha\)):**

**TLC:** \(R_f\) 0.57 (1:1 hexanes-EtOAc)

**\(^1\)H NMR:**

\[(300 \text{ MHz, CDCl}_3) \delta \text{H} 7.71-7.66 \text{ (m, 4H, ortho aromatics)}, 7.44-7.39 \text{ (m, 6H, meta and para aromatics)}, 4.98 \text{ (s, 1H, H1)}, 4.32-3.98 \text{ (m, 4H, H2, H3, H4 and OH)}, 3.86 \text{ (dd, 1H, } J = 11.3 \text{ and 2.3 Hz, H5a)}, 3.76 \text{ (dd, 1H, } J = 11.3 \text{ and 1.5 Hz, H5b)}, 3.41 \text{ (s, 3H, OCH}_3\text{)}, 3.17 \text{ (br s, 1H, OH)}, 1.07 \text{ (s, 9H, C(CH}_3\text{)_3}).

**\(^{13}\)C NMR:**

\[(75 \text{ MHz, CDCl}_3) \delta \text{C} 135.4 \text{ (ortho)}, 135.3 \text{ (ortho)}, 131.7 \text{ (ipso)}, 131.6 \text{ (ipso)}, 129.9 \text{ (para)}, 129.8 \text{ (para)}, 127.8 \text{ (meta)}, 127.7 \text{ (meta)}, 109.2 \text{ (C1)}, 86.8 \text{ (C4)}, 78.4 \text{ (C3)}, 77.7 \text{ (C2)}, 63.9 \text{ (C5)}, 54.7 \text{ (OCH}_3\text{)}, 26.6 \text{ (C(CH}_3\text{)_3}}, 18.9 \text{ (C(CH}_3\text{)_3}}\).

**IR:** \(\nu_{\text{max}}\text{(CHCl}_3)/\text{cm}^{-1} 3411, 2965, 1701, 1688, 1474, 1222, 1212, 1104, 1044, 994, 971, 940.\)
EIMS: 403 (M+1, 2%), 387 (M+ - CH3, 1%), 371 (M+ - OCH3, 3%), 293 (M+ - Ph - OCH3, 100%), 239 (TBDPS, 2%).

**Minor isomer (β):**

TLC: Rf 0.48 (1:1 hexanes-EtOAc)

**1H NMR:** (300 MHz, CDCl3) δH 7.69-7.67 (m, 4H, ortho aromatics), 7.42-7.37 (m, 6H, meta and para aromatics), 4.80 (d, 1H, J =4.2 Hz, H1), 4.26-3.97 (m, 2H, H2 and H3), 3.89 (unresolved td, 1H, J =4.9 Hz, H4), 3.77 (dd, 2H, J = 10.8 and 4.9 Hz, H5a and H5b), 3.35 (s, 3H, OCH3), 2.89 (v br s, 2H, OH), 1.07 (s, 9H, C(CH3)3).

**13C NMR:** (75 MHz, CDCl3) δC 135.4 (ortho), 135.3 (ortho), 133.1 (ipso × 2), 129.9 (para), 129.7 (para), 127.6 (meta × 2), 101.6 (C1), 81.8 (C4), 78.0 (C3), 76.8 (C2), 64.9 (C5), 55.3 (OCH3), 26.8 (C(CH3)3), 19.2 (C(CH3)3).

**Methyl 5-O-(tert-Butyldiphenylsilyl)-2,3-bis-DHP-d-arabinose (5.31)**

The general route towards the protection using bis-DHP, in CHCl3, in the presence of CSA (4.31) was used to protect Methyl 5-O-(tert-butyldiphenylsilyl)-d-arabinose (500 mg, 1.244 mmol). Column chromatography (hexanes-EtOAc) afforded the bis-DHP-protected product (250 mg, 0.440 mmol, 35%).

TLC: Rf 0.75 (4:1 hexanes-EtOAc)
\[^1^\text{H NMR:} \ (300 \text{ MHz, CDCl}_3) \ \delta_\text{H} \ 7.73-7.68 \ (m, 4H, \text{ortho aromatics}), 7.39-7.36 \ (m, 6H, \text{meta and para aromatics}), 4.98 \ (d, 1H, J = 6.6 \text{ Hz, H1}), 4.29 \ (dd, 1H, J = 10.5 \text{ and } 9.6 \text{ Hz, H3}), 4.14 \ (dt, 1H, J = 9.6 \text{ and } 3.0 \text{ Hz, H4}), 4.11 \ (dd, 1H, J = 10.5 \text{ and } 6.6 \text{ Hz, H2}), 3.87 \ (dd, 1H, J = 11.7 \text{ and } 3.0 \text{ Hz, H5a}), 3.80 \ (dd, 1H, J = 11.7 \text{ and } 3.0 \text{ Hz, H5b}), 3.79-3.53 \ (m, 4H, \text{OCH}_2 \text{ of DHP x } 2), 3.48 \ (s, 3H, \text{OCH}_3), 2.90-1.40 \ (m, 12H, \text{CH}_2 \text{ of DHP x 6}), 1.06 \ (s, 9H, \text{C(CH}_3)_3).\]

\[^{13}\text{C NMR:} \ (75 \text{ MHz, CDCl}_3) \ \delta_\text{C} \ 135.6 \ (\text{ortho}), 135.4 \ (\text{ortho}), 133.4 \ (\text{ipso}), 133.1 \ (\text{ipso}), 129.5 \ (\text{para}), 127.5 \ (\text{meta}), 127.4 \ (\text{meta}), 102.2 \ (\text{C1}), 98.1 \ (1'\text{A}), 97.9 \ (1'\text{B}), 76.5 \ (\text{C4}), 74.1 \ (\text{C2}), 67.1 \ (\text{C3}), 63.0 \ (\text{C5}), 60.7 \ (5'\text{A}), 60.6 \ (5'\text{B}), 56.3 \ (\text{OCH}_3), 28.7 \ (2'\text{A}), 26.7 \ (\text{C(CH}_3)_3), 24.7 \ (2'\text{B}), 24.6 \ (4'\text{A}), 22.4 \ (4'\text{B}), 20.2 \ (3'\text{A}), 19.3 \ (\text{C(CH}_3)_3), 17.9 \ (3'\text{B}).\]

\text{IR:} \quad \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \ 2945, 1702, 1686, 1498, 1475, 1396, 1219, 1115, 1069, 1048, 784.

\text{EIMS:} \quad 596 (M+1, 1\%), 537 (M^+ - \text{OCH}_3, 3\%), 511 (M^+ - \text{tert}-\text{Bu, 1\%}), 400 (M^+ - \text{DHP, 1\%}), 167 (100\%).

\text{Methyl 2,3-}\text{bis-DHP-}\text{d-arabinofuranose (5.32)}

\text{The general route for the removal of a TBDPS primary protection, using HF.Pyridine (4.38), was carried out to remove the primary protection of methyl 5-}\text{O-(tert-butyldiphenylsilyl)-2,3-bis-DHP-d-arabinose (200 mg, 0.352 mmol). Chromatography (2:1 hexanes-EtOAc) of the crude residue gave the deprotected product as a mixture of}
isomers (major isomer 28 mg, 0.085 mmol, 24%, minor isomer 18 mg, 0.043 mmol, 12%, total yield: 40%).

**Major isomer (α):**

TLC: \[ R_f 0.20 \text{ (2:1 hexanes-EtOAc)} \]

\[^{1}H\text{ NMR:}\] \((300 \text{ MHz, CDCl}_3\) \(\delta_H 4.77 \text{ (d, } 1H, J = 3.3 \text{ Hz, H1)}, 4.21 \text{ (dd, } 1H, J = 10.5 \text{ and } 3.3 \text{ Hz, H2}), 4.11 \text{ (dd, } 1H, J = 10.5 \text{ and } 3.3 \text{ Hz, H3)}, 3.96-3.18 \text{ (m, } 1H, H4), 3.81 \text{ (unresolved dd, } 1H, J = 12.5 \text{ Hz, H5a)}, 3.72 \text{ (dd, } 1H, J = 12.5 \text{ and } 1.7 \text{ Hz, H5b)}, 3.66-3.54 \text{ (m, } 4H, \text{ OCH}_2 \text{ of DHP} \times 2), 3.40 \text{ (s, } 3H, \text{ OCH}_3), 2.58 \text{ (s, } 1H, \text{ OH)}, 1.86-1.48 \text{ (m, } 12H, \text{ CH}_2 \text{ of DHP} \times 6).\]

\[^{13}C\text{ NMR: (75 MHz, CDCl}_3\) \(\delta_C 99.9 \) (C1), 98.6 (1’A), 97.4 (1’B), 68.1 (C4), 64.8 (C2), 64.3 (C3), 62.4 (C5), 60.5 (5’A and 5’B), 55.2 (OCH_3), 28.4 (2’A and 2’B), 24.8 (4’A), 24.6 (4’B), 18.1 (3’A and 3’B).

**Minor isomer (β):**

TLC: \[ R_f 0.32 \text{ (2:1 hexanes-EtOAc)} \]

\[^{1}H\text{ NMR:}\] \((300 \text{ MHz, CDCl}_3\) \(\delta_H 4.95 \text{ (d, } 1H, J = 4.5 \text{ Hz, H1)}, 4.10-4.06 \text{ (m, } 3H, H2, H3, OH), 3.86 \text{ (unresolved dt, } 1H, J = 12.0 \text{ Hz, H4)}, 3.75 \text{ (dd, } 1H, J = 10.8 \text{ and } 3.6 \text{ Hz, H5a)}, 3.68 \text{ (dd, } 1H, J = 10.8 \text{ and } 4.1 \text{ Hz, H5b)}, 3.67-3.56 \text{ (m, } 4H, \text{ OCH}_2 \text{ of DHP} \times 2), 3.46 \text{ (s, } 3H, \text{ OCH}_3), 1.83-1.74 \text{ and } 1.53-1.49 \text{ (m, } 12H, \text{ CH}_2 \text{ of DHP} \times 6).\]

\[^{13}C\text{ NMR: (75 MHz, CDCl}_3\) \(\delta_C 102.6 \) (C1), 98.3 (1’A), 98.0 (1’B), 76.5 (C4), 74.4 (C2), 66.1 (C3), 61.3 (C5), 60.7 (5’A), 60.6 (5’B), 56.4 (OCH_3), 28.8 (2’A), 28.7 (2’B), 24.6 (4’A and 4’B), 18.0 (3’A), 17.9 (3’B).
Methyl-5-C-cyano-5-deoxy-2,3-bis-DHP-D-arabinose (5.33)

The general route for the introduction of a triflate, using triflic anhydride and pyridine in DCM, followed by displacement with a nitrile functionality, using KCN, 18-crown-6 in acetonitrile (5.3 via Route b), was carried out on 5-O-hydroxy-2,3-bis-DHP-1-O-methyl-D-arabinose (50 mg, 0.152 mmol).

**Major isomer:**

Yield: 36%

TLC: \( R_f \) 0.52 (2:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \( \delta_H \) 4.74 (d, 1H, \( J = 3.3 \) Hz, H1), 4.26 (dd, 1H, \( J = 11.1 \) and 9.9 Hz, H3), 3.92-3.59 (m, 6H, H2, H4 and OCH\(_2\) of DHP \( \times 2 \)), 3.42 (s, 3H, OCH\(_3\)), 2.91 (dd, 1H, \( J = 11.1 \) and 6.6Hz, H5a), 2.88 (dd, 1H, \( J = 11.1 \) and 6.6 Hz, H5b), 1.89-1.47 (m, 12H, CH\(_2\) of DHP \( \times 6 \)).

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \( \delta_C \) 116.6 (C6), 98.49 (C1), 97.7 (1’A), 97.6 (1’B), 68.5 (C4), 64.2 (C2), 60.9 (5’A and 5’B), 58.5 (C3), 55.5 (OCH\(_3\)), 32.4 (C5), 28.4 (2’A), 28.1 (2’B), 24.7 (4’A and 4’B), 17.8 (3’A and 3’B).

IR: \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 2934, 2372, 1675, 1650, 1639, 1633, 901, 785, 773

EIMS: 339 (M\(^+\), 1%), 322 (M+1 - H\(_2\)O, 97%), 168 (DHP, 1%), 145 (M\(^+\) - DHP - CN, 1%), 115 (M\(^+\) - DHP - CN - OCH\(_3\), 4%), 100 (M\(^+\) - DHP 0 CH\(_2\)CN - OCH\(_3\), 20%).
Benzyl 2,5-di-\(O\)-benzyl-d-arabinose or Benzyl 3,5-di-\(O\)-benzyl-d-arabinose

The general route for the benzylation of sugar derivatives (0 °C, NaH, DMF, benzyl bromide) \((3.15a)\) was used for the tribenzylation of 5-\(O\)-tert-butylidiphenylsilyl-d-arabinose (1 g, 2.6 mmol). Unfortunately this resulted in the removal of the primary protection and benzylation at the primary position in addition two of the three desired sites.

Yield: 230 mg, 0.547 mmol, 21%
TLC: \(R_f\) 0.55 (5:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl\(_3\)) \(\delta \)H 7.62-7.20 (m, 15H aromatics), 5.03 (d, 1H, \(J = 4.2 \) Hz, H1), 4.86-4.53 (m, 6H, OCH\(_2\)Ph \(\times\) 2), 4.28-4.20 (m, 1H, H4), 4.10 (dd, 1H, \(J = 9.9\) and 3.6 Hz, H5a), 4.02 (dd, 1H, \(J = 9.9\) and 3.3 Hz, H5b), 3.85 (unresolved dd, 1H, H3), 3.76 (unresolved dd, 1H, H2).

\(^{13}\)C NMR: (75 MHz, CDCl\(_3\)) \(\delta \)C 138.6 (ipso), 138.5 (ipso), 138.2 (ipso), Aromatics – 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 98.8 (C1), 84.1 (C4), 80.3 (C3), 76.3 (C2), 73.2 (OCH\(_2\)Ph), 72.6 (OCH\(_2\)Ph), 72.1 (OCH\(_2\)Ph), 68.6 (C5).

IR: \(\nu_{\text{max}}\)(CHCl\(_3\))/cm\(^{-1}\) 3060, 2870, 1721, 1716, 1209, 1090, 1087, 754.

EIMS: 421 (M+1, 1%), 403 (M+1 - H\(_2\)O, 64%), 313 (M+1 - OBn, 6%), 295 (M\(^+\) - OBn - H\(_2\)O, 45%), 206 (M\(^+\) - 2OBn, 3%), 181 (C\(_{14}\)H\(_{13}\), 65%), 91 (Bn, 100%).
Benzyl 2,3,5-tri-O-benzyl-α-D-arabinofuranoside

The general route for the benzylation of sugar derivatives (0 °C, NaH, DMF, benzyl bromide) (3.15a) was used for the tribenzylation of 5-O-tert-butyldiphenylsilyl-D-arabinofuranose (1 g, 2.6 mmol) and this tetra-protected derivative was obtained.

TLC: \[ R_f 0.48 \text{ (5:1 hexanes-EtOAc)} \]

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 7.35-7.17 (m, 20H aromatics), 4.91-4.47 (m, 8H, OCH$_2$Ph $\times$ 4), 4.39 (d, 1H, $J = 6.8$ Hz, H1), 4.01 (dd, 1H, $J = 12.6$ and 3.3 Hz, H5a), 3.83 (dd, 1H, $J = 9.0$ and 6.8 Hz, H2), 3.65-3.62 (m, 1H, H4), 3.98 (dd, 1H, $J = 9.0$ and 3.3 Hz, H3), 3.21 (dd, 1H, $J = 12.6$ and 1.5 Hz, H5b).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 138.4 (ipso), 138.2 (ipso), 138.0 (ipso), 137.5 (ipso), Aromatics – 128.1, 127.9, 127.8, 127.6, 127.6, 127.4, 127.3, 102.2 (C1), 79.4 (C4), 78.8 (C3), 74.8 (C2), 72.2 (OCH$_2$Ph), 72.1 (OCH$_2$Ph), 71.1 (OCH$_2$Ph), 70.4 (C5), 62.5 anomeric OCH$_2$Ph).

IR: $\nu_{max}$(CHCl$_3$)/cm$^{-1}$ 2873, 1721, 1702, 1219, 1210, 1094, 768.

EIMS: 511 (M+1, 20%), 403 (M$^+$ - OBn, 100%), 295 (M+1 - 2OBn, 26%), 189 (M$^+$ - 3OBn, 2%), 181 (C$_{14}$H$_{13}$, 44%), 91 (Bn, 63%).
The general procedure for trityl primary protection (4.8) was carried out on D-ribose (1 g, 6.661 mmol). Column chromatography yielded the desired silyl ether (2.30 g, 5.86 mmol, 88%).

**TLC:** \( R_f 0.13 \) (1:1 hexanes-EtOAc)

**\(^1\)H NMR:** (300 MHz, CDCl\(_3\)) \( \delta_H \) 7.45 - 7.39 (m, 6H\(^\alpha\) and 6H\(^\beta\), \textit{ortho}), 7.29 - 7.17 (m, 9H\(^\alpha\) and 9H\(^\beta\), \textit{meta} and \textit{para}), 5.34 (s, 1H\(^\alpha\)), 5.23 (s, 1H\(^\beta\)), 4.22 – 3.88 (m, 3H\(^\alpha\), 3H\(^\beta\), 3OH\(^\alpha\) and 3OH\(^\beta\)), 3.51 (dd, 1H\(^\alpha\), \( J = 10.2 \) and 2.6 Hz, H5\(^a\)), 3.36 (dd, 1H\(^\beta\), \( J = 10.2 \) and 3.9 Hz, H5\(^b\)), 3.26 (dd, 1H\(^\beta\), \( J = 10.2 \) and 4.8 Hz, H5\(^b\)), 3.19 (dd, 1H\(^\alpha\), \( J = 10.2 \) and 2.6 Hz, H5\(^a\)).

**\(^{13}\)C NMR:** (75 MHz, CDCl\(_3\)) \( \delta_C \) 143.3 (ipso\(^\beta\)), 142.8 (ipso\(^\alpha\)), 128.6 (ortho\(^\alpha\) and \(^\beta\)), 127.8 (meta\(^\alpha\)), 127.7 (meta\(^\beta\)), 127.2 (para\(^\alpha\)), 127.0 (para\(^\beta\)), 102.8 (C1\(^\alpha\)), 95.9 (C1\(^\beta\)), 87.8 (C4\(^\alpha\)), 87.2 (C4\(^\beta\)), 84.9 (C(Ph)\(^\alpha\)), 80.9 (C(Ph)\(^\beta\)), 79.9 (C2\(^\alpha\)), 77.8 (C3\(^\alpha\)), 77.2 (C2\(^\beta\)), 76.3 (C3\(^\beta\)), 64.7 (C5), 63.7 (C5\(^\alpha\)).
Benzyl 2,3-di-O-benzyl-5-O-(triphenylmethyl)-D-arabinofuranoside \(^{(5.35)}\)

The general route for the benzylation of sugar derivatives (room temperature, benzyl bromide, KOH, minimal DMF to dissolve sugar) \((3.15b)\) was used for the tribenzylation of 5-O-triphenylmethyl-D-Arabinose (1.3 g, 3.3 mmol). Chromatography (hexanes-EtOAc) of the crude residue gave the desired product as a mixture of isomers (major isomer 704 mg, 1.063 mmol, 32%, minor isomer 167 mg, 0.252 mmol, 8%, total yield 40%).

**Major isomer (α):**

**TLC:** \(R_f 0.47\) (10:1 hexanes-EtOAc)

**\(^1\)H NMR:**

\[
\begin{align*}
\text{(300 MHz, CDCl}_3\text{)} & \delta_H 7.67-7.36 \text{ (m, 30H, aromatics), 5.37 (s, 1H, H1),} \\
& 5.01 \text{ (d, 1H, } J = 12.0 \text{ Hz, OCH}_2\text{H}_2\text{Ph), 4.79-4.56 \text{ (m, 5H, OCH}_2\text{H}_2\text{Ph and OCH}_2\text{Ph} \times 2),} \\
& 4.51 \text{ (ddd, 1H, } J = 6.2, 5.1 \text{ and 4.3 Hz, H4),} \\
& 4.30 \text{ (d, 1H, } J = 2.6 \text{ Hz, H2),} \\
& 4.23 \text{ (dd, 1H, } J = 6.2 \text{ and } J = 2.6 \text{ Hz, H3),} \\
& 3.54 \text{ (dd, 1H, } J = 10.2 \text{ and 4.3 Hz, H5a),} \\
& 3.49 \text{ (dd, 1H, } J = 10.2 \text{ and 5.1 Hz, H5b).}
\end{align*}
\]

**\(^{13}\)C NMR:**

\[
\begin{align*}
\text{(75 MHz, CDCl}_3\text{)} & \delta_C 143.7 \text{ (ipso C(Ph)\text{)_3), 137.7 (ipso), 137.6 (ipso), 137.3} \\
& (ipso), \text{ Aromatics – 128.6, 128.2, 128.1, 127.8, 127.7, 127.6, 127.0, 126.8,} \\
& 104.9 (C1), 88.1 (C4), 86.4 (C3), 83.6 (C2), 81.0 \text{ (C(Ph)\text{)_3), 71.8 (OCH}_2\text{Ph}} \\
& \times 2), 68.7 \text{ (anomeric OCH}_2\text{Ph), 63.6 (C5).}
\end{align*}
\]

*Product NMR analysis agreed with published results.* \(^5\)

**IR:**

\[
\begin{align*}
& \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} 2934, 2370, 1675, 1655, 1639, 902, 785, 773, 762, 633.
\end{align*}
\]

**EIMS:**

\[
\begin{align*}
& 662 \text{ (M}^+, 1\%), \\& 555 \text{ (M}^+ - \text{OBn, 1\%), 448 (M}^+ - 2\text{OBn, 1\%), 243 (Trityl,} \\
& 100\%), 91 \text{ (Bn, 14\%).}
\end{align*}
\]
Minor isomer (β)

TLC: $R_f$ 0.39 (10:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$ 7.61-7.55 and 7.39-7.26 (m, 30H, aromatics), 5.03 (d, 1H, $J = 4.5$ Hz, H1), 4.80-4.47 (m, 6H, OCH$_2$Ph $\times$ 3), 4.32 (dd, 1H, $J = 7.0$ and 6.2 Hz, H3), 4.20 (dd, 1H, $J = 6.2$ and 5.4 Hz, H4), 4.16 (dd, 1H, $J = 7.0$ and 4.5 Hz, H2), 3.40 (d, 2H, $J = 5.4$ Hz, H5a and H5b).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 143.7 (ipso C(Ph)$_3$), 138.0 (ipso), 137.4 (ipso), 137.2 (ipso), Aromatics – 128.6, 128.2, 128.1, 128.0, 127.8, 127.6, 127.5, 127.4, 126.8, 98.6 (C1), 86.5 (C4), 84.0 (C3), 82.76 (C2), 80.4 (C(Ph)$_3$), 72.3 (OCH$_2$Ph), 72.2 (OCH$_2$Ph), 68.6 (anomic OCH$_2$Ph), 65.8 (C5).

Product NMR analysis agreed with published results.\(^4\)

EIMS: 661 (M-1, 1%), 585 (M$^+$ - Ph, 1%), 555 (M$^+$ - OBn, 1%), 447 (M-1 - 2OBn, 1%), 243 (Trityl, 100%).

Benzyl 2,3-di-O-benzyl-\textit{d}-arabinofuranoside (5.36)

To a solution of Benzyl 2,3-di-O-benzyl-5-O-(triphenylmethyl)-\textit{d}-arabinofuranoside (200 mg, 0.302 mmol) in DCM (7 mL) was added a solution of BF$_3$.(OEt)$_2$ (0.14 mL) in MeOH (0.3 mL) at room temperature. The reaction mixture was allowed to stir overnight, thereafter poured over water, washed with NaHCO$_3$ and dried over MgSO$_4$. Column chromatography (7:1 hexanes-EtOAc) afforded the title compound in good yield (108 mg, 0.257 mmol, 85%).
The general route for the protection with a triflate group, using triflic anhydride and pyridine in DCM, followed by displacement with a nitrile functionality, using KCN, 18-crown-6 in acetonitrile (5.3 via Route b), was carried out on benzyl 2,3-di-O-benzyl-D-arabinofuranose (220 mg, 0.524 mmol). Column chromatography (5:1 hexanes-EtOAc) afforded the desired product (146 mg, 0.340 mmol, 65%, on conversion 70%).
**1H NMR:** (300 MHz, CDCl$_3$) $\delta$H 7.40-7.33 (m, 15H, aromatics), 5.17 (s, 1H, H1), 4.82 (d, 1H, $J$ = 12.0 Hz, OCH$_2$H$_3$Ph), 4.67-4.46 (m, 5H, OCH$_2$H$_3$Ph and OCH$_2$Ph $\times$ 2), 4.28 (ddd, 1H, $J$ = 5.7, 5.7 and 4.9 Hz, H4), 4.14 (d, 1H, $J$ = 3.0 Hz, H2), 3.88 (dd, 1H, $J$ = 5.7 and 3.0 Hz, H3), 2.71 (dd, 1H, $J$ = 17.0 and 4.9 Hz, H5a), 2.62 (dd, 1H, $J$ = 17.0 and 5.7 Hz H5b).

**13C NMR:** (75 MHz, CDCl$_3$) $\delta$C 137.1 ($ipso \times 2$), 136.9 ($ipso$), Aromatics – 128.3, 128.2, 127.9, 127.8, 127.7, 116.4 (C6), 105.1 (C1), 87.8 (C4), 85.9 (C3), 76.2 (C2), 72.3 (OCH$_2$Ph), 72.1 (OCH$_2$Ph), 69.1 (anomeric OCH$_2$Ph), 21.6 (C5).

**IR:** $\nu$$_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3027, 1755, 1710, 1705, 1222, 1211, 1209, 768.

**CIMS:** 429 (M$^+$, 100%), 322 (M$^+$ - OBn, 7%), 215 (M+1 - 2 OBn, 14%), 181 (C$_{14}$H$_{13}$, 9%), 91 (Bn, 82%).

5-O-(t-Butyldimethylsilyl)-2,3-O-isopropylidene-D-ribofuranose (5.40) – see 4.9

5-O-(t-butyldimethylsilyl)-2,3-O-isopropylidene-D-ribofuranosyl pivaloate (5.41)

A solution of 5-O-(t-butyldimethylsilyl)-2,3-O-isopropylidene-D-ribofuranose (2.0g, 6.6 mmol) in dry pyridine (5 mL) was cooled to -10 °C. To this solution was slowly added pivaloylchloride (1.0 mL, 7.9 mmol). The reaction was allowed to warm to room temperature and left to stir for approximately 52 hours (monitor by TLC). Once the reaction was complete (TLC) the solvent was reduced to a minimum in vacuo. DCM was added and the organic layer was washed with water. Drying over MgSO$_4$ and
evaporation of solvent *in vacuo* at or below 40 °C gave the crude product. This residue was purified by flash chromatography to afford the title compound (2.3 mg, 5.9 mmol, 89%).

TLC: \( R_f \ 0.44 \) (10:1 hexanes-EtOAc)

\(^1\text{H NMR:}\ (300 \text{ MHz, CDCl}_3) \ \delta_H 6.07 \) (d, 1H, \( J = 4.5 \text{ Hz, H1} \)), 4.78 (dd, 1H, \( J = 6.6 \) and 4.5 Hz, H2), 4.71 (dd, 1H, \( J = 6.6 \) and 1.8 Hz, H3), 4.29-4.21 (m, 1H, H4), 3.74 (dd, 1H, \( J = 11.1 \) and 2.7 Hz, H5a), 3.66 (dd, 1H, \( J = 11.1 \) and 2.7 Hz, H5b), 1.52 (s, 3H, CH\(_3\)isopropylidene), 1.33 (s, 3H, CH\(_3\)isopropylidene), 1.23 (s, 9H, OCC(CH\(_3\))\(_3\)), 0.87 (s, 9H, C(CH\(_3\))\(_3\)), 0.04 (s, 6H, SiCH\(_3\))

\(^{13}\text{C NMR:}\ (75 \text{ MHz, CDCl}_3) \ \delta_C 177.1 \) (OC\(\text{C(CH}_3\)_3\)), 113.9 (acetal-C), 97.9 (C1), 83.1 (C4), 80.8 (C3), 80.2 (C2), 64.2 (C5), 38.7 (OCC(CH\(_3\))\(_3\)), 27.2 (OCC(CH\(_3\))\(_3\)), 26.3 (CH\(_3\)-isopropylidene), 25.8 (C(CH\(_3\))\(_3\)), 25.2 (CH\(_3\)-isopropylidene), 18.2 (C(CH\(_3\))\(_3\)), -5.3 (SiCH\(_3\) × 2).

IR: \( \nu_{\text{max}}(\text{CHCl}_3) / \text{cm}^{-1} 2961, 2936, 1735, 1385, 1376, 1226, 1135, 1023, 975, 868. 

EIMS: 388 (M\(^+\), 1%), 303 (M\(^+\) - Piv, 1%), 287 (M\(^+\) - OPiv, 16%), 167 (100%).
2,3-O-isopropylidene-D-ribofuranosyl pivaloate (5.42)

To a solution of 5-O-(t-butyldimethylsilyl)-2,3-O-isopropylidene-D-ribofuranosyl pivaloate (500 mg, 1.29 mmol) in THF (2 mL) was added TBAF (447 mg, 1.42 mmol). The reaction mixture was allowed to stir at room temperature for approximately 4 hours. Once the reaction was complete (TLC) the solvent was reduced to a minimum in vacuo. DCM was added and the organic layer was washed with water. Drying over MgSO$_4$ and evaporation of solvent in vacuo gave the crude product. This residue was purified by flash chromatography to afford the title compound (178 mg, 0.65 mmol, 50%), along with two interesting byproducts: the diprotected pivaloyl product (6%) and the rearranged product, where the pivaloyl had moved from the anomeric position to the primary position (24%).

**Major isomer (α):**

TLC: $R_f$ 0.33 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 6.07 (d, 1H, $J = 4.2$ Hz, H1), 4.75 (dd, 1H, $J = 6.9$ and 4.2 Hz, H2), 4.69 (dd, 1H, $J = 6.9$ and 2.9 Hz, H3), 4.27-4.15 (m, 1H, H4), 3.75 (unresolved dd, 1H, H5a), 3.64 (unresolved dd, 1H, H5b), 2.84 (br s, 1H, OH), 1.49 (s, 3H, CH$_3$-isopropylidene), 1.29 (s, 3H, CH$_3$-isopropylidene), 1.18 (s, 9H, OCC(CH$_3$)$_3$).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 177.4 (OCC(CH$_3$)$_3$), 115.3 (acetal-C), 96.3 (C1), 83.3 (C4), 80.1 (C3), 80.0 (C2), 62.3 (C5), 38.8 (OCC(CH$_3$)$_3$), 26.9 (OCC(CH$_3$)$_3$), 26.1 (CH$_3$-isopropylidene), 25.0 (CH$_3$-isopropylidene).

IR: $\nu_{max}$(CHCl$_3$/cm$^{-1}$) 3602, 3024, 2983, 1738, 1728, 1700, 1378, 1228, 1226, 1205, 943.
CIMS: 275 (M+1, 65%), 257 (M+1 - H₂O, 100%), 217 (M⁺ - C₄H₉, 8%), 173 (M+2 - H₂O - Piv, 78%).

**Minor isomer (β):**

TLC: Rₐ 0.27 (4:1 hexanes-EtOAc)

¹H NMR: (300 MHz, CDCl₃) δ_H 6.22 (s, 1H, H1), 4.75 (d, 1H, J = 6.0 Hz, H2), 4.67 (d, 1H, J = 6.0 Hz, H3), 4.14 (dd, 1H, J = 5.4 and 5.1 Hz H4), 3.76-3.52 (unresolved dd × 2, 2H, H5a and H5b), 2.09 (br s, 1H, OH), 1.49 (s, 3H, CH₃-isopropylidene), 1.32 (s, 3H, CH₃-isopropylidene), 1.18 (s, 9H, OCC(CH₃)₃).

¹³C NMR: (75 MHz, CDCl₃) δ_C 176.4 (OCC(CH₃)₃), 112.8 (acetal-C), 102.7 (C1), 88.6 (C4), 85.6 (C3), 81.1 (C2), 63.5 (C5), 38.7 (OCC(CH₃)₃), 26.9 (OCC(CH₃)₃), 26.4 (CH₃-isopropylidene), 24.8 (CH₃-isopropylidene).

IR: ν_max(CHCl₃)/cm⁻¹ 3603, 3023, 1730, 1720, 1386, 1233, 1200, 1004.

CIMS: 274 (M⁺, 100%), 257 (M+1 - H₂O, 25%), 217 (M⁺ - C₄H₉, 4%), 172 (M+1 - H₂O - Piv, 98%).

**2,3- O-isopropylidene-1,5-di-O-pivaloyl-d-ribofuranose (5.43)**

TLC: Rₐ 0.52 (4:1 hexanes-EtOAc)

¹H NMR: (300 MHz, CDCl₃) δ_H 6.13 (d, 1H, J = 4.5 Hz, H1), 4.85 (dd, 1H, J = 6.9 and 4.7 Hz, H2), 4.66 (dd, 1H, J = 6.9 and 2.7 Hz, H3), 4.44-4.41 (m, 1H, H4), 4.26 (dd, 1H, J = 12.0 and 3.6 Hz, H5a), 4.18 (dd, 1H, J = 12.0 and
3.6 Hz, H5b), 1.56 (s, 3H, CH₃-isopropylidene), 1.36 (s, 3H, CH₃-isopropylidene), 1.26 (s, 9H, OCC(CH₃)₃), 1.22 (s, 9H, OCC(CH₃)₃).

**1³C NMR:**
(75 MHz, CDCl₃) δC 177.8 (OCC(CH₃)₃), 177.1 (OCC(CH₃)₃), 115.4 (acetal-C), 96.9 (C1), 80.6 (C4), 80.5 (C3), 80.1 (C2), 64.1 (C5), 38.8 (OCC(CH₃)₃), 38.7 (OCC(CH₃)₃), 27.2 (OCC(CH₃)₃), 27.1 (OCC(CH₃)₃), 26.3 (CH₃-isopropylidene), 25.2 (CH₃-isopropylidene).

**IR:** νmax(CHCl₃)/cm⁻¹ 1746, 1717, 1386, 1376, 1105, 1030, 864.

**CIMS:** 358 (M⁺, 1%), 301 (M+1 - C₄H₉, 1%), 273 (M⁺ - Piv, 1%), 257 (M+1 - OPiv, 100%).

2,3-O-isopropylidene-5-O-pivaloyl-D-ribofuranose (5.44)

**TLC:** Rₐ 0.33 (2:1 hexanes-EtOAc)

**¹H NMR:**
(300 MHz, CDCl₃) δH 5.41 (s, 1H, H1), 4.66 (d, 1H, J = 5.6 Hz, H2), 4.60 (d, 1H, J = 5.6 Hz, H3), 4.36-4.25 (m, 1H, H4), 4.14-4.05 (m, 2H, H5a and H5b), 3.70 (br s, 1H, OH), 1.44 (s, 3H, CH₃-isopropylidene), 1.29 (s, 3H, CH₃-isopropylidene), 1.18 (s, 9H, OCC(CH₃)₃).

**¹³C NMR:**
(75 MHz, CDCl₃) δC 178.4 (OCC(CH₃)₃), 112.4 (acetal-C), 102.9 (C1), 85.7 (C4), 84.6 (C3), 81.8 (C2), 65.2 (C5), 38.8 (OCC(CH₃)₃), 27.1 (OCC(CH₃)₃), 26.4 (CH₃-isopropylidene), 24.9 (CH₃-isopropylidene).

**IR:** νmax(CHCl₃)/cm⁻¹ 3678, 3023, 1738, 1728, 1720, 1483, 1228, 1115, 1080.

**CIMS:** 274 (M⁺, 1%), 257 (M+1 - H₂O, 100%), 217 (M⁺ - C₄H₉, 8%).
The general route for the protection with a triflate group, using triflic anhydride and pyridine in DCM, followed by displacement with a nitrile functionality, using KCN, 18-crown-6 in acetonitrile (5.3 via Route b), was carried out on 2,3-O-isopropylidene-D-ribofuranosyl pivaloate (300 mg, 1.095 mmol). Column chromatography (5:1 hexanes-EtOAc) afforded the product (227 mg, 0.802 mmol, 73%).

**TLC:** Rf 0.0.17 (5:1 hexanes-EtOAc)

**1H NMR:** (300 MHz, CDCl₃) δ_H 6.11 (d, 1H, J = 4.5 Hz, H1), 4.86 (dd, 1H, J = 7.5 and 4.5 Hz, H2), 4.57 (dd, 1H, J = 7.5 and 4.5 Hz, H3), 4.26 (ddd, 1H, J = 5.1, 4.8 and 4.5 Hz, H4), 2.73 (dd, 1H, J = 17.0 and 5.1 Hz, H5a), 2.66 (dd, 1H, J = 17.0 and 4.8 Hz, H5b), 1.48 (s, 3H, CH₃-isopropylidene), 1.29 (s, 3H, CH₃-isopropylidene), 1.16 (s, 9H, OCC(CH₃)₃).

**13C NMR:** (75 MHz, CDCl₃) δ_C 176.6 (OCC(CH₃)₃), 116.5 (C6), 115.9 (acetal-C), 95.5 (C1), 82.0 (C4), 80.0 (C3), 78.0 (C2), 38.6 (OCC(CH₃)₃), 26.8 (OCC(CH₃)₃), 26.0 (CH₃-isopropylidene), 24.9 (CH₃-isopropylidene), 21.6 (C5).

**IR:** ν_max(CHCl₃)/cm⁻¹ 3028, 1737, 1387, 1378, 1207, 1161, 1126, 762.

**CIMS:** 283 (M⁺, 3%), 257 (M⁺ - CN, 6%), 242 (M+1 - isopropylidene, 28%), 182 (100%).
The general procedure to deprotonate using LDA (5.3b) was used to deprotonate methyl 5-C-cyano-5-deoxy-2,3-O-isopropylidene d-ribofuranoside (78 mg, 0.366 mmol). The reaction mixture was allowed to stir at –78 °C for approximately 15 minutes. At this point BF$_3$·(OEt)$_2$ (0.9 equivalents) was added. The reaction mixture was left to stir for a further 2 hours. The reaction was quenched at -78 °C with 1:1 mixture of NaCl (sat.):NaHCO$_3$ (sat.), extracted with DCM and dried over MgSO$_4$. The solvent removed in vacuo and the product purified by column chromatography (14 mg, 0.077 mmol, 21%, on conversion 27%).

TLC: R$_f$ 0.19 (2:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta$H 9.53 (d, 1H, $J = 2.7$ Hz, H6), 6.65 (dd, 1H, $J = 16.2$ and 4.2 Hz, H3), 5.73 (dd, 1H, $J = 16.2$ and 2.1 Hz, H2), 4.94 (ddd, 1H, $J = 7.8$, 4.2 and 2.1 Hz, H4), 4.52 (dd, 1H, $J = 7.8$ and 2.7 Hz, H5), 1.61 (s, 3H, CH$_3$-isopropylidene), 1.44 (s, 3H, CH$_3$-isopropylidene).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta$C 200.3 (C6), 146.6 (C3), 116.2 (C1), 112.1 (acetal-C), 101.8 (C2), 81.6 (C5), 76.2 (C4), 27.1 (CH$_3$-isopropylidene), 25.2 (CH$_3$-isopropylidene).

IR: $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3352, 2997, 2936, 1755, 1728, 1703, 1460, 1418, 1387, 1225, 1203, 1164, 1150, 1076.

CIMS: 182 (M+1, 100%), 155 (M$^+$ - CN, 6%).

(2E,4R,5R)-4,5-O-isopropylidene-6-oxo-hex-2-enenitrile (5.4)
(2E,4R,5R)-4,5-\textit{O}-isopropylidene-6-oxo-hex-2-enenitrile (5.4)

The general procedure to form an aldehyde using LDA and BF$_3$.(OEt)$_2$ was carried out with 5-\textit{C}-cyano-5-deoxy-2,3-\textit{O}-isopropylidene-\textit{D}-ribofuranosyl pivaloate. After workup and column chromatography (3:1 hexanes-EtOAc) the desired aldehyde analogue was obtained as a minor product (5%). The major product obtained from the reaction contains the $\alpha,\beta$-unsaturated nitrile but the aldehyde has been reduced to an alcohol (40%).

\textit{The aldehyde product has been characterised above.}

\textbf{Major product:}

(2E,4R,5S)-6-Hydroxy-4,5-\textit{O}-isopropylidene-hex-2-enenitrile

\begin{align*}
\text{TLC:} & \quad R_f 0.17 \text{ (2:1 hexanes-EtOAc)} \\
\text{\textsuperscript{1}H NMR:} & \quad (300 \text{ MHz, CDCl}_3) \delta_H 6.74 \text{ (dd, 1H, } J = 16.4 \text{ and } 4.7 \text{ Hz, H3), 5.71 \text{ (dd, 1H, } J = 16.4 \text{ and } 1.8 \text{ Hz, H2), 4.76 \text{ (ddd, 1H, } J = 7.1 \text{, 4.7 and } 1.8 \text{ Hz, H4), 4.36 \text{ (dt, 1H, } J = 7.1 \text{ and } 5.7 \text{ Hz, H5), 3.59 \text{ (dd, 2H, } J = 5.7 \text{ and } 5.4 \text{ Hz, H6a and b), 1.50 \text{ (s, 3H, CH}_3\text{-isopropylidene), 1.38 \text{ (s, 3H, CH}_3\text{-isopropylidene).}}}
\end{align*}
\textbf{13C NMR:} (75 MHz, CDCl$_3$) $\delta$C 149.3 (C3), 116.7 (C1), 109.8 (acetal-C), 101.2 (C2), 77.8 (C5), 75.8 (C4), 61.3 (C6), 27.4 ($\text{CH}_3$-isopropylidene), 27.1 ($\text{CH}_3$-isopropylidene).

\textbf{IR:} $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3022, 3015, 2992, 1766, 1659, 1655, 1459, 1387, 1075, 869.

\textbf{CIMS:} 184 (M+1, 100%), 157 (M$^+$ - CN, 1%), 126 (M$^+$ - CN – CH$_2$OH, 4%).

(2\textit{E},4\textit{R},5\textit{R})-4,5-di(benzyloxy)-6-oxohex-2-enenitrile (5.26)

\begin{center}
\begin{tikzpicture}
\node at (0,0) {\includegraphics[width=1cm]{chemical_structure.png}};
\end{tikzpicture}
\end{center}

The general procedure to form an aldehyde using LDA and BF$_3$.(OEt)$_2$ (5.4) was carried out with benzyl 2,3-di-O-benzyl-5-C-cyano-5-deoxy-D-ribofuranose. After workup and column chromatography (hexanes-EtOAc) the desired aldehyde analogue was obtained (Major isomer 66%, minor isomer 27%, total yield 92%).

\textbf{Major isomer (\(\alpha\)):

\textbf{TLC:} \(R_f\) 0.33 (3:1 hexanes-EtOAc)

\textbf{\(^1\text{H NMR:} \) (300 MHz, CDCl$_3$) $\delta$H 9.57 (d, 1H, $J = 1.8$ Hz, H6), 7.35- 7.19 (m, 10H, aromatics), 6.65 (dd, 1H, $J = 16.2$ and 5.4 Hz, H3), 5.65 (dd, 1H, $J = 16.2$ and 1.8 Hz, H2), 4.68-4.47 (m, 4H, OCH$_2$Ph $\times$ 2), 4.32 (ddd, 1H, $J = 5.4$, 5.1 and 1.7 Hz, H4), 3.87 (dd, 1H, $J = 5.1$ and 1.8 Hz, H5).

\textbf{\(^{13}\text{C NMR:} \) (75 MHz, CDCl$_3$) $\delta$C 200.1 (C6), 149.9 (C3), 136.3 ($\text{\textit{ipso}}$), 136.2 ($\text{\textit{ipso}}$), Aromatics – 128.6, 128.4, 128.3, 128.1, 127.9, 127.8, 116.4 (C1), 102.7 (C2), 83.5 (C4), 77.8 (C5), 73.4 (OCH$_2$Ph), 72.3 (OCH$_3$Ph).

\textbf{IR:} $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3039, 2926, 1848, 1760, 1737, 1458, 1238, 1230, 1102, 800, 791, 787.
CIMS: \(322 (M+1, 23\%), 303 (M^+ - H_2O, 1\%), 214 (M^+ - OBn, 17\%), 181 (C_{14}H_{13}, 27\%), 91 (Bn, 58\%), 89 (100\%). 155 (M^+ - CN, 6\%).

**Minor isomer (β):**

TLC: \(R_f 0.51\) (3:1 hexanes-EtOAc)

\(^1\)H NMR: (300 MHz, CDCl$_3$) \(\delta_H 9.58\) (d, 1H, \(J = 1.8\) Hz, H6), 7.34-7.21 (m, 10H, aromatics), 6.66 (dd, 1H, \(J = 16.2\) and 5.4 Hz, H3), 5.66 (dd, 1H, \(J = 16.2\) and 1.8 Hz, H2), 4.69-4.48 (m, 4H, OCH$_2$Ph \(\times\) 2), 4.33 (ddd, 1H, \(J = 5.4, 4.9\) and 1.5 Hz, H4), 3.89 (dd, 1H, \(J = 4.8\) and 1.8 Hz, H5).

\((2E,4R,5R)-4,5\text{-di(benzyloxy)-6-oxohex-2-enenitrile (5.26)}\)

![Chemical Structure](image)

The general procedure to form an aldehyde using LDA and BF$_3$.(OEt)$_2$ (5.4) was carried out with Methyl 2,3-di-O-benzyl-5-C-cyano-5-deoxy-D-ribose. After workup and column chromatography (hexanes-EtOAc) the desired aldehyde analogue was obtained (41\%, after two columns).

*Product characterised above when obtained tribenzyl analogue*
The general procedure to form an aldehyde using LDA and BF$_3$(OEt)$_2$ (5.4) was carried out with benzyl 2,3-di-O-benzyl-5-C-cyano-5-deoxy-D-arabinofuranoside. After workup and column chromatography (4:1 hexanes-EtOAc) the desired aldehyde analogue was obtained as a mixture of isomers (43%, on conversion 58%).

TLC: \( R_f \) 0.32 and 0.24 (3:1 hexanes-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 9.64 (d, 1H, $J = 1.2$ Hz, H6), 9.62 (d, 1H, $J = 1.2$ Hz, H6), 7.48-7.30 (m, 20H, aromatics and aromatics), 6.66 (dd, 1H, $J = 16.2$ and 5.3 Hz, H3), 6.53 (dd, 1H, $J = 11.1$ and 8.7 Hz, H3), 5.65 (dd, 1H, $J = 16.2$ and 1.5 Hz, H2), 5.51 (dd, 1H, $J = 11.1$ and 1.2 Hz, H2), 4.77-4.39 (m, 8H, OCH$_2$Ph $\times$ 2 and OCH$_2$Ph $\times$ 2), 4.34-4.31 (m, 2H, H4 and H4), 3.92 (dd, 1H, $J = 4.2$ and 1.2 Hz, H5), 3.81 (dd, 1H, $J = 4.2$ and 1.2 Hz, H5).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 201.2 (C6), 200.5 (C6), 149.7 (C3), 149.5 (C3), 136.3 ($ipso$), 136.2 ($ipso$), 136.1 ($ipso$), 136.0 ($ipso$), Aromatics – 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 116.4 (C1), 114.6 (C1), 103.0 (C2), 102.5 (C2), 83.6 (C4), 82.7 (C4), 76.8 (C5), 76.5 (C5), 73.7 (OCH$_2$Ph), 73.6 (OCH$_2$Ph), 72.64 (OCH$_2$Ph), 72.2 (OCH$_2$Ph).

IR: $\nu_{\text{max}}$(CHCl$_3$/cm$^{-1}$) 3067, 2934, 1807, 1772, 1638, 1616, 1500, 1458, 1421, 1341, 1181, 1096, 795.

CIMS: 321 (M$^+$, 17%), 303 (M$^+$ - H$_2$O, 8%), 295 (M$^+$ - CN, 1%), 214 (M$^+$ - OBn, 38%), 107 (OBn, 28%), 91 (Bn, 100%).
6.5.2 Samarium diiodide studies

7-cyanomethyl-3,3-dimethyl-2,4-dioxabicyclo[3.2.0]heptan-6-ol (5.47)

General procedure to form monomers with SmI$_2$, in THF in the presence of HMPA via normal addition (4.53) was used to form monomers from (2E,4R,5R)-4,5-O-isopropylidene-6-oxo-hex-2-enenitrile (38 mg, 0.21 mmol). The residue was purified by column chromatography (3:1 hexanes-EtOAc). A single monomer was obtained (7 mg, 0.036 mmol, 17%).

TLC: $R_f$ 0.33 (1:1 hexane-EtOAc)

$^1$H NMR: (300 MHz, CDCl$_3$) $\delta_H$ 4.71 (dd, 1H, $J$ = 5.7 and 5.1 Hz, H6), 4.36 (unresolved dd, 1H, H5), 3.94 (unresolved dd, 1H, H1), 2.60 (d, 2H, $J$ = 7.5 Hz, CH$_2$CN), 2.34 (br s, 1H, OH), 2.28-2.22 (m, 1H, H7), 1.50 (s, 3H, CH$_3$-isopropylidene), 1.28 (s, 3H, CH$_3$-isopropylidene).

$^{13}$C NMR: (75 MHz, CDCl$_3$) $\delta_C$ 118.2 (CN), 115.2 (acetal), 80.4 (C5), 79.0 (C1), 71.3 (C6), 37.5 (C7), 26.6 (CH$_3$-isopropylidene), 25.8 (CH$_3$-isopropylidene), 15.3 (CH$_2$CN).

IR: $\nu_{max}$(CHCl$_3$/cm$^{-1}$ 3240, 2970, 2086, 1810, 1740, 1715, 1666, 1560, 1391, 1250, 1223.

HRMS: Found 183.0899. Calculated for C$_9$H$_{13}$NO$_6$ 183.0895.

CIMS: 184 (M+1, 100%), 166 (M+1 - H$_2$O, 4%), 126 (M+1 - H$_2$O - CH$_2$CN, 18%), 100 (M-1 - CN - H$_2$O - isopropylidene, 25%).

$[\alpha]_D$: +2.3 ($c$ = 0.75, CHCl$_3$).
6.6 REFERENCES

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8  Horton, D., Liav, A. Carbohydrate Research 1976, 47, 326.