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# Synthesis of 2,3-*O*-benzyl-ribose and xylose and their equilibration

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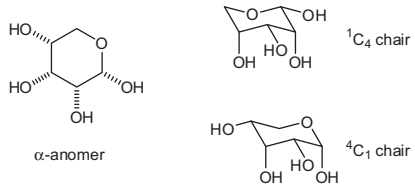
ABSTRACT

The preparation and NMR analysis of 2,3-di-*O*-benzyl D-ribose and 2,3-di-*O*-D-xylose are described. In DMSO-$d_6$ the sugars adopt a conformation in which the hydroxyl groups are in an equatorial position. In $CDCl_3$ and $CD_2Cl_2$ the sugars adopts a conformation in which intramolecular hydrogen bonding plays an important role in determining the equilibrium composition. These findings were also confirmed by DFT studies and, in the solid phase, by X-ray single crystal diffraction.



## 1. Introduction

Carbohydrates are essential biochemical building blocks for complex life forms to develop. Major strides have been made in the synthesis of complex structures encompassing carbohydrates over the last decade. However a universal strategy for glycosylation that readily results in the synthesis of oligosaccharides has remained elusive.[1] Understanding the biological activity of saccharides and of their oligomers by its very nature necessitates that we know the structure and stability of the different conformations that these molecules can adopt. A major obstacle in obtaining a basic structure is due to that fact that these can form strong hydrogen bonds in water and other polar solvents, which in turn can result in conformational changes taking place that may lead to a different biological effect being observed. As a result of these observations, a number of investigations into the conformations of 2-deoxy-D-ribose have been reported[2] using Fourier-transform microwave spectroscopy in conjunction with UV spectroscopy using a laser source. In aqueous solution D-ribose exists primarily as α- and β-pyranose[3] forms whilst in RNA it is present as a furanose. In aqueous solution D-ribose exists as a mixture of α- and β-pyranoses that are present in their low energy chair conformations, $^4C_1$ and $^1C_4$. These configurations proceed through ring inversion leading to an axial or equatorial OH group for each conformer. Additionally, extra stabilisation provided by the anomeric effect results in the preference for an axial OH group at the $C_1$ carbon over the empirically expected equatorial orientation[4] (Scheme 1).




**Scheme 1.**

We have recently reported NMR equilibration studies leading to the synthesis of arabinofuranosides using an iterative protocol.[5] Herein we report on our findings relating to 2,3-*O*-dibenzylribo- and xylo-furanosides and the former use for the synthesis of oligosaccharides.

Following on from these studies, we reasoned that ribosides and their xylo analogues should be capable of providing access to oligosaccharides using similar procedures. In addition these studies should provide insight into the conformation of these pentoses and the stereochemical effects as a result of the change in the substitution patterns at C-2 and C-3. Furthermore, we wished to control the mutarotation of these partially protected sugars with the specific goal of being able to selectively prepare furanosides from a mixture of isomers. The success of the proposed strategy depends upon the selectivity of the attack of the primary hydroxyl group on the glycosyl intermediate species that results.[5] At the outset we wished to study the equilibrium composition of these two sugars and compare the experimental findings with theoretical predictions arising from the use of the density functional theory with respect to the possible conformations arising in solution and the effect the solvents have on these.

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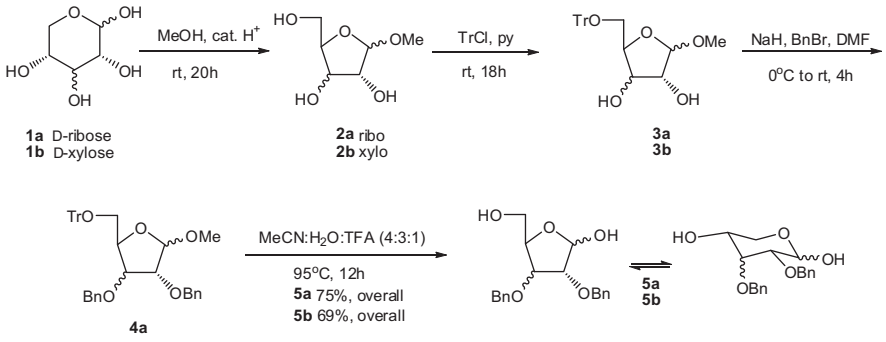



**Scheme 2.** Preparation of 2,3-di-*O*-benzyl ribose **5a** and 2,3-di-*O*-benzyl xylose **5b**.

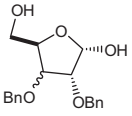
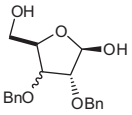
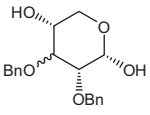
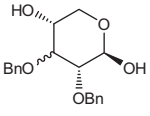
## 2. Results and discussion

2,3-Di-O-benzylated D-ribose was synthesized from the commercially available D-ribose (Scheme 2). The methyl furanoside[6] was protected selectively at the primary hydroxyl group using trityl chloride[7] followed by benzylation to give the fully protected sugars. Removal of the trityl group and the anomeric methyl group was accomplished in one step to yield the desired compounds. 2,3-Di-*O*-benzyl-D-xylose was also synthesized from commercially available D-xylose using the same procedures.

The pure 2,3-di-*O*-benzyl derivatives **5a** and **5b** obtained after column chromatography were analysed using one dimensional and two-dimensional NMR in three solvents: $CDCl_3$, $CD_2Cl_2$ and DMSO-$d_6$. The equilibrium proportions of the various isomers in solution were determined by integration of the anomeric proton NMR signals.

The $^1$H NMR spectrum of **5a** in deuterated chloroform showed the presence of four major anomers; the α- and β-pyranoses and the α- and β-furanoses. Neither the acyclic aldehyde nor hydrate was detected by natural abundance of NMR. The anomeric protons of the furanoses resonated at lower fields than those of the pyranoses, with chemical shifts of 5.30 and 5.31 ppm for the α- and β-anomers, respectively, (Table 1).

**Table 1**
Chemical shift data for compounds **5a** and **5b** in $CDCl_3$[a]

| | | 5a | | 5b | |
|---|---|---|---|---|---|
| α-Furanose | H-1, C-1 | 5.30 | 96.3 | 5.47 | 95.5 |
|  | H-2, C-2 | 3.61 | 76.9 | 4.00 | 82.4 |
| | H-3, C-3 | 3.69 | 62.4 | 4.18 | 82.9 |
| | H-4, C-4 | 3.82 | 80.6 | 4.35 | 81.2 |
| | H-5a, 5b, C-5* | 3.83, 3.86 | 62.2 | 3.73,3.89 | 62.2 |
| β-Furanose | H-1, C-1 | 5.31 | 99.8 | 5.30 | 101.2 |
|  | H-2, C-2 | 4.22 | 82.0 | 4.02 | 87.4 |
| | H-3, C-3 | 4.25 | 82.0 | 4.16 | 82.0 |
| | H-4, C-4 | 3.69 | 72.8 | 4.29 | 77.7 |
| | H-5a, 5b, C-5* | 3.92, 3.88 | 64.6 | 3.72, 3.83 | 61.9 |
| α-Pyranose | H-1, C-1 | 5.21 | 93.5 | 5.01 | 91.8 |
|  | H-2, C-2 | 3.75 | 66.0 | 3.52 | 77.2 |
| | H-3, C-3 | 3.88 | 77.8 | 3.83 | 76.8 |
| | H-4, C-4 | 3.77 | 65.9 | 3.63 | 67.6 |
| | H-5a, 5b, C-5* | 3.89, 3.93 | 67.6 | 3.83, 3.85 | 64.9 |
| β-Pyranose | H-1, C-1 | 4.91 | 92.4 | 4.96 | 94.1 |
|  | H-2, C-2 | 3.96 | 77.3 | 3.48 | 76.0 |
| | H-3, C-3 | 3.87 | 78.0 | 3.72 | 76.6 |
| | H-4, C-4 | 3.54 | 61.7 | 3.69 | 67.0 |
| | H-5a, 5b, C-5* | 4.18, 4.20 | 76.8 | 3.83, 3.85 | 61.7 |

[a] All values are given as chemical shifts in ppm.
* H-5a and H-5b unassigned.

The ratios of the four anomers were obtained by integration of the anomeric resonance in its $^1$H spectrum (Table 2).

**Table 2**
Percent pyranose and furanose forms of **5a** in $CDCl_3$, DMSO-$d_6$ and $CD_2Cl_2$*

| | $CDCl_3$ | DMSO-$d_6$ | $CD_2Cl_2$ |
|---|---|---|---|
| α-Furanose | 18 | — | 15 |
| β-Furanose | 13 | — | 17 |
| α-Pyranose | 24 | — | 21 |
| β-Pyranose | 45 | 100 | 47 |

* Ratios calculated using spectra obtained immediately after dissolution in the respective solvents.

Benzylation of the 2,3-hydroxy groups of ribose results in a thermodynamic equilibrium which results in the β-pyranose being the sole isomer that is observed in DMSO and the solid state, in contrast to the unprotected sugar which gives a mixture of all four isomers in water (Table 3).

**Table 3**
% pyranose and furanose forms of D-ribose **1a** and D-xylose **1b** in $D_2O$[3b]

| | 1a | 1b |
|---|---|---|
| α-Furanose | 6.5 | <1 |
| β-Furanose | 13.5 | <1 |
| α-Pyranose | 21.5 | 36.5 |
| β-Pyranose | 58.5 | 63.0 |

For **5a** in $CDCl_3$ and $CD_2Cl_2$, the composition of the four isomers were similar with the two pyranose forms occurring in 69% and 68%, respectively, indicative of similar solvent effects. In the more polar DMSO-$d_6$ only the β-pyranose isomer was detected upon immediate dissolution and subsequent acquisition of the NMR data. The resonances observed, excluding the benzyl signals are detailed in Table 4 for the sake of clarity. This indicated that in solid **5a**, the β-pyranose isomer was the sole observed component upon dissolution and immediate accumulation of the spectroscopic data. The anomeric resonance occurred at $\delta$ 4.88 and in its $^{13}$C spectrum the resonance was observed at $\delta$ 93.34.

**Table 4**
Chemical shift data for **5a** in DMSO-$d_6$

| β-Pyranose in DMSO-$d_6$ | | |
|---|---|---|
| OH-1 | 6.62 $J$ = 6.00 Hz | |
| H-1, C-1 | 4.88 | 93.34 |
| H-2, C-2 | 3.32 | 79.02 |
| H-3, C-3 | 3.93 | 76.5 |
| OH-4, H-4, C-4 | 4.62, 3.70 | 67.4 |
| H-5, H-5′, C-5 | 3.53, 3.60 | 63.7 |

We were able to crystallise the pure β-anomer of **5a** from ethyl acetate by allowing the slow evaporation of the solvent to obtain thin white needles with a mp of 82–83 °C, $[\alpha]_D = -19.6$ ($c$ 1.0, $CHCl_3$). With this isomer in hand we undertook single X-ray crystallographic analysis. This confirmed that crystalline **5a** existed in a pyranose structure, which was in agreement with the solution structure observed in DMSO. The crystal structure belongs to the monoclinic P21 space group with $a = 10.558(3)$, $b = 6.878(2)$, $c = 12.275(4)$ and $b = 97.543(4)°$ with $Z = 2$ thus showing two independent molecules in the unit cell. The ring puckering analysis performed on the crystalline structure[8] evidenced the presence of a chair conformation as reported in Table 5. More interestingly, the structure presents no solvent accessible voids, being available only two small volumes of less than 15 Å$^3$ which are not suitable for any small solvent molecule to fit, and a resulting high packing index[9] (64.2%). The solid state hydrogen bond network is reported in Table 6. There are both inter- and intra-molecular hydrogen bonds as well as weak π stacking interactions between the aromatic rings of the structure, particularly along the $1 - x$, $-1/2 + y$, $1 - z$ direction (Fig. 1).

Prior to the commencement of these studies we had undertaken density functional theory (DFT) calculations of 2,3-di-*O*-benzyl and 2,3-di-*O*-methyl ribosides along with the xylose analogues, using B3LYP/6-31G** and Schrodinger's Jaguar software, version 7.6, on geometries generated by conformation searches using MacroModel (BatchMin v9.7) and the OPLS_2005 force field. These calculations indicated that the major isomer in DMSO, (Table 7), would have a β-pyranose structure. This is in agreement with our experimental findings in both the solution and solid states. When dissolved in $CD_2Cl_2$ and $CDCl_3$ the crystalline β-ribopyranoside afforded a mixture of furanosides and pyranosides.

In DMSO-$d_6$ the anomer with the least steric interactions was the most abundant.[10] The hydrogen bond interaction between the solvent and the hydroxyl groups increases the effective size of the substituents. In $CDCl_3$, which does not interact with the solute via hydrogen bonding, other effects come into play including the anomeric effect and ring strain or torsional strain. Intramolecular hydrogen bonding also influences the equilibrium because conformations containing these interactions are preferentially stabilized.[11]

In order to account for possible stereoelectronic effects we undertook DFT calculations with D-arabinose. These suggested that in a polar solvent the pyranose structure should predominate. This was at variance with our experimental findings[5] wherein it was established that the furanose and pyranose ring systems occurred in equal percentages. These findings suggest that the stereochemistry of the C-2 hydroxy group plays a predominant role in determining the ring size of pentoses. This is not too surprising since the C-2 hydroxy function in both ribose and xylose is in the preferred equatorial orientation whilst in the case of D-arabinose it has a higher energy axial geometry.

**Table 5**
Ring puckering coordinates and their e.s.d. for the Cremer and Pople analysis performed on the anomeric ring and its resulting conformation

| Q (Å) | $q_2$ (Å) | $\phi_2$ (°) | $q_3$ (Å) | $\theta$ (°) | Conformation |
|---|---|---|---|---|---|
| 0.570 (5) | 0.016 (5) | 353 (20) | −0.570 (5) | 177.9 (5) | Chair |

**Table 6**
Potential hydrogen bonds analysis. Bond lengths, together with their standard uncertainties (s.u.) are given in Å; bond angles (D–H···A) in (°)

| Bond type | Donor | –H | Acceptor | D–H | H···A | D···A | D–H···A |
|---|---|---|---|---|---|---|---|
| Inter-[i] | O3 | –H30 | ..O2 | 0.79 (7) | 1.96 (7) | 2.738 (5) | 166 (7) |
| Inter-[ii] | C19 | –H19 | ..O3 | 0.93 | 2.59 | 3.503 (7) | 166 |
| Intra- | O2 | –H20 | ..O5 | 0.83 (7) | 2.00 (8) | 2.696 (6) | 141 (7) |
| Intra- | C19 | –H19 | ..O3 | 0.93 | 2.59 | 3.503 (7) | 166 |

Symmetry codes: (i) $x$, $-1 + y$, $z$; (ii) $x$, $1 + y$, $z$.

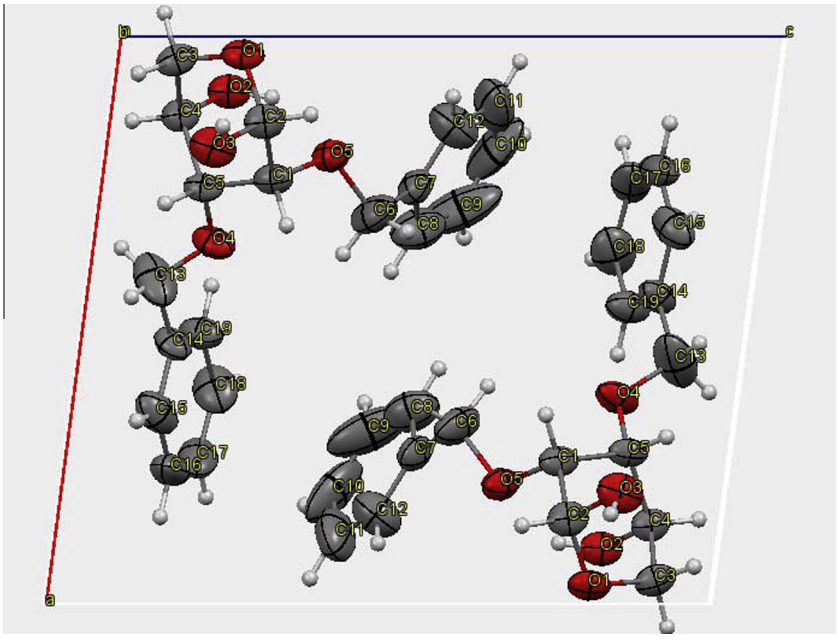



**Figure 1.** Packing diagram viewed down the $b$ axis. Hydrogens are shown as fixed-size spheres of an arbitrary radius of 0.15 Å and the ellipsoids probability level set to 30% for the sake of clarity.

**Table 7**

| | 2,3,Di-*O*-Bn ribose | | | 2,3-Di-*O*-Me ribose | | 2,3-Di-*O*-Bn xylose | | |
|---|---|---|---|---|---|---|---|---|
| | Model % | Exp DMSO % | Exp $CDCl_3$ % | ab initio | B3LYP | Model DMSO | Exp DMSO | Exp $CDCl_3$ |
| α-Furanose | 0.0 | 0.0 | 18.0 | 0.0 | 0.6 | 0.0 | 0.0 | 6.9 |
| β-Furanose | 0.0 | 00 | 13.0 | 0.0 | 0.0 | 0.0 | 0.0 | 5.6 |
| α-Pyranose | 4.8 | 0.0 | 24.0 | 2.0 | 44.2 | 13.0 | 44.4 | 31.2 |
| β-Pyranose | 95.2 | 100.0 | 45.0 | 98.0 | 55.2 | 87.0 | 55.6 | 56.3 |
| | Arabinose | | | 2,3-Di-*O*-Me arabinose | | 2,3-Di-*O*-Bn arabinose | | |
| | Model dry | Model $H_2O$ | Literature[3b] | Model DMSO | | Model DMSO | Exp DMSO | Exp $CDCl_3$ |
| α-Furanose | 0.0 | 0.0 | 2.5 | 6.7 | | 8.7 | 35.0 | 26.0 |
| β-Furanose | 0.0 | 0.0 | 2.0 | 48.1 | | 11.9 | 16.0 | 21.0 |
| α-Pyranose | 2.0 | 10.0 | 60.0 | 0.0 | | 0.0 | 24.0 | 26.0 |
| β-Pyranose | 98.0 | 90.0 | 35.5 | 45.2 | | 79.4 | 25.0 | 27.0 |

Differences in the chemical shifts and the coupling constants of the anomeric protons when the solvent was changed from $CDCl_3$ to DMSO-$d_6$ were related to a change in conformation, particularly in the pyranose forms. Both 2,3-di-*O*-benzyl-β-D-ribopyranose **5a** and 2,3-di-*O*-benzyl-β-D-xylopyranose **5b** experienced conformational changes due to the change in solvent as indicated by the values of the $J_{1,2}$ coupling constants (Table 8).

In $CDCl_3$, 2,3-di-*O*-benzyl-β-D-ribopyranose **5a** exists primarily as the $^1C_4$ conformer as indicated by the $J_{1,2}$ value of 1.99 Hz (Table 8). In DMSO-$d_6$, however, a $J_{1,2}$ value of 5.6 Hz suggests that this anomer exists as a mixture of the $^1C_4$ and $^4C_1$ conformers, with the equilibrium favouring the latter.[3e] Similarly, 2,3-di-*O*-benzyl-β-D-xylopyranose **5b** exists primarily in the $^4C_1$ conformation, in which all substituents are in an equatorial position, in DMSO-$d_6$ but as a mixture of the two chair conformations in the less polar, non-hydrogen bonding $CDCl_3$ with the equilibrium in favour of the $^1C_4$ conformer. In 2,3-di-*O*-benzyl-α,D-xylopyranose **5b** the conformation was assigned based on the well-known fact that an equatorial proton resonates at a lower field than a chemically similar but axial proton. Thus 2,3-di-*O*-benzyl-α,D-xylopyranose **5b**, exists primarily as the $^1C_4$ conformer in $CDCl_3$.[12] while 2,3-di-*O*-benzyl-α,D-ribopyranose **5a** exists as a mixture of both conformers in either solvent. These observations suggest that intramolecular hydrogen bonding is present in the absence of a hydrogen bonding solvent.[13] This intramolecular hydrogen bonding occurs even in the presence of bulky benzyl substituents and stabilizes the conformer in which these groups are axial, in spite of unfavourable 1,3-diaxial interactions[14] (Fig. 2).

Having this information in hand, we will begin to investigate the application of these findings to the synthesis of furano-oligosaccharides. In particular we wish to undertake an iterative synthesis of 1-*O*-linked ribosides. We reason that we should be able to selectively react the equilibrium mixture in order to obtain the desired furano linked ribosides.

**Table 8**
Comparison of chemical shifts in ppm and coupling constants (in Hz) of anomeric protons of compounds **5a** and **5b**

| | **5a** | | | **5b** | | |
|---|---|---|---|---|---|---|
| | $CDCl_3$ | $CD_2Cl_2$ | DMSO-$d_6$ | $CDCl_3$ | $CD_2Cl_2$ | DMSO-$d_6$ |
| α-Furanose | 5.30 (6.1) | 5.27 (4.0) | | 5.47 (4.2) | 5.44 (3.85) | |
| β-Furanose | 5.31 (3.8) | 5.35 (4.7) | | 5.30 | 5.23 | |
| α-Pyranose | 4.91 (10.0) | 4.88 (10.0) | | 5.01 (2.2) | 5.01 (2.28) | 5.20 (5.4) |
| β-Pyranose | 5.21 (1.99) | 5.23 | 4.88 (5.6) | 4.96 (2.6) | 4.92 (3.5) | 4.47 (6.6) |

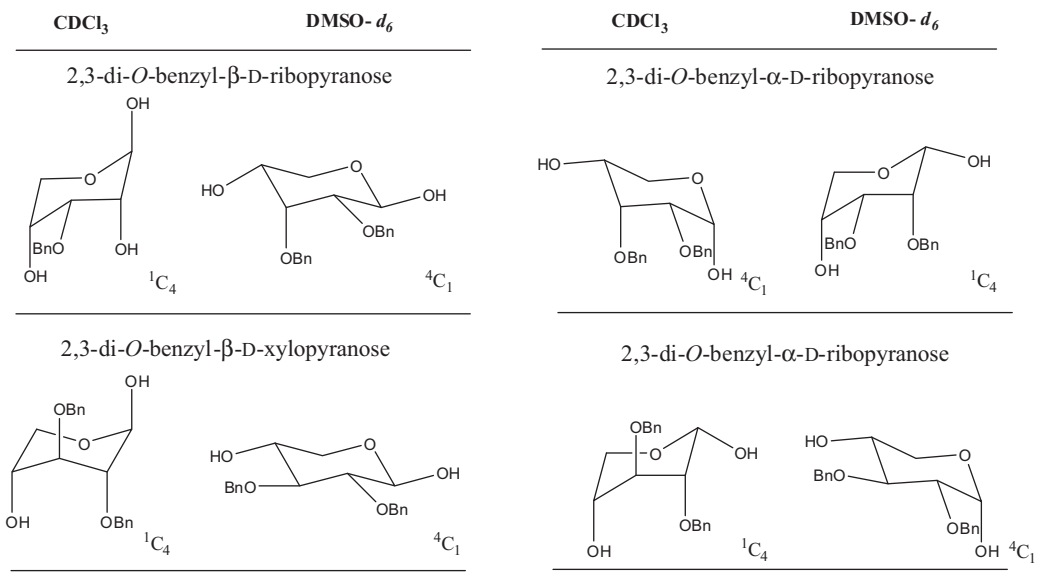



**Figure 2.** Major chair conformations of **5a** and **5b**.

## 3. Conclusion

In conclusion, we have investigated the equilibria present in 2,3-di-*O*-benzylated pentose sugars and established that in polar solvents, the β-pyranose form is the major isomer, whilst in less polar solvents a mixture of both furanose and pyranose isomers can be found.

## 4. Experimental

### 4.1. General

All chemicals used were reagent or HPLC grade and used as supplied without prior purification unless otherwise stated. Solvents: DCM and diethyl ether were dried over calcium hydride for 24 h, distilled and stored over 4 Å molecular sieves. Flash column chromatography was carried out using forced flow of the indicated solvent on Merck (230–400 mesh) silica gel. TLC was performed using pre-coated silica gel 60 $F_{254}$ plates; compounds were visualized using acidic ammonium molybdate solution [ammonium molybdate(VI) tetrahydrate (25 g) in 1 M $H_2SO_4$ (500 mL)]. Anhydrous reactions were performed under argon in oven dried apparatus; anhydrous transfers were carried out with standard syringe techniques.

$^1H$, $^{13}C$ and $^{31}P$ NMR spectra were recorded on Bruker 600, 400 MHz spectrometers in the deuterated solvent stated. For ease of interpretation, protons are expressed as multiples of 1. Refer to the main text for equilibrium ratios. IR spectra were recorded on a Perkin Elmer Spectrum RXI FT-IR spectrometer. High resolution mass data was obtained using a Bruker Daltonics micrOTof-Q instrument in the electron spray ionization mode. Melting points were measured in open capillaries and are uncorrected.

### 4.2. Crystallographic structure determination

The single crystals used for structure determination were mounted on a glass capillary; the small dimensions and some twinning did not allow collection of high quality data and resolution, but were nevertheless perfectly suitable for satisfactory structural determination. Single crystal X-ray diffraction data were collected at $T = 293$ K using the MoKα radiation ($\lambda = 0.71073$ Å) on a SMART APEX2 diffractometer. Lorentz, polarization and absorption corrections were applied.[15] The structure was solved by direct methods using SIR2004[16] and refined by full-matrix least-squares on all F2 using SHELXL-2013[17] implemented in the Olex2 package.[18] Hydrogen atoms were introduced in calculated positions riding on their carrier atoms with the exception of hydroxylic hydrogens that were located on the difference map and refined isotropically. Anisotropic displacement parameters were refined for all non-hydrogen atoms. Due to slight twinning the Flack parameter does not converge to zero, although the absolute structure is assessed by chemical argumentation. Hydrogen bonds have been analysed with SHELXL2013[17] and PARST97[19] and extensive use was made of the Cambridge Crystallographic Data Centre packages[20] for the analysis of crystal packing. CCDC 1022046 contains the Supplementary crystallographic data for this paper. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: (+44) 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk).

### 4.3. General procedure for preparation of 2,3-di-*O*-benzyl sugars

The starting sugar (5.0 g, 33.3 mmol) was suspended in methanol,[6] after which *p*-TSA (290 mg, 1.5 mmol) was added and the mixture was stirred at 40 °C for 20 h. The solvent was removed in vacuo and the crude product dissolved in pyridine (50 mL). Trityl chloride[7] (9.3 g, 33.3 mmol) was added and the mixture was stirred at rt overnight. The reaction mixture was then poured into an ice-water mixture and allowed to warm up to room temperature. The mixture was then extracted with chloroform (3 × 50 mL). The organic layers were then combined and washed using saturated aqueous ammonium chloride (2 × 50 mL) and water (2 × 50 mL). The organic layer was then dried ($Na_2SO_4$) and the solvents removed in vacuo. The solvent was removed under reduced pressure and the residue obtained purified via column chromatography ($CHCl_3$ followed by $CHCl_3$/MeOH; 9:1). The tritylated methyl glycoside was then benzylated under standard benzylation conditions. Deprotection of the trityl and methyl groups was carried out by refluxing in a solution of $CH_3CN/H_2O$/TFA (4:3:1; 1:20 w/v) at 95 °C for 12 h. The solvent was then removed in vacuo and the residue neutralized using saturated aqueous $NaHCO_3$ (20 mL) and solid $NaHCO_3$. The mixture was then extracted using EtOAc (2 × 20 mL). The organic layers were combined and dried ($Na_2SO_4$) and the solvent removed under reduced pressure. The residue obtained was purified via column chromatography using $CHCl_3$/MeOH (95:5).

### 4.4. 2,3-Di-*O*-benzyl-D-ribose 5a

The resultant light yellow oil solidified on standing, 75% yield overall. A portion of this was recrystallized from EtOAc mp of 82–83 °C, $[\alpha]_D^{23} = -19.6$ ($c$ 1.0, $CHCl_3$). NMR (600 MHz) $CDCl_3$ $\delta_H$ (ppm): shared resonances: 7.2–7.4 (40H, m, aromatic protons), 4.5–4.8 (4H, benzylic protons + 1 hydroxyl proton), 4.25 (1H, 1 hydroxyl proton), 3.5–4.0 (3H, 3 hydroxyl protons) 1.55–2.85 (3H, 3 hydroxyl protons); α-furanose: 5.30 (1H, d, $J = 6.1$ Hz, H-1), 3.61 (1H, H-2), 3.69 (1H, H-3), 3.82 (1H, H-4), 3.83 (1H, H-$5_a$), 3.86 (1H, H-$5_b$); β-furanose: 5.31 (1H, d, $J = 3.8$ Hz, H-1), 4.22 (1H, H-2), 4.25 (1H, H-3), 3.69 (1H, H-4), 3.92 (1H, H-$5_b$), 3.88 (1H, H-$5_a$); β-pyranose: 4.91 (1H, d, $J = 1.99$ Hz, H-1), 3.96 (1H, H-2), 3.87 (1H, H-3), 3.54 (1H, H-4), 4.18 (1H, H-$5_a$), 4.20 (1H, H-$5_b$); α-pyranose: 5.21 (1H, d, $J = 10$ Hz, H-1), 3.75 (1H, H-2), 3.88 (1H, H-3), 3.77 (1H, H-4), 3.89 (1H, H-$5_b$), 3.93 (1H, H-$5_a$); $^{13}C$ (150 MHz) $CDCl_3$ $\delta_C$ (ppm): shared resonances: 138.1, 137.7, 137.7, 137.6, 137.4, 137.3, 137.3, 128.7, 128.7, 128.7, 128.7, 128.7128.6, 128.5, 128.5, 128.4, 128.4,128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.9, 127.7, 127.7, 127.7, 127.7 (aromatic-C), 76.1, 73.8, 73.6, 73.0, 73.0, 72.8, 72.3, 70.6 (benzylic-C); α-furanose: 96.3 (C-1), 76.9 (C-2), 62.4 (C-3), 80.6 (C-4), 62.2 (C-5); β-furanose: 99.8 (C-1), 82.0 (C-2), 82.0 (C-3),72.8 (C-4), 64.6 (C-5); α-pyranose: 92.4 (C-1), 77.3 (C-2), 78.0 (C-3), 61.7 (C-4), 76.8 (C-5); β-pyranose: 93.5 (C-1), 66.0 (C-2), 77.8 (C-3), 65.9 (C-4), 67.6 (C-5).

$^1H$ NMR (600 MHz) $CD_2Cl_2$ $\delta_H$ (ppm): shared resonances: 7.2–7.4 (40H, m, aromatic protons), 4.4–4.8 (4H, benzylic protons + 1 hydroxyl proton), 3.5–4.0 (3H, 3 hydroxyl protons) 3.09 (1H, br s; hydroxyl proton), 1.24–2.73 (3H; hydroxyl protons); α-furanose: 5.29 (1H, d, $J = 4.0$ Hz, H-1), 3.72 (1H, H-2), 3.90 (1H, H-3), 3.60 (1H, H-4), 3.77 (1H, H-$5_a$), 3.73 (1H, H-$5_b$); β-furanose: 5.32 (1H, d, $J = 4.7$ Hz, H-1), 3.92 (1H, H-2), 4.21 (1H, H-3), 3.63 (1H, H-4), 4.83 (1H, H-$5_b$), 4.84 (1H, H-$5_a$); β-pyranose: 5.35 (1H, H-1), 3.98 (1H, H-2), 4.21 (1H, H-3), 3.88 (1H, H-4), 4.19 (1H, H-$5_a$), 4.22 (1H, H-$5_b$); α-pyranose: 4.88 (1H, d, $J = 10$ Hz, H-1), 3.64 (1H, H-2), 3.52 (1H, H-3), 3.77 (1H, H-4), 3.44 (1H, H-$5_b$), 3.46 (1H, H-$5_a$); $^{13}C$ (150 MHz) $CD_2Cl_2$ $\delta_C$ (ppm): shared resonances: 138.8, 138.4, 138.3, 138.2, 138.1, 138.1, 129.0, 128.9, 128.8, 128.8, 128.8, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0 (aromatic-C), 73.5, 73.4, 73.1, 73.0, 72.8, 71.0 (benzylic-C, overlapping resonances); α-furanose: 97.8

(C-1), 77.9 (C-2), 67.8 (C-3), 62.2 (C-4), 65.2 (C-5); β-furanose: 100.3 (C-1), 78.6 (C-2), 77.4 (C-3),78.6 (C-4), 74.2 (C-5); α-pyranose: 92.8 (C-1), 76.9 (C-2), 63.0 (C-3), 66.5 (C-4), 67.8 (C-5); β-pyranose: 94.0 (C-1), 78.0 (C-2), 82.4 (C-3), 81.6 (C-4), 85.6 (C-5).

$^1$H NMR (600 MHz) DMSO-$d_6$ $\delta_H$ (ppm): 7.2–7.4 (10H, m, aromatic protons), 4.71–4.77 (4H, benzylic protons) 4.62 (1H, br s, hydroxyl proton, OH-4); β-pyranose: 6.62 (1H, d, $J$ = 6.0 Hz; OH-1), 4.88 (1H, overlapping dd, $J$ = 6.8 Hz, H-1), 3.32 (1H, H-2), 3.93 (1H, H-3), 3.70 (1H, H-4), 3.60 (1H, dd, $J$ = 10.8 Hz, 3.6 Hz, H-5$_a$), 3.53 (1H, dd, $J$ = 7.8 Hz, 3.6 Hz, H-5$_b$); $^{13}$C (150 MHz) DMSO-$d_6$ $\delta_C$ (ppm): 139.3, 138.8, 128.1, 128.0, 127.3, 127.3, 127.2, 127.0 (aromatic-C), 72.3, 71.7 (benzylic-C); β pyranose: 93.3 (C-1), 79.0 (C-2), 76.5 (C-3), 67.4 (C-4), 63.7 (C-5); $m/z$ found ($M^+$) 330.1453; $C_{19}H_{22}O_5$ requires 330.1467.

### 4.5. 2,3-Di-*O*-benzyl-D-xylose 5b

Colourless oil which solidified after storage under vacuum to give an off-white solid. 69% yield overall; mp 80–82 °C, $[\alpha]_D^{26} = -4.4$ ($c$ 1.1 $CHCl_3$); $\nu_{max}$(film)/cm$^{-1}$ 3406, 2928, 1721, 1453, 1357, 1274, 1215 and 1094. $^1$H NMR (600 MHz) $CDCl_3$ $\delta_H$ (ppm): shared resonances: 7.2–7.4 40H/m (aromatic protons), 4.4–4.7 (16H; benzylic protons), 3.40–4.20 (4H; hydroxyl protons); 2.55–3.30 (4H; hydroxyl protons); α-furanose: 5.47 (1H, d, $J$ = 4.2 Hz, H-1), 4.00 (1H, H-2), 4.18 (1H, H-3), 4.35 (1H, H-4), 3.73 (H-5$_a$) 3.89 (H-5$_b$); β-furanose: 5.30 (1H, s, H-1), 4.02 (1H, H-2), 4.16 (1H, H-3), 4.29 (1H, H-4), 3.72 (1H, H-5$_a$), 3.83 (1H, H-5$_b$); α-pyranose: 5.01 (1H, d, $J$ = 2.2 Hz, H-1), 3.52 (1H, H-2), 3.83 (1H, H-3), 3.63 (1H, H-4), 3.83 (1H, H-5$_a$), 3.85 (1H, H-5$_b$); β-pyranose: 4.96 (1H, d, $J$ = 2.6 Hz, H-1), 3.48 (1H, H-2), 3.72 (1H, H-3), 3.69 (1H, H-4), 3.55 (1H, H-5$_a$), 4.13 (1H, H-5$_b$) $^{13}$C (150 MHz) $CDCl_3$ $\delta_C$ (ppm): shared resonances: 137.9, 137.3, 137.2, 137.1, 137.0, 136.9, 128.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.6, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.1, 128.00, 128.0, 127.9, 127.9, 127.8, 127.7 (aromatic-C) 73.7, 73.7.6, 73.3, 73.1, 73.1, 72.8, 72.5, 72.0 (benzylic-C); α-furanose: 95.5 (C-1), 82.4 (C-2), 82.9 (C-3), 81.2 (C-4), 62.2 (C-5); β-furanose: 101.2 (C-1), 87.4 (C-2), 82.0 (C-3), 77.7 (C-4), 61.9 (C-5); α-pyranose: 91.8 (C-1), 77.2 (C-2), 76.8 (C-3), 67.6 (C-4), 64.9 (C-5); β-pyranose: 94.1 (C-1), 76.0 (C-2), 76.6 (C-3), 67.0 (C-4), 61.7 (C-5);

$^1$H NMR (600 MHz) $CD_2Cl_2$ $\delta_H$ (ppm): shared resonances: 7.2–7.4 40H/m (aromatic protons), 4.4–4.7 (16H; benzylic protons), 3.40–4.20 (4H; hydroxyl protons); 2.55–3.30 (4H; hydroxyl protons); α-furanose: 5.44 (1H, d, $J$ = 3.85 Hz, H-1), 4.02 (1H, H-2), 4.18 (1H, H-3), 4.33 (1H, H-4), 3.74 (H-5$_a$) 3.90 (H-5$_b$); β-furanose: 5.23 (1H, s), 4.01 (1H, H-2), 4.12 (1H, H-3), 4.24 (1H, H-4), 3.69 (1H, H-5$_a$), 3.78 (1H, H-5$_b$); α-pyranose: 5.01 (1H, d, $J$ = 2.28 Hz, H-1), 3.52 (1H, H-2), 3.83 (1H, H-3), 3.63 (1H, H-4), 3.83 (1H, H-5$_a$), 3.85 (1H, H-5$_b$); β-pyranose: 4.92 (1H, d, $J$ = 3.5 Hz, H-1), 3.47 (1H, H-2), 3.71 (1H, H-3), 3.69 (1H, H-4), 3.49 (1H, H-5$_a$), 4.10 (1H, H-5$_b$) $^{13}$C (150 MHz) $CDCl_3$ $\delta_C$ (ppm): shared resonances: 138.7, 137.9, 137.9, 137.7, 129.0, 129.0, 129.0, 129.0, 129.0, 128.6, 128.6, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1 (aromatic-C) 74. 73.9, 73.5, 73.5, 73.4, 73.2, 72.8, 72.3 (benzylic-C); α-furanose: 96.0 (C-1), 82.4 (C-2), 82.8 (C-3), 81.7 (C-4), 62.6 (C-5); β-furanose: 101.7 (C-1), 88.0 (C-2), 82.8 (C-3), 78.2 (C-4), 62.2 (C-5); α-pyranose: 92.1 (C-1), 78.2 (C-2), 77.3 (C-3), 68.1 (C-4), 65.2 (C-5); β-pyranose: 94.7 (C-1), 76.9 (C-2), 77.3 (C-3), 67.5 (C-4), 62.2 (C-5);

$^1$H NMR (600 MHz) DMSO-$d_6$ $\delta_H$ (ppm): shared resonances: 7.2–7.4 (20H, m, aromatic protons), 4.6–4.9 (8H, benzylic protons + 2H; hydroxyl protons); α-pyranose: 6.89 (1H, d, $J$ = 6.5 Hz; OH-1), 5.14 (1H, m, H1) 3.31 (1H, H-2), 3.57 (1H, H-3), 3.45 (1H, H-4), 3.38 (1H, H-5$_a$), 3.53 (1H, H-5$_b$); β-pyranose: 5.20 (1H, d, $J$ = 5.4 Hz; OH-1), 4.47 (1H, overlapping dd, $J$ = 6.6 Hz, H-1), 3.09 (1H, H-2), 3.30 (1H, H-3), 3.51 (1H, H-4), 3.09 (1H, H-5$_a$), 3.66 (1H, H-5$_b$); $^{13}$C (150 MHz) DMSO-$d_6$ $\delta_C$ (ppm): shared resonances: 139.4, 139.1, 138.9, 138.7, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.9, 127.5, 127.4, 127.3, 127.3, 127.2, 127.1, 127.0, 126.7 (aromatic-C), 74.0 (2C), 73.7, 71.5 (benzylic-C); α-pyranose: 89.9 (C-1), 79.6 (C-2), 81.2 (C-3), 70.0 (C-4), 61.1 (C-5); β-pyranose: 97.5 (C-1), 82.5 (C-2), 84.3 (C-3), 69.9 (C-4), 65.4 (C-5). $m/z$ found ($M^+$) 330.1530; $C_{19}H_{22}O_5$ requires 330.1467.

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