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Note

Conversion of D-xylose to protected D-lyxose derivatives and to D-lyxose, via the corresponding 1,2-anhydride

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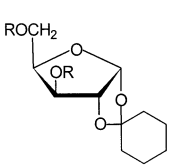
Abstract

Acid hydrolysis of 3,5-di-*O*-benzyl-1,2-*O*-cyclohexylidene-α-D-xylofuranose gave the corresponding lactol, which was subsequently converted to the 3,5-di-*O*-benzyl-2-*O*-mesyl-D-xylofuranose. This compound readily reacted with sodium methoxide, sodium benzylate or sodium hydroxide (presumably via the corresponding 1,2-anhydride) to give the protected D-lyxofuranosides. These compounds were finally converted to methyl α-D-lyxopyranoside or to D-lyxose. © 1999 Elsevier Science Ltd. All rights reserved.

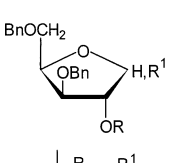
Keywords: 1,2-Anhydro sugar; D-Lyxose; D-Lyxosides, protected; Mutarotation; D-Xylofuranose, protected

1. Introduction

Remarkable progress has been made in the synthesis of *O*-glycosides by regioselective nucleophilic ring opening of 1,2-anhydrohexopyranose derivatives with various alcohols [1,2], aryloxy anions [3] or with suitably protected monosaccharides [2–4]. Conversely, a possibility of using 1,2-anhydroaldopentose derivatives as intermediates in the synthesis of certain pentopyranosides has been recognized [5] but not extensively exploited. 1,2-Anhydro pentoses are usually prepared in situ by intramolecular displacement of leaving groups at C-1 (or C-2) with free C-2 (or C-1) hydroxyl group, under basic conditions. Subsequent opening of the 1,2-anhydro ring with an appropriate alkoxide anion leads to the corresponding glycopyranoside. This methodology has been used earlier for the preparation of methyl β-D-ribopyranoside by treatment of 2-*O*-mesyl-D-arabinose with sodium methoxide [5]. Now the use of similar reaction conditions for the preparation of certain D-lyxofuranosides from suitably protected 2-*O*-mesyl-D-xylose derivative has been studied. The preparation of the 2-*O*-mesyl-D-xylofuranose derivative **4** was first attempted.



1 R = H
2 R = Bn



	R	R^1
3	H	OH
4	Ms	OH

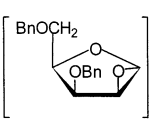


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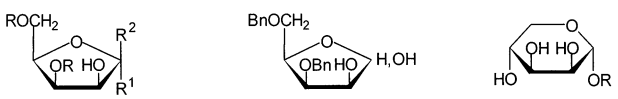
Table 1
^{13}C NMR data for **6**, **7** and **11** (in D_2O) and comparison with Ref. [10]

Compound	C-1	C-2	C-3	C-4	C-5	CH_3O	Reference
6	109.1	77.0	72.0	81.4	61.1	56.9	This work
	109.2	77.0	72.2	81.4	61.5	56.9	[10]
7	102.3	70.4	71.9	67.5	63.9	55.2	This work
	102.0	70.4	71.6	67.7	63.3	55.9	[10]
α-**11**	94.9	70.8	71.3	68.4	63.9		This work
	94.9	71.0	71.4	68.4	63.9		[10]
β-**11**	95.1	70.9	73.5	67.3	65.1		This work
	95.0	70.9	73.5	67.4	65.0		[10]

1,2-*O*-Cyclohexylidene-α-D-xylofuranose (**1**), readily available from D-xylose [6], reacted with benzyl chloride in the presence of powdered potassium hydroxide (Me_2SO, 60 °C) to afford the corresponding 3,5-di-*O*-benzyl derivative **2** in 71% yield. The cyclohexylidene group was removed from **2** by hydrolysis with aqueous acetic acid to give the crystalline lactol **3** in 71% yield. The product was mainly the α anomer since a chloroform solution mutarotated to a less positive equilibrium value (see Section 2). Treatment of **3** with mesyl chloride and triethylamine in dichloromethane gave the desired 2-*O*-mesyl derivative **4** accompanied by at least an equal amount of a less-polar component (presumably [7] the corresponding glycosyl chloride), as estimated by TLC (1:1 hexane–EtOAc). Treatment of the mixture with an excess of silica gel in dichloromethane converted, almost completely, the less-polar component to the crystalline 2-*O*-mesyl derivative **4**. In contrast to the lactol **3**, compound **4** was not observed to mutarotate in chloroform solution[1].

Reaction of 3,5-di-*O*-benzyl-2-*O*-methanesulfonyl-D-xylofuranose (**4**) with sodium methoxide gave the methyl 3,5-di-*O*-benzyl-α-D-lyxofuranoside (**5**) in 57% yield. A possible mechanism for this transformation presumably involves initial formation of the corresponding 1,2-anhydro derivative as an intermediate[2]. The subsequent step could involve a nucleophilic attack of the methoxide ion at C-1 to give **5** as the main reaction product. Apart from the isolated product **5**, the reaction mixture contained a small amount of a more polar component. Although this material was chromatographically homogeneous in different solvent systems, it appeared to be a mixture of several products, with the most prominent one presumably being the methyl 3,5-di-*O*-benzyl-β-D-lyxofuranoside, as indicated by NMR spectral data [δ_H 4.79 (d, $J_{1,2}$ 1.7 Hz, H-1), 3.39 (s, OCH_3); δ_C 109.50 (C-1), 55.59 (OCH_3)]. Compound **5** was further debenzylated (H_2–Pd/C) to the known [9] methyl α-D-lyxofuranoside (**6**). Moreover, acid-catalysed methanolysis of **6** (HCl, MeOH) afforded the known [11] methyl α-D-lyxopyranoside (**7**) in 90% yield. The ^{13}C NMR spectral data (Table 1), as well as the physical constants of both products **6** and **7**, were in reasonable agreement with those already reported in the literature [9–11]. Compound **7** represents a convenient starting material for the preparation of 1,2,3,5-tetra-*O*-acetyl-4-thio-L-ribofuranose and the corresponding nucleoside analogs [11].



	R	R^1	R^2
5	Bn	OMe	H
6	H	OMe	H
8	Bn	OBn	H
9	Bn	H	OBn

10

7 R = Me
11 R = H

[1] According to ^1H NMR spectral data, it appeared to be an 1:4 mixture of α and β anomer, as established by integration of the corresponding proton signals [δ 5.27 (d, $J_{1,2}$ 1.5 Hz, H-1β) and 5.59 (δ, $J_{1,2}$ 4.1 Hz, H-1α)]. The initial 1:4 α–β anomeric ratio (recorded immediately after dissolution of the sample) remains unchanged after storing the solution at room temperature for 3 days. Similarly to compound **4**, the 2-*O*-mesyl-D-arabinose derivative [8] shows no mutarotation in 2 days.

[2] All attempts to isolate the 1,2-anhydro intermediate failed due to its instability and/or high reactivity.

Treatment of 3,5-di-*O*-benzyl-2-*O*-methanesulfonyl-D-xylofuranose (**4**) with sodium benzylate afforded a 5:1 mixture of two anomeric benzyl lyxofuranosides in a 46% combined yield. The major product was the α anomer **8**, as indicated by its highly positive optical rotation {$[\alpha]_D$ +112.9° (*c* 1.02)}. This was additionally confirmed by ^{1}H NMR spectroscopy since the anomeric signal [δ 5.13 (s, 1 H, H-1)] showed no vicinal coupling with H-2 [δ 4.20 (dd, $J_{2,OH}$ 10.2, $J_{2,3}$ 4.8 Hz)]. The minor product was the β anomer **9**, as indicated by a less positive optical rotation {$[\alpha]_D$ +82.1° (*c* 1.43)}, as well as by a significant vicinal coupling between H-1 and H-2 ($J_{1,2}$ 4.7 Hz), compatible with a cis relationship of these protons. The stereochemistry of the minor product **9** was additionally confirmed by an NOE experiment. Upon irradiation of the multiplet at δ_H 4.08 (dd, 1 H, H-3), a significant enhancement of the anomeric proton signal was observed. This confirmed a spatial vicinity of H-1 and H-3 in **9** and consequently, a β configuration at the anomeric position. Both protected lyxofuranosides **8** and **9** represent suitable building blocks for the preparation of oligosaccharides containing the (1→2)-*O*-glycosidic bond, with D-lyxose at the reducing end.

Moreover, it has also been shown that sodium hydroxide could be used for the direct C-2 epimerization of the 2-*O*-mesyl-D-*xylo* derivative **4** to the corresponding D-*lyxo* derivative **10**. This surprisingly clean and smooth transformation was carried out with an equimolar amount of the base in aqueous *N*,*N*-dimethylformamide, whereupon syrupy 3,5-di-*O*-benzyl-D-lyxofuranose (**10**) was obtained in 75% yield. No products of hydrolysis or elimination of the C-2 sulfonyloxy group could be detected in the reaction mixture. Conversely, treatment of 2-*O*-tosyl-D-xylose with aqueous sodium hydroxide gave D-lyxose contaminated with small amounts of D-xylose, D-arabinose and 2-D-*threo*-pentos-2-ulose [12]. The structure of **10** was confirmed by NMR and MS data, as well as by its independent preparation from methyl lyxoside **5**. Hydrolysis of **5** in boiling aqueous acetic acid furnished the lactol **10** in 70% yield. The ^{1}H and ^{13}C NMR spectral data of **10** thus obtained were identical to those already recorded for the sample prepared by C-2 epimerization of **4**.

Catalytic hydrogenolysis of the lactol **10** over Pd/C gave D-lyxose (**11**), with ^{13}C NMR spectral data (Table 1), as well as the physical constants in good agreement with those already reported in the literature [10,13]. The sequence **2**→**4**→**10**→**11** then affords a convenient and novel synthesis of D-lyxose from D-xylose.

2. Experimental

General methods.—Melting points were determined on a Büchi SMP 20 apparatus and were not corrected. Optical rotations were measured on a Perkin–Elmer 141 MC polarimeter. NMR spectra were recorded on a Bruker AC 250 E instrument and chemical shifts are expressed in ppm downfield from Me_4Si. Chemical ionization mass spectra were recorded on a Finnigan-MAT 8230 mass spectrometer with isobutane as a reagent gas. TLC was performed on DC Alufolien Kieselgel 60 F_{254} (E. Merck). Column chromatography was carried out using Kieselgel 60 (under 0.063 mm; E. Merck). Flash column chromatography was performed using ICN silica 32-63. All organic extracts were dried with anhyd Na_2SO_4. Organic solutions were concentrated in a rotary evaporator under diminished pressure at a bath temperature below 35 °C.

*3,5-Di-*O*-benzyl-1,2-*O*-cyclohexylidene-α-D-xylofuranose* (**2**).—1,2-*O*-cyclohexylidene-α-D-xylofuranose [6] (**1**; 9.34 g, 40.61 mmol) was dissolved in Me_2SO (60 mL), and then powdered KOH (10 g, 178.22 mmol) and benzyl chloride (43 mL, 373.65 mmol) were added. The reaction mixture was stirred for 1 h at 60 °C, then poured into cold water (200 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The extracts were washed with water (3 × 50 mL), dried and concentrated to a yellow syrup. Crystallisation from MeOH afforded pure **2** (11.79 g, 71%) as white needles: mp 89–91 °C; $[\alpha]_D$ −39° (*c* 0.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.41–7.25 (m, 10 H, 2 Ph), 5.96 (d, 1 H, H-1), 4.61 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-2), 4.64 and

4.58 (2 d, each 2 H, J_{gem} 12 Hz, 2 PhC**H**$_2$), 4.23 (td, 1 H, H-4), 4.01 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 3.81 (dd, 1 H, $J_{4,5b}$ 6.1 Hz, H-5b), 3.75 (dd, 1 H, $J_{5a,5b}$ 9.8, $J_{4,5a}$ 6.1 Hz, H-5a), 1.77–1.34 (m, 10 H, cyclohexylidene residue); ^{13}C NMR ($CDCl_3$): δ 138.03 and 137.61 (aromatic), 128.40, 128.34, 127.77, 127.62, 127.50, 112.37 (quaternary C from cyclohexylidene residue), 104.61 (C-1), 81.91 (C-2), 81.86 (C-3), 79.13 (C-4), 73.51 and 71.97 (2 PhC**H**$_2$), 67.52 (C-5), 36.43 (5 C**H**$_2$ from cyclohexylidene residue), 35.80, 24.87, 23.85, 23.57; CIMS: m/z 411 $[M+H]^+$. Anal. Calcd for $C_{25}H_{30}O_5$: C, 73.14; H, 7.31. Found: C, 73.28; H, 7.42.

*3,5-Di-*O*-benzyl-*D*-xylofuranose* (**3**).—A solution of **2** (2.76 g, 6.73 mmol) in aq 70% AcOH (80 mL) was stirred at reflux temperature for 8 h, then concentrated and co-evaporated with toluene. The syrupy residue was purified by flash chromatography (7:3 toluene–EtOAc) to give pure **3** (1.59 g, 71%): mp 70–71 °C (toluene–hexane); $[\alpha]_D$ + 20.8° → + 14.7° (24 h) (*c* 1.15, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.40–7.25 (m, 10 H, 2 Ph), 5.48 and 5.18 (s and d, 1 H, H-1β and H-1α), 4.72–4.40 (m, 5 H, 2 PhCH_2 and H-4), 4.23 and 4.14 (dd and d, 1 H, α anomer: $J_{1,2}$ 4.3 Hz, H-2α, and H-2β), 3.99 (m, 1 H, α anomer: $J_{2,3}$ 2.8, $J_{3,4}$ 5 Hz, β anomer: $J_{2,3}$ 2.2 Hz, H-3), 3.78 and 3.69 (2 d, 2 H, α anomer: $J_{4,5}$ 5.2 Hz, β anomer: $J_{4,5}$ 5.1 Hz, 2 H-5), 3.50 (bs, exchangeable with D_2O, 2 H, 2 OH); ^{13}C NMR ($CDCl_3$): δ 137.72–127.45 (aromatic), 103.24 (C-1β), 95.99 (C-1α), 83.39 (C-3α), 82.69 (C-3β), 79.80 (C-4β), 78.87 (C-2β), 77.24 (C-4α), 75.26 (C-2α), 73.50 and 73.37 (4 PhC**H**$_2$), 72.49, 71.78, 69.00 (C-5α); CIMS: m/z 331 $[M+H]^+$, 313 $[M–OH]^+$. Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.31; H, 6.66. Found: C, 69.11; H, 6.98.

*3,5-Di-*O*-benzyl-2-*O*-methanesulfonyl-*D*-xylofuranose* (**4**).—To a stirred and cooled solution (−10 °C) of **3** (1.7 g, 5.15 mmol) in dry CH_2Cl_2 (30 mL) was added Et_3N (2 mL, 8.44 mmol) and mesyl chloride (0.9 mL, 11.64 mmol). Stirring was continued for 1.5 h and the mixture was diluted with CH_2Cl_2 (30 mL), washed successively with cold water, aq 10% HCl, satd aq $NaHCO_3$ and brine. The organic solution was dried and stirred with silica gel (6 g) at room temperature (rt) overnight. The mixture was filtered and the precipitate washed with EtOAc. The filtrates were evaporated, and the residue was submitted to flash-chromatography (2:1 hexane–EtOAc) to furnish pure product **4** (1.3 g, 62%): mp 104–105 °C (CH_2Cl_2–hexane); $[\alpha]_D$ + 3.5° (*c* 0.88, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.36–7.28 (m, 10 H, 2 Ph), 5.59 (d, H-1α), 5.27 (d, H-1β), 5.06 (dd, $J_{1,2}$ 1.5 Hz, H-2β), 5.00 (t, $J_{1,2}$ 4.1, $J_{2,3}$ 4.2 Hz, H-2α), 4.82–4.54 (m, 4 H, 2 PhCH_2), 4.48 (m, $J_{3,4}$ 6.1 Hz, H-4α), 4.37 (m, H-3α and H-4β), 4.31 (dd, $J_{2,3}$ 3.5, $J_{3,4}$ 6.1 Hz, H-3β), 4.23 (d, exchangeable with D_2O, 1 H, $J_{1,OH}$ 11.9 Hz, OH), 3.80–3.60 (m, 2 H, α anomer: $J_{4,5}$ 5.7, J_{gem} 11 Hz, β anomer: $J_{4,5}$ 3.8, J_{gem} 10.1 Hz, 2 H-5), 3.05 (s, 3 H, CH_3SO_2); ^{13}C NMR ($CDCl_3$): δ 137.70 and 136.99 (aromatic), 136.64, 128.39, 128.34, 128.20, 128.04, 127.88, 127.80, 127.63, 127.51, 127.38, 100.34 (C-1β), 94.20 (C-1α), 86.35 (C-2β), 81.74 (C-2α), 80.41 (C-3β), 80.09 (C-3α), 79.25 (C-4β), 76.08 (C-4α), 73.27 and 72.68 (2 PhC**H**$_2$ from β anomer), 73.54 and 72.59 (2 PhC**H**$_2$ from α anomer), 68.43 (C-5α), 68.11 (C-5β), 38.22 (**C**H_3SO_2 from α anomer), 38.14 (**C**H_3SO_2 from β anomer); CIMS: m/z 409 $[M+H]^+$, 391 $[M–OH]^+$. Anal. Calcd for $C_{20}H_{24}O_7S$: C, 58.50; H, 5.70; S, 7.88. Found: C, 58.81, H, 5.92; S, 7.85.

*Methyl 3,5-di-*O*-benzyl-α-*D*-lyxofuranoside* (**5**).—To a solution of **4** (0.5135 g, 1.26 mmol) in dry benzene (5 mL) and MeOH (2 mL) was added NaOMe (0.3 g, 5.56 mmol) and the mixture was stirred for 3 days at ambient temperature. The solution was diluted with ether (20 mL), washed successively with aq 10% NH_4Cl (3 × 10 mL) and water (10 mL), dried and evaporated. Flash chromatography (7:2 hexane–EtOAc) of the residue gave oily **5** (0.2478 g, 57%): $[\alpha]_D$ + 58.2° (*c* 0.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.40–7.17 (m, 10 H, 2 Ph), 4.89 (s, 1 H, H-1), 4.64 (2 d, 2 H, J_{gem} 11.8 Hz, PhC**H**$_2$), 4.62 (2 d, 2 H, J_{gem} 11.4 Hz, PhC**H**$_2$), 4.45 (bs, exchangeable with D_2O, 1 H, OH), 4.44 (dd, 1 H, H-3), 4.33 (dt, 1 H, $J_{3,4}$ 8 Hz, H-4), 4.08 (d, 1 H, $J_{2,3}$ 4.8 Hz, H-2), 3.71 (dd, 1 H, $J_{4,5b}$ 3.1 Hz, H-5b), 3.64 (dd, 1 H, $J_{4,5a}$ 2.4, $J_{5a,5b}$ 10.5 Hz, H-5a), 3.37 (s, 3 H, OC**H**$_3$); ^{13}C NMR ($CDCl_3$): δ 137.61 and 137.11 (aromatic), 127.28, 128.27, 127.76,

127.69, 108.31 (C-1), 77.51 (C-3), 77.27 (C-4), 73.73 and 72.36 (2 Ph**C**H_2), 71.95 (C-2), 67.78 (C-5), 54.89 (O**C**H_3); CIMS: *m/z* 345 $[M+H]^+$, 313 $[M-OCH_3]^+$, 295 $[M-OCH_3-H_2O]^+$.

Methyl α-D-lyxofuranoside (**6**).—Compound **5** (0.65 g, 1.89 mmol) was hydrogenated over 10% Pd–C (0.61 g) in EtOH (15 mL) at rt for 2 h. The mixture was filtered and the catalyst was washed successively with 2:1 EtOH–EtOAc (75 mL) and EtOH (25 mL). The filtrate and washings were combined and concentrated. Flash chromatography (9:1 $CHCl_3$–MeOH) of the residue yielded pure **6** (0.17 g, 55%): mp 95–96 °C (EtOAc), lit. 97.5–98.5 °C [9]; $[\alpha]_D$ +111° (*c* 0.1, MeOH), lit. +128° (*c* 1, MeOH) [9]; ^{1}H NMR (Me_2SO-d_6): δ 5.20 (d, exchangeable with D_2O, 1 H, 2-OH), 4.89 (t, exchangeable with D_2O, 1 H, 5-OH), 4.83 (d, exchangeable with D_2O, 1 H, 3-OH), 4.65 (d, 1 H, H-1), 4.02 (m, after addition of D_2O t, 1 H, H-3), 3.91 (m, 1 H, $J_{3,4}$ 4.6 Hz, H-4), 3.80 (m, after addition of D_2O dd, 1 H, $J_{1,2}$ 2.9, $J_{2,3}$ 4.7, $J_{2,OH}$ 7 Hz, H-2), 3.56 (m, after addition of D_2O dd, 1 H, $J_{4,5b}$ 4.6 Hz, H-5b), 3.45 (m, after addition of D_2O dd, 1 H, $J_{4,5a}$ 5.6, $J_{5a,5b}$ 11.5 Hz, H-5a), 3.23 (s, 3 H, OCH_3). For ^{13}C NMR data see Table 1. CIMS: *m/z* 165 $[M+H]^+$, 133 $[M-OCH_3]^+$.

Methyl α-D-lyxopyranoside (**7**).—Compound **6** (0.0928 g, 0.56 mmol) was refluxed for 30 min with 2% methanolic hydrogen chloride (2 mL). The mixture was diluted with MeOH (4 mL), then neutralised [Amberlyte IRA 45 resin (OH form)], filtered and evaporated. Flash chromatography (6:1 $CHCl_3$–MeOH) of the residue gave pure **7** (0.084 g, 90%) as a white solid. Recrystallised from EtOAc, **7** had mp 104–105 °C, lit. 108–109 °C [11]; $[\alpha]_D$ +56.5° (*c* 0.6, H_2O), lit. +52° (*c* 0.6, H_2O) [11]; ^{1}H NMR (Me_2SO-d_6): δ 4.80 and 4.77 (3 d, exchangeable with D_2O, each 1 H, 3 OH), 4.65, 4.41 (d, 1 H, $J_{1,2}$ Hz, H-1), 3.36–3.60 (m, 4 H, H-2, H-3, H-4, H-5b), 3.24 (s, 3 H, OC**H**$_3$), 3.20 (m, 1 H, H-5a). For ^{13}C NMR data see Table 1. CIMS: *m/z* 165 $[M+H]^+$, 133 $[M-OCH_3]^+$.

Benzyl 3,5-di-O-benzyl-α- (**8**) *and β-D-lyxofuranoside* (**9**).—To a solution of **4** (0.6142 g, 1.5 mmol) in dry benzene (10 mL) was added a solution of NaOBn in BnOH (15 mL of 0.2 M solution, 3.0 mmol), and the resulting mixture was stirred for 20 h at rt. The mixture was then poured into satd aq NH_4Cl (15 mL) and extracted with EtOAc (3 × 10 mL). The extract was dried and evaporated, and the remaining benzyl alcohol was removed by distillation in high vacuum (oil pump). Column chromatography (19:1 toluene–EtOAc) of the residue (0.8958 g) furnished the pure α anomer **8** (0.2439 g, 38.6%) as a colourless syrup: $[\alpha]_D$ +112.9° (*c* 1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.44–7.32 (m, 15 H, 3 Ph), 5.13 (s, 1 H, H-1), 4.81–4.48 (m, 7 H, 3 C**H**$_2$Ph and H-3), 4.41 (m, 2 H, $J_{3,4}$ 6 Hz, OH and H-4), 4.20 (dd, 1 H, $J_{2,OH}$ 10.2, $J_{2,3}$ 4.8 Hz, H-2), 3.74 (dd, 1 H, $J_{4,5b}$ 3.2 Hz, H-5b), 3.66 (dd, 1 H, $J_{4,5a}$ 2.4, $J_{5a,5b}$ 10.5 Hz, H-5a); ^{13}C NMR ($CDCl_3$): δ 137.71 and 137.60 (aromatic), 137.15, 128.34, 127.83, 127.81, 127.76, 127.72, 127.65, 106.49 (C-1), 77.79 (C-3), 77.51 (C-4), 72.08 (C-2), 73.81 and 72.44 (3 **C**H_2Ph), 69.15, 67.82 (C-5). CIMS: *m/z* 421 $[M+1]^+$, 313 $[M-OBn]^+$. Further elution with 4:1 toluene–EtOAc gave the pure β anomer **9** (0.0466 g; 7.4%) as a colourless syrup: $[\alpha]_D$ +82.1° (*c* 1.43, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.45–7.25 (m, 15 H, 3 Ph), 5.25 (d, 1 H, H-1), 4.96–4.54 (m, 6 H, 3 PhC**H**$_2$), 4.51 (m, 1 H, H-4), 4.31 (m, 1 H, $J_{1,2}$ 4.7 Hz, H-2), 4.08 (dd, 1 H, $J_{2,3}$ 4.1, $J_{3,4}$ 6 Hz, H-3), 3.80 (dd, 1 H, $J_{4,5b}$ 4.3 Hz, H-5b), 3.72 (dd, 1 H, $J_{5a,5b}$ 10.6, $J_{4,5a}$ 6.7 Hz, H-5a), 2.86 (d, exchangeable with D_2O, 1 H, $J_{2,OH}$ 7.6 Hz, OH); ^{13}C NMR ($CDCl_3$): δ 138.13 and 137.88 (aromatic), 137.07, 128.43, 128.29, 128.28, 128.02, 127.92, 127.68, 127.58, 127.51, 127.45, 99.86 (C-1), 83.55 (C-3), 77.49 (C-4), 77.04 (C-2), 73.80 and 71.38 (3 Ph**C**H_2), 69.88, 68.99 (C-5). CIMS: *m/z* 421 $[M+1]^+$, 313 $[M-OBn]^+$.

3,5-Di-O-benzyl-D-lyxofuranose (**10**).—(a) The 2-*O*-mesyl derivative **4** (0.3317 g, 0.80 mmol) was dissolved in *N*,*N*-dimethylformamide (3 mL), and 0.1 M aq NaOH (8 ml) was added slowly at rt during 1 h, whereupon the solution became alkaline to phenolphthalein. The mixture was stirred at rt for an additional 0.5 h, then neutralized with glacial AcOH and concentrated by co-distillation with toluene. The syrupy residue was purified by flash column chromatography (4:1 toluene–EtOAc) to afford syrupy **10** (0.1995 g, 75%) as a 1:1 mixture of anomers.

(b) A solution of **5** (0.2082 g, 0.61 mmol) in 70% aq AcOH (10 mL) was stirred at reflux temperature for 8 h, then concentrated and co-evaporated with toluene. The syrupy residue (0.1894 g) was purified by flash chromatography (1:1 hexane–EtOAc) to give pure **10** (0.1408 g, 70%) as a colourless syrup: $[\alpha]_D$ + 24.6° (*c* 1.32, $CHCl_3$); ^1H NMR ($CDCl_3$ + D_2O): δ 7.42–7.28 (m, 20 H, 4 Ph), 5.34 (s, 1 H, H-1α), 5.17 (d, 1H, H-1β), 4.81–4.47 (m, 9 H, H-3 and 4 PhC**H**$_2$), 4.42 (dt, 1 H, $J_{3,4}$ 7.9 Hz, H-4α), 4.20 (m, 2 H, H-3α and H-4β), 4.10 (d, 1 H, $J_{2,3}$ 4.7 Hz, H-2α), 4.05 (t, 1 H, $J_{1,2}$ 3.9, $J_{2,3}$ 4.6 Hz, H-2β), 3.75–3.57 (m, 4 H, α anomer: $J_{4,5}$ 2.7 Hz, β anomer: $J_{4,5}$ 4.2 Hz, 2 H-5α and 2 H-5β); ^{13}C NMR ($CDCl_3$): δ 137.65–127.81 (aromatic), 102.14 (C-1α), 96.82 (C-1β), 77.77 and 77.55 (C-3β and C-4β), 77.44 (C-3α), 73.80 (Ph**C**H$_2$), 73.34 (C-4α), 72.73 (Ph**C**H$_2$), 72.55 (C-2α), 70.09 (C-2β), 68.57 (C-5β), 67.91 (C-5α); CIMS: *m*/*z* 331 $[M + H]^+$, 313 $[M–OH]^+$.

D-*Lyxose* (**11**).—Compound **10** (0.3506 g, 1.06 mmol) was hydrogenated over 10% Pd–C (0.2348 g) in EtOH (15 mL) at rt for 18 h. The mixture was filtered and the catalyst was washed with EtOH. The filtrate and washings were combined and concentrated to a colourless syrup (0.1564 g; 98%). Trituration with cooled EtOH (+4 °C) gave pure D-lyxose (**11**): mp 104–105 °C, lit. 106–107 °C [13]; $[\alpha]_D$ −13.6° (*c* 1.5, H_2O), lit. −14° (*c* 0.8, H_2O) [13]. For ^{13}C NMR data see Table 1.

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