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Convenient preparation of L-*arabino*-hexos-5-ulose derivatives from lactose☆

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Abstract

2,6-Di-*O*-benzyl- (**9**), 2-*O*-benzyl-3,4-*O*-isopropylidene- (**19**), and 2-*O*-benzyl-6-*O*-*m*-chlorobenzoyl-L-*arabino*-hexos-5-ulose (**20**) have been prepared using 4′-deoxy-4′-eno- and 6′-deoxy-5′-eno lactose dimethyl acetal derivatives **7** and **14** as key intermediates. The synthesis of enol ethers **7** and **14** has been performed with good yields by base-promoted elimination of acetone or *p*-toluenesulfonic acid from 2′,6′-di-*O*-benzyl-, and 6′-*O*-*p*-toluenesulfonyl-2,3:5,6:3′,4′-tri-*O*-isopropylidenelactose dimethyl acetal, respectively. The epoxidation with MCPBA of **7** and **14** in methanol or dichloromethane furnishes C-5′-methoxy and C-5′-*m*-chlorobenzoyloxy derivatives, easily transformed with good yields into L-*arabino* 5-ketoaldohexoses **9**, **19** and **20**.

Keywords: L-*arabino*-Hexos-5-uloses; Lactose; Ketopyranose glycals; Epoxidation

1. Introduction

Monosaccharides having two unprotected carbonyl functions (dialdoses, diuloses and aldosuloses) have long been known as intermediates in several degradation reactions as well as constituents of few naturally occurring compounds.[2] Little attention has, however, been devoted to the class of hexos-5-uloses (**3**), the sole known member of which was, until 20 years ago, the D-*xylo* stereoform.[3–6] More recently, these compounds have attracted attention as synthetic precursors both of 1,5-dideoxy-1,5-iminoalditols[7,8] (1-deoxynojirimycin and its stereo analogues, **4**) and cyclitols[9,10] (**5**) (Scheme 1). Two conceptually similar general approaches to hexos-5-uloses (Scheme 1) are based on the epoxydation of 4-deoxy-hex-4-enopyranosides[11,12] (**1**) or 6-deoxy-hex-5-enopyranosides[13] (**2**), two classes of unsaturated sugars, that can be considered as endo- or exo-ketopyranose glycals, respectively.

As a part of an ongoing project on the chemical valorisation of milk-derived sugars,[1] we present here a convenient preparation from lactose of some differently protected L-*arabino*-hexos-5-ulose derivatives,[14] some of which have been previously used for the stereoselective synthesis of 1-deoxy-D-galactostatin[8] and *epi*-inositol.[9]

2. Results and discussion

A first approach to 2,6-di-*O*-benzyl-L-*arabino*-hexos-5-ulose (**9**) was based on the preparation of the enol ether **7** (Scheme 2) by treatment of 2′,6′-di-*O*-benzyl-2,3:5,6:3′,4′-tri-*O*-isopropylidenelactose dimethyl acetal (**6**)[15] with *t*-BuOK in DMF following the method previously applied[11] to the methyl β-galactopyranoside analogue.

The yield of the expected 4′-hexeno derivative **7** was, however, depressed by the formation of two by-products, the disaccharide diene **10** and the known[16] D-glucose derivative **11**.

☆ See Ref. 1.

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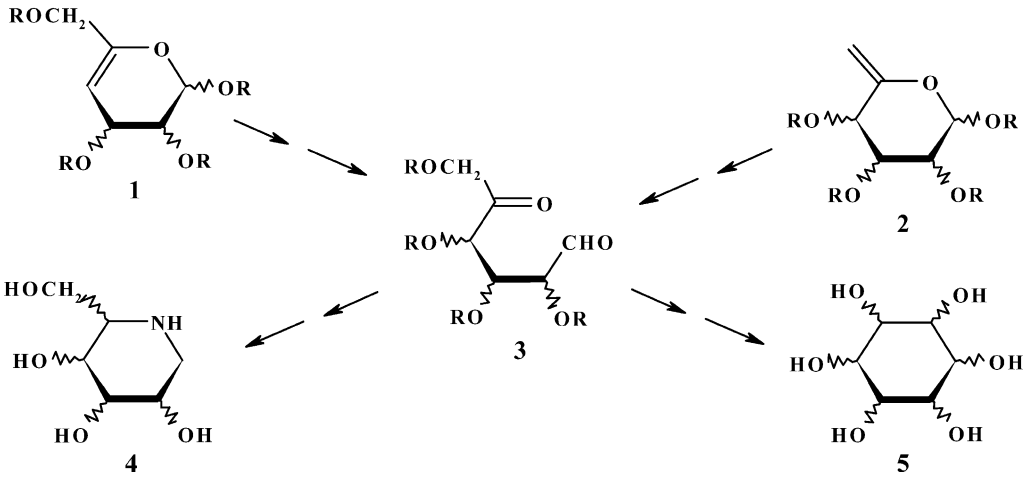
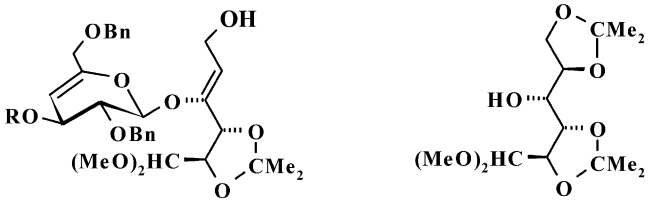


Scheme 1.



Under selected reaction conditions (rt, 24 h, Table 1, run 4) and quenching the reaction with a large excess of triethylammonium chloride before concentration of the solvent, **7** was obtained in good yield (65%), after chromatographic separation from the two side-products **10** (10%) and **11** (15%).

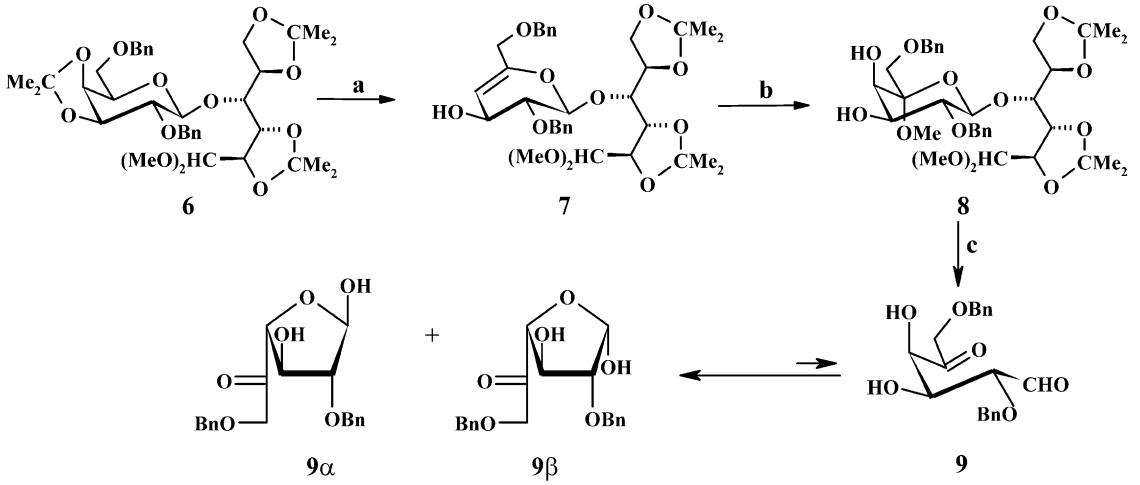
The structure of **7** was firmly confirmed through NMR analysis; in particular, the hex-4-enopyranoside ring shows diagnostic ^{1}H parameters very close to those reported for the corresponding methyl glycoside,[11] suggesting also a similar conformational situation, i.e., a large preference ($>80\%$) of the conformer having three axially oriented substituents.[17] The location in 4,5

Table 1
Products distribution[a] in the base-promoted acetone elimination from **6**.

Run	Reaction conditions[b]	7	10	11
1	80 °C, 2 h		15	35
2	50 °C, 1 h	21	18	55
3	rt, 24 h	48	15	12
4	rt, 24 h, then Et_3NHCl	65	10	15

[a] Isolated yields after flash chromatography.
[b] In all cases, the same excess of *t*-BuOK (10 equiv) and the same concentration of **6** (0.1 M) were used (see Section 3).

of the other double bond of the diene **10** was deduced from the deshielding of the C-6 carbon atom ($\Delta\delta$ 8.2 ppm) with respect to that of **7**, indicating that the second elimination of acetone involves the 5,6-*O*-isopropylidene group rather than the more hindered 3,4 one. It should also be noted that the formation of **11**, caused by an interglycoside bond cleavage, rather unexpected in



Scheme 2. (a) *t*-BuOK, DMF; (b) MCPBA, MeOH; (c) CF_3COOH, 4:1 CH_3CN–water.

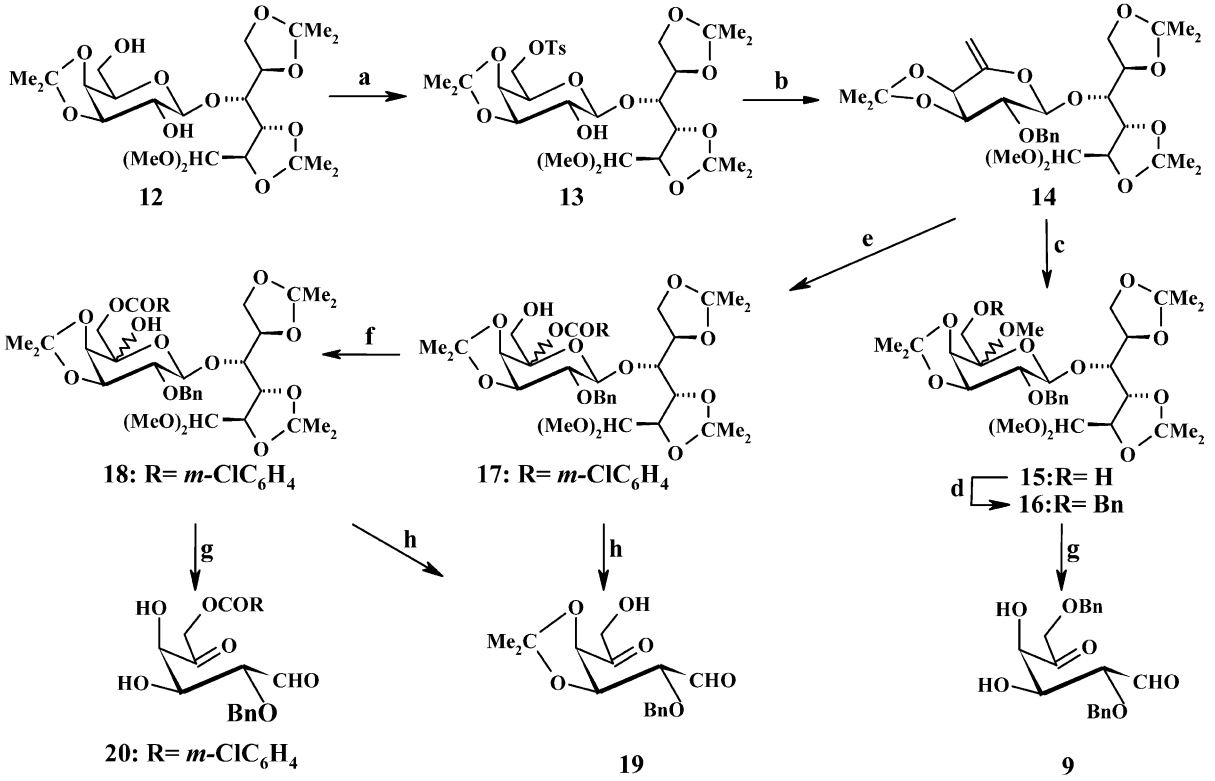
the strong basic reaction conditions, was also previously observed during the $LiAlH_4$ reduction of 2′-oximino disaccharide derivatives of **6**,[18] suggesting the presence, in both cases, of a base-promoted degradative pathway of the non-reducing ring.

The epoxidation of **7** with MCPBA in methanol led in 67% yield to the diol **8** (Scheme 2), as a result of a C-5′ regioselective and anti-stereoselective "in situ" opening of an intermediate epoxide formed, in turn, with a complete stereospecific manner owing to the syn-directing effect of the free allyl OH group of **7**.[11] The C-5′ configuration of **8** was not directly attributed, but is reasonably assigned as (*R*) by analogy with the product obtained in the epoxidation–methanolysis of the methyl monosaccharide analogous.[11]

2,6-Di-*O*-benzyl-L-*arabino*-hexos-5-ulose (**9**) was, finally, obtained by treatment of **8** with CF_3COOH in CH_3CN–water (50 °C, 14 h) and isolated in high yield (83%) after separation from D-glucose by extraction with EtOAc. As previously reported,[11] **9** was present in CD_3CN soln as an anomeric mixture (**9α**:**9β** ≈ 4:1) of 1,4-furanose tautomers.

The second way to L-*arabino*-hexos-5-ulose derivatives (Scheme 3) follows the Murphy's approach[13] based on the epoxidation of a 6-deoxy-hex-5-enopyranoside. An efficient preparation of the enol ether disaccharide **14** was made starting by the previously unreported 6′-*O*-tosylate **13**, easily obtained with an overall 73% yield by selective tosylation (TsCl, CH_2Cl_2–Py, rt, 48 h) of the crude diol **12**, available by a two-step, "one-pot" procedure of acetonation–demethoxyisopropylation of lactose.[15] The treatment of **13** with NaH in DMF followed, after 3 h, by addition of BnBr led directly to the fully protected hex-5′-enopyranoside **14**, as a crystalline solid in 78% yield.

The epoxidation of **14** with MCPBA in CH_2Cl_2 led with almost quantitative yield to a crude product, the ^1H NMR analysis of which (CD_3CN) showed four separated doublets characteristic for H-1′ at δ 5.35, 5.27, 5.19, and 5.14 with relative intensities 60:19:7:14. NMR parameters of the more abundant component suggested a structure corresponding to a 5′-*C*-*m*-chlorobenzoate **17**. We suppose that one of the other three components of the crude mixture could correspond to the other C-5′ anomer **17**, even if any structural determination of the three minor components was not possible on the basis of the NMR analysis. An attempt at separation of this crude mixture through silica gel chromatography led to recovery of a different product identified as a 4:1 mixture of 6′-*O*-*m*-chlorobenzoates **18** (81% yield from **14**), evidently arising by a silica gel promoted intramolecular shift of the benzoate group from the anomeric OH-5′ to the primary OH-6′ function. The structure of **18** was confirmed by NMR analysis, in particular the migration of the benzoate group was deduced from the contemporary ^{13}C NMR deshielding of the C-6′ meth-



Scheme 3. (a) TsCl-Py; (b) BnBr, NaH, DMF; (c) MCPBA, MeOH; (d) BnBr, 18-crown-6, KOH, THF; (e) MCPBA, CH_2Cl_2; (f) SiO_2 chromatography; (g) CF_3COOH; (h) NEt_3, 5:1 MeOH–water.

ylene ($\Delta\delta$ 5.0 ppm) and shielding of the C-5′ methine ($\Delta\delta$ 8.7 ppm), with respect to **17**.

It is worthy of note that the expected spontaneous scission of **18** into the alcohol **11** and the pertinent dicarbonyl hexose (**19**) was not observed either during the chromatographic process or the storage. The formation of a stable glycopyranoside having a C-5 hemiacetal group has been observed in a specific case by Murphy,[13] as an apparent consequence of the pattern of protecting groups.

The epoxidation–methanolysis of **14** (Scheme 3), as described above for **7**, took place in a manner which was not completely selective leading, after flash chromatography, to an approximately 4:1 C-5′ anomeric mixture of 1′,5′-bis-glycosides **15**, obtained as the main reaction products with 70% yield, and to minor amounts (20%) of the 6′-*O*-*m*-chlorobenzoate **18**, evidently derived by the above described transformation over silica of the benzoates **17**, in turn arising from the opening of the intermediate epoxides by the *m*-chlorobenzoate present in the reaction medium.

The stereochemistry at position C-5′ of **15**, **17** or **18** could not be inferred by routine NMR analysis, owing to the absence of diagnostic vicinal proton couplings. The absolute configuration of the two bis-glycosides **15** formed during the epoxidation–methanolysis of **14** (Scheme 3) was, however, assigned transforming **8** into the C-5′ anomerically pure (5*R*)-**16** by acetonation (DMP, TsOH) and verifying (NMR) that it corresponds to the major constituent of the anomeric mixture of **16** obtained by benzylation of **15**.

The mixture of bis-glycosides **16** was, finally, hydrolysed as described above for **8**, to give with high yield **9** (Scheme 3).

In order to obtain differently protected L-*arabino*-hexos-5-ulose derivatives, compound **17** was treated with Et_3N in aq MeOH (Scheme 3), as reported[19] for the hydrolysis of benzoate groups. In these conditions, the deprotection of the C-5′-hemiacetal OH was followed by the loss of the protected D-glucose moiety (**11**) with contemporary formation of the dicarbonyl sugar **19**. An identical result was obtained submitting the 6′-*O*-benzoate **18** to the same treatment. Evidently, the presence of NEt_3 considerably accelerates the chain-ring tautomerism of the reducing unit, leading to the unmasking of the ketone function. The chromatographic separation of the reaction products gave with acceptable yield (65%) 2-*O*-benzyl-3,4-*O*-isopropylidene-L-*arabino*-hexos-5-ulose (**19**) as an approximately 11:9 mixture of the two tautomers **19a** and **19b** (Scheme 4). These bicyclic tautomers, derived from a first hemiacetalisation of the aldehyde group with OH-6 followed by a second one between the 5-keto group and the hemiacetalic OH-1, were recently identified by Murphy[13] as the sole components of the tautomeric equilibrium of **19**.

The 4:1 mixture of 6′-*O*-*m*-benzoates **18** was, finally, hydrolysed with CF_3COOH (Scheme 3) in CH_3CN–H_2O (rt, 1 h) to give, after separation from D-glucose by extraction with EtOAc and chromatography purification, 2-*O*-benzyl-6-*O*-*m*-chlorobenzoyl-L-*arabino*-hexos-5-ulose **20** (80% yield), the NMR spectra of which revealed that it exists in CD_3CN–D_2O exclusively as a mixture of the α- and β-1,4-furanose forms (α/β ratio ≈ 7:3) (Scheme 4) analogously to the above described 2,6-di-*O*-benzyl derivative **9**.

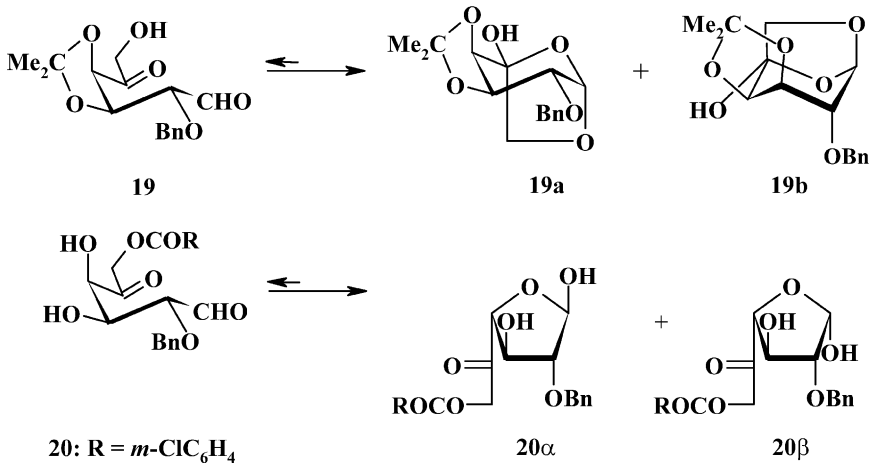
3. Experimental

3.1. General methods

Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 polarimeter at 20 ± 2 °C. ^{1}H NMR spectra were recorded with a Bruker AC 200 instrument at 200 MHz and with a Varian Unity Inova instrument at 500 MHz in the stated solvent (Me_4Si was used as the internal standard). ^{13}C NMR spectra were recorded with a Bruker AC 200 instrument at 50 MHz. Assignments were made, when possible, with the aid of DEPT experiments, for comparison with values for known compounds and applying the known[20] additivity rules, and, in the case of anomeric mixtures, referring to the differences in the peak intensities. All reactions were followed by TLC on Kieselgel 60 F_{254} with detection by UV light and/or with ethanolic 10% phosphomolybdic or sulphuric acid, and heating. Kieselgel 60 (E. Merck, 70–230 and 230–400 mesh, respectively) was used for column and flash chromatography. Solvents were dried by distillation according to standard procedure,[21] and storage over 4 Å molecular sieves activated at least 24 h at 400 °C. $MgSO_4$ was used as the drying agent for solns.

3.2. Base-promoted acetone elimination from 4-*O*-(2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-β-D-galactopyranosyl)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (6)

A soln of **6**[15] (3.84 g, 5.58 mmol) in 55 mL of anhyd DMF was treated under stirring at rt with solid commercial *t*-BuOK (Fluka) (6.26 g, 55.9 mmol). After 24 h stirring, the starting material was consumed (TLC, 1:1 hexane–EtOAc, R_f 0.60) and the mixture was treated with solid triethylammonium chloride (10.4 g, 75.4 mmol), stirred for 20 min and concentrated under diminished pressure. The residue was partitioned between brine (120 mL) and CH_2Cl_2 (120 mL), the water phase extracted further with CH_2Cl_2 (4 × 20 mL) and the combined organic phases were dried and concentrated to dryness to give a crude residue (4.78 g),



Scheme 4.

containing three components with R_f 0.51, 0.41, and 0.12 (TLC, 1:1 hexane–EtOAc). The flash chromatography of the crude product eluting in the order with 7:3 hexane–EtOAc, 1:1 hexane–EtOAc and 1:4 hexane–EtOAc, led to the three following compounds.

3.2.1. 4-*O*-(2,6-Di-*O*-benzyl-4-deoxy-α-L-*threo*-hex-4-enopyranosyl)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (7). Clear syrup, (2.29 g, 65% yield), $[\alpha]_D$ −38.3° (*c* 1.5, $CHCl_3$); R_f 0.51 (1:1 hexane–EtOAc); ^{1}H NMR (200 MHz, CD_3CN): δ 7.37–7.31 (m, 10 H, aromatic H), 5.60 (dd, 1 H, $J_{1',2'}$ 3.3 Hz, $J_{1',3'}$ 1.2 Hz, H-1′), 5.18 (m, 1 H, H-4′), 4.67 (s, 2 H, CH_2Ph), 4.54, and 4.50 (AB system, 2 H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.33 (d, 1 H, $J_{1,2}$ 6.3 Hz, H-1), 4.26 (dddd, 1 H, $J_{4,5}$ 3.2 Hz, $J_{5,6a}$ 6.3 Hz, $J_{5,6b}$ 7.4 Hz, H-5), 4.14 (dd, 1 H, H-4), 4.07 (dd, 1 H, $J_{3,4}$ 1.5 Hz, H-3), 3.99 (dd, 1 H, $J_{2,3}$ 5.2 Hz, H-2), 3.95 (ddd, 1 H, $J_{3',4'}$ 4.9 Hz, $J_{2',3'}$ 2.7 Hz, H-3′), 3.93 (m, 2 H, H-6a, H-6b), 3.92 (m, 2 H, $J_{4',6'a}$ = $J_{4',6'b}$ 0.3 Hz, H-6′a, H6′b), 3.75 (ddd, 1 H, $J_{2',4'}$ 1.27 Hz, H-2′), 3.38, 3.34 (2 s, each 3 H, 2 OMe); 1.36, 1.35, 1.31, 1.30 (4 s, each 3 H, 2 CMe_2). ^{13}C NMR (50 MHz, CD_3CN): δ 148.8 (C-5′), 139.4, 139.2 (2 aromatic C), 129.3–128.4 (aromatic CH), 110.9, 108.8 (2 *C*Me_2), 106.4 (C-1), 102.5 (C-4′), 99.0 (C-1′), 78.6 (C-5), 78.4 (C-3), 77.5 (C-2), 77.2 (C-2′), 75.1 (C-4), 73.0, 72.8 (2 *C*H_2Ph), 69.9 (C-6′), 65.6 (C-6), 63.8 (C-3′), 56.7, 54.7 (2 OMe), 27.3, 27.3, 26.8, 25.3 (2 CMe_2). Anal. Calcd for $C_{34}H_{46}O_{11}$: C, 64.75; H, 7.35. Found: C, 65.11; H, 7.29.

3.2.2. 2,3:5,6-Di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (11). Syrup, identical to an authentic sample,[18] (0.26 g, 15% yield), R_f 0.41 (1:1 hexane–EtOAc). NMR data were in good agreement with the reported ones.[16]

3.2.3. 4-*O*-(2,6-Di-*O*-benzyl-4-deoxy-α-L-*threo*-hex-4-enopyranosyl)-2,3-*O*-isopropylidene-*aldehydo*-L-*threo*-hex-4-enose dimethyl acetal (10). Syrup (0.32 g, 10% yield), $[\alpha]_D$ −59.6° (*c* 0.5, $CHCl_3$); R_f 0.12 (1:1 hexane–EtOAc); ^{1}H NMR (200 MHz, CD_3CN): δ 7.39–7.25 (m, 10 H, aromatic H), 5.70 (dd, 1 H, $J_{1',2'}$ 3.4 Hz, $J_{1',3'}$ 1.0 Hz, H-1′), 5.41 (t, 1 H, $J_{5,6a} = J_{5,6b}$ 7.6 Hz, H-5), 5.16 (dd, 1 H, $J_{3',4'}$ 4.4 Hz, $J_{4',6'a} = J_{4',6'b}$ 0.7 Hz, H-4′), 4.82 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.76, and 4.68 (AB system, 2 H, $J_{A,B}$ 11.7 Hz, CH_2Ph), 4.49 (s, 2 H, CH_2Ph), 4.39 (d, 1 H, $J_{2,3}$ 6.3 Hz, H-3), 4.08 (m, 2 H, H-2, H-3′), 4.06 (m, 2 H, H-6a, H-6b), 3.91 (bs, 2 H, H-6′a, H-6′b), 3.80 (ddd, 1 H, $J_{2',3'}$ 1.2 Hz, H-2′), 2.91 (d, 1 H, $J_{3',OH}$ 4.5 Hz, OH-3′), 2.73 (bs, 1 H, OH-6), 3.31, 3.28 (2 s, each 3 H, 2 OMe), 1.36, 1.35 (2 s, each 3 H, CMe_2). ^{13}C NMR (50 MHz, CD_3CN): δ 150.8 (C-4), 148.8 (C-5′), 139.4, 139.3 (2 aromatic C), 129.3–127.3 (aromatic CH), 111.0 (*C*Me_2), 110.6 (C-5), 105.5 (C-1), 103.3 (C-1′), 96.0 (C-4′), 78.1, 77.1 (C-2, C-2′), 74.4 (C-3), 72.9, 71.6 (2 *C*H_2Ph), 69.9 (C-6′), 64.3 (C-3′), 57.4 (C-6), 55.3, 54.7 (2 OMe), 27.2, 26.6 (CMe_2). Anal. Calcd for $C_{31}H_{40}O_{10}$: C, 65.02; H, 7.04. Found: C, 65.16; H, 7.11.

3.3. 4-*O*-[(5*R*)-2,6-Di-*O*-benzyl-5-*C*-methoxy-α-L-*arabino*-hexopyranosyl]-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (8)

A solution of **7** (3.00 g, 4.76 mmol) in MeOH (30 mL) was cooled at 0 °C and treated, under stirring, with commercial (Fluka) 70% MCPBA (1.76 g, 7.16 mmol). The mixture was slowly warmed at rt, with continuous stirring until **7** was consumed (3 h, TLC, 1:1 hexane–EtOAc); the reaction mixture was made alkaline by adding satd aq $NaHCO_3$ (10 mL), stirred for 30 min, concentrated to dryness. The semisolid residue was partitioned between water (30 mL) and CH_2Cl_2 (50 mL) and the aqueous phase extracted with CH_2Cl_2 (5 × 50 mL); the combined organic extracts were dried ($MgSO_4$) and concentrated to give a crude residue (2.87 g). A flash chromatographic purification (1:1

hexane–EtOAc) give pure **8** (2.16 g, 67% yield) as a white solid, mp 100–103 °C (from EtOAc), $[\alpha]_D$ +2.1° (*c* 0.9, $CHCl_3$); R_f 0.38 (1:1 hexane–EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.37–7.26 (m, 10 H, aromatic H), 4.90 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1′), 4.95, and 4.57 (AB system, 2 H, $J_{A,B}$ 12.2 Hz, CH_2Ph), 4.65, and 4.50 (AB system, 2 H, $J_{A,B}$ 11.4 Hz, CH_2Ph), 4.49 (dd, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.32 (d, 1 H, $J_{1,2}$ 6.4 Hz, H-1), 4.23 (m, 1 H, H-5), 4.18 (dd, 1 H, $J_{6a,6b}$ 8.5 Hz, $J_{5,6b}$ 5.8 Hz, H-6b), 4.06–3.88 (m, 5 H, H-3′, H-4′, H-3, H-4, H-6a), 3.57, and 3.50 (AB system, 2 H, $J_{A,B}$ 10.4 Hz, H-6′a, H-6′b), 3.48 (dd, 1 H, $J_{2',3'}$ 9.5 Hz, H-2′), 2.51 (d, 1 H, *J* 2.6 Hz, OH), 2.44 (d, 1 H, *J* 3.8 Hz, OH), 3.30, 3.28, 3.25 (3 s, each 3 H, 3 OMe), 1.43, 1.42, 1.41, 1.32 (4 s, each 3 H, 2 CMe_2). ^{13}C NMR (50 MHz, $CDCl_3$): δ 138.4, 137.7 (2 aromatic C), 128.5–127.7 (aromatic CH), 110.0, 108.5 (2 CMe_2), 105.5 (C-1), 100.5 (C-5′), 98.9 (C-1′), 79.0, 77.7, 77.5 (C-2′, C-3, C-5), 74.6, 74.4 (C-2, C-4), 74.5, 73.4 (2 CH_2Ph), 70.1 (C-3′), 69.4 (C-4′), 65.2, 64.9 (C-6, C-6′), 55.7, 52.7 (2 OMe-1), 48.0 (OMe-5), 27.3, 26.6, 26.3, 25.1 (2 CMe_2). Anal. Calcd for $C_{35}H_{50}O_{13}$: C, 61.93; H, 7.42. Found: C, 62.13; H, 7.49.

3.4. 4-*O*-(3,4-*O*-Isopropylidene-6-*O*-*p*-toluenesulfonyl-β-D-galactopyranosyl)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (13)

A crude sample of **12** obtained, as previously described,[15] by acetonation–demethoxyisopropylation of lactose (6.91 g, 20.2 mmol) was dissolved in a 1:1 mixture of pyridine and CH_2Cl_2 (66 mL) and treated at rt under stirring with solid TsCl (4.82 g, 28.0 mmol). After 24 h the diol **12** was completely consumed (TLC, 3:7 hexane–EtOAc); the mixture was treated with satd aq $NaHCO_3$ (40 mL), stirred for 15 min and extracted with CH_2Cl_2 (4 × 50 mL). The organic extracts were collected, dried ($MgSO_4$) and concentrated by repeated co-evaporation with toluene (3 × 50 mL), the residue partitioned between CH_2Cl_2 (40 mL) and water (40 mL), and the aqueous phase extracted with CH_2Cl_2 (3 × 40 mL). The organic phases were collected, dried ($MgSO_4$) and concentrated under diminished pressure. The crude residue was directly applied to a flash chromatography column eluting with 3:7 hexane–EtOAc+1‰ Et_3N to give pure **13** as a foam solid (9.77 g, 73% yield from lactose), mp 57–59 °C, $[\alpha]_D$ +15.8° (*c* 1.1, $CHCl_3$); R_f 0.47 (3:7 hexane–EtOAc); ^{1}H NMR (200 MHz, CD_3CN): δ 7.81, 7.45 (2 d, each 2 H, *J* 8.1 Hz, aromatic H), 4.40 (d, 1 H, $J_{1',2'}$ 8.1 Hz, H-1′), 4.38 (dd, 1 H, $J_{6'a,6'b}$ 12.1 Hz, $J_{5',6'b}$ 6.2 Hz, H-6′b), 4.32 (dd, 1 H, $J_{5',6'a}$ 6.4 Hz, H-6′a), 4.23 (m, 1 H, H-5), 4.15–3.91 (m, 8 H, H-3′, H-4′, H-5′, H-1, H-2, H-3, H-6a, H-6b), 3.84 (dd, 1 H, $J_{3,4}$ 1.6 Hz, $J_{4,5}$ 4.7 Hz, H-4), 3.30 (ddd, 1 H, $J_{2',3'}$ 6.9 Hz, $J_{2',OH}$ 3.1 Hz, H-2′), 3.60 (d, 1 H, OH-2′), 3.38, 3.35 (2 s, each 3 H, 2 OMe), 2.44 (s, 3 H, *Me*Ph), 1.39, 1.36, 1.32, 1.31, 1.29, 1.22 (6 s, each 3 H, 3 CMe_2). ^{13}C NMR (50 MHz, CD_3CN): δ 145.6, 133.3 (2 aromatic C), 131.1, 128.8 (aromatic CH), 110.6, 110.5, 109.7 (3 CMe_2), 106.1 (C-1), 104.0 (C-1′), 80.0, 78.4, 77.6, 77.9, 77.6 (C-2, C-3, C-5, C-3′), 76.3 (C-4), 74.4, 73.8 (C-2′, C-4′), 71.3 (C-5′), 69.5 (C-6′), 66.0 (C-6), 56.4, 54.3 (2 OMe), 28.2, 27.5, 27.0, 26.5, 26.4, 25.2 (3 CMe_2), 21.7 (*Me*Ph). Anal. Calcd for $C_{30}H_{46}O_{14}S$: C, 54.37; H, 7.00. Found: C, 54.11; H, 7.10.

3.5. 4-*O*-(2-*O*-Benzyl-6-deoxy-3,4-*O*-isopropylidene-α-L-*arabino*-hex-5-enopyranosyl)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (14)

A suspension of pre-washed (hexane) 60% NaH in mineral oil (637 mg, 16.3 mmol) in dry DMF (20 mL) was cooled at 0 °C and treated under argon with a soln of **13** (2.17 g, 3.27 mmol) in dry DMF (15 mL). The mixture was gently warmed at rt, left under stirring until **13** was consumed (3 h, TLC, 3:7 hexane–EtOAc), treated with neat BnBr (0.8 mL, 6.54 mmol) and further stirred for 45 min. The reaction mixture was cooled at 0 °C, treated with crushed ice (30 mL) and extracted with Et_2O (5 × 20 mL); the collected organic extracts were dried ($MgSO_4$) and concentrated to give a crude residue (2.03 g), that was directly subjected to a flash chromatographic purification, eluting with 7:3 hexane–EtOAc+1‰ Et_3N, to give pure **14** (1.48 g, 78% yield) as a white crystalline solid, mp 93–95 °C (from hexane); $[\alpha]_D$ +21.9° (*c* 1.2, $CHCl_3$); R_f 0.28 (7:3 hexane–EtOAc); ^{1}H NMR (200 MHz, CD_3CN): δ 7.37–7.30 (m, 5 H, aromatic H), 4.94 (d, 1 H, $J_{1',2'}$ 7.6 Hz, H-1′), 4.75 (s, 1 H, H-6′a), 4.81, and 4.71 (AB system, 2 H, $J_{A,B}$ 11.9 Hz, CH_2Ph), 4.66 (s, 1 H, H-6′b), 4.63 (d, 1 H, $J_{3',4'}$ 7.0 Hz, H-4′), 4.40 (dd, 1 H, $J_{2,3}$ 7.1 Hz, H-2), 4.38 (d, 1 H, $J_{1,2}$ 6.2 Hz, H-1), 4.22 (m, 1 H, H-5), 4.21 (dd, 1 H, $J_{2',3'}$ 7.6 Hz, H-3′), 4.10 (dd, 1 H, $J_{3,4}$ 1.3 Hz, H-3), 4.05 (dd, 1 H, $J_{6a,6b}$ 8.5 Hz, $J_{5,6a}$ 6.1 Hz, H-6a), 3.96 (dd, 1 H, $J_{4,5}$ 5.3 Hz, H-4), 3.93 (dd, 1 H, $J_{5,6b}$ 6.4 Hz, H-6b), 3.43 (t, 1 H, $J_{1',2'} = J_{2',3'}$ 7.6 Hz, H-2′); 3.41, 3.39 (2 s, each 3 H, 2 OMe), 1.37, 1.36, 1.35, 1.34, 1.33, 1.28, (6 s, each 3 H, 3 CMe_2). ^{13}C NMR (50 MHz, CD_3CN): δ 154.3 (C-5′), 139.4 (aromatic C), 129.1–127.5 (aromatic CH), 111.0, 110.6, 109.2 (3 CMe_2), 98.9 (C-6′), 106.7 (C-1), 103.0 (C-1′), 80.1 (C-2′), 78.5, 78.1, 77.9 (C-3′, C-3, C-4), 76.9, 76.3 (C-2, C-5), 74.17 (2 CH_2Ph), 73.9 (C-4′), 66.3 (C-6), 56.5, 54.3 (2 OMe), 27.7, 27.5, 27.2, 26.9, 26.0, 25.5 (3 CMe_2). Anal. Calcd for $C_{30}H_{44}O_{11}$: C, 62.05; H, 7.64. Found: C, 61.85; H, 7.52.

3.6. 4-*O*-[(5*R*)- and/or (5*S*)-2-*O*-Benzyl-3,4-*O*-isopropylidene-5-*C*-*m*-chlorobenzoyloxy-α-L-*arabino*-hexopyranosyl]-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal [(5*R*)- and/or (5*S*)-17]

A soln of **14** (1.50 g, 2.58 mmol) in dry CH_2Cl_2 (28 mL) was treated at 0 °C with a pre-dried ($MgSO_4$) soln of

70% MCPBA (751 mg, 3.05 mmol) in CH_2Cl_2 (37 mL) and stirred until the starting material was consumed (2.5 h, TLC, 3:2 hexane–EtOAc). The reaction mixture was washed with 10% aq $Na_2S_2O_3$ (3×40 mL), dried ($MgSO_4$) and concentrated to give a mixture (clear syrup, 189 g, 97% yield) of four products, as judged through ^1H NMR analysis (200 MHz, CD_3CN) showing four separated doublets attributed to H-1′ at δ 5.35 ($J_{1',2'}$ 8.5 Hz), 5.27 ($J_{1',2'}$ 8.3 Hz), 5.19 ($J_{1',2'}$ 8.4 Hz), and 5.14 ($J_{1',2'}$ 7.8 Hz) in a 60:19:7:14 ratio. Selected NMR signals of the more abundant component: ^1H NMR (200 MHz, $CDCl_3$): δ 5.42 (d, 1 H, $J_{1',2'}$ 8.5 Hz, H-1′). ^{13}C NMR (50 MHz, $CDCl_3$): δ 162.7 (C=O), 137.8, 134.4, 131.8 (3 aromatic C), 133.3–127.4 (aromatic CH), 110.3, 109.6, 108.3 (3 CMe_2), 106.9 (C-1), 104.6 (C-5′), 98.7 (C-1′), 78.2, 78.2, 78.1, 77.8 (C-3, C-5, C-3′, C-2′), 75.4, 73.8, 73.5 (C-2, C-4, C-4′), 73.3 (CH_2Ph), 62.1 (C-6′), 65.0 (C-6), 57.3, 54.4 (2 OMe), 27.5, 27.1, 26.5, 26.3, 26.2, 25.2 (3 CMe_2).

3.7. 4-*O*-[(5*R* and (5*S*)-2-*O*-Benzyl-6-*O*-*m*-chlorobenzoyl-3,4-*O*-isopropylidene-5-hydroxy-α-L-*arabino*-hexopyranosyl]-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (18)

A sample (820 mg) of the above crude product derived by epoxidation with MCPBA in CH_2Cl_2 of **14** was subjected to flash chromatography over silica gel eluting with 1:1 hexane–EtOAc recovering an approximately 4:1 mixture of (5′*R* and 5′*S*)-**18** (580 mg, 81% yield from **14**) as a colourless syrup, $[\alpha]_D$ −33.3° (*c* 1.5, $CHCl_3$); R_f 0.49 (1:1 hexane–EtOAc); NMR data of the major component: ^1H (500 MHz, $CDCl_3$): δ 8.03, 7.94, 7.55 (3 m, each 1 H, aromatic H), 7.41–7.25 (m, 6 H, aromatic H), 5.21 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 4.82, and 4.76 (AB system, 2 H, $J_{A,B}$ 12.0 Hz, CH_2Ph), 4.57 (dd, 1 H, $J_{1,2}$ 6.5 Hz, $J_{2,3}$ 7.5 Hz, H-2), 4.65, and 4.37 (AB system, 2 H, $J_{A,B}$ 11.5 Hz, H-6′a, H-6′b), 4.34 (d, 1 H, H-1), 4.30 (m, 2 H, H-3′, H-5), 4.17 (dd, 1 H, $J_{6a,6b}$ 9.0 Hz, $J_{5,6b}$ 5.7 Hz, H-6b), 4.14 (d, 1 H, $J_{3',4'}$ 5.5 Hz, H-4′), 4.07 (dd, 1 H, $J_{3,4}$ 1.5 Hz, H-3), 3.97 (dd, 1 H, $J_{5,6a}$ 6.5 Hz, H-6a), 3.93 (dd, 1 H, $J_{4,5}$ 5.5 Hz, H-4), 3.41 (dd, 1 H, $J_{2',3'}$ 5.5 Hz, H-2′), 3.44, 3.43 (2 s, each 3 H, 2 OMe), 1.88 (bs, 1 H, OH), 1.42, 1.41, 1.40, 1.34, 1.32, 1.31 (6 s, each 3 H, 3 CMe_2). ^{13}C (50 MHz, $CDCl_3$): δ 165.4 (C=O), 138.1, 134.5, 131.4 (3 aromatic C), 133.2–126.9 (aromatic CH), 109.9, 109.7, 108.6 (3 CMe_2), 106.3 (C-1), 97.8 (C-1′), 95.9 (C-5′), 78.8, 78.1, 77.5, 77.0 (C-2′, C-3′, C-3, C-5), 75.9, 75.4, 75.2 (C-4′, C-2, C-4), 73.4 (CH_2Ph), 67.1 (C-6′), 65.6 (C-6), 56.2, 54.1 (2 OMe), 27.6, 27.2, 26.6, 26.5, 26.2, 25.2 (3 CMe_2). Selected NMR data of the minor component: ^1H (500 MHz, $CDCl_3$): δ 5.19 (d, 1 H, $J_{1',2'}$ 6.7 Hz, H-1′). ^{13}C (50 MHz, $CDCl_3$): δ 164.5 (C=O), 138.1, 134.3, 131.4 (3 aromatic C), 133.2–126.9 (aromatic CH), 110.7, 110.0, 108.1 (3 CMe_2), 105.2 (C-1), 99.6 (C-1′), 95.1 (C-5′), 80.3, 78.1, 77.2, 77.0 (C-2′, C-3′, C-3, C-5), 76.8, 75.9, 74.2 (C-4′, C-2, C-4), 73.1 (CH_2Ph), 67.9 (C-6′), 65.0 (C-6), 56.1, 53.7 (2 OMe), 27.3, 27.1, 26.7, 26.5, 24.8, 24.7 (3 CMe_2). Anal. Calcd for $C_{37}H_{49}ClO_{14}$: C, 59.0; H, 6.56. Found: C, 59.21; H, 6.62.

3.8. 4-*O*-[(5*R*)- and (5*S*)-2-*O*-Benzyl-3,4-*O*-isopropylidene-5-*C*-methoxy-α-L-*arabino*-hexopyranosyl]-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal [(5*R*)- and (5*S*)-15]

A soln of **14** (899 mg, 1.55 mmol) in MeOH (9 mL) was treated at 0 °C under stirring with a soln of 70% commercial MCPBA (470 mg, 1.90 mmol) in MeOH (4 mL), warmed at rt and stirred until the starting material was consumed (6 h, TLC, 1:1 hexane–EtOAc). The reaction mixture was neutralised by addition of satd aq $NaHCO_3$, stirred for 15 min, concentrated and partitioned between CH_2Cl_2 (30 mL) and satd aq $NaHCO_3$ (20 mL). The aqueous phase was extracted with CH_2Cl_2 (3×35 mL), the combined extracts were collected, dried ($MgSO_4$) and concentrated to give a crude reaction product (1.02 g) that was subjected to flash chromatography (1:1 hexane–EtOAc) to give, after a first fraction with R_f 0.30 (1:1 hexane–EtOAc), corresponding to the 4:1 mixture of 6-*O*-*m*-chlorobenzoates **18** (239 mg, 20% yield), a 4:1 mixture of the title compounds (686 mg, 70% yield) as a colourless syrup, $[\alpha]_D$ +2.2° (*c* 1.4, $CHCl_3$); R_f 0.20 (1:1 hexane–EtOAc); selected ^1H NMR (200 MHz, CD_3CN) signals: (5*R*)-**15**: δ 4.83 (d, 1 H, $J_{1',2'}$ 8.3 Hz, H-1′), 4.81, and 4.68 (AB system, 2 H, $J_{A,B}$ 12.1 Hz, CH_2Ph), 4.11 (dd, 1 H, $J_{6a,6b}$ 8.7 Hz, $J_{5,6b}$ 5.2 Hz, H-6b), 3.93 (dd, 1 H, $J_{5,6a}$ 6.3 Hz, H-6a), 3.90 (dd, 1 H, $J_{3,4}$ 1.3 Hz, $J_{4,5}$ 5.5 Hz, H-4), 3.70, and 3.48 (AB system, 2 H, $J_{A,B}$ 12.2 Hz, H-6′a, H-6′b), 3.27 (dd, 1 H, $J_{2',3'}$ 7.0 Hz, H-2′), 3.39, 3.38, 3.33 (3 s, each 3 H, 3 OMe); (5*S*)-**15**: δ 4.94 (d, 1 H, $J_{1',2'}$ 8.4 Hz, H-1′), 4.74 (s, 2 H, CH_2Ph), 4.54 (dd, 1 H, $J_{1,2}$ 6.5 Hz, $J_{2,3}$ 7.4 Hz, H-2), 3.85 (dd, 1 H, $J_{6a,6b}$ 8.5 Hz, $J_{5,6a}$ 5.9 Hz, H-6a), 3.82 (dd, 1 H, $J_{3,4}$ 1.4 Hz, $J_{4,5}$ 6.8 Hz, H-4), 3.65, and 3.43 (AB system, 2 H, $J_{A,B}$ 12.7 Hz, H-6′a, H-6′b), 3.35 (m, 1 H, H-2′), 3.40, 3.37, 3.32 (3 s, each 3 H, 3 OMe). ^{13}C NMR (50 MHz, CD_3CN): (5*R*)-**15**: δ 139.6 (aromatic C), 110.2, 110.1, 109.2 (3 CMe_2), 106.9 (C-1), 100.6 (C-5′), 98.7 (C-1′), 80.5 (C-2′), 79.0, 78.8, 78.5, (C-3′, C-3, C-5), 76.1, 76.4, 75.8 (C-4′, C-2, C-4), 74.3 (CH_2Ph), 66.1 (C-6), 60.0 (C-6′), 56.8, 54.1 (2 OMe-1), 48.7 (OMe-5); (5*S*)-**15**: δ 137.4 (aromatic C), 111.7, 110.4, 110.1 (3 CMe_2), 106.9 (C-1), 100.8 (C-1′), 100.7 (C-5′), 80.5 (C-2′), 78.5, 78.0, 77.4 (C-3′, C-3, C-5), 76.6, 76.2, 75.0 (C-4′, C-2, C-4), 73.6 (CH_2Ph), 66.8 (C-6), 62.4 (C-6′), 56.9, 54.5 (2 OMe-1), 50.1 (OMe-5). Clusters of signals for both anomers: δ 129.0–128.4 (aromatic CH), 28.3–25.5 (CMe_2). Anal. Calcd for $C_{31}H_{48}O_{13}$: C, 59.22; H, 7.70. Found: C, 59.01; H, 7.60.

3.9. 4-*O*-[(5*R*)-2,6-Di-*O*-benzyl-3,4-*O*-isopropylidene-5-*C*-methoxy-α-L-*arabino*-hexopyranosyl]-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal [(5*R*)-16]

A soln of **8** (182 mg, 0.27 mmol) in 2,2-dimethoxypropane (3 mL) was treated with *p*-TsOH (5 mg), stirred at rt until the starting material was consumed (1 h, TLC, 1:1 hexane–EtOAc), treated with Et_3N (0.2 mL) and concentrated under diminished pressure. Flash chromatographic purification of the crude residue (2.03 g), eluting with 3:2 hexane–EtOAc + 1‰ Et_3N, gave pure (5*R*)-**16** (172.5 mg, 92% yield) as a syrup, R_f 0.52 (1:1 hexane–EtOAc); $[\alpha]_D$ +22.1° (*c* 1.6, $CHCl_3$); ^{1}H NMR (200 MHz, CD_3CN): δ 7.38–7.29 (m, 10 H, aromatic H), 4.81 (d, 1 H, $J_{1',2'}$ 8.4 Hz, H-1′), 4.82, and 4.67 (AB system, 2 H, $J_{A,B}$ 12.1 Hz, CH_2Ph), 4.56, and 4.49 (AB system, 2 H, $J_{A,B}$ 12.0 Hz, CH_2Ph), 4.30 (m, 2 H, H-1, H-2), 4.21 (m, 1 H, H-5), 4.09 (dd, 1 H, $J_{6a,6b}$ 8.6 Hz, $J_{5,6b}$ 5.7 Hz, H-6b), 4.12 (d, 1 H, H, $J_{3',4'}$ 2.2 Hz, H-4′), 4.10 (dd, 1 H, $J_{2',3'}$ 5.4 Hz, H-3′), 4.02 (dd, 1 H, $J_{2,3}$ 7.3 Hz, $J_{3,4}$ 1.3 Hz, H-3), 3.91 (dd, 1 H, $J_{5,6a}$ 6.3 Hz, H-6a), 3.83 (dd, 1 H, $J_{4,5}$ 5.6 Hz, H-4), 3.65, and 3.40 (AB system, 2 H, $J_{A,B}$ 10.5 Hz, H-6′a, H-6′b), 3.30 (m, 1 H, H-2′), 3.31, 3.27, 3.26 (2 s, each 3 H, 2 OMe), 1.34, 1.33, 1.31, 1.27, 1.26, 1.23 (6 s, each 3 H, 3 C*Me*$_2$). ^{13}C NMR (50 MHz, CD_3CN): δ 139.6, 139.2 (2 aromatic C), 129.6–128.4 (aromatic CH), 111.4, 110.0, 109.2 (3 *C*Me$_2$), 106.7 (C-1), 100.2 (C-5′), 98.6 (C-1′), 80.5 (C-2′), 78.8, 78.5, 77.9 (C-3′, C-3, C-5), 76.6, 76.1, 76.0 (C-4′, C-2, C-4), 74.3, 74.9 (2 CH_2Ph), 66.9, 66.1 (C-6′, C-6), 48.6 (OMe-5), 56.6, 53.7 (2 OMe-1), 28.3, 27.6, 27.0, 26.9, 26.7, 25.6 (3 C*Me*$_2$). Anal. Calcd for $C_{38}H_{54}O_{13}$: C, 63.49; H, 7.57. Found: C, 63.58; H, 7.63.

3.10. 4-*O*-[(5*R*)- and (5*S*)-2,6-Di-*O*-benzyl-3,4-*O*-isopropylidene-5-*C*-methoxy-α-L-*arabino*-hexopyranosyl]-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal [(5*R*)- and (5*S*)-16]

A 4:1 mixture of **15** (1.00 g, 1.59 mmol) was dissolved in wet THF (10 mL) and the soln was treated with 18-crown-6 (10 mg) and crushed KOH (712 mg, 12.7 mmol). The mixture was stirred at rt for 1 h, treated with BnBr (0.38 mL, 3.20 mmol) and stirred until the starting material was consumed (2 h, TLC, 1:1 hexane–EtOAc). MeOH (2 mL) was added, the soln stirred for 15 min, concentrated under diminished pressure and the residue partitioned between CH_2Cl_2 (50 mL) and H_2O (25 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL), the organic extracts collected, dried, concentrated and the crude residue (1.24 g) subjected to flash chromatography (7:3 hexane–EtOAc) to give an approximately 4:1 anomeric mixture of **16** (1.04 g, 91% yield) as a syrup, $[\alpha]_D$ +12.7° (*c* 1.1, $CHCl_3$); R_f 0.54 (1:1 hexane–EtOAc); NMR analysis of the crude mixture shown for the major constituent spectral parameters identical to those of (5*R*)-**16** and the following selected signals for (5*S*)-**16**: ^{1}H NMR (200 MHz, CD_3CN): δ 7.57–7.23 (m, 10 H, aromatic H), 4.96 (d, 1 H, $J_{1',2'}$ 8.3 Hz, H-1′), 4.77, and 4.71 (AB system, 2 H, $J_{A,B}$ 11.3 Hz, CH_2Ph), 4.60, and 4.50 (AB system, 2 H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 3.79 (dd, 1 H, $J_{3,4}$ 1.4 Hz, $J_{4,5}$ 6.8 Hz, H-4), 3.63, and 3.53 (AB system, 2 H, $J_{A,B}$ 10.7 Hz, H-6′a, H-6′b), 3.44, 3.33, 3.32 (3 s, each 3 H, 3 OMe). ^{13}C NMR (50 MHz, CD_3CN): δ 139.7, 139.4 (2 aromatic C), 129.2–128.4 (aromatic CH), 111.4, 110.5, 109.2 (3 *C*Me$_2$), 106.9 (C-1), 100.8 (C-5′), 100.7 (C-1′), 80.7 (C-2′), 78.8, 78.5, 78.4, 77.4 (C-3′, C-2, C-3, C-5), 74.9, 74.3 (C-4′, C-4), 74.3, 73.6 (2 CH_2Ph), 70.6 (C-6′), 66.9 (C-6), 56.6, 54.4 (2 OMe-1), 50.1 (OMe-5). Anal. Calcd for $C_{38}H_{54}O_{13}$: C, 63.49; H, 7.57. Found: C, 63.47; H, 7.60.

3.11. 2,6-Di-*O*-benzyl-L-*arabino*-hexos-5-ulose (9)

A 4:1 anomeric mixture of **16** (728 mg, 1.01 mmol) was dissolved in 4:1 (v/v) CH_3CN–water (15 mL), treated with 90% aq CF_3COOH (1.5 mL) and warmed at 50 °C for 16 h. The soln was concentrated under diminished pressure and repeatedly co-evaporated with toluene (3 × 20 mL). The crude residue was extracted three times with EtOAc (50 mL) and the turbid solns were filtered, collected, dried ($MgSO_4$) and concentrated to give pure **9** (299 mg, 83% yield), having NMR parameters identical to those of a sample previously prepared by us,[11] and constituted by an approximately 4:1 mixture of α- and β-1,4-furanose anomers.

The treatment with an identical procedure of pure **8** led to **9** in analogous yield.

3.12. 2-*O*-Benzyl-5-*C*-hydroxy-3,4-*O*-isopropylidene-1,6-anhydro-β-L-talopyranose (19a) and 2-*O*-benzyl-5-*C*-hydroxy-3,4-*O*-isopropylidene-1,6-anhydro-β-D-galactopyranose (19b)

A 4:1 mixture of crude *m*-chlorobenzoates **17** (324 mg, 0.45 mmol) was dissolved in 5:1 MeOH–water (5 mL), treated at rt with Et_3N (1.5 mL) and stirred until the starting material was consumed (3 h, TLC, 1:1 hexane–EtOAc). The reaction mixture was concentrated under diminished pressure and the residue partitioned between EtOAc (25 mL) and water (10 mL). The organic phase was dried ($MgSO_4$), concentrated and submitted to column chromatography (9:1 CH_2Cl_2–Et_2O) to give in the order an approximately 9:11 mixture (NMR immediately after dissolution) of the title compounds as a clear syrup (86 mg, 65% yield) and **11** (170 mg, quantitative yield). The treatment with an identical procedure of pure **18** led to **19** in analogous yield. Some of the following NMR signals closely corresponded to those reported by Murphy.[13]

3.12.1. NMR signals of 19a. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.38–7.24 (m, 5 H, aromatic H), 5.42 (d, 1 H, $J_{1,2}$ 2.7 Hz, H-1), 4.79, and 4.60 (AB system, 2 H, $J_{A,B}$ 12.0 Hz, CH_2Ph), 4.43 (dd, 1 H, H-3), 4.31 (d, 1 H, $J_{3,4}$ 6.7 Hz, H-4), 3.86, and 3.62 (AB system, 2 H, $J_{A,B}$ 8.1 Hz, H-6a, H-6b), 3.48 (dd, 1 H, $J_{2,3}$ 4.6 Hz, H-2), 1.53, 1.34 (2 s, each 3 H, CMe_2). ^{13}C NMR (50 MHz, $CDCl_3$): δ 137.3 (aromatic C), 128.4–126.9 (aromatic CH), 111.6 (*C*Me$_2$), 100.9 (C-5), 99.9 (C-1), 78.7, 78.0, 76.8 (C-2, C-3, C-4), 71.4, 69.2 (C-6, CH_2Ph), 27.4, 26.2 (CMe_2).

3.12.2. NMR signals of 19b. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.38–7.24 (m, 5 H, aromatic H), 5.48 (s, 1 H, H-1), 4.71, and 4.60 (AB system, 2 H, $J_{A,B}$ 11.5 Hz, CH_2Ph), 4.40–4.33 (m, 2 H, H-3, H-4), 4.16 (d, 1 H, $J_{6a,6b}$ 7.8 Hz, H-6b), 3.61 (d, 1 H, $J_{2,3}$ 0.9 Hz, H-2), 3.25 (dd, 1 H, $J_{4,6a}$ 1.5 Hz, H-6a), 1.45, 1.38 (2 s, each 3 H, CMe_2). ^{13}C NMR (50 MHz, $CDCl_3$): δ 137.0 (aromatic C), 128.4–126.9 (aromatic CH), 108.8 (*C*Me$_2$), 101.9 (C-5), 100.8 (C-1), 77.5, 76.4, 75.1 (C-2, C-3, C-4); 72.1 (CH_2Ph), 65.8 (C-6), 25.9, 24.1 (CMe_2).

3.13. 2-*O*-Benzyl-6-*O*-*m*-chlorobenzoyl-L-*arabino*-hexos-5-ulose (20)

A 4:1 anomeric mixture of **18** (550 mg, 0.73 mmol) was dissolved in 4:1 (v/v) CH_3CN–water (10 mL), treated with 90% aq CF_3COOH (1.0 mL) and left at rt. After disappearance of the starting material (1 h, TLC, 1:1 hexane–EtOAc) the soln was concentrated under diminished pressure and repeatedly co-evaporated with toluene (3 × 30 mL). The crude residue was extracted four times with EtOAc (100 mL) and the turbid solns were filtered, collected, dried ($MgSO_4$) and concentrated under reduced pressure giving a residue (400 mg), which was purified by chromatography on silica gel (2:3 hexane–EtOAc) to give pure **20** (238 mg, 80% yield), as a 7:3 mixture of α- and β-1,4-furanose anomers, syrup, R_f 0.31 (2:3 hexane–EtOAc); $[\alpha]_{Diniz}$ +41° (*c* 1.0, MeOH); $[\alpha]_{D\infty.}$ +20° (*c* 1.0, MeOH).

3.13.1. NMR signals of 20α. ^{1}H NMR (200 MHz, CD_3CN–D_2O): δ 7.91, 7.63, 7.48 (3 m, each 1 H, aromatic H), 7.34–7.25 (m, 6 H, aromatic H), 5.45 (d, 2 H, $J_{1,2}$ 0.5 Hz, H-1), 5.23, and 5.10 (AB system, 2 H, $J_{A,B}$ 17.9 Hz, H-6a, H-6b), 4.67 (d, 1 H, $J_{3,4}$ 2.8 Hz, H-4), 4.53 (s, 2 H, CH_2Ph), 4.39 (dd, 1 H, H-3), 3.86 (dd, 1 H, $J_{2,3}$ 1.7 Hz, H-2). ^{13}C NMR (50 MHz, CD_3CN–D_2O): δ 204.1 (C-5), 165.6 (C=O), 138.5, 135.1, 132.4 (3 aromatic C), 134.2–128.8 (aromatic CH), 102.8 (C-1), 89.6 (C-4), 87.5 (C-2), 77.9 (C-3), 72.2 (CH_2Ph), 68.5 (C-6).

3.13.2. NMR signals of 20β. ^{1}H NMR (200 MHz, CD_3CN–D_2O): δ 7.91, 7.63, 7.48 (3 m, each 1 H, aromatic H), 7.34–7.25 (m, 6 H, aromatic H), 5.48 (d, 2 H, $J_{1,2}$ 3.5 Hz, H-1), 5.36, and 5.21 (AB system, 2 H, $J_{A,B}$ 18.0 Hz, H-6a, H-6b), 4.57 (s, 2 H, CH_2Ph), 4.44 (dd, 1 H, $J_{2,3}$ 3.7 Hz, $J_{3,4}$ 4.0 Hz, H-3), 4.29 (d, 1 H, H-4); 3.77 (dd, 1 H, H-2). ^{13}C NMR (50 MHz, CD_3CN–D_2O): δ 205.3 (C-5), 165.6 (C=O), 138.5, 135.1, 132.4 (3 aromatic C), 134.2–128.8 (aromatic CH), 98.6 (C-1), 87.0 (C-4), 82.9 (C-2), 76.7 (C-3), 72.9 (CH_2Ph), 68.8 (C-6).

Anal. Calcd for $C_{20}H_{19}ClO_7$: C, 59.05; H, 4.71. Found: C, 58.89; H, 4.68.

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