STEREOSELECTIVE PREPARATION OF 2,3-DIDEOXY-3-*C*-[(α-D-GALACTOPYRANOSYL)METHYL]-D-*arabino*-HEXOPYRANOSE AND 2,3-DIDEOXY-3-*C*-[(α-D-GALACTOPYRANOSYL)METHYL]-L-*arabino*-HEXOPYRANOSE

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The diastereomeric substituted 2*H*-dihydropyran derivatives **2b** and **3b** were obtained by the stereoselective cycloaddition of (*E*)-4-(tetra-*O*-benzyl-α-D-galactopyranosyl)-1-(thiazol-2-yl)but-2-en-1-one (**1**) with either of the enantiomeric chiral vinyl ethers (*R*)-**4** or (*S*)-**4**. Reduction of the ester group, transformation of the thiazole ring into an aldehyde group and reaction with an excess of borane afforded the final *C*-(1→3)-disaccharide structures. The obtained *C*-(1→3)-disaccharides, containing an L- or D-deoxy-*arabino*-hexopyranose moiety at the reducing end, were characterized as peracetylated methyl glycosides **9a**, **9b** and **12a**, **12b**.
Keywords: *C*-Disaccharides; Stereoselective synthesis; Saccharide chemistry.

As a result of their great structural variability, saccharides represent very suitable "structural units" for the construction of the so-called sugar codes[1]. The interactions of sugar codes with protein receptors play a key role in cell/cell or cell/pathogen communication and, inter alia, even control such important processes as cell adhesion, fertilization, inflammation, immune response and cancer metastasis. A deeper understanding of molecular details of these recognition processes has led to the discovery of various saccharide derivatives of significant therapeutic potential[2]. However, the search for new carbohydrate-based therapeutics or vaccines is often complicated by the fact that oligosaccharides used in forming the sugar codes are labile compounds in vivo, because they undergo hydrolysis by ubiquitous glycosidases. The solution to this problem may rest in the use of stable carbohydrate mimicks, such as *C*-disaccharides, which nominally preserve the

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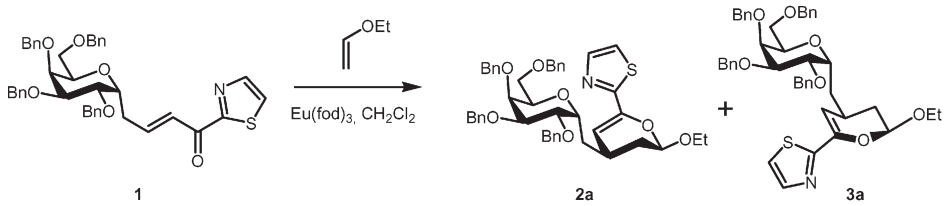
structural information of natural disaccharides but are chemically as well as enzymatically non-hydrolyzable[3].

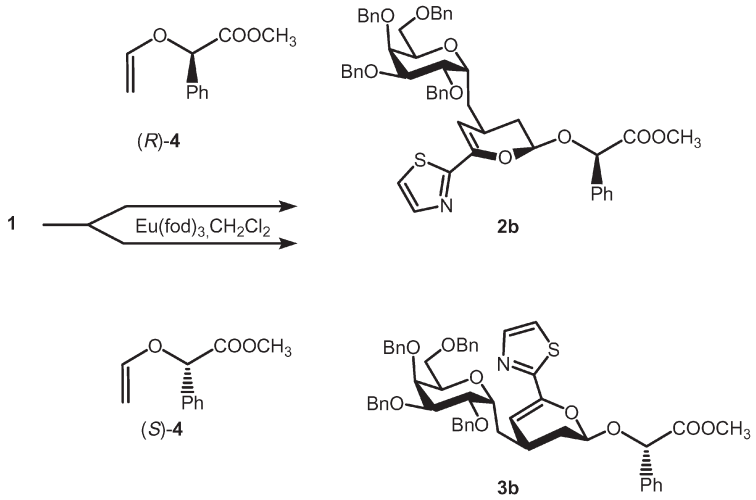
Recently we described a short and efficient synthesis of α-*C*-(1→3)-disaccharides in which D-glucopyranose was linked to an L- or D-2-deoxy-*arabino*-hexopyranose moiety[4]. Later on, we found that the stereoselectivity of the key step in our synthesis, namely the cycloaddition of the substituted oxadiene with ethyl vinyl ether, can be markedly increased by the use of chiral vinyl ethers. This has made possible the facile stereoselective preparation of further *C*-(1→3)-disaccharide derivatives[5]. As an example of this approach we now report the preparation of previously unknown disaccharide mimetics, in which the α-D-galactopyranosyl moiety is linked by a methylene bridge to C-3 of an L- or D-2-deoxy-*arabino*-hexopyranose. The α-D-galactopyranosyl moiety, attached by a (1→3) glycosidic bond to the oligosaccharide chain, is present as the terminal monosaccharide, e.g., in the B blood group antigen and in the so-called α-galactosyl epitope, which is responsible for the hyperacute rejection of organs in xenotransplantation[6]. The synthesized compounds represent non-hydrolyzable mimetics of this structural motif, and further synthetic transformations of the deoxy-*arabino*-hexopyranose ring (i.e., via the corresponding glycals) make possible their linkage into oligosaccharide chains and the synthesis of non-hydrolyzable analogs of natural epitopes. A stereoisomeric compound, 2,3-dideoxy-3-*C*-[(β-D-galactopyranosyl)methyl]D-*lyxo*-hexopyranose, was recently prepared from isolevoglucosen, using a longer and more laborious procedure[7].

Using our original procedure[4], the reaction of (*E*)-4-(tetra-*O*-benzyl-α-D-galactopyranosyl)-1-(thiazol-2-yl)but-2-en-1-one (**1**) with ethyl vinyl ether led to a 1:1 mixture of two diastereomeric endo cycloadducts **2a** and **3a** which were inseparable by preparative chromatography (Scheme 1).



SCHEME 1

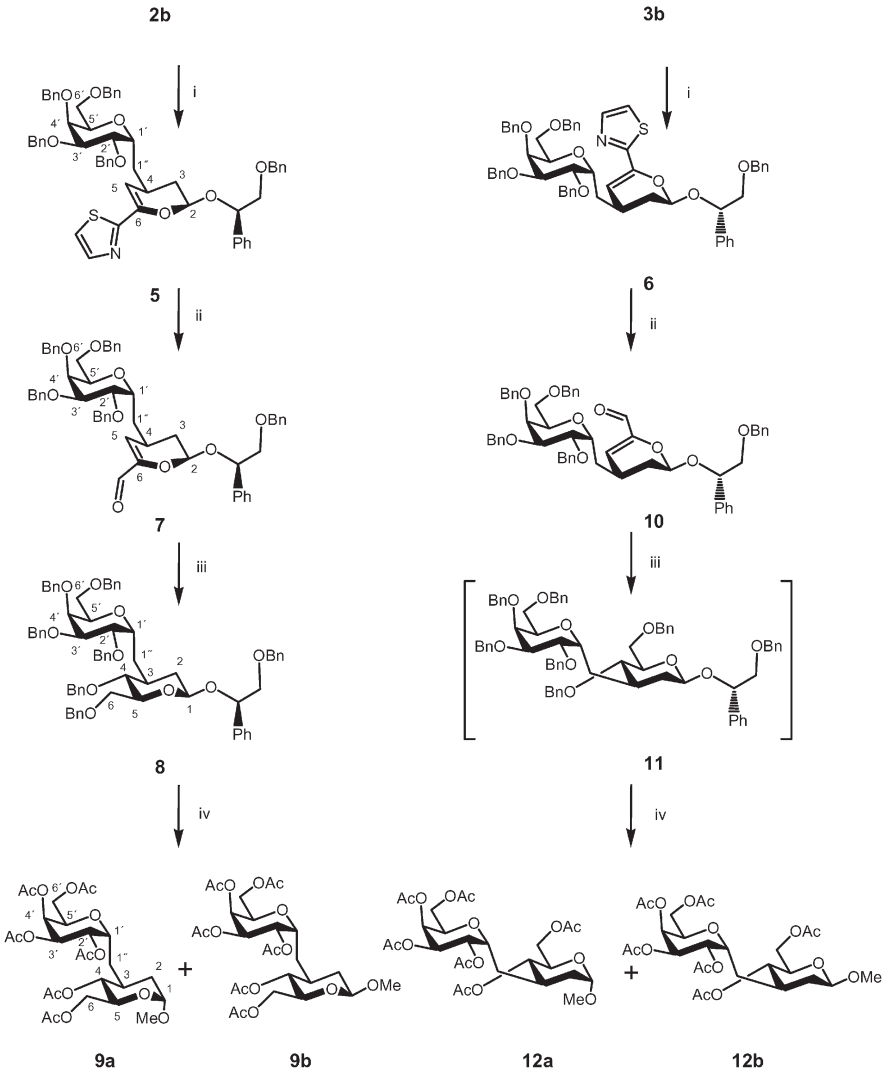
On the contrary, cycloaddition with the enantiopure vinyl ethers (*R*)-**4** and (*S*)-**4**, easily obtainable from the cheap and commercially accessible enantiomers of mandelic acid, was highly stereoselective[5]. The reaction with enantiomer (*R*)-**4** afforded almost pure cycloadduct **2b**, while the reaction with enantiomer (*S*)-**4** led to almost pure cycloadduct **3b** (Scheme 2).



SCHEME 2

Unfortunately, preliminary experiments demonstrated that the subsequent transformation of the thiazole ring in cycloadducts **2b** and **3b** into an aldehyde functionality (unlike the similar conversion in cycloadducts **2a** and **3a**) proceeded with problems. The desired aldehydes were obtained in only low yields and were accompanied by other unidentified compounds. Originally, we intended to circumvent this synthetic problem by replacing the chiral moiety of mandelic acid in cycloadducts **2b** and **3b** with simpler substituents (e.g., methoxy or ethoxy). However, all such attempts led only to mixtures of several compounds. The attempted acid-catalyzed transglycosidation was probably accompanied by cleavage of the unsaturated dihydropyran ring and subsequent decomposition of the intermediates.

To avoid this problem, we reduced the ester group in cycloadducts **2b** and **3b** with $LiAlH_4$ and protected the resulting primary alcohols by benzylation (Scheme 3). The benzyl ethers **5** and **6** then underwent transformation of the thiazole ring to an aldehyde in the usual manner without difficulty. Compound **5** gave pure aldehyde **7** (yield 70%) which, on reaction with excess of borane and benzylation of the newly generated hydroxy



(i) 1. $LiAlH_4$, THF, 2. NaH, BnBr, THF; (ii) 1. TfOMe, MeCN, 2. $NaBH_4$, MeOH, 3. $AgNO_3$, H_2O, MeCN; (iii) 1. $BH_3 \cdot Me_2S$, THF, 30% NaOH, 30% H_2O_2, 2. NaH, BnBr, THF; (iv) 1. MeOH, 3 M HCl, THF, 2. H_2, Pd/C, 3. Ac_2O, pyridine

SCHEME 3
Synthesis of (1→3)-*C*-disaccharides

groups, afforded the desired structure, *C*-disaccharide **8**, as the sole reaction product. Although the mass spectrum of the compound obtained agreed with the assumed structure **8**, it was not possible to confirm the relative configuration of the new deoxypyranose directly from its complex ^{1}H NMR spectrum. However, the chiral aglycon was easily exchanged by treatment of compound **8** in tetrahydrofuran with methanolic solution of HCl, the reaction afforded a mixture of only two anomers, which, after exchange of the benzyl protecting groups for acetates, was characterized as a mixture of the peracetyl methyl glycosides **9a** and **9b**. As determined from the NMR spectra, the anomeric methyl glycosides **9a** and **9b** were formed in the 4:1 ratio (as estimated by integration of the ^{1}H NMR signals of the methoxy group at 3.27 ppm in the major anomer and at 3.41 ppm in the minor one). The coupling constants of the major anomer **9a** unequivocally show that the substituents on carbon atoms 4 and 5 of the new deoxyhexopyranose are in the equatorial positions (J(H-4,H-5) = 9.9 Hz). The configurations of the remaining carbon atoms in this compound were determined using NOE experiments: a marked NOE was observed between protons H-3 and H-5, but there was no interaction with proton H-1. On the contrary, protons H-3 and H-5 showed a strong NOE with the methoxy group in the anomeric position. These results confirm that the substituents at positions 3, 4 and 5 are equatorial whereas the anomeric methoxy group is axial. This means that the major stereoisomer **9a** is the α-methyl glycoside of the substituted 2-deoxy-*arabino*-hexopyranose. As follows from the coupling constants of the ^{1}H NMR spectrum of the minor anomer **9b**, the substituents on carbon atoms 1, 4 and 5 of this deoxyhexopyranose are in equatorial position (J(H-1,H-2ax) = 9.4 Hz, J(H-1,H-2eq) = 1.8 Hz, J(H-4,H-5) = 9.6 Hz). Moreover, the spectrum of this anomer displayed marked NOEs between protons H-1, H-3 and H-5; thus confirming that in this case all the substituents are equatorial and thus **9b** is the β-methyl glycoside of the substituted 2-deoxy-*arabino*-hexopyranose. Since the absolute configuration of the starting compound **2b** was unequivocally determined by X-ray diffraction in our previous study[5], the deoxy-*arabino*-hexopyranose in methyl glycosides **9a** and **9b** must have the L-configuration.

Using the same reaction scheme as above, we converted the diastereoisomeric compound **6** into aldehyde **10**, which, via intermediate **11** (in this case not isolated), was converted into a mixture of peracetylated methyl glycosides **12a** and **12b**. The NMR spectra of the obtained mixture of **12a** and **12b** were almost identical with those of compounds **9a** and **9b**. Also in this case, the two methyl glycosides were formed in the ca. 4:1 ratio (as determined by integration of ^{1}H NMR signals of OMe at 3.34 ppm for the

major anomer and at 3.49 ppm for the minor one). As in the preceding case, the interaction constants and NOE experiments unequivocally confirm that the major stereoisomer **12a** is the α-methyl glycoside of the substituted 2-deoxy-*arabino*-hexopyranose whereas the minor stereoisomer **12b** is the β-methyl glycoside. As follows from the absolute configuration[5] of the starting compound **3b**, the new deoxy-*arabino*-hexopyranose in the methyl glycosides **12a**, **12b** must have the D-configuration.

In conclusion, we have demonstrated that stereoselective cycloaddition of the enantiomeric vinyl ethers (*R*)-**4** and (*S*)-**4** with the suitably substituted oxadiene **1** enables a facile and simple preparation of the previously unknown (1→3)-disaccharide mimetics, containing an α-D-galactopyranosyl moiety at the non-reducing end and a 2-deoxy-*arabino*-hexopyranose moiety of L- or D-configuration at the reducing end. Compounds **12a** and **12b** may serve as precursors for the synthesis of non-hydrolyzable glycoprotein or glycolipid epitopes containing the α-D-galactopyranosyl-(1→3)-structural motif.

EXPERIMENTAL

The synthesis of compounds **2b** and **3b** has already been described in our previous paper[5].

The melting points are uncorrected. TLC was performed on HF_{254} plates (Merck), detection was by UV light or by spraying with a solution of $Ce(SO_4)_2(H_2O)_4$ (5 g) in 10% H_2SO_4 (500 ml) and subsequent heating. Flash column chromatography was performed on silica gel (MERCK, 100–160 μm) in solvents, distilled prior to use. Optical rotations were measured at 25 °C on a JASCO DIP-370 spectropolarimeter. ^1H and ^{13}C NMR spectra were taken on a Bruker DRX 500 Avance spectrometer at 500.132 MHz (^1H NMR) and at 125.767 MHz (^{13}C NMR) using tetramethylsilane as internal standard. Chemical shifts in the ^1H and ^{13}C NMR spectra are given in ppm (δ-scale), coupling constants (*J*) in Hz. ^1H and ^{13}C NMR signal assignments were confirmed by 2D COSY and HMQC when necessary. NOE connectivities were obtained using the 1D ^1H DPFGSE-NOE experiment. For numbering of atoms see Scheme 3. Mass spectra and HPLC were performed on a 250 × 4.6 mm column packed with 5 μm Supelco BDS Hypersil C-18, mobile phase methanol–water, using an HP 1100 instrument equipped with a gradient pump, column thermostat, and in addition to a UV detector, also with an Agilent G1956B single quadrupole system as an MS detector.

(2*S*,4*S*)-2-[(2*R*)-2-(Benzyloxy)-1-phenylethoxy]-4-[(2,3,4,6-tetra-*O*-benzyl-α-D-galacto pyranosyl)methyl]-6-(thiazol-2-yl)-3,4-dihydro-2*H*-pyran (**5**)

Lithium aluminum hydride (0.3 g, 7.95 mmol) was added portionwise under nitrogen to a solution of compound **2b** (2.3 g, 2.65 mmol) in tetrahydrofuran (50 ml), cooled to 0 °C, and the reaction mixture was stirred at room temperature for 2 h. The mixture was then quenched by the cautious addition of 1 M NaOH (5 ml), the solid salts were removed by filtration and the filtrate was taken down. The residue was partitioned between ethyl acetate and water. The organic phase was dried, the solvent evaporated and the residue flash-

chromatographed on a short column of silica gel in petroleum ether–ethyl acetate (5:1). A solution of the obtained alcohol (2.1 g, R_F 0.4 in petroleum ether–ethyl acetate (2:1), *m/z* 841.8 $[M + H]^+$) in tetrahydrofuran (60 ml) was stirred with NaH (0.2 g, 5 mmol; 60% suspension in mineral oil) at room temperature for 1 h. Benzyl bromide (0.49 ml, 3.75 mmol) and tetrabutylammonium iodide (0.23 g, 0.63 mmol) were added, and the reaction mixture was stirred at 40 °C for 15 min and then at room temperature for 14 h. After the addition of methanol (3 ml), the solvent was evaporated in vacuo and the residue was partitioned between dichloromethane and saturated solution of $NaHCO_3$. The organic phase was dried and then evaporated. The residue was chromatographed on silica gel in petroleum ether–ethyl acetate (4:1). Yield 1.97 g (80%) of compound **5**, R_F 0.65 (petroleum ether–ethyl acetate 2:1). $[\alpha]_D$ +52.2 (*c* 1.02, $CHCl_3$). ^{1}H NMR ($CDCl_3$): 1.78 m, 1 H (H-1″a); 1.92 ddd, 1 H, *J*(3ax,3eq) = 13.7, *J*(3ax,4) = 6.8, *J*(3ax,2) = 6.8 (H-3ax); 2.00 ddd, 1 H, *J*(1″a,1″b) = 15.1, *J*(1″b,1′) = 10.3, *J*(1″b,4) = 5.5 (H-1″b); 2.24 ddd, 1 H, *J*(3eq,3ax) = 13.7, *J*(3eq,4) = 6.6, *J*(3eq,2) = 1.4 (H-3eq); 2.62 m, 1 H (H-4); 3.59–3.75 m, 5 H (BnOC**H**$_2$CHPh, H-2′, H-3′, H-6a′); 3.92 m, 1 H (6b′); 4.02 m, 1 H (H-4′); 4.11 m, 1 H (H-5′); 4.25 bd, 1 H, *J*(1″b,1′) = 10.3 (H-1′); 4.47–4.80 m, 10 H (5 × OC**H**$_2$Ph); 5.00 dd, 1H, *J* = 8.1, 3.6 (BnOCH$_2$C**H**Ph); 5.50 dd, 1 H, *J*(2,3eq) = 1.4, *J*(2,3ax) = 6.8 (H-2); 6.01 d, 1 H, *J*(5,4) = 3.4 (H-5); 7.12 d, 1 H, *J* = 3.2 (H-thiazole); 7.19–7.41 m, 30 H (6 × Ph); 7.71 d, 1 H, *J* = 3.2 (H-thiazole). ^{13}C NMR ($CDCl_3$): 27.61 (C-4), 34.15 (C-1″), 34.17 (C-3), 67.61 (C-6′), 72.40 (C-1′), 72.95, 73.07, 73.27, 73.34, 73.52 (5 × OCH$_2$Ph), 74.35, 76.78, 77.01, 77.24 (C-2′, C-3′, C-4′, C-5′), 76.92 (BnOCH$_2$CHPh), 81.16 (BnOCH$_2$CHPh), 100.78 (C-2), 103.76 (C-5), 118.49 (CH-thiazole), 126.56–128.29 (25 × C_6H_5), 138.16, 138.32, 138.41, 138.50, 139.75 (5 × *ipso* C_6H_5), 142.79 (CH-thiazole); 143.58 (C-6) 164.46 (C-2 thiazole). For $C_{58}H_{59}NO_8S$ calculated relative molecular mass 930.16. MS (ESI), *m/z*: 931.4 $[M + H]^+$.

(2*S*,4*S*)-2-[(2*R*)-2-(Benzyloxy)-1-phenylethoxy]-4-[(2,3,4,6-tetra-*O*-benzyl-α-D-galacto pyranosyl)methyl]-6-formyl-3,4-dihydro-2*H*-pyran (**7**)

Molecular sieves (4Å, 1.5 g) were added to a solution of compound **5** (1.5 g, 1.6 mmol) in acetonitrile (10 ml), and methyl triflate (0.24 ml, 2.1 mmol) was added dropwise. After stirring at room temperature for 15 min, methanol (3 ml) was added and the solvent was evaporated in vacuo. The residue was treated with methanol (20 ml) and then $NaBH_4$ (0.20 g, 5.2 mmol) was added in portions. After stirring at room temperature for 15 min, acetone (5 ml) was added, the reaction mixture was filtered through Supercel and the filtrate was evaporated in vacuo. The residue was dissolved in acetonitrile (15 ml) and a solution of $AgNO_3$ (0.41 g, 2.4 mmol) in water (1.5 ml) was added under vigorous stirring. After stirring for 10 min, phosphate buffer (10 ml, pH 7) was added and after an additional 10 min the acetonitrile was evaporated in vacuo and the residue was partitioned between dichloromethane and phosphate buffer (pH 7). The organic phase was dried and evaporated. The resulting residue was flash-chromatographed through a short column of silica gel in petroleum ether–ethyl acetate (4:1). Yield 1.14 g (70%) of aldehyde **7**, R_F 0.4 (petroleum ether–ethyl acetate 3:1). $[\alpha]_D$ +33.6 (*c* 1.03, $CHCl_3$). ^{1}H NMR ($CDCl_3$): 1.92–2.07 m, 4 H (H-1″a, H-1″b, H-3ax, H-3eq); 2.57 m, 1 H (H-4); 3.54–3.65 m, 3 H (BnOC**H**$_2$CHPh, H-6a′); 3.71–3.78 m, 2 H (H-2′, H-3′); 3.87 m, 1 H (H-6b′); 3.99 m, 1 H (H-4′); 4.02–4.10 m, 2 H (H-1′, H-5′); 4.45–4.77 m, 10 H (5 × OC**H**$_2$Ph); 4.94 dd, 1 H, *J* = 8.0, 3.4 (BnOCH$_2$C**H**Ph); 5.56 m, 1 H (H-2); 5.81 d, 1 H, *J*(5,4) = 4.2 (H-5), 7.14–7.37 m, 30 H (6 × Ph); 8.74 s, 1 H (CHO). ^{13}C NMR ($CDCl_3$): 26.54 (C-4), 32.11 (C-1″), 32.15 (C-3), 67.68 (C-6′), 72.01 (C-1′), 72.8, 73.04, 73.21, 73.24, 73.34 (5 ×

OCH_2Ph), 74.31, 76.78, 77.01, 77.26 (C-2′, C-3′, C-4′, C-5′), 76.84 ($BnOCH_2CHPh$), 79.60 ($BnOCH_2CHPh$), 98.30 (C-2), 125.66 (C-5), 127.39–128.36 (25 × C_6H_5), 138.13, 138.20, 138.38, 139.47, 139.34 (5 × *ipso* C_6H_5), 148.72 (C-6), 186.40 (CHO). For $C_{56}H_{58}O_9$ calculated relative molecular mass 875.05. MS (ESI), *m/z*: 876.1 $[M + H]^+$.

(2*R*)-2-(Benzyloxy)-1-phenylethyl 2,3-Dideoxy-3-*C*-[(2,3,4,6-tetra-*O*-benzyl-α-D-galacto pyranosyl)methyl]-4,6-di-*O*-benzyl-β-L-*arabino*-hexopyranoside (**8**)

A 2 M solution of $BH_3{\cdot}Me_2S$ in tetrahydrofuran (2.1 ml, 4.1 mmol) was added dropwise to a cool (0 °C) solution of aldehyde **7** (1.03 g, 1.18 mmol) in tetrahydrofuran (35 ml) and the reaction mixture was stirred at room temperature for 16 h. The mixture was quenched by the gradual addition of 30% NaOH (2.2 ml) and 30% H_2O_2 (2.2 ml), and stirred at room temperature for 30 min. The reaction mixture was partitioned between dichloromethane and a saturated aqueous NaCl solution. The organic phase was dried and evaporated in vacuo. The residue was dissolved in tetrahydrofuran (20 ml) and stirred with NaH (60% suspension in mineral oil; 0.21 g, 5.3 mol) at room temperature for 1 h. Benzyl bromide (0.56 ml, 4.7 mmol) and tetrabutylammonium iodide (0.13 g, 0.35 mmol) were added, and the reaction mixture was heated to 40 °C for 15 min. After stirring at room temperature for 14 h, methanol (3 ml) was added and the solvent was evaporated in vacuo. The residue was partitioned between dichloromethane and a saturated solution of $NaHCO_3$. The organic layer was dried, evaporated in vacuo, and chromatographed on silica gel in petroleum ether–ethyl acetate (5:1). Yield 1 g (79%) of compound **8**, R_F 0.4 (petroleum ether–ethyl acetate 3:1). $[\alpha]_D$ +45.6 (*c* 0.26, $CHCl_3$). ^{1}H NMR ($CDCl_3$): 1.31–1.55 m, 2 H (H-1″a, H-2ax); 2.02–2.35 m, 3 H (H-1″b, H-2eq, H-3); 3.40 m, 1 H (H-5), 3.49–3.58 m, 2 H ($BnOCH_2aCHPh$, H-6a); 3.60–3.79 m, 6 H ($BnOCH_2bCHPh$, H-2′, H-3′, H-6′a, H-6b, H-5); 3.86 m, 1 H (H-6′b); 3.97 m, 1 H (H-4′); 4.10 m, 1 H (H-5′); 4.15 m, 1 H (H-1′); 4.34–4.84 m, 15 H (7 × OCH_2Ph, H-1); 4.93 dd, 1 H, *J* = 8.2, 3.5 ($BnOCH_2CHPh$); 7.10–7.43 m, 40 H (8 × Ph). ^{13}C NMR ($CDCl_3$): 29.70 (C-1″), 35.44 (C-3), 35.68 (C-2), 69.35 (C-6′), 69.58 (C-6), 71.27 (C-1′), 72.85, 72.99, 73.05, 73.18, 73.36, 73.43, 73.53 (7 × OCH_2Ph), 74.18, 74.26, 74.49 (C-2′, C-3′, C-4′), 74.72 ($BnOCH_2CHPh$), 76.79 (C-5), 76.85 (C-5′), 78.32 (C-4), 78.36 ($BnOCH_2CHPh$), 93.90 (C-1), 127.18–128.46 (40 × C_6H_5), 138.11, 138.22, 138.26, 138.29, 138.32, 138.41, 138.51, 138.53 (8 × *ipso* C_6H_5). For $C_{70}H_{74}O_{10}$ calculated relative molecular mass 1075.33. MS (ESI), *m/z*: 1076.6 $[M + H]^+$.

Methyl 2,3-Dideoxy-3-*C*-[(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)methyl]-4,6-di-*O*-acetyl-α-L-*arabino*-hexopyranoside (**9a**) and
Methyl 2,3-Dideoxy-3-*C*-[(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)methyl]-4,6-di-*O*-acetyl-β-L-*arabino*-hexopyranoside (**9b**)

Methanol (30 ml) and 3 M HCl (3.6 ml) were successively added to a solution of compound **8** (0.6 g, 0.56 mmol) in tetrahydrofuran (15 ml) and the reaction mixture was stirred at room temperature for 23 h. A saturated solution of $NaHCO_3$ (10 ml) was added cautiously and the resulting mixture was concentrated in vacuo. The residue thus obtained was partitioned between dichloromethane and a saturated solution of $NaHCO_3$. After drying and evaporation of the solvent, the residue was chromatographed on silica gel in petroleum ether–ethyl acetate (8:1). The obtained mixture of methyl glycosides (425 mg), R_F 0.3 (petroleum ether–ethyl acetate 3:1), *m/z* 879.4 $[M + H]^+$, was dissolved in methanol (10 ml) and hydrogenated over Pd/C (10%; 100 mg) at room temperature for 2 h. The catalyst was re-

moved by filtration, the solvent was evaporated and the residue dissolved in pyridine (2 ml). Acetic anhydride (2 ml) was added and the mixture was stirred at room temperature for 1 h. The reaction mixture was poured onto ice and then partitioned between water and ethyl acetate. The organic phase was dried and evaporated in vacuo. Chromatography of the residue on silica gel in petroleum ether–ethyl acetate (2:1) afforded 248 mg (75%) of product as a mixture of two anomers **9a** and **9b** in the ratio 4:1, R_F 0.7 (petroleum ether–ethyl acetate 2:1).

Anomer **9a**: ^{1}H NMR ($CDCl_3$): 1.37 m, 1 H (H-1″a); 1.49–1.58 m, 2 H (H-2ax, H-1″b); ca. 1.95 m, overlapped by Ac, 1 H (H-2eq); 1.95 s, 3 H (1 × Ac); 1.98 s, 3 H (1 × Ac); 2.00 s, 3 H (1 × Ac); 2.01 s, 3 H (1 × Ac); 2.02 s, 3 H (1 × Ac); 2.05 s, 3 H (1 × Ac); 2.19 m, 1 H (H-3); 3.27 s, 3 H (OCH_3); 3.77 ddd, 1 H, *J*(5,6a) = 2.3, *J*(5,6b) = 4.8, *J*(5,4) = 9.9 (H-5); 3.91 dd, 1 H, *J*(6a,5) = 2.3, *J*(6a,6b) = 12.1 (H-6a); 3.93–4.03 m, 2 H (H-5′, H-6a′); 4.13–4.16 m, 2 H (H-1′, H-6b′); 4.18 dd, overlapped, 1 H, *J*(6b,5) = 4.8, *J*(6b,6a) = 12.1 (H-6b); 4.61–4.71 m, 2 H (H-1, H-4); 5.04 dd, 1 H, *J*(3′,4′) = 3.2, *J*(3′,2′) = 9.6 (H-3′); 5.10 dd, 1 H, *J*(2′,1′) = 5.0, *J*(2′,3′) = 9.6 (H-2′); 5.31 dd, 1 H, *J*(4′,3′) = 3.2, *J*(4′,5′) = 5.5 (H-4′). ^{13}C NMR ($CDCl_3$): 20.48, 20.57, 20.62, 20.63, 20.74, 20.76 (6 × CH_3CO), 28.22 (C-1″), 32.33 (C-3), 36.07 (C-2), 54.36 (OCH_3), 61.67 and 62.73 (C-6 and C-6′), 67.48 and 67.57 (C-3′ and C-4′), 68.02 and 68.22 (C-2′ and C-5′), 68.53 (C-5), 71.35 (C-1′), 71.94 (C-4), 97.46 (C-1), 169.82, 169.88, 169.96, 170.43, 170.60, 170.74 (6 × CH_3CO). For $C_{26}H_{38}O_{15}$ calculated relative molecular mass 590.57. MS (ESI), *m/z*: 591.3 $[M + H]^+$.

Anomer **9b**: ^{1}H NMR ($CDCl_3$): 1.82 m, 1 H (H-3); 3.41 s, 3 H (OCH_3); 3.49 ddd, 1 H, *J*(5,6a) = 2.5, *J*(5,6b) = 4.9, *J*(4,5) = 9.6 (H-5); 4.35 dd, 1 H, *J*(1,2ax) = 9.4, *J*(1,2eq) = 1.8 (H-1), other resonances are overlapped by signals of the major isomer. For $C_{26}H_{38}O_{15}$ calculated relative molecular mass 590.57. MS (ESI), *m/z*: 591.3 $[M + H]^+$.

(2*R*,4*R*)-2-[(2*S*)-2-(Benzyloxy)-1-phenylethoxy]-4-[(2,3,4,6-tetra-*O*-benzyl-α-D-galacto pyranosyl)methyl]-6-(thiazol-2-yl)-3,4-dihydro-2*H*-pyran (**6**)

Compound **3b** (5 g) was treated in the same manner as described for the preparation of compound **5**, yielding 4.235 g (79%) of compound **6**, R_F 0.45 (petroleum ether–ethyl acetate 3:1). $[\alpha]_D$ +29.5 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): 1.73 m, 1 H (H-1″a); 1.87 ddd, 1 H, *J*(3ax,3eq) = 13.7, *J*(3ax,4) = 6.9, *J*(3ax,2) = 6.9 ($H\text{-}3_{ax}$); 1.95 ddd, 1 H, *J*(1″a,1″b) = 15.2, *J*(1″b,1′) = 10.3, *J*(1″b,4) = 5.4 (H-1″b); 2.19 ddd, 1 H, *J*(3eq,3ax) = 13.7, *J*(3eq,4) = 6.8, *J*(3eq,2) = 1.2 (H-3eq); 2.62 m, 1 H (H-4); 3.59–3.75 m, 5 H ($BnOC\mathbf{H}_2CHPh$, H-2′, H-3′, H-6a′); 3.87 m, 1 H (H-6b′); 3.98 m, 1 H (H-4′); 4.06 m, 1 H (H-5′); 4.20 bd, 1 H, *J*(1″b,1′) = 10.3 (H-1′); 4.45–4.75 m, 10 H (5 × $OC\mathbf{H}_2Ph$); 4.95 dd, 1 H, *J* = 7.9, 3.4 ($BnOCH_2C\mathbf{H}Ph$); 5.45 dd, 1 H, *J*(2,3eq) = 1.4, *J*(2,3ax) = 6.8 (H-2); 6.01 d, 1 H, *J*(5,4) = 3.2 (H-5); 7.12 d, 1 H, *J* = 3.1 (H-thiazole); 7.19–7.35 m, 30 H (6 × Ph); 7.66 d, 1 H, *J* = 3.1 (H-thiazole). ^{13}C NMR ($CDCl_3$): 27.65 (C-4), 34.15 (C-1″), 34.17 (C-3), 67.61 (C-6′), 72.40 (C-1′), 72.95, 73.07, 73.27, 73.34, 73.52 (5 × OCH_2Ph), 74.35, 76.78, 77.01, 77.24 (C-2′, C-3′, C-4′, C-5′), 76.92 ($BnOCH_2CHPh$), 81.16 ($BnOCH_2CHPh$), 100.78 (C-2), 103.76 (C-5), 118.49 (CH-thiazole), 126.56–128.29 (25 × C_6H_5), 138.16, 138.32, 138.41, 138.50, 139.75 (5 × *ipso* C_6H_5), 142.79 (CH-thiazole), 143.58 (C-6), 164.46 (C-2 thiazole). For $C_{58}H_{59}NO_8S$ calculated relative molecular mass 930.16. MS (ESI), *m/z*: 931.4 $[M + H]^+$.

(2*R*,4*R*)-2-[(2*S*)-2-(Benzyloxy)-1-phenylethoxy]-4-[(2,3,4,6-tetra-*O*-benzyl-α-D-galacto pyranosyl)methyl]-6-formyl-3,4-dihydro-2*H*-pyran (**10**)

Compound **6** (2.25 g) was treated in the same manner as described for the preparation of compound **7**, yielding 1.60 g (75%) of aldehyde **10**, R_F 0.4 (petroleum ether–ethyl acetate 3:1). $[\alpha]_D$ + 23.8 (*c* 0.92, $CHCl_3$). ^{1}H NMR ($CDCl_3$): 1.90–2.06 m, 4 H (H-1″a, H-1″b, H-3ax, H-3eq); 2.57 m, 1 H (H-4); 3.50–3.65 m, 3 H (BnOC**H**$_2$CHPh, H-6a′); 3.73–3.80 m, 2 H (H-2′, H-3′); 3.87 m, 1 H (H-6b′); 3.99 m, 1 H (H-4′); 4.02–4.11 m, 2 H (H-1′, H-5′); 4.45–4.75 m, 10 H (5 × OC**H**$_2$Ph); 4.94 dd, 1 H, *J* = 8.1, 3.5 (BnOCH$_2$C**H**Ph); 5.56 m, 1 H (H-2); 5.81 d, 1 H, *J*(5,4) = 4.2 (H-5); 7.12–7.40 m, 30 H (6 × Ph); 8.74 s, 1 H (CHO). ^{13}C NMR ($CDCl_3$): 26.54 (C-4), 32.11 (C-1″), 32. 15 (C-3), 67.68 (C-6′), 72.01 (C-1′), 72.8, 73.04, 73.21, 73.24, 73.34 (5 × CH_2Ph), 74.31, 76.78, 77.01, 77.26 (C-2′, C-3′, C-4′, C-5′), 76.84 (BnOCH_2CHPh), 79.60 (BnOCH_2CHPh), 98.30 (C-2), 125.66 (C-5), 127.39–128.36 (25 × **C**$_6$H$_5$), 138.13, 138.20, 138.38, 139.47, 139.34 (5 × *ipso* C_6H_5), 148.72 (C-6), 186.40 (**C**HO). For $C_{56}H_{58}O_9$ calculated relative molecular mass 875.05. MS (ESI), *m/z*: 876.1 $[M + H]^+$.

Methyl 2,3-Dideoxy-3-*C*-[(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)methyl]-4,6-di-*O*-acetyl-α-D-*arabino*-hexopyranoside (**12a**) and
Methyl 2,3-Dideoxy-3-*C*-[(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)methyl]-4,6-di-*O*-acetyl-β-D-*arabino*-hexopyranoside (**12b**)

Compoud **10** (1.60 g) was treated in the same manner as described for the preparation of compound **8**, yielding compound **11** (1.69 g), R_F 0.45 (petroleum ether–ethyl acetate 3:1), *m/z* 1076.6 $[M + H]^+$, which was immediately processed as described for the preparation of compounds **9a** and **9b**, yielding 650 mg (60%) of a mixture of anomers **12a** and **12b** in the ratio 4:1, R_F 0.7 (petroleum ether–ethyl acetate 2:1).

Anomer **12a**: ^{1}H NMR ($CDCl_3$): 1.47 m, 1 H (H-1″a); 1.56–1.66 m, 2 H (H-2ax, H-1″b); ca. 2.00 m, overlapped by Ac, 1 H (H-2eq); 2.02 s, 3 H (1 × Ac); 2.05 s, 3 H (1 × Ac); 2.06 s, 3 H (1 × Ac); 2.07 s, 3 H (1 × Ac); 2.08 s, 3 H (1 × Ac); 2.12 s, 3 H (1 × Ac); 2.26 m, 1 H (H-3); 3.34 s, 3 H (OCH_3); 3.84 ddd, 1 H, *J*(5,6a) = 2.1, *J*(5,6b) = 4.6, *J*(5,4) = 9.7 (H-5); 3.99 dd, 1 H, *J*(6a,5) = 2.1, *J*(6a,6b) = 12.2 (H-6a); 4.01–4.09 m, 2 H (H-5′, H-6a′); 4.20–4.25 m, 2 H (H-1′, H-6b′); 4.27 dd, overlapped, 1 H, *J*(6b,5) = 4.6, *J*(6a,6b) = 12.2 (H-6b), 4.71–4.77 m, 2 H (H-1, H-4); 5.10 dd, 1 H, *J*(3′,4′) = 3.2, *J*(3′,2′) = 9.5 (H-3′); 5.17 dd, 1 H, *J*(2′,1′) = 5.1, *J*(2′,3′) = 9.5 (H-2′); 5.38 m, 1 H (H-4′). ^{13}C NMR ($CDCl_3$): 20.48, 20.52, 20.57, 20.62, 20.64, 20.76 (6 × CH_3CO), 28.25 (C-1′), 32.34 (C-3), 36.07 (C-2), 54.54 (CH_3O), 61.64 and 62.73 (C-6 and C-6′), 67.49 and 67.55 (C-3′ and C-4′), 68.04 and 68.23 (C-2′ and C-5′), 68.54 (C-5), 71.35 and 71.94 (C-4 and C-1′), 97.47 (C-1), 169.83, 169.90, 169.97, 170.45, 170.62, 170.77 (6 × CH_3CO). For $C_{26}H_{38}O_{15}$ calculated relative molecular mass 590.57. MS (ESI), *m/z*: 591.3 $[M + H]^+$.

Anomer **12b**: ^{1}H NMR ($CDCl_3$): 1.86 m, 1 H (H-3); 3.49 s, 3 H (OCH_3); 3.56 ddd, 1 H, *J*(5,6a) = 2.4, *J*(5,6b) = 5.0, *J*(4,5) = 9.6 (H-5); 4.42 dd, 1 H, *J*(1,2ax) = 9.5, *J*(1,2eq) = 1.9 (H-1), other resonances are overlapped by signals of the major isomer. For $C_{26}H_{38}O_{15}$ calculated relative molecular mass 590.57. MS (ESI), *m/z*: 591.3 $[M + H]^+$.

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