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Synthesis of 2-deoxy-D-*arabino*/*lyxo*-hexopyranosyl disaccharides

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Abstract—Synthesis of 2-deoxy-D-*arabino*/*lyxo*-hexopyranosyl disaccharides is reported. In these, the disaccharides contain 2-deoxy-*arabino*-hexopyranosyl and 2-deoxy-*lyxo*-hexopyranosyl sugars as either the reducing or the non-reducing or both the sugar units of the disaccharides. The activated 2-deoxy-1-thioglycosides served as the common precursors to prepare the 2-deoxy disaccharides with the above configurations.

Keywords: Deoxysugars; Glycals; Glycosylations; Thioglycosides

1. Introduction

Among various deoxy sugars, 2-deoxysugars assume significance as integral components of several natural products.[1] The biological functions of, for example, antibiotics require the presence of the deoxy sugar units in these molecules.[2] Associated with the importance of 2-deoxy sugar units for biological functions, a number of synthetic methods have been developed.[3] An approach relying on utilizing an activated 2-deoxy-1-thioglycoside has been developed by us recently. An easy access to activated 2-deoxy-1-thioglycoside involves the reaction of readily available 1,2-unsaturated sugars, namely glycals, with EtSH in the presence of catalytic amount of ceric ammonium nitrate (CAN).[4] The synthetic utility of the activated 2-deoxy-1-thioglycoside has been established in glycosylations involving both aglycosyl and glycosyl acceptors.[4] Methods have also been established to prepare either anomers of aryl 2-deoxy-glycosides, from activated 2-deoxy-1-thioglycoside donors.[5] Continuing our efforts, the synthesis of 2-deoxy disaccharides were undertaken. These disaccharides contain 2-deoxy-*arabino*-hexopyranosyl and 2-deoxy-*lyxo*-hexopyranosyl sugars as either the reducing or the non-reducing or both the sugar units of the disaccharides. 2-Deoxy disaccharides with maltose and lactose configuration are studied previously in detail. For example, the 2-deoxy maltosyl oligosaccharides have been studied to understand the enzymatic glycosylations and the functions of enzyme, such as amylases, glycosylases and cyclodextrin-glucano-transferases.[6] The 2-deoxylactose derivatives, on the other hand, are known to be the high-affinity substrates for bacterial phosphotransferases[7] and the enzymatic products of galactosyltransferases.[8] The readily available 2-deoxy-thioglycosides have thus been considered as suitable precursors to synthesize 2-deoxy sugar containing disaccharides. Synthesis of six new 2-deoxy-*arabino*-hexopyranosyl and 2-deoxy-*lyxo*-hexopyranosyl sugar containing disaccharides are described in this report. These are (i) 2-deoxy-α-D-*arabino*-hexopyranosyl-(1→4)-D-glucopyranose (2′-deoxy maltose); (ii) α-D-glucopyranosyl-(1→4)-2-deoxy-D-*arabino*-hexopyranose (2-deoxy maltose); (iii) 2-deoxy-α-D-*arabino*-hexopyranosyl-(1→4)-2-deoxy-D-*arabino*-hexopyranose (2,2′-dideoxy maltose); (iv) 2-deoxy-α-D-*lyxo*-hexopyranosyl-(1→4)-D-glucopyranose; (v) 2-deoxy-α-D-*lyxo*-hexopyranosyl-(1→4)-2-deoxy-D-*arabino*-hexopyranose and (vi) β-D-galactopyranosyl-(1→4)-2-deoxy-D-*arabino*-hexopyranoside (2-deoxy lactose).

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2. Results and discussion

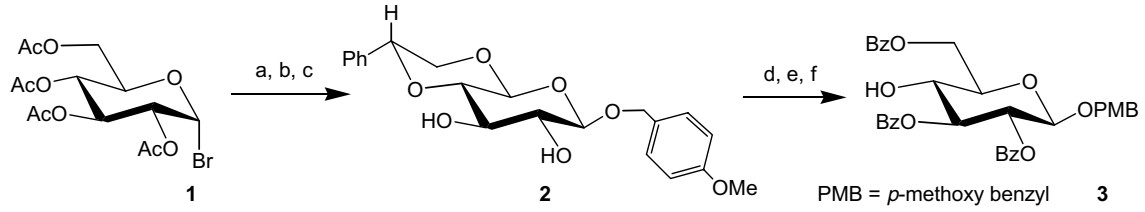
2.1. Synthesis of 2′-deoxy- and 2,2′-dideoxy-disaccharides

Synthesis of this series of disaccharides was accomplished through a glycosylation between a 2-deoxy glycosyl donor and appropriately protected either a glycosyl or a 2-deoxyglycosyl acceptor. The formation of the α-glycosidic linkage was anticipated from the 2-deoxy glycosyl donor, due to the absence of neighbouring group effects. Also, the formation of the α-glycosidic linkage with 2-deoxy-1-thioglycoside donor was established previously.[4,5] The required acceptors for glycosylation with 2-deoxy-1-thioglycoside having free hydroxyl group at C-4 were synthesized as described below.

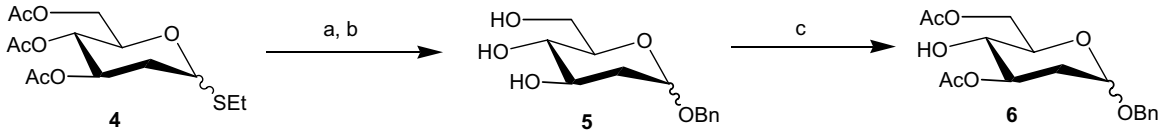
2.1.1. Synthesis of *p*-methoxybenzyl 2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside (3). Synthesis of the acceptor **3** was performed with a modification of a known procedure.[9] Thus, reaction of acetobromo glucose (**1**)[10] with *p*-methoxybenzyl alcohol (PMB–OH), followed by de-O-acetylation and 4,6-O-benzylidination afforded diol **2** (Scheme 1). The following reactions were performed subsequently: (i) O-benzoylation of **2** with BzCl and pyridine; (ii) deprotection of benzylidene group and (iii) the reaction of the resulting product with $^{n}Bu_2SnO$, followed by treatment with BzCl afforded the acceptor alcohol **3**, in an overall yield of 44%, on the basis of **1** (Scheme 1).

2.1.2. Synthesis of benzyl 2-deoxy-3,6-di-*O*-acetyl-D-*arabino*-hexopyranoside (6). Synthesis of **6** was initiated from the known 2-deoxy-1-thioglycoside **4**.[4] Glycosylation of BnOH with **4**, followed by de-O-acetylation led to isolation of benzyl 2-deoxy-*arabino*-hexopyranoside (**5**) (Scheme 2). Partial acetylation of **5** was performed with AcCl upon the reaction of **5** with $^{n}Bu_2SnO$, to afford alcohol **6**, in an overall yield of 67%, on the basis of **4**.

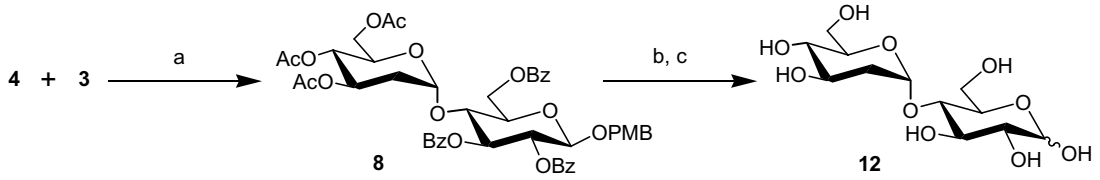
The glycosylation reactions were then performed, involving acceptors **3** and **6** and the donor **4** and ethyl 2-deoxy-3,4,6-tri-*O*-acetyl-1-thio-D-*lyxo*-hexopyranoside (**7**).[4] Syntheses of 2′-deoxy maltose (**12**) and 2,2′-dideoxy maltose (**14**) were thus accomplished by the reaction of 2-deoxy-1-thioglycoside **4**, with acceptors **3** and **6**, promoted by NIS/TfOH (Schemes 3 and 4). The glycosylations led to the isolation of disaccharides **8**



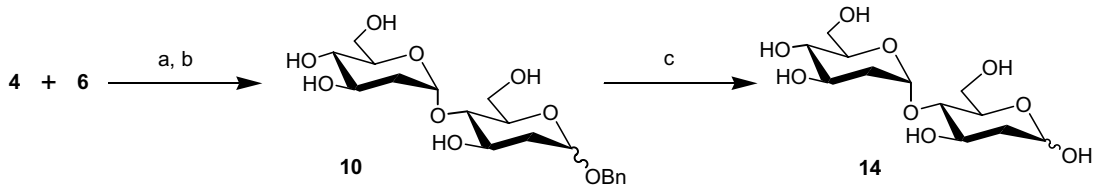
Scheme 1. Reagents and conditions: (a) Ag_2O, PMB–OH, I_2 (cat.), 4 Å MS, CH_2Cl_2, rt, 24 h; (b) NaOMe (cat.), MeOH, rt, 6 h; (c) α,α-dimethoxytoluene, *p*-TsOH, DMF, 60 °C, 2 mm of Hg, 1.5 h; (d) BzCl, C_5H_5N, 0 °C–rt, 24 h; (e) *p*-TsOH, MeOH/THF (1:1), 3 h; (f) (i) $^{n}Bu_2SnO$, PhMe, reflux, 16 h; (ii) BzCl, rt, 5 min.



Scheme 2. Reagents and conditions: (a) BnOH, NIS, TfOH (cat.), 4 Å MS, CH_2Cl_2, 0 °C, 30 min; (b) NaOMe (cat.), MeOH, rt, 6 h; (c) (i) $^{n}Bu_2SnO$, MeOH, reflux, 16 h; (ii) AcCl, PhMe, rt, 1 h.



Scheme 3. Reagents and conditions: (a) NIS, TfOH (cat.), 4 Å MS, CH_2Cl_2, 0 °C, 30 min; (b) CAN, MeCN/H_2O (9:1 v/v), rt, 4 h; (c) NaOMe (cat.), MeOH, rt, 6 h.



Scheme 4. Reagents and conditions: (a) NIS, TfOH (cat.), 4 Å MS, CH_2Cl_2, 0 °C, 30 min; (b) NaOMe (cat.), MeOH, rt, 6 h; (c) H_2, Pd/C (10%), MeOH, rt, 3 d.

and **10**. Subsequent deprotection afforded disaccharides **12** and **14**.

Similarly, glycosylation of acceptors **3** and **6** with 2-deoxy-1-thioglycoside **7** provided protected disaccharides **9** and **11** (Schemes 5 and 6). Deprotection of the protecting groups in **9** and **11** afforded the free hydroxyl group containing disaccharides **13** and **15**.

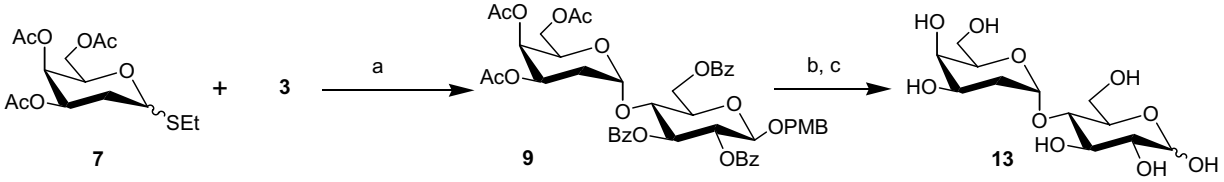
The anomeric configurations of the newly formed glycosidic linkages were confirmed by ^1H and ^{13}C NMR spectroscopies. In the case of **8** and **9**, the H-1′ appeared as an apparent doublet at ~5.20 ppm ($J_{1,2} \sim 4.0$ Hz). The dideoxy disaccharides **10** and **11** showed anomeric H-1′ resonance at ~5.32 ppm, with $J_{1,2} \sim 3.0$ Hz. The anomeric H-1 in **10** and **11** resonated at ~4.92 ppm and 4.34 ppm, corresponding to the presence of α- and β-anomeric configuration at the reducing end of the disaccharides.

An analysis of the anomeric protons in the case of free mono- and dideoxy disaccharides **12**–**15** showed the following trend: (i) H-1′ in **12** and **13** resonated at 5.35 ppm as an apparent doublet with $J_{1,2a} \sim 2.7$ Hz; (ii) H-1 resonated at ~5.06 ppm ($J_{1,2a} \sim 3.6$ Hz) and at 4.50 ppm ($J_{1,2} \sim 7.8$ Hz); (iii) H-1′ in **14** and **15** appeared at ~5.50 ppm as a broad singlet and (iv) H-1 in **14** and **15** appeared at 5.35 ppm ($J_{1,2a} \sim 3.0$ Hz) and 4.91 ppm ($J_{1,2e} \sim 2.0$ Hz and $J_{1,2a} \sim 10.0$ Hz). The above observations for H-1′ and H-1 resonances for the monodeoxy (**12**, **13**) and dideoxy (**14**, **15**) disaccharides indicated the presence of α-anomeric configuration at the non-reducing end and a mixture of α- and β-anomeric configurations at the reducing end of the disaccharides. The α/β ratio of the anomeric configurations at the reducing end was found to be ~2:1, in all the disaccharides.

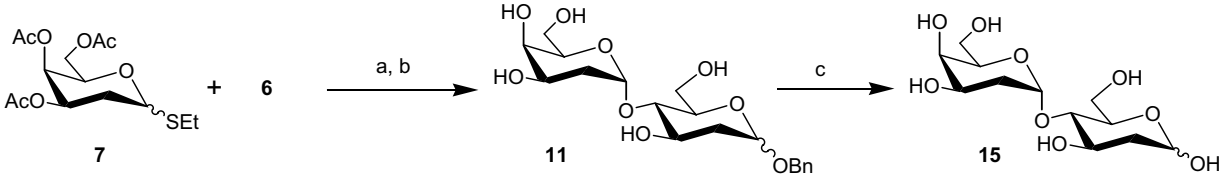
In ^{13}C NMR spectrum of **12**–**15**, the C-1′ nuclei appeared at 98.5 ppm, whereas the C-1 appeared as the set of resonances at ~91 ppm and 93–96 ppm. These observations further confirmed the α-anomeric configuration at the non-reducing end and α,β-anomeric mixtures at the reducing end of the disaccharides.

2.2. Synthesis of 2-deoxy disaccharides

The preparations of 2-deoxy disaccharides were performed directly from the 1,2-unsaturated disaccharide glycals. It is noted that disaccharide glycals have been shown before as precursors for the synthesis of 2-deoxy disaccharides. Maltal and lactal have been subjected to hydration across the vinylic double bond, under the acid-catalyzed condition, to form 2-deoxy maltose[11a] and 2-deoxy lactose, respectively.[11b] In the present



Scheme 5. Reagents and conditions: (a) NIS, TfOH (cat.), 4 Å MS, CH_2Cl_2, 0 °C, 30 min; (b) CAN, MeCN/H_2O (9:1 v/v), rt, 4 h; (c) NaOMe (cat.), MeOH, rt, 6 h.



Scheme 6. Reagents and conditions: (a) NIS, TfOH (cat.), 4 Å MS, CH_2Cl_2, 0 °C, 30 min; (b) NaOMe (cat.), MeOH, rt, 6 h; (c) H_2, Pd/C (10%), MeOH, rt, 3 d.

study, it was intended to explore the 2-deoxy-1-thioglycoside route to prepare the 2-deoxydisaccharides. Thus, *hexa-O*-acetyl maltal (**16**)[12] and *hexa-O*-acetyl lactal (**17**)[12] were converted to the corresponding 2-deoxy-1-thioglycosides **18** and **19**, respectively, by treatment with EtSH/CAN reagent system (Scheme 7). The yields were poor, only 10–15% of **18** and **19** were obtained, the remaining products were found to be 2,3-unsaturated thioglycosides, corresponding to the Ferrier products. With a desire to obtain 2-deoxy-1-thioglycoside disaccharides in higher yields, an alternate procedure was undertaken. In this procedure, the glycals **16** and **17** were converted first to C-1 acetylated 2-deoxy disaccharides **20** and **21**, respectively, utilizing the method by Lam and Gervey-Hague.[13] Thus, the glycals **16** and **17** were treated with HBr/AcOH, followed by treatment with Ac_2O/AcOH that led to the formation of **20** and **21** (Scheme 8). The C-1 acetylated 2-deoxy disaccharides **20** and **21** were subjected subsequently to a reaction with BF_3–Et_2O and EtSH at −40 °C, which furnished 2-deoxythioglycosides **18** and **19**. The overall yield of the formation of **18** and **19** were ∼75%, on the basis of glycals **16** and **17**. Thus, an alternative method of synthesizing the activated 2-deoxy-1-thioglycosides has also been identified, which does not require reaction with CAN. Hydrolysis of the thioglycosides in **18** and **19** was conducted in the presence of NBS in acetone–H_2O, followed by de-O-acetylation under Zemplén condition, that afforded 2-deoxydisaccharides **22** and **23**, in good yields. Alternatively, the disaccharides **22** and **23** could also be secured by direct de-O-acetylation of **20** and **21**, under Zemplén condition.

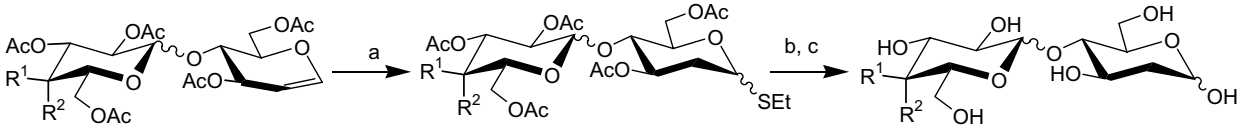
The constitutions of **22** and **23** were established by ^1H and ^{13}C NMR spectroscopies. The anomeric H-1′ appeared at 5.30 ppm, as a broad singlet for **22**, whereas that for **23** was observed at 4.33 ppm, overlapped with H-1 proton of the reducing end. The anomeric H-1 was observed as a set of resonances corresponding to α- and β-configurations, in the order: (i) 5.04 ppm for **22** and 5.39 ppm for **23**; (ii) 4.90 ppm ($J_{1,2e} \sim 2.0$ Hz and $J_{1,2a} \sim 10.0$ Hz) for **22** and 4.33 ppm as a multiplet for **23**. The anomeric C-1′ resonated at 95.4 ppm and 102.9 ppm, for **22** and **23**, respectively. The C-1 nucleus of the α-anomer was observed at 92.2 and 93.1 ppm for **22** and **23**, respectively. The corresponding values for the β-anomer were observed at 94.5 ppm for **22** and 98.0 ppm for **23**.

In conclusion, a series of 2-deoxy, 2′-deoxy and 2,2′-dideoxy disaccharides, presenting *arabino*-hexopyranosyl and *lyxo*-hexopyranosyl sugar units, were prepared through glycosylations involving 2-deoxy-1-thioglycoside donors. Activated 2-deoxy-1-thioglycoside disaccharide donors have also been explored to secure the 2-deoxy disaccharides. Few of the 2′-deoxy- and 2,2′-dideoxy disaccharides are known previously through enzymatic methods.[6–8,14] The glycosylations studied herein, involving orthogonally protected 2-deoxy-1-thioglycosides, allow the preparation of a range of 2 or 2′-monodeoxy and 2,2′-dideoxy disaccharides.

3. Experimental

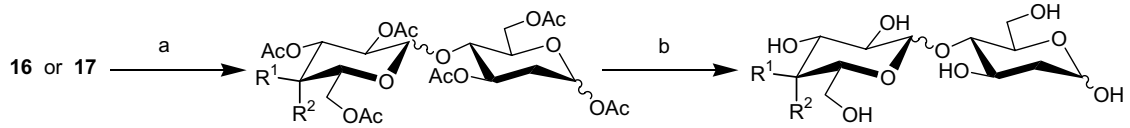
3.1. General methods

Chemicals were purchased from commercial sources and were used without further purification. Solvents were dried and distilled according to the literature procedures. Analytical TLC was performed on commercial Merck plates coated with Silica Gel GF_{254} (0.25 mm). Silica gel (100–200 mesh) was used for column chromatography. Optical rotations were recorded on a Jasco



16: (1-4)α linkage: R^1 = OAc, R^2 = H
17: (1-4)β linkage: R^1 = H, R^2 = OAc
18: (1-4)α linkage: R^1 = OAc, R^2 = H
19: (1-4)β linkage: R^1 = H, R^2 = OAc
22: (1-4)α linkage: R^1 = OH, R^2 = H,
23: (1-4)β linkage: R^1 = H, R^2 = OH

Scheme 7. Reagents and conditions: (a) CAN (cat.), EtSH, MeCN, 0 °C–rt, 16 h; (b) NBS, acetone/H_2O (5:1, v/v), rt, 5 min; (c) NaOMe (cat.), MeOH, rt, 1 h.



20: (1-4)α linkage: R^1 = OAc, R^2 = H
21: (1-4)β linkage: R^1 = H, R^2 = OAc
22: (1-4)α linkage: R^1 = OH, R^2 = H,
23: (1-4)β linkage: R^1 = H, R^2 = OH

Scheme 8. Reagents and conditions: (a) HBr/AcOH (cat.) (33% w/v), Ac_2O, AcOH, CH_2Cl_2, 0 °C–rt, 16 h; (b) NaOMe (cat.), MeOH, rt, 6 h.

Model P-1020 polarimeter at the sodium D line at 24 °C. High-resolution mass spectra were obtained from Q-TOF instrument by electron spray ionization (ESI) technique. ^{1}H and ^{13}C NMR spectral analysis were performed on a 300/400 MHz and 75/100 MHz spectrometer, respectively, with residual solvent signal acting as the internal standard. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; m, multiplet; band, several overlapping signals; br, broad.

3.2. 4-Methoxybenzyl 2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside (3)

To a mixture of BzCl (3 mL, 0.042 mol) and pyridine (6 mL) in CH_2Cl_2 (15 mL), 4-methoxybenzyl 4,6-*O*-benzylidene-β-D-glucopyranoside (**2**)[9] (3.68 g, 0.012 mol) in CH_2Cl_2 (15 mL) was added dropwise at 0 °C. After 24 h, the reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with ice-cold aq HCl (5%) solution, satd aq $NaHCO_3$ solution, water, dried (Na_2SO_4) and concentrated. The resulting crude 4-methoxybenzyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranoside (5.5 g) was dissolved in MeOH/THF (20 mL, 1:1, v/v) and was added with *p*-TsOH (2.46 g). After 3 h, the reaction was quenched with Et_3N (4 mL), concentrated and purified by column chromatography (SiO_2, 100–200 mesh) to afford 4-methoxybenzyl 2,3-di-*O*-benzoyl-β-D-glucopyranoside (4.37 g, 86%, after 2 steps), as a foamy solid. $R_f = 0.27$ (1:1 EtOAc/PhMe); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.95–7.07 (m, 10H, aromatic), 7.08 (d, 2H, $J = 8.6$ Hz, aromatic), 6.68 (d, 2H, $J = 8.6$ Hz, aromatic), 5.43 (dd, 1H, $J = 7.8$, 9.3 Hz, H-2), 5.33 (app. t, 1H, $J = 9.3$ Hz, H-3), 4.78 (d, 1H, $J = 12.3$ Hz, PhCH_2), 4.59 (d, 1H, $J = 7.8$ Hz, H-1), 4.67 (d, 1H, $J = 12.3$ Hz, PhCH_2), 4.02–3.74 (m, 3H, H-6$_a$, H-6$_b$, H-5), 3.73 (s, 3H, OCH_3), 3.55–3.49 (m, 1H, H-4), 3.33 (br s, 2H, –OH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.5, 159.3, 133.5, 133.2, 129.9, 129.8, 129.5, 129.3, 129.0, 128.8, 128.6, 128.4, 128.3, 113.7, 99.1 (C-1), 76.5 (C-2), 75.8 (C-3), 71.4 (Ph*C*H$_2$), 70.6 (C-4), 69.9 (C-5), 62.2 (C-6), 55.2 (OCH_3). HR-MS *m*/*z*: $[M+Na]^+$ calcd for $C_{28}H_{28}O_9$, 531.1631; found, 531.1635.

A suspension of ^{n}Bu$_2$SnO (2.9 g, 0.01 mol), 4-methoxybenzyl 2,3-di-*O*-benzoyl-β-D-glucopyranoside (4.37 g, 9.6 mmol) in PhMe was refluxed, with azotropic removal of water. After 16 h, the reaction mixture was cooled, BzCl (1.34 mL, 0.012 mol) was added and stirred for 5 min. Removal of the solvent and purification of the resulting residue afforded **3** (4.90 g, 93%), as a foamy solid. $R_f = 0.43$ (20% EtOAc/PhMe); $[\alpha]_D^{24}$ +24.8 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.13–7.25 (m, 15H, aromatic), 7.09 (d, 2H, $J = 8.7$ Hz, aromatic), 6.68 (d, 2H, $J = 8.7$ Hz, aromatic), 5.49 (dd, 1H, $J = 7.8$, 9.3 Hz, H-2), 5.38 (app. t, 1H, $J = 9.3$, H-3), 4.84–4.59 (m, 5H, H-1, H-6$_a$, H-6$_b$, PhCH_2), 3.91 (ddd, 1H, $J = 3.8$, 4.5, 9.3 Hz, H-4), 3.79–3.75 (band, 4H, H-5, OCH_3), 3.50 (d, 1H, $J = 4.5$ Hz, –OH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.4, 166.9, 165.2, 159.4, 133.5, 133.4, 130.0, 129.9, 129.8, 129.6, 129.3, 128.9, 128.6, 128.5, 128.4, 128.3, 113.7, 98.7 (C-1), 74.5 (C-2), 71.4 (C-3, Ph*C*H$_2$), 70.1 (C-4), 69.7 (C-5), 63.5 (C-6), 55.2 (OCH_3). HR-MS *m*/*z*: $[M+Na]^+$ calcd for $C_{35}H_{32}O_{10}$, 635.1893; found, 635.1919.

3.3. Benzyl 2-deoxy-3,6-di-*O*-acetyl-D-*arabino*-hexopyranoside (6)

A mixture of benzyl 2-deoxy-D-*arabino*-hexopyranoside (**5**)[4] (1.23 g, 4.86 mmol) and ^{n}Bu$_2$SnO (2.49 g, 0.01 mol) was dissolved in MeOH (40 mL) and refluxed for 16 h. The solvents were evaporated and the resulting residue was dried at 60 °C, dissolved in PhMe (20 mL) and AcCl (728 μL, 0.01 mol) was added. After stirring for 1 h in room temperature, the solvents were evaporated and the crude product was purified to obtain **6** (1.31 g, 80%, α/β = 2:1), as a gum, along benzyl 2,3,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranoside (0.22 g, 12%). $R_f = 0.48$ (1:1 EtOAc/pet ether); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.35–7.27 (band, aromatic), 5.20 (ddd, $J = 5.4$, 9.3, 12.0 Hz, H-3β), 5.00 (d, $J = 3.0$ Hz, H-1α), 4.93–4.79 (m, H-4β, PhCH_2), 4.69–4.58 (m, PhCH_2), 4.50–4.43 (m, H-1β, H-5α, H-6$_a$α, H-6$_a$β), 4.37 (dd, $J = 2.1$, 12.3 Hz, H-6$_b$α), 4.25 (dd, $J = 2.1$, 12.0 Hz, H-6$_b$β), 3.85 (ddd, $J = 2.1$, 4.8, 9.9 Hz, H-5β), 3.54–3.40 (m, H-3α, H-4α), 3.29–3.25 (band, –OH), 2.33–2.20 (m, H-2$_a$α, H-2$_e$β), 2.13–2.09 (band, $COCH_3$), 1.80–1.63 (m, H-2$_e$α, H-2$_a$β); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.6, 171.5, 171.4, 171.1, 137.1, 136.9, 128.3, 127.9, 127.8, 127.7, 98.0 (C-1β), 96.1 (C-1α), 74.0, 73.3, 71.9, 70.4, 70.3, 69.6, 69.0, 68.9, 63.4, 63.3, 36.9 (C-2β), 34.7 (C-2α), 21.0, 20.9, 20.8. HR-MS *m*/*z*: $[M+Na]^+$ calcd for $C_{17}H_{22}O_7$, 361.1263; found, 361.1261.

3.4. 4-Methoxybenzyl 4-*O*-(2-deoxy-3,4,6-tri-*O*-acetyl-α-D-*arabino*-hexopyranosyl)-2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside (8)

Compound **4**[4] (0.31 g, 0.93 mmol) and **3** (0.31 g, 0.51 mmol) were dissolved in CH_2Cl_2 (10 mL) and stirred for 1 h in the presence of 4 Å MS (0.8 g), under N_2 atmosphere. *N*-Iodosuccinimide (0.25 g, 1.12 mmol) and catalytic TfOH (10 μL, 0.11 mmol) were added at 0 °C, stirred for 30 min. and neutralized with a few drops of Et_3N. The reaction mixture was diluted with CH_2Cl_2 (25 mL), filtered and the filtrate was washed with aq $Na_2S_2O_3$ solution, brine, dried and concentrated. Purification of the crude product afforded disaccharide **8** (0.25 g, 55%), as a white foamy solid. $R_f = 0.20$ (EtOAc/pet ether 1:2); $[\alpha]_D^{24}$ +38.6 (*c* 1.04, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.16–7.35 (m,

15H, aromatic), 7.07 (d, 2H, $J = 8.7$ Hz, aromatic), 6.68 (d, 2H, $J = 8.7$ Hz, aromatic), 5.67 (app. t, 1H, $J = 9.0$ Hz, H-3), 5.42 (dd, 1H, $J = 7.8$, 9.0 Hz, H-2), 5.19 (d, 1H, $J = 3.6$ Hz, H-1′), 4.88–4.53 (m, 7H, PhCH_2, H-1, H-6$_a$, H-6$_b$, H-3′, H-4′), 4.28–4.13 (m, 3H, H-5, H-6′$_a$, H-6′$_b$), 4.04 (ddd, 1H, $J = 3.5$, 4.7, 9.0 Hz, H-5′), 3.86–3.75 (band, 4H, H-4, OCH_3), 2.13–1.89 (band, 11H, $COCH_3$, H-2′$_a$, H-2′$_e$); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.5, 169.8, 169.7, 166.1, 165.3, 165.1, 159.3, 133.5, 133.4, 133.1, 130.0, 129.8, 129.8, 129.7, 129.6, 129.5, 128.3, 128.2, 113.7, 98.4 (C-1), 98.3 (C-1′), 75.5, 75.4, 72.7, 71.7, 70.1, 69.2, 68.9, 68.0, 63.4, 62.0, 55.1 (OCH_3), 34.7 (C-2′), 20.7, 20.6. HR-MS m/z: $[M+Na]^+$ calcd for $C_{47}H_{48}O_{17}$, 907.2789; found, 907.2783.

3.5. 4-Methoxybenzyl 4-*O*-(2-deoxy-3,4,6-tri-*O*-acetyl-α-D-*lyxo*-hexopyranosyl)-2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside (9)

Compound **9** was prepared according to the method described for the synthesis of compound **8**, using **7**[4] (0.35 g, 1.05 mmol), **3** (0.520 g, 0.95 mmol), 4 Å MS (1 g), CH_2Cl_2 (12 mL), NIS (0.28 g, 1.26 mmol) and TfOH (11 μL, 0.13 mmol). Purification of the crude reaction mixture afforded disaccharide **9** (0.39 g, 52%), as a white foamy solid. $R_f = 0.18$ (EtOAc/pet ether 1:2); $[\alpha]_D^{24}$ +36.0 (*c* 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.14–7.35 (m, 15H, aromatic), 7.06 (d, 2H, $J = 8.4$ Hz, aromatic), 6.67 (d, 2H, $J = 8.4$ Hz, aromatic), 5.65 (app. t, 1H, $J = 9.0$ Hz, H-3), 5.42 (dd, 1H, $J = 7.8$, 9.0 Hz, H-2), 5.27 (app. s, 1H, H-4′), 5.22 (d, 1H, $J = 4.5$ Hz, H-1′), 5.16–5.14 (m, 1H, H-3′), 4.80 (app. t, 2H, $J = 11.7$ Hz, PhCH_2), 4.69 (d, 1H, $J = 7.8$ Hz, H-1), 4.59–4.53 (m, 2H, H-6$_a$, H-6$_b$). 4.27 (app. t, 1H, $J = 6.0$ Hz, H-5′), 4.13 (app. t, 1H, $J = 9.0$ Hz, H-4), 3.98–3.94 (m, 2H, H-6′$_a$, H-6′$_b$), 3.88–3.84 (m, 1H, H-5), 3.75 (br s, 3H, OCH_3), 2.03–1.77 (band, 11H, H-2′$_e$, $COCH_3$, H-2′$_a$); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.4, 170.0, 169.8, 165.4, 165.2, 159.4, 148.1, 133.5, 133.3, 133.2, 129.8, 129.7, 129.2, 128.8, 128.7, 128.5, 128.3, 128.2, 128.1, 113.7, 99.4 (C-1), 98.4 (C-1′), 76.1, 75.4, 72.9, 71.7, 70.0, 69.1, 68.0, 67.9, 66.2, 65.4, 63.6, 62.1, 55.1 (OCH_3), 30.1 (C-2′), 20.7, 20.6. HR-MS m/z: $[M+Na]^+$ calcd for $C_{47}H_{48}O_{17}$, 907.2789; found, 907.2762.

3.6. Benzyl 4-*O*-(2-deoxy-α-D-*arabino*-hexopyranosyl)-2-deoxy-D-*arabino*-hexopyranoside (10)

Compound **10** was prepared according to the method described for the synthesis of compound **8**, using **4** (0.38 g, 1.13 mmol), **6** (0.36 g, 1.07 mmol), 4 Å MS (0.8 g), CH_2Cl_2 (8 mL), NIS (0.3 g, 1.35 mmol) and TfOH (12 μL, 0.13 mmol). After work-up and concentration, the crude product was admixed with NaOMe (cat.) and MeOH (8 mL), stirred for 6 h at room temperature, quenched with a few drops of AcOH/MeOH (1:10, v/v) and concentrated. Purification afforded **10** (0.28 g, 66% conversion after 2 steps, α/β = 2:1), as a white foamy solid. $R_f = 0.34$ (12% MeOH/$CHCl_3$); ^{1}H NMR (D_2O, 300 MHz): δ 7.26–7.23 (band, aromatic), 5.32 (app. d, $J = 2.7$ Hz, H-1′), 5.07 (m, H-3β), 4.93 (br s, H-1α), 4.82–4.64 (band, H-3′, H-4′, PhCH_2, H-5α, H-4β), 4.52–4.49 (m, H-6$_a$α, H-6$_b$α), 4.35 (app. d, $J = 11.3$ Hz, H-1β), 3.85–3.13 (band, H-5′, H-6′$_a$, H-6′$_b$, H-3α, H-4α, H-6$_a$β, H-6$_b$β, H-5β), 2.08–1.78 (m, H-2$_e$β, H-2′$_a$, H-2′$_e$, H-2$_a$α, H-2$_e$α), 1.64–1.55 (m, H-2$_a$β); ^{13}C NMR (D_2O, 75 MHz): δ 137.6, 137.3, 129.5, 129.4, 129.3, 129.1, 99.3 (C-1β), 97.4 (C-1α, C-1′), 77.1, 77.0, 75.5, 74.0, 71.9, 71.8, 71.7, 71.6, 70.2, 69.7, 68.8, 61.9, 61.4, 39.7 (C-2β), 38.0 (C-2′), 37.6 (C-2α). HR-MS m/z: $[M+Na]^+$ calcd for $C_{19}H_{28}O_9$, 423.1631; found, 423.1625.

3.7. Benzyl 4-*O*-(2-deoxy-α-D-*lyxo*-hexopyranosyl)-2-deoxy-D-*arabino*-hexopyranoside (11)

Compound **11** was prepared according to the method described for the synthesis of compound **10**, using **6** (0.28 g, 0.82 mmol), **7** (0.32 g, 0.97 mmol), 4 Å MS (0.8 g), CH_2Cl_2 (8 mL), NIS (0.26 g, 1.16 mmol) and TfOH (10 μL, 0.11 mmol). Purification afforded **11** (0.21 g, 64% conversion after 2 steps, α/β = 2:1), as a white foamy solid. $R_f = 0.23$ (12% MeOH/$CHCl_3$); ^{1}H NMR (D_2O, 300 MHz): δ 7.27–7.24 (band, aromatic), 5.33 (br s, H-1′), 5.09 (m, H-3β), 4.92 (br s, H-1α), 4.73–4.65 (band, H-3′, H-4′, PhCH_2, H-5α, H-4β), 4.52–4.49 (m, H-6$_a$α, H-6$_b$α), 4.34 (app. d, $J = 10.8$ Hz, H-1β), 3.84–3.18 (band, H-5′, H-6′$_a$, H-6′$_b$, H-3α, H-4α, H-6$_a$β, H-6$_b$β, H-5β), 2.04–1.78 (m, H-2$_e$β, H-2′$_a$, H-2′$_e$, H-2$_a$α), 1.64–1.55 (m, H-2$_e$α), 1.45–1.34 (m, H-2$_a$β); ^{13}C NMR (D_2O, 75 MHz): δ 137.7, 137.3, 129.5, 129.4, 129.3, 129.2, 129.1, 99.5 (C-1β), 97.4 (C-1α, C-1′), 77.2, 75.5, 72.6, 71.9, 70.0, 69.7, 68.3, 65.4, 62.3, 61.8, 61.3, 39.7 (C-2β), 38.0 (C-2α), 32.3 (C-2′). HR-MS m/z: $[M+Na]^+$ calcd for $C_{19}H_{28}O_9$, 423.1631; found, 423.1628.

3.8. 2-Deoxy-α-D-*arabino*-hexopyranosyl-(1→4)-D-glucopyranose (12)

To a solution of **8** (0.22 g, 0.25 mmol) in MeCN/H_2O (5:1, v/v, 8 mL), CAN (0.16 g, 0.3 mmol) was added and stirred at room temperature. After 4 h, the reaction mixture was diluted with EtOAc (30 mL), washed with aq $NaHSO_3$, water, dried and concentrated. The residue was admixed with MeOH (8 mL), NaOMe (cat.) and stirred for 6 h at room temperature, neutralized with IR 120 resin (H^+) and evaporated. The residue was purified and freeze-dried to afford **12** (0.07 g, 85%, α/β = 36:64), as an amorphous solid. $R_f = 0.18$ (7:2:1

EtOAc/CH_3OH/H_2O); $[\alpha]_D^{24}$ +50.5 (*c* 1, H_2O); ^1H NMR (D_2O, 300 MHz): δ 5.36 (d, 1H, $J = 2.7$ Hz, H-1′), 5.08 (d, 1H, $J = 3.6$ Hz, H-1α), 4.48 (d, 1H, $J = 7.8$ Hz, H-1β), 3.76–3.38 (band, 15H, H-4α, H-5α, H-$6_{a,b}$α, H-2β, H-3β, H-4β, H-5β, H-$6_{a,b}$β, H-3′, H-4′, H-5′, H-$6'_{a,b}$), 3.23 (app. t, 1H, $J = 9.3$ Hz, H-3α), 3.10 (dd, 1H, $J = 7.8$, 9.3 Hz, H-2α), 2.13–2.07 (m, 1H, H-$2'_e$), 1.59 (ddd, 1H, $J = 3.6$, 11.7, 12.6 Hz, H-$2'_a$); ^{13}C NMR (D_2O, 75 MHz): δ 99.4 (C-1′), 96.6 (C-1β), 92.6 (C-1α), 77.2, 76.9, 75.4, 74.2, 74.0, 73.9, 72.3, 71.6, 70.8, 69.5, 68.8, 61.6, 61.5, 37.7 (C-2′). HR-MS *m*/*z*: $[M+Na]^+$ calcd for $C_{12}H_{22}O_{10}$, 349.1111; found, 349.1115. Anal. Calcd for $C_{12}H_{22}O_{10}\cdot H_2O$: C, 41.86; H, 6.98. Found: C, 41.76; H, 7.30.

3.9. 2-Deoxy-α-D-*lyxo*-hexopyranosyl-(1→4)-D-glucopyranose (13)

Compound **13** was prepared according to the method described for the synthesis of compound **12**, using **9** (0.3 g, 0.34 mmol), CAN (0.22 g, 0.4 mmol), MeCN/H_2O (5:1, v/v, 8 mL), followed by NaOMe (cat.) in MeOH (10 mL). After neutralization and evaporation, the residue was purified to afford **13** (0.086 g, 78%, α/β = 36:64), as an amorphous solid. $R_f = 0.16$ (7:2:1 EtOAc/CH_3OH/H_2O); $[\alpha]_D^{24}$ +86.3 (*c* 0.9, H_2O); ^1H NMR (D_2O, 400 MHz): δ 5.35 (br s, 1H, H-1′), 5.05 (d, 1H, $J = 3.6$ Hz, H-1α), 4.49 (d, 1H, $J = 8.0$ Hz, H-1β), 4.08–3.44 (band, 17H, H-2α, H-3α, H-4α, H-5α, H-$6_{a,b}$α, H-2β, H-3β, H-4β, H-5β, H-$6_{a,b}$β, H-3′, H-4′, H-5′, H-$6'_{a,b}$), 2.51–2.34 (m, 1H, H-$2'_e$), 1.94–1.86 (m, 1H, H-$2'_a$); ^{13}C NMR (D_2O, 100 MHz): δ 98.9 (C-1′), 95.8 (C-1β), 92.5 (C-1α), 76.4, 75.4, 75.2, 74.1, 73.4, 72.2, 71.9, 71.5, 70.1, 67.5, 64.6, 63.1, 61.7, 31.6 (C-2′). HR-MS *m*/*z*: $[M+Na]^+$ calcd for $C_{12}H_{22}O_{10}$, 349.1111; found, 349.1128. Anal. Calcd for $C_{12}H_{22}O_{10}\cdot H_2O$: C, 41.86; H, 6.98. Found: C, 41.08; H, 7.08.

3.10. 2-Deoxy-α-D-*arabino*-hexopyranosyl-(1→4)-2-deoxy-D-*arabino*-hexopyranose (14)

A solution of **10** (0.28 g, 0.7 mmol) in MeOH (10 mL) was hydrogenolyzed over Pd/C (10%, 0.05 g) at room temperature under positive pressure of H_2 for 3 days, filtered through Celite pad and evaporated. The residue was purified and freeze-dried to obtain **14** (0.2 g, 90%, α/β = 2:3), as an amorphous solid. $R_f = 0.28$ (7:2:1 EtOAc/CH_3OH/H_2O); $[\alpha]_D^{24}$ +77.5 (*c* 2, H_2O), lit.[6] $[\alpha]_D^{20}$ +126.6 (*c* 0.47, H_2O); ^1H NMR (D_2O, 400 MHz): δ 5.51 (br s, H-1′), 5.35 (d, $J = 2.8$ Hz, H-1α), 4.91 (dd, $J = 2.0$, 10.0 Hz, H-1β), 4.08 (ddd, $J = 5.2$, 9.6, 12.4 Hz, H-3α), 3.88–3.72 (band, H-5α, H-$6_{a,b}$α, H-3β, H-$6_{a,b}$β, H-3′, H-$6'_{a,b}$), 3.66 (ddd, $J = 2.2$, 5.1, 9.5 Hz, H-5′), 3.56 (app. t, $J = 9.6$ Hz, H-4α), 3.50 (app. t, $J = 9.6$ Hz, H-4β), 3.43 (ddd, $J = 2.0$, 5.4, 9.7 Hz, H-5β), 3.38 (app. t, $J = 9.7$ Hz, H-4′), 2.25 (m, H-2_eβ, H-$2'_e$), 2.10 (d, $J = 5.2$, 13.6 Hz, H-2_eα), 1.81–1.68 (m, H-2_aα, H-$2'_a$), 1.55 (ddd, $J = 9.0$, 10.0, 12.4 Hz, H-2_aβ); ^{13}C NMR (D_2O, 100 MHz): δ 98.4 (C-1′), 93.3 (C-1β), 90.9 (C-1α), 76.5, 76.0, 74.5, 73.2, 71.1, 70.8, 70.6, 68.5, 67.9, 61.7, 60.7, 60.5, 37.7 (C-2β), 36.8 (C-2′), 36.4 (C-2α). HR-MS *m*/*z*: $[M+Na]^+$ calcd for $C_{12}H_{22}O_9$, 333.1162; found, 333.1151. Anal. Calcd for $C_{12}H_{22}O_9\cdot 2H_2O$: C, 41.62; H, 7.51. Found: C, 41.14; H, 7.48.

3.11. 2-Deoxy-α-D-*lyxo*-hexopyranosyl-(1→4)-2-deoxy-D-*arabino*-hexopyranose (15)

Compound **15** was prepared according to the method described for the synthesis of compound **14**, using **11** (0.21 g, 0.52 mmol), MeOH (10 mL), Pd/C (10%, 0.05 g) and H_2 gas. After filtration and solvent evaporation, the residue was purified and freeze-dried to obtain **15** (0.16 g, 95%, α/β = 45:55), as an amorphous solid. $R_f = 0.26$ (7:2:1 EtOAc/CH_3OH/H_2O); $[\alpha]_D^{24}$ +125.8 (*c* 2, H_2O); ^1H NMR (D_2O, 400 MHz): δ 5.52 (br s, H-1′), 5.36 (d, $J = 3.2$ Hz, H-1α), 4.91 (dd, $J = 1.6$, 9.5 Hz, H-1β), 4.07 (ddd, $J = 5.1$, 9.4, 12.3 Hz, H-3α), 4.04–3.89 (band, H-5α, H-$6_{a,b}$α, H-3β, H-$6_{a,b}$β, H-3′, H-4′, H-5′, H-$6'_{a,b}$), 3.58 (app. t, $J = 9.4$ Hz, H-4α), 3.49 (app. t, $J = 9.5$ Hz, H-4β), 3.42 (ddd, $J = 2.1$, 5.2, 9.7 Hz, H-5β), 2.24 (app. d, $J = 4.8$, 13.5 Hz, H-$2'_e$), 2.10 (app. d, $J = 5.2$, 12.8 Hz, H-2_eα), 2.00–1.91 (m, H-2_eβ, H-$2'_a$), 1.75 (ddd, $J = 3.2$, 12.3, 13.7 Hz, H-2_aα), 1.55 (ddd, $J = 9.5$, 11.7, 12.8 Hz, H-2_aβ); ^{13}C NMR (D_2O, 100 MHz): δ 98.7 (C-1′), 93.4 (C-1β), 91.1 (C-1α), 76.7, 76.3, 74.6, 71.8, 71.1, 71.2, 70.6, 68.6, 67.6, 64.7, 61.6, 60.8, 37.8 (C-2β), 37.7 (C-2α), 31.5 (C-2′). HR-MS *m*/*z*: $[M+Na]^+$ calcd for $C_{12}H_{22}O_9$, 333.1162; found, 333.1163. Anal. Calcd for $C_{12}H_{22}O_9\cdot 2H_2O$: C, 41.62; H, 7.51. Found: C, 41.13; H, 7.61.

3.12. Ethyl 4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-2-deoxy-3,6-di-*O*-acetyl-1-thio-D-*arabino*-hexopyranoside (18)

3.12.1. Method A. Compound **18** was synthesized according to the previously described method,[4] **16**[12] (1.0 g, 1.78 mmol), CAN (0.1 g, 0.18 mmol), EtSH (0.7 mL, 9.45 mmol) and MeCN (15 mL). The crude product was purified to afford **18** (0.167 g, 15%, α/β = 5:1), as a colourless syrup, along with ethyl 4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-6-*O*-acetyl-2,3-dideoxy-1-thio-D-*erythro*-hex-2-enopyranoside (Ferrier product) 0.66 g (66% yield, α/β = 90:10).

3.12.2. Method B. To a solution of **20** (0.61 g, 0.9 mmol) and EtSH (0.4 mL, 0.54 mmol) in CH_2Cl_2 (7 mL), BF_3–Et_2O was added at −40 °C. The reaction mixture was allowed to come to room temperature over a 4 h period of time, quenched with Et_3N, concentrated

and purified to afford **18** (0.47 g, 76%, α/β = 6:1), as a colourless syrup. $R_f = 0.46$ (1:1 EtOAc/pet ether); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.57 (d, $J = 4.0$ Hz, H-1′), 5.43–5.37 (m, H-4′, H-1), 5.16–4.85 (band, H-3, H-3′, H-2′), 4.38–3.84 (band, H-6′$_a$, H-6′$_b$, H-5′, H-4, H-5, H-6$_a$, H-6$_b$), 2.68–2.49 (m, SCH_2), 2.18–1.81 (band, H-2$_e$, H-2$_a$, CH_3CO), 1.30 (t, $J = 7.8$ Hz, CH_3); characteristic resonances for β-anomer found: 4.64 (dd, $J = 2.4$, 10.0 Hz, H-1), 3.70–3.67 (m, H-5); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.6, 170.5, 170.3, 169.9, 169.8, 169.4, 95.4 (C-1′), 79.1 (C-1), 73.5, 72.9, 70.0, 69.4, 68.2, 67.9, 63.3, 61.4, 34.7 (C-2), 24.7 (SCH_2), 21.1, 20.8, 20.7, 20.6, 20.5, 20.4, 20.3, 14.6. HR-MS *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{38}O_{15}S$, 645.1829; found, 645.1833.

3.13. Ethyl 4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)-2-deoxy-3,6-di-*O*-acetyl-1-thio-D-*arabino*-hexopyranoside (19)

3.13.1. Method A. Compound **19** was synthesized according to the previously described method,[4] using **17**[12] (1.37 g, 2.46 mmol), CAN (0.14 g, 0.24 mmol), EtSH (1.0 mL, 0.01 mol) and MeCN (20 mL). The crude product was purified to afford **19** (0.152 g, 11%, α/β = 5:1), as a white foamy solid, as well as ethyl 4-*O*(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-6-*O*-acetyl-2,3-dideoxy-1-thio-D-*erythro*-hex-2-enopyranoside (Ferrier product) 0.977 g (71% yield, α/β = 3:2).

3.13.2. Method B. To a solution of **21** (1.11 g, 1.79 mmol) and EtSH (0.7 mL, 9.45 mmol) in CH_2Cl_2 (12 mL), BF_3–Et_2O was added at −40 °C. The reaction mixture was allowed to come to room temperature over a 4 h period of time, quenched with Et_3N, concentrated and purified to afford **19** (0.902 g, 81% yield, α/β = 5:1), as a white foamy solid. $R_f = 0.41$ (1:1 EtOAc/pet ether); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.35–5.32 (m, H-3′, H-1), 5.20–5.10 (band, H-3, H-4′), 4.99–4.97 (m, H-2′), 4.55–4.52 (m, H-1′, H-5′), 4.30–4.22 (m, H-4, H-5), 4.18–3.85 (band, H-6′$_a$, H-6′$_b$, H-6$_a$, H-6$_b$), 2.70–2.48 (m, SCH_2), 2.18–1.81 (band, H-2$_a$, H-2$_e$, CH_3CO), 1.26 (t, $J = 7.8$ Hz, CH_3); characteristic resonances for β-anomer found: 4.79 (app. d, $J = 10.0$ Hz, H-1), 3.62–3.60 (m, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.5, 170.4, 170.2, 169.8, 169.6, 169.2, 101.1 (C-1′), 79.2 (C-1), 72.3, 70.5, 69.1, 68.7, 66.7, 63.0, 62.2, 60.9, 34.7 (C-2), 24.8 (SCH_2), 21.1, 21.0, 20.9, 20.8, 20.7, 20.5, 14.5. HR-MS *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{38}O_{15}S$, 645.1829; found, 645.1821.

3.14. 4-*O*-(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)-2-deoxy-1,3,6-tri-*O*-acetyl-D-*arabino*-hexopyranoside (20)

Compound **20** was synthesized by a known procedure,[13] using **16**[12] (2.35 g, 4.22 mmol), Ac_2O (4 mL), AcOH (2.2 mL), a catalytic amount of HBr/AcOH (33%, w/v, 206 μL, 0.94 mmol) and CH_2Cl_2 (13 mL). The crude reaction mixture was purified to afford **20** (2.34 g, 91%, α/β = 96:4), as a colourless gum. $R_f = 0.41$ (1:1 EtOAc/pet ether); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.19 (d, 1H, $J = 2.4$ Hz, H-1), 5.60 (d, 1H, $J = 4.0$ Hz, H-1′), 5.40 (app. t, 1H, $J = 10.0$ Hz, H-4′), 5.20 (ddd, 1H, $J = 5.4$, 8.4, 11.4 Hz, H-3), 5.09 (app. t, 1H, $J = 10.0$ Hz, H-3′), 4.89 (dd, 1H, $J = 4.0$, 10.0 Hz, H-2′), 4.38–4.23 (m, 4H, H-4, H-5, H-6′$_a$, H-6′$_b$), 4.08–3.88 (m, 3H, H-5′, H-6$_a$, H-6$_b$), 2.29 (app. dd, 1H, $J = 5.4$, 12.3 Hz, H-2$_e$), 2.16–2.02 (band, 21H, CH_3CO), 1.75 (ddd, 1H, $J = 2.4$, 11.4, 12.3 Hz, H-2$_a$); characteristic resonances for the β-anomer: δ 5.80 (dd, 1H, $J = 2.0$, 9.9 Hz, H-1), 3.86–3.85 (m, 1H, H-5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.5, 170.4, 170.2, 170.0, 169.9, 169.3, 169.0, 95.6 (C-1′), 90.4 (C-1), 72.6, 72.0, 70.1, 70.0, 69.3, 68.3, 67.8, 62.9, 61.3, 33.4 (C-2), 21.1, 21.0, 20.7, 20.6, 20.5, 20.4. HR-MS *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{36}O_{17}$, 643.1850; found, 643.1863.

3.15. 4-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2-deoxy-1,3,6-tri-*O*-acetyl-D-*arabino*-hexopyranoside (21)

Compound **21** was synthesized by a known procedure,[13] using **17**[12] (8.10 g, 0.01 mol), Ac_2O (13.2 mL), AcOH (7.3 mL), a catalytic amount of HBr/AcOH (33%, w/v, 0.7 mL, 2.85 mmol) and CH_2Cl_2 (42 mL). The crude reaction mixture was purified to afford **21** (8.18 g, 84%, α/β = 95:5), as a white foam. $R_f = 0.12$ (1:1 EtOAc/pet ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.09 (d, 1H, $J = 1.6$ Hz, H-1), 5.29–5.27 (m, 2H, H-3, H-4′), 5.07–5.05 (m, 1H, H-2′), 4.89 (dd, 1H, $J = 3.6$, 10.8 Hz, H-3′), 4.49 (d, 1H, $J = 8.0$ Hz, H-1′), 4.30–4.27 (m, 1H, H-6$_b$), 4.09–3.97 (m, 3H, H-6$_a$, H-6′$_a$, H-6′$_b$), 3.90–3.79 (m, 2H, H-5′, H-5), 3.68–3.66 (m, 1H, H-4), 2.22 (app. dd, 1H, $J = 5.0$, 12.8 Hz, H-2$_e$), 2.08–1.98 (band, 21H, CH_3CO), 1.89–1.72 (m, 1H, H-2$_a$); characteristic resonances for the β-anomer: δ 5.89 (dd, 1H, $J = 2.0$, 9.9 Hz, H-1), 3.58–3.55 (m, 1H, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.5, 170.4, 170.2, 170.1, 169.7, 169.3, 101.2 (C-1′), 90.6 (C-1), 71.8, 70.8, 70.7, 70.6, 69.1, 68.9, 67.4, 62.9, 62.3, 33.4 (C-2), 21.2, 21.1, 21.0, 20.9, 20.7, 20.6. HR-MS *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{36}O_{17}$, 643.1850; found, 643.1840.

3.16. α-D-Glucopyranosyl-(1→4)-2-deoxy-D-*arabino*-hexopyranose (22)

3.16.1. Method A. To a solution of **18** (0.17 g, 0.27 mmol) in CH_2Cl_2 (5 mL), NBS (0.06 g, 0.32 mmol) and acetone/H_2O (9:1 v/v, 8 mL) was added. After 5 min, the reaction mixture was diluted with CH_2Cl_2 (25 mL), washed with aq $Na_2S_2O_3$, water, dried and

concentrated. The residue was dissolved in MeOH, treated with NaOMe (cat.) at room temperature for 6 h, neutralized with IR-120 resin (H^+) and evaporated. The resulting residue was purified and freeze-dried to afford **22** (0.07 g, 80%), as an amorphous solid.

3.16.2. Method B. Alternatively, **22** was obtained by treating **20** (0.5 g, 0.91 mmol) with NaOMe (cat.) in MeOH (10 mL) for 6 h, neutralized with IR-120 resin (H^+), solvents were evaporated and residue purified to afford **22** (0.23 g, 88%, $\alpha/\beta = 3{:}2$), as an amorphous solid. $R_f = 0.36$ (6:2:1 EtOAc/CH_3OH/H_2O); $[\alpha]_D^{24}$ +147.4 (*c* 2, H_2O), lit.[6] $[\alpha]_D^{20}$ +126 (*c* 0.14, H_2O), lit.[11a] $[\alpha]_D^{20}$ +30.4 (H_2O), lit.[14b] $[\alpha]_D^{20}$ +136 (H_2O); ^{1}H NMR (D_2O, 400 MHz): δ 5.30 (br s, 1H, H-1′), 5.04 (d, 1H, $J = 3.3$ Hz, H-1α), 4.88 (app. d, 1H, $J = 9.6$ Hz, H-1β), 4.30 (ddd, 1H, $J = 5.4$, 9.8, 11.4 Hz, H-3α), 3.91–3.19 (band, 15H, H-4α, H-5α, H-$6_{a,b}$α, H-3β, H-4β, H-5β, H-$6_{a,b}$β, H-2′, H-3′, H-4′, H-5′, H-$6'_{a,b}$), 2.10–2.06 (m, 1H, H-2_eβ), 1.96–1.92 (m, 1H, H-2_eα), 1.65–1.57 (m, 1H, H-2_aα), 1.45–1.34 (m, 1H, H-2_aβ); ^{13}C NMR (D_2O, 75 MHz): δ 95.4 (C-1′), 94.5 (C-1β), 92.2 (C-1α), 76.0, 75.8, 74.8, 74.2, 73.5, 70.5, 70.0, 69.5, 68.12, 65.3, 61.1, 60.7, 60.3, 34.9 (C-2α, 2β). HR-MS *m*/*z*: $[M+Na]^+$ calcd for $C_{12}H_{22}O_{10}$, 349.1111; found, 349.1104. Anal. Calcd for $C_{12}H_{22}O_{10}\cdot H_2O$: C, 41.86; H, 6.98. Found: C, 41.25; H, 7.34.

3.17. β-D-Galactopyranosyl-(1→4)-2-deoxy-D-*arabino*-hexopyranoside (23)

3.17.1. Method A. Compound **23** was prepared according to the method described for the synthesis of compound **22** using **19** (0.15 g, 0.24 mmol), NBS (0.05 g, 0.29 mmol), and acetone/H_2O (9:1 v/v, 8 mL), followed by NaOMe catalyzed deprotection of acetate group and purification which afforded **23** (0.06 g, 75% yield), as an amorphous solid.

3.17.2. Method B. Similarly, **23** was also obtained (0.174 g, 83% yield, $\alpha/\beta = 1{:}1$) on treatment of **21** (0.4 g, 0.54 mmol) under Zemplén condition. $R_f = 0.4$ (5:4:1 EtOAc/CH_3OH/H_2O); $[\alpha]_D^{24}$ +33.6 (*c* 1.3, H_2O); ^{1}H NMR (D_2O, 400 MHz): δ 5.39 (d, 1H, $J = 5.2$ Hz, H-1α), 4.33–4.31 (m, 2H, H-1β, H-1′), 4.11–4.07 (m, 1H, H-3α), 4.00–3.22 (band, 15H, H-4α, H-5α, H-$6_{a,b}$α, H-3β, H-4β, H-5β, H-$6_{a,b}$β, H-2′, H-3′, H-4′, H-5′, H-$6'_{a,b}$), 2.11–2.07 (m, 1H, H-2_eβ), 1.95–1.90 (m, 2H, H-2_eα, H-2_aα), 1.55–1.52 (m, 1H, H-2_aβ); ^{13}C NMR (D_2O, 100 MHz): δ 102.9 (C-1′), 98.0 (C-1β), 93.1 (C-1α), 79.9, 79.5, 79.3, 78.6, 75.3, 72.5, 70.9, 70.4, 68.4, 67.7, 60.9, 60.4, 60.0, 35.6 (C-2β), 33.2 (C-2α). HR-MS *m*/*z*: $[M+Na]^+$ calcd for $C_{12}H_{22}O_{10}$, 349.1111; found, 349.1118. Anal. Calcd for $C_{12}H_{22}O_{10}\cdot H_2O$: C, 41.86; H, 6.98. Found: C, 41.27; H, 7.48.

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