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Note

4-*O*-Acetyl-3-*O*-*tert*-butyldimethylsilyl-L-rhamnal: a building block in the stereoselective synthesis of 2-deoxy-α-L-rhamnopyranosides

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Abstract—The stereoselective synthesis of 2-deoxy-α-L-glycosides by addition of various acceptors to 4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-L-rhamnal promoted by triphenylphosphine–hydrogen bromide is developed.

Keywords: Glycals; 2-Deoxyglycosides; Stereoselective synthesis

Glycals are versatile synthetic intermediates for the preparation of 2-deoxy glycosides and 2,3-unsaturated glycosides that can be easily functionalised at the C-2 and C-3 positions.[1–4] 2,6-Dideoxyglycosidic linkages are present in many bioactive natural products such as anthracycline antibiotics, aureolic acids and cardiac glycosides. Therefore, utilisation of glycals as building blocks for the total synthesis of various natural products is of great interest in bioorganic and medicinal chemistry.[4–8]

Glycals compare well with fully oxygenated pyranose derivatives due to their relative ease in differentiation of hydroxyl groups by selective protection. Moreover, glycals can be exploited, not only as glycosyl donors, but also as glycosyl acceptors.[2,9,10] This approach enables an efficient, reiterative synthesis of complex oligosaccharides.

One possible way for the exploration of glycals as glycosyl donors is to investigate the direct addition of alcohols to the double bond of glycals. This reaction should take place under mild conditions in order to provide preference over the Ferrier rearrangement, which is a competing reaction.[11] Successful direct addition can be accomplished in the presence of several catalysts, for instance, triphenylphosphine–hydrogen bromide (TPHB),[12] cation-exchange resin Dowex AG 50WX2,[13] BCl_3, BBr_3,[14] CAN[15] or the $CeCl_3$–NaI reagent system.[16] According to these procedures, 2-deoxy-α-glycosides are formed as the major products.

The work described in this report is based on the Falck–Mioskowski route[12] where TPHB is the catalyst for a mild and high-yield protonation, followed by glycosylation of glycals. This procedure has a lot of applications in the synthesis of several precursors of bioactive compounds when specificity and mild conditions are required.[17–21] Stereoselectivity in these procedures depends mostly on the nature of the starting materials.

2,6-Dideoxy-L-*arabino*- and L-*lyxo*-hexopyranoses are common structural units in natural products. Both of them can be obtained from L-rhamnal, the former by direct addition of an alcohol, and the latter by addition, followed by inversion of configuration at C-4.[22,23]

We describe herein our studies on the stereoselectivity in the addition of various acceptors to derivatives of L-rhamnal promoted by TPHB. Stereoselectivity in glycosylation reactions is a key feature, especially since in the synthesis of complex oligosaccharides, the separation of isomeric glycosides is difficult and often even impossible. Therefore, within a synthetic project directed to the preparation of analogues of 2,6-dideoxy-L-*arabino*-hexopyranose we have undertaken studies aiming at

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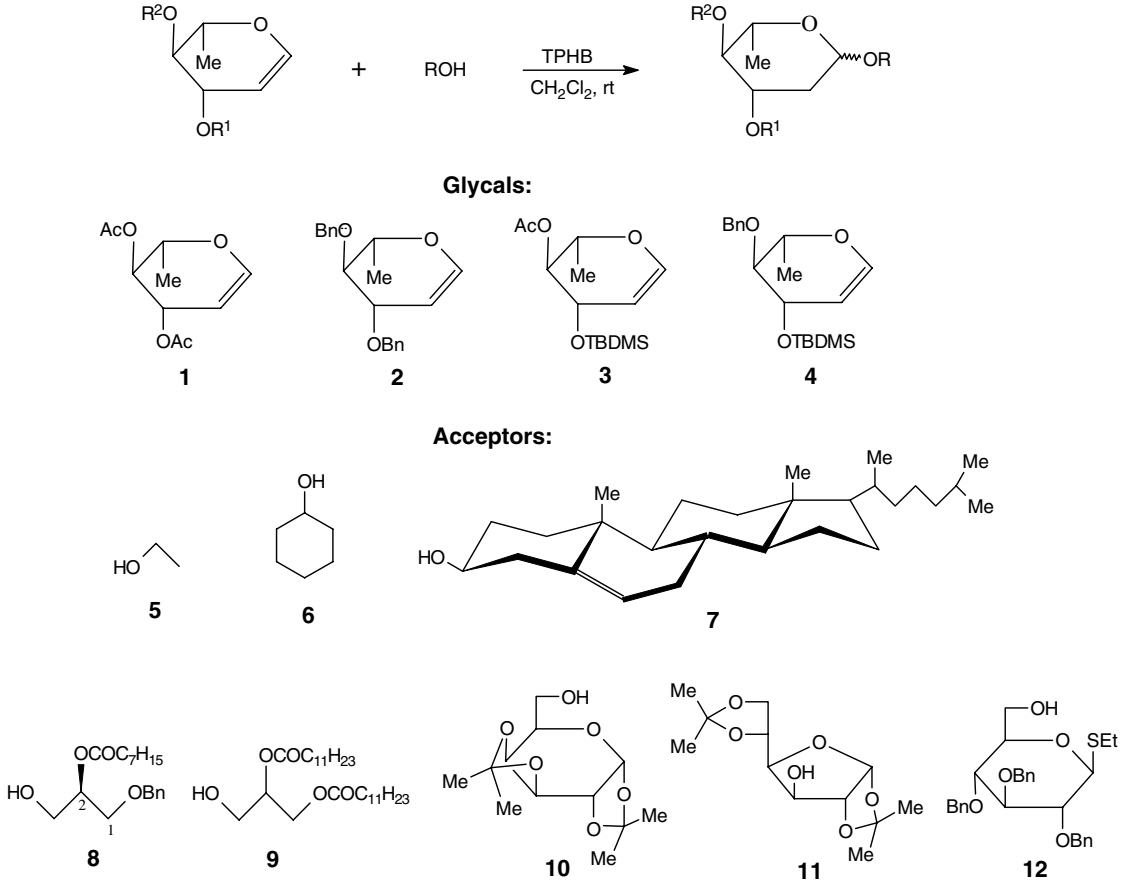
improving stereoselectivity. It was interesting to examine if the stereoselective outcome of the Falck–Mioskowski method is influenced by the protecting group at C-3. Recently we have found that reaction of glycal **3** with 1-*O*-benzyl-2-*O*-octanoyl-*sn*-glycerol (**8**) was highly selective for the α-glycoglycerolipid **23**.[21] Now, in order to evaluate the range of applicability of this process, various acceptors **5**–**12** were reacted with L-rhamnal derivatives **1**–**4** (Scheme 1).

We initially examined the glycosylation of glycals **1** and **2** with a small excess (1.2 equiv) of selected acceptors in the presence of a catalytic amount of TPHB (0.1 equiv) in CH_2Cl_2 at room temperature. Reactions afforded the corresponding 2-deoxy glycosides **13**–**20** as chromatographically inseparable mixtures of α and β anomers regardless of the acceptor applied. As shown in Table 1 (entries 1–8) the α:β ratio may have slightly changed depending on the acceptor used, but in all cases 2-deoxy-α-L-glycosides were preferentially formed. The stereoselectivity was not influenced by the solvent. When toluene was used instead of CH_2Cl_2 in the glycosylation of **3** with **10**, we obtained the same mixture of anomers. Similarly decreasing the reaction temperature to −25 °C did not significantly affect the stereoselectivity of the reaction. Glycosylations of **1** and **2** with **10** (Table 1,

Table 1. Addition of acceptors **5**–**12** to L-rhamnal derivatives **1**–**4**

Entry	Glycal	Acceptor	Product	α:β	Reaction time	Yield (%)
1	**1**	**10**	**13**	5:1	6 h	65
2		**5**	**14**	3:1	10 min	81
3		**6**	**15**	4:1	10 min	71
4		**7**	**16**	4:1	1 h	51
5	**2**	**8**	**17**	5:1	30 min	85[21]
6		**9**	**18**	4.5:1	30 min	59
7		**10**	**19**	6:1	10 min	76
8		**11**	**20**	6:1	2.5 h	55
9		**6**	**21**	4:1	20 min	76
10		**7**	**22**	4:1	1.5 h	58
11		**8**	**23**	15:1	45 min	55[21]
12	**3**	**9**	**24**	15:1	1 h	63
13		**10**	**25**	1:0	1 h	78
14		**11**	**26**	12:1	5 h	45
15		**12**	**27**	1:0	2 h	79
16	**4**	**10**	**28**	5.5:1	20 min	59



TBDMS = *tert*-butyldimethylsilyl
TPHB = triphenylphosphine-hydrogen bromide

Scheme 1.

entries 1 and 7) clearly showed that a similar α:β ratio was obtained irrespective of the protecting group at C-3, which was either electron-donating or electron-withdrawing. However, electron factors associated with the nature of the protecting group affected the reaction rate. Considering the reaction times required for the completion of the reaction, benzyl groups in glycal **2** increased the reaction rate in comparison with acetyl groups in glycal **1**.

The ratio of stereoisomers was determined by examination of the ^{1}H NMR spectra of isomer mixtures. The equatorially oriented H-1α proton of the major α isomer gave the characteristic broad doublet at δ 4.8–5.0 ppm with $J_{1,2ax}$ 2.7–3.2 Hz, while the axially oriented H-1β proton was observed at δ 4.4–4.6 ppm as doublet of doublets with $J_{1,2eq}$ between 2.0 and 2.2 Hz and $J_{1,2ax}$ 9.8 Hz.

Significant predominance of the α anomer was seen when glycal **3** with a bulky group at the C-3 position was applied in reactions with glycerol derivatives **8** and **9** (Table 1, entries 11–12). Glycoglycerolipids **23** and **24** were formed as the predominant 2-deoxy-α-L-glycosides (α:β = 15:1) showing the superiority of glycal **3** over the perbenzylated glycal **2**. Unfortunately, we observed poor stereoselectivity when glycal **3** was employed in reactions with cyclohexanol **6** and cholesterol **7** with an easily accessible hydroxyl group. In final experiments, glycal **3** was coupled with monosaccharides **10**–**12** providing exclusively the α-disaccharides. No signals for the β isomers of compounds **25** and **27** in their ^{13}C NMR spectra were detected.

All 2-deoxy glycosides were purified by column chromatography and characterised on the basis of mass spectrometry and ^{1}H and ^{13}C NMR spectroscopy. Compounds **13**, **16**, **19**, **20** were identified by comparison with literature data.[24] All new compounds gave satisfactory ^{1}H and ^{13}C NMR spectra as well as ESIMS analysis (for details see Section 1).

In the course of our investigations we have found that the presence of a *tert*-butyldimethylsilyloxy group at the C-3 position in L-rhamnal derivative **3** beneficially led to total α-stereoselectivity. An addition to their steric effect, a second factor that influences stereoselectivity is the relative reactivity of the L-rhamnal substrate. When glycal **4** was used in the reaction with acceptor **10**, disaccharide **28** was obtained without significant stereoselectivity, although the sterically demanding *tert*-butyldimethylsilyloxy group was present at the C-3 position. Considering the reaction times, glycal **4** is more reactive than glycal **3**.

Franck and co-workers shed light on the mechanism of the TPHB-mediated addition of acceptors to glycals.[25] They applied the Falck–Mioskowski procedure in deuterated media in the presence of nucleophiles having an OD group. Reaction proceeded via the oxonium ion formed in the first protonation step of the glycal. Once the intermediate was formed, it was attacked by the nucleophile at either the α or β face. The authors concluded that the prevailing axial stereoselectivity at C-1 in the case of glycals with all equatorial substituents arose from the kinetic anomeric effect. Our results suggest that the addition mechanism is not only kinetically, but also sterically controlled. The kinetic anomeric effect can be enhanced by steric factors. Geometries of both oxonium ion and glycosyl acceptor acting as a nucleophile are essential. It is probable that the substituent present at the equatorially oriented C-3 position in the intermediate oxonium ion determines the stereoselectivity of the nucleophilic attack. The *tert*-butyldimethylsilyloxy group at the C-3 position presents significantly more steric hindrance to the approach of the nucleophile than the benzyl or acetyl group does in glycals **1** and **2**, respectively. Thus the approach of the nucleophile from the bottom β-face of the oxonium ion is sterically hindered by *tert*-butyldimethylsilyloxy group. The top α-face of the intermediate is less hindered, and the major product is formed by nucleophilic attack from this direction.

We have proved that the easily prepared glycal **3** can be a useful building block in the synthesis of 2-deoxy-α-L-glycosides. It is reasonable to expect that the stereoselective outcome observed for compounds **23**–**27** would be similar when glycal **3** is applied in the synthesis of trisaccharides and complex 2-deoxy-α-glycosides.

1. Experimental

1.1. Materials and methods

NMR spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Varian spectrometer at a frequency of 300 MHz. Optical rotations were measured with a Perkin–Elmer 141 polarimeter using a sodium lamp (589 nm) at room temperature. Mass spectra were recorded in the positive-ion mode on a Mariner (Perseptive Biosystem) detector using the electrospray-ionisation (ESI) technique.

Reactions were monitored by TLC on precoated plates of silica gel G (E. Merck), and components were detected by charring with 10% sulfuric acid in ethanol. Column chromatography was performed on Silica Gel 60 (70–230 mesh, E. Merck) developed with one of the hexane–EtOAc solvent systems: A, 8:1; B, 15:1 or C, 25:1 (v/v). All evaporations were performed under diminished pressure at 50 °C.

3,4-Di-*O*-acetyl-L-rhamnal (**1**),[26a] 3,4-di-*O*-benzyl-L-rhamnal (**2**),[27] 4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-L-rhamnal (**3**),[28] 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**10**),[26b] 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**11**)[26c] and ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (**12**)[29] were prepared according to the

published procedures. 4-*O*-Benzyl-3-*O*-*tert*-butyldimethylsilyl-L-rhamnal (**4**) was synthesised by benzylation of 3-*O*-*tert*-butyldimethylsilyl-L-rhamnal[28] with benzyl bromide/NaH in DMF; 1,2-di-*O*-dodecanoyl-*rac*-glycerol (**9**) was synthesised via debenzylation of 1-*O*-benzyl-2,3-di-*O*-dodecanoyl-*rac*-glycerol[30] in the presence of a $Pd(OH)_2$/cyclohexene system. Other chemicals were purchased from Aldrich and Fluka Chemical Companies and were used without purification. Solvents were dried and stored over molecular sieves (4 Å) under an inert atmosphere.

1.2. Typical glycosylation procedure

To a solution of glycal **1**, **2**, **3** or **4** (0.3 mmol) and glycosyl acceptors **5**–**12** (0.36 mmol) in dry CH_2Cl_2 (2 mL), a catalytic amount of TPHB (0.03 mmol) was added (Table 1). The mixture was stirred at room temperature for 10 min to 6 h (appropriate reaction times are given in Table 1). After completion (TLC, 8:1 toluene–EtOAc) the reaction mixture was concentrated to give a crude product mixture that was purified directly by column chromatography with an appropriate solvent system as indicated.

1.2.1. Ethyl 3,4-di-*O*-benzyl-2,6-dideoxy-L-*arabino*-hexopyranoside (14). Product **14** as an inseparable α,β-anomeric mixture was purified on a column of silica gel using solvent system B as the eluent; yield 81%, colourless syrup. ^{1}H NMR: (α:β = 3:1) 7.22–7.36 (m, *Ph*CH_2), 4.56–4.98 (m, Ph*C*H_2), 4.86 (br d, *J* 3.2 Hz, H-1α), 4.41 (dd, *J* 2.0, 9.8 Hz, H-1β), 3.97 (ddd, *J* 5.1, 8.8, 11.3, H-3α), 3.74 (dq, *J* 6.1, 9.2 Hz, H-5α), 3.27–3.71 (m, *C*H_2CH$_3$, H-5β, H-3β). 3.13 (t, *J* 9.2 Hz, H-4), 2.34 (m, H-2$_{eq}$β), 2.29 (ddd, *J* 1.2, 5.1, 12.9 Hz, H-2$_{eq}$α), 1.67 (ddd, *J* 3.2, 11.3, 12.9 Hz, H-2$_{ax}$α), 1.62 (m, H-2$_{ax}$β), 1.33 (d, *J* 6.1 Hz, CH$_3$ (H-6β)), 1.28 (d, *J* 6.1 Hz, CH$_3$ (H-6α)), 1.22, 1.17 (2t, *J* 7.1 Hz, CH$_2$*C*H$_3$). Selected ^{13}C NMR data: 138.80, 138.62 (*Ph*CH_2), 99.31 (C-1β), 96.81 (C-1α), 37.10 (C-2β), 35.88 (C-2α), 18.17 (C-6), 15.16 (OCH$_2$*C*H$_3$β), 15.06 (OCH$_2$*C*H$_3$α). HRESIMS: Calcd for $C_{22}H_{28}O_4Na$ ([M+Na]$^+$): *m*/*z* 379.1885, found: *m*/*z* 379.1853.

1.2.2. Cyclohexyl 3,4-di-*O*-benzyl-2,6-dideoxy-L-*arabino*-hexopyranoside (15). Product **15** as an inseparable α,β-anomeric mixture was purified on a column of silica gel using solvent system C as the eluent; yield 71%, colourless syrup. ^{1}H NMR: (α:β = 4:1) 7.22–7.36 (m, *Ph*CH_2), 5.01 (br d, *J* 2.7 Hz, H-1α), 4.53–4.98 (m, Ph*C*H_2), 4.54 (dd, *J* 2.2, 9.8 Hz, H-1β), 3.99 (ddd, *J* 5.1, 9.0, 11.5, H-3α), 3.82 (dq, *J* 6.1, 9.0 Hz, H-5α), 3.56–3.68 (m, C_6H_{11}β, H-3β). 3.51 (m, C_6H_{11}α), 3.32 (m, H-5β), 3.13 (t, *J* 9.0 Hz, H-4β), 3.10 (t, *J* 9.0 Hz, H-4α), 2.30 (m, H-2$_{eq}$β), 2.24 (ddd, *J* 1.2, 5.1, 13.0 Hz, H-2$_{eq}$α), 1.12 (m, C_6H_{11}, CH$_3$ (H-6β), H-2$_{ax}$), 1.27 (d, *J* 6.1 Hz, CH$_3$ (H-6α)). Selected ^{13}C NMR data: 138.84, 138.60 (*Ph*CH_2α), 138.50, 138.45 (*Ph*CH_2β), 97.28 (C-1β), 94.71 (C-1α), 37.53 (C-2β), 36.31 (C-2α), 18.24 (C-6β), 18.14 (C-6α). HRESIMS: Calcd for $C_{26}H_{34}O_4Na$ ([M+Na]$^+$): *m*/*z* 433.2355, found: *m*/*z* 433.2371.

1.2.3. 2,3-Di-*O*-dodecanoylglyceryl 3,4-di-*O*-benzyl-2,6-dideoxy-L-*arabino*-hexopyranoside (18). Product **18** as an inseparable α,β-anomeric mixture was purified on a column of silica gel using solvent system B as the eluent; yield 59%, colourless syrup. ^{1}H NMR: (α:β = 4.5:1) 7.25–7.36 (m, *Ph*CH_2), 5.18 (m, H-2′), 4.55–4.98 (m, Ph*C*H_2), 4.82, 4.84 (2br d, *J* 3.0 Hz, H-1α), 4.44 (m, H-1β), 3.44–4.44 (m, H-3, H-5α, H-1′a, H-1′b, H-3′a, H-3′b), 3.32 (m, H-5β), 3.11 (t, *J* 9.0 Hz, H-4), 2.22–2.37 (m, CH_2 in $C_{11}H_{23}$CO, H-2$_{eq}$), 1.54–1.72 (m, CH_2 in $C_{11}H_{23}$CO, H-2$_{ax}$), 1.19–1.37 (m, CH_2 in $C_{11}H_{23}$-CO, CH$_3$ (H-6)), 0.83–0.92 (m, CH_3 in $C_{11}H_{23}$CO). Selected ^{13}C NMR data: 173.37, 173.02 ($C_{11}H_{23}$*C*O), 138.60, 138.45 (*Ph*CH_2), 99.83, 99.61 (C-1β), 97.59, 97.23 (C-1α), 35.61, 35.51 (C-2β), 34.32, 34.13 (C-2α), 18.13 (C-6). ESIMS: Calcd for $C_{47}H_{74}O_8Na$ ([M+Na]$^+$): *m*/*z* 789.53, found: *m*/*z* 789.5.

1.2.4. Cyclohexyl 4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-L-*arabino*-hexopyranoside (21). Product **21** as an inseparable α,β-anomeric mixture was purified on a column of silica gel using solvent system C as the eluent; yield 76%, colourless syrup. ^{1}H NMR: (α:β = 4:1) 4.97 (d, *J* 3.2 Hz, H-1α), 4.63 (t, *J* 9.2 Hz, H-4), 4.60 (m, H-1β), 4.05 (ddd, *J* 5.3, 9.2, 11.2 Hz, H-3α), 3.80 (dq, *J* 6.3, 9.2 Hz, H-5α), 3.74 (m, H-3β). 3.64 (m, C_6H_{11}β), 3.51 (m, C_6H_{11}α), 3.33 (m, H-5β), 2.06, 2.07 (2s, CH_3CO), 2.06 (m, H-2$_{eq}$β), 1.99 (ddd, *J* ~ 0, 5.3, 20 Hz, H-2$_{eq}$α), 1.22–1.88 (m, C_6H_{11}, H-2$_{ax}$), 1.19 (d, *J* 6.3 Hz, CH$_3$ (H-6β)), 1.13 (d, *J* 6.3 Hz, CH$_3$ (H-6α)), 0.85, (s, Si[C(CH_3)$_3$(CH$_3$)$_2$]α), 0.84 (s, Si[C(CH_3)$_3$-(CH$_3$)$_2$]β), 0.06, 0.04 (2s, Si[C(CH$_3$)$_3$(CH_3)$_2$]α), 0.05, 0.03 (2s, Si[C(CH$_3$)$_3$(CH_3)$_2$]β). Selected ^{13}C NMR data: 170.06, 169.89 (CH$_3$*C*Oα, β), 97.09 (C-1β), 94.96 (C-1α), 41.07 (C-2β), 39.76 (C-2α), 25.59, 25.53 (Si[C(*C*H$_3$)$_3$-(CH$_3$)$_2$]α, β), 21.20 (*C*H$_3$CO), 17.83 (Si[*C*(CH$_3$)$_3$(CH$_3$)$_2$]), 17.79 (C-6β), 17.63 (C-6α), −4.56, −4.87 (Si[C(CH$_3$)$_3$-(*C*H$_3$)$_2$]). HRESIMS: Calcd for $C_{20}H_{38}O_5SiNa$ ([M+Na]$^+$): *m*/*z* 409.2387, found: *m*/*z* 409.2395.

1.2.5. Cholesteryl 4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-L-*arabino*-hexopyranoside (22). Product **22** as an inseparable α,β-anomeric mixture was purified on a column of silica gel using solvent system C as the eluent; yield 58%, colourless syrup. ^{1}H NMR: (α:β = 4:1) 5.28–5.38 (m, H-6′), 4.97 (d, *J* 2.9 Hz, H-1α), 4.55–4.64 (m, H-1β), 4.62, 4.60 (2t, *J* 9.4 Hz, H-4α,β), 4.02 (ddd, *J* 5.3, 9.0, 11.0 Hz, H-3α), 3.79 (dq, *J* 6.1, 9.4 Hz, H-5α), 3.73 (m, H-3β), 3.55 (m, H-3′β), 3.26–3.47 (m, H-3′α, H-5β), 0.80–2.45 (m, H-2$_{eq}$, H-2$_{ax}$,

Si[C(CH_3)$_3$(CH_3)$_2$], Si[C(CH_3)$_3$(CH_3)$_2$], steryl-H) 2.06, 2.07 (2s, CH_3CO), 1.19 (d, *J* 6.1 Hz, CH_3 (H-6β)), 1.11 (d, *J* 6.1 Hz, CH_3 (H-6α)), 1.01 (s, CH_3-19′), 0.68 (s, CH_3-18′). Selected ^{13}C NMR data: 170.26 (CH_3*C*O), 141.05, 140.89 (C-5′α, β), 122.01, 121.94 (C-6′α, β), 97.57 (C-1β), 95.53 (C-1α), 40.40 (C-2β) 39.94 (C-2α), 25.76, 25.81 (Si[C(*C*H$_3$)$_3$(CH_3)$_2$]α, β), 21.30 (*C*H_3CO), 18.96 (C-19′), 18.04 (Si[*C*(CH_3)$_3$(CH_3)$_2$]), 17.84 (C-6), 12.08 (C-18′), −4.20, −4.25, −4.63, −4.58 (Si[C(CH_3)$_3$(*C*H$_3$)$_2$]). HRESIMS: Calcd for $C_{41}H_{72}O_5$SiNa ([M+Na]$^+$): *m*/*z* 695.5047, found: *m*/*z* 659.5074.

1.2.6. 2,3-Di-*O*-dodecanoylglyceryl 4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-L-*arabino*-hexopyranoside (24). Product **24** as an inseparable α,β-anomeric mixture was purified on a column of silica gel using solvent system B as the eluent; yield 63%, colourless syrup. ^{1}H NMR: (α-anomer) 5.21 (m, H-2′), 4.80, 4.83 (2d, *J* 3.5 Hz, H-1), 4.63 (t, *J* 9.3 Hz, H-4), 4.33 (ddd, *J* 3.8, 9.7, 11.6 Hz, H-3), 3.90–4.22 (m, H-3′a,b), 3.60–3.78 (m, H-1′a, H-5), 3.45–3.56 (m, H-1′b), 2.26–2.36 (m, CH_2 in $C_{11}H_{23}$CO), 2.07, 2.08 (2s, CH_3CO), 2.04 (m, H-2$_{eq}$), 1.74 (ddd, *J* 3.5, 11.6, 13.2 Hz, H-2$_{ax}$), 1.55–1.68 (m, CH_2 in $C_{11}H_{23}$CO), 1.20–1.37 (m, CH_2 in $C_{11}H_{23}$CO), 1.13, 1.14 (2d, *J* 6.1 Hz, CH_3 (H-6)), 0.80–0.93 (m, CH_3 in $C_{11}H_{23}$CO, Si[C(CH_3)$_3$(CH_3)$_2$]), 0.03, 0.04 (2s, Si[C(CH_3)$_3$(CH_3)$_2$]). ^{13}C NMR: (α-anomer) 173.60, 173.18 ($C_{11}H_{23}$*C*O), 170.21 (CH_3*C*O), 97.85, 97.47 (C-1), 70.09, 69.83, 67.48, 66.46, 65.35, 62.65 (C-3, C-4, C-5, C-1′, C-2′, C-3′), 39.16, 39.09 (C-2), 34.54, 34.34, 32.13, 29.84, 29.71, 29.56, 29.35, 25.18, 25.12, 22.90, 14.33 (*C*$_{11}$H$_{23}$CO), 25.77 (Si[C(*C*H$_3$)$_3$(CH_3)$_2$]), 21.36 (*C*H_3CO), 18.03 (Si[*C*(*C*H$_3$)$_3$(CH_3)$_2$]), 17.84 (C-6), −4.32, −4.70 (Si[C(CH_3)$_3$(*C*H$_3$)$_2$]). ESIMS: Calcd for $C_{41}H_{78}O_9$SiNa ([M+Na]$^+$): *m*/*z* 765.53, found: *m*/*z* 765.5.

1.2.7. 4-*O*-Acetyl-3-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-*arabino*-hexopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (25). Product **25** was purified on a column of silica gel using solvent system A as the eluent; yield 78%, colourless syrup; [α] −87.7 (*c* 1.1, $CHCl_3$); ^{1}H NMR: 5.53 (d, 1H, *J* 4.9 Hz, H-1), 4.90 (d, 1H, *J* 2.9 Hz, H-1′), 4.63 (t, 1H *J* 9.3 Hz, H-4′), 4.62 (dd, 1H, *J* 2.4, 7.8 Hz, H-3), 4.32 (dd, 1H, *J* 2.4, 4.9 Hz, H-2), 4.24 (dd, 1H, *J* 1.9, 7.8 Hz, H-4), 4.02 (ddd, 1H, *J* 5.4, 9.3, 11.2 Hz, H-3′), 3.97 (m, 1H, H-5), 3.80 (m, 1H, H-5′), 3.77 (dd, 1H, *J* 5.9, 10.5 Hz, H-6a), 3.55 (dd, 1H, *J* 7.8, 10.5 Hz, H-6b), 2.09 (ddd, 1H, *J* 1.2, 5.4, 13.3 Hz, H-2′$_{eq}$) 2.07 (s, 3H, CH_3CO), 1.74 (ddd, 1H, *J* 2.9, 11.2, 13.3 Hz, H-2′$_{ax}$), 1.34, 1.35, 1.44, 1.55 (4s, 12H, 2(CH_3)$_2$C), 1.13 (d, 3H *J* 6.2 Hz, CH_3 (H-6′)), 0.85 (s, 9H, Si[C(CH_3)$_3$(CH_3)$_2$]), 0.03, 0.05 (2s, 6H, Si[C(CH_3)$_3$(CH_3)$_2$]). ^{13}C NMR: 170.03 (CH_3*C*O), 109.28, 108.60 ((CH_3)$_2$*C*), 97.22 (C-1′), 96.24 (C-1), 77.78, 71.19, 70.67, 70.65, 67.53, 67.18, 66.00, 65.49 (C-2, C-3, C-4, C-5, C-6, C-3′, C-4′, C-5′), 39.03 (C-2), 26.09, 25.97, 25.01, 24.38 ((CH_3)$_2$*C*), 25.60 (Si[C(*C*H$_3$)$_3$(CH_3)$_2$]), 21.19 (*C*H_3CO), 17.86 (Si[*C*(*C*H$_3$)$_3$(CH_3)$_2$]), 17.56 (C-6′), −4.50, −4.91 (Si[C(CH_3)$_3$(*C*H$_3$)$_2$]). HRESIMS: Calcd for $C_{26}H_{46}O_{10}$SiNa ([M+Na]$^+$): *m*/*z* 569.2758, found: *m*/*z* 569.2732.

1.2.8. 4-*O*-Acetyl-3-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-*arabino*-hexopyranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucopyranose (26). Product **26** as an inseparable α,β-anomeric mixture was purified on a column of silica gel using solvent system A as the eluent; yield 45%, colourless syrup. ^{1}H NMR (α-anomer): 5.89 (d, 1H, *J* 3.8 Hz, H-1), 5.01 (d, 1H, *J* 3.5 Hz, H-1′), 4.64 (t, 1H *J* 9.3 Hz, H-4′), 4.50 (d, 1H, *J* 3.7 Hz, H-3), 3.66–4.36 (m, 7H, H-2, H-4, H-5, H-6a, H-6b, H-3′, H-5′), 2.05 (s, 3H, CH_3CO), 2.00 (ddd, 1H, *J* ∼ 0, 5.7, 13.5 Hz, H-2′$_{eq}$), 1.81 (ddd, 1H, *J* 3.5, 11.4, 13.5 Hz, H-2′$_{ax}$) 1.31, 1.36, 1.41, 1.51 (4s, 12H, 2(CH_3)$_2$C), 1.10 (d, 3H *J* 6.1 Hz, CH_3 (H-6′)), 0.85 (s, 9H, Si[C(CH_3)$_3$(CH_3)$_2$]), 0.03, 0.05 (2s, 6H, Si[C(CH_3)$_3$(CH_3)$_2$]). ^{13}C NMR (α-anomer): 169.97 (CH_3*C*O), 111.93, 109.12, ((CH_3)$_2$*C*), 105.36 (C-1), 94.26 (C-1′), 81.79, 81.25, 77.55, 76.12, 72.07, 68.12, 67.50, 66.30 (C-2, C-3, C-4, C-5, C-6, C-3′, C-4′, C-5′), 38.99 (C-2), 26.82, 26.72, 26.18, 25.30 ((CH_3)$_2$*C*), 25.58 (Si[C(*C*H$_3$)$_3$(CH_3)$_2$]), 21.12 (*C*H_3CO), 17.85 (Si[*C*(*C*H$_3$)$_3$(CH_3)$_2$]), 17.33 (C-6′), −4.46, −4.88 (Si[C(CH_3)$_3$(*C*H$_3$)$_2$]). HRESIMS: Calcd for $C_{26}H_{46}O_{10}$SiNa ([M+Na]$^+$): *m*/*z* 569.2758, found: *m*/*z* 569.2746.

1.2.9. Ethyl 4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-α-L-*arabino*-hexopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (27). Product **27** was purified on a column of silica gel using solvent system C as the eluent; yield 79%, colourless syrup; [α] −14.9 (*c* 0.8, $CHCl_3$) ^{1}H NMR: 7.24–7.38 (m, 15H, *Ph*CH$_2$), 4.54–4.97 (m, 6H, PhCH_2), 4.78 (d, 1H, *J* 3.4 Hz, H-1′), 4.62 (t, 1H *J* 9.3 Hz, H-4′), 4.47 (d, 1H, *J* 9.7 Hz, H-1), 4.02 (ddd, 1H, *J* 5.5, 9.7, 11.3 Hz, H-3′), 3.39–3.91 (m, 7H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-5′), 2.75 (m, 2H, SCH_2CH$_3$), 2.07 (s, 3H, CH_3CO), 2.01 (ddd, 1H, *J* ∼ 0, 5.5, 12.9 Hz, H-2′$_{eq}$), 1.72 (ddd, 1H, *J* 3.4, 11.3, 12.9 Hz, H-2′$_{ax}$) 1.34 (t, 3H, *J* 9.3 Hz, SCH$_2$CH_3), 1.12 (d, 3H *J* 6.3 Hz, CH_3 (H-6′)), 0.85 (s, 9H, Si[C(CH_3)$_3$(CH_3)$_2$]), 0.03, 0.04 (2s, 6H, Si[C(CH_3)$_3$(CH_3)$_2$]). ^{13}C NMR: 170.00 (CH_3*C*O), 138.30, 137.92, 128.49, 128.41, 128.27, 127.94, 127.89, 127.79 (CH$_2$*Ph*), 97.59 (C-1′), 84.84 (C-1), 86.70, 81.78, 78.59, 78.25 (C-2, C-3, C-4, C-5), 77.70 (C-4′), 75.90, 75.49, 75.09 (*C*H$_2$Ph), 67.42 (C-3′), 66.62 (C-5′), 65.88 (C-6), 39.10 (C-2′) 25.56, (Si[C(*C*H$_3$)$_3$(CH_3)$_2$]), 24.82 (S*C*H$_2$CH$_3$), 21.16 (*C*H_3CO) 17.82 (Si[*C*(*C*H$_3$)$_3$(CH_3)$_2$]), 17.60 (C-6′), 15.28 (SCH$_2$*C*H$_3$), −4.50, −4.87 (Si[C(CH_3)$_3$(*C*H$_3$)$_2$]). ESIMS: Calcd for $C_{43}H_{60}O_9$SSiNa ([M+Na]$^+$): *m*/*z* 803.36, found: *m*/*z* 803.3.

1.2.10. 4-*O*-Benzyl-3-*O*-*tert*-butyldimethylsilyl-2,6-dideoxy-L-*arabino*-hexopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (28). Product **28** as an inseparable α,β-anomeric mixture was purified on a column of silica gel using solvent system A as the eluent; yield 59%, colourless syrup. ^{1}H NMR: (α:β = 5.5:1) 7.26–7.34 (m, *Ph*CH_2), 5.51, 5.52 (2d, *J* 5.0 Hz, H-1α,β), 4.55–4.96 (m, Ph*C*H_2, H-3), 4.86 (d, 1H, *J* 3.3 Hz, H-1′α), 4.48 (m, H-1′β), 4.28, 4.33 (2dd, *J* 2.4, 5.0, H-2α,β), 4.22 (dd, *J* 1.8, 7.9 Hz, H-4), 4.80 (ddd, *J* 5.1, 8.9, 11.2 Hz, H-3′α), 3.66–4.44 (m, H-5, H-6a, H-3′β, H-5′α), 3.51 (dd, *J* 7.0, 10.4 Hz, H-6b), 3.29 (m, H-5′β), 2.99 (t, *J* 8.9 Hz, H-4′) 2.15 (m, H-$2'_{eq}$β) 2.07 (ddd, 1H, *J* ∼ 0, 5.1, 13.2 Hz, H-$2'_{eq}$α), 1.67 (ddd, 1H, *J* 3.3, 11.2, 13.2 Hz, H-$2'_{ax}$α), 1.64 (m, H-$2'_{ax}$β), 1.32, 1.33, 1.43, 1.54 (4s, 2(CH_3)$_2$C), 1.22, 1.28 (2d, *J* 6.2 Hz, CH_3 (H-6′α,β)), 0.91 (s, Si[C(CH_3)$_3$(CH_3)$_2$]), 0.08 (s, Si[C(CH_3)$_3$(CH_3)$_2$]). Selected ^{13}C NMR data: 138.69 (*Ph*CH_2α), 138.37 (*Ph*CH_2β), 109.24, 108.54 ((CH_3)$_2$*C*), 100.15 (C-1′β), 97.24 (C-1′α), 96.28 (C-1), 36.87 (C-2′α), 35.61 (C-2′β), 26.82, 26.72, 26.18, 25.30 ((*C*H$_3$)$_2$*C*), 25.57, 25.80 (Si[C(*C*H$_3$)$_3$(CH$_3$)$_2$]α, β), 17.70 (C-6′β), 17.33 (C-6′α), 17.85 (Si[*C*(*C*H$_3$)$_3$(CH$_3$)$_2$]), −4.46, −4.89 (Si[C(CH$_3$)$_3$(*C*H$_3$)$_2$]). HRESIMS: Calcd for $C_{31}H_{50}O_9SiNa$ ([M+Na]$^+$): *m*/*z* 617.3122, found: *m*/*z* 617.3156.

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Supplementary data

Supplementary data (copies of ^{1}H and ^{13}C NMR spectra of compounds **13**–**28**) associated with this article can be found, in the online version, at doi:10.1016/j.carres.2006.09.007.

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