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Indirect approach to C-3 branched 1,2-*cis*-glycofuranosides: synthesis of aceric acid glycoside analogues

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Abstract—Aceric acid (3-*C*-carboxy-5-deoxy-α-L-xylofuranose) residues are present in pectic polysaccharide rhamnogalacturonan II (RG II) in the form of synthetically challenging 1,2-*cis*-glycofuranosides. To access synthetic fragments of RG II incorporating aceric acid, a four-step procedure based on *C*-2 epimerisation of initially prepared 1,2-*trans*-glycofuranoside was developed. Readily available derivatives of branched-chain L-lyxofuranose bearing a 3-*C*-vinyl group as a masked 3-*C*-carboxyl group were investigated as potential precursors of aceric acid units. In the first step of the procedure, installation of a participating group at *C*-2 of the furanose ring ensured stereocontrol of the O-glycosylation, which was carried out with the thioglycoside of 2-*O*-acetyl-3,5-di-*O*-benzyl-3-*C*-vinyl-L-lyxofuranose. After the glycosylation step, the 2-*O*-acetyl group was removed, the free 2-OH group was oxidised and the resulting ketone was finally reduced to form the *C*-3-vinyl-L-xylofuranoside. The use of L-Selectride in the key reduction reaction was essential to achieve the required stereoselectivity to generate 1,2-*cis*-furanoside.

Keywords: Glycofuranosides; Branched-chain sugars; Aceric acid; Rhamnogalacturonan II

1. Introduction

Rhamnogalacturonan II (RG II), a unique 'mega-oligosaccharide' present in the primary cell walls of all higher plants, plays an essential role in plant growth, development and resistance to disease.[1,2] RG II consists of a main backbone of 7–9 α-1,4-linked D-galacturonic residues to which four structurally different oligosaccharides are attached, the so-called side chains A–D. In total, 16 different kinds of glycosyl residues are present in RG II and it is believed[1] that at least 24 enzymes may be required for the generation of the requisite glycoside linkages. The complex structure of RG II is, remarkably, conserved throughout the plant kingdom with only a few known variations depending on the source.[3,4] Mutant plants having an altered RG II sugar composition showed significant abnormalities in their development.[4,5] This effect is accounted for by a reduced ability of RG II to form a dimer, which is the predominant form of RG II in plants.[6] It is believed that the dimerisation of RG II is mediated by cross-linking through a borate diester formation between apiofuranosyl residues. Although a common motif, β-L-Rha*p*-(1-3′)-β-D-Api*f*-(1-2)-α-L-Gal*p*A, is present in both side chains A and B, only the residue belonging to side chain A is thought to be involved in RG II dimerisation. Fragments of both side chains will be useful in the study of boron complexation and a number of synthetic fragments of RG II has been reported.[7] Reading from the polygalacturonic acid backbone, the first point of difference between side chains A and B lies in the glycosylation of β-L-rhamnopyranosyl residue. Side chain B (Fig. 1) has the branched-chain sugar aceric acid (Ace*f*) attached to *O*-3 of β-L-rhamnopyranose. To date, aceric acid has only been found in nature in the structure of RG II. The synthesis of this unusual monosaccharide and of its C-2 epimer has been reported recently,[8,9]

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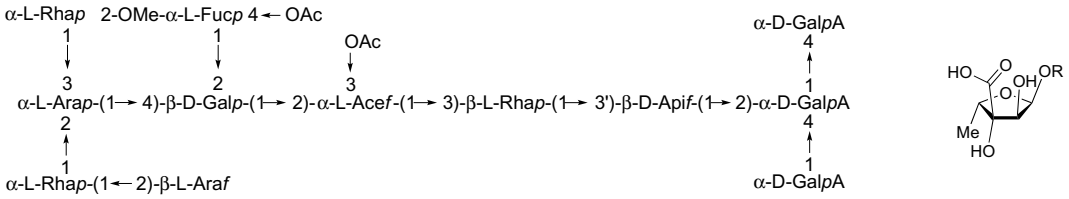


Figure 1. Structure of a fragment of rhamnogalacturonan II representing the side chain B nonasaccharide attached to a trisaccharide region of polygalacturonan backbone[3b] (left) and the aceric acid residue, shown as a generic glycoside with naturally occurring α-L-configuration (right).

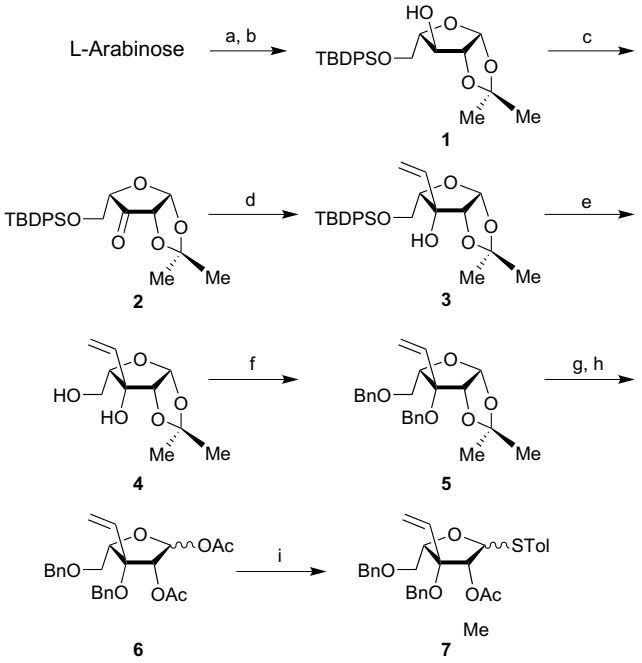
but thus far no synthetic fragments of RG II containing this branched-chain pentose are known.

Chemical synthesis of side chain B requires the construction of a 1,2-*cis*-glycofuranosidic bond between aceric acid and rhamnopyranose units. Stereoselective formation of this type of glycosidic bond remains one of the major challenges of synthetic carbohydrate chemistry because stereoelectronic and steric effects favour the formation of 1,2-*trans*-glycofuranosides, even in reactions with glycofuranosyl donors having non-participating substituents at C-2. Glycofuranosyl fluorides,[10] thioglycofuranosides[11,12] and trichloroacetimidates[13] of glycofuranoses have been employed for the synthesis of 1,2-*cis*-glycofuranosides. Less common reagents such as ditiocarbamates[14] and 2-carboxybenzyl glycosides[15] have also been used for this purpose. Indirect methods based on 2,3-anhydro-glycofuranosyl donors[16] or intramolecular aglycon delivery[17] proved to be useful in syntheses of 1,2-*cis*-arabinofuranosides. More recently, a remarkable stereoselectivity in 1,2-*cis*-arabinofuranosylation was achieved with the aid of a 3,5-*O*-di-*tert*-butylsilyl protecting group.[18] However, the whole arsenal of general 1,2-*cis*-glycosylating methods[19] has not been widely used by synthetic chemists for the construction of 1,2-*cis*-furanosides, apparently because of the rare occurrence of this type of glycosides in nature. Since the only access to aceric acid is via multi-step synthesis, a choice of glycosylation method for the construction of aceric acid glycosides depends on the availability of a suitable glycosyl donor which can serve as an aceric acid precursor. We describe, herein an application of an indirect approach to the construction of 3-*C*-branched 1,2-*cis*-linked glycofuranosides via the inversion of C-2 configuration in more readily available 1,2-*trans*-linked glycofuranosides. This methodology is illustrated by the synthesis of protected methyl 3-*C*-vinyl-β-L-xylofuranoside and methyl 3-*C*-vinyl-β-L-xylofuranosyl-(1→3)-β-L-rhamnopyranoside; the functionalised core furanose moiety of these compounds has the same stereochemistry as aceric acid and can be envisaged as an aceric acid precursor.

2. Results and discussion

The synthesis of 1,2-*cis*-glycosides of aceric acid (Fig. 1) was approached by an indirect strategy consisting of the construction of a 1,2-*trans*-glycofuranosidic bond first, followed by the inversion of the C-2 configuration of the glycofuranose residue. This strategy takes advantage of highly stereoselective glycosylation provided by the possibility of a neighbouring group participation as well as more easy access to C-2 epimers of aceric acid.[8]

Our strategy began with trapping the furanose form of L-arabinose by selective 5-O-silylation, followed by conventional isopropylidenation which gave the known alcohol **1**[20] in an overall 48% yield (Scheme 1). Oxidation of **1** using Dess–Martin periodinane in CH_2Cl_2 gave pentafuranos-2-ulose **2**[20] in a 90% yield. The bicylo-[3.3.0]octane ring system of **2** allows stereoselective introduction of branching point by nucleophilic addition from sterically less demanding *exo*-face of the molecule.[21] Following the classical synthesis of streptose,[22] a branched sugar which has structural similarity to aceric



Scheme 1. Synthesis of glycosyl donor **7**. Reagents and conditions: (a) TBDPSCl, imidazole, DMF, 65 °C; (b) $Me_2C(OMe)_2$, Me_2CO, I_2, 48% over two steps; (c) Dess–Martin periodinane, CH_2Cl_2, 90%; (d) CH_2=CHMgBr, THF, −78→20 °C, 81%; (e) TBAF, THF, 90%, (f) BnBr, NaH, Bu_4NI, DMF, 75%; (g) TFA–H_2O 9:1; (h) Ac_2O, pyridine, 72% over two steps; (i) *p*-$CH_3C_6H_4SH$, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C, 92%.

acid, we made use of vinyl magnesium bromide as a nucleophile. Addition to ketone **2** was highly stereoselective and proceeded with the formation of a single product **3** in 81% yield. The desired stereochemistry of the vinyl adduct **3** was confirmed by X-ray structural analysis which showed that this compound has the *lyxo*-configuration (Fig. 2). It should be noted that other nucleophiles, such as thiazolyl lithium,[8] can also be applied for the introduction of the C-3 branch point. The vinyl group was chosen in this instance because it was expected, due to its relatively small size, not to interfere with subsequent glycosylation steps required for the construction of RG II side chain B. Deprotection of O-5 in **3** under acidic conditions afforded diol **4**, which was benzylated to give dibenzyl ether **5** in overall 68% yield. Several attempts to benzylate the tertiary alcohol in compound **3** prior to desilylation were unsuccessful, leading only to the recovery of starting material. If more vigorous benzylation conditions were applied, including a large excess of reagent and temperature increased to 40 °C, compound **3** was converted into desilylated product **4**. A similar lack of reactivity of a tertiary alcohol having an adjacent silyl group was observed recently in benzylation of a compound with unrelated structure.[23]

Taking into account that the preparation of 5-deoxy-L-arabinose as a precursor of aceric acid will demand a tedious multistep synthesis,[8,24] in these studies, we proceeded with the investigation of the glycosylation methodology required for the construction of 1,2-*cis*-glycofuranosidic bond using the 5-hydroxy analogue of aceric acid. The isopropylidene group of the dibenzylated derivative **5** was hydrolysed in 90% CF_3CO_2H and the resulting diol was acetylated to an anomeric mixture of 1,2-diacetates **6**. Treatment of **6** with *p*-thiocresol-$BF_3{\cdot}Et_2O$ produced thioglycoside **7** as a 1:8 mixture of anomers in 92% yield. The ratio of anomers was determined on the basis of intensities of signals in ^{1}H NMR spectra, specifically resonances of $CH{=}CH_2$ and *p*-$CH_3C_6H_4S$ groups, which were not overlapping. Anomeric configurations were assigned tentatively on the basis of $^3J_{H\text{-}1,H\text{-}2}$ coupling constants, which were measured for individual samples of **α-7** (minor product) and **β-7** (major product) isolated from the mixture. Values of these coupling constants (5.6 Hz for **α-7** and 7.3 Hz for **β-7**) were notably higher than typical $^3J_{H\text{-}1,H\text{-}2}$ values for *O*-glycofuranosides (0–2 Hz for 1,2-*trans* and 3–5 Hz for 1,2-*cis*-glycofuranosides).[25] This observation is in agreement with previous findings that the presence of sulfur at the anomeric position, in particular, in the case of some thioglycofuranosides (e.g. 7.1 Hz for *trans*- and 6.8 Hz for *cis*-isomer of perbenzylated phenylthiomannofuranoside),[11] substantially increases $^3J_{H\text{-}1,H\text{-}2}$ values.

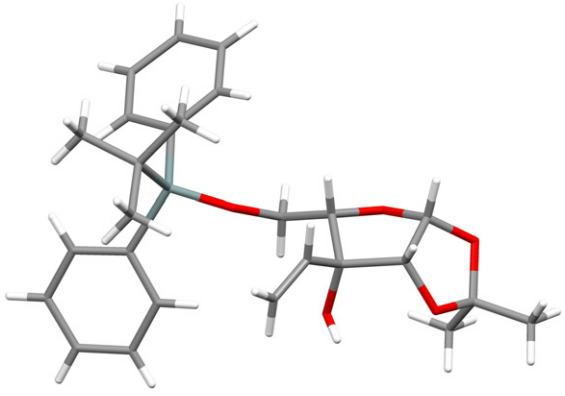
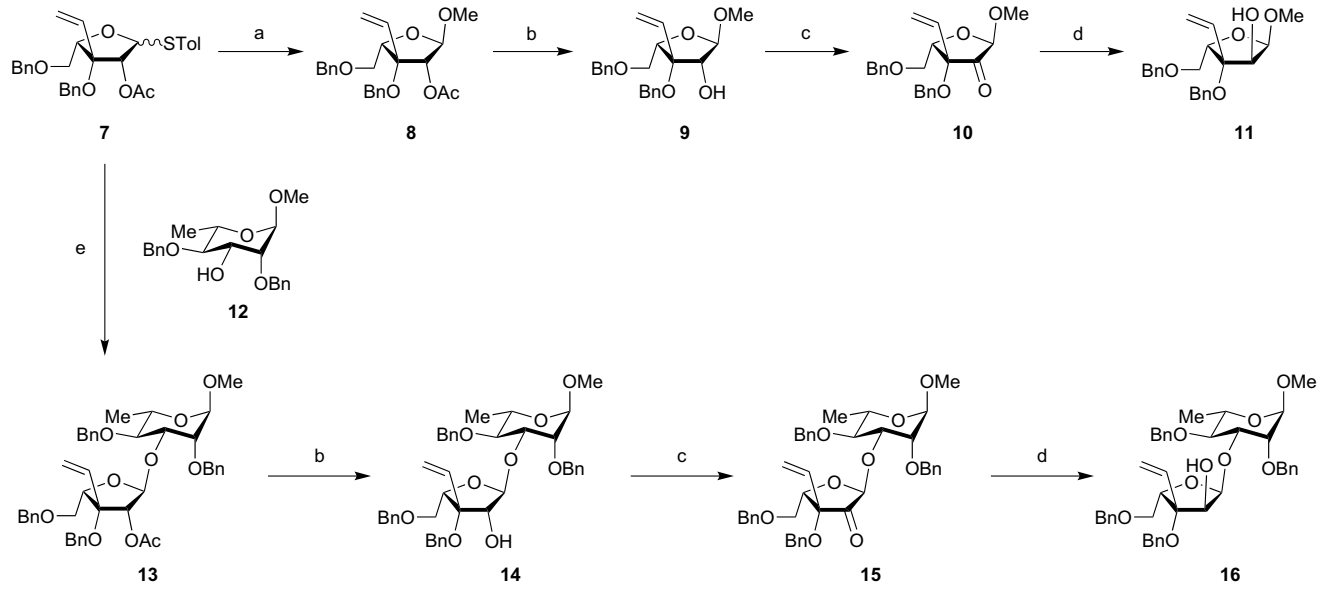


Figure 2. X-ray crystal structure of *exo*-vinyl derivative **3**.

With the donor **7** in hand, NIS/TMSOTf-promoted glycosylation of methanol and known methyl α-L-rhamnopyranoside derivative **12**[26] were executed giving methyl glycofuranoside **8** and disaccharide **13** in 76% and 81% yields, respectively (Scheme 2). The α-L-stereochemistry of the furanosyl residue in these compounds was established from the values of $\delta_{C\text{-}1}$ in ^{13}C NMR spectra of **8** (111.0 ppm) and **13** (107.8 ppm) which lie in the characteristic range of $\delta_{C\text{-}1}$ for 1,2-*trans*-glycofuranosides. Coupling constants $^3J_{H\text{-}1,H\text{-}2}$ for **8** and **13** were 3.1 Hz and 3.7 Hz, respectively. These values are somewhat higher than $^3J_{H\text{-}1,H\text{-}2}$ values (0–2 Hz), which are characteristic[25] for 1,2-*trans*-furanosides and usually allow unambiguous assignment of the anomeric configuration in glycofuranosides.

The key step in the synthesis of target 1,2-*cis*-glycofuranosides from **8** and **13** was the inversion of the C-2 configuration. Epimerisation of C-2 in carbohydrates can be performed by nucleophilic displacement of a 2-triflate with nitrate,[27] acetate[28] or benzoate[29] ions. An alternative approach includes stereoselective reduction of corresponding 2-uloses.[30] This reduction process has been particularly well studied in the course of the development of indirect β-mannosylation methodology[31] but it has not previously been reported for the synthesis of 1,2-*cis*-glycofuranosides. Application of the 2-ulose reduction procedure required conversion of 2-acetates **8** and **13** into derivatives **10** and **15**, respectively (Scheme 2). After deacetylation of compounds **8** and **13**, which proceeded in 91% yield, 2-hydroxy-derivatives **9** and **14** were subjected to oxidation with Dess–Martin periodinane in CH_2Cl_2 to afford 2-uloses **10** and **15** in 87% and 86% yield, respectively. The X-ray crystal structure obtained for methyl glycofuranosid-2-ulose **10** confirmed successful installation of keto group and the correct C-1 stereochemistry of the furanose unit (Fig. 3).

In attempts to reduce the keto group in methyl glycoside **10** using a standard $NaBH_4$ procedure, only the undesired *lyxo*-configured alcohol **9** was obtained. In the pyranose series, a dramatic improvement of the stereoselectivity of C-2 reduction was achieved[32] with the use of sterically demanding $LiB(i\text{Bu})_3H$ (L-Selectride). Mindful of this precedent, L-Selectride was investigated with substrates **10** and **15**. For the former, a mixture of



Scheme 2. Synthesis of methyl glycofuranoside **11** and disaccharide **16**. Reagents and conditions: (a) MeOH, NIS, TMSOTf, 3 Å mol sieves, CH_2Cl_2, −30 °C, 76%; (b) NaOMe, MeOH, 91% (for **9**), 89% (for **14**); (c) Dess–Martin periodinane, CH_2Cl_2, 87% (for **10**), 86% (for **15**); (d) L-Selectride, THF, −65 °C, 72% (for **11**), 80% (for **16**); (e) NIS, TMSOTf, 4 Å mol sieves, CH_2Cl_2, −30 °C, 81%.

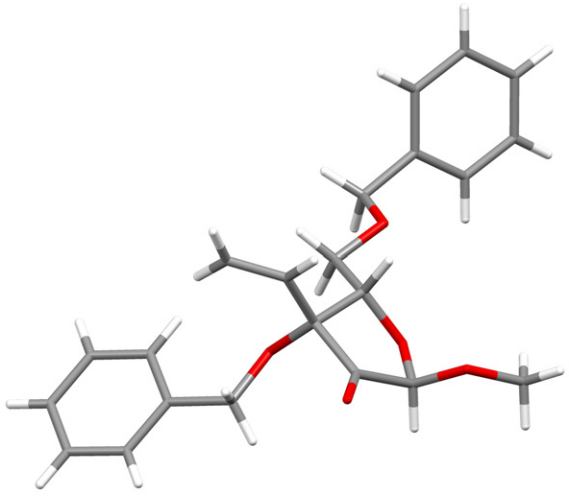


Figure 3. X-ray crystal structure of 2-keto derivative **10**.

C-2 epimers was obtained in 77% yield, favouring the desired *xylo*-configured alcohol **11** (*xylo*:*lyxo* ~ 14:1) when the reaction was performed at −65 °C. Conveniently, the disaccharide 2-ulose **15** was reduced under these conditions into alcohol **16** in 80% yield with the formation of the undesired epimer being not observed. These results can be rationalised on the basis of the assumption that the attack by bulky borohydride nucleophile on the carbonyl group occurs preferentially from the (slightly) less hindered β-face of C-3-branched glycofuranosid-2-ulose. This suggestion is supported by higher stereoselectivity of the reduction of glycofuranosid-2-ulose **15** compared to glycoside **10**. The former has a bigger aglycon than the latter that can further reduce accessibility to the α-face of ketone disaccharide **15**.

3. Conclusion

In summary, an indirect four-step procedure has been developed for the construction of 1,2-*cis*-glycofuranosides in relation to the synthesis of aceric acid-containing fragments of rhamnogalacturonan II. The procedure involves stereospecific 1,2-*trans*-glycosylation, 2-OH group deprotection followed by oxidation to ketone and final reduction with L-Selectride. This sequence of reactions has been successfully applied to the synthesis of methyl glycoside **11** and disaccharide **16**. The branched-chain pentofuranosyl units in these compounds have the correct anomeric configuration and possess the potential to be transformed into aceric acid derivatives present in the natural pectic polysaccharide RG II. Introduction of the 5-deoxy group into the pentofuranosyl unit can be achieved by a variety of methods, as it has been described earlier.[8] The 3-*C*-vinyl group in our scheme represents a precursor for the carboxyl group and it is convenient for the construction of larger fragments of RG II incorporating aceric acid. The carboxyl group can be unmasked via ozonolysis and subsequent aldehyde oxidation at a later stage of the oligosaccharide assembly. The described epimerisation procedure also conveniently leads to a free C-2 hydroxyl group, which is required for further extension of the oligosaccharide chain by chemical glycosylation. Synthesis of larger fragments of side chain B of RG II (Fig. 1) employing this strategy is currently under way in our laboratories.

4. Experimental

All solvents were used as supplied, except for CH_2Cl_2, which was freshly distilled from CaH_2. Cation-exchange resin (Amberlite IRA120, H^+-form, Fluka) was pre-washed with water and dry MeOH before use. Dess–Martin periodinane was prepared according to the literature procedures.[33] Reagents and dry solvents were added via syringes through septa. Solns of reaction products were dried with $MgSO_4$. Evaporation of solvents was performed under reduced pressure at 30–40 °C. Thin-layer chromatography was performed on aluminium-backed, pre-coated Silica gel plates 60 F_{254}, (E. Merck); spots were detected by charring plates treated with 5% H_2SO_4 in EtOH. Products were purified by column chromatography on silica gel (40–63 μm) using SP4 flash purification system (Biotage). Melting points were determined using Gallenkamp melting point apparatus and are uncorrected. Optical rotations were measured at 20–21 °C using Perkin–Elmer 341 polarimeter. IR spectra were recorded on Perkin Elmer Spectrum BX FT IR Spectrometer equipped with SensiIR diamond ATR accessory. ^{1}H and ^{13}C NMR spectra were recorded at 20–21 °C with a Varian Gemini 2000 spectrometer at 300 and 75 MHz, respectively, or with a Varian Unity Plus spectrometer at 400 and 100.6 MHz, respectively, using Me_4Si as an internal standard. Resonance allocations were made with the aid of COSY and HSQC experiments when necessary. High resolution electrospray ionisation mass spectra (ESIMS) were obtained on Finnigan MAT 900 XLT mass spectrometer.

4.1. 5-*O*-*tert*-Butyldiphenylsilyl-1,2-*O*-isopropylidene-β-L-arabinofuranose (1)

L-Arabinose (10.0 g, 66.6 mmol) was added to a stirred solution of *tert*-butyl(chloro)diphenylsilane (17.5 mL, 67.3 mmol) and imidazole (9.0 g, 132 mmol) in DMF (120 mL). After 2 h at 60 °C, the reaction mixture was concentrated, poured into aqueous 1 M HCl (100 mL) and extracted with CH_2Cl_2 (3 × 80 mL). The combined organic extracts were washed with water (2 × 100 mL) and saturated aqueous $NaHCO_3$ solution (2 × 100 mL), dried and concentrated. Column chromatography (8:2→3:7 petroleum ether–EtOAc) gave 5-*O*-*tert*-butyldiphenylsilyl-α,β-L-arabinofuranose as an oil (14.2 g, 55%); R_f 0.25 (CH_2Cl_2/MeOH, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.28 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1, β-anomer), 5.40 (s, 1H, H-1, α-anomer). The purified product was dissolved in a mixture of acetone (150 mL) and 2,2-dimethoxypropane (6.8 mL, 55.0 mmol) and, I_2 (2.6 g, 10.2 mmol) was added. After 1 h, satd aq $NaHCO_3$ soln was added until the reaction mixture turned colourless. The reaction mixture was concentrated and the residue was purified by column chromatography (9:1→6:4 petroleum ether–EtOAc) to afford compound **1** as a colourless oil (13.8 g, 48% over two steps); R_f 0.41 (hexane/EtOAc 7:3); $[\alpha]_D$ −4.7 (*c* 1.2, $CHCl_3$), lit.[20] −5; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (s, 9H, *t*-Bu), 1.28 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 2.08 (s, 1H, OH), 3.80–3.84 (m, 2H, H-5a, H-5b), 4.03–4.08 (m, 1H, H-4), 4.34–4.45 (m, 1H, H-3), 4.54 (d, 1H, $J_{1,2} = 3.9$ Hz, H-2), 5.88 (d, 1H, H-1), 7.36–7.43 (m, 6H, Ph), 7.65–7.68 (m, 4H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.1 ($C(CH_3)_3$), 26.0 ($C(CH_3)_2$), 26.8 (4C, $C(CH_3)_3$, $C(CH_3)_2$), 63.7 (C-5), 76.4 (C-4), 87.1 (C-3), 87.4 (C-2), 105.6 (C-1), 112.6 ($C(CH_3)_2$), 127.8, 129.9 (2C), 133.3 (2C), 135.7 (2C).

4.2. 5-*O*-*tert*-Butyldiphenylsilyl-1,2-*O*-isopropylidene-β-L-*threo*-pentofuranos-3-ulose (2)

Dess–Martin periodinane (3.4 g, 8.0 mmol) was added to stirred soln of alcohol **1** (2.0 g, 4.7 mmol) in dry CH_2Cl_2 (50 mL), the mixture was stirred for 2 h at 20 °C, then poured into stirred satd aq $NaHCO_3$ soln (70 mL) containing $Na_2S_2O_3$ (6.6 g, 16 mmol), and extracted with CH_2Cl_2 (2 × 60 mL). The combined organic extracts were dried and the solvent was removed by evaporation. The resulting residue was purified by column chromatography (9:1→7:3 petroleum ether–EtOAc) to give **2** as an amorphous solid (1.79 g, 90%); R_f 0.35 (8:2 hexane–EtOAc); $[\alpha]_D$ −12 (*c* 1.0, $CHCl_3$), lit.[20] −12.0; mp 31–33 °C (hexane–petroleum ether), IR: *v* 1772 (CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04–1.06 (m, 9H, *t*-Bu), 1.36 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 3.96–3.97 (m, 2H, H-5a, H-5b), 4.29 (m, 1H, H-4), 4.38 (d, 1H, $J_{1,2} = 6.0$ Hz, H-2); 6.03 (d, 1H, H-1), 7.36–7.44 (m, 6H, Ph), 7.63–7.73 (m, 4H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.5 ($C(CH_3)_3$), 26.8 (3 C, $C(CH_3)_3$), 27.0 ($C(CH_3)_2$), 27.7 ($C(CH_3)_2$), 64.7 (C-5), 77.0 (C-4), 82.5 (C-2), 102.8 (C-1), 115.0 ($C(CH_3)_2$), 128.0, 128.2 (2C), 130.0 (2C), 133.0, 133.3, 135.8, 135.9, 136.0 (C-Ar), 207.4 (C-3).

4.3. 5-*O*-*tert*-Butyldiphenylsilyl-1,2-*O*-isopropylidene-3-*C*-vinyl-β-L-lyxofuranose (3)

A 1.0 M soln of vinylmagnesium bromide in THF (3.0 mL, 3.0 mmol) was slowly added to a stirred soln of the ketone **2** (1.00 g, 2.34 mmol) in dry THF (10 mL) at −78 °C. After 15 min, the mixture was allowed to warm to −20 °C and left at this temperature for 1.5 h. The reaction was quenched with a mixture of satd aq NH_4Cl soln and crushed ice and then extracted with CH_2Cl_2 (3 × 40 mL). The combined organic extracts were dried and the solvent was removed in vacuo. The residue was purified by column chromatography (1:0→75:25 petroleum ether–EtOAc) to give **3** as a white solid (0.86 g, 81%); R_f 0.49 (8:2 hexane–EtOAc); mp 73–75 °C (hexane); $[\alpha]_D$ −4.0 (*c* 1.0, $CHCl_3$); IR: *v*

3507 (OH), 1640 (C=C), no peaks near 1770 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.05 (s, 9H, *t*-Bu), 1.36 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 3.37 (s, 1H, OH), 3.86–3.94 (m, 2H, H-5a, H-5b), 4.09 (dd, 1H, $J_{4,5a} = 5.0$ Hz, $J_{4,5b} = 10.3$ Hz, H-4), 4.36 (d, 1H, $J_{1,2} = 4.1$ Hz, H-2), 5.18 (dd, 1H, $J_{a,b} = 10.7$ Hz, $J_{b,c} = 1.2$ Hz, CHa=C*H*bHc), 5.45 (dd, 1H, $J_{a,c} =$ 17.2 Hz, $J_{b,c}$, CHa=CHb*H*c), 5.75 (d, 1 H, H-1), 5.86 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 7.34–7.43 (m, 6H, Ph), 7.67–7.70 (m, 4H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4 ($C(CH_3)_3$), 27.0 (3 C, $C(CH_3)_3$), 27.1 ($C(CH_3)_2$), 27.2 ($C(CH_3)_2$), 63.2 (C-5), 78.2 (C-4), 85.6 (2 C, C-2 and C-3), 104.9 (C-1), 114.8 (HC=CH_2), 114.9 ($C(CH_3)_2$), 127.9 (2C), 129.9, 133.3, 135.9 (2C, C-Ar), 139.8 (H*C*=CH_2); HRESIMS: found *m*/*z* 455.2248; calcd for $C_{26}H_{35}O_5Si$ $[M+H]^+$, 455.2248.

4.4. 1,2-*O*-Isopropylidene-3-*C*-vinyl-β-L-lyxofuranose (4)

A 1 M soln of TBAF in THF (15 mL, 15 mmol) was added to a stirred soln of the silyl ether **3** (3.0 g, 6.6 mmol) in THF (15 mL). The mixture was stirred for 2 h at 20 °C, concentrated and the residue was purified by column chromatography (8:2→1:1 petroleum ether–EtOAc) to afford the title compound **4** as an oil (1.28 g, 90%); R_f 0.35 (6:4 hexane–EtOAc); $[\alpha]_D$ +2.0 (*c* 0.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.41 (s, 3H, CH_3), 1.65 (s, 3H, CH_3), 3.87 (d, 2H, $J_{4,5} = 5.2$ Hz, H-5a, H-5b), 3.97 (t, 1H, $J_{4,5}$, H-4), 4.48 (br s, 2H, OH), 4.40 (d, 1H, $J_{1,2} = 4.2$ Hz, H-2), 5.26 (d, 1H, $J_{a,b} = 10.8$ Hz, CHa=C*H*bHc), 5.50 (d, 1H, $J_{a,c} = 17.2$ Hz, CHa=CHb*H*c), 5.84 (d, 1H, H-1), 5.91 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.0 (2C, CH_3), 61.6 (C-5), 78.5 (C-4), 85.1 (C-2), 85.7 (C-3), 105.0 (C-1), 114.7 ($C(CH_3)_2$), 114.9 (HC=CH_2), 139.5 (H*C*=CH_2); HRESIMS: found *m*/*z* 234.1335 $[M+NH_4]^+$; calcd for $C_{10}H_{20}O_5N$, 234.1336.

4.5. 3,5-Di-*O*-benzyl-1,2-*O*-isopropylidene-3-*C*-vinyl-β-L-lyxofuranose (5)

Sodium hydride (60% suspension in mineral oil, 3.6 g, 90 mmol) was added to a stirred soln of the diol **4** (2.1 g, 9.7 mmol), benzyl bromide (3.5 mL, 29 mmol) and Bu_4NI (1.1 g, 3.0 mmol) in DMF (30 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 3 h. MeOH (10 mL) was added carefully and the reaction mixture was concentrated. The residue was dissolved in CH_2Cl_2 (100 mL), washed with water (2 × 20 mL) and saturated aq $NaHCO_3$ soln (2 × 20 mL), dried and concentrated. Column chromatography of the residue (1:0→8:2 petroleum ether–EtOAc) gave compound **5** as an oil (2.9 g, 75%). R_f 0.45 (8:2 hexane–EtOAc); $[\alpha]_D$ −24.1 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 3.98 (m, 2H, H-5a, H-5b), 4.27 (dd, 1H, $J_{4,5a} = 7.3$ Hz, $J_{4,5b} = 3.9$ Hz, H-4), 4.51–4.64 (m, 5H, 2 × C*H*$_2$Ph, H-2), 5.41 (d, 1H, $J_{a,b} = 11.2$ Hz, CHa=C*H*bHc), 5.41 (d, 1H, $J_{a,c} = 17.8$ Hz, CHa=CHb*H*c), 5.78 (d, 1H, $J_{1,2} = 3.8$ Hz, H-1), 6.00 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 7.26–7.34 (m, 10H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.2 (CH_3), 26.7 (CH_3), 67.5 (CH_2Ph), 70.4 (C-5), 73.5 (CH_2Ph), 82.0 (C-2), 84.4 (C-3), 86.0 (C-4), 105.6 (C-1), 113.8 ($C(CH_3)_2$), 117.8 (HC=CH_2), 127.4, 127.6 (2C), 128.0, 128.5, 138.7 (C-Ar), 138.8 (2C, C-Ar and H*C*=CH_2); HRESIMS: found *m*/*z* 414.2275 $[M+NH_4]^+$; calcd for $C_{24}H_{32}O_5N$ 414.2276.

4.6. 1,2-Di-*O*-acetyl-3,5-di-*O*-benzyl-3-*C*-vinyl-α,β-L-lyxofuranose (6)

A soln of compound **5** (1.4 g, 3.5 mmol) in CH_2Cl_2 (1 mL) was treated with 90% aq CF_3CO_2H (5 mL) at 0 °C and the mixture was stirred at 20 °C for 1 h, diluted with water (5 mL) and extracted with CH_2Cl_2 (2 × 30 mL). The organic extracts were dried, solvent was evaporated and the residue was purified by chromatography (8:2→6:4 petroleum ether–EtOAc) to give 1,2-diol as an oil (1.10 g, 88%). R_f 0.45 (1:1 hexane–EtOAc); IR: *v* 3399 (OH), 1640 (C=C) cm^{-1}; ^{13}C NMR (100 MHz, $CDCl_3$): δ 97.8 (C-1β), 104.4 (C-1α); HRESIMS: found *m*/*z* 374.1962 $[M+NH_4]^+$; calcd for $C_{21}H_{28}O_5N$ 374.1962. The purified product (0.60 g, 1.68 mmol) was dissolved in pyridine (2 mL), Ac_2O (2.0 mL, 32 mmol) was added and the mixture was kept for 17 h at 20 °C. The mixture was repeatedly diluted with toluene and concentrated. The residual solid was dissolved in 15 mL of CH_2Cl_2, and the soln was washed with 0.1 M aq HCl soln (2 × 5 mL) and saturated aq $NaHCO_3$ soln (5 mL), dried over $MgSO_4$ and concentrated. Purification of the residue by column chromatography (9:1→7:3 petroleum ether–EtOAc) gave **6** (0.60 g, 71%) as a 8.5:1 mixture of anomers. Minor anomer of **6**: R_f 0.22 (8:2 hexane–EtOAc), ^1H NMR (400 MHz, $CDCl_3$): δ 2.02 (s, Ac), 2.07 (s, Ac), 5.58 (d, $J_{1,2} = 4.9$ Hz, H-2), 6.40 (d, H-1). Analytical sample of the major anomer of **6**: R_f 0.25 (8:2 hexane–EtOAc); $[\alpha]_D$ −29.9 (*c* 1.2, $CHCl_3$); IR: *v* 1746 (C=O) no peaks near 3650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.04 (s, 3H, Ac), 2.09 (s, 3H, Ac), 3.78 (dd, 1H, $J_{4,5a} =$ 6.7 Hz, $J_{5a,5b} = 10.8$ Hz, H-5a), 3.89 (dd, 1H, $J_{4,5b} = 4.0$ Hz, H-5b), 4.41 (dd, 1H, H-4), 4.49 (d, 1H, $J_{gem} = 12.0$ Hz, C*H*Ph), 4.58 (d, 1H, J_{gem}, C*H*Ph), 4.59 (d, 1H, J_{gem}, C*H*Ph), 4.68 (d, 1H, C*H*Ph), 5.44 (d, 1H, $J_{a,b} = 11.1$ Hz, CHa=C*H*bHc), 5.53 (d, 1H, $J_{a,c} =$ 17.7 Hz, CHa=CHb*H*c), 5.71 (d, 1H, $J_{1,2} = 3.6$ Hz, H-2), 5.97 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 6.31 (d, 1H, H-1), 7.26–7.34 (m, 10H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0 (CH_3), 21.4 (CH_3), 68.3 (CH_2Ph), 68.5 (C-5), 73.7 (CH_2Ph), 79.6 (C-2), 85.0 (C-3), 85.7 (C-4),

99.7 (C-1), 119.7 (HC=*C*H_2), 126.9, 127.5, 127.9, 128.0, 128.5 (2C), 128.6, 134.4, 138.1 (C-Ar), 139.2 (H*C*=CH_2), 169.8 (CO), 170.2 (CO); HRESIMS: found *m*/*z* 463.1728 $[M+Na]^+$; calcd for $C_{25}H_{28}O_7Na$ 463.1727.

4.7. *p*-Tolyl 2-*O*-acetyl-3,5-di-*O*-benzyl-1-thio-3-*C*-vinyl-α,β-L-lyxofuranoside (7)

A soln of acetate **6** (0.20 g, 0.45 mmol) and thiocresol (65 mg, 0.52 mmol) in dry CH_2Cl_2 (5 mL) was carefully treated with $BF_3{\cdot}OEt_2$ (45 μL, 0.90 mmol) at 0 °C and the mixture was kept at 5 °C for 1 h. Triethylamine (0.5 mL) was added and the resulting soln was diluted with CH_2Cl_2 and washed with satd aq $NaHCO_3$ soln and water. The organic layer was dried, filtered and concentrated. The product was purified by column chromatography (1:0→9:1 petroleum ether–EtOAc) to yield **7** (0.21 g, 92%, α:β 1:8) as a colourless syrup. Repeated purification of a small sample of **7** afforded pure β-anomer, R_f 0.28 and α-anomer, R_f 0.21 (9:1 hexane–EtOAc). Thioglycoside **β-7**: $[\alpha]_D$ −72.0 (*c* 1.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 2.10 (s, 3H, Ac), 2.33 (s, 3H, C*H*$_3$C$_6$H$_4$S), 3.74 (dd, 1H, $J_{4,5a}$ = 4.7 Hz, $J_{5a,5b}$ = 10.8 Hz, H-5a), 3.91 (dd, 1H, $J_{4,5b}$ = 6.3 Hz, H-5b), 4.20 (dd, 1H, H-4), 4.49 (d, 1H, J_{gem} = 12.0 Hz, C*H*Ph), 4.59 (m, 2H, PhC*H*), 4.75 (d, 1H, J_{gem} = 12.0 Hz, PhC*H*), 5.36 (d, 1H, $J_{a,b}$ = 11.2 Hz, CHa=C*H*bHc), 5.43 (d, 1H, $J_{1,2}$ = 7.3 Hz, H-1), 5.44 (d, 1H, $J_{a,c}$ = 17.8 Hz, CHa=CHb*H*c), 5.65 (d, 1H, H-2), 5.91 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 7.12–7.46 (m, 14H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2 (*C*H$_3$C$_6$H$_4$S), 21.4 (OC(O)*C*H$_3$), 68.2 (C-5), 68.4 (PhCH_2), 73.5 (PhCH_3), 78.3 (C-2), 84.4 (C-3), 84.6 (C-4), 88.4 (C-1), 119.6 (HC=*C*H_2), 126.9–138.4 (Ph), 139.5 (H*C*=CH_2), 169.6 (CO); HRESIMS: found *m*/*z* 522.2309 $[M+NH_4]^+$; calcd for $C_{30}H_{40}O_5NS$ 522.2309. Thioglycoside **α-7**: ^1H NMR (400 MHz, $CDCl_3$): δ 2.13 (s, 3H, Ac), 2.31 (s, 3H, C*H*$_3$C$_6$H$_4$S), 3.91 (dd, 1H, $J_{4,5a}$ = 4.5 Hz, $J_{5a,5b}$ = 10.7 Hz, H-5a), 4.00 (dd, 1H, $J_{4,5b}$ = 6.9 Hz, H-5b), 4.24 (dd, 1H, H-4), 4.55 (d, 1H, J_{gem} = 12.0 Hz, C*H*Ph), 4.57 (2H, m, C*H*Ph), 4.65 (1H, d, J_{gem} 12.0 Hz, C*H*Ph), 4.69 (1H, d, J_{gem}, C*H*Ph), 5.63 (d, 1H, H-1 or H-2, $J_{1,2}$ = 5.8 Hz), 5.67 (d, 1H, H-1 or H-2), 5.46 (d, 1H, $J_{a,b}$ = 11.2 Hz, CHa=C*H*bHc), 5.47 (d, 1H, $J_{a,c}$ = 17.7 Hz, CHa=CHb*H*c), 6.00 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 7.09–7.39 (m, 14H, Ph); HRESIMS: found *m*/*z* 527.1869 $[M+Na]^+$; calcd for $C_{30}H_{40}O_5NS$ 527.1863.

4.8. Methyl 2-*O*-acetyl-3,5-di-*O*-benzyl-3-*C*-vinyl-α-L-lyxofuranoside (8)

A mixture of thioglycoside **7** (0.21 g, 0.42 mmol), MeOH (175 μL, 4.32 mmol) and 3 Å mol sieves (0.5 g) in CH_2Cl_2 (12 mL) was stirred for 20 min at 20 °C and then cooled to −30 °C. After addition of *N*-iodosuccinimide (0.12 g, 0.53 mmol) and TMSOTf (16 μL, 0.086 mmol,), the mixture was stirred for 1 h at −30 °C and then treated with a few drops of Et_3N. Diluted aq $Na_2S_2O_3$ soln (10 mL) was added at 20 °C, the mixture was stirred for 30 min, extracted with CH_2Cl_2 (3 × 10 mL), dried and concentrated. The residue was purified by column chromatography (1:0→8:2 hexane–EtOAc) to give methyl glycofuranoside **8** as an oil (0.13 g, 76%); R_f 0.37 (8:2 hexane–EtOAc); $[\alpha]_D$ −51.0 (*c* 1.0, $CHCl_3$); IR: *v* 1746 (C=O), no peaks near 3400 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.02 (s, 3H, $COCH_3$), 3.43 (3H, s, OCH_3), 3.80 (dd, 1H, $J_{4,5a}$ = 7.1 Hz, $J_{5a,5b}$ = 10.8 Hz, H-5a), 3.90 (dd, 1H, $J_{4,5b}$ = 3.8, H-5b), 4.33 (dd, 1H, H-4), 4.52 (d, 1H, J_{gem} = 12.0 Hz, C*H*Ph), 4.58–4.60 (m, 2H, 2 × C*H*Ph), 4.64 (d, 1H, J_{gem} = 12.0 Hz, C*H*Ph), 5.08 (d, 1H, $J_{1,2}$ = 3.1 Hz, H-2), 5.38 (d, 1H, $J_{a,b}$ = 11.1 Hz, CHa=C*H*bHc), 5.50 (d, 1H, $J_{a,c}$ = 17.7 Hz, CHa=CHb*H*c), 5.52 (d, 1H, H-1), 5.99 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 7.26–7.34 (m, 10H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1 (Ac), 55.9 (O*C*H$_3$), 68.0 (*C*H$_2$Ph), 70.0 (C-5), 73.6 (*C*H$_2$Ph), 79.9 (C-2), 84.5 (C-4), 85.3 (C-3), 107.0 (C-1), 118.9 (HC=*C*H_2), 126.8, 127.4, 127.8, 128.0, 128.5, 128.6, 135.4, 138.4 (C-Ar), 139.4 (H*C*=CH_2), 169.9 (CO); HRESIMS: found *m*/*z* 435.1779 $[M+Na]^+$; calcd for $C_{24}H_{28}O_6Na$ 435.1778.

4.9. Methyl 3,5-di-*O*-benzyl-3-*C*-vinyl-α-L-lyxofuranoside (9)

A soln of monoacetate **8** (0.22 g, 0.53 mmol) in CH_2Cl_2 (2 mL) was treated with 1.0 M NaOMe in MeOH (0.6 mL), the mixture was stirred for 1 h at 20 °C., diluted with MeOH (10 mL) and treated with Amberlite IRA-120 (H^+) ion exchange resin. After removal of the resin by filtration, the filtrate was concentrated and the residue was purified by column chromatography (1:0→8:2 hexane–EtOAc) to afford alcohol **9** as an oil (0.18 g, 91%). R_f 0.29 (8:2 hexane–EtOAc); $[\alpha]_D$ −64.5 (*c* 1.1, $CHCl_3$); IR: *v* 3381 (O–H) cm^{-1}, no peaks near 1750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.40 (s, 3H, OCH_3), 3.69 (dd, 1H, $J_{4,5a}$ = 3.7 Hz, $J_{5a,5b}$ = 10.5 Hz, H-5a), 3.77 (dd, 1H, $J_{4,5b}$ = 2.9, H-5b), 4.07 (br s, 1H, H-2), 4.23 (d, 1H, $J_{4,5}$ = 3.2 Hz, H-4), 4.53 (d, 1H, J_{gem} = 11.8 Hz, PhC*H*), 4.57–4.60 (m, 2H, C*H*Ph), 4.64 (d, 1H, J_{gem} = 11.2 Hz, PhC*H*), 4.99 (br s, 1H, H-1), 5.37 (d, 1H, $J_{a,b}$ = 11.1 Hz, CHa=C*H*bHc), 5.47 (d, 1H, $J_{a,c}$ = 17.7 Hz, CHa=CHb*H*c), 6.20 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 7.26–7.33 (m, 10H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.8 (O*C*H$_3$), 67.5 (*C*H$_2$Ph), 68.8 (C-5), 74.1 (*C*H$_2$Ph), 77.8 (C-2), 84.2 (C-3), 85.9 (C-4), 111.0 (C-1), 117.3 (HC=*C*H_2), 127.6 (2C), 128.0, 128.1, 128.5, 128.7, 137.5, 137.9 (C-Ar),

139.0 (H*C*=CH_2); HRESIMS: found *m*/*z* 393.1676 $[M+Na]^+$; calcd for $C_{22}H_{26}O_5Na$ 393.1672.

4.10. Methyl 3,5-di-*O*-benzyl-3-*C*-vinyl-α-L-*erythro*-pentofuranosid-2-ulose (10)

Dess–Martin periodinane (0.53 g, 1.25 mmol) was added to a stirred soln of the alcohol **9** (0.23 g, 0.62 mmol) in dry CH_2Cl_2 (10 mL) at 20 °C. After 2 h, the reaction mixture was poured into stirred saturated aq $NaHCO_3$ soln (10 mL) containing $Na_2S_2O_3$ (1.0 g, 6.3 mmol), and extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were dried, solvent was removed in vacuo and the residue was purified by column chromatography (9:1→8:2 petroleum ether–EtOAc) to give **10** as a white solid (0.20 g, 87%); R_f 0.54 (8:2 hexane–EtOAc); mp 76–77 °C (hexane); IR: *ν* 1772 (C=O), 1640 (C=C), no peaks near 3400 cm^{-1}; $[\alpha]_D$ +61.0 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): *δ* 3.50 (s, 3H, OC*H*$_3$), 3.87 (dd, 1H, $J_{4,5a}$ = 6.2 Hz, $J_{5a,5b}$ = 10.8 Hz, H-5a,), 3.97 (dd, 1H, $J_{4,5b}$ = 4.0 Hz, H-5b), 4.46 (dd, 1H, H-4), 4.51 (d, 1H, J_{gem} = 11.6 Hz, C*H*Ph), 4.54 (d, 1H, C*H*Ph, J_{gem} = 11.6 Hz), 4.62 (d, 1H, J_{gem} = 12.4 Hz, C*H*Ph), 4.65 (d, 1H, J_{gem} = 12.4 Hz, C*H*Ph), 4.89 (s, 1H, H-1), 5.47 (dd, 1H, $J_{a,c}$ = 17.6 Hz, $J_{b,c}$ = 0.8 Hz, CHa=CHb*H*c), 5.53 (dd, 1H, $J_{a,b}$ = 11.2 Hz, $J_{b,c}$, CHa=C*H*bHc), 5.87 (dd, 1H, $J_{a,b}$, $J_{a,c}$ C*H*a=CHbHc), 7.22–7.34 (m, 10H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 56.5 (O*C*H$_3$), 67.1 (*C*H$_2$Ph), 68.0 (C-5), 73.8 (*C*H$_2$Ph), 79.8 (C-3), 83.8 (C-4), 99.1 (C-1), 121.7 (HC=*C*H$_2$), 127.3, 127.8, 127.9 (2C), 128.6, 131.5, 138.2 (C-Ar), 138.2 (H*C*=CH$_2$), 205.4 (C-2); HRESIMS: found *m*/*z* 391.1519 $[M+Na]^+$; calcd for $C_{22}H_{24}O_5Na$ 391.1516.

4.11. Methyl 3,5-di-*O*-benzyl-3-*C*-vinyl-α-L-xylofuranoside (11)

A 1.0 M soln of lithium tri-*sec*-butylborohydride (L-Selectride) in THF (0.53 mL) was added slowly under nitrogen to a soln of the ulose **10** (150 mg, 0.407 mmol) in THF (3 mL) at −55 °C. After 40 min, satd aq $NaHCO_3$ soln (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried, solvent was evaporated and the residue was purified by column chromatography (1:0→7:3 hexane–EtOAc) to give alcohol **11** as a colourless oil (108 mg, 72%) along with the C-2 epimer **9** (8 mg, 5%). Compound **11**: R_f 0.22 (8:2 hexane–EtOAc); $[\alpha]_D$ −20.1 (*c* 1.0, $CHCl_3$), IR: *ν* 3521 (OH), no peaks near 1770 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 3.52 (s, 3H, CH_3), 3.76 (dd, 1H, $J_{4,5a}$ = 7.4 Hz, $J_{5a,5b}$ = 11.2 Hz, H-5a), 3.83 (dd, 1H, $J_{4,5b}$ = 2.6 Hz, H-5b), 4.27 (dd, 1H, H-4), 4.33 (d, 1H, $J_{1,2}$ = 4.6 Hz, H-2), 4.52 (d, 1H, J_{gem} = 12.4 Hz, C*H*Ph,), 4.53 (d, 1H, J_{gem} = 12.4 Hz, C*H*Ph), 4.62 (d, 1H, J_{gem} = 12.2 Hz, C*H*Ph), 4.64 (d, 1H, J_{gem} = 12.2 Hz, C*H*Ph), 4.83 (br s, 1H, OH), 5.10 (d, 1H, H-1,), 5.37 (dd, 1H, $J_{a,c}$ = 17.6 Hz, $J_{b,c}$ = 1.3 Hz, CHa=CHb*H*c), 5.38 (dd, 1H, $J_{a,b}$ = 11.3 Hz, $J_{b,c}$, CHa=C*H*bHc), 6.06 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 7.25–7.34 (m, 10H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 56.1 (*C*H$_3$), 66.9 (*C*H$_2$Ph), 68.9 (C-5), 73.6 (*C*H$_2$Ph), 76.3 (C-2), 83.5 (C-4), 87.1 (C-3), 102.5 (C-1), 117.7 (HC=*C*H$_2$), 126.6, 127.4, 127.7, 127.9, 128.5 (C-Ar), 133.6 (H*C*=CH$_2$), 138.5, 139.2 (C-Ar); HRESIMS: found *m*/*z* 388.2115 $[M+NH_4]^+$; calcd for $C_{22}H_{30}O_5N$ 388.2118.

4.12. Methyl 2,4-di-*O*-benzyl-3-*O*-(2-*O*-acetyl-3,5-di-*O*-benzyl-3-*C*-vinyl-α-L-lyxofuranosyl)-α-L-rhamnopyranoside (13)

A mixture of thioglycosides **7** (0.20 g, 0.40 mmol), methyl 2,4-di-*O*-benzyl-α-L-rhamnopyranoside (**12**)[26] (0.15 g, 0.42 mmol) and 4 Å molecular sieves (0.5 g) in CH_2Cl_2 (8 mL) was stirred under nitrogen for 20 min at 20 °C and then cooled to −30 °C. *N*-Iodosuccinimide (0.11 g, 0.49 mmol) and TMSOTf (10 μL, 0.055 mmol) were added and the mixture was stirred at this temperature for 40 min. The mixture was treated with Et_3N (0.5 mL) and diluted aq $Na_2S_2O_3$ soln to remove the yellow colour. After dilution with CH_2Cl_2 (10 mL) the mixture was washed with water (2 × 10 mL), organic layer was concentrated in vacuo and the residue was purified by column chromatography (1:0→8:2 petroleum ether–EtOAc). The disaccharide **13** was obtained as a colourless oil (0.24 g, 81%); R_f 0.28 (8:2 hexane–EtOAc); $[\alpha]_D$ −71.0 (*c* 1.0, $CHCl_3$); IR: *ν* 1747 (C=O), no peaks near 3400 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 1.31 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6), 1.72 (s, 3H, Ac), 3.28 (s, 3H, OCH_3), 3.57 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, H-4), 3.68 (dq, 1H, $J_{4,5}$, $J_{5,6}$, H-5), 3.76 (dd, 1H, $J_{4',5'a}$ = 6.8 Hz, $J_{5'a,5'b}$ = 10.8 Hz, H-5′a), 3.87 (dd, 1H, $J_{4',5'b}$ = 4.0 Hz, $J_{5'a,5'b}$, H-5′b), 3.95 (dd, 1H, $J_{1,2}$ = 1.5 Hz, $J_{2,3}$ = 3.0 Hz, H-2), 4.03 (dd, 1H, H-3,), 4.34 (dd, 1H, $J_{4',5'a}$, $J_{4',5'b}$, H-4′), 4.48 (d, 1H, J_{gem} = 11.6 Hz, C*H*Ph,), 4.51–4.55 (m, 2H, H-2′, C*H*Ph), 4.58 (d, 1H, J_{gem} = 12 Hz, C*H*Ph), 4.59 (d, 1H, J_{gem} = 11.2 Hz, C*H*Ph,), 4.64 (d, 1H, J_{gem} = 12.0 Hz, C*H*Ph), 4.65 (d, 1H, J_{gem} = 12.4 Hz, C*H*Ph), 4.81 (d, 1H, J_{gem} = 12.4 Hz, C*H*Ph), 4.85 (d, 1H, J_{gem} = 11.6 Hz, C*H*Ph), 5.36 (d, 1H, $J_{a,b}$ = 11.0 Hz, CHa=C*H*bHc), 5.51 (br s, 1H, H-1), 5.53 (d, 1H, $J_{a,c}$ = 17.8 Hz, CHa=CHb*H*c), 5.75 (d, 1H, $J_{1',2'}$ = 3.7 Hz, H-1′), 5.96 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 7.36–7.24 (m, 20H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 17.9 (C-6), 20.4 (OCO*C*H3), 54.6 (O*C*H$_3$), 67.7 (C-5), 67.9 (*C*H$_2$Ph), 68.9 (C-5′), 73.3 (*C*H$_2$Ph), 73.4 (*C*H$_2$Ph), 74.9 (*C*H$_2$Ph), 78.4 (C-2′), 79.8 (C-3), 80.2 (C-2), 80.7 (C-4), 84.3 (C-4′), 85.0 (C-3′), 99.2 (C-1), 107.8 (C-1′), 118.9 (HC=*C*H$_2$), 126.6, 127.2, 127.3, 127.4, 127.5, 127.6, 127.7, 128.2, 128.3 (C-Ar), 134.7 (H*C*=CH$_2$), 138.2, 138.7, 138.8, 139.2 (C-Ar), 169.5

(CO); HRESIMS: found m/z 761.3306 $[M+Na]^+$; calcd for $C_{44}H_{50}O_{10}Na$ 761.3296.

4.13. Methyl 2,4-di-*O*-benzyl-3-*O*-(3,5-di-*O*-benzyl-3-*C*-vinyl-α-L-lyxofuranosyl)-α-L-rhamnopyranoside (14)

The disaccharide **13** (0.25 g, 0.34 mmol) was dissolved in CH_2Cl_2 (1 mL) and treated with 1.0 M soln of NaOMe in MeOH (0.30 mL). The resulting soln was stirred at room temperature for 1 h, diluted with MeOH (10 mL) and treated with Amberlite IRA-120 (H^+) ion exchange resin. The mixture was filtered and concentrated in vacuo. Column chromatography (1:0→8:2 petroleum ether–EtOAc) gave the title compound **14** as an oil (0.21 g, 89%); R_f 0.24 (8:2 hexane–EtOAc); IR thin film: ν 3374 (OH), no peaks near 1750 cm^{-1}; $[\alpha]_D$ +37.4 (c 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (d, 3H, $J_{5,6} = 6.0$ Hz, H-6), 3.29 (s, 3H, OCH_3), 3.58 (t, 1H, $J_{3,4} = J_{4,5} = 9.4$ Hz, H-4), 3.64–3.71 (m, 1H, H-5), 3.68 (dd, 1H, $J_{4',5'a} = 3.4$ Hz, $J_{5'a,5'b} = 10.4$ Hz, H-5′a), 3.76 (dd, 1H, $J_{4',5'b} = 2.9$ Hz, $J_{5'a,5'b}$, H-5′b), 3.88 (br s, 1H, H-2′), 4.01 (dd, 1H, $J_{2,3} = 3.1$ Hz, H-3), 4.17 (m, 1H, H-4′), 4.24 (m, 1H, H-2), 4.53–4.63 (m, 6H, H-1, C*H*Ph,), 4.65 (d, 1H, $J_{gem} = 10.9$ Hz, C*H*Ph), 4.74 (d, 1H, $J_{gem} = 12.0$ Hz, C*H*Ph), 4.80 (br s, 1H, OH), 4.91 (d, 1H, C*H*Ph, $J_{gem} = 10.7$ Hz), 5.28 (d, 1H, $J_{a,b} = 11.1$ Hz, CHa=C*H*bHc), 5.41 (d, 1H, $J_{1',2'} = 0.9$ Hz, H-1′), 5.48 (d, 1H, $J_{a,c} = 17.7$ Hz, CHa=CHb*H*c), 6.29 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 7.24–7.40 (m, 20H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.2 (C-6), 54.9 (OCH_3), 67.5 (C-5), 68.0 (*C*H_2Ph), 68.9 (C-5′), 73.4 (CH_2Ph), 74.0 (*C*H_2Ph), 74.0 (*C*H_2Ph), 75.7 (*C*H_2Ph), 78.6, 78.9 (C-2, C-2′), 80.4 (2C, C-3, C-4), 84.2 (C-3′), 85.9 (C-4′), 99.3 (C-1), 112.0 (C-1′), 117.4 (HC=*C*H_2), 127.5, 127.6, 127.7, 127.8, 128 (3C), 128.5 (3C), 128.7, 137.5 (C-Ar), 137.7 (H*C*=CH_2), 138.6, 138.6, 138.9, 139.0 (C-Ar); HRESIMS: found m/z 714.3637 $[M+NH_4]^+$; calcd for $C_{42}H_{52}O_9N$ 714.3637.

4.14. Methyl 2,4-di-*O*-benzyl-3-*O*-(3,5-di-*O*-benzyl-3-*C*-vinyl-α-L-*erythro*-pentofuranosyl-2-ulose)-α-L-rhamnopyranoside (15)

Dess–Martin periodinane (0.25 g, 0.59 mmol) was added to stirred soln of the alcohol **14** (0.21 g, 0.30 mmol) in dry CH_2Cl_2 (10 mL) at 20 °C. After 2 h, the reaction mixture was poured into stirred satd aq $NaHCO_3$ soln (10 mL) containing $Na_2S_2O_3$ (1.0 g, 6.3 mmol), and extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were dried and the solvent was removed in vacuo. The residue was purified by column chromatography (9:1→8:2 petroleum ether–EtOAc) to give **15** as an oil (0.18 g, 86%); R_f 0.34; $[\alpha]_D$ +4.0 (c 1.0; $CHCl_3$); IR: ν 1730 (C=O), no peaks near 3400 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.34 (d, 3H, $J_{5,6}$, H-6,), 3.28 (s, 3H, OCH_3), 3.59 (t, 1H, $J_{3,4} = J_{4,5} = 9.4$ Hz, H-4), 3.68 (dq, 1H, $J_{4,5} = 12.2$ Hz, $J_{5,6} = 6.0$ Hz, H-5), 3.84 (dd, 1H, $J_{4',5'a} = 6.2$ Hz, $J_{5'a,5'b} = 10.8$ Hz, H-5′a), 3.87–3.91 (m, 1H, H-2), 3.94 (dd, 1H, $J_{4',5'b} = 3.6$ Hz, $J_{5'a,5'b}$, H-5′b), 4.11 (dd, 1H, $J_{2,3} = 3.1$ Hz, $J_{3,4} = 9.4$ Hz, H-3), 4.47–4.63 (m, 10H, H-1, H-4′, 8 × C*H*Ph), 4.76 (d, 1H, $J_{gem} = 12.1$ Hz, PhCH), 5.01 (d, 1H, $J_{gem} = 10.4$ Hz, PhCH), 5.33 (s, 1H, H-1′), 5.50 (d, 1H, $J_{a,c} = 17.8$ Hz, CHa=CHb*H*c), 5.51 (d, 1H, $J_{a,b} = 11.1$ Hz, CHa=C*H*bHc), 5.89 (dd, 1H, $J_{a,b}$, $J_{a,c}$, C*H*a=CHbHc), 7.21–7.43 (m, 20H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.2 (C-6), 54.9 (OCH_3), 67.2 (*C*HPh), 68.1 (2C, C-5, C-5′), 73.5 (*C*HPh), 73.8 (*C*HPh), 75.8 (*C*HPh), 78.8 (C-2), 79.9 (C-4), 80.3 (C-3′), 81.4 (C-3), 83.8 (C-4′), 99.2 (C-1), 100.1 (C-1′), 121.6 (HC=*C*H_2), 127.3, 127.7, 127.8 (2C), 127.9, 128.0, 128.5, 128.6 (3C), 128.7 (C-Ar), 131.8 (H*C*=CH_2), 138.3 (2C), 138.6, 138.8 (C-Ar), 205.0 (C-2′); HRESIMS: found m/z 712.3481 $[M+NH_4]^+$; calcd for $C_{42}H_{50}O_9N$ 712.3480.

4.15. Methyl 2,4-di-*O*-benzyl-3-*O*-(3,5-di-*O*-benzyl-3-*C*-vinyl-α-L-xylofuranosyl)-α-L-rhamnopyranoside (16)

A 1.0 M soln of lithium tri-*sec*-butylborohydride (L-Selectride) in THF (0.4 mL) was added slowly under nitrogen to a soln of the ulose **15** (0.20 g, 0.29 mmol) in 2.5 mL of THF at −40 °C. After 1 h, satd aq $NaHCO_3$ soln (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried and solvent was removed in vacuo. The residue was purified by column chromatography (1:0→8:2 hexane–EtOAc) to give **16** as a colourless oil (0.16 g, 80%); R_f 0.24 (8:2 hexane–EtOAc); $[\alpha]_D$ −63.0 (c 1.0, $CHCl_3$); IR: ν 3491, no peaks near 1750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.36 (d, 3H, $J_{5,6} = 9.5$ Hz, H-6), 3.30 (s, 3H, OCH_3), 3.59 (t, 1H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 3.66–3.79 (m, 1H, H-5), 3.75 (dd, 1H, $J_{4',5'a} = 7.4$ Hz, $J_{5'a,5'b} = 11.2$ Hz, H-5′a), 3.84 (dd, 1H, $J_{4,5b} = 2.4$ Hz, $J_{5'a,5'b}$, H-5′b), 3.95–3.99 (m, 1H, H-2), 4.16 (dd, 1H, $J_{2,3} = 3.2$ Hz, H-3), 4.25 (d, 1H, $J_{1',2'} = 4.4$ Hz, H-2′), 4.34 (dd, 1H, H-4′), 4.37–4.78 (m, 9H, H-1, C*H*Ph), 4.81 (br s, 1H, OH), 5.32–5.42 (m, 2H, CHa=C*H*b*H*c), 5.48 (d, 1H, $J_{1',2'}$, H-1′), 6.09 (dd, 1H, Ha, $J_{a,b} = 10.9$ Hz, $J_{a,c} = 18.1$ Hz, C*H*a=CHbHc), 7.24–7.37 (m, 20H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.3 (C-6), 55.0 (OCH_3), 65.8 (*C*HPh), 68.0 (C-5), 68.9 (*C*HPh), 73.5 (2C, *C*HPh), 75.6 (*C*HPh), 76.0 (C-2′), 78.7 (C-2), 79.6 (C-3), 80.7 (C-4), 83.7 (C-4′), 87.3 (C-3′), 99.1 (C-1), 103.7 (C-1′), 118.0 (H*C*=CH_2), 126.7, 127.7, 127.8, 127.9 (2C), 128.0, 128.1, 128.5, 128.6 (2C), 128.7 (C-Ar), 133.3 (HC=*C*H_2), 138.3, 138.6, 138.7, 139.1 (C-Ar); HRESIMS: found m/z 714.3635 $[M+NH_4]^+$; calcd for $C_{42}H_{52}O_9N$ 714.3637.

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Supplementary data

Complete crystallographic data for the structural analysis of compounds **3** and **10** have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 658522 and 658523, respectively. Copies of this information may be obtained free of charge from Cambridge Crystallographic Data Centre, (e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk). Copies of ^{1}H and ^{13}C NMR spectra for compounds **1**–**16** and crystallographic data for compounds **3** and **10**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2007.10.035.

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