Carbohydrate Research 345 (2010) 369–376

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Lactose as an inexpensive starting material for the preparation of aldohexos-5-uloses: synthesis of L-*ribo* and D-*lyxo* derivatives ☆

Lorenzo Guazzelli, Giorgio Catelani *, Felicia D'Andrea

Dipartimento di Scienze Farmaceutiche, Università di Pisa, Via Bonanno, 33 I-56126 Pisa, Italy

ARTICLE INFO

Article history:
Received 27 October 2009
Received in revised form 18 November 2009
Accepted 23 November 2009
Available online 26 November 2009

Keywords:
Lactose
L-*ribo*-Aldohexos-5-ulose
D-*lyxo*-Aldohexos-5-ulose
1,5-Bis-glycopyranosides
Epimerisation

ABSTRACT

Partially protected derivatives of L-*ribo*- and D-*lyxo*-aldohexos-5-ulose have been prepared starting from triacetonlactose dimethyl acetal derivatives. Key steps of the synthetic sequences are (a) the synthesis of 4′-deoxy-4′-eno- and 6′-deoxy-5′-eno lactose derivatives, and (b) the epoxidation–methanolysis of the above-mentioned enol ethers to give 1,5-bis-glycopyranosides, masked form of the target 1,5-dicarbonyl hexoses.

1. Introduction

Aldohexos-5-uloses (**3**) represent an interesting, although yet poorly investigated class of dicarbonyl hexoses[2] that are useful synthetic intermediates for the preparation of high value-added compounds such as imino sugars[3] and cyclitols, as well as inositols[4] and polyhydroxycyclopentanes.[5]

A useful approach (Chart 1) to aldohexos-5-uloses (**3**) is based on a selective C-5 oxidation by epoxidation of 4-deoxy-hex-4-eno[6] (**1**) or 6-deoxy-hex-5-enopyranosides[7] (**2**). In the frame of a general research project aimed at the chemical valorisation of lactose as cheap and renewable starting material, we planned the preparation of a representative of each diastereomeric series of aldohexos-5-uloses and attained the goal by preparing the L-*arabino*,[7c,d] the D-*xylo*[7e] and the L-*lyxo*[7e] examples.

In this communication, we present the preparation of partially protected L-*ribo* and D-*lyxo* derivatives following either the hex-4- or hex-5-enopyranoside approach. Some unexpected results observed during the planned synthetic routes are also described and discussed.

2. Results and discussion

To prepare a representative of the remaining aldohexos-5-ulose stereoseries, that is the *ribo* example, from lactose, we decided to investigate a different strategy with respect to that reported starting from monosaccharide precursors.[8] We thus considered to perform the epimerisation of the C-2′ position on the D-galactopyranoside moiety in an earlier stage of the synthetic sequence (Scheme 1). Compound **4**[7c,d] was subjected to an oxidation with the tetra-*n*-propyl ammonium perruthenate–*N*-methylmorpholine-*N*-oxide (TPAP–NMO) system in CH_2Cl_2, obtaining a crude mixture of the uloside **5** and its hydrate **6** (about 3:1). The reduction ($NaBH_4$/MeOH) of the crude mixture gave in an overall 90% yield the corresponding D-*talo*-derivative **7** as the sole isolated diastereoisomer. The C-2′ epimerisation was firmly confirmed by the changes in the $J_{1',2'}$ and $J_{2',3'}$ coupling constant values from 8.1 and 6.9 Hz in compound **4**[7c,d] to 2.5 and 4.1 Hz, respectively.

The tosylate **7** was then transformed into 6-deoxy-hex-5-enol ether by treatment with NaH in DMF under the conditions reported[7c,d] for the transformation of the *galacto* epimer **4**, but only the 2,5-anhydro derivative **8** was obtained in almost quantitative yield (96%) as a result of an intramolecular S_N2 displacement. The presence of this concurrent pathway was not unexpected in view of the favourable axial orientation of the C-2′ alkoxide. Furthermore, the conformational flattening caused by the 3′,4′-*cis*-dioxolane ring, and the high stability of the 2,5-dioxabicyclo[2,2,2]octane system† could explain the exclusive formation of **8**.

In order to suppress this unwanted reaction, we considered the preparation of a 6′-*O*-sulfonate analog of **4**, protected as benzyl ether at HO-2′. The alcohol **10** was first prepared, which was easily

☆ Part 28 of the series 'Chemical Valorisation of Milk-derived Carbohydrates'. For part 27 see Ref. 1.

* Corresponding author. Tel.: +39 0502219700; fax: +39 0502219660.
E-mail address: giocate@farm.unipi.it (G. Catelani).

† The high stability of this kind of bicyclooctane system originates the unexpected high preference for the ring-closed hemiacetal form of 6-OH-3,4-*O*-isopropylidene-β-D-*lyxo*-2-ulopyranosides (Ref. 9).

0008-6215/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2009.11.027

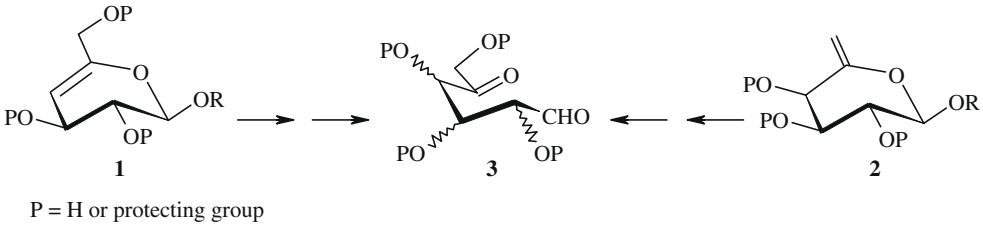
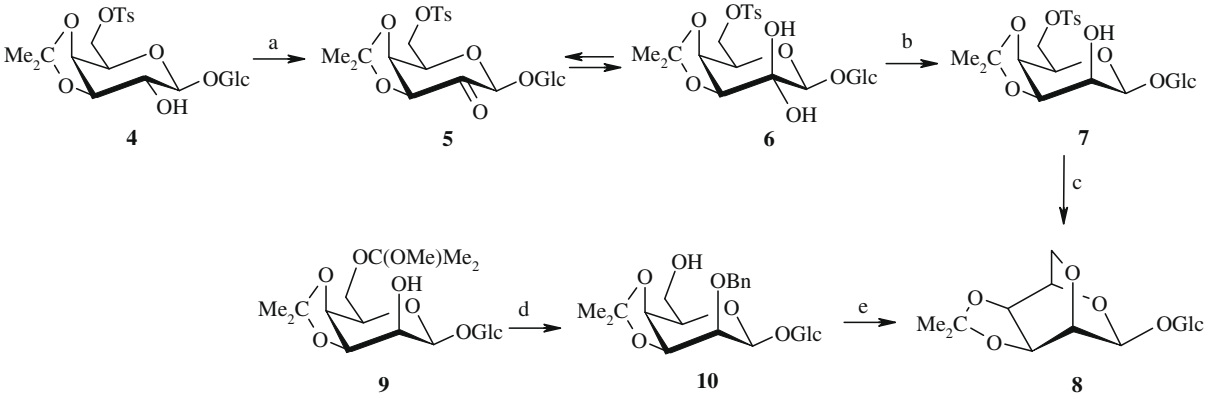


Chart 1. General approach to aldohexos-5-uloses from hex-4- and hex-5-enopyranosides.



Scheme 1. Attempts to prepare a β-D-*talo*-6-deoxy-hex-5-enopyranoside. Reagent and conditions: (a) TPAP, NMO, CH_2Cl_2, 4 Å, rt, 1 h (91%); (b) $NaBH_4$, MeOH, rt, 1 h, (90% from **4**); (c) NaH, DMF, rt, 1.5 h (96%); (d) BnBr, NaH, DMF, rt, 40 min, then 5% aq HCl, CH_2Cl_2 (90%); (e) NaH·DMF, Im_2SO_2, −30 °C, 3 h (96%).

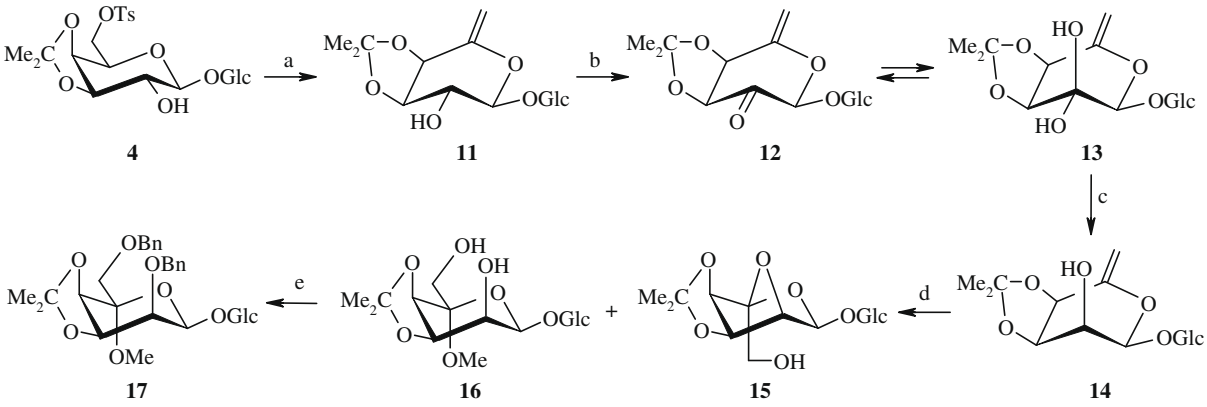
obtained in 90% yield by treatment (Scheme 1) of the known alcohol **9**[10] with NaH and BnBr in dry DMF, followed by selective removal of the mixed acetal 6′-O-protecting group by mild acid treatment of the crude benzylation product in a biphasic system (CH_2Cl_2–5% aq HCl). However, the subsequent introduction of a leaving group in the primary position failed using Ts_2O in pyridine, leaving alcohol **10** completely unchanged, probably because of the steric hindrance of either the 3′,4′-*O*-isopropylidene or the 2′-*O*-benzyl ether protecting group. An effective activation of the alcohol **10** was obtained using the conditions (NaH–DMF followed by Im_2SO_2) usually employed for the preparation of imidazylates,[11] but, surprisingly, derivative **8** was again obtained in excellent yield (96%) as the sole reaction product. Although intramolecular substitution involving a benzyl ether group as a nucleophile is known,[12] the observed behaviour corroborates the above-mentioned hypothesis of a high conformational strain due to the *talo*-configuration and the 3′,4′-*O*-isopropylidene ring fusion which facilitates this reaction.

This problem was obviated by following a different strategy, which first involved the elimination reaction and then the C-2′ inversion (Scheme 2). Compound **4** was treated with NaH in DMF, and the hex-5-enopyranoside **11** was obtained in 85% yield. However, the oxidation of **11** with the TPAP–NMO system was much less evident than expected.

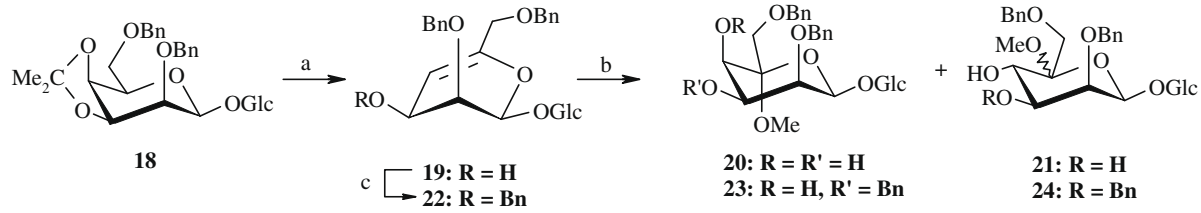
A complete conversion of the alcohol **4** into a 1:4 mixture of the uloside **12** and its hydrate **13** was obtained by operating at low temperature (0 °C) and by employing 9:1 CH_2Cl_2–CH_3CN as the solvent, which is reported in some cases to enhance the catalytic turnover.[13] A reduced stability of the hex-5-eno-2-ulopyranoside **12**–**13** was evidenced by the loss of material observed during the silica gel chromatographic purification, lowering the yield to a rather modest 55%. The following reduction step was accomplished with high stereoselectivity, but in a rather modest overall yield (50%) by treating a crude sample of **12–13** with $NaBH_4$ in MeOH at −40 °C. When the reduction was run at higher temperatures, a substantial drop of the yield was observed, pointing out again the low stability of **12–13**. Furthermore, the presence of some fragmentation pathways was evidenced by the formation of appreciable amounts of the known[14] 2,3:5,6-di-*O*-isopropylidene-*aldehydo* dimethyl acetal (not shown). The L-*ribo* configuration of the 6′-deoxy-hex-5′-enopyranoside **14** was well confirmed by the $J_{1',2'}$ coupling constant value (3.3 Hz), which highlighted the new H-1′, H-2′ axial–equatorial disposition.

Compound **14** was then subjected to the epoxidation–methanolysis reaction (MCPBA–MeOH) in order to oxidise the C-5′ enol ether group. This reaction gave some unexpected results, showing the formation of **15** (13%) and of only one of the two possible C-5′ anomers (**16**, 47%). The C-5′ configuration of **15** and **16** was assigned on the basis of 1D NOE experiments. Thus, the irradiation of the H-1′ resonance for **16** gave enhancements for the H-3′ and 5′-OMe resonances, whereas **15** gave enhancements for the H-3′, H-6′a and H-6′b resonances. On the basis of the epoxidation–methanolysis results of analogous *exo*-glycals,[7] one could suppose the formation of two non-isolable epoxide intermediates, which were opened in an *anti* fashion, in the case of the β-epoxide by means of an intermolecular α-attack of methanol, and in the case of the α one by means of an intramolecular 2′-OH β-attack. Derivative **16** was then benzylated by treatment with powdered KOH and BnBr in wet THF, which led to the formation of **17** in excellent yield (94%).

Although with this sequence the targeted 1,5-bis-L-*ribo*-hexopyranosides were obtained, the rather modest yields of the overall process (about 20% from the tosylate **4**), as well as the chemical fragility of some intermediates, pushed us to explore the complementary hex-4-enopyranoside approach as illustrated in the Scheme 3. Known compound **18**[10] was subjected to an acetone



Scheme 2. Synthesis of L-*ribo*-hexos-5-ulose-1,5-bis-glycopyranosides through the hex-5-enopyranosides approach. Reagent and conditions: (a) NaH, DMF, rt, 3.2 h (85%); (b) TPAP, NMO, 9:1 CH_2Cl_2–CH_3CN, 4 Å, rt, 2.5 h; (c) $NaBH_4$, MeOH, −40 °C, 2.5 h, (50% from **11**); (d) MCPBA, MeOH, rt, 4.5 h (**15**: 13% + **16**: 47%); (e) KOH, BnBr, 18-crown-6, rt, 4.5 h (94%).



Scheme 3. Synthesis of L-*ribo*-hexos-5-ulose 1,5-bis-glycopyranosides and D-*lyxo*-hexos-5-ulose 1,5-bis-glycopyranosides through the hex-4-enopyranoside approach. Reagents and conditions: (a) *t*-BuOK, THF, reflux, 15 min, (81%); (b) MCPBA, MeOH, rt, 24 h (**20**: 58%, **21**: 15%, **23**: 17%, **24**: 48%); (c) BnBr, NaH, DMF, rt, 30 min, (88%).

elimination employing *t*-BuOK in THF (reflux, 15 min), and **19** was obtained in good yield (81%).

It is noteworthy to emphasise that the acetone elimination on **18** required milder conditions with respect to those used for 3,4-*O*-isopropylidene-D-galactopyranosides[7c,d] analogues, giving rise to complex mixtures of inseparable products using *t*-BuOK in DMF at 80 °C or lower temperatures. Probably the enhanced reactivity of the *talo* series is due to the unfavourable *syn* interaction between the axial 2′-OR group and the 3′,4′-*O*-isopropylidene group, giving rise to a higher strain release with the acetone elimination. Derivative **19** was subjected to the epoxidation–methanolysis reaction (MCPBA–MeOH) that gave the two 1,5-bis-glycosides **20** and **21**, easily isolated in 58% and 15% yield, respectively, through chromatography. The structure of **20** was confirmed by NMR spectroscopy ($J_{3',4'}$ 3.0 Hz), and its C-5′ configuration was established by its transformation into **17** through an acid-promoted transacetalation reaction with TsOH in 2,2-dimethoxypropane (DMP, 93% yield). In the case of **21**, the D-*lyxo* configuration was easily assigned by NMR spectroscopy ($J_{3',4'}$ 10.0 Hz), but the anomeric C-5′ configuration could not be inferred by routine NMR analysis.

The rather low diastereoselection (L-*ribo*/D-*lyxo* ratio of about 4:1) observed in the epoxidation–methanolysis was somewhat unexpected, owing to the influence of a complete *syn*-directing effect, which is generally observed for a free allylic hydroxyl group in the epoxidation reaction.[15] The presence of an appreciable amount of the bis-glycoside **21** arising from a peroxide attack *anti* to the allylic 3′-OH group, followed by epoxide opening by MeOH, could reasonably be attributed to the steric hindrance of the axial 2′-OBn, which shields the β face of **19**. Reasoning on this point, we tried to reverse the stereoselectivity of the formation of 1,5-bis-glycosides by performing the epoxidation–methanolysis on the 3′-*O*-benzyl derivative **22**, which is easily obtained in good yield by routine benzylation of **19**. This objective was achieved, although in a not complete manner, as we obtained a mixture of the D-*lyxo*- and L-*ribo*-1,5-bis-pyranosides **24** and **23** in an about 3:1 ratio and in an overall 65% yield. The C-5′ configuration of **23** is suggested considering the close analogy between its NMR data and those of **20**.

The final transformation of the 1,5-bis-glycopyranosides into hexos-5-uloses, thereby exposing both the dicarbonyl groups, was performed by acid hydrolysis (90% aq CF_3COOH in 4:1 CH_3CN–water at 50 °C) of the two L-*ribo* derivatives **17** and **20** (Scheme 4). After separation from D-glucose, the known dicarbonyl hexose **25**[8] was obtained in satisfactory isolated yield (66–73%). In an identical way bis-glycoside **21** gave **26**, which is the enantio-form of the previously reported 2,6-di-*O*benzyl-L-*lyxo*-aldohexos-5-ulose, in 72% yield, as an anomeric mixture of 1,4-furanose tautomers (**26α**:**26β** 66:34).[16]

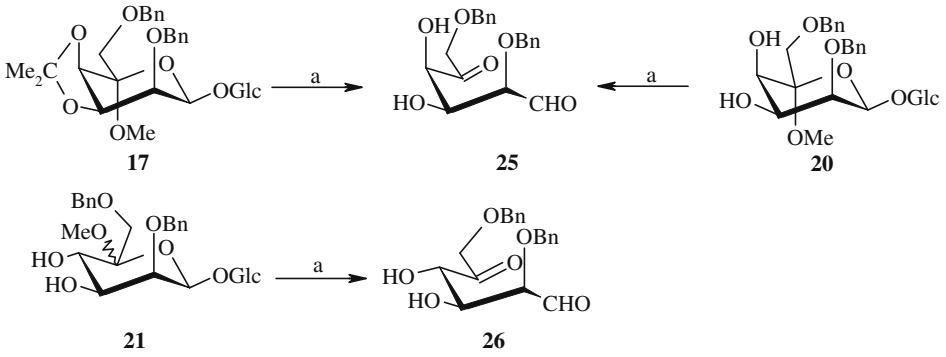
In conclusion, with this work the usefulness of lactose as the starting material for accessing all the diastereoisomeric series of aldohexos-5-uloses has been demonstrated, opening the way to a new synthetic channel for the valorisation of whey, a waste product of the cheese industry, into sophisticated chemical synthons for the preparation of biologically active compounds. Some examples of synthetic use of hexos-5-uloses belonging to the *lyxo*-series are reported,[4b,17] while synthetic elaboration of L-*ribo*-hexos-5-ulose derivatives are currently under investigation in our group and will be reported in a forthcoming paper.[‡]

3. Experimental

3.1. General methods

General methods are those reported in Ref. 19. Compounds **4**,[7c] **9**[10] and **18**[10] were prepared according to the described procedures.

[‡] The stereoselective synthesis of *cis*- and *epi*-inositol derivatives have been recently achieved starting from L-*ribo*-hexos-5-ulose precursors (Ref. 18).



Scheme 4. Synthesis of 2,6-di-*O*-benzyl-L-*ribo*- and 2,6-di-*O*-benzyl-D-*lyxo*-hexos-5-uloses. Reagent and conditions: (a) 90% aq CF_3COOH, 4:1 CH_3CN–H_2O, 50 °C, 4–5 h (**25**: 66% from **17** and 73% from **20**, **26**: 72%).

3.2. 3,4-*O*-Isopropylidene-6-*O*-*p*-toluenesulfonyl-α-D-*lyxo*-hex-2-ulopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (5) and its hydrate (6)

A suspension of **4**[7c] (2.02 g, 3.00 mmol) in dry CH_2Cl_2 (20 mL) and pre-dried 4-methylmorpholine-*N*-oxide (NMO) (618 mg, 5.30 mmol) containing 4 Å powdered molecular sieves (240 mg) was stirred under an argon atmosphere for 30 min at room temperature. Tetrapropylammonium perruthenate (TPAP) (106 mg, 10%) was added, and the resulting green mixture was stirred at room temperature (1 h). The reaction mixture was filtered through alternate pads of Celite and silica gel and was extensively washed with CH_2Cl_2 and then EtOAc. The combined organic phases were concentrated under diminished pressure to give a syrup (2.00 g) consisting of a mixture of **5** and **6** in a ratio of about 3:2, as estimated on the basis of the relative C-1′ NMR signal intensities (δ 99.5 and 103.7, respectively). Flash chromatographic purification of a crude sample, eluting with 9:1 CH_2Cl_2–Me_2CO, afforded a 3:1 mixture of **5** and **6** (1.81 g, combined yield about 91%) as a colourless syrup; $[\alpha]_D$ −9.9 (*c* 1.17, $CHCl_3$); R_f 0.45 (9:1 CH_2Cl_2–Me_2CO); selected ^{13}C NMR (50 MHz, $CDCl_3$) signals: *major component* **5**: δ 196.4 (C-2′), 144.9, 132.0 (2 × Ar–C), 111.1, 110.2, 107.7 (3 × Me_2C), 104.7 (C-1), 99.5 (C-1′), 77.4, 77.3, 77.0, 76.9 (C-4, C-2, C-3, C-5), 75.7, 74.7 (C-3′, C-4′), 70.2 (C-5′), 67.5 (C-6′), 64.8 (C-6), 55.4, 53.1 (2 × OMe-1), 27.0, 26.6, 25.9, 25.8, 25.7, 25.3 (3 × CMe_2), *minor component* **6**: δ 144.6, 132.1 (2 × Ar–C), 110.1, 109.7, 107.9 (3 × Me_2C), 104.3 (C-1), 103.7 (C-1′), 90.0 (C-2′), 77.6, 77.5, 77.2, 76.3 (C-4, C-2, C-3, C-5), 74.4, 72.2 (C-3′, C-4′), 70.0 (C-5′), 68.1 (C-6′), 64.2 (C-6), 55.8, 52.6 (2 × OMe-1), 26.8, 26.1, 25.6, 25.5, 24.4, 24.0 (3 × CMe_2). Cluster of signals for both components: δ 129.7, 127.6 (Ar–CH), 21.2 (*Me*Ph). The mixture was directly used for the preparation of **7**, which follows in Section 3.3.

3.3. 3,4-*O*-Isopropylidene-6-*O*-*p*-toluenesulfonyl-β-D-talopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (7)

A crude mixture of **5** and **6** (800 mg) was dissolved in dry MeOH (14 mL). The solution was cooled to 0 °C, treated with $NaBH_4$ (228 mg, 6.03 mmol) and gently warmed to room temperature. The reaction mixture was stirred until the TLC analysis (9:1 CH_2Cl_2–Me_2CO) showed the complete disappearance of the starting material (1 h). The mixture was treated with satd aq NH_4Cl (10.0 mL), stirred for 15 min and extracted with CH_2Cl_2 (4 × 30 mL). The collected organic extracts were dried, filtered and concentrated under diminished pressure to give a residue (740 mg), which was directly subjected to flash chromatographic purification (3:2 hexane–EtOAc) affording **7** (728 mg, 90% yield calculated from **4**) as a colourless syrup; $[\alpha]_D$ −2.2 (*c* 1.16, $CHCl_3$); R_f 0.40 (9:1 CH_2Cl_2–Me_2CO); ^1H NMR (200 MHz, $CDCl_3$): δ 7.80, 7.36 (AA′XX′ system, 4H, Ar–H), 4.93 (d, 1H, $J_{1',2'}$ 2.5 Hz, H-1′), 4.47 (dd, 1H, $J_{2,3}$ 7.1 Hz, H-2), 4.38 (d, 1H, $J_{1,2}$ 6.2 Hz, H-1), 4.32 (dd, 1H, $J_{3',4'}$ 6.7 Hz, H-3′), 4.28–4.00 (m, 7H, H-4′, H-6′a, H-6′b, H-4, H-5, H-6a, H-6b), 3.93 (m, 1H, H-5′), 3.92 (dd, 1H, $J_{3,4}$ 1.4 Hz, H-3), 3.79 (dd, 1H, $J_{2',3'}$ 4.1 Hz, H-2′), 3.42, 3.41 (2s, each 3H, 2 × OMe), 2.46 (s, 3H, *Me*Ph), 2.45 (br s, 1H, OH), 1.49, 1.42, 1.37, 1.36, 1.35, 1.28 (6s, each 3H, 3 × CMe_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 144.8, 132.4 (2 × Ar–C), 129.8, 127.8 (Ar–CH), 110.1, 110.1, 107.8 (3 × CMe_2), 104.7 (C-1), 100.5 (C-1′), 77.9, 77.7, 76.0, 74.7 (C-2, C-4, C-3, C-5), 73.7, 71.0, 70.0 (C-3′, C-4′, C-5′), 68.3 (C-6′), 66.5 (C-2′), 64.8 (C-6), 55.6, 53.0 (2 × OMe), 27.1, 26.2, 26.1, 25.4, 25.1, 24.8 (3 × CMe_2), 21.5 (*Me*Ph). Anal. Calcd for $C_{30}H_{46}O_{14}S$: C, 54.37; H, 7.00. Found: C, 54.41; H, 7.08.

3.4. 2-*O*-Benzyl-3,4-*O*-isopropylidene-β-D-talopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (10)

A suspension of pre-washed (hexane) 60% NaH in mineral oil (417 mg, 10.4 mmol) in dry DMF (20 mL) was cooled to 0 °C and treated under argon atmosphere with a solution of **9**[10] (2.02 g, 3.48 mmol) in dry DMF (30 mL). The mixture was warmed to room temperature and stirred for 10 min, cooled again to 0 °C and then treated with BnBr (0.66 mL, 5.57 mmol). The mixture was warmed to room temperature and further stirred until the starting material was consumed (40 min, TLC, 3:7 hexane–EtOAc). MeOH (5 mL) and water (20 mL) were slowly added, and the mixture was extracted with CH_2Cl_2 (4 × 20 mL). The collected organic layers were treated with 5% aq HCl until TLC analysis (3:7 hexane–EtOAc) revealed the complete disappearance of the product with R_f 0.58 and the formation of a slower moving product (R_f 0.39). The aqueous phase was further extracted with CH_2Cl_2 (20 mL), and the organic extracts were dried, filtered and concentrated under diminished pressure. The residue was subjected to flash chromatography, eluting with 1:1 hexane–EtOAc, to give **10** (1.87 g, 90% yield) as a colourless syrup; $[\alpha]_D$ +19.3 (*c* 1.23, $CHCl_3$); R_f 0.17 (4:6 hexane–EtOAc); ^1H NMR (200 MHz, $CDCl_3$): δ 7.45–7.22 (m, 5H, Ar–H), 4.89, 4.83 (AB system, 2H, $J_{A,B}$ 12.8 Hz, CH_2Ph), 4.71 (dd, 1H, $J_{2,3}$ 7.9 Hz, H-2), 4.57 (s, 1H, H-1′), 4.38 (d, 1H, $J_{1,2}$ 6.7 Hz, H-1), 4.30–4.15 (m, 2H, H-3′, H-4′), 4.15–4.05 (m, 3H, H-5, H-6a, H-6b), 3.95 (m, 2H, H-6a', H-6b'), 3.90 (dd, 1H, $J_{3,4}$ 1.4 Hz, H-3), 3.81 (m, 1H, H-5′), 3.71 (d, 1H, $J_{2',3'}$ 5.5 Hz, H-2′), 3.69 (m, 1H, H-4), 3.48 (s, 6H, 2 × OMe), 1.50, 1.35, 1.34, 1.31, 1.26, 1.25 (6s, each 3H, 3 × CMe_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 138.1 (Ar–C), 127.7–126.9 (Ar–CH), 110.2, 109.5, 107.4 (3 × CMe_2), 106.4 (C-1), 102.1 (C-1′), 78.2, 77.5, 74.9, 74.8, 74.7, 74.6 (C-2, C-3, C-4, C-5, C-3′, C-4′), 74.0 (CH_2Ph), 72.0 (C-2′), 70.8 (C-5′), 64.6 (C-6), 62.0 (C-6′), 57.0, 53.1 (2 × OMe-1), 26.5, 26.3, 26.1, 25.5, 25.4, 25.2 (3 × CMe_2). Anal. Calcd for $C_{30}H_{46}O_{12}$: C, 60.19; H, 7.74. Found: C, 60.25; H, 7.81.

3.5. 2,6-Anhydro-3,4-*O*-isopropylidene-β-D-talopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (8)

3.5.1. From 7 with NaH in DMF

To a suspension of pre-washed (hexane) 60% NaH in mineral oil (90 mg, 1.51 mmol) in dry DMF (2.0 mL) was added, under argon atmosphere at 0 °C, a solution of **7** (200 mg, 0.30 mmol) in dry DMF (5 mL). After warming to room temperature and stirring for 1.5 h , TLC analysis (3:7 hexane–EtOAc) showed the disappearance of the starting material. MeOH (5 mL) and water (13 mL) were slowly added, and the mixture was extracted with Et_2O (2 × 30 mL). The collected organic layers were dried, filtered and concentrated under diminished pressure. The residue (150 mg) was purified by flash chromatography (3:7 hexane–EtOAc) to give **8** (142 mg, 96% yield) as a colourless syrup; $[\alpha]_D$ −19.6 (*c* 1.2, $CHCl_3$); R_f 0.55 (3:7 hexane–EtOAc); ^{1}H NMR (200 MHz, CD_3CN): δ 5.04 (d, 1H, $J_{1',2'}$ 1.7 Hz, H-1′), 4.47 (t, 1H, $J_{2,3}$ 6.6 Hz, H-2), 4.36 (d, 1H, $J_{1,2}$ 6.6 Hz, H-1), 4.34 (m, 1H, H-5), 4.22 (dd, 1H, $J_{3',4'}$ 6.1 Hz, H-3′), 4.18 (dd, 1H, $J_{4',5'}$ 4.6 Hz, H-4′), 4.08 (dd, 1 H, $J_{3,4}$ 1.5 Hz, H-3), 4.05–3.90 (m, 5H, H-5′, H-6′a, H-6′b, H-6a, H-6b), 3.89 (dd, 1H, $J_{4,5}$ 4.5 Hz, H-4), 3.79 (t, 1H, $J_{2',3'}$ 1.7 Hz, H-2′), 3.38, 3.36 (2s, each 3H, 2 × OMe), 1.48, 1.39, 1.34, 1.33, 1.32, 1.28 (6s, each 3H, 3 x C*Me*$_2$); ^{13}C NMR (200 MHz, CD_3CN): δ 112.5, 111.3, 109.0 (3 × C*Me*$_2$), 106.4 (C-1), 99.8 (C-1′), 78.6, 78.0, 76.8 76.6 (C-2, C-4, C-3, C-5), 74.7, 71.3, (C-2′, C-3′), 69.8, 68.0 (C-4′, C-5′), 65.8 (C-6), 63.3 (C-6′), 56.5, 54.0 (2 × OMe), 27.7, 26.9, 26.7, 26.1, 25.3, 24.9 (3 × C*Me*$_2$). Anal. Calcd for $C_{23}H_{38}O_{11}$: C, 56.32; H, 7.81. Found: C, 56.41; H, 7.90.

3.5.2. From 10 with NaH, Im_2SO_2 in DMF

To a suspension of pre-washed (hexane) 60% NaH in mineral oil (95 mg, 2.37 mmol) in dry DMF (2.4 mL) was added, under argon atmosphere at 0 °C, a solution of **10** (284 mg, 0.47 mmol) in dry DMF (9.5 mL). The mixture was warmed to room temperature and stirred for 30 min, then cooled to −30 °C and treated with *N,N*-sulfonyldiimidazole (Im_2SO_2) (142 mg, 0.71 mmol, 1.5 equiv). After 3 h at −30 °C, TLC analysis (EtOAc) showed the disappearance of the starting material, and the mixture was cooled to −40 °C, treated with MeOH and water (5 mL) and extracted with Et_2O (2 × 20 mL). The organic extracts collected, dried, filtered and concentrated under diminished pressure afforded a residue (240 mg) which was subjected to a filtration over silica gel (3:7 hexane–EtOAc) to give pure **8** (221 mg, 96% yield) as a colourless syrup, identical to the above-described sample.

3.6. 6-Deoxy-3,4-*O*-isopropylidene-α-L-*arabino*-hex-5-enopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (11)

A suspension of pre-washed (hexane) 60% NaH in mineral oil (1.91 g, 47.4 mmol) in dry DMF (60 mL) was cooled to 0 °C and treated under argon atmosphere with a solution of **4**[7c] (6.30 g, 9.51 mmol) in dry DMF (45 mL). The mixture was gently warmed to room temperature, left under stirring until **4** was consumed (TLC: 3:7 hexane–EtOAc). After 3.2 h, the reaction mixture was cooled to 0 °C, treated with crushed ice (50 mL) and extracted with Et_2O (5 × 40 mL). The collected organic extracts were dried, filtered and concentrated under diminished pressure to give a residue (4.83 g), which was directly subjected to flash chromatographic purification (7:3 hexane–EtOAc + 0.1% Et_3N) to give **11** (3.96 g, 85% yield); as a clear syrup; $[\alpha]_D$ −22.8 (*c* 1.3, $CHCl_3$); R_f 0.22 (7:3 hexane–EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.85 (d, 1H, $J_{1',2'}$ 8.0 Hz, H-1′), 4.82 (br t, 1H, $J_{6'a,6'b} = J_{4',6'a}$ 1.0 Hz, H-6′a), 4.73 (br t, 1H, $J_{6'a,6'b} = J_{4',6'b}$ 1.1 Hz, H-6′b), 4.67 (dd, 1H, $J_{1,2}$ 6.2 Hz, $J_{2,3}$ 7.7 Hz, H-2), 4.65 (m, 1H, H-4′), 4.48 (d, 1H, H-1), 4.29 (ddd, 1H, $J_{5,6a}$ 6.0 Hz, $J_{4,5}$ 2.0 Hz, H-5), 4.17 (m, 1H, H-4), 4.28–4.13 (m, 2H, H-3′, H-6a), 4.07 (dd, 1H, $J_{6a,6b}$ 8.7 Hz, $J_{5,6b}$ 6.9 Hz, H-6b), 3.99 (dd, 1H, $J_{3,4}$ 1.5 Hz, H-3), 3.76 (t, 1H, $J_{2',3'}$ 8.0 Hz, H-2′), 3.50, 3.51 (2s, each 3H, 2 × OMe), 1.60, 1.57, 1.48, 1.47, 1.46, 1.39 (6s, each 3H, 3 × C*Me*$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 153.1 (C-5′), 110.9, 110.1, 108.1 (3 × C*Me*$_2$), 105.0 (C-1), 103.1 (C-1′), 96.8 (C-6′), 78.9, 77.8, 77.2 76.9, (C-2, C-3, C-4, C-5), 74.8, 73.8, 72.8 (C-2′, C-3′, C-4′); 64.4 (C-6), 55.9, 52.9 (2 × OMe), 27.3, 27.7, 26.3, 25.5, 25.4, 23.9 (3 × C*Me*$_2$). Anal. Calcd for $C_{23}H_{38}O_{11}$: C, 56.32; H, 7.81. Found: C, 56.13; H, 7.77.

3.7. Oxidation–reduction of 6-deoxy-3,4-*O*-isopropylidene-α-L-*arabino*-hex-5-enopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (11)

3.7.1. Oxidation of 11

A suspension of **11** (1.02 g, 2.08 mmol) in dry 9:1 CH_2Cl_2–CH_3CN (14 mL) and pre-dried 4-methylmorpholine-*N*-oxide (NMO) (410 mg, 3.5 mmol) containing 4Å powdered molecular sieves (380 mg) was stirred under an argon atmosphere for 30 min at room temperature. Tetrapropylammonium perruthenate (TPAP) (73 mg, 208 mmol, 10%) was added, and the resulting green mixture was stirred at room temperature. After 2.5 h, TLC analysis (9:1 CH_2Cl_2–acetone) showed the complete disappearance of **11**, and the reaction mixture was filtered through alternate pads of Celite and silica gel and extensively washed first with CH_2Cl_2 and then with EtOAc. The combined organic phases were concentrated under diminished pressure to give a syrup (882 mg, combined yield about 84%) consisting of a mixture of **12** and its hydrate **13** in a ratio of 1:4 established on the basis of the integration of the H-1′ signals (δ 5.15 and 5.64, respectively). The flash chromatographic purification (7:3 hexane–EtOAc) of a sample (210 mg), gave a 1:1 mixture of **12** and **13** (135 mg, combined yield about 55%); as a clear syrup; $[\alpha]_D$ −19.4 (*c* 1.18, $CHCl_3$); R_f 0.09 (7:3 hexane–EtOAc); Selected ^{1}H NMR (200 MHz, C_6D_6) signals *component* ***12***: δ 5.17, 4.85 (2 br s, each 1H, H-6′a, H-6′b), 5.15 (s, 1H, H-1′), 4.76 (dd, 1H, $J_{2,3}$ 7.5 Hz, H-2), 4.28 (d, 1H, $J_{1,2}$ 5.7 Hz, H-1), 4.15 (dd, 1H, $J_{3,4}$ 1.5 Hz, H-3), 3.30, 3.19 (2s, each 3H, 2 × OMe-1); *component* ***13***: δ 5.64 (s, 1H, H-1′), 4.96 (dd, 1H, $J_{2,3}$ 7.9 Hz, H-2), 4.37 (d, 1H, $J_{1,2}$ 5.7 Hz, H-1), 4.08 (dd, 1H, $J_{3,4}$ 1.7 Hz, H-3), 4.85, 4.69 (2 br s, each 1H, H-6′a, H-6′b), 3.25, 3.17 (2s, each 3H, 2 × OMe-1); selected ^{13}C NMR (50 MHz, C_6D_6) signals: *component* ***12***: δ 197.8 (C-2′), 152.6 (C-5′), 111.6, 110.3, 108.3 (3 × C*Me*$_2$), 105.7 (C-1), 102.4 (C-6′), 100.4 (C-1′), 78.3, 78.1, 77.0, 76.4, 76.3, 75.3 (C-3, C-2, C-4, C-5, C-3′, C-4′), 65.3 (C-6), 56.6, 53.7 (2 × OMe-1); *component* ***13***: δ 154.7 (C-5′), 112.2, 110.6, 108.5 (3 × C*Me*$_2$), 106.1 (C-1), 103.0 (C-1′), 94.2 (C-6′), 91.4 (C-2′), 78.6, 78.4, 78.2, 77.6 (C-2, C-4, C-5, C-3′), 75.6, 73.1 (C-3, C-4′), 65.3 (C-6), 56.7, 53.3 (2 × OMe-1); Cluster of signals for both components: δ 27.5–24.9 (3 × C*Me*$_2$). The crude mixture was directly used in the reduction, which follows (Section 3.7.2).

3.7.2. Reduction of the mixture of 12 and 13

A solution of the crude mixture of **12** and **13** in dry MeOH (15 mL) was treated, under argon atmosphere, at −40 °C with $NaBH_4$ (132 mg, 3.5 mmol) and then stirred at the same temperature until TLC analysis (9:1 CH_2Cl_2–Me_2CO) revealed the complete disappearance of the starting material (2.5 h). The mixture was diluted with CH_2Cl_2 (20 mL) and treated with water (20 mL), warmed to room temperature and then extracted with CH_2Cl_2 (4 × 30 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated under diminished pressure. The residue (642 mg) was subjected to flash chromatography (3:1 hexane–EtOAc) to give **14** (390 mg) in 50% yield calculated from **11**.

3.7.2.1. 6-Deoxy-3,4-*O*-isopropylidene-α-L-ribo-hex-5-enopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-aldehydo-D-glucose dimethyl acetal (14). Colourless syrup; $[\alpha]_D$ +18.6 (*c* 0.97, $CHCl_3$); R_f 0.56 (3:7 hexane–EtOAc); ^1H NMR (200 MHz, C_6D_6): δ 5.39 (d, 1H, $J_{1',2'}$ 3.3 Hz, H-1′), 4.85 (br s, 1H, H-6′b), 4.83 (d, 1H, $J_{2',OH}$ 10.5 Hz, OH), 4.78 (dd, 1H, $J_{2,3}$ 8.0 Hz, H-2), 4.70 (br s, 1H, H-6′a), 4.35 (m, 1H, H-4), 4.32 (d, 1H, $J_{1,2}$ 5.6 Hz, H-1), 4.26 (m, 1H, H-5), 4.23–4.03 (m, 2H, H-6a, H-6b), 4.15 (d, 1H, $J_{3',4'}$ 6.7 Hz, H-4′), 4.05 (dd, 1H, $J_{2',3'}$ 4.2 Hz, H-3′), 4.00 (dd, 1H, $J_{3,4}$ 1.6 Hz, H-3), 3.67 (b dt, 1H, H-2′), 3.26, 3.15 (2s, each 3H, 2 × OMe), 1.58, 1.57, 1.44, 1.33, 1.26, 1.20 (6s, each 3H, 3 × C*Me*$_2$); ^{13}C NMR (50 MHz, C_6D_6): δ 154.2 (C-5′), 110.9, 109.8, 108.3 (3 × *C*Me$_2$), 105.7 (C-1), 101.4 (C-1′), 97.5 (C-6′), 78.5, 78.4, 77.9, 75.5 (C-2, C-3, C-4, C-5), 74.1, 72.6 (C-3′, C-4′), 67.3 (C-2′), 65.7 (C-6); 56.2, 53.3 (2 × OMe), 27.3, 27.2, 27.0, 26.4, 25.6, 25.5 (3 × C*Me*$_2$). Anal. Calcd for $C_{23}H_{38}O_{11}$: C, 56.32; H, 7.81. Found: C, 56.41; H, 7.92.

3.8. Epoxidation of 6-deoxy-3,4-*O*-isopropylidene-α-L-*ribo*-hex-5-enopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (14)

A solution of **14** (655 mg, 1.32 mmol) in MeOH (12 mL) was cooled to 0 °C, treated with 70% commercial MCPBA (Fluka, 407 mg, 1.98 mmol), warmed to room temperature and left stirring. After 4.5 h, TLC analysis (3:7 hexane–EtOAc) showed the complete disappearance of the starting material and the formation of three spots at R_f 0.56, 0.40 and 0.29. Satd aq $NaHCO_3$ (40 mL) was added, and the solution was further stirred for 15 min and concentrated under diminished pressure. The residue was partitioned between water (30 mL) and CH_2Cl_2 (75 mL), the aq phase was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic extracts were dried, filtered and concentrated under diminished pressure. The residue (623 mg) was subjected to flash chromatography (7:3 hexane–EtOAc) to give **15** (87 mg, 13% yield) and **16** (337 mg, 47% yield).

3.8.1. (5*S*)-2,5-Anhydro-3,4-*O*-isopropylidene-α-L-*ribo*-hexopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (15)

Colourless syrup; $[\alpha]_D$ −48.3 (*c* 1.0, $CHCl_3$); R_f 0.40 (3:7 hexane–EtOAc); ^1H NMR (600 MHz, $CDCl_3$): δ 5.09 (s, 1H, H-1′), 4.60 (s, 1H, H-2′), 4.40 (dd, 1H, $J_{2,3}$ 7.2 Hz, H-2), 4.35 (d, 1H, $J_{1,2}$ 6.0 Hz, H-1), 4.34 (d, 1H, $J_{3',4'}$ 5.5 Hz, H-3′), 4.26 (d, 1H, H-4′), 4.25 (m, 1H, H-5), 4.09, 4.08 (AB system, 2H, $J_{A,B}$ 13.0 Hz, H-6′a, H-6′b), 4.00 (m, 3H, H-4, H-6a, H-6b), 3.91 (dd, 1H, $J_{3,4}$ 2.1 Hz, H-3), 3.46, 3.45 (2s, each 3H, 2 × OMe), 1.44, 1.40, 1.37, 1.36, 1.34, 1.28 (6s, each 3H, 3 × C*Me*$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 113.9 (C-5′), 110.3, 108.3, 107.8 (3 × *C*Me$_2$), 105.6 (C-1), 98.3 (C-1′), 82.7 (C-2′), 80.8 (C-4′), 80.1 (C-3′), 80.0, 77.9 (C-3, C-5), 75.9 (C-2), 73.5 (C-4), 64.7 (C-6); 58.4 (C-6′), 56.6, 54.2 (2 × OMe), 27.7, 26.3, 26.1, 25.9, 25.4, 24.9 (3 × C*Me*$_2$). Anal. Calcd for $C_{23}H_{38}O_{12}$: C, 54.54; H, 7.56. Found: C, 54.48; H, 7.52.

3.8.2. (5*R*)-3,4-*O*-Isopropylidene-5-*C*-methoxy-α-L-*ribo*-hexopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (16)

Colourless syrup; $[\alpha]_D$ −15.8 (*c* 1.25, $CHCl_3$); R_f 0.29 (3:7 hexane–EtOAc); ^1H NMR (600 MHz, $CDCl_3$): δ 5.10 (d, 1H, $J_{1',2'}$ 3.1 Hz, H-1′), 4.53 (dd, 1H, $J_{2,3}$ 7.8 Hz, H-2), 4.40 (dd, 1H, $J_{2',3'}$ 4.5 Hz, $J_{3',4'}$ 7.2 Hz, H-3′), 4.38 (d, 1H, $J_{1,2}$ 6.4 Hz, H-1), 4.25 (dt, 1H, *J* 6.8 Hz, *J* 2.4 Hz, H-5), 4.16 (d, 1H, H-4′), 4.08 (m, 3H, H-4, H-6a, H-6b), 4.00 (m, 1H, H-2′), 3.91 (dd, 1H, $J_{3,4}$ 1.6 Hz, H-3), 3.80, 3.72 (AB system, 2H, $J_{A,B}$ 12.0 Hz, H-6′a, H-6′b), 3.44, 3.43 (2s, each 3H, 2 × OMe-1), 3.37 (s, 3H, OMe-5′), 2.99 (br d, 1H, OH), 2.21 (br s, 1H, OH), 1.56, 1.44, 1.40, 1.37, 1.35, 1.34 (6s, each 3H, 3 × C*Me*$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 109.9, 109.8, 107.9 (3 × *C*Me$_2$), 105.4 (C-1), 98.4 (C-5′), 98.2 (C-1′), 77.9 (C-3), 77.8 (C-5), 76.8 (C-4), 74.5 (C-2), 73.2 (C-4′), 72.5 (C-3′), 65.5 (C-2′), 64.9 (C-6); 60.7 (C-6′), 56.2, 52.8 (2 × OMe-1), 48.7 (OMe-5′), 26.9, 26.2, 26.0, 25.7, 25.0, 24.5 (3 × C*Me*$_2$). Anal. Calcd for $C_{24}H_{42}O_{13}$: C, 53.52; H, 7.86. Found: C, 53.61; H, 7.90.

3.9. (5*R*)-2,6-Di-*O*-benzyl-3,4-*O*-isopropylidene-5-*C*-methoxy-α-L-*ribo*-hexopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (17)

To a solution of **16** (276 mg, 0.51 mmol) in THF containing 0.5% of water (4.1 mL) were added 18-crown-6 (14 mg) and powdered KOH (230 mg, 4.09 mmol), and the mixture was stirred at room temperature for 30 min. BnBr (0.24 mL, 2.05 mmol) was added, and the suspension was stirred at room temperature until TLC analysis (3:7 hexane–EtOAc) revealed the complete disappearance of the starting material (4.5 h, R_f 0.20) and the formation of a major faster moving product (R_f 0.64). MeOH (10 mL) was added, and the reaction mixture was further stirred at room temperature for 30 min. Solvents were removed under diminished pressure, and the residue was partitioned between CH_2Cl_2 (50 mL) and water (15 mL). The aq phase was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic extracts were dried, filtered and concentrated under diminished pressure. The residue (630 mg) was subjected to flash chromatography (first hexane, then 3:1 hexane–EtOAc) to give **17** (345 mg, 94% yield) as a colourless syrup; $[\alpha]_D$ +0.9 (*c* 1.12, $CHCl_3$); R_f 0.64 (3:7 hexane–EtOAc); ^1H NMR (200 MHz, $CDCl_3$): δ 7.43–7.23 (m, 10H, Ar–H), 4.91 (d, 1H, $J_{1',2'}$ 1.4 Hz, H-1′), 4.82 (s, 2H, *CH*$_2$Ph), 4.68, 4.50 (AB system, 2H, $J_{A,B}$ 12.3 Hz, *CH*$_2$Ph), 4.54 (dd, 1H, $J_{1,2}$ 6.5 Hz, $J_{2,3}$ 7.6 Hz, H-2), 4.33 (d, 1H, H-1), 4.31 (dd, 1H, $J_{2',3'}$ 5.0 Hz, $J_{3',4'}$ 6.1 Hz H-3′), 4.15 (d, 1H, H-4′), 4.20 (dt, 1H, *J* 3.3 Hz, *J* 6.6 Hz, H-5), 4.02 (dd, 1H, $J_{6a,6b}$ 8.9 Hz, $J_{5,6a}$ 6.7 Hz, H-6b), 3.96–3.88 (m, 3H, H-3, H-4, H-6a), 3.75 (d, 1H, H-2′), 3.67, 3.57 (AB system, 2H, $J_{A,B}$ 10.3 Hz, H-6′a, H-6b), 3.30, 3.29, 3.23 (3s, each 3H, 2 × OMe-1, OMe-5′), 1.50, 1.36, 1.33, 1.30, 1.28, 1.25 (6s, each 3H, 3 × C*Me*$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 138.2, 137.9 (2 × Ar–C), 128.2–127.2 (Ar–CH), 109.9, 109.7, 107.8 (3 × *C*Me$_2$), 105.1 (C-1), 99.0 (C-5′), 96.9 (C-1′), 77.9, 77.7, 76.6 (C-3, C-4, C-5), 73.9, 73.3 (2 × CH_2Ph), 73.3, 73.0 (C-2, C-4′), 72.5, 72.0 (C-2′, C-3′), 66.2 (C-6′), 64.9 (C-6), 55.9, 51.6 (2 × OMe-1), 47.8 (OMe-5′), 26.8, 26.7, 26.4, 25.7, 25.5, 25.0 (3 × C*Me*$_2$). Anal. Calcd for $C_{38}H_{54}O_{13}$: C, 63.49; H, 7.57. Found: C, 63.51; H, 7.58.

3.10. 2,6-Di-*O*-benzyl-4-deoxy-α-L-*erythro*-hex-4-enopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (19)

A solution of **18**[10] (5.45 g, 7.90 mmol) in dry THF (100 mL) was warmed to reflux and treated with solid *t*-BuOK (9.70 g, 79.2 mmol). After 15 min, TLC analysis (1:1 hexane–EtOAc) showed the complete disappearance of the starting material, and satd aq $NaHCO_3$ (100 mL) was then added. The aq phase was extracted with CH_2Cl_2 (3 × 200 mL), and the collected organic extracts were dried, filtered and concentrated under diminished pressure. The residue (5.35 g) was subjected to flash chromatography (3:2 hexane–EtOAc, 0.1% Et_3N) to give **19** (4.04 g, 81% yield) as a colourless syrup; $[\alpha]_D$ −25.1 (*c* 1.0, $CHCl_3$); R_f 0.4 (3:2 hexane–EtOAc); ^1H NMR (250 MHz, CD_3CN): δ 7.43–7.27 (m, 10H, Ar–H), 5.62 (dd, 1H, $J_{1',2'}$ 2.3 Hz $J_{1',3'}$ 1.1 Hz, H-1′), 5.17 (dt, 1H, $J_{3',4'}$ 5.3 Hz, $J_{4',6'a} = J_{4',6'b}$ 0.8 Hz, H-4′), 4.77, 4.64 (AB system, 2H, $J_{A,B}$ 11.6 Hz, *CH*$_2$Ph), 4.52 (s, 2H, *CH*$_2$Ph), 4.32 (d, 1H, $J_{1,2}$ 6.6 Hz, H-1), 4.23 (ddd, 1H, $J_{4,5}$ 3.8 Hz, $J_{5,6a}$ 6.3 Hz, $J_{5,6b}$ 7.0 Hz, H-5), 4.18 (m, 1H, $J_{2',3'}$ 4.0 Hz, H-3′), 4.12 (dd, 1H, $J_{2,3}$ 7.1 Hz, $J_{3,4}$ 1.4 Hz, H-3), 4.07 (dd, 1H, H-4), 4.05- 3.88 (m, 4H, H-6a, H-6b, H-6′a, H-6′b), 4.02 (dd, 1 H, H-2), 3.73 (dd, 1H, H-2′), 3.38, 3.34 (2s, each 3H,

2 × OMe), 3.12 (d, 1H, $J_{3',OH}$ 10.1 Hz, OH), 1.37, 1.31, 1.30, 1.28 (4s, each 3H, 2 × C*Me*$_2$); ^{13}C NMR (62.9 MHz, CD_3CN): δ 149.0 (C-5′), 139.7, 139.6 (2 × Ar–C), 129.3–128.5 (Ar–CH), 110.7, 108.9 (2 × C*Me*$_2$), 106.6 (C-1), 102.9 (C-4′), 98.8 (C-1′), 78.5, 78.5 (C-4, C-5), 77.3 (C-2), 75.3 (C-2′), 75.0 (C-3), 73.1, 71.7 (2 × *CH*$_2$Ph), 69.6 (C-6′), 65.8 (C-6), 61.3 (C-3′), 56.8, 54.7 (2 × OMe-1), 27.3, 27.2, 26.8, 25.4 (2 × C*Me*$_2$). Anal. Calcd for $C_{34}H_{46}O_{11}$: C, 64.75; H, 7.35. Found: C, 64.77; H, 7.38.

3.11. Epoxidation–methanolysis of 2,6-di-*O*-benzyl-deoxy-α-L-*erythro*-hex-4-enopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (19)

A solution of **19** (5.81 g, 9.21 mmol) in MeOH (180 mL) was cooled to 0 °C and treated with 70% commercial MCPBA (2.95 g, 11.9 mmol,). After 5 min the reaction mixture was gently warmed to room temperature and left under stirring until **19** was consumed (TLC, 1:1 hexane–EtOAc, 24 h). Satd aq $NaHCO_3$ (50 mL) was added, the solution was further stirred for 30 min and the solvent was removed under diminished pressure. The residue was partitioned between water (60 mL) and CH_2Cl_2 (150 mL), the aq phase was extracted with CH_2Cl_2 (2 × 150 mL), and the collected organic extracts were dried, filtered and concentrated under diminished pressure. The residue (5.4 g) was subjected to flash chromatography (3:2 hexane–EtOAc) to give **20** (3.63 g, 58% yield) and the 4′-epimer **21** (920 mg, 15% yield).

3.11.1. (5*R*)-2,6-Di-*O*-benzyl-5-*C*-methoxy-α-L-*ribo*-hexopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (20)

Colourless syrup, $[\alpha]_D$ −22.8 (*c* 1.3, $CHCl_3$); R_f 0.33 (1:1 hexane–EtOAc); ^{1}H NMR (200 MHz, CD_3CN): δ 7.39–7.31 (m, 10H, Ar H), 4.97, 4.69 (AB system, 2H, $J_{A,B}$ 11.4 Hz, *CH*$_2$Ph), 4.60, 4.45 (AB system, 2H, $J_{A,B}$ 11.9 Hz, *CH*$_2$Ph), 4.88 (d, 1H, $J_{1',2'}$ 0.9 Hz, H-1′), 4.44 (dd, 1H, $J_{1,2}$ 6.5 Hz, $J_{2,3}$ 7.0 Hz, H-2), 4.34 (d, 1H, H-1), 4.25 (m, 1H, H-5), 4.10–3.90 (m, 5H, H-3, H-4, H-6a, H-6b, H-4′), 3.99 (dd, 1H, $J_{2',3'}$ 1.5 Hz, H-2′), 3.85 (dt, 1H, $J_{3',4'}$ 3.0 Hz, $J_{3',OH}$ 2.3 Hz, H-3′), 3.67, 3.53 (AB system, 2H, $J_{A,B}$ 10.2, H-6′a, H-6′b), 3.30, 3.26, 3.24 (3s, each 3H, 2 × OMe-1, OMe-5′), 1.36, 1.31, 1.30, 1.26 (4s, each 3H, 2 × C*Me*$_2$); ^{13}C NMR (50 MHz, CD_3CN): δ 139.2, 139.1 (2 × Ar–C), 128.8–128.6 (Ar–CH), 110.3, 108.7 (2 × C*Me*$_2$), 106.3 (C-1), 102.6 (C-5′), 99.1 (C-1′), 80.3 (C-2′), 78.6, 78.5, 77.7, 75.6 (C-2, C-3, C-4, C-5), 76.0, 73.8 (2 × *CH*$_2$Ph), 71.1 (C-3′), 66.8 (C-4′), 65.9, 65.5 (C-6, C-6′), 56.4, 53.1 (2 × OMe-1), 48.8 (OMe-5′), 27.1, 27.0, 26.9, 25.2 (2 × C*Me*$_2$). Anal. Calcd for $C_{35}H_{50}O_{13}$: C, 61.93; H, 7.42. Found: C, 61.96; H, 7.45.

The structure of **20** was confirmed by transformation into **17** by treatment of **20** (0.112 g, 0.165 mmol) with TsOH (3 mg, 0.0167 mmol) in DMP (3 mL) at room temperature. After 4 h, the TLC (1:1 hexane–EtOAc) revealed the complete disappearance of the starting material, Et_3N (0.4 mL) was added, and the solution was stirred at room temperature. After 15 min the solution was concentrated under diminished pressure and the residue (125 mg) was subjected to flash chromatography (7:3 hexane–EtOAc) to give **17** (0.110 g, 93% yield) as a colourless syrup, identical to the sample described above.

3.11.2. (5*S* or 5*R*)-2,6-Di-*O*-benzyl-5-*C*-methoxy-β-D-*lyxo*-hexopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (21)

Colourless syrup; $[\alpha]_D$ −42.0 (*c* 1.07, $CHCl_3$); R_f 0.13 (1:1 hexane–EtOAc); ^{1}H NMR (200 MHz, CD_3CN): δ 7.39–7.25 (m, 10H, Ar–H), 4.95, 4.69 (AB system, 2H, $J_{A,B}$ 11.8 Hz, *CH*$_2$Ph), 4.72, 4.45 (AB system, 2H, $J_{A,B}$ 11.7 Hz, *CH*$_2$Ph), 4.53 (dd, 1H, $J_{1,2}$ 6.3 Hz, $J_{2,3}$ 7.6 Hz, H-2), 4.39 (d, 1H, $J_{1',2'}$ 1.0 Hz, H-1′), 4.35 (d, 1H, H-1), 4.25 (dt, 1H, *J* 3.4 Hz, *J* 6.6 Hz, H-5), 4.05–3.94 (m, 4H, H-3, H-4, H-6a, H-6b), 3.95 (d, 1H, 1H, $J_{3',4'}$ 10.0 Hz, H-4′), 3.89 (dd, 1H, $J_{2',3'}$ 3.2 Hz, H-2′), 3.75, 3.58 (AB system, 2H, $J_{A,B}$ 10.5, H-6′a, H-6′b), 3.67 (dd, 1H, H-3′), 3.36, 3.31 (2s, each 3H, 2 × OMe-1), 3.29 (s, 3H, OMe-5′), 1.36, 1.30, 1.28, 1.23 (4s, each 3H, 2 × C*Me*$_2$); ^{13}C NMR (50 MHz, CD_3CN): δ 140.1, 139.4 (2 × Ar–C), 129.2–128.2 (Ar–CH), 110.3, 108.2 (2 × C*Me*$_2$), 106.7 (C-1), 100.3 (C-5′), 99.4 (C-1′), 79.4 (C-2′), 78.7, 78.5, 78.1, 76.3 (C-2, C-3, C-4, C-5), 75.2, 74.3 (2 × *CH*$_2$Ph), 70.8, 71.8 (C-3′, C-4′), 70.7 (C-6′), 65.6 (C-6), 56.7, 54.0 (2 × OMe-1), 49.0 (OMe-5′), 27.1, 27.0, 26.9, 25.1 (2 × C*Me*$_2$). Anal. Calcd for $C_{35}H_{50}O_{13}$: C, 61.93; H, 7.42. Found: C, 61.97; H, 7.44.

3.12. 2,3,6-Tri-*O*-benzyl-deoxy-α-L-*erythro*-hex-4-enopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (22)

A solution of **19** (317 mg, 0.50 mmol) in dry DMF (8 mL) was treated at 0 °C with a 60% NaH in mineral oil (60 mg, 2.50 mmol), and the mixture was stirred for 15 min at 0 °C. Benzyl bromide (160 μL, 0.65 mmol) was added, and the reaction mixture was warmed to room temperature and further stirred. After 30 min, TLC analysis (3:2 hexane–EtOAc) showed the disappearance of the starting material (R_f 0.31) and the formation of a major faster moving product (R_f 0.51). Excess NaH was decomposed with MeOH (0.5 mL) under stirring for 10 min at 0 °C, CH_2Cl_2 (15 mL) and H_2O (8 mL) were added, and the aq phase was further extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were dried, filtered and concentrated under diminished pressure, and the crude product (350 mg) was subjected to flash chromatography (7:3 hexane–EtOAc) to give pure **22** (318 mg, 88% yield) as a colourless syrup, R_f 0.31 (3:2 hexane–EtOAc); $[\alpha]_D$ −25.0 (*c* 1.04, $CHCl_3$); ^{1}H NMR (250 MHz, CD_3CN): δ 7.41–7.24 (m, 15H, Ar–H), 5.32 (t, 1H, $J_{1',2'} = J_{1',3'}$ 1.0 Hz, H-1′), 4.94 (dt, 1H, $J_{3',4'}$ 2.8 Hz, $J_{4',6'a} = J_{4',6'b}$ 0.8 Hz, H-4′), 4.86, 4.73 (AB system, 2H, $J_{A,B}$ 11.6 Hz, *CH*$_2$Ph), 4.56, 4.52 (AB system, 2H, $J_{A,B}$ 12.0 Hz, *CH*$_2$Ph), 4.53, 4.47 (AB system, 2H, $J_{A,B}$ 11.8 Hz, *CH*$_2$Ph), 4.43 (dd, 1H, $J_{1,2}$ 6.3 Hz, $J_{2,3}$ 7.2 Hz, H-2), 4.35 (d, 1H, H-1), 4.26 (dt, 1H, $J_{4,5}$ 3.8 Hz, $J_{5,6a} = J_{5,6b}$ 6.3 Hz, H-5), 4.24 (m, 1H, $J_{2',3'}$ 5.4 Hz, H-3′), 4.08 (dd, 1H, $J_{6a,6b}$ 10.5 Hz, H-6b), 4.07 (dd, 1H, $J_{3,4}$ 2.0 Hz, H-3), 4.04 (dd, 1H, H-4), 3.97 (m, 2H, H-6a, H-2′), 3.90 (m, 2H, H-6′a, H-6′b), 3.35, 3.33 (2s, each 3H, 2 × OMe), 1.34, 1.31, 1.30, 1.29 (4s, each 3H, 2 × C*Me*$_2$); ^{13}C NMR (62.9 MHz, CD_3CN): δ 150.4 (C-5′), 139.8, 139.7, 139.5 (3 × Ar–C), 129.2–128.4 (Ar–CH), 110.6, 108.7 (2 × C*Me*$_2$), 106.3 (C-1), 101.0 (C-1′), 100.4 (C-4′), 78.7 (C-3), 78.5 (C-5), 76.9 (C-4), 76.0 (C-2), 73.9, 72.8, 71.4 (3 × *CH*$_2$Ph), 73.6 (C-2′), 71.8 (C-3′), 69.9 (C-6′), 65.9 (C-6), 56.2, 53.8 (2 × OMe-1), 27.3, 27.2, 26.9, 25.1 (2 × C*Me*$_2$). Anal. Calcd for $C_{41}H_{52}O_{11}$: C, 68.31; H, 7.27. Found: C, 68.28; H, 7.29.

3.13. Epoxidation–methanolysis of 2,3,6-tri-*O*-benzyl-deoxy-α-L-*erythro*-hex-4-enopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (22)

A solution of **22** (233 mg, 0.323 mmol) in MeOH (12 mL) was cooled to 0 °C and treated with 70% commercial MCPBA (111.4 mg, 0.388 mmol). After 5 min, the reaction mixture was gently warmed to room temperature and left under stirring until **22** was consumed (TLC, 1:1 hexane–EtOAc, 14 h). Satd aq $NaHCO_3$ (10 mL) was added, the solution was further stirred for 10 min, and the solvent was removed under diminished pressure. CH_2Cl_2 (20 mL) was added, the aq phase was extracted with CH_2Cl_2 (2 × 20 mL), and the collected organic extracts were dried, filtered and concentrated under diminished pressure. The residue was subjected to flash chromatography (3:2 hexane–EtOAc) to give **23** (42.8 mg, 17% yield) and the 4′-epimer **24** (120 mg, 48% yield).

3.13.1. (5*R*)-2,3,6-Tri-*O*-benzyl-5-*C*-methoxy-α-L-*ribo*-hexopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (23)

Colourless syrup, $[\alpha]_D$ −14.6 (*c* 0.96, $CHCl_3$); R_f 0.33 (3:2 hexane–EtOAc); ^{1}H NMR (250 MHz, CD_3CN): δ 7.43–7.26 (m, 15H, Ar H), 4.88, 4.74 (AB system, 2H, $J_{A,B}$ 11.4 Hz, CH_2Ph), 4.63, 4.50 (AB system, 2H, $J_{A,B}$ 11.9 Hz, CH_2Ph), 4.60, 4.44 (AB system, 2H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.81 (d, 1H, $J_{1',2'}$ 1.1 Hz, H-1′), 4.42 (dd, 1H, $J_{1,2}$ 6.5 Hz, $J_{2,3}$ 7.5 Hz, H-2), 4.33 (d, 1H, H-1), 4.24 (dt, 1H, $J_{4,5}$ 3.4 Hz, $J_{5,6a} = J_{5,6b}$ 6.6 H-5), 4.09 (m, 1H, H-2′), 4.01 (dd, 1H, $J_{6a,6b}$ 8.5 Hz, H-6b), 3.96 (m, 3H, H-3, H-4, H-6a), 3.82 (ddd, 1H, $J_{3',4'}$ 3.1 Hz, $J_{4',OH}$ 9.9 Hz, $J_{2',4'}$ 1.2 Hz, H-3′), 3.81 (d, 1H, OH-4′),3.74 (dd, 1H, $J_{2',3'}$ 2.9 Hz, H-3′), 3.70, 3.50 (AB system, 2H, $J_{A,B}$ 10.2, H-6′a, H-6′b), 3.28, 3.25, (2s, each 3H, 2 × OMe-1), 3.19 (s, 3H, OMe-5′), 1.30 (s, 12H, 2 × CMe_2); ^{13}C NMR (62.9 MHz, CD_3CN): δ 139.5, 139.3, 139.2 (3 × Ar–C), 129.3–128.6 (Ar–CH), 110.4, 108.7 (2 × CMe_2), 106.3 (C-1), 102.9 (C-5′), 98.8 (C-1′), 78.6 (C-3), 78.5 (C-5), 78.2 (C-2′), 77.7 (C-4), 75.9, 73.9, 70.5 (3 × CH_2Ph), 75.6 (C-2), 74.0 (C-3′), 68.5 (C-4′), 65.9 (C-6′), 65.5 (C-6), 56.4, 53.1 (2 × OMe-1), 48.9 (OMe-5′), 27.1, 27.0, 26.9, 25.1 (2 × CMe_2). Anal. Calcd for $C_{42}H_{56}O_{13}$: C, 65.61; H, 7.34. Found: C, 65.58; H, 7.28.

3.13.2. (5*S* or 5*R*)-2,3,6-Tri-*O*-benzyl-5-*C*-methoxy-β-D-*lyxo*-hexopyranosyl-(1→4)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose dimethyl acetal (24)

Colourless syrup; $[\alpha]_D$ −54.6 (*c* 0.99, $CHCl_3$); R_f 0.44 (3:2 hexane–EtOAc); ^{1}H NMR (250 MHz, CD_3CN): δ 7.39–7.236 (m, 15H, Ar–H), 4.93, 4.70 (AB system, 2H, $J_{A,B}$ 11.8 Hz, CH_2Ph), 4.73, 4.47 (AB system, 2H, $J_{A,B}$ 11.7 Hz, CH_2Ph), 4.59 (s, 2H, CH_2Ph), 4.90 (d, 1H, $J_{1',2'}$ 0.7 Hz, H-1′), 4.53 (dd, 1H, $J_{1,2}$ 6.2 Hz, $J_{2,3}$ 7.5 Hz, H-2), 4.35 (d, 1H, H-1), 4.26 (dt, 1H, *J* 3.2 Hz, *J* 6.7 Hz, H-5), 4.18 (d, 1H, 1H, $J_{3',4'}$ 10.1 Hz, H-4′), 4.05 (m, 1H, H-6b), 4.04 (dd, 1H, $J_{2',3'}$ 3.0 Hz, H-2′), 3.98 (dd, 1H, $J_{3,4}$ 1.3 Hz, H-3), 3.96 (m, 2H, H-4, H-6a,), 3.59 (dd, 1H, H-3′), 3.78, 3.61 (AB system, 2H, $J_{A,B}$ 10.5, H-6′a, H-6′b), 3.37, 3.32 (2s, each 3H, 2 × OMe-1), 3.30 (s, 3H, OMe-5′), 1.31, 1.30, 1.29, 1.27 (4s, each 3H, 2 × CMe_2); ^{13}C NMR (62.9 MHz, CD_3CN): δ 140.2, 139.9, 139.5 (3 × Ar–C), 129.2–128.1 (Ar–CH), 110.4, 108.7 (2 × CMe_2), 106.7 (C-1), 100.3 (C-5′), 99.3 (C-1′), 78.8 (C-5), 78.6 (C-3), 78.5 (C-3′), 77.9 (C-4), 76.9 (C-2′), 76.3 (C-2), 75.0, 74.3, 72.4 (3 × CH_2Ph), 68.8 C-4′), 70.7 (C-6′), 65.5 (C-6), 56.7, 54.0 (2 × OMe-1), 49.0 (OMe-5′), 27.2, 27.1, 26.9, 25.2 (2 × CMe_2). Anal. Calcd for $C_{42}H_{56}O_{13}$: C, 65.61; H, 7.34. Found: C, 65.58; H, 7.31.

3.14. 2,6-Di-*O*-benzyl-L-*ribo*-hexos-5-ulose (25)

A solution of **17** (344 mg, 0.479 mmol) in a 4:1 CH_3CN–H_2O (8.5 mL) was treated with 90% aq CF_3COOH (24.2 mL) and stirred at 50 °C until the TLC analysis (EtOAc) showed the complete disappearance of the starting material (5 h). The mixture was concentrated under diminished pressure and repeatedly co-evaporated with toluene (4 × 30 mL). The crude residue was partitioned between brine (20 mL) and EtOAc (40 mL) and the aq phase was extracted with EtOAc (3 × 40 mL). The organic phases were collected, dried and concentrated under diminished pressure to give a residue that was directly subjected to a flash chromatographic purification, eluting with 3:7 hexane–EtOAc, to give **25** (113 mg, 66% yield) as an amorphous solid constituted (NMR) by a mixture of α- and β-1,4-furanose anomers in a ratio of about 7:3, estimated on the basis of the relative C-1′ NMR signal intensities (δ 100.9 and 97.4, respectively); R_f 0.31 (1:1 hexane–EtOAc); mp 121–125 °C; lit.[8] mp 120–124 °C; $[\alpha]_D$ −20.5 (*c* 0.7; $CHCl_3$).

Hydrolysis of **20** (456 mg, 0.67 mmol) was performed in 4:1 (v/v) CH_3CN–H_2O (11 mL) with 90% aq CF_3COOH (2.3 mL) according to the procedure described above. After 4 h, the reaction mixture was subjected to the workup described above, and the crude reaction product was flash chromatographated (2:3 hexane–EtOAc) to give **25** (175 mg, 73% yield) as an amorphous solid, identical to the sample described above.

3.15. 2,6-Di-*O*-benzyl-D-*lyxo*-hexos-5-ulose (26)

Compound **26** was obtained by the method described above for **25**, with the following reagents: 331 mg of **21** (0.49 mmol) in 2:1 (v/v) CH_3CN–H_2O (18 mL) and 90% aq CF_3COOH (1.4 mL). After 1.5 h at 60 °C, TLC analysis showed the complete disappearance of the starting material, and the reaction mixture was subjected to the workup described above for **25**. The residue (135 mg) was subjected to a flash chromatographic purification, eluted with 3:7 hexane–EtOAc, to give **26** (126 mg, 72% yield) as a white solid; constituted (^{13}C NMR, CD_3CN) by a mixture of α- and β-1,4-furanose anomers in a ratio of about 65:35 estimated on the basis of the relative C-1 signal intensities (δ 101.6 and 97.4, respectively); $[\alpha]_D$ −15.5 (*c* 1.0, $CHCl_3$); R_f 0.29 (4:1 CH_2Cl_2–Et_2O); lit.[16] for the L-enantiomer $[\alpha]_{D\infty}$ +15.1 (*c* 0.96, $CHCl_3$).

Acknowledgement

This research was partly supported by Ministero dell'Università e della Ricerca (MIUR, Rome, Italy) in the frame of the COFIN national project.

References

1. Bonaccorsi, F.; Catelani, G.; Oscarson, S. *Carbohydr. Res.* **2009**, *344*, 1442–1448.
2. (a) Theander, O. Acids and other oxidation products. In *The Carbohydrates: Chemistry and Biochemistry*, 2nd ed.; Pigman, W., Horton, D., Eds., Academic Press: New York, 1980; Vol. 1B, pp 1013–1099; (b) De Lederkremer, R. M.; Marino, C. *Adv. Carbohydr. Chem. Biochem.* **2003**, *58*, 199–306.
3. (a) Baxter, E. W.; Reitz, A. B. *J. Org. Chem.* **1994**, *59*, 3175–3185; (b) Barili, P. L.; Berti, G.; Catelani, G.; D'Andrea, F.; De Rensis, F.; Puccioni, L. *Tetrahedron* **1997**, *53*, 3407–3416.
4. (a) Pistarà, V.; Barili, P. L.; Catelani, G.; Corsaro, A.; D'Andrea, F.; Fisichella, S. *Tetrahedron Lett.* **2000**, *41*, 3253–3256; (b) Catelani, G.; Corsaro, A.; D'Andrea, F.; Mariani, M.; Pistarà, V. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 3313–3315.
5. Adinolfi, M.; Barone, G.; Iadonisi, A.; Mangoni, L. *Tetrahedron Lett.* **1998**, *39*, 2021–2024.
6. (a) Barili, P. L.; Berti, G.; Catelani, G.; D'Andrea, F. *Gazz. Chim. Ital.* **1992**, *122*, 135–142; (b) Barili, P. L.; Berti, G.; Catelani, G.; D'Andrea, F.; De Rensis, F. *Tetrahedron* **1997**, *53*, 8665–8674.
7. (a) Enright, P. M.; O'Boyle, K. M.; Murphy, P. V. *Org. Lett.* **2000**, *2*, 3929–3932; (b) Enright, P. M.; Tosin, M.; Nieuwenhuyzen, M.; Cronin, L.; Murphy, P. V. *J. Org. Chem.* **2002**, *67*, 3733–3741; (c) Catelani, G.; Corsaro, A.; D'Andrea, F.; Mariani, M.; Pistarà, V.; Vittorino, E. *Carbohydr. Res.* **2003**, *338*, 2349–2358; (d) Corsaro, A.; Catelani, G.; D'Andrea, F.; Fisichella, S.; Mariani, M.; Pistarà, V. *Environ. Sci. Pollut. Res.* **2003**, *10*, 325–328; (e) Guazzelli, L.; Catelani, G.; D'Andrea, F.; Pistarà, V. *Carbohydr. Res.* **2009**, *344*, 717–724.
8. Barili, P. L.; Bergonzi, M. C.; Berti, G.; Catelani, G.; D'Andrea, F.; De Rensis, F. *J. Carbohydr. Chem.* **1999**, *18*, 1037–1049.
9. Barili, P. L.; Berti, G.; D'Andrea, F.; Di Bussolo, V.; Gaudiosi, A. *Tetrahedron Lett.* **1992**, *33*, 7061–7064.
10. Attolino, E.; Catelani, G.; D'Andrea, F. *Eur. J. Org. Chem.* **2006**, 5279–5292.
11. Hanessian, S. *Preparative Carbohydrate Chemistry*; Marcel Dekker: New York, 1997. pp 127–149.
12. (a) Martin, O. R.; Yang, F.; Xie, F. *Tetrahedron Lett.* **1995**, *36*, 47–50; (b) Cipolla, L.; Lay, L.; Nicotra, F. *J. Org. Chem.* **1997**, *62*, 6678–6681; (c) Juers, S.; Thiem, J. *J. Carbohydr. Chem.* **2009**, *28*, 293–297.
13. Ley, S. V.; Griffith, W. P.; Norman, J.; Marsden, S. P. *Synthesis* **1994**, 639–666.
14. Stevens, J. D. *Carbohydr. Res.* **1975**, *45*, 143–150.
15. (a) Berti, G. *Top. Stereochem.* **1972**, *7*, 130–152; (b) Barili, P. L.; Berti, G.; Catelani, G.; Colonna, F.; D'Andrea, F. *Carbohydr. Res.* **1989**, *190*, 13–21.
16. Barili, P. L.; Catelani, G.; D'Andrea, F.; De Rensis, F.; Goracci, G. *J. Carbohydr. Chem* **1998**, *17*, 1167–1180.
17. (a) O'Brien, J. L.; Tosin, M.; Murphy, P. V. *Org. Lett.* **2001**, *3*, 3353–3356; (b) Steiner, A. J.; Stütz, A. E.; Tarling, C. A.; Withers, G. S.; Wrodnigg, T. M. *Carbohydr. Res.* **2007**, *342*, 1850–1858.
18. 18. Catelani, G.; D'Andrea, F.; Guazzelli, L.; Masi, L.; Pistarà, V. *XI Conference-School on Carbohydrate Chemistry*, 22-26 June 2008, Siena (Italy); OR 15.
19. Attolino, E.; Bonaccorsi, F.; Catelani, G.; D'Andrea, F. *Carbohydr. Res.* **2008**, *343*, 2545–2556.