A reinvestigation of the synthesis and revision of spectral data of 1,2-*O*-isopropylidene-α-l-sorbofuranose, 1,2:4,6-di-*O*-isopropylidene-α-l-sorbofuranose and derivatives

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PII: S0008-6215(13)00225-5
DOI: http://dx.doi.org/10.1016/j.carres.2013.05.019
Reference: CAR 6495

To appear in: *Carbohydrate Research*

Received Date: 10 May 2013
Accepted Date: 30 May 2013

Please cite this article as: Biela-Banas, A., Gallienne, E., Martin, O.R., A reinvestigation of the synthesis and revision of spectral data of 1,2-*O*-isopropylidene-α-l-sorbofuranose, 1,2:4,6-di-*O*-isopropylidene-α-l-sorbofuranose and derivatives, *Carbohydrate Research* (2013), doi: http://dx.doi.org/10.1016/j.carres.2013.05.019

CARBOHYDRATE RESEARCH Manuscript

NOTE

A reinvestigation of the synthesis and revision of spectral data of 1,2-*O*-isopropylidene- -L-sorbofuranose, 1,2:4,6-di-*O*-isopropylidene- -L-sorbofuranose and derivatives

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Abstract

Mono- and di-*O*-isopropylidene-L-sorbofuranose derivatives are important starting materials for the synthesis of modified sugars and useful chiral compounds. However, several inconsistencies in the spectral data of these compounds and erroneous structural assignments have been noted in the literature. The unambiguous synthesis of 1,2:4,6-di-*O*-isopropylidene- -L-sorbofuranose and of derivatives of 1,2- and 2,3-*O*-isopropylidene- -L-sorbofuranoses has been achieved and definitive spectral data on these compounds are provided.

1. Introduction

1,2:4,6-Di-*O*-isopropylidene- -L-sorbofuranose **1** (Figure 1) is a useful starting material for the synthesis of various modified sugar derivatives including iminosugars,[1,2,3] as well as ligands and catalysts for asymmetric synthesis.[4,5,6] As part of our on-going program on the synthesis of iminosugar derivatives of biological interest,[7,8] we required this L-sorbofuranose derivative as starting material. This compound is now commercially available, but our experience with a commercial sample, which was found to be heterogeneous and to contain a significant amount of L-sorbose, led us to reinvestigate the synthesis of **1** and its derivatives, and to examine literature data on these compounds. We have identified a number of errors in literature reports, with instances of confusion between the 1,2:4,6-di-*O*-isopropylidene derivative **1** and the more common 2,3:4,6-di-*O*-isopropylidene- -L-sorbofuranose **2**, as well as between the corresponding mono-*O*-isopropylidene derivatives. We report in this note the results of our investigations and corrections of data from literature reports with definitive spectral data on both families of compounds.

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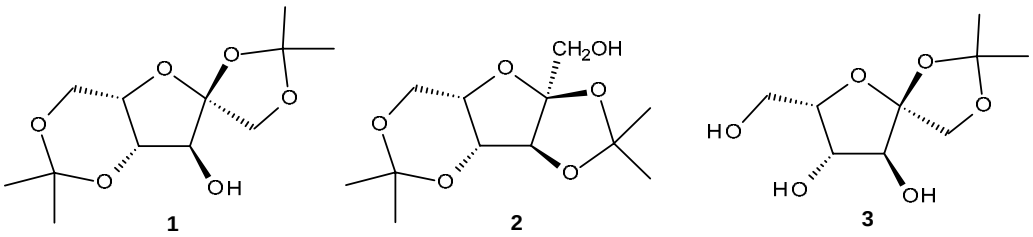


Figure 1. Mono- and di-*O*-isopropylidene derivatives of L-sorbofuranose

2. Results and Discussion

It is well known since Reichstein's work in the 30's that the reaction of L-sorbose with acetone under acidic conditions provides 2,3:4,6-di-*O*-isopropylidene- -L-sorbofuranose **2** in high yield.[9] The 1,2:4,6-isomer **1** has been observed for the first time as a minor product in the reaction mixture from the acetonation of L-sorbose using acetone diethyl acetal in the presence of *p*TsOH, and was characterized (mp and optical activity) by Tokuyama and Honda in 1964.[10] Further investigations on the reaction of L-sorbose with acetone acetals were performed by Maeda and co-workers who isolated also one mono-*O*-isopropylidene-L-sorbofuranose derivative[11] and reported the first NMR data on this family of compounds.[12] It should be noted that in Maeda's paper,[12] the spectrum shown in Fig. 6 corresponds to that of the -anomer VIIa and not to that of the -anomer IXa (incorrect structure number). The first convenient method for the selective preparation of 1,2:4,6-di-*O*-isopropylidene- -L-sorbose **1** was reported in 1988 by Chen and Whistler,[13] as a prelude to their synthesis of L-fructose. The method consists in refluxing L-sorbose in 2,2-dimethoxypropane containing 1,2-dimethoxyethane (DME) in the presence of a catalytic amount of **$SnCl_2$** as a Lewis acidic catalyst, which is the key feature of this protocol. This procedure has been used subsequently by other groups (Tyler,[2] Overkleeft,[3,] Wang[4], Zhao[14]) with yields in the order of 40% when the acetonation was coupled with subsequent reactions (mesylation for example). Behling and co-workers have modified the protocol in order to obtain 1,2-*O*-isopropylidene- -L-sorbofuranose **3** (Figure 1) as the major product, and as the starting material for a short synthesis of 1-deoxynojirimycin.[1]

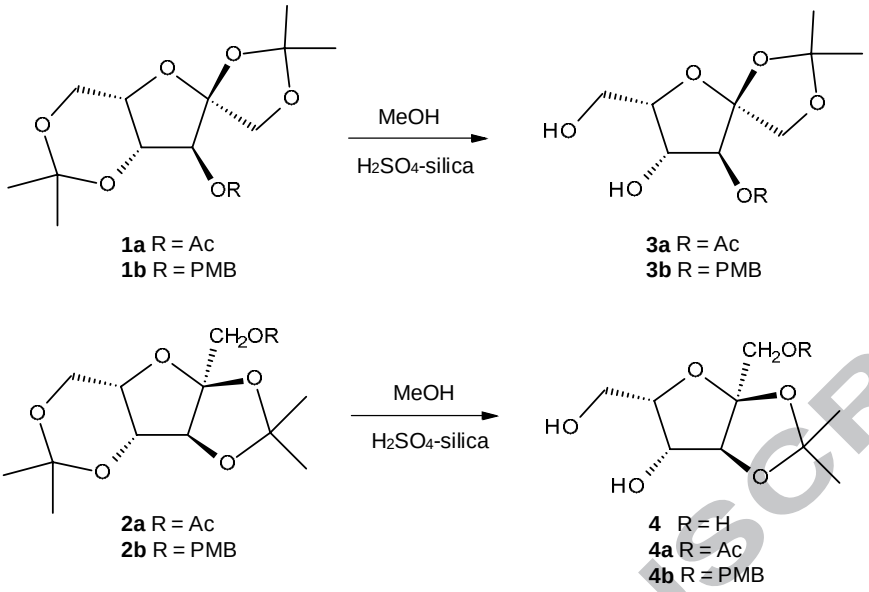
Initially we have experienced difficulties with the protocols of Wang[4] or Chen[13] which consisted in refluxing the reaction mixture until complete disappearance of starting material (the solution becomes clear after 3-4h on a 5g-scale). In our hands, these conditions led to a

In this article, the catalyst is indicated as $SnCl_4$; this is a mistake (H. Overkleeft, personal communication)

mixture of **1** and **2** that could not be separated by crystallisation. As suggested by Zhao,[14] we decreased the reaction temperature to 70°C and stopped it before the solution became clear (1h, 10g-scale). Although the reaction was not complete (66% of L-sorbose was recovered), we were able to obtain mainly the desired isomer **1** that could be purified by recrystallisation from hexane. The purity of 1,2:4,6-di-*O*-isopropylidene- -L-sorbose **1** obtained by this procedure was sufficient to continue the synthesis (yield of 16%, 46% based on consumed L-sorbose).

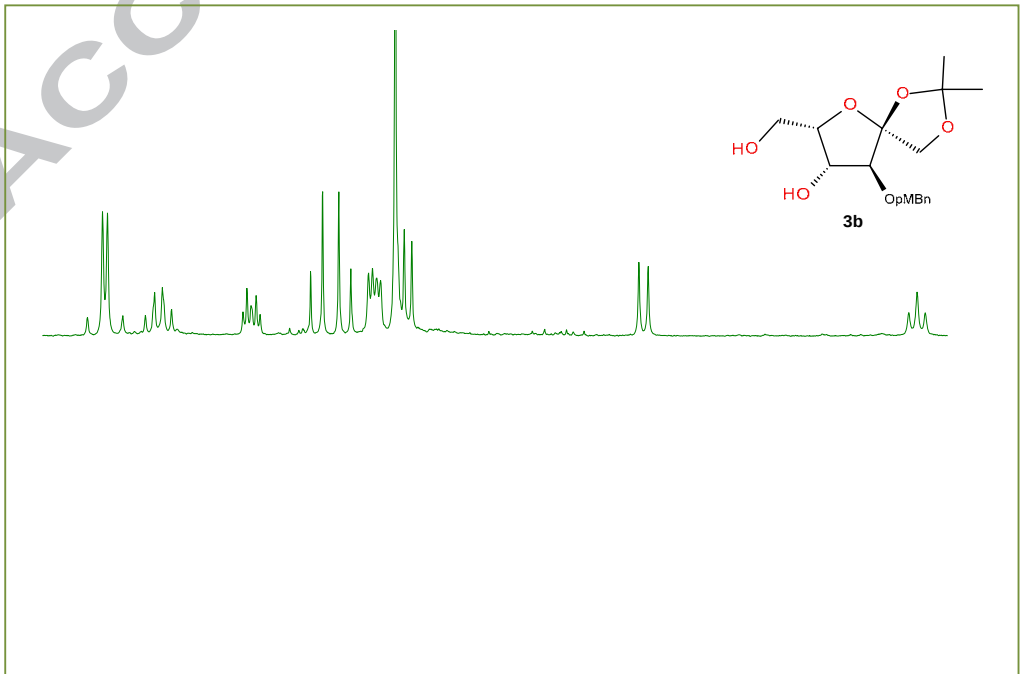
More recently, Mukhopadhyay and co-workers[15] reported a method of synthesis of *O*-isopropylidene and di-*O*-isopropylidene sugar derivatives using sulfuric acid immobilized on silica as the catalyst in refluxing acetone. Among the reported applications of this convenient procedure, the authors indicated that L-sorbose was converted into 1,2:4,6-di-*O*-isopropylidene- -L-sorbofuranose **1** in 86% yield. However, the ^{1}H and ^{13}C-NMR spectra of the isolated compound shown in supplementary materials clearly do not match those of **1**, but matched the spectra of the isomeric 2,3:4,6-di-*O*-isopropylidene- -L-sorbofuranose **2**.

Furthermore, the same authors reported the same year[16] the use of the same supported acidic catalyst for the selective hydrolysis of the less stable *O*-isopropylidene group in common di-*O*-isopropylidene derivatives of hexoses and hexuloses. The reported applications included the selective cleavage of the 4,6-*O*-isopropylidene group in **1**, as well as in the 3-*O*-acetyl, 3-*O*-benzoyl, 3-*O*-benzyl, and 3-*O*-*p*-methoxybenzyl derivatives of **1**, to form the corresponding 1,2-*O*-isopropylidene derivatives of L-sorbose. Considering the error in the first paper, we decided to repeat the synthesis of two of these derivatives, and of the corresponding derivatives in the 2,3:4,6-di-*O*-isopropylidene- -L-sorbofuranose series in order to verify this report.



Scheme 1. Selective hydrolysis of di-*O*-isopropylidene- -L-sorbofuranose derivatives

Thus the *O*-acetyl and *O*-*p*-methoxybenzyl derivatives of **1** and **2**, compounds **1a**,[11,12] **1b**, **2a**,[12,17] and **2b** (Scheme 1), were prepared by standard procedures and then submitted to the selective hydrolysis procedure of Mukhopadhyay et al.[16] Compounds **3a**, **3b**, **4a**,[17,20] and **4b** were isolated generally in good yields (21-80%), and their NMR spectra recorded. For reference, the ^{1}H and ^{13}C-NMR of the important compounds **3b** and **4b** are shown in Figures 2 and 3 (others are provided in supplementary materials). Comparison of these data with the spectra provided in supplementary materials by Mukhopadhyay show clearly that the compounds that they have made are not the 1,2-*O*-isopropylidene derivatives, but the 2,3-*O*-isopropylidene derivatives. That compound **3b** is the correct isomer is further supported by the large chemical shift of the H-3 proton in the 3-*O*-acetyl derivative **3a** (=4.403 ppm).



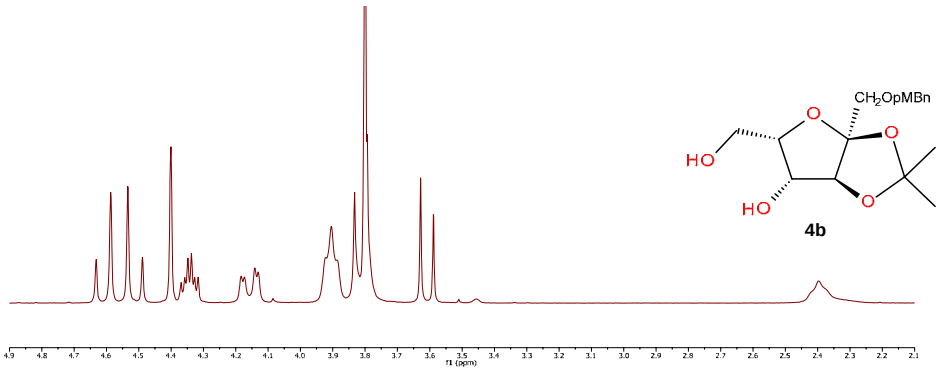


Figure 2. Partial ^{1}H-NMR spectra of **3b** and **4b** ($CDCl_3$, 250 MHz)

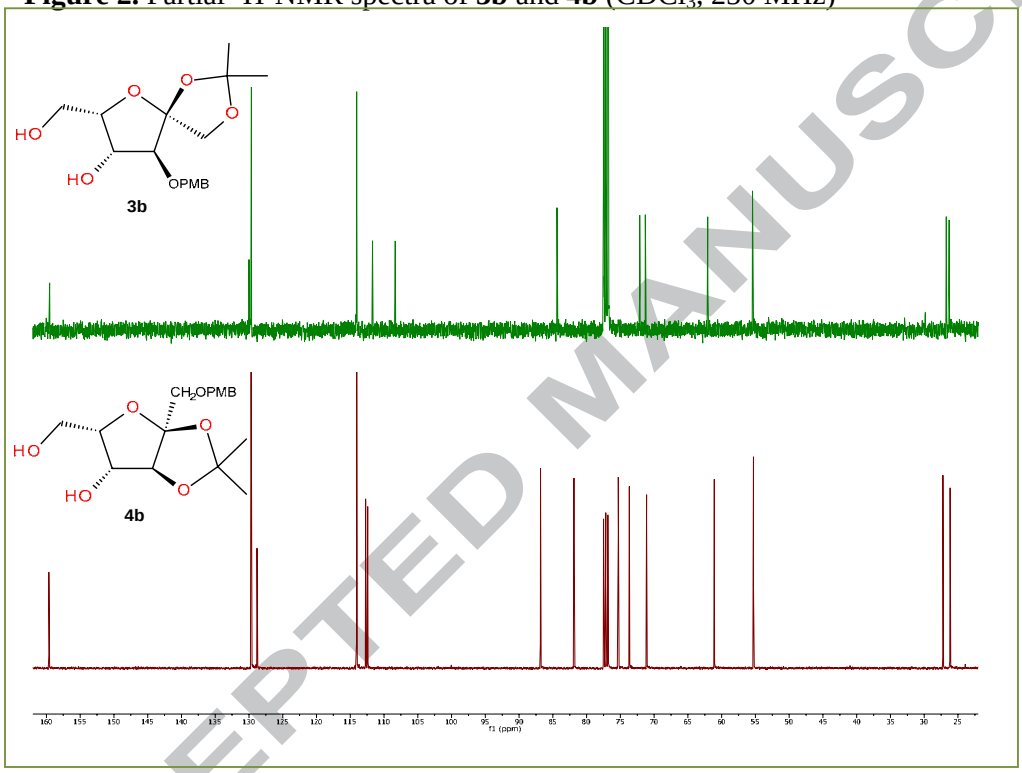


Figure 3. ^{13}C-NMR spectra of **3b** and **4b** ($CDCl_3$, 100 MHz)

Thus it appears clearly that the entire series of compounds made by these authors in the L-sorbose series arises from 2,3:4,6-di-*O*-isopropylidene **2**, which they had incorrectly assigned in the preceding paper. Such compounds are important starting materials and therefore it is significant to note this correction. The same error appears in the 2010 review by Rauter and co-workers on zeolites and other silicon-based promoters in carbohydrate chemistry.[18]

A further correction is required in a study by Rauter and co-workers.[19] This group reported in 1995 the use of zeolite HY as a catalyst for the acetonation of various free sugars. L-Sorbose was submitted to these conditions, and reported to give 2,3:4,6-di-*O*-isopropylidene derivative **2** in 37% yield; however, spectral data provided for this compound indicate that they have obtained the 1,2:4,6-di-*O*-isopropylidene derivative **1.** Thus the procedure reported by this group provides an alternative synthesis of **1**, although the reported yield is not significantly better than that of the $SnCl_2$-catalyzed method.

3. Conclusion

We have achieved in this study the unambiguous synthesis of mono- and di-*O*-isopropylidene- -L-sorbofuranose derivatives in order to verify a number of literature reports. Definitive spectral and characterization data are provided herein for the 3-*O*-acetyl and 3-*O*-*p*-methoxybenzyl derivatives of 1,2-*O*-isopropylidene- -L-sorbofuranose and for the isomeric 1-*O*-substituted 2,3-*O*-isopropylidene- -L-sorbofuranose. These compounds are readily available and therefore constitute useful starting materials for the synthesis of other sugar derivatives or sugar-derived biologically important compounds.

4. Experimental section

4.1. General methods

All reactions requiring anhydrous conditions were carried out using oven-dried glassware under an atmosphere of dry Ar. All reagent-grade chemicals were obtained from commercial suppliers and were used as received. Analytical thin layer chromatography was performed using Silica Gel $60F_{254}$ precoated plates (Merck) with visualization by ultraviolet light and phosphomolybdic acid or ceric sulfate/ammonium molybdate solutions. Flash chromatography was performed on Silica Gel 60 (230-400 mesh).

Melting points were determined in capillary tubes with a Büchi apparatus and are uncorrected. Optical rotations were measured in appropriate solvent at the indicated temperature in a 1-dm cell with a Perkin-Elmer 341 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance DPX 250 or Bruker Avance 400 spectrometers. Chemical shifts are given in ppm and are referenced to the residual solvent signal or to TMS as internal standard. Carbon multiplicities were assigned by distortionless enhancement by polarization transfer (DEPT) experiments. ^{1}H and ^{13}C signals were attributed on the basis of H-H and H-C correlations. High resolution mass spectra were recorded on a Bruker Q-TOF MaXis spectrometer .

4.2. 1,2:4,6-Di-*O*-isopropylidene- -L-sorbofuranose (1)[10,11,12]

The reaction was conducted under argon. To a suspension of L-sorbose (10 g, 0.056 mol) in 2,2-dimethoxypropane (30 mL) was added $SnCl_2$ (50 mg, 0.005 eq) in DME (1 mL). The reaction was left stirring 1h at 70°C and then quenched with Et_3N (0.26 mL, 0.06 eq). The remaining sorbose was removed by filtration and the filtrate was concentrated under vacuum. The residue was dissolved in EtOAc (100 mL) and washed with H_2O (2x50 mL). The organic phase was dried over $MgSO_4$ and concentrated under vacuum. The crude product was obtained as a yellow oil which crystallized overnight. Recrystallization from *n*-hexane gave pure **1** as a white solid (2.275 g, 16%; 46% based on consumed L-sorbose): ^{1}H NMR (250 MHz, $CDCl_3$) 4.26 (dd, 1H, H-4, $J_{4\text{-}3}$=1.3 Hz, $J_{4\text{-}5}$=2.8 Hz), 4.17-4.14 (m, 3H, 2H-1, H-5), 4.00-3.95 (m, 3H, 2H-6, H-3), 2.85 (d, 1H, OH, J=2.3 Hz), 1.54 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.36 (s, 3H, CH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$) 111.23, 110.51 (C^{IV}iPr), 97.42 (C-2), 79.31 (C-3), 74.34 (C-4), 72.90 (C-1), 72.43 (C-5), 60.43 (C-6), 28.49, 26.33, 25.42, 19.23 (CH_3).

4.3. General procedure for acetylation

To a solution of **1** or **2** (1 eq) in pyridine (0.5 M) was added Ac_2O (5 eq). The reaction was left stirring overnight at room temperature. CH_2Cl_2 (13 mL/mL of pyridine) was then added. The organic phase was separated, washed with 1N aqueous HCl, then with water and dried over $MgSO_4$. After concentration under vacuum, **1a** or **2a** were obtained as clean products.

4.3.1. 3-*O*-Acetyl 1,2:4,6-di-*O*-isopropylidene- -L-sorbofuranose (1a)[11,12]

From **1** (150 mg, 0.58 mmol), **1a** was obtained as a colorless oil (173 mg, 99 %): [ ]$_D$ -64.7 (*c* 1.12, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 5.15 (br s, 1H, H-3), 4.31 (dd, 1H, H-4, $J_{4\text{-}3}$=1.4 Hz, $J_{4\text{-}5}$=2.8 Hz), 4.29 (d, 1H, H-1$_b$, $J_{1b\text{-}1a}$=9.2 Hz), 4.18 (d, 1H, H-1$_a$, $J_{1a\text{-}1b}$=9.2 Hz), 4.14 (q, 1H, H-5, J~2.8 Hz), 4.03 (dd, 1H, H-6$_b$, $J_{6b\text{-}5}$=2.8 Hz, $J_{6b\text{-}6a}$=13.2 Hz), 3.95 (dd, 1H, H-6$_a$, $J_{6a\text{-}5}$=2.8 Hz, $J_{6a\text{-}6b}$=13.2 Hz), 2.12 (s, 3H, OAc), 1.50 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 169.44 (C=O), 111.03, 110.25 (C^{IV}iPr), 97.90 (C-2), 79.31 (C-3), 73.59 (C-1), 73.31 (C-4), 72.06 (C-5), 60.36 (C-6), 28.47, 25.94, 25.79, 19.52 (CH_3), 20.73 (CH_3CO); HRMS Calcd for $C_{14}H_{26}NO_7$ $[M+NH_4]^+$

m/z = 320.170379. Found: 320.169904. Calcd for $C_{14}H_{22}NaO_7$ $[M+Na]^+$ *m/z* = 325.125774. Found: 325.125450.

4.3.2. 1-*O*-Acetyl 2,3:4,6-di-*O*-isopropylidene- -L-sorbofuranose (2a)[12,17]

From **2** (200 mg, 0.77 mmol), **2a** was obtained as a colorless oil (233 mg, quant): $[\ ]_D$ -13.9 (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 4.56 (d, 1H, H-1_b, J_{1b-1a}=12.0 Hz), 4.43 (s, 1H, H-3), 4.33 (d, 1H, H-4, J_{4-5}=2.0 Hz), 4.17 (d, 1H, H-1_a, J_{1a-1b}=12.0 Hz), 4.12 (q, 1H, H-5, *J*~2.0 Hz), 4.10-4.00 (m, 2H, 2H-6), 2.11 (s, 3H, OAc), 1.51 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.39 (s, 3H, CH_3) , 1.37 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 169.97 (C=O from OAc), 112.56, 112.16 (C^{IV}iPr), 97.28 (C-2), 84.55 (C-3), 73.11 (C-4), 72.34 (C-5), 63.42 (C-1), 60.04 (C-6), 28.82, 27.34, 26.26, 18.57 ($\underline{C}H_3$), 20.76 ($\underline{C}H_3$OAc); HRMS Calcd for $C_{14}H_{23}O_7$ $[M+H]^+$ *m/z* = 303.143829. Found: 303.140610. Calcd for $C_{14}H_{26}NO_7$ $[M+NH_4]^+$ *m/z* = 320.170379. Found: 320.170543. Calcd for $C_{14}H_{22}NaO_7$ $[M+Na]^+$ *m/z* = 325.125774. Found: 325.125708.

4.4. General procedure for protection with a *p*-methoxybenzyl group

To a solution of **1** or **2** (1 eq) in anhydrous DMF (0.5 M) at 0°C was added sodium hydride (60% dispersion in oil, 2 eq). When H_2 evolution ceased (5 min), *p*-methoxybenzyl chloride (1.5 eq) was added dropwise. The reaction mixture was left stirring overnight at room temperature. The reaction was quenched with ice-water. EtOAc (4 mL/mL of DMF) was added. The organic phase was washed with water, saturated $NaHCO_3$ and then dried over $MgSO_4$. After concentration under vacuum, the crude product was purified by flash column chromatography on silica gel (Pet. Ether/EtOAc 8:2) to afford pure **1b** or **2b**.

4.4.1. 3-*O*-*p*-Methoxybenzyl-1,2:4,6-di-*O*-isopropylidene- -L-sorbofuranose (1b)

From **1** (100 mg, 0.38 mmol), **1b** was obtained as a slightly yellow solid (136 mg, 93%): mp 98-99 °C; $[\ ]_D$ -18.7 (*c* 1.86, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 7.29 (d, 2H, H_{ar}, *J*=8.5 Hz), 6.87 (d, 2H, H_{ar}, *J*=8.75 Hz), 4.71 (d, 1H, C$\underline{H}_2$OPMB, *J*=11.8 Hz), 4.61 (d, 1H, C$\underline{H}_2$OPMB, *J*=11.8 Hz), 4.26 (dd, 1H, H-4, J_{4-3}=1.8 Hz, J_{4-5}=3.5 Hz), 4.19 (br q, 1H, H-5, *J*=3.5 Hz), 4.14 (d, 1H, H-1_b, *J*=9.5 Hz), 4.02 (d, 1H, H-1_a, *J*=9.5 Hz), 3.96 (dd, 1H, H-6_b, J_{6b-5}=3.5 Hz, J_{6b-6a}=12.8 Hz), 3.84 (dd, 1H, H-6_a, J_{6a-5}=3.5 Hz, J_{6a-6b}=12.8 Hz), 3.80 (s, 4H, C$\underline{H}_3$O, H-3), 1.54 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 159.42 (C^{IV}_{ar}), 129.84 (C^{IV}_{ar}), 129.61 (C_{ar}), 113.85 (C_{ar}), 110.94, 110.80 (C^{IV}iPr), 97.96 (C-2), 84.55 (C-3), 74.01 (C-4), 73.27 ($\underline{C}H_2$OPMB), 72.67 (C-1),72.14

(C-5), 60.59 (C-6), 55.31 ($\underline{C}H_3O$), 28.02, 26.30, 26.12, 20.28 ($4CH_3$); HRMS Calcd for $C_{20}H_{29}O_7$ $[M+H]^+$ *m/z* = 381.190780. Found: 381.190771. Found: 398.217264. Calcd for $C_{20}H_{28}NaO_7$ $[M+Na]^+$ *m/z* = 403.172724. Found: 403.172306.

4.4.2. 1-*O*-*p*-Methoxybenzyl-2,3:4,6-di-*O*-isopropylidene- -L-sorbofuranose (2b)

From **1** (100 mg, 0.38 mmol), **2b** was obtained as a colorless oil (127 mg, 87%):[ ]$_D$ -4.80 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 7.27 (d, 2H, H_{ar}, *J*=8.4 Hz), 6.86 (d, 2H, H_{ar}, *J*=8.4 Hz), 4.65 (d, 1H, $C\underline{H}_2$OPMB, *J*=11.6 Hz), 4.52 (d, 1H, $C\underline{H}_2$OPMB, *J*=11.6 Hz), 4.48 (s, 1H, H-3), 4.29 (d, 1H, H-4, $J_{4\text{-}5}$=2.4 Hz), 4.10-4.07 (m, 1H, H-5), 4.04 (dd, 1H, H-6_b, $J_{6b\text{-}5}$=2.2 Hz, $J_{6b\text{-}6a}$=13.6 Hz), 3.98 (d, 1H, H-6_a, $J_{6a\text{-}6b}$=13.6 Hz), 3.79 (s, 3H, CH_3), 3.77 (d, 1H, H-1_b, $J_{1b\text{-}1a}$=10.8 Hz), 3.69 (d, 1H, H-1_a, $J_{1a\text{-}1b}$=10.8 Hz), 1.51 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.29 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 159.17 (C^{IV}_{ar}), 130.37 (C^{IV}_{ar}), 129.30 (C_{ar}), 114.24 (C^{IV}iPr), 113.76 (C_{ar}), 112.27 (C^{IV}iPr), 97.30 (C-2), 84.37 (C-3), 73.32 (C-4), 73.30 ($\underline{C}H_2$OPMB), 72.16 (C-5), 69.63 (C-1), 60.40 (C-6), 55.31 ($\underline{C}H_3$OBn), 28.97, 27.66, 26.60, 18.69 ($\underline{C}H_3$); HRMS Calcd for $C_{20}H_{32}NO_7$ $[M+NH_4]^+$ *m/z* = 398.217329. Found: 398.217460. Calcd for $C_{20}H_{28}NaO_7$ $[M+Na]^+$ *m/z* = 403.172724. Found: 403.172497.

4.5. General procedure for selective cleavage of the 4,6-*O*-isopropylidene group[16]

H_2SO_4 on silica was prepared according to the protocol of Mukhopadhyay.[15] To a solution of **1a**, **2a**, **1b** or **2b** (1 mmol) in MeOH (5 mL), silica-H_2SO_4 (100 mg) was added. The mixture was left stirring at room temperature until completion of the reaction (TLC, 1h-4h). The suspension was filtered on a membrane and the filtrate was concentrated under vacuum to give respectively crude **3a**, **4a**, **3b** or **4b**. Flash column chromatography on silica gel (CH_2Cl_2/MeOH 95:5) afforded the pure products.

4.5.1. 3-*O*-Acetyl-1,2-*O*-isopropylidene- -L-sorbofuranose (3a)

From **1a** (67 mg, 0.22 mmol), **3a** was obtained as a white solid (44 mg, 76%): mp 133-135 °C; [ ]$_D$ -111.4 (*c* 1.23, MeOH); ^{1}H NMR (400 MHz, CD_3OD) (d, 1H, H-3, $J_{3\text{-}4}$=5.2 Hz), 4.40 (t, 1H, H-4, $J_{4\text{-}3}$=5.2 Hz, $J_{4\text{-}5}$=5.6 Hz), 4.20 (d, 1H, H-1_b, *J*=9.2 Hz), 4.16 (q, 1H, H-5, *J*~5 Hz), 4.05 (d, 1H, H-1_a, *J*=9.2 Hz), 3.75 (dd, 1H, H6_b, $J_{5\text{-}6b}$=4.4 Hz, $J_{6a\text{-}6b}$=12.0 Hz), 3.71 (dd, 1H, H6_a, $J_{5\text{-}6a}$=5.2 Hz, $J_{6a\text{-}6b}$=12.0 Hz), 2.10 (s, 3H, OAc), 1.44 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (100 MHz, CD_3OD) 171.90 (C=O), 112.11, 109.58 (C^{IV}iPr, C-2), 80.48

(C-5), 80.44 (C-3), 74.77 (C-4), 73.13 (C-1), 61.79 (C-6), 26.49, 26.31 (2x$\underline{C}H_3$), 20.67 ($\underline{C}H_3CO$); HRMS Calcd for $C_{11}H_{18}NaO_7$ $[M+Na]^+$ *m/z* = 285.094474. Found: 285.094838.

4.5.2. 1-*O*-Acetyl 2,3-*O*-isopropylidene- -L-sorbofuranose (4a)[17,20]

From **2a** (100 mg, 0.33 mmol), **4a** was obtained (30 mg, 34%) along with deacetylated **4** (39 mg, 53%) as yellow oils. **4a**: ^{1}H NMR (250 MHz, CD_3OD) 4.46 (d, 1H, H-1_b, J_{1b-1a}=11.8 Hz), 4.40 (s, 1H, H-3), 4.28 (ddd, 1H, H-5, J_{5-4}=2.8 Hz, J_{5-6b}=5.0 Hz, J_{5-6a}=6.25 Hz), 4.17 (d, 1H, H-4, J_{4-5}=2.8 Hz), 4.09 (d, 1H, H-1_a, J_{1a-1b}=11.8 Hz), 3.80 (dd, 1H, H-6_b, J_{5-6b}=5.0 Hz, J_{6a-6b}=11.8 Hz), 3.74 (dd, 1H, H-6_a, J_{5-6a}=6.25 Hz, J_{6a-6b}=11.75 Hz), 2.07 (s, 3H, OAc), 1.47 (s, 3H, CH_3), 1.36 (s, 3H, CH_3); ^{13}C NMR (100 MHz, CD_3OD) 171.98 (C=O), 113.67, (C^{IV}iPr), (C-2), 87.00 (C-3), 83.41 (C-5), 75.76 (C-4), 64.49 (C-1), 61.13 (C-6), 27.72, 26.77 ($\underline{C}H_3$), 20.75 ($\underline{C}H_3$OAc).

4.5.3. 2,3-*O*-Isopropylidene- -L-sorbofuranose (4)[11,21]

^{1}H NMR (250 MHz, CD_3OD) 4.39 (s, 1H, H-3), 4.29 (ddd, 1H, H-5, J_{5-4}=2.8 Hz, J_{5-6b}=5.3 Hz, J_{5-6a}=6.3 Hz), 4.13 (d, 1H, H-4, J_{4-5}=2.8 Hz), 3.81 (dd, 1H, H-6_b, J_{6b-5}=5.3 Hz, J_{ba-6b}=11.5 Hz), 3.73 (dd, 1H, H-6_a, J_{6a-5}=6.3 Hz, J_{6a-6b}=11.5 Hz), 3.68 (s, 2H, 2H-1), 1.48 (s, 3H, $C\underline{H}_3$), 1.36 (s, 3H, $C\underline{H}_3$); ^{13}C NMR (62.5 MHz, CD_3OD) 115.54, 113.12 (C^{IV}iPr, C-2), 86.79 (C-3), 83.33 (C-5), 75.65 (C-4), 63.78 (C-1), 61.13 (C-6), 27.77, 26.86 (2x$\underline{C}H_3$).

4.5.4. 3-*O*-*p*-Methoxybenzyl-1,2-*O*-isopropylidene- -L-sorbofuranose (3b)

From **1b** (136 mg, 0.36 mmol), **3b** was obtained as a white solid (25 mg, 21%): mp 119-120 °C; $[\ ]_D$ -57.6 (*c* 0.86, MeOH); ^{1}H NMR (250 MHz, $CDCl_3$) 7.30 (d, 2H, H_{ar}, *J*=8.5 Hz), 6.89 (d, 2H, H_{ar}, *J*=8.7 Hz), 4.74 (d, 1H, $C\underline{H}_2$OPMB, *J*=11.8 Hz), 4.68 (d, 1H, $C\underline{H}_2$OPMB, *J*=11.8 Hz), 4.54 (dt, 1H, H-4, J_{4-5}=7.0 Hz, J_{4-3}=6.0 Hz, J_{4-OH}=7 Hz), 4.25 (dt, 1H, H-5, J_{5-6}=3.25 Hz, J_{4-5}=7.0 Hz), 4.05 (d, 1H, H-1, *J*=9.25 Hz), 3.97 (d, 1H, H-1, *J*=9.25 Hz), 3.87 (dd, 2H, 2H6, J_{6-5}=3.25 Hz, J_{6-OH}=6.25 Hz), 3.81 (s, 3H, $C\underline{H}_3O$), 3.77 (d, 1H, H-3, J_{3-4} =6.0 Hz), 3.04 (d, 1H, 4-OH, *J*=7.25 Hz), 2.20 (t, 1H, $CH_2\underline{OH}$, *J*=6.5 Hz), 1.51 (s, 3H, CH_3), 1.46 (s, 3H, CH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$) 159.53, 129.99 (C^{IV}_{ar}), 129.64, 114.04 (C_{ar}), 111.70, 108.33 (C^{IV}iPr, C-2), 84.37 (C-3), 77.13 (C-4), 76.89 (C-5), 72.12 (C-1), 71.29 ($\underline{C}H_2$OPMB), 62.07 (C-6), 55.43 ($\underline{C}H_3O$), 26.74, 26.31 (2x$\underline{C}H_3$); HRMS Calcd for $C_{17}H_{28}NO_7$ $[M+NH_4]^+$ *m/z* = 358.186029. Found: 358.185917. Calcd for $C_{17}H_{24}NaO_7$ $[M+Na]^+$ *m/z* = 363.141424. Found: 363.141514.

4.5.5. 1-*O*-*p*-Methoxybenzyl-2,3-*O*-isopropylidene- -L-sorbofuranose (4b)

From **2b** (127 mg, 0.33 mmol), **4b** was obtained as a white solid (90 mg, 80%): mp 60-61 °C; [ ]$_D$ +4.15 (*c* 1.42, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) 7.24 (d, 2H, H_{ar}, *J*=8.5 Hz), 6.86 (d, 2H, H_{ar}, *J*=8.6 Hz), 4.60 (d, 1H, C$\underline{H}_2$OPMB, *J*=11.3 Hz), 4.51 (d, 1H, C$\underline{H}_2$OPMB, *J*=11.3 Hz), 4.40 (br s, 1H, H-3), 4.33 (td, 1H, H-5, $J_{4\text{-}5}$=2.8 Hz, $J_{5\text{-}6}$=5.2 Hz), 4.16 (dd, 1H, H-4, $J_{4\text{-}5}$=2.7 Hz, $J_{4\text{-OH}}$= 10.6 Hz), 3.89 (br t, 2H, 2H-6, $J_{5\text{-}6}$=5.6 Hz), 3.84 (d, 1H, OH, *J*=10.6 Hz), 3.80 (d, 1H, H-1, J=10.0 Hz), 3.79 (s, 3H, C$\underline{H}_3$O), 3.61 (d, 1H, H-1, *J*=10.0 Hz), 2.63 (t, 1H, $CH_2\underline{OH}$, *J*=6.1 Hz), 1.50 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 159.63 (C^{IV}_{ar}), 129.66 (C_{ar}), 128.82 (C^{IV}_{ar}), 114.05 (C_{ar}), 112.72, 112.41 (C^{IV}iPr, C-2), 86.82 (C-3), 81.87 (C-5), 75.31 (C-4), 73.67 (C$\underline{H}_2$OPMB), 71.13 (C-1), 61.09 (C-6), 55.29 (C$\underline{H}_3$O), 27.23, 26.18 (2xC$\underline{H}_3$); HRMS Calcd for $C_{17}H_{25}NO_7$[M+H]$^+$ *m/z* = 341.159480. Found: 341.159301. Calcd for $C_{17}H_{24}NaO_7$ [M+Na]$^+$ *m/z* = 363.141424. Found: 363.141371.

Acknowledgements

The authors want to thank Pr. Arnaud Tatibouët for the gift of compound **2**, the "Ministère de l'Enseignement Supérieur et de la Recherche" for a PhD fellowship (ABB) and the LABEX *SynOrg* (ANR-11-LABX-0029) for financial support.

Supplementary data

Supplementary data associated with this article can be found, in the on-line version, at http://

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