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Carbohydrate Research 340 (2005) 753–758
Carbohydrate RESEARCH

Note

Stereoselective synthesis of a ketohexofuranose from an aldohexopyranose by a [6+1−1] strategy

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Received 25 May 2004; received in revised form 28 December 2004; accepted 5 January 2005

This paper is dedicated to Professor G. Descotes, Université Claude Bernard, Lyon I, France

Abstract—Ozonolysis of 2-acetoxymethyl-1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol gave 1-*O*-acetyl-3,4,6-tri-*O*-benzyl-4-*O*-formyl-D-*arabino*-hex-2-ulose (**5**). Subsequent hydrolysis and acetylation of **5** provided 1,2-di-*O*-acetyl-3,4,6-tri-*O*-benzyl-D-fructofuranose **6** in excellent yield. This methodology allows specific deuteration at C-1 of a protected D-fructofuranose derivative. This approach therefore could serve as [6+1−1] formulation for hexose series inter-conversion, that is, aldohexopyranose to ketohexofuranose.

Keywords: Glycal; Fructofuranose; Deuterated fructofuranose; Ozonolysis; Isotopic labelling; Ketohexofuranose; Aldohexopyranose

D-Fructofuranose is seldom available as a distinct isomeric entity because D-fructose rapidly mutarotates through acyclic keto forms and can exist in as many as five tautomers.[3] In aqueous solution D-fructose exists predominantly in the pyranose form with a very small amount of the furanose form.[4]

Synthesis of furanose oligosaccharides and their related analogues is important because they form the core structure of bacterial cell walls and can act as either glycosyl transferase substrates or inhibitors.[5] Generally, furanose oligosaccharides are synthesized using unprotected reducing sugars in a controlled Fischer glycosylation reaction or via sugar dithioacetals.[6] D'Souza et al., have reported the synthesis of furanose oligosaccharides by ozonolysis of protected pyranose glycals.[7]

As part of our ongoing research in glycal chemistry,[8] we envisaged a synthetic route for the synthesis of highly functionalized D-fructofuranose and its C-1 deuterated counterpart from 2-acetoxymethyl-1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (**4**). Conceptually, we introduced a one carbon unit at the C-2 position of the aldopyranose glucal, which in turn will form the C-1 of the fructofuranose compound at the expense of one carbon loss from the ring during the course of the reaction.

The synthesis of **4** was reported previously by our laboratory[1,2,†] starting from 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (**1**) as outlined in Scheme 1.

Glycal **4** was subjected to ozonolysis to give the ketoformate **5** in excellent yield. Hydrolysis of **5** afforded the diol **11**, (Scheme 2) which was directly acetylated to give 1,2-di-*O*-acetyl-3,4,6-tri-*O*-benzyl-D-fructofuranose (**6**) in good yield. The ^{1}H NMR and ^{13}C NMR spectra indicate that this product is not a mixture of anomers but a single anomer. Efforts were not undertaken to establish the stereochemistry at the anomeric center. An important point to note is that the furanose derivative **6** cannot re-open and recyclize to give the pyranose form

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† For preliminary communications, see in parts Refs. 1,2.

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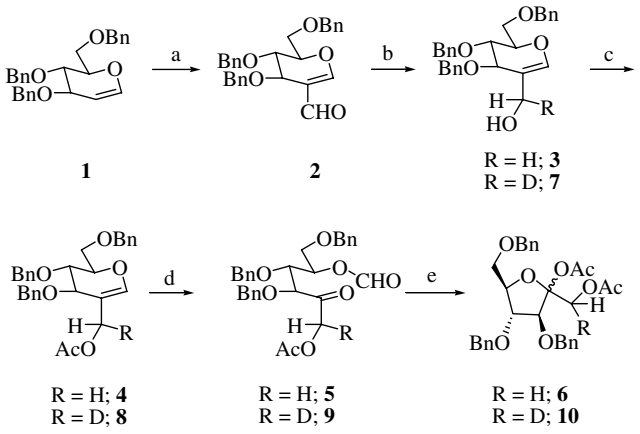
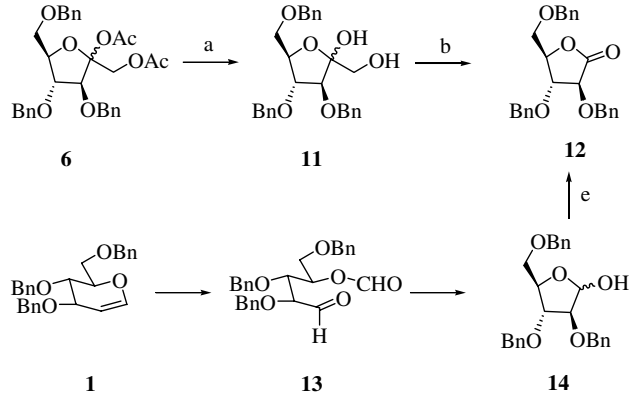
doi:10.1016/j.carres.2005.01.008



Scheme 1. Reagents and conditions: (a) DMF, $POCl_3$, 0 °C to rt, 60%;[1] (b) (R = H) $NaBH_4$, MeOH, 90% or (R = D) $LiAlD_4$, THF, 86%; (c) Ac_2O, Et_3N, cat DMAP, CH_2Cl_2, 92%;[2] (d) O_3, PPh_3, CH_2Cl_2, −78 °C, 90%; (e) Na_2CO_3/MeOH, Ac_2O, Et_3N, cat DMAP, CH_2Cl_2, 92%.



Scheme 2. Reagents and conditions: (a) Na_2CO_3, MeOH, 90%; (b) $NaIO_4$, CH_2Cl_2, 78%; (c) O_3, PPh_3, −78 °C, 86%; (d) Na_2CO_3, MeOH, 90%; (e) PDC, EtOAc, 84%.

because the C-6 hydroxyl group is protected as benzyl ether in the furanose form (Scheme 1).

This synthetic route offers scope for specific deuterium labelling in the furanose product at the C-1 position. Reduction of 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-formyl-D-*arabino*-hex-1-enitol (**2**) with $LiAlD_4$ furnished the alcohol **7**, which was acetylated to give the 2-acetoxymonodeuteromethyl-1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (**8,** Scheme 1). By virtue of introduction of a deuterium atom, one could expect the formation of diastereomers in the reduction of aldehyde **2** by lithium aluminum deuteride. In the ^{1}H NMR spectrum of **8**, the signal due to the proton attached to the newly generated chiral center bearing the deuterium and acetoxy group overlapped with the signals of the benzylic protons in the region of δ 4.43–4.72 ppm and could not be identified distinctly. The ^{1}H NMR spectrum of **8** did not throw any light on this point and it was not possible to determine whether it was a single diastereomer. As a result, no useful information about the diastereoselectivity could be obtained from the ^{1}H NMR spectrum of **8**. Fortunately, an answer to this question was provided by careful analysis of the ^{1}H NMR spectra of **9** and **5** derived from the ozonolysis of monodeuteroacetate glycal **8** and undeuterated acetate glycal **4**, respectively.

The ^{1}H NMR spectrum of **5** displayed a distinct AB quartet pattern for the diastereotopic methylene protons of –$COCH_aH_b$–OAc, with a doublet at δ 4.78 ppm (J 18.1 Hz) and the other doublet at δ 5.04 ppm (J 18.1 Hz). This AB quartet was clearly absent in the ^{1}H NMR spectrum of **9**. The doublet seen at δ 5.04 ppm due to one of the diastereotopic proton of –$COCH_aH_b$–OAc of **5** disappeared almost completely in the case of **9**. Also the doublet at δ 4.78 ppm due to the other geminal diastereotopic proton of **5** had collapsed into a singlet, integrating nearly for one proton in the case of the monodeuteroacetate **9**. From the ^{1}H NMR spectral data, it is evident that the lithium aluminum deuteride reduction of **2** exhibited high diastereoselectivity to the tune of 95:5, although the configuration of the new chiral center could not be determined from the available data.

Deuteroglycal **8** was successfully subjected to ozonolysis to provide the deutero-keto-formate **9**, which was subsequently hydrolyzed, cyclized and acetylated to give the C-1 deuterated furanose sugar viz., 1,2-di-*O*-acetyl-3,4,6-tri-*O*-benzyl-1′-deutero-D-fructofuranose **10** in 90% yield.

The presence of the intact furanose ring in **6** was also established by chemical means. Hydrolysis of **6** with Na_2CO_3/MeOH gave the diol **11** (Scheme 2) which, upon subsequent periodate oxidation, afforded 2,3,5-tri-*O*-benzyl-D-*arabinono*-1,4-lactone **12** in 78% yield with a rotation in agreement with the reported literature value.[9] Lactone **12** was also compared with an authentic sample, prepared by an unambiguous route starting with the ozonolysis of **1** to yield the formate aldehyde **13** in 86% yield (Scheme 2). Hydrolysis of **13** followed by oxidation of the acetal **14** with PDC afforded **12** in 84% yield, which was identical in all respects with the product obtained from degradation of the fructofuranose compound **6**.

In summary, we have developed a stereoselective synthetic route to 1,2-di-*O*-acetyl-3,4,5-tri-*O*-benzyl-D-fructofuranose (**6**), which is useful for the introduction of specific labelling at C-1 position as in **10**. This approach therefore could serve as [6 + 1 − 1] strategy for hexose series interconversion, that is, aldohexopyranose to ketohexofuranose. This methodology can be extended to other glycals also, enabling the synthesis of other ketohexofuranose sugars viz., D-tagatofuranose, D-sorbofuranose and D-psicofuranose.

1. Experimental

1.1. General

1.1.1. Procedure for the reduction of glycal 2 with $NaBH_4$ or $LiAlD_4$. To a soln of aldehyde **2** (1 mmol) in MeOH (5 mL) [THF 5 mL in the case of $LiAlD_4$] was added $NaBH_4$ or $LiAlD_4$ (2 mmol) and the reaction mixture was stirred at room temperature for 16 h (0 °C to room temperature for 6 h in the case of $LiAlD_4$). The reaction mixture was quenched with satd NH_4Cl and extracted with ether (3 × 25 mL). The combined organic washings were evaporated under diminished pressure and the products, **3** and **7** were subjected to acetylation without purification.

1.1.2. Procedure for the acetylation of 3, 7, 11. To compound **3** or **7**, **11** (1 mmol) in dry CH_2Cl_2 (10 mL) was added Ac_2O (2.5 mmol), Et_3N (4 mmol) and DMAP (5 mol % with respect to Et_3N) and the reaction mixture was stirred for 3 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 and washed successively with 2 N HCl (2 × 25 mL), satd $NaHCO_3$ and water. The organic layer was evaporated under diminished pressure, purified by column chromatography over silica gel using 9:1 hexane–EtOAc as eluent to afford 1,2-di-*O*-acetyl-3,4,6-tri-*O*-benzyl-D-fructofuranose **4**, **8** and **6**, respectively.

1.1.3. General procedure for the ozonolysis of glycals 1, 4 and 8. Compound **1** or **4** or **8** (1 mmol) in dry CH_2Cl_2 (15 mL) was treated with O_3 at −78 °C until the soln became light blue in colour (~45 min). Subsequently, PPh_3 (2 mmol) was added and the reaction mixture was allowed to warm up to room temperature and stirred for 3 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL), concentrated under diminished pressure, purified by column chromatography over silica gel using 4:1 hexane–EtOAc, as eluent.

1.1.4. General procedure for the hydrolysis of 5, 6, 9 and 13. To compound **5** or **6** or **9** or **13** (1 mmol) in MeOH (15 mL) was added anhyd Na_2CO_3 (2 mmol). The reaction mixture was stirred at room temperature for 30 min. The solids were removed by filtration and the filtrate was evaporated under diminished pressure. The thick syrup was used further without purification.

1.2. 1,5-Anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-formyl-D-*arabino*-hex-1-enitol (2)

To a soln of 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (**1** (0.5 g, 1.2 mmol) in DMF (2 mL) was added $POCl_3$ (0.33 mL, 3.6 mmol) slowly at 0 °C. The reaction was stirred at room temperature for 4 h followed by the addition of satd $NaHCO_3$ (10 mL). The reaction mixture was then extracted with ether (3 × 25 mL). The combined organic washings were evaporated under diminished pressure and the product was purified by column chromatography over silica gel using 9:1 hexane–EtOAc as eluent to give **2** (0.32 g, 60%) as a viscous liquid; R_f 0.4 (4:1 hexane–EtOAc); $[\alpha]_D^{25}$ +6.8 (*c* 0.34, $CHCl_3$); IR (CCl_4) *ν* (cm^{-1}): 3080, 3020, 2860, 2725, 1665, 1620, 1450, 1365, 1270, 1200, 1060, 870, 700; ^1H NMR (400 MHz): 9.39 (s, 1H, C*H*O), 7.20–7.50 (m, 16H's, Ar–H, H-1), 4.40–4.70 (m, 8H, 3 × –OCH_2Ph, H-6a, H-5), 3.50–3.90 (m, 3H, H-6b, H-4, H-3); ^{13}C NMR (100 MHz): *δ* 190.40 (d, C*H*O), 164.34 (d, C-1), 138.11 (s, Ar–*C*), 137.58 (s, Ar–*C*), 137.17 (s, Ar–*C*), 128.55 (d, Ar–*C*H), 128.44 (d, Ar–*C*H), 128.35 (d, Ar–*C*H), 128.05 (d, Ar–*C*H), 127.89 (d, Ar–*C*H), 127.83 (d, Ar–*C*H), 127.76 (d, Ar–*C*H), 127.71 (d, Ar–*C*H), 117.69 (s, C-2), 79.34 (d, C-5), 73.36 (t), 72.43 (t), 71.63 (t), 71.29 (d), 68.39 (t), 65.22 (d). Anal. Calcd for $C_{28}H_{28}O_5$: C, 75.67; H, 6.30. Found: C, 75.29, H, 6.05.

1.3. 1,5-Anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-hydroxymethyl-D-*arabino*-hex-1-enitol (3)

From **2** (0.44 g); viscous liquid (0.34 g, 76%); R_f 0.2 (4:1 hexane–EtOAc); $[\alpha]_D^{26}$ +40.4 (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) *ν* (cm^{-1}): 3410, 2916, 2881, 1651, 1590, 1486, 1454, 1397, 1362, 1321, 1261, 1220, 1202, 1163, 1089, 906, 655; ^1H NMR (400 MHz): *δ* 7.16–7.29 (m, 15H's, Ar–H), 6.44 (s, 1H, H-1), 4.47–4.70 (m, 6H, 3 × –OCH_2Ph), 4.21 (m, 1H, H-5), 4.06 (dd, 1H, $J_{6a,6b}$ 12.2 Hz, $J_{5,6a}$ 4.4 Hz, H-6a), 3.92 (m, 2H, H-3, H-4), 3.66–3.78 (m, 3H, H-6b, –CH_2OH), 2.30–2.40 (br s, 1H, –OH); ^{13}C NMR (100 MHz): *δ* 143.12 (d, C-1), 137.79 (s, Ar–*C*), 137.70 (s, Ar–*C*), 137.61 (s, Ar–*C*), 128.37 (d, Ar–*C*H), 128.28 (d, Ar–*C*H), 128.23 (d, Ar–*C*H), 128.08 (d, Ar–*C*H), 127.90 (d, Ar–*C*H), 127.80 (d, Ar–*C*H), 127.76 (d, Ar–*C*H), 127.70 (d, Ar–*C*H), 127.56 (d, Ar–*C*H), 127.53 (d, Ar–*C*H), 127.26 (d, Ar–*C*H), 126.73 (d, Ar–*C*H), 117.76 (s, C-2), 75.95 (d, C-5), 74.80 (d, C-3), 73.65 (d, C-4), 73.72 (t), 72.80 (t), 72.46 (t), 67.79 (t), 61.38 (t). Anal. Calcd for $C_{28}H_{30}O_5$: C, 75.33; H, 6.72. Found: C, 75.12; H, 6.63.

1.4. 2-Acetoxymethyl-1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (4)

From **3** (0.25 g); viscous liquid (0.25 g, 92%); R_f 0.4 (4:1 hexane–EtOAc); $[\alpha]_D^{29}$ +48.1 (*c* 1, $CHCl_3$); IR ($CHCl_3$) (cm^{-1}): 3038, 2912, 2880, 1738, 1593, 1491, 1452, 1392, 1363, 1324, 1257, 1222, 1206, 1161, 1088, 908, 654; ^1H NMR (400 MHz): *δ* 7.24–7.33 (m, 15H, Ar–H), 6.55 (s, 1H, H-1), 4.43–4.72 (m, 8H, 3 × –OCH_2Ph, –CH_2OAc), 4.24–4.28 (m, 1H, H-5), 4.11 (d, 1H, $J_{3,4}$

4.88 Hz, H-3), 3.93 (dd, $J_{4,5}$ 6.35 Hz, $J_{3,4}$ 4.86 Hz, H-4), 3.79 (dd, 1H, $J_{6a,6b}$ 10.74 Hz, $J_{5,6b}$ 5.86 Hz, H-6b), 3.69 (dd, 1H, $J_{6a,6b}$ 10.74 Hz, $J_{5,6a}$ 3.9 Hz, H-6a), 1.94 (s, 3H, $OCOCH_3$); ^{13}C NMR (100 MHz): δ 170.91 (s, –O*C*OCH$_3$), 145.45 (d, C-1), 138.03 (s, Ar–*C*), 137.85 (s, Ar–*C*), 128.42 (d, Ar–*C*H), 128.35 (d, Ar–*C*H), 128.32 (d, Ar–*C*H), 127.83 (d, Ar–*C*H), 127.78 (d, Ar–*C*H), 127.71 (d, Ar–*C*H), 127.64 (d, Ar–*C*H), 107.98 (s, C-2), 76.36 (d, C-4), 73.87 (d, C-5), 73.50 (t), 73.35 (d), 72.91 (t), 72.33 (t), 67.94 (t), 62.55 (t), 20.96 (q, –OCO*C*H$_3$). Anal. Calcd for $C_{30}H_{32}O_6$: C, 73.77; H, 6.55. Found: C, 73.67; H, 6.60.

1.5. 1-*O*-Acetyl-3,4,6-tri-*O*-benzyl-4-*O*-formyl-D-*arabino*-hex-2-ulose (5)

From **4** (0.25 g); viscous liquid (0.23 g, 90%); R_f 0.4 (4:1 hexane–EtOAc); $[\alpha]_D^{29}$ −4.2 (*c* 1.45, $CHCl_3$); IR ($CHCl_3$) ν (cm^{-1}): 3050, 2912, 2880, 1753, 1738, 1593, 1491, 1452, 1392, 1363, 1324, 1257, 1222, 1206, 1161, 1088, 908, 654; ^1H NMR (400 MHz): δ 7.83 (s, 1H, OCHO), 7.17–7.32 (m, 15H's, Ar–H), 5.23 (m, 1H, H-5), 5.04 (d, B of AB, 1H, *J* 18.06 Hz, H-1b), 4.78 (d, A of AB, 1H, *J* 18.06 Hz, H-1a), 4.41-4.68 (m, 6H, 3 × –OCH_2Ph), 4.18 (dd, $J_{4,5}$ 7.81 Hz, $J_{3,4}$ 3.45 Hz, H-4), 4.12 (d, 1H, $J_{3,4}$ 2.93 Hz, H-3), 3.80 (dd, 1H, $J_{6a,6b}$ 11.2 Hz, $J_{5,6b}$ 2.45 Hz, H-6b), 3.73 (dd, 1H, $J_{6a,6b}$ 11.2 Hz, $J_{5,6a}$ 4.4 Hz, H-6a), 2.15 (s, 3H, $OCOCH_3$); ^{13}C NMR (50 MHz): δ 205.17 (s, C=O), 170.20 (s, –O*C*OCH$_3$), 159.79 (d, –O*C*HO), 136.95 (s, Ar–C), 137.44 (s, Ar–C), 136.11 (s, Ar–C), 128.83 (d, Ar–CH), 128.38 (d, Ar–CH), 128.24 (d, Ar–CH), 128.00 (d, Ar–CH), 127.81 (d, Ar–CH), 127.75 (d, Ar–CH), 83.10 (d, C-3), 77.99 (d, C-5), 74.83 (t, –OCH_2Ar), 74.29 (t, –OCH_2Ar), 73.28 (t, –OCH_2Ar), 71.40 (d, C-4), 68.14 (t, C-1), 67.56 (t, C-6), 20.42 (q, –OCO*C*H$_3$). MS: *m*/*z* 463 (M^+−CH_2OAc), 277, 199, 183, 105, 91, 77, 65.

1.6. 1,2-Di-*O*-acetyl-3,4,6-tri-*O*-benzyl-D-fructofuranose (6)

From **5** (0.2 g); viscous liquid (0.18 g, 92%); R_f 0.5 (1:1 hexane–EtOAc); $[\alpha]_D^{29}$ +20.6 (*c* 3.1, $CHCl_3$); IR ($CHCl_3$) ν (cm^{-1}): 2944, 2880. 1737, 1494, 1452, 1369, 1107, 998; ^1H NMR (200 MHz): δ 7.20–7.38 (m, 15H, Ar–H), 4.39-4.74 (m, 10H, 3 × –OCH_2Ph, H-5, H-3, H-1a, H-1b), 4.01 (dd, 1H, $J_{4,5}$ 5.42 Hz, $J_{3,4}$ 3.03 Hz, H-4), 3.64 (dd, 1H, $J_{6a,6b}$ 10.75 Hz, $J_{5,6b}$ 5.10 Hz, H-6b), 3.57 (dd, 1H, $J_{6a,6b}$ 10.75 Hz, $J_{5,6a}$ 5.07 Hz, H-6a), 2.00 (s, 6H, 2 × $OCOCH_3$); ^{13}C NMR (50 MHz): δ 170.06 (s, –O*C*OCH$_3$), 169.53 (s, –O*C*OCH$_3$), 137.85 (s, Ar–C), 137.53 (s, Ar–C), 137.14 (s, Ar–C), 128.33 (d, Ar–CH), 128.20 (d, Ar–CH), 127.85 (d, Ar–CH), 127.78 (d, Ar–CH), 127.68 (d, Ar–CH), 127.60 (d, Ar–CH), 109.38 (s, C-2), 85.79 (d, C-3), 82.77 (d, C-4), 82.68 (d, C-5), 73.22 (t, –OCH_2Ar), 72.58 (t, –OCH_2Ar), 71.89 (t, –OCH_2Ar), 69.22 (t, C-6), 62.51 (t, C-1), 21.68 (q, –OCO*C*H$_3$), 20.60 (q, –OCO*C*H$_3$); MS: *m*/*z* 534 (M^+), 461, 384, 313, 292, 278, 248, 235, 216, 175, 131, 105, 77, 65.

1.7. 2-Acetoxymonodeuteromethyl1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (8)

From **7** (0.25 g); viscous liquid (0.22 g, 80%); R_f 0.4 (4:1 hexane–EtOAc); $[\alpha]_D^{29}$ +25.7 (*c* 1, $CHCl_3$); IR ($CHCl_3$) (cm^{-1}): 2928, 2848, 1731, 1603, 1491, 1452, 1366, 1308, 1283, 1107, 992, 972, 908; ^1H NMR (200 MHz): δ 7.22–7.55 (m, 15H, Ar–H), 6.46 (s, 1H, H-1), 4.38-4.87 (m, 7H, 3 × –O*C*H$_2$ Ph, –*C*HDOAc), 4.24–4.31 (m, 1H, H-5), 4.19 (d, 1H, $J_{3,4}$ 3.73 Hz, H-3), 3.93 (t, $J_{4,5} = J_{3,4}$ 3.58 Hz, H-4), 3.80 (dd, 1H, $J_{6a,6b}$ 10.40 Hz, $J_{5,6b}$ 7.16 Hz, H-6b), 3.69 (dd, 1H, $J_{6a,6b}$ 10.44 Hz, $J_{5,6a}$ 4.97 Hz, H-6a), 1.94 (s, 3H, $OCOCH_3$); ^{13}C NMR (50 MHz): δ 170.88 (s, –O*C*OCH$_3$), 144.86 (d, C-1), 138.24 (s, Ar–*C*), 138.05 (s, Ar–*C*), 137.89 (s, Ar–*C*), 128.32 (d, Ar*C*H), 127.85 (d, Ar*C*H), 127.81 (d, Ar*C*H), 127.78 (d, Ar*C*H), 127.73 (d, Ar*C*H), 127.65 (d, Ar*C*H), 127.62 (d, Ar*C*H), 108.20 (s, C-2), 75.33 (d), 73.33 (t), 73.23 (t), 73.07 (t), 71.75 (d), 70.99 (d), 67.95 (t), 20.99 (q, –OCO*C*H$_3$).

1.8. 1-*O*-Acetyl-1-deutero-3,4,6-tri-*O*-benzyl-4-*O*-formyl-D-*arabino*-hex-2-ulose (9)

From **8** (0.2 g); viscous liquid (0.19 g, 90%); R_f 0.4 (4:1 hexane–EtOAc); $[\alpha]_D^{29}$ −13.2 (*c* 1.4, $CHCl_3$); IR ($CHCl_3$) ν (cm^{-1}): 2944, 2880, 1755, 1728, 1600, 1491, 1452, 1369, 1331, 1270, 1158, 1150, 992, 905; ^1H NMR (200 MHz): δ 7.83 (s, 1H, OCHO), 7.15–7.42 (m, 15H, Ar–H), 5.20–5.27 (m, 1H, H-5), 4.76 (s, 1H, H-1a), 4.35–4.69 (m, 6H, 3 × –OCH_2Ph), 4.18 (dd, $J_{4,5}$ 7.50 Hz, $J_{3,4}$ 3.01 Hz, H-4), 4.12 (d, 1H, $J_{3,4}$ 3.05 Hz, H-3), 3.80 (dd, 1H, $J_{6a,6b}$ 11.16 Hz, $J_{5,6b}$ 2.95 Hz, H-6b), 3.72 (dd, 1H, $J_{6a,6b}$ 11.16 Hz, $J_{5,6a}$ 4.15 Hz, H-6a), 2.14 (s, 3H, $OCOCH_3$); ^{13}C NMR (50 MHz): δ 205.13 (s, *C*=O), 170.12 (s, –OCO*C*H$_3$), 159.74 (d, –O*C*HO), 137.37 (s, Ar–*C*), 136.89 (s, Ar–*C*), 136.05 (s, Ar–*C*), 128.54 (d, Ar–*C*H), 128.29 (d, Ar–*C*H), 128.16 (d, Ar–*C*H), 127.91 (d, Ar–*C*H), 127.72 (d, Ar–*C*H), 127.67 (d, Ar–*C*H), 126.90 (d, Ar–*C*H), 83.04 (d, C-3), 77.92 (d, C-5), 74.73 (t, –O*C*H$_2$Ar), 74.18 (t, –O*C*H$_2$Ar), 73.18 (t, –O*C*H$_2$Ar), 71.30 (d, C-4), [67.49,67.79, 68.22-C-1], 67.49 (t, C-6), 20.31 (q, –OCO*C*H$_3$).

1.9. 1,2-Di-*O*-acetyl-3,4,6-tri-*O*-benzyl-1′-deutero-D-fructofuranose (10)

From **9** (0.15 g); viscous liquid (0.14 g, 92%); R_f 0.5 (1:1 hexane–EtOAc); $[\alpha]_D^{29}$ +17.9 (*c* 4.9, $CHCl_3$); IR ($CHCl_3$)

ν (cm^{-1}): 2928, 2804, 1737, 1600, 1491, 1452, 1366, 1308, 1276, 1107, 992, 940, 902, 807, 601; ^1H NMR (200 MHz): δ 7.20–7.38 (m, 15H, Ar–H), 4.32–4.67 (m, 9H, 3 × –OCH_2Ph, H-5, H-3, H-1), 4.00 (dd, 1H, $J_{4,5}$ 5.32 Hz, $J_{3,4}$ 2.97 Hz, H-4), 3.63 (dd, 1H, $J_{6a,6b}$ 10.95 Hz, $J_{5,6b}$ 5.34 Hz, H-6b), 3.57 (dd, 1H, $J_{6a,6b}$ 10.62 Hz, $J_{5,6a}$ 5.07 Hz, H-6a), 2.00 (s, 6H, 2 × $OCOCH_3$); ^{13}C NMR (50 MHz): δ 170.11 (s, –O*C*OCH$_3$), 169.57 (s, –O*C*OCH$_3$), 137.87 (s, Ar–CH), 137.55 (s, Ar–CH), 137.16 (s, Ar–C), 128.36 (d, Ar–CH), 128.26 (d, Ar–CH), 128.23 (d, Ar–CH), 127.88 (d, Ar–CH), 127.81 (d, Ar–CH), 127.70 (d, Ar–CH), 127.62 (d, Ar–CH), 127.55 (d, Ar–CH), 109.37 (s, C-2), 85.82 (d, C-3), 82.80 (d, C-4), 82.71 (d, C-5), 73.25 (t, –OCH_2Ar), 72.60 (t, –OCH_2Ar), 71.91 (t, –OCH_2Ar), 69.24 (t, C-6), 21.70 (q, –OCO*C*H$_3$), 20.62 (q, –OCO*C*H$_3$); MS: *m*/*z* 535 (M^+), 475, 473, 384, 313, 278, 235, 221, 181, 105, 91, 77, 65.

1.10. 2,3,5-Tri-*O*-benzyl-D-*arabinono*-1,4-lactone (12)

From **11**: To the diol **11** (0.1 g, 0.22 mmol) in CH_2Cl_2 (3 mL) was added $NaIO_4$ (0.094 g, 0.44 mmol) followed by satd $NaHCO_3$ (0.1 mL). The reaction mixture was stirred at room temperature for 1.5 h. Work-up involves filtration of the solid material by Celite and washings with CH_2Cl_2 (2 × 25 mL). The combined CH_2Cl_2 filtrate were evaporated under diminished pressure and the product was purified by column chromatography over silica gel using 4:1 hexane–EtOAc as eluent to give **12** (0.072 g, 78%).

From **14**: To the acetal **14** (0.1 g, 0.23 mmol) in EtOAc (5 mL) containing AcOH (0.05 mL) was added finely ground PDC (0.98 g, 0.26 mmol). The reaction mixture was stirred at room temperature for 2 h. Work-up involves filtration of the solid material through a sintered-glass funnel and the filtrate was evaporated under diminished pressure and purified by column chromatography over silica gel using 4:1 hexane–EtOAc as eluent to give **12** (0.083 g, 84%). Semi-solid; R_f 0.6 (3:2 hexane–EtOAc); $[\alpha]_D^{29}$ +6.58 (*c* 1.1, $CHCl_3$), lit.[9] $[\alpha]_D^{22}$ +6.8 (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) ν (cm^{-1}): 2928, 2864, 1785, 1737, 1600, 1491, 1452, 1363, 1315, 1116, 988, 905, 867; ^1H NMR (300 MHz): δ 7.18–7.36 (m, 15H, Ar–H), 5.04 (d, B of AB, 1H, *J* 11.4 Hz, $PhCH_B$), 4.75 (d, A of AB, 1H, *J* 11.4 Hz, $PhCH_A$), 4.40–4.63 (m, 5H, 2 × –OCH_2Ph, H-2), 4.29 (s, 2H, H-3, H-4), 3.67 (d, 1H, $J_{5a,5b}$ 11.4 Hz, H-5b), 3.55 (d, 1H, $J_{5a,5b}$ 11.4 Hz, H-5a); ^{13}C NMR (75 MHz): δ 172.12 (s, –O–*C*O–), 137.33 (s, Ar–*C*), 136.99 (s, Ar–*C*), 136.69 (s, Ar–*C*), 129.63 (d, Ar*C*H), 128.42 (d, Ar*C*H), 128.34 (d, Ar*C*H), 128.08 (d, Ar*C*H), 127.97 (d, Ar*C*H), 127.81 (d, Ar*C*H), 127.73 (d, Ar*C*H), 127.61 (d, Ar*C*H), 79.04 (d, C-2), 78.91 (d, C-3/C-4), 78.66 (d, C-3/C-4), 73.39 (t, –O*C*H$_2$Ar), 72.51 (t, –O*C*H$_2$Ar), 72.28 (t, –O*C*H$_2$Ar), 67.77 (t, C-5).

1.11. (2*S*, 3*R*, 4*R*)-2,3,5-Tri-*O*-benzyl-4-*O*-formyl-pentanal (13)

From **1** (0.2 g, 0.48 mmol); viscous liquid (0.18 g, 86%); R_f 0.4 (4:1 hexane–EtOAc); $[\alpha]_D^{29}$ +3.8 (*c* 1.45, $CHCl_3$); IR ($CHCl_3$) ν (cm^{-1}): 3072, 2926, 2880, 1724, 1600, 1491, 1449, 1363, 1158, 1100, 992, 905; ^1H NMR (400 MHz): δ 9.62 (s, 1H, –CHO), 7.80 (s, 1H, –OCHO), 7.14–7.32 (m, 15H's, Ar–H), 5.26 (m, 1H, H-4), 4.41–4.73 (m, 6H, 3 × –OC*H*$_2$Ph), 4.18 (dd, $J_{3,4}$ 7.5 Hz, $J_{2,3}$ 3.3 Hz, H-3), 3.86 (d, 1H, $J_{2,3}$ 2.1 Hz, H-2), 3.68–3.78 (m, 2H, H-5a, H-5b); ^{13}C NMR (50 MHz): δ 202.48 (d, –*C*HO), 159.57 (d, –O*C*HO), 137.50 (s, Ar–*C*), 137.01 (s, Ar–*C*), 136.46 (s, Ar–*C*), 128.68 (d, Ar–*C*H), 128.58 (d, Ar–*C*H), 128.41 (d, Ar–*C*H), 128.38 (d, Ar–*C*H), 128.33 (d, Ar–*C*H), 128.11 (d, Ar–*C*H), 128.01 (d, Ar–*C*H), 127.78 (d, Ar–*C*H), 127.73 (d, Ar–*C*H), 82.37 (d), 76.57 (d), 74.22 (t, –O*C*H$_2$Ar), 73.38 (t, –O*C*H$_2$Ar), 73.27 (t, –O*C*H$_2$Ar), 71.22 (d), 67.61 (t, C-5).

Acknowledgements

The authors thank the Department of Science and Technology, India, for financial support, and RSIC, IIT, Chennai, SPIC Science Foundation, Chennai and Sun Pharmaceutical Advanced Research Center, Baroda for spectral data. One of us (S.B.B.) also thanks Dr. K. Vijayakumaran, Director, R&D, Chimique Laboratories, Chennai for useful discussions.

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