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Preparation of 2-, 3-, and 4-deoxy derivatives of L-rhamnose, and derivatives of 2-azido-2-deoxy-L-rhamnose and 2,6-dideoxy-2-fluoro-L-glucose, for use in glycosylation reactions

Mikael Bols*,
Leo Pharmaceutical Products, Industriparken 55, DK-2750 Ballerup (Denmark)
Inge Lundt, and Erik Rytter Ottosen
Department of Organic Chemistry, The Technical University of Denmark, Building 201, DK-2800 Lyngby (Denmark)

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ABSTRACT

The following compounds have been prepared for use as glycosyl donors: 1,3,4-tri-*O*-acetyl-2,6-dideoxy-2-fluoro-α,β-L-glucopyranose (**5a**), 1,3,4-tri-*O*-acetyl-2,6-dideoxy-α,β-L-*arabino*-hexopyranose (**7a**), 1,3,4-tri-*O*-acetyl-2-azido-2,6-dideoxy-α,β-L-mannopyranose (**8a**), 1,2,4-tri-*O*-acetyl-3,6-dideoxy-α,L-*arabino*-hexopyranose (**13a**), and 1,2,3-tri-*O*-acetyl-4,6-dideoxy-α- (**15a**) and -β-L-*lyxo*-hexopyranose (**15b**).

INTRODUCTION

In work on the preparation of analogues of an anthracycline antibiotic, the acetylated 2-, 3-, and 4-deoxy, and 2-azido-2-deoxy derivatives of L-rhamnose, as well as the 2,6-dideoxy-2-fluoro derivative of L-glucose, were needed for use as glycosyl donors for the preparation of α-L-glycosides. Trimethylsilyl triflate-catalysed glycosylation with this type of derivative has been used to obtain α-L-rhamnosides[1]. We now report the synthesis of these compounds.

RESULTS AND DISCUSSION

An attractive approach to the synthesis of the 2-deoxy, 2-azido-2-deoxy, and 2-deoxy-2-fluoro derivatives was from known 2-bromo-2-deoxy-L-rhamnono-1,4-lactone[2] (**1**) as a common intermediate, since these functionalities can be introduced in 2-bromo-2-deoxyaldonolactones by direct substitution[2,3] or *via* the 2,3-epoxide[4]. Reaction of **1** with potassium fluoride in dry acetone gave a quantitative yield of 2,3-anhydro-6-deoxy-L-mannono-1,4-lactone[5] (**2**). No δ-lactone was formed as in the reaction[4] of 2-bromo-2-deoxypentonolactones with potassium fluoride.

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* To whom correspondence should be addressed. Present address: Department of Organic Chemistry, The Technical University of Denmark, Building 201, DK-2800 Lyngby, Denmark.

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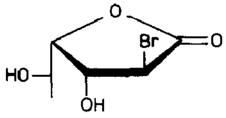
Reaction of **2** with triethylamine tris(hydrogen fluoride) at 70° for 6 days resulted in regioselective reaction at position 2 to give 85% of a mixture of 2,6-dideoxy-2-fluoro-L-glucono-1,4- (**3**) and -1,5-lactones (**4**). No compounds with fluorine at C-3 were detected. The structures of **3** and **4** were confirmed by COSY and ^{13}C-n.m.r. spectroscopy. The former showed that each compound had a fluorine substituent at C-2, and the latter showed that **3** was a γ-lactone with the characteristic signal at 82.9 p.p.m. for C-4; **4** lacked such a signal. The regioselectivity in this reaction accords with results obtained with other 2,3-epoxylactones[4].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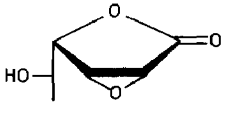
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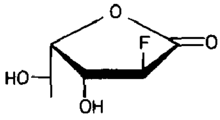
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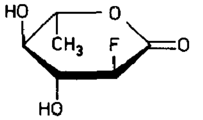
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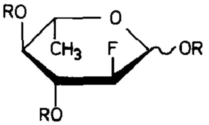
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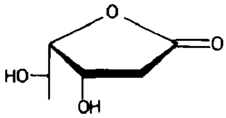
5a R = Ac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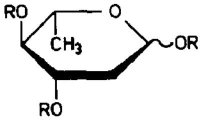
Reduction of the mixture of lactones **3** and **4**, using disiamylborane in tetrahydrofuran, gave 65% of 2,6-dideoxy-2-fluoro-L-glucose (**5**). Acetylation of **5**, using acetic anhydride–pyridine, then gave 83% of 1,3,4-tri-*O*-acetyl-2,6-dideoxy-2-fluoro-L-glucopyranose (**5a**) with an α,β-ratio of 1:1. The pure β anomer (25%) was crystallised from the mixture. Previously, **5** and **5a** have been synthesised from L-rhamnose in 5 or 6 steps, respectively, *via* addition of trifluoromethoxyfluoride to 3,4-di-*O*-acetyl-L-rhamnal[6]. This reaction gave 2-epimeric fluorides that were difficult to separate. Our synthesis has the same number of steps and overall yield (30–35%) but is more convenient, since the fluorination is regio- and stereo-selective and isomers were not formed.

2,6-Dideoxy-L-*arabino*-hexono-1,4-lactone (**6**) was obtained readily by hydrogenation[2] of **1**. Reduction of **6** with disiamylborane to give the lactol **7**, analogously to the method[2] used to obtain the enantiomer of **7**, proceeded satisfactorily, and no alditol derivative was formed. Acetylation of **7** gave 70% of 1,3,4-tri-*O*-acetyl-2,6-dideoxy-L-*arabino*-hexopyranose[7] (**7a**) with an α,β-ratio of 1:2.

Compounds **7** and **7a** can also be prepared from 3,4-di-*O*-acetyl-L-rhamnal. This makes **7** available in 5 steps[8], and **7a** in 4 steps, from L-rhamnose[7], compared to 4 and 5 steps, respectively, in the above syntheses.

2-Azido-2-deoxy-L-rhamnose (**8**), prepared from **1** in two steps[3], was acetylated to give 88% of 1,3,4-tri-*O*-acetyl-2-azido-2,6-dideoxy-L-mannopyranose (**8a**) with an α,β-ratio of 2:1; a 1:1 α,β-mixture was crystallised in a yield of 43%.

Oxidation of L-rhamnose with bromine[9] and acetylation of the products gave a mixture of the acetylated 1,4- (**9**) and the 1,5-lactone (**10**). Hydrogenation (Pd/C) of this mixture in the presence of triethylamine resulted[10] in elimination and stereospecific hydrogenation to give a mixture of the 3-deoxylactones **11a** and **12a**. Deacetylation of



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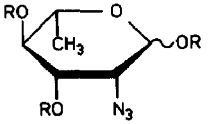

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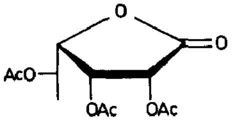

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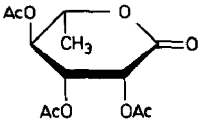

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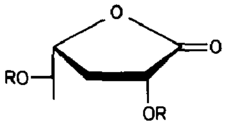

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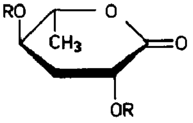

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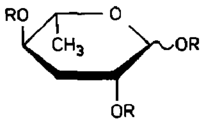

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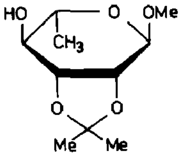
13a R = Ac



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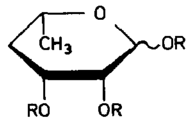

15 R = H
15a R = Ac, α
15b R = Ac, β

this mixture with methanolic hydrogen chloride gave a mixture of **11** and **12**, which were reduced with disiamylborane to give, 3,6-dideoxy-L-*arabino*-hexose (**13**, 66% from L-rhamnose). The previous synthesis[11] of **13** from L-rhamnono-1,5-lactone gave a somewhat lower overall yield (54%). However, the use of 1,5-lactones could be advantageous, when pyranose derivatives are required.

In contrast to **5**, **7**, **8**, and **15**, **13** was not exclusively in the pyranose form (see Experimental). N.m.r. spectroscopy showed that the equilibrium mixture of **13** in pyridine at 25° contained ~35% of the furanose form, and 50% at 100°. When **13** was acetylated at 0° in pyridine, chromatography of the mixture of products gave 27% of 1,2,4-tri-*O*-acetyl-α-L-*arabino*-hexopyranose (**13**).

4,6-Dideoxy-L-*lyxo*-hexose (**15**) was prepared conveniently from methyl 2,3-*O*-isopropylidene-α-L-rhamnoside (**14**) through radical deoxygenation[12] of the methyl dithiocarbonate derivative. Acetylation of **15**[12,13] with acetic anhydride/pyridine gave 86% of 1,2,3-tri-*O*-acetyl-4,6-dideoxy-α- (**15a**) and -β-L-*lyxo*-hexopyranose (**15b**), which could be separated by chromatography, and their respective configurations were determined by n.m.r. spectroscopy. Only the β anomer **16b** showed an n.O.e. between H-1 and H-5.

EXPERIMENTAL

General. — N.m.r. spectra were measured on solutions in $CDCl_3$ (internal Me_4Si) with a Bruker AC-300 instrument unless otherwise specified. Melting points were measured on a Buchi apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer PE241 instrument. Microanalyses were performed by the Leo microanalytical laboratory. Column chromatography was performed on Kieselgel 60 (Merck 0.4–0.63 mm), using the flash technique. T.l.c. was performed on Kieselgel 60 F_{254} (Merck) with detection with 1% cerium sulfate and 1.5% molybdic acid in aqueous 10% H_2SO_4 at 200° for 5 min. Evaporations were carried out *in vacuo* at 40°, unless otherwise specified.

*2,3-Anhydro-6-deoxy-*L*-mannono-1,4-lactone*[5] (**2**). — A solution of 2-bromo-2,6-dideoxy-L-glucono-1,4-lactone (**1**, 2.39 g) in dry acetone (21 mL) was stirred with KF (2.13 g, spray-dried) for 17 h at room temperature. T.l.c. (EtOAc–pentane, 1:1) then revealed a single product. The solution was filtered through a short column of silica gel with acetone (3 vol.), and the combined eluates were concentrated to give **2** as a clear syrup (1.54 g, 100%), $[\alpha]_D^{20}$ +56° (*c* 1, water) which was pure as seen from the n.m.r. spectra. The product was used immediately in the next reaction after drying *in vacuo*. N.m.r. data [$(CD_3)_2CO$]: ^1H, δ 1.25 (d, 3 H, H-6,6,6), 3.86 (dq, 1 H, $J_{5,6}$ 6.2 Hz, H-5), 3.98 (d, 1 H, H-2), 4.25 (dd, 1 H, $J_{4,5}$ 8.6 Hz, H-4), and 4.40 (dd, 1 H, $J_{2,3}$ 2.7, $J_{3,4}$ 1.5 Hz, H-3); ^{13}C, δ 21.0 (C-6), 51.5 and 56.5 (C-2,3), 65.7 (C-5), 83.0 (C-4), and 171.4 (C-1).

*2,6-Dideoxy-2-fluoro-*L*-glucono-1,4-* (**3**) *and -1,5-lactone* (**4**). — A solution of **2** (1.1 g) in triethylamine tris(hydrogen fluoride) (11 mL) in a polyethylene flask was stirred at 70° for 6 days. The reaction was monitored by treating samples with an equal volume of Ac_2O for 4 h at 25°, H_2O was added, the mixture was extracted with CH_2Cl_2, the extract was concentrated, and the residue was analysed by n.m.r. spectroscopy. After 1 day, ~20% of **2** had reacted. The final solution was cooled to 25°, then stirred with acetone (60 mL) and silica gel (6 g) for 30 min. The mixture was added to a column (2 × 10 cm) of silica gel and eluted with acetone. The first 300 mL of eluate was concentrated to give a syrupy 1:1 mixture of **3** and **4** (1.1 g, 86%). N.m.r. data [$(CD_3)_2CO$]: **3** ^1H, δ 1.37 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6,6,6), 4.30 (m, 1 H, H-5), 4.46 (dd, 1 H, $J_{4,5}$ 5.0 Hz, H-4), 4.85 (ddd, 1 H, $J_{3,4}$ 6.5, $J_{3,F}$ 20.0 Hz, H-3), 5.34 (dd, 1 H, $J_{2,3}$ 6.2, $J_{2,F}$ 52.0 Hz, H-2); ^{13}C, δ 18.4 (C-6), 67.4 (C-5), 73.0 (d, $J_{3,F}$ 20.0 Hz, C-3), 82.9 (d, $J_{4,F}$ 6.8 Hz, C-4), 91.5 (d, $J_{2,F}$ 188 Hz, C-2), 170.5 (d, $J_{1,F}$ 21.4 Hz, C-1); **4** ^1H, δ 1.43 (d, 3 H, $J_{5,6}$ 6.0 Hz, H-6), 3.61 (dd, 1 H, $J_{4,5}$ 9.2 Hz, H-4), 4.03 (ddd, 1 H, $J_{3,4}$ 9.2, $J_{3,F}$ 16.0 Hz, H-3), 4.40 (m, 1 H, H-5), 4.92 (dd, 1 H, $J_{2,3}$ 9.4, $J_{2,F}$ 48.0 Hz, H-2); ^{13}C, δ 19.8 (C-6), 73.4 (d, C-4), 73.5 (d, C-3), 78.1 (C-5), 89.6 (d, $J_{2,F}$ 189.0 Hz, C-2), and 167.3 (d, $J_{1,F}$ 20.0 Hz, C-1).

Anal. Calc. for $C_6H_9FO_4$: C, 44.73; H, 5.63; Found: C, 44.63; H, 6.31.

*2,6-Dideoxy-2-fluoro-*L*-glucose* (**5**). — To a solution of 10M borane–dimethyl sulfide complex (1.4 mL) in dry tetrahydrofuran (5 mL) at 0° was added 2-methyl-2-butene (2.9 mL). The solution was kept under N_2 at 25° for 5 h, then cooled to 0°, and a solution of the mixture of **3** and **4** (437 mg) in dry tetrahydrofuran (3.0 mL) was added. The mixture was kept at 25° for 18 h, water (2.5 mL) was then added slowly, and the mixture was boiled under reflux for 1 h. After evaporation of the tetrahydrofuran, more H_2O (15 mL) was added, the aqueous phase was extracted with $CHCl_3$ (3 × 15 mL), then concentrated, and MeOH was evaporated twice from the syrupy residue to leave **5** (293 mg, 65%, α,β-ratio 2:3). Flash chromatography (EtOAc) gave **5** (150 mg, 34%), $[\alpha]_D^{20}$ −35° (c 0.27, D_2O); lit.[6] $[\alpha]_D^{20}$ −49.6° (water). N.m.r. data (D_2O): α anomer ^{1}H, δ 1.09 (d, 3 H, H-6,6,6), 3.08 (m, 1 H, H-4), 3.38 (dq, 1 H, $J_{4,5}$ 9.5, $J_{5,6}$ 6.2 Hz, H-5), 3.78 (m, 1 H, H-3), 4.27 (d, 1 H, $J_{2,3}$ 9.5, $J_{2,F}$ 49.0 Hz, H-2), 5.23 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1); ^{13}C, δ 19.4 (C-6), 70.1, 77.3 (C-4,5), 73.7 (d, $J_{3,F}$ 17.4 Hz, C-3), 92.3 (d, $J_{1,F}$ 21.3 Hz, C-1), and 93.3 (d, $J_{2,F}$ 185.0 Hz, C-2); β anomer ^{1}H, δ 1.14 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6,6), 3.08 (m, 1 H, H-4), 3.59 (ddd, 1 H, $J_{4,5}$ 9.2, $J_{3,F}$ 15.0 Hz, H-3), 3.75 (m, 1 H, H-5), 3.94 (ddd, 1 H, $J_{2,3}$ 9.1, $J_{2,F}$ 52.0 Hz, H-2), 4.73 (dd, 1 H, $J_{1,2}$ 7.9, $J_{1,F}$ 2.5 Hz, H-1); ^{13}C, δ 19.4 (C-6), 74.9, 77.4 (C-4,5), 76.6 (d, $J_{3,F}$ 17.2 Hz, C-3), 96.0 (d, $J_{2,F}$ 182.0 Hz, C-2), 96.2 (d, $J_{1,F}$ 23.1 Hz, C-1).

*1,3,4-Tri-O-acetyl-2,6-dideoxy-2-fluoro-α,β-*L*-glucopyranose* (**5a**). — A solution of **5** (150 mg) in pyridine (1.3 g) and acetic anhydride (1 g) was kept at 25° for 20 h, ice–water (5 mL) was added, and the mixture was extracted with $CHCl_3$ (3 × 5 mL). The combined extracts were dried ($MgSO_4$) and concentrated, and toluene was evaporated twice from the residue to leave a partly crystalline ~1:1 α,β-mixture (220 mg, 83%) of **5a**. The pure β-acetate (67 mg, 25%) was crystallised from MeOH and had m.p. 154–155°, $[\alpha]_D^{20}$ −72° (c 0.44, chloroform); lit.[6] (for a 1:2 α,β-mixture), m.p. 126°, $[\alpha]_D^{20}$ −152° (chloroform). N.m.r. data ($CDCl_3$): α-acetate ^{1}H, δ 1.19 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6,6), 2.06, 2.08, and 2.19 (3 s, each 3 H, 3 AcO), 3.98 (dq, 1 H, H-5), 4.65 (ddd, 1 H, $J_{2,F}$ 49.0 Hz, H-2), 4.80 (dd, 1 H, H-4), 5.50 (dt, 1 H, $J_{2,3}$ 9.6, $J_{3,4}$ 9.6, $J_{3,F}$ 22.0 Hz, H-3), 6.35 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1); ^{13}C, δ 17.2 (C-6), 20.6–20.9 (3 CH_3CO), 67.6, 72.7 (C-4,5), 70.8 (d, $J_{3,F}$ 19.0 Hz, C-3), 86.6 (d, $J_{2,F}$ 195.0 Hz, C-2), 88.4 (d, $J_{1,F}$ 22.0 Hz, C-1), 169.0–170.3 (3 CH_3CO; β-acetate ^{1}H, δ 1.24 (d, 3 H, H-6,6,6), 2.06, 2.09, and 2.18 (3 s, each 3 H, 3 AcO), 3.73 (dq, 1 H, $J_{5,6}$ 6.2 Hz, H-5), 4.42 (ddd, 1 H, $J_{2,F}$ 51.0 Hz, H-2), 4.79 (dd, 1 H, $J_{4,5}$ 9.8 Hz, H-4), 5.32 (ddd, 1 H, $J_{2,3}$ 9.0, $J_{3,4}$ 9.4, $J_{3,F}$ 14.0 Hz, H-3), 5.76 (dd, 1 H, $J_{1,2}$ 8.2, $J_{1,F}$ 3.2 Hz, H-1); ^{13}C, δ 17.1 (C-6), 20.6–20.8 (3 CH_3CO), 72.6 (d, $J_{3,F}$ 14.0 Hz, C-3), 70.9, 72.7 (C-4,5), 88.5 (d, $J_{2,F}$ 192.0 Hz, C-2), 91.1 (d, $J_{1,F}$ 24.0 Hz, C-1), 168.9, 169.7, and 169.9 (3 CH_3CO).

Anal. Calc. for $C_{12}H_{17}FO_7$: C, 49.32; H, 5.86. Found: C, 49.57; H, 5.94.

*2,6-Dideoxy-*L-arabino*-hexose* (**7**). — 2,6-Dideoxy-L-*arabino*-hexono-1,4-lactone[2] (**6**, 137 g) was reduced with $BH_3 \cdot SMe_2$ (5 mL, 10.0M) and 2-methyl-2-butene (11 mL) in tetrahydrofuran (22.5 mL), as described[2] for the enantiomer of **7**, to afford **7** (0.88 g, 63%; α,β-ratio 3:4), $[\alpha]_D^{20}$ −20° (c 0.8, water); lit.[8] $[\alpha]_D^{20}$ −18.2° (water). No alditol derivative was formed in this reaction.

*1,3,4-Tri-O-acetyl-2,6-dideoxy-α,β-*L-arabino*-hexopyranose* (**7a**). — A solution of **7** (0.87 g) in pyridine (6 g) and acetic anhydride (5 g) was kept at 25° for 18 h. Ice–water (25 mL) was then added, the mixture was extracted with $CHCl_3$ (3 × 25 mL), and the combined extracts were dried ($MgSO_4$) and concentrated. Flash chromatography (EtOAc–pentane, 1:5) of the residue (1.63 g) gave **7a** (1.12 g, 70%; α,β-ratio 1:2) as a clear syrup, $[\alpha]_D^{20}$ −53° (c 0.6; chloroform); lit.[7] (for a 3:4 α,β-mixture) $[\alpha]_D^{20}$ −98° (chloroform). N.m.r. data ($CDCl_3$): α-pyranose ^{1}H, δ 1.18 (d, 3 H, H-6,6,6), 1.95 (m, H-2*ax*), 2.05, 2.07, 2.12 (3 s, each 3 H, 3AcO), 2.23 (bdd, 1 H, H-2*eq*), 3.60 (dq, 1 H, $J_{4,5}$ 12.0, $J_{5,6}$ 6.2 Hz, H-5), 4.80 (dd, 1 H, H-4), 5.27 (ddd, 1 H, H-3), 6.19 (bd, 1 H, H-1); ^{13}C, δ 17.6 (C-6), 20.8–21.1 (3 *C*H$_3$CO), 34.0 (C-2), 68.5 (2 C, C-3,4), 74.0 (C-5), 90.9 (C-1), and 169.8–170.3 (3 CH$_3$*C*O); β-pyranose ^{1}H, δ 1.27 (d, 3 H, H-6,6,6), 1.84 (ddd, H-2*ax*), 2.03, 2.06, 2.11 (3 s, each 3 H, 3 AcO), 2.34 (ddd, 1 H, $J_{2ax,2eq}$ 12.4 Hz, H-2*eq*), 3.60 (dq, 1 H, $J_{5,6}$ 6.2 Hz, H-5), 4.70 (dd, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 5.02 (ddd, 1 H, $J_{2eq,3}$ 5.2, $J_{2ax,3}$ 11.4, $J_{3,4}$ 9.3 Hz, H-3), 5.77 (dd, 1 H, $J_{1,2eq}$ 2.2, $J_{1,2ax}$ 10.2 Hz, H-1); ^{13}C, δ 17.6 (C-6), 20.8–21.1 (3 *C*H$_3$CO), 35.1 (C-2), 70.2, 71.0, 73.6 (C-3,4,5), 91.0 (C-1), 168.8–171.3 (3 CH$_3$*C*O).

*1,3,4-Tri-O-acetyl-2-azido-2,6-dideoxy-α,β-*L-mannopyranose (**8a**). — A solution of 2-azido-2,6-dideoxy-L-mannopyranose[3] (**8**, 2.40 g) in pyridine (14.3 g) and acetic anhydride (11.0 g) was kept at 0° for 18 h. Ice–water (40 mL) was then added, the mixture was extracted with CHCl$_3$ (2 × 40 mL), and the combined extracts were dried (MgSO$_4$) and concentrated. Flash chromatography (EtOAc–pentane, 1:2) of the residue (3.90 g) gave **8a** (3.53 g, 88%; α,β-ratio 2:1) as a clear syrup. Colourless crystals of a 1:1 α,β-mixture obtained from ethanol (1.71 g, 43%) had m.p. 84–86°, $[\alpha]_D^{20}$ −34° (*c* 1, chloroform). N.m.r. data (CDCl$_3$): α-pyranose ^{1}H, δ 1.22 (d, 3 H, H-6,6,6), 2.08, 2.12, 2.16 (3 s, each 3 H, 3 AcO), 3.91 (dq, 1 H, $J_{5,6}$ 6.2 Hz, H-5), 4.03 (dd, 1 H, H-2), 5.34 (dd, 1 H, $J_{2,3}$ 3.8, $J_{3,4}$ 9.9 Hz, H-3), 5.15 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), and 6.05 (d, 1 H, $J_{1,2}$ 1.9 Hz, H-1); ^{13}C, δ 17.4 (C-6), 20.6, 20.7, 20.9 (3 *C*H$_3$CO), 68.9, 70.5, 70.6 (C-3,4,5), 91.4 (C-1), 60.8 (C-2), 168.5, 169.7, 170.2 (3 CH$_3$*C*O); β-pyranose ^{1}H, δ 1.26 (d, 3 H, H-6,6,6), 2.06, 2.11, 2.19 (3 s, each 3 H, 3 AcO), 3.61 (dq, 1 H, $J_{5,6}$ 6.1 Hz, H-5), 5.04 (m, 2 H, H-3,4), 4.15 (dd, 1 H, $J_{2,3}$ 3.2 Hz, H-2), and 5.82 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1); ^{13}C, δ 17.3 (C-6), 20.6–20.9 (3 *C*H$_3$CO), 61.5 (C-2), 70.0, 71.5, 71.9 (C-3,4,5), 91.1 (C-1), 168.5, 169.6, 170.2 (3 CH$_3$*C*O).

Anal. Calc. for $C_{12}H_{17}N_3O_7$: C, 45.72; H, 5.43; Found; C, 45.57; H, 5.43.

*3,6-Dideoxy-*L-arabino-*hexose* (**13**). — To a solution of α-L-rhamnose monohydrate (20.0 g) in H$_2$O (400 mL) was added BaCO$_3$ (40 g). Bromine (6.5 mL) was added slowly to the suspension, the mixture was stirred at 25° overnight, more bromine (0.5 mL) was added, and stirring was continued for 2 h. The yellow suspension was filtered, H$_2$SO$_4$ was added to pH 3, BaSO$_4$ was removed by filtration, the filtrate was concentrated, and toluene was evaporated from the residue.

To the resulting crude L-rhamnonolactone was added acetic anhydride (180 mL) and aqueous 70% HClO$_4$ (0.75 mL), and the mixture was stirred for 5 days. H$_2$O (180 mL) was added slowly, the aqueous phase was extracted with CH$_2$Cl$_2$ (4 × 200 mL), and the combined extracts were washed with a saturated aqueous NaHCO$_3$ and H$_2$O, dried (MgSO$_4$), filtered, and concentrated to give a pale-yellow, syrupy 2:1 mixture (22.3 g, 71%) of 2,3,5-tri-*O*-acetyl-6-deoxy-L-mannono-1,4-lactone (**9**) and 2,3,4-tri-*O*-acetyl-6-deoxy-L-mannono-1,5-lactone (**10**). The mixture also contained 5–10% of a by-product, presumably 2,3-di-*O*-acetyl-6-deoxy-L-mannono-1,4-lactone. N.m.r. data (CDCl$_3$); **9** ^{1}H, δ 1.42 (d, 3 H, H-6,6,6), 4.44 (dd, 1 H, H-4), 5.20 (dq, 1 H, H-5), 5.67 (dd, 1 H, H-3), and 5.75 (m, 1 H, H-2); ^{13}C, δ 17.4 (C-6), 65.9 (C-5), 68.2, 68.6 (C-2,3), 79.4 (C-4); **10** ^{1}H, δ 1.42 (d, 3 H, H-6,6,6), 4.51 (dq, 1 H, H-5), 4.81 (dd, 1 H, H-4), 5.45 (dd, 1 H, H-3), 5.76 (m, 1 H, H-2); ^{13}C, 18.8 (C-6), 66.7 (C-2), 70.8 (C-3), 73.8, 74.3 (C-4,5).

A solution of the mixture (5.06 g) of **9** and **10** in ethyl acetate (45 mL) and dry triethylamine (7 mL) was stirred under hydrogen together with 10% Pd/C (350 mg) at 1200 kPa for 3 days. The catalyst was removed, and the filtrate was washed with 4M HCl (2 × 20 mL), dried (Na_2SO_4), and concentrated to give a syrupy 2:1 mixture (3.92 g, 97%) of 2,5-di-*O*-acetyl-3,6-dideoxy-L-*arabino*-hexono-1,4-lactone (**11a**) and 2,4-di-*O*-acetyl-3,6-dideoxy-L-*arabino*-hexono-1,5-lactone (**12a**). N.m.r. data ($CDCl_3$): **11a** ^{1}H, δ 1.30 (d, 3 H, H-6,6,6), 2.0–2.2 (2 s, 6 H, 2 Ac), 2.15 (m, 1 H, H-3b), 2.76 (dd, 1 H, H-3a), 4.48 (ddd, 1 H, H-4), 5.17 (dq, 1 H, H-5), 5.50 (dd, 1 H, H-2); ^{13}C, δ 15.0 (C-6), 20.6, 21.0 (2 *C*H$_3$CO), 29.9 (C-3), 68.1, 69.5 (C-2,5), 77.6 (C-4), 169.0, 169.7, 171.7, (C-1 and 2 CH$_3$*C*O); **12a** ^{13}C, δ 19.0 (C-6), 20.4, 20.9 (2 *C*H$_3$CO), 29.7 (C-3), 64.9, 69.8 (C-2,4), 77.1 (C-5), 168.1–171.7 (C-1 and 2 CH$_3$*C*O).

A solution of the mixture of **11a** and **12a** (3.81 g) in 1% HCl in MeOH (100 mL) was kept at 25° for 5 days, then concentrated. MeOH was evaporated from the residue to leave a 2:1 mixture (2.36 g, 97%) of 3,6-dideoxy-L-*arabino*-hexono-1,4- (**11**) and -1,5-lactone (**12**). N.m.r. data (CD_3OD): **11** ^{13}C, δ 18.4 (C-6), 32.5 (C-3), 68.1, 69.2 (C-2,5), 81.1 (C-4), 179.0 (C-1); **12** ^{13}C, δ 18.7 (C-6), 37.9 (C-3), 68.7, 71.9, 72.7 (C-2,4,5), 178.1 (C-1).

A solution of disiamylborane (76.8 mmol) was prepared by adding 2-methyl-2-butene (16 mL) to $BH_3 \cdot SMe_2$ (7.7 mL) in dry tetrahydrofuran (20 mL) at 0° and stirring at 25° for 5 h under N_2. To this solution was added a solution of the mixture (2.14 g, 14.7 mmol) of **11** and **12** in tetrahydrofuran (15 mL) at 0°. The mixture was stored for 3 days at 25°, H_2O (10 mL) was added, and the mixture was boiled under reflux for 1 h, then concentrated. H_2O (60 mL) was added, the solution was extracted with $CHCl_3$ (2 × 60 mL), and the aqueous phase was concentrated. MeOH was evaporated from the residue to leave **13** (2.16 g, 66% from L-rhamnose), which gave one spot in t.l.c. (EtOAc) and which consisted of ~65% pyranoses and ~35% of a furanose (n.m.r. data), $[\alpha]_D^{20}$ −33° (*c* 0.1, water); lit.[11] $[\alpha]_D^{20}$ −23.6° (water). N.m.r. data (pyridine-d_5): α-pyranose ^{1}H, δ 1.66 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6,6), 5.74 (s, 1 H, H-1); ^{13}C, δ 19.1 (C-6), 36.7 (C-3), 68.3, 70.2, 70.5 (C-2,4,5), 94.9 (C-1), β-pyranose ^{1}H, δ 1.61 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6,6), 5.64 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1); ^{13}C, δ 19.0 (C-6), 40.1 (C-3), 67.6, 69.5, 77.1 (C-2,4,5), 96.5 (C-1); furanose δ 1.66 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 5.98 (s, 1 H, H-1); ^{13}C, δ 20.7 (C-6), 32.8 (C-3), 68.2, 76.0 (C-2,5), 83.0 (C-4), 104.1 (C-1).

*1,2,4-Tri-O-acetyl-3,6-dideoxy-α-*L-arabino-*hexopyranose* (**13a**). — A solution of **13** (1.78 g) in pyridine (13.0 g) and acetic anhydride (10.0 g) was kept at 0° for 17 h. Ice–water (40 mL) was added, the mixture was extracted with $CHCl_3$ (2 × 40 mL), the combined extracts were dried ($MgSO_4$) and concentrated, and toluene was evaporated twice from the residue to leave a syrupy mixture (3.92 g) of the acetylated pyranoses and an acetylated furanose (*αp*:*βp*:*f*-ratio 6:4:3). Flash chromatography (EtOAc–pentane, 1:4) of the mixture twice gave, as the faster moving component, **13a** (0.88 g, 27%), isolated as a clear syrup, $[\alpha]_D^{20}$ −84° (*c* 0.9, chloroform). The β-pyranose and furanose forms could not be separated. The remaining fractions contained 2.02 g (62%) of product. N.m.r. data ($CDCl_3$): **13a** ^{1}H, δ 1.21 (d, 3 H, H-6,6,6), 1.98 (m, H-3*ax*), 2.06, 2.08, 2.13 (3 s, each 3 H, 3 AcO), 3.88 (dq, 1 H, $J_{5,6}$ 6.2 Hz, H-5), 2.24 (m, 1 H, H-3*eq*), 4.84 (ddd, 1 H, $J_{4,3eq}$ 4.8, $J_{4,3ax}$ 11.2, $J_{4,5}$ 9.7 Hz, H-4), 4.93 (bdd, 1 H, $J_{2,3eq}$ 3.3, $J_{2,3ax}$ 4.8 Hz, H-2), 5.94 (bs, 1 H, H-1); ^{13}C, δ 17.7 (C-6), 20.9, 21.0, 21.1 (3 CH_3CO), 29.3 (C-3), 68.6, 68.8, 69.2 (C-2,4,5), 89.9 (C-1), 168.6, 169.9, and 171.1 (3 CH_3CO); β-pyranose ^{1}H, δ 1.30 (d, 3 H, H-6,6,6), 1.81 (ddd, 1 H, $J_{2,3ax}$ 3.4 Hz, H-3*ax*), 2.09, 2.10, 2.15 (3 s, each 3 H, 3 AcO), 2.36 (ddd, 1 H, $J_{2,3eq}$ 4.6, $J_{3ax,3eq}$ 14.0 Hz, H-3*eq*), 3.76 (dq, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 4.83 (ddd, 1 H, $J_{4,3eq}$ 4.6, $J_{4,3ax}$ 10.2, $J_{4,5}$ 8.3 Hz, H-4), 5.24 (m, 1 H, H-2), 5.85 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1); ^{13}C, δ 18.2 (C-6), 20.6–21.1 (3 CH_3CO), 31.3 (C-3), 67.0, 69.4, 74.4 (C-2,4,5), 91.9 (C-1), 169.4, 170.0, 170.2 (3 CH_3CO); furanose δ 1.27 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6,6,6), 1.80–2.00 (ddd, 1 H, H-3b), 2.07–2.15 (9 H, 3 AcO), 2.47 (ddd, 1 H, $J_{4,3b}$ 8.2, $J_{3a,3b}$ 15.0 Hz, H-3a), 4.75 (m, 1 H, H-5), 4.99 (dd, 1 H, $J_{4,3a}$ 6.2 Hz, H-4), 5.14 (dd, 1 H, $J_{2,3b}$ 1.8, $J_{2,3a}$ 6.5 Hz, H-2), 6.23 (s, 1 H, H-1); ^{13}C, δ 16.3 (C-6), 20.9, 21.0, 21.2 (3 CH_3CO), 31.6 (C-3), 71.0, 76.9 (C-2,5), 81.6 (C-4), 100.1 (C-1), 169.3, 169.9, 170.0 (3 CH_3CO).

Anal. Calc. for $C_{12}H_{18}O_7$: C, 52.55; H, 6.61; Found: C, 52.56; H, 6.80.

1,2,3-Tri-O-acetyl-4,6-dideoxy-α- (**15a**) *and -β-*L-lyxo*-hexopyranose* (**15b**). — A solution of 4,6-dideoxy-L-*lyxo*-hexose[13] (**15**, 0.99 g) in pyridine (6.5 g) and acetic anhydride (5.0 g) was kept at 25° for 23 h. Ice–water (25 mL) was added, the mixture was extracted with $CHCl_3$ (3 × 25 mL), and the combined extracts were dried ($MgSO_4$) and concentrated. Flash chromatography (EtOAc–pentane, 1:2) of the residue (1.97 g) afforded, first, **15a** (0.63 g, 34%), m.p. 73–74°, $[\alpha]_D^{20}$ +20° (*c* 3.4, chloroform).

Anal. Calc. for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62. Found: C, 52.56; H, 6.64.

Eluted second was **15b** (0.30 g, 16%), m.p. 83–85°, $[\alpha]_D^{20}$ −63.2° (*c* 0.5, chloroform).

Anal. Calc. for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62. Found: C, 52.56; H, 6.64.

A mixture (0.67 g, 36%) of **15a** and **15b** was also obtained. N.m.r. data ($CDCl_3$): **15a** ^{1}H, δ 1.24 (d, 3 H, $J_{5,6}$ 5.8 Hz, H-6,6,6), 1.85 (m, 2 H, H-4*ax*,4*eq*), 2.03, 2.14, 2.15 (3 s, each 3 H, 3 AcO), 4.05 (m, 1 H, H-5), 5.08 (dd, 1 H, H-2), 5.27 (ddd, 1 H, H-3), 6.06 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1); ^{13}C, δ 20.8, 20.9, 21.1 (3 CH_3CO), 21.1 (C-6), 33.0 (C-4), 66.5, 66.8 (3 C, C-2,3,5), 91.8 (C-1), 168.6, 169.9, 170.1 (3 CH_3CO): **15b** ^{1}H, δ 1.34 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6,6), 1.6–1.9 (m, 2 H, H-4*ax*,4*eq*), 2.02, 2.09, 2.19 (3 s, each 3 H, 3 AcO), 3.76 (ddq, 1 H, H-5), 5.03 (ddd, 1 H, $J_{3,4eq}$ 5.7, $J_{3,4ax}$ 11.6 Hz, H-3), 5.37 (dd, 1 H, $J_{2,3}$ 3.0 Hz, H-2), 5.74 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1); ^{13}C, δ 20.8–20.9 (4 C, 3 CH_3CO and C-6), 32.6 (C-4), 67.0, 68.6, 69.4 (C-2,3,5), 91.2 (C-1), 168.6, 169.9, 170.4 (3 CH_3CO).

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REFERENCES

1 H. Paulsen and M. Paal, *Carbohydr. Res.*, 135 (1984) 53–69; T. Ogawa, K. Beppu, and S. Nakabagashi, *ibid.*, 93 (1981) c6–c9; M. Trumptel, A. Veyrieres, and P. Sinaÿ, *Tetrahedron. Lett.*, 30 (1989) 2529–2532.
2 K. Bock, I. Lundt, and C. Pedersen, *Carbohydr. Res.*, 90 (1981) 7–16.
3 K. Bock, I. Lundt, and C. Pedersen, *Acta Chem. Scand., Ser. B*, 41 (1987) 435–441.

4 M. Bols and I. Lundt, *Acta Chem. Scand.*, 44 (1990) 252–256.
5 I. Lundt and C. Pedersen, unpublished data.
6 G. C. Butchard and P. W. Kent, *Tetrahedron*, 35 (1979) 2439–2443.
7 A. F. Hadfield, L. Cunningham, and A. C. Sartorelli, *Carbohydr. Res.*, 72 (1979) 93–104.
8 B. Iselin and T. Reichstein, *Helv. Chim. Acta*, 27 (1944) 1146–1149.
9 H. S. Isbell and H. L. Frush, *Bur. Stand. J. Res.*, 11 (1933) 649–664.
10 K. Bock, I. Lundt, and C. Pedersen, *Acta Chem. Scand., Ser. B*, 35 (1981) 155–162.
11 O. J. Varela, A. F. Cirelli, and R. M. de Lederkremer, *Carbohydr. Res.*, 70 (1979) 27–35.
12 V. Pozsgay and A. Neszmelyi, *Carbohydr. Res.*, 85 (1980) 143–150.
13 K. Kefurt, Z. Kefurtova, and J. Jary, *Collect. Czech, Chem. Commun.*, 36 (1971) 1701–1704.