Preparation of Some Acetylated Deoxy-pento- and -hexofuranoses and their Deacetylation

Christian Pedersen* and Hanne Stampe Jensen

The Technical University of Denmark, Department of Organic Chemistry, 2800 Lyngby, Denmark

In previous papers the preparation of a number of acetylated mono-, di- and tri-deoxy-pentono- and -hexono-1,4-lactones has been described.1-4 The reduction of such lactones may yield the corresponding acetylated furanoses, which are of potential synthetic use, e.g., for the synthesis of nucleoside analogues2 or for the preparation of free deoxy sugars by deacetylation. Unprotected aldolactones have been reduced to the corresponding hemiacetals with several reagents such as sodium amalgam,5 sodium borohydride,6 bis(2-butyl)aluminiun hydride6 (DIBAL) or bis(3-methyl-2-butyl)borane (dissiamylborane).5 For the reduction of acetylated lactones only dissiamylborane can be used since the other three reagents will cleave off the acetyl groups. Reduction of acetylated and benzoylated aldolactones with dissiamylborane was first described by Kohn et al.,9 who used this reagent to prepare a number of benzoylated hexofuranoses. They also synthesized 2,3,5,6-tetra-O-acetyl-D-galactofuranose in 83% yield by reduction of the corresponding acetylated lactone. Dyong et al., on the other hand, reported that they obtained complex mixtures of products on reduction of tetra-O-acetyl-D-galactono-1,4-lactone and some acetylated deoxyhexonolactones with dissiamylborane.9

When a lactone is reduced with dissiamylborane an addition of the latter to the double bond of the carbonyl group takes place. Subsequent hydrolysis then gives the hemiacetal and dissiamylboronic acid.9 In the normal procedure used to isolate the product the boronic acid is oxidized by simultaneous addition of hydrogen peroxide and aqueous sodium hydroxide, keeping the pH at 7.5-8. This converts the boronic acid into boric acid and 3-methyl-2-butanol, both of which are easily removed by evaporation. In our opinion this procedure should not be used for the reduction of acetylated lactones, because the addition of sodium hydroxide is likely to cause partial decylation, even with careful control of pH, and this may explain the mixture of products obtained in some cases.9 We have now found that the dissiamylborinic acid can be completely removed from the reaction mixture simply by coevaporation with water and with methanol.

Results and discussion

To achieve complete reduction of an acetylated aldolactone it is necessary to use two to four times the calculated amount of dissiamylborane and a reaction time of about 18 h at room temperature. Acetylated 2-deoxy- and 2,3-dideoxy-lactones are reduced relatively easily, whereas 3-deoxy-lactones require more time and more reagent to be reduced completely. Thus the acetylated 2,6-dideoxy-D- and -L-arabinono-hexofuranoses (1 and 3, respectively), the 2,6-dideoxy-D-ribo- (5) and the 2,3,6-trideoxy-D-erythro-hexofuranose (9a) were all obtained in virtually quantitative yields by reduction of the corresponding acetylated lactones. For complete formation of the acetylated 2-deoxy-D-ribo-hexofuranose (7a) a 40 h reaction time was necessary under the same conditions. The synthesis of the acetylated 3-deoxy-D-threo-pento-furanose (10a), 3-deoxy-D-arabino-hexofuranose (11a), 3-deoxy-D-xylo-hexofuranose (12a), 3-deoxy- and 3,6-dideoxy-D-gluco-heptofuranose (13a and 13b, respectively), from the corresponding lactones, required four equivalents of dissiamylborane and a 48-72 h reaction time for complete reduction. The electronnegative acetox
groups probably inhibit the reaction of the electrophilic borane with the carbonyl group of the lactone, and this becomes more pronounced when an acetoxy group is present at the 2-position.

**Scheme 2.**

Some of the acetylated furanoses, prepared as described above, were deacetylated in order to obtain the corresponding free sugars. Acetylated 3-deoxy- and 2,3-dideoxy-furanoses were readily deacetylated with catalytic amounts of sodium methoxide in methanol to give high yields of the free sugars. Deacetylation of acetylated 2-deoxyfuranoses, on the other hand, gave mixtures of products which contained O-methyl groups. Thus deacetylation of 3,5-di-O-acetyl-2,6-dideoxy-D-arabinohexofuranose (1) gave a mixture of the expected 2,6-dideoxy-D-arabinohexose (2a) and 2,6-dideoxy-3-O-methyl-D-arabinohexose (2b); the latter was isolated in 39% yield. The formation of 2b must proceed via elimination of the 3-O-acetyl group from the aldehyde form of 1 and subsequent addition of a methoxy group to the resulting unsaturated aldehyde. Apparently the addition was, in this case, highly stereoselective since no isomeric product was observed. Deacetylation of 5 and 7a with methoxide gave mixtures of O-methyl derivatives. However, all the acetylated furanoses could be deacetylated smoothly when the less basic reagents, potassium cyanide or magnesium oxide were used.

**Experimental**

Melting points are uncorrected. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. NMR spectra were recorded on Bruker AC-250 or AM-500 instruments. Tetramethylsilane was used as an internal reference for CDCl₃ solutions and dioxane (67.4 ppm) for ¹³C NMR spectra measured in D₂O solutions. Unless
otherwise stated NMR spectra were measured for samples in CDCl₃ solution. Chromatographic separations were performed on columns of silica gel using the flash technique.

3.5-Di-O-acetyl-2,6-dideoxy-β-D-arabinofuranose (7a). A solution of diis amylnitroborene was prepared by addition of 2-methyl-2-butene (6.9 ml, 65 mmol) in CH₂Cl₂ (15 ml) to borane·dimethyl sulfide complex (3.2 ml, 34 mmol) in CH₂Cl₂ (10 ml) at 0 °C under an N₂ atmosphere. After 2.5 h, 3.5-di-O-acetyl-2,6-dideoxy-β-D-arabinofuranose (2.5 g, 11 mmol) in CH₂Cl₂ (10 ml) was added and the mixture was kept at 20 °C for 18 h. Water (10 ml) was then added and the mixture was stirred for 1 h. The organic phase was separated and the aqueous phase was extracted with CH₂Cl₂. The combined organic phases were concentrated and the residue was coevaporated three times with 20 ml portions of water at 40 °C (to remove the boronic acid) and three times with MeOH to leave the title compound as a syrup (2.5 g, 100%)., which crystallized from Et₂O–pentane to give 2.2 g (88%) of 7a, m.p. 75–78 °C. Recrystallization gave a product with m.p. 83–85 °C. [α]D +11.1 → +16.8 (c 3.2, CHCl₃). Anal. C₁₅H₁₉O₅: C, H. H NMR: δ 5.55 (dd, 1 H, J₂, 3 5.0 Hz, J₂, 4 2.0 Hz, H-1), 5.25 (dd, 1 H, J₂, 3 2.5, H-3), 5.04 (m, 1 H, J₃, ₄ 3.2, J₅, ₆ 6.0, H-5), 4.37 (dd, 1 H, J₅, ₆ 12.0, H-6), 4.31 (m, 1 H, J₅, ₆ 6.5, J₆, ₇ 2.0, H-4), 4.11 (dd, 1 H, H-6'), 2.30 (m, 1 H, J₃, ₄ 1.5, H-2), 2.10 (m, 1 H, J₂, 3 7.0, H₂-2'), 2.10, 2.00 (3 OAc); 13C NMR, δ 79.8 (C-1), 81.5 (C-4), 74.9, 70.9 (C-3, 5), 62.5 (C-6), 39.2 (C-2), 20.6, 20.5, 20.4 (OAc); 1H NMR, β-7a: δ 5.65 (dd, 1 H, J₂, 3 5.5 Hz, J₂, 4 3.2, H-1), 5.32 (dd, 1 H, J₂, 3 2.5, H-3), 5.17 (dd, 1 H, J₃, ₄ 3.0, J₅, ₆ 5.5, H-5), 4.43 (dd, 1 H, J₅, ₆ 12.0, H-6), 4.18 (dd, 1 H, H-6'), 4.08 (m, 1 H, J₅, ₆ 7.8, J₆, ₇ 1.5, H-4), 2.50 (m, 1 H, J₃, ₄ 14.5, J₅, ₆ 7.0, H-2'), 2.17 (dd, 1 H, J₂, 3 5.5, H₂-2'), 2.10, 2.00 (OAc); 13C NMR, β-7a: δ 98.1 (C-1), 81.5 (C-4), 74.3, 70.3 (C-3, 5), 62.3 (C-6), 39.0 (C-2), 20.7, 20.6, 20.3 (OAc).

5-O-Acetyl-2,3,6-trideoxy-β-D-erythro-hexofuranose (9a). Reduction of 5-O-acetyl-2,3,6-trideoxy-β-D-erythro-hexono-1,4-lactone (1.5 g, 8.7 mmol) with diis Amylborene (27 mmol) for 16 h at 20 °C as described above gave 1.5 g (100%) of syrup 9a in an αβ ratio of 5:6. 13C NMR, δ 98.2 (C-1), 79.2 (C-4), 71.1 (C-5), 32.0 (C-2), 24.1 (C-3), 15.2 (C-6); β-9a, 97.8 (C-1), 81.6 (C-4), 71.3 (C-5), 32.8 (C-2), 24.3 (C-3), 15.5 (C-6). The product readily undergoes self-condensation to form mixtures of 1:1 linked disaccharides; it should therefore be used immediately after preparation.

5-O-Acetyl-1,0-benzyl-2,3,6-trideoxy-β-D-erythro-hexofuranose (9b). Treatment of 9a (0.55 g) with benzoyl chloride (1.2 ml) in pyridine (10 ml) followed by processing in the usual way gave 0.82 g (93%) of product. Column chromatography using Et₂O–pentane (1:1) as the eluent gave 230 mg (26%) of 9b, m.p. 64–66 °C. Recrystallization from pentane gave a product with m.p. 70–71 °C. [α]D +57.7° (c 0.6, CHCl₃). Anal. C₁₅H₁₆O₅: C, H. H NMR: δ 8.1–7.4 (5 H, Bz), 6.59 (br d, 1 H, J₂, 3 4.0 Hz, J₂, 4: ca. 0, H-1), 4.98 (dq, 1 H, J₃, ₄ 6.5, H-5, 5), 4.34 (dt, 1 H, J₃, ₄ 4.5, H-4), 2.23–2.1 (m, 3 H, J₅, ₆ 7.5, H₂-2', H-3), 2.05 (s, 3 H, OAc), 1.88–1.95 (m, 1 H, H-3'), 1.22 (d, 3 H, H-6). 13C NMR: δ 99.6 (C-1), 81.4 (C-4), 71.0 (C-5), 31.4 (C-2), 23.7 (C-3), 21.0 (OAc), 15.6 (C-6).
for 72 h at 20°C to give 1.0 g (100%) of **10a** as a syrup. When only 3 equiv. of the borane had been used 20%, of unreduced lactone remained. **13** NMR: **1 H** NMR: δ 8.0–7.4 (Bz), 6.46 (s, 1 H, J=5.0 Hz, H-1), 5.33 (dd, 1 H, J=3.5, 6.5, J=2.0, H-2), 5.25 (dd, 1 H, J=5.0, 5.5, J=7.0, H-5), 4.54 (dt, 1 H, J=5.0, H-4), 4.87 (dd, 1 H, J=6.0, 12.0, H-6), 4.16 (dd, 1 H, H-6’), 2.65 (dd, 1 H, J=3.5, 15.0, J=6.0, H-3), 2.12 (2 OAc, 2.03 ppm) (OAc), 1.91 (dd, 1 H, J=6.0, H=3’). **13** C NMR: δ 133.3–128.2 (Bz), 100.1 (C-1), 77.8, 76.5, 71.2 (C-2,4,5), 62.7 (C-6), 31.5 (C-3), 20.6, 20.4 (OAc).

2.5,6,7-Tetra-O-acetyl-3-deoxy-β-D-glucopyranose (13a). **13** NMR: δ 5.40 (br s, 1 H, J=0.0 Hz, H-1), 5.30 (t, 1 H, J=6.0, H-5), 5.23 (dt, 1 H, J=2.5, J=6.0, H-6), 5.05 (dd, 1 H, J=7.0, J=2.0, H=2), 4.48 (dt, 1 H, J=5.0, H-4), 4.40 (dd, 1 H, J=7.0, H=7), 4.40 (dd, 1 H, H=7’), 2.55 (dd, 1 H, J=13.5, 14.5, J=8.0, H=3), 2.13–2.02 (4 OAc). 1.76 (dd, 1 H, J=6.0, H=3) ppm. **13** C NMR: δ 100.3 (C-1), 77.8, 75.3 (C-2,4), 71.1, 70.3 (C-5,6), 61.7 (C-7), 31.3 (C-3), 20.7–20.4 (4 OAc).

2.5,6,7-Tetra-O-acetyl-3,7-dideoxy-β-D-glucopyranose (13b). Reduction of 2.5,6,7-Tri-O-acetyl-3,7-dideoxy-β-D-gluco-heptono-1,4-lactone (2.0 g, 6.62 mmol) with diisobutyric acid (27.2 mmol) for 48 h gave 2.1 g (100%) of **13b** (δ 3.58 (5 H, Bz), 6.48 (s, 1 H, J=0.0 Hz, H-1), 5.30 (dd, 1 H, J=8.5, J=3.0, J=6.0, H-5), 4.50 (dd, 1 H, J=6.0, 12.0, H=6), 4.48 (m, 1 H, J=6.5, H-4), 4.12 (dd, 1 H, H-6’), 2.60 (dd, 1 H, J=14.0, 3.0, H=3), 2.10, 2.07, 2.02 (OAc), 1.99 (dd, 1 H, J=3.0, 7.0, H=3’). **13** C NMR: δ 133.4–128.3 (Bz), 100.2 (C-1), 77.8, 76.5, 71.2 (C-2,4,5), 62.3 (C-6), 31.7 (C-3), 20.8, 20.6 (3 OAc).

2.6,2-Dideoxy-3-O-methyl-β-D-arabino-heptopyranose (2b). To a solution of **1** (2.0 g) in MeOH (70 ml) was added 1 M methanolic sodium methoxide (18 ml, 2 mol equiv.). The solution was stirred for 2 h and then
neutralized with ion-exchange resin (Amberlite IR-120, H⁺) and concentrated. The residue (1.4 g) was chromatographed twice using first Et₂O–MeOH (9:1) and then 2% MeOH in Et₂O as the eluent. The first fraction gave 480 mg (36%v) of 2b as a syrup. ³H NMR, α-2b: δ 5.27 (br d, 1 H, J₁,₂ 1.5 Hz, J₂,₃ 3.5, H-1), 3.87 (dq, 1 H, J₃,₆ 6.0, H-5), 3.53 (dd, 1 H, J₁,₃ 9.0, H-3), 3.35 (s, 3 H, OMe), 3.09 (t, 1 H, J₃,₅ 9.0, H-4), 2.22 (dd, 1 H, J₂,₃ 12.5, J₃,₅ 11.5, H-2'), 1.43 (dd, 1 H, J₃,₅ 3.5, H-2'), 1.22 (d, 3 H, H-6); ¹¹C NMR, α-2b: δ 91.7 (C-1), 77.8, 75.8 (C-3,4), 67.4 (C-5), 56.3 (OMe), 33.9 (C-2), 17.7 (C-6).

A second fraction gave 520 mg (39%v) of 2,6-dideoxy-α-D-arabino-hexopyranose (α-D-olivose) (2a) as a syrupy α,β-mixture. A ¹³C NMR spectrum was identical with that reported previously.¹

2,6-Dideoxy-3-O-methyl-D-arabino-hexonic acid phenylhydrazide. To crude 2b (200 mg) in water (3.4 ml) was added bromine (0.09 ml) and the mixture was kept for 18 h. The excess of bromine was then removed with air and the solution was neutralized with silver carbonate, filtered and concentrated. The residue was heated at 100°C with phenylhydrazine (0.12 ml) for 0.5 h. Addition of Et₂O precipitated the title compound, which was recrystallized from EtOH, m.p. 133.5–135°C, [α]₂⁰Be = 19.6° (c 0.4, MeOH); (lit.¹⁵ for the L-enantiomer m.p. 135–136°C, [α]₂⁰Be = 20.3°). Anal. C₃₁H₄₀N₂O₁₄; C, H. ¹¹C NMR (D₂O): δ 173.5 (C-1), 130.2–114.2 (Ph), 78.4, 77.5 (C-3,4), 67.6 (C-5), 59.8 (OMe), 36.6 (C-2), 19.3 (C-6).

Methyl 2,6-dideoxy-3,4-di-O-p-nitrobenzoyl-α-D-arabino-hexopyranoside (α-D-2d). A solution of 1 (700 mg) in MeOH (45 ml) containing KCN (98 mg, 0.5 mol equiv.) was kept overnight. It was then neutralized with an acidic ion-exchange resin (Amberlite IR-120, H⁺) and concentrated leaving 410 mg (92%) of 2,6-dideoxy-D-arabino-hexose (2a), pure as seen from its ¹³C NMR spectrum. The product was kept overnight in MeOH (10 ml) which contained 3 drops of sulfuric acid. The solution was then neutralized with barium carbonate, filtered and concentrated to leave 400 mg of methyl 2,6-dideoxy-β-D-arabino-hexopyranoside (2c), (α:β ratio 5:1). Subsequent p-nitrobenzoylation in pyridine gave 1.0 g (88%) of crude 2d. Chromatography with Et₂O–pentane (1:1) as the eluent yielded α-2d, m.p. 149–150°C, [α]₂⁰Be = -71° (c 0.7, CHCl₃); (lit.¹ m.p. 149–151°C, [α]₂⁰Be = -72°).

When 1 (230 mg) was stirred in MeOH (15 ml) with MgO (1.0 g) for 72 h, then filtered and concentrated, 130 mg (88%) of 2a were obtained. A ¹³C NMR spectrum showed no other products.

2,6-Dideoxy-3-O-methyl-D-arabino-hexopyranose (1-oleandrose, 4b). Reaction of 3 with methanolic sodium methoxide as described above for the D-enantiomer followed by chromatography gave 38% of 4b. Oxidation and subsequent reaction with phenylhydrazine as described above yielded 2,6-dideoxy-3-O-methyl-L-arabino-hexonic acid phenylhydrazide, m.p. 134–135°C, [α]₂⁰Be = +20.0° (c 0.4, MeOH); (lit.¹¹ m.p. 135–136°C, [α]₂⁰Be = +20.3°).

A second fraction gave 30% of 2,6-dideoxy-L-arabino-hexopyranose (l-olivose, 4a). It was converted into methyl 2,6-dideoxy-3,4-di-O-p-nitrobenzoyl-α-L-arabino-hexopyranoside (α-4c) as described above for α-2d, m.p. 150–151°C, [α]₂⁰Be = 70.9° (c 0.7, CHCl₃). Anal. C₂₁H₂₃N₂O₁₄; C, H, N. ¹¹C NMR spectra were identical with those of α-2d.

2,6-Dideoxy-α-L-ribo-hexose (l-digiotioside 6). A solution of 5 (270 mg) in MeOH (15 ml) was stirred with KCN (37 mg) for 2.5 h. The solution was then neutralized with Amberlite IR-120(H⁺), filtered and concentrated. The residue (160 mg, 94%) contained only 6 as seen from its ¹³C NMR spectrum.² Recrystallization from acetone gave a product with a m.p. 104–105°C, [α]₂⁰Be = -46.8° (c 0.5, H₂O); (lit.¹⁴ m.p. 105–107°C, [α]₂⁰Be = -47.0°).

When the deacetylation of 5 was carried out with sodium methoxide (0.2 mol equiv.) in MeOH as described above the main product was 6 in admixture with ca. 20% of an α-methyl derivative.

2-Deoxy-β-L-ribo-hexopyranose (β-8). A solution of 7a (800 mg) was treated with KCN in MeOH as described above to give 460 mg (100%) of 8. A ¹³C NMR spectrum showed that it was a mixture of the α- and β-pyranoses and small amounts of the furanoses. Crystallization from EtOH gave 100 mg (22%v) of β-8, m.p. 135–137°C. Recrystallization gave a product with m.p. 136–137°C, [α]₂⁰Be = -49.4° – 55.5° (c 0.6, H₂O); (lit.¹³ for the D-enantiomer, m.p. 135–136°C, [α]₂⁰Be = +57.9°). Anal. C₃₁H₄₀N₂O₁₄; C, H. ¹¹C NMR (D₂O): δ 92.4 (C-1), 74.5 (C-4), 68.3, 67.7 (C-3,5), 62.3 (C-6), 38.9 (C-2).

2,3,6-Trideoxy-D-erythro-hexose (amincose) was obtained by treatment of 9a (500 mg) in MeOH (20 ml) with 1 M methanolic sodium methoxide (0.7 ml, 0.25 mol equiv.) for 1 h followed by neutralisation and concentration as described above. The product was a mixture of furanoses and pyranoses as seen from the ¹³C NMR spectrum. Treatment with 2,4-dinitrophenylhydrazine in 2 M hydrochloric acid precipitated 2,3,6-trideoxy-D-erythro-hexose, 2,4-dinitrophenylhydrazine, which was recrystallized from MeOH-benzene, m.p. 151–152°C, [α]₂⁰Be = -9.8° (c 0.5, pyridine); (lit.¹⁶ m.p. 152–153°C, [α]₂⁰Be = -10.0°).

3-Deoxy-α-D-gluco-heptopyranose (14). Treatment of 13a (1.7 g, 4.5 mmol) with sodium methoxide (4.5 mmol) in MeOH (45 ml) for 50 min, followed by neutralisation and evaporation, gave a syrup which crystallized from EtOH–water to give 500 mg (55%) of 14, m.p. 115–120°C.
Recrystallization from 2-propanol gave a product with m.p. 126–128°C, [α]D 55.0 → +9.6° (c 1.5, H2O); [lit.17] m.p. 126–128°C, [α]D +10° (equil.).

References

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