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Carbohydrate Research 342 (2007) 2132–2137
Carbohydrate RESEARCH

Note

Glucuronic acid-based ulosyl donors for introducing α-D-GlcA and β-D-ManA units[☆]

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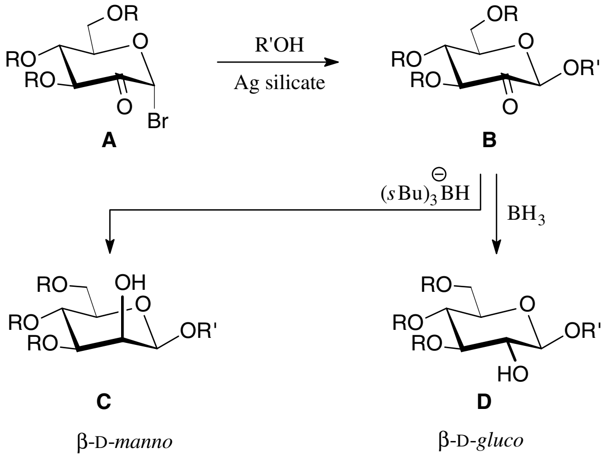
Received 2 April 2007; received in revised form 3 May 2007; accepted 7 May 2007
Available online 18 May 2007

Abstract—Practical protocols are described for a five-step conversion of D-glucuronolactone into α-D-*arabino*-2-ketoglucuronyl bromides, which due to their α-selective or β-specific glycosidation, and *gluco*- or *manno*-specific carbonyl reductions of the glucurono-2-ulosides formed, are expedient indirect donor substrates for the efficient introduction of α-D-GlcA or β-D-ManA residues.

Keywords: Glycosylation; β-D-Mannuronyl donor; Ulosyl bromides; Glucurono-2-ulosides

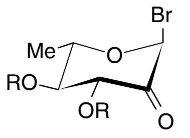
The 2-ulosyl donor approach for the expedient synthesis of β-D-mannosides has successfully been employed for the construction of various β-D-mannose-containing oligosaccharides up to the hexasaccharide level.[2] Central to this procedure are the ready preparations of variously blocked α-D-*arabino*-2-ketohexosyl bromides of type **A** from D-glucose,[2,3] their essentially β-specific glycosidation (→**B**)—the electron-withdrawing 2-carbonyl group suppresses oxocarbenium ion formation at the anomeric center implementing direct S_N2 displacement of the bromine—and manno-specific (**B**→**C**) or gluco-selective (**B**→**D**) reduction[4] of the resulting β-D-glycosiduloses (Scheme 1). Aside from its preparative simplicity, the methodology has the advantage of providing β-D-glycosides with a free 2-OH group, that is, acceptors ready for further glycosylations toward (1→2)-oligosaccharides.



R = Ac, Bz, Bn; R' = alkyl, glycosyl

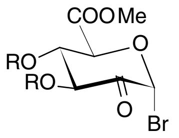
Scheme 1. The 'ulosyl donor approach' to β-D-mannosides or β-D-glucosides with a free 2-OH.

Whilst the 6-deoxy-L-ulosyl bromides of type **E** have already been prepared and utilized for the straightforward synthesis of β-L-rhamnose-containing oligosaccharides,[5] we here report on a simple, five-step conversion of D-glucuronolactone into ulosyl bromides **F** with a 6-carboxyl functionality, which are practical donor substrates for the generation of α-D-GlcA and β-D-ManA linkages:



E

R = Ac, Bz, Bn



F

R = Ac, Bz

[☆] Sugar-Derived Building Blocks, Part 41; for Part 40, see Ref. 1.

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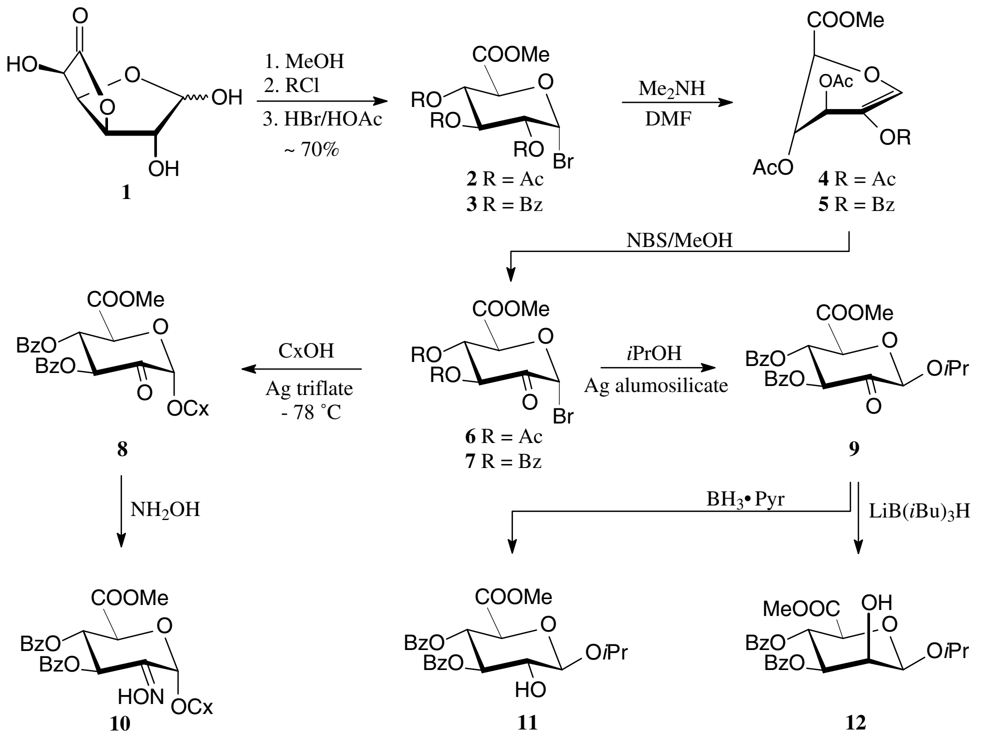
doi:10.1016/j.carres.2007.05.008



Cx = cyclohexyl

Scheme 2.

Commercially available glucuronolactone **1** was converted into its methyl ester,[6] then acylated with either acetic anhydride[6] or benzoyl chloride,[7] followed by exposure to HBr/HOAc[6,7] to give glucuronyl bromides **2** and **3**, overall yields for the three steps being in the 75% range. The subsequent HBr elimination was effected by dimethylamine/tetrabutylammonium bromide in DMF, affording 2-acyloxyglucuronals **4**[8] and **5** in nicely crystalline form each. Interestingly, yet not entirely unexpected,[†] **4** and **5** adopt the uncommon $^5H_4$ half-chair conformation in solution as well as in the solid state: in $CDCl_3$, the H-4/H-5 couplings are small (2.2 and 2.3 Hz, respectively) and the occurrence of a 1.4-Hz long-range coupling between H-3 and H-5 indicates these hydrogens to be in a W arrangement as depicted in the formulae (Scheme 2); this steric disposition, 'inverse' to that in the parent glucal esters, is even more lucidly exposed in the solid-state structure of **4** (Fig. 1), revealing an essentially antiparallel arrangement (dihedral angle O4–C4–C5–C6: 175.8°) of the 4-acetoxy and 5-carbomethoxy groups perpendicular to the ring plane.

Exposure of either 2-acetoxyglucuronals **4** or **5** to methoxybromination conditions (NBS/methanol in dichloromethane, 15 min, 25 °C) smoothly afforded the respective ulosyl bromides **6** and **7** in 66–70% yield. Particularly compound **7**, isolable in crystalline form and storable for weeks, appeared to lend itself as a suitable donor substrate, as glycosidations can simply be effected in either an α- or β-specific manner: When exposed to cyclohexanol in dichloromethane in the presence of silver triflate at −78 °C, α-D-uloside **8** is formed exclusively (isolated yield: 85%)[‡] as the reaction obviously proceeds through a β-triflate intermediate, which then undergoes S_N2-type alcoholysis. When using an insoluble silver catalyst, such as silver aluminosilicate,[5,10] however, and 2-propanol as the acceptor, the well-crystallizing β-D-glucuronosidulose **9** is generated in essentially quantitative yield.

Reductions of the carbonyl group in β-D-2-ketoglucuronide **9** follow the stereoselectivity patterns observed previously with β-D-glucosiduloses:[3,4] exposure to BH_3·pyridine in THF at −78 °C generates an approximate 10:1 mixture of glucuronide **11** and its manno-isomer **12**, from which **11** is isolable in useful yield (76%), whereas the selectride reduction of **9** provides mannuronide **12** in an essentially stereospecific manner (84% isolated yield).

[†] The parent 3,4,6-tri-*O*-acetyl-D-glucuronal, in acetone solution, predominantly adopts the $^5H_4$ half-chair conformation as evidenced by a small $J_{4,5}$ value (3.9 Hz) and the appearance of a long range coupling (1.2 Hz) between H-3 and H-5.[9]

[‡] On performing the silver triflate-induced glycosidation of **9** with cyclohexanol at 0 °C or at ambient temperature α/β-mixtures are obtained with the latter anomer preponderating, conceivably due to extensive direct S_N2-type displacement of the bromine.

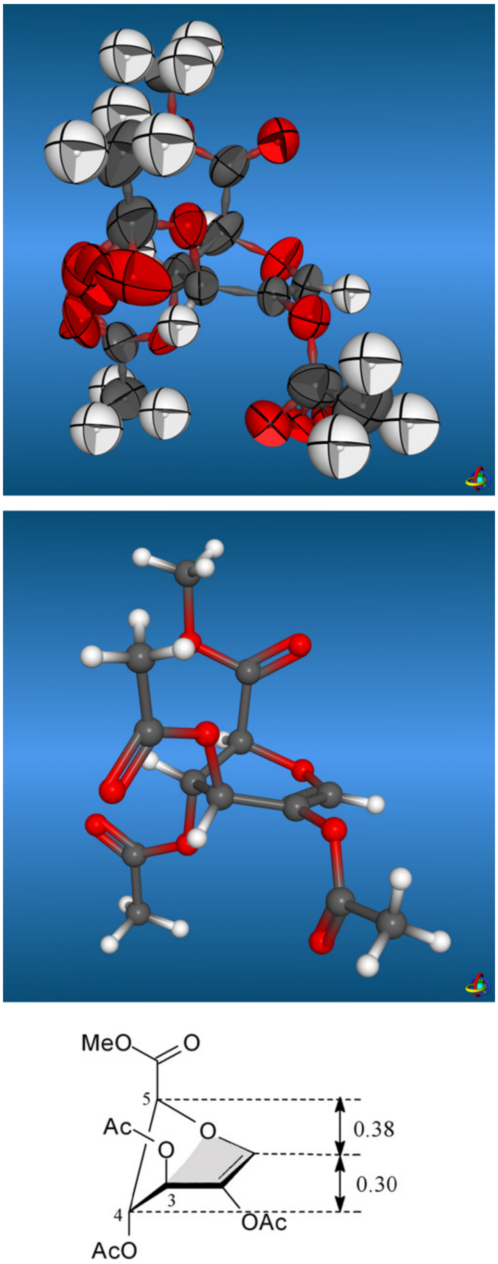


Figure 1. X-ray structure of methyl 2-acetoxy-3,4-di-*O*-acetyl-D-*arabino*-hex-1-enopyranuronate (**4**) with a view accentuating the antiparallel arrangement of 3-OAc, 4-OAc, and 5-COOMe. Selected torsional angles: H3–C3–C4–H-4 +78, H4–C4–C5–H5 −63, O51–C1–C2–C3 +1.5, O51–C5–C4–C3 +56.9, O31–C3–C4–O41 −162.0, O4–C4–C5–C6 +175.8. The deviations of C4 (−0.30) and C5 (+0.38) from the plane formed by the ring oxygen, C1, C2, and C3 are given in Å.

Although only verified with a single secondary alcohol (2-propanol), the experiments described suffice to extend the ulosyl donor approach[2–5] to 2-ketoglucuronyl bromides for the straightforward assembly of oligosaccharides with α-D-GlcA or, preparatively more important, with β-D-ManA units, thereby complementing the use of 2-oximinoglucuronyl bromides[8] as effective indirect β-D-ManNAcA donors. As the 2-ketoglucuronides are readily converted into their oximes, as shown here for **8** (→**10**), they may also be utilized for the generation of β-D-ManNAcA oligosaccharides.

1. Experimental

1.1. General

Melting points were determined with a Bock hot-stage microscope, and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 polarimeter at 20 °C using a cell of 1 dm path length; concentration (*c*) in g/100 mL and solvent are given in parantheses. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX-300 spectrometer in the solvents given. Mass spectra were acquired on Varian MAT 311 and MAT 212 spectrometers. Microanalyses were determined on a Perkin–Elmer 240 elemental analyzer. Analytical thin-layer chromatography (TLC) was performed on precoated E. Merck plastic sheets (0.2 mm Silica Gel 60 F_{254}) with detection by UV (254 nm) and/or spraying with H_2SO_4 (50%) and heating. Column and flash chromatography was carried out on Fluka Silica Gel 60 (70–230 mesh) using the specified eluents.

1.2. Methyl 2-acetoxy-3,4-di-*O*-acetyl-D-*arabino*-hex-1-enopyranuronate (4)

The product was prepared by HBr elimination from methyl (2,3,4-tri-*O*-acetyl-α-D-glucopyranosyl)uronate bromide (**2**) according to Kaji et al.[8] Crystals suitable for X-ray structure determination were obtained by recrystallization from diisopropyl ether: well-formed rodlets of mp 92–93 °C and $[\alpha]_D^{20}$ −51.5 (*c* 1.1, $CHCl_3$); lit.:[8] mp 101–101.5 °C and $[\alpha]_D^{20}$ −51 (*c* 1.0, $CHCl_3$);[8] mp 76 °C and $[\alpha]_D^{20}$ −54 (*c* 0.5, $CHCl_3$).[11]

X-ray diffraction analysis was carried out on an Euraf–Nonius CAD diffractometer with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). Details for crystal data, data collection, and refinement parameters are given in Table 1. Programs used for structure solution, refinement, and analysis include SHELXS97,[12] and SHELXL97.[13] The ball-and-stick model representation of Figure 1 was generated by the MolArch™ program.[14] Hydrogen atoms were positioned geometrically; the carbonyl oxygens of the acetyl groups are disordered.

1.3. Methyl 3,4-di-*O*-benzoyl-2-benzoyloxy-D-*arabino*-hex-1-enopyranuronate (5)

A solution of methyl (2,3,4-tri-*O*-benzoyl-α-D-glucopyranosyl)uronate bromide (**3**)[7] (15.8 g, 27.1 mmol) in 150 mL of dry DMF was cooled to −20 °C, followed by the addition of tetrabutylammonium bromide (9.20 g, 28.5 mmol) and 3 Å molecular sieves (4 g) with stirring. Then, a solution of Me_2NH (4.36 mL, 42 mmol)

Table 1. Crystal data and structure refinement for **4**

Empirical formula	$C_{13}H_{16}O_9$
Formula weight	316.29
Temperature (K)	299
Wavelength (Å)	0.71069
Crystal system, space group	Orthorombic, $P2_12_12_1$
Unit cell dimensions	
A (Å)	8.4500(10)
B (Å)	9.0720(10)
C (Å)	20.410(2)
α (°)	90
β (°)	90
γ (°)	90
Volume (Å^3)	1.564.6(3)
Z, Calculated density (mg/m^3)	4, 1.343
Absorption coefficient (mm^{-1})	0.075
F(000)	664
Crystal size (mm)	0.55 × 0.20 × 1.00
θ Range for data collection (°)	2.00–22.96
Index ranges	$-9 \leqslant h \leqslant 9$, $0 \leqslant k9$, $0 \leqslant l \leqslant 22$
Reflections collected	2386 [R(int) = 0.0281]
Data/restraints/parameters	2170/0/253
Goodness-of-fit on F^2	1.094
Final *R* indices [$I > \sigma(I)$]	$R_1 = 0.0525$, $wR_2 = 0.1269$
R indices (all data)	$R_1 = 0.0585$, $wR_2 = 0.1337$
Largest difference in peak and hole (Å^{-3})	0.166 and −0.276

in DMF (50 mL) was added dropwise during the course of 1 h, and the mixture was stirred for 1 d at −20 °C and another at −10 °C. The dark-red solution was then diluted with CH_2Cl_2 (200 mL), filtered through kieselgur, and successively washed with 2 N HCl (3 × 100 mL), satd aq $NaHCO_3$ (3 × 50 mL) and water (50 mL). Drying (Na_2SO_4), removal of the solvent in vacuo and coevaporation of the residue with toluene left a syrup that was eluted from a silica gel column (5.5 × 12 cm) with 50:1 toluene–EtOAc. Evaporation of the eluate to dryness left crude glucuronal **5** as a yellowish foam (9.2 g, 67%, R_f 0.46 in 3:2 cyclohexane–EtOAc), containing about 3% of methyl 2,3,4-tri-*O*-benzoyl-D-glucopyranuronate (R_f 0.42). This product was used for the methoxybromination of **5**→**7**.

A 500 mg portion of crude **5** was subjected to purification on a silica gel column (2 × 20 cm, elution with 50:1 toluene–EtOAc) to give upon evaporation of the eluate containing **5** in vacuo and trituration of the residual foam with 2-propanol 295 mg (59%) of **5** as wad-like crystals: mp 123 °C; $[\alpha]_D^{20}$ −167.4 (*c* 1, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 3.56 (s, 3H, CH_3O), 5.10 (dd, 1H, H-5), 5.82 (d, 1H, H-3), 5.89 (dd, 1H, H-4), 7.07 (s, 1H, H-1), 7.35–8.11 (m, 15H, $3C_6H_5$); $J_{3,4}$ 2.4; $J_{4,5}$ 2.3; $J_{3,5}$ 1.4 Hz; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 51.8 ($\mathit{C}H_3O$), 63.9 (C-3), 67.5 (C-4), 71.5 (C-5), 126.6 (C-2), 127.5–133.9 ($3C_6H_5$), 139.3 (C-1), 165.0, 165.1, 165.2, 166.8 ($3C_6H_5\mathit{C}O$, C-6). Anal. Calcd for $C_{28}H_{22}O_9$ (502.48): C, 66.93; H, 4.41. Found C, 66.83; H, 4.39.

1.4. Methyl (3,4-di-*O*-acetyl-α-D-*arabino*-hexos-2-ulopyranosyl)uronate bromide (6)

MeOH (260 µL, 0.63 mmol) and 3 Å molecular sieves were added to a CH_2Cl_2 solution of D-gluronal **4** (2.00 g, 6.3 mmol, in 50 mL), followed, after stirring for 15 min, by *N*-bromosuccinimide (1.13 g, 6.3 mmol). Upon another 15 min of stirring the mixture was diluted with CH_2Cl_2 (50 mL), washed with 10% aq $Na_2S_2O_3$ (50 mL) and water (2 × 50 mL), dried (Na_2SO_4), and evaporated to dryness in vacuo, to give 1.46 g (66%) of ulosyl bromide **6** as a chromatographically uniform (R_f 0.05 in 5:1 toluene–EtOAc), colorless syrup: $[\alpha]_D^{20}$ +192.4 (*c* 0.7, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 2.04, 2.12 (two 3H-s, $AcCH_3$), 3.73 (s, 3H, OCH_3), 4.73 (d, 1H, H-5), 5.45 (dd, 1H, H-4), 6.02 (d, 1H, H-3), 6.34 (s, 1H, H-1), $J_{3,4} = J_{4,5}$ 10.4 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.4, 20.6 ($2\mathit{C}H_3CO$), 53.5 (CH_3O), 69.0 (C-4), 71.6 (C-3), 72.2 (C-5), 81.6 (C-1), 165.9, 169.1, 169.5 ($2CH_3\mathit{C}O$, C-6), 188.0 (C-2). FDMS (5 mA): *m*/*z* 352, 354 [M^+]. Anal. Calcd for $C_{11}H_{13}BrO_8$ (353.13): C, 37.41; H, 3.71. Found: C, 37.53; H, 3.80. The compound is liable to decomposition, stable in a refrigerator no longer than 24 h.

1.5. Methyl (3,4-di-*O*-benzoyl-α-D-*arabino*-hexos-2-ulopyranosyl)uronate bromide (7)

MeOH (0.45 mL, 11 mmol) and 3 Å molecular sieves were added to a solution of 5.00 g (10 mmol) of crude glucuronal **5**, as obtained above, in 50 mL of CH_2Cl_2. After stirring for 15 min, *N*-bromosuccinimide (2.0 g, 11 mmol) was added, and stirring at ambient temperature was continued for 3 h. Subsequent washing with 10% aq $Na_2S_2O_3$ (10 mL) and water (2 × 10 mL), followed by drying (Na_2SO_4) and evaporation to dryness, left a syrup that crystallized on trituration with CH_2Cl_2–diisopropyl ether: 3.34 g (70%) of ulosyl bromide **7** as colorless needles: mp 171–173 °C; $[\alpha]_D^{20}$ +151.6 (*c* 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 3.71 (s, 3H, CH_3O), 5.04 (d, 1H, H-5), 5.96 (dd, 1H, H-4), 6.52 (s, 1H, H-1), 6.57 (d, 1H, H-3), 7.40–8.05 (m, 10H, $2C_6H_5$). $J_{3,4} = J_{4,5}$ 10.4 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 53.5 (CH_3O), 69.6 (C-5), 72.1 (C-3), 72.5 (C-4), 81.8 (C-1), 128.3–134.1 ($2C_6H_5$), 164.8, 165.2, 166.0 ($2C_6H_5\mathit{C}O$, C-6), 188.0 (C-2); FDMS (15 mA): *m*/*z* 479, 477 [M^++H], 478, 476 [M^+], 397 [M^+−Br]. Anal. Calcd for $C_{21}H_{17}BrO_8$ (477.27): C, 52.85; H, 3.59. Found: C, 52.93; H, 3.51.

1.6. Methyl (cyclohexyl 3,4-di-*O*-benzoyl-α-D-*arabino*-hexos-2-ulopyranosid)uronate (8)

A solution of cyclohexanol (105 mg, 1.05 mmol) in CH_2Cl_2 (10 mL) containing 3 Å molecular sieves (500 mg) was cooled to −78 °C. Then ulosyl bromide **7**

(500 mg, 1.05 mmol) and silver triflate were added with vigorous stirring, followed by letting the temperature rise to −35 °C. After 5 h, the mixture was filtered through kieselgur, the filtrate was diluted with CH_2Cl_2 (40 mL) and washed consecutively with satd aq $NaHCO_3$, 10% aq $Na_2S_2O_3$ and water (20 mL each). Drying of the organic phase (Na_2SO_4) and removal of the solvent in vacuo left a syrup that was purified by elution from a silical gel column with 5:1 toluene–EtOAc to give 445 mg (85%) of **8** as a colorless foam: ^1H NMR (300 MHz, $CDCl_3$): δ 1.05–2.20 (m, 10H, $5CH_2$), 3.71 (s, 3H, CH_3O), 3.78 (m, 1H, CH), 4.99 (d, 1H, H-5), 5.21 (s, 1H, H-1), 5.87 (dd, 1H, H-4), 6.20 (d, 1H, H-3), 7.40–8.05 (m, 10H, 2 C6H5); $J_{3,4}$ 0.3; $J_{4,5}$ 10.1 Hz. Anal. Calcd for $C_{27}H_{28}O_9$ (496.49): C, 65.31; H, 5.68. Found: C, 65.19; H, 5.60.

1.7. Methyl (isopropyl 3,4-di-*O*-benzoyl-β-D-*arabino*-hexos-2-ulopyranosid)uronate (9)

To a suspension of silver aluminosilicate[10] (2.0 g, 6.2 mmol) and 3 Å molecular sieves (2 g) in CH_2Cl_2 (20 mL) containing 380 μL (5.0 mmol) of 2-propanol was added ulosyl bromide **7** (2.0 g, 2.1 mmol). The mixture was stirred at ambient temperature for 10 min, then filtered through kieselgur and evaporated to dryness in vacuo to give 1.85 g (97%) of uloside **9** as colorless crystals: mp 152–153 °C; $[\alpha]_D^{20}$ −91.1 (*c* 1.6, $CHCl_3$); R_f 0.48 in 5:1 CH_2Cl_2–EtOAc. ^1H NMR (300 MHz, $CDCl_3$): δ 1.24, 1.24 (two 3H-d, $CH(CH_3)_2$), 3.75 (s, 3H, CH_3O), 4.15 (qq, 1H, $CH(CH_3)_2$), 4.73 (d, 1H, H-5), 5.18 (s, 1H, H-1), 6.06 (d, 1H, H-3), 6.21 (dd, 1H, H-4), 7.30–8.10 (m, 10H, $2C_6H_5$); $J_{3,4} = 10.5$; $J_{4,5} = 7.8$ Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.4, 22.8 ($CH(CH_3)_2$), 53.0 (CH_3O), 69.3 (C-4), 72.9 ($CH(CH_3)_2$), 73.5 (C-5), 75.4 (C-3), 97.0 (C-1), 128.6–133.7 ($2C_6H_5$), 164.8, 165.5, 168.4 ($2C_6H_5CO$, C-6), 193.4 (C-2). Anal. Calcd for $C_{24}H_{24}O_9$ (456.45): C, 63.15; H, 5.30. Found C, 62.95; H, 5.18.

The product contained about 3% of the hydrated form as evidenced by a second set of ring protons: δ 4.74 (H-1), 5.53 (H-3), 5.78 (H-4) and 4.28 (H-5) with $J_{3,4} = J_{4,5}$ 9.9 Hz. The water of hydration could only partially be removed by extensive drying over P_2O_5 at 56 °C.

1.8. Methyl (cyclohexyl 3,4-di-*O*-benzoyl-α-D-*arabino*-hexos-2-ulopyranosid)uronate *Z*-oxime (10)

To a solution of α-glycosidulose **8** in 10 mL of 1:1 pyridine–MeOH was added $NH_2OH{\cdot}HCl$ (350 mg, 5 mmol), and the mixture was stirred for 24 h at ambient temperature, followed by dilution with CH_2Cl_2 (50 mL) and washings with 2 N HCl (2 × 10 mL), satd aq $NaHCO_3$ (10 mL) and water (10 mL). Drying (Na_2SO_4), removal of the solvent in vacuo, purification of the yellowish syrup by elution from a silica gel column (3 × 15 cm) with 8:1 cyclohexane–EtOAc and evaporation to dryness of the fractions with R_f 0.45 (3:2 cyclohexane–EtOAc) left 245 mg (51%) of **10** as a syrup: $[\alpha]_D^{20}$ +12.5 (*c* 0.6, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 1.10–1.83 (m, 10H, $5CH_2$), 3.66 (s, 3H, CH_3O), 3.65–3.72 (m, 1H, CH), 4.77 (d, 1H, H-5), 5.70 (dd, 1H, H-4), 6.18 (s, 1H, H-1), 6.26 (d, 1H, H-3), 7.35–8.00 (m, 10H, $2C_6H_5$), 8.87 (s, 1H, NOH); $J_{3,4}$ 9.7; $J_{4,5}$ 9.8 Hz; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 24.1, 24.4, 25.9, 31.7, 33.6 ($5CH_2$), 53.2 (CH_3O), 69.5 (C-5), 69.6 (C-3), 71.6 (C-4), 77.6 (cyclohexyl-*C*H), 89.3 (C-1), 128.7–133.8 ($2C_6H_5$), 148.8 (C-2), 165.5, 165.6, 168.5 ($2C_6H_5CO$, C-6); $J_{C\text{-}1,1\text{-}H}$ 176.6 Hz. Anal. Calcd for $C_{27}H_{29}NO_9$ (511.51): C, 63.40; H, 5.71; N, 2.74. Found C: 63.32; H, 5.57; N, 2.63.

1.9. Methyl (isopropyl 3,4-di-*O*-benzoyl-β-D-gluco-pyranosid)uronate (11)

A THF solution of uloside **9** (460 mg, 1 mmol, in 5 mL) was added in portions to a cooled (−78 °C) solution of $BH_3{\cdot}$pyridine (0.5 mL, 5 mmol) in THF (10 mL). The mixture was stirred for 1 h, then allowed to warm to ambient temperature, and quenched with water (2 mL). After removal of the solvents the syrupy residue was dissolved in CH_2Cl_2 (20 mL), followed by vigorous stirring with 2 N HCl (5 mL) for 30 min, separation of the layers and washing of the organic phase with satd aq $NaHCO_3$ (5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent led to a crude product, comprising (^1H NMR) an approximate 10:1 mixture of glucuronide **11** and its manno isomer **12**. Purification by elution from a silica gel column (3 × 15 cm) with 30:1 CH_2Cl_2–acetone gave 320 mg (76%) of **11** as a hard foam. ^1H NMR (300 MHz, $CDCl_3$): δ 1.24, 1.27 (2d, 3H each, $CH(CH_3)_2$), 2.55 (d, 1H, 2-OH), 3.69 (3H-s, OCH_3), 3.78 (ddd, 1H, H-2) 4.05 (m, 2H, H-5, $CH(CH_3)_2$), 4.63 (d, 1H, H-1), 5.55 (dd, 1H, H-4), 5.63 (dd, 1H, H-3); $J_{1,2}$ 7.7; $J_{2,3}$ 9.4; $J_{2,OH}$ 2.5; $J_{3,4} = J_{4,5}$ 9.5 Hz. Anal. Calcd for $C_{21}H_{26}O_9$ (422.4): C, 59.71; H, 6.20. Found C: 59.60; H, 6.11.

1.10. Methyl (isopropyl 3,4-di-*O*-benzoyl-β-D-manno-pyranosid)uronate (12)

A M solution of L-selectride (lithium tri-*sec*-butyl borohydride, 1 mL) was added under Ar to a cooled (−78 °C), stirred solution of uloside **9** (460 mg, 1 mmol) in THF (5 mL). After 1 min the reaction was quenched by the addition of HOAc (0.2 mL). Dilution with CH_2Cl_2 (20 mL), followed by washing with 2 M HCl (10 mL) and satd aq $NaHCO_3$ (10 mL), drying ($MgSO_4$) and evaporation of the solvent in vacuo left a residue that was purified by flash elution from a silica gel column with 50:1 CH_2Cl_2–EtOAc to give, after removal of the solvents from the appropriate fraction, 360 mg

(84%) of **12** as a colorless foam: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21, 1.27 (2d each, 3H, $CH(CH_3)_2$), 2.56 (d, 1H, 2-OH), 3.71 (3H-s, OCH_3), 4.09 (ddd, 1H, H-5), 4.10 (qq, 1H, $OCH(CH_3)_2$), 4.33 (m, 1H, H-2) 4.87 (d, 1H, H-1), 5.40 (dd, 1H, H-3), 5.95 (dd, 1H, H-4); $J_{1,2}$ 0.9, $J_{2,3}$ 3.2, $J_{3,4}$ 9.8, $J_{4,5}$ 9.6 Hz. Anal. Calcd for $C_{21}H_{26}O_9$ (422.4): C, 59.71; H, 6.20. Found C: 59.66; H, 6.09.

2. Supplementary data

Crystallographic data, excluding structure factors, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication with CCDC No. 630545. Copies of the data can be obtained free of charge on application with the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgements

Our thanks are due to Mrs. Sabine Foro for collecting the X-ray data and Priv. Doz. Dr. Stefan Immel for the color graphic in Figure 1, generated with his MolArch™ program.

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