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Note

From lactose towards a novel galactosylated cyclooctenone

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Dedicated to the memory of Professor Zoltán Györgydeák

Abstract—Lactose was converted into a disaccharide precursor incorporating an allyl vinyl ether substructure within the glucose residue by vinylation, regioselective silylation, tosylation and subsequent elimination. The thermal Claisen rearrangement led to a novel galactosylated cyclooctenone exhibiting a boat-chair conformation.

Keywords: Claisen rearrangement; Allyl vinyl ether; Lactose; Stannylene; Cyclooctenone; Boat chair

Glycosides of functionalized eight-membered carbocycles represent important structural motifs that can be found as backbones in a variety of natural products such as taxane derivatives[1] and fusicoccane terpenoids.[2] Moreover, synthetic access to specifically glycosylated and oxygenated carbocycles is highly desirable, since such compounds may serve as mimetics[3] of naturally occurring inositol glycoside structures such as the glycosylphosphatidylinositol unit in GPI anchors.[4] In a recent contribution we reported approaches towards glycosylated eight-membered rings via Claisen rearrangement of either a disaccharide derivative or a monosaccharide derivative and subsequent glycosylation.[5] Further studies of this work involved the synthesis of a novel galactosylated cyclooctenone derived from lactose that we wish to describe here.

Lactose was initially converted into the known α-lactosylbromide **1**,[6] which was subjected to a Grignard reaction with vinylmagnesiumbromide[7] to give after peracetylation the C-vinylated lactoside **2** as an inseparable anomeric mixture (Scheme 1). The deacetylated lactoside **3** was obtained by treatment with sodium methoxide in methanol[8] in quantitative yield. In order to efficiently generate the enol ether double bond between C-7 and C-8 of the glucose residue the other primary hydroxyl group had to be selectively protected. This was accomplished in good yield by generation of the stannylene intermediate[9] derived from **3** using Bu_2SnO followed by silylation with *t*-butyldimethylsilyl chloride. The regioselective substitution does not occur at C-3′ of the galactose residue as one would normally expect when using a stannylene derivative of a galactose unit. Instead, C-6′ is silylated almost exclusively, which can be rationalized by a fast equilibrium of different stannylene intermediates, the one involving O-6′ reacting faster with the bulky silylation reagent.[10] To convert the hydroxyl group at C-8 selectively into a good leaving group, lactoside **4** was treated with TsCl, however, in addition to the desired monotosylate the formation of substantial amounts of the 8,3′-ditosylate (ca. 40%) could not be suppressed. Both compounds were acetylated in situ to give compounds **5** and **6** as an inseparable mixture. The enol ether double bond was then introduced by substitution of the tosylate by an iodide and subsequent basic elimination using DBU.[11] At this stage both allyl vinyl ethers **7** and **8** could be separated without difficulty.

For the Claisen rearrangement step compound **7** was heated in a *n*-decane/toluene mixture (ratio: 2:1) at 185 °C under microwave irradiation, a procedure that had proved effective previously for thermal Claisen rearrangements of carbohydrate derivatives.[12,13] The

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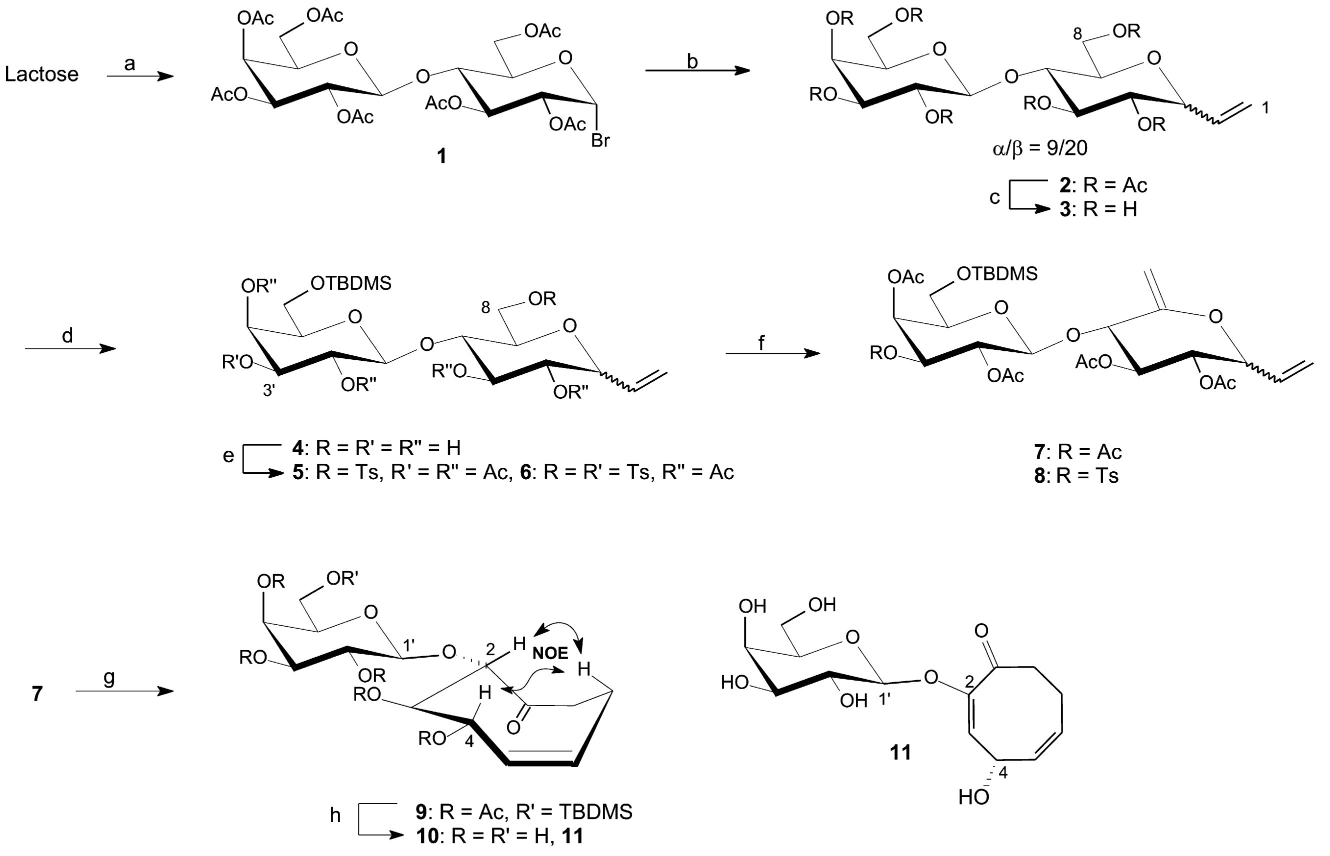

Scheme 1. Reagents and conditions: (a) lit.,[6] (b) (i) $CH_2{=}CHMgBr$, THF, (ii) Ac_2O, py, 46%; (c) NaOMe, MeOH, 100%; (d) (i) Bu_2SnO, MeOH, (ii) TBDMSCl, THF, 81%; (e) (i) TsCl, py, (ii) Ac_2O, py; (f) (i) TBAI, NaI, DMSO, 80 °C, (ii) DBU, DMSO, 80 °C, 67%; (g) *n*-decane/toluene 2:1, microwave 185 °C, 69%; (h) (i) NaOMe, MeOH, (ii) TBAF, THF, 90%.

expected rearrangement product **9** was obtained in 69% yield. Longer reaction times will drive the Claisen rearrangement to completion, however, the elimination of acetic acid in ketone **9** to the α,β-unsaturated ketone increases and becomes a major drawback. Thorough analysis of coupling constants as well as observed NOE interactions between H-2 and H-7 as well as H-4 and H-7 lead to the conclusion that ketone **9** adopts a boat-chair conformation with the oxygenated functionalities being equatorially oriented. For global deprotection ketone **9** was first deacetylated under Zemplén conditions followed by treatment with tetrabutylammoniumfluoride to yield a mixture of ketone **10** along with the α,β-unsaturated ketone **11** (ratio: **10**/**11** ≈ 11:9), which is the result of an elimination of acetic acid under the basic deacetylation conditions. As soon as the acetyl group at C-3 is removed, this elimination is impeded since a negatively charged oxide substituent ($R{-}O^-$) is unable to act as a leaving group. Further, there is no possibility for any of the deprotonated hydroxyl functions for a nucleophilic attack of the carbonyl group due to steric reasons. These structural properties render ketone **10** relatively stable under basic conditions compared to ketone **9**.

HPLC separation of a mixture of **10** and **11** resulted in three fractions a–c, which were analyzed by ESI-MS. Fraction c proved to be the pure elimination product **11** (M+Na, $m/z = 339$). Fraction b in addition to **11** contained the cyclooctenone galactopyranoside **10** (M+Na, $m/z = 357$) and an unknown degradation product of **10**, which was also obtained in fraction a (M+Na, $m/z = 275$). Apparently, even under such comparatively mild separation conditions, the unblocked target compound **10** did not prove to be stable.

Overall, we have explored one more alternative for the construction of glycosylated eight-membered ring systems in addition to our previous works, which is superior in that it involves fewer steps, avoids complex glycosylation procedures and reaches higher yields. Further efforts will focus on the employment of different protecting groups to circumvent the formation of product mixtures generated during the deprotection steps.

1. Experimental

1.1. General methods

Anhydrous solvents were purchased from the manufacturers Fluka and Merck. TLC was performed on silica gel 60-coated aluminium sheets (Merck or Macherey-Nagel), with detection by UV at 254 nm and by heating with H_2SO_4 (10% in EtOH). Flash chromatography was carried out on silica gel 60 (0.04–0.063 mm; Merck, Macherey-Nagel or ICN). Petroleum ether used refers to bp 50–70 °C. The microwave experiments were performed in a CEM microwave system (Discover, 300 W maximum power output) by using sealed tubes with temperature control via infrared sensor. NMR spectra were recorded on a Bruker AMX-400 and DRX-500 NMR spectrometer (^{1}H: 400/500 MHz; ^{13}C: 100 MHz) and analyzed with the respective solvent peaks as references. Assignments of the anomers to either α or β were made on the basis of the H-3/H-4 coupling constants: In the β-anomer $^3J_{3,4}$ is usually around 9–10 Hz due to the diaxial arrangement of the hydrogens whereas $^3J_{3,4}$ in the α-anomer is considerably smaller (around 3–5 Hz) as a result of the axial–equatorial orientation. For the majority of compounds only the β-anomer was characterized from the α/β-mixture, while signals of both α- and β-anomers are marked accordingly. Mass spectra were recorded either with a Bruker Biflex III (MALDI-TOF, positive reflection mode, matrix: 2,5-dihydroxybenzoic acid) or with a Thermo Electron MAT 95 XL Trap (ESI-MS, high resolution, water/MeOH 1:1) from Thermo Fisher Scientific Inc. The HPLC separation was performed using a Grace Vydac column (Vydac 218TP510) with water and acetonitrile as eluents both containing trifluoroacetic acid (0.1%). The optical rotations were measured on a Perkin–Elmer 243 polarimeter at 20 °C.

1.2. 4,5,8-Tri-*O*-acetyl-3,7-anhydro-1,2-dideoxy-D-*glycero*-D-*gulo*-oct-1-enitol-6-yl-2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranoside [β-anomer]; 4,5,8-tri-*O*-acetyl-3,7-anhydro-1,2-dideoxy-D-*glycero*-D-*ido*-oct-1-enitol-6-yl-2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranoside [α-anomer] (2)

Under an argon atmosphere a solution of **1**[6] (7.007 g, 10.02 mmol) in dry THF (100 mL) was added dropwise to a solution of vinylmagnesium bromide in THF (190 mL, 1 M, 190 mmol). After the end of the exothermic reaction heating under reflux was continued for 5 h. The reaction mixture was poured into ice water and neutralized with acetic acid. The aqueous phase was evaporated and the residue dried several hours in vacuo. After suspension of the residue in pyridine (60 mL) and addition of Ac_2O (30 mL) at 0 °C the reaction mixture was stirred for 2 days. The mixture was then poured into ice water and extracted with CH_2Cl_2. After evaporation of the solvent the residue was purified by column chromatography (petroleum ether/ethyl acetate 5:1–3:1) to give 2.961 g of **2** (4.579 mmol, 46%, colourless syrup) as an inseparable anomeric mixture (α/β ≈ 9:20). However, a partial separation of the β-anomer for NMR spectroscopic characterization could be realized.

β-Anomer: $[\alpha]_D^{20}$ +1.3 (*c* 1, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ 1.54, 1.63, 1.65, 1.70, 1.73, 1.93, 1.98 (7 × s, 7 × 3H, Ac), 3.27 (ddd, 1H, H-7, $^3J_{6,7} = 9.7$, $^3J_{7,8a} = 2.0$ Hz), 3.46–3.51 (m, 2H, H-3, H-5′, $^3J_{2,3} = 6.6$, $^3J_{3,4} = 9.7$ Hz), 3.59 (dd ∼ vt, 1H, H-6, $^3J_{5,6} = {}^3J_{6,7} = 9.7$ Hz), 4.07–4.17 (m, 3H, H-8b, H-6′a/b), 4.35 (d, 1H, H-1′, $^3J_{1',2'} = 7.9$ Hz), 4.48 (dd, 1H, H-8a, $^3J_{7,8a} = 2.0$, $^2J_{8a,8b} = 11.7$ Hz), 4.98 (ddd ∼ dt, 1H, H-1b, $^2J_{1a,1b} = 1.0$, $^3J_{1b,2} = 10.4$ Hz), 5.03 (dd ∼ t, 1H, H-4, $^3J_{3,4} = {}^3J_{4,5} = 9.7$ Hz), 5.11 (dd, 1H, H-3′, $^3J_{2',3'} = 10.4$, $^3J_{3',4'} = 3.3$ Hz), 5.18 (ddd ∼ dt, 1H, H-1a, $^2J_{1a,1b} = 1.0$, $^3J_{1a,2} = 17.3$ Hz), 5.36 (dd ∼ t, 1H, H-5, $^3J_{4,5} = {}^3J_{5,6} = 9.2$ Hz), 5.47 (dd, 1H, H-4′, $^3J_{3',4'} = 3.3$, $^3J_{4',5'} = 1.0$ Hz), 5.53 (dd, 1H, H-2′, $^3J_{1',2'} = 7.9$, $^3J_{2',3'} = 10.4$ Hz), 5.65–5.74 (m, 1H, H-2, $^3J_{1a,2} = 17.3$, $^3J_{1b,2} = 10.4$, $^3J_{2,3} = 6.6$ Hz); ^{13}C NMR (100 MHz, C_6D_6): δ 20.38, 20.47, 20.57, 20.65, 20.70, 20.80, 21.18 (7C, Ac), 61.29 (1C, C-6′), 63.43 (1C, C-8), 67.26, 70.01, 71.14, 71.86, 72.49, 74.93, 76.94, 77.65, 79.06 (9C, C-1, C-2, C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 101.94 (1C, C-1′), 119.14 (1C, C-2), 134.43 (1C, C-1), 169.24, 169.60, 169.69, 170.03, 170,12, 170.37 (7C, Ac); MALDI-TOF (DHB, positive mode): $C_{28}H_{38}O_{17}$ *m*/*z* = 669 $[M+Na]^+$, 685 $[M+K]^+$.

1.3. 3,7-Anhydro-1,2-dideoxy-D-glycero-D-*gulo*-oct-1-enitol-6-yl-β-D-galactopyranoside [β-anomer]; 3,7-anhydro-1,2-dideoxy-D-*glycero*-D-*ido*-oct-1-enitol-6-yl-β-D-galactopyranoside [α-anomer] (3)

To a solution of **2** (2.906 g, 4.494 mmol) in dry MeOH (60 mL) was added sodium methoxide (NaOMe) until pH 9 was reached. The reaction mixture was stirred for several hours until TLC control (CH_2Cl_2/MeOH 10:1) confirmed complete reaction. After neutralization with Amberlite IR-120 H^+ the solution was filtered and the solvent evaporated to give 1.584 g of **3** (4.495 mmol, 100%, white amorphous solid) as an inseparable anomeric mixture (α/β ≈ 9:20). Purified β-**2** was deacetylated as well and separately characterized.

β-Anomer: $[\alpha]_D^{20}$ +4.0 (*c* 1, DMSO); ^{1}H NMR (400 MHz, DMSO): δ 2.93–3.77 (m, 13H, H-1, H-2, H-3, H-4, H-5, H-6a/b, H-2′, H-3′, H-4′, H-5′, H-6′a/b), 4.20 (d, 1H, H-1′, $^3J_{1',2'} = 7.4$ Hz), 4.45–4.88 (br m, 5H, 5 × OH), 5.12–5.15 (m, 3H, 2 × OH, H-1b, $^2J_{1a,1b} = 2.0$, $^3J_{1b,2} = 10.7$ Hz), 5.30 (ddd ∼ dt, 1H, H-1a, $^2J_{1a,1b} = 2.0$, $^3J_{1a,2} = 17.8$ Hz), 5.89 (ddd, 1H, H-2, $^3J_{1a,2} = 17.8$, $^3J_{1b,2} = 10.7$, $^3J_{2,3} = 5.2$ Hz); ^{13}C NMR (100 MHz, DMSO): δ 60.72, 61.14 (2C, C-8, C-6′), 68.48, 70.93, 73.62, 73.97, 75.86, 76.68, 78.77, 79.31, 81.73 (9C, C-3, C-4, C-5, C-6, C-7, C-2′, C-3′, C-4′, C-5′), 104.21 (1C, C-1′), 116.52 (1C, C-1), 136.74 (1C, C-2); MALDI-TOF (DHB, positive mode): $C_{14}H_{24}O_{10}$ *m*/*z* = 375 $[M+Na]^+$, 391 $[M+K]^+$.

1.4. 3,7-Anhydro-1,2-dideoxy-D-*glycero*-D-*gulo*-oct-1-enitol-6-yl-6′-*O*-*tert*-butyldimethyl-silyl-β-D-galactopyranoside [β-anomer]; 3,7-anhydro-1,2-dideoxy-D-*glycero*-D-*ido*-oct-1-enitol-6-yl-6′-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranoside [α-anomer] (4)

A solution of **3** (661 mg, 1.876 mmol) in MeOH (18 mL) with molecular sieves 4 Å was treated with dibutyltin oxide ($\mathrm{Bu_2SnO}$, 472 mg, 1.896 mmol) and refluxed for 2 h. After evaporation of the solvent and co-distillation with toluene the residue was taken up in THF (18 mL). Following addition of TBDMSCl (311 mg, 2.063 mmol) the solution was stirred at rt until TLC control confirmed the complete consumption (TLC: $\mathrm{CH_2Cl_2}$/MeOH 9:1). The solvent was removed under reduced pressure and the residue purified by column chromatography ($\mathrm{CH_2Cl_2}$/MeOH 95:5 + 1% $\mathrm{Et_3N}$) to give 537 mg of **4** (1.151 mmol, 61%, colourless syrup) as an inseparable anomeric mixture (α/β ≈ 9:20).

β-Anomer: ^{1}H NMR (400 MHz, MeOH): δ 0.11 (s, 6H, Me), 0.92 (s, 9H, *tert*-Bu), 3.14–3.19, 3.38–3.91 (2 × m, 13H, H-1, H-2, H-3, H-4, H-5, H-6a/b, H-2′, H-3′, H-4′, H-5′, H-6′a/b), 4.37 (d, 1H, H-1′, $^3J_{1',2'} = 7.6$ Hz), 5.20–5.23 (m, 1H, H-1b, $^2J_{1a,1b} = 1.8$, $^3J_{1b,2} = 10.7$ Hz), 5.39–5.42 (m, 1H, H-1a, $^2J_{1a,1b} = 1.8$, $^3J_{1a,2} = 17.5$ Hz), 5.93 (ddd, 1H, H-2, $^3J_{1a,2} = 17.5$, $^3J_{1b,2} = 10.7$, $^3J_{2,3} = 5.6$ Hz); ^{13}C NMR (100 MHz, MeOH): δ 8.01 (2C, Me), 26.43 (3C, *tert*-Bu), 62.26, 62.92 (2C, C-8, C-6′), 69.66, 72.51, 74.91, 75.17, 76.78, 77.81, 79.95, 81.22, 81.42 (9C, C-3, C-4, C-5, C-6, C-7, C-2′, C-3′, C-4′, C-5′), 105.21 (1C, C-1′), 117.78 (1C, C-1), 136.76 (1C, C-2); MALDI-TOF (DHB, positive mode): $\mathrm{C_{20}H_{38}O_{10}Si}$ $m/z = 489$ $[\mathrm{M+Na}]^+$, 505 $[\mathrm{M+K}]^+$; Anal. Calcd for $\mathrm{C_{20}H_{38}O_{10}Si}$: C, 51.47; H, 8.22. Found: C, 51.61; H, 8.28.

1.5. 4,5-Di-*O*-acetyl-3,7-anhydro-1,2-dideoxy-8-*O*-tosyl-D-*glycero*-D-*gulo*-oct-1-enitol-6-yl-2′,3′,4′-tri-*O*-acetyl-6′-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranoside [β-anomer]; 4,5-di-*O*-acetyl-3,7-anhydro-1,2-dideoxy-8-*O*-tosyl-D-*glycero*-D-*ido*-oct-1-enitol-6-yl-2′,3′,4′-tri-*O*-acetyl-6′-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranoside [α-anomer] (5)

A solution of **4** (524 mg, 1.123 mmol) in pyridine (20 mL) was treated with TsCl (336 mg, 1.762 mmol). After complete consumption of starting material (TLC: $\mathrm{CH_2Cl_2}$/MeOH 10:1), $\mathrm{Ac_2O}$ (10 mL) was added and stirring continued until the reaction was complete (TLC: PE/EE 1:1). The mixture was diluted with water, extracted with $\mathrm{CH_2Cl_2}$ and purified by column chromatography (PE/EE 3:1 + 1% $\mathrm{Et_3N}$) to give 421 mg (0.507 mmol, 45%) **5**/**6** as colourless foam (anomeric ratio: α/β ≈ 1:5). The product mixture contained approximately 40% of the 8,3′-ditosylate **6**.

β-Anomer: ^{1}H NMR (400 MHz, $\mathrm{C_6D_6}$): δ −0.02, 0.00 (2 × s, 2 × 3H, Me), 0.92 (s, 9H, *tert*-Bu), 1.61, 1.70, 1.76, 1.93, 2.02 (5 × s, 5 × 3H, Ac), 1.90 (s, 3H, Ts–Me), 2.94–3.00 (m, 1H, H-7), 3.34–3.46 (m, 2H, H-3, H-5′), 3.56–3.84 (m, 3H, H-6, H-6′a/b), 4.22–4.34 (m, 2H, H-8a/b), 4.38 (d, 1H, H-1′, $^3J_{1',2'} = 7.9$ Hz), 4.87–5.10 (m, 3H, H-1a/b, H-4), 5.16 (dd, 1H, H-3′, $^3J_{2',3'} = 10.4$, $^3J_{3',4'} = 3.3$ Hz), 5.31 (dd ~ t, 1H, H-5, $^3J_{4,5} = {}^3J_{5,6} = 9.1$ Hz), 5.46–5.60 (m, 2H, H-2, H-2′, $^3J_{1a,2} = 17.3$, $^3J_{1b,2} = 10.4$, $^3J_{2,3} = 6.6$ Hz), 5.74–5.76 (m, 1H, H-4′), 6.77, 7.78 (2 × d, 2 × 2H, Ar); ^{13}C NMR (100 MHz, $\mathrm{C_6D_6}$): δ 20.03, 20.31, 20.41, 20.89, 21.19 (5C, Ac), 25.91 (3C, *tert*-Bu), 60.41 (1C, C-6′), 66.89 (1C, C-4′), 67.87 (1C, C-8), 70.00, 71.97, 72.06 (3C, C-4, C-2′, C-3′), 73.58, 74.70, 75.81, 76.17 (4C, C-5, C-6, C-7, C-5′), 78.76 (1C, C-3), 101.37 (1C, C-1′), 118.69 (1C, C-1), 128.59, 130.00 (2 × 2C, Ar), 133.97 (1C, C-2), 169.24, 169.46, 169.76 (5C, Ac); MALDI-TOF (DHB, positive mode): $\mathrm{C_{37}H_{54}O_{17}SSi}$ $m/z = 853$ $[\mathrm{M+Na}]^+$, 872 $[\mathrm{M+K}]^+$.

1.5.1. 4,5-Di-*O*-acetyl-3,7-anhydro-1,2-dideoxy-8-*O*-tosyl-D-*glycero*-D-*gulo*-oct-1-enitol-6-yl-2′,4′-di-*O*-acetyl-6′-*O*-*tert*-butyldimethylsilyl-3′-*O*-tosyl-β-D-galactopyranoside [β-anomer]; 4,5-Di-*O*-acetyl-3,7-anhydro-1,2-dideoxy-8-*O*-tosyl-D-*glycero*-D-*ido*-oct-1-enitol-6-yl-2′,4′-di-*O*-acetyl-6′-*O*-*tert*-butyldimethylsilyl-3′-*O*-tosyl-β-D-galactopyranoside [α-anomer] (6). Anomeric ratio: α/β ≈ 1:5; ^{1}H NMR (400 MHz, $\mathrm{C_6D_6}$): δ 1.82 (s, 3H, Ts–Me_α), 1.90 (s, 3H, Ts–Me_β), 4.97 (dd, 1H, H-$3'_{\alpha/\beta}$); ^{13}C NMR (100 MHz, $\mathrm{C_6D_6}$): δ 77.45 (1C, C-$3'_{\alpha/\beta}$), 128.48, 129.84 (2 × 2C, $\mathrm{Ar}_{\alpha/\beta}$); MALDI-TOF (DHB, positive mode): $\mathrm{C_{42}H_{58}O_{18}S_2Si}$ $m/z = 965$ $[\mathrm{M+Na}]^+$.

1.6. 4,5-Di-*O*-acetyl-3,7-anhydro-1,2,8-trideoxy-D-*gulo*-octa-1,7-dienitol-6-yl-2′,3′,4′-tri-*O*-acetyl-6′-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranoside [β-anomer]; 4,5-di-*O*-acetyl-3,7-anhydro-1,2,8-trideoxy-D-*ido*-octa-1,7-dienitol-6-yl-2′,3′,4′-tri-*O*-acetyl-6′-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranoside [α-anomer] (7)

A solution of the product mixture **5**/**6** (395 mg, 475 μmol), TBAI (88 mg, 238 μmol) and NaI (356 mg, 2.377 mmol) in DMSO (4 mL) was stirred for 2 h at 80 °C. After addition of DBU (142 μL, 145 mg, 951 μmol) stirring was continued for another 2 h until TLC control confirmed complete consumption of the intermediate iodide (PE/EE 3:1). The solution was diluted with water and extracted with $\mathrm{CH_2Cl_2}$. Evaporated of the solvent and purification of the residue by column chromatography (PE/EE 4:1 + 1% $\mathrm{Et_3N}$) gave 133 mg of **7** (202 μmol, 43%, white foam) and 86 mg of **8** (112 μmol, 24%, colourless syrup).

Anomeric ratio: α/β ≈ 1:5; β-anomer: ^{1}H NMR (400 MHz, $\mathrm{C_6D_6}$): δ −0.02, 0.01 (2 × s, 2 × 3H, Me), 0.93 (s, 9H, *tert*-Bu), 1.60, 1.61, 1.73, 1.75, 1.78 (5 × s, 5 × 3H, Ac), 3.31 (ddd ~ t, 1H, H-5′, $^3J_{5',6'a} = 6.1$, $^3J_{5',6'b} = 7.5$ Hz), 3.60 (dd, 1H, H-6′b, $^2J_{6'a,6'b} = 9.7$, $^3J_{5',6'b} = 7.5$ Hz), 3.71 (dd, 1H, H-6′a, $^2J_{6'a,6'b} = 9.7$, $^3J_{5',6'a} = 6.1$ Hz), 4.36 (dd, 1H, H-3, $^3J_{2,3} = 7.0$, $^3J_{3,4} = 9.9$ Hz), 4.42 (d, 1H, H-6, $^3J_{5,6} = 5.6$ Hz), 4.53 (d, 1H, H-1′, $^3J_{1',2'} = 8.1$ Hz), 4.58 (s, 1H, H-8b), 4.85 (s, 1H, H-8a), 5.03 (d, 1H, H-1b, $^2J_{1a,1b} = 1.0$, $^3J_{1b,2} = 10.4$ Hz), 5.18 (dd, 1H, H-3′, $^3J_{2',3'} = 10.4$, $^3J_{3',4'} = 3.3$ Hz), 5.25 (dd, 1H, H-4, $^3J_{3,4} = 9.9$, $^3J_{4,5} = 6.4$ Hz), 5.32 (ddd ~ dt, 1H, H-1a, $^2J_{1a,1b} = 1.0$, $^3J_{1a,2} = 17.3$ Hz), 5.49 (dd, 1H, H-5, $^3J_{4,5} = 6.4$, $^3J_{5,6} = 5.6$ Hz), 5.64 (dd, 1H, H-4′, $^3J_{3',4'} = 3.3$, $^3J_{4',5'} = 1.8$ Hz), 5.67 (dd, 1H, H-2′, $^3J_{1',2'} = 8.1$, $^3J_{2',3'} = 10.4$ Hz), 5.75–5.84 (m, 1H, H-2, $^3J_{1a,2} = 17.3$, $^3J_{1b,2} = 10.4$ Hz); ^{13}C NMR (100 MHz, C_6D_6): δ 20.06, 20.30, 20.33, 20.44, 20.51 (5C, Ac), 25.93 (3C, *tert*-Bu), 61.04 (1C, H-6′), 67.35 (1C, C-4′), 69.63 (1C, C-2′), 71.79, 72.65, 73.86, 74.06 (4C, C-4, C-5, C-3′, C-5′), 75.90 (1C, C-6), 77.56 (1C, C-3), 95.65 (1C, C-8), 99.13 (1C, C-1′), 119.51 (1C, C-1), 134.35 (1C, C-2), 153.90 (1C, C-7), 168.94, 169.04, 169.24, 169.83, 169.85 (5C, Ac); MALDI-TOF (DHB, positive mode): $C_{30}H_{46}O_{14}Si$ $m/z = 681$ [M+Na]$^+$, 697 [M+K]$^+$.

1.6.1. 4,5-Di-*O*-acetyl-3,7-anhydro-1,2,8-trideoxy-D-*gulo*-octa-1,7-dienitol-6-yl-2′,4′-di-*O*-acetyl-6′-*O*-*tert*-butyldimethylsilyl-3′-*O*-tosyl-β-D-galactopyranoside [β-anomer]; 4,5-di-*O*-acetyl-3,7-anhydro-1,2,8-trideoxy-D-*ido*-octa-1,7-dienitol-6-yl-2′,4′-di-*O*-acetyl-6′-*O*-*tert*-butyldimethylsilyl-3′-*O*-tosyl-β-D-galactopyranoside [α-anomer] (8). Anomeric ratio: $\alpha/\beta \approx 1{:}5$; ^{1}H NMR (400 MHz, C_6D_6): δ 1.80 (s, 3H, Ts–Me), 4.94 (dd, 1H, H-3′); ^{13}C NMR (100 MHz, C_6D_6): δ 20.75 (1C, Ts–Me$_{\alpha/\beta}$), 77.34 (1C, C-3′$_{\alpha/\beta}$), 128.48, 129.84 (2 × 2C, Ar); MALDI-TOF (DHB, positive mode): $C_{35}H_{50}O_{15}SSi$ $m/z = 793$ [M+Na]$^+$, 809 [M+K]$^+$.

1.7. (2*S*,3*R*,4*S*,5*Z*)-3,4-Diacetoxy-2-(2′,3′,4′-tri-*O*-acetyl-6′-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranosyloxy)-cyclooct-5-ene-1-one (9)

A solution of **7** (26 mg, 39 μmol) in a *n*-decane/toluene mixture (2:1, 6 mL) was heated under microwave irradiation for 1 h at 185 °C (TLC control: PE/EE 2:1). After evaporation of the solvent the residue was purified by column chromatography (PE/EE 4:1) to give 18 mg of **9** (27 μmol, 69%) as a colourless syrup besides 4 mg of recovered starting material **8** (6 μmol, 15%). Based on the actual conversion the yield amounts to 82%.

$[\alpha]_{546}^{20}$ −23.3 (*c* 0.5, EtOAc); ^{1}H NMR (500 MHz, C_6D_6): δ −0.02, 0.01 (2 × s, 2 × 3H, Me), 0.92 (s, 9H, *tert*-Bu), 1.58, 1.62, 1.74, 1.80 (4 × s, 4 × 3H, Ac), 1.76–1.83, 2.20–2.34 (2 × m, 3H, H-7a/b, H-8b), 2.73 (ddd, 1H, H-8a), 3.38 (ddd ~ t, 1H, H-5′, $^3J_{5',6'a} = 6.0$, $^3J_{5',6'b} = 7.6$ Hz), 3.74 (dd, 1H, H-6′b, $^2J_{6'a,6'b} = 9.7$, $^3J_{5',6'b} = 7.6$ Hz), 3.92 (dd, 1H, H-6′a, $^2J_{6'a,6'b} = 9.7$, $^3J_{5',6'a} = 6.0$ Hz), 4.19 (d, 1H, H-1′, $^3J_{1',2'} = 8.2$ Hz), 4.45 (d, 1H, H-2, $^3J_{2,3} = 4.4$ Hz), 5.13 (dd, 1H, H-3′, $^3J_{2',3'} = 10.4$, $^3J_{3',4'} = 3.5$ Hz), 5.39–5.43 (m, 1H, H-5, $^3J_{4,5} = 8.5$, $^3J_{5,6} = 10.7$ Hz), 5.52 (dd, 1H, H-3, $^3J_{2,3} = 4.4$, $^3J_{3,4} = 10.1$ Hz), 5.60–5.67 (m, 2H, H-6, H-2′), 5.69 (dd, 1H, H-4′, $^3J_{3',4'} = 3.5$ Hz), 5.87–5.91 (m, 1H, H-4, $^3J_{3,4} = 10.1$, $^3J_{4,5} = 8.5$, $^4J_{4,6} = 1.0$ Hz); ^{13}C NMR (100 MHz, C_6D_6): δ 20.19 (1C, C-7), 20.12, 20.29, 20.34, 20.45, 20.56 (5C, Ac), 23.66 (1C, –Si*C*Me$_3$), 25.95 (3C, *tert*-Bu), 41.76 (1C, C-8), 60.82 (1C, C-6′), 67.35 (1C, C-4′), 69.44, 69.65 (2C, C-4, C-2′), 71.42 (1C, C-3′), 72.15 (1C, C-3), 74.11 (1C, C-5′), 83.27 (1C, C-2), 101.29 (1C, C-1′), 127.68 (1C, C-5), 132.30 (1C, C-6), 169.01 (5C, Ac); MALDI-TOF (DHB, positive mode): $C_{30}H_{46}O_{14}Si$ $m/z = 681$ [M+Na]$^+$, 697 [M+K]$^+$.

1.7.1. (2*S*,3*R*,4*S*,5*Z*)-2-(β-D-Galactopyranosyloxy)-cyclooct-5-ene-3,4-diol-1-one (10); (2*E*,4*S*,5*Z*)-2-(β-D-galactopyranosyloxy)-cyclooct-2,5-diene-4-ol-1-one (11). To a solution of **9** (15.4 mg, 23 μmol) in MeOH (1 mL) was added NaOMe at −10 °C until pH 10 was reached. The solution was then allowed to warm to rt and stirred until TLC control confirmed complete deacetylation (CH_2Cl_2/MeOH 5:1). The solvent was evaporated under reduced pressure and taken up in THF (0.4 mL). After addition of a solution of TBAF in THF (1 M, 0.035 mL, 35 μmol) the mixture was stirred at rt until the reaction was complete (TLC control: CH_2Cl_2/MeOH 5:1). The solvent was evaporated and the residue purified by column chromatography (CH_2Cl_2/MeOH 10:1) to yield 7 mg (ca. 90%) of an inseparable mixture, which contained ca. 55% of **10** and ca. 45% of the elimination product **11**.

Compound **10**: ^{1}H NMR (500 MHz, D_2O): δ 4.15 (d, 1H, H-2, $^3J_{2,3} = 5.9$ Hz), 4.47 (d, 1H, H-1′, $^3J_{1',2'} = 7.4$ Hz), 4.50 (dd, 1H, H-3, $^3J_{2,3} = 5.9$, $^3J_{3,4} = 7.4$ Hz), 4.59 (dd, 1H, H-4, $^3J_{3,4} = 7.4$, $^3J_{4,5} = 5.6$ Hz), 5.70–5.75 (m, 1H, H-5), 5.92–5.96 (m, 1H, H-6); ^{13}C NMR (100 MHz, D_2O): δ 84.26 (1C, C-2), 103.40 (1C, C-1′), 128.34 (1C, C-5); MALDI-TOF (DHB, positive mode): $C_{14}H_{22}O_9$ $m/z = 357$ [M+Na]$^+$, 373 [M+K]$^+$, ESI-MS (high resolution): 357.1161 [M+Na]$^+$.

Compound **11**: ^{1}H NMR (500 MHz, D_2O): δ 4.87 (d, 1H, H-1′, $^3J_{1',2'} = 7.9$ Hz), 5.00 (dd, 1H, H-4, $^3J_{3,4} = 2.3$, $^3J_{4,5} = 4.8$ Hz), 5.38 (d, 1H, H-3, $^3J_{3,4} = 2.3$ Hz), 5.79–5.85 (m, 1H, H-6, $^3J_{5,6} = 10.7$ Hz), 5.96–6.00 (m, 1H, H-5); ^{13}C NMR (100 MHz, D_2O): δ 102.18 (1C, C-3), 102.88 (1C, C-1′), 133.26 (1C, C-6); MALDI-TOF (DHB, positive mode): $C_{14}H_{20}O_8$ $m/z = 339$ [M+Na]$^+$, 355 [M+K]$^+$, ESI-MS (high resolution): 339.1059 [M+Na]$^+$.

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