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Observations on the oxirane ring opening reactions of a 2-acetamido-3,4-anhydro sugar and on the inversion of the derived alcohols

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Abstract

A novel methodology for the preparation of L-enantiomers of 2,4- and 2,3-diacetamido-2,4,6- and 2,3,6-trideoxy-pyranoses is described. Factors influencing both the steric course of the epoxide ring opening and substitution are discussed.

1. Introduction

Sugar epoxides have attracted a great amount of attention as very useful intermediates in the synthesis and modification of the various mono- and oligosaccharides. An oxirane ring is able to react with nucleophiles under neutral, basic or acidic conditions.[1] Although factors directing the regioselectivity of oxirane ring cleavage have been well recognized,[2] the steric course of the reaction is in many cases unpredictable.

Little is known about the influence of the allylic acetamido group on the stereochemistry of the epoxide ring formation.[3,4] We thought, some knowledge of this question could be gained by application of a suitable starting material for the synthesis of isomeric 2,4-diamido-2,4,6-trideoxy-pyranoses. These compounds of D-*gluco* and D-*galacto* configuration play important biological roles as constituents of bacterial polysaccharides.[5] All other isomers and their L-enantiomers have been recognized as C-4–C-9 fragments of structure of the corresponding 5,7-diamino-3,5,7,9-tetradeoxy-*glycero*-nonulosonic acids, identified as components of *O*-antigenic lipopolysaccharides (LPS) of the clinically important gram-negative bacteria.[6] One isomer, i.e. 2,4-diacetamido-2,4,6-trideoxy-L-gulopyranose, has recently been utilized in the synthesis of 5,7-diacetamido-3,5,7,9-tetradeoxy-L-*glycero*-D-*talo*- and L-*glycero*-D-*galacto*-nonulosonic acids.[7]

In a previous paper[4] we have reported a methodology for synthesis of diamino sugars starting from 2-acetamido-2,3,4,6-tetradeoxy-α-L-*threo*-hex-2-enopyranoside **1**. This olefin was prepared from L-rhamnal in a reaction sequence involving: (i) Ferrier rearrangement to the corresponding

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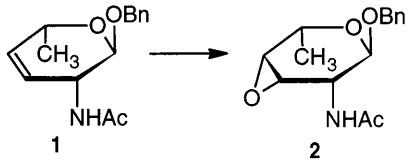
benzyl α-L-*erythro*-hex-2-enopyranoside;[8] (ii) conversion of configuration at C-4 via Mitsunobu reaction;[9] (iii) Overman [3,3]-sigmatropic rearrangement of 4-trichloroacetamidate[10] with subsequent hydrolysis/acetylation reaction to afford **1**. Utilizing again olefin **1** as a key starting material, a new synthesis of isomeric 2,4-diamino-2,4,6-trideoxy- and 2,3-diamino-2,3,6-trideoxy-α-L-pyranosides was elaborated.

2. Results and discussion

It has been reported that ethyl 2,3,4-trideoxy-2-trichloro-acetamido-α-D-*threo*-hex-3-enopyranoside[3] as well as benzyl 2-acetamido-2,3,4,6-tetradeoxy-hex-3-enopyranoside,[4] upon treatment with MCPBA, furnished the corresponding epoxides, *syn*-oriented to the vicinal 2-acetamido group. Analogously, the anomeric α-L-olefin **1**, submitted to the reaction with MCPBA, afforded epoxide **2** as a single product (Scheme 1).

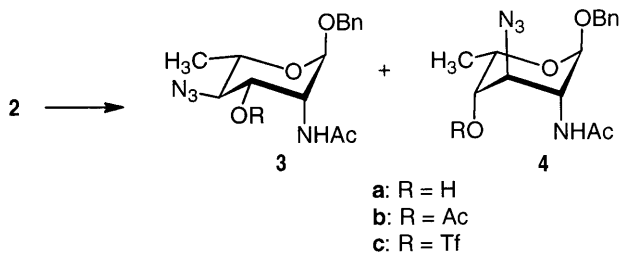


Scheme 1.

All these results are consistent with an existence of a transistent hydrogen bond between an oxygen of MCPBA and the allylic acetamido group, by an analogy to the directing role of the allylic hydroxyl group in epoxidation reactions of allylic alcohols.[11]

Our study focused, in the next step, on the ring opening of epoxide **2** by an azide. Using two different types of reagents, i.e. $Me_3SiN_3/BF_3{\cdot}OEt_2$ or NaN_3/NH_4Cl it should be possible to direct an attack of the reagent at C-4 or C-3 of epoxide **2**. Although little is known on the use of the first reagent for the opening of the sugar epoxides,[12] this procedure is commonly applied for oxirane ring cleavage of the various epoxy alcohols.[13] The steric course of the reaction has been rationalized by invoking coordination of the epoxy alcohol to the metal center of a Lewis acid in a rigid bidentate manner.[13] This is opposite to those in the dianion case (NaN_3/NH_4Cl) involving the participation of a *cis* hydroxyl group in the direct course of epoxide opening.[13,14]

Indeed, reaction of **2** with $TMSN_3/BF_3{\cdot}OEt_2$, performed in CH_2Cl_2 solution proceeded very quickly, to afford the *trans*-diequatorial product 4-azido sugar **3a** highly predominantly; its 3-amido *trans*-diaxial isomer **4a** was isolated as a minor product (**3a**:**4a** ~ 3:1) (Scheme 2).



Scheme 2.

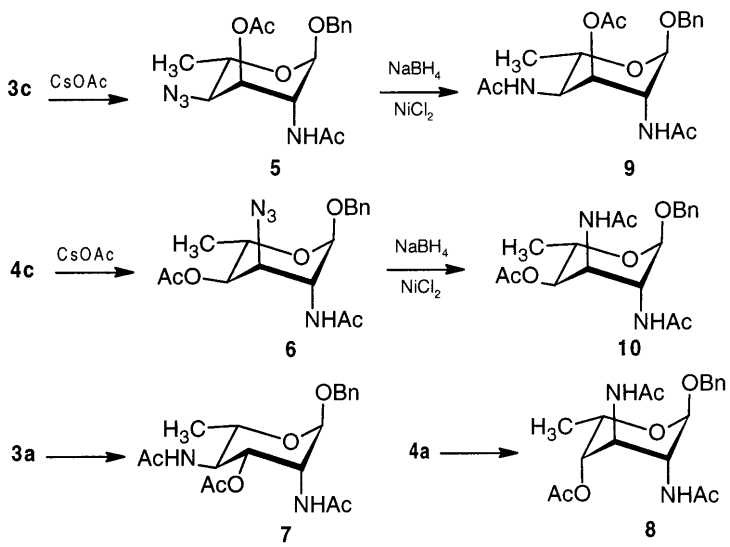
It seems more probable that the 'abnormal' product **3a** arises from a change of the less stable $^0H_1$ conformation (steric and electrostatic interactions between the dipoles associated with the oxirane and pyranoid ring oxygen atoms, supported by 2-OH *pseudo*-axial) to its $^1H_0$ or an *E* conformation, which results in a *trans*-diaxial opening of **2**.

In contrast, the reaction of **2** with NaN_3/NH_4Cl reagents proceeded sluggishly at 90°C to give mainly 3-azido sugar **3** (**3a**:**4a** ~3.5:1), presumably via the less favored $^0H_1$ conformation (two 1,3-diaxial interactions in the transition state). Evidently, this is due to the stabilizing effect of the hydrogen bond between the epoxide oxygen and 2-acetamido group, similar to that of the 2-hydroxyl group.[14]

Compounds **3** and **4** were considered to be converted to their epimers. Inversion of configuration is one of the most important problems in carbohydrate chemistry. Among different methodologies developed, a direct Mitsunobu reaction is usually applied.[9] However, attempts to invert the configuration at C-3 in **3a** under Mitsunobu condition failed. More forcing conditions (large excess of reagents, longer reaction time, higher temperature) caused the formation of a *p*-nitrobenzoic ester with retention of configuration, albeit in a low yield. Evidently, the vicinal axial acetamido group renders the approaching reagent to 3-OH difficult, thus preventing an inversion.

Epimerization of **3a** and **4a** was successfully achieved by a nucleophilic displacement of the triflate group in **3c** and **4c** by CsOAc.[15] Compound **3a** (**4a**) in CH_2Cl_2 solution, when treated with Tf_2O/Py at −10→0°C over 15 min afforded **3c** (**4c**), which is stable enough to purify by filtration through silica gel column. After drying by evaporation with toluene, **3c** dissolved in toluene was heated with CsOAc and 18-crown-6 at 60–70°C overnight, furnishing a single benzyl 2-acetamido-3-*O*-acetyl-2-azido-2,4,6-trideoxy-α-L-altropyranoside **5** in a moderate yield. The substitution reaction of triflate **4c** proceeded much faster to give enantiomer **6** after ~3 h at 60°C.

All azido sugars **3**, **4**, **5** and **6** were converted to the corresponding diacetamido derivatives **7**, **8**, **9** and **10**, respectively (Scheme 3). For reduction of the azido group, $NaBH_4/NiCl_2$ reagent was the best choice.[16] The reaction proceeded smoothly giving, after acetylation, benzyl



Scheme 3.

2,4-diacetamido- and/or 2,3-diacetamido-2,4,6-α-L-pyranosides. Their structure was confirmed by NMR data. In the case of compound **8** $^1C_4$ conformation was a little distorted, as it was indicated by coupling constants ($J_{2,3}$ 4.7, $J_{3,4}$ 6.1, $J_{4,5}$ 3.6 Hz). This probably resulted from two 1,3-diaxial interactions in $^1C_4$ conformation, exerted by 1,3 and 2,4 substituents.

It is noteworthy that the observations described here can be also suitable for preparation of other isomeric diamino sugars.

3. Experimental

General information: Optical rotations were measured with a JASCO Dip-360 Digital polarimeter at room temperature. ^{1}H NMR spectra were recorded on Bruker AM-500 (500 MHz) and Varian AC-200 (200 MHz) spectrometers with Me_4Si as internal standard. Mass spectra were taken on a AMD-604 mass spectrometer. IR spectra were taken with a Perkin–Elmer FT-IR-1600 spectrophotometer. Reactions were controlled by TLC on silica [Merck alu-plates (0.2 mm)]. All reagents and solvents were purified and dried according to common methods. CsOAc was dried by stirring with Ac_2O overnight and evaporated with toluene. Reaction products were purified and separated by flash chromatography, using Merck's Kieselgel 60 (240–400 mesh or 70–230 mesh).

3.1. Benzyl 2-acetamido-3,4-anhydro-2,6-dideoxy-α-L-talopyranoside **2**

To a solution of **1**[4] (2.61 g, 10 mmol) in CH_2Cl_2 (20 ml), MCPBA (4 g) and $NaHCO_3$ (1 g) were added and the mixture was stirred overnight (TLC hexane–AcOEt, 3:7). After filtration through Celite, the filtrate was diluted with CH_2Cl_2 and the solution was washed with aqueous $NaHCO_3$. Evaporation left a syrup, which was purified by chromatography (hexane–AcOEt, 3:7→1:1) to yield **2** (2.56 g, 92%) as a colorless oil; HRMS (LSIMS): MH^+, found 278.1400. $C_{15}H_{19}O_4N$ requires 278.1392; $[\alpha]_D$ −87.7 (*c* 0.7, $CHCl_3$); ν_{max} ($CHCl_3$) 3300, 2934, 1659, 1144, 1090 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.26–7.35 (5H, m, Ph), 6.01–5.59 (1H, d, *J* 8.8 Hz, NH), 4.66 (1H, d, *J* 11.8 Hz, CH_2OBn), 4.57 (1H, bs, H-1), 4.34 (1H, qd, *J* 0.8, 5.5, 8.8 Hz, H-2), 4.11 (1H, q, *J* 6.7 Hz, H-5), 3.48 (1H, dtd, *J* 1.1, 4.2, 5.5 Hz, H-3), 3.15 (1H, dd, *J* 1.0, 4.2 Hz, H-4), 2.02 (3H, s, NAc), 1.35 (3H, d, *J* 6.7 Hz, Me); δ_C ($CDCl_3$) 169.7, 137.0, 128.5, 127.9, 127.8, 97.4, 69.6, 60.9, 53.9, 50.4, 43.9, 23.2, 17.4.

3.2. Benzyl 2-acetamido-4-azido-2,4,6-trideoxy-α-L-mannopyranoside **3a** *and benzyl 2-acetamido-3-azido-2,3,6-trideoxy-α-L-idopyranoside* **4a**

Method a: A solution of **2** (1.69 g, 6.1 mmol) in CH_2Cl_2 (5 ml) was treated with Me_3SiN_3 (2.47 ml, 27 mmol), then with $BF_3{\cdot}OEt_2$ (0.66 ml, 3.47 mmol) and the mixture was stirred for 2 h (TLC hexane–AcOEt, 3:7). After neutralization with triethylamine, the solvent was evaporated. The residue was chromatographed on a silica gel column (hexane–AcOEt, 1:1). Eluted first was **3a** (1.26 g, 64.5%): colorless oil; HRMS (LSIMS): MH^+, found 321.1571. $C_{15}H_{20}O_4N_4$ requires 321.1563; $[\alpha]_D$ −105.6 (*c* 0.96, $CHCl_3$); ν_{max} ($CHCl_3$) 3313, 2929, 2112, 1726, 1652 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.29–7.38 (5H, m, Ph), 5.74 (1H, d, *J* 7.7 Hz, NH), 4.76 (1H, d, *J* 1.4 Hz, H-1), 4.66 (1H, d, *J* 12.0 Hz, CH_2OBn), 4.48 (1H, d, *J* 12.0 Hz, CH_2OBn), 4.40 (1H, ddd, *J* 1.4, 4.4, 7.7 Hz, H-2), 4.18 (1H, dd, *J* 4.4, 9.8 Hz, H-3), 3.63 (1H, pq, *J* 6.3, 10.0 Hz, H-5), 3.38 (1H, bs,

OH), 3.09 (1H, t, *J* 10.0 Hz, H-4), 2.05 (3H, s, NAc), 1.31 (3H, d, *J* 6.3 Hz, Me); δ_C ($CDCl_3$) 169.7, 137.0, 128.5, 127.9, 127.8, 97.4, 69.6, 60.9, 53.9, 50.4, 43.9, 23.2, 17.4.

Eluted second was **4a** (0.42 g, 21.6%): colorless crystals; mp 131–132°C; HRMS (LSIMS): MH^+, found 321.1574. $C_{15}H_{20}O_4N_4$ requires 321.1563; $[\alpha]_D$ −107.1 (*c* 0.76, $CHCl_3$); ν_{max} ($CHCl_3$) 3419, 2926, 2112, 1671, 1515 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.26–7.38 (5H, m, Ph), 6.73 (1H, d, *J* 9.0 Hz, NH), 4.79 (1H, bs, H-1), 4.73 (1H, d, *J* 12.2 Hz, CH_2OBn), 4.57 (1H, d, *J* 12.2 Hz, CH_2OBn), 4.29 (1H, dq, *J* 1.3, 2.6, 9.0 Hz, H-2), 4.22 (1H, qd, *J* 1.2, 6.7 Hz, H-5), 3.87 (1H, td, *J* 1.0, 4.0 Hz, H-4), 3.47 (1H, m, H-3), 2.30 (1H, bs, OH), 1.98 (3H, s, NAc), 1.19 (3H, d, *J* 6.7 Hz, Me); δ_C ($CDCl_3$) 169.3, 137.5, 128.4, 127.6, 127.4, 98.4, 69.7, 69.6, 61.9, 59.1, 46.5, 23.4, 15.9.

Method b*:* To a solution of **2** (138 mg, 0.5 mmol) in DMF (5 ml) were added NaN_3 (130 mg, 1 mmol) and NH_4Cl (130 mg). The mixture was heated at ~90°C overnight. Evaporation of the solvent left a residue, which after usual work-up and chromatography gave **3a** (29 mg, 18%) and **4a** (97 mg, 60%).

*3.3. Benzyl 2-acetamido-3-*O*-acetyl-4-azido-2,4,6-trideoxy-α-L-mannopyranoside* ***3b***

Acetylation of **3a** (32 mg, 0.1 mmol) was performed using pyridine and Ac_2O. Usual work-up and purification of the product by chromatography ($CHCl_3$–Me_2CO, 95:5) gave the title compound **3b** as a colourless oil: HRMS (LSIMS): MH^+, found 363.1657. $C_{17}H_{23}O_5N_4$ requires 363.1668; $[\alpha]_D$ −154.2 (*c* 0.90, $CHCl_3$); ν_{max} ($CHCl_3$) 3442, 2110, 1748, 1678, 1512 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.26–7.36 (5H, m, Ph), 5.55 (1H, d, *J* 9.4 Hz, NH), 5.25 (1H, dd, *J* 4.3, 10.4 Hz, H-3), 4.69 (1H, d, *J* 1.5 Hz, H-1), 4.66 (1H, d, *J* 12.0 Hz, CH_2OBn), 4.60 (1H, ddd, *J* 1.5, 4.3, 9.4 Hz, H-2), 4.51 (1H, d, *J* 12.0 Hz, CH_2OBn), 3.70 (1H, pq, *J* 6.2, 10.3 Hz, H-5), 3.25 (1H, t, *J* 10.3 Hz, H-4), 2.05, 2.02 (2×3H, 2s, OAc, NAc), 1.33 (3H, d, *J* 6.2 Hz, Me); δ_C ($CDCl_3$) 169.7, 136.3, 128.5, 128.1, 128.0, 97.9, 70.8, 69.4, 67.7, 62.9, 49.7, 23.3, 20.8, 18.4.

*3.4. Benzyl 2-acetamido-4-*O*-acetyl-3-azido-2,3,6-trideoxy-α-L-idopyranoside* ***4b***

Compound **4a** (32 mg, 0.1 mmol) was converted to the title **4b** according to the above described procedure: white solid; mp 151–152°C; HRMS (LSIMS): MH^+, found 363.1651. $C_{17}H_{23}O_5N_4$ requires 363.1668; $[\alpha]_D$ −92.4 (*c* 1.14, $CHCl_3$); ν_{max} ($CHCl_3$) 3442, 2110, 1748, 1679, 1512 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.26–7.38 (5H, m, Ph), 6.10 (1H, d, *J* 9.3 Hz, NH), 4.81 (1H, d, *J* 0.8 Hz, H-1), 4.81–4.72 (1H, m, H-4), 4.65, 4.56 (2×1H, 2d, *J* 12.2 Hz, 2×CH_2OBn), 4.32 (1H, pq, *J* 1.8, 6.6 Hz, H-5), 4.23 (1H, pq, *J* 0.8, 3.3, 9.2 Hz, H-2), 3.85 (1H, td, *J* 0.8, 3.3 Hz, H-3), 2.15, 1.99 (2×3H, 2s, OAc, NAc), 1.10 (3H, d, *J* 6.6 Hz, Me); δ_C ($CDCl_3$) 169.3, 137.0, 128.5, 127.8, 127.6, 97.9, 70.3, 69.8, 61.5, 57.4, 46.9, 23.3, 20.8, 15.8.

*3.5. Benzyl 2-acetamido-3-*O*-acetyl-4-azido-2,4,6-trideoxy-α-L-altropyranoside* ***5***

To a stirred solution of **3a** (320 mg, 1 mmol) in CH_2Cl_2 (10 ml) containing pyridine (2.25 ml, 3 mmol) triflic anhydride (0.22 ml, 1.3 mmol) was added dropwise at −10°C under Ar. Then the temperature was allowed to rise to −5°C continuing stirring until no starting material remained (~10 min. TLC, hexane–AcOEt, 1:1). The reaction was then diluted with CH_2Cl_2 and filtered through a short silica gel column. The solvent was removed to give a relatively stable crude triflate **3c**, which was used directly for the conversion to **5**. Thus, **3c** was dried by evaporation

with dry toluene in vacuo, redissolved in toluene (15 ml) and the solution was treated with 18-crown-6 (790 mg, 3 mmol) followed by cesium acetate (580 mg, 3 mmol). The reaction mixture was stirred at 60–70°C for ~18 h (TLC), whereupon the solvent was evaporated in vacuo and the product was isolated by column chromatography (hexane–AcOEt, 17:5) to afford **5** (220 mg, 61%) as a white solid: mp 61–62°C; HRMS (LSIMS): MNa^+, found 385.1484. $C_{17}H_{22}O_5N_4Na$ requires 385.1487; $[\alpha]_D$ −122.5 (*c* 1.02, $CHCl_3$); ν_{max} ($CHCl_3$) 3281, 2932, 1744, 1656, 1548 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.30–7.40 (5H, m, Ph), 5.63 (1H, d, *J* 8.8 Hz, NH), 5.23 (1H, t, *J* 3.5 Hz, H-5), 4.75 (1H, d, *J* 12.0 Hz, CH_2OBn), 4.72 (1H, d, *J* 1.7 Hz, H-1), 4.49 (1H, d, *J* 12.0 Hz, CH_2OBn), 4.41 (1H, ddd, *J* 1.7, 4.0, 8.8 Hz, H-2), 4.21 (1H, pq, *J* 6.4, 9.6 Hz, H-5), 3.23 (1H, dd, *J* 3.5, 9.6 Hz, H-4), 2.08, 2.01 (2×3H, 2s, OAc, NAc), 1.30 (3H, d, *J* 6.4 Hz, Me); δ_C ($CDCl_3$) 169.7, 169.1, 137.3, 128.4, 127.8, 127.4, 98.2, 69.6, 68.9, 63.5, 60.6, 49.6, 23.3, 20.8, 18.3.

*3.6. Benzyl 2-acetamido-4-*O*-acetyl-3-azido-2,3,6-trideoxy-α-L-altropyranoside* **6**

Compound **4a** (160 mg, 0.5 mmol) was converted into the title **6** according to the procedure described for **5**, using pyridine (1.2 ml, 1.5 mmol) and Tf_2O (0.11 ml, 0.66 mmol) in CH_2Cl_2 to give **4c**. This was subjected to the substitution reaction with 18-crown-6 (400 mg), cesium acetate (290 mg) in toluene (10 ml). The reaction proceed at 60°C for 3 h (TLC, hexane–Me_2CO, 7:3), furnishing after column chromatography compound **6** (115 mg, 63.5%) as a white solid: mp 112°C; HRMS (LSIMS): MNa^+, found 385.1484. $C_{17}H_{22}O_5N_4Na$ requires 385.1487; $[\alpha]_D$ −119.5 (*c* 0.83, $CHCl_3$); ν_{max} ($CHCl_3$) 3436, 2936, 2112, 1739, 1682 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.15–7.30 (5H, m, Ph), 5.27 (1H, d, *J* 8.2 Hz, NH), 4.93 (1H, dd, *J* 4.0, 8.7 Hz, H-4), 4.59 (1H, d, *J* 12.0.4 Hz, CH_2OBn), 4.56 (1H, d, *J* 2.1 Hz, H-1), 4.38 (1H, ddd, *J* 2.1, 4.0, 8.2 Hz, H-2), 4.29 (1H, d, *J* 12.4 Hz, CH_2OBn), 4.25 (1H, pq, *J* 6.4, 8.7 Hz, H-5), 4.10 (1H, t, *J* 4.0 Hz, H-3), 1.67, 1.40 (2×3H, 2s, OAc, NAc), 1.10 (3H, d, *J* 6.4 Hz, Me); δ_C ($CDCl_3$) 169.9, 169.4, 136.8, 128.5, 127.9, 127.8, 97.2, 71.4, 69.6, 63.1, 58.4, 51.1, 23.3, 20.6, 17.0.

3.7. General procedure for the reduction of azido group in sugars

To a solution of azido sugar (1 mmol) in EtOH (10 ml) were added $NaBH_4$ (160 mg) and a 0.16 M solution of $NiCl_2$ in EtOH (0.2 ml). The mixture was stirred for 30 min at room temperature, then neutralized with AcOH and evaporated in vacuo to dryness. The residue was treated with Ac_2O (5 ml) and anhydrous NaOAc (500 mg) and stirred at 40°C until TLC showed consumption of the starting material. The solvent was removed, water was added to the residue and the product was extracted with $CHCl_3$. The combined organic extracts were washed with brine, dried $MgSO_4$ and evaporated. The residue was purified by flash column chromatography.

*3.8. Benzyl 3-*O*-acetyl-2,4-diacetamido-2,4,6-trideoxy-α-L-mannopyranoside* **7**

Based on the general procedure compound **3a** (160 mg, 0.5 mmol) afforded, after purification by column chromatography ($CHCl_3$–MeOH, 17:1) the title **7** (164 mg, 87%) as a colorless oil: HRMS (LSIMS): MNa^+, found 401.1692. $C_{19}H_{26}O_6N_2Na$ requires 401.1689; $[\alpha]_D$ −103.5 (*c* 0.57, $CHCl_3$); ν_{max} ($CHCl_3$) 3431, 2935, 1729, 1679 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.32 (5H, m, Ph), 5.85 (1H, d, *J* 9.1 Hz, NH), 5.45 (1H, d, *J* 9.3 Hz, NH), 5.25 (1H, dd, *J* 4.5, 11.1 Hz, H-3), 4.79 (1H, d, *J* 1.5 Hz, H-1), 4.66, 4.59 (2×1H, 2d, *J* 11.8 Hz, CH_2OBn), 4.53 (1H, m, H-2), 4.39 (1H, dd,

J 10.2, 11.1 Hz, H-4), 3.68 (1H, pq, *J* 6.2, 10.0 Hz, H-5), 2.05, 2.01, 1.96 (3×3H, 3s, OAc, 2×NAc), 1.24 (3H, d, *J* 6.2 Hz, Me); δ_C ($CDCl_3$) 171.3, 170.4, 170.1, 136.6, 128.5, 128.1, 128.0, 98.2, 69.6, 68.9, 68.1, 51.7, 50.0, 23.4, 23.3, 20.9, 17.8.

3.9. Benzyl 4-O-acetyl-2,3-diacetamido-2,3,6-trideoxy-α-L-idopyranoside **8**

Prepared according to the general procedure from **4a** (64 mg, 0.2 mmol). Chromatography ($CHCl_3$–MeOH, 17:1) afforded the title **8** (60 mg, 79.4%) as a white solid: mp 185°C (destruction); HRMS (LSIMS): MNa^+, found 401.1684. $C_{19}H_{26}O_6N_2Na$ requires 401.1689; $[\alpha]_D$ −72.6 (*c* 0.70, $CHCl_3$); ν_{max} ($CHCl_3$) 3446, 2928, 1751, 1678 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.28–7.36 (5H, m, Ph), 4.93 (1H, dd, *J* 3.5, 6.0 Hz, H-4), 4.80 (3H, m, H-1, 2× NH), 4.74 (1H, d, *J* 12.0 Hz, CH_2OBn), 4.57 (1H, d, *J* 12.0 Hz, CH_2OBn), 4.29 (1H, pq, *J* 3.5, 6.6 Hz, H-5), 4.09 (1H, dd, *J* 6.0, 7.8 Hz, H-3), 3.98 (1H, dd, *J* 4.7, 7.9 Hz, H-2), 2.08, 1.98, 1.93 (3×3H, 3s, OAc, 2×NAc), 1.13 (3H, d, *J* 6.6 Hz, Me); δ_C ($CDCl_3$) 168.8, 168.8, 168.3, 136.6, 128.7, 128.4, 127.8, 98.9, 69.9, 69.8, 61.9, 47.9, 47.0, 23.4, 23.2, 20.9, 16.3.

3.10. Benzyl 3-O-acetyl-2,4-diacetamido-2,4,6-trideoxy-α-L-altropyranoside **9**

Prepared according to the general procedure from **5** (74 mg, 0.2 mmol). Chromatography (AcOEt–EtOH, 17:1) gave the title **9** (66 mg, 87%) as a colorless oil: HRMS (LSIMS): MNa^+, found 401.1683. $C_{19}H_{26}O_6N_2Na$ requires 401.1689; $[\alpha]_D$ −115.0 (*c* 1.03, $CHCl_3$); ν_{max} ($CHCl_3$) 3281, 2932, 1744, 1656 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.25–7.30 (5H, m, Ph), 6.10 (1H, d, *J* 9.2 Hz, NH), 5.69 (1H, d, *J* 9.6 Hz, NH), 4.82 (1H, t, *J* 3.3 Hz, H-3), 4.75 (1H, s, H-1), 4.68 (1H, d, *J* 11.7 Hz, CH_2OBn), 4.52–4.44 (1H, m, H-2), 4.50–4.44 (1H, d, *J* 11.7 Hz, CH_2OBn), 4.22 (1H, ddd, *J* 9.6, 9.4, 3.3 Hz, H-4), 4.05 (1H, pq, *J* 6.4, 9.4 Hz, H-5), 2.02, 2.00, 1.99 (3×3H, 3s, OAc, 2×NAc), 1.23 (3H, d, *J* 6.6 Hz, Me); δ_C ($CDCl_3$) 169.9, 169.8, 169.5, 137.4, 128.5, 128.3, 127.5, 98.4, 70.3, 69.9, 64.7, 48.8, 48.5, 23.3, 23.2, 20.9, 17.8.

3.11. Benzyl 4-O-acetyl-2,3-diacetamido-2,3,6-trideoxy-α-L-altropyranoside **10**

Prepared according to the general procedure from **6** (100 mg, 0.27 mmol). Chromatography (AcOEt–EtOH, 17:1) afforded the title compound (86 mg, 82.7%) as a white solid: HRMS (LSIMS): MNa^+, found 401.1683. $C_{19}H_{26}O_6N_2Na$ requires 401.1689; $[\alpha]_D$ −66.4 (*c* 1.03, $CHCl_3$); ν_{max} ($CHCl_3$) 3287, 2935, 1740, 1660, 1537 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.32–7.41 (5H, m, Ph), 6.81 (1H, d, *J* 8.7 Hz, NH), 6.02 (1H, d, *J* 8.3 Hz, NH), 4.78 (1H, s, H-1), 4.75 (1H, d, *J* 11.4 Hz, CH_2OBn), 4.69 (1H, dd, *J* 4.0, 9.6 Hz, H-4), 4.56 (1H, d, *J* 11.4 Hz, CH_2OBn), 4.48 (1H, ddd, *J* 3.6, 4.0, 8.3 Hz, H-3), 4.26 (1H, pq, *J* 1.9, 3.6, 8.7 Hz, H-2), 4.01 (1H, pq, *J* 6.3, 9.6, Hz, H-5), 2.03, 2.02, 1.90 (3×3H, 3s, OAc, 2×NAc), 1.24 (3H, d, *J* 6.3 Hz, Me); δ_C ($CDCl_3$) 170.3, 169.7, 169.6, 136.6, 128.7, 128.4, 128.1, 98.3, 70.6, 70.3, 69.9, 50.7, 47.4, 23.3, 23.2, 20.8, 17.3.

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