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Studies of the stereoselective reduction of 2-hydroxyimino-hexopyranosides: $LiBH_4$–Me_3SiCl, a mild reducing agent of oximes to amines *

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ABSTRACT

Reduction of the title compounds of types **1** and **2** under mild conditions using $LiBH_4$–Me_3SiCl species, followed by acetylation, yielded the corresponding 2-amino sugars of α-D-*gluco* (**5**) and β-D-*manno* (**6**) configuration, respectively, with full stereoselectivity. Analogously, the β-D-*lyxo* isomer of type **4** afforded the β-D-talosamine **9** exclusively. The stereochemical outcome of the reduction of oximes of type **3** is controlled by the configuration of the substrate and the chemical features of the C-1–C-4 substituents, leading to *talo* (**8**) and/or *galacto* (**7**) isomers.

INTRODUCTION

As is well known[1,2], 2-amino-2-deoxy-D-hexopyranoses are widely distributed in Nature. They are components of antibiotics but, more importantly, D-glucosamine, D-galactosamine, and D-mannosamine occur in the oligosaccharide part of glycoconjugates.

Among all of the glycosamines, only D-glucosamine is a cheap commercial product. The other isomers are very expensive (D-galactosamine and D-mannosamine) or not available at all (D-talosamine). On the other hand, the preparation of di- or oligo-saccharides containing glycosamine units may be accomplished more conveniently by a sequence of stereo- and regio-selective transformations of lactose[3] or maltose[4], leading to the amino group, as compared with the creation of a desired α- or β-glycosidic linkage from monosaccharide units. For the above reasons, considerable interest has been devoted to the conversion of the hydroxyl group into the amino function in sugars.

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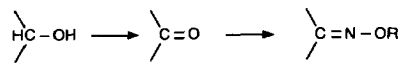


Scheme 1.

A generally useful method involves the reduction of oximes[3–7] readily available through the reaction sequence in Scheme 1.

However, studies of the generation of the amino group from oximes have demonstrated[4–8] that the reduction of oximes is capricious. In fact, this reaction is strongly dependent on the reagent used (H_2–Pd–C, $LiAlH_4$, BH_3, $TiCl_3$–$NaBH_3CN$, $ZrCl_4$–$NaBH_4$[3–10], etc.) and, to a greater extent, on the substrate to be reduced. This relationship specially concerns the sugar oximes owing to the influence of stereoelectronic factors governing their behaviour in these reactions[3–8].

Our interest in this subject was recently rekindled when we used an appropriate oxime of type **1** as a substrate in the synthesis of neotrehaloses[11]. When trying to apply one of the above-mentioned methods for the reduction of the oxime function, we observed a mixture of products. To overcome these difficulties, we decided to examine the generation of the amino function from oximes by the use of a new species composed of $LiBH_4$–Me_3SiCl in THF. This complex, effective for the reduction of nitro and cyano groups[12], may be considered to exist as a borane–silyl mixture $[(Me_3SiCl)_n$–$(BH_3)_n]$ because its reducing ability is connected with the assistance of an excess of Me_3SiCl. This study defines the conditions for a mild stereoselective reduction of pyranoside 2-oximes of *α,β-arabino* and *α,β-lyxo* configuration.

RESULTS AND DISCUSSION

Our studies were performed with differently substituted stereoisomeric oximes of *α*-D-*arabino*- (**1**), *β*-D-*arabino*- (**2**), *α*-D-*lyxo*- (**3**), and *β*-D-*lyxo* (**4**) configuration. All oxime derivatives under investigation were readily accessible by one of the known procedures involving: (*a*) the reaction of the 2-keto group in *α*- or *β*-glycosides with NH_2OH[13], followed by methylation of the oxime with MeI–Ag_2O; (*b*) the treatment of acetylated glycals with nitrosyl chloride, followed by the reaction with alcohols and methylation[14]; (*c*) conversion of 2-hydroxyglycal esters into oximes by the reaction with NH_2OH, followed by benzoylation, photobromination, and condensation of the bromide with alcohols[15,16].

It is worth noting that when removal of the 6-*O*-trityl and 3,4-*O*-isopropylidene groups from oxime **3d** was attempted with pyridinium *p*-toluenesulfonate in boiling methanol (conditions described for deprotection of these groups[17]), **3a** was isolated after acetylation, i.e., deprotection was accompanied by the transglycosylation reaction. In this way also, oxime **4** was transformed into **3e**.

All oxime derivatives **1–4** readily undergo the reaction with the species com-

posed of $LiBH_4$–Me_3SiCl (Scheme 2). Thus, treatment of oxime derivatives of α-(1) and β-D-*arabino* (2) configuration with $LiBH_4$–Me_3SiCl in THF at $0 \rightarrow 25°C$, followed by acetylation, provides the appropriate 2-acetamido-2-deoxy-α-D-glucopyranosides **5** and 2-acetamido-2-deoxy-β-D-mannopyranosides **6**, respectively, in high yield. At higher temperatures $20 \rightarrow 80°C$, the reduction is accompanied by removal of the benzoyl groups. The reduction of the oxime group proceeds with strong anomeric stereoelectronic control: the hydride attacks exclusively from the opposite side to the aglycon, analogously to the literature data[3].

The anomeric stereoelectronic control is also operative in the case of the β-D-*lyxo* isomer **4**, leading nearly exclusively to talosaminide **9**.

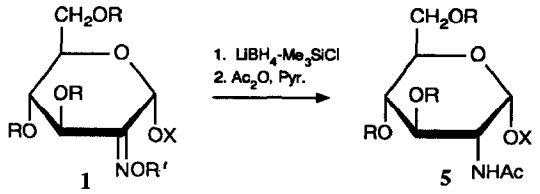
The stereochemical outcome of the reduction of α-D-*lyxo* oximes of type **3** is more complex owing to the trans-diaxial disposition of the C-1–C-4 substituents, hindering in a similar manner both the equatorial and the axial attack of the hydride ion. As a result, the ratio of the *galacto* (**7**) and *talo* (**8**) isomers formed seems to be dependent on the nature of the aglycon as well as on the character of the protecting groups. Thus, the substrates with sterically undemanding aglycons (Me, Bn, cyclohexyl) and OAc groups in the molecule undergo the reduction with a moderate stereoselectivity, with the *talo* isomer (**8**) preponderating. Substrates with OBn protecting groups favour the formation of equatorial amine [*galacto* (**7**)–*talo* (**8**) ~ 6 : 1].

A fully stereoselective course of the reduction of α-D-*lyxo* isomers, leading to an α-D-talosaminide as sole product, was observed in two cases: on reduction of **3d** and **3e**. In the case of **3d**, the exclusively equatorial attack of the hydride ion appears to be the result of conformational deviation caused by the 3,4-*O*-isopropylidene group. Similar behaviour was noticed on reduction of **3d** with $LiAlH_4$[18]. The deformation of the chair shape is demonstrated by "abnormal" coupling constants for the product **8d**: $J_{1,2}$ 6.6, $J_{2,3}$ 3.08, $J_{3,4}$ 7.6 Hz. After hydrolysis of the protecting groups of **8d**, followed by acetylation, the coupling constants assumed the "normal" values: $J_{1,2}$ 1.1, $J_{2,3}$ 5.0, $J_{3,4}$ 3.4 Hz, and additionally $J_{2,4}$ 1.1 Hz, characteristic of the $^4C_1$ conformation of the *talo* isomer **8f**. Moreover, the signal of H-2, in the form of a quartet of triplets for all of the *O*-acetyl derivatives of α-talosaminides, is unique in the series of 2-acetamido-2-deoxyhexopyranosides.

The reason for the formation of talosaminide **8e** from oxime **3e** is not clear. Evidently, the anomeric *tert*-butyl group exerts insufficient steric hindrance for equatorial attack of the hydride ion, and other factors determine the steric course of the reduction.

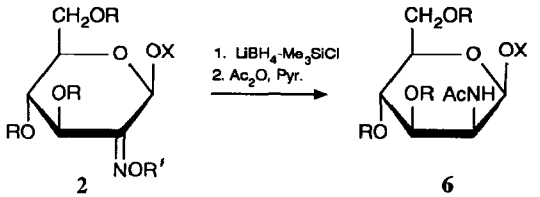
It is worth noting that the procedure we have devised represents the first simple approach to talosaminides, usually prepared by multistep transformations of D-galactose[19].

The methodology of the generation of the amino function from oximes, as here described, seems to be applicable to structurally complex substrates with other functional groups, including those which may be acid-sensitive (trityl, isopropylidene) and/or easily reducible (phthalimido)[11].



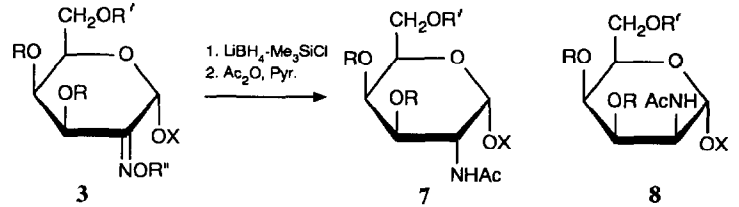
1 5

1a, 5a: X = cyclohexyl, R = Ac, R′ = Me
1b, 5b: X = 1,2:3,4-di-*O*-iP-α-D-Gal*p*, R = R′ = Bz
5c: X= 1,2:3,4-di-*O*-iP-α-D-Gal*p*, R = Ac



2 6

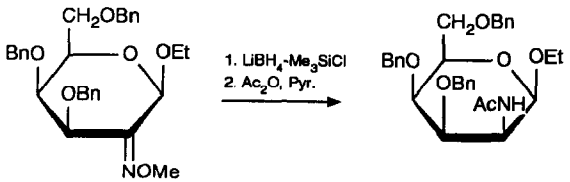
2a, 6a: X = cyclohexyl, R = R′ = Bz
6c: X = cyclohexyl, R = Ac
2b, 6b: X = 1,2:3,4-di-*O*-iP-α-D-Gal*p*, R = R′ = Bz



3 7 8

3a, 7a, 8a: X = R" = Me, R′ = R = Ac
3b, 7b, 8b: X = cyclohexyl, R = R′ = Ac, R"= Me
3c, 7c, 8c: X = R" = Me, R = R′ = Bn
3d, 8d: X = Bn, R = iP , R′ = Tr, R" = Me
3e, 8e: X = *t*-Bu, R = R′ = Ac, R" = Me
8f: X = Bn, R = R′ = Ac

3	7	:	8	yield
a	2	:	3	56%
b	1	:	2	69%
c	6	:	1	68%
d	0	:	100	89%
e	5	:	95	74%



4 9

EXPERIMENTAL

General methods.—Optical rotations were determined with a Jasco DIP-360 automatic polarimeter for solutions in chloroform. ^{1}H NMR spectra were recorded with a Bruker AM-500 (500 MHz) spectrometer for solutions in $CDCl_3$ (internal

Me_4Si). Melting points were measured on a Kofler hot-stage apparatus and are uncorrected. Reactions were monitored by TLC on silica gel coated plates (Merck), and column chromatography was performed on Silica Gel G (Merck 230–400 mesh).

A. General procedures for the preparation of methoxyimino and benzoyloxyimino glycosides.—The title compounds were prepared by standard methods: (*a*) based on the reaction of the 2-keto group in α- or β-glycosides with NH_2OH[13], followed by methylation of the oxime with MeI–Ag_2O; (*b*) based on the reaction of alcohols with nitrosyl chloride adducts of acetylated glycals[14] and then methylation; (*c*) via conversion of 2-hydroxyglycal esters into oximes by the reaction with NH_2OH, followed by benzoylation, photobromination, and condensation of the bromide with alcohols[15,16].

*Cyclohexyl 2-(acetoxyimino)-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D-arabino-*hexopyranoside* (**1a**).—Prepared by method (*b*)[14]. Characterization data: $[\alpha]_D$ +35.2° (*c* 1.17). ^1H NMR: δ 1.4–2.0 (m, 10 H, several br peaks of cyclohexyl), 2.11, 2.10, 2.08 (3 s, 9 H, 3 OAc), 3.64 (m, 1 H, H-1 of cyclohexyl), 3.85 (s, 3 H, OMe), 4.09 (dd, 1 H, H-6a), 4.24 (ddd, 1 H, H-5), 4.29 (dd, 1 H, H-6b), 5.19 (t, 1 H, H-4), 5.76 (d, 1 H, H-3), 6.02 (s, 1 H, H-1); $J_{3,4}$ 9.7, $J_{4,5}$ 9.9, $J_{5,6a}$ 2.2, $J_{5,6b}$ 4.7, $J_{6a,6b}$ 12.1 Hz. Anal. Calcd for $C_{19}H_{29}NO_9$: C, 54.93; H, 7.04; N, 3.37. Found: C, 55.20; H, 7.29; N, 3.14.

*1,2 : 3,4-Di-*O*-isopropylidene-6-*O*-[3,4,6-tri-*O*-benzoyl-2-(benzoyloxyimino)-2-deoxy-α-*D-arabino-*hexopyranosyl]-α-*D-*galactopyranose* (**1b**).—Prepared by method (*c*)[15,16]. Characterization data: $[\alpha]_D$ +44.2° (*c* 0.81). ^1H NMR: δ 1.21, 1.34, 1.39, 1.60 (4 s × 3 H, 2 CMe_2), 3.98–4.05 (m, 2 H, H-6a,6b), 4.12 (ddd, 1 H, H-5), 4.27 (dd, 1 H, H-4), 4.34 (dd, 1 H, H-2), 4.51 (dd, 1 H, H-6'a), 4.61 (dd, 1 H, H-3), 4.67 (dd, 1 H, H-6'b), 4.78 (ddd, 1 H, H-5'), 5.55 (d, 1 H, H-1), 5.96 (t, 1 H, H-4'), 6.25 (s, 1 H, H-1'), 6.42 (d, 1 H, H-3'), 7.3–8.2 (m, 20 H, arom.); $J_{1,2}$ 5.0, $J_{2,3}$ 7.9, $J_{3,4}$ 2.4, $J_{4,5}$ 1.8, $J_{5,6a}$ 5.9, $J_{6a,6b}$ 10.3, $J_{3',4'}$ 9.8, $J_{4',5'}$ 9.9, $J_{5',6'a}$ 2.8, $J_{5',6'b}$ 4.3, $J_{6'a,b'b}$ 12.4 Hz. Anal. Calcd for $C_{46}H_{45}NO_{15} \cdot 0.5H_2O$: C, 64.18; H, 5.39; N, 1.63. Found: C, 64.37; H, 5.27; N, 1.25.

*Cyclohexyl 3,4,6-tri-*O*-benzoyl-2-(benzoyloxyimino)-2-deoxy-β-*D-arabino-*hexopyranoside* (**2a**).—Prepared by method (*c*)[20]. Characterization data: $[\alpha]_D$ −80.6° (*c* 1.33). ^1H NMR: δ 1.30–2.20 (m, 10 H, several peaks of cyclohexyl), 3.96–4.10 (m, 1 H, H-1 of cyclohexyl), 4.46 (ddd, 1 H, H-5), 4.86 (d, 2 H, H-6a,6b), 5.89 (t, 1 H, H-4), 6.19 (d, 1 H, H-3), 6.25 (s, 1 H, H-1), 7.35–8.10 (m, 20 H, arom.); $J_{3,4}$ 4.6, $J_{4,5}$ 4.9 (both coupling constants indicate that the $^4C_1$ conformation is substantially flattened around the anomeric center, compare ref 3), $J_{5,6a}$ 6.9, $J_{5,6b}$ 6.8 Hz. Anal. Calcd for $C_{40}H_{37}NO_{10}$: C, 69.45; H, 5.39; N, 2.02. Found: C, 61.21,; H, 5.21; N, 2.12.

*1,2 : 3,4-Di-*O*-isopropylidene-6-*O*-[3,4,6-tri-*O*-benzoyl-2-(benzoyloxyimino)-2-deoxy-β-*D-arabino-*hexopyranosyl]-α-*D-*galactopyranose* (**2b**).—Prepared by method (*c*)[20]; its optical rotation and ^1H NMR data were identical with the reported data[20].

*Methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(methoxyimino)-α-*D-lyxo-*hexopyranoside* (**3a**).

—Prepared by method (*b*)[14]. Characterization data: $[\alpha]_D$ +44.9° (*c* 0.82). ^{1}H NMR: δ 2.06, 2.10, 2.15 (3 s × 3 H, 3 OAc), 3.45 and 3.91 (2 s, 2 × 3 H, 2 OMe), 4.12 (d, 2 H, H-6a,6b), 4.36 (bt, 1 H, H-5), 5.48 (dd, 1 H, H-4), 5.83 (d, 1 H, H-3), 5.85 (s, 1 H, H-1); $J_{3,4}$ 3.5, $J_{4,5}$ 0.9, $J_{5,6a}$ 6.7, $J_{5,6b}$ 6.7 Hz. Anal. Calcd for $C_{14}H_{21}NO_9$: C, 48.41; H, 6.09; N, 4.03. Found: C, 48.38; H, 6.35; N, 3.96.

*Cyclohexyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(methoxyimino)-α-*D-lyxo-*hexopyranoside* (**3b**).—Prepared by method (*b*)[14]. Amorphous powder; $[\alpha]_D$ +81.6° (*c* 1.38). ^{1}H NMR: δ 1.30–2.20 (m, 10 H, several peaks of cyclohexyl), 2.05, 2.10, 2.15 (3 s, 9 H, 3 OAc), 3.90 (s, 3 H, OMe), 4.09 (m, 2 H, H-6a,6b), 4.46 (t, 1 H, H-5), 5.48 (dd, 1 H, H-4), 5.87 (d, 1 H, H-3), 6.11 (s, 1 H, H-1); $J_{3,4}$ 3.5, $J_{4,5}$ 0.9, $J_{5,6}$ 6.8, $J_{5,6b}$ 6.4, $J_{6a,6b}$ 11.3 Hz. Anal. Calcd for $C_{19}H_{29}NO_9$: C, 54.93; H, 7.04; N, 3.37. Found: C, 54.98; H, 7.06; N, 3.19.

*Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-(methoxyimino)-α-*D-lyxo-*hexopyranoside* (**3c**). —Compound **3c** was prepared by heating oxime **4** (1 mmol) with pyridinium *p*-toluenesulfonate (1 mmol) in MeOH (7 mL) during 6 h. Neutralization with Dowex 1 (HO^-), followed by evaporation, dissolution of the syrup in 20:1 benzene–EtOAc, filtration through silica gel, and evaporation gave **3** as a syrup (82% yield); $[\alpha]_D$ +44.9° (*c* 0.82). ^{1}H NMR: δ 3.39 (s, 3 H, OMe), 3.51 (m, 2 H, H-6a,6b), 3.96 (s, 3 H, OMe), 3.99 (dd, 1 H, H-4), 4.02 (t, 1 H, H-5), 4.40 (d, 1 H of OCH_2Ph), 4.43 (d, 1 H, H-3), 4.44, 4.58, 4.68 (3 d, 3 H of OCH_2Ph), 4.99 (AB, 2 H, OCH_2Ph), 5.85 (s, 1 H, H-1), 7.25–7.48 (m, 15 H, arom.); $J_{3,4}$ 2.7, $J_{4,5}$ 1.1, $J_{5,6a}$ 6.6, $J_{5,6b}$ 6.0, $J_{6a,6b}$ 9.5 Hz. Anal. Calcd for $C_{29}H_{33}NO_6$: C, 70.85; H, 6.77; N, 2.85. Found: C, 70.53; H, 6.89; N, 2.82.

*Benzyl 2-deoxy-3,4-*O*-isopropylidene-2-(methoxyimino)-6-*O*-trityl-α-*D-lyxo-*hexopyranoside* (**3d**).—Compound **3d**, prepared by method (*a*)[13], had mp 173°C; $[\alpha]_D$ +71.3° (*c* 0.81). ^{1}H NMR: δ 1.32, 1.35 (2 s × 3 H, 2 CMe_2), 3.31 (dd, 1 H, H-6a), 3.51 (dd, 1 H, H-6b), 3.98 (s, 3 H, OMe), 4.10 (ddd, 1 H, H-5), 4.22 (dd, 1 H, H-4), 4.73 and 4.96 (AB, 2 H, OCH_2Ph), 5.29 (d, 1 H, H-3), 5.24 (s, 1 H, H-1); $J_{3,4}$ 7.45, $J_{4,5}$ 1.8, $J_{5,6a}$ 4.4, $J_{5,6b}$ 7.0, $J_{6a,6b}$ 10.0 Hz. Anal. Calcd for $C_{36}H_{37}NO_6$: C, 74.59; H, 6.43; N, 2.42. Found: C, 74.73; H, 6.30; N, 2.40.

tert-*Butyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(methoxyimino)-α-*D-lyxo-*hexopyranoside* (**3e**).—Prepared by method (*b*)[14]. Syrup; $[\alpha]_D$ +87.3° (*c* 1.3). ^{1}H NMR: δ 1.28 (s, 9 H, *tert*-Bu), 2.05, 2.10, 2.14 (3 s × 3 H, 3 OAc), 3.89 (s, 3 H, OMe), 4.20 (dd, 1 H, H-6a), 4.30 (dd, 1 H, H-6b), 4.53 (ddd, 1 H, H-5), 5.47 (dd, 1 H, H-4), 5.89 (d, 1 H, H-3), 6.30 (s, 1 H, H-1); $J_{3,4}$ 3.4, $J_{4,5}$ 1.1, $J_{5,6a}$ 6.5, $J_{5,6b}$ 6.4 Hz. Anal. Calcd for $C_{17}H_{27}NO_9$: C, 52.43; H, 6.99; N, 3.60. Found: C, 52.39; H, 7.00; N, 3.71.

*Ethyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-(methoxyimino)-β-*D-lyxo-hexopyranoside (**4**). —Compound **4** was prepared by method (*a*)[13], starting from ethyl 3,4,6-tri-*O*-benzyl-β-D-galactopyranoside. Syrup; $[\alpha]_D$ −49.1° (*c* 0.6). ^{1}H NMR: δ 1.18 (t, 3 H, Me of OEt), 3.55 (m, 1 H of OEt), 3.80 (dd, 1 H, H-6a), 3.85 (m, 2 H, H-5,6b), 3.91 (s, 3 H, OMe), 4.02 (m, 1 H of OEt), 4.30–4.40 (m, 3 H, unresolved), 4.50–4.60 (m, 3 H, unresolved), 4.66 (AB, 2 H, OCH_2Ph), 5.73 (s, 1 H, H-1); $J_{5,4}$ 2.1, $J_{5,6a}$ 6.2, $J_{5,6b}$ 5.1, $J_{6a,6b}$ 9.6 Hz. Anal. Calcd for $C_{30}H_{35}NO_6$: C, 71.26; H, 6.98; N, 2.77. Found: C, 70.95; H, 6.87; N, 2.85.

*B. General procedure for the reduction of derivatives of isomeric 2-hydroxyimino-*D*-hexopyranosides.*—To a mixture of $LiBH_4$ (22 mg, 1 mmol) in dry THF (2 mL) was added Me_3SiCl (2.71 mg, 0.319 mL, 2.5 mmol) at −20°C (bath) under Ar, and the mixture was stirred for 2 h at room temperature. Then the mixture was recooled to −20°C, and a solution of the substrate (0.2 mmol) was added dropwise. Stirring was continued at room temperature until disappearance of the substrate (TLC, 3–12 h). Then MeOH was cautiously added, followed by neutralization with Et_3N. Evaporation in vacuo left a residue which was acetylated with Ac_2O–pyridine. Ice–water was then added and the mixture was extracted with CH_2Cl_2. The extract was dried, then concentrated, and the residue was chromatographed on silica gel.

*Cyclohexyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-glucopyranoside* (**5a**).—Substrate **1a** (0.20 g, 0.48 mmol) was reduced according to the general procedure. After acetylation, one product was observed in TLC (1:2 EtOAc–hexane). Filtration on a short column of silica gel gave **5a** (0.13 g, 58%) as an amorphous powder; $[\alpha]_D$ +90.2° (*c* 1.17). ^1H NMR (Varian GEM 200 MHz): δ 1.20–1.95 (m, 10 H, several peaks of cyclohexyl), 1.95, 2.03, 2.04, 2.09 (4 s, 12 H, 3 OAc, NAc), 3.56 (m, 1 H, H-1 of cyclohexyl), 4.00–4.20 (m, 1 H, H-5), 4.10 (dd, 1 H, H-6a), 4.20 (d, 1 H, H-6b), 4.30 (ddd, 1 H, H-2), 4.90 (d, 1 H, H-1), 5.18 (dt, 2 H, H-3,4), 5.63 (d, 1 H, NH); $J_{1,2}$ 3.9, $J_{2,3}$ 9.7, $J_{2,NH}$ 9.3, $J_{3,4}$ 10.1, $J_{4,5}$ 9.6, $J_{5,6a}$ 4.4, $J_{5,6b}$ 2.3, $J_{6a,6b}$ 12.2 Hz. Anal. Calcd for $C_{19}H_{29}NO_9$: C, 54.93; H, 7.04; N, 3.37. Found: C, 55.23; H, 7.29; N, 3.04.

*6-*O*-(2-Acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-α-*D*-glucopyranosyl)-1,2 : 3,4-di-*O*-isopropylidene-α-*D*-galactopyranose* (**5b**).—Substrate **1b** (85 mg, 0.1 mmol) was reduced according to the general procedure at 30°C until disappearance of starting material (TLC; 3:1 hexane–EtOAc). The usual workup and then chromatography on a silica gel column (5:1 hexane–EtOAc) gave **5b** (43 mg, 53%) as the first fraction. The second fraction (12 mg) consisted of a mixture of partially debenzoylated products. Characterization data: $[\alpha]_D$ +35.9° (*c* 0.77). ^1H NMR: δ 1.25, 1.34, 1.45, 1.56 (4 s × 3 H, 2 CMe_2), 1.88 (s, 3 H, NAc), 3.80 (dd, 1 H, H-6a), 3.97 (dd, 1 H, H-6b), 4.05 (m, 1 H, H-5′), 4.23 (dd, 1 H, H-4), 4.37 (dd, 1 H, H-2), 4.41–4.46 (m, 2 H, H-2′,6′a), 4.55–4.64 (m, 2 H, H-5′,6′b), 4.66 (dd, 1 H, H-3), 5.00 (d, 1 H, H-1′), 5.57 (d, 1 H, H-1), 5.69–5.73 (m, 2 H, H-3′,4′), 6.10 (d, 1 H, NH), 7.32–8.08 (m, 15 H, arom.); $J_{1,2}$ 5.6, $J_{2,3}$ 2.5, $J_{3,4}$ 7.8, $J_{4,5}$ 2.0, $J_{5,6a}$ 7.6, $J_{5,6b}$ 4.4, $J_{6a,6b}$ 11.1, $J_{1',2'}$ 3.6, $J_{2',NH}$ 9.5, $J_{3',4'}$ 9.8, $J_{6'a,6'b}$ 10.1 Hz. Anal. Calcd for $C_{46}H_{45}NO_{15} \cdot 0.5H_2O$: C, 64.18; H, 5.39; N, 1.63. Found: C, 64.37; H, 5.27; N, 1.25.

The second fraction from chromatography was dissolved in dry MeOH and treated with K_2CO_3. After being stirred overnight, the solution was filtered through Celite and concentrated to give one product (TLC; 17:3 $CHCl_3$–MeOH). Acetylation, of the product gave 6-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**5c**); mp 108–110°C; $[\alpha]_D$ +27.2° (*c* 0.4). ^1H NMR: δ 1.33, 1.34, 1.45, 1.52 (4 s × 3 H, 2 CMe_2), 1.96, 2.01, 2.03, 2,10 (4 s × 3 H, 3 OAc, NAc), 3.71 (dd, 1 H, H-6a), 3.86 (dd, 1 H,

H-6b), 3.97 (ddd, 1 H, H-5), 4.04 (ddd, 1 H, H-5′), 4.06 (m, 1 H, H-6′a), 4.19 (dd, 1 H, H-4), 4.26 (dd, 1 H, H-6′b), 4.38 (ddd, 1 H, H-2′), 4.64 (dd, 1 H, H-3), 4.86 (d, 1 H, H-1′), 5.14 (t, 1 H, H-4′), 5.23 (t, 1 H, H-3′), 5.53 (d, 1 H, H-1), 5.90 (d, 1 H, NH); $J_{1,2}$ 5.0, $J_{2,3}$ 2.5, $J_{3,4}$ 7.8, $J_{4,5}$ 1.8, $J_{5,6a}$ 7.9, $J_{5,6b}$ 7.9, $J_{6a,6b}$ 11.1, $J_{1',2'}$ 3.6, $J_{2',3'}$ 10.7, $J_{2',NH}$ 9.6, $J_{3',4'}$ 9.6, $J_{4',5'}$ 9.9, $J_{5',6'a}$ 4.2, $J_{5',6'b}$ 2.2, $J_{6',6'b}$ 12.4 Hz. Anal. Calcd for $C_{26}H_{39}NO_{14}$: C, 52.96; H, 6.67; N, 2.38. Found: C, 53.15; H, 6.78; N, 2.54.

*Cyclohexyl 2-acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-β-*D*-mannoside* (**6a**).—Reduction of **2a** (69 mg, 0.1 mmol) was performed by the general procedure. After *N*-acetylation, one product was detected by TLC (2:1 hexane–EtOAc). Filtration through a short column of silica gel gave **6a** (51 mg, 82%); mp 231–232°C; $[\alpha]_D$ −62.4° (*c* 1.35). ^{1}H NMR: δ 1.15–1.90 (m, 10 H, several peaks of cyclohexyl); 2.02 (s, 3 H, NAc), 3.67 (m, 1 H, H-1 of cyclohexyl), 4.10 (ddd, 1 H, H-5), 4.59 (m, 2 H, H-6a,6b), 4.91 (ddd, 1 H, H-2), 4.99 (d, 1 H, H-1), 5.46 (dd, 1 H, H-3), 5.59 (t, 1 H, H-4), 5.88 (d, 1 H, NH), 7.35–8.20 (m, 15 H, arom.); $J_{1,2}$ 2.0, $J_{2,3}$ 3.9, $J_{2,NH}$ 8.7, $J_{5,6a}$ 4.2, $J_{5,6b}$ 6.4, $J_{6a,6b}$ 11.8 Hz. Anal. Calcd for $C_{35}H_{37}NO_9$: C, 68.28; H, 6.06: N, 2.28. Found: C, 68.02; H, 5.98; N, 2.24.

*Cyclohexyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-mannoside* (**6c**).—Reduction of **2a** (69 mg, 0.1 mmol) was performed at 80°C (bath) during 2 h. Usual workup, followed by acetylation, gave **6c** (25 mg, 58%) as the sole product; $[\alpha]_D$ −32.2° (*c* 0.8). ^{1}H NMR: δ 1.2–1.9 (m, 10 H, several peaks of cyclohexyl), 2.01, 2.05, 2.06, 2.09 (4 s × 3 H, 3 OAc, NAc); 3.63 (m, 2 H, H-1 of cyclohexyl, H-5), 4.09 (dd, 1 H, H-6a), 4.30 (dd, 1 H, H-6b), 4.64 (ddd, 1 H, H-2), 4.78 (d, 1 H, H-1), 4.96 (dd, 1 H, H-3), 5.08 (t, 1 H, H-4), 5.75 (d, 1 H, NH); $J_{1,2}$ 1.7, $J_{2,3}$ 4.0, $J_{2,NH}$ 8.3, $J_{3,4}$ 9.8, $J_{4,5}$ 9.7, $J_{5,6a}$ 2.8, $J_{5,6b}$ 5.7, $J_{6a,6b}$ 12.2 Hz. Anal. Calcd for $C_{20}H_{31}NO_9$: C, 55.93; H, 7.27; N, 3.26. Found: C, 56.13; H, 7.51; N, 3.11.

*6-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-*D*-mannopyranosyl)-1,2 : 3,4-di-*O*-isopropylidene-α-*D*-galactopyranose* (**6b**).—Reduction of **2b** (85 mg, 0.1 mmol) was performed as described for **1b**. Acetylation of the product yielded **6b** (58 mg, 72%) identical by its optical rotation and ^{1}H NMR spectra with the authentic compound[20].

*Methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-galacto- and -talo-pyranosides* (**7a** *and* **8a**).—Reduction of **3a** (69 mg, 0.2 mmol) was performed according to the general procedure. After acetylation, TLC (19:1 $CHCl_3$–MeOH) showed a mixture of two products, which were not separated. The ratio of **7a** : **8a**, elucidated from ^{1}H NMR data, was 2:3. ^{1}H NMR data of **7a**: δ 1.97, 2.00, 2.06, 2.17 (4 s × 3 H, 3 OAc, NAc), 3.40 (s, 3 H, OMe), 4.07–4.15 (m, 3 H, H-5,6a,6b), 4.59 (ddd, 1 H, H-2), 4.77 (d, 1 H, H-1), 5.16 (dd, 1 H, H-3), 5.37 (d, 1 H, H-4); 5.60 (d, 1 H, NH); $J_{1,2}$ 3.6, $J_{2,3}$ 11.3, $J_{2,NH}$ 9.7, $J_{3,4}$ 3.3, $J_{4,5}$ 1.0, $J_{5,6a}$ 9.9, $J_{5,6b}$ 4.3, $J_{6a,6b}$ 10.0 Hz.

^{1}H NMR data of **8a**: δ 1.99, 2.03, 2.07, 2.18 (4 s × 3 H, 3 OAc, NAc), 4.10–4.14 (m, 2 H, H-6a,6b), 4.20 (t, 1 H, H-5), 4.40 (dd, 1 H, H-2), 4.71 (s, 1 H, H-1), 5.31 (t, 1 H, H-3), 5.37 (d, 1 H, H-4), 6.30 (d, 1 H, NH); $J_{2,3}$ 4.7, $J_{2,NH}$ 9.4, $J_{3,4}$ 3.8, $J_{4,5}$ 0.9, $J_{5,6a}$ 6.1, $J_{5,6b}$ 3.1 Hz.

*Cyclohexyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-galacto- and -talo-pyrano-*

sides (**7b** and **8b**).—Reduction of **3b** (83 mg, 0.2 mmol) was performed according to the general procedure. After acetylation, two products (TLC; 1:2 hexane–EtOAc) were separated on a silica gel column, using 1:1 EtOAc–hexane as eluant. First to be eluted (35 mg, 46%) was **8b**; $[\alpha]_D$ +75.2° (*c* 0.64). ^{1}H NMR: δ 0.8–1.9 (m, 10 H, several peaks of cyclohexyl), 1.97, 2.01, 2.02, 2.15 (4 s × 3 H, 3 OAc, NAc), 3.53 (m, 1 H, H-1 of cyclohexyl), 4.00 (d, 1 H, H-6a), 4.10–4.30 (m, 2 H, H-5,6b), 4.50 (td, H-2), 4.94 (d, 1 H, H-1), 5.33 (t, 1 H, H-3), 5.40 (t, 1 H, H-4), 6.28 (d, 1 H, NH); $J_{1,2}$ 1.1, $J_{2,3}$ 4.6, $J_{2,NH}$ 9.6, $J_{3,4}$ 3.5, $J_{4,5}$ 1.1, $J_{5,6a}$ 5.9, $J_{5,6b}$ 7.1, $J_{6a,6b}$ 11.3 Hz. Anal. Calcd for $C_{20}H_{31}NO_9$: C, 55.93; H, 7.27; N, 3.26. Found: C, 55.84; H, 7.41; N, 3.28.

The second compound to be eluted was **7b** (17 mg, 23%); $[\alpha]_D$ +35.7° (*c* 0.9). ^{1}H NMR: δ 0.9–1.9 (m, 10 H, several peaks of cyclohexyl), 1.96, 2.00, 2.04, 2.17 (4 s × 3 H, 3 OAc, NAc), 3.56 (m, 1 H, H-1 of cyclohexyl), 4.06 (m, 2 H, H-6a,6b), 4.25 (dt, 1 H, H-5), 4.54 (ddd, 1 H, H-2), 5.08 (d, 1 H, H-1), 5.16 (d, 1 H, H-3), 5.37 (dd, 1 H, H-4), 5.55 (d, 1 H, NH); $J_{1,2}$ 3.7, $J_{2,3}$ 11.3, $J_{2,NH}$ 9.7, $J_{3,4}$ 3.3, $J_{4,5}$ 1.1, $J_{5,6a}$ 6.1, $J_{5,6b}$ 7.1, $J_{6a,6b}$ 11.3 Hz. Anal. Calcd for $C_{20}H_{31}NO_9$: C, 55.93; H, 7.27; N, 3.26. Found: C, 55.73; H, 7.30; N, 3.09.

*Methyl 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-α-*D*-galacto- and -talo-pyranoside* (**7c** *and* **8c**).—After reduction of **3c** (98 mg, 0.2 mmol) followed by acetylation, two products (TLC; 9:1 $CHCl_3$–Me_2CO) were separated by chromatography to afford **7c** (60 mg, 60%) as the main product; mp 140–141°C; $[\alpha]_D$ +110° (*c* 0.9). Anal. Calcd for $C_{30}H_{35}NO_6$: C, 71.26; H, 6.98; N, 2.77. Found: C, 71.00; H, 7.28; N, 2.70.

The minor product was **8c** (9 mg, 9%); mp 144–145°C; $[\alpha]_D$ +100.0° (*c* 0.8). Anal. Calcd for $C_{30}H_{35}NO_6$: C, 71.26; H, 6.98; N, 2.77. Found: C, 70.95; H, 6.87; N, 2.85.

Catalytic hydrogenolysis of benzyl groups (H_2–Pd–C) followed by acetylation afforded **7a** and **8a** identical by their ^{1}H NMR data with those obtained from **3a**.

*Benzyl 2-acetamido-2-deoxy-3,4-*O*-isopropylidene-6-*O*-trityl-α-*D*-talopyranoside* (**8d**).—Reduction of **3d** (58 mg, 0.1 mmol) followed by acetylation gave **8d** (52 mg, 88%) as the sole product (TLC: 19:1 benzene–Me_2CO); mp 174–175; $[\alpha]_D$ +54.8° (*c* 0.8). ^{1}H NMR: δ 1.25, 1.34 (2 s × 3 H, CMe_2), 3.25 (dd, 1 H, H-6a), 3.42 (dd, 1 H, H-6b), 3.94 (ddd, 1 H, H-5), 4.24 (dd, 1 H, H-4), 4.32 (ddd, 1 H, H-2), 4.43 (dd, 1 H, H-3), 4.61 and 4.91 (AB, 2 H, OCH_2Ph), 4.68 (d, 1 H, H-1), 5.68 (d, 1 H, NH); $J_{1,2}$ 6.5, $J_{2,3}$ 3.2, $J_{2,NH}$ 9.4, $J_{3,4}$ 7.6, $J_{4,5}$ 1.9, $J_{5,6a}$ 4.9, $J_{5,6b}$ 7.4, $J_{6a,6b}$ 9.8 Hz. Anal. Calcd for $C_{37}H_{39}NO_6$: C, 74.85; H, 6.62; N, 2.36. Found: C, 74.73; H, 6.60; N, 2.42.

tert-*Butyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-talopyranoside* (**8e**).—Reduction of **3e** (68 mg, 0.17 mmol) followed by acetylation and then filtration of the product through a silica gel column afforded **8e** (53 mg, 75%); mp 101–102°C; $[\alpha]_D$ +66.0° (*c* 0.27). ^{1}H NMR *: δ 1.25 (s, 9 H of *tert*-Bu); 1.99, 2.02, 2.04, 2.17 (4 s × 3 H, 3 OAc, NAc), 4.06–4.14 (m, 2 H, H-6a,6b), 4.24 (qt, 1 H, H-2), 4.43 (ddd, 1 H, H-5), 5.09 (d, 1 H, H-1), 5.34 (dd, 1 H, H-3), 5.40 (m, 1 H, H-4), 6.31 (d, 1 H,

* In the spectrum were also found signals which could be ascribed to **7e** (**7e**:**8e** ~ 1:19).

NH); $J_{1,2}$ 1.1, $J_{2,3}$ 4.8, $J_{2,4}$ 1.1, $J_{2,NH}$ 9.5, $J_{3,4}$ 3.5, $J_{4,5}$ 1.3, $J_{5,6a}$ 6.7 Hz. Anal. Calcd for $C_{18}H_{29}NO_9$: C, 53.58; H, 7.25; N, 3.47. Found: C, 53.43; H, 7.44; N, 3.63.

*Benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-*D*-talopyranoside* (**8f**).—A solution of **8d** (200 mg, 0.34 mmol) in MeCN (2 mL) and water (2 mL) was treated with CAN (500 mg) and the mixture was stirred at 60°C for ca. 1 h. Filtration through Celite, then evaporation left a syrup which was purified by chromatography (eluant 97:3 $CHCl_3$–MeOH). The product was acetylated using Ac_2O–pyridine. Isolation by the usual procedure yielded **8e** (113 mg, 77%); mp 115–116°C; $[\alpha]_D$ +68.8° (*c* 0.89). ^{1}H NMR: δ 1.99, 2.03, 2.07, 2.18 (4 s × 3 H, 3 OAc, NAc), 4.12 (ddd, 2 H, H-6a,6b), 4.27 (ddd, 1 H, H-5), 4.48 (qt, 1 H, H-2), 4.62 and 4.69 (AB, 2 H, OCH_2Ph), 4.91 (d, 1 H, H-1), 5.41 (m, 1 H, H-4), 5.34 (dd, 1 H, H-3), 6.28 (d, 1 H, NH), 7.32–7.39 (m, 5 H, arom.); $J_{1,2}$ 1.1, $J_{2,3}$ 4.8, $J_{2,4}$ 1.1, $J_{2,NH}$ 9.7, $J_{4,5}$ 1.2, $J_{5,6a}$ 6.2, $J_{5,6b}$ 7.1, $J_{6a,6b}$ 11.0, J_{OBn} 11.7 Hz. Anal. Calcd for $C_{21}H_{27}NO_9$: C, 57.66; H, 6.22; N, 3.20. Found: C, 57.71; H, 6.54; N, 2.94.

*Ethyl 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-*D*-talopyranoside* (**9**).—Reduction of **4** (101 mg, 0.2 mmol) followed by acetylation gave **9** (83 mg, 80%) as the sole product (TLC; 3:7 hexane–EtOAc); syrup; $[\alpha]_D$ −51.6° (*c* 0.7). ^{1}H NMR: δ 1.19 (t, 3 H, Me of OEt), 1.78 (s, 3 H, NAc), 3.54 (dd, 1 H of OEt), 3.50–3.60 (m, 2 H, H-5, H of OEt), 3.66 (dd, 1 H, H-6a), 3.79 (dd, 1 H, H-6b), 3.85 (dt, 1 H, H-2), 3.89 (dd, 1 H, H-4), 4.37 (d, 1 H, H-1), 4.47, 4.49, 4.50, 4.57, 4.79 (5 d × 1 H, 5 H of OCH_2Ph), 4.82 (dt, 1 H, H-3), 4.87 (d, 1 H of OCH_2Ph), 6.80 (d, 1 H, NH); $J_{1,2}$ 1.7, $J_{2,3}$ 3.4, $J_{2,NH}$ 9.7, $J_{3,4}$ 2.7, $J_{4,5}$ 1.4, $J_{5,6a}$ 7.5, $J_{5,6b}$ 7.0, $J_{6a,6b}$ 9.0, J_{OBn} 11.8, 11.8, 11.7, 10.2 Hz. Anal. Calcd for $C_{31}H_{37}NO_6$: C, 71.65; H, 7.18; N, 2.70. Found: C, 71.65; H, 7.26; N, 2.78.

REFERENCES

1 J. Montreuil, *Adv. Carbohydr. Chem. Biochem.*, 37 (1980) 157–223.
2 H. Jennings, *Adv. Carbohydr. Chem. Biochem.*, 41 (1983) 155–208.
3 F.W. Lichtenthaler, E. Kaji, and S. Weprek, *J. Org. Chem.*, 50 (1985) 3505–3515.
4 J.N. Glushka and A.S. Perlin, *Carbohydr. Res.*, 205 (1990) 305–321.
5 R.U. Lemieux and S.W. Gunner, *Can. J. Chem.*, 46 (1968) 397–400.
6 R.U. Lemieux, K. James, T.L. Nagabhushan, and Y. Ito, *Can. J. Chem.*, 51 (1973) 33–41.
7 R.U. Lemieux, K. James, and T.L. Nagabhushan, *Can. J. Chem.*, 51 (1973) 48–52.
8 J.P. Leeds and H.A. Kirst, *Synth. Commun.*, 18 (1988) 777–782.
9 S. Itsuno, Y. Sakurai, and K. Ito, *Synthesis*, (1988) 995–996.
10 P. Kočovsky, *Synlett*, (1900) 677–679.
11 W. Karpiesiuk and A. Banaszek, *J. Carbohydr. Chem.*, 9 (1990) 909–914.
12 A. Giannis and S. Sandhoff, *Angew. Chem. Int. Ed. Engl.*, 28 (1989) 218–220.
13 C.L. Stevens and C.P. Bryant, *Methods Carbohydr. Chem*, VI (1972) 235–238.
14 R.U. Lemieux and T.L. Nagabhushan, *Methods Carbohydr. Chem.*, VI (1972) 487–496.
15 F.W. Lichtenthaler, P. Jarglis, and W. Hampe, *Liebigs Ann. Chem.*, (1983) 1959–1972.
16 F.W. Lichtenthaler and E. Kaji, *Liebigs Ann. Chem.*, (1985) 1659–1668.
17 R. von Rysbergen, M.J.O. Anteunis, and A.D. Bruyn, *J. Carbohydr. Chem.*, 2 (1983) 395–404.
18 J. Ramza, Ph.D. Thesis, Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw, 1991.
19 R.W. Jeanloz, Z. Tarasiejska-Glazer, and D.A. Jeanloz, *J. Org. Chem.*, 26 (1961) 532–536.
20 E. Kaji, F.W. Lichtenthaler, T. Nishino, A. Yamane, and S. Zen, *Bull. Chem. Soc. Jpn.*, 61 (1988) 1291–1297.