Preparation of 1,6-di-deoxy-D-*galacto* and 1,6-di-deoxy-L-*altro* nojirimycin derivatives by aminocyclization of a 1,5-dicarbonyl derivative

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Abstract

Iminosugars are known glycosidase inhibitors which are the subject of drug development efforts against several diseases. The access to structurally-related families of iminosugars is of primary importance for running structure-activity relationship studies. In this work, the double reductive amination (aminocyclization) reaction of a dicarbonyl derivative of the L-*arabino* series, in turn obtained from lactose, is reported. Different ratios of 1,6-di-deoxy-D-*galacto* and 1,6-di-deoxy-L-*altro* nojirimycin derivatives were obtained depending on the amine employed in this transformation which provided an insight into the effects of their structure on the outcome of the reaction. Of particular interest were the results obtained when two enantiomeric amino acids (D-Phe-OMe and L-Phe-OMe) were used, which resulted in the inversion of the reaction stereoselectivity.

1. Introduction

Carbohydrates play key roles in almost every major biological event and are receiving increasing attention both for elucidating the interaction of cells with their surroundings and as potential drug targets [1-8]. Carbohydrate mimics represent intriguing structural variation of the naturally occurring sugar glycan structures. Within this class fall iminosugars, also known as azasugars, where the endocyclic oxygen is replaced by a basic nitrogen atom [9]. This apparently simple modification confers to these structures significant biological activities. Indeed, iminosugars are known as inhibitors of glycosidases which are enzymes responsible for the hydrolysis of the glycosidic bonds in biologically relevant processes such as intestinal digestion, post-translational processing of the sugar chain of glycoproteins and lysosomal catabolism of glycoconjugates [10].

Iminosugars are a class of structurally diverse molecules (polyhydroxylated piperidines and pyrrolidines and their derivatives) which have been investigated as antiviral agents (against HIV-1, herpes simplex virus, bovine viral diarrhoea virus (BVDV), and hepatitis C

virus (HCV)), as antidiabetics, in the treatment of lysosomal storage disorders such as Gaucher's and Niemann Pick type C, in immune modulation and as anticancer agents [11]. In the last 50 years, a great number of compounds have been synthesized and tested against different biological targets, while only few glycosidase inhibitors have been progressed to clinical trials [12]. Their structures are closely related to 1-deoxy-D-nojirimycin (DNJ) and nowadays the following compounds are available on the market: the Acarbose DNJ analogue Miglitol or Glyset [13-15], the carbamino sugar Voglibose [16] (used in the treatment of diabetes type II), Miglustat or Zavesca [17] for the treatment of Gaucher's disease and the antiviral drug Tamiflu or Oseltamivir [18] (**Figure1**).

Usually, the main limitation associated with the use of iminosugars is the lack of adequate selectivity, which results into detrimental side effects associated to their therapeutic application. In order to improve the binding affinity between substrate and domain, some efforts in the design and synthesis of new selective iminosugars have been carried out. [19-21]

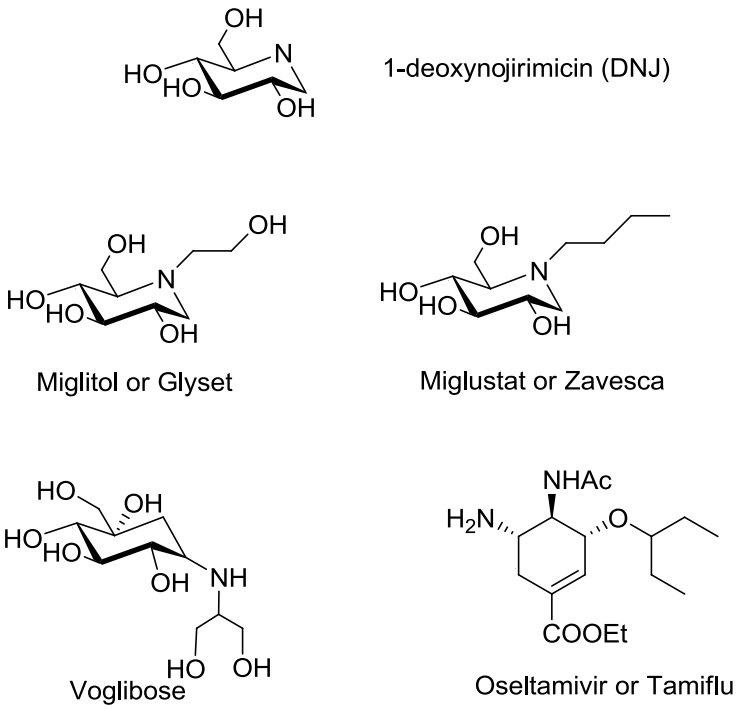


Figure 1. Chemical structure of glycosidase inhibitors.

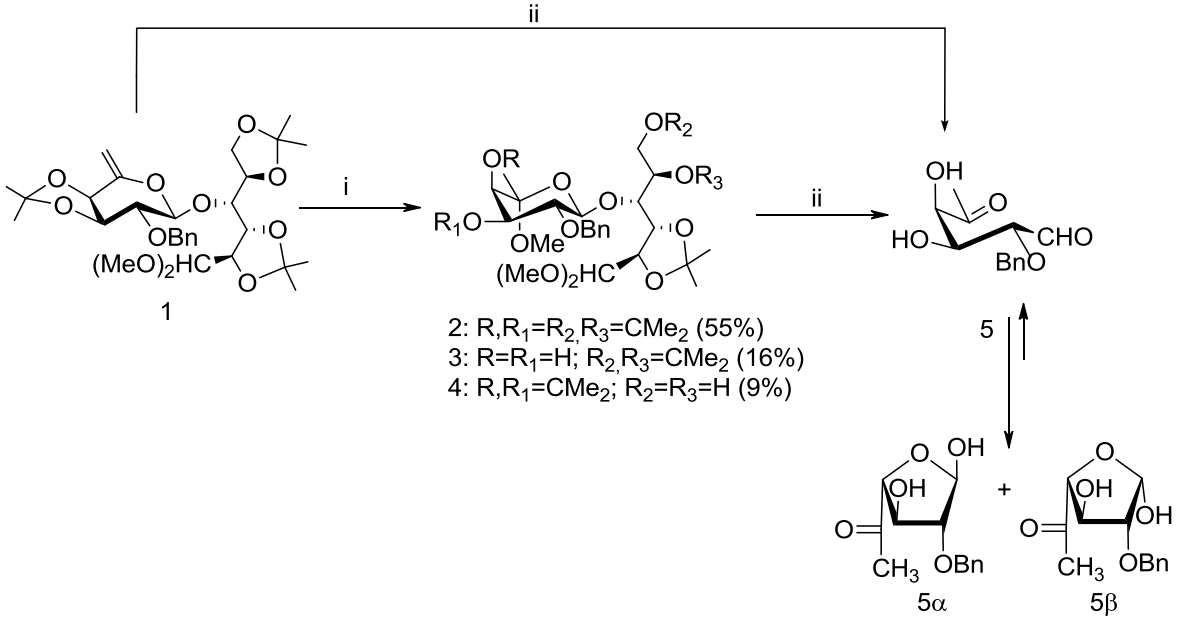
The synthesis of iminosugar derivatives is quite complex due to the polar nature and stereochemical complexity of the target structures [22]. Different approaches have been explored in the past years to address this challenge. Some works reported the syntheses of 1-deoxynojirimycin and its isomers employing as starting materials substrates from the chiral pool such as carbohydrates [23-25] or amino acids [26, 27]. Other strategies started

instead from different open chain precursors and were based on chemoenzymatic [28, 29] or asymmetric reactions such as dihydroxylation [30], aldol reaction coupled with a reductive amination [31] or aminohydroxylation [32] transformations.

As part of an ongoing project aimed at converting lactose into valuable compounds [33, 34] by means of dicarbonyl intermediates [35-37], we report here the intramolecular double reductive amination (aminocyclization) reaction of a partially protected 6-deoxy-L-*arabino*-hexos-5-ulose to access 1,6-dideoxy-D-*galacto* and 1,6-dideoxy-L-*altro* nojirimycin derivatives. The influence of the amines' steric hindrance and of the stereochemistry of two enantiomeric amino acids, all employed as reagents, was evaluated with a particular emphasis on the aminocyclization reaction outcome.

2. Results and discussion

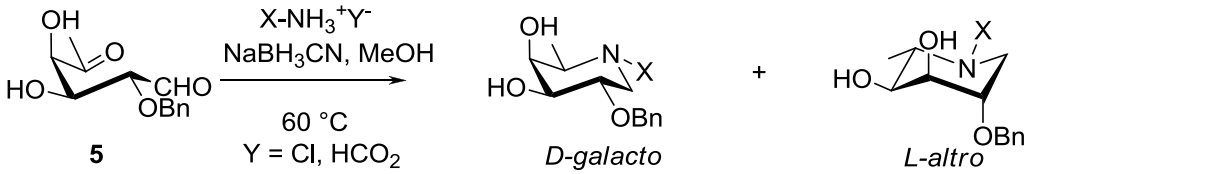
The synthetic pathway started with the synthesis of the 2-*O*-benzyl-6-deoxy-L-*arabino*-hexos-5-ulose **5** as the key intermediate (**Scheme 1**). Dicarbonyl derivative **5** was prepared from the previously reported enol ether **1** [38] which in turn can be obtained from lactose on a multi gram scale. By applying the original protocol of Mioskovski [39] enol ether **1** was converted into a complex mixture of derivatives (**2-4**, 80% overall yield) due to the instability of the isopropylidene protecting groups under these conditions (PPh_3·HBr, MeOH).



Scheme 1. *Reagents and conditions*: (i) PPh_3·HBr, MeOH, 0.5 h, rt; (ii) CF_3COOH, 4:1 CH_3CN-H_2O, 18 h, r.t. (yield of **5**: 76% from the crude mixture of **2**, **3** and **4**; 85% from **1**).

The following treatment of the mixture of 1,5-*bis*-glycosides **2-4** with trifluoroacetic acid caused the hydrolysis of all the acetal groups thus affording the desired compound in a satisfactory yield (**5**, 76%). It is worth mentioning that it was also possible to prepare **5**, even in a higher yield (85%), by adding trifluoroacetic acid directly to **1** (Scheme 1). As expected, 1,5-dicarbonyl intermediate **5** was obtained as a mixture of furanose forms **5**α and **5**β (ca 4:1 ratio) as assessed by NMR. In the proton spectrum, the presence of only two doublet signals at δ 5.41 ($J_{1,2}$ =1.1 Hz) and δ 5.43 ($J_{1,2}$ =3.9 Hz), related to anomeric protons, confirmed the almost exclusive presence of furanose tautomers. The low values of these coupling constants as well as of $J_{2,3}$ (2.2 and 5.0 Hz) strongly suggest the absence of pyranose tautomers. The observed composition is in good agreement with the tautomeric equilibrium previously reported for other aldohexos-5-ulose derivatives, where the furanose forms are the prevalent species provided that the 4-OH is free to engage in the emiacetalization process [36].

Derivative **5** was reacted with quaternary ammonium salts characterized by an increasing substitution around the nitrogen (-H, -OH, $-CH_3$, CH_2Ph, $-CH(Ph)_2$), and with selected amino acids (Gly, D-Phe, L-Phe) protected as methyl esters (Scheme 2). The reaction was performed following a protocol previously reported by us ($NaBH_3CN$, MeOH, 60°C) [38]. Azasugars **6a-h** and **7a-h** were isolated in satisfactory overall yields (Table 1) after chromatographic purification, and their structures and stereochemistries were established by NMR analysis. In particular, the known effects caused by the nitrogen atom on the chemical shifts of vicinal protons (H-1ax, H-1eq and H-5), which give resonance signals at higher fields (δ 1.80-3.40, see experimental section) than those in alpha to the oxygen atom, and the related $J_{1,2}$ and $J_{4,5}$ coupling constants allowed for the identification of the C-5 epimers **6a-h** and **7a-h**. In addition, in the case of ^{13}C spectra again the signals of carbons adjacent to the nitrogen (C-1 and C-5), which are shielded and easily recognisable by DEPT experiments, were diagnostics for the C-5 epimers.



6a: X=H
6b: X=Me
6c: X=CH_2Ph
6d: X=$CHPh_2$
6e: X=OH
6f: X=CH_2COOMe
6g: X= (D)-CH(Bn)COOMe
6h: X= (L)-CH(Bn)COOMe

7a: X=H
7b: X=Me
7c: X=CH_2Ph
7d: X=$CHPh_2$
7f: X=CH_2COOMe
7g: X= (D)-CH(Bn)COOMe
7h: X= (L)-CH(Bn)COOMe

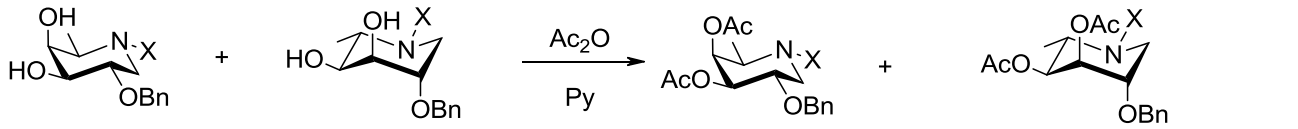
Scheme 2. Intramolecular double reductive amination (aminocyclization) reaction of **5**.

Table 1. Yields of isolated products and selectivity of the aminocyclization reaction

Entry	Amine	Products (Isolated yield)	D-galacto/L-altro ratio[a]
1	NH_3	**6a**+**7a** (68%)	75:25
2	CH_3NH_2	**6b**+**7b** (62%)	80:20
3	$PhCH_2NH_2$	**6c** (40%) and **7c** (16%)	70:30
4	Ph_2CHNH_2	**6d**+**7d** (64%)	45:55
5	NH_2-OH	**6e** (56%)	100:0
6	Gly-OMe	**6f** (39%) and **7f** (17%)	70:30
7	D-Phe-OMe	**6g** (14%) and **7g** (49%)	25:75
8	L-Phe-OMe	**6h**+**7h** (58%)	65:35

[a]Ratios were determined by NMR analysis of the crude product.

For **6c**, **7c** and mixture **6d**/**7d** and **6h**/**7h**, in order to complete the NMR characterization or to simplify the purification process, an acetylation reaction (Ac_2O/Py 1:2, 24h, Scheme 3) was performed affording products **8-13** in good yields. It is of interest to highlight that it was possible to separate the diastereoisomeric mixture of iminosugars only when $PhCH_2NH_2$, Gly-OMe or D-Phe-OMe was used as reacting partner (entries 3, 6, 7, Table 1).



6c: X=CH_2Ph **7c**: X=CH_2Ph **8**: X=CH_2Ph **9**: X=$CHPh_2$
6d: X=$CHPh_2$ **7d**: X=$CHPh_2$ **10**: X=$CHPh_2$ **11**: X=$CHPh_2$
6h: X= (L)-CH(Bn)COOMe **7h**: X= (L)-CH(Bn)COOMe **12**: X= (L)-CH(Bn)COOMe **13**: X= (L)-CH(Bn)COOMe

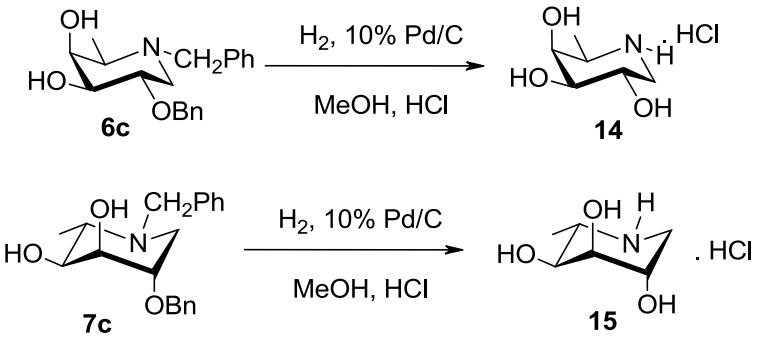
Scheme 3. Acetylation of iminosugars **6c**/**7c**, **6d**/**7d** and **6h**/**7h**.

The stereoselectivity of the aminocyclization reaction of aldohexos-5-uloses is commonly accepted to be governed by the direction of hydride attack on a cyclic iminium ion intermediate. The latter is formed through two consecutive steps: the condensation of the amino group with the more reactive aldehyde function followed by a second amination on the C-5 keto group. Stereoelectronic effects (preferential axial attack of the hydride) as well as conformational effects (stability of the half chair conformers) can be invoked to rationalise the experimental results [40]. For D-*xylo* aldohexos-5-ulose derivatives almost only one iminosugar (D-*gluco*) is obtained with a negligible influence of the structure of the amine used and of the protecting group pattern present on the dicarbonyl substrate [33, 41], while a more complicated picture is found for L-*arabino* aldohexos-5-ulose derivatives. For the deprotected compound, again only a sole iminosugar (D-*galacto*) was isolated even when performing the reaction with the quite hindered benzhydrylamine, whereas the two possible stereoisomers (D-*galacto*/L-*altro* 4:1 ratio) were obtained when using the 2,6-di-*O*-benzyl L-*arabino* aldohexos-5-ulose derivative. [42] Furthermore, the steric hindrance of the employed amine had an effect on the stereoselectivity. Therefore, these literature results suggest that both the different C-4 stereochemistry of L-*arabino* aldohexos-5-ulose derivatives and the protecting groups present can play an important role in determining the stereochemical outcome of the reaction. Indeed, for the 6-deoxy 2-*O*-benzyl-L-*arabino*-derivative studied here, the results are in line with the previous findings for most of the amines (Table 1). Usually both D-*galacto* and L-*altro* 1,6-dideoxy nojirimycin derivatives were isolated with the first being the most abundant. The ratio between these two isomers span from 8:2 to 7:3 (entries 1-3, 6 and 8) with the exception of the more hindered benzhydrylamine derivative (entry 4) where an almost equal amount of the two isomeric iminosugars was obtained. The results obtained with hydroxylamine (entry 5), when complete selectivity for the D-*galacto* configuration was observed, and with D- or L-Phe-OMe (entries 7 and 8), where the ratio of the two iminosugars product was reversed, point to the need to consider other features of the amine partner beside its steric hindrance.

Indeed, it appears that additional interactions between the reacting amine, the substituents or the hydroxy groups present on the dicarbonyl compound can come into play in determining the conformation and the reactivity of the preferred cyclic iminium ion. Further studies in this direction are currently underway.

It has also to be mentioned that an aminocyclization reaction employing amino acids has already been reported in the literature [43]. However, in that case the amino group involved in the reaction was on the side chain of a protected lysine, which is probably too far from the chiral centre to affect the stereoselectivity of the reaction.

To compare the experimental data with the literature, compounds **6c** and **7c** were further transformed into the deprotected compounds **14** [44] and **15** [44, 45] (Scheme 4) by means of catalytic hydrogenolysis (H_2, Pd/C 10% in MeOH) in the presence of HCl, a set of conditions employed to avoid the previously reported *N*-methylation side reaction [46].



Scheme 4. Catalytic hydrogenolysis of iminosugars **6c** and **7c.**

3. Conclusions

The preparation of a 2-*O*-benzyl-6-deoxy-L-*arabino*-hexos-5-ulose from lactose and its conversion into 1,6-di-deoxy-D-*galacto* and 1,6-di-deoxy-L-*altro* nojirimycin derivatives exploiting a reductive aminocyclization reaction were reported. This approach allowed for the preparation of a structurally-related family of iminosugars by simply selecting different ammonium salts. However, a limitation of the method lies in the difficulty encountered in the separation of the diastereoisomeric iminosugars. Of a certain interest is the observed inversion of selectivity when the enantiomeric amino acids were employed in the aminocyclization reaction, and the formation of only the iminosugar of the D-*galacto* configuration with hydroxylamine.

4. Experimental

4.1. General methods

Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. Optical rotations were measured at room temperature (20±2 °C) in a 1 dm cell with a Perkin-Elmer 241 polarimeter. NMR spectra were recorded with a Bruker AC 200 instrument operating at 200.13 MHz (^{1}H) and 50.33 MHz (^{13}C) in the stated solvent (Me_4Si was used as the internal standard, unless stated otherwise). Assignments were made, when possible, with the aid of DEPT, HETCOR, by comparison of values for known compounds and applying the additivity rules [47]. In the case of mixtures, assignments were made by referring to the differences in the peak intensities. All reactions were followed by TLC on Kieselgel 60 F_{254} (Merk) with detection by UV light and/or with 10% phosphomolybdic acid or sulphuric acid in EtOH and heating, or exposure to I_2 vapours. Kieselgel 60 (E. Merck, 70-230 and 230-400 mesh, respectively) was used for column and flash chromatography. Solvents were dried and purified by distillation according to standard procedures [48], and stored over 4Å molecular sieves activated for at least 24 h at 250 °C. $MgSO_4$ was used as the drying agent for solutions. Unless otherwise stated, all reactions requiring anhydrous conditions were carried out under Argon or Nitrogen. Elemental analysis was used to determine the purity of compounds. Analytical results are within ± 0.40% of the theoretical values.

The following standard procedure was used for acetylation: a solution of the compound (1.0 mmol) in a 2:1 (v/v) mixture (6 mL) of pyridine and Ac_2O was stirred at room temperature for 12-24 h, and then repeatedly co-evaporated under diminished pressure with toluene, and the residue was purified by flash chromatography on silica. “Solid foam” refers to amorphous compounds, recovered pure by chromatography for which all attempts to crystallize failed.

4.2. Experimental procedures

4.2.1. Reaction of 4-*O*-(2-*O*-benzyl-6-deoxy-3,4-*O*-isopropylidene-α-L-*arabino*-hex-5-enopyranosyl)-2,3:5,6-di-*O*-isopropylidene-*aldehydo*-dimethyl acetal (1) with MeOH catalyzed by PPh_3·HBr.

A solution of **1** [34] (2.02 g, 3.48 mmol) in dry CH_2Cl_2 (17.0 mL) was treated at room temperature with PPh_3·HBr (60.2 mg, 0.175 mmol) and dry MeOH (1.40 mL, 34.2 mmol), and the mixture reaction was stirred at room temperature until the starting material

completely disappeared (TLC, 1:3 Et_2O-toluene). After 30 min, TLC analysis (EtOAc) showed the prevalent formation of **2** (R_f 0.73) and small amount of products **3** (R_f 0.54) and **4** (R_f 0.50). The reaction solution was washed with satd aq $NaHCO_3$ (3×30 mL) and the aqueous phases were collected and extracted with CH_2Cl_2 (4×30 mL). The combined organic phases were dried, filtered and concentrated. Purification of the crude residue (syrup, 2.96 g) by flash chromatography on silica gel (7:3 *n*-hexane-EtOAc + 0.1% of Et_3N) afforded pure **2** (1.17 g, 55% yield), **3** (319 mg, 16% yield) and **4** (159 mg, 8% yield).

4-O-*[(5R)-(2*-O-*Benzyl-6-deoxy-3,4*-O-*isopropylidene-5*-C-*methoxy-α-L-hexopyranosyl]-2,3:5,6-di*-O-*isopropylidene*-aldehydo-*D-glucose dimethyl acetal (**2**).* Clear syrup; R_f 0.73 (EtOAc); $[\alpha]_D$ +7.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (CD_3CN, 200.13 MHz): δ 7.38-7.28 (m, 5H, Ar-*H*), 4.75 (d, 1H, $J_{1',2'}$ 8.4 Hz, H-1'), 4.80, 4.68 (AB system, 2H, $J_{A,B}$ 12.1 Hz, C*H*$_2$Ph), 4.47 (dd, 1H, $J_{1,2}$ 6.4 Hz, $J_{2,3}$ 7.2 Hz, H-2), 4.38 (d, 1H, H-1), 4.23 (d, 1H, $J_{4,5}$=$J_{5,6a}$ =$J_{5,6b}$ 5.9 Hz, H-5), 4.15-4.06 (m, 3H, H-3', H-4, H-6a), 3.93 (d, 1H, $J_{3',4'}$ 5.3 Hz, H-4'), 3.91 (dd, 1H, $J_{6a,6b}$ 8.6 Hz, H-6b), 3.86 (dd, 1H, $J_{3,4}$ 1.3 Hz, H-3), 3.38, 3.39 (2s, each 3H, OMe-1), 3.29 (s, 3H, OMe-5'), 3.25 (bt, 1H, $J_{2',3'}$ 8.0 Hz, H-2'); 2.20 (s, 3H, H-6'), 1.37, 1.36, 1.35, 1.29, 1.28, 1.27 (6s, each 3H, 3×C*Me*$_2$); ^{13}C NMR **(**CD_3CN, 50.33 MHz): δ 139.7 (Ar-*C*), 129.1, 129.0, 128.4 (Ar-*C*H), 110.5, 109.9, 109.3 (3×*C*Me$_2$), 106.7 (C-1), 100.5 (C-5'), 98.7 (C-1'), 80.3, 78.9, 78.9, 77.8, 78.8 (C-2', C-3', C-2, C-3, C-4), 76.8, 76.1 (C-4', C-5), 74.3 (*C*H$_2$Ph), 66.2 (C-6), 56.5, 53.8 (2×OMe-1), 48.3 (OMe-5'), 28.3, 27.5, 27.1, 26.9, 26.6, 25.6 (3×C*Me*$_2$), 19.4 (C-6'). Anal. Calcd for $C_{31}H_{48}O_{12}$: C, 60.77; H, 7.90. Found: C, 60.49; H, 7.61.

4-O-*[(5R)-(2*-O-*benzyl-6-deoxy-5*-C-*methoxy-α-L-hexopyranosyl]-2,3:5,6-di*-O-*isopropylidene*-aldehydo-*D-glucose dimethyl acetal (**3**).* Clear syrup; R_f 0.54 (EtOAc); $[\alpha]_D$ -7.4 (*c* 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 7.34-7.27 (m, 5H, Ar-H), 4.91 (d, 1H, $J_{1',2'}$ 7.8 Hz, H-1'), 4.96, 4.80 (AB system, 2H, $J_{A,B}$ 11.6 Hz, *CH*$_2$Ph), 4.75-4.49 (m, 2H, H-2, H-5), 4.40 (d, 1H, $J_{1,2}$ 6.4 Hz, H-1), 4.34-3.83 (m, 6H, H-3, H-4, H-6a, H-6b, H-2', H-3'), 3.68 (d, 1H, $J_{3',4'}$ 3.2 Hz, H-4'), 3.43, 3.41 (2s, each 3H, 2×OMe-1), 3.29 (s, 3H, OMe-5'), 1.47, 1.44, 1.43, 1.38, 1.34 (5s, each 3H, 2×C*Me*$_2$, H-6'); ^{13}C NMR ($CDCl_3$, 50.33 MHz): δ 138.4 (Ar-*C*), 128.5, 128.2, 127.8 (Ar-*C*H), 110.0, 108.4 (2×*C*Me$_2$), 105.3 (C-1), 100.9 (C-5'), 98.8 (C-1'), 78.7, 77.9, 77.7, 77.6 (C-2', C-2, C-3, C-4), 74.5 (C-5), 74.4 (*CH*$_2$Ph), 72.5, 70.2 (C-3', C-4'), 65.2 (C-6), 55.6, 52.7 (2×OMe-1), 47.8 (OMe-5'), 27.3, 26.7, 26.5, 25.1 (2×C*Me*$_2$), 18.6 (C-6'). Anal. Calcd for $C_{28}H_{44}O_{12}$: C, 58.73; H, 7.74. Found: C, 58.65; H, 7.70.

4-O-*[(5R)-(2*-O-*benzyl-6-deoxy-3,4*-O-*isopropylidene-5*-C-*methoxy-*α-L-*hexopyranosyl]-2,3*-O-*isopropylidene*-aldehydo-*D-glucose dimethyl acetal (**4**).* Clear syrup; R_f 0.40 (EtOAc); $[\alpha]_D$ = -12.8 (*c* 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 7.41-7.27 (m, 5H, Ar-H), 4.88, 4.72 (AB system, 2H, $J_{A,B}$ 11.4 Hz, CH_2Ph), 4.71 (d, 1H, $J_{1',2'}$ 7.2 Hz, H-1'), 4.60 (dd, 1H, $J_{1,2}$ 6.4 Hz, $J_{2,3}$ 7.4 Hz, H-2), 4.39 (d, 1 H, H-1), 4.07- 3.72 (m, 7H, H-3, H-4, H-5, H-6a, H-6b, H-3', H-4'), 3.42 (m, 1H, H-2'), 3.43, 3.41 (2s, each 3H, 2 x OMe-1), 3.30 (s, 3H, OMe-5'), 1.44, 1.43, 1.41, 1.38, 1.34 (5s, each 3H, 2×CMe_2, H-6'); ^{13}C NMR ($CDCl_3$, 50.33 MHz): δ 137.4 (Ar-*C*), 128.4, 128.2, 127.7 (Ar-*C*H), 110.0, 109.3 (2×*C*Me_2), 105.4 (C-1), 99.6 (C-5'), 97.8 (C-1'), 79.2, 78.4, 77.9, 77.6, 77.5 (C-2', C-3', C-2, C-3, C-4), 75.2 (C-4'), 73.45 (C-5), 73.2 (CH_2Ph), 62.5 (C-6), 56.1, 52.7 (2×OMe-1), 47.5 (OMe-5'), 27.9, 27.2, 26.4, 26.3 (2×CMe_2), 19.1 (C-6'). Anal. Calcd for $C_{28}H_{44}O_{12}$: C, 58.73; H, 7.74. Found: C, 58.55; H, 7.70.

4.2.2. 6-deoxy-2-*O*-benzyl-L-*arabino*-hexos-5-ulose (5).

Method A (*from 1 with TFA-H_2O*): A solution **1** [34] (6.10 g, 10.5 mmol) in 4:1 (v/v) CH_3CN-H_2O (160 mL) was treated with 90% aq CF_3COOH (14.4 mL) and stirred at room temperature. After 18 h, TLC analysis (3:7 hexane-EtOAc) showed the complete disappearance of the starting material and the formation of two products (R_f 0.47 and 0.0), the first of them (R_f 0.47) visible under UV light. The solution was concentrated under diminished pressure and repeatedly co-evaporated with toluene (5×20 mL). The crude residue was partitioned between EtOAc (80 mL) and satd aq $NaHCO_3$ (40 mL) and the aqueous phase extracted with EtOAc (4×30 mL). The combined organic extracts were dried and concentrated to give a crude residue (2.41 g, 91% yield) constituted (NMR) exclusively by a 4:1 mixture of α- and β-1,4-furanose anomers (**5α** and **5β**) measured on the relative intensities two C-1 signals at δ 102.3 and 97.6 respectively. Purification of the crude product by flash chromatography on silica gel (3:2 hexane-EtOAc) gave pure **5** (2.25 g, 85% yield) as white foam; R_f 0.47 (3:7 hexane-EtOAc); $[\alpha]_D$ +6.9° (*c* 1.2, $CHCl_3$); ^{1}H NMR (CD_3CN, 200.13 MHz): anomer **5α**: δ 5.41 (d, 1H, $J_{1,2}$ 1.1 Hz, H-1), 4.48 (d, 1H, $J_{3,4}$ 3.8 Hz, H-4), 4.27 (dd, 1H, $J_{2,3}$ 2.2 Hz, H-3), 3.84 (dd, 1H, H-2), 2.14 (s, 3H, H-6); anomer **5β**: δ 5.43 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 4.10 (d, 1H, $J_{3,4}$ 4.5 Hz, H-4), 4.38 (dd, 1H, $J_{2,3}$ 5.0 Hz, H-3), 3.79 (dd, 1H, H-2), 2.21 (s, 3H, H-6), cluster of signals for both anomers δ 7.39-7.25 (m, 10H, Ar-*H*), 4.62-4.45 (m, 4H, 2×CH_2Ph); ^{13}C NMR (CD_3CN, 50.33 MHz) anomer **5α**: δ 209.8 (C-5), 102.3 (C-1), 90.0 (C-4), 88.7 (C-2), 77.8 (C-3), 72.3 (CH_2Ph), 26.7 (C-6); anomer **5β**: δ 211.2 (C-5), 97.6 (C-1), 87.8 (C-4), 83.9 (C-2), 76.3 (C-3), 72.8

(*CH*$_2$Ph), 26.7 (C-6), cluster of signals for both anomers δ 138.7 (2×Ar-*C*), 129.4-127.8 (Ar-*C*H). Anal. Calcd for $C_{13}H_{16}O_5$ (252.10): C, 61.90; H, 6.39. Found: C, 61.75; H, 6.35.

Method B (*from crude mixture* **2**, **3** and **4**, *with TFA-H$_2$O*): the crude mixture of 5-*C*-methoxy derivatives **2**, **3** and **4**, obtained by MeOH addition of **1** (760 mg, 1.31 mmol), was dissolved in 4:1 (*v*/*v*) CH_3CN/H_2O and treated with 90% aq CF_3COOH in CH_3CN-H_2O according to the procedure described above for the reaction of **1**. Purification of the crude product (280 mg) by flash chromatography on silica gel (3:2 hexane-EtOAc) led to a 4:1 mixture of **5α** and **5β** (251 mg, 76% yield) having NMR parameters identical to those of the samples prepared above.

4.2.3. General procedures for the double reductive amination of 6-deoxy-2-*O*-benzyl-L-*arabino*-hexos-5-ulose (5).

Method A - To a solution of the 4:1 mixture of **5α,β** (1.0 mmol) in dry MeOH (15 mL), a solution of the opportune amine salt (10 mmol) in dry MeOH (22 mL) and then a solution of $NaBH_3CN$ (2.2 mmol) in dry MeOH (15 mL) were added. The mixture was warmed to 60 °C and left under stirring until the starting material was completely disappeared (TLC analysis, 5-24 h). The reaction mixture was cooled to room temperature, quenched by addition of 1% methanolic HCl, and stirred until a persistent pH 1 value was reached (50 min). The solution was neutralized by addition of solid $NaHCO_3$ (pH 7-8), stirred at room temperature (30 min) and the suspension was filtered, the residue washed with MeOH and the organic phase was concentrated under diminished pressure. The crude residue was partitioned between EtOAc (40 mL) containing Et_3N (0.5 mL) and $NaHCO_3$ satd aq solution (30 mL) and the aqueous phase extracted with EtOAc (4×30 mL). The combined organic extracts were dried and concentrated at diminished pressure. The crude residue was analyzed by NMR (^{1}H and ^{13}C) and subjected to a flash chromatographic purification on silica gel eluting with opportune solvent mixtures.

Method B – A solution of the 4:1 mixture of **5α,β** (1.0 mmol) in dry MeOH (6 mL) was treated with a solution of opportune amine salt (1.0 mmol) in dry MeOH (9 mL) and with a solution of $NaBH_3CN$ (2.0 mmol) in dry MeOH (6 mL). The reaction mixture was stirred at 60 °C until the starting material was completely disappeared (TLC analysis, 18-24 h). The solution was concentrated under diminished pressure and the crude residue was partitioned between with EtOAc (40 mL) and satd aq $NaHCO_3$ solution (20 mL). The aqueous phase was extracted with EtOAc (4×30 mL) and the organic layers were collected, dried and concentrated in diminished pressure. The crude residue was analyzed

by NMR (^{1}H and ^{13}C) and subjected to a flash chromatographic purification on silica gel eluting with opportune solvent mixtures.

4.2.4. 2-*O*-benzyl-1,5,6-trideoxy-1,5-imino-D-galactitol (6a) and 2-*O*-benzyl-1,5,6-trideoxy-1,5-imino-L-altritol (7a).

A solution of **5α,β** (300 mg, 1.19 mmol) was subjected to double reductive amination with ammonium formate (748 mg, 11.9 mmol) and $NaBH_3CN$ (149 mg, 2.38 mmol) according to the general procedure (Method A). The reaction was complete after 17 h and TLC analysis (6:4 EtOAc-MeOH) showed the formation of only one spot (R_f 0.30). The crude residue (syrup, 203 mg) was constituted (NMR, CD_3CN) by a mixture of compounds **6a** and **7a** in a 75:25 ratio, measured on the relative intensities of the C-1 signals at δ 45.7 and 42.9 respectively. Compound **6a** and **7a** were inseparable by TLC with several elution systems and purification of the crude product by flash chromatography on silica gel (3:1 EtOAc-MeOH + 0.1% Et_3N) afforded pure mixture of **6a+7a** (193 mg, 68% yield) as a clear syrup; R_f 0.30 (6:4 EtOAc-MeOH); selected ^{1}H NMR ($CDCl_3$, 200.13 MHz) signals: compound **6a** δ 4.58 (s, 2H, O*CH*$_2$Ph), 1.01 (d, 1H, $J_{5,6}$ 6.4 Hz, H-6); for **7a** δ 4.54, 4.46 (AB system, 2H, $J_{A,B}$ 12.2 Hz, O*CH*$_2$Ph), 1.17 (d, 1H, $J_{5,6}$ 7.0 Hz, H-6); ^{13}C NMR ($CDCl_3$, 50.33 MHz): compound **6a**: δ 138.3 (Ar-*C*), 76.9 (C-2), 75.2 (C-3), 72.2 (O*CH*$_2$Ph), 72.1 (C-4), 53.8 (C-5), 47.7 (C-1), 17.2 (C-6); compound **7a**: δ 137.9 (Ar-*C*), 76.8 (C-2), 72.0 (C-3), 70.0 (O*CH*$_2$Ph); 68.7 (C-4), 50.9 (C-5), 45.7 (C-1), 17.6 (C-6); cluster of signals for both diastereoisomers: δ 128.2-127.5 (Ar-*C*H). Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.83; H, 8.10; N, 5.92.

4.2.5. 2-*O*-benzyl-1,5,6-trideoxy-1,5-imino-*N*-methyl-D-galactitol (6b) and 2-*O*-benzyl-1,5,6-trideoxy-1,5-imino-*N*-methyl-L-altritol (7b).

The double reductive amination of **5α,β** (354 mg, 1.40 mmol) with CH_3NH_3Cl (1.02 g, 15.1 mmol) and $NaBH_3CN$ (192 mg, 3.05 mmol) was performed in accordance to the general procedure (Method A). After 5 h, TLC analysis (EtOAc) showed the complete disappearance of the starting material and the formation of only one spot (R_f 0.10). The crude residue (350 mg) was constituted (NMR) by a mixture of **6b** and **7b** in a 80:20 ratio, estimated on the relative intensities of two separated singlets attributed to *N*-CH_3 at δ 2.23 and 2.31, respectively. Several attempts to separate the components of the mixture through TLC gave negative results. Purification of the crude product by flash chromatography on silica gel (6:4 CH_2Cl_2-^{i}PrOH + 0.1% Et_3N) gave a mixture of pure **6b**

and **7b** (217 mg, 62% yield) as a clear syrup; R_f 0.15 (6:4 CH_2Cl_2-^{i}PrOH); ^{1}H NMR ($CDCl_3$, 200.13 MHz) compound **6b**: δ 4.69, 4.62 (AB system, 2H, $J_{A,B}$ 11.7 Hz, O*CH*$_2$Ph), 3.70 (m, 2H, H-2, H-4), 3.44 (dd, 1H, $J_{2,3}$ 9.3 Hz, $J_{3,4}$ 3.3Hz, H-3), 3.06 (dd, 1H, $J_{1ax,1eq}$ 11.2 Hz, $J_{1eq,2}$ 5.0 Hz, H-1eq), 2.50 (bs, 2H, 2×OH), 2.24 (s, 3H, N*CH*$_3$), 2.12 (dq, 1H, $J_{5,6}$ 6.6 Hz, $J_{4,5}$ 1.1 Hz, H-5), 1.98 (dd, 1H, $J_{1ax,2}$ 10.7 Hz, H-1ax), 1.11 (d, 3H, H-6); compound **7b**: selected signals δ 4.56 (s, 2H, O*CH*$_2$Ph), 2.31 (s, 3H, N*CH*$_3$), 1.05 (d, 3H, $J_{5,6}$ 6.8 Hz, H-6); cluster of signals for both diastereoisomers: δ 7.37-7.27 (m, 10H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 50.33 MHz): compound **6b**: δ 138.3 (Ar-*C*), 76.3 (C-2), 75.5 (C-3), 73.4 (C-4), 72.2 (O*CH*$_2$Ph); 60.7 (C-5), 58.5 (C-1), 42.1 (N*CH*$_3$), 16.4 (C-6); compound **7b**: δ 138.1 (Ar-*C*), 75.8 (C-2), 71.8 (O*CH*$_2$Ph), 71.5 (C-3), 69.4 (C-4), 59.1 (C-5), 51.8 (C-1), 41.9 (N*CH*$_3$), 10.7 (C-6); cluster of signals for both diastereoisomers: δ 128.2-127.6 (Ar-*C*H). Anal. Calcd for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42; N, 5.57. Found: C, 66.89; H, 8.38; N, 5.54.

4.2.6. 2-*O*-benzyl-*N*-benzyl-1,5,6-trideoxy-1,5-imino-D-galactitol (6c) and 2-*O*-benzyl-*N*-benzyl-1,5,6-trideoxy-1,5-imino-L-altritol (7c).

A solution of **5α,β** (1.09 g, 4.30 mmol) was subjected to double reductive amination with $PhCH_2NH_3Cl$ (618 mg, 4.30 mmol) and $NaBH_3CN$ (541 mg, 8.61 mmol) in accordance to the general procedure (Method B). After 18 h, TLC analysis (EtOAc) showed the complete disappearance of the starting material and the formation of two spots (R_f 0.40 and 0.27). NMR analysis of the crude residue (350 mg) showed a mixture of azapyranoses **6c** and **7c** in a 70:30 ratio, measured on the relative intensities of the C-1 signals at δ 54.1 and 47.8, respectively. Purification of the crude product by flash chromatography on silica gel (96:4 CH_2Cl_2-^{i}PrOH + 0.1% Et_3N) afforded pure **6c** (565 mg, 40% yield) and pure **7c** (225 mg, 16% yield).

2-O-*benzyl*-N-*benzyl-1,5,6-trideoxy-1,5-imino-D-galactitol (**6c**)*. Crystalline solid; R_f 0.27 (EtOAc); mp 84-87 °C (from Et_2O); $[\alpha]_D$ -11.7 (*c* 1.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 7.21-7.36 (m, 10H, Ar-*H*), 4.57, 4.50 (AB system, 2H, $J_{A,B}$ 11.6 Hz, O*CH*$_2$Ph), 3.74, 3.22 (AB system, 2H, $J_{A,B}$ 13.5 Hz, N*CH*$_2$Ph), 3.61 (dd, 1H, $J_{3,4}$ 3.0 Hz, $J_{4,5}$ 1.4 Hz, H-4), 3.51 (ddd, 1H, $J_{1ax,2}$ 9.8 Hz, $J_{2,3}$ 9.1 Hz, $J_{1eq,2}$ 4.6 Hz, H-2), 3.43 (dd, 1H, H-3), 3.06 (dd, 1H, $J_{1ax,1eq}$ 11.3 Hz, H-1eq), 2.49 (dq, 1H, $J_{5,6}$ 6.5 Hz, H-5), 2.47 (bs, 2H, 2×OH), 1.83 (dd, 1H, H-1ax), 1.36 (d, 3H, H-6); ^{13}C NMR ($CDCl_3$, 50.33 MHz): δ 138.2, 137.9 (2×Ar-*C*), 128.7-126.9 (Ar-*C*H), 76.5 (C-2), 75.6 (C-3), 74.0 (C-4), 72.1 (O*CH*$_2$Ph), 58.6 (C-5), 56.4 (N*CH*$_2$Ph), 53.9 (C-1), 16.8 (C-6). Anal. Calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28. Found: C, 73.36; H, 7.68; N, 4.30.

2-O-*benzyl*-N-*benzyl-1,5,6-trideoxy-1,5-imino-L-altritol (**7c**)*. Clear syrup; R_f 0.40 (EtOAc); $[\alpha]_D$ +18.6 (*c* 1.16, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 7.38-7.21 (m, 10H, Ar-*H*), 4.65, 4.57 (AB system, 2H, $J_{A,B}$ 12.0 Hz, O*CH*$_2$Ph), 3.67 (m, 3H, H-2, H-3, H-4), 3.62 (s, 2H, N*CH*$_2$Ph), 2.49 (bs, 2H, 2×OH), 3.08 (dq, 1H, $J_{5,6}$ 6.9 Hz, $J_{4,5}$ 2.3 Hz, H-5), 2.79 (dd, 1H, $J_{1ax,1eq}$ 11.5 Hz, $J_{1eq,2}$ 5.3 Hz, H-1eq), 2.42 (dd, 1H, $J_{1ax,2}$ 9.8 Hz, H-1ax), 1.01 (d, 3H, H-6); δ ^{13}C NMR ($CDCl_3$, 50.33 MHz): δ 138.5, 138.4 (2×Ar-*C*), 128.8-126.9 (Ar-*C*H), 77.3 (C-2), 73.2 (C-3), 72.2 (O*CH*$_2$Ph), 71.6 (C-4), 57.9 (N*CH*$_2$Ph), 57.4 (C-5), 47.8 (C-1), 8.1 (C-6). Anal. Calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28. Found: C, 73.34; H, 7.67; N, 4.26.

4.2.7. 2-*O*-benzyl-*N*-benzydryl-1,5,6-trideoxy-1,5-imino-D-galactitol (6d) and 2-*O*-benzydryl-*N*-benzydryl-1,5,6-trideoxy-1,5-imino-L-altritol (7d).

The double reductive amination of **5α,β** (300 mg, 1.19 mmol) was performed with Ph_2CHNH_3Cl (261 mg, 1.19 mmol) and $NaBH_3CN$ (149.4 mg, 2.34 mmol) according to the general procedure (Method B). The reaction was complete after 18 h and TLC analysis (EtOAc) showed the complete disappearance of the starting material and the formation of a major spot (R_f 0.57). NMR analysis of the crude residue (405 mg) showed a mixture of azapyranoses **6d** and **7d** in a 45:55 ratio estimated on the relative intensities of the C-1 signals at δ 49.0 and 45.6 respectively. Several attempts to separate the components of the mixture through TLC gave negative result. Purification of the crude product by flash chromatography on silica gel (60:35:5 hexane-EtOAc-^{i}PrOH + 0.1% Et_3N) gave a mixture of pure **6d** and **7d** (312 mg, 64% yield) as a clear syrup; R_f 0.30 (60:35:5 hexane-EtOAc-^{i}PrOH). ^{1}H NMR ($CDCl_3$, 200.13 MHz) compound **6d**: δ 3.67 (dd, 1H, $J_{3,4}$ 3.3 Hz, $J_{4,5}$ 1.6 Hz, H-4), 3.62 (ddd, 1H, $J_{1ax,2}$ 10.0 Hz, $J_{2,3}$ 8.8 Hz, $J_{1eq,2}$ 4.6 Hz, H-2), 3.33 (dd, 1H, H-3), 3.05 (dd, 1H, $J_{1ax,1eq}$ 11.5 Hz, H-1eq), 2.53 (dq, 1H, $J_{5,6}$ 6.5 Hz, H-5), 1.77 (dd, 1H, H-1ax), 1.40 (d, 3H, H-6); compound **7d**: 3.67 (m, 3H, H-2, H-3, H-4), 3.20 (dq, 1H, $J_{5,6}$ 7.0 Hz, $J_{4,5}$ 1.1 Hz, H-5), 2.93 (dd, 1H, $J_{1ax,1eq}$ 11.7 Hz, $J_{1eq,2}$ 4.3 Hz, H-1eq), 2.27 (dd, 1H, $J_{1ax,2}$ 10.0 Hz, H-1ax), 0.96 (d, 3H, H-6); cluster of signals for both diastereoisomers: δ 7.43-7.08 (m, 30H, Ar-*H*), 4.75-4.40 (m, 6H, 2×O*CH*$_2$Ph, 2×*NCH*Ph$_2$); ^{13}C NMR ($CDCl_3$, 50.33 MHz) compound **6d**: δ 75.2 (C-2), 73.9 (C-3), 70.8 (C-4), 56.3 (C-5), 49.1 (C-1), 15.9 (C-6); compound **7d**: δ 76.9 (C-2), 73.4 (C-3), 71.9 (C-4), 54.8 (C-5), 45.7 (C-1), 7.6 (C-6); cluster of signals for both diastereoisomers: δ 143.2, 142.1, 141.5, 138.4, 138.1, 137.7 (6×Ar-*C*), 129.8-126.6 (Ar-*C*H), 72.0 (2×OCH_2Ph), 64.7 (2×$CHPh_2$). Anal. Calcd for $C_{26}H_{29}NO_3$: C, 77.39; H, 7.24; N, 3.47. Found: C, 77.36; H, 7.27; N, 3.49.

4.2.8. 2-*O*-benzyl-*N*-hydroxy-1,5,6-trideoxy-1,5-imino-D-galactitol (6e).

To a solution of **5α,β** (400 mg, 1.59 mmol, 40 mL of dry MeOH) a solution of $NH_2OH \cdot HCl$ (176 mg, 2.54 mmol, 30 mL of dry MeOH) and a solution of $NaBH_3CN$ (199 mg, 3.17 mmol, 34 mL of dry MeOH) were added and the reaction was conducted according to the general procedure (Method B). After 26 h, TLC analysis (8:2 EtOAc-MeOH) revealed the complete disappearance of the starting material and the formation of one spot (R_f 0.18). The ^{1}H NMR spectrum of the residue (426 mg) showed that the crude was mainly (ca 95%) constituted by azapyranose **6e** and purification of the crude product by flash chromatography on silica gel (95:5 EtOAc-*i*-PrOH + 0.1% Et_3N) afforded pure **6e** (224 mg, 56% yield) as a white solid; R_f 0.23 (95:5 EtOAc-^{i}PrOH); mp 115-117°C (chrom); $[\alpha]_D$ +17.8 (c 1.0, $CHCl_3$); ^{1}H NMR (CD_3CN-D_2O, 200.13 MHz): δ 7.39-7.27 (m, 5H, Ar-*H*), 4.63 (d, 2H, *CH*$_2$Ph), 3.68 (m, 1H, H-2, H-4), 3.39 (dd, 1H, $J_{2,3}$ 9.6 Hz, $J_{3,4}$ 3.4 Hz, H-3), 3.44 (dd, 1H, $J_{1ax,1eq}$ 10.4 Hz, $J_{1eq,2}$ 4.6 Hz, H-1eq), 2.43 (m, 1H, H-5), 2.29 (bdd, 1H, $J_{1ax,2}$ 10.1 Hz, H-1ax), 1.13 (d, 3H, $J_{5,6}$ 6.4 Hz, H-6);^{13}C NMR (CD_3CN-D_2O, 50.33 MHz): δ 139.7 (Ar-*C*), 129.2, 128.8, 128.5 (Ar-*C*H), 76.4 (C-2), 75.4 (C-3), 73.1 (O*CH*$_2$Ph), 73.0 (C-4), 64.9 (C-5), 61.1 (C-1), 15.7 (C-6); Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.60; H, 7.51; N, 5.50.

4.2.9. 2-*O*-benzyl-*N*-(1'-carbomethoxyethyl)-1,5,6-trideoxy-1,5-imino-D-galactitol (6f) and 2-*O*-benzydryl-*N*-(1'-carbomethoxyethyl)-1,5,6-trideoxy-1,5-imino-L-altritol (7f).

The double reductive amination of **5α,β** (500 mg, 1.98 mmol) was performed with Gly-OMe·HCl (249 mg, 1.98 mmol) and $NaBH_3CN$ (249 mg, 3.96 mmol) following the general procedure (Method B). After 20 h, TLC analysis (EtOAc) showed the complete disappearance of the starting material and the formation of two spots (R_f 0.24 and 0.19). The crude residue (537 mg), analyzed by NMR ($CDCl_3$), showed a mixture of azapyranoses **6f** and **7f** in a 70:30 ratio, measured on the relative intensities of the C-6 signals at δ 15.9 and 10.3 respectively. Purification of the crude product by flash chromatography on silica gel (EtOAc +0.1% of 30% aq NH_3 solution) gave pure **6f** (239 mg, 39% yield) and **7f** (104 mg, 17% yield).

2-O-benzyl-N-*(1'-carbomethoxyethyl)-1,5,6-trideoxy-1,5-imino-D-galactitol (**6f**).* Clear syrup, R_f 0.19 (EtOAc); $[\alpha]_D$ +31.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (CD_3CN-D_2O, 200.13 MHz): δ 7.36-7.26 (m, 5H, Ar-*H*), 4.63, 4.57 (AB system, 2H, $J_{A,B}$ 11.8 Hz, OC*H*$_2$Ph), 3.62 (s, 3H, OMe), 3.57 (ddd, 1H, $J_{1ax,2}$ 10.5 Hz, $J_{2,3}$ 9.4 Hz, $J_{1eq,2}$ 5.0 Hz, H-2), 3.53 (dd, 1H, $J_{3,4}$ 3.3

Hz, $J_{4,5}$ 1.5 Hz, H-4), 3.39, 3.31 (AB system, 2H, $J_{A,B}$ 17.3 Hz, H-2'), 3.30 (dd, 1H, H-3), 3.03 (dd, 1H, $J_{1ax,1eq}$ 11.1 Hz, H-1eq), 2.73 (dq, 1H, $J_{5,6}$ 6.6 Hz, H-5), 2.32 (dd, 1H, H-1ax), 1.06 (d, 3H, H-6); ^{13}C NMR (CD_3CN-D_2O, 50.33 MHz): δ 173.1 (C=O), 139.9 (Ar-*C*), 129.2, 128.7, 128.4 (Ar-*C*H), 77.0 (C-2), 76.1 (C-3), 74.3 (C-4), 72.8 (O*CH*$_2$Ph), 57.8 (C-5), 55.9 (C-2'), 54.2 (C-1), 52.1 (OMe); 16.4 (C-6); Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.53. Found: C, 62.07; H, 7.45; N, 4.51.

2-O-benzyl-N-*(1'-carbomethoxyethyl)-1,5,6-trideoxy-1,5-imino-*L*-altritol (**7f**)***.*** Clear syrup, R_f 0.24 (EtOAc); $[\alpha]_D$ +27.8 (*c* 1.1, $CHCl_3$); ^{1}H NMR (CD_3CN-D_2O, 200.13 MHz): δ 7.36-7.26 (m, 5H, Ar-*H*), 4.61, 4.53 (AB system, 2H, $J_{A,B}$ 11.9 Hz, O*CH*$_2$Ph), 3.63 (s, 3H, OMe), 3.71 (dd, 1H, $J_{2,3}$ 6.2 Hz, $J_{3,4}$ 3.2 Hz,H-3), 3.58 (ddd, 1H, $J_{1ax,2}$ 6.0 Hz, $J_{1eq,2}$ 3.5 Hz, H-2), 3.46 (dd, 1H, $J_{4,5}$ 6.5 Hz, H-4), 3.39, 3.27 (AB system, 2H, $J_{A,B}$ 17.1 Hz, H-2'); 2.89 (dq, 1H, $J_{5,6}$ 6.7 Hz, H-5), 2.84 (dd, 1H, $J_{1ax,1eq}$ 12.2 Hz, H-1eq), 2.57 (dd, 1H, H-1ax), 1.00 (d, 3H, H-6); ^{13}C NMR (CD_3CN-D_2O, 50.33 MHz): δ 172.6 (C=O), 140.0 (Ar-*C*), 129.2, 128.6, 128.3 (Ar-*C*H), 77.4 (C-2), 73.2 (C-3), 71.8 (O*CH*$_2$Ph), 70.7 (C-4), 55.1 (C-2'), 57.1 (C-5), 51.8 (OMe), 50.2 (C-1), 13.1 (C-6). Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.53. Found: C, 62.08; H, 7.52; N, 4.56.

4.2.10. 2-*O*-benzyl-*N*-[(2'R)-1'-carbomethoxy-2'-benzylethyl]-1,5,6-trideoxy-1,5-imino-D-galactitol (6g) and 2-*O*-benzydryl- *N*-[(2'R)-1'-carbomethoxy-2'-benzylethyl]-1,5,6-trideoxy-1,5-imino-L-altritol (7g).

A solution of **5α,β** (500 mg, 1.98 mmol) was treated with D-Phe-OMe·HCl (427 mg, 1.98 mmol) and $NaBH_3CN$ (249 mg, 3.96 mmol) according to the general procedure (Method B). The reaction was complete in 24 h and TLC analysis (3:7 hexane-EtOAc) revealed the complete disappearance of the starting material and the formation of two spots (R_f 0.28 and 0.16). NMR analysis of the crude product (756 mg) showed a mixture of azapyranoses **6g** and **7g** in a 25:75 ratio estimated on the relative intensities of the C-6 signals at δ 16.7 and 7.1 respectively. Purification of the crude product by flash chromatography on silica gel (1:1 hexane-EtOAc + 0.1% Et_3N) gave pure **6g** (110 mg, 14% yield) and **7g** (389 mg, 49% yield).

2-O-benzyl-N-*[(2'R)-1'-carbomethoxy-2'-benzylethyl]-1,5,6-trideoxy-1,5-imino-D-galactitol (**6g**).* Clear syrup; R_f 0.16 (3:7 hexane-EtOAc); $[\alpha]_D$ +37.7 (*c* 1.1, $CHCl_3$); ^{1}H NMR (CD_3CN-D_2O, 200.13 MHz): δ 7.40-7.19 (m, 10H, Ar-H), 4.64 (s, 2H, *OCH*$_2$Ph), 3.74 (dd, 1H, $J_{2',a}$ 5.1 Hz, $J_{2',b}$ 9.4 Hz, H-2'), 3.56 (s, 3H, OMe), 3.51 (dd, 1H, $J_{3,4}$ 3.4 Hz, $J_{4,5}$ 1.4 Hz,

H-4), 3.49 (ddd, 1H, $J_{1ax,2}$ 9.8 Hz, $J_{2,3}$ 8.8 Hz, $J_{1eq,2}$ 4.9 Hz, H-2), 3.30 (dd, 1H, H-3), 3.29 (dd, 1H, $J_{1ax,1eq}$ 11.3 Hz, H-1eq), 3.00 (dd, 1H, $J_{a,b}$ 13.4 Hz, CH_b-Ph), 2.83 (dd, 1H, CH_a-Ph), 2.65 (dq, 1H, $J_{5,6}$ 6.6 Hz, H-5), 2.26 (dd, 1H, H-1ax), 1.13 (d, 3H, H-6); ^{13}C NMR (CD_3CN-D_2O, 50.33 MHz): δ 173.6 (C=O), 140.0, 139.8 (2×Ar-*C*), 130.1-127.2 (Ar-*C*H), 77.6 (C-2), 76.3 (C-3), 74.6 (C-4), 72.6 (O*CH*$_2$Ph), 64.0 (C-2'), 57.6 (C-5), 52.3 (OMe), 50.6 (C-1), 31.8 (*N*CH_2Ph), 16.7 (C-6). Anal. Calcd for $C_{23}H_{29}NO_5$: C, 69.15; H, 7.32; N, 3.51. Found: C, 69.11; H, 7.30; N, 3.54.

2-O-benzyl-N-*[(2'R)-1'-carbomethoxy-2'-benzylethyl]-1,5,6-trideoxy-1,5-imino-*L*-altritol* ***(7g)*****.** Clear syrup; R_f 0.28 (3:7 hexane-EtOAc); $[\alpha]_D$ +70.7 (*c* 1.2, $CHCl_3$). ^{1}H NMR (CD_3CN-D_2O, 200.13 MHz): δ 7.38-7.16 (m, 10H, Ar-H), 4.63, 4.54 (AB system, 2H, $J_{A,B}$ 11.9 Hz, O*CH*$_2$Ph), 3.81 (dd, 1H, $J_{2',a}$ 7.2 Hz, $J_{2',b}$ 7.7 Hz, H-2'), 3.78 (dd, 1H, $J_{4,5}$ 6.0 Hz, $J_{3,4}$ 3.1 Hz, H-4), 3.58 (s, 3H, OMe), 3.52 (ddd, 1H, $J_{2,3}$ 7.9 Hz, $J_{1ax,2}$ 4.6 Hz, $J_{1eq,2}$ 3.0 Hz, H-2), 3.27 (dd, 1H, H-3), 3.05 (dd, 1H, $J_{a,b}$ 13.6 Hz, CH_b-Ph), 2.99 (dd, 1H, $J_{1ax,1eq}$ 12.7 Hz, H-1eq), 2.85 (dd, 1H, CH_a-Ph), 2.78 (dq, 1H, $J_{5,6}$ 6.4 Hz, H-5), 2.73 (dd, 1H, H-1ax), 1.01 (d, 3H, H-6); ^{13}C NMR (CD_3CN-D_2O, 50.33 MHz): δ 173.3 (C=O), 139.9, 139.8 (2×Ar-*C*), 130.3-127.1 (Ar-*C*H), 77.5 (C-2), 73.2 (C-3), 71.8 (O*CH*$_2$Ph), 70.5 (C-4), 64.2 (C-2'), 56.7 (C-5), 51.6 (OMe), 45.1 (C-1), 36.8 (*N*CH_2Ph), 7.1 (C-6). Anal. Calcd for $C_{23}H_{29}NO_5$: C, 69.15; H, 7.32; N, 3.51. Found: C, 69.12; H, 7.29; N, 3.48.

4.2.11. 2-*O*-benzyl-*N*-[(2'S)-1'-carbomethoxy-2'-benzylethyl]-1,5,6-trideoxy-1,5-imino-D-galactitol (6h) and 2-*O*-benzydryl-*N*-[(2'S)-1'-carbomethoxy-2'-benzylethyl]-1,5,6-trideoxy-1,5-imino-L-altritol (7h).

A solution of **5α,β** (400 mg, 1.59 mmol) was treated with L-Phe-OMe·HCl (342 mg, 1.59 mmol) and $NaBH_3CN$ (199 mg, 3.17 mmol) and the reaction was performed according to the general procedure (Method B). After 24 h, TLC analysis (2:8 hexane-EtOAc) showed the complete disappearance of the starting material and the formation of one spot (R_f 0.39). The NMR spectrum of residue (665 mg) showed a mixture of azapyranoses **6h** and **7h** in a 65:35 ratio measured on the relative intensities of the C-6 signals at δ 16.3 and 11.5 respectively. Several attempts to separate the components of the mixture through TLC gave negative result. Purification of the crude product by flash chromatography on silica gel (98:2 $CHCl_3$-^{i}PrOH + 0.1% Et_3N) gave a mixture of pure **6h** and **7h** (370 mg, 58% yield) as a clear syrup; R_f 0.39 (2:8 hexane-EtOAc); ^{1}H NMR (CD_3CN, 200.13 MHz,): Compound **6h**: δ 4.68, 4.57 (AB system, 2H, $J_{A,B}$ 12.2 Hz, O*CH*$_2$Ph), 3.70 (dd, 1H, $J_{2',a}$ 6.3 Hz, $J_{2',b}$ 9.7 Hz, H-2'), 3.64 (s, 3H, OMe), 3.50 (dd, 1H, $J_{2,3}$ 8.3 Hz, $J_{3,4}$ 3.1 Hz, H-3), 3.35

(ddd, 1H, $J_{1ax,2}$ 9.2 Hz, $J_{1eq,2}$ 4.1 Hz, H-2), 3.32 (dd, 1H, $J_{4,5}$ 1.0 Hz, H-4), 3.24 (dd, 1H, $J_{1ax,1eq}$ 12.4 Hz, H-1eq), 2.75 (dd, 1H, $J_{a,b}$ 13.7 Hz, CH_b-Ph), 2.70 (dd, 1H, CH_a-Ph), 2.64 (dq, 1H, $J_{5,6}$ 6.4 Hz, H-5), 2.56 (dd, 1H, H-1ax), 0.93 (d, 3H, H-6); compound **7h**: δ 4.70, 4.56 (AB system, 2H, $J_{A,B}$ 12.0 Hz, OCH_2Ph), 3.61 (dd, 1H, $J_{2',a}$ 4.6 Hz, $J_{2',b}$ 8.4 Hz, H-2'), 3.60 (dd, 1H, $J_{a,b}$ 13.4 Hz, CH_b-Ph), 3.53 (s, 3H, OMe), 3.12 (dd, 1H, CH_a-Ph); 3.25 (m, 4H, H-1eq, H-2, H-3, H-4), 2.88 (bq, 1H, $J_{5,6}$ 6.8 Hz, H-5), 1.83 (dd, 1H, $J_{1ax,1eq}$ 11.3 Hz, $J_{1ax,2}$ 4.8 Hz, H-1ax), 0.97 (d, 3H, H-6); cluster of signals for both diastereoisomers: δ 7.44-7.08 (m, 20H, Ar-*H*); ^{13}C NMR (CD_3CN,, 50.33 MHz): compound **6h**: δ 172.8 (C=O), 140.1, 139.8 (2×Ar-*C*), 77.2 (C-2), 76.7 (C-3), 74.9 (C-4), 72.8 (OCH_2Ph), 61.0 (C-2'), 58.6 (C-5), 51.8 (OMe), 49.1 (C-1), 36.0 (*N*CH_2Ph), 16.3 (C-6); compound **7h**: δ 174.3 (C=O), 140.0, 139.4 (2×Ar-*C*), 77.5 (C-2), 74.1 (C-3), 72.3 (OCH_2Ph), 71.9 (C-4), 66.9 (C-2'), 61.3 (C-5), 52.0 (OMe), 43.0 (C-1), 36.2 (*N*CH_2Ph), 11.5 (C-6); cluster of signals for both diastereoisomers: δ 129.9-127.1 (Ar-*C*H). Anal. Calcd for $C_{23}H_{29}NO_5$: C, 69.15; H, 7.32; N, 3.51. Found: C, 69.17; H, 7.35; N, 3.53.

4.2.12. 3,4-di-*O*-Acetyl-2-*O*-benzyl-*N*-benzyl-1,5,6-trideoxy-1,5-imino-D-galactitol (8).

Routine acetylation of **6c** (104 mg, 0.32 mmol) and purification of the crude product by flash chromatography on silica gel (4:6 hexane-EtOAc + 0.1% Et_3N) gave pure **8** (104 mg, 79% yield) as a clear syrup; R_f 0.42 (4:6 hexane-EtOAc); $[\alpha]_D$= +7.1 (c 0.80, $CHCl_3$); ^{1}H NMR (CD_3CN, 200.13 MHz,): δ 7.38-7.19 (m, 10H, Ar-H), 5.25 (dd, 1H, $J_{3,4}$ 3.6 Hz, $J_{4,5}$ 2.1 Hz, H-4), 4.76 (dd, 1H, $J_{2,3}$ 9.6 Hz, H-3), 4.48 (s, 2H, OCH_2Ph), 3.83, 3.27 (sistema AB, 2H, $J_{A,B}$ 13.7 Hz, NCH_2Ph), 3.73 (ddd, 1H, $J_{1ax,2}$ 9.6 Hz, $J_{1eq,2}$ 4.7 Hz, H-2), 3.04 (dd, 1H, $J_{1ax,1eq}$ 11.7 Hz, H-1eq), 2.71 (dq, 1H, $J_{5,6}$ 6.5 Hz, H-5), 2.08, 1.93 (2s, each 3H, 2×CH_3CO), 2.01 (dd, 1H, H-1ax), 1.13 (d, 3H, H-6); ^{13}C NMR (CD_3CN, 50.33 MHz): δ 171.2, 171.1 (2×C=O), 139.8, 139.7 (2×Ar-*C*), 129.8-127.9 (Ar-*C*H), 75.7 (C-2), 74.0 (C-3), 73.2 (C-4), 72.8 (OCH_2Ph), 57.7 (C-5), 57.1 (NCH_2Ph), 54.6 (C-1), 21.0, 20.9 (2×CH_3CO), 15.9 (C-6). Anal. Calcd for $C_{24}H_{29}NO_5$: C, 70.05; H, 7.10; N, 3.40. Found: C, 69.98; H, 7.06; N, 3.36.

4.2.13. 3,4-di-*O*-Acetyl-2-*O*-benzyl-*N*-benzyl-1,5,6-trideoxy-1,5-imino-L- altritol (9).

Routine acetylation of **7c** (94 mg, 0.29 mmol) and purification of the crude product by flash chromatography on silica gel (4:6 hexane-EtOAc + 0.1% Et_3N) gave pure **9** (95 mg, 77% yield) as a clear syrup; R_f 0.50 (4:6 hexane-EtOAc); $[\alpha]_D$= +32.5 (c 0.75, $CHCl_3$); ^{1}H NMR (CD_3CN, 200.13 MHz,): 7.38-7.23 (m, 10H, Ar-H), 5.10 (dd, 1H, $J_{2,3}$ 7.5 Hz, $J_{3,4}$ 3.4 Hz, H-3), 3.95 (dd, 1H, $J_{4,5}$ 5.2 Hz, H-4), 4.74 (ddd, 1H, $J_{1ax,2}$ 6.7 Hz, $J_{1eq,2}$ 4.9 Hz, H-2), 4.51,

4.43 (AB system, 2H, $J_{A,B}$ 11.8 Hz, O*C*H_2Ph), 3.85, 3.49 (AB system, 2H, $J_{A,B}$ 13.8 Hz, NCH_2Ph), 2.93 (dq, 1H, $J_{5,6}$ 6.7 Hz, H-5), 2.75 (dd, 1H, $J_{1ax,1eq}$ 12.4 Hz, H-1eq), 2.67 (dd, 1H, H-1ax), 2.03, 1.99 (2s, each 3H, 2×CH_3CO), 1.01 (d, 3H, H-6); ^{13}C NMR (CD_3CN, 50.33 MHz): δ 171.1 (2×C=O), 140.4, 139.6 (2×Ar-*C*), 129.8-127.9 (Ar-*C*H), 74.5 (C-2), 73.8 (C-3), 72.2 (O*C*H_2Ph), 71.3 (C-4), 58.0 (*N*CH_2Ph), 55.9 (C-5), 49.8 (C-1), 21.1 (2×*C*H_3CO), 11.3 (C-6). Anal. Calcd for $C_{24}H_{29}NO_5$: C, 70.05; H, 7.10; N, 3.40. Found: C, 69.99; H, 7.07; N, 3.37.

4.2.14. 3,4-di-*O*-Acetyl-2-*O*-benzyl-*N*-benzydryl-1,5,6-trideoxy-1,5-imino-D-galactitol (10) and 3,4-di-*O*-acetyl-2-*O*-benzydryl-*N*-benzydryl-1,5,6-trideoxy-1,5-imino-L-altritol (11).

Routine acetylation of **6d** and **7d** (45:55 mixture, 150 mg, 0.37 mmol) and purification of the crude product by flash chromatography on silica gel (1:9 hexane-EtOAc + 0.1% Et_3N) gave pure **10** and **11** (164 mg, 91% yield) as a 45:55 mixture estimated on the relative intensities of two separated signals (ddd) attributed to H-2 at δ 3.61 and 3.80 respectively. The mixture of title compounds is a clear syrup; R_f 0.66 (EtOAc); ^{1}H NMR ($CDCl_3$, 200.13 MHz,): compound **10**: δ 5.25 (bt, 1H, $J_{4,5} = J_{3,4}$ 3.4 Hz, H-4), 4.86 (dd, 1H, $J_{2,3}$ 7.4 Hz, H-3), 3.61 (ddd, 1H, $J_{1ax,2}$ 7.4 Hz, $J_{1eq,2}$ 3.6 Hz, H-2), 2.80 (m, 2H, H-1eq, H-5), 2.20 (m, 1H, H-1ax), 1.08 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6); compound **11**: δ 5.06 (dd, 1H, $J_{2,3}$ 10.0 Hz, $J_{3,4}$ 3.6 Hz, H-3), 4.99 (dd, 1H, $J_{4,5}$ 2.4 Hz, H-4), 3.80 (ddd, 1H, $J_{1ax,2}$ 10.0 Hz, $J_{1eq,2}$ 5.1 Hz, H-2), 3.10 (bq, 1H, $J_{5,6}$ 7.0 Hz, H-5), 2.80 (dd, 1H, $J_{1ax,1eq}$ 12.1 Hz, H-1eq), 2.35 (dd, 1H, H-1ax), 0.96 (d, 3H, H-6); clusters of signals for both diastereoisomers δ 7.44-7.08 (m, 2×15H, Ar-H), 4.50-4.30 (m, 2×3H, O*C*H_2Ph, N-*C*HPh_2), 2.32, 2.16, 1.99, 1.98 (4s, each 3H, 4x*C*H_3CO); ^{13}C NMR (CD_3CN, 50.33 MHz): compound **10**: δ 74.2 (C-2), 73.1 (C-3), 71.5 (C-4), 53.1 (C-5), 46.9 (C-1), 12.3 (C-6); compound **11**: δ 73.9 (C-2), 71.8 (C-3), 70.4 (C-4), 52.7 (C-5), 45.9 (C-1), 8.3 (C-6); clusters of signals for both diastereoisomers δ 170.3, 170.1, 170.0, 169.9 (4×CH_3*CO*), 143.2, 142.6, 142.0, 138.6, 138.3, 138.2 (6×Ar-*C*), 129.1-125.1 (Ar-*C*H), 72.0, 71.7 (2×O*C*H_2Ph); 66.7 (2×NCHPh_2), 20.9-20.8 (4×*C*H_3CO). Anal. Calcd for $C_{30}H_{33}NO_5$: C, 73.90; H, 6.82; N, 2.87. Found: C, 73.93; H, 6.85; N, 2.90.

4.2.15. 3,4-di-*O*-Acetyl-2-*O*-benzyl-*N*-[(2'S)-1'-carbomethoxy-2'-benzylethyl]-1,5,6-trideoxy-1,5-imino-D-galactitol (12) and 3,4-di-*O*-Acetyl-2-*O*-benzyl-*N*-[(2'S)-1'-carbomethoxy-2'-benzylethyl]-1,5,6-trideoxy-1,5-imino-L-altritol (13).

Routine acetylation of **6h** and **7h** (65:35 mixture, 172 mg, 0.43 mmol), and purification of the crude product by flash chromatography on silica gel (99:1 $CHCl_3$-iPrOH+ 0.1% Et_3N) gave pure **12** and **13** (186 mg, 88% yield) as a 65:55 mixture measured on the relative intensities two separated signals (d) attributed to H-6 at δ 0.64 and 0.83 respectively. The mixture of title compounds is a clear syrup; R_f 0.38 (98:2 $CHCl_3$-^{i}PrOH); ^{1}H NMR (1:1 CD_3CN-C_6D_6, 200.13 MHz): compound **12** δ 4.84 (bt, 1H, $J_{3,4}$ 3.7 Hz $J_{4,5}$ 1.6 Hz, H-4), 4.50 (dd, 1H, $J_{2,3}$ 9.8 Hz, H-3), 4.46, 4.36 (AB system, 2H, $J_{A,B}$ 12.0 Hz, O*CH*$_2$Ph), 3.55 (dd, 1H, $J_{2',a}$ 6.0 Hz, $J_{2',b}$ 9.6 Hz, H-2'), 3.44 (s, 3H, OMe), 3.33 (ddd, 1H, $J_{1ax,2}$ 10.2 Hz, $J_{1eq,2}$ 4.9 Hz, H-2), 3.16 (dd, 1H, $J_{1ax,1eq}$ 11.5 Hz, H-1eq), 2.82 (dd, 1H, $J_{a,b}$ 14.0 Hz, C*H*$_b$-Ph), 2.70(dq, 1H, $J_{5,6}$ 6.5 Hz, H-5); 2.64 (dd, 1H, C*H*$_a$-Ph), 1.91 (dd, 1H, H-1ax), 1.71, 1.65 (2s, each 3H, 2×*CH*$_3$CO), 0.64 (d, 3H, H-6); compound **13**: δ 4.78 (dd, 1H, $J_{2,3}$ 8.7 Hz, $J_{3,4}$ 3.4 Hz, H-3), 4.60 (dd, 1H, $J_{4,5}$ 3.6 Hz, H-4), 4.43, 4.32 (AB system, 2H, $J_{A,B}$ 11.9 Hz, O*CH*$_2$Ph), 3.46 (m, 1H, H-2'), 3.38 (s, 3H, OMe), 3.26 (ddd, 1H, $J_{1ax,2}$ 4.2 Hz, $J_{1eq,2}$ 4.8 Hz, H-2), 3.10 (m, 1H, C*H*$_b$-Ph), 3.05 (dd, 1H, $J_{1ax,1eq}$ 12.7 Hz, H-1eq), 2.85 (bq, 1H, $J_{5,6}$ 6.9 Hz, H-5), 2.76 (dd, 1H, $J_{a,b}$ 14.2 Hz, $J_{2',a}$ 6.9 C*H*$_a$-Ph), 2.70 (dd, 1H, H-1ax), 1.75, 1.60 (2s, each 3H, 2×*CH*$_3$CO), 0.83 (d, 3H, H-6); cluster of signals for both diastereoisomers: δ 7.38-6.94 (m, 10H, 2×Ar-H); ^{13}C NMR (1:1 CD_3CN-C_6D_6, 50.33 MHz): Compound **12**: δ 172.8, 170.9 (2×C=O), 75.8 (C-2), 74.2 (C-3), 73.0 (C-4), 72.8 (O*C*H$_2$Ph), 61.4 (C-2'), 56.5 (C-5), 51.7 (OMe), 49.2 (C-1), 35.8 (N*C*H$_2$Ph), 15.7 (C-6); compound **13**: δ 174.5, 171.0 (2×C=O), 74.5 (C-2), 73.6 (C-3), 72.3 (O*CH*$_2$Ph), 71.9 (C-4), 66.5 (C-2'), 58.5 (C-5), 52.0 (OMe), 43.8 (C-1), 36.1 (*N*CH$_2$Ph), 11.8 (C-6); cluster of signals for both diastereoisomers: δ 139.7-139.3 (Ar-*C*), 130.3-126.9 (Ar-*C*H), 21.1-20.7 (*C*H$_3$CO). Anal. Calcd for $C_{27}H_{33}NO_7$: C, 67.06; H, 6.88; N, 2.90. Found: C, 67.10; H, 6.91; N, 2.88.

4.2.16. 1,5,6-trideoxy-1,5-imino-D-galactitol hydrochloride (14).

A solution of **6c** (393 mg, 1.2 mmol) in MeOH (15.0 mL) was treated with 1% methanolic HCl (pH 2) and 10% Pd on charcoal (125 mg). The suspension was stirred at room temperature under an H_2 atmosphere until TLC analysis (7:3 EtOAc-MeOH) showed the complete disappearance of the starting material (24 h). The mixture was filtered over Celite, washed with MeOH and the solution concentrated under diminished pressure to give a crude solid (209 mg, 95%) constituted (NMR) exclusively by **14**. Trituration of the crude residue with EtOH afforded pure **14** as a white foam; $[\alpha]_D$ +29.8 (*c* 0.9, MeOH); lit. [36] $[\alpha]_D$ +31 (*c* 1.0, MeOH); NMR data (^{1}H and ^{13}C) agreed with those reported in the literature [36].

4.2.17. 1,5,6-trideoxy-1,5-imino-L-altritol hydrochloride (15).

A sample of **7c** (250 mg, 0.76 mmol) was treated under the same conditions described above for **14**, giving a crude solid (136 mg, 97%) constituted (NMR) exclusively by the title compound. Trituration of crude residue (EtOH) afforded **15** as a white foam; $[\alpha]_D$ -8.8 (*c* 0.75, MeOH); lit. [36] $[\alpha]_D$ -10 (*c* 1.0, MeOH); lit. [37] $[\alpha]_D$ -2 (*c* 1.0, MeOH); NMR data (^{1}H and ^{13}C) agreed with those reported in the literature [36, 37].

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