JOC Article

A General Strategy for the Practical Synthesis of Nojirimycin *C*-Glycosides and Analogues. Extension to the First Reported Example of an Iminosugar 1-Phosphonate

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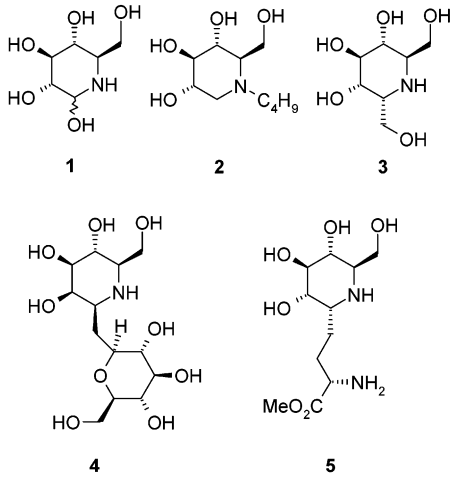
An efficient and versatile strategy for the synthesis of nojirimycin *C*-glycosides and related compounds with full stereocontrol is reported. The key steps of the process are the addition of organometallic reagents onto an L-sorbose-derived imine (**13**) followed by an internal reductive amination. The addition step, which controls the α- vs *β*-configuration at the pseudoanomeric center in the final product, is highly diastereoselective (*re*-face addition), and the stereoselectivity can be effectively inverted by adding an external monodentate Lewis acid (*si*-face addition). The complete synthesis could be achieved in 10 steps only from commercially available 2,3;4,6-di-*O*-isopropylidene-α-L-sorbofuranose and provided α- or *β*-1-*C*-substituted 1-deoxynojirimycin derivatives in 27−52% overall yield. The strategy was successfully extended to the first example of an iminosugar 1-phosphonate. The methodology provides access to a wide range of biologically relevant glycoconjugate mimetics in which the glycosidic function is replaced by an imino-*C*-glycosidic linkage.

Introduction

Since the discovery of nojirimycin **1**[1] as the first glucose mimetic with nitrogen instead of the ring oxygen (Chart 1), the spectacular development of iminosugars, prompted primarily by their properties as glycosidase inhibitors,[2−4] has opened a dynamic research field at the interface between glycobiology and organic chemistry. In addition, the scope of biological activities has been extended in recent years to the inhibition of glycosyltransferases,[5] of nucleoside[6] and glycogen[7] phosphorylases, and of sugar nucleotide mutase (UDP-Gal*p* mutase).[8] These remarkable properties promise a new generation of iminosugar-based medicines in a wide range of diseases[3,9] such as diabetes,[10] viral infections,[11] and tumor metastasis.[12] New

CHART 1



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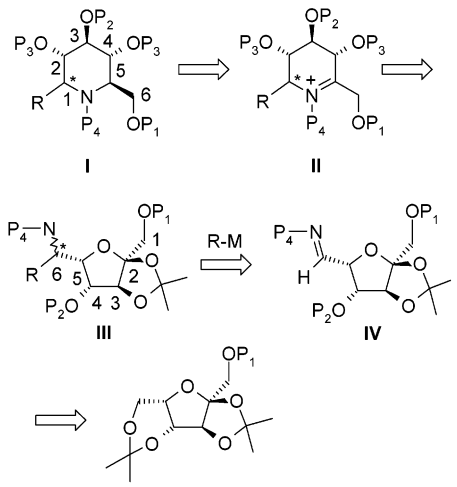
therapeutic applications are being uncovered. For example, *N*-butyl-1-deoxynojirimycin **2** (Chart 1) has been engaged recently in a clinical trial as a potential therapy for Gaucher disease, a severe lysosomal storage disorder.[13−15] The first promising results obtained have warranted further exploration of *N*-alkyliminosugars.[16]

Considering the high potential of azaglycoside mimetics as modified biological substrates, the design of a general and efficient access to iminosugar *C*-glycosides appears to be a major issue in bioorganic and medicinal chemistry. As stable analogues of azapyranosides, iminosugar *C*-glycosides have attracted much attention since the first synthesis[17] and isolation[18] of α-homonojirimycin **3**, the simplest example of this class of compounds. A diversity-oriented synthesis of iminosugar *C*-glycosides would facilitate the exploration of new biological targets, the finding of more potent/selective inhibitors, and the elucidation of carbohydrate-processing enzyme mechanisms by probing further their binding specificities.[19] In addition, from a chemical point of view, properly protected and functionalized iminosugar intermediates could be particularly useful as building blocks for the synthesis of more complex targets such as glycosyltransferase inhibitors (i.e., unreactive sugar nucleotide or bisubstrate analogues)[5] and oligosaccharide or glycoprotein mimetics (see, for example, **4**[20] and **5**,[21] Chart 1). Despite a large amount of synthetic effort in this area,[22] there is still a need for an efficient and general methodology to iminosugar *C*-glycosides of predictable configuration from simple precursors.

In this context and as part of our continuing studies on azaglycoside mimics,[23] we have designed a versatile synthetic strategy for the preparation of various types of iminosugar *C*-glycosides from L-sorbose based on the stereoselective addition of organometallic reagents onto an advanced imine intermediate. In a preliminary study,[24] this approach was partially validated with the preparation of two protected analogues of nojirimycin α-*C*-glycosides. Herein, we wish to report the generalization of this strategy to the stereocontrolled and practical synthesis of various α- and *β*-1-*C*-substituted-1-deoxynojirimycins and protected analogues. Extension of the methodology to a phosphorus nucleophile led to the synthesis of the first reported example of an iminosugar 1-phosphonate.

SCHEME 1



Synthetic Design. Besides the highly oxygenated piperidine structure of our target **I** and its five contiguous stereogenic centers, the main challenge of our synthetic strategy lies in its generality (Scheme 1). To generate diversity from advanced intermediates, we concentrated on three directions: the aglycon part (R), the control of the α/*β* configuration at the pseudoanomeric center, and the rapid access to other series: D-allo, D-galacto, D-manno, and L-ido.

Our retrosynthetic analysis takes advantage of the chirality of L-sorbose, which provides three stereogenic centers (C2, C3, and C4) of our target **I** and secures the stereocontrol of the addition reactions.[25] The key step of our synthetic strategy is the diastereoselective chain extension of imine **IV**. At this stage, the careful choice of reaction conditions can give selectively one or the other of two possible epimers at C6 in **III**, i.e., the precursors of the α- or *β*-epimer of imino-*C*-glycoside **I**. In addition, structural diversity may be introduced at the "anomeric" position by using the wide library of organometallic

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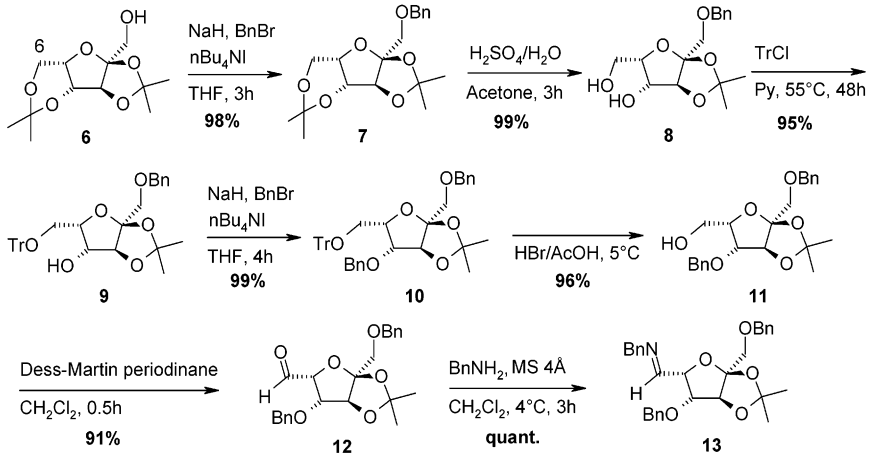
SCHEME 2



nucleophiles available. This point is particularly significant if one wants to explore the affinity of the aglycon binding site within a range of glycosidases in order to increase the selectivity of potential inhibitors. The last steps of the synthetic plan consisted of generating the final iminosugar *C*-glycosidic structure **I** by way of the intramolecular reductive amination of the latent keto function of the aminosorbofuranose derivative, a reaction that was expected to be highly stereoselective and to give the desired epimer in the D-series.[26] Finally, an orthogonal protecting group strategy was designed to facilitate the differentiation of the sugar hydroxyl groups, notably at C3, thus opening the way to oligosaccharide analogues or to iminosugars of other configurations by controlled epimerization of one of the OH group (see Scheme 1). The strategy was first tested for the stereocontrolled synthesis of α- and *β*-1-*C*-substituted-1-deoxynojirimycin **I**.

Results and Discussion

Preparation of Imine 13. As our approach required an easy access to multigram quantities of imine **13**, the first goal of our synthesis was the efficient preparation of this key intermediate from commercially available 2,3;4,6-di-*O*-isopropylidene-α-L-sorbofuranose **6**.[27] We followed a protecting group strategy to isolate and then oxidize the hydroxyl group at C6 (Scheme 2). The synthesis began with the benzylation of the primary alcohol at C1, followed by the selective deprotection of the less stable isopropylidene acetal under aqueous acidic conditions, in the presence of acetone, to afford the diol **8**[28] in 97% yield from **6**. Benzylation of the secondary hydroxyl group was performed by way of the temporary protection of the primary hydroxyl group of **8** as a trityl ether, benzylation of the secondary OH and cleavage of the trityl group using HBr in glacial acetic acid. This three-step procedure provided the primary alcohol **11** in 90% yield. The aldehyde **12** was then cleanly generated in 91% yield using Dess−Martin periodinane in dichloromethane at room temperature.[29] This reaction was readily scaled-up for the preparation of **12** in 10 g quantities. On the contrary, standard PCC oxidation of **11** was found to be less efficient (85% yield)[24] and less reproducible on a multigram scale. Finally, condensation of **12** with benzylamine in dichloromethane in the presence of molecular sieves (4 Å)[30] afforded the imine **13** in quantitative yield, as judged by proton NMR spectroscopy. In summary, the advanced intermediate **13** was efficiently prepared on a multigram scale from commercially available 2,3;4,6-di-*O*-isopropylidene-α-L-sorbofuranose in seven steps and 80% overall yield (Scheme 2).

Stereocontrolled Addition to Imine 13. With the desired imine **13** in hand, the addition of organometallic nucleophiles to the C=N bond[31] was first investigated without Lewis acid (Table 1, entries 1−5). The allyl- and vinylmagnesium bromides were chosen because of the synthetic potential offered by the C=C bond at a later stage of the synthesis. The reaction was found to be highly diastereoselective with organolithium as well as organomagnesium reagents. In a typical experimental procedure, a solution of 3 equiv of the organometallic reagent in ether was added dropwise to a cooled solution (−78 or 0 °C) of the *N*-benzylimine **13** in ether. The reaction mixture was slowly warmed to 0 °C (for RLi) or to room temperature (for RMgBr) and stirred for a few hours. In each case, ^{1}H NMR analysis of the crude product after workup revealed the presence of a single diastereoisomer with the exception of vinylmagnesium bromide (de = 90%, Table 1, entry 3). Purification by flash chromatography afforded amines **14** in good yields (Table 1, entries 1−5). The absolute configuration of the newly created stereocenter was unambiguously established to be *R* at the stage of cyclic products **16** and **17**. The high stereoselectivity of the addition of the organometallic species to the *re* face of imine **13** can be rationalized by the chelated intermediate **A** involving as ligands the nitrogen atom of the *N*-benzylimine and the ring oxygen atom of the sorbofuranose moiety (Scheme

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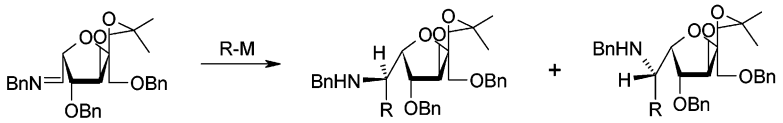
TABLE 1

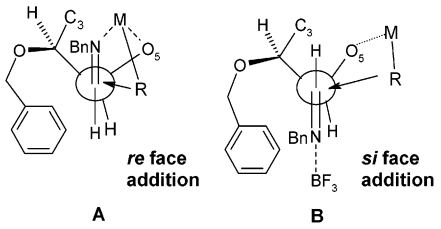


13 14a-e 15a-c

entry	R−M	Lewis acid	*T*, °C	**14**/**15**[a]	product	yield[b] (%)
1	allylMgBr		0 → rt	>98/2	**14a**	84
2	*n*BuLi		−78 → 0	>98/2	**14b**	65
3	vinylMgBr		0 → rt	95/5	**14c**	90
4	EtMgBr		0 → rt	>98/2	**14d**	75
5	$Me_3SiC{\equiv}CMgBr$		0 → rt	>98/2	**14e**	60
6	allylMgBr	$BF_3{\cdot}Et_2O$	−40 → 0	40/60	**14a**/**15a**	90
7	allylMgBr	$BF_3{\cdot}Et_2O$	−78 → 0	20/80	**14a**/**15a**	42
8	*n*BuLi	$BF_3{\cdot}Et_2O$	−78 → 0	>2/98	**15b**	69
9	vinylMgBr	$BF_3{\cdot}Et_2O$	−78 → 0	>2/98	**15c**	72

[a] Diastereomer ratio from ^1H and ^{13}C NMR analysis of the crude products. [b] Isolated yield after chromatography on silica gel.

SCHEME 3



3). In furanoid systems, it is well established that the endocyclic oxygen acts as a coordinating Lewis base in additions of organometallic reagents to 5-*aldehydo*-pentofuranose derivatives.[32]

With the goal of reversing the stereoselectivity of the addition, we performed the reaction in the presence of 5 equiv of $BF_3{\cdot}Et_2O$.[33] It was expected that imine **13** would be engaged in an open complex with the monodentate Lewis acid (open transition state model **B**)[31] and that chelation effects would be suppressed. According to this prevision, addition of BuLi or vinylmagnesium bromide (3 equiv) to a cold solution of imine **13** thus preactivated provided after purification the epimeric amines **15b**,**c** in good yield (Table 1, entries 8 and 9) and with a very high stereoselectivity (*si*-face addition). In contrast, the addition of allylmagnesium bromide to imine **13** at 0 °C under the same conditions gave a separable mixture of the two amines **14a** and **15a** with a lower degree of stereoselectivity (Table 1, entry 6). The diastereomeric excess could be improved by lowering the addition temperature to −78 °C but to the detriment of the yield (Table 1, entry 7). The lower diastereoselectivity of this process is attributed to a change in mechanism from inter- to intramolecular delivery of allylmagnesium reagents as it has been previously observed for 1,2-diastereoselective addition to α-alkoxy ketones or aldimines.[34]

Intramolecular Reductive Amination. The next key step of the strategy was the intramolecular reductive amination of the unmasked aminosorbose hemiketal. The pivotal issues of this one-pot process were the critical acidic hydrolysis of the relatively stable 2,3-*O*-isopropylidene group[35] and the control of the newly created stereocenter C5 (Table 2). We first focused our attention on the synthesis of nojirimycin α-*C*-glycosides from the 6(*R*) aminosorbose derivatives **14**. The optimized experimental conditions for the hydrolysis step consisted in using 90% aqueous CF_3COOH at room temperature at a substrate concentration of 0.15 M for 30 h.[36] After concentration of the reaction mixture and removal of solvent traces by coevaporation with toluene, the crude intermediate was treated with $NaBH_3CN$ for the reduction step. Our previously reported conditions using acetic acid as the solvent[24] were notably improved after careful optimization: the amount of acetic acid was decreased to 1 equiv, the solvent changed to methanol, and the reaction time extended to 24 h (Table 2). This process afforded diastereomerically pure diols **16**[37] or fully protected piperidines **17** after acetylation in very good overall yields. The relative configurations of the substituents in the piperidine ring system were unambiguously established by the ^1H NMR spectra (COSY and NOESY) of **16** and **17**. Removal of the benzyl protecting groups in **16b** and **16d** by hydrogenolysis provided the expected α-1-*C*-butyl-1-deoxynojirimycin **18**[38] and α-1-*C*-ethyl-1-deoxynojirimycin **19**[38] in very good yields (Scheme 4) (see ^1H NMR data for **18** in Table 3). The diastereoselectivity of the reduction step may be explained by the addition of hydride to a favorable half-chair conformation of the cyclic iminium intermediate in which all substituents are in pseudoequatorial position except the R group (Scheme 5). Hydride delivery in the axial direction is sterically unhindered and minimizes torsional strain during the

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(37) Diol **16c** with the vinyl group at C1 was found to decompose after a few days of storage at −20 °C. To avoid this degradation, **16c** was directly acetylated after the reductive amination reaction.

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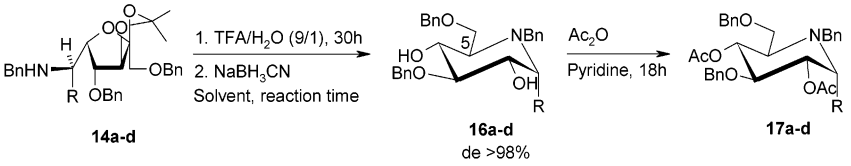
TABLE 2



entry	R	reductive amination	solvent	reaction time (h)	product	yield[a] (%)
1	allyl	$NaBH_3CN$ (4 equiv)	AcOH	3	**17a**	45
2	allyl	$NaBH_3CN$ (3 equiv), AcOH (1 equiv)	MeOH	24	**17a**	75
3	butyl	$NaBH_3CN$ (3 equiv), AcOH (1 equiv)	MeOH	24	**16b**	72
4	vinyl	$NaBH_3CN$ (4 equiv)	AcOH	3	**17c**	44
5	vinyl	$NaBH_3CN$ (3 equiv), AcOH (1 equiv)	MeOH	24	**17c**	72
6	ethyl	$NaBH_3CN$ (3 equiv), AcOH (1 equiv)	MeOH	24	**16d**	53

[a] Isolated yield from **14** after chromatography on silica gel.

SCHEME 4

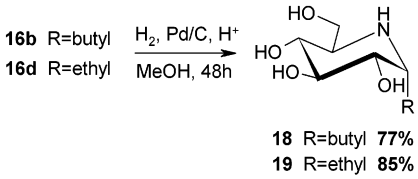
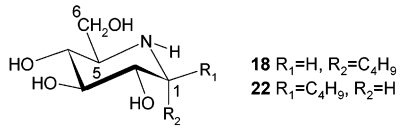
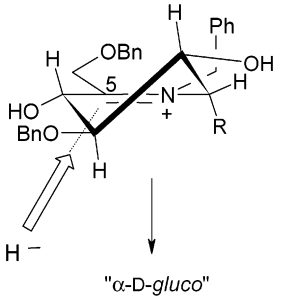


TABLE 3



J (Hz)	**18**	**22**
$J_{1,2}$	5.4	9.2−9.4
$J_{2,3}$	9.8	9.2−9.4
$J_{3,4}$	9.8	9.2−9.4
$J_{4,5}$	9.8	9.2−9.4
$J_{5,6A}$	3.0	2.8
$J_{5,6B}$	6.6	8.2

SCHEME 5



transition to the final chair conformation of the piperidine ring.[39]

Under the same conditions, the reductive amination of the 6(*S*)-epimers **15a**,**b** afforded quite unexpectedly an equimolar mixture of the pseudo-*β*-D-gluco and pseudo-α-L-ido products **20a**,**b** and **21a**,**b**, respectively, as determined on the basis of mass and NMR spectral data (Scheme 6). The complete loss of stereoselectivity at C5 may be rationalized by the partial destabilization of the cyclic iminium ion in conformation **A**: in this conformer, all the substituents are in a pseudoequatorial position, which generates $A_{1,2}$ strain between the C1 substituent and the *N*-benzyl group (Scheme 7).[26a,39] Hydride addition may thus also occur in the axial direction on the alternate half-chair conformation **B** of the iminium ion and thus lead to a substantial proportion of pseudo-α-L-ido product. The decisive influence of $A_{1,2}$ strain was demonstrated by the dramatic increase of the diastereomeric excess to 70% with the slightly less sterically demanding vinyl group (sp^2 instead of sp^3 carbon linked to C1). According to this analysis, it was predicted that removal of the *N*-benzyl group prior to internal reductive amination would suppress $A_{1,2}$ strain effects and increase the stereoselectivity of the reduction toward the desired D configuration. This hypothesis was verified by performing the following three-step sequence without purification of the intermediates: removal of the benzyl protecting groups of the amino-sorbofuranose derivatives **15b**,**c** by hydrogenolysis, cleavage of the isopropylidene group, and reductive amination under classical conditions (Scheme 8). Purification of the product by ion-exchange chromatography provided the expected *β*-1-*C*-butyl-1-deoxynojirimycin **22**[38] and *β*-1-*C*-ethyl-1-deoxynojirimycin **23** in good overall yields from **15b** and **15c** respectively (see the ^1H NMR data for **22** in Table 3). No trace of the other epimer was detected. This three-step procedure provides an efficient access to nojirimycin *β*-*C*-glycoside analogues bearing a C1 substituent compatible with catalytic hydrogenation.

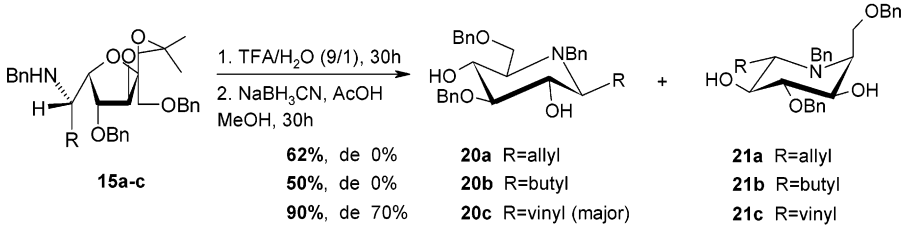
Synthesis of Iminosugar 1-Phosphonate 25. The operational simplicity and predictive power of the synthetic strategy outlined in this paper have been successfully applied to the efficient synthesis of the first example of an iminosugar 1-phosphonate. Due to their central role in the metabolism and the biosynthesis of carbohydrates,[40,41] glycosyl phosphates represent valuable tools for the comprehension of such fundamental biological mechanisms as glycolysis, gluconeogenesis, and glycosylation. The synthesis of glycosyl phosphate mimetics that could regulate those processes may lead to the discovery of new carbohydrate-based therapeutics. In the pyranoid series, several examples of glycosylmethylphosphonates,[42] the isosteric and isopolar *C*-glycosyl equivalents of gly-

(39) Baxter, E. W.; Reitz, A. B. *J. Org. Chem.* **1994**, *59*, 3175.

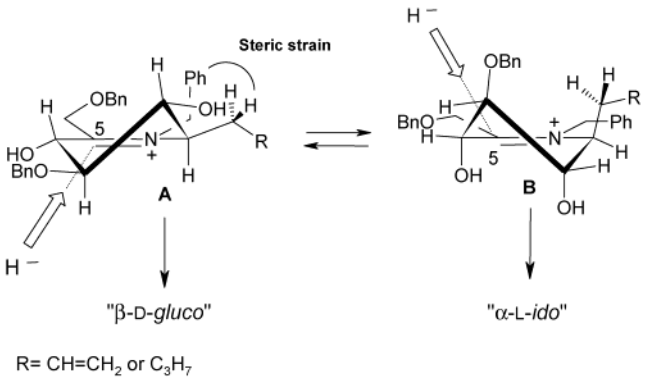
(40) Hers, H. G. *Biochem. Soc. Trans.* **1984**, *12*, 729.

(41) Macdonald, D. L. In *The Carbohydrates: Chemistry and Biochemistry*; Pigman, W., Horton, D., Eds.; Academic Press: New York, 1972; Vol. 1A, pp 253−277.

SCHEME 6



SCHEME 7



cosyl phosphates, as well as a number of the isopolar glycosylphosphonates[43] have been reported and prepared by various routes. While examples of "iminoglycosyl"-methylphosphonates have been described,[44] there has been no report of the corresponding iminosugar-derived glycosylphosphonates. Extension of our synthetic strategy to a phosphorus nucleophile provided access to this new class of stable glycosyl phosphate mimetics that combine an iminosugar moiety and a nonisosteric phosphate analogue (Scheme 9). Compound **25** was designed to display a strong affinity toward certain carbohydrate-processing enzymes: the ability of iminosugars to become protonated in biological medium and to form a cation which can interact strongly with an anionic group (i.e., carboxylate) at the enzyme active site is well established. In addition, glycosyl phosphate mimetics that consist of a phosphonate directly bound to the pseudo anomeric carbon were found to have a polarity similar to that of the natural sugar 1-phosphates.[45] Diethyl phosphite was converted in situ to its trimethylsilyloxy P(III) derivative **26**[46] in the presence of TMSCl and then reacted with imine **13** in CH_2Cl_2 to afford the α-amino phosphonate **24a** as a single diastereoisomer (6*S*) in high yield (Scheme 9). It is noteworthy that the diastereoselectivity was completely lost with the more sterically demanding phosphorus nucleophile generated from dibenzyl phosphite. According to Rees et al.,[46] the electrophilicity of the carbon atom of the C═N bond in this reaction is increased by the formation of a transient *N*-silylated iminium cation. The *S* configuration of the newly created stereogenic center may be explained by an open transition state model of type **B** having an antiperiplanar conformation due to steric and electrostatic repulsion (Scheme 3). The sense of addition could be reversed using the bidentate Lewis acid $ZrCl_4$ (chelated intermediate of type **A**). Following the mild experimental procedure recently described by Yadav et al.,[47] the epimeric α-amino phosphonate **24b** was obtained with a diastereomeric excess of 85%. Surprisingly, the acetal function of the α-amino phosphonates **24** was found to be particularly resistant to various hydrolysis conditions. To overcome this unexpected difficulty, we took advantage of the observation that deketalization of **15** was easier after complete debenzylation of the hydroxyl and amino functions (Scheme 8). We therefore completed the synthesis of the deprotected iminosugar 1-phosphonate **25** from **24a** by way of a one-pot deprotection (acetal and benzyl groups) and intramolecular reductive amination using hydrogen over a palladium catalyst in aqueous CF_3COOH. This process provided 1-deoxynojirimycin *β*-1-phosphonate **25** in a single operation and in 70% yield, the new stereogenic center (C5) being created with a diastereomeric excess of 80% according to the ^1H and ^{31}P NMR spectra of the crude product. So far, the conversion of epimeric **24b** into the corresponding 1-deoxynojirimycin α-1-phosphonate was unsuccessful, as the same sequence of reactions led to an unexploitable mixture of products. As shown clearly by NMR data, compound **25** has a pseudo-*β*-D-gluco configuration and adopts a chair conformation in which all substituents are in equatorial position.

Conclusion

The synthetic strategy based on the addition of organometallic reagents onto the L-sorbose-derived imine **13**, followed by an internal reductive amination, provides an efficient, practical and general access to nojirimycin *C*-glycosides and analogues. The tactical combination of these two reactions allows the stereocontrolled synthesis of α- and *β*-1-*C*-substituted-1-deoxynojirimycin and protected analogues in 10 steps and in an overall yield of 27 to 52% from commercially available 2,3;4,6-di-*O*-isopropylidene-α-L-sorbofuranose **6**. Future work will focus on the extension of this strategy to other series (D-allo,

(42) Nicotra, F. In *Carbohydrate Mimics: Concepts and Methods*; Chapleur, Y., Ed.; Wiley-VCH: New York, 1997; pp 67−85.

(43) (a) Vasella, A.; Baudin, G.; Panza, L. *Heteroatom Chem.* **1991**, *2*, 151 and references therein. (b) Vaghefi, M. M.; Bernacki, R. J.; Dalley, N. K.; Wilson, B. E.; Robins, R. K. *J. Med. Chem.* **1987**, *30*, 1383. (c) Chmielewski, M.; BeMiller, J. N.; Cerretti, D. P. *Carbohydr. Res.* **1981**, *97*, C1. (d) Meuwly, R.; Vasella, A. *Helv. Chim. Acta* **1986**, *69*, 25.

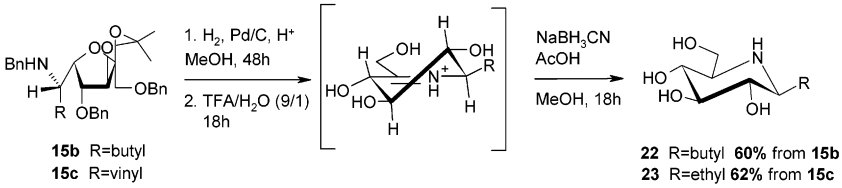
(44) For examples of iminosugar *C*-glycoside analogues of glycosyl 1-phosphate, see: (a) Reference 5b. (b) Bosco, M.; Bisseret, P.; Bouix-Peter, C.; Eustache, J. *Tetrahedron Lett.* **2001**, *42*, 7949. (c) Schuster, M.; He, W.-F.; Blechert, S. *Tetrahedron Lett.* **2001**, *42*, 2289. (d) Gautier-Lefebvre, I.; Behr, J.-B.; Guillerm, G.; Ryder, N. S. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1483. (e) Kajimoto, T.; Chen, L.; Liu, K. K.-C.; Wong, C.-H. *J. Am. Chem. Soc.* **1991**, *113*, 6678.

(45) Briner, K.; Vasella, A. *Helv. Chim. Acta* **1987**, *70*, 1341.

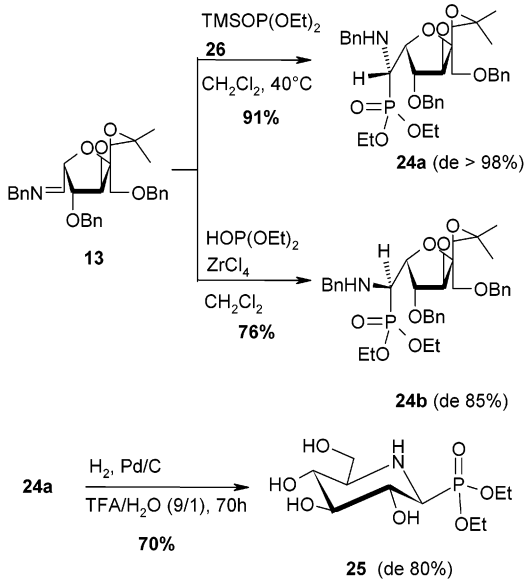
(46) Afarinkia, K.; Rees, C. W.; Cadogan, J. I. G. *Tetrahedron* **1990**, *46*, 7175.

(47) Yadav, J. S.; Reddy, B. V. S.; Sarita Raj, K.; Bhaskar Reddy, K.; Prasad, A. R. *Synthesis* **2001**, 2277.

SCHEME 8



SCHEME 9



D-galacto, and D-manno) from diols **16** and to various types of functionalized nucleophiles. Investigations on the activity of the synthesized iminosugars as glycosidase inhibitors, especially in the field of lysosomal storage disorders, are in progress and will be reported in due course. The synthesis of potential glycosyltransferase inhibitors based on a new type of sugar nucleotide mimetics with an unusual β pseudo-anomeric configuration from **24a** is currently being investigated. According to a remarkable observation reported very recently by Schmidt et al.,[48] such original donor analogues might be extremely useful to probe the poorly understood mechanism of glycosyl transfer by retaining transferases.

Experimental Section

General Methods. All reactions requiring anhydrous conditions were carried out under Ar. Diethyl ether and tetrahydrofuran were freshly distilled from sodium/benzophenone under Ar prior to use. Infrared spectra were recorded using films on NaCl windows or KBr pellets. Mass spectra (MS) were recorded by ion spray (IS). Melting points were determined in open capillary tubes and are uncorrected. Specific rotations were measured at room temperature (20 °C). Analytical thin-layer chromatography was performed using silica gel $60F_{254}$ precoated plates (Merck). Flash chromatography was perfomed on silica gel 60 (230−400 mesh) with ethyl acetate (AcOEt) and petroleum ether (PE) as eluants. ^{1}H and ^{13}C NMR spectra were recorded at 250 or 500 MHz and 62.9 MHz, respectively. Carbon multiplicities were assigned by distortionless enhancement by polarization transfer (DEPT) experiments.

1-*O*-Benzyl-2,3:4,6-di-*O*-isopropylidene-α-L-sorbofuranose (7).[28] To a stirred solution of **6** (40 g, 150 mmol) in anhydrous THF (40 mL) was added NaH (12.5 g, 312.5 mmol) at 0 °C. After 30 min at room temperature, benzyl bromide (30 mL, 250 mmol) and tetrabutylammonium iodide (3 g, 10 mmol) were added. After 3 h, the reaction was quenched by the careful addition of MeOH (25 mL) and ice (100 g). The mixture was extracted with CH_2Cl_2 (2 × 150 mL). The combined organic layer was washed with water (100 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification of the residual product by silica gel chromatography (PE/EtOAc 5:2) afforded **7** (52.5 g, 98%) as a clear syrup: $[\alpha]^{20}_D$ +34.5 (*c* 1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3H), 1.41 (s, 3H), 1.42 (s, 3H), 1.51 (s, 3H), 3.72 (d, 1H, J = 10.8 Hz), 3.80 (d, 1H, J = 10.8 Hz), 4.02 (m, 2H), 4.09 (d, 1H, J = 1.7 Hz), 4.30 (d, 1H, J = 1.7 Hz), 4.49 (s, 1H), 4.58 (d, 1H, J = 12.2 Hz), 4.72 (d, 1H, J = 12.2 Hz), 7.25−7.3 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 26.6, 27.7, 29.0, 60.4, 70.0, 72.2, 73.4, 73.7, 84.4, 97.4, 112.4, 114.2, 127.6, 127.7, 128.4, 138.3; MS *m*/*z* 351 (MH^+). Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 64.74; H, 7.34.

1-*O*-Benzyl-2,3-*O*-isopropylidene-α-L-sorbofuranose (8).[28] To a cold solution (ice bath) of **7** (51.8 g, 148 mmol) in acetone (530 mL) were cautiously added concentrated H_2SO_4 (45 mL) and water (235 mL). After 3 h at room temperature, the reaction mixture was neutralized by the slow addition of 2 M aqueous NaOH (500 mL). The mixture was extracted with EtOAc (3 × 500 mL). The combined organic layer was washed with water (300 mL), dried ($MgSO_4$), and concentrated to afforded **8** (45.4 g, 99%) as a white foam. An analytical sample was obtained by purification by silica gel chromatography (PE/EtOAc 1:9): $[\alpha]^{20}_D$ +41 (*c* 1.34, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 3H), 1.50 (s, 3H), 2.1 (m, 1H), 3.63 (d, 1H, J = 9.8 Hz), 3.73 (d, 1H, J = 11 Hz), 3.84 (d, 1H, J = 9.8 Hz), 3.89−3.98 (m, 2H), 4.18 (dd, 1H, J = 2.7, 10.3 Hz), 4.31 (dt, 1H, J = 3.1, 5.1 Hz), 4.43 (s, 1H), 4.59 (d, 1H, J = 11.7 Hz), 4.68 (d, 1H, J = 11.7 Hz), 7.25−7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 26.5, 27.6, 61.7, 71.8, 74.41, 75.9, 82.1, 87.3, 112.8, 113.0, 128.4, 128.7, 129.1, 137.0; MS *m*/*z* 311.5 (MH^+). Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C 61.84; H, 7.23.

1-*O*-Benzyl-2,3-*O*-isopropylidene-6-*O*-triphenylmethyl-α-L-sorbofuranose (9). To a solution of **8** (30 g, 96.6 mmol) in pyridine (140 mL) was added trityl chloride (30 g, 107.6 mmol) at room temperature. The mixture was stirred for 24 h at 50 °C. After removal of pyridine by coevaporation with toluene in vacuo, the crude product was taken in CH_2Cl_2 (200 mL). The solution was washed with saturated aqueous $NaHCO_3$ (3 × 100 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification of the residual product by silica gel chromatography (PE/EtOAc 95:5 to 6:4) afforded **9** (50.6 g, 95%) as a clear syrup: $[\alpha]^{20}_D$ +39 (*c* 1.32, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 3H), 1.52 (s, 3H), 3.39 (d, 1H, J = 2 Hz), 3.42 (s, 1H), 3.64 (d, 1H, J = 10 Hz), 3.79 (d, 1H, J = 10.2 Hz), 4.13 (dd, 1H, J = 2.2, 10.6 Hz), 4.38 (d, 1H, J = 2.7 Hz), 4.41 (s, 1H), 4.53 (d, 1H, J = 11.7 Hz), 4.62 (d, 1H, J = 11.7 Hz), 7.2−7.39 (m, 14H), 7.41−7.59 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 26.3, 27.4, 61.9, 71.5, 74.1, 75.1, 81.1, 86.5, 87.0, 112.3, 112.8, 127.1, 127.9, 128.2, 128.7, 128.9, 136.9, 144.0; MS *m*/*z* 553 (MH^+).

(48) Very recently, Schmidt et al. observed that the presence of UDP on the β-side of the sugar donor moiety of a bisubstrate analogue led to higher inhibition of a retaining glycosyltransferase (galactosyltransferase LgtC from *Neisseria meningitidis*) than when UDP was on the α-side as in the natural sugar nucleotide donor: Waldscheck, B.; Streiff, M.; Notz, W.; Kinzy, W.; Schmidt, R. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 4007.

1,4-Di-*O*-benzyl-2,3-*O*-isopropylidene-6-*O*-triphenylmethyl-α-L-sorbofuranose (10). To a solution of **9** (27.2 g, 49.2 mmol) in anhydrous THF (130 mL) was added NaH (3.14 g, 78.5 mmol) at 0 °C. After 30 min at room temperature, benzyl bromide (7.6 mL, 63.9 mmol) and tetrabutylammonium iodide (0.9 g, 3 mmol) were added. After 4 h, the reaction was quenched by the slow addition of MeOH (15 mL) and ice (80 g). The mixture was extracted with CH_2Cl_2 (3 × 400 mL). The combined organic layer was washed with water (250 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification of the residual product by silica gel chromatography (PE/EtOAc 95:5−85:15) afforded **10** (31.4 g, 99%) as a white crystalline material: mp 46−48 °C; $[\alpha]^{20}_D$ +23.5 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 3H), 1.55 (s, 3H), 3.28 (dd, 1H, J = 6.9, 9.1 Hz), 3.48 (dd, 1H, J = 6, 9.4 Hz), 3.57 (d, 1H, J = 11 Hz), 3.72 (d, 1H, J = 11 Hz), 4.03 (d, 1H, J = 3.1 Hz), 4.39 (d, 1H, J = 11.9 Hz), 4.46 (ddd, 1H, J = 3.1, 5.9, 6.2 Hz), 4.50 (d, 1H, J = 12.2 Hz), 4.55 (d, 1H, J = 11.9 Hz), 4.58 (s, 1H), 4.65 (d, 1H, J = 12.2 Hz), 7.10 (m, 2H), 7.15−7.35 (m, 17H), 7.38−7.50 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 26.7, 27.8, 61.5, 70.3, 71.8, 73.6, 80.3, 81.7, 82.1, 87.0, 112.4, 114.0, 127.1, 127.5, 127.6, 127.7, 127.9, 128.4, 128.8, 137.8, 138.3, 144.1; MS *m*/*z* 643.5 (MH^+).

1,4-Di-*O*-benzyl-2,3-*O*-isopropylidene-α-L-sorbofuranose (11). To a solution of **10** (4.2 g, 6.54 mmol) in acetic acid (25 mL) was added a 33% (w/v) solution of HBr in acetic acid (2 mL) at 10 °C. After 2−4 min at 10−15 °C, EtOAc (50 mL) and cold aqueous $NaHCO_3$ (50 mL) were added quickly to the reaction mixture. The organic layer was separated, dried ($MgSO_4$), and concentrated in vacuo. Purification of the residual product by silica gel chromatography (PE/EtOAc 4:1−3:2) afforded **11** (2.51 g, 96%) as a colorless oil: $[\alpha]^{20}_D$ +33.5 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 3H), 1.51 (s, 3H), 3.66 (d, 1H, J = 11 Hz), 3.78 (d, 1H, J = 11 Hz), 3.82 (dd, 1H, J = 4.9, 12 Hz), 3.89 (dd, 1H, J = 5.4, 11.7 Hz), 4.03 (d, 1H, J = 3.4 Hz), 4.37 (dt, 1H, J = 3.4, 5.3 Hz), 4.40 (d, 1H, J = 12 Hz), 4.56 (d, 1H, J = 12.2 Hz), 4.63 (d, 1H, J = 12 Hz), 4.66 (s, 1H), 4.69 (d, 1H, J = 11 Hz), 7.20−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 27.1, 28.0, 61.5, 70.6, 72.1, 74.0, 81.3, 82.4, 83.1, 112.8, 114.3, 128.0, 128.1, 128.5, 128.7, 129.0, 137.5, 138.5; MS *m*/*z* 401.5 (MH^+). Anal. Calcd for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 69.08; H, 6.97.

3,6-Di-*O*-benzyl-4,5-*O*-isopropylidene-D-*xylo*-*aldehydo*-hexos-5-ulo-2,5-furanose (12). To a solution of **11** (4.6 g, 11.5 mmol) in anhydrous CH_2Cl_2 (60 mL) was added a 15 wt % Dess−Martin periodinane solution (26.3 mL, 12.65 mmol) in CH_2Cl_2. After 30 min, aqueous NaOH (200 mL) and Et_2O (400 mL) were added under vigorous stirring. The organic layer was washed with aqueous NaOH (200 mL) and then with water (100 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification of the residual product by silica gel chromatography (PE/EtOAc 8:2−1:1) afforded **12** (4.16 g, 91%) as a colorless oil: $[\alpha]^{20}_D$ +1 (*c* 1.02, $CHCl_3$); IR (NaCl, neat) 1736 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 3H), 1.50 (s, 3H), 3.77 (d, 1H, J = 11 Hz), 3.87 (d, 1H, J = 11 Hz), 4.34 (d, 1H, J = 3.8 Hz), 4.40 (d, 1H, J = 12 Hz), 4.55 (d, 1H, J = 12 Hz), 4.58 (d, 1H, J = 12 Hz), 4.63 (dd, 1H, J = 1.5, 4.1 Hz), 4.68 (s, 1H), 4.71 (d, 1H, J = 12 Hz), 7.17−7.32 (m, 10H), 9.61 (d, 1H, J = 1.6 Hz); ^{13}C NMR ($CDCl_3$) δ 26.4, 27.5, 69.7, 72.2, 73.7, 81.6, 83.9, 85.1, 113.0, 115.4, 127.6, 127.7, 128.1, 128.3, 128.4, 128.5, 136.4, 137.4, 200.3; MS *m*/*z* 399.0 (MH^+). Anal. Calcd for $C_{23}H_{26}O_6$ + $0.5H_2O$: C, 67.80; H, 6.68. Found: C, 68.15; H, 6.70.

3,6-Di-*O*-benzyl-4,5-*O*-isopropylidene-D-*xylo*-*aldehydo*-hexos-5-ulo-2,5-furanose *N*-Benzylimine (13). To a solution of **12** (3.6 g, 9.05 mmol) in anhydrous CH_2Cl_2 (45 mL) were added powdered 4 Å molecular sieves (450 mg) and benzylamine (1.04 mL, 9.5 mmol) at room temperature. After 3 h at 4 °C without stirring, the solids were removed by filtration and washed with anhydrous CH_2Cl_2 (45 mL). The filtrate was concentrated in vacuo to afford homogeneous **13** (4.38 g, quant.) as a colorless oil: $[\alpha]^{20}_D$ +43 (*c* 1.07, $CHCl_3$); IR (NaCl, neat) 1672 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 3H), 1.50 (s, 3H), 3.74 (d, 1H, J = 11 Hz), 3.83 (d, 1H, J = 11 Hz), 4.16 (d, 1H, J = 3.4 Hz), 4.37 (d, 1H, J = 12 Hz), 4.53 (d, 1H, J = 12 Hz), 4.58 (d, 1H, J = 12 Hz), 4.60−4.69 (m, 3H), 4.68 (s, 1H), 4.86 (m, 1H), 7.15−7.31 (m, 15H), 7.79 (d, 1H, J = 5 Hz); ^{13}C NMR ($CDCl_3$) δ 26.8, 27.7, 65.0, 70.2, 72.1, 73.8, 82.3, 82.5, 84.7, 112.8, 114.8, 127.0, 127.3, 127.5, 127.7, 127.9, 128.3, 128.5, 128.6, 128.7, 137.4, 138.2, 138.4, 163.2.

General Procedure A: Synthesis of (6*R*)-6-*C*-Alkyl-1,4-di-*O*-benzyl-6-benzylamino-6-deoxy-2,3-*O*-isopropylidene-α-L-sorbofuranose (14). To a 0.33 M solution of organolithium reagent (3 equiv) or organomagnesium bromide reagent (3 equiv) in anhydrous Et_2O at −78 or at 0 °C, respectively, was added slowly a 0.15 M solution of **13** (1 equiv) in anhydrous Et_2O. The mixture was then warmed slowly to 0 °C or to room temperature, respectively, and stirred for 3−12 h. The reaction was quenched by the slow addition of a saturated aqueous NH_4Cl at room temperature. The phases were separated, the organic layer was dried ($MgSO_4$), and concentrated under reduced pressure. The product was purified by flash silica gel chromatography.

General Procedure B: Synthesis of (6*S*)-6-*C*-Alkyl-1,4-di-*O*-benzyl-6-benzylamino-6-deoxy-2,3-*O*-isopropylidene-α-L-sorbofuranose (15). To a 0.06 M solution of **13** (1 equiv) in anhydrous Et_2O at −78 °C was added $BF_3{\cdot}Et_2O$ (5 equiv). After 10 min, a solution of organolithium reagent (3 equiv) or organomagnesium bromide reagent (3 equiv) in anhydrous Et_2O or THF (1−3 M) was added to the imine solution. After 3 h at 0 °C, the reaction was quenched by the slow addition of saturated aqueous NH_4Cl. The phases were separated, and the organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The product was purified by silica gel flash chromatography.

(6*R*)-6-*C*-Allyl-1,4-di-*O*-benzyl-6-benzylamino-6-deoxy-2,3-*O*-isopropylidene-α-L-sorbofuranose (14a). Compound **13** (2 g, 4.1 mmol) was treated with allylmagnesium bromide (12.3 mmol) according to general procedure A. Purification of the crude product by silica gel chromatography (PE/AcOEt 3:1) provided **14a** (1.82 g, 84%) as a yellow oil: $[\alpha]^{20}_D$ −10 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.41 (s, 3H), 1.50 (s, 3H), 2.05 (m, 1H), 2.20 (m, 1H), 3.07 (ddd, 1H, J = 6.8, 8.7, 14.2 Hz), 3.60 (d, 1H, J = 11 Hz), 3.73 (d, 1H, J = 11 Hz), 3.74 (d, 1H, J = 12.5 Hz), 3.83 (d, 1H, J = 12.5 Hz), 3.88 (d, 1H, J = 3.2 Hz), 4.16 (dd, 1H, J = 3.2, 8.8 Hz), 4.36 (d, 1H, J = 11.5 Hz), 4.55 (d, 1H, J = 12.2 Hz), 4.64 (d, 1H, J = 11.5 Hz), 4.66 (d, 1H, J = 12.2 Hz), 4.67 (s, 1H), 5.01 (ddd, 2H, J = 2.5, 7, 11.5 Hz), 5.84 (m, 1H), 7.22−7.29 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 26.8, 27.7, 34.9, 51.8, 55.5, 70.6, 71.4, 73.8, 81.5, 81.7, 83.5, 112.3, 113.6, 116.9, 126.9, 127.7, 128.0, 128.0, 128.4, 128.5, 128.6, 135.5, 137.5, 138.4; MS *m*/*z* 530.5 (MH^+).

(6*R*)-1,4-Di-*O*-benzyl-6-benzylamino-6-*C*-butyl-6-deoxy-2,3-*O*-isopropylidene-α-L-sorbofuranose (14b). Compound **13** (1 g, 2.11 mmol) was treated with butyllithium (6 mmol) according to general procedure A. Purification of the crude product by silica gel chromatography (PE/AcOEt 3:1) provided **14b** (745 mg, 65%) as a yellow oil: $[\alpha]^{20}_D$ −16 (*c* 1.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.85 (t, 3H, J = 6.5 Hz), 1.20−1.40 (m, 6H), 1.38 (s, 3H), 1.51 (s, 3H), 2.40 (d, 2H, J = 5.6 Hz), 3.04 (dd, 1H, J = 3.2, 12 Hz), 3.71 (d, 1H, J = 12 Hz), 3.73 (d, 1H, J = 12.7 Hz), 3.81 (d, 1H, J = 12 Hz), 3.82 (d, 1H, J = 12.7 Hz), 3.92 (d, 1H, J = 3.2 Hz), 4.23 (dd, 1H, J = 3.2, 8.6 Hz), 4.38 (d, 1H, J = 11.5 Hz), 4.67 (s, 1H), 4.71 (d, 1H, J = 11.5 Hz), 7.20−7.32 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 14.4, 23.4, 27.1, 27.8, 27.9, 30.2, 51.4, 58.8, 64.4, 72.0, 82.3, 82.4, 83.7, 112.3, 114.2, 127.3, 128.5, 128.7, 128.8, 128.9, 137.3, 140.8; MS *m*/*z* 546.5 (MH^+). Anal. Calcd for $C_{34}H_{43}NO_5$: C, 74.83; H, 7.94; N, 2.57. Found: C, 74.42; H, 7.44; N, 2.68.

(6*R*)-1,4-Di-*O*-benzyl-6-benzylamino-6-deoxy-6-*C*-ethenyl-2,3-*O*-isopropylidene-α-L-sorbofuranose (14c). Compound **13** (500 mg, 1.05 mmol) was treated with vinylmagnesium bromide (3 mmol) according to general procedure A. Purification of the crude product by silica gel chromatography (PE/AcOEt 5:1) provided **14c** (482 mg, 90%) as a yellow oil:

$[\alpha]^{20}_D$ −23 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 3H), 1.50 (s, 3H), 3.57 (t, 1H, *J* = 8.1 Hz), 3.59 (d, 1H, *J* = 13 Hz), 3.62 (d, 1H, *J* = 11 Hz), 3.73 (d, 1H, *J* = 11 Hz), 3.73 (d, 1H, *J* = 13 Hz), 3.85 (d, 1H, *J* = 2.9 Hz), 4.21 (dd, 1H, *J* = 2.9, 9.3 Hz), 4.34 (d, 1H, *J* = 11.2 Hz), 4.53 (d, 1H, *J* = 12.2 Hz), 4.55 (d, 1H, *J* = 11.2 Hz), 4.65 (s, 1H), 4.66 (d, 1H, *J* = 12.2 Hz), 5.21 (dd, 1H, *J* = 1.7, 17.1 Hz), 5.31 (dd, 1H, *J* = 1.9, 10.3 Hz), 5.39 (ddd, 1H, *J* = 8.1, 10, 17.6 Hz), 7.19−7.59 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 26.8, 27.7, 51.4, 60.4, 69.4, 70.8, 73.7, 81.5, 82.5, 82.9, 112.5, 114.0, 119.3, 126.8, 127.6, 127.7, 127.8, 128.2, 128.3, 128.4, 128.7, 136.4, 137.6, 138.2, 140.4; MS *m*/*z* 516.5 (MH^+). Anal. Calcd for $C_{32}H_{37}NO_5$: C, 74.54; H, 7.23; N, 2.72. Found: C, 74.76; H, 7.30; N, 2.77.

(6*R*)-1,4-Di-*O*-benzyl-6-benzylamino-6-deoxy-6-*C*-ethyl-2,3-*O*-isopropylidene-α-L-sorbofuranose (14d). Compound **13** (500 mg, 1.05 mmol) was treated with ethylmagnesium bromide (3.15 mmol) according to general procedure A. Purification of the crude product by silica gel chromatography (CH_2Cl_2/MeOH 99:1 to 95:5) provided **14d** (410 mg, 75%) as a yellow oil: $[\alpha]^{20}_D$ −11 (*c* 0.89, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.93 (t, 3H, *J* = 7.4 Hz), 1.30−1.53 (m, 2H), 1.42 (s, 3H), 1.51 (s, 3H), 3.02 (ddd, 1H, *J* = 6.1, 9.3, 10 Hz), 3.62 (d, 1H, *J* = 11 Hz), 3.70 (d, 1H, *J* = 13 Hz), 3.74 (d, 1H, *J* = 11 Hz), 3.78 (d, 1H, *J* = 13 Hz), 3.87 (d, 1H, *J* = 2.7 Hz), 4.22 (dd, 1H, *J* = 2.9, 9 Hz), 4.34 (d, 1H, *J* = 11.5 Hz), 4.52 (d, 1H, *J* = 12.3 Hz), 4.55 (d, 1H, *J* = 11.2 Hz), 4.67 (s, 1H), 4.66 (d, 1H, *J* = 12.2 Hz), 7.13−7.40 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 10.2, 23.1, 27.2, 28.1, 51.6, 57.1, 70.9, 71.9, 74.1, 81.9, 82.4, 83.5, 112.5, 113.9, 127.1, 128.0, 128.0, 128.2, 128.3, 128.7, 128.8, 128.8, 128.8, 137.9, 138.7, 141.5; MS *m*/*z* 518.5 (MH^+). Anal. Calcd for $C_{32}H_{39}NO_5$: C, 74.25; H, 7.59; N, 2.71. Found: C, 74.50; H, 7.73; N, 2.84.

(6*R*)-1,4-Di-*O*-benzyl-6-benzylamino-6-deoxy-2,3-*O*-isopropylidene-6-*C*-(trimethylsilylethynyl)-α-L-sorbofuranose (14e). To a solution of ethynyltrimethylsilane (580 μL, 4.1 mmol) in anhydrous Et_2O (15 mL) was added at 0 °C a solution of ethylmagnesium bromide in Et_2O (1.18 mL, 3.54 mmol). The mixture was stirred at 40 °C for 1 h. Compound **13** (420 mg, 0.86 mmol) was then treated with the solution of trimethylsilylethynylmagnesium bromide thus prepared according to general procedure A. Purification of the crude product by silica gel chromatography (EP/AcOEt 4:1) provided **14e** (300 mg, 60%) as a yellow oil: $[\alpha]^{20}_D$ −4 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.18 (s, 9H), 1.41 (s, 3H), 1.51 (s, 3H), 3.58 (d, 1H, *J* = 11 Hz), 3.70 (d, 1H, *J* = 11 Hz), 3.82 (d, 1H, *J* = 13 Hz), 3.88 (d, 1H, *J* = 9.5 Hz), 3.92−4.10 (m, 1H), 4.43 (dd, 1H, *J* = 2.9, 8.3 Hz), 4.46 (d, 1H, *J* = 12 Hz), 4.53−4.62 (m, 2H), 4.60 (s, 1H), 4.61 (d, 1H, *J* = 12 Hz), 7.13−7.40 (m, 15H);; ^{13}C NMR ($CDCl_3$) δ -0.06, 26.5, 27.5, 50.4, 51.3, 70.0, 73.0, 73.6, 81.5, 83.0, 83.1, 89.3, 103.6, 112.2, 114.5, 126.8, 127.5, 127.5, 127.7, 128.2, 128.3, 137.7, 138.1, 139.8; MS *m*/*z* 586.5 (MH^+). Anal. Calcd for $C_{35}H_{43}NO_5Si$: C, 71.76; H, 7.40; N, 2.39. Found: C, 72.01; H, 7.56; N, 2.55.

(6*S*)-6-*C*-Allyl-1,4-di-*O*-benzyl-6-benzylamino-6-deoxy-2,3-*O*-isopropylidene-α-L-sorbofuranose (15a). Compound **13** (825 mg, 1.7 mmol) was treated with BF_3·Et_2O (8.5 mmol) and allylmagnesium bromide (5.1 mmol) according to general procedure B. The isomers were separated by silica gel chromatography (PE/AcOEt 4:1). Isomer 6*S* (**15a**) eluted first (300 mg, 33%): yellow oil; $[\alpha]^{20}_D$ +24 (*c* 1.34, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 3H), 1.50 (s, 3H), 2.33 (m, 1H), 2.46 (m, 1H), 3.18 (dd, 1H, *J* = 5.6, 13.5 Hz), 3.60 (d, 1H, *J* = 10.9 Hz), 3.73 (d, 1H, *J* = 10.9 Hz), 3.72 (d, 1H, *J* = 12.7 Hz), 3.91 (d, 1H, *J* = 12.7 Hz), 4.10 (s, 1H), 4.13 (dd, 1H, *J* = 3.1, 9.1 Hz), 4.44 (d, 1H, *J* = 11.6 Hz), 4.55 (d, 1H, *J* = 11.6 Hz), 4.64 (d, 1H, *J* = 11.6 Hz), 4.68 (d, 1H, *J* = 11.6 Hz), 4.66 (s, 1H), 5.04 (ddd, 2H, *J* = 2.2, 7.8 Hz, 11 Hz), 5.75 (m, 1H), 7.22−7.29 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 26.8, 27.8, 34.9, 51.7, 54.4, 70.5, 71.8, 73.8, 81.6, 81.9, 82.3, 112.2, 113.6, 118.3, 127.2, 127.7, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 128.6, 134.5, 137.6, 138.2; MS *m*/*z* 530.5 (MH^+). The second fraction contained homogeneous **14a** (80 mg, 9%).

(6*S*)-1,4-Di-*O*-benzyl-6-benzylamino-6-*C*-butyl-6-deoxy-2,3-*O*-isopropylidene-α-L-sorbofuranose (15b). Compound **13** (825 mg, 1.7 mmol) was treated with BF_3·Et_2O (8.5 mmol) and butyllithium (5.1 mmol) according to general procedure B. Purification of the crude product by silica gel chromatography (PE/AcOEt 5:1 to 3:1) provided **15b** (630 mg, 69%) as a yellow oil: $[\alpha]^{20}_D$ +15 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.87 (m, 3H), 1.10−1.70 (m, 6H), 1.46 (s, 3H), 1.51 (s, 3H), 3.13 (m, 1H), 3.64 (d, 1H, *J* = 11 Hz), 3.74 (d, 1H, *J* = 11 Hz), 3.85 (m, 2H), 4.19 (dd, 1H, *J* = 2.8, 7.8 Hz), 4.40−4.70 (m, 6H), 7.0−7.40 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 23.1, 26.8, 27.4, 27.8, 30.8, 51.9, 55.4, 70.6, 71.8, 73.8, 81.5, 82.1, 112.3, 113.7, 127.4, 127.7, 127.8, 128.2, 128.5, 128.5, 128.6, 128.7, 128.8, 138.3; MS *m*/*z* 546.5 (MH^+).

(6*S*)-1,4-Di-*O*-benzyl-6-benzylamino-6-deoxy-6-*C*-ethenyl-2,3-*O*-isopropylidene-α-L-sorbofuranose (15c). Compound **13** (830 mg, 1.7 mmol) was treated with BF_3·Et_2O (6.13 mmol) and vinylmagnesium bromide (7 mmol) according to general procedure B . Purification of the crude product by silica gel chromatography (PE/AcOEt 5:1−1:1) provided **15c** (635 mg, 72%) as a yellow oil: $[\alpha]^{20}_D$ +7 (*c* 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 3H), 1.49 (s, 3H), 3.51 (t, 1H, *J* = 8.3 Hz), 3.57 (d, 1H, *J* = 13.1 Hz), 3.63 (d, 1H, *J* = 11.2 Hz), 3.72 (d, 1H, *J* = 11.2 Hz), 3.78 (d, 1H, *J* = 13.1 Hz), 4.09 (d, 1H, *J* = 2.9 Hz), 4.13 (dd, 1H, *J* = 3.2, 8.5 Hz), 4.43 (d, 1H, *J* = 11.7 Hz), 4.55 (d, 1H, *J* = 12.2 Hz), 4.62 (d, 1H, *J* = 11.7 Hz), 4.65 (s, 1H), 4.66 (d, 1H, *J* = 12.2 Hz), 5.22 (m, 2H), 5.77 (ddd, 1H, *J* = 7.8, 10.7, 18.6 Hz), 7.20−7.28 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 27.0, 28.0, 51.4, 59.6, 70.6, 72.2, 73.9; 81.8, 82.0, 83.6, 112.5, 114.1, 118.2, 127.3, 127.8, 128.0, 128.1, 128.2, 128.5, 128.7, 128.9, 137.9, 138.7; 141.0; MS *m*/*z* 516.5 (MH^+).

General Procedure C: Synthesis of (1*R*)-1-*C*-Alkyl-*N*-benzyl-3,6-di-*O*-benzyl-1,5-dideoxy-1,5-imino-D-glucitol (16). A ∼0.15 M solution of precursor **14** in trifluoroacetic acid was prepared at 0 °C; H_2O was then added to form a 9:1 (v/v) TFA/H_2O mixture. The reaction mixture was warmed to room temperature and stirred for 20−30 h. The solvents were removed by three coevaporations with toluene, and the residual product was taken up in MeOH to form a ∼0.05 M solution. Acetic acid (1 equiv) and $NaBH_3CN$ (3 equiv) were added at 0 °C. The reaction mixture was stirred for 24 h at room temperature. The mixture was then concentrated under reduced pressure. The crude product was taken up in CH_2Cl_2, and the solution was washed with saturated aqueous $NaHCO_3$ and then with water. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The product (**16**) was purified by silica gel chromatography.

(1*R*)-1-*C*-Allyl-*N*-benzyl-3,6-di-*O*-benzyl-1,5-dideoxy-1,5-imino-D-glucitol (16a) and Diacetate (17a). Compound **14a** (2.4 g, 4.53 mmol) was treated according to general procedure C. Purification of the crude product by silica gel chromatography (PE/AcOEt 3:1 to 2:1) provided **16a** (1.6 g, 75%) as a yellow oil: $[\alpha]^{20}_D$ +24 (*c* 1.21, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.36 (m, 2H), 3.02 (dd, 1H, *J* = 5.6, 8.1 Hz), 3.07 (ddd, 1H, *J* = 13.7, 13.5, 4.6 Hz), 3.69 (d, 1H, *J* = 4.9 Hz), 3.70 (t, 1H, *J* = 8.3 Hz), 3.71 (m, 2H), 3.79 (d, 1H, *J* = 13.7 Hz), 3.86 (dd, 1H, *J* = 4.9, 8.8 Hz), 4.42 (d, 1H, *J* = 11.7 Hz), 4.73 (d, 1H, *J* = 11.7 Hz), 4.93 (d, 1H, *J* = 11.7 Hz), 4.96 (d, 1H, *J* = 10.3 Hz), 5.03 (dd, 1H, *J* = 10.2, 17.1 Hz), 5.74 (ddd, 1H, *J* = 7.8, 10.3, 17.0 Hz), 7.10−7.49 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 29.7, 53.4, 58.1, 59.1, 65.4, 70.3, 72.8, 73.5, 74.6, 83.5, 115.9, 126.9−128.9, 132.1, 137.4, 137.8, 138.8; MS *m*/*z* 474.5 (MH^+). Compound **16a** (1.3 g, 2.75 mmol) was acetylated under standard conditions (acetic anhydride/pyridine), and the crude diacetate was purified by silica gel chromatography (PE/AcOEt 4:1) to give **17a** (1.53 g, quant) as a yellow oil: $[\alpha]^{20}_D$ +26 (*c* = 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.89 (s, 3H), 1.95 (s, 3H), 2.24 (m, 1H), 2.37 (m, 1H), 3.19 (m, 2H), 3.58 (m, 2H), 3.80 (t, 1H, *J* = 8.3 Hz), 3.96 (s, 2H), 4.33 (s, 2H), 4.62 (d, 1H, *J* = 11.7 Hz), 4.66 (d, 1H, *J* = 11.7 Hz), 4.96 (dd, 1H, *J* = 1.5, 10.3 Hz), 4.99 (dd, 1H, *J* = 1.5, 17.1 Hz), 5.15 (dd, 1H, *J* = 5.4, 8.8 Hz), 5.23 (t, 1H, *J* = 8.5

Hz), 5.62 (ddd, 1H, J = 6.8, 10.3, 17.1 Hz), 7.10−7.45 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 21.2, 30.7, 52.6, 55.8, 56.0, 69.6, 71.4, 71.8, 73.2, 74.2, 78.6, 116.1, 126.0−128.5, 136.1, 138.0, 138.4, 140.1, 170.0, 170.1; MS m/z 558.5 (MH^+). Anal. Calcd for $C_{34}H_{39}NO_6$: C, 73.23; H, 7.05; N, 2.51. Found: C, 73.02; H, 7.15; N, 2.61.

(1*R*)-*N*-Benzyl-3,6-di-*O*-benzyl-1-*C*-butyl-1,5-dideoxy-1,5-imino-D-glucitol (16b). Compound **14b** (220 mg, 0.4 mmol) was treated according to general procedure C. Purification of the crude product by silica gel chromatography (PE/AcOEt 2:3) provided **16b** (140 mg, 72%) as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 0.85 (t, 3H, J = 7.3 Hz), 1.16−1.28 (m, 4H), 1.53 (m, 2H), 2.30 (br s, 1H), 2.85 (m, 1H), 3.00 (br s, 1H), 3.08 (m, 1H), 3.52 (t, 1H, J = 8.5 Hz), 3.70−3.96 (m, 6H), 4.12 (dd, 1H, J = 7.3, 14 Hz), 4.44 (s, 2H), 4.74 (d, 1H, J = 11.4 Hz), 4.96 (d, 1H, J = 11.3 Hz), 7.23−7.39 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 14.2, 14.3, 21.2, 22.8, 24.6, 29.4, 53.3, 57.3, 59.1, 60.5, 69.6, 71.5, 73.0, 73.6, 74.9, 84.3, 126.9, 127.8, 127.9, 127.9, 128.2, 128.3, 128.6, 128.7, 137.7, 139.0, 140.9; MS m/z 490.5 (MH^+).

(1*R*)-2,4-Di-*O*-acetyl-*N*-benzyl-3,6-di-*O*-benzyl-1,5-dideoxy-1-*C*-ethenyl-1,5-imino-D-glucitol (17c). Compound **14c** (370 mg, 0.72 mmol) was submitted to deprotection−reductive amination according to general procedure C. The resulting crude product (**16c**) was acetylated under standard conditions, and the diacetate was purified by silica gel chromatography (PE/AcOEt 5:1−3:1), which provided **17c** (280 mg, 72%) as a yellow oil: $[\alpha]^{20}_D$ + 33.6 (c = 1.23, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.86 (s, 3H), 1.90 (s, 3H), 3.16 (dt, 1H, J = 3.9, 9.8 Hz), 3.51 (d, 2H, J = 3.9 Hz), 3.59 (dd, 1H, J = 5.4, 8.8 Hz), 3.68 (d, 1H, J = 14.2 Hz), 3.76 (t, 1H, J = 9.5 Hz), 4.08 (d, 1H, J = 14.2 Hz), 4.33 (d, 1H, J = 11.7 Hz), 4.38 (d, 1H, J = 11.7 Hz), 4.58 (d, 1H, J = 11.7 Hz), 4.67 (d, 1H, J = 11.7 Hz), 5.05 (dd, 1H, J = 5.4, 9.8 Hz), 5.12 (dd, 1H, J = 10.2, 17.1 Hz), 5.14 (t, 1H, J = 9.8 Hz), 5.36 (dd, 1H, J = 10.2, 17.1 Hz), 5.93 (ddd, 1H, J = 8.8, 10.2, 17.1 Hz), 7.10−7.45 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 21.0, 52.7, 57.9, 59.8, 69.0, 72.1, 72.8, 73.2, 74.2, 79.1, 121.4, 126.0−128.7, 130.7, 137.9, 138.5, 139.7, 169.8, 170.1; MS m/z 544.5 (MH^+). Anal. Calcd for $C_{33}H_{37}NO_6$: C, 72.91; H, 6.86; N, 2.58. Found: C, 72.73; H, 6.98; N, 2.71.

(1*R*)-1-*C*-Butyl-1,5-dideoxy-1,5-imino-D-glucitol (18). To a solution of **16b** (60 mg, 0.12 mmol) in MeOH (4 mL) were added 10% Pd/C (0.2 equiv) and two drops of 5 N aqueous HCl. The flask was purged 3× with Ar and then filled with H_2. After 48 h, the solids were removed by filtration, and the filtrate was concentrated under reduced pressure. The crude product was filtered through Amberlyst ion-exchange resin IRA-400 (OH^-) (elution with H_2O), and the filtrate was concentrated under reduced pressure. The residual product was purified by chromatography on Amberlyst ion-exchange resin IR-120(H^+) (loading, washing with H_2O, elution with aqueous ammonia (7.5% NH_4OH)); the fractions containing the product were pooled and concentrated under reduced pressure to afforded pure **18** (21 mg, 77%) as a colorless oil: $[\alpha]^{20}_D$ +50 (c = 0.13, H_2O); ^{1}H NMR (D_2O, 500 MHz) δ 0.91 (t, 3H, J = 6.6 Hz), 1.1−1.49 (m, 4H), 1.50−1.70 (m, 2H), 2.92 (ddd, 1H, J = 3, 6.6, 9.8 Hz), 3.23 (ddd, 1H, J = 4.6, 5.5, 9.8 Hz), 3.28 (dd, 1H, J = 9.5, 9.8 Hz), 3.58 (dd, 1H, J = 9.5, 9.8 Hz), 3.64 (dd, 1H, J = 6.6, 12 Hz), 3.69 (dd, 1H, J = 5.4, 9.8 Hz), 3.88 (dd, 1H, J = 2.9, 11.7 Hz); ^{13}C NMR (D_2O) δ 13.7, 22.4, 24.1, 28.2, 54.7, 55.9, 61.3, 71.7, 72.3, 74.1. HR-FABMS (relative intensity) calcd for $C_{10}H_{22}NO_4$ (MH^+) m/z 220.1550, found 220.1550 (100).

(1*R*)-1,5-Dideoxy-1-*C*-ethyl-1,5-imino-D-glucitol (19). Compound **14d** (300 mg, 0.58 mmol) was submitted to deprotection−reductive amination according to general procedure C. The resulting crude iminoalditol **16d** was then debenzylated and purified as described for **18**, which provided **19** (49 mg, 45%) as a colorless oil: $[\alpha]^{20}_D$ +52 (c 1.15, H_2O); ^{1}H NMR (D_2O, 500 MHz) δ 0.95 (t, 3H, J = 7.5 Hz), 1.50 (m, 1H), 1.70 (m, 1H), 2.70 (ddd, 1H, J = 3.4, 8.3, 10.7 Hz), 2.91 (ddd, 1H, J = 3.9, 5.4, 9.3 Hz), 3.10 (t, 1H, J = 9.3 Hz), 3.45 (t, 1H, J = 9.3 Hz), 3.49 (dd, 1H, J = 7.8, 10.7 Hz), 3.60 (dd, 1H, J = 5.4, 9.3 Hz), 3.88 (dd, 1H, J = 2.9, 10.7 Hz); ^{13}C NMR (D_2O) δ 10.1, 17.4, 54.2, 57.3, 62.1, 72.4, 72.8, 74.4; HR-FABMS (relative intensity) calcd for $C_8H_{18}NO_4$ (MH^+) m/z 192.12358, found 192.12314 (100).

(1*S*)-*N*-Benzyl-3,6-di-*O*-benzyl-1,5-dideoxy-1-*C*-ethenyl-1,5-imino-D-glucitol (20c). Compound **15c** (150 mg, 0.29 mmol) was treated according to general procedure C, and the resulting crude product mixture was filtered through silica gel to afford 120 mg (90%) of a mixture of **20c** and its L-ido epimer (de 70%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.84 (ddd, 1H, J = 3.9, 4.4, 8.3 Hz), 3.14 (t, 1H, J = 9.3 Hz), 3.22 (ddd, 0.15H, J = 3.3, 5.4, 10.3 Hz), 3.30 (dd, 1H, J = 3.9, 9.8 Hz), 3.44 (dd, 1H, J = 3.4, 10.3 Hz), 3.55 (t, 1H, J = 8.3 Hz), 3.75 (dd, 0.15H, J = 2.9, 6.3 Hz), 3.89 (d, 1H, J = 16.1 Hz), 4.03 (d, 1H, J = 16.1 Hz), 4.14 (s, 2H), 4.60 (s, 2H), 5.00 (t, 0.15H, J = 9.3 Hz), 5.06 (t, 1H, J = 9.3 Hz), 5.12 (dd, 1H, J = 1.5, 10.3 Hz), 5.20 (dd, 1H, J = 1.5, 17.6 Hz), 5.26 (t, 1H, J = 7.8 Hz), 5.66 (m, 1H), 7.17−7.40 (m, 15H); ^{13}C NMR ($CDCl_3$) δ (major product) 21.0, 21.2, 54.5, 68.5, 68.6, 71.4, 72.8, 73.0, 81.4, 119.7, 126.4−128.6, 137.9, 138.1, 140.2; MS m/z 460.4 (MH^+).

General Procedure D: Synthesis of (1*S*)-1-*C*-Alkyl-1,5-dideoxy-1,5-imino-D-glucitol. To a solution of precursor **15** (1 equiv) in MeOH were added 10% Pd/C (0.2 equiv) and two drops of 5 N aqueous HCl. The flask was purged 3× with Ar and then filled with H_2. After 48 h, the solids were removed by filtration, and the filtrate was concentrated under reduced pressure. The crude intermediate was then dissolved in a 9:1 (v/v) mixture of trifluoroacetic acid and H_2O (final concentrated ~0.15 M). The reaction mixture was stirred for 18 h at room temperature. The solvent was removed under reduced pressure by coevaporation with toluene (3×), the residual product was taken in MeOH (to a concentration of ~0.05 M), and CH_3COOH (1 equiv) and $NaBH_3CN$ (3 equiv) were added. After 12 h, the mixture was concentrated under reduced pressure. The crude product was filtered through Amberlyst ion-exchange resin IRA-400(OH^-) (elution with H_2O), and the filtrate was concentrated under reduced pressure. The residual product was purified by chromatography on Amberlyst ion-exchange resin IR-120(H^+) (loading, washing with H_2O, elution with aqueous ammonia (7.5% NH_4OH)); the fractions containing the product were pooled and concentrated under reduced pressure to afforded pure 1-*C*-alkyl-1,5-dideoxy-1,5-imino-D-glucitol.

(1*S*)-1-*C*-Butyl-1,5-dideoxy-1,5-imino-D-glucitol (22). Compound **15b** (170 mg, 0.31 mmol) was submitted to general procedure D, which provided **22** (41 mg, 60%) as a colorless oil: $[\alpha]^{20}_D$ +2 (c = 1.4, H_2O); ^{1}H NMR (CD_3OD) δ 0.90 (t, 3H, J = 6.3 Hz), 1.20−1.40 (m, 5H), 1.80−1.90 (m, 1H), 2.36 (m, 1H), 2.52 (m, 1H), 2.94 (t, 1H, J = 9.2 Hz), 3.06 (t, 1H, J = 9.4 Hz), 3.17 (t, 1H, J = 9.2 Hz), 3.46 (dd, 1H, J = 8.2, 11 Hz), 3.90 (dd, 1H, J = 2.8, 10.7 Hz); ^{13}C NMR (CD_3OD) δ 14.4, 24.0, 29.0, 32.6, 60.7, 62.4, 63.6, 73.7, 76.6, 80.6; HR-FABMS (relative intensity) calcd for $C_{10}H_{22}NO_4$ (MH^+) m/z 220.1550, found 220.1548 (100).

(1*S*)-1-*C*-Ethyl-1,5-dideoxy-1,5-imino-D-glucitol (23). Compound **15c** (146 mg, 0.28 mmol) was submitted to general procedure D, which provided **23** (33 mg, 62%) as a colorless oil: $[\alpha]^{20}_D$ −2 (c = 0.3, H_2O); ^{1}H NMR (CD_3OD) δ 1.02 (t, 3H, J = 7.6 Hz), 1.66 (m, 1H), 1.96 (m, 1H), 2.89 (m, 1H), 3.03 (m, 1H), 3.31 (m, 2H), 3.50 (t, 1H, J = 9.5 Hz), 3.86 (m, 2H); ^{13}C NMR (CD_3OD) δ 10.5, 23.9, 58.7, 61.8, 62.1, 69.1, 72.8, 78.2; HR-FABMS (relative intensity) calcd for $C_8H_{18}NO_4$ (MH^+) m/z 192.12358, found 192.12389 (23).

(6*S*)-1,4-Di-*O*-benzyl-6-benzylamino-6-deoxy-2,3-*O*-isopropylidene-6-*C*-diethylphosphono-α-L-sorbofuranose (24a). Trimethylsilyl chloride (360 μL, 2.85 mmol) was added to a mixture of diethyl phosphite (360 μL, 2.85 mmol) and triethylamine (400 μL, 2.85 mmol) in anhydrous CH_2Cl_2 (24 mL) at 0 °C. The reaction mixture was stirred for 15 min, and then **13** (1 g, 2.05 mmol) in anhydrous CH_2Cl_2 (12 mL) was added at room temperature. The reaction was warmed to 40 °C during 45 min. The reaction mixture was diluted with

CH_2Cl_2 and washed with 2 M NaOH (2×) and water. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to provided homogeneous **24a** (1.17 g, 91%) as a yellow oil. For analysis, a small amount of **24a** was purified by silica gel chromatography (PE/AcOEt 2:1): $[\alpha]^{20}_D$ −3.4 (*c* 1.65, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.29 (m, 6H), 1.42 (s, 3H), 1.52 (s, 3H), 2.34 (br s, 1H), 3.45 (d, 1H, J = 7.6 Hz), 3.50 (d, 1H, J = 7.8 Hz), 3.65 (d, 1H, J = 11 Hz), 3.77 (d, 1H, J = 11 Hz), 3.85 (d, 1H, J = 13 Hz), 3.97 (d, 1H, J = 13 Hz), 4.08−4.18 (m, 4H), 4.29 (d, 1H, J = 2.8 Hz), 4.50 (ddd, 1H, J = 2.8, 4, 10.4 Hz), 4.53 (d, 1H, J = 12.3 Hz), 4.57 (d, 1H, J = 4.7 Hz), 4.62 (d, 1H, J = 1.6 Hz), 4.65 (d, 1H, J = 12.3 Hz), 7.21−7.27 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 16.3 (d, J = 5.9 Hz), 26.6, 27.6, 53.2 (d, J = 151.3 Hz), 53.5, 53.6, 62.4, 70.3, 71.7, 73.6, 80.0, 81.7, 82.6, 112.3, 113.2, 126.7, 127.3, 127.5, 127.5, 128.1, 128.3, 128.3, 128.6, 137.8, 138.1, 140.1; ^{31}P NMR (121.5 MHz, $CDCl_3\{^1H\}$) δ 25.82 (s); MS *m*/*z* 626.5 (MH^+). Anal. Calcd for $C_{34}H_{44}NO_8P$: C, 65.27; H, 7.09, N, 2.24; P, 4.95. Found: C, 65.13; H, 7.16; N, 2.29; P, 5.07.

(6*R*)-1,4-Di-*O*-benzyl-6-benzylamino-6-deoxy-2,3-*O*-isopropylidene-6-*C*-diethylphosphono-α-L-sorbofuranose (24b). To a solution of **13** (490 mg, 1 mmol) were added diethyl phosphite (175 μL, 1.36 mmol) and $ZrCl_4$ (27 mg, 0.11 mmol) in anhydrous CH_3CN (3 mL), at 0 °C. The reaction mixture was stirred for 1.5 h at room temperature. Water (5 mL) was added, and the product was extracted in CH_2Cl_2 (2×). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. A ^{31}P NMR spectrum taken before purification indicated a de of 80%. Purification of the crude product by silica gel chromatography (PE/AcOEt 3:1−2:1) provided **24b** (475 mg, 76%) as a colorless oil: $[\alpha]^{20}_D$ −15 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.29 (m, 6H), 1.42 (s, 3H), 1.53 (s, 3H), 2.33 (br s, 1H), 3.62 (d, 1H, J = 9.7 Hz), 3.64 (d, 1H, J = 11 Hz), 3.66 (d, 1H, J = 9.7 Hz), 3.80 (d, 1H, J = 11 Hz), 4.00 (d, 1H, J = 14 Hz), 4.12 (d, 1H, J = 14 Hz), 4.13−4.30 (m, 4H), 4.58 (d, 1H, J = 12.3 Hz), 4.58−4.72 (m, 3H), 4.71 (d, 1H, J = 12.3 Hz), 4.73 (s, 1H), 7.14−7.35 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 16.3, 26.6, 27.6, 53.2 (d, J = 160.5 Hz), 53.5, 53.6, 62.4, 70.3, 71.7, 73.6, 80.0, 81.7, 82.6, 112.3, 113.2, 126.7, 127.3, 127.5, 127.5, 128.1, 128.3, 128.3, 128.6, 137.8, 138.1, 140.1; ^{31}P NMR (121.5 MHz, $CDCl_3\{^1H\}$) δ 24.02 (s, 1P), 25.82 (s, 0.082P) de = 86%; MS *m*/*z* 626.5 (MH^+). Anal. Calcd for $C_{34}H_{44}NO_8P$: C, 65.27; H, 7.09, N, 2.24. Found: C, 64.56; H, 7.21; N, 2.30.

(1*S*)-1-*C*-Diethylphosphono-1-deoxynojirimycin (25). To a solution of **24a** (100 mg, 0.16 mmol) in TFA/H_2O 9:1 (3 mL) was added 10% Pd/C (0.2 equiv). The flask was purged three times with argon and then filled with H_2. After 70 h, the crude mixture was filtered using MeOH, and the filtrate was concentrated under reduced pressure. The crude product was filtered through Amberlyst ion-exchange resin IRA-400 (OH^-) (elution with H_2O), and the filtrate was concentrated under reduced pressure to provided **25** (33 mg, 70%) (de 80%) as a colorless oil: ^{1}H NMR (CD_3OD) δ 1.32 (t, 6H, J = 7.1 Hz), 2.53 (dt, 1H, J = 3, 11 Hz), 2.90 (dd, 1H, J = 10, 11.7 Hz), 3.07 (t, 1H, J = 9 Hz), 3.20 (dt, 1H, J = 1.2, 8.8 Hz), 3.43 (dd, 1H, J = 2.9, 8.6 Hz), 3.49 (t, 1H, J = 9 Hz), 3.90 (dd, 1H, J = 3.2, 11 Hz), 4.17 (m, 4H); ^{13}C NMR (CD_3OD) δ 16.7 (d, J = 5.4 Hz), 58.0 (d, J = 158.1 Hz), 63.3, 63.5, 63.6, 64.2−64.5, 72.9 (d, J = 5.4 Hz), 73.4, 80.8 (d, J = 19.4 Hz); ^{31}P NMR (121.5 MHz, $CD_3OD\{^1H\}$) δ 25.63 (s, 1P), 26.58 (s, 0.11P); HR-FABMS (relative intensity) calcd for $C_{10}H_{23}NO_7P$ (MH^+) *m*/*z* 300.12121, found 300.12050 (100).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for selected compounds (**10**, **13**, **14a**, **15a**, **16b**, **17c**, **18**, **19**, and **22**−**25**). This material is available free of charge via the Internet at http://pubs.acs.org.

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