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A convenient synthesis of iminosugar-*C*-glycosides via organometallic addition to *N*-benzyl-*N*-glycosylhydroxylamines

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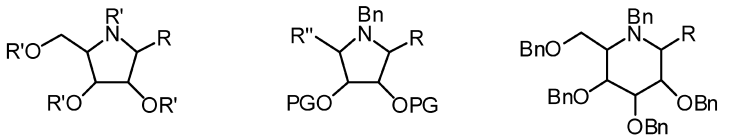
Abstract—*N*-Benzyl-*N*-glycosylhydroxylamines were prepared in very good yield via condensation of furanoses and pyranoses with *N*-benzylhydroxylamine at 110°C for 30 min under solvent-free conditions. These anomeric sugar-hydroxylamines exist in equilibrium with the open-chain nitrone form. In fact upon treatment with various organometallic reagents, the corresponding adducts were obtained with good to high diastereoselectivity. These adducts were converted into iminosugar-*C*-glycosides by reductive dehydroxylation and intramolecular cyclization.

1. Introduction

Interest in polyhydroxylated pyrrolidines and piperidines (iminosugars) for their biological properties as glycosidase and glycosyltransferase inhibitors has been extensively documented.[1] Glycosidases and glycosyltransferases act on the glycosidic linkage of oligosaccharides and glycopeptides by stabilizing an intermediate oxonium ion, thus facilitating the lysis and modification of the anomeric center.[2] The ability of these iminosugars to function as glycosidase and glycosyltransferase inhibitors is generally attributed to their potency in mimicking the oxonium ion intermediate which participates in both enzymatic reactions. Glycosidases are involved in a wide range of important biological processes, such as intestinal digestion, post-translational processing of glycoproteins and lysosomal catabolism of glycoconjugates. Glycosidase inhibitors have potential application in the treatment of viral infections,[3] cancer,[4] and diabetes and other metabolic disorders.[5]

In earlier studies of our group we developed a stereoselective chemical synthesis of amino and iminosugars based on the nucleophilic addition to chiral nitrones.[6] Subsequently we have found that *N*-benzyl-*N*-glycosylhydroxylamines (hidden *N*-benzylnitrones) derived from sugars are suitable substrates for the synthesis of iminosugars.[7] In fact, in recent papers we have demonstrated the ability of several *N*-benzyl-*N*-furanosylhydroxylamines, to act as versatile synthetic precursors of pyrrolidine homoazasugars **1** (Fig. 1) by their reaction with 2-lithiothiazole followed by suitable transformations of resulting adducts. The formyl aza-*C*-glycosides **2**, the precursor of **1**, were employed for the synthesis of more complex derivatives, namely, aza-*C*-disaccharides.[7b,8]

As an extension of our previous work, we would like to report here, a convenient synthesis of various fully protected C1 substituted iminosugars via the stereoselective addition of organometallic reagents to *N*-benzyl-*N*-glycosylhydroxylamines derived from furanoses and pyranoses. To this aim, starting from different sugars and changing the organometallic reagents, a variety of pyrrolidines and piperidines of type **3** and **4** were obtained with different saturated and unsaturated appendages R at the carbon adjacent to the nitrogen atom.



1 R = CH_2OH, R' = H
2 R = CHO, R' = Bn

3 R = carbon chain
R'' = H or CH_2OBn

4 R = carbon chain

Figure 1.

Keywords: nitrones; *N*-benzyl-*N*-glycosylhydroxylamines; iminosugars; glycosidase inhibitors; organometallic addition.
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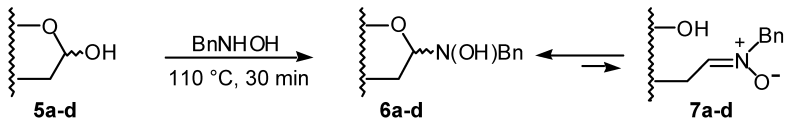
Biological evaluations have suggested that the presence of short *N*- or *C*-alkyl appendages often leads to an increase in either potency and/or specificity of the iminosugar,[9] as in the case of some α-L-fucosidase inhibitors.[10] The above suggestions provided growing interest in the synthesis of C1 substituted iminosugars.[11]

2. Results and discussion

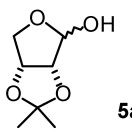
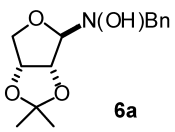
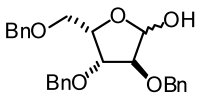
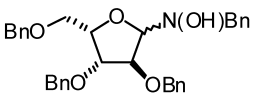
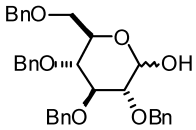
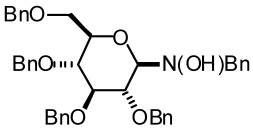
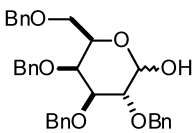
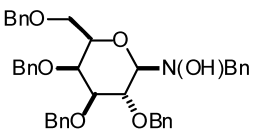
As a first objective of this work, we applied our improved synthesis of sugar hydroxylamines[7b] to prepare various derivatives on a multigram scale starting from the readily available sugars **5a-d** (Table 1). Heating these compounds with 1.5 equiv. of *N*-benzylhydroxylamine for 30 min at 110°C in the absence of solvent, the corresponding *N*-benzyl-*N*-glycosylhydroxylamines **6a-d** were obtained. Pure products were isolated at the end of the reaction by crystallization or flash chromatography. The yields (75–82%) were well comparable with those reported by others,[12] employing more complex reaction conditions, such as highly boiling solvents or Lewis acids and long reaction time. The configuration at the anomeric center of **6a-d** was assigned on the base of their spectroscopic properties. The anomeric signals for **6a** ($J_{1,2}$=0 Hz), **6c** ($J_{1,2}$=9.0 Hz) and **6d** ($J_{1,2}$=8.5 Hz) were consistent with the presence of β-anomers, according to the known spectral properties of β-glycosyl derivatives.[13] Only compound **6b** afforded a mixture of α and β anomers with the open-chain tautomer **7b** in approximately 15%. The presence of the nitrone **7b** was substantiated by its ^{1}H NMR spectrum showing a doublet at δ 6.74 ppm corresponding to the C*H* proton of the nitrone group. This spectroscopic evidence confirmed the assumption that *N*-glycosylhydroxylamines exist as anomeric mixtures in equilibrium through the nitrone form, as already observed.[7,12] Nevertheless, in the other cases the open-chain tautomer was not detectable by NMR spectroscopy, whereas the thermodynamically most stable glycosylhydroxylamine was present as a single compound.

With the desired glycosylhydroxylamines **6a-d** in hand, in order to synthesize iminosugar-*C*-glycosides, we decided to investigate their reactivity toward various types of organometallic nucleophiles,[14] particularly 2-lithiothiazole, 1-trimethylsilylethynyllithium and allylmagnesium bromide. The results of the addition reactions are summarized in Table 2. In all experiments 3.5 equiv. of organometallic reagent in diethyl ether or THF were added dropwise to a cooled solution (−75 or −30°C) of the glycosylhydroxylamines **6** in THF. The resulting mixtures were stirred for a few hours to provide, after the usual aqueous work-up, mixtures of *syn* and *anti* hydroxylamines **8-17** in good yields (65–95%). On the contrary, if a stoichiometric amount of organometallic reagent was used, the reactions did not go to completion. The diastereomeric ratios of the products were determined by ^{1}H NMR analysis of the crude mixtures. The configuration of the newly created stereocenters was assigned on the base of NOE experiments, after the

Table 1. Synthesis of *N*-benzyl-*N*-glycosylhydroxylamines from the corresponding sugars

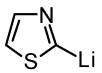
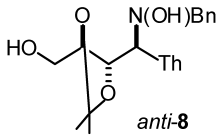
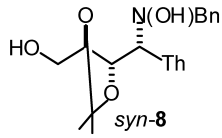
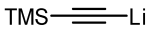
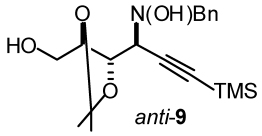
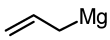
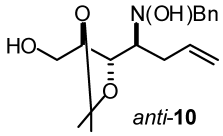
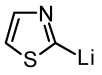
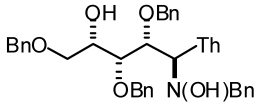
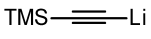
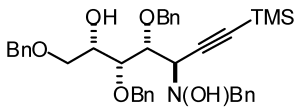
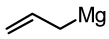
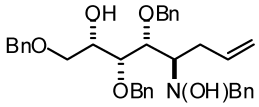
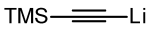
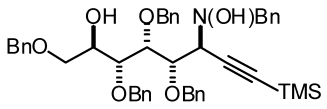
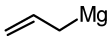
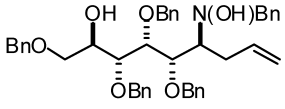
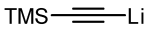
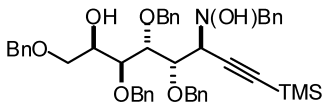
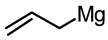
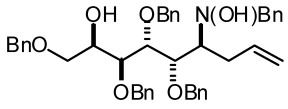


5a-d **6a-d** **7a-d**

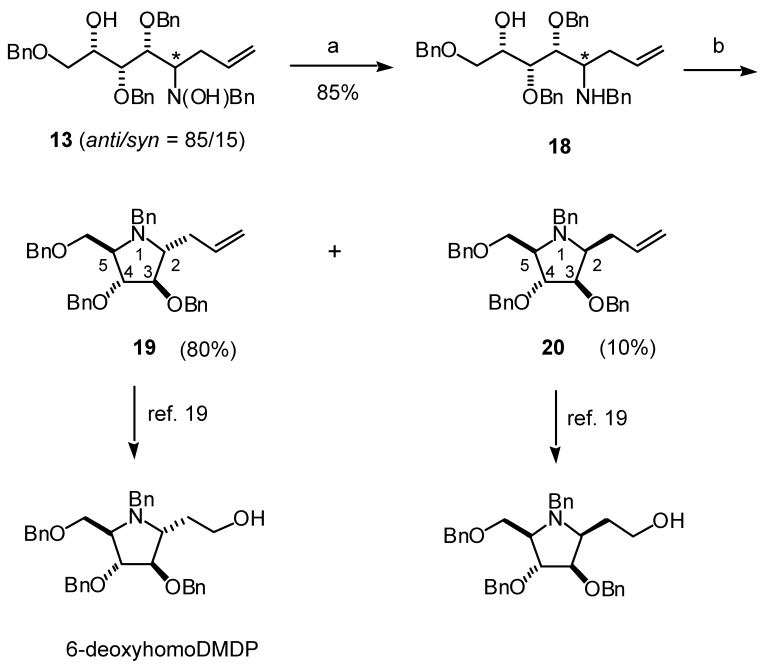
Sugar	Product	Yield[a] (%)	α/β[b]
 **5a**	 **6a**	81	0/100
 **5b**	 **6b**	82	Not determined[c]
 **5c**	 **6c**	75	0/100
 **5d**	 **6d**	75	0/100

[a] Isolated chemical yield after crystallization or flash chromatography.
[b] The ratio was determined by ^{1}H NMR analysis of the crude product.
[c] See text and Section 4.

Table 2. Addition of organometallic reagents (RM) to *N*-benzyl-*N*-glycosylhydroxylamines

Entry	Glycosyl-hydroxylamine	RM	Yield[a] (%)	Products		*anti*/*syn*[b]
1	**6a**		65	 *anti*-**8**	 *syn*-**8**	98/2
2	**6a**		72	 *anti*-**9**	*syn*-**9**	70/30
3	**6a**		95	 *anti*-**10**	*syn*-**10**	96/4
4	**6b**		72	 *anti*-**11**	*syn*-**11**	80/20
5	**6b**		82	 *anti*-**12**	*syn*-**12**	90/10
6	**6b**		80	 *anti*-**13**	*syn*-**13**	85/15
7	**6c**		85	 *anti*-**14**	*syn*-**14**	85/15
8	**6c**		85	 *anti*-**15**	*syn*-**15**	50/50
9	**6d**		85	 *anti*-**16**	*syn*-**16**	75/25
10	**6d**		90	 *anti*-**17**	*syn*-**17**	50/50

[a] Isolated chemical yield of the mixture after flash chromatography.
[b] The diastereomeric ratio was determined by ^{1}H NMR on the crude mixture. Th=2-thiazolyl; TMS=trimethylsilyl.



Scheme 1. *Reagents and conditions*: (a) $(AcO)_2Cu$, Zn, AcOH, H_2O, 70°C; (b) MsCl, pyridine, rt.

conversion of the hydroxylamines **8**-**17** into the final cyclic compounds. The reactions of **6a** and **6b** showed good levels of diastereoselectivity with organolithium (entries 1, 2, 4 and 5) as well as organomagnesium (entries 3 and 6) reagents. Also, the reactions of the pyranosylhydroxylamines **6c** and **6d** with 1-trimethylsilylethynyllithium proceeded with good diastereofacial selectivity (entries 7 and 9). In contrast, both **6c** and **6d** were found to be unreactive toward 2-lithiothiazole and afforded a 1:1 mixture of diastereomeric adducts with allylmagnesium bromide (entries 8 and 10). The stereoselectivity degree was not improved by lowering the reaction temperature to −50°C, while at this temperature the yields dramatically decreased (40–45%). The same poor diastereoselectivity has been previously observed for additions of allylmagnesium reagents to aldimine or α-alkoxy ketones.[11h,15]

The next step of this work, was the conversion of hydroxylamines **8**-**17** into iminosugar-*C*-glycosides. As an example, this transformation is illustrated for compound **13** (Scheme 1). The *syn* and *anti* mixture of hydroxylamines **13** was subjected to reductive dehydroxylation using zinc-copper (II) acetate as we have described in earlier work.[16] Because of the difficulty in separation, the resulting mixture of crude benzylamines **18** (85% yield, 95% pure by ^{1}H NMR) was converted into pyrrolidines **19** and **20** by treating at room temperature with 2.5 equiv. of methansulfonyl chloride[17] in pyridine and in presence of activated powdered molecular sieves. The cyclization products **19** and **20** were easily separated by flash chromatography (CH_2Cl_2) in 90% overall yield.

Examination of nuclear Overhauser effects (NOE) on **19** and **20** allowed the assignment of the configuration at the newly formed stereocenter C2, and at C5. The *trans*-relationship between the allyl and the CH_2OBn groups in **19** was assigned on the basis of a NOE of H2 with H4 and of H5 with H3, while the presence of a NOE between the allylic protons and the methylenic protons of the CH_2OBn confirmed the *cis*-relationship in the epimer **20**. Consequently, the stereochemistry at C5 was opposite to that in the starting sugar **5b**, as a result of the stereoselective intramolecular cyclization process occurring via an S_N2-like mechanism. Moreover, from this result it can be inferred that the major isomer (85%) in the mixture of hydroxylamines **13** is the *anti* adduct.[18] The same stereochemical outcomes were reported for the addition of 2-lithiothiazole to *N*-benzyl-*N*-furanosylhydroxylamines.[7] However, it is worth mentioning that the addition of nucleophiles to nitrones affords preferentially *syn* adducts, while *anti* adducts are obtained when the nitrones are precomplexed with Lewis acids.[6] Hence, also in this case the *anti* selectivity can be rationalized by a preferential conformation adopted by the open-chain nitrone form **7b** due to the magnesium coordination involving the nitrone oxygen and the free hydroxyl group (Fig. 2). Consequently the addition occurs to the less hindered side of this complex to give the *anti*-product.

It is worth noting that the pyrrolidines **19** and **20** have been recently employed for the synthesis of two natural iminosugars with specific glycosidase inhibitory properties: 6-deoxy-homo DMDP and the gulo-epimer.[19]

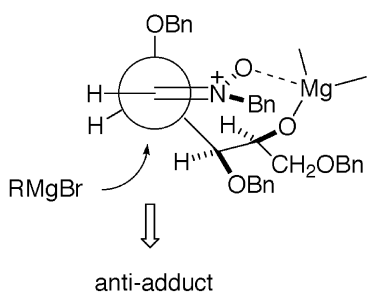
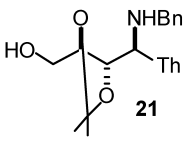
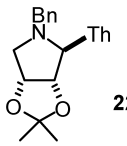
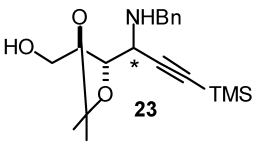
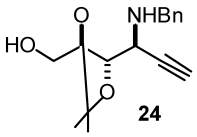
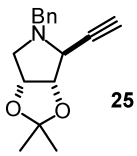
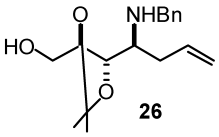
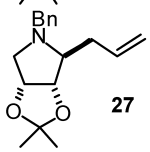
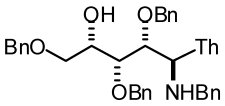
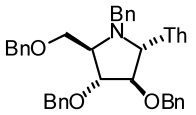
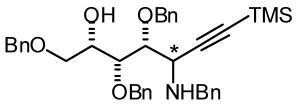
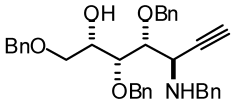
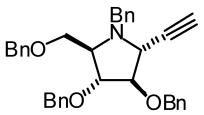
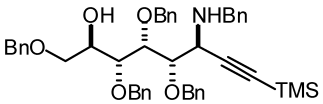
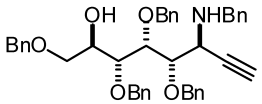
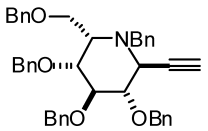
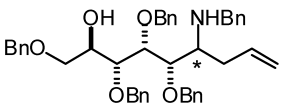
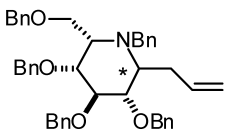
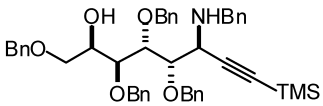
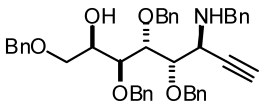
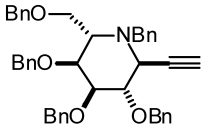
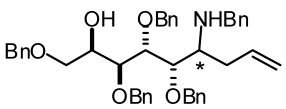
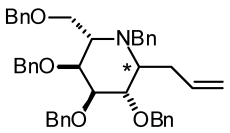


Figure 2.

Table 3. Conversion of hydroxylamines **8**-**12** and **14**-**16** into iminosugar-*C*-glycosides **22**, **25**, **27**, **29**, **32**, **35**, **37**, **40** and **42**

Hydroxylamine	Benzylamine	Ethynyl derivative	Iminosugar-*C*-glycoside	Yield[a] (%)
anti-**8**	 **21**		 **22**	63
anti-syn-**9**	 **23**	 **24**	 **25**	58
anti-**10**	 **26**		 **27**	80
anti-**11**	 **28**		 **29**	67[b]
anti-syn-**12**	 **30**	 **31**	 **32**	54
anti-syn-**14**	 **33**	 **34**	 **35**	48
anti-syn-**15**	 **36**		 **37**	57
anti-syn-**16**	 **38**	 **39**	 **40**	58
anti-syn-**17**	 **41**		 **42**	72

The minor *syn* isomers (not shown) of **24**, **31**, **33** and **38** were separated by flash chromatography (see Section 4).
[a] Overall yield of conversion.
[b] See Ref. 7b. Th=2-thiazolyl; TMS=trimethylsilyl.

By the same reaction sequence shown in Scheme 1, the *anti*-benzylhydroxylamines **8**, **10** and **11** were transformed into the protected iminosugar-*C*-glycosides **22** (63% yield), **27** (80% yield) and **29** (67% yield) (Table 3). The structure of these compounds was established on the basis of NOE experiments. On the contrary, the cyclic products **37** and **42**, (Table 3) were isolated as diastereomeric mixtures, since these compounds and their precursors **15**, **17**, **36**, and **41**, were inseparable by flash chromatography. Finally the conversion of the mixtures of *anti*–*syn*-benzylhydroxylamines

9, **12**, **14** and **16** into the iminosugar-*C*-glycosides **25**, **32**, **35** and **40**, required an additional step to remove the trimethylsilyl group (Table 3). Briefly, compounds **9**, **12**, **14** and **16** were reduced into the benzylamines **23**, **30**, **33**, and **38** which were treated with an aqueous solution of NaOH to afford the ethynyl derivatives **24**, **31**, **34** and **39** as pure major diastereomers. Finally, all these compounds were subjected to intramolecular cyclization with methanesulfonyl chloride to give the C1 substituted iminosugars **25**, **32**, **35** and **40** with good yields (65–91%), the structure of which was assigned by the aid of NOE experiments. In all cases the structure of these final cyclic products confirmed the *anti* selectivity of the addition of 1-trimethylsilylethynyllithium to the glycosylhydroxylamines **6a-d**.

3. Conclusion

In summary, our synthetic strategy based on the stereoselective addition of organometallic reagents onto *N*-benzyl-*N*-glycolsylhydroxylamines followed by intramolecular cyclization, provides an efficient and practical access to various fully protected iminosugar-*C*-glycosides. These compounds can be regarded as multifunctional key intermediates for further derivatizations, since they possess as substituents, allyl, ethynyl and thiazolyl groups, which are easily convertible in other functional groups. Finally, the stereochemistry at the newly created stereocenter appears to be reproducible, so that employing different *N*-alkyl-*N*-glycosylhydroxylamines and other types of functionalized nucleophiles a larger collection of iminosugar-*C*-glycosides of predictable configuration could be obtained starting from simple precursors.

4. Experimental

4.1. General

All moisture-sensitive reactions were performed under a nitrogen atmosphere using oven-dried glassware. Solvents were dried over standard drying agent[20] and freshly distilled prior to use. Commercially available powdered 4 Å molecular sieves (5 μm average particle size) were used without further activation. Reactions were monitored by TLC on silica gel 60 F_{254} with detection by charring with sulfuric acid, or alcoholic solutions of ninhydrin. Flash column chromatography[21] was performed on silica gel 60 (230–400 mesh). Melting points were determined with a capillary apparatus. Optical rotations were measured at 20±2°C in the stated solvent; $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Infrared spectra were recorded in KBr pellets on a Nicolet 510 P FT-IR instrument. ^{1}H (300 or 400 MHz) and ^{13}C (75 MHz) NMR spectra were recorded in $CDCl_3$ solutions at room temperature. Assignments were aided by homo-two-dimensional experiments. MALDI-TOF mass spectra were acquired using α-cyano-4-hydroxycinnamic acid as the matrix. Glucopyranose **5c** was commercially available. Erythrofuranose **5a**,[22] galactopyranose **5d**,[23] benzylxylosylhydroxylamine **6b**,[7b] benzylhydroxylamine *anti*-**11**,[7b] benzylamine **28**[7b] and pyrrolidine **29**[7b] were synthesized as described.

4.2. General procedure for the synthesis of *N*-benzyl-*N*-glycosylhydroxylamines 6

A mixture of sugar **5** (20.0–30.0 mmol) and *N*-benzylhydroxylamine (1.2 equiv.) was stirred at 110°C for 45 min. The resulting residue was cooled to rt and purified by crystallization or by flash chromatography (*h*: 10 cm).

4.2.1. 1-(*N*-Benzylhydroxylamino)-2,3-*O*-isopropylidene-1-deoxy-β-D-erythrose (6a). Purification by flash chromatography afforded pure **6a** (81%) as a white solid: mp 93–94°C (cyclohexane); $[\alpha]_D^{20}=-70.0$ (*c* 1.1, $CHCl_3$). IR ν_{O-H} 3540 cm^{-1}. ^{1}H NMR (400 MHz) δ 7.40–7.25 (m, 5H, Ph), 4.92 (d, 1H, $J_{2,3}$=6.0 Hz, H-2), 4.87 (ddd, 1H, $J_{3,2}$=6.0 Hz, $J_{3,4a}$=4.0 Hz, $J_{3,4b}$=1.0 Hz, H-3), 4.73 (s, 1H, H-1), 4.65 (s, 1H, OH), 4.27 (dd, 1H, $J_{4a,3}$=4.0 Hz, $J_{4a,4b}$=9.5 Hz, H-4a), 4.08 and 3.88 (2d, 2H, *J*=13.5 Hz, PhCH_2N), 4.07 (dd, 1H, $J_{4b,3}$=1.0 Hz, $J_{4b,4a}$=9.5 Hz, H-4b), 1.50 and 1.35 (2 s, 6H, 2CH_3). ^{13}C NMR (75 MHz) δ 136.8, 129.5, 128.3, 127.4, 111.9, 99.4, 83.6, 81.0, 76.2, 59.2, 26.4, 24.7. MALDI-TOF MS (265.31): 266.5 (M+H), 288.4 (M+Na), 304.3 (M+K). Anal. calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.13; H, 7.37; N, 5.12.

4.2.2. 1-(*N*-Benzylhydroxylamino)-2,3,4,6-*O*-tetrabenzyl-1-deoxy-β-D-glucose (6c). Purification by crystallization from cyclohexane afforded pure **6c** (75%) as a white solid: mp 135–136°C; $[\alpha]_D^{20}=+21.1$ (*c* 0.8, $CHCl_3$). IR ν_{O-H} 3530 cm^{-1}. ^{1}H NMR (400 MHz) δ 7.40–7.15 (m, 25H, 5Ph), 5.02 and 4.77 (2d, 2H, *J*=11.0 Hz, PhCH_2), 4.94 and 4.82 (2d, 2H, *J*=11.5 Hz, PhCH_2), 4.83 and 4.57 (2d, 2H, *J*=11.0 Hz, PhCH_2), 4.60 (s, 2H, PhCH_2), 4.34 (s, 1H, OH), 4.24 and 4.07 (2d, 2H, *J*=13.0 Hz, PhCH_2N), 4.05 (d, 1H, $J_{1,2}$=9.0 Hz, H-1), 3.89 (dd, 1H, $J_{2,1}=J_{2,3}$=9.0 Hz, H-2), 3.78 (dd, 1H, $J_{6a,5}$=2.0 Hz, $J_{6a,6b}$=10.5 Hz, H-6a), 3.72 (dd, 1H, $J_{6b,5}$=5.0 Hz, $J_{6b,6a}$=10.5 Hz, H-6b), 3.66 (dd, 1H, $J_{3,2}=J_{3,4}$=9.0 Hz, H-3), 3.56 (dd, 1H, $J_{4,3}=J_{4,5}$= 9.0 Hz, H-4), 3.46 (ddd, 1H, $J_{5,4}$=9.0 Hz, $J_{5,6a}$=2.0 Hz, $J_{5,6b}$=5.0 Hz, H-5). ^{13}C NMR (75 MHz) δ 138.6, 138.5, 138.1, 138.0, 137.1, 129.0–127.3 (Ph), 92.5, 85.7, 78.0, 77.8, 76.3, 75.6, 74.9, 74.3, 73.3, 69.1, 60.2. MALDI-TOF MS (645.78): 646.2 (M+H), 668.1 (M+Na), 684.3 (M+K). Anal. calcd for $C_{41}H_{43}NO_6$: C, 76.25; H, 6.71; N, 2.17. Found: C, 76.35; H, 6.63; N, 2.29.

4.2.3. 1-(*N*-Benzylhydroxylamino)-2,3,4,6-*O*-tetrabenzyl-1-deoxy-β-D-galactose (6d). Purification by crystallization from cyclohexane afforded pure **6d** (75%) as a white solid: mp 92–93°C; $[\alpha]_D^{20}=+7.8$ (*c* 1.0, $CHCl_3$). IR ν_{O-H} 3530 cm^{-1}. ^{1}H NMR (400 MHz) δ 7.42–7.20 (m, 25H, 5Ph), 5.01 and 4.62 (2d, 2H, *J*=11.0 Hz, PhCH_2), 4.97 and 4.81 (2d, 2H, *J*=11.5 Hz, PhCH_2), 4.77 and 4.72 (2d, 2H, *J*=12.0 Hz, PhCH_2), 4.55 (s, 1H, OH), 4.51 and 4.46 (2d, 2H, *J*=12.0 Hz, PhCH_2), 4.25 (dd, 1H, $J_{2,1}=J_{2,3}$=8.5 Hz, H-2), 4.22 and 4.04 (2d, 2H, *J*=13.5 Hz, PhCH_2N), 4.06 (d, 1H, $J_{1,2}$=8.5 Hz, H-1), 3.92–3.89 (m, 1H, H-4), 3.65 (dd, 1H, $J_{6a,5}$=6.0 Hz, $J_{6a,6b}$=9.0 Hz, H-6a), 3.62 (dd, 1H, $J_{6b,5}$=6.0 Hz, $J_{6b,6a}$=9.0 Hz, H-6b), 3.59–3.52 (m, 2H, H-3, H-5). ^{13}C NMR (75 MHz) δ 138.8, 138.7, 138.5, 137.8, 137.3, 129.0–127.2 (Ph), 93.0, 83.2, 75.4, 74.7, 74.6, 74.3, 73.5, 73.4, 72.8, 68.8, 60.0. MALDI-TOF MS (645.78): 646.8 (M+H),

668.4 (M+Na), 684.7 (M+K). Anal. calcd for $C_{41}H_{43}NO_6$: C, 76.25; H, 6.71; N, 2.17. Found: C, 76.38; H, 6.92; N, 2.05.

4.3. General procedure for the addition of 2-lithiothiazole to *N*-benzyl-*N*-glycosylhydroxylamines 6

To a cooled (−78°C) and stirred solution of *n*-BuLi (3.5 equiv. of a 1.6 M solution in hexane) in dry Et_2O (0.25 M) was added dropwise a solution of freshly distilled 2-bromothiazole (3.5 equiv.) in dry Et_2O (0.8 M). The rate of addition was adjusted so as to keep the temperature of the reaction mixture below −70°C. After the pale yellow solution of 2-lithiothiazole had been stirred at this temperature for 20 min, a solution of *N*-benzyl-*N*-glycosylhydroxylamine **6** (1.00 mmol) in dry THF (0.2 M) was added slowly while the temperature of the mixture was maintained below −65°C. The reaction mixture was stirred at −70°C for 5 h, then aqueous phosphate buffer (20 mL, pH 7) was added, and the mixture was allowed to warm to rt. The layers were separated, and the aqueous layer was extracted with AcOEt (3×20 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated.

4.4. General procedure for the addition of 1-trimethylsilylethynyllithium to *N*-benzyl-*N*-glycosylhydroxylamines 6

To a cooled (−30°C) and stirred solution of ethynyltrimethylsilane (3.5 equiv.) in THF (0.25 M) was added *n*-BuLi (3.5 equiv. of a 1.6 M solution in hexane). After 30 min a solution of *N*-benzyl-*N*-glycosylhydroxylamine **6** (1.00 mmol) in dry THF (0.3 M) was added. The resulting mixture was stirred at this temperature for 3.5 h, then treated with aqueous phosphate buffer (20 mL, pH 7) and allowed to warm to rt. The layers were separated, and the aqueous layer was extracted with AcOEt (3×20 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated.

4.5. General procedure for the addition of allylmagnesium bromide to *N*-benzyl-*N*-glycosylhydroxylamines 6

To a cooled (−30°C) and stirred solution of *N*-benzyl-*N*-glycosylhydroxylamine **6** (1.00 mmol) in dry THF (0.3 M) was added a solution of freshly prepared allylmagnesium bromide (3.5 equiv. of a 1.0 M solution in Et_2O). The resulting mixture was stirred at this temperature for 3.5 h, then treated with aqueous phosphate buffer (20 mL, pH 7) and allowed to warm to rt. The layers were separated, and the aqueous layer was extracted with AcOEt (3×20 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated.

4.5.1. (2*R*,3*S*,4*R*) and (2*R*,3*S*,4*S*)-4-*N*-Benzylhydroxylamino-2,3-*O*-isopropylidene-4-(2-thiazolyl)-1,2,3-butanetriol (*anti*-8 and *syn*-8).

Crude **8** was a 98/2 mixture of 4*S*/4*R* epimers (by ^{1}H NMR). Purification by crystallization from cyclohexane afforded pure *anti*-**8** (60% yield) as a white solid: mp 179–180°C; $[\alpha]_D^{20}=-10.3$ (*c* 0.4, $CHCl_3$). IR ν_{O-H} 3500–3200 cm^{-1}. ^{1}H NMR (300 MHz) δ 7.94 and 7.49 (2d, 2H, *J*=3.2 Hz, Th), 7.43–7.25 (m, 5H, Ph), 4.94 (dd, 1H, $J_{3,2}$=5.5 Hz, $J_{3,4}$=9.5 Hz, H-3), 4.52–4.42 (m, 2H, H-2, OH), 4.46 (d, 1H, $J_{4,3}$=9.5 Hz, H-4), 3.90 and 3.76 (2d, 2H, *J*=12.5 Hz, PhCH_2N), 3.75 (dd, 1H, $J_{1a,1b}$=12.0 Hz, $J_{1a,2}$=5.0 Hz, H-1a), 3.64 (dd, 1H, $J_{1b,1a}$=12.0 Hz, $J_{1b,2}$=8.5 Hz, H-1b), 1.18 and 1.15 (2 s, 6H, 2CH_3). ^{13}C NMR (75 MHz) δ 165.1, 141.7, 135.1, 129.7, 128.5, 128.0, 120.0, 108.5, 77.6, 76.9, 64.7, 62.0, 60.1, 27.6, 25.0. MALDI-TOF MS (350.43): 351.3 (M+H), 373.1 (M+Na), 389.3 (M+K). Anal. calcd for $C_{17}H_{22}N_2O_4S$: C, 58.27; H, 6.33; N, 7.99. Found: C, 58.09; H, 6.41; N, 7.85.

4.5.2. (2*R*,3*S*,4*S*) and (2*R*,3*S*,4*R*)-4-*N*-Benzylhydroxylamino-2,3-*O*-isopropylidene-4-(1-trimethylsilylethynyl)-1,2,3-butanetriol (*anti*-9 and *syn*-9).

Crude **9** was a 70/30 mixture of 4*S*/4*R* epimers (by ^{1}H NMR). Purification by flash chromatography (3:1 cyclohexane–AcOEt) afforded the not separable syrup *anti-syn*-**9** in 72% yield. IR ν_{O-H} 3500–3200 cm^{-1}; $\nu_{C\equiv C}$ 2235 cm^{-1}. ^{1}H NMR (300 MHz, selected data) δ 7.42–7.30 (m, 5H, Ph), 6.05–5.80 (m, 0.7H, OH), 5.60 (s, 0.3H, OH), 4.55 (dd, 0.3H, $J_{3,2}$=6.0 Hz, $J_{3,4}$=7.5 Hz, H-3), 4.42 (dd, 0.7H, $J_{3,2}$=6.0 Hz, $J_{3,4}$=9.0 Hz, H-3), 4.05 and 3.93 (2d, 1.4H, *J*=12.5 Hz, PhCH_2N), 3.68 (dd, 0.3H, $J_{1a,1b}$=12.0 Hz, $J_{1a,2}$=7.0 Hz, H-1a), 3.51 (dd, 0.7H, $J_{1a,1b}$=12.0 Hz, $J_{1a,2}$=6.0 Hz, H-1a), 3.30 (dd, 0.7H, $J_{1b,1a}$=12.0 Hz, $J_{1b,2}$=8.5 Hz, H-1b), 1.50 and 1.40 (2 s, 3H, CH_3), 1.39 and 1.38 (2 s, 3H, CH_3), 0.30 and 0.25 (2 s, 9H, 3CH_3). MALDI-TOF MS (363.52): 364.5 (M+H), 386.2 (M+Na), 402.4 (M+K).

4.5.3. (2*R*,3*S*,4*S*) and (2*R*,3*S*,4*R*)-4-*N*-Benzylhydroxylamino-2,3-*O*-isopropylidene-5-vinyl-1,2,3-pentanetriol (*anti*-10 and *syn*-10).

Crude **10** was a 96/4 mixture of 4*S*/4*R* epimers (by ^{1}H NMR). Purification by crystallization from cyclohexane afforded pure *anti*-**10** (88% yield) as a white solid: mp 128–129°C; $[\alpha]_D^{20}=-8.1$ (*c* 0.9, $CHCl_3$). IR ν_{O-H} 3500–3200 cm^{-1}; $\nu_{C=C}$ 1634 cm^{-1}. ^{1}H NMR (400 MHz) δ 7.40–7.23 (m, 5H, Ph), 6.15–6.00 (m, 2H, H-2′, OH), 5.26–5.17 (m, 2H, H-1′a, OH), 5.11–5.06 (m, 1H, H-1′b), 4.31 (dd, 1H, $J_{3,2}$=5.5 Hz, $J_{3,4}$=9.5 Hz, H-3), 4.14 (ddd, 1H, $J_{2,1a}$=9.0 Hz, $J_{2,1b}$=4.5 Hz, $J_{2,3}$=5.5 Hz, H-2), 3.98 and 3.81 (2d, 2H, *J*=13.0 Hz, PhCH_2N), 3.45 (dd, 1H, $J_{1a,1b}$=11.5 Hz, $J_{1a,2}$=9.0 Hz, H-1a), 3.32 (dd, 1H, $J_{1b,1a}$=11.5 Hz, $J_{1b,2}$=4.5 Hz, H-1b), 3.18–3.12 (m, 1H, H-4), 2.82–2.74 (m, 1H, H-5a), 2.65–2.57 (m, 1H, H-5b), 1.38 and 1.32 (2s, 6H, 2CH_3). ^{13}C NMR (75 MHz) δ 137.2, 136.1, 129.9, 128.4, 127.8, 116.0, 107.6, 77.8, 77.3, 76.9, 76.5, 64.6, 60.6, 60.2, 30.5, 27.8, 25.2. MALDI-TOF MS (307.38): 308.2 (M+H), 330.4 (M+Na), 346.6 (M+K). Anal. calcd for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.38; H, 8.35; N, 4.54.

4.5.4. (2*S*,3*R*,4*R*,5*R*) and (2*S*,3*R*,4*R*,5*S*)-5-*N*-Benzylhydroxylamino-1,3,4-*O*-tribenzyl-5-(1-trimethylsilylethynyl)-1,2,3,4-pentanetetrol (*anti*-12 and *syn*-12).

Crude **12** was a 90/10 mixture of 5*R*/5*S* epimers (by ^{1}H NMR). Purification by flash chromatography (3:1 cyclohexane–AcOEt) afforded the not separable syrup *anti-syn*-**12** in 82% yield. IR ν_{O-H} 3500–3200 cm^{-1}; $\nu_{C\equiv C}$ 2245 cm^{-1}. ^{1}H NMR (300 MHz, selected data for the major compound *anti*-**12**) δ 7.45–7.20 (m, 20H, 4Ph), 5.73 (s, 1H, OH), 4.77 and 4.62 (2d, 2H, *J*=11.0 Hz, PhCH_2), 4.53 (s, 2H, PhCH_2), 4.51 and 4.45 (2d, 2H, *J*=11.5 Hz, PhCH_2), 4.13 and 3.88 (2d, 2H, *J*=13.0 Hz, PhCH_2N), 4.07 (ddd, 1H, $J_{2,1a}$=5.0 Hz, $J_{2,1b}$=7.0 Hz, $J_{2,3}$=3.5 Hz, H-2),

4.00 (dd, 1H, $J_{3,2}$=3.5 Hz, $J_{3,4}$=8.0 Hz, H-3), 3.90 (dd, 1H, $J_{4,3}$=$J_{4,5}$=8.0 Hz, H-4), 3.86 (d, 1H, $J_{5,4}$=8.0 Hz, H-5), 3.56 (dd, 1H, $J_{1a,1b}$=9.5 Hz, $J_{1a,2}$=5.0 Hz, H-1a), 3.48 (dd, 1H, $J_{1b,1a}$=9.5 Hz, $J_{1b,2}$=7.0 Hz, H-1b), 0.26 (s, 9H, $3CH_3$). MALDI-TOF MS (623.85): 624.9 (M+H).

4.5.5. (2*S*,3*R*,4*R*,5*R*) and (2*S*,3*R*,4*R*,5*S*)-5-*N*-Benzylhydroxylamino-1,3,4-*O*-tribenzyl-6-vinyl-1,2,3,4-hexanetetrol (*anti*-13 and *syn*-13). Crude **13** was an 85/15 mixture of 5*R*/5*S* epimers (by ^{1}H NMR). Purification by flash chromatography (3:1 cyclohexane–AcOEt) afforded the not separable syrup *anti-syn*-**13** in 80% yield. IR ν_{O-H} 3500–3200 cm^{-1}; $\nu_{C=C}$ 1637 cm^{-1}.^{1}H NMR (300 MHz, selected data) δ 7.45–7.20 (m, 20H, 4Ph), 6.14–6.98 (m, 0.85H, H-2′), 5.89 (s, 0.85H, OH), 5.78–5.62 (m, 0.15H, H-2′), 5.55 (s, 0.15H, OH), 5.18–5.00 (m, 2H, H-1′a, H-1′b), 3.26–3.20 (m, 0.15H, H-5), 3.20–3.12 (m, 0.85H, H-5), 2.87–2.46 (m, 2H, H-6a, H-6b). MALDI-TOF MS (567.71): 568.8 (M+H).

4.5.6. (2*R*,3*R*,4*R*,5*S*,6*S*) and (2*R*,3*R*,4*R*,5*S*,6*R*)-6-*N*-Benzylhydroxylamino-1,3,4,5-*O*-tetrabenzyl-6-(1-trimethylsilylethynyl)-1,2,3,4,5-hexanepentol (*anti*-14 and *syn*-14). Crude **14** was an 85/15 mixture of 6*S*/6*R* epimers (by ^{1}H NMR). Purification by flash chromatography (3:1 cyclohexane–AcOEt) afforded the not separable syrup *anti-syn*-**14** in 85% yield. IR ν_{O-H} 3500–3200 cm^{-1}; $\nu_{C\equiv C}$ 2245 cm^{-1}. ^{1}H NMR (300 MHz, selected data) δ 7.42–7.15 (m, 25H, 5Ph), 5.06 (d, 0.15H, J=11.0 Hz, $PhCH_2$), 5.04 (d, 0.85H, J=11.0 Hz, $PhCH_2$), 3.66 (dd, 0.85H, $J_{1a,1b}$=9.5 Hz, $J_{1a,2}$=3.5 Hz, H-1a), 3.55 (dd, 0.85H, $J_{1b,1a}$=9.5 Hz, $J_{1b,2}$=5.0 Hz, H-1b), 0.25 (s, 9H, $3CH_3$). MALDI-TOF MS (744.00): 745.5 (M+H).

4.5.7. (2*R*,3*R*,4*R*,5*S*,6*S*) and (2*R*,3*R*,4*R*,5*S*,6*R*)-6-*N*-Benzylhydroxylamino-1,3,4,5-*O*-tetrabenzyl-7-vinyl-1,2,3,4,5-heptanepentol (*anti*-15 and *syn*-15). Crude **15** was a 50/50 mixture of 6*S*/6*R* epimers (by ^{1}H NMR). Purification by flash chromatography (5:1 cyclohexane–AcOEt) afforded the not separable syrup *anti-syn*-**15** in 85% yield. IR ν_{O-H} 3500–3200 cm^{-1}; $\nu_{C=C}$ 1633 cm^{-1}. ^{1}H NMR (300 MHz, selected data) δ 7.40–7.10 (m, 25H, 5Ph), 6.06–5.95 (m, 0.5H, H-2′), 5.68–5.56 (m, 0.5H, H-2′), 5.39 (s, 1H, OH), 3.19–3.13 (m, 0.5H, H-6), 2.88–2.83 (m, 0.5H, H-6), 2.74–2.44 (m, 2H, H-7a, H-7b). MALDI-TOF MS (687.86): 688.8 (M+H).

4.5.8. (2*R*,3*S*,4*R*,5*S*,6*S*) and (2*R*,3*S*,4*R*,5*S*,6*R*)-6-*N*-Benzylhydroxylamino-1,3,4,5-*O*-tetrabenzyl-6-(1-trimethylsilylethynyl)-1,2,3,4,5-hexanepentol (*anti*-16 and *syn*-16). Crude **16** was a 75/25 mixture of 6*S*/6*R* epimers (by ^{1}H NMR). Purification by flash chromatography (4:1 cyclohexane–AcOEt) afforded the not separable syrup *anti-syn*-**16** in 85% yield. IR ν_{O-H} 3500–3200 cm^{-1}; $\nu_{C\equiv C}$ 2247 cm^{-1}. ^{1}H NMR (300 MHz, selected data) δ 7.45–7.15 (m, 25H, 5Ph), 5.20–5.38 (m, 1H, OH), 4.98 and 4.71 (2d, 1.5H, J=11.5 Hz, $PhCH_2$), 4.86 and 4.81 (2d, 0.5H, J=11.5 Hz, $PhCH_2$), 4.65 and 4.57 (2d, 1.5H, J=11.5 Hz, $PhCH_2$), 4.52 and 4.45 (2d, 1.5H, J=12.0 Hz, $PhCH_2$), 4.46 and 4.38 (2d, 1.5H, J=12.0 Hz, $PhCH_2$), 4.26 and 3.82 (2d, 1.5H, J=13.0 Hz, $PhCH_2N$), 3.54 (dd, 0.75H, $J_{1a,1b}$=9.0 Hz, $J_{1a,2}$=5.5 Hz, H-1a), 3.38 (dd, 0.25H, $J_{1a,1b}$=9.5 Hz, $J_{1a,2}$=7.0 Hz, H-1a), 0.28 (s, 2.25H, $3CH_3$), 0.25 (s, 6.75H, $3CH_3$). MALDI-TOF MS (744.00): 745.2 (M+H).

4.5.9. (2*R*,3*S*,4*R*,5*S*,6*S*) and (2*R*,3*S*,4*R*,5*S*,6*R*)-6-*N*-Benzylhydroxylamino-1,3,4,5-*O*-tetrabenzyl-7-vinyl-1,2,3,4,5-heptanepentol (*anti*-17 and *syn*-17). Crude **17** was a 50/50 mixture of 6*S*/6*R* epimers (by ^{1}H NMR). Purification by flash chromatography (5:1 cyclohexane–AcOEt) afforded the not separable syrup *anti-syn*-**17** in 90% yield. IR ν_{O-H} 3500–3200 cm^{-1}; $\nu_{C=C}$ 1635 cm^{-1}. ^{1}H NMR (300 MHz, selected data) δ 7.40–7.15 (m, 25H, 5Ph), 6.09–5.96 (m, 0.5H, H-2′), 5.74–5.61 (m, 0.5H, H-2′), 5.29 (s, 1H, OH) 3.06–2.98 (m, 0.5H, H-6), 2.88–2.95 (m, 0.5H, H-6), 2.80–2.45 (3 m, 2H, H-7a, H-7b). MALDI-TOF MS (687.86): 688.9 (M+H).

4.6. General procedure for the reduction of *N*-benzylhydroxylamines 8-17 into *N*-benzylamines 18, 21, 23, 26, 28, 30, 33, 36, 38 and 41

To a solution of $(AcO)_2Cu{\cdot}H_2O$ (20%) in AcOH (0.1 M) was added Zn dust (10 equiv.). The resulting suspension was vigorously stirred at rt for 10 min, then a solution of *N*-benzylhydroxylamine (**8**-**17**) in 3:1 AcOH–H_2O (0.2 M) was added and the mixture was warmed to 70°C for 1 h. After this time, the resulting suspension was filtered through Celite and the collected solution was neutralized with an aqueous solution of NaOH (3 M), extracted with AcOEt (3×10 mL) and washed with a saturated aqueous solution of EDTA (30 mL). The organic phase was dried (Na_2SO_4) and concentrated.

4.7. General procedure for the hydrolysis of trimethylsilyl group of compounds: 23, 30, 33 and 38. Synthesis of the ethynyl derivative: 24, 31, 34 and 39

To a stirred solution of trimethylsilyl ethynylbenzylamine (**23**, **30**, **33** and **38**) in 5:1 CH_3OH–Et_2O (0.05 M) was added a solution of NaOH (2 equiv. of a 1.0 M aqueous solution). The resulting mixture was stirred at rt for 1 h, then diluted with aqueous phosphate buffer and concentrated to remove CH_3OH. The residue was extracted with AcOEt, dried (Na_2SO_4) and concentrated.

4.8. General procedure for the cyclization reaction with methanesulfonyl chloride. Synthesis of iminosugar-*C*-glycosides: 19, 20, 22, 25, 27, 29, 32, 35, 37, 40 and 42

A mixture of *N*-benzylamine (**18**, **21**, **24**, **26**, **28**, **31**, **34**, **36**, **39** and **41**) in dry pyridine (0.1 M) and activated 4 Å powdered molecular sieves (200 mg/0.1 mmol) was stirred ar rt for 10 min and then treated with MsCl. The resulting suspension was stirred at rt (1–3 h) for the synthesis of pyrrolidines, and at 100°C (1–3 h) for the synthesis of piperidines, then filtered through Celite and concentrated.

4.8.1. (2*S*,3*R*,4*R*,5*R*) and (2*S*,3*R*,4*R*,5*S*)-5-*N*-Benzylamino-1,3,4-*O*-tribenzyl-6-vinyl-1,2,3,4-hexanetetrol (18). Compound **18** was an 85/15 mixture of 5*R*/5*S* epimers (by ^{1}H NMR), not separable by flash chromatography. Crude **18** (85% yield; ca. 95% pure by ^{1}H NMR) was used for the next reaction without further purification. ^{1}H NMR (300 MHz, selected data) δ 7.50–7.20 (m, 20H, 4Ph),

5.80–5.48 (m, 1H, H-2′), 5.20–5.05 (m, 2H, H-1′a, H-1′b), 3.10–3.20 (m, 0.15H, H-5), 3.08–2.96 (m, 0.85H, H-5), 2.62–2.20 (m, 2H, H-6a, H-6b). MALDI-TOF MS (551.72): 552.9 (M+H).

4.8.2. (2*R*,3*R*,4*R*,5*R*) and (2*S*,3*R*,4*R*,5*R*)-*N*-Benzyl-3,4-dibenzyloxy-5-benzyloxymethyl-2-(2-propenyl)pyrrolidine (19) and (20). Chromatography on silica gel (CH_2Cl_2) of the crude mixture afforded as first eluate the pyrrolidine **19** (80% yield) as a syrup: $[\alpha]_D^{20}=-24.0$ (*c* 0.6, $CHCl_3$). IR $\nu_{C=C}$ 1634 cm^{-1}. ^1H NMR (300 MHz) δ 7.42–7.20 (m, 20H, 4Ph), 5.84–5.69 (m, 1H, H-2′), 5.06–4.96 (m, 2H, H-1′a, H-1′b) 4.54 and 4.47 (2d, 2H, *J*=12.0 Hz, PhCH_2), 4.49 and 4.45 (2d, 2H, *J*=11.5 Hz, PhCH_2), 4.48 (s, 2H, PhCH_2), 4.06 and 3.73 (2d, 2H, *J*=14.0 Hz, PhCH_2N), 3.98 (dd, 1H, $J_{4,3}$=2.5 Hz, $J_{4,5}$=3.0 Hz, H-4), 3.86 (dd, 1H, $J_{3,2}$=4.0 Hz, $J_{3,4}$=2.5 Hz, H-3), 3.60 (dd, 1H, $J_{6a,5}$=5.0 Hz, $J_{6a,6b}$=9.5 Hz, H-6a), 3.56 (dd, 1H, $J_{6b,5}$=6.5 Hz, $J_{6b,6a}$=9.5 Hz, H-6b), 3.30–3.24 (ddd, 1H, $J_{5,4}$=3.0 Hz, $J_{5,6a}$=5.0 Hz, $J_{5,6b}$=6.5 Hz, H-5), 3.21–3.14 (m, 1H, H-2), 2.52–2.41 (m, 1H, H-3′a), 2.36–2.23 (m, 1H, H-3′b). ^{13}C NMR (75 MHz) δ 139.4, 138.4, 138.3, 135.2, 128.2–127.4 (Ph), 126.6, 117.0, 85.9, 87.7, 73.1, 71.3, 71.2, 69.4, 64.5, 64.2, 51.0, 32.4. MALDI-TOF MS (533.70): 534.5 (M+H). Anal. calcd for $C_{36}H_{39}NO_3$: C, 81.02; H, 7.37; N, 2.62. Found: C, 81.11; H, 7.45; N, 2.60.

Eluted next was the pyrrolidine **20** (10% yield) as a syrup: $[\alpha]_D^{20}=+32.0$ (*c* 0.7, $CHCl_3$). IR $\nu_{C=C}$ 1634 cm^{-1}. ^1H NMR (400 MHz) δ 7.38–7.15 (m, 20H, 4Ph), 5.77–5.65 (m, 1H, H-2′), 5.07–5.01 (m, 1H, H-1′a), 4.97–4.93 (m, 1H, H-1′b), 4.54 and 4.47 (2d, 2H, *J*=12.0 Hz, PhCH_2), 4.43 and 4.25 (2d, 2H, *J*=12.0 Hz, PhCH_2), 4.37 and 4.30 (2d, 2H, *J*=12.0 Hz, PhCH_2), 3.99 and 3.70 (2d, 2H, *J*=14.0 Hz, PhCH_2N), 3.88–3.87 (m, 1H, H-4), 3.77 (d, 1H, $J_{3,2}$=4.5 Hz, H-3), 3.31 (dd, 1H, $J_{6a,5}=J_{6a,6b}$=10.5 Hz, H-6a), 3.12–3.03 (m, 3H, H-2, H-5, H-6b), 2.52–2.43 (m, 1H, H-3′a), 2.35–2.27 (m, 1H, H-3′b). ^{13}C NMR (75 MHz) δ 139.2, 138.4, 138.1, 136.0, 129.2–127.3 (Ph), 126.8, 116.2, 82.3, 82.1, 72.7, 71.8, 71.5, 70.5, 68.9, 66.4, 58.2, 32.8. MALDI-TOF MS (533.70): 534.7 (M+H). Anal. calcd for $C_{36}H_{39}NO_3$: C, 81.02; H, 7.37; N, 2.62. Found: C, 81.20; H, 7.48; N, 2.53.

4.8.3. (2*R*,3*S*,4*R*)-4-*N*-Benzylamino-2,3-*O*-isopropylidene-4-(2-thiazolyl)-1,2,3-butanetriol (21). Crude **21** (syrup; 78% yield; ca. 95% pure by ^1H NMR) was used for the next reaction without further purification. ^1H NMR (300 MHz) δ 7.90 and 7.40 (2d, 2H, *J*=3.2 Hz, Th), 7.40–7.22 (m, 5H, Ph), 4.53 (ddd, 1H, $J_{2,1a}$=4.5 Hz, $J_{2,1b}$=9.5 Hz, $J_{2,3}$=5.5 Hz, H-2), 4.38 (dd, 1H, $J_{3,2}$=5.5 Hz, $J_{3,4}$=9.5 Hz, H-3), 4.22 (d, 1H, $J_{4,3}$=9.5 Hz, H-4), 3.84 (dd, 1H, $J_{1a,1b}$=11.5 Hz, $J_{1a,2}$=4.5 Hz, H-1a), 3.71 (dd, 1H, $J_{1b,1a}$=11.5 Hz, $J_{1b,2}$=9.5 Hz, H-1b), 3.72 and 3.64 (2d, 2H, *J*=12.0 Hz, PhCH_2N), 1.43 and 1.30 (2 s, 6H, 2CH_3). MALDI-TOF MS (334.43): 335.6 (M+H).

4.8.4. (2*R*,3*S*,4*R*)-*N*-Benzyl-3,4-*O*-isopropylidenoxy-2-(2-thiazolyl)pyrrolidine (22). Chromatography on silica gel (4:1 cyclohexane–AcOEt) afforded pure **22** (80% yield) as a white solid: mp 78–79°C (cyclohexane); $[\alpha]_D^{20}=+12.6$ (*c* 0.8, $CHCl_3$).^1H NMR (300 MHz) δ 7.80 (d, 1H, *J*=3.2 Hz, Th), 7.40–7.22 (m, 6H, Ph and Th), 4.85–4.76 (m, 2H, H-3, H-4), 4.31 (d, 1H, $J_{2,3}$=2.5 Hz, H-2), 3.95 and 3.60 (2d, 2H, *J*=13.0 Hz, PhCH_2N), 3.32 (dd, 1H, $J_{5a,4}$=5.0 Hz, $J_{5a,5b}$=11.0 Hz, H-5a), 2.79 (dd, 1H, $J_{5b,4}$=2.5 Hz, $J_{5b,5a}$=11.0 Hz, H-5b), 1.65 and 1.35 (2s, 6H, 2CH_3). ^{13}C NMR (75 MHz) δ 175.1, 142.6, 138.0, 128.9, 128.8, 127.8, 119.2, 110.1, 79.6, 77.8, 59.9, 58.9, 51.6, 27.9, 25.1. MALDI-TOF MS (316.42): 317.3 (M+H). Anal. calcd for $C_{17}H_{20}N_2O_2S$: C, 64.53; H, 6.37; N, 8.85. Found: C, 64.51; H, 6.48; N, 8.71.

4.8.5. (2*R*,3*S*,4*S*) and (2*R*,3*S*,4*R*)-4-*N*-Benzylamino-2,3-*O*-isopropylidene-4-(1-trimethylsilylethynyl)-1,2,3-butanetriol (23). Compound **23** was a 70/30 mixture of 4*S*/4*R* epimers (by ^1H NMR), not separable by flash chromatography. Crude **23** (90% yield; ca. 95% pure by ^1H NMR) was used for the next reaction without further purification. ^1H NMR (300 MHz, selected data) δ 7.40–7.30 (m, 5H, Ph), 4.21 (dd, 0.7H, $J_{3,2}$=6.0 Hz, $J_{3,4}$=8.0 Hz, H-3), 4.10 and 3.85 (2d, 1.4H, *J*=12.0 Hz, PhCH_2N), 4.08 and 3.86 (2d, 0.6H, *J*=12.0 Hz, PhCH_2N), 3.78 (d, 0.7H, $J_{4,3}$=8.0 Hz, H-4), 1.50 and 1.48 (2s, 3H, CH_3), 1.40 and 1.38 (2s, 3H, CH_3), 0.24 (s, 9H, 3CH_3). MALDI-TOF MS (347.52): 348.7 (M+H).

4.8.6. (2*R*,3*S*,4*S*)-4-*N*-Benzylamino-2,3-*O*-isopropylidene-4-ethynyl-1,2,3-butanetriol (24). Chromatography on silica gel (1:1 cyclohexane–AcOEt) of the crude mixture afforded as first eluate the ethynyl derivative **24** (71% yield) as a syrup contaminated by a small amount of the 4*R*-epimer (by ^1H NMR analysis). ^1H NMR (400 MHz) δ 7.40–7.25 (m, 5H, Ph), 4.38 (ddd, 1H, $J_{2,1a}$=4.5 Hz, $J_{2,1b}$=9.0 Hz, $J_{2,3}$=5.5 Hz, H-2), 4.17 (dd, 1H, $J_{3,2}$=5.5 Hz, $J_{3,4}$=9.0 Hz, H-3), 4.09 and 3.82 (2d, 2H, *J*=12.0 Hz, PhCH_2N), 3.79 (dd, 1H, $J_{1a,1b}$=12.0 Hz, $J_{1a,2}$=4.5 Hz, H-1a), 3.70 (dd, 1H, $J_{4,1'}$=2.0 Hz, $J_{4,3}$=9.0 Hz, H-4), 3.57 (dd, 1H, $J_{1b,1a}$=12.0 Hz, $J_{1b,2}$=9.0 Hz, H-1b), 2.50 (d, 1H, $J_{1',4}$=2.0 Hz, H-1′), 1.46 and 1.36 (2s, 6H, 2CH_3). MALDI-TOF MS (275.34): 276.4 (M+H), 298.2 (M+Na), 315.3 (M+K). Anal. calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.83; H, 7.55; N, 4.91.

Eluted next was the 4*R*-epimer of **24** (10% yield) as a syrup: $[\alpha]_D^{20}=-73.5$ (*c* 0.8, $CHCl_3$): ^1H NMR (300 MHz) δ 7.42–7.30 (m, 5H, Ph), 4.45 (dd, 1H, $J_{3,2}$=2.5 Hz, $J_{3,4}$=7.0 Hz, H-3), 4.27 (ddd, 1H, $J_{2,1a}$=4.5 Hz, $J_{2,1b}$=7.0 Hz, $J_{2,3}$=2.5 Hz, H-2), 4.12 and 3.86 (2d, 2H, *J*=12.5 Hz, PhCH_2N), 3.89 (dd, 1H, $J_{1a,1b}$=12.5 Hz, $J_{1a,2}$=4.5 Hz, H-1a), 3.68–3.62 (m, 2H, H-1b, H-4), 2.52 (d, 1H, $J_{1',4}$=2.5 Hz, H-1′), 1.50 and 1.40 (2s, 6H, 2CH_3). MALDI-TOF MS (275.34): 276.5 (M+H), 298.2 (M+Na), 315.5 (M+K). Anal. calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 70.08; H, 7.81; N, 5.04.

4.8.7. (2*S*,3*S*,4*R*)-*N*-Benzyl-3,4-*O*-2-ethynylpyrrolidine (25). Chromatography on silica gel (3:1 cyclohexane–AcOEt) afforded pure **25** (91% yield) as a white solid: mp 76–77°C (cyclohexane); $[\alpha]_D^{20}=+76.0$ (*c* 0.5, $CHCl_3$). IR $\nu_{C\equiv C-H}$ 3288 cm^{-1}; $\nu_{C\equiv C}$ 2100 cm^{-1}. ^1H NMR (400 MHz) δ 7.40–7.20 (m, 5H, Ph), 4.72 (dd, 1H, $J_{4,3}$=6.0 Hz, $J_{4,5b}$=4.5 Hz, H-4), 4.67 (d, 1H, $J_{3,4}$=6.0 Hz, H-3), 3.77 (d, 1H, $J_{2,1'}$=2.0 Hz, H-2), 3.76 and 3.72 (2d, 2H, *J*=13.0 Hz, PhCH_2N), 2.94 (d, 1H, $J_{5a,5b}$=11.0 Hz, H-5a), 2.64 (dd, 1H, $J_{5b,4}$=4.5 Hz, $J_{5b,5a}$=11.0 Hz, H-5b), 2.35 (d,

1H, $J_{1',2}$=2.0 Hz, H-1′) 1.55 and 1.30 (2s, 6H, $2CH_3$). ^{13}C NMR (75 MHz) δ 138.4, 128.5, 128.1, 126.9, 111.9, 84.7, 79.1, 78.0, 75.2, 58.8, 56.7, 54.6, 26.4, 25.3. MALDI-TOF MS (257.33): 258.0 (M+H). Anal. calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.51; H, 7.53; N, 5.15.

4.8.8. (2*R*,3*S*,4*S*)-4-*N*-Benzylamino-2,3-*O*-isopropylidene-5-vinyl-1,2,3-pentanetriol (26). Crude **26** (syrup; 90% yield; ca. 95% pure by ^1H NMR) was used for the next reaction without further purification. ^1H NMR (300 MHz) δ 7.40–7.25 (m, 5H, Ph), 5.94–5.79 (m, 1H, H-2′), 5.31–5.22 (m, 2H, H-1′a, H-1′b), 4.42–4.35 (m, 1H, H-2), 4.03 (dd, 1H, $J_{3,2}$=5.5 Hz, $J_{3,4}$=9.5 Hz, H-3), 3.90 and 3.71 (2d, 2H, J=12.0 Hz, PhCH_2N), 3.76–3.70 (m, 2H, H-1a, H-1b), 3.17–3.09 (m, 1H, H-4), 2.64–2.58 (m, 2H, H-5a, H-5b), 1.45 and 1.36 (2s, 6H, $2CH_3$). MALDI-TOF MS (291.39): 292.8 (M+H).

4.8.9. (2*S*,3*S*,4*R*)-*N*-Benzyl-3,4-*O*-isopropylidenoxy-2-(2-propenyl)pyrrolidine (27). Chromatography on silica gel (6:1 cyclohexane–AcOEt) afforded pure **27** (89% yield) as an oil: $[\alpha]_D^{20}$=+68.1 (*c* 0.6, $CHCl_3$). IR $\nu_{C=C}$ 1643 cm^{-1}. ^1H NMR (300 MHz) δ 7.40–7.20 (m, 5H, Ph), 5.98–5.82 (m, 1H, H-2′), 5.22–5.11 (m, 2H, H-1′a, H-1′b), 4.61 (ddd, 1H, $J_{4,3}$=7.0 Hz, $J_{4,5a}$=6.0 Hz, $J_{4,5b}$=4.5 Hz, H-4), 4.43 (dd, 1H, $J_{3,2}$=3.5 Hz, $J_{3,4}$=7.0 Hz, H-3), 4.00 and 3.46 (2d, 2H, J=13.0 Hz, PhCH_2N), 3.08 (dd, 1H, $J_{5a,4}$=6.0 Hz, $J_{5a,5b}$=10.0 Hz, H-5a), 2.86–2.79 (m, 1H, H-2), 2.51 (dd, 1H, $J_{5b,4}$=4.5 Hz, $J_{5b,5a}$=10.0 Hz, H-5b), 2.51–2.43 (m, 1H, H-3′a), 2.31–2.19 (m, 1H, H-3′b), 1.55 and 1.34 (2 s, 6H, $2CH_3$). ^{13}C NMR (75 MHz) δ 138.6, 134.5, 128.6, 128.1, 126.9, 117.2, 112.5, 83.6, 77.9, 67.7, 58.0, 56.8, 33.7, 27.1, 25.1. MALDI-TOF MS (273.37): 274.6 (M+H). Anal. calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.78; H, 8.63; N, 5.04.

4.8.10. (2*S*,3*R*,4*R*,5*R*) and (2*S*,3*R*,4*R*,5*S*)-5-*N*-Benzylamino-1,3,4-*O*-tribenzyl-5-(1-trimethylsilylethynyl)-1,2,3,4-pentanetetrol (30). Compound **30** was a 90/10 mixture of 5*R*/5*S*-epimers (by ^1H NMR), not separable by flash chromatography. Crude **30** (90% yield; ca. 95% pure by ^1H NMR) was used for the next reaction without further purification. ^1H NMR (300 MHz, selected data for the major 5*R*-epimer) δ 7.50–7.20 (m, 20H, 4Ph), 4.79 and 4.73 (2d, 2H, J=10.0 Hz, PhCH_2), 4.75 and 4.56 (2d, 2H, J=10.5 Hz, PhCH_2), 4.51 and 4.44 (2d, 2H, J=11.5 Hz, PhCH_2), 4.04 and 3.78 (2d, 2H, J=13.0 Hz, PhCH_2N), 3.98 (ddd, 1H, $J_{2,1a}$=$J_{2,1b}$=6.0 Hz, $J_{2,3}$=2.5 Hz, H-2), 3.93 (dd, 1H, $J_{3,2}$=2.5 Hz, $J_{3,4}$=6.0 Hz, H-3), 3.87 (dd, 1H, $J_{4,3}$=$J_{4,5}$=6.0 Hz, H-4), 3.72 (d, 1H, $J_{5,4}$=6.0 Hz, H-5), 3.56 (dd, 1H, $J_{1a,1b}$=9.5 Hz, $J_{1a,2}$=6.0 Hz, H-1a), 3.47 (dd, 1H, $J_{1b,1a}$=9.5 Hz, $J_{1b,2}$=6.0 Hz, H-1b), 0.22 (s, 9H, $3CH_3$). MALDI-TOF MS (607.85): 609.0 (M+H).

4.8.11. (2*S*,3*R*,4*R*,5*R*)-5-*N*-Benzylamino-1,3,4-*O*-tribenzyl-5-ethinyl-1,2,3,4-pentanetetrol (31). Chromatography on silica gel (3:1 cyclohexane–AcOEt) of the crude mixture afforded as first eluate the 5*S*-epimer of **31** (9% yield) as a syrup contaminated by a small amount of **31** (by ^1H NMR analysis). ^1H NMR (300 MHz) δ 7.45–7.15 (m, 20H, 4Ph), 4.71 and 4.64 (2d, 2H, J=11.0 Hz, PhCH_2), 4.53 and 4.48 (2d, 2H, J=12.0 Hz, PhCH_2), 4.53 and 4.43 (2d, 2H, J=12.0 Hz, PhCH_2), 4.10 and 3.78 (2d, 2H, J=12.0 Hz, PhCH_2N), 4.09 (ddd, 1H, $J_{2,1a}$=5.5 Hz, $J_{2,1b}$=9.0 Hz, $J_{2,3}$=1.0 Hz, H-2), 3.93 (dd, 1H, $J_{5,1'}$=2.5 Hz, $J_{5,4}$=1.0 Hz, H-5), 3.89 (dd, 1H, $J_{4,3}$=6.0 Hz, $J_{4,5}$=1.0 Hz, H-4), 3.76 (dd, 1H, $J_{3,2}$=1.0 Hz, $J_{3,4}$=6.0 Hz, H-3), 3.62 (dd, 1H, $J_{1a,1b}$=9.0 Hz, $J_{1a,2}$=5.5 Hz, H-1a), 3.53 (dd, 1H, $J_{1b,1a}$=$J_{1b,2}$=9.0 Hz, H-1b), 2.42 (d, 1H, $J_{1',5}$=2.5 Hz, H-1′). MALDI-TOF MS (535.67): 536.8 (M+H). Anal. calcd for $C_{35}H_{37}NO_4$: C, 78.48; H, 6.96; N, 2.61. Found: C, 78.58; H, 7.15; N, 2.55.

Eluted next was **31** (80% yield) as a syrup: $[\alpha]_D^{20}$=−13.9 (*c* 1.4, $CHCl_3$). ^1H NMR (300 MHz) δ 7.40–7.20 (m, 20H, 4Ph), 4.78 and 4.58 (2d, 2H, J=11.5 Hz, PhCH_2), 4.77 and 4.74 (2d, 2H, J=11.0 Hz, PhCH_2), 4.52 and 4.45 (2d, 2H, J=11.5 Hz, PhCH_2), 4.05 and 3.78 (2d, 2H, J=13.0 Hz, PhCH_2N), 4.00–3.90 (m, 3H, H-2, H-3, H-4), 3.70 (dd, 1H, $J_{5,1'}$=2.5 Hz, $J_{5,4}$=5.0 Hz, H-5), 3.57 (dd, 1H, $J_{1a,1b}$=9.5 Hz, $J_{1a,2}$=6.0 Hz, H-1a), 3.49 (dd, 1H, $J_{1b,1a}$=9.5 Hz, $J_{1b,2}$=6.0 Hz, H-1b), 2.43 (d, 1H, $J_{1',5}$=2.5 Hz, H-1′). ^{13}C NMR (75 MHz) δ 139.1, 138.0, 128.3–127.0 (Ph), 82.3, 81.1, 79.5, 74.5, 73.4, 73.1, 71.1, 69.2, 50.9, 50.8. MALDI-TOF MS (535.67): 536.5 (M+H). Anal. calcd for $C_{35}H_{37}NO_4$: C, 78.48; H, 6.96; N, 2.61. Found: C, 78.51; H, 7.17; N, 2.48.

4.8.12. (2*R*,3*R*,4*R*,5*R*)-*N*-Benzyl-5-benzyloxymethyl-3,4-dibenzyloxy-2-ethynylpyrrolidine (32). Chromatography on silica gel (10:1 cyclohexane–AcOEt) afforded pure **32** (75% yield) as a syrup: $[\alpha]_D^{20}$=−57.7 (*c* 1.1, $CHCl_3$). IR $\nu_{C\equiv C-H}$ 3290 cm^{-1}; $\nu_{C\equiv C}$ 2100 cm^{-1}. ^1H NMR (400 MHz) δ 7.45–7.22 (m, 20H, 4Ph), 4.52 and 4.44 (2d, 2H, J=12.0 Hz, PhCH_2), 4.52 and 4.39 (2d, 2H, J=12.0 Hz, PhCH_2), 4.51 and 4.49 (2d, 2H, J=12.0 Hz, PhCH_2), 4.19 and 3.71 (2d, 2H, J=13.5 Hz, PhCH_2N), 4.05 (dd, 1H, $J_{3,2}$=1.5 Hz, $J_{3,4}$=2.5 Hz, H-3), 3.83 (ddd, 1H, $J_{4,2}$=1.0 Hz, $J_{4,3}$=2.5 Hz, $J_{4,5}$=6.0 Hz, H-4), 3.75–3.73 (m, 1H, H-2), 3.66 (dd, 1H, $J_{6a,5}$=4.5 Hz, $J_{6a,6b}$=9.0 Hz, H-6a), 3.64 (dd, 1H, $J_{6b,5}$=5.0 Hz, $J_{6a,6b}$=9.0 Hz, H-6b), 3.13 (ddd, 1H, $J_{5,4}$=6.0 Hz, $J_{5,6a}$=4.5 Hz, $J_{5,6b}$=5.0 Hz, H-5), 2.45 (d, 1H, $J_{1',2}$=2.5 Hz, H-1′). ^{13}C NMR (75 MHz) δ 138.8, 138.2, 138.1, 137.6, 128.8–126.8 (Ph), 87.1, 85.6, 79.6, 75.6, 73.1, 71.6, 70.5, 65.6, 56.4, 52.8. MALDI-TOF MS (517.66): 518.5 (4M+H). Anal. calcd for $C_{35}H_{35}NO_3$: C, 81.21; H, 6.81; N, 2.71. Found: C, 81.45; H, 7.02; N, 2.53.

4.8.13. (2*R*,3*R*,4*R*,5*S*,6*S*)-6-*N*-Benzylamino-1,3,4,5-*O*-tetrabenzyl-6-(1-trimethylsilylethynyl)-1,2,3,4,5-hexanepentol (33). Chromatography on silica gel (5:1 cyclohexane–AcOEt) of the crude mixture afforded as first eluate the 6*R*-epimer of **33** (10% yield) as a syrup: $[\alpha]_D^{20}$=−53.2 (*c* 1.5, $CHCl_3$).^1H NMR (400 MHz) δ 7.40–7.15 (m, 25H, 5Ph), 4.98 and 4.81 (2d, 2H, J=11.0 Hz, PhCH_2), 4.83 and 4.64 (2d, 2H, J=11.0 Hz, PhCH_2), 4.56 and 4.53 (2d, 2H, J=11.0 Hz, PhCH_2), 4.46 and 4.22 (2d, 2H, J=11.5 Hz, PhCH_2), 4.22 (dd, 1H, $J_{4,3}$=3.0 Hz, $J_{4,5}$=7.5 Hz, H-4), 4.08 (ddd, 1H, $J_{2,1a}$=3.5 Hz, $J_{2,1b}$=6.0 Hz, $J_{2,3}$=6.5 Hz, H-2), 4.04 (dd, 1H, $J_{5,4}$=7.5 Hz, $J_{5,6}$=3.0 Hz, H-5), 4.02 and 3.70 (2d, 2H, J=13.0 Hz, PhCH_2N), 3.64 (dd, 1H, $J_{1a,1b}$=10.0 Hz, $J_{1a,2}$=3.5 Hz, H-1a), 3.58 (dd, 1H, $J_{1b,1a}$=10.0 Hz, $J_{1b,2}$=6.0 Hz, H-1b), 3.44 (dd, 1H, $J_{3,2}$=6.5 Hz, $J_{3,4}$=3.0 Hz, H-3), 3.31 (d, 1H, $J_{6,5}$=3.0 Hz, H-6). MALDI-TOF MS (728.00): 729.3 (M+H). Anal.

calcd for $C_{46}H_{53}NO_5Si$: C, 75.89; H, 7.34; N, 1.92. Found: C, 76.01; H, 7.53; N, 1.78.

Eluted next was **33** (78% yield) as a syrup: $[\alpha]_D^{20}=+40.3$ (*c* 0.9, $CHCl_3$).^{1}H NMR (300 MHz) δ 7.40–7.10 (m, 25H, 5Ph), 4.83 and 4.79 (2d, 2H, J=11.0 Hz, PhCH_2), 4.74 and 4.70 (2d, 2H, J=11.0 Hz, PhCH_2), 4.56 and 4.46 (2d, 2H, J=12.0 Hz, PhCH_2), 4.51 (s, 2H, PhCH_2), 4.23 (dd, 1H, $J_{4,3}$=4.0 Hz, $J_{4,5}$=5.5 Hz, H-4), 4.02–3.95 (m, 1H, H-2), 3.95 and 3.67 (2d, 2H, J=13.0 Hz, PhCH_2N), 3.92 (dd, 1H, $J_{5,4}=J_{5,6}$=5.5 Hz, H-5), 3.73 (dd, 1H, $J_{3,2}$=7.0 Hz, $J_{3,4}$=4.0 Hz, H-3), 3.68–3.56 (m, 3H, H-1a, H-1b, H-6), 3.10–2.90 (m, 1H, OH), 0.21 (s, 9H, $3CH_3$). ^{13}C NMR (75 MHz) δ 139.8, 138.5, 138.3, 138.1, 137.9, 129.0–126.8 (Ph), 105.3, 89.9, 80.0, 78.8, 77.1, 74.3, 74.0, 73.2, 73.0, 71.1, 71.0, 51.6, 50.1, 0.0. MALDI-TOF MS (728.00): 729.4 (M+H). Anal. calcd for $C_{46}H_{53}NO_5Si$: C, 75.89; H, 7.34; N, 1.92. Found: C, 75.78; H, 7.48; N, 1.83.

4.8.14. (2*R*,3*R*,4*R*,5*S*,6*S*)-6-*N*-Benzylamino-6-ethynyl-1,3,4,5-*O*-tetrabenzyl-1,2,3,4,5-hexanepentol (34). Crude **34** (syrup; 95% yield; ca. 95% pure by ^{1}H NMR) was used for the next reaction without further purification.^{1}H NMR (300 MHz) δ 7.40–7.15 (m, 25H, 5Ph), 4.85 and 4.79 (2d, 2H, J=11.0 Hz, PhCH_2), 4.80 and 4.71 (2d, 2H, J=11.0 Hz, PhCH_2), 4.56 and 4.50 (2d, 2H, J=12.0 Hz, PhCH_2), 4.47 (s, 2H, PhCH_2), 4.21 (dd, 1H, $J_{4,3}$=3.5 Hz, $J_{4,5}$=7.0 Hz, H-4), 4.00 (dd, 1H, $J_{5,4}$=7.0 Hz, $J_{5,6}$=4.5 Hz, H-5), 4.05–3.98 (m, 1H, H-2), 3.94 and 3.63 (2d, 2H, J=13.0 Hz, PhCH_2N), 3.70–3.56 (m, 3H, H-1a, H-1b, H-3), 3.54 (dd, 1H, $J_{6,1'}$=2.0 Hz, $J_{6,5}$=4.5 Hz, H-6), 2.39 (d, 1H, $J_{1',6}$=2.0 Hz, H-1′). MALDI-TOF MS (655.82): 656.9 (M+H).

4.8.15. (2*S*,3*S*,4*R*,5*R*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-2-ethynyl-3,4,5-tribenzyloxypiperidine (35). Chromatography on silica gel (10:1 cyclohexane–AcOEt) afforded pure **35** (65% yield) as a syrup: $[\alpha]_D^{20}=+1.9$ (*c* 0.5, $CHCl_3$). IR $\nu_{C\equiv C-H}$ 3280 cm^{-1}; $\nu_{C\equiv C}$ 2100 cm^{-1}. ^{1}H NMR (400 MHz) δ 7.40–7.15 (m, 25H, 5Ph), 4.96 and 4.85 (2d, 2H, J=10.5 Hz, PhCH_2), 4.87 and 4.77 (2d, 2H, J=11.0 Hz, PhCH_2), 4.52 and 4.49 (2d, 2H, J=11.0 Hz, PhCH_2), 4.49 and 4.47 (2d, 2H, J=12.0 Hz, PhCH_2), 4.37 and 3.96 (2d, 2H, J=14.0 Hz, PhCH_2N), 4.05 (dd, 1H, $J_{2,1'}$=2.5 Hz, $J_{2,3}$=9.5 Hz, H-2), 3.82–3.65 (m, 5H, H-3, H-4, H-5, H-7a, H-7b), 3.20–3.15 (m, 1H, H-6), 2.40 (d, 1H, $J_{1',2}$=2.5 Hz, H-1′). ^{13}C NMR (75 MHz) δ 139.6, 138.4, 138.3, 138.2, 128.3–126.7 (Ph), 82.9, 82.7, 78.8, 75.5, 75.3, 73.6, 73.1, 72.4, 65.4, 55.4, 54.7, 53.8, 53.4, 29.6. MALDI-TOF MS (637.81): 638.8 (M+H). Anal. calcd for $C_{43}H_{43}NO_4$: C, 80.97; H, 6.80; N, 2.20. Found: C, 81.13; H, 6.91; N, 2.21.

4.8.16. (2*R*,3*R*,4*R*,5*S*,6*S*) and (2*R*,3*R*,4*R*,5*S*,6*R*)-6-*N*-Benzylamino-1,3,4,5-*O*-tetrabenzyl-7-vinyl-1,2,3,4,5-heptanepentol (36). Compound **36** was a 50/50 mixture of 6*S*/6*R*-epimers (by ^{1}H NMR), not separable by flash chromatography. Crude **36** (88% yield; ca. 95% pure by ^{1}H NMR) was used for the next reaction without further purification. ^{1}H NMR (300 MHz, selected data) δ 7.40–7.15 (m, 25H, 5Ph), 5.84–5.72 (m, 0.5H, H-2′), 5.65–5.53 (m, 0.5H, H-2′), 2.90–2.84 (m, 0.5H, H-6), 2.63–2.56 (m, 0.5H, H-6), 2.48–2.20 (m, 2H, H-7a, H-7b). MALDI-TOF MS (671.86): 672.8 (M+H).

4.8.17. (2*S*,3*S*,4*R*,5*R*,6*S*) and (2*R*,3*S*,4*R*,5*R*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-3,4,5-tribenzyloxy-2-(2-propenyl)piperidine (37). Compound **37** (65% yield) was a 50/50 mixture of 2*S*/2*R* epimers (by ^{1}H NMR), not separable by chromatography. A small amount of the 2*R*-epimer (contaminated by ca. 10% of the 2*S*-epimer) was isolated after flash chromatography (12:1 cyclohexane–AcOEt). IR $\nu_{C=C}$ 1640 cm^{-1}. ^{1}H NMR (400 MHz) δ 7.40–7.20 (m, 25H, 5Ph), 5.93–5.81 (m, 1H, H-2′), 5.01–4.91 (m, 2H, H-1′a, H-1′b), 4.83 and 4.80 (2d, 2H, J=10.5 Hz, PhCH_2), 4.62 and 4.56 (2d, 2H, J=11.5 Hz, PhCH_2), 4.57 and 4.54 (2d, 2H, J=11.5 Hz, PhCH_2), 4.49 (s, 2H, PhCH_2), 4.13 and 4.07 (2d, 2H, J=15.0 Hz, PhCH_2N), 3.83 (dd, 1H, $J_{7a,6}$=5.5 Hz, $J_{7a,7b}$=10.0 Hz, H-7a), 3.78–3.70 (m, 3H, H-4, H-5, H-7b), 3.64 (dd, 1H, $J_{3,2}$=5.5 Hz, $J_{3,4}$=9.0 Hz, H-3), 3.54–3.49 (m, 1H, H-6), 3.23–3.17 (m, 1H, H-2), 2.54–2.45 (m, 1H, H-3′a), 2.39–2.31 (m, 1H, H-3′b). MALDI-TOF MS (653.85): 654.5 (M+H). Anal. calcd for $C_{44}H_{47}NO_4$: C, 80.82; H, 7.25; N, 2.14. Found: C, 80.75; H, 7.41; N, 2.03.

4.8.18. (2*R*,3*S*,4*R*,5*S*,6*S*)-6-*N*-Benzylamino-1,3,4,5-*O*-tetrabenzyl-6-(1-trimethylsilylethynyl)-1,2,3,4,5-hexanepentol (38). Chromatography on silica gel (4:1 cyclohexane–AcOEt) of the crude mixture afforded as first eluate the 6*R*-epimer of **38** (15% yield) as a syrup: $[\alpha]_D^{20}=-55.5$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz) δ 7.50–7.20 (m, 25H, 5Ph), 4.96 and 4.80 (2d, 2H, J=11.0 Hz, PhCH_2), 4.82 and 4.78 (2d, 2H, J=11.5 Hz, PhCH_2), 4.68 and 4.42 (2d, 2H, J=11.5 Hz, PhCH_2), 4.48 and 4.41 (2d, 2H, J=12.0 Hz, PhCH_2), 4.34 (dd, 1H, $J_{4,3}$=3.0 Hz, $J_{4,5}$=7.0 Hz, H-4), 4.07 and 3.73 (2d, 2H, J=13.0 Hz, PhCH_2N), 4.02 (ddd, 1H, $J_{2,1a}$=6.0 Hz, $J_{2,1b}$=7.0 Hz, $J_{2,3}$=2.0 Hz, H-2), 3.92 (dd, 1H, $J_{5,4}$=7.0 Hz, $J_{5,6}$=3.0 Hz, H-5), 3.66 (dd, 1H, $J_{3,2}$=2.0 Hz, $J_{3,4}$=3.0 Hz, H-3), 3.60 (d, 1H, $J_{6,5}$=3.0 Hz, H-6), 3.56 (dd, 1H, $J_{1a,1b}$=9.0 Hz, $J_{1a,2}$=6.0 Hz, H-1a), 3.48 (dd, 1H, $J_{1b,1a}$=9.0 Hz, $J_{1b,2}$=7.0 Hz, H-1b), 0.25 (s, 9H, $3CH_3$). MALDI-TOF MS (728.00): 729.5 (M+H). Anal. calcd for $C_{46}H_{53}NO_5Si$: C, 75.89; H, 7.34; N, 1.92. Found: C, 75.71; H, 7.42; N, 2.13.

Eluted next was **38** (70% yield) as a syrup: $[\alpha]_D^{20}=+8.9$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz) δ 7.40–7.20 (m, 25H, 5Ph), 4.81 (s, 2H, PhCH_2), 4.89 (s, 2H, PhCH_2), 4.63 and 4.45 (2d, 2H, J=11.5 Hz, PhCH_2), 4.45 and 4.38 (2d, 2H, J=12.0 Hz, PhCH_2), 4.33 (dd, 1H, $J_{4,3}$=4.5 Hz, $J_{4,5}$=6.0 Hz, H-4), 4.01 (ddd, 1H, $J_{2,1a}$=5.0 Hz, $J_{2,1b}$=6.5 Hz, $J_{2,3}$=2.0 Hz, H-2), 4.00 and 3.67 (2d, 2H, J=13.0 Hz, PhCH_2N), 3.78 (dd, 1H, $J_{3,2}$=2.0 Hz, $J_{3,4}$=4.5 Hz, H-3), 3.75 (dd, 1H, $J_{5,4}$=6.0 Hz, $J_{5,6}$=5.0 Hz, H-5), 3.66 (d, 1H, $J_{6,5}$=5.0 Hz, H-6), 3.55 (dd, 1H, $J_{1a,1b}$=9.0 Hz, $J_{1a,2}$=5.0 Hz, H-1a), 3.48 (dd, 1H, $J_{1b,1a}$=9.0 Hz, $J_{1b,2}$=6.5 Hz, H-1b), 3.28–3.20 (m, 1H, OH), 0.22 (s, 9H, $3CH_3$). ^{13}C NMR (75 MHz) δ 139.8, 138.6, 138.1, 138.0, 128.3–127.0 (Ph), 105.0, 90.5, 81.0, 80.7, 75.1, 74.2, 73.2, 72.7, 70.9, 70.0, 51.9, 51.1, 29.7, 0.1. MALDI-TOF MS (728.00): 729.3 (M+H). Anal. calcd for $C_{46}H_{53}NO_5Si$: C, 75.89; H, 7.34; N, 1.92. Found: C, 75.92; H, 7.48; N, 1.80.

4.8.19. (2*R*,3*S*,4*R*,5*S*,6*S*)-6-*N*-Benzylamino-6-ethynyl-1,3,4,5-*O*-tetrabenzyl-1,2,3,4,5-hexanepentol (39). Crude **39** (syrup; 95% yield; ca. 95% pure by ^{1}H NMR) was used for the next reaction without further purification.^{1}H NMR

(300 MHz) δ 7.40–7.20 (m, 25H, 5Ph), 4.85 and 4.82 (2d, 2H, J=11.0 Hz, PhCH_2), 4.84 and 4.76 (2d, 2H, J=11.5 Hz, PhCH_2), 4.65 and 4.49 (2d, 2H, J=11.5 Hz, PhCH_2), 4.45 and 4.38 (2d, 2H, J=12.0 Hz, PhCH_2), 4.32 (dd, 1H, $J_{4,3}$=4.0 Hz, $J_{4,5}$=6.5 Hz, H-4), 4.08 (ddd, 1H, $J_{2,1a}$=5.5 Hz, $J_{2,1b}$=6.5 Hz, $J_{2,3}$=2.0 Hz, H-2), 4.00 and 3.64 (2d, 2H, J=13.0 Hz, PhCH_2N), 3.85 (dd, 1H, $J_{5,4}$=6.5 Hz, $J_{5,6}$=4.5 Hz, H-5), 3.78 (dd, 1H, $J_{3,2}$=2.0 Hz, $J_{3,4}$=4.0 Hz, H-3), 3.63 (dd, 1H, $J_{6,1'}$=2.5 Hz, $J_{6,5}$=4.5 Hz, H-6), 3.56 (dd, 1H, $J_{1a,1b}$=9.0 Hz, $J_{1a,2}$=5.5 Hz, H-1a), 3.49 (dd, 1H, $J_{1b,1a}$=9.0 Hz, $J_{1b,2}$=6.5 Hz, H-1b), 2.42 (d, 1H, $J_{1',6}$=2.5 Hz, H-1′), 1.65–1.50 (m, 1H, OH). MALDI-TOF MS (655.82): 656.7 (M+H).

4.8.20. (2*S*,3*S*,4*R*,5*S*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-2-ethynyl-3,4,5-tribenzyloxypiperidine (40). Chromatography on silica gel (9:1 cyclohexane–AcOEt) afforded pure **40** (88% yield) as a syrup: $[\alpha]_D^{20}$=+17.9 (*c* 0.5, $CHCl_3$). IR $\nu_{C\equiv C-H}$ 3280 cm^{-1}; $\nu_{C\equiv C}$ 2100 cm^{-1}. ^{1}H NMR (300 MHz) δ 7.50–7.20 (m, 25H, 5Ph), 4.62 and 4.54 (2d, 2H, J=12.0 Hz, PhCH_2), 4.52 and 4.48 (2d, 2H, J=12.0 Hz, PhCH_2), 4.51 (s, 2H, PhCH_2), 4.45 and 4.38 (2d, 2H, J=12.0 Hz, PhCH_2), 4.38 and 3.79 (2d, 2H, J=13.5 Hz, PhCH_2N), 3.97 (dd, 1H, $J_{3,2}$=$J_{3,4}$=6.0 Hz, H-3), 3.92 (dd, 1H, $J_{5,4}$=3.5 Hz, $J_{5,6}$=6.0 Hz, H-5), 3.78 (dd, 1H, $J_{2,1'}$=2.5 Hz, $J_{2,3}$=6.0 Hz, H-2), 3.75 (dd, 1H, $J_{4,3}$=6.0 Hz, $J_{4,5}$=3.5 Hz, H-4), 3.69 (dd, 1H, $J_{7a,6}$=4.0 Hz, $J_{7a,7b}$=10.0 Hz, H-7a), 3.60 (dd, 1H, $J_{7b,6}$=5.0 Hz, $J_{7b,7a}$=10.0 Hz, H-7b), 3.32 (ddd, 1H, $J_{6,5}$=6.0 Hz, $J_{6,7a}$=4.0 Hz, $J_{6,7b}$=5.0 Hz, H-6), 2.35 (d, 1H, $J_{1',2}$=2.5 Hz, H-1′). ^{13}C NMR (75 MHz) δ 139.6, 138.5, 138.2, 138.1, 128.7–126.8 (Ph), 80.9, 77.1, 74.9, 73.8, 73.1, 71.7, 71.4, 67.0, 56.0, 53.4, 52.0. MALDI-TOF MS (637.81): 638.6 (M+H). Anal. calcd for $C_{43}H_{43}NO_4$: C, 80.97; H, 6.80; N, 2.20. Found: C, 80.71; H, 6.71; N, 2.23.

4.8.21. (2*R*,3*S*,4*R*,5*S*,6*S*) and (2*R*,3*S*,4*R*,5*S*,6*R*)-6-*N*-Benzylamino-1,3,4,5-*O*-tetrabenzyl-7-vinyl-1,2,3,4,5-heptanepentol (41). Compound **41** was a 50/50 mixture of 6*S*/6*R* epimers (by ^{1}H NMR), not separable by flash chromatography. Crude **41** (90% yield; ca. 95% pure by ^{1}H NMR) was used for the next reaction without further purification. ^{1}H NMR (300 MHz, selected data) δ 7.40–7.18 (m, 25H, 5Ph), 5.83–5.70 (m, 0.5H, H-2′), 5.69–5.61 (m, 0.5H, H-2′), 2.86–2.80 (m, 0.5H, H-6), 2.70–2.62 (m, 0.5H, H-6). MALDI-TOF MS (671.86): 672.9 (M+H).

4.8.22. (2*S*,3*S*,4*R*,5*S*,6*S*) and (2*R*,3*S*,4*R*,5*S*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-3,4,5-tribenzyloxy-2-(2-propenyl)-piperidine (42). Compound **42** (80% yield) was a 50/50 mixture of 2*S*/2*R* epimers (by ^{1}H NMR), not separable by chromatography. A small amount of the 2*S*-epimer was isolated after flash chromatography (10:1 cyclohexane–AcOEt): $[\alpha]_D^{20}$=+13.9 (*c* 0.5, $CHCl_3$). IR $\nu_{C=C}$ 1640 cm^{-1}. ^{1}H NMR (400 MHz) δ 7.40–7.15 (m, 25H, 5Ph), 5.93–5.80 (m, 1H, H-2′), 5.00–5.09 (m, 2H, H-1′a, H-1′b), 4.82 and 4.56 (2d, 2H, J=11.5 Hz, PhCH_2), 4.53 and 4.48 (2d, 2H, J=12.0 Hz, PhCH_2), 4.52 and 4.42 (2d, 2H, J=12.0 Hz, PhCH_2), 4.36 and 4.29 (2d, 2H, J=12.0 Hz, PhCH_2), 4.16 and 3.82 (2d, 2H, J=13.5 Hz, PhCH_2N), 3.96 (dd, 1H, $J_{5,4}$=$J_{5,6}$=3.5 Hz, H-5), 3.83 (dd, 1H, $J_{3,2}$=$J_{3,4}$=7.5 Hz, H-3), 3.71 (dd, 1H, $J_{4,3}$=7.5 Hz, $J_{4,5}$=3.5 Hz, H-4), 3.57 (dd, 1H, $J_{7a,6}$=5.0 Hz, $J_{7a,7b}$=10.0 Hz, H-7a), 3.46 (dd, 1H, $J_{7b,6}$=7.0 Hz, $J_{7b,7a}$=10.0 Hz, H-7b), 3.30 (ddd, 1H, $J_{6,5}$=3.5 Hz, $J_{6,7a}$=5.0 Hz, $J_{6,7b}$=7.0 Hz, H-6), 2.98–2.91 (m, 1H, H-2), 2.76–2.68 (m, 1H, H-3′a), 2.54–2.45 (m, 1H, H-3′b). ^{13}C NMR (75 MHz) δ 140.2, 138.7, 138.5, 138.1, 136.4, 128.6–127.3 (Ph), 126.5, 115.7, 79.9, 77.2, 74.5, 74.1, 72.8, 71.6, 71.2, 67.8, 59.1, 55.0, 51.2, 32.0. MALDI-TOF MS (653.85): 654.7 (M+H). Anal. calcd for $C_{44}H_{47}NO_4$: C, 80.82; H, 7.25; N, 2.14. Found: C, 80.71; H, 7.23; N, 2.43.

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References

1. (a) Sears, P.; Wong, C.-H. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 2300. (b) Asano, N.; Nash, R. J.; Molyneux, R. J.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **2000**, *11*, 1645.
2. (a) Sinnot, M. L. *Chem. Rev.* **1990**, *90*, 1171. (b) Legler, G. In *Carbohydrate Mimics Concepts and Methods*; Chapleur, Y., Ed.; Wiley-VCH: Weinheim, 1998. (c) In *Iminosugars as Glycosidase Inhibitors. Nojirimycin and Beyond*; Stütz, A. E., Ed.; Wiley-VCH: Weinheim, 1999.
3. (a) Häusler, H.; Kawakami, P.; Mlaker, E.; Severn, W. B.; Wrodnigg, T. M.; Stütz, A. E. J. *Carbohydr. Chem.* **2000**, *19*, 435. (b) Durantel, D.; Branza-Nichita, N.; Carrouee-Durantel, S.; Butters, T. D.; Dwek, R. A.; Zitzmann, N. *J. Virol.* **2001**, *75*, 8987.
4. (a) Humphries, M. J.; Matsumoto, K.; White, S. L.; Olden, K. *Cancer Res.* **1986**, *46*, 5215. (b) Goss, P. E.; Baker, M. A.; Carver, J. P.; Dennis, J. W. *Clin. Cancer Res.* **1995**, *1*, 935. (c) Nishimura, Y.; Satoh, T.; Adachi, H.; Kondo, S.; Takeuchi, T.; Azetaka, M.; Fukuyasu, H.; Lizuka, Y. *J. Med. Chem.* **1997**, *40*, 2626.
5. (a) Dimitriadis, G. D.; Tessari, P.; Go, V. L. W.; Gerich, J. E. *Metabolism* **1985**, *34*, 261. (b) Bolle, M.; Stalmans, W. *Eur. J. Biochem.* **1989**, *181*, 775. (c) Anzeveno, P. B.; Creemer, L. J.; Daniel, J. K.; King, C.-H. R.; Liu, P. S. *J. Org. Chem.* **1989**, *54*, 2539. (d) Andersen, B.; Rassov, A.; Westergaard, N.; Lundgren, K. *Biochem. J.* **1999**, *342*, 545.
6. Dondoni, A.; Franco, S.; Junquera, F.; Merchán, F. L.; Merino, P.; Tejero, T.; Bertolasi, V. *Chem. Eur. J.* **1995**, *1*, 505.
7. (a) Dondoni, A.; Perrone, D. *Tetrahedron Lett.* **1999**, *40*, 9375. (b) Dondoni, A.; Giovannini, P. P.; Perrone, D. *J. Org. Chem.* **2002**, *67*, 7203.
8. Dondoni, A.; Giovannini, P. P.; Marra, A. *Tetrahedron Lett.* **2000**, *41*, 6195.
9. (a) Ikeda, K.; Takahashi, M.; Nishida, M.; Miyauchi, M.; Kizu, H.; Kameda, Y.; Arisawa, M.; Watson, A. A.; Nash, R. J.; Fleet, G. W. J.; Asano, N. *Carbohydr. Res.* **2000**, *323*, 73. (b) Butters, T. D.; van den Broek, L. A. G. M.; Fleet, G. W. J.; Krulle, T. M.; Wormald, M. R.; Dwek, R. A.; Platt, F. M. *Tetrahedron: Asymmetry* **2000**, *11*, 113.
10. (a) Fleet, G. W. J.; Namgoong, S. K.; Barker, C.; Baines, S.; Jacob, G. S.; Winchester, B. *Tetrahedron Lett.* **1989**, *30*, 4439. (b) Sifferlen, T.; Defoin, A.; Streith, J.; Le Nouën, D.; Tarnus, C.; Dosbaâ, I.; Foglietti, M.-J. *Tetrahedron* **2000**, *56*, 971.

11. (a) Cipolla, L.; Lay, L.; Nicotra, F.; Pangrazio, C.; Panza, L. *Tetrahedron* **1995**, *51*, 4679. (b) Johnson, C. R.; Johns, B. A. *J. Org. Chem.* **1997**, *62*, 6046. (c) Defoin, A.; Sifferlen, Th.; Streith, J.; Dosbaa, I.; Foglietti, M.-J. *Tetrahedron: Asymmetry* **1997**, *8*, 363. (d) Shilvock, J. P.; Wheatley, J. R.; Nash, R. J.; Watson, A. A.; Griffiths, R. C.; Butters, T. D.; Müller, M.; Watkin, D. J.; Winkler, D. A.; Fleet, G. W. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2735. (e) Shilvock, J. P.; Wheatley, J. R.; Nash, R. J.; Watson, A. A.; Winters, A. L.; Butters, T. D.; Raymond, A. D.; Winkler, D. A.; Fleet, G. W. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2747. (f) Dransfield, P. J.; Gore, P. M.; Shipman, M.; Slawin, A. M. Z. *Chem. Commun.* **2002**, 150. (g) Cipolla, L.; Palma, A.; La Ferla, B.; Nicotra, F. *Chem. Soc., Perkin Trans. 1* **2002**, 2161. (h) Godin, G.; Compain, P.; Masson, G.; Martin, O. R. *J. Org. Chem.* **2002**, *67*, 6960.
12. The synthesis *N*-alkyl-*N*-glycosylhydroxylamines have been the subject of two recent communications: (a) Merino, P.; Franco, S.; Merchan, F. L.; Tejero, T. *Synth. Commun.* **1997**, *27*, 3529. (b) Cicchi, S.; Corsi, M.; Marradi, M.; Goti, A. *Tetrahedron Lett.* **2002**, *43*, 2741.
13. (a) Ohrui, H.; Jones, G. H.; Moffatt, J. G.; Maddox, M. L.; Christensen, A. T.; Byram, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 4602. (b) Collins, P.; Ferrier, R. *Monosaccharides*; Wiley: Chichester, 1995.
14. For recent reviews on nucleophilic additions to C=N bonds, including nitrones, see: (a) Bloch, R. *Chem. Rev.* **1998**, *98*, 1407. (b) Lombardo, M.; Trombini, C. *Synthesis* **2000**, 759.
15. (a) Compain, P.; Goré, J.; Vatèle, J.-M. *Tetrahedron Lett.* **1995**, *36*, 4059. (b) Veith, U.; Schwardt, O.; Jäger, V. *Synlett* **1996**, 1181. (c) Akhoon, K. M.; Myles, D. C. *J. Org. Chem.* **1997**, *62*, 6041.
16. Dondoni, A.; Perrone, D.; Rinaldi, M. *J. Org. Chem.* **1998**, *63*, 9252.
17. We have observed that the use of methansulfonyl chloride instead of triflic anhydride (Ref. 7) in many cases improved the yield of the cyclization products.
18. A *syn* selectivity has been reported in the procedure described by Nicotra and co-workers (see Ref. 11a) involving the addition of Grignard reagents to glycosylamines.
19. For the first synthesis of 6-deoxy-homo DMDP and its C5-epimer see: Behr, J.-B.; Guillerm, G. *Tetrahedron: Asymmetry* **2002**, *13*, 111.
20. Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*; 4th ed. Butterworth-Heinemann: Oxford, 1996.
21. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
22. De Napoli, L.; Messere, A.; Palomba, D.; Piccialli, V. *J. Org. Chem.* **2000**, *65*, 3432.
23. Koto, S.; Morishima, N.; Miyata, Y.; Zen, S. *Bull. Chem. Soc. Jpn* **1976**, *46*, 2639.