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Access to Piperidine Imino-*C*-glycosides via Stereoselective Thiazole-Based Aminohomologation of Pyranoses

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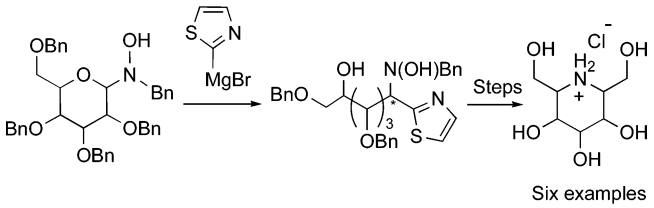
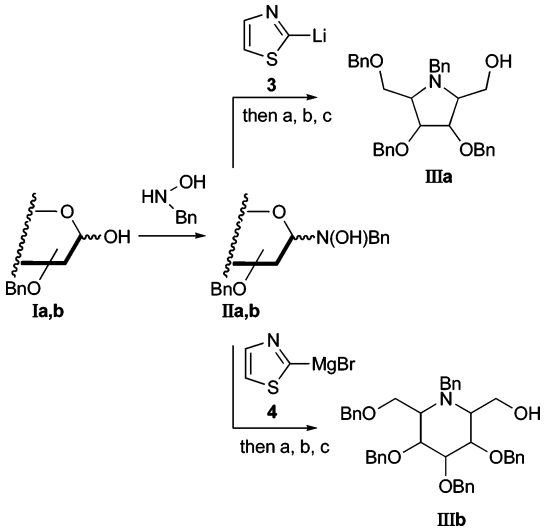


The access to piperidine homoazasugars (dideoxyiminoheptitols) from pyranoses via formal one-carbon chain elongation and exchange of the ring oxygen with the NH group is described. The key process involves the stereoselective addition of 2-thiazolylmagnesium bromide to an *N*-glycosylhydroxylamine, i.e., a hidden open-chain sugar nitrone. The *N*-thiazolylalkylhydroxylamine formed in this way is reduced to amine, and this transformed into a substituted piperidine via intramolecular cyclization by an S_N2 process. Cleavage of the thiazole residue attached to C2 of the piperidine ring reveals the formyl group, and this is reduced to hydroxymethyl to give the target homoazasugar. A collection of six stereodiversified compounds with free OH and NH groups and isolated as hydrochlorides has been prepared.

Introduction

Recent disclosures from these laboratories have shown the effectiveness of the thiazole-based transformation of 2,3,5-tri-*O*-benzyl D- and L-furanoses into *N*-benzylpyrrolidines bearing a hydroxymethyl group at the carbon atom adjacent to nitrogen, namely the so-called pyrrolidine homoazasugars[1] (Scheme 1). The whole procedure can be considered as an aminohomologation process because it entails the substitution of the furanose ring oxygen with the NH group and the insertion of a methylene group into the anomeric C−OH bond. These structural changes are achieved via a five-step reaction sequence involving the following: (i) the conversion of the furanose **Ia** into the *N*-benzyl-*N*-glycosylhydroxylamine **IIa**; (ii) the stereoselective addition of 2-lithiothiazole **3** to the minor tautomer of **IIa**, viz. an open-chain *N*-benzyl sugar nitrone (not shown), to give a mixture of *N*-thiazolylalkylhydroxylamine diastereoisomers Th(R)CH*-N(Bn)OH (Th = 2-thiazolyl; R = $BnOCH_2CH(OH)$-$CH(OBn)CH(OBn)$−); (iii) the separation and reductive *N*-dehydroxylation of each isomer to give a secondary amine Th(R)CH*-NHBn; (iv) the pyrrolidine ring formation via activation of the free hydroxyl group in the alkyl chain R as a mesylate and displacement of the latter with the amino group; (v) the cleavage of the thiazole ring to formyl group and reduction of the latter to give the target alcohol **IIIa**. We embarked

SCHEME 1[a]



[a] Key: (a) N(OH)Bn → NHBn in the open-chain adduct; (b) cyclization via SN_2 of OSO_2CH_3 by NHBn; (c) one-pot thiazole → CHO → CH_2OH.

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in this research because in the diversity of natural and synthetic azasugars (*alias* iminosugars) that have been isolated and prepared in the last three decades[2,3] due to their intense activity as specific glycosidase and glycosyltransferase inhibitors, those compounds having a hydroxymethyl group or a polyhydroxylated carbon chain linked to the carbon adjacent to nitrogen of either a pyrrolidine or piperidine ring have gained special importance.[4] These homoazasugars have been found to retain the same type of enzymatic inhibition of the lower homologues and at the same time exibit higher selectivity and potency.[5] Moreover, they present high stability toward chemical and enzymatic degradation, a serious drawback of the parent azasugars due to the lability of the *O*,*N*-acetal function. In line with this concept, the synthesis of aza-*C*-glycosides with various functional aglycons, suitable for further modification, are attracting great interest as the next generation of glycoprocessing enzyme inhibitors.[4c] The thiazole-based aminohomologation methodology appears to fit quite well in this program because the mild and neutral reaction conditions of the thiazole-to-formyl protocol (methylation, reduction, hydrolysis) permit rather unstable aza-*C*-glycosyl aldehydes to be isolated and transformed into more complex aza-*C*-glycosides. We have taken advantage of this opportunity by performing Wittig-type coupling reactions of 2-formyl *N*-benzylpyrrolidines with sugar phosphoranes en route to (1→6)- and (1→5)-linked aza-*C*-disaccharides,[1] i.e., compounds in which the azasugar moiety is anomerically linked through an all-carbon tether to a normal monosaccharide.[4c,6]

Unfortunately, the use of the above aminohomologation sequence was restricted to pentofuranoses **Ia**. Attempts to extend the methodology to pyranoses **Ib** to access piperidine homoazasugars **IIIb** met with failure.[1] The crucial process involving the introduction of the thiazole ring at the anomeric carbon of the *N*-hexopyranosylhydroxylamine **IIb** was unsuccessful by the use of 2-lithiothiazole **3** at −70 °C in Et_2O. Performing the reaction under these conditions was required since substantial decomposition of **3** occurred at higher temperatures.[7] We sought a simple solution to this shortcoming by the use of another thiazole-based organometallic reagent that was enough stable and reactive at higher temperature. Thus, guided by the observation[8] that Grignard reagents reacted with two *N*-hexopyranosylhydroxylamines **IIb,** attention was focused on the use of 2-thiazolylmagnesium bromide **4.** This was a previously scarcely exploited organometallic reagent very likely because of the lack of a standard preparation procedure. Fortunately enough the preparation of **4** was recently optimized in our laboratory.[9] To our delight, the Grignard reagent **4** reacted smoothly with *N*-hexopyranosylhydroxylamines **IIb** at 0 °C in THF, thus paving the way to the target piperidine homoazasugars **IIIb**. The results of this work are presented below.

We considered three model 2,3,4,6-tetra-*O*-benzyl-D-hexopyranoses (D-*gluco* **1a**, D-*manno* **1b**, D-*galacto* **1c**) as readily available starting materials to study the feasibility of the thiazole-based route toward a small yet representative collection of stereodiversified piperidine homoazasaugars. We were aware that in the case of a successful synthesis via the reaction sequence employed for the pyrrolidine homoazasugar synthesis,[1] the products will belong to the L-series of carbohydrates. L-Azasugars which in the past attracted little attention, have been recently reevaluated because while mimicking L-sugars[10] they have been found to be also noncompetitive inhibitors of D-glycohydrolases.[11] Moreover, it has been recently reported a

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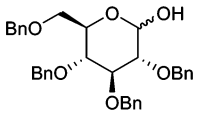
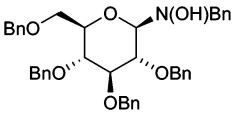
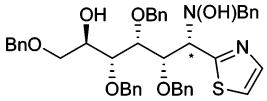
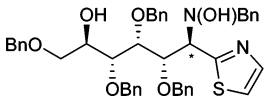
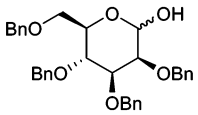
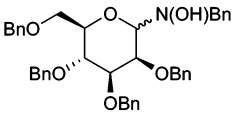
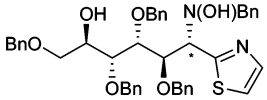
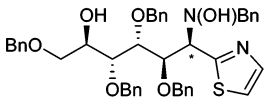
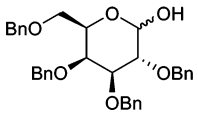
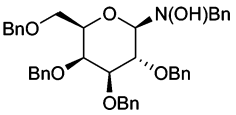
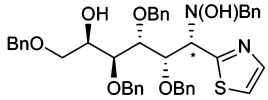
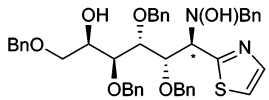
TABLE 1. ***N*-Glycosylhydroxylamines 2 Prepared[a] from Pyranoses 1 and Their Adducts[b] 5a−c, 6a−c with 2-Thiazolylmagnesium Bromide 4**

Pyranose	Hydroxylamine (% yield)	Product (dr, % yield)[c]		
			(75:25, 80%)	
1a	**2a** (70%)	**5a**		**6a**[d]
			(60:40, 82%)	
1b	**2b** (81%)	**5b**		**6b**
			(67:33, 77%)	
1c	**2c** (88%)	**5c**		**6c**

[a] Neat **1** and BnNHOH at 110 °C, 1 h. [b] 5 equiv of **4** in THF at 0 °C. [c] dr ratios determined by ^{1}H NMR analysis. [d] Not isolated in pure form.

synthetic azasugar with the L-*altro* configuration featuring great potential as immunosuppressive agent.[12] Hence compounds **1a−c** were conveniently transformed into the corresponding *N*-benzyl-*N*-glycosylhydroxylamines **2a−c** (Table 1) on heating their mixtures with *N*-benzylhydroxylamine at 110 °C for 1 h in the absence of solvent. While the β-configuration of the D-*gluco* **2a** and D-*galacto* **2c** derivatives was previously assigned on the basis of the $J_{1,2}$ values,[8] the assignment of the anomeric configuration of the D-*manno* isomer **2b** appeared to be problematic. In fact, ROESY experiments were inconclusive. Moreover, the measurement of the $^1J_{C1-H1}$ (157.5 Hz) appeared to us of scarce utility because of the unavailable value of the other anomer and the absence of an extensive set of data for α- and β-*N*-glycosylhydroxylamines.[13] Therefore, the structure of **2b** remains at present unassigned. No one of compounds **2a−c** showed by NMR analysis the presence of the open-chain nitrone form. Nevertheless treatment of these hydroxylamines with excess (5.0 equiv) of 2-thiazolylmagnesium bromide **4** in THF at 0 °C for 2 h afforded three pairs of formal adducts to nitrones, i.e., the thiazolylalkylhydroxylamine diastereoisomers **5a−6a**, **5b−6b**, and **5c−6c** respectively, in good overall yield but modest selectivity (Table 1). Unfortunately, attempts to separate **5a** and **6a** by flash chromatography were unsuccessful. Only a pure sample of **5a** was obtained by preparative TLC. On the other hand, each isomer of the pairs **5b−6b** and **5c−6c** was separated by flash chromatography. The configuration of the newly formed stereocenter in all compounds **5** and **6** was established following the conversion of their mixtures or individually isolated pure compounds into piperidines (see below). Thus, it appeared that the major diastereoisomers **5a** and **5c** were both *syn*-adducts, whereas the main product **5b** was an *anti*-adduct. Evidently, the configuration of the carbon stereocenter adjacent to the nitrone group affects substantially the selectivity of these reactions. Variable *syn*/*anti* selectivities in the additions of organometallic reagents to nitrones derived from chiral polyalkoxy aldehydes and aldehydo sugars were recorded in a number of cases studied in our[14] and other [15] laboratories.

Either the individually isolated hydroxylamines **5** and **6** or their mixtures were transformed into polyhydroxylated 2-thiazolylpiperidines **9** and **10** (Table 2). Improved conditions were used with respect to those employed for the synthesis of the pyrrolidine derivatives.[1] Specifically, the reductive dehydroxylation of the N(OH)Bn group was first carried out by Zn−Cu $(OAc)_2 \cdot H_2O$ to give the amino alcohols **7** and **8**. Attempts of cyclization of these compounds to piperidine derivatives via activation of the free hydroxyl group with triflic anhydride as reported[1] gave complex mixtures of products. This crucial operation was conveniently carried out via *O*-mesylate formation at 0−5 °C in toluene employing methanesulfonyl chloride (MsCl) in the presence of Et_3N (1.5 equiv) and catalytic *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, TMEDA, as a promoter,[16] followed by heating the crude product in MeCN at 85 °C. Under these conditions, the piperidines **9a** and **10a** (from D-glucose), **9b** (from D-mannose), and **9c**, **10c** (from D-galactose)

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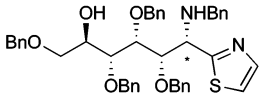
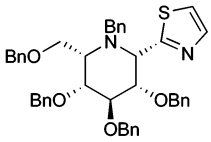
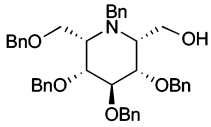
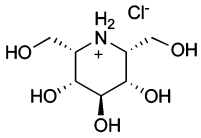
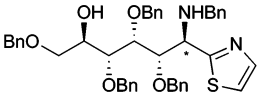
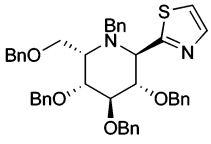
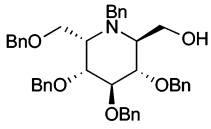
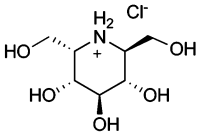
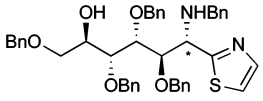
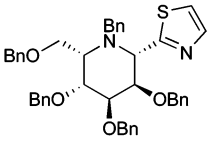
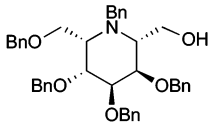
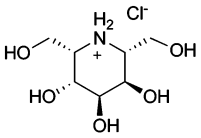
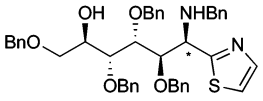
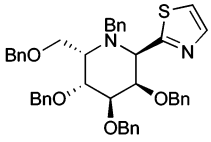
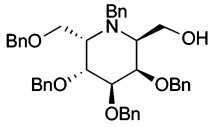
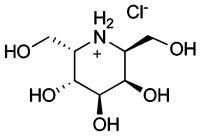
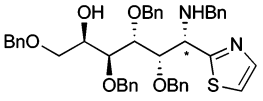
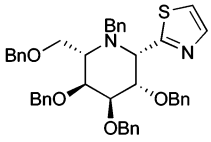
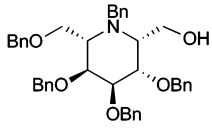
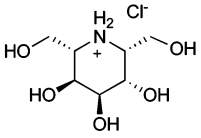
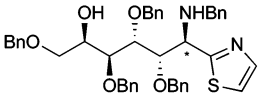
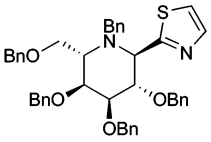
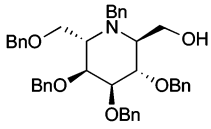
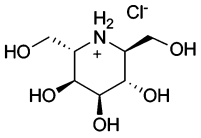
TABLE 2. Protected (11a−c, 12a−c) and Free (13a−c, 14a−c) Piperidine Homoazasugars Prepared from Sugar Hydroxylamines 5a−c, 6a−c

Hydroxylamine	Amine	Piperidine (% yield)	Protected homoazasugar (% yield)	Free homoazasugar (% yield)
5a	 **7a**	 **9a** (80%)	 **11a** (56%)	 **13a** (92%)
6a	 **8a**	 **10a** (70%)	 **12a** (71%)	 **14a** (89%)
5b	 **7b**	 **9b** (70%)	 **11b** (36%)	 **13b** (56%)
6b	 **8b**	 **10b** (52%)[a]	 **12b** (31%)	 **14b** (88%)
5c	 **7c**	 **9c** (76%)	 **11c** (37%)	 **13c** (87%)
6c	 **8c**	 **10c** (70%)	 **12c** (50%)	 **14c** (86%)

[a] A side product (ca. 30%) has been isolated (ref 17).

were obtained as the sole diastereoisomers in good isolated yields (70−80%). Only the piperidine **10b** was obtained in low yield (52%) because an unexpected byproduct was also formed, which was characterized as a *C*-furanosyl substituted thiazolylalkylamine.[17] The configuration of the C2 carbon bearing the thiazole ring in all piperidines **9** and **10** was established by analysis of their ^{1}H NMR spectra and determination of coupling constant values of all protons of the heterocyclic ring. Hence, based on the reasonable assumption that the ring closure reaction occurred via an S_N2 mechanism, the configuration of the corresponding open-chain amine and hydroxylamine precursors was assigned with high degree of confidence.

With the three pairs of thiazolylpiperidine epimers **9a**−**10a**, **9b**−**10b**, and **9c**−**10c** in hand, their transformation into the corresponding homoazasugars **11a**−**12a**, **11b**−**12b**, and **11c**−**12c** commenced by cleavage of the thiazole ring. Although earlier work in our laboratory showed that the presence of the NBn group was incompatible with the thiazole-to-aldehyde unmasking protocol,[18] this shortcoming did not occur with the thiazolyl-piperidines **9** and **10**. Hence, these compounds were subjected to the one-pot sequence consisting of microwave (MW)-assisted[19] methylation (MeI), reduction ($NaBH_4$), and $HgCl_2$-promoted hydrolysis. Crude piperidine aldehydes thus formed were reduced by $NaBH_4$ to the corresponding alcohols **11** and **12**. The isolated overall yields of these products varied from 31 to 71% without any apparent reason. Finally, the removal of the *O*-Bn and *N*-Bn protective groups from compounds **11** and **12** by H_2 (100psi) and $Pd(OH)_2$/C in the presence

of HCl afforded the three pairs of epimers, i.e., free dideoxyiminoheptitol hydrochlorides **13a**−**14a**, **13b**−**14b**, and **13c**−**14c**. These salts, with the exception of **13b**, were isolated in very good yields. Compounds **13b**[20] and **13c**[21] showed characteristics identical to those of the literature.

In conclusion, the results of the present work demonstrate the successful extension of the thiazole-based aminohomologation strategy to pyranoses. The reactions in this sequence while being nontrivial are operationally simple and do not show limitations by the structural change of the reactants employed. Hence, since this methodology works quite well with both furanoses and pyranoses, we believe that significant collections of pyrrolidine and piperidine homoazasugars with a wide range of stereochemical diversity will become accessible.

Experimental Section

All moisture-sensitive reactions were performed under a nitrogen atmosphere using oven-dried glassware. Solvents were dried over standard drying agent and freshly distilled prior to use. Reactions were monitored by TLC on silica gel 60 F_{254} with detection by charring with ethanolic solution of sulfuric acid or ninhydrin. Flash column chromatography was performed on silica gel 60 (230−400 mesh). The microwave (MW) irradiation was performed by a Biotage Initiator apparatus. Optimization experiments were performed in the "single-run" mode, i.e., by manual filling of reaction vials and by specifying the irradiation time and maximum temperature. 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}. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded for $CDCl_3$ solutions at room temperature unless otherwise specified. Assignments were aided by homo-2D experiments. MALDI-TOF mass spectra were acquired using 2,6-dihydroxy benzoic acid (DHB) as matrix. *N*-Benzyl-*N*-glycosylhydroxylamines **2a** and **2c**,[8] 2,6-dideoxy-2,6-imino heptitol hydrochloride **13b**,[20] and the free amine of **13c**[21] were known compounds.

General Procedure for the Preparation of *N*-Benzyl-*N*-glycosylhydroxylamines 2a−c. A mixture of 2,3,4,6-tetra-*O*-benzylhexopyranose **1a**−**c** (5.00 g, 9.25 mmol) and *N*-benzylhydroxylamine (1.71 g, 13.88 mmol) was stirred at 110 °C for 1 h. The resulting residue was cooled to room temperature and purified by crystallization.

***N*-Benzyl *N*-2,3,4,6-tetra-*O*-benzyl-D-mannopyranosylhydroxylamine (2b).** Crystallization from cyclohexane afforded **2b** (4.85 g, 81%) as a white solid. Mp = 101−103 °C. $[\alpha]_D$ = 16.3 (*c* 0.6, $CHCl_3$). ^{1}H NMR (C_6D_6): δ = 7.40−7.00 (m, 25 H, Ph), 4.84 and 4.48 (2 d, 2 H, J = 11.5 Hz, CH_2Ph), 4.64 and 4.60 (2 d, 2 H, J = 11.5 Hz, CH_2Ph), 4.55 (d, 1 H, $J_{1,2}$ = 3.0 Hz, H-1), 4.48 and 4.41 (2 d, 2 H, J = 11.5 Hz, CH_2Ph), 4.48 (s, 2 H, CH_2Ph), 4.38 and 3.54 (2 d, 2 H, J = 13.5 Hz, N−CH_2Ph), 4.35 (ddd, 1 H, $J_{5,4}$ = 8.5 Hz, $J_{5,6a}$ = 4.0 Hz, $J_{5,6b}$ = 4.5 Hz, H-5), 4.24 (t, 1 H, $J_{2,1}$ = $J_{2,3}$ = 3.0 Hz, H-2), 4.15 (t, 1 H, $J_{4,3}$ = $J_{4,5}$ = 8.5 Hz, H-4), 4.11 (s, 1 H, N(OH)), 4.02 (dd, 1 H, $J_{3,2}$ = 3.0 Hz, $J_{3,4}$ = 8.5 Hz, H-3), 3.75 (m, 2 H, H-6a and H-6b). ^{13}C NMR (C_6D_6): δ = 138.9, 138.1, 137.2, 129.9−127.0, 90.3, 79.9, 75.5, 74.8, 74.3, 73.9, 73.1, 72.6, 70.1, 60.1, $^1J_{C1-H1}$ = 157.5 Hz. MALDI-TOF MS: 668.2 (M + Na), 684.5 (M + K). Anal. Calcd for $C_{41}H_{43}NO_6$ (645.3): C, 76.25; H, 6.71; N, 2.17. Found: C, 76.35; H, 6.63; N, 2.29.

General Procedure for the Addition of 2-Thiazolylmagnesium Bromide 4 to *N*-Benzyl-*N*-glycosylhydroxylamines 2a−c. To a cooled (0 °C), stirred mixture of ethylmagnesium bromide (12.9 mL, 38.74 mmol of a 3 M solution in Et_2O) and anhydrous THF (82 mL) was added dropwise a solution of freshly distilled 2-bromothiazole (3.49 mL, 38.74 mmol) in dry THF (15 mL) in ca. 15 min. The resulting pale yellow-orange solution was kept at 0 °C for an additional 10 min and then warmed to room temperature and stirred for 1.5−2 h until the color of the solution changed to red-violet. The mixture was then cooled to 0 °C, and a solution of *N*-benzyl-*N*-glycosyl hydroxylamine **2a**−**c** (5.00 g, 7.75 mmol) in anhydrous THF (35 mL) was added dropwise in ca. 20 min. The mixture was stirred at 0 °C for 1−2 h and then quenched with 1 M aqueous phosphate buffer (25 mL). The layers were separated, and the aqueous phase was extracted with AcOEt (2 × 50 mL). The collected organic phases were washed with 1 M aqueous phosphate buffer (2 × 50 mL), dried over Na_2SO_4, filtered, and concentrated. The residue was eluted from a column of silica gel with the suitable elution system to give the corresponding thiazolyl derivatives **5a**−**c**, **6a**−**c**.

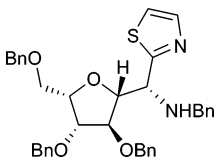
(2*R*,3*R*,4*R*,5*S*,6*R*)- and (2*R*,3*R*,4*R*,5*S*,6*S*)-6-*N*-Benzylhydroxylamino-1,3,4,5-tetra-*O*-benzyl-6-thiazolyl-1,2,3,4,5-hexanepentol (5a and 6a). Column chromatography with 3:1 cyclohexane−AcOEt afforded **5a** and **6a** (4.54 g, 80%) as a 3:1 unseparable mixture of diastereoisomers. The above mixture was subjected to preparative TLC analysis with 4:1 cyclohexane−AcOEt.

Eluted first was **5a**. $[\alpha]_D$ = 4.6 (*c* 0.5, MeOH). ^{1}H NMR (C_6D_6): δ = 7.55 (d, 1 H, J = 3.2 Hz, Th), 7.40−7.00 (m, 25 H, Ph), 6.62 (d, 1 H, J = 3.2 Hz, Th), 6.05 (s, 1 H, N(OH)Bn), 5.04 (d, 1 H, $J_{6,5}$ = 6.0 Hz, H-6), 4.76 (s, 2 H, CH_2Ph), 4.73 and 4.52 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.59 (dd, 1 H, $J_{5,4}$ = 5.5 Hz, $J_{5,6}$ = 6.0 Hz, H-5), 4.49 (s, 2 H, CH_2Ph), 4.30 and 4.24 (2 d, 2 H, J = 12.0 Hz, CH_2Ph), 4.21 (m, 1 H, H-2), 4.05 (dd, 1 H, $J_{4,3}$ = 4.5 Hz, $J_{4,5}$ = 5.0 Hz, H-4), 3.97 and 3.70 (2 d, 2 H, J = 13.0 Hz, N−CH_2-Ph), 3.87 (dd, 1 H, $J_{3,2}$ = 7.0 Hz, $J_{3,4}$ = 4.5 Hz, H-3), 3.59 (dd, 1 H, $J_{1a,1b}$ = 9.5 Hz, $J_{1a,2}$ = 3.5 Hz, H-1a), 3.56 (dd, 1 H, $J_{1b,1a}$ = 9.5 Hz, $J_{1b,2}$ = 5.5 Hz, H-1b), 2.85 (s, 1 H, OH). ^{13}C NMR (C_6D_6): δ = 164.9, 143.9, 141.7, 139.3, 139.2, 138.9, 138.6, 137.9, 130.1, 128.5−127.6, 120.9, 120.5, 80.8, 79.2, 74.9, 74.3, 74.0, 73.4, 71.6, 67.4, 62.0. MALDI-TOF MS: 731.8 (M), 753.8 (M + Na). Anal. Calcd for $C_{44}H_{46}N_2O_6S$ (730.3): C, 72.30; H, 6.34; N, 3.83. Found C, 72.31; H, 6.36; N, 3.85.

Eluted second was **6a** contaminated by **5a**. ^{1}H NMR for **6a** (C_6D_6, selected data): δ = 7.52 (d, 1 H, J = 3.2 Hz, Th), 6.60 (d, 1 H, J = 3.2 Hz, Th).

(2*R*,3*R*,4*R*,5*R*,6*R*)- and (2*R*,3*R*,4*R*,5*R*,6*S*)-6-*N*-Benzylhydroxylamino-1,3,4,5-tetra-*O*-benzyl-6-thiazolyl-1,2,3,4,5-hexanepentol (5b and 6b). Column chromatography with 4:1 cyclohexane−AcOEt afforded, first, **5b** (2.27 g, 40%) as a foam. $[\alpha]_D$ = 14.9 (*c* 0.3, $CHCl_3$). ^{1}H NMR (C_6D_6): δ = 7.55 (d, 1 H, J = 3.2 Hz,

(17) NMR and mass spectral data are consistent with the structure shown below. ^{1}H NMR (400 MHz, C_6D_6): δ = 7.52 (d, 1 H, J = 3.2 Hz, Th), 7.25−7.00 (m, 20 H, Ph), 6.67 (d, 1 H, J = 3.2 Hz, Th), 4.57 (dd, 1 H, $J_{4,3}$ = 2.0 Hz, $J_{4,5}$ = 0.5 Hz, H-4), 4.56 (d, 1 H, $J_{2,3}$ = 9.0 Hz, H-2), 4.54 and 4.18 (2 d, 2 H, J = 11.5 Hz, CH_2Ph), 4.49 (ddd, 1 H, $J_{6,5}$ = 4.5 Hz, $J_{6,7a}$ = $J_{6,7b}$ = 6.0 Hz, H-6), 4.35 (dd, 1 H, $J_{3,2}$ = 9.0 Hz, $J_{3,4}$ = 2.0 Hz, H-3), 4.35 and 4.29 (2 d, 2 H, J = 12.0 Hz, CH_2Ph), 4.10 and 4.02 (2 d, 2 H, J = 12.0 Hz, CH_2Ph), 3.90 (dd, 1 H, $J_{5,4}$ = 0.5 Hz, $J_{5,6}$ = 4.5 Hz, H-5), 3.82 (dd, 1 H, $J_{7a,6}$ = 6.0 Hz, $J_{7a,7b}$ = 10.0 Hz, H-7a), 3.72 and 3.47 (2 d, 2 H, J = 13.5 Hz, N-CH_2Ph), 3.71 (dd, 1 H, $J_{7b,6}$ = 6.0 Hz, $J_{7b,7a}$ = 10.0 Hz, H-7b), 2.84 (bs, 1 H, NH). MALDI-TOF MS: 629.54 (M+Na), 645.46 (M+K). The formation of this compound from the precursor **8b** can be explained to occur by intramolecular C−O bond formation via mesylate displacement by the OBn group at C2 followed by elimination of the benzyl cation.



(18) (a) Dondoni, A.; Marra, A. *Chem. Rev.* **2004**, *104*, 2557−2600. (b) Dondoni, A. *Synthesis* **1998**, 1681−1706.

(19) It is worth pointing out that under these new conditions (i.e., MW, 110 °C, 35 equiv of MeI) the *N*-methylation of the thiazole ring went to completion in 10−15 min.

(20) Bruce, I.; Fleet, G. W. J.; Cenci di Bello, I.; Winchester, B. *Tetrahedron Lett.* **1989**, *51*, 7257−7260.

(21) Shilvock, J. P.; Nash, R. J.; Watson, A. A.; Winters, A. L.; Butters, T. D.; Dwek, R. A.; Winkler, D. A.; Fleet, G. W. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2747−2754.

Th), 7.40−7.00 (m, 25 H, Ph), 6.64 (d, 1 H, J = 3.2 Hz, Th), 5.13 (d, 1 H, $J_{6,5}$ = 7.5 Hz, H-6), 4.98 and 4.85 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.90 and 4.65 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.80 (dd, 1 H, $J_{5,4}$ = 3.0 Hz, $J_{5,6}$ = 7.5 Hz, H-5), 4.57 and 4.46 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.33 (dd, 1 H, $J_{3,2}$ = 12.0 Hz, $J_{3,4}$ = 6.0 Hz, H-3), 4.30 (dd, 1 H, $J_{4,3}$ = 6.0 Hz, $J_{4,5}$ = 3.0 Hz, H-4), 4.22 (s, 2 H, CH_2Ph), 4.18 (ddd, 1 H, $J_{2,1a}$ = 5.5 Hz, $J_{2,1b}$ = 3.5 Hz, $J_{2,3}$ = 12.0 Hz, H-2), 3.93 and 3.68 (2 d, 2 H, J = 13.0 Hz, N−CH_2Ph), 3.69 (dd, 1 H, $J_{1a,1b}$ = 9.0 Hz, $J_{1a,2}$ = 3.5 Hz, H-1a), 3.58 (dd, 1 H, $J_{1b,1a}$ = 9.0 Hz, $J_{1b,2}$ = 5.5 Hz, H-1b). ^{13}C NMR: δ = 166.6, 141.5, 138.7, 138.5, 138.0, 137.0, 129.3−127.3, 119.9, 81.1, 80.1, 79.5, 74.5, 74.3, 73.5, 73.3, 71.3, 71.2, 67.2, 62.0. MALDI-TOF MS: 752.7 (M + Na). Anal. Calcd. for $C_{44}H_{46}N_2O_6S$ (730.3): C, 72.30; H, 6.34; N, 3.83. Found: C, 72.18; H, 6.34; N, 3.84.

Eluted second was a 2:1 mixture of **6a** and **6b** (0.83 g, 15%).

Eluted third was pure **6b** (1.53 g, 27%) as a syrup. $[\alpha]_D$ = −8.8 (*c* 0.8, MeOH). ^{1}H NMR: δ = 7.84 (d, 1 H, J = 3.2 Hz, Th), 7.40−7.10 (m, 26 H, Ph and Th), 5.95 (s, 1 H, N(OH)), 4.90 (d, 1 H, $J_{6,5}$ = 5.5 Hz, H-6), 4.72 and 4.68 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.66 and 4.58 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.58 and 4.46 (2 d, 2 H, J = 11.5 Hz, CH_2Ph), 4.49 and 4.47 (2 d, 2 H, J = 10.0 Hz, CH_2Ph), 4.48 (t, 1 H, $J_{5,4}$ = $J_{5,6}$ = 5.5 Hz, H-5), 4.14 (dd, 1 H, $J_{4,3}$ = 4.0 Hz, $J_{4,5}$ = 5.5 Hz, H-4), 4.00 (ddd, 1 H, $J_{2,1a}$ = 3.0 Hz, $J_{2,1b}$ = 5.5 Hz, $J_{2,3}$ = 7.5 Hz, H-2), 3.85 and 3.73 (2 d, 2 H, J = 13.5 Hz, N−CH_2Ph), 3.73 (dd, 1 H, $J_{3,2}$ = 7.5 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 3.64 (dd, 1 H, $J_{1a,1b}$ = 9.5 Hz, $J_{1a,2}$ = 3.0 Hz, H-1a), 3.57 (dd, 1 H, $J_{1b,1a}$ = 9.5 Hz, $J_{1b,2}$ = 5.5 Hz, H-1b), 2.90 (s, 1 H, OH). ^{13}C NMR: δ = 165.4, 141.8, 138.5, 138.2, 137.9, 137.5, 129.2−127.2, 120.3, 80.9, 79.6, 78.4, 74.2, 73.3, 73.1, 71.2, 70.5, 67.7, 61.4. MALDI-TOF MS: 731.9 (M+H), 753.9 (M + Na). Anal. Calcd for $C_{44}H_{46}N_2O_6S$ (730.3): C, 72.30; H, 6.34; N, 3.83. Found C, 72.13; H, 6.36; N, 3.81.

(2*R*,3*S*,4*R*,5*S*,6*R*)- and (2*R*,3*S*,4*R*,5*S*,6*S*)-6-*N*-Benzylhydroxylamino-1,3,4,5-tetra-*O*-benzyl-6-thiazolyl-1,2,3,4,5-hexanepentol (5c and 6c). Column chromatography with 10:1 CH_2Cl_2−isopropyl ether afforded, first, **6c** (0.83 g, 15%) as a foam. $[\alpha]_D$ = −18.2 (*c* 0.5, $CHCl_3$). ^{1}H NMR (C_6D_6): δ = 7.60 (d, 1 H, J = 3.2 Hz, Th), 7.30−6.90 (m, 25 H, 5Ph), 6.66 (d, 1 H, J = 3.2 Hz, Th), 5.02 (d, 1 H, $J_{6,5}$ = 9.0 Hz, H-6), 4.77 and 4.72 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.71 and 4.31 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.66 and 4.43 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.65 (dd, 1 H, $J_{5,4}$ = 4.0 Hz, $J_{5,6}$ = 9.0 Hz, H-5), 4.50 (dd, 1 H, $J_{4,3}$ = 6.0 Hz, $J_{4,5}$ = 4.0 Hz, H-4), 4.43 (ddd, 1 H, $J_{2,1a}$ = 5.5 Hz, $J_{2,1b}$ = 7.5 Hz, $J_{2,3}$ = 2.0 Hz, H-2), 4.35 (dd, 1 H, $J_{3,2}$ = 2.0 Hz, $J_{3,4}$ = 6.0 Hz, H-3), 4.19 and 4.09 (2 d, 2 H, J = 12.0 Hz, CH_2Ph), 3.83 and 3.72 (2 d, 2 H, J = 13.0 Hz, N−CH_2Ph), 3.52 (dd, 1 H, $J_{1a,1b}$ = 9.0 Hz, $J_{1a,2}$ = 5.5 Hz, H-1a), 3.42 (dd, 1 H, $J_{1b,1a}$ = 9.0 Hz, $J_{1b,2}$ = 7.5 Hz, H-1b), 3.17 (s, 1 H, OH). ^{13}C NMR: δ = 166.1, 141.6, 138.1, 136.8, 129.5−127.3, 120.2, 100.0, 80.5, 79.8, 77.9, 75.1, 73.6, 73.4, 73.3, 70.7, 69.8, 68.5, 61.7. MALDI-TOF MS: 731.7 (M + H). Anal. Calcd for $C_{44}H_{46}N_2O_6S$ (730.3): C, 72.30; H, 6.34; N, 3.83. Found: C, 72.23; H, 6.33; N, 3.84.

Eluted second was a 3:1 mixture of **5c** and **6c** (1.17 g, 21%).

Eluted third was pure **5c** (2.34 g, 41%) as a foam. $[\alpha]_D$ = −8.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR: δ = 7.91 (d, 1 H, J = 3.3 Hz, Th), 7.41 (d, 1 H, J = 3.3 Hz, Th), 7.35−7.14 (m, 25 H, 5Ph), 6.10 (s, 1 H, N(OH)), 4.83 and 4.77 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.79 (d, 1 H, $J_{6,5}$ = 6.0 Hz, H-6), 4.67 and 4.64 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.63 and 4.49 (2 d, 2 H, J = 11.5 Hz, CH_2Ph), 4.36 (t, 1 H, $J_{5,4}$ = $J_{5,6}$ = 6.0 Hz, H-5), 4.23 and 4.18 (2 d, 2 H, J = 11.5 Hz, CH_2Ph), 4.10 (m, 2 H, H-3 and H-2), 3.93 (t, 1 H, $J_{4,3}$ = $J_{4,5}$ = 5.5 Hz, H-4), 3.80 and 3.66 (2 d, 2 H, J = 13.0 Hz, N−CH_2Ph), 3.43 (dd, 1 H, $J_{1a,1b}$ = 9.0 Hz, $J_{1a,2}$ = 5.5 Hz, H-1a), 3.36 (dd, 1 H, $J_{1b,1a}$ = 9.0 Hz, $J_{1b,2}$ = 7.5 Hz, H-1b), 3.02 (s, 1 H, OH). ^{13}C NMR: δ = 164.6, 142.1, 138.6, 138.3, 138.2, 137.6, 137.2, 129.6−127.3, 120.3, 80.3, 79.8, 75.0, 73.4, 73.1, 72.8, 70.5, 69.4, 67.9, 61.9. MALDI-TOF MS: 768.8 (M + K). Anal. Calcd for $C_{44}H_{46}N_2O_6S$ (730.3): C, 72.30; H, 6.34; N, 3.83. Found: C, 72.48; H, 6.32; N, 3.82.

(2*R*,3*S*,4*R*,5*R*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-2-thiazolyl-3,4,5-tribenzyloxypiperidine and (2*S*,3*S*,4*R*,5*R*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-2-thiazolyl-3,4,5-tribenzyloxypiperidine (9a and 10a). To a stirred solution of $(AcO)_2Cu\cdot H_2O$ (13 mg, 0.11 mmol) in AcOH (1.0 mL) was added Zn dust (0.36 g, 0.56 mmol) in one portion. The resulting suspension was vigorously stirred at room temperature for 10 min, and then a solution of a 3:1 mixture of **5a** and **6a** (1.02 g, 1.4 mmol) in AcOH (13.0 mL) and H_2O (5.0 mL) was added dropwise. The resulting mixture was warmed to 80 °C for 1 h. The suspension was filtered through a pad of Celite, neutralized with aqueous 3 M NaOH, and extracted with AcOEt (3 × 25 mL). The organic layer was washed with a saturated aqueous solution of EDTA (30 mL), dried over Na_2SO_4, filtered, concentrated, and eluted from a column of silica gel with 4:1 cyclohexane−AcOEt to afford, first, **7a** (0.54 g, 54%) and, second, **8a** (0.29 g, 20%), both as syrups.

To a cooled (0 °C), stirred mixture of the above amine **7a** or **8a**, anhydrous toluene (6.0 mL), Et_3N (0.28 mL, 0.84 mmol), and TMEDA (9.0 μL, 0.057 mmol) was added MsCl (65 μL, 0.84 mmol) dropwise. The resulting mixture was stirred for 1 h, and then MeOH (100 μL) and Et_3N (0.28 mL) were added in one portion and the mixture was stirred for an additional 5 min. The solvent was then evaporated, and the crude was taken up in CH_3CN (6.0 mL) and Et_3N (0.28 mL, 0.84 mmol). The solution was warmed to 85 °C for 4−20 h. Then, the mixture was cooled to room temperature and concentrated. The resulting crude material was diluted in AcOEt (10 mL), washed with saturated $NaHCO_3$ (2 × 10 mL), dried over Na_2SO_4, filtered, concentrated, and eluted from a column of silica gel with the suitable elution system to give the corresponding piperidines **9a** and **10a**.

(2*R*,3*S*,4*R*,5*R*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-2-thiazolyl-3,4,5-tribenzyloxypiperidine (9a). Column chromatography with 6:1 cyclohexane−AcOEt afforded **9a** (321 mg, 80%) as a syrup. $[\alpha]_D$ = −20.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR: δ = 7.80 (d, 1 H, J = 3.1 Hz, Th), 7.40−7.10 (m, 26 H, 5Ph and Th), 4.87 and 4.82 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.65 and 4.55 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.50 and 4.43 (2 d, 2 H, J = 12.0 Hz, CH_2Ph), 4.45 (d, 1 H, $J_{2,3}$ = 5.5 Hz, H-2), 4.36 (dd, 1 H, $J_{4,3}$ = 7.0 Hz, $J_{4,5}$ = 8.5 Hz, H-4), 4.23 and 4.16 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.16 and 4.09 (2 d, 2 H, J = 15.0 Hz, N−CH_2Ph), 3.91 (dd, 1 H, $J_{3,2}$ = 5.5 Hz, $J_{3,4}$ = 7.0 Hz, H-3), 3.83 (dd, 1 H, $J_{5,4}$ = 8.5 Hz, $J_{5,6}$ = 5.5 Hz, H-5), 3.68 (dd, 1 H, $J_{7a,6}$ = 4.5 Hz, $J_{7a,7b}$ = 9.5 Hz, H-7a), 3.57 (ddd, 1 H, $J_{6,5}$ = 5.5 Hz, $J_{6,7a}$ = 4.5 Hz, $J_{6,7b}$ = 6.5 Hz, H-6), 3.50 (dd, 1 H, $J_{7b,6}$ = 6.5 Hz, $J_{7b,7a}$ = 9.5 Hz, H-7b). ^{13}C NMR: δ = 142.1, 139.1−137.9, 128.5−127.1, 119.3, 80.2, 79.9, 79.2, 74.5, 72.8, 72.6, 72.3, 69.4, 59.2, 59.1, 58.1. MALDI-TOF MS: 718.8 (M + Na). Anal. Calcd for $C_{44}H_{44}N_2O_4S$ (696.3): C, 75.83; H, 6.36; N, 4.02. Found: C, 75.91; H, 6.38; N, 4.03.

(2*S*,3*S*,4*R*,5*R*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-2-thiazolyl-3,4,5-tribenzyloxypiperidine (10a). Column chromatography with 6:1 cyclohexane−AcOEt afforded **10a** (281 mg, 70%) as a syrup. $[\alpha]_D$ = −28.2 (*c* 0.94, $CHCl_3$). ^{1}H NMR: δ = 7.78 (d, 1 H, J = 3.1 Hz, Th), 7.40−6.95 (m, 26 H, 5Ph and Th), 4.93 and 4.78 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.65 (d, 1 H, $J_{2,3}$ = 9.0 Hz, H-2), 4.60 and 4.00 (2 d, 2 H, J = 10.0 Hz, CH_2Ph), 4.57 and 4.53 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.55 (s, 2 H, CH_2Ph), 3.96 (t, 1 H, $J_{4,3}$ = $J_{4,5}$ = 9.0 Hz, H-4), 3.95 and 3.92 (dd, 1 H, $J_{7a,6}$ = 5.0 Hz, $J_{7a,7b}$ = 9.5 Hz, H-7a), 3.89 (t, 1 H, $J_{3,2}$ = $J_{3,4}$ = 9.0 Hz, H-3), 3.83 (dd, 1 H, $J_{5,4}$ = 9.0 Hz, $J_{5,6}$ = 2.5 Hz, H-5), 3.79 (dd, 1 H, $J_{7b,6}$ = 5.0 Hz, $J_{7b,7a}$ = 9.5 Hz, H-7b), 3.74 and 3.49 (2 d, 2 H, J = 14.0 Hz, N−CH_2Ph), 3.31 (ddd, 1 H, $J_{6,5}$ = 2.5 Hz, $J_{6,7a}$ = $J_{6,7b}$ = 5.0 Hz, H-6). ^{13}C NMR: δ = 141.9, 138.9, 138.3, 138.2, 128.3−126.8, 119.8, 85.5, 82.6, 79.8, 75.2, 75.0, 73.3, 72.4, 64.8, 64.6, 56.0, 53.1. MALDI-TOF MS: 696.4 (M), 720.1 (M + Na). Anal. Calcd for $C_{44}H_{44}N_2O_4S$ (696.3): C, 75.83; H, 6.36; N, 4.02. Found: C, 75.74; H, 6.35; N, 4.02.

General Procedure for the Synthesis of Piperidines 9b−c, 10b−c. To a stirred solution of $(AcO)_2Cu\cdot H_2O$ (13 mg, 0.11 mmol) in AcOH (1.0 mL) was added Zn dust (0.36 g, 0.56 mmol) in one

portion. The resulting suspension was vigorously stirred at room temperature for 10 min, and then a solution of *N*-benzylhydroxylamines **5b**−**c**, **6b**−**c** (0.41 g, 0.57 mmol) in AcOH (5.0 mL) and H_2O (2.0 mL) was added dropwise. The resulting mixture was warmed to 80 °C for 1 h. The suspension was filtered through a pad of Celite, neutralized with aqueous 3 M NaOH, and extracted with AcOEt (3 × 15 mL). The organic layer was washed with a saturated aqueous solution of EDTA (30 mL), dried over Na_2SO_4, filtered, and concentrated to give crude **7b**−**c**, **8b**−**c**.

To a cooled (0 °C), stirred mixture of the above crude amine, anhydrous toluene (6.0 mL), Et_3N (0.28 mL, 0.84 mmol), and TMEDA (9.0 μL, 0.057 mmol) was added MsCl (65 μL, 0.84 mmol) dropwise. The resulting mixture was stirred for an additional 1 h, and then MeOH (100 μL) and Et_3N (0.28 mL) were added in one portion and stirred for an additional 5 min. The solvent was then evaporated, and the crude was taken up in CH_3CN (6.0 mL) and Et_3N (0.28 mL, 0.84 mmol). The solution was warmed to 85 °C for 4−20 h. Then, the mixture was cooled to room temperature and concentrated. The resulting crude material was diluted in AcOEt (10 mL), washed with saturated $NaHCO_3$ (2 × 10 mL), dried over Na_2SO_4, filtered, concentrated, and eluted from a column of silica gel with the suitable elution system to give the corresponding piperidines **9b**−**c**, **10b**−**c**.

(2*R*,3*R*,4*R*,5*R*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-2-thiazolyl-3,4,5-tribenzyloxypiperidine (9b). Column chromatography with 6:1 cyclohexane−AcOEt afforded **9b** (282 mg, 70%) as a pale yellow solid. Mp = 80−82 °C. $[\alpha]_D$ = 24.9 (*c* 0.7, $CHCl_3$). ^{1}H NMR (300 MHz, C_6D_6, 70 °C): δ = 7.50−7.00 (m, 26 H, 5Ph and Th), 6.65 (d, 1 H, *J* = 3.1 Hz, Th), 4.76 (d, 1 H, $J_{2,3}$ = 6.5 Hz, H-2), 4.71 and 4.61 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.66 (dd, 1 H, $J_{3,2}$ = 6.5 Hz, $J_{3,4}$ = 2.5 Hz, H-3), 4.48 (s, 2 H, CH_2Ph), 4.35 and 4.26 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.27 (dd, 1 H, $J_{5,4}$ = 7.0 Hz, $J_{5,6}$ = 4.0 Hz, H-5), 4.17 and 3.91 (2 d, 2 H, *J* = 15.0 Hz, N−CH_2Ph), 4.12 (dd, 1 H, $J_{4,3}$ = 2.5 Hz, $J_{4,5}$ = 7.0 Hz, H-4), 4.08 (s, 2 H, CH_2Ph), 3.72 (dd, 1 H, $J_{7a,6}$ = 6.5 Hz, $J_{7a,7b}$ = 9.0 Hz, H-7a), 3.64 (ddd, 1 H, $J_{6,5}$ = 4.0 Hz, $J_{6,7a}$ = 6.5 Hz, $J_{6,7b}$ = 6.0 Hz, H-6), 3.46 (dd, 1 H, $J_{7b,6}$ = 6.0 Hz, $J_{7b,7a}$ = 9.0 Hz, H-7b). ^{13}C NMR (C_6D_6): δ = 173.2, 141.5, 140.1, 139.1, 138.7, 128.4−126.6, 119.2, 79.6, 75.3, 74.1, 72.9, 72.7, 72.4, 72.2, 69.1, 63.0, 60.7, 58.1. MALDI-TOF MS: 697.55 (M + H), 719.55 (M + Na). Anal. Calcd for $C_{44}H_{44}N_2O_4S$ (696.3): C, 75.83; H, 6.36; N, 4.02. Found: C, 75.99; H, 6.38; N, 4.00.

(2*S*,3*R*,4*R*,5*R*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-2-thiazolyl-3,4,5-tribenzyloxypiperidine (10b). Column chromatography with 6:1 cyclohexane−AcOEt afforded **10b** (209 mg, 52%) as a syrup. $[\alpha]_D$ = −26.3 (*c* 0.6, $CHCl_3$). ^{1}H NMR (C_6D_6, 70 °C): δ = 7.60 (d, 1 H, *J* = 3.2 Hz, Th), 7.45−7.00 (m, 25 H, 5Ph), 6.73 (d, 1 H, *J* = 3.2 Hz, Th), 4.96 (d, 1 H, $J_{2,3}$ = 3.0 Hz, H-2), 4.91 and 4.58 (2 d, 2 H, *J* = 11.0 Hz, CH_2Ph), 4.66 and 4.59 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.53 and 4.38 (2 d, 2 H, *J* = 11.5 Hz, CH_2Ph), 4.44 (dd, 1 H, $J_{5,4}$ = 9.0 Hz, $J_{5,6}$ = 5.0 Hz, H-5), 4.38 (t, 1 H, $J_{3,2}$ = $J_{3,4}$ = 3.0 Hz, H-3), 4.32 (s, 2 H, CH_2Ph), 4.06 and 3.95 (2 d, 2 H, *J* = 15.0 Hz, N−CH_2Ph), 4.02 (dd, 1 H, $J_{4,3}$ = 3.0 Hz, $J_{4,5}$ = 9.0 Hz, H-4), 3.87 (dd, 1 H, $J_{7a,6}$ = 5.0 Hz, $J_{7a,7b}$ = 10.0 Hz, H-7a), 3.82 (dd, 1 H, $J_{7b,6}$ = 4.0 Hz, $J_{7b,7a}$ = 10.0 Hz, H-7b), 3.68 (ddd, 1 H, $J_{6,5}$ = 5.0 Hz, $J_{6,7a}$ = 5.0 Hz, $J_{6,7b}$ = 4.0 Hz, H-6). ^{13}C NMR (C_6D_6): δ = 170.5, 142.5, 141.1, 140.2, 139.4, 139.3, 139.1, 138.7, 128.2, 128.1, 128.0, 127.9, 127.7, 127.4, 127.3, 127.2, 127.1, 126.7, 120.2, 80.3, 77.8, 75.9, 74.9, 73.0, 72.8, 72.5, 71.3, 67.0, 63.1, 57.2, 54.3, 51.6. MALDI-TOF MS: 697.1 (M + H), 719.8 (M + Na). Anal. Calcd for $C_{44}H_{44}N_2O_4S$ (696.3): C, 75.83; H, 6.36; N, 4.02. Found: C, 75.97; H, 6.43; N, 4.05.

(2*R*,3*S*,4*R*,5*S*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-2-thiazolyl-3,4,5-tribenzyloxypiperidine (9c). Column chromatography with 6:1 cyclohexane−AcOEt afforded **9c** (305 mg, 76%) as a syrup. $[\alpha]_D$ = 17.6 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ = 7.74 (d, 1 H, *J* = 3.1 Hz, Th), 7.45−7.10 (m, 26 H, 5Ph and Th), 4.72 (d, 1 H, $J_{2,3}$ = 3.5 Hz, H-2), 4.58 and 4.54 (2 d, 2 H, *J* = 11.0 Hz, CH_2Ph), 4.51 and 4.45 (2 d, 2 H, *J* = 11.5 Hz, CH_2Ph), 4.29 and 4.11 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.19 (dd, 1 H, $J_{5,4}$ = 2.5 Hz, $J_{5,6}$ = 8.5 Hz, H-5), 4.16 and 4.10 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.04 and 3.81 (2 d, 2 H, *J* = 16.0 Hz, N-CH_2Ph), 3.90 (dd, 1 H, $J_{3,2}$ = 3.5 Hz, $J_{3,4}$ = 5.0 Hz, H-3), 3.83 (dd, 1 H, $J_{4,3}$ = 5.0 Hz, $J_{4,5}$ = 2.5 Hz, H-4), 3.67 (dd, 1 H, $J_{7a,6}$ = 3.5 Hz, $J_{7a,7b}$ = 10.0 Hz, H-7a), 3.52 (dd, 1 H, $J_{7b,6}$ = 3.5 Hz, $J_{7b,7a}$ = 10.0 Hz, H-7b), 3.26 (ddd, 1 H, $J_{6,5}$ = 8.5 Hz, $J_{6,7a}$ = $J_{6,7b}$ = 3.5 Hz, H-6). ^{13}C NMR: δ = 141.0, 139.1, 138.6, 138.5, 138.4, 138.0, 128.5−126.4, 120.2, 77.3, 74.1, 73.1, 72.8, 72.5, 72.1, 71.9, 67.7, 62.6, 60.5, 57.1. MALDI-TOF MS: 697.2 (M + H), 719.7 (M + Na). Anal. Calcd for $C_{44}H_{44}N_2O_4S$ (696.3): C, 75.83; H, 6.36; N, 4.02. Found: C, 75.75; H, 6.35; N, 4.03.

(2*S*,3*S*,4*R*,5*S*,6*S*)-*N*-Benzyl-6-benzyloxymethyl-2-thiazolyl-3,4,5-tribenzyloxypiperidine (10c). Column chromatography with 6:1 cyclohexane−AcOEt afforded **10c** (282 mg, 70%) as a syrup. $[\alpha]_D$ = −4.2 (*c* 1.6, $CHCl_3$). ^{1}H NMR (C_6D_6, 70 °C): δ = 7.50−7.00 (m, 26 H, 5Ph and Th), 6.70 (d, 1 H, *J* = 3.1 Hz, Th), 4.79 (dd, 1 H, $J_{3,2}$ = 6.5 Hz, $J_{3,4}$ = 7.0 Hz, H-3), 4.66 (d, 1 H, $J_{2,3}$ = 6.5 Hz, H-2), 4.63 and 4.36 (2 d, 2 H, *J* = 11.0 Hz, CH_2Ph), 4.55 and 4.48 (2 d, 2 H, *J* = 12.0 Hz, CH_2Ph), 4.46 (s, 2 H, CH_2Ph), 4.19 (s, 2 H, CH_2Ph), 4.07 (dd, 1 H, $J_{5,4}$ = 3.0 Hz, $J_{5,6}$ = 5.0 Hz, H-5), 4.02 and 3.93 (2 d, 2 H, *J* = 14.0 Hz, N−CH_2Ph), 3.98 (dd, 1 H, $J_{4,3}$ = 7.0 Hz, $J_{4,5}$ = 3.0 Hz, H-4), 3.78 (q, 1 H, $J_{6,5}$ = $J_{6,7a}$ = $J_{6,7b}$ = 5.0 Hz, H-6), 3.61 (dd, 1 H, $J_{7a,6}$ = 5.0 Hz, $J_{7a,7b}$ = 10.0 Hz, H-7a), 3.54 (dd, 1 H, $J_{7b,6}$ = 5.0 Hz, $J_{7b,7a}$ = 10.0 Hz, H-7b). ^{13}C NMR: δ = 173.5, 141.7, 141.1, 139.3−137.9, 128.5−126.5, 120.3, 119.9, 81.4, 78.2, 76.8, 74.5, 74.2, 73.3, 72.9, 72.6, 72.2, 72.0, 71.6, 70.8, 67.7, 66.4, 63.9, 62.7, 54.5, 52.9. MALDI-TOF MS: 718.5 (M + Na). Anal. Calcd for $C_{44}H_{44}N_2O_4S$ (696.3): C, 75.83; H, 6.36; N, 4.02. Found: C, 75.85; H, 6.39; N, 4.00.

General Procedure for the Synthesis of Piperidine Homoiminosugars 11a−c, 12a−c. A 2.0−5.0 mL process vial was filled with piperidine **9a**−**c**, **10a**−**c** (100 mg, 0.14 mmol), MeI (0.45 mL, 7.2 mmol), and CH_3CN (4.0 mL). The vial was sealed with a Teflon septum and aluminum crimp, using an appropriate crimping tool. The vial was then placed in its correct position in the Biotage Initiator cavity and irradiated for 15 min at 110 °C. After the full irradiation sequence was completed, the vial was cooled to room temperature and then opened. The solution was transferred into a round-bottom flask, and the solvent was removed under reduced pressure. The residue was dissolved in a 3:1 mixture of CH_2Cl_2−MeOH (2.0 mL), cooled to 0 °C in an ice bath; to the resulting mixture $NaBH_4$ (30 mg, 0.72 mmol) was added in one portion while the solution was vigorously stirred. The ice bath was then removed, and after an additional 40 min the solution was treated with acetone (1.0 mL) and diluted with CH_2Cl_2. The resulting mixture was washed with saturated aqueous $NaHCO_3$, and the extracted organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was taken up in a 10:1 mixture of CH_3CN−H_2O (2.0 mL) where some drops of CH_2Cl_2 were added. Then, $HgCl_2$ (43 mg, 0.16 mmol) was added in one portion. After the mixture was stirred for 5 min, a 10% aqueous solution of KI (6.0 mL) was added dropwise. The solution was stirred for an additional 5 min and then extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was taken up in a 3:1 mixture of CH_2Cl_2−MeOH (2.0 mL). The solution was cooled to −35 °C, and $NaBH_4$ (30 mg, 0.72 mmol) was added in one portion. After being stirred for 40 min, the solution was treated with acetone (1.0 mL) and then diluted with CH_2Cl_2. The solution was washed with saturated aqueous $NaHCO_3$ and the extracted organic phase was dried over Na_2SO_4, filtered, concentrated, and eluted from a column of silica gel with the suitable elution system to give the corresponding piperidine homoiminosugars **11a**−**c**, **12a**−**c**.

***N*-Benzyl-2,6-dideoxy-2,6-imino-3,4,5,7-tetra-*O*-benzyl-L-*glycero*-D-*ido*-heptitol (11a).** Column chromatography with 4:1 cyclohexane−AcOEt afforded **11a** (52 mg, 56%) as a syrup. $[\alpha]_D$ = −3.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (C_6D_6): δ = 7.40−7.00 (m, 25 H, 5Ph), 4.85 and 4.80 (2 d, 2 H, *J* = 11.0 Hz, CH_2Ph), 4.44 and 4.36 (2 d, 2 H, *J* = 11.5 Hz, CH_2Ph), 4.39 and 4.34 (2 d, 2 H, *J* =

11.5 Hz, CH_2Ph), 4.32 and 4.21 (2 d, 2 H, J = 11.5 Hz, CH_2Ph), 4.02 (m, 1 H, H-1a), 3.93 (s, 2 H, N-CH_2Ph), 3.91 (dd, 1 H, $J_{1b,1a}$ = 11.5 Hz, $J_{1b,2}$ = 8.0 Hz, H-1b), 3.80 (t, 1 H, $J_{4,3} = J_{4,5}$ = 9.0 Hz, H-4), 3.76 (dd, 1 H, $J_{5,4}$ = 10.0 Hz, $J_{5,6}$ = 5.0 Hz, H-5), 3.70 (dd, 1 H, $J_{3,2}$ = 6.5 Hz, $J_{3,4}$ = 9.0 Hz, H-3), 3.65 (dd, 1 H, $J_{7a,6}$ = 2.0 Hz, $J_{7a,7b}$ = 8.0 Hz, H-7a), 3.63 (dd, 1 H, $J_{7b,6}$ = 2.0 Hz, $J_{7b,7a}$ = 8.0 Hz, H-7b), 3.46 (ddd, 1 H, $J_{6,5}$ = 5.0 Hz, $J_{6,7a} = J_{6,7b}$ = 2.0 Hz, H-6), 3.39 (ddd, 1 H, $J_{2,1b}$ = 8.0 Hz, $J_{2,3}$ = 6.5 Hz, H-2). ^{13}C NMR: δ = 139.9, 138.8, 138.1, 137.9, 128.5−127.2, 79.9, 79.6, 79.2, 75.7, 73.4, 73.2, 72.9, 70.2, 61.3, 60.7, 60.4, 57.5. MALDI-TOF MS: 666.7 (M + Na), 682.7 (M + K). Anal. Calcd for $C_{42}H_{45}NO_5$ (643.3): C, 78.35; H, 7.05; N, 2.18. Found: C, 78.43; H, 7.08; N, 2.17.

***N*-Benzyl-2,6-dideoxy-2,6-imino-3,4,5,7-tetra-*O*-benzyl-L-*glycero*-D-*gulo*-heptitol (12a).** Column chromatography with 6:1 cyclohexane−AcOEt afforded **12a** (66 mg, 71%) as a syrup. $[\alpha]_D$ = −21.1 (*c* 0.9, $CHCl_3$). ^{1}H NMR (acetone-d_6): δ = 7.40−7.20 (m, 25 H, 5Ph), 4.93 and 4.76 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.92 and 4.68 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.55 and 4.51 (2 d, 2 H, J = 11.5 Hz, CH_2Ph), 4.54 (s, 2 H, CH_2Ph), 4.22 and 4.00 (2 d, 2 H, J = 14.0 Hz, N-CH_2Ph), 3.96 (dd, 1 H, $J_{1a,1b}$ = 11.5 Hz, $J_{1a,2}$ = 3.0 Hz, H-1a), 3.95 (dd, 1 H, $J_{7a,6}$ = 6.0 Hz, $J_{7a,7b}$ = 10.5 Hz, H-7a), 3.85 (dd, 1 H, $J_{7b,6}$ = 3.0 Hz, $J_{7b,7a}$ = 10.5 Hz, H-7b), 3.84 (dd, 1 H, $J_{4,3}$ = 8.0 Hz, $J_{4,5}$ = 9.0 Hz, H-4), 3.84 (dd, 1 H, $J_{1b,1a}$ = 11.5 Hz, $J_{1b,2}$ = 4.0 Hz, H-1b), 3.68 (dd, 1 H, $J_{5,4}$ = 9.0 Hz, $J_{5,6}$ = 5.5 Hz, H-5), 3.63 (dd, 1 H, $J_{3,2}$ = 9.0 Hz, $J_{3,4}$ = 8.5 Hz, H-3), 3.37 (ddd, 1 H, $J_{6,5}$ = 5.5 Hz, $J_{6,7a}$ = 6.0 Hz, $J_{6,7b}$ = 3.0 Hz, H-6), 3.24 (s, 1 H, OH), 3.10 (ddd, 1 H, $J_{2,1a}$ = 3.0 Hz, $J_{2,1b}$ = 4.0 Hz, $J_{2,3}$ = 9.0 Hz, H-2). ^{13}C NMR: δ = 141.7, 140.4, 140.2, 139.8, 139.5, 129.3−127.4, 84.1, 80.2, 79.7, 75.3, 75.1, 73.6, 72.5, 66.7, 61.9, 60.0, 57.1, 53.2. MALDI-TOF MS: 644.8 (M + H), 666.9 (M + Na). Anal. Calcd for $C_{42}H_{45}NO_5$ (643.3): C, 78.35; H, 7.05; N, 2.18. Found: C, 78.51; H, 7.06; N, 2.19.

***N*-Benzyl-2,6-dideoxy-2,6-imino-3,4,5,7-tetra-*O*-benzyl-L-*glycero*-D-*talo*-heptitol (11b).** Column chromatography with 6:1 cyclohexane−AcOEt afforded **11b** (33 mg, 36%) as a syrup. $[\alpha]_D$ = 10.3 (*c* 1.1, $CHCl_3$). ^{1}H NMR (C_6D_6): δ = 7.35−7.00 (m, 25 H, 5Ph), 4.58 and 4.49 (2 d, 2 H, J = 12.0 Hz, CH_2Ph), 4.43 (s, 2 H, CH_2Ph), 4.37 and 4.33 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.16 and 4.12 (2 d, 2 H, J = 11.0 Hz, CH_2Ph), 4.10 (dd, 1 H, $J_{5,4}$ = 6.0 Hz, $J_{5,6}$ = 3.0 Hz, H-5), 4.06 (dd, 1 H, $J_{3,2}$ = 8.0 Hz, $J_{3,4}$ = 2.5 Hz, H-3), 3.91 and 3.82 (2 d, 2 H, J = 16.0 Hz, N-CH_2Ph), 3.78 (dd, 1 H, $J_{4,3}$ = 2.5 Hz, $J_{4,5}$ = 6.0 Hz, H-4), 3.76 (dd, 1 H, $J_{1a,1b}$ = 11.5 Hz, $J_{1a,2}$ = 3.5 Hz, H-1a), 3.75 (dd, 1 H, $J_{7a,6}$ = 6.0 Hz, $J_{7a,7b}$ = 11.5 Hz, H-7a), 3.63 (dd, 1 H, $J_{1b,1a}$ = 11.5 Hz, $J_{1b,2}$ = 4.0 Hz, H-1b), 3.56 (dd, 1H, $J_{7b,6}$ = 6.0 Hz, $J_{7b,7a}$ = 11.5 Hz, H-7b), 3.56 (ddd, 1 H, $J_{6,5}$ = 3.0 Hz, $J_{6,7a}$ = 6.0 Hz, $J_{6,7b}$ = 6.0 Hz, H-6), 3.29 (ddd, 1 H, $J_{2,1a}$ = 3.5 Hz, $J_{2,1b}$ = 4.0 Hz, $J_{2,3}$ = 8.0 Hz, H-2), 2.61 (s, 1 H, OH). ^{13}C NMR (75 MHz, C_6D_6): δ = 141.7, 139.4, 139.1, 138.8, 128.6−126.9, 76.1, 75.3, 73.7, 73.1, 72.7, 72.2, 70.4, 63.0, 60.5, 59.5, 58.1. MALDI-TOF MS: 667.4 (M + Na). Anal. Calcd for $C_{42}H_{45}NO_5$ (643.3): C, 78.35; H, 7.05; N, 2.18. Found: C, 78.26; H, 7.05; N, 2.16.

***N*-Benzyl-2,6-dideoxy-2,6-imino-3,4,5,7-tetra-*O*-benzyl-L-*glycero*-D-*galacto*-heptitol (12b).** Column chromatography with 4:1 cyclohexane−AcOEt afforded **12b** (29 mg, 31%) as a syrup. $[\alpha]_D$ = −35.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR: δ = 7.40−7.15 (m, 25 H, 5Ph), 4.73−4.35 (8 d, 8 H, CH_2Ph), 4.12 (dd, 1 H, $J_{3,2} = J_{3,4}$ = 5.0 Hz, H-3), 4.05 (t, 1 H, $J_{1a,1b} = J_{1a,2}$ = 10.0 Hz, H-1a), 3.92 and 3.68 (2 d, 2 H, J = 14.0 Hz, N−CH_2Ph), 3.92 (dd, 1 H, $J_{4,3}$ = 5.0 Hz, $J_{4,5}$ = 9.0 Hz, H-4), 3.80 (bs, 1 H, H-5), 3.74 (dd, 1 H, $J_{7a,6}$ = 6.0 Hz, $J_{7a,7b}$ = 9.0 Hz, H-7a), 3.69 (dd, 1 H, $J_{7b,6}$ = 6.5 Hz, $J_{7b,7a}$ = 9.0 Hz, H-7b), 3.66 (dd, 1 H, $J_{1b,1a}$ = 10.0 Hz, $J_{1b,2}$ = 4.5 Hz, H-1b), 3.56 (m, 1 H, H-6), 3.10 (ddd, 1 H, $J_{2,1a}$ = 10.0 Hz, $J_{2,1b}$ = 4.5 Hz, $J_{2,3}$ = 5.0 Hz, H-2), 2.45 (s, 1 H, OH). ^{13}C NMR: δ = 140.9, 138.4, 128.6, 128.3, 127.7, 127.6, 127.0, 73.3, 73.0, 72.8, 71.5, 68.4, 60.4, 58.5, 53.4, 26.9, 21.0, 14.8. MALDI-TOF MS: 644.7 (M + H), 666.6 (M + Na). Anal. Calcd for $C_{42}H_{45}NO_5$ (643.3): C, 78.35; H, 7.05; N, 2.18. Found: C, 78.29; H, 7.11; N, 2.23.

***N*-Benzyl-2,6-dideoxy-2,6-imino-3,4,5,7-tetra-*O*-benzyl-L-*glycero*-L-*gluco*-heptitol (11c).** Column chromatography with 4:1 cyclohexane−AcOEt afforded **11c** (34 mg, 37%) as a syrup. $[\alpha]_D$ = 17.4 (*c* 0.8, $CHCl_3$). ^{1}H NMR (acetone-d_6): δ = 7.42−7.06 (m, 25 H, 5Ph), 4.72 and 4.64 (2 d, 2 H, J = 12.0 Hz, CH_2Ph), 4.67 (s, 2 H, CH_2Ph), 4.62 and 4.57 (2 d, 2 H, J = 12.0 Hz, CH_2Ph), 4.33 and 4.29 (2 d, 2 H, J = 11.5 Hz, CH_2Ph), 4.25 (dd, 1 H, $J_{3,2}$ = 4.5 Hz, $J_{3,4}$ = 7.5 Hz, H-3), 4.18 and 4.06 (2 d, 2 H, J = 15.0 Hz, N−CH_2Ph), 4.07 (dd, 1 H, $J_{5,4}$ = 3.0 Hz, $J_{5,6}$ = 5.5 Hz, H-5), 3.99 (dd, 1 H, $J_{4,3}$ = 7.5 Hz, $J_{4,5}$ = 3.0 Hz, H-4), 3.71 (dd, 1 H, $J_{1a,1b}$ = 11.0 Hz, $J_{1a,2}$ = 7.0 Hz, H-1a), 3.64 (dd, 1 H, $J_{7a,6}$ = 5.0 Hz, $J_{7a,7b}$ = 9.5 Hz, H-7a), 3.55 (dd, 1 H, $J_{7b,6}$ = 5.5 Hz, $J_{7b,7a}$ = 9.5 Hz, H-7b), 3.52 (dd, 1 H, $J_{1b,1a}$ = 11.0 Hz, $J_{1b,2}$ = 7.0 Hz, H-1b), 3.38 (ddd, 1 H, $J_{6,5} = J_{6,7b}$ = 5.5 Hz, $J_{6,7a}$ = 5.0 Hz, H-6), 3.34 (dd, 1 H, $J_{2,1a} = J_{2,1b}$ = 7.0 Hz, $J_{2,3}$ = 4.5 Hz, H-2). ^{13}C NMR (C_6D_6): δ = 140.8, 139.1, 139.0, 138.8, 138.3, 128.4−126.9, 76.2, 75.9, 73.2, 72.8, 72.1, 72.0, 70.1, 61.5, 61.1, 59.8, 59.5. MALDI-TOF MS: 666.7 (M + Na). Anal. Calcd for $C_{42}H_{45}NO_5$ (643.3): C, 78.35; H, 7.05; N, 2.18. Found: C, 78.45; H, 7.03; N, 2.18.

***N*-Benzyl-2,6-dideoxy-2,6-imino-3,4,5,7-tetra-*O*-benzyl-L-*glycero*-L-*manno*-heptitol (12c).** Column chromatography with 4:1 cyclohexane−AcOEt afforded **12c** (46 mg, 50%) as a syrup. $[\alpha]_D$ = −1.6 (*c* 0.5, $CHCl_3$). ^{1}H NMR (C_6D_6): δ = 7.40−7.00 (m, 25 H, 5Ph), 4.74 and 4.53 (2 d, 2 H, J = 12.0 Hz, CH_2Ph), 4.47 and 4.40 (2 d, 2 H, J = 12.0 Hz, CH_2Ph), 4.39 (s, 2 H, CH_2Ph), 4.13 (s, 2 H, CH_2Ph), 4.11 and 3.81 (2 d, 2 H, J = 14.0 Hz, N−CH_2Ph), 4.04 (t, 1 H, $J_{3,2} = J_{3,4}$ = 7.0 Hz, H-3), 4.00 (dd, 1 H, $J_{5,4}$ = 3.0 Hz, $J_{5,6}$ = 5.5 Hz, H-5), 3.94 (dd, 1 H, $J_{1a,1b}$ = 11.0 Hz, $J_{1a,2}$ = 5.5 Hz, H-1a), 3.83 (dd, 1 H, $J_{4,3}$ = 7.0 Hz, $J_{4,5}$ = 3.0 Hz, H-4), 3.74 (dd, 1 H, $J_{1b,1a}$ = 11.0 Hz, $J_{1b,2}$ = 4.5 Hz, H-1b), 3.57 (ddd, 1 H, $J_{6,5}$ = 5.5 Hz, $J_{6,7a}$ = 5.5 Hz, $J_{6,7b}$ = 6.0 Hz, H-6), 3.47 (dd, 1 H, $J_{7a,6}$ = 5.5 Hz, $J_{7a,7b}$ = 11.0 Hz, H-7a), 3.38 (dd, 1 H, $J_{7b,6}$ = 5.5 Hz, $J_{7b,7a}$ = 11.0 Hz, H-7b), 3.03 (ddd, 1 H, $J_{2,1b}$ = 4.5 Hz, $J_{2,1a}$ = 5.5 Hz, $J_{2,3}$ = 7.0 Hz, H-2). ^{13}C NMR (C_6D_6): δ = 140.9, 139.4, 139.3, 139.2, 138.7, 128.9−127.2, 79.4, 77.1, 74.6, 74.1, 73.2, 72.1, 71.8, 68.1, 61.3, 59.9, 56.0, 52.6. MALDI-TOF MS: 644.7 (M + H), 666.8 (M + Na). Anal. Calcd for $C_{42}H_{45}NO_5$ (643.3): C, 78.35; H, 7.05; N, 2.18. Found: C, 78.49; H, 7.08; N, 2.17.

General Procedure for the Synthesis of 2,6-Dideoxy-2,6-iminoheptitol Hydrochlorides 13a−c, 14a−c. To a solution of piperidine homoiminosugar **11a−c**, **12a−c** (80 mg, 0.12 mmol) in a 2:1 mixture of MeOH and THF (3.0 mL) was added $Pd(OH)_2$/C (80 mg). After the reaction flask was purged with hydrogen, 7 drops of 6 M HCl were added, and the reaction mixture was stirred for 2 days at room temperature under hydrogen (100 psi). The mixture was then filtered through a pad of Celite, concentrated, and eluted from a column of Sephadex LH-20 (2 × 60 cm) with MeOH to afford the corresponding pure heptitol hydrochlorides **13a−c**, **14a−c**.

2,6-Dideoxy-2,6-imino-L-*glycero*-D-*ido*-heptitol Hydrochloride (13a). 13a (26 mg, 92%) as an amorphus solid. $[\alpha]_D$ = 0.0 (*c* 0.8, MeOH). ^{1}H NMR (CD_3OD): δ = 4.02 (t, 1 H, $J_{4,3} = J_{4,5}$ = 3.0 Hz, H-4), 3.98 (m, 2 H, H-3 and H-5), 3.89 (m, 4 H, H-1a and H-1b, H-7a and H-7b), 3.55 (m, 2 H, H-2 and H-6). ^{13}C NMR (CD_3OD): δ = 68.8, 67.7, 59.9, 58.1. MALDI-TOF MS: 193.8 (M_{amine}), 215.6 (M_{amine} + Na). Anal. Calcd for $C_7H_{16}ClNO_5$ (229.1): C, 36.61; H, 7.02; N, 6.10. Found: C, 36.57; H, 7.03; N, 6.11.

2,6-Dideoxy-2,6-imino-L-*glycero*-D-*gulo*-heptitol Hydrochloride (14a). 14a (25 mg, 89%) as an amorphus solid. $[\alpha]_D$ = −38.2 (*c* 0.8, MeOH). ^{1}H NMR (CD_3OD): δ = 3.99 (dd, 1 H, $J_{1a,1b}$ = 13.0 Hz, $J_{1a,2}$ = 5.5 Hz, H-1a), 3.97 (dd, 1 H, $J_{7a,6}$ = 6.0 Hz, $J_{7a,7b}$ = 12.5 Hz, H-7a), 3.89 (dd, 1 H, $J_{7b,6}$ = 6.5 Hz, $J_{7b,7a}$ = 12.5 Hz, H-7b), 3.87 (dd, 1 H, $J_{1b,1a}$ = 13.0 Hz, $J_{1b,2}$ = 3.5 Hz, H-1b), 3.85 (dd, 1 H, $J_{5,4}$ = 8.5 Hz, $J_{5,6}$ = 5.5 Hz, H-5), 3.68 (t, 1 H, $J_{4,3} = J_{4,5}$

= 8.5 Hz, H-4), 3.63 (ddd, 1 H, $J_{6,5}$ = 5.5 Hz, $J_{6,7a}$ = 6.0 Hz, $J_{6,7b}$ = 6.5 Hz, H-6), 3.61 (t, 1 H, $J_{3,2} = J_{3,4}$ = 8.5 Hz, H-3), 3.39 (ddd, 1 H, $J_{2,1a}$ = 5.5 Hz, $J_{2,1b}$ = 3.5 Hz, $J_{2,3}$ = 8.5 Hz, H-2). ^{13}C NMR (CD_3OD): δ = 73.8, 69.9, 69.3, 58.2, 58.1, 57.5, 57.1. MALDI-TOF MS: 216.3 (M_{amine} + Na). Anal. Calcd for $C_7H_{16}ClNO_5$ (229.1): C, 36.61; H, 7.02; N, 6.10. Found: C, 36.68; H, 7.01; N, 6.10.

2,6-Dideoxy-2,6-imino-L-*glycero*-D-*talo*-heptitol Hydrochloride (13b). 13b (16 mg, 56%) as an amorphus solid. $[\alpha]_D$ = 30.8 (*c* 0.9, H_2O) [lit.[20] $[\alpha]_D$ = 31.1 (*c* 1.0, H_2O)]. ^{1}H NMR (D_2O): δ = 3.96−3.89 (m, 3 H), 3.82−3.62 (m, 4 H), 3.51−3.42 (m, 1 H), 3.24 (m, 1 H). ^{13}C NMR (D_2O) spectrum was consistent with that reported in the literature.[20] MALDI-TOF MS: 194.2 (M_{amine} + H). Anal. Calcd for $C_7H_{16}ClNO_5$ (229.1): C, 36.61; H, 7.02; N, 6.10. Found: C, 36.59; H, 7.00; N, 6.09.

2,6-Dideoxy-2,6-imino-L-*glycero*-D-*galacto*-heptitol Hydrochloride (14b). 14b (25 mg, 88%) as an amorphus solid. $[\alpha]_D$ = −39.4 (*c* 0.7, MeOH). ^{1}H NMR (D_2O): δ = 4.04−3.99 (m, 2 H), 3.85 (dd, 1 H, *J* = 4.5 Hz, *J* = 12.0 Hz), 3.75−3.60 (m, 5 H), 3.45 (t, 1 H, $J_{3,2} = J_{3,4}$ = 6.0 Hz, H-3). ^{13}C NMR (D_2O): δ = 69.1, 66.1, 65.9, 58.2, 55.4, 55.3, 55.0. MALDI-TOF MS: 217.7 (M_{amine} + Na). Anal. Calcd for $C_7H_{16}ClNO_5$ (229.1): C, 36.61; H, 7.02; N, 6.10. Found: C, 36.55; H, 6.97; N, 6.01.

2,6-Dideoxy-2,6-imino-L-*glycero*-L-*gluco*-heptitol Hydrochloride (13c). 13c (24 mg, 87%) as an amorphus solid. $[\alpha]_D$ = −20.0 (*c* 0.3, MeOH). ^{1}H NMR (CD_3OD): δ = 4.02−3.92 (m, 4 H), 3.87−3.80 (m, 3 H), 3.51 (t, 1 H). ^{13}C NMR (D_2O): δ = 70.6, 68.3, 64.7, 59.9, 59.4, 57.8, 57.1. MALDI-TOF MS: 217.6 (M_{amine} + Na). Anal. Calcd for $C_7H_{16}ClNO_5$ (229.1): C, 36.61; H, 7.02; N, 6.10. Found: C, 36.58; H, 6.93; N, 6.03.

Compound **13c** was previously characterized as a free amine.[21] Therefore, the hydrochloride **13c** was dissolved in a minimum of water and stirred with DOWEX 1X8−200 ion-exchange resin until pH = 11.55. After filtration, the filtrate was concentrated under vacuum to give the free amine. $[\alpha]_D$ = −40.7 (c 0.7, H_2O) [lit.[21] $[\alpha]_D$ = −41.0 (c 0.69, H_2O)]. ^{1}H and ^{13}C NMR spectra were identical to those reported in the literature.[21]

2,6-Dideoxy-2,6-imino-L-*glycero*-L-*manno*-heptitol Hydrochloride (14c). 14c (24 mg, 86%) as an amorphus solid. $[\alpha]_D$ = −19.9 (*c* 1.6, MeOH). ^{1}H NMR (CD_3OD): δ = 4.04 (dd, 1 H, $J_{5,4}$ = 3.0 Hz, $J_{5,6}$ = 6.5 Hz, H-5), 4.00 (dd, 1 H, $J_{1a,1b}$ = 12.0 Hz, $J_{1a,2}$ = 8.0 Hz, H-1a), 3.92 (dd, 1 H, $J_{7a,6}$ = 4.5 Hz, $J_{7a,7b}$ = 12.0 Hz, H-7a), 3.90 (t, 1 H, $J_{3,2} = J_{3,4}$ = 6.5 Hz, H-3), 3.87 (dd, 1 H, $J_{1b,1a}$ = 12.0 Hz, $J_{1b,2}$ = 4.0 Hz, H-1b), 3.84 (dd, 1 H, $J_{7b,6}$ = 7.0 Hz, $J_{7b,7a}$ = 12.0 Hz, H-7b), 3.80 (dd, 1 H, $J_{4,3}$ = 6.5 Hz, $J_{4,5}$ = 3.0 Hz, H-4), 3.50 (ddd, 1 H, $J_{6,5}$ = 6.5 Hz, $J_{6,7a}$ = 4.5 Hz, $J_{6,7b}$ = 7.0 Hz, H-6), 3.36 (m, 1 H, H-2). ^{13}C NMR (CD_3OD): δ = 71.7, 67.9, 67.0, 60.0, 58.4, 57.6. MALDI-TOF MS: 215.7 (M_{amine} + Na). Anal. Calcd for $C_7H_{16}ClNO_5$ (229.1): C, 36.61; H, 7.02; N, 6.10. Found: C, 36.69; H, 7.03; N, 6.12.

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