Chemical Synthesis of β-Homonojirimycin, of Its *N*-Butyl Derivative, and of "Methyl Homoazacellobioside"

Oscar M. Saavedra and Olivier R. Martin*

Department of Chemistry, State University of New York, P.O. Box 6016, Binghamton, New York 13902-6016

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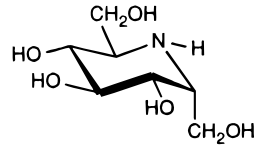
β-Homonojirimycin (**2**) was prepared by the highly stereoselective double reductive amination of a 2,6-heptodiulose derivative (**6** or **13**) using ammonium formate and $NaBH_3CN$. The process was unsuccessful with primary amines. The synthesis of *N*-butyl-β-homonojirimycin (**19**) was achieved by the *N*-butanoylation of a derivative of **2** followed by the reduction of the resulting tertiary amide. Compound **19** was found to be completely devoid of anti-HIV activity, in marked contrast with *N*-butyl-1-deoxynojirimycin. The coupling of the 1-*O*-*p*-toluenesulfonyl derivative of **2**, compound **20**, with methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside, followed by a deprotection step, provided pseudodisaccharide **23**, the "homoaza" analog of methyl α-cellobioside and a potential inhibitor of β-glucan-processing enzymes.

Introduction

Judging by their potent biological activities, most prominently as glycosidase inhibitors, azasugars[1] constitute undoubtedly the most remarkable class of "glycomimetics" designed by Nature. As a result of the lability of the O/N-acetal function[2] that would characterize glycosides of azasugars, most natural and non-natural piperidine azasugars,[1c,3] including the archetypal 1-deoxynojirimycin, are, in fact, derivatives of 1,5-dideoxy-1,5-iminohexitols and lack a substituent at the "anomeric" position. The concept of *C*-glycosidation, now extensively developed in furanoid and pyranoid systems,[4] becomes particularly significant in azasugar chemistry: the replacement of the anomeric oxygen atom in azaglycosides by a methylene group or the insertion of a methylene group into the "glycosidic" linkage provides means of generating stable analogs of such elusive species as, for example, azadisaccharides.[5] Several types of significant azasugar-containing pseudoglycoconjugates become accessible by way of this structural modification. The so-called homoazasugars (e.g., **1** and **2**) represent the simplest examples of aza-*C*-glycosyl compounds. The isolation of **1** (α-homonojirimycin) from the moth *Urania fulgens*[6a] and from its larval food plant *Omphalea diandra*[6b] prompted the synthesis of several homoazasugars including **1**,[7−9] the homo analogs of mannojirimycin,[9−11] of L-fuconojirimycin,[12] and, recently, of galactostatin in our laboratory.[13] A number of pyrrolidine homoazasugars have also been reported,[10,14,15] and one of them has been used for the construction of a homoazanucleoside.[14a] While retaining the powerful biological activity of the parent azasugars, homoazasugars were shown in several instances[6a,9] to exhibit greater selectivity in their inhibition of glycosidases. The addition of a substituent recognizing the aglycon-binding site of the enzyme is expected to further increase this selectivity, for example, toward oligosaccharidases. This proposition is supported by the potent activity of the 7-*O*-β-D-glucopyranosyl derivative of **1**[7] toward intestinal sucrase and other disaccharidases of the digestive system. Few other types of aza-*C*-glycosyl compounds have been



α-Homonojirimycin

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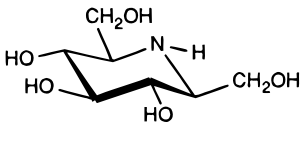

β-Homonojirimycin

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[⊗] Abstract published in *Advance ACS Abstracts,* August 15, 1996.

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described so far:[16−20] therefore particularly noteworthy are the recent first examples of aza-*C*-disaccharides.[19,20]

We report in this article[21] the first chemical synthesis of the β-epimer of **1**, namely β-homonojirimycin (**2**), of its *N*-butyl derivative **19**, and of the pseudodisaccharide **23**, the "homoaza" analog of methyl α-cellobioside. A chemoenzymatic preparation of **2** was recently reported by Holt and co-workers,[11a] but no physical data on this compound were given. Compound **19** is the homolog of *N*-butyl-1-deoxynojirimycin, the azasugar exhibiting the strongest inhibition of HIV-induced cytopathogenicity;[1c] compound **23** is the first example of a homoaza analog of a natural disaccharide and constitutes a potential selective inhibitor of cellobiohydrolases and cellulases.

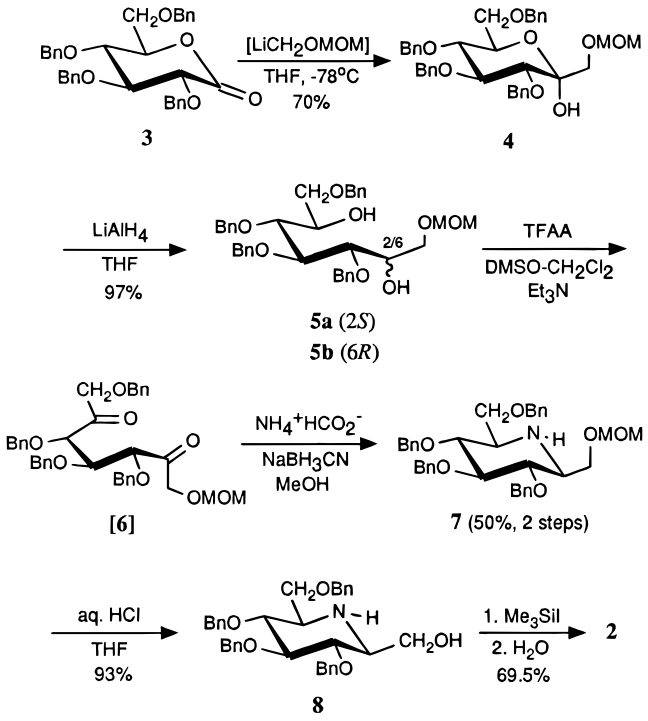
Results and Discussion

Our synthesis of β-homonojirimycin (**2**) and its derivatives relies on the double reductive amination[22] of a 2,6-heptodiulose. This strategy appeared to be particularly well suited to the preparation of an *all-equatorial* piperidine derivative. From the results of extensive studies on the synthesis of 1-deoxynojirimycin by internal reductive amination[1b,23] as well as from dicarbonyl sugars,[22b] the reduction step was expected to provide predominantly, if not exclusively, the desired configuration at C-2 and C-6.

Two different approaches to the required D-*xylo*-2,6-heptodiulose were investigated: (i) the addition of an (alkoxyalkyl)lithium reagent to a D-gluconolactone derivative (**3**) and (ii) a Wittig chain extension of tetra-*O*-benzyl-D-glucopyranose (**9**) followed by the dihydroxylation of the resulting heptenitol. Both approaches were designed to provide a differentially protected 2,6-heptodiulose and, ultimately, nonsymmetric β-homonojirimycin derivatives having different protecting groups at C-1 and C-7.

In approach i (see Scheme 1), tetra-*O*-benzyl-D-glucono-1,5-lactone **3** was treated with ((methoxymethoxy)methyl)lithium[24] under the conditions described by Shiozaki;[25] the resulting α-D-*gluco*-heptulopyranose derivative **4** was reduced in high yield to a mixture of heptitols **5a** and **5b** (∼1:1 ratio) using $LiAlH_4$. The configuration[26] of these epimers was determined as described later in the discussion. The oxidation of the mixture of **5a** and **5b** to the heptodiulose **6** was achieved using DMSO−trifluoroacetic anhydride, conditions that were used by Fukase and Horii[27] to produce related diketones. As a result of the tendency of 1,5-diketones such as **6** to undergo internal aldol reaction,[27] compound **6** was immediately submitted to reductive amination using ammonium formate in the presence of $NaBH_3CN$. This process afforded the desired β-homonojirimycin derivative **7** in 50% yield (from **5a**/**5b**) *as a single stereoisomer*. Thorough analysis of the reaction mixture did not reveal the presence of any other isomer. Although no evidence is available on the nature of the intermediates involved in this multistep process, the very high degree of stereoselectivity observed appears to exclude the amination of one of the carbonyl groups of the diketone in the open chain form that would produce an aminoheptulose in the first step. Rather, the reaction involves probably only cyclic intermediates (starting with a bis-hemiaminal and the corresponding cyclic imine/iminium salt) and the stereoselectivity of the hydride addition (axial attack) appears to be due primarily to torsional effects.[1b,22b]

Scheme 1



Cleavage of the MOM group of **7** under mildly acidic conditions gave the amino alcohol **8**, a key precursor of β-(D)-homonojirimycin derivatives (see below). Debenzylation of **8** by catalytic hydrogenation, by treatment with Li/NH_3, or with iodotrimethylsilane gave β-homonojirimycin (**2**), the best results being obtained using the latter reagent. The simple ^1H and ^{13}C NMR spectra of **2** (five and four signals, respectively) and the absence of optical activity were evidence for its symmetrical structure, and the magnitude of the $^3J_{H,H}$ coupling constants between the ring protons (9.5 Hz) confirmed its all-equatorial configuration.

The reductive amination of **6** was also attempted with primary alkylamines (benzylamine, butylamine) in the presence of acetic acid and $NaBH_3CN$. However, these reactions were completely unsuccessful.

In approach ii (see Scheme 2), the chain extension was achieved by the efficient Wittig reaction of tetra-*O*-

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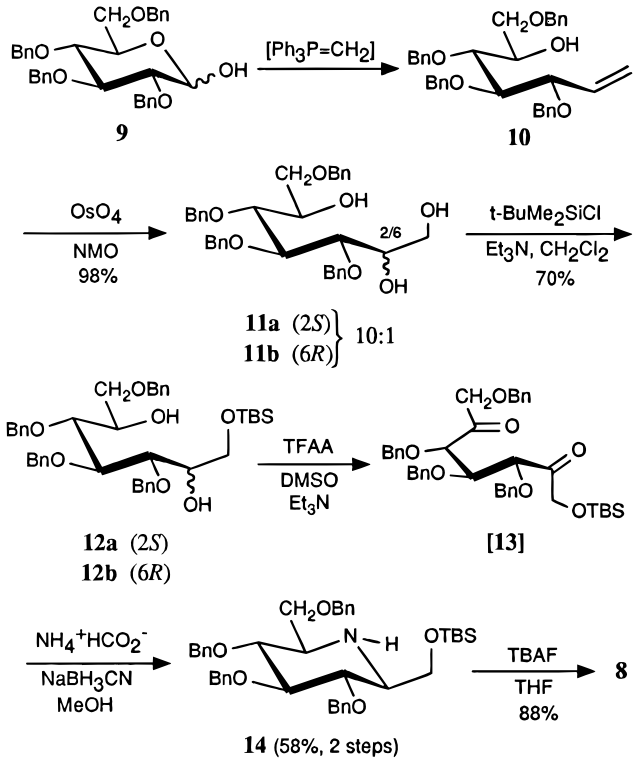
Scheme 2

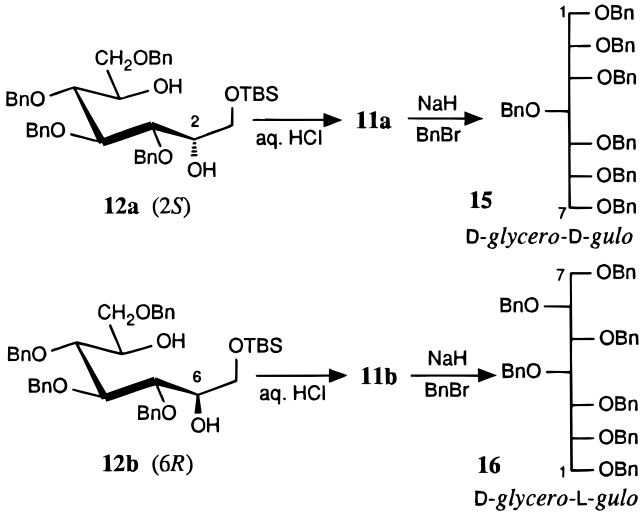


benzyl-D-glucopyranose **9** with $Ph_3P{=}CH_2$.[28] The resulting heptenitol **10** was submitted to dihydroxylation using catalytic OsO_4, which afforded the D-*glycero*-D-*gulo*- and D-*glycero*-L-*gulo*-heptitols **11a** and **11b** in a ratio of 10:1; the major stereoisomer was the one predicted from the Kishi empirical rule.[29] Selective silylation of the mixture of epimers gave primary silyl ethers **12a** and **12b**, which could be readily separated by flash chromatography at this stage. Oxidation of **12a**/**12b** and reductive amination of the resulting 2,6-heptodiulose **13** gave β-homonojirimycin derivative **14** in 58% overall yield, again as a single stereoisomer. Desilylation of **14** led to **8**, thus completing this alternative synthesis of β-homonojirimycin. Overall, the second approach is the preferred one for both better yields and simpler experimental conditions.

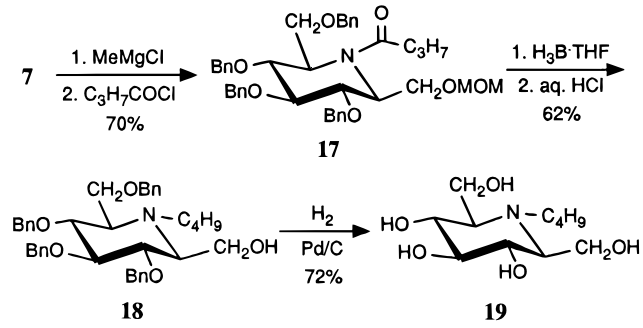
With pure **12a** and **12b** available, their configuration could be determined as follows (see Scheme 3): desilylation of **12a** and **12b**, separately, afforded pure samples of **11a** and **11b**. The two triols were then perbenzylated: compound **11a** led to **15**, a heptitol derivative exhibiting simple NMR spectra and zero optical activity, and **11b** led to **16**, an optically active compound exhibiting seven ^{13}C signals for its heptitol chain. On the basis of these data, the D-*glycero*-D-*gulo* and D-*glycero*-L-*gulo* configurations (see footnote 26) were assigned unambiguously to **11a** and **11b**.

The preparation of *N*-substituted derivatives of **2** met with considerable difficulties: for example, the *N*-benzylation of precursor **7** could not be achieved under any of the direct benzylation conditions attempted. *N*-Benzoylation was successful if the amine was first deprotonated with a Grignard reagent. Upon cleavage of the MOM group from the *N*-benzoyl derivative of **7**, the

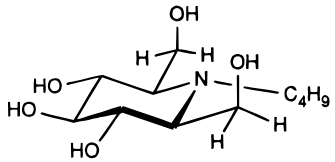
Scheme 3



Scheme 4



benzoyl group underwent immediate N → O migration.[30] These preliminary investigations indicated the route to follow for the preparation of **19** (see Scheme 4): butanoylation of the magnesium amide derived from **7** gave **17** in 70% yield. The amide was then reduced to the corresponding tertiary amine by treatment of **17** with the BH_3·THF complex, and the protecting groups were removed in two steps. This lengthy procedure provided *N*-butyl-β-homonojirimycin (**19**). *N*-Alkylation of **2** promoted a marked change of conformation about the C(1)−C(2) and C(6)−C(7) bonds: while the conformation of the hydroxymethyl groups in **2** appears to be flexible, with two predominant forms for each group, compound **19** has clearly both hydroxymethyl groups in the unusual *gauche*−*gauche* conformation (both values of $^3J = 1.7$ Hz).



19

It has been suggested that this conformation is an important structural feature of azasugar derivatives exhibiting antiviral activity.[1c] Compound **19** was found, however, to be completely devoid of anti-HIV activity (*in vitro* screening at the National Cancer Institute), in marked contrast with *N*-butyl-1-deoxynojirimycin.[1c]

The low reactivity of the amino function in **2** and its derivatives is clearly due to steric effects: the substitu-

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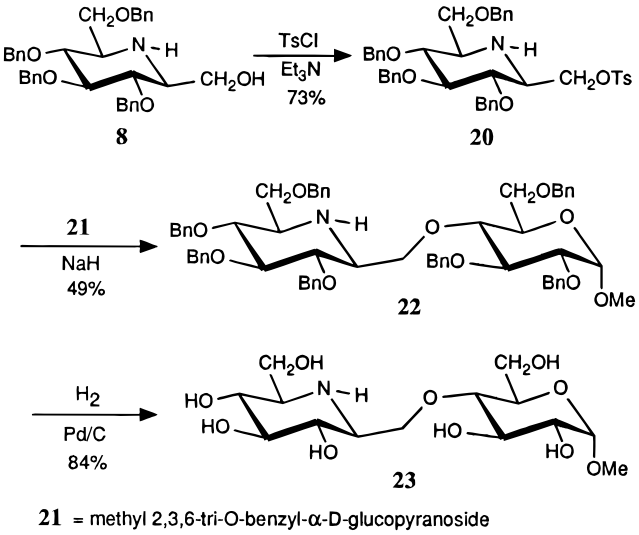
Scheme 5



21 = methyl 2,3,6-tri-O-benzyl-α-D-glucopyranoside

ents at C-2 and C-6 reduce the accessibility to nitrogen. Steric factors may also be responsible for the failure of the double reductive amination with alkylamines:[31] the presence of a substituent at nitrogen makes the ring closure substantially less favorable than that without a substituent.

Advantage was taken of this low reactivity at nitrogen to prepare derivatives of **2** at O-1: tosylation of amino alcohol **8** afforded exclusively the reactive *O*-tosylate **20**[32] (see Scheme 5). Compound **20** constitutes a convenient precursor for the preparation of a wide variety of β-linked "homoazadisaccharides": upon reaction with methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (**21**), compound **20** gave the expected pseudodisaccharide **22** in 49% yield, without rearrangement of the piperidine ring.[33] Compound **22** was deprotected to afford **23**, the homo analog of an elusive azacellobioside; it is the first example of an homoaza analog of a natural disaccharide and constitutes a potential inhibitor of β-glucan-processing enzymes.

In conclusion, we have developed an efficient method for the chemical synthesis of symmetric β-homonojirimycin (**2**) and of optically active derivatives. These derivatives are convenient precursors of homoaza analogs of β-linked disaccharides, a class of significant glycomimetics. Investigations on the activity of the new azasugar derivatives as glycosidase inhibitors are in progress and will be reported in due course.

Experimental Section

Optical rotations were measured with an automatic polarimeter for solutions in a 0.1 dm cell at 22 ± 3 °C. ^{1}H and ^{13}C NMR spectra were recorded at 360 and 90 MHz, respectively, using chloroform-*d* as the solvent unless otherwise indicated. Chemical shifts (in ppm) and coupling constants (in Hz) were obtained from first-order analysis of the spectra. A minus sign (−) is used to designate those signals that are negative in ^{13}C NMR spectra acquired in the DEPT mode (θ_y = 135°). Mass spectra were recorded at the Nebraska Center for Mass Spectrometry in the FAB mode [matrix: 3-nitrobenzyl alcohol in the absence or in the presence of an alkali metal cation (Li^+, Na^+)].

Analytical TLC was performed on precoated glass plates with silica gel 60 F-254 as the adsorbant (layer thickness: 0.25 mm). The developed plates were air-dried, exposed to UV light for inspection, sprayed with a solution of ammonium phosphomolybdate, and heated to 120−140 °C. Flash chromatography was performed using silica gel 60 (230−400 mesh). The following hexane−ethyl acetate solvent systems were used: A, 1:1; B, 2:1; C, 3:1; D, 4:1; E, 5:1.

Separations by HPLC were achieved using a preparative HPLC system equipped with a gradient programmer, a variable wavelength UV detector, and a 21.2 × 250 mm preparative column containing silica gel 60 (10 μm).

Solvents were evaporated under reduced pressure below 40 °C. Catalytic hydrogenations and hydrogenolyses were performed in a stainless steel benchtop pressure reactor equipped with a magnetic stirring drive and a pressure and temperature controller (maximum pressure: 2000 psi).

Heptitols 5a and 5b. 3,4,5,7-Tetra-*O*-benzyl-1-*O*-(methoxymethyl)-α-D-*gluco*-2-heptulopyranose (**4**) was prepared in 70% yield by the reaction of ((methoxymethoxy)methyl)lithium [from ((methoxymethoxy)methyl)tributylstannane[24]] with 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone (**3**),[34] as described by Shiozaki.[25] To **4** (3.56 g, 5.8 mmol) was added dropwise a 1 N solution of $LiAlH_4$ in THF (15 mL), and the mixture was stirred overnight at room temperature. Excess $LiAlH_4$ was then destroyed by the careful addition of EtOAc (10 mL). An additional volume of EtOAc (150 mL) was added, and the resulting mixture was washed with 2 N aqueous HCl (75 mL); the organic phase was separated, washed successively with saturated aqueous $NaHCO_3$ (75 mL) and brine (75 mL), dried (Na_2SO_4), and concentrated, thus affording a homogeneous mixture of heptitols **5a** and **5b** (3.46 g, 98%; 1:1 ratio). A small sample of the mixture was resolved by flash chromatography (solvent A).

3,4,5,7-Tetra-*O*-benzyl-1-*O*-(methoxymethyl)-D-*glycero*-D-*gulo*-heptitol (5a): syrup; $[\alpha]_D$ +1.74 (*c* 3.5, $CHCl_3$); IR ν_{max} (film) 3462 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.95 (br s, 1 H, OH), 3.12 (br, 1 H, OH), 3.32 (s, 3 H, OCH_3), 3.60−3.74 (m, 4 H, H-1A, 1B, 7A, 7B), 3.82 (dd, 1 H, J = 6.8, 4.5 Hz) and 3.88 (dd, 1 H, J = 6.5, 4.6 Hz) (H-3, 5), 3.98 (t, 1 H, $J_{3,4} \cong J_{4,5}$ = 4.5 Hz, H-4), 3.99−4.06 (m, 2 H, H-2, 6), 4.51 (AB, 2 H), 4.60 (AB, 2 H), 4.61 (s, 2 H), 4.64 (s, 2 H), and 4.67 (s, 2 H) (4 OC*H*$_2$Ph, OC*H*$_2$OCH$_3$), 7.20−7.35 (m, 20 H, 4 C$_6$*H*$_5$); ^{13}C NMR ($CDCl_3$) δ 55.36 (OCH_3), 69.79 [(−), C-7], 71.12 (2 C, C-2, 6), 71.19 [(−), C-1], 73.37, 73.61 (2 C), and 74.22 [all (−), 4 OC*H*$_2$Ph], 77.67 and 77.82 (C-3, 5), 79.05 (C-4), 97.12 [(−), OC*H*$_2$O], 127.64−128.37 (Ar *C*H), 138.14 and 138.21 (Ar *C*). Anal. Calcd for $C_{37}H_{44}O_8$: C, 72.06; H, 7.19. Found: C, 71.88; H, 7.27.

1,3,4,5-Tetra-*O*-benzyl-7-*O*-(methoxymethyl)-D-*glycero*-L-*gulo*-heptitol (5b): syrup; $[\alpha]_D$ +2.5 (*c* 2.5, $CHCl_3$); IR ν_{max} (film) 3450 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.75 (br s, 1 H, OH), 2.95 (br s, 1 H, OH), 3.30 (s, 3 H, OCH_3), 3.42 (dd, 1 H, J = 10.0, 5.5 Hz), 3.51 (dd, 1 H, J = 10.0, 6.7 Hz), and 3.66 (narrow ABX, 2 H) (H-1A, 1B, 7A, 7B), 3.75 (dd, 1 H, J = 7.2, 3.0 Hz) and 3.90 (dd, 1 H, J = 7.8, 1.9 Hz) (H-3, 5), 4.09 (dd, 1 H, J = 7.7, 2.7 Hz, H-4), 3.85 (br m, 1 H) and ~4.05 (br m, 1 H) (H-2, 6), 4.48−4.85 (5 AB, 10 H, 4 OC*H*$_2$Ph, OC*H*$_2$OCH$_3$), 7.22−7.35 (m, 20 H, 4 C$_6$*H*$_5$); ^{13}C NMR ($CDCl_3$) δ 55.31 (OCH_3), 69.79 [(−), C-1], 69.95 and 70.63 (C-2, 6), 71.26 [(−), C-7], 73.15, 73.44, 74.70, and 74.89 [all (−), 4 OC*H*$_2$Ph], 77.48, 78.44, and 79.17 (C-3−5), 96.87 [(−), OC*H*$_2$O], 127.72−128.32 (Ar *C*H), 137.95, 138.00, 138.06, and 138.14 (Ar *C*).

3,4,5,7-Tetra-*O*-benzyl-1-*O*-(methoxymethyl)-D-*xylo*-2,6-heptodiulose (6). To a solution of DMSO (2.3 mL) in anhydrous CH_2Cl_2 (21 mL) at −78 °C was added dropwise, under N_2, a solution of trifluoroacetic anhydride (3.4 mL, 24.1 mmol) in CH_2Cl_2 (2.5 mL), and the mixture was stirred for 20 min at low temperature. A solution of a mixture of diols **5a** and **5b** (3.26 g, 5.3 mmol) in CH_2Cl_2 (21 mL) was then added

(31) By contrast with **6**, both 2,5-hexodiuloses and hexos-5-uloses (e.g., "5-*keto*-D-glucose") undergo double reductive amination with primary alkylamines. For several examples, see: ref 22b.

(32) A small amount of the dimer resulting from the reaction of **8** with **20** could be detected in the mass spectrum of **20**. This byproduct was not apparent in the NMR spectra of **20**.

(33) Expansion of the six-membered ring was observed in related systems carrying a tertiary nitrogen atom: Martin O. R.; Liu, L. Unpublished results.

(34) Hanessian, S.; Ugolini, A. *Carbohydr. Res.* **1984**, *130*, 265−275.

dropwise; the temperature of the reaction mixture was maintained below −60 °C during the addition. The mixture was stirred for 1.5 h at −78 °C. A solution of Et_3N (6 mL) in CH_2Cl_2 (21 mL) was then added dropwise, and the mixture was allowed to warm to room temperature. After 30 min, the solvents were removed *in vacuo*, and the residue (crude **6**) was used without further purification in the following step. A sample of crude product **6** was rapidly processed (extraction with aqueous $NaHCO_3$ and brine) for analysis by NMR: ^{13}C NMR ($CDCl_3$) (content of diketone **6** > 90%) δ 55.49 (OCH_3), 71.62, 73.19, 73.83, 73.91, 74.25, and 74.45 [all (−), C-1, 7; 4 OCH_2Ph], 80.67, 81.03, and 81.07 (C-3−5), 96.51 [(−), OCH_2O], 127.8−128.5 (Ar *C*H), 136.75 (3 C) and 137.33 (Ar *C*), 206.22 and 206.38 (C-2, 6).

3,4,5,7-Tetra-*O*-benzyl-2,6-dideoxy-2,6-imino-1-*O*-(methoxymethyl)-D-*glycero*-D-*gulo*-heptitol (7). To a mixture of crude **6** (product from previous reaction, 5.3 mmol scale), dry ammonium formate (630 mg, 10 mmol), and powdered 3 Å molecular sieves (0.5 g) in MeOH (45 mL) was added $NaBH_3CN$ (720 mg, 11.5 mmol) in one portion. The reaction mixture was stirred for 30 min at room temperature.[35] The solids were then removed by filtration through a Celite bed, the solids were washed with CH_2Cl_2 (100 mL), and the filtrate was concentrated. The residue was dissolved in EtOAc (150 mL). The solution was washed successively with saturated aqueous $NaHCO_3$ (75 mL) and with brine (75 mL), dried (Na_2SO_4), and concentrated. Crude **7** thus obtained was purified by flash chromatography (solvent A) in a yield of 1.57 g (50%): mp 83−84 °C (EtOH−water 1:1); $[\alpha]_D$ +10.3 (*c* 5.6, $CHCl_3$); IR ν_{max} (KBr) 3338 cm^{-1} (w, NH); ^{13}C NMR ($CDCl_3$) δ 55.34 (OCH_3), 58.74 and 58.79 (C-2, 6), 67.92 [(−), C-7], 69.94 [(−), C-1], 73.28, 75.02 (2 C), and 75.53 [all (−), 4 OCH_2Ph], 80.50 (2 C, C-3, 5), 88.15 (C-4), 96.86 [(−), OCH_2O], 127.6−128.5 (Ar *C*H), 138.24, 138.47 (2 C), and 138.92 (Ar *C*). FABMS (rel intensity) 598 (100, $[M + H]^+$), 522 (18, $[M - CH_2OMOM]^+$), 476 (37, $[M - CH_2OBn]^+$); HR-FABMS calcd for $C_{37}H_{44}NO_6$ (MH^+) *m*/*z* 598.3168, found 598.3167. Anal. Calcd for $C_{37}H_{43}NO_6$: C, 74.34; H, 7.25; N, 2.34. Found: C, 74.23; H, 7.26; N, 2.33.

3,4,5,7-Tetra-*O*-benzyl-2,6-dideoxy-2,6-imino-D-*glycero*-D-*gulo*-heptitol (8). A suspension of **7** (370 mg, 0.62 mmol) in a mixture of THF (0.7 mL), water (3.4 mL), and 6 N aqueous HCl (8.4 mL) was stirred overnight at 50 °C. Solid $NaHCO_3$ was then added to neutralize the mixture, followed by water (30 mL). The mixture was extracted with CH_2Cl_2 (2 × 60 mL), the organic phases were combined, washed with brine (30 mL), dried (Na_2SO_4), and concentrated to afford homogeneous **8** (320 mg, 93%): mp 129−130 °C (MeOH−water 1:1); $[\alpha]_D$ + 7.0 (*c* 6.1, $CHCl_3$); IR ν_{max} (KBr) 3281 (w, NH), 3143 (m, OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.36 (br s, 2 H, NH, OH), 2.66 (ddd, 1 H, $J_{1A,2}$ = 4.9 Hz, $J_{1B,2}$ = 3.0 Hz, $J_{2,3}$ = 9.5 Hz, H-2), 2.80 (ddd, 1 H, $J_{5,6}$ = 9.5 Hz, $J_{6,7A}$ = 6.0 Hz, $J_{6,7B}$ = 2.5 Hz, H-6), 3.39 (t, 2 H, $J_{3,4}$ = 9.5 Hz, $J_{4,5}$ = 9.5 Hz, H-3, 5), 3.52 (dd, 1 H, $J_{7A,7B}$ = 9.0 Hz, H-7A), 3.16 (dd, 1 H, $J_{1A,1B}$ = 11.0 Hz, H-1A), 3.63 (t, 1 H, H-4), 3.67 (dd, 1 H, H-7B), 3.74 (dd, 1 H, H-1B), 4.45 (AB, 2 H, *J* = 12.0 Hz), 4.49 (d, 1 H, *J* = 10.9 Hz), 4.65 (d, 1 H, *J* = 11.0 Hz), 4.83 (d, 1 H, *J* = 11.0 Hz), 4.88 (d, 1 H, *J* = 11.0 Hz), and 4.90 (s, 2 H) (4 OCH_AH_BPh), 7.14−7.38 (m, 20 H, 4 C_6H_5); ^{13}C NMR ($CDCl_3$; assignments verified by H,C-COSY) δ 58.79 (C-6), 60.11 (C-2), 62.42 [(−), C-1], 70.02 [(−), C-7], 73.41, 75.04, 75.07, and 75.55 [all (−), 4 OCH_2Ph], 80.11 and 80.41 (C-3, 5), 88.02 (C-4), 127.3−130.5 (Ar *C*H), 137.60, 137.73 (2 C), and 137.91 (Ar *C*); FABMS (rel intensity) 554 (100, $[M + H]^+$). Anal. Calcd for $C_{35}H_{39}NO_5$: C, 75.92; H, 7.10; N, 2.53. Found: C, 75.70; H, 7.07; N, 2.47.

2,6-Dideoxy-2,6-imino-D-*glycero*-D-*gulo*-heptitol (β-homonojirimycin) (2). To a solution of **8** (65.5 mg, 0.118 mmol) in CH_2Cl_2 (3.5 mL) was added, dropwise at 0 °C, iodotrimethylsilane (0.13 mL). The reaction mixture was allowed to warm up to room temperature and stirred for 12 h. Water (25 mL) and ether (25 mL) were then added, the organic phase was separated, and the aqueous phase was extracted with another 25 mL portion of ether. The aqueous phase was then concentrated to 2 mL, and the solution was submitted to a column of Dowex 1X2-200 (OH^-) ion-exchange resin. The product was eluted with water (40 mL), and the fractions containing **2** were combined and lyophilized to afford **2** (16 mg, 69.5%) as a solid: mp > 200 °C (dec); $[\alpha]_D$ 0 (*c* 1.4, H_2O); ^1H NMR (D_2O, CH_3OD internal standard at δ 3.35) δ 2.65 (ddd, 2 H, *J* = 2.8, 6.6, and 9.5 Hz, H-2, 6), 3.25 (t, 2 H, *J* = 9.5 Hz, H-3, 5), 3.39 (t, 1 H, *J* = 9.0 Hz, H-4), 3.63 (dd, 2 H, *J* = 6.6 and 11.6 Hz, H-1A, 7A), 3.88 (dd, 2 H, *J* = 2.8 and 11.6 Hz, H-1B, 7B); ^{13}C NMR (D_2O, CH_3OD internal standard at δ 49.6) δ 60.37 (C-2,6), 62.14 [(−), C-1,7], 72.16 (C-3,5), 78.88 (C-4); FABMS (rel intensity) 200 (100, $[M + Li]^+$); HR-FABMS calcd for $C_7H_{15}NO_5Li$ *m*/*z* 200.1110, found 200.1104.

Heptitols 11a and 11b. To a solution of heptenitol **10** (ref 28) (1.03 g, 1.9 mmol) in acetone (4 mL) were added water (1 mL), 4-methylmorpholine *N*-oxide (225 mg, 1.92 mmol), and a 2.5% (w/v) solution of OsO_4 in *t*-BuOH (0.2 mL). The mixture was stirred overnight at room temperature. A solution of $NaHSO_3$ (300 mg) in water (20 mL) was then added, and the resulting mixture was passed through a bed of Florisil. The Florisil layer was washed with EtOAc (20 mL), and the eluate was collected in the flask containing the aqueous phase. The aqueous phase was acidified with dilute H_2SO_4. The organic phase was then separated, and the aqueous phase was extracted again with two 20 mL portions of fresh EtOAc. The organic phases were combined, washed with brine (50 mL), dried (Na_2SO_4), and concentrated to afford a homogeneous mixture of epimers **11a** and **11b** (∼10:1, 1.07 g, 98%). These epimers could be separated after silylation (see below).

Silylation of 11a and 11b. To a solution of **11a** and **11b** (∼10:1, 1.0 g, 1.75 mmol) in anhydrous CH_2Cl_2 (6.7 mL) were added *tert*-butyldimethylsilyl chloride (316 mg, 2.1 mmol), DMAP (51 mg), and Et_3N (0.4 mL). The mixture was stirred overnight at room temperature. CH_2Cl_2 (100 mL) was then added, and the solution was washed successively with 2 N aqueous HCl (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and brine (50 mL), dried (Na_2SO_4), and concentrated. The residue was submitted to flash chromatography (solvent E) which afforded **12a** (767 mg, 64%, R_f 0.25) and **12b** (72 mg, 6%, R_f 0.12).

3,4,5,7-Tetra-*O*-benzyl-1-*O*-(*tert*-butyldimethylsilyl)-D-*glycero*-D-*gulo*-heptitol (12a): syrup; $[\alpha]_D$ +4.4 (*c* 5.9, $CHCl_3$); IR ν_{max} (film) 3476 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.18 (s, 6 H) and 1.02 (s, 9 H) ($OSiMe_2$-*t*-Bu), 2.98 (br d, 1 H, OH), 3.13 (br d, 1 H, OH), 3.71−3.89 (2 narrow ABX, 4 H, H-1A, 1B, 7A, 7B), 3.96−4.03 (m, 3 H), 4.10 (t, 1 H, *J* = 4.2 Hz) and ∼4.17 (br m, 1 H) (H-2−6), 4.62 (AB, 2 H, *J* = 11.9 Hz), 4.73 (AB, 2 H, *J* = 11.4 Hz), 4.76 (s, 2 H), and 4.79 (s, 2 H) (4 OCH_AH_B-Ph), 7.35−7.45 (m, 20 H, 4 C_6H_5); ^{13}C NMR ($CDCl_3$) δ −5.45, −5.38, 18.16, and 25.83 ($SiMe_2$-*t*-Bu), 63.99 [(−), C-1], 71.20 [(−), C-7], 71.16 and 72.13 (C-2, 6), 73.28, 73.56, 73.65, and 74.25 [all (−), 4 OCH_2Ph], 77.42, 77.92, and 79.23 (C-3−5), 127.54−128.28 (Ar *C*H), 137.86, 138.03, and 138.15 (2 C) (Ar *C*). Anal. Calcd for $C_{41}H_{54}O_7Si$: C, 71.69; H, 7.92. Found: C, 71.58; H, 7.96.

1,3,4,5-Tetra-*O*-benzyl-7-*O*-(*tert*-butyldimethylsilyl)-D-*glycero*-L-*gulo*-heptitol (12b): syrup; $[\alpha]_D$ +2.3 (*c* 8.5, $CHCl_3$); IR ν_{max} (film) 3456 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.08 (s, 6 H) and 0.91 (s, 9 H) ($OSiMe_2$-*t*-Bu), ∼2.65 (br, 1 H, OH), ∼3.05 (br, 1 H, OH), 3.48 (dd, 1 H, *J* = 9.7, 6.6 Hz), 3.64 (dd, 1 H, *J* = 9.7, 6.7 Hz), and 3.66−3.74 (narrow ABX) (H-1A, 1B, 7A, 7B), ∼3.82 (m, 1 H) and ∼4.14 (m, 1 H) (H-2, 6), 3.83 (dd, 1 H, *J* = 7.3, 3.0 Hz) and 4.04 (dd, 1 H, *J* = 7.8, 1.6 Hz) (H-3, 5), 4.17 (dd, 1 H, *J* = 7.8, 3.0 Hz, H-4), 4.58 (AB, 2 H, *J* = 11.9 Hz), 4.65 (s, 2 H), 4.70 and 4.91 (2 d, 2 H, *J* = 11.3 Hz), and 4.73 and 4.83 (2 d, 2 H, *J* = 11.2 Hz) (4 OCH_AH_BPh), 7.30−7.42 (4 C_6H_5); ^{13}C NMR ($CDCl_3$) δ −5.46, 18.15, and 25.84 ($SiMe_2$-*t*-Bu), 64.08 [(−), C-7], 70.55 and 71.25 (C-2, 6), 71.25 [(−), C-1], 73.08, 73.37, 74.61, and 74.87 [all (−), 4 OCH_2Ph], 77.45, 77.69, and 79.25 (C-3−5), 127.64−128.29 (Ar *C*H), 137.97, 138.02, 138.11, and 138.27 (Ar *C*). Anal. Calcd for $C_{41}H_{54}O_7Si$: C, 71.69; H, 7.92. Found: C, 71.84; H, 8.04.

3,4,5,7-Tetra-*O*-benzyl-D-*glycero*-D-*gulo*-heptitol (11a). To a solution of **12a** (102.5 mg, 0.15 mmol) in anhydrous THF (1 mL) was added a 1 M solution of tetra-*n*-butylammonium fluoride in THF (0.3 mL). The mixture was stirred for 2 h at

(35) It is imperative to use anhydrous conditions. Otherwise, the reaction is slow and the yields are lower.

0 °C. The solvent was then evaporated, the residue dissolved in EtOAc (50 mL), and the resulting solution was washed with brine (25 mL), dried (Na_2SO_4), and concentrated. The product was purified by flash chromatography (solvent A) which afforded **11a** (74.7 mg, 87%) as a syrup: $[\alpha]_D$ − 0.7 (*c* 4.4, $CHCl_3$); IR ν_{max} (film) 3445 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.90 (br, 1 H, OH), ~3.38 (v br, 1 H, OH), 3.62 (d, 2 H, J = 4.6 Hz), ~3.63 (dd, 1 H, J = ?, 4.3 Hz), and 3.71 (dd, 1 H, J = 11.4, 3.3 Hz) (2 H-1, 2 H-7), 3.81 (dd, 1 H, J = 7.3, 4.9 Hz), 3.87 (m, 2 H), 3.93 (t, 1 H, $J \cong$ 4 Hz), and 4.05 (br q, 1 H) (H-2−6), 4.52 (narrow AB, 2 H, J = 11.8 Hz), 4.59 (narrow AB, 2 H), 4.595 (s, 2 H), and 4.62 (narrow AB, 2 H, J = 11.3 Hz) (4 OCH_AH_B-Ph), 7.22−7.35 (m, 20 H, 4 C_6H_5); ^{13}C NMR ($CDCl_3$) δ 63.65 [(−), C-1], 70.89 and 72.00 (C-2, 6), 71.13 [(−), C-7], 73.50, 73.60, 73.87, and 74.00 [all (−), 4 OCH_2Ph], 77.16, 77.63, and 79.01 (C-3−5), 127.82−128.47 (Ar *C*H), 137.49, 137.77, 137.84, and 137.96 (Ar *C*). Anal. Calcd for $C_{35}H_{40}O_7$: C, 73.40; H, 7.04. Found: C, 73.31; H, 7.13.

1,3,4,5-Tetra-*O*-benzyl-D-*glycero*-L-*gulo*-heptitol (11b). Compound **12b** (65 mg, 0.094 mmol) was desilylated under the same conditions as **12a** to provide heptitol **11b** (39.2 mg, 72%) as a syrup: $[\alpha]_D$ −3.7 (*c* 3.8, $CHCl_3$); IR ν_{max} (film) 3440 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.94 (br, OH), 3.35 (dd, 1 H, J = 11.2, 4.6 Hz), 3.48 (dd, 1 H, J = 11.2, 6.3 Hz), 3.62 (br m, 1 H), 3.66 (~d, 2 H), 3.74 (2 dd overlapping, 2 H), and 4.05 (dd overlapping br m, 2 H, J = 7.4, 3.3 Hz) (2 H-1, H-2−6, 2 H-7), 4.49−4.81 (4 AB, 8 H, 4 OCH_AH_BPh), 7.22−7.35 (m, 20 H, 4 C_6H_5); ^{13}C NMR ($CDCl_3$) δ 64.17 [(−), C-7], 70.64 and 71.15 (C-2, 6), 71.17 [(−), C-1], 73.19, 73.48, and 74.79 (2 C) [all (−), 4 OCH_2Ph], 77.39, 78.93, and 79.00 (C-3−5), 127.79−128.47 (Ar *C*H), 137.83 (2 C) and 137.89 (2 C) (Ar *C*).

Hepta-*O*-benzyl-D-*glycero*-D-*gulo*-heptitol (15). Compound **11a** (32.4 mg, 0.057 mmol) was benzylated under standard conditions (NaH, BnBr in DMF). Purification of the product by flash chromatography (solvent E) afforded perbenzylated heptitol **15** (41 mg, 86%) as a syrup: $[\alpha]_D$ 0 (*c* 4.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 70.27 [(−), 2 C, C-1,7], 72.03 (2 C), 73.31 (2 C), 74.01 (2 C), 75.07 (1 C) [all (−), 7 OCH_2Ph], 79.64 (4 C, C-2,3 and 5,6), 80.06 (1 C, C-4), 127.24−128.43 (Ar *C*H), 138.51, 138.84 (Ar *C*). Anal. Calcd for $C_{56}H_{58}O_7$: C, 79.78; H, 6.93. Found: C, 79.62; H, 7.00.

Hepta-*O*-benzyl-D-*glycero*-L-*gulo*-heptitol (16). Compound **11b** (22.9 mg, 0.040 mmol) was benzylated under standard conditions (NaH, BnBr in DMF). Purification of the product by flash chromatography (solvent E) afforded perbenzylated heptitol **16** (28 mg, 83%) as a syrup: $[\alpha]_D$ −4.5 (*c* 2.4, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 70.26 and 70.52 [(−), C-1, 7], 71.93, 72.94, 73.20, 73.30, 73.83, 74.62, and 74.72 [all (−), 7 OCH_2-Ph], 78.10, 78.94, 79.11, 79.29, and 79.51 (C-2−6), 127.24−128.18 (Ar *C*H), 138.5−139.5 (Ar *C*). Anal. Calcd for $C_{56}H_{58}O_7$: C, 79.78; H, 6.93. Found: C, 79.39; H, 7.28.

3,4,5,7-Tetra-*O*-benzyl-1-*O*-(*tert*-butyldimethylsilyl)-D-*xylo*-2,6-heptodiulose (13). A mixture of epimers **12a** and **12b** (883 mg, 1.28 mmol) was submitted to the same oxidation procedure as the **5a**/**5b** mixture. The resulting crude diketone **13** was used in the following step without further purification. For **13**: ^{13}C NMR ($CDCl_3$) δ 205.88 and 207.05 (C-2, 6).

3,4,5,7-Tetra-*O*-benzyl-1-*O*-(*tert*-butyldimethylsilyl)-2,6-dideoxy-2,6-imino-D-*glycero*-D-*gulo*-heptitol (14). Reductive amination of crude **13** (prepared from 1.28 mmol of **11a**/**11b**) using ammonium formate (155 mg) and $NaBH_3CN$ (176 mg) in MeOH (11 mL) (see preparation of **7**) followed by purification of the product by flash chromatography (solvent E) afforded compound **14** (497 mg, 58% from **12a**/**12b**) as a solid: mp 88−89 °C (EtOH−water 1:1); $[\alpha]_D$ +8.9 (*c* 3.1, $CHCl_3$); IR ν_{max} (KBr) 3342 (NH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.05 (s, 3 H) and 0.89 (s, 9 H) (OSiMe$_2$-*t*-Bu), 2.66 (m, 1 H) and 2.78 (m, 1 H) (H-2, 6), 3.43 (t, 1 H, J = 9.4 Hz), and 3.47 (t, 1 H, J = 9.5 Hz) (H-3, 5), 3.60−3.68 [ABX and t (δ = 3.65, $J \cong$ 9 Hz), 3 H, H-4, 2 H-1 or H-7], 3.73 (dd, 1 H, J = 9.8, 4.8 Hz) and 3.79 (dd, 1 H, J = 9.8, 2.4 Hz) (2 H-7 or H-1), 4.46 (AB, 2 H, J = 11.9 Hz), 4.53 (d, 1 H, J = 11.0 Hz), 4.62 (d, 1 H, J = 11.0 Hz), 4.87 (d, 1 H), 4.89 (d, 1 H), and 4.91 (s, 2 H) (4 OCH_AH_BPh), 7.22−7.35 (m, 20 H, 4 C_6H_5); ^{13}C NMR ($CDCl_3$) δ −5.47, −5.39, 18.13, and 25.82 (SiMe$_2$-*t*-Bu), 58.53 and 59.84 (C-2, 6), 62.65 [(−), C-1], 69.75 [(−), C-7], 73.18, 75.08 (2 C), and 75.69 [all (−), 4 OCH_2Ph], 80.37 and 80.68 (C-3, 5), 88.19 (C-4), 127.54−128.39 (Ar *C*H), 138.46−138.76 (Ar *C*). Anal. Calcd for $C_{41}H_{53}NO_5Si$: C, 73.72; H, 8.00; N, 2.10. Found: C, 73.80; H, 8.03; N, 2.15.

Compound 8 from 14. To a solution of **14** (398 mg, 0.596 mmol) in THF (4 mL) was added, at 0 °C, a 1 N solution of tetrabutylammonium fluoride in THF (1.2 mL), and the mixture was stirred for 4 h at 0 °C. The solvent was then evaporated and the residue taken up in CH_2Cl_2 (20 mL). The solution was washed with brine (15 mL), dried (Na_2SO_4), and concentrated. Crystallization of the residue from EtOH−water (1:1) afforded pure **8** (260 mg). The mother liquors were concentrated, and the residue was submitted to flash chromatography (solvent B) which gave an additional sample of pure **8** (32 mg; overall yield of 88%).

3,4,5,7-Tetra-*O*-benzyl-*N*-butanoyl-2,6-dideoxy-2,6-imino-1-*O*-(methoxymethyl)-D-*glycero*-D-*gulo*-heptitol (17). To a solution of **7** (103.3 mg, 0.17 mmol) in anhydrous THF (0.5 mL) was added dropwise 3 N methylmagnesium bromide in THF (0.08 mL), and the mixture was stirred for 5 min (room temperature). Butanoyl chloride (0.04 mL) was then added, and the mixture was stirred for 2 h at room temperature. The solvent was evaporated, and the residue was taken up in CH_2Cl_2 (25 mL). The resulting mixture was washed with brine (15 mL), dried (Na_2SO_4), and concentrated. The crude product was submitted to flash chromatography (solvent C) which afforded **17** (80.1 mg, 70%) as a syrup: $[\alpha]_D$ +4.0 (*c* 18.5, $CHCl_3$); IR ν_{max} (film) 1651 (*s*, C=O, doublet) cm^{-1}; ^{13}C NMR (~1:1 mixture of amide rotamers; $CDCl_3$) δ 13.88, 18.71 [(−)], and 35.54 [(−), *C*H$_3$*C*H$_2$*C*H$_2$CO], 55.48 (OCH$_3$), 55.50, 55.92, 58.07, and 58.15 (C-2, 6), 66.16, 68.43, and 69.79 [(−), C-1, 7], 71.89, 72.13, 73.11, 73.31, 73.53, 73.78, 74.40, and 74.48 [all (−), OCH_2Ph], 75.41, 75.71, 80.00, 80.67, 82.98, and 83.18 (C-3−5), 96.55 [(−), OCH_2O], 127.6−128.3 (Ar *C*H), 138.03−138.4 (Ar *C*), 173.40 (CO). Anal. Calcd for $C_{41}H_{49}NO_7$: C, 73.74; H, 7.40; N, 2.10. Found: C, 73.46; H, 7.45; N, 1.99.

3,4,5,7-Tetra-*O*-benzyl-*N*-butyl-2,6-dideoxy-2,6-imino-D-*glycero*-D-*gulo*-heptitol (18). A solution of **17** (76.1 mg, 0.11 mmol) in anhydrous THF (1 mL) was added to a 1 N solution of BH_3 in THF (0.2 mL) at 0 °C, and the mixture was heated under reflux for 1.5 h. The mixture was treated with 6 N aqueous HCl (1 mL). The acid was neutralized after 10 min by the addition of solid $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2 (2 × 15 mL), and the organic phases were combined, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (solvent D) to afford the MOM derivative of **18** (61.2 mg, 82%) as a solid: mp 66−67 °C; $[\alpha]_D$ +0.9 (*c* 13, $CHCl_3$). The MOM group was cleaved under the same conditions as that of **7** (see preparation of **8**), and the product was purified by flash chromatography (solvent B) to afford **18** in 75% yield: mp 53−54 °C; $[\alpha]_D$ +7.5 (*c* 6.9, $CHCl_3$); IR ν_{max} (KBr) 3441 (m, OH) cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 13.86, 20.30 [(−)], 26.63 [(−)], and 49.39 [(−), C_4H_9N], 58.74 [(−), C-1], 62.09 and 62.85 (C-2, 6), 68.04 (C-7), 73.25, 74.22, 74.36, and 74.69 [all (−), 4 OCH_2Ph], 78.04 and 78.48 (C-3, 5), 86.63 (C-4), 127.4−128.3 (Ar *C*H), 137.85, 138.39, 138.43, and 138.60 (Ar *C*). Anal. Calcd for $C_{39}H_{47}NO_5$: C, 76.82; H, 7.77; N, 2.30. Found: C, 76.56; H, 7.67; N, 2.21.

***N*-Butyl-2,6-dideoxy-2,6-imino-D-*glycero*-D-*gulo*-heptitol (*N*-Butyl-*β*-homonojirimycin) (19).** Compound **18** (67.8 mg, 0.11 mmol) was hydrogenolyzed in EtOH (40 mL) in the presence of 10% palladium-on-carbon (100 mg) under H_2 (120 psig) for 12 h at 50 °C. The solid was removed by filtration, and the filtrate was concentrated. The residue was dissolved in water (1 mL), and the solution was passed through LC-8 reverse phase silica gel (1 mL Supelclean extraction tube, Supelco; H_2O eluant). Concentration of the fractions containing the product afforded **19** (19.7 mg, 72%) as a solid: $[\alpha]_D$ 0 (*c* 1.6, H_2O); ^1H NMR (D_2O) δ 0.93 (t, 3 H, J = 7.4 Hz), 1.33 (sextet, 2 H, J = 7.4 Hz), 1.55 (quintet, 2 H), and 3.12 (br t, 2 H) ($CH_3CH_2CH_2CH_2N$), 2.88 (br d, 2 H, J = 9.8 Hz, H-2, 6), 3.42 (t, 1 H, J = 9.3 Hz, H-4), 3.56 (t, 2 H, J = 9.7 Hz, H-3, 5), 3.98 (narrow ABX, 4 H, $J_{AX} \cong J_{BX} \cong$ 1.7 Hz, $J_{AB} \cong$ 11.4 Hz, H-1A, 7A and H-1B, 7B); ^{13}C NMR (D_2O) δ 13.71, 20.23 [(−)], 23.77 [(−)], and 47.78 [(−), C_4H_9N], 57.12 [(−), C-1, 7], 64.60 (C-2, 6), 68.88 (C-3, 5), 77.87 (C-4); FABMS (rel intensity) 250

(100, $[M + H]^+$); HR-FABMS calcd for $C_{11}H_{24}NO_5$ *m/z* 250.1654, found 250.1652.

3,4,5,7-Tetra-*O*-benzyl-2,6-dideoxy-2,6-imino-1-*O*-(*p*-toluenesulfonyl)-D-*glycero*-D-*gulo*-heptitol (20). To a solution of **8** (60.2 mg, 0.11 mmol) in CH_2Cl_2 (1 mL) were added *p*-toluenesulfonyl chloride (31.1 mg), Et_3N (0.03 mL), and DMAP (3 mg). The mixture was stirred for 2 h at room temperature. The solvent was then evaporated, and the residue was submitted to flash chromatography (solvent B) which afforded **20** (57.4 mg, 73%) as a solid: mp 138−139 °C (EtOH); $[\alpha]_D$ +4.0 (*c* 2.5, $CHCl_3$); IR ν_{max} (KBr) 3343 (w, NH), 1365, 1175 (s, SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 (s, 3 H, ArCH_3), 2.70 (ddd, 1 H, J = 2.6, 5.3, 9.6 Hz) and 2.77 (ddd, 1 H, J = 2.6, 5.1, 9.8 Hz) (H-2, 6), 3.32 (t, 1 H, J = 9.5 Hz) and 3.39 (t, 1 H, J = 9.5 Hz) (H-3, 5), 3.515 (A of ABX, 1 H, $J_{6,7A}$ = 5.3 Hz, $J_{7A,7B}$ = 9.2 Hz, H-7A), 3.57 (t, 1 H, $J \cong$ 9.2 Hz, H-4), 3.585 (B of ABX, 1 H, $J_{6,7B}$ = 2.8 Hz, H-7B), 4.13 (A of ABX, 1 H, $J_{1A,2}$ = 5.1 Hz, $J_{1A,1B}$ = 9.6 Hz, H-1A), 4.18 (B of ABX, 1 H, $J_{1B,2}$ = 2.5 Hz, H-1B), 4.41−4.51 (m, 4 H) and 4.78−4.91 (m, 4 H) (4 OCH_AH_BPh), 7.14 (∼d, 2 H) and 7.75 (∼d, 2 H) ($pCH_3C_6H_4SO_2$), 7.22−7.36 (m, 20 H, 4 C_6H_5); ^{13}C NMR ($CDCl_3$) δ 21.57 (ArCH_3), 57.73 and 58.72 (C-2, 6), 69.44 and 70.13 (C-1, 7), 73.35, 74.98, 75.09, and 75.53 (4 OCH_2Ph), 79.36 and 80.19 (C-3, 5), 87.95 (C-4), 127.53−129.85 (Ar *C*H), 132.66, 137.87, 137.91, 138.14, 138.56, and 144.87 (Ar *C*); FABMS (rel intensity) 708.7 (26, $[M + H]^+$), also observed 554.7 (28, [**8** + $H]^+$). Anal. Calcd for $C_{42}H_{45}NO_7S$: C, 71.26; H, 6.41; N, 1.98; S, 4.53. Found: C, 71.32; H, 6.44; N, 1.91; S, 4.32.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(3,4,5,7-tetra-*O*-benzyl-2,6-dideoxy-2,6-imino-D-*glycero*-D-*gulo*-heptit-1-yl)-α-D-glucopyranoside (22). To a solution of methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (**21**)[36] (105.6 mg, 0.23 mmol) was added NaH (20 mg), and the mixture was stirred for 20 min at room temperature. A solution of **20** (155.4 mg, 0.22 mmol) in DMF (1.5 mL) was then added, and the mixture was stirred for 2 h. MeOH (0.5 mL) was then carefully added, followed by water (20 mL); the mixture was extracted with ether (2 × 25 mL), and the organic phases were combined, washed with brine (15 mL), dried (Na_2SO_4), and concentrated. The residue was submitted to flash chromatography (solvent C) which afforded pseudodisaccharide **22** (107 mg, 49% based on **20**) as a solid: mp 88−89 °C; $[\alpha]_D$ +20.0 (*c* 1.3, $CHCl_3$); IR ν_{max} (KBr) 3355 (w, NH) cm^{-1}; ^1H NMR (C_6D_6; assignments verified by H,H-COSY) δ 2.91−2.98 (2 overlapping m, 2 H, H-2′, 6′), 3.17 (OCH_3), 3.46 (t, 1 H, J = 9.4 Hz, H-3′), 3.51 (t, 1 H, $J \cong$ 9.5 Hz, H-5′), 3.52 (dd, 1 H, $J_{1,2}$ = 3.4 Hz, $J_{2,3}$ = 9.3 Hz, H-2), 3.55 (dd, 1 H, $J_{6',7'A}$ = 6.4 Hz, $J_{7'A,7'B} \cong$ 9 Hz, H-7′A), 3.67−3.76 (m, 4 H, H-4, 4′, 6A, 7′B), 3.83−3.90 (m, 3 H, H-1′A, 5, 6B), 4.18 (t, 1 H, J = 9.3 Hz, H-3), 4.45 (dd, 1 H, $J_{1'B,2}$ = 2.4 Hz, H-1′B), 4.65 (d, 1 H, H-1), 4.20 (AB, 2 H, J = 12.0 Hz), 4.39−4.60 (several d and AB, 6 H), 4.85−4.94 (2 d, AB, 4 H), and 4.99 (s, 2 H) (7 OCH_AH_BPh), 7.05−7.50 (m, 35 H, 7 C_6H_5); ^{13}C NMR (C_6D_6; assignments verified by H,C-COSY) δ 54.93 (OCH_3), 59.33 and 59.80 (C-2′, 6′), 69.71 [(−), C-6], 70.96 [(−), C-7′], 71.14 (C-5), 73.69 [(−), C-1′], 72.92, 73.24, 73.55, 74.82, 74.97, and 75.51 (2 C) [all (−), 7 OCH_2Ph], 78.67 (C-4), 81.16, 81.26, and 81.40 (C-2, 3′, 5′), 81.97 (C-3), 88.84 (C-4′), 98.38 (C-1), 127.4−128.6 (Ar *C*H), 138.8−139.9 (Ar *C*); FABMS (rel intensity) 1022 (100, $[M + Na]^+$), 1000 (30, $[M + H]^+$). Anal. Calcd for $C_{63}H_{69}NO_{10}$: C, 75.65; H, 6.95; N, 1.40. Found: C, 75.52; H, 6.99; N, 1.35.

Methyl 4-*O*-(2,6-Dideoxy-2,6-imino-D-*glycero*-D-*gulo*-heptit-1-yl)-α-D-glucopyranoside (23). To a solution of **22** (98.2 mg, 0.098 mmol) in EtOH (60 mL) were added AcOH (3 mL) and 10% palladium-on-carbon (200 mg). The mixture was stirred under hydrogen (140 psig) for 12 h at 50 °C. The catalyst was then removed by filtration, and the filtrate was concentrated. The residue was washed with CH_2Cl_2 (5 mL), dried, and then dissolved in water (5 mL). The product was loaded on a column of Dowex 50X8 (H^+) ion-exchange resin (100−200 mesh, 2 mL), the column was washed with water (50 mL), and the product was eluted with 2% aqueous NH_3 to afford homogeneous **23** (28.2 mg, 84%): $[\alpha]_D$ +65.9 (*c* 0.9, H_2O); ^{13}C NMR (D_2O; CH_3CN internal standard at δ 1.49) δ 55.69 (OCH_3), 58.91 and 60.36 (C-2′, 6′), 60.97 and 61.29 [(−), C-6, 7′], 71.17, 71.35, 71.66, 71.98 (2 C including C-1′), 73.42, 78.53, and 78.73 (C-2, 3, 3′, 4, 4′, 5, 5′), 99.83 (C-1); FABMS (rel intensity) 392 (100 $[M + Na]^+$); HR-FABMS calcd for $C_{14}H_{27}NO_{10}Na$ *m/z* 392.1533, found 392.1538.

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