Short and Convergent Synthesis of (1→3)-C-Linked Imino Disaccharides (Aza-C-disaccharides)

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Glycosidases and glycosyltransferases are key enzymes in the biosynthesis and processing of glycoproteins, which are molecules involved in recognition (cell−cell, host−pathogen interactions) and in control of biological mechanisms and structures.[1] Thus, substances able to inhibit these enzymes have become potential antibacterial, antiviral, antimetastatic, antidiabetes, antihyperglycemic, antiadhesive, or immunostimulatory agents.[2,3] A new class of selective glycosidase inhibitors has emerged with the C-linked imino disaccharides (aza-C-disaccharides)[4,5] which contains not only the steric and charge information of the glycosyl moiety, which is liberated during the enzyme-catalyzed hydrolysis, but also that of the aglycon to which the glycon is attached. The first example of a C-linked imino disaccharide (1,5-dideoxy-1,5-imino-D-mannitol linked at C(6) of D-galactose through a CH_2 unit) was prepared by Johnson and co-workers.[6] Other examples of "linear" C-linked imino disaccharides were obtained by the groups of Martin[7] and Van Boom.[8] We have prepared the first examples of "branched" disaccharides.[4,9] Further examples were reported by Johnson and co-workers.[5] The current syntheses of "branched" disaccharide mimetics are rather lengthy, which limits their development and the search for better glycosidase inhibitors from among highly diverse candidates. We report here a new approach which condenses a dideoxyiminoaldose with an isolevoglucosenone-derived enolate.[10] The aldol so obtained can be transformed readily into C-linked iminodisaccharides in which L-*glycero*-1,2,4-trideoxy-1,4-iminotetritol is linked through a CH(OH) moiety at position C(3) of methyl D-*gluco*- or methyl D-*galacto*-pyranoside.

Conjugate addition of benzyl alcohol to isolevoglucosenone **1** (derived in four steps from D-glucose[11]) afforded ketone **2** in 90% yield with high stereoselectivity. The enolates of ketone **2** did not induce β-elimination at low temperature, probably because of the rigid bicyclic system.[10] The dichlorozinc enolate of **2**, generated by deprotonation with $(Me_3Si)_2NK$ followed by treatment with anhydrous $ZnCl_2$, added to aldehyde **3**.[12] This produced a single aldol **4** which partially decomposed during attempts at purification (chromatography on silica gel or Florisil).[13,14] Therefore, the crude aldol **4** was directly reduced with L-Selectride into the D-galactose derivative **5** (53% based on **2**).[15] Desilylation of **5** with *n*-Bu_4NF afforded triol **6** in 96% yield. Debenzylation of **6** gave **7** in 96% yield, which was refluxed in anhydrous methanol saturated with gaseous HCl, producing a 3:2 mixture of methyl α- and β-D-*galacto*-pyranosides **8α** and **8*β***, respectively, in 82% yield.

Reduction of the crude aldol **4** with $Me_4NBH(OAc)_3$,[16] on the other hand, formed the D-glucose derivative **9** (59% based on **2**) which was deprotected as above, giving first **10** in 94% yield, then **11** in 93% yield, and finally a 7:3 mixture of methyl α- and β-D-*gluco*-pyranosides **12α** and **12*β***, respectively, in 90% yield.

The structures of the new compounds were given by their mode of formation and their spectral data. Further proof was given by the vicinal coupling constants and the NOE's (Figure 1) measured in the ^{1}H NMR spectra of acetonides **13** and **14** derived from diols **5** and **9**, respectively, under standard conditions ($Me_2C(OMe)_2$, acetone, TsOH, and Drierite). The $\delta_{C(Me)} = 24.8$ and 24.2 ppm observed in the ^{13}C NMR spectrum of **13** suggest a twist-boat conformation for the acetonide.[17] Coupling

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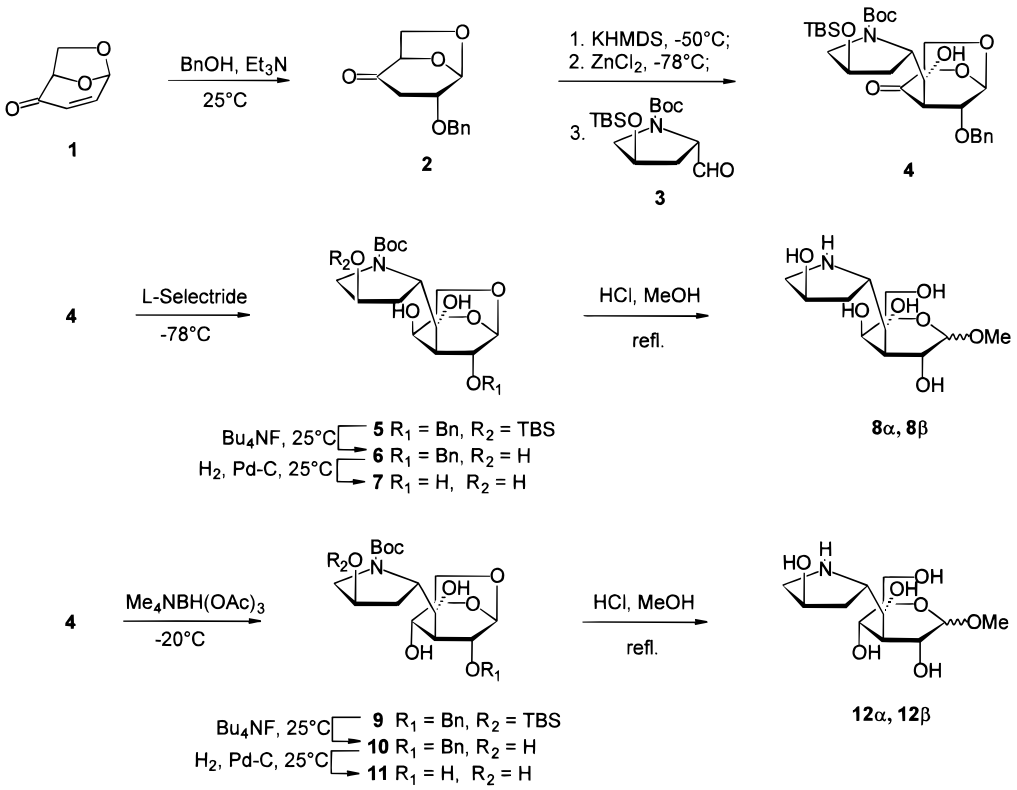
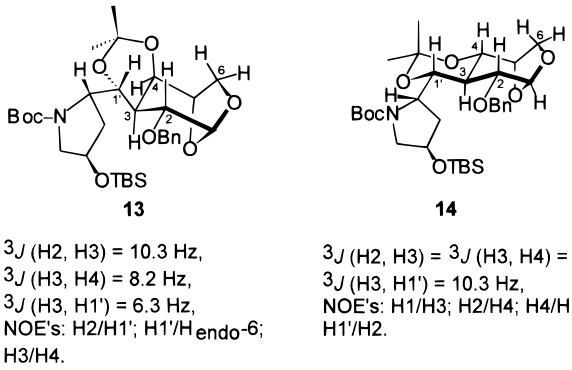
Scheme 1





13

^3J (H2, H3) = 10.3 Hz,
^3J (H3, H4) = 8.2 Hz,
^3J (H3, H1') = 6.3 Hz,
NOE's: H2/H1'; H1'/H$_{endo}$-6; H3/H4.

14

^3J (H2, H3) = ^3J (H3, H4) = ^3J (H3, H1') = 10.3 Hz,
NOE's: H1/H3; H2/H4; H4/H1'; H1'/H2.

Figure 1. Selected ^{1}H NMR data for **13** and **14**.

constants between vicinal protons at C(2,3,4) suggest a boat conformation for the tetrahydropyran ring (O−C1−C2−C3−C4−C5) in which H-2 and H-3 are axial. For **14**, the ^{13}C NMR spectrum displays $\delta_{C(Me)}$ = 29.9 and 19.9 ppm for the acetonide moiety, suggesting a chair conformation for it. Coupling constants between vicinal protons at C2, C3, and C4 also confirm a boat conformation for the tetrahydropyran ring as shown in Figure 1. This also appears to be the case for the 1,6-anhydro-β-glucopyranose derivatives **9**, **10**, and **11** for which vicinal coupling constants ^3J(H3, H4) = 8.7, 9.8, and 10.5 Hz, respectively, were measured. These data confirmed that the cross-aldolization between **2** and **3** follows the Zimmerman−Traxler model.[10,18]

An expedient method for the stereoselective synthesis of (1→3)-C-linked imino disaccharides has been realized. It will now be applied to a large number of iminodideoxyaldoses and sugar-derived carbaldehydes in order to generate a large variety of C-disaccharides and analogues.

Experimental Section

General remarks, see ref 4b.

1,6-Anhydro-2-*O*-benzyl-3-deoxy-D-*erythro*-hexopyrano-4-ulose (2). A mixture of isolevoglucosenone **1** (185 mg, 1.47 mmol),[11] benzyl alcohol (8.2 mL), and triethylamine (0.1 mL, 0.72 mmol) was stirred at 20 °C for 15 h. Et_3N was then eliminated by evaporation. Excess of BnOH was recovered by bulb-to-bulb distillation in vacuo. The residue was chromatographed on silica gel (15:85 EtOAc/light petroleum ether), affording a colorless syrup (310 mg, 90%). $[\alpha]^{25}_D = -57$ (*c* 1.2, $CHCl_3$). IR (film): 1736 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45−7.22 (m, 5H), 5.62 (s, 1H), 4.63 and 4.57 (2d, J = 12.0 Hz, 2H), 4.55 (d, J = 5.0 Hz, 1H), 3.92 (d, J = 8.0 Hz, 1H), 3.84 (dd, J = 8.0, 5.0 Hz, 1H), 3.78 (ddd, J = 6.5, 3.5, 1.2 Hz, 1H), 2.68 (dd, J = 12.5, 6.5 Hz, 1H), 2.61 (dd, J = 12.5, 3.5 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 204.1, 137.2, 128.6, 128.1, 127.7, 101.5, 79.1, 75.5, 71.6, 66.8, 39.2. MS (CI, NH_3): 252 ([M + NH_4]$^+$). Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.56; H, 6.01.

1,6-Anhydro-2-*O*-benzyl-3-deoxy-3-[(1′*R*)-4′-*O*-*tert*-butyldimethylsilyl-*N*-*tert*-butyloxycarbonyl-2′,3′,5′-trideoxy-2′,5′-imino-L-*erythro*-pentitol-1′-*C*-yl]-β-D-galactopyranose (5). A solution of potassium bis(trimethylsilyl)amide (0.75 M in toluene, 0.24 mL, 0.18 mmol) was added to a solution of **2** (32 mg, 0.14 mmol) in anhydrous THF (1.3 mL) stirred at −50 °C under a nitrogen atmosphere. After being stirred at this temperature for 1 h, the mixture was cooled to −78 °C and a 1 M solution of $ZnCl_2$ in ether (0.18 mL, 0.18 mmol) was added dropwise. After being stirred for 15 min, a solution of aldehyde **3**[12] (58 mg, 0.18 mmol) in anhydrous THF (0.3 mL) was added. The reaction mixture was warmed to −45 °C and stirred at this temperature for 5 h. A saturated aqueous solution of NH_4Cl (0.6 mL) was added, and the mixture was allowed to warm to 20 °C with stirring. EtOAc (2 mL) was added. The aqueous phase was separated and extracted with EtOAc (3 mL, three times). The combined organic phases were dried (anhydrous Na_2SO_4), and

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the solvent was removed in vacuo to yield the crude aldol product **4**, the ^{1}H NMR spectrum of which showed 75% conversion. This crude product was used for the following reaction without further purification.

A solution of L-Selectride (1 M in THF, 0.69 mL, 0.69 mmol) was added dropwise to a THF (2 mL) solution of above crude product at −78 °C under a nitrogen atmosphere. The resulting yellow solution was stirred at this temperature for 1 h. After being warmed to 20 °C, MeOH (0.5 mL), followed by 3 M aqueous NaOH (1 mL) and 35% H_2O_2 (1 mL), was added to the reaction mixture. The mixture was stirred vigorously at 20 °C for 1 h. MeOH (2 mL) was added, and the mixture was extracted with CH_2Cl_2 (6 mL, three times). The combined organic phases were dried (anhydrous Na_2SO_4), and the solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel (35:65 EtOAc/light petroleum ether), giving a colorless oil (41 mg, 53%). $[\alpha]^{25}_D = -29$ (*c* 1.73, $CHCl_3$). IR (film): 3364, 1673 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 323 K): δ 7.37−7.15 (m, 5H), 5.40 (s, 1H), 4.60 (s, 2H), 4.54 (dd, J = 5.8, 4.8 Hz, 1H), 4.51 (t, J = 6.1 Hz, 1H), 4.43−4.28 (m, 3H), 4.20 (m, 1H), 3.62−3.50 (m, 2H), 3.40 (d, J = 4.5 Hz, 1H), 3.23 (dd, J = 11.4, 4.2 Hz, 1H), 2.15 (ddd, J = 13.0, 7.9, 5.1 Hz, 1H), 2.05 (ddd, J = 7.6, 6.1, 4.5 Hz, 1H), 1.89 (dddd, J = 13.0, 7.7, 3.0, 1.6 Hz, 1H), 1.43 (s, 9H), 0.88 (s, 9H), 0.05 (s, 6H). ^{13}C NMR (100.6 MHz, $CDCl_3$, 323 K): δ 156.3, 137.8, 128.6, 128.0, 127.7, 100.9, 80.5, 77.2, 74.7, 73.3, 71.6, 70.5, 66.6, 62.8, 60.7, 56.3, 41.0, 35.4, 28.4, 25.8, 18.0, −4.7, −4.8. MS (CI, NH_3): 566 ([M + H]$^+$). Anal. Calcd for $C_{29}H_{47}O_8NSi$: C, 61.56;; H, 8.37; N, 2.48.. Found: C, 61.66; H, 8.42; N, 2.45.

1,6-Anhydro-2-*O*-benzyl-3-deoxy-3-[(1′*R*)-*N*-*tert*-butyloxycarbonyl-2′,3′,5′-trideoxy-2′,5′-imino-L-*erythro*-pentitol-1′-*C*-yl]-*β*-D-galactopyranose (6). A tetrabutylammonium fluoride solution (1 M in THF, 0.40 mL, 0.40 mmol) was added to a solution of **5** (60 mg, 0.11 mmol) in THF (2.5 mL) at 20 °C. After being stirred at 20 °C for 15 h, the solvent was evaporated and the residue purified by chromatography on silica gel (1% MeOH in EtOAc), affording a colorless oil (48 mg, 96%). $[\alpha]^{25}_D = -17$ (*c* 0.48, $CHCl_3$). IR (film): 3374, 1668 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 323 K): δ 7.40−7.25 (m, 5H), 5.38 (s, 1H), 4.62 (d, J = 11.9 Hz, 1H), 4.53 (d, J = 11.9 Hz, 1H), 4.54 (dd, J = 6.4, 4.8 Hz, 1H), 4.50 (m, 1H), 4.45 (m, 1H), 4.36 (m, 1H), 4.28 (d, J = 7.6 Hz, 1H), 4.07 (m, 1H), 3.60 (d, J = 11.8 Hz, 1H), 3.54 (dd, J = 7.3, 4.8 Hz, 1H), 3.35 (d, J = 4.8 Hz, 1H), 3.30 (dd, J = 11.8, 4.2 Hz, 1H), 2.22 (ddd, J = 13.6, 7.6, 4.8 Hz, 1H), 2.00 (ddd, J = 8.8, 6.4, 4.8 Hz, 1H), 1.81 (dddd, J = 13.3, 7.8, 3.0, 2.1 Hz, 1H), 1.43 (s, 9H). ^{13}C NMR (100.6 MHz, $CDCl_3$, 323K): δ 156.0, 137.8, 128.6, 128.0, 100.7, 80.7, 77.9, 74.6, 72.8, 71.7, 70.0, 66.3, 62.7, 60.3, 56.1, 41.1, 34.6, 28.5. MS (CI, NH_3): 452 ([M + H]$^+$). Anal. Calcd for $C_{23}H_{33}O_8N\cdot H_2O$: C, 58.84; H, 7.51; N, 2.98. Found: C, 58.96; H, 7.42; N, 3.35.

1,6-Anhydro-3-deoxy-3-[(1′*R*)-*N*-*tert*-butyloxycarbonyl-2′,3′,5′-trideoxy-2′,5′-imino-L-*erythro*-pentitol-1′-*C*-yl]-*β*-D-galactopyranose (7). A degassed mixture of **6** (48 mg, 0.10 mmol), 10% Pd on charcoal (12 mg, 0.011 mmol), and MeOH (5 mL) was stirred under H_2 at 20 °C for 15 h. The catalyst was filtered off and solvent evaporated in vacuo. The residue was chromatographed (5% MeOH in EtOAc) to afford a white solid (37 mg, 96%). Mp 209−210 °C. $[\alpha]^{25}_D = -47$ (*c* 0.75, MeOH). IR (KBr): 3495, 3397, 3254, 1650 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD, 323 K): δ 5.22 (d, J = 1.2 Hz, 1H), 4.64 (m, 1H), 4.56−4.38 (m, 3H), 4.30 (d, J = 7.6 Hz, 1H), 4.22 (dd, J = 8.2, 5.7 Hz, 1H), 3.60 (m, 2H), 3.56 (d, J = 11.4 Hz, 1H), 3.40 (dd, J = 11.4, 4.2 Hz, 1H), 2.35 (dt, J = 13.3, 5.7 Hz, 1H), 1.95 (dddd, J = 13.3, 8.2, 3.3, 1.8 Hz, 1H), 1.96−1.88 (m, 1H), 1.52 (s, 9H). ^{13}C NMR (100.6 MHz, CD_3OD, 323 K): δ 156.7, 103.9, 81.5, 76.8, 73.8, 70.7, 68.3, 63.9, 60.9, 56.5, 44.7, 34.4, 28.9. MS (CI, NH_3): 362 ([M + H]$^+$). Anal. Calcd for $C_{16}H_{27}O_8N$: C, 53.18; H, 7.53; N 3.88. Found: C, 53.23; H, 7.64; N, 3.83..

Methyl 3-Deoxy-3-[(1′*R*)-2′,3′,5′-trideoxy-2′,5′-imino-L-*erythro*-pentitol-1′-*C*-yl]-α(and *β*)-D-galactopyranoside (8α, 8*β*). A mixture of **7** (10.0 mg, 0.0277 mmol) and anhydrous MeOH saturated with gaseous HCl (1 mL) was refluxed under N_2 for 20 h. After cooling, the solution was poured onto a column (5 cm length) of Dowex 50WX8 (100−200 mesh). The column was washed sequentially with MeOH (20 mL), H_2O (5 mL), and 5% $NH_3\cdot H_2O$ (40 mL). The fractions containing products **8α** and **8*β*** were concentrated in vacuo and purified by flash chromatography on silica gel (5% aqueous NH_3:*i*-PrOH = 1:2.5) to afford a colorless oil (7.4 mg, 82%). $[\alpha]^{25}_D = +38$ (*c* 0.15, H_2O). IR (film): 3375 cm^{-1}. ^{1}H NMR (400 MHz, D_2O): δ 4.72 (d, J = 3.6 Hz, 0.6H, H-1 of **8α**), 4.56 (m, 1H), 4.30 (d, J = 7.9 Hz, 0.4H, H-1 of **8*β***), 4.24 (ddd, J = 10.3, 7.3, 4.5 Hz, 1H), 4.18 (m, 0.4 H), 4.15 (dd, J = 7.9, 4.5 Hz, 0.6 H), 4.12 (m, 0.6 H), 4.08 (d, J = 2.7 Hz, 0.4 Hz), 3.96 (dd, J = 11.5, 3.6 Hz, 0.6H), 3.82 (dd, J = 7.3, 4.8 Hz, 0.6H), 3.73−3.65 (m, 1.4H), 3.61 (dd, J = 11.2, 7.9 Hz, 0.4H), 3.55 (s, 1.2H), 3.41 (s, 1.8H), 3.18 (dd, J = 11.5, 4.5 Hz, 0.6 H), 3.15 (dd, J = 10.6, 4.5 Hz, 0.4H), 3.10 (d, J = 11.5 Hz, 0.6H), 3.07 (d, J = 10.6 Hz, 0.4H), 2.12 (dd, J = 13.3, 7.3 Hz, 1H), 2.04 (ddd, J = 13.3, 10.3, 4.2 Hz, 1H), 1.95 (ddd, J = 11.2, 7.9, 2.7 Hz, 0.6 H), 1.81 (ddd, J = 10.6, 6.0, 3.0 Hz, 0.4H). ^{13}C NMR (100.6 MHz, D_2O): δ 106.5 (d, ^1J(C, H) = 157 Hz, C1 of **8*β***), 99.9 (d, ^1J(C, H) = 171 Hz, C1 of **8α**),[19] 79.0, 72.6, 71.8, 71.7, 71.3, 71.1, 68.0, 67.2, 67.1, 66.0, 62.4, 62.1, 61.7, 61.5, 58.3, 56.0, 54.3, 48.5, 44.0, 36.3, 35.9. MS (CI, NH_3): 294 ([M + H]$^+$). Anal. Calcd for $C_{12}H_{23}O_7N\cdot 1.8H_2O$: C, 44.25; H, 8.23; N, 4.30. Found: C, 44.26; H, 8.53; N, 4.44.

1,6-Anhydro-2-*O*-benzyl-3-deoxy-3-[(1′*R*)-4′-*O*-*tert*-butyldimethylsilyl-*N*-*tert*-butyloxycarbonyl-2′,3′,5′-trideoxy-2′,5′-imino-L-*erythro*-pentitol-1′-*C*-yl]-*β*-D-glucopyranose (9). A solution of crude aldol product **4** derived from 32 mg (0.14 mmol) of **2** (see above) in MeCN (0.3 mL) was added to a stirred solution of $Me_4NBH(OAc)_3$ (330 mg, 1.3 mmol) in CH_3CN (1 mL) and AcOH (1 mL) at −40 °C. The flask containing **4** was rinsed with CH_3CN (0.3 mL, twice). The mixture was warmed to −20 °C and stirred at this temperature for 20 h. A 1 M aqueous potassium sodium tartrate solution (1 mL) was added, and the mixture was warmed to 20 °C. The phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 mL, three times). The combined organic phases were washed with a saturated aqueous solution of $NaHCO_3$ (5 mL), which was counter-extracted with CH_2Cl_2 (3 mL, four times). The washing and extraction procedure was repeated once more. The combined organic phases were dried (anhydrous Na_2SO_4), and the solvent was evaporated in vacuo. Chromatography on silica gel (2:3 EtOAc/light petroleum ether) afforded a colorless oil (32 mg, 59%). $[\alpha]^{25}_D = -32$ (*c* 1.5, $CHCl_3$). IR (film): 3428, 1674 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 323 K): δ 7.39−7.26 (m, 5H), 5.42 (s, 1H), 4.60 (s, 2H), 4.49 (d, J = 5.2 Hz, 1H), 4.33 (p, J = 3.9 Hz, 1H), 4.14 (td, J = 7.5, 3.0 Hz, 1H), 3.98 (dd, J = 8.1, 2.6 Hz, 1H), 3.84 (m, 2H), 3.66 (dd, J = 7.3, 5.2 Hz, 1H), 3.55 (d, J = 11.5 Hz, 1H), 3.26 (dd, J = 11.5, 3.9 Hz, 1H), 3.16 (d, J = 3.9 Hz, 1H), 2.11 (ddd, J = 13.3, 7.7, 3.9 Hz, 1H), 1.93 (dddd, J = 13.3, 7.7, 3.9, 1.8 Hz, 1H), 1.87 (ddd, J = 8.7, 8.5, 3.9 Hz, 1H), 1.44 (s, 9H), 0.86 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, 323 K): δ 156.1, 137.7, 128.5, 127.9, 127.7, 100.4, 80.3, 77.6, 77.3, 73.8, 71.3, 70.6, 68.9, 66.3, 59.7, 56.3, 45.4, 35.2, 28.5, 25.8, 18.0, −4.8, −4.9. MS (CI, NH_3): 566 ([M + H]$^+$). Anal. Calcd for $C_{29}H_{47}O_8NSi$: C, 61.56; H, 8.37; N, 2.48. Found: C, 61.51; H, 8.35; N, 2.44.

1,6-Anhydro-2-*O*-benzyl-3-deoxy-3-[(1′*R*)-*N*-*tert*-butyloxycarbonyl-2′,3′,5′-trideoxy-2′,5′-imino-L-*erythro*-pentitol-1′-*C*-yl]-*β*-D-glucopyranose (10). The same procedure as for the preparation of **6** was used, starting from **9** (119 mg, 0.211 mmol), yielding a colorless oil (93 mg, 94%) which crystallized from CH_2Cl_2. Mp 80−81 °C. $[\alpha]^{25}_D = -49$ (*c* 1.75, MeOH). IR (KBr): 3414, 1656 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD, 323 K): δ 7.45−7.28 (m, 5H), 5.45 (s, 1H), 4.64 (s, 2H), 4.45 (m, 1H), 4.43 (m, 1H), 4.10−3.98 (m, 1H), 4.03 (d, J = 9.8 Hz, 1H), 3.93 (m, 1H), 3.82 (d, J = 7.6 Hz, 1H), 3.67 (dd, J = 7.6, 5.9 Hz, 1H), 3.52 (d, J = 11.3 Hz, 1H), 3.43 (dd, J = 11.3, 4.9 Hz, 1H), 3.22 (br s, 1H), 2.33 (br s, 1H), 1.89 (ddd, J = 13.3, 7.9, 3.0 Hz, 1H), 1.75 (dt, J = 9.8, 3.0 Hz, 1H), 1.44 (s, 9H). ^{13}C NMR (100.6 MHz, CD_3OD, 323 K): δ 156.6, 139.3, 129.6, 129.1, 129.0, 101.5, 81.3, 78.8, 75.8, 73.1, 72.2, 70.8, 68.3, 66.3, 60.7, 56.2, 47.2, 34.4, 28.8. Anal. Calcd for $C_{23}H_{33}O_8N\cdot H_2O$: C, 58.84; H, 7.51; N, 2.98. Found: C, 59.16; H, 7.40; N, 2.73.

1,6-Anhydro-3-deoxy-3-[(1′*R*)-*N*-*tert*-butyloxycarbonyl-2′,5′-imino-2′,3′,5′-trideoxy-L-*erythro*-pentitol-1′-*C*-yl]-*β*-D-glucopyranose (11). The same procedure as for the preparation

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of **7** was used, starting from **10** (50 mg, 0.11 mmol): white solid (37 mg, 93%). Mp 164−165 °C. $[\alpha]^{25}_D = -74$ (*c* 1.2, MeOH). IR (KBr): 3463, 3379, 1649 cm^{-1}. ^1H NMR (400 MHz, CD_3OD, 323 K): δ 5.27 (s, 1H), 4.45 (d, *J* = 5.4 Hz, 1H), 4.42 (m, 1H), 4.24 (m, 1H), 4.07 (dd, *J* = 10.4, 1.5 Hz, 1H), 3.92 (m, 1H), 3.82 (d, *J* = 7.6 Hz, 1H), 3.67 (dd, *J* = 7.6, 5.4 Hz, 1H), 3.55 (d, *J* = 11.5 Hz, 1H), 3.42 (dd, *J* = 11.5, 4.6 Hz, 1H), 3.40 (d, *J* = 3.1 Hz, 1H), 2.32 (dt, *J* = 13.4, 6.0 Hz, 1H), 1.96 (dddd, *J* = 13.3, 8.1, 3.1, 1.5 Hz, 1H), 1.59 (dt, *J* = 10.5, 3.1 Hz, 1H), 1.52 (s, 9H).^{13}C NMR (100.6 MHz, CD_3OD, 323 K): δ 156.8, 104.2, 81.2, 78.8, 73.3, 70.8, 69.2, 68.8, 66.5, 60.6, 56.4, 49.8, 34.3, 28.9. MS (CI, NH_3): 362 ($[M + H]^+$). Anal. Calcd for $C_{16}H_{27}O_8N$: C, 53.18; H, 7.53; N, 3.88. Found: C, 53.02; H, 7.68; N, 3.83.

Methyl 3-Deoxy-3-[(1′*R*)-2′,5′-imino-2′,3′,5′-trideoxy-L-*erythro*-pentitol-1′-*C*-yl]-α (and *β*)-D-glucopyranoside (12*α*, 12*β*). The same procedure as for the preparation of **8**α and **8*β*** was used, starting from **11** (10.0 mg, 0.0277 mmol), chromatography on silica gel (5% aqueous NH_3:MeOH = 1:12): colorless oil (7.8 mg, 90%). $[\alpha]^{25}_D = +43$ (*c* 0.29, H_2O). IR (film): 3354 cm^{-1}. ^1H NMR (400 MHz, D_2O): δ 4.71 (d, *J* = 3.7 Hz, 0.7H, H-1 of **12**α), 4.59 (t, *J* = 4.2 Hz, 1H), 4.35 (d, *J* = 7.9 Hz, 0.3H, H-1 of **12*β***), 4.26 (dd, *J* = 6.0, 2.6 Hz, 1H), 4.14 (dt, *J* = 11.4, 6.0 Hz, 1H), 3.88 (dd, *J* = 12.1, 2.1 Hz, 0.3H), 3.83 (dd, *J* = 12.1, 2.1 Hz, 0.7H), 3.70 (d, *J* = 12.1, 0.3H), 3.67 (d, *J* = 12.1, 0.7H), 3.68−3.58 (m, 2H), 3.65 (dd, *J* = 10.6, 3.7 Hz, 0.7 H), 3.54 (s, 0.9H), 3.41 (s, 2.1H), 3.34 (dd, *J* = 12.8, 4.2 Hz, 1H), 3.28 (d, *J* = 7.7, 0.3H), 3.21 (d, *J* = 12.6, 1H), 2.18 (dd, *J* = 14.0, 6.0 Hz, 1H), 1.98 (ddd, *J* = 14.0, 11.4, 4.2 Hz, 1H), 1.96 (td, *J* = 10.9, 3.5 Hz, 0.7H), 1.80 (td, *J* = 10.3, 2.3 Hz, 0.3H). ^{13}C NMR (100.6 MHz, D_2O): δ 105.7 (d, ^1J (C, H) = 163 Hz, C1 of **12*β***), 99.4 (d, ^1J (C, H) = 167 Hz, C1 of **12**α),[19] 79.3, 72.8, 70.8, 70.0, 69.9, 69.9, 68.1, 64.9, 64.5, 62.4, 62.1, 61.9, 61.7, 58.1, 55.9, 54.1, 49.5, 45.4, 37.2, 37.0. MS (CI, NH_3): 294 ($[M + H]^+$). Anal. Calcd for $C_{12}H_{23}O_7N \cdot 1.2H_2O$: C, 45.76; H, 8.13; N, 4.45. Found: C, 45.83; H, 7.99; N, 4.53.

1,6-Anhydro-2-*O*-benzyl-3-deoxy-1′,4-*O*-isopropylidene-3-[(1′*R*)-4′-*O*-*tert*-butyldimethylsilyl-*N*-*tert*-butyloxycarbonyl-2′,3′,5′-trideoxy-2′,5′-imino-L-*erythro*-pentitol-1′-*C*-yl]-*β*-D-galactopyranose (13). A mixture of **5** (39 mg, 0.069 mmol), 2,2-dimethoxypropane (2 mL), Drierite (2 g, powder), dry acetone (4 mL), and *p*-toluenesulfonic acid (1 mg) was stirred at 20 °C for 15 h. After addition of K_2CO_3 (10 mg), the precipitate was filtered off and the solvent evaporated in vacuo. The residue was purified by chromatography on silica gel (8:92 EtOAc/light petroleum ether), affording a colorless oil (37 mg, yield 89%). $[\alpha]^{25}_D = +5$ (*c* 1.65, $CHCl_3$). IR (film): 1694 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 333 K): δ 7.40−7.22 (m, 5H), 5.42 (s, 1H), 4.63 (s, 2H), 4.57 (dd, *J* = 7.9, 5.6 Hz, 1H), 4.45 (p, *J* = 5.2 Hz, 1H), 4.38 (t, *J* = 8.2 Hz, 1H), 4.36−3.98 (m, 2H), 4.22 (d, *J* = 7.5, 1H), 3.52 (dd, *J* = 7.5, 5.6 Hz, 1H), 3.41 (dd, *J* = 10.7, 5.4 Hz, 1H), 3.43−3.21 (m, 2H), 2.23 (dt, *J* = 12.6, 5.4 Hz, 1H), 1.90 (ddd, *J* = 10.3, 8.2, 6.3 Hz, 1H), 1.79 (ddd, *J* = 12.4, 8.6, 5.6 Hz, 1H), 1.49 (s, 9H), 1.32 (s, 3H), 1.31 (s, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, 333K): δ 154.3, 137.8, 128.4, 127.8, 127.7, 101.8, 80.4, 79.4, 71.3, 70.6, 70.5, 70.2, 62.5, 61.9, 57.3, 55.1, 40.0, 34.9, 28.7, 25.8, 24.8, 24.2, 18.0, −4.8, −4.9. MS (CI, NH_3): 606 ($[M + H]^+$). Anal. Calcd for $C_{32}H_{51}O_8NSi$: C, 63.44; H, 8.48; N: 2.31. Found: C, 63.53; H, 8.56; N, 2.41.

1,6-Anhydro-2-*O*-benzyl-3-deoxy-1′,4-*O*-isopropylidene-3-[(1′*R*)-4′-*O*-*tert*-butyldimethylsilyl-*N*-*tert*-butyloxycarbonyl-2′,3′,5′-trideoxy-2′,5′-imino-L-*erythro*-pentitol-1′-*C*-yl]-*β*-D-glucopyranose (14). The same procedure as for the preparation of **13** was used, starting from **9** (32 mg, 0.057 mmol): colorless oil (29 mg, 85%). $[\alpha]^{25}_D = -11$ (*c* 1.45, $CHCl_3$). IR (film): 1690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 323 K): δ 7.40−7.28 (m, 5H), 5.32 (s, 1H), 4.60 (s, 2H), 4.44 (p, *J* = 5.6 Hz, 1H), 4.42 (m, 1H), 4.23 (m, 1H), 4.18 (m, 1H), 3.63 (m, 1H), 3.48 (m, 2H), 3.38 (dd, *J* = 10.7, 5.4 Hz, 1H), 3.25 (m, 1H), 3.19 (m, 1H), 2.23 (ddd, *J* = 12.8, 5.6, 4.4 Hz, 1H), 1.77 (m, 1H), 1.60 (q, *J* = 10.3 Hz, 1H), 1.46 (s, 9H), 1.39 (s, 6H), 0.86 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$, 323 K): δ 154.3, 137.5, 128.5, 127.9, 102.0, 79.0, 78.8, 75.7, 73.1, 71.7, 70.7, 69.3, 58.1, 55.1, 38.7, 34.5, 29.9, 28.6, 25.9, 19.9, 18.0, −4.8, −4.9. MS (CI, NH_3): 606 ($[M + H]^+$). Anal. Calcd for $C_{32}H_{51}O_8NSi$: C, 63.44; H, 8.48; N, 2.31. Found: C, 63.48; H, 8.46; N, 2.37.

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Supporting Information Available: Detailed ^1H and ^{13}C NMR spectra and signal assignments, further optical rotation data, and UV, IR, and MS spectra (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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