C-Glycosyl Aldehydes: Synthons for *C*-Linked Disaccharides

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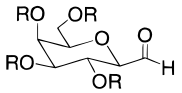
The emerging role of carbohydrate molecules as central determinants of biological function has stimulated tremendous interest in the synthesis of carbohydrate analogs with therapeutic potential. Carbon-linked glycosides (*C*-glycosides) are a particularly interesting class of derivatives by virtue of their resistance to chemical and enzymatic hydrolysis of the glycosidic linkage and their ability to interact with protein receptors similarly to their *O*-linked counterparts.[1,2] In our efforts to construct *C*-glycosyl analogs of biologically active glycoconjugates, we developed an expedient synthesis of *C*-glycosyl aldehydes such as compound **1**.[3] These versatile synthons are constructed in three steps from simple monosaccharides and are available in both α- and *β*-linked forms. Aldehyde **1** proved to be extremely useful in the synthesis of *C*-linked glycopeptides[4] and *C*-linked glycolipids.[5] Here we extend the utility of compound **1** in a general method for the synthesis of *C*-linked disaccharides.



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Current strategies for the synthesis of *C*-disaccharides fall largely into two categories: those in which an acyclic precursor is appended to a pyranose unit and later cyclized to form the second pyranose of the *C*-disaccharide[6] and those in which two intact pyranose units are coupled directly to afford the *C*-disaccharide.[7] The intellectual appeal of the latter approach derives from the availability of monosaccharide starting materials with the desired hydroxyl group stereochemistry already in place. However, this strategy requires the functionalization of pyranose units with mutually reactive centers, which are often incompatible with neighboring alkoxy substituents.

Scheme 1

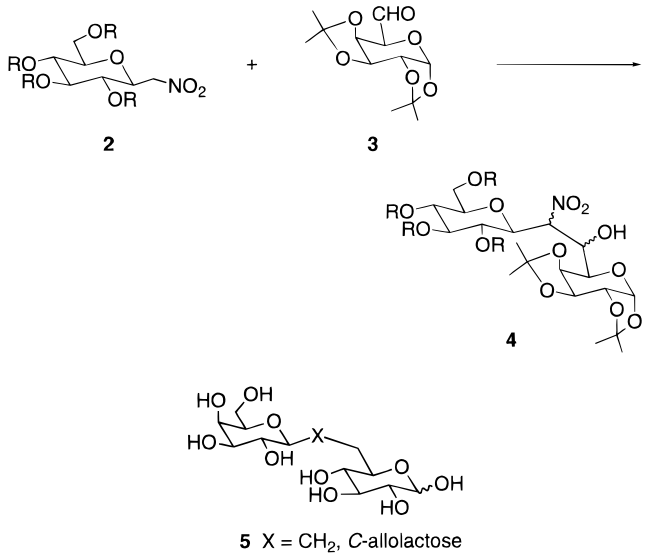

Figure 1.

Martin and Lai have taken advantage of a mild nitro-aldol (Henry) condensation in their synthesis of (1,6)- and (1,1)-linked *C*-disaccharides.[8] For example, *C*-glycosyl nitrate **2** was condensed with a second pyranose functionalized with a C-6 aldehyde (**3**) (Scheme 1). The resulting adduct **4** was then converted to the target *C*-disaccharide. The low pK_a of the proton adjacent to the nitro group (ca. 10) allows formation of the nitronate anion under mildly basic conditions (KF in CH_3CN), avoiding concurrent *β*-elimination of the neighboring alkoxy group. We reasoned that aldehyde **1** could be utilized in a similar approach, in which the polarity of the nitro-aldol reaction is the reverse of that employed by Martin and Lai. The target *C*-disaccharide in this study possesses a 1,6 linkage. However, the nitro group can be installed at any position in a monosaccharide unit,[9] thereby generalizing this method to other disaccharide linkages.

The utility of aldehyde **1** was demonstrated in the synthesis of a *C*-linked analog of a biologically active disaccharide, allolactose (gal*β*1,6glc, **5**, Figure 1). Allolactose is a potent inducer of the *lac* repressor protein, which exerts negative control over the expression of the lactose operon.[10−12] The operon comprises several genes encoding proteins involved in galactose metabolism, such as *β*-galactosidase. The *lac* operon has been used extensively for the control of gene expression in bacterial cloning systems. Allolactose is susceptible to rapid enzymatic hydrolysis by *β*-galactosidase, rendering this molecule unusable in cloning systems.[13] In contrast, *C*-allolactose could serve as a potent inducer of the *lac* repressor protein.

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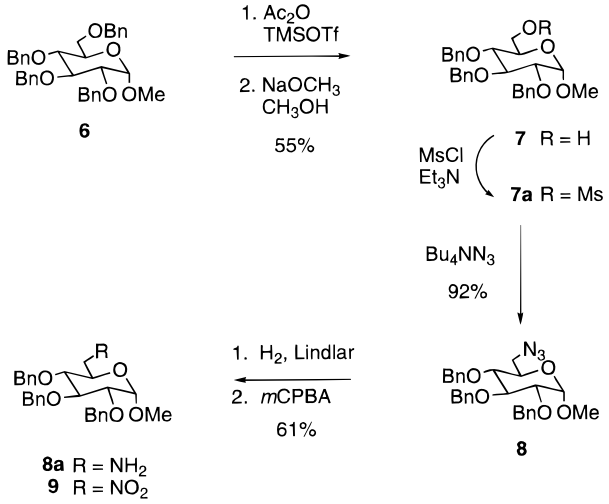
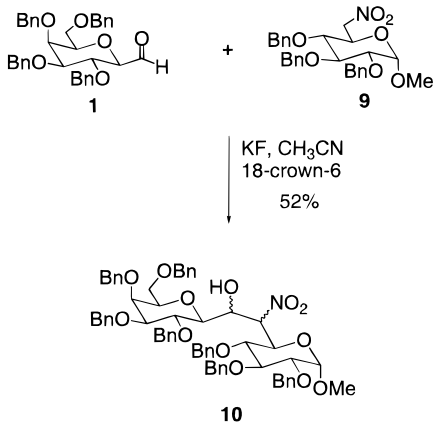
Scheme 2



Scheme 3



The nitro sugar coupling partner was synthesized as depicted in Scheme 2. Selective acetoxylation of methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (**6**)[14] followed by deacetylation afforded compound **7**, which was converted to azido sugar **8** using standard methods. The azide was reduced to the amine by hydrogenation over Lindlar's catalyst and then oxidized with *m*-CPBA to afford nitro sugar **9**.

Aldehyde **1** was condensed with compound **9** using the conditions reported by Martin and Lai[8] to afford the adduct **10** as a mixture of diastereomers (Scheme 3). At this stage, removal of the hydroxyl and nitro groups can be accomplished in the same manner as previously reported.[8] We explored an alternative approach utilizing a radical-promoted elimination reaction.[15] The hydroxyl group in compound **10** was converted to the corresponding phenyl thiocarbonate ester **11** by treatment with 2 equiv of *n*-BuLi followed by phenyl chlorothionocarbonate (PTC-Cl) (Scheme 4).[16] Treatment with Bu_3SnH and a radical initiator effected the elimination reaction, yielding only *trans* olefin **12**. The overall yield for these two steps was ~10% unoptimized.[17] The limiting step is the conversion of the alcohol into the phenyl thionocarbonate ester whereas the radical-promoted elimination reaction proceeds in good yield. In spite of the low yield, this two-step, one-pot procedure has the advantage of only one purification step. Once conditions are optimized for these two steps, this method will facilitate the conversion of Henry condensation products into their fully reduced form. Finally, the olefin was reduced with diimide (generated in situ) and the benzyl ethers were removed by dissolving metal reduction to afford target disaccharide **14**.[18]

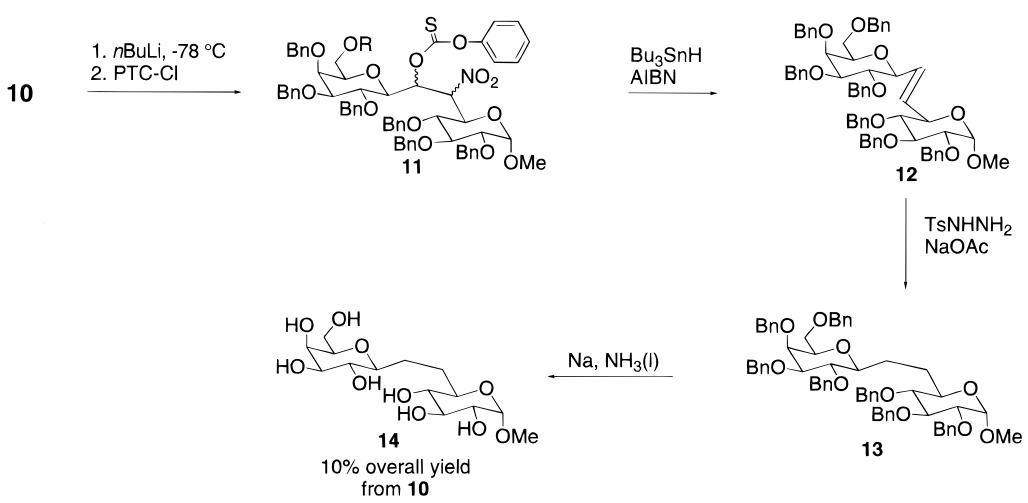
In summary, a new method for the synthesis of *C*-disaccharides has been presented that utilizes a nitro-aldol condensation between readily available *C*-glycosyl aldehydes and nitro sugars. Evaluation of the generality of this method by extension to (1,2)-, (1,3)-, and (1,4)-linked *C*-disaccharides will come in due course.

Experimental Section

General Procedures. Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. Melting points (Pyrex capillary) are uncorrected. The silica gel used in column chromatography was Universal Adsorbents DCC. ^1H NMR spectra were determined at 400 or 500 MHz. ^{13}C NMR spectra were proton decoupled and measured at 100.6 or 125.7 MHz. Chemical shifts are reported in δ values, positive values indicating shifts downfield of tetramethylsilane. Coupling constants are in hertz. Fast atom bombardment (FAB^+) mass spectra were recorded at the U.C. Berkeley Mass Spectral Laboratory.

Methyl 2,3,4-Tri-*O*-benzyl-α-D-glucopyranoside (7). A solution of 27.4 g (49.4 mmol) of methyl 2,3,4,6-tetra-*O*-benzyl)-α-D-glucopyranoside (**6**) in 230 mL of acetic anhydride and 230 mL of dry CH_2Cl_2 was cooled to −61 °C under a N_2 atmosphere. A solution of 11.7 g (49.4 mmol) of trimethylsilyl trifluoromethanesulfonate in 15 mL of dry CH_2Cl_2 was then added over a 45-min period. The resulting orange solution was stirred for 90 min, and then the reaction was quenched with saturated

Scheme 4



$NaHCO_3$. The solution was diluted with CH_2Cl_2, washed with water, and dried over $MgSO_4$. The crude product was dissolved in 500 mL of methanol with a catalytic amount of sodium methoxide. After 3 h, the reaction was neutralized with acidic methanol. Purification of the crude product by silica gel chromatography eluting with 5:1 cyclohexane/ethyl acetate afforded 12.7 g (55%) of a thick syrup: IR (thin film) 3473, 2931, 1652, 1497, 1455, 1363, 1211, 1195, 1162, 1074, 1027, 912, 735, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.40 (s, 3 H), 3.53−3.60 (m, 2 H), 3.67−3.82 (m, 3 H), 4.06 (app t, 1 H, J = 9.2), 4.61 (d, 1 H, J = 3.5), 4.68 (d, 1 H, J = 5.4), 4.70 (d, 1 H, J = 6.5), 4.82−4.94 (m, 3 H), 5.03 (d, 1 H, J = 11.9), 7.28−7.40 (m, 15 H); ^{13}C NMR δ 55.05, 61.64, 70.60, 73.28, 74.90, 75.61, 77.27, 79.85, 81.82, 98.03, 127.50, 127.73, 127.82, 127.84, 127.89, 127.99, 128.28, 128.35, 137.99, 138.03, 138.61; mass spectrum (FAB^+) 471 $(M + Li)^+$.

Methyl 6-*O*-Methanesulfonyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (7a). A solution of 8.95 g (19.3 mmol) of compound **7** in 40 mL of dry CH_2Cl_2 was cooled to 0 °C under a N_2 atmosphere after which 4.1 mL (29 mmol) of Et_3N was added. After 10 min, methanesulfonyl chloride (1.7 mL, 21 mmol) was added dropwise via syringe and the solution was stirred for 1 h. The reaction was quenched with saturated NH_4Cl, and the solution diluted with CH_2Cl_2, washed with water, and dried over $MgSO_4$. Removal of solvents afforded a yellow syrup which was used in the next step without further purification: IR (thin film) 3032, 2919, 1497, 1455, 1359, 1178, 1087, 966, 930, 819, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.98 (s, 3 H), 3.38 (s, 3 H), 3.47−3.54 (m, 2 H), 3.82−3.87 (m, 1 H), 4.02 (app t, 1 H, J = 9.3), 4.35−4.37 (m, 2 H), 4.59−4.68 (m, 3 H), 4.78−4.85 (m, 2 H), 4.91 (d, 1 H, J = 10.8), 5.00 (d, 1 H, J = 10.9), 7.26−7.40 (m, 15 H); ^{13}C NMR δ 37.5, 55.4, 68.3, 68.6, 73.4, 75.1, 75.7, 76.9, 79.7, 81.7, 98.1, 127.7, 127.9, 128.0, 128.0, 128.4, 128.5, 128.5, 137.7, 137.9, 138.4; high-resolution mass spectrum (FAB^+) calcd for $C_{29}H_{34}O_8SLi$ $(M + Li)^+$ 549.2134, found 549.2143.

Methyl 6-Azido-6-deoxy-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (8). To a stirring solution of 10.5 g (19.3 mmol) of compound **7a** in 40 mL of dry CH_3CN was added 6.6 g (23 mmol) of Bu_4NN_3[19] under a nitrogen atmosphere. The solution was heated at reflux for 8 h and cooled to room temperature, and the solvent was removed *in vacuo*. Purification of the crude product by silica gel chromatography eluting with 5:1 cyclohexane/ethyl acetate afforded 8.7 g (92% from alcohol **7**) of a colorless syrup: IR (thin film) 3089, 3065, 3032, 2924, 2246, 2100, 1497, 1454, 1360, 1290, 1286, 1193, 1158, 1077, 1001, 910, 736, 698, 647 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.33 (dd, 1 H, J = 5.6, 13.0), 3.41 (s, 3 H), 3.41−3.47 (m, 2 H), 3.55 (dd, 1 H, J = 3.6, 9.6), 3.77−3.82 (m, 1 H), 4.00 (app t, 1 H, J = 9.2), 4.59 (d, 1 H, J = 11.0), 4.62 (d, 1 H, J = 3.5), 4.68 (d, 1 H, J = 12.1), 4.79−4.84 (m, 2 H), 4.92 (d, 1 H, J = 11.0), 5.01 (d, 1 H, J = 11.0), 7.22−7.40 (m, 15 H); ^{13}C NMR δ 51.31, 55.30, 69.87, 73.36, 75.08, 75.71, 78.27, 79.90, 81.77, 97.96, 127.62, 127.90, 128.03, 128.38, 128.44, 137.87, 137.96, 138.53; high-resolution mass spectrum (FAB^+) calcd for $C_{28}H_{31}N_3O_5Li$ $(M + Li)^+$ 496.2424, found 496.2415.

Methyl 6-Amino-6-deoxy-2,3,4-tri-*O*-benzyl)-α-D-glucopyranoside (8a). To a stirring solution of compound **8** (8.71 g, 17.8 mmol) in 180 mL of EtOH was added 2.61 g (30% by weight) of $Pd/CaCO_3$ poisoned with PbO (Lindlar's catalyst). Hydrogen gas was bubbled through the solution for 1 h, and the reaction was stirred under a H_2 atmosphere for an additional 12-h period. The mixture was filtered through Celite, and the catalyst was rinsed with ethyl acetate. The filtrate was concentrated, and the crude product was purified by silica gel chromatography eluting with a gradient of 2:1 ethyl acetate/cyclohexane to ethyl acetate (2% Et_3N) affording 7.28 g (88%) of a colorless syrup which solidified upon standing: mp 86−89 °C; IR (thin film) 3387, 3031, 2908, 1643, 1495, 1453, 1358, 1069, 735, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.70 (dd, 1 H, J = 6.5, 13.4), 2.97 (dd, 1 H, J = 2.7, 13.4), 3.31−3.36 (m, 1 H), 3.36 (s, 3 H), 3.49 (dd, 1 H, J = 3.6, 9.6), 3.53−3.58 (m, 1 H), 3.99 (app t, 1 H, J = 9.2), 4.55 (d, 1 H, J = 3.5), 4.60 (d, 1 H, J = 11.1), 4.66 (d, 1 H, J = 12.1), 4.78−4.84 (m, 2 H), 4.87 (d, 1 H, J = 11.1), 4.99 (d, 1 H, J = 10.9), 7.27−7.40 (m, 15 H); ^{13}C NMR δ 42.7, 55.0, 71.6, 73.3, 74.8, 75.6, 78.5, 80.0, 82.0, 97.8, 127.5, 127.8, 127.8, 127.9, 128.0, 128.0, 128.3, 128.4, 138.0, 138.0, 138.6; high-resolution mass spectrum (FAB^+) calcd for $C_{28}H_{34}NO_5$ $(MH)^+$ 464.2437, found 464.2431.

Methyl 6-Deoxy-6-nitro-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (9). A stirring solution of 50% *m*-chloroperbenzoic acid (*m*-CPBA) (19.7 g, 62.8 mmol) in 300 mL of 1,2-dichloroethane was heated to reflux under a N_2 atmosphere. A solution of compound **8a** (7.28 g, 15.7 mmol) in 50 mL of 1,2-dichloroethane was added to the solution over a 30-min period, and the reaction was stirred for an additional 2 h at reflux. The solution was cooled to room temperature, the reaction was quenched with a saturated $NaHCO_3$, and the solution was diluted with CH_2Cl_2. The organic layer was washed repeatly with saturated $NaHCO_3$ until all of the *m*-chlorobenzoic acid was removed. The acid free organic layer was dried over $MgSO_4$, and the solvents were removed *in vacuo*. Purification of the crude product by silica gel chromatography eluting with 15:1 cyclohexane/ethyl acetate afforded 5.32 g (69%) of a waxy solid. Recrystallization from hexanes/ethyl acetate afforded white needles: mp 62−63 °C; IR (thin film) 3072, 3024, 2937, 1726, 1558, 1497, 1454, 1362, 1221, 908, 740, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.33 (app t, 1 H, J = 9.9), 3.37 (s, 1 H), 3.52 (dd, 1 H, J = 3.5, 9.6), 4.07 (app t, 1 H, J = 9.2), 4.20 (dd, 1 H, J = 9.3, 12.6), 4.37 (dt, 1 H, J = 2.5, 9.8), 4.48 (d, 1 H, J = 2.6), 4.51−4.53 (m, 1 H), 4.58 (d, 1 H, J = 11.3), 4.65 (d, 1 H, J = 12.0), 4.79−4.86 (m, 1 H), 4.93 (d, 1 H, J = 11.3), 5.04 (d, 1 H, J = 10.8), 7.22−7.37 (m, 15 H); ^{13}C NMR δ 55.58, 67.38, 73.41, 74.84, 75.81, 76.10, 77.66, 79.71, 81.71, 97.90, 127.76, 127.97, 128.05, 128.09, 128.12, 128.20, 128.44, 128.50, 128.61, 137.40, 137.77, 138.30; high-resolution mass spectrum (FAB^+) calcd for $C_{28}H_{31}NO_7Li$ $(M + Li)^+$ 500.2261, found 500.2271.

Anal. Calcd for $C_{28}H_{31}NO_7$: C, 68.14; H, 6.33; N, 2.84. Found: C, 68.34; H, 6.42; N, 2.67.

Methyl 6-*C*-(2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-d-glycero-L-*manno*-heptitol-1-yl)-6-deoxy-6-nitro-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (10). To a stirring solution of 1.80 g (3.62 mmol) of compound **9** in 15 mL of dry CH_3CN were added 2.20 g (3.98 mmol) of (2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)methanal (**1**), 0.23 g (4.0 mmol) of KF, and 0.21 g (0.80 mmol) of 18-crown-6 under a N_2 atmosphere. The solution was stirred at room temperature for 7 h, and the solvent was removed *in vacuo*. Purification of the crude product by silica gel chromatography eluting with 5:1 pentane/ether afforded 1.97 g (52%) of a thick syrup, which consisted of an inseparable mixture of four diastereomers as determined by ^1H and ^{13}C NMR spectroscopy. The mixture was characterized by IR spectroscopy and mass spectrometry: IR (thin film) 3442, 3090, 3064, 3033, 2924, 2871, 1548, 1498, 1452, 1362, 1212, 1087, 1047, 1029, 999, 911, 736, 698 cm^{-1}; high-resolution mass spectrum (FAB^+) calcd for $C_{63}H_{67}NO_{13}Li$ $(M + Li)^+$ 1052.4772, found 1052.4793.

Methyl 6-*C*-(2,6-Anhydro-1-*O*-(phenylthionocarbonyl)-3,4,5,7-tetra-*O*-benzyl-D-*glycero*-L-*manno*-heptitol-1-yl)-6-deoxy-6-nitro-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (11). A solution of 37 mg (0.35 mmol) of compound **10** in 3.5 mL of THF was placed in a flame-dried flask under a N_2 atmosphere. The solution was cooled to −78 °C, and 280 μL (0.70 mmol) of a 2.5 M solution of *n*-BuLi in hexanes was added slowly. The resulting yellow solution was stirred for 15 min, after which 60 μL (0.42 mmol) of phenyl chlorothionocarbonate was added dropwise. The reaction mixture was warmed to −42 °C for 45 min and then to room temperature for 5 min. The reaction was quenched with saturated NH_4Cl, and the solution was diluted with ether, washed with water and brine, and dried over $MgSO_4$. Removal of the solvents afforded a yellow syrup which decomposed readily upon exposure to silica gel. The crude product was therefore used in the next step without further purification; mass spectrum (FAB^+) 1182.6 $(MH)^+$.

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(14) Angibeaud, P.; Utille, J.-P. *Synthesis* **1991**, 737.

(15) A similar reaction has been used for the conversion of β-nitro sulfides and sulfones to the corresponding olefins: Ono, N.; Kaji, A. *Synthesis* **1986**, 693.

(16) Robins, M. J.; Wilson, J. S.; Hansske, F. *J. Am. Chem. Soc.* **1983**, *105*, 4059.

(17) Unfortunately, optimization of this step was not possible due to closure of the laboratory.

(18) Compound **12** was refractory to hydrogenation of both the olefin and the benzyl ethers.

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Methyl 6-*C*-(2,6-Anhydro-1-deoxy-1-dehydro-3,4,5,7-tetra-*O*-benzyl-D-*glycero*-L-*manno*-heptitol-1-yl)-6-deoxy-6-dehydro-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (12). To a stirring, degassed solution of crude **11** (41 mg, 0.35 mmol) in 3.5 mL of dry, degassed toluene were added 280 μL (1.1 mmol) of tributyltin hydride and 114 mg (0.70 mmol) of AIBN. The solution was heated at reflux for 1 h, cooled to room temperature, and then concentrated *in vacuo*. The resulting syrup was dissolved in acetonitrile and washed extensively with pentane. The acetonitrile layer was concentrated, and the crude product was purified by silica gel chromatography eluting with 15:1 cyclohexane/ethyl acetate to afford an amorphous gel. Subsequent treatment with pentane resulted in the formation of white crystals. Isolation by vacuum filtration afforded 33 mg of the desired product in an overall yield of 10% based on compound **10**. The product was exclusively in the *trans* configuration as determined by an olefin coupling constant of 15.5 Hz: mp 95−97 °C; IR (KBr) 3097, 3064, 3031, 2913, 2863, 1453, 1360, 1266, 1212, 1094, 1072, 1052, 1031, 913, 740, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.18 (app t, 1 H, J = 9.3), 3.32 (s, 3 H), 3.50 (dd, 1 H, J = 3.6, 9.6), 3.55−3.60 (m, 4 H), 3.67−3.71 (m, 1 H), 3.74 (dd, 1 H, J = 5.8, 9.2), 3.95 (app t, 1 H, J = 9.3), 3.99 (d, 1 H, J = 2.7), 4.09 (dd, 1 H, J = 5.9, 9.8), 4.37−4.44 (m, 2 H), 4.46−4.52 (m, 2 H), 4.58−4.72 (m, 7 H), 4.77−4.83 (m, 2 H), 4.91−4.96 (m, 2 H), 5.90 (dd, 1 H, J = 6.2, 15.5), 5.98 (dd, 1 H, J = 6.1, 15.5), 7.15−7.40 (m, 35 H); ^{13}C NMR δ 55.14, 68.78, 70.71, 72.41, 73.35, 73.52, 74.00, 74.57, 74.99, 75.17, 75.80, 79.25, 79.59, 79.82, 81.66, 82.22, 84.18, 98.04, 127.47, 127.54, 127.75, 127.84, 127.92, 127.95, 127.96, 128.04, 128.07, 128.11, 128.18, 128.25, 128.34, 128.38, 128.42, 130.31, 130.76, 137.85, 138.16, 138.23, 138.42, 138.48, 138.85, 138.87; high-resolution mass spectrum (FAB^+) calcd for $C_{63}H_{66}O_{10}Li$ $(M + Li)^+$ 989.4816, found 989.4828.

Methyl 6-*C*-(2,6-Anhydro-1-deoxy-3,4,5,7-tetra-*O*-benzyl-D-*glycero*-L-*manno*-heptitol-1-yl)-6-deoxy-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (13). A solution of 29 mg (0.029 mmol) of alkene **12** and 16 mg (0.087 mmol) of (*p*-toluenesulfonyl)-hydrazine in 3 mL of dimethoxyethane was heated to reflux. A solution of 7.1 mg (0.087 mmol) of NaOAc in 1.5 mL of H_2O was then added to the solution via syringe pump over a 12-h period. The reaction was stirred at reflux for an additional 12 h and cooled to room temperature. The solution was diluted with ether, washed with water and brine, and dried over $MgSO_4$. The solution was concentrated and coevaporated twice with ethanol to afford a fluffy white solid (28 mg, 98%) that was used in the next step without further purification: ^1H NMR (500 MHz, $CDCl_3$) δ 1.40−1.53 (m, 4 H), 3.16 (app t, 1 H, J = 9.4), 3.20 (m, 1 H), 3.30 (s, 3 H), 3.49−3.60 (m, 6 H), 3.67 (app t, 1 H, J = 9.3), 3.94 (app t, 1 H, J = 9.3), 4.01 (app d, 1 H, J = 2.5), 4.40 (d, 1 H, J = 11.7), 4.46 (d, 1 H, J = 11.7), 4.54 (d, 1 H, J = 3.6), 4.56 (d, 1 H, J = 10.8), 4.62 (d, 1 H, J = 11.2), 4.64 (d, 1 H, J = 13.0), 4.68 (app d, 2 H, J = 11.9), 4.76 (d, 1 H, J = 11.7), 4.80 (d, 1 H, J = 12.2), 4.81 (d, 1 H, J = 10.8), 4.84 (d, 1 H, J = 10.8), 4.93 (d, 1 H, J = 10.9), 4.96 (d, 1 H, J = 11.7), 4.97 (d, 1 H, J = 10.8), 7.25−7.38 (m, 35 H); ^{13}C NMR δ 27.77, 29.60, 54.80, 68.82, 70.38, 72.07, 73.14, 73.42, 73.65, 74.37, 75.13, 75.36, 75.64, 76.82, 79.25, 79.85, 80.07, 82.00, 82.26, 84.82, 97.60, 127.39, 127.42, 127.48, 127.65, 127.75, 127.80, 127.92, 127.98, 128.09, 128.20, 128.27, 128.31, 128.34, 137.88, 138.19, 138.28, 138.35, 138.44, 138.77; high-resolution mass spectrum (FAB^+) calcd for $C_{63}H_{68}O_{10}Li$ $(M + Li)^+$ 991.4973, found 991.4973.

Methyl 6-*C*-(2,6-Anhydro-1-deoxy-D-*glycero*-L-*manno*-heptitol-1-yl)-6-deoxy-α-D-glucopyranoside (14). Compound **13** was dissolved in 1.5 mL of dry dimethoxyethane and cooled to −78 °C under a N_2 atmosphere. Ammonia (5 mL) was condensed into the reaction flask, and the solution was warmed to −33 °C. Sodium metal was added to the stirring solution until a dark blue color persisted. The reaction mixture was stirred for an additional 15 min, and then the reaction was quenched with solid NH_4Cl. The resulting suspension was concentrated and diluted with ethanol, and the insoluble salts were filtered. The filtrate was concentrated and passed down a column of Bio-Rad AG501-X8 (D) resin (mixed bed desalting resin), and the eluate was concentrated to afford 11 mg (100%) of a white solid. The product was further purified by reversed-phase HPLC eluting with H_2O: ^1H NMR (400 MHz, D_2O) δ 1.29−1.33 (m, 2 H), 1.89−1.94 (m, 2 H), 3.00−3.06 (m, 2 H), 3.21 (s, 3 H), 3.24 (app t, 1 H, J = 9.5), 3.34−3.43 (m, 6 H), 4.38 (dd, 1 H, J = 4.3, 11.6), 3.55 (dd, 1 H, J = 8.1, 11.7), 3.74 (d, 1 H, J = 3.2); ^{13}C NMR δ 29.48, 30.04, 57.90, 64.30, 72.08, 73.81, 74.25, 74.27, 75.94, 76.25, 76.92, 81.39, 82.72, 101.95; high-resolution mass spectrum (FAB^+) calcd for $C_{14}H_{26}O_{10}Li$ $(M + Li)^+$ 361.1686, found 361.1706.

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Supporting Information Available: ^1H NMR spectra for compounds **7**−**10** and **12**−**14**; ^{13}C NMR specta for compounds **7**−**9** and **12**−**14** (17 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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