An Olefin Metathesis Route for the Preparation of (1→6)-Linked *C*-Disaccharide Glycals. A Convergent and Flexible Approach to *C*-Saccharide Synthesis

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A convergent route to a variety of *C*-1-disaccharide glycals based on the olefin metathesis reaction of enol ethers and alkenes is described. The DCC-mediated coupling reaction of a variety of pentose enitols (**1a**−**c**) with a number of C-5- and C-6-monosaccharide carboxylic acids (**2a**−**e**) gave the corresponding esters **3a**−**l** in good yield. Methylenation of these compounds was followed by ring-closing metathesis, mediated by the Schrock molybdenum catalyst **8** in warm toluene, to provide the target *C*-disaccharide glycals **5a**−**l**. The formed enol ether double bond in **5a** was then transformed, via standard manipulations, into a variety of *C*-disaccharide derivatives **21**−**25**.

It has been well established that cell surface carbohydrates are involved in key molecular recognition events with protein receptors. These interactions are important for normal cell functions, such as recognition and binding, but they can also be harmful since they are a launch point for bacterial and viral infections as well as cell adhesion in inflammation and tumor metastasis[1] One strategy to prevent these events from occurring is to prepare small carbohydrate-based therapeutics which will inhibit the recognition event by preferentially binding to the protein receptor. The disadvantage of using carbohydrates for these purposes is that they are easily hydrolyzed by a large number of extra- and intracellular glycosidases. It is here that *C*-saccharides show their strength; with their stability at low pH and resistance to enzymatic cleavage, they make ideal sugar mimics.

Inhibitors of glycosidase have been shown to exhibit both antiviral[2] and antitumor[3,4] activity in a variety of models. Inhibitors of α-glucosidase also have potential for therapeutic use in the treatment of diabetes.[5]

The importance of sugar-based enzyme inhibitors cannot be understated. The main problem with carbohydrate-based therapeutics, however, is their instability to enzymatic cleavage and chemical hydrolysis. One way to increase the stability of the anomeric linkage is to replace the interglycosidic oxygen atom with a methylene group to furnish a *C*-saccharide. There has been some debate over the validity of this substitution since the conformation and, hence, the binding affinity of the *C*-saccharide mimic may not be the same as that of the parent *O*-saccharide.[6−11] In these above cases, the only change from the natural substrate to the *C*-saccharides was the replacement of the interglycosidic oxygen atom with a methylene group. From these works,[8−10] it was shown that, although substitution of the interglycosidic oxygen atom with a methylene group may change the conformation during binding, the change does not interfere with the binding of the *C*-glycoside substrate to the active site. Although there has been much synthetic work in the area of *C*-glycosides, relatively little has appeared in regard to biological evaluation of *C*-saccharides and *C*-saccharide glycals. *C*-Glycosides are extremely stable entities which will not be fragmented by biological or chemical hydrolysis.[12,13] If carbohydrates are to be used as potential drug candidates, then stable compounds, such as *C*-saccharides, are an excellent starting point.

There have been interesting and novel approaches to *C*-saccharide synthesis over the past decade, and many of these have been reviewed.[14] Recently, Armstrong employed an approach to the preparation of *C*-trisaccharides that relied on nonstereoselective methods in conjunction with de novo ring synthesis to gain access to a number of stereochemically diverse *C*-trisaccharides.[15,16]

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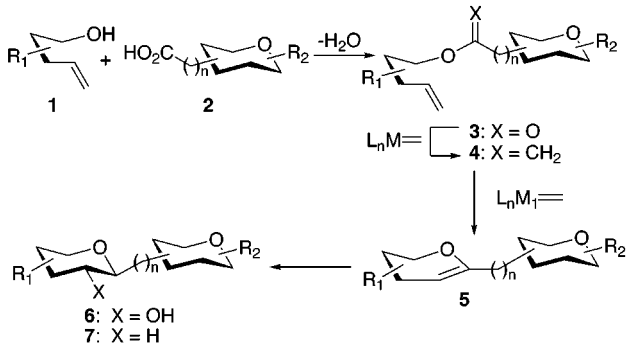
Scheme 1



Schmidt employed *C*-1-lithiated glycals that were then coupled to the appropriate sugar aldehydes.[17] Recent work by Sinaÿ relied on the use of tethered 8- and 9-*endo* tin hydride mediated radical closures to prepare *C*-disaccharides.[18] Skrydstrup and Beau have used organosamarium chemistry to construct α-manno-*C*-disaccharides,[19] while a very recent approach for *C*-disaccharide preparation relied on the novel use of the Ramberg−Bäcklund reaction.[20]

We have previously shown that olefin metathesis can be used to prepare alkyl and aryl *C*-glycosides[21] as well as (1→6)-linked *C*-disaccharides.[22] In this full paper, we describe the details of our metathesis-based approach for the formation of (1→6)-*C*-disaccharide glycals. Conceptually, it was thought that olefin metathesis and carbohydrate chemistry could mesh together[23] quite well to provide a convergent and flexible route to a wide variety of *C*-disaccharides (Scheme 1). The sequence begins with a dehydrative coupling of an appropriate olefin alcohol **1** with generic acid **2** to give carbohydrate-based ester **3**. Methylenation of **3** to acyclic enol ether **4**, via standard methods, is then followed by ring-closing metathesis to give the *C*-disaccharide glycal **5**. Compound **5** can serve as an intermediate to both the *β*-*C*-saccharides with the general structures **6** and **7** by hydroboration[24,25] (followed by oxidative workup) or stereoselective reduction,[26] respectively. Access to other types of linked saccharide structures should be possible by simply changing the stereochemical disposition and/or location of the acid function on the carbohydrate ring.

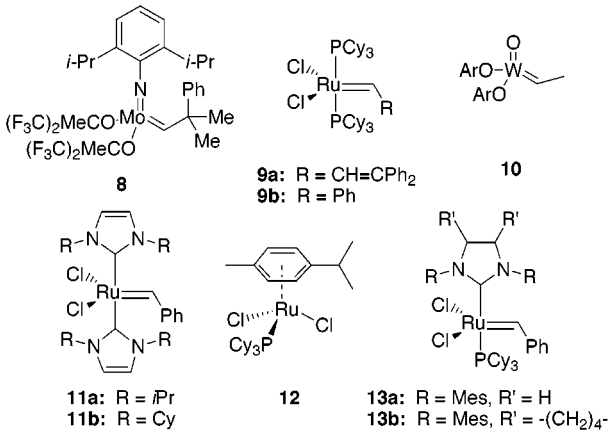


Figure 1.

Initial work by Grubbs established the viability of employing ring-closing metathesis for the preparation of cyclic enol ethers from simple substrates.[27] Subsequent work by Nicolaou focused on the one-pot preparation of cyclic enol ethers directly from esters using stoichiometric titanium reagents for the convergent assembly of polyethers.[28,29] This one-pot methodology has recently been employed by Hirama and co-workers for the convergent preparation of the IJKLM ring fragment of Ciguatoxin CTX3C.[30] The preparation of polyether-based cyclic enol ethers from olefinic acyclic enol ethers using a two-step protocol has also been reported.[31] The same group has also studied metathesis-based ring closures involving olefinic alkynyl ethers to give cyclic alkenyl enol ethers.[32] This two-step protocol was also later used as an iterative method of fusing glycals onto a carbohydrate to gain access to polyether-type structures.[33] In addition, scientists at Merck-Frosst have found that some unsubstituted (on the enol ether olefin) enol ethers can undergo ring-closing metathesis, albeit in low yield, with the use of the Grubbs catalyst **9b** (Figure 1) to give unsubstituted glycals.[34]

The use of olefin metathesis[35] to prepare functionalized organic structures has been made possible by the availability of the appropriate precatalysts, Figure 1. The Schrock catalyst **8**[36] has been available for several years now, and the ruthenium-based carbenes **9a** and **9b**, developed by Grubbs,[37] have become very popular due

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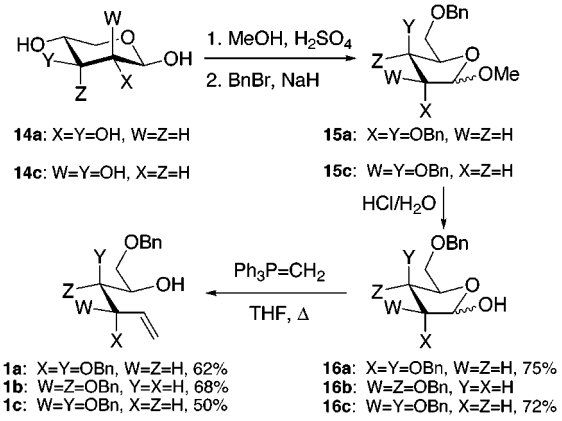
to their increased stability to air and various solvents over **8**. Several other variants based on both ruthenium (**11**,[38] **12**[39]) and tungsten (**10**[40]) have also appeared. Recently, catalyst **13** in which one of the tricyclohexylphosphine ligands of **9b** has been replaced with an imazolidine group has been prepared.[41] Both catalysts **11** and **13** are more reactive than the parent catalyst **9b** and both possess greater stability to air and moisture than the Schrock catalyst **8**. Catalysts **11** and **13** are capable of forming tri- and tetrasubstituted cycloalkenes by ring-closing metathesis.[41,42]

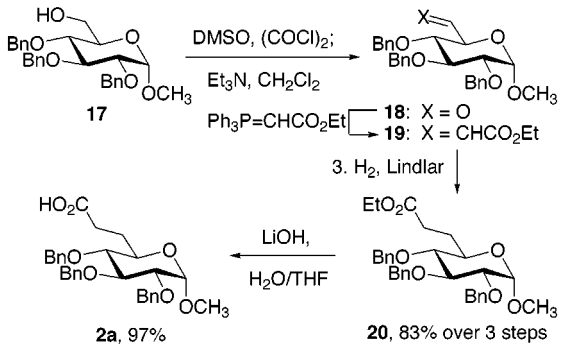
This work outlines the preparation of 1,6-linked *C*-disaccharides, compounds in which two monosaccharide units are joined at the 1- and 6′-positions by a $-CH_2-CH_2-$ linker.[43] We wished to determine whether our metathesis-based methodology was suitable for *C*-disaccharide synthesis, since the substrates are more densely oxygenated than simple *C*-glycosides, and it was not clear whether the methylenation or metathesis chemistry would proceed efficiently. In previous cases of cyclic enol ether formation via olefin metathesis,[28,29,33,44,45] the two reactive ends (olefin and acyclic enol ether) were fused onto an existing ring, bringing them proximal to each other for cyclization. In this case, no fused ring system is present since benzyl groups were chosen for protection of the hydroxyl functionality. Our concerns were unwarranted, and the results described below demonstrate that glycal formation via olefin metathesis is a viable synthetic approach to this class of carbohydrate mimics.

The preparation of the needed olefin alcohols was straightforward and modeled upon literature guidelines as shown in Scheme 2.[46] We targeted three olefin alcohols

Scheme 2



Scheme 3



that would lead to the *galacto*, *gulo*, and *gluco* 1,6-linked *C*-disaccharide glycals. Methanol solutions of D-xylose (**14a**) and D-lyxose (**14c**) were treated with acid to furnish the kinetically favored furanosides which were then benzylated to give **15a** and **15c**. Anomeric deprotection then gave lactols **15a** and **15c** as mixtures of anomers. The first three steps were routinely carried out without purification of the intermediates. Only the lactols were purified and characterized when necessary. Wittig reaction of lactols **16a**−**c** with the ylide derived from methyltriphenylphosphonium bromide and *n*-butyllithium gave the three olefin alcohols **1a**,[47] **1b**[48] and **1c** corresponding to the *gulo*, *gluco*, and *galacto* sugars, respectively. The *arabino* lactol **16b** is commercially available.[49]

The starting acids were prepared by simple chain extension of a suitably protected free *O*-6-monosaccharide derivative.[50,51] The sequence is described with the *gluco* derivative **17** (Scheme 3). Swern oxidation of alcohol **17** was followed by Wittig reaction of the crude aldehyde **18** to give **20** after reduction of the double bond (81% over three steps). Saponification of **20** then delivered the requisite acid **2a**.[52] All the acids used for the preparations of esters **3a**−**l** (Table 1) were prepared in a fashion analogous to that employed for **2a**. Thus far, only benzyl, methyl, and acetonide protecting groups have been examined.

The general strategy is delineated in Scheme 4 and follows our approach to *C*-glycoside synthesis.[21] Coupling

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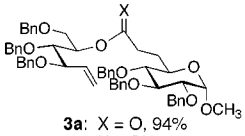
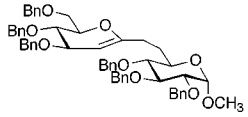
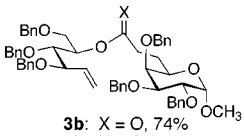
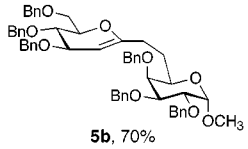
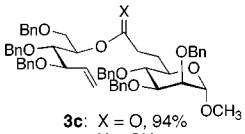
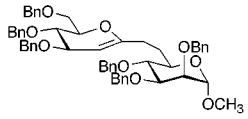
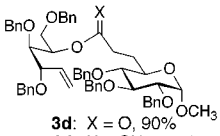
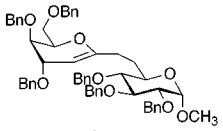
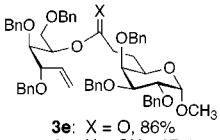
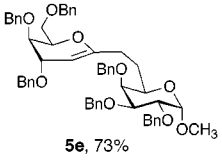
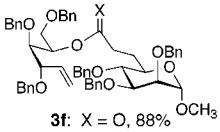
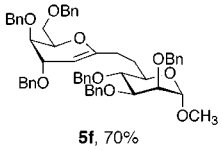
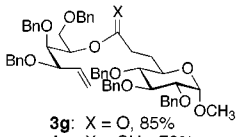
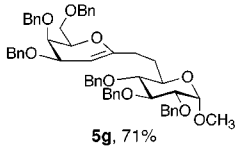
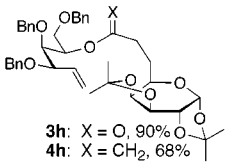
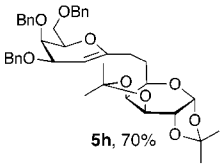
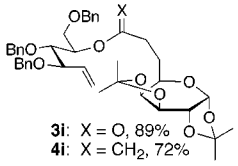
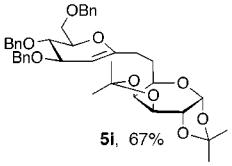
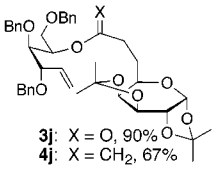
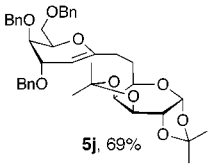
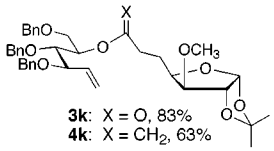
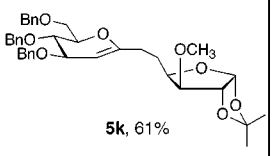
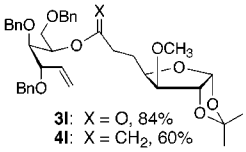
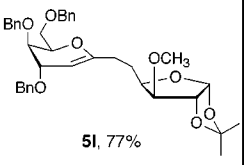
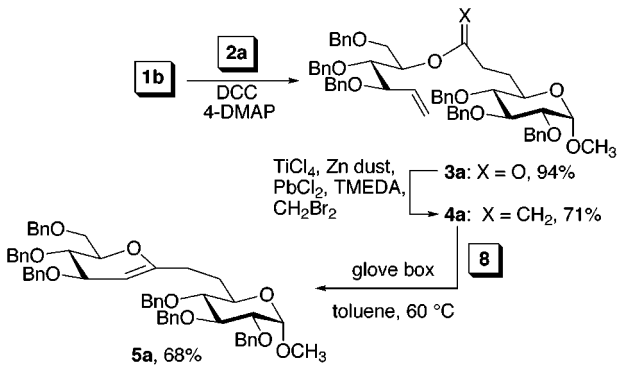
(52) Detailed procedures for the preparations of these compounds can be found in the Supporting Information.

Table 1. Preparation of 1,6-Linked *C*-Disaccharide Glycals

Entry	Ester **3**/Acyclic Enol Ether **4**	Glycal, **5**, (% Yield)[a, b]
1	 **3a**: X = O, 94% **4a**: X = CH_2, 71%	 **5a**, 68%
2	 **3b**: X = O, 74% **4b**: X = CH_2, 71%	 **5b**, 70%
3	 **3c**: X = O, 94% **4c**: X = CH_2, 71%	 **5c**, 72%
4	 **3d**: X = O, 90% **4d**: X = CH_2, 71%	 **5d**, 75%
5	 **3e**: X = O, 86% **4e**: X = CH_2, 67%	 **5e**, 73%
6	 **3f**: X = O, 88% **4f**: X = CH_2, 68%	 **5f**, 70%
7	 **3g**: X = O, 85% **4g**: X = CH_2, 70%	 **5g**, 71%
8	 **3h**: X = O, 90% **4h**: X = CH_2, 68%	 **5h**, 70%
9	 **3i**: X = O, 89% **4i**: X = CH_2, 72%	 **5i**, 67%
10	 **3j**: X = O, 90% **4j**: X = CH_2, 67%	 **5j**, 69%
11	 **3k**: X = O, 83% **4k**: X = CH_2, 63%	 **5k**, 61%
12	 **3l**: X = O, 84% **4l**: X = CH_2, 60%	 **5l**, 77%

[a] Yields refer to chromatographically homogeneous (^{1}H NMR, 500 MHz) material. [b] 20-60 mg scale at 0.01−0.02 M in substrate using 15−30 mol % metathesis catalyst **8**.

Scheme 4



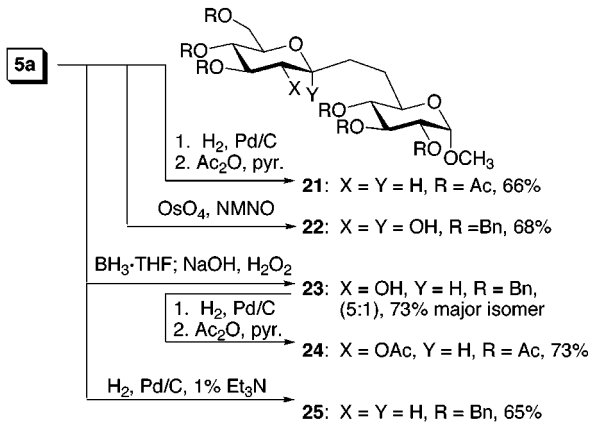
of olefin alcohol **1b** with the sugar-based acid **2a** gave ester **3a** in 94% yield. Methylenation of **3a** to **4a** was performed in the usual way[53] and exposure of the resulting enol ether to the Schrock catalyst **8** (10−15 mol %) in a glovebox delivered the target *C*-disaccharide glycal **5a** in 68% yield.

The key esterification reaction was carried out with DCC in the presence of 4-DMAP, and the acids were used in slight excess. Yields for these couplings were good as seen from Table 1. Methylenations were carried out using the modified Takai conditions[53] with an excess of reagent and gave fair yields of the acyclic enol ethers.[54] Purification of the acyclic enol ethers was important since impurities impeded the subsequent ring-closing metathesis step.[27] Exposure of the pure acyclic enol ethers to catalyst **8** then gave the (1→6)-*C*-glycals **5** (Table 1).[54] The reactions were generally complete within 30−60 min at 60 °C in dry degassed toluene. We briefly examined the use of catalyst **9b** to effect the key RCM reaction. Exposure of **4a** to 50 mol % **9b** in hot toluene gave only 50% conversion to **5a** after 8 h as observed by ^{1}H NMR. These results are consistent with what has been observed previously with much simpler, but related systems.[34] We are currently screening the remaining catalysts shown in Figure 1 for their ability to mediate the key conversion (**4** → **5**).

(53) Takai, K.; Kakiuchi, T.; Kataoka, Y.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 2668.

(54) The compounds are stable to silica gel chromatography provided that 1% triethylamine is used in the eluting solvent.

Scheme 5



Glycal **5a** was employed to explore the functionalization chemistry of the double bond (Scheme 5). Hydrogenation of the double bond and removal of the benzyl groups in one pot were also tried and gave **21** (66%), after acetylation. An NOE enhancement of 5% at *H*-1 was observed when *H*-5 was irradiated. Osmylation was also performed on **5a** and gave the keto-*C*-disaccharide **22** in 68% yield. Hydroboration of **5a** gave **23** as the major product (5:1, ^{1}H NMR, 500 MHz) fully characterized as its peracetate.[55] The stereochemistry of the major isomer was assigned on the basis of the large coupling constants of the *C*-2 proton (J = 9.5, 9.5 Hz) in acetylated **23** (where X = OAc, Y = H, and R = Bn), indicating an all-axial relationship among *H*-1, *H*-2, and *H*-3. Selective reduction of the double bond in **5a** using slightly poisoned (1% Et_3N) Pd/C catalyst gave the *β*-*C*-disaccharide **25** in 65% yield.[26]

The flexibility of our route is illustrated by the different types of glycals that have been prepared from readily available monosaccharides (Table 1). The nature of the acid can be varied although we have not yet examined *C*-2 amino sugars or deoxygenation of the remaining positions either prior to or after cyclization. Acetonide blocking groups (entries 8−12) as well as benzyl moieties are tolerant of the reaction conditions. Entries 4−6 and 10 (Table 1) show that the stereochemistry of the adjacent allylic benzyloxy group does not interfere with the ring-closing metathesis reaction.

Our metathesis-based approach to *C*-saccharide formation allows for structural diversity in both the olefin and acid portions as evidenced from the data shown in Table 1. The starting acids and olefin alcohols are readily prepared in good yield from known and inexpensive monosaccharide derivatives. The route is convergent since two pieces of roughly equal molecular weight are joined together during the initial esterification step to eventually deliver target *C*-saccharide structures in good overall yield. The preparation of the 1,6-linked *C*-saccharide mimics described above opens the door for the preparation of more complex and biologically relevant *C*-saccharides.

Experimental Section

General Procedures. Unless otherwise noted, reagents were commercially available and were used without purification. Tetrahydrofuran (THF) was freshly distilled from sodium−benzophenone ketyl. Dichloromethane and TMEDA were distilled from calcium hydride, while benzene and toluene were distilled from sodium. All reactions were conducted in oven- or flame-dried glassware under an atmosphere of argon. Organic solutions were dried over magnesium sulfate. TLC analyses were carried out using (Merck 60F-254) thin-layer chromatography plates and visualized under UV light or by charring with phosphomolybdic solution. Silica gel for flash chromatography was Merck type 60 (230−400 mesh).

General Procedure for the Wittig Reaction Exemplified by the Preparation of Ethyl (Methyl 6,7-dideoxy-α-D-*gluco*-octo-6(*Z*)-enopyranosid)uronate (19a). Dry DMSO (1.23 mL, 17.3 mmol) was added dropwise to a −78 °C solution of oxalyl chloride (1.23 mL, 12.9 mmol) in dry CH_2Cl_2 (20 mL). After the reaction mixture was stirred for 15 min at −78 °C, a CH_2Cl_2 (10 mL plus 5 mL rinse) solution of alcohol **17a** (5.20 g, 11.2 mmol) was cannulated into it dropwise over a period of 3 min. After the resulting mixture was stirred at −78 °C for 30 min, Et_3N (7.7 mL, 54.3 mmol) was added, and the mixture was allowed to warm to 0 °C, at which point H_2O (20 mL) was added. The mixture was allowed to warm to room temperature, and the aqueous layer was separated and extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo to afford a yellow oil.

A benzene (30 mL) solution of $Ph_3P{=}CHCO_2Et$ (5.4 g, 15.5 mmol) was added to a cool (0 °C) solution of the crude product obtained above in dry benzene (30 mL). The reaction mixture was allowed to warm to ambient temperature, stirred for an additonal 4 h, and then concentrated in vacuo. Flash chromatography of the residue over silica gel using 20% Et_2O−hexanes gave unsaturated ester **19a** (5.10 g, 85%) as a pure (TLC, silica 30% ether−hexanes; ^{1}H NMR, 500 MHz) white solid: mp = 69 °C; $[\alpha]_D$ = +16.8 (c = 0.28, $CHCl_3$); FT-IR (neat) 3063, 3031, 2982, 2940, 2906, 1721, 1303; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.27 (m, 15 H, Ph), 7.02 (dd, 1 H, J = 15.7, 4.9 Hz, *H*-6), 6.11 (dd, 1 H, J = 15.7, 1.8 Hz, *H*-7), 4.96 (d, 1 H, J = 10.7 Hz, OC*H*$_2$Ph), 4.83 (d, 1 H, J = 10.6 Hz, OC*H*$_2$Ph), 4.81 (d, 1 H, J = 10.7 Hz, OC*H*$_2$Ph), 4.79 (d, 1 H, J = 11.9 Hz, OC*H*$_2$Ph), 4.66 (d, 1 H, J = 11.9 Hz, OC*H*$_2$Ph), 4.59 (d, 1 H, J = 3.5 Hz, *H*-1), 4.56 (d, 1 H, J = 10.9 Hz, OC*H*$_2$Ph), 4.25 (ddd, 1 H, J = 9.9, 4.6, 1.5 Hz, *H*-5), 4.19 (q, 2 H, J = 7.1 Hz, OC*H*$_2$-CH_3), 4.00 (dd, 1 H, J = 9.3, 9.3 Hz, *H*-3), 3.51 (dd, 1 H, J = 9.6, 3.6 Hz, *H*-2), 3.34 (s, 3 H, OC*H*$_3$), 3.23 (dd, 1 H, J = 9.9, 8.9 Hz, *H*-4), 1.28 (t, 1 H, J = 7.1 Hz, CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 143.8, 138.5, 137.9, 137.6, 128.5, 128.4, 128.4, 128.1, 128.1, 127.9, 127.9, 127.6, 122.1, 98.1, 81.8, 81.7, 79.7, 77.2, 77.0, 76.7, 75.8, 75.4, 73.4, 69.2, 60.4, 55.3, 14.2; HRMS (EI) calcd for $C_{25}H_{29}O_7$ (M − C_7H_7)$^+$ 441.1913, found 441.1912.

General Procedure for Hydrogenation Exemplified with the Preparation of Ethyl (Methyl 2,3,4-tri-*O*-benzyl-6,7-dideoxy-α-D-*gluco*-octopyranosid)uronate (20a). Lindlar catalyst (2.00 g) was added in portions to a solution of the unsaturated ester **19a** (2.16 g, 4.058 mmol) in EtOAc (35 mL), and the resulting suspension was agitated in a Parr shaker apparatus under an atmosphere of H_2 (35 psi) for 12 h at ambient temperature. The reaction mixture was filtered through a pad of Celite using EtOAc (50 mL) as the eluent, and the resulting soultion was concentrated in vacuo. Flash chromatography of the residue over silica gel using 20% Et_2O−hexanes gave saturated ester **20a** (2.06 g, 95%) as a pure (TLC, silica 40% ether−hexanes; ^{1}H NMR, 500 MHz) white solid: mp = 69 °C; $[\alpha]_D$ = +22.6 (c = 1.7, $CHCl_3$); FT-IR (neat) 3030, 2981, 2926, 1731, 1255 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.27 (m, 15 H, Ph), 4.95 (d, 1 H, J = 10.8 Hz, OC*H*$_2$Ph), 4.88 (d, 1 H, J = 10.9 Hz, OC*H*$_2$Ph), 4.80−4.76 (m, 2 H, OC*H*$_2$-Ph), 4.64 (d, 1 H, J = 12.1 Hz, OC*H*$_2$Ph), 4.61 (d, 1 H, J = 10.9 Hz, OC*H*$_2$Ph), 4.49 (d, 1 H, J = 3.5 Hz, *H*-1), 4.09 (q, 1 H, J = 7.1 Hz, OC*H*$_2$CH$_3$), 3.93 (dd, 1 H, J = 9.3, 9.3 Hz, *H*-3), 3.57 (ddd, 1 H, J = 9.6, 9.6, 2.2 Hz, *H*-5), 3.48 (dd, 1 H, J = 9.6, 3.5 Hz, *H*-2), 3.32 (s, 3 H, OC*H*$_3$), 3.17 (dd, 1 H, J = 9.2, 9.2 Hz, *H*-4), 2.41−2.27 (m, 2 H, *H*-7), 2.19−2.15 (m, 1 H, *H*-6), 1.69−1.63 (m, 1 H, *H*-5), 1.21 (t, 3 H, J = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 138.9, 138.3, 128.6, 128.6,

(55) (a) Hanessian, S.; Martin, M.; Desai, R. C. *J. Chem. Soc., Chem. Commun.* **1986**, 926−927. (b) Schmidt, R. R.; Preuss, R.; Betz, R. *Tetrahedron Lett.* **1987**, *28*, 6591−6594.

128.5, 128.3, 128.2, 128.1, 128.1, 127.9, 127.8, 98.0, 82.2, 82.0, 80.3, 76.0, 75.4, 73.5, 69.6, 60.5, 55.2, 30.8, 27.2, 14.4; HRMS (EI) calcd for $C_{25}H_{31}O_7$ $(M - C_7H_7)^+$ 443.2069, found 443.2067.

General Procedure for Saponification Exemplified with the Preparation of Methyl 2,3,4-Tri-*O*-benzyl-6,7-dideoxy-α-D-*gluco*-octopyranosiduronic Acid (2a). LiOH (1.03 g, 24.5 mmol) was added to a 0 °C solution of saturated ethyl ester **20a** (655 mg, 1.23 mmol) in THF (15 mL). Water (15 mL) was then added to the resulting suspension, and the mixture was vigorously stirred at 0 °C for 1 h, allowed to warm to ambient temperature, and stirred overnight. The mixture was cooled to 0 °C and acidified by the addition of HCl (20 mL, 2 M) until litmus red was obtained. The resulting solution was extracted with EtOAc, dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography of the residue over silica gel using 20% → 60% EtOAc−hexanes gave carboxylic acid **2a** (600 mg, 97%) as a pure (TLC, silica 40% ether−hexanes, ^{1}H NMR, 500 MHz) oil: $[\alpha]_D = +140.2$ ($c = 1.32$, $CHCl_3$); FT-IR (neat) 3220, 3062, 3031, 2927, 1738 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.29 (m, 15 H, Ph), 5.00 (d, 1 H, $J = 11$ Hz, OC*H*$_2$Ph), 4.92 (d, 1 H, $J = 10.5$ Hz, OC*H*$_2$Ph), 4.83 (d, 1 H, $J = 11$ Hz, OC*H*$_2$Ph), 4.81 (d, 1 H, $J = 11.5$ Hz, OC*H*$_2$Ph), 4.68 (d, 1 H, $J = 12.2$ Hz, OC*H*$_2$Ph), 4.64 (d, 1 H, $J = 10.9$ Hz, OC*H*$_2$Ph), 4.54 (d, 1 H, $J = 3.5$ Hz, *H*-1), 3.98 (dd, 1 H, $J = 9.2$, 9.2 Hz, *H*-3), 3.63 (ddd, 1 H, $J = 9.6$, 9.6, 2.6 Hz, *H*-5), 3.52 (dd, 1 H, $J = 9.6$, 3.6 Hz, *H*-2), 3.36 (s, 3 H, OC*H*$_3$), 3.21 (dd, 1 H, $J = 9.1$, 9.1 Hz, *H*-4), 2.52−2.38 (m, 2 H, *H*-7), 2.24−2.18 (m, 1 H, *H*-6), 1.73−1.67 (m, 1 H, *H*-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.2, 138.6, 138.0, 137.9, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 97.7, 81.8, 81.6, 79.9, 75.7, 75.2, 73.3, 69.2, 55.1, 30.1, 26.6; HRMS (EI) calcd for $C_{23}H_{27}O_7$ $(M - C_7H_7)^+$ 415.1756, found 443.1761.

General Procedure for DCC-Mediated Esterification Exemplified by the Preparation of 3,4,6-Tri-*O*-benzyl-1,2-dideoxy-D-*arabino*-hex-1-enyl (Methyl 2,3,4-tri-*O*-benzyl-6,7-dideoxy-α-D-*gluco*-octopyranosid)uronate (3a). 4-DMAP (30 mg, 0.25 mmol) and DCC (236 mg, 1.15 mmol) were added in one portion to a solution of acid **2a** (387 mg, 0.764 mmol) and alcohol **1b** (250 mg, 0.60 mmol) in dry CH_2Cl_2 (3 mL). The resulting solution was then stirred for 18 h at ambient temperature, at which point TLC (2 × silica, 50% ether−hexanes) showed the reaction was complete. The reaction mixture was diluted with ether (30 mL) and filtered by gravity through cotton to remove most of the formed dicyclohexylurea. The resulting organic solution was washed with NH_4Cl (1 × 30 mL), dried, and concentrated in vacuo. Gravity chromatography over silica gel using 10% → 20% ether−hexanes gave ester **3a** (508 mg, 94%) as a pure (TLC, silica 40% ether−hexanes; ^{1}H NMR, 500 MHz) viscous oil: $[\alpha]_D = +22.0$ ($c = 2.5$, CH_2Cl_2); FT-IR (neat) 3082, 3054, 3025, 2913, 1731 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.20 (m, 30 H, Ph), 5.85 (ddd, 1 H, $J = 17.5$, 10.4, 8.1 Hz, *H*-2), 5.29−5.19 (m, 3 H, *H*-1, *H*-5), 4.94 (d, 1 H, $J = 11.9$ Hz, OC*H*$_2$Ph), 4.85 (d, 1 H, $J = 10.9$ Hz, OC*H*$_2$Ph), 4.77 (d, 1 H, $J = 10.9$ Hz, OC*H*$_2$Ph), 4.76 (d, 1 H, $J = 12.1$ Hz, OC*H*$_2$Ph), 4.66 (d, 1 H, $J = 11.2$ Hz, OC*H*$_2$Ph), 4.63 (d, 1 H, $J = 12.3$ Hz, OC*H*$_2$Ph), 4.60 (d, 1 H, $J = 11.4$ Hz, OC*H*$_2$Ph), 4.56 (d, 1 H, $J = 11.6$ Hz, OC*H*$_2$Ph), 4.55 (d, 1 H, $J = 11.7$ Hz, OC*H*$_2$Ph), 4.48 (d, 1 H, $J = 3.6$ Hz, *H*-1′), 4.44 (d, 1 H, $J = 11.9$ Hz, OC*H*$_2$Ph), 4.41 (d, 1 H, $J = 11.9$ Hz, OC*H*$_2$Ph), 4.28 (d, 1 H, $J = 11.6$ Hz, OC*H*$_2$-Ph), 3.92 (dd, 1 H, $J = 9.3$, 9.3 Hz, *H*-3′), 3.87 (dd, 1 H, $J = 7.9$, 5.1 Hz, *H*-3), 3.76−3.73 (m, 3 H, *H*-4, 2 × *H*-6), 3.55 (ddd, 1 H, $J = 9.6$, 9.6, 2.2 Hz, *H*-5′), 3.46 (dd, 1 H, $J = 9.6$, 3.5 Hz, *H*-2′), 3.28 (s, 3 H, OC*H*$_3$), 3.13 (dd, 1 H, $J = 9.2$, 9.2 Hz, *H*-4′), 2.36−2.20 (m, 2 H, *H*-6′), 2.18−2.12 (m, 1 H, *H*-7′), 1.64−1.54 (m, 1 H, *H*-7′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 138.6, 138.2, 138.1, 138.0, 135.1, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 119.3, 97.7, 81.9, 81.9, 80.8, 80.7, 80.0, 75.7, 75.1, 75.0, 73.3, 73.0, 72.5, 70.4, 69.2, 68.1, 55.0, 30.4, 26.7; HRMS (FAB) calcd for $C_{57}H_{62}O_{10}Na$ $(M + Na)^+$ 929.4240, found 929.4226.

General Procedure for the Methylenation Exemplified by the Preparation of Methyl 8-*O*-(3,4,6-Tri-*O*-benzyl-1,2-dideoxy-D-*arabino*-hex-1-enyl)-6,7,9-trideoxy-α-D-*gluco*-nona-8-enopyranoside (4a). A solution of titanium tetrachloride (1.5 mL, 2 M in CH_2Cl_2, 3.07 mmol) was added to cool (0 °C) THF (6 mL). The resulting mixture was stirred for 5 min, at which point TMEDA (0.89 mL, 5.93 mmol) was added in one portion. The resulting yellow-brown suspension was allowed to warm to ambient temperature and stirred for 15 min. At this point, zinc dust (437 mg, 6.69 mmol) and lead(II) chloride (5 mg, 0.18 mmol) were added in portions and stirring at ambient temperature was continued for 15 min. A solution of ester **3a** (164 mg, 0.18 mmol) and dibromomethane (0.12 mL, 1.68 mmol) in THF (2 mL) was then added via cannula to the reaction flask in one portion. The mixture was stirred at 60 °C for 45 min, cooled to 0 °C, and then quenched by the addition of saturated potassium carbonate (1.5 mL). The resulting mixture was stirred for 30 min, while being warmed to ambient temperature, diluted with ether (20 mL), and stirred vigorously for 15 min. The resulting mixture was filtered through neutral alumina using 3% triethylamine−ether as the eluent. The green-blue precipitate that resulted was crushed (mortar and pestle) and thoroughly extracted by vigorous stirring over diethyl ether (15−20 mL) for 30 min. The combined ethereal extracts were concentrated in vacuo, and gravity chromatography of the residue over silica using 18% Et_2O−hexanes−1% triethylamine gave **4a** (116 mg, 71%) as a pure ($R_f = 0.22$, TLC silica, 30% Et_2O−hexanes; ^{1}H NMR, 500 MHz) oil: $[\alpha]_D = +21.1$ ($c = 0.81$, CH_2Cl_2); FT-IR (neat) 3087, 3063, 3030, 2919, 2866, 1652 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.35−7.02 (m, 30 H, Ph), 5.88 (ddd, 1 H, $J = 17.4$, 10.3, 7.0 Hz, *H*-2), 5.20 (d, 1 H, $J = 17.2$ Hz, *H*-1), 5.05 (d, 1 H, $J = 10.4$, 1.3 Hz, *H*-1), 4.98 (d, 1 H, $J = 11.2$ Hz, OC*H*$_2$Ph), 4.88 (d, 1 H, $J = 11.4$ Hz, OC*H*$_2$Ph), 4.76−4.74 (m, 3 H, OC*H*$_2$-Ph), 4.71−4.68 (m, 1 H, *H*-5), 4.59 (d, 1 H, $J = 3.6$ Hz, *H*-1′), 4.56−4.50 (m, 3 H, OC*H*$_2$Ph), 4.45 (d, 1 H, $J = 11.9$ Hz, OC*H*$_2$-Ph), 4.31 (d, 1 H, $J = 11.7$ Hz, OC*H*$_2$Ph), 4.29 (s, 2 H, OC*H*$_2$-Ph), 4.17 (dd, 1 H, $J = 9.1$, 9.1 Hz, *H*-3′), 4.13 (dd, 1 H, $J = 5.3$, 5.3 Hz, *H*-3), 4.10−4.07 (m, 3 H, *H*-4, 2 × *H*-9′), 3.96 (dd, 1 H, $J = 10.4$, 3.3 Hz, *H*-6), 3.83 (dd, 1 H, $J = 9.3$, 1.7 Hz, *H*-5′), 3.79 (dd, 1 H, $J = 10.4$, 4.3 Hz, *H*-6), 3.51 (dd, 1 H, $J = 9.6$, 3.6 Hz, *H*-2′), 3.21 (dd, 1 H, $J = 9.1$, 9.1 Hz, *H*-4′), 3.10 (s, 3 H, OC*H*$_3$), 2.58−2.52 (m, 1 H, *H*-7′), 2.36−2.26 (m, 2 H, *H*-6′, *H*-7′), 1.82−1.74 (m, 1 H, *H*-6′); ^{13}C NMR (125 MHz, C_6D_6) δ 161.8, 140.1, 139.9, 139.6, 139.5, 139.5, 139.4, 136.5, 128.8, 128.8, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 118.9, 98.4, 83.1, 82.9, 82.6, 81.7, 81.7, 81.6, 75.9, 75.8, 75.6, 75.6, 73.7, 73.1, 71.4, 70.2, 68.8, 55.3, 32.2, 30.5; MS (FAB) m/z 927 $(M + Na)^+$, 905 $(M + H)^+$, 873, 799, 647, 591, 541, 474, 398, 329, 271, 181, 154, 107.

General Procedure for the Metathesis Exemplified by the Preparation of Methyl 6-*C*-(2,6-Anhydro-4,5,7-tri-*O*-benzyl-1,3,-dideoxy-D-*arabino*-hept-2-enit-1-yl)-2,3,4-tri-*O*-benzyl-6-deoxy-α-D-*gluco*-pyranoside (5a). In the Box. To a toluene (3.6 mL) solution of **4a** (33 mg, 0.036 mmol) was added catalyst **8** (7 mg, 0.009 mmol, 25 mol %) in one portion, and the resulting mixture was heated to 60 °C for 1 h. The resulting solution was taken out of the box and concentrated in vacuo. Flash chromatography of the residue over silica using 18% Et_2O−hexanes−1% Et_3N gave **5a** (22 mg, 68%) as a pure ($R_f = 0.15$, TLC silica, 30% Et_2O−hexanes; ^{1}H NMR, 500 MHz) white solid: mp = 100−101 °C; $[\alpha]_D = +23.3$ ($c = 0.82$, CH_2Cl_2); FT-IR (neat) 3087, 3062, 3030, 2920, 2864, 1673 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.31−7.22 (m, 10 H, Ph), 7.16−7.02 (m, 20 H, Ph), 4.99 (d, 1 H, $J = 11.1$ Hz, OC*H*$_2$Ph), 4.89 (d, 1 H, $J = 11.3$ Hz, OC*H*$_2$Ph), 4.77−4.74 (m, 3 H, *H*-2, 2 × OC*H*$_2$Ph), 4.59 (d, 1 H, $J = 3.8$ Hz, *H*-1′), 4.58 (d, 1 H, $J = 11.2$ Hz, OC*H*$_2$Ph), 4.55 (d, 1 H, $J = 11.7$ Hz, OC*H*$_2$Ph), 4.51 (d, 1 H, $J = 11.9$ Hz, OC*H*$_2$Ph), 4.46 (d, 1 H, $J = 11.9$ Hz, OC*H*$_2$Ph), 4.45 (d, 1 H, $J = 12.1$ Hz, OC*H*$_2$Ph), 4.39 (d, 1 H, $J = 11.4$ Hz, OC*H*$_2$Ph), 4.36 (d, 1 H, $J = 11.1$ Hz, OC*H*$_2$Ph), 4.32 (d, 1 H, $J = 12.1$ Hz, OC*H*$_2$Ph), 4.21−4.19 (m, 2 H, *H*-3, *H*-3′), 4.17−4.14 (m, 1 H, *H*-5), 4.01 (dd, 1 H, $J = 8.1$, 5.8 Hz, *H*-4), 3.82−3.78 (m, 2 H, *H*-6), 3.75 (dd, 1 H, $J = 10.4$, 3.1 Hz, *H*-5′), 3.50 (dd, 1 H, $J = 9.6$, 3.6 Hz, *H*-2′), 3.21 (dd, 1 H, $J = 9.4$, 9.4 Hz, *H*-4′), 3.13 (s, 3 H, OC*H*$_3$), 2.48−2.43 (m, 1 H, *H*-7′), 2.28−2.23 (m, 2 H, *H*-7′, *H*-6′), 1.75−1.69 (m, 1 H, *H*-6′); ^{13}C NMR (125 MHz, C_6D_6) δ 156.4, 140.1, 139.8, 139.6, 139.6, 139.3, 128.8, 128.8, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2,

128.1, 128.1, 128.0, 127.9, 127.8, 127.6, 127.4, 98.4, 96.0, 82.7, 82.7, 81.6, 77.7, 77.0, 75.8, 75.5, 75.3, 73.8, 73.8, 73.1, 70.6, 70.1, 69.5, 55.3, 30.4, 29.8; HRMS (FAB) calcd for $C_{56}H_{60}O_9Na$ $(M + Na)^+$ 899.4135, found 899.4119.

Methyl 6-*C*-(2,6-Anhydro-4,5,7-tri-*O*-acetyl-1,3-dideoxy-D-*glycero*-D-*gulo*-heptit-1-yl)-2,3,4-tri-*O*-acetyl-6-deoxy-α-D-*gluco*-pyranoside (21). To a solution of **5a** (28 mg, 31 umol) in EtOAc/MeOH (5 mL) was added Pd/C (10 mg), and the resulting suspension was stirred under an atmosphere of H_2 (40 psi) for 6 h. The reaction mixture was filtered through Celite using MeOH (20 mL) as the eluent, and the resulting solution was concentrated. The residue was dissolved in pyridine (2 mL), 4-DMAP (5 mg) and Ac_2O (1 mL) were sequentially added, and the resulting solution was stirred at ambient temperature for 12 h. The solution was diluted with ether (20 mL) and washed with saturated NH_4Cl and brine. The ethereal solution was dried and concentrated. Flash chromatography of the residue over silica using 40% EtOAc−hexanes gave **21** (12 mg, 66%) as a fairly pure ($R_f = 0.20$, TLC silica, 40% EtOAc−hexanes; ^{1}H NMR, 500 MHz) off-white foam: $[\alpha]_D = +27.0$ ($c = 0.75$, $CHCl_3$); FT-IR (neat) 2958, 2938, 1368, 1327, 1226 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 5.83 (dd, 1 H, J = 9.6, 9.1 Hz, *H*-3′), 5.12 (dd, 1 H, J = 9.6, 9.6 Hz, *H*-4), 5.07−4.98 (m, 3 H, *H*-2′, *H*-3, *H*-4′), 4.85 (d, 1 H, $J = 3.5$ Hz, *H*-1′), 4.30 (dd, 1 H, J = 12.1, 5.0 Hz, *H*-6), 4.03 (dd, 1 H, J = 12.2, 2.0 Hz, *H*-6), 3.67−3.63 (m, 1 H, *H*-5′), 3.21 (ddd, 1 H, J = 7.6, 5.6, 2.5 Hz, *H*-5), 2.91 (s, 3 H, OCH_3), 2.86−2.81 (m, 1 H, *H*-1), 1.75 (s, 3 H, CH_3), 1.72 (s, 3 H, CH_3), 1.73−1.66 (m, 1 H, *H*-2), 1.69 (s, 3 H, CH_3), 1.67 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 1.59 (s, 3 H, CH_3), 1.49−1.39 (m, 1 H, *H*-7′), 1.36−1.30 (m, 2 H, *H*-7′,6′), 1.26−1.19 (m, 2 H, *H*-6′,2); ^{13}C NMR (125 MHz, C_6D_6) δ 170.0, 169.7, 169.6, 169.5, 169.3, 96.8, 76.2, 75.4, 72.7, 72.2, 71.5, 70.6, 69.7, 68.5, 62.6, 54.6, 36.7, 30.9, 27.7, 20.4, 20.2, 20.2, 20.2, 20.2, 20.1; HRMS (FAB) calcd for $C_{26}H_{38}O_{15}Na$ $(M + Na)^+$ 613.2108, found 613.2109.

Methyl 6-*C*-(2,6-Anhydro-4,5,7-tri-*O*-benzyl-1-deoxy-D-*glycero*-D-*gulo*-hept-2-ulo-1-yl)-2,3,4-tri-*O*-benzyl-6-deoxy-α-D-*gluco*-pyranoside (22). To a solution of *C*-disaccharide glucal **5a** (20.2 mg, 23.1 μmol) in THF (0.4 mL) and *t*-BuOH (0.4 mL) were sequentially added pyridine (100 μL), H_2O (200 μL), NMNO (65 mg, 0.55 mmol), and OsO_4 (1 crystal). The mixture was heated to reflux for 1 h, cooled to room temperature, and quenched by the addition of aqueous $NaHSO_3$ (1 mL, 20%, w/v). The resulting brown mixture was stirred for 3 h over ether (5 mL) and then extracted with Et_2O. The combined ethereal extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography of the residue over silica gel using 40% → 80% Et_2O−hexanes gave diol **22** (14 mg, 68%) as a pure ($R_f = 0.35$, TLC, silica, 80% Et_2O−hexanes; ^{1}H NMR 500 MHz] oil: $[\alpha]_D = +18.1$ (c = 0.77, $CHCl_3$); FT-IR (neat) 3403, 3063, 3030, 2924, 2854, 1496, 1453 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.35−7.01 (m, 30 H, Ph), 4.95 (d, 1 H, J = 11.2 Hz, OCH_2Ph), 4.91 (m, 2 H, OCH_2Ph, O-*H*), 4.87 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.83 (d, 1 H, J = 11.2 Hz, OCH_2Ph), 4.74−4.71 (m, 2 H, OCH_2Ph), 4.63 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.48 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.46 (d, 1 H, $J = 3.5$ Hz, *H*-1′), 4.45 (d, 1 H, J = 12.2 Hz, OCH_2Ph), 4.41 (d, 1 H, J = 12.2 Hz, OCH_2Ph), 4.37 (d, 1 H, J = 12.1 Hz, OCH_2Ph), 4.35 (d, 1 H, J = 12.2 Hz, OCH_2Ph), 4.26 (ddd, 1 H, J = 10.1, 4.1, 2.0 Hz, *H*-5), 4.10 (dd, 1 H, J = 9.1, 9.1 Hz, *H*-3′), 3.92 (dd, 1 H, J = 9.1, 9.1 Hz, *H*-3), 3.77−3.69 (m, 3 H, *H*-4, 2 × *H*-6), 3.64 (ddd, 1 H, J = 9.6, 9.6, 1.5 Hz, *H*-5′), 3.49 (dd, 1 H, J = 8.6, 8.6 Hz, *H*-2), 3.36 (dd, 1 H, J = 9.6, 3.5 Hz, *H*-2′), 3.12 (dd, 1 H, J = 9.6, 9.6 Hz, *H*-4′), 3.08 (s, 3 H, OCH_3), 2.10−2.00 (m, 2 H, *H*-7′), 1.97−1.90 (m, 1 H, *H*-6′), 1.81 (ddd, 1 H, J = 13.1, 8.1, 5.0 Hz, *H*-6′); ^{13}C NMR (125 MHz, C_6D_6) δ 139.6, 139.5, 139.3, 139.0, 138.9, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.8, 127.8, 127.7, 127.5, 127.4, 98.1, 97.5, 84.7, 82.3, 81.8, 80.7, 78.5, 76.8, 75.4, 75.2, 75.2, 74.7, 73.3, 72.7, 71.9, 71.7, 69.6, 55.1, 35.3, 30.3, 24.3; HRMS (FAB) calcd for $C_{56}H_{62}O_{11}Na$ $(M + Na)^+$ 933.4189, found 933.4165.

Methyl 6-*C*-(2,6-Anhydro-4,5,7-tri-*O*-benzyl-1-deoxy-D-*glycero*-D-*gulo*-heptit-1-yl)-2,3,4-tri-*O*-benzyl-6-deoxy-α-D-*gluco*-pyranoside (23). Borane−tetrahydrofuran complex (66 μL, 66 μmol) was added dropwise to a solution of **5a** (29 mg, 33 μmol) in 2 mL of THF cooled in an ice bath. After being stirred for 4 h at 0 °C, the mixture was treated with NaOH (0.8 mL of a 1 M solution), followed by H_2O_2 (0.1 mL, 30%, w/w). The biphasic mixture was allowed to warm to room temperature and stirred vigorously for 1 h. The resulting solution was extracted with Et_2O, washed with NH_4Cl and brine, and dried. Flash chromatography of the residue over silica gel using 40−80% Et_2O−hexanes gave compound **23** (22 mg, 73%) as a pure (TLC silica, 40% Et_2O−hexanes; ^{1}H NMR, 500 MHz) white solid: mp = 155−156 °C; $[\alpha]_D = +23.7$ (c = 0.9, $CHCl_3$); FT-IR (KBr pellet) 3437, 3088, 3063, 3029, 2986, 2923, 2907 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 7.31−7.02 (m, 30 H, Ph), 5.0 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 4.93 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.85 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.78 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.77 (d, 1 H, J = 11.2 Hz, OCH_2Ph), 4.65 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.62 (d, 1 H, J = 5.1 Hz, *H*-1′), 4.61 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.51 (d, 1 H, J = 12.2 Hz, OCH_2Ph), 4.46−4.49 (m, 2 H, OCH_2Ph), 4.35 (d, 1 H, J = 12.1 Hz, OCH_2Ph), 4.21 (dd, 1 H, J = 9.3, 9.3 Hz, *H*-3′), 3.84−3.80 (m, 1 H, *H*-5′), 3.73 (dd, 1 H, J = 9.3, 9.3 Hz, *H*-4), 3.69 (dd, 1 H, J = 11.2, 4.1 Hz, *H*-6), 3.65 (dd, 1 H, J = 10.6, 2.0 Hz, *H*-6), 3.53 (dd, 1 H, J = 9.7, 3.6 Hz, *H*-2′), 3.41 (dd, 1 H, J = 8.8, 8.8 Hz, *H*-3), 3.34−3.30 (m, 2 H, *H*-5, *H*-2), 3.27 (dd, 1 H, J = 9.8, 9.8 Hz, *H*-4′), 3.19−3.16 (m, 1 H, *H*-1), 3.12 (s, 3 H, OCH_3), 2.36−2.26 (m, 2 H, *H*-7′), 1.78 (bs, 1 H, O*H*), 1.70−1.60 (m, 2 H, *H*-6′); ^{13}C NMR (125 MHz, C_6D_6) δ 139.7, 139.4, 139.3, 139.1, 138.9, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 127.4, 127.3, 97.8, 87.1, 82.6, 82.2, 81.2, 80.0, 79.5, 78.8, 75.4, 75.0, 74.9, 74.6, 74.5, 73.5, 72.6, 70.8, 69.5, 54.6, 28.3, 27.9; HRMS (FAB) calcd for $C_{56}H_{62}O_{10}Na$ $(M + Na)^+$ 917.4241, found 917.4206.

Methyl 6-*C*-(2,6-Anhydro-4,5,7-tri-*O*-acetyl-1-deoxy-D-*glycero*-D-*gulo*-heptit-1-yl)-2,3,4-tri-*O*-acetyl-6-deoxy-α-D-*gluco*-pyranoside (24). Pd on carbon (10%, 100 mg) was added to a solution of **23** (16 mg, 17 μmol) in 4 mL of 3:1 EtOAc−MeOH. The heterogeneous mixture was shaken in a Parr hydrogenation apparatus for 9 h, filtered through Celite, and washed with MeOH (3 × 4 mL). The solution was concentrated, and the residue was dried on the pump. The crude product was treated with excess acetic anhydride and pyridine (1 mL of each), and the mixture was stirred overnight at room temperature. After the reaction was quenched with MeOH (3 mL), the solvents were evaporated and the crude product was purified by flash chromatography over silica gel using 5:3 hexanes−EtOAc to give compound **24** (8 mg, 73%) as a pure (TLC silica, 40% Et_2O−hexanes; ^{1}H NMR, 500 MHz) white solid: mp = 166−168 °C; $[\alpha]_D = +15.3$ (c = 0.56, $CHCl_3$); FT-IR (neat) 2920, 1750, 1224, 1171 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 5.82 (dd, 1 H, J = 9.7, 9.6 Hz, *H*-3′), 5.32 (dd, 1 H, J = 9.6, 9.1 Hz, *H*-3), 5.18 (dd, 1 H, J = 10.2, 9.6 Hz, *H*-4), 5.05 (dd, 1 H, J = 9.6, 9.6 Hz, *H*-4′), 5.04−4.99 (m, 2 H, *H*-2, *H*-2′), 4.83 (d, 1 H, $J = 4.0$ Hz, *H*-1′), 4.17 (dd, 1 H, J = 12.6, 5.0 Hz, *H*-6), 3.99 (dd, 1 H, J = 12.1, 1.5 Hz, *H*-6), 3.66−3.63 (m, 1 H, *H*-5′), 3.19 (ddd, 1 H, J = 7.1, 5.1, 2.1 Hz, *H*-5), 3.08−3.05 (m, 1 H, *H*-1), 2.90 (s, 3 H, OCH_3), 1.82−1.80 (m, 2 H, CH_2), 1.76 (s, 3 H, CH_3), 1.72 (s, 3 H, CH_3), 1.68 (s, 3 H, CH_3), 1.67 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 1.63 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3), 1.48−1.31 (m, 2 H, CH_2); ^{13}C NMR (125 MHz, C_6D_6) δ 169.9, 169.8, 169.6, 169.5, 169.4, 169.1, 169.0, 96.7, 77.9, 76.0, 74.6, 72.6, 72.1, 71.6, 70.5, 68.9, 68.5, 62.0, 54.7, 27.2, 26.9, 20.2, 20.2, 20.2, 20.1, 20.0, 20.0, 20.0; HRMS (FAB) calcd for $C_{28}H_{40}O_{17}Na$ $(M + Na)^+$ 671.2163, found 671.2139.

Methyl 6-*C*-(2,6-Anhydro-4,5,7-tri-*O*-benzyl-1,3-dideoxy-D-*glycero*-L-*manno*-heptit-1-yl)-2,3,4-tri-*O*-acetyl-6-deoxy-α-D-*gluco*-pyranoside (25). Glycal **5a** (11 mg, 12 μmol) was dissolved in a mixture of 2 mL of EtOAc, 2 mL of EtOH, and 40 μL of Et_3N, and the solution stirred under hydrogen (1 atm) for 7 h. The reaction mixture was filtered through Celite and washed with EtOAc and the solvent evaporated in vacuo. Flash chromatography of the residue over silica gel using 30% Et_2O−hexanes gave compound **25** (7 mg, 65%) as a pure (TLC silica, 40% Et_2O−hexanes; ^{1}H NMR, 500 MHz) oil: $[\alpha]_D = +15.2$ (c = 0.32, $CHCl_3$); FT-IR (neat) 3080, 3063, 3030, 3005, 1311,

1207, 1155, 1086 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.32−7.01 (m, 30 H, Ph), 5.02 (d, 1 H, J = 11.6 Hz, OCH_2Ph), 5.01 (d, 1 H, J = 11.7 Hz, OCH_2Ph), 4.94 (d, 1 H, J = 11.1 Hz, OCH_2-Ph), 4.78 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.64 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.61 (d, 1 H, J = 3.5 Hz, *H*-1′), 4.59 (d, 1 H, J = 11.1 Hz, OCH_2Ph), 4.53−4.48 (m, 2 H, OCH_2Ph), 4.47 (d, 1 H, J = 12.2 Hz, OCH_2Ph), 4.45 (d, 1 H, J = 12.2 Hz, OCH_2Ph), 4.40 (d, 1 H, J = 12.1 Hz, OCH_2Ph), 4.39 (d, 1 H, J = 12.7 Hz, OCH_2Ph), 4.22 (dd, 1 H, J = 9.6, 9.1 Hz, *H*-3′), 3.79−3.75 (m, 3 H, *H*-5′, 2 × *H*-6), 3.64 (dd, 1 H, J = 9.6, 9.1 Hz, *H*-4), 3.53 (dd, 1 H, J = 9.7, 3.56 Hz, *H*-2′), 3.50−3.45 (m, 1 H, *H*-1), 3.37 (ddd, 1 H, J = 6.1, 3.6, 2.5 Hz, *H*-5), 3.26 (dd, 1 H, J = 9.7, 9.1 Hz, *H*-4′), 3.11 (s, 3 H, OCH_3), 3.08−3.03 (m, 1 H, *H*-3), 2.17−2.11 (m, 1 H, *H*-7′), 1.84 (ddd, 1 H, J = 6.6, 5.1, 1.5 Hz, *H*-2), 1.75−1.61 (m, 2 H, *H*-7′, *H*-6′), 1.52−1.45 (m, 1 H, *H*-6′), 1.38−1.31 (m, 1 H, *H*-2); ^{13}C NMR (125 MHz, C_6D_6) δ 139.6, 139.6, 139.5, 139.2, 139.1, 139.1, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.5, 127.5, 127.4, 97.9, 82.2, 81.3, 81.2, 79.6, 79.0, 75.6, 75.4, 74.9, 74.9, 73.4, 72.6, 71.0, 70.3, 70.2, 54.6, 37.1, 31.9, 28.3; HRMS (FAB) calcd for $C_{56}H_{62}O_9Na$ $(M + Na)^+$ 901.4292, found 901.4314.

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Supporting Information Available: Experimental procedures for the preparation of **1c**, **2b**−**e**, **3b**−**l**, **4b**−**l**, **5b**−**l**, **19b**−**e**, **20b**−**e**, and acids **2b**−**e** and spectral data listing for as well as copies of ^1H NMR spectra of **1c, 2a**−**e, 3a**−**l, 4a**−**l, 5a**−**l, 21**−**25, 19b**−**e**, and **20b**−**e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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