Linear Total Synthetic Routes to β-D-*C*-(1,6)-Linked Oligoglucoses and Oligogalactoses up to Pentaoses by Iterative Wittig Olefination Assembly†

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Two complementary routes, A and B, have been followed for the stepwise iterative assembly of β-D-(1,6)-glucopyranose and galactopyranose residues through methylene bridges. In route A the building block was constituted by 2,3,4-tri-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl (*O*-TBDPS) β-linked galactosylmethylenephosphorane, while in route B the building block was a β-linked formyl *C*-glycopyranoside with a similar orthogonal protection of hydroxy groups. In route A each cycle consisted of the reaction of the phosphorane building block with a sugar residue bearing a formyl group at the C-5 carbon atom (*coupling*) and transformation of the *O*-TBDPS-protected primary alcohol into the formyl group (*arming*). Accordingly, route A is defined as the aldehyde route. On the other hand, each cycle in route B involved the coupling of the sugar aldehyde building block with a substrate bearing a phosphorus ylide at C-6 and introduction of the phosphonium group in the arming step as a precursor of the ylide functionality. Accordingly, route B is defined as the ylide route. The efficiency of route A proved to be seriously hampered by the 1,2-elimination of BnOH under the basic reaction conditions of the Wittig olefination, giving rise to the formation of substantial amounts of enopyranose. On the other hand, the ylide route B proved to be more efficient since very good yields (70−93%) of the isolated Wittig products were obtained throughout four consecutive cycles. Individual olefins and polyolefins obtained by routes A and B using *gluco* and *galacto* substrates were reduced and debenzylated in one pot by H_2/$Pd(OH)_2$ to give the corresponding β-D-*C*-(1,6)-linked oligosaccharides up to the pentaose stage. The latter compounds were fully characterized by high-field NMR spectroscopy (500 MHz).

Introduction

Oligosaccharides and glycoconjugates deeply influence many fundamental biological processes in living organisms.[1] They mediate a variety of events, including inflammation, immunological response, fertilization, cancer metastasis, and viral and bacterial infection.[2] Hence, there is a great need for usable quantities of natural carbohydrates with a well-defined structure and composition for biological studies aiming at a better understanding of those phenomena at the molecular level. Given the intrinsic difficulty to obtain complex natural oligosaccharides and glycoconjugates in a pure and homogeneous form from natural sources because of the presence of mixtures of glycosylated species (glycoforms), a major opportunity is provided by chemical synthesis.[3] Complementary synthetic efforts must also be directed toward the supply of structurally modified sugar-containing molecules, the so-called glycomimetics,[4] which may serve as tools for studying conformational preferences of their parent natural products as well as probes of recognition specificity, and may provide important insight into the mechanism of glycoside elaboration by carbohydrate-processing enzymes. In turn glycomimetics may become effective inhibitors of those enzymes and therefore evolve into lead compounds of pharmaceutical relevance. The simplest modification that can be made in natural oligosaccharides and glycoconjugates to obtain chemically and enzymatically resistant analogues is the replacement of the oxygen atom of the glycosidic linkage with a methylene group. Many synthetic approaches to these analogues have therefore been devised, most of which have been restricted to *C*-disaccharides.[5] Only in recent years increasing attention has been addressed to

† Dedicated to Professor Albert I. Mayers.

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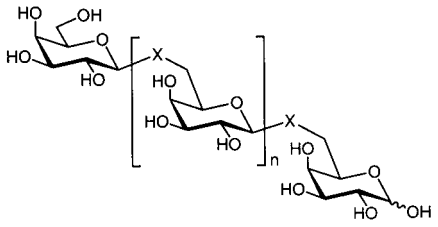

Figure 1. β-D-**(1,6)-Galactans (X = O) and methylene isosteres (X = CH_2).**

the synthetic challenge of preparing higher oligomers. Thus, engaged with their NMR studies on the preference of the *C*-glycosidic bond for the *exo*-anomeric conformation, Kishi and co-workers described the synthesis of various *C*-trisaccharides with 1,2 and 1,4 methylene bridges.[6] Sutherlin and Armstrong prepared a collection of 12 stereochemically and structurally diverse *C*-trisaccharides as potential inhibitors for the cell surface proteins of the bacterium *Helicobacter pylori*,[7] a pathogen associated with gastritis and peptic ulcers and implicated in gastric carcinoma. Skrydstrup and co-workers reported the synthesis of a branched *C*-trisaccharide analogue of the high-mannose core which is present in asparagine-linked oligosaccharides.[8] Also the preparations of mixed *O*,*C*-trisaccharides have been carried out in the laboratories of Sinaÿ (*O*,*C*-analogue of the Lewis^x trisaccharide)[9] and Martin (*O*,*C*-analogue of methyl 4′-*O*-β-D-glucopyranosylgentiobioside).[10] Quite recently, we[11] and Sinaÿ and co-workers[12] developed iterative synthetic protocols based on Wittig olefination and sugar lactone−alkyne coupling, respectively, which afforded β-D-*C*-(1,6)-oligogalactosides up to the tetrasaccharide term. These works provided the first totally synthetic route to tetrasaccharide methylene isosteres of β-D-(1,6)-galactans, which have been shown by Glaudemans to bind to various monoclonal immunoglobulins[13] (Figure 1). Subsequently we have developed an improved synthetic protocol yet based on a Wittig olefination strategy, which allowed us to prepare for the first time a carbon-linked pentasaccharide of this class of carbohydrate mimics.[14] Following these preliminary reports, we describe here in full view the implementation of our iterative strategy.

Results and Discussion

Synthetic Planning. Our intention in the present work was the achievement of an iterative assembly of carbohydrate units through methylene bridges holding the C-1 of one residue and the C-6 of the other. This accomplishment had to be accompanied by full stereochemical control to give exclusively a β-D-linkage to the C-1 carbon atom. Guided by the earlier experience that we acquired in the synthesis of *C*-(1,6)-disaccharides[5a] as well as in the related work regarding the preparation of *C*-glycosyl amino acids[15] via Wittig olefination, it seemed logical to adopt the same synthetic strategy by a suitable adjustment of the tactic. To this aim we envisaged two possible routes (Scheme 1). Route A employs as a building block a sugar derivative, **A**, carrying a methylenephosphonium group at C-1 and a differentially protected hydroxyl group at C-6. The initial base-promoted reaction of **A** with the sugar aldehyde **B** would lead to the olefin **C** (*coupling*). This can be transformed into the aldehyde **D** (*arming*), which in turn will be subjected to the coupling with **A** to start the second cycle of the iterative process. Route B employs as a building block a suitably protected formyl *C*-glycoside, **E**, which in the first cycle is coupled with a glycopyranose 6-phosphorane derived from the phosphonium species **F**. The resulting olefin **C** would be transformed into the phosphonium salt **G**, which in turn will be subjected to the subsequent olefination with **E** to start a second cycle. Quite evidently, since the same identical coupling product **C** is obtained by the two routes, one should be able to switch from one route to the other as may be required. Each cycle can be interrupted at the level of the coupling product whose double bond(s) can be reduced to give the target dimer, trimer, and so on.

Synthesis of the Building Blocks. Quite crucial in both routes was the efficient and fast regeneration of the reactive functional group in the arming step, i.e., the formyl group in route A and the phosphorus ylide in route B. This operation appeared to be finalized by an orthogonal protection of the hydroxy groups in the building block types **A** and **E**. To this aim it was decided to use the benzyl group and the *tert*-butyldiphenylsilyl group to differentiate the secondary from the primary hydroxy groups. The synthesis of these building blocks involved common intermediates as shown in Scheme 2 starting from a sugar lactone. In particular the galactonolactone **1** was allowed to react with 2-lithiobenzothiazole[16] (**2**) to give the corresponding ketose **3**, which following activation to the *O*-acetate **4** was deoxygenated to the benzothiazolyl *C*-glycoside **5**. The selective removal of the *O*-benzyl group from the primary alcohol via acetolysis and transesterification, followed by silylation with *tert*-butyldiphenylsilyl chloride, afforded the differentially hydroxy-protected glycoside **6**. The application of the

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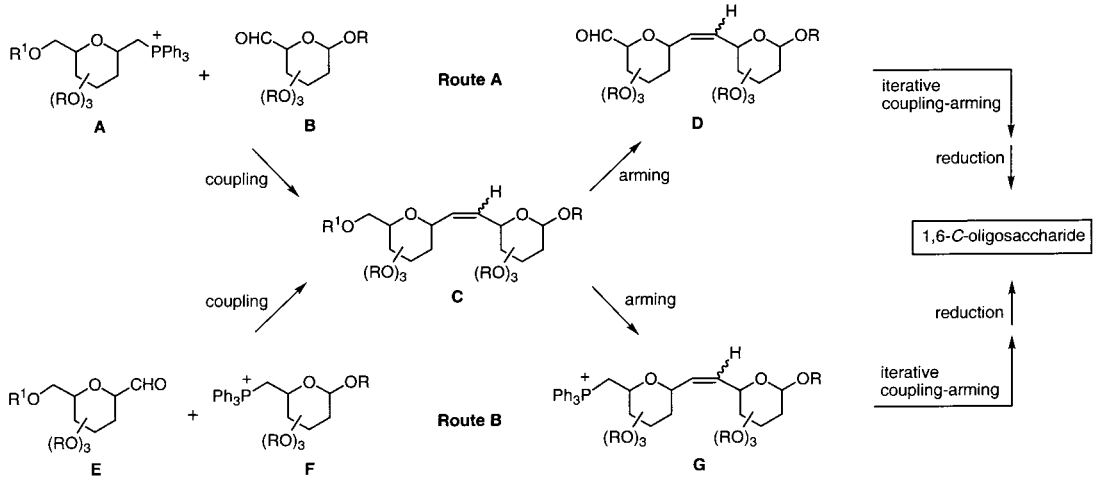
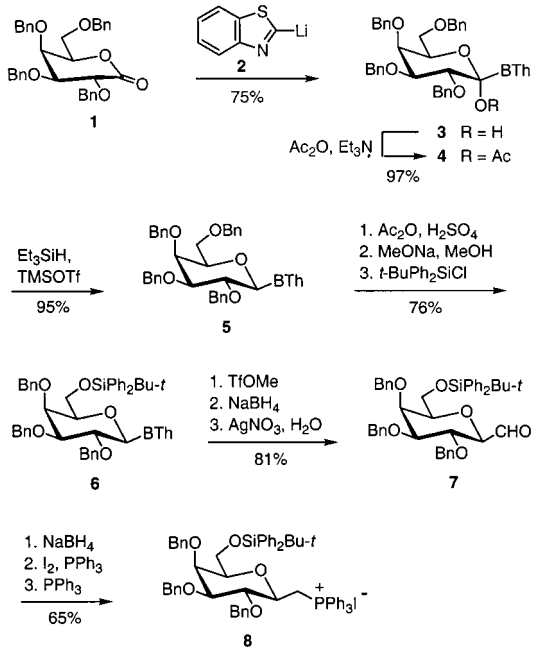
Scheme 1



Scheme 2[a]



[a] BTh = 2-benzothiazolyl.

formyl unmasking protocol to **6** under the conditions required by the benzothiazole ring[16] produced the formyl *C*-galactoside **7**, the first target building block. The conversion of the latter into the galactosylmethylene-phosphonium iodide **8**, the second building block, was carried out by elaboration of the formyl group via reduction to alcohol ($NaBH_4$), iodination (I_2, PPh_3), and phosphanation (PPh_3).

Aldehyde Route A. We first considered route A more attractive than route B because of the straightforward transformation of the primary hydroxy group into the formyl group in the arming step (**C** to **D** in Scheme 1). Hence, the ylide generated from the phosphonium iodide **8** by treatment with BuLi at −50 °C in THF−HMPA (3:1) was allowed to react with an excess of the readily available galactose-derived aldehyde **9** according to our earlier protocol[5a] to give the olefin **10** (mixture of *E*,*Z* isomers) in very good yield (70%) (Scheme 3). Then, the silyl protective group was removed and the primary alcohol was oxidized to the aldehyde **11** in excellent overall yield (70%). Treatment of this aldehyde with the ylide of **8** generated as described above revealed the existence of a serious problem in this approach since the desired trisglycosylated bisolefin **12** was isolated in only 36% yield while a side product, **12a** (Chart 1), featuring an endocyclic double bond in one pyranose ring was formed in almost comparable amount. This problem became even more dramatic in the subsequent cycle because the side product **14a** was isolated in much higher yield (28%) than the desired product **14** (11%). It seems logical to suggest that **12a** and **14a** are formed by the coupling of the ylide derived from **8** with the enals arising from **11** and **13** by elimination of a molecule of benzyl alcohol. This elimination is due to the basic medium required for the generation of the ylide and by the ylide itself, causing abstraction of the proton at the α-position adjacent to the formyl group. Evidently, this reaction becomes more substantial when the rate of the aldehyde coupling with the phosphorus ylide diminishes as a consequence of the increase of the complexity of the system. It should be noted that the elimination reaction should be especially favored in the case of C-5 formyl galactopyranose derivatives due to the 1,2-transdiaxial arrangement of the hydrogen atom and the C-4 benzyloxy group. It is worth noting that we observed a competing E2 reaction also in the Wittig coupling of a sugar phosphorane with a formyl *β*-D-*C*-mannopyranoside, an aldehyde featuring the same stereochemical arrangement of the α-hydrogen atom and the adjacent benzyloxy group.[5a] The elimination of benzyl alcohol from sugar-based aldehydes under the conditions of Wittig reactions has been reported in other instances.[17] Nevertheless, despite the low efficiency of the strategy, the olefins **10**,

(16) Extensive work in our laboratory has been dealing with the use of thiazole as formyl protective group (Dondoni, A. *Synthesis* **1998**, 1681−1706). However, the replacement of thiazole with benzothiazole in the synthesis of formyl *C*-glycosides gives rise to considerable economical advantages and produces, in many cases, crystalline compounds which can be more easily purified and handled. The crucial step with the use of benzothiazole remains its cleavage to the formyl group. In particular the hydrolysis of the benzothiazoline in the final step of the unmasking process requires the assistance of silver ion to obtain a good yield of aldehyde.

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Scheme 3

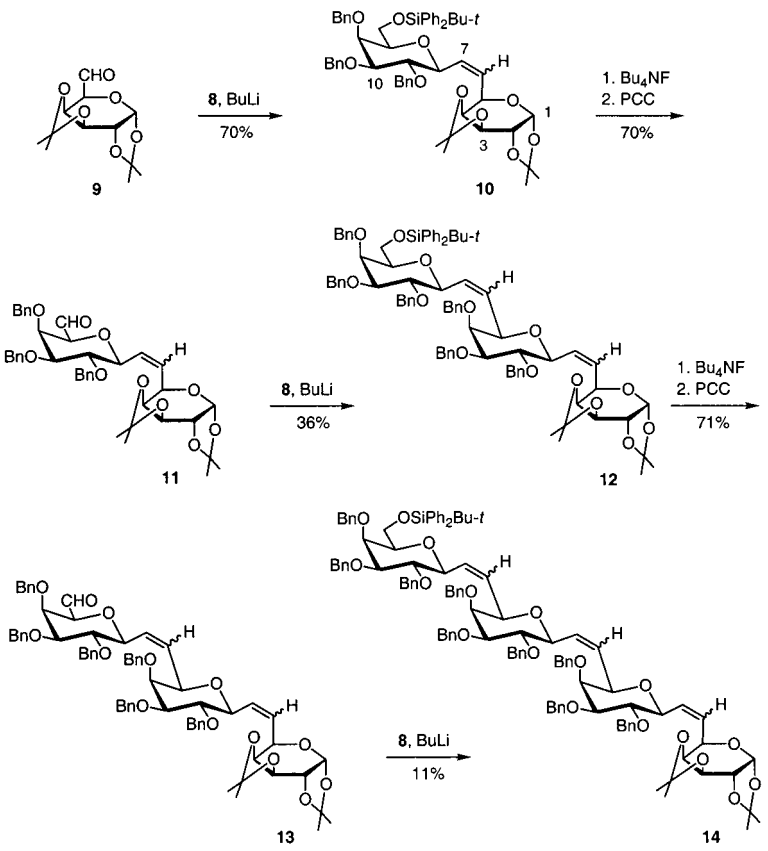


Chart 1

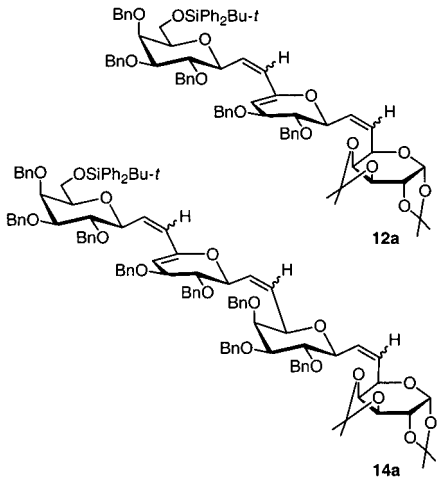
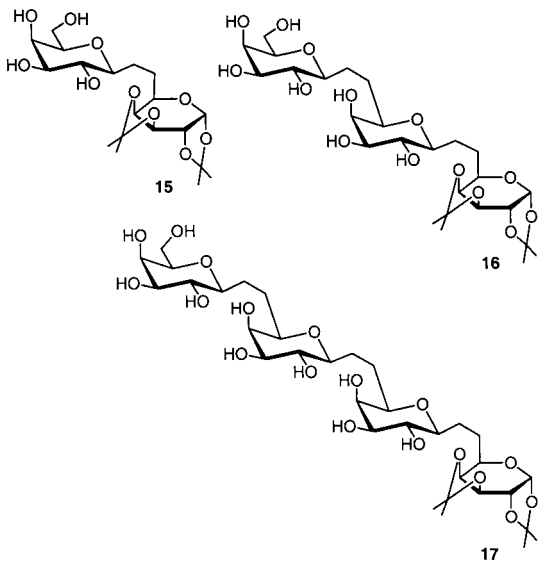


Chart 2

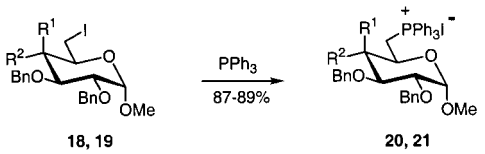


12, and **14** were transformed into the corresponding β-D-*C*-(1,6)-linked oligogalactoses **15**, **16**, and **17** via treatment with $H_2/Pd(OH)_2$ (Chart 2). All compounds were characterized through their *O*-acetyl derivatives.

Ylide Route B. We next turned to this route with some confidence because some earlier experiments showed the lack of substantial benzylic elimination.[11] While the aldehyde building block **7** was available via the reaction sequence shown in Scheme 2, the substrate phosphonium salt **20**, which was required in the first cycle of this route, was prepared by coupling the iodogalactose **18** with neat triphenylphosphine at 120 °C (Scheme 4). These solvent-free conditions gave the target product in much higher yield and shorter reaction time than those employing a solution of triphenylphosphine in tetramethylenesulfolane (120 °C, 3 days) as we reported earlier[5a] for the preparation of the corresponding *gluco* derivative **21**. Hence, also this compound whose use will be described later on in this work was prepared in a similar way as shown in Scheme 4.

Not surprisingly the coupling of the excess aldehyde **7** with the ylide generated from the phosphonium salt **20** under the usual conditions (BuLi in THF−HMPA at −20 °C) afforded the corresponding bisglycosylated olefin **22** in very good yield (81%) (Scheme 5). The preservation of the original configuration at C-5 and C-8 in **22** was confirmed by the $J_{8,9}$ value of 9.3 Hz, in agreement with a β-D-linkage at the anomeric center of one sugar residue

Scheme 4[a]



[a] Key: **18**, **20**, R^1 = OBn, R^2 = H (*galacto* series); **19**, **21**, R^1 = H, R^2 = OBn (*gluco* series).

and the $J_{4,5}$ value of 0.8 Hz consistent with the D-*galacto* configuration in the other moiety. Moreover, the subsequent arming step requiring the installation of the phosphonium group via desilylation (Bu_4NF), iodination (I_2, PPh_3), and phosphanation (PPh_3) turned out to be a quite effective operation, affording the sugar phosphonium iodide **23** in excellent yield (88%). Quite rewardingly, and with elimination of our anxiety, the corresponding ylide coupled with the aldehyde **7** to give the bisolefin **24** in similarly high yield (87%) without any substantial side product formation. A similar satisfactory scenario appeared in two subsequent cycles, both being characterized by a high-yield arming sequence and Wittig olefination, the latter step leading to the sugar polyolefins **26** and **28** in excellent yields (93 and 92%). After having removed the silyl protective group from compounds **22**, **24**, **26**, and **28**, we could reductively debenzylate and saturate the double bond(s) by catalytic hydrogenation to give the β-*C*-(1,6)-linked oligogalactoses **29**−**32** (Chart 3). The complete assignment of the proton signals of the *O*-acetyl derivative of the galactopentaose **32** by NMR analysis at 500 MHz confirmed the β-D-linkage at the anomeric center of the carbohydrate units B−E, since a $J_{1,2}$ value of 9.3 Hz was observed in each case. Moreover, ROESY experiments indicated a *cis*-relationship between the H-5 and H-3 protons of all monosaccharide residues, proving that the original D-*galacto* configuration was retained in each chain elongation step. Evidently, having established the structure of **32**, it can be safely assumed that the sugar moieties in the lower oligomers **29**−**31** have an identical configuration. These results demonstrate that the Wittig reactions in all four consecutive cycles did not affect the configuration of the anomeric carbon atom of the building block **7** nor that of the stereocenters in the various phosphorus ylide intermediates. In closing this section, a comparison of routes A and B appears worthwhile. Route A is plagued by substantial side product formation in the coupling step, which makes the approach unpractical after a few iterative cycles. On the other hand, route B is characterized by high yields in both the coupling and arming steps throughout four consecutive cycles. This indicates that we did not reach the limit of application of the method, and therefore, oligomers higher that **32** can be in principle prepared by this route.

To further prove the scope of route B, attention could now be focused on the synthesis of β-*C*-(1,6)-linked oligoglucoses, i.e., the isosteres of the β-(1,6)-glucooligosaccharides known as gentiooligosaccharides which are found in lichen.[18] The required phosphonium iodide **21** was prepared as shown in Scheme 4 starting from the iodoglucose **19**, while the formyl *C*-glucoside building block **36** having orthogonal protective groups was obtained in a way similar to that of the *C*-galactoside derivative **7** (see Scheme 2) via the benzothiazole-based formylation technique of the gluconolactone **33** through the benzothiazolyl *C*-glucoside intermediates **34** and **35** (Scheme 6).

The construction of the sugar−olefin chain was carried out using the same coupling−arming sequence described above in the *galacto* series. Scheme 7 shows details of this stepwise oligomerization in which very good yields of products were obtained both in the Wittig olefination step (70−84%) and in the installation of the phosphonium group (56−73%) over four consecutive cycles. Also in this case it was carefully ascertained by NMR analysis of the first adduct **37** that the β-D-linkage was preserved in one sugar moiety ($J_{8,9}$ = 9.0 Hz) as well as the D-*gluco* configuration in the other sugar residue ($J_{4,5}$ = 10.0 Hz). The sugar olefin **37** and the polyolefins **39**, **41**, and **43** were transformed via desilylation and hydrogenation into the corresponding *C*-(1,6)-linked glucose di-, tri-, tetra-, and pentasaccharides **44**−**47** (Chart 4). All of these compounds were isolated and characterized as their *O*-acetyl derivatives. In particular the acetate of the glucopentaose **47**, which was analyzed by 500 MHz NMR spectroscopy, showed large coupling constant values between the H-1 and H-2 (9.5−9.9 Hz) as well as the H-4 and H-5 protons (9.6−10.1 Hz) of the B−E moieties. These values indicated a transdiaxial arrangement of the above-mentioned protons and therefore a β-D-*gluco* configuration for the B−E sugar units.

In conclusion, a novel and reasonably efficient method for the synthesis of artificial carbon-linked (1,6)-oligosaccharides has been developed and its scope demonstrated by the synthesis of di-, tri-, tetra-, and pentagalacto and -gluco oligomers. The high yields registered over four consecutive cycles indicated the possibility of access to higher oligomers. Moreover, the method should be extensible to other sugars and readily adaptable to techniques using solid supports or polymer-supported reagents.

Experimental Section

All moisture-sensitive reactions were performed under a nitrogen atmosphere using oven-dried glassware. Solvents were dried over standard drying agent[19] and freshly distilled prior to use. Commercially available powdered 4 Å molecular sieves (5 μm average particle size) were used without further activation. Reactions were monitored by TLC on silica gel 60 F_{254} with detection by charring with sulfuric acid. Flash column chromatography[20] was performed on silica gel 60 (230−400 mesh). Melting points were determined with a capillary apparatus. Optical rotations were measured out at 20 ± 2 °C in the stated solvent; $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. ^{1}H (300 and 500 MHz), ^{13}C (75 MHz), and ^{31}P (121 MHz) NMR spectra were recorded for $CDCl_3$ solutions at room temperature unless otherwise specified. Assignments were aided by homo- and heteronuclear two-dimensional experiments. MALDI-TOF mass spectra were acquired using α-cyano-4-hydroxycinnamic acid as the matrix. Sugar lactones **1**[21] and **33**[22] were prepared by oxidation of the corresponding hemiacetal with pyridinium chlorochromate.[23] Aldehyde **9**[24] and iodides **18**[25] and **19**[26] were synthesized as described.

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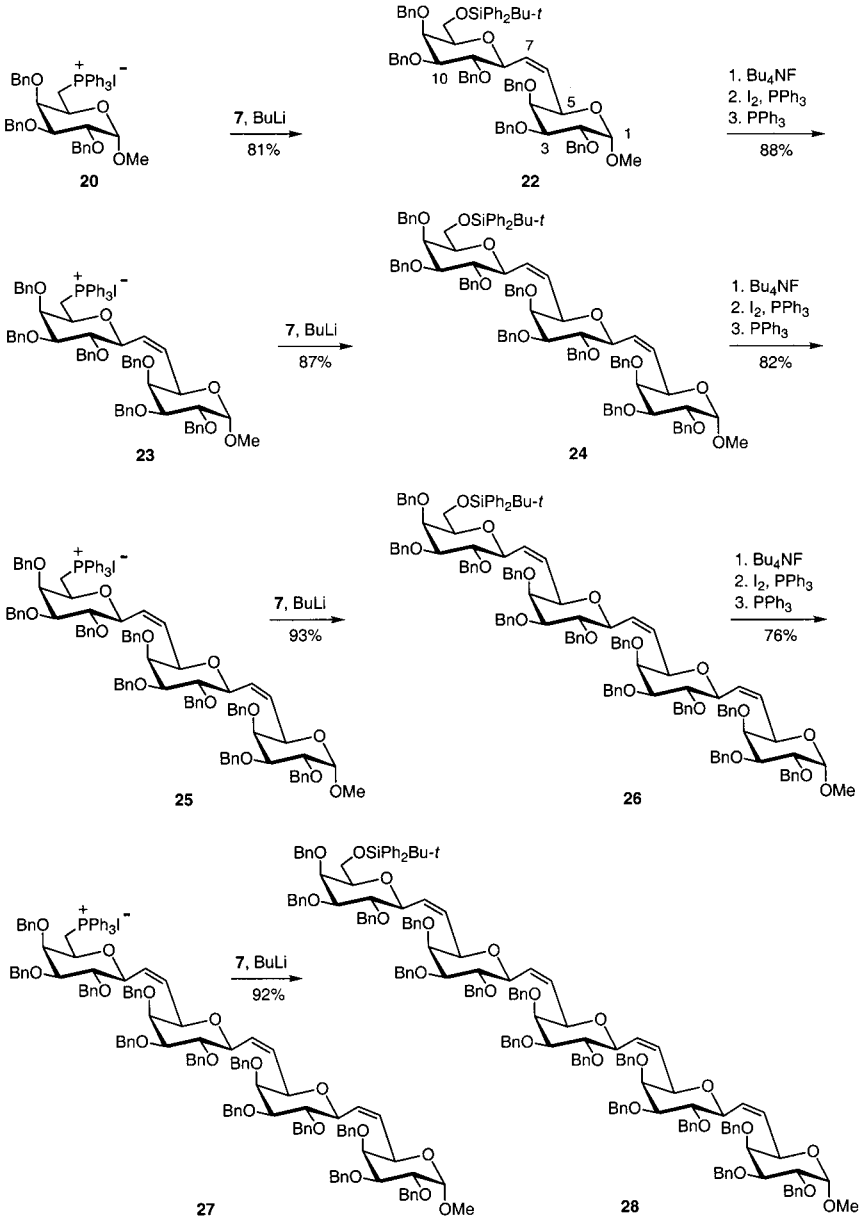
Scheme 5



2,3,4,6-Tetra-*O*-benzyl-1-*C*-(2-benzothiazolyl)-α-D-galactopyranose (3). To a cooled (−65 °C), stirred solution of *n*-BuLi (4.2 mL, 6.72 mmol, of a 1.6 M solution in hexane) in anhydrous Et_2O (15 mL) was added dropwise a solution of freshly distilled 2-benzothiazole (0.91 g, 6.72 mmol) in anhydrous Et_2O (8 mL) over a 30 min period. The yellow solution was stirred at −65 °C for 30 min, and then a solution of galactonolactone **1** (2.62 g, 4.86 mmol) in anhydrous Et_2O (20 mL) was added slowly (20 min). After an additional 1 h at −65 °C the mixture was allowed to warm to −50 °C in 30 min and then poured into 100 mL of a 1 M phosphate buffer at pH 7. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 15:1 to 9:1) to give **3** (2.45 g, 75%) as a syrup. $[\alpha]_D$ = −15.8 (*c* 1.6, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.13−8.05 and 7.91−7.85 (2 m, 2 H, BTh), 7.60−6.97 (m, 22 H, 4 Ph, BTh), 5.06 and 4.72 (2 d, 2 H, J = 11.3 Hz, PhCH_2), 4.82 and 4.78 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.78 and 4.42 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.52 (d, 1 H, $J_{2,3}$ = 9.7 Hz, H-2), 4.51 and 4.46 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.37 (ddd, 1 H, $J_{4,5}$ = 1.0, $J_{5,6a}$ = 8.0, $J_{5,6b}$ = 5.5 Hz, H-5), 4.15 (dd, 1 H, $J_{3,4}$ = 2.8 Hz, H-4), 4.10 (dd, 1 H, H-3), 3.73 (dd, 1 H, H-6a), 3.63 (dd, 1 H, H-6b). Anal. Calcd for $C_{41}H_{39}NO_6S$ (673.83): C, 73.08; H, 5.83; N, 2.08. Found: C, 73.26; H, 5.91; N, 2.00.

1-*O*-Acetyl-2,3,4,6-tetra-*O*-benzyl-1-*C*-(2-benzothiazolyl)-α-D-galactopyranose (4). To a solution of **3** (4.72 g, 7.00 mmol) in anhydrous CH_2Cl_2 (50 mL) were added at rt distilled triethylamine (10 mL) and acetic anhydride (10 mL). The solution was kept at rt for 24 h and then concentrated to give syrupy **4** (5.01 g, ca. 100%) at least 95% pure by ^{1}H NMR analysis. An analytical sample was obtained by column chromatography on silica gel (4:1 cyclohexane−AcOEt). $[\alpha]_D$ = +20.4 (*c* 1.4, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.11−8.03 and 7.88−7.80 (2 m, 2 H, BTh), 7.51−6.91 (m, 22 H, 4 Ph, BTh), 5.05 and 4.68 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.85 and 4.80 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.59 and 4.40 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.56 and 4.48 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.19−4.14 (m, 3 H, H-2, H-3, H-4), 4.04 (ddd, 1 H, $J_{4,5}$ = 0.8, $J_{5,6a}$ = 8.0, $J_{5,6b}$ = 5.3 Hz, H-5), 3.85 (dd, 1 H, $J_{6a,6b}$ = 9.0 Hz,

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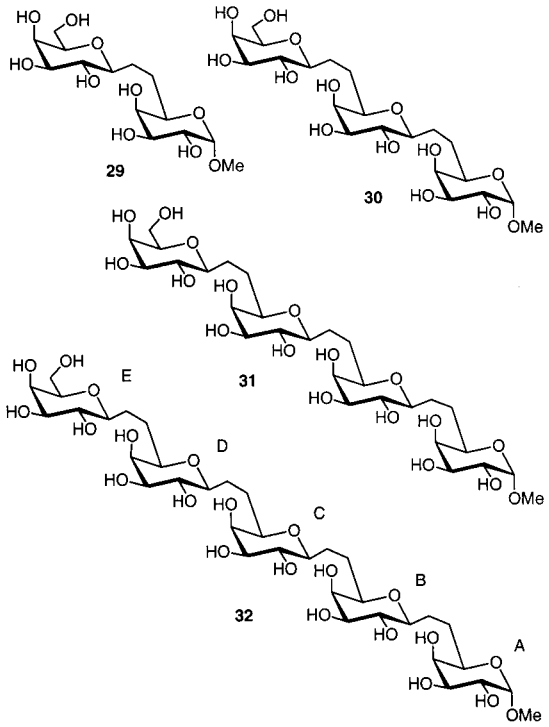
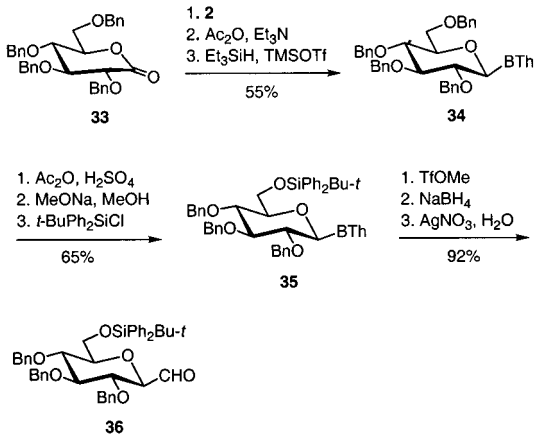
Chart 3



Scheme 6[a]



[a] BTh = 2-benzothiazolyl.

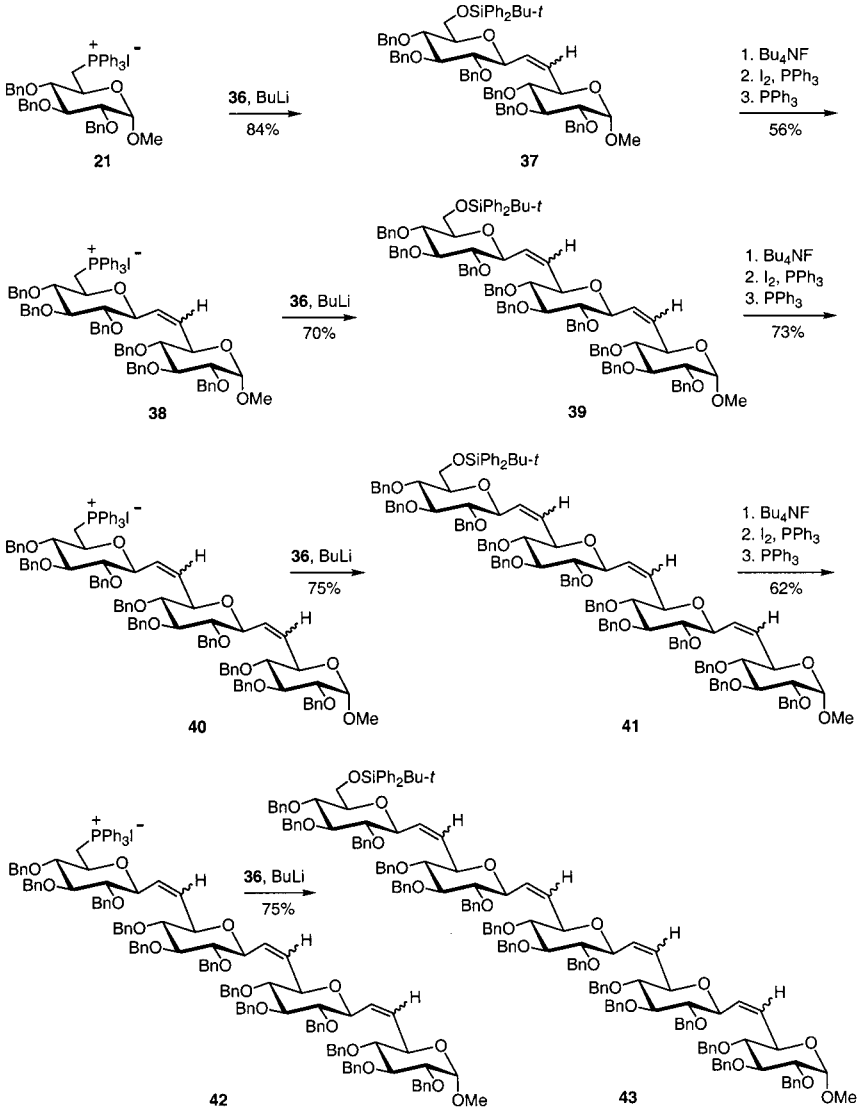
H-6a), 3.70 (dd, 1 H, H-6b), 2.22 (s, 3 H, Ac). Anal. Calcd for $C_{43}H_{41}NO_7S$ (715.87): C, 72.15; H, 5.77; N, 1.96. Found: C, 72.33; H, 5.86; N, 1.91.

2-(2,3,4,6-tetra-*O*-benzyl-*β*-D-galactopyranosyl)benzothiazole (5). To a stirred mixture of **4** (4.29 g, 6.00 mmol), activated 4 Å powdered molecular sieves (6.0 g), and triethylsilane (9.6 mL, 60.0 mmol) in anhydrous CH_2Cl_2 (50 mL) was added TMSOTf (1.63 mL, 9.00 mmol). The mixture was stirred at rt for 1.5 h and then diluted with triethylamine (2 mL), filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with 5:1 cyclohexane−AcOEt to give **5** (3.74 g, 95%) as a syrup. $[\alpha]_D = -20.5$ (*c* 1.5, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.11−8.04 and 7.92−7.86 (2 m, 2 H, BTh), 7.56−7.00 (m, 22 H, 4 Ph, BTh), 5.05 and 4.70 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.81 (s, 2 H, PhCH_2), 4.76 (d, 1 H, $J_{1,2}$ = 9.5 Hz, H-1), 4.70 and 4.40 (2 d, 2 H, J = 10.8 Hz, PhCH_2), 4.52 and 4.45 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.26 (dd, 1 H, $J_{2,3}$ = 9.5 Hz, H-2), 4.09 (dd, 1 H, $J_{3,4}$ = 2.8, $J_{4,5}$ = 0.6 Hz, H-4), 3.82 (dt, 1 H, $J_{5,6}$ = 6.4 Hz, H-5), 3.80 (dd, 1 H, H-3), 3.68 (d, 2 H, 2 H-6). Anal. Calcd for $C_{41}H_{39}NO_5S$ (657.83): C, 74.86; H, 5.98; N, 2.13. Found: C, 74.78; H, 6.09; N, 2.08.

2-(2,3,4-tri-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-*β*-D-galactopyranosyl)benzothiazole (6). To a solution of **5** (5.26 g, 8.00 mmol) in acetic anhydride (60 mL) was added a solution of 96% H_2SO_4 (0.8 mL) in acetic acid (28 mL). The reaction mixture was kept at rt for 1.5 h, then diluted with AcOEt (300 mL), washed with H_2O (3 × 100 mL) and saturated aqueous Na_2CO_3 (2 × 100 mL), dried (Na_2SO_4), and concentrated. The crude 6-*O*-acetylated derivative was treated with a freshly prepared ~0.1 M solution of CH_3ONa in CH_3OH (50 mL) at rt for 3 h, then neutralized with acetic acid, and concentrated. The residue was eluted from a column of silica gel with 3:1 cyclohexane−AcOEt to give 2-(2,3,4-tri-*O*-benzyl-*β*-D-galactopyranosyl)benzothiazole (3.59 g) as a syrup. $[\alpha]_D = -31.6$ (*c* 1.5, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.12−8.06 and 7.94−7.87 (2 m, 2 H, BTh), 7.58−7.00 (m, 22 H, 4 Ph, BTh), 5.07 and 4.75 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.85 (s, 2 H, PhCH_2), 4.76 (d, 1 H, $J_{1,2}$ = 9.5 Hz, H-1), 4.72 and 4.41 (2 d, 2 H, J = 10.7 Hz, PhCH_2), 4.30 (dd, 1 H, $J_{2,3}$ = 9.5 Hz, H-2), 3.98 (dd, 1 H, $J_{3,4}$ = 2.8, $J_{4,5}$ = 0.6 Hz, H-4), 3.89 (ddd, 1 H, $J_{5,6a}$ = 6.6, $J_{6a,6b}$ = 11.0, $J_{6a,OH}$ = 3.4 Hz, H-6a), 3.81 (dd, 1 H, H-3), 3.67 (ddd, 1 H, $J_{5,6b}$ = 4.9 Hz, H-5), 3.58 (ddd, 1 H, $J_{6b,OH}$ = 8.4 Hz, H-6b), 1.80 (dd, 1 H, OH). Anal. Calcd for $C_{34}H_{33}NO_5S$ (567.71): C, 71.93; H, 5.86; N, 2.47. Found: C, 71.72; H, 5.92; N, 2.38. To a stirred solution of this alcohol in pyridine (60 mL) was added *tert*-butylchlorodiphenylsilane (2.46 mL, 9.48 mmol). Stirring was continued for an additional 16 h, and then the reaction mixture was diluted with CH_3OH (2 mL) and concentrated. The residue was eluted from a column of silica gel with 10:1 cyclohexane−AcOEt (containing 0.3% triethylamine) to give **6** (4.90 g, 76% from **5**) as a syrup. $[\alpha]_D = -15.6$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.12−8.04 and 7.90−7.82 (2 m, 2 H, BTh), 7.68−7.00 (m, 27 H, 5 Ph, BTh), 5.10 and 4.73 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.88 and 4.82 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.70 (d, 1 H, $J_{1,2}$ = 9.5 Hz, H-1), 4.68 and 4.38 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.22 (dd, 1 H, $J_{2,3}$ = 9.5 Hz, H-2), 4.14 (dd, 1 H, $J_{3,4}$ = 2.8, $J_{4,5}$ = 0.7 Hz, H-4), 3.92 (dd, 1 H, $J_{5,6a}$ = 8.0, $J_{6a,6b}$ = 10.0 Hz, H-6a), 3.83 (dd, 1 H, $J_{5,6b}$ = 5.5 Hz, H-6b), 3.78 (dd, 1 H, H-3), 3.65 (ddd, 1 H, H-5), 1.07 (s, 9 H, *t*-Bu). Anal. Calcd for $C_{50}H_{51}NO_5SSi$ (806.11): C, 74.50; H, 6.38; N, 1.74. Found: C, 74.72; H, 6.44; N, 1.68.

2,6-Anhydro-3,4,5-tri-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-*aldehydo*-D-*glycero*-L-*manno*-heptose (7). A mixture of **6** (1.46 g, 1.81 mmol), activated 4 Å powdered molecular sieves (2.71 g), and anhydrous CH_3CN (18 mL) was stirred at rt for 10 min, and then methyl triflate (307 μL, 2.71 mmol) was added. The suspension was stirred at rt for 20 min and then concentrated to dryness without filtering off the molecular sieves. To a cooled (0 °C), stirred suspension of the crude *N*-methylbenzothiazolium salt in CH_3OH (18 mL) was added $NaBH_4$ (103 mg, 2.71 mmol). The mixture was stirred at rt for an additional 10 min, diluted with acetone, filtered through a pad of Celite, and concentrated. To a vigorously stirred solution of the diastereomeric benzothiazolines in CH_2Cl_2 (3 mL) and CH_3CN (15 mL) were added H_2O (1.8 mL) and then $AgNO_3$ (0.92 g, 5.43 mmol). The mixture was stirred at rt for 15 min, and then diluted with 1 M phosphate buffer at pH 7 (1.8 mL). Stirring was continued for an additional 15 min, and then the reaction mixture was diluted with 1 M phosphate buffer at pH 7 (50 mL) and partially concentrated to remove CH_3CN (bath temperature not exceeding 40 °C). The suspension was extracted with Et_2O (2 × 100 mL), and the combined organic phases were dried (Na_2SO_4), filtered through a pad of Celite, and concentrated. The residue was eluted from a short column (3 × 10 cm, diameter × height) of silica gel with 5:1 cyclohexane−AcOEt to afford syrupy **7** (1.03 g, 81%) ca. 95% pure by ^{1}H NMR analysis. ^{1}H NMR (300 MHz): δ 9.59 (d, 1 H, $J_{1,2}$ = 1.2 Hz, H-1), 7.66−7.60 and 7.50−7.25 (2 m, 25 H, 5 Ph), 5.00 and 4.67 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.90 and 4.69 (2 d, 2 H, J = 10.6 Hz, PhCH_2), 4.81 (s, 2 H, PhCH_2), 4.07 (dd, 1 H, $J_{4,5}$ = 2.6, $J_{5,6}$ = 0.7 Hz, H-5), 4.06 (dd, 1 H, $J_{2,3}$ = 10.0, $J_{3,4}$ = 9.0 Hz, H-3), 3.88 (dd, 1 H, $J_{6,7a}$ = 8.2, $J_{7a,7b}$ = 10.3 Hz, H-7a), 3.83 (dd, 1 H, $J_{6,7b}$ = 5.7 Hz, H-7b), 3.71 (dd, 1 H, H-2), 3.68 (dd, 1 H, H-4), 3.48 (ddd, 1 H, H-6), 1.08 (s, 9 H, *t*-Bu).

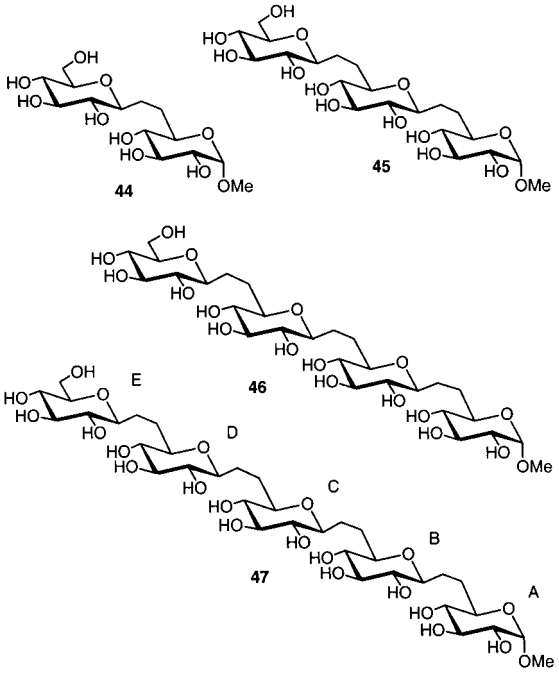
Scheme 7



(2,6-Anhydro-3,4,5-tri-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-1-deoxy-D-*glycero*-L-*manno*-heptitol-1-yl)triphenylphosphonium Iodide (8). To a cooled (0 °C), stirred solution of aldehyde **7** (3.14 g, 4.48 mmol) in Et_2O (22 mL) and CH_3OH (22 mL) was added $NaBH_4$ (170 mg, 4.48 mmol). The mixture was stirred at rt for an additional 10 min, then diluted with acetone (1 mL), and concentrated. The residue was suspended in Et_2O (200 mL), washed with H_2O (2 × 50 mL), dried (Na_2SO_4), and concentrated to afford 2,6-anhydro-3,4,5-tri-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-D-*glycero*-L-*manno*-heptitol (3.12 g). ^{1}H NMR (300 MHz): δ 7.75−7.72, 7.68−7.63, and 7.46−7.25 (3 m, 25 H, 5 Ph), 4.99 and 4.64 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 4.93 and 4.66 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.79 (s, 2 H, PhCH_2), 4.03 (dd, 1 H, $J_{4,5}$ = 2.7, $J_{5,6}$ = 0.5 Hz, H-5), 3.92 (dd, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, H-3), 3.81−3.73 and 3.68−3.61 (2 m, 2 H, 2 H-1), 3.76 (d, 2 H, $J_{6,7}$ = 6.8 Hz, 2 H-7), 3.62 (dd, 1 H, H-4), 3.46 (dt, 1 H, H-6), 3.30 (ddd, 1 H, $J_{1a,2}$ = 2.2, $J_{1b,2}$ = 5.4 Hz, H-2), 1.06 (s, 9 H, *t*-Bu). To a vigorously stirred solution of the crude alcohol, triphenylphosphine (1.76 g, 6.72 mmol), and imidazole (0.91 g, 13.44 mmol) in anhydrous toluene (45 mL) was added iodine (1.71 g, 6.72 mmol). The mixture was stirred at 80 °C for 2 h, then cooled to rt, filtered through a pad of Celite, and concentrated. A solution of the residue in Et_2O (200 mL) was washed with 5% aqueous $Na_2S_2O_3$ (2 × 50 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 4:1 cyclohexane−AcOEt to give 2,6-anhydro-3,4,5-tri-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-1-deoxy-1-iodo-D-*glycero*-L-*manno*-heptitol (3.18 g). ^{1}H NMR (300 MHz): δ 7.75−7.60 and 7.44−7.17 (2 m, 25 H, 5 Ph), 5.01 and 4.65 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.98 and 4.72 (2 d, 2 H, J = 10.8 Hz, PhCH_2), 4.78 and 4.73 (2 d, 2 H, J = 11.9 Hz, PhCH_2), 4.02 (dd, 1 H, $J_{4,5}$ = 2.6, $J_{5,6}$ = 0.5 Hz, H-5), 3.81 (dd, 1 H, $J_{2,3}$ = 8.9, $J_{3,4}$ = 9.3 Hz, H-3), 3.79 (d, 2 H, $J_{6,7}$ = 6.8 Hz, 2 H-7), 3.62 (dd, 1 H, H-4), 3.46 (dt, 1 H, H-6), 3.45 (dd, 1 H, $J_{1a,2}$ = 2.5, $J_{1a,1b}$ = 10.6 Hz, H-1a), 3.30 (dd, 1 H, $J_{1b,2}$ = 6.6 Hz, H-1b), 3.09 (ddd, 1 H, H-2), 1.06 (s, 9 H, *t*-Bu). A mixture of iodide (3.18 g, 3.91 mmol) and triphenylphosphine (10.25 g, 39.10 mmol) was stirred at 120 °C under a nitrogen atmosphere for 2 h, then cooled to ca. 80 °C, diluted with toluene (20 mL), cooled to rt, and diluted with Et_2O (40 mL). The white solid was filtered, washed with Et_2O, and dried to give **8** (3.13 g, 65% from **7**). Mp 182−183 °C. $[\alpha]_D$ = −9.3 (*c* 0.8, $CHCl_3$). ^{1}H NMR (300 MHz): δ 7.83−7.18 (m, 40 H, 8 Ph), 5.06 and 4.92 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 4.99 and 4.60 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.78 (s, 2 H, PhCH_2), 3.98 (dd, 1 H, $J_{4,5}$ = 2.6, $J_{5,6}$ = 0.6 Hz, H-5), 3.95 (dd, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, H-3), 3.60 (dd, 1 H, H-4), 3.56−3.45 (m, 2 H, H-1a, H-2), 3.40 (dd, 1 H, $J_{6,7a}$ = 8.5, $J_{7a,7b}$ = 9.8 Hz, H-7a), 3.28−3.18 (m, 1 H, H-1b), 3.10 (dd, 1 H, $J_{6,7b}$ = 5.4 Hz, H-6), 2.91 (dd, 1 H, H-7b), 1.00 (s, 3 H, *t*-Bu). ^{31}P NMR (121 MHz): δ 23.7. Anal. Calcd for $C_{62}H_{64}IO_5PSi$ (1075.16): C, 69.26; H, 6.00. Found: C, 68.98; H, 5.96.

(*E*,*Z*)-8,12-Anhydro-9,10,11-tri-*O*-benzyl-13-*O*-*tert*-butyldiphenylsilyl-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-L-*manno*-D-*galacto*-tridec-6-eno-1,5-pyranose (10). To a cooled (−50 °C), stirred mixture of **8** (1.08 g,

Chart 4



1.00 mmol) and activated 4 Å powdered molecular sieves (1.0 g) in anhydrous THF (4 mL) and HMPA (2 mL) were added *n*-BuLi (625 μL, 1.00 mmol, of a 1.6 M solution in hexane) and, after 5 min, a solution of **9** (387 mg, 1.50 mmol) in anhydrous THF (2 mL). The mixture was allowed to reach −20 °C in 3 h, then diluted with Et_2O (150 mL), filtered through a pad of Celite, washed with 1 M phosphate buffer at pH 7 (30 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 6:1 cyclohexane−AcOEt (containing 0.5% triethylamine) to give syrupy **10** (0.65 g, 70%) as a ca. 9:1 *Z*,*E* mixture. ^{1}H NMR (300 MHz) of the *Z*-isomer: δ 7.64−7.54 and 7.46−7.24 (2 m, 25 H, 5 Ph), 5.77 (dd, 1 H, $J_{5,6}$ = 8.0, $J_{6,7}$ = 11.2 Hz, H-6), 5.66 (dd, 1 H, $J_{7,8}$ = 8.0 Hz, H-7), 5.48 (d, 1 H, $J_{1,2}$ = 5.0 Hz, H-1), 4.99 and 4.65 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.91 and 4.62 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.76 (s, 2 H, PhCH_2), 4.63 (dd, 1 H, $J_{4,5}$ = 2.6 Hz, H-5), 4.27 (dd, 1 H, $J_{2,3}$ = 2.2, $J_{3,4}$ = 8.0 Hz, H-3), 4.22 (dd, 1 H, H-2), 4.11 (d, 1 H, $J_{10,11}$ = 3.0 Hz, H-11), 4.01 (dd, 1 H, $J_{8,9}$ = 9.4 Hz, H-8), 3.84 (dd, 1 H, $J_{9,10}$ = 9.4 Hz, H-9), 3.78−3.71 (m, 3 H, H-10, 2 H-13), 3.58 (dd, 1 H, H-4), 3.42 (dd, 1 H, $J_{12,13a}$ = 5.0, $J_{12,13b}$ = 8.5 Hz, H-12), 1.48, 1.44, 1.42, and 1.33 (4 s, 12 H, 4 CH_3), 1.08 (s, 9 H, *t*-Bu). Anal. Calcd for $C_{56}H_{66}O_{10}Si$ (927.23): C, 72.54; H, 7.17. Found: C, 72.41; H, 7.25.

(*E*,*Z*)-8,12-Anhydro-9,10,11-tri-*O*-benzyl-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-L-*manno*-D-*galacto*-tridec-6-eno-1,5-pyranodialdose (11). A solution of **10** (0.63 g, 0.68 mmol) and *n*-$Bu_4NF{\cdot}3H_2O$ (0.32 g, 1.02 mmol) in distilled THF (14 mL) was kept at rt for 3 h, then diluted with 1 M phosphate buffer at pH 7 (20 mL), and extracted with Et_2O (2 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with 2:1 cyclohexane−AcOEt to give (*E*,*Z*)-8,12-anhydro-9,10,11-tri-*O*-benzyl-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-L-*manno*-D-*galacto*-tridec-6-eno-1,5-pyranose (0.42 g) as a syrup. ^{1}H NMR (300 MHz) selected data for the *Z*-isomer: δ 7.38−7.26 (m, 15 H, 3 Ph), 5.84 (dd, 1 H, $J_{5,6}$ = 8.0, $J_{6,7}$ = 11.4 Hz, H-6), 5.76 (dd, 1 H, $J_{7,8}$ = 7.6 Hz, H-7), 5.51 (d, 1 H, $J_{1,2}$ = 5.1 Hz, H-1), 4.97 and 4.68 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.93 and 4.66 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.78 and 4.74 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.33 (dd, 1 H, $J_{2,3}$ = 2.4, $J_{3,4}$ = 7.9 Hz, H-3), 4.24 (dd, 1 H, H-2), 4.07 (dd, 1 H, $J_{8,9}$ = 9.3 Hz, H-8), 3.59 (dd, 1 H, $J_{9,10}$ = 9.3, $J_{10,11}$ = 2.8 Hz, H-10), 1.54, 1.44, 1.33, and 1.17 (4 s, 12 H, 4 CH_3). To a vigorously stirred mixture of this alcohol, activated 4 Å powdered molecular sieves (1.2 g), and anhydrous CH_2Cl_2 (12 mL) was added pyridinium chlorochromate (0.40 g, 1.83 mmol). The reaction mixture was stirred at rt for 30 min, then diluted with Et_2O (24 mL) and cyclohexane (12 mL), stirred for an additional 10 min, and eluted from a short column of silica gel (4 × 3 cm, diameter × height) with 2:1 cyclohexane−Et_2O to give syrupy **11** (0.33 g, 70% from **10**) ca. 95% pure by ^{1}H NMR analysis. ^{1}H NMR (300 MHz) selected data for the *Z*-isomer: δ 9.60 (s, 1 H, H-13), 7.35−7.26 (m, 15 H, 3 Ph), 5.92 (dd, 1 H, $J_{5,6}$ = 8.0, $J_{6,7}$ = 11.3 Hz, H-6), 5.84 (dd, 1 H, $J_{7,8}$ = 8.0 Hz, H-7), 5.50 (d, 1 H, $J_{1,2}$ = 5.1 Hz, H-1), 4.32 (dd, 1 H, $J_{2,3}$ = 2.3, $J_{3,4}$ = 7.9 Hz, H-3), 4.23 (dd, 1 H, H-2), 4.18 (dd, 1 H, $J_{8,9}$ = 9.1 Hz, H-8), 3.82 (dd, 1 H, $J_{9,10}$ = 9.3 Hz, H-9), 3.76 (d, 1 H, $J_{11,12}$ = 1.2 Hz, H-12), 3.72 (dd, 1 H, $J_{4,5}$ = 1.7 Hz, H-4), 3.59 (dd, 1 H, $J_{10,11}$ = 2.7 Hz, H-10), 1.44, 1.42, 1.30, and 1.18 (4 s, 12 H, 4 CH_3). MALDI-TOF MS (686.81): *m*/*z* 710.0 (M + Na), 725.9 (M + K).

Trisaccharide 12. Aldehyde **11** (137 mg, 0.20 mmol) was treated with **8** (237 mg, 0.22 mmol) as described for the preparation of **10**. The crude product was eluted from a column of silica gel with 4:1 cyclohexane−AcOEt (containing 0.3% triethylamine) to give first **12a** (45 mg, 18%) as a syrup. ^{1}H NMR (300 MHz) selected data: δ 5.92 (dd, 1 H, $J_{5,6}$ = 8.8, $J_{6,7}$ = 11.5 Hz, H-6), 5.86 (d, 1 H, $J_{13,14}$ = 11.7 Hz, H-13), 5.70 (dd, 1 H, $J_{7,8}$ = 8.3 Hz, H-7), 5.50 (dd, 1 H, $J_{14,15}$ = 8.9 Hz, H-14), 5.50 (d, 1 H, $J_{1,2}$ = 4.5 Hz, H-1), 5.10 (dd, 1 H, $J_{10,11}$ = 2.1 Hz, H-11). MALDI-TOF MS (1247.6): *m*/*z* 1270.9 (M + Na), 1287.0 (M + K). Eluted second was syrupy **12** (98 mg, 36%) as a ca. 9:1 *E*,*Z*-mixture. ^{1}H NMR (300 MHz) selected data for the 6*Z*,13*E*-isomer: δ 7.66−7.61, 7.44−7.23, and 7.14−6.98 (3 m, 40 H, 8 Ph), 5.86 (dd, 1 H, $J_{12,13}$ = 7.0, $J_{13,14}$ = 16.0 Hz, H-13), 5.82−5.75 (m, 2 H, H-6, H-7), 5.71 (dd, 1 H, $J_{14,15}$ = 3.6 Hz, H-14), 5.46 (d, 1 H, $J_{1,2}$ = 4.8 Hz, H-1), 4.05 (dd, 1 H, $J_{7,8}$ = 7.1, $J_{8,9}$ = 9.4 Hz, H-8), 3.53 (dd, 1 H, $J_{9,10}$ = 9.7, $J_{10,11}$ = 2.9 Hz, H-10), 3.43 (ddd, 1 H, $J_{18,19}$ = 0.6, $J_{19,20a}$ = 5.1, $J_{19,20b}$ = 8.6 Hz, H-19), 1.51, 1.41, 1.30, and 1.28 (4 s, 12 H, 4 CH_3), 1.07 (s, 9 H, *t*-Bu). MALDI-TOF MS (1355.76): *m*/*z* 1379.4 (M + Na), 1395.4 (M + K). Anal. Calcd for $C_{84}H_{94}O_{14}Si$: C, 74.42; H, 6.99. Found: C, 74.23; H, 7.15.

Trisaccharide 13. Trisaccharide **12** (203 mg, 0.15 mmol) was desilylated and oxidized as described for the preparation of **11** to give syrupy **13** (119 mg, 71%) ca. 95% pure by ^{1}H NMR analysis. ^{1}H NMR (300 MHz) selected data for the 13*E*-isomer: δ 9.59 (s, 1 H, H-20), 7.49−7.13 (m, 30 H, 5 Ph), 6.00 (dd, 1 H, $J_{12,13}$ = 7.0, $J_{13,14}$ = 16.0 Hz, H-13), 5.48 (d, 1 H, $J_{1,2}$ = 5.0 Hz, H-1), 1.45, 1.41, 1.32, and 1.09 (4 s, 12 H, 4 CH_3). MALDI-TOF MS (1115.34): *m*/*z* 1138.5 (M + Na), 1154.8 (M + K).

Tetrasaccharide 14. Aldehyde **13** (112 mg, 0.10 mmol) was treated with **8** (161 mg, 0.15 mmol) as described for the preparation of **10**. The crude product was eluted from a column of silica gel with 4:1 cyclohexane−AcOEt (containing 0.3% triethylamine) to give first **14a** (47 mg, 28%) as a syrup. ^{1}H NMR (300 MHz) selected data: δ 6.00 (dd, 1 H, J = 6.3, 16.0 Hz), 5.76 (dd, 1 H, J = 7.8, 11.0 Hz), 5.56 (dd, 1 H, J = 8.8, 12.0 Hz), 5.44 (d, 1 H, $J_{1,2}$ = 4.9 Hz, H-1), 5.17 (d, 1 H, $J_{17,18}$ = 2.7 Hz, H-18). MALDI-TOF MS (1676.15): *m*/*z* 1699.2 (M + Na), 1715.6 (M + K). Eluted second was **14** (20 mg, 11%) slightly contaminated by **14a**. An analytical sample was obtained by preparative thin-layer chromatography on silica gel (6:3:1 pentane−CH_2Cl_2−Et_2O). ^{1}H NMR (300 MHz) selected data: δ 7.66−7.61, 7.53−7.11, and 7.05−6.99 (3 m, 55 H, 11 Ph), 5.47 (d, 1 H, $J_{1,2}$ = 4.6 Hz, H-1), 1.56, 1.41, 1.34, and 1.27 (4 s, 12 H, 4 CH_3), 1.07 (s, 9 H, *t*-Bu). MALDI-TOF MS (1784.29): 1808.0 (M + Na), 1824.0 (M + K). Anal. Calcd. for $C_{112}H_{122}O_{18}Si$: C, 75.39; H, 6.89. Found: C, 75.56; H, 7.01.

9,10,11,13-Tetra-*O*-acetyl-8,12-anhydro-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-L-*manno*-D-*galacto*-trideco-1,5-pyranose (15Ac). Disaccharide **10** (139 mg, 0.15 mmol) was desilylated as described for the preparation of **11**. A vigorously stirred mixture of the resulting alcohol, 20% palladium hydroxide on carbon (60 mg), and 1:1 CH_3OH−AcOEt (10 mL) was degassed under a vacuum and saturated with hydrogen (by a H_2-filled balloon) three times. The suspension was stirred at rt for 6 h under a positive pressure of hydrogen (4 bar), then filtered through a plug of cotton, and concentrated. A solution of crude **15** in pyridine (2 mL) and

acetic anhydride (2 mL) was kept at rt for 4 h, and then concentrated. The residue was eluted from a column of silica gel with 2:1 cyclohexane−AcOEt to give **15Ac** (62 mg, 70%) as a syrup. $[\alpha]_D = -32.1$ (*c* 1.9, $CHCl_3$). ^1H NMR (300 MHz): δ 5.51 (d, 1 H, $J_{1,2} = 5.1$ Hz, H-1), 5.41 (dd, 1 H, $J_{10,11} = 3.3$, $J_{11,12} = 1.1$ Hz, H-11), 5.09 (dd, 1 H, $J_{8,9} = 9.7$, $J_{9,10} = 10.0$ Hz, H-9), 4.99 (dd, 1 H, H-10), 4.58 (dd, 1 H, $J_{2,3} = 2.3$, $J_{3,4} = 6.9$ Hz, H-3), 4.29 (dd, 1 H, H-2), 4.14 (dd, 1 H, $J_{12,13a} = 6.6$, $J_{13a,13b} = 11.5$ Hz, H-13a), 4.12 (dd, 1 H, $J_{4,5} = 1.8$ Hz, H-4), 4.07 (dd, 1 H, $J_{12,13b} = 6.8$, H-13b), 3.84 (dd, 1 H, H-12), 3.69 (ddd, 1 H, $J_{4,5} = J_{5,6a} = 2.0$, $J_{5,6b} = 8.4$ Hz, H-5), 3.44 (ddd, 1 H, $J_{7a,8} = 2.0$, $J_{7b,8} = 9.5$ Hz, H-8), 2.17, 2.06, 2.05, and 1.99 (4 s, 12 H, 4 Ac), 1.88−1.76, 1.77−1.65, and 1.50−1.44 (3 m, 4 H, 2 H-6, 2 H-7), 1.52, 1.48, 1.36, and 1.34 (4 s, 12 H, 4 CH_3). Anal. Calcd for $C_{27}H_{40}O_{14}$ (588.62): C, 55.09; H, 6.85. Found: C, 54.94; H 6.97.

Peracetylated Trisaccharide 16Ac. Trisaccharide **12** (68 mg, 0.05 mmol) was desilylated as described for the preparation of **13**. A vigorously stirred mixture of the resulting alcohol, 20% palladium hydroxide on carbon (30 mg), and 1:1 CH_3OH−AcOEt (5 mL) was degassed under a vacuum and saturated with hydrogen (by a H_2-filled balloon) three times. The suspension was stirred at rt for 9 h under a positive pressure of hydrogen (4 bar), then filtered through a plug of cotton, and concentrated to give **16**. ^1H NMR (CD_3OD, 300 MHz) selected data: δ 5.44 (d, 1 H, $J_{1,2} = 4.9$ Hz, H-1), 4.59 (dd, 1 H, $J_{2,3} = 2.2$, $J_{3,4} = 7.8$ Hz, H-3), 4.30 (dd, 1 H, H-2), 4.16 (dd, 1 H, $J_{4,5} = 0.8$ Hz, H-4), 1.48, 1.38, 1.33, and 1.32 (4 s, 12 H, 4 CH_3). A solution of crude **16** in pyridine (2 mL) and acetic anhydride (2 mL) was kept at rt for 8 h, and then concentrated. The residue was eluted from a column of silica gel with 1.5:1 cyclohexane−AcOEt to give **16Ac** (26 mg, 59%) as a syrup. $[\alpha]_D = -20.2$ (*c* 0.6, $CHCl_3$). ^1H NMR (300 MHz): δ 5.51 (d, 1 H, $J_{1,2} = 5.1$ Hz, H-1), 5.40 (dd, 1 H, $J_{17,18} = 3.2$, $J_{18,19} = 1.0$ Hz, H-18), 5.29 (dd, 1 H, $J_{10,11} = 3.2$, $J_{11,12} = 0.7$ Hz, H-11), 5.08 (dd, 1 H, $J_{8,9} = 9.8$, $J_{9,10} = 10.0$ Hz, H-9), 5.07 (dd, 1 H, $J_{15,16} = 9.8$, $J_{16,17} = 10.0$ Hz, H-16), 4.98 (dd, 1 H, H-17), 4.97 (dd, 1 H, H-10), 4.58 (dd, 1 H, $J_{2,3} = 2.2$, $J_{3,4} = 7.1$ Hz, H-3), 4.28 (dd, 1 H, $J_{2,3} = 2.2$ Hz, H-2), 4.18−4.03 (m, 3 H, H-4, 2 H-20), 3.85 (dd, 1 H, $J_{19,20a} = 5.8$, $J_{19,20b} = 6.8$ Hz, H-19), 3.70−3.66 (m, 1 H, H-5), 3.52−3.48 (m, 1 H, H-12), 3.43−3.32 (m, 2 H, H-8, H-15), 2.18, 2.16, 2.05, 2.04, and 1.97 (5 s, 21 H, 7 Ac), 1.86−1.78 (m, 2 H, 2 H-6), 1.72−1.60 (m, 4 H, 2 H-7, 2 H-14), 1.47−1.42 (m, 2 H, 2 H-13), 1.50, 1.46, 1.35, 1.32 (4 s, 12 H, 4 CH_3). ^{13}C NMR (75.1 MHz): δ 20.7, 20.8, 24.3, 25.0, 26.1, 16.0, 26.4, 27.2, 28.4, 61.7, 67.7, 68.6, 69.7, 69.7, 70.5, 70.9, 72.2, 72.9, 73.0, 74.0, 76.9, 77.2, 77.7, 78.3, 96.5, 108.3, 109.1, 169.8, 169.9, 170.2, 170.3, 170.5, 170.7. MALDI-TOF MS (874.90): *m*/*z* 898.2 (M + Na), 914.6 (M + K). Anal. Calcd for $C_{40}H_{58}O_{21}$: C, 54.91; H, 6.68. Found: C, 55.20; H, 6.52.

Peracetylated Tetrasaccharide 17Ac. Tetrasaccharide **14** (89 mg, 0.05 mmol) was desilylated as described for the preparation of **13**. A vigorously stirred mixture of the resulting alcohol, 20% palladium hydroxide on carbon (30 mg), and 1:1 CH_3OH−AcOEt (5 mL) was degassed under a vacuum and saturated with hydrogen (by a H_2-filled balloon) three times. The suspension was stirred at rt for 9 h under a positive pressure of hydrogen (4 bar), then filtered through a plug of cotton, and concentrated to give **17**. ^1H NMR (CD_3OD, 300 MHz) selected data: δ 5.48 (d, 1 H, $J_{1,2} = 5.1$ Hz, H-1), 4.59 (dd, 1 H, $J_{2,3} = 2.2$, $J_{3,4} = 8.0$ Hz, H-3), 4.31 (dd, 1 H, H-2), 4.18 (dd, 1 H, $J_{4,5} = 1.3$ Hz, H-4), 1.49, 1.40, 1.32, and 1.29 (4 s, 12 H, 4 CH_3). A solution of crude **17** in pyridine (2 mL) and acetic anhydride (2 mL) was kept at rt for 16 h, and then concentrated. The residue was eluted from a column of silica gel with 1:2 cyclohexane−AcOEt to give **17Ac** (35 mg, 61%) as a syrup. $[\alpha]_D = -12.0$ (*c* 0.2, $CHCl_3$). ^1H NMR (300 MHz) selected data: δ 5.51 (d, 1 H, $J_{1,2} = 4.9$ Hz, H-1), 5.40 (dd, 1 H, $J_{24,25} = 3.3$, $J_{25,26} = 0.6$ Hz, H-25), 5.28 (dd, 1 H, $J_{17,18} = 3.2$, $J_{18,19} = 0.5$ Hz, H-18), 5.28 (dd, 1 H, $J_{10,11} = 3.2$, $J_{11,12} = 0.5$ Hz, H-11), 5.09 (dd, 1 H, $J_{22,23} = J_{23,24} = 9.8$ Hz, H-23), 5.07 (dd, 1 H, $J_{15,16} = J_{16,17} = 9.8$ Hz, H-16), 5.04 (dd, 1 H, $J_{8,9} = J_{9,10} = 9.8$ Hz, H-9), 4.58 (dd, 1 H, $J_{2,3} = 2.2$, $J_{3,4} = 7.8$ Hz, H-3), 4.29 (dd, 1 H, H-2), 3.84 (ddd, 1 H, $J_{26,27a} = 5.6$, $J_{26,27b} = 7.3$ Hz, H-26), 3.69−3.66 (m, 1 H, H-5), 2.19, 2.18, 2.16, 2.06, 2.05, 2.04, 1.98, and 1.97 (8 s, 30 H, 10 Ac), 1.87−1.79 (m, 2 H, 2 H-6), 1.73−1.60 (m, 6 H, 2 H-7, 2 H-14, 2 H-21), 1.52−1.43 (m, 4 H, 2 H-13, 2 H-20), 1.51, 1.48, 1.35, and 1.33 (4 s, 12 H, 4 CH_3). MALDI-TOF MS (1161.19): *m*/*z* 1184.8 (M + Na), 1201.3 (M + K). Anal. Calcd for $C_{53}H_{76}O_{28}$: C, 54.82; H, 6.60. Found: C, 55.01; H, 6.65.

(Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-D-galactopyranosid-6-yl)triphenylphosphonium Iodide (20). A mixture of iodide **18** (2.64 g, 4.60 mmol) and triphenylphosphine (12.05 g, 46.00 mmol) was stirred at 120 °C under a nitrogen atmosphere for 4 h, and then cooled to room temperature. A solution of the residue in CH_2Cl_2 (20 mL) was added dropwise to a stirred volume of Et_2O (ca. 1.2 L), and the white solid was filtered, washed with Et_2O, and dried to give **20** (3.42 g, 89%). Mp 93−94 °C. $[\alpha]_D = +50.5$ (*c* 0.7, $CHCl_3$). ^1H NMR (300 MHz): δ 7.81−7.23 (m, 30 H, 6 Ph), 5.14 and 4.89 (2 d, 2 H, $J = 11.2$ Hz, PhCH_2), 5.09 (ddd, 1 H, $J_{5,6a} = 3.0$, $J_{6a,6b} = J_{6a,P} = 16.0$ Hz, H-6a), 4.96 (ddd, 1 H, $J_{3,4} = 2.6$, $J_{4,5} = J_{4,P} = 1.0$ Hz, H-4), 4.92 and 4.82 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.85 and 4.67 (2 d, 2 H, $J = 12.3$ Hz, PhCH_2), 4.45 (dddd, 1 H, $J_{5,6b} = 10.7$, $J_{5,P} = 10.0$ Hz, H-5), 4.39 (d, 1 H, $J_{1,2} = 3.6$ Hz, H-1), 4.07 (dd, 1 H, $J_{2,3} = 10.3$ Hz, H-3), 3.98 (dd, 1 H, H-2), 3.50 (ddd, 1 H, $J_{6b,P} = 10.3$ Hz, H-6b), 2.48 (s, 3 H, CH_3). ^{31}P NMR (121 MHz): δ 24.9. Anal. Calcd for $C_{46}H_{46}IO_5P$ (836.75): C, 66.03, H, 5.54. Found: C, 66.21, H, 5.59.

(Methyl 2,3,4-tri-*O*-benzyl-6-deoxy-D-glucopyranosid-6-yl)triphenylphosphonium Iodide (21). Iodide **19** (5.00 g, 8.70 mmol) was treated with triphenylphosphine (22.82 g, 87.00 mmol) as described for the preparation of **20** to give **21** (6.34 g, 87%) identical in all respects to the product that we prepared using different reaction conditions.[5a]

Methyl 8,12-Anhydro-2,3,4,9,10,11-hexa-*O*-benzyl-13-*O*-*tert*-butyldiphenylsilyl-6,7-dideoxy-α-D-*glycero*-L-*manno*-D-*galacto*-tridec-6-(*Z*)-eno-1,5-pyranoside (22). To a cooled (−20 °C), stirred mixture of aldehyde **7** (1.05 g, 1.50 mmol), iodide **20** (0.84 g, 1.00 mmol), activated 4 Å powdered molecular sieves (1.5 g), anhydrous THF (12 mL), and anhydrous HMPA (4 mL) was added *n*-BuLi (0.62 mL, 1.00 mmol, of a 1.6 M solution in hexane) by a syringe-pump apparatus over 4 h. After that period the reaction mixture was diluted with Et_2O (150 mL), filtered through a pad of Celite, washed with 1 M phosphate buffer (30 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 15:1 cyclohexane−AcOEt to give **22** (1.28 g, 81%) as a syrup. $[\alpha]_D = +5.7$ (*c* 1.5, $CHCl_3$). ^1H NMR (300 MHz) selected data: δ 7.68−7.56 (m, 4 H, Ar), 7.48−7.15 (m, 36 H, Ar), 5.87 (dd, 1 H, $J_{5,6} = 9.0$, $J_{6,7} = 11.2$ Hz, H-6), 5.65 (dd, 1 H, $J_{7,8} = 8.3$ Hz, H-7), 4.66 (d, 1 H, $J_{1,2} = 3.5$ Hz, H-1), 4.59 (dd, 1 H, $J_{4,5} = 0.6$ Hz, H-5), 4.10 (dd, 1 H, $J_{10,11} = 2.9$, $J_{11,12} = 0.6$ Hz, H-11), 3.99 (dd, 1 H, $J_{2,3} = 10.0$ Hz, H-2), 3.97 (dd, 1 H, $J_{8,9} = 9.6$ Hz, H-8), 3.84 (dd, 1 H, $J_{12,13a} = 8.0$, $J_{13a,13b} = 9.6$ Hz, H-13a), 3.83 (dd, 1 H, $J_{3,4} = 2.4$ Hz, H-3), 3.76 (dd, 1 H, $J_{9,10} = 9.3$ Hz, H-9), 3.72 (dd, 1 H, $J_{12,13b} = 5.6$ Hz, H-13b), 3.64 (dd, 1 H, H-10), 3.60 (dd, 1 H, H-4), 3.40 (ddd, 1 H, H-12), 3.27 (s, 3 H, OCH_3), 1.05 (s, 9 H, *t*-Bu). MALDI-TOF MS (1131.50): *m*/*z* 1154.8 (M + Na), 1170.6 (M + K). Anal. Calcd for $C_{72}H_{78}O_{10}Si$: C, 76.43; H, 6.95. Found: C, 76.30; H, 7.07.

When the reaction was performed using an excess of phosphonium iodide **20** (1.2 equiv), the *C*-disaccharide **22** was isolated in 61% yield.

(Methyl 8,12-anhydro-2,3,4,9,10,11-hexa-*O*-benzyl-6,7,-13-trideoxy-α-D-*glycero*-L-*manno*-D-*galacto*-tridec-6-(*Z*)-eno-1,5-pyranosid-13-yl)triphenylphosphonium Iodide (23). A solution of **22** (1.13 g, 1.00 mmol) and *n*-$Bu_4NF{\cdot}3H_2O$ (0.95 g, 3.00 mmol) in distilled THF (20 mL) was refluxed for 2 h, then cooled to rt, diluted with 1 M phosphate buffer at pH 7 (40 mL), and extracted with Et_2O (2 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 2:1 to 1:1) to give methyl 8,12-anhydro-2,3,4,9,10,11-hexa-*O*-benzyl-6,7-dideoxy-α-D-*glycero*-L-*manno*-D-*galacto*-tridec-6-(*Z*)-eno-1,5-pyranoside (0.86 g). ^1H NMR (300 MHz) selected data: δ 5.90 (dd, 1 H, $J_{5,6} = 8.8$, $J_{6,7} = 11.2$ Hz, H-6), 5.73 (dd, 1 H, $J_{7,8} = 8.0$ Hz, H-7), 3.36 (s, 3 H, CH_3). To a vigorously stirred solution of the alcohol,

triphenylphosphine (0.50 g, 1.92 mmol), and imidazole (0.26 g, 3.83 mmol) in anhydrous toluene (20 mL) was added iodine (0.49 g, 1.92 mmol). The mixture was refluxed for 1 h, then cooled to rt, filtered through a pad of Celite, and concentrated. A solution of the residue in CH_2Cl_2 (100 mL) was washed with 5% aqueous $Na_2S_2O_3$ (2 × 30 mL), dried (Na_2SO_4), and concentrated. Column chromatography of the residue (2:1 CH_2Cl_2–cyclohexane, and then 9:1 cyclohexane−AcOEt) gave methyl 8,12-anhydro-2,3,4,9,10,11-hexa-*O*-benzyl-6,7,13-trideoxy-13-iodo-α-D-*glycero*-L-*manno*-D-*galacto*-tridec-6-(*Z*)-eno-1,5-pyranoside (0.94 g). ^{1}H NMR (300 MHz) selected data: δ 7.40−7.20 (m, 30 H, 6 Ph), 5.88 (dd, 1 H, $J_{5,6}$ = 8.8, $J_{6,7}$ = 11.7 Hz, H-6), 5.70 (dd, 1 H, $J_{7,8}$ = 7.2 Hz, H-7), 4.69 (d, 1 H, $J_{1,2}$ = 3.2 Hz, H-1), 4.15 (dd, 1 H, $J_{10,11}$ = 2.4, $J_{11,12}$ = 0.5 Hz, H-11), 4.02 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, H-2), 4.01 (dd, 1 H, $J_{8,9}$ = 9.3 Hz, H-8), 3.89 (dd, 1 H, $J_{3,4}$ = 2.8 Hz, H-3), 3.77 (dd, 1 H, $J_{9,10}$ = 9.2 Hz, H-9), 3.71 (dd, 1 H, $J_{4,5}$ = 0.5 Hz, H-4), 3.64 (dd, 1 H, H-10), 3.54 (ddd, 1 H, $J_{12,13a}$ = 6.0, $J_{12,13b}$ = 7.2 Hz, H-12), 3.34 (s, 3 H, CH_3), 3.18 (dd, 1 H, $J_{13a,13b}$ = 10.0 Hz, H-13a), 3.14 (dd, 1 H, H-13b). The iodide was treated with triphenylphosphine (2.46 g, 9.37 mmol) as described for the preparation of **20** to give **23** (1.11 g, 88%) as a white solid. Mp 213−214 °C dec (CH_3OH). $[\alpha]_D$ = +66.1 (*c* 0.6, $CHCl_3$). ^{1}H NMR (300 MHz) selected data: δ 7.78−7.50 and 7.43−7.10 (2 m, 45 H, 9 Ph), 5.57 (dd, 1 H, $J_{5,6}$ = 8.1, $J_{6,7}$ = 11.5 Hz, H-6), 5.01 (dd, 1 H, $J_{7,8}$ = 8.5 Hz, H-7), 4.50 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.29 (dd, 1 H, $J_{4,5}$ = 0.6 Hz, H-5), 3.92 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, H-2), 3.80 (dd, 1 H, $J_{8,9}$ = 9.4 Hz, H-8), 3.76 (dd, 1 H, $J_{9,10}$ = 9.1, $J_{10,11}$ = 1.6 Hz, H-10), 3.64 (dd, 1 H, $J_{3,4}$ = 2.7 Hz, H-3), 3.56 (dd, 1 H, H-9), 3.29 (dd, 1 H, H-4), 3.08 (s, 3 H, CH_3). ^{31}P NMR (121 MHz): δ 24.9. Anal. Calcd for $C_{74}H_{74}IO_9P$ (1265.28): C, 70.25; H, 5.90. Found: C, 70.42; H, 5.99.

Trisaccharide 24. The aldehyde **7** (420 mg, 0.60 mmol) was treated with **23** (633 mg, 0.50 mmol) as described for the preparation of **22** to give syrupy **24** (679 mg, 87%) slightly contaminated by the *Z*,*E*-isomer. ^{1}H NMR (300 MHz) selected data: δ 5.86 (dd, 1 H, $J_{5,6}$ = 8.3, $J_{6,7}$ = 11.5 Hz, H-6), 5.83 (dd, 1 H, $J_{12,13}$ = 8.4, $J_{13,14}$ = 11.6 Hz, H-13), 5.71 (dd, 1 H, $J_{7,8}$ = 7.5 Hz, H-7), 5.65 (dd, 1 H, $J_{14,15}$ = 7.5 Hz, H-14), 4.73 (dd, 1 H, $J_{4,5}$ = 0.5 Hz, H-5), 4.68 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.31 (dd, 1 H, $J_{11,12}$ = 0.5 Hz, H-12), 4.00 (dd, 1 H, $J_{2,3}$ = 10.1 Hz, H-2), 3.98 (dd, 1 H, $J_{8,9}$ = 9.5 Hz, H-8), 3.28 (s, 3 H, CH_3). MALDI-TOF MS (1560.03): *m*/*z* 1582.8 (M + Na), 1599.0 (M + K). Anal. Calcd for $C_{100}H_{106}IO_{14}Si$: C, 76.99; H, 6.85. Found: C, 76.81; H, 6.98.

Trisaccharide 25. A solution of **24** (624 mg, 0.40 mmol) and *n*-$Bu_4NF{\cdot}3H_2O$ (310 mg, 1.20 mmol) in distilled THF (16 mL) was refluxed for 2 h, then cooled to rt, diluted with 1 M phosphate buffer at pH 7 (20 mL), and extracted with Et_2O (2 × 80 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 3:1 to 1:1.5) to give the corresponding alcohol (510 mg) as the pure *Z*,*Z*-isomer. $[\alpha]_D$ = +11.3 (*c* 0.9, $CHCl_3$). ^{1}H NMR (300 MHz) selected data: δ 5.90 (dd, 1 H, *J* = 8.5, 11.3 Hz), 5.88 (dd, 1 H, *J* = 9.0, 12.0 Hz), 5.73 (dd, *J* = 7.6, 11.3 Hz), 5.72 (dd, 1 H, *J* = 7.8, 12.0 Hz), 3.33 (s, 3 H, CH_3). To a vigorously stirred solution of the alcohol, triphenylphosphine (203 mg, 0.78 mmol), and imidazole (106 mg, 1.55 mmol) in anhydrous toluene (8 mL) was added iodine (197 mg, 0.78 mmol). The mixture was refluxed for 1 h, then cooled to rt, filtered through a pad of Celite, and concentrated. A solution of the residue in CH_2Cl_2 (100 mL) was washed with 5% aqueous $Na_2S_2O_3$ (2 × 30 mL), dried (Na_2SO_4), and concentrated. Column chromatography of the residue (2:1 CH_2Cl_2–cyclohexane, and then 6:1 cyclohexane−AcOEt) gave the corresponding iodide (510 mg). ^{1}H NMR (300 MHz) selected data: δ 5.88 (dd, 2 H, *J* = 8.9, 11.0 Hz), 5.73 (dd, 1 H, *J* = 7.4, 11.0 Hz), 5.69 (dd, 1 H, *J* = 7.3, 11.0 Hz), 3.33 (s, 3 H, CH_3). A mixture of iodide and triphenylphosphine (0.94 g, 3.57 mmol) was stirred at 120 °C under a nitrogen atmosphere for 4 h, and then cooled to room temperature. The solid was triturated at rt with 4:1 cyclohexane−Et_2O (20 mL), and then cooled to 0 °C. After 15 min the solution was removed, and the formed syrup was dried under a vacuum to give **25** (557 mg, 82%) as an amorphous solid slightly contaminated by triphenylphosphine. ^{1}H NMR (300 MHz) selected data: δ 5.91 (dd, 1 H, *J* = 8.8, 11.5 Hz), 5.75 (dd, 1 H, *J* = 9.0, 11.3 Hz), 5.73 (dd, 1 H, *J* = 7.6, 11.5 Hz), 5.02 (dd, 1 H, *J* = 8.5, 11.3 Hz), 3.29 (s, 3 H, CH_3). ^{31}P NMR (121 MHz): δ 24.7.

Tetrasaccharide 26. The aldehyde **7** (273 mg, 0.39 mmol) was treated with **25** (508 mg, 0.30 mmol) as described for the preparation of **22** to give **26** (554 mg, 93%) as a syrup. $[\alpha]_D$ = −11.3 (*c* 1.2, $CHCl_3$). ^{1}H NMR (300 MHz) selected data: δ 5.83 (dd, 1 H, *J* = 9.0, 11.6 Hz), 5.81−5.66 (4 dd, 4 H, 2 CH=CH), 5.63 (dd, 1 H, *J* = 7.5, 11.4 Hz), 3.21 (s, 3 H, CH_3). MALDI-TOF MS (1988.56): *m*/*z* 2012.3 (M + Na), 2027.6 (M + K). Anal. Calcd for $C_{128}H_{134}O_{18}Si$: C, 77.31; H, 6.79. Found: C, 77.40; H, 6.88.

Tetrasaccharide 27. The tetrasaccharide **26** (398 mg, 0.20 mmol) was treated as described for the preparation of **25** to give **27** (322 mg, 76%) slightly contaminated by triphenylphosphine. ^{1}H NMR (300 MHz) selected data: δ 6.00 (dd, 1 H, *J* = 9.0, 12.0 Hz), 3.24 (s, 3 H, CH_3). ^{31}P NMR (121 MHz): δ 24.4.

Pentasaccharide 28. To a cooled (−20 °C), stirred mixture of aldehyde **7** (91 mg, 0.13 mmol), iodide **27** (212 mg, 0.10 mmol), activated 4 Å powdered molecular sieves (130 mg), anhydrous THF (3 mL), and anhydrous HMPA (1 mL) was added a solution of *n*-BuLi (63 μL, 0.10 mmol, of a 1.6 M solution in hexane) in anhydrous THF (0.3 mL) by a syringe-pump apparatus over 4 h. After that period the reaction mixture was diluted with Et_2O (100 mL), filtered through a pad of Celite, washed with 1 M phosphate buffer at pH 7 (20 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 9:1 cyclohexane−AcOEt to give **28** (222 mg, 92%) as a syrup. $[\alpha]_D$ = −21.1 (*c* 1.1, $CHCl_3$). ^{1}H NMR (300 MHz) selected data: δ 5.82 (dd, 2 H, *J* = 8.8, 11.5 Hz), 5.75−5.61 (6 dd, 6 H, 3 CH=CH), 5.10 and 4.67 (2 d, 2 H, *J* = 11.5 Hz, PhCH_2), 3.19 (s, 3 H, CH_3), 1.04 (s, 9 H, *t*-Bu). MALDI-TOF MS (2417.10): *m*/*z* 2439.8 (M + Na), 2456.2 (M + K). Anal. Calcd for $C_{156}H_{162}O_{22}Si$: C, 77.52; H, 6.76. Found: C, 77.76; H, 6.83.

Methyl 2,3,4,9,10,11,13-Hepta-O-acetyl-8,12-anhydro-6,7-dideoxy-α-D-*glycero*-L-*manno*-D-*galacto*-trideco-1,5-pyranoside (29Ac). The disaccharide **22** (90 mg, 0.08 mmol) was desilylated, hydrogenated, and acetylated as described for the preparation of **15Ac** to give, after column chromatography (1:1 AcOEt−cyclohexane), **29Ac** (43 mg, 82%) as a syrup. $[\alpha]_D$ = +58.5 (*c* 1.1, $CHCl_3$). ^{1}H NMR (C_6D_6, 300 MHz): δ 5.72 (dd, 1 H, $J_{2,3}$ = 10.8, $J_{3,4}$ = 3.3 Hz, H-3), 5.54 (dd, 1 H, $J_{1,2}$ = 3.7 Hz, H-2), 5.53 (dd, 1 H, $J_{4,5}$ = 1.0 Hz, H-4), 5.50 (dd, 1 H, $J_{10,11}$ = 3.3, $J_{11,12}$ = 1.2 Hz, H-11), 5.42 (dd, 1 H, $J_{8,9}$ = 9.6, $J_{9,10}$ = 10.2 Hz, H-9), 5.12 (dd, 1 H, H-10), 5.09 (d, 1 H, H-1), 4.08 (d, 2 H, $J_{12,13}$ = 6.7 Hz, 2 H-13), 3.61 (ddd, 1 H, $J_{5,6a}$ = 4.5, $J_{5,6b}$ = 8.3 Hz, H-5), 3.32 (dt, 1 H, H-12), 3.13 (ddd, 1 H, $J_{7a,8}$ = 2.5, $J_{7b,8}$ = 7.8 Hz, H-8), 3.00 (s, 3 H, OCH_3), 1.73, 1.71, 1.69, 1.64, and 1.59 (5 s, 21 H, 7 Ac). Anal. Calcd for $C_{28}H_{40}O_{17}$ (648.63): C, 51.85; H, 6.22. Found: C, 51.60; H, 6.41.

Trisaccharide 30Ac. The trisaccharide **24** (109 mg, 0.07 mmol) was desilylated, hydrogenated, and acetylated as described for the preparation of **15Ac** to give, after column chromatography (2:1 AcOEt−cyclohexane), **30Ac** (52 mg, 80%) as a syrup. $[\alpha]_D$ = +15.5 (*c* 0.7, $CHCl_3$). ^{1}H NMR (300 MHz) selected data: δ 5.42 (dd, 1 H, *J* = 0.8, 3.0 Hz), 5.31 (dd, 2 H, *J* = 0.7, 3.2 Hz), 3.40 (s, 3 H, OCH_3). MALDI-TOF MS (934.91): *m*/*z* 958.2 (M + Na), 973.9 (M + K). Anal. Calcd for $C_{41}H_{58}O_{24}$: C, 52.67; H, 6.25. Found: C, 52.58; H, 6.32.

Tetrasaccharide 31Ac. A solution of **26** (100 mg, 0.05 mmol) and *n*-$Bu_4NF{\cdot}3H_2O$ (47 mg, 0.15 mmol) in distilled THF (5 mL) was refluxed for 2 h, then cooled to rt, diluted with 1 M phosphate buffer at pH 7 (10 mL), and extracted with Et_2O (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 3:1 to 2:1) to give the corresponding alcohol. A vigorously stirred mixture of this alcohol, 10% palladium on carbon (80 mg), and 1:1 CH_3OH−AcOEt (5 mL) was degassed under a vacuum and saturated with hydrogen (by a H_2-filled balloon) three times. The suspension was stirred at rt for 6 h under a positive pressure of hydrogen (7 bar), then filtered through a plug of

cotton, washed with distilled DMF, and concentrated to give **31**. A solution of crude **31** in pyridine (2 mL) and acetic anhydride (2 mL) was kept at rt for 8 h, and then concentrated. The residue was eluted from a column of silica gel with 2:1 AcOEt−cyclohexane to give **31Ac** (55 mg, 90%) as an amorphous solid. $[\alpha]_D = +39.9$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz) selected data: δ 5.41 (dd, 1 H, $J = 0.6$, 3.0 Hz), 3.38 (s, 3 H, OCH_3). MALDI-TOF MS (1221.20): *m*/*z* 1244.6 (M + Na), 1260.2 (M + K). Anal. Calcd for $C_{54}H_{76}O_{31}$: C, 53.11; H, 6.27. Found: C, 53.22; H, 6.30.

Pentasaccharide 32Ac. The pentasaccharide **28** (48 mg, 0.20 mmol) was desilylated, hydrogenated, and acetylated as described for the preparation of **31Ac**. The crude product was eluted from a column of silica gel with AcOEt−cyclohexane (from 2:1 to 4:1) to give **32Ac** (26 mg, 86%) as an amorphous solid. $[\alpha]_D = +32.8$ (*c* 0.6, $CHCl_3$). ^{1}H NMR (500 MHz): δ 5.40 (dd, 1 H, $J_{3,4} = 3.5$, $J_{4,5} = 1.1$ Hz, H-4E), 5.34 (dd, 1 H, $J_{3,4} = 3.5$, $J_{4,5} = 0.7$ Hz, H-4A), 5.31 (dd, 1 H, $J_{2,3} = 10.8$ Hz, H-3A), 5.28 (dd, 3 H, $J_{3,4} = 3.5$, $J_{4,5} = 0.7$ Hz, H-4B, H-4C, H-4D), 5.13 (dd, 1 H, $J_{1,2} = 3.7$, $J_{2,3} = 10.6$ Hz, H-2A), 5.06, 5.04, and 5.03 (3 dd, 4 H, $J_{1,2} = 9.3$, $J_{2,3} = 10.3$ Hz, H-2B, H-2C, H-2D, H-2E), 4.99 (dd, 1 H, H-3E), 4.96, 4.95, and 4.94 (3 dd, 3 H, H-3B, H-3C, H-3D), 4.96 (d, 1 H, H-1A), 4.11 (dd, 1 H, $J_{5,6a} = 6.8$, $J_{6a,6b} = 11.4$ Hz, H-6aE), 4.06 (dd, 1 H, $J_{5,6b} = 6.5$ Hz, H-6bE), 3.91 (ddd, 1 H, $J_{5,6a} = 6.0$, $J_{5,6b} = 8.0$ Hz, H-5A), 3.84 (ddd, 1 H, $J_{5,6a} = J_{5,6b} = 6.5$ Hz, H-5E), 3.52−3.48 (m, 3 H, H-5B, H-5C, H-5D), 3.38 (s, 3 H, OCH_3), 3.38 (ddd, 1 H, $J = 2.0$, 8.2, 9.3 Hz, H-1E), 3.32 and 3.30 (2 ddd, 3 H, $J = 2.0$, 8.2, 9.3 Hz, H-1B, H-1C, H-1D), 2.18−1.96 (9 s, 48 H, 16 Ac), 1.72−1.58 and 1.48−1.40 (2 m, 16 H, 4 CH_2CH_2). MALDI-TOF MS (1507.49): *m*/*z* 1530.9 (M + Na), 1547.4 (M + K). Anal. Calcd for $C_{67}H_{94}O_{38}$: C, 53.38; H, 6.28. Found: C, 53.44; H, 6.35.

2-(2,3,4,6-Tetra-*O*-benzyl-*β*-D-glucopyranosyl)benzothiazole (34). To a cooled (−65 °C), stirred solution of *n*-BuLi (22.1 mL, 35.35 mmol, of a 1.6 M solution in hexane) in anhydrous Et_2O (80 mL) was added dropwise a solution of freshly distilled 2-benzothiazole (4.78 g, 35.35 mmol) in anhydrous Et_2O (40 mL) over a 30 min period. The yellow solution was stirred at −65 °C for 30 min, and then a solution of gluconolactone **33** (13.60 g, 25.25 mmol) in anhydrous Et_2O (80 mL) was added slowly (30 min). After an additional 1 h at −65 °C the mixture was allowed to warm to −50 °C in 30 min, then diluted with Et_2O (200 mL), and poured into 200 mL of a 1 M phosphate buffer at pH 7. The layers were separated, and the organic phase was filtered to collect the benzothiazolylketose which crystallized during the extraction. The white solid was washed with H_2O and Et_2O (10 mL) and dried to give pure 2,3,4,6-tetra-*O*-benzyl-1-*C*-(2-benzothiazolyl)-α-D-glucopyranose (9.87 g, 58%). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 4:1 to 3:1) to give the benzothiazolylketose (3.40 g, 20%) as a white solid. Mp 115−117 °C (Et_2O). $[\alpha]_D = -19.7$ (*c* 0.4, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.16−8.05 and 7.92−7.86 (2 m, 2 H, BTh), 7.60−6.95 (m, 22 H, 4 Ph, BTh), 4.94 (s, 2 H, PhCH_2), 4.71 (s, 1 H, OH), 4.89 and 4.67 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.66 and 4.54 (2 d, 2 H, $J = 12.5$ Hz, PhCH_2), 4.61 and 4.31 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.21 (ddd, 1 H, $J_{4,5} = 1.8$, $J_{5,6a} = 11.0$, $J_{5,6b} = 4.0$ Hz, H-5), 4.07 (dd, 1 H, $J_{2,3} = 10.5$, $J_{3,4} = 8.0$ Hz, H-3), 4.03 (d, 1 H, H-2), 3.86 (dd, 1 H, H-4), 3.83 (dd, 1 H, $J_{6a,6b} = 11.5$ Hz, H-6a), 3.66 (dd, 1 H, H-6b). Anal. Calcd for $C_{41}H_{39}NO_6S$ (673.83): C, 73.08; H, 5.83; N, 2.08. Found: C, 73.01; H, 5.90; N, 2.01. To a solution of the benzothiazolylketose (5.60 g, 8.31 mmol) in anhydrous CH_2Cl_2 (50 mL) were added at rt distilled triethylamine (15 mL) and acetic anhydride (15 mL). The solution was kept at rt for 24 h, and then concentrated. The residue was triturated with Et_2O (2 × 20 mL) to give pure 1-*O*-acetyl-2,3,4,6-tetra-*O*-benzyl-1-*C*-(2-benzothiazolyl)-α-D-glucopyranose (5.23 g, 88%). Mp 136−137 °C (cyclohexane). $[\alpha]_D = +27.0$ (*c* 1.1, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.11−8.05 and 7.92−7.86 (2 m, 2 H, BTh), 7.55−7.00 (m, 22 H, 4 Ph, BTh), 4.99 and 4.93 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.90 and 4.68 (2 d, 2 H, $J = 10.5$ Hz, PhCH_2), 4.78 and 4.65 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 4.51 and 4.28 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.22 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 4.11 (dd, 1 H, $J_{4,5} = 9.0$ Hz, H-4), 3.92 (dd, 1 H, $J_{5,6a} = 3.2$, $J_{6a,6b} = 11.8$ Hz, H-6a), 3.87−3.78 (m, 2 H, H-5, H-6b), 3.68 (d, 1 H, H-2), 2.25 (s, 3 H, Ac). Anal. Calcd for $C_{43}H_{41}NO_7S$ (715.87): C, 72.15; H, 5.77; N, 1.96. Found: C, 72.24; H, 5.71; N, 1.91. To a stirred mixture of acetate (5.73 g, 8.00 mmol), activated 4 Å powdered molecular sieves (8.0 g), and triethylsilane (12.8 mL, 80.0 mmol) in anhydrous CH_2Cl_2 (65 mL) was added TMSOTf (2.17 mL, 12.00 mmol). The mixture was stirred at rt for 1.5 h, then diluted with triethylamine (3 mL) and CH_2Cl_2 (100 mL), and filtered through Celite. The solution was washed with H_2O (30 mL), dried (Na_2SO_4), and concentrated to afford a ca. 1.5:1 mixture of **34** and its α-anomer. The residue was triturated with cyclohexane (2 × 20 mL) to give pure **34** (3.16 g, 60%) as a white solid. The mother liquor was concentrated, and the residue was treated with a 0.2 M solution of CH_3ONa in CH_3OH (50 mL). After 24 h at rt the reaction mixture was neutralized with acetic acid, concentrated, diluted with CH_2Cl_2 (100 mL), washed with H_2O (20 mL), dried (Na_2SO_4), and concentrated. The residue was triturated with cyclohexane (2 × 10 mL) to give **34** (1.05 g, 20%) as a white solid. Mp 137−139 °C. $[\alpha]_D = -10.6$ (*c* 0.8, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.06−8.03 and 7.98−7.95 (2 m, 2 H, BTh), 7.58−7.00 (m, 22 H, 4 Ph, BTh), 4.98 and 4.92 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.88 and 4.65 (2 d, 2 H, $J = 10.8$ Hz, PhCH_2), 4.79 (d, 1 H, $J_{1,2} = 9.2$ Hz, H-1), 4.67 and 4.59 (2 d, 2 H, $J = 12.2$ Hz, PhCH_2), 4.56 and 4.26 (2 d, 2 H, $J = 10.5$ Hz, PhCH_2), 3.94−3.76 (m, 5 H), 3.70 (ddd, 1 H, $J_{4,5} = 10.5$, $J_{5,6a} = J_{5,6b} = 3.2$ Hz, H-5). Anal. Calcd for $C_{41}H_{39}NO_5S$ (657.83): C, 74.86; H, 5.98; N, 2.13. Found: C, 74.92; H, 5.95; N, 2.08.

2-(2,3,4-Tri-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-*β*-D-glucopyranosyl)benzothiazole (35). To a solution of **34** (4.60 g, 7.00 mmol) in acetic anhydride (50 mL) was added a solution of 96% H_2SO_4 (0.7 mL) in acetic acid (24 mL). The reaction mixture was kept at rt for 1.5 h, then diluted with AcOEt (300 mL), washed with H_2O (3 × 100 mL) and saturated aqueous Na_2CO_3 (2 × 100 mL), dried (Na_2SO_4), and concentrated. The crude 6-*O*-acetylated derivative was treated with a freshly prepared ∼0.1 M solution of CH_3ONa in CH_3OH (50 mL) at rt for 3 h, then neutralized with acetic acid, and concentrated. The residue was eluted from a column of silica gel with 2.5:1 cyclohexane−AcOEt to give 2-(2,3,4-tri-*O*-benzyl-*β*-D-glucopyranosyl)benzothiazole (2.94 g) as a white solid. Mp 131−132 °C (Et_2O). $[\alpha]_D = -23.4$ (*c* 0.7, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.13−8.07 and 7.94−7.88 (2 m, 2 H, BTh), 7.65−6.90 (m, 17 H, 3 Ph, BTh), 5.00 and 4.94 (2 d, 2 H, $J = 10.5$ Hz, PhCH_2), 4.83−4.77 (m, 1 H, H-1), 4.88 and 4.73 (2 d, 2 H, $J = 10.5$ Hz, PhCH_2), 4.59 and 4.27 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 3.98−3.72 (m, 5 H), 3.61 (ddd, 1 H, $J_{4,5} = 10.0$, $J_{5,6a} = 2.5$, $J_{5,6b} = 1.5$ Hz, H-5). Anal. Calcd for $C_{34}H_{33}NO_5S$ (567.71): C, 71.93; H, 5.86; N, 2.47. Found: C, 72.02; H, 5.80; N, 2.36. To a stirred solution of this alcohol in pyridine (50 mL) was added *tert*-butylchlorodiphenylsilane (2.02 mL, 7.77 mmol). Stirring was continued for an additional 16 h, and then the reaction mixture was diluted with CH_3OH (2 mL) and concentrated. A solution of the residue in CH_2Cl_2 (200 mL) was washed with 1 M phosphate buffer at pH 7 (50 mL), dried (Na_2SO_4), and concentrated. The residue was triturated with CH_3CN (2 × 10 mL) to give **35** (3.00 g, 53% from **34**) as a white solid. The mother liquor was concentrated and eluted from a column of silica gel with 10:1 cyclohexane−AcOEt (containing 0.3% triethylamine) to give **35** (0.67 g, 12% from **34**) as a white solid. Mp 125−126 °C (cyclohexane). $[\alpha]_D = +32.6$ (*c* 0.9, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.13−8.07 and 7.94−7.88 (2 m, 2 H, BTh), 7.85−7.00 (m, 27 H, 5 Ph, BTh), 4.99 and 4.82 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.98 and 4.94 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.83 (d, 1 H, $J_{1,2} = 9.5$ Hz, H-1), 4.59 and 4.24 (2 d, 2 H, $J = 10.5$ Hz, PhCH_2), 4.07 (dd, 1 H, $J_{3,4} = 9.3$, $J_{4,5} = 9.5$ Hz, H-4), 4.04 (dd, 1 H, $J_{5,6a} = 2.8$, $J_{6a,6b} = 11.5$ Hz, H-6a), 3.99 (dd, 1 H, $J_{5,6b} = 2.0$ Hz, H-6b), 3.92 (dd, 1 H, $J_{2,3} = 9.0$ Hz, H-3), 3.81 (dd, 1 H, H-2), 3.57 (ddd, 1 H, H-5), 1.11 (s, 9 H, *t*-Bu). Anal. Calcd for $C_{50}H_{51}NO_5SSi$ (806.11): C, 74.50; H, 6.38; N, 1.74. Found: C, 74.46; H, 6.57; N, 1.86.

2,6-Anhydro-3,4,5-tri-*O*-benzyl-7-*O*-*tert*-butyldiphenylsilyl-*aldehydo*-D-*glycero*-D-*gulo*-heptopyranose (36). Ben-

zothiazolyl *C*-glucoside **35** (2.42 g, 3.00 mmol) was treated as described for the preparation of **7**. After a similar workup the residue was eluted from a short column (3 × 10 cm, diameter × height) of silica gel with 5:1 cyclohexane−AcOEt to afford syrupy **36** (1.94 g, 92%) ca. 95% pure by ^{1}H NMR analysis. ^{1}H NMR (300 MHz): δ 9.62 (d, 1 H, $J_{1,2}$ = 1.5 Hz, H-1), 7.55−7.15 (m, 25 H, 5 Ph), 4.95 (s, 2 H, PhCH_2), 4.94 and 4.81 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.86 and 4.70 (2 d, 2 H, J = 10.5 Hz, PhCH_2), 4.02−3.97 (m, 2 H, 2 H-7), 3.89 (dd, 1 H, $J_{3,4}$ = 8.2, $J_{4,5}$ = 9.0 Hz, H-4), 3.83 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, H-2), 3.81 (dd, 1 H, $J_{5,6}$ = 9.5 Hz, H-5), 3.70 (dd, 1 H, H-3), 3.42 (ddd, 1 H, $J_{6,7a}$ = $J_{6,7b}$ = 2.0 Hz, H-6), 1.11 (s, 9 H, *t*-Bu).

Methyl 8,12-Anhydro-2,3,4,9,10,11-hexa-*O*-benzyl-13-*O*-*tert*-butyldiphenylsilyl-6,7-dideoxy-α-D-*glycero*-D-*gulo*-D-*gluco*-tridec-6-(*Z*,*E*)-eno-1,5-pyranoside (37). The aldehyde **36** (1.05 g, 1.50 mmol) was treated with **21** (0.84 g, 1.00 mmol) as described for the preparation of **22** to give, after column chromatography on silica gel (10:1 cyclohexane−AcOEt), syrupy **37** as a ca. 7:1 mixture of *Z*,*E*-isomers (0.95 g, 84%). Analytical samples of (*Z*)-**37** and (*E*)-**37** were obtained by column chromatography on silica gel (15:1 cyclohexane−AcOEt). Eluted first was (*Z*)-**37**. $[\alpha]_D$ = +0.7 (*c* 1.5, $CHCl_3$). ^{1}H NMR (C_6D_6, 300 MHz): δ 8.05−6.95 (m, 40 H, 8 Ph), 5.80 (dd, 1 H, $J_{5,6}$ = 7.0, $J_{6,7}$ = 11.0 Hz, H-6), 5.72 (dd, 1 H, $J_{7,8}$ = 7.2 Hz, H-7), 5.11 and 4.95 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 5.01 and 4.82 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.94 (s, 2 H, PhCH_2), 4.80 (dd, 1 H, $J_{4,5}$ = 10.0 Hz, H-5), 4.78 and 4.71 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.75 and 4.64 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.68 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.56 and 4.48 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.50 (dd, 1 H, $J_{8,9}$ = 9.0 Hz, H-8), 4.27 (dd, 1 H, $J_{2,3}$ = 9.8, $J_{3,4}$ = 8.8 Hz, H-3), 4.04 (dd, 1 H, $J_{10,11}$ = $J_{11,12}$ = 9.5 Hz, H-11), 4.03 (dd, 1 H, $J_{12,13a}$ = 1.0, $J_{13a,13b}$ = 12.0 Hz, H-13a), 3.92 (dd, 1 H, $J_{12,13b}$ = 1.5 Hz, H-13b), 3.71 (dd, 1 H, $J_{9,10}$ = 9.5 Hz, H-10), 3.57 (dd, 1 H, H-2), 3.47 (dd, 1 H, H-9), 3.41 (dd, 1 H, H-4), 3.20 (ddd, 1 H, H-12), 3.13 (s, 3 H, OCH_3), 1.20 (s, 9 H, *t*-Bu). Anal. Calcd for $C_{72}H_{78}O_{10}Si$ (1131.50): C, 76.43; H, 6.95. Found: C, 76.61; H, 7.04. Eluted second was (*E*)-**37**. $[\alpha]_D$ = +5.0 (*c* 1.5, $CHCl_3$). ^{1}H NMR (C_6D_6, 300 MHz) selected data: δ 6.32 (dd, 1 H, $J_{6,7}$ = 15.5, $J_{7,8}$ = 5.5 Hz, H-7), 6.24 (dd, 1 H, $J_{5,6}$ = 4.5 Hz, H-6), 4.69 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.43 (dd, 1 H, $J_{8,9}$ = 9.3 Hz, H-8), 4.30 (dd, 1 H, $J_{2,3}$ = 9.5, $J_{3,4}$ = 9.2 Hz, H-3), 4.04 (d, 2 H, $J_{12,13}$ = 2.0 Hz, 2 H-13), 3.97 (dd, 1 H, $J_{10,11}$ = 8.7, $J_{11,12}$ = 9.0 Hz, H-11), 3.80 (dd, 1 H, $J_{4,5}$ = 9.2 Hz, H-5), 3.69 (dd, 1 H, $J_{9,10}$ = 9.3 Hz, H-10), 3.62 (dd, 1 H, H-2), 3.42 (dd, 1 H, H-4), 3.37 (dd, 1 H, H-9), 3.28 (dt, 1 H, H-12), 3.18 (s, 3 H, OCH_3), 1.20 (s, 9 H, *t*-Bu). MALDI-TOF MS (1131.50): *m*/*z* 1154.5 (M + Na), 1170.6 (M + K). Anal. Calcd for $C_{72}H_{78}O_{10}Si$: C, 76.43; H, 6.95. Found: C, 76.68; H, 7.06.

(Methyl 8,12-anhydro-2,3,4,9,10,11-hexa-*O*-benzyl-6,7,-13-trideoxy-α-D-*glycero*-D-*gulo*-D-*gluco*-tridec-6-(*Z*,*E*)-eno-1,5-pyranosid-13-yl)triphenylphosphonium Iodide (38). A solution of **37** (905 mg, 0.80 mmol) and *n*-$Bu_4NF{\cdot}3H_2O$ (757 mg, 2.40 mmol) in distilled THF (16 mL) was refluxed for 2 h, then cooled to rt, diluted with 1 M phosphate buffer at pH 7 (30 mL), and extracted with Et_2O (2 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with 2:1 cyclohexane−AcOEt to give methyl 8,12-anhydro-2,3,4,9,10,-11-hexa-*O*-benzyl-6,7-dideoxy-α-D-*glycero*-D-*gulo*-D-*gluco*-tridec-6-(*Z*,*E*)-eno-1,5-pyranoside (543 mg). ^{1}H NMR (300 MHz) selected data for the *Z*-isomer: δ 5.79 (dd, 1 H, $J_{5,6}$ = 6.5, $J_{6,7}$ = 11.5 Hz, H-6), 5.61 (dd, 1 H, $J_{7,8}$ = 8.5 Hz, H-7), 4.54 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.16 (dd, 1 H, $J_{4,5}$ = 9.5 Hz, H-5), 3.41 (s, 3 H, CH_3), 2.54 (dd, 1 H, $J_{13a,OH}$ = $J_{13b,OH}$ = 6.9 Hz, OH). MALDI-TOF MS (893.10): *m*/*z* 915.5 (M + Na), 931.6 (M + K). To a vigorously stirred solution of the alcohol, triphenylphosphine (320 mg, 1.22 mmol), and imidazole (166 mg, 2.43 mmol) in anhydrous toluene (12 mL) was added iodine (310 mg, 1.22 mmol). The mixture was refluxed for 1 h, then cooled to rt, filtered through a pad of Celite, and concentrated. A solution of the residue in CH_2Cl_2 (100 mL) was washed with 5% aqueous $Na_2S_2O_3$ (2 × 30 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with CH_2Cl_2–cyclohexane (from 2:1 to 10:1) to give methyl 8,12-anhydro-2,3,4,9,10,11-hexa-*O*-benzyl-6,7,13-trideoxy-13-iodo-α-D-*glycero*-D-*gulo*-D-*gluco*-tridec-6-(*Z*,*E*)-eno-1,5-pyranoside (537 mg). ^{1}H NMR (300 MHz) selected data for the *Z*-isomer: δ 5.72−5.67 (m, 2 H, H-6, H-7), 4.56 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.01 (dd, 1 H, $J_{2,3}$ = 10.0, $J_{3,4}$ = 8.5 Hz, H-3), 3.53 (dd, 1 H, H-2), 3.43 (s, 3 H, CH_3). MALDI-TOF MS (1002.99): *m*/*z* 1026.9 (M + Na), 1043.1 (M + K). A mixture of iodide and triphenylphosphine (1.40 g, 53.50 mmol) was stirred at 120 °C under a nitrogen atmosphere for 4 h, cooled to rt, triturated with toluene (10 mL) and then Et_2O (3 × 10 mL), and dried to give **38** (570 mg, 56%) as a white solid. ^{1}H NMR (300 MHz) selected data for the *Z*-isomer: δ 5.47 (dd, 1 H, $J_{5,6}$ = 5.0, $J_{6,7}$ = 11.5 Hz, H-6), 5.12 (dd, 1 H, $J_{7,8}$ = 5.5 Hz, H-7), 4.57 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 3.86 (dd, 1 H, $J_{2,3}$ = 9.5, $J_{3,4}$ = 9.0 Hz, H-3), 3.45 (dd, 1 H, H-2), 3.17 (dd, 1 H, $J_{4,5}$ = 10.0 Hz, H-4), 3.10 (s, 3 H, CH_3). Anal. Calcd for $C_{74}H_{74}IO_9P$ (1265.28): C, 70.25; H, 5.90. Found: C, 70.51; H, 6.04.

Trisaccharide 39. The aldehyde **36** (182 mg, 0.26 mmol) was treated with **38** (253 mg, 0.20 mmol) as described for the preparation of **22** to give, after column chromatography on silica gel (6:1 cyclohexane−AcOEt), syrupy **39** as a ca. 1.5:1 mixture of *Z*,*E*-isomers (219 mg, 70%). ^{1}H NMR (300 MHz) selected data for the 6*Z*,13*Z*-isomer: δ 5.85 (dd, 1 H, $J_{5,6}$ = 5.0, $J_{6,7}$ = 11.0 Hz, H-6), 5.79 (dd, 1 H, $J_{7,8}$ = 4.5 Hz, H-7), 5.78−5.71 (m, 2 H, H-13, H-14), 3.35 (s, 3 H, OCH_3), 1.23 (s, 9 H, *t*-Bu). ^{1}H NMR (300 MHz) selected data for the 6*Z*,13*E*-isomer: δ 6.31 (dd, 1 H, J = 6.0, 16.0 Hz), 6.21 (dd, 1 H, J = 4.8, 16.0 Hz), 5.85 (dd, 1 H, $J_{5,6}$ = 5.0, $J_{6,7}$ = 11.0 Hz, H-6), 5.79 (dd, 1 H, $J_{7,8}$ = 4.5 Hz, H-7), 3.40 (s, 3 H, CH_3), 1.20 (s, 9 H, *t*-Bu). MALDI-TOF MS (1560.03): *m*/*z* 1582.8 (M + Na), 1599.4 (M + K). Anal. Calcd for $C_{100}H_{106}IO_{14}Si$: C, 76.99; H, 6.85. Found: C, 77.36; H, 7.12.

Trisaccharide 40. The trisaccharide **39** (780 mg, 0.50 mmol) was treated as described for the preparation of **38**. The crude product was eluted from a column of silica gel with 1:1 CH_2Cl_2–acetone to give **40** (618 mg, 73%) as an amorphous solid ca. 95% pure by TLC and NMR analysis.

Tetrasaccharide 41. The aldehyde **36** (363 mg, 0.52 mmol) was treated with **40** (677 mg, 0.40 mmol) as described for the preparation of **22** to give, after column chromatography on silica gel (9:1 cyclohexane−AcOEt), **41** as a syrup (596 mg, 75%). MALDI-TOF MS (1988.56): *m*/*z* 2012.3 (M + Na), 2027.6 (M + K). Anal. Calcd for $C_{128}H_{134}O_{18}Si$: C, 77.31; H, 6.79. Found: C, 77.09; H, 6.90.

Tetrasaccharide 42. The tetrasaccharide **41** (595 mg, 0.30 mmol) was treated as described for the preparation of **38**. The crude product was eluted from a column of silica gel with 1:1 CH_2Cl_2–acetone to give **42** (396 mg, 62%) as an amorphous solid ca. 95% pure by TLC and NMR analysis.

Pentasaccharide 43. The aldehyde **36** (91 mg, 0.13 mmol) was treated with **42** (212 mg, 0.10 mmol) as described for the preparation of **28** to give, after column chromatography on silica gel (9:1 cyclohexane−AcOEt), **43** as a syrup (180 mg, 75%). MALDI-TOF MS (2417.10): *m*/*z* 2439.8 (M + Na), 2455.6 (M + K). Anal. Calcd for $C_{156}H_{162}O_{22}Si$: C, 77.52; H, 6.76. Found: C, 77.79; H, 6.88.

Methyl 2,3,4,9,10,11,13-Hepta-*O*-acetyl-8,12-anhydro-6,7-dideoxy-α-D-*glycero*-D-*gulo*-D-*gluco*-trideco-1,5-pyranoside (44Ac). The disaccharide **37** (113 mg, 0.10 mmol) was desilylated as described for the preparation of **38** to give, after column chromatography (2:1 cyclohexane−AcOEt), methyl 8,-12-anhydro-2,3,4,9,10,11-hexa-*O*-benzyl-6,7-dideoxy-α-D-*glycero*-D-*gulo*-D-*gluco*-tridec-6-(*Z*,*E*)-eno-1,5-pyranoside. A mixture of this alcohol, 20% palladium hydroxide on carbon (100 mg), and 1:1 CH_3OH−AcOEt (5 mL) was degassed under a vacuum and saturated with hydrogen (by a H_2-filled balloon) three times. The suspension was stirred at rt for 6 h under a positive pressure of hydrogen (7 bar), then filtered through a plug of cotton, washed with CH_3OH and H_2O, and concentrated to give **44**. $[\alpha]_D$ = +56.0 (*c* 0.8, CH_3OH) (lit.[5a] $[\alpha]_D$ = +61 (*c* 0.6, CH_3OH); lit.[27] $[\alpha]_D$ = +88 (*c* 1, CH_3OH)). A solution of **44** and

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4-(dimethylamino)pyridine (5 mg) in pyridine (2 mL) and acetic anhydride (2 mL) was kept at rt for 8 h, and then concentrated. The residue was eluted from a column of silica gel with 1:1 cyclohexane−AcOEt to give **44Ac** (57 mg, 88%) as a white solid. Mp 175−176 °C (AcOEt−cyclohexane). $[\alpha]_D = +69.5$ (*c* 0.9, $CHCl_3$) (lit.[27] mp 172 °C). $[\alpha]_D = +55$ (*c* 1, $CHCl_3$) (lit.[5m] mp 166−168 °C). $[\alpha]_D = +15.3$ (*c* 0.6, $CHCl_3$) (lit.[5h] $[\alpha]_D = +65$ (*c* 0.5, $CHCl_3$); lit.[5a] $[\alpha]_D = +63$ (*c* 0.7, $CHCl_3$)). ^{1}H NMR (300 MHz): δ 5.42 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.8$ Hz, H-3), 5.16 (dd, 1 H, $J_{9,10} = J_{10,11} = 9.5$ Hz, H-10), 5.02 (dd, 1 H, $J_{11,12} = 9.7$ Hz, H-11), 4.90−4.79 (m, 4 H), 4.23 (dd, 1 H, $J_{12,13a} = 5.5$, $J_{13a,13b} = 12.5$ Hz, H-13a), 4.07 (dd, 1 H, $J_{12,13b} = 2.0$ Hz, H-13b), 3,73 (ddd, 1 H, $J_{4,5} = 9.5$, $J_{5,6a} = 7.0$, $J_{5,6b} = 1.5$ Hz, H-5), 3.61 (ddd, 1 H, H-12), 3.38 (ddd, 1 H, $J_{7a,8} = 10.0$, $J_{7b,8} = 1.0$, $J_{8,9} = 9.0$ Hz, H-8), 3.35 (s, 3 H, OCH_3), 2.10−1.99 (7 s, 21 H, 7 Ac), 1.84−1.74 and 1.46−1.38 (2 m, 4 H, 2 H-6, 2 H-7). Anal. Calcd for $C_{28}H_{40}O_{17}$ (648.63): C, 51.85; H, 6.22. Found: C, 51.72; H, 6.20.

Trisaccharide 45Ac. The trisaccharide **39** (78 mg, 0.05 mmol) was desilylated as described for the preparation of **40**. A mixture of the resulting alcohol, 20% palladium hydroxide on carbon (70 mg), and 1:1 CH_3OH−AcOEt (5 mL) was degassed under a vacuum and saturated with hydrogen (by a H_2-filled balloon) three times. The suspension was stirred at rt for 8 h under a positive pressure of hydrogen (7 bar), then filtered through a plug of cotton, washed with distilled DMF and H_2O, and concentrated to give **45** as an amorphous solid. $[\alpha]_D = +40.5$ (*c* 0.4, H_2O). A solution of **45** and 4-(dimethylamino)pyridine (5 mg) in pyridine (2 mL) and acetic anhydride (2 mL) was kept at rt for 12 h, and then concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 1:1 to 1:2) to give **45Ac** (38 mg, 81%) as a white solid. Mp 168−169 °C (AcOEt−cyclohexane). $[\alpha]_D = +37.1$ (*c* 1.1, $CHCl_3$). ^{1}H NMR (300 MHz) selected data: δ 5.45 (dd, 1 H, $J_{2,3} = 10.0$, $J_{3,4} = 10.5$ Hz, H-3), 5.06 (dd, 1 H, $J_{17,18} = 9.0$, $J_{18,19} = 10.5$ Hz, H-18), 4.84 (dd, 1 H, $J_{1,2} = 5.5$ Hz, H-2), 4.24 (dd, 1 H, $J_{19,20a} = 5.0$, $J_{20a,20b} = 12.5$ Hz, H-20a), 4.12 (dd, 1 H, $J_{19,20b} = 2.5$ Hz, H-20b), 3.65 (ddd, 1 H, H-19), 3.37 (s, 3 H, OCH_3), 2.13−1.99 (10 s, 30 H, 10 Ac). MALDI-TOF MS (934.91): *m*/*z* 958.0 (M + Na), 974.4 (M + K). Anal. Calcd for $C_{41}H_{58}O_{24}$: C, 52.67; H, 6.25. Found: C, 52.79; H, 6.30.

Tetrasaccharide 46Ac. The tetrasaccharide **41** (80 mg, 0.04 mmol) was desilylated and hydrogenated as described for the preparation of **45** to give **46** as an amorphous solid. $[\alpha]_D = +32$ (*c* 0.5, H_2O). A solution of **46** and 4-(dimethylamino)-pyridine (10 mg) in pyridine (2 mL) and acetic anhydride (2 mL) was kept at rt for 12 h, and then concentrated. The residue was eluted from a column of silica gel with 1:1 cyclohexane−AcOEt to give **46Ac** (34 mg, 69%) as a white solid. Mp 86−90 °C (AcOEt−cyclohexane). $[\alpha]_D = +30$ (*c* 0.3, $CHCl_3$). ^{1}H NMR (300 MHz) selected data: δ 5.45 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 4.22 (dd, 1 H, $J_{26,27a} = 2.5$, $J_{27a,27b} = 12.0$ Hz, H-27a), 4,10 (dd, 1 H, $J_{26,27b} = 5.5$ Hz, H-27b), 3.74−3.71 (m, 1 H, H-5), 3.65 (ddd, 1 H, H-26), 2.13−1.99 (13 s, 39 H, 13 Ac). MALDI-TOF MS (1221.20): *m*/*z* 1244.0 (M + Na), 1260.3 (M + K). Anal. Calcd for $C_{54}H_{76}O_{31}$: C, 53.11; H, 6.27. Found: C, 53.34; H, 6.38.

Pentasaccharide 47Ac. The pentasaccharide **43** (73 mg, 0.03 mmol) was desilylated and hydrogenated as described for the preparation of **45** to give **47** as an amorphous solid. $[\alpha]_D = +6.3$ (*c* 0.3, H_2O). A solution of **47** and 4-(dimethylamino)-pyridine (5 mg) in pyridine (1 mL) and acetic anhydride (1 mL) was kept at rt for 16 h, and then concentrated. The residue was eluted from a column of silica gel with 2:1 AcOEt−cyclohexane to give **47Ac** (28 mg, 60%) as a white solid. Mp 196−198 °C (CH_3OH). $[\alpha]_D = +24.4$ (*c* 0.4, $CHCl_3$). ^{1}H NMR (500 MHz) selected data: δ 5.43 (dd, 1 H, $J_{2,3} = 9.9$, $J_{3,4} = 9.4$ Hz, H-3A), 5.17 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.4$ Hz, H-3E), 5.11 and 5.10 (2 dd, 3 H, $J_{2,3} = J_{3,4} = 9.4$ Hz, H-3B, H-3C, H-3D), 5.03 (dd, 1 H, $J_{4,5} = 10.1$ Hz, H-4E), 4.89 (d, 1 H, $J_{1,2} = 3.7$ Hz, H-1A), 4.88 (dd, 1 H, $J_{1,2} = 9.9$ Hz, H-2E), 4.87 (dd, 1 H, $J_{4,5} = 9.6$ Hz, H-4A), 4.86 (dd, 1 H, H-2A), 4.83, 4.82, 4.81, and 4.80 (4 dd, 6 H, $J = 9.5$, 9.5 Hz, H-2B, H-2C, H-2D, H-4B, H-4C, H-4D), 4.20 (dd, 1 H, $J_{5,6a} = 5.6$, $J_{6a,6b} = 12.2$ Hz, H-6aE), 4.10 (dd, 1 H, $J_{5,6b} = 2.3$ Hz, H-6bE), 3.71 (ddd, 1 H, $J_{5,6a} = 2.0$, $J_{5,6b} = 8.5$ Hz, H-5A), 3.64 (ddd, 1 H, H-5E), 3.37 (s, 3 H, OCH_3), 2.10−1.99 (14 s, 48 H, 16 Ac). MALDI-TOF MS (1507.49): *m*/*z* 1530.4 (M + Na), 1547.1 (M + K). Anal. Calcd for $C_{67}H_{94}O_{38}$: C, 53.38; H, 6.28. Found: C, 53.50; H, 6.33.

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