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Stereoselective Syntheses of the Conjugation-Ready, Downstream Disaccharide and Phosphorylated Upstream, Branched Trisaccharide Fragments of the O-PS of *Vibrio cholerae* O139

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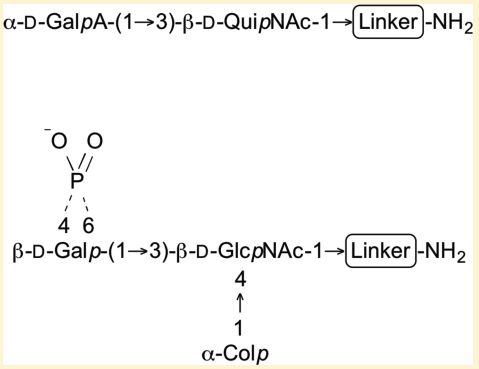
Supporting Information

ABSTRACT: *N*-Bromosuccinimide-mediated 4,6-*O*-benzylidene ring opening in 8-azido-3,6-dioxaoctyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-*β*-D-glucopyranoside afforded the corresponding 4-*O*-benzoyl-6-bromo-6-deoxy analogue, which was coupled with 3,4,6-tri-*O*-acetyl-2-*O*-benzyl-*α*-D-galactopyranosyl chloride to give the 1,2-*cis* *α*-linked disaccharide as the major product. Conventional hydroxyl group manipulation in the latter and products of further conversions gave the desired, functionalized disaccharide *α*-D-Gal*p*A-(1→3)-*β*-D-Qui*p*NAc. The rare, foregoing sequence forms the downstream end in the O-specific polysaccharide of both *Vibrio cholerae* O22 and O139. Halide-assisted glycosylation at 4[I]-OH in 8-azido-3,6-dioxaoctyl 6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)-2-trichloroacetamido-*β*-D-glucopyranoside, obtained by regioselective reductive opening of the acetal ring in the parent 4[I],6[I]-*O*-benzylidene derivative, with 2,4-di-*O*-benzyl-*α*-colitosyl bromide, gave exclusively the *α*-linked trisaccharide. The latter was sequentially deacetylated and selectively benzylated to give 8-azido-3,6-dioxaoctyl 2,4-di-*O*-benzyl-3,6-dideoxy-*α*-L-*xylo*-hexopyranosyl-(1→4)-[3-*O*-benzyl-*β*-D-galactopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-*β*-D-glucopyranoside. Subsequent selective phosphorylation of the triol, thus obtained, with 2,2,2-trichloroethyl phosphorodichloridate afforded isomeric (*R*,*S*)-(P)-4[II],6[II]-cyclic phosphates, which were both obtained in crystalline form and fully characterized. Each of the latter was globally deprotected by catalytic (Pd/C) hydrogenation/hydrogenolysis to give the desired, amino-functionalized, spacer-equipped, phosphorylated upstream trisaccharide fragment of the O-PS of *V. cholerae* O139.



INTRODUCTION

This laboratory has been engaged in developing conjugate vaccines from fragments of bacterial lipopolysaccharides for a number of years.[1−4] To evaluate specificity,[5,6] we often use in these studies synthetic oligosaccharide probes that mimic O-antigens. We intend to perform such a study also in connection with our ongoing work toward a synthetic vaccine for a disease caused by *Vibrio cholerae* O139.[7−9] The O-antigen of *V. cholerae* O139 is a phosphorylated hexasaccharide [sequence FD(E)-CBA, Figure 1] consisting of five different monosaccharides.[10] Collecting a wide range of fragments of the protective antigen requires extensive synthetic work. We often synthesize[11−13] such fragments in spacer-equipped form to make them amenable for conjugation to proteins because use of glycoconjugates made from such substances often helps in solving questions that arise during immunological/immunogenicity studies. Synthesis of every individual fragment of the hexasaccharide (Figure 1) presents its own problems, the most formidable challenge being construction of the 1,2-*cis* glycosidic linkage, which is present also in target compounds of this communication. Construction of the *α*-colitosyl linkage to form fragments of the hexasaccharide (Figure 1) has been largely

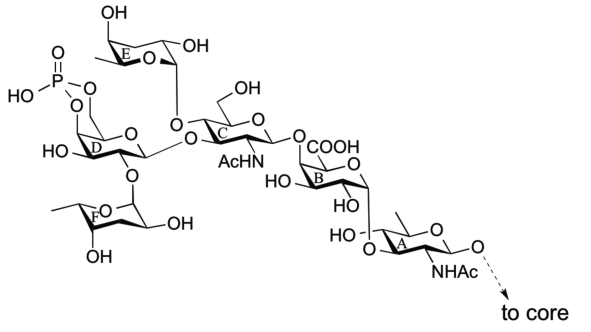


Figure 1. Structure of the O-antigen of *V. cholerae* O139 lipopolysaccharide.

solved,[12,14] but the first synthesis of the sequence *α*-D-Gal*p*A-(1→3)-*β*-D-Qui*p*NAc (sequence BA) is yet to be reported. The latter forms the downstream end in the O-PS of both *V. cholerae* O139 and O22 (Figures 1 and 2, respectively).[10,15] Because synthesis of virtually any disaccharide is generally not

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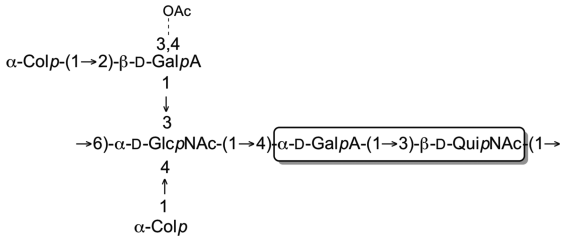

Figure 2. Structure of the repeating unit of O-PS of *V. cholerae* O22, the highlighted disaccharide showing the sequence BA present also in O-PS of *V. cholerae* O139.

considered difficult, the absence of synthesis of the sequence BA underscores the difficulty of the task. Here, we report on the first syntheses of the linker-equipped downstream disaccharide **10** and the phosphorylated upstream trisaccharide **20** [sequences BA and D(E)C, respectively, Figure 1]. The syntheses of the aforementioned, end fragments were important for choosing and optimizing the synthetic and protecting group strategy to be used in the planned synthesis of the complete hexasaccharide, which is a much more involved, yet to be solved task.

RESULTS AND DISCUSSION

Synthesis of the downstream disaccharide **10** started (Scheme 1) with the spacer-equipped glycosyl acceptor 8-azido-3,6-dioxaoctyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-*β*-D-glucopyranoside (**1**).[16] Construction of the 1,2-*cis* *α*-D-galactopyranosidic linkage, to arrive at sequence BA, required use of a glycosyl donor bearing at C-2 a group incapable of anchimeric assistance.[17] For that purpose, we chose 2-*O*-benzylated galactosyl chloride **2**[18] and treated it in CH_2Cl_2 with **1** at subzero temperature under silver triflate catalysis. These conditions are known[19] to favor 1,2-*cis* glycosidation. The reaction was fast and high yielding (4 h, ∼90%), but the stereoselectivity of formation of the *α*-glycosidic linkage was poor (*α*/*β* = 2:1). It is known that stereoselectivity of glycosylation can vary depending on solvent and that ether-type solvents, such as 1,2-dimethoxyethane[20] and particularly diethyl ether,[21] favor formation of the 1,2-*cis* glycosidic linkage. Therefore, in an attempt to enhance formation of the desired *α*-linkage by solvent effect, limited by solubility of **1** in Et_2O, we performed condensation of **1** with **2** in 1:1 CH_2Cl_2–Et_2O. The selectivity improved (*α*/*β* = 4:1), but we deemed looking for ways to further enhance the yield of the *α*-linked product warranted. Experimental evidence has shown[22] that unlike fast substitution reactions, the slow S_N1-type reactions, such as glycosylations with donors bearing nonparticipating groups at C-2, tend to occur without inversion of configuration. In addition, reactivity of hydroxyl groups in carbohydrates can be controlled to some extent by substituents at neighboring positions;[23] namely, their reactivity can be increased by vicinal electron-donating substituents and vice versa. Accordingly, regioselective ring opening in the 4,6-*O*-benzylidene acetal in **1** with *N*-bromosuccinimide,[24] to form **4** (85%, Scheme 1), positioned the electron-withdrawing benzoyl group at C-4 and simultaneously deoxygenated position 6, which was desirable to effect later conversion of Glc*p*NAc into Qui*p*NAc. Subsequent silver triflate mediated glycosylation of **4** with galactosyl chloride **2**, in CH_2Cl_2 as solvent, gave predominantly the desired *α*-linked disaccharide **5*α***, together with a small amount of the *β*-anomer **5*β*** (overall yield of glycosylation, 84%; *α*/*β* = 11:1). Unlike in the case of coupling product **3**, running the reaction in solvent containing a large proportion of Et_2O had no effect on stereoselectivity and only made the reaction considerably slower. The ^{13}C NMR spectrum of disaccharide **5*α*** showed signals characteristic of the presence of both donor and acceptor moieties, while the *α*-configuration of the interglycosidic linkage was established from the ^1H NMR spectrum (*δ* 4.93, H-1^{II}, $J_{1,2}$ = 3.6 Hz).

Zemplén de-*O*-acylation of **5*α*** gave tetraol **6** in virtually quantitative yield, and subsequent isopropylidenation (2,2-dimethoxypropane and camphorsulfonic acid in DMF at 45 °C) gave selectively the 3^{II},4^{II}-*O*-isopropylidene derivative **7**. The location of the isopropylidene group in **7** (Scheme 1) was evident from the comparison of ^{13}C NMR spectra of **6** and **7**, the latter showing downfield shifts for C-3^{II} and C-4^{II} (from δ_C 69.5 to 76.5 and from 70.3 to 75.0 ppm, respectively), as a result of isopropylidenation at those positions.

The primary hydroxyl group in **7** was then regioselectively oxidized with [bis(acetoxy)iodo]benzene (BAIB) in the presence of 2,2,6,6-tetramethylpiperidinyloxy free radical (TEMPO).[25] For confirmation of structure and easier purification, the crude product of the oxidation was treated with benzyl bromide and potassium carbonate[26] in anhydrous DMF to provide benzyl uronate **8** (73% over two steps). The ^{13}C NMR spectrum of **8** showed a signal at δ_C 167.3 ppm, which confirms the presence of a carboxyl group in the oxidation product. It is worth noting that attempts to convert **6** directly into **9** (not described in the Experimental Section) gave complex mixtures. *O*-Deisopropylidenation (80% aq AcOH, 80 °C) of **8** was followed by catalytic hydrogenation/hydrogenolysis (Pd/C, H_2, rt), which affected one-pot transformation of azide to amine, multiple debenzylations, debromination at C-6^I, as well as conversion of the *N*-trichloroacetyl to *N*-acetyl group to afford the desired disaccharide **10**. The expected structure **10** was confirmed by mass and NMR spectra.

Thus far, only very few attempts to synthesize fragments of the hexasaccharide antigen of *V. cholerae* O139 have been reported.[11−14] Most notable are the two syntheses of the upstream, terminal tetrasaccharide sequence FD(E)C (Figure 1),[12,14] each having its characteristic advantage. The present synthesis of trisaccharide **20** (Scheme 2) incorporates the salient features of both approaches. First, it starts with compound **11** where the linker/spacer is already in place.[12] Thus, chemical manipulation with the fully assembled sequence,[14] other than final deprotection, can be avoided. Second, the synthesis was designed with the isomers yielding phosphorylation as the penultimate step,[14] but choosing protecting groups that allow global deprotection in one step, to afford the final product **20** in increased overall yield.

Accordingly, the 4^I,6^I-*O*-benzylidene ring in 8-azido-3,6-dioxaoctyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)-2-trichloroacetamido-*β*-D-glucopyranoside[16] (**11**) was regioselectively opened with $NaCNBH_3$ and HCl in THF[27] to give the crystalline 6^I-*O*-benzyl derivative **12** (92%). Compared to the ^{13}C NMR spectrum of **11**,[16] the signal for C-4^I in **12** showed significant upfield shift (by ∼ 10 ppm) because of the absence of the positive shift effect[28] of the benzylidene group, and the ^1H–^1H COSY cross-peak between H-4^I (*δ* 3.57 ppm) and the proton of the newly generated hydroxyl group (*δ* 3.66 ppm) confirmed that the reductive opening of the benzylidene acetal produced the 6^I- and not 4^I-benzyl ether. Because the shift effect of alkylation and alkylidination is similar, the difference in chemical shift for C-

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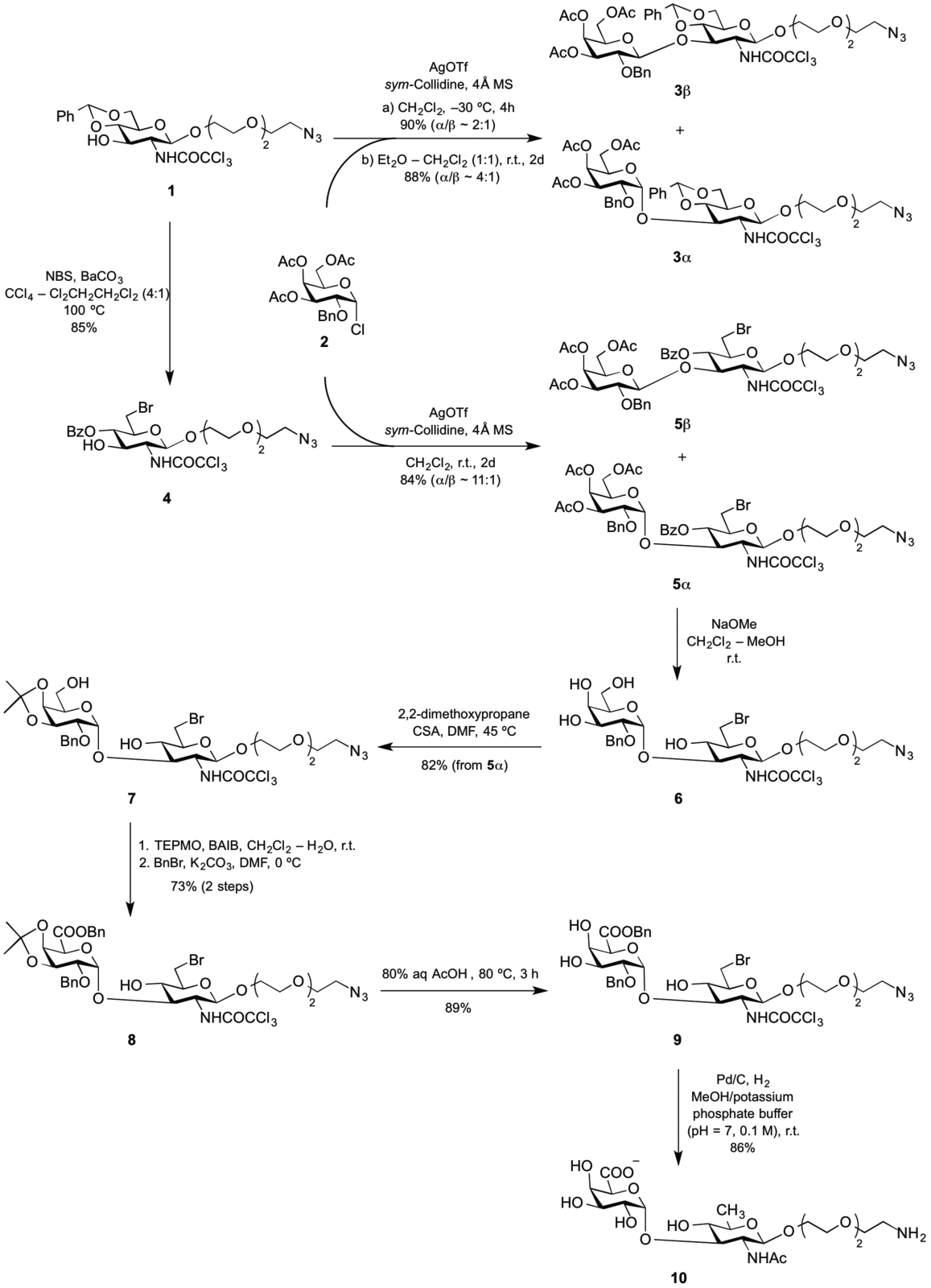
Scheme 1. Synthesis of the Spacer-Equipped Disaccharide 10



6^{I} in **11** and **12** is small and not diagnostic for the mode of opening of the benzylidene ring. The disaccharide acceptor **12**, thus formed, was subjected to halide-assisted[29] glycosylation with the α-colitosyl bromide **14** (made by treatment[30] of the corresponding β-ethyl thioglycoside **13**[31] with bromine) to give the trisaccharide **15** (95%). Identification of the coupling product **15** was based on its ^{1}H and ^{13}C NMR spectra, which included signals characteristic for presence of both the donor and the acceptor moieties. As expected, compared to the ^{13}C NMR spectrum of **12**, the signal of C-4^{I} (the site of glycosylation) was shifted downfield. The coupling constant (J = 3.0 Hz) shown by the doublet for the anomeric proton of

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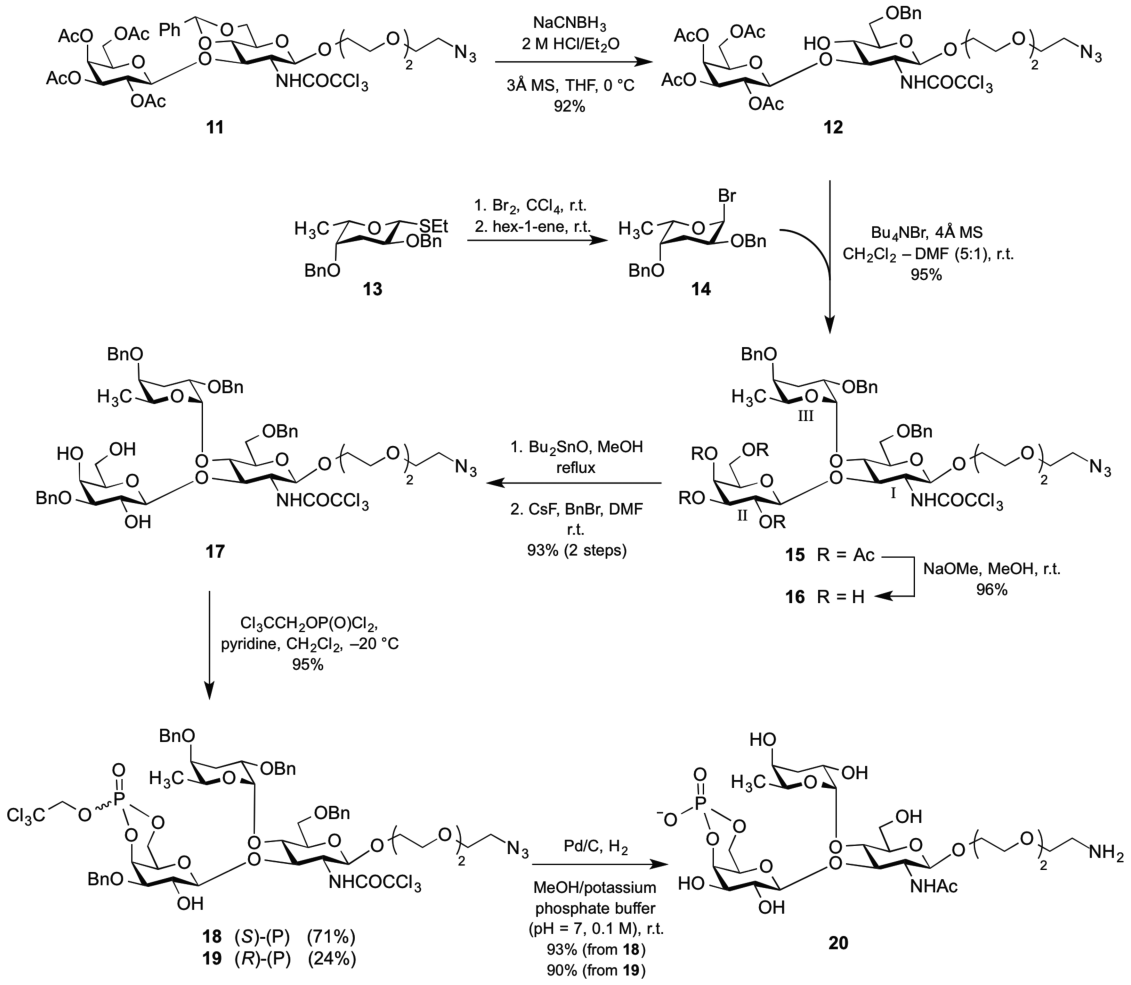
Scheme 2. Synthesis of the Spacer-Equipped, Phosphorylated Trisaccharide 20



the colitose residue (δ 5.07 ppm) confirmed formation of the α-glycosidic linkage, which was also supported[32] by the $^{1}J_{C\text{-}1,H\text{-}1}$ = 170.2 Hz.

De-*O*-acetylation of **15** through transesterification with methanolic sodium methoxide afforded 8-azido-3,6-dioxaoctyl 2,4-di-*O*-benzyl-3,6-dideoxy-α-L-*xylo*-hexopyranosyl-(1→4)-[β-D-galactopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**16**) in virtually theoretical yield. Subsequent selective benzylation at the 3^{II}-OH via stannylation gave the 3^{II}-*O*-benzyl derivative **17** (93%). Formation of the 4^{II}-*O*-benzyl isomer was not observed (TLC). Identification of compound **17** was based on its ^{13}C NMR spectrum, in which the signal for C-3^{II} was shifted downfield (δ 79.9 ppm) compared to δ 73.6 ppm in the spectrum of **16**.

Treatment of trisaccharide **17** with the phosphorylating reagent, 2,2,2-trichloroethyl phosphorodichloridate,[33,34] gave isomeric (*S*,*R*)-(P)-4^{II},6^{II}-cyclic 2,2,2-trichloroethyl phosphates **18** and **19** (~3:1, ^{31}P NMR). The isomers **18** and **19** were separated by chromatography and isolated in excellent combined yield. Both substances were obtained crystalline and fully characterized.

Global deprotection of the foregoing phosphate **18** was achieved in one step by catalytic hydrogenation/hydrogenolysis in the presence of Pd/C catalyst and pH = 7, 0.1 M potassium phosphate buffer, to protect the acid-labile[9] α-colitosyl group. In this way, the desired phosphorylated trisaccharide **20** was obtained in 93% yield. Contrary to our previous observation,[12] elevated pressure and temperature were not required to achieve smooth, complete deprotection by catalytic hydrogenation/hydrogenolysis. Because the same protecting groups were transformed in both situations, the likely explanation for the harsher conditions required previously was different activity of the Pd/C catalyst used.

Similar global deprotection of the other phosphate isomer **19** gave the same product **20** (^{1}H NMR, ^{13}C NMR, ^{31}P NMR, TLC, MS) in 90% yield. In addition to MS, the presence of the cyclic phosphate in **20** followed from the ^{31}P NMR spectrum, showing $^{3}J_{P,H}$ = 22.2 Hz.[35]

Many features in the present, successful synthetic approach will be incorporated in the future synthesis of the full O-antigen, the phosphorylated hexasaccharide [sequence FD(E)-CBA, Figure 1], which will be a much more involved project, not realized to date.

■ CONCLUSIONS

We have developed an efficient approach to synthesize the rare disaccharide sequence **10**, which forms the downstream end in the O-PS of both *V. cholerae* O22 and O139 and the phosphorylated upstream, branched trisaccharide **20**, which is one of the terminal determinants of the O-specific polysaccharide of *V. cholerae* O139. The final, amino-functionalized spacer-equipped fragments **10** and **20** are ready for conjugation to proteins.

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EXPERIMENTAL SECTION

General Methods. Optical rotations were measured at ambient temperature for solution in $CHCl_3$ unless stated otherwise. All reactions were monitored by thin-layer chromatography (TLC) on silica gel 60 coated glass slides. Column chromatography was performed by elution from prepacked columns of silica gel and monitored with the evaporative light scattering detector. Nuclear magnetic resonance (NMR) spectra were measured at 500 or 600 MHz for ^{1}H, 125 or 150 MHz for ^{13}C, and 162 MHz for ^{31}P. Solvent peaks were used as internal reference relative to TMS for ^{1}H and ^{13}C chemical shifts (ppm); ^{31}P chemical shifts (ppm) were reported relative to 85% H_3PO_4 in D_2O external reference. Assignments of NMR signals were made by homonuclear and heteronuclear two-dimensional correlation spectroscopy, run with the software supplied with the spectrometers. When reporting assignments of NMR signals, nuclei associated with the spacer are denoted with a prime; sugar residues are serially numbered, beginning with the one bearing the aglycon, and are identified by a Roman numeral superscript in listings of signal assignments, with nuclei of the colitose residue as III (see Scheme 2, **15**). The density of 2,2,2-trichloroethyl phosphorodichloridate (Aldrich/Sigma, $d \approx 1.7$ g/mL at 20 °C) was determined by weighing of 1 mL of the reagent. Palladium-on-charcoal catalyst (5%, Escat 103) was purchased from Engelhard Industries. Solutions in organic solvents were dried with anhydrous Na_2SO_4 and concentrated at 40 °C/2 kPa.

8-Azido-3,6-dioxaoctyl 4,6-*O*-Benzylidene-2-deoxy-2-trichloroacetamido-3-*O*-(3,4,6-tri-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranosyl)-β-D-glucopyranoside (3α) and 8-Azido-3,6-dioxaoctyl 4,6-*O*-Benzylidene-2-deoxy-2-trichloroacetamido-3-*O*-(3,4,6-tri-*O*-acetyl-2-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside (3β). (a) A mixture of 8-azido-3,6-dioxaoctyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**1**)[16] (2.5 g, 4.39 mmol), powdered AgOTf (1.90 g, 7.46 mmol), and activated molecular sieves (4 Å, 7 g) in anhydrous CH_2Cl_2 (150 mL) was stirred under nitrogen for 1 h. The suspension was cooled to −30 °C, and a solution of 3,4,6-tri-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranosyl chloride (**2**)[18] (2.80 g, 6.76 mmol) in anhydrous CH_2Cl_2 (50 mL) containing *sym*-collidine (1.20 mL, 7.5 mmol) was added dropwise. The cooling was removed, and with continued stirring, the mixture was allowed to warm to room temperature. After 4 h, analysis by TLC (6:1 chloroform−acetone) indicated that all acceptor was consumed. The mixture was diluted with CH_2Cl_2 (100 mL) and filtered through a Celite pad. The filtrate was washed successively with 0.5 M aq HCl, aq $NaHCO_3$, and brine. The organic phase was coevaporated with water to remove excess *sym*-collidine, and chromatography (9:1 chloroform−acetone) gave first the β-linked disaccharide **3β** (1.25 g, 30%).

*Data for **3β**.* $[\alpha]_D^{20}$ = +13.2 (*c* 0.7, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.49−7.19 (m, 10 H, 2 Ph), 7.10 (d, 1 H, $J_{2,NH}$ = 7.2 Hz, NH), 5.59 (s, 1H, PhC*H*), 5.29 (dd, 1 H, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 1.0 Hz, H-4^{II}), 5.22 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1^{I}), 4.88 (dd, 1 H, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 3.5 Hz, H-3^{II}), 4.75 (d, 1 H, ^2J = 11.8 Hz, PhC*H*H), 4.65 (t partially overlapped, 1 H, *J* = 9.5 Hz, H-3^{I}), 4.63 (d, 1 H, $J_{1,2}$ = 7.7 Hz, H-1^{II}), 4.58 (d, 1 H, ^2J = 11.8 Hz, PhC*H*H), 4.37 (dd, 1 H, *J* = 4.8, 10.4 Hz, H-6$^{I}_a$), 4.13 (dd, 1 H, *J* = 6.8, 11.2 Hz, H-6$^{II}_a$), 3.99−3.96 (m, 1 H, H-6$^{II}_b$), 3.95−3.91 (m, 1 H, H-1′$_a$), 3.84−3.81 (m, 1 H, H-6$^{I}_b$), 3.80−3.75 (m, 2 H, H-4^{I}, H-1′$_b$), 3.73 (dt, 1 H, *J* = 1.0, 6.8, 7.6 Hz, H-5^{II}), 3.69−3.67 (m, 1 H, H-2^{II}), 3.67−3.61 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.58−3.54 (m, 1 H, H-5^{I}), 3.49−3.44 (m, 1 H, H-2^{I}), 3.39 (t, 2 H, *J* = 5.1 Hz, H-6′), 2.07, 2.01, 1.88 (3 s, 9 H, 3 COC*H*$_3$). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.4−170.0 (3 $OCOCH_3$), 162.0 ($NCOCCl_3$), 138.2, 136.9 (2 *ipso* Ph), 129.1−126.0 (Ar), 102.4 (C-1^{II}), 101.2 (PhCH), 99.4 (C-1^{I}), 92.2 (CCl_3), 78.9 (C-4^{I}), 76.8 (2C, C-2^{II}, C-3^{I}), 75.2 ($PhCH_2$), 72.4 (C-3^{II}), 70.7, 70.6, 70.5, 70.1 (C-2′, C-3′, C-4′, C-5′), 70.6 (C-5^{II}), 69.1 (C-1′), 68.6 (C-6^{I}), 67.3 (C-4^{II}), 66.2 (C-5^{I}), 61.4 (C-6^{II}), 59.6 (C-2^{I}), 50.6 (C-6′), 20.65, 20.64, 20.61 (3 $COCH_3$). HRMS (ESI-TOF): *m*/*z* $[M + NH_4]^+$ calcd for $C_{40}H_{53}Cl_3N_5O_{16}$ 964.2553, found 964.2549. Anal. Calcd for $C_{40}H_{49}Cl_3N_4O_{16}$: C, 50.67; H, 5.21; N, 5.91. Found: C, 50.76; H, 5.01; N, 5.65.

Continued elution gave the desired α-linked disaccharide **3α** (2.49 g, 60%, 90% overall, $\alpha/\beta \sim 2{:}1$).

*Data for **3α**.* $[\alpha]_D^{20}$ = +47.6 (*c* 0.7, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.38−7.04 (m, 10 H, 2 Ph), 7.21 (d, 1 H, $J_{2,NH}$ = 7.6 Hz, NH), 5.69 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1^{II}), 5.38 (dd, 1 H, $J_{3,4}$ = 3.2 Hz, $J_{4,5}$ = 1.1 Hz, H-4^{II}), 5.34 (s, 1H, PhC*H*), 5.27 (dd, 1 H, $J_{2,3}$ = 10.7 Hz, $J_{3,4}$ = 3.2 Hz, H-3^{II}), 5.12 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1^{I}), 4.62 (t, 1 H, *J* = 9.4 Hz, H-3^{I}), 4.50 (d, 1 H, ^2J = 12.4 Hz, PhC*H*H), 4.37 (d, 1 H, ^2J = 12.4 Hz, PhC*H*H), 4.33 (dd, 1 H, *J* = 5.0, 10.5 Hz, H-6$^{I}_a$), 4.28−4.25 (m, 1 H, H-5^{II}), 4.07 (dd, 1 H, *J* = 8.1, 10.9 Hz, H-6$^{II}_a$), 3.98−3.93 (m, 2 H, H-1′$_a$, H-6$^{II}_b$), 3.80−3.78 (m, 1 H, H-1′$_b$), 3.77−3.73 (m, 3 H, H-6$^{I}_b$, H-4^{I}, H-2^{II}), 3.70−3.64 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.63−3.61 (m, 1 H, H-2^{I}), 3.60−3.56 (m, 1 H, H-5^{I}), 3.41 (t, 2 H, *J* = 5.0 Hz, H-6′), 2.03, 2.02, 1.95 (3 s, 9 H, 3 COC*H*$_3$). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.4−169.9 (3 $OCOCH_3$), 162.0 ($NCOCCl_3$), 137.8, 139.8 (2 *ipso* Ph), 129.4−126.2 (Ar), 101.8 (PhCH), 99.5 (C-1^{I}), 96.3 (C-1^{II}), 92.4 (CCl_3), 82.8 (C-4^{I}), 72.8 (C-3^{I}), 72.5 (C-2^{II}), 71.7 ($PhCH_2$), 70.6, 70.5, 70.4, 70.0 (C-2′, C-3′, C-4′, C-5′), 68.9 (C-1′), 68.8 (C-3^{II}), 68.7 (C-6^{I}), 67.9 (C-4^{II}), 66.2 (C-5^{II}), 65.5 (C-5^{I}), 61.0 (C-6^{II}), 58.2 (C-2^{I}), 50.6 (C-6′), 20.7−20.5 (3 $COCH_3$). HRMS (ESI-TOF): *m*/*z* $[M + NH_4]^+$ calcd for $C_{40}H_{53}Cl_3N_5O_{16}$ 964.2553, found 964.2552. Anal. Calcd for $C_{40}H_{49}Cl_3N_4O_{16}$: C, 50.67; H, 5.21; N, 5.91. Found: C, 50.55; H, 5.30; N, 6.07.

(b) A suspension of glycosyl acceptor **1** (833 mg, 1.46 mmol), powdered AgOTf (633 mg, 2.49 mmol), and activated molecular sieves (4 Å, 2 g) in anhydrous CH_2Cl_2 (15 mL) and anhydrous Et_2O (30 mL) was stirred under nitrogen for 1 h. A solution of galactosyl donor **2** (933 mg, 2.25 mmol) and *sym*-collidine (0.4 mL, 2.5 mmol) in anhydrous CH_2Cl_2 (15 mL) was added at room temperature. The reaction mixture was stirred for 2 days until TLC (6:1 chloroform−acetone) indicated that all acceptor was consumed. The mixture was worked up as described above and chromatographed. The combined yield of **3α** and **3β** was 88% ($\alpha/\beta \sim 4{:}1$).

8-Azido-3,6-dioxaoctyl 4-*O*-Benzoyl-6-bromo-2,6-dideoxy-2-trichloroacetamido-β-D-glucopyranoside (4). *N*-Bromosuccinimide (812 mg, 4.6 mmol) was added at 100 °C, under argon, to a stirred mixture of 8-azido-3,6-dioxaoctyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**1**)[16] (2.0 g, 3.5 mmol) and barium carbonate (3.47 g, 17.6 mmol) in 4:1 carbon tetrachloride−tetrachloroethane (75 mL). The mixture was kept at reflux for 2.5 h, cooled to room temperature, and filtered. The filtrate was concentrated, and the residue was chromatographed (12:1 → 6:1 chloroform−acetone) to afford **4** (1.93 g, 85%). $[\alpha]_D^{20}$ = −18.2 (*c* 0.8, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.05−7.45 (m, 5 H, Ph), 7.57 (d, 1 H, $J_{2,NH}$ = 7.6 Hz, NH), 5.11 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.3 Hz, H-4), 5.04 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1), 4.30−4.25 (m, 1 H, H-3), 4.04−4.00 (m, 1 H, H-1′$_a$), 3.92−3.88 (m, 1 H, H-1′$_b$), 3.87−3.84 (m, 1 H, H-5), 3.75−3.72 (m, 1 H, H-2), 3.78−3.65 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.58 (d, 1 H, $J_{3,OH}$ = 6.2 Hz, 3-OH), 3.55 (dd, 1 H, *J* = 2.4, 11.3 Hz, H-6$_a$), 3.48 (dd, 1 H, *J* = 7.7, 11.3 Hz, H-6$_b$), 3.45−3.42 (m, 2 H, H-6′). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.2 (*C*O), 163.0 (CO), 133.7−128.5 (Ar), 128.7 (*ipso* Ph), 99.8 (C-1), 92.2 (CCl_3), 74.3 (C-4), 73.5 (C-5), 71.8 (C-3), 70.7, 70.5, 70.2, 69.9 (C-2′, C-3′, C-4′, C-5′), 68.7 (C-1′), 59.1 (C-2), 50.4 (C-6′), 31.3 (C-6). HRMS (ESI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{26}Cl_3BrN_4O_8Na$ 668.9897, found 668.9884. Anal. Calcd for $C_{21}H_{26}Cl_3BrN_4O_8$: C, 38.88; H, 4.04; N, 8.64. Found: C, 39.02; H, 4.09; N, 8.64.

8-Azido-3,6-dioxaoctyl 4-*O*-Benzoyl-6-bromo-2,6-dideoxy-2-trichloroacetamido-3-*O*-(3,4,6-tri-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranosyl)-β-D-glucopyranoside (5α) and 8-Azido-3,6-dioxaoctyl 4-*O*-Benzoyl-6-bromo-2,6-dideoxy-2-trichloroacetamido-3-*O*-(3,4,6-tri-*O*-acetyl-2-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside (5β). A suspension of the glycosyl acceptor **4** (2.49 g, 3.84 mmol), powdered AgOTf (218.4 mg, 0.85 mmol), and activated molecular sieves (4 Å, 10 g) in anhydrous CH_2Cl_2 (150 mL) was stirred under nitrogen for 1 h. A solution of 3,4,6-tri-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranosyl chloride (**2**)[18] (2.47 g, 5.76 mmol) and *sym*-collidine (1.1 mL, 7.7 mmol) in anhydrous CH_2Cl_2 (50 mL) was added portionwise at room temperature. Stirring was continued for 2 days, when analysis by TLC (6:1 toluene−

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acetone) indicated that all acceptor was consumed. The mixture was diluted with CH_2Cl_2 (100 mL) and filtered through a Celite pad. The filtrate was washed successively with 0.5 M aq HCl, aq $NaHCO_3$, and brine. The organic phase was coevaporated with water to remove excess *sym*-collidine, and chromatography (9:1 toluene−acetone) gave first the desired α-linked disaccharide **5α** (3.03 g, 77%).

Data for **5α**. $[\alpha]_D^{20}$ = +28.0 (*c* 0.7, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.04−7.04 (m, 11 H, 2 Ph, NH), 5.35 (br s, 1 H, H-4^{II}), 5.34 (d, 1 H, $J_{1,2}$ = 7.4 Hz, H-1^I), 5.31 (dd, 1 H, *J* = 8.1 Hz, *J* = 8.9 Hz, H-4^I), 5.18 (dd, 1 H, $J_{2,3}$ = 10.6 Hz, $J_{3,4}$ = 3.3 Hz, H-3^{II}), 4.93 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1^{II}), 4.56 (dd, 1 H, *J* = 8.1 Hz, *J* = 8.7 Hz, H-3^I), 5.31 (dd, 1 H, *J* = 1.3 Hz, *J* = 7.1 Hz, H-5^{II}), 4.23 (d, 1 H, ^2J = 12.3 Hz, PhC*H*H), 4.10 (d, 1 H, ^2J = 12.3 Hz, PhC*H*H), 4.07−4.04 (m, 2 H, H-1′$_a$, H-6$^{II}_a$), 3.95 (ddd, 1 H, *J* = 3.2, 8.5, 11.8 Hz, H-5^I), 3.85−3.81 (m, 2 H, H-1′$_b$, H-6$^{II}_b$), 3.71−3.65 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.63 (dd, 1 H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.5 Hz, H-2^{II}), 3.58 (dd, 1 H, *J* = 3.3, 11.2 Hz, H-6^I_a), 3.53−3.49 (m, 2 H, H-6^I_b, H-2^I), 3.41 (t, 2 H, *J* = 5.1 Hz, H-6′), 2.04, 2.03, 1.87 (3 s, 9 H, 3 COC*H*$_3$). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.5−169.7 (3 OCOCH$_3$), 165.1 (*C*O), 162.0 (*C*O), 137.6, 129.2 (2 *ipso* Ph), 133.5−127.7 (Ar), 98.3 (C-1^I), 97.8 (C-1^{II}), 92.2 (*C*Cl$_3$), 76.9 (C-3^I), 73.8 (C-5^I), 73.1 (PhCH$_2$), 73.0 (C-2^{II}), 71.9 (C-4^{II}), 70.7, 70.6, 70.4, 70.1 (C-2′, C-3′, C-4′, C-5′), 69.4 (C-3^{II}), 69.2 (C-1′), 68.2 (C-4^I), 67.5 (C-5^{II}), 62.2 (C-6^{II}), 58.6 (C-2^I), 50.7 (C-6′), 31.5 (C-6^I), 20.7−20.6 (3 COC*H*$_3$). HRMS (ESI-TOF): *m*/*z* [M + NH$_4$]$^+$ calcd for $C_{40}H_{52}Cl_3BrN_5O_{16}$ 1042.1658, found 1042.1652. Anal. Calcd for $C_{40}H_{48}Cl_3BrN_4O_{16}$: C, 46.78; H, 4.71; N, 5.46. Found: C, 47.03; H, 4.71; N, 5.45.

Continued elution gave the β-linked disaccharide **5β** (0.28 g, 7%, 84% overall, $\alpha/\beta \sim$ 11:1).

Data for **5β**. $[\alpha]_D^{20}$ = +3.4 (*c* 0.8, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.06−7.25 (m, 10 H, 2 Ph), 6.92 (d, 1 H, $J_{2,NH}$ = 6.9 Hz, NH), 5.27 (d, 1 H, $J_{1,2}$ = 8.2 Hz, H-1^I), 5.20 (t, 1 H, *J* = 9.3 Hz, H-4^I), 5.14 (br d, 1 H, *J* = 3.3 Hz, H-4^{II}), 4.76 (dd, 1 H, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 3.3 Hz, H-3^{II}), 4.69 (t partially overlapped, 1 H, *J* = 9.4 Hz, H-3^I), 4.68 (d, 1 H, ^2J = 11.7 Hz, PhC*H*H), 4.61 (d, 1 H, ^2J = 11.7 Hz, PhC*H*H), 4.44 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H-1^{II}), 4.02−3.98 (m, 1 H, H-1′$_a$), 3.90−3.87 (m, 1 H, H-5^I), 3.85−3.81 (m, 1 H, H-1′$_b$), 3.71−3.63 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.61 (t, 1 H, *J* = 6.8 Hz, H-5^{II}), 3.57−3.53 (m, 2 H, H-6^I_a, H-6$^{II}_a$), 3.49−3.46 (m, 2 H, H-6^I_b, H-2^{II}), 3.44 (dd, 1 H, *J* = 7.7, 11.1 Hz, H-6$^{II}_b$), 3.40 (t, 2 H, *J* = 5.1 Hz, H-6′), 3.37−3.33 (m, 1 H, H-2^I), 2.00, 1.87, 1.85 (3 s, 9 H, 3 COC*H*$_3$). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.2−169.9 (3 OCOCH$_3$), 165.3 (*C*O), 162.1 (*C*O), 138.4, 129.5 (2 *ipso* Ph), 133.6−127.8 (Ar), 102.8 (C-1^{II}), 98.4 (C-1^I), 92.0 (*C*Cl$_3$), 77.1 (C-2^{II}), 75.6 (C-3^I), 75.4 (PhCH$_2$), 73.5 (C-5^I), 72.4 (C-3^{II}), 71.8 (C-4^I), 70.7, 70.6, 70.5, 70.0 (C-2′, C-3′, C-4′, C-5′), 70.3 (C-5^{II}), 69.2 (C-1′), 66.9 (C-4^{II}), 60.5 (C-6^{II}), 59.9 (C-2^I), 50.7 (C-6′), 31.2 (C-6^I), 20.6−20.3 (3 COCH$_3$). HRMS (ESI-TOF): *m*/*z* [M + NH$_4$]$^+$ calcd for $C_{40}H_{52}Cl_3BrN_5O_{16}$ 1042.1658, found 1042.1652. Anal. Calcd for $C_{40}H_{48}Cl_3BrN_4O_{16}$: C, 46.78; H, 4.71; N, 5.46. Found: C, 47.07; H, 4.84; N, 5.15.

8-Azido-3,6-dioxaoctyl 6-Bromo-2,6-dideoxy-2-trichloroacetamido-3-*O*-(2-*O*-benzyl-3,4-*O*-isopropylidene-α-D-galactopyranosyl)-β-D-glucopyranoside (7). A solution of sodium methoxide in methanol (1 M, 0.7 mL) was added under argon to a solution of **5α** (520 mg, 0.5 mmol) in 1:9 CH_2Cl_2−MeOH (20 mL), and the reaction mixture was stirred at room temperature for 6 h. The mixture was neutralized with Amberlite IR-120 (H$^+$) resin and filtered, and the solids were washed with MeOH (25 mL). The filtrate was concentrated to give compound **6** as an amorphous solid in almost theoretical yield. For identification and spectral analysis, a portion was purified by chromatography (12:1 CH_2Cl_2−MeOH). ^{1}H NMR (600 MHz, $CDCl_3$ + D_2O): δ = 7.36−7.30 (m, 5 H, Ph), 5.08 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1^{II}), 4.86 (d, 1 H, $J_{1,2}$ = 8.4 Hz, H-1^I), 4.83 (d, 1 H, ^2J = 11.7 Hz, PhC*H*H), 4.70 (d, 1 H, ^2J = 11.7 Hz, PhC*H*H), 4.03−3.99 (m, 2 H, H-3^{II}, H-4^{II}), 3.94−3.88 (m, 3 H, H-3^I, H-5^{II}, H-1′$_a$), 3.80−3.75 (m, 4 H, H-2^{II}, H-6^{II}, H-1′$_b$), 3.74−3.69 (m, 1 H, H-6^I_a), 3.68−3.58 (m, 9 H, H-2^I, H-2′, H-3′, H-4′, H-5′), 3.52−3.49 (m, 2 H, H-5^I, H-4^I), 3.48−3.43 (m, 1 H, H-6^I_b), 3.42−3.39 (m, 2 H, H-6′). ^{13}C NMR (150 MHz, $CDCl_3$ + D_2O): δ = 162.7 (NCOCCl$_3$), 137.0 (*ipso* Ph), 128.7−128.4 (Ar), 100.0 (C-1^{II}), 99.9 (C-1^I), 92.4 (*C*Cl$_3$), 82.7 (C-3^I), 77.0 (C-2^{II}), 74.4 (C-5^I), 74.3 (PhCH$_2$), 73.1 (C-4^I), 70.7, 70.5, 70.2 (C-2′, C-3′, C-4′), 70.3 (C-4^{II}), 70.2 (C-5^{II}), 69.8 (C-5′), 69.5 (C-3^{II}), 68.6 (C-1′), 62.0 (C-6^{II}), 57.3 (C-2^I), 50.5 (C-6′), 32.6 (C-6^I). HRMS (ESI-TOF): *m*/*z* [M + NH$_4$]$^+$ calcd for $C_{27}H_{42}Cl_3BrN_5O_{12}$ 812.1073, found 812.1075.

To a solution of the deacetylated product **6** in anhydrous DMF (6 mL) were added 2,2-dimethoxypropane (95 μL, 0.75 mmol) followed by dry camphorsulfonic acid (12 mg, 0.05 mmol). The mixture was stirred at 45 °C for 16 h, neutralized with Et_3N (50 μL), concentrated to dryness, and coevaporated with toluene (twice) to remove traces of Et_3N. A solution of the crude product in 10:1 MeOH−H_2O (22 mL) was boiled under reflux for 3 h. The solvents were evaporated and the residue was purified by flash chromatography (5:1 toluene−acetone) to afford the isopropylidene derivative 7 (345 mg, 82% over two steps). $[\alpha]_D^{20}$ = +46.2 (*c* 0.4, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.36−7.30 (m, 5 H, Ph), 7.18 (d, 1 H, $J_{2,NH}$ = 8.4 Hz, NH), 4.99 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H-1^{II}), 4.92 (d, 1 H, ^2J = 12.1 Hz, PhC*H*H), 4.86 (s, 1 H, 4^I-OH), 4.83 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1^I), 4.73 (d, 1 H, ^2J = 12.1 Hz, PhCH*H*), 4.44 (dd, 1 H, $J_{2,3}$ = 7.6 Hz, $J_{3,4}$ = 5.8 Hz, H-3^{II}), 4.27 (dd, 1 H, $J_{3,4}$ = 5.5 Hz, $J_{4,5}$ = 4.3 Hz, H-4^{II}), 4.17 (dd, 1 H, $J_{4,5}$ = 4.4 Hz, $J_{5,6}$ = 7.4 Hz, H-5^{II}), 3.96−3.93 (m, 1 H, H-1′$_a$), 3.88−3.84 (m, 2 H, H-6^{II}), 3.83−3.81 (m, 2 H, H-1′$_b$, H-3^I), 3.76−3.72 (m, 2 H, H-6^I_a, H-2^I), 3.70−3.60 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.58 (dd, 1 H, $J_{1,2}$ = 3.4 Hz, $J_{2,3}$ = 7.8 Hz, H-3^{II}), 3.50−3.46 (m, 3 H, H-4^I, H-5^I, H-6^I_b), 3.42−3.40 (m, 2 H, H-6′), 2.41 (d, 1 H, $J_{6,OH}$ = 6.2 Hz, 6^{II}-OH), 1.41, 1.36 (2 s, 6 H, C(C*H*$_3$)$_2$). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.4 (NCOCCl$_3$), 136.7 (*ipso* Ph), 128.6−128.3 (Ar), 109.7 (*C*(CH$_3$)$_2$), 101.0 (C-1^{II}), 100.4 (C-1^I), 92.5 (*C*Cl$_3$), 82.3 (C-3^I), 76.6 (C-2^{II}), 76.5 (C-3^{II}), 75.0 (C-4^{II}), 74.4 (C-5^I), 73.1 (C-4^I), 72.7 (PhCH$_2$), 71.0, 70.5, 70.3 (C-2′, C-3′, C-4′), 69.9 (C-5′), 68.3 (C-1′), 67.8 (C-5^{II}), 62.9 (C-6^{II}), 57.1 (C-2^I), 50.4 (C-6′), 32.4 (C-6^I), 28.2, 26.4 (C(*C*H$_3$)$_2$). HRMS (ESI-TOF): *m*/*z* [M + NH$_4$]$^+$ calcd for $C_{30}H_{46}Cl_3BrN_5O_{12}$ 852.1392, found 852.1395. Anal. Calcd for $C_{30}H_{42}Cl_3BrN_4O_{12}$: C, 43.05; H, 5.06; N, 6.69. Found: C, 43.34; H, 5.32; N, 6.60.

8-Azido-3,6-dioxaoctyl 6-Bromo-2,6-dideoxy-2-trichloroacetamido-3-*O*-(benzyl 2-*O*-benzyl-3,4-*O*-isopropylidene-α-D-galactopyranosyluronate)-β-D-glucopyranoside (8). To a flask charged with compound 7 (200 mg, 0.24 mmol), TEMPO (15 mg, 0.10 mmol), and BAIB (232 mg, 0.72 mmol) was added CH_2Cl_2−H_2O (2:1, v/v, 15 mL), and the two-phase reaction mixture was stirred vigorously at room temperature until analysis by TLC (3:1 toluene−acetone) showed complete conversion of the starting material to a slower moving product (~24 h). The mixture was diluted with EtOAc (100 mL) and washed with 1:1 (v/v) aq $Na_2S_2O_3$ and aq NaH_2PO_4 (2 × 50 mL). The combined aqueous washes were extracted with EtOAc (2 × 100 mL), and the organic phases were combined, dried, and concentrated.

Anhydrous K_2CO_3 (57.16 mg, 0.31 mmol) followed by BnBr (40 μL, 0.32 mmol) was added at 0 °C under argon to a solution of the foregoing material in DMF (15 mL). After being stirred for 15 min at 0 °C, the mixture was allowed to warm to room temperature (~2 h), diluted with CH_2Cl_2 (150 mL), and washed with water (2 × 50 mL). The organic layer was dried, concentrated, and coevaporated with toluene (twice). Chromatography (6:1 toluene−acetone) afforded the benzyl uronate **8** (164 mg, 73% over two steps) as a colorless foam. $[\alpha]_D^{20}$ = +17.2 (*c* 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.36−7.30 (m, 10 H, 2Ph), 6.98 (d, 1 H, $J_{2,NH}$ = 8.8 Hz, NH), 5.36 (d, 1 H, ^2J = 12.3 Hz, PhC*H*H), 5.13 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1^{II}), 5.01 (d, 1 H, ^2J = 12.3 Hz, PhC*H*H), 4.94 (d, 1 H, ^2J = 12.1 Hz, PhC*H*H), 4.91 (d, 1 H, $J_{4,OH}$ = 1.8 Hz, 4^I-OH), 4.75 (d, 1 H, $J_{1,2}$ = 8.2 Hz, H-1^I), 4.74−4.72 (m, 2 H, PhCH*H*, H-5^{II}), 4.49 (dd, 1 H, $J_{3,4}$ = 5.5 Hz, $J_{4,5}$ = 3.1 Hz, H-4^{II}), 4.46 (dd, 1 H, $J_{2,3}$ = 7.5 Hz, $J_{3,4}$ = 5.5 Hz, H-3^{II}), 3.91−3.87 (m, 1 H, H-1′$_a$), 3.85−3.83 (m, 1 H, H-1′$_b$), 3.79 (t, 1 H, $J_{1,2}$ = $J_{2,3}$ = 8.5 Hz, H-2^I), 3.74−3.69 (m, 2 H, H-3^I, H-6^I_a), 3.68−3.59 (m, 9 H, H-2^{II}, H-2′, H-3′, H-4′, H-5′), 3.52−3.45 (m, 3 H, H-4^I, H-5^I, H-6^I_b), 3.44−3.37 (m, 2 H, H-6′), 1.37, 1.27 (2 s, 6 H, C(C*H*$_3$)$_2$). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.3 (COOBn), 162.4 (NCOCCl$_3$), 136.6, 135.2 (2 *ipso* Ph), 128.7−128.2 (Ar), 109.6 (*C*(CH$_3$)$_2$), 101.3 (C-1^{II}), 100.8 (C-1^I), 92.4 (*C*Cl$_3$), 85.9 (C-3^I), 76.1 (C-3^{II}), 75.9 (C-2^{II}), 74.4

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(C-5^{I}), 73.5 (C-4^{II}), 73.3 (C-4^{I}), 72.9 (PhCH$_2$), 71.0, 70.5, 70.3 (C-2′, C-3′, C-4′), 69.9 (C-5′), 68.3 (C-1′), 68.2 (C-5^{II}), 66.8 (PhCH$_2$), 56.4 (C-2^{I}), 50.5 (C-6′), 32.3 (C-6^{I}), 28.0, 26.1 (C(CH$_3$)$_2$). HRMS (ESI-TOF): m/z [M + NH$_4$]$^+$ calcd for $C_{37}H_{50}Cl_3BrN_5O_{13}$ 956.1654, found 956.1638. Anal. Calcd for $C_{37}H_{46}Cl_3BrN_4O_{13}$: C, 47.22; H, 4.93; N, 5.95. Found: C, 47.45; H, 5.08; N, 5.80.

8-Azido-3,6-dioxaoctyl 6-Bromo-2,6-dideoxy-2-trichloroacetamido-3-*O*-(benzyl 2-*O*-benzyl-α-D-galactopyranosyluronate)-β-D-glucopyranoside (9). Compound **8** (360 mg, 0.38 mmol) was dissolved in 80% aq AcOH (5 mL) and stirred at 80 °C for 3 h, when TLC (3:1 toluene−acetone) showed complete conversion of the starting material into a product with lower mobility. The solvents were evaporated, the residue was coevaporated with toluene (twice) to remove AcOH, and chromatography (4:1 toluene−acetone) gave **9** (307 mg, 89%). $[\alpha]_D^{20}$ = +25.7 (c 0.3, CHCl$_3$). ^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.38−7.30 (m, 10 H, 2Ph), 7.17 (d, 1 H, $J_{2,NH}$ = 8.5 Hz, NH), 5.26 (d, 1 H, ^2J = 12.2 Hz, PhC*H*H), 5.16 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1^{II}), 5.08 (d, 1 H, ^2J = 12.3 Hz, PhC*H*H), 4.86 (d, 1 H, ^2J = 11.8 Hz, PhC*H*H), 4.80 (d, 1 H, $J_{1,2}$ = 8.4 Hz, H-1^{I}), 4.75 (d, 1 H, ^2J = 11.8 Hz, PhC*H*H), 4.69 (d, 1 H, $J_{4,OH}$ = 1.2 Hz, 4^{I}-OH), 4.53 (d, 1 H, $J_{4,5}$ = 1.5 Hz, H-5^{II}), 4.28 (br s, 1 H, H-4^{II}), 4.22−4.19 (m, 1 H, H-3^{II}), 3.89−3.86 (m, 1 H, H-1′$_a$), 3.84−3.79 (m, 3 H, H-2^{II}, H-3^{I}, H-1′$_b$), 3.75−3.68 (m, 2 H, H-2^{I}, H-6$^{I}_a$), 3.67−3.56 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.52−3.49 (m, 2 H, H-5^{I}, H-4^{I}), 3.48−3.44 (m, 1 H, H-6$^{I}_b$), 3.43−3.36 (m, 2 H, H-6′), 2.47 (d, 1 H, $J_{3,OH}$ = 5.8 Hz, 3^{II}-OH), 2.42 (br s, 1 H, 4^{II}-OH). ^{13}C NMR (150 MHz, CDCl$_3$): δ = 168.1 (COOBn), 162.6 (NCOCCl$_3$), 136.6, 135.1 (2 *ipso* Ph), 128.9−128.4 (Ar), 101.3 (C-1^{II}), 100.6 (C-1^{I}), 92.4 (CCl$_3$), 85.0 (C-3^{I}), 75.9 (C-2^{II}), 74.7 (PhCH$_2$), 74.3 (C-5^{I}), 73.6 (C-4^{I}), 71.1 (C-5^{II}), 70.8 (C-4^{II}), 70.9, 70.5, 70.3 (C-2′, C-3′, C-4′), 69.9 (C-5′), 69.4 (C-3^{II}), 68.5 (C-1′), 67.1 (PhCH$_2$), 56.8 (C-2^{I}), 50.5 (C-6′), 32.4 (C-6^{I}). HRMS (ESI-TOF): m/z [M + NH$_4$]$^+$ calcd for $C_{34}H_{46}Cl_3BrN_5O_{13}$ 916.1341, found 916.1337. Anal. Calcd for $C_{34}H_{42}Cl_3BrN_4O_{13}$: C, 45.33; H, 4.70; N, 6.22. Found: C, 45.57; H, 4.49; N, 5.86.

8-Amino-3,6-dioxaoctyl 2,6-Dideoxy-2-acetamido-3-*O*-(α-D-galactopyranosyluronate)-β-D-glucopyranoside (10). A mixture of **9** (250 mg, 0.28 mmol) and Pd/C (250 mg) in a mixture of MeOH (10 mL) and 0.1 M potassium phosphate buffer (10 mL; pH = 7) was stirred under H$_2$ (1 atm) at room temperature. After 2 days, when TLC (25:1 MeOH−25% NH$_4$OH) showed complete conversion of the starting material into a more polar product, the mixture was filtered through a Celite pad, the catalyst was washed with H$_2$O (15 mL), and the filtrate was concentrated. Chromatography (30:1 MeOH−25% NH$_4$OH) followed by lyophilization afforded the desired disaccharide **10** (122 mg, 86%) as a white solid. ^{1}H NMR (600 MHz, D$_2$O): δ = 5.27 (d, 1 H, $J_{1,2}$ = 3.1 Hz, H-1^{II}), 4.47 (d, 1 H, $J_{1,2}$ = 8.5 Hz, H-1^{I}), 4.17 (br s, 1 H, H-4^{II}), 4.08 (br s, 1 H, H-5^{II}), 3.91−3.88 (m, 1 H, H-1′$_a$), 3.78−3.74 (m, 2 H, H-2^{II}, H-3^{II}), 3.71−3.66 (m, 2 H, H-2^{I}, H-1′$_b$), 3.64−3.61 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.60−3.57 (m, 1 H, H-3^{I}), 3.46−3.42 (m, 1 H, H-5^{I}), 3.35 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.2 Hz, H-4^{I}), 3.10 (t, 2 H, J = 5.2 Hz, H-6′), 1.91 (s, 3H, COC*H*$_3$), 1.23 (d, 3 H, J = 6.1 Hz, H-6^{I}). ^{13}C NMR (150 MHz, D$_2$O): δ = 175.6 (CO), 174.7 (CO), 101.3 (C-1^{I}), 100.5 (C-1^{II}), 81.1 (C-3^{I}), 76.2 (C-4^{I}), 72.4 (C-5^{II}), 71.8 (C-5^{I}), 71.0 (C-4^{II}), 69.9, 69.9, 69.8 (C-2′, C-3′, C-4′), 69.7 (C-2^{II} or C-3^{II}), 69.3 (C-5′), 68.4 (C-2^{II} or C-3^{II}), 66.8 (C-1′), 54.4 (C-2^{I}), 39.3 (C-6′), 22.4 (COC*H*$_3$), 16.7 (C-6^{I}). HRMS (ESI-TOF): m/z [M − H]$^-$ calcd for $C_{20}H_{35}N_2O_{13}$ 511.2145, found 511.2149.

8-Azido-3,6-dioxaoctyl 6-*O*-Benzyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-trichloroacetamido-β-D-glucopyranoside (12). A mixture of the benzylidene acetal **11**[16] (1.0 g, 1.11 mmol) and freshly activated powdered molecular sieves (3 Å, 1.5 g) in dry THF (20 mL) was stirred under argon for 2 h at room temperature. The solution was cooled to 0 °C (ice−water bath), and NaCNBH$_3$ (0.84 g, 13.32 mmol) was added portionwise. After the mixture was stirred for 20 min at 0 °C, 2 M HCl−Et$_2$O was added dropwise at 0 °C until the effervescence ceased and the pH remained acidic. The mixture was stirred for an additional 15 min at room temperature, diluted with CH$_2$Cl$_2$ (25 mL), and filtered through Celite. The filtrate was washed with cold satd aq NaHCO$_3$ (20 mL) and brine (20 mL), and the organic extract was dried and concentrated. Chromatography (6:1 toluene−acetone) afforded **12** (919 mg, 92%). Mp: 85−86 °C (EtOAc−Et$_2$O). $[\alpha]_D^{20}$ = −1.7 (c 0.5, CHCl$_3$). ^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.36−7.26 (m, 5 H, Ph), 6.94 (d, 1 H, $J_{2,NH}$ = 7.5 Hz, NH), 5.38 (d, 1 H, $J_{3,4}$ = 3.3 Hz, H-4^{II}), 5.24 (dd, 1 H, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 10.4 Hz, H-2^{II}), 4.92 (dd, 1 H, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.4 Hz, H-3^{II}), 4.88 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1^{I}), 4.63 (d, 1 H, ^2J = 12.3 Hz, PhC*H*H), 4.60 (d, 1 H, ^2J = 12.3 Hz, PhCH*H*), 4.56 (d, 1 H, $J_{1,2}$ = 8.0 Hz, H-1^{II}), 4.55 (dd, 1 H,, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 8.1 Hz, H-3^{I}), 4.16−4.10 (m, 2 H, H-6^{II}), 3.99 (t, 1 H, J = 6.6 Hz, H-5^{II}), 3.96−3.93 (m, 1 H, H-1′$_a$), 3.87−3.85 (dd, 1 H, J = 1.2, J = 10.7 Hz, H-6$^{I}_b$), 3.80−3.76 (m, 1 H, H-1′$_b$), 3.71−3.68 (m, 1 H, H-6$^{I}_a$), 3.68−3.65 (m, 3 H, H-5′, 4^{I}-OH), 3.64−3.59 (m, 6 H, H-2′, H-3′, H-4′), 3.57 (t, 1 H, J = 8.5 Hz, H-4^{I}), 3.53−3.48 (m, 2 H, H-2^{I}, H-5^{I}), 3.39 (t, 2 H, J = 5.0 Hz, H-6′), 2.16, 2.08, 2.03, 1.97 (4 s, 12 H, 4 COC*H*$_3$). ^{13}C NMR (150 MHz, CDCl$_3$): δ = 170.4, 170.1, 170.0, 169.5 (4 OCOCH$_3$), 162.0 (NCOCCl$_3$), 138.2 (*ipso* Ph), 128.3−127.6 (Ar), 100.9 (C-1^{I}), 99.1 (C-1^{II}); 92.4 (CCl$_3$), 82.3 (C-3^{I}), 75.3 (C-5^{I}), 73.5 (PhCH$_2$), 71.1 (C-5^{II}), 70.8 (C-3^{II}), 70.7, 70.6, 70.5 (C-2′, C-3′, C-4′), 69.9 (C-5′), 69.5 (C-6^{I}), 69.2 (C-4^{I}), 68.4 (C-1′), 68.3 (C-2^{II}), 66.8 (C-4^{II}), 61.2 (C-6^{II}), 58.0 (C-2^{I}), 50.6 (C-6′), 20.9, 20.6, 20,5, 20.4 (4 OCOC*H*$_3$). HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{35}H_{47}Cl_3N_4O_{17}Na$ 923.1899, found 923.1896. Anal. Calcd for $C_{35}H_{47}Cl_3N_4O_{17}$: C, 46.60; H, 5.25; N, 6.21. Found: C, 46.45; H, 5.24; N, 6.16.

8-Azido-3,6-dioxaoctyl 2,4-Di-*O*-benzyl-3,6-dideoxy-α-L-*xylo*-hexopyranosyl-(1→4)-[3,4,6-tri-*O*-acetyl-β-D-galactopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (15). Bromine (113 μL, 2.2 mmol) was added to a solution of ethyl 2,4-di-*O*-benzyl-3,6-dideoxy-1-thio-β-L-*xylo*-hexopyranoside (**13**)[31] (410 mg, 1.1 mmol) in CCl$_4$ (6 mL). The mixture was shaken gently for 10 min, and then hex-1-ene (555 μL, 4.4 mmol) was added. After concentration and coevaporation with CCl$_4$ (3 × 6 mL), a solution of the crude bromide **14** in dry CH$_2$Cl$_2$ (2 mL) was added to a stirred mixture of **12** (330 mg, 0.366 mmol), Bu$_4$NBr (354 mg, 1.1 mmol), and powdered molecular sieves (4 Å, 750 mg) in 2.5:1 CH$_2$Cl$_2$−DMF (2.8 mL). After being stirred under argon atmosphere for 48 h at room temperature, when TLC (4:1 toluene−acetone) showed that all glycosyl acceptor **12** had been consumed, the mixture was diluted with CH$_2$Cl$_2$ (10 mL) and filtered through a Celite pad, and the solids were washed with CH$_2$Cl$_2$ (2 × 5 mL). The combined filtrate and washings were successively washed with satd aq NaHCO$_3$ (15 mL) and H$_2$O (15 mL), dried, and concentrated. Chromatography (6:1 toluene−acetone) gave trisaccharide **15** (422 mg, 95%) as a colorless solid. $[\alpha]_D^{20}$ = −29.5 (c 0.9, CHCl$_3$). ^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.34−7.26 (m, 15 H, Ph), 7.04 (d, 1 H, $J_{2,NH}$ = 8.5 Hz, NH), 5.34 (d, 1 H, $J_{3,4}$ = 3.1 Hz, H-4^{II}), 5.14 (dd, 1 H, $J_{1,2}$ = 8.3, $J_{2,3}$ = 10.4 Hz, H-2^{II}), 5.07 (d, 1 H, $J_{1,2}$ = 3.0 Hz, H-1^{III}), 4.90 (dd, 1 H, $J_{2,3}$ = 10.5, $J_{3,4}$ = 3.4 Hz, H-3^{II}), 4.82 (d, 1 H, $J_{1,2}$ = 8.2 Hz, H-1^{II}), 4.75 (d, 1 H, $J_{1,2}$ = 7.2 Hz, H-1^{I}), 4.59 (d, 1 H, ^2J = 12.4, PhC*H*H), 4.54 (s, 2 H, PhC*H*$_2$), 4.46 (s, 2 H, PhC*H*$_2$), 4.44 (m, 1 H, H-5^{III}), 4.33 (d, 1 H, ^2J = 12.4, PhCH*H*), 4.15 (t, 1 H, J = 7.2 Hz, H-3^{I}), 4.11−4.02 (m, 3 H, H-4^{I}, H-6^{II}), 3.92−3.84 (m, 4 H, H-6$^{I}_a$, H-1′$_a$, H-2^{III}, H-5^{II}), 3.81 (m, 1 H, H-2^{II}), 3.73−3.66 (m, 3 H, H-1′$_b$, H-6$^{I}_b$, H-5^{I}), 3.65−3.55 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.38 (m, 3 H, H-4^{III}, H-6′), 2.15 (dt, 1 H, $J_{2,3}$ = $J_{3,4}$ = 3.6, ^2J = 12.8 Hz, 1 H, H-3$^{III}_{eq}$), 2.08, 2.01, 1.94, 1.84 (4 s, 12 H, 4 COC*H*$_3$), 1.80 (dt, 1 H, $J_{3,4}$ = 1.9, $J_{2,3}$ = ^2J = 12.2 Hz, 1 H, H-3$^{III}_{ax}$), 1.25 (d, 3 H, $J_{5,6}$ = 6.2 Hz, H-6^{III}). ^{13}C NMR (150 MHz, CDCl$_3$): δ = 170.3, 170.0, 169.9, 169.5 (4 OCOCH$_3$), 161.6 (NCOCCl$_3$), 138.3, 138.1, 138.0 (3 *ipso* Ph), 128.4−127.5 (Ar), 100.0 ($J_{C,H}$ = 161.4 Hz, C-1^{II}), 99.5 ($J_{C,H}$ = 164.3 Hz, C-1^{I}), 95.7 ($J_{C,H}$ = 170.2 Hz, C-1^{III}), 92.5 (CCl$_3$), 76.6 (C-3^{I}), 75.5 (C-4^{III}), 75.2 (C-5^{I}), 73.3 (PhCH$_2$), 71.5 (C-4^{I}), 71.3 (PhCH$_2$), 70.7, 70.6, 70.5 (PhCH$_2$, C-2′, C-3′, C-4′), 70.9 (C-3^{II}), 70.8 (C-2^{III}), 70.6 (C-5^{II}), 70.0 (C-5′), 68.3 (C-1′), 68.1 (C-2^{II}), 68.1 (C-6^{I}), 66.9 (C-4^{II}), 66.3 (C-5^{III}), 60.5 (C-6^{II}), 57.2 (C-2^{I}), 50.6 (C-6′), 26.8 (C-3^{III}), 20.7, 20.6, 20.5, 20.4 (4 OCOC*H*$_3$), 16.5 (C-6^{III}). HRMS (ESI-TOF): m/z [M + NH$_4$]$^+$ calcd for $C_{55}H_{73}Cl_3N_5O_{20}$ 1228.3914, found 1228.3962. Anal. Calcd for $C_{55}H_{69}Cl_3N_4O_{20}$: C, 54.48; H, 5.74; N, 4.62. Found: C, 54.26; H, 5.79; N, 4.45.

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8-Azido-3,6-dioxaoctyl 2,4-Di-*O*-benzyl-3,6-dideoxy-α-L-*xylo*-hexopyranosyl-(1→4)-[β-D-galactopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (16). Compound **15** (903 mg, 0.76 mmol) was dissolved in 6:1 CH_2Cl_2−MeOH (35 mL), a solution of sodium methoxide in methanol (1 M, 1.0 mL) was added, and the reaction mixture was stirred at room temperature for 3 h. The mixture was processed as described above for preparation of **6**, and chromatography (9:1 CH_2Cl_2−MeOH) gave **16** in virtually theoretical yield. $[\alpha]_D^{20} = -13.4$ (*c* 0.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.02 (d, 1 H, $J_{2,NH}$ = 7.2 Hz, NH), 7.34−7.26 (m, 15 H, Ph), 5.12 (d, 1 H, $J_{1,2}$ = 7.1 Hz, H-1^I), 4.99 (d, 1 H, $J_{1,2}$ = 3.1 Hz, H-1^{III}), 4.52 (d, 1 H, ^2J = 12.1, PhC*H*H), 4.44 (s, 2 H, PhCH_2), 4.43−4.39 (m, 4 H, H-1^{II}, PhCH_2, H-3^I), 4.38 (d, 1 H, ^2J = 12.1, PhC*H*H), 4.20 (dd, 1 H, $J_{4,5}$ = 12.7, $J_{5,6}$ = 6.3 Hz, H-5^{III}), 3.98 (m, 1 H, H-1′$_b$), 3.94 (m, 1 H, H-4^I), 3.91 (dd, 1 H, *J* = 4.6, *J* = 10.7 Hz, H-6^I_a), 3.88 (d, 1 H, $J_{3,4}$ = 2.7 Hz, H-4^{II}), 3.83 (m, 1 H, H-6$^{II}_a$), 3.82 (m, 1 H, H-2^{III}), 3.77 (m, 1 H, H-6$^{II}_b$), 3.74 (m, 1 H, H-6^I_b), 3.71 (m, 1 H, H-1′$_a$), 3.67 (m, 1 H, H-5^I), 3.64−3.61 (m, 9 H, H-2^I, H-2′, H-3′, H-4′, H-5′), 3.58 (m, 1 H, H-2^{II}), 3.56 (dd, 1 H, $J_{2,3}$ = 9.7, $J_{3,4}$ = 2.9 Hz, H-3^{II}), 3.49 (m, 1 H, H-5^{II}), 3.43 (br s, 1 H, H-4^{III}), 3.38 (t, 2 H, *J* = 5.1 Hz, H-6′), 2.11 (dt, 1 H, $J_{2,3}$ = $J_{3,4}$ = 3.7, ^2J = 12.9 Hz, 1 H, H-3$^{III}_{eq}$), 1.81 (dt, 1 H, $J_{3,4}$ = 2.1, $J_{2,3}$ = ^2J = 12.8 Hz, 1 H, H-3$^{III}_{ax}$), 1.17 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6^{III}). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.1 ($NCOCCl_3$), 138.2, 138.1, 137.9 (3 *ipso* Ph), 128.4−127.6 (Ar), 100.0 (C-1^{II}), 98.9 (C-1^I), 97.5 (C-1^{III}), 92.5 (CCl_3), 77.1 (C-3^I), 75.7 (C-4^{III}), 75.7 (C-5^{II}), 74.6 (C-4^I), 74.5 (C-5^I), 73.6 (C-3^{II}), 73.1 (PhCH$_2$), 71.4 (PhCH$_2$), 71.2 (C-2^{III}), 71.0 (PhCH$_2$), 70.8 (C-2^{II}), 70.5, 70.4, 70.3, 69.8 (C-2′, C-3′, C-4′, C-5′), 68.7 (C-1′), 68.6 (C-4^{II}), 68.5 (C-6^I), 67.3 (C-5^{III}), 62.2 (C-6^{II}), 56.1 (C-2^I), 50.6 (C-6′), 27.1 (C-3^{III}), 16.4 (C-6^{III}). HRMS (ESI-TOF): *m*/*z* [M + NH_4]$^+$ calcd for $C_{47}H_{65}Cl_3N_5O_{16}$ 1060.3486, found 1060.3487. Anal. Calcd for $C_{47}H_{61}Cl_3N_4O_{16}$: C, 54.05; H, 5.89; N, 5.36. Found: C, 53.92; H, 6.01; N, 5.17.

8-Azido-3,6-dioxaoctyl 2,4-Di-*O*-benzyl-3,6-dideoxy-α-L-*xylo*-hexopyranosyl-(1→4)-[3-*O*-benzyl-β-D-galactopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (17). A suspension of compound **16** (773 mg, 0.74 mmol) and dibutyltin oxide (204 mg, 0.82 mmol) in dry MeOH (25 mL) was boiled under reflux until the solution became clear (∼2 h). The mixture was cooled to room temperature, the solvent was evaporated, a solution of the residue was concentrated with toluene (3 × 5 mL), and the white residue was dried under vacuum for 3 h. A mixture of the stannylene derivative, thus obtained, CsF (225 mg, 1.48 mmol), and benzyl bromide (176 μL, 1.48 mmol) in anhyd DMF (15 mL) was stirred at room temperature overnight and concentrated (∼13 kPa). A solution of the residue in toluene (5 mL) was concentrated, and chromatography (first toluene, to remove the tin derivatives, followed by 4:1 toluene−acetone) afforded **17** (781 mg, 93%) as a colorless syrup. $[\alpha]_D^{20} = -12.8$ (*c* 0.7, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.87 (d, 1 H, $J_{2,NH}$ = 7.3 Hz, NH), 7.38−7.22 (m, 20 H, Ph), 5.09 (d, 1 H, $J_{1,2}$ = 6.5 Hz, H-1^I), 5.03 (d, 1 H, $J_{1,2}$ = 3.0 Hz, H-1^{III}), 4.85 (d, 1 H, ^2J = 12.0, PhC*H*H), 4.74 (d, 1 H, ^2J = 12.0, PhC*H*H), 4.53 (d, 1 H, ^2J = 12.0, PhC*H*H), 4.54−4.41 (m, 4 H, 2 PhCH_2), 4.40−4.35 (m, 3 H, H-1^{II}, H-3^I, PhC*H*H), 4.14 (dd, 1 H, $J_{4,5}$ = 12.9 Hz, $J_{5,6}$ = 6.3 Hz, H-5^{III}), 3.99−3.95 (m, 2 H, H-1′$_b$, H-4^I), 3.92 (dd, 1 H, *J* = 5.0, *J* = 10.7 Hz, H-6^I_a), 3.89 (br s, 1 H, H-4^{II}), 3.87−3.82 (m, 2 H, H-6$^{II}_a$, H-2^{III}), 3.78−3.73 (m, 4 H, H-6$^{II}_b$, H-6^I_b, H-2^{II}, H-5^I), 3.72−3.65 (m, 2 H, H-1′$_a$, H-2^I), 3.63−3.58 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.43−3.39 (m, 3 H, H-4^{III}, H-5^{II}, H-3^{II}), 3.34 (t, 2 H, *J* = 5.0 Hz, H-6′), 2.10 (dt, 1 H, $J_{2,3}$ = $J_{3,4}$ = 3.5, ^2J = 12.9 Hz, 1 H, H-3$^{III}_{eq}$), 1.83 (dt, 1 H, $J_{3,4}$ = 2.3, $J_{2,3}$ = ^2J = 13.0 Hz, 1 H, H-3$^{III}_{ax}$), 1.19 (d, 3 H, $J_{5,6}$ = 6.4 Hz, H-6^{III}). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 163.0 ($NCOCCl_3$), 138.3, 138.3, 138.04, 138.01 (4 *ipso* Ph), 128.5−127.5 (Ar), 100.5 (C-1^{II}), 99.0 (C-1^I), 97.2 (C-1^{III}), 92.5 (CCl_3), 79.9 (C-3^{II}), 76.9 (C-3^I), 75.8 (C-4^{III}), 74.6 (C-5^{II}), 74.5 (C-5^I), 74.2 (C-4^I), 73.1 (PhCH$_2$), 72.7 (PhCH$_2$), 71.4 (PhCH$_2$), 71.2 (C-2^{III}), 71.0 (PhCH$_2$), 70.8 (C-2^{II}), 70.6, 70.5, 70.4, 69.9 (C-2′, C-3′, C-4′, C-5′), 68.9 (C-6^I), 68.7 (C-1′), 67.6 (C-4^{II}), 67.4 (C-5^{III}), 62.3 (C-6^{II}), 55.4 (C-2^I), 50.6 (C-6′), 27.3 (C-3^{III}), 16.4 (C-6^{III}). HRMS (ESI-TOF): *m*/*z* [M + NH_4]$^+$ calcd for $C_{54}H_{71}Cl_3N_5O_{16}$ 1150.3956, found 1150.3959. Anal. Calcd for $C_{54}H_{67}Cl_3N_4O_{16}$: C, 57.17; H, 5.95; N, 4.94. Found: C, 57.43; H, 5.93; N, 4.91.

8-Azido-3,6-dioxaoctyl 2,4-Di-*O*-benzyl-3,6-dideoxy-α-L-*xylo*-hexopyranosyl-(1→4)-[3-*O*-benzyl-β-D-galactopyranosyl-(*S*)-(*P*)-4,6-cyclic 2,2,2-trichloroethyl phosphate-(1→3)]-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (18) and 8-Azido-3,6-dioxaoctyl 2,4-Di-*O*-benzyl-3,6-dideoxy-α-L-*xylo*-hexopyranosyl-(1→4)-[3-*O*-benzyl-β-D-galactopyranosyl-(*R*)-(*P*)-4,6-cyclic 2,2,2-trichloroethyl phosphate-(1→3)]-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (19). 2,2,2-Trichloroethyl phosphorodichloridate (95 μL, 0.593 mmol) was added dropwise at −20 °C to a solution of **17** (560 mg, 0.494 mmol) and pyridine (400 μL, 4.94 mmol) in CH_2Cl_2 (7 mL). After 30 min, when TLC (3:1 toluene−acetone) indicated incomplete conversion of **17**, an additional portion of 2,2,2-trichloroethyl phosphorodichloridate (95 μL, 0.593 mmol) was added, and stirring was continued for 30 min at −20 °C. Excess reagent was destroyed by addition of MeOH (0.5 mL), the mixture was concentrated, and EtOAc (5 mL) was added to the residue. The precipitate was filtered off and washed with EtOAc (2 × 3 mL). The combined filtrates were concentrated, and chromatography (3:1 toluene−acetone) gave **18** (464 mg, 71%) and **19** (160 mg, 24%), in that order, as colorless solids.

Data for ***18****.* Mp: 152−153 °C (EtOH). $[\alpha]_D^{20} = -17.4$ (*c* 0.6, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57 (d, 1 H, $J_{2,NH}$ = 7.4 Hz, NH), 7.36−7.23 (m, 20 H, Ph), 5.04 (d, 1 H, $J_{1,2}$ = 3.3 Hz, H-1^{III}), 5.01 (d, 1 H, $J_{1,2}$ = 6.7 Hz, H-1^I), 4.74 (m, 3 H, H-4^{II}, PhCH_2), 4.68−4.59 (m, 2 H, CH_2CCl$_3$), 4.55−4.47 (m, 7 H, H-6^{II}, H-1^{II}, 2 PhCH_2), 4.46−4.36 (m, 4 H, H-3^I, H-5^{III}, PhCH_2), 4.04 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 7.9 Hz, H-4^I), 4.03−3.96 (m, 3 H, H-4^I, H-6$^{II}_a$, H-1′$_a$), 3.90−3.84 (m, 2 H, H-2^{III}, H-2^{II}), 3.79 (br s, 1 H, 2^{II}-OH), 3.74−3.65 (m, 5 H, H-6$^{II}_b$, H-1′$_b$, H-4^{III}, H-2^I, H-5^I), 3.64−3.57 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.46 (br s, 1 H, H-5^{II}), 3.41 (dt, 1 H, $J_{2,3}$ = 9.4, $J_{3,4}$ = 3.8 Hz, H-3^{II}), 3.34 (t, 2 H, *J* = 5.0 Hz, H-6′), 2.09 (dt, 1 H, $J_{2,3}$ = $J_{3,4}$ = 3.5, ^2J = 12.8 Hz, 1 H, H-3$^{III}_{eq}$), 1.82 (dt, 1 H, $J_{3,4}$ = 2.2, $J_{2,3}$ = ^2J = 12.7 Hz, 1 H, H-3$^{III}_{ax}$), 1.24 (d, 3 H, $J_{5,6}$ = 6.5 Hz, H-6^{III}). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.0 ($NCOCCl_3$), 138.8, 138.2, 138.0, 137.2 (4 *ipso* Ph), 128.7−127.3 (Ar), 101.4 (C-1^{II}), 98.6 (C-1^I), 96.9 (C-1^{III}), 95.0 (d, $J_{C,P}$ = 10.3 Hz, CH_2CCl_3), 92.3 ($COCCl_3$), 77.0 (C-3^{II}), 76.9 (d, $J_{C,P}$ = 3.9 Hz, CH_2CCl_3), 76.3 (C-4^{III}), 76.2 (C-4^{II}), 76.21 (C-3^I), 74.7 (C-5^I), 73.1 (PhCH$_2$), 72.8 (C-4^I), 72.1 (PhCH$_2$), 72.0 (PhCH$_2$), 71.0 (PhCH$_2$), 70.9 (C-2^{III}), 70.7 (d, $J_{C,P}$ = 7.5 Hz, C-6^{II}), 70.6, 70.5, 69.9 (C-2′, C-3′, C-4′, C-5′), 69.6 (C-2^{II}), 68.2 (C-6^I), 68.1 (C-1′), 67.0 (C-5^{III}), 66.3 (d, $J_{C,P}$ = 6.2 Hz, C-5^{II}), 56.7 (C-2^I), 50.6 (C-6′), 27.4 (C-3^{III}), 16.4 (C-6^{III}). ^{31}P NMR (162 MHz, $CDCl_3$): δ = −10.95. HRMS (ESI-TOF): *m*/*z* [M + NH_4]$^+$ calcd for $C_{56}H_{71}Cl_6N_5O_{18}P$: 1342.2657, found 1342.2660. Anal. Calcd for $C_{56}H_{67}Cl_6N_4O_{18}P$: C, 50.66; H, 5.09; N, 4.22. Found: C, 50.96; H, 5.09; N, 4.24.

Data for ***19****.* Mp: 75−76 °C (EtOH). $[\alpha]_D^{20} = -15.0$ (*c* 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (d, 1 H, $J_{2,NH}$ = 8.0 Hz, NH), 7.40−7.27 (m, 20 H, Ph), 5.00 (br d, 2 H, H-1^{III}, H-1^I), 4.88 (d, 1 H, $J_{3,4}$ = 3.0 Hz, H-4^{II}), 4.81 (d, 1 H, ^2J = 12.1, PhC*H*H), 4.76 (d, 1 H, ^2J = 12.2, PhC*H*H), 4.65−4.57 (m, 3 H, H-6$^{II}_b$, CH_2CCl$_3$), 4.56−4.41 (m, 7 H, H-1^{II}, H-6$^{II}_a$, 2 PhCH_2, PhC*H*H), 4.39 (d, 1 H, ^2J = 12.0, PhC*H*H), 4.24 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 7.2 Hz, H-3^I), 4.11 (br. q, 1 H, $J_{5,6}$ = 6.5 Hz, H-5^{III}), 4.04 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 7.0 Hz, H-4^I), 4.01 (m, 1 H, H-1′$_a$), 3.95 (dd, 1 H, *J* = 5.1, *J* = 10.4 Hz, H-6^I_a), 3.87−3.81 (m, 3 H, H-2^{II}, H-2^{III}, H-2^I), 3.78 (m, 1 H, H-5^I), 3.72 (dd, 1 H, *J* = 3.3, *J* = 10.5 Hz, H-6^I_b), 3.67 (m, 2 H, H-1′$_b$), 3.65−3.59 (m, 8 H, H-2′, H-3′, H-4′, H-5′), 3.56 (br s, 1 H, H-5^{II}), 3.51 (dt, 1 H, $J_{2,3}$ = 9.4, $J_{3,4}$ = 3.5 Hz, H-3^{II}), 3.45 (br s, 1 H, H-4^{III}), 3.35 (t, 2 H, *J* = 5.0 Hz, H-6′), 2.13 (dt, 1 H, $J_{2,3}$ = $J_{3,4}$ = 3.6, ^2J = 12.6 Hz, 1 H, H-3$^{III}_{eq}$), 1.79 (dt, 1 H, $J_{3,4}$ = 1.9, $J_{2,3}$ = ^2J = 12.8 Hz, 1 H, H-3$^{III}_{ax}$), 1.21 (d, 3 H, $J_{5,6}$ = 6.6 Hz, H-6^{III}). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.2 ($NCOCCl_3$), 138.2, 138.1, 137.9, 137.3 (4 *ipso* Ph), 128.6−127.8 (Ar), 100.5 (C-1^{II}), 99.2 (C-1^{III}), 96.7 (C-1^I), 94.4 (d, $J_{C,P}$ = 9.6 Hz, CH_2CCl_3), 92.2 ($COCCl_3$), 77.7 (d, $J_{C,P}$ = 4.6 Hz, CH_2CCl_3), 77.4 (C-3^I), 76.9 (C-3^{II}), 75.6 (C-4^{III}), 75.2 (d, $J_{C,P}$ = 4.5 Hz, C-4^{II}), 74.2 (C-5^I), 73.2 (C-4^I), 73.1 (PhCH$_2$), 72.2 (PhCH$_2$), 71.3 (PhCH$_2$), 71.1 (PhCH$_2$), 70.8 (C-2^{III}), 70.6, 70.5, 70.4, 69.9 (C-2′, C-3′, C-4′, C-5′), 70.0 (d, $J_{C,P}$ = 2.4 Hz, C-6^{II}), 69.7 (C-2^{II}), 68.8 (C-6^I), 68.4 (C-1′), 67.5 (C-5^{III}), 66.8 (d, $J_{C,P}$ =

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6.3 Hz, C-5^{II}), 54.1 (C-2^{I}), 50.6 (C-6′), 27.3 (C-3^{III}), 16.5 (C-6^{III}). ^{31}P NMR (162 MHz, $CDCl_3$): δ = −7.06. HRMS (ESI-TOF): m/z [M + NH_4]$^+$ calcd for $C_{56}H_{71}Cl_6N_5O_{18}P$ 1342.2657, found 1342.2669. Anal. Calcd for $C_{56}H_{67}Cl_6N_4O_{18}P$: C, 50.66; H, 5.09; N, 4.22. Found: C, 50.54; H, 4.94; N, 4.16.

8-Amino-3,6-dioxaoctyl 3,6-Dideoxy-α-L-*xylo*-hexopyranosyl-(1→4)-[β-D-galactopyranosyl-4,6-cyclic phosphate-(1→3)]-2-deoxy-2-acetamido-β-D-glucopyranoside (20). (a) A mixture of **18** (214 mg, 0.16 mmol) and Pd/C (214 mg) in a mixture of MeOH (8 mL) and 0.1 M potassium phosphate buffer (8 mL; pH = 7) was stirred under H_2 (1 atm) at room temperature. After 3 days, when TLC (2:1 *i*-PrOH−30% NH_4OH) showed complete conversion of the starting material into a more polar product, the mixture was filtered through a Celite pad, the catalyst was washed with H_2O (10 mL), and the filtrate was concentrated. Chromatography (2:1:0.1 *i*-PrOH−H_2O−30% NH_4OH) followed by lyophilization afforded the desired trisaccharide **20** (106 mg, 93%) as a white powder. $[\alpha]_D^{20}$ = −36.4 (*c* 0.3, H_2O). ^{1}H NMR (600 MHz, D_2O): δ = 4.85 (d, 1 H, $J_{1,2}$ = 3.8 Hz, H-1^{III}), 4.73 (q, 1 H, $J_{5,6}$ = 6.7 Hz, H-5^{III}), 4.50 (d, 1 H, $J_{3,4}$ = 3.5 Hz, H-4^{II}), 4.48 (d, 1 H, $J_{1,2}$ = 8.8 Hz, H-1^{I}), 4.46 (d, 1 H, $J_{1,2}$ = 8.1 Hz, H-1^{II}), 4.33 (br d, 1 H, J = 12.5 Hz, H-6$^{II}_b$), 4.23 (m, 1 H, H-6$^{II}_a$), 4.05 (br s, 1 H, H-4^{III}), 3.87−3.88 (m, 4 H, H-3^{I}, H-2^{III}, H-6$^{I}_a$, H-1′$_a$), 3.84 (t, 1 H, $J_{1,2}$ = $J_{2,3}$ = 9.3 Hz, H-2^{I}), 3.80 (dd, 1 H, J = 4.3, J = 12.3 Hz, H-6$^{I}_b$), 3.71−3.66 (m, 4 H, H-4^{I}, H-1′$_b$, H-5′), 3.65−3.59 (m, 7 H, H-3^{II}, H-2′, H-3′, H-4′), 3.55 (br s, 1 H, H-5^{II}), 3.49−3.43 (m, 2 H, H-5^{I}, H-2^{II}), 3.13 (t, 2 H, J = 4.9 Hz, H-6′), 1.95 (s, 3 H, COCH_3), 1.92 (dt, 1 H, $J_{2,3}$ = $J_{3,4}$ = 2.5, ^2J = 12.9 Hz, 1 H, H-3$^{III}_{eq}$), 1.81 (dt, 1 H, $J_{3,4}$ = 3.9, $J_{2,3}$ = ^2J = 12.9 Hz, 1 H, H-3$^{III}_{ax}$), 1.06 (d, 3 H, $J_{5,6}$ = 6.8 Hz, H-6^{III}). ^{13}C NMR (150 MHz, D_2O): δ = 174.5 ($COCH_3$), 103.2 (C-1^{II}), 101.1 (C-1^{I}), 98.1 (C-1^{III}), 77.1 (C-3^{I}), 76.0 (d, $J_{C,P}$ = 4.3 Hz, C-4^{II}), 75.7 (C-5^{I}), 72.9 (C-4^{I}), 71.3 (d, $J_{C,P}$ = 7.3 Hz, C-3^{II}), 69.8, 69.8, 69.6 (C-2′, C-3′, C-4′), 69.7 (C-2^{II}), 69.2 (C-1′), 68.8 (d, $J_{C,P}$ = 5.4 Hz, C-6^{II}), 68.3 (C-4^{III}), 67.5 (d, $J_{C,P}$ = 4.9 Hz, C-5^{II}), 66.7 (C-5^{III}), 66.6 (C-5′), 63.3 (C-2^{III}), 59.8 (C-6^{I}), 55.9 (C-2^{I}), 39.3 (C-6′), 32.8 (C-3^{III}), 22.5 ($COCH_3$), 15.6 (C-6^{III}). ^{31}P NMR (162 MHz, D_2O): δ = −3.88 ($^3J_{P,H}$ 22.2 Hz). HRMS (ESI-TOF): m/z [M − H]$^-$ calcd for $C_{26}H_{46}N_2O_{18}P$ 705.2489, found 705.2488.

(b) Compound **19** (150 mg, 0.11 mmol) was treated with Pd/C (150 mg) and worked up, as described for **18**, to afford **20** (72 mg, 90%), which was in all aspects identical with the compound described above.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00562.

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Notes

The authors declare no competing financial interest.

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