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Synthesis of Phosphorylated, Conjugation-Ready Di-, Tri- and Tetrasaccharide Fragments of the O-Specific Polysaccharide of *V. cholerae* O139

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The fragments described contain a galactose residue with cyclic 4,6-phosphate and are equipped with an amino-functionalized spacer, allowing further derivatization or direct conjugation to suitable carriers. The core Gal-(1→3)-GlcNAc disaccharide was obtained by condensation of 8-azido-3,6-dioxaoctyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide under Helferich conditions. Reductive opening of the benzylidene acetal, followed by deacetylation and selective benzylation gave 8-azido-3,6-dioxaoctyl 2-acetamido-6-*O*-benzyl-3-*O*-(3-*O*-benzyl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside, which was regioselectively phosphorylated to give two isomeric 4,6-cyclic 2,2,2-trichloroethyl phosphates. The (*R*)-phosphate was subjected to catalytic hydrogenation/hydrogenolysis to give the fully deprotected title disaccharide fragment. Glycosylation of the (*S*)-phosphate diol with 2,4-di-*O*-benzyl-3,6-dideoxy-α-L-xy*lo*-hexopyranosyl bromide under halide-assisted conditions yielded a mixture of the tetrasaccharide and a trisaccharide, which were readily separable by chromatography. Their hydrogenation/hydrogenolysis effected global deprotection as well as reduction of the azide, to furnish the deprotected title tri- and tetrasaccharide.

Introduction

Cholera,[1] caused by *Vibrio cholerae*, is a serious enteric disease. Its main symptoms are severe diarrhea and dehydration, which can lead to hypotensive shock and death. Until 1992, *V. cholerae* O1 was the only strain associated with epidemic and pandemic cholera. In 1992, a new serotype, *V. cholerae* O139, emerged as an additional threat to public health in Third World countries because the population in *V. cholerae* O1 endemic regions lacked protective immunity against the new strain.[2] Serotype O139 has evolved from serotype O1 through acquisition of new genes encoding for enzymes involved in the biosynthesis of O-specific polysaccharides (O-PS),[3] and consequently, the main differences between the two strains are in the constitution of the cell surface.[4] *V. cholerae* O139 expresses a capsular polysaccharide (CPS) whose repeating unit is identical to the O-PS.[4,5] Both the CPS and the O-PS are virulence factors,[4] and a critical level of serum immunoglobulin G (IgG) antibodies against these cell surface components is required for immunity to the parent vibrio.[6]

Carbohydrates are poor immunogens because they activate antibody-producing B cells in T-cell independent (TI) fashion and fail to generate memory B cells.[7] The inferior immunogenicity of carbohydrates is most noticeable in young children, whose immune system is not fully developed. Avery and Goebel first demonstrated that inoculation with neoglycoproteins, obtained by chemical conjugation of carbohydrates to proteins, elicited anticarbohydrate antibodies in T-cell dependant fashion, thus not only initiating immunologic memory but also inducing a stronger and earlier response to a subsequent challenge.[8] These observations initiated the use of glycoconjugates from cell surface carbohydrates as experimental vaccines against the parent microorganism.[9] Initially, haptens were harvested from pathogens, but recent progress in oligosaccharide synthesis enabled preparation of conjugate vaccines from synthetic carbohydrate antigens.[10] Clinical trials with the first synthetic conjugate vaccine provided proof of principle and demonstrated the feasibility of a synthetic approach.[11]

The O-antigen of *V. cholerae* O139 is a hexasaccharide (**1**, Figure 1) consisting of five different monosaccharides, two of which are rare deoxysugars.[5b,5c,12] Within a project focused on the development of a synthetic conjugate vaccine for cholera from this hexasaccharide, we prepare fragments of the O-PS, which will aid to identify epitopes that are crucial for protective capacity. Recently, we reported the synthesis of a linker-equipped phosphorylated disaccharide fragment (**2**, Figure 1),[13] amenable to conjugation with proteins by squaric acid chemistry.[14] Here, we describe experimental details of our synthesis of additional phosphorylated fragments, disaccharide **12**, trisaccharide **17** and the tetrasaccharide **16** (Scheme 1), which were not included in

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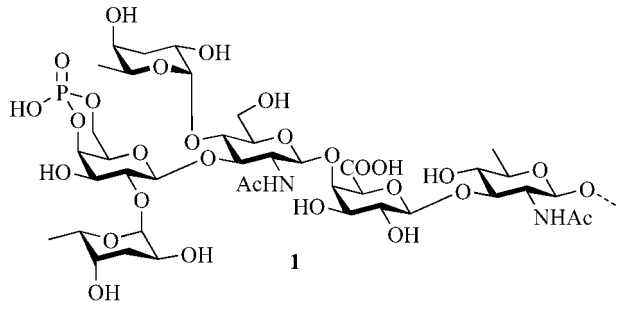
the preliminary report.[15] The compounds are equipped with an amino-functionalized spacer allowing direct conjugation to proteins, or further derivatization for conjugation by a method of choice.



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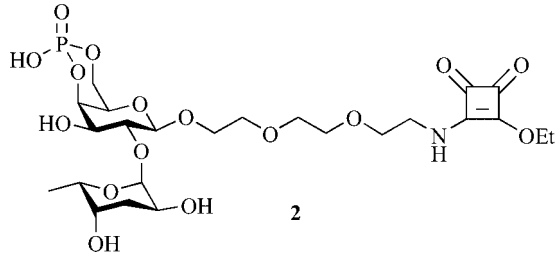

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Figure 1. Structure of the O-antigen of *V. cholerae* O139 (**1**) and of its terminal, disaccharide fragment amenable to conjugation by squaric acid chemistry.

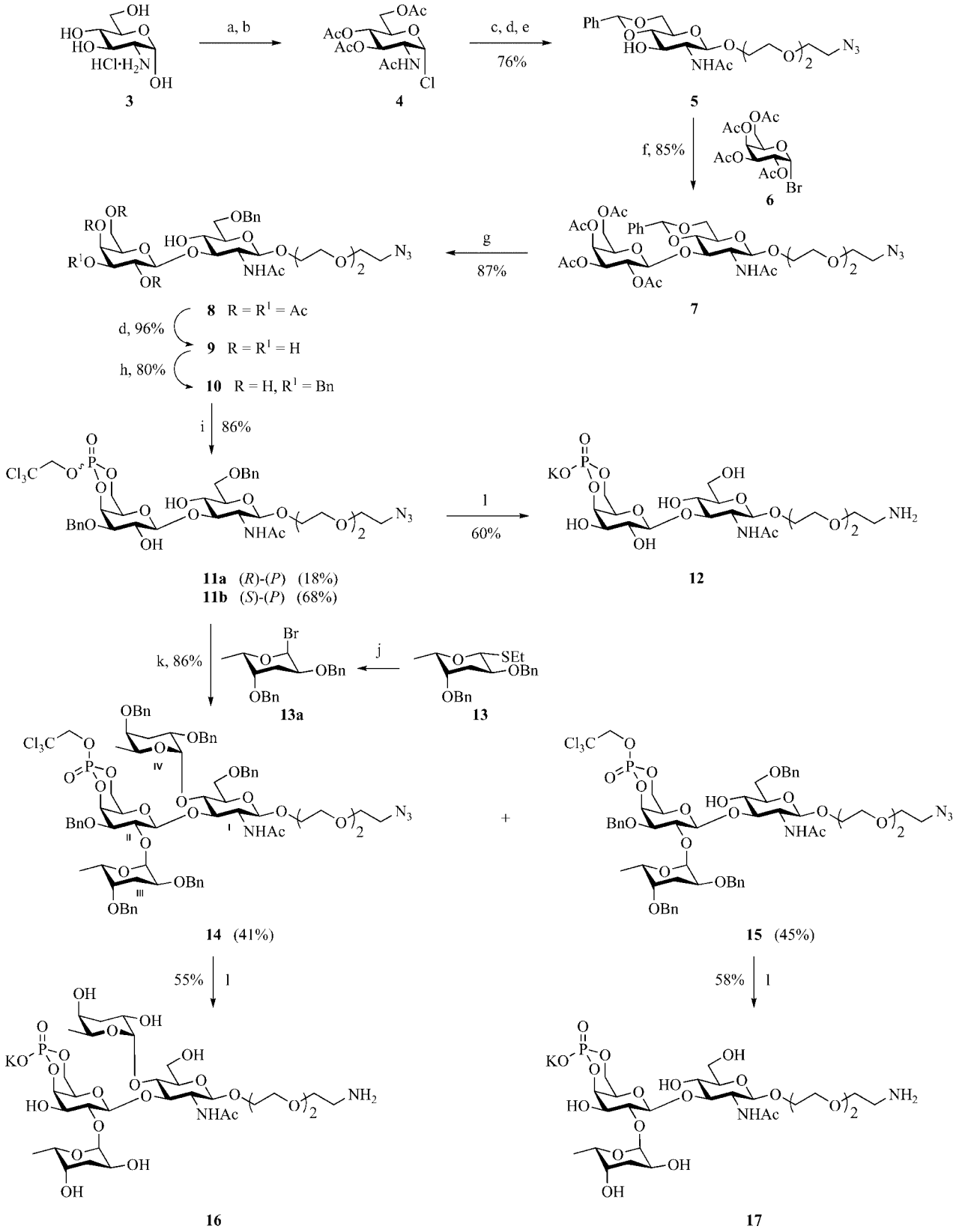
Oscarson and co-workers have recently reported[16] an alternative preparation of a linker-equipped, phosphorylated tetrasaccharide fragment of the *V. cholerae* O139 O-PS. The two approaches are fully independent. For example, a different colitosyl donor and different phosphorylation strategy were used, and the functionalized linker in the final tetrasaccharide was also different. The advantage of Oscarson and co-workers' approach is that their tetrasaccharide thioglycoside can be used as a glycosyl donor to be coupled with a GalA-QuiNAc disaccharide acceptor, to construct the complete hexasaccharide (**1**, Figure 1). On the other hand, our strategy allows preparation of several smaller fragments and requires fewer chemical manipulations with precious oligosaccharides.

Results and Discussion

The synthesis of the tetrasaccharide fragment **16** (Scheme 1) was designed based on the previous[13] observation that the 4,6-cyclic 2,2,2-trichloroethyl phosphate was formed in excellent yield from a galactose derivative with more than two free hydroxy groups. This selectivity is probably the result of a considerable difference in reactivity of the primary and secondary hydroxy groups under the reaction conditions. Initial attack of the primary hydroxy group on the phosphorus dihalide reagent is followed by intramolecular closure to form two stable six-membered ring epimers, rather than intermolecular polymerization. Thus, we expected phosphorylation of linker-equipped key intermediate **10** to lead to two disaccharide phosphate isomers[17] **11a** and **11b**, with the remaining free hydroxy groups available for glycosylation with a colitose donor. Substance **10** represents a motif common in human milk and blood group Lewis oligosaccharides, whose synthesis was first described by Flowers and Jeanloz.[18] Compound **7**, a precursor of **10**, is an intermediate for the preparation of several linker-equipped upstream[19] di-, tri- and tetrasaccharide fragments of the O-antigen of *V. cholerae* O139.

8-Azido-3,6-dioxaoctyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (**5**),[20] the acceptor needed for the preparation of **7**, was synthesized from 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride (**4**),[21] according to the same sequence of reactions as described by Amvam-Zollo and Sinaÿ,[20] albeit using different reagents and reaction conditions. Crude **4**, prepared as reported by Horton,[21] contains a small amount of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-glucopyranoses that co-crystallizes with the chloride.[22] We found chromatographic removal of this impurity prior to crystallization the most efficient way to obtain pure **4**. Condensation of **5** and 2,3,4,6-tetra-*O*-acetyl-α-D-galactosyl bromide (**6**) under Helferich conditions,[23] according to a procedure that is a slight modification of that described by Khare et al.,[24] gave disaccharide **7** in good yield (85%, Scheme 1). The disaccharide was obtained as a crystalline solid after spontaneous evaporation of solvent from its solution in CH_2Cl_2, but all attempts to crystallize it from common solvents failed.

The synthesis described required opening of the 4,6-*O*-benzylidene ring. DeNinno et al. introduced the use of Et_3SiH/CF_3COOH for reductive cleavage of benzylidene acetals in carbohydrates.[25] The method is described as highly selective and to effect exclusive formation of the 6-*O*-benzyl derivatives. However, the reaction has been reported as poor yielding and sluggish, with concomitant cleavage of the acetal to form the 4,6-*O*-deprotected compounds.[26] Kiessling and co-workers engaged Et_3SiH/CF_3SO_3H as an alternative reagent,[27] and a more detailed study of the trialkylsilane/acid reducing system showed that substitution of TFA by TfOH resulted in a more efficient reagent.[28] Indeed, reductive cleavage of acetal **7** with Et_3SiH/TfOH at –78 °C led to 6-*O*-benzyl derivative **8**, with only a small amount of the diol (8%). Examination of the NMR spectra of **8** showed that the compound exists as two conformers, whose ratio is strongly solvent-dependent (NMR). The presence of a mixture is most prominent in [D_6]benzene (ratio of conformers ca. 80:20, based on integration). The amount of the less abundant conformer decreases in [D]-chloroform (ca. 85:15), and it becomes negligible in [D_5]-pyridine, [D_4]methanol, [D_6]dimethyl sulfoxide and [D_4]acetic acid (<5%). At 50 °C in [D]chloroform, the presence of the conformers is hardly noticeable, but interpretation of the spectrum was difficult due to line broadening. The diol byproduct of the reductive cleavage displays similar behavior, with a conformer ratio of 85:15 in [D]chloroform at room temperature. These observations are in accord with a recent report that oligosaccharides containing *N*-acetylglucosamine can adopt unexpected conformations as a result



Scheme 1. Reagents and conditions: (a) (1) NaOMe, MeOH, room temp., (2) Ac_2O, room temp.; (b) AcCl, room temp.; (c) 8-azido-3,6-dioxaoctan-1-ol, AgOTf, tetramethylurea, CH_2Cl_2, room temp.; (d) anhydr. K_2CO_3, MeOH, room temp.; (e) $PhCH(OMe)_2$, CSA, CH_3CN, room temp.; (f) $Hg(CN)_2$, MS (4 Å), CH_3NO_2/benzene (1:1), 40 °C; (g) Et_3SiH, CF_3SO_3H, MS (4 Å), CH_2Cl_2, –78 °C; (h) (1) Bu_2SnO, toluene, reflux, (2) CsF, BnBr, DMF, room temp.; (i) $Cl_3CCH_2OP(O)Cl_2$, pyridine, CH_2Cl_2, –15 °C; (j) (1) Br_2, CCl_4, room temp., (2) hex-1-ene, room temp.; (k) Bu_4NBr, MS (4 Å), CH_2Cl_2/DMF (5:1), room temp.; (l) Pd/C, H_2, *i*PrOH/potassium phosphate buffer (pH = 7, 0.1 M), room temp.

of formation of hydrogen bonds involving the amide group.[29] Liao et al. studied the coupling constants for the *N*-acetylglucosamine residue in small oligosaccharides and found that they were inconsistent with a $^4C_1$ chair conformation in non-hydrogen bond-accepting solvents. However, they did not observe the presence of different conformers. We presume that, in our case, the long polyethylene glycol spacer slows down formation of the equilibrium between conformations sufficiently to lead, in solution, to the existence of different conformers on the NMR time scale. In [D]chloroform, the ^{13}C NMR spectrum of the major conformer of **8** shows a significant upfield shift of the signal for C-4^{I} (by ca. 11 ppm; for numbering of sugar residues, see Scheme 1, structure **14**) and downfield shifts of signals for C-3^{I} (by ca. 7 ppm) and for C-6^{I} (by ca. 1 ppm) compared to those in the spectra of **7**, which is consistent with reductive opening of the acetal to form the 6-benzyl ether. Additional proof that the intended opening of the benzylidene ring had occurred was provided by the cross peak between 4^{I}-H and the HO group observed in the COSY spectra of **8** taken in [D]chloroform and [D_6]dimethyl sulfoxide. Deacetylation of substance **8** (→ **9**), followed by benzylation at the 3-position of the galactose residue (→ **10**) and selective phosphorylation[13] with 2,2,2-trichloroethyl phosphorodichloridate, gave a mixture (ca. 1:3.8) of (*R*)- and (*S*)-(*P*)-4,6-cyclic 2,2,2-trichloroethyl phosphates **11a** and **11b**, respectively.

The (*S*)-phosphate acceptor **11b** was subjected to halide-assisted[30] glycosylation with the colitosyl bromide (**13a**) obtained from ethyl 1-thio-β-colitoside[31] (**13**) by treatment with Br_2. As expected from the well-known fact that the 4-OH group of the GlcNAc residues is quite unreactive, these glycosylation conditions furnished not only the desired tetrasaccharide **14**, but also the trisaccharide **15**, whose deprotected forms are useful haptens for immunological studies. Oscarson and co-workers[16] reported similar formation of a mixture of a trisaccharide and a tetrasaccharide, albeit with a better yield of the latter. It is interesting to note that this was accomplished with fewer equivalents of a colitosyl bromide donor under very similar reaction conditions. It seems that the use of electron-withdrawing protecting groups instead of benzyl ethers increased the stability of their donor to allow prolonged reaction time (7 d) resulting in more complete conversion. We found that with bromide **13a** the reaction was finished within 48 h, and that the yield of oligosaccharides **14** and **15** depended on the excess of glycosyl donor used. With 5 equiv. of **13a**, the glycosylation furnished more of the trisaccharide **15** (48%, in addition to 34% of **14**), while with 6 equiv. of **13a** similar yields of **14** and **15** (41 and 45%, respectively) were obtained. Both compounds were fully characterized and their structure was confirmed by NMR spectrioscopy and high-resolution mass spectrometry. For trisaccharide **15**, the significant downfield shift of the signal for 2^{II}-H (by 0.32 ppm, compared to that in the spectrum of **11b**) and the COSY crosspeak between 4^{I}-H and the hydroxy group confirmed the point of attachment of the colitose residue at O-2 in galactose, while the coupling constant of the doublet for 1^{III}-H at δ = 5.50 ppm ($J_{1^{III},2^{III}}$ = 3.3 Hz) evidenced formation of the α-colitosyl linkage. As expected, downfield shifts were observed in the spectrum of tetrasaccharide **14** of signals for 2^{II}-H and 4^{I}-H (by 0.24 and 0.48 ppm, respectively, compared to those in the spectrum of **11b**), and the coupling constants of the doublets for 1^{III}-H at δ = 5.62 ppm ($J_{1^{III},2^{III}}$ = 3.4 Hz) and 1^{IV}-H at δ = 5.02 ppm ($J_{1^{IV},2^{IV}}$ = 3.5 Hz) are consistent with the α-linkage of colitose residues. Unlike in the NMR spectra of trisaccharide **15**, coupling constants for 1^{I}-H ($J_{1^{I},2^{I}}$ = 6.7 Hz, $J_{C\text{-}1^{I},H\text{-}1^{I}}$ = 166.7 Hz) in NMR spectra of **14** differ from those usually found for a β-glucosamine residue in a $^4C_1$ conformation.[32] They are in accord, however, in particular $J_{C\text{-}1^{I},H\text{-}1^{I}}$, with a distorted conformation of the β-glucosamine unit due to the involvement of the acetamido group in hydrogen-bond formation.[29] Bush and co-workers[33] analyzed the conformation of the tetrasaccharide portion of the hexasaccharide repeating unit of the CPS of *V. cholerae* O139 by NMR spectroscopy and molecular modeling. They showed that the tetrasaccharide adopts a compact and tightly folded conformation in which the cyclic phosphate is in close contact with the colitose residue linked to the β-glucosamine unit. Though protected, NMR spectroscopic data found for the synthetic tetrasaccharide fragment **14** reflect these findings. Deshielding, as a result of the interaction between the phosphate group and the colitose residue attached to β-GlcNAc, leads to a downfield shift (by 7.11 ppm) of the ^{31}P signal compared to that in the spectrum of trisaccharide **15**, and downfield shifts of the signals for 3^{IV}-H_{ax} (by 0.09 ppm), 4^{IV}-H (by 0.1 ppm), 5^{IV}-H (by 0.4 ppm) and 6^{IV}-H (by 0.05 ppm), compared to those for 3^{III}-H_{ax}, 4^{III}-H, 5^{III}-H and 6^{III}-H, respectively.

Unusually high hydrogen pressure (160 psi) was required to maintain a practicable reaction rate of hydrogenolysis/hydrogenation of **14** (→ **16**) in the presence of palladium-on-charcoal catalyst, probably because the aforementioned compact conformation impedes interaction of reaction sites with the catalyst surface. Global deprotection of **11a** (→ **12**) and **15** (→ **17**) with concomitant reduction of the azide to an amine was possible to achieve at considerably lower hydrogen pressure (70 psi). As reported previously,[13] deprotection was done in a buffered solution, to protect the acid-labile α-colitosyl bonds. Oscarson and co-workers[16] did not report problems with catalytic hydrogenolysis of the benzyl groups in their tetrasaccharide. However, they had two fewer benzyl groups to remove from the tetrasaccharide. The benzoyl groups used instead to protect the 4-OH groups in the colitose residues were very resistant to base-catalyzed deacylation, indicating that this position in the tetrasaccharide is rather unreactive. Furthermore, the *p*-chlorobenzyl ethers at C-2 of the colitosyl residues[16] can be expected to be more easily cleaved than their non-halogenated counterparts. Finally, it is possible that the buffered reaction medium deactivated the catalyst, thus necessitating the use of substantially higher hydrogen pressure. This seems to be confirmed by the fact that deprotection of **12** and **15** also required more than atmospheric hydrogen pressure to effect the conversion. After chromatography to re-

move several less polar byproducts, the deprotected oligosaccharides **12**, **16** and **17** were obtained in yields of 60%, 55% and 58%, respectively. Extended reaction times led to lower yields of the desired oligosaccharides and more extensive formation of the byproducts (TLC). This indicates that these materials were not the products of incomplete deprotection, but their nature was not further investigated.

Conclusions

An efficient synthesis has been developed for the preparation of three fragments of the O-PS of *V. cholerae* O139. The key step is the regioselective phosphorylation of a polyol disaccharide intermediate, which greatly reduces the number of synthetic steps. The phosphorylated di-, tri- and tetrasaccharide fragments are equipped with an amino-functionalized spacer to allow direct conjugation to proteins or further derivatization for conjugation by a method of choice.

Experimental Section

General Methods: HPLC grade solvents were used, and reactions requiring anhydrous conditions were carried out under nitrogen or argon. A Parr mini bench top reactor, series 4560, was used for reactions under H_2. Tetramethylurea was stored over KOH pellets, pyridine over CaH_2. The density of 2,2,2-trichloroethyl phosphorodichloridate was determined by differential weighing of 1 mL of reagent ($d \approx 1.7$ g/mL at 20 °C). Compound **6** was purchased from Sigma. The palladium-on-charcoal catalyst (5%, Escat 147) was a product of Engelhard Industries. Reversed phase purifications were done on Analogix SuperFlash-Sepra C18 columns. Reactions were monitored by thin-layer chromatography (TLC) on silica gel 60 glass slides. Spots were visualized by heating, after spraying with H_2SO_4 in EtOH (5% v/v) or ninhydrine in EtOH (5% w/v) for primary amines. For purification of **4** and **6**, silica gel 60 was dried overnight at 160 °C. Melting points were determined with a Kofler hot stage. Optical rotations were measured with a Perkin–Elmer automatic polarimeter, Model 341. NMR spectra were measured at 25 °C with a Varian Mercury spectrometer, at 300 MHz for ^1H, 75 MHz for ^{13}C and 121 MHz for ^{31}P, or with a Bruker Avance spectrometer, at 600 MHz for ^1H and 150 MHz for ^{13}C. Assignments of NMR signals were made by first-order analysis of the spectra and, when feasible, the assignments were supported by homonuclear decoupling experiments or homonuclear and heteronuclear 2-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 in listings of signal assignments are serially numbered by a Roman numeral superscript, beginning with the one bearing the aglycon (see Scheme 1, **14**). ^{31}P-^{13}C coupling was observed for all phosphates. Chemical shifts are reported relative to tetramethylsilane (TMS) or acetone[34] as internal standard. Chemical shifts for ^{31}P NMR spectra are reported relative to H_3PO_4 in D_2O as an internal standard (stem coaxial insert). No elemental analyses or optical rotations were collected for the di-, tri- and tetrasaccharide phosphate salts. The structure of these compounds follows unequivocally from the mode of synthesis and the *m*/*z* values found in their low- and high-resolution mass spectra, and their purity was verified by TLC and NMR spectroscopy. Unless stated otherwise, solutions in organic solvents were dried with anhydrous Na_2SO_4 and concentrated at ca. 40 °C/2 kPa.

2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl Chloride (4): Prepared from D-glucosamine hydrochloride (**3**) as described by Horton,[21] except that crude **4** was chromatographed (dry silica gel/crude material: 20:1, hexane/EtOAc: 1:2, sample loaded as a solution in CH_2Cl_2) before crystallization, to remove 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-glucopyranose.

8-Azido-3,6-dioxaoctyl 2-Acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (5): A solution of **4** (15.68 g, 42.84 mmol) and tetramethylurea (3.25 mL, 27.13 mmol) in CH_2Cl_2 (60 mL) was added slowly (exothermic!) to a stirred mixture of AgOTf (11.74 g, 45.69 mmol) and 8-azido-3,6-dioxaoctan-1-ol[13] (5.0 g, 28.56 mmol) in CH_2Cl_2 (40 mL). Stirring was continued in the dark for 24 h. The mixture was treated with Et_3N (8 mL, 57.11 mmol), filtered through a Celite pad, and the solids were washed with CH_2Cl_2. The combined filtrates (ca. 500 mL) were washed with H_2O (500 mL), ice-cold 10% aqueous H_2SO_4 (500 mL), saturated $NaHCO_3$ (500 mL) and H_2O (500 mL), dried, and concentrated. The residue (14.82 g) was dissolved in MeOH (100 mL) and anhydrous K_2CO_3 (1.0 g, 7.14 mmol) was added. The mixture was stirred for 4 h and neutralized with IR-120 (H^+) resin. The resin was filtered off, washed with MeOH, and the combined filtrates were concentrated. A solution of the residue in CH_3CN (3×100 mL) was concentrated to remove residual MeOH, and dried. A mixture of the residue, CSA (665 mg, 2.86 mmol), α,α-dimethoxytoluene (8.6 mL, 57.11 mmol) and CH_3CN (200 mL) was stirred at room temp. After 14 h, Et_3N (1 mL, 7.14 mmol) was added and the solvent was evaporated. The residue was chromatographed (CH_2Cl_2/*i*PrOH: 95:5→90:10) to give **5**, containing ca. 5% of the α-anomer (11.615 g, 87%). Crystallization from EtOH gave pure **5** (8.646 g, 65%). Column chromatography (reversed phase, MeOH/H_2O: 1:1) of the mother liquor, followed by crystallization from EtOH gave an additional crop of pure **5** (1.505 g, 11%). M.p. 184–187 °C (ref.[20] 193–194 °C). $[\alpha]_D^{25}$ = –78 [*c* = 1.63, $CHCl_3$; ref.[20] –76 (*c* = 1.6, $CHCl_3$)]. ^1H NMR (600 MHz, $CDCl_3$): δ = 2.02 (s, 3 H, $COCH_3$), 3.40 (br. t, *J* = 5.0 Hz, partial overlap, 2 H, CH_2N_3), 3.41 (m, partial overlap, 1 H, 5-H), 3.56 (t, $J_{3,4} = J_{4,5}$ = 9.2 Hz, 1 H, 4-H), 3.60 (dt, $J_{1,2a}$ = 3.1, $J_{2a,2b}$ = 11.0 Hz, 1 H, 2′a-H), 3.62–3.65 (m, 6 H, 3′-H, 4′-H, 5′-H), 3.68 (m, 1 H, 2′b-H), 3.73 (m, 1 H, 2-H), 3.75 (t, $J_{5,6a} = J_{6a,6b}$ = 10.4 Hz, partial overlap, 1 H, 6a-H), 3.78 (ddd, $J_{1a,2a}$ = 2.8, $J_{1a,2b}$ = 8.7, $J_{1a,1b}$ = 12.0 Hz, partial overlap, 1 H, 1′a-H), 3.86 (br. dt, $J_{3,OH}$ = 2.4, $J_{2,3} = J_{3,4}$ = 9.5 Hz, 1 H, 3-H), 3.92 (dt, $J_{1b,2a} = J_{1b,2b}$ = 3.2, $J_{1a,1b}$ = 12.0 Hz, 1 H, 1′b-H), 4.30 (dd, $J_{5,6b}$ = 5.0, $J_{6a,6b}$ = 10.4 Hz, 1 H, 6b-H), 4.66 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1-H), 4.86 (d, $J_{3,OH}$ = 2.9 Hz, 1 H, HO-3), 5.51 (s, 1 H, C*H*Ph), 6.85 (d, $J_{2,NH}$ = 6.6 Hz, 1 H, NH), 7.31–7.36 (m, 3 H, Ph), 7.47–7.50 (m, 2 H, Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 22.97 ($COCH_3$), 50.41 (CH_2N_3), 58.11 (C-2), 66.15 (C-5), 68.43 (C-6), 68.85 (C-1′), 69.73, 70.26, 70.43 (C-3′, C-4′, C-5′), 70.86 (C-2′), 72.62 (C-3), 81.47 (C-4), 101.68 (*C*HPh), 101.69 (C-1), 126.28, 128.07, 128.95, 137.08 (Ph), 172.53 (*C*$COCH_3$) ppm.

2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl Bromide (6): Commercial bromide (30 g) was purified by chromatography (hexane/EtOAc: 3:1) to remove the stabilizer ($CaCO_3$) and other impurities. Crystallization of the resulting material (25.55 g) from diisopropyl ether gave **6** (20.67 g), whose purity and structure was confirmed by ^1H NMR spectroscopy.

8-Azido-3,6-dioxaoctyl 2-Acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (7): Powdered anhydrous $CaSO_4$ (30 g) and $Hg(CN)_2$ (9.56 g,

37.84 mmol) were added to a stirred solution of **5** (8.82 g, 18.92 mmol) in CH_3NO_2/benzene (1:1; 520 mL). After 1 h, a solution of **6** (11.67 g, 28.38 mmol) in the same solvent (75 mL) was added, and the mixture was stirred at 40 °C for 16 h. After filtration through a Celite pad, the solids were washed with CH_2Cl_2 (5 × 250 mL), the filtrate was concentrated and a solution of the residue in CH_2Cl_2 (1.5 L) was washed with 10% KBr in brine (1 L), saturated $NaHCO_3$ (1 L) and H_2O (1 L). The organic phase was dried, and concentrated, and the residue was chromatographed (CH_2Cl_2/*i*PrOH: 100:2.5 and petroleum ether/acetone: 3:2) to give disaccharide **7** (12.86 g, 85%). A portion was dissolved in CH_2Cl_2 and the solvent was allowed to evaporate. The solid obtained after drying under reduced pressure at 40 °C showed m.p. 129.0–132.5 °C (see Results and Discussion). $[a]_D^{25}$ = –16.8 (*c* = 0.51, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.95, 1.96, 2.00, 2.02, 2.12 (5 s, 15 H, 5 CH_3CO), 3.24 (m, 1 H, 2^I-H), 3.43 (m, 2 H, CH_2N_3), 3.53 (m, 1 H, 5^I-H), 3.61 (m, partial overlap, 1 H, 5^{II}-H), 3.62–3.70 (m, 9 H, 4^I-H, 2′-H, 3′-H, 4′-H, 5′-H), 3.75 (m, partial overlap, 1 H, 1′b-H), 3.78 (t, partial overlap, $J_{5,6a}$ = $J_{6a,6b}$ = 10.4 Hz, 1 H, 6^{I}a-H), 3.93 (dd, partial overlap, $J_{5,6a}$ = 5.9, $J_{6a,6b}$ = 11.1 Hz, 1 H, 6^{II}a-H), 3.94 (m, partial overlap, 1 H, 1′a-H), 4.06 (dd, $J_{5,6b}$ = 7.8, $J_{6a,6b}$ = 11.1 Hz, 1 H, 6^{II}b-H), 4.31 (dd, $J_{5,6b}$ = 4.9, $J_{6a,6b}$ = 10.4 Hz, 1 H, 6^{I}b-H), 4.60 (t, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, 1 H, 3^I-H), 4.74 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1^{II}-H), 4.93 (dd, $J_{2,3}$ = 10.4, $J_{3,4}$ = 3.4 Hz, 1 H, 3^{II}-H), 5.12 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1^I-H), 5.17 (dd, $J_{1,2}$ = 8.0, $J_{2,3}$ = 10.3 Hz, 1 H, 2^{II}-H), 5.29 (dd, $J_{3,4}$ = 3.4, $J_{4,5}$ = 1.0 Hz, 1 H, 4^{II}-H), 5.52 (s, 1 H, C*H*Ph), 6.10 (d, $J_{NH,2}$ = 7.4 Hz, 1 H, NH), 7.36–7.39 (m, 3 H, arom.), 7.46–7.49 (m, 2 H, arom.) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 20.49, 20.53, 20.57, 20.69, 23.53 (5 *C*H_3CO), 50.54 (CH_2N_3), 57.78 (C-2^I), 60.92 (C-6^{II}), 65.89 (C-5^I), 66.77 (C-4^{II}), 68.69 (C-6^I), 68.81 (C-1′), 69.23 (C-2^{II}), 70.35 (C-5^{II}), 69.89, 70.40, 70.49, 70.60 (C-2′, C-3′, C-4′, C-5′), 71.03 (C-3^{II}), 76.92 (C-3^I), 80.44 (C-4^I), 99.86 (C-1^I), 100.39 (C-1^{II}), 101.32 (*C*HPh), 126.00, 128.24, 129.15, 137.06 (Ph), 169.46, 170.09, 170.15, 170.19, 170.71 (5 CH_3CO) ppm. ES-TOF-MS (pos. ion): *m*/*z* = 803.3179 ([M + Li]$^+$; calcd. 803.3175). $C_{35}H_{48}N_4O_{17}$ (796.30): calcd. C 52.76, H 6.07, N 7.03; found C 52.59, H 6.08, N 7.01.

8-Azido-3,6-dioxaoctyl 2-Acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (8): Powdered molecular sieves (4 Å, 2.5 g) were added to a stirred solution of **7** (5.0 g, 6.28 mmol) in CH_2Cl_2 (50 mL). After 30 min, the mixture was cooled to –78 °C, and Et_3SiH (3.0 mL, 18.84 mmol) and TfOH (1.42 mL, 12.56 mmol) was added. Stirring was continued at –78 °C, and after 2 h the reaction was quenched by addition of solid $NaHCO_3$ (5.0 g) and MeOH (25 mL). The mixture was allowed to reach room temperature, filtered through a Celite pad, and the solids were washed with CH_2Cl_2. The combined filtrates (500 mL) were washed with saturated aq. $NaHCO_3$ (250 mL) and H_2O (250 mL), dried, and concentrated. The residue was chromatographed (toluene/EtOH: 9:1→8:2) to give first **8** (4.343 g, 87%). M.p. 103.5–104.0 °C (from *i*PrOH). $[a]_D^{25}$ = +1.7 (*c* = 0.54, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$; major conformer): δ = 1.98, 2.00, 2.02, 2.09, 2.15 (5 s, 15 H, 5 CH_3CO), 3.28 (m, 1 H, 2^I-H), 3.40–3.52 (m, 4 H, 5^I-H, 4^I-H, CH_2N_3), 3.60–3.70 (m, 9 H, 6a^I-H, 2′-H, 3′-H, 4′-H, 5′-H), 3.76 (m, 1 H, 1a′-H), 3.80 (s, 1 H, OH), 3.86 (dd, $J_{5,6b}$ = 1.6, $J_{6a,6b}$ = 10.9 Hz, 1 H, 6b^I-H), 3.95 (m, 1 H, 1b′-H), 4.01 (m, 1 H, 5^{II}-H), 4.12 (m, 2 H, 6^{II}-H), 4.23 (dd, *J* = 7.8, *J* = 10.3 Hz, 1 H, 3^I-H), 4.59 (d, $J_{1,2}$ = 8.0 Hz, partial overlap, 1 H, 1^{II}-H), 4.58, 4.61 (2 d, ^2J = 12.2 Hz, partial overlap, 2 H, CH_2Ph), 4.86 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1^I-H), 5.01 (dd, $J_{3,4}$ = 3.4, $J_{2,3}$ = 10.5 Hz, 1 H, 3^{II}-H), 5.22 (dd, $J_{1,2}$ = 8.0, $J_{2,3}$ = 10.5 Hz, 1 H, 2^{II}-H), 5.37 (dd, $J_{4,5}$ = 0.9, $J_{3,4}$ = 3.4 Hz, 1 H, 4^{II}-H), 5.98 (d, $J_{NH,2}$ = 7.6 Hz, 1 H, NH), 7.24–7.30 (m, 2 H, Ph), 7.30–7.36 (m, 3 H, Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$; major conformer): δ = 20.47, 20.49, 20.57, 20.71, 23.64 (5 *C*H_3CO), 50.53 (CH_2N_3), 56.85 (C-2^I), 61.41 (C-6^{II}), 66.88 (C-4^{II}), 68.48 (C-1′), 68.74 (C-2^{II}), 69.43 (C-4^I), 69.65 (C-6^I), 69.86, 70.35, 70.59, 70.71 (C-2′, C-3′, C-4′, C-5′), 70.76 (C-3^{II}), 70.94 (C-5^{II}), 73.51 (*C*H_2Ph), 75.26 (C-5^I), 83.89 (C-3^I), 99.71 (C-1^I), 101.36 (C-1^{II}), 127.45, 127.52, 128.25, 138.33 (Ph), 169.15, 170.00, 170.09, 170.41, 170.64 (5 CH_3CO) ppm. ^{1}H NMR (600 MHz, [D$_6$]DMSO; major conformer): δ = 1.82, 1.90, 1.98, 2.02, 2.11 (5 s, 15 H, 5 CH_3CO), 3.20 (dt, $J_{4,OH}$ = 4.0, $J_{3,4}$ = $J_{4,5}$ = 9.0 Hz, 1 H, 4^I-H), 3.35–3.39 (m, 3 H, 5^I-H, CH_2N_3), 3.45–3.60 (m, 11 H, 1a′-H, 6a^I-H, 2^I-H, 2′-H, 3′-H, 4′-H, 5′-H), 3.64 (br. t, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, 1 H, 3^I-H), 3.71–3.79 (m, 2 H, 1b′-H, 6b^I-H), 4.01 (dd, $J_{5,6a}$ = 5.9, $J_{6a,6b}$ = 11.2 Hz, 1 H, 6a^{II}-H), 4.10 (dd, $J_{5,6b}$ = 7.3, $J_{6a,6b}$ = 11.2 Hz, 1 H, 6b^{II}-H), 4.21 (br. t, $J_{4,5}$ ≈ 0, $J_{5,6a}$ = $J_{5,6b}$ = 6.9 Hz, 1 H, 5^{II}-H), 4.40 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1^I-H), 4.51, 4.53 (2 d, ^2J = 12.1 Hz, partial overlap, 2 H, CH_2Ph), 4.52 (d, $J_{4,OH}$ = 3.7 Hz, partial overlap, 1 H, OH), 4.78 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1^{II}-H), 4.93 (dd, $J_{1,2}$ = 8.1, $J_{2,3}$ = 10.4 Hz, 1 H, 2^{II}-H), 5.13 (dd, $J_{3,4}$ = 3.6, $J_{2,3}$ = 10.4 Hz, 1 H, 3^{II}-H), 4.26 (br. d, $J_{4,5}$ ≈ 0, $J_{3,4}$ = 3.6 Hz, 1 H, 4^{II}-H), 7.26–7.36 (m, 5 H, Ph), 7.79 (d, $J_{NH,2}$ = 9.0 Hz, 1 H, NH) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO; major conformer): δ = 20.30, 20.41 (2 C), 20.42, 22.95 (5 *C*H_3CO), 49.97 (CH_2N_3), 53.83 (C-2^I), 61.02 (C-6^{II}), 67.18 (C-4^{II}), 67.90 (C-1′), 68.31 (C-2^{II}), 68.52 (C-4^I), 69.22, 69.45, 69.69, 69.83 (C-2′, C-3′, C-4′, C-5′), 69.51 (C-6^I), 69.93 (C-5^{II}), 70.39 (C-3^{II}), 72.28 (*C*H_2Ph), 75.14 (C-5^I), 82.74 (C-3^I), 100.10 (C-1^{II}), 100.51 (C-1^I), 127.33, 128.20, 138.57 (Ph), 169.01, 169.29, 169.48, 169.89, 169.95 (5 CH_3CO) ppm. ES-TOF-MS (pos. ion): *m*/*z* = 805.3347 ([M + Li]$^+$; calcd. 805.3331). $C_{35}H_{50}N_4O_{17}$ (798.3): calcd. C 52.63, H 6.31, N 7.01; found C 52.81, H 6.42, N 6.99. Next eluted was **8-Azido-3,6-dioxaoctyl 2-Acetamido-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside** (353 mg, 8%). ^{1}H NMR (600 MHz, $CDCl_3$; major conformer): δ = 1.98, 2.01, 2.06, 2.10, 2.16 (5 s, 15 H, 5 CH_3CO), 2.47 (t, $J_{6,OH}$ = 6.7 Hz, 1 H, 6-OH), 3.35 (m, 1 H, 2^I-H), 3.41 (m, 1 H, 5^I-H), 3.42–3.46 (m, 2 H, CH_2N_3), 3.49 (m, 1 H, 4^I-H), 3.63–3.72 (m, 8 H, 2′-H, 3′-H, 4′-H, 5′-H), 3.74–3.80 (m, 2 H, 1a′-H, 6a^I-H), 3.88–3.95 (m, 3 H, 1b′-H, 6b^I-H, 4-OH), 4.04 (br. ddd, $J_{4,5}$ = 1.1, $J_{5,6a}$ = 5.9, $J_{5,6b}$ = 7.1 Hz, 1 H, 5^{II}-H), 4.13 (m, 2 H, 6^{II}-H), 4.18 (dd, *J* = 8.4, *J* = 10.3 Hz, 1 H, 3^I-H), 4.60 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1^{II}-H), 4.88 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1^I-H), 5.02 (dd, $J_{3,4}$ = 3.5, $J_{2,3}$ = 10.5 Hz, 1 H, 3^{II}-H), 5.21 (dd, $J_{1,2}$ = 8.0, $J_{2,3}$ = 10.5 Hz, 1 H, 2^{II}-H), 5.38 (dd, $J_{4,5}$ = 1.0, $J_{3,4}$ = 3.5 Hz, 1 H, 4^{II}-H), 6.27 (d, $J_{NH,2}$ = 7.8 Hz, 1 H, NH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$; major conformer): δ = 20.48, 20.51, 20.57, 20.69, 23.56 (5 *C*H_3CO), 50.48 (CH_2N_3), 56.42 (C-2^I), 61.42 (C-6^{II}), 62.75 (C-6^I), 66.87 (C-4^{II}), 68.63 (C-1′), 68.67 (C-2^{II}), 69.83, 70.31, 70.56, 70.80 (C-2′, C-3′, C-4′, C-5′), 69.93 (C-4^I), 70.72 (C-3^{II}), 70.93 (C-5^{II}), 75.24 (C-5^I), 83.86 (C-3^I), 100.09 (C-1^I), 101.34 (C-1^{II}), 169.24, 170.03, 170.11, 170.44, 170.76 (5 CH_3CO) ppm. ES-TOF-MS (pos. ion): *m*/*z* = 715.2882 ([M + Li]$^+$; calcd. 715.2862).

8-Azido-3,6-dioxaoctyl 2-Acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(β-D-galactopyranosyl)-β-D-glucopyranoside (9): Anhydrous K_2CO_3 (727 mg, 5.26 mmol) was added to a solution of **8** (4.2 g, 5.26 mmol) in MeOH (50 mL). The mixture was stirred at room temperature for 2.5 h, neutralized with IR-120 (H$^+$) resin, the resin was filtered off, washed with MeOH, and the filtrate was concentrated. The residue was chromatographed (CH_2Cl_2/10% NH_4OH in MeOH: 85:15→80:20) to give, after freeze-drying, amorphous **9** (3.194 g, 96%). $[a]_D^{25}$ = –13.8 (*c* = 0.55, MeOH). ^{1}H NMR (600 MHz, D_2O): δ = 2.02 (s, 3 H, CH_3CO), 3.47 (m, 2 H, CH_2N_3), 3.52 (dd, $J_{1,2}$ = 7.7, $J_{2,3}$ = 10.0 Hz, 2^{II}-H, 1 H, partial overlap),

3.54 (dd, J = 8.5, J = 10.0 Hz, 1 H, 4^{I}-H), 3.60 (m, 1 H, 5^{I}-H), 3.63 (dd, $J_{3,4}$ = 3.4, $J_{2,3}$ = 10.0 Hz, 1 H, 3^{II}-H), 3.64–3.71 (m, 9 H, 5^{II}-H, 2′-H, 3′-H, 4′-H, 5′-H), 3.71–3.79 (m, 5 H, 3^{I}-H, 6a^{I}-H, 6^{II}-H, 1a′-H), 3.83 (dd, $J_{1,2}$ = 8.5, $J_{2,3}$ = 10.4 Hz, 1 H, 2^{I}-H), 3.89–3.93 (m, 2 H, 6b^{I}-H, 4^{II}-H), 3.95 (ddd, $J_{1b,2a}$ = 3.1, $J_{1b,2b}$ = 5.6, $J_{1a,1b}$ = 11.7 Hz, 1 H, 1b′-H), 4.41 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1^{II}-H), 4.57 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1^{I}-H), 4.62, 4.64 (2 d, ^{2}J = 11.8 Hz, 2 H, CH_2Ph), 7.38–7.46 (m, 5 H, Ph) ppm. ^{13}C NMR (150 MHz, D_2O): δ = 25.01 (CH_3CO), 52.87 (CH_2N_3), 57.24 (C-2^{I}), 63.79 (C-6^{II}), 71.29 (C-4^{II}), 71.74 (C-6^{I}), 71.76 (C-4^{I}), 71.82 (C-1′), 71.98, 72.33, 72.42, 72.43 (C-2′, C-3′, C-4′, C-5′), 73.44 (C-2^{II}), 75.25 (C-3^{II}), 75.99 (CH_2Ph), 77.01 (C-5^{I}), 78.04 (C-5^{II}), 85.16 (C-3^{I}), 103.59 (C-1^{I}), 106.31 (C-1^{II}), 131.07, 131.18, 131.48, 140.04 (Ph), 177.37 (CH_3CO) ppm. ES-TOF-MS (pos. ion): m/z = 637.2905 ([M + Li]$^{+}$; calcd. 637.2908). $C_{27}H_{42}N_4O_{13}$ (630.3): calcd. C 51.42, H 6.71, N 8.88; found C 51.18, H 6.69, N 8.89.

8-Azido-3,6-dioxaoctyl 2-Acetamido-6-*O*-benzyl-3-*O*-(3-*O*-benzyl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (10): A mixture of **9** (3.0 g, 4.76 mmol), Bu_2SnO (1.185 g, 4.76 mmol) and toluene (150 mL) was heated under reflux in a Soxhlet apparatus containing molecular sieves (4 Å). After 6 h, the mixture was cooled to room temperature, CsF (1.45 g, 9.52 mmol) was added, and the solvent was evaporated under reduced pressure. The residue was dissolved in DMF (50 mL) and BnBr (1.15 mL, 9.52 mmol) was added to the stirred solution. After 20 h, the mixture was concentrated and the residue was partitioned between CH_2Cl_2 (500 mL) and brine (500 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 250 mL), the combined organic layers were dried, concentrated, and the residue was chromatographed (CH_2Cl_2/MeOH: 100:0→95:5) to give **10** (2.753 g, 80%). $[\alpha]_D^{25}$ = –1.90 (c = 0.59, MeOH). ^{1}H NMR (600 MHz, CD_3OD): δ = 1.98 (s, 3 H, CH_3CO), 3.35–3.38 (m, 3 H, 3^{II}-H, CH_2N_3), 3.45 (t, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, partial overlap, 1 H, 4^{I}-H), 3.44–3.52 (m, 2 H, 5^{II}-H, 5^{I}-H), 3.60–3.66 (m, 8 H, 2′-H, 3′-H, 4′-H, 5′-H), 3.67–3.73 (m, 5 H, 2^{II}-H, 3^{I}-H, 6a^{I}-H, 6a^{II}-H, 1a′-H), 3.74–3.78 (m, 2 H, 2^{I}-H, 6b^{II}-H), 3.87 (dd, $J_{5,6b}$ = 1.6, $J_{6a,6b}$ = 11.0 Hz, 1 H, 6b^{I}-H), 3.93 (m, 1 H, 1b′-H), 4.00 (br. d, $J_{3,4}$ = 3.2 Hz, 1 H, 4^{II}-H), 4.30 (d, $J_{1,2}$ = 7.8 Hz, 1 H, 1^{II}-H), 4.56 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1^{I}-H), 4.59 (s, 2 H, CH_2Ph), 4.67, 4.76 (2 d, ^{2}J = 11.8 Hz, 2 H, CH_2Ph), 7.24–7.29 (m, 2 H, Ph), 7.30–7.37 (m, 6 H, Ph), 7.42–7.45 (m, 2 H, Ph) ppm. ^{13}C NMR (150 MHz, CD_3OD): δ = 23.23 (CH_3CO), 51.72 (CH_2N_3), 56.23 (C-2^{I}), 62.46 (C-6^{II}), 67.12 (C-4^{II}), 70.01 (C-1′), 70.69 (C-4^{I}), 70.85 (C-6^{I}), 71.06, 71.51, 71.53, 71.65 (C-2′, C-3′, C-4′, C-5′), 71.74 (C-2^{II}), 72.64, 74.50 (CH_2Ph), 76.63 (C-5^{I}), 76.97 (C-5^{II}), 81.99 (C-3^{II}), 85.02 (C-3^{I}), 102.42 (C-1^{I}), 105.51 (C-1^{II}), 128.62, 128.64, 128.81, 129.07, 129.27, 129.36, 139.70, 139.82 (2 Ph), 174.21 (CH_3CO) ppm. ES-TOF-MS (pos. ion): m/z = 727.3398 ([M + Li]$^{+}$; calcd. 727.3378). $C_{34}H_{48}N_4O_{13}$ (720.3): calcd. C 56.66, H 6.71, N 7.77; found C 56.83, H 6.76, N 7.64.

8-Azido-3,6-dioxaoctyl 2-Acetamido-6-*O*-benzyl-3-*O*-[3-*O*-benzyl-β-D-galactopyranosyl-(*R*)-(*P*)-4,6-cyclic 2,2,2-trichloroethyl phosphate]-2-deoxy-β-D-glucopyranoside (11a) and 8-Azido-3,6-dioxaoctyl 2-Acetamido-6-*O*-benzyl-3-*O*-[3-*O*-benzyl-β-D-galactopyranosyl-(*S*)-(*P*)-4,6-cyclic 2,2,2-trichloroethyl phosphate]-2-deoxy-β-D-glucopyranoside (11b): 2,2,2-Trichloroethyl phosphorodichloridate (160 μL, 1.0 mmol) was added dropwise at –15 °C and with stirring to a solution of **10** (600 mg, 0.83 mmol) and pyridine (675 μL, 8.33 mmol) in CH_2Cl_2 (8.5 mL). After 5 min, when TLC (reversed phase, CH_3CN/H_2O: 1:1) indicated incomplete reaction, more 2,2,2-trichloroethyl phosphorodichloridate (160 μL, 1.0 mmol) was added while stirring was continued at –15 °C. One additional portion of reagent (160 μL, 1.0 mmol) was required to drive the reaction to completion. The reaction was quenched with MeOH (1 mL), the mixture concentrated, and EtOAc was added to the residue. The precipitate was filtered off, washed with EtOAc and the combined filtrates were concentrated. The residue was chromatographed (CH_2Cl_2/MeOH: 95:5) to give **11a** and **11b**, in that order. Further purification of both compounds by reversed phase chromatography (CH_3CN/H_2O: 2:3→1:1) gave **11a** (136 mg, 18%) as an oil, and **11b** (521 mg, 68%) as a white solid.

Data for 11a: $[\alpha]_D^{25}$ = –9.03 (c = 0.54, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, CH_3CO), 3.40 (m, 2 H, CH_2N_3), 3.45–3.57 (m, 5 H, 5^{II}-H, 4^{I}-H, 5^{I}-H, 2^{I}-H, 3^{II}-H), 3.60–3.67 (m, 8 H, 2′-H, 3′-H, 4′-H, 5′-H), 3.70 (dd, $J_{5,6a}$ = 5.7, $J_{6a,6b}$ = 10.8 Hz, 1 H, 6a^{I}-H), 3.77 (ddd, $J_{1a,2a}$ = 4.3, $J_{1a,2b}$ = 6.6, $J_{1a,1b}$ = 11.8 Hz, 1 H, 1a′-H), 3.85 (br. d, $J_{4,OH}$ = 0.7 Hz, partial overlap, 1 H, OH^{I}), 3.85 (dd, $J_{5,6b}$ = 2.3, $J_{6a,6b}$ = 10.8 Hz, partial overlap, 1 H, 6b^{I}-H), 3.94 (br. dt, $J_{1b,2a}$ = $J_{1b,2b}$ = 4.0, $J_{1a,1b}$ = 11.8 Hz, 1 H, 1b′-H), 3.96–4.01 (m, 2 H, 3^{I}-H, 2^{II}-H), 4.21 (br. d, $J_{2,OH}$ = 2.6 Hz, 1 H, OH^{II}), 4.33 (d, $J_{1,2}$ = 7.8 Hz, 1 H, 1^{II}-H), 4.40–4.49 (m, 2 H, 6^{II}-H), 4.57, 4.60 (2 d, ^{2}J = 12.1 Hz, partial overlap, 2 H, CH_2Ph), 4.58 (dd, $J_{H,P}$ = 7.0, ^{2}J = 11.2 Hz, partial overlap, 1 H, CH_2CCl_3), 4.60 (dd, $J_{H,P}$ = 6.9, ^{2}J = 11.2 Hz, partial overlap, 1 H, CH_2CCl_3), 4.74 (d, ^{2}J = 12.1 Hz, partial overlap, 1 H, CH_2Ph), 4.75 (br. d, $J_{3,4}$ = 3.8 Hz, partial overlap, 1 H, 4^{II}-H), 4.79 (d, ^{2}J = 12.3 Hz, 1 H, CH_2Ph), 4.87 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1^{I}-H), 6.71 (d, $J_{2,NH}$ = 7.6 Hz, 1 H, NH), 7.25–7.38 (m, 10 H, 2 Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 23.50 (CH_3CO), 50.54 (CH_2N_3), 56.02 (C-2^{I}), 66.26 (d, $J_{C,P}$ = 6.5 Hz, C-5^{II}), 68.63 (C-1′), 69.40 (C-2^{II}), 69.46 (C-4^{I}), 69.82, 70.35, 70.45, 70.56 (C-2′, C-3′, C-4′, C-5′), 69.90 (C-6^{I}), 70.74 (d, $J_{C,P}$ = 7.4 Hz, C-6^{II}), 72.27, 73.44 (2 CH_2Ph), 74.87 (C-5^{I}), 76.78 (d, $J_{C,P}$ = 7.1 Hz, partial overlap, C-4^{II}), 76.84 (d, $J_{C,P}$ = 5.4 Hz, partial overlap, CH_2CCl$_3$), 77.52 (d, $J_{C,P}$ = 7.0 Hz, C-3^{II}), 84.69 (C-3^{I}), 94.85 (d, $J_{C,P}$ = 9.5 Hz, CCl_3), 100.14 (C-1^{I}), 104.07 (C-1^{II}), 127.51, 127.65, 127.76, 127.85, 128.30, 128.46, 137.78, 138.29 (2 Ph), 172.30 (CH_3CO) ppm. ^{31}P NMR (121 MHz, $CDCl_3$): δ = –10.61 ppm. ES-TOF-MS (pos. ion): m/z = 919.2075 ([M + Li]$^{+}$; calcd. 919.2079). $C_{36}H_{48}Cl_3N_4O_{15}P$ (912.19): calcd. C 47.30, H 5.29, N 6.13; found C 47.44, H 5.44, N 6.12.

Data for 11b: M.p. 166–168 °C (from *i*PrOH; dec.). $[\alpha]_D^{25}$ = –2.54 (c = 0.50, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.01 (s, 3 H, CH_3CO), 3.37–3.53 (m, 5 H, 4^{I}-H, 5^{I}-H, 3^{II}-H, CH_2N_3), 3.59–3.69 (m, 10 H, 2^{I}-H, 6a^{I}-H, 2′-H, 3′-H, 4′-H, 5′-H), 3.71 (br. s, 1 H, OH^{I}), 3.73 (br. d, $J_{2,OH}$ = 2.3 Hz, 1 H, OH^{II}), 3.80 (ddd, $J_{1a,2a}$ = 3.1, $J_{1a,2b}$ = 8.2, $J_{1a,1b}$ = 12.1 Hz, partial overlap, 1 H, 1a′-H), 3.81–3.86 (m, 2 H, 3^{I}-H, 6b^{I}-H), 3.87 (ddd, $J_{2,OH}$ = 2.3, $J_{1,2}$ = 7.7, $J_{2,3}$ = 9.8 Hz, 1 H, 2^{II}-H), 3.93 (br. dt, $J_{1b,2a}$ = $J_{1b,2b}$ = 3.4, $J_{1a,1b}$ = 12.1 Hz, 1 H, 1b′-H), 4.33 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1^{II}-H), 4.41 (ddd, $J_{5,6a}$ = 1.5, $J_{6a,6b}$ = 12.6, $J_{6a,P}$ = 20.1 Hz, 1 H, 6a^{II}-H), 4.58 (d, ^{2}J = 12.0 Hz, partial overlap, 1 H, CH_2Ph), 4.58 (dd, $J_{H,P}$ = 7.9, ^{2}J = 11.3 Hz, partial overlap, 1 H, CH_2CCl_3), 4.60 (d, ^{2}J = 12.0 Hz, partial overlap, 1 H, CH_2Ph), 4.61 (dd, $J_{H,P}$ = 7.6, ^{2}J = 11.3 Hz, partial overlap, 1 H, CH_2CCl_3), 4.65 (ddd, J = 2.3, J = 3.7, $J_{6a,6b}$ = 12.6 Hz, 1 H, 6b^{II}-H), 4.70 (d, ^{2}J = 12.0 Hz, 1 H, CH_2Ph), 4.78 (d, $J_{1,2}$ = 8.5 Hz, partial overlap, 1 H, 1^{I}-H), 4.79 (d, ^{2}J = 12.0 Hz, partial overlap, 1 H, CH_2Ph), 4.90 (br. d, $J_{3,4}$ = 3.1 Hz, 1 H, 4^{II}-H), 6.70 (d, $J_{2,NH}$ = 7.8 Hz, 1 H, NH), 7.26–7.38 (m, 10 H, 2 Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 23.41 (CH_3CO), 50.47 (CH_2N_3), 55.81 (C-2^{I}), 66.73 (d, $J_{C,P}$ = 7.2 Hz, C-5^{II}), 68.54 (C-1′), 69.40 (C-4^{I}), 69.52 (C-2^{II}), 69.66 (C-6^{I}), 69.71, 70.26, 70.58, 70.98 (C-2′, C-3′, C-4′, C-5′), 69.85 (d, $J_{C,P}$ = 5.9 Hz, C-6^{II}), 71.85, 73.54 (2 CH_2Ph), 75.01 (d, $J_{C,P}$ = 5.5 Hz, partial overlap, C-4^{II}), 75.05 (C-5^{I}), 77.14 (d, $J_{C,P}$ = 6.9 Hz, partial overlap, C-3^{II}), 77.73 (d, $J_{C,P}$ = 5.0 Hz, CH_2CCl$_3$), 85.78 (C-3^{I}), 94.35 (d, $J_{C,P}$ = 10.1 Hz, CCl_3), 100.55 (C-1^{I}), 103.91 (C-1^{II}), 127.55, 127.59, 127.99, 128.08, 128.31, 128.56, 137.17, 138.15 (2 Ph), 172.28 (CH_3CO) ppm. ^{31}P NMR

(121 MHz, $CDCl_3$): δ = –8.71 ppm. ES-TOF-MS (pos. ion): *m*/*z* = 919.2057 ([M + Li]$^+$; calcd. 919.2079). $C_{36}H_{48}Cl_3N_4O_{15}P$ (912.19): calcd. C 47.30, H 5.29, N 6.13; found C 47.14, H 5.39, N 6.14.

Ethyl 2,4-Di-*O*-benzyl-3,6-dideoxy-1-thio-β-L-*xylo*-hexopyranoside (13): This compound was prepared as described.[31] When prepared on large scale, it solidified spontaneously. M.p. 32–33 °C (from diisopropyl ether/hexane). $[\alpha]_D^{25}$ = +71.8 (*c* = 1, $CHCl_3$). $C_{22}H_{28}O_3S$ (372.5): calcd. C 70.93, H 7.58; found C 70.86, H 7.54.

2,4-Di-*O*-benzyl-3,6-dideoxy-α-L-*xylo*-hexopyranosyl Bromide (13a): Br_2 (1.28 mL, 25.0 mmol) was added to a solution of **13**[31] (4.656 g, 12.50 mmol) in CCl_4 (50 mL). Occasionally, the mixture was shaken gently manually and, after 5 min, hex-1-ene (6.5 mL, 52.08 mmol) was added. The mixture was concentrated and a solution of the residue in CCl_4 was concentrated (twice). Crude **13a** was used immediately in the next step without purification.

8-Azido-3,6-dioxaoctyl 2,4-Di-*O*-benzyl-3,6-dideoxy-α-L-*xylo*-hexopyranosyl-(1→4)-[2,4-di-*O*-benzyl-3,6-dideoxy-α-L-*xylo*-hexopyranosyl-(1→2)-3-*O*-benzyl-β-D-galactopyranosyl-(*S*)-(*P*)-4,6-cyclic 2,2,2-trichloroethyl phosphate-(1→3)]-2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranoside (14): A solution of **13a** in CH_2Cl_2 (15 mL) was added to a stirred mixture of **11b** (1.9 g, 2.08 mmol), Bu_4NBr (2.686 g, 8.33 mmol) and powdered molecular sieves (4 Å, 4.5 g) in CH_2Cl_2/DMF (2:1, 15 mL). Stirring was continued at room temperature for 36 h before MeOH (5 mL) was added. After 30 min, the mixture was diluted with CH_2Cl_2 (100 mL), filtered through a Celite pad, and the solids were washed with CH_2Cl_2 (200 mL). The combined filtrates (ca. 500 mL) were washed with saturated aq. $NaHCO_3$ (500 mL) and H_2O (500 mL), dried, and concentrated. The residue was chromatographed (toluene/acetone: 50:50→0:100) to give first **14** (1.308 g, 41%; after further purification by chromatography with CH_2Cl_2/MeOH: 19:1→16:1). $[\alpha]_D^{25}$ = –36.75 (*c* = 0.55, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.20 (d, $J_{5,6}$ = 6.5 Hz, 3 H, 6^{III}-H), 1.25 (d, $J_{5,6}$ = 6.6 Hz, 3 H, 6^{IV}-H), 1.71 (dt, $J_{3,4}$ = 2.2, $J_{2,3}$ = ^2J = 12.8 Hz, partial overlap, 1 H, 3^{III}-H$_{ax}$), 1.73 (s, 3 H, CH_3CO), 1.80 (dt, $J_{3,4}$ = 2.2, $J_{2,3}$ = ^2J = 12.7 Hz, 1 H, 3^{IV}-H$_{ax}$), 2.12 (dt, $J_{2,3}$ = $J_{3,4}$ = 3.8, ^2J = 13.0 Hz, partial overlap, 1 H, 3^{III}-H$_{eq}$), 2.15 (dt, $J_{2,3}$ = $J_{3,4}$ = 3.8, ^2J = 12.7 Hz, partial overlap, 1 H, 3^{IV}-H$_{eq}$), 3.25 (br. q, *J* = 7.0 Hz, 1 H, 2^I-H), 3.33 (t, *J* = 5.1 Hz, 2 H, CH_2N_3), 3.47 (br. s, 1 H, 4^{III}-H), 3.53 (br. s, 1 H, 5^{II}-H), 3.54–3.65 (m, 11 H, 3^{II}-H, 5^I-H, 4^{IV}-H, 2′-H, 3′-H, 4′-H, 5′-H), 3.69 (dd, $J_{5,6a}$ = 2.9, $J_{6a,6b}$ = 10.7 Hz, 1 H, 6a^I-H), 3.71–3.79 (m, 2 H, 1′-H), 3.82–3.88 (m, 2 H, 2^{III}-H, 2^{IV}-H), 3.89 (dd, $J_{5,6b}$ = 3.8, $J_{6a,6b}$ = 10.7 Hz, partial overlap, 1 H, 6b^I-H), 3.99 (t, $J_{3,4}$ = $J_{4,5}$ = 8.4 Hz, 1 H, 4^I-H), 4.11 (t, $J_{1,2}$ = $J_{2,3}$ = 8.8 Hz, 1 H, 2^{II}-H), 4.20 (br. q, $J_{5,6}$ = 6.5 Hz, 1 H, 5^{III}-H), 4.33 (d, ^2J = 11.9 Hz, 1 H, C*H*$_2$Ph$_A$), 4.35–4.45 (m, 6 H, 3^I-H, 6a^{II}-H, C*H*$_2$Ph$_B$, C*H*$_2$Ph$_C$, C*H*$_2$Ph$_D$), 4.45 (d, ^2J = 11.8 Hz, partial overlap, 1 H, C*H*$_2$Ph$_C$), 4.46 (d, ^2J = 12.1 Hz, partial overlap, 1 H, C*H*$_2$Ph$_A$), 4.47 (d, ^2J = 11.8 Hz, 1 H, C*H*$_2$Ph$_E$), 4.48 (d, ^2J = 15.5 Hz, partial overlap, 1 H, C*H*$_2$Ph$_F$), 4.51 (d, ^2J = 12.2 Hz, 1 H, C*H*$_2$Ph$_F$), 4.52 (d, ^2J = 12.1 Hz, 1 H, C*H*$_2$Ph$_D$), 4.62–4.68 (m, 3 H, 6b^{II}-H, 1^{II}-H, 5^{IV}-H), 4.62 (dd, $J_{H,P}$ = 10.2, ^2J = 11.5 Hz, partial overlap, 1 H, CH_2CCl_3), 4.68 (dd, $J_{H,P}$ = 9.1, ^2J = 11.5 Hz, partial overlap, 1 H, CH_2CCl_3), 4.77 (d, ^2J = 11.8 Hz, 1 H, C*H*$_2$Ph$_E$), 4.97 (d, $J_{3,4}$ = 3.3 Hz, 1 H, 4^{II}-H), 5.02 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1^{IV}-H), 5.06 (d, $J_{1,2}$ = 6.7 Hz, 1 H, 1^I-H), 5.62 (d, $J_{1,2}$ = 3.4 Hz, 1 H, 1^{III}-H), 6.35 (d, $J_{2,NH}$ = 7.0 Hz, 1 H, NH), 7.16–7.32 (m, 30 H, 6 Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 16.28 (C-6^{IV}), 16.39 (C-6^{III}), 23.17 (*C*H$_3$CO), 27.24 (C-3^{IV}), 28.07 (C-3^{III}), 50.64 (CH_2N_3), 58.11 (C-2^I), 66.51 (C-5^{IV}), 66.64 (C-5^{III}), 67.02 (d, $J_{C,P}$ = 5.7 Hz, C-5^{II}), 68.05 (C-1′), 68.29 (C-6^I), 69.97, 70.49, 70.51, 70.76 (C-2′, C-3′, C-4′, C-5′), 70.01 (C-2^{II}), 70.23 (d, $J_{C,P}$ = 4.5 Hz, C-6^{II}), 70.44 (*C*H$_2$Ph$_E$), 70.66 (*C*H$_2$Ph$_A$), 70.86 (C-2^{III}), 71.06 (C-2^{IV}), 71.12, 71.21, 71.35 (*C*H$_2$Ph$_B$, *C*H$_2$Ph$_C$, *C*H$_2$Ph$_D$), 72.39 (C-4^I), 73.21 (*C*H$_2$Ph$_F$), 74.00 (d, $J_{C,P}$ = 4.4 Hz, C-4^{II}), 74.79 (C-5^I), 75.47 (C-4^{III}), 76.69 (C-4^{IV}), 77.64 (d, $J_{C,P}$ = 2.8 Hz, *C*H$_2$CCl$_3$), 78.13 (C-3^I), 79.96 (d, $J_{C,P}$ = 7.6 Hz, C-3^{II}), 94.59 (d, $J_{C,P}$ = 7.2 Hz, CCl_3), 95.73 ($J_{C,H}$ = 172.8 Hz, C-1^{III}), 96.22 ($J_{C,H}$ = 167.0 Hz, C-1^{IV}), 98.86 ($J_{C,H}$ = 166.7 Hz, C-1^I), 101.98 ($J_{C,H}$ = 158.8 Hz, C-1^{II}), 127.29, 127.37, 127.38, 127.45, 127.52, 127.58, 127.60, 127.68, 127.75, 127.76, 127.81, 127.94, 128.17, 128.23 (2 C), 128.24, 128.29, 128.44, 136.86, 138.13, 138.15, 138.17, 138.40, 138.95 (6 Ph), 170.59 (CH$_3$*C*O) ppm. ^{31}P NMR (121 MHz, $CDCl_3$): δ = –2.30 ppm. ES-TOF-MS (pos. ion): *m*/*z* = 1539.5226 ([M + Li]$^+$; calcd. 1539.5217). $C_{76}H_{92}Cl_3N_4O_{21}P$ (1532.51): calcd. C 59.47, H 6.04, N 3.65; found C 59.77, H 6.13, N 3.72. Next eluted was **8-Azido-3,6-dioxaoctyl [2,4-Di-*O*-benzyl-3,6-dideoxy-α-L-*xylo*-hexopyranosyl-(1→2)-3-*O*-benzyl-β-D-galactopyranosyl-(*S*)-(*P*)-4,6-cyclic 2,2,2-trichloroethyl phosphate-(1→3)]-2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranoside (15)** (1.15 g, 45%; after further purification by chromatography with CH_2Cl_2/MeOH: 25:1→15:1). $[\alpha]_D^{25}$ = –9.02 (*c* = 0.55, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.17 (d, $J_{5,6}$ = 6.6 Hz, 3 H, 6^{III}-H), 1.75 (dt, $J_{3,4}$ = 1.9, $J_{2,3}$ = ^2J = 12.4 Hz, 1 H, 3^{III}-H$_{ax}$), 1.96 (s, 3 H, CH_3CO), 2.07 (dt, $J_{2,3}$ = $J_{3,4}$ = 3.9, ^2J = 12.9 Hz, 1 H, 3^{III}-H$_{eq}$), 3.22 (m, 1 H, 2^I-H), 3.31–3.39 (m, 2 H, CH_2N_3), 3.42 (br. t, $J_{3,4}$ = $J_{4,5}$ = 9.2 Hz, 1 H, 4^I-H), 3.46 (br. s, 1 H, OH^I), 3.48–3.54 (m, 2 H, 4^{III}-H, 5^I-H), 3.58–3.68 (m, 10 H, 6a^I-H, 5^{II}-H, 2′-H, 3′-H, 4′-H, 5′-H), 3.68–3.76 (m, 2 H, 1a′-H, 3^{II}-H), 3.79–3.85 (m, 2 H, 6b^I-H, 2^{III}-H), 3.92 (m, 1 H, 1b′-H), 4.16–4.22 (m, 2 H, 5^{III}-H, 2^{II}-H), 4.26 (d, ^2J = 12.3 Hz, partial overlap, 1 H, C*H*$_2$Ph$_A$), 4.29 (br. t, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, partial overlap, 1 H, 3^I-H), 4.38 (d, ^2J = 12.0 Hz, 1 H, C*H*$_2$Ph$_B$), 4.43 (d, ^2J = 12.3 Hz, partial overlap, 1 H, C*H*$_2$Ph$_A$), 4.45 (m, 1 H, 6a^{II}-H), 4.50 (d, ^2J = 12.0 Hz, partial overlap, 1 H, C*H*$_2$Ph$_B$), 4.51 (d, ^2J = 11.5 Hz, partial overlap, 1 H, C*H*$_2$Ph$_C$), 4.55–4.66 (m, 6 H, 1^{II}-H, 6b^{II}-H, CH_2CCl_3, OC*H*$_2$Ph$_D$), 4.75 (d, ^2J = 11.5 Hz, 1 H, C*H*$_2$Ph$_C$), 4.82 (d, $J_{1,2}$ = 8.2 Hz, 1 H, 1^I-H), 4.98 (br. d, $J_{3,4}$ = 2.5 Hz, 1 H, 4^{II}-H), 5.50 (d, $J_{1,2}$ = 3.3 Hz, 1 H, 1^{III}-H), 6.07 (d, $J_{2,NH}$ = 7.4 Hz, 1 H, NH), 7.12–7.34 (m, 20 H, 4 Ph) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 16.17 (C-6^{III}), 23.60 (*C*H$_3$CO), 27.58 (C-3^{III}), 50.49 (CH_2N_3), 56.98 (C-2^I), 66.40 (d, $J_{C,P}$ = 7.9 Hz, C-5^{II}), 66.61 (C-5^{III}), 68.45 (C-1′), 69.38 (C-4^I), 69.58 (C-6^I), 69.76, 70.28, 70.50, 70.55 (C-2′, C-3′, C-4′, C-5′), 69.87 (d, $J_{C,P}$ = 6.2 Hz, C-6^{II}), 70.50 (*C*H$_2$Ph$_A$), 70.73 (C-2^{III}), 71.02 (*C*H$_2$Ph$_C$), 71.28 (*C*H$_2$Ph$_B$), 71.64 (C-2^{II}), 73.40 (*C*H$_2$Ph$_D$), 74.56 (d, $J_{C,P}$ = 5.4 Hz, C-4^{II}), 75.29 (C-5^I), 75.63 (C-4^{III}), 79.47 (d, $J_{C,P}$ = 6.4 Hz, C-3^{II}), 80.59 (C-3^I), 94.40 (d, $J_{C,P}$ = 9.9 Hz, CCl_3), 96.56 ($J_{C,H}$ = 172.8 Hz, C-1^{III}), 100.05 ($J_{C,H}$ = 161.0 Hz, C-1^I), 101.33 ($J_{C,H}$ = 159.3 Hz, C-1^{II}), 127.17, 127.38, 127.42, 127.43, 127.44, 127.62, 127.73, 128.15, 128.16, 128.16, 128.17, 128.35, 136.97, 138.16, 138.22, 138.33 (4 Ph), 171.02 (CH$_3$*C*O) ppm. ^{31}P NMR (121 MHz, $CDCl_3$): δ = –9.41 ppm. ES-TOF-MS (pos. ion): *m*/*z* = 1229.3718 ([M + Li]$^+$; calcd. 1229.3648). $C_{56}H_{70}Cl_3N_4O_{18}P$ (1222.4): calcd. C 54.93, H 5.76, N 4.58; found C 54.67, H 5.78, N 4.58.

8-Amino-3,6-dioxaoctyl 2-Acetamido-2-deoxy-3-*O*-(β-D-galactopyranosyl-4,6-cyclic potassium phosphate)-β-D-glucopyranoside (12): Pd/C (540 mg) was added to a mixture of **11a** (540 mg, 0.59 mmol), *i*PrOH (21 mL) and potassium phosphate buffer (21 mL; pH = 7, 0.1 M). The mixture was stirred at room temperature in a Parr reactor under H_2 (160 psi). After 2 d, when TLC showed complete conversion, the mixture was filtered through a Celite pad, the catalyst was washed with MeOH and H_2O, and the filtrate was concentrated. The residue was purified by normal phase chromatography (MeOH/H_2O:100:0→10:1) to give, after freeze-drying, **12** (218 mg, 60%). ^{1}H NMR (600 MHz, D_2O): δ = 1.99 (s, 3 H, CH_3CO), 3.18

(br. t, J = 5.1 Hz, 2 H, CH_2NH$_2$), 3.45 (ddd, $J_{5,6b}$ = 2.3, $J_{5,6a}$ = 5.6, $J_{4,5}$ = 10.0 Hz, 1 H, 5^{I}-H), 3.52 (dd, $J_{3,4}$ = 8.5, $J_{4,5}$ = 10.0 Hz, 1 H, 4^{I}-H), 3.56 (dd, $J_{1,2}$ = 7.9, $J_{2,3}$ = 10.0 Hz, 1 H, 2^{II}-H), 3.63–3.70 (m, 6 H, 3 CH'_2O), 3.71–3.77 (m, 7 H, 3^{I}-H, 5^{II}-H, 6a^{I}-H, 3^{II}-H, 1a′-H, CH'_2O), 3.81 (dd, $J_{1,2}$ = 8.4, $J_{2,3}$ = 10.4 Hz, 1 H, 2^{I}-H), 3.89 (dd, $J_{5,6b}$ = 2.3, $J_{6a,6b}$ = 12.4 Hz, 1 H, 6b^{I}-H), 3.98 (ddd, $J_{1b,2a}$ = 3.2, $J_{1b,2b}$ = 5.9, $J_{1a,1b}$ = 11.6 Hz, 1 H, 1b′-H), 4.22 (ddd, $J_{5,6a}$ = 1.7, $J_{6a,6b}$ = 12.8, $J_{6a,P}$ = 22.3 Hz, 1 H, 6a^{II}-H), 4.38 (br. d, $J_{6a,6b}$ = 12.8 Hz, 1 H, 6b^{II}-H), 4.48 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1^{II}-H), 4.55 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1^{I}-H), 4.56 (br. d, $J_{3,4}$ = 3.5 Hz, 1 H, 4^{II}-H) ppm. ^{13}C NMR (150 MHz, D$_2$O): δ = 22.42 (*C*H$_3$CO), 39.25 (CH$_2$NH$_2$), 54.57 (C-2^{I}), 60.80 (C-6^{I}), 66.48, 69.63, 69.76, 69.84 (C-2′, C-3′, C-4′, C-5′), 67.47 (d, $J_{C,P}$ = 4.7 Hz, C-5^{II}), 68.34 (d, $J_{C,P}$ = 5.4 Hz, C-6^{II}), 68.68 (C-4^{I}), 69.18 (C-1′), 69.93 (C-2^{II}), 71.15 (d, $J_{C,P}$ = 7.4 Hz, C-3^{II}), 75.50 (C-5^{I}), 76.08 (d, $J_{C,P}$ = 5.1 Hz, C-4^{II}), 82.69 (C-3^{I}), 101.12 (C-1^{I}), 103.30 (C-1^{II}), 174.62 (CH$_3$*C*O) ppm. ^{31}P NMR (121 MHz, D$_2$O): δ = –3.75 ppm. ES-TOF-MS (neg. ion): *m*/*z* = 575.1836 ([M – K]$^-$; calcd. 575.1853).

8-Amino-3,6-dioxaoctyl 3,6-Dideoxy-α-L-*xylo*-hexopyranosyl-(1→4)-[3,6-dideoxy-α-L-*xylo*-hexopyranosyl-(1→2)-β-D-galactopyranosyl-4,6-cyclic potassium phosphate-(1→3)]-2-acetamido-2-deoxy-β-D-glucopyranoside (16): Pd/C (1.2 g) was added to a mixture of **14** (1.2 g, 0.78 mmol), *i*PrOH (47 mL) and potassium phosphate buffer (47 mL; pH = 7, 0.1 M). The mixture was stirred at room temperature in a Parr reactor under H_2 (160 psi). After 24 h, when TLC showed complete conversion, the mixture was filtered through a Celite pad, the catalyst was washed with MeOH and H_2O, and the filtrate was concentrated. The residue was purified by reversed phase chromatography (H_2O/MeOH: 100:0→95:5) to give, after freeze-drying, **16** (378 mg, 55%). ^{1}H NMR (600 MHz, D$_2$O): δ = 1.19 (d, $J_{5,6}$ = 6.7 Hz, partial overlap, 3 H, 6^{III}-H), 1.19 (d, $J_{5,6}$ = 6.8 Hz, partial overlap, 3 H, 6^{IV}-H), 1.80–1.89 (m, 3 H, 3^{III}-H, 3^{IV}-H$_{eq}$), 2.02 (s, 3 H, C*H*$_3$CO), 2.05 (m, 1 H, 3^{IV}-H$_{ax}$), 3.15 (br. t, J = 5.0 Hz, 2 H, CH_2NH$_2$), 3.47 (br. dt, J = 3.0, J = 9.8 Hz, 1 H, 5^{I}-H), 3.59 (dd, $J_{1,2}$ = 7.9, $J_{2,3}$ = 9.7 Hz, partial overlap, 1 H, 2^{II}-H), 3.60 (br. s, partial overlap, 1 H, 5^{II}-H), 3.62–3.73 (m, 10 H, 4^{I}-H, 1a′-H, 2′-H, 3′-H, 4′-H, 5′-H), 3.76 (br. t, $J_{3,4}$ = 3.5 Hz, 1 H, 4^{III}-H), 3.81 (dd, $J_{1,2}$ = 8.5, $J_{2,3}$ = 10.6 Hz, 1 H, 2^{I}-H), 3.86 (dd, $J_{5,6a}$ = 3.7, $J_{6a,6b}$ = 12.7 Hz, partial overlap, 1 H, 6a^{I}-H), 3.88 (m, 1 H, 3^{II}-H), 3.91–4.01 (m, 4 H, 2^{IV}-H, 2^{III}-H, 6b^{I}-H, 1b′-H), 4.03 (dd, $J_{3,4}$ = 9.3, $J_{2,3}$ = 10.6 Hz, 1 H, 3^{I}-H), 4.21 (br. t, J = 3.6 Hz, 1 H, 4^{IV}-H), 4.28 (br. q, $J_{5,6}$ = 6.7 Hz, 1 H, 5^{III}-H), 4.30–4.41 (m, 2 H, 6^{II}-H), 4.39 (d, $J_{1,2}$ = 8.5 Hz, partial overlap, 1 H, 1^{I}-H), 4.54 (d, $J_{3,4}$ = 3.8 Hz, 1 H, 4^{II}-H), 4.69 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1^{II}-H), 4.75 (br. q, $J_{5,6}$ = 6.8 Hz, 1 H, 5^{IV}-H), 4.89 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1^{IV}-H), 4.97 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1^{III}-H) ppm. ^{13}C NMR (150 MHz, D$_2$O): δ = 15.61 (C-6^{III}), 15.72 (C-6^{IV}), 22.33 (*C*H$_3$CO), 32.68 (C-3^{IV}), 32.84 (C-3^{III}), 39.35 (CH$_2$NH$_2$), 55.86 (C-2^{I}), 59.46 (C-6^{I}), 63.41 (C-2^{IV}), 63.66 (C-2^{III}), 66.27 (C-5^{III}), 66.93, 69.76, 70.00, 70.05 (C-2′, C-3′, C-4′, C-5′), 66.96 (C-5^{IV}), 67.53 (d, $J_{C,P}$ = 4.9 Hz, C-5^{II}), 68.55 (C-4^{IV}), 68.85 (d, $J_{C,P}$ = 4.2 Hz, partial overlap, C-6^{II}), 68.87 (C-4^{III}), 69.32 (C-1′), 72.50 (d, $J_{C,P}$ = 7.0 Hz, C-3^{II}), 72.60 (C-4^{I}), 75.44 (C-3^{I}), 75.63 (C-5^{I}), 76.32 (C-2^{II}), 76.60 (d, $J_{C,P}$ = 5.2 Hz, C-4^{II}), 97.90 (C-1^{IV}), 99.68 (C-1^{III}), 101.19 (C-1^{II}), 101.97 (C-1^{I}), 173.99 (CH$_3$*C*O) ppm. ^{31}P NMR (121 MHz, D$_2$O): δ = –3.68 ppm. ES-TOF-MS (neg. ion): *m*/*z* = 835.3127 ([M – K]$^-$; calcd. 835.3113), ES-TOF-MS (pos. ion): *m*/*z* = 837.3282 ([M – K + 2 H]$^+$; calcd. 837.3270).

8-Amino-3,6-dioxaoctyl [3,6-Dideoxy-α-L-*xylo*-hexopyranosyl-(1→2)-β-D-galactopyranosyl-4,6-cyclic potassium phosphate-(1→3)]-2-acetamido-2-deoxy-β-D-glucopyranoside (17): Pd/C (0.2 g) was added to a mixture of **15** (0.2 g, 0.16 mmol), *i*PrOH (8 mL) and potassium phosphate buffer (8 mL; pH = 7, 0.1 M). The mixture was stirred at room temperature in a Parr reactor under H_2 (160 psi). After 3 d, TLC showed complete conversion. The mixture was filtered through a Celite pad, the catalyst was washed with MeOH and H_2O, and the filtrate was concentrated. The residue was purified by reversed phase chromatography (H_2O/MeOH: 100:0→97:3) to give, after freeze-drying, **17** (70 mg, 58%). ^{1}H NMR (600 MHz, D$_2$O): δ = 1.15 (d, $J_{5,6}$ = 6.7 Hz, 3 H, 6^{III}-H), 1.80 (dt, J = 2.8, ^2J = 12.9 Hz, 1 H, 3^{III}-H$_{ax}$), 1.91 (br. dt, J = 4.0, ^2J = 12.9 Hz, 1 H, 3^{III}-H$_{eq}$), 2.03 (s, 3 H, CH$_3$CO), 3.20 (t, J = 5.0 Hz, 2 H, CH_2NH$_2$), 3.47–3.51 (m, 2 H, 4^{I}-H, 5^{I}-H), 3.63–3.79 (m, 14 H, 2^{I}-H, 6a^{I}-H, 2^{II}-H, 5^{II}-H, 4^{III}-H, 4 CH'_2O, 1a′-H), 3.89–3.95 (m, 3 H, 3^{I}-H, 6b^{I}-H, 3^{II}-H), 3.96–4.02 (m, 2 H, 2^{III}-H, 1b′-H), 4.23 (br. q, $J_{5,6}$ = 6.7 Hz, 1 H, 5^{III}-H), 4.31 (ddd, $J_{5,6a}$ = 1.5, $J_{6a,6b}$ = 12.7, $J_{6a,P}$ = 22.0 Hz, 1 H, 6a^{II}-H), 4.40 (br. d, $J_{6a,6b}$ = 12.7 Hz, 1 H, 6b^{II}-H), 4.43 (d, $J_{1,2}$ = 8.5 Hz, 1 H, 1^{I}-H), 4.57 (d, $J_{3,4}$ = 3.4 Hz, 1 H, 4^{II}-H), 4.71 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1^{II}-H), 5.08 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1^{III}-H) ppm. ^{13}C NMR (150 MHz, D$_2$O): δ = 18.12 (C-6^{III}), 24.96 (*C*H$_3$CO), 35.55 (C-3^{III}), 41.93 (CH$_2$NH$_2$), 57.48 (C-2^{I}), 63.43 (C-6^{I}), 65.95 (C-2^{III}), 69.04 (C-5^{III}), 69.18, 71.96, 72.36, 72.52, 72.55 (C-1′, C-2′, C-3′, C-4′, C-5′), 70.00 (d, $J_{C,P}$ = 5.0 Hz, C-5^{II}), 70.97 (d, $J_{C,P}$ = 5.3 Hz, C-6^{II}), 71.26, 71.28 (C-4^{III}, C-4^{I} or C-5^{I}), 74.75 (d, $J_{C,P}$ = 7.2 Hz, C-3^{II}), 78.19 (C-4^{I} or C-5^{I}), 78.52 (C-2^{II}), 79.30 (d, $J_{C,P}$ = 4.9 Hz, C-4^{II}), 80.97 (C-3^{I}), 101.92 (C-1^{III}), 102.85 (C-1^{II}), 104.59 (C-1^{I}), 176.56 (CH$_3$*C*O) ppm. ^{31}P NMR (121 MHz, D$_2$O): δ = –3.73 ppm. ES-TOF-MS (neg. ion): *m*/*z* = 705.2466 ([M – K]$^-$; calcd. 705.2483).

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