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Iterative Synthesis of *Leishmania* Phosphoglycans by Solution, Solid-Phase, and Polycondensation Approaches without Involving Any Glycosylation

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A general strategy (solution, solid-phase, and polycondensation) for the synthesis of antigenic phosphoglycans (PG) of the protozoan parasite *Leishmania* is presented. Phosphoglycans constitute the variable structural and functional domain of major cell-surface lipophosphoglycan (LPG) and secreted proteophosphoglycan (PPG), the molecules involved in infectivity and survival of the *Leishmania* parasite inside human macrophages. We have shown that the chemically labile, anomerically phosphodiester-linked phosphoglycan repeats can be assembled in an iterative and efficient manner from a single key intermediate, *without* involving any glycosylation steps. Furthermore, the phosphoglycan chain can be extended toward either the nonreducing (6′-OH) or the reducing (1-OH) end. We also describe a new and efficient solid-phase methodology to construct phosphoglycans based on design and application of a novel *cis*-allylphosphoryl solid-phase linker that enabled the selective cleavage of the first anomeric-phosphodiester linkage without affecting any of the other internal anomeric-phosphodiester groups of the growing PG chain on the solid support. The strategy to construct larger phosphoglycans in a one-pot synthesis by polycondensation of a single key intermediate is also described, enabling CD spectrometric measurements to show the helical nature of phosphoglycans. Our versatile synthetic approach provides easy access to *Leishmania* phosphoglycans and the opportunity to address key immunological, biochemical, and biophysical questions pertaining to the phosphoglycan family (LPG and PPG) unique to the parasite.

Introduction

The protozoan parasite *Leishmania*, responsible for multiple diseases including fatal visceral leishmaniasis (kala-azar), has a remarkable ability to survive and proliferate in extreme microbicidal environments during its digenetic life cycle in the sandfly vector and the human host. All life-cycle stages of *Leishmania* species produce an abundance ($>10^7$ copies/cell) of a unique class of glycoconjugates[1a−f] named phosphoglycans. These include the most abundant cell-surface molecule lipophosphoglycan (LPG) expressed by the infectious promastigote stage and proteophosphoglycans (PPG) secreted by the intracellular amastigote form of the parasite. The phosphoglycans have been referred[2] to as "molecules with insidious intent" due to their critical role in subverting the host immune system, in binding of the parasite to the sandfly midgut epithelial cells and to human macrophages, and in receptor-mediated phagocytosis via direct interaction with carbohydrate binding sites. There is now substantial evidence[1,2] that LPG and PPG are antigenic and multifunctional virulence factors essential for infectivity and survival of the parasite and dramatically inhibit[3] (in the nM range) protein kinase C (PKC) dependent signaling and *c-fos* gene transcription[4] in host cells. Interestingly, the phosphoglycan-deficient genetic mutants of *Leishmania* cannot survive in the sandfly vector or infect mammalian macrophages, and both these functions can be restored[1e] on insertion of exogenous LPG into the plasma membrane of deficient strains. The role of LPG/PPG in parasite virulence is currently a topic of intense debate[5,6] in parasite biology.

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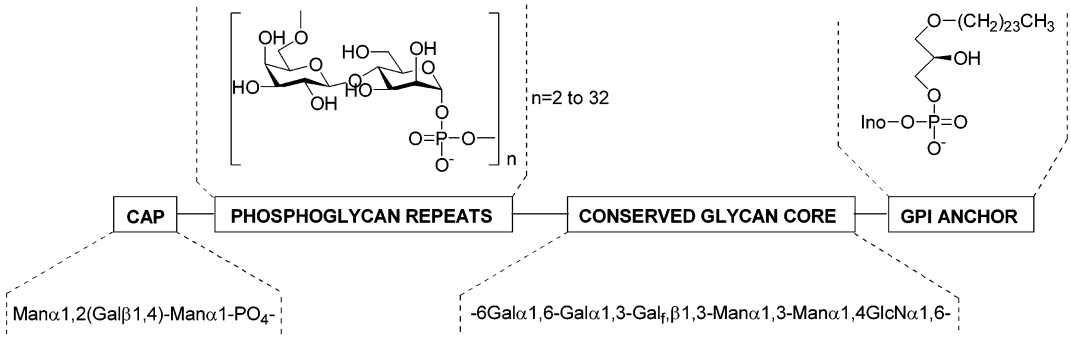

FIGURE 1. Structure of the lipophosphoglycan (LPG) of *Leishmania donovani*.

The intriguing structure[7,8] of the lipophosphoglycan (LPG) of *Leishmania donovani* (Figure 1) consists of four distinct domains: (i) alkyl-*lyso*-glycosyl-phosphatidylinositol (GPI) lipid-anchor; (ii) conserved glycan core with an internal galactofuranose residue; (iii) variable phosphoglycan repeats, and (iv) neutral oligosaccharide cap. The proteophosphoglycans[1b] (PPG) are also made up of similar phosphoglycan repeats except that they are linked to a polypeptide scaffold rather than to the lipid anchor present in LPG.

The most distinct fine structural feature of LPG/PPG is the variable phosphoglycan repeat domain, unique among all the eukaryotic carbohydrates, made of phosphodisaccharide [6Gal*p*-β1,4-Man*p*-α1-phosphate]$_n$ repeats (n = 2−32) linked to each other through a phosphodiester group between anomeric-OH of the mannose of one repeat and 6-OH of the galactose of the adjoining repeat. Distinct biological roles have been attributed[1,2] to each of the LPG structural domains; e.g., the PG repeats form a spring like helical supramolecular structure[8] around the parasite, providing resistance to host hydrolytic enzymes and antibodies, and constitute functional epitopes for recognition by macrophage receptors.[9] The GPI core serves as an anchor[10] to attach PG repeats to the outer leaflet of plasma membrane, and the neutral oligomannose cap provides biosynthetic termination signals during PG assembly.[1d] The dynamic structure of the phosphoglycans and their role in host−parasite interaction have led to significant biological interest, and their biosynthetic pathway has emerged as a novel target[11a−e] for drug design and development[11f,g] of synthetic carbohydrate vaccines.

Immunological, biochemical, and biophysical experiments to probe the function, biosynthesis, and conformation of the *Leishmania* phosphoglycans require efficient chemical synthetic approaches for construction of phosphoglycans of defined lengths and repeats. The natural material is extremely difficult to isolate (10 L of *Leishmania* culture yields 5 mg of LPG) and is always a mixture of sub-populations of LPGs due to the microheterogeneity present in the lipid and glycan domains. In addition, it is not possible to get pure PG domain from intact LPG or PPG with the current methods[7,8] because PG repeats fall apart during mild acid hydrolysis, the step necessary to remove the glycan core or peptide anchor. Synthetic approaches are challenging because the PGs are extremely labile due to anomeric phosphodiester linkages present between each repeat unit. Synthesis of the anomeric phosphodiesters is complicated, as compared to that of nonanomeric types such as oligonucleotides, by the requirement of anomeric stereocontrol and instability due to the propensity of the glycosyl ring to form a stabilized carbocation by expulsion of the anomeric phosphomonoester leaving group. For these reasons, only a few syntheses of anomerically linked phospho-oligomers of carbohydrates have been reported.[12−15] The first synthesis of *Leishmania* phosphoglycans, reported by the Dundee group,[14−15] used monosaccharide building blocks from suitably protected galactose donor and mannose acceptors. This elegant approach, however, involved multiple protection, deprotection, glycosylation, phosphorylation, and cumbersome purification steps even before undertaking phosphoglycan assembly by use of H-phosphonate chemistry.

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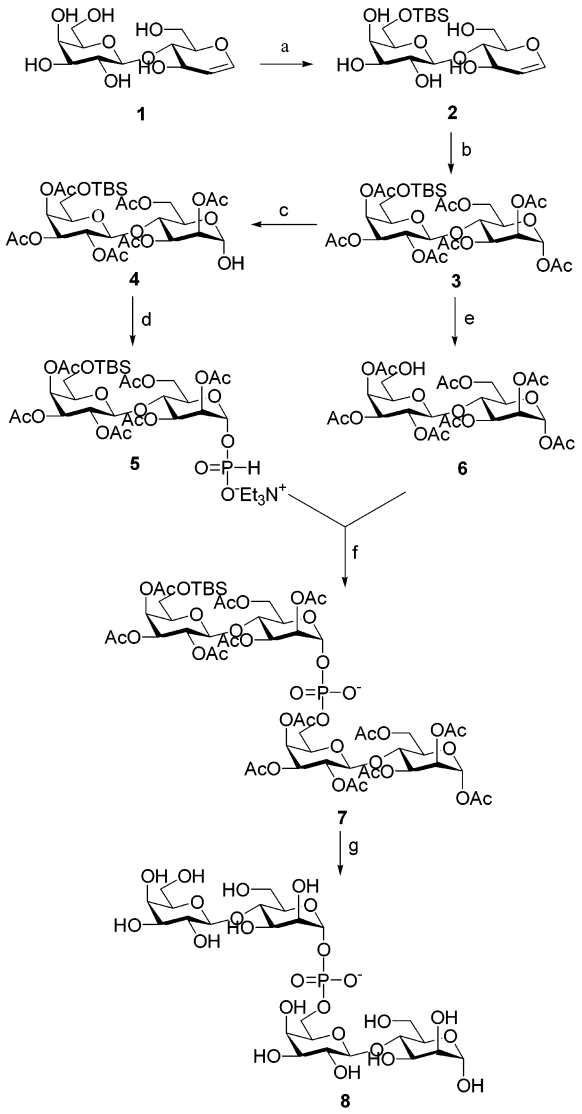
In our ongoing work on the organic synthesis[16−19] biosynthesis,[20] and immunology[21] of *Leishmania* cell surface glycoconjugates, an efficient route to construct phosphoglycans was required for the immunological evaluation of synthetic carbohydrate based anti-leishmania vaccines as well as for total synthesis of LPG. To circumvent the usual problems associated with glycosylation and multiple protection, deprotection, and glycosylation steps, we have designed a glycosylation-free synthetic approach[22] to construct phosphoglycans rapidly from disaccharide lactose as the starting material. Herein, we report a comprehensive (solution, solid-phase, and polycondensation) and efficient synthetic approach, without involving any glycosylation steps, that includes (a) gluco → manno transformation by glycal chemistry and regioselective 6′-protection to convert the easily available starting material lactose (Galβ1,4Glu) into a strategically protected central Galβ1,4Man building block that (b) can be used either as PG-phosphate donor or acceptor for (c) chain extension of PG repeats in either direction by selective deprotection at nonreducing or reducing ends and for (d) iterative PG coupling cycles in either direction. For the solid-phase synthesis of the phosphoglycans, we have designed a new *cis*-allyloxyphosphoryl linker to attach the first PG repeat to the solid support (via anomeric phosphodiester), followed by iterative PG coupling cycles. This new linker strategy allows selective cleavage of the first anomeric phosphodiester from the solid support without affecting other internal anomeric phosphodiester linkages. We have also observed that larger phosphoglycan oligomers (19−22 repeats) can be assembled from a single key intermediate in a one-pot polycondensation reaction.

Results and Discussion

Synthesis of Phosphoglycans in Solution. The first key intermediate lactal (**1**) was prepared[23] from lactose (Scheme 1) in four straightforward steps (acetylation, bromination, reductive-elimination, and deacetylation), and a high yield could be obtained in the reductive-elimination step by the application[18,19] of Zn/Vitamin-B_{12} reagent.[24] The next task was to selectively protect the 6-position of the galactose residue of lactal (**1**), and this was achieved, after considerable experimentation, by dibutyltin oxide mediated silylation ($Bu_2SnO-CH_3OH$ reflux followed by TBDMSCl), which led exclusively to 6′-*O*-(*tert*-butyldimethylsilyl) lactal (**2**). It should be mentioned here that under similar conditions most of the other protecting groups tested (benzyl, *p*-methoxybenzyl, and allyl) led to C3′-OH-protected lactals. The structure of compound **2** was determined by $^1H-^1H$ COSY, $^1H-^{13}C$ HETCOR, and HMBC NMR experiments, and placement of the TBDMS group at the 6-position of the Gal residue was further confirmed by silyl group induced shift in C-6 (δ 59.57) as compared to C-6 (δ 60.89) of the Man residue. The stereoselective gluco → manno transformation was completed by *m*-CPBA oxidation of 6′-*O*-(*tert*-butyldimethylsilyl) lactal **2** under biphasic conditions which led exclusively to 6′-*O*-(*tert*-butyldimethylsilyl)-galactopyranosyl-(1 → 4)-β-D-mannopyranose. Without further purification of this heptahydroxylated disaccharide, direct peracetylation provided the key intermediate

SCHEME 1. Synthesis of Phosphoglycan Donor and Acceptor from Common Intermediate 3 and Coupling to Phosphotetrasaccharide[a]



[a] Reagents and conditions: (a) Bu_2SnO, MeOH, reflux, 4 h; TBSCl, THF, rt, 48 h, 80%; (b) (1) *m*-CPBA, ether−H_2O, 0 °C, 4 h, (2) Ac_2O, pyridine, rt, 16 h, 84%; (c) Me_2NH, CH_3CN, −20 °C, 3 h, 99%; (d) PCl_3, imidazole, CH_3CN, 0 °C, 3 h, TEAB workup, 86%; (e) 48% aq HF−CH_3CN (5:95), 0 °C, 2 h, 85%; (f) compounds **5** and **6**, pivaloyl chloride, pyridine, rt, 1 h, then I_2 in 95% aq pyridine, 30 min, TEAB workup, 74%; (g) (1) 48% aq HF−CH_3CN (5:95), 0 °C, 2 h, (2) NaOMe−MeOH, 12 h, rt, 94%.

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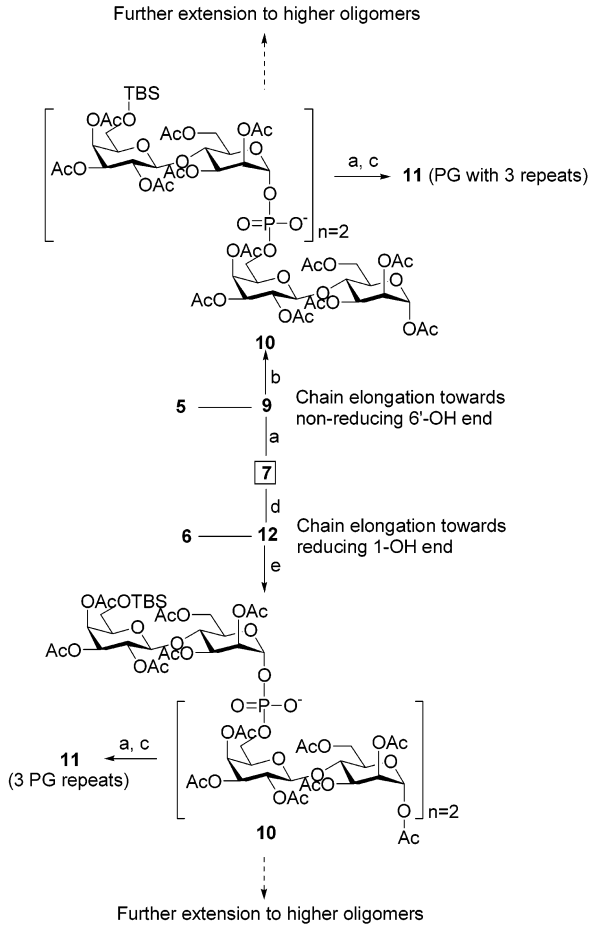
1,2,3,6-tetra-*O*-acetyl-4-*O*-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl]-α-D-mannopyranose (**3**) as the major product. The latter served as a central agent for both the donor as well as acceptor for iterative assembly of the phosphoglycan repeats. A portion of compound **3** was transformed to the phosphoglycan H-phosphonate donor by selective deacylation (Me_2NH at -20 °C) at the anomeric position leading to **4**, followed by phosphitylation (triimidazolylphosphine generated in situ from PCl_3 and imidazole) to provide 2,3,6-tri-*O*-acetyl-4-*O*-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl]-α-D-mannopyranosyl H-phosphonate, isolated as the triethylammonium bicarbonate (TEAB) salt (**5**). A second portion of compound **3** was converted to the hepta-*O*-acetylphosphoglycan acceptor (**6**) by removal of the TBDMS group from the 6-position of the Gal residue. The trimethylacetyl chloride (pivaloyl chloride) mediated coupling of the phosphoglycan H-phosphonate donor **5** with the acceptor compound **6**, followed by in situ iodine oxidation, afforded fully protected phosphotetrasaccharide (**7**) characterized as 2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl-(1 → 4)-1,2,3,6-tetra-*O*-acetyl-α-D-mannopyranoside 6-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl-(1 → 4)-1,2,3,6-tetra-*O*-acetyl-α-D-mannopyranosyl phosphate] triethylammonium salt. The presence of (1 → 6)-phosphodiester linkages between the PG repeats in compound **7** was confirmed by $^{31}P-^{13}C$ coupling (doublets, 5 and 7 Hz in ^{13}C NMR) for C-1 and C-2 of the α-mannose phosphate units and for C-5 and C-6 of the corresponding galactose units. These ^{13}C signals were found to be shifted due to α- and β-phosphorylation effects. The α-configuration of the mannosyl phosphate linkage was confirmed by ^1H NMR analysis that showed characteristic coupling (5.45 ppm, J_{HH} = 1.9 Hz and J_{HP} = 7 Hz) for the corresponding anomeric proton. This was further confirmed from the ^{13}C signals of the mannose C-3 and C-5 positions, corresponding to those reported[13] for α-mannosyl phosphate containing phoshphoglycans. The protected phosphotetrasaccharide (**7**), on global deprotection with $HF-CH_3CN$ and $NaOMe-CH_3OH$ conditions, provided free phosphoglycan **8** having two PG repeats.

The protected phosphotetrasaccharide **7** intermediate was ideally suited to further extension (Scheme 2) of phosphoglycan chain either upstream (nonreducing 6′-end) or downstream (reducing 1-OH end). For the upstream extension, the TBDMS group from **7** was removed, and the resulting phosphotetrasaccharide **9** was coupled with the phosphoglycan H-phosphonate donor **5** (from Scheme 1) to provide phosphohexasaccharide **10** in high yield. Global deprotection (TBDMS group removal with 48% aq $HF-CH_3CN$ (5:95) and deacetylation with $NaOMe-MeOH$) yielded free phosphoglycan **11** with three PG repeats.

For downstream extension of the PG domain, the phosphotetrasaccharide intermediate **7** was first selectively deacetylated at the reducing-end anomeric position by treatment with a saturated solution of dimethyamine in acetonitrile at -20 °C, followed by direct conversion to the corresponding H-phosphonate (**12**) as described above, giving an overall 86% yield over two steps. The H-phosphonate donor **12**, when coupled with the hepta-*O*-acetyldisaccharide acceptor **6** (from Scheme 1) using pivaloyl chloride, provided the phosphohexasaccharide **10**

SCHEME 2. Iterative Synthesis of *Leishmania* Phosphoglycans: Extension toward the Nonreducing 6′-OH or Reducing 1-OH End[a]



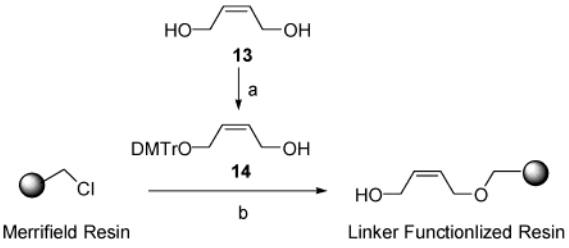
[a] Reagents and conditions: (a) 48% aqueous $HF-CH_3CN$ (5:95), 0 °C, 2 h, 85%; (b) (1) compound **5**, pivaloyl chloride, pyridine, rt, 1 h, (2) I_2 in 95% aq pyridine, 30 min, TEAB workup, 63%; (c) $MeOH/H_2O/Et_3N$ (5:2:1), rt, 48 h, 95%; (d) (1) Me_2NH-CH_3CN, -20 °C, 3 h, (2) PCl_3, imidazole, CH_3CN, 0 °C, 2 h, TEAB workup, 86%; (e) (1) compound **6**, pivaloyl chloride, pyridine, rt, 1 h, (2) I_2 in 95% aq pyridine, 30 min, TEAB, 61%.

identical to that obtained from the upstream extension sequence described above, ready for global deprotection to get PGs with three repeats or for further extension toward either end to get higher oligomers. The molecular masses of these oligomeric phosphoglycans were confirmed by negative-ion ESMS.

It is obvious from the above that the phosphoglycan chain can further be extended to the desired length in either direction, and instead of 2 + 4 (disaccharide+tetrasaccharide) coupling, 4 + 4 coupling can also be carried out for rapid access to desired phosphoglycans.

Solid-Phase Synthesis of Phosphoglycan. The synthesis of *Leishmania* phosphoglycans by solid-phase methodology presented a specific problem because of the presence of a labile anomeric phosphodiester between each PG repeat unit. If a single PG H-phosphonate donor (**5**) was used in iterative coupling cycles, removal of the final product from the solid-support would necessitate selective hydrolysis of the first terminal anomeric phosphodiester without affecting internal ones. This selectiv-

SCHEME 3. Synthesis of *cis*-Allyloxy Linker Functionized Resin[a]



[a] Reagents and conditions: (a) dimethoxytrityl chloride (DMTrCl), pyridine, rt, 15 h, 80%; (b) (1) compound **14**, DMF, NaH, tetrabutylammonium iodide, rt, 12 h, (2) 3% TFA in CH_2Cl_2, rt.

ity requirement was a formidable obstacle, and there was no literature precedent for this chemistry. After considerable experimentation and molecular modeling, we reasoned that a *cis*-allyloxy linker group adjacent to the first anomeric phosphodiester was marginally susceptible to organometallic catalysis under mild acidic conditions while other anomeric phosphodiesters survived. To examine this proposition, we designed and synthesized a new *cis*-allyloxyphosphoryl linker (Scheme 3) from *cis*-2-butene-1,4-diol (**13**) by dimethoxytritylation with 1 equiv of dimethoxytrityl chloride to obtain 4-(4,4′-dimethoxytrityl)-*cis*-2-butenol (**14**). The latter was coupled to the Merrifield resin (chloromethylated polystyrene cross-linked with 1% divinylbenzene, Sigma) using NaH and tetrabutylammonium iodide (TBAI) as catalyst. The unreacted sites on the functionalized resin were blocked by treatment with more NaH followed by CH_3OH quenching. Now the DMTr group was removed by treatment with 3% TFA in CH_2Cl_2 to obtain ready to couple linker-resin.

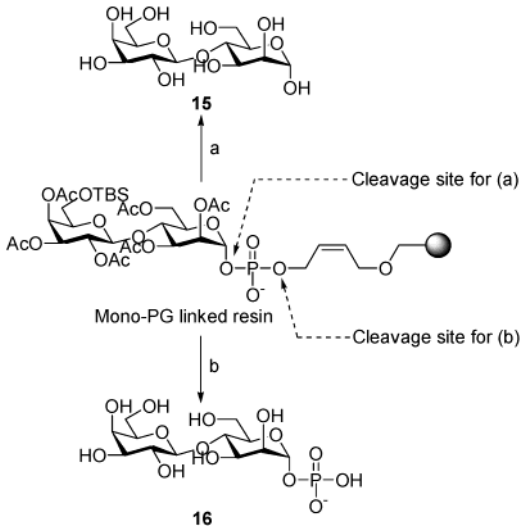
The molar quantity of loading of allyloxy linker onto the Merrifield resin was determined by the amount of dimethoxytrityl (DMTr) cation released on treatment with 3% TFA solution in CH_2Cl_2, measured at 503 nm by a UV spectrophotometric method.[25] This highly sensitive method showed fairly high (0.43 mmol/g) loading efficiency of the linker onto the solid support.

To the best of our knowledge, this is the first example of the design and application of a *cis*-allyloxy phosphoryl linker strategy to construct phosphorylated glycans on solid support, quite different from the octenediol linker designed by Seeberger[26] used for glycosylations on the solid phase and cleaved by olefin metathesis.

The linker-functionalized resin was swollen in the required solvent and coupled to the phosphoglycan H-phosphonate donor **5** (from Scheme 1) using pivaloyl chloride as the coupling agent, followed by iodine oxidation to afford a single PG repeat, linked by an anomeric phosphodiester group to the resin. This first cycle of coupling turned out to be efficient (95%).

To test our hypothesis regarding the directed selective cleavage of the allyloxyphosphoryl linker (Scheme 4), a small portion of the PG-linker-resin was treated with 0.1

SCHEME 4. Selective Cleavage of Allylphosphoryl Linker[a]



[a] Reagents and conditions: (a) (1) 0.1 N HCl, 100 °C, 1 min, (2) 48% aq HF−CH_3CN (5:95), 0 °C, 2 h, and MeOH−H_2O−Et_3N (5:2:1), rt, 48 h; (b) (1) Wilkinson's catalyst, 0.01 N HCl in toluene−PrOH−H_2O (2:1:0.08), rt, 24 h, (2) 48% aq HF−CH_3CN (5:95), 0 °C, 2 h and MeOH−H_2O−Et_3N (5:2:1), rt, 48 h.

N HCl at 100 °C for 1 min, this condition being known to cleave the phosphodiester at the anomeric position.[7] The cleaved product was characterized as 2,3,6-tri-*O*-acetyl-4-*O*-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl]-α-D-mannopyranose, identical to the authentic compound **4** already prepared by our solution method (see Scheme 1), and full deprotection led to the known compound Gal1−4βMan (**15**).

To our satisfaction, when the same PG-linked resin was treated with tris(triphenylphosphine)rhodium(I) chloride (Wilkinson's catalyst) in an argon-purged solution of toluene−PrOH−H_2O (2:1:0.08) containing 0.01 N HCl at room temperature for 7 h, the only product that was cleaved off under these mild conditions was 2,3,6-tri-*O*-acetyl-4-*O*-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl]-α-D-mannopyranosyl phosphate, which on complete deprotection provided the known Gal1−4βMan-1α-phosphate (**16**), identical to the authentic sample reported[18] by us earlier. This clearly demonstrated that our use of milder Wilkinson's reagent-catalyzed condition at room temperature led to selective cleavage of the anomeric phosphodiester group from the resin-bound intermediate at the allylic site to give compound **16** with its anomeric-phosphate linkage intact. The yield of this first iteration (attachment, one condensation, and selective cleavage) was 95% as determined by taking into the account the linker loading (0.43 mmol/g) of the functionalized resin and measuring the amount of the cleaved product. We did not observe any byproduct formed due to a competing mechanism (olefin isomerization and acidic enol hydrolysis toward the resin end). The selective cleavage of the *cis*-allyloxyphosphoryl linker toward the phosphate end is due to greater charge delocalization and weaker P−O−C bonds, as shown by a molecular modeling study.

With the validity of our linker design proven, we decided to extend the PG synthesis to the solid support

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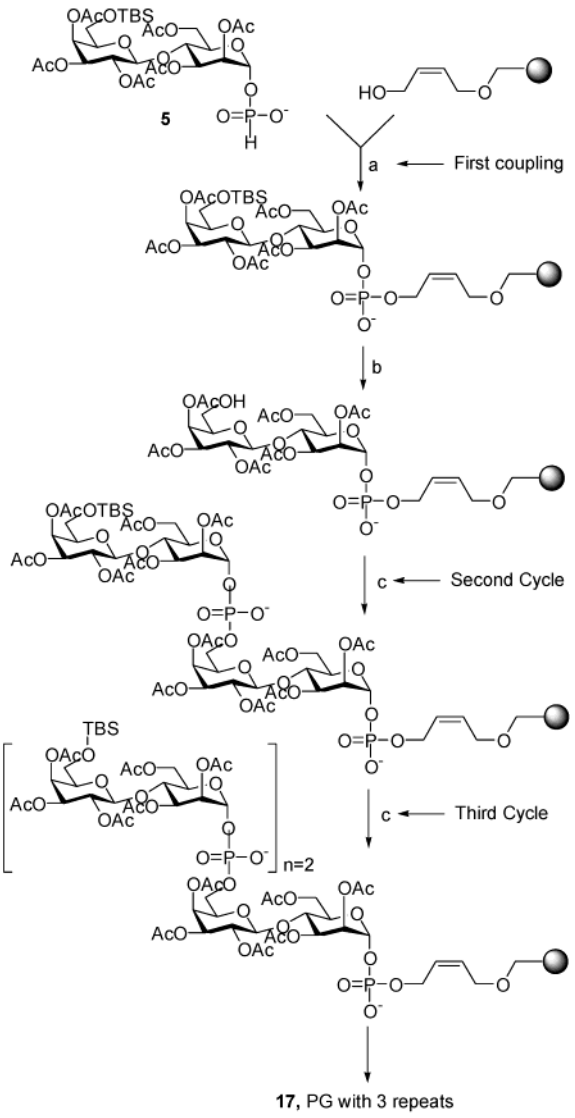
(26) Andrade, R. B.; Plante, O. J.; Melean, L. G., Seeberger, P. H. *Org. Lett.* **1999**, *1*, 1814−1814.

SCHEME 5. Solid-Phase Synthesis of Phosphoglycan Repeats[a]



[a] Reagents and conditions: (a) (1) pivaloyl chloride, pyridine, rt, 2 h, (2) I_2, 95% aq pyridine, 1 h; (b) 48% aq HF−CH_3CN (5:95), 0 °C, 3 h; (c) (1) **5**, pivaloyl chloride, pyridine, rt, 2 h, (2) I_2 in 95% aq pyridine, 1 h; (d) (1) tris(triphenylphosphine)rhodium(I) chloride (Wilkinson's catalyst), 0.01 N HCl in toluene−PrOH−H_2O (2:1:0.08), rt, 24 h, (2) 48% aq HF−CH_3CN (5:95), 0 °C, 2 h and MeOH−H_2O−Et_3N (5:2:1), rt, 48 h.

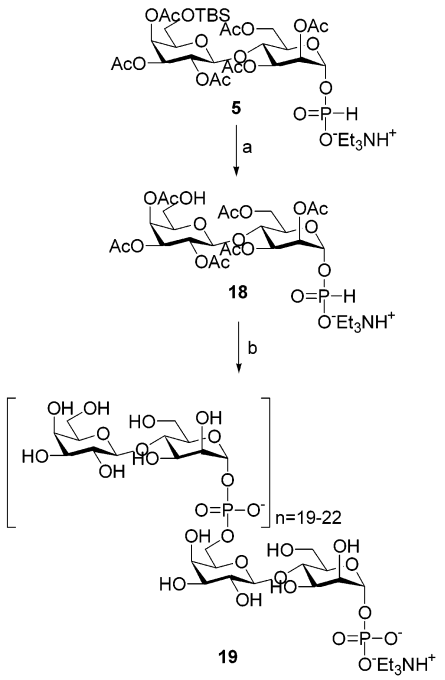
(Scheme 5). The mono-PG coupled resin was treated with 48% aq HF−CH_3CN (5:95) to remove the terminal TBDMS group from the galactose residue to provide a free 6′ hydroxyl which was used for the second cycle of coupling with the phosphoglycan H-phosphonate donor **5**. This coupled resin so obtained had two PG repeats and two anomeric phosphodiesters to test our selective cleavage. Wilkinson's catalyst mediated selective hydrolysis, as described above, led to 2,3,4-tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-α-D-mannopyranosyl phosphate 6-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl-(1→4)-1,2,3,6-tetra-*O*-acetyl-α-D-mannopyranosyl phosphate, which when treated directly with 48% aq HF−CH_3CN (5:95) and CH_3OH−H_2O−Et_3N for global deprotection (desilylation and deacetylation) provided free phosphotetrasaccharide with two PG repeats (80% yield), characterized by comparison with authentic sample (**8**) prepared by the solution method described above. The third coupling and cleavage cycle was carried out essentially as described above, which provided phosphohexasaccharide **17** with three phosphoglycan repeats.

The coupling efficiency of each iterative cycle was more than 90% as determined by cleavage after each cycle and analysis of the deprotected product. The progress of these PG coupling cycles could be easily monitored by taking a small aliquot of the reaction mixture and treating it with the cleavage reagent for negative-ion ESMS analysis.

Hence, we have been able to design a new allyoxyphosphoryl linker and establish a straightforward synthetic strategy for construction of Leishmania phosphoglycans on solid phase, starting from a single and easily available intermediate **5**, without involving any glycosylation step. This synthetic methodology has the obvious advantage of solid-phase synthesis and is eminently suitable for easy access to *Leishmania* phosphoglycans for biological and immunological studies and also for combinatorial synthesis of structural and functional mimics of phosphoglycans. For example, one major obvious advantage of our solid-phase approach is that the cleaved phosphoglycan can be easily activated as a phosphoro-imidazolide intermediate, ready to couple with the amino groups of an antigenic carrier protein for preparation of anti-leishmania vaccines. Currently, we are exploiting this approach, and the results will be communicated separately.

Synthesis of Phosphoglycans by Polycondensation. With the essential methodology established and larger amounts of two key building blocks, **5** and **6**, in hand for the construction of *Leishmania* phosphoglycans by solution or solid-phase approaches, we turned toward exploring the possibility of assembling linear PGs by one-pot polycondensation, following the methodology reported by Nikolaev et al.[15] The rationale (Scheme 6) involved selective removal of the TBDMS group from the 6′-position of our key intermediate **5** to give 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-*β*-D-galactopyranosyl)-α-D-mannopyranosyl H-phosphonate (**18**), which would serve as a bifunctional monomer building block for the polycondensation reaction. Attempts to remove the TBDMS group selectively by standard methods (TBAF, HF, PTSA, PPTS, Lewis acids, etc.) caused simultaneous loss of the anomeric H-phosphonate group, necessitating milder conditions for this deprotection. Thus, treatment of the PG-donor **5** with AcOH/H_2O/THF (3:1:1) at 40 °C for 9 h led to clean TBDMS deprotection. The product was obtained without any chromatographic purification, and the ^{1}H-coupled ^{31}P NMR spectrum of **18** showed a clear signal at 0.22 ppm with the characteristic J_{H-P} of 637 Hz for the H-phosphonate group. The polycondensation of the bifunctional monomer block **18** was now carried out by pivaloyl chloride in pyridine−Et_3N (10:1) using a high concentration of both the monomer and the coupling reagent to avoid formation of cyclic products. The progress of the polycondensation reaction could be easily monitored by in situ ^{31}P NMR that showed the disappearance of the starting monomer signal at 0.22 ppm after 3 h and the appearance of a major new signal at 8.00 ppm due

SCHEME 6. Synthesis of PG Repeats by Polycondensation[a]



[a] Reagents and conditions: (a) AcOH/THF/H_2O (3:1:1), 40 °C, 9 h, 97%; (b) (1) pivaloyl chloride, pyridine−Et_3N (10:1), rt, 3 h, (2) I_2 in 95% aq pyridine, 2 h, TEAB, (3) 0.1 M NaOMe in methanol−dioxane−chloroform, 23 h, 4 °C.

to H-phosphonic diesters. The reaction mixture was then treated with iodine solution in aqueous pyridine to oxidize the H-phosphonic diesters to phosphoric diesters to obtain fully protected phosphoglycan which was directly used for final deprotection (0.1 M NaOMe in CH_3-OH−dioxane−$CHCl_3$) followed by filtration through Dowex X8 (H^+) resin to provide free phosphoglycan as a triethylammonium salt (**19**), which showed a major ^{31}P NMR signal at −1.73 ppm. This material was further purified by anion-exchange (DEAE) chromatography to give partially purified product.

The size of the polycondensation product (**19**) was determined by two independent methods using negative-ion ESMS and ^{31}P NMR analysis. The ESMS analysis of the multiply charged ions, by the MaxEnt transformation and deconvolution method, showed that the product contained a major sub-population of phosphoglycans having 19−22 repeats. There were four major peaks in transformed spectra for 19−22 repeats with the difference of *m*/*z* 403 Da each corresponding to an incremental PG unit. It needs to be mentioned here that under normal negative-ion ESMS conditions (capillary voltage, 4.9 kV and cone voltage, 170 V), deprotected phosphoglycans were found to be rather unstable (due to cleavage of anomeric phosphodiester linkages), but under milder ionization conditions (capillary, 2.3 kV, and cone, 70 V), they provided excellent ESMS data of intact molecules. The number of PG repeats was also indicated by ^{31}P NMR analysis of the integration ratio of signals due to one terminal phosphomonoester (0.88 ppm) and other internal phosphodiester groups (−1.73 ppm).

CD Analysis of Polycondensation Product. Although this polycondensation did not provide homogeneous phosphoglycan, it efficiently led to a mixture containing larger phosphoglycans (with 19−22 repeats) in a single straightforward step, and their numbers could be estimated either by ESMS or ^{31}P NMR methods. Currently, there is no practical methodology available, due to lack of a chromophore, to separate the individual phosphoglycans for NMR analysis. However, the availability of this unique material allowed us to initiate conformational studies on *Leishmania* phosphoglycan by another powerful biophysical method for conformational analysis, i.e., circular dichroism. In fact, the heterogeneity present in our polycondensation product turned out to be advantageous because it nicely mimicked the biological situation where LPG and PPG both have significant heterogeneity in terms of the number of repeats present in their phosphoglycan domains, when isolated from parasite culture.

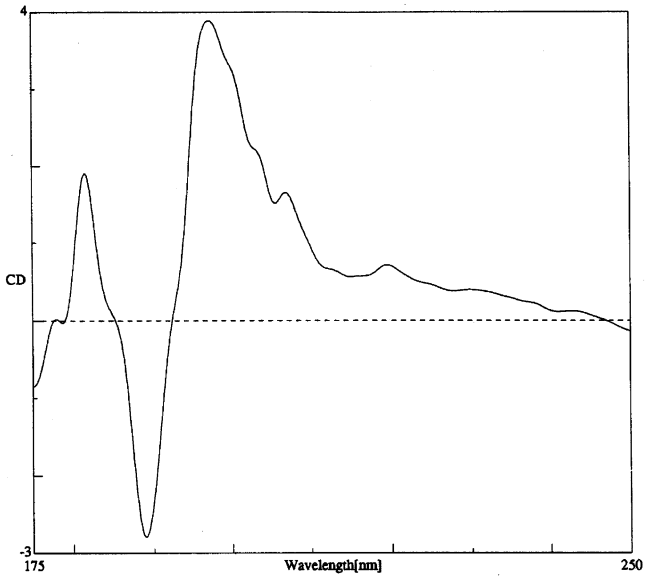


FIGURE 2. CD spectrum of the polycondensation product (19−22 repeats) in the vacuum−UV range.

For CD analysis, the polycondensation product **19** was lyophilized repeatedly and dissolved in water (15% w/v) and CD spectra acquired (Figure 2) in a vacuum-UV region (between 175 and 250 nm) at 25 °C. For a reference, the CD spectrum of Agarose (15% w/v), a known polysaccharide with helical conformation,[27] was recorded under the identical conditions. The analysis of the CD data of our polycondensation product clearly showed that these larger phosphoglycan repeats contain a significant amount of helicity in aqueous solution. Interestingly, this helical conformation was not seen in CD analysis of smaller PGs prepared by solution synthesis described in the first section of this paper. This preliminary CD observation is extremely significant in view of the prevailing biological hypothesis that *Leishmania* phosphoglycans form springlike helical supramolecular structures[8] around the parasite cell surface, which provide resistance to host hydrolytic enzymes and antibodies and also constitute functional epitopes for recognition by macrophage receptors.[9] Our current interest is to exploit this observation, and the detailed conforma-

(27) Liang, J. N.; Stevens, E. S. *Biopolymers* **1979**, *18*, 327−333.

tional analysis of these larger PGs will be reported in due course.

Experimental Section

Lactal (1). A solution of cyanocobalamin (vitamin B_{12}, 1.5 g, 1.14 mmol) in anhyd CH_3OH (400 mL) was thoroughly purged with nitrogen gas for 30 min, and zinc powder (87.5 g, 1.338 mol) and ammonium chloride (71 g, 1.33 mol) were added to the solution. The reaction was stirred for another 45 min, and hepta-*O*-acetyl lactosyl bromide (47 g, 67.5 mmol), freshly prepared from lactose by a known method, dissolved in CH_3OH (150 mL) was added. Immediately after addition of the bromide, the dark red solution changed to reddish yellow and then back to dark red in 5 min. The solution was filtered through Celite to remove zinc, the Celite pad was washed with CH_3OH, and the filtrate was concentrated to give a white and red solid. This mixture was dissolved in water (500 mL) and extracted with CH_2Cl_2 (300 mL × 3). Organic extracts were combined, dried over Na_2SO_4, and concentrated to provide hexa-*O*-acetyl lactal (36 g, 87%) as an amorphous solid: mp 113 °C (lit.[23] mp 114 °C); $[\alpha]_D = -18$ (*c* 1.0, $CHCl_3$) [lit.[23] $[\alpha]_D = -18$ (*c* 1.0, $CHCl_3$)]. In the next step of complete deacylation, hexa-*O*-acetyl lactal (36 g, 64.5 mmol) and freshly dried Na_2CO_3 (45 g, 425 mmol) were suspended in anhyd CH_3OH (750 mL) and stirred for 90 min at room temperature. The suspension was filtered to remove excess Na_2CO_3, and the filtrate was concentrated under reduced pressure to give deprotected lactal (**1**) as an amorphous solid (19.4 g, 98%): $R_f = 0.2$ in 30% CH_3OH in CH_2Cl_2; mp 191−193 °C; $[\alpha]_D = +27$ (*c* 1.6, H_2O) [lit.[23] $[\alpha]_D = +27$ (*c* 1.6, H_2O)].

6′-*O*-(*tert*-Butyldimethylsilyl)lactal (2). A solution of lactal (**1**, 10 g, 32.4 mmol) and Bu_2SnO (8 g, 32.5 mmol) in anhyd CH_3OH (1000 mL) was heated to reflux for 4 h followed by removal of solvent, which provided a yellow powder. The dibutyltin complex was dissolved in anhyd THF (1000 mL), TBDMSCl (4.9 g, 32.3 mmol) was added, and the solution was stirred for 48 h at rt. After completion of the reaction, the solvent was concentrated to give a residue which was purified by silica chromatography (8% CH_3OH in CH_2Cl_2) to provide compound **2** (10.8 g, 79.5%): $R_f = 0.47$ in 15% CH_3OH in CH_2Cl_2; $[\alpha]_D = +3.45$ (*c* 0.29, MeOH); ^{1}H NMR (D_2O, 300 MHz) δ 0.01 (s, 6H), 0.82 (s, 9H), 3.48 (m, 1H), 3.58 (m, 1H), 3.65 (m, 1H), 3.76 (m, 4H), 3.82 (d, $J = 3.1$ Hz, 1H), 3.92 (m, 1H), 4.38 (m, 1H), 4.31 (d, $J = 5.7$ Hz, 1H), 4.46 (d, $J = 7.8$ Hz, 1H), 4.76 (dd, $J = 3.6$ and 6.3 Hz, 1H), 6.37 (dd, $J = 1.1$ and 6.2 Hz, 1H); ^{13}C NMR (D_2O, 75 MHz) δ −4.84, 25.23, 59.57, 60.89, 67.14, 68.45, 70.87, 72.52, 101.73, 76.68, 77.43, 75.23, 102.87, 143.88; ESMS *m*/*z* 445.10 $(M + Na)^+$; HRMS (FAB) calcd for $(M + Li)^+$ $C_{18}H_{34}O_9SiLi$ 429.2132, found 429.2126.

1,2,3,6-Tetra-*O*-acetyl-4-*O*-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl]-α-D-mannopyranose (3). A solution of **2** (5 g, 11.8 mmol) in water (50 mL) was stirred, and then a solution of *m*-CPBA (6.5 g, 36 mmol) in diethyl ether (50 mL) was added dropwise at −10 °C. The reaction mixture was brought to 0 °C and stirred for 4 h, and the aqueous layer was extracted thoroughly with ether and lyophilized to afford a white solid. This was dissolved in anhyd pyridine (25 mL), and acetic anhydride (25 mL) was added dropwise at 0 °C. The mixture was gradually brought to rt and stirred for 16 h, and after completion of the reaction it was quenched with ice and diluted with CH_2Cl_2. The organic layer was washed with water, dried (Na_2SO_4), and concentrated to give a syrup which was purified by silica column (20% ethyl acetate in hexane) to provide compound **3** as a white amorphous solid (7.5 g, 84%): $[\alpha]_D = +6.72$ (*c* 0.55, $CHCl_3$); $R_f = 0.69$ in 70% ethyl acetate in hexane; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.01 (s, 6H), 0.84 (s, 9H), 1.95−2.14 (m, 21H), 3.56−3.64 (m, 4H), 4.17−5.04 (m, 2H), 4.53 (d, $J = 7.8$ Hz, 1H), 5.01 (dd, $J = 3.3$, 7.8 Hz, 2H), 5.12 (dd, $J = 2.1$, 7.8 Hz, 1H), 5.21 (dd, $J = 2.1$, 3.6 Hz, 1H), 5.34 (dd, $J = 3.6$, 4.5 Hz, 1H), 5.41 (d, $J = 3.3$ Hz, 1H), 6.01 (d, $J = 2.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.85, 17.94, 20.40−20.86, 25.54, 60.01, 62.14, 66.45, 68.18, 69.25, 69.39, 70.58, 70.79, 73.38, 73.62, 90.25, 101.14, 168.08−170.23; ESMS *m*/*z* 773.24 $(M + Na)^+$; HRMS (ESMS) calcd for $(M + NH_4)^+$ $C_{32}H_{54}NO_{18}Si$ 768.3110, found 768.3139.

2,3,6-Tri-*O*-acetyl-4-*O*-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl]-α-D-mannopyranose (4). Compound **3** (100 mg, 0.132 mmol) was dissolved in saturated Me_2NH solution in anhyd CH_3CN (20 mL) at −20 °C and stirred for 3 h, after which time TLC confirmed the disappearance of the starting material. Excess of Me_2NH was removed under reduced pressure below 30 °C, and the reaction mixture was concentrated to give the desired anomeric deprotected compound **4** in quantitative yield: $R_f = 0.45$ in 70% ethyl acetate in hexane; $[\alpha]_D = +3.75$ (*c* 0.16, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.01 (s, 6H), 0.84 (s, 9H), 1.95−2.19 (m, 18H), 3.56−3.66 (m, 4H), 3.91 (m, 1H), 4.12−4.16 (m, 2H), 4.40 (d, $J = 4.5$ Hz, 1H), 4.40 (d, $J = 7.8$ Hz, 1H), 4.99 (dd, $J = 3.3$, 7.8 Hz), 5.09 (dd, $J = 2.1$, 7.8 Hz, 1H), 5.17 (dd, $J = 2.1$, 3.6 Hz, 1H), 5.23 (dd, $J = 3.6$, 4.5 Hz, 1H), 5.43 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.77, 17.98, 20.40−21.38, 25.58, 60.06, 62.62, 66.56, 68.78, 69.30, 69.51, 70.06, 71.21, 73.37, 74.15, 91.82, 101.04, 169.10−170.52; ESMS *m*/*z* 731.3 $(M + Na)^+$; HRMS (ESMS) calcd for $(M + Na)^+$ $C_{30}H_{48}O_{17}SiNa$ 731.2558, found 731.2570.

Triethylammonium 2,3,6-Tri-*O*-acetyl-4-*O*-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl]-α-D-mannopyranosyl Hydrogen Phosphonate (5). To a stirred solution of imidazole (224 mg, 3.28 mmol) in anhyd CH_3CN (5 mL) at 0 °C were added PCl_3 (160 μL, 1.8 mmol) and Et_3N (480 μL, 3.44 mmol). The mixture was stirred for 20 min, after which time a solution of compound **4** dissolved in anhyd CH_3CN (5 mL) was added dropwise. The mixture was stirred at 0 °C for 3 h and quenched with 1 M triethylammonium bicarbonate (TEAB) buffer (pH 7, 2 mL). The clear solution was stirred for 15 min and diluted with CH_2Cl_2 (20 mL), and the organic layer was washed with ice-cold water (10 mL × 2) and cold 1 M TEAB solution (10 mL × 2), dried over Na_2SO_4, and concentrated to yield phosphoglycan donor **5** (100 mg, 86%): $R_f = 0.45$ in 20% CH_3OH in CH_2Cl_2; $[\alpha]_D = -4.5$ (*c* 0.27, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.01 (s, 6H), 0.82 (s, 9H), 1.30 (t, 9H), 1.95−2.09 (m, 18H), 3.00 (q, 6H), 3.49−3.68 (m, 4H), 3.88 (m, 1H), 4.14 (m, 1H), 4.36 (d, $J = 4.5$ Hz, 1H), 4.47 (d, $J = 7.8$ Hz, 1H), 4.95 (dd, $J = 3.3$, 7.8 Hz, 1H), 5.05 (dd, $J = 2.1$, 7.8 Hz, 1H), 5.21 (dd, $J = 2.1$, 3.6 Hz, 1H), 5.41 (d, $J = 3.3$ Hz, 1H), 5.48 (dd, $J = 2.1$, 7.8 Hz, 1H), 6.92 (d, $J_{H,P} = 637.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.80, 17.98, 8.5 and 45.5, 20.48−20.76, 25.57, 60.10, 62.42, 66.57, 69.36, 69.53, 69.69, 71.20, 73.30, 73.86, 91.59, 92.54, 101.09, 169.13−170.49; ^{31}P NMR δ 0.13; ESMS *m*/*z* 771.26 $(M - Et_3N - H)^-$; HRMS (ESMS) calcd for $(M - Et_3N - H)^-$ $C_{30}H_{48}O_{19}PSi$ 771.2297, found 771.2276.

1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-*β*-D-galactopyranosyl)-α-D-mannopyranose (6). A solution of 48% aq HF in CH_3CN (5:95, 8 mL) was added to compound **3** (100 mg, 0.132 mmol) at 0 °C, and the solution was stirred for 2 h. The reaction was quenched with aq $NaHCO_3$ solution until effervescence ceased and diluted with CH_2Cl_2. The organic layer was washed thoroughly with water, dried over Na_2SO_4, and concentrated to give **6** (72 mg, 86%): $R_f = 0.3$ in 70% ethyl acetate in hexane; $[\alpha]_D = +4.6$ (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.97−2.16 (m, 21H), 3.67−3.74 (m, 3H), 4.08−4.14 (m, 3H), 4.58 (d, $J = 7.8$ Hz, 1H), 5.16 (dd, $J = 2.1$, 7.8 Hz, 1H), 5.23 (dd, $J = 2.1$, 3.6 Hz, 1H), 5.32 (d, $J = 3.3$ Hz, 1H), 5.41 (dd, $J = 3.6$, 4.5 Hz, 1H), 6.01 (d, $J = 2.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.42−20.77, 60.74, 62.25, 67.56, 68.31, 69.35, 69.43, 70.77, 70.83, 73.98, 74.32, 90.45, 101.30, 168.32−170.80; ESMS *m*/*z* 659.28 $(M + Na)^+$; HRMS (ESMS) calcd for $(M + NH_4)^+$ $C_{26}H_{40}NO_{18}$ 654.2245, found 654.2272.

2,3,4-Tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-1,2,3,6-tetra-*O*-acetyl-α-D-mannopyranoside 6-[2,3,4-Tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl-(1→4)-

1,2,3,6-tetra-*O*-acetyl-α-D-mannopyranosyl phosphate] Triethylammonium Salt (7). A mixture of H-phosphonate donor **5** (32 mg, 0.036 mmol) and acceptor **6** (23 mg, 0.036 mmol) was dried by evaporation of pyridine (500 μL × 3). The residue was dissolved in anhyd pyridine (600 μL), and pivaloyl chloride (15 μL, 0.123 mmol) was added. The reaction mixture was stirred for 1 h at rt, and a freshly prepared iodine solution (600 μL, 18 mg, 0.078 mmol in pyridine−water, 95:5) was added. After 30 min, CH_2Cl_2 (10 mL) was added, and the solution was washed successively with a cold 1 M aqueous solution of $Na_2S_2O_3$ (5 mL × 2) and ice-cold 1 M TEAB buffer (5 mL × 2), dried over Na_2SO_4, and concentrated. Column chromatography on silica gel (3% MeOH in CH_2Cl_2 with 1% Et_3N) afforded product **7** (40 mg, 74%): $R_f = 0.21$ in 10% CH_3OH in CH_2Cl_2; $[\alpha]_D = -6.1$ (*c* 0.18, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz; assignments confirmed by $^1H-^1H$ COSY and HMQC experiments) δ 0.01 (s, 6H), 0.84 (s, 9H), 1.30 (t, 9H), 1.96−2.15 (m, 39H), 3.00 (q, 6H),3.50 (m, 4H), 3.87 (m, 1H), 3.94 (m, 1H), 4.07−4.14 (m, 2H), 4.35 (m, 1H), 4.39 (m, 4H), 4.40 (m, 1H), 4.48 (m, 1H), 4.52 (m, 1H), 4.94 (d, $J = 7.7$ Hz, 2H), 5.28 (m, 5H), 5.43 (m, 1H), 5.45 (dd, $J_{HH} = 1.9$ and $J_{HP} = 7.0$ Hz, 1H), 5.46 (m, 1H), 6.01 (d, $J = 2.7$ Hz, 1H); ^{13}C NMR −5.75, 17.95, 25.57, 8.5 and 45.50 (TEA ion), 20.48−20.79 (13 peaks), 60.06, 60.42 (d, $J_{CP} = 8$ Hz), 62.22, 62.63, 66.55, 67.46, 68.27, 68.64, 69.37, 69.66, 69.84, 70.14, 70.75, 70.88, 71.20, 73.31, 73.76, 74.24, 77.15, 78.95, 90.41 (d), 91.69, 101.08, 101.29, 168; ^{31}P NMR: δ −2.90 (dt, J_{PH} 7.5 and 10); ESMS *m/z* 1405.2 (M − Et_3N − H)$^-$; HRMS (ESMS) calcd for (M − Et_3N − H)$^-$ $C_{56}H_{82}O_{37}PSi$ 1405.4042, found 1405.4105.

***β*-D-Galactopyranosyl-(1→4)-α-D-mannopyranoside 6-[*β*-D-Galactopyranosyl-(1→4)-α-D-mannopyranosyl phosphate] Triethylammonium Salt (8).** A solution of 48% aq HF in CH_3CN (5:95, 1.5 mL) was added to compound **7** (15 mg, 0.01 mmol) at 0 °C. The solution was stirred at 0 °C for 2 h. The reaction was quenched by the addition of aq $NaHCO_3$ solution until effervescence ceased and diluted with CH_2Cl_2 (5 mL). The organic layer was washed with water, dried over Na_2SO_4, and concentrated. The residue was dissolved in anhyd CH_3OH (500 μL), NaOMe (15 mg) was added, the solution was stirred overnight at rt, deionized with AG-X8 resin (H^+), filtered, and immediately neutralized with Et_3N. After concentration, water (500 μL × 3) was evaporated off from the residue to afford tetrasaccharide phosphodiester **8** (7.9 mg, 94%): $[\alpha]_D = 34$ (*c* 0.15, H_2O); ^1H NMR (D_2O; $^1H-^1H$ COSY assignments) δ 1.30 (t, 9H), 3.00 (q, 6H), 3.45 (m, 2H), 3.46 (m, 1H), 3.55 (m, 1H), 3.56−3.53 (m, 2H), 3.60 (m, 2H), 3.68 (m, 4H), 3.76 (m, 2H), 3.80 (m, 4H), 3.83 (m, 2H), 3.85 (m, 1H), 3.94 (m, 1H), 4.32 (m, 1H), 4.37 (d, $J = 7.6$ Hz, 1H), 4.35 (d, $J = 7.6$ Hz, 1H), 5.09 (d, $J = 1.8$ Hz, 1H), 5.36 (dd, $J_{HH} = 1.9$ Hz, $J_{HP} = 6.8$ Hz, 1H); ^{13}C NMR δ 8.5 and 45 (TEA ion), 61.37, 61.37, 62.30, 65.53, 69.28, 69.83, 70.84, 71.08, 72.13, 72.34, 73.69, 74.89, 76.52, 77.05, 78.14, 97.0, 102.9; ^{31}P NMR δ −1.29; ESMS *m/z* 745.38 (M − Et_3N − H)$^-$; HRMS (ESMS) calcd for (M − Et_3N − H)$^-$ $C_{24}H_{42}O_{24}P$ 745.1804, found 745.1830.

2,3,4-Tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-1,2,3,6-tetra-*O*-acetyl-α-D-mannopyranoside 6-(2,3,4-Tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-α-D-mannopyranosyl phosphate) Triethylammonium Salt (9). A solution of 48% aq HF in CH_3CN (5:95, 5 mL) was added to compound **7** (20 mg, 0.015 mmol) at 0 °C and stirred at 0 °C for 2 h. The reaction was quenched by the addition of aq $NaHCO_3$ solution until effervescence ceased and diluted with CH_2Cl_2 (5 mL). The organic layer was washed with water, dried over Na_2SO_4, and filtered through a small silica column to give compound **9** (15.6 mg, 85%): ^1H NMR ($CDCl_3$, 300 MHz) δ 1.30 (t, 9H), 3.00 (q, 6H), 1.96−2.15 (m, 39H), 3.50 (m, 4H), 3.87 (m, 1H), 3.94 (m, 1H), 4.07−4.10 (m, 1H), 4.07−4.14 (m, 1H), 4.35 (m, 1H), 4.39 (m, 4H), 4.40 (m, 1H), 4.48 (m, 1H), 4.52 (m, 1H), 4.94 (d, 1H), 5.28 (m, 4H), 5.29 (m, 1H), 5.43 (m, 1H), 5.45 (dd, 1H), 5.46 (m, 1H), 6.01 (d, 1H); ^{13}C NMR δ 8.00 and 45.50 (TEA ion), 20.48−20.7, 60.06, 60.42, 62.22, 62.63, 66.55, 67.46, 68.27, 68.64, 69.37, 69.66, 69.84, 70.14, 70.75, 70.88, 71.20, 73.31, 73.76, 74.24, 77.15, 78.95, 90.41, 91.69, 101.08, 101.29, 168−171; ^{31}P NMR δ δ −2.90 (dt, J_{PH} 7.5 and 10); ESMS *m/z* 1290.4 (M − Et_3N − H); HRMS (ESMS) calcd for (M − Et_3N − H)$^-$ $C_{50}H_{68}O_{37}P$ 1291.3177, found 1291.3188.

2,3,4-Tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-1,2,3,6-tetra-*O*-acetyl-α-D-mannopyranoside 6-[2,3,4-Tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-α-D-mannopyranosyl phosphate 6-[2,3,4-tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-α-D-mannopyranosyl phosphate]] Bis-triethylammonium Salt (10). A mixture of phosphotetrasaccharide acceptor **9** (15.6 mg, 0.015 mmol) and H-phosphonate donor **5** (20.8 mg, 0.024 mmol) was dried by evaporation of pyridine (500 μL × 3). The residue was dissolved in anhydrous pyridine (500 μL), and pivaloyl chloride (10 μL, 0.083 mmol) was added. The mixture was stirred for 1 h at rt after which time a freshly prepared solution of iodine (500 μL, 16 mg, 0.06 mmol in pyridine/water 95:5) was added. After 30 min, CH_2Cl_2 was added, and the solution was washed successively with cold 1 M aq $Na_2S_2O_3$ solution (5 mL × 2) and ice-cold 1 M TEAB buffer (5 mL × 2), dried over Na_2SO_4, and concentrated. The silica column purification using 5% MeOH in CH_2Cl_2 with 1% Et_3N afforded compound **10** (16 mg, 63%): $R_f = 0.11$ in 10% CH_3OH in CH_2Cl_2; ^1H NMR ($CDCl_3$) δ 0.01 (s, 6H), 0.84 (s, 9H), 1.30 (t, 9H, TEA ion), 3.00 (q, 6H, TEA ion), 2.15−1.96 (m, 57H), 3.50 (m, 6H), 3.87−3.94 (m, 3H), 4.14−4.07 (m, 3H), 4.30−4.35 (m, 3H), 4.39 (m, 6H), 4.48 (m, 2H), 4.52 (m, 1H), 4.94 (m, 3H), 5.28 (m, 6H), 5.29 (m, 1H), 5.43 (m, 2H), 5.45 (dd, $J_{HH} = 1.9$ and $J_{HP} = 7.0$ Hz, 2H), 5.46 (m, 3H), 6.01 (d, $J = 1.9$ Hz, 1H); ^{31}P NMR δ δ −1.94; ESMS *m/z* 2061.44 (M − 2Et_3N − H), 2062.35 (M − 2Et_3N); HRMS (ESMS) calcd for (M − Et_3N − H)$^-$ $C_{80}H_{115}O_{56}P_2Si$ 2061.5396, found 2061.5399.

***β*-D-Galactopyranosyl-(1→4)-α-D-mannopyranoside [6-*β*-D-Galactopyranosyl-(1→4)-α-D-mannopyranosyl phosphate 6-[*β*-D-galactopyranosyl-(1 → 4)-α-D-mannopyranosyl phosphate]] Bis-triethylammonium Salt (11).** The global deprotection of fully protected phosphohexasaccharide **10** was carried out by same method as given for the preparation of compound **8** earlier: ^1H NMR (D_2O) δ 1.38 (t, 9H), 3.30 (q, 6H),3.45 (m, 3H), 3.46 (m, 2H), 3.55 (m, 1H), 3.56−3.53 (m, 3H), 3.60 (m, 3H), 3.68 (m, 6H), 3.76 (m, 3H), 3.80 (m, 6H), 3.83 (m, 3H), 3.85 (m, 1H), 3.94 (m, 2H), 3.90−4.20 (m, 4H), 5.09 (d, $J = 1.8$ Hz, 1H, H-1), 5.29 (brd, 2H); ^{31}P NMR δ −1.29; ESMS *m/z* 574.12 ([M − 2Et_3N − 2H]$^{2-}$; HRMS (ESMS)t calcd for (M − Et_3N − H)$^-$ $C_{36}H_{62}O_{37}P_2$ 574.1222, found 574.1234.

2,3,4-Tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-1,2,3,6-tetra-*O*-acetyl-α-D-mannopyranoside 6-[2,3,4-Tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-α-D-mannopyranosyl hydrogen phosphonate] Triethylammonium Salt (12). Compound **7** (50 mg, 0.03 mmol) was dissolved in a saturated solution of Me_2NH in anhyd CH_3CN (2 mL) at −20 °C, and the solution was stirred for 3 h after which time TLC confirmed disappearance of the starting material. Excess Me_2NH was removed under reduced pressure below 30 °C, and the reaction mixture was concentrated to give the anomeric deprotected product. To a stirred solution of imidazole (60 mg, 8.7 mmol) in anhyd CH_3CN (2.50 mL) at 0 °C were added PCl_3 (100 μL, 1.12 mmol) and Et_3N (300 μL, 2.15 mmol). The mixture was stirred for 20 min, after which time a solution of the above anomeric deprotected compound dissolved in anhyd CH_3CN (500 μL) was added dropwise. The mixture was stirred at 0 °C for 2 h and quenched with 1 M TEAB solution (pH = 7, 1 mL). The clear solution was stirred for 15 min, after which time CH_2Cl_2 was added and the organic layer was washed with ice-cold water (5 mL × 2) and cold 1 M TEAB buffer (5 mL × 2), dried over Na_2SO_4, and concentrated to yield compound **12** (51 mg, 86%): ^1H NMR δ 0.01 (s, 6H), 0.84 (s, 9H), 1.30 (t, 9H), 1.96−2.15 (m, 36H, 3.10 (q, 6H),3.50 (m, 4H), 3.87 (m, 1H), 3.94 (m,

1H), 4.07−4.10 (m, 1H), 4.07−4.14 (m, 1H), 4.35 (m, 1H), 4.39 (m, 4H), 4.40 (m, 1H), 4.48 (m, 1H), 4.52 (m, 1H), 4.94 (d, 2H), 5.28 (m, 4H), 5.29 (m, 1H), 5.43 (m, 1H), 5.45 (dd, 1H, H-1), 5.46 (m, 1H), 6.90 (d, $J_{H,P}$ = 642 Hz, 1H); ^{13}C NMR δ −8.00 and 45.50 (TEA ion), 5.75, 17.95, 25.57, 20.48−20.79, 60.06, 60.42, 62.22, 62.63, 66.55, 67.46, 68.27, 68.64, 69.37, 69.66, 69.84, 70.14, 70.75, 70.88, 71.20, 73.31, 73.76, 74.24, 77.15, 78.95, 90.41, 91.69, 101.08, 101.29, 168−171; ^{31}P NMR δ δ −2.90 (dt, J_{PH} = 7.5, 10 Hz); ESMS *m*/*z* 1427.9 (M − Et_3N − H); HRMS (ESMS) calcd for (M − Et_3N − H)$^-$ $C_{54}H_{81}O_{38}P_2Si$ 1427.3650, found 1427.3770.

Solid-Phase Phosphoglycan Synthesis. Synthesis of Solid-Phase Linker (4-(4,4′-Dimethoxytrityl)-*cis*-2-butenol). To a solution of commercially available *cis*-butene-1,4-diol (**13**, 4.7 mL, 5 g, 56.7 mmol) in anhyd pyridine (100 mL) at 0 °C was added 4,4′-dimethoxytrityl chloride (6.4 g, 18.9 mmol). The reaction mixture was gradually brought to rt over 3 h and stirred for an additional 12 h. Ethyl acetate (200 mL) was added, and the organic phase was washed with water (150 mL), saturated aq $NaHCO_3$ (200 mL), saturated aq NaCl (200 mL), and water (150 mL). The organic layer was dried (Na_2SO_4) and concentrated. The crude product was purified by silica column chromatography (20% ethyl acetate in hexane with 1% Et_3N) to afford **14** (4.2 g, 80%): R_f = 0.3 in 50% ethyl acetate in hexane; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.03 (s, 1H), 3.68 (d, *J* = 4.8 Hz, 2H), 3.78 (s, 6H), 4.03 (d, *J* = 5.4 Hz, 2H), 5.73−5.75 (m, 2H), 6.82 (tt, *J* = 1.2, 9.0 Hz, 4H), 7.25−7.44 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 55.12, 55.13, 58.75, 59.93, 113.05, 126.68, 127.76, 127.99, 128.95, 129.87, 130.92, 136.07, 144.79, 158.37; ESMS *m*/*z* 413.39 (M + Na)$^+$.

Preparation of Allyloxy-Linker Functionalized Resin. 4-(4,4′-Dimethoxytrityl)-2-*cis*-butenol (**14**, 1 g, 2.56 mmol) was dissolved in anhyd DMF (8 mL). Upon cooling to 0 °C, sodium hydride (60% dispersion in mineral oil, 150 mg, 3.75 mmol) was added and the solution was stirred for 1 h. Merrifield's resin (650 mg, chloromethylated polystyrene cross-linked with 1% divinylbenzene, Fluka-63865) was added along with tetrabutylammonium iodide (95 mg, 0.256 mmol), and shaking was continued for an additional 1 h at 0 °C, after which time the reaction mixture was brought to rt and shaken for 12 h. The capping of unreacted sites on resin was accomplished by addition of CH_3OH (100 μL) and sodium hydride (100 mg) and shaking the contents for another 4 h, after which time more CH_3OH (5 mL) was added and the resin was washed sequentially with 1:1 CH_3OH/DMF (10 mL), THF (10 mL × 3), and CH_2Cl_2 (10 mL × 3). The resin was dried over P_2O_5 under vacuum to afford 836 mg of the linker-attached resin.

To quantify loading of linker onto the solid support, a stock solution of 3% TFA in CH_2Cl_2 (10 mL) was prepared which contained effectively 0.167 mg of the protected resin. The resulting orange color formed by release of dimethoxytrityl (DMTr) cation was measured by UV at 503 nm, and the loading of the linker onto the resin was calculated to be 0.43 mmol/g of resin.

The deprotection of the entire DMT-linker functionalized resin was then carried out by treating the resin with 3% TFA in CH_2Cl_2 (10 mL). Further washing with CH_2Cl_2 (20 mL × 3), 1% Et_3N in CH_2Cl_2 (10 mL), and CH_2Cl_2 (10 mL) and drying under vacuum afforded 640 mg of deprotected resin ready for coupling with phosphoglycan donors.

Coupling of Phosphoglycan to Solid Phase and Regioselective Cleavage. Allyloxy-functionalized resin (50 mg, 0.43 mmol/g, 0.021 mmol) was swollen in anhyd pyridine (100 μL) for 15 min, followed by addition of phosphoglycan H-phosphonate donor **5** (26 mg, 0.03 mmol) dissolved in anhyd pyridine (500 μL). Then pivaloyl chloride (20 μL) was added, and the resin mixture was shaken for 2 h. Thereafter, a 200 μL solution of iodine (4 mg) in 95% aqueous pyridine was added and stirring continued for another 1 h. The resin was then thoroughly washed with CH_3OH (700 μL × 3) and dried over P_2O_5 overnight to afford PG-linked resin (50 mg). The coupled PG intermediate was characterized by positive-ion ESMS after cleaving it off from the resin (20 mg) by treatment with 0.1 N HCl (100 μL) at 100 °C for 1 min. The product cleaved under this condition was characterized as 2,3,6-tri-*O*-acetyl-4-*O*-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl-α-D-mannopyranose, which was identical to compound **4**, already synthesized by solution method described earlier: ESMS *m*/*z* 731.3 (M + Na)$^+$. This compound, on full deprotection with 48% aq HF−CH_3CN (5:95) and MeOH−H_2O−Et_3N (5:2:1), provided known disaccharide Gal1-4β-Man (**15**, 2.5 mg, 93% yield): ^{1}H NMR δ 5.12 (d, *J* = 1.67 Hz, 1H), 4.85 (d, 1H, *J* = 0.98 Hz, 1H), 4.40−4.36 (m, 2H), 3.75 (dd, 1H), 3.94−3.92 (m, 2H), 3.89−3.83 (m, 2H), 3.81−3.79 (dd, 1H, *J* = 6, 2 Hz, 1H), 3.75−3.71 (m, 2H), 3.63−3.59 (dd, 1H), 3.51−3.46 (m, 2H, H-5); ESMS *m*/*z* 341.0 [M − H]$^-$.

To a part of the PG-loaded resin (15 mg) was added 48% aq HF−CH_3CN (5:95, 500 μL) at 0 °C, and the mixture was stirred on a orbital shaker for 3 h. The resin was then washed with CH_3OH (500 μL × 2) and dried under vacuum to afford acceptor-bound resin with free 6′ hydroxyl groups. This intermediate was again characterized by ESMS after cleaving it off from a small part of the resin (2 mg) by treatment with 0.1 N HCl (100 μL) at 100 °C for 1 min. The product that got cleaved under this condition was characterized as 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-α-D-mannopyranose. The authenticity of this compound was confirmed by its comparison (TLC, NMR, ESMS) with standard separately prepared via solution synthesis by deprotection (HF−CH_3CN) of TBDMS group from compound **4** (Scheme 1).

Selective cleavage of phosphoglycans from the resin was accomplished by taking the PG-loaded resin (50 mg) and Wilkinson's catalyst (2 mg) in argon-purged solvent mixture (1 mL, toluene−PrOH−H_2O, 2:1:0.08 containing 0.01 N HCl) and shaking it for 24 h at rt. Cleavage after the first cycle of coupling provided 2,3,6-tri-*O*-acetyl-4-*O*-[2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl]-α-D-mannopyranosyl phosphate, which was directly subjected to full deprotection in two steps. First, it was treated with 48% HF in CH_3CN (5:95, 1.5 mL) at 0 °C for 2 h, diluted with $CHCl_3$, washed with aq bicarbonate solution, and concentrated. Then it was dissolved in a mixture of CH_3OH−H_2O−Et_3N (5:2:1, 2 mL) and the solution stirred for 48 h and concentrated. The product was purified on a small silica column using 10% CH_3OH in $CHCl_3$ containing 1% triethylamine to give the known β-D-galactopyranosyl-α-D-mannopyranosyl phosphate (**16**, 8.3 mg, 95%), identified by comparison with the authentic sample prepared[18] by us: $[\alpha]_D$ = +10 (*c* 0.1, H_2O); ^{1}H NMR (D_2O, assignments by 2D COSY and TOCSY experiments) δ 3.45 (dd, *J* = 6.67, 1.5 Hz, 1H), 3.46 (m, 1H), 3.60 (m, 1H), 3.53−3.56 (m, 2H), 3.68 (m, 2H), 3.76 (t, *J* = 7.11, 2.64 Hz, 1H), 3.83 (m, 2H), 3.83 (m, 1H), 3.94 (m, 1H), 4.38 (d, *J* = 9.65 Hz, 1H), 4.38 (d, *J* = 7.6 Hz, 1H), 5.27 (dd, J_{1H-P} = 6.8 Hz, $J_{1,2}$ = 1.9 Hz, 1H); ^{31}P NMR δ −2.07; ESMS 421.2 [M − 1H]$^-$; HRMS (ESMS) calcd for [M − H]$^-$ $C_{12}H_{22}O_{14}P$ 421.2720, found 421.2718.

Iterative Solid-Phase Synthesis of Phosphoglycans. (1) First Coupling Cycle. Allyloxy-linker functionalized resin (300 mg, 0.43 mmol/g, 0.126 mmol) was swelled in anhyd pyridine (500 μL) for 15 min, followed by the addition of the H-phosphonate donor **5** (150 mg, 0.172 mmol) dissolved in anhyd pyridine (500 μL) and pivaloyl chloride (80 μL). The resin was shaken for 2 h followed by addition of 800 μL of iodine solution (16 mg) in 95% aq pyridine with stirring continued for another 1 h. Next the resin was thoroughly washed with CH_3OH (1 mL × 3) and dried over P_2O_5 overnight. For removal of the TBS group, the resin was shaken in 48% aq HF−CH_3CN (5:95, 200 μL) at 0 °C for 3 h, washed with CH_3OH (600 μL × 3), and dried under vacuum. **(2) Second Coupling Cycle.** The first PG-bound resin was swelled in anhyd pyridine (500 μL) for 15 min, followed by the addition of the same H-phosphonate donor **5** (150 mg, 0.172 mmol) in anhyd pyridine and pivaloyl chloride (80 μL), and shaking was continued for 2 h. Thereafter, 800 μL of iodine solution as

described above was added with stirring for another 1 h. The resin was thoroughly washed with CH_3OH (500 μL × 3), dried over P_2O_5, and treated with 200 μL of 48% aq HF−CH_3CN (5:95) at 0 °C for 3 h for removal of the TBS group, centrifuged, and washed with CH_3OH (500 μL × 3). **(3) Third Coupling Cycle.** A portion of the above TBS-deprotected resin (200 mg) with free 6′ hydroxyl groups was swelled in anhyd pyridine for 15 min, followed by the addition of H-phosphonate donor **5** (100 mg) and pivaloyl chloride (3 μL). The resin was shaken for 2 h after which time 400 μL of iodine solution was added, shaking was continued for another 1 h, and the solution was washed with CH_3OH and dried over P_2O_5 to afford the phosphohexasaccharide-bound resin. **(4) Cleavage from Solid Support.** A part of the above resin (30 mg) and Wilkinson's catalyst (1 mg) were taken in argon-purged solvent mixture (600 μL, toluene−PrOH−H_2O, 2:1:0.08 containing 0.01 N HCl) and shaken for 7 h at rt. The catalyst and resin were filtered off, and the mixture was concentrated, followed by treatment with 500 μL 48% aq HF−CH_3CN (5:95, 200 μL) at 0 °C for 3 h and 1 mL $CH_3OH/H_2O/Et_3N$, 5:2:1) for 48 h for global deprotection of the phosphohexasaccharide (**17**, 10.3 mg, 70% yield over three coupling cycles) which was characterized by ^{1}H, ^{31}P NMR and negative-ion ESMS analysis and by comparison with standards prepared by the solution method: ^{1}H NMR (D_2O, due to oligomeric nature of the molecule with three identical PG repeats, NMR peaks assignments were not possible) δ 1.30 (t, 9H), 3.00 (q, 6H), 3.45 (m, 3H), 3.46 (m, 2H), 3.55 (m, 1H), 3.56−3.53 (m, 3H), 3.60 (m, 3H), 3.68 (m, 6H), 3.76 (m, 3H), 3.80 (m, 6H), 3.83 (m, 3H), 3.85 (m, 1H), 3.94 (m, 2H), 4.0 (m, 3H), 5.57 (d, 3H), 5.09 (brd, 1H), 5.29 (m, 3H); ^{31}P NMR δ −1.29; ESMS for $C_{36}H_{62}O_{40}P_3$ calcd 1227.2030, found 1227.30 for (M − Et_3N − H)$^-$, 613.60 for (M − Et_3N − 2H)$^{2-}$, and 409.10 for (M − Et_3N − 3H)$^{3-}$.

Synthesis of Phosphoglycans by Polycondensation. Triethylammonium 2,3,6-Tri-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-*β*-D-galactopyranosyl)-α-D-mannopyranosyl Hydrogen Phosphonate (18). Compound **5** (30 mg, 0.034 mmol) was dissolved in a mixture of acetic acid−water−THF (3:1:1, 2.5 mL). The mixture was stirred at 40 °C for 9 h, after which time the solvent was evaporated off under vacuum at rt. To remove excess of acid, water (1 mL) was added and evaporated off twice to afford **18** in quantitative yield: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.30 (t, 9H), 1.95−2.09 (m, 21H), 3.00 (q, 6H), 3.49−3.68 (m, 4H), 3.88 (m, 1H), 4.14 (m, 1H), 4.36 (d, J = 4.5 Hz, 1H), 4.47 (d, J = 7.8 Hz, 1H), 4.95 (dd, J = 3.3, 7.8 Hz, 1H), 5.05 (dd, J = 2.1, 7.8 Hz, 1H), 5.21 (dd, J = 2.1, 3.6 Hz, 1H), 5.41 (d, J = 3.3 Hz, 1H), 5.48 (dd, J = 2.1, 7.8 Hz, 1H), 7.99 (d, $J_{H,P}$ = 637.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 8.40 and 45 (TEA ion), 20.48−20.76, 60.10, 62.42, 66.57, 69.36, 69.53, 69.69, 71.20, 73.30, 73.86, 91.59, 92.54, 101.9, 169.13−170.49; ^{31}P ($CDCl_3$) δ 0.22; ESMS *m/z* 657.3 (M − Et_3N − H)$^-$; HRMS (ESMS) calcd for [M − H]$^-$ $C_{24}H_{34}O_{19}P$ 657.1432, found 657.1440

Polycondensation. The bifunctional intermediate compound **18** (25 mg, 0.033 mmol) was dissolved in dry pyridine (500 μL) and the solvent evaporated under high vacuum. This procedure was repeated three times to remove traces of residual moisture The dried compound was dissolved in a mixture of anhyd pyridine and triethylamine (10:1, 40 μL), followed by dropwise addition of pivaloyl chloride (9 μL, 0.073 mmol). After 30 min, a fresh lot of pivaloyl chloride (6 μL, 0.048 mmol) was added. The reaction mixture was stirred at rt for 3 h, a freshly prepared iodine solution (220 μL, 35 mg, 0.137 mmol in pyridine−water, 95:5) was added, and stirring was continued for another 2 h. Next the reaction was quenched by addition of $CHCl_3$, and the organic layer washed with ice-cold solutions of $Na_2S_2O_3$ (1 M) and TEAB buffer, dried over Na_2SO_4, and concentrated under high vacuum. For final deprotection, above product was dissolved in 0.1 M NaOMe solution in CH_3OH (440 μL), 1,4-dioxane (800 μL), and $CHCl_3$ (800 μL). The mixture was stirred at rt for 7 h, left at 4 °C for 16 h, diluted with CH_3OH, deionized by addition of Dowex 50W-X4 (H^+) resin, filtered, and neutralized with drops of triethylamine. The mixture was further purified by anion-exchange chromatography to provide fully deprotected polymeric phosphoglycans (**19**, 9 mg, 58%): ^{1}H NMR (D_2O) δ 1.30 (t, 9H), 3.00 (q, 6H), 3.45 (m), 3.46 (m), 3.55 (m), 3.56−3.53 (m), 3.60 (m), 3.68 (m), 3.76 (m), 3.80 (m), 3.83 (m), 3.85 (m), 3.94 (m), 4.32 (m), 4.37 (m), 4.5 (m), 5.09 (m), 5.30 (m); ^{31}P NMR δ −1.73, 0.88; ESMS (after MaxEnt deconvolution of multiply changed ions) *m/z* 7238 (18 repeats), 7640 (19 repeats), 8043 (20 repeats), 8446 (21 repeats), 8849 (22 repeats).

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for new compounds **2**−**12**, **14**, **17**, and **18**, and a ^{31}P NMR spectrum and MS data for polycondensation product **19**. This material is available free of charge via the Internet at http://pubs.acs.org.

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