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Synthesis of a series of maltotriose phosphates with an evaluation of the utility of a fluorous phosphate protecting group

Lin Liu [a], Nicola L. B. Pohl [a,b,*]

[a] Department of Chemistry, Department of Chemical and Biological Engineering, and the Plant Sciences Institute, Hach Hall, Iowa State University, Ames, IA 50011-3111, USA
[b] Department of Chemistry, Simon Hall, Indiana University, Bloomington, IN 47405, USA

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ABSTRACT

A series of methyl maltotrioside phosphates were synthesized for application in the determination of the actual molecular substrate of the Lafora enzyme involved in Lafora disease. Several different synthetic routes were applied for the successful synthesis of six methyl maltotrioside phosphate regioisomers. The utility of a new fluorous phosphate protecting group was also evaluated, but its utility was found to be limited in this particular late stage introduction.

1. Introduction

α-Glucans, including starch and glycogen, are important in biological systems functioning as energy storage.[1] A series of specific enzymes are involved in the synthesis of these glucan polymers and determine their structures and properties.[2] Mistakes in this polymer biosynthesis can lead to problems such as Lafora disease,[3] or Lafora progressive myoclonic epilepsy—a fatal disease with no known cure or treatment.[4] Hyperphosphorylation of glycogen is the cause of Lafora disease and it is related to mutations in the genes that code for the protein laforin. In the synthesis of glycogen, phosphates are added to the 2- or 3-position hydroxyls of glucose at a rate of one phosphate per every 10,000 glucose residues.[5,6] Laforin should remove those phosphate groups subsequently.[7] However, with the mutated laforin, this dephosphorylation reaction cannot take place and eventually Lafora disease sets in.[8,9] To date, the actual molecular mechanism of the laforin enzyme is still unknown. In order to gain a detailed understanding of enzyme function, especially its positional requirements for phosphorylation of a glucose residue, molecules with well-defined chemical structures were needed as substrates. To this end, a series of maltotriose analogs with phosphate groups at one of either the 2- or 3-position hydroxyl was designed and synthesized as substrates for the dephosphorylation enzyme (Fig. 1).

Although the synthesis of α-glucans has been extensively studied and reviewed,[10] the synthesis of maltose analogs with phosphate at the 2-or 3-hydroxyl of a sugar ring remains relatively understudied. The desired 1,4-α-glycosidic linkage generally requires non-participating protecting groups at the 2-position of the donor, which would need to be cleaved selectively later to install the phosphate at the 2-position. The temporary protecting group at the 3-position should also be chosen carefully, since the protecting group could also affect the glycosylation reaction itself.

Ideally, the synthesis could be achieved via a set of orthogonal protecting groups, preferably using six protecting groups that could be cleaved under conditions that do not affect any of the other groups. This would allow us to synthesize the six desired compounds from a single precursor, thus greatly simplifying the synthesis. However, the limited choice of non-participating protecting groups is a major challenge of that task when material is needed in a short time frame. The other difficulty in using orthogonal protecting groups is the lack of convenient methods to selectively install an ether protecting group at the 2-position. In thinking about an efficient strategy to form all six desired regioisomers under these constrains, we also considered the possible use of our recently developed fluorous protecting group for phosphate groups.[11] This group can easily be added to a phosphate and then be used as a tag to separate the sugar chain from other reagents using fluorous solid-phase extraction (FSPE).[12,13] In our previous work, this approach was used for the synthesis of a disaccharide from *Leishmania* and had the advantage of easy purification and deprotection under mild conditions. However, in the current

* Corresponding author.
E-mail address: npohl@indiana.edu (N.L.B. Pohl).

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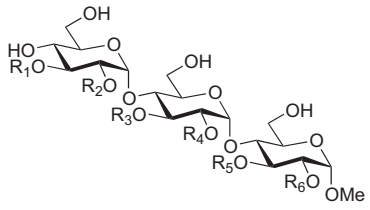


Figure 1. Six methyl maltotrioside phosphates as potential substrates for the laforin protein involved in Lafora disease.

case, it was unclear whether, first, introduction of the group so close to the anomeric center might negatively affect the glycosylation and, second, whether a relatively late stage introduction of the fluorous group would actually significantly facilitate the synthesis of the various methyl maltotrioside phosphate regioisomers. In many cases of the synthesis of a phosphate bearing compound, the phosphate group is installed in the last few steps.[14] We reasoned that if the purification of the non-fluorous phosphate group-bearing compound was problematic, it might be still useful to perform a late stage fluorous phosphate installation; otherwise the practicality of such a late stage installation would be questionable. As opposed to a late stage installation strategy, the other possibility is to perform an early stage installation of the fluorous phosphate group and to then carry the fluorous group throughout the synthesis. In this way, the fluorous group functions as a tag. In the previous cases of fluorous tag-assisted synthesis, most tags were attached at the anomeric position of the reducing end of the oligosaccharide, so the tag is remote from the reaction center. In the synthesis of the desired maltose phosphates, however, the fluorous phosphate group would inevitably be closer to the reaction site. Although fluorous groups could be used as a convenient method of purification, if the stereoselectivity is not ideal in the synthesis of the α-glycosidic linkage, it might be difficult to separate the α/β mixture, thus diminishing the usefulness of the fluorous-assisted synthesis. Since our initial report, Van der Marel reported another fluorous phosphate protecting group earlier this year to be used in the synthesis of carbohydrates.[15] The reaction utilized in their study did not involve the glycosidic bond formation, so the fluorous tag proved to be very efficient in their synthesis. Herein we probe how the fluorous tag would perform in a situation when the selectivity of the reaction might not be ideal, but in which normal chromatography could then be used for that particular step alone.

2. Results and discussion

The desired six methyl maltotrioside phosphates (Fig. 1) can be broken into three categories depending on the position of the phosphate group: phosphates at the reducing end, phosphates at the non-reducing end, and phosphates in the middle saccharides. We started the synthesis of the analogs with phosphates at the reducing end. In this case, the temporary protecting group for future installation of phosphates only exists in the acceptor, simplifying the glycosylation reaction.

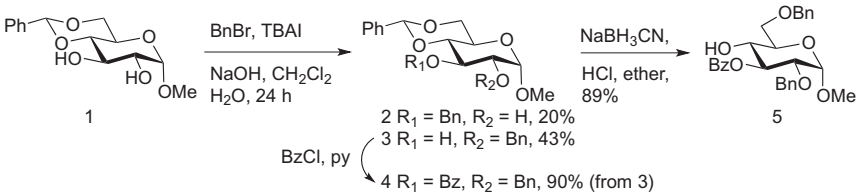
Initially, a *p*-methoxybenzyl (PMB) group was chosen as the temporary protecting group on the reducing end. However, although the survival of PMB groups under HCl/ether/$NaBH_3CN$ conditions used for selective benzylidene opening has been reported,[16] we experienced extensive decomposition in the benzylidene opening reactions using either TfOH/Et_3SiH[17] or $NaBH_3CN$/HCl[18] conditions. A milder condition using DIBALH in CH_2Cl_2[19] only resulted in modest yields of the desired product.

To circumvent this problem, we attempted to use benzoyl groups instead of the acid-labile PMB groups as the temporary protecting group at the reducing end of maltotriose. Known acceptor **5**[20] was synthesized by a modified route (Scheme 1).

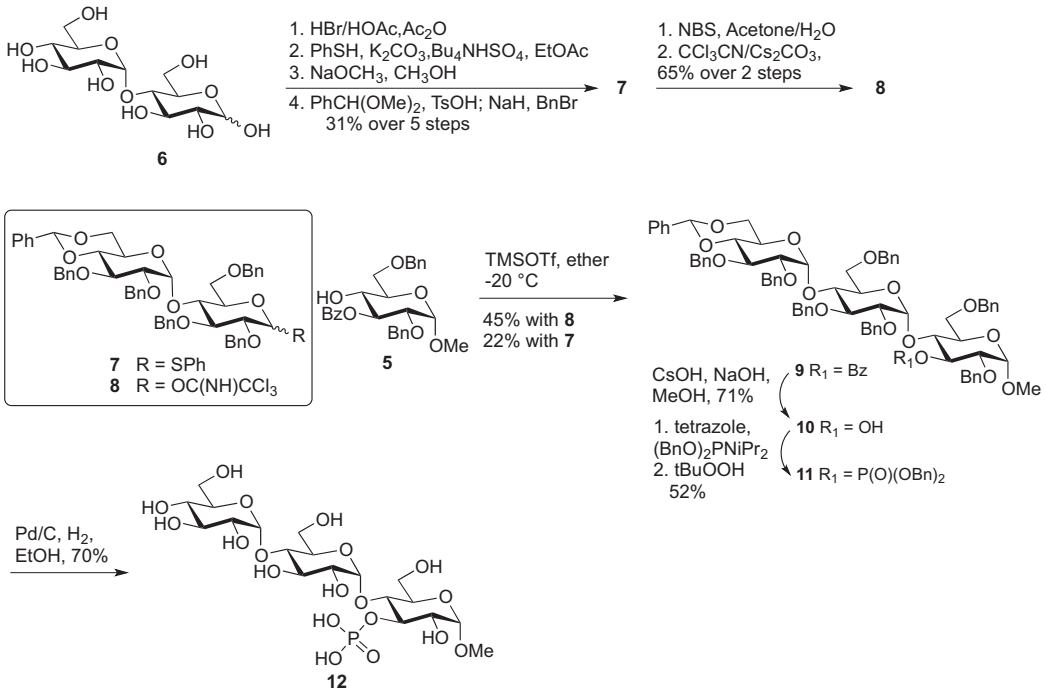
When designing the maltose donor, we decide to use the benzylidene-protected donors. The perbenzylated donors sometimes proved too armed and will decompose too quickly upon treatment of promoter. Also, the solubility of the benzylidene-protected donors is generally better than perbenzylated donors in relatively more polar solvents like ether. The maltose disaccharide donors **7** and **8** (Scheme 2) were synthesized with modifications on the known procedure starting from maltose **6**. One pot acetylation and bromination of maltose afforded the maltose bromide, which was converted to a thioglycoside under phase-transfer conditions.[21] Deacetylation, followed by benzylidene acetal formation and benzylation yielded the previously reported fully protected maltose thioglycoside donor **7**.[22]

The glycosylation reaction was performed using the thioglycoside donor **7** first (Scheme 2). In the presence of NIS and TMSOTf at 0 °C in ether/dichloromethane (1:1), the reaction proceeded well to give a mixture of α/β glycosides in the ratio of 2:3, and the α glycoside was separated using silica gel chromatography in a 22% isolated yield. To try to improve the stereoselectivity of this glycosylation reaction, we carried out the glycosylation of benzoylated acceptors with maltose imidate donors **8** in light of Motawia's work on the 'blockwise three-stage glycosylation strategy'[23] by converting the thiophenyl group to a trichloroacetimidate using standard chemistry. In this case, in a mixture of ether/dichloromethane, the glycosylation between the imidate donor and the acceptor gave the desired α product **9** in 45% yield with no β anomer detected.

To remove the 3-position benzoyl group in trisaccharide **9** for installation of the phosphate, various conditions were screened. Interestingly, routine conditions, including using sodium methoxide in methanol or using NaOH in water/THF could only remove the benzoyl group slowly to give **10**, probably due to steric hindrance. However, a combination of cesium hydroxide and sodium hydroxide together could speed up the reaction greatly and provide a better result for the deprotection of the benzoyl ester, possibly due to the cesium effect.[21] Proton NMR was used to determine when the deprotection reaction had finished. The doublet peak from the benzoyl group moves slightly down field, indicating



Scheme 1. The synthesis of benzoyl-protected reducing end building block of methyl maltotriose and the benzylidene acetal opening reaction.

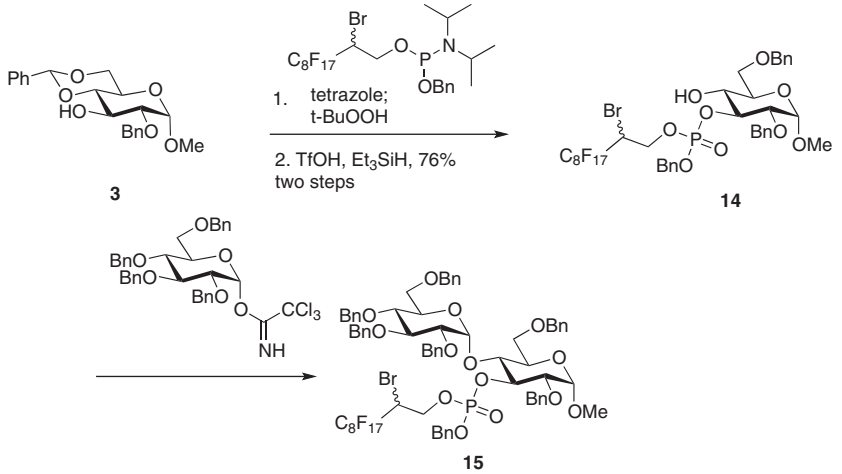


Scheme 2. Synthesis of the 3-position phosphorylated methyl maltotrioside via a benzoyl-protected acceptor.

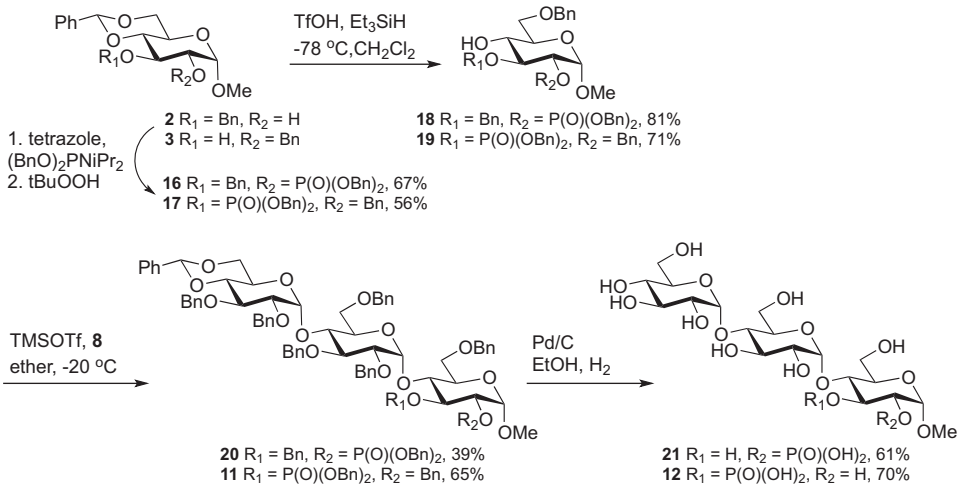
the formation of benzoic acid. We envisioned that if there would be any problem in the purification of trisaccharide **11**, the fluorous phosphate protecting group would be beneficial. After the benzoyl deprotection, a phosphate group was installed on the resulting hydroxyl moiety using standard phosphoramidite chemistry[24] to yield **11**, followed by hydrogenolysis to provide the desired phosphate **12**. No problems were encountered in the purification of trisaccharide **11**—a finding that eliminates the need for installing a fluorous phosphate group at this late stage.

Although late stage installation of the fluorous phosphate group was not required for synthetic ease in this particular case, an early stage installation could still be useful. Van der Marel recently reported the synthesis of teichoic acids using a fluorous phosphate group.[15] In their synthesis, the fluorous protecting group is far away from the reaction center, and no glycosylation was involved in the synthesis. However, remote electron-withdrawing effects and certainly neighboring protecting groups can readily affect glycosylation outcomes. The size of the fluorous protecting group and the change of the molecule's polarity due to the attachment of the fluorous portion might influence the reaction and the subsequent separation in a reaction that can give product mixtures such as many glycosylation reactions. Not many reports focus on the situation when the reaction would lead to a mixture; however, if the fluorous protecting group-modified product is inseparable from undesired products by any means, a fluorous assisted-synthesis would not prove efficient or practical.

Alcohol **3** was chosen as a model compound to test the early stage installation of the fluorous phosphate protecting group (Scheme 3). Compound **3** was coupled with the fluorous phosphoramidate **13** followed by selective benzylidene-acetal opening to provide glycosyl acceptor **14**. However, the glycosylation between **14** and the perbenzylated donor **12** gave an inseparable α/β mixture in low yield. In our synthesis of the *Leishmania* saccharide, we also witnessed a phenomenon with a change of stereochemical



Scheme 3. Early stage introduction of the fluorous phosphate protecting group.



Scheme 4. Synthesis of methyl maltotrioside phosphates using phosphorylated acceptors.

outcomes. These results showed that even though fluorous protecting groups and tags can provide a convenient way of purification, tags too closely attached to the sugar building block itself can lead to subtle changes in the reaction that might render its usage impractical.

Since using benzoyl as a temporary protecting group worked well, and the early stage installation of the fluorous phosphate group leads to a mixture, we wanted to further examine the possibility of using phosphorylated acceptors directly. In this way, the protection/deprotection could be omitted by using phosphate directly as the protecting group. The free hydroxyl in compounds **2** or **3** was directly protected as dibenzyl phosphates to give **16** or **17** (Scheme 4). The benzylidene acetal was opened smoothly to provide the phosphorylated acceptor **18** or **19**. The glycosylation reaction between donor **8** and acceptor **18** or **19** in ether at −20 °C also resulted in an anomeric mixture of products, but this mixture was readily separable to isolate methyl maltotriose phosphate isomers in an α/β ratio of 3:1. Hydrogenolysis of **20** or **11** gave the desired compound **21** or **12**, respectively (Scheme 4).

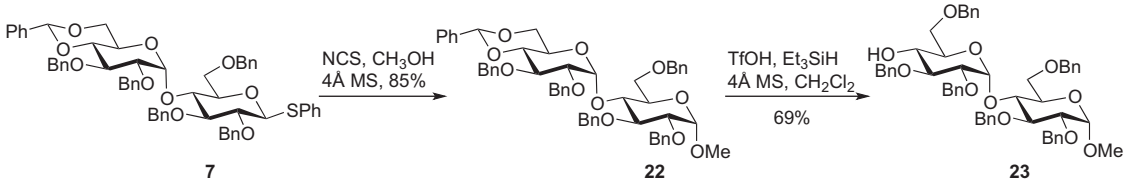
Encouraged by these results, we moved to synthesize the maltotriose with a phosphate at the non-reducing end. To prepare the maltose acceptor, the thiophenyl group on the maltose donor **7** was converted to an α-methoxy group by reacting with methanol in the presence of *N*-chlorosuccinimide (Scheme 5).[22,25] It was found that the formation of methyl glycoside **22** required the presence of molecular sieves, otherwise large amounts of a side product, presumably the NHS-substituted maltoside, would be formed. We also found that using freshly recrystallized NCS would slow the reaction down; the un-recrystallized NCS gave much better results. Selective opening of the benzylidene acetal using TfOH/Et_3SiH afforded the acceptor **23** with a free hydroxyl group at the 4-position (Scheme 5).

To obtain the desired α-linkage, a PMB-substituted donor was used. Donors **27** and **28** with the desired protecting group patterns were synthesized following the route shown in Scheme 6. Glycosylation using the thioglycoside donor **27** and maltose acceptor **23** was studied under different conditions. Using Tf_2O/PhS_2O/TTBP at −78 °C failed to give the desired glycosylation product **29**, and using NIS/TfOH as the promoter at −45 °C led to an inseparable mixture of α/β products in the ratio of 2:1. Changing the donor from thioglycoside to imidate did not improve the stereoselectivity of the glycosylation reaction. Fortunately the mixture became separable after the cleavage of the PMB group. It was found that the deprotection of PMB on **29** using ceric ammonium nitrate (CAN) gave a much cleaner reaction than using DDQ; however, if the reaction using CAN took too long, the acidic conditions could cleave the benzylidene. The desired α-linked product **31** was phosphorylated to give **33**, and hydrogenolysis gave the desired final product **35**. Compound **36** was then synthesized via an analogous route (Scheme 7).

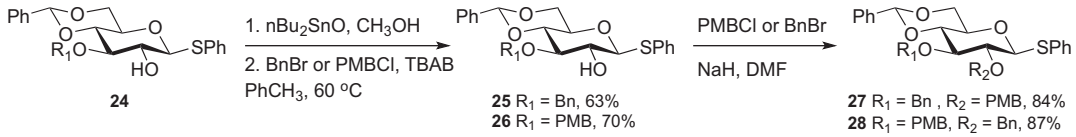
For the maltotriose with phosphates on the middle saccharide, we surveyed the methods that could potentially lead to selective protection and differentiation of hydroxyls on maltose, in the hope of finding an easier way of installing the phosphates. However, the selective protection of hydroxyls on disaccharides is far from developed, so we decided to synthesize the desired maltotriose via two glycosylation reactions.

The glycosylation between the donor **27** with a PMB group at the 2-position and acceptor **37** gave an inseparable mixture of α/β stereoisomers in the ratio of 3:1 (Scheme 8). As in the case of the previous trisaccharide, the mixture became separable after PMB cleavage. The free hydroxyl in **40** was phosphorylated to give disaccharide **42**, followed by selective benzylidene acetal opening to provide disaccharide acceptor **44**. The glycosylation between acceptor **44** and donor **44** in ether gave the desired methyl maltotrioside 2′-phosphate **47**, followed by hydrogenolysis to give **49**. The methyl maltotrioside 3′-phosphate **50** was synthesized in a similar straightforward fashion to successfully provide the last of the desired phosphate regioisomers (Scheme 8).

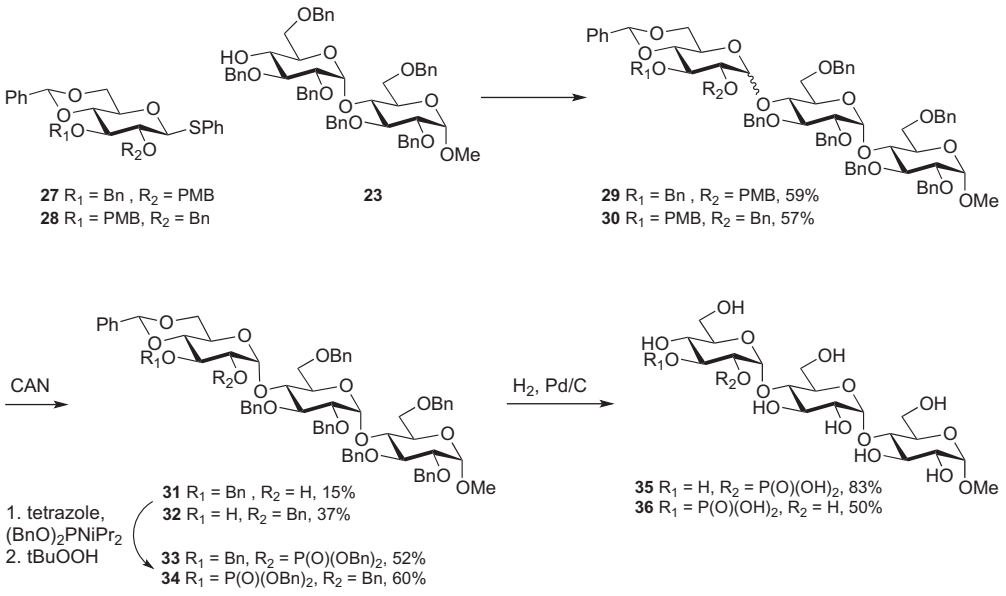
We have reported the first fluorous phosphate protecting group previously[11] and here show the limitations of using this particular protecting group in the context of the synthesis of maltotrioside



Scheme 5. Preparation of the methyl maltoside acceptor.



Scheme 6. Synthesis of the glucose donor.



Scheme 7. Synthesis of methyl maltotrioside 2″ and 3″-phosphates.

phosphate isomers. In the studies of *Leishmania*-associated carbohydrates, we reported the synthesis of a phosphorylated disaccharide utilizing our fluorous phosphate protecting group. However, our current attempts to explore the scope of this protecting group alerted us to an interesting result. In the glycosylation coupling between the donor and a per-acetylated galactose donor, a mixture of α/β isomers was formed instead of the desired β product, which was not readily separable from the mixture. Interestingly, most of the previously reported fluorous-assisted synthesis focused on fairly straightforward reactions, so the formation of a mixture with a fluorous tag is minimized. For example, in our automated solution-phase synthesis of oligosaccharides,[26,27] the fluorous tag is attached at the anomeric position of the reducing end, so the tag remains far away from the reaction site and is also mediated by a longer linker region.

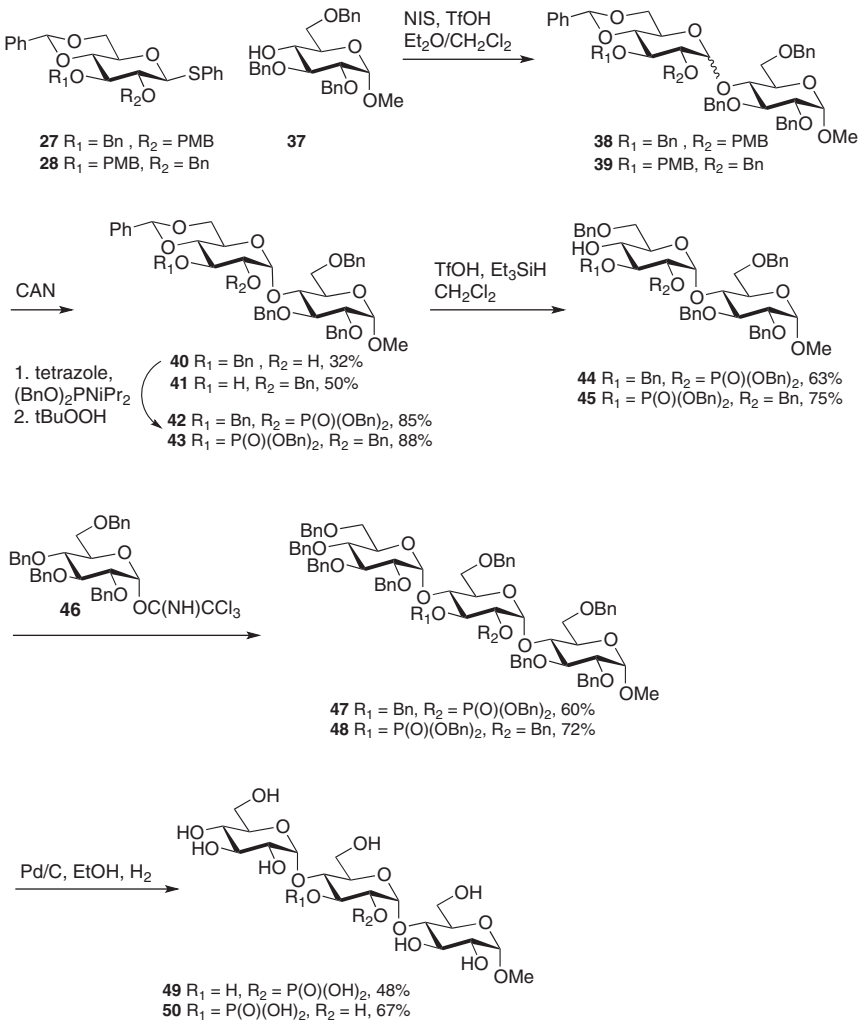
In this study, a series of methyl maltotrioside phosphate regioisomers were synthesized via a modular synthesis. Different strategies were used to introduce the phosphate groups to the maltotriose. Performing glycosylations on phosphorylated acceptors would greatly simplify the transformations needed at the trisaccharide stage. We found out that the glycosylation reactions were not affected when phosphate esters were present at either 2 or 3 position of the acceptor, so the 2-, 3-, 2′-, and 3′-phosphorylated maltotriose were synthesized using phosphorylated monosaccharides or disaccharides as acceptors. However, due to the participating nature of the phosphate group, using a pre-phosphorylated donor with a phosphate at the 2-position could not generate the desired α-glycosidic linkage. Therefore, in the synthesis of the 2″ phosphorylated maltotriose, the post-phosphorylation strategy was used.

The formation of an α-glucosidic bond is still a significant challenge when new protecting groups are introduced, as shown in the synthesis of maltotriose. Different protecting groups and glycosylations can easily alter the outcome of the glycosylations. Although fluorous tags and protecting groups can provide a convenient method of purification, this work demonstrates that the tag can introduce some subtle changes in reactions at nearby sites and provide little advantage in some cases when introduced at a late stage of a synthesis. Until better separation methods on normal phase silica gel are found for fluorous-containing compound mixtures, the fluorous protecting groups show more promise when used with sufficient distance from a reactive site. Future studies include testing of these synthetic methyl maltotrioside phosphate isomers to probe the activity of the Laforin enzyme and thereby determining the most likely in vivo substrate for this enzyme.

3. Experimental

3.1. General experimental methods

Reactions were performed using flame-dried glassware under argon using anhydrous solvents unless otherwise noted. Thin layer chromatography (TLC) was performed using glass-backed silica gel plates w/UV254. Visualization of TLC plates was performed by UV light and 5% sulfuric acid/ethanol. Silica gel flash chromatography (SGC) was performed using silica gel (60 Å, 40–63 μm) from ZEOChem AG. NMR spectra were recorded on a 400 MHz for ^{1}H (101 MHz for ^{13}C, 162 MHz for ^{31}P) spectrometer or on a 600 MHz for ^{1}H (150 MHz for ^{13}C, 243 MHz for ^{31}P). ^{1}H NMR and ^{13}C NMR taken in $CDCl_3$ spectra were referenced to the solvent peak at 7.260 ppm (^{1}H) and 77.0 ppm (^{13}C). ^{31}P NMR was not referenced. High resolution mass spectra (HRMS, ESI mode) were obtained using a Q-TOF LC/MS.



Scheme 8. Synthesis of methyl maltotrioside 2′ and 3′ phosphate.

3.2. General procedure for selective benzylidene opening reaction

The substrate (1 equiv) was dissolved in CH_2Cl_2 (0.1 M), and ASW-3000 (powder, 100 mg/mol) was added. The reaction was cooled to −78 °C, and Et_3SiH (3 equiv) was added followed by TfOH (1.5 equiv). The reaction was stirred at −78 °C until TLC indicated the conversion was complete. Methanol and Et_3N were added, and the reaction was filtered, concentrated under reduced pressure, and subject to SGC for purification.

3.3. General procedure for thioglycoside removal

The substrate (1 equiv) was dissolved in acetone/water (9:1, 0.1 M). *N*-Bromosuccinimide (NBS, 2 equiv) was added and the reaction was stirred until TLC indicated the conversion had finished. The reaction was quenched with adding solid $NaHCO_3$, concentrated under reduced pressure, diluted with EtOAc, washed with $Na_2S_2O_3$, $NaHCO_3$, brine, and dried. The resulting organic layer was concentrated under reduced pressure and the crude mixture was purified via SGC.

3.4. General procedure for PMB removal

The substrate (1 equiv) was dissolved in CH_3CN/H_2O (9:1 0.05 M), and CAN (4 equiv) was added. The reaction was stirred at ambient temperature until TLC indicated the conversion had finished. The reaction was diluted with EtOAc, washed with water and $NaHCO_3$ (aq), dried, concentrated and purified via SGC.

3.5. General procedure for glycosylation using thioglycoside donor

The acceptor (1 equiv) and donor (1.5 equiv) were co-evaporated with toluene for 3 times and dissolved in Et_2O/CH_2Cl_2 (3:1, 0.05 M). ASW-3000 (powder, 100 mg/mmol) was added, and the reaction was cooled to −78 °C. NIS (1.8 equiv) was added, and the reaction was stirred at −78 °C for 20 min then warmed up to −45 °C. TfOH (1.8 equiv) was added and the reaction was stirred at −45 °C until TLC indicated the conversion had finished. The reaction was quenched by adding Et_3N, concentrated, and purified via SGC.

3.6. General procedure for trichloroacetimidate formation

The substrate (1 equiv) was dissolved in CH_2Cl_2 (0.1 M), Cs_2CO_3 (0.5 equiv) was added, followed by CCl_3CN (3 equiv). The reaction was stirred at ambient temperature until TLC indicated the conversion was complete. The reaction was filtered through Celite, and concentrated under reduced pressure to give the crude imidate.

3.7. General procedure for glycosylation using trichloroacetimidate donor

The acceptor (1 equiv) and donor (1.5 equiv) were co-evaporated with toluene 3 times and dissolved in Et_2O (0.05 M). The reaction was cooled to −20 °C, and TMSOTf (0.1 equiv, 0.0268 M in CH_2Cl_2) was added; the reaction was stirred at −20 °C until TLC indicated the conversion was complete. The reaction was quenched by adding Et_3N, concentrated under reduced pressure, and purified via SGC.

3.8. General procedure for phosphorylation

The substrate (1 equiv) was dissolved in CH_2Cl_2 (0.1 M). Dibenzyl *N,N*-di isopropylphosphoramidite (2 equiv) was added followed by 1-H tetrazole (3 equiv, 0.45 M in CH_3CN). The reaction was stirred at ambient temperature until TLC indicated the conversion was complete. *t*-BuOOH (5 equiv, 5–6 M in decane) was added, and the reaction was stirred for 1 h. The mixture was concentrated under reduced pressure, and purified via SGC.

3.9. General procedure for global deprotection

The substrate was dissolved in EtOH, and Pd/C was added. The reaction was stirred under 800 psi of H_2 for 8 h, filtered, and concentrated to give the product.

3.10. Synthetic procedures

3.10.1. Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,6-di-*O*-benzyl-3-benzoyl-α-D-glucopyranoside (9)

Compound **7** (500 mg, 0.513 mmol) was subjected to the conditions in the general method for thiolphenol removal to give the hemiacetal (320 mg, 0.367 mmol). The hemiacetal was treated with CCl_3CN and Cs_2CO_3 as described in the general procedure for trichloroacetimidate formation to give **8** as a yellow foam (350 mg, 0.34 mmol, 67% for two steps) and used without further purification. Donor **8** (98 mg, 0.98 mmol) and acceptor **5** (28 mg, 0.058 mmol) were glycosylated using the general glycosylation method and purified via SGC (hexanes/EtOAc 3:1) to give **9** (35 mg, 0.026 mmol, 45%) as a syrup. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–7.94 (m, 2H, PhH), 7.54–7.00 (m, 43H, PhH), 5.88 (t, J = 9.58 Hz, 1H, H-3), 5.73 (d, J = 3.87 Hz, 1H, H-1′), 5.53 (s, 1H, PhCH), 4.92 (d, J = 3.24 Hz, 1H, H-1″), 4.87 (d, J = 11.20 Hz, 1H, OC*H*HPh), 4.81–4.75 (m, 2H, 2 × OC*H*HPh), 4.75–4.63 (m, 2H, 2 × OC*H*HPh), 4.63–4.53 (m, 6H, 6 × OC*H*HPh), 4.49 (d, J = 11.79 Hz, 1H, OC*H*HPh), 4.42 (dd, J = 5.65, 12.06 Hz, 2H, 2 × OC*H*HPh), 4.19 (d, J = 12.25 Hz, 1H, H-6″a), 4.16–4.05 (m, 3H, H-5, H-4″, H-6a), 4.05–3.90 (m, 5H, H-3, H-4, H-6′a, H-3″), 3.91–3.76 (m, 3H, H-5′, H-6″b), 3.72–3.70 (m, 2H, H-2″, H-4′), 3.67–3.55 (m, 3H, H-2′, H-3′, H-6′b), 3.55–3.46 (m, 2H, H-5″, H-6b), 3.43 (s, 3H, OCH_3), 3.29–3.27 (m, 1H, H-2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 138.9, 138.7, 138.1, 137.9, 137.9, 137.9, 137.7, 137.6, 132.7, 130.7, 129.8, 128.8, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.2, 128.1, 128.0, 128.0, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 127.4, 127.0, 126.5, 126.1, 101.1, 97.8, 97.7, 96.9, 82.2, 81.3, 79.7, 78.9, 78.7, 76.9, 75.5, 75.2, 73.8, 73.5, 73.4, 73.3, 73.2, 72.8, 72.4, 71.2, 70.6, 69.9, 68.7, 63.2, 55.3; HRMS (ESI) calcd for $C_{82}H_{84}O_{17}Na$ [M+Na]$^+$: 1363.5601, found 1363.5561.

3.10.2. Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,6-tri-*O*-benzyl-α-D-glucopyranoside (10)

Compound **9** (23 mg, 0.017 mmol) was dissolved in CH_3OH (3 mL). $CsOH–H_2O$ (50 mg) was added, followed by Na (23 mg). The reaction was stirred for 16 h, concentrated, extracted with EtOAc, and purified with SGC (hexanes/EtOAc 3:1) to give **10** (15 mg, 0.012 mmol, 71%) as a syrup. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61–7.04 (m, 40H, PhH), 5.69 (d, J = 3.83 Hz, 1H, H-1′), 5.55 (s, 1H, PhCH), 5.00–4.79 (m, 5H, H-1″), 4.79–4.66 (m, 4H, 4 × OCH *H*Ph), 4.66–4.52 (m, 5H, 4 × OCH *H*Ph, H-1), 4.51–4.41 (m, 2H, 2 × OCH *H*Ph), 4.35 (d, J = 11.79 Hz, 1H, OCH*H*Ph), 4.15 (dd, J = 5.23, 10.96 Hz, 1H, H-6″a), 4.12–4.03 (m, 2H, H-5, H-4″), 4.02–3.90 (m, 2H, H-3, H-4), 3.88–3.80 (m, 1H, H-5″), 3.78–3.42 (m, 10H, H-3′, H-2″, H-3″, H-4′, H-6″b, H-6a, H-2′, H-6b, H-6′a, H-6′b), 3.37 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.6, 138.6, 138.2, 137.9, 137.7, 137.6, 136.8, 128.9, 128.8, 128.6, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.2, 126.5, 126.0, 101.2, 100.4, 98.4, 97.6, 82.3, 82.1, 82.1, 80.3, 78.7, 78.7, 78.0, 77.3, 75.3, 74.3, 74.3, 74.0, 73.4, 73.3, 73.1, 71.9, 70.8, 69.0, 68.8, 68.6, 63.4, 55.2; HRMS (ESI) calcd for $C_{75}H_{80}O_{16}Na$ [M+Na]$^+$: 1259.5339, found 1259.5326.

3.10.3. Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,6-di-*O*-benzyl-3-dibenzylphosphate-α-D-glucopyranoside (11)

Compound **10** (15 mg, 0.012 mmol) was subjected to the general procedure for phosphorylation described above and purified via SGC (hexanes/EtOAc 3:2) to give **11** (9.3 mg, 0.006 mmol, 52%) as a syrup. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–6.97 (m, 50H, PhH), 5.86 (d, J = 3.45 Hz, 1H, H-1), 5.76 (d, J = 3.89 Hz, 1H, H-1″), 5.53 (s, 1H, PhCH), 5.05–4.76 (m, 9H, 9 × OC*H*HPh), 4.70 (s, 2H, 2 × OC*H*HPh), 4.68–4.60 (m, 4H, 4 × OC*H*HPh), 4.58–4.47 (m, 5H, 4 × OC*H*HPh H-1′), 4.43 (d, J = 12.19 Hz, 2H, 2 × OC*H*HPh), 4.24 (d, J = 9.54 Hz, 2H, 2 × OC*H*HPh), 4.17 (t, J = 9.07 Hz, 1H, H-4), 4.10 (dd, J = 4.68, 10.17 Hz, 1H, H-5′), 4.01 (t, J = 8.84 Hz, 1H, H-3), 3.93 (t, J = 9.27 Hz, 1H, H-3″), 3.90–3.74 (m, 4H, H-4″, H-5, H-6a, H-3′), 3.72–3.56 (m, 5H, H-6′a, H-6′b, H-6b, H-2′, H-6″a), 3.55-3.45 (m, 3H, H-2, H-2″, H-6″b), 3.28 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.7, 138.3, 138.2, 137.8, 137.6, 137.5, 136.0, 128.8, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 1281.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.4, 127.4, 127.3, 127.1, 127.0, 126.7, 126.11, 101.1, 97.4, 96.8, 93.8, 82.3, 81.9, 81.8, 81.3, 79.8, 79.1, 78.7, 78.7, 75.0, 73.8, 73.5, 73.3, 73.0, 72.3, 71.1, 70.4, 69.9, 69.8, 69.8, 69.3, 69.2, 68.9, 68.8, 68.7, 68.1, 65.4, 63.1, 55.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ −2.96; HRMS (ESI) calcd for $C_{89}H_{93}O_{19}PNa$ [M+Na]$^+$: 1519.5914, found 1519.5949.

3.10.4. Methyl α-D-glucopyranosyl-(1→4)-α-D-glucopyranosyl-(1→4)-3-phosphate-α-D-glucopyranoside (12)

Hydrogenolysis of **11** (12 mg, 0.007 mmol) according to the general method for global deprotection gave **12** (3 mg, 0.005 mmol, 71%) as a syrup. ^{1}H NMR (400 MHz, CD_3OD) δ 5.44 (d, J = 3.4 Hz, 1H, H-1′), 5.15 (d, J = 3.7 Hz,1H, H-1″), 4.69 (d, J = 4.4 Hz,1H, H-1), 4.55–4.47 (m, 1H, H-3), 3.90–3.74 (m, 5H, H-6a, H-6′a, H-6′b, H-6″a, H-6″b), 3.73–3.56 (m, 5H, H-2, H-3′, H-6b, H-4′, H-4″), 3.57–3.47 (m, 3H, H-3″, H-4, H-5), 3.42–3.34 (m, 4H, H-2′, H-5′, H-2″), 3.34–3.15 (m, 4H, OCH_3); ^{13}C NMR (101 MHz, CD_3OD) δ 101.5, 99.4, 99.1, 79.9, 78.2, 75.3, 73.6, 73.3, 72.9, 71.8, 70.7, 70.1, 61.3, 60.8, 60.7, 54.1, 46.4; ^{31}P NMR (162 MHz, CD_3OD) δ 1.57; HRMS (ESI) calcd for $C_{19}H_{34}O_{19}P$ [M−H]$^-$: 597.1437, found 597.1447.

3.10.5. Methyl 2-dibenzylphosphate-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (16)

Compound **2** (76 mg, 0.20 mmol) was subjected to the general procedure for phosphorylation described above to and purified

via SGC (hexanes/EtOAc 2:1) give **16** (85 mg, 0.134 mmol, 67%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.14 (m, 20H, PhH), 5.57 (s, 1H, PhCH), 5.04 (d, J = 7.51 Hz, 2H, OCH_2Ph), 5.02–4.94 (m, 3H, OCH_2Ph, H-1), 4.91 (d, J = 11.35 Hz, 1H, OC*H*HPh), 4.73 (d, J = 11.32 Hz, 1H, OC*H*HPh), 4.41 (ddd, J = 3.81, 7.70, 9.40 Hz, 1H, H-2), 4.30 (dd, J = 4.66, 10.12 Hz, 1H, H-6a), 4.06 (t, J = 9.28 Hz, 1H, H-3), 3.87 (td, J = 4.66, 9.90 Hz, 1H, H-5), 3.76 (t, J = 10.25 Hz, 1H, H-6b), 3.67 (t, J = 9.34 Hz, 1H, H-4), 3.37 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.2, 137.2, 135.7, 129.0, 128.5, 128.5, 128.5, 128.3, 128.2, 128.2, 127.9, 127.8, 127.7, 127.6, 126.0, 101.3, 98.6, 82.0, 82.0, 75.0, 69.4, 69.3, 69.3, 69.2, 68.9, 62.2, 55.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ −1.77; HRMS (ESI) calcd for $C_{35}H_{38}O_9P$ $[M+H]^+$: 633.2248, found 633.2244.

3.10.6. Methyl 2-*O*-benzyl-3-dibenzylphosphate-4,6-*O*-benzylidene-α-D-glucopyranoside (17)

Compound **3** (220 mg, 0.59 mmol) was subjected to the general procedure for phosphorylation described above and purified via SGC (hexanes/EtOAc 3:2) to give **17** (210 mg, 0.33 mmol, 56%) as a white foam. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73–6.95 (m, 20H, PhH), 5.52 (s, 1H, PhCH), 5.08–4.88 (m, 5H, 4 × OCH*H*Ph, H-3), 4.80 (d, J = 12.19 Hz, 1H, OCH*H*Ph), 4.73–4.55 (m, 2H, OCH*H*Ph, H-1), 4.30 (dd, J = 4.86, 10.30 Hz, 1H, H-6a), 3.90 (td, J = 4.79, 9.89 Hz, 1H, H-6b), 3.83–3.62 (m, 3H, H-4, H-2, H-5), 3.40 (s, 3H, OCH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.8, 136.9, 136.2, 136.2, 136.2, 129.2, 128.5, 128.3, 128.3, 128.3, 128.3, 128.1, 128.1, 128.0, 128.0, 127.5, 127.4, 126.4, 102.0, 99.0, 80.2, 80.2, 78.4, 78.4, 76.9, 76.9, 73.4, 69.1, 69.0, 69.0, 69.0, 69.0, 62.2, 55.4; ^{31}P NMR (243 MHz, $CDCl_3$) δ 15.82; HRMS (ESI) calcd for $C_{35}H_{38}O_9P$ $[M+H]^+$: 633.2248, found 633.2257.

3.10.7. Methyl 2-dibenzylphosphate-3,6-di-*O*-benzyl-α-D-glucopyranoside (18)

Compound **16** (104 mg, 0.165 mmol) was subjected to the conditions described in the general procedure for selective benzylidene opening and purified via SGC (hexanes/EtOAc 2:1) to give **18** (84 mg, 0.133 mmol, 81%) as a syrup. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.16 (m, 20H, PhH), 5.05 (d, J = 7.64 Hz, 2H, OCH_2Ph), 5.03–4.96 (m, 3H, OCH_2Ph, H-1), 4.87 (d, J = 11.45 Hz, 1H, OCH*H*Ph), 4.71 (d, J = 11.37 Hz, 1H, OCH*H*Ph), 4.64–4.52 (m, 2H, OCH_2Ph), 4.36 (ddd, J = 3.67, 7.22, 9.60 Hz, 1H, H-2), 3.84 (t, J = 9.14 Hz, 1H, H-3), 3.80–3.61 (m, 4H, H-4, H-6ab, H-5), 3.35 (s, 3H, OCH_3), 2.56 (d, J = 2.75 Hz, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 137.9, 135.8, 135.7, 135.6, 128.6, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 97.9, 80.2, 80.1, 77.0, 75.2, 73.6, 71.2, 71.2, 69.8, 69.6, 69.4, 69.4, 69.3, 69.2, 55.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ −1.59; HRMS (ESI) calcd for $C_{35}H_{39}O_9PNa$ $[M+Na]^+$: 657.2224, found 657.2209.

3.10.8. Methyl 2,6-di-*O*-benzyl-3-dibenzylphosphate-α-D-glucopyranoside (19)

Compound **17** (91 mg, 0.143 mmol) was subjected to the conditions described in the general procedure for selective benzylidene opening and purified via SGC (hexanes/EtOAc 3:2) to give **19** (64 mg, 0.101 mmol, 71%) as a syrup. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (m, 20H, PhH), 5.25–5.00 (m, 4H, 4 × OC*H*HPh), 4.81–4.69 (m, 3H, OC*H*HPh, H-1, H-3), 4.69–4.57 (m, 3H, 3 × OC*H*HPh), 3.88–3.72 (m, 4H, H-4, H-5, H-6a, H-6b), 3.59 (dd, J = 4.03, 10.10, Hz, 1H, H-2), 3.40 (s, 3H, OCH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.2, 137.7, 135.6, 135.6, 128.7, 128.7, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.3, 128.1, 128.0, 128.0, 128.0, 127.9, 127.6, 127.6, 127.6, 97.8, 82.0, 81.9, 73.6, 73.2, 70.3, 70.0, 70.0, 69.9, 69.8, 69.7, 68.9, 55.2; ^{31}P NMR (243 MHz, $CDCl_3$) δ 18.83; HRMS (ESI) calcd for $C_{35}H_{40}O_9P$ $[M+H]^+$: 635.2404, found 635.2411.

3.10.9. Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→4)-3-dibenzylphosphate-,6-di-*O*-benzyl-α-D-glucopyranoside (20)

Donor **8** (72 mg, 0.071 mmol) and acceptor **18** (30 mg, 0.047 mmol) were subjected to the conditions in the general method of glycosylation and purified via SGC (hexanes/EtOAc 2:1) to give **20** (27 mg, 0.018 mmol, 39%) as a syrup.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–6.85 (m, 50H, PhH), 5.65 (d, J = 3.52 Hz, 1H, H-1′), 5.50 (s, 1H, PhCH), 5.41 (d, J = 2.90 Hz, 1H, H-1″), 4.99–4.91 (m, 4H, 4 × OCH*H*Ph), 4.90–4.76 (m, 5H, 4 × OCH*H*Ph, H-1), 4.73–4.57 (m, 3H, 3x4 × OCH*H*Ph), 4.57–4.33 (m, 7H, 6x4 × OCH*H*Ph, H-2), 4.16–3.84 (m, 7H, H-4′, H-3″, H-4″, H-6″a, H-5″, H-3, H-4), 3.82−−3.74 (m, 2H, H-6″, H-5′), 3.72–3.51 (m, 5H, H-6a, H-6b, H-6′a, H-5, H-3′), 3.53–3.39 (m, 3H, H-2′, H-2″, H-6′b), 3.31 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.3, 138.1, 138.0, 137.9, 137.6, 137.6, 137.5, 137.2, 137.1, 135.3, 135.2, 135.1, 135.1, 128.4, 128.0, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 127.4, 127.4, 127.3, 127.3, 127.2, 127.2, 127.2, 127.1, 127.1, 127.1, 127.1, 127.0, 127.0, 127.0, 126.7, 126.7, 126.6, 126.3, 126.2, 126.1, 125.6, 100.7, 97.3, 97.1, 96.8, 96.3, 91.4, 81.8, 81.2, 80.2, 80.1, 79.9, 79.8, 79.1, 78.4, 78.2, 74.7, 73.5, 73.5, 73.3, 73.0, 73.0, 72.9, 72.7, 72.6, 71.5, 70.9, 70.5, 70.1, 69.4, 68.9, 68.8, 68.8, 68.7, 68.7, 68.5, 68.2, 68.0, 62.7, 54.8, 54.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ −1.74; HRMS (ESI) calcd for $C_{89}H_{93}O_{19}PNa$ $[M+Na]^+$: 1519.5914, found 1519.5934.

3.10.10. Methyl α-D-glucopyranosyl-(1→4)-α-D-glucopyranosyl-(1→4)-2-phosphate-α-D-gluco pyranoside (21)

Hydrogenation of **20** (5 mg, 0.003 mmol) according to the general method for global deprotection gave **12** (1 mg, 0.002 mmol, 61%) as a syrup. ^{1}H NMR (400 MHz, CD_3OD) δ 5.15 (s, 1H, H-1″), 5.11 (d, J = 3.14 Hz, 1H, H-1′), 4.63–4.55 (m, 1H, H-1), 4.06–3.92 (m, 2H), 3.87–3.70 (m, 7H), 3.70–3.51 (m, 5H), 3.51–3.41 (m, 2H), 3.37 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 101.5, 101.1, 97.9, 79.8, 79.5, 73.6, 73.5, 73.3, 72.8, 72.4, 72.0, 71.9, 70.6, 70.2, 70.1, 61.3, 60.7, 60.5, 54.3, 54.2; ^{31}P NMR (162 MHz, CD_3OD) δ −0.43, HRMS (ESI) calcd for $C_{19}H_{34}O_{19}P$ $[M-H]^-$: 597.1437, found 597.1433.

3.10.11. Methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (23)

Compound **22** (59 mg, 0.066 mol) was subjected to the conditions according to the general procedure for selective benzylidene opening to and purified via SGC (hexanes/EtOAc 3:1) afford **23** (41 mg, 0.046 mmol, 69%) as white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.06 (m, 30H, PhH), 5.72 (d, J = 3.59 Hz, 1H, H-1), 5.07 (d, J = 11.62 Hz, 1H, OCH*H*Ph), 4.91 (d, J = 11.29 Hz, 1H, OCH*H*Ph), 4.82 (d, J = 11.70 Hz, 1H, OCH*H*Ph), 4.77–4.68 (m, 2H, 2 × OCH*H*Ph), 4.66–4.41 (m, 7H, H-1′, 6 × OCH*H*Ph), 4.35 (d, J = 12.09 Hz, 1H, OCH*H*Ph), 4.10 (d, J = 8.80 Hz, 2H, H-3′, H-5′), 3.96–3.81 (m, 2H, H-6′a), 3.81–3.42 (m, 8H, H-6′b, H-3, H-6a, H-4, H-6b, H-2′, H-4′, H-2), 3.40 (s, 3H, OCH_3), 2.52 (d, J = 2.43 Hz, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 138.8, 138.2, 137.9, 137.9, 137.9, 128.5, 128.4, 128.3, 128.3, 128.3, 128.2, 127.9, 127.9, 127.7, 127.7, 127.7, 127.6, 127.4, 127.3, 127.1, 126.7, 97.7, 96.5, 82.0, 81.3, 80.2, 79.0, 75.3, 74.4, 73.5, 73.4, 73.2, 73.1, 72.3, 71.5, 70.5, 69.8, 69.5, 69.0, 55.2; HRMS(ESI): calcd for $C_{55}H_{61}O_{11}$ $[M+H]^+$: 897.4206, found 897.4208.

3.10.12. Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (31)

Donor **27** (19 mg, 0.033 mmol) and acceptor **23** (22 mg, 0.023 mmol) were glycosylated using the general glycosylation

method for thioglycosides to give a 3:1 α/β mixture of **29** (17.5 mg, 0.013 mmol). Compound **29** was treated with DDQ according to the conditions in the general method for PMB removal, and purified by SGC (hexanes/ethyl acetate 3:1) to give **31** (6 mg, 0.005 mmol, 15% for two steps) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64–6.95 (m, 40H, PhH), 5.69 (d, J = 3.59 Hz, 1H, H-1″), 5.54 (s, 1H, PhCH), 5.19 (d, J = 3.53 Hz, 1H, H-1′), 5.06 (dd, J = 11.33, 22.77 Hz, 2H, 2 × OCH*H*Ph), 4.84–4.66 (m, 5H, 5 × OCH*H*Ph), 4.66–4.31 (m, 11H, 10 × OCH*H*Ph, H-1), 4.13–4.02 (m, 3H, H-6″a, H-3, H-4′), 4.00–3.81 (m, 4H, H-6″b, H-4″, H-4, H-5′), 3.80–3.42 (m, 10H, H-5, H-2″, H-3″, H-6a, H-6b, H-6′a, H-6′b, H-2, H-2′), 3.39 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 137.6, 137.0, 136.9, 136.9, 136.6, 136.4, 136.4, 127.9, 127.4, 127.4, 127.3, 127.3, 127.3, 127.3, 127.2, 127.2, 127.2, 127.0, 126.9, 126.8, 126.8, 126.8, 126.7, 126.7, 126.6, 126.5, 126.5, 126.4, 126.4, 126.3, 126.1, 125.7, 125.6, 125.0, 100.1, 100.0, 96.7, 95.0, 80.9, 80.4, 79.3, 79.2, 78.8, 78.3, 74.1, 73.6, 73.4, 72.6, 72.4, 72.3, 72.2, 71.8, 71.3, 70.0, 68.6, 67.9, 67.3, 62.8, 54.2; HRMS (ESI) calcd for $C_{75}H_{80}O_{16}Na$ $[M+Na]^+$: 1259.5339, found 1559.5337.

3.10.13. Methyl 2-dibenzylphosphate-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (33)

Compound **31** (13 mg, 0.011 mmol) was subjected to the general procedure for phosphorylation described above and purified by SGC (hexanes/ethyl acetate 4:1) to give **33** (8.6 mg, 0.0055 mmol, 52%) as a syrup. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61–6.98 (m, 50H, PhH), 5.82 (d, J = 3.69 Hz, 1H, H-1″), 5.62 (d, J = 3.49 Hz, 1H, H-1′), 5.55 (s, 1H, PhCH), 5.06–4.97 (m, 2H, 2 × OCH*H*Ph), 4.97–4.80 (m, 6H, 6 × OCH*H*Ph), 4.81–4.63 (m, 6H, 6 × OCH*H*Ph), 4.63–4.37 (m, 8H, 6 × OCH*H*Ph, H-1, H-2″), 4.19–4.11 (m, 2H, H-4″, H-5″), 4.09–3.94 (m, 5H, H-3′, H-3″, H-6″a, H-5), 3.95–3.75 (m, 4H, H-3 H-4′, H-6″b, H-5′, H-4), 3.74–3.55 (m, 4H, H-2, H-6a, H-6b, H-6′a), 3.54–3.39 (m, 2H, H-2′, H-6′b), 3.37 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 138.5, 138.3, 138.1, 138.0, 137.9, 137.4, 128.9, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.2, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 127.5, 127.4, 127.4, 127.3, 127.3, 127.1, 127.0, 126.7, 126.7, 126.0, 101.2, 97.8, 96.0, 82.2, 82.0, 81.0, 80.1, 79.6, 77.2, 76.8, 74.8, 74.3, 74.0, 73.4, 73.3, 73.1, 73.0, 72.1, 71.5, 70.5, 69.5, 69.3, 68.8, 68.6, 68.6, 63.0, 55.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ −1.19; HRMS (ESI) calcd for $C_{89}H_{93}O_{19}PNa$ $[M+Na]^+$: 1519.5914, found 1519.5942.

3.10.14. Methyl 2-phosphate-α-D-glucopyranosyl-(1→4)-α-D-glucopyranosyl-(1→4)-D-glucopyranoside (35)

Compound **33** (8.6 mg, 0.0055 mmol) was subjected to the general procedure for global deprotection described above to give **35** (2.7 mg, 0.0045 mmol, 83%) as a syrup.

^{1}H NMR (400 MHz, CD_3OD) δ 5.52 (d, J = 3.50 Hz, 1H, H-1″), 5.15 (d, J = 3.20 Hz, 1H, H-1′), 4.66 (d, J = 3.20 Hz, 1H, H-1), 4.07–3.92 (m, 2H), 3.92–3.72 (m, 11H), 3.72–3.56 (m, 2H), 3.56–3.34 (m, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 101.1, 99.7, 98.7, 80.3, 74.8, 73.5, 73.2, 72.7, 72.3, 71.7, 70.8, 70.5, 61.4, 60.7, 54.2, 45.9; ^{31}P NMR (162 MHz, CD_3OD) δ 3.43; HRMS (ESI) calcd for $C_{19}H_{34}O_{19}P$ $[M-H]^-$: 597.1437, found 597.1455.

3.10.15. Methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (32)

Donor **28** (72 mg, 0.126 mmol) and acceptor **23** (63 mg, 0.078 mmol) were glycosylated using the general glycosylation method for thioglycoside to give a 3:1 α/β mixture of **30** (56 mg, 0.040 mmol, 52%). Compound **30** (22 mg, 0.016 mmol) was treated with DDQ according to the conditions in the general method for PMB removal, and purified by SGC (hexanes/EtOAc 3:1) to give **32** (8 mg, 0.006 mmol, 37%) as a syrup. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–6.82 (m, 40H, PhH), 5.68 (d, J = 3.76 Hz, 1H, H-1″), 5.55 (d, J = 3.52 Hz, 1H, H-1′), 5.41 (s, 1H, PhCH), 4.98 (d, J = 11.65 Hz, 1H, OCH*H*Ph), 4.91 (d, J = 11.78 Hz, 1H, OCH*H*Ph), 4.73 (dd, J = 9.98, 10.69 Hz, 2H, 2 × OCH*H*Ph), 4.68–4.57 (m, 1H, OCH*H*Ph), 4.57–4.45 (m, 4H, H-1), 4.45–4.26 (m, 5H, 5 × OCH*H*Ph), 4.15–3.89 (m, 6H, H-6″a, H-6″b, H-4″, H-3, H-4′, H-5), 3.90–3.64 (m, 5H, H-5′, H-2″, H-3″), 3.59–3.49 (m, 3H, H-6′a, H-6′b, H-2), 3.49–3.36 (m, 3H, H-6a, H-6b, H-2′), 3.30 (s, 3H, OCH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.8, 138.3, 138.1, 138.0, 137.8, 137.6, 137.3, 129.1, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.7, 127.5, 127.4, 127.4, 127.3, 127.1, 126.8, 126.6, 126.4, 101.8, 97.8, 96.4, 96.0, 81.9, 81.8, 81.3, 80.1, 79.7, 79.2, 74.4, 73.9, 73.4, 73.2, 72.9, 72.6, 71.4, 70.5, 70.2, 69.6, 68.9, 68.8, 68.6, 62.9, 55.2, 29.7; HRMS (ESI) calcd for $C_{75}H_{80}O_{16}Na$ $[M+Na]^+$: 1259.5339, found 1559.5332.

3.10.16. Methyl 2-*O*-benzyl-3-dibenzylphosphate-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-D-glucopyranoside (34)

Compound **32** (12 mg, 0.01 mmol) was subjected to the general procedure for phosphorylation described above and purified by SGC (hexanes/EtOAc 2:1) to give **34** (8 mg, 0.006 mmol, 60%) as a syrup. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55–7.06 (m, 50H, PhH), 5.80 (d, J = 3.80 Hz, 1H, H-1″), 5.67 (d, J = 3.48 Hz, 1H, H-1′),5.08–4.87 (m, 6H, 5 × OCH*H*Ph, H-3″), 4.86–4.69 (m, 3H, × OCH*H*Ph), 4.71–4.60 (m, 3H, H-1, 2 × OCH*H*Ph), 4.60–4.38 (m, 8H, 8 × OCH*H*Ph), 4.20–4.09 (m, 4H, H-4″, H-5″, H-6″a, H-3″), 4.09–4.03 (m, 1H, H-3′), 3.97–3.77 (m, 5H, H-5′, H-4, H-6″b, H-3, H-4′), 3.77–3.66 (m, 3H, H-6a, H-6a), 3.63–3.48 (m, 4H, H-2, H-2′, H-6′b, H-6b), 3.42 (s, 3H, OCH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0, 138.9, 138.3, 138.2, 138.0, 137.6, 137.1, 135.8, 135.8, 129.1, 128.7, 128.6, 128.6, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 127.4, 127.4, 127.3, 127.3, 127.3, 127.3, 127.1, 127.1, 126.8, 126.5, 126.5, 126.4, 101.9, 97.8, 96.8, 96.0, 82.0, 81.7, 80.1, 79.7, 78.0, 75.0, 74.4, 73.8, 73.4, 73.3, 73.1, 72.9, 72.5, 71.7, 70.4, 69.6, 69.3, 69.3, 69.0, 68.9, 68.7, 68.5, 63.0, 55.2; ^{31}P NMR (243 MHz, $CDCl_3$) δ 16.09; HRMS (ESI) calcd for $C_{89}H_{93}O_{19}PNa$ $[M+Na]^+$: 1519.5914, found 1519.5944.

3.10.17. Methyl 3-phosphate-α-D-glucopyranosyl-(1→4)-α-D-glucopyranosyl-(1→4)-α-D-gluco pyranoside (36)

Hydrogenation of **34** (10 mg, 0.006 mmol) according to the general method for global deprotection gave **36** (2.5 mg, 0.003 mmol, 50%) as a syrup.^{1}H NMR (600 MHz, MeOD) δ 5.23 (d, J = 3.40 Hz, 1H, H-1′), 5.18 (d, J = 3.71 Hz, 1H, H-1″), 4.70 (d, J = 3.69 Hz, 1H, H-1), 3.36–3.30 (m, 8H), 3.91–3.78 (m, 9H), 5.12–5.10 (m, 1H), 3.70–3.55 (m, 5H), 3.53 (m, 4H); ^{13}C NMR (101 MHz, MeOD) δ 101.3, 101.2, 99.7, 89.7, 80.2, 80.1, 73.5, 73.0, 72.3, 71.8, 71.7, 70.7, 61.0, 60.7, 54.2, 52.6; ^{31}P NMR (162 MHz, MeOD) δ 1.25; HRMS (ESI) calcd for $C_{19}H_{34}O_{19}P$ $[M-H]^-$: 597.1437, found 597.1425.

3.10.18. Methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*–benzyl-α-D-glucopyranoside (41)

Donor **28** (82 mg, 0.144 mmol) and acceptor **37** (38 mg, 0.082 mmol) were subjected to the conditions in the general method of glycosylation to give **39** as a mixture, followed by PMB removal and purified by SGC (hexanes/EtOAc 4:1) to give **41** (33 mg, 0.041 mmol, 50%) as a white foam. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.59–7.16 (m, 25H), 5.80 (d, J = 3.69 Hz, 1H, H-1′), 5.50 (s, 1H, PhCH), 5.12 (d, J = 11.73 Hz, 1H, OCH*H*Ph), 4.78 (d, J = 11.80 Hz, 1H, OCH*H*Ph), 4.71 (d, J = 12.11 Hz, 2H, OCH_2Ph), 4.68–4.45 (m, 5H, H-1, 4 × OCH*H*Ph), 4.21–4.05 (m, 4H, H-3, H-3′, H-6′a, H-4′), 3.93–3.78 (m, 3H, H-6′b, H-4, H-5′), 3.74–3.57 (m, 3H, H-2, H-6a, H-6b), 3.48 (t, J = 9.46 Hz, 1H, H-5), 3.44–3.28 (m, 4H, H-2′, OCH_3), 2.48 (br s, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 138.1, 137.9, 137.6, 137.2, 129.1, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.9, 127.5, 127.4, 127.2, 126.7, 126.3, 101.8, 97.7, 96.5, 82.1, 81.3, 80.3, 79.1, 74.2, 73.4, 73.3, 73.0, 71.5, 70.2, 69.4, 68.9, 68.7, 63.0, 55.2; HRMS (ESI) calcd for $C_{48}H_{56}NO_{11}$ $[M+NH_4]^+$: 822.3848, found 822.3834.

3.10.19. Methyl 2-*O*-benzyl-3-dibenzylphosphate-4,6-*O*-benzylidene-α-D-gluco pyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (43)

Compound **41** (33 mg, 0.041 mmol) was subjected to the general procedure for phosphorylation described above and purified by SGC (hexanes/EtOAc 4:1) to give **43** (38 mg, 0.036 mmol, 88%) as a white foam. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60–6.99 (m, 35H, PhH), 5.84 (d, J = 3.67 Hz, 1H, H-1′), 5.50 (s, 1H, PhCH), 5.18–5.04 (m, 5H, 5 × OCH*H*Ph), 5.04–4.91 (m, 2H, OCH*H*Ph, H-3′), 4.86 (dd, J = 7.69, 12.12 Hz, 1H, OCH*H*Ph), 4.75–4.67 (m, 3H, H-1, 2 × OCH*H*Ph), 4.66–4.57 (m, 2H, 2 × OCH*H*Ph), 4.54 (d, J = 11.69 Hz, 1H, OCH*H*Ph), 4.23–4.11 (m, 3H, H-6′a, H-4, H-5), 3.98–3.88 (m, 3H, H-6′b, H-3, H-5′), 3.72–3.65 (m, 3H, H-2, H-6a, H-6b), 3.61 (dd, J = 3.76, 9.57 Hz, 1H, H-2′), 3.45 (s, 3H, OCH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0, 138.2, 137.9, 137.5, 137.1, 136.3, 136.2, 136.1, 135.6, 135.6, 129.1, 128.7, 128.7, 128.6, 128.5, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 127.6, 127.6, 127.5, 127.4, 127.3, 127.1, 126.6, 126.5, 101.9, 97.7, 96.9, 82.0, 80.4, 80.2, 78.1, 74.1, 73.4, 73.3, 72.9, 71.7, 69.4, 69.1, 69.0, 69.0, 69.0, 68.9, 68.8, 67.3, 67.3, 63.2, 55.3; ^{31}P NMR (243 MHz, $CDCl_3$) δ 16.02; HRMS (ESI) calcd for $C_{62}H_{65}O_{14}PK$ $[M+K]^+$: 1103.3744, found 1103.3756.

3.10.20. Methyl 2,6-di-*O*-benzyl-3-dibenzylphosphate-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (45)

Compound **43** (38 mg, 0.036 mmol) was subjected to the conditions according to the general procedure for selective benzylidene opening and purified by SGC (hexanes/EtOAc 3:2) to afford **45** (29 mg, 0.027 mmol, 75%) as a syrup. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55–7.09 (m, 35H, PhH), 5.77 (d, J = 3.68 Hz, 1H, H-1′), 5.18–4.95 (m, 7H, 7 × OCH*H*Ph), 4.75 (d, J = 11.86 Hz, 1H, OCH*H*Ph), 4.72 (d, J = 12.33 Hz, 1H, OCH*H*Ph), 4.68–4.57 (m, 4H, H-1, H-3′, OCH*H*Ph, H-4′), 4.58–4.44 (m, 5H, 5 × OCH*H*Ph), 4.12–4.03 (m, 2H, H-3, H-4), 3.86–3.81 (m, 3H, H-5, H-5′, H-6a), 3.75 (dd, J = 3.62, 10.72 Hz, 1H, H-6′a), 3.70–3.58 (m, 3H, H-6b, H-2, H-6′a), 3.52 (dd, J = 2.52, 10.88 Hz, 1H, H-6′b), 3.49 (dd, J = 3.58, 9.60 Hz, 1H, H-2′), 3.44 (s, 3H, OCH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0, 138.2, 138.2, 138.0, 137.6, 135.6, 135.6, 135.6, 135.5, 128.7, 128.7, 128.6, 128.5, 128.5, 128.3, 128.3, 128.3, 128.2, 128.2, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 127.4, 127.1, 126.6, 97.7, 96.5, 82.0, 82.0, 81.9, 80.2, 74.3, 73.6, 73.3, 73.2, 73.0, 72.8, 71.1, 69.9, 69.8, 69.7, 69.7, 69.5, 69.0, 68.6, 67.3, 67.3, 55.3; ^{31}P NMR (243 MHz, $CDCl_3$) δ 18.69; HRMS (APCI) calcd for $C_{62}H_{68}O_{14}P$ $[M+H]^+$: 1067.4341, found 1067.4342.

3.10.21. Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (40)

Donor **27** (50 mg, 0.088 mmol) and acceptor **37** (22 mg, 0.047 mmol) were subjected to the conditions in the general method of glycosylation to give **38** as a mixture, followed by PMB removal and purified by SGC (hexanes/EtOAc 4:1) to give **40** (12 mg, 0.015 mmol, 32%) as a syrup. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.21 (m, 25H, PhH), 5.52 (s, 1H, PhCH), 5.26 (d, J = 3.47 Hz, 1H, H-1′), 5.09 (d, J = 10.91 Hz, 1H, OCH*H*Ph), 4.81–4.73 (m, 2H, 2 × OCH*H*Ph), 4.73–4.51 (m, 6H, 5 × OCH*H*Ph, H-1), 4.13 (dd, J = 4.84, 10.27 Hz, 1H, H-6′a), 3.99 (t, J = 9.29 Hz, 1H, H-3), 3.95–3.80 (m, 3H, H-5, H-4', H-5′), 3.77–3.51 (m, 6H, H-4, H-2', H-6′b, H-2, H-6a, H-6b), 3.46–3.30 (m, 4H, H-3′, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.6, 137.8, 137.8, 137.7, 137.4, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.7, 127.6, 127.5, 126.0, 101.2, 100.9, 97.8, 81.5, 80.7, 80.3, 79.2, 77.2, 76.8, 75.3, 74.7, 73.5, 73.4, 73.2, 69.9, 68.9, 68.5, 63.7, 55.3; HRMS (ESI) calcd for $C_{48}H_{52}O_{11}Na$ $[M+Na]^+$: 827.3402, found 827.3402.

3.10.22. Methyl 2-dibenzylphosphate-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (42)

Compound **40** (11 mg, 0.015 mmol) was subjected to the general procedure for phosphorylation described above and purified by SGC (hexanes/EtOAc 3:1) to give **42** (13 mg, 0.013 mmol, 85%) as a syrup. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47–7.20 (m, 35H, PhH), 5.91 (d, J = 3.81 Hz, 1H, H-1′), 5.59 (s, 1H, PhCH), 5.16–4.84 (m, 7H, 7 × OCH*H*Ph), 4.80–4.67 (m, 3H, OCH_2Ph), 4.64 (d, J = 3.56 Hz, 1H, H-1), 4.59 (dd, J = 6.56, 12.17 Hz, 2H, OCH_2Ph), 4.51–4.44 (m, 1H, H-2′),4.21 (dd, J = 4.84, 10.31 Hz, 1H, H-6′a), 4.16 (t, J = 9.15 Hz, 1H, H-3), 4.10 (t, J = 9.05 Hz, 1H, H-5), 4.05 (t, J = 9.34 Hz, 1H, H-3′), 3.96 (dd, J = 5.43, 9.92, 1H, H-5′), 3.90–3.81 (m, 2H, H-6′b, H-4), 3.77–3.67 (m, 3H, H-4′, H-6a, H-6b), 3.59 (dd, J = 3.46, 8.60 Hz, 1H, H-2), 3.40 (s, 3H, OCH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.7, 138.4, 138.1, 138.0, 137.4, 137.2, 137.1, 128.7, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.7, 127.6, 127.5, 127.5, 101.8, 97.9, 96.1, 82.2, 81.4, 80.4, 76.6, 76.6, 74.9, 74.5, 73.5, 73.4, 71.7, 69.5, 69.4, 68.9, 68.8, 67.3, 67.3, 67.2, 67.2, 63.1, 55.3; ^{31}P NMR (243 MHz, $CDCl_3$) δ 12.20; HRMS (ESI) calcd for $C_{62}H_{65}O_{14}PNa$ $[M+Na]^+$: 1087.4004, found 1087.3988.

3.10.23. Methyl 3-dibenzylphosphate-2,6-di-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (44)

Compound **42** (8 mg, 0.008 mmol) was subjected to the conditions according to the general procedure for selective benzylidene opening and purified by SGC (hexanes/EtOAc 3:1) to afford **44** (5 mg, 0.005 mmol, 63%) as a syrup. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–6.99 (m, 35H), 5.69 (d, J = 3.57 Hz, 1H, H-1′), 4.98–4.70 (m, 7H, 7 × OCH*H*Ph), 4.70–4.55 (m, 2H, 2 × OCH*H*Ph), 4.54–4.42 (m, 3H, 2 × OCH*H*Ph, H-1), 4.36 (d, J = 12.00 Hz, 1H, OCH*H*Ph), 4.32–4.23 (m, 2H, H-2′, OCH*H*Ph), 4.02–3.91 (m, 2H, H-3, H-5′), 3.84–3.68 (m, 4H, H-3′, H-6′a, H-5), 3.68–3.54 (m, 3H, H-4′, H-6′b, H-6a), 3.48-3.42 (m, 2H, H-2, H-6b), 3.28 (s, 3H, OCH_3), 2.53 (d, J = 2.51 Hz, 1H, OH); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.5, 138.1, 137.9, 135.8, 135.7, 128.7, 128.6, 128.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 127.3, 97.9, 95.7, 81.4, 80.2, 79.6, 75.0, 74.5, 73.6, 73.4, 73.3, 72.5, 72.1, 70.3, 70.0, 69.6, 69.4, 69.3, 68.9, 67.3, 55.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ −0.99; HRMS (ESI) calcd for $C_{62}H_{68}O_{14}P$ $[M+H]^+$: 1067.4341, found 1067.4319.

3.10.24. Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl-(1→4)-3-dibenzyl phosphate-2,6-di-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (48)

Donor **46** (29 mg, 0.042 mmol) and acceptor **45** (15 mg, 0.014 mmol) were subjected to the conditions according to the glycosylation procedure and purified by SGC (hexanes/EtOAc 4:1) to give **48** (16 mg, 0.010 mmol, 72%) as a syrup. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50–6.98 (m, 55H, PhH), 5.83 (d, J = 3.58 Hz, 1H, H-1″),

5.66 (d, J = 3.54 Hz, 1H, H-1′), 5.05–4.95 (m, 3H, H-3′, 2 × OCH*H*Ph), 4.95–4.89 (m, 1H, OCH*H*Ph), 4.89–4.83 (m, 5H, 5 × OCH*H*Ph), 4.83–4.79 (m, 2H, 2 × OCH*H*Ph), 4.77 (d, J = 11.12 Hz, 1H, OCH*H*Ph), 4.75–4.68 (m, 1H, OCH*H*Ph), 4.66–4.58 (m, 6H, H-1, 5 × OCH*H*Ph), 4.56–4.38 (m, 8H, 8 × OCH*H*Ph), 4.32 (dd, J = 12.11, 16.95 Hz, 2H, 2 × OCH*H*Ph), 4.27 (dd, J = 6.52, 9.76 Hz, 1H, H-4′), 4.06–3.99 (m, 2H, H-4″, H-3), 3.87–3.81 (m, 2H, H-3″, H-4), 3.79–3.74 (m, 2H, H-5), 3.74–3.66 (m, 3H, H-6″a, H-6″b), 3.66–3.51 (m, 5H, H-2′, H-6a, H-2, H-6b, H-6′a), 3.51–3.42 (m, 5H, H-5″, H-5′, H-2″, OCH_3, H-6′b); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 138.8, 138.7, 138.4, 138.2, 138.2, 138.1, 138.0, 137.9, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.4, 127.4, 127.4, 127.4, 127.3, 127.2, 126.9, 97.8, 95.2, 94.5, 82.0, 81.7, 80.2, 80.1, 75.4, 74.9, 74.3, 73.4, 73.3, 73.3, 72.9, 72.6, 72.3, 71.8, 71.0, 70.4, 69.5, 69.4, 69.4, 69.2, 69.2, 68.8, 68.7, 68.5, 55.3; ^{31}P NMR (243 MHz, $CDCl_3$) δ 15.13; HRMS (ESI) calcd for $C_{96}H_{101}O_{19}PNa$ $[M+Na]^+$: 1611.6567, found 1611.6524.

3.10.25. Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2-dibenzylphosphate-3,6-di-*O*-benzyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (47)

Donor **46** (10 mg, 0.012 mmol) and acceptor **44** (5 mg, 0.005 mmol) were subjected to the conditions according to the glycosylation procedure and purified by SGC ($PhCH_3$/EtOAc 8:1) to give **48** (5 mg, 0.003 mmol, 60%) as a syrup. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65–7.00 (m, 50H, PhH), 5.73 (d, J = 3.51 Hz, 1H, H-1′), 5.59 (d, J = 3.63 Hz, 1H, H-1″), 5.09–4.98 (m, 2H, 2 × OCH*H*Ph), 4.98–4.88 (m, 2H, 2 × OCH*H*Ph), 4.88–4.77 (m, 6H, 6 × OCH*H*Ph), 4.77–4.68 (m, 3H, 3 × OCH*H*Ph), 4.66–4.41 (m, 11H, 10 × × OCH*H*Ph, H-1, H-2′), 4.32 (d, J = 12.19 Hz, 1H), 4.19–4.08 (m, 2H, H-3′, H-5″), 4.08–4.02 (m, 2H, H-3, H-5), 4.02–3.94 (m, 1H, H-4′), 3.94–3.87 (m, 2H, H-6″a, H-3″), 3.80 (d, J = 7.13 Hz, 1H, H-4), 3.79–3.73 (m, 2H, H-6″b, H-5′), 3.72–3.66 (m, 2H, H-6′a, H-4″), 3.57 (m, 2H, H-6′b, H-6a), 3.54–3.47 (m, 2H, H-2″, H-2), 3.41 (dd, J = 2.00, 10.75 Hz, 1H, H-6b), 3.38 (s, 3H, OCH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.0, 138.7, 138.4, 138.2, 138.0, 129.0, 128.6, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.0, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.4, 127.2, 127.1, 126.7, 97.9, 97.1, 95.7, 82.1, 81.2, 80.0, 79.5, 77.6, 75.4, 74.9, 74.7, 73.7, 73.5, 73.3, 73.1, 71.1, 71.1, 69.7, 69.2, 68.8, 68.2, 55.3; ^{31}P NMR (243 MHz, $CDCl_3$) δ 16.68; HRMS (ESI) calcd for $C_{96}H_{101}O_{19}PNa$ $[M+Na]^+$: 1611.6567, found 1611.6565.

3.10.26. Methyl α-D-glucopyranosyl-(1→4)-2-phosphate-α-D-glucopyranosyl-(1→4)-α-D-gluco pyranoside (49)

Hydrogenation of **48** (3 mg, 0.0018 mmol) according to the general method for global deprotection gave **12** (0.5 mg, 0.001 mmol, 48%) as a syrup.^{1}H NMR (700 MHz, MeOD) δ 5.75 (m, 1H, H-1′), 5.24 (m, 1H, H-1″), 4.73 (m, 1H, H-1), 4.20–4.02 (m, 3H), 3.99–3.81 (m, 5H), 3.79–3.58 (m, 6H), 3.54–3.14 (m, 6H); ^{13}C NMR (176 MHz, MeOD) δ 104.1, 102.3, 99.0, 82.1, 80.8, 80.4, 78.4, 76.5, 76.3, 76.1, 75.5, 74.4, 74.1, 73.0, 72.9, 72.8, 64.0, 63.6, 63.3, 56.9; ^{31}P NMR (243 MHz, MeOD) δ 3.20; HRMS (ESI) calcd for $C_{19}H_{34}O_{19}P$ $[M-H]^-$: 597.1437, found 597.1435.

3.10.27. Methyl α-D-glucopyranosyl-(1→4)-3-phosphate-α-D-glucopyranosyl-(1→4)-α-D-gluco pyranoside (50)

Hydrogenation of **48** (10 mg, 0.006 mmol) according to the general method for global deprotection gave **50** (3 mg, 0.004 mmol, 67%) as a syrup. ^{1}H NMR (600 MHz, MeOD) δ 5.49 (br s, 1H, H-1′), 5.19 (br s, 1H, H-1″), 4.60 (br s, 1H, H-1), 4.07–3.76 (m, 4H), 3.76–3.58 (m, 5H), 3.58–3.36 (m, 6H), 3.24–3.14 (m, 6H); ^{13}C NMR (151 MHz, MeOD) δ 99.7, 96.8, 92.6, 76.7, 76.6, 74.9, 73.5, 73.0, 72.5, 71.6, 71.4, 70.5, 70.4, 61.5, 61.4, 60.8, 54.2; ^{31}P NMR (162 MHz, MeOD) δ 2.20; HRMS (ESI) calcd for $C_{19}H_{34}O_{19}P$ $[M-H]^-$: 597.1437, found 597.1436.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2012.12.015.

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