Synthesis of α- and *β*-Carbon-Linked Serine Analogues of the P^k Trisaccharide

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The synthesis of glycopeptide ligands for a range of biomedically relevant carbohydrate-binding proteins is a topic of great importance to the glycobiology community. This task is impeded by the inherent instability of glycosyl linkages to serine/threonine, the normal sites of O-glycosylation in proteins. We have previously developed methodology for the preparation of C-glycosylated serines based on catalytic asymmetric hydrogenation of the corresponding enamide esters with the DuPHOS−Rh^+ catalysts. Here we report further development of the methodology in the preparation of the *C*-glycosyl serine analogue of the P^k trisaccharide (α-Gal(1→4)*β*-Gal(1→4)*β*-Glc-CH_2-serine); we require these ligands for our continuing investigations of the binding subunit of the shiga-like toxin. Catalytic asymmetric hydrogenation was used to prepare both α- and *β*-*C*-glycosides in the *R* and *S* serine series. We report here on the tolerance of the DuPHOS catalysts toward acetate, benzoate, and benzyl hydroxyl protecting groups. Additionally, we have developed an amino acid protecting group strategy compatible with both asymmetric hydrogenation and solid-phase peptide synthesis. In the course of our studies, we have also developed a new methodology for regioselective reductive cleavage of benzylidene protecting groups.

Introduction

Protein−carbohydrate interaction plays a central role in biological recognition. In addition to myriad functions in normal human biology, an array of pathological recognition events are mediated by protein−carbohydrate interaction.[1] In the earliest phases of infection by a variety of viral, parasitic, mycoplasmal, and bacterial infections a pathogen recognizes and adheres to its host through a protein−carbohydrate interaction. Because of the importance of carbohydrate-mediated recognition, the development of high-affinity soluble ligands designed to inhibit pathogens−host adhesion is an area of intense activity. The development of such inhibitors has been frustrated to date by the exceptionally weak affinities with which native, monovalent saccharides adhere to their protein receptors; such interactions typically proceed with millimolar to micromolar dissociation constants. Much contemporary glycoscience thus seeks general strategies for overcoming this weak native affinity.

Two strategies have been explored toward this goal. The first involves modification of the monovalent ligand in a search for adventitious contacts between various pendant moieties and the protein, either in or out of the binding site. Some of the most successful demonstrations of this strategy have been offered by Wong and coworkers,[2] who have shown that much of the specificity of an oligosaccharide binding event is provided by a single monosaccharide.[3] Derivatized monosaccharides, prepared randomly and identified with high throughput screens, thus act as effectively as the parent oligosaccharide as ligands for both lectins and antibodies. A second general strategy for the preparation of high-affinity ligands involves the use of multivalency. Lectins are seldom found in vivo as monomeric species; rather they are aggregated into higher order oligomers. A reasonable suggestion following from this observation is that Nature has solved the "tight binding" problem through multivalency. From this premise a wide range of high-affinity multivalent carbohydrate ligands have been prepared for myriad carbohydrate-binding proteins.[4]

Toward the development of high-affinity ligands for carbohydrate-binding proteins of immediate concern for human health, we sought to prepare libraries of bivalent, peptide-linked oligosaccharide ligands. Our rationale for this exercise was to access the advantages of both adventitious contacts between linker and protein outside the binding site and multivalency. From this perspective, peptides are attractive tethers for several reasons. First, the amide linkage is robust to both chemical and enzymatic degradation, especially following the incorporation of nonproteinaceous amino acids. Second, the peptide backbone provides sufficient flexibility for optimal placement of saccharide recognition epitopes within the carbohydrate-binding sites while at the same time providing sufficient rigidity to reduce the conformational entropy barrier encountered during restriction of the linker region during binding. Third, a wide range of functionalities are available with even the 20 proteinaceous amino acids in the search for favorable interactions between ligand and protein. Finally, the facile and well-developed synthetic

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methodology available for peptide synthesis allows rapid preparation of ligands on solid supports.

We have previously reported the preparation of bivalent, peptide-linked ligands for the plant lectin concanavalin A.[5] This work demonstrated that "shaving" protocols effectively generate beads with low-density, spatially segregated recognition sequences on the bead surface that enforce exclusive intramolecular binding but with high-density interior sequences suitable for sequencing by mass spectroscopic techniques.[6] We are now utilizing this strategy in a search for high-affinity ligands for the shiga-like toxin (SLT). The shiga and shiga-like toxins are members of a group of bacterial two-component toxins that includes the heat labile and cholera toxins. The proteins are structurally and mechanistically related to the diphtheria and pertussis toxins, and to the toxic plant lectins abrin and ricin. All members of this group produce their toxic effects by recognizing and adhering to host cell surfaces through a multimeric lectin recognition subdomain. Following endocytosis, a second, enzymatically active, subdomain is transported to the cytosol, where it exerts its toxic effects.[7]

The shiga toxin and shiga-like toxins bind the P^k trisaccharide recognition domain of the glycolipid receptor globotriosylceramide (α-Gal(1→4)*β*-Gal(1→4)*β*Glc-*O*-cer).[8] Originally isolated from *Shigella dysenteria*, the toxin is now secreted by several strains of *Escherichia coli*; to date more than 25 strains of SLT-producing *Escherichia* have been identified in North America. The most notorious of these, *E. coli* O157, produces a set of symptoms functionally equivalent to those of shigellosis, primarily a unique hemmorrhagic colitis. In children and elderly patients, occasional progression to hemolytic uremic syndrome and kidney failure is a complication of the disease; the renal toxicity is thought to reflect the high concentration of glycolipid receptor on kidney tissue.[9] There is currently no treatment for the disease following the onset of symptoms, although high-affinity mimics of the cell surface glycolipid receptor might serve as effective therapeutic agents even following the onset of bloody diarrhea.

A prerequisite for the synthesis of peptide-linked ligands is access to sufficient quantities of P^k trisaccharide-derivatized amino acid suitably protected for solid-phase glycopeptide synthesis. Naturally occurring *O*-glycopeptides and proteins are glycosylated through either serine or threonine. To avoid problems associated with the instability of the *O*-glycosyl serine linkage, we instead sought to utilize the C-linked analogue α-Gal(1→4)*β*-Gal(1→4)*β*Glc-CH_2-serine.[10] A variety of methods have been reported for the production of *C*-glycosyl amino acids with both natural and unnatural stereochemistry at the α-amino acid center.[11] We have previously reported methodology based on catalytic asymmetric hydrogenation of glycosylated enamides to produce the carbon-linked glycosyl serines in either *R* or *S* stereochemistry from a common starting material.[12] In our original communication amino acids were produced N-protected as the *tert*-butyl carbamates and carboxyl protected as the methyl esters; such protection is incompatible with solid-phase synthesis. Here, we extend our methodology beyond monosaccharides to produce gram quantities of the P^k trisaccharide protected as the TMSE esters and *tert*-butyl carbamates, appropriate for solid-phase glycopeptide synthesis. Finally, we report the use of triethylsilane/$BF_3{\cdot}Et_2O$ for the selective conversion of a 4,6-di-*O*-benzylidene protecting group to the corresponding 6-*O*-benzyl ether. This methodology represents a significant improvement over the widely used methodology involving $NaBCNH_3$ and HCl_g.[13]

Results and Discussion

Preparation of the α-Analogue of the P^k Trisaccharide. The two key aspects of the synthetic strategy are disconnection of the trisaccharide and installation of a moiety that facilitates incorporation of a *C*-glycoside into the amino acid backbone. Several syntheses of the P^k trisaccharide have been reported; all make the key bond disconnection at the α-galactose(1→4)lactose linkage.[14] Our strategy toward the amino acid component involves asymmetric hydrogenation of an enamide precursor. The enamide is prepared as the *E*/*Z* mixture by Horner−Emmons olefination of a *C*-glycosyl aldehyde, in turn prepared from the corresponding *C*-allyl glycoside by ozonolysis. With these considerations in mind, we chose to functionalize lactose as the *C*-allyl derivative prior to installation of the terminal galactose residue.

Although the naturally occurring ligand possesses the *β*-configuration at the glucosyl anomeric center, we sought to produce all four diastereomers at the *C*-glycosyl anomeric and the α-amino acid centers. We first considered synthesis of the two diastereomers of the α-*C*-glycosyl compound, a route that requires preparation of the α-*C*-allyl lactoside. A variety of methodologies have been developed for the preparation of α-*C*-glycosides; we considered both acid-catalyzed and radical additions to α-*C*-allyl lactose.[15] Gannis and co-workers[16] report that

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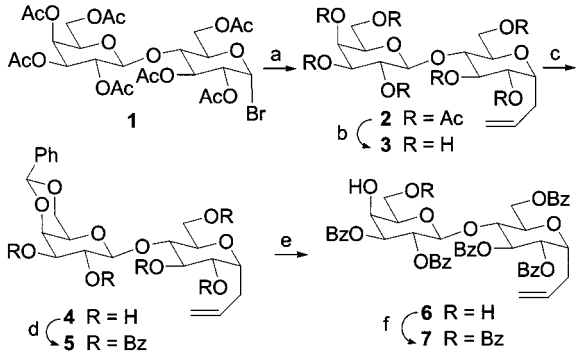
Scheme 1. Synthesis of α-Trisaccharide Acceptor 7[a]



[a] Conditions: (a) allyl phenyl sulfone, $(Bu_3Sn)_2$, PhH, *hν*, 53%; (b) K_2CO_3, MeOH, 99%; (c) PhCHO, formic acid, 61%; (d) BzCl, pyridine, 100%; (e) TFA, H_2O 80%; (f) 2.0 equiv of BzCl, pyridine, 2 days, 100%.

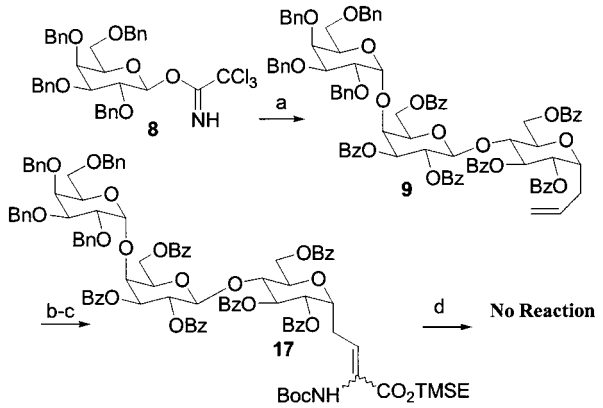
treatment of peracetylated lactose with $BF_3{\cdot}Et_2O$ and allyltrimethylsilane provides the required *C*-allyl lactoside **2** in 55% yield. In our hands the reaction was complicated by low yields (<30%) and significant contamination by the *β*-isomer. We thus turned to the radical protocol of Magnusson and co-workers.[17] Photochemically initiated allylation of acetobromolactose (**1**) with allyl phenyl sulfone and bistributyltin afforded the desired α-analogue **2** exclusively, but in only moderate yield (∼50%). Alterations of reaction conditions failed to significantly improve the yield. Removal of the acetate protecting groups was effected in quantitative yield with K_2CO_3 in methanol (Scheme 1).

With the installation of the α-*C*-allyl moiety complete, it was necessary to differentially functionalize the disaccharide in preparation for addition of the terminal α-galactosyl residue. Installation of the 4′,6′-di-*O*-benzylidene by treatment of *C*-allyl lactoside **3** with benzaldehyde and formic acid followed by perbenzoylation provided **5** in 61% yield for the two steps. Removal of the benzylidene and selective benzoylation of the primary hydroxyl provided the lactose-derived acceptor **7** in 24% overall yield from lactose (Scheme 1). Coupling of the C4′ axial hydroxyl with perbenzylated galactosyl trichloroacetimidate **8**[18] with TMSOTf promotion in dichloromethane provided **9** in 66% yield (Scheme 2). Finally, ozonolysis of the terminal furnished the required aldehyde in 78% yield.

Our previously reported strategy next required Horner−Emmons olefination to a glycine *O*-methyl ester-derived phosphonate.[12] While the methyl ester is compatible with hydrogenation, orthogonal deprotection considerations render the product unsuitable for solid-phase synthesis. Accordingly, we explored alternate protecting group strategies.

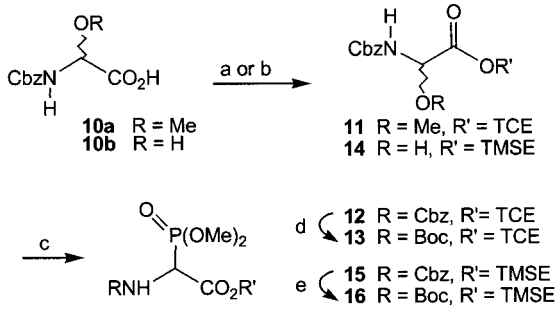
Ideal protecting groups for the enamide precursor should be stable to phosphonate ester preparation (PCl_3/$P(OMe)_3$), not interfere with asymmetric catalytic hydrogenation, and be cleavable in the presence of carbohydrate acetate protecting groups. Additionally, the carboxyl protecting group should be stable to *tert*-butyl carbamate

Scheme 2. Synthesis of the α-Trisaccharide Enamide Ester 17[a]



[a] (a) **7**, 0.25 equiv of TMSOTf, CH_2Cl_2, 60%; (b) O_3, then Me_2S, 75%; (c) **16**, TMG, THF, −78 °C; 65%; (d) (*R*,*R*)-Et-DuPHOS, THF, 90 psi of H_2.

Scheme 3. Synthesis of TCE- or TMSE-Protected Phosphonate Ester[a]



[a] Conditions: (a) 2,2,2-trichloroethanol, DMAP, DCC, 75%; (b) 2-(trimethylsilyl)ethanol, DMAP, DCC, 50%; (c) PCl_3, then $P(OMe)_3$, 88%; (d) 30% HBr/AcOH, then Boc_2O, <8%. (e) Pd/C, H_2, Boc_2O, MeOH, 98%.

deprotection. With these considerations in mind, trichloroethyl esters (TCE) were investigated for carboxyl protection. The TCE group is stable to both organic acids and amine bases, permitting subsequent utilization of either Boc or Fmoc amino protecting groups.[19] The TCE ester was installed using standard DCC coupling to provide **11** in 71% yield.[20,21] Treatment of **11** with PCl_3 followed by $P(OMe)_3$ afforded the ester **12** in 88% yield (Scheme 3).

Catalytic asymmetric hydrogenation using the DuPHOS ligands requires amide or carbamate protection of the enamide nitrogen.[22] The conditions required for amide hydrolysis preclude the use of amide protecting groups. Although the phosphonate ester is initially

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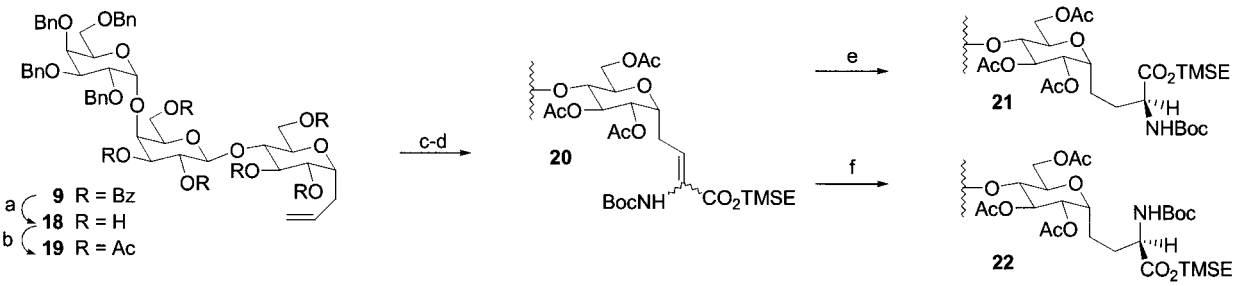
Scheme 4. Synthesis of the α-Trisaccharide Glycosylated Serine Derivatives 21 and 22[a]



[a] (a) K_2CO_3, MeOH, 96%; (b) Ac_2O, pyridine, DMAP, 93%; (c) O_3, then Me_2S, 75%; (d) **16**, TMG, THF, −78 °C; 65%; (e) [(COD)Rh−((*S*,*S*)-Et-DuPHOS)]$^+$OTf$^-$, 90 psi of H_2, THF, 98% yield, >95% de; (f) [(COD)Rh−((*R*,*R*)-Et-DuPHOS)]$^+$OTf$^-$, 90 psi of H_2, THF, 88% yield, >95% de.

prepared N-protected as the benzyl carbamate, a protection strategy compatible with solid-phase peptide synthesis was required. Accordingly, the Cbz amine protecting group was converted to the corresponding *tert*-butyl carbamate. Selective hydrogenolysis of benzyl carbamates in the presence of TCE esters is not feasible due to palladium/halogen exchange. Alternatively, cleavage of the Cbz group was effected with HBr/HOAc. Immediate treatment of the free amine with di-*tert*-butyl dicarbonate (Boc_2O) provided **13** in less than 8% yield. Numerous attempts to increase the yield of this transformation were unsuccessful, and the method was abandoned.

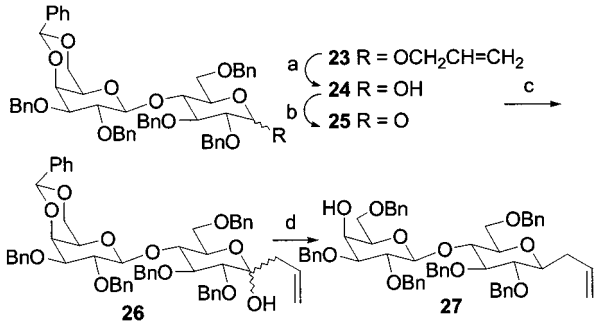
We next considered (trimethylsilyl)ethyl (TMSE) carboxyl protection. Conversion of **10b** to the corresponding TMSE ester **14** with (trimethylsilyl)ethanol and DCC (Scheme 1) proceeded in 50% isolated yield. Conversion to the phosphonate ester followed by catalytic hydrogenolysis in the presence of Boc_2O furnished the phosphonate ester **16** in 28% overall isolated yield for the three steps. This phosphonate is both stable to all conditions required for completion of the *C*-glycosyl serine synthesis and appropriately protected for peptide synthesis. We note parenthetically that reaction of the free amine with Fmoc-chloroformate would produce the corresponding Fmoc-protected derivative.

Horner−Emmons olefination of the unstable *C*-glycosyl aldehyde with phosphonate **16** at −78 °C furnished enamide ester **17**. Unfortunately, catalytic asymmetric hydrogenation with either (*R*,*R*)-Et-DuPHOS or (*R*,*R*)-Me-DuPHOS catalysts in THF at 90 psi of H_2 failed completely.[22] Variation of solvent and reaction time also failed to produce any reduced product (Scheme 2).

Our initial report of catalytic asymmetric hydrogenation of glycosylated enamides utilized acetylated monosaccharides. Accordingly, we decided to return to the less sterically demanding protecting group. Methanolysis of **9** followed by immediate acetylation provided **19** in 89% yield for the two steps. Ozonolysis of the alkene followed by immediate Horner−Emmons olefination of the resultant aldehyde afforded **20** (Scheme 4).

With diminished steric bulk, enamide ester **20** was reduced smoothly using the (*S*,*S*)-Et-DuPHOS catalyst at 90 psi of H_2 in THF for 48 h, providing the glycosylated α-amino acid derivative **21** in 88% yield and >95% diastereomeric excess.[23] Alternatively, hydrogenation with the *R* enantiomer of the catalyst provided the *R* diastereomer **22**, again in >95% stereoisomeric purity (Scheme 4).

Scheme 5. Synthesis of *β*-Acceptor 27[a]



[a] Conditions: (a) (i) $Rh(PPh_3)_3Cl$, DABCO, (ii) HgO, $HgCl_2$, 67%; (b) DMSO, Ac_2O, 95%; (c) allyl magnesium bromide, THF, 89%; (d) Et_3SiH, BF_3Et_2O, 73%.

Preparation of the *β*-Analogue of the P^k Trisaccharide. A parallel synthetic strategy that was utilized for the successful synthesis of the α-*C*-glycosyl serine was adopted for preparation of the *β*-analogue; accordingly, a synthesis of *β*-*C*-allyl lactose was required. Several methods are available for installation of carbon functionality to glycosides with exclusive equatorial selectivity.[15] Our approach to this species followed the report of Kishi that Grignard addition to a perbenzylated sugar lactone followed by deoxygenation of the resulting hemiketal yields *β*-carbon-linked glycosides.[24] To adapt this methodology to our synthesis, the protected lactose−lactone **25** was required.

Allyl lactoside was converted to the 4′,6′-di-*O*-benzylidene and perbenzylated to yield **23** according to literature protocol.[25] Removal of the allyl glycoside was affected by treatment with Wilkinson's catalyst (Rh-[$(PPh_3)_3$]$^+$Cl$^-$) and diazabicyclo[2.2.2]octane (DABCO) followed by $HgO/HgCl_2$ hydrolysis of the vinyl ether (Scheme 5).

Reducing sugar **24** was oxidized to the corresponding lactone **25** in 98% yield with DMSO and acetic anhydride.[26] Treatment with allylmagnesium bromide in THF at −78 °C produced the *β*-*C*-allyl lactose derivative **26** as an interconverting mixture of anomers.[24,27] Deoxygenation of the hemiketal with triethylsilane and $BF_3{\cdot}Et_2O$

(23) Diastereomeric excess was determined by ^{1}H NMR (300 or 400 MHz). The Si(CH_3)$_3$ and Boc peaks are almost baseline resolved in all cases.

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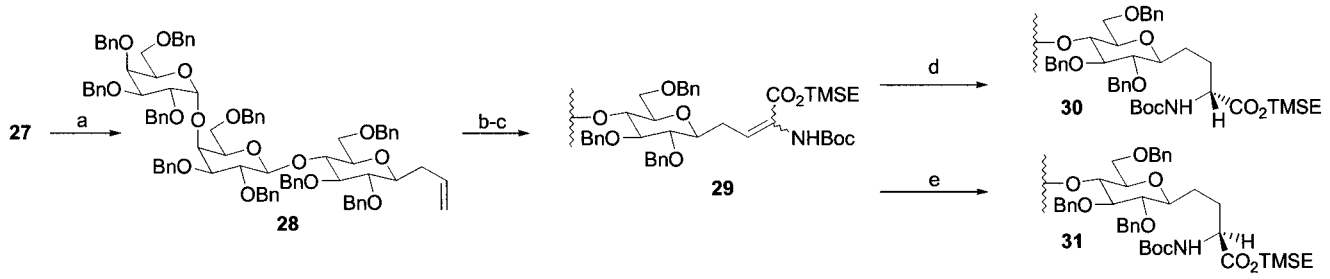
Scheme 6. Synthesis of β-Trisaccharide Glycosylated Serine Derivatives 30 and 31[a]



[a] Conditions: (a) **8**, TMSOTf, Et_2O, 64%; (b) O_3, then Me_2S, 69%; (c) **16**, TMG, THF, −78 °C, 84%; (d) (*R*,*R*)-Et-DuPHOS, THF, 90 psi of H_2, 98% yield, >95% de; (e) (*S*,*S*)-Et-DuPHOS, THF, 90 psi of H_2, 98% yield, >95% de.

proceeded smoothly *with concomitant reduction of the benzylidene to directly afford the desired acceptor* ***27***. Although literature precedent exists for the reduction of a benzylidene with Et_3SiH and TFA, we are unaware of prior use of $BF_3{\cdot}Et_2O$ in this regard.[28] Indeed, TFA catalysis failed to effect the selective benzylidene reduction on galactose-derivated substrates. We are currently exploring the scope of these reaction conditions and will report our results in due course.

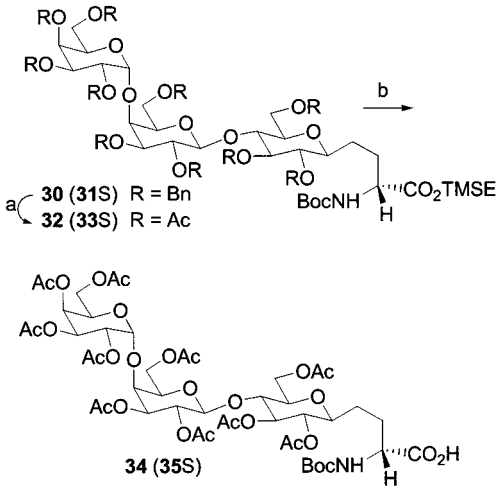
Coupling of acceptor **27** with the galactosyl trichloroacetimidate donor **8** in diethyl ether provided the perbenzylated trisaccharide **28** in 84% yield. Use of dichloromethane as a solvent resulted in minor contamination of **28** with the β-isomer. Ozonolysis of the *C*-allyl glycoside and Horner−Emmons olefination as before provided enamide ester **29** for catalytic asymmetric hydrogenation (Scheme 6).

Asymmetric hydrogenation with the (*R*,*R*)-Et-DuPHOS catalyst in THF afforded the *R* diastereomer **30** in excellent yield and selectivity (>95% de). The *S* diastereomer **31** was also isolated in >95% de after hydrogenation with the *S* enantiomer of the catalyst. Alternatively, catalytic hydrogenation of the acetylated β-trisaccharide enamide under the same conditions proceeds with a diastereomeric excess of only 52%. This result was somewhat surprising in light of the previous observation that the perbenzoylated derivative of the α-anomer failed to react under equivalent hydrogenation conditions. In contrast, asymmetric hydrogenation of peractylated monosaccharides proceeds in excellent diastereoselectivity (>95%). Apparently a complex and subtle interplay of steric and electronic effects control diastereoselectivities during RhDuPHOS-catalyzed hydrogenations, and a thorough exploration of substrate−catalyst interactions is required to achieve high stereoselectivity.

To complete the synthesis of a trisaccharide derivative compatible with solid-phase peptide synthesis, the benzyl ether protecting groups were removed and replaced with acetates, producing both the *R* (**32**) and *S* (**33**) diastereomers in good yield. Finally, removal of the TMSE ester with TBAF provided the free carboxylic acids **34** and **35**, ready for peptide coupling (Scheme 7).

In conclusion, we have utilized catalytic asymmetric hydrogenation methodology to produce four diastereomers of the P^k trisaccharide as the *C*-glycosyl serine derivative. The synthesis is concise and expeditious, and

Scheme 7. Deprotection of the Carboxylic Acids 34 and 35[a]



[a] Conditions: (a) Pd/C, MeOH/THF, 90 psi of H_2, then Ac_2O, pyridine, 76% (**32***R*), 66% (**33***S*); (b) TBAF, 88% (**34***R*), 99% (**35***S*).

amenable to scale-up. Our development of a novel phosphonate ester provides *C*-glycosyl serines appropriately protected for solid-phase peptide synthesis. Using the reported methodology, we have prepared *C*-glycosyl amino acid derivatives suitable for peptide synthesis on a multigram scale. Additionally, the tolerance of the DuPHOS−Rh catalyst was tested with respect to three various hydroxyl protecting groups. The complex results of this study reveal that no simple prescription for effective hydrogenation exists. Finally, we have reported a novel synthetic methodology for the regioselective reduction of the 4,6-di-*O*-benzylidene protecting group. We are currently evaluating the activity of the *C*-glycosyl serine adducts as ligands for the SLT and will report our results in due course.

Experimental Section

General Methods. All reactions were conducted under an inert argon atmosphere. THF and diethyl ether were distilled from sodium benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Methanol was distilled from magnesium. Solutions of compounds in organic solvents were dried over sodium sulfate prior to rotary evaporation. DMF was 99.5% pure and anhydrous (Amresco). Benzyl bromide was filtered through alumina prior to use. TLC plates were Kieselgel 60 F254 (Merck Art. 5554). Carbohydrate compounds were visualized on TLC by charring with H_2SO_4/EtOH/H_2O (1:10:10). Flash column chromatography was done with silica gel 60 (230−400 mesh, Merck). Although not technically correct, compounds are named as derivatives of the corresponding *O*-glycosides for ease of identification.

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Preparation of the Trisaccharide α-Acceptor. 1-(*O*-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl)-2-propene (2). To a solution of acetobromolactose **1** (2.40 g, 3.40 mmol) in toluene (7.0 mL) and CH_2Cl_2 (2.0 mL) were added allyl phenyl sulfone (3.0 equiv, 1.6 mL) and bistributyltin (1.4 equiv, 2.42 mL). The solution was degassed with argon for 30 min before being irradiated with a mercury lamp for 15 h. The solution was concentrated and purified via chromatography eluting with 1:1 petroleum ether/EtOAc. **2** (1.19 g, 53%) was isolated as a white foam: R_f = 0.52 (1:1 EtOAc/petroleum ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.74−5.64 (m, 1H), 5.37−5.34 (m, 2H), 5.15−5.09 (m, 3H), 4.99−4.97 (dd, J = 5.2, 8.6 Hz, 1H), 4.96−4.96 (m, 1H), 4.51−4.50 (d, J = 7.6 Hz, 1H), 4.35−4.33 (dd, J = 2.4, 11.6 Hz, 1H), 4.18−4.15 (dd, J = 5.2, 10.5 Hz, 1H), 4.14−4.08 (m, 3H), 3.90−3.88 (br t, J = 6.8 Hz, 1H), 3.82−3.79 (m, 1H), 3.63−3.60 (t, J = 7.6 Hz, 1H), 2.52−2.44 (m, 1H), 2.30−2.17 (m, 1H), 2.11 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 2.01 (br s, 6H), 2.01 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.37, 170.31, 170.05, 169.99, 169.86, 169.53, 169.11, 133.02, 117.71, 101.27, 76.52, 71.43, 70.95, 70.67, 69.98, 69.73, 66.66, 62.21, 60.83, 30.97, 20.83, 20.77, 20.70, 20.58, 20.46.

1-(*β*-D-Galactopyranosyl-(1→4)-α-D-glucopyranosyl)-2-propene (3). To a 1.0 M solution of $NaOCH_3$ at 0 °C was added a solution of **2** (1.858 g, 2.82 mmol) in anhydrous MeOH (6.0 mL). The reaction mixture was stirred at 25 °C for 15 h and then quenched by the addition of Dowex acid resin until the pH was neutral by pH paper. The solution was filtered and concentrated in vacuo to yield **3** as a pale yellow foam (1.1 g), which was used without further purification: ^{1}H NMR (400 MHz, D_2O) δ 5.73−5.65 (m, 1H), 5.08−5.04 (br d, J = 9.0 Hz, 1H), 5.01−4.98 (br d, J = 9.0 Hz, 1H), 4.31−4.29 (d, J = 7.6 Hz, 1H), 3.96−3.91 (ddd, J = 3.0, 3.8, 12.6 Hz, 1H), 3.78−3.77 (d, J = 3.2 Hz, 1H), 3.74−3.37 (m, 12H), 2.39−2.24 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 134.43, 117.43, 102.83, 79.04, 75.27, 74.75, 72.45, 71.63, 71.15, 70.85, 70.63, 68.44, 60.91, 60.09, 28.86. HRMS *m/e* calcd for M + Na 389.152597, found 389.1424.

1-((4,6-*O*-Benzylidene-*β*-D-galactopyranosyl)-(1→4)-α-D-glucopyranosyl))-2-propene (4). Benzaldehyde and formic acid were freshly distilled prior to use. To a solution of **3** (77.6 mg, 0.212 mmol) in 99% formic acid (175 μL) was added benzaldehyde (375 μL). The reaction mixture was stirred for 45 min at 25 °C. After removal of formic acid by rotary evaporation, NEt_3 (0.5 mL) was added. The remaining solvents were removed in vacuo. The compound was purified via flash chromatography eluting with 8:1 EtOAc/MeOH, affording **4** as a colorless oil (58.5 mg, 61% yield): R_f = 0.56 (1:4 MeOH/CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.14 (m, 5H), 5.74−5.65 (m, 1H), 5.40 (s, 1H), 5.17 (br s, 1H), 5.06−5.01 (m, 2H), 4.52 (br s, 1H), 4.43−4.41 (d, J = 8.0 Hz, 1H), 4.25 (br s, 1H), 4.16−4.13 (d, J = 12.0 Hz, 1H), 4.00−3.83 (m, 4H), 3.67−3.53 (m, 4H), 3.40−3.38 (d, J = 8.4 Hz, 1H), 3.31 (s, 1H), 2.30 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.18, 134.67, 129.26, 129.00, 128.49, 128.18, 126.31, 125.26, 116.90, 102.38, 101.34, 75.53, 75.14, 73.161, 72.03, 71.17, 69.07, 66.94, 61.57, 28.89. Anal. Calcd for $C_{22}H_{30}O_{10}\cdot H_2O$: C, 55.94; H, 6.83. Found: C, 55.43; H, 6.79.

1-((2,3-Di-*O*-benzoyl-4,6-benzylidene-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-glucopyranosyl)-2-propene (5). To a solution of **4** (740.2 mg, 1.63 mmol) in dry pyridine (11.0 mL) was added 4-(dimethylamino)pyridine (40 mg, 20 mol %). After the reaction mixture was cooled to 0 °C, benzoyl chloride (1.9 mL, 16.3 mmol) was added dropwise. The reaction was stirred for 24 h, during which time the solution warmed to 25 °C. After dilution with CH_2Cl_2, the organic layer was washed with water, 1 M HCl, and saturated aqueous $NaHCO_3$ and dried ($MgSO_4$). Recrystallization from petroleum ether/EtOAc yielded **5** as a pale yellow solid (1.592 g, 100%): R_f = 0.73 (1:1 EtOAc/petroleum ether); $[\alpha]^{20}_D$ +69.1° (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04−7.83 (m, 10H), 7.55−7.25 (m, 18H), 7.15−7.11 (t, J = 7.6 Hz, 2H), 6.02−5.97 (t, J = 8.0 Hz, 1H), 5.81−5.76 (dd, J = 8.4, 10.4 Hz, 1H), 5.71−5.62 (m, 2H), 5.36−5.32 (dd, J = 5.6, 9.6 Hz, 1H), 5.30 (s, 1H), 5.19−5.15 (dd, J = 4.0, 10.6 Hz, 1H), 5.11−5.06 (dd, J = 1.6, 17.2 Hz, 1H), 4.98−4.95 (dd, J = 0.8, 10.6 Hz, 1H), 4.89−4.87 (d, J = 8.4 Hz, 1H), 4.48−4.45 (dd, J = 2.4, 11.4 Hz, 1H), 4.41−4.35 (ddd, J = 3.3, 3.9, 12.3 Hz, 1H), 4.32−4.28 (m, 1H), 4.13−4.09 (t, J = 8.0 Hz, 1H), 4.00−3.95 (m, 1H), 3.87−3.83 (dd, J = 1.2, 12.4 Hz, 1H), 3.61−3.58 (dd, J = 2.0, 12.0 Hz, 1H), 3.00 (s, 1H), 2.73−2.65 (m, 1H), 2.42−2.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.88, 166.11, 165.57, 164.88, 161.07, 137.42, 133.32, 133.21, 133.08, 132.96, 129.88, 129.65, 129.60, 129.56, 128.90, 128.76, 128.50, 128.42, 128.34, 127.92, 126.33, 117.84, 101.69, 100.59, 77.47, 73.10, 72.63, 72.25, 71.81, 71.76, 69.58, 69.46, 68.07, 66.47, 62.84, 34.02, 30.43. Anal. Calcd for $C_{57}H_{50}O_{15}$: C, 70.22; H, 5.17. Found: C, 70.15; H, 5.21.

1-((2,3-Di-*O*-benzoyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-glucopyranosyl)-2-propene (6). To a solution of **5** (171.6 mg, 0.1765 mmol) in CH_2Cl_2 (2.0 mL) were added water (2 drops) and trifluoroacetic acid (204 μL, 2.65 mmol). The reaction mixture was stirred at 25 °C for 5 h, diluted with CH_2Cl_2, washed with water and saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated. Purification via flash chromatography eluting with a gradient of 1:9 to 2:8 EtOAc/CH_2Cl_2 provided **6** as a white foam (124.8 mg, 80%): R_f = 0.40 (1:1 EtOAc/petroleum ether); $[\alpha]^{20}_D$ +86.2° (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05−8.02 (m, 4H), 7.91−7.89 (m, 5H), 7.57−7.52 (m, 4H), 7.47−7.37 (m, 6H), 7.33−7.27 (m, 4H), 7.22−7.18 (m, 2H), 6.04−6.00 (t, J = 7.6 Hz, 1H), 5.78−5.67 (m, 2H), 5.41−5.38 (dd, J = 4.8, 7.8 Hz, 1H), 5.14−5.11 (dd, J = 3.2, 10.0 Hz, 1H), 5.07 (s, 1H), 4.98−4.95 (d, J = 10.0 Hz, 1H), 4.88−4.86 (d, J = 8.0 Hz, 1H), 4.52−4.48 (dd, J = 6.4, 11.8 Hz, 1H), 4.44−4.40 (m, 2H), 4.22−4.21 (d, J = 2.8 Hz, 1H), 4.15−4.10 (m, 1H), 4.03−4.00 (t, J = 6.8 Hz, 1H), 3.54−3.44 (m, 3H), 2.89 (br s, 1H), 2.73−2.65 (m, 1H), 2.43−2.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.88, 165.74, 165.47, 165.16, 133.56, 133.49, 133.23, 133.06, 129.84, 129.75, 129.59, 129.53, 129.39, 129.12, 128.99, 128.90, 128.62, 128.55, 128.29, 128.22, 117.84, 101.98, 76.90, 74.56, 71.29, 70.76, 70.54, 70.11, 69.67, 67.91, 62.73, 62.25, 31.42. Anal. Calcd for $C_{50}H_{46}O_{15}$: C, 67.70; H, 5.23. Found: C, 67.63; H, 5.30.

1-((2,3,6-Tri-*O*-benzoyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-glucopyranosyl)-2-propene (7). To a solution of **6** (148.4 mg, 0.168 mmol) in pyridine (6.0 mL) at 0 °C was added 4-(dimethylamino)pyridine (3.2 mg, 15 mol %). Benzoyl chloride (19.5 μL, 0.168 mmol) was added dropwise. The solution was stirred for 3 h at 0 °C and 15 h at 25 °C. At this time, TLC (1:1 petroleum ether/EtOAc) showed approximately 50% conversion to product. A second equivalent of benzoyl chloride was added, and the reaction mixture was allowed to stir at 25 °C for 20 h. Benzoyl chloride (40 μL, 2.0 eq) was added, and the reaction was stirred for 24 h. After dilution with CH_2Cl_2 the organic layer was washed with water, 1 M HCl, and saturated aqueous $NaHCO_3$, dried, and concentrated. Purification via flash chromatography eluting with 1:1 petroleum ether/EtOAc provided **7** as a white foam (186.7 mg, 100%). R_f = 0.6 (1:1 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +67.8° (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−7.91 (m, 10H), 7.57−7.19 (m, 20H), 6.00−5.96 (t, J = 8.9 Hz, 1H), 5.83−5.68 (m, 2H), 5.49−5.45 (dd, J = 5.8, 9.2 Hz, 1H), 5.24−5.21 (dd, J = 3.1, 10.2 Hz, 1H), 5.12−5.08 (d, J = 17.1 Hz, 1H), 5.00−4.97 (d, J = 10.3 Hz, 1H), 4.90−4.88 (d, J = 7.9 Hz, 1H), 4.55−4.45 (m, 3H), 4.27−4.22 (m, 2H), 4.17−4.07 (m, 2H), 3.84−3.79 (m, 2H), 2.90 (br s, 1H), 2.79−2.71 (m, 1H), 2.43−2.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.94, 165.80, 165.72, 165.53, 165.36, 165.02, 133.30, 133.25, 133.17, 133.11, 133.05, 132.98, 129.75, 129.72, 129.52, 129.48, 128.96, 128.82, 128.76, 128.37, 128.27, 128.23, 128.21, 117.70, 101.49, 76.75, 74.28, 74.28, 72.66, 72.06, 71.11, 70.53, 70.08, 69.64, 66.69, 62.80, 62.17, 30.49. Anal. Calcd for $C_{57}H_{50}O_{16}$: C, 69.08; H, 5.09. Found: C, 68.99; H, 5.37.

1-((2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)−(2,3,6-tri-*O*-benzoyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-glucopyranosyl)-2-propene (9). 7 and **8** were azeotroped with toluene (3 × 5 mL) and dried in vacuo for 15 h prior to use. Molecular sieves (4 Å) (∼20 mg) were added to each flask. To a solution of acceptor **7** (77.0 mg, 0.078 mmol) in CH_2Cl_2 (2 mL, 0.04 M) at −5 °C was added TMSOTf (0.25 equiv, 3.9 μL). A solution of donor **8** (104.6 mg, 2 equiv)

in CH_2Cl_2 (5.2 mL, 0.015 M) was added via cannula over 1.5 h. After the addition, TMSOTf (0.1 equiv, 2 μL) was added and the solution warmed to 25 °C over 6 h. Following the addition of $NaHCO_3$, the solution was filtered and concentrated. Purification via flash chromatography eluting with 3:1 petroleum ether/EtOAc (R_f = 0.3) afforded **9** as a white foam (66.6 mg, 60%): R_f = 0.6 (1:1 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +53.1° (*c* 1.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11−7.01 (m, 50H), 5.94−5.89 (t, *J* = 9.2 Hz, 1H), 5.81−5.65 (m, 2H), 5.51−5.47 (dd, *J* = 5.8, 9.5 Hz, 1H), 5.37−5.34 (dd, *J* = 3.1, 15.2 Hz, 1H), 5.26−5.23 (d, *J* = 11.6 Hz, 1H), 5.19 (s, 1H), 5.13−5.05 (m, 1H), 4.98−4.93 (m, 1H), 4.83−4.81 (d, *J* = 7.5 Hz, 1H), 4.75−4.38 (m, 8H), 4.33−3.93 (m, 9H), 3.65−3.62 (t, *J* = 6.4 Hz, 1H), 3.29−3.24 (t, *J* = 8.8 Hz, 1H), 2.93−2.90 (dd, *J* = 4.0, 8.8 Hz, 1H), 3.26−3.23 (m, 2H), 2.75−2.67 (m, 1H), 2.42−2.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.71, 165.66, 165.63, 165.34, 164.57, 139.21, 138.82, 138.44, 137.75, 133.23, 133.16, 132.98, 130.12, 129.69, 129.56, 128.41, 128.34, 128.22, 128.16, 128.14, 128.07, 127.95, 127.92, 127.58, 127.50, 127.41, 127.37, 127.32, 127.71, 127.01, 117.64, 104.00, 100.98, 81.50, 79.25, 75.86, 75.09, 74.88, 74.78, 73.91, 73.26, 73.18, 72.88, 72.77, 72.52, 72.29, 72.08, 70.87, 70.50, 70.28, 69.91, 68.19, 62.94, 62.78, 30.43, 20.90, 14.08. HRMS *m/e* calcd for $(M - H)^+$ 1511.5505, found 1511.5471.

2,2,2 Trichloroethyl α-Methoxy-*N*-benzyloxycarbonylglycinate (11). 10a (167.6 mg, 0.701 mmol), 2,2,2-trichloroethanol (1.2 equiv, 83.4 μL), and DMAP (0.5 equiv, 42.9 mg) were dissolved in CH_2Cl_2 (3.5 mL) and cooled to 0 °C. DCC (1.2 equiv, 173.4 mg) was added, and the reaction was allowed to warm to 25 °C over 15 h. The reaction was filtered through Celite, diluted with CH_2Cl_2, washed with 1.0 N HCl, water, and saturated Na_2CO_3, and dried. Purification via column chromatography eluting with 2:1 petroleum ether/EtOAc afforded **11** as a pale yellow oil (190 mg, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.32 (m, 5H), 6.04−6.02 (br d, *J* = 8.0, 1H), 5.49−5.46 (d, *J* = 7.2, 1H), 5.15 (s, 2H), 4.81 (s, 2H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.09, 155.46, 135.56, 128.49, 128.31, 128.10, 93.97, 80.55, 74.49, 67.42, 56.56.

2,2,2-Trichloroethyl α-(Dimethoxyphosphoryl)-*N*-benzyloxycarbonylglycinate (12). 11 was azeotroped with toluene and dried in vacuo for 15 h prior to use. **11** (5.00 g, 13.5 mmol) was dissolved in $PhCH_3$ (135 mL), and the solution was heated to 70 °C. PCl_3 (1 equiv, 1.18 mL) was added, and the solution was stirred at 70 °C for 15 h. $P(OMe)_3$ (1 equiv, 1.60 mL) was added, and the reaction was stirred for 2 h before removal of solvent by rotary evaporation. The residue was diluted with CH_2Cl_2 and washed with water, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried ($MgSO_4$) and concentrated. Recrystallization from EtOH yielded **12** (3.726 g, 71% yield) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.30 (m, 5H), 5.80−5.78 (br d, *J* = 6.0 Hz, 1H), 5.15 (s, 2H), 5.12−5.07 (m, 1H), 5.03−5.01 (d, *J* = 8.0 Hz, 1H), 4.90−4.87 (d, *J* = 12.0 Hz, 1H), 4.80−4.77 (d, *J* = 12.0 Hz, 1H), 3.85 (s, 1H), 3.84 (s, 2H), 3.82 (s, 1H), 3.81 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.64, 128.52, 128.34, 128.12, 75.01, 74.57, 67.75, 54.28, 54.03, 52.77, 51.29.

2-(Trimethylsilyl)ethyl α-Methoxy-*N*-benzyloxycarbonylglycinate (14). 10b was azeotroped with toluene and dried under high vacuum for 15 h prior to use. To a solution of **10b** (325 mg, 1.36 mmol), DMAP (0.5 equiv, 140 mg), and 2-(trimethylsilyl)ethanol (2 equiv, 0.400 mL) in CH_2Cl_2 (0.2 M, 7 mL) at 0 °C was added DCC (1.2 equiv, 199 mg). The reaction was allowed to warm to 25 °C over 15 h. The solution was filtered through Celite, concentrated, and purified via flash chromatography eluting with 3:1 petroleum ether/EtOAc to afford **14** (224.8 mg, 50%) as a colorless oil: R_f = 0.5 (1:3 EtOAc/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.29 (m, 5H), 6.03−6.01 (br d, *J* = 9.2 Hz, 1H), 5.33−5.30 (br d, *J* = 9.2 Hz, 1H), 5.14 (s, 2H), 4.27−4.25 (m, 2H), 3.45 (s, 3H), 1.06−1.02 (m, 2H), 0.042 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.51, 155.62, 135.71, 128.43, 128.19, 128.03, 80.66, 67.18, 64.51, 56.07, 17.15, −1.69; HRMS (FAB) calcd for $(M + Na)^+$ $C_{15}H_{23}NO_5SiNa$ 348.1243, found 348.1237.

2-(Trimethylsilyl)ethyl α-(Dimethoxyphosphoryl)-*N*-benzyloxycarbonylglycinate (15). 14 was azeotroped with toluene and dried in vacuo for 15 h prior to use. **14** (3.641 g, 10.7 mmol) was dissolved in toluene (135 mL) and heated to 70 °C before the addition of PCl_3 (1.0 equiv, 0.934 mL). The reaction was stirred for 15 h before the dropwise addition of $P(OMe)_3$ (1.0 equiv, 1.26 mL). The reaction was stirred for 2 h before removal of the solvent by rotary evaporation. The residue was dissolved in CH_2Cl_2, washed with saturated $NaHCO_3$, dried ($MgSO_4$), and concentrated. Purification via flash chromatography eluting with a gradient of 2:1 to 1:1 petroleum ether/EtOAc provided **15** (3.826 g, 88%) as a colorless oil: R_f = 0.10 (1:2 EtOAc/petroleum ether); ^{1}H NMR (400 MHz, CDCl3) δ 7.50−7.45 (m, 5H), 5.75−5.73 (br d, *J* = 8.0 Hz, 1H), 5.28−5.27 (m, 2H), 5.06−4.98 (dd, *J* = 9.2, 14.8 Hz, 1H), 4.47−4.42 (m, 2H), 3.97 (s, 2H), 3.94 (s, 1H), 3.93 (s, 2H), 3.91 (s, 1H), 1.41−1.17 (m, 2H), 0.179 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.65, 155.55, 135.78, 128.21, 128.44, 128.04, 67.48, 65.14, 54.02, 53.96, 52.90, 51.43, 18.25, −1.68. Anal. Calcd for $C_{17}H_{28}NO_7PSi$: C, 48.91; H, 6.76; N, 3.36. Found: C, 48.85; H, 6.82; N, 3.31.

2-(Trimethylsilyl)ethyl α-(Dimethoxyphosphoryl)-*N*-*tert*-butyloxycarbonylglycinate (16). To a solution of **15** (95.3 mg, 0.228 mmol) in anhydrous MeOH (3.0 mL) was added Boc_2O (1.5 equiv, 75 mg). The solution was degassed with argon for 20 min before the addition of 10% Pd/C (5 mol %, 12.1 mg). The vessel was pressurized to 90 psi of H_2 and stirred vigorously for 15 h. The reaction was filtered through Celite and concentrated. Purification via flash chromatography eluting with a gradient of 1:1 to 2:1 EtOAc/petroleum ether provided **16** (60.6 mg, 98%) as a white solid: R_f = 0.60 (1:1 EtOAc/petroleum ether), visualized with $KMnO_4$; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33−5.31 (br d, *J* = 8.0 Hz, 1H), 4.82−4.74 (dd, *J* = 9.2, 22.4 Hz, 1H), 4.27−4.23 (m, 2H), 3.79 (s, 2H), 3.78 (s, 1H), 3.76 (s, 2H), 3.75 (s, 1H), 1.39 (s, 9H), 1.03 (m, 2H), −0.01 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.91, 80.73, 64.97, 53.93, 53.86, 52.48, 51.01, 28.10, 17.26, −1.67. Anal. Calcd for $C_{14}H_{30}NO_7PSi$: C, 43.98; H, 7.89; N, 3.54. Found: C, 43.98; H, 7.90; N, 3.54.

1-((2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-(β-D-galactopyranosyl)-(1→4)-α-D-glucopyranosyl)-2-propene (18). To a solution of **9** (275.2 mg, 0.182 mmol) in anhydrous MeOH (2.0 mL) and THF (2.5 mL) was added K_2CO_3 (20 mg, 0.8 equiv). The reaction was stirred at 25 °C for 15 h, filtered through Celite, and concentrated. Purification via flash chromatography eluting with 15% MeOH/85% CH_2Cl_2 afforded **18** as a colorless oil (154.6 mg, 96%): R_f = 0.7 (20% MeOH/80% CH_2Cl_2); $[\alpha]^{20}_D$ 13.2 (*c* 0.80, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD) δ 7.31−7.14 (m, 20H), 5.83−5.73 (m, 1H), 5.06−5.01 (d, *J* = 17.2 Hz, 1H), 4.98−4.96 (d, *J* = 10 Hz, 1H), 4.93−4.92 (d, *J* = 2.4 Hz, 1H), 4.76−4.62 (m, 5H), 4.46−4.29 (m, 5H), 3.95−3.85 (m, 5H), 3.81−3.66 (m, 5H), 3.64−3.52 (m, 5H), 3.5−3.39 (m, 5H); ^{13}C NMR (100 MHz, CD_3OD) δ 140.00, 139.60, 139.42, 136.43, 134.20, 130.45, 129.56, 129.40, 129.29, 129.20, 129.10, 128.78, 128.61, 116.98, 105.40, 101.21, 82.02, 80.24, 79.82, 77.67, 76.87, 76.65, 76.25, 75.88, 74.82, 74.71, 74.37, 73.57, 72.83, 72.70, 72.59, 71.33, 69.78, 62.25, 62.04, 30.53; HRMS *m/e* calcd for $(M + H)^+$ 889.3932, found 889.4040.

1-((2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl)-2-propene (19). To a solution of **18** (141.8 mg, 0.160 mmol) in pyridine (3.5 mL) were added Ac_2O (0.20 mL, 12 equiv) and DMAP (0.5 equiv, 17 mg). The reaction was stirred for 15 h, diluted with CH_2Cl_2, and washed with 1 M HCl and saturated $NaHCO_3$. Purification via flash chromatography eluting with 2:1 petroleum ether/EtOAc provided **19** (169.5 mg, 93%) as a colorless foam: R_f = 0.6 (1:1 petroleum ether/EtOAc); $[\alpha]^{20}_D$ 41.9 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.22 (m, 20H), 5.78−5.68 (m, 1H), 5.34−5.30 (t, *J* = 9.2 Hz, 1H), 5.18−5.08 (m, 3H), 5.01−4.97 (dd, *J* = 5.6, 9.2 Hz, 1H), 4.93−4.90 (d, *J* = 11.2 Hz, 1H), 4.83−4.75 (m, 4H), 4.69−4.66 (d, *J* = 11.6 Hz, 1H), 4.57−4.55 (d, *J* = 11.2 Hz, 1H), 4.51−4.36 (m, 5H), 4.31−4.27 (m, 2H), 4.21−4.16 (m, 2H), 4.13−4.03 (m, 2H), 3.99−3.98 (d, *J* = 2.4 Hz, 1H), 3.79−3.75 (m, 1H), 3.69−3.60 (m, 4H), 3.45−3.42 (m, 2H), 2.61−2.45 (m, 1H), 2.37−2.22 (m, 1H), 2.09 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 1.92 (s, 3H), 1.87 (s, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 170.66, 170.39, 170.32, 169.87, 169.81, 169.80, 138.78, 138.71, 138.12, 137.93, 133.13, 128.41, 128.29, 128.26, 128.20, 128.09, 128.05, 127.95, 127.62, 127.59, 127.37, 127.29, 117.63, 101.31, 101.26, 79.17, 76.58, 75.86, 75.40, 74.91, 74.58, 74.12, 73.29, 72.82, 72.52, 72.37, 71.70, 70.11, 69.90, 67.56, 62.30, 61.19, 30.72, 20.79, 20.73, 20.68, 20.57. Anal. Calcd for $C_{61}H_{72}O_{22}$: C, 64.20; H, 6.36. Found: C, 63.93; H, 6.41.

2-(Trimethylsilyl)ethyl 1-((2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl)-2-ene-2-(*N*-*tert*-butyloxycarbonyl)butenoate (20). 19 was dried under high vacuum for 15 h prior to use. To a solution of **19** (114.6 mg, 0.127 mmol) in distilled CH_2Cl_2 (8.0 mL) and anhydrous MeOH (4.0 mL) was added solid $NaHCO_3$ (~200 mg). The solution was cooled to −78 °C under argon. O_3 was bubbled through the solution until a blue color persisted for 10 min. The solution was then purged with O_2 for 15 min followed by argon for 15 min. Me_2S (0.50 mL) was added to the reaction and allowed to warm to 25 °C over 15 h. The solution was filtered through Celite and concentrated. Purification via flash chromatography eluting with 1:1 petroleum ether/EtOAc provided the aldehyde (108.7 mg, 75%) as a white foam: R_f = 0.25 (1:1 petroleum ether/EtOAc); (select NMR data) ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.67, 170.62, 170.26, 169.88, 169.77, 169.62, 168.65, 138.74, 138.66, 138.07, 137.86, 137.29, 132.56, 129.66, 128.39, 128.34, 128.22, 128.17, 128.15, 128.06, 128.01, 127.9., 127.85, 127.71, 127.60, 127.57, 127.34, 127.23, 101.28, 100.95, 79.11, 79.04, 76.79, 76.07, 75.91, 75.79, 75.29, 74.87, 74.53, 74.13, 73.44, 73.25, 72.74, 72.67, 72.55, 72.46, 72.26, 71.50, 71.22, 69.57, 69.45, 69.02, 67.50, 67.31, 66.95, 62.06, 61.76, 61.15, 60.99, 20.73, 20.52, 18.98. **16** was azeotroped with toluene (3 × 15 mL) and stored under high vacuum for 15 h prior to use. To a solution of **16** (695 mg, 1.5 equiv) in THF (15.0 mL) at −78 °C was added TMG (1.5 equiv, 228 μL). The solution was stirred at −78 °C for 10 min before the addition of the aldehyde (1.377 g, 1.21 mmol) in THF (15.0 mL) via cannula. After 4 h, the reaction was diluted with CH_2Cl_2, washed with 1 N HCl and saturated $NaHCO_3$, dried, and concentrated. Purification via chromatography eluting with a gradient of 2:1 to 1:1 to 1:2 petroleum ether/EtOAc provided **20** (1.080 g, 65%) as a colorless film: R_f = 0.6 (1:1 petroleum ether/EtOAc); $[\alpha]^{20}_D$ 33.6 (*c* 1.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98−7.13 (m, 20H), 6.40 (br s, 2H), 5.15−5.10 (m, 2H), 4.93−4.90 (d, *J* = 11.2 Hz, 1H), 4.84−4.79 (m, 2H), 4.78−4.74 (m, 2H), 4.69−4.66 (d, *J* = 11.6 Hz, 1H), 4.57−4.54 (d, *J* = 11.2 Hz, 1H), 4.46−4.39 (m, 2H), 4.28−4.24 (m, 2H), 4.16−4.04 (m, 4H), 3.98−3.97 (d, *J* = 2.1 Hz, 1H), 3.97−3.86 (m, 4H), 3.68−3.60 (m, 2H), 3.57−3.54 (m, 3H), 3.44−3.41 (dd, *J* = 5.2, 8.6 Hz, 2H), 2.49−2.42 (m, 2H,), 2.39−2.29 (m, 2H), 2.14 (s, 3H), 1.044 (s, 3H), 2.040 (s, 3H), 2.03 (s, 3H), 1.87 (s, 3H), 1.86 (s, 3H), 1.45 (s, 9H), 1.07−1.02 (m, 2H) 0.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.70, 170.54, 170.33, 170.02, 169.80, 168.76, 164.65, 153.08, 138.82, 138.75, 138.16, 137.94, 129.74, 128.42, 128.61, 128.29, 128.23, 128.14, 128.10, 128.01, 127.67, 127.64, 127.42, 127.35, 101.36, 101.12, 80.44, 79.12, 76.83, 76.47, 75.97, 75.37, 74.95, 74.62, 74.19, 73.71, 73.34, 72.82, 72.55, 72.34, 71.53, 69.64, 69.56, 67.59, 63.72, 62.29, 61.08, 29.96, 29.68, 28.15, 20.84, 20.77, 20.68, 20.60, 17.35, −1.53; HRMS *m/e* calcd for $C_{72}H_{92}NO_{25}Si$ $(M - H)^+$ 1398.5727, found 1398.5756. Anal. Calcd for $C_{72}H_{93}NO_{25}Si\cdot H_2O$: C, 60.96; H, 6.75; N, 0.99. Found: C, 60.75; H, 6.82; N, 0.96.

(2*S*)-(Trimethylsilyl)ethyl 1-((2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl)-2-(*N*-*tert*-butyloxycarbonyl)butanoate (21). In a drybox, [(COD)Rh−((*S*,*S*)-Et-DuPHOS)]$^+$OTf$^-$ catalyst precursor (1 mg, 0.0014 mmol) and **20** (25.0 mg0.018 mmol) were dissolved in deoxygenated anhydrous THF (3.0 mL) in a Fischer−Porter tube. The reaction vessel was pressurized with 90 psi of H_2 after five vacuum/H_2 cycles and stirred at 25 °C for 48 h. The vessel was then depressurized and the mixture concentrated. The product was purified via flash chromatography eluting with 3:1 petroleum ether/EtOAc to yield **21** as a colorless oil (25 mg, 98%, >95% de): R_f = 0.5 (1:1 EtOAc/petroleum ether); $[\alpha]^{20}_D$ +50.2° (*c* 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25−7.01 (m, 20H), 5.12−5.07 (t, *J* = 9.0 Hz, 1H), 5.00−4.98 (d, *J* = 7.5 Hz, 1H), 4.97−4.94 (d, *J* = 7.5 Hz, 1H), 4.80−4.77 (m, 1H), 4.75−4.71 (d, *J* = 11.4 Hz, 1H), 4.64−4.47 (m, 6H), 4.40−4.36 (d, *J* = 11.4 Hz, 1H), 4.27−4.22 (m, 7H), 4.18−4.18 (d, *J* = 2.4 Hz, 1H), 4.13−4.01 (m, 3H), 3.97−3.87 (m, 7H), 3.81−3.80 (d, *J* = 2.7 Hz, 1H), 3.54−3.40 (m, 5H), 3.27−3.23 (dd, *J* = 4.8, 8.4 Hz, 1H), 1.93 (s, 3H), 1.87 (s, 3H), 1.85 (s, 3H), 1.83 (s, 3H), 1.74 (s, 3H), 1.68 (s, 3H), 1.26 (s, 9H), 0.85−0.79 (m, 2H), −0.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.07, 170.36, 170.02, 169.53, 169.44, 168.41, 154.96, 138.58, 138.50, 137.91, 137.74, 128.23, 128.04, 127.89, 127.85, 127.74, 127.38, 127.08, 101.25, 101.18, 79.66, 79.07, 76.38, 75.76, 75.31, 74.82, 74.52, 74.03, 73.18, 72.75, 72.44, 72.31, 71.93, 69.96, 69.45, 67.48, 63.70, 62.11, 61.11, 53.17, 28.49, 28.23, 21.72, 20.73, 20.58, 17.39, −1.53. Anal. Calcd for $C_{72}H_{95}NO_{25}Si\cdot H_2O$: C, 60.87; H, 6.88; N, 0.99. Found: C, 60.77; H, 6.79; N, 1.02.

(2*R*)-(Trimethylsilyl)ethyl 1-((2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl)-2-(*N*-*tert*-butyloxycarbonyl)butanoate (22). In a drybox, [(COD)Rh−((*R*,*R*)-Et-DuPHOS)]$^+$OTf$^-$ catalyst precursor (1 mg, 0.0014 mmol) and **20** (25.0 mg, 0.018 mmol) were dissolved in deoxygenated anhydrous THF (3.0 mL) in a Fischer−Porter tube. The reaction vessel was pressurized with 90 psi of H_2 after five vacuum/H_2 cycles and stirred at 25 °C for 48 h. The vessel was then depressurized and the mixture concentrated. The product was purified via flash chromatography eluting with 3:1 petroleum ether/EtOAc to yield **22** as a colorless oil (22 mg, 88%, >95% de): R_f = 0.5 (1:1 EtOAc/petroleum ether); $[\alpha]^{20}_D$ +42.2° (*c* 0.93, $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.17 (m, 20H), 5.14−5.06 (m, 2H), 4.91−4.89 (d, *J* = 11.2 Hz, 1H), 4.82−4.81 (d, *J* = 2.0 Hz, 1H), 4.77−4.73 (m, 2H), 4.64−4.57 (m, 6H), 4.55−4.52 (d, *J* = 10.8 Hz, 1H), 4.47−4.37 (m, 6H), 4.28−4.24 (dd, *J* = 5.2, 8.8 Hz, 1H), 4.21−4.14 (m, 5H), 4.05−4.01 (m, 5H), 3.96−3.95 (d, *J* = 2.8 Hz, 1H), 3.65−3.58 (m, 5H), 3.42−3.39 (dd, *J* = 4.8, 12.4 Hz, 1H), 2.11 (s, 3H), 2.02 (s, 6H), 2.00 (s, 3H), 1.85 (s, 3H), 1.54 (s, 3H), 1.42 (s, 9H), 1.01−0.96 (m, 2H), 0.03 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.73, 170.45, 170.36, 170.09, 169.80, 168.78, 138.84, 138.77, 138.17, 137.96, 128.42, 128.33, 128.30, 128.25, 128.15, 128.11, 128.03, 127.69, 127.65, 127.44, 127.38, 101.38, 101.14, 79.14, 76.89, 76.00, 75.42, 74.97, 74.66, 74.22, 73.95, 73.35, 72.87, 72.57, 72.34, 72.05, 69.66, 69.55, 67.61, 63.71, 62.49, 61.10, 53.42, 28.33, 28.14, 27.50, 20.85, 20.73, 20.63, 17.40, −1.53. Anal. Calcd for $C_{72}H_{95}NO_{25}Si\cdot H_2O$ C, 60.87; H, 6.88; N, 0.99. Found: C, 60.98; H, 6.78; N, 1.01.

(2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α,*β*-D-glucopyranose (24). A solution of **23** (15.6 g, 16.0 mmol) in EtOH (70 mL), toluene (30 mL), and water (10 mL) was heated to 70 °C. $Rh(PPh_3)_3Cl$ (0.1 equiv, 1.6 g) and DABCO (0.25 equiv, 475 mg) were added. The reaction was heated to reflux for 24 h. The mixture was cooled to 25 °C and concentrated. Filtration through a short plug of SiO_2 followed by concentration provided an orange foam that was dissolved in wet acetone (0.1 M, 170 mL). HgO (0.04 equiv, 150.0 mg) was added followed by $HgCl_2$ (0.25 equiv, 1.15 g). The reaction was stirred at 25 °C for 24 h before dilution with CH_2Cl_2. The organic layer was washed with water and saturated aqueous KI, dried, and concentrated. Purification via flash chromatography eluting with 2:1 petroleum ether/EtOAc afforded **24** as a colorless foam (10.0 g, 67% yield): R_f = 0.20 (1:2 EtOAc/petroleum ether); $[\alpha]^{20}_D$ +20.7° (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.16 (m, 30H), 5.45−5.44 (d, *J* = 6.4 Hz, 1H), 5.24−5.16 (m, 2H), 4.89−4.71 (m, 6H), 4.69−4.61 (m, 2H), 4.54−4.48 (t, *J* = 12.0 Hz, 1H), 4.40−4.34 (dd, *J* = 7.6, 17.2 Hz, 1H), 4.26−4.18 (m, 2H), 4.00−3.91 (m, 3H), 3.85−3.72 (m, 2H), 3.66−3.52 (m, 2H), 3.38−3.30 (m, 2H), 2.91−2.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.96, 138.79, 138.71, 138.46, 138.36, 138.28, 138.18, 138.09, 138.03, 128.77, 128.68, 128.48, 128.33, 128.28, 128.21, 128.15, 128.04, 128.01, 127.93, 127.75, 127.72, 127.64, 127.61, 127.48, 127.37, 127.22, 126.48, 108.85, 102.88, 102.80, 101.27, 97.91, 97.23, 91.15, 82.83, 82.70, 79.97, 79.53, 79.38, 79.24,

78.70, 77.55, 77.39, 77.01, 76.69, 75.83, 75.62, 75.20, 74.78, 73.60, 73.51, 72.92, 71.50, 70.21, 68.86, 68.27, 66.23, 63.76, 60.34. Anal. Calcd for $C_{54}H_{56}O_{11}\cdot 2H_2O$: C, 70.71; H, 6.60. Found: C, 70.80; H, 6.29.

(2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-D-glucuronic Acid (25). To a solution of DMSO (3.6 mL) and Ac_2O (2.5 mL) was added **24** (10.0 g, 11.4 mmol), and the solution was stirred at 25 °C for 20 h. The reaction was diluted with CH_2Cl_2, washed with water, dried ($MgSO_4$), and concentrated to provide **25** as a colorless foam (9.5 g, 95%), which was used without further purification: R_f = 0.2 (1:2 EtOAc/petroleum ether); $[\alpha]^{20}_D$ +50.8° (*c* 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.18 (m, 30H), 5.47 (s, 1H), 4.85−4.83 (d, *J* = 6.0 Hz, 1H), 4.82−4.80 (d, *J* = 5.2 Hz, 1H), 4.77 (s, 1H), 4.73 (s, 1H), 4.71 (s, 1H), 4.68 (s, 1H), 4.61−4.56 (m, 3H), 4.49−4.46 (d, *J* = 11.6 Hz, 1H), 4.43−4.41 (d, *J* = 7.6 Hz, 1H), 4.36−4.33 (d, *J* = 12.0 Hz, 1H), 4.23−4.2 (dd, *J* = 4.0, 9.0 Hz, 1H), 4.13−4.09 (m, 3H), 4.06−4.06 (d, *J* = 3.4 Hz, 1H), 3.90−3.86 (dd, *J* = 1.6, 12.4 Hz, 1H), 3.80−3.75 (m, 2H), 3.73−3.72 (d, *J* = 3.6 Hz, 1H), 3.64−3.61 (dd, *J* = 2.4, 10.8 Hz, 1H), 3.45−3.42 (dd, *J* = 3.6, 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.76, 166.31, 138.49, 138.17, 137.86, 137.69, 136.76, 128.88, 128.36, 128.31, 128.25, 128.22, 128.11, 128.07, 127.97, 127.84, 127.74, 127.70, 127.64, 127.58, 127.54, 127.51, 126.39, 103.53, 101.15, 79.76, 76.27, 78.28, 77.91, 76.64, 75.32, 73.37, 73.16, 73.08, 72.91, 71.61, 68.87, 67.96, 66.33, 22.07.

1-Hydroxy-1-((2,3-di-*O*-benzyl-4,6-*O*-benzylidene-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-2-propene (26). 25 was azeotroped with toluene and stored under vacuum for 15 h prior to use. To a solution of **25** (12.1 g, 13.7 mmol) in THF (137 mL) at −78 °C was added a solution of 1.0 M allylmagnesium bromide (1.5 equiv, 21.0 mL). The solution was stirred for 2 h at −78 °C. Water was added and the mixture allowed to stir for 20 min before extraction with EtOAc. Purification via flash chromatography eluting with 2:1 petroleum ether/EtOAc afforded **26** (11.2 g, 89% yield) as a colorless oil: R_f = 0.6 (1:2 EtOAc/petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.16 (m, 30H), 5.91−5.80 (m, 1H), 5.46 (s, 1H), 5.34−5.31 (d, *J* = 10.8 Hz, 1H), 5.17−5.15 (d, *J* = 10.0 Hz, 1H), 5.13−5.09 (d, *J* = 17.2 Hz, 1H), 5.01−4.98 (d, *J* = 11.2 Hz, 1H), 4.81 (s, 2H), 4.73 (s, 2H), 4.69−4.66 (m, 4H), 4.65−4.63 (d, *J* = 11.2 Hz, 1H), 4.60−4.57 (d, *J* = 12.0 Hz, 1H), 4.52−4.50 (d, *J* = 7.6 Hz, 1H), 4.38−4.35 (d, *J* = 12.4 Hz, 1H), 4.29−4.26 (d, *J* = 12.4 Hz, 1H), 4.08−3.87 (m, 6H), 3.80−3.75 (m, 1H), 3.60−3.57 (d, *J* = 11.6 Hz, 1H), 3.47−3.45 (d, *J* = 8.8 Hz, 1H), 3.42−3.39 (dd, *J* = 4.0, 9.8 Hz, 1H), 2.89 (br s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 132.36, 128.96, 128.81, 128.32, 128.17, 128.04, 128.00, 127.89, 127.67, 127.45, 127.31, 126.57, 119.80, 102.72, 101.45, 97.43, 82.15, 80.79, 79.50, 78.90, 75.97, 75.35, 73.86, 72.93, 71.72, 71.60, 68.97, 68.12, 66.38, 43.07. Anal. Calcd for $C_{57}H_{60}O_{11}$: C, 74.31; H, 6.57. Found: C, 74.02; H, 6.59.

1-((2,3,6-Tri-*O*-benzyl-α-D-galactopyranosyl)-(1→4)−(2,3,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-2-propene (27). 26 (3.44 g, 3.7 mmol) was azeotroped with toluene and stored under vacuum for 15 h prior to use. To a solution of **26** in CH_2Cl_2 (0.08 M, 45.0 mL) at −78 °C were added Et_3SiH (3.55 mL, 6 equiv) and $BF_3\cdot Et_2O$ (1.89 mL, 4 equiv). The reaction was stirred at −78 °C for 5 h. Saturated aqueous $NaHCO_3$ was added, and the solution was extracted with CH_2Cl_2. Purification via flash chromatography eluting with 3:1 petroleum ether/EtOAc provided **27** (2.463 g, 73%) as a colorless amorphous solid: R_f = 0.5 (1:3 EtOAc/petroleum ether); $[\alpha]^{20}_D$ +8.5° (*c* 0.69, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.18 (m, 30H), 5.96−5.85 (m, 1H), 5.13−5.10 (d, *J* = 10.8 Hz, 1H), 5.06−5.04 (d, *J* = 10.8 Hz, 1H), 4.82−4.79 (d, *J* = 11.2 Hz, 1H), 4.77−4.75 (d, *J* = 11.2 Hz, 1H), 4.72−4.64 (m, 3H), 4.60−4.59 (d, *J* = 4.8 Hz, 1H), 4.58−4.56 (d, *J* = 6.0 Hz, 2H), 4.49−4.44 (m, 2H), 4.42−4.41 (d, *J* = 4.4 Hz, 1H), 4.39−4.38 (d, *J* = 4.0 Hz, 1H), 4.01−3.97 (m, 2H), 3.38−3.79 (dd, *J* = 3.6, 7.6 Hz, 1H), 3.69−3.58 (m, 4H), 3.51−3.47 (dd, *J* = 5.2, 9.6 Hz, 1H), 3.39−3.25 (m, 6H), 2.59−2.54 (m, 1H), 2.32−2.25 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 139.09, 138.54, 138.40, 138.25, 137.90, 134.78, 128.38, 128.32, 128.29, 128.19, 127.84, 127.76, 127.67, 127.60, 127.56, 127.49, 127.32, 127.21, 116.88, 102.43, 85.39, 81.02, 80.87, 79.42, 79.26, 78.75, 75.26, 75.02, 73.45, 73.02, 72.84, 72.02, 68.36, 68.24, 66.14, 36.05.

1-((2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-2-propene (28). 8 and **27** were azeotroped with toluene and dried under vacuum for 15 h prior to use. To a solution of **27** (114.7 mg, 0.127 mmol) in Et_2O (3.1 mL) at 0 °C were added 4 Å molecular sieves (25 mg) and TMSOTf (0.25 equiv, 6.3 μL). A suspension of **8** (2 equiv, 170.4 mg) and 4 Å molecular sieves (50 mg) in Et_2O (8.5 mL) was added over 1 h. The reaction was warmed to 25 °C and stirred for an additional 4 h. The reaction was quenched by the addition of NEt_3, filtered through Celite, and concentrated. Purification via chromatography eluting with 5:1 petroleum ether/EtOAc afforded **28** (115 mg, 64%) as a colorless foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.03 (m, 50H), 5.94−5.73 (m, 1H), 5.20−5.17 (d, *J* = 10.8 Hz, 1H), 5.11−5.03 (m, 2H), 4.86−4.66 (m, 8H), 4.63−4.29 (m, 10H), 4.19−4.13 (m, 1H), 4.10−3.82 (m, 7H), 3.73−3.46 (m, 7H), 3.37−3.22 (m, 6H), 3.19−3.15 (dd, *J* = 4.8, 8.4 Hz, 1H), 2.56−2.53 (m, 1H,), 2.30−2.23 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.23, 138.97, 138.90, 138.80, 138.77, 138.69, 138.56, 138.10, 134.93, 128.75, 128.55, 128.52, 128.36, 128.26, 128.09, 127.96, 127.89, 127.83, 127.80, 127.73, 127.59, 127.56, 127.46, 127.40, 127.35, 127.11, 116.84, 102.73, 100.63, 93.59, 85.14, 83.43, 81.70, 81.13, 80.85, 79.56, 79.45, 79.34, 78.80, 78.72, 76.06, 75.27, 75.19, 75.10, 75.02, 74.86, 73.72, 73.56, 73.45, 73.18, 73.08, 73.03, 72.76, 72.44, 72.20, 69.73, 69.49, 68.99, 68.37, 67.93, 36.10.

2-(Trimethylsilyl)ethyl 1-((2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-2-ene-2-(*N*-*tert*-butyloxycarbonyl)butenoate (29). To a solution of **28** (90.1 mg, 0.063 mmol) in CH_2Cl_2 (8.0 mL) and anhydrous MeOH (4.0 mL) was added $NaHCO_3$ (100 mg). The solution was cooled to −78 °C, and O_3 was bubbled through until a blue color persisted for 10 min. The solution was purged with O_2 for 10 min and argon for 20 min before addition of Me_2S (1.0 mL). The reaction was allowed to warm to 25 °C over 15 h, then filtered, and concentrated. Purification via chromatography eluting with a gradient of 5:1 to 4:1 petroleum ether/EtOAc provided the aldehyde (63.4 mg, 69%) as a clear oil. The aldehyde was used immediately (R_f = 0.2 (4:1 petroleum ether/EtOAc)). **16** was azeotroped with toluene and stored under high vacuum for 15 h prior to use. To a solution of **16** (946.0 mg, 1.3 equiv) in THF (19.0 mL) at −78 °C was added tetramethylguanidine (312 μL, 1.3 equiv). The mixture was stirred for 15 min before the addition of a solution of the aldehyde (2.719 g, 1.90 mmol) in THF (19.0 mL). The solution was warmed to 25 °C. After 5 h, the reaction was diluted with CH_2Cl_2, washed with 1 N HCl and saturated $NaHCO_3$, dried ($MgSO_4$), and concentrated. Purification via chromatography eluting with 4:1 petroleum ether/EtOAc afforded **29** (2.702 g, 84%) as a colorless foam: R_f = 0.4 (4:1 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +12.6° (*c* 1.05, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.01 (m, 50H), 6.55 (s, 1H), 6.36 (br s, 1H), 5.17−5.13 (d, *J* = 11.1 Hz, 1H), 5.04−5.02 (d, *J* = 3.6 Hz, 1H), 4.84−4.65 (m, 6H), 4.57−4.53 (d, *J* = 12.0 Hz, 1H), 4.49−4.39 (m, 6H), 4.34−4.29 (m, 4H), 4.23−4.17 (m, 2H), 4.14−4.04 (m, 4H), 4.02−3.79 (m, 7H), 3.63−3.51 (m, 4H), 3.49−3.43 (t, *J* = 8.7 Hz, 1H), 3.33−3.31 (m, 2H), 3.28−3.24 (dd, *J* = 2.4, 9.9 Hz, 1H), 3.21−3.13 (m, 3H), 2.66−2.59 (m, 1H), 2.39−2.30 (m, 1H), 1.39 (s, 9H), 1.26−1.00 (m, 2H), 0.02 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.72, 153.09, 138.94, 138.79, 138.58, 138.50, 138.38, 138.20, 138.03, 137.90, 129.59, 128.64, 128.25, 128.14, 127.98, 127.69, 127.61, 127.46, 127.32, 126.98, 102.64, 100.56, 84.71, 81.56, 80.60, 80.19, 79.43, 78.91, 78.45, 75.23, 75.07, 74.82, 73.71, 73.36, 73.16, 73.06, 72.41, 72.11, 69.46, 68.24, 67.85, 63.48, 30.37, 28.27, 17.37, −1.34. Anal. Calcd for $C_{102}H_{117}NO_{19}Si$: C, 72.53; H, 6.98; N, 0.83. Found: C, 72.52; H, 7.02; N, 0.92.

(2*R*)-(Trimethylsilyl)ethyl 1-((2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-*β*-D-glucopyra-

nosyl)-2-ene-2-(*N*-*tert*-butyloxycarbonyl)butanoate (30). In a drybox, [(COD)Rh−((*R*,*R*)-Et-DuPHOS)]$^+$OTf$^-$ catalyst precursor (1 mg, 0.0014 mmol) and **29** (940 mg, 0.56 mmol) were dissolved in deoxygenated anhydrous THF (3 mL) in a Fischer−Porter tube. The reaction vessel was pressurized to 90 psi of H_2 after five vacuum/H_2 cycles and stirred at 25 °C for 48 h. The vessel was then depressurized and the mixture concentrated. The product was purified via flash chromatography eluting with 3:1 petroleum ether/EtOAc to yield **30** as a clear oil (920 mg, 98%, >95% de): R_f = 0.4 (4:1 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +16.5° (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−6.87 (m, 50H), 5.01−4.97 (d, *J* = 11.0 Hz, 1H), 4.92−4.89 (d, *J* = 8.5 Hz, 1H), 4.88−4.87 (d, *J* = 3.3 Hz, 1H), 4.69−4.50 (m, 9H), 4.39−4.35 (d, *J* = 12.0 Hz, 1H), 4.32−4.25 (m, 6H), 4.24−4.20 (d, *J* = 9.9 Hz, 1H), 4.24−4.12 (m, 5H), 4.04−3.79 (m, 6H), 3.75−3.74 (t, *J* = 2.1 Hz, 1H), 3.71−3.70 (d, *J* = 2.7 Hz, 1H), 3.68−3.63 (m, 2H), 3.50−3.36 (m, 4H), 3.35−3.33 (d, *J* = 6.3 Hz, 1H), 3.30−3.27 (d, *J* = 8.7 Hz, 1H), 3.18−3.12 (m, 2H), 3.10−3.09 (d, *J* = 2.4 Hz, 1H), 3.06 (br s, 1H), 2.99−2.97 (m, 4H), 1.22 (s, 9H), 0.82−0.75 (m, 2H); −0.16 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.69, 170.97, 155.23, 138.99, 138.77, 138.61, 138.35, 138.25, 138.08, 137.87, 128.64, 128.14, 127.98, 127.70, 127.61, 127.46, 127.34, 126.97, 102.59, 100.62, 84.91, 81.61, 81.26, 79.58, 79.42, 79.16, 78.87, 75.26, 75.09, 74.83, 74.75, 73.68, 73.28, 73.15, 73.02, 72.37, 72.09, 69.41, 68.31, 67.79, 63.56, 60.42, 53.62, 28.95, 28.39, 27.83, 21.16, 17.43, 14.31, −1.38. Anal. Calcd for $C_{102}H_{119}NO_{19}Si$: C, 72.44; H, 7.09; N, 0.83. Found: C, 72.44; H, 7.17; N, 0.87.

(2*S*)-(Trimethylsilyl)ethyl 1-((2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-2-ene-2-(*N*-*tert*-butyloxycarbonyl)butanoate (31). In a drybox, [(COD)Rh−((*S*,*S*)-Et-DuPHOS)]$^+$OTf$^-$ catalyst precursor (1 mg, 0.0014 mmol) and **29** (940 mg, 0.56 mmol) were dissolved in deoxygenated anhydrous THF (3.0 mL) in a Fischer−Porter tube. The reaction vessel was pressurized to 90 psi of H_2 after five vacuum/H_2 cycles, and the mixture was stirred at 25 °C for 48 h. The vessel was depressurized and the mixture concentrated. The product was purified via flash chromatography eluting with 3:1 petroleum ether/EtOAc to yield **31** as a colorless oil (922 mg, 98%, >95% de): R_f = 0.4 (4:1 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +1.5° (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23−6.90 (m, 50H), 5.01−4.97 (d, *J* = 10.8 Hz, 1H), 4.89−4.87 (d, *J* = 3.6 Hz, 1H), 4.82−4.79 (d, *J* = 8.4 Hz, 1H), 4.69−4.50 (m, 6H), 4.38−4.27 (m, 7H), 4.24−4.19 (d, *J* = 12.6 Hz, 1H), 4.17−4.12 (m, 2H), 4.03−3.94 (m, 2H), 3.91−3.89 (m, 2H), 3.85−3.79 (m, 3H), 3.75−3.74 (t, *J* = 2.1 Hz, 1H), 3.71−3.71 (d, *J* = 2.4 Hz, 1H), 3.67−3.66 (d, *J* = 3.6 Hz, 1H), 3.64−3.62 (d, *J* = 3.3 Hz, 1H), 3.48−3.27 (m, 8H), 3.18−3.12 (m, 1H), 3.08−2.93 (m, 6H), 1.69−1.64 (m, 4H), 1.25 (s, 9H), 0.80−0.74 (m, 2H), −0.17 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.70, 138.99, 138.78, 138.61, 138.36, 138.16, 137.88, 128.67, 128.25, 128.15, 127.98, 127.71, 127.63, 127.53, 127.46, 127.35, 126.97, 102.59, 100.64, 84.96, 81.61, 81.15, 79.58, 79.53, 79.43, 79.21, 79.12, 78.52, 75.18, 74.94, 74.83, 74.75, 74.01, 73.69, 73.57, 73.30, 73.15, 73.03, 72.37, 72.09, 69.42, 68.30, 67.79, 63.56, 53.49, 29.78, 28.61, 28.41, 27.77, 17.42, −1.39. Anal. Calcd for $C_{102}H_{119}NO_{19}Si\cdot H_2O$: C, 71.75; H, 7.03; N, 0.82. Found: C, 71.41; H, 7.00; N, 0.79.

(2*R*)-(Trimethylsilyl)ethyl 1-((2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-glucopyranosyl)-2-ene-2-(*N*-*tert*-butyloxycarbonyl)butanoate (32). A solution of **30** (833.5 mg, 0.49 mmol) in THF (2.0 mL) and anhydrous MeOH (2.0 mL) was degassed with argon for 15 min. Ten percent Pd/C (∼75 mg) was added and the vessel pressurized to 90 psi of H_2 after five vacuum cycles. The reaction was stirred for 4 days and was then filtered through Celite and concentrated (R_f = 0.7 (5:3:1 EtOAc/MeOH/H_2O)). The residue was dissolved in pyridine (5.0 mL, 0.1 M). Ac_2O (15 equiv, 0.7 mL) was added and the reaction stirred for 15 h at 25 °C. The mixture was diluted with CH_2Cl_2, washed with water, 1.0 N HCl, and saturated $NaHCO_3$, dried ($MgSO_4$), and concentrated. Purification via chromatography eluting with a gradient of 1:1 to 2:1 EtOAc/petroleum ether provided **32** (511.6 mg, 76%) as a colorless foam: $[\alpha]^{20}_D$ +28.2° (*c* 1.07, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.52−5.51 (d, *J* = 3.0 Hz, 1H), 5.36−5.31 (dd, *J* = 3.0, 10.5 Hz, 1H), 5.22−5.21 (d, *J* = 3.9 Hz, 1H), 5.17−5.06 (m, 4H), 4.79−4.70 (m, 2H), 4.52−4.47 (t, *J* = 5.4 Hz, 1H), 4.43−4.34 (m, 3H), 4.20−4.03 (m, 8H), 3.78−3.77 (d, *J* = 1.8 Hz, 1H), 3.69−3.63 (m, 2H), 3.55−3.44 (m, 2H), 3.39−3.34 (m, 2H), 2.10 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H), 1.98 (s, 3H), 1.94 (s, 3H), 1.60−1.43 (m, 4H), 1.39 (s, 9H), 0.96−0.89 (m, 2H), 0.00 (s, 9H);^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 170.3, 170.25, 170.1, 170.0, 169.9, 169.7, 169.6, 169.2, 101.1, 99.4, 81.2, 79.7, 76.7, 76.574.4, 72.5, 72.3, 72.1, 71.7, 68.3, 68.1, 67.7, 66.7, 63.7, 62.7, 61.9, 61.1, 53.428.4, 28.2, 27.5, 20.9, 20.8, 20.7, 20.6, 17.4, 14.3, −1.4. Anal. Calcd for $C_{52}H_{79}NO_{29}Si$: C, 51.61; H, 6.58; N, 1.16. Found: C, 51.53; H, 6.53; N, 1.08.

(2*S*)-(Trimethylsilyl)ethyl 1-((2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-glucopyranosyl)-2-ene-2-(*N*-*tert*-butyloxycarbonyl)butanoate (33). A solution of **31** (822.9 mg, 0.49 mmol) in THF (2.0 mL) and anhydrous MeOH (2.0 mL) was degassed with argon for 15 min. Ten percent Pd/C (75 mg) was added and the vessel pressurized to 90 psi of H_2 after five vacuum cycles. The reaction was stirred for 4 days, filtered through Celite, and concentrated (R_f = 0.7 (5:3:1 EtOAc/MeOH/H_2O)). The residue was dissolved in pyridine (4.0 mL, 0.1 M). Ac_2O (15 equiv, 0.60 mL) was added and the reaction stirred for 15 h at 25 °C. The mixture was diluted with CH_2Cl_2, washed with water, 1.0 N HCl, and saturated $NaHCO_3$, dried ($MgSO_4$), and concentrated. Purification via chromatography eluting with a gradient of 1:1 to 2:1 EtOAc/petroleum ether provided **33** (382.6 mg, 66%) as a colorless foam: $[\alpha]^{20}_D$ +46.0° (*c* 1.18, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.53−5.52 (d, *J* = 2.4 Hz, 1H), 5.36−5.31 (dd, *J* = 3.0, 11.1 Hz, 1H), 5.15−4.98 (m, 4H), 4.94−4.93 (d, *J* = 3.6 Hz, 1H), 4.76−4.66 (m, 2H); 4.47−4.35 (m, 4H), 4.18−3.96 (m, 8H), 3.72−3.65 (m, 3H), 3.52−3.48 (m, 1H), 3.39−3.33 (m, 1H), 2.08 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.01 (s, 6H), 2.00 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.93 (s, 3H), 1.83−1.56 (m, 4H), 1.38 (s, 9H), 0.97−0.92 (m, 2H), −0.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 170.4, 170.2, 169.8, 169.5, 169.2, 168.6, 101.0, 99.5, 76.8, 76.7, 76.3, 74.4, 72.8, 72.0, 71.7, 68.9, 68.8, 67.8, 67.1, 63.6, 62.5, 61.3, 60.2, 53.1, 28.3, 27.9, 27.1, 20.7, 20.5, 17.4, −1.5. Anal. Calcd for $C_{52}H_{79}NO_{29}Si$: C, 51.61; H, 6.58; N, 1.16. Found: C, 51.48; H, 6.52; N, 1.21.

(2*R*)-1-((2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-glucopyranosyl)-2-ene-2-(*N*-*tert*-butyloxycarbonyl)butanoic Acid (34). To a solution of **32** (524.7 mg, 0.43 mmol) in THF (5.0 mL) was added 1.0 M TBAF (1.70 mL). The reaction was stirred at 25 °C for 4 h, diluted with CH_2Cl_2, washed with 1 N HCl, dried ($MgSO_4$), and concentrated. Purification via flash chromatography eluting with 4:1 EtOAc/petroleum ether provided **34** (425.0 mg, 88%) as a pale yellow foam: R_f = 0.8 (4:1 EtOAc/petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.54−5.53 (d, *J* = 3.0 Hz, 1H), 5.37−5.32 (dd, *J* = 3.0, 11.1 Hz, 1H), 5.21−5.19 (m, 1H), 5.16−5.02 (m, 5H), 4.94−4.93 (d, *J* = 3.6 Hz, 1H), 4.77−4.67 (m, 2H), 4.48−4.41 (m, 4H), 4.21−4.19 (m, 1H), 4.16−4.00 (m, 6H), 3.97−3.96 (d *J* = 2.1 Hz, 1H), 3.74−3.65 (m, 2H), 3.54−3.49 (m, 1H), 3.40−3.35 (m, 1H), 2.08 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.997 (s, 3H), 1.995 (s, 3H), 1.98 (s, 3H), 1.94 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3, 170.5, 170.3, 169.9, 169.6, 169.3, 168.7, 101.0, 99.5, 76.8, 76.4, 74.4, 72.8, 72.1, 71.8, 69.0, 68.9, 67.9, 67.0, 62.6, 61.4, 60.3, 28.3, 27.4, 21.0, 20.8. Anal. Calcd for $C_{47}H_{67}NO_{29}$: C, 50.86; H, 6.08; N, 1.26. Found: C, 50.64; H, 6.17; N, 1.32.

(2*S*)-1-((2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-*β*-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-glucopyranosyl)-2-ene-2-(*N*-*tert*-butyloxycarbonyl)butanoic Acid (35). To a solution of **33** (377.4 mg, 0.31 mmol) in THF (5.0 mL) was added 1.0 M TBAF (1.2 mL). The reaction was stirred at 25 °C for 4 h, diluted with CH_2Cl_2, washed with 1 N HCl, dried ($MgSO_4$), and concen-

trated. Purification via flash chromatography eluting with 4:1 EtOAc/petroleum ether provided **35** (351.7 mg, 99%) as a colorless foam: $R_f = 0.8$ (4:1 EtOAc/petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.55−5.54 (d, J = 3.3 Hz, 1H), 5.37−5.33 (dd, J = 3.3, 11.1 Hz, 1H), 5.17−5.03 (m, 4H), 4.95−4.94 (d, J = 3.6 Hz, 1H), 4.78−4.68 (m, 2H), 4.49−4.32 (m, 5H), 4.20−3.98 (m, 8H), 3.75−3.67 (m, 3H), 3.55−3.48 (m, 2H), 3.41−3.37 (m, 1H), 2.09 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H), 2.02 (s, 9H), 2.01 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.94 (s, 3H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 170.5, 170.3, 170.2, 170.0, 169.9, 169.5, 169.3, 168.7, 155.6, 101.0, 99.5, 80.1, 76.9, 76.7, 76.4, 74.4, 72.8, 72.0, 71.8, 69.0, 68.8, 67.9, 67.1, 62.5, 61.3, 60.3, 53.0, 28.3, 27.4, 27.0, 21.0, 20.9, 20.8, 20.6. Anal. Calcd for $C_{47}H_{67}NO_{29}$: C, 50.86; H, 6.08; N, 1.26. Found: C, 50.83; H, 6.20; N, 1.27.

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