JOC The Journal of Organic Chemistry

Featured Article

pubs.acs.org/joc

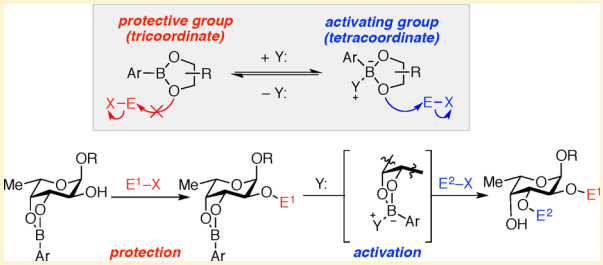
Sequential Functionalizations of Carbohydrates Enabled by Boronic Esters as Switchable Protective/Activating Groups

Ross S. Mancini, Jessica B. Lee, and Mark S. Taylor*

Department of Chemistry, University of Toronto, Toronto, Ontario M5S 3H6, Canada

Supporting Information

ABSTRACT: Processes for site-selective, sequential functionalizations of carbohydrate derivatives are described. In these processes, a tricoordinate boronic ester initially serves as a protective group for a sugar-derived 1,2- or 1,3-diol motif, permitting functionalization of free OH groups. In a second step, addition of a Lewis base generates a tetracoordinate adduct, which serves as an activating group, enabling functionalization of one of the boron-bound oxygen atoms by a second electrophile. By combining an initial acylation, alkylation, or glycosylation step with an amine-mediated glycosylation of the boronic ester, a variety of selectively protected di- and trisaccharide derivatives can be accessed in an operationally simple fashion without purification of intermediates. This Lewis base-triggered switching of behavior from "latent" to "active" nucleophile is a unique feature of boronic esters relative to other protective groups for diol moieties in carbohydrate chemistry.



INTRODUCTION

Efficient laboratory syntheses of oligosaccharides are needed to advance glycobiology research and to explore the development of carbohydrate-based therapeutic agents such as vaccines.[1,2] The preparation of appropriately functionalized building blocks for oligosaccharide synthesis often requires sequential, site-selective chemical transformations of monosaccharides. Most often, such sequential functionalizations are achieved by taking advantage of differences in the relative reactivity of hydroxyl (OH) groups in sugars due to steric and electronic effects. Catalytic processes that enable sequential, multistep functionalizations via acetal intermediates have also been developed.[3,4] Here, we describe an approach for sequential functionalization of carbohydrate derivatives that takes advantage of the ability of boronic esters to serve as either protective groups or activating groups for diols, depending on the coordination number at the boron center. This approach enables the one-pot synthesis of a variety of selectively protected disaccharide and branched trisaccharide derivatives.

The most well-established applications of boronic esters in carbohydrate chemistry involve their use as protective groups for 1,2- or 1,3-diol motifs.[5,6] Transient protection via tricoordinate boronic ester formation has been used to accomplish selective acylations, glycosylations, sulfations, alkylations, and silylations of carbohydrate derivatives.[7−15] Variants employing polymer-supported boronic acids have also been developed.[16−18] A complementary and less widely exploited mode of reactivity for organoboron complexes of sugars is the activation of OH groups by formation of tetracoordinate adducts. Aoyama and co-workers demonstrated that boronic esters of carbohydrates could be activated toward reactions of electrophiles by coordination of a nitrogen-[19] or oxygen-centered Lewis base.[20] Our group has developed methods for site-selective activation of sugars via tetracoordinate organoboron adducts, using either arylborinic acids (Ar_2BOH)[21,22] or boronic acid/Lewis base combinations.[23,24] Methods for intramolecular aglycon delivery via tetracoordinate organoboron adducts have also been reported.[25] On the whole, the observations described above suggest that the behavior of boronic esters can be switched from protective group (tricoordinate) to activating group (tetracoordinate) by addition of a Lewis base. We aimed to make use of this property to develop reaction sequences in which the boronic ester group serves initially as a protective group and then as an activating group for coupling with a second electrophile (Scheme 1).

RESULTS AND DISCUSSION

Sequential Acylation and Glycosylation. The preparation of selectively protected gentiobiose derivative **5a** from methyl α-D-glucopyranoside (**1a**) through a bis-benzoylation/glycosylation sequence was targeted in our initial studies (Table 1). Benzoylation of arylboronates **2a** (benzoyl chloride, pyridine solvent, 0−23 °C) proceeded effectively as judged by ^{1}H nuclear magnetic resonance (NMR) spectroscopy. Previous work has shown that these conditions result in acylation of free OH groups in carbohydrate-derived aryboronic esters. Whereas trialkylamine bases are able to form Lewis acid−base adducts with the boronic ester, causing reactivity of the boron-bound oxygens with electrophiles (see below), this reactivity was not observed in the presence of pyridine, a

Received: June 28, 2017

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 1. Design Plan for Sequential Functionalization of Carbohydrates via Boronic Esters

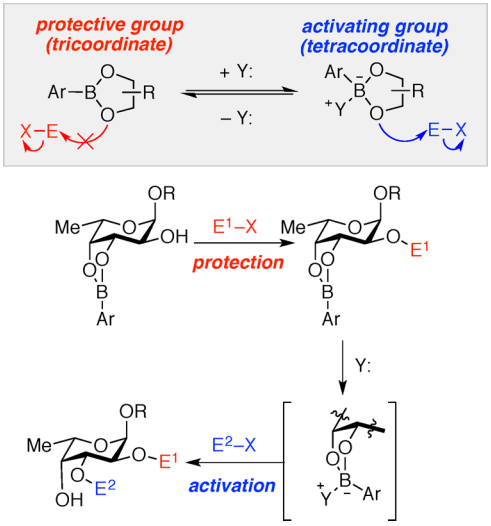
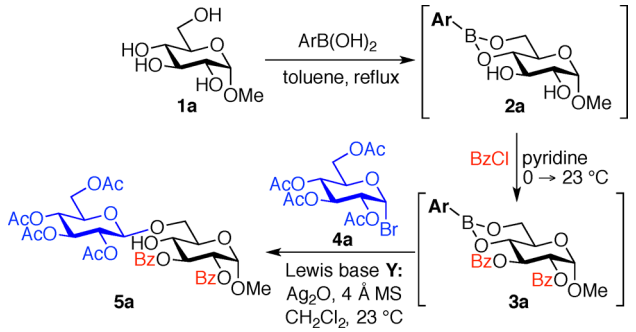


Table 1. Optimization of Conditions for the Synthesis of Protected Gentiobiose Derivative 5a by Sequential Benzoylation and Glycosylation



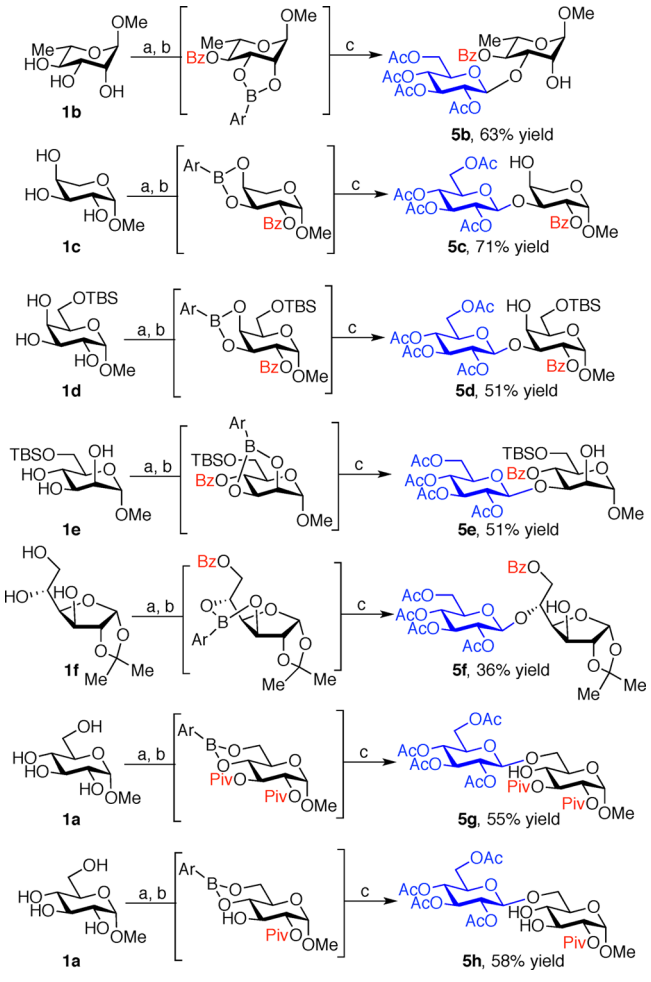
entry	Ar	Y	yield of **5a**[a] (%)
1	Ph	Et_3N	36
2	4-(MeO)C_6H_4	Et_3N	44
3	4-(CF_3)C_6H_4	Et_3N	50
4	4-(CF_3)C_6H_4	Me_2NCHO	<5
5	4-(CF_3)C_6H_4	Bu_3PO	<5
6	4-(CF_3)C_6H_4	*N*,*N*-dimethylpiperazine	31
7	4-(CF_3)C_6H_4	*N*-methylmorpholine	41

[a]Yield after purification by flash column chromatography on silica gel.

weaker Lewis base. The pyridinium hydrochloride byproduct from the benzoylation step was removed by dilution with toluene, filtration through Celite, and removal of the solvent under vacuum. This operation was carried out because preliminary optimization experiments (data not shown) indicated that pyridinium hydrochloride had an adverse effect on the yield of the glycosylation reaction, perhaps due to side reactions with the Ag_2O activator and/or the glycosyl bromide. Without further purification, the intermediate bis-*O*-benzoylated boronic esters **3a** were subjected to acetobromoglucose (**4a**) in the presence of a Lewis basic activator (Y:) and silver(I) oxide as halide scavenger and base. Along with disaccharide **5a** and unreacted glycosyl acceptor, byproducts resulting from glycosyl donor hydrolysis and elimination were observed under these conditions. The yield of **5a** was dependent on both the arylboronic acid and the Lewis base employed: electron-deficient 4-(trifluoromethyl)phenylboronic acid provided higher yields than 4-methoxyphenylboronic acid and the parent phenylboronic acid, and triethylamine was the optimal activating agent for the boronic acid. This observation appeared to be qualitatively consistent with our previous work in which an electron-deficient boronic acid in combination with a trialkylamine provided optimal results for activation of a pyranoside toward reaction with a glycosyl halide donor.[24] Previous research from our laboratory had also identified 4-(trifluoromethyl)phenylboronic acid as a useful protective group for acylations, alkylations, and glycosylations of carbohydrate derivatives,[14] indicating that a range of sequential transformations could potentially be achieved. It should be noted, however, that the data shown in Table 1 reflect an interplay between the reactivity of the Lewis base—boronic acid adduct and that of the Ag_2O-activated glycosyl bromide: a different result was obtained when an "armed" glycosyl chloride was used (see below).

The sequential acylation/glycosylation protocol was employed to generate a series of partially protected disaccharide derivatives (Scheme 2). For pyranoside triols having the *manno*

Scheme 2. Synthesis of Partially Protected Disaccharides from Boronic Esters by Sequential Acylation and Coupling with Acetobromoglucose[a]



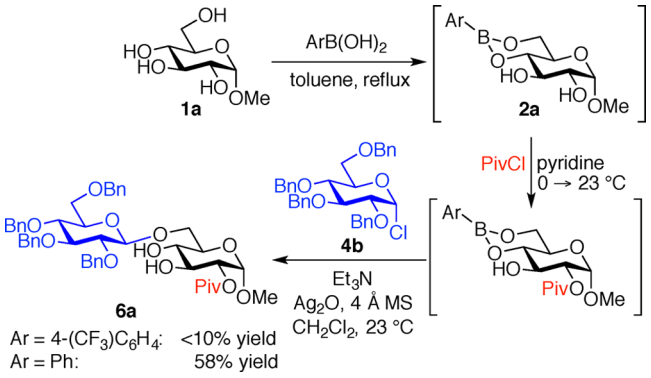
[a]Reagents and conditions: (a) 4-(CF_3)$C_6H_4B(OH)_2$, toluene, 110 °C; (b) RCOCl, pyridine, 0 °C (*T* = 50 °C for product **5g**); (c) **4a** (1.5 equiv), Et_3N (6 equiv), Ag_2O (1.5 equiv), 4 Å MS, CH_2Cl_2, 23 °C.

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX–XXX

configuration (e.g., α-rhamnopyranoside **1b**, α-mannopyranoside **1e**), benzoylation occurred at the 4-OH group, followed by glycosylation at O-3. For galacto-configured substrates (β-arabinopyranoside **1c**, α-galactopyranoside **1d**), the 2-*O*-benzoylated, β-1,3-linked products were obtained. The selectivity for activation of the equatorial OH group of *cis*-1,2-diol motifs that is generally observed for activation via tetracoordinate boron adducts is thus maintained for these substrates, despite the deactivating effect of the vicinal acyl protective group.[26] A glucofuranoside substrate was also employed, leading to acylation of the 6-OH group and glycosylation at O-5. The regiochemical outcomes of both steps are consistent with previous results for acylation[14] and glycosylation[22] of this substrate (via boronic and borinic ester intermediates, respectively). The use of pivaloyl chloride in place of BzCl led to the formation of gentiobiose-derived bis-pivaloate ester **5g** from α-glucopyranoside **1a**. Selective monoacylation at the less sterically hindered 2-OH group could also be achieved using this reagent, resulting in a triol-derived boronate that underwent selective mono-*O*-glycosylation (product **5h**). In each case, the glycosylation step was highly stereoselective (>20:1 β:α), with no evidence for the formation of α-configured byproducts as judged by ^{1}H NMR spectroscopy. Although the overall yields of these processes were relatively modest, the three-step sequence (protection, acylation, and deprotection via glycosylation) is operationally simple and does not require purification of the intermediates.

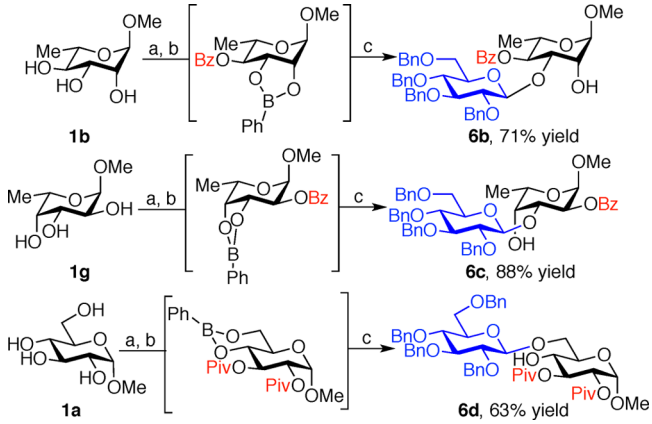
Couplings with an "armed"[27] glycosyl halide bearing ether rather than ester protective groups were also pursued. Such couplings would provide access to orthogonally protected disaccharides and were also of interest from the perspective of stereocontrol, given that anchimeric assistance could not be relied upon to deliver the β-linkage when using a per-benzylated donor. A significant effect of arylboronic acid substitution on the efficiency of coupling with tetra-*O*-benzyl-α-D-glucopyranosyl chloride (**4b**) was observed (Scheme 3).

Scheme 3. Effect of Boronic Acid Substitution on Efficiency of Sequential Acylation/Coupling with an Armed Glycosyl Donor



Whereas the glycosylation did not proceed to a useful extent upon activation of the 4-(trifluoromethyl)boronate intermediate with triethylamine, the disaccharide **6a** was isolated in 58% yield using the phenylboronic ester. We speculate that the inductive electron-withdrawing effect of the trifluoromethyl group may attenuate the nucleophilicity of the tetracoordinate boronate adduct to the point where coupling with the less reactive donor becomes challenging. (Although the benzyl protective groups have an arming effect, **4b** was found to be less reactive than **4a** under these conditions, presumably due to the poorer leaving group of chloride versus bromide. This lower reactivity is reflected in the longer reaction times needed for the glycosylation using the former (48 h) versus the latter (12 h).) The glycosylation showed high (>20:1) β-selectivity, with ^{1}H NMR spectroscopy providing no evidence for the presence of the α-anomer in the unpurified reaction mixture. This observation is consistent with our previous studies of borinic acid-catalyzed couplings of α-configured glycosyl chlorides, which proceeded with inversion of configuration at the anomeric center, likely through an associative mechanism.[28,29] The protocol was further applied to the synthesis of disaccharides **6b–d** with high levels of β-selectivity (no detectable formation of α-configured side products) observed in each case (Scheme 4).

Scheme 4. Synthesis of Partially Protected Disaccharides from Boronic Esters by Sequential Acylation and Coupling with Tetra-*O*-benzyl-α-D-glucopyranosyl Chloride[a]



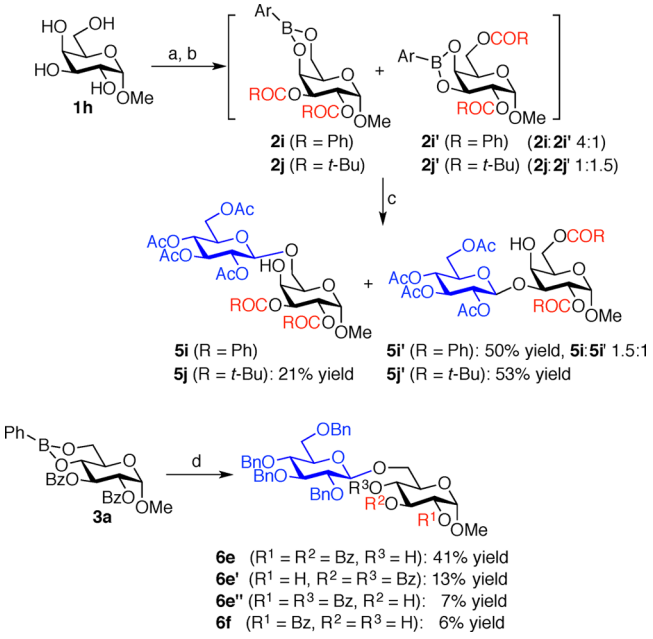
[a]Reagents and conditions: (a) $PhB(OH)_2$, toluene, 110 °C; (b) RCOCl, pyridine, 0 °C (*T* = 50 °C for product **6d**); (c) **4b** (1.1 equiv), Et_3N (6 equiv), Ag_2O (1.1 equiv), 4 Å MS, CH_2Cl_2, 23 °C.

Acyl and Boronate Group Migration. When methyl α-D-galactopyranoside (**1h**) was subjected to the arylboronic acid mediated benzoylation/glycosylation sequence, a mixture of isomeric disaccharides **5i** and **5i′** was formed (Scheme 5). Boronic ester migration under the conditions of benzoylation was partially responsible for this outcome: a 4:1 mixture of isomeric benzoylated arylboronates **2i** and **2i′** was obtained prior to the glycosylation step. The galactopyranoside substrate is prone to this type of rearrangement because both the 4,6- and 3,4-diol motifs are able to form relatively stable boronic esters.[14] Based on the 1.5:1 ratio of isomeric benzoylated disaccharides, it is likely that further rearrangement—in this case, a concomitant migration of acyl and boronate groups—occurred under the basic conditions of the glycosylation reaction.[30] Using pivaloyl chloride in place of benzoyl chloride for this series of reactions also resulted in a pair of regioisomers, **5j** and **5j′**. With this electrophile, acylation of the primary OH group was favored, and the 3-*O*-glycosylated isomer (**5j′**) was ultimately obtained as the major product.

Acyl migrations were also observed for couplings of perbenzylated glucopyranosyl chloride **4b**. For example, four disaccharide products could be identified when bis-benzoylated boronic ester **3a** was coupled with **4b**. These include three

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX–XXX

Scheme 5. Acylation/Glycosylation Sequences Resulting in Mixtures of Regioisomeric Disaccharides[a]

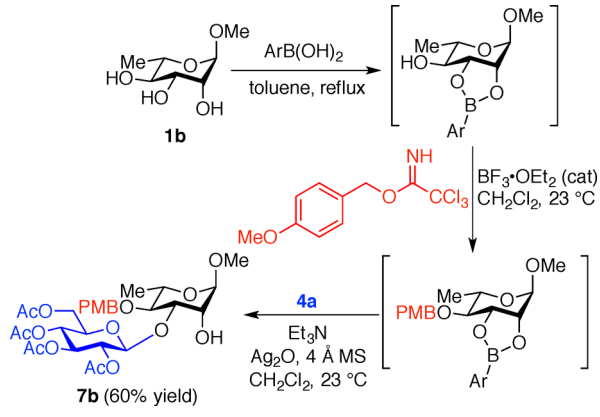


[a]Reagents and conditions: (a) 4-$(CF_3)C_6H_4B(OH)_2$, toluene, 110 °C; (b) RCOCl, pyridine, 0 °C (R = Ph) or 50 °C (R = *t*-Bu); (c) **4a** (1.5 equiv), Et_3N (6 equiv), Ag_2O (1.5 equiv), 4 Å MS, CH_2Cl_2, 23 °C; (d) **4b** (1.1 equiv), Et_3N (6 equiv), Ag_2O (1.1 equiv), 4 Å MS, CH_2Cl_2, 23 °C.

products of intramolecular acyl migration (**6e**, **6e′** and **6e″**) along with monobenzoate **6f**. Analogous migration products were not observed under the conditions of Scheme 2, presumably because the rate of glycosylation was higher with **4a** than with **4b**, as described above.

Sequential *p*-Methoxybenzyl (PMB) Protection and Glycosylation. Taking advantage of a protocol developed in our laboratory for coupling of boronic ester-protected carbohydrate derivatives with *p*-methoxybenzyl trichloroacetimidate,[14] we investigated the sequential installation of PMB and glycosyl moieties using the protection/activation approach (Scheme 6). Our previous work had shown that the 4-(trifluoromethyl)-substituted arylboronic ester was the optimal protective group for the PMB etherification step. As described

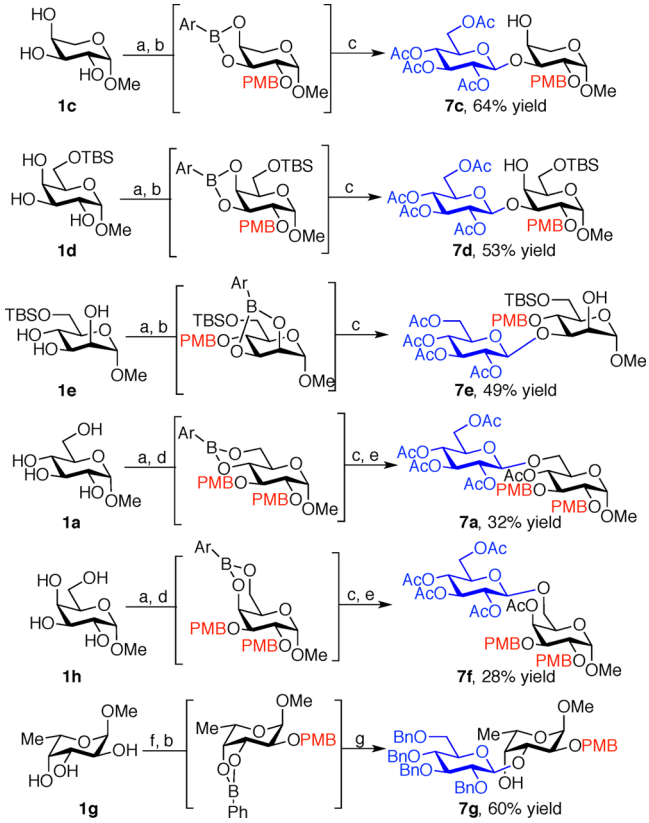
Scheme 6. Sequential Installation of *p*-Methoxybenzyl and Glycosyl Moieties



above, this substitution pattern also provided superior results for the amine-mediated glycosylation step using disarmed donor **4a**. Condensation of pyranoside derivative **1b** with 4-(trifluoromethyl)phenylboronic acid, followed by treatment with PMB trichloroacetimidate and catalytic boron trifluoride diethyl etherate ($BF_3{\cdot}OEt_2$) in dichloromethane with 4 Å molecular sieves, resulted in a PMB-protected boronic ester intermediate that was activated toward coupling with glycosyl donor **4a** by addition of triethylamine and Ag_2O. Protected disaccharide **7b** was isolated in 60% yield.

This approach was amenable to the synthesis of other PMB-protected disaccharides (Scheme 7). Sequences involving bis-

Scheme 7. Preparation of PMB-Protected Disaccharides by Sequential Etherification and Glycosylation[a]



[a]Conditions: (a) 4-$(CF_3)C_6H_4B(OH)_2$, toluene, 110 °C; (b) $PMBOC(=NH)CCl_3$ (3 equiv), $BF_3{\cdot}OEt_2$ (2 mol %), CH_2Cl_2, 0 °C; (c) **4a** (1.5 equiv), Et_3N (6 equiv), Ag_2O (1.5 equiv), 4 Å MS, CH_2Cl_2, 23 °C; (d) $PMBOC(=NH)CCl_3$ (6 equiv), $La(OTf)_3$ (1 mol %), CH_2Cl_2/toluene, 0 °C; (e) Ac_2O, pyridine, 23 °C; (f) $PhB(OH)_2$, toluene, 110 °C; (g) **4b** (1.1 equiv), Et_3N (6 equiv), Ag_2O (1.1 equiv), 4 Å MS, CH_2Cl_2, 23 °C.

etherification of 4,6-*O*-boronates (**1a** → **7a**, **1h** → **7f**) required lanthanum(III) trifluoromethanesulfonate ($La(OTf)_3$) in place of $BF_3{\cdot}OEt_2$ as Lewis acid and proceeded in lower yield than those in which only a single PMB group was installed. Separation of product from hydrolyzed glycosyl donor was challenging in these cases but could be achieved after acetylation of the free OH groups by treatment with Ac_2O and pyridine. For the coupling of **1g** with armed glycosyl chloride **4b**, the phenylboronic ester was used in place of the trifluoromethyl-substituted derivative due to its increased reactivity in the glycosylation step.

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

Synthesis of Branched Trisaccharides by Sequential Glycosylation Reactions. Application of a glycosyl donor as the electrophile in the first step of the boronic ester protection−activation sequence was investigated as a way to generate branched trisaccharides. The groups of Boons, Kaji, and Madsen have described conditions for glycosylation of free OH groups in sugar-derived boronates using thioglycoside donors.[10−12,17,18] Building on the conditions described in the preceding section for incorporation of PMB groups, we pursued the glycosylation of boronates using trichloroacetimidate donors under Lewis acid catalysis. Such a protocol was employed recently by Nagorny, Sherman, and co-workers to achieve selective glycosylations of the macrolide antibiotic 6-deoxyerythronolide B.[15] The reaction of rhamnopyranoside-derived boronic ester **2b** with armed mannosyl trichloroacetimidate **4c** in the presence of catalytic trimethylsilyl trifluoromethanesulfonate (TMSOTf) resulted in an 85% yield of disaccharide **8** (>10:1 α:β selectivity). To isolate the disaccharide product, the boronic ester group was deprotected by transesterification with aqueous basic sorbitol solution[14] using Hall's "phase-switching" protocol (Scheme 8).[31] Activation of the intermediate boronate-protected disaccharide with triethylamine enabled its coupling with glycosyl bromide **4a**, generating branched trisaccharide **9**. A comparison of the yields of disaccharide **8** and trisaccharide **9** indicates that the second glycosylation is the problematic step, perhaps due to the deactivating inductive and steric effects of the previously introduced glycosyl group. A still lower yield was obtained for the synthesis of trisaccharide **10** using armed donor **4b**, in keeping with its generally lower reactivity under the conditions developed here for *O*-glycosylation of boronic esters. Trisaccharide **11** was obtained from fucopyranoside **1g** by initial glycosylation with a xylopyranosyl trichloroacetimidate, followed by Lewis base-mediated coupling with **4b**.

Sequential coupling of two different glycosyl halide donors was also investigated. Boronic ester **2b** underwent glycosylation at the free OH group upon treatment with acetobromoglucose **4a** in the presence of AgOTf and Ag_2CO_3 and without an amine additive (dichloromethane, 23 °C: Scheme 9). After removal of the silver salts by filtration through Celite, the resulting glycosylated boronic ester intermediate was activated by triethylamine toward coupling with glycosyl chloride **4b**. Isomeric trisaccharides **12** and **12′** were isolated in 36% and 17% yields, respectively. Presumably, the relatively low level of site selectivity arose because 3-*O*-glycosylation was hampered by the steric and electronic effects of the adjacent glycosyl moiety.

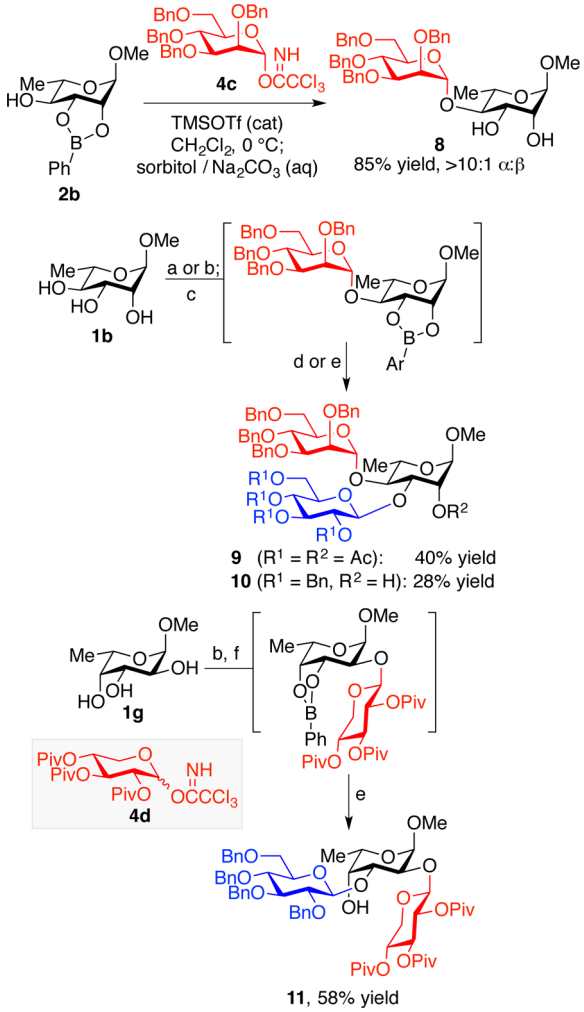
Multistep Protection−Activation Reaction Sequences. Couplings of glucopyranoside substrate **1a** with three distinct electrophiles could be achieved by carrying out two functionalization steps prior to the boronate-cleaving glycosylation (Scheme 10). Selective installation of a benzoyl ester at the less sterically hindered 2-OH group of the 4,6-*O*-boronic ester (Ar = 4-$CF_3C_6H_4$) was followed by a second esterification of the 3-OH group with PivCl. The resulting intermediate underwent 6-*O*-glycosylation upon activation by triethylamine (product **5k**). In a similar way, an esterification/glycosylation/glycosylation sequence led to the formation of branched trisaccharide **13** in 46% yield.

CONCLUSIONS

The ability to switch the behavior of boronic esters from protective groups to activating groups by formation of a tetracoordinate adduct has been exploited to achieve sequential, site-selective functionalizations of carbohydrate derivatives. A variety of selectively protected disaccharide derivatives have been prepared by acylation or etherification of free OH groups in the tricoordinate boronic ester intermediate followed by addition of triethylamine and glycosylation of the resulting tetracoordinate complex. Branched trisaccharides have been accessed by conducting successive couplings of glycosyl donors with the carbohydrate-derived boronic ester acceptor. The sequence of boronate formation, functionalization, and deprotection/glycosylation can be conducted without purification of intermediates.

Although parallels can often be drawn between the properties of boronic esters and acetals/ketals, the other commonly used protective groups for 1,2- or 1,3-diol motifs, the present study

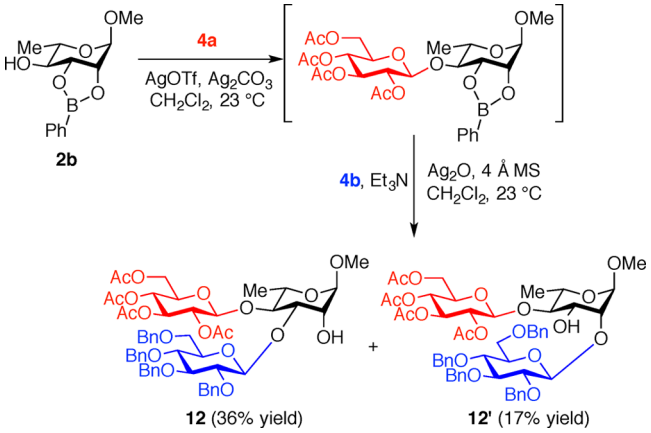
Scheme 8. Coupling of a Boronic Ester Protected Acceptor with a Glycosyl Trichloroacemidate and Synthesis of Branched Trisaccharides by Sequential Glycosylations of Boronic Esters with Trichloroacetimidate and Glycosyl Halide Donors[a]



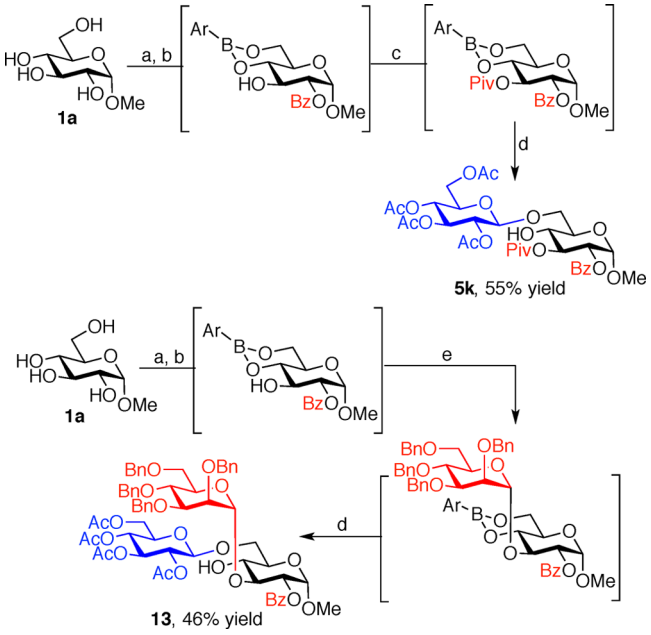
[a]Reagents and conditions: (a) 4-$(CF_3)C_6H_4B(OH)_2$, toluene, 110 °C; (b) $PhB(OH)_2$, toluene, 110 °C; (c) **4c** (1.5 equiv), TMSOTf (5 mol %), CH_2Cl_2, 0 °C; (d) **4a** (1.5 equiv), Et_3N (6 equiv), Ag_2O (1.5 equiv), 4 Å MS, CH_2Cl_2, 23 °C (Ar = 4-$(CF_3)C_6H_4$), then Ac_2O, pyridine; (e) **4b** (1.1 equiv), Et_3N (6 equiv), Ag_2O (1.1 equiv), 4 Å MS, CH_2Cl_2, 23 °C (Ar = Ph); (f) **4d** (1.5 equiv), TMSOTf (10 mol %), CH_2Cl_2, 0 °C.

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 9. Sequential Couplings with Two Glycosyl Halide Donors



Scheme 10. Boronic Acid Mediated Reactions of Glucopyranoside 1a with Three Distinct Electrophiles[a]



[a]Reagents and conditions: (a) 4-$(CF_3)C_6H_4B(OH)_2$, toluene, 110 °C; (b) BzCl, pyridine, 0 °C; (c) PivCl, pyridine, 50 °C; (d) **4a** (1.5 equiv), Et_3N (6 equiv), Ag_2O (1.5 equiv), 4 Å MS, CH_2Cl_2, 23 °C. (e) **4c** (1.5 equiv), TMSOTf (2 × 10 mol %), CH_2Cl_2, 0 °C.

illustrates how a distinct reactivity mode of boronic esters can be exploited to achieve unique multistep transformations. Benzylidene acetals can be regioselectively converted to monobenzyl ethers by reductive C−O bond cleavage,[32] but protective group removal via selective glycosylation has not been achieved to date. In principle, the approach described here could be generalized by developing conditions for selective *O*-functionalization of boronic esters with electrophiles other than glycosyl donors. Room also exists to improve upon the existing method, both in terms of the efficiency of the final glycosylation step and the practicality of the reaction conditions (glycosyl halide donors activated by stoichiometric Ag_2O). The property of boronic esters as "latent"[33] glycosyl acceptors whose reactivity can be triggered by addition of a Lewis base is thus worthy of further investigation.

EXPERIMENTAL SECTION

Experimental procedures and characterization data are provided below for all new compounds reported here.

General Considerations. Stainless steel syringes were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed using 35−75 μm particle size silica gel. Thin-layer chromatography (TLC) was performed using aluminum-backed silica gel plates, and products were visualized by UV irradiation at 254 nm and by staining with $KMnO_4$ solution.

Materials. Dichloromethane was purified by passing through two columns of activated alumina under nitrogen. Deionized water was acquired from an in-house supply. The remainder of reagents and solvents were purchased from commercial suppliers and used without further purification.

Instrumentation. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a 400, 500, or 600 MHz spectrometer. Chemical shifts for protons are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CDCl_3$: δ 7.26). Chemical shifts for carbon (^{13}C NMR) are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.16). Boron (^{11}B NMR) chemical shifts are reported in parts per million downfield from boron trifluoride diethyl etherate and are uncorrected. Fluorine (^{19}F NMR) chemical shifts are reported in parts per million downfield from trichlorofluoromethane and are uncorrected. Data are represented as follows; chemical shift (δ, ppm); multiplicity (s, singlet; d, doublet; app t, apparent triplet; br s, broad singlet; m, multiplet); integration; coupling constant (*J*, Hz), proton assignment. Proton resonances were assigned based on 2-D COSY, HSQC, and HMBC experiments. Glycosidic linkages were confirmed by 2-D COSY and HMBC experiments. Attenuated total reflectance infared (IR) spectra were obtained in the solid form or as neat liquids. High-resolution mass spectra (HRMS) experiments were carried out using a time-of-flight (TOF) mass spectrometer using an electrospray ionization (ESI) method. Optical rotations were measured using an automatic polarimeter.

General Procedure A: Preparation of Carbohydrate Boronates. Methyl glycoside (2.00 mmol) and arylboronic acid (2.00 mmol, 1.00 equiv) were placed in a round-bottom flask equipped with a stir bar. Toluene (10.0 mL) was added to the flask, and the solution was placed in an oil bath set at 110 °C and stirred overnight. The solution was then cooled to room temperature, and solvent was removed under reduced pressure. Residual water was removed from the resulting material via azeotroping with toluene three times, followed by drying under high vacuum to yield the desired boronic ester. Products were used without further purification. All compounds were found to be stable to prolonged storage on the benchtop at room temperature and were stored in a desiccator to limit exposure to moisture.

General Procedure B: Sequential Reactions of Carbohydrate Boronates with Benzoyl Chloride and Glycosyl Donor 4a. 4-(Trifluoromethyl)phenylboronic acid-derived carbohydrate boronate (0.200 mmol, prepared according to general procedure A) was dissolved in anhydrous pyridine (0.400 mL) and cooled to 0 °C with stirring. Benzoyl chloride (0.035 mL, 0.300 mmol, 1.50 equiv) was added quickly to the reaction vessel, and the solution was removed from the ice bath and allowed to warm to room temperature with stirring for 30 min. Once complete, the reaction was diluted with toluene and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was then dissolved in anhydrous dichloromethane (1.00 mL) and transferred via syringe to an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (0.123 g, 0.300 mmol, 1.50 equiv) and silver(I) oxide (0.070 g, 0.300 mmol, 1.50 equiv) were added to the solution followed by triethylamine (0.166 mL, 1.20 mmol, 6.00 equiv), and the reaction was stirred vigorously (800 rpm or higher) at room temperature overnight. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

flash column chromatography on silica gel to yield the functionalized disaccharide.

General Procedure C: Sequential Reactions of Carbohydrate Boronates with 4-Methoxybenzyl Trichloroacetimidate and Glycosyl Donor 4a. 4-(Trifluoromethyl)phenylboronic acid derived carbohydrate boronate (0.200 mmol, prepared according to general procedure A) was transferred to an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. The reaction vessel was purged with argon and kept under an atmosphere of argon using a balloon. Anhydrous dichloromethane (1.00 mL) was added to the flask followed by 4-methoxybenzyl trichloroacetimidate (0.125 mL, 0.600 mmol, 3.00 equiv), and the solution was cooled to 0 °C with stirring. A 0.1 M solution of boron trifluoride diethyl etherate in dichloromethane was prepared fresh, and 0.040 mL of this solution (0.004 mmol, 0.020 equiv) was added slowly dropwise to the reaction mixture. The solution was allowed to stir at 0 °C for an additional 5 min before the ice bath was removed. Triethylamine (0.166 mL, 1.20 mmol, 6.00 equiv) was added to the reaction vessel followed by 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (0.123 g, 0.300 mmol, 1.50 equiv) and silver(I) oxide (0.070 g, 0.300 mmol, 1.50 equiv), and the reaction was stirred vigorously (800 rpm or higher) at room temperature overnight. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel to yield the functionalized disaccharide.

General Procedure D: Sequential Reactions of Carbohydrate Boronates with Benzoyl Chloride and Glycosyl Donor 4b. Phenylboronic acid-derived carbohydrate boronate (0.200 mmol, prepared according to general procedure A) was dissolved in anhydrous pyridine (0.400 mL) and cooled to 0 °C with stirring. Benzoyl chloride (0.035 mL, 0.300 mmol, 1.50 equiv) was added quickly to the reaction vessel, and the solution was removed from the ice bath and allowed to warm to room temperature with stirring for 30 min. Once complete, the reaction was diluted with toluene and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was then dissolved in anhydrous dichloromethane (1.00 mL) and transferred via syringe to an oven-dried round-bottom flask charged with a stir bar and 4 Å molecular sieves. 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.123 g, 0.220 mmol, 1.10 equiv) and silver(I) oxide (0.051 g, 0.220 mmol, 1.10 equiv) were added to the solution followed by triethylamine (0.166 mL, 1.20 mmol, 6.00 equiv), and the reaction was stirred vigorously (800 rpm or higher) at room temperature for 48 h. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel to yield the functionalized disaccharide.

General Procedure E: Sequential Reactions of Carbohydrate Boronates with 4-Methoxybenzyl Trichloroacetimidate and Glycosyl Donor 4b. Phenylboronic acid derived carbohydrate boronate (0.200 mmol, prepared according to general procedure A) was transferred to an oven-dried round-bottom flask charged with a stir bar and 4 Å molecular sieves. The reaction vessel was purged with argon and kept under an atmosphere of argon using a balloon. Anhydrous dichloromethane (1.00 mL) was added to the flask followed by 4-methoxybenzyl trichloroacetimidate (0.125 mL, 0.600 mmol, 3.00 equiv), and the solution was cooled to 0 °C with stirring. A 0.1 M solution of boron trifluoride diethyl etherate in dichloromethane was prepared fresh, and 0.040 mL of this solution (0.004 mmol, 0.020 equiv) was added slowly dropwise to the reaction mixture. The solution was allowed to stir at 0 °C for an additional 5 min before the ice bath was removed. Triethylamine (0.166 mL, 1.20 mmol, 6.00 equiv) was added to the reaction vessel followed by 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.123 g, 0.220 mmol, 1.10 equiv) and silver(I) oxide (0.051 g, 0.220 mmol, 1.10 equiv), and the reaction was stirred vigorously (800 rpm or higher) at room temperature for 48 h. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel to yield the functionalized disaccharide.

*Methyl 2,3-Bis-O-benzoyl-6-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**5a**).* Prepared from methyl 4,6-*O*-(4-(trifluoromethyl)phenylboronate)-α-D-glucopyranoside (0.056 g, 0.200 mmol) according to general procedure B with the following amendment: benzoyl chloride (0.058 mL, 0.500 mmol, 2.50 equiv). The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield a white amorphous solid (0.073 g, 50%). TLC: R_f = 0.47 (ethyl acetate/hexanes 1:1). $[\alpha]^{20}_D$ = 38.3 (*c* 1.15 in $CHCl_3$). FTIR (powder, cm^{-1}): 3446 (br), 2960 (w), 2903 (w), 1749 (s), 1716 (s), 1366 (m), 1219 (s), 1030 (s), 917 (m), 709 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.98−7.95 (m, 4H, ArH), 7.53−7.48 (m, 2H, ArH), 7.38−7.33 (m, 4H, ArH), 5.69 (dd, 1H, *J* = 10.1, 9.2 Hz, H-3), 5.25−5.20 (m, 2H, H-2, H-3′), 5.11−5.04 (m, 3H, H-1, H-2′, H-4′), 4.67 (d, 1H, *J* = 8.0 Hz, H-1′), 4.25 (dd, 1H, *J* = 12.3, 4.7 Hz, H-6′), 4.20−4.16 (m, 2H, H-6, H-6′), 3.96−3.87 (m, 2H, H-5, H-6), 3.825 (app td, 1H, *J* = 9.4, 5.0 Hz, H-4), 3.76−3.72 (m, 1H, H-5′), 3.41 (s, 3H, OCH_3), 3.11 (d, 1H, *J* = 5.0 Hz, 4-OH), 2.06 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.9, 170.4, 169.5, 169.4, 167.7, 166.0, 133.6, 133.5, 130.0, 130.0, 129.3, 129.3, 128.6, 128.5, 101.2, 97.1, 74.5, 72.9, 72.1, 71.4, 71.3, 70.8, 70.1, 68.7, 68.5, 62.0, 55.5, 20.8, 20.77, 20.75, 20.72. HRMS (ESI, *m*/*z*): calcd for $[C_{35}H_{44}NO_{17}]$ $(M + NH_4)^+$ 750.2604, found 750.2598.

*Methyl 3-O-(2′,3′,4′,6′-Tetra-O-acetyl-β-D-glucopyranosyl)-4-O-benzoyl-α-L-rhamnopyranoside (**5b**).* Prepared from methyl 2,3-*O*-(4-(trifluoromethyl)phenylboronate)-α-L-rhamnopyranoside (0.066 g, 0.200 mmol) according to general procedure B. The title compound was purified by flash column chromatography on silica gel (ethyl acetate/hexanes 1:1) to yield a white amorphous solid (0.077 g, 63%). TLC: R_f = 0.23 (ethyl acetate/hexanes 1:1). $[\alpha]^{20}_D$ = −17.4 (*c* 0.97 in $CHCl_3$). FTIR (powder, cm^{-1}): 3506 (br), 2938 (w), 1748 (s), 1725 (s), 1367 (m), 1213 (s), 1029 (s), 907 (m), 712 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.04−8.01 (m, 2H, *o*-ArH), 7.60−7.56 (m, 1H, *p*-ArH), 7.47−7.44 (m, 2H, *m*-ArH), 5.33 (app t, 1H, *J* = 9.7 Hz, H-4), 5.05−4.95 (m, 2H, H-3′, H-4′), 4.93 (dd, 1H, *J* = 9.2, 7.9 Hz, H-2′), 4.76 (d, 1H, *J* = 1.6 Hz, H-1), 4.62 (d, 1H, *J* = 7.9 Hz, H-1′), 4.21 (dd, 1H, *J* = 12.2, 5.5 Hz, H-6′), 4.15−4.10 (m, 2H, H-2, H-6′), 4.04 (dd, 1H, *J* = 9.5, 3.3 Hz, H-3), 3.92−3.84 (m, 1H, H-5), 3.71−3.67 (m, 1H, H-5′), 3.40 (s, 3H, OCH_3), 2.73 (d, 1H, *J* = 2.4 Hz, 2-OH), 2.08 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.90 (s, 3H, CH_3CO), 1.41 (s, 3H, CH_3CO), 1.22 (d, 3H, *J* = 6.3 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.8, 170.3, 169.4, 169.2, 165.3, 133.4, 129.9, 129.8, 128.7, 101.5, 100.3, 79.6, 72.7, 72.5, 71.9, 70.9, 70.5, 68.6, 66.2, 61.9, 55.1, 20.7, 20.66, 20.61, 19.7, 17.6. HRMS (ESI, *m*/*z*): calcd for $[C_{28}H_{40}NO_{15}]$ $(M + NH_4)^+$ 630.2392, found 630.2390.

*Methyl 2-O-Benzoyl-3-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-β-L-arabinopyranoside (**5c**).* Prepared from 3,4-*O*-(4-(trifluoromethyl)phenylboronate)-β-L-arabinopyranose (0.064 g, 0.200 mmol) according to general procedure B. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield a white amorphous solid (0.085 g, 71%). TLC: R_f = 0.49 (ethyl acetate/hexanes 3:2). $[\alpha]^{20}_D$ = 39.1 (*c* 1.26 in $CHCl_3$). FTIR (powder, cm^{-1}): 3527 (br), 2973 (w), 2941 (w), 2927 (w), 2903 (w), 1748 (s), 1725 (s), 1364 (m), 1245 (s), 1214 (s), 1030 (s), 997 (s), 906 (m), 779 (m), 706 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.04−8.02 (m, 2H, *o*-ArH), 7.59−7.55 (m, 1H, *p*-ArH), 7.47−7.43 (m, 2H, *m*-ArH), 5.41 (dd, 1H, *J* = 10.0, 3.6 Hz, H-2), 5.08 (app t, 1H, *J* = 9.3 Hz, H-3′), 5.02 (app t, 1H, *J* = 9.3 Hz, H-4′), 4.97−4.93 (m, 2H, H-1, H-2′), 4.74 (d, 1H, *J* = 8.0 Hz, H-1′), 4.23−4.12 (m, 4H, H-3, H-4, H-5, H-5), 3.84 (app d, 1H, *J* = 12.0 Hz, H6′), 3.78 (dd, 1H, *J* = 12.5, 2.1 Hz, H-6′), 3.73−3.68 (m, 1H, H-5), 3.37 (s, 3H, OCH_3), 2.75 (s, 1H, 4-OH), 2.07 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.91 (s, 3H, CH_3CO), 1.45 (s, 3H, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.6, 170.2, 169.4, 169.2, 165.7, 133.5, 129.9, 129.7, 128.6, 101.6, 98.0, 76.9, 72.7, 72.0, 71.0, 70.1, 69.2, 68.4, 61.8, 61.5, 55.6, 20.8, 20.63, 20.59, 19.9. HRMS

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

(ESI, m/z): calcd for $[C_{27}H_{34}NaO_{15}]$ $(M + Na)^+$ 621.1790, found 621.1801.

*Methyl 2-O-Benzoyl-3-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-6-O-(tert-butyldimethylsilyl)-α-D-galactopyranoside (**5d**).* Prepared from methyl 3,4-*O*-(4-(trifluoromethyl)phenylboronate)-6-*O*-(*tert*-butyldimethylsilyl)-α-D-galactopyranoside (0.092 g, 0.200 mmol) according to general procedure B. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to give a white solid. This material was purified further by flash column chromatography on silica gel (gradient elution, acetone in dichloromethane) to yield the pure compound as a white amorphous solid (0.076 g, 51%). TLC: R_f = 0.25 (ethyl acetate/hexanes 2:3). $[\alpha]^{20}_D$ = 27.4 (*c* 0.87 in $CHCl_3$). FTIR (powder, cm^{-1}): 3510 (br), 2961 (w), 2932 (w), 2857 (w), 1748 (s), 1723 (s), 1365 (m), 1214 (s), 1034 (s), 836 (s), 777 (m), 711 (s). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.06−8.03 (m, 2H, *o*-ArH), 7.60−7.56 (m, 1H, *p*-ArH), 7.48−7.43 (m, 2H, *m*-ArH), 5.42 (dd, 1H, *J* = 9.6, 3.8 Hz, H-2), 5.11−5.01 (m, 2H, H-3′, H-4′), 5.01 (d, 1H, *J* = 3.8 Hz, H-1), 4.97 (dd, 1H, *J* = 9.3, 8.0 Hz, H-2′), 4.77 (d, 1H, *J* = 8.0 Hz, H-1′), 4.23 (dd, 1H, *J* = 12.4, 4.7 Hz, H-6′), 4.21−4.16 (m, 2H, H-3, H-4), 4.13 (dd, 1H, *J* = 12.4, 2.5 Hz, H-6′), 3.92−3.81 (m, 3H, H-5, H-6, H-6), 3.72−3.68 (m, 1H, H-5′), 3.37 (s, 3H, OCH_3), 2.63 (s, 1H, 4-OH), 2.08 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.92 (s, 3H, CH_3CO), 1.45 (s, 3H, CH_3CO), 0.89 (s, 9H, $(CH_3)_3CSi$), 0.09 (s, 3H, CH_3Si), 0.09 (s, 3H, CH_3Si). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.7, 170.3, 169.4, 169.2, 165.8, 133.5, 129.9, 129.8, 128.7, 101.7, 97.5, 77.5, 72.8, 72.0, 71.0, 70.4, 70.1, 69.3, 68.4, 62.4, 61.9, 55.3, 26.0, 20.8, 20.7, 20.6, 19.9, 18.4, − 5.2, − 5.3. HRMS (ESI, m/z): calcd for $[C_{34}H_{54}NO_{16}Si]$ $(M + NH_4)^+$ 760.3206, found 760.3214.

*Methyl 3-O-(2′,3′,4′,6′-Tetra-O-acetyl-β-D-glucopyranosyl)-4-O-benzoyl-6-O-(tert-butyldimethylsilyl)-α-D-mannopyranoside (**5e**).* Prepared from methyl 2,3-*O*-(4-(trifluoromethyl)phenylboronate)-6-*O*-(*tert*-butyldimethylsilyl)-α-D-mannopyranoside (0.092 g, 0.200 mmol) according to general procedure B. The title compound was purified by flash column chromatography on silica gel (gradient elution, acetone in dichloromethane) to yield a white amorphous solid (0.076 g, 51%). TLC: R_f = 0.37 (acetone:dichloromethane 1:9). $[\alpha]^{20}_D$ = 1.0 (*c* 1.02 in $CHCl_3$). FTIR (powder, cm^{-1}): 3500 (br), 2929 (w), 2861 (w), 1745 (s), 1366 (m), 1251 (s), 1216 (s), 1035 (s), 835 (s), 711 (s). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.05−8.02 (m, 2H, *o*-ArH), 7.58−7.54 (m, 1H, *p*-ArH), 7.43−7.40 (m, 2H, *m*-ArH), 5.37 (app t, 1H, *J* = 9.7 Hz, H-4), 5.13 (app t, 1H, *J* = 9.6 Hz, H-3′), 7.95 (app t, 1H, *J* = 9.6 Hz, H-4′), 4.90 (dd, 1H, *J* = 9.6, 7.9 Hz, H-2′), 4.80 (d, 1H, *J* = 1.7 Hz, H-1), 4.63 (d, 1H, *J* = 7.9 Hz, H-1′), 4.15 (dd, 1H, *J* = 9.4, 3.3 Hz, H-3), 3.94−3.83 (m, 3H, H-2, H-5, H-6), 3.78−3.69 (m, 2H, H-6′, H-6′), 3.51−3.45 (m, 2H, H-5′, H-6), 3.44 (s, 3H, OCH_3), 2.46 (d, 1H, *J* = 2.7 Hz, 2-OH), 1.99 (s, 3H, CH_3CO), 1.96 (s, 3H, CH_3CO), 1.95 (s, 3H, CH_3CO), 1.92 (s, 3H, CH_3CO), 0.83 (s, 9H, $(CH_3)_3CSi$), 0.00 (s, 3H, CH_3Si), − 0.02 (s, 3H, CH_3CSi). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.6, 170.4, 169.7, 169.3, 165.3, 133.4, 130.1, 129.9, 128.5, 100.5, 100.0, 79.4, 72.7, 72.0, 71.9, 71.8, 69.6, 68.0, 67.9, 63.3, 61.5, 55.1, 26.0, 20.8, 20.7, 20.7, 20.6, 18.4, − 5.2, − 5.3. HRMS (ESI, m/z): calcd for $[C_{34}H_{54}NO_{16}Si]$ $(M + NH_4)^+$ 760.3206, found 760.3202.

*1,2-O-Isopropylidene-5-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-6-O-benzoyl-α-D-glucofuranose (**5f**).* Prepared from 1,2-*O*-isopropylidene-3,5-*O*-(4-(trifluoromethyl)phenylboronate)-α-D-glucofuranose (0.075 g, 0.200 mmol) according to general procedure B. The title compound was purified by flash column chromatography on silica gel (gradient elution, acetone in dichloromethane) to yield a white amorphous solid (0.047 g, 36%). TLC: R_f = 0.39 (acetone:dichloromethane 1:9). $[\alpha]^{20}_D$ = 4.6 (*c* 1.19 in $CHCl_3$). FTIR (powder, cm^{-1}): 3513 (br), 2997 (w), 2939 (w), 1748 (s), 1721 (s), 1373 (m), 1273 (m), 1211 (s), 1164 (m), 1067 (s), 1028 (s), 713 (s). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.06−8.03 (m, 2H, *o*-ArH), 7.61−7.57 (m, 1H, *p*-ArH), 7.49−7.45 (m, 2H, *m*-ArH), 5.91 (d, 1H, *J* = 3.6 Hz, H-1), 5.17 (app t, 1H, *J* = 9.6 Hz, H-3′), 5.03−4.98 (m, 2H, H-2′, H-4′), 4.84 (d, 1H, *J* = 8.0 Hz, H-1′), 4.76 (dd, 1H, *J* = 12.2, 1.7 Hz, H-6), 4.54 (d, 1H, *J* = 3.6 Hz, H-2), 4.38−4.33 (m, 2H, H-3, H-6), 4.27 (dd, 1H, *J* = 12.4, 2.4 Hz, H-6′), 4.25−4.12 (m, 2H, H-4, H-5), 4.07 (dd, 1H, *J* = 12.4, 6.7 Hz, H-6′), 3.83−3.78 (m, 1H, H-5′), 3.53 (d, 1H, *J* = 4.0 Hz, 3-OH), 2.11 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO), 1.77 (s, 3H, CH_3CO), 1.48 (s, 3H, CH_3), 1.31 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.7, 170.1, 169.5, 169.4, 166.2, 133.5, 129.8, 129.7, 128.7, 112.1, 105.6, 101.1, 84.7, 79.0, 75.2, 74.0, 72.4, 72.2, 70.8, 68.5, 65.8, 62.1, 27.0, 26.4, 20.7, 20.66, 20.64, 20.4. HRMS (ESI, m/z): calcd for $[C_{30}H_{42}NO_{16}]$ $(M + NH_4)^+$ 672.2498, found 672.2489.

*Methyl 2,3-Bis-O-trimethylacetyl-6-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**5g**).* Prepared from methyl 4,6-*O*-(4-(trifluoromethyl)phenylboronate)-α-D-glucopyranoside (0.070 g, 0.200 mmol) according to general procedure B with the following amendment: instead of benzoyl chloride, trimethylacetyl chloride (98.0 μL, 0.800 mmol, 4.00 equiv) was used as the acylating agent and the acylation step was run for 16 h at 50 °C. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield a white amorphous solid (0.077 g, 55%). TLC: R_f = 0.34 (ethyl acetate/hexanes 1:1). $[\alpha]^{20}_D$ = 27.6 (*c* 1.03 in $CHCl_3$). FTIR (powder, cm^{-1}): 3502 (br), 2962 (w), 2936 (w), 1757 (s), 1732 (s), 1367 (m), 1217 (s) 1145 (s), 1033 (s), 906 (m). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.26 (dd, 1H, *J* = 10.1, 9.3 Hz, H-3), 5.20 (app t, 1H, *J* = 9.6 Hz, H-3′), 5.07 (app t, 1H, *J* = 9.6 Hz, H-4′), 5.03 (dd, 1H, *J* = 9.6, 7.9 Hz, H-2′), 4.88 (d, 1H, *J* = 3.8 Hz, H-1), 4.77 (dd, 1H, *J* = 10.1, 3.8 Hz, H-2), 4.61 (d, 1H, *J* = 7.9 Hz, H-1′), 4.23 (dd, 1H, *J* = 12.3, 4.6 Hz, H-6′), 4.16 (dd, 1H, *J* = 12.3, 2.5 Hz, H-6′), 4.12−4.09 (m, 1H, H-6), 3.81−3.76 (m, 2H, H-5, H-6), 3.73−3.69 (m, 1H, H-5′), 3.58−3.52 (m, 1H, H-4), 3.34 (s, 3H, OCH_3), 2.81 (d, 1H, *J* = 5.7 Hz, 4-OH), 2.08 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.18 (s, 9H, $(CH_3)_3CCO$), 1.16 (s, 9H, $(CH_3)_3CCO$). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 179.8, 177.8, 170.8, 170.4, 169.5, 169.4, 101.3, 96.8, 73.4, 72.8, 72.1, 71.2, 70.7, 70.5, 70.1, 68.7, 68.4, 61.9, 55.5, 39.1, 38.9, 27.2, 27.1, 20.9, 20.74, 20.74, 20.72. HRMS (ESI, m/z): calcd for $[C_{31}H_{52}NO_{17}]$ $(M + NH_4)^+$ 710.3230, found 710.3232.

*Methyl 2-O-Trimethylacetyl-6-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**5h**).* Prepared from methyl 4,6-*O*-(4-(trifluoromethyl)phenylboronate)-α-D-glucopyranoside (0.070 g, 0.200 mmol) according to general procedure B with the following amendment: instead of benzoyl chloride, trimethylacetyl chloride (29.5 μL, 0.240 mmol, 1.20 equiv) was used as the acylating agent. The title compound was isolated by flash column chromatography on silica gel (gradient elution, acetone in dichloromethane) as a yellow solid. Color was removed by stirring over charcoal in methanol solvent followed by filtration through a pad of tightly packed Celite. Solvent was removed under reduced pressure to yield the pure compound as a white amorphous solid (0.070 g, 58%). TLC: R_f = 0.29 (acetone/dichloromethane 1:4). $[\alpha]^{20}_D$ = 25.5 (*c* 1.28 in $CHCl_3$). FTIR (powder, cm^{-1}): 3486 (br), 2938 (w), 1729 (s), 1367 (m), 1216 (s), 1151 (m), 1029 (s), 908 (m), 772 (w). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.21 (apt t, 1H, *J* = 9.6 Hz, H-3′), 5.08 (dd, 1H, *J* = 9.6 Hz, H-4′), 5.02 (dd, 1H, *J* = 9.6, 8.0 Hz, H-2′), 4.85 (d, 1H, *J* = 3.7 Hz, H-1), 4.60 (dd, 1H, *J* = 10.0, 3.7 Hz, H-2), 4.25 (dd, 1H, *J* = 12.3, 4.5 Hz, H-6′), 4.19 (dd, 1H, *J* = 12.3, 2.6 Hz, H-6′), 4.07 (dd, 1H, *J* = 11.0, 2.7 Hz, H-6), 3.94 (dd, 1H, *J* = 9.8, 9.1 Hz, H-3), 3.81 (dd, 1H, *J* = 11.0, 5.4 Hz, H-6), 3.75−3.70 (m, 2H, H-5, H-5′), 3.50 (apt t, 1H, *J* = 9.3 Hz, H-4), 3.34 (s, 3H, OCH_3), 2.09 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.22 (s, 9H, $(CH_3)_3CCO$). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.6, 170.9, 170.4, 169.6, 169.5, 101.1, 97.2, 73.3, 72.8, 72.1, 71.9, 71.3, 71.2, 70.0, 68.9, 68.5, 61.9, 55.5, 39.0, 27.2, 20.9, 20.8, 20.74, 20.72. HRMS (ESI, m/z): calcd for $[C_{26}H_{44}NO_{16}]$ $(M + NH_4)^+$ 626.2655, found 626.2663.

*Methyl 2,3-Bis-O-benzoyl-6-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-galactopyranoside (**5i**).* Prepared from methyl 4,6-*O*-(4-(trifluoromethyl)phenylboronate)-α-D-galactopyranoside (0.070 g, 0.200 mmol) according to general procedure B with the following amendment: benzoyl chloride (0.058 mL, 0.500 mmol, 2.50 equiv). The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

hexanes) to yield a white amorphous solid (0.072 g). This material was found to be an inseparable mixture of **5i**:**5i′** (4:1). Yield of **5i** was determined to be 30% based on this ratio. TLC: R_f = 0.57 (ethyl acetate/hexanes 1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.10−7.94 (m, ArH), 7.60−7.40 (m, ArH), 7.35−7.32 (m, ArH), 5.65−5.61 (m, 2H, H-2, H-3), 5.18 (app t, 1H, J = 9.5 Hz, H-3′), 5.12 (d, 1H, J = 3.6 Hz, H-1), 5.05 (app t, 1H, J = 9.5 Hz, H-4′), 4.97 (dd, 1H, J = 9.5, 8.0 Hz, H-2′), 4.61 (d, 1H, J = 8.0 Hz, H-1′), 4.33−4.32 (m, 1H, H-4), 4.23 (dd, 1H, J = 12.3, 2.3 Hz, H-6′) 4.14−4.10 (m, 2H, H-5, H-6′), 4.05−4.02 (m, 1H, H-6), 3.88 (dd, 1H, J = 10.4, 6.6 Hz, H-6), 3.71−3.68 (m, 1H, H-5′), 3.38 (s, 3H, OCH_3), 2.93 (d, 1H, J = 4.4 Hz, 4-OH), 2.03 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 170.8, 170.3, 169.5, 169.4, 166.8, 166.2, 133.6, 133.3, 130.0, 129.9, 129.8, 129.6, 129.5, 128.7, 101.1, 97.6, 72.8, 72.1, 71.8, 71.2, 71.0, 68.9, 68.6, 68.4, 67.8, 61.8, 55.5, 20.7, 20.7, 20.6, 20.6. HRMS (ESI, m/z): calcd for $[C_{35}H_{44}NO_{17}]$ $(M + NH_4)^+$ 750.2604, found 750.2604 The yield of regioisomer methyl 2,6-bis-*O*-benzoyl-3-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-D-galactopyranoside (**5i′**) was determined to be 20% based on the 4:1 ratio of **5i**/**5i′** observed in the ^{1}H NMR spectrum. TLC: R_f = 0.57 (ethyl acetate/hexanes 1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.10−7.94 (m, ArH), 7.60−7.40 (m, ArH), 7.35−7.32 (m, ArH), 5.65−5.61 (m, 1H, H-4), 5.32 (dd, 1H, J = 10.3, 3.7 Hz, H-2), 5.13 (app t, 1H, J = H-3′), 5.12 (d, 1H, J = 3.7 Hz, H-1), 5.03 (app t, 1H, J = 9.5 Hz, H-4′), 4.97 (dd, 1H, J = 9.5, 8.0 Hz, H-2′), 4.51 (d, 1H, J = 8.0 Hz, H-1′), 4.47−4.44 (m, 1H, H-3), 4.26−4.24 (m, 1H, H-5), 4.16 (dd, 1H, J = 12.4, 5.0 Hz, H-6), 4.04−4.02 (m, 1H, H-6), 3.97 (dd, 1H, J = 10.8, 3.3 Hz, H-6′), 3.66−3.62 (m, 2H, H-5′, H-6′), 3.38 (s, 3H, OCH_3), 2.67 (d, 1H, J = 4.2 Hz, 4-OH), 2.00 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO), 1.96 (s, 3H, CH_3CO). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 170.7, 170.3, 169.5, 169.3, 166.4, 165.8, 133.5, 133.3, 130.0, 129.8, 129.7, 129.6, 129.3, 128.6, 101.1, 97.5, 72.8, 72.3, 71.9, 71.3, 69.4, 69.1, 68.7, 68.4, 67.2, 61.7, 55.5, 20.7, 20.7, 20.6, 20.6.

*Methyl 2,3-Bis-O-trimethylacetyl-6-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-galactopyranoside (**5j**).* Prepared from methyl 4,6-*O*-(4-(trifluoromethyl)phenylboronate)-α-D-galactopyranoside (0.070 g, 0.200 mmol) according to general procedure B with the following amendment: instead of benzoyl chloride, trimethylacetyl chloride (98.0 μL, 0.800 mmol, 4.00 equiv) was used as the acylating agent and the acylation step was run for 16 h at 50 °C. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield a white amorphous solid (0.029 g, 21%). TLC: R_f = 0.22 (ethyl acetate/hexanes 2:3). $[\alpha]^{20}_D$ = 33.5 (c 0.76 in $CHCl_3$). FTIR (powder, cm^{-1}): 3530 (br), 2966 (w), 2942 (w), 2876 (w), 1757 (s), 1728 (s), 1367 (m), 1217 (s), 1145 (s), 1034 (s), 905 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.20−5.06 (m, 3H, H-2, H-3, H-3′), 5.00 (app t, 1H, J = 9.8 Hz, H-4′), 4.92 (dd, 1H, J = 9.8, 8.0 Hz, H-2′), 4.88 (d, 1H, J = 3.6 Hz, H-1), 4.53 (d, 1H, J = 8.0 Hz, H-1′), 4.17−4.10 (m, 2H, H-6′, H-6′), 4.08−4.04 (m, 1H, H-4), 3.96−3.90 (m, 2H, H-5, H-6), 3.76−3.72 (m, 1H, H-6), 3.68−3.64 (m, 1H, H-5′), 3.28 (s, 3H, OCH_3), 2.34 (d, 1H, J = 4.3 Hz, 4-OH), 2.03 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO), 1.96 (s, 3H, CH_3CO), 1.93 (s, 3H, CH_3CO), 1.13 (s, 9H, $(CH_3)_3CCO$), 1.10 (s, 9H, $(CH_3)_3CCO$). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.1, 177.4, 170.8, 170.3, 169.5, 169.4, 101.1, 97.3, 72.8, 72.0, 71.2, 69.8, 68.8, 68.5, 68.4, 68.3, 67.7, 62.1, 55.6, 39.0, 38.9, 27.3, 27.1, 20.8, 20.75, 20.71, 20.70. HRMS (ESI, m/z): calcd for $[C_{31}H_{52}NO_{17}]$ $(M + NH_4)^+$ 710.3230, found 710.3229. Methyl 2,6-bis-*O*-trimethylacetyl-3-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-D-galactopyranoside (**5j′**) was also isolated from the reaction as a white amorphous solid (0.073 g, 53%). TLC: R_f = 0.31 (ethyl acetate/hexanes 2:3). $[\alpha]^{20}_D$ = 24.5 (c 0.98 in $CHCl_3$). FTIR (powder, cm^{-1}): 3510 (br), 2961 (w), 2921 (w), 2876 (w), 2855 (w), 1749 (s), 1728 (s), 1366 (m), 1214 (s), 155 (s), 1034 (s), 906 (m), 777 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.12−5.05 (m, 3H, H-2, H-3′, H-4′), 4.99 (dd, 1H, J = 9.4, 8.0 Hz, H-2′), 4.88 (d, 1H, J = 3.8 Hz, H-1), 4.75 (d, 1H, J = 8.0 Hz, H-1′), 4.33 (dd, 1H, J = 11.7, 4.5 Hz, H-6), 4.28−4.21 (m, 2H, H-6, H-6′), 4.13−4.04 (m, 3H, H-3, H-4, H-6′), 3.97−3.94 (m, 1H, H-5), 3.69−3.64 (m, 1H, H-5′), 3.34 (s, 3H, OCH_3), 2.54 (s, 1H, 4-OH), 2.09 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO), 1.96 (s, 3H, CH_3CO), 1.23 (s, 9H, $(CH_3)_3CCO$), 1.19 (s, 9H, $(CH_3)_3CCO$). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.3, 177.6, 170.7, 170.3, 169.4, 169.3, 100.8, 97.0, 75.2, 72.7, 72.1, 71.1, 70.2, 69.4, 68.4, 67.8, 63.7, 61.8, 55.4, 38.6, 29.8, 27.3, 27.2, 20.8, 20.7, 20.7, 20.7. HRMS (ESI, m/z): calcd for $[C_{31}H_{52}NO_{17}]$ $(M + NH_4)^+$ 710.3230, found 710.3229.

*Methyl 2-O-Benzoyl-3-O-trimethylacetyl-6-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**5k**).* In an oven-dried 1 dram screw-cap vial equipped with a stir bar was dissolved methyl 4,6-*O*-(4-(trifluoromethyl)phenylboronate)-α-D-glucopyranoside (0.070 g, 0.200 mmol) in anhydrous pyridine (0.400 mL) and cooled to 0 °C. Benzoyl chloride (0.028 mL, 0.240 mmol, 1.20 equiv) was added quickly to the reaction, and the solution was allowed to warm to room temperature with stirring. The reaction was allowed to stir for 1 h at room temperature before the addition of trimethylacetyl chloride (0.074 mL, 0.600 mmol, 3.00 equiv). The solution was then heated to 50 °C and allowed to stir for 24 h before cooling to room temperature. The reaction was diluted with toluene and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was then dissolved in anhydrous dichloromethane (1.00 mL) and transferred to an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (0.123 g, 0.300 mmol, 1.50 equiv), silver(I) oxide (0.070 g, 0.300 mmol, 1.50 equiv) and triethylamine (0.166 mL, 1.20 mmol, 6.00 equiv) were added to the flask and the reaction was stirred vigorously (800 rpm or higher) at room temperature overnight. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield the title compound as a white amorphous solid (0.097 g, 55%). TLC: R_f = 0.33 (ethyl acetate/hexanes 1:1). $[\alpha]^{20}_D$ = 31.7 (c 0.90 in $CHCl_3$). FTIR (powder, cm^{-1}): 3508 (br), 2962 (w), 1754 (s), 1725 (s), 1366 (m), 1216 (s), 1031 (s), 908 (m), 712 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.01−7.98 (m, 2H, *o*-ArH), 7.57−7.53 (m, 1H, *p*-ArH), 7.44−7.40 (m, 2H, *m*-ArH), 5.42 (dd, 1H, J = 10.1, 9.2 Hz, H-3), 5.22 (app t, 1H, J = 9.4 Hz, H-3′), 5.11−5.02 (m, 3H, H-2, H-2′, H-4′), 5.01 (d, 1H, J = 3.7 Hz, H-1), 4.64 (d, 1H, J = 8.0 Hz, H-1′), 4.25 (dd, 1H, J = 12.4, 4.5 Hz, H-6′), 4.19−4.13 (m, 2H, H-6, H-6′), 3.87−3.81 (m, 2H, H-5, H-6), 3.75−3.71 (m, 1H, H-5′), 3.67−3.61 (m, 1H, H-4), 3.36 (s, 3H, OCH_3), 2.92 (d, 1H, J = 5.5 Hz, 4-OH), 2.08 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.06 (s, 9H, $(CH_3)_3CCO$). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 179.7, 170.8, 170.4, 169.5, 169.4, 165.8, 133.6, 130.0, 129.2, 128.6, 101.3, 97.0, 73.4, 72.8, 72.0, 71.25, 71.23, 70.9, 69.9, 68.7, 68.4, 61.9, 55.4, 39.0, 27.0, 20.8, 20.72, 20.72, 20.70. HRMS (ESI, m/z): calcd for $[C_{33}H_{48}NO_{17}]$ $(M + NH_4)^+$ 730.2917, found 730.2916.

*Methyl 2-O-Trimethylacetyl-6-O-(2′,3′,4′,6′-tetra-O-benzyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**6a**).* Prepared from methyl 4,6-*O*-(phenylboronate)-α-D-glucopyranoside (0.056 g, 0.200 mmol) according to general procedure D with the following amendment: instead of benzoyl chloride, trimethylacetyl chloride (29.5 μL, 0.240 mmol, 1.20 equiv) was used as the acylating agent. The title compound was purified by flash column chromatography on silica gel (gradient elution, acetone in dichloromethane) to yield a white amorphous solid (0.093 g, 58%). TLC: R_f = 0.28 (acetone/dichloromethane 1:9). $[\alpha]^{20}_D$ = 25.4 (c 1.06 in $CHCl_3$) FTIR (powder, cm^{-1}): 3496 (br), 2969 (w), 2898 (w), 2872 (w), 1706 (m), 1454 (m), 1358 (m), 1284 (m), 1173 (m), 1146 (s), 1088 (s), 1068 (s), 1046 (s), 1028 (s), 1000 (s), 919 (m), 736 (s), 695 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39−7.27 (m, 18H, ArH), 7.18−7.16 (m, 2H, ArH), 4.98 (d, 1H, J = 11.1 Hz, PhCH), 4.49 (d, 1H, J = 11.1 Hz, PhCH), 4.90 (d, 1H, J = 3.8 Hz, H-1), 4.83 (d, 1H, J = 10.9 Hz, PhCH), 4.82 (d, 1H, J = 11.0 Hz, PhCH), 4.76 (d, 1H, J = 10.9 Hz, PhCH), 4.63 (dd, 1H, J = 10.0, 3.8 Hz, H-2), 4.62 (d, 1H, J = 12.1 Hz, PhCH), 4.56−4.52 (m, 2H, PhCH, PhCH), 4.52 (d, 1H, J = 7.8 Hz, H-1′), 4.16 (dd, 1H, J = 10.8, 2.8 Hz, H-6′), 3.93 (app dd, 1H, J = 9.8, 3.0 Hz, H-3), 3.88−3.79 (m, 2H, H-5′, H-6′), 3.75 (dd, 1H, J = 10.8,

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

2.0, H-6), 3.71−3.65 (m, 2H, H-5, H-6), 3.61 (app t, 1H, J = 9.1 Hz, H-3′), 3.55−3.49 (m, 3H, H-2′, H-4, H-4′), 3.33 (s, 3H, OCH_3), 3.17 (d, 1H, J = 3.5 Hz, 4-OH), 2.50 (d, 1H, J = 3.8 Hz, 3-OH), 1.25 (s, 9H, $(CH_3)_3CCO$). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.5, 138.6, 138.5, 138.1, 138.0, 128.6, 128.5, 128.5, 128.5, 128.2, 128.1, 128.0, 127.95, 127.89, 127.85, 127.81, 127.7, 103.9, 97.2, 84.8, 82.1, 77.9, 75.8, 75.1, 74.9, 74.9, 73.6, 73.3, 71.9, 71.7, 70.1, 69.3, 69.0, 55.5, 39.0, 27.2. HRMS (ESI, m/z): calcd for $[C_{46}H_{60}NO_{12}]$ $(M + NH_4)^+$ 818.4110, found 818.4112.

*Methyl 3-O-(2′,3′,4′,6′-Tetra-O-benzyl-β-D-glucopyranosyl)-4-O-benzoyl-α-L-rhamnopyranoside (**6b**).* Prepared from methyl 2,3-*O*-(phenylboronate)-α-L-rhamnopyranoside (0.053 g, 0.200 mmol) according to general procedure D. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield a white amorphous solid (0.115 g, 71%). TLC: R_f = 0.65 (ethyl acetate/hexanes 2:3). $[\alpha]^{20}_D$ = 1.6 (c 1.13 in $CHCl_3$). FTIR (powder, cm^{-1}): 3532 (br), 2918 (W), 2837 (s), 1744 (s), 1514 (m), 1367 (m), 1216 (s), 1033 (s), 907 (m), 800 (m). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.94−7.91 (m, 2H, ArH), 7.45−7.41 (m, 1H, ArH), 7.35−7.32 (m, 4H, ArH), 7.31−7.25 (m, 6H, ArH), 7.25−7.20 (m, 3H, ArH), 7.17−7.10 (m, 5H, ArH), 7.08−7.03 (m, 2H, ArH), 6.89−6.86 (m, 2H, ArH), 5.48 (app t, 1H, J = 9.4 Hz, H-4), 4.78−4.71 (m, 3H, H-1, PhCH, PhCH), 4.64 (d, 1H, J = 11.0 Hz, PhCH), 4.55−4.47 (m, 5H, H-1′, PhCH, PhCH, PhCH, PhCH), 4.35 (d, 1H, J = 11.6 Hz, PhCH), 4.20−4.16 (m, 2H, H-2, H-3), 3.96−3.91 (m, 1H, H-5), 3.68 (dd, 1H, J = 10.3, 1.2 Hz, H-6′), 3.56−3.46 (m, 4H, H-3′, H-4′, H-5′, H-6′), 3.44−3.39 (m, 4H, H-2′, OCH_3), 3.22 (d, 1H, J = 2.7 Hz, 2-OH), 1.26 (d, 3H, J = 6.3 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 165.8, 138.5, 138.2, 138.1, 138.1, 133.1, 129.9, 129.8, 128.6, 128.52, 128.48, 128.37, 128.2, 128.1, 128.0, 127.95, 127.87, 127.82, 127.7, 127.6, 127.3, 103.5, 100.7, 84.7, 81.8, 79.5, 77.8, 75.7, 75.1, 74.7, 74.5, 73.7, 72.8, 69.8, 69.3, 66.3, 55.1, 17.7. HRMS (ESI, m/z): calcd for $[C_{48}H_{56}NO_{11}]$ $(M + NH_4)^+$ 822.3848, found 822.3848.

*Methyl 2-O-Benzoyl-3-O-(2′,3′,4′,6′-tetra-O-benzyl-β-D-glucopyranosyl)-α-L-fucopyranoside (**6c**).* Prepared from methyl 3,4-*O*-(phenylboronate)-α-L-fucopyranoside (0.053 g, 0.200 mmol) according to general procedure D. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield a white amorphous solid (0.142 g, 88%). TLC: R_f = 0.78 (ethyl acetate/hexanes 2:3). $[\alpha]^{20}_D$ = −24.4 (c 1.05 in $CHCl_3$). FTIR (powder, cm^{-1}): 3470 (br), 3030 (w), 2906 (w), 1717 (m), 1496 (w), 1452 (m), 1274 (m), 1052 (s), 1027 (s), 999 (s), 960 (m), 912 (m), 735 (s), 693 (s). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.14−8.11 (m, 2H, *o*-Bz), 7.53−7.48 (m, 1H, *p*-Bz), 7.37−7.28 (m, 20H, ArH), 7.19−7.17 (m, 2H, ArH), 5.46 (dd, 1H, J = 10.3, 3.8 Hz, H-2), 5.09 (dm 1H, J = 3.8 Hz, H-1), 4.92 (d, 1H, J = 11.0 Hz, PhCH), 4.87−4.84 (m, 3H, PhCH, PhCH, PhCH), 4.80 (d, 1H, J = 10.7 Hz, PhCH), 4.59−4.47 (m, 4H, H-1′, PhCH, PhCH, PhCH), 4.46 (dd, 1H, J = 10.2, 3.2 Hz, H-3), 4.02−3.95 (m, 2H, H-4, H-5), 3.67−3.59 (m, 4H, H-3′, H-4′, H-6′, H-6′), 3.44 (dd, 1H, J = 8.8, 7.9 Hz, H-2′), 3.42−3.37 (m, 4H, H-5′, OCH_3), 1.34 (d, 3H, J = 6.6 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 166.3, 138.5, 138.2, 138.1, 137.9, 133.0, 130.3, 130.0, 128.6, 128.5, 128.5, 138.46, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.76, 127.73, 127.67, 99.8, 97.7, 85.1, 81.8, 78.0, 75.6, 75.5, 75.4, 75.1, 74.7, 73.7, 69.7, 69.3, 68.7, 65.3, 55.4, 16.3. HRMS (ESI, m/z): calcd for $[C_{48}H_{56}NO_{11}]$ $(M + NH_4)^+$ 822.3848, found 822.3856.

*Methyl 2,3-Bis-O-trimethylacetyl-6-O-(2′,3′,4′,6′-tetra-O-benzyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**6d**).* Prepared from methyl 4,6-*O*-(phenylboronate)-α-D-galactopyranoside (0.056 g, 0.200 mmol) according to general procedure D with the following amendment: instead of benzoyl chloride, trimethylacetyl chloride (98.0 μL, 0.800 mmol, 4.00 equiv) was used as the acylating agent and the acylation step was run for 16 h at 50 °C. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield a white amorphous solid (0.112 g, 63%). TLC: R_f = 0.62 (ethyl acetate/hexanes 2:3). $[\alpha]^{20}_D$ = 26.5 (c 1.30 in $CHCl_3$). FTIR (powder, cm^{-1}): 3458 (br), 2969 (w), 2933 (w), 2915 (w), 2876 (w), 1732 (s), 1454 (m), 1281 (m), 1146 (s), 1043 (s), 734 (s), 696 (s). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.38−7.26 (m, 18H, ArH), 7.17−7.15 (m, 2H, ArH), 5.35 (app t, 1H, J = 10.2, 9.2 Hz, H-3), 5.00 (d, 1H, J = 10.9 Hz, PhCH), 4.94 (d, 1H, J = 11.0 Hz, PhCH), 4.94 (d, 1H, J = 3.7 Hz, H-1), 4.83−4.79 (m, 3H, H-2, PhCH, PhCH), 4.73 (d, 1H, J = 10.9 Hz, PhCH), 4.63 (d, 1H, J = 12.2 Hz, PhCH), 4.56−4.51 (m, 3H, H-1′, PhCH, PhCH), 4.22−4.18 (m, 1H, H-6), 3.92−3.86 (m, 2H, H-4′, H-6), 3.74 (dd, 1H, J = 10.7, 2.0 Hz, H-6′), 3.70−3.64 (m, 3H, H-4, H-5, H-6′), 3.59 (app t, 1H, J = 9.2 Hz, H-3′), 3.53−3.48 (m, 2H, H-2′, H-5′), 3.35 (s, 3H, OCH_3), 2.90 (d, 1H, J = 5.6 Hz, 4-OH), 1.19 (s, 9H, $(CH_3)_3CCO$), 1.18 (s, 9H, $(CH_3)_3CCO$). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 179.4, 177.9, 138.7, 138.5, 138.2, 138.2, 138.52, 128.50, 128.49, 128.49, 128.48, 128.2, 128.1, 128.0, 127.9, 127.8, 127.76, 127.72, 104.0, 95.8, 84.8, 82.1, 77.9, 75.8, 75.1, 75.0, 74.9, 73.6, 73.2, 70.8, 70.7, 70.6, 69.0, 68.9, 55.5, 39.0, 38.9, 27.3, 27.1. HRMS (ESI, m/z): calcd for $[C_{51}H_{68}NO_{13}]$ $(M + NH_4)^+$ 902.4685, found 902.4694.

*Methyl 2,3-Bis-O-benzoyl-6-O-(2′,3′,4′,6′-tetra-O-benzyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**6e**).* 2,3-Bis-*O*-benzoyl-α-D-glucopyranoside[14] (0.053 g, 0.132 mmol, 1.00 equiv) and phenylboronic acid (0.016 g, 0.132 mmol, 1.00 equiv) were placed in a round-bottom flask equipped with stir bar. Toluene (1.00 mL) was added to the flask, and the solution was placed in an oil bath set at 110 °C and stirred overnight. The solution was then cooled to room temperature, and solvent was removed under reduced pressure. Residual water was removed from the resulting material via azeotroping with toluene three times, followed by drying under high vacuum to yield a white solid. The resulting material was then dissolved in anhydrous dichloromethane (1.00 mL) and transferred via syringe to an oven-dried round-bottom flask charged with a stir bar and 4 Å molecular sieves. 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.081 g, 0.145 mmol, 1.10 equiv) and silver(I) oxide (0.034 g, 0.145 mmol, 1.10 equiv) were added to the solution followed by triethylamine (0.110 mL, 0.792 mmol, 6.00 equiv), and the reaction was stirred vigorously (800 rpm or higher) at room temperature for 48 h. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to give a white solid. This material was purified further by flash column chromatography on silica gel (acetone/toluene 1:9) to yield the pure compound as a white amorphous solid (0.050 g, 41%). TLC: R_f = 0.34 (ethyl acetate/hexanes 1:1). $[\alpha]^{20}_D$ = 33.1 (c 0.98 in $CHCl_3$) FTIR (powder, cm^{-1}): 3446 (br), 3031 (w), 2908 (w), 1722 (s), 1452 (m), 1275 (s), 1092 (s), 1063 (s), 1026 (s), 914 (w), 735 (m), 693 (s). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.96−7.90 (m, 4H, *o*-Bz), 7.48−7.47 (m, 2H, *p*-Bz), 7.34−7.17 (m, 22H, ArH), 7.12−7.10 (m, 2H, ArH), 5.72 (dd, 1H, J = 10.1, 9.1 Hz, H-3), 5.19 (dd, 1H, J = 10.1, 3.7 Hz, H-2), 5.10 (d, 1H, J = 3.7 Hz, H-1), 4.97 (d, 1H, J = 11.0 Hz, PhCH), 4.89 (d, 1H, J = 11.0 Hz, PhCH), 4.78−4.71 (m, 3H, PhCH, PhCH, PhCH), 4.55−4.44 (m, 2H, PhCH, PhCH), 4.50 (d, 1H, J = 7.7 Hz, H-1′), 4.18 (dd, 1H, J = 10.5, 2.0 Hz, H-6), 3.98−3.90 (m, 3H, H-5, H-6), 3.88 (app t, 1H, J = 9.1 Hz, H-4), 3.69 (dd, 1H, J = 10.7, 1.9 Hz, H-6′), 3.65−3.44 (m, 5H, H-2′, H-3′, H-4′, H-5′, H-6′), 3.35 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.3, 166.1, 138.7, 138.5, 138.2, 138.1, 133.4, 133.4, 129.99, 129.97, 129.5, 129.4, 128.53, 128.50, 128.50, 128.50, 128.50, 128.48, 128.1, 128.05, 127.96, 127.96, 127.89, 127.8, 127.76, 127.74, 103.9, 97.2, 84.8, 82.1, 77.9, 75.8,75.1, 75.0, 75.0, 74.2, 73.6, 71.7, 70.8, 70.3, 68.9, 68.8, 55.5. HRMS (ESI, m/z): calcd for $[C_{55}H_{60}NO_{13}]$ $(M + NH_4)^+$ 942.4059, found 942.4053. Acyl migration byproducts **6e′**, **6e″**, and **6f** were also isolated from the reaction. ^1H and ^{13}C NMR characterization data are provided. Methyl 3,4-Bis-*O*-benzoyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**6e′**). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.96−7.90 (m, 4H, *o*-Bz), 7.51−7.47 (m, 2H, *p*-Bz), 7.41−7.23 (m, 22H, ArH), 7.16−7.13 (m, 2H, ArH), 5.70 (app t, 1H, J = 9.8 Hz, H-3), 5.38 (app t, 1H, J = 9.8 Hz, H-4), 5.06 (d, 1H, J = 10.9 Hz, PhCH), 4.92 (d, 1H, J = 11.0 Hz, PhCH), 4.89 (d, 1H, J = 3.7 Hz, H-1), 4.81 (d, 1H, J = 10.7 Hz, PhCH), 4.77 (d, 1H, J = 10.7 Hz, PhCH), 4.69 (d, 1H, J = 11.0 Hz, PhCH), 4.54−4.50 (m, 2H, PhCH, PhCH), 4.47−4.42 (m, 2H, H-1′, PhCH), 4.29−4.24 (m, 1H, H-5), 4.09 (dd, 1H, J =

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

11.0, 2.1, H-6) 3.85 (dd, J = 9.8, 3.6 Hz, H-2), 3.77 (dd, 1H, J = 11.0, 7.4 Hz, H-6), 3.66−3.62 (m, 3H, H-5′, H-6′, H-6′), 3.58 (app t, 1H, J = 9.1 Hz, H-4′), 3.48−3.39 (m, 5H, H-2′, H-3′, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.0, 165.6, 138.7, 138.6, 138.24, 138.22, 133.5, 133.3, 130.0, 129.5, 129.1, 128.54, 128.50, 128.49, 128.48, 128.45, 128.42, 128.3, 128.1, 128.0, 127.86, 127.85, 127.8, 127.71, 127.69, 104.2, 99.3, 84.7, 82.5, 77.8, 75.8, 75.1, 75.0, 74.9, 74.2, 73.6, 71.6, 69.5, 69.4, 69.0, 68.8, 55.8. Methyl 2,4-*O*-Benzoyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**6e″**). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.01−7.96 (m, 4H, ArH), 7.53−7.49 (m, 2H, ArH), 7.40−7.15 (m, 24H, ArH), 5.77 (dd, 1H, J = 10.2, 9.0 Hz, H-4), 5.25 (dd, 1H, J = 10.2, 3.6 Hz, H-2), 5.15 (d, 1H, J = 3.6 Hz, H-1), 5.02 (d, 1H, J = 11.0 Hz, PhCH), 4.95 (d, 1H, J = 11.2 Hz, PhCH), 4.87−4.69 (m, 3H, H-1′, PhCH, PhCH), 4.62−4.48 (m, 4H, PhCH, PhCH, PhCH, PhCH), 4.24 (dd, 1H, J = 10.6, 2.1 Hz, H-6), 4.01−3.91 (m, 3H, H-3, H-6′, H-6′), 3.75 (dd, 1H, J = 10.6, 2.1 Hz, H-6), 3.71−3.53 (m, 5H, H-2′, H-3′, H-4′, H-5, H-5′), 3.41 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.3, 166.1, 138.6, 138.5, 138.2, 138.1, 133.4, 130.0, 129.9, 129.5, 129.3, 128.5, 128.5, 128.50, 128.5, 128.5, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 103.9, 97.2, 84.8, 82.1, 77.9, 75.8, 75.1, 75.0, 74.2, 73.6, 71.7, 70.8, 70.4, 70.2, 68.9, 68.7, 55.5. Methyl 2-*O*-benzoyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**6f**): ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.11−8.08 (m, 2H, *o*-ArH), 7.61−7.56 (m, 1H, *p*-ArH), 7.48−7.44 (m, 2H, *m*-ArH), 7.40−7.25 (m, 18H, ArH), 7.18−7.16 (m, 2H, ArH), 5.03 (d, 1H, J = 3.8 Hz, H-1), 4.98 (d, 1H, J = 11.1 Hz, PhCH), 4.93 (d, 1H, J = 10.9 Hz, PhCH), 4.92 (dd, 1H, J = 9.7, 3.8 Hz, H-2), 4.84−4.74 (m, 3H, H-1′, PhCH, PhCH), 4.62 (d, 1H, J = 12.2 Hz, PhCH), 4.56−4.52 (m, 3H, PhCH, PhCH, PhCH), 4.15 (dd, 1H, J = 11.0, 3.1 Hz, H-6), 4.09 (dd, 1H, J = 9.7, 9.0 Hz, H-3), 3.91 (dd, 1H, J = 10.9, 4.9 Hz, H-6′), 3.87−3.83 (m, 1H, H-5), 3.76 (dd, 1H, J = 10.9, 2.0 Hz, H-6′), 3.71−3.51 (m, 6H, H-2′, H-3′, H-4, H-4′, H-5′, H-6), 3.35 (s, 3H, OCH_3).

*Methyl 2,3-Bis-O-(p-methoxybenzyl)-4-O-acetyl-6-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**7a**).* Methyl 4,6-*O*-(4-(trifluoromethyl)phenylboronate)-α-D-glucopyranoside (0.070 g, 0.200 mmol) was dissolved in a 1:1 (v/v) mixture of toluene and dichloromethane (1.00 mL) and cooled to 0 °C. 4-Methoxybenzyl trichloroacetimidate (0.250 mL, 1.20 mmol, 6.00 equiv) was added to the solution followed by lanthanum(III) trifluoromethanesulfonate (0.001 g, 0.002 mmol, 0.010 equiv), and the reaction was stirred at 0 °C for 15 min before being quenched with triethylamine. The solution was concentrated under reduced pressure, and the crude material was dissolved in anhydrous dichloromethane (1.00 mL) and transferred to an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (0.123 g, 0.300 mmol, 1.50 equiv), silver(I) oxide (0.070 g, 0.300 mmol, 1.50 equiv), and triethylamine (0.166 mL, 1.20 mmol, 6.00 equiv) were added to the flask, and the reaction was stirred vigorously (800 rpm or higher) at room temperature overnight. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel (gradient elution, acetone in dichloromethane) to give an inseparable mixture of the desired disaccharide and hydrolyzed donor. The mixture was dissolved in pyridine (0.500 mL), and acetic anhydride (0.190 mL, 2.00 mmol, 10.0 equiv) was added to the solution. Once complete, excess pyridine and was removed via azeotroping with toluene and the crude material was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield the title compound as an amorphous white solid (0.052 g, 32%). TLC: R_f = 0.22 (ethyl acetate/hexanes 1:1). $[\alpha]^{20}_D$ = −1.08 (c 0.93 in $CHCl_3$). FTIR (powder, cm^{-1}): 2934 (w), 2843 (w), 1742 (s), 1513)m), 1366 (m), 1215 (s), 1029 (s), 906 (m), 820 (m), 729 (m). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.27−7.25 (m, 2H, ArH), 7.19−7.17 (m, 2H, ArH), 6.86−6.83 (m, 4H, ArH), 5.17 (app t, 1H, J = 9.6 Hz, H-3′), 5.05 (app t, 1H, J = 9.6 Hz, H-4′), 4.98 (dd, 1H, J = 9.6, 7.9 Hz, H-2′), 4.79−4.72 (m, 3H, H-4, ArCH, ArCH), 4.56−4.51 (m, 2H, ArCH, ArCH), 4.50 (d, 1H, J = 7.9 Hz, H-1′), 4.48 (d, 1H, J = 3.6 Hz, H-1), 4.24 (dd, 1H, J = 12.3, 4.6 Hz, H-6′), 4.10 (dd, 1H, J = 12.3, 2.2 Hz, H-6′), 3.87−3.71 (m, 9H, H-3, H-5, H-6, $ArOCH_3$, $ArOCH_3$), 3.67−3.63 (m, 1H, H-5′), 3.48 (dd, 1H, J = 9.6, 3.6 Hz, H-2), 3.43 (dd, 1H, J = 11.0, 6.8 Hz, H-6), 3.34 (s, 3H, OCH_3), 2.05 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO), 1.92 (s, 3H, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.7, 170.3, 169.9, 169.5, 169.4, 159.5, 159.2, 130.8, 130.1, 129.9, 129.5, 114.0, 113.8, 101.0, 98.1, 79.2, 78.8, 75.0, 73.2, 72.8, 71.9, 71.1, 70.5, 68.7, 68.6, 68.5, 61.9, 55.4, 55.4, 55.3, 21.0, 20.8, 20.72, 20.68, 20.67. HRMS (ESI, m/z): calcd for $[C_{39}H_{54}NO_{18}]$ $(M + NH_4)^+$ 824.3335, found 824.3348.

*Methyl 3-O-(2′,3′,4′,6′-Tetra-O-acetyl-β-D-glucopyranosyl)-4-O-(p-methoxybenzyl)-α-L-rhamnopyranoside (**7b**).* Prepared from methyl 2,3-*O*-(4-(trifluoromethyl)phenylboronate)-α-L-rhamnopyranoside (0.066 g, 0.200 mmol) according to general procedure C. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to give a white solid. This material was purified further by flash coloumn chromatography on silica gel (acetone:dichloromethane 1:1) to yield the pure compound a white amorphous solid (0.075 g, 60%). TLC: R_f = 0.20 (ethyl acetate/hexanes 1:1). $[\alpha]^{20}_D$ = −16.4 (c 1.12 in $CHCl_3$). FTIR (powder, cm^{-1}): 3528 (br), 2919 (w), 1740 (s), 1514 (m), 1368 (m), 1216 (s), 1096 (m), 1032 (s), 907 (m), 800 (m). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.28−7.24 (m, 2H, *o*-ArH), 6.89−6.86 (m, 2H, *m*-ArH), 5.23 (app t, 1H, J = 9.4 Hz, H-3′), 5.13−5.03 (m, 2H, H-2′, H-4′), 4.79 (d, 1H, J = 7.9 Hz, H-1′), 4.67 (d, 1H, J = 10.7 Hz, PhCH), 4.66 (d, 1H, J = 1.6 Hz, H-1), 4.45 (d, 1H, J = 10.7 Hz, PhCH), 4.22 (dd, 1H, J = 12.3, 5.7 Hz, H-6′), 4.14 (dd, 1H, J = 12.3, 2.6 Hz, H-6′), 4.02−4.00 (m, 1H, H-2), 3.94 (dd, 1H, J = 9.2, 3.1 Hz, H-3), 3.79 (s, 3H, $ArOCH_3$), 3.75−3.70 (m, 1H, H-5′), 3.68−3.62 (m, 1H, H-5), 3.44 (app t, 1H, J = 9.3 Hz, H-4), 3.33 (s, 3H, OCH_3), 2.70 (d, 1H, J = 2.8 Hz, 2-OH), 2.08 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.82 (s, 3H, CH_3CO), 1.26 (d, 3H, J = 6.3 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.8, 170.3, 169.5, 169.5, 159.4, 130.5, 129.4, 114.0, 101.0, 100.2, 82.4, 78.8, 74.7, 73.0, 72.0, 71.5, 70.4, 68.6, 67.3, 62.0, 55.4, 54.8, 20.7, 20.7, 20.7, 20.6, 18.0. HRMS (ESI, m/z): calcd for $[C_{29}H_{44}NO_{15}]$ $(M + NH_4)^+$ 646.2705, found 646.2699.

*Methyl 2-O-(p-Methoxybenzyl)-3-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-β-L-arabinopyranoside (**7c**).* Prepared from methyl 3,4-*O*-(4-(trifluoromethyl)phenylboronate)-β-L-arabinopyranose (0.064 g, 0.200 mmol) according to general procedure C. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield a white amorphous solid (0.079 g, 64%). TLC: R_f = 0.29 (ethyl acetate/hexanes 3:2). $[\alpha]^{20}_D$ = 8.1 (c 0.80 in $CHCl_3$). FTIR (powder, cm^{-1}): 3528 (br), 2936 (w), 2840 (w), 1747 (s), 1513 (m), 1366 (m), 1213 (s), 1091 (s), 1031 (s), 905 (m), 821 (m). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.28−7.25 (m, 2H, *o*-ArH), 6.88−6.86 (m, 2H, *m*-ArH), 5.20 (app t, 1H, J = 9.5 Hz, H-3′), 5.11−5.04 (m, 2H, H-2′, H-4′), 4.84 (d, 1H, J = 7.9 Hz, H-1′), 4.65 (d, 1H, J = 11.7 Hz, ArCH), 4.50 (d, 1H, J = 3.5 Hz, H-1), 4.41 (d, 1H, J = 11.7 Hz, ArCH), 4.21 (dd, 1H, J = 12.3, 5.0 Hz, H-6′), 4.11 (dd, 1H, J = 12.3, 2.5 Hz, H-6′), 4.04−4.01 (m, 2H, H-3, H-4), 3.80 (s, 3H, $ArOCH_3$), 3.77−3.64 (m, 4H, H2, H-5, H-5, H-5′), 3.34 (s, 3H, OCH_3), 2.06 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.7, 170.3, 169.54, 169.50, 159.6, 130.2, 129.8, 114.1, 101.3, 99.0, 78.3, 75.1, 73.3, 72.8, 72.0, 71.4, 69.1, 68.5, 61.9, 61.3, 55.6, 55.4, 20.83, 20.79, 20.72, 20.70. HRMS (ESI, m/z): calcd for $[C_{28}H_{42}NO_{15}]$ $(M + NH_4)^+$ 632.2549, found 632.2547.

*Methyl 2-O-(p-Methoxybenzyl)-3-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-6-O-(tert-butyldimethylsilyl)-α-D-galactopyranoside (**7d**).* Prepared from methyl 3,4-*O*-(4-(trifluoromethyl)-phenylboronate)-6-*O*-(*tert*-butyldimethylsilyl)-α-D-galactopyranoside (0.092 g, 0.200 mmol) according to general procedure C. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to give a yellow mixture. This material was purified further by flash column chromatography on silica gel (gradient elution, acetone in dichloromethane) to yield the pure compound a white amorphous solid (0.081 g, 53%). TLC: R_f =

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

0.64 (ethyl acetate/hexanes 1:1). $[\alpha]^{20}_{D}$ = 5.52 (*c* 0.82 in $CHCl_3$). FTIR (powder, cm^{-1}): 3504 (br), 2958 (w), 2933 (w), 2857 (w), 1749 (s), 1513 (m), 1365 (m), 1214 (s), 1090 (s), 1033 (s), 835 (s), 744 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.28−7.25 (m, 2H, *o*-ArH), 6.89−6.85 (m, 2H, *m*-ArH), 5.20 (app t, 1H, *J* = 9.4 Hz, H-3′), 5.11−5.06 (m, 2H, H-2′, H-4′), 4.87 (d, 1H, *J* = 8.0 Hz, H-1′), 4.65 (d, 1H, *J* = 11.7 Hz, PhCH), 4.50 (d, 1H, *J* = 3.7 Hz, H-1), 4.40 (d, 1H, *J* = 11.7 Hz, PhCH), 4.22 (dd, 1H, *J* = 12.4, 4.8 Hz, H-6′), 4.10−4.06 (m, 2H, H-4, H-6′), 4.00 (dd, 1H, *J* = 9.8, 3.3 Hz, H-3), 3.82−3.77 (m, 5H, H-2, H-6, $ArOCH_3$), 3.76−3.71 (m, 2H, H-5, H-6), 3.69−3.65 (m, 1H, H-5), 3.33 (s, 3H, OCH_3), 2.57 (s, 1H, 4-OH), 2.07 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO), 0.87 (s, 9H, $(CH_3)_3CSi$), 0.05 (s, 3H, CH_3Si), 0.05 (s, 3H, CH_3Si). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.7, 170.3, 169.6, 169.5, 159.6, 130.2, 129.8, 114.1, 101.2, 98.4, 78.8, 75.3, 73.3, 72.9, 71.9, 71.4, 69.9, 68.9, 68.4, 62.5, 61.9, 55.4, 55.3, 26.0, 20.9, 20.8, 20.73, 20.71, 18.4, − 5.26, − 5.31. HRMS (ESI, *m*/*z*): calcd for $[C_{35}H_{54}NaO_{16}Si]$ $(M + Na)^+$ 781.3073, found 781.3078.

*Methyl 3-O-(2′,3′,4′,6′-Tetra-O-acetyl-β-D-glucopyranosyl)-4-O-(p-methoxybenzyl)-6-O-(tert-butyldimethylsilyl)-α-D-mannopyranoside (**7e**).* Prepared from methyl 2,3-*O*-(4-(trifluoromethyl)-phenylboronate)-6-*O*-(*tert*-butyldimethylsilyl)-α-D-mannopyranoside (0.092 g, 0.200 mmol) according to general procedure C. The title compound was purified by flash column chromatography on silica gel (gradient elution, acetone in dichloromethane) to yield a white amorphous solid (0.074 g, 49%). TLC: R_f = 0.51 (acetone:dichloromethane 1:9). $[\alpha]^{20}_{D}$ = 9.6 (*c* 0.62 in $CHCl_3$). FTIR (powder, cm^{-1}): 3457 (br), 2958 (w), 2930 (w), 2856 (w), 1750 (s), 1514 (m), 1366 (m), 1215 (s), 1091 (s), 1032 (s), 973 (s), 834 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.27−7.25 (m, 2H, *o*-ArH), 6.85−6.82 (m, 2H, *m*-ArH), 5.21 (app t, 1H, *J* = 9.4 Hz, H-3′), 5.14 (app t, 1H, *J* = 9.6 Hz, H-4′), 5.04 (dd, 1H, *J* = 9.4, 7.9 Hz, H-2′), 4.86 (d, 1H, *J* = 10.4 Hz, $ArCH_2$), 4.71−4.69 (m, 2H, H-1, H-1′), 4.45 (d, 1H, *J* = 10.4 Hz, ArCH), 4.29 (dd, 1H, *J* = 12.4, 4.4 Hz, H-6′), 4.08−4.03 (H-3, H-6′), 3.87−3.84 (m, 1H, H-2), 3.82−3.76 (m, 5H, H-6, H-6, $ArOCH_3$), 3.70−3.65 (m, 2H, H-4, H-5′), 3.55−3.51 (m, 1H, H-5), 3.33 (s, 3H, OCH_3), 2.07 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 0.89 (s, 9H, $(CH_3)_3CSi$), 0.06 (s, 3H, CH_3Si), 0.06 (s, 3H, CH_3CSi). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.8, 170.4, 169.9, 169.5, 159.4, 130.9, 129.8, 113.8, 100.1, 99.8, 81.1, 74.5, 73.0, 72.6, 72.4, 72.2, 72.0, 68.9, 68.3, 62.6, 62.0, 55.4, 54.8, 26.1, 20.82, 20.80, 20.74, 20.72, 18.5, − 5.0, − 5.2. HRMS (ESI, *m*/*z*): calcd for $[C_{35}H_{58}NO_{16}Si]$ $(M + NH_4)^+$ 776.3519, found 776.3528.

*Methyl 2,3-Bis-O-(p-methoxybenzyl)-4-O-acetyl-6-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-galactopyranoside (**7f**).* Methyl 4,6-*O*-(4-(trifluoromethyl)phenylboronate)-α-D-galactopyranoside (0.070 g, 0.200 mmol) was dissolved in a 1:1 (v/v) mixture of toluene and dichloromethane (1.00 mL) and cooled to 0 °C. 4-Methoxybenzyl trichloroacetimidate (0.250 mL, 1.20 mmol, 6.00 equiv) was added to the solution followed by lanthanum(III) trifluoromethanesulfonate (0.001 g, 0.002 mmol, 0.010 equiv). The reaction was stirred at 0 °C for 15 min before being quenched with triethylamine. The solution was concentrated under reduced pressure, and the crude material was dissolved in anhydrous dichloromethane (1.00 mL) and transferred to an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (0.123 g, 0.300 mmol, 1.50 equiv), silver(I) oxide (0.070 g, 0.300 mmol, 1.50 equiv), and triethylamine (0.166 mL, 1.20 mmol, 6.00 equiv) were added to the flask, and the reaction was stirred vigorously (800 rpm or higher) at room temperature overnight. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel (gradient elution, acetone in dichloromethane) to give an inseparable mixture of the desired disaccharide and hydrolyzed donor. The mixture was dissolved in pyridine (0.500 mL), and acetic anhydride (0.190 mL, 2.00 mmol, 10.0 equiv) was added to the solution. Once complete, excess pyridine was removed via azeotroping with toluene and the crude material was purified by flash column chromatography on silica gel (ethyl acetate/hexanes 1:1) to yield the title compound as an amorphous white solid (0.045 g, 28%). TLC: R_f = 0.22 (ethyl acetate/hexanes 1:1). $[\alpha]^{20}_{D}$ = 9.7 (*c* 1.04 in $CHCl_3$). FTIR (powder, cm^{-1}): 2938 (w), 2912 (w), 2840 (w), 1741 (s), 1513 (m), 1367 (m), 1215 (s), 1030 (s), 906 (m), 820 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.26−7.24 (m, 4H, ArH), 6.86−6.83 (m, 4H, ArH), 5.44 (dd, 1H, *J* = 3.5, 1.2 Hz, H-4), 5.17 (app t, 1H, *J* = 9.6 Hz, H-3′), 5.07 (app t, 1H, *J* = 9.6 Hz, H-4′), 4.97 (dd, 1H, *J* = 9.6, 7.9 Hz, H-2′), 4.76 (d, 1H, *J* = 11.7 Hz, ArCH), 4.64 (d, 1H, *J* = 10.8 Hz, ArCH), 4.58−4.52 (m, 3H, H-1, H-1′, ArCH), 4.47 (d, 1H, *J* = 10.8 Hz, ArCH), 4.26 (dd, 1H, *J* = 12.3, 4.5 Hz, H-6′), 4.12 (dd, 1H, *J* = 12.3, 2.4 Hz, H-6′), 4.03−4.00 (m, 1H, H-5), 3.89 (dd, 1H, *J* = 10.0, 3.5 Hz, H-3), 3.82−3.77 (m, 7H, H-6, $ArOCH_3$, $ArOCH_3$), 3.72−3.66 (H-2, H-5′), 3.56 (dd, 1H, *J* = 10.7, 8.0 Hz, H-6), 3.34 (s, 3H, OCH_3), 2.10 (CH_3CO), 2.07 (CH_3CO), 2.01 (CH_3CO), 2.00 (CH_3CO), 1.99 (s, 3H, CH_3CO). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.8, 170.4, 170.3, 169.5, 169.3, 159.5, 159.3, 130.7, 130.3, 129.8, 129.7, 113.9, 113.8, 100.8, 99.0, 75.8, 74.9, 73.4, 72.9, 72.1, 71.9, 71.3, 68.8, 68.7, 68.4, 68.2, 61.9, 55.44, 55.39, 55.36, 21.0, 20.8, 20.76, 20.72, 20.70. HRMS (ESI, *m*/*z*): calcd for $[C_{39}H_{54}NO_{18}]$ $(M + NH_4)^+$ 824.3335, found 824.3345.

*Methyl 2-O-(p-Methoxybenzyl)-3-O-(2′,3′,4′,6′-tetra-O-benzyl-β-D-glucopyranosyl)-α-L-fucopyranoside (**7g**).* Prepared from methyl 3,4-*O*-(phenylboronate)-α-L-fucopyranoside (0.053 g, 0.200 mmol) according to general procedure E. The title compound was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield a white amorphous solid (0.142 g, 62%). TLC: R_f = 0.36 (ethyl acetate/hexanes 2:3). $[\alpha]^{20}_{D}$ = −5.88 (*c* 0.80 in $CHCl_3$). FTIR (powder, cm^{-1}): 3030 (w), 2903 (w), 1612 (w), 1586 (w), 1512 (m), 1454 (m), 1359 (m), 1246 (m), 1048 (s), 1028 (s), 957 (m), 819 (m), 734 (s), 696 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.36−7.26 (m, 20H, ArH), 7.19−7.17 (m, 2H, ArH), 6.83−6.80 (m, 2H, ArH), 4.93−4.81 (m, 5H, five of PhCH), 4.75 (d, 1H, *J* = 12.0 Hz, PhCH), 4.64−4.52 (m, 6H, H-1, H-1′, four of PhCH), 4.24 (dd, 1H, *J* = 10.0, 3.2 Hz, H-3), 3.88−3.65 (m, 10H, H-2, H-3′, H-4, H-4′, H-5, H-6′, H-6′, $ArOCH_3$), 3.50 (dd, 1H, *J* = 8.8, 7.9 Hz, H-2′), 3.45−3.40 (m, 1H, H-5′), 3.35 (s, 3H, OCH_3), 1.23 (d, 3H, *J* = 6.6 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.3, 138.5, 138.2, 138.1, 138.0, 130.9, 129.9, 128.6, 128.5, 128.5, 128.48, 128.2, 128.1, 127.99, 127.97, 127.94, 127.81, 127.77, 127.7, 133.8, 99.7, 98.9, 85.3, 82.0, 78.1, 77.0, 75.7, 75.4, 75.3, 75.2, 73.7, 73.6, 73.1, 69.4, 68.8, 65.0, 55.4, 55.4, 16.3. HRMS (ESI, *m*/*z*): calcd for $[C_{49}H_{60}NO_{11}]$ $(M + NH_4)^+$ 838.4161, found 838.4169.

*Methyl 4-O-(2′,3′,4′,6′-Tetra-O-benzyl-α-D-mannopyranosyl)-α-L-rhamnopyranoside (**8**).* Methyl 2,3-*O*-(phenylboronate)-α-L-rhamnopyranoside (0.066 g, 0.200 mmol) and 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl trichloroacetimidate (0.205 g, 0.300 mmol, 1.50 equiv) were dissolved in anhydrous dichloromethane (1.00 mL) and added to an oven-dried round-bottom flask charged with a stir bar and 4 Å molecular sieves under an atmosphere of argon. The solution was cooled to 0 °C. A 0.1 M solution of trimethylsilyl trifluoromethanesulfonate in dichloromethane was prepared fresh, and 0.100 mL of this solution (0.010 mmol, 0.050 equiv) was added slowly dropwise to the reaction mixture. The solution was allowed to stir at 0 °C for 20 min before the ice bath was removed and the reaction was quenched with triethylamine. The solution was filtered through a pad of tightly packed Celite, and the solvent was removed under reduced pressure. This material was then dissolved in ethyl acetate and placed in a separatory funnel. A solution of 1.0 M aqueous sodium carbonate and D-sorbitol (25 mL) was added to the funnel, and the biphasic mixture was shaken by hand for 5 min. The organic phase was collected, dried over magnesium sulfate, and filtered, and solvent was removed under reduced pressure. The crude isolate was purified by flash column chromatography on silica gel (acetone:dichloromethane 1:9) to yield the title compound a clear viscous oil (0.119 g, 85%). TLC: R_f = 0.70 (acetone/dichloromethane 1:4). $[\alpha]^{20}_{D}$ = 5.61 (*c* 1.23 in $CHCl_3$). FTIR (neat, cm^{-1}): 3418 (br), 3070 (w), 3031 (w), 2973 (w), 2917 (w), 2869 (w), 1724 (m), 1597 (w), 1496 (w), 1453 (m), 1362 (m), 1205 (w), 1098 (s), 1049 (s), 979 (s), 909(s), 826 (s), 723 (s), 698 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39−7.29 (m, 18H,

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

ArH), 7.21−7.19 (m, 2H, ArH), 4.86 (d, 1H, J = 12.4 Hz, PhCH), 4.85 (d, 1H, J = 3.5 Hz, H-1′), 4.77 (d, 1H, J = 12.3 Hz, PhCH), 4.71−4.58 (m, 4H, PhCH, PhCH, PhCH, PhCH), 4.67 (d, 1H, J = 1.6 Hz, H-1), 4.54 (d, 1H, J = 12.0 Hz, PhCH), 4.50 (d, 1H, J = 11.0 Hz, PhCH), 4.05−4.00 (m, 1H, H-3′), 3.91 (dd, 1H, J = 3.6, 1.6 Hz, H-2), 3.87−3.81 (m, 2H, H-4′, H-5′), 3.74−3.71 (m, 2H, H3, H-6′), 3.68−3.63 (m, 2H, H-2′, H-6′), 3.58−3.53 (m, 1H, H-5), 3.36 (s, 3H, OCH_3), 3.29 (app t, 1H, J = 9.1 Hz, H-4), 1.12 (d, 3H, J = 6.2 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 138.2, 138.1, 137.8, 137.79, 128.53, 128.51, 128.44, 128.42, 128.2, 128.0, 128.0, 127.97, 127.9, 127.89, 127.8, 127.5, 100.2, 100.1, 85.3, 79.2, 75.3, 75.1, 74.9, 73.4, 73.2, 72.7, 72.5, 70.6, 69.8, 69.3, 65.7, 54.9, 17.7. HRMS (ESI, m/z): calcd for $[C_{41}H_{52}NO_{10}]$ $(M + NH_4)^+$ 718.3583, found 718.3586.

*Methyl 2-O-Acetyl-3-O-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-4-O-(2″,3″,4″,6″-tetra-O-benzyl-α-D-mannopyranosyl)-α-L-rhamnopyranoside (**9**).* Methyl 2,3-*O*-(4-(trifluoromethyl)-phenylboronate)-α-L-rhamnopyranoside (0.066 g, 0.200 mmol) was placed in an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. The reaction vessel was purged with argon and kept under an atmosphere of argon using a balloon. 2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl trichloroacetimidate (0.206 g, 0.300 mmol, 1.50 equiv) was dissolved in anhydrous dichloromethane (1.00 mL) and added to the flask, and the solution was cooled to 0 °C. A 0.1 M solution of trimethylsilyl trifluoromethanesulfonate in dichloromethane was prepared fresh, and 0.100 mL of this solution (0.001 mmol, 0.050 equiv) was added slowly dropwise to the reaction mixture. The solution was allowed to stir at 0 °C for 30 min before the ice bath was removed. Triethylamine (0.166 mL, 1.20 mmol, 6.00 equiv) was added to the reaction vessel followed by 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (0.123 g, 0.300 mmol, 1.50 equiv) and silver(I) oxide (0.070 g, 0.300 mmol, 1.50 equiv), and the reaction was stirred vigorously (800 rpm or higher) at room temperature overnight. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to give an inseparable mixture of various products as a yellow solid. This material was dissolved in pyridine (1.00 mL), and acetic anhydride (0.190 mL, 2.00 mmol, 10.0 equiv) was added to the solution. Once complete, excess pyridine and was removed via azeotroping with toluene, and the crude material was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to yield the title compound as a white amorphous solid (0.085 g, 40%). TLC: R_f = 0.43 (ethyl acetate/hexanes 1:1). $[\alpha]^{20}_D$ = 9.8 (c 1.04 in $CHCl_3$). FTIR (powder, cm^{-1}): 2920 (w), 2858 (w), 1745 (s), 1366 (m), 1214 (s), 1137 (m), 1036 (s), 906 (m), 737 (m), 698 (m). ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.41−7.37 (m, 4H, ArH), 7.34−7.23 (m, 16H, ArH), 5.13 (dd, 1H, J = 3.8, 2.1 Hz, H-2), 5.08 (app t, 1H, J = 9.4 Hz, H-3′), 4.94−4.90 (m, 3H, H-1″, H-4′, PhCH), 4.84 (dd, 1H, J = 9.4, 7.8 Hz, H-2′), 4.80 (d, 1H, J = 7.8 Hz, H-1′), 4.76 (d, 1H, J = 12.0 Hz, PhCH), 4.68 (d, 1H, J = 11.9 Hz, PhCH), 4.64−4.55 (m, 6H, H-1, PhCH, PhCH, PhCH, PhCH), 3.99−3.93 (m, 3H, H-3, H-5″, H-6′), 3.91 (dd, 1H, J = 12.2, 2.4 Hz, H-6′), 3.86−3.82 (m, 2H, H-3″, H-4″), 3.76 (dd, 1H, J = 10.4, 2.0 Hz, H-6″), 3.73 (dd, 1H, J = 10.4, 5.6 Hz, H-6″), 3.63 (app t, 1H, J = 2.3 Hz, H-2″), 3.58−3.53 (m, 1H, H-5), 3.37 (dd, 1H, J = 10.6, 8.7 Hz, H-4), 3.34 (s, 3H, OCH_3), 3.06−3.03 (m, 1H, H-5′), 2.08 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.96 (s, 3H, CH_3CO), 1.91 (s, 3H, CH_3CO), 1.09 (d, 3H, J = 6.2 Hz, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 170.8, 170.5, 170.2, 170.1, 169.5, 138.7, 138.41, 138.39, 138.1, 128.47, 128.46 128.45, 128.41, 128.2, 128.1, 127.8, 127.8, 127.8, 127.76, 127.6, 127.5, 100.8, 98.5, 98.1, 79.5, 79.1, 77.6, 75.3, 75.2, 75.0, 73.1, 73.1, 72.9, 72.8, 72.3, 72.0, 71.8, 70.9, 70.4, 68.3, 66.3, 61.8, 55.0, 21.1, 21.0, 20.70, 20.67, 20.65, 18.4. HRMS (ESI, m/z): calcd for $[C_{57}H_{72}NO_{20}]$ $(M + NH_4)^+$ 1090.4642, found 1090.4655.

*Methyl 3-O-(2′,3′,4′,6′-Tetra-O-benzyl-β-D-glucopyranosyl)-4-O-(2″,3″,4″,6″-tetra-O-benzyl-α-D-mannopyranosyl)-α-L-rhamnopyranoside (**10**).* Methyl 2,3-*O*-(phenylboronate)-α-L-rhamnopyranoside (0.040 g, 0.150 mmol) was placed in an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. The reaction vessel was purged with argon and kept under an atmosphere of argon using a balloon. 2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl trichloroacetimidate (0.154 g, 0.225 mmol, 1.50 equiv) was dissolved in anhydrous dichloromethane (1.00 mL) and added to the flask, and the solution was cooled to 0 °C. A 0.1 M solution of trimethylsilyl trifluoromethanesulfonate in dichloromethane was prepared fresh, and 0.075 mL of this solution (0.008 mmol, 0.050 equiv) was added slowly dropwise to the reaction mixture. The solution was allowed to stir at 0 °C for 30 min before removal of the ice bath. Triethylamine (0.125 mL, 0.900 mmol, 6.00 equiv) was added to the reaction vessel followed by 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.092 g, 0.165 mmol, 1.10 equiv) and silver(I) oxide (0.038 g, 0.165 mmol, 1.10 equiv), and the reaction was stirred vigorously (800 rpm or higher) at room temperature for 48 h. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to give a white solid. This material was purified further by flash column chromatography on silica gel (ether/hexanes 1:1) to yield the title compound as a pale yellow gum (0.044 g, 28%). TLC: R_f = 0.35 (ether/hexanes 7:3). $[\alpha]^{20}_D$ = 4.6 (c 0.41 in $CHCl_3$). FTIR (powder, cm^{-1}): 3510 (br), 3030 (w), 2908 (w), 2870 (w), 1453 (m), 1361 (w), 1097 (s), 1046 (s), 972 (m), 733 (s), 694 (s). ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.36−7.12 (m, 20H, ArH), 5.10 (d, 1H, J = 1.8 Hz, H-1″), 4.99 (d, 1H, J = 11.0 Hz, PhCH), 4.80−4.63 (m, 10H, H-1, H-1′, eight of PhCH), 4.54−4.99 (m, 6H, six of PhCH), 4.35 (d, 1H, J = 11.7 Hz, PhCH), 4.27 (d, 1H, J = 11.7 Hz, PhCH), 4.21 (ddd, 1H, J = 10.0, 4.5, 1.8 Hz, H-3″), 4.05−3.99 (m, 3H, H-2,H-3, H-4″), 3.85−3.81 (m, 2H, H-4, H-6″), 3.77−3.72 (m, 3H, H-2″, H-5″, H-6″), 3.71−3.67 (m, 1H, H-5), 3.63−3.58 (m, 2H, H-4′, H-6′), 3.55−3.46 (m, 3H, H-2′, H-3′, H-5′), 3.44 (dd, 1H, J = 10.2, 5.6 Hz, H-6′), 3.36 (s, 3H, OCH_3), 1.15 (d, 3H, J = 6.3 Hz, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 138.9, 138.8, 138.7, 138.6, 138.5, 138.4, 138.1, 137.9, 128.53, 128.52, 128.50, 128.49, 128.46, 128.37, 128.36, 128.3, 128.2, 128.1, 128.04, 128.01, 128.00, 127.9, 127.8, 127.79, 127.77, 127.7, 127.6, 127.54, 127.53, 127.52, 127.4, 127.3, 101.9, 100.9, 98.7, 85.0, 81.6, 80.3, 80.2, 78.0, 77.7, 75.3, 75.1, 75.1, 75.0, 74.7, 74.6, 74.5, 73.6, 73.4, 72.8, 72.7, 72.4, 69.6, 69.4, 69.0, 67.5, 55.1, 18.6. HRMS (ESI, m/z): calcd for $[C_{75}H_{86}NO_{15}]$ $(M + NH_4)^+$ 1240.5992, found 1240.5978.

*Methyl 2-O-(2′,3′,4′-Tris-O-trimethylacetyl-β-D-xylopyranosyl)-3-O-(2″,3″,4″,6″-tetra-O-benzyl-β-D-glucopyranosyl)-α-L-fucopyranoside (**11**).* Methyl 3,4-*O*-(phenylboronate)-α-L-fucopyranoside (0.026 g, 0.100 mmol) and 2,3,4-tris-*O*-trimethylacetyl-α/β-D-xylopyranosyl trichloroacetimidate (0.082 g, 0.150 mmol, 1.50 equiv) were placed in an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. The reaction vessel was purged with argon and kept under an atmosphere of argon using a balloon. Anhydrous dichloromethane (1.00 mL) was added to the flask, and the solution was cooled to 0 °C. A 0.1 M solution of trimethylsilyl trifluoromethanesulfonate in dichloromethane was prepared fresh, and 0.100 mL of this solution (0.010 mmol, 0.100 equiv) was added slowly dropwise to the reaction mixture. The solution was allowed to stir at 0 °C for 45 min before removal of the ice bath. Triethylamine (0.084 mL, 0.600 mmol, 6.00 equiv) was added to the reaction vessel followed by 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.061 g, 0.110 mmol, 1.10 equiv) and silver(I) oxide (0.025 g, 0.110 mmol, 1.10 equiv), and the reaction was stirred vigorously (800 rpm or higher) at room temperature for 48 h. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel (gradient elution, hexanes in diethyl ether) to yield the title compound as a white amorphous solid (0.058 g, 54%). TLC: R_f = 0.24 (hexanes/diethyl ether 2:3). $[\alpha]^{20}_D$ = −25.1 (c 1.29 in $CHCl_3$). FTIR (powder, cm^{-1}): 2970 (w), 2931 (w), 2879 (w), 1739 (s), 1479 (m), 1454 (m), 1397 (w), 1363 (m), 1278 (m), 1140 (s), 1066 (s), 734 (s), 696 (s). ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.39−7.26 (m, 18H, ArH), 7.17−7.16 (m, 2H, ArH), 5.28 (app t, 1H, J = 8.8 Hz, H-3′), 4.98−4.86 (m,

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

6H, H-2′, H-4′, PhCH, PhCH, PhCH, PhCH), 4.81 (d, 1H, J = 10.7 Hz, PhCH), 4.78 (d, 1H, J = 3.1 Hz, H-1), 4.68 (d, 1H, J = 12.2 Hz, PhCH), 4.59−4.55 (m, 2H, PhCH, PhCH), 4.55 (d, 1H, J = 7.8 Hz, H-1″), 4.53 (d, 1H, J = 6.7 Hz, H-1′), 4.20−4.15 (m, 3H, H-2, H-3, H-5′), 3.87−3.84 (m, 2H, H-4, H-5), 3.78 (dd, 1H, J = 11.0, 2.0 Hz, H-6″), 3.73 (dd, 1H, J = 11.0, 4.5 Hz, H-6″), 3.72−3.65 (m, 2H, H-3″, H-4″), 3.51−3.49 (m, 1H, H-5″), 3.46 (dd, 1H, J = 8.8, 7.8 Hz, H-2″), 3.35 (s, 3H, OCH_3), 3.19 (dd, 1H, J = 12.0, 8.1 Hz, H-5′), 1.27 (d, 3H, J = 6.8 Hz, CH_3), 1.20 (s, 9H, $(CH_3)_3CCO$) 1.18 (s, 9H, $(CH_3)_3CCO$), 1.14 (s, 9H, $(CH_3)_3CCO$). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 177.3, 177.3, 176.5, 138.6, 138.3, 138.2, 138.0, 128.6, 128.5, 128.5, 128.5, 128.47, 128.46, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 99.2, 98.8, 97.5, 85.4, 81.1, 78.2, 75.7, 75.4, 75.1, 75.0, 75.0, 73.6, 72.4, 71.6, 71.5, 69.6, 69.0, 68.8, 65.2, 62.6, 55.2, 38.8, 38.8, 38.8, 27.3, 27.3, 27.2, 16.2. HRMS (ESI, m/z): calcd for $[C_{61}H_{84}NO_{17}]$ $(M + NH_4)^+$ 1102.5734, found 1102.5714.

*Methyl 3-O-(2′,3′,4′,6′-Tetra-O-benzyl-β-D-glucopyranosyl)-4-O-(2″,3″,4″,6″-tetra-O-acetyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**12**).* Methyl 2,3-*O*-(phenylboronate)-α-L-rhamnopyranoside (0.053 g, 0.200 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide were placed in an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. The reaction vessel was purged with argon and kept under an atmosphere of argon using a balloon. Anhydrous dichloromethane (1.00 mL) was added to the flask, and the solution was cooled to 0 °C. Silver(I) carbonate (0.083 g, 0.300 mmol, 1.50 equiv) and silver(I) trifluoromethanesulfonate (0.77 g, 0.300 mmol, 1.50 equiv) were added, and the reaction was covered with aluminum foil and allowed to stir overnight, gradually warming to room temperature. The solution was then filtered through a pad of tightly packed Celite, and solvent was removed under reduced pressure. The crude material was then dissolved in anhydrous dichloromethane (1.00 mL) and transferred to an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.123 g, 0.220 mmol, 1.10 equiv), silver(I) oxide (0.051 g, 0.220 mmol, 1.10 equiv), and triethylamine (0.166 mL, 1.20 mmol, 6.00 equiv) were added to the flask, and the solution was stirred vigorously (800 rpm or higher) at room temperature for 48 h. The reaction was quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to give a white solid. This material was further purified by flash column chromatography on silica gel (acetone/dichloromethane 5:95) to yield the pure compound as a white amorphous solid (0.074 g, 36%). TLC: R_f = 0.24 (ethyl acetate/hexanes 2:3). $[\alpha]^{20}_D$ = −10.8 (c 1.15 in $CHCl_3$). FTIR (powder, cm^{-1}): 3497 (br), 3032 (w), 2933 (w), 2909 (w), 2873 (w), 1754 (s), 1364 (m), 1215 (s), 1054 (s), 1028 (s), 975 (m), 907 (m), 735 (m), 697 (s). ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.42−7.40 (m, 2H, ArH), 7.37−7.35 (m, 2H, ArH), 7.34−7.25 (m, 14H, ArH), 7.19−7.17 (m, 2H, ArH), 5.01 (d, 1H, J = 10.9 Hz, PhCH), 4.99 (app t, 1H, = 9.3 Hz, H-3″), 4.91−4.83 (m, 7H, H-1″, H-2″, H-4″, PhCH, PhCH, PhCH, PhCH), 4.75 (d, 1H, J = 7.0 Hz, H-1′), 4.65 (d, 1H, J = 1.6 Hz, H-1), 4.58−4.56 (m, 2H, PhCH, PhCH), 4.54 (d, 1H, J = 12.2 Hz, PhCH), 4.04 (dd, 1H, J = 3.4, 1.6 Hz, H-2), 3.96−3.92 (m, 2H, H-3, H-6″), 3.90 (dd, 1H, J = 12.3, 2.5 Hz, H-6″), 3.78−3.69 (m, 4H, H-4, H-3′, H-4′, H-6′), 3.65−3.60 (m, 2H, H-5, H-6′), 3.57 (dd, 1H, J = 7.7, 7.0 Hz, H-2′), 3.50−3.47 (m, 1H, H-5′), 3.34 (s, 3H, OCH_3), 2.95 (br s, 1H, 2-OH), 2.61−2.58 (m, 1H, H-5″), 2.04 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO), 1.25 (d, 3H, J = 6.3 Hz, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 170.7, 170.2, 169.4, 169.3, 138.5, 138.4, 138.2, 137.9, 128.8, 128.56, 128.54, 128.53, 128.53, 128.1, 128.0, 127.94, 127.93, 127.8, 127.7, 127.2, 102.7, 100.4, 99.1, 84.7, 81.9, 79.7, 77.8, 75.3, 75.1, 74.9, 74.3, 73.7, 72.9, 72.2, 70.9, 68.7, 68.3, 66.3, 61.7, 54.9, 21.2, 20.8, 20.76, 20.74, 17.8. HRMS (ESI, m/z): calcd for $[C_{55}H_{70}NO_{19}]$ $(M + NH_4)^+$ 1048.4537, found 1048.4550. The regioisomer methyl 2-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-β-D-glucopyranosyl)-4-*O*-(2″,3″,4″,6″-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**12′**) was also isolated from the reaction as a white amorphous solid (0.035 g, 17%). TLC: R_f = 0.33 (ethyl acetate/hexanes 2:3). $[\alpha]^{20}_D$ = −6.6 (c 0.35 in $CHCl_3$). FTIR (powder, cm^{-1}): 3487 (br), 2933 (w), 2873 (w), 1750 (m), 1365 (m), 1217 (s), 1055 (s), 2028 (s), 972 (m), 907 (m), 736 (m), 696 (s). ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.45−7.40 (m, 3H, ArH), 7.37−7.35 (m, 2H, ArH), 7.34−7.31 (m, 6H, ArH), 7.31−7.27 (m, 5H, ArH), 7.25−7.23 (m, 2H, ArH), 7.21−7.18 (m, 2H, ArH), 5.01−4.98 (m, 3H, H-3″, PhCH, PhCH), 4.90 (app t, 1H, J = 9.7 Hz, H-4″), 4.86−4.78 (m, 5H, H-1, H-2″, PhCH, PhCH, PhCH), 4.60−4.54 (m, 4H, H-1′, PhCH, PhCH, PhCH) 4.23 (d, 1H, J = 8.0 Hz, H-1″), 4.05 (dd, 1H, J = 12.2, 5.3 Hz, H-6″), 3.97 (dd, 1H, J = 12.2, 2.4 Hz, H-6″), 3.88 (dd, 1H, J = 3.4, 1.5 Hz, H-2), 3.78−3.66 (m, 4H, H-3, H-3′, H-6′, H-6′), 3.61 (app t, 1H, J = 9.3 Hz, H-4′), 3.58−3.52 (m, 2H, H-2′, H-5), 3.48−3.45 (m, 1H, H-5′), 3.29 (s, 3H, OCH_3), 3.20 (app t, 1H, J = 9.4 Hz, H-4), 2.98−2.95 (m, 1H, H-5″), 2.79 (d, 1H, J = 9.9 Hz, 3-OH), 2.05 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.26 (d, 3H, J = 6.2 Hz, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 170.7, 170.3, 169.9, 169.6, 138.3, 138.2, 138.2, 138.1, 128.9, 128.6, 128.53, 128.51, 128.2, 128.06, 128.04, 128.0, 127.9, 127.8, 127.7, 126.6, 105.0, 101.9, 100.1, 85.0, 83.1, 82.0, 8.6, 78.1, 75.8, 75.4, 75.2, 74.6, 73.5, 72.7, 71.6, 71.5, 71.2, 68.9, 68.7, 66.2, 62.2, 57.8, 20.85, 20.82, 20.77, 20.74, 17.8. HRMS (ESI, m/z): calcd for $[C_{55}H_{70}NO_{19}]$ $(M + NH_4)^+$ 1048.4537, found 1048.4546.

*Methyl 2-O-Trimethylacetyl-3-O-(2′,3′,4′,6′-tetra-O-benzyl-α-D-mannopyranosyl)-6-O-(2″,3″,4″,6″-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**13**).* In an oven-dried 1 dram screw-cap vial equipped with stir bar was dissolved methyl 4,6-*O*-(4-(trifluoromethyl)phenylboronate)-α-D-glucopyranoside (0.070 g, 0.200 mmol) in anhydrous pyridine (0.400 mL) and the mixture cooled to 0 °C with stirring. Trimethylacetyl chloride (0.030 mL, 0.240 mmol, 1.20 equiv) was added quickly to the reaction vessel, and the solution was removed from the ice bath and allowed to warm to room temperature with stirring for 30 min. Once complete, the reaction was diluted with toluene and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was then dissolved in anhydrous dichloromethane (1.00 mL) and transferred via syringe to an oven-dried round-bottom flask charged with stir bar and 4 Å molecular sieves. 2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl trichloroacetimidate (0.154 g, 0.225 mmol, 1.50 equiv) was dissolved in anhydrous dichloromethane (1.00 mL) and added to the flask and the solution was cooled to 0 °C. A 0.1 M solution of trimethylsilyl trifluoromethanesulfonate in dichloromethane was prepared fresh and 0.200 mL of this solution (0.020 mmol, 0.100 equiv) was added slowly dropwise to the reaction mixture. The solution was allowed to stir at 0 °C for 30 min before a 25.0 μL aliquot of the reaction mixture was taken and analyzed by ^1H NMR, revealing no conversion of the mannosyl donor. An additional 200 μL of 0.1 M trimethylsilyl trifluoromethanesulfonate in dichloromethane (0.020 mmol, 0.100 equiv) was added, and the reaction mixture was allowed to stir for 10 min before addition of another 200 μL of 0.1 M trimethylsilyl trifluoromethanesulfonate in dichloromethane (0.020 mmol, 0.100 equiv). The reaction mixture was allowed to stir for an additional 10 min, after which NMR analysis of a 25.0 μL aliquot of the reaction mixture showed complete consumption of the mannosyl donor as judged by disappearance of the imine proton. The reaction mixture was then warmed to room temperature, followed by addition of triethylamine (0.125 mL, 0.900 mmol, 6.00 equiv), 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl bromide (0.123 g, 0.300 mmol, 1.50 equiv) and silver(I) oxide (0.070 g, 0.300 mmol, 1.50 equiv). The reaction mixture was stirred vigorously (800 rpm or higher) at room temperature for 20 h and then quenched with methanol and filtered through a pad of tightly packed Celite followed by removal of the solvent under reduced pressure. The crude material was purified by flash column chromatography on silica gel (gradient elution, ethyl acetate in hexanes) to give a white solid. This material was purified further by flash column chromatography on silica gel (gradient elution, acetone in toluene) to yield the title compound as a white amorphous solid (0.103 g, 46%). TLC: R_f = 0.55 (ethyl acetate/hexanes 2:3). $[\alpha]^{20}_D$ = 20.7 (c 1.35 in $CHCl_3$). FTIR (powder, cm^{-1}): 3502 (br), 2935 (w), 1754 (m), 1732 (m), 1454 (w), 1366 (w), 1217

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX

(s), 1154 (m), 1034 (s), 907 (w), 736 (m), 697 (m). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.43−7.43 (m, 2H, ArH), 7.39−7.35 (m, 4H, ArH), 7.33−7.24 (m, 12H, ArH), 7.21−7.19 (m, 2H, ArH), 5.26 (m, 1H, J = 1.9 Hz, H-1′), 5.16 (app t, 1H, J = 9.6 Hz, H-3″), 5.05 (dd, 1H, J = 10.0, 9.6 Hz, H-4″), 4.98 (dd, 1H, J = 8.0, 9.6 Hz, H-2″), 4.93 (dd, 1H, J = 10.6, 4.0 Hz, H-2), 4.90 (d, 1H, J = 11.1 Hz, PhCH), 4.76 (d, 1H, J = 12.3 Hz, PhCH), 4.74 (d, 1H, J = 4.0 Hz, H-1), 4.69 (d, 1H, J = 12.3 Hz, PhCH), 4.57 (d, 1H, J = 11.7 Hz, PhCH), 4.50 (d, 1H, J = 11.7 Hz, PhCH), 4.49 (d, 1H, J = 11.1 Hz, PhCH), 4.46 (s, 2H, $PhCH_2$), 4.25 (d, 1H, J = 5.8 Hz, 4-OH), 4.23−4.19 (m, 2H, H-5′, H-6″), 4.18 (d, 1H, J = 8.0 Hz, H-1″), 4.13 (dd, 1H, J = 12.3, 2.5 Hz, H-6″), 3.99 (dd, 1H, J = 10.6, 9.6 Hz, H-3), 3.91 (dd, 1H, J = 10.9, 2.1 Hz, H-6), 3.88 (dd, 1H, J = 9.2, 3.0 Hz, H-3′), 3.83 (dd, 1H, J = 9.6, 2.0 Hz, H-6′), 3.78−3.74 (m, 1H, H-4), 3.70 (app t, 1H, J = 9.6 Hz, H-4′), 3.69−3.66 (m, 1H, H-5), 3.65 (dd, 1H, J = 3.0, 1.9 Hz, H-2′), 3.58−3.52 (m, 2H, H-5″, H-6), 3.51 (dd, 1H, J = 9.6, 8.7 Hz, H-6′), 3.33 (s, 3H, OCH_3), 2.07 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO), 1.15 (s, 9H, $(CH_3)_3CCO$). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 177.8, 170.9, 170.5, 169.5, 169.5, 138.6, 138.5, 138.4, 137.7, 129.2, 128.6, 128.43, 128.37, 128.1, 128.0, 127.92, 127.89, 127.7, 127.65, 127.62, 127.61, 101.4, 97.6, 93.0, 79.8, 78.4, 75.3, 75.2, 75.0, 73.8, 72.9, 72.4, 71.80, 71.78, 71.6, 71.3, 70.7, 70.5, 69.1, 68.6, 68.1, 67.3, 62.1, 55.4, 38.8, 27.2, 20.9, 20.78, 20.75, 20.7. HRMS (ESI, m/z): calcd for $[C_{60}H_{78}NO_{21}]$ $(M + NH_4)^+$ 1148.5061, found 1148.5074.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01605.

Additional optimization data, spectral data for boronic ester intermediates, and copies of ^{1}H and ^{13}C NMR spectra for new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: mtaylor@chem.utoronto.ca.

ORCID

Mark S. Taylor: 0000-0003-3424-4380

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by NSERC (Discovery Grants and Canada Research Chairs programs), the Canada Foundation for Innovation (Project Nos. 17545 and 19119), and the Province of Ontario.

■ REFERENCES

(1) Seeberger, P. H.; Werz, D. B. *Nature* **2007**, *446*, 1046−1051.
(2) Boltje, T. J.; Buskas, T.; Boons, G.-J. *Nat. Chem.* **2009**, *1*, 611−622.
(3) Wang, C.-C.; Lee, J.-C.; Luo, S.-Y.; Kulkarni, S. S.; Huang, Y.-W.; Lee, C.-C.; Chang, K.-L.; Hung, S.-C. *Nature* **2007**, *446*, 896−899.
(4) Français, A.; Urban, D.; Beau, J.-M. *Angew. Chem., Int. Ed.* **2007**, *46*, 8662−8665.
(5) Ferrier, R. J. *Adv. Carbohydr. Chem. Biochem.* **1978**, *35*, 31−80.
(6) Duggan, P. J.; Tyndall, E. M. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1325−1339.
(7) Dahlhoff, W. V. *Synthesis* **1987**, *1987*, 366−368.
(8) Langston, S.; Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1994**, *77*, 2341−2353.
(9) Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2002**, *124*, 8867−8869.
(10) Kaji, E.; Nishino, T.; Ishige, K.; Ohya, Y.; Shirai, Y. *Tetrahedron Lett.* **2010**, *51*, 1570−1573.
(11) Fenger, T. H.; Madsen, R. *Eur. J. Org. Chem.* **2013**, *2013*, 5923−5933.
(12) Kaji, E.; Yamamoto, H.; Shirai, Y.; Ishige, K.; Arai, Y.; Shirahata, T.; Makino, K.; Nishino, T. *Eur. J. Org. Chem.* **2014**, *2014*, 3536−3539.
(13) Fukuhara, K.; Shimada, N.; Nishino, T.; Kaji, E.; Makino, K. *Eur. J. Org. Chem.* **2016**, *2016*, 902−905.
(14) Mancini, R. S.; Lee, J. B.; Taylor, M. S. *Org. Biomol. Chem.* **2017**, *15*, 132−143.
(15) Tay, J.-H.; Argüelles, A. J.; DeMars, M. D., II.; Zimmerman, P. M.; Sherman, D. H.; Nagorny, P. *J. Am. Chem. Soc.* **2017**, *139*, 8570−8578.
(16) Fréchet, J. M. J.; Nuyens, L. J.; Seymour, E. *J. Am. Chem. Soc.* **1979**, *101*, 432−436.
(17) Belogi, G.; Zhu, T.; Boons, G.-J. *Tetrahedron Lett.* **2000**, *41*, 6969−6972.
(18) Belogi, G.; Zhu, T.; Boons, G.-J. *Tetrahedron Lett.* **2000**, *41*, 6965−6968.
(19) Oshima, K.; Kitazono, E.-I.; Aoyama, Y. *Tetrahedron Lett.* **1997**, *38*, 5001−5004.
(20) Oshima, K.; Aoyama, Y. *J. Am. Chem. Soc.* **1999**, *121*, 2315−2316.
(21) Lee, D.; Williamson, C. L.; Chan, L.; Taylor, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 8260−8267.
(22) D'Angelo, K. A.; Taylor, M. S. *J. Am. Chem. Soc.* **2016**, *138*, 11058−11066.
(23) Lee, D.; Taylor, M. S. *Org. Biomol. Chem.* **2013**, *11*, 5409−5412.
(24) Mancini, R. S.; McClary, C. A.; Anthonipillai, S.; Taylor, M. S. *J. Org. Chem.* **2015**, *80*, 8501−8510.
(25) Nakagawa, A.; Tanaka, M.; Hanamura, S.; Takahashi, D.; Toshima, K. *Angew. Chem., Int. Ed.* **2015**, *54*, 10935−10939.
(26) Kalikanda, J.; Li, Z. *Tetrahedron Lett.* **2010**, *51*, 1550−1553.
(27) Mootoo, D. R.; Konradsson, P.; Udodong, U.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1988**, *110*, 5583−5584.
(28) Gouliaras, C.; Lee, D.; Chan, L.; Taylor, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 13926−13929.
(29) Beale, T. M.; Moon, P. J.; Taylor, M. S. *Org. Lett.* **2014**, *16*, 3604−3607.
(30) Roslund, M. U.; Aitio, O.; Wärna, J.; Maaheimo, H.; Murzin, D. Y.; Leino, R. *J. Am. Chem. Soc.* **2008**, *130*, 8769−8772.
(31) Mothana, S.; Grassot, J.-M.; Hall, D. G. *Angew. Chem., Int. Ed.* **2010**, *49*, 2883−2887.
(32) Garegg, P. G. *Pure Appl. Chem.* **1984**, *56*, 845−858.
(33) Boons, G.-J.; Isles, S. *J. Org. Chem.* **1996**, *61*, 4262−4271.

DOI: 10.1021/acs.joc.7b01605
J. Org. Chem. XXXX, XXX, XXX−XXX