Regioselective Activation Of Glycosyl Acceptors By A Diarylborinic Acid Catalyst

by

Christina Gouliaras

A thesis submitted in conformity with the requirements for the degree of Master of Science
Department of Chemistry
University of Toronto

© Copyright by Christina Gouliaras 2011
Regioselective Activation Of Glycosyl Acceptors By A Diarylborinic Acid Catalyst

Christina Gouliaras

Master of Science

Department of Chemistry
University of Toronto

2011

Abstract

The realization that oligosaccharides play a central role in many biological processes has led to increasing interest in the preparation of synthetic targets for use in medical or biochemical research and drug discovery. The preparation of oligosaccharides from simple carbohydrate derivatives requires efficient methods for the construction of O-glycosidic bonds. Much effort has been made towards the development of selective methods for the preparation of oligosaccharide targets. The most common method to overcome the challenge of regioselectivity is the use of protecting group manipulations to suppress glycosylation at undesired positions. This is highly inefficient in terms of atom and step economy. Organoboron catalysis is a recent strategy that imparts regioselective activation of the equatorial hydroxy group of cis-vicinal diols towards functionalization. Following the initial findings that diarylborinic acid catalyzes the regioselective acylation of carbohydrate derivatives, an analogous method for regioselective glycosylation under Koenigs-Knorr conditions has been developed.
Acknowledgments

I would like to thank all the wonderful mentors and colleagues I have had the opportunity to work with over the past four years. I would not be able to rank them in order of importance because each had a unique impact on my growth as both a chemist and as a person, so I will simply list them chronologically. First, thank you to Mark Lautens for accepting a student with no experience into his group and for the recommendation that gave me the opportunity to spend a summer at Merck-Frosst. Thank you to Praew Thansandote who made me “everything I am”. Thank you for teaching me how to run my first column and how to be resilient when chemistry fails. Thank you to my big sister and brothers: Alena Rudolph, Christopher Bryan and Michael Langer, for their friendship. There began Schmoopy’s love of wine and cheese, and rock climbing. Thank you to (Master) Jean-François Fournier from his Padawan for being such a good friend and dedicated mentor, and for your wise words: “Chemistry is like shit, it happens”. Thank you Keith Fagnou for even the short time I had to learn from you. Thank you for showing us that a great chemist can earn the title without sacrificing the people and hobbies they love. And thank you for the constant reminder that “it is what it is”. Thank you to the Fagnou group, where I learned to work hard and play (drink) hard. Thank you to Nicolas Guimond and David Stuart for all the chemistry discussions and for guaranteed lab fun, even on the worst of days. Thank you Mark Taylor for your support and guidance throughout my M.Sc. Thank you for taking the time to discuss chemistry and for giving me so many opportunities to expand my skill set and grow as a chemist. I didn’t think anyone could ever convince me that sugar chemistry was fun - I learned so much from working on this project! Thank you especially for the encouragement you gave when it seemed that there was no end in sight. Thank you to all the Taylor group members, particularly Lina Chan, Doris Lee and Caitlin Williamson. Also, thanks to Corey McClary, who we could always count on for comic relief. Finally, thank you to Mark Nitz for helpful discussions and for reading my thesis, and to Anna Liza for answering all my questions and giving advice, always with a smile.
# Table of Contents

Table of Contents .................................................................................................................. iv
List of Tables .......................................................................................................................... vi
List of Figures .......................................................................................................................... vii
List of Schemes ....................................................................................................................... viii

1 Introduction ................................................................................................................................. 1
  1.1 Carbohydrates in Biological Systems ..................................................................................... 1
  1.2 Chemical Synthesis of Glycosides: Koenigs-Knorr Method .................................................... 2
  1.3 Methods for Regioselective Glycosylation ............................................................................. 4
    1.3.1 Carbohydrates: Complex Biopolymers .............................................................................. 4
    1.3.2 Protective Group Manipulations ...................................................................................... 5
    1.3.3 Enzymatic Methods ....................................................................................................... 6
    1.3.4 Tin- and Boron- Mediated Approaches .......................................................................... 7
  1.4 Organoboron Compounds in Chemical Recognition & Catalysis ......................................... 10

2 Results and Discussion ............................................................................................................... 13
  2.1 Research Goals ...................................................................................................................... 13
  2.2 Substrate Synthesis ............................................................................................................... 13
    2.2.1 Synthesis of Glycosyl Acceptors ...................................................................................... 13
    2.2.2 Synthesis of Glycosyl Donors ...................................................................................... 16
  2.3 Optimization of Borinic Acid-Catalyzed Glycosylation .......................................................... 17
    2.3.1 Preliminary Investigation ............................................................................................... 17
    2.3.2 Catalyst, Promoter & Solvent Optimization .................................................................. 20
    2.3.3 Optimizations of Difficult Glycosylations ..................................................................... 27
  2.4 Attempt to Change Stereoselectivity: Halide Catalysis Method ............................................ 32
  2.5 Glycosylations with Non-Glucosyl Donors .......................................................................... 33
2.6 Acceptors Incompatible with the Borinic Acid-Catalyzed Glycosylation .................. 36
2.7 Glycosylations with Acceptors Unprotected at the 6' Hydroxyl ................................ 37
2.8 Glycosylations with Non-Halide Donors ................................................................ 39
2.9 Glycosylation Scope ............................................................................................... 40
3 Conclusions .................................................................................................................. 43
4 Experimental .................................................................................................................. 44
   4.1 General Experimental Procedures ........................................................................... 44
   4.2 Characterization Data ............................................................................................. 45
List of Tables

Table 2.1 Preparation of monosaccharide acceptor substrates. .................................................. 14
Table 2.2 Preparation of disaccharide acceptor substrates. .......................................................... 14
Table 2.3 Optimization of the borinic acid-catalyzed glycosylation between 57 and 34. ............ 19
Table 2.4 Optimization of the borinic acid-catalyzed glycosylation between 57 and 33. .......... 20
Table 2.5 Optimization of boron catalyst for regioselective glycosylation................................. 21
Table 2.6 Optimization of the identity of Ag (I) promoter ............................................................ 25
Table 2.7 Optimization of the stoichiometry of Ag₂O promoter ................................................... 25
Table 2.8 Solvent optimization for regioselective glycosylation ....................................................... 26
Table 2.9 Effect of water on the borinic acid-catalyzed glycosylation ........................................... 27
Table 2.10 Optimization of glycosylation conditions with rhamnose-derived acceptor ............ 28
Table 2.11 Optimization of glycosylation conditions with fucose-derived acceptor ................. 29
Table 2.12 Optimization of glycosylation with anhydromannose-derived acceptor ............... 30
Table 2.13 Optimization of glycosylation with anhydrogalactose-derived acceptor .................. 31
Table 2.14 Optimization of glycosylation with 4,6-O-ethylidene-α-D-glucose ....................... 32
Table 2.15 Optimization of glycosylation with fucopyranosyl bromide ................................... 34
Table 2.16 Borinic acid-catalyzed glycosylation with a trichloroacetimidate donor .................... 40
Table 2.17 Scope of glycosyl acceptors in the borinic acid-catalyzed glycosylation ................. 41
Table 2.18 Scope of glycosyl donors in the borinic acid-catalyzed glycosylation ................. 42
List of Figures

Figure 1.1 Biologically relevant glycoconjugates: Blood group B and Globo H antigens............ 2

Figure 1.2 Diversity of stereo- and regio- centers in blood group H-type II tetrasaccharide. ....... 5

Figure 1.3 Mechanism of transglycosylation catalyzed by *Agrobacterium* sp. β-glucosidase..... 7

Figure 1.4 Early examples of boronic acid-based carbohydrate receptors. ............................. 11

Figure 1.5 Calculated Fukui indices (B3LYP/6-311+G(d,p)) of diphenylborinates. ................ 12

Figure 2.1 Boron catalysts screened for activity in regioselective glycosylation....................... 20

Figure 2.2 Crude ¹H NMR of glycosylation reactions run between 57 and 33 under Hanessian’s reported conditions (A), and the current optimized conditions with (C) and without (B) catalyst 59. The ¹H NMR of purified 63 (D) is displayed for comparison. ............................................ 24

Figure 2.3 Boronate esters of mannose and galactose derivatives........................................... 30
List of Schemes

Scheme 1.1 Reaction components in chemical glycoside synthesis .................................................. 2
Scheme 1.2 Mechanism of the Koenig’s-Knorr glycosylation .......................................................... 3
Scheme 1.3 Lemieux halide catalysis method for glycosylation ......................................................... 4
Scheme 1.4 Preparation of a fragment of saponin pentasaccharide ................................................. 6
Scheme 1.5 Glycosylation using an engineered glycosyltransferase .................................................. 6
Scheme 1.6 Activation of OH groups through O-stannyl ethers and O-stannylene acetals ............... 8
Scheme 1.7 Typical conditions for tin-mediated regioselective glycosylation ................................. 8
Scheme 1.8 Regioselective glycosylation via arylboronic acid activation ........................................ 9
Scheme 1.9 Regioselective glycosylation via transient arylboronic acid protection ..................... 10
Scheme 1.10 Activation of cyclic boronates with tertiary amines .................................................. 11
Scheme 1.11 Regioselective borinic acid-catalyzed acylation of carbohydrate derivatives .......... 12
Scheme 2.1 Preparation of glycosyl sulfide and sulfoxide acceptors .............................................. 15
Scheme 2.2 Preparation of 2-deoxy glycosylamine derivatives ........................................................ 15
Scheme 2.3 Preparation of a peracetylated fucopyranosyl bromide donor ...................................... 16
Scheme 2.4 Preparation of electron-deficient glycosyl bromide donors .......................................... 16
Scheme 2.5 Preparation of mannopyranosyl bromide donors ........................................................ 17
Scheme 2.6 Preparation of a trichloroacetimidate donor ................................................................. 17
Scheme 2.7 Borinic acid-catalyzed glycosylation of cis-1,2-cyclopentanediol ............................... 18
Scheme 2.8 Glycosylation products observed with phenylboronic acid catalyst. .................. 22
Scheme 2.9 Borinic acid-catalyzed glycosylation under halide catalysis conditions. .......... 33
Scheme 2.10 Glycosylation with galactopyranosyl bromide donor. ............................. 34
Scheme 2.11 Glycosylation with an electron-deficient fucopyranosyl bromide donor. ........ 35
Scheme 2.12 Glycosylation with arabinopyranosyl bromide donors. ............................ 35
Scheme 2.13 Organoboron-catalyzed mannosylations. ............................................. 36
Scheme 2.14 Glycosylation of a thiogalactoside-derived acceptor. ............................... 36
Scheme 2.15 Glycosylation of a galactose-derived sulfoxide acceptor. ......................... 37
Scheme 2.16 Glycosylation of a glucose-derived acceptor. ......................................... 37
Scheme 2.17 Glycosylation of mannose and galactose derivatives at the 3' OH and 6' OH. .... 38
Scheme 2.18 Attempted glycosylation at the 6' OH of glucose derivatives. ...................... 38
Scheme 2.19 Borinic acid-catalyzed glycosylation with a thiophenyl donor. ...................... 39
1 Introduction

1.1 Carbohydrates in Biological Systems

Carbohydrates are present in biological systems as a source of energy, as structural materials (e.g., cellulose in plants, chitin in invertebrates), and as glycoconjugates, which include glycoproteins and glycolipids. The carbohydrate components of these glycoconjugates are responsible for a wide range of biological processes. They mediate protein folding, cellular development, and the organization of cells into different tissues. Carbohydrates present on cell walls mediate signaling and recognition, including antigen recognition. This ultimately leads to control of, for example, hormone activity and the innate immune response. Certain human disorders can arise as a result of defects in protein glycosylation and unique oligosaccharide patterns can characterize tumour cells, bacteria, and viruses. Carbohydrate-based vaccines and therapeutics are therefore of great interest. A major challenge in glycobiology and glycomedicine however, is the limited access to useful quantities of pure and structurally well-defined carbohydrates and glycoconjugates. They are present in low concentrations and as heterogeneous mixtures in biological systems, making purification difficult. Laboratory syntheses are therefore necessary and although much effort has gone into their development, no single general method exists. An array of complementary tools, including chemical and enzymatic methods, are often employed and must be chosen carefully based on the linkages present in each oligosaccharide target. Figure 1.1 shows two examples of biologically relevant oligosaccharides that were prepared either by

---


enzymatic or chemical methods: the blood group B antigen 1 and the glycolipid Globo H antigen 2, found on prostate and breast cancer cells.

Figure 1.1 Biologically relevant glycoconjugates: Blood group B and Globo H antigens.

1.2 Chemical Synthesis of Glycosides: Koenigs-Knorr Method

The chemical synthesis of glycosides usually involves glycosylation of a suitably protected glycosyl acceptor (the nucleophile), which generally contains only one free hydroxy (OH) group. The electrophilic partner is the glycosyl donor, a fully protected sugar with a leaving group at its anomeric center (Scheme 1.1).

Scheme 1.1 Reaction components in chemical glycoside synthesis.

---


The Fischer glycoside synthesis, an acid-catalyzed condensation suitable for the preparation of lower alkyl glycosides, was the earliest report on the construction of O-glycosidic bonds. The reversibility of this reaction and harsh acidic conditions required limits its usefulness in the synthesis of complex oligosaccharides. Soon after Fischer’s report Koenigs and Knorr reported a method for the irreversible exchange of the anomeric oxygen atom through preactivation of the anomeric center, and this has become the most well known method for glycoside synthesis. The Koenigs-Knorr method makes use of a glycosyl halide (bromide or chloride) donor and a heavy metal ion promoter such as silver oxide or silver carbonate. As shown in Scheme 1.2, this affords a 1,2-trans-glycoside 4 from the corresponding peracetylated glycosyl halide 3. The reaction can either proceed by an S_N2-like mechanism or an S_N1-like mechanism. The latter would involve the intermediacy of oxocarbenium intermediate 5. Participation of the protecting group at C-2 would favour attack of one face but could also result in formation of orthoester byproduct 6. Undesired byproducts can also arise from reaction of the halide with water, which is formed in the reaction. As a result, drying agents such as molecular sieves or Drierite are often used to improve yields.

Scheme 1.2 Mechanism of the Koenig’s-Knorr glycosylation.

---

8 Fischer, E. Ber. 1893, 26, 2400–2412.


The 1,2-\emph{cis}-glycoside can be accessed using the halide ion catalysis method developed by Lemieux, which makes use of glycosyl halides containing a nonparticipating (benzyl) group at the C-2 position and a tetrabutylammonium halide salt (\textbf{Scheme 1.3}).\textsuperscript{11} An equilibrium is set up with the added halide so that both the \(\alpha\)- and \(\beta\)-glycosyl halides (7 and 8, respectively) exist in solution. The thermodynamically less stable \(\beta\)-anomer will react much faster than the \(\alpha\)-anomer to give the 1,2-\emph{cis}-glycoside 9.

\textbf{Scheme 1.3 Lemieux halide catalysis method for glycosylation.}

\begin{center}
\includegraphics[width=0.5\textwidth]{Scheme1.3.png}
\end{center}

\section{1.3 Methods for Regioselective Glycosylation}

\subsection{1.3.1 Carbohydrates: Complex Biopolymers}

Of the biopolymers, oligosaccharides are unique in that many isomeric structures can result from the formation of a single linkage. The stereochemistry of the glycosidic linkage can be either \(\alpha\) or \(\beta\), and multiple regioisomers are possible depending on which OH group acts as the nucleophilic partner. The diversity of linkages present in the blood group H-type II tetrasaccharide\textsuperscript{12} are highlighted in \textbf{Figure 1.2}. Oligosaccharides can therefore have branched structures, as opposed to peptides and oligonucleotides, which are usually linear. As a result, a biological template for carbohydrate amplification does not exist as it does for nucleic acids (polymerase chain reaction) or proteins (bacterial expression systems), and instead oligosaccharide synthesis relies on a variety of enzymes.


1.3.2 Protective Group Manipulations

Tremendous efforts have been made toward the development of methods for selective oligosaccharide synthesis.\(^{13}\) The problem of stereoselectivity can be overcome through the control of neighbouring group participation, the stereochemistry of the glycosyl donor, as well as the reaction conditions. The problem of regioselectivity, however, has generally been addressed through the use of protective groups to suppress glycosylation at undesired positions. This requires multiple additional steps to install and remove these protective groups, which is inefficient both in terms of time and resources. In the example shown in Scheme 1.4, disaccharide 13 is obtained by coupling of acceptor 11 with donor 12. In order to selectively functionalize the 3' OH of arabinose, the protected derivative 11 must be prepared in five steps from 10. Differential protection of O2 and O4 was necessary in order for O2 to be selectively unmasked and subsequently glycosylated. This represents only a fragment of the synthesis towards a saponin pentasaccharide.\(^{14}\)

---


1.3.3 Enzymatic Methods

Glycosyltransferases and glycosidases, enzymes used in nature for the biosynthesis and degradation of oligosaccharides, have been exploited for the laboratory syntheses of these molecules. Glycosyltransferases (GTs) function by creating a glycosidic linkage, specific in terms of position and configuration, between a sugar nucleoside phosphate (the glycosyl donor) and an acceptor. These enzymes are highly specific, however the range of available enzymes and glycosides that can be accessed is limited. Genetic engineering and recombinant techniques have helped to expand the availability of GTs. In one example Thorson and coworkers were able to glucosylate a diverse range of acceptors, including bioactive natural products, using a triple mutant of the oleandomycin (OleD) GT (Scheme 1.5).

Scheme 1.4 Preparation of a fragment of saponin pentasaccharide.

Scheme 1.5 Glycosylation using an engineered glycosyltransferase.

---


Glycosynthases are mutant glycosidases and function through the mechanism shown in Figure 1.3. A covalent glycosyl-enzyme intermediate is formed and instead of being hydrolyzed by water, which is the normal function of a glycosidase enzyme, is intercepted by a glycosyl acceptor. The glycosidic linkage is formed through acid/base catalysis. Although not depicted in Figure 1.3, the glycosyl donor is normally an *in situ* generated glycosyl fluoride. Glycosidases are more widely available and less costly compared to GTs, but may be limited by low specificities and yields.

![Figure 1.3](image)

**Figure 1.3** Mechanism of transglycosylation catalyzed by *Agrobacterium* sp. β-glucosidase.

1.3.4 Tin- and Boron- Mediated Approaches

Protecting group manipulations facilitate regioselective glycosylation through deactivation, or masking, of hydroxy groups that are not to be glycosylated. An alternative approach employs activating agents that enhance the reactivity of specific OH groups in the presence of others. The use of organotin derivatives in this respect has become a common method to promote regioselective reactions of carbohydrate derivatives with a variety of electrophiles, including glycosyl donors. Bis(trialkyltin) oxide and dialkyltin oxide have been used to form carbohydrate O-stannyly ethers 16 and O-stannylene acetals 17, respectively (Scheme 1.6). The tin-bound oxygen atoms have enhanced nucleophilicity and so are activated towards glycosylation.

---

Scheme 1.6 Activation of OH groups through O-stannyl ethers and O-stannylene acetals.

Most common is the formation of α/β-(1–6)-glycosidic linkages, however there are a few cases where β-(1–3)-linkages have been made. These glycosylations are usually carried out under Koenigs-Knorr conditions but there are some examples that make use of thioglycoside donors. Shortcomings of the tin-based approaches are: (1) the scope is limited and the yields are moderate to good, at best; (2) the required use of stoichiometric amounts of toxic organotin compounds; (3) the activated sugar-tin complex must first be generated under harsh conditions, followed by a low temperature glycosylation step that can proceed in some cases for multiple days. Typical conditions are shown in Scheme 1.7, with the examples chosen showing formation of both an α-(1–6)- and β-(1–6)-glycosidic linkage. These represent some of the higher-yielding examples of tin-mediated glycosylations.

Scheme 1.7 Typical conditions for tin-mediated regioselective glycosylation.

---


Aoyama and coworkers have shown that boronic acids can also be used to mediate regioselective glycosylation through an activation strategy. Formation of the activated cyclic boronate complex can occur through binding at either a 1,3-diol or a cis-1,2-diol to activate the less hindered primary or equatorial OH group, respectively (Scheme 1.8). Similar to the tin procedure, the synthesis is quite lengthy. Stoichiometric amounts of boronic acid promoter must first be stirred with the donor, acceptor and molecular sieves at reflux. Addition of TBAI and Ag$_2$CO$_3$ are carried out separately, at different temperatures, and the glycosylation proceeds for several days. Although the use of boron is an improvement compared to the tin-based protocol, the scope and yields are still quite limited. Additionally, a regioselective glycosylation protocol has been developed that employs stoichiometric 4-methoxyphenylboronic acid (Scheme 1.9). In this case, the regiochemical outcome has been interpreted in terms of transient protection, rather than activation, of a diol moiety by the organoboron reagent. Boronic acid would bind to the cis-1,2-diol in 21, leaving only the 2' OH free for glycosylation.

Scheme 1.8 Regioselective glycosylation via arylboronic acid activation.

---


Scheme 1.9 Regioselective glycosylation via transient arylboronic acid protection.

1.4 Organoboron Compounds in Chemical Recognition & Catalysis

The reversible covalent interaction of organoboron compounds with diols is well precedented, having been used extensively in the design of carbohydrate receptors. The first reports elucidating the structures and association constants of boronic acid-saccharide complexes in aqueous solution appeared as early as the 1950s. There is now general agreement that boronic acids covalently and reversibly interact with 1,2- or 1,3-diole to form five or six membered cyclic esters. The pioneering work of Czarnik and Shinkai demonstrated the ability of boronic acids, such as 23 and 24, to function as fluorescent sensors for carbohydrates (Figure 1.4). There have since been many reported examples of boronic acid-based carbohydrate sensors, including fluorescent, colorimetric, electrochemical, and polymer- and surface-bound sensors.

Figure 1.4 Early examples of boronic acid-based carbohydrate receptors.

Although formation of a boronate ester generally constitutes protection of a diol motif\textsuperscript{30}, Aoyama and co-workers reported generation of ‘ate’ complex 25 upon addition of triethylamine (Scheme 1.10), which activated fucose- and arabinose-derived boronate esters toward alkylation at O3.\textsuperscript{31} More recently, the Taylor group has reported that borinate ester 26 can act as a pre-catalyst for the regioselective acylation and alkylation of carbohydrate derivatives.\textsuperscript{32} The same catalyst had also been used earlier in the development of a boron-catalyzed direct aldol reaction of pyruvic acids.\textsuperscript{33} The mechanistic model for the regioselectivity observed involves formation of a tetracoordinate borinate complex 27 from 26 and cis-diol motifs (Scheme 1.11). The enhanced nucleophilicity of the boron-bound oxygen atoms activates them toward electrophilic attack.

Scheme 1.10 Activation of cyclic boronates with tertiary amines.


Scheme 1.11 Regioselective borinic acid-catalyzed acylation of carbohydrate derivatives.

Computational studies suggest an electronic basis for the observed selectivity: the boron-bound oxygen in the equatorial position is predicted to be the most nucleophilic based on Fukui index calculations, and this corresponds to the site of observed reactivity. The results for this study are summarized in Figure 1.5, showing that O-3 of the borinate esters derived from the galacto 28 and manno 29 series have the highest Fukui indices. Adducts of anhydro[1,6]galactose 30 and anhydro[1,6]mannose 31 show the highest nucleophilic reactivity at O-4 and O-2, respectively.

<table>
<thead>
<tr>
<th>atom</th>
<th>Fukui index</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-2</td>
<td>0.039</td>
</tr>
<tr>
<td>O-3</td>
<td>0.177</td>
</tr>
<tr>
<td>O-4</td>
<td>0.132</td>
</tr>
</tbody>
</table>

Figure 1.5 Calculated Fukui indices (B3LYP/6-311+G(d,p)) of diphenylborinates.
2 Results and Discussion

2.1 Research Goals

Based on the observed catalytic reactivity of borinic acids in the regioselective acylation of carbohydrate derivatives, it was postulated that this small molecule could also be used to catalyze regioselective glycosylation reactions. The electrophilic species would be a glycosyl donor, as opposed to an acyl halide. The challenge would lie in identifying conditions for glycosylation that would be compatible with the borinic acid catalyst. If successful, this would represent the first example of a small molecule catalyst for glycosylation. Besides enzymes, the only way of achieving regioselective glycosylation without the use of extensive protecting group manipulations is through organotin- or organoboron-mediated processes, which are themselves not very general and limited in terms of substrate scope and yields.

2.2 Substrate Synthesis

2.2.1 Synthesis of Glycosyl Acceptors

The primary hydroxy groups of methyl-α-D-mannopyranose, methyl-β-D-galactopyranose and methyl-α-D-galactopyranose were protected with the tert-butyldimethylsilyl group, as shown in Table 2.1 to give 33, 34 and 35, respectively. Protection of the primary OH groups of acceptor substrates would avoid complications arising from binding of the organoboron catalyst to two different diols: the cis-1,2-diol (O-3 and O-4) and the 1,3-diol (O-6 and O-4). The tert-butyldimethylsilyl groups were later removed from disaccharides prepared by the borinic acid-catalyzed glycosylation to give acceptor substrates 36 and 37, shown in Table 2.2.34 These substrates, already functionalized at O-3, could be used to access higher order oligosaccharides by taking advantage of the two-point binding of the organoboron catalyst to O-6 and O-4.

Table 2.1 Preparation of monosaccharide acceptor substrates.

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>35</td>
</tr>
<tr>
<td>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>21</td>
</tr>
</tbody>
</table>

* Isolated yield.

Table 2.2 Preparation of disaccharide acceptor substrates.

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>37</td>
</tr>
<tr>
<td>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>78</td>
</tr>
</tbody>
</table>

* Isolated yield.

The primary OH group of isopropyl-β-D-thiogalactoside 38 was protected with the tert-butylidimethylsilyl group and then oxidized to the corresponding sulfoxide 40, providing two different acceptor sugars, 39 and 40, shown in Scheme 2.1.<sup>35</sup> Acceptor substrates such as these, possessing an anomeric group other than an alkoxide, were of interest. Following glycosylation with a glycosyl halide under Koenigs-Knorr conditions, the new disaccharide would have the

potential to be activated under orthogonal conditions\textsuperscript{7} (with the sulfide or sulfoxide as the leaving group) in a second glycosylation reaction.

**Scheme 2.1 Preparation of glycosyl sulfide and sulfoxide acceptors.**

Anomeric protection of 2-deoxy sugars to be used subsequently as acceptors in glycosylation reactions was also attempted. Glycosylamines (GlcNAc and GalNAc) are common subunits in biologically relevant oligosaccharides.\textsuperscript{36} The method developed by Nitz and coworkers\textsuperscript{37} was used to prepare glucopyranoside 42 (**Scheme 2.2**). In order to increase the solubility of the substrate in organic solvents, synthesis of octyl-galactopyranoside 44 was attempted. The second step of the synthesis was not successful, neither for the methyl 45 nor octyl 44 derivatives, and the desired products were not observed after purification by column chromatography. Differences in the electronic nature of the galactopyranoside compared to the glucopyranoside (resulting from dipole orientations created by the polar OH groups) may result in differences in reactivity between the substrates.\textsuperscript{38}

**Scheme 2.2 Preparation of 2-deoxy glycosylamine derivatives.**

---

\textsuperscript{36} Marcaurelle, L.A.; Bertozzi, C.R. *Glycobiology* 2002, 12, 69R–77R.


2.2.2 Synthesis of Glycosyl Donors

The bromination procedure outlined in Scheme 2.3 was used to prepare fucopyranosyl bromide donor 46. The electron-deficient arabinopyranosyl bromide 49 and fucopyranosyl bromide 50 donors were prepared by the route shown in Scheme 2.4. Preparation of a more highly electron-deficient arabinose donor 51 by addition of chloroacetate protecting groups was also attempted. Starting material was consumed, however no product was observed by TLC nor by $^1$H NMR. A possible explanation could be degradation of the starting material, which may have occurred under the harsh reaction conditions.

Scheme 2.3 Preparation of a peracetylated fucopyranosyl bromide donor.

Scheme 2.4 Preparation of electron-deficient glycosyl bromide donors.

The synthetic routes towards mannopyranosyl bromide donors 52 and 54 are outlined in Scheme 2.5. Trichloroacetimidate donor 56 was prepared by the route shown in Scheme 2.6.

---

2.3 Optimization of Borinic Acid-Catalyzed Glycosylation

2.3.1 Preliminary Investigation

In order to simplify analysis, conditions for glycosylation were initially evaluated using 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide 57 as the donor and cis-1,2-clycopentanediol 58 as the acceptor, on 0.2 mmol scale. As shown in Scheme 2.7, reactions were run using 10 mol % of 2-aminoethyl diphenylborinate precatalyst 59 and a silver (I) promoter to abstract the halide and act as the acid acceptor. Silver oxide and silver carbonate are most commonly used in Koenigs-Knorr glycosylation reactions, however it has also been demonstrated that other silver salts of organic acids as well as different heavy-metal (eg. mercury) salts, and organic bases (eg. pyridine) are effective. By TLC the reaction with silver oxide looked most promising and isolation yielded 86% of the glycosylated product 60 as a mixture of diastereomers. A control reaction was run without borinic acid catalyst, which showed mostly unreacted starting materials. The glycosylated product was isolated in less than 13% yield, coeluting with an unidentified impurity. These results lead to the conclusion that borinic acid catalyst 59, previously employed for acylation chemistry, was also active under conditions for glycosylation.
Scheme 2.7 Borinic acid-catalyzed glycosylation of cis-1,2-cyclopentanediol.

The first attempt to synthesize a disaccharide was carried out using 57 and galactose derivative 34. As illustrated in Table 2.3, under the same conditions used previously with acceptor 58, the \( \beta-1,3 \)-linked disaccharide 61 was formed in 60% isolated yield along with 15% of a trisaccharide 62 resulting from difunctionalization of the acceptor. Without catalyst, no product was observed by crude \(^1\)H NMR and recoveries of donor and acceptor starting materials based on mesitylene as a quantitative internal standard were estimated to be 90% and 80%, respectively (Entry 1). In addition to calculating yields by \(^1\)H NMR using mesitylene as a quantitative internal standard, in many cases the products were isolated to more accurately determine yields. Overlapping peaks of electronically very similar side products or starting materials would be a source of error when calculating \(^1\)H NMR yields and often yields were slightly overestimated this way. Analysis by GC/MS was attempted, however glycosylation reagents and products were not observed by this method. In an attempt to improve yield and reduce difunctionalization, the stoichiometries of donor and acceptor were varied (Entries 2, 3, 4). Different silver (I) sources were screened (Entries 6, 7) and the reaction time reduced (Entry 5). The results of this preliminary optimization are summarized in Table 2.3. Of all the conditions, those listed in Entry 3 were considered ideal. Yield of trisaccharide was minimal and donor and acceptor were used in almost equimolar amounts, which is preferable to using a large excess of one reagent. A more extensive optimization was carried out using mannose derivative 33 as the acceptor, which was easier to handle as a solid at room temperature. Galactose derivative 34, on the other hand, did not always solidify and had to be weighed out as a viscous oil.
Table 2.3 Optimization of the borinic acid-catalyzed glycosylation between 57 and 34.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Change from above conditions</th>
<th>Result</th>
</tr>
</thead>
</table>
| 1     | No catalyst                  | 90 % 57<sup>a</sup>  
       |                              | 80 % 34<sup>a</sup>  |
| 2     | 57 (1.1 equiv)               | 84 % 61<sup>b</sup>  
       |                              | 13 % 62<sup>b</sup>  |
| 3     | 57 (1.0 equiv)               | 74 % 61<sup>b</sup>  
       | 34 (1.1 equiv)               | 9 % 62<sup>b</sup>  
       | Ag₂O (1.2 equiv)             |        |
| 4     | 57 (1.0 equiv)               | 100 % 61<sup>a</sup> |
       | 34 (1.5 equiv)               |        
       | Ag₂O (1.6 equiv)             |        |
| 5     | 4 hrs                        | 85 % 61<sup>a</sup> |
       | 57 (1.0 equiv)               |        
       | 34 (1.1 equiv)               |        
       | Ag₂O (1.2 equiv)             |        |
| 6     | 57 (1.0 equiv)               | 85 % 61<sup>a</sup> |
       | 34 (1.1 equiv)               |        
       | Ag₂CO₃ (1.2 equiv)            |        |
| 7     | 57 (1.0 equiv)               | 16 % 61<sup>b</sup> |
       | 34 (1.1 equiv)               |        
       | AgOTf (2.4 equiv)             |        
       | DIPEA (2.4 equiv)             |        |

* Yield determined by <sup>1</sup>H NMR with mesitylene as a quantitative internal standard.

<sup>b</sup> Isolated yield.
2.3.2 Catalyst, Promoter & Solvent Optimization

The reaction between glucose donor 57 and mannose acceptor 33 was carried out under the conditions listed in Table 2.4, Entry 3 and gave β-1,3-linked disaccharide 63 in 78% isolated yield. The yield was essentially unchanged when the stoichiometry of donor and acceptor was reversed, as shown in Table 2.4. An extensive catalyst screen was carried out with various borinic acids (Table 2.5, Entries 1–7), boronic acids (Entries 8–13), boric acid (Entry 14) and triphenylborane (Entry 15), the structures of which are summarized in Figure 2.1.

![Chemical Reaction Diagram]

Table 2.4 Optimization of the borinic acid-catalyzed glycosylation between 57 and 33.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Donor (equiv)</th>
<th>Acceptor (equiv)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.0</td>
<td>1.1</td>
<td>78(^a) (100)%</td>
</tr>
<tr>
<td>2</td>
<td>1.1</td>
<td>1.0</td>
<td>80(^b) (100)%</td>
</tr>
</tbody>
</table>

\(^a\) Yield determined by \(^1\)H NMR with mesitylene as a quantitative internal standard.  
\(^b\) Isolated yield.

![Chemical Structures](images)

Figure 2.1 Boron catalysts screened for activity in regioselective glycosylation.
carried out on a 1.0 mmol scale, is shown in Table 2.5 Optimization of boron catalyst for regioselective glycosylation.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst $^c$</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>59 (5 mol%)</td>
<td>40$^a$</td>
</tr>
<tr>
<td>2</td>
<td>59</td>
<td>78$^b$</td>
</tr>
<tr>
<td>3</td>
<td>59 (2 x 10 mol%)</td>
<td>72$^b$</td>
</tr>
<tr>
<td>4</td>
<td>59 (1.0 mmol scale)</td>
<td>99$^b$</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>53$^b$ (85)$^a$</td>
</tr>
<tr>
<td>6</td>
<td>65</td>
<td>83$^b$</td>
</tr>
<tr>
<td>7</td>
<td>66</td>
<td>83$^b$</td>
</tr>
<tr>
<td>8</td>
<td>67</td>
<td>36$^b$ (80)$^a$</td>
</tr>
<tr>
<td>9</td>
<td>67 (1.0 mmol scale)</td>
<td>52$^b$</td>
</tr>
<tr>
<td>10</td>
<td>67 (with Ag$_2$CO$_3$)</td>
<td>40$^a$</td>
</tr>
<tr>
<td>11</td>
<td>68</td>
<td>57$^b$ (60)$^a$</td>
</tr>
<tr>
<td>12</td>
<td>69</td>
<td>50$^b$</td>
</tr>
<tr>
<td>13</td>
<td>70</td>
<td>60$^b$</td>
</tr>
<tr>
<td>14</td>
<td>71</td>
<td>83$^b$</td>
</tr>
<tr>
<td>15</td>
<td>72</td>
<td>55$^a$</td>
</tr>
</tbody>
</table>

$^a$ Yield determined by $^1$H NMR with mesitylene as a quantitative internal standard.  
$^b$ Isolated yield.  
$^c$ Reactions run on 0.2 mmol scale with 10 mol% catalyst and Ag$_2$O as promoter, unless otherwise noted.

Yields of disaccharide obtained using boronic acid catalysts were lower than with borinic acid catalysts. In addition, orthoester 73 was consistently observed as a side product in reactions with boronic acids, generally in yields ranging from 12–20%. The result with phenylboronic acid, carried out on a 1.0 mmol scale, is shown in Scheme 2.8.
Scheme 2.8 Glycosylation products observed with phenylboronic acid catalyst.

It was found that reducing the catalyst loading of 59 to 5 mol % resulted in a reduced yield of disaccharide (Table 2.5, Entry 1). Adding more catalyst 5 hours into the reaction did not improve the yield (Entry 3). This confirmed that catalyst turnover was not compromised by decomposition or inactivation over the course of the reaction time. Using “free-based” catalyst 64, obtained by stirring catalyst 59 with 1M HCl in methanol/acetone to hydrolyze the ethanolamine, did not improve the yield of 63 (Entry 5). Finally, when run on 1.0 mmol scale in a 50 mL round-bottom flask as opposed to on 0.2 mmol scale in a 2-dram vial, the yield of 63 increased from 78% to 99% (Entry 4). This is thought to be a result both of increased accuracy when working on a larger scale and of the increased surface area of silver (I) oxide in the round-bottom flask. Changing the electronic properties of catalyst 59 to either an electron poor 65 or an electron rich 66 borinic acid resulted in similar yields (Entry 6 and 7, respectively).

Interestingly, boric acid as the catalyst also gave a high yield of 63 (Entry 14). However, when tested on one of the lower-yielding glycosylations from the scope (donor 57 with rhamnose-derived acceptor 74), none of the desired product was isolated and an unidentifiable mixture of products was instead observed. Triphenylborane also proved to be a less efficient catalyst compared to the borinic acids (Entry 15).

The results summarized in Table 2.5 indicated that borinic acid 59 was the most promising catalyst for the glycosylation reaction. It gave a single disaccharide in high yield and no side products were observed. It is also commercially available, as opposed to the other borinic acids, which had to be prepared.

Control reactions were run in order to evaluate whether regioselective synthesis of 63 might be possible without the use of a catalyst. Figure 2.2 shows the $^1$H NMR spectra of purified
disaccharide 63 (spectrum D), the crude $^1$H NMR of the reaction run under optimized conditions (spectrum C), the crude $^1$H NMR of the reaction run under the optimized conditions but without catalyst (spectrum B), and the crude $^1$H NMR of the glycosylation reaction run under Hanessian’s reported conditions (spectrum A). The crude reaction mixtures were each filtered through Celite before being submitted for $^1$H NMR analysis. Mesitylene was added as a quantitative internal standard and appears at approximately 6.7 ppm in spectra A, B and C. Based on these results it is clear that catalyst 59 has a significant effect on glycosylation rate and regioselectivity. Without catalyst, unreacted starting material was evident as the major component of the crude mixture (spectrum B). Under Hanessian’s reported glycosylation conditions the starting materials appear to be consumed however the crude $^1$H NMR indicates a complex mixture of products and no selectivity. The crude $^1$H NMR of the reaction with borinic acid catalyst (spectrum C) is quite clean when compared with the isolated material (spectrum D).

---

Figure 2.2 Crude $^1$H NMR of glycosylation reactions run between 57 and 33 under Hanessian’s reported conditions (A), and the current optimized conditions with (C) and without (B) catalyst 59. The $^1$H NMR of purified 63 (D) is displayed for comparison.

The effects of the identity and stoichiometry of the Ag (I) promoter were evaluated. Silver oxide proved to be a superior promoter in comparison to other silver additives (Table 2.6). It was found that using more than 1.0 equivalent of silver (I) oxide made no improvement to the yield however yields decreased with less than 1.0 equivalent (Table 2.7).
Table 2.6 Optimization of the identity of Ag (I) promoter.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ag (I) promoter (equiv.)</th>
<th>Yield (%) (^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ag₂O (1.0)</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>Ag₂CO₃ (1.0)</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>AgOAc (2.0)</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>AgOTf (2.0) + DIPEA (1.1)</td>
<td>&lt; 5</td>
</tr>
</tbody>
</table>

\(^a\) Yield determined by \(^1\)H NMR with mesitylene as a quantitative internal standard.

Table 2.7 Optimization of the stoichiometry of Ag₂O promoter.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Equivalents Ag₂O</th>
<th>Yield (%) (^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>0.75</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>1.0</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>1.2</td>
<td>78</td>
</tr>
</tbody>
</table>

\(^a\) Isolated yield.
A solvent screen, summarized in **Table 2.8**, demonstrated that the borinic acid-catalyzed glycosylation proceeded well not only in acetonitrile but also in dichloromethane and tetrahydrofuran. The yield was lower, however, in toluene. The sensitivity of the glycosylation reaction to moisture was evaluated by carrying out the reaction with additions of increasing volumes of water (**Table 2.9**). The results show that the reaction is quite tolerant of water and addition of 1 volume percent (4 equivalents) had only a moderate effect on the yield of 63 (Entry 1). The vast majority of glycosylation reactions must be carried out with strict exclusion of water, however it was observed that the reaction did not proceed when molecular sieves were added (**Table 2.9**, Entry 5).

![Chemical structure](image)

**Table 2.8 Solvent optimization for regioselective glycosylation.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>acetonitrile</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>chloroform</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>tetrahydrofuran</td>
<td>100</td>
</tr>
<tr>
<td>4</td>
<td>toluene</td>
<td>70</td>
</tr>
</tbody>
</table>

<sup>a</sup> Yield determined by <sup>1</sup>H NMR with mesitylene as a quantitative internal standard.
2.3.3 Optimizations of Difficult Glycosylations

Glycosylation of rhamnose-derived acceptor 75 and fucose-derived acceptor 78 with donor 57 proved to be more challenging. Compared to the mannose- and galactose-derived acceptors (33 and 34, respectively), 75 and 78 lack the 6’ OTBS group. It is expected that having one less electron-withdrawing oxygen atom would result in a relative decrease in the acidity of the OH groups. Deprotonation would therefore be more difficult and once the borinate ester formed, it would be more stable. The decrease in reactivity of the borinate ester is one explanation for the lower yields observed. Additionally, it is predicted that the bulky 6’ OTBS group helps to bias selectivity for the equatorial boron-bound oxygen atom, in addition to the electronic preferences discussed previously. 32 Acceptors 75 and 78 do not have this additional steric factor to enhance selectivity for the equatorial boron-bound OH group. As shown in the scope table at the end of the chapter (Table 2.17), a mixture of regioisomers was observed with arabinose- and lyxose-derived acceptors 108 and 110, respectively. This is also predicted to be a result of the absence of a large group at C5 in these sugars. This may result in a lower thermodynamic preference for

Table 2.9 Effect of water on the borinic acid-catalyzed glycosylation.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Volume % H₂O</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>72b(90)a</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>50a</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>25a</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>10a</td>
</tr>
<tr>
<td>5</td>
<td>0 (4A MS)</td>
<td>NP, 50 % donorb</td>
</tr>
</tbody>
</table>

a Yield determined by 1H NMR with mesitylene as a quantitative internal standard.  
b Isolated yield.
one of the two conformational isomers of the acceptor, allowing the borinic acid to interact with both and give two different products.

Results for the attempted optimization using rhamnose-derived acceptor 75 are summarized in Table 2.10. Under the original optimized conditions, disaccharide 76 was obtained in 68% yield (Entry 1). A mixture of side products was observed and these were tentatively assigned as higher-order (eg. tri-) saccharides, regioisomeric disaccharides and/or orthoesters. Changing the catalyst, reaction temperature, reaction time, and protecting groups on the donor did not give improved results. Also attempted but not shown in the table, was substituting propionitrile for acetonitrile as the reaction solvent. Only complex product mixtures were observed with no apparent formation of desired disaccharide 76. When pivaloyl-protected glucopyranosyl bromide 74 was used, 13% of a regioisomeric disaccharide coeluted with 71% of 77 as a result of the decreased polarity of the products (Entry 7). Results for the optimization using fucose-derived acceptor 78 are summarized in Table 2.11. A minor regioisomeric disaccharide was consistently observed in this coupling and the best result was obtained when 74 was used as the donor (Entries 7, 8).

![Chemical structure](image)

**Table 2.10 Optimization of glycosylation conditions with rhamnose-derived acceptor.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Donor</th>
<th>Catalyst</th>
<th>Time (hrs)</th>
<th>Temp (°C)</th>
<th>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>59</td>
<td>16</td>
<td>23</td>
<td>68</td>
</tr>
<tr>
<td>2</td>
<td>57</td>
<td>59</td>
<td>16</td>
<td>40</td>
<td>67</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>59</td>
<td>48</td>
<td>23</td>
<td>68</td>
</tr>
<tr>
<td>4</td>
<td>57</td>
<td>71&lt;sup&gt;c&lt;/sup&gt;</td>
<td>16</td>
<td>23</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>5</td>
<td>57</td>
<td>66</td>
<td>16</td>
<td>23</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>6</td>
<td>57&lt;sup&gt;d&lt;/sup&gt;</td>
<td>59</td>
<td>16</td>
<td>23</td>
<td>57</td>
</tr>
<tr>
<td>7</td>
<td>74</td>
<td>59</td>
<td>16</td>
<td>23</td>
<td>71</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reactions run on 0.2 mmol scale unless otherwise noted.

<sup>b</sup> Isolated yield.

<sup>c</sup> Also carried out using stoichiometric boric acid (same result observed).

<sup>d</sup> Reaction run on 1.0 mmol scale.
Mannose- and galactose-derived anhydro sugars 81 and 84, respectively, are interesting because they force these pyranosides to assume their otherwise less-favoured conformations. Based on the previously discussed mechanistic model and as depicted in Figure 2.3, this should result in functionalization of the 2' OH and 4' OH (which are now equatorial) of 81 and 84, respectively, instead of the 3' OH. The yields for the reactions with 81 and 84 were lower compared to the reactions with 33 and 34, which may be due to the increased rigidity of the anhydro sugars. Binding with the borinic acid catalyst may be more difficult if the sugar is less able to distort.

Table 2.11 Optimization of glycosylation conditions with fucose-derived acceptor.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Donor&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Time (hrs)</th>
<th>Temp (°C)</th>
<th>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Side product(s) (% Yield)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57&lt;sup&gt;b&lt;/sup&gt;</td>
<td>16</td>
<td>23</td>
<td>58</td>
<td>regioisomer + coeluted 79 (25) trisaccharide (13)</td>
</tr>
<tr>
<td>2</td>
<td>57&lt;sup&gt;c&lt;/sup&gt;</td>
<td>16</td>
<td>23</td>
<td>69</td>
<td>regioisomer (9)</td>
</tr>
<tr>
<td>3</td>
<td>57&lt;sup&gt;d&lt;/sup&gt;</td>
<td>16</td>
<td>23</td>
<td>58</td>
<td>regioisomer (12) trisaccharide (5)</td>
</tr>
<tr>
<td>4</td>
<td>57</td>
<td>16</td>
<td>40</td>
<td>70</td>
<td>regioisomer (8)</td>
</tr>
<tr>
<td>5</td>
<td>57</td>
<td>16</td>
<td>60</td>
<td>70</td>
<td>--</td>
</tr>
<tr>
<td>6</td>
<td>57</td>
<td>48</td>
<td>40</td>
<td>70</td>
<td>regioisomer (8)</td>
</tr>
<tr>
<td>7</td>
<td>74</td>
<td>16</td>
<td>23</td>
<td>85</td>
<td>regioisomer (9)</td>
</tr>
<tr>
<td>8</td>
<td>74&lt;sup&gt;d&lt;/sup&gt;</td>
<td>16</td>
<td>23</td>
<td>81</td>
<td>regioisomer (9)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reactions run using 0.2 mmol donor unless otherwise noted.
<sup>b</sup> Stoichiometry reversed: 0.22 mmol 57, 0.2 mmol 78.
<sup>c</sup> With excess 78 (0.3 mmol).
<sup>d</sup> Reaction run on 1.0 mmol scale.
<sup>e</sup> Isolated yield.
Unreacted donor was observed in reactions with both anhydro sugars, which indicates a lower activity. Additionally, 10-20% of a mixture of side products was isolated from these reactions. The results for the optimizations are shown in Table 2.12 and Table 2.13 below. Once again, when using pivaloyl-protected donor 74 purification became more difficult and unidentified side products often eluted with the desired disaccharides. Using mannose-derivative 81 as the acceptor was particularly challenging because the equatorial OH of the cis-1,2-diol that is expected to be functionalized is both sterically and electronically deactivated.

![Boronate esters of mannose and galactose derivatives.](image)

**Figure 2.3** Boronate esters of mannose and galactose derivatives.

![Optimization of glycosylation with anhydromannose-derived acceptor.](image)

**Table 2.12** Optimization of glycosylation with anhydromannose-derived acceptor.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Donor&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Temp (°C)</th>
<th>Yield (%)&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>23</td>
<td>56</td>
</tr>
<tr>
<td>2</td>
<td>57</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>57&lt;sup&gt;b&lt;/sup&gt;</td>
<td>23</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>74&lt;sup&gt;c&lt;/sup&gt;</td>
<td>23</td>
<td>product mixtures, no separation</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reactions run on 0.2 mmol scale unless otherwise noted.  
<sup>b</sup> With excess 81 (0.3 mmol).  
<sup>c</sup> Reaction run on 1.0 mmol scale.  
<sup>d</sup> Isolated yield.
Table 2.13 Optimization of glycosylation with anhydrogalactose-derived acceptor.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Donor</th>
<th>Temp (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>23</td>
<td>68</td>
</tr>
<tr>
<td>2</td>
<td>57</td>
<td>40</td>
<td>66</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>60</td>
<td>83</td>
</tr>
<tr>
<td>4</td>
<td>57&lt;sup&gt;b&lt;/sup&gt;</td>
<td>60</td>
<td>73</td>
</tr>
<tr>
<td>5</td>
<td>74</td>
<td>23</td>
<td>58 (impure)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reactions run on 0.2 mmol scale unless otherwise noted.
<sup>b</sup> Reaction run on 1.0 mmol scale.
<sup>c</sup> Isolated yield.

Carrying out a glycosylation with 4,6-O-ethylidene-α-D-glucose 87 would be interesting because the anomeric position is unprotected and the borinic acid is expected to bind to the only cis-1,2-diol: the 1' and 2' OH groups of the α anomer. Unfortunately, the yield of this reaction could not be improved above 50% of α-1,1-linked disaccharide 88, as tentatively assigned by ¹H/¹H COSY analysis. This was surprising, as functionalization of the equatorial OH group over the axial had been observed in all previous borinic acid-catalyzed glycosylations. The 1' OH should be less nucleophilic compared to the 2' OH, however it is also more acidic. The various conditions screened are summarized in Table 2.14. In all cases, mixtures of unidentifiable side products were isolated in addition to disaccharide 88/89 and unreacted donor was also observed. What appeared to be a mixture of two different monofunctionalized products was isolated from the reaction with the electron-rich borinic acid catalyst (Entry 3).
2.4 Attempt to Change Stereoselectivity: Halide Catalysis Method

It was thought that α-glycosidic linkages could be achieved using the Lemieux halide catalysis method. The addition of halide anion in the form of a halide salt should set up an equilibrium between the α- and β-halide donors, as discussed previously. The more reactive β-halide would undergo glycosylation with the glycosyl acceptor to yield a disaccharide having an α-glycosidic linkage. As shown in Scheme 2.9 below, the addition of both TBAB and TBAI resulted in very messy reactions with unidentifiable product mixtures. It is unclear why the addition of these salts is incompatible with the developed borinic acid-catalyzed glycosylation conditions. Reaction

![Reaction scheme](image)

**Table 2.14 Optimization of glycosylation with 4,6-O-ethylidene-α-D-glucose.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Donor*</th>
<th>Catalyst</th>
<th>Temp (°C)</th>
<th>Yield (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>59</td>
<td>23</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>57</td>
<td>59</td>
<td>40</td>
<td>37</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>66</td>
<td>23</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>4</td>
<td>57b</td>
<td>59</td>
<td>23</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>5</td>
<td>57c</td>
<td>59</td>
<td>23</td>
<td>32</td>
</tr>
<tr>
<td>6</td>
<td>74</td>
<td>59</td>
<td>23</td>
<td>48</td>
</tr>
<tr>
<td>7</td>
<td>74d</td>
<td>59</td>
<td>23</td>
<td>50</td>
</tr>
</tbody>
</table>

*a Reactions run using 0.2 mmol donor unless otherwise noted.
*b With excess 87 (0.3 mmol).
*c With excess donor: 0.3 mmol 57, 0.2 mmol 87.
*d Reaction run on 1.0 mmol scale.
*e Isolated yield.
conditions developed by group member Lina Chan demonstrated that TBAI could be used with K₂CO₃ for the borinic acid-catalyzed regioselective alkylation of carbohydrate derivatives.⁴³

Scheme 2.9 Borinic acid-catalyzed glycosylation under halide catalysis conditions.

2.5 Glycosylations with Non-Glucosyl Donors

Changing the identity of the glycosyl donor can result in significant variations in reactivity. As mentioned previously, differences in the orientations of the OH groups will result in differences in electron density at the anomeric carbon (through dipole effects).³⁸ Carbohydrates having OH groups occupying axial positions are activated (armed) and show higher reactivity as glycosyl donors.⁴⁴ These so-called ‘armed’ donors have a higher electron density at the anomeric position and therefore include donors with electron-donating protecting groups. Additionally, carbohydrate derivatives lacking a 6' OH group, such as fucose-derived donors, are considered armed and will be more reactive. Conversely, donors that have low electron density at the anomeric position – a result of having electron-withdrawing protecting groups and/or many equatorially-oriented OH groups as well as the additional 6' OH – are deactivated (disarmed) and will display lower reactivity.⁴

When a glycosylation was carried out with galactopyranosyl bromide donor 90 and arabinose-derived acceptor 91, disaccharide 92 was obtained in 78% yield (Scheme 2.10). A complex mixture of products was observed, however, when fucopyranosyl bromide 46 was used as the donor with mannose-derived acceptor 33. Multiple spots were observed by TLC and attempted

---

⁴³ Chan, L.; Taylor, M.S. Unpublished results.

isolation resulted in co-elution of unidentifiable product mixtures. This result was not surprising, as fucose has one less electron-withdrawing oxygen atom on its ring compared to glucose and galactose, rendering it a more reactive donor. Lowering the reaction temperature, using different acceptors or using the electron-rich borinic acid catalyst 66 did not improve this glycosylation (Table 2.15, entries 2–5). Employing the less reactive 4-nitrobenzoyl-protected fucopyranosyl bromide 50 gave disaccharide 93 in 40% yield (Scheme 2.11). Introducing electron-withdrawing protecting groups is expected to decrease reactivity by destabilizing oxocarbenium-like intermediates in favor of a pathway with S_N2 character. The same trend was observed with arabinopyranosyl bromide donors 94 and 49 (Scheme 2.12). Doris Lee was able to further increase yields by synthesizing and using peracetylated fucopyranosyl and arabinopyranosyl chloride donors in the glycosylation reaction. Success with these reagents is attributed to the lower reactivity of chloride relative to bromide donors. 

Scheme 2.10 Glycosylation with galactopyranosyl bromide donor.

![Scheme 2.10](image)

Table 2.15 Optimization of glycosylation with fucopyranosyl bromide.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Acceptor</th>
<th>Catalyst</th>
<th>Temp (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33</td>
<td>59</td>
<td>23</td>
</tr>
<tr>
<td>2</td>
<td>33</td>
<td>59</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>34</td>
<td>59</td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td>75</td>
<td>59</td>
<td>23</td>
</tr>
<tr>
<td>5</td>
<td>33</td>
<td>66</td>
<td>23</td>
</tr>
</tbody>
</table>
Organoboron-catalyzed mannosylations were also attempted. Reaction of mannopyranosyl bromide donor 52 with 34 yielded 38% orthoester 96 (Scheme 2.13). In an attempt to minimize neighbouring group participation and formation of the orthoester, the more sterically demanding pivaloyl-protected mannopyranosyl bromide 54 was used as the donor. The result, as shown in Scheme 2.13, was 72% of a 1:1 mixture of orthoester 97 and what appeared to be the expected disaccharide 98. Reactions of this donor with either fucose- or anhydro galactose-derived acceptors (78 and 84, respectively) did not give improved results.
Scheme 2.13 Organoboron-catalyzed mannosylations.

Scheme 2.14 Glycosylation of a thiogalactoside-derived acceptor.

2.6 Acceptors Incompatible with the Borinic Acid-Catalyzed Glycosylation

It was of interest to explore glycosyl acceptors bearing anomeric substituents that could subsequently be activated in a second glycosylation event. Unfortunately, neither thiogalactoside-derived acceptor 39 nor the corresponding sulfoxide 40 reacted with donor 57 to give the expected disaccharides (Scheme 2.14 and Scheme 2.15). What appeared to be a derivative of the donor was observed from reactions with 39, as well as complex product mixtures. Based on TLC, crude \(^1\)H NMR and attempted isolation, the glycosylation reaction seemed to be shut down with 40. Only unreacted starting material and derivatives (tentatively assigned as decomposition products) were observed. It is speculated that the sulfur is interacting unfavourably with silver. In the case of the sulfoxide, the anionic oxygen may be complexing with the borinic acid catalyst, thereby inhibiting the reaction.
Scheme 2.15 Glycosylation of a galactose-derived sulfoxide acceptor.

As expected, reaction with glucose-derived acceptor 99 resulted in mostly unreacted starting material and minor amounts of a product that integrated for a disaccharide (Scheme 2.16). There are no cis-diols in glycopyranoside 99 and the borinic acid is not expected to bind well to trans-diols therefore the low activity is not surprising.

Scheme 2.16 Glycosylation of a glucose-derived acceptor.

2.7 Glycosylations with Acceptors Unprotected at the 6’ Hydroxyl

Glycosylation reactions were also attempted with acceptors unprotected at the 6’ OH. With acceptors 100 and 102, 2.2 equivalents of donor 57 were used in an attempt to glycosylate at both the 3’ and 6’ positions. This was expected to occur through binding of the borinic acid to both the 1,2-diol and 1,3-diol moieties. Binding of organoboron compounds, specifically boronic acids, to the 4’ OH and 6’ OH of carbohydrate derivatives is a known mode of coordination. Moderate yields of trisaccharides 101 and 103 were obtained (Scheme 2.17). With glucose-derived acceptor 104 the hope was to glycosylate at the 6’ OH. It was anticipated

---

that the borinic acid would bind only to the 1,3-diol, as the 1,2-diols have \textit{trans} arrangements. The reaction was not very clean as observed by both TLC and crude $^1$H NMR, indicating a complex mixture of products (Scheme 2.18). No reaction occurred with the 2-deoxy-$N$-acetylated glucose acceptor 42, which was insoluble in acetonitrile, which is also shown in Scheme 2.18.

**Scheme 2.17 Glycosylation of mannose and galactose derivatives at the 3' OH and 6' OH.**

**Scheme 2.18 Attempted glycosylation at the 6' OH of glucose derivatives.**
2.8 Glycosylations with Non-Halide Donors

The major limitation of the Koenigs-Knorr method is the requirement of at least equimolar amounts of a heavy metal salt promoter.\textsuperscript{46} Additionally, the nature of the leaving group at the anomeric position is an important factor affecting the outcome of the glycosylation.\textsuperscript{4} Depending on the nature and complexity of the oligosaccharide, Koenigs-Knorr activation conditions may not be ideal. It was therefore of interest to investigate the compatibility of the borinic acid catalyst with a wider range of donors and activation conditions. Preliminary studies were carried out with thiophenyl and trichloroacetimidate donors \textbf{106} and \textbf{56}, respectively. Reaction with the thiophenyl donor under both NIS/TMSOTf and NIS/AgOTf activation conditions resulted in complex product mixtures and/or decomposition products by TLC analysis (\textbf{Scheme 2.19}). Reactions with the trichloroacetimidate donor were carried out under either BF\textsubscript{3}•OEt\textsubscript{2} or TMSOTf activation at various temperatures, as summarized in \textbf{Table 2.16}. Reactions were monitored every hour for two hours and then left at room temperature overnight when TLC analysis indicated minimal reaction progression. Based on TLC analysis, the reaction under TMSOTf activation appeared most promising when compared by TLC to the previously isolated disaccharide \textbf{63}. Remaining starting material indicated that the reaction had not gone to completion and the use of stoichiometric rather than catalytic TMSOTf could improve results. The reactions with BF\textsubscript{3}•OEt\textsubscript{2} showed mostly starting material and may also have been improved by using stoichiometric promoter.

\textbf{Scheme 2.19 Borinic acid-catalyzed glycosylation with a thiophenyl donor.}

\textbf{Promoter:} NIS (1.3 equiv.)/TMSOTf (0.5 equiv.)
\textbf{NIS} (1.15 equiv.)/AgOTf (1.1 equiv.)

Table 2.16 Borinic acid-catalyzed glycosylation with a trichloroacetimidate donor.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Promoter</th>
<th>Temp (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BF₃ OEt₂</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>BF₃ OEt₂</td>
<td>-40</td>
</tr>
<tr>
<td>3</td>
<td>BF₃ OEt₂</td>
<td>-78</td>
</tr>
<tr>
<td>4</td>
<td>TMSOTf</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>TMSOTf</td>
<td>-40</td>
</tr>
<tr>
<td>6</td>
<td>TMSOTf</td>
<td>-78</td>
</tr>
</tbody>
</table>

2.9 Glycosylation Scope

The scope of the borinic acid-catalyzed glycosylation with various acceptors and donors is summarized in Table 2.17 and Table 2.18, respectively. Yields of the borinic acid-catalyzed glycosylations and the range of acceptors and donors that can be applied are superior to what has been achieved with organotin- and boronic acid-mediated approaches. ¹⁹,²⁰,²¹,²²,²³ Further examples expanding on the scope of the glycosyl donors were demonstrated by Doris Lee.⁴⁷

Table 2.17 Scope of glycosyl acceptors in the borinic acid-catalyzed glycosylation.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Acceptor</th>
<th>Product</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Structure 1" /></td>
<td><img src="image2" alt="Structure 2" /></td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Structure 3" /></td>
<td><img src="image4" alt="Structure 4" /></td>
<td>56</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Structure 5" /></td>
<td><img src="image6" alt="Structure 6" /></td>
<td>94</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="Structure 7" /></td>
<td><img src="image8" alt="Structure 8" /></td>
<td>74</td>
</tr>
<tr>
<td>5</td>
<td><img src="image9" alt="Structure 9" /></td>
<td><img src="image10" alt="Structure 10" /></td>
<td>73&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td><img src="image11" alt="Structure 11" /></td>
<td><img src="image12" alt="Structure 12" /></td>
<td>89</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(10:1 mixture of regioisomers)</td>
</tr>
<tr>
<td>7</td>
<td><img src="image13" alt="Structure 13" /></td>
<td><img src="image14" alt="Structure 14" /></td>
<td>57</td>
</tr>
<tr>
<td>8</td>
<td><img src="image15" alt="Structure 15" /></td>
<td><img src="image16" alt="Structure 16" /></td>
<td>50</td>
</tr>
<tr>
<td>9</td>
<td><img src="image17" alt="Structure 17" /></td>
<td><img src="image18" alt="Structure 18" /></td>
<td>72</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(10:1 mixture of regioisomers)</td>
</tr>
<tr>
<td>10</td>
<td><img src="image19" alt="Structure 19" /></td>
<td><img src="image20" alt="Structure 20" /></td>
<td>76</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2:1 mixture of regioisomers)</td>
</tr>
<tr>
<td>11</td>
<td><img src="image21" alt="Structure 21" /></td>
<td><img src="image22" alt="Structure 22" /></td>
<td>72</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yield.
<sup>b</sup> Reaction run at 60 °C.
Table 2.18 Scope of glycosyl donors in the borinic acid-catalyzed glycosylation.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Donor</th>
<th>Product</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Donor Image" /></td>
<td><img src="image2.png" alt="Product Image" /></td>
<td>78</td>
</tr>
<tr>
<td>2&lt;sup&gt;b&lt;/sup&gt;</td>
<td><img src="image3.png" alt="Donor Image" /></td>
<td><img src="image4.png" alt="Product Image" /></td>
<td>41</td>
</tr>
<tr>
<td>3&lt;sup&gt;b&lt;/sup&gt;</td>
<td><img src="image5.png" alt="Donor Image" /></td>
<td><img src="image6.png" alt="Product Image" /></td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7.png" alt="Donor Image" /></td>
<td><img src="image8.png" alt="Product Image" /></td>
<td>61</td>
</tr>
<tr>
<td>5</td>
<td><img src="image9.png" alt="Donor Image" /></td>
<td><img src="image10.png" alt="Product Image" /></td>
<td>88</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yield.

<sup>b</sup> R = 4-nitrobenzoyl.
3 Conclusions

What is known about the interactions of organoboron compounds with diols, specifically from the chemical sensing literature, has been applied to the development of novel reactivity. A small molecule borinic acid has been used as a catalyst to activate diol moieties in carbohydrate derivatives through formation of a nucleophilic borinate ester. As an extension of previous work in the Taylor group on the borinic acid-catalyzed regioselective acylation of carbohydrate derivatives, a regioselective glycosylation protocol has been developed. Using glycosyl halide donors and Koenigs-Knorr type activation conditions, a range of di- and tri-saccharides having 1,2-trans glycosidic linkages can be accessed in good to excellent yields and with high regioselectivity for the equatorial OH of the cis diol moiety. This represents the first example of a small molecule catalyst for regioselective glycosylation. Preliminary work has been carried out in an attempt to access 1,2-cis glycosidic linkages using Lemieux conditions, and to extend the catalytic method to other classes of glycosyl donors and activation conditions. Efforts in these areas have not yet been successful, however with further optimization and catalyst development it is hopeful that this catalytic method for regioselective glycosylation can be made more general. Changing the regioselectivity of the glycosylation to target new linkages is another goal that will be explored through the design and development of novel catalysts.
4 Experimental

4.1 General Experimental Procedures

**General Procedure A: TBS-Protection of Primary Hydroxy Group**

The glycoside substrate (1.0 equiv.) and *tert*-butyldimethylsilyl chloride (1.2 equiv.) were dissolved in pyridine (0.7 M). The flask was capped with a septum and stirred at room temperature for 16 hours. The resulting mixture was poured into saturated aqueous NaHCO₃ and extracted several times with dichloromethane. The combined organic layers were dried over MgSO₄, filtered, and concentrated *in vacuo*. Toluene was added and the solution was concentrated *in vacuo* to azeotrope pyridine. The resulting crude material was purified by silica gel chromatography.

**General Procedure B: TBS-Deprotection**

An 80% aqueous acetic acid solution (0.042 M) was added to a stirred solution of TBS-protected disaccharide (1.0 equiv.) in acetonitrile (0.084 M). The solution was stirred at 40 ºC for 18 hours, cooled to room temperature then diluted in ethyl acetate an washed twice with brine. The organic layer was dried over MgSO₄, filtered, and concentrated *in vacuo*. The resulting crude material was purified by silica gel chromatography.

**General Procedure C: Preparation of *p*-Toluenesulfonyl-hydrazides.**

To a round-bottom flask were added *N*-acetyl-D-glycosamine (1.0 equiv.) and *p*-toluenesulfonyl hydrazide (1.3 equiv.). The flask was purged with argon and DMF (1.13 M) and water (4.52 M) were added. Glacial acetic acid (0.1 equiv.) was added dropwise while stirring. The reaction was stirred at 37 ºC for 24 hours, then poured into diethyl ether (0.03 M) and stirred for 1–2 hours. The precipitate was filtered and washed with ether and DCM to yield the desired product.

**General Procedure D: Bromination**

To the corresponding peracetylated sugar was added 33% HBr in AcOH (0.427 M), under an argon atmosphere. The reaction was stirred at room temperature for 1 hour, diluted with dichloromethane and extracted with ice water to pH neutral. The organic layer was dried over
MgSO₄, filtered, and concentrated in vacuo. The resulting crude material was purified by passing through a short plug of silica.

**General Procedure E: 4-Nitrobenzoyl Protection of Pyranose Sugars.**

To a solution of the corresponding methyl pyranose (1.0 equiv.) in pyridine (0.4 M), was added 4-nitrobenzoyl chloride (5.0 equiv.). The mixture was stirred at 60 °C for 20 hours, diluted in dichloromethane and washed twice with water and brine. The organic layer was dried over MgSO₄, filtered, and concentrated in vacuo. Toluene was added and the solution was concentrated in vacuo to azeotrope pyridine. The resulting crude material was purified by silica gel chromatography.

**General Procedure F: Borinic Acid-Catalyzed Glycosylation**

Donor sugar (1.0 equiv.), acceptor sugar (1.1 equiv.), silver (I) oxide (1.0 equiv.) and 2-aminoethyl diphenylborinate (10 mol %) were added to an oven-dried round bottom flask, under an argon atmosphere. Dry acetonitrile (0.13 M) was added and the resulting mixture was stirred at room temperature (unless otherwise noted). After 16 hours, the reaction was quenched with a few drops of methanol, diluted with dichloromethane and filtered through a plug of Celite®. The resulting crude material was purified by silica gel chromatography.

### 4.2 Characterization Data

**Methyl-6-O-tert-butyldimethylsilyl-α-D-mannopyranose (33).** Synthesized according to general procedure A, from methyl-α-D-mannopyranoside (5.0 mmol), 85% yield, white solid. ¹H NMR (400 MHz, CDCl₃): δ 4.72 (d, J = 1.5 Hz, 1H, H-1), 3.94–3.76 (m, 5H, H-6a, H-6b, H-2, H-3 and H-4), 3.60 (ddd, J = 11.6, 6.4, 4.8 Hz, 1H, H-5), 3.38 (s, 3H, OCH₃), 3.29 (d, J = 1.5 Hz, 1H, C₄-OH), 2.66 (d, J = 4.8 Hz, 1H, C₃-OH), 2.39 (d, J = 4.3 Hz, 1H, C₂-OH), 0.91 (s, 9H,
Si(C(CH₃)₃)(CH₃)₂, 0.11 (s, 3H, Si(C(CH₃)₃)(CH₃)₂), 0.11 (s, 3H, Si(C(CH₃)₃)(CH₃)₂). **Rf:** 0.30 (ethyl acetate/pentanes 7:3).

Methyl-6-O-tert-butyldimethylsilyl-β-D-galactopyranose (34). Synthesized according to general procedure A, from methyl-β-D-galactopyranoside (2.45 mmol), 92% yield, transparent viscous oil. **¹H NMR (400 MHz, CDCl₃):** δ 4.16 (d, J = 7.5 Hz, 1H, H-1), 4.05 (dd, J = 3.4, 3.4, 0.8 Hz, 1H, H-4), 3.94 (dd, J = 10.5, 6.0 Hz, 1H, H-6a), 3.88 (dd, J = 10.5, 5.0 Hz, 1H, H-6b), 3.64 (dd, J = 9.5, 7.5, 2.0 Hz, 1H, H-2), 3.60–3.56 (m, 1H, H-3), 3.55 (s, 3H, OCH₃), 3.49 (dd, J = 6.0, 5.0, 0.8 Hz, 1H, H-5), 2.87 (d, J = 3.6 Hz, 1H, C₄-OH), 2.68 (d, J = 6.2 Hz, 1H, C₃-OH), 2.52 (d, J = 2.1 Hz, 1H, C₂-OH), 0.90 (s, 9H, Si(C(CH₃)₃)(CH₃)₂), 0.10 (s, 3H, Si(C(CH₃)₃)(CH₃)₂), 0.09 (s, 3H, Si(C(CH₃)₃)(CH₃)₂). **Rf:** 0.20 (ethyl acetate/pentanes 7:3).

Methyl-6-O-tert-butyldimethylsilyl-α-D-galactopyranose (35). Synthesized according to general procedure A, from methyl-α-D-galactopyranoside (5.0 mmol), 21% yield, white fluffy solid. **¹H NMR (400 MHz, CDCl₃):** δ 4.82 (d, J = 3.9 Hz, 1H, H-1), 4.10 (dd, J = 3.2, 0.9 Hz, 1H, H-4), 3.91 (dd, J = 10.6, 5.4 Hz, 1H, H-6a), 3.86 (dd, J = 10.6, 5.0 Hz, 1H, H-6b), 3.84 (dd, J = 9.6, 3.6 Hz, 1H, H-2), 3.76–3.71 (m, 2H, H-3 and H-5), 3.42 (s, 3H, OCH₃), 0.90 (s, 9H, Si(C(CH₃)₃)(CH₃)₂), 0.10 (s, 6H, Si(C(CH₃)₃)(CH₃)₂). **Rf:** 0.15 (ethyl acetate/pentanes 7:3).
Methyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-mannopyranoside  (36).
Synthesized according to general procedure B, from 63 (0.61 mmol), 75% yield, white solid. $^1$H NMR (400MHz, CDCl$_3$): δ 5.23 (dd, $J = 9.6, 9.6$ Hz, 1H, H-3'), 5.05–5.00 (m, 2H, H-4' and H-2'), 4.74 (d, $J = 1.2$ Hz, 1H, H-1'), 4.61 (d, $J = 8.0$ Hz, 1H, H-1'), 4.22 (dd, $J = 12.4, 2.8$ Hz, 1H, H-6a'), 4.14 (dd, $J = 12.4, 6.4$ Hz, 1H, H-6b'), 3.93–3.83 (m, 4H, H-6a, H-6b, H-4 and H-2), 3.79 (ddd, $J = 9.6, 6.4, 2.4$ Hz, 1H, H-5'), 3.72 (dd, $J = 9.2, 3.6$ Hz, 1H, H-3), 3.59–3.55 (m, 2H, H-5 and C$_4$-OH), 3.37 (s, 3H, OCH$_3$), 2.76 (br s, 1H, C$_2$-OH), 2.48 (br s, 1H, C$_6$-OH), 2.08 (s, 3H, OCOCH$_3$), 2.06 (s, 3H, OCOCH$_3$), 2.03 (s, 3H, OCOCH$_3$), 2.01 (s, 3H, OCOCH$_3$). $^{13}$C NMR (100MHz, CDCl$_3$): δ 170.7, 170.2, 169.9, 169.5, 101.6, 100.4, 84.4, 72.3, 72.2, 71.6, 71.6, 71.0, 68.6, 66.3, 62.6, 62.1, 55.0, 20.8, 20.7, 20.7, 20.7. R$_f$: 0.25 (isopropanol/toluene 1:5). IR (Powder, cm$^{-1}$): 2922 (w), 1754 (s), 1369 (w), 1212 (s), 1171 (w), 1130 (m), 1053 (s), 1029 (s), 970 (s), 805 (m). HRMS (ESI, m/z): Calculated for C$_{21}$H$_{32}$O$_{15}$Na ((M+Na$^+$)): 547.1633; Found: 547.1627. m.p.: 68–70 °C.

Methyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-galactopyranoside  (37).
Synthesized according to general procedure B, from 61 (0.1 mmol), 78% yield, white solid. $^1$H NMR (400MHz, CDCl$_3$): δ 5.24 (dd, $J = 9.6, 9.6$ Hz, 1H, H-3'), 5.05 (dd, $J = 10.0, 9.2$ Hz, 1H, H-4'), 5.02 (dd, $J = 9.6, 8.0$ Hz, 1H, H-2'), 4.82 (d, $J = 8.0$ Hz, 1H, H-1'), 4.21 (dd, $J = 12.4, 4.8$ Hz, 1H, H-6a'), 4.18 (d, $J = 8.0$ Hz, 1H, H-1'), 4.17 (dd, $J = 12.4, 3.2$ Hz, 1H, H-6b'), 4.03 (m, 1H, H-4), 3.97 (ddd, $J = 11.2, 6.8, 4.0$ Hz, 1H, H-6a), 3.83 (ddd, $J = 12.0, 7.7, 4.6$ Hz, 1H, H-6b), 3.77–3.71 (m, 2H, H-2 and H-5'), 3.59 (dd, $J = 9.5, 3.4$ Hz, 1H, H-3), 3.56 (s, 3H, OCH$_3$), 3.56–3.54 (m, 1H, H-5), 2.75 (br s, 1H, C$_4$-OH), 2.51 (d, $J = 2.5$ Hz, 1H, C$_2$-OH), 2.39–2.35 (m, 1H, C$_6$-OH), 2.08 (s, 3H, OCOCH$_3$), 2.04 (s, 3H, OCOCH$_3$), 2.03 (s, 3H, OCOCH$_3$), 2.01 (s, 3H, OCOCH$_3$). $^{13}$C NMR (100MHz, CDCl$_3$): δ 170.8, 170.3, 170.0, 169.5, 104.0, 101.6, 82.6, 74.2, 72.4, 72.1, 71.5, 70.5, 68.7, 68.5, 62.4, 61.9, 57.2, 20.8, 20.8, 20.7, 20.7. R$_f$: 0.10
(isopropanol/toluene 1:5). **IR (Powder, cm⁻¹):** 1747 (s), 1221 (m), 1203 (s), 1113 (w), 1036 (s), 787 (m). **HRMS (ESI, m/z):** Calculated for C₂₁H₃₂O₁₅Na ((M+Na)⁺): 547.1633; Found: 547.1638. **m.p.:** 174–175 °C.

**Isopropyl-6-O-tert-butyldimethylsilyl-β-D-thiogalactopyranoside (39).** Synthesized according to general procedure A, from isopropyl-α-D-thiogalactopyranoside (4.0 mmol), 58% yield, transparent sticky solid. **1H NMR (400 MHz, CDCl₃):** δ 4.37 (d, J = 9.5 Hz, 1H, H-1), 4.09 (dd, J = 3.2, 3.2 Hz, 1H, H-4), 3.90 (dd, J = 10.5, 6.0 Hz, 1H, H-6a), 3.85 (dd, J = 10.5, 5.0 Hz, 1H, H-6b), 3.65 (ddd, J = 9.2, 8.8, 1.8 Hz, 1H, H-2), 3.58 (ddd, J = 9.0, 5.9, 3.2 Hz, 1H, H-3), 3.52 (ddd, J = 6.0, 5.2, 0.8 Hz, 1H, H-5), 3.21 (septet, J = 6.8 Hz, 1H, SCH(CH₃)₂), 2.88 (d, J = 3.7 Hz, 1H, C₂-OH), 2.76 (d, J = 6.0 Hz, 1H, C₃-OH), 2.50 (d, J = 1.7 Hz, 1H, C₂-OH), 1.35 (d, J = 3.0 Hz, 3H, SCH(CH₃)₂), 1.33 (d, J = 2.9 Hz, 3H, SCH(CH₃)₂), 0.89 (s, 9H, Si(C(CH₃)₃)(CH₃)₂), 0.09 (s, 3H, Si(C(CH₃)₃)(CH₃)₂), 0.08 (s, 3H, Si(C(CH₃)₃)(CH₃)₂). **Rf:** 0.20 (isopropanol/toluene 1:9).

**6-O-tert-butyldimethylsilyl-β-D-galactopyranosyl isopropylthiosulfoxide (40).** To a solution of 39 (1.09 mmol, 0.37 g) in dry dichloromethane (50 mL) at 0 ºC was added mCPBA (77% pure, 1.42 mmol, 0.25 g), dropwise as a solution in dichloromethane (5 mL). The solution was stirred at 0 ºC for 1 hour, quenched with saturated aqueous NaHCO₃ (2.4 mL) and washed with brine. The organic layer was dried over MgSO₄, filtered, and concentrated in vacuo. The resulting crude material was purified by silica gel chromatography to afford 40 as a white solid in 61% yield. **1H NMR (400 MHz, CDCl₃):** (both isomers) δ 5.52 (d, J = 5.1 Hz, 1H), 4.84 (d, J = 8.2 Hz, 1H), 4.53 (d, J = 2.3 Hz, 1H), 4.37–4.30 (m, 3H), 4.11 (d, J = 9.4 Hz, 1H), 4.06 (apparent t, J = 2.7 Hz, 1H), 4.02 (d, J = 9.7 Hz, 1H), 3.93 (dd, J = 8.0, 3.2 Hz, 1H), 3.86–3.82
(m, 3H), 3.71–3.55 (m, 4H), 3.50 (quintet, $J = 6.9$ Hz, 1H), 3.36 (d, $J = 2.1$ Hz, 1H), 3.18 (quintet, $J = 6.9$ Hz, 1H), 1.89 (s, 1H), 1.41 (d, $J = 7.0$ Hz, 3H), 1.35 (d, $J = 6.8$ Hz, 3H), 1.33 (d, $J = 7.2$ Hz, 3H), 1.15 (d, $J = 6.8$ Hz, 3H), 0.88 (s, 18H), 0.06 (s, 6H), 0.05 (s, 6H). $R_f$: 0.35 (isopropanol/toluene 1:4).

$N'$(2-acetamido-2-deoxy-$\beta$-D-glucopyranosyl)-$p$-toluenesulfonyl-hydrazide (41). Synthesized according to general procedure C, from $N$-acetyl-D-glucosamine (11.3 mmol), 18% yield, white solid. $^1$H NMR (400 MHz, CD$_3$OD): $\delta$ 7.72 (d, $J = 8.3$ Hz, 2H, Ar-H), 7.38 (d, $J = 8.0$ Hz, 2H, Ar-H), 3.93 (d, $J = 9.6$ Hz, 1H, $H$-1), 3.88 (dd, $J = 11.6$, 1.5 Hz, 1H, $H$-6a), 3.62–3.57 (m, 1H, $H$-6b), 3.45 (dd, $J = 9.6$, 9.6 Hz, 1H, $H$-2), 3.41–3.36 (m, 1H, $H$-3), 3.19–3.17 (m, 2H, $H$-4 and $H$-5), 2.43 (s, 3H, Ar-CH$_3$), 2.01 (s, 3H, NCOCH$_3$).

Methyl-2-acetamido-2-deoxy-$\beta$-D-glucopyranoside (42). To a solution of 41 (2.03 mmol, 0.79 g) in anhydrous DMF (8 mL) and methanol (3.3 mL) was added $N$-bromosuccinimide (4.87 mmol, 0.87 g), dropwise as a solution in anhydrous DMF (8 mL). The reaction was stirred at room temperature for 1 hour, cooling periodically in an ice bath. Basic amberlite resin activated with methanol was added and the solution stirred for 2 hours. The resin was filtered off and the solution concentrated under vacuum. A stream of air was blown over the flask overnight to remove DMF and the resulting crude material was purified by silica gel chromatography to yield 42 as a white solid in 47% yield. $^1$H NMR (400 MHz, CD$_3$OD): $\delta$ 4.31 (d, $J = 8.4$ Hz, 1H, $H$-1), 3.89 (dd, $J = 11.9$, 2.2 Hz, 1H, $H$-6a), 3.69 (dd, $J = 11.9$, 5.6 Hz, 1H, $H$-6b), 3.64 (dd, $J = 10.2$, 8.5 Hz, 1H, $H$-2), 3.46 (s, 3H, OCH$_3$), 3.43 (dd, $J = 10.2$, 8.4 Hz, 1H, $H$-3), 3.29-3.24 (m, 2H, $H$-4 and $H$-5), 1.98 (s, 3H, NCOCH$_3$). $R_f$: 0.45 (isopropanol/toluene 1:1).
$N^\prime$-(2-acetamido-2-deoxy-$\beta$-D-galactopyranosyl)-$p$-toluenesulfono-hydrazide  \((43)\).

Synthesized according to general procedure C, from $N$-acetyl-D-galactosamine (11.3 mmol), 99% yield, white solid. \(^1\)H NMR \((400\) MHz, CD$_3$OD): $\delta$ 7.72 (d, $J = 8.3$ Hz, 2H, Ar-H), 7.38 (d, $J = 8.0$ Hz, 2H, Ar-H), 3.90 (d, $J = 9.6$ Hz, 1H, H-1), 3.78–3.64 (m, 4H, H-6a, H-6b, H-2 and H-4), 3.54 (dd, $J = 10.5$, 3.2 Hz, 1H, H-3), 3.42 (ddd, $J = 7.6$, 4.6, 0.8 Hz, 1H, H-5), 2.43 (s, 3H, Ar-CH$_3$), 2.01 (s, 3H, NCOCH$_3$).

2,3,4-Tri-O-acetyl-$\alpha$-L-fucopyranosyl bromide  \((46)\). Synthesized according to general procedure D, from 1,2,3,4-tetra-O-acetyl-D-fucopyranose (1.5 mmol), 92% yield, white solid. \(^1\)H NMR \((400\) MHz, CDCl$_3$): $\delta$ 6.69 (d, $J = 3.9$ Hz, 1H, H-1), 5.41 (dd, $J = 10.6$, 3.2 Hz, 1H, H-3), 5.36 (d, $J = 3.3$ Hz, 1H, H-4), 5.02 (dd, $J = 10.6$, 3.9 Hz, 1H, H-2), 4.40 (q, $J = 6.5$ Hz, 1H, H-5), 2.17 (s, 3H, OCOCH$_3$), 2.10 (s, 3H, OCOCH$_3$), 2.01 (s, 3H, OCOCH$_3$), 1.21 (d, $J = 6.5$ Hz, 3H, CH$_3$). \(R_f\): 0.30 (isopropanol/toluene 3:17).

Methyl-(2,3,4-tri-O-para-nitrobenzoyl)-$\beta$-D-arabinopyranose  \((47)\). Synthesized according to general procedure E, from 91 (1.0 mmol), 93% yield, pale yellow solid. \(^1\)H NMR \((400\) MHz, CDCl$_3$): $\delta$ 8.37–8.34 (m, 2H, OCHPh), 8.27–8.23 (m, 4H, OCHPh), 8.18–8.13 (m, 4H, OCHPh), 8.00–7.96 (m, 2H, OCHPh), 5.96 (dd, $J = 10.7$, 3.6 Hz, 1H, H-3), 5.83–5.82 (m, 1H, H-4), 5.73 (dd, $J = 10.6$, 3.4 Hz, 1H, H-2), 5.24 (d, $J = 3.6$ Hz, 1H, H-1), 4.22 (dd, $J = 13.4$, 1.0 Hz, 1H, H-5).
Hz, 1H, H-5a), 3.99 (dd, J = 13.2, 2.0 Hz, 1H, H-5b), 3.52 (s, 3H, OCH₃). ¹³C NMR (100MHz, CDCl₃): δ 164.2, 164.1, 163.8, 151.1, 151.0, 150.9, 134.6, 134.3, 134.3, 131.1, 131.1, 130.8, 124.0, 123.8, 123.8, 97.7, 71.0, 69.9, 69.0, 60.4, 56.0. Rf: 0.3 (ethyl acetate/toluene 1:9). IR (Powder, cm⁻¹): 1726 (s), 1607 (m), 1523 (s), 1410 (w), 1347 (m), 1320 (w), 1257 (s), 1197 (w), 1094 (s), 1071 (s), 1014 (m), 1000 (m), 909 (w), 871 (m), 844 (m), 782 (m), 715 (s).

**Methyl-(2,3,4-tri-O-para-nitrobenzoyl)-α-L-fucopyranose (48).** Synthesized according to general procedure E, from 78 (1.5 mmol), quantitative yield, pale yellow solid. ¹H NMR (400MHz, CDCl₃): δ 8.38−8.35 (m, 2H, OCHPh), 8.28−8.22 (m, 4H, OCHPh), 8.17−8.12 (m, 4H, OCHPh), 7.96−7.93 (m, 2H, OCHPh), 5.97 (dd, J = 10.7, 3.4 Hz, 1H, H-3), 5.78 (dd, J = 3.4, 1.1 Hz, 1H, H-4), 5.67 (dd, J = 10.7, 3.6 Hz, 1H, H-2), 5.22 (d, J = 3.6 Hz, 1H, H-1), 4.44 (q, J = 6.9 Hz, 1H, H-5), 3.51 (s, 3H, OCH₃), 1.32 (d, J = 6.6 Hz, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 164.4, 164.3, 163.8, 151.2, 151.0, 150.9, 134.4, 134.4, 134.4, 131.1, 131.1, 130.8, 124.1, 123.8, 123.8, 97.4, 73.0, 69.9, 69.8, 64.7, 56.0, 16.2. Rf: 0.3 (ethyl acetate/toluene 1:9). IR (Powder, cm⁻¹): 2942 (w), 1727 (s), 1607 (w), 1524 (s), 1410 (w), 1346 (m), 1259 (s), 1096 (s), 870 (m), 782 (m), 715 (s).

**2,3,4-Tri-O-para-nitrobenzoyl-β-D-arabinopyranosyl bromide (49).** To a solution of 47 (0.65 mmol, 0.40 g) in dichloromethane (1.0 mL), was added hydrogen bromide (33% solution in acetic acid, 1.5 mL) and glacial acetic acid (1.5 mL). The mixture was stirred for 1 hour at 45
°C then reduced to 35 °C for another 18 hours. The crude mixture was cooled to room temperature, diluted in dichloromethane and washed twice with ice-cold water to pH neutral. The organic layer was dried over MgSO₄, filtered, and concentrated in vacuo. The resulting crude material was purified over a plug of silica (10 cm) to yield 49 as a yellow solid in 38% yield. **¹H NMR (400MHz, CDCl₃):** δ 8.38–8.35 (m, 2H, OCHPh), 8.29–8.23 (m, 4H, OCHPh), 8.20–8.16 (m, 4H, OCHPh), 8.02–7.98 (m, 2H, OCHPh), 6.90 (d, J = 3.6 Hz, 1H, H-1), 6.02 (dd, J = 10.4, 3.6 Hz, 1H, H-3), 5.91–5.90 (m, 1H, H-4), 5.72 (dd, J = 10.4, 3.6 Hz, 1H, H-2), 4.53 (d, J = 13.2 Hz, 1H, H-5a), 4.26 (dd, J = 13.6, 2.0 Hz, 1H, H-5b). **¹³C NMR (100MHz, CDCl₃):** δ 163.9, 163.8, 163.6, 151.3, 151.3, 151.0, 134.2, 133.9, 133.6, 131.3, 131.1, 130.9, 124.1, 124.0, 123.9, 88.5, 69.7, 69.6, 69.0, 64.9. **Rf:** 0.3 (ethyl acetate/pentanes 1:4). **IR (Powder, cm⁻¹):** 3113 (w), 2922 (w), 1729 (s), 1608 (m), 1523 (s), 1410 (w), 1347 (m), 1320 (w), 1254 (s), 1089 (m), 1014 (m), 870 (m), 844 (m), 818 (w), 781 (m), 715 (s).

2,3,4-Tri-O-para-nitrobenzoyl-α-L-fucopyranosyl bromide (50). To a solution of 48 (0.80 mmol, 0.50 g) in dichloromethane (5.7 mL), was added hydrogen bromide (33% solution in acetic acid, 1.9 mL). The mixture was stirred for 24 hours at 35 °C. The crude mixture was cooled to room temperature, diluted in dichloromethane and washed twice with ice-cold water to pH neutral. The organic layer was dried over MgSO₄, filtered, and concentrated in vacuo. The resulting crude material was purified over a plug of silica (10 cm) to yield 50 as a yellow solid in 14% yield. **¹H NMR (400MHz, CDCl₃):** δ 8.39–8.36 (m, 2H, OCHPh), 8.28–8.23 (m, 4H, OCHPh), 7.98–7.94 (m, 2H, OCHPh), 6.89 (d, J = 4.0 Hz, 1H, H-1), 6.02 (dd, J = 10.5, 3.3 Hz, 1H, H-3), 5.86 (dd, J = 3.2, 1.1 Hz, 1H, H-4), 5.64 (dd, J = 10.5, 4.0 Hz, 1H, H-2), 4.73 (q, J = 6.6 Hz, 1H, H-5), 1.39 (d, J = 6.5 Hz, 3H, CH₃). **¹³C NMR (100 MHz, CDCl₃):** δ 164.2, 163.8, 163.7, 151.3, 151.2, 151.0, 134.0, 134.0, 133.7, 131.3, 131.1, 130.8, 124.2, 124.0, 123.8, 88.1, 71.8, 70.4, 70.4, 69.0, 15.9. **Rf:** 0.7 (ethyl acetate/pentanes 1:5).
IR (Powder, cm$^{-1}$): 2865 (w), 1730 (s), 1608 (w), 1524 (s), 1411 (w), 1346 (m), 1257 (s), 1090 (s), 1013 (m), 870 (m), 845 (m), 715 (s).

2,3,4,6-Tetra-O-acetyl-α-D-mannopyranosyl bromide (52). Synthesized according to general procedure D, from 1,2,3,4,6-penta-O-acetyl-α-D-mannopyranose (0.85 mmol), 75% yield, white solid. $^1$H NMR (400 MHz, CDCl$_3$): δ 6.29 (br s, 1H, H-1), 5.72 (dd, $J = 10.3$, 3.2 Hz, 1H, H-3), 5.45 (br s, 1H, H-2), 5.37 (dd, $J = 10.2$, 10.2 Hz, 1H, H-4), 4.33 (dd, $J = 12.6$, 4.9 Hz, 1H, H-6a), 4.24–4.20 (m, 1H, H-5), 4.15–4.09 (m, 1H, H-6b), 2.17 (s, 3H, OCOCH$_3$), 2.10 (s, 3H, OCOCH$_3$), 2.07 (s, 3H, OCOCH$_3$), 2.01 (s, 3H, OCOCH$_3$). $R_f$: 0.7 (ethyl acetate/pentanes 1:4).

1,2,3,4,6-Penta-O-pivaloyl-α-D-mannopyranose (53). D-mannose (5.0 mmol, 0.90 g) was dissolved in pyridine (18 mL). Pivaloyl chloride (60.0 mmol, 7.4 mL) was added dropwise at 0 $^\circ$C. The reaction was stirred at reflux for 24 hours then diluted with dichloromethane and washed twice with water. The organic layer was dried over MgSO$_4$, filtered, and concentrated in vacuo. Toluene was added and the solution was concentrated in vacuo to azeotrope pyridine. The resulting crude material was purified by silica gel chromatography to afford 53 as a viscous oil in 99% yield. $^1$H NMR (400 MHz, CDCl$_3$): (major isomer) δ 5.83 (d, $J = 1.1$ Hz, 1H, H-1), 5.47–5.45 (m, 2H, H-4 and H-2), 5.16 (dd, $J = 10.1$, 3.1 Hz, 1H, H-3), 4.21 (dd, $J = 12.4$, 4.1 Hz, 1H, H-6a), 4.19–4.14 (m, 1H, H-6b), 3.84 (ddd, $J = 10.0$, 4.1, 2.1 Hz, 1H, H-5), 1.29 (s, 9H, OCO(CH$_3$)$_3$), 1.22 (s, 9H, OCO(CH$_3$)$_3$), 1.22 (s, 9H, OCO(CH$_3$)$_3$), 1.16 (s, 9H, OCO(CH$_3$)$_3$), 1.15 (s, 9H, OCO(CH$_3$)$_3$), 1.11 (s, 9H, OCO(CH$_3$)$_3$). $R_f$: 0.3 (ethyl acetate/pentanes 1:19).
2,3,4,6-Tetra-O-pivaloyl-\(\alpha\)-D-mannopyranosyl bromide (54). To a solution of 53 (1.88 mmol, 1.13 g) in dry dichloromethane (13.5 mL) was added 33% HBr in AcOH (4.4 mL), dropwise at 0 °C. The reaction was stirred at room temperature for 5 hours and then washed several times with water. The organic layer was dried over MgSO\(_4\), filtered, and concentrated \textit{in vacuo}. The resulting crude material was purified by running through a short plug of silica to afford 54 as a viscous yellow oil in 70% yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 6.26 (d, \(J = 1.5\) Hz, 1H, \(H-1\)), 5.75 (dd, \(J = 10.3, 3.2\) Hz, 1H, \(H-3\)), 5.58 (dd, \(J = 10.2, 10.2\) Hz, 1H, \(H-4\)), 5.46 (dd, \(J = 3.2, 1.6\) Hz, 1H, \(H-2\)), 4.29--4.14 (m, 3H, \(H-6a, H-6b\) and \(H-5\)), 1.27 (s, 9H, OCOC(CH\(_3\))\(_3\)), 1.23 (s, 9H, OCOC(CH\(_3\))\(_3\)), 1.18 (s, 9H, OCOC(CH\(_3\))\(_3\)), 1.13 (s, 9H, OCOC(CH\(_3\))\(_3\)). \(R\_f\): 0.45 (ethyl acetate/toluene 1:19).

2,3,4,6-Tetra-O-acetyl-\(\alpha\)-D-glucose (55). In a round-bottom flask were combined 1,2,3,4,6-penta-O-acetyl-\(\alpha\)-D-glucopyranose (5.0 mmol, 1.95 g) and imidazole (5.0 mmol, 0.34 g). The flask was purged with argon and dry methanol (25 mL) was added. The reaction was stirred at 40 °C for 24 hours, following which it was concentrated in vacuo and partitioned between ethyl acetate and water. The organic layer was washed with 1 N HCl and then dried over MgSO\(_4\), filtered, and concentrated \textit{in vacuo}. The resulting crude material was purified by silica gel chromatography to afford 55 as a colourless oil in 41% yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 5.53 (dd, \(J = 9.8, 9.8\) Hz, 1H, \(H-4\)), 5.47 (d, \(J = 3.3\) Hz, 1H, \(H-1\)), 5.08 (dd, \(J = 9.8, 9.8\) Hz, 1H, \(H-3\)), 4.91 (dd, \(J = 10.2, 3.6\) Hz, 1H, \(H-2\)), 4.29--4.11 (m, 3H, \(H-6a, H-6b\) and \(H-5\)), 2.10 (s, 3H, OCOC\(_2\)H\(_3\)), 2.08 (s, 3H, OCOC\(_2\)H\(_3\)), 2.03 (s, 3H, OCOC\(_2\)H\(_3\)), 2.02 (s, 3H, OCOC\(_2\)H\(_3\)). \(R\_f\): 0.15 (pentanes/ethyl acetate 6:4).
2,3,4,6-Tetra-O-acetyl-α-D-glucopyranosyl trichloroacetimidate (56). Into an oven-dried, round-bottom flask was added 55 (2.0 mmol, 0.70 g). The flask was purged with argon and dry dichloromethane (14 mL) was added, followed by trichloroacetonitrile (15.0 mmol, 1.5 mL) at 0 °C. The solution was stirred at 0 ºC for 1 hour and then DBU (0.4 mmol, 60 µL) was added. The reaction was stirred at room temperature for 1 hour, concentrated, and purified through a short plug of silica to afford 56 as a viscous yellow oil in 81% yield. 

1H NMR (400 MHz, CDCl₃): δ 8.69 (s, 1H, NH), 6.56 (d, J = 3.7 Hz, 1H, H-1), 5.56 (dd, J = 9.8, 9.8 Hz, 1H, H-4), 5.18 (dd, J = 9.9, 9.9 Hz, 1H, H-3), 5.13 (dd, J = 10.2, 3.7 Hz, 1H, H-2), 4.28 (dd, J = 12.3, 4.1 Hz, 1H, H-6a), 4.21 (ddd, J = 10.2, 4.1, 2.0 Hz, 1H, H-5), 4.13 (dd, J = 12.4, 2.0 Hz, 1H, H-6b), 2.08 (s, 3H, OCOCCH₃), 2.05 (s, 3H, OCOCCH₃), 2.03 (s, 3H, OCOCCH₃), 2.02 (s, 3H, OCOCCH₃). Rf: 0.60 (ethyl acetate/pentanes, 1:1).

Methyl-6-O-tert-butyldimethylsilyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-galactopyranoside (61). Synthesized according to general procedure F, from 57 (1.0 mmol) and 34, 94% yield, white solid. 1H NMR (400 MHz, CDCl₃): δ 5.25 (dd, J = 9.2, 9.2 Hz, 1H, H-3'), 5.09 (dd, J = 9.6, 9.6 Hz, 1H, H-4'), 5.04 (dd, J = 10.0, 8.0 Hz, 1H, H-2'), 4.88 (d, J = 8.0 Hz, 1H, H-1'), 4.25 (dd, J = 12.4, 4.4 Hz, 1H, H-6a'), 4.15 (d, J = 7.6 Hz, 1H, H-1'), 4.12 (dd, J = 12.4, 2.4 Hz, 1H, H-6b'), 4.03 (dd, J = 2.4, 2.4 Hz, 1H, H-4), 3.92 (dd, J = 10.0, 6.4 Hz, 1H, H-6a), 3.82 (dd, J = 10.0, 5.6 Hz, 1H, H-6b), 3.75 (ddd, J = 9.6, 8.0, 2.4 Hz, 1H, H-2), 3.71 (ddd, J = 6.8, 4.4, 2.4 Hz, 1H, H-5'), 3.60 (dd, J = 9.2, 3.2 Hz, 1H, H-3), 3.54 (s, 3H, OCH₃), 3.49 (dd, J = 6.4, 5.6 Hz, 1H, H-5), 2.54 (dd, J = 2.4, 1.6 Hz, 1H, C₆-OH), 2.33 (d, J = 2.4 Hz, 1H, C₂-OH), 2.09 (s, 3H, OCOCH₃), 2.04 (s, 3H, OCOCH₃), 2.03 (s, 3H, OCOCH₃), 2.02 (s, 3H, OCOCH₃), 0.89 (s, 9H, Si(C(CH₃)₃)(CH₃)₂), 0.08 (s, 6H, Si(C(CH₃)₃)(CH₃)₂). 13C NMR (100 MHz, CDCl₃): δ 170.8, 170.4, 169.9, 169.5, 103.8, 101.4, 82.5, 74.8, 72.5, 72.1, 71.5, 70.9, 68.4, 67.8,
Methyl-6-O-tert-butyldimethylsilyl-2-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-galactopyranoside (62). To an oven-dried 2-dram vial under an argon atmosphere were added 57 (0.30 mmol, 0.12 g), 34 (0.20 mmol, 0.059 g), silver (I) oxide (0.22 mmol, 0.051 g) and 2-aminoethyl diphenylborinate (0.02 mmol, 4.5 mg). Dry acetonitrile (1.5 mL) was added and the resulting mixture was stirred at room temperature. After 16 hours, the reaction was quenched with a few drops of methanol, diluted with dichloromethane and filtered through a plug of Celite®. The resulting crude material was purified by silica gel chromatography to afford 62 as a white solid in 15% yield.

**1H NMR (400 MHz, CDCl₃)**: δ 5.30 (dd, J = 9.4, 9.4 Hz, 1H, H-3''), 5.18−5.07 (m, 3H, H-3', H-4' and H-4''), 4.97−4.86 (m, 4H, H-2'', H-2', H-1'' and H-1'), 4.32 (d, J = 7.6 Hz, 1H, H-1), 4.28 (dd, J = 12.2, 4.6 Hz, 1H, H-6a''), 4.24 (dd, J = 12.4, 4.8 Hz, 1H, H-6b''), 4.13 (dd, J = 12.3, 2.3, 2H, H-6a' and H-6b'), 3.98 (br s, 1H, H-4), 3.94−3.78 (m, 4H, H-6a, H-6b, H-3 and H-2), 3.75−3.68 (m, 2H, H-5'' and H-5'), 3.50 (s, 3H, OCH₃), 3.43 (dd, J = 6.2, 6.2 Hz, 1H, H-5), 2.70 (br s, 1H, C₄-OH), 2.11 (s, 3H, OCOCH₃), 2.09 (s, 3H, OCOCH₃), 2.08 (s, 3H, OCOCH₃), 2.07 (s, 3H, OCOCH₃), 2.03 (s, 3H, OCOCH₃), 2.01 (s, 3H, OCOCH₃), 2.00 (s, 3H, OCOCH₃), 1.99 (s, 3H, OCOCH₃). **Rₛ**: 0.25 (isopropanol/toluene 1:9).
Methyl-6-O-tert-butyldimethylsilyl-3-O-(2',3',4',6'-tetra-O-acetyl-\(\beta\)-D-glucopyranosyl)-\(\alpha\)-D-mannopyranoside (63). Synthesized according to general procedure F, from 57 (1.0 mmol) and 33, 99% yield, white solid. \(\textsuperscript{1}H\) NMR (400 MHz, CDCl\(_3\)): \(\delta\) 5.23 (dd, \(J = 9.6, 9.6\) Hz, 1H, \(H-3')\), 5.06–5.01 (m, 2H, \(H-4'\) and \(H-2')\), 4.73 (d, \(J = 1.6\) Hz, 1H, \(H-1')\), 4.61 (d, \(J = 8.0\) Hz, 1H, \(H-1'\)), 4.21 (dd, \(J = 12.4, 2.4\) Hz, 1H, \(H-6a')\), 4.15 (dd, \(J = 12.4, 6.0\) Hz, 1H, \(H-6b')\), 3.96 (dd, \(J = 11.2, 2.4\) Hz, 1H, \(H-6a\)), 3.83–3.69 (m, 5H, \(H-6b, H-2, H-3, H-5'\) and \(H-4\)), 3.54 (dddd, \(J = 8.8, 6.0, 2.4\) Hz, 1H, \(H-5\)), 3.37 (s, 3H, OCH\(_3\)), 3.36 (d, \(J = 1.6\) Hz, 1H, C\(_4\)-OH), 2.21 (d, \(J = 3.6\) Hz, 1H, C\(_2\)-OH), 2.08 (s, 3H, OCOC\(_3\)), 2.06 (s, 3H, OCOC\(_3\)), 2.03 (s, 3H, OCOC\(_3\)), 2.01 (s, 3H, OCOC\(_3\)), 0.89 (s, 9H, Si(C(CH\(_3\))\(_3\))(CH\(_3\))\(_2\)), 0.07 (s, 6H, Si(C(CH\(_3\))\(_3\))(CH\(_3\))\(_2\)). \(\textsuperscript{13}C\) NMR (100 MHz, CDCl\(_3\)): \(\delta\) 170.7, 170.2, 169.7, 169.5, 101.5, 100.2, 84.3, 72.6, 72.4, 72.2, 71.5, 70.0, 68.6, 66.2, 63.3, 62.1, 54.8, 26.1, 20.8, 20.7, 20.7, 20.7, 18.5, -5.1. \(R_f\): 0.4 (isopropanol/toluene 1:9). IR (Powder, cm\(^{-1}\)): 3522 (w), 2929 (w), 1751 (s), 1367 (m), 1212 (s, \(\delta\)). HRMS (ESI, m/z): Calculated for C\(_{27}\)H\(_{37}\)O\(_{15}\)Si ((M+H): 639.2678; Found: 639.2702.

Methyl-6-O-tert-butyldimethylsilyl-3-O-(3',4',6'-tri-O-acetyl-\(\alpha\)-D-glucopyranose-1,2-orthoacetyl)-\(\alpha\)-D-mannopyranoside (73). To an oven-dried round bottom flask under an argon atmosphere were added 57 (1.0 mmol, 0.41 g), 33 (1.1 mmol, 0.34 g), silver (I) oxide (1.0 mmol, 0.41 g), phenylboronic acid (0.23 mmol, 0.23 g) and acetonitrile (7.5 mL) was added and the resulting mixture was stirred at room temperature. After 16 hours, the mixture was quenched with a few drops of methanol, diluted with dichloromethane and filtered through a plug of celite. The resulting crude material was purified by silica gel chromatography to yield 73 as a white solid in 15% yield. \(\textsuperscript{1}H\) NMR (400MHz, CDCl\(_3\)): \(\delta\) 5.86 (d, \(J = 5.2\) Hz, 1H, \(H-1'\)), 5.18 (apparent t, \(J = 3.2\) Hz, 1H, \(H-3'\)), 4.91 (ddd, \(J = 9.6, 3.2, 0.4\) Hz, 1H, \(H-4'\)), 4.68 (d, \(J = 1.6\) Hz, 1H, \(H-1\)), 4.46 (ddd, \(J = 5.2, 3.2, 0.8\) Hz, 1H, \(H-2'\)), 4.22 (dd, \(J = 12.4, 5.2\) Hz, 1H, \(H-6a'\)), 4.17 (dd, \(J =
12.4, 2.8 Hz, 1H, H-6b'), 3.96–3.76 (m, 6H, H-5', H-2, H-3, H-6a, H-6b and H-4), 3.60 (ddd, J = 9.6, 5.6, 5.6 Hz, 1H, H-5), 3.37 (s, 3H, OCH$_3$), 3.03 (d, J = 2.0 Hz, 1H, C$_4$-OH), 2.21 (d, J = 3.2 Hz, 1H, C$_2$-OH), 2.11 (s, 3H, COOCH$_3$), 2.09 (s, 3H, COOCH$_3$), 1.80 (s, 3H, COOCH$_3$), 0.90 (s, 9H, Si(C(CH$_3$)$_3$)(CH$_3$)$_2$), 0.09 (s, 6H, Si(C(CH$_3$)$_3$)(CH$_3$)$_2$).

$^{13}$C NMR (100MHz, CDCl$_3$): δ 170.7, 170.2, 169.8, 169.5, 101.5, 100.2, 84.3, 72.6, 72.4, 72.2, 71.5, 70.0, 68.6, 66.2, 63.3, 62.1, 54.8, 26.1, 20.8, 20.7, 20.7, 18.5, -5.2. R$_f$: 0.3 (isopropanol/toluene 1:9). IR (Powder, cm$^{-1}$): 3507 (w), 2930 (w), 1749 (s), 1368 (m), 1214 (s), 1135 (m), 1036 (s).

HRMS (ESI, m/z): Calculated for C$_{27}$H$_{50}$NO$_{15}$Si ((M+NH$_4$)$^+$): 656.2950; Found: 656.2948.

Methyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (76).

Synthesized according to general procedure F, from 57 (1.0 mmol) and 75, 57% yield, white solid. $^1$H NMR (400 MHz, CDCl$_3$): δ 5.23 (dd, J = 9.2, 9.6 Hz, 1H, H-3'), 5.05 (dd, J = 10.0, 9.6 Hz, 1H, H-4'), 5.03 (dd, J = 8.0, 8.0 Hz, 1H, H-2'), 4.70 (d, J = 1.6 Hz, 1H, H-1), 4.68 (d, J = 8.0 Hz, 1H, H-1'), 4.23–4.15 (m, 2H, H-6a' and H-6b'), 3.99 (ddd, J = 3.2, 3.2, 2.0 Hz, 1H, H-2), 3.77–3.70 (m, 2H, H-5' and H-4), 3.68–3.59 (m, 2H, H-3 and H-5), 3.36 (s, 3H, OCH$_3$), 2.66 (d, J = 3.2 Hz, 1H, C$_2$-OH), 2.27 (d, J = 2.8 Hz, 1H, C$_4$-OH), 2.08 (s, 3H, COOCH$_3$), 2.05 (s, 3H, COOCH$_3$), 2.03 (s, 3H, COOCH$_3$), 2.01 (s, 3H, COOCH$_3$), 1.32 (d, J = 5.6 Hz, 3H, CH$_3$).

$^{13}$C NMR (100 MHz, CDCl$_3$): δ 170.8, 170.3, 170.1, 169.5, 101.4, 100.5, 83.3, 72.5, 72.2, 71.7, 71.0, 69.7, 68.5, 67.6, 61.9, 54.9, 20.9, 20.8, 20.7, 20.7, 17.7. R$_f$: 0.3 (isopropanol/toluene, 1:9). IR (Powder, cm$^{-1}$): 3545 (w), 3477 (w), 2908 (w), 1748 (s), 1438 (w), 1368 (m), 1261 (m), 1224 (s), 1172 (m), 1132 (m), 1052 (s), 1035 (s). HRMS (ESI, m/z): Calculated for C$_{27}$H$_{36}$NO$_{14}$ ((M+NH$_4$)$^+$): 526.2130; Found: 526.2107. m.p.: 126–128 °C.
Methyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-α-L-fucopyranoside (79).

Synthesized according to general procedure F, from 57 (1.0 mmol) and 78, 58% yield, white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 5.22 (dd, \(J = 9.6, 9.6\) Hz, 1H, H-3'), 5.06 (dd, \(J = 10.0, 9.6\) Hz, 1H, H-4'), 5.03 (dd, \(J = 9.6, 8.0\) Hz, 1H, H-2'), 4.82 (d, \(J = 3.9\) Hz, 1H, H-1), 4.67 (d, \(J = 8.0\) Hz, 1H, H-1'), 4.23 (dd, \(J = 12.4, 2.5\) Hz, 1H, H-6a'), 4.16 (dd, \(J = 12.4, 5.4\) Hz, 1H, H-6b'), 3.98 (ddd, \(J = 9.6, 4.0, 4.0\) Hz, 1H, H-2), 3.92 (q, \(J = 6.6\) Hz, 1H, H-5), 3.82 (dd, \(J = 9.6, 3.3\) Hz, 1H, H-3), 3.74 (ddd, \(J = 10.0, 5.4, 2.6\) Hz, 1H, H-5'), 3.70 (m, 1H, H-4), 3.41 (s, 3H, OCH\(_3\)), 3.15 (d, \(J = 4.2\) Hz, 1H, C-2-OH), 2.27 (br s, 1H, C-4-OH), 2.09 (s, 3H, OCOC\(_3\)H\(_3\)), 2.06 (s, 3H, OCOC\(_3\)H\(_3\)), 2.03 (s, 3H, OCOC\(_3\)H\(_3\)), 2.01 (s, 3H, OCOC\(_3\)H\(_3\)), 1.30 (d, \(J = 6.6\) Hz, 3H, CH\(_3\)). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 170.7, 170.3, 169.7, 169.4, 100.9, 99.5, 82.6, 72.4, 72.2, 71.6, 71.0, 68.3, 67.2, 65.3, 61.7, 55.5, 20.8, 20.8, 20.7, 20.7, 16.1. \(R_f\): 0.2 (isopropanol/toluene 1:9). IR (Powder, cm\(^{-1}\)) \(\nu\): 3470 (w), 2903 (w), 1737 (s), 1365 (m), 1219 (s), 1148 (w), 1090 (m), 1033 (s), 961 (m), 911 (m). HRMS (ESI, m/z): Calculated for C\(_{21}\)H\(_{36}\)NO\(_{14}\) ((M+NH\(_4^+\))\(^+\)): 526.2130; Found: 526.2149. m.p.: 161–163 °C.

Methyl-3-O-(2',3',4',6'-tetra-O-pivaloyl-β-D-glucopyranosyl)-α-L-fucopyranoside (80).

Synthesized according to general procedure F, from 74 (1.0 mmol) and 78, 81% yield, white solid. Inseparable unidentified regioisomer: 9% yield, \(^1\)H NMR peaks visible at \(\delta\) 4.66 (d, \(J = 4.0\) Hz, 1H), 4.60 (d, \(J = 8.0\) Hz, 1H). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 5.34 (dd, \(J = 9.6, 9.6\) Hz, 1H, H-3'), 5.15 (dd, \(J = 10.0, 9.6\) Hz, 1H, H-4'), 5.08 (dd, \(J = 9.6, 8.0\) Hz, 1H, H-2'), 4.82 (d, \(J = 3.6\) Hz, 1H, H-1), 4.69 (d, \(J = 7.6\) Hz, 1H, H-1'), 4.30 (dd, \(J = 12.8, 2.0\) Hz, 1H, H-6a'), 4.03 (dd, \(J = 12.4, 4.8\) Hz, 1H, H-6b'), 3.95 (ddd, \(J = 10.0, 8.0, 4.0\) Hz, 1H, H-2), 3.89 (q, \(J = 6.8\) Hz, 1H, H-5), 3.81 (dd, \(J = 9.6, 3.2\) Hz, 1H, H-3), 3.76 (ddd, \(J = 10.0, 4.8, 1.6\) Hz, 1H, H-5'), 3.68 (ddd, \(J = 3.2, 1.6, 1.6\) Hz, 1H, H-4), 3.40 (s, 3H, OCH\(_3\)), 3.10 (d, \(J = 4.0\) Hz, 1H, C-2-OH), 2.22 (dd, \(J = 1.6, 1.6\) Hz, 1H, C-4-OH), 1.28 (d, \(J = 6.8\) Hz, 3H, CH\(_3\)), 1.22 (s, 9H, OCOC(CH\(_3\))\(_3\)), 1.16 (s, 9H,
1,6-Anhydro-2-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-mannopyanoside (82). Synthesized according to general procedure F in an oven-dried 2-dram vial, from 57 (0.2 mmol) and 81, 56% yield, white solid. \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 5.38 (dd, \( J = 1.6, 1.6 \) Hz, 1H, \( H-1 \)), 5.22 (dd, \( J = 9.6, 9.2 \) Hz, 1H, \( H-3' \)), 5.07 (dd, \( J = 10.4, 9.2 \) Hz, 1H, \( H-4' \)), 5.05 (dd, \( J = 9.6, 8.0 \) Hz, 1H, \( H-2' \)), 4.71 (d, \( J = 8.0 \) Hz, 1H, \( H-1' \)), 4.51–4.50 (m, 1H, \( H-5 \)), 4.32 (dd, \( J = 7.3, 0.9 \) Hz, 1H, \( H-6a \)), 4.22 (dd, \( J = 12.4, 4.9 \) Hz, 1H, \( H-6a' \)), 4.16 (dd, \( J = 12.4, 2.6 \) Hz, 1H, \( H-6b' \)), 4.07–4.05 (m, 1H, \( H-2 \)), 3.91 (d, \( J = 8.2 \) Hz, 1H, \( H-4 \)), 3.77–3.71 (m, 3H, \( H-3, H-6b \) and \( H-5' \)), 2.86 (d, \( J = 1.6 \) Hz, 1H, \( C_3-OH \)), 2.27 (d, \( J = 8.4 \) Hz, 1H, \( C_4-OH \)), 2.09 (s, 3H, OCOCH\(_3\)), 2.06 (s, 3H, OCOCH\(_3\)), 2.03 (s, 3H, OCOCH\(_3\)), 2.01 (s, 3H, OCOCH\(_3\)). \( ^{13}C \) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 170.8, 170.4, 169.5, 169.4, 100.8, 99.7, 76.4, 75.6, 72.5, 72.4, 71.6, 71.2, 71.2, 68.3, 65.0, 61.8, 20.8, 20.8, 20.7, 20.7. R\(_f\): 0.20 (isopropanol/toluene 3:17). IR (Powder, cm\(^{-1}\)): 3266 (w), 2962 (w), 2901 (w), 1739 (s), 1429 (w), 1370 (m), 1222 (s), 1124 (m), 1028 (s), 979 (s), 897 (m). HRMS (ESI, m/z): Calculated for C\(_{20}\)H\(_{28}\)O\(_{14}\)Na ((M+Na\(^{+}\)): 515.1371; Found: 515.1392.

1,6-Anhydro-4-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-galactopyanoside (85). Synthesized according to general procedure F at 60 °C, from 57 (1.0 mmol) and 84, 73% yield, white solid. \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 5.38 (dd, \( J = 1.2, 1.2 \) Hz, 1H, \( H-1 \)), 5.23 (dd,
\( J = 9.6, 9.6 \text{ Hz}, 1 \text{H}, \ H-3' \), 5.05 (dd, \( J = 10.0, 9.2 \text{ Hz}, 1 \text{H}, \ H-4' \)), 5.00 (dd, \( J = 9.6, 8.0 \text{ Hz}, 1 \text{H}, \ H-2' \)), 4.69 (d, \( J = 8.0 \text{ Hz}, 1 \text{H}, \ H-1' \)), 4.54 (apparent t, \( J = 5.2 \text{ Hz}, 1 \text{H}, \ H-5 \)), 4.29 (d, \( J = 7.6 \text{ Hz}, 1 \text{H}, \ H-6a \)), 4.22 (dd, \( J = 12.0, 4.8 \text{ Hz}, 1 \text{H}, \ H-6a' \)), 4.16 (dd, \( J = 12.0, 2.4 \text{ Hz}, 1 \text{H}, \ H-6b' \)), 4.04–4.00 (m, 2H, \( H-4 \) and \( H-3 \)), 3.83 (br s, 1H, \( H-2 \)), 3.74 (ddd, \( J = 10, 4.8, 2.4 \text{ Hz}, 1 \text{H}, \ H-5' \)), 3.67 (dd, \( J = 7.2, 5.2 \text{ Hz}, 1 \text{H}, \ H-6b \)), 2.46 (br s, 1H, C\(_3\)-OH), 2.09–2.08 (m, 1H, C\(_2\)-OH), 2.09 (s, 3H, OCOCH\(_3\)), 2.05 (s, 3H, OCOCH\(_3\)), 2.03 (s, 3H, OCOCH\(_3\)), 2.01 (s, 3H, OCOCH\(_3\)). \(^{13}\text{C NMR (100 MHz, CDCl}\_3\): \( \delta \) 170.7, 170.2, 169.8, 169.5, 101.4, 100.7, 73.9, 73.3, 72.4, 72.3, 71.7, 71.5, 70.0, 68.4, 64.5, 61.9, 20.8, 20.8, 20.7, 20.7. \( \text{Rf} \): 0.25 (isopropanol/toluene 3:17). \( \text{IR (Powder, cm}^{-1}\)): 3472 (w), 2940 (w), 1747 (s), 1725 (s), 1435 (w), 1368 (m), 1228 (s), 1228 (s), 1122 (m), 1034 (s). \( \text{HRMS (ESI, m/z):} \) Calculated for C\(_{20}\)H\(_{32}\)NO\(_{14}\) ((M+NH\(_4\))\(^+\)): 510.1823; Found: 510.1832. \( \text{m.p.:} \) 172–174 °C.

1-O-(2',3',4',6'-tetra-O-acetyl-\( \beta \)-D-glucopyranosyl)-4,6-O-ethylidene-\( \alpha \)-D-glucopyranoside (88). Synthesized according to general procedure F in an oven-dried 2-dram vial, from 57 (0.2 mmol) and 87, 50% yield, white solid. \(^1\text{H NMR (400 MHz, CDCl}_3\): \( \delta \) 5.25 (dd, \( J = 9.6, 9.6 \text{ Hz}, 1 \text{H}, \ H-3' \)), 5.06–5.00 (m, 3H, \( H-2' \), \( H-4' \) and \( H-1 \)), 4.70 (q, \( J = 5.0 \text{ Hz}, 1 \text{H}, \ CH_3CHO_2 \)), 4.64 (d, \( J = 7.9 \text{ Hz}, 1 \text{H}, \ H-1' \)), 4.20 (dd, \( J = 12.3, 5.2 \text{ Hz}, 1 \text{H}, \ H-6a' \)), 4.15 (dd, \( J = 12.5, 2.6 \text{ Hz}, 1 \text{H}, \ H-6b' \)), 4.05 (dd, \( J = 10.1, 5.0 \text{ Hz}, 1 \text{H}, \ H-6a \)), 3.90 (ddd, \( J = 9.6, 9.6, 4.8 \text{ Hz}, 1 \text{H}, \ H-5' \)), 3.86 (dd, \( J = 9.2, 9.2 \text{ Hz}, 1 \text{H}, \ H-3 \)), 3.75 (ddd, \( J = 10.3, 5.2, 2.6 \text{ Hz}, 1 \text{H}, \ H-5' \)), 3.52 (ddd, \( J = 10.4, 10.4, 4.0 \text{ Hz}, 1 \text{H}, \ H-2 \)), 3.46 (dd, \( J = 10.0, 10.0 \text{ Hz}, 1 \text{H}, \ H-6b \)), 3.28 (dd, \( J = 9.6, 9.6 \text{ Hz}, 1 \text{H}, \ H-4 \)), 2.62 (br s, 1H, C\(_3\)-OH), 2.10 (s, 3H, OCOCH\(_3\)), 2.07 (s, 3H, OCOCH\(_3\)), 2.04 (s, 3H, OCOCH\(_3\)), 2.02 (s, 3H, OCOCH\(_3\)), 2.02 (s, 1H, C\(_2\)-OH), 1.37 (d, \( J = 5.0 \text{ Hz}, 3 \text{H}, \ CH_2CHO_2 \)). \(^{13}\text{C NMR (100 MHz, CDCl}_3\): \( \delta \) 170.7, 170.7, 170.2, 169.6, 101.3, 101.1, 99.8, 80.0, 73.0, 72.5, 72.2, 71.9, 71.8, 68.4, 68.0, 63.3, 62.3, 20.9, 20.8, 20.7, 20.7, 20.4. \( \text{Rf} \): 0.20 (isopropanol/toluene 1:9). \( \text{IR (Powder, cm}^{-1}\)): 3508 (w), 2952 (w), 1742 (s), 1376 (m), 1215 (s), 1035 (s), 907 (m). \( \text{HRMS (ESI, m/z):} \) Calculated for C\(_{22}\)H\(_{36}\)NO\(_{15}\) ((M+NH\(_4\))\(^+\)): 554.2085; Found: 554.2065.
Synthesized according to general procedure F, from 90 (1.0 mmol) and 91, 78% yield, white solid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 5.40 (dd, $J = 3.6$, 1.2 Hz, 1H, $H$-4’), 5.24 (dd, $J = 10.8$, 8.0 Hz, 1H, $H$-2’), 5.03 (dd, $J = 10.4$, 3.2 Hz, 1H, $H$-3’), 4.85 (d, $J = 3.6$ Hz, 1H, $H$-1), 4.61 (d, $J = 8.0$ Hz, 1H, $H$-1’), 4.17 (dd, $J = 11.2$, 6.0 Hz, 1H, $H$-6a’), 4.13 (dd, $J = 11.6$, 7.2 Hz, 1H, $H$-6b’), 4.01 (dd, $J = 9.2$, 3.6, 3.6 Hz, 1H, $H$-2), 3.97 (dd, $J = 7.2$, 6.4 Hz, 1H, $H$-5’), 3.89 (m, 1H, $H$-4), 3.84 (dd, $J = 9.2$, 3.6 Hz, 1H, $H$-3), 3.80–3.76 (m, 1H, $H$-5), 3.73 (dd, $J = 3.6$ Hz, 1H, C$_2$-OH), 2.43 (br s, 1H, C$_4$-OH), 2.16 (s, 3H, OCOC$_3$H$_3$), 2.08 (s, 3H, OCOC$_3$H$_3$), 2.06 (s, 3H, OCOC$_3$H$_3$), 1.99 (s, 3H, OCOC$_3$H$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 170.5, 170.2, 170.1, 169.9, 101.8, 99.8, 82.1, 71.4, 70.6, 69.3, 68.4, 67.7, 66.9, 61.7, 61.5, 55.6, 20.9, 20.8, 20.7, 20.7. $R_f$: 0.2 (isopropanol/toluene 1:9). IR (Powder, cm$^{-1}$): 3507 (w), 2934 (w), 1741 (s), 1432 (w), 1368 (m), 1214 (s), 1139 (m), 1054 (s).

HRMS (ESI, m/z): Calculated for C$_{20}$H$_{34}$NO$_{14}$ ([M+NH$_4$]$^+$): 512.1979; Found: 512.1961.

Methyl-3-O-(2’,3’,4’-tri-para-nitrobenzoyl-β-L-fucopyranosyl)-α-D-mannopyranoside (93). Synthesized according to general procedure F in an oven-dried 2-dram vial, from 50 (0.10 mmol) and 33, 40% yield, white solid. $^1$H NMR (400MHz, CDCl$_3$): $\delta$ 8.39–8.36 (m, 2H, OCHPh), 8.28–8.20 (m, 4H, OCHPh), 8.18–8.13 (m, 4H, OCHPh), 7.98–7.94 (m, 2H, OCHPh), 5.73 (dd, $J = 3.4$, 0.8 Hz, 1H, $H$-4’), 5.69 (dd, $J = 10.5$, 7.8 Hz, 1H, $H$-2’), 5.60 (dd, $J = 10.4$, 3.4 Hz, 1H, $H$-3’), 5.16 (d, $J = 7.8$ Hz, 1H, $H$-1’), 4.72 (d, $J = 1.5$ Hz, 1H, $H$-1), 4.17–4.12 (m, 1H, $H$-5’), 4.08–4.06 (m, 1H, $H$-2), 3.92 (dd, $J = 9.1$, 3.4 Hz, 1H, $H$-3), 3.87–3.79 (m, 2H, $H$-6a and $H$-4), 3.71 (dd, $J = 10.0$, 7.6 Hz, 1H, $H$-6b), 3.55 (ddd, $J = 9.0$, 7.7, 4.9 Hz, 1H, $H$-5), 3.38 (s,
Methyl-3-O-(2',3',4'-tri-O-para-nitrobenzoyl-α-D-arabinopyranosyl)-α-D-mannopyranoside (95). Synthesized according to general procedure F in an oven-dried 2-dram vial, from 49 (0.20 mmol) and 33, 41% yield, white solid. ¹H NMR (400MHz, CDCl₃): δ 8.36–8.33 (m, 2H, OCH₃Ph), 8.26–8.24 (m, 2H, OCH₃Ph), 8.24–8.22 (m, 2H, OCH₃Ph), 8.20–8.19 (m, 2H, OCH₃Ph), 8.18–8.17 (m, 2H, OCH₃Ph), 8.06–8.03 (m, 2H, OCH₃Ph), 5.76–5.72 (m, 2H, H-4' and H-2'), 5.62 (dd, J = 10.0, 3.6 Hz, 1H, H-3'), 5.14 (d, J = 7.6 Hz, 1H, H-1'), 4.71 (d, J = 1.6 Hz, 1H, H-1), 4.32 (dd, J = 13.2, 2.8 Hz, 1H, H-5a'), 4.04 (dd, J = 3.2, 1.6 Hz, 1H, H-2), 3.97 (dd, J = 12.4, 1.6 Hz, 1H, H-5b'), 3.94 (dd, J = 9.6, 3.6 Hz, 1H, H-3'), 3.88–3.80 (m, 2H, H-6a and H-4), 3.71 (dd, J = 10.0, 7.6 Hz, 1H, H-6b), 3.56 (dd, J = 9.2, 7.6, 4.8 Hz, 1H, H-5), 3.38 (s, 3H, OCH₃), 3.19 (br s, 1H, C₄=OH), 2.43 (br s, 1H, C₂=OH), 0.83 (s, 9H, Si(C(CH₃)₃)(CH₃)₂), 0.05 (s, 3H, Si(C(CH₃)₃)(CH₃)₂), 0.02 (s, 3H, Si(C(CH₃)₃)(CH₃)₂). ¹³C NMR (100MHz, CDCl₃): δ 164.1, 164.1, 163.8, 151.2, 151.0, 150.9, 134.7, 134.4, 134.1, 131.2, 131.1, 131.0, 124.0, 123.8, 123.7, 102.3, 100.4, 81.0, 71.8, 71.0, 70.8, 70.1, 69.6, 69.6, 65.8, 63.8, 55.2, 25.8, 18.2, -5.5, -5.6. Rf: 0.3 (ethyl acetate/toluene 1:3). IR (Powder, cm⁻¹): 3508 (w), 2931 (w), 1731 (s), 1608 (m), 1525 (s), 1471 (w), 1410 (w), 1348 (m), 1320 (w), 1257 (s), 1086 (s), 1014 (s), 871 (m), 836 (s), 781 (m), 717 (s).
Methyl-6-O-tert-butylidemethylsilyl-3-O-(3',4',6'-tri-O-acetyl-β-D-mannopyranose-1,2-orthoacetyl)-β-D-galactopyranoside (96). Synthesized according to general procedure F in an oven-dried 2-dram vial, from 52 (0.20 mmol) and 34, 38% yield, white solid. \[ ^1H \text{NMR (400MHz, CDCl}_3 \]: \[ \delta \] 5.55 (d, \( J = 2.8 \) Hz, 1H, \( H-1' \)), 5.28 (dd, \( J = 9.6, 9.6 \) Hz, 1H, \( H-4' \)), 5.19 (dd, \( J = 10.0, 4.0 \) Hz, 1H, \( H-3' \)), 4.70 (dd, \( J = 4.0, 2.8 \) Hz, 1H, \( H-2' \)), 4.25 (dd, \( J = 12.0, 4.8 \) Hz, 1H, \( H-6a' \)), 4.17 (d, \( J = 7.6 \) Hz, 1H, \( H-1 \)), 4.15 (dd, \( J = 12.4, 2.8 \) Hz, 1H, \( H-6b' \)), 3.96 (ddd, \( J = 3.2, 3.2, 0.4 \) Hz, 1H, \( H-4 \)), 3.91 (dd, \( J = 10.4, 6.0 \) Hz, 1H, \( H-6a \)), 3.83 (dd, \( J = 10.4, 5.2 \) Hz, 1H, \( H-6b \)), 3.73–3.68 (m, 2H, \( H-2 \) and \( H-5' \)), 3.62 (dd, \( J = 9.6, 3.2 \) Hz, 1H, \( H-3 \)), 3.54 (s, 3H, OCH\(_3\)), 3.44 (apparent t, \( J = 5.6 \) Hz, 1H, \( H-5 \)), 2.63 (d, \( J = 1.6 \) Hz, 1H, \( C_2-OH \)), 2.53 (dd, \( J = 2.8, 0.8 \) Hz, 1H, \( C_4-OH \)), 2.10 (s, 3H, OCOCH\(_3\)), 2.07 (s, 3H, OCOCH\(_3\)), 2.05 (s, 3H, OCOCH\(_3\)), 1.85 (s, 3H, OCOCH\(_3\)), 0.89 (s, 9H, Si(C(CH\(_3\))\(_3\))(CH\(_3\))\(_2\)), 0.08 (s, 6H, Si(C(CH\(_3\))\(_3\))(CH\(_3\))\(_2\)). \[ ^{13}C \text{NMR (100MHz, CDCl}_3 \]: \[ \delta \] 170.7, 170.4, 169.5, 124.4, 104.0, 97.5, 76.6, 76.4, 74.6, 71.8, 70.1, 69.8, 68.8, 65.5, 62.5, 62.4, 56.9, 26.0, 25.4, 20.8, 20.8, 18.4, -5.2. \( R_f \): 0.2 (isopropanol/toluene, 1:9). \( \text{IR (Powder, cm}^{-1}\)): 3507 (w), 2935 (w), 2857 (w), 1742 (s), 1371 (m). Methyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-6-O-(2",3",4",6"-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-mannopyranoside (101). Synthesized according to general procedure F in an oven-dried 2-dram vial, from 57 (0.20 mmol) and 36, 72% yield, transparent sticky solid. \[ ^1H \text{NMR (400MHz, CDCl}_3 \]: \[ \delta \] 5.23 (dd, \( J = 9.6, 9.6 \) Hz, 1H, \( H-3' \)), 5.19 (dd, \( J = 9.6, 9.2 \) Hz, 1H, \( H-3' \)), 5.08 (dd, \( J = 9.6, 9.6 \) Hz, 1H, \( H-4' \)), 5.05–4.98 (m, 3H, \( H-4", H-2" \) and \( H-2' \)), 4.70 (d, \( J = 1.4 \) Hz, 1H, \( H-1 \)), 4.65 (d, \( J = 7.9 \) Hz, 1H, \( H-1" \)), 4.58 (d, \( J = 8.0 \) Hz, 1H, \( H-1' \)), 4.28–4.10 (m, 5H, \( H-6a' \), \( H-6b' \), \( H-6a" \), \( H-6b" \) and \( H-6a \)), 3.80–3.67 (m, 7H, \( H-6b \), \( H-2 \), \( H-3 \), \( H-4 \), \( H-5" \), \( H-5' \) and \( H-5 \)), 3.35 (s, 3H, OCH\(_3\)), 3.34 (br s, 1H, \( C_4-OH \)), 2.30 (d, \( J = 3.0 \) Hz, 1H, \( C_2-\)}}
Methyl-3-O-(2',3',4',6'-tetro-O-acetyl-β-D-gluco.pyranosyl)-6-O-(2",3",4",6"-tetro-O-acetyl-β-D-gluco.pyranosyl)-β-D-galactopyranoside (103). To an oven-dried 2-dram vial under an argon atmosphere were added 57 (0.44 mmol, 0.18 g), 102 (0.20 mmol, 0.039 g), silver (I) oxide (0.52 mmol, 0.12 g) and 2-aminoethyl diphenylborinate (0.02 mmol, 4.5 mg). Dry acetonitrile (1.5 mL) was added and the resulting mixture was stirred at room temperature. After 16 hours, the reaction was quenched with a few drops of methanol, diluted with dichloromethane and filtered through a plug of Celite®. The resulting crude material was purified by silica gel chromatography to afford 103 as a white solid in 56% yield. 1H NMR (400MHz, CDCl3): δ 5.24 (dd, J = 9.6, 9.6 Hz, 1H, H-3'), 5.18 (dd, J = 9.5, 9.5 Hz, 1H, H-3''), 5.09-4.97 (m, 4H, H-4', H-2', H-4" and H-2''), 4.82 (d, J = 8.0 Hz, 1H, H-1'), 4.63 (d, J = 8.0 Hz, 1H, H-1''), 4.26-4.21 (m, 2H, H-6a' and H-6a''), 4.17-4.11 (m, 3H, H-6b', H-4 and H-1), 4.02 (dd, J = 11.2, 3.6 Hz, 1H, H-6b''), 3.94-3.90 (m, 2H, H-6a and H-6b), 3.75-3.67 (m, 3H, H-2, H-5' and H-5''), 3.63 (dd, J = 7.6, 3.6 Hz, 1H, H-5), 3.57 (dd, J = 9.6, 3.6 Hz, 1H, H-3), 3.55 (s, 3H, OCH3), 2.61 (dd, J = 1.8, 1.8 Hz, 1H, C4-OH), 2.36 (d, J = 2.4 Hz, 1H, C2-OH), 2.09 (s, 3H, OCOCH3), 2.09 (s, 3H, OCOCH3), 2.04 (s, 3H, OCOCH3), 2.03 (s, 3H, OCOCH3), 2.02 (s, 3H, OCOCH3), 2.02 (s, 3H, OCOCH3), 2.01 (s, 3H, OCOCH3), 2.00 (s, 3H, OCOCH3). Rf: 0.15 (isopropanol/toluene 1:9).
IR (Powder, cm⁻¹): HRMS (ESI, m/z): 3552 (w), 2940 (w), 1740 (s), 1432 (w), 1367 (m), 1210 (s), 1032 (s), 906 (m).

Methyl-6-O-tert-butylidemethylsilyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-galactopyranoside (107). Synthesized according to general procedure F, from 57 (1.0 mmol) and 35, 74% yield, white solid. ¹H NMR (400 MHz, CDCl₃): δ 5.23 (dd, J = 9.6, 9.6 Hz, 1H, H-3'), 5.07 (dd, J = 10, 9.6 Hz, 1H, H-4'), 5.02 (dd, J = 10, 8 Hz, 1H, H-2'), 4.81 (d, J = 8 Hz, 1H, H-1'), 4.79 (d, J = 3.6 Hz, 1H, H-1), 4.23 (dd, J = 12.4, 4.8 Hz, 1H, H-6a'), 4.12 (dd, J = 12.4, 2.4 Hz, 1H, H-6b'), 4.06 (d, J = 3.2 Hz, 1H, H-4), 3.97 (dd, J = 9.2, 3.6 Hz, 1H, H-2), 3.85 (ddd, J = 8.8, 4.8, 4.8 Hz, 1H, H-5), 3.80–3.74 (m, 3H, H-6a, H-6b, and H-3), 3.71 (ddd, J = 10, 4.8, 2.4 Hz, 1H, H-5'), 3.42 (s, 3H, OCH₃), 2.08 (s, 3H, OCOCH₃), 2.05 (s, 3H, OCOCH₃), 2.02 (s, 3H, OCOCH₃), 2.01 (s, 3H, OCOCH₃), 0.88 (s, 9H, Si(CH₃)₃(CH₃)₂), 0.07 (s, 6H, Si(C(CH₃)₃)(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 170.7, 170.3, 170.0, 169.5, 101.6, 99.4, 81.1, 72.5, 72.0, 71.6, 70.3, 68.5, 68.4, 68.2, 62.5, 61.8, 55.3, 26.0, 20.9, 20.8, 20.7, 20.7, 18.4, -5.2, -5.3. Rₘ: 0.35 (isopropanol/toluene 1:9). IR (Powder, cm⁻¹): 3527 (w), 2931 (w), 2856 (w), 1747 (s), 1434 (w), 1366 (m), 1215 (s), 1147 (m), 1034 (s). HRMS (ESI, m/z): Calculated for C₂₇H₅₉NO₁₅Si (M+NH₄)⁺: 656.2950; Found: 656.2958.

Methyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-α-L-arabinopyranoside (109). Synthesized according to general procedure F in an oven-dried 2-dram vial, from 57 (0.20 mmol) and 109, 72% yield (10:1 mixture of regioisomers), white solid. ¹H NMR (400 MHz, CDCl₃): δ 5.23 (dd, J = 9.6, 9.6 Hz, 1H, H-3'), 5.06 (dd, J = 9.6, 9.6 Hz, 1H, H-4'), 5.02 (10.0, 8.0 Hz, 1H, H-2'), 4.77 (d, J = 8.0 Hz, 1H, H-1'), 4.76 (d, J = 3.2 Hz, 1H, H-1), 4.21 (dd, J = 12.3, 5.1 Hz, 1H, H-6a'), 4.14 (dd, J = 12.3, 2.6 Hz, 1H, H-6b'), 4.00 (br s, 1H, H-4), 3.95 (ddd, J = 10.8, 7.6,
4.0 Hz, 1H, H-2), 3.82 (dd, J = 9.3, 3.4 Hz, 1H, H-3), 3.78–3.70 (m, 3H, H-5a, H-5b and H-5'), 3.43 (s, 3H, OCH$_3$), 2.68 (br s, 1H, C$_4$-OH), 2.07 (s, 3H, OCOCH$_3$), 2.05 (s, 3H, OCOCH$_3$), 2.02 (s, 3H, OCOCH$_3$), 2.01 (s, 3H, OCOCH$_3$). Inseparable, unidentified regioisomer peaks visible at: 4.72 (d, J = 8.0 Hz, H-1'), 2.17 (s, OCOCH$_3$), 2.15 (s, OCOCH$_3$), 2.02 (s, OCOCH$_3$), 2.00 (s, OCOCH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 170.7, 170.3, 170.0, 169.5, 101.7, 99.8, 80.6, 72.4, 72.0, 71.5, 68.5, 68.4, 68.2, 61.9, 61.7, 55.6, 20.8, 20.8, 20.7, 20.7. $R_f$: 0.10 (isopropanol/toluene 1:9). IR (Powder, cm$^{-1}$): 3522 (w), 2928 (w), 1751 (s), 1368 (m), 1215 (s), 1135 (m), 1034 (s), 966 (m), 835 (s), 780 (m). HRMS (ESI, m/z): Calculated for C$_{20}$H$_{34}$NO$_{14}$ ((M+NH$_4$)$^+$): 512.1973; Found: 512.1987.

Methyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-lyxopyranoside (111).
Synthesized according to general procedure F in an oven-dried 2-dram vial, from 57 (0.20 mmol) and 110, 76% yield (2:1 mixture of regioisomers), white solid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 5.27–5.19 (m, 1.5H), 5.09–4.98 (m, 3H), 4.67 (d, J = 2.0 Hz, 1H), 4.61 (d, J = 8.0 Hz, 1H), 4.58 (d, J = 8.0 Hz, 0.5H), 4.53 (d, J = 3.0 Hz, 0.5H), 4.26 (dd, J = 12.0, 2.4 Hz, 1H), 4.22–4.17 (m, 1H), 4.12 (dd, J = 12.3, 6.3 Hz, 1H), 4.03–3.97 (m, 1H), 3.85–3.72 (m, 5.5H), 3.66 (dd, J = 8.6, 3.4 Hz, 1H), 3.47–3.36 (m, 2H), 3.39 (s, 1.5H), 3.38 (s, 3H), 3.32 (d, J = 2.2 Hz, 1H), 2.81 (d, J = 8.4 Hz, 0.5H), 2.34 (br s, 0.5H), 2.32 (d, J = 2.8 Hz, 1H), 2.10 (s, 1.5H), 2.10 (s, 3H), 2.07 (s, 3H), 2.06 (s, 1.5H), 2.04 (s, 3H), 2.03 (s, 1.5H), 2.02 (s, 3H), 2.01 (s, 1.5H). (both isomers) $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 170.8, 170.7, 170.3, 170.2, 169.8, 169.5, 169.5, 169.5, 101.7, 101.0, 100.6, 99.8, 84.2, 79.7, 72.4, 72.3, 72.3, 72.2, 71.6, 71.1, 71.1, 70.0, 68.5, 68.4, 68.4, 65.7, 62.9, 62.0, 61.8, 61.8, 55.4, 55.2, 31.0, 20.8, 20.8, 20.7, 20.7, 20.7, 20.7, 20.7. (both isomers) $R_f$: 0.15 (isopropanol/toluene 1:9). IR (Powder, cm$^{-1}$): 3450 (w), 2941 (w), 2896 (w), 1738 (s), 1429 (w), 1379 (m), 1220 (s), 1134 (w), 1032 (s), 904 (m). HRMS (ESI, m/z): Calculated for C$_{20}$H$_{34}$NO$_{14}$ ((M+NH$_4$)$^+$): 512.1979; Found: 512.1976.
Methyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-6-O-(2'',3'',4'',6''-tetra-O-acetyl-α-D-galactopyranosyl)-β-D-galactopyranoside (112). Synthesized according to general procedure F in an oven-dried 2-dram vial, from 90 (0.20 mmol) and 37, 61% yield, white solid.

$^1$H NMR (400 MHz, CDCl$_3$): δ 5.38 (dd, $J = 3.4$, 0.8 Hz, 1H, $H$-4''), 5.24 (dd, $J = 9.6$, 9.6 Hz, 1H, $H$-3'), 5.19 (dd, $J = 10.4$, 8.0 Hz, 1H, $H$-2''), 5.05 (dd, $J = 9.6$, 9.6 Hz, 1H, $H$-4'), 5.03–4.97 (m, 2H, $H$-2' and $H$-3''), 4.82 (d, $J = 8.0$ Hz, 1H, $H$-1''), 4.60 (d, $J = 8.0$ Hz, 1H, $H$-1''), 4.22 (dd, $J = 12.4$, 5.0 Hz, 1H, $H$-6a'), 4.16–4.11 (m, 4H, $H$-6b', $H$-6a'', $H$-6b'' and $H$-1''), 4.03 (dd, $J = 11.1$, 3.7 Hz, 1H, $H$-6a), 3.94–3.88 (m, 3H, $H$-6b, $H$-4 and $H$-5''), 3.75–3.69 (m, 2H, $H$-5' and $H$-2), 3.65–3.62 (m, 1H, $H$-5), 3.57 (dd, $J = 9.5$, 3.4 Hz, 1H, $H$-3), 3.54 (s, 3H, OCH$_3$), 2.60 (dd, $J = 1.8$, 1.8 Hz, 1H, C$_4$-OH), 2.41 (d, $J = 2.4$ Hz, 1H, C$_2$-OH), 2.14 (s, 3H, OCOCH$_3$), 2.08 (s, 3H, OCOCH$_3$), 2.05 (s, 3H, OCOCH$_3$), 2.04 (s, 3H, OCOCH$_3$), 2.03 (s, 3H, OCOCH$_3$), 2.03 (s, 3H, OCOCH$_3$), 2.01 (s, 3H, OCOCH$_3$), 1.97 (s, 3H, OCOCH$_3$). $^{13}$C NMR (100MHz, CDCl$_3$): δ 170.7, 170.5, 170.3, 170.2, 169.9, 169.5, 169.5, 103.7, 101.6, 101.5, 82.3, 74.0, 72.3, 72.2, 71.5, 71.0, 70.9, 70.7, 69.3, 69.0, 68.4, 68.4, 67.2, 61.9, 61.5, 57.1, 21.0, 20.9, 20.8, 20.8, 20.8, 20.8, 20.7, 20.7, 20.7. R$: 0.2 (isopropanol/toluene 1:9). IR (Powder, cm$^{-1}$): 1742 (s), 1366 (m), 1210 (s), 1032 (s), 906 (w). HRMS (ESI, m/z): Calculated for C$_{33}$H$_{50}$O$_{24}$Na ((M+Na)$^+$): 877.2584; Found: 877.2564. m.p.: 88–90 °C.

Methyl-3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-6-O-(2'',3'',4'',6''-tetra-O-acetyl-β-D-galactopyranosyl)-α-D-mannopyranoside (113). Synthesized according to general procedure F in an oven-dried 2-dram vial, from 90 (0.20 mmol) and 36, 88% yield, white solid.

$^1$H NMR (400MHz, CDCl$_3$): δ 5.38 (dd, $J = 3.2$, 0.8 Hz, 1H, $H$-4''), 5.26–5.21 (m, 2H, $H$-2'' and
$H-3'$), 5.05–4.98 (m, 3H, $H-4'$, $H-2'$ and $H-3''$), 4.71 (d, $J = 1.6$ Hz, 1H, $H-1$), 4.59 (d, $J = 8.0$ Hz, 1H, $H-1'$), 4.58 (d, $J = 8.0$ Hz, 1H, $H-1''$), 4.25–4.10 (m, 5H, $H-6a'$, $H-6b'$, $H-6a''$, $H-6b''$ and $H-6a$), 3.91 (ddd, $J = 6.4$, 6.4, 0.8 Hz, 1H, $H-5''$), 3.81–3.68 (m, 6H, $H-6b$, $H-2$, $H-3$, $H-5'$, $H-4$ and $H-5$), 3.36 (s, 3H, OCH$_3$), 3.34 (br s, 1H, C$_4$-OH), 2.30 (d, $J = 3.6$ Hz, 1H, C$_2$-OH), 2.13 (s, 3H, OCOCH$_3$), 2.08 (s, 3H, OCOCH$_3$), 2.06 (s, 3H, OCOCH$_3$), 2.04 (s, 3H, OCOCH$_3$), 2.04 (s, 3H, OCOCH$_3$), 2.03 (s, 3H, OCOCH$_3$), 2.01 (s, 3H, OCOCH$_3$), 1.97 (s, 3H, OCOCH$_3$). $^{13}$C NMR (100MHz, CDCl$_3$): δ 170.7, 170.5, 170.4, 170.3, 170.2, 169.8, 169.7, 169.5, 102.0, 101.5, 100.2, 84.2, 72.3, 72.2, 71.5, 71.1, 71.0, 70.7, 69.9, 69.5, 69.1, 68.5, 67.2, 65.9, 62.0, 61.4, 55.0, 20.9, 20.8, 20.8, 20.7, 20.7, 20.7, 20.7. $R_f$: 0.2 (isopropanol/toluene 1:9). IR (Powder, cm$^{-1}$): 2942 (w), 1740 (s), 1367 (m), 1212 (s), 1132 (m). HRMS (ESI, m/z): Calculated for C$_{33}$H$_{50}$O$_{24}$Na ((M+Na)$^+$): 877.2584; Found: 877.2600. m.p.: 90–91 °C.