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Structure-reactivity relationships in glycosylation chemistry

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Chapter 7: summary and future prospects

Summary

One of the key challenges in synthetic carbohydrate chemistry is the formation of a glycosidic bond between two carbohydrate building blocks. The main reason that synthesis of carbohydrate oligomers is more challenging than other biomolecules, such as peptides and oligonucleotides, is that with glycosylation a new stereocenter is introduced. And where *1,2-trans* glycosidic bonds can usually be synthesised by means of neighbouring group participation, for the stereoselective and high yielding formation of *1,2-cis* glycosidic bonds no universally applicable technique exists.
In a typical glycosylation reaction, a donor is activated to form a (variety of) electrophilic species which can react with a nucleophilic acceptor, following a reaction mechanism having both S_N1 and S_N2 character. On the S_N1-side of the spectrum oxocarbenium ions partake in the mechanism while covalent intermediates act as the product forming intermediates on the S_N2-side. The result of a glycosylation reaction is influenced by the properties of both donor and acceptor and can be affected by external factors as well. Because the challenges in carbohydrate synthesis are typically solved for a specific synthetic problem, a general understanding of what effect changing a single variable has on the mechanistic pathway, and thus the (stereochemical) outcome is not available. This in turn means that synthesis of glycosidic bonds typically requires a considerable amount of optimisation at the expense of a significant amount of time and resources. The goal of this thesis is to systematically investigate how changes in stereochemistry and protecting group patterns on the donor and acceptor affect the mechanism and outcome of glycosylation reactions, to enable a more rational design of synthesis routes.

Chapter 1 presents the challenges associated with the chemical synthesis of carbohydrates and shows some solutions that have been developed for stereoselective glycosylation. Here, the S_N1/S_N2 mechanism continuum is described, as well as methods for investigating both ends of the spectrum together with some key results. Finally, the role of the reactivity of the acceptor in the outcome of the glycosylation reaction is discussed.

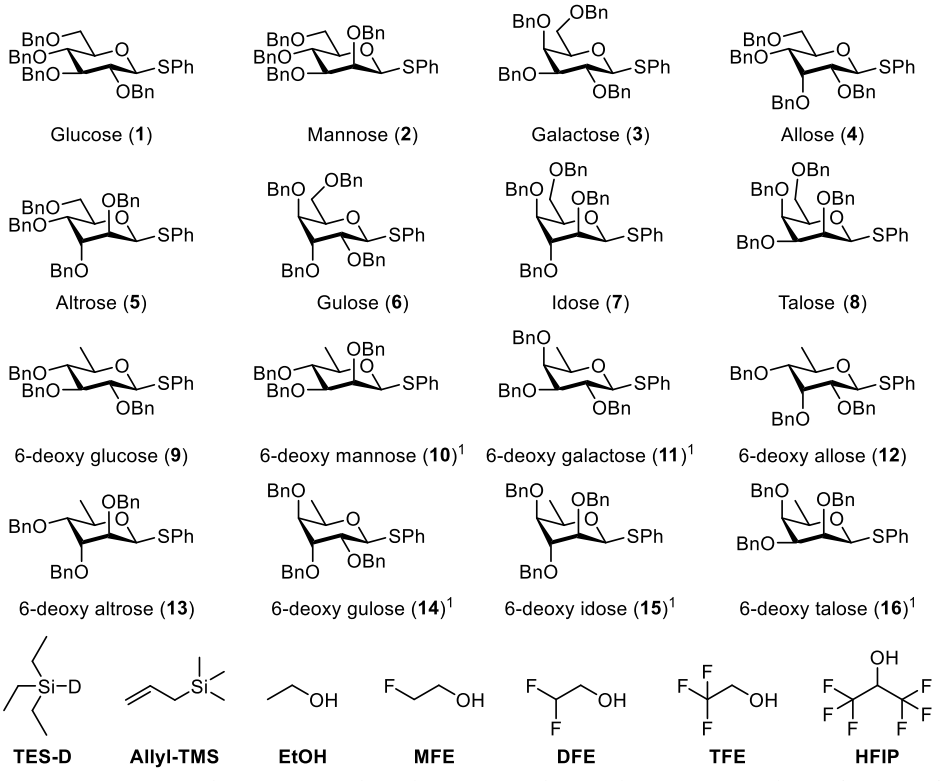


Figure 1: *Donors and acceptors used in chapters* ***2*** *and* ***3****. 1: the* D*-isomer is shown for ease of comparison, but the* L*-isomer was used in the experiments.*

Chapter 2 describes an investigation to the influence of the stereochemistry of the donor on the S_N1 mechanistic pathway of the glycosylation reaction via a combination of computational chemistry and glycosylation experiments. First, all eight diastereomeric per-*O*-benzyl pyranosyl donors, as well as their 6-deoxy analogues (**1-8** and **9-16** respectively, ***Figure 1***) were synthesised. Next, conformation energy landscape (CEL)-maps for all the corresponding oxocarbenium ions were generated to theoretically determine the conformational preference of the oxocarbenium ions, thereby predicting the expected stereochemical outcome of a glycosylation reaction which follows a S_N1 pathway. Finally, all donors were reacted with two nucleophiles which typically react following an S_N1-type mechanism, namely TES-D and allyl-TMS.
The stability of the conformers found in CEL maps can be explained by considering the "preferences" of the substituents to stabilize (or minimize destabilization of) the oxocarbenium ions. Oxocarbenium ions where the C-3 and C-4 alkoxy groups are placed in a pseudo-axial fashion are more stable compared to their pseudo-equatorial equivalents. For C-2 and C-5 a pseudo-equatorial orientation is preferred. When all 4 substituents can be placed in the preferred orientations, as is the case for gulose/6-

deoxy gulose, the ion has a strong preference for that conformation ($^4H_3$ half chair). Also, with 3 out of 4 substituents optimally orientated, the ions show a strong preference for that conformation. When only 2 substituents can be placed in the preferred orientation, the energy differences between conformations are a lot smaller. One further observation is that the preferences for 6-deoxy oxocarbenium ions are very similar to those of their 6-OBn analogues in most cases, although the absolute energy differences are different. This is also apparent in the outcome of the glycosylation reactions.

For the reactions with TES-D, the orientation of the C-2 substituent is the most important in determining the stereochemical outcome, as all of these reactions are highly *1,2-cis* selective. This in agreement with the CEL maps in most cases, except for talose and 6-deoxy glucose, where a ~1:1 mixture is predicted and for idose, where α-selectivity was predicted, but complete β-selectivity was observed.

Reactions with Allyl-TMS gave different results. When the C-2 group is equatorial, the reaction proceeds with full α-selectivity like with TES-D. When the C-2 group is placed in an axial manner however, the reaction shifts from β-selectivity for the TES-D reactions to α-selectivity with allyl-TMS. A possible explanation are the steric interactions between the substituents and the nucleophile that disfavour attack on the *cis*-side. Following a Curtin-Hammett kinetic scenario, attack can then take place on a higher energy oxocarbenium ion conformer *via* a lower energy transition state leading to the *trans*-product. Understanding the possible Curtin-Hammett scenarios occurring during the nucleophilic addition of allyl-TMS to an oxocarbenium ion is currently a topic of active research.[1]

Chapter 3 focuses on the mechanistic pathways which involve a covalent intermediate. Variable temperature (VT) NMR was used to characterise the covalent species formed upon activation of donors **1-8** (see ***Figure 1***). The observed species were either a mixture of α-triflate and α-oxosulfonium triflate, a mixture of α-triflate and α,β-oxosulfonium triflates or a mixture of α,β-oxosulfonium triflates. β-Triflates were not observed for any of the donors.

Next, the donors were coupled with five alcohol acceptors of varying nucleophilicity (EtOH-HFIP, see ***Figure 1***) to probe the influence of the nucleophilicity on the reaction path and the stereochemical outcome of the glycosylations. In the reactions with the EtOH-MFE-DFE-TFE series, the configuration of C-3 appeared to be a key determining factor in the relation between nucleophilicity and stereoselectivity. When the C-3 substituent is equatorial, a clear trend is observed where more nucleophilic acceptors give higher β-selectivity and less nucleophilic acceptors provide higher α-selectivity. When the C-3 groups are axial, α:β mixtures are obtained with no clear relation between nucleophilicity and stereoselectivity. A possible mechanistic explanation for these observations is that for the donors having an equatorially oriented

C-3 group, the most reactive acceptors can substitute the more stable covalent α-species, yielding the β-products, while less reactive acceptors can only react with the more reactive β-species to yield the α-product. When the substituent at C-3 is axial, the reactivity difference between the covalent α- and β-species is smaller because of destabilizing 1,3-diaxial interactions between the triflate and the C-3 group. The S_N2 substitution of the β-species, is also hindered by the group on C-3. These steric interactions counteract one another leading to overall poor selectivity.
The glycosylations with HFIP were all completely α-selective, regardless of the stereochemistry of C-2 or C-3. This stands in contrast to the outcome of related reactions with TES-D, the nucleophile used to benchmark S_N1 reaction pathways, where reactions are always highly *1,2-cis* selective, suggesting that the glycosylations with weak *O*-nucleophiles occurs via a different mechanism than nucleophilic addition to an oxocarbenium ion.

In **Chapter 4** a system based on the use of two conformationally restricted glucosyl donors is described to unravel the structure-reactivity relations of a set of 60 acceptors. The stereochemical outcome of the glycosylation reactions of these two donors is highly dependent on the nucleophilicity of the acceptor, as determined by glycosylations with the EtOH-HFIP model acceptors. The most nucleophilic acceptors react with full β-selectivity, while decreasing the nucleophilicity of the acceptor gradually leads to full α-selectivity.
This property was used to measure the reactivity of a large set of carbohydrate acceptors. By systematically varying the protecting group pattern on D-glucose, D-mannose, D-galactose, L-rhamnose and L-fucose acceptors and "measuring" their reactivity, it was possible to determine which structural features determine the reactivity of the acceptor. Two kinds of model acceptors were also introduced. The first kind consist of carbohydrate-like acceptors stripped to only their "essential" substituents, based on 1,2,6-trideoxy glucose and galactose with varying protecting group patterns. The second kind of model acceptors are C-2-OH glycerol acceptors with a cyclic protecting group on C-1 and C-3. These acceptors resemble carbohydrates acceptors in the sense that they are secondary alcohols next to two protected oxygen atoms. Unlike carbohydrate acceptors however, they are not chiral, so the stereochemical outcome of the glycosylation reactions is not determined by diastereomeric interactions.
Analysis of the results from the glycosylation reactions reveals that both the configuration as well as the protecting group pattern of the acceptor play a key role in determining the reactivity of the acceptor (***Figure 2***). With regard to the configuration of the acceptor, equatorial alcohols are more reactive than axial alcohols (light blue circles and blue squares vs black triangles). The orientation of the functional group next to the nucleophilic alcohol is also important, and alcohols having only equatorial

neighbours are more reactive than alcohols which are next to an axial neighbour (light blue circles vs blue squares). With regard to the protecting group pattern, benzoyl protected acceptors are less reactive than their benzyl protected counterparts. The magnitude of this effect depends on which benzyl group is replaced with a benzoyl group, since the effect is much larger when an equatorial benzyl group next to the alcohol is changed for a benzoyl group than when the same is done with an axial benzyl group next to the alcohol (blue squares, red diamonds and yellow triangles).

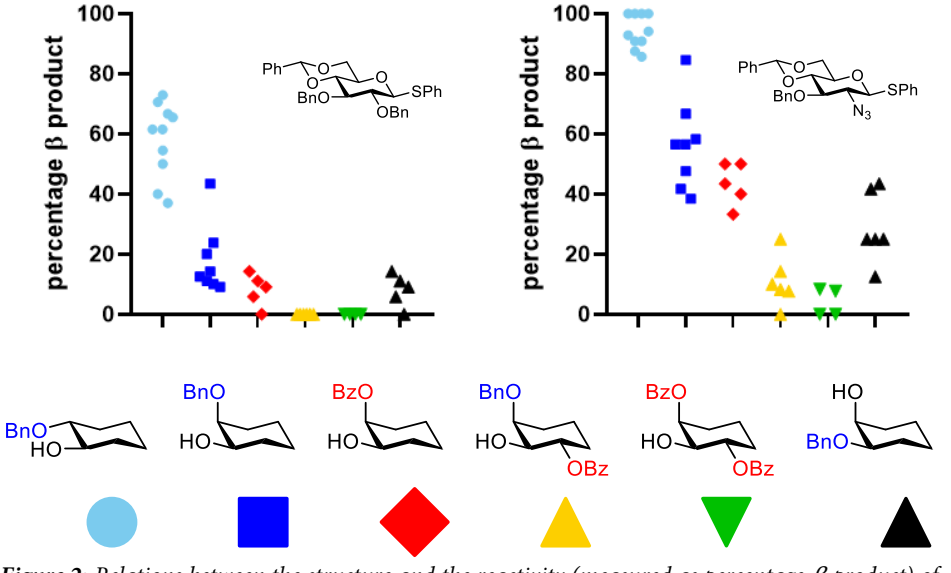


Figure 2: *Relations between the structure and the reactivity (measured as percentage β-product) of glycosyl acceptors found in chapter 4.*

Chapter 5 builds on chapter 4, by using the same methodology that was applied on benzyl/benzoyl protected acceptors to determine the influence of common *N*-protecting groups (*i.e* azide, tricholoroacetamide (TCA) and trifluoroacetamide (TFA)) on the reactivity of glycosyl acceptors. The acceptors used in this study were C-4-OH glucosamine acceptors, since the C-4-OH *N*-acetylglucosamine acceptors are notorious for their poor nucleophilicity and C-3-OH glucosamine acceptors, to investigate the effect of different protecting groups next to the nucleophilic alcohol. The C-4-OH and C-3-OH mannosamine acceptors were added in order to determine the influence of the configuration of the protected amine on the reactivity of the acceptor.

Like with benzyl/benzoyl protected acceptors, both the configuration and the nature of the protecting group are important for the reactivity of the acceptor. For both the C-4-OH glucosamine and mannosamine acceptors, the nature of the protecting group has little influence on the reactivity of the acceptors, since all glycosylations within the same acceptor series proceeded with similar stereoselectivity and high yield. With the C-3-

OH glucosamine and mannosamine acceptors, similar trends were observed as in the acceptor series in chapter 4. The first observation is that an azide has a disarming effect that is comparable to that of a *O*-benzoyl group and that acetamides have a larger disarming effect, with the trifluoroacetamides being more disarming than the trichloroacetamides. The configuration of the protected amine next to the alcohol was also found to be important for the reactivity of the acceptor. As observed for the ether protected acceptors, the C-3-OH glucosazide acceptor is more reactive than the C-3-OH mannosazide acceptor. Also, in line to the results of chapter 4, the disarming effect of the N-protecting groups on equatorial amines next to the alcohol is much more significant than the disarming effect of the N-protecting groups of the neighboring axial amines.

In **Chapter 6**, the obtained knowledge described in Chapters 2-5 is used to synthesize the repeating unit of a capsular polysaccharide found on Acinetobacter baumannii LUH 5554, a Gram-negative bacterium that has been designated by the World Health Organization as a high risk pathogen due to its high level of antibiotic resistance. This polysaccharide is built up from repeating tetramers with the structure [→4)-β-D-GlcpNAc3NAcA-(1→3)-α-D-QuipNAc4NAc-(1→3)-α-D-QuipNAc4NAc-(1→4)-β-D-GlcpNAc3NAcA-(1→] (***Figure 3***) which encompass the two rare sugars 2,4-di-*N*-acetyl-α-D-quinovose (2,4-di-*N*-acetyl bacillosamine, QuiNAc4NAc) and 2,3-di-*N*-acetyl-β-D-glucuronic acid (GlcNAc3NAcA). What makes this structure special, is that it contains *N*-acetyl groups, carboxylates and deoxy centers, but not a single hydroxyl group!

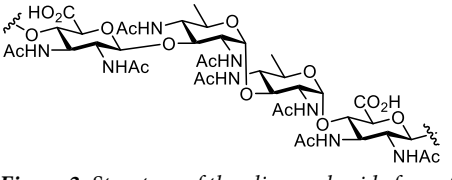


Figure 3: *Structure of the oligosaccharide from A. Baumannii LUH 5554.*

Synthetic routes for producing multi-gram quantities of the bacillosamine and 2,3-di-*N*-acetyl glucuronic acid building blocks were developed starting from D-fucose and D-glucosamine-HCl. The reactivity of the bacillosamine donors was then studied to develop methods for the construction of the 1,2-*cis* linkages. Model glycosylations with fluorinated ethanol acceptors showed that the stereoselectivity of the studied selenophenol bacillosamine donor strongly depends on the nucleophilicity of the acceptor under pre-activation conditions, with ethanol providing complete β-selectivity and 2,2,2-trifluoroethanol nearly complete α-selectivity. The azides and methyl esters on the carbohydrate acceptors should have a disarming effect on the nucleophilic alcohol based on previous studies and, as expected, glycosylation with both the 2,3-di-

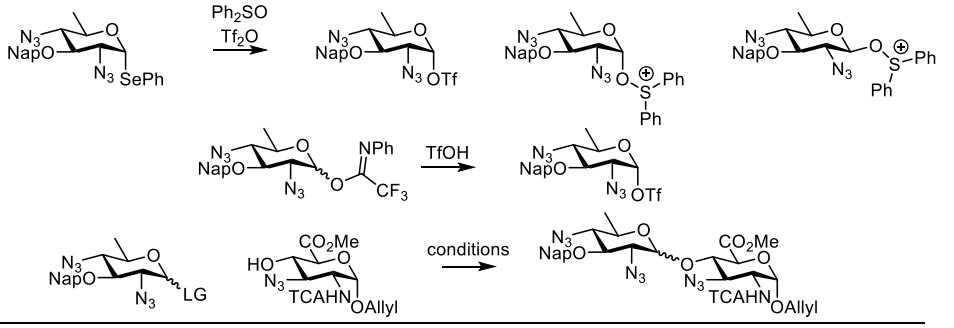
N-acetyl glucuronic acid acceptors and the bacillosamine acceptors proceed with high α-selectivity.
In order to investigate the mechanism underlying this selectivity, VT-NMR was used to study the reactive intermediates formed from the bacillosamine donors. When the selenophenol donor was activated with Ph_2SO and Tf_2O, a mixture of the α-triflate, α-oxosulfonium triflate and β-oxosulfonium triflate was formed. The β-oxosulfonium triflate appeared to be the most reactive, as judged by the lowest decomposition temperature. On the other hand, activation of the corresponding PTFAI donor with TfOH, led to the formation of only the α-triflate. Based on observations in glycosylations between the selenophenol donor or imidate donor with the 2,3-di-*N*-acetyl glucuronic acid acceptors (see below) it is expected that the oxosulfonium triflates play a role in determining the selectivity of the selenophenol donor.
With this knowledge in hand, the tetrasaccharide could be assembled. Eventually 855 mg (670 μmol) of protected tetrasaccharide building block was obtained, which can be deprotected, or used for the synthesis of larger oligomers (see below).

Future prospects

The goal of this thesis has been to systematically map structure-reactivity relationships for both donor and acceptor building blocks and shine light on the different mechanisms of the glycosylation reaction to enable the rational design of synthetic routes towards complex oligosaccharides. The following section describes some suggestions for follow-up studies to further increase the understanding of the glycosylation reaction.

Influence of oxosulfonium species on the outcome of the glycosylation reaction

Chapter 6 shows the use of VT-NMR to characterise the reactive species that are formed when either a selenophenol or an imidate donor are activated with Ph_2SO/Tf_2O or TfOH, respectively (***Figure 4***). The selenophenol donor provided a mixture of α-triflate, α-oxosulfonium triflate and β-oxosulfonium triflate, while the imidate only delivered the α-triflate. The glycosylations with the 2,3-di-*N*-acetyl glucuronic acid acceptor suggest a prominent role for the oxosulfonium triflates in determining the stereoselectivity of the reaction. When this acceptor was reacted with the selenophenol donor under pre-activation conditions, high α-selectivity was obtained. While the reaction with the imidate donor led to a mixture of α- and β-products. The α-selectivity could be restored in the reaction with the imidate donor by adding Ph_2SO, suggesting an important role for the intermediate oxosulfonium species.



Entry	LG	Activation	α:β
1	**α-SePh**	**Ph_2SO/Tf_2O**	**10-13:1**
2	**α,β-OC(=NPh)CF_3**	**TMSOTf**	**1:1**
3	**α,β-OC(=NPh)CF_3**	**TMSOTf+Ph_2SO**	**9:1**

***Figure 4**: Selected observations from chapter 6*

Figure 5 shows an example from literature where the difference in reactivity between triflates and oxosulfonium triflates was used. When Crich and Li reacted sialic acid donor **I** with a stoichiometric amount of Ph_2SO, triflate **II** was formed, followed by immediate elimination to give glycal **III**. However, when an excess of Ph_2SO was used under otherwise similar conditions, a mixture of oxosulfonium triflates IV and V was formed. These species enabled the formation of the glycosylation products with a variety of acceptors.[2]

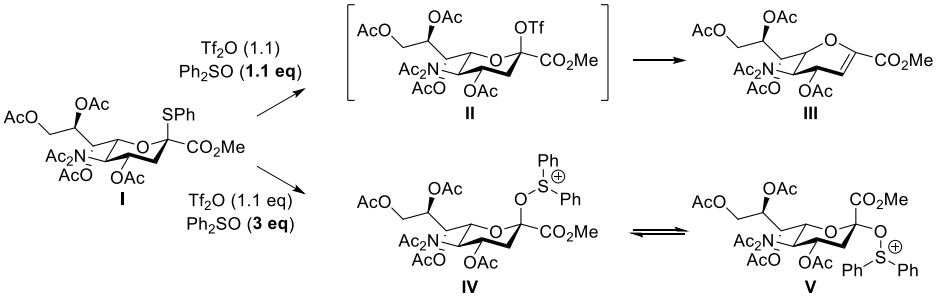


***Figure 5:** A literature example which illustrates the reactivity difference between triflates and oxosulfonium triflates. When sialic acid donor I gets activated with Tf_2O and an stoichiometric amount of Ph_2SO, triflate II is formed, followed by immediate elimination to glycal III. When an excess of Ph_2SO was used, oxosulfonium triflates IV and V are formed, which can successfully react with different acceptors.[2]*

When thiophenol donors **1**-**8** (***Figure 1***) were activated with Ph_2SO and Tf_2O, oxosulfonium species were generated as determined by the VT-NMR measurements. Based on the observations described above, it is not unreasonable to expect that these

oxosulfonium species play a role in shaping the stereochemical outcome of the glycosylation reactions, as reported in chapter 3. An interesting follow-up study would be to transform these thiophenol donors into the corresponding (PTFAI) imidates and use transform these into the corresponding triflates and perform glycosylations with the EtOH-HFIP acceptors to systematically investigate the role that the oxosulfonium species play in glycosylation reactions.

Relative reactivity values of acceptors with donors that react via an S_N1 or an S_N2 mechanism

In chapter 4 and chapter 5 structure-reactivity relationships for glycosyl acceptors are established based on the stereoselectivity of these acceptors in reactions with two glycosyl donors. A quantitative expression of the nucleophilicity of acceptors remains challenging nonetheless. Although multiple attempts, both computational and experimental, have been undertaken,[3] an acceptor equivalent to the widely used relative reactivity values (RRVs) used to describe the reactivity of glycosyl donors[4-6] does not yet exist. In a recent paper by Wong, Wang and coworkers the "AKa" value was proposed as a measurement of acceptor reactivity. This value can be determined by measuring the relative reaction rate between an acceptor hydroxyl group and dihydropyran under acidic conditions in a flow system.[7]

A problem in competition experiments in which two acceptors are made to compete for one donor in a "real" glycosylation reaction, is the potential occurrence of four different products, that are formed via different pathways. The relative reactivity of an acceptor may depend on the mechanistic pathway, complicating the interpretation of the obtained values. To establish how relative acceptor reactivity depends on the mechanistic pathway, acceptor competition experiments can be probed using two different kinds of donors that react via different mechanisms on opposite ends of the S_N1/ S_N2 mechanism continuum (***Figure 6***). Glycosylation of donor **D1**, a tetra-benzoyl PTFAI galactosyl donor, proceed via a displacement of a dioxolenium ion in an S_N2-type mechanism (***Figure 6A***).[8-10] While glycosylations of donor **D2**, a DTBS protected galactopyranose PTFAI donor, follow an S_N1-type mechanism to form the α-product.[11] ***Figure 6C*** shows a selection of acceptors, described in chapter 4 and 5, for a set of competition experiments (**A1**-**A11**, ***Figure 6C***).

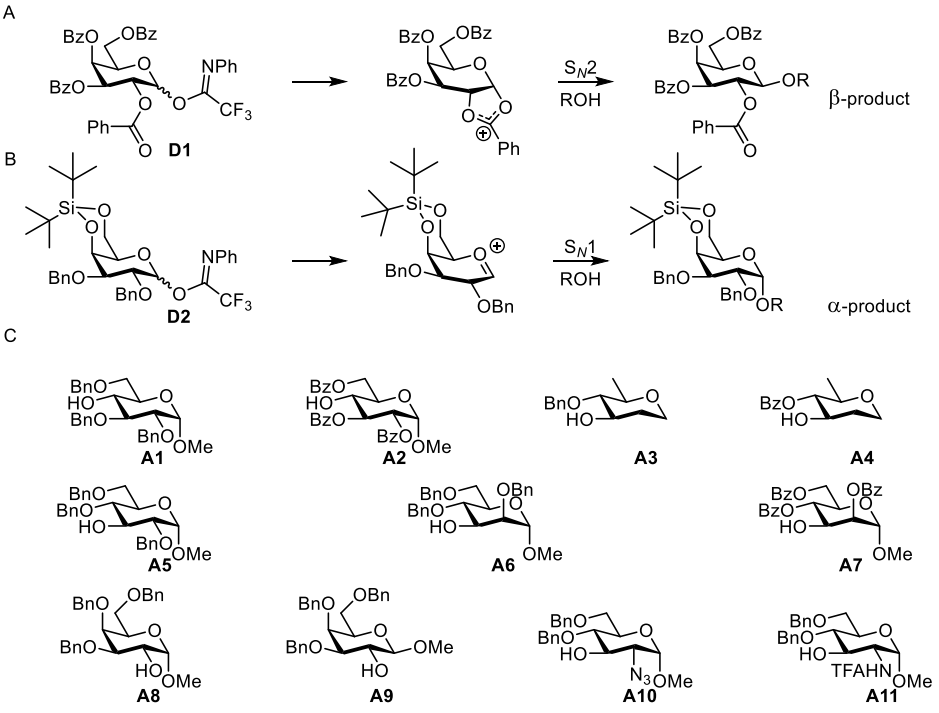


Figure 6: *A) reaction mechanism of donor D1; B) reaction mechanism of donor D2; C) acceptors tested in this work.*

For the competition experiments, a limiting amount of donor was reacted under *in situ* activation conditions with 2 equivalents of acceptor to ensure that an excess of each acceptor was always present. Due to the stereoselective nature of the reactions, only two products are formed in each reaction: product I and product II according to equation (1). The ratio between the two formed products can be used as a measure for the relative reactivity of two acceptors in a given mechanistic pathway.

$$\boldsymbol{Donor}\ (\mathbf{1}\ \boldsymbol{eq}) + \boldsymbol{Acceptor\ I}\ (\mathbf{2}\ \boldsymbol{eq}) + \boldsymbol{Acceptor\ II}\ (\mathbf{2}\ \boldsymbol{eq}) \rightarrow \boldsymbol{product\ I} + \boldsymbol{product\ II}\ (\mathbf{1})$$

The results of the competition experiments are summarised in ***Table 1***. These results show that with S_N2-donor **D1**, the relative reactivity of the acceptors parallels the structure-reactivity relations found in chapter 4 and chapter 5. Benzyl protected acceptors are more reactive than benzoyl protected acceptors (**A1**>**A2**; **A3**>**A4** and **A6**>**A7**), alcohols next to equatorial ethers are more reactive than alcohols next to axial ethers (**A5**>**A6** and **A9**>**A8**) and TFA groups are more disarming than azides (**A10**>**A11**).

With S_N1-donor **D2** on the other hand, benzoyl protected acceptors **A2** and **A4** appear to be more reactive than their benzylated counterparts **A1** and **A3**. Alcohols next to equatorial ethers appear to be (slightly) more reactive than alcohols next to axial ethers (**A5**>**A6**).

These results indicate that the relative nucleophilicity of the acceptors in glycosylation reactions proceeding with different mechanisms are governed by different factors. While the trend for the S_N2-substitutions seems to be correlated to the electron density on the acceptor alcohol oxygen, which decreases with increasing electron withdrawing capacity of the protecting/functional groups, the relative reactivity of the acceptors in the S_N1-substitutions correlate to the relative acidity of the alcohols, with the more acidic alcohols being more reactive in the substitution reactions. More acceptors need to be screened to shed further light on the relative acceptor reactivity under these conditions.

Table 1: *results of the competition experiments*

Entry	Donor	Acceptor I	Acceptor II	Product I:II	yield
1	**D1**	**A1**	**A2**	**>20:1**	**80%**
2	**D1**	**A3**	**A4**	**3.5:1**	**89%**
3	**D1**	**A5**	**A6**	**11:1**	**92%**
4	**D1**	**A6**	**A7**	**9:1**	**90%**
5	**D1**	**A8**	**A9**	**1:2**	**85%**
6	**D1**	**A10**	**A11**	**16:1**	**79%**
7	**D2**	**A1**	**A2**	**1:3.5**	**100%**
8	**D2**	**A3**	**A4**	**1:3.9**	**100%**
9	**D2**	**A5**	**A6**	**1.5:1**	**100%**

Conditions: 0.05M Donor in DCM 1 eq donor, 2 eq acceptor I, 2 eq acceptor II, 0.1 eq TMSOTf ***D1****: 0°C,* ***D2****: -40 °C to 0 °C.*

Synthesis of oligomers of the A. Baumannii LUH 5554 tetrasaccharide

Chapter 6 describes the synthesis of the tetrasaccharide repeating unit of the A. Baumannii LUH 5554 capsular polysaccharide. Since a relatively large amount of protected tetrasaccharide building block was obtained, the synthesis of oligomers is an attractive perspective. A strategy for this oligomer synthesis is depicted in ***Figure 7***. The tetrasaccharide building block is orthogonally protected at the reducing and the non-reducing end. This property can be used to generate tetramer donor and acceptor building blocks. For the synthesis of the acceptor, the levulinoyl ester can be removed selectively with H_2NNH_2-HOAc,[12] while the allyl group at the reducing end can be removed with catalytic $PdCl_2$ and turned into the imidate with conditions similar to those described in chapter 6 to generate a donor synthon. After glycosylation, the

obtained octasaccharide can then be treated with H_2NNH_2-HOAc to generate an acceptor, which can react with the tetrameric donor. This process can be repeated multiple times to get the octa-, dodeca-, hexadeca- and icosasaccharides.

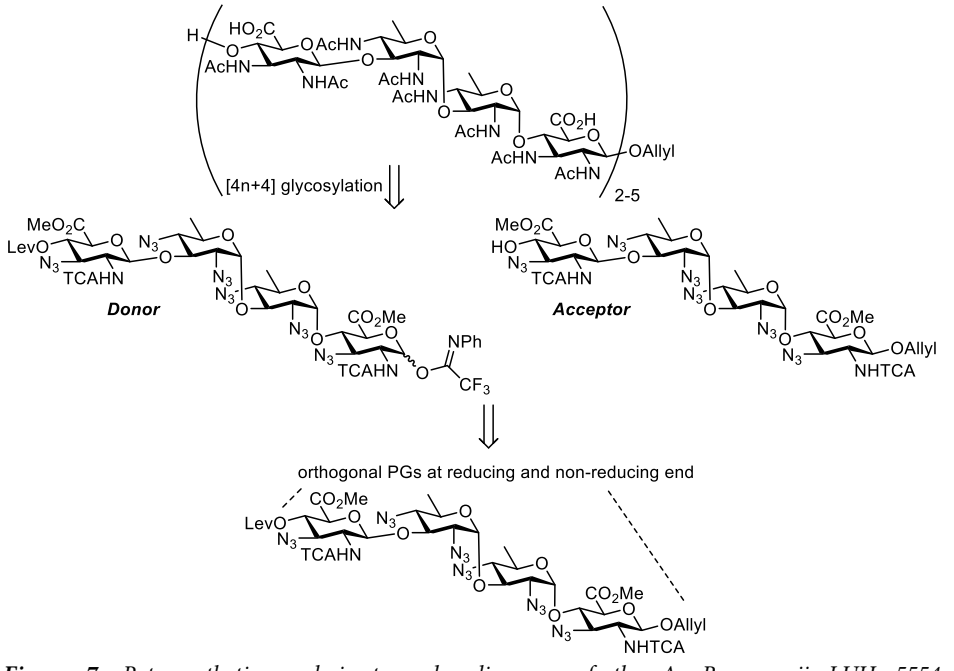


Figure 7: *Retrosynthetic analysis towards oligomers of the A. Baumannii LUH 5554 tetrasaccharide.*

With the obtained oligosaccharides the structure of the oligomers can be investigated by an approach combining NMR spectroscopy and computational chemistry. It will be of interest to see how the "lack of oxygen" substituents and the presence of all the acetamides affects the secondary structure of the saccharides. These structural studies can be followed by the immunological evaluation to investigate whether antibodies can be elicited by protein conjugates of the oligomers (the generation of which can be done exploiting the allyl group as a conjugation handle) that recognize the capsular polysaccharide, and if so, what the minimal epitope is.[13]

Experimental

General procedure I: Glycosylation with D1 or D2

Donor **D1** or **D2** (1 eq) and the acceptor (1-2 eq) were coevaporated twice with toluene and dissolved in DCM (0.05 M donor). 3A molecular sieves were added and the mixture was stirred for 30 min at RT, after which it was cooled to 0 °C and 0.1-0.2 eq of TMSOTf was added. After full conversion after the starting material, the reaction was quenched with sat. aq. $NaHCO_3$ and extracted with DCM. The organic phase was dried with $MgSO_4$ and concentrated under reduced pressure. The disaccharides were isolated by size-exclusion chromatography (Sephadex LH-20 1:1 DCM/MeOH)

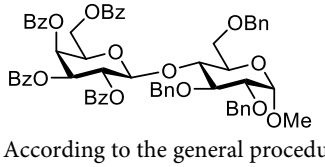
Competition experiments with D1

Donor **D1** (1 eq), acceptor I (2 eq) and acceptor II were coevaporated twice with toluene and dissolved in DCM (0.05 M donor). 3A molecular sieves were added and the mixture was stirred for 30 min at RT, after which it was cooled to 0 °C and 0.1 eq of TMSOTf was added. After full conversion after the starting material, the reaction was quenched with sat. aq. $NaHCO_3$ and extracted with DCM. The organic phase was dried with $MgSO_4$ and concentrated under reduced pressure. The mixture of disaccharide products was isolated by size-exclusion chromatography (Sephadex LH-20 1:1 DCM/MeOH). Selection of diagnostic peaks for determining the ratio of product I to product II was done by comparing the 1H-NMR spectrum of the mixture to the 1H-NMR spectra of both reference compounds.

Competition experiments with D2

Competition experiments with **D2** were done in a procedure similar to those for **D1**. The only difference is that TMSOTf was added at -40 °C, after which the reaction mixture was allowed to warm to 0 °C.

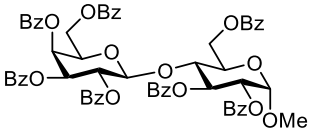
Disaccharide D1A1



According to the general procedure **I** from D1 and A1. Yield: 88 mg, 84 µmol, 84% α:β <1:20. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 – 8.00 (m, 2H), 7.94 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.87 – 7.83 (m, 2H), 7.79 – 7.74 (m, 2H), 7.58 – 7.52 (m, 2H), 7.52 – 7.45 (m, 5H), 7.44 – 7.34 (m, 9H), 7.33 – 7.20 (m, 9H), 7.19 – 7.14 (m, 1H), 5.86 (dd, *J* = 3.5, 1.1 Hz, 1H), 5.70 (dd, *J* = 10.4, 8.1 Hz, 1H), 5.30 (dd, *J* = 10.4, 3.5 Hz, 1H), 5.18 (d, *J* = 11.1 Hz, 1H), 4.91 (d, *J* = 11.1 Hz, 1H), 4.84 – 4.74 (m, 3H), 4.65 (d, *J* = 12.3 Hz, 1H), 4.58 (d, *J* = 3.7 Hz, 1H), 4.40 (dd, *J* = 11.2, 6.2 Hz, 1H), 4.32 (d, *J* = 12.2 Hz, 1H), 4.19 (dd, *J* = 11.2, 7.6 Hz, 1H), 4.03 (dd, *J* = 10.0, 9.0 Hz, 1H), 3.92 (td, *J* = 9.2, 8.3, 3.6 Hz, 2H), 3.70 (dd, *J* = 10.8, 2.8 Hz, 1H), 3.53 (ddd, *J* = 13.2, 10.8, 3.0 Hz, 2H), 3.44 (dd, *J* = 10.8, 1.9 Hz, 1H), 3.30 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 165.5, 165.5, 165.0, 139.5, 138.4, 137.9, 133.5, 133.4, 133.3, 129.9, 129.9, 129.8, 129.8, 129.7, 129.6, 129.2, 129.1, 128.9, 128.7, 128.5, 128.5, 128.4, 128.4, 128.2, 128.2, 127.9, 127.3, 127.3, 100.5, 98.6, 79.9, 78.7, 76.8, 75.3, 73.7, 73.7,

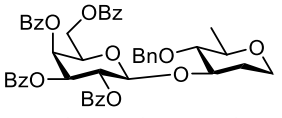
71.9, 71.0, 70.4, 69.6, 67.9, 67.6, 61.5, 55.5; HRMS: $[M+NH_4]^+$ calcd for $C_{62}H_{58}O_{15}NH_4$ 1060.41140, found 1060.41099

Disaccharide D1A2



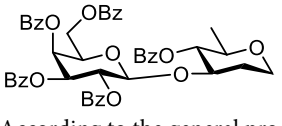
According to the general procedure **I** from D1 and A2. Yield: 75 mg, 70 µmol, 70%, α:β <1:20. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 – 8.03 (m, 2H), 8.01 – 7.96 (m, 8H), 7.90 – 7.87 (m, 2H), 7.76 – 7.71 (m, 2H), 7.62 (ddt, *J* = 8.8, 7.3, 1.3 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.50 – 7.27 (m, 13H), 7.24 – 7.16 (m, 5H), 6.09 (dd, *J* = 10.3, 9.0 Hz, 1H), 5.78 – 5.71 (m, 2H), 5.40 (dd, *J* = 10.3, 3.4 Hz, 1H), 5.24 (dd, *J* = 10.3, 3.7 Hz, 1H), 5.13 (d, *J* = 3.8 Hz, 1H), 4.92 (d, *J* = 7.9 Hz, 1H), 4.59 (dd, *J* = 12.1, 2.0 Hz, 1H), 4.53 (dd, *J* = 12.1, 4.2 Hz, 1H), 4.22 (dd, *J* = 10.1, 9.0 Hz, 1H), 4.13 (ddd, *J* = 10.1, 4.2, 1.9 Hz, 1H), 3.94 – 3.89 (m, 1H), 3.84 (dd, *J* = 11.2, 6.3 Hz, 1H), 3.76 (dd, *J* = 11.3, 7.1 Hz, 1H), 3.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 166.0, 165.7, 165.6, 165.4, 165.4, 164.9, 133.6, 133.6, 133.5, 133.5, 133.4, 133.3, 133.2, 130.1, 130.1, 130.0, 130.0, 129.9, 129.9, 129.9, 129.8, 129.8, 129.7, 129.7, 129.7, 129.7, 129.5, 129.2, 128.9, 128.8, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 101.2, 97.0, 76.4, 72.0, 72.0, 71.4, 70.5, 70.0, 68.4, 67.6, 62.5, 61.2, 55.6; HRMS: $[M+NH_4]^+$ calcd for $C_{62}H_{52}O_{18}NH_4$ 1102.34919, found 1102.34951.

Disaccharide D1A3



According to the general procedure **I** from D1 and A3. Yield: 80 mg, 99 µmol, 99%, α:β <1:20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.94 (m, 6H), 7.83 – 7.77 (m, 2H), 7.63 – 7.48 (m, 5H), 7.47 – 7.35 (m, 7H), 7.34 – 7.28 (m, 2H), 7.28 – 7.21 (m, 4H), 6.01 (dd, *J* = 3.4, 1.1 Hz, 1H), 5.83 (dd, *J* = 10.4, 7.8 Hz, 1H), 5.63 (dd, *J* = 10.4, 3.4 Hz, 1H), 5.19 (d, *J* = 10.6 Hz, 1H), 5.02 (d, *J* = 7.9 Hz, 1H), 4.73 – 4.59 (m, 2H), 4.39 (dd, *J* = 11.0, 7.4 Hz, 1H), 4.31 (ddd, *J* = 7.2, 5.9, 1.2 Hz, 1H), 4.05 (ddd, *J* = 11.4, 8.5, 5.2 Hz, 1H), 3.80 (ddd, *J* = 11.7, 4.9, 1.7 Hz, 1H), 3.33 – 3.19 (m, 2H), 3.05 (t, *J* = 8.9 Hz, 1H), 2.03 – 1.93 (m, 1H), 1.48 (tdd, *J* = 12.8, 11.4, 4.9 Hz, 1H), 1.27 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 165.7, 165.6, 165.3, 138.9, 133.6, 133.5, 133.4, 130.0, 129.9, 129.9, 129.7, 129.5, 129.2, 128.9, 128.8, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 127.7, 98.7, 82.5, 79.9, 76.0, 75.2, 71.9, 71.3, 70.4, 68.1, 64.9, 61.8, 31.1, 18.6; HRMS: $[M+NH_4]^+$ calcd for $C_{47}H_{44}O_{12}NH_4$ 818.31710, found 818.31713.

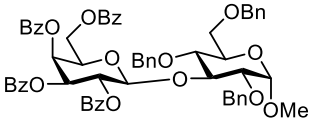
Disaccharide D1A4



According to the general procedure **I** from D1 and A4. Yield: 81 mg, 100 µmol, 100%, α:β = 1:10. Data for the β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 – 8.10 (m, 2H), 8.02 – 7.97 (m, 2H),

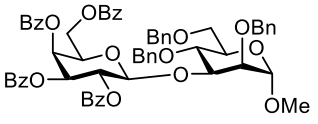
7.97 – 7.90 (m, 2H), 7.87 – 7.81 (m, 2H), 7.80 – 7.73 (m, 2H), 7.61 – 7.33 (m, 15H), 7.28 – 7.14 (m, 5H), 5.85 (dd, *J* = 3.4, 1.1 Hz, 1H), 5.62 (dd, *J* = 10.4, 7.7 Hz, 1H), 5.51 (dd, *J* = 10.4, 3.4 Hz, 1H), 4.96 (t, *J* = 9.2 Hz, 1H), 4.92 (d, *J* = 7.9 Hz, 1H), 4.18 (dd, *J* = 10.9, 6.0 Hz, 1H), 4.06 (dddd, *J* = 20.4, 9.1, 6.0, 2.5 Hz, 2H), 3.94 (dd, *J* = 10.9, 7.4 Hz, 1H), 3.89 (ddd, *J* = 11.9, 5.3, 2.0 Hz, 1H), 3.49 – 3.44 (m, 1H), 3.39 (td, *J* = 12.3, 2.2 Hz, 1H), 2.03 – 1.90 (m, 1H), 1.78 – 1.65 (m, 2H), 1.25 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 165.6, 165.4, 164.9, 133.5, 133.4, 133.3, 133.2, 133.1, 130.3, 129.9, 129.8, 129.8, 129.7, 129.7, 129.6, 129.4, 128.9, 128.8, 128.6, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.0, 100.3, 78.8, 75.7, 75.1, 71.8, 71.0, 70.1, 67.7, 65.2, 61.3, 31.7, 18.2; diagnostic peaks for the α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (dd, *J* = 3.4, 1.3 Hz, 1H), 5.89 (dd, *J* = 10.9, 3.4 Hz, 1H), 4.76 (t, *J* = 6.4 Hz, 1H), 4.43 (dd, *J* = 11.4, 4.7 Hz, 1H), 2.19 (dd, *J* = 12.8, 5.3 Hz, 1H), 1.13 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 98.3, 77.4, 76.8, 68.2, 63.0, 32.6; HRMS: $[M+NH_4]^+$ calcd for $C_{47}H_{42}O_{13}NH_4$ 832.29637, found 832.29592.

Disaccharide D1A5



According to the general procedure **I** from D1 and A5. Yield: 104 mg, 100 μmol, 100%, α:β <1:20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (td, *J* = 8.6, 1.4 Hz, 4H), 7.90 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.81 – 7.76 (m, 2H), 7.55 – 7.46 (m, 3H), 7.43 – 7.30 (m, 10H), 7.29 – 7.19 (m, 11H), 7.10 – 7.04 (m, 2H), 6.01 (dd, *J* = 3.5, 1.1 Hz, 1H), 5.88 (dd, *J* = 10.5, 8.0 Hz, 1H), 5.69 (dd, *J* = 10.5, 3.5 Hz, 1H), 5.51 (d, *J* = 8.0 Hz, 1H), 5.29 (d, *J* = 10.5 Hz, 1H), 4.67 – 4.53 (m, 4H), 4.49 – 4.43 (m, 2H), 4.41 – 4.28 (m, 3H), 4.18 (d, *J* = 12.3 Hz, 1H), 3.73 – 3.55 (m, 4H), 3.37 (dd, *J* = 9.6, 3.5 Hz, 1H), 3.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 165.7, 165.5, 165.4, 138.7, 138.0, 138.0, 133.4, 133.4, 133.3, 133.2, 130.0, 129.9, 129.8, 129.5, 129.5, 129.1, 128.9, 128.6, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 128.1, 128.1, 127.9, 127.8, 127.7, 101.1, 97.9, 80.9, 78.7, 75.4, 75.0, 73.9, 73.6, 71.8, 71.0, 70.7, 69.7, 68.5, 68.2, 61.6, 55.1; HRMS: $[M+NH_4]^+$ calcd for $C_{62}H_{58}O_{15}NH_4$ 1060.41140, found 1060.41118.

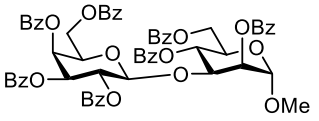
Disaccharide D1A6



According to the general procedure **I** from D1 and A6. Yield: 96 mg, 92 μmol, 92%, α:β <1:20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (ddd, *J* = 8.5, 3.6, 1.4 Hz, 4H), 7.92 – 7.87 (m, 2H), 7.80 – 7.74 (m, 2H), 7.60 – 7.50 (m, 2H), 7.48 – 7.13 (m, 23H), 7.03 (dd, *J* = 6.8, 2.7 Hz, 2H), 5.97 (dd, *J* = 3.5, 1.1 Hz, 1H), 5.90 (dd, *J* = 10.5, 7.9 Hz, 1H), 5.60 (dd, *J* = 10.4, 3.4 Hz, 1H), 5.12 (d, *J* = 10.9 Hz, 1H), 4.99 (d, *J* = 7.9 Hz, 1H), 4.67 (d, *J* = 2.1 Hz, 1H), 4.62 (d, *J* = 12.1 Hz, 1H), 4.56 – 4.47 (m, 3H), 4.42 – 4.28 (m, 4H), 4.25 – 4.18 (m, 1H), 4.01 – 3.91 (m, 1H), 3.77 – 3.70 (m, 4H), 3.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 165.7, 165.6, 165.2, 138.9, 138.5, 138.1, 133.6, 133.4, 133.3, 130.0, 129.9, 129.9, 129.8, 129.5, 129.3, 129.1, 128.8, 128.7, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.5, 127.5, 99.5, 98.8, 79.1, 75.6, 74.7, 73.7, 73.4, 72.9, 72.0, 71.9, 71.4,

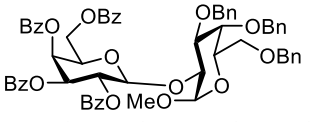
70.4, 69.4, 68.1, 61.7, 54.8; HRMS: $[M+NH_4]^+$ calcd for $C_{62}H_{58}O_{15}NH_4$ 1060.41140, found 1060.41145.

Disaccharide D1A7



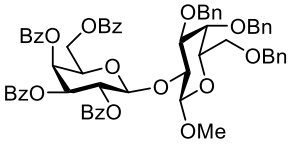
According to the general procedure **I** from D1 and A7. Yield: 86 mg, 79 µmol, 79%, α:β = 1:1. Data reported for a 1:1 mixture of anomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 – 8.21 (m, 2H), 8.19 – 8.13 (m, 3H), 8.11 – 7.97 (m, 12H), 7.75 – 7.71 (m, 2H), 7.70 – 7.67 (m, 2H), 7.66 – 7.60 (m, 6H), 7.59 – 7.50 (m, 9H), 7.48 – 7.40 (m, 12H), 7.38 – 7.29 (m, 13H), 7.22 – 7.05 (m, 13H), 6.02 (dd, *J* = 3.4, 1.4 Hz, 1H), 5.92 – 5.84 (m, 3H), 5.79 (dd, *J* = 10.1, 3.3 Hz, 1H), 5.72 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.64 – 5.59 (m, 3H), 5.47 (dd, *J* = 10.3, 3.3 Hz, 1H), 5.37 (dd, *J* = 3.5, 1.9 Hz, 1H), 5.02 – 4.96 (m, 2H), 4.93 (dd, *J* = 6.9, 1.8 Hz, 2H), 4.69 – 4.61 (m, 4H), 4.60 – 4.53 (m, 2H), 4.45 (dd, *J* = 12.1, 4.7 Hz, 1H), 4.41 – 4.31 (m, 3H), 4.29 – 4.22 (m, 2H), 4.17 (ddd, *J* = 10.1, 5.2, 3.0 Hz, 1H), 3.97 (dd, *J* = 10.9, 6.9 Hz, 1H), 3.46 (s, 3H), 3.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 166.2, 166.2, 166.1, 166.0, 165.6, 165.6, 165.5, 165.4, 165.1, 164.9, 164.5, 133.6, 133.6, 133.4, 133.4, 133.3, 133.2, 133.1, 133.0, 132.8, 130.3, 130.0, 130.0, 129.9, 129.9, 129.8, 129.8, 129.8, 129.7, 129.6, 129.5, 129.5, 129.4, 129.2, 128.8, 128.8, 128.7, 128.7, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 99.6, 98.6, 98.5, 98.3, 74.4, 74.0, 72.0, 71.8, 71.1, 70.0, 69.4, 69.4, 69.0, 68.9, 68.9, 68.4, 68.1, 68.0, 67.7, 67.5, 63.3, 63.1, 61.6, 55.6, 55.3; HRMS: $[M+NH_4]^+$ calcd for $C_{62}H_{52}O_{18}NH_4$ 1102.34919, found 1102.34904.

Disaccharide D1A8



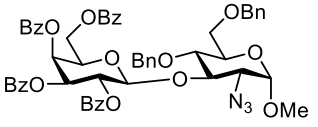
According to the general procedure **I** from D1 and A8. Yield: 90 mg, 86 µmol, 86%, α:β <1:20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.09 (m, 2H), 8.02 – 7.97 (m, 2H), 7.87 – 7.82 (m, 2H), 7.81 – 7.74 (m, 2H), 7.64 – 7.57 (m, 1H), 7.54 – 7.45 (m, 3H), 7.43 – 7.35 (m, 4H), 7.34 – 7.15 (m, 21H), 7.08 – 7.03 (m, 2H), 6.04 – 5.95 (m, 2H), 5.59 (dd, *J* = 10.3, 3.5 Hz, 1H), 5.13 (d, *J* = 8.0 Hz, 1H), 5.07 (d, *J* = 3.6 Hz, 1H), 4.84 (d, *J* = 11.5 Hz, 1H), 4.61 (dd, *J* = 11.3, 6.7 Hz, 1H), 4.46 (dt, *J* = 11.6, 5.7 Hz, 4H), 4.41 – 4.32 (m, 3H), 4.28 (dd, *J* = 10.2, 3.6 Hz, 1H), 3.91 – 3.82 (m, 2H), 3.76 (dd, *J* = 3.1, 1.3 Hz, 1H), 3.51 (dd, *J* = 6.4, 1.9 Hz, 2H), 3.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 165.7, 165.7, 165.3, 138.7, 138.1, 133.7, 133.4, 133.3, 133.1, 130.2, 129.9, 129.8, 129.4, 129.4, 129.1, 128.8, 128.7, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 127.8, 127.7, 127.3, 127.2, 103.3, 99.8, 80.0, 77.2, 76.0, 74.9, 73.5, 73.3, 72.2, 71.6, 69.9, 69.2, 69.1, 68.3, 62.4, 55.6; HRMS: $[M+NH_4]^+$ calcd for $C_{62}H_{58}O_{15}NH_4$ 1060.41140, found 1060.41120.

Disaccharide D1A9



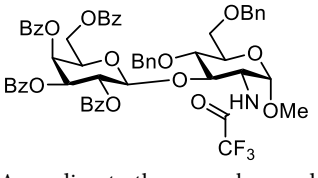
According to the general procedure **I** from D1 and A9. Yield: 94 mg, 90 μmol, 90%, α:β <1:20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 – 8.08 (m, 2H), 8.03 – 7.98 (m, 2H), 7.89 – 7.84 (m, 2H), 7.84 – 7.78 (m, 2H), 7.65 – 7.58 (m, 1H), 7.57 – 7.45 (m, 3H), 7.44 – 7.36 (m, 4H), 7.34 – 7.15 (m, 19H), 7.07 (ddd, *J* = 5.7, 2.7, 1.5 Hz, 2H), 6.03 (dd, *J* = 3.5, 1.1 Hz, 1H), 5.89 (dd, *J* = 10.4, 8.1 Hz, 1H), 5.55 (dd, *J* = 10.4, 3.4 Hz, 1H), 5.34 (d, *J* = 8.1 Hz, 1H), 4.72 (dd, *J* = 10.9, 5.9 Hz, 1H), 4.55 – 4.45 (m, 3H), 4.44 – 4.31 (m, 6H), 4.24 (d, *J* = 12.0 Hz, 1H), 4.07 (dd, *J* = 9.7, 7.6 Hz, 1H), 3.59 (d, *J* = 2.8 Hz, 1H), 3.53 (s, 4H), 3.49 – 3.40 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 165.7, 165.5, 138.6, 138.3, 137.9, 133.6, 133.4, 133.3, 133.0, 130.2, 129.9, 129.9, 129.8, 129.7, 129.5, 129.2, 129.0, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.6, 127.5, 104.0, 102.2, 80.7, 80.3, 73.9, 73.5, 73.4, 73.2, 72.3, 71.7, 70.9, 68.9, 68.3, 62.2, 57.3; HRMS: $[M+NH_4]^+$ calcd for $C_{62}H_{58}O_{15}NH_4$ 1060.41140, found 1060.41110.

Disaccharide D1A10



According to the general procedure **I** from D1 and A10. Yield: Yield: 88 mg, 90 μmol, 90%, α:β <1:20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.97 (m, 4H), 7.95 – 7.90 (m, 2H), 7.82 – 7.75 (m, 2H), 7.57 – 7.48 (m, 4H), 7.41 (dt, *J* = 10.1, 7.6 Hz, 6H), 7.35 – 7.27 (m, 9H), 7.26 – 7.18 (m, 6H), 5.99 (d, *J* = 3.4 Hz, 1H), 5.84 (dd, *J* = 10.4, 7.9 Hz, 1H), 5.65 (dd, *J* = 10.4, 3.4 Hz, 1H), 5.28 (d, *J* = 7.9 Hz, 1H), 5.23 (d, *J* = 10.7 Hz, 1H), 4.79 (d, *J* = 3.5 Hz, 1H), 4.60 – 4.51 (m, 3H), 4.48 (d, *J* = 12.1 Hz, 1H), 4.37 – 4.24 (m, 3H), 3.78 – 3.71 (m, 2H), 3.70 – 3.60 (m, 2H), 3.39 (s, 3H), 3.26 (dd, *J* = 10.2, 3.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 165.6, 165.6, 165.5, 138.5, 137.9, 133.5, 133.4, 133.4, 133.3, 129.9, 129.9, 129.9, 129.5, 129.4, 129.1, 128.9, 128.7, 128.5, 128.5, 128.5, 128.4, 128.0, 127.9, 127.7, 101.1, 98.5, 78.1, 75.6, 75.1, 73.6, 71.8, 71.3, 70.4, 70.3, 68.4, 68.1, 63.6, 61.5, 55.3; HRMS: $[M+NH_4]^+$ calcd for $C_{55}H_{51}N_3O_{14}NH_4$ 995.37093, found 995.37058.

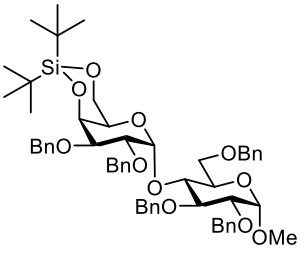
Disaccharide D1A11



According to the general procedure **I** from D1 and A10. Yield: 80 mg, 76 μmol, 76%, α:β <1:20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dt, *J* = 8.4, 1.6 Hz, 2H), 7.95 – 7.87 (m, 4H), 7.77 – 7.71 (m, 2H), 7.61 – 7.25 (m, 19H), 7.23 – 7.15 (m, 5H), 6.59 – 6.48 (m, 1H), 5.98 (dd, *J* = 3.5, 1.0 Hz, 1H), 5.80 (dd, *J* = 10.4, 7.8 Hz, 1H), 5.52 (dd, *J* = 10.4, 3.4 Hz, 1H), 5.20 (d, *J* = 10.9 Hz, 1H), 5.03 (d, *J* = 7.9 Hz, 1H), 4.66 – 4.56 (m, 4H), 4.50 (d, *J* = 12.1 Hz, 1H), 4.36 – 4.22 (m, 4H), 3.78 – 3.70 (m,

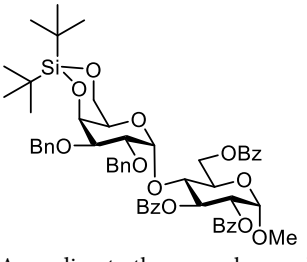
3H), 3.68 – 3.63 (m, 1H), 3.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 165.8, 165.6, 165.6, 138.4, 138.0, 133.6, 133.5, 133.4, 133.4, 130.0, 130.0, 129.9, 129.9, 129.8, 129.5, 129.1, 129.0, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 127.9, 127.9, 127.8, 127.8, 100.8, 97.8, 77.3, 75.7, 75.0, 73.6, 71.8, 71.3, 70.8, 70.3, 68.5, 67.9, 61.4, 55.2, 53.3; HRMS: $[M+NH_4]^+$ calcd for $C_{57}H_{52}F_3NO_{15}NH_4$ 1065.36273, found 1065.36259.

Disaccharide D2A1



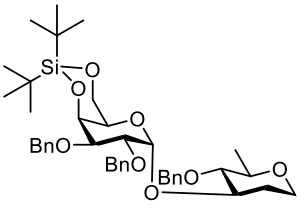
According to the general procedure **I** from D2 and A1. Yield: 95 mg, 100 μmol, 100%, α:β >20:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.15 (m, 25H), 5.75 (d, *J* = 3.9 Hz, 1H), 5.04 (d, *J* = 11.2 Hz, 1H), 4.78 (dd, *J* = 11.7, 7.9 Hz, 3H), 4.73 – 4.67 (m, 2H), 4.66 – 4.57 (m, 3H), 4.52 (d, *J* = 12.1 Hz, 1H), 4.44 (d, *J* = 12.2 Hz, 1H), 4.37 – 4.32 (m, 1H), 4.10 (dd, *J* = 9.5, 8.5 Hz, 1H), 4.04 – 3.95 (m, 2H), 3.94 – 3.87 (m, 2H), 3.78 (dd, *J* = 12.4, 2.0 Hz, 1H), 3.75 – 3.66 (m, 2H), 3.59 (ddd, *J* = 12.8, 10.1, 2.8 Hz, 2H), 3.50 (d, *J* = 5.2 Hz, 1H), 3.46 – 3.37 (m, 4H), 1.08 (s, 9H), 1.01 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 138.7, 138.3, 138.1, 138.0, 128.5, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 127.8, 127.8, 127.7, 127.6, 127.6, 127.3, 127.2, 97.9, 96.8, 82.2, 80.4, 77.8, 74.5, 74.0, 73.6, 73.6, 73.6, 71.1, 71.0, 70.9, 69.4, 69.2, 67.7, 66.9, 55.2, 27.7, 27.4, 23.4, 20.8; HRMS: $[M+NH_4]^+$ calcd for $C_{56}H_{70}O_{11}SiNH_4$ 964.50256, found 964.50209.

Disaccharide D2A2



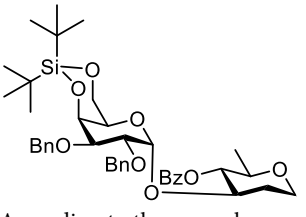
According to the general procedure **I** from D2 and A2. Yield: 99 mg, 100 μmol, 100%, α:β >20:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.05 (m, 2H), 8.00 (dt, *J* = 8.4, 1.2 Hz, 4H), 7.63 – 7.57 (m, 1H), 7.53 – 7.44 (m, 5H), 7.43 – 7.26 (m, 10H), 7.11 (s, 5H), 6.19 (dd, *J* = 10.0, 8.5 Hz, 1H), 5.22 – 5.09 (m, 3H), 4.70 – 4.58 (m, 3H), 4.51 (dd, *J* = 12.0, 3.9 Hz, 1H), 4.44 – 4.36 (m, 2H), 4.33 – 4.23 (m, 2H), 4.21 (d, *J* = 11.9 Hz, 1H), 3.92 (d, *J* = 1.8 Hz, 2H), 3.83 – 3.71 (m, 2H), 3.57 (q, *J* = 1.5 Hz, 1H), 3.41 (s, 3H), 0.97 (s, 9H), 0.78 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 166.2, 165.6, 139.0, 138.1, 133.5, 133.4, 133.1, 130.1, 130.0, 130.0, 130.0, 129.9, 129.8, 129.7, 129.7, 129.2, 128.7, 128.6, 128.5, 128.5, 128.5, 128.4, 128.3, 127.7, 127.5, 98.5, 96.9, 77.6, 73.2, 72.9, 72.8, 72.6, 72.5, 71.2, 71.1, 68.5, 68.4, 67.0, 63.5, 55.4, 27.7, 27.2, 23.4, 20.6; HRMS: $[M+NH_4]^+$ calcd for $C_{56}H_{64}O_{14}SiNH_4$ 1006.44036, found 1006.44041.

Disaccharide D2A3



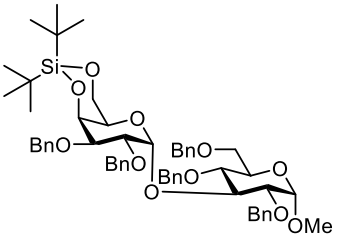
According to the general procedure **I** from D2 and A3. Yield: 71 mg, 100 µmol, 100%, α:β >20:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 2H), 7.34 – 7.28 (m, 2H), 7.27 – 7.22 (m, 8H), 7.21 – 7.17 (m, 3H), 5.13 (d, *J* = 11.4 Hz, 1H), 5.07 (d, *J* = 3.6 Hz, 1H), 4.79 (dd, *J* = 12.0, 5.5 Hz, 2H), 4.69 (dd, *J* = 14.4, 12.0 Hz, 2H), 4.61 – 4.54 (m, 2H), 4.23 (dd, *J* = 12.4, 2.1 Hz, 1H), 4.06 (dd, *J* = 12.4, 1.7 Hz, 1H), 3.99 (dd, *J* = 10.2, 3.6 Hz, 1H), 3.88 (dd, *J* = 10.2, 2.9 Hz, 1H), 3.82 (ddd, *J* = 11.8, 4.9, 1.6 Hz, 1H), 3.78 – 3.68 (m, 2H), 3.34 (td, *J* = 12.2, 2.0 Hz, 1H), 3.26 (dq, *J* = 9.2, 6.1 Hz, 1H), 3.03 (t, *J* = 8.9 Hz, 1H), 2.01 (ddt, *J* = 12.9, 5.3, 1.5 Hz, 1H), 1.74 – 1.62 (m, 1H), 1.22 (d, *J* = 6.1 Hz, 3H), 1.06 (s, 9H), 0.97 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 138.5, 128.4, 128.4, 128.3, 128.0, 127.6, 127.6, 127.6, 127.4, 100.3, 83.5, 82.0, 77.6, 76.2, 74.9, 74.0, 73.8, 71.1, 70.7, 67.8, 67.2, 65.3, 33.8, 27.8, 27.4, 23.6, 20.8, 18.7; HRMS: $[M+NH_4]^+$ calcd for $C_{41}H_{56}O_8SiNH_4$ 722.40827, found 722.40806.

Disaccharide D2A4



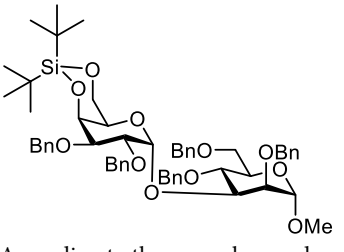
According to the general procedure **I** from D2 and A4. Yield: 72 mg, 100 µmol, 100%, α:β >20:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 7.99 (m, 2H), 7.55 – 7.47 (m, 1H), 7.40 – 7.27 (m, 8H), 7.17 – 7.11 (m, 3H), 7.01 – 6.94 (m, 2H), 5.02 (t, *J* = 9.3 Hz, 1H), 4.88 (t, *J* = 1.5 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 11.9 Hz, 1H), 4.43 (t, *J* = 1.3 Hz, 1H), 4.31 (d, *J* = 12.2 Hz, 1H), 4.23 – 4.15 (m, 2H), 4.05 (dd, *J* = 12.4, 1.7 Hz, 1H), 3.99 – 3.93 (m, 1H), 3.89 (ddd, *J* = 11.3, 9.1, 5.2 Hz, 1H), 3.75 (t, *J* = 1.4 Hz, 2H), 3.70 (q, *J* = 1.6 Hz, 1H), 3.54 – 3.39 (m, 2H), 2.03 (ddt, *J* = 13.0, 4.1, 1.9 Hz, 1H), 1.86 (ddt, *J* = 12.8, 11.3, 6.3 Hz, 1H), 1.23 (d, *J* = 6.2 Hz, 3H), 1.02 (s, 9H), 0.89 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 139.2, 138.6, 133.0, 130.4, 129.9, 128.4, 128.3, 128.1, 128.1, 127.7, 127.4, 127.3, 99.7, 78.2, 77.8, 76.6, 75.3, 73.3, 72.8, 71.4, 71.1, 68.0, 67.2, 65.5, 33.3, 27.8, 27.3, 23.5, 20.7, 18.2; HRMS: $[M+NH_4]^+$ calcd for $C_{41}H_{54}O_9SiNH_4$ 736.38754, found 736.38728.

Disaccharide D2A5



According to the general procedure **II** from D2 and A5. Yield: 93 mg, 98 µmol, 98%, α:β >20:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.42 (m, 2H), 7.36 – 7.19 (m, 17H), 7.18 – 7.08 (m, 5H), 7.04 – 6.98 (m, 2H), 5.46 (d, *J* = 3.6 Hz, 1H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.81 (d, *J* = 11.6 Hz, 1H), 4.76 – 4.71 (m, 2H), 4.65 (dd, *J* = 11.7, 4.4 Hz, 2H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 10.8 Hz, 1H), 4.42 (d, *J* = 12.0 Hz, 1H), 4.38 (dd, *J* = 11.2, 4.2 Hz, 2H), 4.26 (dd, *J* = 9.8, 8.7 Hz, 1H), 4.22 (dd, *J* = 3.0, 1.1 Hz, 1H), 3.99 – 3.94 (m, 2H), 3.91 (dd, *J* = 12.6, 1.6 Hz, 1H), 3.86 (dd, *J* = 10.1, 2.9 Hz, 1H), 3.78 (dd, *J* = 10.0, 8.7 Hz, 1H), 3.72 – 3.68 (m, 1H), 3.65 (dd, *J* = 10.6, 3.3 Hz, 1H), 3.61 – 3.50 (m, 3H), 3.34 (s, 3H), 1.00 (s, 9H), 0.93 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 138.4, 138.3, 138.0, 137.9, 128.6, 128.5, 128.5, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.8, 127.6, 127.5, 127.4, 127.1, 97.9, 97.5, 79.1, 79.0, 78.1, 74.5, 74.1, 73.7, 73.6, 73.5, 73.1, 70.8, 70.6, 69.9, 68.5, 67.1, 66.9, 55.1, 27.8, 27.4, 23.5, 20.7; HRMS: $[M+NH_4]^+$ calcd for $C_{56}H_{70}O_{11}SiNH_4$ 964.50256, found 964.50252.

Disaccharide D2A6



According to the general procedure **II** from D2 and A6. Yield: 87 mg, 92 µmol, 92%, α:β >20:1.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 6.86 (m, 25H), 5.09 (d, *J* = 11.4 Hz, 1H), 5.05 (d, *J* = 3.5 Hz, 1H), 4.84 (d, *J* = 1.9 Hz, 1H), 4.78 – 4.68 (m, 4H), 4.66 – 4.56 (m, 2H), 4.50 (d, *J* = 12.1 Hz, 1H), 4.40 (dd, *J* = 11.9, 10.2 Hz, 2H), 4.30 (d, *J* = 2.9 Hz, 1H), 4.06 (dd, *J* = 9.2, 3.2 Hz, 1H), 3.97 – 3.89 (m, 3H), 3.88 – 3.80 (m, 2H), 3.75 (ddd, *J* = 12.9, 5.2, 2.9 Hz, 1H), 3.72 – 3.65 (m, 3H), 3.42 (s, 1H), 3.36 (s, 3H), 1.02 (s, 9H), 0.93 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 139.1, 138.6, 138.5, 138.4, 128.4, 128.4, 128.3, 128.2, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.3, 100.4, 97.7, 79.5, 77.4, 77.4, 74.6, 74.6, 74.0, 73.5, 73.4, 71.9, 71.3, 71.0, 70.7, 69.5, 67.7, 67.2, 55.0, 27.8, 27.4, 23.5, 20.7; HRMS: $[M+NH_4]^+$ calcd for $C_{56}H_{70}O_{11}SiNH_4$ 964.50256, found 964.50245.

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