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Selective Acetylation of Non-anomeric Groups of per-*O*-Trimethylsilylated Sugars

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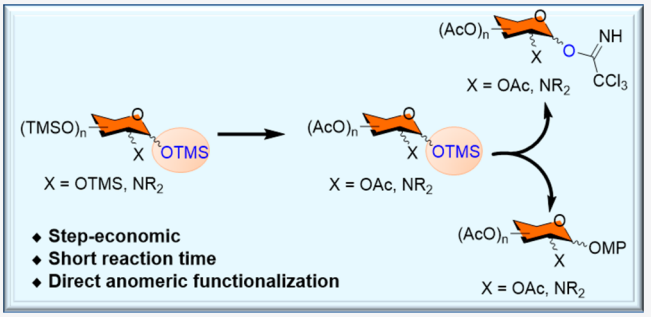
ABSTRACT: Selective modification of the hydroxyl groups of sugars has been a long-standing challenge due to their proximate relative reactivity. Herein, we report a TMSOTf-catalyzed selective acetylation of the non-anomeric hydroxyl groups of several per-*O*-TMS-protected sugar substrates while leaving their anomeric group unaffected. In addition to standing versatile by itself, the anomeric *O*-TMS group left intact can be functionalized to afford key sugar precursors such as imidate donors, which could otherwise be synthesized via a stepwise anomeric deprotection-functionalization procedure.



Apart from the obvious roles of carbohydrates as energy sources and structural components, their involvement in molecular recognition events attributed to their prevalence at the surface of cells[1] has long been the focus of scientific curiosity questing to decipher the mechanism of their functions. Although the most ubiquitous in nature, accessing carbohydrates of interest in pure form and adequate quantity for biological evaluation has been almost formidable mainly due to their structural complexity and diversity.[2] In this regard, synthesis has become one of the most reliable ways of obtaining the target molecules of biological values. Nevertheless, the multifunctionality of carbohydrates also poses invincible difficulties during synthesis. The hydroxyl groups that are not required to make subsequent reaction should be masked with appropriate protecting groups which can easily be removed when needed. Meanwhile, this circuitous protection-deprotection process during the preparation of carbohydrate building blocks remains a tedious task in organic synthesis demanding innovative strategies.[3,4]

In the customary practice, the installation of carbohydrate protecting groups often begins with the modification of the anomeric hydroxyl group owing to the unique reactivity features rendered by its hemiacetal functionality.[5] As the anomeric center is also the site of glycosidic linkage formation in subsequent glycosylation reactions, its alteration should be made prudently based on the synthetic design. In this case, if the building block of interest is a glycosyl donor, the anomeric center should be equipped with a leaving group, whereas, if an acceptor is needed for glycosylations other than 1,1′-glycosidic linkage formation, the anomeric hydroxyl moiety should be masked with a protecting group compatible with ensuing reaction conditions.[6] Because of their ease of preparation and good stability, per-acetylated sugars are commonly used as precursors for such kinds of adjustments.[7] The majority of per-acetylation reactions are carried out using excess acetic anhydride (Ac_2O) as an acetylating agent in the presence of pyridine[8] or its derivatives like 4-(dimethylamino)pyridine[9,10] as catalysts, though plenty of other protocols are also available.[11] In order to address the issue of regioselectivity in acetylations, a number of attempts have been made over the past several years involving reactions by both chemical[12−16] and enzymatic[17,18] methods. However, these reactions utilize building blocks where the anomeric hydroxyl functionality is either already protected or free but is one of the target groups in the acetylation process. In the meantime, when the anomeric center is required to undergo base-mediated nucleophilic reactions such as during the preparation of imidate donors and *tert*-butyldimethylsilyl functionalized acceptors,[19,20] anomeric deprotection is needed, leading to the incessant protecting group manipulation procedure.

Ascribed to their role as temporary masking agents and enhancing the solubility of sugar building blocks,[3] per-*O*-trimethylsilylated (per-*O*-TMS-protected) sugars—with a different anomeric substituent such as thiotoluene (STol), thiophenyl (SPh), or methoxy (OMe) groups—have been used as transient precursors in numerous carbohydrate synthetic protocols. Hung and co-workers used per-*O*-silylated sugars to construct various orthogonally protected carbohydrate building blocks via a regioselective sequential one-pot

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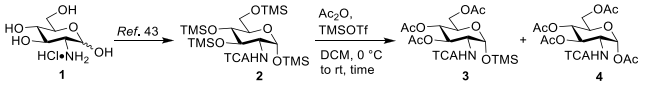
protection procedure under trimethylsilyl trifluoromethanesulfonate (TMSOTf) catalysis.[21−23] Beau's group also followed a similar approach but under different catalytic conditions,[24,25] showing the indispensable role of TMS-protected sugars as starting materials for multiple transformations. Likewise, fully *O*-silylated (i.e., including the anomeric center) sugars have been widely applied in different sugar derivatizations where the anomeric *O*-TMS is mainly the reaction site. For instance, Gervay-Hague's group used this strategy to obtain per-*O*-silylated glycosyl iodides which were employed in subsequent transformations,[26−28] while Wang and co-workers followed a similar approach for microwave-assisted synthesis of 1,6-anhydrosugars via intramolecular anomeric protection and to obtain orthogonally protected thioglycoside donors.[29,30] On the other hand, regioselective modifications of per-*O*-TMS-protected sugars without affecting the anomeric *O*-TMS group have also been reported.[31,32] However, further manipulations through the ordinary protection-deprotection pathways are inevitable in order to access 1-*O*-TMS glycosyl precursors which can either be directly used in ensuing glycosylation reactions or be transformed into other leaving groups such as imidates.

Over the past several years, a plethora of reports have shown the synthetic versatility of 1-*O*-TMS-equipped sugars in which they have been employed as either glycosyl donors or acceptors in the construction of various carbohydrate scaffolds.[33−41] Unfortunately, the preparation of these building blocks from per-acetylated starting materials through the step-uneconomic anomeric deprotection-silylation procedures—requiring high energy and time for workup and purification—has limited their synthetic utility. On the other hand, 1-*O*-TMS per-acetyl sugars can still be synthesized in two steps (anomeric deacetylation to obtain a hemiacetal and silylation) from commercially available per-acetyl precursors. However, per-acetyl sugars are more expensive and may not be commercially available compared to the free sugar starting materials. Moreover, the silylation of a free anomeric hydroxyl group needs tremendous effort to optimize the conditions for the stereoselective formation of the new bond.[42] Herein, we report an expeditious synthesis of per-acetylated 1-*O*-TMS containing sugars through TMSOTf-catalyzed acetylation of the non-anomeric hydroxyl groups of per-*O*-TMS-protected carbohydrates while leaving their 1-*O*-TMS group intact with the retention of its precedent stereochemistry. Thus, our established methodology can be applied to speed up chemical glycosylation by alleviating the cumbersome protection-deprotection challenges.

We commenced our investigation with the synthesis of a per-*O*-silylated amino sugar derivative of commercially available D-glucosamine hydrochloride (**1**) based on our reported method in two steps.[43] The resulting compound **2** was then treated with various equivalents of Ac_2O under TMSOTf catalysis as shown in Table 1. The formation of the fully acetylated compound **4** as the sole product required 20 h under treatment of substrate **2** with 10 equiv of Ac_2O and 0.4 equiv of TMSOTf (added in two portions), resulting in 86% yield (Table 1, entry 1). Close scrutiny of the reaction progress by thin layer chromatography (TLC) under the same reaction condition showed the full consumption of the starting material and the formation of two major spots after stirring for 4 h. Neutralizing the reaction mixture with triethyl amine (Et_3N), followed by workup, gave compounds **3** (35%) and **4** (55%) (Table 1, entry 2) as verified with three bonds separated

Table 1. Optimization of Selective Acetylation Condition



				yield (%)	
entry	Ac_2O (equiv)	TMSOTf (equiv)	time (h)	**3**	**4**
1	10	0.4	20	[a]	86
2	10	0.4	4	35	55
3	6	0.2	1	91	2
4	4	0.2	2	88	[a]

[a]No product isolated.

HMBC correlations (Figure S1). Encouraged by the unprecedented formation of 1-*O*-TMS-equipped product **3**, we intended to optimize the acetylation reaction condition so as to obtain an improved yield. Gratifyingly, sagacious reduction of the Ac_2O and TMSOTf equivalences to 6 and 0.2, respectively, and quenching the reaction after 1 h gave **3** in an excellent yield (91%) with a trace amount of **4** (2%) (Table 1, entry 3). Further decrement of Ac_2O to 4 equiv did not significantly alter the yield of **3** but took longer reaction time, and thus, 6 equiv of Ac_2O and 0.2 equiv of TMSOTf were taken as the optimum conditions for further acetylation attempts.

Our finding reveals that the non-anomeric hydroxyl groups of per-*O*-TMS sugar **2** are acetylated, leaving the anomeric *O*-TMS group unaffected. On the other hand, Gervay-Hague observed that the anomeric *O*-TMS group of *N*-acetamido-protected sugar analogue of **2** was acetylated next to the primary *O*-TMS (6-*O*-TMS) group, thereby obtaining 1,6-di-*O*-acetylated species, while the 3- and 4-*O*-TMS groups remained intact.[12]

With this discovery and the optimized selective acetylation condition at our disposal, we investigated the viability of the methodology in other per-*O*-TMS-protected amino-sugars prepared in accordance with reported silylation and *N*-functionalization procedures.[43] To this end, commercially available D-glucosamine (**1**), D-galactosamine (**5**), and D-mannosamine (**6**) hydrochloride monosaccharides were used to prepare per-*O*-TMS substrates **7**, **8**, and **9**, respectively. These easily accessed per-*O*-silylated sugars were subsequently subjected to our established selective acetylation condition, and the results are shown in Table 2. To our delight, the respective 1-*O*-TMS acetylated products **10**−**12** (Table 2, entries 1−3) were obtained in good yields within 1 h reaction time, proving that the anomeric *O*-TMS group is still the least reactive regardless of the type and the conformation of the amino substituent at C-2. Likewise, the use of benzoic anhydride (Bz_2O) as an acylating agent could also provide per-benzoylated 1-*O*-TMS product **13** in a moderate yield after a longer reaction time despite the low reactivity of the bulky Bz_2O (Table 2, entry 4).[44,45] On the other hand, treatment of the per-*O*-TMS substrate **2** with acetyl chloride (AcCl) did not form any acetylated product, likely due the inertness of AcCl toward activation by the TMSOTf catalyst (Scheme S1).

Our early premise regarding the observed difference in the acetylation order of the TMS-masked hydroxyl groups of the sugar substrates **2**, **7**, and **8** targeted at the presence of the amino substituent at C-2. Accordingly, we asserted that the pre-installed electron withdrawing C-2 substituents, namely, the trichloroacetamido (TCANH) and the azido (N_3) groups,

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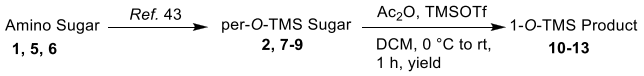
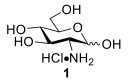
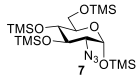
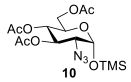
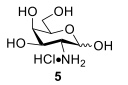
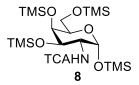
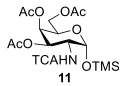
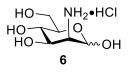
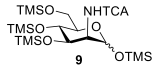
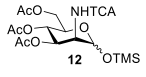
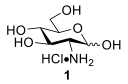
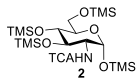
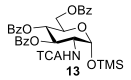
Table 2. Selective Acetylation of Amino Sugar Substrates 2, 7−9 with Pre-installed C-2 Substituent



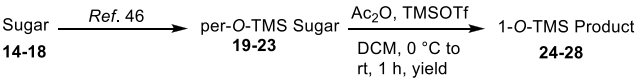
Entry	Amino Sugar	per-*O*-TMS Sugar	1-*O*-TMS Product	Yield (%)
1				86
2				86
3				70[a]
4[b]				48

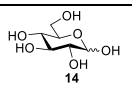
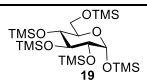
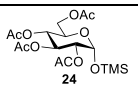
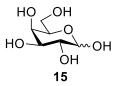
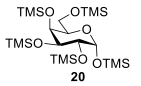
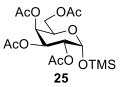
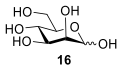
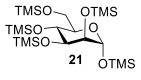
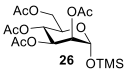
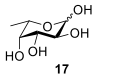
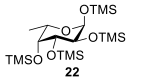
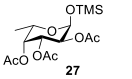
[a]Yield of β-isomer of **12** was determined from NMR. [b]Condition: Bz_2O (6 equiv), TMSOTf (0.3 equiv), 4 h.

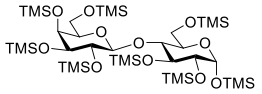
in addition to the endocyclic oxygen atom, were playing a role in attenuating the nucleophilicity of the oxygen moiety at the anomeric *O*-TMS group, thereby rendering it the least reactive in the acetylation process. In order to vindicate this presumption, we investigated the acetylation of per-*O*-TMS-protected sugars without a pre-installed substituent at C-2. Thus, we first tested our protocol in a per-*O*-TMS-protected derivative of D-glucose (**14**) and was then extended to other analogous sugar substrates. Accordingly, we prepared the respective per-*O*-TMS-protected sugars from commercially available **14**, D-galactose (**15**), D-mannose (**16**), L-fucose (**17**), and the disaccharide lactose (**18**) based on a procedure from the literature.[46] Then, the resulting per-*O*-TMS-protected products **19**−**23** were subjected to our developed acetylation condition. Astonishingly, the respective per-acetylated sugars **24**−**28** (Table 3, entries 1−5) were obtained in good to moderate yields in which the non-anomeric hydroxyl groups were acetylated, while leaving the anomeric *O*-TMS group intact. These results indicate that the oxygen atom in the anomeric *O*-TMS group is still the least reactive, even compared to the axial groups in the per-*O*-TMS substrates **20**−**23** which are typically considered less reactive for steric reasons. To this effect, the yield of **25** (Table 3, entry 2) is particularly the lowest presumably due to the poor reactivity of the 4-*O*-TMS group of **20**. On the other hand, previous works utilizing different acetylation conditions revealed that the anomeric *O*-TMS group of both per-*O*-silylated monosaccharides and disaccharides was among the first groups to undergo the silyl exchange reaction.[12,13,16] Meanwhile, the attainment of per-acetylated 1-*O*-TMS lactose **28** (Table 3, entry 5) shows that our established acetylation protocol can effectively differentiate the slight reactivity variations in multi-hydroxylated sugars.

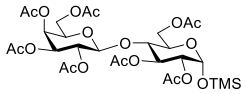
The exploitation of the marginal nucleophilicity differences in the hydroxyl groups of glycopyranose sugars has been a common strategy to separately modify each group using a variety of reaction conditions; it is well-recognized that the electron density around a nucleophile is influenced by its inductive and steric environments. Accordingly, the primary

Table 3. Selective Acetylation of Sugar Substrates 19−23 without Pre-installed C-2 Substituent



Entry	Sugar	per-*O*-TMS Sugar	1-*O*-TMS Product	Yield (%)
1				78
2				65
3				76
4				75
5	Lactose (**18**)	**23**	**28**	73

23 = 

28 = 

hydroxyl groups are considered the most reactive due to less steric congestion. Likewise, excluding the anomeric hydroxyl group because of its unique reactivity features, the secondary hydroxyl groups are usually differentiated based on their spatial orientation as either axial or equatorial where the former is usually deemed less reactive due to stereoelectronic factors.[47−50] Therefore, we presumed that the order of the reactivity of each *O*-TMS group in our TMSOTf-catalyzed acetylation reaction is an extrapolation of the order of the reactivity of the respective hydroxyl groups. In order to substantiate this preposition, we decided to probe the order of acetylation of each *O*-TMS group of **2** by treating a limited amount of the acetylating agent. To this end, **2** was treated with 1.5 equiv of Ac_2O and 0.2 equiv of TMSOTf. To the contrary of our assumption where the less sterically hindered primary 6-*O*-TMS group was perceived as the most reactive, the 3-*O*-TMS group was acetylated first, providing **29** in 56% yield, together with 3,6-di-*O*-acetylated compound **30** as a minor product (Scheme 1). Although not clear as to why this difference occurred, the 6-*O*-TMS group was reported to be the first to be acetylated under Gervay-Hague's slightly basic condition.[12] Meanwhile, treatment of **8** with 1.5 equiv of Ac_2O resulted in a mixture of inseparable products, making it difficult to identify each product formed, and thus, the use of 2.0 equiv of Ac_2O afforded the 1,3-di-*O*-TMS containing product **31** in 30% yield, along with the 1-*O*-TMS product **11** in 42%. Similarly, treatment of **20** with 3.0 equiv of Ac_2O gave majorly the 1-*O*-TMS product **25**, together with the partially acetylated products **32** and **33** in 13% and 8% yields, respectively (Scheme 1). With these results of selective acetylation reactions in hand, we proposed the plausible mechanism of our method as shown in Scheme 2 for the acetylation of substrate **2**.

As depicted in Scheme 2, the TMSOTf catalyst first activates the acetylating agent (Ac_2O), resulting in the formation of

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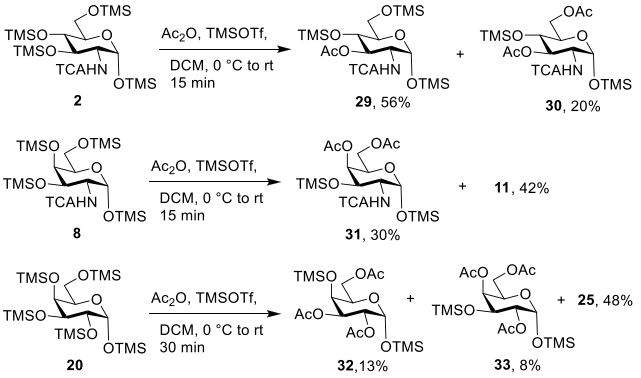
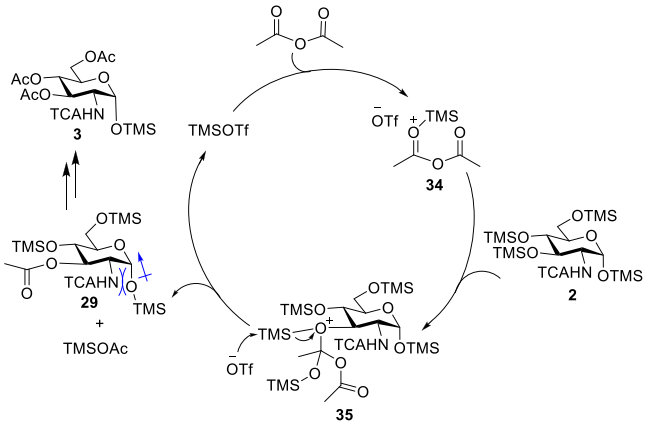
Scheme 1. Selective Acetylation Reactions of 2, 8, and 20



Scheme 2. Plausible Mechanism of TMSOTf-Catalyzed Selective Acetylation

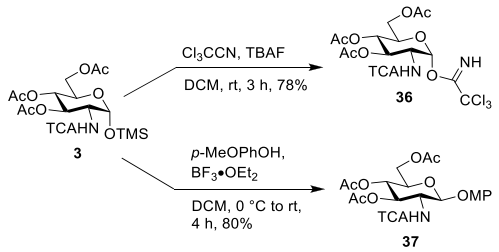


adduct **34** which, then, initially reacts with the most nucleophilic *O*-TMS group of **2**, yielding intermediate **35**. Subsequent bond cleavage and rearrangement in **35** gives the partially acetylated sugar **29**, regenerating the catalyst to resume the reaction cycle, and successive reactions of the remaining *O*-TMS groups of **29** based on the order of their reactivity afford the final per-acetylated 1-*O*-TMS desired product **3**.

Although convenient to separately modify using hemiacetal chemistry, the anomeric hydroxyl group when considered alone is less reactive as a nucleophile since its lone pair electrons are tightly held by the hemiacetal environment.[5] Therefore, we postulate that the proximity of the anomeric group to the electron withdrawing endocyclic oxygen (i.e., its hemiacetal functionality) plays a prominent role in enfeebling the nucleophilicity of the 1-*O*-TMS moiety by withholding its lone pair of electrons, hence making it remain unaffected until the other groups are acetylated. Furthermore, steric congestion of the 1-*O*-TMS group due to 1,2-*cis* interaction may be considered as an additional factor contributing to its low reactivity with the exception of mannose derivatives such as **21** which gave a good selectivity irrespective of such steric influence. Unlike Gervay-Hague's condition that proceeds through prior cleavage of the most electrophilic TMS group by an acetate anion,[13] there is no co-reagent in our protocol that can cleave the TMS group before reaction with the acetylating agent. Thus, the most nucleophilic *O*-TMS group is believed to attack the activated acetylating agent like **34**, thereby leading to a subsequent cascade of acetylation reactions with the remaining *O*-TMS groups.

Myriads of research outputs have shown the synthetic versatility of 1-*O*-TMS-equipped sugar substrates which are employed as both glycosyl donors and acceptors such as in the synthesis of *O*-alkylated glycosides and 1,1′-disaccharides including trehalose.[33,37,39−41] On the other hand, the acquisition of the per-acetylated 1-*O*-TMS sugars in such short steps and with no sophisticated workup or purification procedures can provide a unique opportunity for the expeditious synthesis of carbohydrate building blocks of interest. Moreover, the possibility of modifying the 1-*O*-TMS group under either basic or acidic conditions is another captivating feature of our methodology as demonstrated for product **3** as a representative example (Scheme 3). In this

Scheme 3. Preparation of Versatile Carbohydrate Precursors from 1-*O*-TMS Sugars



regard, with the use of 1-*O*-TMS precursor **3**, imidate donors can easily be prepared which could otherwise be synthesized through the commonly employed time-consuming anomeric deprotection of fully acetylated sugars such as **4**.[51] In the meantime, imidate donor **36** was synthesized in a single step from the reaction of 1-*O*-TMS sugar **3** and trichloroacetonitrile (Cl_3CCN) in DCM utilizing tetrabutylammonium fluoride (TBAF) to cleave the TMS group *in situ*. Likewise, the same sugar building block **3** was used to prepare *p*-methoxyphenyl (MP)-protected sugar **37** which is usually synthesized from fully acetylated precursor **4** under triflic acid-mediated reaction.[52] In our case, the mixture of **3** and *p*-methoxyphenol (*p*-MeOPhOH) in DCM was treated with $BF_3{\cdot}OEt_2$ to afford **37** in a good yield. Interestingly, Scheme 3 is a manifestation that the easily accessible 1-*O*-TMS group can serve the purpose of a free hydroxyl or an anomeric acetyl group provided that suitable reaction conditions are used and, thus, can also be used to prepare thioglycosides.[53]

It is to be noted from Scheme 3 that the ability of 1-*O*-TMS substrates to react as either nucleophiles or electrophiles has an extraordinary consequence in determining the stereochemistry of the final products. In this respect, with the driving force of F−Si bond formation, the TBAF-mediated reaction of **3** cleaves the O−Si bond,[54] generating intermediate **38** which consists of a negatively charged oxygen nucleophile that attacks the electrophilic center of Cl_3CCN to give tetrabutylammonium ion-stabilized intermediate **39**. Therefore, the stereochemistry at C-1 of **3** is also retained in the imidate donor **36**, providing only a single isomer (Scheme 4a). On the other hand, under the Lewis acid $BF_3{\cdot}OEt_2$-mediated condition, the *O*-TMS group of **3** is activated to form complex **40**, thereby serving as a leaving group to generate the incipient oxocarbenium intermediate **41** which has been detected via cold-ion infrared spectroscopy.[55] The suitably placed sub-

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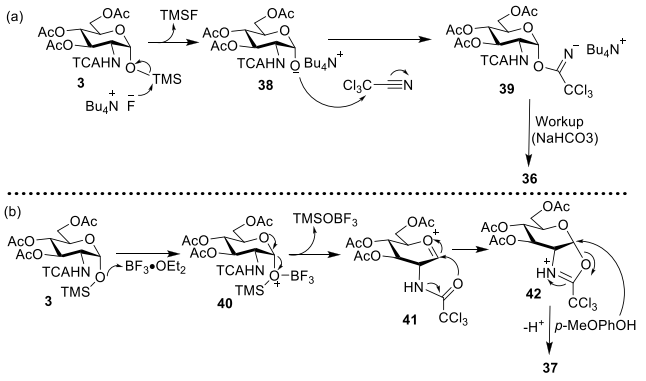
Scheme 4. Proposed Mechanism of Imidate Formation (a) and *p*-Methoxyphenyl Installation (b) Reactions of Substrate 3



stituent at C-2 of **41** instigates the well-known neighboring group participation to give the five-membered ring oxazolinium intermediate[56] **42** which dictates the stereochemistry of the resulting product **37**. Consequently, nucleophilic attack by *p*-MeOPhOH on the open β-face of **42** with concomitant loss of proton (H^+) yields **37** with inversion of stereochemistry relative to that of **3** (Scheme 4b).

In conclusion, we have developed an expeditious protocol that enables accessing a versatile class of sugar precursors which can significantly abate the main bottleneck of carbohydrate synthesis: notably prolonged reaction time due to the protection-deprotection manipulation of protecting groups. Thus, our methodology can remarkably speed up chemical glycosylation in conjunction with other proven strategies such as orthogonal protection.[7,57]

EXPERIMENTAL SECTION

General Information. All reagents obtained from commercial sources were used without further purification. All reactions were carried out under a nitrogen atmosphere and in flame-dried glassware. All solvents were purified and dried from a sealed purification system equipped with activated Al_2O_3. Flash column chromatography was conducted using Silica Gel Geduran Si 60 (0.040−0.063 mm, E. Merck). TLC was performed on precoated glass plates of Silica Gel 60 F254 (0.25 mm, E. Merck), and detection was executed either by spraying with a solution of $Ce(SO_4)_2$, $(NH_4)_2MoO_4$, and H_2SO_4 in water and subsequently heating on a hot plate or UV light (254 nm). ^{1}H NMR, ^{13}C NMR, DEPT, HSQC, and HMBC spectra were recorded by Bruker AV400, Av500, or N600 MHz. ^{1}H and ^{13}C chemical shifts are in ppm designated relative to Me_4Si using the $CDCl_3$ lock signal at δ 7.24 and 77.23, respectively. Multiplicities are reported by using the following symbols: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constant (J) values are stated in hertz. Mass spectra were analyzed by a Waters Premier XE instrument using a TOF mass analyzer with ESI mode. Structural assignments were made with additional information from selective 1D-TOCSY experiments. Specific rotations were measured on a Jasco P-2000 digital polarimeter using a 50 mm cell at 589 nm and are reported in 10^{-1}·deg·cm^2·g^{-1} at ambient temperature; the sample concentrations are in g·dL^{-1}. IR spectra were analyzed with a PerkinElmer Paragon 1000 FT-IR spectrometer. Melting points were determined with an MP-2D melting apparatus.

General Procedure for Silylation and N-Functionalization of Amino Sugars.[43] To a stirring solution of the free amino sugar hydrochlorides **1**, **5**, or **6** (2.5 g each) in 50 mL of acetonitrile (CH_3CN) was added hexamethyldisilazane (HMDS, 2.5 equiv) at room temperature (rt) under a N_2 atmosphere, and the mixture was allowed to stir for 3 h at the same temperature. After checking its completion by TLC, the reaction mixture was filtered, the residue was washed with ethyl acetate (EA), and the filtrate was concentrated to get the respective *O*-silylated desired free amino products. To the suspension of each silylated product in dichloromethane/pyridine (7/3, 0.2 M solution) under a N_2 atmosphere was then added trichloroacetyl chloride (1.1 equiv) at 0 °C under a N_2 atmosphere. After stirring for 2 h, the reaction mixture was concentrated in *rota* and was filtered with a *Celite pad* by washing it with EA/hexane (1/10). The filtrate was then evaporated in *vacuo*. Resilylation of partially cleaved TMS groups using HMDS (2.5 equiv) and TMSOTf (0.1 equiv) and direct *rota* after checking completion of reaction (roughly 30 min) furnished the desired *N*-functionalized per-*O*-TMS products **2**, **8**, and **9**, respectively.

After silylating glucosamine hydrochloride **1** (2.5 g) with HMDS as described above, it was subjected to the following azide transfer reaction. To a cooled (in ice bath) suspension of the *O*-silylated product in DCM (0.5 M solution) was added 4-dimethylaminopyridine (3.0 equiv), followed by direct addition of TfN_3 which was prepared separately from reaction of NaN_3 (4 equiv) and Tf_2O (1.2 equiv) in a mixture of water and DCM (1:2, 0.2 M solution). After stirring for 12 h at rt, the reaction mixture was quenched with glycine (1.5 equiv) and filtered by washing the residue with hexane. The filtrate was concentrated *in vacuo* and resilylated as already mentioned above to get the desired per-*O*-trimethylsilylated azido product **7**.

General Procedure for Silylation of Non-amino Sugars.[26,46] To a stirring solution of the free sugars **14**−**18** (2.5 g each) in dimethylformamide (DMF, 0.2 M solution) was added triethyl amine (Et_3N, 1.1 equiv for each free hydroxyl group). This content was placed in an ice bath, and trimethylsilyl chloride (TMSCl, 1.1 equiv for each free hydroxyl group) was added. After stirring the reaction mixture at rt for 4 h for the monosaccharides and 8 h for the disaccharide, it was diluted with hexane and crushed ice was added. The organic layer was separated, and the aqueous layer was washed one more time with hexane. The combined organic layers were washed three times with water, dried over $MgSO_4$, and concentered *in vacuo* to get the desired per-*O*-silylated products **19**−**23**.[26,46]

General Procedure for the Synthesis of 1-*O*-TMS Products. A solution of each per-*O*-silylated sugars **2**, **8**, and **9** (1.0 g, 1.63 mmol) in DCM (8.2 mL, 0.2 M solution) was placed in an ice bath, to which were successively added Ac_2O (1.0 mL, 9.80 mmol) and TMSOTf (61 μL, 0.33 mmol). To a suspension of **7** (1.0 g, 2.03 mmol) in DCM (10 mL, 0.2 M solution) in an ice bath were sequentially added Ac_2O (1.2 mL, 9.80 mmol) and TMSOTf (76 μL, 0.41 mmol). Similarly, each solution of **19**−**21** (1.0 g, 1.85 mmol) in DCM (9 mL, 0.2 M) was treated with Ac_2O (1.1 mL, 11.1 mmol) and TMSOTf (68 μL, 0.37 mmol). Suspensions of **22** (1.0 g, 2.21 mmol) in DCM (11.1 mL) and **23** (1.0 g, 1.09 mmol) in DCM (5.5 mL) were, respectively, treated with Ac_2O (1.0 mL, 9.95 mmol) and TMSOTf (81 μL, 0.44 mmol) and Ac_2O (1.2 mL, 11.45 mmol) and TMSOTf (41 μL, 0.22 mmol). The ice bath was then removed, and after stirring each reaction mixture for 1 h at rt, it was diluted with DCM and neutralized with Et_3N. Then, saturated $NaHCO_3$ solution was added and the organic layer separated. The organic layer was further washed with saturated $NaHCO_3$ solution twice, concentrated *in vacuo*, and purified by flash column chromatography using EtOAc/Hexane as eluent to obtain the respective per-acetylated 1-*O*-TMS products **3**, **10**−**13**, and **24**−**28**.

General Procedure for Selective Acetylation Reactions of 2, 8, and 20. To each 0.2 M DCM solution of **2** (1.0 g, 1.63 mmol), **8** (1.0 g, 1.63 mmol), and **20** (1.0 g, 1.85 mmol) in an ice bath were, respectively, added Ac_2O (0.24 mL, 2.45 mmol; 0.33 mL, 3.3 mmol; 0.54 mL, 5.55 mmol), and TMSOTf (0.2 equiv each). After removing the ice bath and stirring each reaction mixture for 15−30 min at rt, it was diluted with DCM and neutralized with Et_3N. Then, saturated $NaHCO_3$ solution was added and the organic layer separated. The organic layer was further washed with saturated $NaHCO_3$ solution twice, concentrated *in vacuo*, and purified by flash column chromatography using EA/Hexane or EtOAc/Toluene as eluent to obtain the respective partially acetylated products **29**−**33**.

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*Trimethylsilyl 3,4,6-Tri-O-acetyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranoside (**3**).* TLC: EtOAc/Hexane = 1:3, R_f = 0.3. Colorless syrup (Yield: 775 mg, 91%). $[\alpha]_D^{30}$ +71.9° (*c* 1.3, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 3425, 2959, 1747, 1721, 1515, 1224, 1049, 848 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, *J* = 9.0 Hz, 1H, NH), 5.29 (t, *J* = 9.7 Hz, 1H, H-3), 5.24 (d, *J* = 3.4 Hz, 1H, H-1), 5.08 (t, *J* = 9.7 Hz, 1H, H-4), 4.22 (dd, *J* = 11.6, 4.4 Hz, 1H, H-6a), 4.13 (ddd, *J* = 10.5, 9.1, 3.5 Hz, 1H, H-2), 4.08−4.00 (m, 2H, H-5, H-6b), 2.06 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 0.16 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.4, 170.6, 169.5, 161.9 (all C═O), 92.3 (CCl_3), 91.6 (C-1), 70.8, 68.2, 68.0 (all CH), 62.3 (CH_2), 55.0 (CH), 20.8, 20.8, 20.7 (all CH_3), −0.1 (CH_3) ppm. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{26}NO_9NaSiCl_3$ 544.0335; found 544.0328.

*Trimethylsilyl 3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranoside (**10**).* TLC: EtOAc/Hexane = 1:3, R_f = 0.3. Colorless syrup (Yield: 703 mg, 86%). $[\alpha]_D^{30}$ +160.7° (*c* 1.4, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 2951, 2108, 1750, 1224, 1048, 848 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.46 (t, *J* = 9.6 Hz, 1H, H-3), 5.26 (d, *J* = 3.2 Hz, 1H, H-1), 4.98 (t, *J* = 9.8 Hz, 1H, H-4), 4.24 (dd, *J* = 12.1, 4.8 Hz, 1H, H-6a), 4.11 (m, 1H, H-5), 3.99 (dd, *J* = 12.2, 2.0 Hz, 1H, H-6b), 3.14 (dd, *J* = 10.5, 3.1 Hz, H-2), 2.04 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 0.19 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.7, 170.3, 169.9 (all C═O), 93.0 (C-1), 70.3, 68.9, 67.6 (all CH), 62.3 (CH_2), 61.7 (CH), 20.9, 20.9, 20.8 (all CH_3), −0.1 (CH_3) ppm. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{15}H_{25}N_3O_8NaSi$ 426.1303; found 426.1298.

*Trimethylsilyl 3,4,6-Tri-O-acetyl-2-deoxy-2-trichloroacetamido-α-D-galactopyranoside (**11**).* TLC: EtOAc/Hexane = 1:3, R_f = 0.3. Sticky solid (Yield: 733 mg, 86%). $[\alpha]_D^{30}$ +89.0° (*c* 1.0, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 3422, 3340, 2960, 1750, 1719, 1518, 1372, 1226, 1079, 848 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, *J* = 9.3 Hz, 1H, NH), 5.38 (d, *J* = 2.9 Hz, 1H, H-4), 5.29 (d, *J* = 3.5 Hz, 1H, H-1), 5.25 (dd, *J* = 11.1, 3.2 Hz, 1H, H-3), 4.40 (m, 1H, H-2), 4.27 (t, *J* = 6.5 Hz, 1H, H-5), 4.10−4.02 (m, 2H, H-6), 2.14 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 0.17 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.0, 170.6, 170.4, 162.1 (all C═O), 92.5 (CCl_3), 92.3 (C-1), 68.4, 67.5, 67.1 (all CH), 62.2 (CH_2), 50.9 (CH), 20.9, 20.8, 20.8 (all CH_3), −0.1 (CH_3) ppm. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{26}NO_9NaSiCl_3$ 544.0335; found 544.0327.

*Trimethylsilyl 3,4,6-Tri-O-acetyl-2-deoxy-2-trichloroacetamido-α/β-D-mannopyranoside (**12**).* Yield: 596 mg, 70%, α:β = 8:1. **12-α**: TLC: EtOAc/Hexane = 1:2, R_f = 0.4. White solid, mp = 120−121 °C. $[\alpha]_D^{26}$ +33.2° (*c* 1.0, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 3361, 2958, 2922, 2851, 1738, 1703, 1519, 1367, 1226, 1048, 844 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 6.82 (d, *J* = 9.4 Hz, 1H, NH), 5.42 (dd, *J* = 10.1, 4.1 Hz, 1H, H-3), 5.17−5.13 (m, 2H, H-1, H-4), 4.44 (m, 1H, H-2), 4.19 (dd, *J* = 12.1, 4.4 Hz, 1H, H-6a), 4.12−4.05 (m, 2H, H-5, H-6b), 2.06 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 0.20 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 170.7, 170.3, 169.9, 163.3 (all C═O), 93.2 (C-1), 92.5 (CCl_3), 69.4, 68.2, 65.7 (all CH), 62.4 (CH_2), 53.9 (CH), 20.9 (CH_3), −0.1 (CH_3) ppm. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{26}NO_9NaSiCl_3$ 544.0335; found 544.0341. **12-β**: TLC: EtOAc/Hexane = 1:2, R_f = 0.3. Sticky solid. $[\alpha]_D^{27}$ −9.0° (*c* 0.7, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 3416, 2957, 2924, 2852, 1748, 1727, 1513, 1371, 1227, 1057, 847 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 6.92 (d, *J* = 7.9 Hz, 1H, NH), 5.09−5.02 (m, 3H, H-1, H-3, H-4), 4.49 (m, 1H, H-2), 4.18−4.11 (m, 2H, H-6), 3.68 (m, 1H, H-5), 2.06 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 0.14 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 170.7, 170.7, 169.9, 163.2 (all C═O), 93.8 (C-1), 92.7 (CCl_3), 72.8, 71.9, 65.8 (all CH), 62.5 (CH_2), 54.4 (CH), 20.9, 20.9 (CH_3), −0.2 (CH_3) ppm. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{26}NO_9NaSiCl_3$ 544.0335; found 544.0339.

*Trimethylsilyl 3,4,6-Tri-O-benzoyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranoside (**13**).* TLC: EtOAc/Hexane = 1:3, R_f = 0.5. White foam (Yield: 555 mg, 46%). $[\alpha]_D^{27}$ +23.6° (*c* 1.3, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 34423, 3064, 2958, 1722, 1515, 1267, 1105, 1095, 846, 709 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (m, 2H, ArH), 7.93−7.87 (m, 4H, ArH), 7.53 (m, 1H, ArH), 7.50−7.45 (m, 2H, ArH), 7.40 (m, 2H, ArH), 7.33 (m, 4H, ArH), 7.13 (d, *J* = 8.6 Hz, 1H, NH), 5.80 (t, *J* = 10.3 Hz, 1H, H-3), 5.68 (t, *J* = 9.4 Hz, 1H, H-4), 5.42 (d, *J* = 3.0 Hz, 1H, H-1), 4.56−4.37 (m, 4H, H-2, H-5, H-6), 0.23 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.4, 166.4, 165.4, 162.1 (all C═O), 133.8, 133.7, 133.3, 130.1, 130.0, 130.0 (all CH), 129.8, 129.0, 128.8 (all C), 128.6, 128.6 (CH), 92.2 (C), 91.8 (C-1), 71.4, 69.2, 68.4 (all CH), 63.3 (CH_2), 55.6 (CH), 0.1 (CH_3) ppm. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{32}H_{32}NO_9NaSiCl_3$ 730.0804; found 730.0801.

*Trimethylsilyl 2,3,4,6-Tetra-O-acetyl-α-D-glucopyranoside (**24**).*[58] TLC: EtOAc/Hexane = 1:2, R_f = 0.3. Colorless syrup (Yield: 607 mg, 78%). $[\alpha]_D^{27}$ +107.3° (*c* 1.1, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 2958, 1745, 1367, 1219, 1040, 847 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.45 (t, *J* = 9.7 Hz, 1H, H-3), 5.34 (d, *J* = 3.2 Hz, 1H, H-1), 5.00 (t, *J* = 9.7 Hz, 1H, H-4), 4.77 (dd, *J* = 10.1, 3.4 Hz, 1H, H-2), 4.22 (dd, *J* = 12.4, 4.9 Hz, 1H, H-6a), 4.11 (m, 1H, H-5), 4.00 (dd, *J* = 12.2, 2.2 Hz, 1H, H-6b), 2.04 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 0.12 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 170.9, 170.4, 170.3, 169.8 (all C═O), 90.5 (C-1), 72.0, 70.3, 68.9, 67.2 (all CH), 62.3 (CH_2), 20.9, 20.9, 20.9, 20.8 (all CH_3), −0.1 (CH_3) ppm. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{28}O_{10}NaSi$ 443.1344; found 443.1349.

*Trimethylsilyl 2,3,4,6-Tetra-O-acetyl-α-D-galactopyranoside (**25**).*[42] TLC: EtOAc/Hexane = 1:2, R_f = 0.4. White solid (Yield: 506 mg, 65%). Mp = 116−118 °C. $[\alpha]_D^{28}$ +124.8° (*c* 1.1, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 2960, 1746, 1371, 1223, 1061, 847 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.40−5.38 (m, 2H, H-1, H-4), 5.30 (dd, *J* = 10.7, 3.2 Hz, 1H, H-3), 5.01 (dd, *J* = 10.8, 3.3 Hz, 1H, H-2), 4.30 (m, 1H, H-5), 4.05−3.99 (m, 2H, H-6), 2.08 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 1.94 (s, 3H, CH_3), 0.11 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 170.6, 170.5, 170.4, 170.3 (all C═O), 90.9 (C-1), 69.2, 68.4, 67.8, 66.2 (all CH), 62.1 (CH_2), 20.9, 20.8, 20.8, 20.8 (all CH_3), −0.2 (CH_3) ppm. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{28}O_{10}NaSi$ 443.1344; found 443.1344.

*Trimethylsilyl 2,3,4,6-Tetra-O-acetyl-α-D-mannopyranoside (**26**).*[59] TLC: EtOAc/Hexane = 1:2, R_f = 0.4. Colorless syrup (Yield: 591 mg, 76%). $[\alpha]_D^{28}$ +39.1° (*c* 1.1, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 2960, 1745, 1368, 1218, 1143, 1075, 1048, 875, 847 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.39 (dd, *J* = 10.1, 2.7 Hz, 1H, H-3), 5.22 (t, *J* = 10.0 Hz, 1H, H-4), 5.09 (m, 2H, H-1, H-2), 4.22 (dd, *J* = 12.0, 5.3 Hz, 1H, H-6a), 4.08−4.01 (m, 2H, H-5, H-6a), 2.11 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 0.15 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 170.8, 170.4, 170.1, 169.9 (all C═O), 90.7 (C-1), 71.3, 69.0, 68.5, 66.5 (all CH), 62.8 (CH_2), 21.1, 20.9 (CH_3), −0.1 (CH_3) ppm. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_{28}O_{10}NaSi$ 443.1344; found 443.1341.

*Trimethylsilyl 2,3,4-Tri-O-acetyl-α-L-fucopyranoside (**27**).* TLC: EtOAc/Hexane = 1:2, R_f = 0.5. Pale yellow syrup (Yield: 591 mg, 76%). $[\alpha]_D^{28}$ −135.4° (*c* 1.1, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 2960, 1746, 1370, 1250, 1222, 1060, 982, 803 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.35−5.31 (m, 2H, H-1, H-3), 5.25 (d, *J* = 3.2 Hz, 1H, H-4), 5.02 (dd, *J* = 10.7, 3.3 Hz, 1H, H-2), 4.25 (q, *J* = 6.6 Hz, 1H, H-5), 2.12 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 1.08 (d, *J* = 6.6 Hz, 3H, H-6), 0.11 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 170.9, 170.6, 170.5 (all C═O), 91.0 (C-1), 71.5, 69.3, 68.3, 64.3 (all CH), 21.0, 20.9, 20.9, 16.1 (all CH_3), −0.1 (CH_3) ppm. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{15}H_{26}O_8NaSi$ 385.1289; found 385.1288.

*Trimethylsilyl 2,3,6-Tri-O-acetyl-4-O-(2′,3′,4′,6′-tetra-O-acetyl-α-D-galactopyranosyl)-α-D-glucopyranoside (**28**).* TLC: EtOAc/Hexane = 1:1, R_f = 0.3. Colorless syrup (Yield: 591 mg, 76%). $[\alpha]_D^{28}$ +58.4° (*c* 1.0, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 2958, 1747, 1370, 1220, 1051, 847 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.45 (t, *J* = 9.6 Hz, 1H, H-3), 5.32 (d, *J* = 3.0 Hz, 1H, H-4′), 5.26 (d, *J* = 3.4 Hz, 1H, H-1), 5.09 (dd, *J* = 10.4, 8.0 Hz, 1H, H-2′), 4.92 (dd, *J* = 10.4, 3.5 Hz, 1H, H-3′), 4.70 (dd, *J* = 10.1, 3.4 Hz, 1H, H-2), 4.45 (d, *J* = 7.9 Hz, 1H, H-1′), 4.35 (dd, *J* = 11.8, 1.7 Hz, 1H, H-6a), 4.14−4.01 (m, 4H, H-5, H-6b, H-6′), 3.84 (t, *J* = 6.9 Hz, 1H, H-5′), 3.68 (t, *J* = 9.5 Hz, 1H, H-4), 2.13 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.02 (s, 3H,

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CH_3), 2.00 (s, 3H, CH_3), 1.94 (s, 3H, CH_3), 0.12 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.6, 170.5, 170.4, 170.3, 169.8, 169.4 (all C=O), 101.5 (C-1′), 90.4 (C-1), 77.0, 72.3, 71.3, 70.8, 70.2, 69.4, 68.1, 66.8 (all CH), 62.4, 61.0 (both CH_2), 21.2, 21.0, 20.9, 20.8, 20.7 (CH_3), −0.0 (CH_3) ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{29}H_{44}O_{18}NaSi$ 731.2189; found 731.2181.

*Trimethylsilyl 3-O-Acetyl-4,6-bis-O-trimethylsilyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranoside (**29**).* TLC: EtOAc/Hexane = 1:6, R_f = 0.7. Colorless syrup (Yield: 532 mg, 56%). $[\alpha]_D^{27}$ +68.3° (*c* 1.4, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 3425, 2958, 1748, 1721, 1513, 1250, 1229, 1145, 1054, 839, 751 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 6.89 (d, *J* = 9.0 Hz, 1H, NH), 5.22−5.18 (m, 2H, H-1, H-3), 3.99 (m, 1H, H-2), 3.81 (t, *J* = 9.0 Hz, 1H, H-4), 3.76−3.67 (m, 3H, H-5, H-6), 2.05 (s, 3H, CH_3), 0.14 (s, 9H, CH_3), 0.10 (m, 18H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 171.5, 162.0 (all C=O), 92.5 (C), 91.7 (C-1), 73.8, 72.8, 68.9 (all CH), 61.4 (CH_2), 55.5 (CH), 21.3 (CH_3), 0.5, 0.0, −0.2 (all CH_3) ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{38}NO_7NaSi_3Cl_3$ 604.0914; found 604.0923.

*Trimethylsilyl 3,6-Di-O-acetyl-4-O-trimethylsilyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranoside (**30**).* TLC: EtOAc/Hexane = 1:3, R_f = 0.4. Colorless syrup (Yield: 180 mg, 20%). $[\alpha]_D^{27}$ +67.7° (*c* 1.4, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 3423, 2959, 1745, 1720, 1514, 1252, 1223, 1057, 841, 752 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.88 (d, *J* = 8.8 Hz, 1H, NH), 5.23−5.19 (m, 2H, H-1, H-3), 4.27 (m, 1H, H-6a), 4.15 (dd, *J* = 12.0, 4.6 Hz, 1H, H-6b), 4.03 (m, 1H, H-2), 3.94 (m, 1H, H-5), 3.79 (t, *J* = 9.1 Hz, 1H, H-4), 2.08 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 0.15 (s, 9H, CH_3), 0.09 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.5, 170.9, 162.0 (all C=O), 92.4 (C), 91.7 (C-1), 73.4, 70.2, 69.4 (all CH), 63.0 (CH_2), 55.4 (CH), 21.3, 21.0 (CH_3), 0.5, −0.0, (CH_3) ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{32}NO_8NaSi_2Cl_3$ 574.0624; found 574.0625.

*Trimethylsilyl 4,6-Di-O-acetyl-3-O-trimethylsilyl-2-deoxy-2-trichloroacetamido-α-D-galactopyranoside (**31**).* TLC: EtOAc/Hexane = 1:4, R_f = 0.4. Colorless syrup (Yield: 270 mg, 30%). $[\alpha]_D^{24}$ +82.4° (*c* 1.1, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 3424, 2958, 1746, 1727, 1511, 1440, 1370, 1251, 1223, 1117, 1065, 843, 755 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 6.59 (d, *J* = 9.0 Hz, 1H, NH), 5.28 (d, *J* = 3.4 Hz, 1H, H-1), 5.23 (m, 1H, H-4), 4.20 (m, 2H, H-2, H-5), 4.11 (dd, *J* = 11.5, 4.8 Hz, 1H, H-6a), 4.00 (dd, *J* = 11.5, 7.7 Hz, 1H, H-6b), 3.93 (dd, *J* = 10.3, 3.4 Hz, 1H, H-3), 2.12 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 0.16 (s, 9H, CH_3), 0.09 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 170.7, 170.6, 161.9 (all C=O), 92.8 (C), 92.3 (C-1), 70.0, 67.7, 67.4 (all CH), 63.0 (CH_2), 53.2 (CH), 21.0, 20.9 (CH_3), 0.1, −0.1, (CH_3) ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{26}O_8NaSi$ 574.0624; found 574.0627.

*Trimethylsilyl 2,3,6-Tetra-O-acetyl-4-O-trimethylsilyl-α-D-galactopyranoside (**32**).* TLC: EtOAc/Toluene = 1:10, R_f = 0.4. Colorless syrup (Yield: 108 mg, 13%). $[\alpha]_D^{25}$ +109.6° (*c* 1.3, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 2959, 1745, 1371, 1249, 1225, 1161, 1066, 996, 875, 842, 754 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.39 (d, *J* = 3.3 Hz, 1H, H-1), 5.22 (dd, *J* = 10.7, 2.8 Hz, 1H, H-3), 5.08 (dd, *J* = 10.7, 3.4 Hz, 1H, H-2), 4.1 (m, 3H, H-4, H-5, H-6a), 4.01 (dd, *J* = 13.6, 9.0 Hz, 1H, H-6b), 2.06 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 0.10 (m, 18H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.6, 170.5 (all C=O), 91.0 (C-1), 70.3, 69.5, 69.5, 68.0 (all CH), 63.0 (CH_2), 21.4, 21.0, 21.0 (CH_3), 0.4, −0.1, (CH_3) ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{26}O_8NaSi$ 473.1634; found 473.1640.

*Trimethylsilyl 2,4,6-Tetra-O-acetyl-3-O-trimethylsilyl-α-D-galactopyranoside (**33**).* TLC: EtOAc/Toluene = 1:10, R_f = 0.3. Colorless syrup (Yield: 67 mg, 8%).$[\alpha]_D^{25}$ +116.7° (*c* 1.4, CH_2Cl_2). IR (CH_2Cl_2) $\bar{\nu}$ 2959, 1746, 1371, 1250, 1225, 1157, 1122, 883, 843, 754 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.39 (d, *J* = 3.4 Hz, 1H, H-1), 5.22 (m, 1H, H-4), 4.78 (dd, *J* = 9.9, 3.4 Hz, 1H, H-2), 4.25 (m, 1H, H-5), 4.08 (m, 2H, H-3, H-6a), 3.99 (dd, *J* = 11.3, 7.6 Hz, 1H, H-6b), 2.07 (s, 3H, CH_3), 2.02 (m, 6H, CH_3), 0.11 (s, 9H, CH_3), 0.08 (m, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.8, 170.6 (all C=O), 91.1 (C-1), 72.6, 71.0, 66.6 (all CH), 62.9 (CH_2), 21.1, 20.9 (CH_3), 0.1, −0.1, (CH_3) ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{26}O_8NaSi$ 473.1634; found 473.1634.

*Trichloroacetimidoyl 3,4,6-Tri-O-acetyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranoside (**36**).*[51] To a suspension of **3** (100 mg, 0.19 mmol) in DCM (2.0 mL, 0.1 M solution) were successively added trichloroacetonitrile (0.2 mL, 1.9 mmol) and TBAF (l M solution in THF; 2 mL, 1.9 mmol). After stirring for 3 h at rt, the reaction mixture was diluted with DCM and saturated $NaHCO_3$ was added. The organic layer was separated and washed with saturated $NaHCO_3$ one more time, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification using flash column chromatography with EtOAc/Hexane (1/2) afforded **36** as a white solid (88 mg, 78%). Mp = 152−154 °C. $[\alpha]_D^{30}$ +56.6° (*c* 1.1, CH_2Cl_2). (Literature: mp = 160−161 °C; $[\alpha]_D$ +75° (*c* 1, $CHCl_3$).[51] IR (CH_2Cl_2) $\bar{\nu}$ 3414, 3339, 2957, 1722, 1680, 1518, 1224, 1040, 823, 797 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1 H, C=NH), 6.98 (d, *J* = 8.5 Hz, 1H, NH), 6.47 (d, *J* = 3.6 Hz, 1H, H-l), 5.41 (t, *J* = 10.3, 1H, H-3), 5.27 (t, *J* = 10.0 Hz, 1H, H-4), 4.42 (m, 1H, H-2), 4.27 (dd, *J* = 12.8, 4.4 Hz, 1H, H-6a), 4.15−4.09 (m, 2H, H-5, H-6b), 2.07 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.04 (s, 3H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.7, 170.8, 169.3, 162.3 (all C=O), 160.2 (C=NH), 93.9 (C-1), 91.9, 90.7 (both CCl_3), 70.7, 70.3, 67.1 (all CH), 61.5 (CH_2), 54.1 (CH), 20.9, 20.8, 20.7 (all CH_3) ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{18}N_2O_9NaCl_6$ 614.9036; found 614.9034.

*p-Methoxyphenyl 3,4,6-Tri-O-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (**37**).*[52] To a cooled (in ice bath) suspension of **3** (100 mg, 0.19 mmol) and *p*-methoxyphenol (47.2 mg, 0.38 mmol) in DCM (2.0 mL, 0.1 M solution) was added $BF_3{\cdot}OEt_2$ (44 μL, 0.42 mmol). After stirring for 4 h at rt, the reaction mixture was concentrated *in vacuo* and purified using flash column chromatography with EtOAc/Hexane (1/1) to get **37** as a white powder (85 mg, 80%). Mp = 187−188 °C. $[\alpha]_D^{30}$ −11.2° (*c* 1.1, CH_2Cl_2). (Literature: mp = 176−177 °C; $[\alpha]_D$ −10° (*c* 1, $CHCl_3$).[52] IR (CH_2Cl_2) $\bar{\nu}$ 3332, 2958, 1746, 1530, 1507, 1368, 1214, 1040, 823 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.9 Hz, 1H, NH), 6.94 (m, 2H, ArH), 6.76 (m, 2H, ArH), 5.41 (t, *J* = 10.1 Hz, 1H, H-3), 5.14 (t, *J* = 9.6 Hz, 1H, H-4), 5.06 (d, *J* = 8.1 Hz, 1H, H-1), 4.28 (dd, *J* = 12.2, 5.3 Hz, 1H, H-6a), 4.24−4.14 (m, 2H, H-2, H-6b), 3.82 (m, 1H, H-5), 3.74 (s, 3H, OCH_3), 2.07 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.99 (s, 3H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.1, 170.8, 169.5, 162.3 (all C=O), 156.2, 151.2 (both ArC), 119.3, 114.8 (both ArCH), 100.6 (C-1), 92.4 (CCl_3), 72.3, 71.6, 68.6 (all CH), 62.3 (CH_2), 56.2 (CH), 55.8 (OCH_3), 20.9, 20.8 (both CH_3) ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{24}NO_{10}NaCl_3$ 578.0358; found 578.0348.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02813.

All NMR spectroscopic data for compounds **3**, **10**−**13**, **24**−**33**, **36**, and **37** (PDF)

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Notes

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