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Why Is Direct Glycosylation with *N*-Acetylglucosamine Donors Such a Poor Reaction and What Can Be Done about It?

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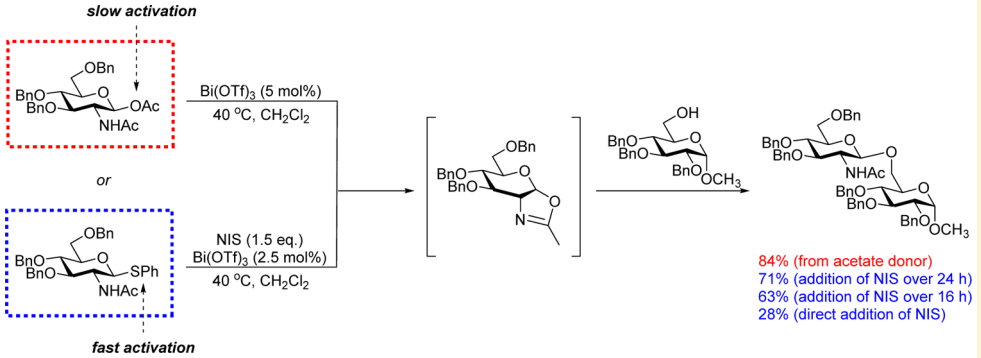
Supporting Information



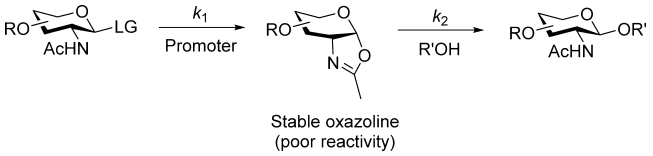
ABSTRACT: The monosaccharide *N*-acetyl-D-glucosamine (GlcNAc) is an abundant building block in naturally occurring oligosaccharides, but its incorporation by chemical glycosylation is challenging since direct reactions are low yielding. This issue, generally agreed upon to be caused by an intermediate 1,2-oxazoline, is often bypassed by introducing extra synthetic steps to avoid the presence of the NHAc functional group during glycosylation. The present paper describes new fundamental mechanistic insights into the inherent challenges of performing direct glycosylation with GlcNAc. These results show that controlling the balance of oxazoline formation and glycosylation is key to achieving acceptable chemical yields. By applying this line of reasoning to direct glycosylation with a traditional thioglycoside donor of GlcNAc, which otherwise affords poor glycosylation yields, one may obtain useful glycosylation results.

INTRODUCTION

Glycosylation chemistry has become increasingly important since the emergence of glycomics in cellular and molecular biology as an important field of study.[1] Indeed, the vast majority of functional proteins have been shown to be heavily and diversely glycosylated in vivo. The role of these abundant post-translational modifications in such matters as protein localization, function regulation, and stability toward degradation has been probed only superficially even today. Access via synthetic organic chemistry to analytically pure samples of relevant oligosaccharides is required for further in-depth investigation of the roles of such carbohydrates.

N-Acetyl-D-glucosamine (GlcNAc) is the most abundant monosaccharide building block in mammalian glycoconjugates,[2] and their incorporation into synthetic oligosaccharides for biological studies is therefore a necessity. Chemical manipulation of this particular unit is, however, far from trivial due to solubility issues and to the fact that GlcNAc derivatives function poorly both as glycosyl donors[3,4] and acceptors.[5−7] A well-accepted general presumption is that an intermediate oxazoline (Scheme 1)[8,9] is the cause of this poor donor reactivity. Many protecting group strategies prevent the formation of such oxazolines by ensuring the lack of a proton on the nitrogen (e.g., N_3, NAc_2, NPhth). Thus, even if neighboring group participation is possible during glycosylation, no stable intermediate can be formed (Scheme 2A).

Scheme 1. General Scheme for Direct Glycosylation with GlcNAc with Oxazolines as the Presumed Critical Intermediate during the Reaction



Other well-studied and high-yielding protecting group strategies, however, preserve the NH functionality in the glycosyl donor (e.g., NHTroc and $NHC(O)CH_2Cl$), thus maintaining the possibility of forming the oxazoline (or a derivative thereof, see Scheme 2B). In fact, the existence and stability of such oxazolines has been investigated and

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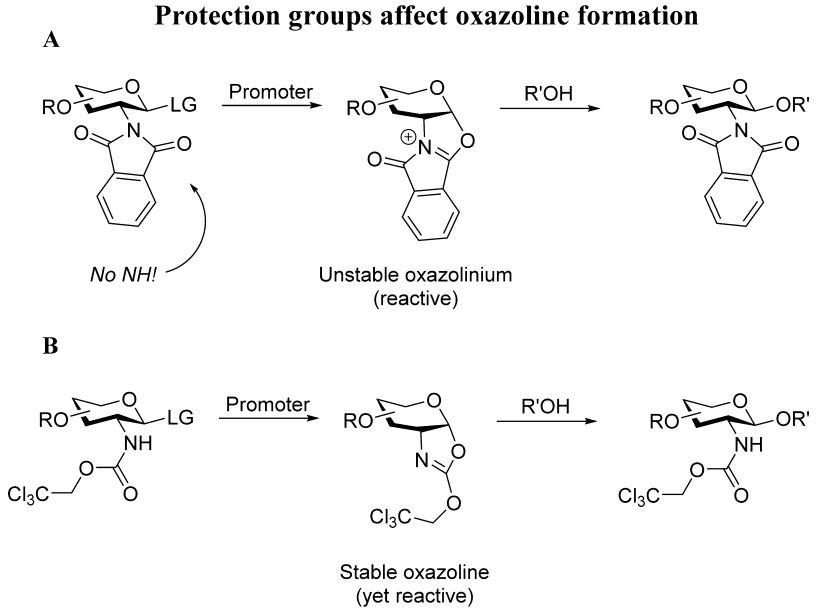
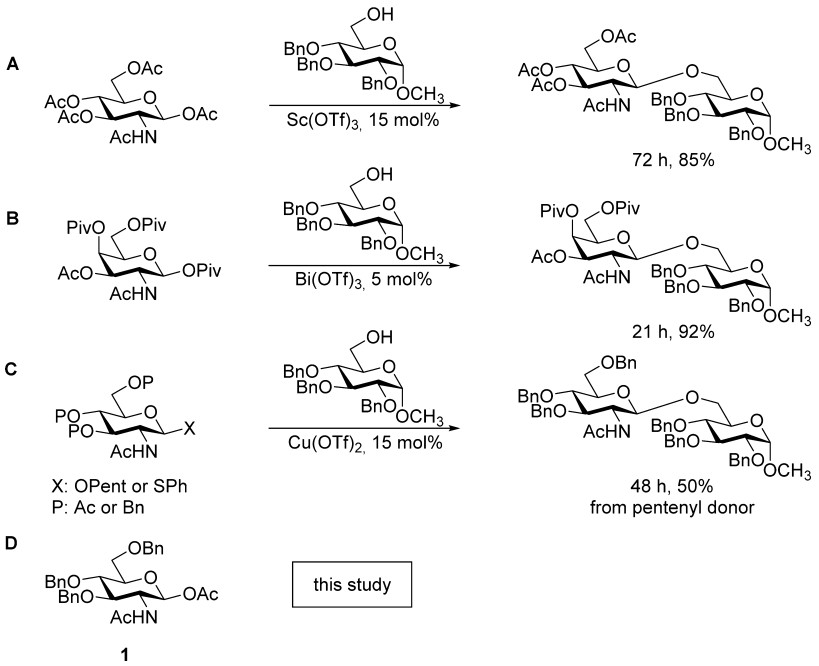
Scheme 2. *N*-Protecting Groups Typically Participate in Glycosylation through Oxazoline/Oxazolinium Ion Formation during Glycosylation



Scheme 3. Overview of Previous Direct and Catalytic GlyNAc-ylation[a]



[a]For refs, see (A) ref 12; (B) ref 17; (C) ref 18.

established for both NHTroc-[10] and NHC(O)CH_2Cl-protected[11] derivatives of GlcNAc.

We[12] and others[13,14] have recently addressed the issue of performing direct glycosylation reactions using GlcNAc donors (GlcNAc-ylation) in the presence of the 2-acetamido functionality. Through investigations of the catalytic activation of tetra-*O*-acetyl-β-GlcNAc with various Lewis acidic promotors, we found that the β-anomeric acetyl ester was a suitable leaving group in such systems to give acceptable glycosylation yields (Scheme 3A).[12] Similarly, we have recently demonstrated that β-configured anomeric pivalates (Scheme 3B), which can be readily synthesized from GlcNAc,[15,16] are good donors of *N*-acetyl-D-galactosamine (GalNAc).[17]

In an attempt to increase the reaction rate for GlcNAc-ylation by exchanging the donor functionality to either 1-SPh or 1-*O*-pentenyl, we found the donor fully activated instantly regardless of the arming/disarming character of the *O*-protecting groups. This system, however, only returned diminished yields of glycosylation products (Scheme 3C).[18]

Given the results listed in Scheme 3, we speculated that balancing the rate of the donor activation (k_1, Scheme 1) with that of the reaction between the oxazoline intermediate and the acceptor alcohol (k_2, Scheme 1) could lead to an improved

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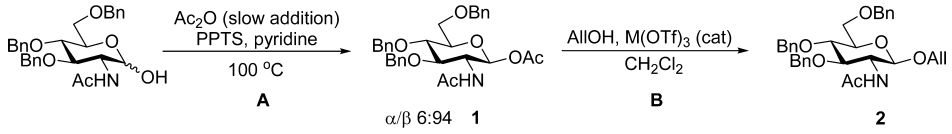
Scheme 4. Formation of Donor 1 and Glycosylation with Allyl Alcohol



overall reaction outcome. In this paper, we report on the effect of having arming benzyl protection groups on the donor while maintaining the slowly activating anomeric β-acetate (donor **1**, Scheme 3D), thereby tuning the reaction rates (small k_1, large k_2) in a way that keeps the oxazoline concentration low in solution. Our studies have led to fundamental insights into the reasons for the disappointing results found with conventional GlcNAc donors.

RESULTS AND DISCUSSION

We synthesized donor **1** from commercially available D-GlcNAc using a modified diastereoselective acetylation of 2-acetamido-2-deoxy-3,4,6-tri-*O*-benzyl-D-glucopyranose to give donor **1** with a satisfying crude α/β-ratio of 6:94 (Scheme 4A).[19]

In accordance with previous work a range of Lewis acids was screened to establish the behavior of the newly synthesized donor in chemical glycosylation. The most efficient catalysts with respect to reaction time were $Bi(OTf)_3$, $Fe(OTf)_3$, and TfOH. Using the metal catalyst in combination with the base tri-*tert*-butylpyrimidine (TTBP)[20] or as their dimethyl sulfoxide (DMSO) complexes[21] led to a significant deterioration in overall reaction rate, and the magnitude of which for TTBP-added reactions is in contrast to that reported by Beau and co-workers, where only a slight rate decrease with TTBP was observed.[13]

Going to only 5 mol % catalyst loading still provided a fast turnover and produced allyl glycoside **2** in a useful timespan (entries 14−18, Table 1). As expected, reaction times were considerably shorter for donor **1** than for its α-anomer (entry 20, Table 1) and for the corresponding tetra-*O*-acetyl-β-GlcNAc (entry 19, Table 1), which we had previously reported.

A series of more complex and relevant glycosyl acceptors were explored as substrates to establish the scope of this new glycosylation system. Of the most time-efficient catalysts, we carried on with the easily handled $Bi(OTf)_3$. In addition, we tested $Fe(OTf)_3$·6.2DMSO, which has been reported as a catalyst in similar glycosylation reactions[13] with the advantage of a lower hygroscopicity than $Fe(OTf)_3$ itself.[21] Excellent glycosylation yields, shorter reaction times, and stoichiometry were found with primary acceptor alcohols compared to previous studies (entries 1−8, Table 2).[12,13] The secondary acceptor **7** (entries 9 and 10, Table 2) posed more of a challenge, as has often been the case in previous studies. The yield could be optimized to 37% with reisolation of most (58%) of the unreacted acceptor. This resulted is an improvement of our earlier findings with the corresponding tetra-*O*-acetylated donor (21% yield, 15 mol % $Sc(OTf)_3$), where 4 equiv of glycosyl donor was used.[12] In general, reactions with challenging acceptors were found to be improved by using less forcing conditions such as less catalyst or a milder one. This is in accordance with our previous observations for GalNAc-ylation (Scheme 3B).[17]

The extended reaction time needed for reaction with the secondary acceptor alcohol **7** resulted in significant amounts of the unexpected benzyl β-glycoside **13** (23%, Scheme 5A), which was also formed in the absence of acceptor (Scheme 5B).

Table 1. Catalytic Activation of Donor 1 According to Scheme 4B[a]

entry	cat.	loading[b] (%)	time[c]	yield[d] (%)
1	$Bi(OTf)_3$	15	20 min	83
2	$Bi(OTf)_3$ + TTBP	15	>6 h 30 min	87
3	$Bi(OTf)_3$·7.8DMSO	15	40 min	74
4	$Bi(OTf)_3$·7.8DMSO + TTBP	15	4 h 30 min	91
5[e]	$Fe(OTf)_3$	15	25 min	88
6	$Fe(OTf)_3$·6.2DMSO	15	50 min	86
7	$Fe(OTf)_3$·6.2DMSO + TTBP	15	5 h 20 min	88
8	$Cu(OTf)_2$	15	20 min	74
9	$Yb(OTf)_3$	15	35 min	70
10	$FeCl_3$	15	45 min	83
11	$BiCl_3$	15	4 h	87
12	$CuCl_2$	15	6 h	86
13	TfOH	15	30 min	82
14	$Bi(OTf)_3$	5	40 min	90
15	$Fe(OTf)_3$	5	60 min	87
16	$Sc(OTf)_3$	5	60 min	88
17	$Cu(OTf)_2$	5	70 min	86
18	$Yb(OTf)_3$	5	115 min	91
19[f]	$Bi(OTf)_3$	15	110 min	83
20[g]	$Bi(OTf)_3$	15	18 h	73

[a]All reactions performed in CH_2Cl_2 at reflux with 3 equiv of allyl alcohol as the acceptor with or without 2 equiv of TTBP. [b]Catalyst loading relative to donor. [c]Time required for full conversion of donor as determined by TLC analysis. [d]Isolated yield after chromatography. [e]Catalyst added in a glovebox due to catalyst hygroscopicity. [f]Tetra-*O*-acetyl β-GlcNAc with benzyl alcohol.[12] [g]1-Epimer of donor **1** (**1**α) used.

This surprising side reaction will be discussed further below (see Scheme 9).

Detailed Reaction Monitoring. We considered that more detailed knowledge about the course of these glycosylation reactions might result in important fundamental insights necessary for future developments in the field. Therefore, representative glycosylation reactions were performed in an NMR tube at 40 °C with $CDCl_3$ as the solvent and 1,3,5-tris(trifluoromethyl)benzene as internal reference for quantification (Scheme 6).

Figures 1 and 2 contain normalized integral values as a function of reaction time for selected experiments. Glycosylation with donor **1**, AllOH, or *i*PrOH (3 equiv) and 2.5 mol % of $Bi(OTf)_3$ at 40 °C both proceeded cleanly, forming product and consuming donor in a synchronous manner across the course of the reaction. A similar result, albeit with a considerably longer reaction time, was obtained under similar conditions using 1 equiv of the acceptor (−)-L-menthol (Figure 1 and Scheme 6). In none of these reactions did the signals from an oxazolinium species appear integratable in the obtained spectra.

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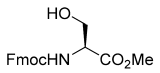
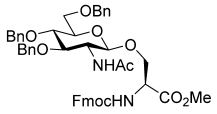
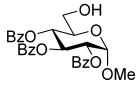
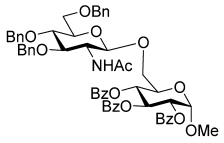
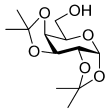
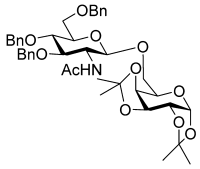
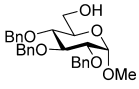
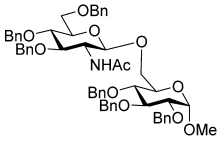
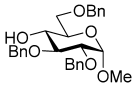
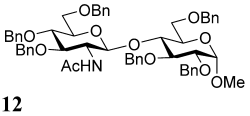
Table 2. Glycosylation of Various Alcohols with Donor 1[a]

Entry	Acceptor	Product	Catalyst[b]	Temp[c]	Time[d]	Yield[e]
1	 **3**	 **8**	5% $Bi(OTf)_3$	Reflux	50 h	80% (16)
2	 **4**	 **9**	5% $Bi(OTf)_3$	Reflux	48 h	90%
3	 **5**	 **10**	5% $Bi(OTf)_3$	Reflux	50 h	71% (22)
4	**5**	**10**	2.5% $Fe(OTf)_3$ ·6.2DMSO	45 °C	16 h	87%
5	 **6**	 **11**	5% $Bi(OTf)_3$	Reflux	48 h	84% (16)
6	**6**	**11**	5% $Bi(OTf)_3$	80 °C[f]	1.5 h	50% (39)
7	**6**	**11**	2.5% $Bi(OTf)_3$	Reflux	43 h	98%
8	**6**	**11**	2.5% $Fe(OTf)_3$ ·6.2DMSO	45 °C	16 h	88%
9	 **7**	 **12**	2.5% $Bi(OTf)_3$	Reflux	6 days	29% (71)
10	**7**	**12**	2.5% $Fe(OTf)_3$ ·6.2DMSO	45 °C	72 h	37% (58)

[a]Reactions were conducted in CH_2Cl_2 with donor and acceptor in a 2:1 ratio. [b]Catalyst loading with respect to donor. [c]All reactions were conducted in sealed vials except where marked "Reflux". [d]No further conversion as determined by TLC analysis. [e]Isolated yield; percent reisolation of acceptor shown in parentheses. [f]Reaction carried out under microwave irradiation.

The results changed considerably on going from 2.5 to 15 mol % catalyst (Figure 2). Under these more forcing conditions, (−)-L-menthol consumption and product formation occurred more slowly than the donor activation, and oxazolinium ion was in this case observable throughout the reaction to a level corresponding to the catalyst loading. At the 33 min data point, 15% of donor is unaccounted for. The same overall observation was made using 15 mol % of TfOH as the catalyst.

Based on these observations, reaction yields might be expected to decrease upon going from low to high catalyst loading. Indeed, with a fixed reaction time of 16 h, we observed

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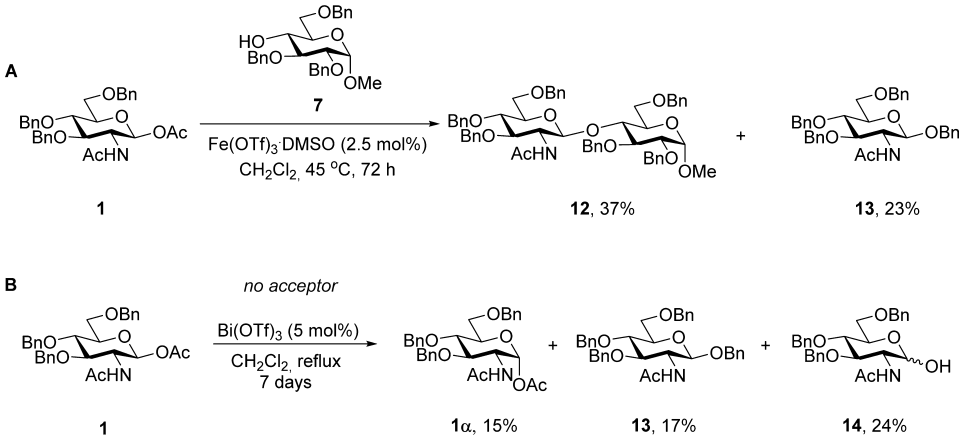
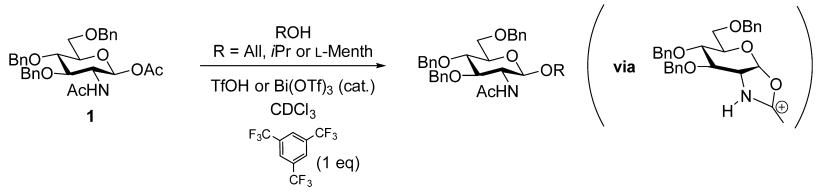
Scheme 5. Reaction of Donor 1 over Prolonged Reaction Times with Acceptor 7 or in the Absence of Acceptor



Scheme 6. Reaction Conditions for GlcNAc-ylation Monitored by ^{1}H NMR Analysis (See Figures 1 and 2)



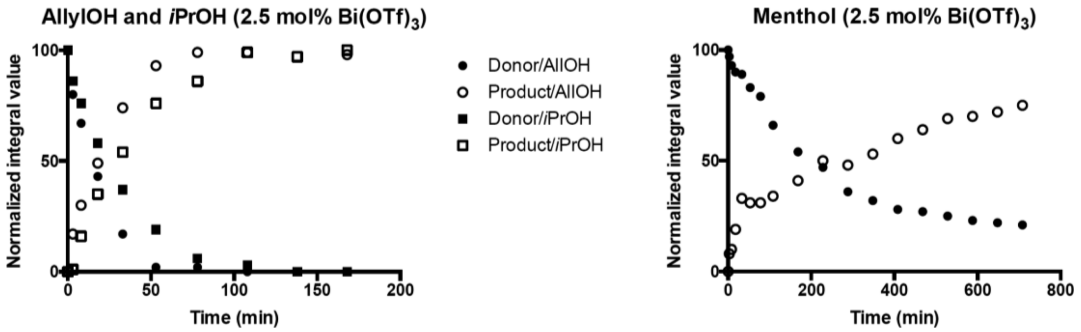


Figure 1. GlcNAc-ylation reaction course according to Scheme 6 by ^{1}H NMR integrals of donor **1** and product in glycosylation of AllOH or *i*PrOH (2.5 mol % $Bi(OTf)_3$) (left). Closed symbols: donor. Open symbols: product. Circles: iPrOH. Squares: AllOH. (−)-L-Menthol (2.5 mol % $Bi(OTf)_3$) (right). Closed symbols: donor. Open symbols: product. The integrals were normalized according to the internal standard 1,3,5-tris(trifluoromethyl)benzene.

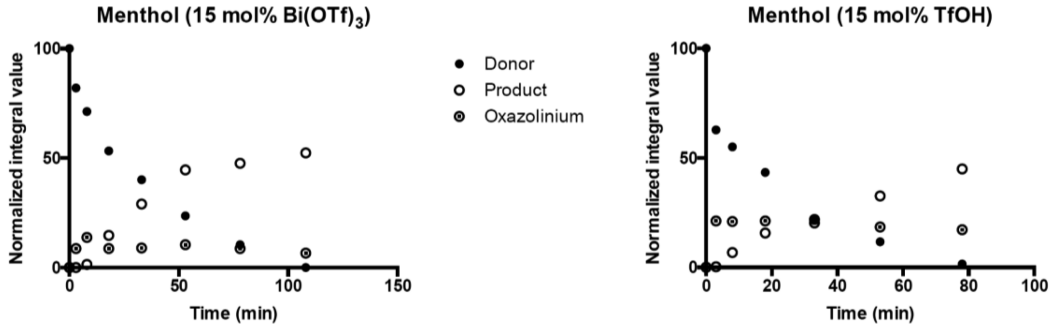


Figure 2. GlcNAc-ylation reaction course according to Scheme 6 by ^{1}H NMR integrals of donor **1** and product in glycosylation of (−)-L-menthol (15 mol % $Bi(OTf)_3$, left; 15 mol % TfOH, right). Closed symbols: donor. Open symbols: product. Dotted symbols: oxazolinium. The integrals were normalized according to the internal standard 1,3,5-tris(trifluoromethyl)benzene.

a significantly higher yield of the corresponding reaction using (−)-L-menthol when the catalyst loading was lowered from 15 to 2.5 mol % (Scheme 7A). Yields could also be optimized with acceptors **5** and **6** as shown in Table 2.

As shown by NMR, glycosylation with 15 mol % of TfOH or $Bi(OTf)_3$, as compared to 2.5 mol %, clearly resulted in the presence of oxazolinium ion in increased concentrations. Furthermore, separate ^{1}H NMR experiments indicated that

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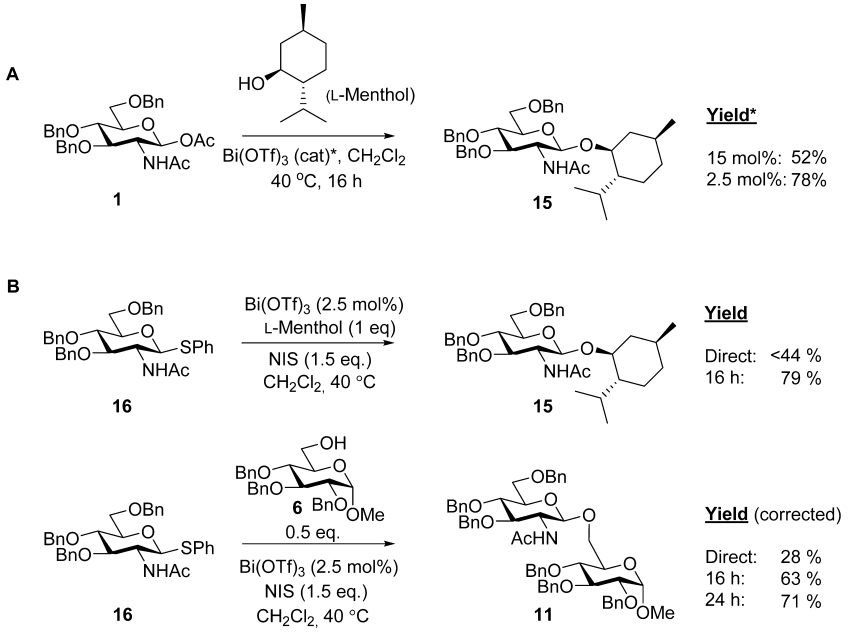
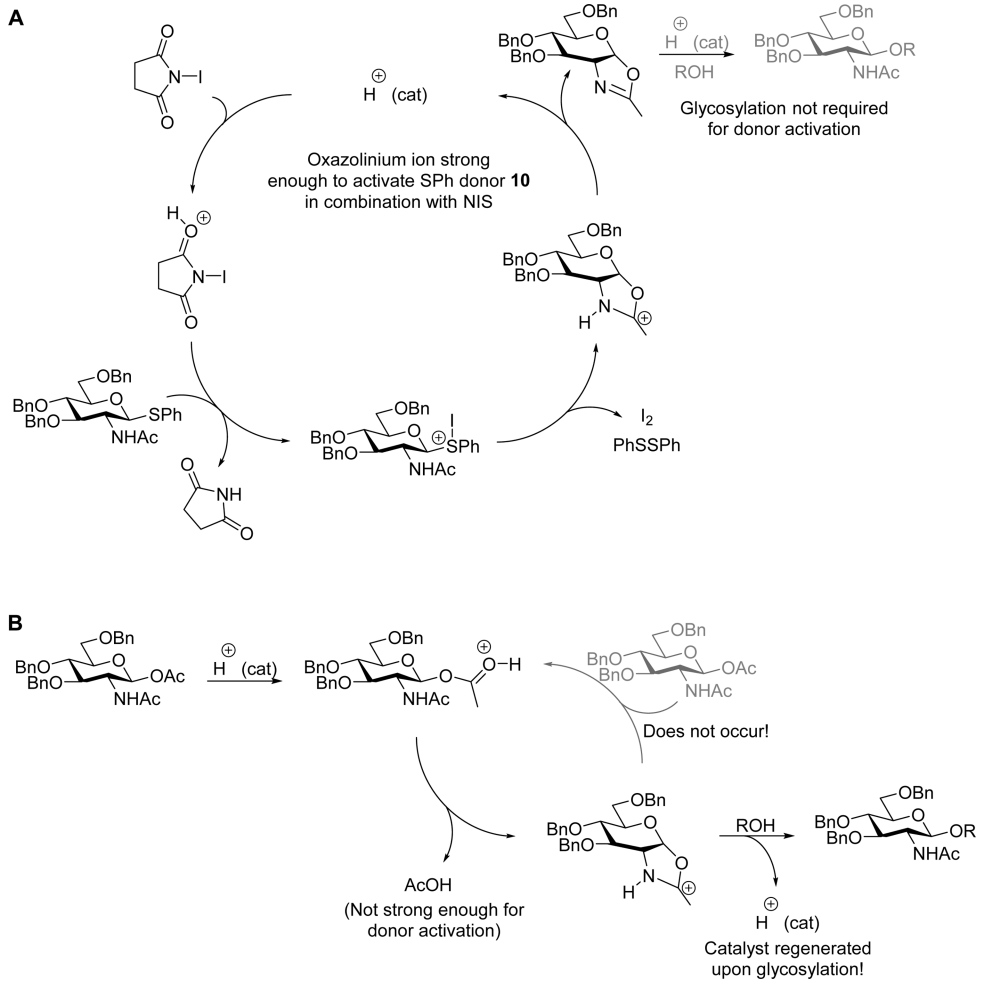
Scheme 7. Isolated Yields of (A) Reactions Corresponding to the ^{1}H NMR Time Course Experiments with (−)-L-Menthol as the Acceptor Using High (15 mol %) or Low (2.5 mol %) Catalyst Loading and (B) Reactions with Conventional Thioglycoside Donor 16 and (−)-L-Menthol or 6 as the Acceptor Adding NIS Either Directly or over Extended Periods of Time



Scheme 8. (A) Activation of GlcNAc Thioglycosides Are Acceptor-Independent; (B) Activation of GlcNAc 1-OAc Donors Are Glycosylation Dependent for Regeneration of the Acid Catalyst



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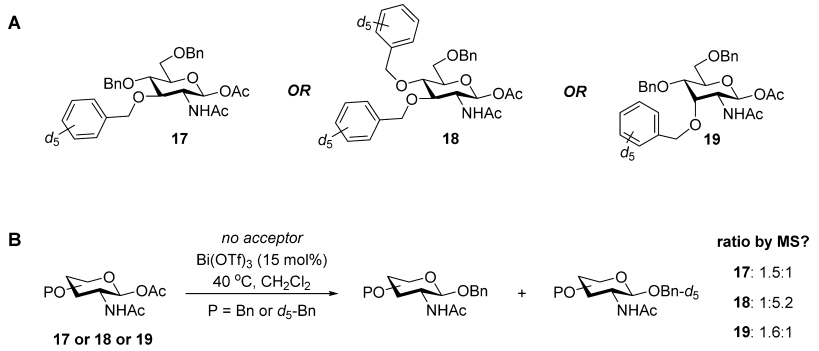
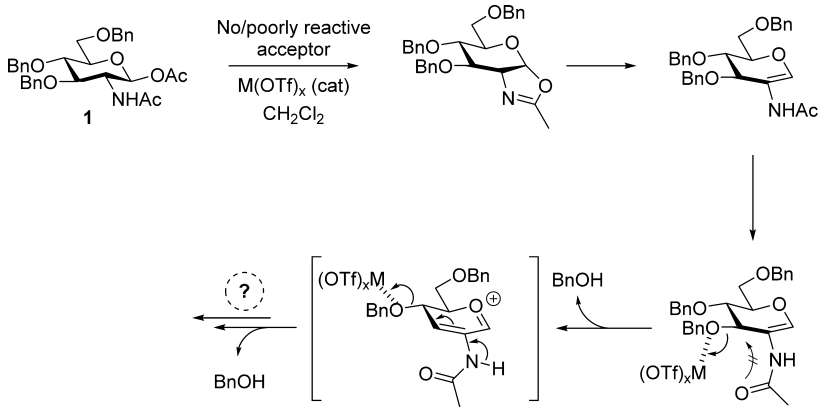
Scheme 9. (A) Deuterium-Labeled Glycosyl Donors To Study the Origin of Benzyl Alcohol in Formation of Glycoside 13. (B) Experimental Conditions Used To Study Product Distributions by HRMS



Scheme 10. Proposed Mechanism for the Formation of BnOH from Donor 1 per Analogy to Related Observations by Lichtenthaler and Co-workers[23,24]



1 equiv of TfOH would convert the acetate donor quantitatively to the oxazolinium species in a few minutes (data not shown), and this species (or the oxazoline) was readily observable as a single spot by TLC analysis. These and the above observations led to the hypothesis that, as a consequence of high catalyst loading, a high concentration of oxazoline during reaction would lead to formation of side products and diminished yields.

We hereupon turned to a conventional donor type, thioglycoside **16** (Scheme 7B). TLC analysis revealed that with this donor activation was in all cases complete after a few minutes when 2.5 mol % of $Bi(OTf)_3$, acceptor, and 1.5 equiv of NIS in CH_2Cl_2 at 40 °C were introduced. After this time, oxazoline could be observed on TLC analysis for the remaining reaction time. As shown above, this is in stark contrast to the acetate **1**, which activates slowly and in an acceptor-dependent fashion (Figure 1). We speculate that the reason for the generally observed poor performance of this donor in 2-acetamido systems is that activation of these thioglycosides is catalytic and acceptor independent (Scheme 8A). This would lead to an extreme case of the high-catalyst scenario from above. During activation of the thioglycoside, formation of the relatively acidic oxazolinium species could activate another equivalent of thioglycoside (Scheme 8A). Oxazolinium, however, would not constitute a strong enough acid to activate the less labile acetate donor (Scheme 8B). This donor requires glycosylation of the acceptor to regenerate the acid catalyst for continuation of the activation cycle.

For the above hypothesis to hold true, in accordance with the NMR studies above, the yields of the glycosylation reactions would be expected to increase if activation of the donor could be slowed down. Accordingly, we performed glycosylation reactions under modified conditions as shown in Scheme 7B. To control the activation of the thioglycoside, NIS was added directly to the reaction at the start in one portion or gradually over the 16 h reaction time via syringe pump. Scheme 7B reveals that slow activation of the thioglycoside **16** does indeed increase the glycosylation yield of 1 equiv of (−)-L-menthol from below 44% to 79%. Furthermore, the reaction became cleaner with slow activation, allowing the isolation of pure product. This trend extends to the carbohydrate-based acceptor **6**; when subjected to similar reaction conditions, the glycosylation yield increased from the rather poor 28% to a more pleasing 63%. Increasing the addition time from 16 to 24 h led to a further enhanced yield of 71%.

Given the above observations, it is interesting to note that when subjected to 2.5 mol % of $Bi(OTf)_3$ and 1.5 equiv of NIS in CH_2Cl_2 at 40 °C without acceptor, an analogous Troc-protected thioglycoside activated immediately, much like the observations we had just made with thioglycoside **16** (data not shown). We attribute the high yields usually obtained with this donor type in spite of this to a higher glycosylation rate (k_2).

Donor Degradation. Keen on understanding what becomes of the donor in situations like the one in Figure 2 where the activation (k_1) and glycosylation (k_2) rates are mismatched, we set out to identify some of the donor derived byproducts. Under glycosylation conditions with no acceptor present three major products could be identified (Scheme 5B). One dominating side reaction was found to be donor anomerization, which will lower the yield of the overall

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reaction since **1α** is a less reactive donor (entry 20, Table 1). Lactol is a commonly formed byproduct in glycosylation reactions[22] and could therefore also be expected. More puzzling was the discovery of benzyl glycoside **13** as a major byproduct, the same compound as observed in the glycosylation of acceptor **7** in Scheme 5A. As no source of benzyl alcohol had been added, the donor (**1**) must itself have been the source. This should lead to the realization that in a glycosylation like the one in Scheme 5 not only has 23% of the donor **1** been converted to benzyl glycoside **13** but another unknown quantity of **1** will have presumably provided the benzyl alcohol, making this a very important donor degradation pathway indeed. In order to investigate the origin of this benzyl alcohol, we synthesized three deuterium-labeled analogues **17**−**19** (Scheme 9A) including an *allo*-epimer (**19**) and subjected them to glycosylation conditions (Scheme 9B). Each reaction was monitored using HRMS, and the product distributions of nonlabeled (light) and labeled (heavy) glycosides were determined for each donor (Scheme 9B).[19]

Assuming equal ionizability of these mono-, bis-, and tris-labeled benzyl glycosides, HRMS indicates the source of the anomeric benzyl group of **13**. We were surprised to find that the combined results indicated that the 3-OBn and the 4-OBn account for roughly 40% of the liberated benzyl alcohol each.[19] We speculate that the Ferrier-type rearrangements reported by Lichtenthaler et al.[23,24] in similar systems might at least partially explain these findings (Scheme 10). Participation of the NHAc was contraindicated by experiments with the *allo*-configured analogue **19**, which yielded the benzyl glycosides in roughly the same ratio as did the corresponding *gluco*-configured **17** (1.6:1 and 1.5:1, respectively).[19]

CONCLUSION

We have shown that donor **1** performs excellently as a glycosyl donor in direct GlcNAc-ylation with primary alcohol acceptors and that this is an improvement compared to previous donor types investigated in terms of reaction time, catalyst loading, and excess of donor used. Compared to existing methodology, the glycosylation yield has been significantly improved, but for reactions with a secondary carbohydrate based acceptor yields remain moderate.

More importantly, this study demonstrates the power of balancing the rate of oxazoline formation (k_1, Scheme 1) controlled by, e.g., catalyst loading/Lewis acidity and glycosylation (k_2, Scheme 1) influenced by the nature of the acceptor nucleophile. Time−course experiments showed a correlation between the synchronous nature of the glycosylation reaction and the success of a direct GlcNAc-ylation. The gained insight led to the controlled activation of a GlcNAc thioglycoside secured by slow addition of NIS to a reaction mixture containing glycosyl donor, acceptor, and Lewis acid catalyst. In the case of a carbohydrate-based acceptor the yield could be rescued from 28% under conditions with direct addition to 71% with slow addition over 24 h, approaching the yield obtained with the slowly activating acetate donor function.

We have furthermore found that a significant side reaction of the glycosyl donor is loss of benzyl alcohol and that this does not proceed through neighboring group participation since the analogous AllNAc donor behaved similarly as the GlcNAc donor.

We strongly believe we have shed much needed scientific light upon paramount fundamental issues concerning GlyNAc-derived donors. It is our hope to see these insights kindle a renewed interest in GlyNAc-chemistry. The question remains whether direct GlyNAc-ylation can indeed be optimized significantly beyond the results disclosed herein.

EXPERIMENTAL SECTION

General Remarks. Air- and moisture-sensitive reactions were conducted in flame-dried glassware under an atmosphere of Ar or N_2. Anhydrous solvents were dried over aluminum oxide and dispensed from a solvent purification system. DMF and dioxane were purchased as anhydrous. Solvents were removed under reduced pressure at 40 °C. Flash column chromatography was performed using silica gel (230−400 mesh) unless otherwise noted. TLC analysis was conducted on silica gel coated aluminum foil (Kieselgel 60 F_{254}) and observed under UV light or visualized by staining in 10% H_2SO_4 with orcinol followed by vigorous heating. NMR spectra were recorded on a 400 spectrometer. Chemical shifts (δ) are reported in ppm relative to the residual signals (^{1}H NMR: $CDCl_3$, 7.26; CD_3OD, 4.87; DMSO-d_6, 2.50 and ^{13}C NMR: $CDCl_3$, 77.2; CD_3OD, 49.0; DMSO-d_6, 39.5). ^{1}H and ^{13}C NMR spectra were interpreted on the basis of *g*COSY, *g*HMQC, and DEPT-135 techniques and where necessary 1D-selective ^{1}H-TOCSY, proton-coupled ^{13}C, or HMBC spectra. Mass spectra were recorded on a TOF-Q high performance MS system. Optical rotations were measured in concentrations reported in g/100 mL on a polarimeter and reported in units of deg·cm^2·g^{-1}. Sonication of reactions was carried out in a ultrasonic bath. Microwave experiments were carried out in a Biotage Initiator (external sensor type). Reaction times listed in these cases refer to "hold time" at the specified temperature.

General Procedure for Glycosylation. 2-Acetamido-1-*O*-acetyl-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranose (**1**) (2 equiv) and acceptor (1 equiv) were dissolved in dry CH_2Cl_2 to an acceptor concentration of 0.10 M. Lewis acid (2.5 or 5 mol % with respect to donor according to Table 2.) was added and the reaction mixture stirred at 45 °C. The reaction was monitored by TLC analysis until there was no further indication of reaction development. The reaction mixture was poured into a separation funnel, diluted with CH_2Cl_2, and washed with water. The aqueous layer was extracted twice with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$, filtered, concentrated under reduced pressure, and purified using flash column chromatography which afforded the desired glycoside products (Table 2.).

^{1}H NMR Time Course Experiments (Figures 1 and 2). 2-Acetamido-1-*O*-acetyl-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranose (**1**) (48 mg, 0.09 mmol, 1 equiv), acceptor (3 equiv for AllOH and *i*PrOH, 1 equiv for (−)-L-menthol), and the internal standard 1,3,5-tris(trifluoromethyl)benzene (16.8 μL, 1 equiv) were dissolved in dry $CDCl_3$ (600 μL) and transferred to an NMR tube. Lewis acid ($Bi(OTf)_3$ or TfOH, 2.5 or 15 mol %) was added whereupon the sample was heated to 40 °C while obtaining ^{1}H NMR spectra at selected time points (see the SI for stacked spectra). Integral values from each spectrum corresponding to baseline-separated signals from donor and product (and oxazolinium where relevant) were normalized using the internal standard and plotted against time in Figures 1 and 2.

Glycosylation According to Scheme 7A. Two reactions were set up. 2-Acetamido-1-*O*-acetyl-2-deoxy-3,4,6-tri-*O*-benzyl-β-D-glucopyranose (**1**) (48 mg, 0.09 mmol, 1 equiv), (−)-L-menthol (14.1 mg, 0.09 mmol, 1 equiv), and $Bi(OTf)_3$ (2.5 or 15 mol %) were dissolved in dry CH_2Cl_2 (0.6 mL) and heated to 40 °C for 16 h. The reactions were then evaporated onto Celite and subjected to flash column chromatography (5 → 10% EtOAc in toluene), which afforded the desired product **15**. R_f: 0.56 (20% EtOAc in toluene). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.36−7.20 (m, 15H, Ar*H*), 5.70 (d, $J_{2,NH}$ 7.9 Hz, 1H, NH), 4.96 (d, $J_{1,2}$ 8.2 Hz, 1H, H1), 4.85 (d, J_{gem} 11.5 Hz, 1H, OC*H*HPh), 4.81 (d, J_{gem} 10.8 Hz, 1H, OC*H*HPh), 4.68 (d, 1H, OCH*H*Ph), 4.64 (d, 1H, OCH*H*Ph), 4.63 (d, J_{gem} 12.9 Hz, 1H, OC*H*HPh), 4.55 (d, 1H, OCH*H*Ph), 4.33 (t, $J_{2,3} = J_{3,4}$ 9,5 Hz, 1H, H3), 3.75 (dd, J_{gem} 11.0, $J_{5,6a}$ 4.1 Hz, 1H, H6a), 3.69 (dd, $J_{5,6b}$ 1.9 Hz, 1H, H6b), 3.63 (t, $J_{3,4} = J_{4,5}$ 9,2 Hz, 1H, H4), 3.52 (ddd, 1H, H5), 3.42 (dt, *J* 4.3 Hz, *J* 10.7 Hz, 1H, C*H*OGlcNAc), 3.15 (dt, 1H, H2), 2.32 (d

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septet, *J* 2.5 Hz, *J* 7.1 Hz, 1H, C*H*$(CH_3)_2$), 1.93 (dt, *J* 3.9 Hz, *J* 12.2 Hz, 1H) 1.84 (s, 3H, NHC(O)CH_3), 1.68−1−58 (m, 2H), 1.40−1.25 (m, 1H), 1.24−1.14 (m, 1H), 1.06−0.72 (m, 3H), 0.89 (d, *J* 6.8 Hz, 6H, CH_3CHCH_3), 0.80 (d, *J* 7.0 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.5 (*C*═O), 138.8, 138.4, 138.3, 128.5, 128.4, 128.03, 127.99, 127.8, 127.72, 127.70, 127.6 (Ar), 97.5 (C1), 80.5 (C3), 79.2 (C4), 78.2, 74.81 (C5, OCH_2Ph), 74.78, 73.76 (OCH_2Ph), 69.3 (C6), 58.6 (C2), 47.9, 41.0, 34.4, 31.4, 25.1, 23.7 (NHC(O)CH_3), 23.1, 22.4 (CH_3), 21.2 (CH_3), 15.8 (CH_3). HRMS(ES): calcd for $C_{39}H_{51}NO_6H^+$ 630.3789, found 630.3866. The NMR data were in accordance with those previously published.[18]

Glycosylation According to Scheme 7B. Two identical reactions were set up in parallel. Phenyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside[18] (**16**) (53 mg, 0.09 mmol, 1 equiv), (−)-L-menthol (14.1 mg, 0.09 mmol, 1 equiv), and $Bi(OTf)_3$ (1.5 mg, 2.3 μmol, 2.5 mol %) were dissolved in dry CH_2Cl_2 (0.6 mL) and heated to 40 °C. NIS (30 mg, 0.14 mmol, 1.5 equiv) was added as a solution in dry dioxane (0.5 mL) either directly or over 16 h via syringe pump (0.52 μL/min). TLC analysis (20% EtOAc in toluene) indicated full conversion of donor after 30 min with direct addition of NIS. After 16 h, TLC also indicated full conversion of donor with slow addition of NIS. Both reactions were evaporated onto Celite and subjected to flash column chromatography (0 → 5→10% EtOAc in toluene), which afforded the desired product **15**.

The glycosylation of methyl 2,3,4-tri-*O*-benzyl-*β*-D-glucopyranoside (**6**) with phenyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside (**16**)[18] was carried out as described above with addition of NIS as described in the scheme.

Isolation of Donor-Derived Byproducts According to Scheme 5B. 2-Acetamido-1-*O*-acetyl-2-deoxy-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranose (**1**) (86 mg, 0.16 mmol, 1 equiv) and $Bi(OTf)_3$ (5 mg, 8.1 μmol, 5 mol %) were dissolved in dry CH_2Cl_2 (1.1 mL) and heated to 40 °C for 7 days. The resulting mixture was diluted and washed with half-saturated $NaHCO_3$ (aq), which was back-extracted three times with CH_2Cl_2. The combined organics were dried over $MgSO_4$, filtered, and evaporated to give a crude which was subjected to flash column chromatography (2:1 → 1:1 → 2:3 → 1:2 pentane/EtOAc then EtOAc/CH_2Cl_2 9:1), which afforded benzyl 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-*β*-D-glucopyranoside (**13**) (15.8 mg, 17%), 2-acetamido-1-*O*-acetyl-2-deoxy-3,4,6-tri-*O*-benzyl-*α*-D-glucopyranose (**1*α***) (13.2 mg, 15%), and 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose (**14**) (18.5 mg, 24%).

2-Acetamido-1-*O*-acetyl-2-deoxy-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranose (1). 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose (14.3 g, 29.0 mmol, 1 equiv) was dissolved in dry pyridine to a concentration of 0.17 M. Pyridinium *p*-toluenesulfonate (PPTS) (11.0 g, 43.6 mmol, 1.5 equiv) was added, and the reaction mixture was heated to 100 °C for 15 min under stirring. Ac_2O (8.2 mL, 87 mmol, 3 equiv) was added as a solution in dry pyridine (1.4 M) to the reaction over 15 min using a syringe pump. The reaction mixture was quenched with CH_3OH (2 mL) and concentrated under reduced pressure to dryness. The resulting crude was dissolved in CH_2Cl_2 and washed with 1 M HCl (aq), satd $NaHCO_3$ (aq), and H_2O. The combined aqueous layers were extracted twice with CH_2Cl_2 which was washed with 1 M HCl (aq), satd $NaHCO_3$ (aq), and H_2O. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude (16.4 g) with an *α*/*β* ratio according to NMR of 7:93. The crude was recrystallized from EtOAc, filtered and washed with cold Et_2O to afford the desired compound **1** (9.85 g, 64%) as a white solid. R_f: 0.28 (EtOAc/toluene 1:1). $[\alpha]_D^{20}$: +28.0 (*c* 1, $CHCl_3$) [lit.[25] +34 (*c* 0.5, $CHCl_3$)]. Mp: 148.1−148.8 °C (EtOAc) [lit.[25] mp 159−162 °C (EtOAc)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.37−7.27 (m, 13H, Ar*H*), 7.19 (dd, *J* 2.2 Hz, *J* 7.2 Hz, 2H, Ar*H*), 5.69 (d, $J_{1,2}$ 7.8 Hz, 1H, H1), 5.19 (d, $J_{NH,2}$ 8.8 Hz, 1H, NH), 4.80 (d, J_{gem} 11.7 Hz, 1H, OC*H*HPh), 4.76 (d, J_{gem} 10.5 Hz, 1H, OC*H*HPh), 4.65 (d, 1H, OCH*H*Ph), 4.61 (d, J_{gem} 12.0 Hz, 1H, OC*H*HPh), 4.58 (d, 1H, OCH*H*Ph), 4.50 (d, 1H, OCH*H*Ph), 4.03 (dt, $J_{2,3}$ 9,2 Hz, 1H, H2), 3.79 (t, $J_{3,4} = J_{4,5}$ 8.3 Hz, 1H, H4), 3.75−3.72 (m, 2H, H6a, H6b), 3.68 (dd, 1H, H3), 3.66 (td, 1H, $J_{5,6}$ 3.5 Hz, H5), 2.06 (s, 3H, OCOCH_3), 1.79 (s, 3H, NHCOCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.1, 169.8 (*C*═O), 138.1, 137.9, 137.8 (*ipso*-Ar*C*), 128.5, 128.5, 128.4, 128.2, 128.0, 127.9, 127.9, 127.7 (Ar), 92.8 (C1), 80.7 (C4), 77.5 (C3), 75.6, 74.6, 74.3 (OCH_2Ph), 73.5 (C5), 68.5 (C6), 53.6 (C2), 23.4 (NHC(O)CH_3), 21.1 (OC(O)CH_3). HRMS(ES): calcd for $C_{31}H_{35}NO_7Na^+$ 556.2306, found 556.2312. The NMR data were in accordance with those previously published.[11,25]

2-Acetamido-1-*O*-acetyl-2-deoxy-3,4,6-tri-*O*-benzyl-*α*-D-glucopyranose (1*α*). 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose (380 mg, 0.77 mmol, 1 equiv) was dissolved in dry pyridine (3.8 mL) before Ac_2O (220 μL, 2.3 mmol, 3 equiv) was added to the mixture and the resulting mixture stirred for 20 h. The reaction mixture was poured into ice−water before extracting with EtOAc and washing with 1 M HCl (aq), satd $NaHCO_3$ (aq), and brine. The organic layer was dried over $MgSO_4$, filtered, concentrated under reduced pressure, and purified by flash column chromatography (EtOAc/CH_2Cl_2 1:5 → 1:4 → 1:3) to separate the anomeric mixture and afford the desired compound **1*α*** (106 mg, 26%) as a colorless amorphous solid, which was recrystallized in EtOAc to afford colorless crystals (59 mg). R_f (EtOAc/toluene 1:1): 0.19. $[\alpha]_D^{20}$ +94.7 (*c* 1.0, $CHCl_3$) [lit.[26] +149 (*c* 0.29, MeOH)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.40−7.27 (m, 13H, Ar*H*), 7.22−7.19 (m, 2H, Ar*H*), 6.14 (d, $J_{1,2}$ 3.5 Hz, 1H, H1), 4.95−4.88 (m, 1H, N*H*), 4.89 (d, J_{gem} 11.8 Hz, 1H, OC*H*HPh), 4.82 (d, J_{gem} 10.6 Hz, 1H, OC*H*HPh), 4.65 (d, 1H, OCH*H*Ph), 4.64 (d, 1H, J_{gem} 12.1 Hz, OC*H*HPh), 4.59 (d, 1H, OCH*H*Ph), 4.51 (d, 1H, OCH*H*Ph), 4.32 (ddd, $J_{2,NH}$ 8.6 Hz, $J_{2,3}$ 10.7 Hz, 1H, H2), 3.87 (dd, $J_{3,4}$ 8.7 Hz, $J_{4,5}$ 9.7 Hz, 1H, H4), 3.83−3.76 (m, 2H, H5, H6a), 3.71 (dd, 1H, H3), 3.69−3.64 (m, 1H, H6b), 2.07 (s, 3H, OCOCH_3), 1.79 (s, 3H, NHCOCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 169.9, 169.0 (*C*═O), 138.3, 138.0, 137.8 (ipso-Ar*C*), 128.7, 128.6, 128.5, 128.3, 128.1, 128.0, 127.9, 127.7 (Ar), 91.7 (C1), 79.0 (C3), 77.9 (C4), 75.2, 74.6, 73.6 (OCH_2Ph), 73.4 (C5), 68.2 (C6), 51.5 (C2), 23.3 (NHCOCH_3), 21.0 (OCOCH_3). HRMS(ES): calcd for $C_{31}H_{35}NO_7Na^+$ 556.2306, found 556.2309.

Allyl 2-Acetamido-2-deoxy-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranoside (2). *From Allyl 2-Acetamido-2-deoxy-β-D-glucopyranoside (20).* Allyl 2-acetamido-2-deoxy-*β*-D-glucopyranoside (12.7 g, 48.6 mmol, 1 equiv) was dissolved in dry DMF (130 mL). 60% NaH on mineral oil (7.58 g, 190 mmol, 3.9 equiv) was added slowly under vigorous stirring before BnBr (19.1 mL, 160 mmol, 3.3 equiv) was added in small portions over a total of 30 min, after which time the mixture was allowed to stir overnight at room temperature. The mixture was poured onto ice/water, the precipitate was filtered off, and the mother liquor was extracted with EtOAc (3 × 100 mL). The precipitate and the combined organics were co-evaporated to dryness with toluene and then purified by flash column chromatography (0 → 25% EtOAc in $CHCl_3$) to give the desired product **2** (14.1 g, 54%) as a colorless solid.

From 2-Acetamido-1-O-acetyl-2-deoxy-3,4,6-tri-O-benzyl-β-D-glucopyranose (1). Donor **1** (1 equiv) was dissolved in dry CH_2Cl_2 to a concentration of 0.15 M. Acceptor (3 equiv) and Lewis acid (according to Table 1) were added, and the resulting mixture stirred under reflux. The reaction was monitored by TLC analysis, and upon completion, the mixture was evaporated onto Celite and purified by column chromatography to afford the desired allyl glycoside **2** in yields according to Table 1. R_f (EtOAc/CH_2Cl_2 1:5): 0.26. Mp: 144.5−145.9 °C (CH_2Cl_2) [lit.[27] mp 146.5−149 °C (MeOH)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.35−7.27 (m, 13H, Ar*H*), 7.22−7.19 (m, 2H, Ar*H*), 5.88 (ddt, J_{trans} 16.9 Hz, J_{cis} 10.5 Hz, J_{vic} 5.5 Hz, 1H, CH_2CH═CH_2), 5.56 (d, $J_{NH,2}$ 7.8 Hz, 1H, N*H*), 5.25 (dq, J_{gem} = ^4J 1.4 Hz, 1H, CH═C*H*H), 5.16 (dq, 1H, CH═CH*H*), 4.85 (d, $J_{1,2}$ 7.7 Hz, 1H, H1), 4.81 (d, J_{gem} 11.6 Hz, 1H, OC*H*HPh), 4.78 (d, J_{gem} 11.1 Hz, 1H, OC*H*HPh), 4.67 (d, 1H, OCH*H*Ph), 4.61 (d, J_{gem} 12.3 Hz, 1H, OC*H*HPh), 4.59 (d, 1H, OCH*H*Ph), 4.55 (d, 1H, OCH*H*Ph), 4.33 (ddt, J_{gem} 13.0 Hz, 1H, OC*H*HCH═CH_2), 4.11 (dd, $J_{2,3}$ 9.4 Hz, $J_{3,4}$ 8.0 Hz, 1H, H3), 4.07 (ddt, 1H, OCH*H*CH), 3.77 (dd, J_{gem} 10.7 Hz, $J_{5,6a}$ 2.6 Hz, 1H, H6a), 3.72 (dd, $J_{5,6b}$ 4.3 Hz, 1H, H6b), 3.64 (dd, $J_{4,5}$ 9.1 Hz, 1H, H4), 3.60 (ddd, 1H, H5), 3.46 (dt, 1H, H2), 1.85 (s, 3H, NHCOCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.4 (*C*═O), 138.5, 138.2, 138.1 (*ipso*-Ar*C*), 134.1 (CH_2CH═CH_2), 128.3, 128.3, 128.3, 127.9, 127.8, 127.7, 127.6, 127.5 (Ar), 117.0 (CH═CH_2), 99.4 (C1),

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80.9 (C4), 78.5 (C3), 74.8, 74.5 (OCH_2Ph), 73.3 (C5), 69.6 (OCH_2CH), 69.0 (C6), 56.3 (C2), 23.5 ($NHCOCH_3$). LRMS(ES): calcd for $C_{32}H_{37}NO_6Na^+$ 554.3, found 553.9. The NMR data were in nearly complete accordance with those previously published,[28] although we disagree with a few of the assignments.

***N*-(9-Fluorenylmethoxycarbonyl)-*O*-(2-acetamido-2-deoxy-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-L-serine Methyl Ester (8).** The general glycosylation procedure was followed using donor **1** (211 mg, 0.40 mmol), $Bi(OTf)_3$ (5 mol %), and *N*-(9-fluorenylmethoxycarbonyl)-L-serine methyl ester **3** (68.4 mg, 0.20 mmol). TLC analysis indicated reaction cessation after 50 h. Flash column chromatography afforded the desired product **8** (131 mg, 80%) as a clear colorless glass and reisolated *N*-(9-fluorenylmethoxycarbonyl)-L-serine methyl ester (**3**) (11 mg, 16%). R_f (Et_2O/CH_2Cl_2 2:5): 0.32. Mp: 166.8−167.8 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.74 (d, *J* 7.5 Hz, 2H, Ar*H*), 7.68−7.60 (m, 2H, Ar*H*), 7.38 (t, *J* 7.5 Hz, 2H, Ar*H*), 7.34−7.25 (m, 15H, Ar*H*), 7.21−7.16 (m, 2H, Ar*H*), 5.98 (d, $J_{NHSer,H\alpha}$ 8.2 Hz, 1H, N*H*Ser), 5.50 (d, $J_{NH,2}$ 6.6 Hz, 1H, N*H*), 4.87 (d, $J_{1,2}$ 7.7 Hz, 1H, H1), 4.81 (d, J_{gem} 11.6 Hz, 1H, OC*H*HPh), 4.77 (d, J_{gem} 10.9 Hz, 1H, OC*H*HPh), 4.64 (d, 1H, OCH*H*Ph), 4.59 (d, J_{gem} 12.1 Hz, 1H, OC*H*HPh), 4.57 (d, 1H, OCH*H*Ph), 4.51 (d, 1H, OCH*H*Ph), 4.48−4.40 (m, 2H, H*α*, H9), 4.33 (dd, J_{gem} 10.5 Hz, $J_{H\alpha,H\beta}$ 7.5 Hz, 1H, H*β*), 4.29−4.21 (m, 2H, H10), 3.98 (t, $J_{2,3}$ 8.8 Hz, 1H, H3), 3.83 (dd, 1H, J 3.1 Hz, H*β*′), 3.74−3.68 (m, 5H, C*H*$_3$, H6), 3.64 (t, $J_{3,4}$ 8.7 Hz, 1H, H4), 3.54 (dt, $J_{4,5}$ 9.2 Hz, $J_{5,6}$ 3.1 Hz, 1H, H5), 3.39 (broad q, 1H, H2), 1.81 (s, 3H, NHC(O)C*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 170.9, 170.5 (*C*═O), 156.3 (NHC(O)O), 144.0, 143.8, 141.3 (Ar*C*), 138.4, 138.0 (ipso-Ar*C*), 128.5, 128.4, 128.4, 128.0, 127.8, 127.7, 127.7, 127.1, 125.3, 125.3, 120.0 (Ar), 100.4 (C1), 80.6 (C4), 78.4 (C3), 75.0 (C5), 74.7, 74.6, 73.5 (OCH_2Ph), 68.8 (C6), 68.7 (C*β*), 67.1 (C10), 56.5 (C2), 54.5 (C*α*), 52.6 (*C*H$_3$), 47.2 (C9), 23.4 ($NHCOCH_3$). HRMS(ES): calcd for $C_{48}H_{50}N_2O_{10}Na^+$ 837.3363, found 837.3381.

Methyl *O*-(2-Acetamido-2-deoxy-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside (9). The general glycosylation procedure was followed using donor **1** (213 mg, 0.40 mmol), $Bi(OTf)_3$ (5 mol %), and methyl 2,3,4-tri-*O*-benzoyl-*α*-D-glucopyranoside **4**[29] (102 mg, 0.20 mmol). TLC analysis indicated reaction cessation after 48 h. Flash column chromatography afforded the desired disaccharide **9** (178 mg, 90%) as an amorphous solid. R_f ($EtOAc/CH_2Cl_2$ 1:5): 0.42. Mp: 153.0−153.5 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.99−7.95 (m, 2H, Ar*H*), 7.92 (dd, *J* 8.3 Hz, *J* 1.2 Hz, 2H, Ar*H*), 7.82 (dd, *J* 8.4 Hz, *J* 1.3 Hz, 2H, Ar*H*), 7.56−7.26 (m, 22H, Ar*H*), 7.18 (dd, *J* 7.4 Hz, *J* 2.1 Hz, 2H, Ar*H*), 6.13 (t, $J_{2,3}$ = $J_{3,4}$ 9.4 Hz, 1H, H3), 5.95 (d, $J_{NH,2}$ 8.1 Hz, 1H, N*H*), 5.61 (t, $J_{3,4}$ = $J_{4,5}$ 9.8 Hz, 1H, H4), 5.26−5.20 (m, 2H, H1, H2), 4.81 (d, J_{gem} 11.5 Hz, 1H, OC*H*HPh), 4.78 (d, J_{gem} 11.1 Hz, 1H, OC*H*HPh), 4.71 (d, 1H, OC*H*HPh), 4.56 (d, J_{gem} 12.2 Hz, 1H, OC*H*HPh), 4.55 (d, 1H, OCH*H*Ph), 4.50 (d, $J_{1',2'}$ 8.0 Hz, 1H, H1′), 4.50 (d, 1H, OCH*H*Ph), 4.21−4.11 (m, 2H, H5, H6a), 3.88 (dd, $J_{3',4'}$ 9.6 Hz, $J_{2',3'}$ 8.5 Hz, 1H, H3′), 3.81−3.73 (m, 1H, H2′), 3.71 (dd, $J_{6'a,6'b}$ 10.8 Hz, $J_{5',6'a}$ 2.4 Hz, 1H, H6′a), 3.68−3.59 (m, 2H, H6′b, H4′), 3.55 (dd, J_{gem} 11.7 Hz, $J_{5,6b}$ 4.6 Hz, 1H, H6b), 3.49 (ddd, $J_{4',5'}$ 9.3 Hz, $J_{5',6'b}$ 4.7 Hz, 1H, H5′), 3.44 (s, 3H, OC*H*$_3$), 1.94 (s, 3H, OC(O)C*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 170.4 (*C*═O), 165.8, 165.7, 165.7 (OC(O)Ph), 138.5, 138.3, 138.1 (ipso-Ar*C*, Bz), 133.7, 133.4, 133.1 (ipso-Ar*C*, Bn), 130.0, 129.9, 129.6, 129.3, 129.2, 128.9, 128.6, 128.5, 128.5, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6 (Ar), 101.4 (C1′), 97.0 (C1), 81.8 (C4′), 78.4 (C3′), 75.3 (C5′), 74.8 (C4), 73.4, 72.0 (double intensity) (OCH_2Ph), 70.8, 69.3, 69.1, 68.5, 67.9 (C6′, C6, C5, C3, C2), 56.2 (C2′), 55.6 (OC*H*$_3$), 23.6 (OC(O)C*H*$_3$). LRMS(ES): calcd for $C_{57}H_{57}NO_{14}Na^+$ 1002.4, found 1001.8. The NMR data were in accordance with those previously published.[18]

***O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-*β*-D-glucopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose (10).** The general glycosylation procedure was followed using donor **1** (150 mg, 0.28 mmol), $Fe(OTf)_3$·6.2 DMSO (7 mg, 2.5 mol %) and 1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose (**5**) (37 mg, 0.14 mmol). TLC analysis indicated full conversion of acceptor after 16 h. Flash column chromatography (EtOAc/pentane 1:1 → 1.5:1) afforded the desired disaccharide **10** (90 mg, 87%) as a clear colorless syrup. R_f (CH_3OH/CH_2Cl_2 1:10): 0.71. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 7.36−7.26 (m, 13H, Ar*H*), 7.18 (dd, *J* 7.4 Hz, *J* 1.9 Hz, 2H, Ar*H*), 5.55 (d, $J_{NH,2'}$ 7.9 Hz, 1H, N*H*), 5.50 (d, $J_{1,2}$ 5.0 Hz, 1H, H1), 4.80 (d, J_{gem} 11.5 Hz, 1H, OC*H*HPh), 4.78 (d, J_{gem} 10.9 Hz, 1H, OC*H*HPh), 4.69 (d, $J_{1',2'}$ 7.9 Hz, 1H, H1′), 4.68 (d, 1H, OCH*H*Ph), 4.62 (d, J_{gem} 12.1 Hz, 1H, OC*H*HPh), 4.58−4.51 (m, 3H, OC*H*$_2$Ph, H6a), 4.28 (dd, $J_{2,3}$ 2.4 Hz, 1H, H2), 4.16 (dd, J_{gem} 7.9 Hz, $J_{5,6b}$ 1.8 Hz, 1H, H6b), 4.00 (dd, J_{gem} 11.3 Hz, $J_{5',6'a}$ 3.5 Hz, 1H, H6′a), 3.97−3.90 (m, 2H, H3, H6′b), 3.75−3.61 (m, 5H, H2′, H3′, H4′, H4, H5), 3.54 (dt, $J_{4',5'}$ = $J_{5',6'b}$ 9.4 Hz, 1H, H5′), 1.89 (s, 3H, NHC(O)C*H*$_3$), 1.51 (s, 3H, CC*H*$_3$), 1.42 (s, 3H, CC*H*$_3$), 1.31 (s, 3H, CC*H*$_3$), 1.30 (s, 3H, CC*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): *δ* 170.5 (*C*═O), 138.6, 138.3, 138.3 (ipso-Ar*C*), 128.5, 128.4, 128.1, 127.9, 127.8, 127.8, 127.7, 127.6 (Ar), 109.4, 108.7 (*C*(CH$_3$)$_2$), 101.3 (C1′), 96.4 (C1), 81.4 (C4′), 78.5 (C3′), 75.1, 74.7, 74.5 (OCH_2Ph), 73.6, 71.3, 70.8, 70.5, 69.1 (C2, C3, C4, C5′, C5), 68.9, 67.9 (C6′, C6), 56.2 (C2′), 26.2, 26.1, 25.1, 24.5, 23.7 (NHC(O)*C*H$_3$, C(*C*H3)$_2$). LRMS(ES): calcd for $C_{41}H_{51}NO_{11}Na^+$ 756.3, found 755.9. The NMR data were in accordance with those previously published.[18]

Methyl *O*-(2-Acetamido-2-deoxy-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside (11). The general glycosylation procedure was followed using donor **1** (231 mg, 0.43 mmol), $Bi(OTf)_3$ (2.5 mol %), and methyl 2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside (**6**) (100 mg, 0.22 mmol). TLC analysis indicated reaction cessation after 43 h. Flash column chromatography ($EtOAc/CH_2Cl_2$ 1:5) afforded the desired disaccharide **11** (198 mg, 98%) as an amorphous solid. R_f ($EtOAc/CH_2Cl_2$ 1:5): 0.39. Mp: 203.7−205.2 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.38−7.18 (m, 30H, Ar*H*), 5.43 (d, $J_{NH,2'}$ 7.8 Hz, 1H, NH), 4.98 (d, J_{gem} 10.9 Hz, 1H, OC*H*HPh), 4.84 (d, $J_{1',2'}$ 8.3 Hz, 1H, H1′), 4.84−4.75 (m, 5H, OCH_2Ph), 4.65 (d, J_{gem} 12.2 Hz, 1H, OCH*H*Ph), 4.63 (d, J_{gem} 11.6 Hz, 1H, OCH*H*Ph), 4.60 (d, $J_{1,2}$ 2.9 Hz, 1H, H1), 4.58 (d, J_{gem} 10.3 Hz, 1H, OCH*H*Ph), 4.57 (d, J_{gem} 10.8 Hz, 1H, OCH*H*Ph), 4.56 (d, J_{gem} 12.3 Hz, 1H, OC*H*HPh), 4.51 (d, 1H, OCH*H*Ph), 4.14−4.11 (m, 1H, H4), 4.08 (dd, J_{gem} 10.4 Hz, $J_{5,6a}$ 1.5 Hz, 1H, H6a), 3.98 (t, $J_{2,3}$ = $J_{3,4}$ 9.3 Hz, 1H, H3), 3.77−3.54 (m, 7H, H3′, H4′, H5′, H5, H6′a, H6′b, H6b), 3.51 (dd, 1H, H2), 3.44 (dt, $J_{2',3'}$ 9.4 Hz, 1H, H2′), 3.35 (s, 3H, OC*H*$_3$), 1.71 (s, 3H, NHC(O)C*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 170.2 (*C*═O), 138.9, 138.6, 138.4, 138.4, 138.3, 138.1 (ipso-Ar), 128.6, 128.6, 128.5, 128.5, 128.4, 128.3, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.7, 127.6 (Ar), 99.9 (C1′), 98.2 (C1), 82.2 (C3), 80.3 (C4′), 79.8 (C2), 78.8 (C3′), 77.7, 75.9 (C4, C5′), 75.1, 74.9, 74.7, 74.6, 73.4 (double intensity) (OCH_2Ph), 69.7, 69.2, 67.6 (C5, C6, C6′), 56.9 (C2′), 55.2 (OC*H*$_3$), 23.7 (NHC(O)*C*H$_3$). LRMS(ES): calcd for $C_{57}H_{63}NO_{11}Na^+$ 960.4, found 959.9. The NMR data were in accordance with those previously published.[18]

Methyl *O*-(2-Acetamido-2-deoxy-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-*α*-D-glucopyranoside (12). The general glycosylation procedure was followed using donor **1** (150 mg, 0.28 mmol), $Fe(OTf)_3$·6.2 DMSO (7 mg, 2.5 mol %), and methyl 2,3,6-tri-*O*-benzyl-*α*-D-glucopyranoside (**7**)[30] (65 mg, 0.14 mmol). TLC analysis indicated reaction cessation after 72 h. Flash column chromatography ($EtOAc/CH_2Cl_2$ 1:8 → 1:5) afforded benzyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranoside (**13**) (17 mg), a 1:1 mixture of **13** and the desired disaccharide **12** (36 mg), and the desired disaccharide **12** (27 mg, 21%) as an amorphous solid. Unreacted methyl 2,3,6-tri-*O*-benzyl-*α*-D-glucopyranoside (**7**) was reisolated (23 mg, 55%). The product was recrystallized from acetone to afford colorless grained crystals. The total corrected yield of the desired product **12** was 37%. R_f (CH_3OH/CH_2Cl_2 1:10): 0.74. Mp: 184.1−185.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.38−7.26 (m, 15H, Ar*H*), 7.25−7.16 (m, 15H, Ar*H*), 5.00 (d, J_{gem} 11.6 Hz, 1H, OC*H*HPh), 4.84 (d, $J_{NH,2'}$ 8.3 Hz, 1H, NH), 4.80 (d, 1H, J_{gem} 11.7 Hz, OC*H*HPh), 4.78 (d, J_{gem} 11.4 Hz, 1H, OC*H*HPh) 4.75−4.40 (m, 10H, OCH_2Ph, H1, H1′), 4.32 (d, J 12.2 Hz, 1H, OC*H*HPh), 3.91−3.39 (m, 11H, H2, H2′, H3, H3′, H4, H5, H5′, H6a, H6a′, H6b, H6b′), 3.35 (s, 3H, OC*H*$_3$), 3.34−3.30 (m, 1H, H4′), 1.68 (s, 3H, NHC(O)C*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 170.1 (*C*═O), 139.8, 138.7, 138.6, 138.4, 138.3, 138.2 (ipso-Ar), 128.7, 128.6, 128.5,

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128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.1 (Ar), 99.8 (C1′), 98.5 (C1), 81.5 (C3), 80.4 (C4′), 79.4 (C2), 78.9 (C3′), 76.5 (C5′), 75.2 (double intensity) (C5, OCH_2Ph), 74.8, 74.7, 73.7, 73.5, 73.5 (OCH_2Ph), 69.8 (C4), 69.0, 68.4 (C6, C6′), 57.5, 55.4 (C2′, OCH_3), 23.7 ($NHC(O)CH_3$). HRMS(ES): calcd for $C_{57}H_{63}NO_{11}Na^+$ 960.4299, found 960.4310.

Benzyl 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-*β*-D-glucopyranoside (13). The general glycosylation procedure was followed using donor **1** (109 mg, 0.20 mmol), $Bi(OTf)_3$ (5 mol %) and benzyl alcohol (22 μL 0.21 mmol). After 3 h, TLC analysis indicated reaction completion. Flash column chromatography followed by recrystallization from CH_3OH afforded the desired compound **13** as colorless crystals (100 mg, 84%). R_f (EtOAc/CH_2Cl_2 1:5): 0.41. Mp: 156.2−157.7 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 7.37−7.26 (m, 18H, Ar*H*), 7.20 (dd, *J* 7.4 Hz, *J* 2.0 Hz, 2H, Ar*H*), 5.45 (d, $J_{NH,2}$ 7.7 Hz, 1H, N*H*), 4.89 (d, J_{gem} 12.0 Hz, 1H, OC*H*HPh), 4.83 (d, $J_{1,2}$ 7.7 Hz, 1H, H1), 4.80 (d, J_{gem} 11.5 Hz, 1H, OC*H*HPh), 4.78 (d, 1H, J_{gem} 10.9 Hz, OC*H*HPh), 4.65 (d, 1H, OCH*H*Ph), 4.63 (d, J_{gem} 12.1 Hz, 1H, OCH*H*Ph), 4.59 (d, 1H, OCH*H*Ph), 4.57 (d, 1H, OCH*H*Ph), 4.55 (d, 1H, OCH*H*Ph), 4.04 (dd, $J_{2,3}$ 9.5 Hz, $J_{3,4}$ 8.2 Hz, 1H, H3), 3.79 (dd, J_{gem} 10.7 Hz, $J_{5,6a}$ 2.8 Hz, 1H, H6a), 3.74 (dd, $J_{5,6b}$ 4.3 Hz, 1H, H6b), 3.67 (dd, $J_{4,5}$ 9.1 Hz, 1H, H4), 3.60 (ddd, 1H, H5), 3.55 (dt, 1H, H2), 1.81 (s, 3H, $NHC(O)CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 170.3 (C═O), 138.5, 138.3, 138.2, 137.7 (ipso-ArC), 128.5, 128.5, 128.5, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7 (Ar), 99.4 (C1), 80.5 (C3), 78.6 (C4), 75.0 (C5), 74.6, 74.5, 73.6, 70.8 (OCH_2Ph), 69.2 (C6), 56.5 (C2), 23.6 ($NHC(O)CH_3$). LRMS(ES): calcd for $C_{36}H_{39}NO_6Na^+$ 604.3, found 604.1. The data were in accordance with the previously published values.[31]

2-Acetamido-1-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-*β*-D-glucopyranose (17). In a glovebox as previously described, allyl 2-acetamido-4,6-di-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-*β*-D-glucopyranoside (**25**) (329 mg, 0.61 mmol, 1 equiv) was dissolved in dry dioxane (1.7 mL). $Pd(dba)_2$ (17.6 mg, 31 μmol, 5 mol %), $P(tBu)_3$ (6.2 mg, 31 μmol, 5 mol %), and COgen (CAS: 1072315-89-9) (7.4 mg, 31 μmol, 5 mol %) were mixed separately in dry dioxane (0.3 mL) and subsequently added to the solution containing the allyl glycoside. The reaction vessel was sealed, removed from the glovebox, and heated to 80 °C. After 24 h of heating, a crude ^1H NMR spectrum indicated full conversion. The mixture was concentrated to dryness, and the resulting residue was redissolved in a 1:9 mixture of 1 M HCl (aq) and acetone (5 mL total volume) and heated to 55 °C for 6 h. The mixture was coevaporated with toluene to dryness and taken up in dry pyridine (3.7 mL). Pyridinium *p*-toluenesulfonate (225 mg, 0.90 mmol, 1.5 equiv) was added to the resulting mixture before it was heated to 100 °C. A mixture of Ac_2O (172 μL, 1.8 mmol, 3 equiv) in dry pyridine (7.5 mL) was added by syringe pump over 15 min, whereupon the reaction mixture was concentrated to dryness and purified by flash column chromatography (10 → 40% EtOAc in toluene). This afforded the desired compound **17** (120 mg, 40%) as a white solid. R_f: 0.28 (EtOAc/toluene 1:1). ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.36−7.25 (m, 8H, Ar*H*), 7.22−7.16 (m, 2H, Ar*H*), 5.69 (d, $J_{1,2}$ 7.9 Hz, 1H, H1), 5.39 (d, $J_{NH,2}$ 9.1 Hz, 1H, NH), 4.82 (d, J_{gem} 11.7 Hz, 1H, OC*H*HPh), 4.77 (d, J_{gem} 10.9 Hz, 1H, OC*H*HPh), 4.67 (d, 1H, OCH*H*Ph), 4.61 (d, J_{gem} 12.1 Hz, 1H, OC*H*HPh), 4.57 (d, 1H, OCH*H*Ph), 4.50 (d, 1H, OCH*H*Ph), 4.03 (dt, $J_{1,2}$ = $J_{2,3}$ 9.2 Hz 1H, H2), 3.79 (dd, $J_{3,4}$ 8.4 Hz, $J_{4,5}$ 8.6 Hz, 1H, H4), 3.74 (d, $J_{5,6}$ 3.4 Hz, 2H, H6), 3.70 (dd, 1H, H3), 3.66 (td, 1H, H5), 2.06 (s, 3H, $OC(O)CH_3$), 1.81 (s, 3H, $NHC(O)CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.2, 169.9 (C═O), 138.03, 138.00, 137.9 (ipso-ArC), 128.6, 128.5, 128.1, 127.99, 127.96, 127.8 (Ar), 92.9 (C1), 80.7 (C4), 77.6 (C3), 75.7, 74.7, 74.3 (OCH_2Ph), 73.6 (C5), 68.6 (C6), 53.7 (C2), 23.4 ($NHC(O)CH_3$), 21.1 ($OC(O)CH_3$). HRMS(ES): calcd for $C_{31}H_{30}D_5NO_7Na^+$ 561.2620, found 561.2626. The NMR data were in agreement with those of the unlabeled congener.

2-Acetamido-1-*O*-acetyl-6-*O*-benzyl-2-deoxy-3,4-di-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-*β*-D-glucopyranose (18). In a glovebox as previously described, allyl 2-acetamido-6-*O*-benzyl-2-deoxy-3,4-di-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-*β*-D-glucopyranoside (**26**) (219 mg, 0.40 mmol, 1 equiv) was dissolved in dry dioxane (0.8 mL). $Pd(dba)_2$ (11.6 mg, 20 μmol, 5 mol %), $P(tBu)_3$ (4.1 mg, 20 μmol, 5 mol %), and COgen (CAS: 1072315-89-9) (4.9 mg, 20 μmol, 5 mol %) were mixed separately in dry dioxane (0.3 mL) and subsequently added to the solution containing the allyl glycoside. The reaction vessel was sealed, removed from the glovebox and heated to 80 °C. After 29 h of heating, a crude ^1H NMR spectrum indicated full conversion. The mixture was reduced to dryness, and the resulting residue was redissolved in a 1:9 mixture of 1 M HCl (aq) and acetone (5 mL total volume) and heated to 55 °C for 6 h. The mixture was coevaporated with toluene to dryness and redissolved in dry pyridine (2.4 mL). To the resulting mixture was added pyridinium *p*-toluenesulfonate (152 mg, 0.60 mmol, 1.5 equiv) and the mixture heated to 100 °C. A mixture of Ac_2O (114 μL, 1.2 mmol, 3 equiv) in dry pyridine (0.85 mL) was added by syringe pump over 15 min, whereupon the mixture was evaporated to dryness and purified by flash column chromatography (10 → 40% EtOAc in toluene), which afforded the desired compound **18** (47.5 mg, 24%) as a white solid. R_f: 0.28 (EtOAc/toluene 1:1). ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.39−7.25 (m, 5H, Ar*H*) 5.69 (d, $J_{1,2}$ 7.9 Hz, 1H, H1), 5.28 (d, $J_{NH,2}$ 9.1 Hz, 1H, NH), 4.82 (d, J_{gem} 11.7 Hz, 1H, OC*H*HPh), 4.77 (d, J_{gem} 10.9 Hz, 1H, OC*H*HPh), 4.66 (d, 1H, OCH*H*Ph), 4.61 (d, J_{gem} 12.1 Hz, 1H, OC*H*HPh), 4.58 (d, 1H, OCH*H*Ph), 4.50 (d, 1H, OCH*H*Ph), 4.04 (dt, $J_{1,2}$ = $J_{2,3}$ 9.2 Hz 1H, H2), 3.79 (dd, $J_{3,4}$ 8.4 Hz, $J_{4,5}$ 8.5 Hz, 1H, H4), 3.74 (d, $J_{5,6}$ 3.5 Hz, 2H, H6), 3.69 (dd, 1H, H3), 3.66 (td, 1H, H5), 2.05 (s, 3H, $OC(O)CH_3$), 1.79 (s, 3H, $NHC(O)CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.1, 169.9 (C═O), 138.0, 137.7 (*ipso*-ArC), 128.5, 128.0, 127.5 (Ar), 92.9 (C1), 80.5 (C4), 77.6 (C3), 75.7, 74.6, 74.2 (OCH_2Ph), 73.6 (C5), 68.6 (C6), 53.7 (C2), 23.5 ($NHC(O)CH_3$), 21.2 ($OC(O)CH_3$). HRMS(ES): calcd for $C_{31}H_{25}D_{10}NO_7Na^+$ 566.2933, found 566.2944. The NMR data were in agreement with those of the unlabeled congener.

2-Acetamido-1-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-*β*-D-allopyranose (19). (1,5-Cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate (3 mg, 3 μmol, 3 mol %) was dissolved in dry THF (2 mL), bubbled through with H_2 for 15 min, and then degassed with a flow of argon under sonication for 10 min. Allyl 2-acetamido-4,6-di-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-*β*-D-allopyranoside (**27**) (61.7 mg, 0.12 mmol, 1 equiv) was dissolved in dry THF (3 mL) and added to the catalyst-containing solution. The resulting yellow solution was stirred under an atmosphere of argon at room temperature. After 24 h, a crude ^1H NMR spectrum indicated incomplete conversion. Another 3 mg of catalyst was activated in a separate vial and transferred to the reaction mixture. After 3 days, the mixture was diluted with acetone (9 mL) and a 1 M solution hydrochloric acid and heated to reflux for 2 h. TLC analysis indicated full conversion, and the mixture was coevaporated with toluene to dryness. The resulting crude was redissolved in dry pyridine (0.5 mL), pyridinium *p*-toluenesulfonate (45 mg, 0.18 mmol, 1.5 equiv) was added, and the mixture was heated to 100 °C. A solution of Ac_2O (33 μL, 0.35 mmol, 3 equiv) in dry pyridine (0.25 mL) was added by means of syringe pump during the course of 10 min, and the resulting mixture was left overnight at room temperature. After 16 h, the excess Ac_2O was quenched with MeOH (0.5 mL). The mixture was evaporated to dryness under reduced pressure, redissolved in $CHCl_3$, and washed with 1 M HCl (aq) followed by satd aq $NaHCO_3$, in both cases extracting three times with $CHCl_3$. The combined organic layers were dried over $MgSO_4$, filtered, and evaporated to dryness. Purification by repeated flash column chromatography (30% EtOAc in toluene, then 10% EtOAc in CH_2Cl_2) afforded the desired compound **19** (19.5 mg, 31%) as a white solid. R_f (30% EtOAc in toluene): 0.35. ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.38−7.23 (m, 10H, Ar*H*), 5.83 (d, $J_{1,2}$ 8.1 Hz, 1H, H1), 5.74 (d, $J_{NH,2}$ 9.6 Hz, 1H, N*H*), 4.91 (d, J_{gem} 11.8 Hz, 1H, OC*H*HPh), 4.64 (d, J_{gem} 11.4 Hz, 1H, OC*H*HPh), 4.63 (d, J_{gem} 12.1 Hz, 1H, OCH*H*Ph), 4.55 (d, 1H, OC*H*HPh), 4.50 (d, 1H, OCH*H*Ph), 4.47 (d, 1H, OCH*H*Ph), 4.21−4.11 (m, 2H, H2, H5), 4.02 (t, $J_{2,3}$ = $J_{3,4}$ 2.7 Hz, 1H, H3), 3.79 (dd, $J_{4,5}$ 8.9 Hz, 1H, H4), 3.73 (d, $J_{5,6}$ 3.3 Hz, 2H, H3), 2.05 (s, 3H, $OC(O)CH_3$), 1.71 (s, 3H, $NHC(O)CH_3$). ^{13}C NMR (100 MHz,

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$CDCl_3$): δ_C 170.1, 169.9 (*C*=O), 138.13, 138.09, 137.7 (*ipso*-Ar*C*), 128.7, 128.5, 128.2, 128.1, 128.0, 127.8 (Ar), 92.4 (C1), 75.8 (C4), 74.8 (C3), 74.5 (OCH_2Ph), 74.0 (C5), 73.7, 72.8 (OCH_2Ph), 68.9 (C6), 51.1 (C2), 23.2 ($NHC(O)CH_3$), 21.2 ($OC(O)CH_3$). HRMS-(ES): calcd for $C_{31}H_{30}D_5NO_7Na^+$ 561.2620, found 561.2622.

Allyl 2-Acetamido-2-deoxy-β-D-glucopyranoside (20). *N*-Acetyl-D-glucosamine (10.0 g, 45.1 mmol, 1 equiv) was dissolved in a mixture of dry pyridine (25 mL) and dry CH_2Cl_2 (50 mL) in a predried flask under an atmosphere of nitrogen. The mixture was allowed to stir overnight at room temperature. The mixture was cooled to −10 °C, and pivaloyl chloride (17 mL, 138 mmol, 3 equiv) was added. The mixture was allowed to reach room temperatureand then stir for 2 days before acetic anhydride (21.3 mL, 226 mmol, 5 equiv) was added, and the resulting mixture was stirred for another 3 h. The reaction mixture was then washed several times with hydrochloric acid (1 M) until the aqueous phase stayed acidic according to a pH paper test. The combined organic layers were then washed with water and brine before being dried over Na_2SO_4 and filtered. The mixture was concentrated to give a crude mixture, which was used in the next step without further purification.

The crude mixture was dissolved in dry CH_2Cl_2, and triflic acid (1.80 mL, 20.3 mmol, 45 mol %) was added using a glass syringe. AllOH (9.2 mL, 135 mmol, 3 equiv) was added and the reaction mixture heated to 40 °C overnight before being washed with water and aq $NaHCO_3$. The organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude glycoside mixture was redissolved in dry methanol, and sodium (1.5 g, 65.2 mmol, 1.4 equiv) was added. The reaction mixture was heated to 50 °C for 24 h and then concentrated onto Celite and purified before purified by flash column chromatography (water/2-propanol/EtOAc 1:4:16) to give the desired compound **20** (8.15 g, 69%) as a colorless solid. Mp: 161.4−162.8 °C (lit.[32] 160−163 °C). ^{1}H NMR (400 MHz, CD_3OD): δ_H 5.89 (ddt, J_{trans} 17.3 Hz, J_{cis} 10.6 Hz, J_{vic} 5.3 Hz, 1H, C*H*=CH_2), 5.27 (dd, J_{gem} 1.7 Hz, 1H, CH=C*H*H), 5.13 (dd, 1H, CH=CH*H*), 4.44 (d, $J_{1,2}$ 8.4 Hz, 1H, H1), 4.34 (dd, J_{gem} 13.3 Hz, 1H, OC*H*HCH), 4.07 (dd, 1H, OCH*H*CH), 3.88 (dd, J_{gem} 11.9 Hz, $J_{5,6a}$ 2.1 Hz, 1H, H6a), 3.72−3.63 (m, 2H, H2, H6b), 3.45 (dd, *J* 10.2 Hz, *J* 8.6 Hz, 1H, H3), 3.38−3.21 (m, 3H, H4, H5, NH), 1.97 (s, 3H, $NHCOCH_3$). ^{13}C NMR (100 MHz, CD_3OD): δ_C 173.8 (*C*=O), 135.6 (CH_2CH=CH_2), 116.9 (CH=CH_2), 101.9 (C1), 78.0 (C5), 76.1 (C3), 72.2 (C4), 70.7 (OCH_2CH), 62.8 (C6), 57.3 (C2), 22.9 ($NHCOCH_3$). HRMS (ES): calcd for $C_{11}H_{19}O_6NH^+$ 262.1285, found 262.1290. The NMR data were in accordance with those previously published.[33]

Allyl 2-Acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-glucopyranoside (21). Allyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside[34] (500 mg, 1.4 mmol, 1 equiv) was dissolved in dry DMF (5 mL). The temperature of the resulting solution was buffered with a water bath at ambient temperature prior to the addition of 60% NaH on mineral oil (74 mg, 1.9 mmol, 1.3 equiv). After gas evolution had ceased, 2,3,4,5,6-pentadeuteriobenzyl bromide[35] (0.2 mL, 1.6 mmol, 1.1 equiv) was added in four portions over 10 min, and the mixture was stirred at room temperature. After 4 h, TLC analysis (40% EtOAc in toluene) indicated full conversion. The mixture was diluted with $CHCl_3$ and poured onto a 1:1 mixture of satd aqueous $NaHCO_3$ and brine. This was extracted 5 times with $CHCl_3$, and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated to dryness in vacuo overnight. Recrystallization from MeOH yielded the desired compound **21** (479 mg, 75%) as a white cotton-like solid. R_f (2% MeOH in $CHCl_3$): 0.26. $[\alpha]_D^{298K}$ −13.6 (*c* 0.25, $CHCl_3$). Mp: 263.9−264.6 °C. ^{1}H NMR (10% CD_3OD in $CDCl_3$): δ_H 7.42−7.19 (m, 5H, Ar*H*), 5.81−5.65 (m, 1H, OCH_2CH=CH_2), 5.46 (s, 1H, PhC*H*), 5.14 (d, J_{trans} 17.1 Hz, 1H, OCH_2CH=C*H*H), 5.05 (d, J_{cis} 10.1 Hz, 1H, OCH_2CH=CH*H*), 4.75 (d, J_{gem} 11.8 Hz, 1H, OC*H*HPh), 4.65 (d, $J_{1,2}$ 8.2 Hz, 1H, H1), 4.53 (d, 1H, OCH*H*Ph), 4.27−4.14 (m, 2H, H6a, OC*H*HCHCH$_2$), 4.00−3.84 (m, 2H, H3, OCH*H*CHCH$_2$), 3.68 (t, J_{gem} = $J_{5,6b}$ 9.2 Hz, 1H, H6b), 3.59 (t, $J_{3,4}$ = $J_{4,5}$ 9.3 Hz, 1H, H4), 3.49 (t, $J_{1,2}$ = $J_{2,3}$ 9.0 Hz, 1H, H2), 3.42−3.29 (m, 1H, H5), 1.78 (s, 3H, $NHC(O)CH_3$). ^{13}C NMR (10% CD_3OD in $CDCl_3$): δ_C 171.5 (C=O), 138.0, 137.1 (Ar), 133.6 (OCH_2CH=CH_2), 128.9, 128.2, 125.9 (Ar), 117.2 (OCH_2CH=CH_2), 101.1 (PhCH), 100.1 (C1), 82.2 (C4), 77.3 (C3), 74.1 (OCH_2Ph), 70.1 (OCH_2CH=CH_2), 68.6 (C6), 65.9 (C5), 56.2 (C2), 22.7 ($NHC(O)CH_3$). HRMS(ES): calcd for $C_{25}H_{24}D_5NO_6H^+$ 445.2381, found 445.2388.

Allyl 2-Acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-glucopyranoside (22). Allyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-glucopyranoside **21** (479 mg, 1.1 mmol, 1 equiv) was suspended in dry CH_2Cl_2 (12 mL) and cooled to 0 °C. Et_3SiH (0.34 mL, 2.2 mmol, 2 equiv) was added via syringe followed by the dropwise addition of freshly distilled $BF_3{\cdot}OEt_2$ (0.40 mL, 3.2 mmol, 3 equiv). The reaction mixture was stirred at 0 °C for 6 h, whereupon TLC analysis (4% MeOH in $CHCl_3$) indicated full conversion. The reaction was quenched with satd aq $NaHCO_3$. Brine was added, and the resulting mixture was extracted five times with $CHCl_3$. The combined organic layers were dried over $MgSO_4$ and evaporated onto Celite. Flash column chromatography (10 → 20% EtOAc in CH_2Cl_2) afforded the desired compound **22** (362 mg, 75%) as a white solid. R_f (40% EtOAc in toluene): 0.26. $[\alpha]_D^{301K}$ −19.4 (*c* 1, $CHCl_3$). Mp: 137.5−138.6 °C. ^{1}H NMR ($CDCl_3$): δ_H 7.31−7.18 (m, 5H, Ar*H*), 5.84−5.73 (m, 1H, OCH_2CH=CH_2), 5.17 (dd, J_{trans} 17.2 Hz, J_{gem} 1.6 Hz, 1H, OCH_2CH=C*H*H), 5.07 (dd, J_{cis} 10.4 Hz, 1H, OCH_2CH=CH*H*), 4.73 (d, J_{gem} 11.7 Hz, 1H, OC*H*HPh), 4.66 (d, $J_{1,2}$ 8.3 Hz, 1H, H1), 4.63 (d, 1H, OCH*H*Ph), 4.52 (d, J_{gem} 12.0 Hz, 1H, OC*H*HPh), 4.48 (d, 1H, OCH*H*Ph), 4.23 (dd, J_{gem} 13.1 Hz, J_{vic} 5.1 Hz, 2H, OC*H*HCH=CH_2), 3.98 (dd, 2H, OCH*H*CH=CH_2), 4.00−3.83 (dd, *J* 8.8 Hz, *J* 10.1 Hz, 1H, H3), 3.70 (dd, J_{gem} 10.4 Hz, $J_{5,6a}$ 3.9 Hz, 1H, H6a), 3.64 (dd, $J_{5,6b}$ 5.3 Hz, 1H, H6b), 3.61−3.49 (m, 2H, H2, H4), 3.48−3.40 (m, 1H, H5), 1.82 (s, 3H, $NHC(O)CH_3$). ^{13}C NMR ($CDCl_3$): δ_C 170.8 (*C*=O), 138.4, 137.9 (Ar), 134.0 (OCH_2CH=CH_2), 128.4, 127.69, 127.65 (Ar), 117.2 (OCH_2CH=CH_2), 99.5 (C1), 80.8 (C3), 74.3 (C5), 73.7, 73.5 (OCH_2Ph), 72.3 (C4), 70.4 (C6), 69.7 (OCH_2CH=CH_2), 55.9 (C2), 23.5 ($NHC(O)CH_3$). HRMS(ES): calcd for $C_{25}H_{26}D_5NO_6H^+$ 447.2538, found 447.2548.

Allyl 2-Acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-allopyranoside (23). Allyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-allopyranoside[36] (500 mg, 1.4 mmol, 1 equiv) was dissolved in dry DMF (5 mL). The temperature of the resulting solution was buffered with a water bath at ambient temperature prior to the addition of 60% NaH on mineral oil (74 mg, 1.9 mmol, 1.3 equiv). After gas evolution had ceased, 2,3,4,5,6-pentadeuteriobenzyl bromide[5] (0.2 mL, 1.6 mmol, 1.1 equiv) was added in four portions over 10 min, and the mixture was stirred at room temperature. After 16 h, TLC analysis (40% EtOAc in toluene) indicated incomplete conversion. Another 0.65 equiv of NaH and 0.55 equiv of 2,3,4,5,6-pentadeuteriobenzyl bromide was added. After 3 h, TLC analysis indicated full conversion. The mixture was diluted with $CHCl_3$ and poured onto a 1:1 mixture of satd aq $NaHCO_3$ and brine. This was extracted two times with $CHCl_3$, and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated to dryness in vacuo overnight. The resulting residue was redissolved in $CHCl_3$ and evaporated onto Celite. Flash column chromatography (20 → 30% EtOAc in toluene) afforded the desired product **23** (403 mg, 63%) as a flocculent white solid: R_f (40% EtOAc in toluene): 0.41. $[\alpha]_D^{296K}$ −112.8 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ_H 7.54−7.46 (m, 2H, Ar*H*), 7.42−7.46 (m, 3H, Ar*H*), 5.85 (dddd, J_{trans} 17.2 Hz, J_{cis} 10.6 Hz, J_{vic} 5.9 Hz, J_{vic} 4.9 Hz, 1H, OCH_2CHCH_2), 5.79−5.71 (m, 1H, NH), 5.53 (s, 1H, PhC*H*), 5.27 (dq, 1H, OCH_2CH=C*H*H), 5.16 (dq, 1H, OCH_2CH=CH*H*), 5.02 (d, J_{gem} 11.7 Hz, 1H, OC*H*HPh), 4.65 (d, $J_{1,2}$ 8.6 Hz, 1H, H1), 4.54 (d, 1H, OCH*H*Ph), 4.39 (dd, J_{gem} 10.4 Hz, $J_{5,6a}$ 5.1 Hz, H6a), 4.33 (ddt, 1H, OC*H*HCH=CH_2), 4.17 (dt, $J_{2,3}$ 3.1 Hz, 1H, H2), 4.13−4.05 (m, 2H, H3, H5), 4.03 (ddt, 1H, OCH*H*CH=CH_2), 3.80 (t, J_{gem} = $J_{5,6b}$ 10.4 Hz, 1H, H6b), 3.73 (dd, $J_{3,4}$ 2.0 Hz, $J_{4,5}$ 9.5 Hz, 1H, H4), 1.85 (s, 3H, $NHC(O)CH_3$). ^{13}C NMR ($CDCl_3$): δ_C 169.4 (*C*=O), 138.1, 137.5, (Ar), 133.9 (OCH_2CHCH_2), 129.2, 128.4, 126.2 (Ar), 117.1 (OCH_2CHCH_2), 102.1 (PhCH), 99.7 (C1), 80.2 (C4), 75.9 (C3), 74.7 (OCH_2Ph), 69.9 (OCH_2CHCH_2), 69.3 (C6), 63.8 (C5), 52.0 (C2), 23.3 (NHC(O)

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CH_3). HRMS(ES): calcd for $C_{25}H_{24}D_5NO_6H^+$ 445.2381, found 445.2390.

Allyl 2-Acetamido-4-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-allopyranoside (24). Allyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-allopyranoside **23** (400 mg, 0.90 mmol, 1 equiv) was dissolved in dry CH_2Cl_2 (11 mL) and cooled to −78 °C prior to the addition of Et_3SiH (0.47 mL, 2.9 mmol, 3.3 equiv) and $PhBCl_2$ (0.34 mL, 2.6 mmol, 2.9 equiv), both via syringe. After 80 min, TLC analysis (40% EtOAc in toluene) indicated full conversion. The reaction was quenched with Et_3N (2 mL) and MeOH (2 mL) before being heated to room temperature. The mixture was washed with satd aq $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated in vacuo to yield a crude, which was purified by flash column chromatography (50 → 100% EtOAc in toluene) to afford the desired compound **24** (68.5 mg, 17%) as a white solid: R_f (50% EtOAc in toluene): 0.35. $[\alpha]_D^{298K}$ −72.8 (*c* 1, $CHCl_3$). Mp: 147.9−148.7 °C. ^{1}H NMR ($CDCl_3$): δ_H 7.41−7.28 (m, 5H, Ar*H*), 5.92−5.77 (m, 2H, OCH_2CH=CH_2, N*H*), 5.24 (d, J_{trans} 17.2 Hz, 1H, OCH_2CH=C*H*H), 5.15 (d, J_{cis} 10.4 Hz, 1H, OCH_2CH=CH*H*), 4.91 (d, J_{gem} 11.7 Hz, 1H, OC*H*HPh), 4.71 (d, J_{gem} 11.5 Hz, 1H, OC*H*HPh), 4.67 (d, $J_{1,2}$ 7.4 Hz, 1H, H1), 4.61 (d, 1H, OCH*H*Ph), 4.51 (d, 1H, OCH*H*Ph), 4.28 (d, J_{gem} 13.3 Hz, 1H, OC*H*HCH=CH_2), 4.13 (s, 1H, H3), 4.10−3.95 (m, 3H, OCH*H*CH=CH_2, H2, H5), 3.87 (d, J_{gem} 12.1 Hz, H6a), 3.79−3.71 (m, 1H, H6b), 3.68 (d, $J_{4,5}$ 10.1 Hz, 1H, H4), 2.20−2.12 (m, 1H, OH), 1.79 (s, 3H, NHC(O)CH_3). ^{13}C NMR ($CDCl_3$): δ_C 169.8 (*C*=O), 138.3, 137.6 (Ar), 134.0 (OCH_2CH=CH_2), 128.7, 128.2, 128.1 (Ar), 117.2 (OCH_2CH=CH_2), 99.3 (C1), 76.2 (C4), 74.7 (C3), 74.4 (OCH_2Ph), 73.9 (C5), 72.7 (OCH_2Ph), 69.8 (OCH_2CH=CH_2), 62.6 (C6), 51.6 (C2), 23.4 (NHC(O)CH_3). HRMS(ES): calcd for $C_{25}H_{26}D_5NO_6H^+$ 447.2538, found 447.2544.

Allyl 2-Acetamido-4,6-di-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-glucopyranoside (25). Allyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-glucopyranoside (**22**) (362 mg, 0.81 mmol, 1 equiv) was dissolved in dry DMF (4 mL). The temperature of the resulting solution was buffered with a water bath at ambient temperature prior to the addition of 60% NaH on mineral oil (42 mg, 1.1 mmol, 1.3 equiv). After gas evolution had ceased, benzyl bromide (0.1 mL, 0.89 mmol, 1.1 equiv) was added in two portions over 15 min, and the resulting mixture was stirred at room temperature for 16 h after which TLC analysis (40% EtOAc in CH_2Cl_2) indicated full conversion. The reaction was quenched with satd aq $NaHCO_3$. Brine was added, and the resulting mixture was extracted five times with $CHCl_3$. The combined organic layers were dried over $MgSO_4$ and evaporated onto Celite. Flash column chromatography (10 → 30% EtOAc in $CHCl_3$) afforded the desired compound **25** (329 mg, 76%) as a white solid. R_f (40% EtOAc in toluene): 0.37. ^{1}H NMR ($CDCl_3$): δ_H 7.40−7.17 (m, 10H, Ar*H*), 5.94−5.82 (m, 1H, OCH_2CH=CH_2), 5.64 (d, $J_{NH,2}$ 7.7 Hz, 1H, N*H*), 5.26 (dq, J_{trans} 17.2 Hz, J_{gem} = ^4J 1.6 Hz, 1H, OCH_2CH=C*H*H), 5.16 (dd, J_{cis} 10.4 Hz, 1H, OCH_2CH=CH*H*), 4.84 (d, $J_{1,2}$ 7.7 Hz, 1H, H1), 4.82 (d, J_{gem} 11.5 Hz, 1H, OC*H*HPh), 4.78 (d, J_{gem} 11.0 Hz, 1H, OC*H*HPh), 4.67 (d, 1H, OCH*H*Ph), 4.62 (d, J_{gem} 12.2 Hz, 1H, OC*H*HPh), 4.58 (d, 1H, OCH*H*Ph), 4.55 (d, 1H, OCH*H*Ph), 4.33 (ddt, J_{gem} 12.9 Hz, 1H, OC*H*HCH=CH_2), 4.14−4.03 (m, 2H, H3, OCH*H*CH=CH_2), 3.77 (dd, J_{gem} 10.7 Hz, $J_{5,6a}$ 2.5 Hz, 1H, H6a), 3.72 (dd, $J_{5,6b}$ 4.4 Hz, 1H, H6b), 3.65 (dd, $J_{4,5}$ 9.1 Hz, $J_{3,4}$ 8.0 Hz, 1H, H4), 3.59 (ddd, 1H, H5), 3.47 (dt, 1H, H2), 1.85 (s, 3H, NHCOCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.4 (*C*=O), 138.4, 138.3, 138.1 (*ipso*-ArC), 134.1 (OCH_2CH=CH_2), 128.53, 128.46, 128.0, 127.9, 127.7 (Ar), 117.5 (OCH_2CH=CH_2), 99.1 (C1), 80.3 (C4), 78.6 (C3), 74.8, 74.62, 74.56 (OCH_2Ph), 73.6 (C5), 69.9 (OCH_2CH=CH_2), 69.1 (C6), 56.9 (C2), 23.7 (NHCOCH_3). HRMS(ES): calcd for $C_{32}H_{32}D_5NO_6H^+$ 537.3007, found 537.3010.

Allyl 2-Acetamido-6-*O*-benzyl-2-deoxy-3,4-di-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-glucopyranoside (26). Allyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-glucopyranoside **22** (265 mg, 0.59 mmol, 1 equiv) was dissolved in dry DMF (2.7 mL). The temperature of the resulting solution was buffered with a water bath at ambient temperature prior to the addition of 60% NaH on mineral oil (31 mg, 0.8 mmol, 1.3 equiv). After gas evolution had ceased, 2,3,4,5,6-pentadeuteriobenzyl bromide[5] (0.08 mL, 0.64 mmol, 1.1 equiv) was added, and the resulting mixture was stirred at room temperature overnight. After 16 h, TLC analysis (40% EtOAc in CH_2Cl_2) indicated only half conversion. Another 0.65 equiv of NaH and 0.55 equiv of 2,3,4,5,6-pentadeuteriobenzyl bromide were added, and after 1.5 h at room temperature TLC analysis indicated full conversion. The reaction was quenched with satd aq $NaHCO_3$. Brine was added, and the resulting mixture was extracted five times with $CHCl_3$. The combined organic layers were dried over $MgSO_4$ and evaporated onto Celite. Flash column chromatography (10 → 20% EtOAc in $CHCl_3$) afforded the desired compound **26** (219 mg, 68%) as a white solid: R_f (20% EtOAc in $CHCl_3$): 0.39. ^{1}H NMR ($CDCl_3$): δ_H 7.36−7.25 (m, 5H, Ar*H*), 5.94−5.82 (m, 1H, OCH_2CH=CH_2), 5.72 (d, $J_{NH,2}$ 7.3 Hz, 1H, N*H*), 5.25 (dq, J_{trans} 17.3 Hz, J_{gem} = ^4J 1.6 Hz, 1H, OCH_2CH=C*H*H), 5.16 (dd, J_{cis} 10.4 Hz, 1H, OCH_2CH=CH*H*), 4.83 (d, $J_{1,2}$ 7.7 Hz, 1H, H1), 4.82 (d, J_{gem} 11.5 Hz, 1H, OC*H*HPh), 4.78 (d, J_{gem} 11.0 Hz, 1H, OC*H*HPh), 4.67 (d, 1H, OCH*H*Ph), 4.62 (d, J_{gem} 12.2 Hz, 1H, OC*H*HPh), 4.58 (d, 1H, OCH*H*Ph), 4.55 (d, 1H, OCH*H*Ph), 4.33 (dd, J_{gem} 13.0 Hz, J_{vic} 5.2 Hz, 1H, OC*H*HCH=CH_2), 4.13−4.03 (m, 2H, H3, OCH*H*CH=CH_2), 3.76 (dd, J_{gem} 10.7 Hz, $J_{5,6a}$ 2.6 Hz, 1H, H6a), 3.72 (dd, $J_{5,6b}$ 4.3 Hz, 1H, H6b), 3.65 (dd, $J_{4,5}$ 9.1 Hz, $J_{3,4}$ 8.1 Hz, 1H, H4), 3.59 (ddd, 1H, H5), 3.49 (dt, 1H, H2), 1.85 (s, 3H, NHC(O)CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.4 (*C*=O), 138.3, 138.2, 137.9 (*ipso*-ArC), 134.1 (OCH_2CH=CH_2), 128.4, 127.9, 127.7 (Ar), 117.4 (OCH_2CH=CH_2), 99.1 (C1), 80.4 (C4), 78.6 (C3), 74.8, 74.5(2C) (OCH_2Ph), 73.5 (C5), 69.9 (OCH_2CH=CH_2), 69.1 (C6), 56.8 (C2), 23.7 (NHC(O)CH_3). HRMS(ES): calcd for $C_{32}H_{27}D_{10}NO_6H^+$ 542.3321, found 542.3328.

Allyl 2-Acetamido-4,6-di-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-allopyranoside (27). Allyl 2-acetamido-4-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,5,6-pentadeuteriobenzyl)-β-D-allopyranoside **24** (65 mg, 0.15 mmol, 1 equiv) was dissolved in dry DMF (0.66 mL). The temperature of the resulting solution was buffered with a water bath at ambient temperature prior to the addition of 60% NaH on mineral oil (8 mg, 0.19 mmol, 1.3 equiv). After gas evolution had ceased, benzyl bromide (19 μL, 0.16 mmol, 1.1 equiv) was added, and the resulting mixture was stirred at room temperature overnight. After 16 h, TLC analysis (40% EtOAc in toluene) indicated less than full conversion. Another 0.65 equiv of NaH and 0.55 equiv of BnBr were added, and after 1 h, TLC analysis indicated full conversion. The reaction was quenched with satd aq $NaHCO_3$. Brine was added, and the resulting mixture was extracted five times with $CHCl_3$. The combined organic layers were dried over $MgSO_4$ and concentrated onto Celite. Flash column chromatography (20% EtOAc in toluene) afforded the desired compound **27** (57.8 mg, 78%) as a white solid. R_f (20% EtOAc in toluene): 0.23. $[\alpha]_D^{298K}$ −51.4 (*c* 1, $CHCl_3$). Mp: 116.1−117.2 °C. ^{1}H NMR ($CDCl_3$): δ_H 7.37−7.26 (m, 10H, Ar*H*), 6.26−6.07 (bs, 1H, N*H*), 5.90−5.79 (m, 1H, OCH_2CH=CH_2), 5.26 (dd, J_{trans} 17.2 Hz, J_{gem} 1.4 Hz, 1H, OCH_2CH=C*H*H), 5.14 (dd, J_{cis} 10.4 Hz, 1H, OCH_2CH=CH*H*), 4.78 (d, J_{gem} 11.7 Hz, 1H, OC*H*HPh), 4.68 (d, $J_{1,2}$ 6.2 Hz, 1H, H1), 4.68 (d, J_{gem} 11.3 Hz, 1H, OC*H*HPh), 4.59 (d, 1H, OCH*H*Ph), 4.58 (d, J_{gem} 12.1 Hz, 1H, OC*H*HPh), 4.53 (d, 1H, OCH*H*Ph), 4.51 (d, 1H, OCH*H*Ph), 4.27 (ddt, J_{gem} 13.1 Hz, J_{vic} 4.9 Hz, 1H, OC*H*HCH=CH_2), 4.21−4.11 (m, 1H, H2), 4.14 (dt, $J_{4,5}$ 6.7 Hz, $J_{5,6}$ 4.8 Hz, 1H, H5), 4.08 (t, $J_{2,3}$ = $J_{3,4}$ 3.0 Hz, 1H, H3), 4.00 (dd, J_{vic} 5.8 Hz, 1H, OCH*H*CH=CH_2), 3.78 (dd, 1H, H4), 3.73 (dd, J_{gem} 10.5 Hz, 1H, H6a), 3.67 (dd, 1H, H6b), 1.80 (s, 3H, NHC(O)CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 169.9 (*C*=O), 138.3, 137.9 (*ipso*-ArC), 134.1 (OCH_2CH=CH_2), 128.6, 128.5, 128.10, 128.08, 127.84, 127.77 (Ar), 117.0 (OCH_2CH=CH_2), 99.3 (C1), 76.2 (C4), 74.1 (C5), 73.5, 72.8 (OCH_2Ph), 69.8 (C6), 69.3 (OCH_2CH=CH_2), 51.2 (C2), 23.5 (NHC(O)CH_3). HRMS-(ES): calcd for $C_{32}H_{32}D_5NO_6H^+$ 537.3007, found 537.3014.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02305.

^{1}H and ^{13}C NMR spectra of products and representative stacked 1H NMR spectra (Figures 1 and 2). Synthesis of **1** and detailed screening results for its acetylation. Further details of the synthesis of deuterium-labeled compounds **17**−**19**. MS analysis data of their degradation according to Scheme 9 (PDF)

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Notes

The authors declare no competing financial interest.

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(8) In this paper, we represent oxazolines and their derivatives as a $^4H_5$ half-chair conformation. The actual conformation is debated, but evidence suggests that the sp^2 NCO motif in the oxazoline ring enforces a change to either this or the twist boat (see refs 9 and 10). Both of these are very different from the parent $^4C_1$ chair, and this, we feel, is an important point to consider in these systems.
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