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Glycosylation with 2-Acetamido-2-deoxyglycosyl Donors at a Low Temperature: Scope of the Non-Oxazoline Method

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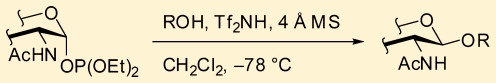
Supporting Information

ABSTRACT: A direct construction of 1,2-*trans*-β-linked 2-acetamido-2-deoxyglycosides was investigated. The 3,4,6-tri-*O*-benzyl- and 3,4,6-tri-*O*-acetyl-protected glycosyl diethyl phosphites and 4,6-*O*-benzylidene-protected galactosyl diethyl phosphite each reacted with a variety of acceptor alcohols in the presence of a stoichiometric amount of Tf_2NH in CH_2Cl_2 at −78 °C to afford the corresponding β-glycosides in good to high yields with complete stereoselectivity. Some experiments provided strong evidence that the corresponding oxazolinium ions are not responsible for the reaction. We demonstrated that glycosylations with the corresponding glycosyl imidate and thioglycoside also proceeded at a low temperature, indicating the possibility of these donors being attractive alternatives to the phosphite. A plausible reaction mechanism, which features glycosyl triflimide and contact ion pair as reactive intermediates, is proposed on the basis of the results obtained with 2-acetamido-2-deoxymannosyl donors.



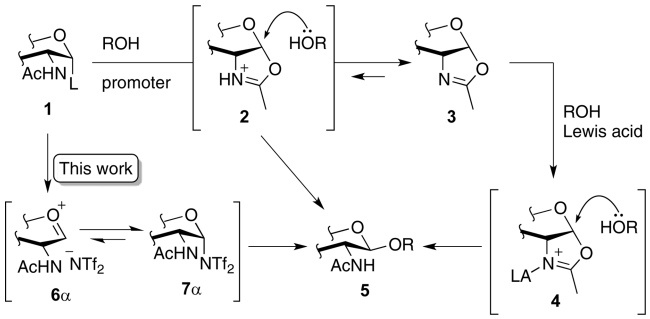
INTRODUCTION

2-Acetamido-2-deoxy-D-glycosides are ubiquitous building blocks of glycolipids, glycoproteins, proteoglycans, and peptidoglycans and are associated with a wide range of biological processes.[1] For example, serine/threonine hydroxy groups in nuclear and cytoplasmic proteins are glycosylated with 2-acetamido-2-deoxy-D-glucoses as a posttranslational modification of proteins that are thought to modulate the functions of proteins in cells. The majority of 2-acetamido-2-deoxysugars are found as β-linked glycosides, whereas 2-acetamido-2-deoxy-D-galactose residues are α-linked to serine/threonine hydroxy groups.[2,3]

For the synthesis of 1,2-*trans*-β-glycosides of 2-acetamido-2-deoxysugars,[4] the most general and extensively developed strategy utilizes donors containing a participating group as the amino-protecting functionality that are replaced by an acetyl group after the glycosylation event. A variety of 2-amino protecting groups such as *N*-phthaloyl,[5] *N*-2,2,2-trichloroethoxycarbonyl (Troc),[6,7] *N*-allyloxycarbonyl (Alloc),[7] *N*-benzyloxycarbonyl (Cbz),[7] *N*-trichloroacetyl (TCA),[8] *N*-tetrachlorophthaloyl (TCP),[9] *N*-dithiasuccinoyl (Dts),[10] *N*,*N*-diacetyl,[11] *N*-4,5-dichlorophthaloyl (DCPhth),[12] *N*-acetyl-*N*-2,2,2-trichloroethoxycarbonyl,[13] *N*-*p*-nitrobenzyloxycarbonyl,[14] *N*-dimethylmaleoyl (DMM),[15] *N*,*N*-dibenzyl,[16] *N*-thiodiglycoloyl (TDG),[17] and *N*-dimethylphosphoryl (DMP)[18] have been employed for this purpose. Despite their electronically nonparticipating nature, the synthetic utility of 2,5-dimethyl-1-pyrrolyl[19] and azido groups[20,21] as amino group equivalents has also been demonstrated.[22,23]

Although these indirect methods provide reliable access to 1,2-*trans*-β-glycosides of 2-acetamido-2-deoxysugars, additional synthetic steps are required for the substrate preparation. Therefore, it is clear that the use of donor **1** with natural *N*-acetyl functionality would constitute an ideal procedure in terms of efficiency and practicality (Scheme 1). In practice,

Scheme 1. Glycosylation with 2-Acetamido-2-deoxyglycosyl Donor 1



however, the reaction of donor **1** generally leads to the preferential formation of oxazoline derivative **3** via neighboring group participation and subsequent abstraction of a proton from the formed oxazolinium ion intermediate **2**.[24] Oxazoline **3** can be activated with Brønsted or Lewis acids to regenerate oxazolinium ion **2** or **4**, which upon treatment with an acceptor alcohol provides 2-acetamido-2-deoxy-β-glycoside **5**,[25] but the harsh reaction conditions required for this conversion have precluded its wide application in the synthesis of complex oligosaccharides.

Over the past 25 years, we have developed novel glycosylation reactions capitalizing on phosphorus-containing leaving groups.[26] Using donors with these leaving groups, various types of glycosidic linkages could be constructed in a stereoselective manner by appropriate choice of reaction conditions.[27−29] We anticipated that, with the proper selection of reaction conditions, high-yielding access to 1,2-*trans*-β-glycosides might be realized by glycosylation with a 2-

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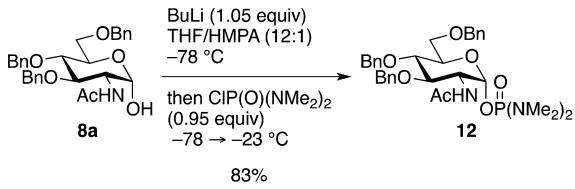
acetamido-2-deoxyglycosyl donor carrying a phosphorus-containing leaving group. In this article, we document the scope and mechanism of Tf_2NH-promoted glycosylation with 2-acetamido-2-deoxyglycosyl diethyl phosphite.[30] An extension of this study using a variety of 2-acetamido-2-deoxyglycosyl donors revealed that 2-acetamido-2-deoxyglycosides could be obtained by glycosylations at a low temperature irrespective of the leaving group employed, although the reaction did not proceed through the intermediacy of the corresponding oxazolinium ions. The details of this investigation are also reported herein.

RESULTS AND DISCUSSION

2-Acetamido-2-deoxy-D-glycosyl donors were prepared according to standard procedures. While α-linked glycosyl diethyl phosphites **9a**, **9c**, **11a**, and **11c** were stereoselectively obtained in excellent yields (87−90%) by phosphitylation of the corresponding hemiacetals with diethyl chlorophosphite,[29a,31] the reaction of 4,6-*O*-benzylidene-protected hemiacetals **8b** and **10b** under identical conditions gave anomeric mixtures, which were recrystallized from *n*-hexane/acetone (4:1) to provide pure α-phosphites **9b** and **11b** (Table 1). Tetramethylphosphorodiamidate **12** was prepared by condensing a lithium alkoxide derived from **8a** with bis(dimethylamino)-phosphorochloridate in THF/HMPA (eq 1).[28] On the other hand, 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucosyl diphenyl phosphate could not be obtained since it decomposed upon purification by silica gel column chromatography, although the reaction of **8a** with diphenyl chlorophosphate and DMAP proceeded in CH_2Cl_2 at 0 °C.

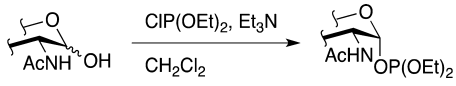


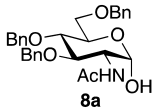
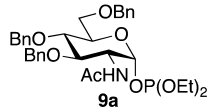
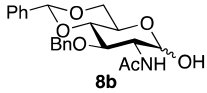
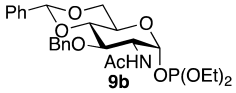
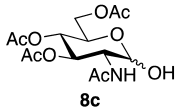
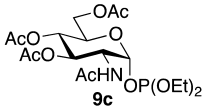
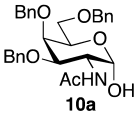
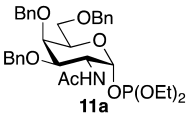
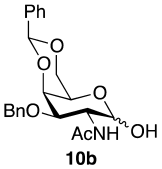
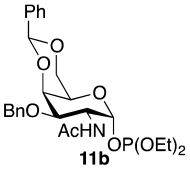
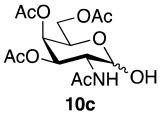
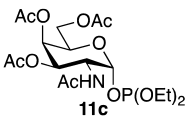
(1)

Having prepared 2-acetamido-2-deoxyglycosyl donors with a phosphorus-containing leaving group, we initially explored TMSOTf-promoted glycosylations of 1.1 equiv of 6-*O*-unprotected glucoside **13** with 3,4,6-tri-*O*-benzyl-protected glucosyl donors **9a** and **12** (Table 2). The reaction involved the addition of a 1.0 M solution of TMSOTf (1.1 equiv) in CH_2Cl_2 to a cooled mixture of a donor and 1.1 equiv of acceptor **13**.[32] To date, glycosylations with 2-acetamido-2-deoxyglycosyl donors have been performed at temperatures above 0 °C. The reaction of phosphite **9a** with alcohol **13** at 0 °C afforded a mixture of β-linked disaccharide **14** and oxazoline **15** in a ratio of 0.3:1 as determined by 500 MHz ^{1}H NMR spectroscopic analysis of the crude mixture (entry 1). An examination of the temperature profile of the reaction demonstrated that a decrease in the reaction temperature is accompanied by a significant increase in the yield of disaccharide **14** (entries 1−3). The temperature limit for smooth reaction was −60 °C, at which β-linked disaccharide **14** was obtained in 36% yield (entry 3). Glycosylation with phosphorodiamidate **12** proceeded at −45 °C to give almost the same result (40% yield), but a protracted reaction time (120 min) was required (entry 4). Given the diversity of promoters available, the phosphite method was chosen for further optimization. Due to its highly crystalline nature, diethyl phosphite **9a** is insoluble in solvents other than CH_2Cl_2 and THF at −60 °C: exclusive formation of oxazoline **15** was observed by the use of THF as a solvent (entry 5), and the addition of either toluene or EtCN as a cosolvent afforded no discernible benefit (entries 6 and 7 vs 3).

In an effort to improve the chemical yield of disaccharide **14**, several promoters were screened in the reaction of diethyl phosphite **9a** with alcohol **13**, and the results are compiled in Table 3. Although the product ratio (**14**:**15**) was improved to 2:1, the use of $BF_3{\cdot}OEt_2$, an effective promoter in the glycosylation with per-O-benzylated glycosyl diethyl phosphites,[29a] did not increase the yield of **14** due to the formation of a number of byproducts. Of various metal triflates examined,[33] $Sn(OTf)_2$ and $Hf(OTf)_4$[34] were found to promote the reaction at −60 °C, affording disaccharide **14** in 46% and 66% yields, respectively. Since some Brønsted acids have been shown to activate glycosyl phosphites,[29b,35] our interest was then directed to the use of promoters with Brønsted acidity. As expected from the precedent,[29c,d] diethyl phosphite **9a** could be activated at lower temperature (−78 °C) with a variety of Brønsted acids than with TMSOTf (entries 5−9). A significantly longer reaction time (12 h) was required to reach completion when $HClO_4$, prepared from *t*-BuBr and $AgClO_4$ in toluene,[36] was employed as a promoter (entry 5). The reaction rate was enhanced by the use of sulfonic acids in place of $HClO_4$

Table 1. Preparation of 2-Acetamido-2-deoxy-α-glycosyl Diethyl Phosphites



entry	hemiacetal	phosphite	yield, %
1	 **8a**	 **9a**	90
2	 **8b**	 **9b**	66[a]
3	 **8c**	 **9c**	89
4	 **10a**	 **11a**	90
5	 **10b**	 **11b**	76[a]
6	 **10c**	 **11c**	87

[a]Pure α-phosphites **9b** and **11b** were obtained upon purification by recrystallization from *n*-hexane/acetone (4:1).

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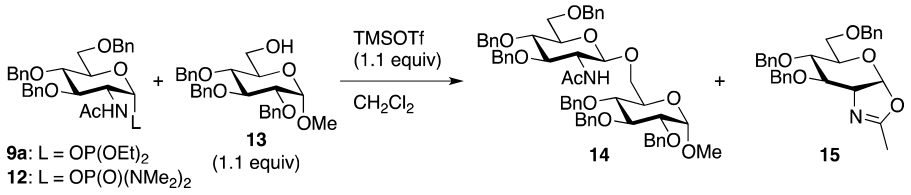
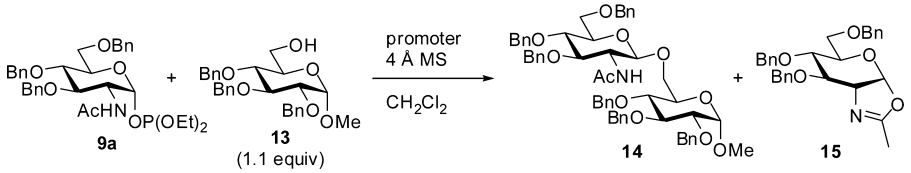
Table 2. TMSOTf-Promoted Glycosylation of Alcohol 13 with 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxyglucosyl Donors[a]



entry	donor	L	solvent	temp (°C)	time (min)	ratio[b] **14**:**15**	yield of **14** (%)
1	**9a**	$OP(OEt)_2$	CH_2Cl_2	0	10	0.3:1	18
2	**9a**	$OP(OEt)_2$	CH_2Cl_2	−23	10	0.4:1	24
3	**9a**	$OP(OEt)_2$	CH_2Cl_2	−60	30	0.7:1	36
4	**12**	$OP(O)(NMe_2)_2$	CH_2Cl_2	−45	120	0.8:1	40
5	**9a**	$OP(OEt)_2$	THF	−60	10	<0.1:1	trace
6	**9a**	$OP(OEt)_2$	$PhMe/CH_2Cl_2$ (1:1)	−60	30	0.7:1	35
7	**9a**	$OP(OEt)_2$	$EtCN/CH_2Cl_2$ (1:1)	−60	30	0.7:1	37

[a]The reaction was carried out on a 0.1 mmol scale. [b]Determined by 500 MHz ^{1}H NMR.

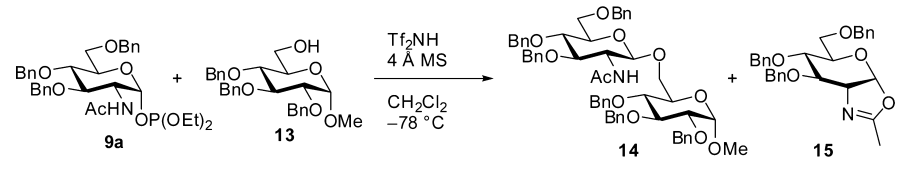
Table 3. Effects of Promoters in the Glycosylation of Alcohol 13 with Diethyl Phosphite 9a[a]



entry	promoter	equiv	temp (°C)	time (h)	ratio[b] **14**:**15**	yield of **14** (%)
1[c]	TMSOTf	1.1	−60	0.5	0.7:1	36
2	$BF_3{\cdot}OEt_2$	1.5	−60	4	2.0:1	39
3	$Sn(OTf)_2$	1.5	−60	1	1.6:1	46
4	$Hf(OTf)_4$	1.5	−60	1	2.9:1	66
5	$HClO_4$[d]	1.5	−78	12	2.2:1	59
6	MsOH	1.5	−78	1	0.8:1	38
7	TsOH	1.5	−78	1	1.8:1	51
8	TfOH	1.5	−78	5	4.2:1	75
9	Tf_2NH	1.1	−78	1	4.1:1	73

[a]The reaction was carried out on a 0.1 mmol scale. [b]Determined by 500 MHz ^{1}H NMR. [c]In the absence of 4 Å MS. [d]Prepared from *t*-BuBr and $AgClO_4$.

Table 4. Effects of Donor/acceptor/Tf_2NH Molar Ratio[a]



entry	Tf_2NH[b] (equiv)	molar ratio **9a**:**13**	time (h)	ratio[c] **14**:**15**	yield of **14** (%)
1[d]	0.2	1.0:1.1	24	0.9:1	22
2	0.5	1.0:1.1	2	2.3:1	57
3	1.1	1.0:1.1	1	4.1:1	73
4	1.5	1.0:1.1	1	4.1:1	73
5	1.1	1.0:1.5	1	5.2:1	77
6	1.1	1.0:2.0	1	7.8:1	84
7	1.1	2.0:1.0	1	–	93

[a]The reaction was carried out on a 0.1 mmol scale. [b]Based on the donor used. [c]Determined by 500 MHz ^{1}H NMR. [d]Donor **9a** was recovered in ca. 50% yield.

(entries 6–8). We noticed that sulfonic acids with greater Brønsted acidity[37] resulted in higher yield of **14**: good chemical yield (75%) was achieved by the TfOH-promoted reaction, albeit with somewhat long reaction time (5 h). Switching the

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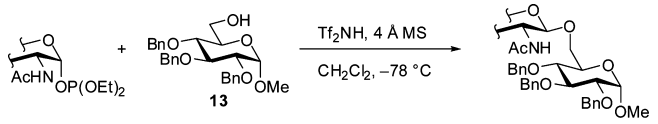
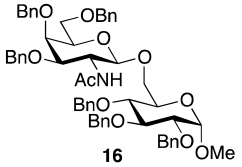
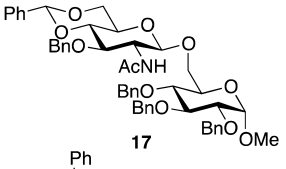
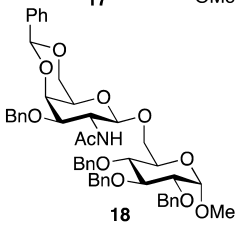
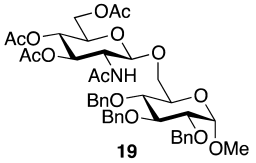
Table 5. Tf_2NH-Promoted Glycosylation of Alcohol 13 with 2-Acetamido-2-deoxyglycosyl Diethyl Phosphites[a,b]



entry	donor	molar ratio donor:**13**	time h	product	yield %
1	**11a**	1.0:2.0	1	 **16**	83
2	**11a**	2.0:1.0	1		87
3	**9b**	1.0:2.0	3	 **17**	49
4	**9b**	2.0:1.0	3		36
5	**11b**	1.0:2.0	3	 **18**	74
6	**11b**	2.0:1.0	3		78
7	**9c**	1.0:2.0	24	 **19**	70
8	**9c**	2.0:1.0	24		72

[a]The reaction was carried out on a 0.1 mmol scale. [b]Donor/Tf_2NH molar ratio =1.0/1.1.

counterion in super Brønsted acids from triflate to triflimide[38,39] significantly shortened the reaction time (5 → 1 h), providing disaccharide **14** in comparable yield (entry 9).[40,41]

Some Brønsted acids have been employed as catalysts to activate glycosyl phosphites.[35a,42] Therefore, we next investigated the glycosylation under catalytic conditions (Table 4). In the presence of 0.2 equiv of Tf_2NH, the glycosylation of alcohol **13** with diethyl phosphite **9a** did not proceed beyond a 50% conversion, providing disaccharide **14** in 22% yield (entry 1). We surmised that the result is attributed to the presence of $HP(O)(OEt)_2$ and oxazoline **15**, which were formed as the reaction progressed and would buffer the acidity of the promoter. While the use of 0.5 equiv of Tf_2NH was found to be sufficient for the reaction to reach completion, product selectivity (**14**:**15**) eroded significantly (entry 2). Since an excess amount of Tf_2NH has essentially no effect on the reaction (entry 4), 1.1 equiv of Tf_2NH was typically employed for the glycosylation. The effect of molar ratio of donor **9a** and acceptor **13** was also examined. When the amount of alcohol **13** used was increased from 1.1 to 2.0 equiv, higher yields were obtained (entries 3 vs 5 and 6). The use of donor **9a** in 2-fold excess afforded the best yield (93% yield, entry 7).[43] These results revealed the possibility that an excess of either reaction component can be used depending on their availability.

Having optimized the reaction conditions, the scope of the Tf_2NH-promoted glycosylation was explored. Results of experiments for probing the scope of the donor component with 6-O-unprotected glucoside **13** are summarized in Table 5.[44] As with donor **9a**, glycosylation with 3,4,6-tri-*O*-benzyl-protected galactosyl diethyl phosphite **11a** proceeded to completion within 1 h to furnish disaccharide **16** in good yields irrespective of the molar ratio (**11a**:**13**) used (entries 1 and 2). Consistent with a general trend of 4,6-*O*-benzylidene-protected glycosyl donors exhibiting reduced reactivities,[45] protracted reaction times were required for the complete consumption of donors **9b** and **11b** (entries 3–6). The use of glucosyl donor **9b** was disappointing because the yields were modest (up to 49%, entries 3 and 4). In stark contrast, glycosylation with galactosyl donor **11b** gave disaccharides **18** in good yields (entries 5 and 6). The difference in reactivity between these donors may be explained by considering that glucosyl donor **9b** is a trans-fused bicyclic compound, whereas galactosyl donor **11b** has a relatively flexible, *cis*-decaline-like architecture. We speculate that the greater conformational rigidity of **9b** relative to **11b** facilitates oxazoline formation.[46] While switching the protecting groups from benzyl to acetyl groups further lowers the reactivity of donors, 3,4,6-tri-*O*-acetyl-protected glucosyl donor **9c** could be activated by

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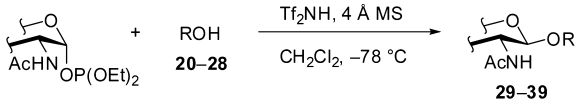
Tf_2NH at −78 °C, affording disaccharide **19** in acceptable yields (entries 7 and 8).[47]

In an effort to define the scope of the glycosylation method, we next examined the reaction employing a range of alcohols with different reactivities as acceptors (Table 6, Figure 1).[44] As expected, glycosylations of reactive primary alcohols such as linker **20** and 6-O-unprotected galactoside **21** gave the corresponding β-glycosides in good to excellent yields (entries 1, 2, and 10). It is noteworthy that even some of the secondary alcohols were successfully utilized in this reaction, leaving the acid-sensitive epoxy or acetal groups unaffected (entries 3−5, 9, and 11). On the other hand, less reactive secondary alcohols **25** and **26** could not be glycosylated under these conditions, indicating the possibility of regioselective glycosylation with 2,3,4-tri-O-unprotected glucoside (entries 4 vs 6 and 7). Isomerization of (*Z*)-trisubstituted olefin was not observed during the reaction between diethyl phosphite **11a** and nerol (**27**, entry 8). We confirmed that similar results could be obtained irrespective of the reaction component employed in excess.

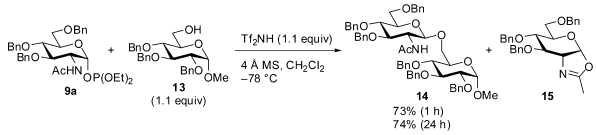
Table 6. Tf_2NH-Promoted Glycosylation of Various Acceptor Alcohols with 2-Acetamido-2-deoxyglycosyl Donors[a]



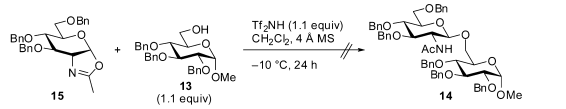
					yield, %	
entry	donor	acceptor	time (h)	product	condition A[b]	condition B[c]
1	**9a**	**20**	1	**29**	80[d]	83[e]
2	**9a**	**21**	1	**30**	89	92
3	**9a**	**22**	1	**31**	79	78
4	**9a**	**23**	1	**32**	65	64
5	**9a**	**24**	1	**33**	57	44
6	**9a**	**25**	1	**34**	0	–
7	**9a**	**26**	1	**35**	0	–
8	**11a**	**27**	1	**36**	81[f]	79[g]
9	**11a**	**28**	1	**37**	74[d]	71[e]
10	**11c**	**21**	24	**38**	67	70
11	**11c**	**22**	24	**39**	59	59

[a]The reaction was carried out on a 0.1 mmol scale. [b]Condition A: donor/acceptor/Tf_2NH molar ratio = 1.0/2.0/1.1 unless otherwise noted. [c]Condition B: donor/acceptor/Tf_2NH molar ratio = 2.0/1.0/2.2 unless otherwise noted. [d]Donor/acceptor/Tf_2NH molar ratio = 1.0/1.5/1.1. [e]Donor/acceptor/Tf_2NH molar ratio = 1.5/1.0/1.7. [f]Donor/acceptor/Tf_2NH molar ratio = 1.0/1.1/1.1. [g]Donor/acceptor/Tf_2NH molar ratio = 1.1/1.0/1.2.

As mentioned above, glycosylations with 2-acetamido-2-deoxyglycosyl donors have been performed at temperatures higher than 0 °C due to the low reactivity of oxazolinium ion intermediates. The feasibility that oxazolinium ions are not reactive intermediates in Tf_2NH-promoted reactions with 2-acetamido-2-deoxyglycosyl diethyl phosphites is suggested by the following: (1) the reaction occurred at −78 °C and (2) prolonged reaction times had no effect on the yield of disaccharides (eq 2). To validate this speculation, we first



(2)



(3)

attempted glycosylation of alcohol **13** with oxazoline **15** in the presence of Tf_2NH in CH_2Cl_2, but desired disaccharide **14** was not formed even at −10 °C (eq 3).[48] To monitor the formation of the oxazolinium ion species, ^1H NMR spectra were recorded

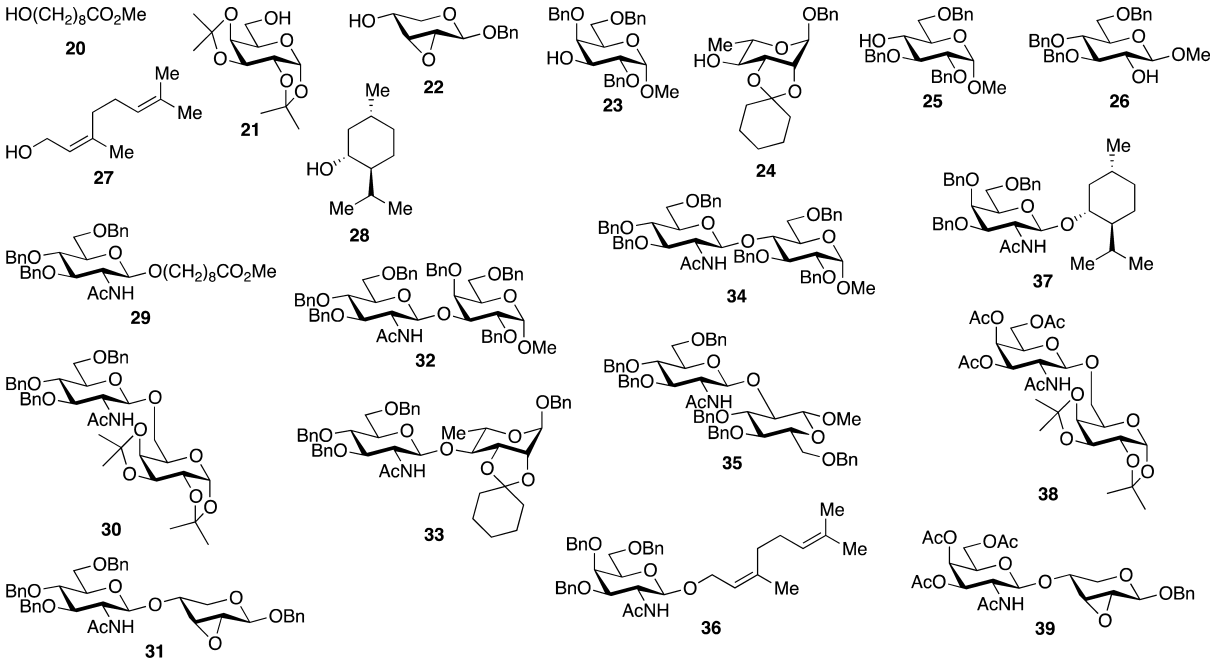


Figure 1. Acceptor alcohols and products in Table 6.

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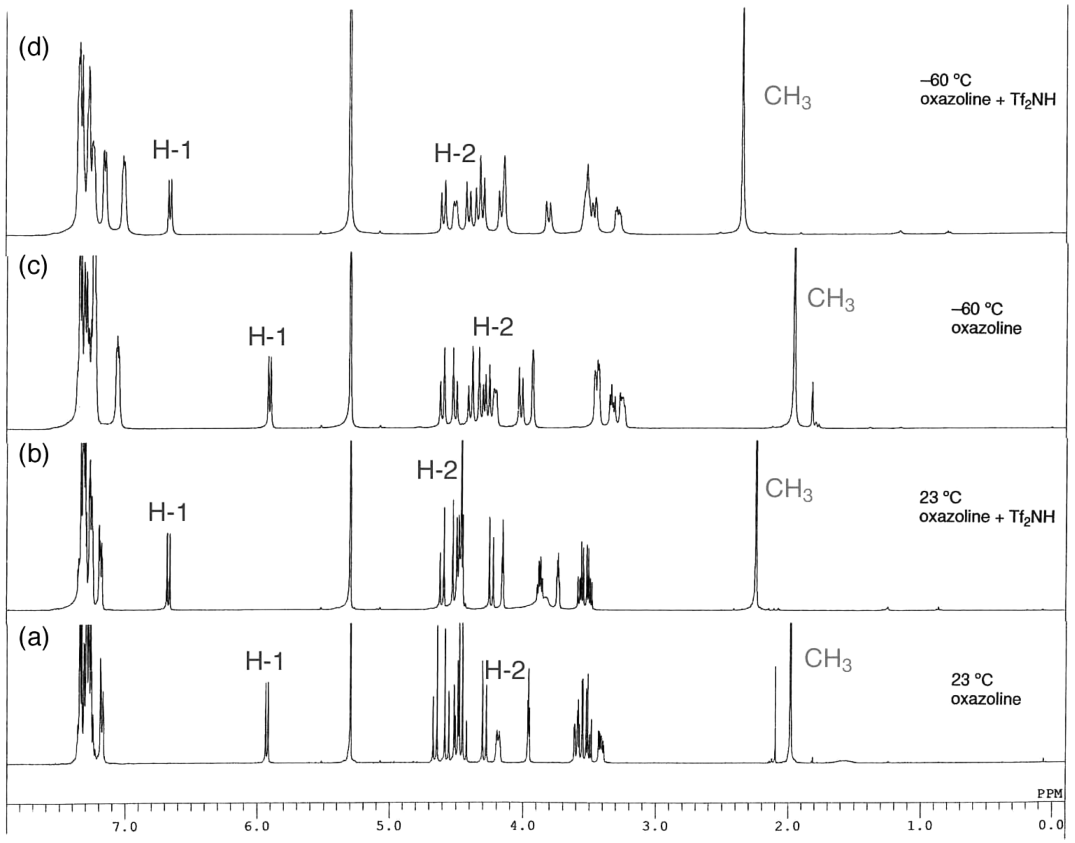
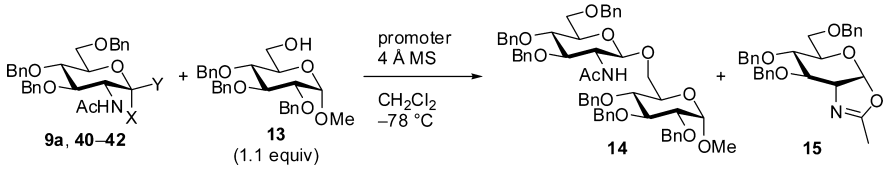


Figure 2. Protonation of oxazoline **15** monitored by ^{1}H NMR in CD_2Cl_2: (a) oxazoline **15** at 23 °C; (b) 23 °C, after addition of Tf_2NH (1.5 equiv); (c) oxazoline **15** at −60 °C; (d) −60 °C, after addition of Tf_2NH (1.5 equiv).

Table 7. Effects of Leaving Group and Anomeric Configuration



	donor			promoter				
entry		X	Y		equiv	time (h)	ratio[a] **14**:**15**	yield of **14** (%)
1	**9a**	$OP(OEt)_2$	H	Tf_2NH	1.1	1	4.1:1	73
2	**40**	$OC(NH)CCl_3$	H	Tf_2NH	1.1	0.5	1.5:1	50
3	**40**	$OC(NH)CCl_3$	H	Tf_2NH	0.5	0.5	2.6:1	56
4	**40**	$OC(NH)CCl_3$	H	Tf_2NH	0.2	40	2.0:1	45
5	**41**	SPh	H	NIS/Tf_2NH	1.1	18	0.6:1	37
6	**42**	H	SPh	NIS/Tf_2NH	1.1	6	0.2:1	16

[a]Determined by 500 MHz ^{1}H NMR.

in CD_2Cl_2 before and after the addition of a 50% excess of Tf_2NH (Figure 2). Inspection of the spectra unambiguously revealed a downfield shift of the resonances of H-1, H-2, and CH_3, which are positioned close to the nitrogen atom.[49] This result clearly indicated that, irrespective of the reaction temperature, oxazoline **15** was protonated to generate the corresponding oxazolinium ion, decreasing the electron density of the oxazoline ring.

The fact that the reaction did not proceed through the common oxazolinium ion intermediate revealed that the glycoside/oxazoline ratio could be influenced by the leaving group and the anomeric configuration of the donor. To provide evidence, we selected the two representative and most successful leaving groups in oligosaccharide synthesis, the trichloroacetimidate[50] and phenylthio groups,[51] and prepared 2-acetamido-2-deoxyglucosyl donors **40**−**42**[52] for the reaction with alcohol **13** at −78 °C (Table 7). Whereas all attempts to obtain 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucosyl diethyl phosphite met with failure in accord with precedents in which a β-oriented anomeric leaving group of a 2-acetamido-2-deoxyglucosyl donor was readily eliminated to form the corresponding oxazoline derivative,[54] β-thioglycoside **42** could be safely obtained. The reaction of 2-acetamido-2-deoxy-α-D-glucosyl trichloroacetimidate **40** under optimized conditions for

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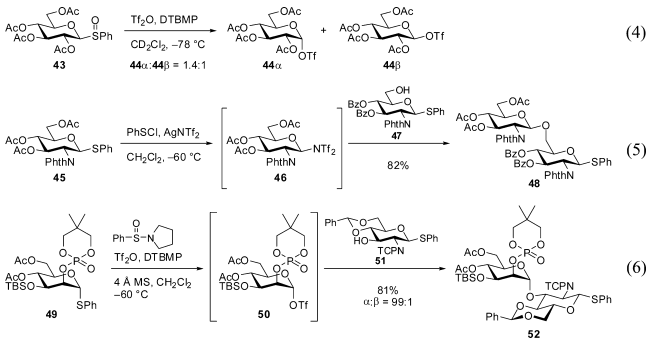
phosphite **9a** was completed within 30 min to give a 1.5:1 mixture of disaccharide **14** and oxazoline **15**, from which disaccharide **14** was obtained in 50% yield after chromatographic separation (entry 2). Interestingly, in contrast to the phosphite method, the chemical yield of disaccharide **14** was somewhat improved (50% → 56%) by a decrease in the amount of Tf_2NH (1.1 → 0.5 equiv), although the reason is not clear at present (entries 2 vs 3). It is also noteworthy that disaccharide **14** was obtained in 45% yield even with the aid of 0.2 equiv of Tf_2NH (entry 4). For the glycosylation with thioglycosides, the effectiveness of the combinational use of NIS and an acid was documented by van Boom and co-workers.[55] In order to preclude the counterion effect, the NIS/Tf_2NH system was chosen for activation of thioglycosides **41** and **42** (entries 5 and 6). Glycosylation with α-thioglycoside **41** in CH_2Cl_2 at −78 °C required 18 h to reach completion, whereas the reaction time was decreased to 6 h under identical conditions when using β-thioglycoside **42**. The difference in reaction rate is a consequence of both the intramolecular assistance of the neighboring acetamido group for elimination of the β-oriented leaving group and the stability of the donor stemming from the anomeric effect. The intramolecular assistance also facilitated formation of the oxazolinium ion, thus leading to preferential production of oxazoline **15** from β-thioglycoside **42**. On the basis of these results, we concluded that the oxazolinium ion formed from these donors is not responsible for the glycosylation at a low temperature. These experiments also indicate that the donors **40** and **41** have the potential to be attractive alternatives to the phosphite **9a**, although the reaction conditions need to be optimized.

In 1997, Crich and Sun revealed on the basis of NMR experiments that glycosyl triflates are cleanly generated from the corresponding glycosyl sulfoxides even with participating protecting groups at O-2 when treated with Tf_2O in the presence of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, eq 4).[56] Stimulated by the pioneering work of Crich, considerable



(4)

(5)

(6)

efforts have been devoted to clarify the mechanism of chemical glycosylation reactions.[57] Very recently, Crich, Pratt, and co-workers suggested on the basis of computed and experimentally determined primary ^{13}C kinetic isotope effect values that β-glucoside formation occurs by an associative mechanism in which the incoming alcohols displace the leaving group from α-glucosyl triflates and/or α-contact ion pair (α-CIP).[58] With regard to the glycosylation with a participating group at O-2, Yamago and co-workers proposed that glycosyl triflates exist in equilibrium through neighboring group participation with short-lived ionic intermediates, which react with alcohols from the less hindered side to give 1,2-*trans*-glycosides, since they monitored the formation of 2-deoxy-2-phthalimido-β-glucosyl triflimide **46** from thioglycoside **45** (eq 5).[59] This proposal seems to be supported by the predominant formation of α-mannoside **52** from thioglycoside **49** (eq 6).[60] On the basis of these reports, we propose plausible reaction pathways for the Tf_2NH-promoted glycosylation with 2-acetamido-2-deoxyglycosyl diethyl phosphites (Scheme 2).

Upon activation by protonation of the phosphorus atom,[61] diethyl phosphite is eliminated to generate an equilibrium mixture of CIPs **6**α and **6**β, solvent-separated ion pair (SSIP) **55**, and glycosyl triflimides **7**α and **7**β, whose equilibrium would heavily lie to α-glycosyl triflimide **7**α on kinetic and thermodynamic grounds.[62] The β-glycosyl triflimide **7**β smoothly undergoes an intramolecular nucleophilic substitution by the adjacent acetamido group, resulting in the exclusive formation of oxazoline **3** through oxazolinium ion **2**. In contrast, α-CIP **6**α and/or α-glycosyl triflimide **7**α would undergo nucleophilic attack by acceptor alcohols at the anomeric carbon from the β-face to provide β-glycosides **5** (path a). However, once the counterion is separated from **6**α and **7**α, the acetamido oxygen atom can access the electrophilic anomeric carbon along the stereoelectronically favored axial direction to generate short-lived intermediate **57** as mentioned by the Yamago group. Although the intramolecular reaction that gives oxazoline **3** via oxazolinium ion **2** is energetically favored compared to the intermolecular process, the possibility of nucleophilic attack of acceptor alcohols from the less hindered β-face of **57** leading to the formation of β-glycosides **5** cannot be excluded (path b). The fact that α-glycosides have not been obtained reveals that the α-face of SSIP is completely shielded by the acetamido group. S_N2-like displacement of protonated phosphite **54** with acceptor alcohols is also a conceivable pathway for the formation of β-glycosides **5** (path c).

While glycosyl triflates and triflimides with participating protecting groups at O-2 were cleanly generated as shown in eqs 4−6, predominant formation of 1,2-*trans*-glycosides was observed in all cases. Therefore, it is not clear from these precedents whether the glycosyl triflates/triflimides are actual reactive species in glycosylation reactions, because nucleophilic substitution of α-CIP, α-glycosyl triflate/triflimide, or short-lived ionic intermediate resulting from neighboring group participation provides β-glycosides in the gluco/galacto series. Since intermediates are prone to oxazoline formation and are labile and NMR experiments were therefore precluded in our case,[63] we decided to investigate the reactions with 2-acetamido-2-deoxy-1-thiomannosides **58** and **59** in order to gain an insight into the reaction pathways for glycosylation with 2-acetamido-2-deoxyglycosyl donors.[64]

The preparation of thioglycosides **58** and **59** began with phosphorylation of 2-azido-2-deoxymannose **60** (Scheme 3).[65] Reaction of diphenyl phosphate **61** with thiophenol in the presence of $BF_3{\cdot}OEt_2$ followed by chromatographic separation gave thioglycosides **62** and **63** in 25% and 67% yields, respectively. A two-step sequence involving reduction of the azido group with Ph_3P in aq THF and acetylation furnished thioglycosides **58** and **59** in 75% and 80% yields, respectively.

Consistent with the general trend,[45d] mannosyl donors **58** and **59** are less reactive than are glucosyl donors **41** and **42**; donors **58** and **59** are unreactive toward NIS/Tf_2NH at −78 °C and were activated upon raising the temperature to −60 °C. While oxazoline **66** was obtained as a major product irrespective of the anomeric configuration of the donor, a mixture of disaccharides **64** and **65** was obtained in ca. 20% yield by the reaction with 6-O-unprotected glycoside alcohol

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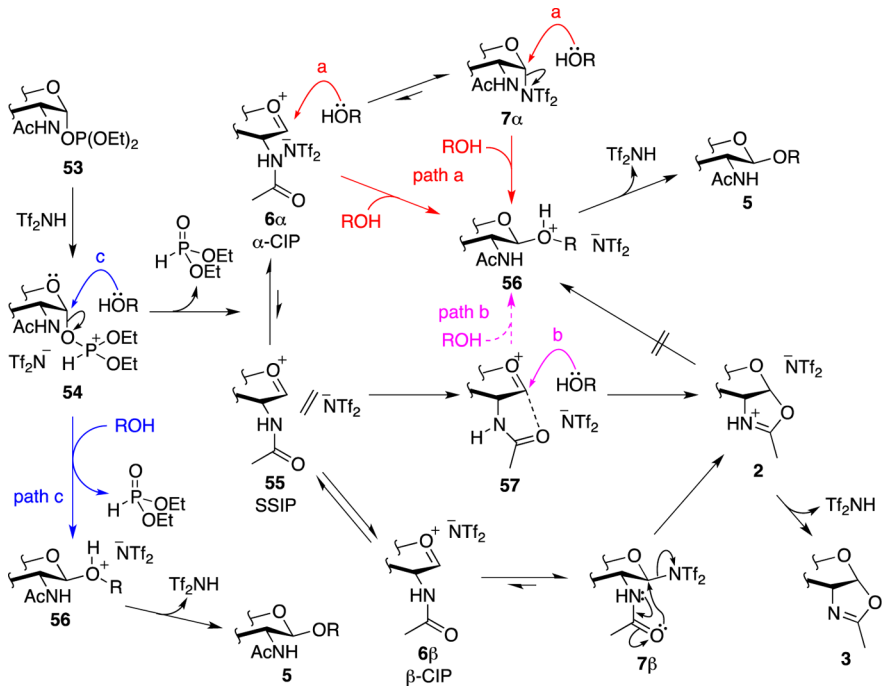
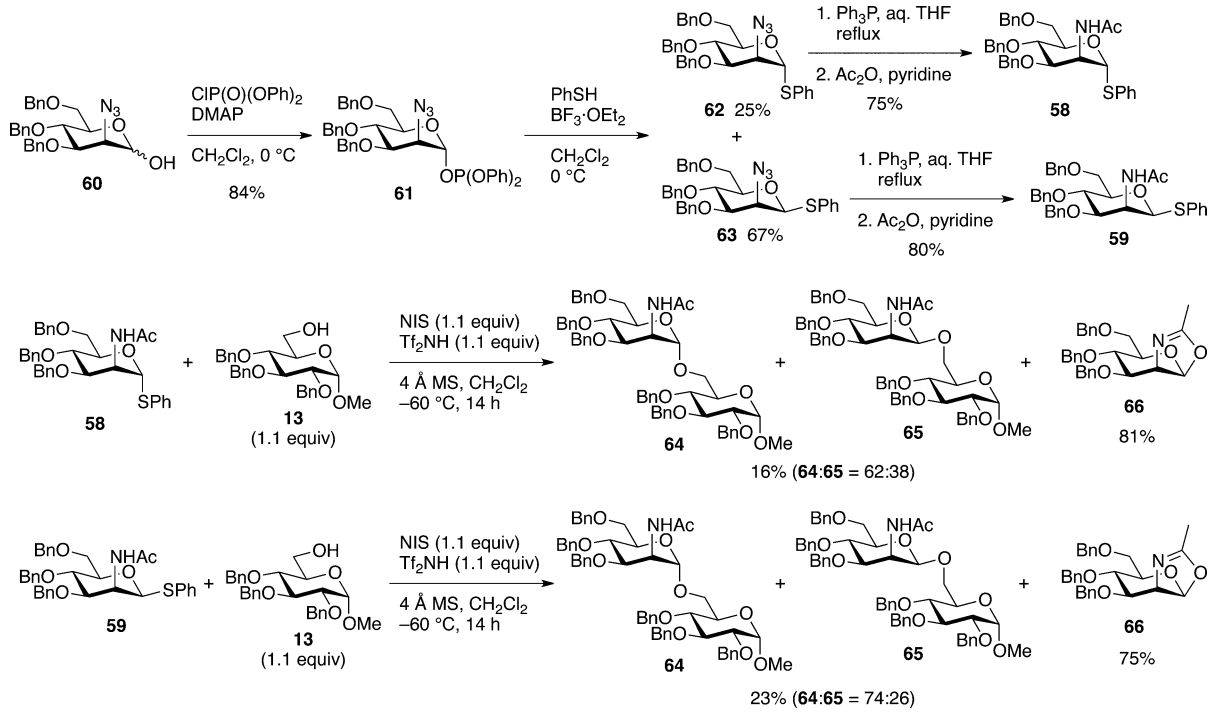
Scheme 2. Plausible Mechanism of Tf_2NH-Promoted Glycosylation with 2-Acetamido-2-deoxyglycosyl Diethyl Phosphites at a Low Temperature



Scheme 3. Preparation and Glycosidation of 2-Acetamido-2-deoxy-1-thiomannosides 58 and 59



13. On the basis of the literature precedents,[51a] 2-acetamido-2-deoxymannosyl triflimide **70***α* would be formed through *α*-CIP **68***α* and/or SSIP **69** upon exposure of donors **58** and **59** to the promoter (Scheme 4). Since both the anomeric effect and the steric repulsion between the acetamido group disposed axially at C-2 and an incoming alcohol uniformly favor the formation of *α*-mannosidic linkages, the formation of thermodynamically less stable *β*-glycoside **65** unambiguously indicates an associative S_N2-like mechanism, wherein *α*-CIP **68***α* and/or *α*-glycosyl triflimide **70***α* undergo nucleophilic attack of acceptor alcohols. To the best of our knowledge, this result is the first example that provides experimental evidence for the S_N2-like displacement of glycosyl triflates/triflimides in a system capable of neighboring group participation. However, participation of the adjacent acetamido group in species **68***α* and **70***α* that leads to the formation of oxazoline **66** competes with the intermolecular process, resulting in low conversion to *β*-linked disaccharide **65**. Due to the steric reason, it is unlikely

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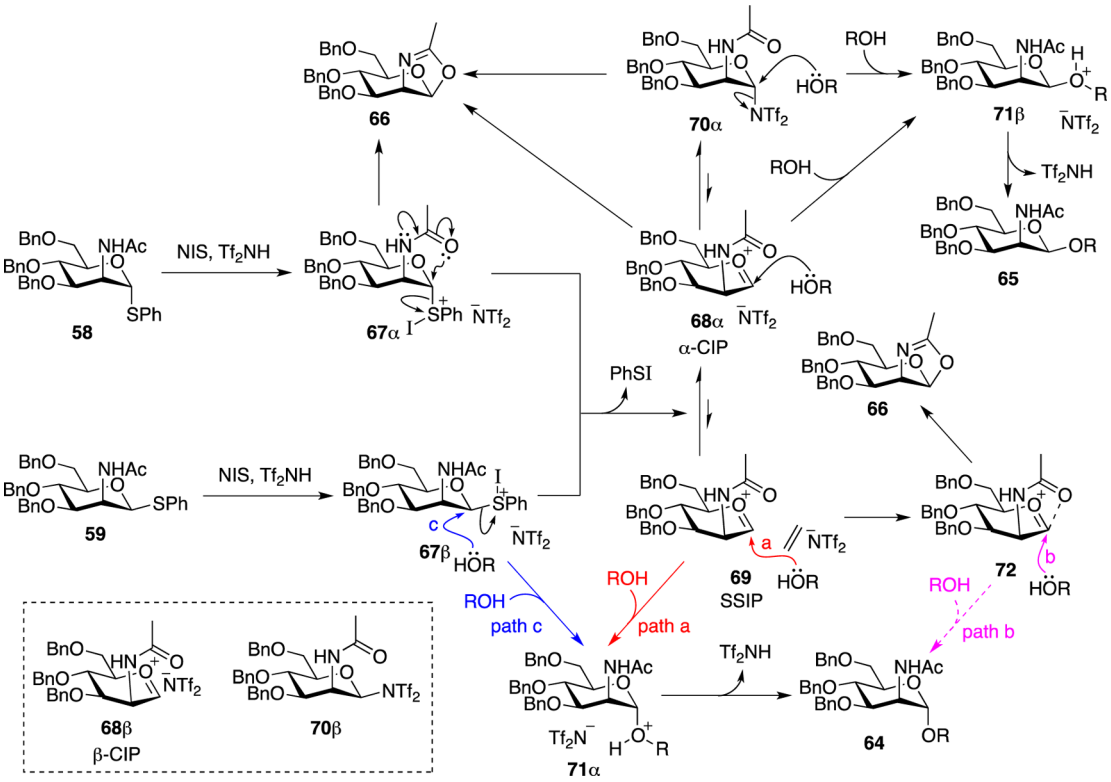
Scheme 4. Plausible Mechanism of the Reaction with 2-Acetamido-2-deoxymannosyl Donors 58 and 59



that β-CIP **68**β and β-triflimide **70**β exist in the reaction mixture. Therefore, the formation of α-glycoside **64** would be attributed to nucleophilic attack from the less hindered face of SSIP **69** (path a) as reported by the Crich group for α-mannoside formation.[58,66] While participation of the acetamido group in SSIP **69** leads to the formation of oxazoline **66** via **72**, access of the oxygen atom from the stereoelectronically unstabilized equatorial orientation permits the formation of α-glycoside **64** from SSIP **69**, albeit in low yield. This result is in stark contrast to the GlcNAc/GalNAc series, in which α-glycosides have never been obtained from SSIP **55**. Nucleophilic attack of acceptor alcohol **13** on transient species **72** to give α-glycoside **64** would be disfavored for steric and electronic reasons (path b).

Because of the alignment of the acetamido group anti to the leaving group, α-thioglycoside **58** underwent cyclization (**67**α → **66**) more easily to give oxazoline **66** than was the case for β-isomer **59**. The slightly higher α-selectivity observed with β-thioglycoside **59** would be a result of the backside attack of alcohol **13** on **67**β (path c). From these results, we conclude that the success of glycosylations at a low temperature is due to the rate retardation of oxazolinium ion formation from α-glycosyl triflimides and α-CIPs, thereby enabling these intermediates to react with acceptor alcohols.

CONCLUSION

A direct construction of 1,2-*trans*-β-linked 2-acetamido-2-deoxyglycosides using 2-acetamido-2-deoxyglycosyl donors has been documented. Tf_2NH was found to be the promoter of choice for activation of diethyl phosphite donors, affording the corresponding β-glycosides in good to high yields with complete stereoselectivity, albeit by the use of either a donor or acceptor in 2-fold excess in most cases. It is noteworthy that lowering the reaction temperature increased the yields of glycosides. A wide range of glycosyl acceptors, including allyl alcohols and some secondary alcohols as well as glycoside alcohols bearing acid-sensitive acetal or epoxy groups, can be employed in this coupling. While a limitation was encountered with less reactive acceptor alcohols, such as 4- or 2-*O*-unprotected glucosides, these results indicate the feasibility of regioselective glycosylation of polyols. The glycosyl donor is not confined to highly reactive per-*O*-benzyl-protected 2-acetamido-2-deoxyglucosyl and galactosyl diethyl phosphites, and the scope of this reaction is extended to include less reactive per-*O*-acetyl-protected 2-acetamido-2-deoxyglycosyl diethyl phosphites and 4,6-*O*-benzylidene-protected galactosyl diethyl phosphite as donors. The use of 2-acetamido-2-deoxyglucosyl trichloroacetimidate or the corresponding thioglycoside clearly revealed that the same coupling could be realized with these donors, though glycosylations with 2-acetamido-2-deoxyglycosyl donors have never been performed at temperatures below 0 °C.

Although the lability of intermediates precludes their direct detection by NMR, some experiments provide strong evidence that the corresponding oxazolinium ions are not responsible for the reaction. On the basis of the literature reports by the groups of Crich and Yamago, we propose a plausible reaction mechanism in which β-glycosides are formed by S_N2-like displacement of α-glycosyl triflimides and/or nucleophilic attack from the less hindered face of α-CIP. The fact that the acetamido group capable of anchimeric assistance behaves as a nonparticipating group in the present glycosylation was supported by the formation of a mixture of α- and β-mannosides from 2-acetamido-2-deoxythiomannosides. The reaction at a low temperature led to the rate retardation of oxazolinium ion formation from α-glycosyl triflimides and α-CIPs through their β-counterparts or SSIPs, thereby enabling these intermediates to react with acceptor alcohols.

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To the best of our knowledge, this protocol represents the first example of glycosylation with 2-acetamido-2-deoxyglycosyl donors that does not proceed through the corresponding oxazolinium ion intermediate. In the following article, we describe the stereoselective synthesis of the tetrasaccharide repeating unit of the polymeric O antigen isolated from *Acinetobacter baumannii* serogroup O18 to demonstrate the synthetic utility of the present method.

EXPERIMENTAL SECTION

Typical Procedure for Preparation of 2-Acetamido-2-deoxyglycopyranosyl Diethyl Phosphite: 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl Diethyl Phosphite (9a). Diethyl chlorophosphite (0.26 mL, 1.78 mmol) was added to a stirred suspension of hemiacetal **8a** (700 mg, 1.42 mmol) and Et_3N (0.60 mL, 4.26 mmol) in CH_2Cl_2 (14 mL) at 0 °C. After 30 min of stirring, the reaction was quenched with crushed ice, followed by stirring at room temperature for 10 min. The mixture was poured into a two-layer mixture of AcOEt (15 mL) and saturated aqueous $NaHCO_3$ (10 mL), and the resulting mixture was extracted with AcOEt (25 mL). The organic extract was washed with brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (945 mg, white solid), which was purified by column chromatography (Wako gel 20 g, 2:1:1 CH_2Cl_2/AcOEt/*n*-hexane with 3% Et_3N) to give diethyl phosphite **9a** (778 mg, 90%) as a white solid. The donors were recrystallized from 4:1 *n*-hexane/acetone when possible for the following glycosylation reaction. R_f 0.50 (2:1:1 CH_2Cl_2/AcOEt/*n*-hexane, with Et_3N-doped silica gel plate); mp 108.0−109.0 °C (colorless needles from 4:1 *n*-hexane/acetone); $[\alpha]_D^{20}$ +101.1 (*c* 1.00, $CHCl_3$); IR (Nujol) 3314, 1642, 1547, 1121, 1065, 1031, 947, 903, 858 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.22 (t, *J* = 7.1 Hz, 6H), 1.80 (s, 3H), 3.65 (dd, *J* = 1.7, 10.9 Hz, 1H), 3.70 (dd, *J* = 9.3, 10.2 Hz, 1H), 3.76−3.89 (m, 6H), 3.97 (m, 1H), 4.25 (ddd, *J* = 3.3, 9.1, 10.5 Hz, 1H), 4.52 (d, *J* = 12.1 Hz, 1H), 4.55 (d, *J* = 10.7 Hz, 1H), 4.63 (d, *J* = 12.1 Hz, 1H), 4.65 (d, *J* = 11.7 Hz, 1H), 4.83 (d, *J* = 10.7 Hz, 1H), 4.87 (d, *J* = 11.7 Hz, 1H), 5.18 (d, *J* = 9.1 Hz, 1H), 5.48 (dd, *J* = 3.3, 8.2 Hz, 1H), 7.21 (m, 2H), 7.21−7.34 (m, 13H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.7 (d, J_{C-P} = 5.3 Hz), 16.8 (d, J_{C-P} = 5.2 Hz), 23.2, 52.7, 58.38 (d, J_{C-P} = 11.1 Hz), 58.42 (d, J_{C-P} = 11.3 Hz), 68.3, 72.0, 73.3, 74.6, 75.0, 78.1, 79.3, 92.7 (d, *J* = 15.3 Hz), 127.5, 127.6, 127.67, 127.73, 127.8, 127.9, 128.2, 128.27, 128.33, 128.4, 137.9, 138.3, 169.6; ^{31}P NMR (109 MHz, $CDCl_3$) δ 141.5; HRMS (FAB) *m*/*z* $[M + H]^+$ calcd for $C_{33}H_{43}NO_8P$ 612.2726; found 612.2749. Anal. Calcd for $C_{33}H_{42}NO_8P$: C, 64.80; H, 6.92; N, 2.29. Found: C, 64.81; H, 6.96; N, 2.19.

2-Acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl Diethyl Phosphite (9b). The reaction was performed according to the typical procedure with hemiacetal **8b** (388 mg, 0.97 mmol), Et_3N (0.41 mL, 2.91 mmol), diethyl chlorophosphite (0.17 mL, 1.17 mmol), and CH_2Cl_2 (15 mL). The crude product was purified by column chromatography (Wako gel 12 g, 5:2:2 CH_2Cl_2/AcOEt/*n*-hexane with 3% Et_3N) to give the corresponding diethyl phosphite (426 mg) as a white solid, which was recrystallized from 4:1 *n*-hexane/acetone (10 mL) to give α-linked diethyl phosphite **9b** (335 mg, 66%) as colorless needles. R_f 0.35 (10:1 CH_2Cl_2/acetone); mp 179.0−179.5 °C; $[\alpha]_D^{23}$ +112.2 (*c* 1.00, $CHCl_3$); IR (KBr) 3314, 1648, 1551, 1371, 1128, 1089, 1029 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.4 Hz, 3H), 1.26 (t, *J* = 7.4 Hz, 3H), 1.89 (s, 3H), 3.72 (t, *J* = 9.7 Hz, 1H), 3.75−3.91 (m, 6H), 4.02 (m, 1H), 4.26 (dd, *J* = 4.6, 10.3 Hz, 1H), 4.29 (m, 1H), 4.65 (d, *J* = 12.6 Hz, 1H), 4.93 (d, *J* = 12.6 Hz, 1H), 5.27 (d, *J* = 8.6 Hz, 1H), 5.49 (dd, *J* = 3.4, 8.0 Hz, 1H), 5.61 (s, 1H), 7.27−7.42 (m, 8H), 7.52 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.8 (d, J_{C-P} = 4.8 Hz), 16.9 (d, J_{C-P} = 4.8 Hz), 23.2, 52.7 (d, J_{C-P} = 3.6 Hz), 58.5 (d, J_{C-P} = 12.0 Hz), 58.6 (d, J_{C-P} = 12.0 Hz), 63.7, 68.8, 73.9, 75.2, 82.4, 92.9 (d, J_{C-P} = 15.6 Hz), 101.2, 125.9, 127.7, 128.1, 128.2, 128.3, 128.9, 137.2, 138.4, 169.7; ^{31}P NMR (202 MHz, $CDCl_3$) δ 142.1; HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{35}NO_8P$ 520.2100; found 520.2104. Anal. Calcd for $C_{26}H_{34}NO_8P$: C, 60.11; H, 6.60; N, 2.70. Found: C, 60.00; H, 6.57; N, 2.65.

2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl Diethyl Phosphite (9c). The reaction was performed according to the typical procedure with hemiacetal **8c** (508 mg, 1.46 mmol), Et_3N (0.61 mL, 4.38 mmol), diethyl chlorophosphite (0.26 mL, 1.83 mmol), and CH_2Cl_2 (10 mL). The crude product (743 mg, slightly yellow amorphous) was purified by column chromatography (Wako gel 14 g, 2:1 AcOEt/*n*-hexane with 3% Et_3N) to give diethyl phosphite **9c** (610 mg, 89%) as a colorless amorphous. R_f 0.39 (1:2 *n*-hexane/AcOEt, with Et_3N-doped silica gel plate); $[\alpha]_D^{19}$ +86.3 (*c* 1.05, $CHCl_3$); IR (Nujol) 3474, 3240, 1744, 1640, 1559, 1292, 1223, 1126, 1031, 922, 831 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.29 (t, *J* = 7.0 Hz, 3H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.95 (s, 3H), 2.03 (s, 3H), 2.04 (s, 3H), 2.09 (s, 3H), 3.88−3.99 (m, 4H), 4.08 (dd, *J* = 2.2, 12.3 Hz, 1H), 4.16 (ddd, *J* = 2.2, 4.4, 9.8 Hz, 1H), 4.24 (dd, *J* = 4.4, 12.3 Hz, 1H), 4.37 (ddd, *J* = 3.3, 9.5, 10.4 Hz, 1H), 5.17 (dd, *J* = 9.8, 10.2 Hz, 1H), 5.24 (dd, *J* = 10.2, 10.4 Hz, 1H), 5.54 (dd, *J* = 3.3, 8.1 Hz, 1H), 5.73 (d, *J* = 9.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.8 (d, J_{C-P} = 5.0 Hz), 16.9 (d, J_{C-P} = 5.2 Hz), 20.5, 20.59, 20.63, 23.0, 52.2 (d, J_{C-P} = 3.4 Hz), 58.7 (d, J_{C-P} = 11.1 Hz), 58.8 (d, J_{C-P} = 11.1 Hz), 61.8, 67.8, 68.1, 68.8, 70.9, 91.8 (d, J_{C-P} = 13.1 Hz), 169.2, 169.8, 170.6, 171.3; ^{31}P NMR (109 MHz, $CDCl_3$) δ 141.1; HRMS (FAB) *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{31}NO_{11}P$ 468.1635; found 468.1623. Anal. Calcd for $C_{18}H_{30}NO_{11}P$: C, 46.25; H, 6.47; N, 3.00. Found: C, 46.11; H, 6.47; N, 2.99.

2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranosyl Diethyl Phosphite (11a). The reaction was performed according to the typical procedure with hemiacetal **10a** (770 mg, 1.57 mmol), Et_3N (0.66 mL, 4.71 mmol), diethyl chlorophosphite (0.30 mL, 2.04 mmol), and CH_2Cl_2 (14 mL). Purification by column chromatography (Wako gel 20 g, 2:1:1 CH_2Cl_2/AcOEt/*n*-hexane with 3% Et_3N) afforded diethyl phosphite **11a** (778 mg, 90%) as a white solid. R_f 0.47 (2:1:1 CH_2Cl_2/AcOEt/*n*-hexane, with Et_3N-doped silica gel plate); mp 134.0−135.0 °C (colorless needles from 4:1 *n*-hexane/acetone); $[\alpha]_D^{23}$ +102.8 (*c* 1.00, $CHCl_3$); IR (Nujol) 3314, 1641, 1539, 1305, 1167, 1124, 1103, 1028, 936, 893 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$; spectrum contains a mixture of rotamers, only the major rotamer signals are reported) δ 1.17 (t, *J* = 7.2 Hz, 6H), 1.87 (s, 3H), 3.51 (dd, *J* = 5.5, 9.2 Hz, 1H), 3.60 (dd, *J* = 2.5, 11.0 Hz, 1H), 3.62 (dd, *J* = 7.5, 9.2 Hz, 1H), 3.70−3.85 (m, 4H), 4.04 (br s, 1H), 4.07 (m, 1H), 4.41 (d, *J* = 11.6 Hz, 1H), 4.42 (d, *J* = 12.3 Hz, 1H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.68 (ddd, *J* = 3.5, 8.7, 11.0 Hz, 1H), 4.72 (d, *J* = 12.3 Hz, 1H), 4.94 (d, *J* = 11.6 Hz, 1H), 5.17 (d, *J* = 8.7 Hz, 1H), 5.54 (dd, *J* = 3.5, 8.0 Hz, 1H), 7.23−7.34 (m, 15H); ^{13}C NMR (126 MHz, $CDCl_3$; spectrum contains a mixture of rotamers, only the major rotamer signals are reported) δ 16.7 (d, J_{C-P} = 4.9 Hz), 16.9 (d, J_{C-P} = 4.9 Hz), 23.3, 49.1 (d, J_{C-P} = 3.7 Hz), 58.3 (d, J_{C-P} = 11.7 Hz), 58.4 (d, J_{C-P} = 11.7 Hz), 68.6, 70.6, 71.1, 72.3, 73.4, 74.5, 76.3, 93.0 (d, J_{C-P} = 15.5 Hz), 127.5, 127.7, 127.81, 127.84, 127.9, 128.0, 128.2, 128.3, 128.4, 137.8, 138.0, 138.4, 169.7; ^{31}P NMR (109 MHz, $CDCl_3$) δ 142.1; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{33}H_{42}NO_8PNa$ 634.2546; found 634.2547. Anal. Calcd for $C_{33}H_{42}NO_8P$: C, 64.80; H, 6.92; N, 2.29. Found: C, 64.60; H, 6.72; N, 2.35.

2-Acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-galactopyranosyl Diethyl Phosphite (11b). The reaction was performed according to the typical procedure with hemiacetal **10b** (218.5 mg, 0.547 mmol), Et_3N (0.23 mL, 1.64 mmol), diethyl chlorophosphite (95 μL, 0.656 mmol), and CH_2Cl_2 (5 mL). Purification by column chromatography (Wako gel 9 g, 4:1:1 CH_2Cl_2/AcOEt/*n*-hexane with 2% Et_3N) afforded the corresponding diethyl phosphite (243.8 mg) as a white solid, which was recrystallized from 4:1 *n*-hexane/acetone (5 mL) to give α-linked diethyl phosphite **11b** (216 mg, 76%) as colorless needles. R_f 0.31 (10:1 CH_2Cl_2/acetone); mp 147.5−148.0 °C; $[\alpha]_D^{23}$ +157.0 (*c* 1.00, $CHCl_3$); IR (KBr) 3318, 1653, 1546, 1368, 1100, 1029 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$; spectrum contains a 10:1 mixture of rotamers, * denotes minor rotamer signals) δ 1.24 (t, *J* = 7.5 Hz, 3H), 1.25 (t, *J* = 7.0 Hz, 3H), *1.26 (t, *J* = 7.0 Hz, 3H), *1.28 (t, *J* = 7.0 Hz, 3H), 1.91 (s, 3H),

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*2.09 (s, 3H), *3.70 (dd, J = 3.4, 10.9 Hz, 1H), 3.76 (dd, J = 3.4, 10.9 Hz, 1H), 3.78−3.94 (m, 5H), 4.05 (dd, J = 2.0, 12.5 Hz, 1H), *4.10 (m, 1H), 4.23 (dd, J = 1.5, 12.5 Hz, 1H), *4.27 (br d, J = 3.4 Hz, 1H), 4.32 (br d, J = 3.4 Hz, 1H), 4.57 (d, J = 12.5 Hz, 1H), *4.62 (d, J = 12.5 Hz, 1H), 4.70 (ddd, J = 3.4, 8.6, 10.9 Hz, 1H), *4.72 (d, J = 12.5 Hz, 1H), 4.75 (d, J = 12.5 Hz, 1H), 5.27 (d, J = 8.6 Hz, 1H), *5.45 (d, J = 8.6 Hz, 1H), 5.52 (s, 1H), *5.54 (s, 1H), *5.63 (dd, J = 3.4, 8.0 Hz, 1H), 5.75 (dd, J = 3.4, 8.0 Hz, 1H), 7.28−7.39 (m, 8H), 7.53 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$; spectrum contains a mixture of rotamers, * denotes minor rotamer signals) δ 16.7 (d, J_{C-P} = 6.0 Hz), 16.8 (d, J_{C-P} = 6.0 Hz), *20.9, 23.2, 48.4 (d, J_{C-P} = 3.6 Hz), *52.5 (d, J_{C-P} = 4.8 Hz), 58.3 (d, J_{C-P} = 3.6 Hz), 58.4 (d, J_{C-P} = 2.4 Hz), *58.6 (d, J_{C-P} = 12.0 Hz), *58.9 (d, J_{C-P} = 12.0 Hz), 63.7, *63.8, 69.2, 70.4, *71.1, *71.4, *72.2, 72.7, 73.3, *75.0, 93.2 (d, J_{C-P} = 14.4 Hz), *93.4 (d, J_{C-P} = 13.2 Hz), *100.5, 100.8, *125.9, 126.2, *127.5, *127.7, 127.76, 127.78, 127.98, *128.01, 128.3, 128.8, 137.5, *137.6, 138.1, 169.7, *173.4; ^{31}P NMR (202.5 MHz, $CDCl_3$; spectrum contains a mixture of rotamers, * denotes minor rotamer signals) δ *142.3, 142.8; HRMS (FAB) m/z $[M + H]^+$ calcd for $C_{26}H_{35}NO_8P$ 520.2100; found 520.2094. Anal. Calcd for $C_{26}H_{34}NO_8P$: C, 60.11; H, 6.60; N, 2.70. Found: C, 60.16; H, 6.62; N, 2.69.

2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl Diethyl Phosphite (11c). The reaction was performed according to the typical procedure with hemiacetal **10c** (500 mg, 1.44 mmol), Et_3N (0.60 mL, 4.32 mmol), diethyl chlorophosphite (0.27 mL, 1.87 mmol), and CH_2Cl_2 (10 mL). The crude product (725 mg, slightly yellow amorphous) was purified by column chromatography (Wako gel 12 g, 2:1 AcOEt/*n*-hexane with 3% Et_3N) to give diethyl phosphite **11c** (588 mg, 87%) as a colorless amorphous. R_f 0.34 (2:1 AcOEt/*n*-hexane, with Et_3N-doped silica gel plate); $[\alpha]_D^{19}$ +99.5 (*c* 1.00, $CHCl_3$); IR (Nujol) 3348, 1746, 1723, 1671, 1539, 1277, 1244, 1167, 1125, 1024, 912, 842 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.29 (t, J = 7.0 Hz, 3H), 1.30 (t, J = 7.0 Hz, 3H), 1.96 (s, 3H), 2.01 (s, 3H), 2.04 (s, 3H), 2.17 (s, 3H), 3.90−3.99 (m, 4H), 4.06 (dd, J = 6.8, 11.3 Hz, 1H), 4.13 (dd, J = 6.2, 11.3 Hz, 1H), 4.35 (dd, J = 6.2, 6.8 Hz, 1H), 4.62 (ddd, J = 3.5, 9.6, 11.3 Hz, 1H), 5.20 (dd, J = 3.2, 11.3 Hz, 1H), 5.41 (br d, J = 3.2 Hz, 1H), 5.58 (dd, J = 3.5, 8.0 Hz, 1H), 5.61 (d, J = 9.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.7 (d, J_{C-P} = 5.3 Hz), 16.8 (d, J_{C-P} = 5.4 Hz), 20.5, 20.57, 20.62, 23.1, 48.0 (d, J_{C-P} = 3.9 Hz), 58.6 (d, J_{C-P} = 11.2 Hz), 58.7 (d, J_{C-P} = 12.4 Hz), 61.7, 67.1, 67.6, 68.0, 92.4 (d, J_{C-P} = 13.2 Hz), 170.0, 170.16, 170.22, 170.8; ^{31}P NMR (109 MHz, $CDCl_3$) δ 141.2: HRMS (FAB) m/z $[M + H]^+$ calcd for $C_{18}H_{31}NO_{11}P$ 468.1635; found 468.1649. Anal. Calcd for $C_{18}H_{30}NO_{11}P$: C, 46.25; H, 6.47; N, 3.00. Found: C, 46.09; H, 6.39; N, 3.01.

2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl *N,N,N′,N′*-Tetramethylphosphorodiamidate (12). *n*-BuLi in *n*-hexane (1.56 M, 0.82 mL, 1.28 mmol) was added to a cooled (−78 °C) suspension of hemiacetal **8a** (600 mg, 1.22 mmol) in 12:1 THF/HMPA (19.5 mL). After 15 min of stirring, bis(dimethylamino)-phosphoryl chloride (0.18 mL, 1.16 mmol) was added, and the reaction mixture was allowed to warm to −23 °C over 30 min. After 1.5 h of stirring at this temperature, the reaction was quenched with crushed ice, followed by stirring at 0 °C for 15 min. The mixture was partitioned between AcOEt (50 mL) and saturated aqueous $NaHCO_3$ (15 mL), and the organic layer was washed with brine (2 × 15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (950 mg), which was purified by flash column chromatography (silica gel 30 g, 3:2 → 1:3 CH_2Cl_2/acetone) to give phosphorodiamidate **12** (633 mg, 83%) as a colorless amorphous. R_f 0.37 (2:3 CH_2Cl_2/acetone); $[\alpha]_D^{22}$ +54.0 (*c* 1.00, $CHCl_3$); IR (Nujol) 3304, 1678, 1547, 1226 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91 (s, 3H), 2.59 (s, 3H), 2.62 (s, 3H), 2.64 (s, 3H), 2.67 (s, 3H), 3.67 (dd, J = 1.8, 10.9 Hz, 1H), 3.72 (dd, J = 9.5, 10.6 Hz, 1H), 3.77 (dd, J = 3.6, 10.9 Hz, 1H), 3.83 (t, J = 9.5 Hz, 1H), 3.97 (ddd, J = 1.8, 3.6, 9.5 Hz, 1H), 4.35 (ddd, J = 2.9, 9.1, 10.6 Hz, 1H), 4.49 (d, J = 11.8 Hz, 1H), 4.53 (d, J = 10.9 Hz, 1H), 4.62 (d, J = 11.8 Hz, 1H), 4.69 (d, J = 11.3 Hz, 1H), 4.836 (d, J = 11.3 Hz, 1H), 4.842 (d, J = 10.9 Hz, 1H), 5.43 (dd, J = 2.9, 7.5 Hz, 1H), 6.32 (d, J = 9.1 Hz, 1H), 7.19 (m, 2H), 7.26−7.33 (m, 13H); ^{13}C NMR (100 MHz, C_6D_6) δ 23.3, 36.48, 36.51, 53.6 (d, J_{C-P} = 4.8 Hz), 69.4, 73.4, 73.9, 74.8, 75.2, 78.5, 80.2, 95.8 (d, J_{C-P} = 3.8 Hz), 127.76, 127.83, 128.1, 128.2, 128.4, 128.51, 128.55, 138.8, 139.0, 139.2, 170.0; ^{31}P NMR (109 MHz, $CDCl_3$) δ 18.5; HRMS (FAB) m/z $[M + H]^+$ calcd for $C_{33}H_{45}N_3O_7P$ 626.2995; found 626.2989.

Typical Procedure for Glycosylation with 2-Acetamido-2-deoxyglycopyranosyl Diethyl Phosphite: Methyl 6-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (14).[22c] A 1.0 M solution of Tf_2NH in EtCN (0.11 mL, 0.11 mmol) was added to a cooled (−78 °C) mixture of diethyl phosphite **9a** (61.2 mg, 0.10 mmol), 6-O-unprotected glucoside **13** (51.2 mg, 0.11 mmol) and pulverized 4 Å molecular sieves (61.2 mg) in CH_2Cl_2 (1.0 mL). After 1 h of stirring at this temperature, the reaction was quenched with Et_3N (0.15 mL). The mixture was diluted with AcOEt (5 mL) and passed through a Celite pad. The filtrate was partitioned between AcOEt (15 mL) and saturated aqueous $NaHCO_3$ (6 mL). The organic layer was washed with brine (6 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude products (138.5 mg), whose ratio was determined to be 4.1:1 by 500 MHz ^{1}H NMR spectroscopic analysis. For easy purification, a solution of the crude mixture in AcOEt (10 mL) and CH_2Cl_2 (2 mL) was vigorously stirred with 10% aqueous HCl (2 mL) for 10 min, during which time the oxazoline **15** was completely hydrolyzed to form the corresponding hemiacetal **8a**. The resulting mixture was extracted with AcOEt (6 mL), and the organic extract was successively washed with saturated aqueous $NaHCO_3$ (6 mL) and brine (6 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by flash column chromatography (silica gel 20 g, 7:1 toluene/acetone) afforded β-linked disaccharide **14** (68.0 mg, 73%) as a white solid. R_f 0.28 (5:1 toluene/acetone); mp 190.0−190.5 °C (lit.[22c] 209−211 °C); $[\alpha]_D^{24}$ +22.4 (*c* 1.00, $CHCl_3$) [lit.[22c] +23.6 (*c* 1.56, $CHCl_3$)]; IR (Nujol) 3279, 3029, 1655, 1564, 1155, 1092, 1067, 949, 912 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.70 (s, 3H), 3.34 (s, 3H), 3.44 (m, 1H), 3.50 (dd, J = 3.7, 9.3 Hz, 1H), 3.52 (t, J = 9.3 Hz, 1H), 3.59−3.61 (m, 2H), 3.66−3.77 (m, 4H), 3.97 (t, J = 9.3 Hz, 1H), 4.06−4.12 (m, 2H), 4.50 (d, J = 12.1 Hz, 1H), 4.55 (d, J = 11.6 Hz, 1H), 4.56 (d, J = 10.8 Hz, 1H), 4.57 (d, J = 10.8 Hz, 1H), 4.59 (d, J = 3.7 Hz, 1H), 4.62 (d, J = 11.6 Hz, 1H), 4.64 (d, J = 12.1 Hz, 1H), 4.76 (d, J = 11.6 Hz, 2H), 4.80 (d, J = 11.6 Hz, 1H), 4.81 (d, J = 11.0 Hz, 1H), 4.80−4.84 (m, 2H), 4.97 (d, J = 11.0 Hz, 1H), 5.44 (d, J = 7.7 Hz, 1H), 7.20 (m, 2H), 7.25−7.35 (m, 28H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.5, 55.0, 56.7, 67.3, 69.0, 69.5, 73.2, 74.4, 74.5, 74.6, 74.8, 75.6, 77.5, 78.6, 79.6, 80.1, 81.9, 97.9, 99.7, 127.35, 127.40, 127.5, 127.58, 127.61, 127.64, 127.67, 127.72, 127.8, 128.0, 128.05, 128.14, 128.2, 128.25, 128.27, 128.30, 137.8, 137.95, 138.03, 138.1, 138.2, 138.6, 169.9.

Methyl 6-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-galactopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (16). The glycosylation was performed according to the typical procedure employing diethyl phosphite **11a** (61.2 mg, 0.10 mmol), 6-O-unprotected glucoside **13** (92.9 mg, 0.20 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Linked disaccharide **16** (78.2 mg, 83%) was obtained as a white solid from the crude product (186.0 mg) after column chromatography (silica gel 18 g, 5:1 toluene/acetone). When the glycosylation was performed employing diethyl phosphite **11a** (122.3 mg, 0.20 mmol), 6-O-unprotected glucoside **13** (46.5 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.22 mL, 0.22 mmol), disaccharide **16** (81.4 mg, 87%) was obtained as a white solid from the crude product (234.0 mg) after column chromatography (silica gel 18 g, 5:1 toluene/acetone). R_f 0.50 (3:1 toluene/acetone); mp 198.5−199.5 °C (colorless needles from CH_2Cl_2/*n*-hexane); $[\alpha]_D^{24}$ +19.1 (*c* 1.00, $CHCl_3$); IR (Nujol) 3295, 3063, 3028, 1651, 1556, 1496, 1310, 1209, 1063, 910 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.78 (s, 3H), 3.33 (s, 3H), 3.49−3.67 (m, 6H), 3.70−3.73 (m, 2H), 3.95−3.98 (m, 2H), 4.04 (m, 1H), 4.33 (dd, J = 2.4, 10.9 Hz, 1H), 4.41 (d, J = 11.8 Hz, 1H), 4.45 (d, J = 11.8 Hz, 1H), 4.46 (d, J = 11.4 Hz, 1H), 4.54 (d, J = 11.2 Hz, 1H), 4.56 (d, J = 10.9 Hz, 1H), 4.59 (d, J = 3.3 Hz, 1H), 4.64 (d, J = 12.2 Hz, 1H), 4.65 (d, J = 11.2 Hz, 1H), 4.76 (d, J = 12.2 Hz, 1H), 4.81 (d, J = 10.9 Hz, 2H),

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4.86 (d, J = 11.4 Hz, 1H), 4.96 (d, J = 10.9 Hz, 1H), 4.99 (d, J = 8.4 Hz, 1H), 5.52 (d, J = 7.2 Hz, 1H), 7.24−7.34 (m, 30H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.8, 54.9, 55.1, 67.1, 68.5, 69.6, 72.3, 72.7, 73.27, 73.34, 73.4, 74.6, 74.8, 75.8, 77.6, 79.6, 82.0, 97.9, 99.8, 127.4, 127.5, 127.6, 127.7, 127.8, 127.90, 127.94, 128.0, 128.1, 128.29, 128.33, 128.4, 137.8, 137.9, 138.0, 138.1, 138.5, 138.7, 170.5; HRMS (FAB) m/z [M + H]$^+$ calcd for $C_{57}H_{64}NO_{11}$ 938.4479; found 938.4485. Anal. Calcd for $C_{57}H_{63}NO_{11}$: C, 72.98; H, 6.77; N, 1.49. Found: C, 73.03; H, 6.88; N, 1.77.

Methyl 6-*O*-(2-Acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-*β*-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside (17). The glycosylation was performed according to the typical procedure employing diethyl phosphite **9b** (52.0 mg, 0.10 mmol), 6-O-unprotected glucoside **13** (92.9 mg, 0.20 mmol), pulverized 4 Å molecular sieves (100 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Linked disaccharide **17** (41.2 mg, 49%) was obtained as a white solid from the crude product (170.8 mg) after column chromatography (silica gel 12 g, 12:1 → 8:1 CH_2Cl_2/AcOEt). When the glycosylation was performed employing diethyl phosphite **9b** (103.9 mg, 0.20 mmol), 6-O-unprotected glucoside **13** (46.5 mg, 0.10 mmol), pulverized 4 Å molecular sieves (100 mg), and Tf_2NH (1.0 M in EtCN, 0.22 mL, 0.22 mmol), disaccharide **17** (30.2 mg, 36%) was obtained as a white solid from the crude product (175.2 mg) after column chromatography (silica gel 12 g, 12:1 → 8:1 CH_2Cl_2/AcOEt). R_f 0.23 (8:1 CH_2Cl_2/AcOEt); mp 248−254 °C (decomp) (colorless needles from CH_2Cl_2/n-hexane); $[\alpha]_D^{20}$ +13.8 (c 1.00, $CHCl_3$); IR (KBr) 3299, 1656, 1559, 1370, 1114, 1062, 737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.68 (s, 3H), 3.27 (ddd, J = 7.4, 8.6, 9.2 Hz, 1H), 3.35 (s, 3H), 3.51 (dd, J = 2.9, 9.7 Hz, 1H), 3.52 (m, 1H), 3.55 (t, J = 9.7 Hz, 1H), 3.67 (t, J = 9.2 Hz, 1H), 3.71−3.76 (m, 2H), 3.77 (t, J = 9.7 Hz, 1H), 3.98 (t, J = 9.7 Hz, 1H), 4.06 (br d, J = 8.6 Hz, 1H), 4.30 (t, J = 9.2 Hz, 1H), 4.31 (dd, J = 4.6, 10.3 Hz, 1H), 4.52 (d, J = 10.3 Hz, 1H), 4.60 (d, J = 2.9 Hz, 1H), 4.61 (d, J = 12.0 Hz, 1H), 4.65 (d, J = 12.0 Hz, 1H), 4.79 (d, J = 12.0 Hz, 1H), 4.81 (d, J = 10.9 Hz, 1H), 4.83 (d, J = 10.3 Hz, 1H), 4.87 (d, J = 12.0 Hz, 1H), 4.98 (d, J = 10.9 Hz, 1H), 5.05 (d, J = 8.6 Hz, 1H), 5.45 (br d, J = 7.4 Hz, 1H), 5.55 (s, 1H), 7.26−7.40 (m, 23H), 7.49 (m, 2H); ^{13}C NMR (126 MHz, 5:1 $CDCl_3$/CD_3OD) δ 22.5, 54.7, 56.3, 65.7, 67.5, 68.4, 69.3, 73.0, 73.9, 74.5, 75.4, 79.5, 81.6, 81.9, 97.7, 100.5, 101.0, 125.7, 127.3, 127.4, 127.5, 127.6, 127.7, 127.8, 127.89, 127.93, 128.0, 128.1, 128.7, 137.0, 137.7, 137.8, 138.0, 138.3, 171.1; HRMS (FAB) m/z [M + H]$^+$ calcd for $C_{50}H_{56}NO_{11}$ 846.3854; found 846.3851. Anal. Calcd for: $C_{50}H_{55}NO_{11}$: C, 70.99; H, 6.55; N, 1.66. Found: C, 70.63; H, 6.55; N, 1.68.

Methyl 6-*O*-(2-Acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-*β*-D-galactopyranosyl)-2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside (18). The glycosylation was performed according to the typical procedure employing diethyl phosphite **11b** (52.0 mg, 0.10 mmol), 6-O-unprotected glucoside **13** (92.9 mg, 0.20 mmol), 4 Å molecular sieves (100 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Linked disaccharide **18** (62.3 mg, 74%) was obtained as a white solid from the crude product (178 mg) after column chromatography (silica gel 12 g, 20:1 → 15:1 CH_2Cl_2/acetone). When the glycosylation was performed employing diethyl phosphite **11b** (103.9 mg, 0.20 mmol), 6-O-unprotected glucoside **13** (46.5 mg, 0.10 mmol), pulverized 4 Å molecular sieves (100 mg), and Tf_2NH (1.0 M in EtCN, 0.22 mL, 0.22 mmol), disaccharide **18** (66.2 mg, 78%) was obtained as a white solid from the crude product (187 mg) after column chromatography (silica gel 12 g, 20:1 → 15:1 CH_2Cl_2/acetone). R_f 0.26 (15:1 CH_2Cl_2/acetone); mp 279−280 °C (decomp) (colorless needles from CH_2Cl_2/n-hexane); $[\alpha]_D^{20}$ +43.3 (c 0.20, $CHCl_3$); IR (KBr) 3299, 1656, 1559, 1370, 1112, 1063, 737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.84 (s, 3H), 3.36 (s, 3H), 3.41 (br s, 1H), 3.52 (dd, J = 3.4, 9.5 Hz, 1H), 3.53 (t, J = 9.5 Hz, 1H), 3.55 (ddd, J = 6.9, 8.6, 10.9 Hz, 1H), 3.74 (dd, J = 4.3, 10.6 Hz, 1H), 3.77 (ddd, J = 2.0, 4.3, 9.5 Hz, 1H), 3.98 (t, J = 9.5 Hz, 1H), 3.99 (dd, J = 2.0, 12.3 Hz, 1H), 4.11 (d, J = 3.4 Hz, 1H), 4.12 (dd, J = 2.0, 10.6 Hz, 1H), 4.27 (dd, J = 1.4, 12.3 Hz, 1H), 4.52 (dd, J = 3.4, 10.9 Hz, 1H), 4.57 (d, J = 10.3 Hz, 1H), 4.60 (d, J = 12.6 Hz, 1H), 4.62 (d, J = 3.4 Hz, 1H), 4.64 (d, J = 12.6 Hz, 1H), 4.65 (d, J = 12.0 Hz, 1H), 4.77 (d, J = 12.0 Hz, 1H), 4.83 (d, J = 10.9 Hz, 1H), 4.84 (d, J = 10.3 Hz, 1H), 4.98 (d, J = 10.9 Hz, 1H), 5.15 (d, J = 8.6 Hz, 1H), 5.46 (s, 1H), 5.64 (br d, J = 6.9 Hz, 1H), 7.26−7.36 (m, 23H), 7.50 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.2, 54.1, 55.0, 66.4, 67.5, 69.2, 69.7, 71.4, 73.0, 73.1, 74.65, 74.68, 75.6, 77.8, 79.8, 81.8, 97.9, 99.6, 100.8, 126.2, 127.4, 127.6, 127.7, 127.75, 127.79, 127.9, 128.0, 128.22, 128.24, 128.3, 128.7, 137.8, 138.0, 138.12, 138.15, 138.6, 171.4; HRMS (FAB) m/z [M + H]$^+$ calcd for $C_{50}H_{56}NO_{11}$ 846.3854; found 846.3856. Anal. Calcd for $C_{50}H_{55}NO_{11}$: C, 70.99; H, 6.55; N, 1.66. Found: C, 70.87; H, 6.57; N, 1.69.

Methyl 6-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-*α*-D-glucopyranoside (19).[67] The glycosylation was performed according to the typical procedure employing diethyl phosphite **9c** (46.7 mg, 0.10 mmol), 6-O-unprotected glucoside **13** (92.9 mg, 0.20 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Linked disaccharide **19** (54.6 mg, 70%) was obtained as a white solid from the crude product (187.5 mg) after column chromatography (silica gel 12 g, 1:2 → 1:3 n-hexane/AcOEt). When the glycosylation was performed employing diethyl phosphite **9c** (93.5 mg, 0.20 mmol), 6-O-unprotected glucoside **13** (46.5 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.22 mL, 0.22 mmol), disaccharide **19** (57.2 mg, 72%) was obtained as a white solid from the crude product (198.5 mg) after column chromatography (silica gel 12 g, 1:2 → 1:3 n-hexane/AcOEt). R_f 0.36 (1:3 n-hexane/AcOEt); mp 186.5−187.5 °C (lit.[67] 187−188 °C); $[\alpha]_D^{21}$ +10.0 (c 1.00, $CHCl_3$); IR (Nujol) 3277, 1746, 1655, 1557, 1232, 1161, 1136, 1044, 910 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.82 (s, 3H), 2.02 (s, 3H), 2.03 (s, 6H), 3.37 (s, 3H), 3.44 (t, J = 9.4 Hz, 1H), 3.50 (dd, J = 3.4, 9.4 Hz, 1H), 3.63 (ddd, J = 2.4, 4.7, 9.8 Hz, 1H), 3.70 (dd, J = 3.8, 10.6 Hz, 1H), 3.75 (m, 1H), 3.82 (dt, J = 10.2, 8.6 Hz, 1H), 3.98 (t, J = 9.4 Hz, 1H), 4.04 (dd, J = 1.8, 10.6 Hz, 1H), 4.09 (dd, J = 2.4, 12.3 Hz, 1H), 4.22 (dd, J = 4.7, 12.3 Hz, 1H), 4.51 (br d, J = 8.6 Hz, 1H), 4.58 (d, J = 11.1 Hz, 1H), 4.63 (d, J = 3.4 Hz, 1H), 4.66 (d, J = 12.1 Hz, 1H), 4.77 (d, J = 12.1 Hz, 1H), 4.79 (d, J = 10.9 Hz, 1H), 4.84 (d, J = 11.1 Hz, 1H), 4.99 (d, J = 10.9 Hz, 1H), 5.04 (t, J = 9.8 Hz, 1H), 5.21 (dd, J = 9.8, 10.2 Hz, 1H), 5.36 (d, J = 8.6 Hz, 1H), 7.27−7.37 (m, 15H).

Methyl 9-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-*β*-D-glucopyranosyl)oxynonanoate (29). The glycosylation was performed according to the typical procedure employing diethyl phosphite **9a** (61.2 mg, 0.10 mmol), hydroxy ester **20** (28.2 mg, 0.15 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Glucoside **29** (52.7 mg, 80%) was obtained as a white solid from the crude product (95.0 mg) after column chromatography (silica gel 9 g, 7:1 toluene/acetone). When the glycosylation was performed employing diethyl phosphite **9a** (91.8 mg, 0.15 mmol), hydroxy ester **20** (18.8 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.17 mL, 0.17 mmol), β-glucoside **29** (54.8 mg, 83%) was obtained as a white solid from the crude product (160.2 mg) after column chromatography (silica gel 12 g, 7:1 toluene/acetone). R_f 0.28 (5:1 toluene/acetone); mp 119.0−120.0 °C (colorless needles from CH_2Cl_2/n-hexane); $[\alpha]_D^{23}$ +11.8 (c 1.00, $CHCl_3$); IR (Nujol) 3263, 3107, 3032, 1739, 1653, 1570, 1194, 1116, 1060 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23−1.35 (m, 8H), 1.50−1.63 (m, 4H), 1.85 (s, 3H), 2.29 (t, J = 7.5 Hz, 2H), 3.38 (dt, J = 9.4, 7.9 Hz, 1H), 3.44 (dt, J = 9.5, 6.9 Hz, 1H), 3.58 (ddd, J = 2.0, 4.3, 9.2 Hz, 1H), 3.61 (dd, J = 8.2, 9.2 Hz, 1H), 3.65 (s, 3H), 3.70 (dd, J = 4.3, 10.8 Hz, 1H), 3.76 (dd, J = 2.0, 10.8 Hz, 1H), 3.84 (dt, J = 9.5, 6.4 Hz, 1H), 4.12 (dd, J = 8.2, 9.4 Hz, 1H), 4.54 (d, J = 12.2 Hz, 1H), 4.58 (d, J = 11.0 Hz, 1H), 4.61 (d, J = 12.2 Hz, 1H), 4.66 (d, J = 11.6 Hz, 1H), 4.78 (d, J = 11.0 Hz, 1H), 4.806 (d, J = 7.9 Hz, 1H), 4.811 (d, J = 11.6 Hz, 1H), 5.67 (d, J = 7.9 Hz, 1H), 7.19 (m, 2H), 7.20−7.32 (m, 13H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.4, 24.7, 25.7, 28.9, 28.98, 29.04, 29.4, 34.0, 51.4, 56.9, 68.9, 69.4, 73.3, 74.47, 74.49, 74.7, 78.6, 80.4, 99.8, 127.5, 127.6, 127.7, 127.8, 127.9, 128.2, 128.30, 128.33, 138.0, 138.1, 138.4, 170.2, 174.3; HRMS (FAB) m/z [M + H]$^+$ calcd for $C_{39}H_{52}NO_8$ 662.3693; found 662.3705. Anal. Calcd for $C_{39}H_{51}NO_8$: C, 70.78; H, 7.77; N, 2.12. Found: C, 70.72; H, 7.93; N, 2.12.

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6-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (30).[25f,68] The glycosylation was performed according to the typical procedure employing diethyl phosphite **9a** (61.2 mg, 0.10 mmol), alcohol **21** (52.0 mg, 0.20 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Linked disaccharide **30** (65.6 mg, 89%) was obtained as a white amorphous solid from the crude product (145.3 mg) after column chromatography (silica gel 12 g, 7:1 → 5:1 toluene/acetone). When the glycosylation was performed employing diethyl phosphite **9a** (122.3 mg, 0.20 mmol), alcohol **21** (26.0 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.22 mL, 0.22 mmol), disaccharide **30** (67.5 mg, 92%) was obtained as a white solid from the crude product (172.3 mg) after column chromatography (silica gel 17 g, 7:1 → 6:1 toluene/acetone). R_f 0.36 (3:1 toluene/acetone); $[\alpha]_D^{25}$ −32.2 (*c* 1.42, $CHCl_3$) [lit. $[\alpha]_D^{25}$ −29 (*c* 0.5, $CHCl_3$),[25f] $[\alpha]_D$ −35 (*c* 1.00, $CHCl_3$)[68]]; IR (Nujol) 3297, 1728, 1657, 1552, 1496, 1310, 1226, 1211, 920, 899 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.30 (s, 3H), 1.31 (s, 3H), 1.42 (s, 3H), 1.51 (s, 3H), 1.88 (s, 3H), 3.54 (ddd, *J* = 2.9, 3.5, 9.3 Hz, 1H), 3.62−3.77 (m, 5H), 3.92−3.96 (m, 2H), 4.00 (dd, *J* = 3.8, 9.3 Hz, 1H), 4.16 (dd, *J* = 1.6, 8.0 Hz, 1H), 4.28 (dd, *J* = 2.4, 5.0 Hz, 1H), 4.54 (d, *J* = 12.1 Hz, 1H), 4.56 (dd, *J* = 2.4, 8.0 Hz, 1H), 4.57 (d, *J* = 11.1 Hz, 1H), 4.62 (d, *J* = 12.1 Hz, 1H), 4.68 (d, *J* = 11.1 Hz, 1H), 4.70 (d, *J* = 7.7 Hz, 1H), 4.78 (d, *J* = 10.7 Hz, 1H), 4.80 (d, *J* = 10.7 Hz, 1H), 5.50 (d, *J* = 5.0 Hz, 1H), 5.55 (d, *J* = 8.2 Hz, 1H), 7.18−7.20 (m, 2H), 7.25−7.34 (m, 13H).

Benzyl 4-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-2,3-anhydro-β-D-ribopyranoside (31). The glycosylation was performed according to the typical procedure employing diethyl phosphite **9a** (61.2 mg, 0.10 mmol), epoxy alcohol **22** (44.4 mg, 0.20 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Glucoside **31** (54.8 mg, 79%) was obtained as a white solid from the crude product (137.3 mg) after column chromatography (silica gel 18 g, 5:1 → 4:1 toluene/acetone). When the glycosylation was performed employing diethyl phosphite **9a** (122.3 mg, 0.20 mmol), epoxy alcohol **22** (22.2 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.22 mL, 0.22 mmol), β-glucoside **31** (54.3 mg, 78%) was obtained as a white solid from the crude product (198.2 mg) after column chromatography (silica gel 18 g, 5:1 → 4:1 toluene/acetone). R_f 0.29 (5:1 toluene/acetone); mp 218.5−219.5 °C (colorless needles from CH_2Cl_2/*n*-hexane); $[\alpha]_D^{25}$ +18.5 (*c* 1.00, $CHCl_3$); IR (Nujol) 3269, 3090, 3063, 3030, 1651, 1564, 1497, 1316, 1116, 1069, 1022, 984, 872 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.86 (s, 3H), 3.18 (d, *J* = 3.8 Hz, 1H), 3.31 (ddd, *J* = 7.4, 8.2, 9.6 Hz, 1H), 3.47 (dd, *J* = 3.2, 12.6 Hz, 1H), 3.52 (dd, *J* = 3.8, 4.1 Hz, 1H), 3.56−3.62 (m, 2H), 3.69 (dd, *J* = 3.5, 10.8 Hz, 1H), 3.72 (br d, *J* = 10.8 Hz, 1H), 3.81 (dd, *J* = 4.6, 12.6 Hz, 1H), 4.07 (ddd, *J* = 3.2, 4.1, 4.6 Hz, 1H), 4.27 (dd, *J* = 8.2, 9.6 Hz, 1H), 4.53 (d, *J* = 11.9 Hz, 2H), 4.58 (d, *J* = 10.9 Hz, 1H), 4.59 (d, *J* = 11.9 Hz, 1H), 4.67 (d, *J* = 11.5 Hz, 1H), 4.77 (d, *J* = 11.5 Hz, 1H), 4.80 (d, *J* = 10.9 Hz, 1H), 4.83 (d, *J* = 11.9 Hz, 1H), 4.98 (s, 1H), 5.17 (d, *J* = 8.2 Hz, 1H), 5.93 (d, *J* = 7.4 Hz, 1H), 7.20 (m, 2H), 7.25−7.36 (m, 18H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.5, 51.5, 52.1, 57.7, 59.6, 69.0, 69.3, 70.3, 73.3, 74.7, 74.9, 78.8, 80.4, 94.9, 98.9, 127.6, 127.65, 127.69, 127.74, 127.8, 128.05, 128.12, 128.3, 128.39, 128.43, 128.5, 137.0, 138.1, 138.2, 138.5, 170.9; HRMS (FAB) *m*/*z* $[M + H]^+$ calcd for $C_{41}H_{46}NO_9$ 696.3173; found 696.3168. Anal. Calcd for $C_{41}H_{45}NO_9$: C, 70.77; H, 6.52; N, 2.01. Found: C, 70.82; H, 6.53; N, 2.17.

Methyl 3-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-2,4,6-tri-*O*-benzyl-α-D-galactopyranoside (32). The glycosylation was performed according to the typical procedure employing diethyl phosphite **9a** (61.2 mg, 0.10 mmol), 3-O-unprotected galactoside **23** (92.9 mg, 0.20 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Linked disaccharide **32** (60.9 mg, 65%) was obtained as a white solid from the crude product (190.2 mg) after column chromatography (silica gel 18 g, 7:1 toluene/acetone). When the glycosylation was performed employing diethyl phosphite **9a** (122.3 mg, 0.20 mmol), 3-O-unprotected galactoside **23** (46.5 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.22 mL, 0.22 mmol), disaccharide **32** (59.6 mg, 64%) was obtained as a white solid from the crude product (220.0 mg) after column chromatography (silica gel 18 g, 7:1 toluene/acetone). R_f 0.28 (5:1 toluene/acetone); mp 127.0−127.5 °C (colorless needles from CH_2Cl_2/*n*-hexane); $[\alpha]_D^{24}$ +9.0 (*c* 1.00, $CHCl_3$); IR (Nujol) 3306, 3088, 3063, 3030, 1952, 1875, 1811, 1657, 1556, 1496, 1205, 1111 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.63 (s, 3H), 3.33 (s, 3H), 3.42 (dd, *J* = 6.0, 9.7 Hz, 1H), 3.50 (dd, *J* = 6.3, 9.7 Hz, 1H), 3.52 (m, 1H), 3.65 (t, *J* = 9.2 Hz, 1H), 3.71−3.75 (m, 3H), 3.89 (dd, *J* = 6.0, 6.3 Hz, 1H), 3.92 (m, 1H), 3.94 (dd, *J* = 3.6, 10.1 Hz, 1H), 4.02 (d, *J* = 2.8 Hz, 1H), 4.08 (dd, *J* = 2.8, 10.1 Hz, 1H), 4.35 (d, *J* = 11.9 Hz, 1H), 4.44 (d, *J* = 11.9 Hz, 1H), 4.48 (d, *J* = 12.2 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 4.56 (d, *J* = 11.8 Hz, 1H), 4.601 (d, *J* = 12.2 Hz, 1H), 4.603 (d, *J* = 10.2 Hz, 1H), 4.61 (d, *J* = 3.6 Hz, 1H), 4.64 (d, *J* = 12.2 Hz, 2H), 4.77 (d, *J* = 8.0 Hz, 1H), 4.785 (d, *J* = 10.2 Hz, 1H), 4.788 (d, *J* = 11.8 Hz, 1H), 4.96 (d, *J* = 11.6 Hz, 1H), 5.01 (d, *J* = 8.9 Hz, 1H), 7.20−7.33 (m, 30H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.4, 55.2, 55.8, 60.3, 68.4, 68.9, 69.31, 69.34, 72.9, 73.3, 74.4, 74.5, 74.8, 76.4, 78.1, 78.2, 78.3, 82.1, 98.2, 102.3, 127.3, 127.4, 127.45, 127.54, 127.6, 127.7, 127.8, 127.9, 128.0, 128.2, 128.30, 128.32, 128.5, 137.8, 137.9, 138.0, 138.2, 138.3, 138.7, 169.7; HRMS (FAB) *m*/*z* $[M + H]^+$ calcd for $C_{57}H_{64}NO_{11}$ 938.4479; found 938.4474. Anal. Calcd for $C_{57}H_{63}NO_{11}$: C, 72.98; H, 6.77; N, 1.49. Found: C, 73.07; H, 6.77; N, 1.57.

Benzyl 4-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-2,3-*O*-cyclohexylidene-α-L-rhamnopyranoside (33).[22c] The glycosylation was performed according to the typical procedure employing diethyl phosphite **9a** (61.2 mg, 0.10 mmol), 4-O-unprotected rhamnoside **24** (66.9 mg, 0.20 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Linked disaccharide **33** (45.8 mg, 57%) was obtained as a white solid from the crude product (168.9 mg) after column chromatography (silica gel 18 g, 12:1 → 10:1 toluene/acetone). When the glycosylation was performed employing diethyl phosphite **9a** (122.3 mg, 0.20 mmol), 4-O-unprotected rhamnoside **24** (33.4 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.22 mL, 0.22 mmol), disaccharide **33** (35.6 mg, 44%) was obtained as a white solid from the crude product (213.3 mg) after column chromatography (silica gel 18 g, 12:1 → 10:1 toluene/acetone). R_f 0.45 (5:1 toluene/acetone); mp 155.0−155.5 °C (lit.[22c] 153−154 °C) (colorless needles from AcOEt/*n*-hexane); $[\alpha]_D^{24}$ −20.5 (*c* 1.00, $CHCl_3$) [lit.[22c] $[\alpha]_D^{25}$ −13.8 (*c* 0.55, $CHCl_3$)]; IR (Nujol) 3341, 3266, 3067, 3032, 1651, 1551, 1456, 1130, 1098, 1067, 1019, 936 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.32 (d, *J* = 6.2 Hz, 3H), 1.35−1.42 (m, 2H), 1.43−1.74 (m, 8H), 1.88 (s, 3H), 3.44 (ddd, *J* = 2.2, 4.0, 9.5 Hz, 1H), 3.46 (dd, *J* = 7.4, 9.9 Hz, 1H), 3.64 (dd, *J* = 9.0, 9.7 Hz, 1H), 3.68−3.74 (m, 3H), 3.74 (dd, *J* = 4.3, 11.2 Hz, 1H), 3.86 (ddd, *J* = 8.1, 8.8, 9.0 Hz, 1H), 4.08 (dd, *J* = 5.5, 7.4 Hz, 1H), 4.11 (d, *J* = 5.5 Hz, 1H), 4.48 (d, *J* = 11.5 Hz, 1H), 4.57 (d, *J* = 12.2 Hz, 1H), 4.62 (d, *J* = 10.8 Hz, 1H), 4.63 (d, *J* = 12.2 Hz, 1H), 4.69 (d, *J* = 11.5 Hz, 2H), 4.71 (d, *J* = 8.1 Hz, 1H), 4.82 (d, *J* = 10.8 Hz, 1H), 4.84 (d, *J* = 11.5 Hz, 1H), 5.06 (s, 1H), 5.52 (d, *J* = 8.8 Hz, 1H), 7.24−7.35 (m, 20H).

1-Neryl 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-galactopyranoside (36). The glycosylation was performed according to the typical procedure employing diethyl phosphite **11a** (61.2 mg, 0.10 mmol), nerol (**27**, 17.0 mg, 0.11 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Glycoside **36** (51.0 mg, 81%) was obtained as a white solid from the crude product (104.7 mg) after column chromatography (silica gel 12 g, 10:1 toluene/acetone). When the glycosylation was performed employing diethyl phosphite **11a** (67.3 mg, 0.11 mmol), nerol (15.4 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.12 mL, 0.12 mmol), β-glycoside **36** (49.6 mg, 79%) was obtained as a white solid from the crude product (124.7 mg) after column chromatography (silica gel 12 g, 10:1 toluene/acetone). R_f 0.33 (5:1 toluene/acetone); mp 148.0−148.5 °C (colorless needles from CH_2Cl_2/*n*-hexane); $[\alpha]_D^{25}$ +9.6 (*c* 1.00, $CHCl_3$); IR (Nujol) 3301, 1653, 1552, 1496, 1167, 1111, 1067, 905

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cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.57 (s, 3H), 1.65 (s, 3H), 1.72 (s, 3H), 1.90 (s, 3H), 1.99−2.06 (m, 4H), 3.44 (ddd, J = 7.0, 8.3, 10.7 Hz, 1H), 3.59 (dd, J = 5.6, 8.8 Hz, 1H), 3.63 (dd, J = 7.1, 8.8 Hz, 1H), 3.67 (dd, J = 5.6, 7.1 Hz, 1H), 3.96 (d, J = 2.4 Hz, 1H), 4.09 (dd, J = 7.6, 11.7 Hz, 1H), 4.27 (dd, J = 6.5, 11.7 Hz, 1H), 4.42 (dd, J = 2.4, 10.7 Hz, 1H), 4.43 (d, J = 12.2 Hz, 1H), 4.478 (d, J = 12.2 Hz, 1H), 4.482 (d, J = 11.4 Hz, 1H), 4.59 (d, J = 11.6 Hz, 1H), 4.64 (d, J = 11.4 Hz, 1H), 4.87 (d, J = 11.6 Hz, 1H), 5.04 (d, J = 8.3 Hz, 1H), 5.05 (m, 1H), 5.30 (dd, J = 6.5, 7.6 Hz, 1H), 5.64 (d, J = 7.0 Hz, 1H), 7.24−7.36 (m, 15H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 17.6, 23.5, 23.7, 25.7, 26.7, 32.1, 55.6, 65.2, 68.6, 72.3, 72.7, 73.2, 73.4, 74.5, 77.5, 98.3, 120.9, 123.8, 127.5, 127.7, 127.80, 127.84, 128.0, 128.12, 128.13, 128.38, 128.44, 131.9, 137.9, 138.1, 138.6, 141.2, 170.7; HRMS (FAB) m/z [M + H]$^+$ calcd for $C_{39}H_{50}NO_6$ 628.3638; found 628.3649. Anal. Calcd for $C_{39}H_{49}NO_6$: C, 74.61; H, 7.87; N, 2.23. Found: C, 74.43; H, 7.72; N, 2.23.

_l_-Menthyl 2-Acetamido-3,4,6-tri-_O_-benzyl-2-deoxy-β-D-galactopyranoside (37). The glycosylation was performed according to the typical procedure employing diethyl phosphite **11a** (61.2 mg, 0.10 mmol), _l_-menthol (**28**, 23.4 mg, 0.15 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Galactoside **37** (46.5 mg, 74%) was obtained as a white solid from the crude product (108.1 mg) after column chromatography (silica gel 12 g, 12:1 toluene/acetone). When the glycosylation was performed employing diethyl phosphite **11a** (91.8 mg, 0.15 mmol), _l_-menthol (15.6 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.17 mL, 0.17 mmol), β-galactoside **37** (44.9 mg, 71%) was obtained as a white solid from the crude product (148.1 mg) after column chromatography (silica gel 14 g, 12:1 toluene/acetone). R_f 0.50 (5:1 toluene/acetone); mp 160.0−161.0 °C (colorless needles from AcOEt/_n_-hexane); $[\alpha]_D^{24}$ −32.8 (_c_ 1.00, $CHCl_3$); IR (Nujol) 3304, 1653, 1550, 1308, 1167, 1105, 1071 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.72 (d, J = 6.8 Hz, 3H), 0.77−0.82 (m, 2H), 0.85 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H), 0.95 (m, 1H), 1.16 (m, 1H), 1.30 (m, 1H), 1.58−1.64 (m, 2H), 1.88 (s, 3H), 1.93 (m, 1H), 2.30 (dquin, J = 2.2, 6.8 Hz, 1H), 3.31−3.39 (m, 2H), 3.54 (dd, J = 5.5, 8.9 Hz, 1H), 3.59 (dd, J = 7.0, 8.9 Hz, 1H), 3.63 (dd, J = 5.5, 7.0 Hz, 1H), 3.92 (d, J = 3.0 Hz, 1H), 4.41 (d, J = 11.8 Hz, 1H), 4.46 (d, J = 11.8 Hz, 1H), 4.48 (dd, J = 3.0, 10.7 Hz, 1H), 4.50 (d, J = 11.6 Hz, 1H), 4.59 (d, J = 11.6 Hz, 1H), 4.62 (d, J = 11.6 Hz, 1H), 4.87 (d, J = 11.6 Hz, 1H), 5.03 (d, J = 8.3 Hz, 1H), 5.66 (d, J = 6.9 Hz, 1H), 7.24−7.35 (m, 15H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 15.5, 21.2, 22.3, 22.9, 23.7, 24.8, 31.4, 34.4, 41.0, 47.7, 55.9, 69.1, 72.3, 73.1, 73.4, 74.4, 77.4, 78.7, 97.6, 127.4, 127.6, 127.70, 127.73, 128.0, 128.07, 128.09, 128.3, 128.4, 128.5, 137.9, 138.0, 138.6, 170.6; HRMS (FAB) m/z [M + H]$^+$ calcd for $C_{39}H_{52}NO_6$ 630.3795; found 630.3797. Anal. Calcd for $C_{39}H_{51}NO_6$: C, 74.21; H, 8.14; N, 2.29. Found: C, 74.37; H, 8.16; N, 2.22.

6-_O_-(2-Acetamido-3,4,6-tri-_O_-acetyl-2-deoxy-β-D-galactopyranosyl)-1,2:3,4-di-_O_-isopropylidene-α-D-galactopyranose (38). The glycosylation was performed according to the typical procedure employing diethyl phosphite **11c** (46.7 mg, 0.10 mmol), alcohol **21** (52.0 mg, 0.20 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Linked disaccharide **38** (39.5 mg, 67%) was obtained as a white solid from the crude product (121.1 mg) after column chromatography (silica gel 12 g, 4:1 → 3:1 CH_2Cl_2/acetone). When the glycosylation was performed employing diethyl phosphite **11c** (93.5 mg, 0.20 mmol), alcohol **21** (26.0 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.22 mL, 0.22 mmol), disaccharide **38** (41.2 mg, 70%) was obtained as a white solid from the crude product (134.2 mg) after column chromatography (silica gel 12 g, 4:1 → 3:1 CH_2Cl_2/acetone). R_f 0.26 (4:1 CH_2Cl_2/acetone); mp 151.5−152.5 °C; $[\alpha]_D^{22}$ −60.8 (_c_ 1.00, $CHCl_3$); IR (Nujol) 3293, 1744, 1665, 1561, 1308, 1258, 1176, 1071, 1015, 966, 895 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (s, 6H), 1.46 (s, 3H), 1.52 (s, 3H), 1.97 (s, 3H), 2.00 (s, 3H), 2.05 (s, 3H), 2.15 (s, 3H), 3.76 (dt, J = 3.7, 9.4 Hz, 1H), 3.91 (t, J = 6.8 Hz, 1H), 3.95−4.00 (m, 2H), 4.11−4.20 (m, 4H), 4.32 (dd, J = 2.4, 5.1 Hz, 1H), 4.59 (dd, J = 2.4, 8.0 Hz, 1H), 4.72 (d, J = 8.6 Hz, 1H), 5.14 (dd, J = 3.3, 11.2 Hz, 1H), 5.34 (d, J = 3.3 Hz, 1H), 5.48 (d, J = 8.7 Hz, 1H), 5.53 (d, J = 5.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.58, 20.63, 23.3, 24.2, 24.9, 25.9, 26.0, 50.9, 61.3, 66.7, 68.2, 68.9, 70.2, 70.56, 70.59, 71.1, 96.2, 102.0, 108.6, 109.3, 170.25, 170.34, 170.5; HRMS (FAB) m/z [M + H]$^+$ calcd for $C_{26}H_{40}NO_{14}$ 590.2449; found 590.2454.

Benzyl 4-_O_-(2-Acetamido-3,4,6-tri-_O_-acetyl-2-deoxy-β-D-galactopyranosyl)-2,3-anhydro-β-D-ribopyranoside (39). The glycosylation was performed according to the typical procedure employing diethyl phosphite **11c** (46.7 mg, 0.10 mmol), epoxy alcohol **22** (44.4 mg, 0.20 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.11 mL, 0.11 mmol). β-Galactoside **39** (32.5 mg, 59%) was obtained as a white solid from the crude product (114.3 mg) after column chromatography (silica gel 12 g, 3:1 CH_2Cl_2/acetone). When the glycosylation was performed employing diethyl phosphite **11c** (93.5 mg, 0.20 mmol), epoxy alcohol **22** (22.2 mg, 0.10 mmol), pulverized 4 Å molecular sieves (61.2 mg), and Tf_2NH (1.0 M in EtCN, 0.22 mL, 0.22 mmol), β-galactoside **39** (32.6 mg, 59%) was obtained as a white solid from the crude product (134.2 mg) after column chromatography (silica gel 12 g, 3:1 CH_2Cl_2/acetone). R_f 0.24 (4:1 CH_2Cl_2/acetone); mp 155.5−156.5 °C (colorless needles from AcOEt/_n_-hexane); $[\alpha]_D^{22}$ −21.3 (_c_ 1.00, $CHCl_3$); IR (Nujol) 3343, 1740, 1667, 1539, 1312, 1258, 1225, 1142, 1084, 1022, 972, 912, 812 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.96 (s, 3H), 2.00 (s, 3H), 2.05 (s, 3H), 2.15 (s, 3H), 3.22 (d, J = 4.0 Hz, 1H), 3.52 (t, J = 4.0 Hz, 1H), 3.58 (dd, J = 2.8, 12.8 Hz, 1H), 3.85 (dt, J = 11.2, 8.5 Hz, 1H), 3.87 (dd, J = 4.6, 12.8 Hz, 1H), 3.97 (t, J = 6.7 Hz, 1H), 4.13 (dd, J = 6.7, 11.2 Hz, 1H), 4.14 (m, 1H), 4.15 (dd, J = 6.7, 11.2 Hz, 1H), 4.57 (d, J = 11.6 Hz, 1H), 4.79 (d, J = 11.6 Hz, 1H), 5.03 (s, 1H), 5.25 (d, J = 8.5 Hz, 1H), 5.38 (d, J = 3.4 Hz, 1H), 5.45 (dd, J = 3.4, 11.2 Hz, 1H), 5.76 (d, J = 8.5 Hz, 1H), 7.32−7.40 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.61, 20.64, 20.7, 23.3, 51.3, 51.7, 51.9, 59.7, 61.6, 66.9, 69.0, 69.5, 70.4, 70.9, 93.9, 99.4, 128.09, 128.10, 128.6, 136.8, 170.17, 170.22, 170.4, 170.8; HRMS (FAB) m/z [M + H]$^+$ calcd for $C_{26}H_{34}NO_{12}$ 552.2081; found 552.2094. Anal. Calcd for $C_{26}H_{33}NO_{12}$: C, 56.62; H, 6.03; N, 2.54. Found: C, 56.29; H, 5.88; N, 2.51.

2-Acetamido-3,4,6-tri-_O_-benzyl-2-deoxy-α-D-glucopyranosyl Trichloroacetimidate (40). DBU (37 μL, 0.25 mmol) was added to an ice-cooled (0 °C) solution of hemiacetal **8a** (600 mg, 1.22 mmol) and trichloroacetonitrile (0.20 mL, 1.95 mmol) in CH_2Cl_2 (30 mL). After 1.5 h of stirring at room temperature, the volatile elements were removed in vacuo, and the residue (1.07 g) was purified by column chromatography (Wako gel 22 g, 2:1:1 _n_-hexane/AcOEt/CH_2Cl_2 with 3% Et_3N) to give trichloroacetimidate **40** (692 mg, 89%) as a colorless crystalline solid. R_f 0.44 (2:1:1 _n_-hexane/AcOEt/CH_2Cl_2, with Et_3N-doped silica gel plate); mp 144.5−145.0 °C (colorless needles from acetone/_n_-hexane); $[\alpha]_D^{20}$ +105.2 (_c_ 1.02, $CHCl_3$); IR (Nujol) 3310, 1672, 1649, 1543, 1285, 1148, 1127, 1105, 1074, 1022, 966, 945, 909, 842, 801 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$; spectrum contains a mixture of rotamers, only the major rotamer signals are reported) δ 1.68 (s, 3H), 3.69 (d, J = 11.2 Hz, 1H), 3.75−3.84 (m, 2H), 3.87−3.95 (m, 2H), 4.30 (ddd, J = 3.5, 8.5, 10.6 Hz, 1H), 4.51 (d, J = 12.0 Hz, 1H), 4.62 (d, J = 10.5 Hz, 1H), 4.65 (d, J = 12.0 Hz, 1H), 4.66 (d, J = 11.9 Hz, 1H), 4.73 (d, J = 8.5 Hz, 1H), 4.86 (d, J = 10.5 Hz, 1H), 4.91 (d, J = 11.9 Hz, 1H), 6.30 (d, J = 3.5 Hz, 1H), 7.22−7.38 (m, 15H), 8.60 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$; spectrum contains a mixture of rotamers, only the major rotamer signals are reported) δ 23.0, 52.1, 67.9, 73.4, 73.8, 74.5, 75.3, 77.7, 77.8, 91.1, 95.9, 127.6, 127.75, 127.80, 127.84, 127.9, 128.0, 128.1, 128.2, 128.3, 128.36, 128.42, 128.6, 128.9, 137.7, 137.8, 137.9, 160.2, 169.9; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{31}H_{33}Cl_3N_2O_6Na$ 657.1302; found 657.1292. Anal. Calcd for $C_{31}H_{33}Cl_3N_2O_6$: C, 58.55; H, 5.23; N, 4.40; Cl, 16.72. Found: C, 58.55; H, 5.22; N, 4.38; Cl, 16.58.

Phenyl 2-Acetamido-3,4,6-tri-_O_-benzyl-2-deoxy-1-thio-α-D-glucopyranoside (41) and Phenyl 2-Acetamido-3,4,6-tri-_O_-benzyl-2-deoxy-1-thio-β-D-glucopyranoside (42).[69] $SnCl_4$ (0.15 mL, 1.22 mmol) was added to an ice-cooled (0 °C) mixture of 2-azido-3,4,6-tri-_O_-benzyl-2-deoxy-D-glucosyl acetate[53] (573 mg, 1.11 mmol), PhSH (0.18 mL, 1.66 mmol), and pulverized 5 Å molecular sieves

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(500 mg) in 1:1 CH_2Cl_2/Et_2O (10 mL). After 5 h of stirring at this temperature, the reaction was quenched with Et_3N (0.4 mL), and the mixture was poured into a two-layer mixture of Et_2O (20 mL) and 10% aqueous NaOH (10 mL) and extracted with AcOEt (20 mL). The organic extract was successively washed with brine (5 mL), saturated aqueous NH_4Cl (10 mL), and brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the yellow oil (780 mg), which was purified by column chromatography (silica gel 20 g, 7:1 *n*-hexane/AcOEt) to give an anomeric mixture of the corresponding thioglycoside (534 mg, 85%, α:β = 60:40) as a colorless oil.

Triphenylphosphine (269 mg, 1.45 mmol) was added to a stirred solution of the 2-azido-2-deoxythioglycoside (530 mg, 0.93 mmol) in THF (6 mL). After 30 min of stirring, H_2O (1 mL) was added and the mixture was heated at 80 °C for 10 h. The resulting mixture was partitioned between AcOEt (30 mL) and brine (10 mL), and the organic layer was dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the 2-amino-2-deoxythioglycoside as a colorless oil, which was dissolved in pyridine (5 mL). Ac_2O (0.26 mL, 2.80 mmol) was added, and the solution was stirred for 3 h. The reaction mixture was partitioned between AcOEt (30 mL) and 10% aqueous HCl (15 mL). The organic layer was successively washed with H_2O (5 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (801 mg, slightly yellow solid), which was purified by flash column chromatography (silica gel 50 g, 5:1 toluene/acetone) to give 2-acetamido-2-deoxy-α-thioglycoside **41** (288 mg, 53%) and its β-isomer **42** (193 mg, 35%) as white solids.

*Data for α-isomer **41**.* R_f 0.33 (5:1 toluene/acetone); mp 168.5−170.0 °C (colorless needles from AcOEt/*n*-hexane); $[\alpha]_D^{21}$ +198.6 (*c* 1.00, $CHCl_3$); IR (KBr) 3314, 1651, 1541, 1127, 1105, 1071 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.79 (s, 3H), 3.63 (dd, *J* = 8.6, 10.9 Hz, 1H), 3.68 (dd, *J* = 1.7, 10.9 Hz, 1H), 3.80 (dd, *J* = 8.6, 9.7 Hz, 1H), 3.84 (dd, *J* = 4.6, 10.9 Hz, 1H), 4.32 (ddd, *J* = 1.7, 4.6, 9.7 Hz, 1H), 4.42 (ddd, *J* = 4.6, 8.6, 10.9 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.58 (d, *J* = 10.9 Hz, 1H), 4.63 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 11.5 Hz, 1H), 4.81 (d, *J* = 10.9 Hz, 1H), 4.87 (d, *J* = 11.5 Hz, 1H), 5.18 (d, *J* = 8.6 Hz, 1H), 5.65 (d, *J* = 4.6 Hz, 1H), 7.21−7.44 (m, 20H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.3, 52.7, 68.3, 72.5, 73.3, 74.5, 74.9, 78.3, 79.4, 88.2, 127.3, 127.56, 127.63, 127.7, 127.8, 127.9, 128.1, 128.27, 128.32, 128.4, 128.6, 129.0, 131.4, 131.8, 137.8, 137.9, 138.0, 169.7; HRMS (FAB) *m*/*z* $[M + H]^+$ calcd for $C_{35}H_{38}NO_5S$ 584.2471; found 584.2469. Anal. Calcd for $C_{35}H_{37}NO_5S$: C, 72.01; H, 6.39; N, 2.40; S, 5.49. Found: C, 71.81; H, 6.41; N, 2.40; S, 5.57.

*Data for β-isomer **42**.* R_f 0.30 (5:1 toluene/acetone); mp 209.5−210.5 °C (colorless needles from AcOEt/*n*-hexane); $[\alpha]_D^{21}$ +16.0 (*c* 1.03, $CHCl_3$) [lit.[69] $[\alpha]_D^{23}$ +14.5 (*c* 1.0, $CHCl_3$)]; IR (KBr) 3286, 1650, 1547, 1129, 1073 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.87 (s, 3H), 3.59 (ddd, *J* = 1.8, 4.6, 9.0 Hz, 1H), 3.62 (dd, *J* = 8.5, 9.0 Hz, 1H), 3.63 (ddd, *J* = 8.0, 8.5, 10.3 Hz, 1H), 3.73 (dd, *J* = 4.6, 10.9 Hz, 1H), 3.78 (dd, *J* = 1.8, 10.9 Hz, 1H), 3.97 (br t, *J* = 9.0 Hz, 1H), 4.53 (d, *J* = 12.1 Hz, 1H), 4.59 (d, *J* = 12.1 Hz, 1H), 4.60 (d, *J* = 11.5 Hz, 1H), 4.64 (d, *J* = 11.5 Hz, 1H), 4.79 (d, *J* = 11.5 Hz, 1H), 4.82 (d, *J* = 11.5 Hz, 1H), 5.03 (d, *J* = 10.3 Hz, 1H), 5.43 (d, *J* = 8.0 Hz, 1H), 7.20−7.23 (m, 5H), 7.26−7.36 (m, 13H), 7.49−7.52 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.5, 55.3, 69.1, 73.4, 74.7, 74.8, 78.5, 79.2, 82.2, 85.6, 127.4, 127.5, 127.6, 127.75, 127.79, 127.82, 128.1, 128.3, 128.4, 128.5, 128.8, 131.9, 133.3, 138.0, 138.2, 138.3, 170.2; HRMS (FAB) *m*/*z* $[M + H]^+$ calcd for $C_{35}H_{38}NO_5S$ 584.2471; found 584.2485. Anal. Calcd for $C_{35}H_{37}NO_5S$: C, 72.01; H, 6.39; N, 2.40; S, 5.49. Found: C, 71.90; H; 6.36; N, 2.38; S, 5.53.

2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-mannopyranosyl Diphenyl Phosphate (61). Diphenylphosphoryl chloride (0.23 mL, 1.13 mmol) was added to an ice-cooled (0 °C) solution of hemiacetal **60**[65] (490 mg, 1.03 mmol) and DMAP (304 mg, 2.49 mmol) in CH_2Cl_2 (10 mL). After 30 min of stirring, the reaction was quenched with crushed ice, followed by stirring at room temperature for 15 min. The mixture was poured into a two-layer mixture of AcOEt (30 mL) and saturated aqueous $NaHCO_3$ (30 mL), and the resulting mixture was extracted with AcOEt (150 mL). The organic extract was successively washed with saturated aqueous $NaHCO_3$ (60 mL) and brine (60 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (737 mg, pale yellow oil), which was purified by column chromatography (silica gel 30 g, 4:1 *n*-hexane/AcOEt with 1% Et_3N) to give α-linked diphenyl phosphate **61** (613 mg, 84%) as a colorless syrup. R_f 0.61 (2:1 *n*-hexane/AcOEt, with Et_3N-doped silica gel plate); $[\alpha]_D^{23}$ +32.8 (*c* 1.06, $CHCl_3$); IR (neat) 3064, 3030, 2913, 2868, 2112, 1590, 1489, 1297, 1188, 957, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.44 (dd, *J* = 2.0, 11.1 Hz, 1H), 3.67 (dd, *J* = 3.6, 11.1 Hz, 1H), 3.83 (ddd, *J* = 2.0, 3.6, 10.1 Hz, 1H), 3.88 (dd, *J* = 1.8, 2.5 Hz, 1H), 3.99 (dd, *J* = 2.5, 9.3 Hz, 1H), 4.01 (dd, *J* = 9.3, 10.1 Hz, 1H), 4.45 (d, *J* = 12.2 Hz, 1H), 4.50 (d, *J* = 10.4 Hz, 1H), 4.62 (d, *J* = 12.2 Hz, 1H), 4.64 (s, 2H), 4.82 (d, *J* = 10.4 Hz, 1H), 5.87 (dd, *J* = 1.8, 6.3 Hz, 1H), 7.13−7.22 (m, 8H), 7.27−7.35 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 61.0 (d, J_{C-P} = 9.6 Hz), 67.7, 72.8, 73.4, 73.5, 73.9, 75.4, 77.2, 78.7, 97.5 (d, J_{C-P} = 5.7 Hz), 120.0 (d, J_{C-P} = 5.7 Hz), 120.1 (d, J_{C-P} = 5.7 Hz), 127.6, 127.8, 127.86, 127.88, 128.0, 128.1, 128.3, 128.4, 128.6, 129.8, 129.9, 137.4, 137.85, 137.89, 150.1 (d, J_{C-P} = 4.8 Hz), 150.2 (d, J_{C-P} = 3.8 Hz); ^{31}P NMR (160 MHz, $CDCl_3$) δ −13.7; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{39}H_{38}N_3O_8PNa$ 730.2294; found 730.2289.

Phenyl 2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-1-thio-α-D-mannopyranoside (62) and Phenyl 2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-1-thio-β-D-mannopyranoside (63). $BF_3{\cdot}OEt_2$ (0.23 mL, 1.88 mmol) was added to an ice-cooled (0 °C) solution of diphenyl phosphate **61** (557 mg, 0.79 mmol) and PhSH (0.18 mL, 1.88 mmol) in CH_2Cl_2 (13 mL). After 5 min of stirring, the reaction was quenched with Et_3N (0.5 mL), and the mixture was poured into a two-layer mixture of AcOEt (50 mL) and saturated aqueous $NaHCO_3$ (50 mL). The resulting mixture was extracted with AcOEt (150 mL), and the organic extract was successively washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (900 mg, pale yellow oil), which was purified by column chromatography (silica gel 27 g, 8:1 *n*-hexane/AcOEt) to give 2-azido-2-deoxy-α-thioglycoside **62** (111 mg, 25%, colorless oil) and its β-isomer **63** (300 mg, 67%, white solid).

*Data for α-isomer **62**.* R_f 0.56 (4:1 *n*-hexane/AcOEt); $[\alpha]_D^{26}$ +93.9 (*c* 1.08, $CHCl_3$); IR (neat) 3062, 3029, 2867, 2105, 1584, 1496, 1454, 1267, 1099, 741, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.68 (dd, *J* = 1.7, 10.9 Hz, 1H), 3.79 (dd, *J* = 4.6, 10.9 Hz, 1H), 3.94 (t, *J* = 9.6 Hz, 1H), 4.02 (dd, *J* = 3.4, 9.6 Hz, 1H), 4.10 (dd, *J* = 1.7, 3.4 Hz, 1H), 4.28 (ddd, *J* = 1.7, 4.6, 9.6 Hz, 1H), 4.46 (d, *J* = 12.6 Hz, 1H), 4.52 (d, *J* = 10.9 Hz, 1H), 4.64 (d, *J* = 12.6 Hz, 1H), 4.75 (s, 2H), 4.85 (d, *J* = 10.9 Hz, 1H), 5.48 (d, *J* = 1.7 Hz, 1H), 7.18 (dd, *J* = 1.7, 7.4 Hz, 2H), 7.24−7.46 (m, 18H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 62.6, 68.5, 72.5, 73.2, 74.5, 75.2, 79.8, 86.1, 127.4, 127.6, 127.65, 127.69, 127.85, 127.94, 128.16, 128.24, 128.5, 129.0, 131.7, 137.3, 137.9, 138.0; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{33}H_{33}N_3O_4SNa$ 590.2089; found 590.2084.

*Data for β-isomer **63**.* R_f 0.50 (4:1 *n*-hexane/AcOEt); mp 99.0−99.5 °C (colorless needles from *n*-hexane/AcOEt); $[\alpha]_D^{25}$ −18.0 (*c* 1.04, $CHCl_3$); IR (KBr) 3030, 2862, 2099, 1583, 1481, 1455, 1362, 1278, 1128, 1070, 741, 689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.46 (ddd, *J* = 1.8, 6.1, 9.3 Hz, 1H), 3.68 (dd, *J* = 6.1, 11.1 Hz, 1H), 3.77 (dd, *J* = 3.6, 9.3 Hz, 1H), 3.78 (dd, *J* = 1.8, 11.1 Hz, 1H), 3.84 (t, *J* = 9.3 Hz, 1H), 4.16 (dd, *J* = 1.4, 3.6 Hz, 1H), 4.54 (d, *J* = 12.2 Hz, 1H), 4.58 (d, *J* = 10.9 Hz, 1H), 4.60 (d, *J* = 12.2 Hz, 1H), 4.71 (d, *J* = 11.8 Hz, 1H), 4.73 (d, *J* = 1.4 Hz, 1H), 4.77 (d, *J* = 11.8 Hz, 1H), 4.87 (d, *J* = 10.9 Hz, 1H), 7.19−7.39 (m, 18H), 7.49−7.52 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.4, 69.2, 72.6, 73.4, 74.3, 75.3, 79.8, 83.1, 85.5, 127.45, 127.47, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.4, 128.6, 129.0, 130.1, 134.4, 137.2, 137.8, 138.2; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{33}H_{33}N_3O_4SNa$ 590.2089; found 590.2079. Anal. Calcd for $C_{33}H_{33}N_3O_4S$: C, 69.82; H, 5.86; N, 7.40; S, 5.65. Found: C, 69.94; H, 5.84; N, 7.37; S, 5.65.

Phenyl 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-1-thio-α-D-mannopyranoside (58). Triphenylphosphine (55.4 mg, 0.21 mmol) was added to a stirred solution of 2-azido-1-thio-α-mannoside **62** (100 mg, 0.18 mmol) in THF (4 mL). After 30 min of stirring,

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H_2O (0.5 mL) was added, and the reaction mixture was heated at 80 °C for 1 h. The reaction mixture was partitioned between AcOEt (50 mL) and brine (10 mL), and the aqueous layer was extracted with AcOEt (40 mL). The combined organic extracts were dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the colorless oil, which was dissolved with pyridine (2 mL). Ac_2O (0.02 mL, 0.22 mmol) was added, and the solution was stirred for 1 h. The reaction was quenched with crushed ice, followed by stirring for 15 min. The mixture was partitioned between AcOEt (100 mL) and 10% aqueous HCl (15 mL), and the organic layer was successively washed with 10% aqueous HCl (30 mL), H_2O (30 mL), saturated aqueous $NaHCO_3$ (30 mL), and brine (30 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (190 mg, slightly yellow oil), which was purified by column chromatography (silica gel 6 g, 4:1 *n*-hexane/AcOEt) to give 2-acetamido-2-deoxy-α-thioglycoside **58** (77.1 mg, 75%) as a colorless oil. R_f 0.51 (1:2 *n*-hexane/AcOEt); $[\alpha]_D^{22}$ +65.4 (*c* 1.04, $CHCl_3$); IR (neat) 3430, 3283, 3061, 3031, 2868, 1655, 1543, 1454, 1370, 1097, 740, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.98 (s, 3H), 3.64 (dd, *J* = 1.7, 10.9 Hz, 1H), 3.78 (t, *J* = 9.5 Hz, 1H), 3.84 (dd, *J* = 3.4, 10.9 Hz, 1H), 4.01 (dd, *J* = 4.3, 9.5 Hz, 1H), 4.33 (ddd, *J* = 1.7, 3.4, 9.5 Hz, 1H), 4.41 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 10.3 Hz, 1H), 4.50 (d, *J* = 10.9 Hz, 1H), 4.59 (d, *J* = 11.5 Hz, 1H), 4.76 (d, *J* = 10.9 Hz, 1H), 4.89 (d, *J* = 10.3 Hz, 1H), 4.93 (ddd, *J* = 1.1, 4.3, 9.2 Hz, 1H), 5.53 (d, *J* = 1.1 Hz, 1H), 6.25 (d, *J* = 9.2 Hz 1H), 7.19−7.45 (m, 20H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.3, 50.5, 68.5, 71.2, 71.6, 73.4, 74.0, 75.1, 77.9, 87.3, 127.4, 127.7, 127.8, 127.9, 128.27, 128.32, 128.4, 128.9, 131.5, 133.8, 137.4, 137.6, 138.1, 170.0; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{35}H_{37}NO_5SNa$ 606.2290; found 606.2290.

Phenyl 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-1-thio-β-D-mannopyranoside (59). Triphenylphosphine (138 mg, 0.53 mmol) was added to a stirred solution of 2-azido-1-thio-β-mannoside **63** (250 mg, 0.44 mmol) in THF (9 mL). After 30 min of stirring, H_2O (1 mL) was added, and the reaction mixture was heated at 80 °C for 1 h. The reaction mixture was partitioned between AcOEt (120 mL) and brine (20 mL), and the aqueous layer was extracted with AcOEt (100 mL). The combined organic extracts were dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the colorless oil, which was dissolved in pyridine (5 mL). Ac_2O (0.05 mL, 0.53 mmol) was added, and the solution was stirred for 1 h. The reaction was quenched with crushed ice, followed by stirring for 15 min. The mixture was partitioned between AcOEt (170 mL) and 10% aqueous HCl (20 mL), and the organic layer was successively washed with 10% aqueous HCl (50 mL), H_2O (50 mL), saturated aqueous $NaHCO_3$ (50 mL), and brine (50 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (465 mg, slightly yellow oil), which was purified by column chromatography (silica gel 15 g, 6:1 *n*-hexane/AcOEt) to give 2-acetamido-2-deoxy-β-thioglycoside **59** (206 mg, 80%) as a colorless amorphous. R_f 0.64 (1:1 *n*-hexane/AcOEt); $[\alpha]_D^{26}$ −69.5 (*c* 1.04, $CHCl_3$); IR (KBr) 3261, 3060, 2866, 1652, 1547, 1454, 1369, 1299, 1075, 735, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.10 (s, 3H), 3.50 (ddd, *J* = 2.1, 4.0, 9.5 Hz, 1H), 3.65 (t, *J* = 9.5 Hz, 1H), 3.72 (dd, *J* = 4.6, 9.5 Hz, 1H), 3.74 (dd, *J* = 4.0, 10.9 Hz, 1H), 3.78 (dd, *J* = 2.1, 10.9 Hz, 1H), 4.49 (d, *J* = 10.9 Hz, 1H), 4.50 (d, *J* = 10.9 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.84 (d, *J* = 1.1 Hz, 1H), 4.89 (d, *J* = 10.9 Hz, 1H), 4.91 (d, *J* = 10.9 Hz, 1H), 5.06 (ddd, *J* = 1.1, 4.6, 10.3 Hz, 1H), 6.03 (d, *J* = 10.3 Hz, 1H), 7.19−7.50 (m, 20H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.4, 50.5, 69.0, 71.3, 73.4, 73.9, 75.1, 79.3, 81.4, 86.5, 127.3, 127.69, 127.73, 127.75, 127.77, 128.3, 128.35, 128.37, 128.44, 128.9, 130.9, 134.2, 137.5, 137.9, 138.1, 170.5; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{35}H_{37}NO_5SNa$ 606.2290; found 606.2290.

Methyl 6-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (64) and Methyl 6-*O*-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (65). Tf_2NH (1.0 M in EtCN, 0.09 mL, 0.09 mmol) was added to a cooled (−60 °C) mixture of thioglycoside **58** (47.6 mg, 0.08 mmol), 6-O-unprotected glucoside **13** (41.7 mg, 0.09 mmol), NIS (20.2 mg, 0.09 mmol), and pulverized 4 Å molecular sieves (82 mg) in CH_2Cl_2 (0.08 mL). After 14 h of stirring, the reaction was quenched with Et_3N (0.1 mL), and the mixture was filtrated through a Celite pad. The filtrate was partitioned between AcOEt (35 mL) and 20% aqueous $Na_2S_2O_3$ (6 mL), and the organic layer was successively washed with 20% aqueous $Na_2S_2O_3$ (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo followed by gel permeation chromatography (Bio-Beads S-X, toluene) afforded a mixture of disaccharides **64** and **65** (12.1 mg, 16%, **64**:**65** = 62:38) as a colorless oil, along with oxazoline **66** (31.3 mg, 81%) as a colorless oil. The ratio of disaccharides **64** and **65** was determined by 500 MHz ^1H NMR spectroscopic analysis. The α- and β-glycosides were separated by column chromatography (silica gel 1 g, 3:1 *n*-hexane/AcOEt). When the glycosylation was performed employing thioglycoside **59** (60.8 mg, 0.10 mmol), 6-O-unprotected glucoside **13** (53.2 mg, 0.12 mmol), NIS (25.9 mg, 0.12 mmol), pulverized 4 Å molecular sieves (100 mg), and Tf_2NH (1.0 M in EtCN, 0.12 mL, 0.12 mmol), a mixture of disaccharides **64** and **65** (22.6 mg, 23%, **64**:**65** = 74:26) and oxazoline **66** (36.9 mg, 75%) were obtained as colorless oils from the crude product (190 mg) after gel permeation chromatography (Bio-Beads S-X, toluene).

*Data for α-anomer **64**.* R_f 0.43 (1:2 *n*-hexane/AcOEt); $[\alpha]_D^{23}$ +39.5 (*c* 0.73, $CHCl_3$); IR (neat) 3306, 3030, 2923, 1662, 1496, 1454, 1362, 1091, 737, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.95 (s, 3H), 3.27 (s, 3H), 3.39 (t, *J* = 9.5 Hz, 1H), 3.44 (dd, *J* = 1.4, 10.6 Hz, 1H), 3.50 (dd, *J* = 3.7, 9.5 Hz, 1H), 3.54 (dd, *J* = 1.1, 10.9 Hz, 1H), 3.57 (dd, *J* = 2.9, 10.6 Hz, 1H), 3.61 (m, 1H), 3.64 (t, *J* = 9.5 Hz, 1H), 3.68 (m, 1H), 3.72 (dd, *J* = 4.6, 10.9 Hz, 1H), 3.93 (t, *J* = 9.5 Hz, 1H), 3.95 (dd, *J* = 4.6, 9.5 Hz, 1H), 4.32 (d, *J* = 12.0 Hz, 1H), 4.36 (d, *J* = 11.5 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.44 (d, *J* = 10.9 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.54 (d, *J* = 3.7 Hz, 1H), 4.64 (d, *J* = 12.6 Hz, 1H), 4.691 (d, *J* = 11.5 Hz, 1H), 4.694 (ddd, *J* = 1.7, 4.6, 9.7 Hz, 1H), 4.740 (d, *J* = 10.3 Hz, 1H), 4.742 (d, *J* = 12.6 Hz, 1H), 4.82 (d, *J* = 1.7 Hz, 1H), 4.83 (d, *J* = 11.5 Hz, 1H), 4.84 (d, *J* = 10.9 Hz, 1H), 4.94 (d, *J* = 10.3 Hz, 1H), 5.84 (d, *J* = 9.7 Hz, 1H), 7.08−7.34 (m, 30H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.5, 49.0, 55.1, 66.2, 68.4, 69.5, 70.5, 71.0, 73.3, 73.5, 73.8, 74.8, 75.0, 75.7, 77.2, 77.6, 80.0, 82.1, 97.8, 99.5, 127.4, 127.50, 127.53, 127.6, 127.7, 127.77, 127.84, 127.9, 128.0, 128.1, 128.2, 128.3, 128.36, 128.39, 128.5, 137.7, 138.1, 138.2, 138.5, 138.6, 170.2; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{57}H_{63}NO_{11}Na$ 960.4299; found 960.4298.

*Data for β-anomer **65**.* R_f 0.70 (1:2 *n*-hexane/AcOEt); $[\alpha]_D^{23}$ +2.5 (*c* 1.09, $CHCl_3$); IR (neat) 3309, 3031, 2927, 2871, 1656, 1520, 1454, 1367, 1270, 1070, 738, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.99 (s, 3H), 3.34 (s, 3H), 3.37 (m, 1H), 3.40 (t, *J* = 9.5 Hz, 1H), 3.48 (dd, *J* = 3.4, 9.7 Hz, 1H), 3.52 (dd, *J* = 5.7, 10.9 Hz, 1H), 3.59 (m, 2H), 3.70 (m, 2H), 3.76 (ddd, *J* = 1.3, 5.6, 10.2 Hz, 1H), 3.98 (dd, *J* = 9.2, 9.7 Hz, 1H), 4.03 (dd, *J* = 1.4, 10.6 Hz, 1H), 4.29 (br s, 1H), 4.45 (d, *J* = 10.9 Hz, 1H), 4.478 (d, *J* = 12.0 Hz, 1H), 4.482 (d, *J* = 10.9 Hz, 1H), 4.53 (d, *J* = 3.4 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 11.5 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.72 (br d, *J* = 9.7 Hz, 1H), 4.79 (d, *J* = 12.0 Hz, 1H), 4.81 (d, *J* = 10.9 Hz, 1H), 4.85 (d, *J* = 10.9 Hz, 1H), 4.87 (d, *J* = 10.3 Hz, 1H), 4.88 (d, *J* = 11.5 Hz, 1H), 4.98 (d, *J* = 10.9 Hz, 1H), 5.80 (d, *J* = 9.7 Hz, 1H), 7.08−7.34 (m, 30H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.3, 49.2, 54.9, 68.1, 68.6, 69.6, 71.0, 73.3, 73.4, 73.9, 74.7, 74.9, 75.6, 77.6, 79.6, 80.2, 82.0, 97.7, 99.6, 127.51, 127.53, 127.6, 127.66, 127.70, 127.73, 127.76, 127.80, 127.82, 127.9, 128.1, 128.25, 128.27, 128.30, 128.34, 137.6, 137.7, 137.9, 138.0, 138.3, 138.5, 170.7; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{57}H_{63}NO_{11}Na$ 960.4299; found 960.4297.

*Data for oxazoline **66**.* R_f 0.56 (1:2 *n*-hexane/AcOEt); $[\alpha]_D^{23}$ +7.8 (*c* 1.06, $CHCl_3$); IR (neat) 3062, 3029, 2866, 1674, 1454, 1108, 1027, 739, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.98 (d, *J* = 1.4 Hz, 3H), 3.531 (d, *J* = 4.0 Hz, 1H), 3.532 (d, *J* = 5.0 Hz, 1H), 3.63 (dd, *J* = 7.4, 8.8 Hz, 1H), 3.71 (ddd, *J* = 4.0, 5.0, 7.4 Hz, 1H), 3.88 (dd, *J* = 5.2, 8.8 Hz, 1H), 4.23 (ddq, *J* = 5.2, 5.9, 1.4 Hz, 1H), 4.51 (d, *J* = 10.9 Hz, 1H), 4.52 (s, 2H), 4.76 (d, *J* = 11.8 Hz, 1H), 4.84 (d, *J* = 10.9 Hz, 1H), 4.87 (d, *J* = 11.8 Hz, 1H), 5.71 (d, *J* = 5.9 Hz, 1H), 7.21 (m, 2H), 7.25−7.34 (m, 11H), 7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

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14.3, 66.7, 70.1, 72.2, 73.4, 74.4, 74.9, 76.1, 76.3, 100.4, 127.6, 127.7, 127.8, 127.96, 128.00, 128.32, 128.34, 137.9, 138.06, 138.12, 165.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{29}H_{31}NO_5Na$ 496.2100; found 496.2107.

■ ASSOCIATED CONTENT

Supporting Information

Additional text with general information and ^1H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(33) The reaction by $La(OTf)_3$, $Zn(OTf)_2$, CuOTf, $Cu(OTf)_2$, $Y(OTf)_3$, $Yb(OTf)_3$, or $Mg(OTf)_2$ did not proceed at a temperature below −23 °C and afforded disaccharide **14** in low yield at higher temperatures.

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(47) Since galactosyl donors **11a** and **11b** and 3,4,6-tri-*O*-acetyl-protected glucosyl donor **9c** were successfully employed, the glycosylation of alcohol **13** with 3,4,6-tri-*O*-acetyl-protected galactosyl donor **11c** has not been examined. The potential of donor **11c** was sufficiently demonstrated by the coupling with alcohols **21** and **22** (Table 6).

(48) It was found that Tf_2NH-promoted reaction of oxazoline **15** with alcohol **13** proceeded at temperatures above approximately 5 °C. The addition of $HP(O)(OEt)_2$, another product of the glycosylation with glycosyl diethyl phosphites, was not effective for the reaction.

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