Glycosyl Phosphites as Glycosylation Reagents: Scope and Mechanism

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The glycosylation reactions with glycosyl phosphites in the presence of catalytic amounts of TMSOTf at low temperature have been studied with different donors and acceptors for the synthesis of several glycosides, including O-glycosides, S-glycosides, C-glycosides, and glycopeptides. Mechanistic investigations of the reactions indicate that the glycosyl phosphite is activated by either TfOH or TMSOTf, depending on how the substrates are mixed. When the acceptor is treated with TMSOTf first, the glycosyl phosphite is activated by the resulting TfOH. The glycosyl phosphite can also be activated by TMSOTf directly. The best result is, however, to mix the acceptor and TMSOTf first, followed by addition of the glycosyl phosphite.

Introduction

As the interest in carbohydrate conjugates with biologically important properties is increasing, the development of new methods for the efficient construction of glycosidic bonds is an objective of current research in this area.[1] The practical and stereocontrolled synthesis of oligosaccharides containing sialic acid, for example, is still of particular interest because of their important roles in biological recognition and cellular communication.[2] However, the steric hindrance of the anomeric center and the ease of elimination during activation and glycosylation make the sialylation reaction particularly difficult to execute in a high-yield and stereoselective manner.

We and others have recently reported a novel and high-yield sialylation using sialyl phosphite as donor[3] and TMSOTf as catalyst. We also have reported the preparation of several other dibenzyl glycosyl phosphites, which can be easily converted to glycosyl phosphates and sugar nucleotides or used as glycosylation reagents in oligosaccharide synthesis[4] (Scheme 1). It is, however, not clear how the activation occurs in the glycosylation reactions, and whether the glycosylation method is applicable to other glycosyl phosphites. We here describe our study on the scope and mechanism of the glycosylation reaction, including its application to the synthesis of O-, S-, and C-glycosides and O-glycopeptides.

Results and Discussion

Glucopyranosyl Phosphites as Glycosyl Donors. We prepared several dibenzyl glycosyl phosphites according to our previously reported method[4] and found that these phosphites were moderately stable and easily handled. We first investigated the coupling reaction using glycosyl phosphites with an acetyl group[5] on C-2 and different acceptors for the formation of O-, S-, and C-linked glycosides and glycopeptides. Contrary to our expectation, the glycosylation of **1** with cyclohexanol **11** or 1,3,5-trimethoxybenzene **12** gave the orthoester-type phosphonate **25** in good yield under the standard conditions (Table 1). The structure of the phosphonate **25** was determined by ^{1}H- and ^{31}P-NMR and compared to known and related structures, e.g., phosphites and phosphonates (Table 2). As expected, the chemical shifts appeared at 5.87 ppm (d, J = 5.2 Hz) and 1.69 ppm (d, J = 10.5 Hz), corresponding to H-1 and the methyl group of the orthoester moiety. In addition, the ^{31}P chemical shift was observed at 17.2 ppm,

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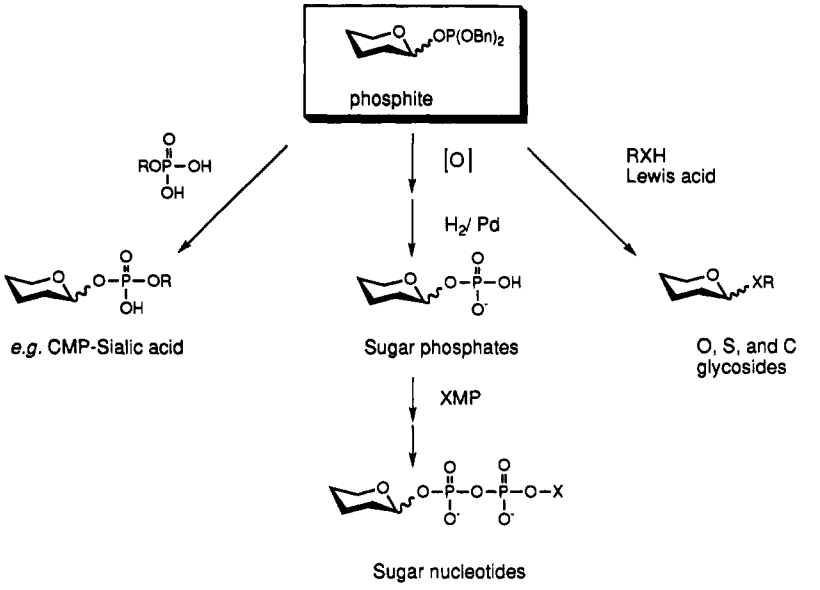
(4) Sim, M. M.; Kondo, H.; Wong, C.-H. *J. Am. Chem. Soc.* **1993**, *115*, 2260.

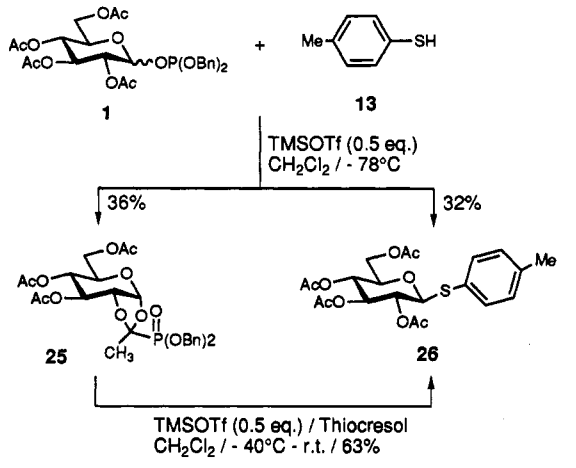
(5) For representative glycosylation with acetyl protecting group: (a) Bochkov, A. F.; Betanely, V. I.; Kochetkov, N. K. *Carbohydr. Res.* **1973**, *30*, 418. (b) Banoub, J.; Bundle, D. R. *Can. J. Chem.* **1979**, *57*, 2091. (c) Garegg, P. J.; Norberg, T. *Acta Chem. Scand. Ser. B* **1979**, *33*, 116. (d) Garegg, P. J.; Konradsson, P.; Kvarnstrom, I.; Norberg, T.; Svensson, S. C. T.; Wigilius, B. *Acta Chem. Scand. Ser. B* **1985**, *39*, 569. (e) Hashimoto, S.-I.; Honda, T.; Ikegami, S. *J. Chem. Soc. Chem. Commun.* **1989**, 685.

0022-3263/94/1959-0864$04.50/0

Scheme 1



Scheme 2



further supporting a pentavalent phosphorus, as the shifts of trivalent phosphites are usually greater than 100 ppm, and that of pentavalent phosphorus compounds such as phosphates or phosphonates are in the range between −10 to 20 ppm.[6] The S-glycosylation of acceptor **13** with **1** in the presence of TMSOTf at −78 °C afforded the desired coupling product **26** in 32% yield, in addition to the byproduct **25** (36%). If a higher reaction temperature (−40 °C) was used, the yield of **26** increased to 63%. We suspected the increase in yield was due to the reaction of **25** with the acceptor at higher temperature. Indeed, compound **25** isolated can be converted to the thioglycoside **26** in the presence of the acceptor **13** and TMSOTf at −40 °C. No further reaction was, however, observed at −78 °C, indicating **25** is not a reactive intermediate. The primary hydroxyl group is not a suitable acceptor in the reaction as methyl 2,3,4-tri-*O*-benzyl glucopyranoside **19** reacts with **1** to give 3,4,6-tri-*O*-acetylglucose and the transacetylation product methyl 2,3,4-tri-*O*-benzyl-6-*O*-acetyl glucopyranoside (**27**).[7]

Galactopyranosyl Phosphites as Glycosyl Donors. The galactopyranosyl phosphite **2** was prepared in high yield (89%) as an anomeric mixture ($\alpha:\beta$ = 1:3).[4] Compounds **11**, **13**, **15**, and **18** were favorable acceptors for the glycosylation and gave the desired glycosides **28**, **30**, **31**, and **32** in moderate yields (Table 1, entries 6–9). Acceptor **11** gave the glycoside **28** and the 2-O-deacetylated product **29** in 47% and 13% yields, respectively. Both **28** and **29** are in the β configuration, presumably due to the participating effect of the acetyl group at the 2-position.[1,5]

It was of interest to note that the glycosylation of galactosyl phosphite **2** with 6-*O*-(*tert*-butyldiphenylsilyl)-*N*-acetylglucosamine (6-*O*-TBDPS-GlcNAc) **18** gave Galβ-(1,3)GlcNAc **32** in 62% yield. In addition, the 3-trimethylsilylated derivative of acceptor **18** (6%)[8] and dibenzyl hydrogen phosphonate **54** were also isolated. In an investigation of the relative reactivity of the α (**2a**) and β (**2b**) anomers of phosphite **2**, it was found that glycosylation of the acceptor **18** with phosphite **2b** afforded the Galβ(1,3)GlcNAc derivative **32** in 72% yield; however, the reaction with phosphite **2a** produced only the 3-*O*-trimethylsilyl derivative of the acceptor **18** as a byproduct in 42%. Therefore, the β phosphite **2b** was the primary reactive species for the formation of **32**. This type of regioselective glycosylation[9] is interesting as the disaccharide Galβ(1,3)GlcNAc (**32**) is part of biologically significant compounds such as Lewis a and sialyl Lewis a (Scheme 3).[10]

Among other acceptors investigated, methyl 2,3,4-tri-*O*-benzylglycoside (**19**) and 6-*O*-TBDPS glycal (**22**) gave the unexpected byproducts **27** and **33**, respectively. The

(6) (a) Gorenstein, D. G. *Prog. NMR Spectrosc.* **1983**, *16*, 1. (b) Phosphonates analogous to **25** were reported previously: Paulsen, H.; Thiem, J. *Chem. Ber.* **1973**, *115*, 131.

(7) Transacetylation is a common phenomenon with the acetyl protecting group (see refs 1b, 5).

(8) TMS product of compound **18**: ^{1}H-NMR ($CDCl_3$) δ 0.10 (9H, s, $Si(CH_3)_3$, 1.06 (9H, s, t-Bu), 2.06 (3H, s, NHAc), 3.33–3.36 (1H, m, H-5), 3.55–3.66 (3H, m, H-2, H-3, and H-4), 3.81 (1H, dd, J = 5.2, 11.0 Hz, H-6), 3.89 (1H, dd, J = 2.4, 11.0 Hz, H-6′), 4.07 (1H, dd, J = 6.5, 12.8 Hz, allylic proton), 4.32–4.36 (1H, m, allylic proton), 4.47 (1H, d, J = 7.5 Hz, H-1), 5.22 (1H, dd, J = 1.2, 10.4 Hz, vinyl proton), 5.28 (1H, dd, J = 1.2, 17.0 Hz, vinyl protons), 5.72 (1H, d, J = 4.3 Hz, NH), 5.87–5.94 (1H, m, vinyl proton), 7.35–7.41 (6H, m, phenyl proton), 7.69–7.72 (4H, m, phenyl proton).

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(10) (a) Tokuzen, R. *Adv. Carbohydr. Chem. Biochem.* **1976**, *32*, 235. (b) Hakomori, S. *Ann. Rev. Immunol.* **1984**, *2*, 103. (c) Feizi, T. *Nature* **1985**, *314*, 53.

Table 1. Glycosylation Reactions Using Glycosyl Phosphites

entry	donor[a]	acceptor[a]	TMSOTf (equiv)	solvent	temp (°C)	product (yield, %)[b,c]	α:β[d]
1	1	11	0.5	CH_2Cl_2	−78	**25** (58)	
2	1	12	0.5	CH_2Cl_2	−78	**25** (66)	
3	1	13	0.5	CH_2Cl_2	−78	**26** (32), **25** (36)	β
4	1	13	0.5	CH_2Cl_2	−40 to rt	**26** (60)	β
5	1	19	0.5	CH_2Cl_2	−78	**27** (25)	β
6	2	11	0.5	CH_2Cl_2	−78	**28** (47), **29** (13)	β
7	2	13	0.5	CH_2Cl_2	−78	**30** (69)	β
8	2	15	0.3	CH_2Cl_2	−78	**31** (66)	β
9	2	18	0.5	CH_2Cl_2	−78	**32** (62)	β(1,3)
10	2	18	0.5	CH_3CN	−40	**32** (58)	β(1,3)
11	2	19	0.3	CH_2Cl_2	−78	**27** (26)	
12	2	22	1.0	CH_2Cl_2	−78	**33** (69)	
13	3	20	0.5	CH_2Cl_2	−78	**34** (49)	β
14	3	20	0.5	CH_3CN	−43	**34** (45)	β
15	4	20	0.5	CH_2Cl_2	−78	**35** (63)	β
16	4	20	0.5	CH_3CN	−43	**35** (32)	β
17	5	11	1.0	CH_2Cl_2	−78	**36** (63)	β
18	5	11	0.5	CH_2Cl_2	−78	**36** (60)	β
19	5	12	0.5	CH_2Cl_2	−78	**37** (52)	β
20	5	13	0.5	CH_2Cl_2	−78	**38** (67)	β
21	5	14	0.5	CH_2Cl_2	−78	**39** (18), **40** (3), **41** (68)	
22	5	16	0.5	CH_2Cl_2	−78	**42** (53)	β
23	5	17	0.5	CH_3CN	−43	**43** (43)	β
24	6	18	0.5	CH_2Cl_2	−78	**44** (18)	β(1,3)
25	7	19	0.5	CH_3CN	−40	**45** (80)	6:1
26	7	23	0.3	CH_3CN	−40	**46** (27)	5:1
27	7	24	0.3	CH_3CN	−40	**47** (44)	6:1
28	8	19	0.5	CH_2Cl_2	−78 to −40	**48** (45)	β
29	9	23	0.5	CH_3CN	−40	**49** (48)	α
30	10	21	0.5	CH_2Cl_2	−43	**50** (40)	β

[a] See Chart 1 for structures of donors and acceptors. [b] See Chart 2 for structures of products. [c] Most of these reactions were designed to study the selectivity (two or more OH groups of the acceptor were exposed for glycosylation) and mechanism. The yields were therefore not optimized. [d] The ratio was determined by 400-MHz ^{1}H-NMR. See ref 2 (Wong, C.-H. et al. *J. Am. Chem. Soc.* **1992**, *114*, 8748).

former is formed via transacetylation as described previously, and the latter is a furan derivative which perhaps is formed via elimination of the 3-*O*-acetyl group followed by an intramolecular cyclization and 1,4-elimination (Scheme 4). The structure of **33** was identified by ^{1}H-NMR, ^{13}C-NMR, and HRMS. The ^{1}H-NMR spectrum showed the characteristic chemical shifts of protons on a furan skeleton at 6.28 (1H), 6.32 (1H), and 7.34 (1H) ppm.[11] Additionally, the diacetate derivative of compound **33** was further characterized by ^{1}H- and ^{13}C-NMR analyses.

Fucosyl Phosphites as Glycosyl Donors. Among the acceptors tested, **11**, **12**, **13**, **16**, and **17** were suitable acceptors for **5** and provided the corresponding β-glycosides in good yields (Table 1, entries 17–23). The peptide acceptor **14** with a Ser group gave the desired O-glycopeptide product **39** in 18%, along with the orthoester **40** (3%) and the phosphonate **41** (68%) (Table 1). Compound **17**, which was two hydroxyl groups, reacted with phosphite **5** to afford the difucosylated trisaccharide **43**.

Sialyl Phosphites as Sialyl Donors. We have already reported that the sialyl phosphite methyl ester **7** is an efficient sialyl donor, giving the α-2,3- or α-2,6-linked sialosides (**45** and **46**, respectively) in good yields (40–85%).[3] To investigate the utility of other sialyl phosphites, we synthesized the 3-bromosialyl phosphite **8** and the sialyl phosphite benzyl ester **9** and examined their sialylation reactions.

The preparation of 3-bromosialyl phosphite **8** was achieved following the chemoenzymatic method shown in Scheme 5 via a chloroperoxidase-catalyzed bromohydration of sialic acid glycal **51**.[12] As indicated in Table 1 (entry 21), 3-bromosialyl phosphite **8** was also an effective sialylating agent, giving the β-2,6-linked sialoside **48** stereoselectively, presumably due to the effective neighboring participation of the C-3 bromo group. The spectral data of **48** agreed well with that reported by Goto et al.[13] Of particular interest was the sialylation with sialyl phosphite benzyl ester **9**; the reaction was more stereoselective than that with the methyl ester, giving only the α sialoside **49**.[14]

Glucuronyl Phosphite 6 as Donor. In a representative reaction as shown in Table 1 (entry 28), the glycosylation of **6** with 6-*O*-TBDPS-GlcNAc **18** gave the disaccharide GlcUAβ(1,3)GlcNAc **44** regio- and stereoselectively. Compound **44** is a key repeating unit of hyaluronic acid (Scheme 3).[15]

Glucosaminyl Phosphites as Donors. To further demonstrate the utility of glycosyl phosphites and to gain more insights into the mechanism of the reaction, this glycosylation was systemically investigated at low temperature using methylene chloride or acetonitrile as solvents and by varying the order of addition of the reacting species. When the phosphite and acceptor were mixed first followed by addition of TMSOTf, the yield of disaccharide was very low (<10%). Addition of the phosphite last, however, increased the yield significantly. In the best case, a 63% yield of the product **35** (a precursor to lipid A)[16] was obtained when the *N*-Troc-protected glycosyl phosphite **4** was added to a mixture of 1 equiv of

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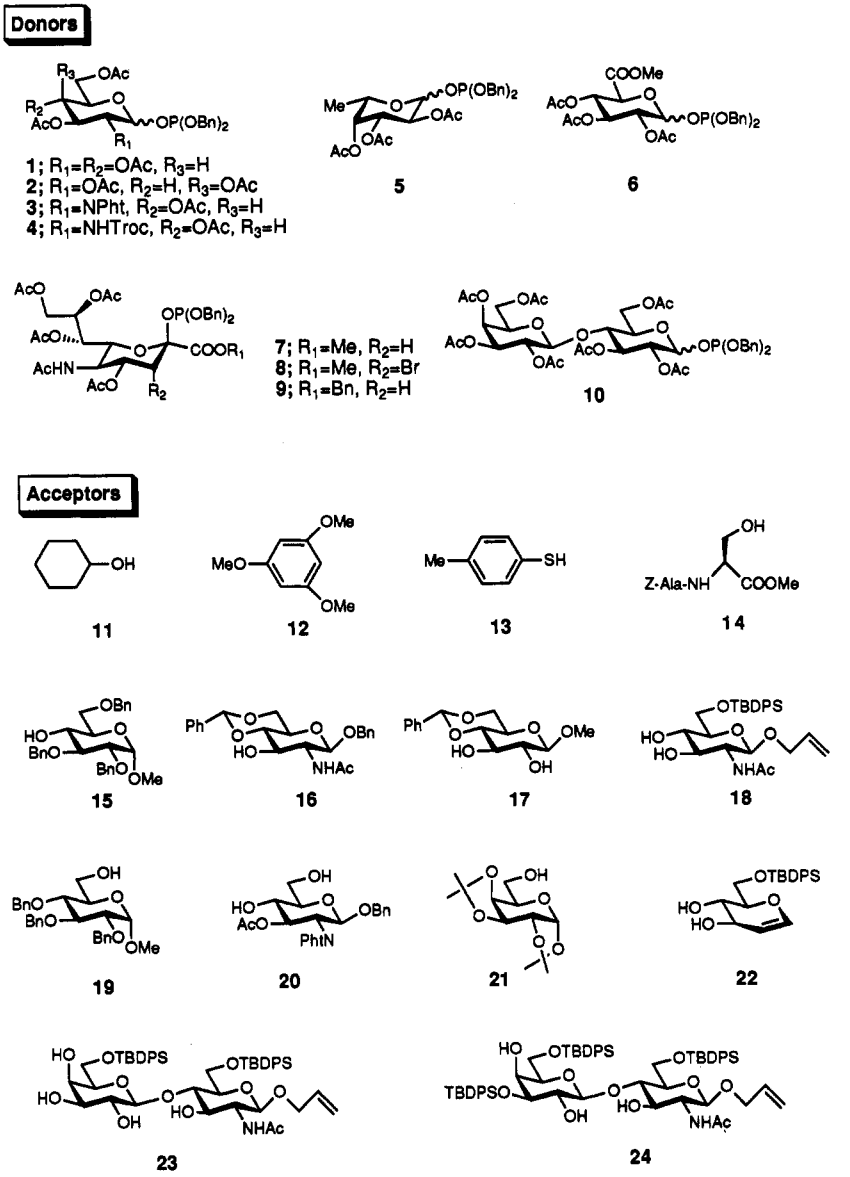
(13) Okamoto, K.; Kondo, T.; Goto, T. *Tetrahedron* **1987**, *43*, 5909.

(14) For the characterization of α2,3-sialosides by NMR (4.69 ppm for Gal-H_3), (a) Kameyama, A.; Ishida, H.; Kiso, M.; Hasegawa, A. *J. Carbohydr. Chem.* **1991**, *10*, 549. (b) Nicolaou, K. C.; Hummel, C. W.; Bockovich, N. J.; Wong, C. H. *J. Chem. Soc., Chem. Commun.* **1991**, *10*, 870.

(15) Banerjee, S. D.; Toole, B. P. *J. Cell Biol.* **1992**, *119*, 643.

(16) Sugai, T.; Ritzen, H.; Wong, C.-H. *Tetrahedron Asymmetry* **1993**, *4*, 1051.

Chart 1. Donors and Acceptors for Glycosylation Reactions (See Table 1)



acceptor **20** and 0.5 equiv of TMSOTf in methylene chloride at −78 °C (Table 1, entry 15). The relationship of these phenomena with the mechanism will be discussed later.

Lactosyl Phosphites as Lactosyl Donors. To investigate the feasibility of using oligosaccharides as donors, lactosyl phosphite **10** was synthesized from lactose octaacetate according to our general procedure.[4] Glycosylation of diisopropylidene-D-galactose with lactosyl phosphite under standard conditions provided the trisaccharide **50** in 40% yield (Table 1). Glycosylations of secondary alcohol acceptors with lactosyl phosphite proved to be unfruitful, resulting predominantly in acetyl transfer from the donor to the free hydroxyl of the acceptor.

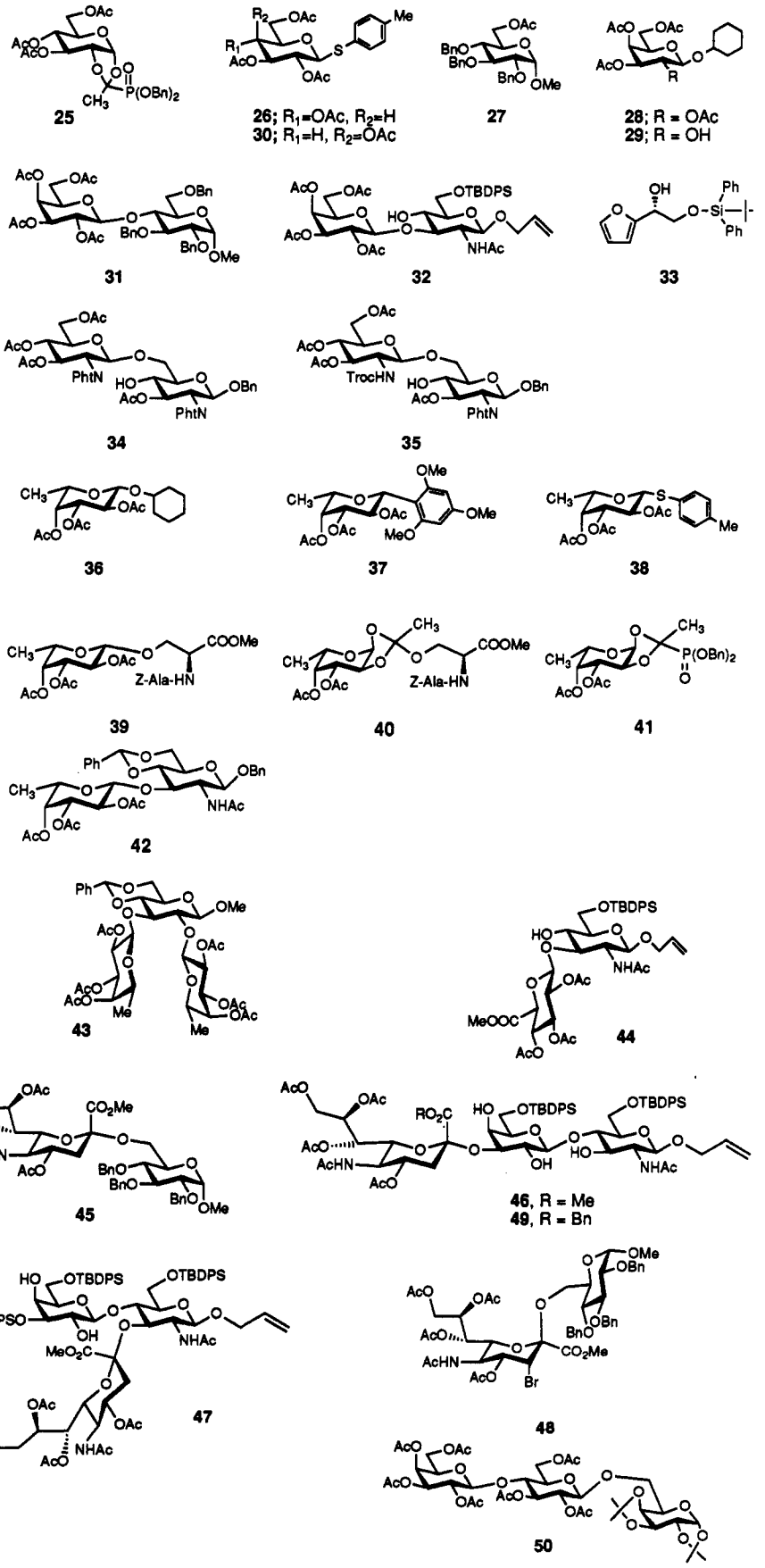
Mechanism of the Glycosylation with Glycosyl Phosphites. On the basis of the results obtained so far, the real catalyst appears to be TfOH, which is generated by reaction of TMSOTf and the acceptor, as an improved yield was obtained when TMSOTf was mixed with the acceptor first. Alternatively, the glycosyl phosphite may be activated by TMSOTf if the glycosyl phosphite and TMSOTf are mixed first. A phosphonate intermediate such as **25** or **41** is, however, produced as byproduct, which can be further converted to the desirable glycoside in the presence of TMSOTf and the acceptor at higher temperature (−40 °C to rt). Though other types of Lewis acid can also activate glycosyl phosphites, they are used as stoichiometric reagents.[3c,17]

To further understand the activation mechanism of glycosyl phosphites by TMSOTf, especially to investigate whether TMSOTf reacts with O or P during the activation, we examined the following reactions.

The trivalent silyl phosphite **56** prepared from *tert*-butyl diphenylsilyl chloride and dibenzyl phosphite **54**[18] was allowed to react with **55** in the presence of AgOTf in methylene chloride at −78 °C (the oxonium cation is formed under this condition). The product isolated was the orthoester **25**. This experiment supports the TMSOP-$(OBn)_2$ is generated in the reaction of TMSOTf with a glycosyl phosphite and then reacts with the oxonium ion triflate complex to form the byproduct phosphonate **25** (Scheme 6). This activation mechanism is consistent with the notion that the Si–O bond is stronger than the Si–P bond.[19] When TMSOTf is mixed with the acceptor first followed by addition of the glycosyl phosphite, the activation mechanism, however, is different: the triflic

(17) Activation of sialyl phosphite with $BiCl_3$: (a) Sugahara, K.; Yamashina, I.; Waard, P. D.; van Halbeek, H. V.; Vliegenthart, J. F. G. *J. Biol. Chem.* **1988**, *263*, 10168. (b) Ekborg, G.; Curenton, T.; Krishna, N. R.; Roden, L. *J. Carbohydr. Chem.* **1990**, *9*, 15.

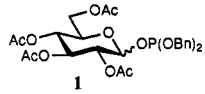
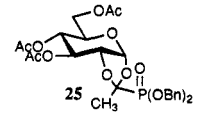
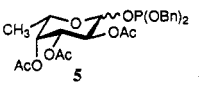
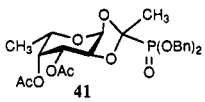
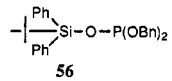
Chart 2. Products of Glycosylation Reactions (See Table 1)



acid generated becomes the catalyst (see Scheme 7a). In this case the byproduct **25** is not observed. This mechanism is further supported by a separate experiment using TfOH as a catalyst (Table 3, entry 3), where **57** was reacted with **19** to give the coupling product **58** in 72% yield.

From this study, we propose that the glycosylation reaction proceeds through two different mechanisms in the presence of a catalytic amount of TMSOTf, depending on how the substrates are mixed (Scheme 7). TMSOTf may react with the acceptor first to generate a more active

Table 2. ^1H (400 MHz) and ^{31}P NMR (162 MHz) Chemical Shifts (ppm) of Phosphites and Phosphonates

Phosphites ^{31}P NMR (125-140 ppm) 	^1H NMR ($CDCl_3$, ppm)	^{31}P NMR (acetone-d_6, ppm)
 1	**H-1**α: 5.77(dd), $J_{1,2}$ = 3.50 Hz, $J_{1,p}$ = 8.33 Hz	140.1 (α)
	H-1β: 4.85–5.15 (m)	139.2 (β)
	OAc: 1.98–2.00	
 25	**H-1**: 5.78 (d, $J_{1,2}$ = 5.2 Hz)	
	OAc: 2.08–2.10	17.2
	CH_3: 1.69 (d, J = 10.5 Hz)	
 5	**H-1**α: 5.82 (dd), $J_{1,2}$ = 4.83 Hz, $J_{1,p}$ = 8.62 Hz	140.4 (α)
	H-1β: 5.32 (dd), $J_{1,2}$ = 4.83 Hz, $J_{1,p}$ = 10.5 Hz	139.2 (β)
	OAc: 1.91–2.19	
 41	**H-1**: 6.08 (d, $J_{1,2}$ = 5.0 Hz)	
	OAc: 2.06–2.12	15.9
	CH_3: 1.66 (d, J = 10.9 Hz)	
	CH_3-Fuc: 1.19 (d, J = 6.5 Hz)	
 56		126.8
 54		9.3

trimethylsilylated acceptor and TfOH. TfOH activates the phosphite to give the oxonium cation–triflate complex and hydrogen phosphite. The oxonium cation–triflate complex then reacts with the trimethylsilylated acceptor to give the glycoside and TMSOTf. The TMSOTf regenerated silylates the acceptor again and generates the catalyst TfOH for the next steps of reactions (Scheme 7a). Alternatively, TMSOTf may react with the donor first to generate the trivalent trimethylsilyl phosphite and the oxonium cation–triflate complex, which reacts with the acceptor to give the glycoside and TfOH (Scheme 7b). Reaction of the released TfOH with the trivalent trimethylsilyl phosphite gives the hydrogen phosphite and TMSOTf, which functions again as a catalyst. In this case, the oxonium cation–triflate complex also reacts with the trivalent trimethylsilyl phosphite to give the orthoester type of the pentavalent phosphonate (**25** or **41**). The pentavalent phosphonate can be converted to the glycoside in the presence of the acceptor and TMSOTf at higher temperature (>–40 °C); presumably, the reaction proceeds through protonation of the phosphonate to form the reactive oxonium cation intermediate. The released TfOH may also enter the TfOH activation pathway. Alternatively, TfOH can be used as a catalyst to activate the phosphite to give the glycoside.

(18) Hata, T.; Sekine, M. *J. Am. Chem. Soc.* **1974**, *96*, 7363. Evans, D. A.; Hurst, K. M.; Takacs, J. M. *J. Am. Chem. Soc.* **1978**, *100*, 3467. Burgerenko, E. F.; Chernyshew, E. A.; Popov, E. M. *Bull. Acad. Sci. USSR* **1966**, *15*, 1334.

(19) Weber, N. P. *Silicon reagents for organic synthesis*; Springer-Verlag: New York, 1983. Hadson, R. F. *Structure and mechanism in organo-phosphorus chemistry*; Academic Press: New York, 1965.

Use of Glycosyl Phosphites without Participating Substituents. To investigate glycosylation using phosphites without participating substituents at C-2, we next prepared 2,3,4,6-tetra-*O*-benzylglucopyranosyl phosphite **57** and examined its reaction with acceptor **19** in the presence of TMSOTf or TfOH. As shown in Scheme 8, both TMSOTf and TfOH served to promote the glycosylation in a catalytic fashion to give the only β glycosides in good yields. The rates are, however, faster than those with acetyl protecting groups, presumably due to the electronic effect and lack of neighboring group participation in the reactive oxonium ion triflate complex.[1a,b] A similar result was observed in the fucosylation of **15** wherein the α-fucoside **60** was obtained as a major product.

In summary, we have investigated the scope and mechanism of the glycosylation reaction using glycosyl phosphites in the presence of TMSOTf at low temperature. The activation proceeds through the reaction of glycosidic oxygen (instead of phosphorus) with the Lewis acid catalyst to form the reactive oxonium cation intermediate. Though the new glycosylation method is particularly useful for sialylation, it also finds use in the synthesis of other kinds of glycosides, including O-, S-, and C-glycosides, and glycopeptides.

Experimental Section

Compounds **1**, **2**, **5**, and **7** were prepared according to the procedures described previously.[4] Compounds **3**, **4**, and **16** were prepared previously.[16] Compounds **23** and **24** were reported.[3a] Compounds **11**–**14** and **21** were from Aldrich Co.

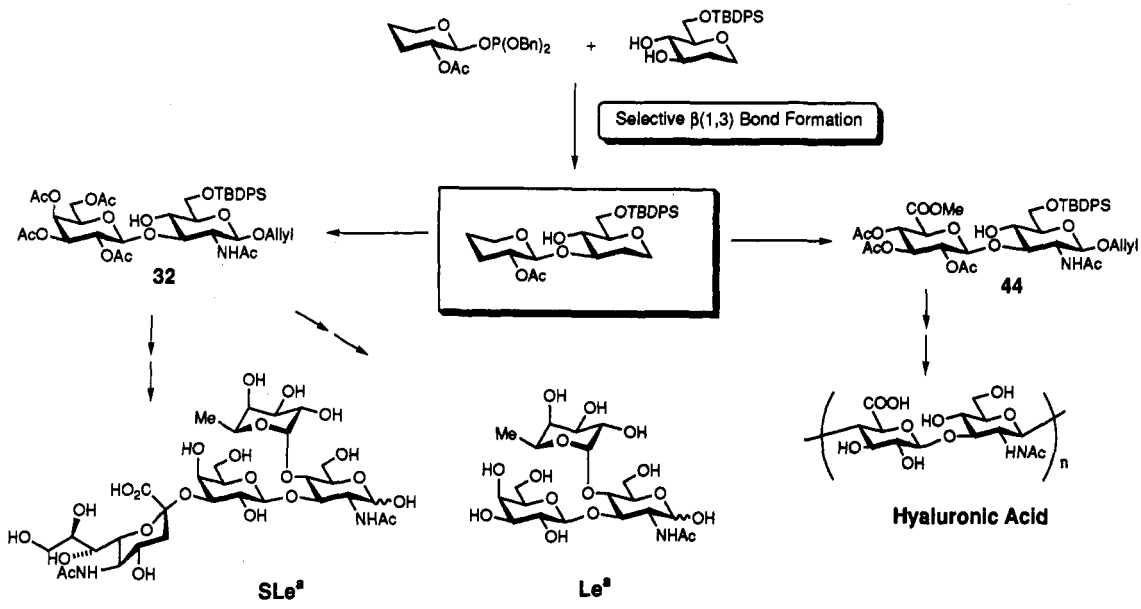
Dibenzyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl Phosphite (3). Dibenzyl *N*,*N*-diethylphosphoramidite (146 mg, 0.46 mmol) was added to a solution of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose (0.1 g, 0.23 mmol) and 1*H*-tetrazole (65 mg, 0.93 mmol) in dry THF (3 mL) under argon atmosphere at room temperature. The mixture was allowed to stir at room temperature for 2 h. The reaction mixture was diluted with CH_2Cl_2 and then washed with ice-cold saturated $NaHCO_3$, saturated NaCl, and water. The organic layer was separated and dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residual syrup was chromatographed by silica gel with EtOAc/hexane (1:3) to give **3** (140 mg, 88%): ^1H-NMR (400 MHz, $CDCl_3$) δ 5.97 (1H, t, J = 8.4 Hz, H-1), 5.89 (1H, dd, J = 9.2, 10.7 Hz, H-3), 5.22 (1H, dd, J = 9.3, 10.0 Hz, H-4), 4.46 (1H, dd, J = 8.4, 10.7 Hz, H-2).

Dibenzyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-[[(2,2,2-trichloroethoxy)carbonyl]amino]-D-glucopyranosyl Phosphite (4). Dibenzyl *N*,*N*-diethylphosphoramidite (527 mg, 1.66 mmol) was added to a solution of 3,4,6-tri-*O*-acetyl-2-deoxy-2-[[(2,2,2-trichloroethoxy)carbonyl]amino]-β-D-glucopyranose (0.2 g, 0.42 mmol) and 1*H*-tetrazole (116 mg, 1.66 mmol) in dry THF (3 mL) under argon atmosphere at room temperature. The mixture was allowed to stir at room temperature for 2 h. The reaction mixture was diluted with CH_2Cl_2 and then washed with ice-cold saturated $NaHCO_3$, saturated NaCl, and water. The organic layer was separated and dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residual syrup was chromatographed by silica gel with EtOAc/hexane (1:2) to give **4** as an anomeric mixture (225 mg, 67%).

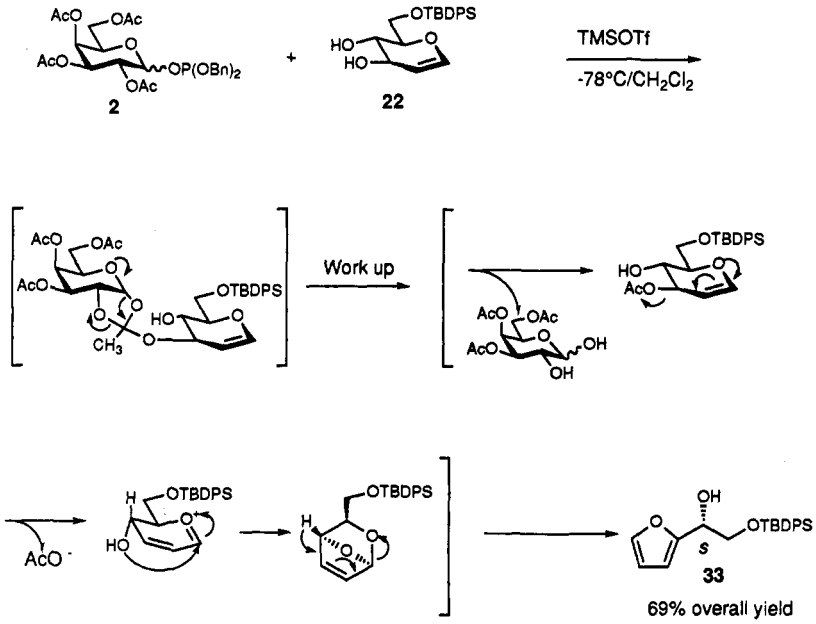
α-**4**: ^1H-NMR ($CDCl_3$) δ 2.01 (3H, s, CH_3CO), 2.02 (6H, s, 2 × CH_3CO), 3.89 (1H, dd, J = 2.2, 12.4 Hz, H-6), 4.00 (1H, m, H-5), 4.08 (1H, dt, J = 3.4, 10.4 Hz, H-2), 4.13 (1H, dd, J = 4.1, 12.5 Hz, H-6'), 4.53 (1H, d, J = 12.0 Hz), 4.76 (1H, d, J = 11.7 Hz), 4.87–4.96 (4H, m), 5.09 (1H, t, J = 9.8 Hz, H-4), 5.16–5.25 (2H, m, H-3, NH), 5.59 (1H, dd, J = 3.4, 7.7 Hz, H-1).

Methyl 2,3,4-Tri-*O*-acetyl-1-*O*-(dibenzylphosphityl)glucopyranuronate (6). Dibenzyl *N*,*N*-diethylphosphoramidite (1.8 g, 5.67 mmol) was added to a solution of methyl 2,3,4-tri-*O*-acetylglucopyranuronate (0.76 g, 2.27 mmol) and 1,2,4-triazole (0.66 g, 9.56 mmol) in dry THF (5 mL) under argon atmosphere at room temperature. The mixture was allowed to stir at room temperature for 2 h. The reaction mixture was diluted with

Scheme 3. Toward the Synthesis of Biologically Active β 1,3-Linked Oligosaccharides



Scheme 4. Proposed Mechanism for the Formation of 33



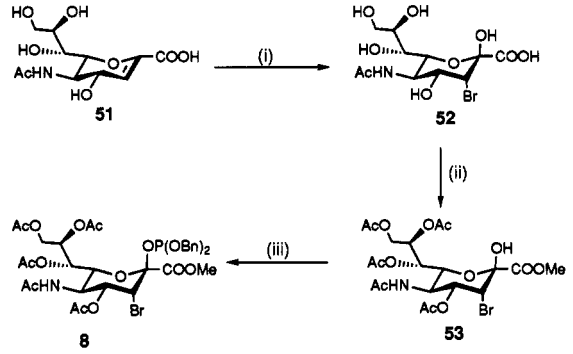
CH_2Cl_2, and then washed with ice-cold saturated $NaHCO_3$ and saturated NaCl. The organic layer was dried and concentrated *in vacuo*. The residual syrup was chromatographed by silica gel with EtOAc/hexane (1:1) to give **6** (0.83 g, 65%) as a 1:1 (α/β) mixture of anomers: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.85, 1.89, 2.01, 2.02, 2.02, 2.03 (3H, each s, OAc), 3.68, 3.70 (3H, each s, COOMe), 4.07 (1H, d, J = 9.6 Hz), 4.10 (1H, q, J = 7.2 Hz), 4.46 (1H, d, J = 10.2 Hz, H-5), 4.82–5.00 (10H, m), 5.12 (1H, dd, J = 2.0, 5.2 Hz), 5.20 (1H, dd, J = 9.7, 9.6 Hz), 5.26–5.28 (1H, m), 5.60 (1H, t, J = 9.7 Hz), 5.83 (1H, dd, J = 3.8, 8.3 Hz, H-1), 7.27–7.35 (10H, m, phenyl protons).

To synthesize methyl 2,3,4-tri-*O*-acetyl glucopyranuronate, glucurono-6,3-lactone (17.6 g, 0.1 mol) was added to MeOH (100 mL) containing sodium methoxide (0.15 g). The mixture was stirred at room temperature for 30 min. After MeOH was removed under reduced pressure, the syrup was dissolved in a mixture of acetic anhydride (50 mL) and pyridine (50 mL), and the reaction mixture was stirred for 24 h at room temperature. After the reaction was over, the reaction solvent was removed. The residue was chromatographed by silica gel column with AcOEt/hexane (1:1) to yield methyl tetra-*O*-acetyl glucopyranuronate (8 g) as a colorless solid: mp 173–175 °C; ^{1}H NMR ($CDCl_3$) δ 2.02, 2.04, 2.05, 2.19 (3H, each s, OAc), 3.75 (3H, s, COOMe), 4.42 (1H, d, J = 10.2 Hz, H-5), 5.12 (1H, dd, J = 3.7, 10.2 Hz, H-2), 5.23 (1H, dd, J = 9.6, 10.2 Hz, H-3), 5.52 (1H, dd, J = 9.6, 10.2 Hz, H-4), 6.40 (1H, d, J = 3.7 Hz, H-1).

This compound (0.9 g) was added to a 30% HBr solutoin, and the reaction mixture was stirred for 5 h at room temperature. After the reaction was over, the solvent was removed to obtain the crude syrup. To the crude residue dissolved in H_2O (10:1, v/v) was added silver carbonate, and the mixture was stirred for 30 min at room temperature. After the reaction was over, the product was isolated by silica gel column chromatography to give methyl 2,3,4-tri-*O*-acetyl glucopyranuronate (0.8 g): ^{1}H NMR ($CDCl_3$) δ 2.03, 2.04, 2.09 (3H, each s, OAc), 3.72 (3H, s, COOMe), 4.59 (1H, d, J = 10.0 Hz, H-5), 4.91 (1H, dd, J = 3.4, 9.6 Hz, H-2), 5.20 (1H, t, J = 9.6 Hz, H-3), 5.55 (1H, d, J = 3.4 Hz, H-1), 5.58 (1H, dd, J = 9.6, 10.0 Hz, H-4).

Methyl-3-Bromo-5-acetamido-4,7,8,9-tetra-*O*-acetyl-2-*O*-(dibenzylphosphityl)-3,5-dideoxy-β-D-*glycero*-D-*galacto*-2-nonulopyranosonate (8). Dibenzyl *N,N*-diethylphosphoramidite (0.14 g, 0.44 mmol) was added to a solution of methyl 3-bromo-5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosonate (0.1 g, 0.175 mmol) and 1,2,4-triazole (51 mg, 0.74 mmol) in dry THF (3 mL) under argon atmosphere at room temperature. The mixture was allowed to stir at room temperature for 2 h. The reaction mixture was diluted with CH_2Cl_2, and then it was washed with ice-cold saturated

Scheme 5. Chemoenzymatic Synthesis of 3-Bromosialyl Phosphite (8)



(i); CPO (chloroperoxydase) / H_2O_2 / KBr / pH3.0. (ii); Dowex 50WX8 (H^+); then $HClO_4$, Ac_2O. (iii); N,N-diethyl dibenzylphosphoramidate (2.5 eq.), 1H-tetrazol (4 eq.), THF, rt (69%).

[a] (i); CPO (chloroperoxydase)/H_2O_2/KBr/pH3.0. (ii); Dowex 50WX8 (H^+); then $HClO_4$, Ac_2O. (iii); N,N-diethyl dibenzylphosphoramidate (2.5 eq.), 1H-tetrazol (4 eq.), THF, rt (69%).

$NaHCO_3$, saturated NaCl, and water. The CH_2Cl_2 layer was separated and dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residual syrup was chromatographed by silica gel with EtOAc/hexane (5:1) to give **6** (125.5 mg, 88%) as a colorless syrup: ^{1}H-NMR ($CDCl_3$) δ 1.85, 2.02, 2.06, 2.07, 2.13 (3H, each s, OAc and NHAc), 3.72 (3H, s, COOMe), 3.89 (1H, dd, J = 2.0, 10.6 Hz, H-6), 4.23 (1H, dd, J = 7.6, 12.4 Hz, H-9′), 4.38 (1H, ddd, J = 10.0, 10.4, 10.6 Hz, H-5), 4.60 (1H, d, J = 3.6 Hz, H-3eq), 4.64 (1H, d, J = 10.0 Hz, NH), 4.75 (1H, dd, J = 2.3, 12.4 Hz, H-9), 4.91–4.96 (4H, m, benzyl protons), 5.09 (1H, dd, J = 3.6, 10.6 Hz, H-4), 5.17 (1H, dd, J = 2.0, 3.5 Hz, H-7), 5.23 (1H, ddd, 2.3, 3.5, 7.6 Hz, H-8), 7.30–7.47 (10H, m, phenyl protons); HRMS calcd for $C_{34}H_{41}NO_{15}BrPCs$ (M + Cs^+) 946.0452, found 946.0450/948. For the synthesis of benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-2-*O*-(dibenzylphosphityl)-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosonate (**9**), dibenzyl *N,N*-diethylphosphoramidite (2.17 g, 6.84 mmol) was added dropwise to a solution of benzyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-β-D-glycero-D-galacto-2-nonulopyranosonate[20] (1.64 g, 2.97 mmol) and 1-tetrazole (875 mg, 12.5 mmol) in THF (40 mL) at room temperature, and the reaction mixture was stirred for 5 h at room temperature. The mixture was diluted with CH_2Cl_2 and successively washed with ice-cold dilute H_2SO_4, water, aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed on SiO_2 with hexane/AcOEt (1:3, v/v) to give a mixture of **9** (740 mg, 31%) as a crude product. This product **9** was used for the next step without further purification.

Dibenzyl 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1,4)-2,3,6-tri-*O*-acetyl-D-glucopyranosyl Phosphite (10). 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1,4)-2,3,6-tri-*O*-acetylglucopyranose is a precursor of the lactosylation donor **10**. A solution of peracetylated lactose (0.5 g, 0.737 mmol) and benzylamine (125 μL) in THF (5 mL) was stirred at room temperature for 38 h. The mixture was added to chloroform (100 mL) and washed with 2 × 50 mL of 0.1 N HCl followed by 50 mL of saturated $NaHCO_3$. The organic layer was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was chromatographed (AcOEt/n-hexane, (1:1–7:3)) to give 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1,4)-2,3,6-tri-*O*-acetylglucopyranose (415 mg, 89%) as a mixture of anomers: ^{1}H-NMR ($CDCl_3$) δ 1.97, 2.03, 2.05, 2.06, 2.07, 2.08, 2.12, 2.13, 2.16 (each s, OAc), 3.62–3.69 (m), 3.78 (t, J = 9.4 Hz), 3.89 (t, J = 7.0 Hz), 4.04–4.22 (m), 4.42 (d, J = 5.7 Hz), 4.45–4.53 (m), 4.74 (t, J = 7.5 Hz), 4.82 (dd, J = 3.5, 10.0 Hz), 4.97 (dd, J = 3.3, 10.4 Hz), 5.08–5.17 (m), 5.23 (t, J = 9.2 Hz), 5.32–5.39 (m), 5.53 (t, J = 9.6 Hz).

A solution of 2,3,4,6-tetra-*O*-acetyl-D-galactopyranosyl-β(1,4)-2,3,6-tri-*O*-acetylglucopyranose (144 mg, 0.212 mmol), 1,2,4-triazole (103 mg), and dibenzyl *N,N*-diethylphosphoramidite (200 μL) in methylene chloride (3 mL) was stirred for 2 h at room temperature. The mixture was added to methylene chloride (20 mL) and washed with 10 mL of saturated $NaHCO_3$ and water (10 mL). The organic layer was dried with Na_2SO_4, filtered, and concentrated under vacuum. The residue was chromatographed (hexane/AcOEt (7:3–1:1)) to give **10** (172 mg, 92%) as a mixture of anomers: ^{1}H-NMR ($CDCl_3$) δ 1.88, 1.92, 1.98, 2.04, 2.05, 2.07, 2.18 (each s, OAc), 3.68 (ddd, J = 1.8, 4.9, 9.9 Hz), 3.74–3.91 (m), 4.02–4.20 (m), 4.43–4.52 (m), 4.80–5.16 (m), 5.22 (t, J = 9.1 Hz), 5.35 (dd, J = 0.8, 3.4 Hz), 5.54 (t, J = 10.1 Hz, H-1β), 5.69 (dd, J = 3.5, 8.5 Hz, H-1α), 7.23–7.45 (m); FAB MS 1013 (M^+).

Allyl 2-Acetamido-2-deoxy-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (18). A solution of allyl 2-acetamido-2-deoxy-β-D-glucopyranoside (7.0 g, 26.8 mmol), imidazole (2.0 g, 29.5 mmol), and *t*-Bu(Ph)$_2$SiCl (8.10 g, 29.5 mmol, 7.66 mL) in DMF (150 mL) was stirred for 10 h at room temperature. Water (2 mL) was added to the cooled mixture, and the mixture was concentrated. The residue was chromatographed on silica gel, with $CHCl_3$ (EtOAc/MeOH (6:3:1)), to give **18** (88%): ^{1}H-NMR ($CDCl_3$) δ 1.03 (9H, s, *t*-Bu), 2.02 (3H, s, NHAc), 3.41 (1H, ddd, J = 3.41, 5.58, 9.31 Hz, H-5), 3.50–3.54 (1H, m, H-2), 3.54 (1H, t, J = 9.20 Hz, H-4), 3.69 (1H, dd, J = 8.65, 10.05 Hz, H-3), 3.87 (1H, dd, J = 5.58, 10.98 Hz, H-6), 3.96 (1H, dd, J = 3.28, 10.98 Hz, H-6′), 4.50 (1H, d, J = 8.21 Hz, H-1), 6.23 (1H, d, J = 6.07 Hz, NH); ^{13}C-NMR ($CDCl_3$) δ 19.2, 23.6, 26.7, 57.6, 64.0, 69.4, 72.0, 75.1, 75.8, 99.3, 117.9, 127.6, 127.7, 129.7, 133.2, 133.3, 133.6, 135.6, 135.7, 172.4.

Benzyl 3-*O*-Acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (20). A solution of benzyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (15.68 g, 2.98 mmol) in methanol (50 mL) was treated with sodium methoxide (1.6 mL of a 25% solution in methanol). After 1 h the solution was neutralized with Dowex 50 H^+ resin, filtered, and concentrated. The residue was dissolved in acetone (180 mL), 2,2-dimethoxypropane (180 mL) and a catalytic amount of *p*-toluenesulfonic acid were added, and the solution was stirred overnight. The precipitate was filtered off, and to the filtrate was added aqueous $NaHCO_3$, which was stirred, filtered, and concentrated *in vacuo*. The residue was diluted with chloroform and washed with brine, dried with Na_2SO_4, filtered, concentrated, and crystallized with chloroform–toluene to give benzyl 2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-D-glucopyranoside (10.41 g, 79%); mp 205 °C; ^{1}H-NMR ($CDCl_3$) δ 1.42, 1.52 (3H, each s, CH_3C), 3.45 (1H, dt, J = 5.4, 9.8 Hz, H-5), 3.65 (1H, t, J = 9.2 Hz, H-4), 3.86 (1H, t, J = 10.4 Hz, H-6), 4.00 (1H, dd, J = 5.5, 10.8 Hz, H-6′), 4.23 (1H, dd, J = 8.5, 10.4 Hz, H-2), 4.45 (1H, dd, J = 8.9, 10.4 Hz, H-3), 4.49 (1H, d, J = 12.3 Hz, $PhCH_2$), 4.81 (1H, d, J = 12.3 Hz, $PhCH_2$), 5.22 (1H, d, J = 8.4 Hz, H-1), 7.00–7.08 (5H), 7.68–7.76 (4H); HRMS calcd for $C_{24}H_{25}NO_7Cs$ (M + Cs^+) 572.0685, found 572.0691.

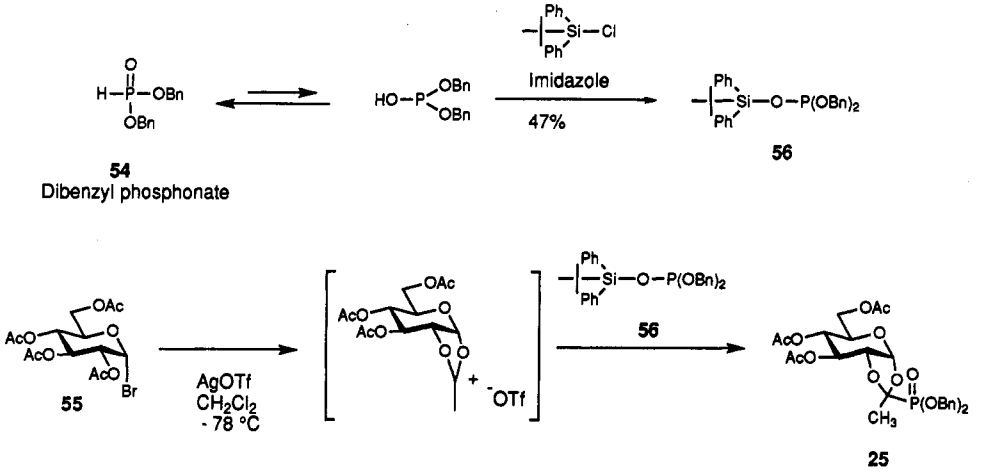
Benzyl 2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-D-glucopyranoside (1.0 g, 2.28 mmol) was stirred in pyridine–acetic anhydride (30 mL, 2:1) for 2.5 h. The solution was evaporated *in vacuo*, coevaporated twice with toluene, dissolved in 60% aqueous acetic acid (40 mL), and stirred at 60 °C for 20 min. The solution was cooled, evaporated, and subjected to column chromatography (AcOEt) to give **20** (739 mg, 72%): ^{1}H-NMR ($CDCl_3$) δ 1.94 (3H, s, OAc), 2.13 (1H, m, 6-OH), 2.96 (1H, d, J = 5.2 Hz, 2-OH), 3.63 (1H, m, H-5), 3.80 (1H, dd, J = 4.9, 9.3 Hz, H-4), 3.88 (1H, m, H-6), 3.99 (1H, m, H-6), 4.28 (1H, dd, J = 8.5, 10.7 Hz, H-2), 4.57 (1H, d, J = 12.2 Hz, $PhCH_2$), 4.82 (1H, d, J = 12.3 Hz, $PhCH_2$), 5.41 (1H, d, J = 8.5 Hz, H-1), 5.65 (1H, dd, J = 8.9, 10.7 Hz, H-3), 7.00–7.14 (5H), 7.71–8,80 (4H); HRMS calcd for $C_{23}H_{23}NO_8Cs$ (M + Cs^+) 574.0478, found 574.0478.

6-*O*-*tert*-Butyldiphenylsilyl Glucal (22). To a solution of glucal (2.14 g, 14.6 mmol) and imidazole (1.1 g, 16.1 mmol) in DMF (60 mL) was added *tert*-butyldiphenylsilyl chloride (4.42 g, 16.1 mmol) slowly at 5 °C. After the reaction was over, water (8 mL) was added and the reaction mixture was stirred at room temperature for 30 min. The precipitated solid was removed with a filter, and the filtrate was concentrated. The obtained crude oil was purified by silica gel column chromatograph ($CHCl_3$/MeOH (15:1)) to give **22** (5.2 g) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 1.08 (9H, s, *t*-Bu), 3.11 (1H, bs, OH), 3.50 (1H, bs, OH), 3.81 (1H, dt, J = 4.0, 9.5 Hz, H-5), 3.90 (1H, dd, J = 7.0, 9.5 Hz, H-4), 3.96 (1H, dd, J = 4.0, 11.2 Hz, H-6), 4.00 (1H, dd, J = 4.0, 11.2 Hz, H-6′), 4.28 (1H, dt, J = 1.8, 7.0 Hz, H-3), 4.72 (1H, dd, J =

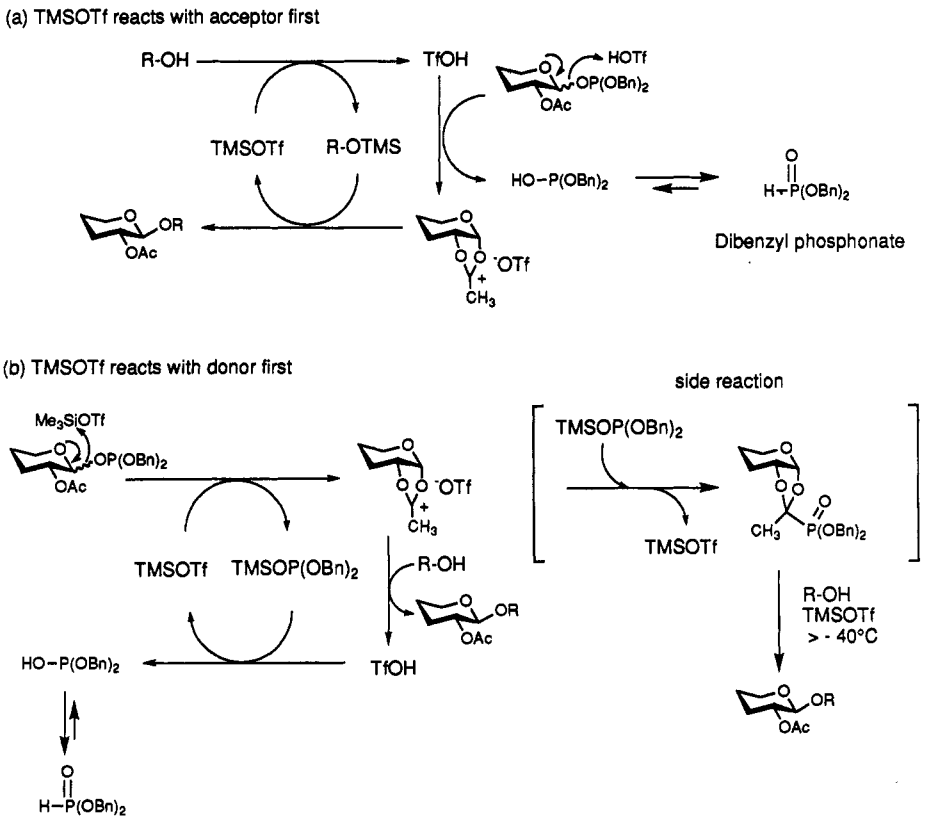
(20) Ratcliffe, M. R.; Venot, A. P.; Abbas, Z. S. Eur. Pat. Appl. EP 319253; *Chem. Abstr.* **1990**, *112*, 175281a.

(21) Garegg, P. J.; Hultberg, H.; Wallin, S. *Carbohydr. Res.* **1982**, *108*, 97.

Scheme 6. Preparation of Silyl Phosphite and its Addition to Orthoester Generated in Situ



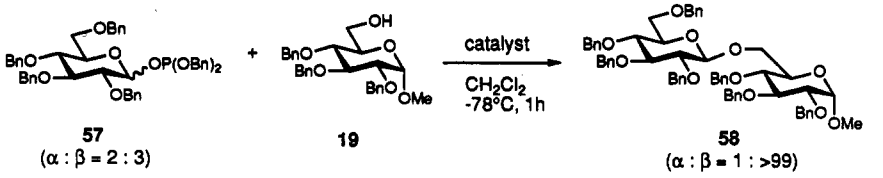
Scheme 7. Proposed Mechanism of Glycosylation Using Phosphites Having a Participating Substituent on C-2



2.2, 6.0 Hz, H-2), 6.31 (1H, dd, J = 1.7, 6.0 Hz, H-1); HRMS calcd for $C_{22}H_{28}O_4SiNa$ (M + Na^+) 407.1655, found 407.1661.

***p*-Methylphenyl 2,3,4,6-Tetra-*O*-acetyl-1-thio-D-glucopyranoside (26).** Dibenzyl 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl phosphite (1) was made according to our previous paper.[3] A solution of 1 (80 mg, 0.135 mmol) and *p*-methylthiophenol (13) (19 mg, 0.135 mmol) and molecular sieves (3 Å) in CH_2Cl_2 (0.8 mL) was cooled to −78 °C, and then TMSOTf (16 mg, 0.067 mmol) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N and washed with saturated

Scheme 8. Results of Glycosylation Using Benzyl-Protected Glycosyl Phosphites (57 and 59)



57 (α : β = 2 : 3) + 19 → 58 (α : β = 1 : >99)

Entry	Catalyst (eq)	Yield (%)
1	TMSOTf (1.2)	62
2	TMSOTf (0.3)	66
3	TfOH (0.3)	72
4	Tf_2O (0.3)	66

59 + 15 → 60 (α : β = 3 : 1)

$NaHCO_3$, aqueous NaCl, and ice–water. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (AcOEt/n-hexane (1:1)) to give **26** (19 mg, 32%) and **25** (29 mg, 36%) as a colorless oil.

26: ^{1}H-NMR ($CDCl_3$) δ 1.98, 2.01, 2.08, 2.09 (3H, each s, OAc), 2.35 (3H, s, phenyl-CH_3), 3.70 (1H, ddd, J = 2.7, 4.7, 10.1 Hz, H-5), 4.15–4.24 (2H, m, H-6 and H-6′), 4.63 (1H, d, J = 10.0 Hz, H-1), 4.93 (1H, dd, J = 9.4, 10.0 Hz, H-2), 5.02 (1H, dd, J = 9.3, 10.1 Hz, H-4), 5.20 (1H, dd, J = 9.3, 9.4 Hz, H-3), 7.12 (2H, d, J = 7.9 Hz, phenyl protons), 7.39 (2H, d, J = 8.1 Hz, phenyl protons); ^{13}C-NMR ($CDCl_3$) δ 20.6, 20.8, 21.2, 62.1, 68.1, 69.8, 73.9, 75.7, 85.8, 129.6, 133.8, 165.6, 165.8, 167.8, 169.2; HRMS calcd for $C_{21}H_{26}NO_9SCs$ (M + Cs^+) 587.0352, found 587.0355.

25: ^{1}H-NMR ($CDCl_3$) δ 1.69 (3H, d, J_{CH_3P} = 10.5 Hz, CH_3), 2.08, 2.094, 2.098 (3H, each s, OAc), 4.00–4.04 (1H, m, H-4), 4.20 (2H, bd, J = 4.1 Hz, H-6 and H-6′), 4.65–4.67 (1H, m, H-5), 4.87 (1H, dd, J = 2.6, 9.5 Hz, H-3), 5.06–5.11 (4H, m, benzyl protons), 5.19 (1H, dd, J = 2.6, 5.2 Hz, H-2), 5.87 (1H, d, J = 5.2 Hz, H-1), 7.34–7.37 (10H, m, phenyl protons); ^{13}P-NMR (acetone-d_6) δ 17.2 ppm; HRMS calcd for $C_{28}H_{33}O_{12}PCs$ (M + Cs^+) 725.0764, found 725.0764.

Synthesis of 26 Using Phosphonate 25. A solution of **25** (20 mg, 0.034 mmol) in CH_2Cl_2 (0.3 mL) was added to a solution of **13** (4.2 mg, 0.034 mmol), TMSOTf (7.5 mg, 0.034 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (0.2 mL) at −40 °C for 20 min. The solution was kept at room temperature and stirred for 1 h. The reaction was quenched with saturated aqueous $NaHCO_3$ diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (AcOEt/n-hexane (1:1) to give **26** (9.6 mg, 63%) as a colorless oil.

Methyl 6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-D-glucopyranoside (27). A mixture of **1** (80 mg, 0.135 mmol), **19** (63 mg, 0.135 mmol) and molecular sieves 3Å in CH_2Cl_2 (0.8 mL) was cooled to −78 °C, and then TMSOTf (16 mg, 0.067 mmol) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N and washed with saturated $NaHCO_3$, aqueous NaCl, and ice–water. The organic solvents were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (Et_2O/n-hexane, (10:1)) to give **27** (15 mg, 25%) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 2.02 (3H, s, OAc), 3.37 (3H, s, OMe), 3.47 (1H, t, J = 9.0 Hz, H-4), 3.53 (1H, dd, J = 3.5, 9.6 Hz, H-2), 3.79–3.83 (1H, m, H-5), 4.0 (1H, dd, J = 9.0, 9.6 Hz, H-3), 4.22–4.26 (2H, m, H-6 and H-6′), 4.55 (1H, d, J = 10.8 Hz, benzyl proton), 4.59 (1H, d, J = 3.5 Hz, H-1), 4.66 (1H, d, J = 12.1 Hz, benzyl proton), 4.78–4.88 (3H, m, benzyl protons), 5.01 (1H, d, J = 10.8 Hz, benzyl proton).

Cyclohexyl 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranoside (28). A mixture of **2** (80 mg, 0.135 mmol), **11** (13.3 mg, 0.135 mmol) and molecular sieves (3 Å) in CH_2Cl_2 (0.8 mL) was cooled to −78 °C, and then TMSOTf (16 mg, 0.067 mmol) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N and washed with saturated $NaHCO_3$, aqueous NaCl, and ice–water. The organic solvent was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (n-hexane/AcOEt (1:1)) to give **28** (27 mg, 47%) and the byproduct **29** (6.8 mg, 13%) as colorless oil.

28: ^{1}H-NMR ($CDCl_3$) δ 1.20–1.90 (10H, m, cyclohexyl protons), 1.98, 2.04, 2.05, 2.14 (3H, each s, OAc), 3.60–3.64 (1H, m, O-cyclohexyl proton), 3.88 (1H, ddd, J = 1.0, 6.5, 7.2 Hz, H-5), 4.11 (1H, dd, J = 7.2, 11.2 Hz, H-6), 4.02 (1H, dd, J = 6.5, 11.2 Hz, H-6′), 4.54 (1H, d, J = 8.0 Hz, H-1), 5.02 (1H, dd, J = 3.4, 10.4 Hz, H-3), 5.19 (1H, dd, J = 8.0, 10.4 Hz, H-2), 5.38 (1H, dd, J = 1.0, 3.4 Hz, H-4).

29: ^{1}H-NMR ($CDCl_3$) δ 1.20–1.80 (10H, m, cyclohexyl protons), 2.04, 2.05, 2.12 (3H, each s, OAc), 3.64–3.69 (1H, m, *O*-cyclohexyl proton), 3.78 (1H, dd, J = 7.8, 10.2 Hz, H-2), 3.89 (1H, ddd, J = 1.1, 6.6, 7.0 Hz, H-5), 4.09 (1H, dd, J = 7.0, 11.1 Hz, H-6), 4.20 (1H, dd, J = 6.6, 11.1 Hz, H-6′), 4.44 (1H, d, J = 7.8 Hz, H-1), 4.94 (1H, dd, J = 3.5, 7.0 Hz, H-3), 5.38 (1H, dd, J = 1.1, 3.5 Hz, H-4); HRMS calcd for $C_{18}H_{28}O_9Cs$ (M + Cs^+) 521.0788, found 521.0780.

***p*-Methylphenyl 2,3,4,6-Tetra-*O*-acetyl-1-thio-D-galactopyranoside (30).** Dibenzyl 2,3,4,6-tetra-*O*-acetyl-D-galactopyranosyl phosphite (**2**) was made according to our previous paper.[4] A mixture of **2** (110 mg, 0.186 mmol), *p*-methylthiophenol (**13**) (26.4 mg, 0.186 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (0.8 mL) was cooled to −78 °C, and then TMSOTf (13.2 mg, 0.06 mmol) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N and washed with saturated $NaHCO_3$, aqueous NaCl, and ice–water. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (AcOEt/n-hexane (1:1)) to give **30** (58 mg, 69%) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 1.97, 2.04, 2.10, 2.11 (3H, each s, OAc), 2.34 (3H, s, phenyl-CH_3), 3.92 (1H, dt, J = 1.0, 6.12 Hz, H-5), 4.11 (1H, dd, J = 6.32, 11.3, Hz, H-6), 4.19 (1H, dd, J = 7.0, 11.3 Hz, H-6′), 4.64 (1H, d, 10.0 Hz, H-1), 5.04 (1H, dd, J = 3.3, 10.0 Hz, H-3), 5.22 (1H, t, J = 10.0 Hz, H-2), 5.40 (1H, dd, J = 1.0, 3.3 Hz, H-4), 7.12 (2H, d, J = 7.8 Hz, phenyl protons), 7.41 (2H, d, J = 8.1 Hz, phenyl protons); HRMS calcd for $C_{21}H_{26}NO_9SCs$ (M + Cs^+) 587.0352, found 587.0351.

Methyl 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1,4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (31). A 10% solution of TMSOTf in CH_2Cl_2 (74 μL, 0.038 mmol) was added dropwise to a mixture of dibenzyl 2,3,4,6-tetra-*O*-acetyl-D-galactopyranosyl phosphite (2.75 mg, 0.13 mmol), methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (15.69 mg, 0.13 mmol), and molecular sieves (4 Å) in anhydrous CH_2Cl_2 (1.6 mL) at −78 °C. After being stirred for 30 min at the same temperature, the reaction was quenched with saturated aqueous $NaHCO_3$, warmed to room temperature, and extracted with CH_2Cl_2. The combined organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The remaining residue was purified by SiO_2 gel column chromatography (AcOEt/*n*-Hex) to provide **31** as colorless syrup (66 mg, 66% yield): ^{1}H NMR ($CDCl_3$) δ 1.95, 1.96, 2.00, 2.09 (3H, each s, O_2CCH_3), 3.37 (3H, s, OCH_3), 3.51 (1H, dd, *J* = 3.6, 9.6 Hz, Glu-H-2), 3.50 (1H, dd, *J* = 9.0, 9.5 Hz, Glu-H-4), 3.59 (1H, dd, *J* = 1.9, 10.5 Hz, Glu-H-6), 3.63 (1H, brddd, Glu-H-5), 3.74 (1H, dd, *J* = 2.8, 10.5 Hz, Glu-H-6), 3.86 (1H, dd, *J* = 9.5, 9.6 Hz, Glu-H-3), 3.89 (2H, m, Gal-H-5, Gal-H-6), 3.96 (1H, dd, *J* = 8.2, 11.2 Hz, Gal-H-6), 4.41 (1H, d, *J* = 12.1 Hz, one of OCH_2Ph), 4.46 (1H, d, *J* = 8.0 Hz, Gal-H-1), 4.59 (1H, d, *J* = 3.6 Hz, Glu-H-1), 4.63 (1H, d, *J* = 12.4 Hz, one of OCH_2Ph), 4.75 (1H, dd, *J* = 3.4, 10.4 Hz, Gal-H-3), 4.75 (1H, d, *J* = 12.9 Hz, two of OCH_2Ph), 4.82 (1H, d, *J* = 10.8 Hz, one of OCH_2Ph), 4.95 (1H, d, *J* = 10.9 Hz, one of OCH_2Ph), 5.08 (1H, dd, *J* = 8.0, 10.4 Hz, Gal-H-2), 5.24 (1H, dd, *J* = 3.4, 0.8 Hz, Gal-H-4), 7.25–7.42 (15H, m, aromatic protons); ^{13}C NMR ($CDCl_3$) δ 20.6, 20.6, 20.8, 29.7, 55.4, 60.6, 66.7, 67.5, 69.6, 70.0, 70.3, 71.1, 73.5, 73.7, 75.2, 78.9, 79.7, 98.4, 100.1, 127.3, 127.5, 127.8, 128.1, 128.2, 128.4, 128.6, 137.6, 138.3, 139.22, 169.1, 170.1, 170.2, 170.2; IR (neat) 3088, 3030, 2932, 2869, 1748, 1497, 1454, 1369, 1223, 1048, 912, 735, 699 cm^{-1}; HRMS calcd for $C_{42}H_{50}O_{15}Cs$ (M + Cs^+) 927.2204, found 927.2211; $[\alpha]^{25}_D$ = −3(*c* 0.5, $CHCl_3$).

Allyl 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1,3)-2-acetamido-2-deoxy-6-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (32). A mixture of **2** (64 mg, 0.128 mmol) and **18** (76 mg, 0.128 mmol) and molecular sieves (3 Å) in CH_2Cl_2 (2 mL) was cooled to −78 °C, and TMSOTf (14 mg, 0.063 mmol) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N–CH_2Cl_2 and washed with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel ($CHCl_3$/MeOH (15:1)) to give **32** (66 mg, 62%) as colorless plates: mp 179–181 °C; ^{1}H-NMR ($CDCl_3$) δ 1.08 (9H, s, t-Bu), 1.72, 1.99, 2.03, 2.06, 2.16 (3H, each s, OAc and NHAc), 3.42 (1H, bd, *J* = 8.7 Hz, GlcN-H-5), 3.54 (1H, ddd, *J* = 7.9, 8.0, 9.5 Hz, GlcN-H-2), 3.80–3.85 (3H, m, GlcN-H-4, GlcN-H-6, Gal-H-6), 3.89–3.95 (2H, m, GlcN-H-6′ and Gal-H-6′), 4.00 (1H, dd, *J* = 9.12, 9.44 Hz, GlcN-H-3), 4.06 (1H, dd, *J* = 6.0, 12.8 Hz, allylic proton), 4.14 (1H, bd, *J* = 6.56 Hz, GalN-H-5), 4.32 (1H, dd, *J* = 5.0, 12.8 Hz, allylic proton), 4.70 (1H, d, *J* = 8.0 Hz, Gal-H-1), 4.77 (1H, d, *J* = 8.0 Hz, GlcN-H-1), 4.97 (1H, dd, *J* = 3.4, 10.4 Hz, Gal-H-3), 5.189 (1H, dd, *J* = 1.16, 10.4 Hz, allylic proton), 5.19 (1H, dd, *J* = 8.0, 10.4 Hz, Gal-H-2), 5.26 (1H, dd, *J* = 1.6, 17.0 Hz, allylic proton), 5.36 (1H, bd, *J* = 3.4 Hz, Gal-H-4), 5.64 (1H, d, *J* = 8.0 Hz, NH), 5.84–5.94 (1H, m, allylic proton), 7.37–7.43 (6H, m, phenyl protons), 7.71–7.75 (4H, m, phenyl protons); ^{13}C-NMR ($CDCl_3$) δ 19.31, 20.31, 20.50, 20.55, 20.60, 23.64, 26.79, 55.66, 61.18, 61.87, 66.85, 68.79, 69.26, 70.75, 71.22, 71.26, 74.52, 79.81, 98.87, 100.90, 117.42, 127.63, 127.65, 127.86, 129.84, 129.89, 133.88, 135.48, 135.93, 169.17, 169.90, 170.10, 170.38, 170.46; HRMS calcd for $C_{41}H_{55}NO_{15}SiCs$ (M + Cs^+) 962.2395, found 962.2380.

1-[(*tert*-Butyldiphenylsilyl)oxy]-2-furanylethanol (33). A mixture of **2** (500 mg, 0.845 mmol), 6-*tert*-butyldiphenylsilyl glucal (**22**) (324 mg, 0.845 mmol), and molecular sieves (4 Å) in CH_2Cl_2 (5 mL) was cooled to −78 °C, and then TMSOTf (187 mg, 0.845 mmol) was added. After being stirred for 2 h at −78 °C, the reaction was quenched with Et_3N–CH_2Cl_2 and washed with saturated $NaHCO_3$, aqueous NaCl, and ice–water. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (AcOEt/n-hexane (1:4)) to give **33** (213 mg, 69%) as a colorless oil: $[\alpha]^{25}_D$ + 52.8 (*c* 0.32, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.06 (9H, s, t-Bu), 2.88 (1H, d, *J* = 4.4 Hz, OH), 3.87–3.95 (2H, m, H-1 and H-1′), 4.82 (1H, dd, *J* = 4.4, 10.6 Hz, H-2), 6.28 (1H, bd, *J* = 3.2 Hz, furanyl proton), 6.32 (1H, dd, *J* = 1.8, 3.2 Hz, furanyl proton), 7.34 (1H, m, furanyl proton), 7.37–7.42 (6H, m, phenyl protons), 7.60–7.66 (4H, m, phenyl protons).

For further characterization, compound **33** was converted to the acetyl derivative by treatment with acetic anhydride–pyridine–DMAP. The product was purified with silica gel preparative TLC: ^{1}H-NMR ($CDCl_3$) δ 1.01 (9H, s, t-Bu), 2.05 (3H, s, OAc), 3.94 (1H, dd, *J* = 5.0, 10.7 Hz, H-1), 4.05 (1H, dd, *J* = 7.6, 10.7 Hz, H-1′), 6.04 (1H, dd, *J* = 5.0, 7.6 Hz, H-2), 6.31 (1H, dd, *J* = 1.18, 3.1 Hz, furanyl proton), 6.34 (1H, bd, *J* = 3.1 Hz, furanyl proton), 7.34 (1H, dd, *J* = 0.9, 1.8 Hz, furanyl proton), 7.35–7.43 (6H, m, phenyl protons), 7.60–7.66 (4H, m, phenyl protons); ^{13}C-NMR ($CDCl_3$) δ 19.2, 20.9, 26.5, 63.7, 69.1, 109.2, 110.2, 127.7, 129.7, 129.7, 135.53, 135.57, 142.53, 150.4, 170.1; HRMS calcd for $C_{24}H_{28}O_4SiCs$ (M + Cs^+) 541.0811, found 541.0818.

Benzyl 3-*O*-Acetyl-6-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (34). A solution of **3** (140 mg, 0.22 mmol) in CH_2Cl_2 (1 mL) was added to a mixture of **20** (99 mg, 0.23 mmol), TMSOTf (22 μL, 0.12 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (2 mL) at −78 °C. After 3 h, when the solution reached room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$, diluted with CH_2Cl_2, and washed with saturated $NaHCO_3$. The organic solvent was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/AcOEt (2:3)) to give **34** (97 mg, 49%) as a colorless syrup: $[\alpha]^{25}_D$ −21.2° (*c* 0.8, $CDCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.84, 1.88, 2.04, 2.13 (3H, each s, OAc), 3.01 (1H, OH), 3.47 (1H, t, *J* = 9.3 Hz, H-4), 3.65–3.71 (1H, m, H-5), 3.79–3.91 (2H, H-5′ and H-6), 4.10–4.35 (4H, H-6, 2 × H-6′, benzyl protons), 4.12 (1H, dd, *J* = 8.5, 10.7 Hz, H-2), 4.41 (1H, dd, *J* = 8.5, 10.7 Hz, H-2′), 4.56 (1H, d, *J* = 12.2 Hz, benzyl protons), 5.21 (1H, t, *J* = 9.6 Hz, H-4′), 5.23 (1H, d, *J* = 8.6 Hz, H-1), 5.55 (1H, dd, *J* = 8.8, 10.6 Hz, H-3), 5.56 (1H, d, *J* = 8.5 Hz, H-1′), 5.82 (1H, dd, *J* = 9.2, 10.6 Hz, H-3′), 6.97–7.11 (5H, phenyl protons), 7.62–7.79 (8H, phthalimido protons); ^{13}C-NMR ($CDCl_3$) δ 20.4, 20.6, 20.7, 54.4, 61.7, 68.7, 70.2, 70.5, 70.6, 71.9, 73.2, 74.9, 96.6, 98.3, 123.4, 136.8, 167.5, 169.4, 170.2, 170.8, 171.2; HRMS calcd for $C_{43}H_{42}N_2O_{17}Cs$ (M + Cs^+) 991.1538, found 991.1546.

Benzyl 3-*O*-Acetyl-6-*O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-[[(2,2,2-trichloroethoxy)carbonyl]amido]-β-D-glucopyranosyl]-2-deoxy-2-phthalimido-β-D-glucopyranoside (35). A solution of **4** (124 mg, 0.17 mmol) in CH_2Cl_2 (1 mL) was added to a mixture of **20** (74 mg, 0.17 mmol), TMSOTf (17 μL, 0.09 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (2 mL) with stirring at −78 °C. After 3 h, when the solution reached room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$/CH_2Cl_2 and washed with saturated $NaHCO_3$. The organic solvent was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/AcOEt (2:3)) to give **35** (97 mg, 63%) as a colorless syrup: $[\alpha]^{25}_D$ −24.7° (*c* 0.8, $CDCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.85, 2.02, 2.05 (3H, each s, OAc), 3.00–3.11 (2H), 3.63–3.80 (4H), 3.92 (1H, dd, *J* = 4.2, 11.4 Hz, H-3), 4.16–4.32 (4H), 4.55 (1H, d, *J* = 12.4 Hz, benzyl proton), 4.66 (1H, d, *J* = 12.4 Hz, CH_2-CCl_3), 4.79 (1H, d, *J* = 12.4 Hz, CH_2-CCl_3), 4.84 (1H, d, *J* = 12.4 Hz, benzyl proton), 5.08 (1H, t, *J* = 9.6 Hz, H-4′), 5.26 (1H, t, *J* = 9.9 Hz, H-3′), 5.35 (2H, d, *J* = 8.4 Hz, H-1 and H-1′), 5.63 (1H, dd, *J* = 8.3, 10.7 Hz, H-3), 7.05–7.12 (5H, phenyl protons), 7.70–7.82 (4H, phenyl protons); ^{13}C-NMR ($CDCl_3$) δ 20.6, 20.7, 54.6, 55.9, 61.9, 68.5, 69.8, 71.1, 71.7, 72.0, 73.2, 74.4, 74.8, 95.3, 97.3, 101.1, 123–137.0, 154.3, 167.6, 169.4, 170.6, 170.8, 171.1; HRMS calcd for $C_{38}H_{41}C_{13}N_2O_{17}Cs$ (M + Cs^+) 1035.0525, found 1035.0558.

Cyclohexyl 6-Deoxy-2,3,4-tri-*O*-acetyl-β-L-galactopyranoside (36). A mixture of **11** (12.8 mg, 0.128 mmol), **5** (70 mg, 0.128 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (0.7 mL) was cooled to −78 °C, and TMSOTf (14.5 mg, 0.064 mmol) was added. After being stirred for 30 min at −78 °C, the reaction was quenched with Et_3N–CH_2Cl_2 and washed with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was separated by preparative TLC (Merck Art 5744, AcOEt/hexane (1:1)) to give **36** (28.5 mg, 60%) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 1.21 (3H, d, *J* = 6.4 Hz, Fuc-CH_3), 1.22–1.85 (10H, m, cyclohexyl protons), 1.98, 2.04, 2.16 (3H, each s, OAc), 3.56–3.64 (1H, m, *O*-cyclohexyl proton), 3.78 (1H, dq, *J* = 0.9, 6.4 Hz, H-5), 4.51 (1H, d, *J* = 7.9

Hz, H-1), 5.01 (1H, dd, J = 3.4, 10.4 Hz, H-3), 5.16 (1H, dd, J = 7.9, 10.4 Hz, H-2), 5.22 (1H, dd, J = 0.9, 3.4 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 16.1, 20.6, 20.7, 20.8, 23.6, 23.7, 25.4, 31.6, 33.3, 69.0, 69.2, 70.3, 71.4, 76.7, 77.0, 77.3, 99.6, 169.5, 170.3, 170.8.

2′,4′,6′-Trimethoxyphenyl 1,6-Dideoxy-2,3,4-tri-*O*-acetyl-β-L-galactopyranoside (37). A mixture of **12** (14 mg, 0.084 mmol), **5** (45 mg, 0.084 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (1 mL) was cooled to −78 °C, and TMSOTf (9 mg, 0.040 mmol) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N and washed with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was separated by preparative TLC (Merck Art 5744, AcOEt/hexane (2:3)) to give **37** (20 mg, 52%) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 1.20 (1H, d, J = 6.4 Hz, Fuc-CH_3), 1.73, 1.99, 2.22 (3H, each s, OAc), 3.781, 3.87 (3H, each s, OCH_3), 3.87 (1H, q, J = 6.4 Hz, H-5), 4.95 (1H, d, J = 9.96 Hz, H-1), 5.12 (1H, dd, J = 3.4, 9.96 Hz, H-3), 5.31 (1H, dd, J = 0.8, 3.4 Hz, H-4), 6.05 (1H, d, J = 2.2 Hz, phenyl proton), 6.10 (1H, t, J = 9.96 Hz, H-2), 6.106 (1H, d, J = 2.2 Hz, phenyl proton); HRMS calcd for $C_{21}H_{28}O_{10}Cs$ (M + Cs^+) 573.0737, found 573.0740.

***p*-Methylphenyl 6-Deoxy-2,3,4-tri-*O*-acetyl-1-thio-β-L-galactopyranoside (38).** A mixture of **13** (5 mg, 0.036 mmol), **5** (20 mg, 0.037 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (1 mL) was cooled to −78 °C, and TMSOTf (4 mg, 0.018 mmol) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N–CH_2Cl_2 and washed with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was separated by preparative TLC (Merck Art 5744, AcOEt/hexane (2:3)) to give **38** (10 mg, 67%) as colorless oil: ^{1}H-NMR ($CDCl_3$) δ 1.23 (1H, d, J = 6.4 Hz, Fuc-CH_3), 1.97, 2.10, 2.14 (3H, each s, OAc), 2.34 (3H, s, Ph-CH_3), 3.80 (1H, q, J = 6.4 Hz, H-5), 4.63 (1H, d, J = 9.92 Hz, H-1), 5.03 (1H, dd, J = 3.32, 9.92 Hz, H-3), 5.20 (1H, t, J = 9.92 Hz, H-2), 5.25 (1H, dd, J = 0.72, 3.22 Hz, H-4), 7.30 (2H, d, J = 7.92 Hz, phenyl protons), 7.41 (2H, d, J = 8.10 Hz, phenyl protons); HRMS calcd for $C_{19}H_{24}O_7SCs$ (M + Cs^+) 529.0252, found 529.0250.

***N*-(Benzyloxycarbonyl)-L-alanyl-*O*-(2,3,4-tri-*O*-acetyl-6-deoxy-β-L-galactopyranosyl)-L-serine Methyl Ester (39).** A mixture of **14** (32.4 mg, 0.1 mmol), **5** (53.4 mg, 0.1 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (1 mL) was cooled to −78 °C, and TMSOTf (11 mg, 0.05 mmol) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N and washed with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was separated by preparative TLC (Merck Art 5744, AcOEt/hexane (2:3)) to give **39** (10 mg, 18%), **40**, and **41**.

39: ^{1}H-NMR ($CDCl_3$) δ 1.22 (3H, d, J = 6.4 Hz, Fuc-CH_3), 1.44 (3H, d, J = 7.0 Hz, Ala-CH_3), 1.98, 2.04, 2.17 (3H, each s, OAc), 3.75 (3H, s, $COOCH_3$), 3.80 (1H, q, J = 6.4 Hz, H-5), 4.05 (2H, bd, J = 2.28 Hz, Ser-CH_2), 4.31 (1H, t, J = 7.0 Hz, Ala-CH), 4.39 (1H, d, J = 7.8 Hz, H-1), 4.723 (1H, dt, J = 2.8, 8.4 Hz, Ser-CH), 4.99 (1H, dd, J = 3.44, 10.5 Hz, H-3), 5.09–5.13 (3H, m, H-2 and benzyl protons), 5.22 (1H, dd, J = 0.96, 3.44 Hz, H-4), 5.46 (1H, d, J = 7.0 Hz, CONH), 6.69 (1H, d, J = 8.44 Hz, CONH), 7.31–7.37 (5H, m, phenyl protons); HRMS calcd for $C_{27}H_{36}N_2O_{13}Cs$ (M + Cs^+) 729.1272, found 729.1276.

40: ^{1}H-NMR ($CDCl_3$) δ 1.18 (3H, d, J = 6.5 Hz, Fuc-CH_3), 1.42 (3H, d, J = 7.0 Hz, Ala-CH_3), 1.57 (3H, s, O-C-CH_3), 2.05, 2.05, 2.12 (3H, each s, OAc), 3.76 (3H, s, COOMe), 3.74–3.79 (1H, m, H-5), 3.97 (1H, dd, J = 3.0, 9.8 Hz), 4.19–4.31 (3H, m), 4.68–4.72 (1H, m), 4.98 (1H, dd, J = 3.2, 7.0 Hz, H-3), 5.11–5.16 (2H, m, benzyl protons), 5.23 (1H, m, H-4), 5.33 (1H, b, NH), 7.32–7.37 (5H, m, Phenyl protons).

41: ^{1}H-NMR ($CDCl_3$) δ 1.19 (3H, d, J = 6.5 Hz, Fuc-CH_3), 1.66 (3H, d, J = 10.9 Hz, PCCH_3), 2.06, 2.12 (3H, each s, OAc), 4.24–4.27 (2H, m, H-2 and H-5), 5.01 (1H, dd, J = 3.4, 7.2 Hz, H-3), 5.05–5.09 (4H, dd, J = 3.3, 7.4 Hz, benzyl protons), 5.20 (1H, dd, J = 1.5, 3.4 Hz, H-4), 6.09 (1H, d, J = 5.0 Hz, H-1), 7.30–7.36 (10H, m, phenyl protons); ^{31}P-NMR (acetone-d_6) δ 15.9 ppm; HRMS calcd for $C_{26}H_{31}O_{10}PCs$ (M + Cs^+) 667.0709, found 667.0728.

Benzyl 2,3,4-Tri-*O*-acetyl-6-deoxy-β-L-galactopyranosyl-(1,3)-2-acetamido-2-deoxy-4,6-*O*-benzylidene-β-D-glucopyranoside (42). A mixture of **16** (30 mg, 0.075 mmol), **5** (40 mg, 0.075 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (1 mL) was cooled to −78 °C, and TMSOTf (10 mg, 0.045 mmol) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N and washed with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel ($CHCl_3$/MeOH (16:1)) to give **42** (33 mg, 65%) as a colorless powder: ^{1}H-NMR ($CDCl_3$) δ 1.16 (1H, d, J = 6.36 Hz, Fuc-CH_3), 1.81, 1.92, 1.96, 2.16 (3H, each s, OAc and NHAc), 3.17 (1H, ddd, J = 6.8, 8.2, 9.08 Hz, GlcN-H-2), 3.52–3.56 (2H, m, GlcN-H-4 and GlcN-H-6), 3.72–3.80 (2H, m, GlcN-H-6′ and Fuc-H-5), 4.36–4.39 (1H, m, GlcN-H-5), 4.51 (1H, dd, J = 9.08, 9.5 Hz, GlcN-H-3), 4.59 (1H, d, J = 11.8, Hz, benzylic proton), 4.66 (1H, d, J = 8.0 Hz, Fuc-H-1), 4.89 (1H, d, J = 11.8 Hz, benzylic proton), 4.96 (1H, dd, J = 3.4, 10.4 Hz, Fuc-H-3), 5.12 (1H, dd, J = 8.0, 10.4 Hz, Fuc-H-2), 5.19 (1H, bd, J = 3.4 Hz, Fuc-H-4), 5.24 (1H, d, J = 8.2 Hz, GlcN-H-1), 5.50 (1H, s, Ph-H), 5.80 (1H, d, J = 6.8 Hz, NH), 7.26–7.50 (10H, m, phenyl proton); ^{13}C-NMR ($CDCl_3$) δ 16.15, 20.57, 20.61, 20.65, 23.64, 57.86, 65.71, 68.74, 68.86, 69.01, 70.16, 71.27, 71.48, 76.07, 76.68, 76.99, 77.31, 81.73, 99.64, 101.18, 101.65, 125.82, 127.89, 127.93, 128.38, 128.42, 129.11, 137.05, 169.61, 170.18, 170.57, 170.80; HRMS calcd for $C_{34}H_{41}NO_{13}Cs$ (M + Cs^+) 804.1632, found 804.1633.

Methyl 2,3-Bis[2,3,4-tri-*O*-acetyl-6-deoxy-β-L-galactopyranosyl-(1,3)]-4,6-*O*-benzylidene-β-D-glucopyranoside (43). A mixture of **17** (50 mg, 0.177 mmol), **5** (180 mg, 0.33 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (1 mL) was cooled to −78 °C, and TMSOTf (31 mg, 0.14 mmol) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N and washed with saturated $NaHCO_3$. The organic solvents were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel ($CHCl_3$/MeOH (20:1)) to give **43** (62 mg, 43%) as colorless oil: ^{1}H-NMR ($CDCl_3$) δ 1.19 (1H, d, J = 6.4 Hz, Fuc_1-CH_3), 1.33 (1H, d, J = 6.4 Hz, Fuc_2-CH_3), 1.92, 1.97, 1.99, 2.06, 2.11, 2.16 (3H, each s, OAc), 3.38–3.44 (1H, m), 3.50 (3H, s, OCH_3), 3.57–3.66 (3H, m), 3.75 (1H, dd, J = 10.2, 10.4 Hz, Glc-H-6), 4.01 (1H, dq, J = 0.84, 6.4 Hz, Fuc_2-H-5), 4.25 (1H, dd, J = 8.0, 8.0 Hz), 4.34 (1H, dd, J = 5.0, 5.2 Hz), 4.36 (1H, d, J = 7.5 Hz, Glc-H-1), 4.76 (1H, d, J = 7.9 Hz, Fuc_2-H-1), 4.95 (1H, dd, J = 3.7, 10.4 Hz, Fuc_1-H-3), 4.96 (1H, d, J = 7.6 Hz, Fuc_1-H-1), 5.24 (1H, dd, J = 0.86, 2.5 Hz, Fuc_2-H-4), 5.51 (1H, s, Ph-H), 7.37–7.42 (3H, m, phenyl protons), 7.44–7.47 (2H, m, phenyl protons); ^{13}C-NMR ($CDCl_3$) δ 15.88, 16.18, 20.60, 20.65, 20.70, 20.72, 20.93, 29.68, 57.64, 65.13, 68.72, 69.16, 69.45, 69.61, 69.85, 70.45, 70.50, 71.08, 71.49, 80.47, 81.01, 99.41, 101.13, 101.24, 103.33, 125.91, 128.37, 129.31, 169.58, 169.78, 170.25, 170.50, 170.73, 170.78; HRMS: calcd for $C_{34}H_{41}NO_{13}Cs$ (M + Cs^+) 959.1950, found 959.1950.

Allyl (Methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosyluronate)-(1,3)-2-acetamido-2-deoxy-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (44). A mixture of **6** (0.29 g, 0.5 mmol), **18** (0.25 g, 0.5 mmol), and molecular sieves (3 Å) in CH_2Cl_2 (5 mL) was cooled to −78 °C, and TMSOTf (56 mg) was added. After being stirred for 1 h at −78 °C, the reaction was quenched with Et_3N and washed with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel ($CHCl_3$/MeOH (15:1)) to give **44** (0.07 g, 18%) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 1.07 (9H, s, t-Bu), 2.02, 2.03, 2.038, 2.40 (3H, each s, OAc and NHAc), 3.40 (1H, bd, J = 9.0 Hz, GlcN-H-5), 3.51 (1H, ddd, J = 8.0, 8.2, 9.0 Hz, GlcN-H-2), 3.75 (3H, s, COOMe), 3.80–3.92 (3H, m, GlcN-H-4, GlcN-H-6, and GlcUA-H-5), 4.04–4.15 (3H, m, GlcN-H-3, GlcN-H-6′, and allyl protons), 4.33 (1H, dd, J = 5.10, 12.8 Hz, allyl proton), 4.79 (1H, d, J = 8.0 Hz, GlcN-H-1), 4.81 (1H, d, J = 7.0 Hz, GlcUA-H-1), 5.02 (1H, dd, J = 8.2, 8.8 Hz, GlcUA-H-3), 5.16–5.30 (4H, m, GlcUA-H-2, GlcUA-H-4, and allyl protons), 5.82 (1H, d, J = 7.8 Hz, NH), 5.85–5.95 (1H, m, allyl proton), 7.36–7.46 (6H, m, phenyl protons), 7.73–7.77 (4H, m, phenyl protons); ^{13}C-NMR ($CDCl_3$) δ 19.3, 20.2, 20.4, 20.5, 23.7, 26.7, 53.2, 56.9, 61.6, 68.8, 69.3, 70.5, 71.2, 71.7, 71.9, 74.3, 80.2, 98.9, 100.2, 117.4, 127.6, 127.9, 129.8, 129.9, 133.9, 135.4, 135.9, 166.6, 168.9, 169.4, 169.8, 170.6; HRMS calcd for $C_{40}H_{53}NO_{15}Cs$ (M + Cs^+) 948.2239, found 948.2206.

Allyl [Methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-α-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate]-(2,3)-[3,6-*O*-bis(*tert*-butyldiphenylsilyl)-β-D-glucopyranosyl]-(1,4)-2-acetamido-2-deoxy-6-*O*-(*tert*-butyldiphenylsilyl)-β-

D-**glucopyranoside (47).** To a stirred solution of **24** (36 mg, 0.032 mmol) and molecular sieves (3 Å) in dry CH_3CN (0.5 mL) was added TMSOTf (2 mg) at 0 °C, and phosphite **7** (28 mg, 0.038 mmol) was then added dropwise over 20 min. After the addition was over, the mixture was allowed to warm to −30 °C to −32 °C and stirred for 2 h at the same temperature. The reaction mixture was diluted with cold AcOEt and quenched with cold saturated aqueous $NaHCO_3$. The organic layer was separated and dried over anhydrous sodium sulfate. The solution was evaporated *in vacuo* to give a crude material, which was chromatographed on a silica gel column ($CHCl_3$–CH_3OH, gradient elution from 25:1 to 15:1). Unreacted **24** (9 mg) was recovered, and **47** (27 mg, 44%) was obtained as a colorless syrup.

47: ^{1}H-NMR ($CDCl_3$) δ 0.95, 0.97, 1.15 (9H each, s, t-Bu), 1.81, 1.86, 2.01 (×2), 2.06, 2.16 (3H each, s, 4 × OAc and 2 × NHAc), 2.67 (1H, dd, J = 4.9, 13.1, H-3 eq of NeuAc), 2.78 (1H, bs), 3.26 (1H, m), 3.50–3.58 (2H, m), 3.62–3.67 (1H, m), 3.68 (3H, s, $COOCH_3$), 3.75–4.12 (11H, m), 4.26–4.30 (2H, m), 4.78–5.10 (5H, m), 5.45–5.55 (2H, m), 5.60 (1H, m, H-8 of NeuAc), 5.78–5.82 (1H, m), 6.99 (1H, d, J = 10.1 Hz), 7.04 (1H, d, J = 6.0 Hz), 7.16–7.42 (20H, m), 7.50 (2H, bd), 7.60 (2H, bd), 7.68 (4H, bd), 7.77 (2H, bd); HRMS calcd for $C_{85}H_{110}N_2O_{23}Si_3Cs$ (M + Cs^+) 1743.5862, found 1743.5747.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-[methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3-bromo-3,5-dideoxy-β-D-*erythro*-L-*manno*-2-nonulopyranosid)onate]-α-D-glucopyranoside (48). A solution of **8** (20 mg, 0.0245 mmol) in CH_3CN (500 μL) was added to a mixture of **19** (34 mg, 0.073 mmol), TMSOTf (4.6 μL), and molecular sieves (3 Å) in CH_3CN (100 μL) at −78 °C. After 3 h, when the solution reached room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$/CH_2Cl_2, and the mixture was washed with saturated $NaHCO_3$. The organic solvent was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel ($CHCl_3$/MeOH (15:1–8:1)) to give **48** (12 mg, 48%) as a colorless syrup. ^{1}H-NMR of **48** was in good accordance with that reported previously.[13]

Allyl [Benzyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-α-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate]-(2,3)-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-galactosyl-(1,4)-2-acetamido-2-deoxy-6-*O*-(*tert*-butyldiphenylsilyl)-β-D-glucopyranoside (49). Following the above method, compound **49** was prepared from **9** (730 mg) and **23** (836 mg) in 8% yield (95 mg). Compound **49** was converted to the acetyl derivative by treatment with acetic anhydride–pyridine–DMAP to identify the structure. The product was quantitatively purified with silica gel preparative TLC: ^{1}H-NMR ($CDCl_3$) δ 1.03, 1.07 (9H, each s, t-Bu), 1.71, 1.82, 1.90, 1.92, 1.99 (×2), 2.01, 2.02, 2.16 (3H, each s, OAc and NHAc), 2.62 (1H, dd, J = 4.66, 12.55 Hz, H-3ax of NeuAc), 3.41 (1H, dd, J = 2.73, 10.7 Hz, H-6 of NeuAc), 3.54 (1H, brt, J = 9.76 Hz, H-6a of Gal), 3.62 (1H, dd, J = 5.06, 9.70 Hz, H-6b of Gal), 3.67 (1H, brq, J = 4.83 Hz, H-5 of GlcNAc), 3.77–3.82 (2H, H-6a of GlcNAc, H-5 of Gal), 3.90–3.97 (3H, H-6b of GlcNAc, H-9a of NeuAc), 4.02–4.11 (3H, H-2 and H-4 of GlcNAc, H-5 of NeuAc), 4.27 (1H, dd, J = 2.44, 12.35 Hz, H-9b of NeuAc), 4.35 (1H, d, J = 6.70 Hz, H-1 of GlcNAc), 4.69 (1H, dd, J = 3.24, 10.1 Hz, H-3 of Gal), 4.77 (1H, d, J = 7.81 Hz, H-1 of Gal), 4.87–4.92 (1H, m, H-4 of NeuAc), 4.90 (1H, dd, J = 7.66, 10.1 Hz, H-2 of Gal), 4.96 (1H, dd, J = 7.94, 10.4 Hz, H-3 of GlcNAc), 5.12 (1H, d, J = 12.1 Hz, benzylic), 5.32 (1H, dd, J = 2.90, 9.65 Hz, H-7 of NeuAc), 5.43 (1H, brd, J = 3.23 Hz, H-4 of Gal), 5.48 (1H, d, J = 12.15 Hz, benzylic), 5.52–5.57 (1H, m, H-8 of NeuAc), 5.72 (1H, d, J = 9.78 Hz, NHAc of GlcNAc), 7.32–7.68 (25H, aromatic); ^{13}C-NMR ($CDCl_3$) δ 14.18, 19.10, 19.21, 20.38, 20.64, 20.73, 21.44, 23.13, 23.19, 29.68, 37.34, 48.82, 52.07, 66.70, 66.79, 68.32, 68.95, 69.44, 70.65, 71.70, 71.76, 72.72, 73.12, 73.91, 75.32, 96.64, 99.45, 99.93, 116.90, 127.56, 127.60, 127.71, 127.77, 128.52, 128.59, 128.83, 129.58, 129.69, 129.84, 129.97, 132.66, 132.76, 133.16, 133.63, 133.67, 135.07, 135.54, 135.59, 135.66, 167.37, 169.56, 169.64, 169.90, 170.00, 170.13, 170.18, 170.31, 170.44, 170.61; HRMS calcd for $C_{81}H_{102}N_2O_4Si_2Cs$ (M + Cs^+) 1707.5314, found 51707.5359.

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1,4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl-(1,6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (50). A solution of **10** (172 mg, 0.195 mmol) and diisopropylidene-D-galactose **21** (74 mg, 0.285 mmol) in CH_2Cl_2 (2 mL) was stirred with crushed 3-Å molecular sieves under argon for 45 min. The mixture was cooled to −42 °C, and TMSOTf (10 μL) was added. After being stirred for 30 min at −42 °C, the mixture was warmed to 0 °C over 20 min and quenched with 1 mL of saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/AcOEt (6:4–3:7)) to give **50** (69.2 mg, 40%): ^{1}H-NMR ($CDCl_3$) δ 1.32 (6H, s, 2 × CH_3), 1.45 (3H, s, CH_3), 1.50 (3H, s, CH_3), 1.98, 2.05, 2.08, 2.14, 2.17 (3H, each s, OAc), 3.58–3.70 (2H, m), 3.75–3.95 (3H, m), 3.99 (1H, dd, J = 3.6, 11.1 Hz), 4.05–4.20 (5H, m), 4.29 (1H, dd, J = 2.4, 4.9 Hz), 4.45–4.52 (2H, m), 4.56–4.62 (2H, m), 4.91 (1H, dd, J = 8.0, 9.6 Hz, H-2′), 4.95 (1H, dd, J = 3.5, 10.5 Hz, H-3″), 5.11 (1H, dd, J = 7.8, 10.4 Hz, H-2′), 5.21 (1H, t, J = 9.3 Hz, H-3′), 5.34 (1H, dd, J = 0.7, 3.3 Hz, H-4′), 5.50 (1H, t, J = 9.3 Hz, H-3′); HRMS calcd for $C_{38}H_{54}O_{23}Cs$ (M + Cs^+) 1011.2110, found 1011.2111.

Synthesis of 56. To a solution of dibenzyl hydrogen phosphonate (0.5 g, 1.9 mmol) and imidazole (0.17 g) in methylene chloride (5 mL) was added a solution of *tert*-butyldiphenylsilyl chloride (0.52 g, 1.9 mmol) in DMF (3 mL) slowly at −78 °C, and the mixture was stirred for 6 h. After the reaction was complete, the reaction mixture was concentrated at low temperature. The crude mixture was chromatographed (AcOEt/n-hexane (1:1)) to give **56** (480 mg) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 1.11 (9H, s, t-Bu), 4.77–4.90 (4H, m, benzyl proton), 7.22–7.44 (16H, m, phenyl proton), 7.70–7.82 (4H, m, phenyl proton).

Dibenzyl 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranosyl Phosphite (57). A solution of dibenzyl *N*,*N*-diethylphosphoramidite (0.9 g, 2.8 mmol) in CH_2Cl_2 was added dropwise to a solution of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (0.80 g, 1.5 mmol, from Fluka Co.) and 1*H*-tetrazole (0.16 g, 2.3 mmol) in anhydrous CH_2Cl_2 (15 mL) under nitrogen at room temperature. After being stirred for 1 day, the mixture was washed with saturated aqueous $NaHCO_3$ and saturated NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. This crude product was passed through Florisil (TLC grade, Aldrich, AcOEt/n-Hex) and purified further by SiO_2 gel column chromatography (AcOEt/n-Hex) to provide a 2:3 mixture of α and β anomers of **57** (0.55 g, 47% yield). This phosphite has been found to be stable at −5 °C over 2 months after its preparation: ^{1}H NMR ($CDCl_3$, only the chemical shifts of anomeric protons are shown) δ 5.03 (1H, dd, J_{HH} = 8.0 Hz, J_{HP} = 8.0 Hz, H-1 of β anomer), 5.65 (1 H, dd, J_{HH} = 3.2 Hz, J_{HP} = 8.3 Hz, H-1 of α anomer); ^{13}C NMR ($CDCl_3$) δ 64.1 (d, J_{CP} = 8.7 Hz), 64.3 (d, J_{CP} = 7.2 Hz), 64.6 (d, J_{CP} = 8.9 Hz), 68.1, 68.6, 71.5, 72.9, 73.4, 73.5, 75.4, 75.7 (d, J_{CP} = 8.2 Hz), 77.1, 77.5, 79.9, 79.9, 81.5, 82.7, 82.7, 84.6, 92.1 (d, J_{CP} = 17.9 Hz), 97.2 (d, J_{CP} = 15.2 Hz), 127.4, 127.5, 127.6, 127.7, 127.7, 127.8, 127.9, 128.0, 128.3, 137.8, 137.9, 138.0, 138.1, 138.2, 138.5, 138.7; ^{13}P NMR ($CDCl_3$) δ 135.1 (α), 135.7 (β); IR (neat) 3063, 3030, 2868, 1951, 1811, 1734, 1606, 1496, 1453, 1363, 1209, 1071, 997, 914, 790, 732, 695 cm^{-1}.

Methyl 2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl-(1,6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (58). A 10% solution of TMSOTf in CH_2Cl_2 (50 μL, 0.026 mmol) was added dropwise to a mixture of **57** (68 mg, 0.087 mmol), methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**19**) (41 mg, 0.088 mmol), and molecular sieves (4 Å) in anhydrous CH_2Cl_2 (1.2 mL) under argon at −78 °C. After being stirred for 1 h at the same temperature, the reaction was quenched with saturated aqueous $NaHCO_3$, warmed to room temperature, and extracted with CH_2Cl_2. The combined organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The remaining residue was purified by SiO_2 gel column chromatography (AcOEt/n-Hex) to provide **58** as a colorless powder (57 mg, 66% yield, mp 191–121 °C, $[\alpha]^{25}_D$ = +23 (*c* 0.9 $CHCl_3$). All data of ^{1}H NMR ($CDCl_3$), ^{13}C NMR ($CDCl_3$), IR, and FABMS were in agreement with those reported previously.[5e]

Dibenzyl 6-Deoxy-2,3,4-tri-*O*-benzyl-L-galactopyranosyl Phosphite (59). A solution of DDP (1.00 g, 3.15 mmol) in THF (8 mL) was added dropwise to a solution of 6-deoxy-2,3,4-tri-*O*-benzyl-L-galactopyranose (755.3 mg, 1.7 mmol) and 1*H*-tetrazole (0.20 g, 2.9 mmol) in THF (8 mL) at room temperature. After being stirred for 2 h at room temperature, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (30 mL × 3). The combined organic layer was washed with saturated aqueous NaCl (20 mL × 2), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The remaining residue was purified by SiO_2 chroma-

tography (AcOEt/n-Hex/Et_3N = 1/10/0.5) to give a 38:62 mixture of α and β anomers of **59** (871.7 mg, 74% yield) which were separated by silica gel chromatography (EtOAc/n-hexane). α-**59**: R_f 0.32 (AcOEt–n-Hex (1:5)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (3H, d, J = 6.5 Hz, CH_3), 3.64 (1H, dd, J = 1.7, 1.7 Hz, H-4), 3.92 (1H, dd, J = 2.8, 10 Hz, H-3), 4.00 (1H, br dq, J = 6.5 Hz, 1.7 Hz, H-5), 4.10 (1H, dd, J = 3.4, 10 Hz, H-2), 4.65 (1H, d, J = 11.6 Hz, one of benzylic protons), 4.69–4.93 (8H, 8 × d, benzylic protons), 4.99 (1H, d, J = 11.6 Hz, one of benzylic protons), 5.66 (1H, dd, J_{HH} = 3.4 Hz, J_{HP} = 8.1 Hz, H-1), 7.25–7.38 (25 H, m, PhH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.61, 64.01 (d, J_{CP} = 8.9 Hz, $POCH_2Ph$), 64.21 (d, J_{CP} = 7.6 Hz, $POCH_2Ph$), 67.68, 72.98, 73.06, 74.85, 76.29 (d, J_{CP} = 4.0 Hz, C-2), 77.51, 78.73, 92.89 (d, J_{CP} = 17.4 Hz, anomeric C-1), 127.38, 127.44, 127.52, 127.61, 127.86, 128.13, 128.20, 128.26, 128.34, 128.39, 138.40, 138.49, 138.76; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 135.43.

β-**59**: R_f 0.27 (AcOEt–n-Hex (1:5)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (3H, d, J = 6.4 Hz, CH_3), 3.51–3.60 (3H, m, H-3,4,5), 3.94 (1H, dd, J = 7.7, 9.4 Hz, H-2), 4.53–5.02 (11H, m, H-1 and benzylic protons), 7.24–7.39 (25H, m, PhH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.72, 64.20, (d, J_{CP} = 7.5 Hz, $POCH_2Ph$), 64.45 (d, J_{CP} = 8.4 Hz, $POCH_2Ph$), 71.09, 73.11, 74.61, 75.20, 76.11, 79.74 (d, J_{CP} = 4.8 Hz, C-2), 82.62, 97.41 (d, J_{CP} = 15.7 Hz, anomeric C-1), 127.34, 127.46, 127.52, 127.57, 127.87, 127.93, 128.18, 128.22, 128.24, 128.30, 128.39, 128.46, 138.09, 138.19, 138.24, 138.41, 138.50, 138.54; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 135.05; HRMS calcd for $C_{41}H_{43}O_7PCs$ (M + Cs^+) 567.1148, found 567.1130.

To prepare 6-deoxy-2,3,4-tri-*O*-benzyl-L-galactopyranose, acetyl chloride (0.3 mL, 3.2 mmol) was added to a solution of L-fucose (5.0 g, 30.5 mmol) in methanol (100 mL) and heated at reflux temperature overnight. The reaction mixture was concentrated under reduced pressure. This crude compound of methyl 6-deoxy-L-galactopyranoside was used for the next step without purification.

NaH (5.4 g, 80%, 0.18 mol) was washed with THF (20 mL), dried, and suspended in DMF (30 mL). A solution of the crude compound of methyl 6-deoxy-L-galactopyranoside described above in DMF (40 mL) was added to the suspension of NaH in DMF at 60 °C. The reaction mixture was stirred for 30 min at the same temperature, and benzyl bromide (20.6 g, 0.12 mmol) was added. After being stirred at 40–50 °C overnight, the reaction mixture was quenched with MeOH (3 mL) and concentrated under reduced pressure. The remaining residue was diluted with AcOEt (200 mL), washed with saturated aqueous $NaHCO_3$ (50 mL × 2) and saturated aqueous NaCl (50 mL × 2), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. This crude product was suspended in acetic acid (120 mL) and 3 M sulfuric acid (15 mL) and stirred at 90 °C for 20 min. To the reaction mixture were added benzene (200 mL) and ice-cold water (100 mL), and the aqueous layer was separated. The organic layer was washed with saturated aqueous $NaHCO_3$ (50 mL × 2) and saturated aqueous NaCl (50 mL × 2), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The remaining residue was purified with silica gel column chromatography (AcOEt/n-Hex = 1/3) to give the desired product (5.0 g, 38% for three steps) as a 65:35 (α/β) anomeric mixture: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (3H, d, J = 6.5 Hz, CH_3 of α), 1.20 (3H, d, J = 6.5 Hz, CH_3 of β), 3.53 (1H, dd, J = 6.5 Hz, H-5 of β), 3.55 (1H, dd, J = 3.0, 9.5 Hz, H-3 of β), 3.59 (1H, dd, J = 0.5, 3.0 Hz, H-4 of β), 3.67 (1H, dd, J = 0.5, 2.5 Hz, H-4 of α), 3.73 (1H, dd, J = 7.5, 9.5 Hz, H-2 of β), 3.89 (1H, dd, J = 3.0, 10.0 Hz, H-3 of α), 4.04 (1H, dd, J = 3.5, 9.5 Hz, H-2 of α), 4.10 (1H, q, J = 6.5 Hz, H-5 of α), 4.63 (1H, dd, J = 4.0, 7.5 Hz, H-1 of β), 4.65–4.99 (12 × d, benzylic protons), 5.26 (1H, dd, J = 2.0, 4.0 Hz, H-1 of α), 4.65–4.99 (benzylic protons), 7.26–7.36 (m, PhH); HRMS calcd for $C_{27}H_{30}O_5Cs$ (M + Cs^+) 567.1148, found 567.1130.

Methyl 6-Deoxy-2,3,4-tri-*O*-benzyl-α-L-galactopyranosyl-(1,4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside and Methyl 6-Deoxy-2,3,4-Tri-*O*-benzyl-β-L-galactopyranosyl-(1,4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (α-**60** and β-**60**). A 10% (v/v) solution of TMSOTf in ether (30 μL, 0.027 mmol) was added dropwise to a mixture of **59** (43.6 mg, 0.094 mmol), **15** (62.4 mg, 0.092 mmol) and molecular sieves (4 Å) in ether (3 mL) at −78 °C under argon. The reaction mixture was stirred for 30 min at −78 °C and quenched with triethylamine (0.1 mL) and saturated aqueous $NaHCO_3$ (5 mL). The mixture was extracted with CH_2Cl_2 (30 mL × 3), and the combined organic layer was washed with saturated aqueous NaCl (20 mL × 2), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The remaining residue was purified by silica gel chromatography (AcOEt/n-Hex = 1/10) to give 9.0 mg of β-**60** (11%), 27.4 mg of α-**60** (34%), and 19 mg of recovered **15** (43%).

α-**60**: R_f 0.55 (AcOEt–n-Hex (1:2)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.66 (3H, d, J = 6.4 Hz, CH_3 of fucose), 3.34 (3H, s, OCH_3), 3.34 (1H, brs, Glc-H-6), 3.57 (1H, dd, J = 3.6 Hz, 9.4 Hz, Glc-H-2), 3.64 (1H, brs, Fuc-H-4), 3.78 (1H, brs, Glc-H-6), 3.79 (1H, dd, J = 9.8, 9.8 Hz, Glc-H-4), 3.84 (1H, dd, J = 2.7, 10.3 Hz, Fuc-H-3), 3.90 (1H, dd, J = 9.2, 9.2 Hz, Glc-H-3), 3.97 (1H, dd, J = 3.6, 10.3 Hz, Fuc-H-2), 3.98–4.00 (1H, m, Fuc-H-5), 4.32 (1H, d, J = 12.2 Hz, benzylic proton), 4.37 (1H, d, J = 12.2 Hz, benzylic proton), 4.53–4.62 (4H, 4 × d, benzylic protons), 4.57 (1H, d, J = 4.0 Hz, Glc-H-1), 4.68–4.78 (5H, 5 × d, benzylic protons), 4.94 (1H, d, J-11.6 Hz, benzylic proton), 4.99 (1H, d, J = 3.6 Hz, Fuc-H-1), 5.05 (1H, d, J = 10.9 Hz, benzylic proton), 7.21–7.41 (30 H, m, PhH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.21, 55.00, 66.62, 68.53, 70.28, 72.70, 73.18, 73.29, 73.68, 74.33, 74.70, 75.56, 76.28, 77.52, 79.45, 80.19, 80.51, 97.58, 97.71, 127.32, 127.50, 127.54, 127.58, 127.65, 127.78, 127.92, 128.01, 128.10, 128.17, 128.21, 128.25, 128.31, 128.38, 128.42; HRMS calcd for $C_{55}H_{66}O_{10}Cs$ (M + Cs^+) 1013.3241, found 1013.3258.

β-**60**: R_f 0.59 (AcOEt–n-Hex (1:2)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (3H, d, J = 6.4 Hz, CH_3 of fucose), 3.29 (1H, dq, J = 6.2, 2.9 Hz, Fuc-H-5), 3.41 (1H, dd, J = 3.0 Hz, 9.7 Hz, Fuc-H-3), 3.42 (3H, s, OCH_3), 3.49 (1H, br d, J = 2.9 Hz, Fuc-H-4), 3.51 (1H, dd, J = 3.5, 9.2 Hz, Glc-H-2), 3.63 (1H, dd, J = 5.2, 10.8 Hz, Glc-H-6), 3.72 (1H, dd, J = 7.8, 9.6 Hz, Fuc-H-2), 3.72–3.75 (1H, m, Glc-H-5), 3.84 (1H, dd, J = 8.7, 10.9 Hz, Glc-H-4), 3.87 (1H, dd, J = 1.9, 10.7 Hz, Glc-H-6), 3.96 (1H, dd, J = 8.9, 9.2 Hz, Glc-H-3), 4.53 (1H, d, J = 12.1 Hz, benzylic proton), 4.60–4.66 (3H, 3 × d, benzylic protons), 4.62 (1H, d, J = 3.6 Hz, Glc-H-1), 4.72–4.85 (6H, 6 × d, benzylic protons), 4.57 (1H, d, J = 3.6 Hz, Glc-H-1), 4.80 (1H, d, J = 7.4 Hz, Fuc-H-1), 4.99 (1H, d, J = 11.8 Hz, benzylic proton), 5.00 (1H, d, J = 11.3 Hz, benzylic proton), 7.20–7.39 (30 H, m, PhH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.67, 55.28, 69.09, 69.76, 70.27, 73.09, 73.35, 73.38, 73.82, 74.70, 75.31, 75.39, 77.34, 79.71, 79.94, 82.21, 82.30, 97.86, 102.93, 127.21, 127.32, 127.45, 127.49, 127.57, 127.92, 127.96, 128.02, 128.13, 128.17, 128.38, 128.46, 128.54, 138.10, 138.66, 138.81, 138.85; HRMS calcd for $C_{55}H_{66}O_{10}Cs$ (M + Cs^+) 1013.3241, found 1013.3260.

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Supplementary Material Available: ^{1}H NMR spectra of **3–4, 6–8, 10, 18, 20, 22, 25, 26, 28–45, 47, 49, 50,** and **56–60** (48 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.