Selected Paper

6-Nitro-2-benzothiazolyl α-Glucoside and α-Mannoside in β-Selective Glycosylations

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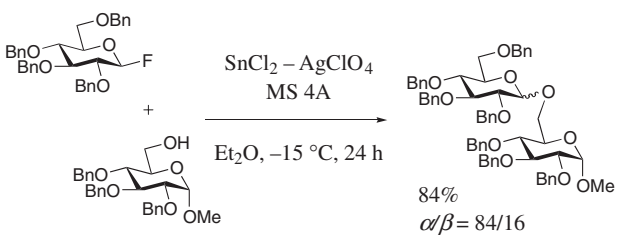
Highly β-selective glucosylations of glycosyl acceptors having a primary hydroxy group with a 6-nitro-2-benzothiazolyl α-glucoside donor **3α** proceeded smoothly in the presence of a catalytic amount of trifluoromethanesulfonic acid (TfOH) in CH_2Cl_2 at −78 °C to afford the corresponding glycosides in high yields. With the use of **3α**, β-saccharides could be obtained more dominantly than other α-glucosyl donors such as thioform- and trichloroacet-imidates or fluoride in the glucosylation under the same conditions. Similarly, highly β-selective mannosylations of glycosyl acceptors with a 6-nitro-2-benzothiazolyl α-mannoside donor **18α** were carried out smoothly in the presence of a catalytic amount of tetrakis(pentafluorophenyl)boric acid $H[B(C_6F_5)_4]$ to afford the corresponding disaccharides in good to high yields; **18α** apparently behaved as a potent donor here for the construction of β-mannoside linkage. Interestingly, in situ anomerization from **18β** to **18α** was observed when β-mannosyl donor **18β** was treated with a catalytic amount of $H[B(C_6F_5)_4]$ in CH_2Cl_2.

To develop stereoselective glycosylation reactions is one of the most fundamental and important topics in carbohydrate chemistry.[1] Concerning syntheses of glycosides, Koenigs–Knorr reaction[2] has long been employed commonly as one of the most useful tools; however, there are several problems. For example, one must use a stoichiometric amount of heavy-metal salt and its reaction conditions are drastic. In order to improve these weak points, many excellent glycosyl donors have been developed[1] during these two decades: e.g., thioglycosides, selenoglycosides, glycosyl sulfoxides, glycosyl trichloroacetimidates, glycosyl acetate, 1-hydroxy sugar, glycals, pentenyl glycoside, and donors having phosphorus-containing leaving groups. These were employed in combination with suitable activators in the syntheses of various saccharide chains. In 1981, it was reported from our laboratory[3] that α-glucosides could be obtained with good stereoselectivities when glucosyl fluoride was treated with various glycosyl acceptors by using a combination of tin(II) chloride ($SnCl_2$) and silver perchlorate ($AgClO_4$) as a promoter in diethyl ether (Et_2O) (Scheme 1). After the above-mentioned combined-catalyst system was introduced, the fluoride became one of the most popular glycosyl donors. Thus, many preparation methods of glycosides using glycosyl fluorides in combination with suitable activators have been established.[4]



Scheme 1.

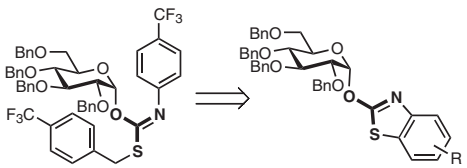


Fig. 1.

Very recently, prominent characteristics were found in a newly devised donor glucosyl *p*-trifluoromethylbenzylthio-*N*-*p*-trifluoromethylphenylformimidate: that is, it was easily prepared in stable crystalline form and in good yield; catalytic and highly α- or β- and chemo-selective glucosylations of several glycosyl acceptors with α-glucosyl thioformimidate were successfully performed in the co-existence of 0.05 molar amounts of trifluoromethanesulfonic acid (TfOH) and molecular sieve 5A (MS 5A) in an ether or nitrile solvent, respectively.[5] Thus, further development of a newer donor, 6-nitro-2-benzothiazolyl glycoside, that possesses a structurally-similar leaving group was planned (Fig. 1). Since a moiety [–O–C(=NR^1)–SR^2] activated easily by Lewis or protic acids was involved in a readily-available benzothiazolyl glycoside, it was expected to be as useful and characteristic a donor as glycosyl thioformimidate in the glycosylation. In this paper, we would like to describe efficient β-stereoselective glycosylations with glucosyl and mannosyl donors.[6]

Results and Discussion

β-Selective Glucosylation Using 6-Nitro-2-benzothiazolyl α-Glucoside. 6-Nitro-2-benzothiazolyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside (**3**) was easily prepared by a direct condensation reaction between anomeric hydroxy group of 2,3,4,6-

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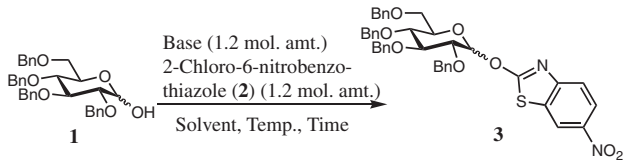
Table 1. Preparation of 6-Nitro-2-benzothiazolyl α-Glucoside



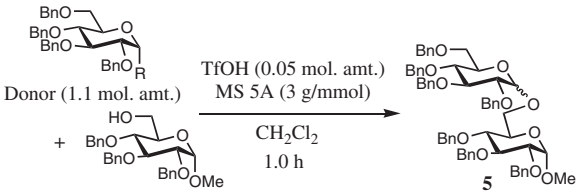
Entry	Base	Solvent	Temp. /°C	Time /h	Yield/% (α/β)[a]
1	KH	THF	0	15	**86** (**29**/**71**)
2	NaH	THF	rt	3	96 (34/66)
3	LiH	THF	rt	21	82 (85/15)
4	$LiN(SiMe_3)_2$	THF	rt	24	71 (83/17)
5	$LiN(SiMe_3)_2$	THF	0	48	74 (76/24)
6	$LiN(SiMe_3)_2$	Et_2O	rt	24	trace
7	$LiN(SiMe_3)_2$	CH_2Cl_2	rt	24	trace
8	$LiN(SiMe_3)_2$	DMF	rt	24	19 (86/14)
9	$LiN(SiMe_3)_2$	THF–DMF[b]	0	48	**92** (**88**/**12**)

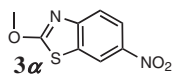
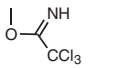
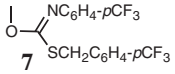
a) The α/β ratios were determined by ^{1}H NMR measurements. b) THF–DMF (9:1).

tetra-*O*-benzyl-D-glucopyranose[7] (**1**) and 2-chloro-6-nitrobenzothiazole[8] (**2**) (Table 1). The reaction smoothly proceeded in THF in the presence of a base and afforded the corresponding 6-nitro-2-benzothiazolyl glucoside **3** in high yield. Interestingly, both of the stereoisomers were prepared selectively depending on the nature of the bases (Entries 1, 3). Though the observed α-selectivity in DMF was high, the chemical yield decreased because of the partial decomposition of the donor during the coupling reaction (Entry 8). The α-selective condensation reaction using lithium bis(trimethylsilyl)amide [$LiN(SiMe_3)_2$] proceeded smoothly in a mixed solvent (THF–DMF, 9/1, v/v) to give a mixture of 6-nitro-2-benzothiazolyl glucosides **3** in 92% chemical yield (Entry 9, $\alpha/\beta = 88/12$). Each isomer of **3α** or **3β** was separated and purified by silica gel chromatography. The former was obtained in 77% and the latter in 7% yields, respectively, based on **1**. It was noted that glucosyl donors having non-substituted benzothiazole were so labile that the product was partly hydrolyzed during the work-up procedure. This result indicated that the introduction of a nitro group at 6-position of benzothiazole ring contributed to the stabilization of the glucosyl donor.

In general, reactivities and stereoselectivies of glucosylations that use conventional donors were influenced considerably by the properties of donors, catalysts, and solvents. Initially, glucosylation[9] of a glycosyl acceptor **4**[10] with **3α** in the presence of 0.05 molar amounts of TfOH in CH_2Cl_2, a nonpolar solvent, was tried under the conditions previously reported[5b] (Table 2). The reaction proceeded smoothly at 0 °C to afford the corresponding disaccharides **5**[11] in high yield with moderate β-selectivity (Entry 1, $\alpha/\beta = 31/69$). Interestingly, β-selectivity of this glucosylation was higher than that using donor **7**,[5d] which afforded the disaccharide with moderate α-selectivity ($\alpha/\beta = 66/34$) under the same conditions as shown in our previous report (Entry 5).[5b] Although the above two donors, **3α** and **7**, possessed similar moieties [–O–C(=NR^1)–SR^2], stereoselectivities of the disaccharides afforded were reversed (Entries 1, 5). The donor **3α** also gave the disaccharides in a higher

Table 2. Glucosylation Using Various Donors by TfOH Catalyst



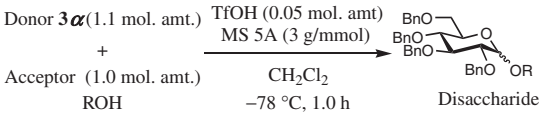
Entry	Donor (R)	Temp./°C	Yield/% (α/β)[a]
1		0	**97** (**31**/**69**)
2	**3α**	–78	**91** (**4**/**96**)
3		0	99 (56/44)
4	**6**	–78	98 (8/92)
5[b]		0	98 (66/34)
6[b]	**7**	–78	97 (43/57)
7		0	96 (57/43)
8	**8**	–78	Not detected

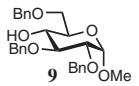
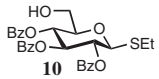
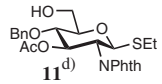
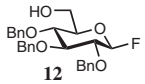
a) The α/β ratios were determined by HPLC analysis. b) These results were previously reported in Ref. 5b.

β-selective manner than the α-glucosyl trichloroacetimidate[12] (**6**) did at 0 °C (Entries 1, 3). The α-glucosyl fluoride[13] (**8**), a less reactive donor compared with the above glucosyl imidates, reacted with acceptor **4** to afford the glucosides with moderate α-selectivity (Entry 7). These results showed that the glucosylation reaction of **3α** under the above-mentioned conditions gave β-saccharide more predominantly than the cases using **6**, **7**, and **8**. Finally, the highest β-selectivity ($\alpha/\beta = 4/96$) was obtained when the donor **3α** was allowed to react at −78 °C (Entry 2).

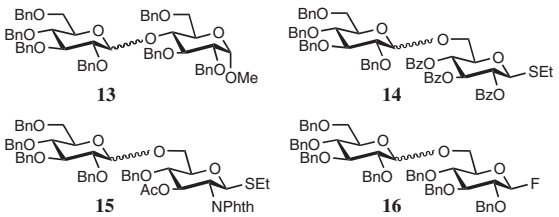
Next, in order to extend the scope of this reaction, β-selective glucosylation of various glycosyl acceptors such as methyl glycoside **9**[14] that contained a hindered secondary hydroxy group, thioglycoside **10**,[15] **11**,[11c] and glycosyl fluoride **12**[5d] with **3α** was examined without utilizing the neighboring effect of 2-*O*-acyl protecting group (Table 3). In those cases that used glycosyl acceptors having primary hydroxy groups, the desired disaccharides were obtained all in high yields with high β-selectivities, while a moderate β-selectivity was observed ($\alpha/\beta = 27/73$) in the case of using **9** (Entry 1), which was the only exception. The donor **3α** gave the β-saccharide more dominantly than α-glucosyl trichloroacetimidate **6** even when the hindered acceptor **9** was used (56%, $\alpha/\beta = 50/50$). Furthermore, the chemoselective glucosylations using acceptors such as ethyl 2,3,4-tri-*O*-benzoyl-1-thio-β-D-glucopyranoside (**10**), ethyl 3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**11**), or 2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl fluoride (**12**) gave good results without giving any damage to a thio-group and to a fluorine-atom linked at their anomeric positions (Entries 2, 3, and 4). These results showed that none of the frequently-employed glycosyl donors such as thioglycoside and glycosyl fluoride were activated un-

Table 3. Glucosylation of Various Acceptors



Entry	Acceptor	Product	Yield/% (α/β)[a]
1	 **9**	**13**	80 (27/73)[b,c]
2	 **10**	**14**	98 (9/91)
3	 **11**[d]	**15**	90 (9/91)
4	 **12**	**16**	89 (7/93)[e]

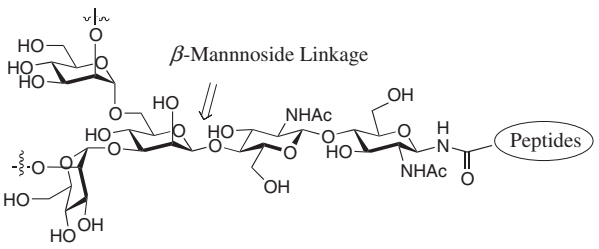
a) The α/β ratios were determined by HPLC analysis. b) The reaction time was 4 h. c) **13** was obtained in 56% yield ($\alpha/\beta = 50/50$) when **6** was used instead of **3α**. d) NPhth: phthalimido. e) The α/β ratio was determined by isolated yields of both isomers.



der these conditions. Therefore, this glucosylation may have broader applicability to the chemoselective synthesis[16] of oligo- and poly-saccharides.

In the presence of a catalytic amount of TfOH, the glucosylation using **3α** enabled higher β-selectivity in CH_2Cl_2 than those using donors **6**, **7**, or **8**. These results imply that benzothiazolyl glycoside has a potent feature to construct β-glycosidic linkage without even utilizing the neighboring effect of the 2-*O*-acyl protecting group. This glycosylation with benzothiazolyl glycoside exhibited further possible applications to the troublesome β-mannosylation.

β-Selective Mannosylation Using 6-Nitro-2-benzothiazolyl α-Mannoside. β-Mannopyranosyl units are the essential constituents of naturally-occurring biologically-active oligosaccharides and glycoconjugates (Scheme 2).[1,17] Formation of

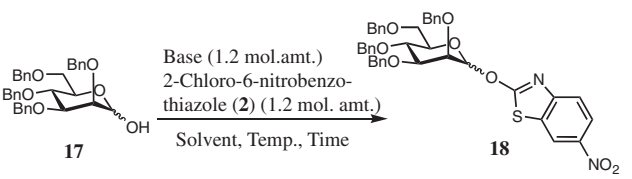


Scheme 2.

β-mannopyranoside is considered rather difficult in chemical synthesis because of the following three reasons: i) α-mannopyranoside formation is favored by its anomeric effect; ii) steric repulsion of hydroxy group at C-2 position; and iii) opposite participation of its neighboring group. However, some useful methods have been developed to date to overcome these problems and to allow the synthesis of β-mannoside; namely, 1) effective epimerization of β-glucoside or galactoside at C-2 position;[18] 2) intramolecular aglycon delivery mannosylation;[19] 3) direct intermolecular mannosylation. Of the methods reported, the catalytic or stoichiometric direct mannosylation[20–27] turned out to be most effective for the convenient construction of β-mannopyranoside. Reactions using mannosyl donors such as mannosyl phosphinothioate,[20] phosphate,[21] halide,[22,23] or sulfoxide[23] in combination with suitable activators, and a donor having 1,2-stannylene acetal[24] were thus reported. The best results were obtained when donors having an electron-withdrawing protecting group at O-2 position[25] or a cyclic acetal protecting group at O-4,6 position[26] were activated by trimethylsilyl triflate, benzenesulfenyl triflate/2,6-di-*t*-butyl-4-methylpyridine (DTBMP), or trifluoromethanesulfonic anhydride/DTBMP. In spite of those reports of success, development of a new and convenient method for the stereoselective synthesis of β-mannopyranosides still remains as one of the most important and challenging topics in carbohydrate chemistry. In the above section, it was pointed out that the benzothiazolyl glycoside had a potent and characteristic feature for the formation of β-saccharide. In this section, the application of the above concept to a direct β-selective mannosylation of several glycosyl acceptors using a newly devised donor, 6-nitro-2-benzothiazolyl α-mannoside is described.

6-Nitro-2-benzothiazolyl 2,3,4,6-tetra-*O*-benzyl-D-mannopyranoside (**18**) was also prepared easily according to a manner similar to that used for glucosyl donor **3**; both stereoisomers were selectively prepared by choosing suitable bases (Table 4, Entries 2, 3). Interestingly, the induction of stereoselectivity depended on the kinds of counter cation of the bases; for example, stereoselective preparation of **18α** was performed by using potassium bis(trimethylsilyl)amide [$KN(SiMe_3)_2$] while **3α** was

Table 4. Preparation of 6-Nitro-2-benzothiazolyl α-Mannoside



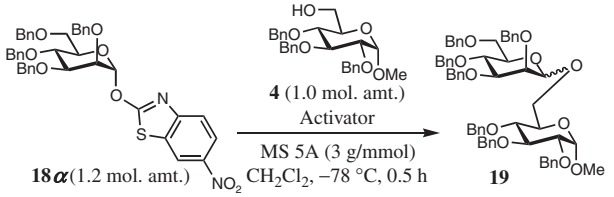
Entry	Base	Solvent	Temp. /°C	Time /h	Yield/% (α/β)[a]
1	$LiN(SiMe_3)_2$	THF	rt	45	27 (40/60)
2	$NaN(SiMe_3)_2$	THF	rt	0.5	**92** (**34**/**66**)
3	$KN(SiMe_3)_2$	THF	rt	0.5	**90** (**73**/**27**)
4	$KN(SiMe_3)_2$	THF–DMF[b]	−20	3	77 (63/37)
5	KH	THF	−20	0.5	68 (63/37)
6	DBU[c]	CH_2Cl_2	rt	12	64 (48/52)

a) The α/β ratios were determined by isolations of both stereoisomers. b) THF–DMF (9:1). c) DBU: 1,8-diazabicyclo-[5.4.0]undec-7-ene.

stereoselectively prepared by using $LiN(SiMe_3)_2$ (Table 1 vs Table 4). It was thought then that the stereoselections were strongly influenced by steric repulsion and chelating effect of the hydroxy group at C-2 position of mannose when condensation reactions were carried out in the presence of bases such as $KN(SiMe_3)_2$. The α-selective condensation reaction between the anomeric hydroxy group of 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose[28] (**17**) and 2-chloro-6-nitrobenzothiazole (**2**) proceeded smoothly to give α-isomer **18α** and β-isomer **18β** in 66% and 24% yields, respectively, under the above conditions (Entry 3).

In the first place, the effect of various activators on the mannosylation of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**4**) with **18α** in CH_2Cl_2 was examined (Table 5). In most cases, the reactions smoothly proceeded at -78 °C to give the corresponding disaccharides **19**[11a] in high yields. It was interesting to note that the activators having anions such as sulfonate (RSO_3^-) or tetrakis(pentafluorophenyl)borate [$^-B(C_6F_5)_4$] gave disaccharides with high β-selectivities (Entries 2, 3, 8–10). The highest β-selectivity was achieved when tetrakis(pentafluorophenyl)boric acid[29] $H[B(C_6F_5)_4]$ was employed (Entry 10, $\alpha/\beta = 16/84$), while weaker acids such as $Et_2O{\cdot}BF_3$ and $H[BF_4]$ induced α-selectivities conversely (Entries 1 and 4). The mechanisms by which the above sulfonates and tetrakis(pentafluorophenyl)borates achieve high β-selectivities are not yet clearly explained. The $H[B(C_6F_5)_4]$-catalyzed-mannosylation in the absence of MS 5A did not proceed as smoothly (29%, $\alpha/\beta = 41/59$) as other glycosylation reactions that used glycosyl fluoride[11c] or thioformimidate[5d] as a donor.

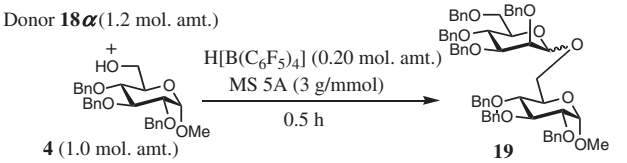
Table 5. Mannosylation Using Various Activators



Entry	Activator (mol. amt. based on acceptor)	Yield/% (α/β)[b)]
1	$Et_2O{\cdot}BF_3$ (1.2)	70 (78/22)
2	TMSOTf (1.2)	95 (25/75)
3	$Tr[B(C_6F_5)_4]$ (1.2)	97[c)] (34/66)
4	$H[BF_4]$ (0.20)	57[d)] (72/28)
5	$H[ClO_4]$ (0.20)[e)]	89 (45/55)
6	$H[NTf_2]$ (0.20)[f)]	92 (43/57)
7	$H[SbF_6]$ (0.20)[f)]	90 (44/56)
8	FSO_3H (0.20)	99 (29/71)
9	TfOH (0.20)	99 (27/73)
10	$H[B(C_6F_5)_4]$ (0.20)[g)]	**96** (**16**/**84**)

a) In the case of using $Ag[B(C_6F_5)_4]$[4c] or CH_3SO_3H as an activator, almost no reaction took place at -78 °C. b) The α/β ratios were determined by isolations of both stereoisomers. c) The reaction time was 1 h. d) The reaction time was 3 h. e) Protic acid was generated from silver salt and ^{t}BuCl in toluene, and the supernatant was used. f) Protic acid was generated from silver salt and ^{t}BuBr in toluene, and the supernatant was used. g) Protic acid was generated from silver salt and ^{t}BuBr in toluene–diethyl ether (1:1), and the supernatant was used.

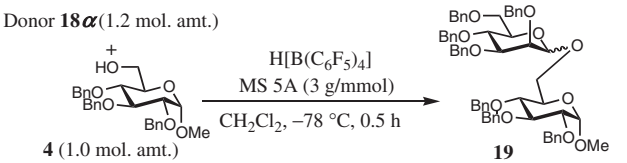
Table 6. Effects of Solvent and Reaction Temperature



Entry	Solvent	Temp./°C	Yield/% (α/β)[a)]
1	EtCN	-78	49[b)] (73/27)
2	Et_2O	-78	89 (38/62)
3	Toluene	-78	91 (14/86)
4	CH_2Cl_2	-78	96 (16/84)
5	CH_2Cl_2	-94	92 (28/72)
6	CH_2Cl_2	-60	98 (22/78)
7	CH_2Cl_2	-30	quant. (45/55)
8	CH_2Cl_2	0	quant. (59/41)

a) The α/β ratios were determined by isolations of both stereoisomers. b) The reaction time was 1 h.

Table 7. Effect of Catalyst Amount



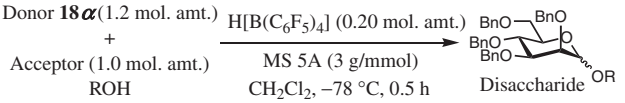
Entry	Catalyst amount/mol. amt.	Yield/% (α/β)[a)]
1	0.30	97 (17/83)
2	0.20	96 (16/84)
3	0.10	quant (17/83)
4	0.05	99 (24/76)
5	0.01	91[b)] (30/70)

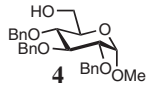
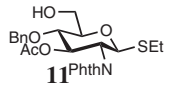
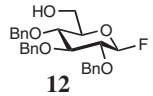
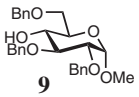
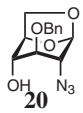
a) The α/β ratios were determined by isolations of both stereoisomers. b) The reaction time was 2 h.

Next, reaction conditions were examined by taking the reaction of **4** with **18α** in the presence of 0.20 molar amounts of $H[B(C_6F_5)_4]$ as a model. High β-selectivity was observed when the mannosylation was carried out in toluene or CH_2Cl_2, a nonpolar solvent (Table 6, Entries 3, 4) and the highest yield for β-mannosylation was obtained when the reaction was carried out in CH_2Cl_2 (Entry 4). On the other hand, the same mannosylation afforded disaccharide with α-selectivity in a nitrile solvent (Entry 1) that was frequently employed for the effective construction of α-mannoside.[21,23] Further, this mannosylation using **18α** proceeded even at -94 °C (Entry 5) and the β-selectivities were observed at the temperatures ranging from -60 °C to -94 °C (Entries 4, 5, and 6), whereas no β-selectivties were recognized at higher temperatures, -30 °C to 0 °C (Entries 7, 8). This was probably because the undesirable S_N1-type process took place competitively under these conditions and thus gave α-mannoside. Concerning the amount of catalyst, only 0.01 molar amounts of $H[B(C_6F_5)_4]$ was enough to carry out the mannosylation at -78 °C. (Table 7, Entry 5). They also proceeded successfully by using at least 0.10 molar amounts of $H[B(C_6F_5)_4]$ to give disaccharide with highest β-selectivities (Entries 1, 2, and 3).

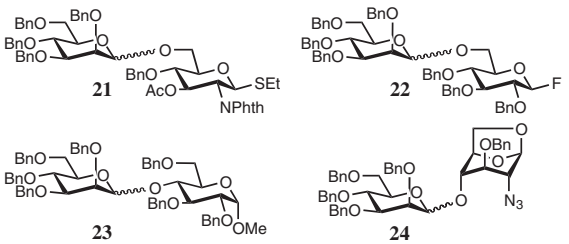
In order to extend the scope of this reaction, β-selective

Table 8. Mannosylation of Several Acceptors



Entry	Acceptor (ROH)	Product	Yield/% (α/β)[a]
1	 **4**	**19**	96 (16/84)
2	 **11**^{PhthN}	**21**	83 (10/90)
3	 **12**	**22**	82 (11/89)
4	 **9**	**23**	77 (25/75)
5	 **20**	**24**	89 (30/70)

a) The α/β ratios were determined by isolations of both stereoisomers.

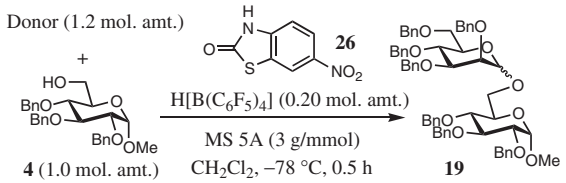


mannosylation of several glycosyl acceptors such as thioglycoside **11**, glycosyl fluoride **12**, methyl glycoside **9**, and glucosamine derivative **20**[30] with **18α** were tried at −78 °C (Table 8). All glycosyl acceptors having primary hydroxy groups reacted smoothly to afford the desired disaccharides with high β-selectivities (Entries 1–3). Furthermore, moderate β-stereoselectivities were observed in the similar mannosylations using **9** and **20** (Entries 4, 5). To the best of our knowledge, these are the highest yields of β-disaccharides, **19**, **23**, and **24**, by direct mannosylations with 2,3,4,6-tetra-*O*-benzyl-mannosyl donor. It should also be noted that the chemoselective mannosylations using glycosyl acceptors such as ethyl 3-*O*-acetyl-4-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**11**) and 2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl fluoride (**12**) gave good results as well without giving any damage to a thio-group or to a fluorine-atom linked at their anomeric positions (Entries 2, 3).

Thus, the donor **18α** is noted to have a potent and characteristic feature for the construction of β-mannoside. This feature enabled us to achieve the mannosylation with high β-selectivity at −78 °C in CH_2Cl_2. The β-selectivity was influenced by the nature of acid catalyst; the highest β-selectivities were observed when $H[B(C_6F_5)_4]$ was used.

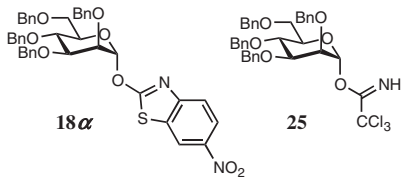
Since 6-nitro-2(3*H*)-benzothiazolone **26** was formed together with the desired mannoside, its influences on β-selectivity and on yield were considered. In order to study the induction of β-selectivity, mannosylation of **4** with **18α** or the corresponding α-mannosyl trichloroacetimidate donor **25**[12] was tried in the presence of **26**; neither β-selectivity nor yield was influenced (Table 9). This may be due to the extreme insolubility of 6-nitro-2(3*H*)-benzothiazolone **26** in CH_2Cl_2. Thus, high β-selectivity is entirely dependent on the characteristic property of **18α**.

Table 9. Effects of 6-Nitro-2(3*H*)-benzothiazolone **26** and Donor

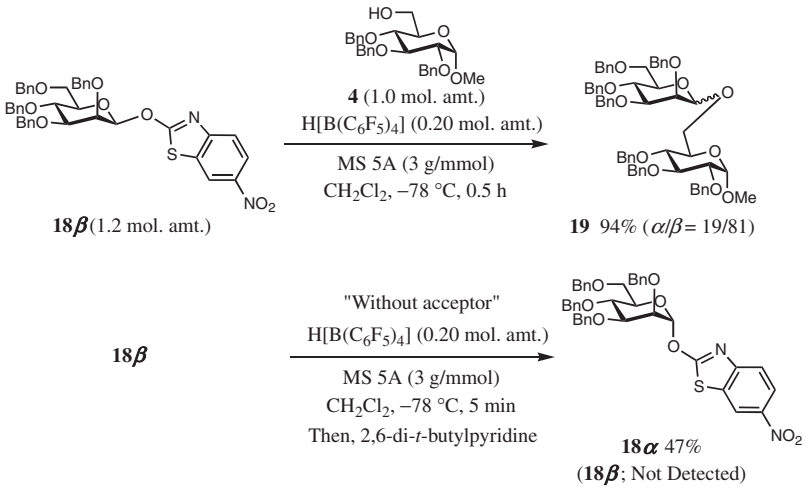


Entry	Donor	Additive **26**/mol. amt.	Yield/% (α/β)[a]
1	**18α**	0	96 (16/84)
2	**18α**	2.4	85 (19/81)
3	**25**	0	67 (36/64)
4	**25**	1.2	71 (35/65)

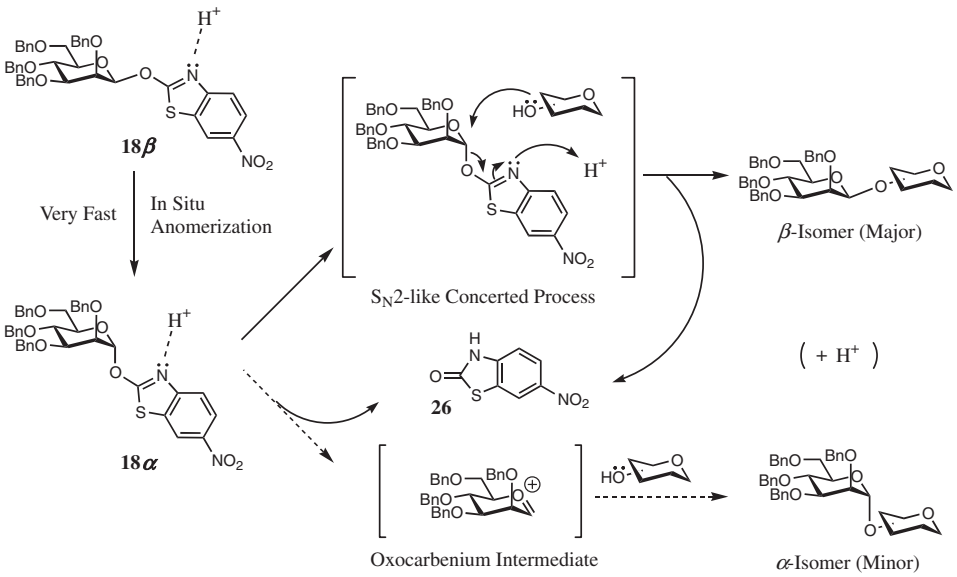
a) The α/β ratios were determined by isolations of both stereoisomers.



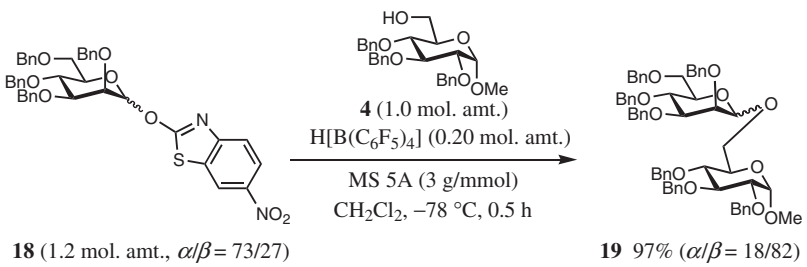
Next, mannosylation of **4** with β-isomer of donor **18β** was tried under the above mentioned conditions (Scheme 3). Interestingly, β-selective mannosylation also proceeded smoothly to give disaccharide in high yield similar to the case of using α-donor **18α**. In order to study its mechanism, a reaction using **18β** was tried in the absence of glycosyl acceptor **4** under the same conditions. After stirring for only 5 minutes, the reaction mixture was swiftly quenched with a proton scavenger, 2,6-di-*t*-butylpyridine. It was interesting to note that the α-isomer **18α** was obtained in 47% yield while β-isomer **18β** was not detected. This result may indicate that in situ anomerization takes place rapidly. As far as we know, this is the first report on the in situ anomerization in which the imidate-type glycosyl donor was treated with acids. As shown in Table 9, 6-nitro-2-benzothiazolyl mannoside donor enabled the mannosylation to achieve higher β-stereoselectivity than mannosyl trichloroacetimidate. It may be considered that the mannosylation reaction using β-donor **18β** proceeded via in situ anomerization to **18α** before forming disaccharide with glycosyl acceptor **4** and that the mannosylation consequently took place via a S_N2-like concerted process between α-isomer **18α** and a glycosyl acceptor more dominantly (Scheme 4). Additionally, it was found that the β-selective mannosylation could be performed by using a mixture of α- and β-donor **18** (α/β = 73/27: obtained by the condensation reaction shown in Table 4, Entry 3) as shown in Scheme 5. This result may extend the utility of 6-nitro-2-benzo-



Scheme 3.



Scheme 4.



Scheme 5.

thiazolyl mannoside donor because a separation procedure of the two isomers, **18α** and **18β**, is not needed.

All stereochemistries of novel mannosides were confirmed by geminal ^{13}C–^{1}H coupling constants of anomeric positions.[31]

Conclusion

It is noted that 1) 6-nitro-2-benzothiazolyl glucoside **3α** was easily prepared by a direct condensation reaction of 1-hydroxy sugar with 2-chloro-6-nitrobenzothiazole in the presence of a base, 2) the glucosyl donor **3α** enabled the glucosylation to achieve higher β-stereoselectivities than the donors **6**, **7**, or **8** when a catalytic amount of TfOH was used in CH_2Cl_2, 3) the donor **18** enabled the mannosylation with high β-selectivities at −78 °C in CH_2Cl_2, and 4) the β-selectivity was influenced by the nature of acid catalyst. The highest β-selectivity was observed when $H[B(C_6F_5)_4]$ was used. Thus, benzothiazolyl glu-

coside and mannoside were found to behave as efficient glycosyl donors and to have a potent feature for the construction of stereoselective β-saccharide linkage.

Experimental

General. All melting points were measured on a Yanaco MP-S3 micro melting point apparatus. Infrared spectra were recorded on a Horiba FT-300 infrared spectrometer. ^{1}H NMR spectra were recorded on a JEOL JNM-EX270 (270 MHz), JNM-EX300 (300 MHz), JNM-LA400 (400 MHz), or JEOL JNM-LA500 (500 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to teteramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C NMR spectra were recorded on a JEOL JNM-EX270L (68 MHz), a JEOL JNM-LA400 (100 MHz), or a JEOL JNM-LA500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$; δ 77.0). High-resolution mass spectra were recorded on a Micromass Q-TOF2 instrument [ESI positive, 0.01 M (1 M = 1 mol dm^{-3}) $AcONH_4$ in H_2O/MeCN]. High-performance liquid chromatography (HPLC) was carried out using a Hitachi LC-Organizer, L-4000 UV Detector, L-6200 Intelligent Pump, and D-2500 Chromato-Integrator with Shodex SIL-5B (normal phase: 120 Å, 5 μm, ϕ4.6 × 250 mm) and YMC J'sphere M80 (reverse phase: 80 Å, 4 μm, ϕ4.6 × 250 mm). Optical rotations were recorded on a Jasco-P-1020 polarimeter. Analytical TLC was done on precoated (0.25 mm) silica gel 60 F_{254} plates (E. Merck). Thin-layer chromatography was performed on Wakogel B-5F. Column chromatography was performed on Silica gel 60 (Merck).

All reactions were carried out under argon atmosphere in dried glassware, unless otherwise noted. All reagents were purchased from Tokyo Kasei Kogyo, Kanto Chemical, or Aldrich and used without further purification, unless otherwise noted. TfOH (donated by Central Glass Co. Ltd.) was simply distilled and used for glycosylation. $H[ClO_4]$, $H[NTf_2]$, $H[SbF_6]$, and $H[B(C_6F_5)_4]$ were generated according to the published procedures.[11c] CH_2Cl_2 was distilled from P_2O_5 and then from CaH_2 and was stored over molecular sieves 4A. Toluene was distilled from P_2O_5 and was stored over molecular sieves 4A. Dry THF and Et_2O were purchased from Kanto Chemical. Powdered and pre-dried (at 260 °C/133 Pa, 6 h) molecular sieves 5A (MS 5A) were used in glycosylation reactions.

2-Chloro-6-nitrobenzothiazole[8] (2). This compound was prepared from 2-chlorobenzothiazole according to a published procedure. Colorless solid; R_f 0.42 (hexane/ethyl acetate, 3/1, v/v); Mp 193–195 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.08 (1H, d, J = 8.9 Hz), 8.39 (1H, dd, J = 2.2, 8.9 Hz), 8.76 (1H, d, J = 2.2 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 117.60, 122.15, 123.22, 136.29, 145.20, 154.55, 158.64; IR (KBr) 748, 1026, 1057, 1334, 1512, 3062 cm^{-1}; HRMS m/z calcd for $C_7H_3ClN_2O_2S$ $[M]^+$ 213.9604, found 213.9606.

6-Nitro-2-benzothiazolyl 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranoside (3). To a solution of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose[7] **1** (50.3 mg, 93.0 μmol) in THF–DMF (1.0 mL, 9/1, v/v) was added lithium bis(trimethylsilyl)amide (0.50 M in THF, 0.22 mL, 0.11 mmol) at 0 °C. After stirring for 0.5 h at the same temperature, **2** (23.8 mg, 0.11 mmol) was added to the reaction mixture. After additional stirring for 48 h at the same temperature, the mixture was quenched by adding sat. aq. $NaHCO_3$. The aqueous layer was extracted with EtOAc, washed with brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford the mixture of **3α** and **3β** (61.5 mg, 92%, α/β = 88/12). The ratios of **3** were determined by ^{1}H NMR measurements. Both anomers were also isolated by preparative TLC (silica gel) to give **3α** (51.5 mg, 77%) and **3β** (5.0 mg, 7%).

3α: colorless oil; R_f 0.36 (hexane/$CHCl_3$/Et_2O, 6/6/1, v/v/v); $[\alpha]_D^{20}$ +122.1° (c 1.00, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.65 (1H, d, J = 10.8 Hz), 3.73–3.88 (3H, m), 3.97 (1H, d, J = 9.7 Hz), 4.12 (1H, t, J = 9.2 Hz), 4.44 (1H, d, J = 12.2 Hz), 4.52 (1H, d, J = 10.8 Hz), 4.58 (1H, d, J = 12.2 Hz), 4.74 (1H, d, J = 11.9 Hz), 4.79 (1H, d, J = 11.9 Hz), 4.87 (1H, d, J = 10.8 Hz), 4.89 (1H, d, J = 10.8 Hz), 5.01 (1H, d, J = 10.8 Hz), 6.61 (1H, d, J = 3.2 Hz, H-1), 7.13–7.38 (20H, m, Ar-H), 7.76 (1H, d, J = 8.9 Hz), 8.26 (1H, dd, J = 2.2, 8.9 Hz), 8.59 (1H, d, J = 2.2 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 67.71, 73.19, 73.38, 73.56, 75.27, 75.77, 79.09, 98.37 (C-1), (127.68–128.39, 137.32, 137.54, 137.78, 138.37) (C-Ar), (117.78, 121.18, 121.84, 132.33, 143.82, 153.65, 174.93) (Benzothiazole); IR (neat) 702, 740, 1119, 1342, 1527, 2931 cm^{-1}; HRMS m/z calcd for $C_{41}H_{38}N_2O_8 \cdot NH_4$ $[M + NH_4]^+$ 736.2693, found 736.2712.

3β: colorless oil; R_f 0.29 (hexane/$CHCl_3$/Et_2O, 6/6/1, v/v/v); $[\alpha]_D^{21}$ +6.3° (c 1.02, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.77–3.83 (6H, m), 4.48 (1H, d, J = 12.2 Hz), 4.58 (2H, t, J = 10.8 Hz), 4.83 (2H, brs), 4.84 (1H, d, J = 12.2 Hz), 4.86 (1H, d, J = 11.1 Hz), 4.93 (1H, d, J = 11.1 Hz), 6.03 (1H, d, J = 7.3 Hz, H-1), 7.13–7.80 (20H, m, Ar-H), 7.78 (1H, d, J = 8.9 Hz), 8.27 (1H, dd, J = 2.2, 8.9 Hz), 8.59 (1H, d, J = 2.2 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 67.98, 73.42, 75.01, 75.68, 76.52, 80.92, 84.35, 101.08 (C-1), (127.68–128.40, 137.49, 137.66, 137.49, 138.09) (C-Ar), (117.80, 121.40, 121.90, 132.45, 143.93, 153.49, 174.72) (Benzothiazole); IR (neat) 702, 748, 1080, 1257, 1342, 1450, 1520, 2870 cm^{-1}; HRMS m/z calcd for $C_{41}H_{38}N_2O_8 \cdot NH_4$ $[M + NH_4]^+$ 736.2693, found 736.2686.

Glucosylation Using TfOH as Catalyst (The General Procedure). To a stirred suspension of MS 5A (150 mg), glucosyl donor (0.055 mmol), and glucosyl acceptor (0.050 mmol) in CH_2Cl_2 (1.25 mL) was successively added TfOH (0.750 mg in toluene, 0.10 mL, 2.5 μmol) at −78 °C. After the completion of the glucosylation reaction by monitoring TLC, the reaction was quenched by adding sat. aq. $NaHCO_3$. Then the mixture was filtered through Celite and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over Na_2SO_4. After filtration and evaporation, the resulting residue was purified by preparative TLC (silica gel) until afforded the corresponding disaccharide. The α to β ratios for **5**,[11c] **13**,[11c] **14**,[11c] and **15**[11c] were determined by HPLC analysis and the ratios for **16**[5d] were determined by isolation of both isomers according to the published conditions.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-α-D-glucopyranoside (5): The ratios were determined by HPLC analysis[11c] (hexane/ethyl acetate = 4/1; flow rate, 1.0 mL/min; 12.4 min, β-isomer; 14.6 min, α-isomer).

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-α-D-glucopyranoside (13): The ratios were determined by HPLC analysis[11c] (MeOH/H_2O = 20/1; flow rate, 1.0 mL/min; 14.4 min, α-isomer; 15.9 min, β-isomer).

Ethyl 2,3,4-Tri-*O*-benzoyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (14): The ratios were determined by HPLC analysis[11c] (hexane/ethyl acetate = 4/1; flow rate, 1.0 mL/min; 10.4 min, β-isomer; 12.1 min, α-isomer).

Ethyl 3-*O*-Acetyl-4-*O*-benzyl-2-deoxy-6-*O*-(2′,3′,4′,6′-tetra-

***O*-benzyl-D-glucopyranosyl)-2-phthalimido-1-thio-β-D-glucopyranoside (15):** The ratios were determined by HPLC analysis[11c] (hexane/ethyl acetate = 4/1; flow rate, 1.0 mL/min; 20.8 min, β-isomer; 23.7 min, α-isomer).

6-Nitro-2-benzothiazolyl 2,3,4,6-Tetra-*O*-benzyl-D-mannopyranoside (18). To a solution of 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose[28] **17** (50.0 mg, 92.5 μmol) in THF (1.0 mL) was added potassium bis(trimethylsilyl)amide (0.50 M in toluene, 0.22 mL, 0.11 mmol) at 0 °C. After stirring for 0.5 h at the same temperature, **2** (23.8 mg, 0.11 mmol) was added to the reaction mixture. Then the reaction mixture was stirring for 0.5 h at room temperature. The reaction was quenched by adding sat. aq. $NaHCO_3$. The aqueous layer was extracted with EtOAc, and the combined organic layer was washed with brine and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford **18α** (44.0 mg, 66%) and **18β** (16.1 mg, 24%).

18α: colorless oil; R_f 0.54 (hexane/ethyl acetate, 7/3, v/v); $[\alpha]_D^{23}$ +63.2° (*c* 1.00, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.74 (1H, dd, *J* = 1.6, 10.8 Hz), 3.82 (1H, dd, *J* = 4.6, 10.8 Hz), 3.95–4.02 (2H, m), 4.08 (1H, t, *J* = 1.9 Hz), 4.17 (1H, t, *J* = 9.5 Hz), 4.52 (1H, d, *J* = 11.9 Hz), 4.55 (1H, d, *J* = 10.5 Hz), 4.60 (1H, d, *J* = 11.3 Hz), 4.65 (1H, d, *J* = 11.9 Hz), 4.66 (1H, d, *J* = 11.3 Hz), 4.83 (2H, s), 4.91 (1H, d, *J* = 10.5 Hz), 6.48 (1H, d, *J* = 1.9 Hz, H-1), 7.16–7.46 (20H, m, Ar-H), 7.74 (1H, d, *J* = 8.9 Hz), 8.25 (1H, dd, *J* = 2.2, 8.9 Hz), 8.55 (1H, d, *J* = 2.2 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 68.52, 72.34, 72.76, 72.97, 73.28, 73.86, 74.69, 75.16, 78.86, 98.68 (C-1, J_{C-H} = 178 Hz), (127.48–128.35, 137.54, 137.86, 137.93, 137.96) (C-Ar), (117.76, 121.18, 121.87, 132.25, 143.84, 153.50, 173.74) (Benzothiazole); IR (neat) 748, 895, 1119, 1342, 1520, 2916 cm^{-1}; HRMS *m/z* calcd for $C_{41}H_{38}N_2O_8 \cdot NH_4$ $[M + NH_4]^+$ 736.2693, found 736.2682.

18β: colorless solid; R_f 0.42 (hexane/ethyl acetate, 7/3, v/v); Mp 109–110 °C; $[\alpha]_D^{23}$ −25.6° (*c* 1.00, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.72–3.86 (4H, m), 4.05 (1H, t, *J* = 8.6 Hz), 4.24 (1H, d, *J* = 1.6 Hz), 4.51 (1H, d, *J* = 12.2 Hz), 4.57 (1H, d, *J* = 10.8 Hz), 4.61 (1H, d, *J* = 12.2 Hz), 4.64 (1H, d, *J* = 11.6 Hz), 4.70 (1H, d, *J* = 11.6 Hz), 4.88 (1H, d, *J* = 10.8 Hz), 4.88 (2H, s), 6.00 (1H, brs, H-1), 7.16–7.72 (20H, m, Ar-H), 7.70 (1H, d, *J* = 9.2 Hz), 8.25 (1H, dd, *J* = 2.2, 9.2 Hz), 8.56 (1H, d, *J* = 2.2 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 68.89, 72.31, 72.86, 73.37, 74.04, 74.12, 74.84, 76.46, 81.06, 99.52 (C-1, J_{C-H} = 162 Hz), (127.53–128.44, 137.77, 137.80, 137.91, 137.96) (C-Ar), (117.79, 121.15, 121.83, 132.41, 143.89, 153.39, 174.30) (Benzothiazole); IR (KBr) 702, 748, 1103, 1342, 1520, 2916 cm^{-1}; HRMS *m/z* calcd for $C_{41}H_{38}N_2O_8 \cdot NH_4$ $[M + NH_4]^+$ 736.2693, found 736.2704.

Mannosylation Using H[B(C$_6$F$_5$)$_4$] as Catalyst (The General Procedure). To a stirred suspension of MS 5A (150 mg), mannosyl donor (0.06 mmol) and glycosyl acceptor (0.050 mmol) in CH_2Cl_2 (1.25 mL) was successively added $H[B(C_6F_5)_4]$ (0.050 M toluene–Et_2O (1:1), 0.20 mL, 0.01 mmol) at −78 °C. After the completion of the mannosylation reaction was verified by monitoring TLC, the reaction was quenched by addition of sat. aq. $NaHCO_3$. Then, the mixture was filtered through Celite and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over Na_2SO_4. After filtration and evaporation, the resulting residue was purified by preparative TLC (silica gel) and afforded the corresponding disaccharide. The α to β ratios for **19**,[11a] **21**, **22**, **23**, and **24** were determined by isolations of both isomers.

Ethyl 3-*O*-Acetyl-4-*O*-benzyl-2-deoxy-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-mannopyranosyl)-2-phthalimido-1-thio-β-D-glucopyranoside (21): This compound was synthesized from mannosyl donor **18α** and glycosyl acceptor **11**.[11c]

21α: colorless oil; R_f 0.41 (hexane/ethyl acetate, 2/1, v/v); $[\alpha]_D^{21}$ +30.2° (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (3H, t, *J* = 7.0 Hz), 1.79 (3H, s), 2.57–2.65 (2H, m), 3.59 (1H, t, *J* = 9.5 Hz), 3.63–3.68 (2H, m), 3.73–3.80 (3H, m), 3.84 (1H, s), 3.89–3.92 (2H, m), 4.02 (1H, t, *J* = 9.5 Hz), 4.24 (1H, t, *J* = 9.5 Hz), 4.50 (1H, d, *J* = 12.5 Hz), 4.53 (1H, d, *J* = 11.0 Hz), 4.54 (2H, s), 4.66 (1H, d, *J* = 12.5 Hz), 4.67 (2H, s), 4.76 (2H, s), 4.92 (1H, d, *J* = 11.0 Hz), 5.07 (1H, s, H-1′), 5.48 (1H, d, *J* = 9.5 Hz, H-1), 5.81 (1H, t, *J* = 9.5 Hz), 7.19–7.37 (23H, m, Ar-H), 7.43 (2H, d, *J* = 7.0 Hz, Ar-H), 7.71–7.74 (2H, m, Ar-H), 7.83–7.88 (2H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.90, 20.43, 24.33, 54.31, 65.63, 69.17, 71.92, 71.95, 72.35, 73.16, 74.06, 74.54, 74.85, 74.89, 76.53, 78.50, 79.36, 80.77 (C-1), 98.31 (C-1′, J_{C-H} = 170 Hz), (123.40, 123.52, 131.20, 131.72, 134.04, 134.20, 167.40, 167.59) (C-Phth), (127.27–128.31, 137.68, 138.26, 138.39, 138.41, 138.47) (C-Ar), 169.85; IR (neat) 702, 748, 1103, 1381, 1712, 2353, 3016 cm^{-1}; HRMS *m/z* calcd for $C_{59}H_{61}NO_{12}S \cdot NH_4$ $[M + NH_4]^+$ 1025.4258, found 1025.4266.

21β: colorless amorphous material; R_f 0.34 (hexane/ethyl acetate, 2/1, v/v); $[\alpha]_D^{22}$ −15.8° (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13 (3H, t, *J* = 7.0 Hz), 1.81 (3H, s), 2.52–2.65 (2H, m), 3.43–3.46 (1H, m), 3.48 (1H, dd, *J* = 2.5, 9.0 Hz), 3.59–3.65 (2H, m), 3.76–3.82 (3H, m), 3.87 (1H, d, *J* = 2.5 Hz), 3.93 (1H, t, *J* = 9.0 Hz), 4.28–4.32 (2H, m), 4.34 (1H, s, H-1′), 4.51–4.68 (7H, m), 4.90 (1H, d, *J* = 12.0 Hz), 4.91 (1H, d, *J* = 11.0 Hz), 4.99 (1H, d, *J* = 11.0 Hz), 5.48 (1H, d, *J* = 10.5 Hz, H-1), 5.85 (1H, t, *J* = 9.5 Hz), 7.19–7.37 (23H, m, Ar-H), 7.50 (2H, d, *J* = 7.0 Hz, Ar-H), 7.72–7.73 (2H, m, Ar-H), 7.85–7.88 (2H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.86, 20.40, 24.02, 54.27, 68.86, 69.52, 71.51, 73.39, 73.69, 73.75, 74.07, 74.29, 74.87, 75.00, 75.96, 77.15, 78.86, 80.63 (C-1), 82.18, 102.05 (C-1′, J_{C-H} = 156 Hz), (123.39, 123.46, 131.21, 131.74, 133.92, 134.18, 167.40, 167.59) (C-Phth), (127.30–128.32, 137.61, 138.12, 138.31, 138.42, 138.68) (C-Ar), 169.80; IR (neat) 748, 1103, 1227, 1381, 1713, 2931 cm^{-1}; HRMS *m/z* calcd for $C_{59}H_{61}NO_{12}S \cdot NH_4$ $[M + NH_4]^+$ 1025.4258, found 1025.4260.

2,3,4-Tri-*O*-benzyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-mannopyranosyl)-β-D-glucopyranosyl Fluoride (22): This compound was synthesized from mannosyl donor **18α** and glycosyl acceptor **12**.[5d]

22α: colorless oil; R_f 0.50 (hexane/ethyl acetate, 2/1, v/v); $[\alpha]_D^{21}$ +36.4° (*c* 1.12, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.53–3.60 (3H, m), 3.63–3.76 (5H, m), 3.84 (1H, s), 3.87–3.90 (2H, m), 4.01 (1H, t, *J* = 9.0 Hz), 4.47–4.53 (3H, m), 4.60–4.65 (3H, m), 4.71–4.81 (5H, m), 4.85–4.91 (3H, m), 5.03 (1H, s, H-1′), 5.26 (1H, dd, *J* = 6.0, 53.0 Hz, H-1), 7.16–7.42 (35H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 65.67, 69.18, 71.85, 72.10, 72.35, 73.19, 74.09 (d, *J* = 1.9 Hz), 74.38 (d, *J* = 3.6 Hz), 74.50, 74.77, 74.82, 74.87, 75.16, 76.52, 79.35, 81.24 (d, *J* = 22.9 Hz), 83.38 (d, *J* = 10.1 Hz), 98.61 (C-1′, J_{C-H} = 170 Hz), 109.48 (d, *J* = 216 Hz, C-1), (127.25–128.37, 137.58, 138.10, 138.33, 138.42, 138.60) (C-Ar); IR (neat) 694, 741, 1095, 1458, 1496, 1604, 1737, 1959, 2931 cm^{-1}; HRMS *m/z* calcd for $C_{61}H_{63}O_{10}F \cdot NH_4$ $[M + NH_4]^+$ 992.4749, found 992.4764.

22β: colorless solid; R_f 0.43 (hexane/ethyl acetate, 2/1, v/v); Mp 129–130 °C; $[\alpha]_D^{22}$ −5.0° (*c* 0.85, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.43–3.46 (2H, m), 3.53–3.62 (3H, m), 3.70–3.82 (4H, m), 3.87 (1H, d, *J* = 3.0 Hz), 3.91 (1H, t, *J* = 9.5 Hz), 4.26 (1H, d, *J* = 10.5 Hz), 4.29 (1H, s, H-1′), 4.50–4.66 (7H,

m), 4.73 (1H, d, $J = 11.0$ Hz), 4.81 (2H, d, $J = 11.0$ Hz), 4.87–5.00 (4H, m), 5.30 (1H, dd, $J = 6.5$, 52.5 Hz, H-1), 7.19–7.50 (35H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 68.40, 69.58, 71.45, 73.37, 73.48, 73.65, 74.15 (d, $J = 1.9$ Hz), 74.64 (d, $J = 4.6$ Hz), 74.85, 74.96, 75.15, 75.95, 76.95, 81.37 (d, $J = 22.0$ Hz), 83.45 (d, $J = 10.1$ Hz), 101.73 (C-1′, $J_{C-H} = 155$ Hz), 109.60 (d, $J = 216$ Hz, C-1), (127.24–128.32, 137.61, 137.79, 138.12, 138.16, 138.33, 138.41, 138.66) (C-Ar); IR (KBr) 694, 741, 1111, 1358, 1458, 1496, 2908 cm^{-1}; HRMS m/z calcd for $C_{61}H_{63}O_{10}F \cdot NH_4$ $[M + NH_4]^+$ 992.4749, found 992.4737.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-mannopyranosyl)-α-D-glucopyranoside (23): This compound was synthesized from mannosyl donor **18α** and glycosyl acceptor **9**.[14]

23α: colorless oil; R_f 0.44 (hexane/ethyl acetate, 2/1, v/v); $[\alpha]_D^{24}$ +18.1° (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.41 (3H, s), 3.56 (1H, dd, $J = 3.6$, 9.6 Hz), 3.59 (1H, dd, $J = 1.6$, 10.4 Hz), 3.68 (1H, dd, $J = 4.4$, 10.4 Hz), 3.73–3.75 (5H, m), 3.79–3.85 (2H, m), 3.88 (1H, dd, $J = 2.8$, 9.2 Hz), 3.99 (1H, t, $J = 9.2$ Hz), 4.23 (1H, d, $J = 12.4$ Hz), 4.33 (1H, d, $J = 12.4$ Hz), 4.44 (1H, d, $J = 12.4$ Hz), 4.45 (1H, d, $J = 12.0$ Hz), 4.51 (1H, d, $J = 10.8$ Hz), 4.53–4.63 (6H, m), 4.63 (1H, d, $J = 3.6$ Hz, H-1), 4.69 (1H, d, $J = 12.4$ Hz), 4.86 (1H, d, $J = 10.8$ Hz), 5.11 (1H, d, $J = 11.6$ Hz), 5.32 (1H, d, $J = 2.0$ Hz, H-1′), 7.12–7.32 (35H, m, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.12, 69.22 × 2, 69.65, 71.90, 72.11, 72.83, 73.02, 73.11, 73.21, 74.78, 74.84, 74.87, 76.13, 77.61, 79.60, 79.83, 81.41, 97.54 (C-1), 100.36 (C-1′, $J_{C-H} = 169$ Hz), (126.56–128.31, 137.72, 138.21, 138.28, 138.42, 138.43, 138.52, 138.68) (C-Ar); IR (neat) 694, 741, 1049, 1103, 1635, 2353, 2931 cm^{-1}; HRMS m/z calcd for $C_{62}H_{66}O_{11} \cdot NH_4$ $[M + NH_4]^+$ 1004.4949, found 1004.4955.

23β: colorless oil; R_f 0.37 (hexane/ethyl acetate, 2/1, v/v); $[\alpha]_D^{24}$ −16.0° (*c* 0.67, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.29 (1H, dd, $J = 2.8$, 9.6 Hz), 3.27–3.30 (1H, m), 3.39 (3H, s), 3.46–3.58 (4H, m), 3.67–3.75 (2H, m), 3.71 (1H, d, $J = 2.8$ Hz), 3.88 (1H, t, $J = 9.6$ Hz), 3.90–3.94 (2H, m), 4.37 (1H, d, $J = 11.2$ Hz), 4.38 (1H, d, $J = 12.0$ Hz), 4.43 (1H, s, H-1′), 4.45 (1H, d, $J = 11.6$ Hz), 4.45 (1H, d, $J = 12.0$ Hz), 4.50 (1H, d, $J = 11.6$ Hz), 4.54 (1H, d, $J = 10.8$ Hz), 4.58 (1H, d, $J = 11.2$ Hz), 4.59 (1H, d, $J = 3.6$ Hz, H-1), 4.61 (1H, d, $J = 12.0$ Hz), 4.76 (1H, d, $J = 11.2$ Hz), 4.78 (1H, d, $J = 12.0$ Hz), 4.84 (2H, brs), 4.86 (1H, d, $J = 10.8$ Hz), 5.16 (1H, d, $J = 11.2$ Hz), 7.15–7.41 (35H, m, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.15, 68.57, 69.41, 69.56, 71.52, 73.33, 73.42, 73.50, 73.95, 74.68, 74.88, 74.91, 75.09, 76.05, 77.01, 78.99, 80.21, 82.46, 98.25 (C-1), 100.73 (C-1′, $J_{C-H} = 154$ Hz), (126.86–128.37, 137.58, 138.18, 138.21, 138.39, 138.69, 138.76, 139.50) (C-Ar); IR (neat) 702, 741, 1049, 1103, 1458, 1720, 2353, 2839 cm^{-1}; HRMS m/z calcd for $C_{62}H_{66}O_{11} \cdot NH_4$ $[M + NH_4]^+$ 1004.4949, found 1004.4979.

1,6-Anhydro-2-azido-3-*O*-benzyl-2-deoxy-4-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-mannopyranosyl)-β-D-glucopyranose (24): This compound was synthesized from mannosyl donor **18α** and glycosyl acceptor **20**.[30]

24α: colorless oil; R_f 0.39 (hexane/ethyl acetate, 2/1, v/v); $[\alpha]_D^{22}$ +58.0° (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.13 (1H, s), 3.47 (1H, brs), 3.62 (1H, dd, $J = 5.2$, 7.2 Hz), 3.67 (1H, s), 3.74–3.82 (2H, m), 3.86 (1H, dd, $J = 1.6$, 2.8 Hz), 3.94–3.96 (2H, m), 4.02 (1H, dd, $J = 2.8$, 6.0 Hz), 4.04 (1H, d, $J = 7.2$ Hz), 4.54 (1H, d, $J = 10.8$ Hz), 4.54 (1H, d, $J = 12.0$ Hz), 4.55 (1H, d, $J = 12.0$ Hz), 4.60 (1H, d, $J = 12.0$ Hz), 4.64 (2H, s), 4.64 (2H, d, $J = 12.0$ Hz), 4.70 (1H, d, $J = 5.2$ Hz), 4.76 (1H, d, $J = 12.0$ Hz), 4.87 (1H, d, $J = 1.6$ Hz, H-1′), 4.91 (1H, d, $J = 10.8$ Hz), 5.52 (1H, s, H-1), 7.16–7.40 (25H, m, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 59.01, 65.12, 69.38, 72.01, 72.13, 72.38, 72.90, 73.17, 73.58, 74.68, 74.72, 74.82, 75.10, 75.71, 79.69, 97.97 (C-1′, $J_{C-H} = 167$ Hz), 100.42 (C-1), (127.40–128.45, 136.93, 137.96, 138.08, 138.15, 138.31) (C-Ar); IR (neat) 702, 748, 1034, 1365, 1458, 1604, 2098, 2924 cm^{-1}; HRMS m/z calcd for $C_{47}H_{49}N_3O_9 \cdot NH_4$ $[M + NH_4]^+$ 817.3813, found 817.3813.

24β: colorless oil; R_f 0.21 (hexane/ethyl acetate, 2/1, v/v); $[\alpha]_D^{23}$ −28.2° (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.27 (1H, s), 3.48–3.52 (1H, m), 3.56 (1H, dd, $J = 2.8$, 9.2 Hz), 3.73–3.81 (3H, m), 3.82 (1H, brs), 3.91 (1H, t, $J = 9.2$ Hz), 3.99 (1H, s), 4.05 (1H, d, $J = 2.8$ Hz), 4.14 (1H, d, $J = 7.6$ Hz), 4.48 (1H, d, $J = 12.0$ Hz), 4.52 (1H, d, $J = 12.0$ Hz), 4.57 (1H, d, $J = 10.8$ Hz), 4.57 (1H, d, $J = 11.6$ Hz), 4.57 (1H, d, $J = 12.0$ Hz), 4.59 (1H, d, $J = 12.0$ Hz), 4.65 (1H, d, $J = 11.6$ Hz), 4.69 (1H, d, $J = 7.2$ Hz), 4.70 (1H, s, H-1′), 4.91 (1H, d, $J = 12.0$ Hz), 4.94 (1H, d, $J = 10.8$ Hz), 5.03 (1H, d, $J = 12.0$ Hz), 5.54 (1H, s, H-1), 7.15–7.48 (25H, m, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 59.27, 64.74, 69.52, 71.19, 72.04, 72.18, 72.58, 73.24, 73.90, 74.05, 74.58, 75.07, 75.94, 77.51, 82.00, 98.52 (C-1′, $J_{C-H} = 154$ Hz), 100.44 (C-1), (127.18–128.32, 137.34, 137.88, 138.06, 138.75) (C-Ar); IR (neat) 702, 741, 1103, 1627, 2098, 2360, 2962 cm^{-1}; HRMS m/z calcd for $C_{47}H_{49}N_3O_9 \cdot NH_4$ $[M + NH_4]^+$ 817.3813, found 817.3809.

In Situ Anomerization Reaction with 18β Using H[B(C$_6$F$_5$)$_4$] as Catalyst. To a stirred suspension of MS 5A (113 mg) and **18β** (0.045 mmol) in CH_2Cl_2 (0.94 mL) was successively added H[B(C_6F_5)$_4$] (0.050 M toluene–Et_2O (1:1), 0.15 mL, 7.50 μmol) at −78 °C. After stirring for 5 min, the reaction was quenched by addition of 2,6-di-*t*-butylpyridine (20.2 μL, 0.090 mmol). To the mixture was then added sat. aq. $NaHCO_3$; the mixture was filtered through Celite and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over Na_2SO_4. After filtration and evaporation, the resulting residue was purified by preparative TLC (silica gel) to afford **18α** (15.3 mg, 47%) as a single isomer.

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