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Protic Acid Catalyzed Stereoselective Glycosylation Using Glycosyl Fluorides

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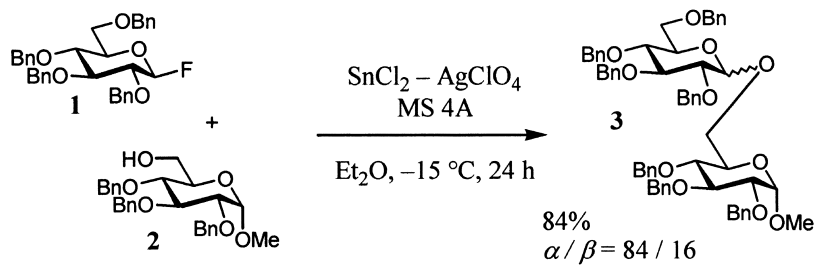
A catalytic and stereoselective glycosylation of various glycosyl acceptors, such as methyl glycosides, thioglycosides, or a disarmed glycosyl fluoride, with benzyl-protected armed glycosyl fluoride was successfully carried out by using various protic acids in the presence of MS 5A. In the cases when trifluoromethanesulfonic acid (TfOH) or perchloric acid ($HClO_4$) was used in diethyl ether (Et_2O), α-glycosides were obtained as major products, while β-stereoselectivity was observed when tetrakis(pentafluorophenyl)boric acid [$HB(C_6F_5)_4$] was used in a mixed solvent of trifluoromethylbenzene (BTF)–pivalonitrile (^tBuCN) = 5:1. Stereoselectivity of this glycosylation was controlled by the properties of counter anions of the catalyst as well as by those of solvents. Also, one-pot trisaccharide synthesis was performed by successive addition of NIS and third-sugar to afford Glcα or β1–6Glcβ1–6Glc and Glcα or β1–6GlcNβ1–6Glc in excellent yields.

Development of stereoselective glycosylation reactions is one of the most fundamental and important topics in carbohydrate chemistry. For syntheses of glycosides including oligosaccharides, the Koenigs–Knorr reaction[1] was most commonly employed for a long time; however, its troublesome use of a stoichiometric amount of heavy-metal salt and its drastic reaction conditions remained to be solved. In the past 20 years, various types of excellent glycosyl donors have been developed and employed in the syntheses of saccharide chains together with suitable activators, that is, thioglycosides, selenoglycosides, glycosyl sulfoxides, glycosyl trichloroacetimidates, glycosyl acetate, 1-OH sugar, glycosyl donors having phosphorus-containing leaving groups, glycals, and pentenyl glycoside.[2] In 1981, use of glycosyl fluoride as a glycosyl donor was first reported from our laboratory.[3] α-Glucosides were obtained with good stereoselectivities when glucosyl fluoride was treated with various glycosyl acceptors by the combined use of tin(II) chloride ($SnCl_2$) and silver perchlorate ($AgClO_4$) as a promoter in diethyl ether (Et_2O) (Scheme 1).

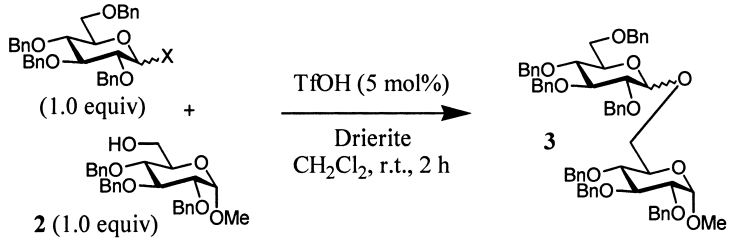
Since glycosyl fluorides that have strong C–F bond were more stable than the corresponding chlorides or bromides, due to their high bond-dissociation energy (C–F: 552 /KJ mol^{-1}, C–Cl: 397 ± 29/KJ mol^{-1}, C–Br: 280 ± 21/KJ mol^{-1}),[4] the fluoride had not been employed. After the above-mentioned combined-catalyst system was introduced, the fluorides became popular glycosyl donors. Preparative methods of glycosides using glycosyl fluorides combined with suitable activators have been developed since then.[5] Activators such as SiF_4,[6] Me_3SiOTf,[6] $BF_3{\cdot}OEt_3$,[7] TiF_4,[8] SnF_4,[8] Cp_2MCl_2–$AgClO_4$ (M = Ti, Zr, Hf),[9] Me_2GaCl,[10] Tf_2O,[11] $LiClO_4$,[12] $Yb(OTf)_3$,[13] $La(ClO_4)_3{\cdot}nH_2O$,[13] SO_4/ZrO_2,[14] and $TrB(C_6F_5)_4$[15] promoted the glycosylation of various glycosyl acceptors and were successfully employed in the syntheses of complex oligosaccharide chains.[16] Of a number of methods developed for activation of glycosyl fluorides using a stoichiometric amount of activators, only a few examples were reported concerning catalytic glycosylation with glycosyl fluorides.[6,7c,13b,15] To the best of our knowledge, only one example has been reported so far for a catalytic and stereoselective glycosylation of various free alcohols as glycosyl acceptors with glycosyl fluoride.[15]

Reviewing methods of glycosylation using glycosyl fluorides, no examples of glycosylation of various glycosyl acceptors using protic acid were found.[17] According to Hard and Soft Acids and Bases (HSAB) rules,[18] proton (H^+) is thought



Scheme 1.

Table 1. Trifluoromethansulfonic Acid Catalyzed Glycosylation with Various Glycosyl Donors



Entry	X	Yield/%	α/β[a)]	Entry	X	Yield/%	α/β[a)]
1	F (β)	83	67/33	5	OH (mix)[b)]	51	73/27
2	F (α)	87	66/34	6	OAc (α)	75	68/32
3	Br (α)	9	45/55	7	OCOOPh (β)	61	72/28
4	Cl (α)	6	52/48	8	SEt (β)	0	—

a) The α/β ratios were determined by HPLC analysis. b) α/β = 7/3.

to be fluorophilic because of its hard character having a higher dissociation energy of H–F bond than those of H–Cl, H–Br, or H–S (H–F: 570 /KJ mol^{-1}, H–Cl: 432 /KJ mol^{-1}, H–Br: 366 / KJ mol^{-1}, H–S: 344 ± 12 /KJ mol^{-1}).[4] Therefore, it was thought that the protic acid would behave as a catalyst in glycosylation using glycosyl fluoride. Based on the above consideration, exploration of a useful method for catalytic activation of glycosyl fluorides was investigated using various protic acids.

In this paper, we would like to report on a new method for catalytic and stereoselective glycosylation of various glycosyl acceptors with glycosyl fluorides using various protic acids in the coexistence of MS 5A in an appropriate solvent to afford the corresponding α- or β-disaccharides in good to excellent yields.[19] Also, the effects of properties of counter anions as well as of solvents on controlling the stereoselectivities of this glycosylation are revealed. Further, one-pot trisaccharide syntheses which show high yields by utilizing the above glycosylation method are demonstrated.

Results and Discussion

In the first place, 5 mol% of protic acid catalysts such as trifluoroacetic acid, methanesulfonic acid, or trifluoromethansulfonic acid (TfOH), were tried in order to examine the suitability of the protic acids for the activation of glycosyl fluoride by taking the reaction of 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl fluoride (**1**),[20] armed glycosyl fluoride, with methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**2**)[21] in the presence of Drierite. It was observed then that only TfOH, the strongest acid, effectively accelerated the glycosylation reaction with glycosyl fluoride in CH_2Cl_2 at room temperature and gave the corresponding disaccharide in good yield (Table 1, Entry 1) while the former two acids did not.

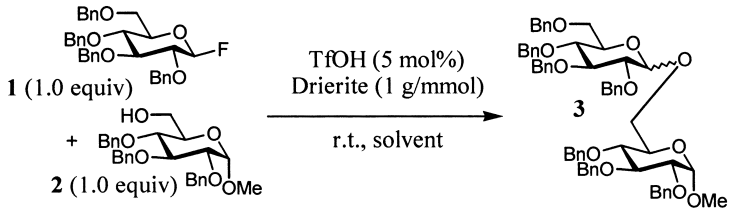
Next, donors which possess other types of leaving groups were examined under the same conditions (Table 1). Interestingly, glycosyl bromide and chloride (Table 1, Entries 1–4) which were less stable compared to glycosyl fluoride were found to be activated not so effectively, whereas the glycosyl fluorides reacted smoothly. Glycosyl acetate, carbonate and 1-hydroxy sugar (Table 1, Entries 5–7) reacted with glycosyl acceptor **2** and afforded the desired disaccharides in moderate yields (not optimized). Since thioglycoside, another frequently employed glycosyl donor, was not activated at all under the present conditions (Table 1, Entry 8), this glycosylation suggested wider applicability to the chemoselective synthesis[22] of oligo- and poly-saccharides (vide post, Table 4).

Next, the effect of solvents on the reaction of glycosyl fluoride **1** having a non-participating protecting group at C(2) position with glycosyl acceptor **2** was studied, because some of the solvents were quite well known to be influential on the stereoselectivity of glycosylation.[23] These reactions were carried out in various solvents by using 5 mol% of TfOH for 2 to 7 h at room temperature. As a result, the glycosylation with glycosyl fluoride **1** took place in all the solvents listed in Table 2 except DMF, which worked as a protic acid capture. The corresponding disaccharide was obtained predominantly in α-form when ethereal solvent was added. The glycosylation proceeded in good yield with high α-stereoselectivity, especially when Et_2O was used as a solvent (Table 2). It was reported that α-glycosides were obtained preferentially when glycosylation using glycosyl fluoride was carried out in diethyl ether.[3,6,11,13]

Then, the α-selective glycosylation was studied further by using 20 mol% of TfOH in Et_2O in order to improve the chemical yield (63%) shown in Table 2. After the effect of various additives[24] in the above reaction was examined, both Drierite and molecular sieve 5A (MS 5A) proved to be useful (Table 3). In this reaction, MS 5A worked more effectively than Drierite, whereas molecular sieve 3A (MS 3A) and molecular sieve 4A (MS 4A) did not work at all, and thus no reactions took place. Owing to their basic characters,[25] it was considered that the latter two molecular sieves captured a strong protic acid catalyst, TfOH. On the other hand, MS 5A, an acidic zeolite,[26] did not interact with protic acid, therefore, the existing TfOH activated glycosyl fluoride, which eventually promoted effective glycosylation.[27]

Then, in order to extend the scope of the present reaction using a catalytic amount of TfOH in the presence of Drierite or MS 5A, the glycosylation using various glycosyl acceptors such as **2**, **4**,[29] **5**,[30] **6**,[31] and **7**[32] was tried (Table 4). The glycosylation proceeded smoothly even in the cases of using the acceptors having secondary alcohols **4** and **5**, which exhibited lower nucleophilic ability than **2**, to afford the corresponding

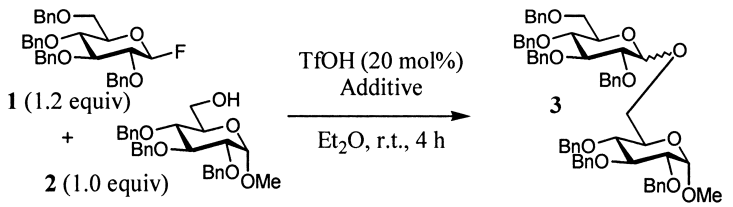
Table 2. Effect of Solvents



Solvent	Time/h	Yield/%[a)]	Solvent	Time/h	Yield/%[a)]
CH_2Cl_2	2	83 (67/33)	Et_2O	**7**	**63 (91/9)**
Toluene	2	87 (60/40)	THF	7	13 (52/48)
Benzene	2	86 (69/31)	$^{i}Pr_2O$[c)]	7	30 (86/14)
Fluorobenzene	2	86 (75/25)	DME	7	2 (86/14)
^{t}BuCN	2	83 (24/76)	$^{n}Bu_2O$	7	66 (87/13)
BTF[b)]	2	90 (68/32)	THP	7	60 (82/18)
$MeNO_2$	2	63 (48/52)	^{t}BuOMe	7	24 (94/6)
AcOEt	2	70 (67/33)	$(ClCH_2CH_2)_2O$	7	83 (72/28)
1,4-Dioxane	2	60 (89/11)	DMF	7	N.R.

a) In parentheses show α/β ratios of the product and which were determined by HPLC analysis. b) BTF = trifluoromethylbenzene. c) Note that the solvent is $^{i}Pr_2O$: it was incorrectly presented as $^{n}Pr_2O$ in our previous communication.[19b]

Table 3. Effect of Additives



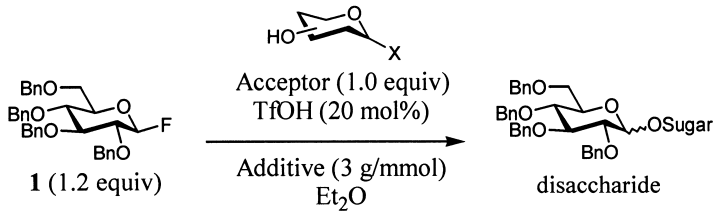
Entry		Additive		Yield/% (α/β)[a)]
1	Drierite	(= $CaSO_4$)	1 g/mmol	92 (87/13)
2	Drierite	(= $CaSO_4$)	3 g/mmol	88 (90/10)
3	Drierite	(= $CaSO_4$)	5 g/mmol	87 (90/10)
4	MS 3A	(= $K_9Na_3[(AlO_2)_{12}(SiO_2)_{12}]$)	3 g/mmol	N.R.
5	MS 4A	(= $Na_{12}[(AlO_2)_{12}(SiO_2)_{12}]$)	3 g/mmol	N.R.
6	**MS 5A**	(= $\mathbf{Ca_{4.5}Na_3[(AlO_2)_{12}]}$)	**3 g/mmol**	**98 (88/12)**
7		None		67 (84/16)

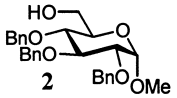
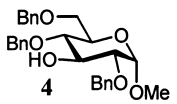
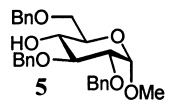
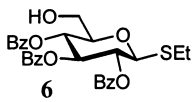
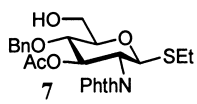
a) The α/β ratios were determined by HPLC analysis.

disaccharides in excellent yields with good α-stereoselectivities when MS 5A was used as an additive (Table 4, Entries 4–9). It was also revealed that MS 5A apparently enhanced the rate of these reactions to afford the glycosides in a shorter period compared with Drierite, though the role of MS 5A has not yet been clear. Now, it should be noted that the chemoselective glycosylation proceeded smoothly with thioglycosides **6** and **7** to give the corresponding disaccharides in excellent yields without damaging the thioglycosidic linkage of their reducing terminus (Table 4, Entries 10–15). Since the ethylthio moiety remained safe in the formed disaccharides, synthesis of trisaccharide would be performed in one-pot by successive activation of the ethylthio group (vide post, Table 11 and 12). α-Selective glycosylation was thus accomplished by using a protic acid, TfOH in the presence of MS 5A in Et_2O. Then, β-selective glycosylation was further studied using glycosyl donor **1** having a substituent so as not to participate in the so-called neighboring effect at C(2) position.

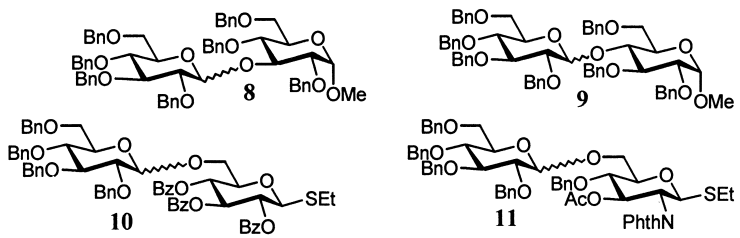
In 1998, it was reported from our laboratory that the glycosylation of glycosyl acceptor **2** with glycosyl fluoride **1** was effectively performed by using trityl tetrakis(pentafluorophenyl)borate [$TrB(C_6F_5)_4$] as a catalyst in trifluoromethylbenzene [alternative name: benzotrifluoride (BTF)][34]–pivalonitrile (^{t}BuCN)[35] = 5:1 mixed solvent to afford the corresponding disaccharide in high yield with high β-stereoselectivity[15] (Scheme 2). In this reaction, it was assumed that the β-stereoselectivity was accomplished by the effect of ^{t}BuCN;[35] therefore, it was thought that the β-selective glycosylation using TfOH would also take place when the glycosylation was tried in the solvent containing ^{t}BuCN. Unexpectedly, however, poor

Table 4. Trifluoromethansulfonic Acid catalyzed α-Selective Glycosylation of Various Glycosyl Acceptors with Glucosyl Donor **1**



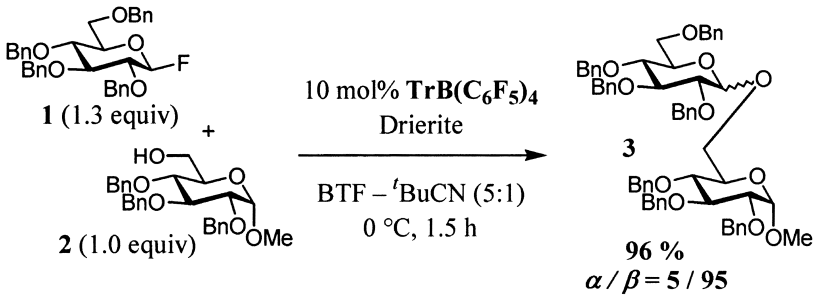
Entry	Acceptor	Product	Additive	h	°C	Yield/% (α/β)[a]
1		**3**	Drierite	6	r.t.	94 (91/9)
2			MS 5A	4	r.t.	98 (88/12)
3			MS 5A	8	0	95 (89/11)
4		**8**	Drierite	22	r.t.	63 (75/25)
5			MS 5A	4	r.t.	97 (78/22)
6			MS 5A	12	0	97 (84/16)
7		**9**	Drierite	22	r.t.	24 (73/27)
8			MS 5A	5	r.t.	82 (73/27)
9			MS 5A	20	0	88 (81/19)
10		**10**	Drierite	4	r.t.	94 (84/16)
11			MS 5A	2	r.t.	95 (81/19)
12			MS 5A	12	0	quant. (86/14)
13		**11**	Drierite	8	r.t.	91 (77/23)
14			MS 5A	2	r.t.	98 (74/26)
15			MS 5A	12	0	quant. (80/20)

a) The α/β ratios were determined by HPLC analysis.

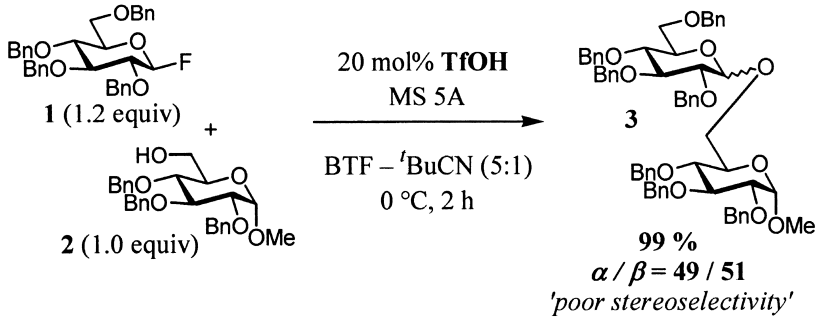


selectivity was observed when the above reaction was tried using TfOH as a catalyst (Scheme 3). Since then, fundamental study on the above glycosylation was further developed by using a catalytic amount of various protic acids in Et_2O or BTF–^{t}BuCN mixed solvent in order to examine the stereoselectivity of this glycosylation (Table 5).

Firstly, in-situ generation of strong protic acids was studied according to the modified procedure of Kevill or Kato by taking the reaction of various silver salts and ^{t}BuCl or ^{t}BuBr.[36] The protic acids shown in Table 5 were effectively generated along with rapid precipitation of AgCl or AgBr. The generated catalysts in supernatant were used in glycosylation reaction of glycosyl acceptor **2** with glucosyl fluoride **1** in Et_2O at room temperature for 4 h or in BTF–^{t}BuCN (5:1) at 0 °C for 2 h, and the corresponding α- or β-disaccharides were obtained in excellent yields. Furthermore, it was clearly recognized that the stereoselectivities of the resulted glycosides varied depending on the combination of a catalyst and a solvent. For example, when the glycosylation was carried out in Et_2O, α-glycoside was obtained as a major product by using a catalytic amount of TfOH, $HClO_4$, or 1,1,2,2,3,3,4,4,4-nonafluorobutanesulfonic acid ($C_4F_9SO_3H$) (Table 5, Entries 1–4). On the other hand, β-stereoselectivity was observed when a catalytic amount of $HNTf_2$, $HSbF_6$, or $HB(C_6F_5)_4$ was used in BTF–^{t}BuCN (5:1) (Table 5, Entries 5–8). It is interesting to note that the stereoselectivities of the formed disaccharides decreased considerably when the combination of the catalyst and solvent was reversed. These results indicated that the counter anions of the

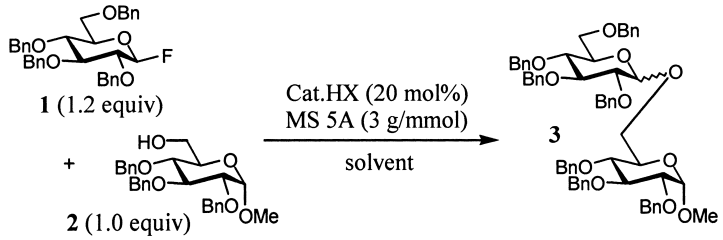


Scheme 2.



Scheme 3.

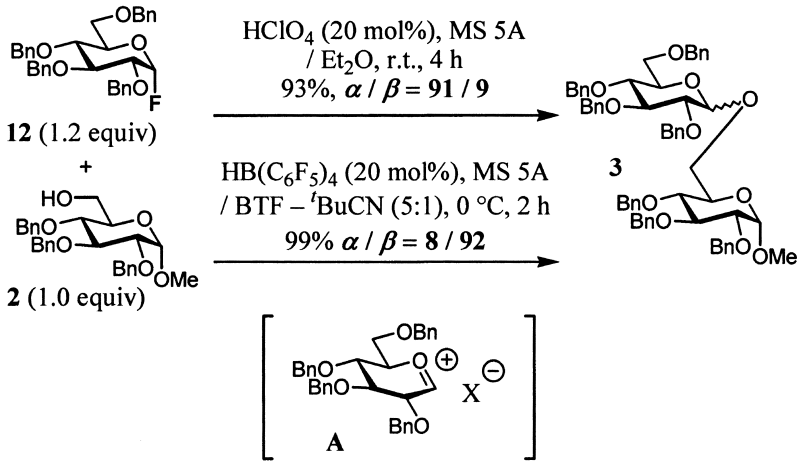
Table 5. Effect of Solvent and the Counter Anion of Protic Acid[a)]



Entry	Cat.	Yield/% (α/β) (Et_2O, r.t., 4 h)	Yield/% (α/β) (BTF–^{t}BuCN (5:1), 0 °C, 2 h)
1	HOTf[b)]	98 (88/12)	quant. (47/53)
2	HOTf[c)]	96 (88/12)	99 (49/51)
3	**$HClO_4$**[c)]	98 (**92/8**)	quant. (60/40)
4	$HOSO_2C_4F_9$[d)]	99 (88/12)	96 (47/53)
5	$HNTf_2$[b)]	quant. (49/51)	99 (9/91)
6	$HNTf_2$[d)]	quant. (50/50)	quant. (9/91)
7	$HSbF_6$[d)]	99 (56/44)	quant. (12/88)
8	**HB (C_6F_5)$_4$**[e)]	95 (55/45)	99 (**7/93**)

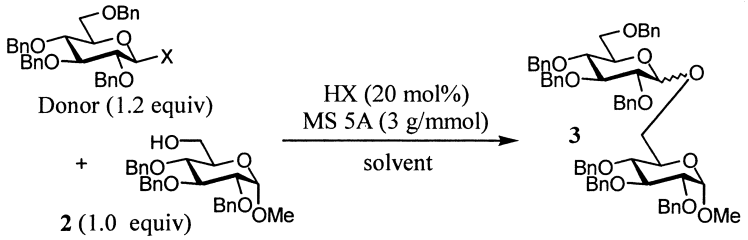
a) In the case of using HBF_4·OMe_2, HOTs, HOMs, or TFA as a catalyst, almost no reaction was observed. b) Commercial substrate. C) Protic acid was generated from silver salt and ^{t}BuCl in toluene, and the supernatant was used. d) Protic acid was generated from silver salt and ^{t}BuBr in toluene, and the supernatant was used. e) Protic acid was generated from AgB(C_6F_5)$_4$ and ^{t}BuBr in toluene–Et_2O (1:1), and the supernatant was used.

catalysts turned out to be as influential on stereoselectivties as the well-known effect of the solvent, although behaviors of these counter anions in detail have not yet been made clear. In this case, formation of α-glycoside by using $HClO_4$ in Et_2O took place in better stereoselectivity compared to the case of using TfOH in Et_2O. On the other hand, β-glycoside was best obtained when a catalytic amount of HB(C_6F_5)$_4$ was used in BTF–^{t}BuCN (5:1).[37]



Scheme 4. Glycosylation with α-D-glucopyranosyl fluoride **12**.

Table 6. Glycosylation with Various Donors



Entry	Donor	Yield/% (α/β) (cat. **$HClO_4$**,[a] r.t. **Et_2O**, 4 h)	Yield/% (α/β) (cat. **$HB(C_6F_5)_4$**,[b] 0 °C **BTF–^{t}BuCN (5 : 1)**, 2 h)
1	SEt (β)	trace (—)	9 (11/89)
2	SEt (β)[c]	89 (90/10)	95 (11/89)
3	OH (mix)	93 (92/8)	93 (8/92)
4	OAc (α)	93 (92/8)	89 (9/91)
5	OC=N(H)CCl_3 (β)	99 (91/9)	97 (10/90)

a) Protic acid was generated from $AgClO_4$ and ^{t}BuCl in toluene, and the supernatant was used. b) Protic acid was generated from $AgB(C_6F_5)_4$ and ^{t}BuBr in toluene–Et_2O (1:1), and the supernatant was used. c) 1.2 equiv of *N*-iodosuccinimide (NIS) was added and stirred for 15 minutes.

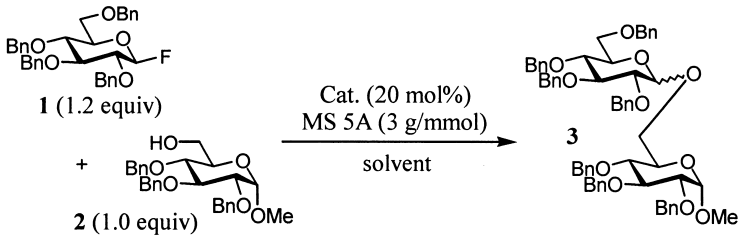
Table 7. Glycosylation with Various Donors*

Entry	Donor	Yield/% (α/β) (cat. **$HB(C_6F_5)_4$**,[b] r.t. **Et_2O**, 4 h)	Yield/% (α/β) (cat. **$HClO_4$**,[a] 0 °C **BTF–^{t}BuCN (5 : 1)**, 2 h)
1	SEt (β)[c]	97 (44/56)	94 (59/41)
2	OH (mix)	88 (43/57)	92 (65/35)
3	OAc (α)	99 (43/57)	90 (54/46)
4	OC=N(H)CCl_3 (β)	97 (43/57)	95 (54/46)

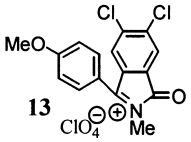
* The reaction scheme and footnotes are the same as those of Table 6.

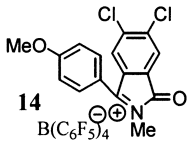
Then, in order to elucidate the mechanism of the above glycosylation, α-oriented glycosyl fluoride **12**[38] was treated with acceptor **2** in the presence of a catalytic amount of $HClO_4$ in Et_2O or $HB(C_6F_5)_4$ in BTF–^{t}BuCN (5:1) as shown in Scheme 4. In the above reactions almost the same stereoselectivities were observed as in the case of using **1**. These results are reasonably explained by assuming that a S_N1 type reaction replaces the fluoro atom with glycosyl acceptors via oxocarbenium

Table 8. Glycosylation Using Various Catalysts



Entry	Catalyst	Yield/% (α/β) (Et_2O, r.t., 4 h)	Yield/% (α/β) (BTF–^{t}BuCN (5:1), 0 °C, 2 h)
1	$TrClO_4$[40]	94 (93/7)	91 (58/42)
2	$TrB(C_6F_5)_4$[15]	85 (47/53)	88 (4/96)
3	$SnCl_2$–$AgClO_4$[3]	97 (92/8)	94 (57/43)
4	$SnCl_2$–$AgB(C_6F_5)_4$[28]	90 (43/57)	95 (8/92)
5	**13**[41]	97 (92/8)	73 (51/49)
6	**14**[41]	88 (40/60)	95 (8/92)





ion intermediate **A** to form the glycosides.

Next, in order to examine the effects of counter anions and solvents, glycosylations with other glucosyl donors such as thioglycoside, 1-hydroxy and 1-*O*-acetyl sugars, and glycosyl trichloroacetimidate were tried using $HClO_4$ or $HB(C_6F_5)_4$ (Tables 6 and 7). In every case, the glycosylation reaction proceeded smoothly to afford the corresponding disaccharides in high yields. In the case of using thioglycoside, further addition of 1.2 equivalent of *N*-iodosuccinimide (NIS)[39] was essential. In the case of using $HClO_4$ in Et_2O, moreover, all the glucosyl donors examined gave high α-stereoselectivities while β-glycosides were obtained predominantly in high yields in the case of using $HB(C_6F_5)_4$ in BTF–^{t}BuCN (5:1) (Table 6). It is noted that the stereoselectivities were poor when catalyst and solvent were used in reversed combination such as $HB(C_6F_5)_4$ in Et_2O or $HClO_4$ in BTF–^{t}BuCN (Table 7).

Then, the glycosylation using various cationic species shown in Table 8 that were paired with the counter anions such as ClO_4^- or $B(C_6F_5)_4^-$ in Et_2O or BTF−^{t}BuCN (5:1), or their reversed combinations was examined. Every catalyst which had ClO_4^- anion in Et_2O or $B(C_6F_5)_4^-$ anion in BTF–^{t}BuCN (5:1) gave high α- or β-stereoselectivities respectively, whereas poor selectivities were observed when the combinations were reversed. The results shown in Tables 6, 7, and 8 also indicate that the nature of counter anion of the catalyst is very influential in controlling the stereoselectivity.[42]

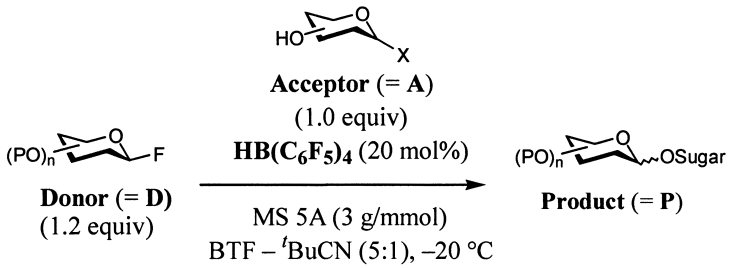
In order to confirm the applicability of the above β-selective glycosylation method, various glycosyl acceptors such as **2**, **4**, **5**, **6**, **7**, **16**,[43] and **17**[33] were allowed to react with glucosyl fluoride **1** or galactosyl fluoride **15** by using a catalytic amount of $HB(C_6F_5)_4$ in the coexistence of MS 5A[44] in BTF–^{t}BuCN (5:1) at −20 °C (Table 9). In all cases, the desired disaccharides were obtained in good to high yields with high β-selectivities even when acceptors having secondary alcohol or thioglycosidic linkage were used (Table 9, Entries 4–6). These protic acid catalysts did not activate the disarmed glycosyl fluoride **17**, an acceptor; therefore, so-called "armed-disarmed"[45] chemoselective glycosylation was performed under the above conditions to afford the desired disaccharide in high yield with good stereoselectivity (Table 9, Entry 7). Since only a few examples were reported in regard to chemoselective glycosylation using glycosyl fluorides,[46] this method is considered to be useful also for oligosaccharide synthesis. Also, the desired disaccharides were obtained in high yields with good β-selectivities when galactosyl derivative **15**[47] was used as a glycosyl donor (Table 9, Entries 8 and 9). It is noted that the mechanism of the above β-selective glycosylations was due to the effect of ^{t}BuCN which worked for the generation of the α-nitrilium ion intermediate; such an effect of nitrile solvent has already been reported.[48]

Next, α-selective glycosylation was reexamined by using $HClO_4$ and TfOH as a catalyst in Et_2O at 0 °C (Table 10). In all cases, the desired disaccharides were obtained in good to high yields with good α-selectivities as in the cases of β-selective glycosylation using $HB(C_6F_5)_4$. Thus, convenient methods for the stereoselective preparation of either α- or β-glycosides are established just by starting from the same glycosyl fluorides.

Then, based on the above results that the disaccharides have been effectively obtained without damaging thioglycosidic linkage, one-pot sequential trisaccharide synthesis,[49] Glcα or β1–6Glcβ1–6Glc and Glcα or β1–6GlcNβ1–6Glc, was attempted (Tables 11 and 12).

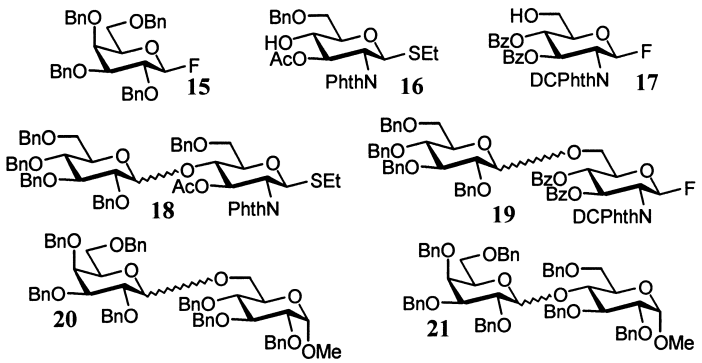
In the first step, **1** was treated with ethylthio glycoside **6** or **7** in the presence of a catalytic amount of either TfOH or $HClO_4$ in Et_2O, or $HB(C_6F_5)_4$ in BTF–^{t}BuCN (5:1) where almost

Table 9. Tetrakis(pentafluorophenyl)boric Acid Catalyzed β-Selective Glycosylation of Various Glycosyl Acceptors with Glycosyl Donors **1** and **15**



Entry	D	A	P	Time/h	Yield/% (α/β)[a)]
1	**1**	**2**	**3**	6	97 (4/96)
2	**1**	**4**	**8**	11	92 (8/92)
3	**1**	**5**	**9**	11	95 (8/92)
4	**1**	**6**	**10**	2	89 (5/95)
5	**1**	**7**	**11**	2	87 (5/95)
6	**1**	**16**	**18**	10.5	78 (15/85)
7	**1**	**17**	**19**	3	96 (6/94)
8	**15**	**2**	**20**	1.5	98 (10/90)
9	**15**	**5**	**21**	2	99 (27/73)[b)]

a) The α/β ratios were determined by HPLC analysis. b) The α/β ratios were determined by ^{1}H NMR analysis.



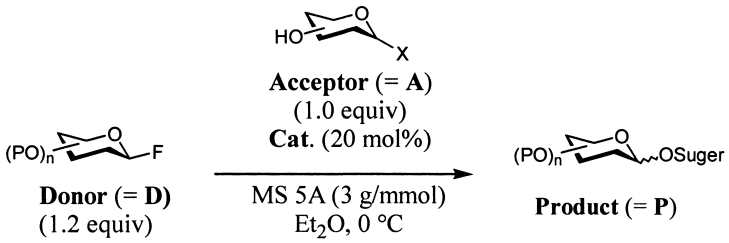
complete consumption of **6** or **7** was confirmed by TLC monitoring. Next, the second glycosylation of glycosyl acceptor **2** with thus formed disaccharide **10** or **11** was tried without work up, and the desired trisaccharide was obtained stereoselectively in high yield by successive addition of NIS and third sugar in one-pot operation. It is noteworthy that these sequential reactions were carried out without further addition of a protic acid and that trisaccharides including 2-deoxy-2-animo sugar moiety were obtained also in excellent yields with good stereoselectivities (Table 12).

Finally, global deprotection of trisaccharides **22** and **23** was demonstrated as shown in Schemes 5 and 6. At first, **22**$\alpha'\beta$ and **22**$\beta'\beta$ were conducted respectively under the conditions of 2 M NaOH in THF–MeOH at room temperature to remove the benzoyl protecting groups. After work up, successive hydrogenolysis of benzyl groups was performed under H_2 (1 atm) atmosphere in the presence of Pd-OH to afford the final products **24**$\alpha'\beta$ and **24**$\beta'\beta$ in excellent yields. Also, Phth protecting groups of amino function in **23**$\alpha'\beta$ and **23**$\beta'\beta$ were firstly removed by using large amounts of ethylenediamine and the successive acetylation of amino function by Ac_2O in MeOH proceeded selectively (Scheme 6). It was followed by deprotection of benzyl group by Pd-OH under H_2 (1 atm) atmosphere to furnish the final products **25**$\alpha'\beta$ and **25**$\beta'\beta$, which were purified by reversed-phase column chloromatography in good yields. Thus, it was finally revealed that the above mentioned one-pot glycosylation method is now applicable for naturally or unnaturally occurring oligosaccharide synthesis.

Conclusion

A convenient method for a catalytic and stereoselective synthesis of either α- or β-glycosides is established by starting just from the same glycosyl fluorides. When the glycosylation was carried out using TfOH or $HClO_4$ in Et_2O, the major product was α-glycosides while β-stereoselectivity was observed when $HB(C_6F_5)_4$ was used in a mixed solvent of BTF–^{t}BuCN (5:1). It was proved that: 1) the stereoselectivity was controlled not only by the effect of solvent but also the nature of counter anion of the catalyst; and 2) MS 5A was an excellent additive for the above protic acid catalyzed glycosylation. Fur-

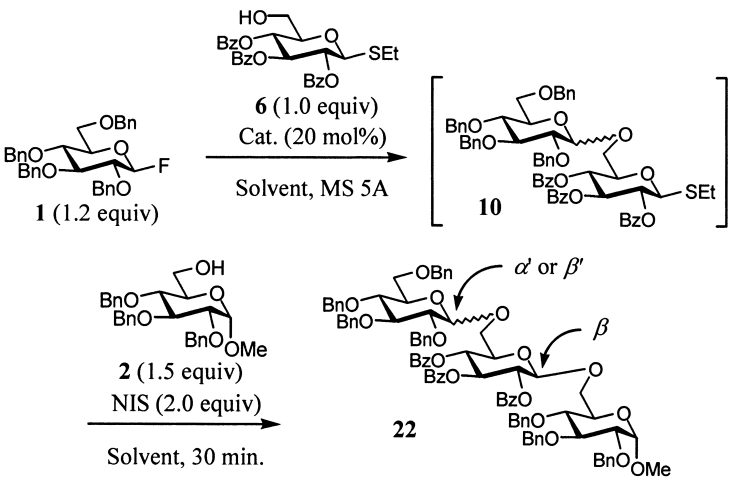
Table 10. Trifluoromethansulfonic Acid Catalyzed α-Selective Glycosylation of Various Glycosyl Acceptors with Glucosyl Donors **1** and **15**



				Cat.			
				TfOH		$HClO_4$	
Entry	D	A	P	h	Yield/% (α/β)[a]	h	Yield/% (α/β)[a]
1	**1**	**2**	**3**	8	95 (89/11)	6	94 (93/7)
2	**1**	**4**	**8**	12	97 (84/16)	7	89 (88/12)
3	**1**	**5**	**9**	20	88 (81/19)	7	93 (83/17)
4	**1**	**6**	**10**	12	quant. (86/14)	4	92 (89/11)
5	**1**	**7**	**11**	12	quant. (80/20)	6	87 (85/15)
6	**1**	**16**	**18**	21	90 (87/13)	19	82 (82/18)
7	**1**	**17**	**19**	4	88 (85/15)	4	96 (90/10)
8	**15**	**2**	**20**	16.5	95 (82/18)	3.5	92 (74/26)
9	**15**	**5**	**21**	7.5	96 (93/7)[b]	15.5	93 (93/7)[b]

a) The α/β ratios were determined by HPLC analysis. b) The α/β ratios were determined by ^{1}H-NMR analysis.

Table 11. One-Pot Trisaccharide (Glcl–6Glcβ1–6Glc) Synthesis



Entry	Cat.	Solvent	Temp/°C	Yield/% ($\alpha'\beta/\beta'\beta$)[a]
1	TfOH	Et_2O	0	93 (85/15)
2	$HClO_4$	Et_2O	0	88 (87/13)
3	$HB(C_6F_5)_4$	BTF–^{t}BuCN (5:1)	−20	93 (7/93)

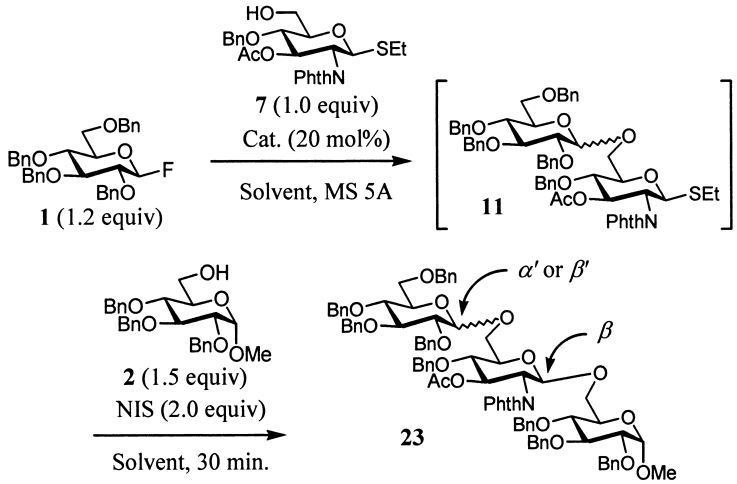
a) The α/β ratios were determined by isolation of each isomer.

ther, one-pot trisaccharide synthesis was performed by the successive addition of NIS and third-sugar in the above glycosylation reaction to afford Glcα or β1–6Glcβ1–6Glc and Glcα or β1–6GlcNβ1–6Glc in excellent yields. Thus it was demonstrated, as a first example, that a catalytic amount of protic acids effectively activate anomeric C–F bond of the glycosyl donors to form the desired glycosides stereoselectively by the reaction with glycosyl acceptors.

Experimental

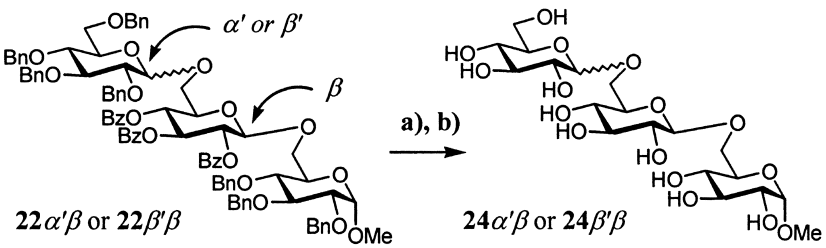
General. All melting points were measured on a Yanaco MP-S3 micro melting point apparatus. Infrared spectra were recorded on a Horiba FT-300 infrared spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-LA500 or JEOL JNM-A500 spectrometer with $CDCl_3$ or $SiMe_4$ as a standard. High-resolution mass spectra were recorded on a Micromass Q-TOF2 instrument

Table 12. One-Pot Trisaccharide (Glcl–6GlcNβ1–6Glc) Synthesis

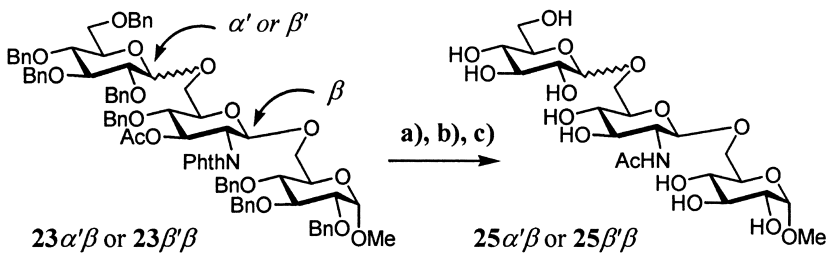


Entry	Cat.	Solvent	Temp/°C	Yield/% ($\alpha'\beta/\beta'\beta$)[a]
1	TfOH	Et_2O	0	91 (81/19)
2	$HClO_4$	Et_2O	0	89 (86/14)
3	$HB(C_6F_5)_4$	BTF–^{t}BuCN (5:1)	−20	88 (6/94)

a) The α/β ratios were determined by HPLC analysis.



Scheme 5. a) 2N NaOH aq/THF–MeOH, 0 °C. b) H_2, Pd-OH/MeOH, r.t.; for **22**$\alpha'\beta$: 2 steps, 87%, for **22**$\beta'\beta$: 2 steps, 88%.



Scheme 6. a) $NH_2CH_2CH_2NH_2$/EtOH, 90 °C. b) Ac_2O/MeOH. c) H_2, Pd-OH/MeOH, r.t., for **23**$\alpha'\beta$: 3 steps, 69%, for **23**$\beta'\beta$: 3 steps, 74%.

(ESI positive, 0.01 M $AcONH_4$ in H_2O/MeCN = 1:1). High-performance liquid chromatography (HPLC) was carried out using a Hitachi LC-Organizer, L-4000 UV Detector, L-6200 Intelligent Pump, and D-2500 Chlomato-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). 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 chlomatography was performed on Silica gel 60 (Merck). Reversed-phase column chlomatography was performed on YMC-Gel ODS-AQ 120-S50.

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 were used without further purification, unless otherwise noted. Trifluoromethanesulfonic acid (TfOH: given by Central Glass Co. Limited) was simply distilled and used for glycosylation. CH_2Cl_2 and pivalonitrile were distilled from P_2O_5 and then from CaH_2 and dried (molecular sieve 4A). Toluene, benzene, fluorobenzene, and (trifluoromethyl)benzene (BTF) were distilled from P_2O_5 and dried (molecular sieve 4A). ^{n}Bu$_2$O, ^{i}Pr$_2$O, DME, and $(ClCH_2CH_2)_2O$ were distilled from CaH_2 and were used immediately.

AcOEt was distilled from K_2CO_3 and dried (molecular sieve 4A). DMF was distilled from CaH_2 under reduced pressure (pre-dried P_2O_5) and dried (molecular sieve 4A). $MeNO_2$ (distilled from hydroquinone) and THP (distilled from $LiAlH_4$) were used immediately after distillation. 1,4-Dioxane was distilled from $LiAlH_4$ (pre-dried KOH) and was used immediately. Dry THF, ^{t}BuOMe, and Et_2O were purchased from Kanto Chemical. Powdered and pre-dried (at 260 °C/1 mmHg, 6 h) molecular sieves 3A, 4A, and 5A were used in glycosylation reactions. Sufficiently crushed and pre-dried (at 260 °C/1 mmHg, 6 h) Drierite from W. A. Hammond Drierite Company was used in the glycosylations.

Generation of Perchloric Acid ($HClO_4$): To a stirred solution of $AgClO_4$ (41 mg, 0.20 mmol) in toluene (1.0 mL) was added ^{t}BuCl (0.22 M in toluene, 1.0 mL, 0.22 mmol) and this mixture was stirred for 30 min at room temperature. After the mixture was left standing for 10 min without stirring, the supernatant was used for glycosylation as a catalyst (0.10 M $HClO_4$ in toluene).

Generation of Tetrakis(pentafluorophenyl)boric Acid [$HB(C_6F_5)_4$]: To a stirred solution of $AgB(C_6F_5)_4$[50] (79 mg, 0.10 mmol) in Et_2O (1.0 mL) and toluene (0.50 mL) was added ^{t}BuBr (0.22 M in toluene, 0.50 mL, 0.11 mmol) and this mixture was stirred for 30 min at room temperature. After the mixture was left standing for 10 min without stirring, the supernatant was used for glycosylation as a catalyst (0.050 M $HB(C_6F_5)_4$ in toluene–Et_2O (1:1)).

Glycosylation Using TfOH (Method A): To a stirred suspension of MS 5A (300 mg), glycosyl donor (glycosyl fluoride **1** or **15**, 65 mg, 0.12 mmol), and glycosyl acceptor (0.10 mmol) in Et_2O (2.5 mL) was successively added TfOH (3.0 mg in toluene, 0.2 mL, 0.020 mol) at 0 °C. After completion of the glycosylation reaction by monitoring TLC, the reaction mixture was quenched by addition of sat. aqueous $NaHCO_3$ (2 mL). Then, the mixture was diluted with EtOAc and 1 M HCl, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with H_2O and brine, and was dried over $MgSO_4$. After filtration and evaporation, the resulting residue was purified by preparative TLC (silica gel) and afforded the corresponding disaccharide.

Glycosylation Using $HClO_4$ (Method B): To a stirred suspension of MS 5A (300 mg), glycosyl donor (glycosyl fluoride **1** or **15**, 65 mg, 0.12 mmol), and glycosyl acceptor (0.10 mmol) in Et_2O (2.5 mL) was successively added $HClO_4$ (0.10 M in toluene, 0.20 mL, 0.020 mol) at 0 °C. After completion of the glycosylation reaction by monitoring TLC, the reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ (2 mL). Then, the mixture was diluted with EtOAc and 1 M HCl, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with $NaHCO_3$ and brine, and was dried over $MgSO_4$. After filtration and evaporation, the resulting residue was purified by preparative TLC (silica gel) and afforded the corresponding disaccharide.

Glycosylation Using $HB(C_6F_5)_4$ (Method C): To a stirred suspension of MS 5A (300 mg), glycosyl donor (glycosyl fluoride **1** or **15**, 65 mg, 0.12 mmol), and glycosyl acceptor (0.10 mmol) in BTF (2.5 mL) and ^{t}BuCN (0.5 mL) was successively added $HB(C_6F_5)_4$ (0.050 M in toluene–Et_2O (1:1), 0.40 mL, 0.020 mol) at −20 °C. After completion of the glycosylation reaction by monitoring TLC, the reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ (2 mL). Then, the mixture was diluted with EtOAc and 1 M HCl, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with $NaHCO_3$ and brine, and was dried over $MgSO_4$. After filtration and evaporation, the resulting residue was purified by preparative TLC (silica gel) and afforded the corresponding disaccharide.

One-Pot Sequential Trisaccharide Synthesis Using TfOH (Method D) : To a stirred suspension of MS 5A (300 mg), **1** (65 mg, 0.12 mmol), and glycosyl acceptor **6** or **7** (0.10 mmol) in Et_2O (2.5 mL) was added TfOH (3.0 mg, 0.020 mol) in toluene (0.20 mL) at 0 °C. After completion of the first glycosylation reaction by monitoring TLC, **2** (70 mg, 0.15 mmol) and NIS (45 mg, 0.20 mmol) were successively added at 0 °C. The reaction mixture was stirred for an additional 30 min at 0 °C and was quenched by addition of saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc and 1 M HCl, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with 10% aqueous $Na_2S_2O_3$, H_2O, and brine, and was dried over $MgSO_4$. After being filtered and evaporated, the resulting residue was purified by preparative TLC (silica gel) to give the corresponding trisaccharide **22** or **23**.

One-Pot Sequential Trisaccharide Synthesis Using $HClO_4$ (method E): To a stirred suspension of MS 5A (300 mg), **1** (65 mg, 0.12 mmol), and glycosyl acceptor **6** or **7** (0.10 mmol) in Et_2O (2.5 mL) was added $HClO_4$ (0.10 M in toluene, 0.2 mL, 0.020 mol) at 0 °C. After completion of the first glycosylation reaction by monitoring TLC, **2** (70 mg, 0.15 mmol) and NIS (45 mg, 0.20 mmol) were successively added at 0 °C. The reaction mixture was stirred for an additional 30 min at 0 °C and was quenched by addition of saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc and 1 M HCl, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with 10% aqueous $Na_2S_2O_3$, $NaHCO_3$, and brine, and was dried over Mg_2SO_4. After being filtered and evaporated, the resulting residue was purified by preparative TLC (silica gel) to give the corresponding trisaccharide **22** or **23**.

One-Pot Sequential Trisaccharide Synthesis Using $HB(C_6F_5)_4$ (method F): To a stirred suspension of MS 5A (300 mg), **1** (65 mg, 0.12 mmol), and glycosyl acceptor **6** or **7** (0.10 mmol) in BTF (2.5 mL) and ^{t}BuCN (0.5 mL) was added $HB(C_6F_5)_4$ (0.050 M in toluene–Et_2O = 1:1 mixture, 0.40 mL, 0.020 mol) at −20 °C. After completion of the first glycosylation reaction by monitoring TLC, **2** (70 mg, 0.15 mmol) and NIS (45 mg, 0.20 mmol) were successively added at −20 °C. The reaction mixture was stirred for an additional 30 min at −20 °C and was quenched by addition of saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc and 1 M HCl, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with 10% aqueous $Na_2S_2O_3$, $NaHCO_3$, and brine, and was dried over Mg_2SO_4. After being filtered and evaporated, the resulting residue was purified by preparative TLC (silica gel) to give the corresponding trisaccharide **22** or **23**.

Ethyl 3-*O*-Acetyl-4-*O*-benzyl-2-deoxy-2-phthalimide-1-thio-β-D-glucopyranoside (7) : To a solution of Ethyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**26**)[33] (2.19 g, 4.53 mmol) and triethylamine–borane complex ($Et_3N{\cdot}BH_3$: 7.16 mL, 45.3 mmol.) in CH_2Cl_2 (76 mL) and Et_2O (15 mL) was added $AlCl_3$ (1.21 g, 9.06 mmol) at 0 °C. After stirring for 30 min at room temperature, sat. aq $NaHCO_3$ was added. Then, the mixture was filtered through celite pad and the aqueous layer was extracted with CH_2Cl_2 (×3). The combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration of the mixture and removal of the solvent, the residue was purified by silica-gel column chromatography (hexane/EtOAc = 4/1 to 1/1 then, hexane/$CHCl_3$/acetone = 10/10/2–10/10/3) to afford **7** (2.16 g, 98.2%) as a foam. $[\alpha]_D^{24}$ + 21 (*c*

1.1, $CHCl_3$). IR (KBr) 3471, 2931, 2877, 1712, 1458, 1381, 1227, 1088, 1034, 964, 717 cm^{-1} ; ^1H NMR (500 MHz, $CDCl_3$) δ 1.20 (t, J = 7.3 Hz, 3 H), 1.77 (s, 3 H), 2.00–2.26 (br, 1 H), 2.64 (dq, J = 12.5, 7.3 Hz, 1 H), 2.70 (dq, J = 12.5, 7.3 Hz, 1 H), 3.66 (ddd, J = 9.5, 4.0, 2.4 Hz, 1 H), 3.80 (dd, J = 9.5, 8.9 Hz, 1 H), 3.77–3.84 (m, 1 H), 3.95–3.99 (m, 1 H), 4.26 (dd, J = 10.4, 10.1 Hz, 1 H), 4.65 (d, J = 11.3 Hz, 1 H), 4.70 (d, J = 11.3 Hz, 1 H), 5.54 (d, J = 10.4 Hz, 1 H, H-1), 5.83 (dd, J = 10.1, 8.9 Hz, 1 H), 7.24–7.36 (m, 5 H), 7.67–7.78 (m, 2 H), 7.80–7.90 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.9, 20.5, 24.4, 54.2, 61.7, 73.8, 74.7, 76.2, 79.4, 81.0(C-1), 123.5, 123.6, 127.7, 127.9, 128.4, 131.2, 131.7, 134.1, 134.3, 137.7, 167.4, 167.7, 170.0; HRMS m/z calcd for $C_{25}H_{31}N_2O_7S$ $[M + NH_4]^+$ 503.1852, found 503.1841.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-α-D-glucopyranoside (3): [51] This compound was synthesized from glycosyl donor **1** and glycosyl acceptor **2** according to method A: 8 h, 95%, α/β = 89/11, method B: 6 h, 94%, α/β = 93/7, method C: 14 h, 93%, α/β = 6/94. The ratios were determined by HPLC analysis (hexane/EtOAc = 4/1). Both anomers were partially separated by thin-layer chromatography (hexane/$CHCl_3$/acetone).

3α: White solid. Mp 98–99 °C; R_f = 0.6 (hexane/EtOAc = 2/1), 0.31 (hexane/$CHCl_3$/acetone = 5/4/1); $[\alpha]_D^{24}$ +53 (c 0.57, $CHCl_3$); IR (KBr) 3032, 2916, 1458, 1365, 1103, 1072, 1034, 741, 694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.35 (s, 3H), 3.44 (dd, J = 9.5, 3.4 Hz, 1 H), 3.52–3.56 (m, 2 H), 3.59–3.68 (m, 3 H), 3.71 (d, J = 11.3 Hz, 1 H), 3.76–3.79 (m, 2 H), 3.82 (dd, J = 11.3, 4.3 Hz, 1 H), 3.96 (dd, J = 9.5, 9.2 Hz, 1 H), 3.98 (dd, J = 9.5, 9.2 Hz, 1 H), 4.41 (d, J = 12.2 Hz, 1 H), 4.45 (d, J = 11.0 Hz, 1 H), 4.55 (d, J = 3.4 Hz, 1 H, H-1), 4.53–4.58 (m, 2 H), 4.62–4.69 (m, 3 H), 4.71 (d, J = 11.9 Hz, 1 H), 4.77 (d, J = 11.0 Hz, 1 H), 4.81 (d, J = 10.7 Hz, 1 H), 4.82 (d, J = 11.0 Hz, 1 H), 4.91 (d, J = 11.6 Hz, 1 H), 4.94 (d, J = 10.7 Hz, 1 H), 4.96 (d, J = 11.0 Hz, 1 H), 4.98 (d, J = 3.7 Hz, 1 H, H-1′), 7.10–7.14 (m, 2 H), 7.20–7.36 (m, 33 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.1, 66.0, 68.5, 70.2, 70.3, 72.3, 73.3, 73.4, 74.85, 74.94, 75.5, 75.7, 77.6, 77.8, 80.0, 80.1, 81.6, 82.1, 97.2 (C-1′), 97.9 (C-1), 127.46, 127.50, 127.51, 127.55, 127.58, 127.68, 127.71, 127.80, 127.84, 127.94, 127.97, 127.98, 128.24, 128.27, 128.29, 128.33, 128.38, 138.0, 138.2, 138.40, 138.43, 138.5, 138.79, 138.81; HRMS m/z calcd for $C_{62}H_{70}NO_{11}$ $[M + NH_4]^+$ 1004.4949, found 1004.4942.

3β: White solid. Mp 133–135 °C; R_f = 0.6 (hexane/EtOAc = 2/1), 0.28 (hexane/$CHCl_3$/acetone = 5/4/1); $[\alpha]_D^{24}$ +19 (c 1.0, $CHCl_3$); IR (KBr) 3032, 2916, 1458, 1358, 1111, 1065, 741, 694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.32 (s, 3 H), 3.42–3.46 (m, 1 H), 3.49 (dd, J = 8.9, 8.2 Hz, 1 H), 3.51 (dd, J = 9.8, 9.5 Hz, 1 H), 3.52 (dd, J = 9.5, 3.7 Hz, 1 H), 3.57 (dd, J = 9.8, 9.2 Hz, 1 H), 3.63 (dd, J = 9.2, 8.9 Hz, 1 H), 3.64–3.74 (m, 3 H), 3.81–3.85 (m, 1 H), 3.99 (dd, J = 9.5, 9.5 Hz, 1 H), 4.16–4.20 (m, 1 H), 4.34 (d, J = 8.2 Hz, 1 H, H-1′), 4.51 (d, J = 11.0 Hz, 1 H), 4.52–4.56 (m, 2 H), 4.57–4.61 (m, 2 H), 4.61 (d, J = 3.7 Hz, 1 H, H-1), 4.65 (d, J = 11.9 Hz, 1 H), 4.71 (d, J = 11.0 Hz, 1 H), 4.75 (d, J = 11.0 Hz, 1 H), 4.77–4.81 (m, 2 H), 4.80 (d, J = 11.0 Hz, 1 H), 4.90 (d, J = 11.0 Hz, 1 H), 4.96 (d, J = 11.0 Hz, 1 H), 4.97 (d, J = 11.0 Hz 1 H), 7.14–7.22 (m, 6 H), 7.23–7.40 (m, 29 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.2, 68.5, 69.0, 69.8, 73.3, 73.4 (C × 2), 74.9 (C × 2), 75.0, 75.68, 75.71, 77.9, 78.0, 79.8, 82.0, 82.1, 84.8, 98.0 (C-1), 103.8 (C-1′), 127.5, 127.60, 127.65, 127.75, 127.85, 127.87, 127.91, 127.94, 127.96, 128.1, 128.33, 128.36, 128.39, 128.44, 138.08, 138.12, 138.2, 138.4, 138.5, 138.8; HRMS m/z calcd for $C_{62}H_{70}NO_{11}$ $[M + NH_4]^+$ 1004.4949, found 1004.4957.

Methyl 2,4,6-Tri-*O*-benzyl-3-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-α-D-glucopyranoside (8): [52] This compound was synthesized from glycosyl donor **1** and glycosyl acceptor **4** according to method A: 12 h, 97%, α/β = 84/16, method B: 7 h, 89%, α/β = 88/12, method C: 11 h, 92%, α/β = 8/92. The ratios were determined by HPLC analysis (hexane/EtOAc = 4/1). Both anomers were partially separated by thin-layer chromatography (hexane/acetone).

8α: colorless oil; R_f = 0.5 (hexane/EtOAc = 2/1), 0.58 (benzene/acetone = 100/6, 2 times); ($[\alpha]_D^{23}$ +59 (c 0.68, $CHCl_3$); IR (KBr) 2916, 1450, 1365, 1103, 1049, 741, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.31 (s, 3H), 3.50–3.55 (m, 2 H), 3.56 (dd, J = 9.2, 3.4 Hz, 1 H), 3.57 (dd, J = 9.5, 3.4 Hz, 1 H), 3.58–3.63 (m, 1 H), 3.65–3.77 (m, 3 H), 3.78 (dd, J = 10.1, 8.5 Hz, 1 H), 4.06 (dd, J = 9.5, 9.2 Hz, 1 H), 4.26 (dd, J = 9.2, 8.5 Hz, 1 H), 4.28–4.35 (m, 1 H), 4.34 (d, J = 12.2 Hz, 1 H), 4.38 (d, J = 11.3 Hz, 1 H), 4.44 (d, J = 11.9 Hz, 1 H), 4.45 (d, J = 11.0 Hz, 1 H), 4.52 (d, J = 11.6 Hz, 1 H), 4.56–4.63 (m, 3 H), 4.63 (d, J = 3.4 Hz, 1 H, H-1), 4.67 (d, J = 11.6 Hz, 1 H), 4.68 (d, J = 11.6 Hz, 1 H), 4.80 (d, J = 11.0 Hz, 1 H), 4.83 (d, J = 10.7 Hz, 1 H), 4.90 (d, J = 10.7 Hz, 1 H), 4.94 (d, J = 11.3 Hz, 1 H), 5.59 (d, J = 3.4 Hz, 1 H, H-1′), 6.98–7.04 (m, 2 H), 7.08–7.36 (m, 33 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.0, 68.37, 68.44, 69.4, 70.2, 73.2, 73.3, 73.5, 74.8, 75.4, 76.6, 78.1, 78.5, 78.7, 79.6, 82.2, 97.3 (C-1′), 97.5 (C-1), 126.8, 127.2, 127.37, 127.40, 127.5, 127.61, 127.64, 127.71, 127.76, 127.83, 127.86, 128.06, 128.14, 128.21, 128.25, 128.31, 128.34, 128.7, 137.8, 138.0, 138.1, 138.3, 138.7, 138.8; HRMS m/z calcd for $C_{62}H_{70}NO_{11}$ $[M + NH_4]^+$ 1004.4949, found 1004.4935.

8β: colorless oil; R_f = 0.5 (hexane/EtOAc = 2/1), 0.52 (benzene/acetone = 100/6, 2 times); $[\alpha]_D^{23}$ +36 (c 1.1, $CHCl_3$); IR (KBr) 3024, 2908, 2870, 1458, 1365, 1041, 741 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.31 (s, 3 H), 3.40–3.44 (m, 1 H), 3.47 (dd, J = 8.9, 7.9 Hz, 1 H), 3.52 (dd, J = 9.5, 3.7 Hz, 1 H), 3.59 (dd, J = 9.8, 8.9 Hz, 1 H), 3.60–3.65 (m, 1 H), 3.67 (dd, J = 9.2, 8.9 Hz, 1 H), 3.67–3.78 (m, 5 H), 4.37 (d, J = 11.9 Hz, 1 H), 3.39 (dd, J = 9.5, 8.9 Hz, 1 H), 4.44 (d, J = 12.2 Hz, 1 H), 4.48 (d, J = 11.0 Hz, 1 H), 4.49 (d, J = 10.1 Hz, 1 H), 4.50 (d, J = 3.7 Hz, 1 H, H-1), 4.50 (d, J = 11.9 Hz, 1 H), 4.58 (d, J = 12.2 Hz, 1 H), 4.60 (d, J = 11.0 Hz, 1 H), 4.65 (d, J = 11.9 Hz, 1 H), 4.82 (d, J = 11.0 Hz, 1 H), 4.86 (d, J = 11.0 Hz, 1 H), 4.89 (d, J = 11.6 Hz, 1 H), 4.99 (d, J = 11.0 Hz, 1 H), 5.04–5.09 (m, 2 H), 5.07 (d, J = 7.9 Hz, 1 H, H-1′), 7.10–7.36 (m, 33 H), 7.40–7.44 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.1, 68.6, 68.9, 69.5, 73.3, 73.6, 74.7, 74.9, 75.0, 75.8, 76.0, 77.5, 78.3, 81.3, 83.2, 85.0, 97.8 (C-1), 102.6 (C-1′), 126.9, 127.2, 127.4, 127.51, 127.55, 127.7, 127.83, 127.86, 127.96, 127.98, 128.1, 128.2, 128.3, 128.4, 137.98, 138.01, 138.2, 138.5, 138.6, 138.7, 138.8; HRMS m/z calcd for $C_{62}H_{70}NO_{11}$ $[M + NH_4]^+$ 1004.4949, found 1004.4959.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-α-D-glucopyranoside (9): [51] This compound was synthesized from glycosyl donor **1** and glycosyl acceptor **5** according to method A: 20 h, 88%, α/β = 81/19, method B: 7 h, 93%, α/β = 83/17, method C: 11 h, 95%, α/β = 8/92. The ratios were determined by HPLC analysis (MeOH/H_2O = 20/1). Both anomers were partially separated by thin-layer chromatography (hexane/$CHCl_3$/acetone).

9α: colorless oil; R_f = 0.6 (hexane/EtOAc = 2/1), 0.44 (hexane/$CHCl_3$/acetone = 5/4/1); $[\alpha]_D^{24}$ +47 (c 0.87, $CHCl_3$); IR (neat) 3032, 2924, 2862, 1450, 1365, 1149, 1095, 1041, 741, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.37 (s, 3H), 3.37–3.42 (m, 1 H), 3.46–3.52 (m, 2 H), 3.59 (dd, J = 8.9, 3.7 Hz, 1 H), 3.64 (dd, J =

9.8, 9.2 Hz, 1 H), 3.65 (dd, J = 9.5, 2.7 Hz, 1 H), 3.68–3.73 (m, 1 H), 3.80–3.87 (m, 2 H), 3.90 (dd, J = 9.5, 9.2 Hz, 1 H), 4.04 (dd, J = 9.2, 8.9 Hz, 1 H), 4.09 (dd, J = 8.9, 8.9 Hz, 1 H), 4.28 (d, J = 12.2 Hz, 1 H), 4.42 (d, J = 11.0 Hz, 1 H), 4.47–4.63 (m, 6 H), 4.60 (d, J = 3.4 Hz, 1 H, H-1), 4.69 (d, J = 11.9 Hz, 1 H), 4.77 (d, J = 10.7 Hz, 1 H), 4.78 (d, J = 10.7 Hz, 1 H), 4.80 (d, J = 11.3 Hz, 1 H), 4.88 (d, J = 10.7 Hz, 1 H), 5.03 (d, J = 11.3 Hz, 1 H), 5.69 (d, J = 3.7 Hz 1 H, H-1′), 7.08–7.10 (m, 2 H), 7.16–7.32 (m, 33 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.1, 68.1, 69.0, 69.5, 70.9, 72.3, 73.1, 73.2, 73.3, 73.4, 74.4, 74.9, 75.5, 77.6, 79.4, 80.2, 82.0, 96.6 (C-1′), 97.7 (C-1), 126.7, 127.1, 127.2, 127.3, 127.46, 127.54, 127.60, 127.68, 127.79, 127.80, 127.9, 128.0, 128.19, 128.23, 128.27, 128.30, 128.4, 137.9, 138.0, 138.2, 138.5, 138.7, 138.9; HRMS m/z calcd for $C_{62}H_{70}NO_{11}$ $[M + NH_4]^+$ 1004.4949, found 1004.4952.

9β: White solid. Mp 83–85 °C; R_f = 0.6 (hexane/EtOAc = 2/1), 0.40 (hexane/$CHCl_3$/acetone = 5/4/1); $[\alpha]_D^{24}$ +21 (c 1.0, $CHCl_3$); IR (KBr) 3016, 2916, 2870, 1450, 1357, 1049, 733, 694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.27–3.33 (m, 1 H), 3.36 (s, 3 H), 3.33–3.40 (m, 1 H), 3.44–3.52 (m, 3 H), 3.54 (dd, J = 11.0, 4.6 Hz, 1 H), 3.56–3.63 (m, 2 H), 3.68–3.73 (m, 1 H), 3.78–3.94 (m, 2 H), 3.96 (dd, J = 9.8, 9.2 Hz, 1 H), 4.38 (d, J = 12.5 Hz, 1 H), 4.38 (d, J = 7.6 Hz, 1 H, H-1′), 4.39 (d, J = 11.3 Hz, 1 H), 4.43 (d, J = 12.5 Hz, 1 H), 4.54–4.60 (m, 2 H), 4.57 (d, J = 4.0 Hz, 1 H, H-1), 4.60 (d, J = 12.5 Hz, 1 H), 4.74–4.83 (m, 6 H), 4.87 (d, J = 11.0 Hz, 1 H), 5.09 (d, J = 11.3 Hz, 1 H), 7.16–7.34 (m, 33 H), 7.39–7.43 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 67.8, 69.0, 69.9, 73.31, 73.32, 73.6, 74.7, 74.9, 75.1, 75.3, 75.6, 76.6, 78.0, 78.8, 80.4, 82.8, 84.8, 98.4 (C-1), 102.5 (C-1′), 127.0, 127.3, 127.49, 127.55, 127.60, 127.72, 127.74, 127.75, 127.9, 128.0, 128.1, 128.2, 128.31, 128.33, 128.4, 137.8, 138.3, 138.4, 138.5, 139.6; HRMS m/z calcd for $C_{62}H_{70}NO_{11}$ $[M + NH_4]^+$ 1004.4949, found 1004.4932.

Ethyl 2,3,4-Tri-*O*-benzoyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (10): This compound was synthesized from glycosyl donor **1** and glycosyl acceptor **6** according to method A: 12 h, 99%, α/β = 86/14, method B: 4 h, 92%, α/β = 89/11, method C: 2 h, 89%, α/β = 5/95. The ratios were determined by HPLC analysis (hexane/EtOAc = 4/1). Both anomers were partially separated by thin-layer chromatography (hexane/$CHCl_3$/acetone).

10α: foam; R_f = 0.5 (hexane/EtOAc = 2/1), 0.48 (hexane/$CHCl_3$/acetone = 5/4/1); $[\alpha]_D^{24}$ +39 (c 1.6, $CHCl_3$); IR (KBr) 2908, 1728, 1450, 1365, 1273, 1095, 1034, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13 (t, J = 7.3 Hz, 3 H), 2.64 (dq, J = 12.2, 7.3 Hz, 1 H), 2.70 (dq, J = 12.2, 7.3 Hz, 1 H), 3.54 (dd, J = 9.5, 3.4 Hz, 1 H), 3.54–3.60 (m, 2 H), 3.63 (dd, J = 9.8, 9.2 Hz, 1 H), 3.65 (dd, J = 10.7, 3.7 Hz, 1 H), 3.84–3.93 (m, 2 H), 3.95 (dd, J = 9.5, 9.2 Hz, 1 H), 4.05–4.12 (m, 1 H), 4.41 (d, J = 12.2 Hz, 1 H), 4.45 (d, J = 11.0 Hz, 1 H), 4.59 (d, J = 12.2 Hz, 1 H), 4.62 (d, J = 12.2 Hz, 1 H), 4.72 (d, J = 3.4 Hz, 1 H, H-1′), 4.75 (d, J = 10.7 Hz, 1 H), 4.77 (d, J = 9.5 Hz, 1 H, H-1), 4.77 (d, J = 12.2 Hz, 1 H), 4.81 (d, J = 11.0 Hz, 1 H), 4.92 (d, J = 10.7 Hz, 1 H), 5.46 (dd, J = 9.5, 9.5 Hz, 1 H), 5.46 (dd, J = 9.5, 9.5 Hz, 1 H), 5.86 (dd, J = 9.5, 9.5 Hz, 1 H), 7.10–7.15 (m, 2 H), 7.16–7.45 (m, 25 H), 7.46–7.54 (m, 2 H), 7.76–7.83 (m, 2 H), 7.90–7.93 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7, 24.4, 66.9, 68.3, 69.8, 70.1, 70.8, 73.26, 73.35, 74.3, 74.8, 75.6, 77.4, 77.6, 80.0, 81.9, 83.6 (C-1), 97.1 (C-1′), 127.4, 127.5, 127.6, 127.7, 127.82, 127.88, 127.93, 128.0, 128.18, 128.25, 128.34, 128.4, 128.9, 129.3, 129.7, 129.86, 129.89, 133.16, 133.21, 133.4, 138.0, 138.3, 138.6, 138.9, 165.2, 165.8; HRMS m/z calcd for $C_{63}H_{66}NO_{13}S$ $[M + NH_4]^+$ 1076.4255, found 1076.4240.

10β: foam; R_f = 0.5 (hexane/EtOAc = 2/1), 0.42 (hexane/$CHCl_3$/acetone = 5/4/1); $[\alpha]_D^{23}$ +7.4 (c 1.0, $CHCl_3$); IR (KBr) 3062, 2862, 1728, 1597, 1450, 1365, 1273, 1072, 741, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13 (t, J = 7.3 Hz, 3 H), 2.63 (dq, J = 12.2, 7.3 Hz, 1 H), 2.68 (dq, J = 12.2, 7.3 Hz, 1 H), 3.38–3.46 (m, 2 H), 3.56–3.68 (m, 4 H), 3.87 (dd, J = 11.6, 7.9 Hz, 1 H), 4.04–4.15 (m, 2 H), 4.43 (d, J = 12.2 Hz, 1 H), 4.50 (d, J = 7.6 Hz, 1 H, H-1′), 4.51 (d, J = 11.0 Hz, 1 H), 4.54 (d, J = 12.2 Hz, 1 H), 4.70 (d, J = 11.0 Hz, 1 H), 4.75 (d, J = 10.1 Hz, 1 H, H-1), 4.77 (d, J = 11.0 Hz, 1 H), 4.80 (d, J = 11.0 Hz, 1 H), 4.91 (d, J = 11.0 Hz, 1 H), 5.00 (d, J = 11.0 Hz, 1 H), 5.42 (dd, J = 10.1, 9.5 Hz, 1 H), 5.51 (dd, J = 10.1, 9.5 Hz, 1 H), 5.89 (dd, J = 9.5, 9.5 Hz, 1 H), 7.12–7.16 (m, 2 H), 7.22–7.45 (m, 25 H), 7.47–7.52 (m, 2 H), 7.78–7.83 (m, 2 H), 7.88–7.97 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7, 24.2, 68.6, 68.9, 70.0, 70.7, 73.5, 74.2, 74.7, 74.8, 75.0, 75.7, 77.6, 78.4, 82.2, 83.6 (C-1), 84.5, 103.9 (C-1′), 127.58, 127.65, 127.72, 127.77, 127.86, 127.92, 128.27, 128.34, 128.36, 128.42, 128.81, 128.85, 129.2, 129.7, 129.8, 133.18, 133.23, 133.5, 138.06, 138.08, 138.5, 138.6, 165.2, 165.4, 165.8; HRMS m/z calcd for $C_{63}H_{66}NO_{13}S$ $[M + NH_4]^+$ 1076.4255, found 1076.4265.

Ethyl 3-*O*-Acetyl-4-*O*-benzyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (11): This compound was synthesized from glycosyl donor **1** and glycosyl acceptor **7** according to method A: 12 h, 99%, α/β = 80/20, method B: 6 h, 87%, α/β = 85/15, method C: 2 h, 87%, α/β = 5/95. The ratios were determined by HPLC analysis (hexane/EtOAc = 4/1). Both anomers were partially separated by thin-layer chromatography (hexane/$CHCl_3$/acetone).

11α: form; R_f = 0.4 (hexane/EtOAc = 2/1), 0.32 (hexane/$CHCl_3$/acetone = 5/4/1); $[\alpha]_D^{27}$ +36 (c 1.2, $CHCl_3$); IR (KBr) 2939, 1720, 1381, 1227, 1103, 1034, 741, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (t, J = 7.3 Hz, 3 H), 1.68 (s, 3H), 2.58 (dq, J = 12.5, 7.3 Hz, 1 H), 2.65 (dq, J = 12.5, 7.3 Hz, 1 H), 3.62–3.79 (m, 5 H), 3.83–3.94 (m, 4 H), 4.03 (dd, J = 9.5, 8.9 Hz, 1 H), 4.23 (dd, J = 10.7, 10.1 Hz, 1 H), 4.46 (d, J = 12.2 Hz, 1 H), 4.47 (d, J = 10.7 Hz, 1 H), 4.62 (d, J = 12.2 Hz, 1 H), 4.63 (d, J = 11.6 Hz, 1 H), 4.68 (d, J = 11.6 Hz, 1 H), 4.76–4.88 (m, 4 H), 5.03 (d, J = 10.7 Hz, 1 H), 5.13 (d, J = 3.7 Hz, 1 H, H-1′), 5.48 (d, J = 10.7 Hz, 1 H, H-1), 5.80 (dd, J = 10.1, 9.2 Hz, 1 H), 7.10–7.15 (m, 2 H), 7.20–7.40 (m, 21 H), 7.43–7.48 (m, 2 H), 7.66–7.76 (m, 2 H), 7.78–7.88 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.0, 20.5, 24.4, 54.5, 65.3, 68.5, 70.3, 72.7, 73.4, 73.9, 74.5, 75.0, 75.6, 76.4, 77.6, 79.2, 80.0, 80.9 (C-1), 81.9, 97.1 (C-1′), 123.5, 123.6, 127.56, 127.68, 127.73, 127.75, 127.84, 127.89, 127.94, 127.98, 128.02, 128.1, 128.29, 128.38, 128.43, 128.5, 131.3, 131.8, 134.0, 134.3, 137.99, 138.01, 138.3, 138.5, 138.8, 167.4, 167.8, 170.1; HRMS m/z calcd for $C_{59}H_{65}N_2O_{12}S$ $[M + NH_4]^+$ 1025.4258, found 1025.4248.

11β: foam; R_f = 0.4 (hexane/EtOAc = 2/1), 0.26 (hexane/$CHCl_3$/acetone = 5/4/1); $[\alpha]_D^{23}$ +12 (c 0.40, $CHCl_3$); IR (KBr) 2924, 2854, 1743, 1720, 1458, 1381, 1227, 1095, 1065, 741, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (t, J = 7.3 Hz, 3 H), 1.74 (s, 3H), 2.55 (dq, J = 12.2, 7.3 Hz, 1 H), 2.60 (dq, J = 12.2, 7.3 Hz, 1 H), 3.40–3.46 (m, 1 H), 3.51 (dd, J = 8.2, 7.6 Hz, 1 H), 3.60–3.67 (m, 2 H), 3.68 (dd, J = 9.8, 9.8 Hz, 1 H), 3.72–3.75 (m, 2 H), 3.78 (dd, J = 11.0, 5.8 Hz, 1 H), 3.83 (dd, J = 9.8, 5.8 Hz, 1 H), 4.24 (d, J = 11.0 Hz, 1 H), 4.28 (dd, J = 10.4, 10.4 Hz, 1 H), 4.44 (d, J = 7.6 Hz, 1 H, H-1′), 4.49 (d, J = 11.0 Hz, 1 H), 4.55 (d, J = 11.0 Hz, 1 H), 4.56 (d, J = 12.2 Hz, 1 H), 4.58 (d, J = 12.2 Hz, 1 H), 4.66 (d, J = 12.2 Hz, 1 H), 4.80 (d, J = 12.2 Hz, 1

H), 4.81 (d, J = 11.0 Hz, 1 H), 4.82 (d, J = 11.0 Hz, 1 H), 4.95 (d, J = 11.0 Hz, 1 H), 5.01 (d, J = 11.0 Hz, 1 H), 5.48 (d, J = 10.4 Hz, 1 H, H-1), 5.83 (dd, J = 10.1, 8.9 Hz, 1 H), 7.14–7.20 (m, 4 H), 7.22–7.42 (m, 21 H), 7.68–7.75 (m, 2 H), 7.80–7.90 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.8, 20.5, 24.2, 54.3, 68.6, 68.8, 73.5, 74.1, 74.5, 74.8, 74.9, 75.0, 75.7, 77.1, 77.8, 78.9, 80.8 (C-1), 82.1, 84.7, 104.0 (C-1′), 123.5, 123.6, 127.48, 127.55, 127.58, 127.72, 127.79, 127.84, 127.9, 128.0, 128.32, 128.36, 128.39, 128.40, 131.3, 131.8, 134.0, 134.3, 137.8, 138.1, 138.2, 138.45, 138.53, 168.0, 168.2, 170.0; HRMS m/z calcd for $C_{59}H_{65}N_2O_{12}S$ $[M + NH_4]^+$ 1025.4258, found 1025.4276.

Ethyl 3-*O*-Acetyl-6-*O*-benzyl-4-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (18): This compound was synthesized from glycosyl donor **1** and glycosyl acceptor **16** according to method A: 21 h, 90%, α/β = 87/13, method B: 19 h, 82%, α/β = 82/18, method C: 10.5 h, 78%, α/β = 15/85. The ratios were determined by HPLC analysis (hexane/EtOAc = 4/1). Both anomers were partially separated by thin-layer chromatography (hexane/$CHCl_3$/EtOAc).

18α: White solid, Mp 116–118 °C; R_f = 0.4 (hexane/EtOAc = 2/1), 0.45 (hexane/$CHCl_3$/EtOAc = 4/4/1); $[\alpha]_D^{23}$ +30 (c 1.2, $CHCl_3$); IR (KBr) 2924, 2862, 1743, 1712, 1458, 1381, 1227, 1080, 1034, 741, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (t, J = 7.3 Hz, 3 H), 1.74 (s, 3H), 2.64 (dq, J = 12.5, 7.3 Hz, 1 H), 2.73 (dq, J = 12.5, 7.3 Hz, 1 H), 3.42–3.47 (m, 1 H), 3.46 (dd, J = 9.5, 3.4 Hz, 1 H), 3.54 (dd, J = 10.3, 3.4 Hz, 1 H), 3.59 (dd, J = 9.8, 9.5 Hz, 1 H), 3.74–3.78 (m, 1 H), 3.78–3.86 (m, 2 H), 3.88 (dd, J = 9.5, 9.5 Hz, 1 H), 4.00 (dd, J = 11.3, 3.4 Hz, 1 H), 4.19 (dd, J = 9.5, 8.6 Hz, 1 H), 4.34 (d, J = 12.2 Hz, 1 H), 4.37 (dd, J = 10.4, 10.1 Hz, 1 H), 4.43 (d, J = 11.0 Hz, 1 H), 4.53 (d, J = 12.2 Hz, 1 H), 4.53–4.58 (m, 2 H), 4.59 (d, J = 11.9 Hz, 1 H), 4.63 (d, J = 11.9 Hz, 1 H), 4.75 (d, J = 10.7 Hz, 1 H), 4.79 (d, J = 11.0 Hz, 1 H), 4.85 (d, J = 10.7 Hz, 1 H), 5.12 (d, J = 3.4 Hz, 1 H, H-1′), 5.47 (d, J = 10.4 Hz, 1 H, H-1), 5.98 (dd, J = 10.1, 8.6 Hz, 1 H), 7.10–7.15 (m, 2 H), 7.15–7.38 (m, 23 H), 7.68–7.78 (m, 2 H), 7.82–7.92 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.0, 20.8, 24.0, 54.2, 68.3, 68.6, 71.2, 73.1, 73.2, 73.4, 73.6, 74.0, 74.8, 75.7, 77.5, 79.2, 79.7, 80.7 (C-1), 81.6, 97.3 (C-1′), 123.5, 123.7, 127.43, 127.48, 127.53, 127.56, 127.7, 127.9, 128.0, 128.16, 128.25, 128.34, 128.37, 128.5, 131.3, 131.8, 134.1, 134.3, 137.8, 137.9, 138.3, 138.4, 138.7, 167.6, 167.7, 170.2; HRMS m/z calcd for $C_{59}H_{65}N_2O_{12}S$ $[M + NH_4]^+$ 1025.4258, found 1025.4269.

18β: form; R_f = 0.4 (hexane/EtOAc = 2/1), 0.39 (hexane/$CHCl_3$/EtOAc = 4/4/1); $[\alpha]_D^{23}$ +21 (c = 2.0, $CHCl_3$); IR (KBr) 2924, 1720, 1458, 1373, 1227, 1080, 733, 710 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (t, J = 7.3 Hz, 3 H), 1.84 (s, 3 H), 2.63 (dq, J = 12.5, 7.3 Hz, 1 H), 2.71 (dq, J = 12.5, 7.3 Hz, 1 H), 3.24–3.30 (m, 1 H), 3.31 (dd, J = 8.9, 7.9 Hz, 1 H), 3.50 (dd, J = 9.2, 8.9 Hz, 1 H), 3.58–3.75 (m, 5 H), 3.84 (dd, J = 11.0, 3.4 Hz, 1 H), 4.05 (dd, J = 9.8, 9.2 Hz, 1 H), 4.36 (dd, J = 10.4, 10.4 Hz, 1 H), 4.39 (d, J = 7.9 Hz, 1 H, H-1′), 4.43 (d, J = 11.9 Hz, 1 H), 4.44 (d, J = 11.0 Hz, 1 H), 4.48 (d, J = 11.9 Hz, 1 H), 4.51 (d, J = 11.0 Hz, 1 H), 4.58 (d, J = 11.0 Hz, 1 H), 4.70 (d, J = 11.3 Hz, 1 H), 4.75–4.83 (m, 3 H), 4.89 (d, J = 11.0 Hz, 1 H), 5.43 (d, J = 10.4 Hz, 1 H, H-1), 5.79 (dd, J = 10.4, 9.2 Hz, 1 H), 7.10–7.17 (m, 2 H), 7.17–7.36 (m, 23 H), 7.67–7.75 (m, 2 H), 7.80–7.88 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 15.0, 20.5, 24.0, 53.9, 67.8, 68.8, 71.5, 73.1, 73.2, 74.4, 74.8, 75.06, 75.10, 75.5, 77.5, 79.4, 80.9 (C-1), 82.5, 84.8, 102.7 (C-1′), 123.6, 127.5, 127.63, 127.66, 127.74, 127.8, 128.3, 128.4, 131.8, 134.1, 134.3, 137.8, 138.1, 138.3, 138.5, 138.7, 167.5, 170.7; HRMS m/z calcd for $C_{59}H_{65}N_2O_{12}S$ $[M + NH_4]^+$ 1025.4258, found 1025.4265.

3,4-Di-*O*-benzoyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranosyl Fluoride (19):[43] This compound was synthesized from glycosyl donor **1** and glycosyl acceptor **17** according to method A: 4 h, 88%, α/β = 85/15, method B: 4 h, 96%, α/β = 90/10, method C: 3 h, 96%, α/β = 6/94. The ratios were determined by HPLC analysis (hexane/EtOAc = 4/1). Both anomers were partially separated by thin-layer chromatography (hexane/$CHCl_3$/EtOAc).

19α: foam; R_f = 0.5 (hexane/EtOAc = 7/3), 0.42 (hexane/$CHCl_3$/EtOAc = 5/4/1); $[\alpha]_D^{23}$ +75 (c 1.3, $CHCl_3$); IR (KBr) 2908, 2854, 1782, 1728, 1450, 1373, 1265, 1103, 1065, 741, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.48 (dd, J = 10.7, 1.5 Hz, 1 H), 3.55 (dd, J = 9.8, 3.7 Hz, 1 H), 3.53–3.70 (m, 3 H), 3.71–3.77 (m, 1 H), 3.90 (dd, J = 11.3, 5.8 Hz, 1 H), 4.00 (dd, J = 9.5, 9.2 Hz, 1 H), 4.22–4.27 (m, 1 H), 4.37 (d, J = 11.9 Hz, 1 H), 4.46 (d, J = 11.0 Hz, 1 H), 4.53 (d, J = 11.9 Hz, 1 H), 4.58–4.67 (m, 2 H), 4.71 (d, J = 3.7 Hz, 1 H, H-1′), 4.77 (d, J = 12.2 Hz, 1 H), 4.82 (d, J = 11.0 Hz, 1 H), 4.82 (d, J = 10.7 Hz, 1 H), 4.97 (d, J = 10.7 Hz, 1 H), 5.66 (dd, J = 9.8, 9.8 Hz, 1 H), 6.18 (dd, J = 9.8, 9.2 Hz, 1 H), 6.22 (dd, J = 51.9, 7.7 Hz, 1 H, H-1), 7.10–7.52 (m, 26 H), 7.72–7.80 (m, 2 H), 7.84–7.98 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.4 (d, J = 23.8 Hz, C-2), 66.7, 68.2, 69.1, 70.5 (d, J = 10.3 Hz, C-3), 73.2 (C × 2), 73.3 (C × 2), 74.9, 75.6, 77.6, 80.1, 81.7, 97.6 (C-1′), 104.2 (d, J = 216.2 Hz, C-1), 125.8, 127.47, 127.53, 127.56, 127.81, 127.84, 127.9, 128.0, 128.1, 128.25, 128.29, 128.31, 128.4, 128.6, 129.8, 129.9, 130.4, 133.49, 133.53, 137.9, 138.3, 138.4, 138.9, 139.0, 139.4, 164.9, 165.5, 165.7; HRMS m/z calcd for $C_{62}H_{58}Cl_2FN_2O_{13}$ $[M + NH_4]^+$ 1127.3300, found 1127.3295.

19β: White solid. Mp 150–151 °C; R_f = 0.5 (hexane/EtOAc = 2/1), 0.39 (hexane/$CHCl_3$/EtOAc = 5/4/1); $[\alpha]_D^{24}$ +39 (c 1.2, $CHCl_3$); IR (KBr) 2924, 2854, 1728, 1381, 1273, 1103, 1072, 741, 710 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.32–3.41 (m, 2 H), 3.45–3.70 (m, 4 H), 3.80 (dd, J = 10.3, 7.6 Hz, 1 H), 4.07 (d, J = 10.3 Hz, 1 H), 4.15–4.22 (m, 1 H), 4.38 (d, J = 7.6 Hz, 1 H, H-1′), 4.37–4.49 (m, 3 H), 4.57 (ddd, J = 12.2, 10.7, 7.6 Hz, 1 H), 4.61 (d, J = 11.0 Hz, 1 H), 4.69 (d, J = 11.0 Hz, 1 H), 4.72 (d, J = 10.7 Hz, 1 H), 4.85 (d, J = 11.0 Hz, 1 H), 4.91 (d, J = 11.0 Hz, 1 H), 5.47 (dd, J = 9.8, 9.2 Hz, 1 H), 6.12 (dd, J = 10.7, 9.2 Hz, 1 H), 6.17 (dd, J = 52.5, 7.6 Hz, 1 H, H-1), 7.05–7.45 (m, 26 H), 7.66 (d, J = 7.3 Hz, 2 H), 7.79–7.83 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 55.3 (d, J = 23.8 Hz, C-2), 68.5, 68.7, 69.5, 70.3 (d, J = 11.8 Hz, C-3), 73.4, 73.8 (d, J = 5.5 Hz, C-4), 74.8, 74.9 (C × 2), 75.6, 77.5, 82.1, 84.5, 104.1 (C-1′), 104.2 (d, J = 209.2 Hz, C-1), 125.8, 127.5, 127.6, 127.7, 128.20, 128,23, 128.31, 128.36, 128.46, 129.67, 129.72, 129.77, 129.84, 130.3, 133.55, 133.59, 138.0, 138.4, 138.6, 139.5, 165.1, 165.5; HRMS m/z calcd for $C_{62}H_{58}Cl_2FN_2O_{13}$ $[M + NH_4]^+$ 1127.3300, found 1127.3285.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-galacto-pyranosyl)-α-D-glucopyranoside (20):[53] This compound was synthesized from glycosyl donor **15** and glycosyl acceptor **2** according to method A: 16.5 h, 95%, α/β = 82/18, method B: 3.5 h, 92%, α/β = 74/26, method C: 1.5 h, 98%, α/β = 10/90. The ratios were determined by HPLC analysis (hexane/EtOAc = 4/1). Both anomers were partially separated by thin-layer chromatography (hexane/$CHCl_3$/acetone).

20α: White solid. Mp 92–94 °C; R_f = 0.4 (hexane/EtOAc = 2/1), 0.37 (hexane/$CHCl_3$/acetone = 20/20/1, 2 times); $[\alpha]_D^{23}$ +51 (c 1.3, $CHCl_3$); IR (KBr) 2916, 1450, 1358, 1103, 1034, 741, 694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.29 (s, 3H), 3.41 (dd, J = 9.2, 3.4 Hz, 1 H), 3.46–3.55 (m, 2 H), 3.59 (dd, J = 9.8, 8.9 Hz, 1

H), 3.70–3.82 (m, 3 H), 3.88–3.97 (m, 3 H), 3.96 (dd, J = 9.8, 9.2 Hz, 1 H), 4.03 (dd, J = 8.5, 3.4 Hz, 1 H), 4.36 (d, J = 11.9 Hz, 1 H), 4.43 (d, J = 11.9 Hz, 1 H), 4.53 (d, J = 3.4 Hz, 1 H, H-1), 4.55 (d, J = 12.5 Hz, 1 H), 4.56 (d, J = 12.5 Hz, 1 H), 4.58 (d, J = 10.7 Hz, 1 H), 4.67–4.75 (m, 4 H), 4.78 (d, J = 11.9 Hz, 1 H), 4.80 (d, J = 11.0 Hz, 1 H), 4.85 (d, J = 10.7 Hz, 1 H), 4.93 (d, J = 12.5 Hz, 1 H), 4.95 (d, J = 11.0 Hz, 1 H), 4.99 (d, J = 3.4 Hz, 1 H, H-1′), 7.18–7.37 (m, 35 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 66.6, 69.2, 69.6, 70.5, 72.8, 73.0, 73.5, 75.0, 75.2, 75.3, 75.9, 77.5, 78.2, 78.5, 80.4, 82.3, 98.1 (C-1), 98.2 (C-1′), 127.57, 127.64, 127.7, 127.86, 127.91, 128.0, 128.2, 128.42, 128.46, 128.51, 128.56, 128.58, 128.62, 138.3, 138.4, 138.7, 138.95, 138.98, 139.09, 139.12; HRMS m/z calcd for $C_{62}H_{70}NO_{11}$ [M + NH_4]$^+$ 1004.4949, found 1004.4956.

20β: White solid. Mp 126–128 °C; R_f = 0.4 (hexane/EtOAc = 2/1), 0.29 (hexane/$CHCl_3$/acetone = 20/20/1, 2 times); $[\alpha]_D^{21}$ +12 (c 1.0, $CHCl_3$); IR (KBr) 2916, 2862, 1458, 1358, 1103, 1065, 741, 694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.29 (s, 3 H), 3.46 (dd, J = 10.1, 9.5 Hz, 1 H), 3.47–3.53 (m, 3 H), 3.56 (dd, J = 9.2, 5.5 Hz, 1 H), 3.57–3.64 (m, 2 H), 3.78–3.86 (m, 1 H), 3.84 (dd, J = 9.8, 7.6 Hz, 1 H), 3.86–3.92 (m, 1 H), 3.97 (dd, J = 9.5, 9.2 Hz, 1 H), 4.13 (dd, J = 9.5, 1.5 Hz, 1 H), 4.30 (d, J = 7.6 Hz, 1 H, H-1′), 4.40 (d, J = 11.6 Hz, 1 H), 4.41 (d, J = 11.6 Hz, 1 H), 4.50 (d, J = 11.3 Hz, 1 H), 4.57 (d, J = 11.3 Hz, 1 H), 4.58 (d, J = 3.4 Hz, 1 H, H-1), 4.64 (d, J = 12.2 Hz, 1 H), 4.68–4.80 (m, 6 H), 4.92 (d, J = 11.3 Hz, 1 H), 4.93 (d, J = 11.6 Hz, 1 H), 4.95 (d, J = 11.0 Hz 1 H), 7.14–7.38 (m, 35 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.1, 68.5, 68.6, 69.9, 72.9, 73.3, 73.5, 74.5, 74.8, 75.1, 75.6, 78.1, 79.2, 79.9, 82.0, 82.3, 97.9 (C-1), 104.2 (C-1′), 127.3, 127.4, 127.5, 127.65, 127.76, 127.85, 127.93, 127.97, 128.10, 128.11, 128.20, 128.25, 128.30, 128.32, 128.4, 137.9, 138.2, 138.4, 138.5, 138.71, 138.73, 138.9; HRMS m/z calcd for $C_{62}H_{70}NO_{11}$ [M + NH_4]$^+$ 1004.4949, found 1004.4966.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2′,3′,4′,6′-tetra-*O*-benzyl-D-galactopyranosyl)-α-D-glucopyranoside (21):[53] This compound was synthesized from glycosyl donor **15** and glycosyl acceptor **5** according to method A: 7.5 h, 96%, α/β = 93/7, method B: 15.5 h, 93%, α/β = 93/7, method C: 2 h, > 99%, α/β = 27/73. The ratios were determined by ^{1}H-NMR analysis. Both anomers were partially separated by thin-layer chromatography (hexane/$CHCl_3$/acetone).

21α: foam; R_f = 0.5 (hexane/EtOAc = 2/1), 0.39 (hexane/$CHCl_3$/acetone = 20/20/1, 2 times); $[\alpha]_D^{23}$ +33 (c 1.3, $CHCl_3$); IR (KBr) 2934, 1458, 1358, 1103, 1041, 741, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.37 (s, 3 H), 3.40–3.52 (m, 2 H), 3.54 (dd, J = 9.5, 3.4 Hz, 1 H), 3.63–3.68 (m, 1 H), 3.70 (dd, J = 10.4, 4.3 Hz, 1 H), 3.78–3.89 (m, 3 H), 3.91–3.98 (m, 2 H), 3.98 (dd, J = 10.7, 4.0 Hz, 1 H), 4.06 (dd, J = 9.5, 8.9 Hz, 1 H), 4.24 (d, J = 11.6 Hz, 1 H), 4.30 (d, J = 11.6 Hz, 1 H), 4.42 (d, J = 12.2 Hz, 1 H), 4.51–4.56 (m, 3 H), 4.57 (d, J = 3.4 Hz, 1 H, H-1), 4.59 (d, J = 12.5 Hz, 1 H), 4.61–4.72 (m, 4 H), 4.81 (d, J = 11.3 Hz, 1 H), 4.86 (d, J = 11.3 Hz, 1 H), 4.96 (d, J = 11.3 Hz, 1 H), 5.75 (d, J = 4.0 Hz, 1 H, H-1′), 7.15–7.33 (m, 35 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.1, 68.7, 69.43, 69.48, 69.9, 72.7, 72.8, 73.1, 73.3, 73.4, 73.8, 74.3, 74.66, 74.75, 75.6, 79.2, 80.2, 82.0, 97.5 (C-1′), 97.7 (C-1), 126.7, 127.0, 127.36, 127.42, 127.50, 127.55, 127.66, 127.8, 127.9, 128.14, 128.19, 128.25, 128.29, 128.32, 128.38, 138.0, 138.3, 138.4, 138.6, 139.0; HRMS m/z calcd for $C_{62}H_{70}NO_{11}$ [M + NH_4]$^+$ 1004.4949, found 1004.4947.

21β: foam; R_f = 0.5 (hexane/EtOAc = 2/1), 0.32 (hexane/$CHCl_3$/acetone = 20/20/1, 2 times); $[\alpha]_D^{23}$ +13 (c 1.1, $CHCl_3$); IR (KBr) 2908, 1458, 1365, 1095, 1049, 741, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.28–3.42 (m, 3 H), 3.37 (s, 3 H), 3.47 (dd, J = 9.8, 3.7 Hz, 1 H), 3.47–3.55 (m, 2 H), 3.57–3.62 (m, 1 H), 3.74 (dd, J = 9.5, 7.6 Hz, 1 H), 3.79–3.85 (m, 2 H), 3.86–3.94 (m, 2 H), 4.24 (d, J = 11.9 Hz, 1 H), 4.30 (d, J = 7.6 Hz, 1 H, H-1′), 4.33 (d, J = 11.9 Hz, 1 H), 4.36 (d, J = 11.9 Hz, 1 H), 4.53 (d, J = 11.9 Hz, 1 H), 4.55 (d, J = 11.3 Hz, 1 H), 4.56 (d, J = 3.7 Hz, 1 H, H-1), 4.63 (d, J = 12.2 Hz, 1 H), 4.67 (d, J = 11.6 Hz, 1 H), 4.71 (d, J = 11.6 Hz, 1 H), 4.72 (d, J = 10.7 Hz, 1 H), 4.76 (d, J = 11.3 Hz, 1 H), 4.80 (d, J = 11.3 Hz, 1 H), 4.82 (d, J = 12.2 Hz, 1 H), 4.96 (d, J = 11.3 Hz, 1 H), 5.02 (d, J = 10.7 Hz 1 H), 7.10–7.39 (m, 35 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 68.0, 68.2, 70.0, 72.6, 73.09, 73.13, 73.4, 73.7, 73.8, 74.7, 75.2, 75.5, 76.6, 78.9, 80.1, 80.3, 82.5, 98.4 (C-1), 102.8 (C-1′), 127.0, 127.36, 127.39, 127.50, 127.53, 127.6, 127.7, 127.8, 127.9, 128.06, 128.12, 128.16, 128.18, 128.29, 128.33, 128.36, 138.1, 138.2, 138.5, 138.9, 139.0, 139.4; HRMS m/z calcd for $C_{62}H_{70}NO_{11}$ [M + NH_4]$^+$ 1004.4949, found 1004.4955.

Methyl 6-*O*-[2′,3′,4′-Tri-*O*-benzoyl-6′-*O*-(2″,3″,4″,6″-tetra-*O*-benzyl-α-D-glucopyranosyl)-β-D-glucopyranosyl]-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (22$\alpha'\beta$) and Methyl 6-*O*-[2′,3′,4′-Tri-*O*-benzoyl-6′-*O*-(2″,3″,4″,6″-tetra-*O*-benzyl-β-D-glucopyranosyl)-β-D-glucopyranosyl]-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (22$\beta'\beta$): These compounds were synthesized from glycosyl donor **1**, glycosyl acceptor **6** and **2** according to method D: 93%, α/β = 85/15, method E: 88%, α/β = 87/13, method F: 93%, α/β = 7/93. The ratios were determined by isolation of each isomer (hexane/EtOAc).

22$\alpha'\beta$: foam; R_f = 0.5 (hexane/EtOAc = 6/4); $[\alpha]_D^{23}$ +23 (c 2.4, $CHCl_3$); IR (KBr) 2931, 2908, 2862, 1736, 1450, 1365, 1265, 1095, 741, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.03 (s, 3H), 3.34–3.43 (m, 2 H), 3.51 (dd, J = 9.8, 3.4 Hz, 1 H), 3.52–3.58 (m, 1 H), 3.58–3.66 (m, 4 H), 3.73 (dd, J = 10.7, 3.4 Hz, 1 H), 3.78–3.83 (m, 1 H), 3.83 (dd, J = 9.5, 9.2 Hz, 1 H), 3.87 (dd, J = 11.3, 6.7 Hz, 1 H), 3.91 (dd, J = 9.8, 9.2 Hz, 1 H), 4.01–4.07 (m, 1 H), 4.10 (d, J = 10.4 Hz, 1 H), 4.20 (d, J = 11.3 Hz, 1 H), 4.35 (d, J = 12.2 Hz, 1 H), 4.38 (d, J = 11.3 Hz, 1 H), 4.44 (d, J = 11.3 Hz, 1 H), 4.45 (d, J = 3.7 Hz, 1 H, H-1), 4.54 (d, J = 12.2 Hz, 1 H), 4.56 (d, J = 12.2 Hz, 1 H), 4.59 (d, J = 12.2 Hz, 1 H), 4.65 (d, J = 11.3 Hz, 1 H), 4.69 (d, J = 12.2 Hz, 1 H), 4.71 (d, J = 10.4 Hz, 1 H), 4.71 (d, J = 10.4 Hz, 1 H), 4.72 (d, J = 3.4 Hz, 1 H, H-1″), 4.76 (d, J = 7.9 Hz, 1 H, H-1′), 4.80 (d, J = 11.3 Hz, 1 H), 4.86 (d, J = 10.4 Hz, 1 H), 4.87 (d, J = 10.4 Hz, 1 H), 5.48 (dd, J = 9.8, 9.8 Hz, 1 H), 5.53 (dd, J = 9.5, 7.9 Hz, 1 H), 5.83 (dd, J = 9.8, 9.5 Hz, 1 H), 6.99 (d, J = 7.0 Hz, 2 H), 7.08–7.13 (m, 2 H), 7.14–7.43 (m, 39 H), 7.48 (dd, J = 7.9, 7.9 Hz, 1 H), 7.79 (d, J = 7.9 Hz, 2 H), 7.87 (d, J = 7.9 Hz, 2 H), 7.92 (d, J = 7.9 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 54.9, 67.1, 67.8, 68.4, 69.4, 69.8, 70.2, 71.9, 73.0, 73.1, 73.36, 73.40, 74.5, 74.8, 75.4, 75.5, 77.1, 77.4, 79.7, 80.1, 81.75, 81.82, 97.3 (C-1″), 97.9 (C-1), 100.8 (C-1′), 127.30, 127.37, 127.47, 127.55, 127.62, 127.79, 127.80, 127.83, 127.87, 128.02, 128.08, 128.18, 128.24, 128.27, 128.30, 128.4, 128.8, 128.9, 129.2, 129.7, 129.8, 133.0, 133.1, 133.3, 138.1, 138.25, 138.28, 138.43, 138.8, 164.8, 165.1, 165.8; HRMS m/z calcd for $C_{89}H_{92}NO_{19}$ [M + NH_4]$^+$ 1478.6264, found 1478.6271.

22$\beta'\beta$: foam; R_f = 0.6 (hexane/EtOAc = 6/4); $[\alpha]_D^{23}$ −0.72 (c 0.74, $CHCl_3$); IR (KBr) 2924, 1736, 1450, 1365, 1095, 1072, 741, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.11 (s, 3H), 3.31 (dd, J = 9.8, 8.9 Hz, 1 H), 3.35–3.43 (m, 3 H), 3.50–3.62 (m, 4 H), 3.62–3.68 (m, 2 H), 3.81 (dd, J = 9.5, 8.9 Hz, 1 H), 3.89 (dd, J = 11.9, 8.5 Hz, 1 H), 4.00–4.09 (m, 3 H), 4.11 (d, J = 11.0 Hz, 1 H), 4.32 (d, J = 11.0 Hz, 1 H), 4.42 (d, J = 12.2 Hz, 1 H), 4.48 (d, J

= 11.0 Hz, 1 H), 4.48 (d, J = 3.4 Hz, 1 H, H-1), 4.52 (d, J = 7.3 Hz, 1 H, H-1″), 4.54 (d, J = 12.2 Hz, 1 H), 4.57 (d, J = 12.2 Hz, 1 H), 4.64 (d, J = 12.2 Hz, 1 H), 4.66 (d, J = 8.2 Hz, 1 H, H-1′), 4.68–4.76 (m, 3 H), 4.76 (d, J = 11.0 Hz, 1 H), 4.85 (d, J = 11.0 Hz, 1 H), 4.86 (d, J = 11.0 Hz, 1 H), 4.94 (d, J = 11.0 Hz, 1 H), 5.39 (dd, J = 9.8, 9.5 Hz, 1 H), 5.53 (dd, J = 9.8, 8.2 Hz, 1 H), 5.84 (dd, J = 9.8, 9.5 Hz, 1 H), 6.90–6.96 (m, 2 H), 7.06–7.14 (m, 2 H), 7.14–7.44 (m, 39 H), 7.47–7.53 (m, 1 H), 7.79 (dd, J = 8.5, 1.2 Hz, 2 H), 7.85 (d, J = 8.2 Hz, 2 H), 7.91 (dd, J = 8.2, 1.2 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.0, 67.9, 68.6, 69.4, 70.0, 71.9, 73.0, 73.3, 73.5, 74.6, 74.8, 74.9, 75.4, 75.5, 77.2, 77.6, 79.7, 81.8, 82.1, 84.7, 98.0 (C-1), 100.8 (C-1′), 103.9 (C-1″), 127.31, 127.37, 127.45, 127.56, 127.67, 127.73, 127.77, 127.82, 127.85, 128.09, 128.11, 128.20, 128.25, 128.31, 128.4, 128.8, 129.1, 129.7, 129.8, 133.0, 133.2, 133.5, 138.06, 138.17, 138.22, 138.5, 138.8, 164.8, 165.4, 165.8; HRMS *m/z* calcd for $C_{89}H_{92}NO_{19}$ $[M + NH_4]^+$ 1478.6264, found 1478.6262.

Methyl 6-*O*-[3′-*O*-Acetyl-4′-*O*-benzyl-6′-*O*-(2″,3″,4″,6″-tetra-*O*-benzyl-α-D-glucopyranosyl)-2′-deoxy-2′-phthalimido-β-D-glucopyranosyl]-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (23α′β) and Methyl 6-*O*-[3′-*O*-Acetyl-4′-*O*-benzyl-6′-*O*-(2″,3″,4″,6″-tetra-*O*-benzyl-β-D-glucopyranosyl)-2′-deoxy-2′-phthalimido-β-D-glucopyranosyl]-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (23β′β): These compounds were synthesized from glycosyl donor **1**, glycosyl acceptor **7** and **2** according to method D: 91%, α/β = 81/19, method E: 89%, α/β = 86/14, method F: 14 h, 88%, α/β = 6/94. The ratios were determined by HPLC analysis (hexane/EtOAc = 2/1). Both anomers were partially separated by thin-layer chromatography (hexane/$CHCl_3$/acetone).

23α′β: foam; R_f = 0.3 (hexane/EtOAc = 6/4), 0.56 (hexane/$CHCl_3$/acetone = 5/4/1, 2 times); $[\alpha]_D^{23}$ +46 (*c* 1.4, $CHCl_3$); IR (KBr) 3101, 2924, 1720, 1458, 1381, 1103, 1034, 741, 694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.68 (s, 3H), 3.03 (s, 3H), 3.25 (dd, J = 9.5, 7.9 Hz, 1 H), 3.26 (dd, J = 9.5, 3.4 Hz, 1 H), 3.53–3.78 (m, 7 H), 3.79 (dd, J = 9.5, 9.5 Hz, 1 H), 3.76–3.84 (m, 1 H), 3.88–3.95 (m, 2 H), 4.01 (dd, J = 9.2, 9.2 Hz, 1 H), 4.04–4.12 (m, 2 H), 4.25 (d, J = 3.4 Hz, 1 H, H-1), 4.27 (dd, J = 10.7, 8.2 Hz, 1 H), 4.35 (d, J = 10.7 Hz, 1 H), 4.44 (d, J = 11.9 Hz, 1 H), 4.43–4.52 (m, 2 H), 4.57–4.70 (m, 5 H), 4.76–4.89 (m, 5 H), 5.03 (d, J = 11.0 Hz, 1 H), 5.15 (d, J = 3.7 Hz, 1 H, H-1″), 5.44 (d, J = 8.2 Hz, 1 H, H-1′), 5.77 (dd, J = 10.7, 9.2 Hz, 1 H), 6.95–6.99 (m, 2 H), 7.10–7.15 (m, 2 H), 7.18–7.38 (m, 34 H), 7.44–7.60 (m, 5 H), 7.67–7.77 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.5, 54.8, 55.3, 65.2, 68.1, 68.6, 69.3, 70.3, 72.6, 73.0, 73.3, 73.4, 74.5, 74.7, 75.0, 75.1, 75.5, 76.3, 77.5, 80.0, 80.2, 81.8, 97.4 (C-1″), 97.7 (C-1), 98.0 (C-1′), 123.4, 127.47, 127.53, 127.64, 127.69, 127.70, 127.74, 127.78, 127.82, 127.85, 127.88, 127.91, 127.97, 128.00, 128.20, 128.26, 128.31, 128.35, 128.39, 128.41, 128.5, 131.2, 131.6, 133.9, 134.0, 137.8, 138.0, 138.2, 138.3, 138.4, 138.8, 138.9, 167.3, 168.1, 170.2; HRMS *m/z* calcd for $C_{85}H_{91}N_2O_{18}$ $[M + NH_4]^+$ 1427.6267, found 1427.6252.

23β′β: foam; R_f = 0.3 (hexane/EtOAc = 6/4), 0.59 (hexane/$CHCl_3$/acetone = 5/4/1, 2 times); $[\alpha]_D^{23}$ +11 (*c* 1.2, $CHCl_3$); IR (KBr) 2916, 2854, 1743, 1720, 1458, 1389, 1227, 1065, 741, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.74 (s, 3H), 3.06 (s, 3H), 3.21 (dd, J = 9.5, 9.5 Hz, 1 H), 3.35 (dd, J = 9.5, 3.7 Hz, 1 H), 3.41 (ddd, J = 9.5, 4.0, 1.8 Hz, 1 H), 3.45–3.53 (m, 3 H), 3.57 (dd, J = 8.9, 8.9 Hz, 1 H), 3.62 (dd, J = 9.5, 8.9 Hz, 1 H), 3.64 (dd, J = 9.5, 8.5 Hz, 1 H), 3.69 (dd, J = 10.7, 4.3 Hz, 1 H), 3.73 (dd, J = 10.7, 1.8 Hz, 1 H), 3.77 (dd, J = 9.5, 9.5 Hz, 1 H), 3.81 (dd, J = 11.3, 6.4 Hz, 1 H), 3.83–3.89 (m, 1 H), 3.96 (d, J = 10.4 Hz, 1 H), 4.05 (d, J = 9.2 Hz, 1 H), 4.22 (d, J = 10.4 Hz, 1 H), 4.21–4.26 (m, 1 H), 4.31 (dd, J = 10.4, 8.5 Hz, 1 H), 4.37 (d, J = 3.7 Hz, 1 H, H-1), 4.46–4.58 (m, 6 H, including H-1″), 4.61 (d, J = 11.0 Hz, 1 H), 4.64 (d, J = 12.2 Hz, 1 H), 4.67 (d, J = 12.2 Hz, 1 H), 4.75 (d, J = 11.0 Hz, 1 H), 4.76–4.84 (m, 3 H), 4.90 (d, J = 11.0 Hz, 1 H), 4.97 (d, J = 11.0 Hz, 1 H), 5.41 (d, J = 8.5 Hz, 1 H, H-1′), 5.79 (dd, J = 10.4, 8.5 Hz, 1 H), 6.89–6.94 (m, 2 H), 7.10–7.39 (m, 38 H), 7.40–7.60 (m, 3 H), 7.63–7.80 (br, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.5, 54.9, 55.0, 68.0, 68.2, 68.8, 69.2, 73.3, 73.5, 74.6, 74.8, 74.9, 75.3, 75.5, 75.6, 77.1, 77.5, 77.8, 79.6, 81.8, 82.1, 84.9, 97.8 (C-1′), 97.9 (C-1), 104.0 (C-1″), 123.2, 127.4, 127.55, 127.63, 127.72, 127.79, 127.83, 127.89, 128.02, 128.04, 128.18, 128.22, 128.31, 128.34, 128.38, 128.39, 128.44, 133.9, 137.64, 137.66, 138.11, 138.15, 138.43, 138.46, 138.7, 165, 170.0; HRMS *m/z* calcd for $C_{85}H_{91}N_2O_{18}$ $[M + NH_4]^+$ 1427.6267, found 1427.6250.

Methyl 6-*O*-[6′-*O*-(α-D-Glucopyranosyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (24α′β): To a solution of **22α′β** (71.0 mg, 0.049 mmol) in THF (2 mL)–MeOH (1 mL), was added 2 M NaOH aq (0.5 mL) at room temperature and stirred for 3 h at the same temperature. Then, the reaction mixture was diluted with EtOAc and H_2O, and the aqueous layer was extracted with EtOAc (×2). The combined organic layer was washed with H_2O and brine, and dried over $MgSO_4$. After filtration and evaporation, the resulting residue was dried in vacuo. Thus obtained crude product was used without further purification. To a solution of the crude product in MeOH (10 mL) was added Pd-OH (20% on Carbon, 50% wet, 150 mg) under argon atmosphere. After purging with H_2 (1 atm) and stirring for 14 h, H_2 was removed. Then the catalyst was filtered off and the mixture was evaporated in vacuo. The crude residue was purified by reversed-phase column (YMC Gel, ODS, MeOH/H_2O = 10/90) to afford **24α′β** (22.0 mg, 87.4%) as a white solid. Mp 143–145 °C; $[\alpha]_D^{22}$ +110 (*c* 0.11, MeOH); IR (KBr) 3386, 3332, 2908, 1643, 1450, 1365, 1041 cm^{-1}; ^{1}H NMR (500 MHz, D_2O, TMS as an external standard) δ 3.11 (dd, J = 8.5, 8.2 Hz, 1 H), 3.22 (s, 3 H), 3.23 (dd, J = 9.5, 8.5 Hz, 1 H), 3.27 (dd, J = 9.8, 9.5 Hz, 1 H), 3.26–3.32 (m, 2 H), 3.35 (dd, J = 9.8, 4.0 Hz, 1 H), 3.36 (dd, J = 9.5, 4.0 Hz, 1 H), 3.41–3.50 (m, 1 H), 3.46 (dd, J = 9.5, 9.5 Hz, 1 H), 3.50–3.56 (m, 1 H), 3.52 (dd, J = 9.8, 9.5 Hz, 1 H), 3.57–3.61 (m, 3 H), 3.64 (dd, J = 12.2, 2.1 Hz, 1 H), 3.68 (dd, J = 11.3, 5.5 Hz, 1 H), 3.76 (dd, J = 11.0, 4.6 Hz, 1 H), 3.95 (dd, J = 11.3, 1.8 Hz, 1 H), 4.32 (d, J = 8.2 Hz, 1 H, H-1′), 4.60 (d, J = 4.0 Hz, 1 H, H-1), 4.75 (d, J = 4.0 Hz, 1 H, H-1″); ^{13}C NMR (125 MHz, D_2O, TMS as an external standard) δ 54.9, 60.1, 65.2, 68.4, 69.04, 69.06, 69.09, 70.3, 70.8, 71.1, 71.4, 72.6, 72.7 (C × 2), 73.9, 75.5, 97.5 (C-1″), 99.0 (C-1), 102.6 (C-1′); HRMS *m/z* calcd for $C_{19}H_{35}O_{16}$ $[M + H]^+$ 519.1925, found 519.1910.

Methyl 6-*O*-[6-*O*-(β-D-Glucopyranosyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (24β′β): To a solution of **22β′β** (197 mg, 0.134 mmol) in THF (5.5 mL)–MeOH (2.7 mL), was added 2 M NaOH aq (1.4 mL) at room temperature and stirred for 3 h in the same temperature. Then, the reaction mixture was diluted with EtOAc and H_2O, and the aqueous layer was extracted with EtOAc (×2). The combined organic layer was washed with H_2O and brine, and dried over $MgSO_4$. After filtration and evaporation, the resulting residue was dried in vacuo. The crude product thus obtained was used without further purification. To a solution of the crude product in MeOH (20 mL) was added Pd-OH (20% on Carbon, 50% wet, 325 mg) in argon atmosphere. After purging with H_2 (1 atm) and stirring for 14 h, H_2 was removed. Then the catalyst was filtered off and the mixture was evaporated in vacuo.

The crude residue was purified by reversed phase column (YMC Gel, ODS, MeOH/H_2O = 10/90) to afforded **24**$\beta'\beta$ (61.1 mg, 88.4%) as a white solid. Mp 137–139 °C; $[\alpha]_D^{23}$ +22 (*c* 1.1, MeOH); IR (KBr) 3410, 2900, 1643, 1450, 1373, 1041 cm^{-1}; ^1H NMR (500 MHz, D_2O, TMS as an external standard) δ 3.09 (dd, *J* = 9.5, 8.2 Hz, 1 H), 3.11 (dd, *J* = 8.9, 8.2 Hz, 1 H), 3.18 (dd, *J* = 9.8, 9.2 Hz, 1 H), 3.21 (s, 3 H), 3.22–3.32 (m, 5 H), 3.35 (dd, *J* = 9.5, 3.7 Hz, 1 H), 3.38–3.44 (m, 1 H), 3.45 (dd, *J* = 9.5, 8.5 Hz, 1 H), 3.51 (dd, *J* = 12.2, 5.8 Hz, 1 H), 3.59 (ddd, *J* = 10.1, 5.8, 1.8 Hz, 1 H), 3.64–3.74 (m, 3 H), 3.96 (dd, *J* = 11.6, 1.8 Hz, 1 H), 3.99 (dd, *J* = 11.6, 1.8 Hz, 1 H), 4.29 (d, *J* = 8.2 Hz, 1 H, H-1′ or H-1″), 4.31 (d, *J* = 8.2 Hz, 1 H, H-1′ or H-1″), 4.59 (d, *J* = 3.7 Hz, 1 H, H-1); ^{13}C NMR (125 MHz, D_2O, TMS as an external standard) δ 54.9, 60.4, 68.2, 68.3, 69.0, 69.1, 69.3, 70.2, 70.8, 72.6, 72.70, 72.74, 74.6, 75.2, 75.3, 75.6, 99.0 (C-1), 102.4 (C-1′ or C-1″), 102.5 (C-1′ or C-1″); HRMS *m*/*z* calcd for $C_{19}H_{35}O_{16}$ $[M + H]^+$ 519.1925, found 519.1908.

Methyl 6-*O*-[2-Deoxy-2-acetoamido-6-*O*-(α-D-glucopyranosyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (25α′-β): To a solution of **23**$\alpha'\beta$ (78.4 mg, 0.0560 mmol) in EtOH (5.6 mL) was added ethylenediamine (0.56 mL) at room temperature and the mixture was stirred for 3 h under reflux condition. After removal of the solvent in vacuo, the residue was used in the next step without further purification. To a solution of the crude product in MeOH (5.6 mL) was added Ac_2O (1.06 mL) at room temperature and this reaction mixture was stirred for a further 14.5 h. Then it was quenched with aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc (×3). The combined organic layer was washed with H_2O and brine, and dried over $MgSO_4$. After filteration and evaporation, the residue was roughly purified by PTLC (Hexane/EtOAc = 3/7) and used for the next step without further purification. To a solution of the crude product in MeOH (7 mL) was added Pd-OH (20% on carbon, 50% wet, 136 mg) in argon atmosphere. After purging with H_2 (1 atm) and stirring for 13 h, H_2 was removed. Then the catalyst was filtered off and the mixture was evaporated in vacuo. The crude residue was purified by reversed phase column (YMC Gel, ODS, MeOH/H_2O = 10/90) to afford **25**$\alpha'\beta$ (21.4 mg, 68.8%) as a white solid. Mp 153–155 °C; $[\alpha]_D^{24}$ +91 (*c* 0.16, MeOH); IR (KBr) 3340, 2985, 1643, 1558, 1419, 1373, 1049 cm^{-1}; ^1H NMR (500 MHz, D_2O, TMS as an external standard) δ 1.82 (s, 3 H), 3.13 (dd, *J* = 9.5, 9.2 Hz, 1 H), 3.18 (s, 3 H), 3.22 (dd, *J* = 9.5, 9.2 Hz, 1 H), 3.31 (dd, *J* = 9.5, 3.7 Hz, 1 H), 3.32–3.38 (m, 3 H), 3.40–3.46 (m, 1 H), 3.43 (dd, *J* = 9.5, 9.2 Hz, 1 H), 3.48–3.63 (m, 8 H), 3.76 (dd, *J* = 11.0, 4.6 Hz, 1 H), 3.87–3.96 (m, 1 H), 4.33 (d, *J* = 8.5 Hz, 1 H, H-1′), 4.55 (d, *J* = 3.7 Hz, 1 H, H-1), 4.75 (d, *J* = 3.7 Hz, 1 H, H-1″); ^{13}C NMR (125 MHz, D_2O, TMS as an external standard) δ 21.9, 54.6, 55.2, 60.1, 65.3, 68.4, 69.1, 69.3, 69.4, 70.0, 70.8, 71.1, 71.5, 72.73, 72.75, 73.6, 73.9, 97.5 (C-1″), 98.7 (C-1), 101.5 (C-1′), 174.1; HRMS *m*/*z* calcd for $C_{21}H_{38}NO_{16}$ $[M + H]^+$ 560.2191, found 560.2184.

Methyl 6-*O*-[2-Deoxy-2-acetoamido-6-*O*-(β-D-glucopyranosyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (25β′β): To a solution of **23**$\beta'\beta$ (66.9 mg, 0.0470 mmol) in EtOH (4.7 mL) was added ethylenediamine (0.47 mL) at room temperature and the mixture was stirred for 3 h in reflux condition. After removal of the solvent in vacuo, the residue was used in the next step without further purification. To a solution of the crude product in MeOH (5.0 mL) was added Ac_2O (1.06 mL, 11.2 mmol) at room temperature and the mixture was stirred for a further 14.5 h. Then it was quenched with aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc (×3). The combined organic layer was washed with H_2O and brine, and dried over $MgSO_4$. After filtration and evaporation, the residue roughly purified by PTLC (hexane/EtOAc = 3/7) and used next step without further purification. To a solution of the crude product in MeOH (8 mL) was added $Pd(OH)_2$ (20% on carbon, 50% wet, 150 mg) in argon atmosphere. After purging with H_2 (1 atm) and stirring for 13 h, H_2 was removed. Then the catalyst was filtered off and the mixture was evaporated in vacuo. The crude residue was purified by reversed phase column (YMC Gel, ODS, MeOH/H_2O = 10/90) to afford **25**$\beta'\beta$ (19.7 mg, 74.2%) as a white solid. Mp 153–155 °C; $[\alpha]_D^{22}$ +26 (*c* 0.22, MeOH); IR (KBr) 3201, 3101, 2939, 1643, 1558, 1373, 1049 cm^{-1}; ^1H NMR (500 MHz, D_2O, TMS as an external standard δ 1.83 (s, 3 H), 3.11 (dd, *J* = 9.2, 8.2 Hz, 1 H), 3.14 (dd, *J* = 9.5, 9.2 Hz, 1 H), 3.18 (s, 3 H), 3.16–3.22 (m, 1 H), 3.22–3.26 (m, 1 H), 3.28 (dd, *J* = 9.5, 9.2 Hz, 1 H), 3.30–3.38 (m, 3 H), 3.38–3.44 (m, 1 H), 3.43 (dd, *J* = 9.5, 9.5 Hz, 1 H), 3.48–3.56 (m, 4 H), 3.66–3.73 (m, 2 H), 3.93–3.98 (m, 1 H), 4.01 (dd, *J* = 11.6, 1.2 Hz, 1 H), 4.31 (d, *J* = 8.2 Hz, 1 H, H-1″), 4.32 (d, *J* = 9.2 Hz, 1 H, H-1′), 4.56 (d, *J* = 4.0 Hz, 1 H, H-1); ^{13}C NMR (125 MHz, D_2O, TMS as an external standard) δ 21.9, 54.7, 55.1, 60.4, 68.2, 68.3, 69.26, 69.28, 69.4, 70.0, 70.8, 72.7 (C × 2), 73.3, 74.6, 75.3, 75.6, 98.9 (C-1), 101.3 (C-1′), 102.5 (C-1″), 174.1; HRMS *m*/*z* calcd for $C_{21}H_{38}NO_{16}$ $[M + H]^+$ 560.2191, found 560.2199.

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