Selected Paper

Convergent Total Syntheses of Oligosaccharides by One-Pot Sequential Stereoselective Glycosylations

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A convergent total synthesis of F1α antigen, a member of the tumor-associated *O*-linked mucin glycosyl amino acid, was tried by one-pot sequential glycosylation. Highly α-selective glycosylation of amino acid **7** with thioglycoside **6** was successfully carried out by combining trityl trifluoromethanesulfonate (TrOTf) and *N*-iodosuccimide (NIS) which gave glycosyl amino acid **21** in high yield (97%, $\alpha/\beta = 83/17$). Next, the glycosylation of thioglycoside **4** with galactosyl phenyl carbonate **2** or fluoride **3** was tried by the promotion of trityl tetrakis(pentafluorophenyl)borate [$TrB(C_6F_5)_4$] or trifluoromethanesulfonic acid (TfOH); protected F1α **25** was afforded in 80 or 89% overall yield, respectively, by the further addition of glycosyl amino acid **5** and NIS. The desired trisaccharide was obtained in high yield after removal of the protecting groups. Next, a convergent total synthesis of branched hepta-β-glucoside **30** having phytoalexin-elicitor activity was efficiently performed by way of two one-pot sequential glycosylation reactions: that is, trisaccharide **34** was synthesized in high yield by TfOH-catalyzed one-pot glycosylation using three given monosaccharides (**31**, **35**, and **36**) as shown in Scheme 12 and by subsequent selective deprotection of 6′-*O*-TBDPS group. The second one-pot glycosylation of trisaccharide **34** with three monosaccharides (**31**, **32**, and **33d**) also proceeded smoothly to afford heptaglucoside **43** stereoselectively in 48% total yield based on monosaccharide **32**. Phytoalexin-elicitor active branched hepta-β-glucoside **30** was afforded by the sequential deprotection.

Development of a stereoselective glycosylation reaction is one of the most fundamental and important topics in carbohydrate chemistry. In the last two decades, various types of superb glycosyl donors combined with suitable activators have been developed[1] since classical Koenigs–Knorr-type reactions[2] were reported. Nowadays, glycosyl fluoride, which was first reported from our laboratory in 1981, is recognized as one of the most excellent glycosyl donors (Scheme 1).[3] Actually, α-glucosides were obtained with good stereoselectivities when the glycosylation reaction of various glycosyl acceptors with glucosyl fluoride was carried out by using stoichiometric amounts of activator formed from tin(II) chloride ($SnCl_2$) and silver perchlorate ($AgClO_4$). After the above-mentioned combined-catalyst system was introduced, the glycosyl fluorides as donors attracted much attention from many research groups. Preparative methods for glycosides using glycosyl fluorides with various activators such as SiF_4,[4] Me_3SiOTf,[4] $Et_2O{\cdot}BF_3$,[5] TiF_4,[6] SnF_4,[6] Cp_2MCl_2–$AgClO_4$ (M = Ti, Zr, Hf),[7] Me_2GaCl,[8] Tf_2O,[9] $LiClO_4$,[10] $Yb(OTf)_3$,[11] $La(ClO_4)_3{\cdot}nH_2O$,[11] SO_4/ZrO_2,[12] $TrB(C_6F_5)_4$,[13] TfOH,[14] $HClO_4$,[15] and $HB(C_6F_5)_4$[15] have been developed since then.[16]

Further development of new strategies and tactics in oligosaccharide synthesis is still of growing importance and many studies have recently been reported; for example, armed-disarmed, two-stage activation, active-latent, orthogonal, one-pot multistep, and solid-phase glycosylation reactions.[1] The one-pot procedure[17] certainly reduced the steps of laborious and time-consuming purification processes of intermediate saccharides. In developing an one-pot sequential glycosylation method, it is very important to choose the most suitable combinations of glycosyl donors and related activating agents. Kahne reported[18] the one-pot glycosylation method first; the synthesis of Ciclamycin trisaccharide moiety was carried out by tuning the reactivity of leaving group, a sulfoxide. Takahashi and Chenault described independently the sequential one-pot glycosylation using two different glycosyl donors such as glycosyl bromide and thioglycoside[19] or isopropenyl glycoside and 4-pentenyl glycoside,[20] respectively. Also, Ley reported[21] the one-pot multistep glycosylation by utilizing his own protecting group strategy. In addition, programmable one-pot oligosaccharide synthesis was developed by Wong.[22]

In our previous papers,[23,24] two types of one-pot sequential glycosylation for the synthesis of trisaccharides were reported. In the first step, the corresponding disaccharide was formed from glycosyl phenyl carbonate or fluoride and thioglycoside by the promotion of a catalytic amount of trityl tetrakis(pentafluorophenyl)borate [$TrB(C_6F_5)_4$] or trifluoromethanesulfonic acid (TfOH), and trisaccharide was afforded in high yield by the subsequent glycosylation of methylglycoside with the above disaccharide and further addition of *N*-iodosuccimide (NIS) (Scheme 2).[19] The results prompted us to search for a rapid total synthesis of biologically active oligosaccharide. In this paper, we would like to report on a convergent and convenient total synthesis of linear- or branched-type oligosaccharide by one-pot sequential glycosylation.

Results and Discussion

A Convergent Total Synthesis of Mucin Related F1α Antigen. During the last decade, mucins have been regarded

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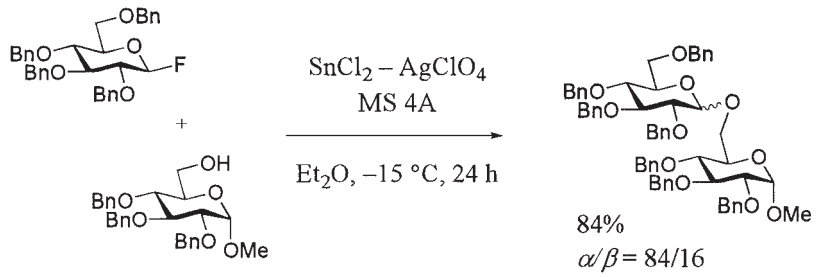
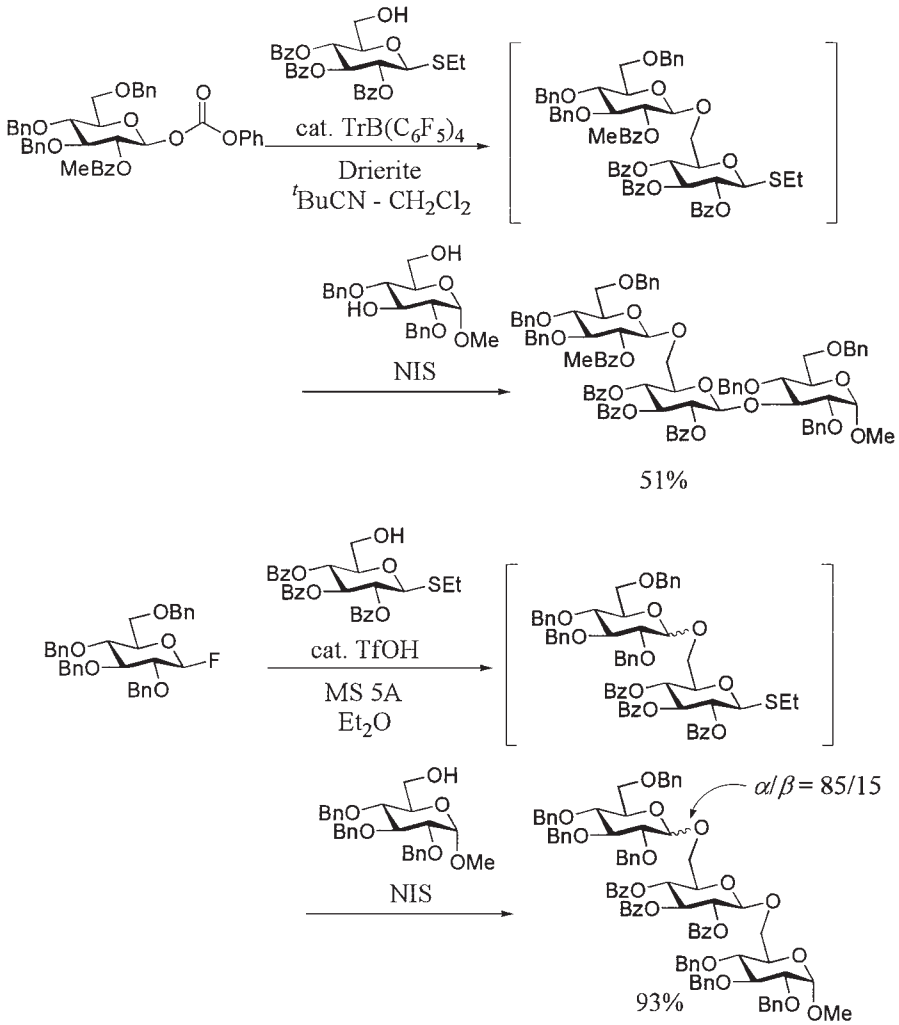


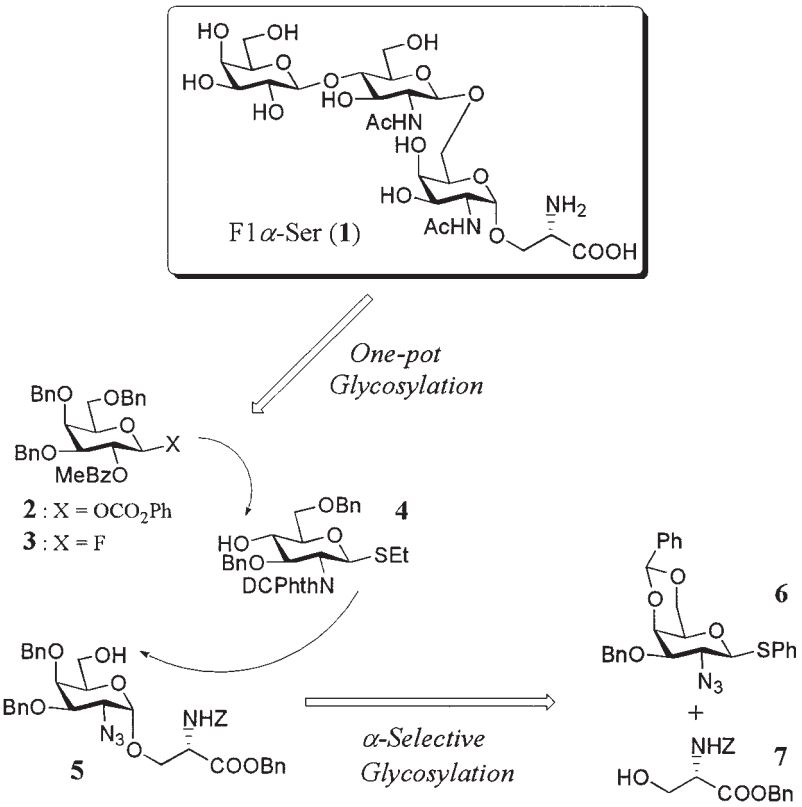
Scheme 1.



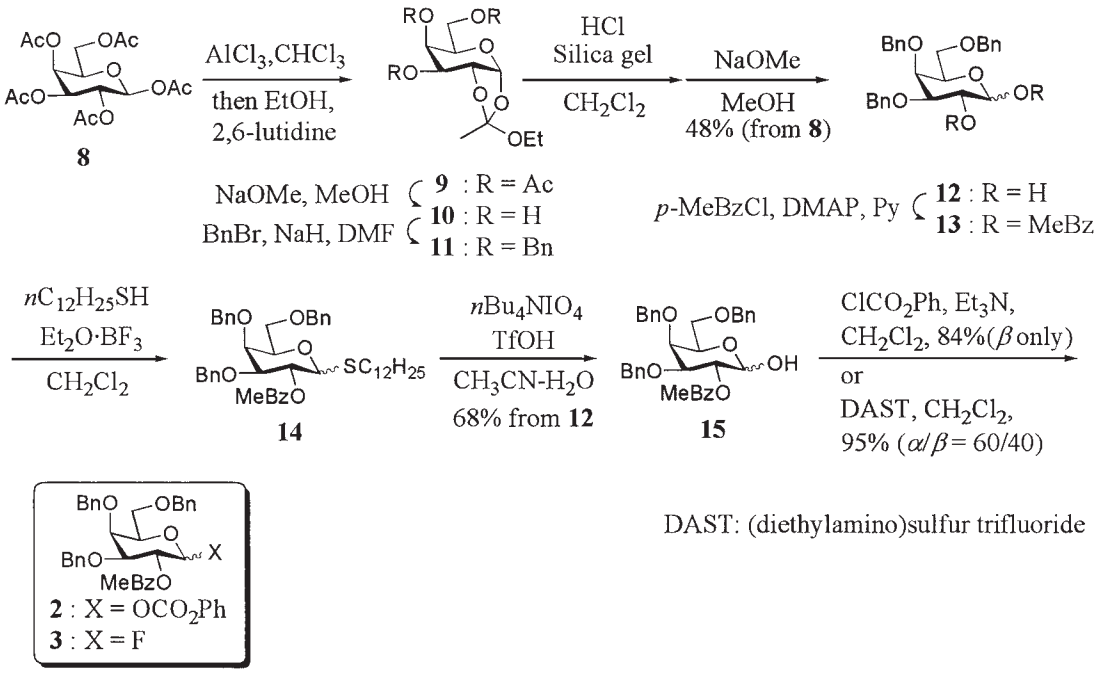
Scheme 2.

as important substances in antitumor immunological studies because of their high expression on epithelial cell surfaces and their high content of clustered α-*O*-linked carbohydrates. Recently, F1α antigens, Galβ-(1→4)GlcNAcβ-(1→6)-GalNAcα-(1→3)Ser and -(1→3)Thr, were found; these represented good examples of aberrant carbohydrate epitopes found on mucins associated with gastric adenocarcinomas.[25] Therefore, total synthesis of F1α antigens[26] continues to be an interesting topic because of their structures and biological properties, and their total synthesis has already been reported by R. R. Koganty et al.[27] in 1997 and S. J. Danishefsky et al.[28] in 1998.

The retro synthetic analysis of F1α (**1**) is shown in Scheme 3. The results of our reported procedure indicated that the fully protected F1α could be synthesized by one-pot sequential glycosylation using galactosyl donor **2** or **3**, thioglycoside **4**, and glycosyl amino acid **5**. Galactosyl donor **2** or **3** having 2-*O*-*para*-methylbenzoyl (*p*-MeBz) and 3,4,6-*O*-tribenzyl groups was prepared according to a procedure similar to that of glucosyl donors.[23,29] By changing benzoyl protecting groups at 3, 4, and 6 positions to benzyl ones, our research group has shown that the reactivity of donor **2** or **3** was improved dramatically compared with that of fully benzoylated one.[14,23a] Thioglycoside **4** having 4,5-dichlorophthaloyl



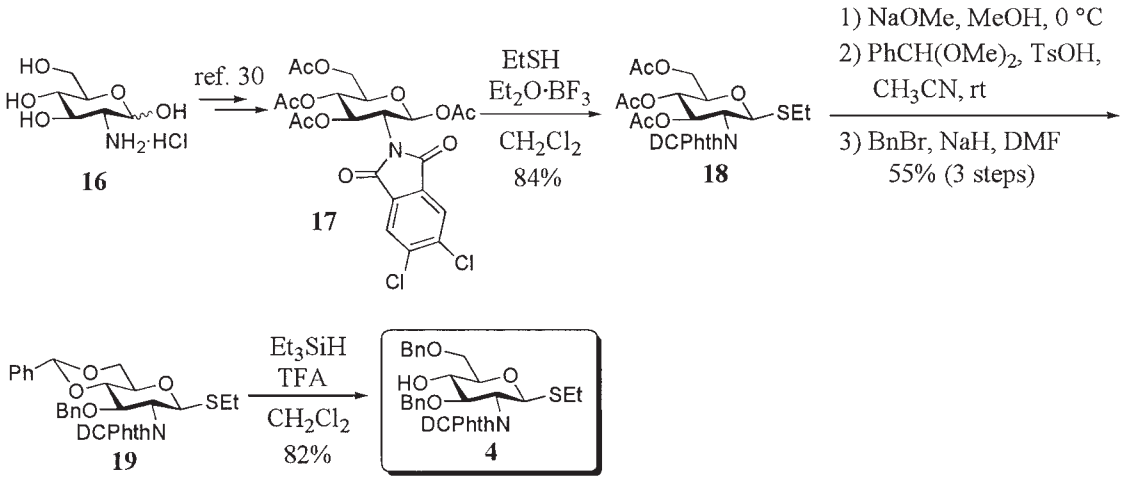
Scheme 3.



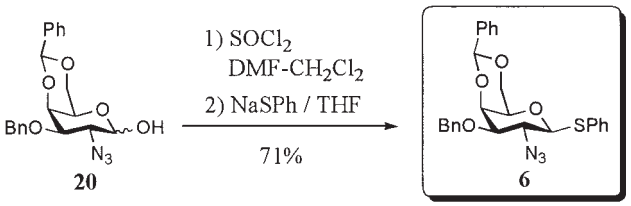
Scheme 4.

(DCPhth) protected amino function was chosen due to ease in removing the amino protecting group; it was prepared by standard protecting group manipulations.[30] It was thought that two β-glycoside linkages would be perfectly controlled by neighboring group participation, and that α-**5** would be prepared by α-selective glycosylation of the protected serine **7** with thioglycoside **6**.[23]

The starting galactosyl donors **2**, **3**, and thioglycoside **4** were successfully prepared from **8** via **9**–**15** and **16** via **17**–**19**, respectively, as shown in Schemes 4 and 5. The hydrolysis of thioglycoside **14** was carried out by using a combination of TfOH and nBu$_4$NIO$_4$ according to our reported procedure.[31]



Scheme 5.

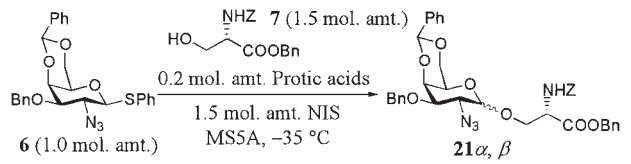


Scheme 6.

Next, stereoselective synthesis of **6** was examined (Scheme 6): that is, the corresponding thioglycoside **6** was obtained in good yield by treating 1-*O*-hydroxy sugar **20** which was prepared by a known procedure,[32] with $SOCl_2$ in DMF, and by the subsequent anomeric substitution with NaSPh.

In the first place, α-selective glycosylation of **7** with **6** was examined using a combination of protic acid such as TfOH and NIS[33] (Table 1), which was already shown as a strong catalyst system for the activation of thioglycoside. Against our expectation, α-selectivity was not observed when the reaction was tried in Et_2O (Entries 1, 4, 5). When the above glycosylation was carried out in toluene using TfOH or perchloric acid ($HClO_4$),[34] on the other hand, significant α-selectivity was observed (Entries 3, 7). However, the yield of saccharide was not sufficient because partial deprotection of the benzylidene acetal took place during this glycosylation.

Table 1. Glycosylation of L-Serine Derivative **7** with Thioglycoside **6**

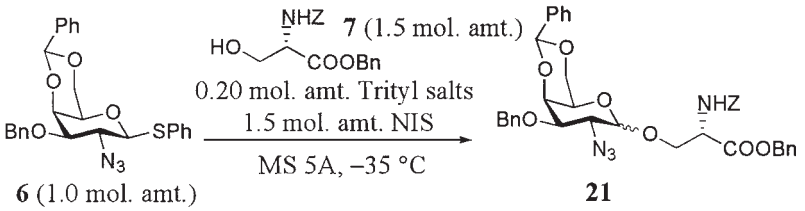


Entry	Protic acid	Solvent	Time/h	Yield/% (α/β)[b]
1	TfOH	Et_2O	4.5	29 (69/31)
2	TfOH	Toluene–Dioxane[c]	4.5	73 (85/15)
3	TfOH	Toluene	2.5	78 (**94**/6)
4	$HClO_4$[a]	Et_2O	2.5	45 (69/31)[d]
5	$HClO_4$	Et_2O	4.5	61 (65/35)
6	$HClO_4$	Toluene–Dioxane[c]	0.5	81 (66/34)
7	$HClO_4$	Toluene	18	36 (>**99**/1)

a) $HClO_4$ was generated from $AgClO_4$ and ^{t}BuCl in toluene, and the supernatant was used. b) The α/β ratios were determined by isolated yields of both isomers. c) Toluene–1,4-Dioxane (v/v = 2/1). d) The reaction was carried out at −20 °C.

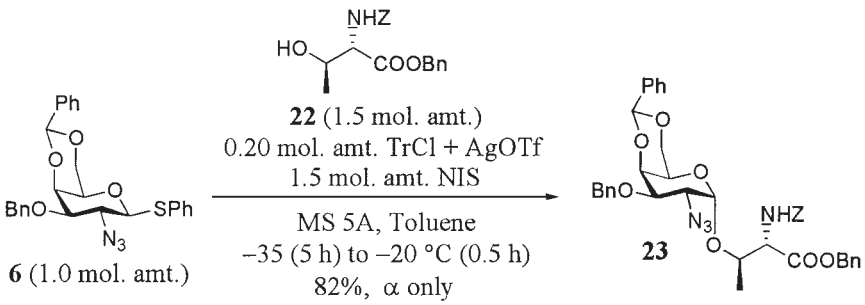
Next, the glycosylation of **7** with **6** was tried by using a combination of trityl salt and NIS (Table 2). It was reported from our laboratory that trityl salts, such as trityl perchlorate ($TrClO_4$) and $TrB(C_6F_5)_4$, could effectively be employed as Lewis acid catalysts[35,36] for aldol, Michael, and glycosylation reactions. Furthermore, glycosylation reaction with thioglycoside using a combination of $TrB(C_6F_5)_4$ and NIS[23] was recently reported to proceed smoothly to afford the disaccharide in high yield as previously noted in Scheme 2. When $TrB(C_6F_5)_4$ was used together with NIS, the glycosyl amino acid **21** was obtained in high yield; however, the undesired β-glycoside was also formed (Entries 1, 2, 3). It was thought that a protic acid would activate an oxygen atom in a benzylidene protecting group, while a Lewis acid having trityl cation would afford the desired **21** in high yield without giving damage to 1,3-benzylidene group. Actually, the TrOTf (generated in situ from trityl chloride and AgOTf)-catalyzed glycosylation afforded **21** in good yield (Entries 4, 5, 6). The highest α-selectivity and chemical yield were observed when the reaction was carried out in toluene (Entry 5), while the $TrClO_4$-catalyzed glycosylation did not proceed at all (Entries 7, 8). It is interesting to note that the stereoselectivity could be reversed only by changing the counter anion of the catalyst, as reported previously from our laboratory. Additionally, the glycosylation of hindered L-threonine derivative **22** with **6** also proceeded smoothly to afford the corresponding α-glycoside **23** in high yield (Scheme 7). It was already noted that the stereoselectivity was strongly influenced by the combined use of counter anion of catalyst and solvent by studying the glycosylation with glycosyl fluoride in detail. In addition, α-selective glycosylation proceeded effectively when $HClO_4$ or TfOH was used[34] (Table 3). It was thought that the high α-selectivity in glycosylation of **7** or **22** with **6** in toluene, a nonpolar solvent, was due to the effect of counter anion (TfO^- or ClO_4^-)

Table 2. Glycosylation Using the Combination of Trityl Salts and NIS



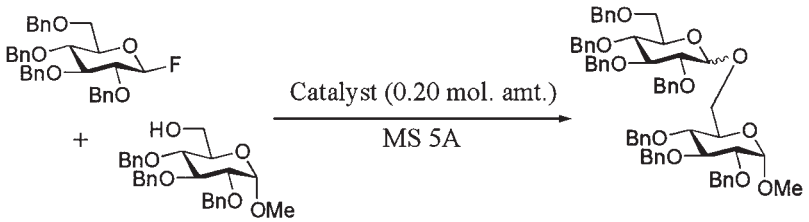
Entry	Trityl salt	Solvent	Time/h	Yield/% (α/β)[a]
1	$TrB(C_6F_5)_4$	Et_2O	1.5	89 (51/49)
2	$TrB(C_6F_5)_4$	Toluene	1.5	90 (36/64)
3	$TrB(C_6F_5)_4$	Toluene–^{t}BuCN (v/v = 3/1)	1.5	68 (10/90)
4	TrCl + AgOTf	Et_2O	4	78 (79/21)
5	TrCl + AgOTf	Toluene	1.5	**97** (**83**/17)
6	TrCl + AgOTf	Toluene–^{t}BuCN (v/v = 3/1)	4	79 (81/19)
7	$TrClO_4$	Toluene	4	trace
8	$TrClO_4$	Et_2O	4	trace

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



Scheme 7.

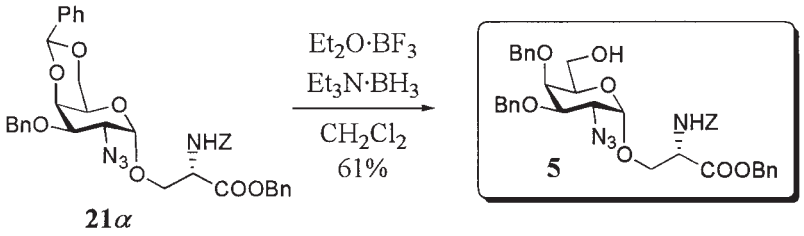
Table 3. Effect of Counter Anion of Catalyst and Solvent



Entry	Catalyst	Yield/% (α/β) (Et_2O, rt, 4 h)	Yield/% (α/β) (BTF–^{t}BuCN, 0 °C, 2 h)
1	HOTf	98 (**88**/12)	>99 (47/53)
2	$HClO_4$	98 (**92**/8)	>99 (60/40)
3	$HB(C_6F_5)_4$	95 (55/45)	99 (7/**93**)
4	$TrB(C_6F_5)_4$	85 (47/53)	88 (4/**96**)
5	$SnCl_2$–$AgB(C_6F_5)_4$	90 (43/57)	95 (8/**92**)

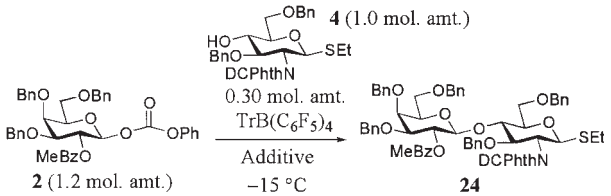
as shown in Tables 1 and 2. After separation of these isomers, a regioselective benzylidene ring opening[37] of **21α** was tried by using a combination of $Et_3N\cdot BH_3$ and $Et_2O\cdot BF_3$ to give alcohol **5** in moderate yield (Scheme 8). This method proved to be effective for the synthesis of mucin basic unit, GalNAcα(1→3)Ser/Thr, and to be applicable for the preparation of related derivatives.

Then, stereo- and chemo-selective glycosylation of thioglycoside **4** with galactosyl donor **2** or **3** were examined in detail according to our previously reported one-pot glycosylation procedure so as to optimize the reaction conditions (Tables 4 and 5). In Table 4, the $TrB(C_6F_5)_4$-catalyzed glycosylation of **4** with phenyl carbonate donor **2** proceeded more smoothly in (trifluoromethyl)benzene (BTF) (Entries 4, 6, 7) than in



Scheme 8.

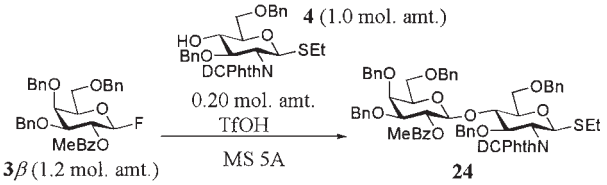
Table 4. Glycosylation of **4** with **2** Using $TrB(C_6F_5)_4$



Entry	Additive	Conditions	Time/h	Yield/%
1	Drierite	CH_2Cl_2	6	14
2	Drierite	Et_2O	6	24
3	Drierite	Toluene	6	7
4	Drierite	BTF	6	61
5	MS 5A	CH_2Cl_2	6	12
6	MS 5A	BTF	4	69
7[a)]	MS 5A	BTF	5	**84**

a) 1.8 mol. amt. of the donor **2** was used.

Table 5. Glycosylation of **4** with Galactosyl Fluoride **3** Using TfOH

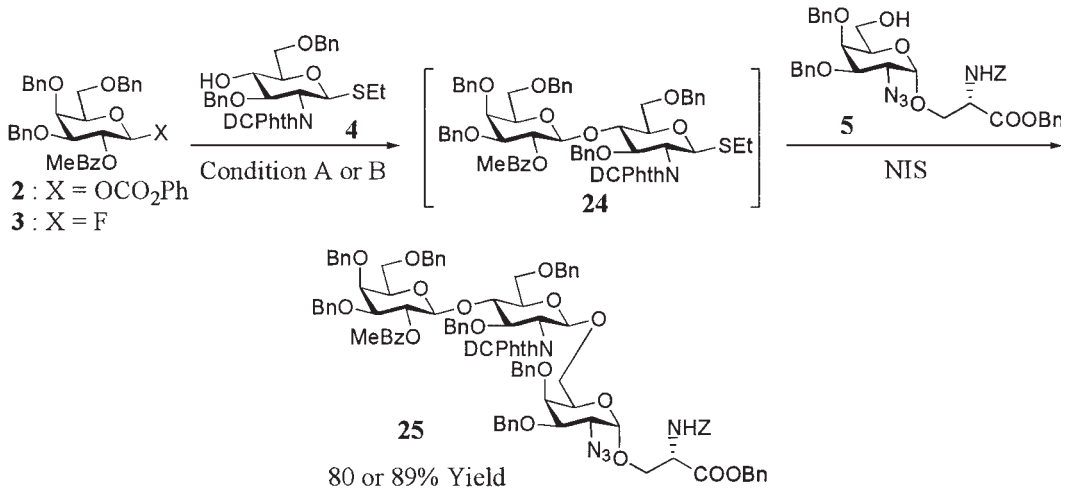


Entry	Conditions	Time/h	Yield/%
1	CH_2Cl_2, 0 °C	0.75	77
2	CH_2Cl_2, −10 °C	1	88
3	CH_2Cl_2, −20 °C	1	**94**
4[a)]	CH_2Cl_2, −20 °C	1.5	91
5	BTF, −10 °C	1	82
6	Et_2O, rt	4.5	91

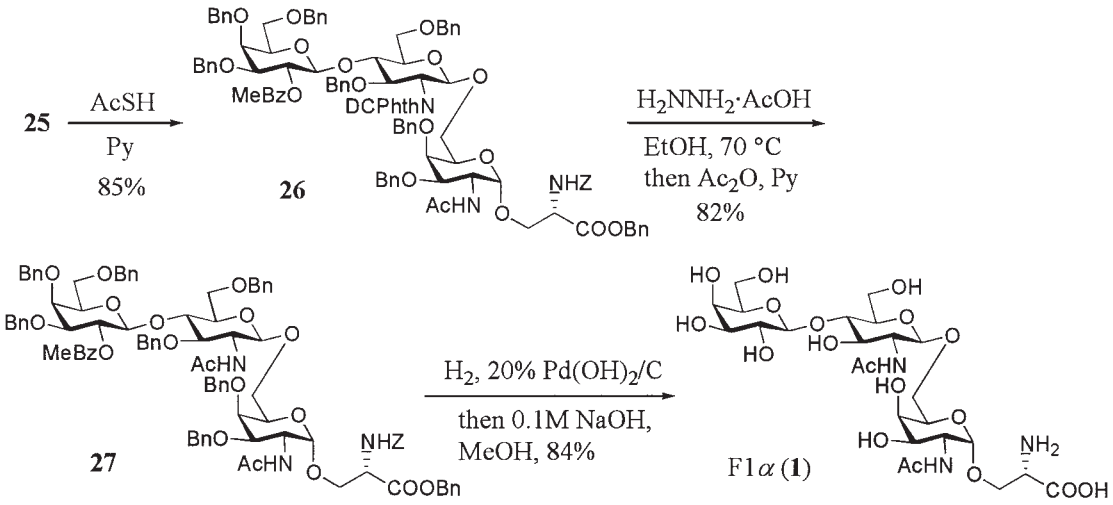
a) **3α** was used in stead of **3β**.

CH_2Cl_2, Et_2O, or toluene (Entries 1, 2, 3, 5). The former solvent was used as a substitute of the above three solvents; it was successively employed in the trityl salt-promoted glycosylation. Further, the yield was improved when the glycosylation was carried out by using MS 5A and 1.8 molar amount of **2** (Entry 7). Next, the glycosylation of **4** with glycosyl fluoride **3** was further examined by using 0.20 molar amount TfOH in CH_2Cl_2 at −20 °C. The desired disaccharide **24** was obtained in excellent yield without giving damage to thio group even when only 1.2 molar amount of glycosyl donor **3** was employed (Table 5, Entry 3). A similar result was also obtained when α-glycosyl fluoride **3α**, a less reactive donor compared with **3β**, was used under the same conditions (Entry 4).

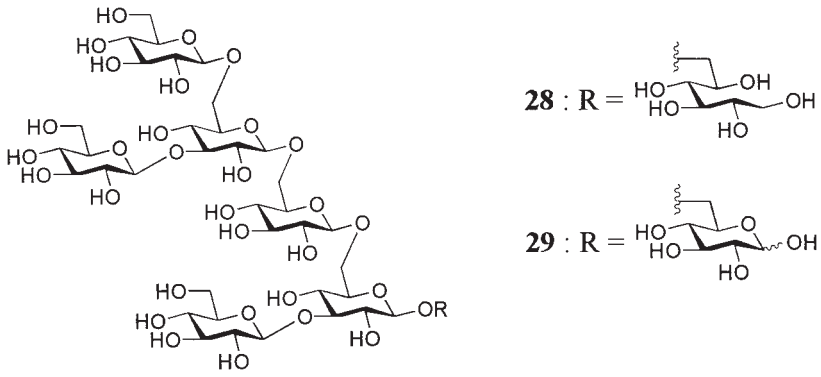
The above results led us to attempt one-pot sequential glycosylations by using glycosyl phenyl carbonate or fluoride, as shown in Scheme 9. In the first step, glycosyl fluoride **3** or phenyl carbonate **2** was treated with thioglycoside **4** in the presence of a catalyst such as TfOH or $TrB(C_6F_5)_4$; **4** was al-



Scheme 9. Condition A: **2** (1.8 mol. amt.), **4** (1.0 mol. amt.), $TrB(C_6F_5)_4$ (0.30 mol. amt.), MS 5A, BTF, −15 °C, 5 h, then **5** (5.0 mol. amt.), NIS (2.0 mol. amt.), BTF–CH_2Cl_2, −30 °C, 2 h, 80% (based on **4**). Condition B: **3** (1.2 mol. amt.), **4** (1.0 mol. amt.), TfOH (0.20 mol. amt.), MS 5A, CH_2Cl_2, −20 °C, 1 h, then **5** (1.5 mol. amt.), NIS (2.0 mol. amt.), CH_2Cl_2, −20 °C, 1 h, 89% (based on **4**).



Scheme 10.



Scheme 11.

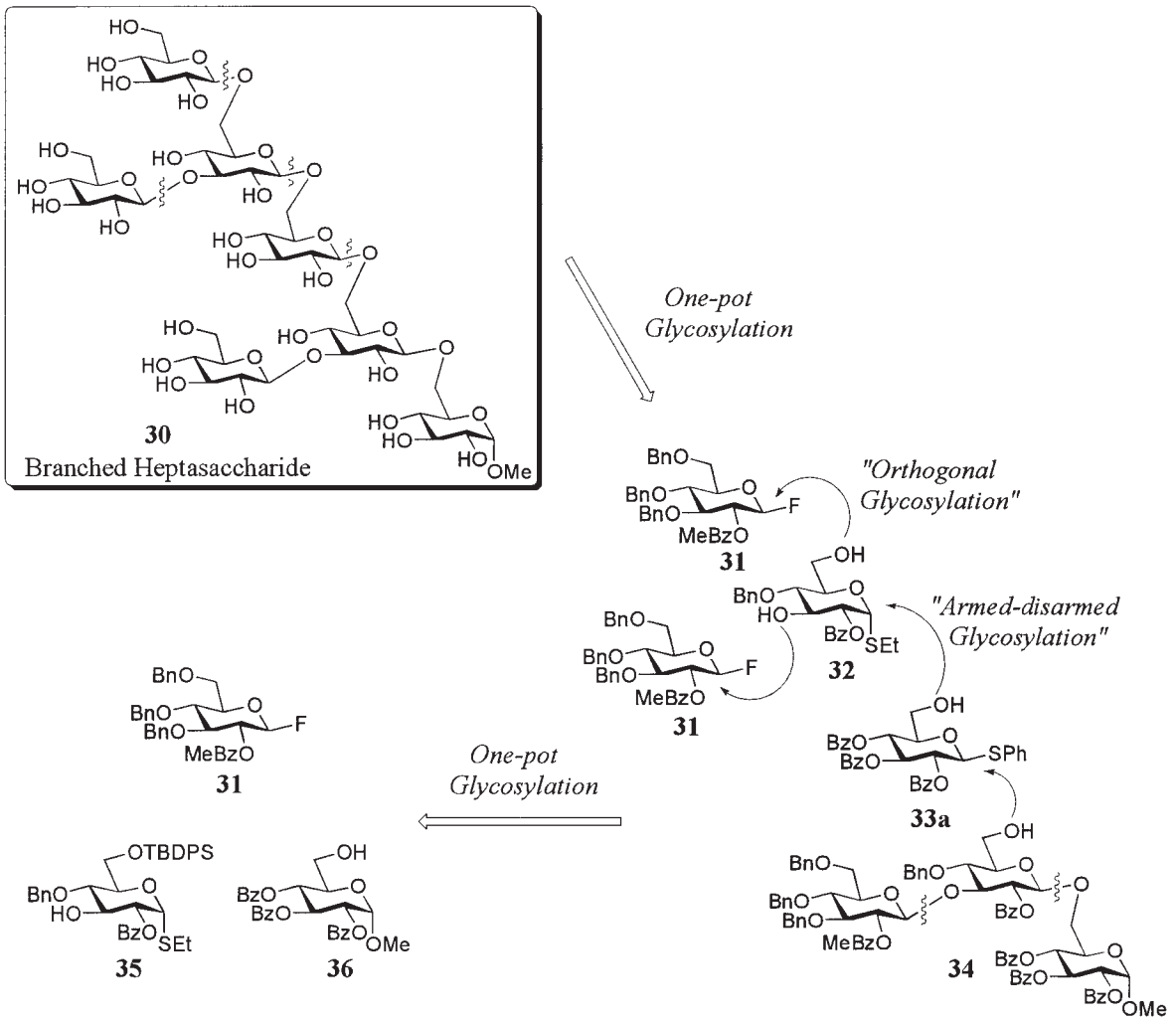
most completely consumed within 1 h or 5 h, respectively, as was confirmed by TLC monitoring. Next, the second glycosylation of glycosyl amino acid **5** with thus formed disaccharide **24** was carried out by successively adding NIS in one-pot operation; fully protected F1α **25** was stereoselectively obtained in high yield (89% or 80%, respectively). Thus, the one-pot sequential glycosylation using glycosyl fluoride **3** was effectively performed in higher yield even when the amount of thioglycoside acceptor **4** was less than that shown in the case of using glycosyl phenyl carbonate **2**.

Transformation of **25** into F1α is shown in Scheme 10. In the first place, the azido group of **25** was reduced with thioacetic acid to give **26** in 85% yield. Successive deprotection of DCPhth group of **26** proceeded smoothly to afford the desired diacetamido glycosyl amino acid **27** in high yield after acetylation (2 steps, 82%) when hydrazine acetate[38] was used in ethanol at 70 °C, while complicated mixtures resulted under standard conditions (hydrazine acetate, ethylenediamine, and $NaBH_4$-reduction followed by AcOH). Finally, removal of benzyl and benzyloxycarbonyl group of compound **27** by hydrogenolysis and careful saponification of *p*-MeBz group afforded the desired product, F1α (**1**), in 84% yield.

A Convergent Total Synthesis of the Phytoalexin-Elicitor Active Heptasaccharide. P. Albersheim et al. reported in 1984 that elicitor-active hexa-β-D-glucopyranosyl-D-glucitol **28**, isolated from the mycelial walls of *Phytophthora megasperma f. sp. Glycinea*, induced antibiotic phytoalexin accumulation in soybeans.[39] Since then, chemical synthesis of phytoalexin elicitor related β-glucans such as **29** have been drawing much attention because of their complex branched-structures (Scheme 11).[19,40]

Recently, it was reported from our laboratory[23,24] that several one-pot sequential glycosylation reactions[19] for convenient synthesis of linear trisaccharides were accomplished by utilizing orthogonal properties[41] of donor and acceptor glycosides as had already been described in the above section: that is, the combination of glycosyl fluorides (or glycosyl phenyl carbonates) and thioglycosides. It is significant to demonstrate extended utility of the above one-pot sequential glycosylations by applying the above-mentioned methods to the synthesis of complex branched-oligosaccharides. In this section, a convergent and convenient total synthesis of methyl heptaglucoside **30** having phytoalexin elicitor activity by one-pot sequential glycosylation is described.[42]

Synthetic strategy for hepta-β-glucoside **30** involved two one-pot glycosylation reactions (Scheme 12). According to our previously reported procedure, it was considered that methyl triglucoside **34** should rapidly be constructed by TfOH-catalyzed one-pot glycosylation using three components: monosaccharides **31**, **35**, and **36**. Next, three independent glycosylation reactions, the armed-disarmed glycosylation using a pair of reactivity-tuned thioglucosides[43] (**32** and **33**) as



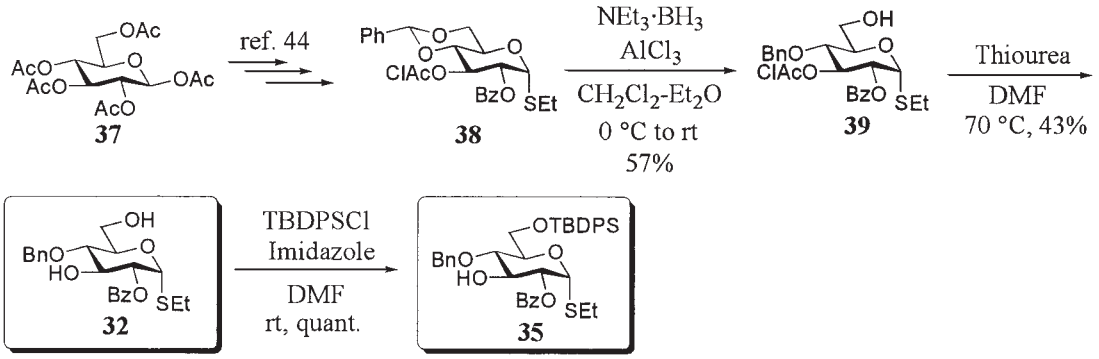
Scheme 12.

well as orthogonal glycosylation[41] using the combination of glucosyl fluoride **31** and thioglucoside **32**, and sequential glycosylation of triglucoside **34** were employed in one-pot for the formation of fully protected heptasaccharide. The assistance of 2-*O*-benzoyl protecting group must have controlled stereochemistries of those glycosylation reactions.

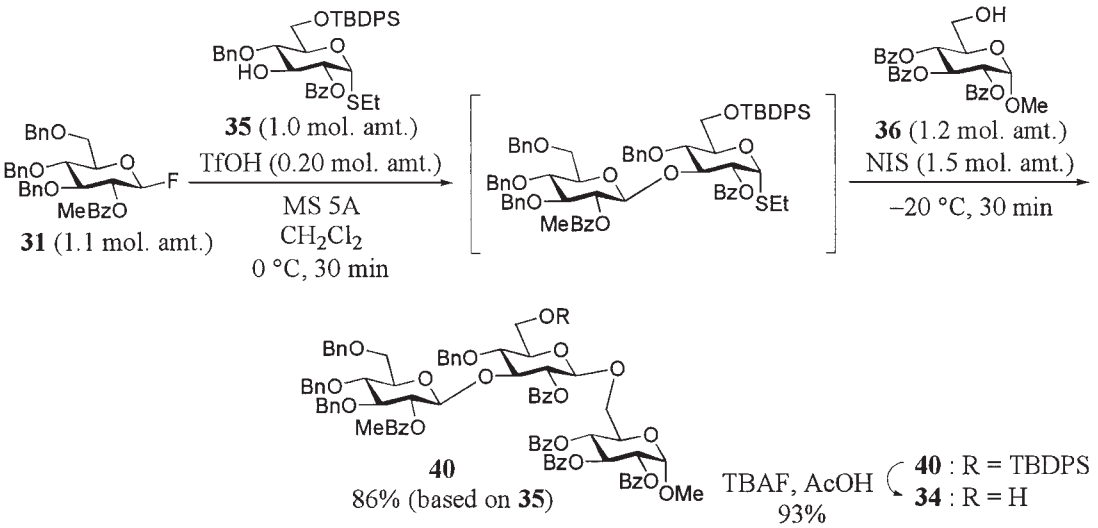
Glucosyl fluoride **31** having 2-*O*-*para*-methylbenzoyl group (*p*-MeBz) was prepared easily by treating the corresponding 1-*O*-hydroxy sugar[23] with (diethylamino)sulfur trifluoride (DAST)[29] in CH_2Cl_2. α-Ethylthio glucosides **32** and **35** corresponding to 3,6-branching positions were synthesized from ethyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-1-thio-α-D-glucopyranoside[44] by standard protecting group manipulations (Scheme 13). In the above procedure, regioselective introduction of benzoyl group to 2-*O*-hydroxy substituent in glucoside with 2 and 3-*O*-free hydroxy groups was carried out by using 4,6-*O*-benzylidene protected glucoside having α-ethylthio moiety.

In the first place, synthesis of trisaccharide unit **34** was carried out according to our previously reported one-pot procedure (Scheme 14):[23,24] that is, TfOH-catalyzed glycosylation[14] of thioglucoside **35** having a free hydroxy group at C-3 position with glucosyl fluoride **31** afforded the corresponding disaccharide, which in turn was followed by glycosylation of methyl glucoside **36** using NIS–TfOH promoter system[33] that gave the corresponding silylated trisaccharide **40** in high yield (86% based on **35**). The desired trisaccharide unit **34** was obtained in 93% yield after selective deprotection of the *t*-butyldiphenylsilyl (TBDPS) group on treatment with tetrabutylammonium fluoride (TBAF) in the presence of acetic acid.

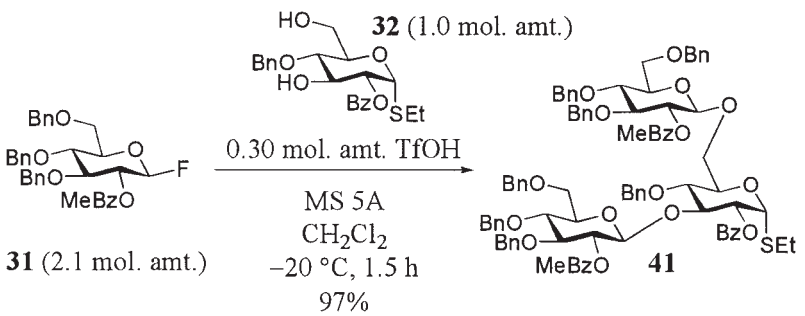
Next, the second one-pot glycosylation of "4-units" was studied in detail. In the first step, double glycosylation of diol **32** having thioglycosidic linkage with 2.1 molar amounts of **31** was attempted in the presence of 0.30 molar amount of TfOH and molecular sieves 5A (MS 5A); terminal branched-trisaccharide **41** was afforded directly in excellent yield, as shown in Scheme 15. Subsequent armed-disarmed glycosylation of several disarmed thioglycoside acceptors with thus formed trisaccharide **41** was tried at low temperature (−60 to −50 °C) using NIS–TfOH. However, the desired tetrasaccharide **42a** was not obtained when β-phenylthio glycoside **33a** was used as an acceptor; instead, self-coupling of **33a** exclusively took place and trisaccharide **41** was recovered (Scheme 16). Tetrasaccharide **42b** was obtained in 51% yield only by changing the leaving group from β-phenylthio to α-ethylthio (Table 6, Entries 2, 3, 4). It should be noted that the reactivity of α-ethylthio group stabilized by the anomeric effect[45] is lower than that of corresponding β-phenylthio group. After screening



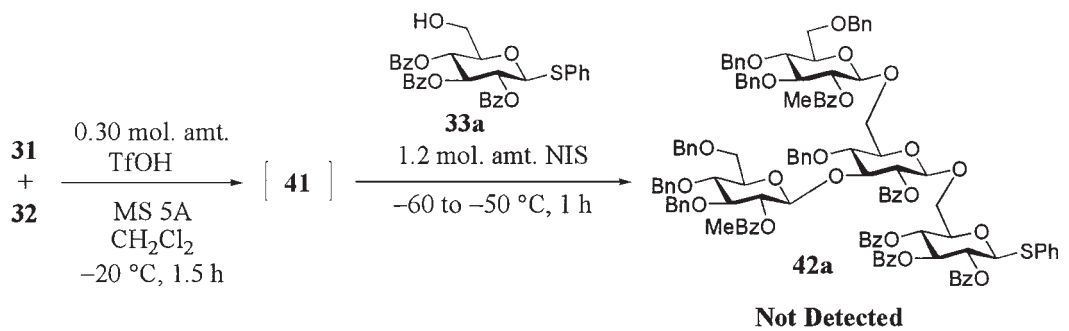
Scheme 13.



Scheme 14.

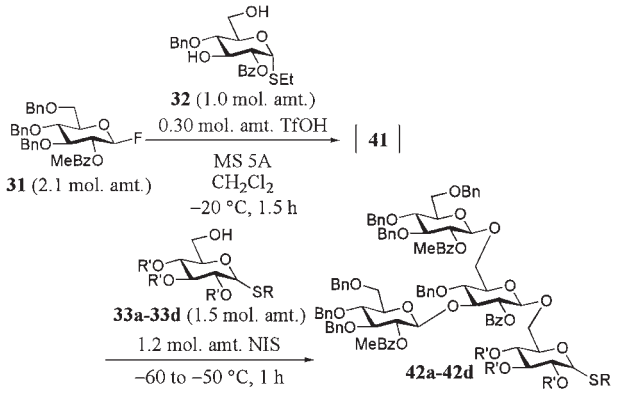


Scheme 15.



Scheme 16.

Table 6. The Second One-Pot Glycosylation of Four Units



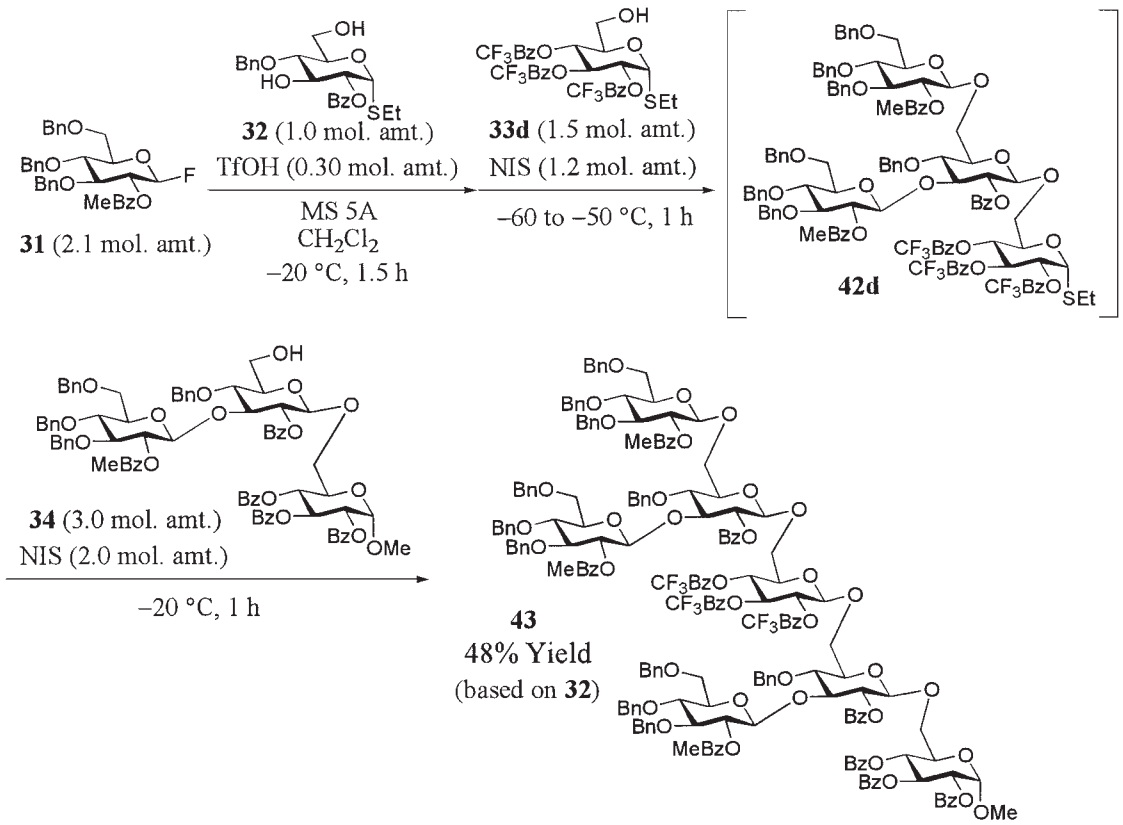
Entry	Thioglycoside	Yield/%
1	**33a**: R = SPh (β), R′ = Bz	Not Detected
2	**33b**: R = SEt (α), R′ = Bz	51
3	**33c**: R = SEt (α), R′ = *p*-ClBz	71
4	**33d**: R = SEt (α), R′ = *p*-CF_3Bz	**76**

several protective groups, the desired tetraglucoside **42d** was synthesized in high yield (total 76% yield based on **32**) when *p*-CF_3Bz-protected α-ethylthio glucoside **33d** was used (Entry 4).

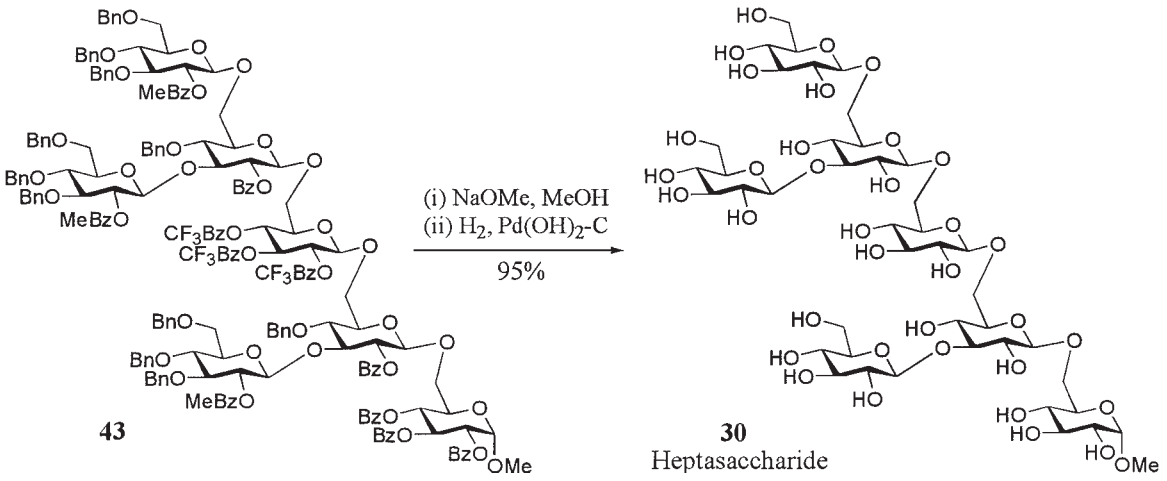
Based on the above results, one-pot sequential heptasaccharide synthesis using four building blocks was attempted, as shown in Scheme 17. First, TfOH-catalyzed double glycosylation of **36** with **35**, followed by the armed-disarmed coupling with *p*-CF_3Bz-protected **33d** afforded tetraglucoside **42d** as a major product, as was confirmed by TLC monitoring. Next, the glycosylation of the above-mentioned trisaccharide unit **34** with **42d** was tried by adding NIS successively. As a result, four glycosidic linkages were formed sequentially in one-pot manners and fully protected heptaglucoside **43** was obtained stereoselectively in 48% yield (based on **32**). Finally, the protected **43** was converted to the final product **30** in 95% yield by saponification of benzoyl groups and subsequent hydrogenolysis (Scheme 18).

Conclusion

Thus, convergent and convenient total syntheses of linear and branched types of oligosaccharides were accomplished by one-pot sequential glycosylations. In the first section, one-pot sequential glycosylation proceeded smoothly by the promotion of $TrB(C_6F_5)_4$ or TfOH using three components and addition of NIS to the reaction mixture afford protected F1α **28** in high yield. It is noted that the high α-selectivity in glycosylation of amino acid **7** with thioglycoside **6** was strongly influenced by the kind of counter anion of the catalyst. In the second section, fully protected heptasaccharide **47** was rapidly assembled in only three steps from the component monosaccharides by two one-pot reactions. It is also noted that a significant reactivity difference was observed between α-ethylthio- and β-phenylthio-glucosides, which indicated that the reactivity tuning of thioglycoside donors is controlled by their anomeric configurations. In summary, it is noted that these methodologies proved to be applicable for the rapid assembly of various types of oligosaccharides.



Scheme 17.



Scheme 18.

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), JEOL JNM-LA500 (500 MHz), or Varian INOVA600 (600 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. 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 ppm). 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]. 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). Reversed-phase column chromatography was performed on YMC-Gel ODS-AQ 120-S50. Ion-exchange column chromatography was performed on Dowex 50WX-8.

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. Trifluoromethanesulfonic acid (TfOH: donated 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 were stored over molecular sieves 4A. Toluene and (trifluoromethyl)benzene (BTF) were distilled from P_2O_5 and 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 4A and 5A were used in glycosylation reactions. Sufficiently crushed and pre-dried (at 260 °C/133 Pa, 6 h) Drierite from W. A. Hammond Drierite Company was used in the glycosylations.

3,4,6-Tri-*O*-benzyl-D-galactopyranose (12). To a solution of pentaacetyl-β-D-galactopyranoside **8** (25.0 g, 128 mmol) in $CHCl_3$ (225 mL) was added $AlCl_3$ (10.3 g, 76.9 mmol) at 0 °C. After stirring for 4 h at the same temperature, 2,6-lutidine (63 mL) was slowly added. To the mixture was successively added EtOH (250 mL) and the reaction mixture was stirred for an additional 16 h at rt. The reaction mixture was diluted with sat. aq. $NaHCO_3$ (250 mL), 2.5 M aq. NaOH (250 mL), and $CHCl_3$ (325 mL). The aqueous layer was extracted with $CHCl_3$ and the combined organic layer was dried over Na_2SO_4. After filtration and evaporation, the residue was dried in vacuo. The crude product was used without further purification. To a solution of the crude product in MeOH (375 mL) was added 28% NaOMe (3 mL) in MeOH at rt. After stirring for 3 h, the solvent was removed by evaporation. The residue was dried in vacuo. To a solution of the crude product in DMF (375 mL) was added portionwise 55% NaH (16.8 g, 385 mmol) oil dispersion during 20 min at 0 °C. After stirring for 30 min at the same temperature, a solution of benzyl bromide (39 mL, 328 mmol) in DMF (50 mL) was added dropwise during 1.5 h. After stirring for 5 h at rt, the reaction mixture was quenched by adding H_2O. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was dried in vacuo. To a solution of the crude product and silica gel (25 g, which was washed with 3 M aq. HCl) in CH_2Cl_2 (500 mL) was added 3 M aq. HCl (50 mL) at rt. After stirring for 3 h at the same temperature, the reaction mixture was diluted with H_2O. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with sat. aq. $NaHCO_3$ and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was dried in vacuo. To a solution of the crude product in MeOH (250 mL) and CH_2Cl_2 (50 mL) was added 28% NaOMe (2 mL) in MeOH at rt. After stirring for 3 h, the reaction mixture was acidified with *Amberlite® IR-120* cation exchange resin (until ca. pH 6). After filtration and evaporation, the residue was purified by silica gel column chromatography to afford **12** (13.75 g, 48%) as oil. α, β-mixture; R_f 0.19 (hexane/ethyl acetate = 1/1, v/v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.36 (dd, J = 2.7, 9.8 Hz), 3.38–3.45 (m), 3.46–3.59 (m), 3.70 (dd, J = 2.7, 10.1 Hz), 3.80–3.91 (m), 4.07–4.14 (m), 4.32–4.57 (m), 4.60–4.71 (m), 4.83 (dd, J = 4.0, 11.6 Hz), 5.26 (d, J = 3.7 Hz), 7.15–7.40 (m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 68.74, 69.08, 69.52, 72.53, 72.57, 73.28, 73.47, 73.56, 74.20, 74.55, 74.62, 79.20, 82.01, 92.69, 97.33, 127.69–128.53, 137.71, 137.75, 138.12, 138.31, 138.38, 138.49; IR (neat): 741, 1065,

1111, 2870, 2939, 3055, 3089, 3186, 3271, 3356 cm^{-1}; HRMS: m/z calcd for $C_{27}H_{30}O_6 \cdot Na$ $[M + Na]^+$ 473.1940, found 473.1941.

3,4,6-Tri-*O*-benzyl-2-*O*-*p*-toluoyl-D-galactopyranose (15). To a solution of **12** (9.00 g, 20.0 mmol) and 4-dimethylaminopyridine (224 mg, 2.00 mmol) in pyridine (40 mL) was added *p*-methylbenzoyl chloride (7.90 mL, 60.0 mmol) at 0 °C. After stirring for 4 h at the same temperature, 2,6-lutidine (63 mL) was slowly added. After additional stirring for 2 h at rt, the reaction mixture was quenched by adding sat. aq. $NaHCO_3$. The aqueous layer was extracted with AcOEt and the combined organic layer was washed with sat. aq. NH_4Cl, H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was dried in vacuo. The crude product was used without further purification. To a solution of the crude product and dodecane-1-thiol (5.7 mL, 24.0 mmol) in CH_2Cl_2 (50 mL) was added $Et_2O \cdot BF_3$ (2.76 mL, 22.0 mmol) at 0 °C; the mixture was stirred for 30 min at the same temperature. After additional stirring for 30 min at rt, the mixture was quenched by adding sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with 1 M aq. NaOH, H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was dried in vacuo. To a solution of the crude product and tetrabutylammonium periodate (2.63 g, 6.08 mmol) in CH_3CN (700 mL) was added 70% aq. TfOH (0.7 mL, 4.94 mmol) at 0 °C. After stirring for 3 h at the same temperature, the reaction mixture was quenched by adding triethylamine (2.0 mL). After evaporation, the mixture was diluted with 10% aq. $Na_2S_2O_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography to afford **15** (7.72 g, 68% from **12**) as colorless amorphous. α, β-mixture; R_f 0.16 (hexane/ethyl acetate = 3/1, v/v); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.38 (s, CH_3Bz), 2.40 (s, CH_3Bz), 3.43 (dd, J = 5.8, 9.5 Hz), 3.50–3.74 (m), 3.89–4.22 (m), 4.31–4.70 (m), 4.86–4.97 (m), 5.45 (dd, J = 7.9, 10.1 Hz), 5.55 (bd), 7.16–7.35 (m, Ar-H), 7.89 (d, J = 7.9 Hz, Ar-H), 7.94 (d, J = 8.2 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.60, 68.34, 69.28, 71.54, 72.02, 72.63, 72.79, 73.44, 73.50, 73.63, 74.45, 74.48, 74.52, 74.63, 76.28, 79.30, 90.88, 96.36, 127.23–129.89, 137.57, 138.10, 138.28, 143.61, 165.99; IR (neat): 694, 1018, 1435, 1481, 1731, 1843, 2006, 2368, 3494 cm^{-1}; HRMS: m/z calcd for $C_{35}H_{36}O_7 \cdot NH_4$ $[M + NH_4]^+$ 586.2805, found 586.2785.

Phenyl 3,4,6-Tri-*O*-benzyl-2-*O*-*p*-toluoyl-β-D-galactopyranosyl Carbonate (2). To a solution of **15** (7.72 g, 13.6 mmol) and triethylamine (12.7 mL, 91.1 mmol) in CH_2Cl_2 (136 mL) was added dropwise phenyl chloroformate (1.81 mL, 14.3 mmol) during 1 h at rt. After stirring for 1 h at the same temperature, the reaction mixture was quenched by adding sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography and recrystallization to afford **2** (7.87 g, 84%) as colorless solid. R_f 0.42 (hexane/$CHCl_3$/acetone, 10/10/1, v/v/v); Mp 111–114 °C; $[\alpha]_D^{20}$ +25.6 (c 1.06, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.43 (3H, s), 3.62–3.76 (3H, m), 3.81 (1H, dd, J = 6.1, 6.1 Hz), 4.07 (1H, brd), 4.44 (1H, d, J = 11.6 Hz), 4.48 (1H, d, J = 11.6 Hz), 4.51 (1H, d, J = 12.2 Hz), 4.64 (1H, d, J = 11.3 Hz), 4.65 (1H, d, J = 12.2 Hz), 5.00 (1H, d, J = 11.3 Hz), 5.69 (1H, d, J = 8.3 Hz, H-1), 5.84 (1H, dd, J = 8.3, 9.8 Hz), 7.00 (2H, d, J = 7.6 Hz, Ar-H), 7.10–7.38 (15H, m, Ar-H), 7.94 (2H, d, J = 8.2 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.66, 67.89, 70.40, 71.89, 72.17, 73.55, 74.60, 74.63, 79.52, 96.66 (C-1), 120.81-129.97, 137.35, 137.64, 138.20, 143.93, 150.73, 152.31, 165.06; IR (KBr) 741, 1103, 1273, 1728, 1774 cm^{-1}; HRMS m/z calcd for $C_{42}H_{40}O_9 \cdot NH_4$ $[M + NH_4]^+$ 706.3016, found 706.3011.

3,4,6-Tri-*O*-benzyl-2-*O*-*p*-toluoyl-D-galactopyranosyl Fluoride (3). To a solution of **15** (100 mg, 0.176 mmol) in CH_2Cl_2 (1.76 mL) was dropwise added (diethylamino)sulfur trifluoride (0.0350 mL, 0.264 mmol) at −35 °C. After stirring for 1 h at the same temperature, the reaction mixture was quenched by adding MeOH and sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford **3** (95.4 mg, 95%, α/β = 60/40), and both anomers were also isolated by preparative TLC (silica gel).

3α: colorless oil; R_f 0.54 (hexane/ethyl acetate, 3/1, v/v); $[\alpha]_D^{26}$ +107.7 (c 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 (3H, s), 3.57–3.66 (2H, m), 4.05–4.12 (2H, m), 4.13–4.20 (1H, m), 4.40 (1H, d, J = 11.6 Hz), 4.50 (1H, d, J = 11.6 Hz), 4.59 (1H, d, J = 11.3 Hz), 4.66 (1H, d, J = 12.2 Hz), 4.70 (1H, d, J = 12.2 Hz), 4.97 (1H, d, J = 11.3 Hz), 5.61 (1H, brdd, J = 10.1, 24.4 Hz), 5.86 (1H, brd, J = 54.3 Hz), 7.20–7.37 (17H, m, Ar-H), 7.94 (2H, d, J = 8.2 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.67, 68.13, 70.61 (d, J = 23.8, C-2), 71.90, 72.44, 73.54, 73.66, 74.84, 75.81, 105.19 (d, J = 225.5 Hz, C-1), (126.78–129.90, 137.62, 137.73, 138.12, 144.02) (C-Ar), 165.89; IR (neat) 748, 1119, 1272, 1728, 2869, 2923 cm^{-1}; HRMS m/z calcd for $C_{35}H_{35}FO_6 \cdot NH_4$ $[M + NH_4]^+$ 588.2761, found 588.2745.

3β: colorless solid; R_f 0.37 (hexane/ethyl acetate, 3/1, v/v); Mp 84–85 °C; $[\alpha]_D^{26}$ +53.3 (c 1.05, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 (3H, s), 3.65–3.81 (4H, m), 4.01 (1H, brs), 4.44 (1H, d, J = 11.7 Hz), 4.50 (1H, d, J = 11.7 Hz), 4.53 (1H, d, J = 12.9 Hz), 4.61 (1H, d, J = 11.5 Hz), 4.64 (1H, d, J = 12.9 Hz), 4.94 (1H, d, J = 11.5 Hz), 5.27 (1H, dd, J = 6.6, 52.9 Hz, H-1), 5.66–5.76 (1H, m), 7.15–7.36 (17H, m, Ar-H), 7.91 (2H, d, J = 6.8 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.69, 68.42, 71.40 (d, J = 24.8 Hz, C-2), 71.97 × 2, 73.63, 74.08 (d, J = 5.0 Hz), 74.33, 78.27 (d, J = 8.3 Hz, C-3), 107.58 (d, J = 217.5 Hz, C-1), 126.85–129.92, 137.39, 137.66, 138.07, 143.99, 165.20; IR (KBr) 741, 1126, 1257, 1728 cm^{-1}; HRMS m/z calcd for $C_{35}H_{35}FO_6 \cdot NH_4$ $[M + NH_4]^+$ 588.2761, found 588.2751.

Ethyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(4,5-dichlorophthalimido)-1-thio-β-D-glucopyranoside (18). To a solution of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(4,5-dichlorophthalimido)-β-D-glucopyranoside **17**[30] (10.0 g, 18.3 mmol) and ethanethiol (5.6 mL, 75.3 mmol) in CH_2Cl_2 (50 mL) was added $Et_2O \cdot BF_3$ (2.76 mL, 22.0 mmol) at 0 °C. The reaction mixture was additionally stirred for 3 days at rt, and then the mixture was quenched by adding sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography and recrystallization to afford **18** (8.40 g, 84%) as colorless solid. R_f 0.30 (hexane/ethyl acetate, 2/1, v/v); Mp 118–121 °C; $[\alpha]_D^{20}$ +44.2 (c 1.04, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (3H, t, J = 7.3 Hz), 1.88 (3H, s), 2.05 (3H, s), 2.11 (3H, s), 2.60–2.75 (2H, m), 3.89 (1H, ddd, J = 2.1, 4.9, 10.1 Hz), 4.18 (1H, dd, J = 2.1, 12.2 Hz), 4.31 (1H, dd, J = 4.9, 12.2 Hz), 4.35 (1H,

dd, $J = 10.1$, 10.4 Hz), 5.18 (1H, dd, $J = 9.5$, 10.1 Hz), 5.45 (1H, d, $J = 10.4$ Hz, H-1), 5.77 (1H, dd, $J = 9.5$, 10.1 Hz), 7.94 (1H, s), 7.96 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.84, 20.42, 20.57, 20.72, 24.38, 54.03, 62.20, 68.62, 71.49, 75.91, 80.93 (C-1), 125.78-131.79, 139.35, 139.54, 165.20, 165.80, 169.42, 170.25, 170.72; IR (KBr) 1034, 1227, 1381, 1712, 1743 cm^{-1}; HRMS m/z calcd for $C_{22}H_{23}Cl_2NO_9S \cdot NH_4$ $[M + NH_4]^+$ 565.0814, found 565.0822.

Ethyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-2-(4,5-dichlorophthalimido)-1-thio-β-D-glucopyranoside (19). To a solution of **18** (9.20 g, 16.8 mmol) in MeOH/CH_2Cl_2 (90 mL, 2/1, v/v) was added 28% NaOMe (0.75 mL) in MeOH at 0 °C. After stirring for 1.5 h at the same temperature, the mixture was acidified with *p*-toluenesulfonic acid monohydrate (until ca. pH 5–6). After evaporation, the residue was dried in vacuo. The crude product was used without further purification. To a solution of *p*-toluenesulfonic acid monohydrate (813 mg, 4.27 mmol) in MeCN (200 mL) was added benzaldehyde dimethyl acetal (2.0 mL, 13.3 mmol) at rt. After stirring at the same temperature for 3 h, benzaldehyde dimethyl acetal (2.0 mL, 13.3 mmol) was added. After additional stirring for 5 h, the mixture was quenched by adding triethylamine (2.0 mL). The mixture was concentrated, diluted with CH_2Cl_2, and fliltrated to remove insoluble substrate. After evaporation, the crude product (6.60 g) was obtained by crystallization; it was used without further purification. To a solution of the crude product (4.12 g) and molecular sieves 4A (4.04 g, activated) in DMF (20 mL) was added dropwise benzyl bromide (9.66 mL, 80.8 mmol) at 0 °C. After stirring for 30 min at the same temperature, 55% NaH (707 mg, 17.6 mmol) oil dispersion was added and the reaction mixture was stirred for 30 min. After additional stirring for 1 h at rt, the reaction mixture was quenched by adding H_2O. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography and recrystallization (hexane/ethyl acetate) to afford **19** (3.45 g, 55% from **18**) as white solid. R_f 0.50 (hexane/ethyl acetate, 4/1, v/v); Mp 179–181 °C; $[\alpha]_D^{20}$ +55.5 (c 1.07, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.16 (3H, t, $J = 7.3$ Hz), 2.60–2.73 (2H, m), 3.65–3.72 (1H, m), 3.77–3.86 (2H, m), 4.24 (1H, dd, $J = 9.8$, 10.7 Hz), 4.38–4.44 (2H, m), 4.48 (1H, d, $J = 12.5$ Hz), 4.80 (1H, d, $J = 12.5$ Hz), 5.28 (1H, d, $J = 10.7$ Hz, H-1), 5.63 (1H, s), 6.90–7.05 (5H, m, Ar-H), 7.35–7.44 (3H, m), 7.52 (2H, dd, $J = 1.2$, 7.6 Hz, Ar-H), 7.67 (1H, s, Ar-H), 7.89 (1H, s, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.84, 24.13, 55.04, 68.07, 70.51, 74.30, 75.43, 81.57 (C-1), 82.93, 101.36, 125.43, 125.54, 126.04, 127.45, 128.12, 128.30, 129.07, 130.61, 137.22, 137.85, 138.75, 138.85, 165.68, 165.68; IR (KBr) 748, 1095, 1373, 1720 cm^{-1}; HRMS m/z calcd for $C_{30}H_{27}Cl_2NO_6S \cdot H$ $[M + H]^+$ 600.1014, found 600.1006.

Ethyl 3,6-Di-*O*-benzyl-2-deoxy-2-(4,5-dichlorophthalimido)-1-thio-β-D-glucopyranoside (4). To a solution of **19** (3.62 g, 4.36 mmol) and triethylsilane (3.48 mL, 21.8 mmol) in CH_2Cl_2 (45 mL) was added dropwise trifluoroacetic acid (1.68 mL, 21.8 mmol) during 15 min at 0 °C. After stirring for 4.5 h at rt, the mixture was quenched by adding sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography and recrystallization (hexane/ethyl acetate) to afford **4** (2.15 g, 82%) as colorless solid. R_f 0.11 (hexane/$CHCl_3$/acetone, 10/10/1, v/v/v); Mp 98–99.5 °C; $[\alpha]_D^{22}$ +38.0 (c 1.01, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.15 (3H, t, $J = 7.3$ Hz), 2.52–2.68 (2H, m), 3.60–3.89 (4H, m), 4.11–4.23 (2H, m), 4.50 (1H, d, $J = 12.2$ Hz), 4.58 (1H, d, $J = 11.9$ Hz), 4.63 (1H, d, $J = 11.9$ Hz), 4.78 (1H, d, $J = 12.2$ Hz), 5.21 (1H, d, $J = 10.1$ Hz, H-1), 6.90–7.06 (5H, m, Ar-H), 7.25–7.41 (5H, m, Ar-H), 7.68 (1H, s), 7.84 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$); δ 14.84, 23.96, 54.71, 70.79, 73.78, 74.59 × 2, 77.54, 79.53, 80.89 (C-1), 125.34–138.72, 165.47, 165.91; IR (KBr) 741, 1056, 1095, 1134, 1373, 1712, 2861, 2923 cm^{-1}; HRMS m/z calcd for $C_{30}H_{29}Cl_2NO_6S \cdot NH_4$ $[M + NH_4]^+$ 619.1436, found 619.1445.

Phenyl 2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-galactopyranoside (6). To a solution of 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranose **20**[31] (793 mg, 2.07 mmol) in CH_2Cl_2/DMF (21 mL, 20/1, v/v) was added thionyl chloride (0.230 mL, 3.12 mmol) at 0 °C. After stirring for 12 h at rt, the mixture was quenched by adding sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was roughly purified by silica gel column chromatography (R_f 0.38, hexane/ethyl acetate, 3/1, v/v) and crystallization (hexane/ethyl acetate). The crude product (572 mg) was used without further purification. To a solution of 55% NaH (84.7 mg, 1.94 mmol) oil dispersion in THF (13 mL) was added dropwise benzenethiol (0.200 mL, 1.94 mmol) at 0 °C. After stirring for 30 min at rt, the crude product (520 mg) was added at 0 °C. After stirring for 3 h at rt, the mixture was filtered through a pad of celite. After evaporation, the residue was purified by silica gel column chromatography to afford **6** (611 mg, 71%) as colorless solid. R_f 0.20 (hexane/ethyl acetate, 3/1, v/v); Mp 122–124 °C; $[\alpha]_D^{23}$ −32.0 (c 0.98, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.38 (1H, brs), 3.44 (1H, dd, $J = 3.4$, 9.8 Hz), 3.79 (1H, dd, $J = 9.8$, 9.8 Hz), 3.97 (1H, brd, $J = 12.2$ Hz), 4.08 (1H, brd, $J = 3.4$ Hz), 4.33–4.40 (2H, m, include H-1), 4.70 (2H, s), 5.44 (1H, s), 7.20–7.75 (15H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 59.80, 69.34, 69.86, 71.62, 72.14, 79.57, 85.22 (C-1), 101.16, 126.45–137.61; IR (KBr); 694, 748, 995, 1095, 1280, 2114 cm^{-1}; HRMS m/z calcd for $C_{26}H_{25}N_3O_4S \cdot H$ $[M + H]^+$ 476.1644, found 476.1658.

***O*-(2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-D-galactopyranosyl)-*N*-(benzyloxycarbonyl)-L-serine Benzyl Ester (21).** To a stirred suspension of trityl chloride (1.70 mg, 6.00 μmol) and MS 5A (90.0 mg, activated) in toluene (1.00 mL) was added AgOTf (1.50 mg, 6.00 μmol) at rt. After stirring for 30 min at the same temperature, thioglycoside **6** (14.3 mg, 30.0 μmol), L-serine **7** (14.8 mg, 45.0 μmol) and NIS (10.1 mg, 45.0 μmol) were added at −35 °C. After additional stirring for 1.5 h at the same temperature, the reaction mixture was quenched by adding sat. aq. $NaHCO_3$ and 10% aq. $Na_2S_2O_3$. The mixture was filtered through a pad of celite. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford **21α** (16.9 mg, 81%) as colorless solid and **21β** (3.40 mg, 16%) as colorless solid. The α/β ratios were determined by isolations of both stereoisomers.

21α: R_f 0.32 (hexane/ethyl acetate, 2/1, v/v); Mp 123–125 °C; $[\alpha]_D^{24}$ +101.5 (c 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.44 (1H, brs), 3.78–4.00 (4H, m), 4.06–4.21 (3H, m), 4.57 (1H, brd), 4.67 (1H, d, $J = 12.2$ Hz), 4.71 (1H, d, $J = 12.2$ Hz), 4.88 (1H, brs, H-1), 5.10 (1H, d, $J = 12.2$ Hz), 5.13 (1H, d, $J = 12.2$ Hz), 5.17 (1H, d, $J = 12.5$ Hz), 5.21 (1H, d, $J = 12.5$ Hz), 5.40

(1H, s), 5.86 (1H, d, $J = 8.1$ Hz), 7.20–7.55 (20H, m, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.66, 58.54, 63.28, 67.14, 67.72, 69.12, 69.98, 71.18, 72.70, 74.09, 99.95 (C-1), 100.78, 126.11–128.99, 135.08, 136.11, 137.47, 137.76, 155.90, 169.73; IR (KBr) 694, 741, 1057, 1281, 1543, 1689, 1736, 2106 cm^{-1}; HRMS m/z calcd for $C_{38}H_{38}N_4O_9 \cdot H$ $[M + H]^+$ 695.2717, found 695.2733.

21β: R_f 0.12 (hexane/ethyl acetate, 2/1, v/v); Mp 119–121 °C; $[\alpha]_D^{23}$ +13.8 (*c* 0.72, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.13 (1H, brs), 3.30 (1H, dd, $J = 2.8$, 10.1 Hz), 3.80 (1H, dd, $J = 8.4$, 9.2 Hz), 3.89 (1H, dd, $J = 2.4$, 10.1 Hz), 3.94 (1H, brd), 4.03 (1H, brd), 4.18 (1H, d, $J = 8.4$ Hz, H-1), 4.23 (1H, brd), 4.40 (1H, brd), 4.58 (1H, brd), 4.72 (2H, s), 5.11 (1H, d, $J =$ 11.9 Hz), 5.14 (1H, d, $J = 11.9$ Hz), 5.18 (1H, d, $J = 12.2$ Hz), 5.22 (1H, d, $J = 12.2$ Hz), 5.46 (1H, s), 5.89 (1H, d, $J = 7.9$ Hz), 7.20–7.56 (20H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 54.42, 61.86, 66.52, 66.92, 67.48, 68.87, 69.49, 71.45, 72.20, 77.53, 101.02, 102.38 (C-1), 126.26–128.99, 135.24, 136.33, 137.55, 137.57, 156.01, 169.49; IR (KBr) 694, 741, 1065, 1697, 1728, 2114 cm^{-1}; HRMS m/z calcd for $C_{38}H_{38}N_4O_9 \cdot H$ $[M + H]^+$ 695.2717, found 695.2711.

***O*-(2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-galactopyranosyl)-*N*-(benzyloxycarbonyl)-L-threonine Benzyl Ester (23).** To a stirred suspension of trityl chloride (1.70 mg, 6.00 μmol) and MS 5A (90.0 mg, activated) in toluene (1.00 mL) was added AgOTf (1.50 mg, 6.00 μmol) at rt. After stirring for 30 min at the same temperature, thioglycoside **6** (14.3 mg, 30.0 μmol), L-threonine **22** (15.5 mg, 45.0 μmol) and NIS (10.1 mg, 45.0 μmol) were added at −35 °C. After stirring for 5 h at the same temperature and for 30 min at −20 °C, the reaction mixture was quenched by adding sat. aq. $NaHCO_3$ and 10% aq. $Na_2S_2O_3$. The mixture was filtered through a pad of celite. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford a single α-isomer **23** (17.5 mg, 82%) as colorless amorphous material. $[\alpha]_D^{25}$ +106.0 (*c* 1.11, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (3H, d, $J = 6.4$ Hz), 3.52 (1H, brs), 3.80–3.89 (2H, m), 3.96 (1H, brd), 4.13 (1H, brs), 4.17 (1H, brd), 4.38–4.45 (2H, m), 4.68 (1H, d, $J = 11.9$ Hz), 4.73 (1H, d, $J = 11.9$ Hz), 4.90 (1H, d, $J = 3.1$ Hz, H-1), 5.10–5.25 (4H, m), 5.42 (1H, s), 5.64 (1H, d, $J = 9.5$ Hz), 7.20–7.52 (20H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.57, 58.82, 59.02, 63.20, 67.24, 67.69, 69.21, 71.29, 72.76, 74.63, 76.47, 99.27 (C-1), 100.86, 126.13–137.79, 156.77, 170.01; IR (KBr) 1728, 2114 cm^{-1}; HRMS m/z calcd for $C_{39}H_{40}N_4O_9 \cdot H$ $[M + H]^+$ 709.2874, found 709.2853.

***O*-(2-Azido-3,4-di-*O*-benzyl-2-deoxy-α-D-galactopyranosyl)-*N*-(benzyloxycarbonyl)-L-serine Benzyl Ester (5).** To a solution of **21α** (1.01 g, 1.45 mmol) and triethylamine–borane (1/1) (4.29 mL, 29.0 mmol) in CH_2Cl_2 (14.5 mL) was added dropwise $Et_2O \cdot BF_3$ (0.460 mL, 3.63 mmol) during 10 min at 0 °C. After stirring for 1 h at rt, the reaction mixture was quenched by adding sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica-gel column chromatography to afford **5** (612 mg, 61%) as colorless solid. R_f 0.13 (hexane/ethyl acetate, 2/1, v/v); Mp 97–97.5 °C; $[\alpha]_D^{24}$ +79.1 (*c* 1.11, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.46 (1H, dd, $J = 4.6$, 11.0 Hz), 3.60–3.90 (5H, m), 3.94 (1H, dd, $J = 2.4$, 10.7 Hz), 4.16 (1H, dd, $J = 2.9$, 10.7 Hz), 4.54 (1H, d, $J = 11.5$ Hz), 4.58 (1H, m), 4.68 (1H, d, $J = 11.2$ Hz), 4.72 (1H, d, $J = 11.2$ Hz), 4.84 (1H, d, $J = 3.2$ Hz, H-1), 4.87 (1H, d, $J = 11.5$ Hz), 5.11 (2H, s), 5.18 (1H, d, $J = 12.0$ Hz), 5.22 (1H, d, $J = 12.0$ Hz), 5.99 (1H, d, $J = 8.1$ Hz), 7.25–7.50 (20H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ 54.72, 59.62, 62.18, 67.12, 67.67 × 2, 70.09, 71.60, 72.40, 72.94, 74.52, 77.07, 99.72 (C-1), 127.82–137.35, 155.90, 169.87; IR (KBr) 733, 1072, 1134, 1242, 1281, 1535, 1689, 1736, 2106 cm^{-1}; HRMS m/z calcd for $C_{38}H_{40}N_4O_9 \cdot Na$ $[M + Na]^+$ 719.2693, found 719.2710.

Ethyl 3,6-Di-*O*-benzyl-4-*O*-(3′,4′,6′-tri-*O*-benzyl-2′-*O*-*p*-toluoyl-β-D-galactopyranosyl)-2-deoxy-2-(4,5-dichlorophthalimido)-1-thio-β-D-glucopyranoside (24). This compound was synthesized from glycosyl donor **2** and glycosyl acceptor **4** as colorless solid (see experimental: compound **25**). R_f 0.32 (hexane/$CHCl_3$/acetone, 10/10/1, v/v/v); $[\alpha]_D^{21}$ +26.1 (*c* 0.91, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.10 (3H, t, $J = 7.4$ Hz), 2.44 (3H, s), 2.46–2.61 (2H, m), 3.37 (1H, dd, $J = 1.8$, 9.8 Hz), 3.45–3.55 (5H, m), 3.64 (1H, dd, $J = 3.7$, 11.0 Hz), 3.97–4.02 (2H, m), 4.11–4.24 (2H, m), 4.28–4.49 (5H, m), 4.53 (1H, d, $J = 11.6$ Hz), 4.59–4.65 (3H, m, include H-1′), 4.88 (1H, d, $J = 12.5$ Hz), 4.96 (1H, d, $J = 11.6$ Hz), 5.06 (1H, d, $J = 10.1$ Hz, H-1), 5.62 (1H, dd, $J = 7.9$, 10.4 Hz), 6.83–6.90 (3H, m, Ar-H), 6.97 (2H, dd, $J = 1.7$, 7.6 Hz, Ar-H), 7.14–7.37 (22H, m, Ar-H), 7.66 (1H, s), 7.81 (1H, s), 7.87 (2H, d, $J = 8.2$, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.85, 21.68, 23.93, 55.15, 67.92, 68.19, 71.05, 72.25, 72.58, 73.25, 73.34, 73.46, 74.39, 74.90, 77.54, 78.12, 78.93, 79.70, 80.76 (C-1), 100.83 (C-1′), 125.34–143.80, 165.10, 165.51, 165.74; IR (KBr) 741, 1095, 1265, 1373, 1720 cm^{-1}; HRMS m/z calcd for $C_{65}H_{63}Cl_2NO_{12}S \cdot NH_4$ $[M + NH_4]^+$ 1169.3792, found 1169.3815.

***O*-[2-Azido-3,4-di-*O*-benzyl-6-*O*-{3′,6′-di-*O*-benzyl-2′-deoxy-2′-(4,5-dichlorophthalimido)-4′-*O*-(3″,4″,6″-tri-*O*-benzyl-2″-*O*-*p*-toluoyl-β-D-galactopyranosyl)-β-D-glucopyranosyl}-2-deoxy-α-D-galactopyranosyl]-*N*-(benzyloxycarbonyl)-L-serine Benzyl Ester (25).** Condition A: To a stirred suspension of MS 5A (150 mg, activated), **2** (37.2 mg, 54.0 μmol), and glycosyl acceptor **4** (18.1 mg, 30.0 μmol) in BTF (2.5 mL) was added $TrB(C_6F_5)_4$ (8.30 mg, 9.0 μmol) at −15 °C. After stirring for 5 h at the same temperature, the completion of the first glycosylation reaction was monitored by TLC, CH_2Cl_2 (0.6 mL), **5** (105 mg, 0.150 mmol), and NIS (13.5 mg, 60.0 μmol) were successively added at −35 °C. The reaction mixture was stirred for an additional 2 h at the same temperature; then the reaction mixture was quenched by adding sat. aq. $NaHCO_3$ and 10% aq. $Na_2S_2O_3$. The mixture was filtered through a pad of celite. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford **25** (42.9 mg, 80%) as colorless solid.

Condition B: To a stirred suspension of MS 5A (90 mg, activated), **3** (20.5 mg, 36.0 μmol), and glycosyl acceptor **4** (18.1 mg, 30.0 μmol) in CH_2Cl_2 (1.0 mL) was added a solution of TfOH (0.90 mg, 6.0 μmol) in toluene (0.100 mL) at −20 °C. After stirring for 1 h at the same temperature, the completion of the first glycosylation reaction was monitored by TLC, CH_2Cl_2 (0.6 mL), **5** (31.4 mg, 45.0 μmol), and NIS (13.5 mg, 60.0 μmol) were successively added at −35 °C. The reaction mixture was stirred for an additional 1 h at the same temperature; then the reaction mixture was quenched by adding sat. aq. $NaHCO_3$ and 10% aq. $Na_2S_2O_3$. The mixture was filtered through a pad of celite. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over

Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford **25** (47.6 mg, 89%) as colorless solid. R_f 0.34 (hexane/ethyl acetate, 2/1, v/v); $[\alpha]_D^{24}$ +37.7 (*c* 1.01, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$); δ 2.44 (3H, s), 3.23 (1H, brd), 3.35–3.69 (12H, m), 3.71–3.80 (2H, m), 3.97 (1H, brd), 4.02 (1H, dd, $J = 8.5$, 9.8 Hz), 4.05–4.20 (3H, m), 4.30 (1H, d, $J = 11.9$ Hz), 4.33–4.64 (12H, m), 4.66 (1H, d, $J = 11.3$ Hz), 4.86 (1H, d, $J = 12.5$ Hz), 4.92–5.15 (6H, m, including H-1′), 5.62 (1H, dd, $J = 8.0$, 10.1 Hz), 5.83 (1H, d, $J = 8.6$ Hz), 6.82–6.94 (5H, m, Ar-H), 7.14–7.40 (42H, m, Ar-H), 7.66 (1H, s), 7.76 (1H, s), 7.84 (2H, d, $J = 8.3$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$); δ 21.68, 54.29, 55.98, 59.20, 66.86, 66.96, 67.28 × 2, 67.50, 68.03, 69.30, 69.53, 71.19, 71.71, 72.08, 72.39, 73.17, 73.22, 73.40, 74.35 × 2, 74.54, 74.74, 76.52, 76.88, 77.32, 79.47, (97.75, 99.22, 100.62) (anomeric positions), 125.07–130.65, 135.01–138.84, 143.82, 155.89, 164.99, 165.59, 165.88, 169.52; IR (KBr) 702, 741, 1057, 1095, 1265, 1381, 1720, 2106 cm^{-1}; HRMS *m/z* calcd for $C_{101}H_{97}Cl_2N_5O_{21}\cdot NH_4$ $[M + NH_4]^+$ 1803.6397, found 1803.6447.

***O*-[2-Acetamido-3,4-di-*O*-benzyl-6-*O*-{3′,6′-di-*O*-benzyl-2′-deoxy-2′-(4,5-dichlorophthalimido)-4′-*O*-(3″,4″,6″-tri-*O*-benzyl-2″-*O*-*p*-toluoyl-β-D-galactopyranosyl)-β-D-glucopyranosyl}-2-deoxy-α-D-galactopyranosyl]-*N*-(benzyloxycarbonyl)-L-serine Benzyl Ester (26).** To a solution of **25** (335 mg, 187 mmol) in pyridine (1.5 mL) was added thioacetic acid (1.5 mL, distilled) at 0 °C. After stirring for 7 h at rt, the reaction mixture was diluted with ethyl acetate and 1 M aq. HCl. The aqueous layer was extracted with ethyl acetate and the combined organic layer was washed with 1 M aq. HCl, sat. aq. $NaHCO_3$, H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford **26** (285 mg, 85%) as yellow solid. R_f 0.44 (hexane/ethyl acetate, 1/2, v/v); $[\alpha]_D^{24}$ +35.3 (*c* 0.71, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$); δ 1.80 (3H, s), 2.44 (3H, s), 3.20–3.74 (14H, m), 3.96–4.09 (3H, m), 4.13–4.27 (3H, m), 4.31 (1H, d, $J = 11.6$ Hz), 4.34–4.64 (12H, m), 4.75 (1H, d, $J = 11.6$ Hz), 4.87 (1H, d, $J = 12.8$ Hz), 4.93 (1H, d, $J = 8.5$ Hz, H-1′), 4.96 (1H, d, $J = 11.9$ Hz), 4.99–5.16 (4H, m), 5.18 (1H, d, $J = 7.6$ Hz), 5.62 (1H, dd, $J = 8.5$, 9.5 Hz), 5.69 (1H, d, $J = 8.5$ Hz), 6.82–6.96 (5H, m, Ar-H), 7.10–7.42 (42H, m, Ar-H), 7.63 (1H, s), 7.74 (1H, s), 7.85 (2H, d, $J =$ 7.9 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$); δ 21.64, 23.21, 48.60, 54.71, 56.14, 67.11, 67.26, 67.57, 67.80 × 2, 68.09, 68.40, 69.93, 71.30, 71.34 × 2, 72.04, 72.13, 72.51, 73.24, 73.39, 74.07, 74.34, 74.71, 76.85, 76.92, 77.00, 79.58, (97.77, 98.75, 100.65) (anomeric positions), 125.41–129.83, 134.84, 136.00, 137.69–138.88, 143.78, 165.00, 165.67, 165.80, 169.66, 169.92; IR (KBr) 694, 741, 1057, 1095, 1265, 1381, 1720 cm^{-1}; HRMS *m/z* calcd for $C_{103}H_{101}Cl_2N_3O_{22}\cdot H$ $[M + H]^+$ 1802.6332, found 1802.6310.

***O*-[2-Acetamido-3,4-di-*O*-benzyl-6-*O*-{2′-acetamido-3′,6′-di-*O*-benzyl-4′-*O*-(3″,4″,6″-tri-*O*-benzyl-2″-*O*-*p*-toluoyl-β-D-galactopyranosyl)-2′-deoxy-β-D-glucopyranosyl}-2-deoxy-α-D-galactopyranosyl]-*N*-(benzyloxycarbonyl)-L-serine Benzyl Ester (27).** To a solution of **26** (268 mg, 0.148 mmol) in EtOH (7.4 mL) was added hydrazine acetate (137 mg, 1.48 mmol) at rt. After stirring for 2 h at 70 °C, the reaction mixture was diluted with $CHCl_3$ and water. The aqueous layer was extracted with $CHCl_3$ and the combined organic layer was washed with brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography to afford **27** (199 mg, 82%) as colorless solid. R_f 0.13 (hexane/ethyl acetate, 1/2, v/v); Mp 169–171 °C; $[\alpha]_D^{17}$ +35.3 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.84 (3H, s), 1.93 (3H, s), 2.37 (3H, s), 3.97 (1H, brs), 3.31–4.09 (17H, m), 4.15–4.80 (18H, m), 4.97 (1H, d, $J = 11.5$ Hz), 5.00–5.20 (4H, m), 5.26 (1H, d, $J = 8.3$ Hz), 5.59 (1H, dd, $J = 8.3$, 9.8 Hz), 6.06 (2H, brd), 7.10–7.45 (47H, m, Ar-H), 7.84 (2H, d, $J = 8.3$ Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.70, 23.24, 23.34, 48.85, 52.66, 54.41, 67.14, 67.35, 67.99, 69.08, 70.13, 71.36, 71.69 × 2, 72.12, 72.53, 72.64, 73.22, 73.51 × 2, 73.55 × 2, 73.64, 74.08, 74.71, 74.99, 76.73, 78.74, 79.20, (98.72, 99.45, 100.87) (anomeric positions), 126.89–138.62, 144.39, 155.99, 166.02, 169.87, 170.15; IR (KBr) 694, 741, 1057, 1095, 1265, 1535, 1666, 1728 cm^{-1}; HRMS *m/z* calcd for $C_{97}H_{103}N_3O_{21}\cdot H$ $[M + H]^+$ 1646.7162, found 1646.7141.

***O*-[2-Acetamido-6-*O*-{2′-acetamido-2′-deoxy-4′-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl}-2-deoxy-α-D-galactopyranosyl]-L-serine (1).** To a solution of **27** (51.2 mg, 31.1 μmol) in $THF/CH_2Cl_2/H_2O$ (4 mL, 4/2/1, v/v/v) was added palladium (II) hydroxide (76.7 mg, 20 wt % on carbon). After purging with H_2 (1.01×10^5 Pa) and stirring for 42 h, H_2 was removed. Then the catalyst was filtered off and the mixture was evaporated in vacuo. The crude residue was used without further purification. To a solution of the crude product in MeOH (0.8 mL) was added 0.1 M aq. NaOH (1.6 mL, 0.16 mmol) at 0 °C. After stirring for 2.5 h at the same temperature, an excess amount of Dowex 50WX-8 was added; then the mixture was purified by ion-exchange column chromatography (MeOH, then aq. NH_3) and reversed-phase column chromatography (H_2O) to afford **1** (17.7 mg, 84% from **27**) as colorless solid. R_f 0.06 (CH_3CN/AcOH/H_2O, 3/1/1, v/v/v); $[\alpha]_D^{20} = +54.0$ (*c* 0.1, H_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.82 (3H, s, Ac), 1.83 (3H, s, Ac), 3.33 (1H, dd, $J = 7.9$, 9.8, H-2″), 3.38–3.42 (1H, m, H-5′), 3.45 (1H, dd, $J = 3.4$, 10.1 Hz, H-3″), 3.47–3.59 (7H, m, H-2′, H-3′, H-4′, H-5″, H-6, H-6′, H-6″), 3.63 (1H, dd, $J = 4.9$, 12.2 Hz, H-6′), 3.66–3.73 (3H, m, H-3, H-4″, Ser), 3.74–3.84 (5H, m, H-4, H-5, H-6′), 3.86 (1H, dd, $J = 3.4$, 10.4 Hz, H-6), 3.96 (1H, dd, $J = 3.7$, 11.0 Hz, H-2), 4.26 (1H, d, $J = 7.9$ Hz, H-1″), 4.36 (1H, d, $J = 7.6$ Hz, H-1′), 4.67 (1H, d, $J = 3.7$ Hz, H-1); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7 (CH_3CO), 21.9 (CH_3CO), 49.2 (C-2), 54.1 (Ser $C(NH_2)COOH$), 54.7 (C-2′), 59.7 (C-6′), 60.7 (C-6″), 66.3 (Ser OCH_2), 67.0 (C-3), 68.1 (C-4), 68.2 (C-4″), 69.4 (C-6), 69.6 (C-5), 70.6 (C-2″), 72.0 (C-3′), 72.2 (C-3″), 74.4 (C-5′), 75.0 (C-5″), 78.2 (C-4′), 97.7 (C-1), 101.1 (C-1′), 102.5 (C-1″), 171.4 (*C*OOH), 174.2 (C=O), 174.4 (C=O); FT-IR (KBr) 1049, 1072, 1643 cm^{-1}; HRMS *m/z* calcd for $C_{25}H_{43}N_3O_{18}\cdot H$ $[M + H]^+$ 674.2620, found 674.2626; Anal. calcd for $C_{25}H_{43}N_3O_{18}\cdot 3H_2O$: C, 41.26, H, 6.79; N, 5.77%, found: C, 41.46; H, 7.17; N, 5.97%.

3,4,6-Tri-*O*-benzyl-2-*O*-*p*-toluoyl-β-D-glucopyranosyl Fluoride (31). To a solution of 3,4,6-tri-*O*-benzyl-2-*O*-*p*-toluoyl-β-D-glucopyranose[23] (13.8 g, 24.2 mmol) in CH_2Cl_2 (100 mL) was added dropwise (diethylamino)sulfur trifluoride (3.84 mL, 29.1 mmol) at −35 °C. After stirring for 1 h at the same temperature, the reaction mixture was quenched by adding MeOH and sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography and crystallization to afford **31** (6.04 g, 44%, 1st crop) as colorless solid. R_f 0.45 (hexane/ethyl acetate, 3/1, v/v), Mp 84–85 °C; $[\alpha]_D^{15}$ +68.0 (*c* 0.71, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 (3H, s), 3.71–3.86 (4H, m), 3.94 (1H, dd, $J = 8.5$, 8.5 Hz), 4.52–4.81 (6H, m), 5.33–5.52 (2H, m, including anomeric posi-

tion), 7.10–7.38 (17H, m, Ar-H), 7.91 (2H, d, $J = 8.1$ Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.67, 68.47, 72.77 (d, $J = 28.9$ Hz), 73.52, 74.18, 74.80, 74.92, 76.47, 81.39 (d, $J = 7.4$ Hz), 106.74 (d, $J = 218.33$ Hz, anomeric position), 126.42–129.85, 137.42, 137.63, 137.77, 144.22, 165.04; IR (KBr) 748, 1111, 1712 cm^{-1}; HRMS m/z calcd for $C_{35}H_{35}FO_6 \cdot Na$ $[M + Na]^+$ 593.2315, found 593.2339.

Ethyl 2,3,4-Tri-*O*-benzoyl-1-thio-α-D-glucopyranoside (33b). To a solution of ethyl 1-thio-α-D-glucopyranoside (2.00 g, 8.92 mmol) and 4-dimethylaminopyridine (327 mg, 2.68 mmol) in pyridine/DMF (25 mL, 5/1, v/v) was added *t*-butyldiphenylsilyl chloride (2.55 mL, 9.81 mmol) at rt; the reaction mixture was stirred for 1.5 h at the same temperature. After additional stirring for 1 h at 60 °C, the completion of the first reaction was monitored by TLC; benzoyl chloride (3.60 mL, 31.2 mmol) was successively added at 0 °C. After stirring for 3 h at rt, the reaction mixture was quenched by adding sat. aq. $NaHCO_3$. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with 0.1 M aq. NaOH, 0.1 M aq. HCl, H_2O, and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was dried in vacuo. The crude product was used without further purification. To a solution of the crude product in THF (12.5 mL) were added acetic acid (1.43 mL) and tetrabutylammonium fluoride (12.5 mL, 1 M in THF) at rt. After stirring for 38 h at the same temperature, the reaction mixture was diluted with Et_2O. The organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography to afford **33b** (3.30 g, 69%, 3 steps) as colorless solid. R_f 0.12 (hexane/ethyl acetate, 3/1, v/v); Mp 114–115 °C; $[\alpha]_D^{14}$ +87.5 (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (3H, t, $J = 7.3$ Hz), 2.55–2.67 (2H, m), 3.77 (1H, dd, $J = 3.3$, 12.8 Hz), 3.83 (1H, dd, $J = 2.1$, 12.8 Hz), 4.49 (1H, ddd, $J = 2.1$, 3.3, 10.1 Hz), 5.48–5.56 (2H, m), 5.97 (1H, d, $J = 5.8$ Hz, anomeric position), 6.13 (1H, dd, $J = 9.8$, 9.8 Hz), 7.25–7.55 (9H, m, Ar-H), 7.86–8.01 (6H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.59, 24.30, 60.99, 69.49, 70.20, 70.62, 71.62, 82.09 (anomeric position), 128.23–129.92, 133.12, 133.37, 133.65, 165.33, 165.58, 166.35; IR (KBr) 702, 1018, 1126, 1157, 1311, 1736 cm^{-1}; HRMS m/z calcd for $C_{29}H_{28}O_8S \cdot H$ $[M + H]^+$ 537.1583, found 537.1573.

Ethyl 2,3,4-Tri-*O*-*p*-chlorobenzoyl-1-thio-α-D-glucopyranoside (33c). This compound was synthesized as colorless solid according to the above-mentioned procedure (see experimental: compound **33b**). R_f 0.38 (hexane/ethyl acetate, 2/1, v/v), Mp 135–136 °C; $[\alpha]_D^{15}$ +66.1 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (3H, t, $J = 7.3$ Hz), 2.43–2.70 (2H, m), 3.75 (1H, dd, $J = 2.9$, 12.9 Hz), 3.83 (1H, brd), 4.47 (1H, brd), 5.44–5.54 (2H, m), 5.92 (1H, d, $J = 5.9$ Hz, anomeric position), 6.04 (1H, dd, $J = 9.8$, 10.0 Hz), 7.26–7.41 (6H, m, Ar-H), 7.78–7.94 (6H, m, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.62, 24.38, 60.92, 69.50, 70.01, 70.92, 71.56, 81.96 (anomeric position), 126.74–131.31, 139.95, 140.13, 140.43, 164.45, 164.78, 165.39; IR (KBr) 764, 1095, 1273, 1713, 1728, 2947 cm^{-1}; HRMS m/z calcd for $C_{29}H_{25}Cl_3O_8S \cdot H$ $[M + H]^+$ 639.0414, found 639.0395.

Ethyl 1-Thio-2,3,4-tri-*O*-*p*-(trifluoromethyl)benzoyl-α-D-glucopyranoside (33d). This compound was synthesized as colorless solid according to the above-mentioned procedure (see experimental: compound **33b**). R_f 0.40 (hexane/ethyl acetate, 2/1, v/v); $[\alpha]_D^{14}$ +67.5 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (3H, t, $J = 7.3$ Hz), 2.57–2.72 (2H, m), 3.78 (1H, dd, $J = 3.4$, 12.9 Hz), 3.87 (1H, brd), 4.54 (1H, brd), 5.55 (1H, dd, $J = 5.6$, 9.8 Hz), 5.62 (1H, dd, $J = 9.8$, 10.0 Hz), 5.96 (1H, d, $J = 5.6$ Hz, anomeric position), 6.11 (1H, dd, $J = 9.8$, 9.8 Hz), 7.55–7.71 (6H, m, Ar-H), 8.00 (2H, d, $J = 8.0$ Hz, Ar-H), 8.06–8.14 (4H, m, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, major signals) δ 14.67, 24.51, 60.97, 69.71, 70.00, 71.42, 71.85, 81.92 (anomeric position), 119.10–135.46, 164.16, 164.55, 164.95; IR (KBr) 694, 771, 856, 1118, 1265, 1327, 1736, 2954 cm^{-1}; HRMS m/z calcd for $C_{32}H_{25}F_9O_8S \cdot Na$ $[M + Na]^+$ 763.1024, found 763.1008.

Ethyl 2-*O*-Benzoyl-4-*O*-benzyl-3-*O*-chloroacetyl-1-thio-α-D-glucopyranoside (39). To a solution of ethyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-chloroacetyl-1-thio-α-D-glucopyranoside **38**[44] (3.63 g, 7.36 mmol) and triethylamine–borane (1/1) (11.6 mL, 73.6 mmol) in CH_2Cl_2 (14.5 mL) was added dropwise a solution of $AlCl_3$[46] (1.96 g, 14.7 mmol) in Et_2O at 0 °C. After stirring for 30 min at rt, the reaction mixture was quenched by adding sat. aq. $NaHCO_3$. The mixture was filtered with a pad of celite. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography and recrystallization (hexane/ethyl acetate) to afford **39** (2.07 g, 57%, 1st crop) as colorless solid. R_f 0.16 (hexane/ethyl acetate, 3/1, v/v); Mp 102–104 °C; $[\alpha]_D^{16}$ +158.8 (*c* 0.38, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (3H, t, $J = 7.3$ Hz), 2.45–2.61 (2H, m), 3.67 (1H, d, $J = 14.6$ Hz), 3.76 (1H, d, $J = 14.6$ Hz), 3.85 (1H, dd, $J = 9.8$, 9.8 Hz), 3.89 (2H, brs), 4.24 (1H, ddd, $J = 2.4$, 2.7, 9.8 Hz), 4.64 (1H, d, $J = 11.5$ Hz), 4.74 (1H, dd, $J = 11.5$ Hz), 5.15 (1H, dd, $J = 5.7$, 10.0 Hz), 5.66 (1H, dd, $J = 9.8$, 10.0 Hz), 5.78 (1H, d, $J = 5.7$ Hz, anomeric position), 7.25–7.61 (8H, m, Ar-H), 7.99 (2H, d, $J = 7.6$ Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.61, 24.26, 40.41, 61.18, 71.12, 71.65, 74.15, 74.69, 75.18, 81.78 (anomeric position), 128.04–137.60, 165.46, 166.37; IR (KBr) 755, 1095, 1273, 1728, 2815, 2985 cm^{-1}; HRMS m/z calcd for $C_{24}H_{27}ClO_7S \cdot H$ $[M + H]^+$ 495.1244, found 495.1239.

Ethyl 2-*O*-Benzoyl-4-*O*-benzyl-1-thio-α-D-glucopyranoside (32). To a solution of **39** (30.0 mg, 60.6 μmol) in DMF (0.6 mL) was added thiourea (9.20 mg, 0.12 mmol). After stirring for 3 h at 70 °C, the reaction mixture was diluted with Et_2O and H_2O. The aqueous layer was extracted with Et_2O and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography and crystallization (hexane/ethyl acetate) to afford **32** (10.8 mg, 43%) as colorless solid. R_f 0.28 (hexane/ethyl acetate, 2/1, v/v); Mp 117–119 °C; $[\alpha]_D^{16}$ +164.1 (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (3H, t, $J = 7.3$ Hz), 2.47–2.59 (2H, m), 3.63 (1H, dd, $J = 9.5$, 9.8 Hz), 3.84 (1H, dd, $J = 3.4$, 11.9 Hz), 3.87 (1H, dd, $J = 2.8$, 11.9 Hz), 4.15 (1H, ddd, $J = 2.8$, 3.4, 9.8 Hz), 4.19 (1H, dd, $J = 9.5$, 9.5 Hz), 4.79 (1H, d, $J = 11.6$ Hz), 4.88 (1H, d, $J = 11.6$ Hz), 5.11 (1H, dd, $J = 5.8$, 9.5 Hz), 5.70 (1H, d, $J = 5.8$ Hz, anomeric position), 7.26–7.60 (8H, m, Ar-H), 8.07 (2H, d, $J = 8.5$ Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.70, 24.29, 61.64, 70.86, 72.60, 73.60, 74.80, 77.44, 81.86 (anomeric position), 127.99–138.01, 165.96; IR (KBr) 702, 1103, 1265, 1728, 3294 cm^{-1}; HRMS m/z calcd for $C_{22}H_{26}O_6S \cdot Na$ $[M + Na]^+$ 441.1348, found 441.1349.

Ethyl 2-*O*-Benzoyl-4-*O*-benzyl-6-*O*-*t*-butyldiphenylsilyl-1-thio-α-D-glucopyranoside (35). To a solution of **32** (1.50 g, 3.58 mmol) and imidazole (730 mg, 10.7 mmol) in DMF (7.2 mL) was added *t*-butyldiphenylsilyl chloride (2.55 mL, 9.81 mmol) at rt. After stirring for 3 h at the same temperature, the re-

action mixture was diluted with Et_2O and H_2O. The aqueous layer was extracted with Et_2O and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography to afford **35** (2.35 g, quant.) as colorless oil. R_f 0.55 (hexane/ethyl acetate, 3/1, v/v); $[\alpha]_D^{16}$ +86.1 (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (9H, s), 1.18 (3H, t, $J = 7.3$ Hz), 2.42–2.58 (2H, m), 3.71 (1H, dd, $J = 9.2$, 9.8 Hz), 3.92 (1H, brd), 3.98 (1H, dd, $J = 4.0$, 11.3 Hz), 4.15–4.24 (2H, m), 4.73 (1H, d, $J = 11.3$ Hz), 4.85 (1H, d, $J = 11.3$ Hz), 5.16 (1H, dd, $J = 5.8$, 9.8 Hz), 5.74 (1H, d, $J = 5.8$ Hz, anomeric position), 7.45–7.76 (18H, m, Ar-H), 8.07 (2H, d, $J = 8.2$ Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.58, 19.27, 23.92, 26.52, 26.78 × 2, 62.79, 71.53, 72.89, 73.79, 74.90, 78.13, 81.29 (anomeric position), 127.55–138.18, 165.97; IR (KBr) 501, 609, 702, 818, 1103, 1265, 1458, 1712, 2931, 3054, 3509 cm^{-1}; HRMS *m/z* calcd for $C_{38}H_{44}O_6SSi \cdot Na$ $[M + Na]^+$ 679.2526, found 679.2521.

Methyl 2,3,4-Tri-*O*-benzoyl-6-*O*-[2-*O*-benzoyl-4-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-*p*-toluoyl-β-D-glucopyranosyl)-6-*O*-*t*-butyldiphenylsilyl-β-D-glucopyranosyl]-α-D-glucopyranoside (40). To a stirred suspension of MS 5A (150 mg, activated), glucosyl fluoride **31** (31.4 mg, 55.0 μmol), and thioglucoside **35** (32.8 mg, 50.0 μmol) in CH_2Cl_2 (1.5 mL) was added the solution of TfOH (1.50 mg, 10.0 μmol) in toluene (0.100 mL) at 0 °C. After stirring for 30 min at the same temperature, the completion of the first glycosylation reaction was monitored by TLC; methyl glucoside **36** (30.4 mg, 60.0 μmol) and NIS (13.5 mg, 60.0 μmol) re successively added at −20 °C. The reaction mixture was stirred for an additional 30 min at the same temperature. Then the reaction mixture was quenched by adding sat. aq. $NaHCO_3$ and 10% aq. $Na_2S_2O_3$. The mixture was filtered through a pad of celite. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford **40** (70.7 mg, 86%) as colorless solid. R_f 0.46 (hexane/$CHCl_3$/acetone, 10/10/1, v/v/v); $[\alpha]_D^{17}$ +55.5 (*c* 1.23, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (9H, s), 2.44 (3H, s), 2.98 (3H, s), 3.37 (1H, brd), 3.46–3.60 (4H, m), 3.67 (1H, brd), 3.72 (1H, brd), 3.78–3.89 (3H, m), 4.02 (1H, d, $J = 11.5$ Hz), 4.08–4.16 (1H, m), 4.31 (1H, dd, $J = 9.0$, 9.0 Hz), 4.37–4.62 (7H, m), 4.74 (1H, d, $J = 10.7$ Hz), 4.83–4.89 (2H, m, anomeric positions), 5.01 (1H, dd, $J = 2.4$, 10.0 Hz), 5.10–5.30 (4H, m), 6.02 (1H, dd, $J = 7.6$, 9.8 Hz), 6.99–7.66 (44H, m, Ar-H), 7.72 (2H, d, $J = 8.1$ Hz, Ar-H), 7.76 (2H, d, $J = 7.1$ Hz, Ar-H), 7.84 (2H, d, $J = 7.1$ Hz, Ar-H), 7.93 (2H, d, $J = 7.1$ Hz, Ar-H), 8.06 (2H, d, $J = 7.3$ Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.07, 21.71, 26.64 × 2, 54.81, 62.63, 68.24, 68.52, 69.14, 69.46, 70.39, 71.97, 73.48 × 2, 73.79, 74.33, 75.01, 75.14 × 2, 75.58, 75.83, 76.03, 78.07, 79.19, 83.06, (96.22, 100.23, 101.50) (anomeric positions), 126.97–143.46, 164.38, 165.17, 165.49, 165.61, 165.64; IR (KBr) 702, 756, 1100, 1265, 1728 cm^{-1}; HRMS *m/z* calcd for $C_{99}H_{98}O_{21}Si \cdot NH_4$ $[M + NH_4]^+$ 1668.6714, found 1668.6680.

Methyl 2,3,4-Tri-*O*-benzoyl-6-*O*-[2-*O*-benzoyl-4-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-*p*-toluoyl-β-D-glucopyranosyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (34). To a solution of the trisaccharide **40** (70.7 mg, 42.8 μmol) in THF (1.0 mL) were added acetic acid (0.049 mL) and tetrabutylammonium fluoride (0.43 mL, 1 M in THF) at rt; the reaction mixture was stirred for 59 h at the same temperature. After stirring for 9 h at 50 °C, the reaction mixture was diluted with Et_2O. The organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by silica gel column chromatography to afford **34** (56.0 mg, 93%) as colorless solid. R_f 0.50 (hexane/ethyl acetate, 1/1, v/v); $[\alpha]_D^{15}$ +56.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.44 (3H, s), 3.10 (3H, s), 3.36 (2H, brd), 3.46–3.64 (5H, m), 3.67 (1H, dd, $J = 8.6$, 8.9 Hz), 3.75–3.86 (2H, m), 3.94 (1H, d, $J = 10.6$ Hz), 4.04–4.13 (1H, m), 4.24–4.31 (1H, m), 4.43–4.62 (7H, m), 4.74 (1H, d, $J = 10.7$ Hz), 4.81 (1H, d, $J = 7.6$ Hz, anomeric position), 4.92 (1H, brs, anomeric position), 4.99–5.10 (3H, m), 5.24 (1H, dd, $J = 7.6$, 8.2 Hz), 5.34 (1H, dd, $J = 9.8$, 9.8 Hz), 6.01 (1H, dd, $J = 9.5$, 10.1 Hz), 6.99–7.70 (34H, m, Ar-H), 7.74 (2H, d, $J = 6.7$ Hz, Ar-H), 7.78 (2H, d, $J = 7.6$ Hz, Ar-H), 7.86 (2H, d, $J = 7.6$ Hz, Ar-H), 7.92 (2H, d, $J = 7.6$ Hz, Ar-H), 8.05 (2H, d, $J = 7.6$ Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.66, 55.07, 61.92, 67.86, 68.08, 69.02, 70.01, 70.22, 71.90, 73.41, 73.72, 73.78, 74.79, 74.97, 75.00, 75.03, 75.28, 75.49, 75.54, 77.95, 78.76, (96.41, 100.07, 100.57) (anomeric positions), 126.93–143.51, 164.22, 165.28, 165.57, 165.61, 165.66; IR (KBr) 756, 1095, 1265, 1728, 2993 cm^{-1}; HRMS *m/z* calcd for $C_{83}H_{80}O_{21} \cdot NH_4$ $[M + NH_4]^+$ 1430.5536, found 1430.5504.

Ethyl 2-*O*-Benzoyl-4-*O*-benzyl-3,6-bis-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-*p*-toluoyl-β-D-glucopyranosyl)-1-thio-α-D-glucopyranoside (41). To a stirred suspension of MS 5A (150 mg, activated), glucosyl fluoride **31** (59.9 mg, 0.105 mmol), and thioglucoside **32** (20.9 mg, 50.0 μmol) in CH_2Cl_2 (1.5 mL) was added the solution of TfOH (2.25 mg, 15.0 μmol) in toluene (0.100 mL) at −20 °C. After stirring for 1.5 h at the same temperature, the reaction mixture was quenched by adding sat. aq. $NaHCO_3$. The mixture was filtered through a pad of celite. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford **41** (73.4 mg, 97%) as colorless solid. R_f 0.35 (hexane/$CHCl_3$/acetone, 10/10/1, v/v/v); $[\alpha]_D^{16}$ +79.0 (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98 (3H, t, $J = 7.3$ Hz), 2.17–2.31 (2H, m), 2.23 (3H, s), 2.25 (3H, s), 3.40 (1H, dd, $J = 8.5$, 10.1 Hz), 3.49–3.64 (5H, m), 3.67–3.81 (6H, m), 4.13 (1H, brd), 4.22 (1H, brdd), 4.29–4.61 (11H, m), 4.64 (1H, d, $J = 11.0$ Hz), 4.69 (1H, d, $J = 11.0$ Hz), 4.75 (1H, d, $J = 10.7$ Hz), 4.79 (1H, d, $J = 11.0$ Hz), 4.88–4.93 (3H, m), 5.21 (1H, dd, $J = 8.2$, 9.2 Hz), 5.29 (1H, dd, $J = 8.2$, 9.2 Hz), 5.49 (1H, d, $J = 5.8$ Hz, anomeric position), 6.99–7.66 (44H, m, Ar-H), 7.85 (2H, d, $J = 8.2$ Hz, Ar-H), 7.99 (2H, d, $J = 7.3$ Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.29, 21.59, 21.66, 23.46, 68.31, 68.81, 69.94, 69.96, 73.43, 73.48, 73.53, 73.78, 74.50, 74.54, 74.92, 74.99, 75.05 × 2, 75.37, 75.59, 75.96, 77.89, 78.00, 78.05, 80.60 (anomeric position), 82.91, 83.04, (100.99, 101.15) (anomeric positions), 126.78–138.68, 143.41, 143.64, 164.72, 165.10, 165.17; IR (KBr) 702, 741, 1095, 1265, 1728, 2985 cm^{-1}; HRMS *m/z* calcd for $C_{92}H_{94}O_{18} \cdot NH_4$ $[M + NH_4]^+$ 1536.6505, found 1536.6555.

Ethyl 2,3,4-Tri-*O*-benzoyl-6-*O*-[2-*O*-benzoyl-4-*O*-benzyl-3,6-bis-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-*p*-toluoyl-β-D-glucopyranosyl)-β-D-glucopyranosyl]-1-thio-α-D-glucopyranoside (42b). To a stirred suspension of MS 5A (180 mg, activated), glucosyl fluoride **31** (59.9 mg, 105 μmol), and thioglucoside **32** (20.9 mg, 50.0 μmol) in CH_2Cl_2 (1.5 mL) was added the solution of TfOH (2.25 mg, 15.0 μmol) in toluene (0.100 mL) at 0 °C. After stirring for 30 min at the same temperature, the completion of the first glycosylation reaction was monitored by TLC; thioglucoside **33b** (40.2 mg, 75.0 μmol) and NIS (13.5 mg, 60.0 μmol) were

successively added at −60 °C. The reaction mixture was allowed to warm to −50 °C over 1 h and quenched by adding sat. aq. $NaHCO_3$ and 10% aq. $Na_2S_2O_3$. The mixture was filtered through a pad of celite. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford **42b** (50.7 mg, 51%) as colorless solid. R_f 0.24 (hexane/$CHCl_3$/acetone, 10/10/1, v/v/v); $[\alpha]_D^{16}$ +52.5 (*c* 0.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03 (3H, t, $J = 7.3$ Hz), 2.25–2.38 (2H, m), 2.37 (3H, s), 2.44 (3H, s), 3.16–3.23 (2H, m), 3.38–3.58 (6H, m), 3.62 (1H, dd, $J = 9.1$, 9.9 Hz), 3.68–3.82 (5H, m), 3.86 (1H, dd, $J = 9.2$, 9.2 Hz), 4.05 (1H, brd), 4.16 (1H, dd, $J = 8.9$, 8.9 Hz), 4.24 (1H, d, $J = 7.6$ Hz, anomeric position), 4.29 (1H, ddd, $J = 3.1$, 4.0, 10.1 Hz), 4.37–4.82 (15H, m), 4.93 (1H, d, $J = 11.3$ Hz), 5.00 (1H, dd, $J = 7.9$, 8.9 Hz), 5.14–5.26 (4H, m), 5.71 (1H, d, $J = 5.5$ Hz, anomeric position), 5.88 (1H, dd, $J = 9.8$, 10.1 Hz), 6.99–7.61 (51H, m, Ar-H), 7.71–7.75 (4H, m, Ar-H), 7.80 (2H, d, $J = 7.3$ Hz, Ar-H), 7.85 (2H, d, $J = 8.2$ Hz, Ar-H), 7.94 (2H, d, $J = 7.0$ Hz, Ar-H), 8.08 (2H, d, $J = 7.3$ Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.33, 21.63, 21.70, 23.68, 67.08, 68.25, 68.63, 68.69, 69.05, 69.61, 69.78, 70.87, 71.59, 73.43, 73.46, 73.69, 73.88, 74.04, 74.50, 74.86, 74.91, 74.99, 75.10, 75.42, 75.57, 75.94, 77.94, 78.07, 78.67, 81.26 (anomeric position), 82.82, 82.97, (99.92, 100.36, 101.29) (anomeric positions), 127.00–138.36, 143.51, 143.62, 164.19, 164.98, 165.02, 165.19, 165.38, 165.50; IR (KBr) 702, 748, 1095, 1265, 1728 cm^{-1}; HRMS *m/z* calcd for $C_{119}H_{116}O_{26}S \cdot NH_4$ $[M + NH_4]^+$ 2010.7819, found 2010.7762.

Ethyl 6-*O*-[2-*O*-Benzoyl-4-*O*-benzyl-3,6-bis-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-*p*-toluoyl-β-D-glucopyranosyl)-β-D-glucopyranosyl]-2,3,4-tri-*O*-*p*-chlorobenzoyl-1-thio-α-D-glucopyranoside (42c). This compound was synthesized as colorless solid (74.7 mg, 71%) according to the above-mentioned procedure (see experimental: compound **42b**). R_f 0.23 (hexane/$CHCl_3$/acetone, 10/10/1, v/v/v); $[\alpha]_D^{16}$ +51.1 (*c* 0.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (3H, t, $J = 7.3$ Hz), 2.25–2.37 (2H, m), 2.38 (3H, s), 2.44 (3H, s), 3.18–3.30 (2H, m), 3.39–3.82 (12H, m), 3.86 (1H, dd, $J = 9.0$, 9.3 Hz), 4.06 (1H, brd), 4.17 (1H, dd, $J = 8.8$, 8.8 Hz), 4.22–4.83 (17H, m), 4.94 (1H, d, $J = 11.2$ Hz), 5.02 (1H, dd, $J = 8.1$, 9.0 Hz), 5.21–5.37 (4H, m), 5.67 (1H, d, $J = 5.6$ Hz, anomeric), 5.80 (1H, dd, $J = 9.8$, 10.0 Hz), 6.98–8.08 (60H, m, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.28, 21.62, 21.71, 23.64, 66.72, 68.15, 68.57 × 2, 69.04, 69.52, 71.18, 71.47, 73.41 × 2, 73.64, 73.80, 73.89, 74.54, 74.91 × 2, 74.98, 75.00, 75.12, 75.36, 75.50, 75.88, 77.85, 78.02, 78.77, 81.05, 82.75, 82.92, 99.96, 100.29, 101.21, 126.91–143.63, 164.13 × 2, 164.24, 164.63, 164.92, 165.34; IR (KBr) 702, 748, 1088, 1265, 1728 cm^{-1}; HRMS *m/z* calcd for $C_{119}H_{113}Cl_3O_{26}S \cdot NH_4$ $[M + NH_4]^+$ 2112.6650, found 2112.668.

Ethyl 6-*O*-[2-*O*-Benzoyl-4-*O*-benzyl-3,6-bis-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-*p*-toluoyl-β-D-glucopyranosyl)-β-D-glucopyranosyl]-1-thio-2,3,4-tri-*O*-*p*-(trifluoromethyl)benzoyl-α-D-glucopyranoside (42d). This compound was synthesized as colorless solid (84.0 mg, 76%) according to the above-mentioned procedure (see experimental: compound **42b**). R_f 0.28 (hexane/$CHCl_3$/acetone, 10/10/1, v/v/v); $[\alpha]_D^{16}$ +61.7 (*c* 0.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (3H, t, $J = 7.3$ Hz), 2.26–2.41 (2H, m), 2.37 (3H, s), 2.44 (3H, s), 3.24–3.33 (2H, m), 3.41–3.64 (7H, m), 3.68–3.84 (5H, m), 3.86 (1H, dd, $J = 9.2$, 9.2 Hz), 4.06 (1H, d, $J = 10.4$ Hz), 4.18 (1H, dd, $J = 8.5$, 8.6 Hz), 4.30 (1H, d, $J = 7.6$ Hz), 4.31–4.62 (11H, m), 4.65–4.82 (5H, m), 4.94 (1H, d, $J = 11.3$ Hz), 5.04 (1H, dd, $J = 8.2$, 8.5 Hz), 5.18–5.30 (4H, m), 5.71 (1H, d, $J = 5.5$ Hz), 5.87 (1H, dd, $J = 9.8$, 9.8 Hz), 7.00–8.08 (60H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$, major signals) δ 14.29, 21.59, 21.67, 23.75, 66.50, 68.18, 68.59, 69.12, 69.75, 71.63, 71.68, 73.44, 73.69, 73.83, 73.92, 74.55, 74.91, 74.94, 75.00, 75.06, 75.11, 75.35, 75.54, 75.91, 77.87, 78.05, 78.85, 81.00, 82.82, 82.96, 99.99, 100.26, 101.25, 122.32–143.64, 163.85, 163.88, 164.18, 164.34, 164.91, 165.31; IR (KBr) 756, 1088, 1265, 1736 cm^{-1}; HRMS *m/z* calcd for $C_{112}H_{113}F_9O_{26}S \cdot NH_4$ $[M + NH_4]^+$ 2214.7441, found 2214.738.

Methyl 2,3,4-Tri-*O*-benzoyl-6-*O*-{2-*O*-benzoyl-4-*O*-benzyl-6-*O*-[2-*O*-benzoyl-4-*O*-benzyl-3,6-bis-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-*p*-toluoyl-β-D-glucopyranosyl)-β-D-glucopyranosyl]-2,3,4-tri-*O*-*p*-(trifluoromethyl)benzoyl-β-D-glucopyranosyl-β-D-glucopyranosyl}-α-D-glucopyranoside (43). To a stirred suspension of MS 5A (180 mg, activated), glucosyl fluoride **31** (59.9 mg, 105 μmol), and thioglucoside **32** (20.9 mg, 50.0 μmol) in CH_2Cl_2 (1.5 mL) was added the solution of TfOH (2.25 mg, 15.0 μmol) in toluene (0.100 mL) at 0 °C. After stirring for 1.5 h at the same temperature, the completion of the first glycosylation reaction was monitored by TLC; thioglucoside **33d** (55.5 mg, 75.0 μmol) and NIS (13.5 mg, 60.0 μmol) were successively added at −60 °C. The reaction mixture was allowed to warm to −50 °C over 1 h. After the completion of the second glycosylation reaction was monitored by TLC; trisaccharide **44** (212 mg, 150 μmol) and NIS (22.5 mg, 100 μmol) were successively added at the same temperature. The reaction mixture was allowed to warm to −20 °C and stirred for 1 h and then quenched by adding sat. aq. $NaHCO_3$ and 10% aq. $Na_2S_2O_3$. The mixture was filtered through a pad of celite. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After filtration and evaporation, the residue was purified by preparative TLC (silica gel) to afford **43** (84.7 mg, 48%) as colorless solid. R_f 0.50 (hexane/$CHCl_3$/acetone, 10/10/2, v/v/v); $[\alpha]_D^{17}$ +26.5 (*c* 0.56, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.33 (3H, s), 2.39 (3H, s), 2.42 (3H, s), 2.87 (3H, s), 2.94 (1H, dd, $J = 8.9$, 9.2 Hz), 3.08–3.28 (3H, m), 3.30–3.91 (22H, m), 3.94–4.05 (4H, m), 4.11 (1H, dd, $J = 8.5$, 9.2 Hz), 4.20–4.26 (3H, m), 4.32–4.60 (15H, m), 4.69–4.98 (13H, m), 5.16–5.26 (4H, m), 5.29 (1H, dd, $J = 9.8$, 10.1 Hz), 5.34 (1H, dd, $J = 8.5$, 9.5 Hz), 5.47 (1H, dd, $J = 9.5$, 10.1 Hz), 5.94 (1H, dd, $J = 9.8$, 9.8 Hz), 6.07 (1H, dd, $J = 9.5$, 10.1 Hz), 6.95–8.03 (104H, m, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$, major signals) δ 21.67, 21.72, 21.73, 54.69, 67.74, 67.87, 67.93, 68.83, 68.96, 69.11, 70.10, 70.21, 71.95, 72.52, 73.36, 73.55, 73.69, 73.83, 74.02, 74.24, 74.29, 74.54, 74.64, 75.02, 75.05, 75.13, 75.17, 75.50, 75.54, 75.70, 75.98, 76.09, 78.02, 78.08. 78.12, 78.19, 78.88, 79.56, 82.87, 82.96, 83.00, (96.49, 100.20, 100.23, 100.40, 100.47, 100.62, 101.25) (anomeric positions), 122.22–143.88, 163.92, 164.02, 164.21, 164.27, 164.58, 165.13, 165.32, 165.41, 165.61, 165.69, 165.86; IR (KBr) 701, 1095, 1265, 1736 cm^{-1}; HRMS *m/z* calcd for $C_{203}H_{187}F_9O_{47} \cdot NH_4$ $[M + 2(NH_4)]^{2+}$ 1791.6393, found 1791.6423.

Methyl 6-*O*-[6-*O*-{6-*O*-[3,6-Di-(β-D-glucopyranosyl)-β-D-glucopyranosyl]-β-D-glucopyranosyl}-3-*O*-(β-D-glucopyranosyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (30). To a solution of heptasaccharide **43** (40.9 mg, 12.2 μmol) in THF/MeOH (6 mL, 2/1, v/v) was added 2 M aq. NaOH (1 mL) at rt. After stirring for 12 h at the same temperature, the reaction mixture was neutralized with *Amberlite® IR-120* cation exchange resin (until ca. pH 7). After filtration and evaporation, the residue

was simply purified by preparative TLC (silica gel). To a solution of the crude product in $THF/CH_2Cl_2/H_2O$ (7 mL, 4/2/1, v/v/v) was added palladium(II) hydroxide (40.7 mg, 20 wt % on carbon). After purging with H_2 (1.01×10^5 Pa) and stirring for 83 h, H_2 was removed. After filtration and evaporation, the residue was purified by reversed-phase column chromatography to afford **3** (13.5 mg, 95%) as colorless solid. $[\alpha]_D^{20} = -3.98$ (*c* 1.0, H_2O), ^{1}H NMR (600 MHz, D_2O, 285 K); δ 3.12–3.76 (41H, m), 4.01–4.06 (4H, m), [4.34 (1H, d, $J = 8.4$ Hz), 4.37 (3H, t, $J = 8.4$ Hz), 4.58 (1H, d, $J = 7.8$ Hz), 4.59 (1H, d, $J = 7.8$ Hz), 4.63 (1H, d, $J = 3.6$ Hz) anomeric positions]; ^{13}C NMR (125 MHz, D_2O); δ 54.98, 60.39 × 2, 60.43, 67.72, 67.74, 68.34 × 2, 68.48, 68.58, 69.04, 69.14, 69.26 × 2, 69.31, 70.22, 70.82, 72.48, 72.50, 72.67, 72.76, 72.78, 73.12, 73.16, 74.25, 74.32, 74.55, 75.23 × 2, 75.27, 75.35, 75.59, 75.66, 75.68, 83.96, 84.05, (99.01, 102.19, 102.41, 102.45, 102.52, 102.62, 102.65) (anomeric positions); IR (KBr): 764, 1033, 3410 cm^{-1}; HRMS *m/z* calcd for $C_{43}H_{74}O_{36}\cdot NH_4$ $[M + NH_4]^+$ 1184.4304, found 1184.4308.

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