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Sequential one-pot glycosylation with glycosyl *N*-trichloroacetylcarbamate and trichloroacetate including dehydrative approach using 1-hydroxy sugars

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ABSTRACT

An efficient sequential one-pot glycosylation has been developed with glycosyl trichlorocarbamate and trichloroacetate activated by the same Lewis acid and enabled by a change in reaction temperature. The αα-selective glycosylation was achieved using glucose, galactose, and mannose substrates after investigation into the reactivities of the two types of glycosyl donors. Sequential one-pot dehydrative glycosylation, including in situ preparation of glycosyl donors followed by generation of two glycosyl bonds, provided three types of trisaccharide.

1. Introduction

Over the past decades the importance of carbohydrates in the life sciences has increased along with advances in glycochemistry and glycobiology. For example, oligosaccharides have been found to play fundamental roles in a series of life processes, such as recognition, growth, function, and the survival of living cells. Carbohydrates remain a relatively undeveloped source of new drugs offering exciting new therapeutic opportunities. Therefore, there is a need for supplying oligosaccharides in sufficient quantities for biological studies. The difficulty in obtaining pure oligosaccharides from natural sources has created the need for new methods in the chemical synthesis of carbohydrates.[1,2] For example, a variety of efficient methods and technologies have been developed for the synthesis of glycosides for application in medicinal tools, such as adjuvants and vaccines.[3,4] In this regard, powerful glycosylation methods and innovative technologies have been disclosed,[5] such as one-pot glycosylation.

One efficient method utilized in glycochemistry is the orthogonal strategy, which is based on selective activation of one leaving group over another. The two chemically different leaving groups are exploited to act either as a leaving group or as a protective group at the anomeric position, resulting in formations of various types of sugars, such as blanched trisaccharides.[6]

Another approach is provided by the chemoselective strategy, which takes advantage of the character of the protective groups of glycosyl donors having the same type of leaving group at the anomeric position. This concept has been achieved by exploiting electron-donating protective groups (armed) and electron-withdrawing protective groups (disarmed).[7]

Furthermore, another operation presented is a preactivation strategy, which utilizes activation of a glycosyl donor in the absence of the glycosyl acceptor to give a highly glycosylating species, which is immediately treated with a second building block that is potentially a glycosyl donor to provide a coupling saccharide, which can be preactivated in situ for further glycosylation.[8]

These methods have some drawbacks in that activation of the donors requires stoichiometric amounts of a promoter and performing the experiments is not always convenient.

Recently, Iadonisi and co-workers reported on a new approach inspired by the recognition of the well-differentiated activation conditions of similarly protected glycosyl-trichloroacetylimidate and (*N*-phenyl) trifluoroacetylimidate with various Lewis acids as activators. This method allows to give oligosaccharides with similar protective groups by simply changing the reaction temperature and adding a Lewis acid at the start of the second step efficiently.[9]

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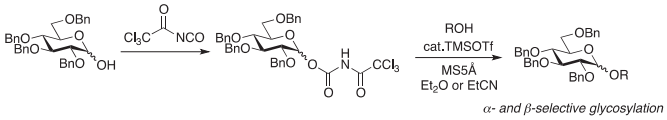
We have described an efficient and straightforward procedure for one-pot dehydrative glycosylation with glycosyl *N*-trichloroacetylcarbamates prepared from the corresponding 1-hydroxy sugars[10] (Scheme 1).



Scheme 1. Stereoselective glycosylation with glycosyl trichloroacetylcarbamate.

In the next stage, we considered whether our convenient methodology would allow sequential one-pot glycosylation, including a dehydrative approach. Isodoli's strategy is particularly desirable in that glycosylation is afforded by a simple and convenient procedure.[9] In order to enhance the method using a glycosyl carbamate donor, a glycosyl donor having weaker reactivity than the carbamate donor in the reaction medium should be developed.

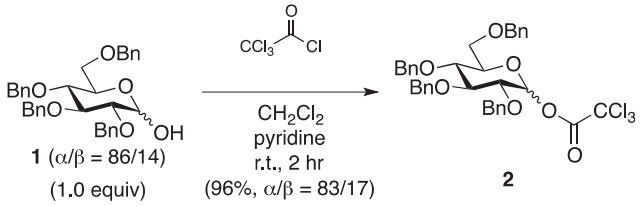
In this paper, we describe (i) the development of a partly protected glycosyl donor as a suitable coupling partner to glycosyl carbamate to synthesize oligosaccharides, (ii) the establishment of sequential one-pot glycosylation, and (iii) the achievement of sequential one-pot dehydrative glycosylation.

2. Results and discussion

2.1. Development of suitable glycosyl donor for sequential one-pot glycosylation

2.1.1. Design and preparation of glycosyl N-trichloroacetate. A key factor in establishing a successful sequential one-pot glycosylation lies in the development of a suitable glycosyl donor as a coupling partner to the glycosyl trichlorocarbamate donor. This coupling partner must have less reactivity in the glycosylation to extend saccharide chain. The carbamate donor reacts with a hard Lewis acid due to the electron-withdrawing nitrogen on the trichloroacetylcarbamate. In this regard, removal of the amide moiety including the nitrogen on the trichloroacetylcarbamate leads to a trichloroacetyl group.[11] Having this functional group as a leaving group in the glycosylation would be attractive for our purposes because of the facile preparation and stability of the glycosyl donor as well as its reduced reactivity in comparison to the glycosyl trichloroacetylcarbamate donor possessing a similar protective group. To the best of our knowledge, although glycosyl trichloroacetate donors protected with acetyl and benzyl groups have been reported,[12] perbenzylated donors have not been investigated in terms of their reactivity and spectral data.

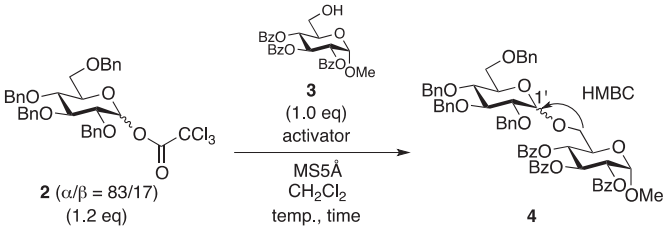
The preparation of glycosyl trichloroacetate donor **2** (α/β=83/17, anomeric ratio determined by ^{1}H NMR in $CDCl_3$) was accomplished by the reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**1**) (α/β=86/14, anomeric ratio determined by ^{1}H NMR in C_6D_6) with trichloroacetyl chloride[13] in dry CH_2Cl_2 and pyridine at room temperature (Scheme 2). The glycosyl donor **2** is stable for a couple of months in a freezer.



Scheme 2. Preparation of glycosyl trichloroacetate.

2.1.2. Glycosylation of perbenzyloxy glycosyl trichloroacetyl donor. With glycosyl donor **2** in hand, we next sought suitable conditions for the sequential one-pot glycosylation by screening the activation conditions for glycosylation of methyl 2,3,4-tri-*O*-benzoyl-D-glucopyranoside (**3**)[14] (1.0 equiv) with **2** in CH_2Cl_2 over 5 Å molecular sieves (MS 5 Å). Soft Lewis acids, such as $Zn(OTf)_2$, AgOTf, $Cu(OTf)_2$, and $Sc(OTf)_3$, were not able to activate donor **2** (Table 1, entries 1–4). However, the glycosylation proceeded moderately using stoichiometric and catalytic amounts of $SnCl_4$ (entries 5 and 6). Decomposition of the glycosyl donor **2** with TfOH in the reaction medium at room temperature, or even at −20 °C, using a catalytic amount of TfOH provided good result (entries 7–9). The use of a stoichiometric amount of TMSOTf also achieved the glycosylation at 0 °C to afford a glucosyl 6,1′-linked disaccharide **4**[15] in good yield as a mixture of anomers (α/β=68/32, anomeric ratio determined by ^{1}H NMR in $CDCl_3$) (entry 10). Employing a catalytic amount of TMSOTf (0.2 equiv) similarly promoted the glycosylation (83% yield, α/β=68/32, entry 11).

Table 1
Glycosylation with glycosyl trichloroacetate promoted by various Lewis acids

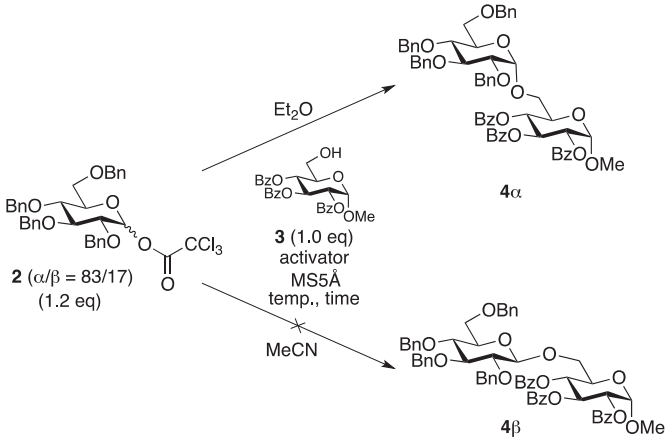


Entry	Activator (equiv)		Temp	Time	Yield[a]	Ratio[b] (α/β)
1	AgOTf	(1.2)	rt	2 h	NR[c]	—
2	$Cu(OTf)_2$	(1.2)	rt	2 h	NR[c]	—
3	$Zn(OTf)_2$	(1.2)	rt	2 h	NR[c]	—
4	$Sc(OTf)_3$	(1.2)	rt	2 h	NR[c]	—
5	$SnCl_4$	(1.2)	rt	4 h	52%	63/37
6	$SnCl_4$	(0.2)	rt	4 h	60%	76/24
7	TfOH	(1.2)	0 °C	30 min	48%	87/13
8	TfOH	(1.2)	−20 °C	1 h	27%	55/45
9	TfOH	(0.2)	0 °C	1 h	83%	69/31
10	TMSOTf	(1.2)	0 °C	20 min	81%	68/32
11	TMSOTf	(0.2)	0 °C	30 min	83%	60/40

[a] Isolated yields.
[b] Determined by ^{1}H NMR (300 MHz) spectroscopy.
[c] NR: no reaction.

Next, we explored the solvent effect for α-selective glycosylation[16] of **3** with **2**. Surprisingly the reaction did not proceed when a stoichiometric amount of TMSOTf was employed at 0 °C in Et_2O (Table 2, entry 1). On the other hand, good reactivity and α-selectivity (α/β=86/14) were observed for the glycosylation at room temperature in Et_2O (entry 2). Furthermore, reducing the amount of Lewis acid (0.2 equiv) gave similar results while maintaining α-selectivity (α/β=87/13, entry 3). To test the stability in a higher temperature medium, the glycosyl donor **2** was applied to glycosylation at 40 °C, resulting in good yield and selectivity (84%, α/β=88/12, entry 4). When a stoichiometric amount of $TMSClO_4$[17] was employed, the α-selectivity ratio was slightly improved (α/β=92/8, entry 5). Even a catalytic amount of $TMSClO_4$ catalyzed the glycosylation efficiently (entries 6 and 7). However, the usage of $TMSClO_4$ was not dramatically changed their yields and ratios comparing with the using TMSOTf. Meanwhile, β-selective glycosylation[18] in MeCN did not proceed (entry 8).

Table 2
Glycosylation with glycosyl trichloroacetate (solvent effect)

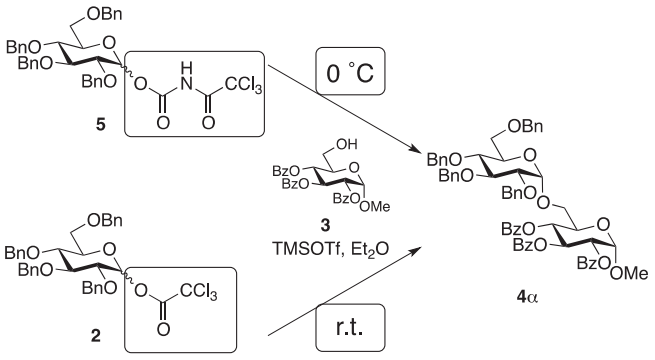


Entry	Activator (equiv)		Solvent	Temp	Time	Yield[a]	Ratio[b] (α/β)
1	TMSOTf	(1.2)	Et_2O	0 °C	2 h	NR[c]	—
2	TMSOTf	(1.2)	Et_2O	rt	2 h	85%	86/14
3	TMSOTf	(0.2)	Et_2O	rt	24 h	90%	87/13
4	TMSOTf	(1.2)	Et_2O	40 °C	4 h	84%	88/12
5	$TMSClO_4$	(1.2)	Et_2O	rt	24 h	76%	92/8
6	$TMSClO_4$	(0.5)	Et_2O	rt	24 h	87%	95/5
7	$TMSClO_4$	(0.2)	Et_2O	rt	24 h	64%	85/15
8	TMSOTf	(1.2)	MeCN	rt	2 h	Decomposed	—

[a] Isolated yields.
[b] Determined by ^1H NMR (300 MHz) spectroscopy.
[c] NR: no reaction.

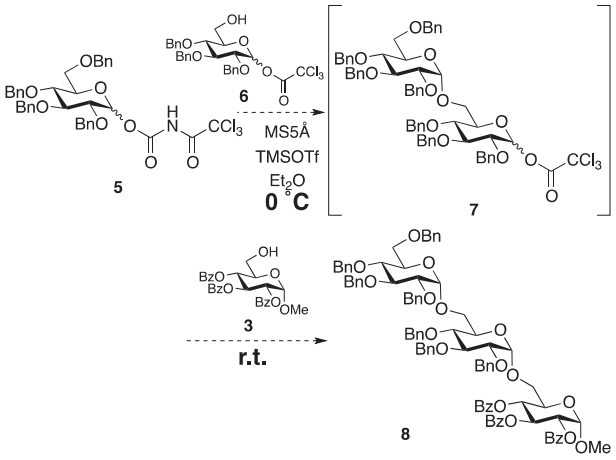
2.2. Development of sequential one-pot glycosylation

2.2.1. Synthetic plan for sequential one-pot glycosylation. Previous research on the glycosyl carbamate **5**[10] and the glycosyl trichloroacetate **2** indicated a difference in reactivity of the glycosyl donors when glycosylation was carried out in Et_2O. For example, the glycosyl carbamate **5** reacts at 0 °C in Et_2O, whereas the less reactive glycosyl trichloroacetate donor only underwent glycosylation at room temperature (Scheme 3).



Scheme 3. Difference in reactivity of two types of glycosyl donor **5**.

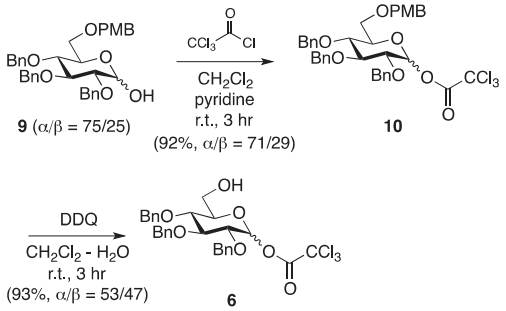
Based on the distinct reactivities of the two glycosyl donors, it was considered that a similar type of sequential one-pot glycosylation to that reported by Iadonisi[9] might be possible. As illustrated in Scheme 4, we envisioned that the first step of glycosylation would be carried out utilizing the glycosyl carbamate **5** and 6-OH glycosyl trichloroacetate **6** in the presence of TMSOTf at 0 °C to provide disaccharyl trichloroacetate **7**. Subsequently, addition of acceptor **3** and an increase in reaction temperature to room temperature as the forcing condition would initiate the second step and ideally provide trisaccharide **8** in a one-pot manner.



Scheme 4. Synthetic plan for trisaccharide using glycosyl *N*-trichloroacetylcarbamate **5** and trichloroacetate **6**.

2.2.2. Preparation of 6-OH glycosyl donor. Execution of the above strategy required preparation of 6-OH glycosyl trichloroacetyl glycosyl donor **6**. Few reports describe the synthesis of 6-OH glycosyl donors because it is difficult to find a protective group that allows regioselective reaction between the more reactive C6-OH and the anomeric hydroxy group. In addition, liberation of the free 6-OH from the protected form might prove difficult due to the presence of the sensitive leaving group at the anomeric position.

One of the few reports on a 6-OH imidate donor was presented by Fraser-Reid[19], in which desilylation of 6-OTBDPS glycosyl imidate with HF/pyridine provides conversion to the 6-OH glycosyl imidate donor. We applied this method to the 6-OTBDPS glycosyl trichloroacetate donor but obtained non-reproducible results, even when using TBAF as a reagent for the deprotection, which suggests that the trichloroacetyl donor is not stable in either acidic or basic conditions. To allow deprotection in neutral conditions, the PMB group was chosen as a suitable protective group at 6-OH (Scheme 5).

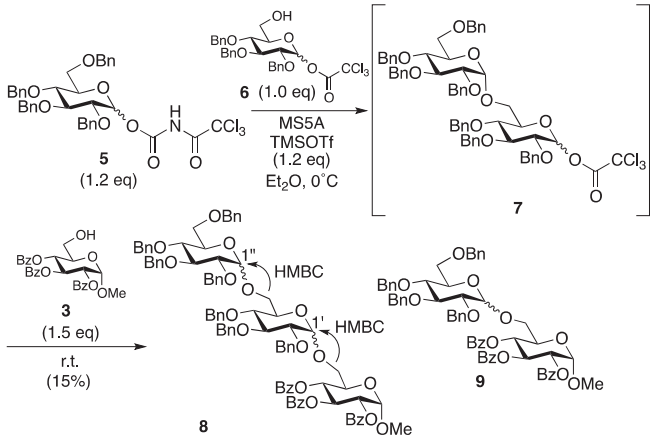


Scheme 5. Synthesis of 6-OH glycosyl donor **6**.

The precursor **9**, derived from penta-*O*-acetyl-β-D-glucopyranoside in seven steps according to previous reports,[20] was treated with trichloroacetyl chloride in the presence of pyridine to afford 2,3,4-tri-*O*-benzyl-6-*O*-*p*-methoxybenzyl-D-glucopyranosyl trichloroacetate (**10**). Subsequently, the 6-OPMB group was deprotected with DDQ to provide the desired 6-OH trichloroacetate donor **6** in good yield. In this case, decomposition of sensitive 1-trichloroacetyl compounds was not observed in the reaction medium. The reproducibility of this reaction allowed for a reliable supply on the gram scale.

2.2.3. Attempt at sequential one-pot glycosylation. With 6-OH glycosyl trichloroacetate **6** in hand, we attempted the sequential one-pot glycosylation. This was performed by stirring with glycosyl trichloroacetylcarbamate **5** (1.2 equiv) and **6** (1.0 equiv) in

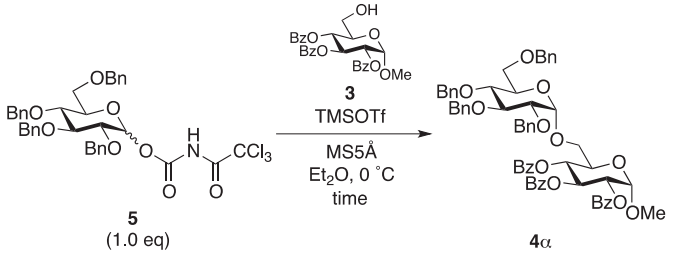
the presence of a stoichiometric amount of TMSOTf at 0 °C until **6** was not detected by TLC, at which point the reaction medium was warmed to ambient temperature and the acceptor **3** added. The desired trisaccharide **8αα** was slightly obtained; however, the undesired disaccharide **9** was also yielded due to coupling between **5** and **3**. To prevent the side reaction, the reactivity of glycosyl carbamate **5** was additively verified in the second-step glycosylation. The structure of **8αα** was determined by HMBC experiments (cross peaks between C6-H and C-1′, and between C6′-H and C-1″), and from the coupling constants matching those expected for an α-glycoside ($^3J_{H1',H2'}$=3.8 Hz, $^3J_{H1'',H2''}$=3.5 Hz) (Scheme 6).



Scheme 6. First attempt at sequential one-pot glycosylation.

The key feature in our solution to the previous problem of the undesired side reaction is to consume the glycosyl carbamate donor in the first-step reaction. To explore conditions in which an excess of the glycosyl acceptor is used in glycosylation with glycosyl carbamate, we re-examined the balance in amounts of glycosyl donor **5**, glycosyl acceptor **3**, and Lewis acid in the glycosylation (Table 3). Changing the amount of the glycosyl acceptor **3** (entries 1–3) revealed that 1.5 equiv of **3** was acceptable (entry 3). TLC analysis showed that the reaction went to completion, providing 94% yield, when an excess (1.5 equiv) of TMSOTf was used (entry 5).

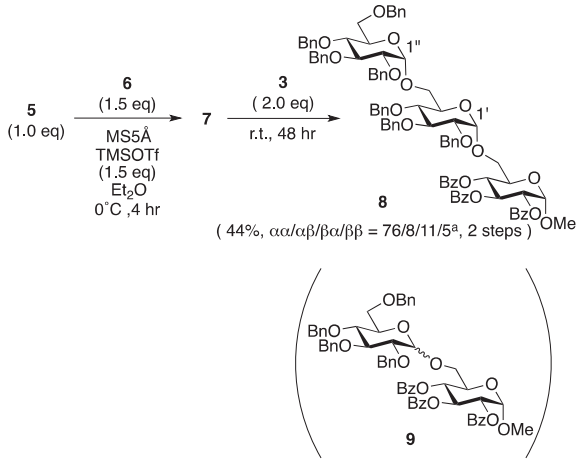
Table 3
Reaction conditions of glycosylation of **3** with glycosyl carbamate **5**



Entry	Acceptor **2** (equiv)	TMSOTf (equiv)	Time (h)	Yield[a] (%)	Ratio[b] (α/β)
1	1.0	1.0	20	85	91/9
2	1.2	1.0	5	86	88/12
3	1.5	1.0	4	85	88/12
4	1.5	1.2	5	82	84/16
5	1.5	1.5	4	94	86/14

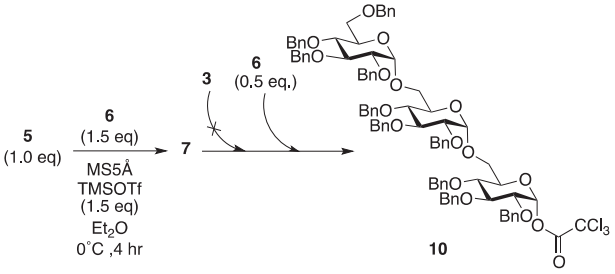
[a] Isolated yields.
[b] Determined by ^{1}H NMR (300 MHz) spectroscopy.

In practice, applying the conditions identified as suitable in Table 3 to the sequential one-pot glycosylation, that is, using 1.5 equiv of the acceptor and TMSOTf, reduced the generation of undesired disaccharide **9**, providing the trisaccharide **8** in moderate yield (Scheme 7).



Scheme 7. Application of suitable conditions identified in Table 3 to the sequential one-pot glycosylation. [a]Anomeric ratio was determined by HPLC [Senshu Pak PEGASIL Silica 60–5 (4.6ø×250 mm), hexane/AcOEt=3/2, UV at 254 nm, flow rate; 0.2 mL/min, 0 °C].

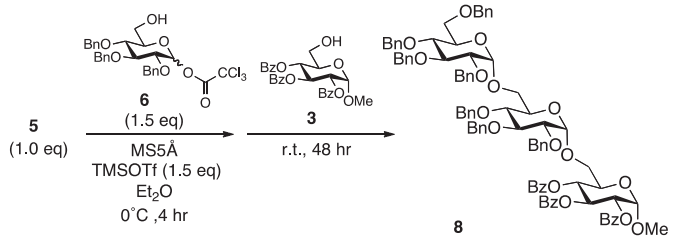
A new side product **10** was identified from the crude product in the previous reaction, explaining why the desired trisaccharide **8** was only obtained in moderated yields. These results suggested that **10αα** was produced by addition of 6-OH acceptor **6** instead of addition of acceptor **3** to the intermediate **7α** as illustrated in Scheme 8.



Scheme 8. Mechanism for the generation of byproduct **10αα**.

To limit generation of **10** by the side reaction in the second glycosylation, we used an excess of acceptor **3** in order to increase the likelihood of reaction by the desired pathway and improve the yield of trisaccharide **8**. Against our expectations, varying the amount of acceptor **3** gave similar results to that observed for 2.0 equiv (Table 4).

Table 4
Sequential one-pot glycosylation (varying the amount of acceptor **3**)



Entry	Acceptor **3** (equiv)	Yield[a] (two steps) (%)	Ratio[b] (αα/αβ/βα/ββ)
1	2.0	44	76/8/11/5
2	2.5	43	76/10/8/6
3	3.0	39	77/11/6/6

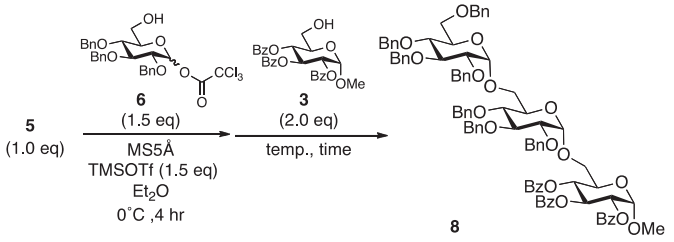
[a] Isolated yields.
[b] Determined by HPLC [Senshu Pak PEGASIL Silica 60–5 (4.6ø×250 mm), hexane/AcOEt=3/2, UV at 254 nm, flow rate; 0.2 mL/min, 0 °C].

It is considered that the poor reactivity of acceptor **3** results in the low observed yield of the desired trisaccharide **8** in sequential one-

pot glycosylation. We expected that the desired glycosylation would be accelerated in warmer reaction conditions at the second step.

Performing glycosylation at 30 °C in the second step provided trisaccharide **8** in improved yield (Table 5, entry 2, 50%). Furthermore, the reaction smoothly proceeded under reflux conditions, providing trisaccharide **8** in 72% yield with reasonable selectivity (entry 3).

Table 5
Sequential one-pot glycosylation with glucose (changing the reaction temperature in the second step)



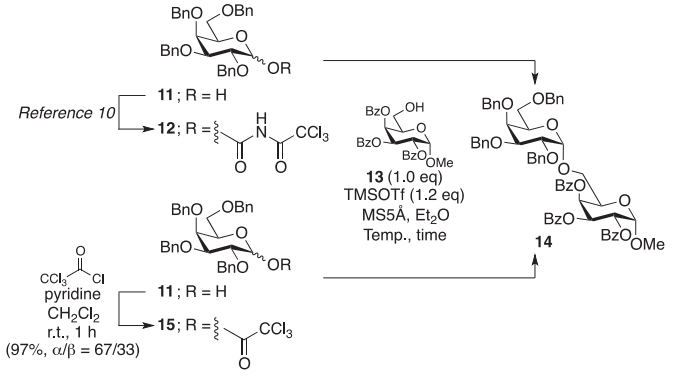
Entry	Temp	Time (h)	Yield[a] (two steps) (%)	Ratio[b] (αα/αβ/βα/ββ)
1	rt	48	44	76/8/11/5
2	30 °C	24	50	77/8/10/5
3	40 °C	24	72	75/10/9/6

[a] Isolated yields.
[b] Determined by HPLC [Senshu Pak PEGASIL Silica 60–5 (4.6ø×250 mm), hexane/AcOEt=3/2, UV at 254 nm, flow rate; 0.2 mL/min, 0 °C].

2.3. Sequential one-pot glycosylation with galactose

2.3.1. Investigating the reactivity for one-pot glycosylation of galactosyl trichloroacetylcarbamate and galactosyl trichloroacetate. The scope and limitations of the sequential one-pot glycosylation with glycosyl *N*-trichloroacetylcarbamate and trichloroacetate were investigated by employing existing galactosyl and mannosyl building blocks. Before attempting the sequential one-pot glycosylation, it is necessary to first identify whether the glycosyl trichlorocarbamate has a different reactivity from the trichloroacetate. Although the preparation and glycosylation of galactosyl carbamate donor **12** has already been described,[10] we did not investigate the effect of reaction temperature. The galactosyl donor **12** underwent glycosylation at −20 °C in reaction with a known perbenzoylated galactosyl acceptor **13**[21] in moderate yield (Table 6, entry 1). In contrast, the perbenzylated galactosyl trichloroacetate **15**, prepared from 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose (**11**), did not undergo glycosylation with the galactosyl acceptor **13** at −20 °C (entry 3). On the other hand, the desired galactosyl disaccharide **14** could be obtained by glycosylation at 0 °C, providing 21% yield (entry 4). The yield of **14** was further increased to 74% at ambient temperature (entry 5). The significant differences identified in the reactivity between the two types of donors, the galactosyl carbamate **12** and the galactosyl trichloroacetate **15**, indicated their suitability for sequential one-pot glycosylation.

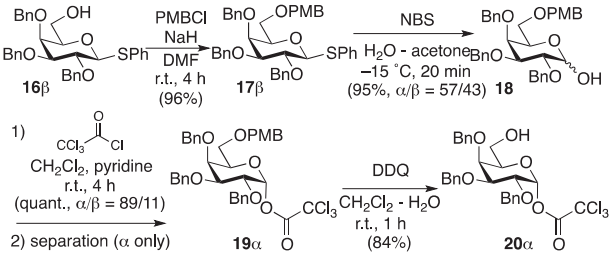
Table 6
Reaction conditions of galactosyl carbamate **12** and trichloroacetate **15**



Entry	Donor	Temp	Time (h)	Yield[a]	Ratio[b] (α/β)
1	**12**	−20 °C	2	56%	68/32
2	**12**	0 °C	2	37%	70/30
3	**15**	−20 °C	9	NR[c]	—
4	**15**	0 °C	2	21%	73/27
5	**15**	rt	14	74%	73/27

[a] Isolated yields.
[b] Determined by ^{1}H NMR (400 MHz) spectroscopy.
[c] NR: no reaction.

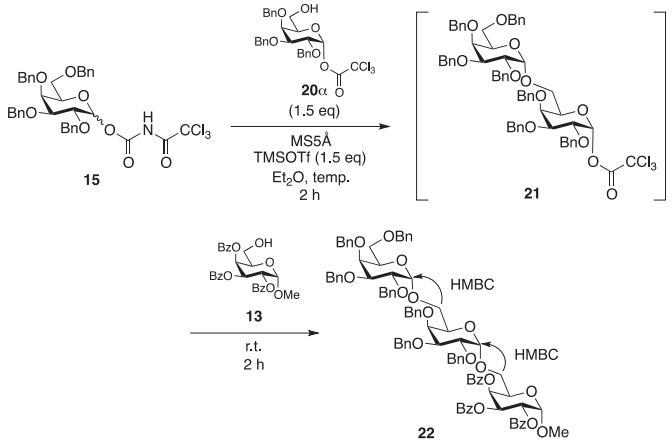
2.3.2. Synthesis of 6-OH galactosyl donor. 2,3,4-Tri-*O*-benzyl-6-*O*-*p*-methoxybenzyl-D-galactopyranose (**18**) was prepared as shown in Scheme 9. A known thioglycoside **16β** was derived from (+)-D-galactose in six steps according to previous reports.[22] The 6-OH of **16β** was masked with PMB group to derive the thioglycoside **17β**. Then the anomeric phenylthionyl moiety of **17β** was oxidized to **18** having a 1-hydroxy group, followed by conversion into 6-OPMB 1-trichloroacetate **19** as an anomeric mixture, which was separated by silica gel column chromatography to provide the stable **α**-isomer **19α**. Deprotection of the 6-OPMB group in **19α** with DDQ according to a similar protocol to that used in the glucose case gave the desired 6-OH galactosyl donor **20α**.[23]



Scheme 9. Synthesis of 6-OH galactosyl donor **20α**.

2.3.3. Sequential one-pot galactosylation. With the three galactosyl building blocks in hand, we attempted the sequential one-pot galactosylation (Table 7). On the basis of the results of our investigations into the galactosyl carbamate **12** and the galactosyl

Table 7
Sequential one-pot galactosylation



Entry	Temp	Acceptor **13** (equiv)	Yield[a] (%)	Ratio[b] (αα/αβ/βα/ββ)
1	−20 °C	2.0	68	44/23/22/11
2	0 °C	2.0	56	45/22/22/11
3	0 °C	3.0	53	43/23/22/12

[a] Isolated yields.
[b] Determined by HPLC [Senshu Pak PEGASIL silica SP 100 (4.6ø×250 mm), hexane/AcOEt=4/1, UV at 254 nm, flow rate; 1.0 mL/min, rt].

trichloroacetate **15**, we envisaged performing the first-step glycosylation at −20 °C and completing the second-step glycosylation at ambient temperature.

Glycosylation of the galactosyl trichloroacetate **20α** with the galactosyl carbamate **15** was carried out at −20 °C in the presence of MS 5 Å and a stoichiometric amount of TMSOTf for the first coupling. Subsequently, addition of the galactosyl acceptor **13**, and warming to ambient temperature provided the desired galactosyl trisaccharide **22** in 68% yield with reasonable anomeric ratios (αα/αβ/βα/ββ=44/23/22/11, Table 7, entry 1).

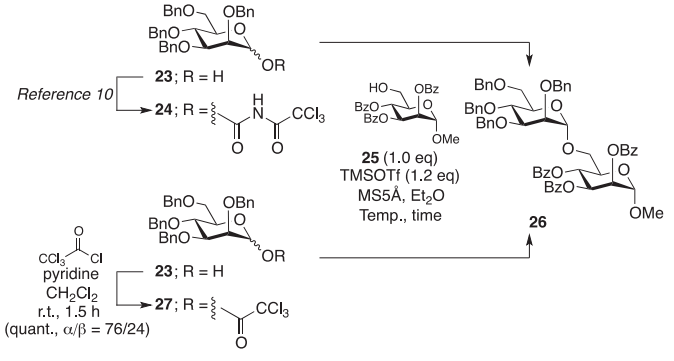
Because it was expected that the galactosyl carbamate **15** would have better reactivity at 0 °C than −20 °C, the first coupling was performed at 0 °C, providing trisaccharide **22** in reduced yield (56%, entry 2). In order to increase the reactivity in the second step, 3.0 equiv of the acceptor **13** was used, although a similar result to entry 2 was obtained (53%, entry 3).

Having higher reactivity than the glucose equivalent, the galactosyl carbamate **15** proved suitable for reaction at a lower temperature in the first step. The structure of **22αα** was determined by HMBC experiments (cross peaks between C6-H and C-1′, and between C6′-H and C-1″), and from the coupling constants ($^3J_{H1',H2'}\sim3.5$ Hz, $^3J_{H1'',H2''}\sim3.5$ Hz) matching those expected for an α-glycoside.

2.4. Sequential one-pot glycosylation with mannose

2.4.1. Investigating the reactivity for one-pot glycosylation of mannosyl trichloroacetylcarbamate and mannosyl trichloroacetate. The mannosyl trichlorocarbamate and trichloroacetate were investigated for their suitability in sequential one-pot glycosylation as in the galactose study. The mannosyl carbamate **24**[10] reacted slightly with the acceptor **25**[24] at −40 °C to obtain **26** (Table 8, entry 1), and was successfully glycosylated at higher temperatures (−20 °C and 0 °C) with improved yield and anomeric ratio (entries 2 and 3). The mannosyl trichloroacetate **27** was derived from 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose (**23**) by the usual procedure and glycosylation was performed at the same temperature (−40 °C) at which mannosyl carbamate **24** was activated. However, in this case no product was obtained (entry 4). Reaction at −20 °C proceeded in moderate yield even after a long reaction time (entry 5); no glycosylated product was observed by TLC after 4 h. Glycosylation could be completed in a shorter reaction time by further increasing the reaction temperature to 0 °C, with a similar yield as the former reaction (entry 6). The mannosylation with **27** was completed at room temperature within 1 h to give a mannosyl disaccharide **26** in good yield and α selectivity (91%, α/β=91/9, entry 7). These results indicate that the difference in reactivity between the two types of donors, the carbamate **24** and the trichloroacetate **27**, is sufficient, as shown by completion of the first-step reaction in 4 h at −20 °C.

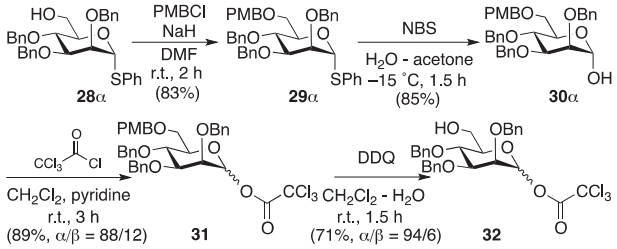
Table 8
Reaction conditions for mannosyl carbamate **24** and trichloroacetate **27**



Entry	Donor	Temp	Time (h)	Yield[a]	Ratio[b] (α/β)
1	**24**	−40 °C	5	14%	58/42
2	**24**	−20 °C	2	70%	69/31
3	**24**	0 °C	2	75%	75/25
4	**27**	−40 °C	3	NR[c]	—
5	**27**	−20 °C	18	45%	75/25
6	**27**	0 °C	4	52%	76/24
7	**27**	rt	1	91%	91/9

[a] Isolated yields.
[b] Determined by ^{1}H NMR (400 MHz) spectroscopy.
[c] NR: no reaction.

2.4.2. Synthesis of 6-OH mannosyl donor. Preparation of 2,3,4-tri-*O*-benzyl-6-*O*-*p*-methoxybenzyl-D-mannnopyranosyl trichloroacetate (**32**) is illustrated in Scheme 10. A partly protected thiomannoside **28**, the precursor of a 6-OH mannosyl donor **32** was prepared in six steps from D-mannose according to previous reports.[25] The 6-hydroxy group of **28α** was masked with a PMB group to provide **29α**, followed by oxidative conversion of the phenylthio group to give the anomeric OH group in **30α**. A 1-trichloroacetyl group was introduced using trichloroacetyl chloride to give the fully protected sugar **31**. After removal of the PMB group, the desired 6-OH mannosyl donor **32** was identified by TLC analysis in the reaction medium, but isolation of the product **32** failed. Because the mannosyl 6-OH donor **32** is sensitive to many factors (e.g., acid, base, and water), a non-aqueous work-up was accomplished by quenching with anhydrous Na_2SO_4 followed by quick filtration through silica gel and a Celite pad to remove any excess reagents and the hydrated Na_2SO_4.



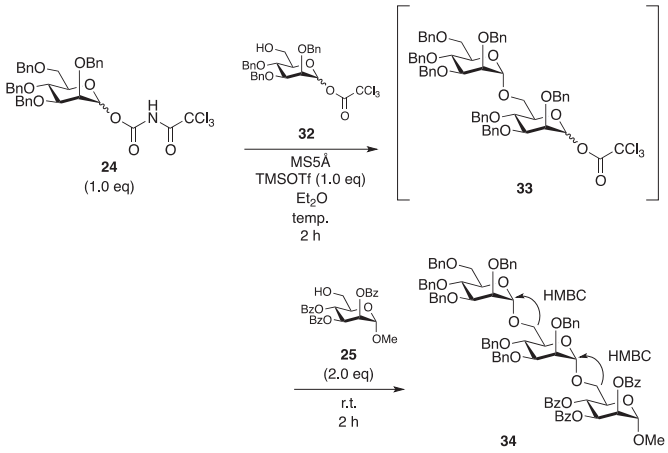
Scheme 10. Synthesis of 6-OH mannosyl donor **32**.

2.4.3. Sequential one-pot mannosylation. With the mannosyl building blocks in hand, one-pot mannosylation was investigated based on the results on the reactivities of the two types of mannosyl donors. The 6-OH mannosyl trichloroacetate **32** was glycosylated with mannosyl carbamate **24** at −20 °C in the presence of a stoichiometric amount of Lewis acid followed by addition of perbenzoylated mannosyl acceptor **25** to furnish the desired trisaccharide **34** in moderate yield with good αα selectivity (Table 9, entry 1). A warmer temperature at the first-step glycosylation reduced the yield of **34** and produced the undesirable tetrasaccharide **35** due to over-glycosylation of disaccharide **33** with **32** at 0 °C, followed by the addition of acceptor **25** (entry 2).

On the other hand, glycosylation with a catalytic amount of Lewis acid was able to be performed, and although the yield was moderate, it was comparable to that obtained with a stoichiometric amount of the activator (entry 3).

The structure of mannose trisaccharide **34** was confirmed as α-configuration by HMBC experiments based on connections between C6-H and C-1′, and between C6′-H and C-1″, as well as GATE-I [$^1J_{C,H}$=168.7 Hz (99.24 ppm, d) for C1′ and $^1J_{C,H}$=168.4 Hz (99.15 ppm, d) for C1″].

Table 9
Sequential one-pot mannosylation



Entry	Temp (°C)	TMSOTf (equiv)	Yield[a] (%)	Ratio[b] (αα/αβ/βα/ββ)
1	−20	1.0	52	71/14/13/2
2	0	1.0	37	75/10/9/6
3	−20	0.2	53	70/12/12/6

[a] Isolated yields.
[b] Determined by HPLC [Senshu Pak PEGASIL silica SP 100 (4.6ø×250 mm), hexane/AcOEt=4/1, UV at 254 nm, flow rate; 0.5 mL/min, rt].

2.5. Sequential one-pot dehydrative glycosylation

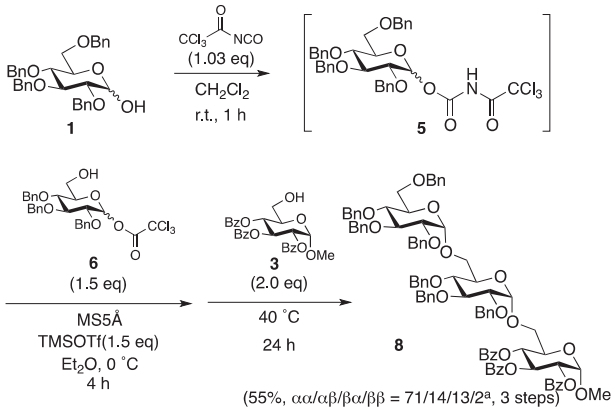
Sequential one-pot glycosylations have usually been performed after preparation of the individual glycosides as donors and acceptors. It would be advantageous to derive the glycosyl carbamate from the corresponding 1-hydroxy glycose in situ, followed by activation, as in so-called dehydrative glycosylation reported by Gin.[26] From this perspective, one-pot glycosylation using glycosyl carbamates could offer a convenient new technology in which the glycosyl donor is prepared and activated in situ to allow synthesis of various trisaccharides in the same flask.

In this sequential one-pot dehydrative glycosylation starting from **1**, a very slightly excess of trichloroacetyl isocyanate was used in pre-glycosylation to prepare the carbamate **5** in situ, followed by the addition of **6**, a Lewis acid, and **3**, resulting in trisaccharide **10** (Scheme 11). Our glycosylation procedure involving preparation of the glycosyl donor in a one-pot procedure was therefore successful.

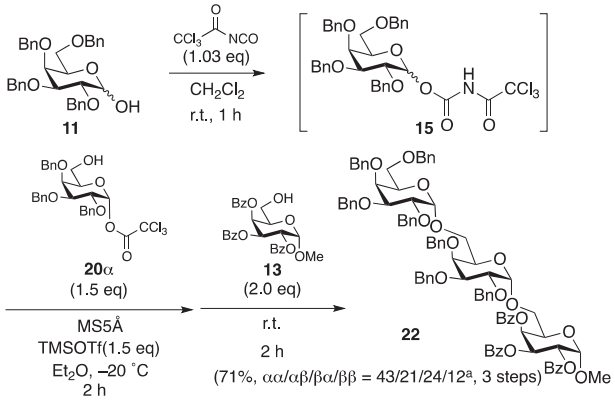
Furthermore, galactosyl trisaccharide **22** was obtained in 71% yield from 1-hydroxy galactose derivative **11** by a one-pot dehydrative technique, which is a better yield than that obtained with the usual one-pot procedure employing the galactosyl carbamate **15** (Scheme 12).

Similarly, the mannosyl trisaccharide **34** was also synthesized in 71% yield from 1-hydroxy mannose **23** in 3 steps by one-pot dehydrative glycosylation (Scheme 13).

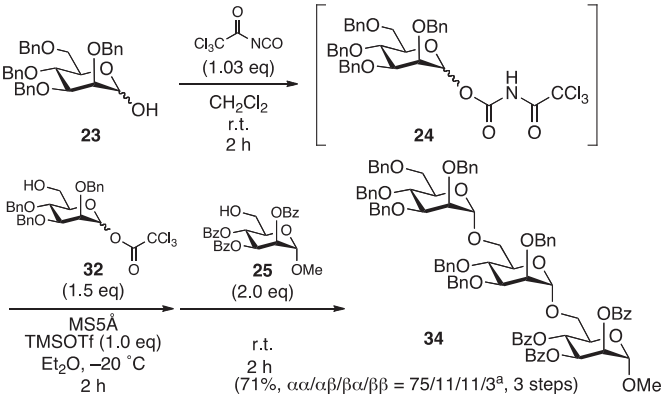
We believe that, in the galactose and mannose cases, a higher yield was obtained for the dehydrative reaction as compared to the reaction starting from the corresponding carbamate because less decomposition of the unstable glycosyl carbamates occurred during the reactions.



Scheme 11. Sequential one-pot dehydrative glycosylation. [a]Anomeric ratio was determined by HPLC [Senshu Pak PEGASIL Silica 60−5 (4.6ø×250 mm), hexane/AcOEt=3/2, UV at 254 nm, flow rate; 0.2 mL/min, 0 °C].



Scheme 12. Sequential one-pot dehydrative galactosylation. [a]Anomeric ratio was determined by HPLC [Senshu Pak PEGASIL silica SP 100 (4.6ø×250 mm), hexane/AcOEt=4/1, UV at 254 nm, flow rate; 1.0 mL/min, rt].



Scheme 13. Sequential one-pot dehydrative mannosylation. [a]Anomeric ratio was determined by HPLC [Senshu Pak PEGASIL silica SP 100 (4.6ø×250 mm), hexane/AcOEt=4/1, UV at 254 nm, flow rate; 0.5 mL/min, rt].

3. Conclusion

In conclusion, we have demonstrated sequential one-pot glycosylation using glycosyl donors with different reactivities (i.e., glycosyl carbamate and trichloroacetate) and enabled by a change in reaction temperature. Derivation of the glycosyl carbamate in situ from the corresponding 1-hydroxy sugars enabled the sequential one-pot dehydrative glycosylation, produce various trisaccharides. The efficient implementation of the present glycosylation approach, in particular for the sequential one-pot dehydrative glycosylation, would be useful in the synthesis of a variety of oligosaccharides.

4. Experimental

4.1. General

All reactions were carried out under argon atmosphere in dried glassware, unless otherwise noted. All reagents were purchased from Tokyo Kasei Kogyo, Kanto Chemical, Fluka or Aldrich companies and used without further purification, unless otherwise noted. Dry THF, toluene, and CH_2Cl_2 were purchased from Kanto Chemical Co. Diethyl ether was freshly distilled from sodium and benzophenone. Precoated silica gel plates with a fluorescent indicator (Merck 60 F_{254}) were used for analytical and preparative thin layer chromatography. Flash column chromatography was carried out with Kanto Chemical silica gel (Kanto Chemical, silica gel 60N, spherical neutral, 0.040–0.050 mm, Cat.-No. 37 563-84). Powdered and predried molecular sieves 4 Å, and 5 Å were used in glycosylation. ^{1}H NMR spectra were recorded at 300, 400, and 600 MHz and ^{13}C NMR spectra were recorded at 75 or 100, 150 MHz on Varian VXR-300 (300 MHz), Varian XL-400 (400 MHz), Varian UNITY-400 (400 MHz), or Varian INOVA (600 MHz) spectrometers. The chemical shifts are expressed in parts per million downfield from the internal solvent peaks for $CHCl_3$ (7.26 ppm, ^{1}H NMR), CH_3OH (3.31, 4.84 ppm, ^{1}H NMR), C_6H_6 (7.27 ppm, ^{1}H NMR), $CDCl_3$ (77.0 ppm, ^{13}C NMR), CD_3OD (49.0 ppm, ^{13}C NMR), or C_6D_6 (128.0 ppm, ^{13}C NMR) and J values are given in Hertz. The coupling patterns are denoted s (singlet), d (doublet), dd (double doublet), ddd (double double doublet), t (triplet), dt (double triplet), q (quartet), m (multiplet), or br (broad). High-performance liquid chromatography (HPLC) was carried out using a Senshu UV–vis Detector (SSC-5410) and Senshu HPLC-pump (SSC-3461, UV; 254 nm) with Senshu Pak PEGASIL Silica 60–5 (normal phase: 4.6ø×250 mm) and Senshu Pak PEGASIL Silica SP 100 (normal phase: 4.6ø×250 mm). All infrared spectra were measured on a JASCO FT/IR-460 spectrometer. High- and low-resolution mass spectra were measured on a JEOL JMS-T100 LP and JEOL JMS-AX505 HA spectrometer. Optical rotations were measured by using JASCO DIP-370 polarimeter. A 0.1 M solution of $TMSClO_4$ in Et_2O was prepared as below; to a solution of $AgClO_4$ (38.4 mg, 185 μmol) in Et_2O (1.85 mL) at 0 °C was added TMSCl (20.5 mg, 189 μmol) and this mixture was stirred. After the mixture was left standing for 10 min without stirring, the supernatant was used for glycosylation as a catalyst.

4.2. Development of suitable glycosyl donor for the sequential one-pot glycosylation

*4.2.1. 2,3,4,6-Tetra-O-benzyl-D-glucopyranosyl trichloroacetate (**2α** and **2β**).* To a stirred solution of 2,3,4,6-tetra-*O*-benzyl-D-gulucopyranose (**1**) (48.3 mg, 0.089 mmol) in dry CH_2Cl_2 (1.0 mL) were added trichloroacetyl chloride (21.9 μL, 0.200 mmol) and pyridine (23.3 μL, 0.300 mmol). After reaction mixture was stirred at room temperature for 2 h, the solvent was evaporated in vacuo with toluene as an azeotropic solvent. The crude product was purified by flash column chromatography (hexane/AcOEt=10/1) to afford **2** (57.2 mg, 0.096 mmol, 96%, α/β=83/17) as yellow syrup. The anomeric ratio was determined by ^{1}H NMR (400 MHz). α: R_f=0.56 (hexane/AcOEt=2/1); $[\alpha]_D^{23}$ +58.4 (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.34–7.25 (m, 18H, Ph–H), 7.17–7.13 (m, 2H, Ph–H), 6.37 (d, *J*=3.5 Hz, 1H, 1-H), 4.92 (d, *J*=11.0 Hz, 1H, $-CH_2Ph$), 4.85 (d, *J*=10.8 Hz, 1H, $-CH_2Ph$), 4.82 (d, *J*=10.8 Hz, 1H, $-CH_2Ph$), 4.72 (d, *J*=11.5 Hz, 1H, $-CH_2Ph$), 4.68 (d, *J*=11.5 Hz, 1H, $-CH_2Ph$), 4.60 (d, *J*=11.9 Hz, 1H, $-CH_2Ph$), 4.52 (d, *J*=11.0 Hz, 1H, $-CH_2Ph$), 4.48 (d, *J*=11.9 Hz, 1H, $-CH_2Ph$), 3.96 (t, *J*=9.4 Hz, 1H, 3-H), 3.95 (ddd, *J*=10.0, 2.5, 2.0 Hz, 1H, 5-H), 3.78 (dd, *J*=10.0, 9.4 Hz, 1H, 4-H), 3.77 (dd, *J*=11.0, 2.5 Hz, 1H, 6-H), 3.76 (dd, *J*=9.4, 3.5 Hz, 1H, 2-H), 3.66 (dd, *J*=11.0, 2.0 Hz, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 160.34, 138.29, 137.79, 137.59, 137.37, 128.43, 128.42, 128.37, 128.28, 128.16, 128.04, 127.97, 127.93, 127.91, 127.85, 127.81, 127.70, 95.68 (C-1), 89.78 ($-CCl_3$), 81.04 (C-3), 78.84 (C-2), 76.40 (C-4), 75.69 ($-CH_2Ph$), 75.40 ($-CH_2Ph$), 73.85 (C-5), 73.51 ($-CH_2Ph$), 73.46 ($-CH_2Ph$), 67.68 (C-6); IR (NaCl) cm^{-1} *ν*: 3030.6, 2923.6, 3867.6, 1771.3, 1496.5, 1454.1, 1361.5, 1241.0, 1072.2; HR-MS (FAB-pos, NBA matrix) *m*/*z* 709.1323 $[M]^+$, calcd for $C_{36}H_{35}O_7Cl_3$: 709.1325 [M].

*4.2.2. Typical procedure for glycosylation of 2,3,4,6-tetra-O-benzyl-D-glucopyranosyl N-trichloroacetylcarbamate to obtain disaccharide; methyl 2,3,4-tri-O-benzoyl-6-O-(2,3,4,6-tetra-O-benzyl-α,β-D-glucopyranosyl)-α-D-glucopyranoside (**4α** and **4β**) (Table 1, entry 11).* To a stirred suspension of MS 5 Å (101.3 mg, MS 5 Å/acceptor=3 g/1 mmol), **2** (30.7 mg, 0.0403 mmol), and acceptor **3** (17.4 mg, 0.0336 mmol) in dry CH_2Cl_2 (1.5 mL) was added TMSOTf (2.0 μL, 0.0067 mmol) at 0 °C. After the reaction mixture was stirred at 0 °C for 30 min, the reaction was quenched by adding satd $NaHCO_3$ solution and the mixture was filtered though Celite pad. The filtrate was extracted with AcOEt, and the combined organic extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by preparative TLC (silica gel, 10/1 benzene/AcOEt) to afford known disaccharide **4** (31.1 mg, 0.0302 mmol, 83%, α/β=60/40) as colorless oil. The anomeric ratio was determined by ^{1}H NMR (300 MHz).

Compound **4α**: R_f=0.44 (hexane/AcOEt=4/1×4); ^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 7.99–7.93 (m, 4H, Ph–H), 7.88–7.84 (m, 2H, Ph–H), 7.54–7.11 (m, 29H, Ph–H), 6.14 (t, *J*=9.7 Hz, 1H, 3-H), 5.52 (dd, *J*=10.4, 9.7 Hz, 1H, 4-H), 5.24–5.19 (m, 2H, 1-H, 2-H), 4.91 (d, *J*=11.0 Hz, 1H, $-CH_2Ph$), 4.82 (d, *J*=11.0 Hz, 1H, $-CH_2Ph$), 4.77 (d, *J*=11.0 Hz, 1H, $-CH_2Ph$), 4.76 (d, *J*=12.3 Hz, 1H, $-CH_2Ph$), 4.74 (d, *J*=3.5 Hz, 1H, 1′-H), 4.62 (d, *J*=12.3 Hz, 1H, $-CH_2Ph$), 4.54 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.45 (d, *J*=11.0 Hz, 1H, $-CH_2Ph$), 4.37 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.32 (ddd, *J*=10.4, 6.7, 2.1 Hz, 1H, 5-H), 3.96 (t, *J*=9.2 Hz, 1H, 3-H), 3.88–3.83 (m, 2H, 6-H), 3.66–3.61 (m, 2H, 4′-H, 5′-H), 3.58 (dd, *J*=11.0, 2.5 Hz, 1H, 6′-H), 3.53 (dd, *J*=9.7, 3.5 Hz, 1H, 2′-H), 3.50 (dd, *J*=11.0, 2.1 Hz, 1H, 6′-H), 3.43 (s, 3H, $-OCH_3$).

Compound **4β**: R_f=0.53 (hexane/AcOEt=4/1×4); ^{1}H NMR (300 MHz, $CDCl_3$), *δ*: 7.99–7.91 (m, 4H, Ph–H), 7.86–7.83 (m, 2H, Ph–H), 7.54–7.12 (m, 29H, Ph–H), 6.17 (t, *J*=9.7 Hz, 1H, 3-H), 5.47 (t, *J*=9.7 Hz, 1H, 4-H), 5.25 (dd, *J*=9.7, 3.5 Hz, 1H, 2-H), 5.20 (d, *J*=3.5 Hz, 1H, 1-H), 5.06 (d, *J*=10.8 Hz, 1H, $-CH_2Ph$), 4.91 (d, *J*=11.0 Hz, 1H, $-CH_2Ph$), 4.80 (d, *J*=11.0 Hz, 1H, $-CH_2Ph$), 4.76 (d, *J*=11.0 Hz, 1H, $-CH_2Ph$), 4.68 (d, *J*=10.8 Hz, 1H, $-CH_2Ph$), 4.53 (d, *J*=12.3 Hz, 1H, $-CH_2Ph$), 4.51 (d, *J*=11.0 Hz, 1H, $-CH_2Ph$), 4.47 (d, *J*=7.8 Hz, 1H, 1′-H), 4.43 (d, *J*=12.3 Hz, 1H, $-CH_2Ph$), 4.41–4.34 (m, 1H, 5′-H), 4.12 (dd, *J*=11.0, 2.1 Hz, 6-H), 3.81 (dd, *J*=11.0, 7.5 Hz, 6-H), 3.67–3.56 (m, 4H, 2′-H, 3′-H, 4′-H, 5′-H), 3.48–3.43 (m, 2H, 6′-H), 3.37 (s, 3H, $-OCH_3$).

4.3. Development of sequential one-pot glycosylation

*4.3.1. 2,3,4-Tri-O-benzyl-6-O-p-methoxybenzyl-α,β-D-glucopyranosyl trichloroacetate (**10α** and **10β**).* To a stirred solution of 2,3,4,6-tetra-*O*-benzyl-α,β-D-gulucopyranose (**9**) (50.0 mg, 0.088 mmol) in dry CH_2Cl_2 were added trichloroacetyl chloride (19.1 μL, 0.175 mmol) and pyridine (21.2 μL, 0.263 mmol). After reaction mixture was stirred at room temperature for 3 h, the solvent was evaporated in vacuo with toluene as an azeotropic solvent. The crude product was purified by flash column chromatography (hexane/AcOEt=10/1) to afford **10** (57.9 mg, 0.081 mmol, 92%, α/β=71/29) as yellow syrup. The anomeric ratio was determined by ^{1}H NMR (400 MHz).

Compound **10α**: R_f=0.67 (hexane/AcOEt=3/1); $[\alpha]_D^{31}$ +46.0 (*c* 1.03, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.28–7.17 (m, 15H, Ph–*H*), 7.11–7.05 (m, 2H, Ph–*H*), 6.82–6.77 (m, 2H, Ph–*H*), 6.32 (d, *J*=3.4 Hz, 1H, 1-H), 4.87 (d, *J*=10.9 Hz, 1H, $-CH_2Ph$), 4.78 (d, *J*=10.4 Hz, 1H, $-CH_2Ph$), 4.77 (d, *J*=10.9 Hz, 1H, $-CH_2Ph$), 4.67 (d, *J*=11.6 Hz, 1H, $-CH_2Ph$), 4.63 (d, *J*=11.6 Hz, 1H, $-CH_2Ph$), 4.51 (d,

J=11.6 Hz, 1H, −CH_2Ph), 4.43 (d, J=10.4 Hz, 1H, −CH_2Ph), 4.35 (d, J=11.6 Hz, 1H, −CH_2Ph), 3.91 (t, J=9.5 Hz, 1H, 3-H), 3.49 (ddd, J=10.0, 2.7, 1.8 Hz, 1H, 5-H), 3.72 (dd, J=10.0, 9.5 Hz, 1H, 4-H), 3.72 (s, 3H, −OCH_3), 3.71 (dd, J=9.5, 3.4 Hz, 1H, 2-H), 3.69 (dd, J=11.1, 2.7 Hz, 1H, 6-H), 3.69 (dd, J=11.1, 1.8 Hz, 1H, 6-H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.34, 159.35, 138.33, 137.82, 137.39, 129.70, 129.61, 128.46, 128.41, 128.38, 128.37, 128.02, 127.98, 127.97, 127.94, 127.93, 127.89, 127.70, 113.82, 95.72 (C-1), 89.79 (−CCl$_3$), 81.06 (C-3), 78.81 (C-2), 76.40 (C-4), 75.68 (−CH$_2$Ph), 75.38 (−CH$_2$Ph), 73.83 (C-5), 73.46 (−CH$_2$Ph), 73.12 (−CH$_2$Ph), 67.17 (C-6), 55.20 (−OCH$_3$); IR (NaCl) cm^{-1} ν: 3030.6, 2909.1, 1770.3, 1512.9, 1245.8, 1072.2; HR-MS (FAB-pos, NBA matrix) m/z 739.1419[M]$^+$, calcd for $C_{37}H_{37}O_8Cl_3$: 739.1431 [M].

*4.3.2. 2,3,4-Tri-O-benzyl-α,β-D-glucopyranosyl trichloroacetate (**6**).* To a solution of **10** (50.0 mg, 0.065 mmol) in CH_2Cl_2 (616 μL) and H_2O (34 μL) at ambient temperature was added DDQ (22.1 mg, 0.098 mmol) in one portion. The reaction mixture was stirred at ambient temperature for 3 h. After this mixture was diluted with CH_2Cl_2 (1 mL), the resultant mixture was filtered through Celite pad, rinsed with CH_2Cl_2 (10 mL). The resultant mixture was washed with satd aq $NaHCO_3$ (20 mL). This satd aq $NaHCO_3$ layer was extracted with CH_2Cl_2 (20 mL). The combined organic layer was dried with sodium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (hexane/AcOEt=3/1→1/1) afforded **6** (39.3 mg, 0.060 mmol, 93%, α/β=53/47) as a colorless oil.

Compound **6α**: R_f=0.33 (hexane/AcOEt=2/1); $[\alpha]_D^{26}$ +61.5 (c 1.03, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38–7.25 (m, 15H, Ph−H), 6.29 (d, J=3.5 Hz, 1H, 1-H), 4.94 (d, J=11.0 Hz, 1H, −CH_2Ph), 4.90 (d, J=11.0 Hz, 1H, −CH_2Ph), 4.85 (d, J=11.0 Hz, 1H, −CH_2Ph), 4.71–4.66 (m, 3H, −CH_2Ph), 3.99 (t, J=9.4 Hz, 1H, 3-H), 3.85 (dt, J=10.0, 2.9 Hz, 1H, 5-H), 3.81 (dd, J=12.5z, 2.9 Hz, 1H, 6-H), 3.74 (dd, J=12.5, 2.9 Hz, 1H, 6-H), 3.71 (dd, J=9.4, 3.5 Hz, 1H, 2-H), 3.67 (dd, J=10.0, 9.4 Hz, 1H, 4-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:160.44, 138.19, 137.65, 137.31, 128.54, 128.47, 128.37, 128.19, 128.08, 128.01, 127.97, 127.88, 127.73, 95.39 (C-1), 89.68 (−CCl$_3$), 80.89 (C-3), 78.88 (C-2), 78.91 (C-4), 75.68 (−CH$_2$Ph), 75.34 (−CH$_2$Ph), 74.54 (C-5), 73.52 (−CH$_2$Ph), 61.06 (C-6); IR (NaCl) cm^{-1} ν: 3448.1, 2924.5, 1771.3, 1240.0, 1072.2; HR-MS (FAB-pos, NBA matrix) m/z 617.0861 [M]$^+$, calcd for $C_{29}H_{29}O_7Cl_3$: 617.0877 [M].

*4.3.3. Methyl 2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzyl-α-D-glucopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-α-D-glucopyranoside (**8αα**) (Table 5, entry 3).* To a stirred suspension of MS 5 Å (103.6 mg, MS 5 Å/acceptor=3 g/1 mmol), **5** (30.6 mg, 0.0412 mmol), and acceptor **6** (41.4 mg, 0.0618 mmol) in dry Et_2O (1.5 mL) was added TMSOTf (12 μL, 0.0618 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 4 h. A solution of acceptor **3** (42.3 mg, 0.0824 mmol) in Et_2O was added, and then reaction temperature was allowed to raise up to ambient temperature. The reaction mixture was stirred at that temperature and warmed up to 40 °C, and stirred for 24 h. The reaction mixture was quenched by adding satd $NaHCO_3$ solution, and filtered through Celite pad. The filtrate was extracted with AcOEt, and the combined organic extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by preparative TLC (hexane/AcOEt=2/1), (toluene/AcOEt=10/1×4) to afford trisaccharide **8** (43.6 mg, 0.0298 mmol, 72%, αα/αβ/βα/ββ=75/10/9/6, two steps) as colorless oil. The anomeric ratio was determined by HPLC analysis [Senshu Pak PEGASIL Silica 60–5 (4.6ø×250 mm), hexane/AcOEt=3/2, UV at 254 nm, flow rate; 0.2 mL/min, 0 °C].

Compound **8αα**: R_f=0.29 (hexane/AcOEt=2/1), 0.47 (toluene/AcOEt=10/1×4); $[\alpha]_D^{25}$ +31.5 (c 1.10, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6) δ: 8.29–8.25 (m, 2H, Ph−H), 8.19–8.16 (m, 2H, Ph−H), 8.14–8.11 (m, 2H, Ph−H), 7.52–6.87 (m, 44H, Ph−H), 6.78 (t, J=10.0 Hz, 1H, 3-H), 6.23 (t, J=10.0 Hz, 1H, 4-H), 5.60 (dd, J=10.0, 3.8 Hz, 1H, 2-H), 5.43 (d, J=3.8 Hz, 1H, 1-H), 5.28 (d, J=3.5 Hz, 1H, 1″-H), 5.26 (d, J=11.0 Hz, 1H, −CH_2Ph), 5.20 (d, J=11.0 Hz, 1H, −CH_2Ph), 5.16 (d, J=11.0 Hz, 1H, −CH_2Ph), 5.11 (d, J=11.0 Hz, 1H, −CH_2Ph), 5.02 (d, J=11.0 Hz, 1H, −CH_2Ph), 5.00 (d, J=11.0 Hz, 1H, −CH_2Ph), 4.99 (d, J=11.0 Hz, 1H, −CH_2Ph), 4.95 (d, J=3.8 Hz, 1H, 1′-H), 4.78 (d, J=11.0 Hz, 1H, −CH_2Ph), 4.70 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.65 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.60 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.57 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.55 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.50–4.37 (m, 2H, 3′-H, 5-H), 4.48 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.41 (t, J=10.0 Hz, 1H, 3″-H), 4.16–4.08 (m, 4H, 4′-H, 5′-H, 6′-H, 5″-H), 4.05 (dd, J=11.0, 5.0 Hz, 1H, 6-H), 3.96 (dd, J=10.0, 8.0 Hz, 1H, 4″-H), 3.90–3.86 (m, 1H, 6′-H), 3.84 (dd, J=11.0 Hz, 4.0 Hz, 1H, 6″-H), 3.73 (dd, J=11.0, 2.0 Hz, 1H, 6″-H), 3.70 (dd, J=11.0, 1.0 Hz, 1H, 6-H), 3.69 (dd, J=10.0, 3.5 Hz, 1H, 2″-H), 3.64 (dd, J=10.0, 3.8 Hz, 1H, 2′-H), 3.23 (s, 3H, −OCH_3); ^{13}C NMR (100 MHz, C_6D_6) δ: 166.7 (−COPh), 166.3 (−COPh), 165.8 (−COPh), 140.3, 140.2, 139.9, 139.7, 139.7, 139.5, 133.6, 133.3, 130.6, 130.6, 130.4, 130.2, 130.1, 129.1, 129.0, 129.0, 128.9, 128.9, 128.9, 128.8, 128.8, 128.5, 128.3, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 98.1 (C-1′), 97.9 (C-1), 97.8 (C-1″), 82.6 (C-3′), 82.5 (C-3″), 81.6 (C-2′), 81.6 (C-2″), 78.8 (C-4″), 78.5 (C-4′), 76.0 (−CH$_2$Ph), 75.9 (−CH$_2$Ph), 75.6 (−CH$_2$Ph), 75.5 (−CH$_2$Ph), 73.9 (−CH$_2$Ph), 73.3 (−CH$_2$Ph), 73.2 (C-2), 72.9 (−CH$_2$Ph), 71.9 (C-5′), 71.8 (C-3), 71.6 (C-5″), 70.3 (C-4), 69.9 (C-6″), 69.8 (C-5), 66.9 (C-6), 66.1 (C-6′), 55.7 (−OCH_3); HR-MS (FAB, NBA matrix) m/z 1483.5774 [M]$^+$, calcd for $C_{89}H_{88}O_{19}Na$: 1483.5818 [M].

Compound **8αβ**: R_f=0.29 (hexane/AcOEt=2/1), 0.44 (toluene/AcOEt=10/1×4); $[\alpha]_D^{27}$ +26.1 (c 1.10, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6) δ: 8.29–8.26 (m, 2H, Ph−H), 8.16–8.10 (m, 4H, Ph−H), 7.67–7.64 (m, 1H, Ph−H), 7.60–7.58 (m, 1H, Ph−H), 7.49–6.90 (m, 42H, Ph−H), 6.81 (t, J=10.0 Hz, 1H, 3-H), 6.06 (t, J=10.0 Hz, 1H, 4-H), 5.69 (dd, J=10.0, 3.8 Hz, 1H, 2-H), 5.44 (d, J=3.8 Hz, 1H each, 1-H, 1″-H), 5.24 (d, J=11.0 Hz, 1H, −CH_2Ph), 5.22 (d, J=11.0 Hz, 1H, −CH_2Ph), 5.12 (d, J=11.0 Hz, 1H, −CH_2Ph), 5.11 (d, J=11.0 Hz, 1H, −CH_2Ph), 5.10 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.99 (d, J=11.0 Hz, 1H, −CH_2Ph), 4.94 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.93 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.92 (d, J=11.0 Hz, 1H, −CH_2Ph), 4.80 (d, J=11.0 Hz, 1H, −CH_2Ph), 4.76 (d, J=11.0 Hz, 1H, −CH_2Ph), 4.70 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.61 (d, J=7.5 Hz, 1H, 1′-H), 4.53 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.48 (ddd, J=10.0, 6.0, 2.0 Hz, 1H, 5-H), 4.44 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.39 (t, J=9.0 Hz, 1H, 3″-H), 4.30 (dd, J=11.0, 2.0 Hz, 6-H), 4.18 (ddd, J=10.0, 4.0, 2.0 Hz, 1H, 6-H), 4.10–4.05 (m, 2H, 4′-H, 6′-H), 4.00 (dd, J=12.0, 1.5 Hz, 1H, 6′-H), 3.95 (dd, J=11.0, 6.0 Hz, 1H, 6-H), 3.90 (dd, J=10.0, 9.0 Hz, 1H, 4″-H), 3.86 (dd, J=10.0, 4.0 Hz, 1H, 6″-H), 3.79 (dd, J=9.0, 6.0 Hz, 1H, 3′-H), 3.77 (dd, J=10.0, 2.0 Hz, 1H, 6″-H), 3.71 (dd, J=9.0, 3.8 Hz, 1H, 2″-H), 3.60 (dd, J=9.0, 7.5 Hz, 1H, 2′-H), 3.40 (ddd, J=9.0, 3.0, 1.5 Hz, 1H, 5′-H), 3.22 (s, 1H, −OCH_3); ^{13}C NMR (100 MHz, C_6D_6) δ: 166.6 (−COPh), 166.4 (−COPh), 166.0 (−COPh), 140.2, 140.0, 139.9, 139.7, 139.7, 139.4, 130.6, 130.5, 130.4, 130.1, 130.0, 130.0, 129.1, 129.1, 128.9, 128.9, 128.9, 128.8, 128.8, 128.7, 128.6, 128.3, 128.3, 128.0, 128.0, 127.9, 127.8, 104.6 (C-1′), 98.0 (C-1″), 97.9 (C-1), 85.3 (C-6″), 83.3 (C-2′), 82.5 (C-3″), 81.6 (C-2″), 78.8 (C-4″), 78.0 (C-4′), 76.1 (C-5′), 75.9 (−CH$_2$Ph), 75.9 (−CH$_2$Ph), 75.5 (−CH$_2$Ph), 75.4 (−CH$_2$Ph), 75.3 (−CH$_2$Ph), 73.9 (−CH$_2$Ph), 73.0 (C-2), 72.7 (−CH$_2$Ph), 71.7 (C-3), 71.6 (C-5″), 70.7 (C-4), 70.2 (C-5), 70.0 (C-3′), 68.7 (C-6′), 66.2 (C-6), 55.8 (−OCH_3). HR-MS (FAB, NBA matrix) m/z 1483.5787 [M]$^+$, calcd for $C_{89}H_{88}O_{19}Na$: 1483.5818 [M].

Compound **8ββ**: R_f=0.35 (hexane/AcOEt=2/1), 0.32 (toluene/AcOEt=10/1×4); $[\alpha]_D^{26}$ +21.0 (c 0.85, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6) δ: 8.28–8.25 (m, 2H, Ph−H), 8.14–8.10 (m, 4H, Ph−H), 7.62–7.58 (m, 4H, Ph−H), 7.53–7.50 (m, 2H, Ph−H), 7.46–7.40 (m, 4H, Ph−H), 7.36–6.86 (m, 34H, Ph−H), 6.79 (t, J=10.0 Hz, 1H, 3-H), 5.95 (t, J=10.0 Hz, 1H, 4-H), 5.66 (dd, J=10.0, 3.8 Hz, 1H, 2-H), 5.39 (d, J=3.8 Hz, 1H, 1-H), 5.30 (d, J=11.5 Hz, 1H, −CH_2Ph), 5.26 (d, J=11.5 Hz, 1H, −CH_2Ph), 5.25 (d, J=11.5 Hz, 1H, −CH_2Ph), 5.10 (d, J=11.5 Hz, 1H, −CH_2Ph), 5.08 (d, J=11.5 Hz, 1H, −CH_2Ph), 5.02 (d, J=11.5 Hz, 1H,

−CH_2Ph), 4.95 (d, J=11.5 Hz, 1H, −CH_2Ph), 4.91 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.88 (d, J=11.5 Hz, 1H, −CH_2Ph), 4.87 (d, J=11.5 Hz, 1H, −CH_2Ph), 4.74 (d, J=8.0 Hz, 1H, 1′-H), 4.71 (d, J=11.5 Hz, 1H, −CH_2Ph), 4.68 (d, J=7.8 Hz, 1H, 1″-H), 4.63 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.61 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.55 (d, J=12.0 Hz, 1H, −CH_2Ph), 4.54 (ddd, J=10.0, 6.0, 3.0 Hz, 1H, 5-H), 4.41 (dd, J=11.5, 3.0 Hz, 1H, 6-H), 4.39 (dd, J=11.0, 2.0 Hz, 1H, 6″-H), 3.99 (dd, J=11.5, 6.0 Hz, 1H, 6-H), 3.94 (t, J=9.0 Hz, 1H, 3′-H), 3.93 (dd, J=11.0, 6.0 Hz, 1H, 6″-H), 3.90−3.83 (m, 3H, 4′-H), 3.80 (t, J=9.0 Hz, 1H, 3″-H), 3.73 (dd, J=9.0, 8.0 Hz, 1H, 2′-H), 3.70−3.67 (m, 1H, 5″-H), 3.68 (dd, J=9.0, 7.8 Hz, 1H, 2″-H), 3.61 (t, J=9.0 Hz, 1H, 4″-H), 3.61−3.57 (m, 1H, 5′-H), 3.20 (s, 3H, −OCH_3); ^{13}C NMR (100 MHz, C_6D_6) δ: 166.6 (−COPh), 166.3 (−COPh), 166.0 (−COPh), 140.1, 139.9, 139.9, 139.8, 139.7, 139.5, 139.4, 133.6, 133.3, 130.6, 130.6, 130.3, 130.2, 130.0, 130.0, 129.0, 129.0, 128.9, 128.9, 128.8, 128.8, 128.7, 128.4, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 105.0 (C-1′), 104.5 (C-1″), 97.7 (C-1), 85.6 (C-3′), 85.4 (C-3″), 83.2 (C-2″), 83.1 (C-2′), 79.0 (C-4″), 78.8 (C-4′), 76.0 (−CH_2Ph, C-5″), 75.9 (−CH_2Ph), 75.7 (C-5′), 75.4 (−CH_2Ph), 75.3 (−CH_2Ph), 75.2 (−CH_2Ph), 75.1 (−CH_2Ph), 74.0 (−CH_2Ph), 73.0 (C-2), 71.7 (C-3), 71.2 (C-4), 70.0 (C-5), 69.9 (C-6′), 69.4 (C-6″), 69.1 (C-6), 55.8 (−OCH_3); HR-MS (FAB, NBA matrix) m/z 1483.5774 $[M+Na]^+$, calcd for $C_{89}H_{88}O_{19}Na$: 1483.5818 [M].

4.4. Sequential one-pot glycosylation with galactose

*4.4.1. Glycosylation with galactosyl carbamate **12**: methyl 2,3,4-tri-O-benzoyl-6-O-(2,3,4,6-tetra-O-benzyl-α,β-D-galactopyranosyl)-α-D-galactopyranoside (**14**) (Table 6, entry 2).* The glycosylation was performed according to the typical procedure employing the carbamate donor **12** (30.7 mg, 0.0505 mmol), acceptor **13** (21.6 mg, 0.0421 mmol), and TMSOTf (9 μL, 0.0505 mmol) at −20 °C for 2 h. The anomeric mixture of the disaccharide **14** (30.3 mg, 0.0294 mmol, 56%, α/β=68/32) was obtained as a colorless oil after purification by preparative TLC (hexane/AcOEt=2/1).

Compound **14α**: R_f=0.21 (hexane/AcOEt=2/1); $[\alpha]_D^{30}$ −13.1 (c 1.06, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06−8.02 (m, 2H, Ph−H), 8.00−7.96 (m, 2H, Ph−H), 7.80−7.76 (m, 2H, Ph−H), 7.60−7.55 (m, 1H, Ph−H), 7.53−7.47 (m, 1H, Ph−H), 7.46−7.19 (m, 27H, Ph−H), 5.97 (dd, J=10.4, 3.5 Hz, 1H, 3-H), 5.93 (dd, J=3.5, 1.0 Hz, 1H, 4-H), 5.62 (dd, J=10.4, 3.5 Hz, 1H, 2-H), 5.23 (d, J=3.5 Hz, 1H, 1-H), 4.92 (d, J=11.6 Hz, 1H, −CH_2Ph), 4.78 (d, J=11.6 Hz, 1H, −CH_2Ph), 4.77 (d, J=3.5 Hz, 1H, 1′-H), 4.72 (d, J=11.6 Hz, 1H, −CH_2Ph), 4.70 (d, J=11.9 Hz, 1H, −CH_2Ph), 4.66 (d, J=11.9 Hz, 1H, −CH_2Ph), 4.56 (d, J=11.6 Hz, 1H, −CH_2Ph), 4.50 (d, J=11.9 Hz, 1H, −CH_2Ph), 4.46 (ddd, J=6.7, 5.7, 1.0 Hz, 1H, 5-H), 4.41 (d, J=11.9 Hz, 1H, −CH_2Ph), 4.04 (dt, J=6.7, 1.0 Hz, 1H, 5′-H), 4.01 (dd, J=10.2, 3.5 Hz, 1H, 2′-H), 3.95 (dd, J=2.7, 1.0 Hz, 1H, 4′-H), 3.90 (dd, J=10.2, 2.7 Hz, 1H, 3′-H), 3.79 (dd, J=10.7, 6.7 Hz, 1H, 6-Ha), 3.69 (dd, J=10.7, 5.7 Hz, 1H, 6-Hb), 3.51 (br d, J=6.7 Hz, 2H, 6′-H), 3.35 (s, 3H, −OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.1 (−OCOPh), 165.6 (−OCOPh), 165.4 (−OCOPh), 138.8, 138.6, 138.5, 138.1, 133.4, 133.3, 133.0, 129.9, 139.8, 139.7, 139.4, 139.30, 129.25, 128.6, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 127.6, 127.50, 127.45, 127.4, 98.2 (C-1′), 97.4 (C-1), 78.6 (C-3′), 76.3 (C-2′), 75.1 (C-4′), 74.7 (−CH_2Ph), 73.34 (−CH_2Ph), 73.31 (−CH_2Ph), 72.9 (−CH_2Ph), 69.63 (2C, C-5′, C-4), 69.60 (C-2), 68.8 (C-6′), 68.4 (C-3), 67.7 (C-5), 66.8 (C-6), 55.5 (−OCH_3), IR (NaCl) cm^{-1} ν: 2924.5, 1727.9, 1601.6, 1494.6, 1453.1, 1282.4, 1095.4; HR-MS (FAB-pos, NBA matrix) m/z 1051.3881 $[M+Na]^+$, calcd for $C_{62}H_{60}O_{14}Na$: 1051.3871 [M+Na].

Compound **14β**: R_f=0.20 (hexane/AcOEt=2/1); $[\alpha]_D^{21}$ +98.8 (c 0.45, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09−8.03 (m, 2H, Ph−H), 8.00−7.95 (m, 2H, Ph−H), 7.80−7.76 (m, 2H, Ph−H), 7.64−7.57 (m, 1H, Ph−H), 7.54−7.18 (m, 28H, Ph−H), 5.95 (dd, J=10.7, 3.5 Hz, 1H, 3-H), 5.90 (dd, J=3.5, 1.0 Hz, 1H, 4-H), 5.64 (dd, J=10.7, 3.5 Hz, 1H, 2-H), 5.27 (d, J=3.5 Hz, 1H, 1-H), 5.00 (d, J=10.7 Hz, 1H, −CH_2Ph), 4.93 (d, J=11.7 Hz, 1H, −CH_2Ph), 4.74 (d, J=10.7 Hz, 1H, −CH_2Ph), 4.73 (d, J=11.9 Hz, 1H, −CH_2Ph), 4.69 (d, J=11.9 Hz, 1H, −CH_2Ph), 4.60 (d, J=11.7 Hz, 1H, −CH_2Ph), 4.50 (br dd, J=8.2, 3.5 Hz, 1H, 5-H), 4.40 (d, J=11.7 Hz, 1H, −CH_2Ph), 4.37 (d, J=7.8 Hz, 1H, 1′-H), 4.35 (d, J=11.7 Hz, 1H, −CH_2Ph), 4.04 (dd, J=10.7, 3.5 Hz, 1H, 6′-Ha), 3.89 (br d, J=2.9 Hz, 1H, 4′-H), 3.83 (dd, J=9.8, 7.8 Hz, 1H, 2′-H), 3.77 (dd, J=10.7, 8.2 Hz, 1H, 6′-Hb), 3.57−3.48 (m, 3H, 5-H, 6-H), 3.49 (dd, J=9.8, 2.9 Hz, 1H, 3′-H), 3.38 (s, 3H, −OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.1 (−OCOPh), 165.5 (−OCOPh), 165.4 (−OCOPh), 138.7, 138.6, 138.5, 137.8, 133.4, 133.3, 133.0, 129.9, 129.8, 129.7, 129.33, 129.27, 129.2, 128.6, 128.41, 128.39, 128.32, 128.25, 128.2, 128.1, 127.9, 127.8, 127.6, 127.52, 127.49, 104.2 (C-1′), 97.4 (C-1), 81.9 (C-3′), 79.6 (C-2′), 75.2 (−CH_2Ph), 74.5 (−CH_2Ph), 73.5 (−CH_2Ph), 73.3 (C-4′), 73.4 (C-5), 72.9 (−CH_2Ph), 69.9 (C-4), 69.6 (C-2), 68.9 (C-6′), 68.7 (2C, C-3, C-6), 68.3 (C-5′), 55.6 (−OCH_3); IR (NaCl) cm^{-1} ν: 2869.6, 1726.9, 1600.6, 1452.1, 1283.4, 1094.4. HR-MS (FAB-pos, NBA matrix) m/z 1051.3881 $[M+Na]^+$, calcd for $C_{62}H_{60}O_{14}Na$: 1051.3870 [M+Na].

*4.4.2. 2,3,4,6-Tetra-O-benzyl-α,β-D-galactopyranosyl trichloroacetate (**15**).* To a stirred solution of 2,3,4,6-tetra-O-benzyl-D-galactopyranose (**11**) (43.3 mg, 0.080 mmol) in dry CH_2Cl_2 were added trichloroacetyl chloride (15.0 μL, 0.138 mmol) and pyridine (15.0 μL, 0.184 mmol). After the reaction mixture was stirred at room temperature for 1 h, the solvent was evaporated in vacuo with toluene as an azeotropic solvent. The crude product was purified by column chromatography (hexane/AcOEt=5/1) to give **15** (52.9 mg, 0.089 mmol, 97%, α/β=67/33) as a yellow oil. The anomeric ratio was determined by ^{1}H NMR (400 MHz).

Compound **15α**: R_f=0.71 (hexane/AcOEt=2/1); $[\alpha]_D^{26}$ +53.5 (c 1.09, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40−7.26 (m, 20H, Ph−H), 6.42 (d, J=3.3 Hz, 1H, 1-H), 4.99 (d, J=11.3 Hz, 1H, −CH_2Ph), 4.81 (d, J=11.9 Hz, 1H, −CH_2Ph), 4.75 (d, J=11.9 Hz, 1H, −CH_2Ph), 4.75 (br d, 2H, −CH_2Ph), 4.60 (d, J=11.3 Hz, 1H, −CH_2Ph), 4.50 (d, J=11.7 Hz, 1H, −CH_2Ph), 4.43 (d, J=11.7 Hz, 1H, −CH_2Ph), 4.25 (dd, J=9.8, 3.3 Hz, 1H, 2-H), 4.13 (ddd, J=7.2, 5.9, 1.2 Hz, 1H, 5-H), 4.07 (dd, J=2.7, 1.2 Hz, 1H, 4-H), 3.94 (dd, J=9.8, 2.7 Hz, 1H, 3-H), 3.61 (dd, J=9.4, 7.2 Hz, 1H, 6-Ha), 3.57 (dd, J=9.4, 5.9 Hz, 1H, 6-Hb); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.3 (−OCOCCl_3), 138.4, 138.1, 137.8, 137.6, 128.4, 128.34, 128.29, 128.2, 128.1, 128.0, 128.92, 127.88, 127.85, 127.80, 127.75, 127.72, 127.69, 127.62, 127.55, 127.5, 96.6 (C-1), 89.9 (−OCOCCl_3), 77.6 (C-3), 75.3 (C-2), 74.9 (−CH_2Ph), 74.2 (C-4), 73.52 (−CH_2Ph), 73.48 (−CH_2Ph), 73.0 (C-5), 72.9 (−CH_2Ph), 68.1 (C-6); IR (NaCl) cm^{-1} ν: 3030.6, 2920.7, 2869.6, 1771.3, 1496.5, 1454.1, 1240.0, 1106.0; HR-MS (FAB-pos, NBA matrix) m/z 709.1325 $[M+Na]^+$, calcd for $C_{36}H_{35}O_7{}^{35}Cl_2{}^{37}ClNa$: 709.1323 [M+Na].

Compound **15β**: R_f=0.61 (hexane/AcOEt=2/1); $[\alpha]_D^{30}$ +16.8 (c 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41−7.22 (m, 20H, Ph−H), 5.62 (d, J=8.0 Hz, 1H, 1-H), 4.94 (d, J=11.3 Hz, 1H, −CH_2Ph), 4.84−4.72 (m, 4H, −CH_2Ph), 4.63 (d, J=11.3 Hz, 1H, −CH_2Ph), 4.50−4.39 (m, 1H, −CH_2Ph), 4.08 (dd, J=9.6, 8.0 Hz, 1H, 2-H), 4.00 (dd, J=2.9, 1.0 Hz, 1H, 4-H), 3.76 (ddd, J=7.2, 5.7, 1.0 Hz, 1H, 5-H), 3.67 (dd, J=9.4, 7.2 Hz, 1H, 6-Ha), 3.64 (dd, J=9.6, 2.9 Hz, 1H, 3-H), 3.62 (dd, J=9.4, 5.7 Hz, 1H, 6-Hb); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.7 (−OCOCCl_3), 138.3, 137.9, 137.8, 137.6, 128.43, 128.35, 128.3, 128.2, 128.1, 128.0, 127.94, 127.87, 127.80, 127.76, 127.7, 127.6, 98.6 (C-1), 89.4 (−OCOCCl_3), 81.9 (C-3), 77.5 (C-2), 75.4 (−CH_2Ph), 74.9 (−CH_2Ph), 74.8 (C-5), 73.5 (−CH_2Ph), 73.03 (C-4), 72.96 (−CH_2Ph), 67.8 (C-6). IR (NaCl) cm^{-1} ν: 3030.6, 2921.6, 2871.5, 1778.1, 1496.5, 1454.1, 1230.4, 1102.1; HR-MS (FAB-pos, NBA matrix) m/z 709.1325 $[M+Na]^+$, calcd for $C_{36}H_{35}O_7{}^{35}Cl_2{}^{37}ClNa$: 709.1307 [M+Na].

*4.4.3. Glycosylation of galactosyl trichloroacetate **15**: methyl 2,3,4-tri-O-benzoyl-6-O-(2,3,4,6-tetra-O-benzyl-α,β-D-galactopyranosyl)-α-D-galactopyranoside (**14**) (Table 6, entry 5).* The glycosylation was performed according to the typical procedure employing trichloroacetate donor **15** (20.2 mg, 0.034 mmol), acceptor **13** (14.2 mg, 0.028 mmol), and TMSOTf (6 μL, 0.034 mmol) at room

temperature for 14 h. The anomeric mixture of the disaccharide **14** (25.8 mg, 0.0251 mmol, 74%, α/β=73/27) was obtained as a colorless oil after purification by preparative TLC (hexane/AcOEt=2/1).

*4.4.4. Phenyl 2,3,4-tri-O-benzyl-6-O-p-methoxybenzyl-1-thio-β-D-galactopyranoside (**17**)*[22]. To a solution of phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranoside (**16**) (5.87 g, 10.8 mmol) in DMF (100 mL) was added NaH (564 mg, 12.9 mmol, 55% disp.) followed by PMBCl (1.61 mL, 11.9 mmol). The reaction mixture was stirred at room temperature for 6 h, and quenched with H_2O. The resultant mixture was extracted with AcOEt. The combined extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by flash column chromatography (hexane/AcOEt=5/1), followed by recrystallization from EtOH to give **17** (6.87 g, 10.6 mmol, 98%) as a white solid. The anomeric ratio was determined by HPLC analysis; R_f=0.68 (hexane/AcOEt=3/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.60–7.52 (m, 2H, Ph–*H*), 7.41–7.15 (m, 20H, Ph–*H*), 6.88–6.82 (m, 2H, Ph–*H*), 4.96 (d, *J*=11.4 Hz, 1H, –C*H*$_2$Ph), 4.78 (d, *J*=10.3 Hz, 1H, –C*H*$_2$Ph), 4.74 (d, *J*=11.9 Hz, 1H, –C*H*$_2$Ph), 4.73 (d, *J*=10.3 Hz, 1H, –C*H*$_2$Ph), 4.69 (d, *J*=11.9 Hz, 1H, –C*H*$_2$Ph), 4.64 (d, *J*=9.8 Hz, 1H, 1-H), 4.58 (d, *J*=11.4 Hz, 1H, –C*H*$_2$Ph), 4.42 (d, *J*=11.3 Hz, 1H, –C*H*$_2$Ph), 4.35 (d, *J*=11.3 Hz, 1H, –C*H*$_2$Ph), 3.98 (br d, *J*=2.6 Hz, 1H, 4-H), 3.93 (t, *J*=9.8 Hz, 1H, 2-H), 3.79 (s, 3H, –OC*H*$_3$), 3.66–3.55 (m, 4H, 3-H, 5-H, 6-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.1, 138.5, 138.1, 138.0, 133.9, 131.2, 129.7, 129.4, 128.5, 128.1, 128.1, 127.9, 127.5, 127.5, 127.4, 127.3, 127.2, 126.7, 113.6, 87.4 (C-1), 83.9 (C-3), 77.0 (C-5), 76.4 (C-2), 75.4 (–*C*H$_2$Ph), 74.2 (–*C*H$_2$Ph), 73.3 (C-4), 72.9 (–*C*H$_2$Ph), 72.4 (–*C*H$_2$Ph), 68.1 (C-6), 55.0 (–O*C*H$_3$). HR-MS (FAB-pos, NBA matrix) *m*/*z* 685.2607 [M+Na]$^+$, calcd for $C_{41}H_{42}O_6SNa$: 685.2600 [M+Na].

*4.4.5. 2,3,4-Tri-O-benzyl-6-O-p-methoxybenzyl-α,β-D-galactopyranose (**18**).* To a solution of **17** (4.85 g, 7.48 mmol) in acetone (72 mL) and H_2O (3 mL) was added NBS (2.00 g, 11.2 mmol) at −15 °C. The reaction mixture was stirred at −15 °C for 20 min, and diluted with AcOEt to stop the reaction. The resultant mixture was extracted with AcOEt, washed with H_2O, brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by preparative flash column chromatography (hexane/AcOEt=5/1→1/1) to afford **18** (4.05 g, 7.10 mmol, 95%, α/β=57/43) as a white solid. Anomeric ratio was determined by HPLC [Senshu Pak PEGASIL Silica SP 100 (4.6ø×250 mm), hexane/AcOEt=3/1, UV at 254 nm, flow rate; 1.0 mL/min, rt]. Compound **18α**: R_f=0.50 (hexane/AcOEt=1/1); $[\alpha]_D^{31}$ +9.99 (*c* 0.74, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42–7.23 (m, 15H, Ph–*H*), 7.23–7.17 (m, 2H, Ph–*H*), 6.89–6.82 (m, 2H, Ph–*H*), 5.28 (dd, *J*=3.5, 2.2 Hz, 1H, 1-H), 4.92 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 4.83 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 4.79 (d, *J*=11.7 Hz, 1H, –C*H*$_2$Ph), 4.74 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 4.71 (d, *J*=11.7 Hz, 1H, –C*H*$_2$Ph), 4.57 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 4.42 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 4.34 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 4.15 (ddd, *J*=6.8, 6.3, 1.0 Hz, 1H, 5-H), 4.03 (dd, *J*=9.8, 3.5 Hz, 1H, 2-H), 3.96 (dd, *J*=2.7, 1.0 Hz, 1H, 4-H), 3.91 (dd, *J*=9.8, 2.7 Hz, 1H, 3-H), 3.80 (s, 3H, –OC*H*$_3$), 3.51 (dd, *J*=9.2, 6.3 Hz, 1H, 6-H), 3.46 (dd, *J*=9.2, 6.8 Hz, 1H, 6-H), 3.10 (br s, 1H, –O*H*).

Compound **18β**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39–7.25 (m, 15H, Ph–H), 7.22–7.17 (m, 2H, Ph–H), 6.88–6.83 (m, 2H, Ph–H), 4.93 (d, *J*=11.5 Hz, 1H, –CH_2Ph), 4.91 (d, *J*=11.0 Hz, 1H, –CH_2Ph), 4.81 (d, *J*=11.0 Hz, 1H, –CH_2Ph), 4.74–4.71 (m, *J*=2H, –CH_2Ph), 4.66 (dd, *J*=7.2, 6.5 Hz, 1H, 1-H), 4.58 (d, *J*=11.5 Hz, 1H, –CH_2Ph), 4.41 (d, *J*=11.5 Hz, 1H, –CH_2Ph), 4.34 (d, *J*=11.5 Hz, 1H, –CH_2Ph), 3.88 (br d, *J*=2.9 Hz, 1H, 4-H), 3.80 (s, 3H, –OCH_3), 3.75 (dd, *J*=9.8, 7.2 Hz, 1H, 2-H), 3.54 (dd, *J*=9.8, 2.9 Hz, 1H, 3-H), 3.62–3.47 (m, 3H, 5-H, 6-H), 3.06 (d, *J*=6.5 Hz, 1H, –OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.3, 159.2, 138.6, 138.5, 138.4, 138.3, 138.2, 129.61, 129.57, 128.31, 128.30, 128.23, 128.20, 128.16, 128.14, 128.09, 127.9, 127.7, 127.53, 127.52, 127.47, 127.4, 113.74, 113.71, 97.7 (C-1β), 91.8 (C-1α), 82.1 (C-3β), 80.7 (C-2β), 78.7 (C-3α), 76.5 (C-2α), 75.0 (–CH_2Ph), 74.7 (C-4α), 74.6 (–CH_2Ph), 74.5 (–CH_2Ph), 73.5 (C-4β), 73.4 (C-5β), 73.3 (–CH_2Ph), 73.1 (–CH_2Ph), 73.0 (–CH_2Ph), 72.8 (–CH_2Ph, 2C), 69.4 (C-5α), 68.6 (C-6α), 68.5 (C-6β), 55.2 (–OCH_3, 2C). IR (NaCl) cm^{-1} ν: 3417.2, 3029.6, 2911.0, 1612.2, 1512.9, 1454.1, 1098.3; HR-MS (FAB-pos, NBA matrix) *m*/*z* 593.2526 [M+Na]$^+$, calcd for $C_{35}H_{38}O_7Na$: 593.2515 [M+Na].

*4.4.6. 2,3,4-Tri-O-benzyl-6-O-p-methoxybenzyl-α,β-D-galactopyranosyl trichloroacetate (**19**).* To a stirred solution of 2,3,4-tri-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α,β-D-galactopyranoside (**18**) (50.0 mg, 0.088 mmol) in dry CH_2Cl_2 (0.9 mL) were added trichloroacetyl chloride (19.1 μL, 0.175 mmol) and pyridine (21.2 μL, 0.263 mmol). After the reaction mixture was stirred at room temperature for 4 h, the solvent was evaporated in vacuo with toluene as an azeotropic solvent. The crude product was purified by flash column chromatography (hexane/AcOEt=7/1) to afford **19** (62.7 mg, 0.088 mmol, quant, α/β=89/11) as yellow syrup.

Compound **19α**: R_f=0.62 (hexane/AcOEt=2/1); $[\alpha]_D^{24}$ +41.9 (*c* 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37–7.24 (m, 15H, Ph–H), 7.22–7.16 (m, 2H, Ph–H), 6.88–6.82 (m, 2H, Ph–H), 6.38 (d, *J*=3.7 Hz, 1H, 1-H), 4.95 (d, *J*=11.3 Hz, 1H, –CH_2Ph), 4.81–4.68 (m, 4H, –CH_2Ph), 4.56 (d, *J*=11.3 Hz, 1H, –CH_2Ph), 4.41 (d, *J*=11.3 Hz, 1H, –CH_2Ph), 4.34 (d, *J*=11.3 Hz, 1H, –CH_2Ph), 4.22 (dd, *J*=10.0, 3.7 Hz, 1H, 2–-H), 4.09 (ddd, *J*=7.4, 5.7 Hz, 1.0 Hz, 1H, 5-H), 4.03 (dd, *J*=2.7, 1.0 Hz, 1H, 4-H), 3.90 (dd, *J*=10.0, 2.7 Hz, 1H, 3-H), 3.79 (s, 3H, –OCH_3), 3.56 (dd, *J*=9.4, 7.4 Hz, 1H, 6-H), 3.52 (dd, *J*=9.4, 5.7 Hz, 1H, 6-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 160.22, 159.32, 138.26, 138.10, 137.77, 129.62, 129.57, 129.54, 128.40, 128.38, 128.30, 128.25, 128.24, 128.18, 128.07, 127.79, 127.72, 127.67, 127.66, 127.62, 127.59, 127.55, 113.80, 96.62 (C-1), 89.92 (–CCl_3), 77.52 (C-3), 75.29 (C-2), 74.93 (–CH_2Ph), 74.15 (C-4), 73.44 (–CH_2Ph), 73.14 (–CH_2Ph), 72.96 (C-5), 72.78 (–CH_2Ph), 67.64 (C-6), 55.20 (–OCH_3). IR (NaCl) cm^{-1} ν: 3030.5, 2922.5, 2869.5, 1770.3, 1612.2, 1512.9, 1454.1, 1246.8, 1102.1, 1029.8. HR-MS (FAB-pos, NBA matrix) *m*/*z* 739.1429[M]$^+$, calcd for $C_{37}H_{37}O_8Cl_3$: 739.1431 [M].

Compound **19β**: R_f=0.53 (hexane/AcOEt=2/1); $[\alpha]_D^{23}$ +17.5 (*c* 0.97, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.36–7.26 (m, 15H, Ph–H), 7.23–7.18 (m, 2H, Ph–H), 6.89–6.84 (m, 2H, Ph–H), 5.62 (d, *J*=8.0 Hz, 1H, 1-H), 4.94 (d, *J*=11.4 Hz, 1H, –CH_2Ph), 4.84–4.81 (m, 2H, –CH_2Ph), 4.73–4.71 (m, 2H, –CH_2Ph), 4.61 (d, *J*=11.4 Hz, 1H, –CH_2Ph), 4.42 (d, *J*=11.4 Hz, 1H, –CH_2Ph), 4.37 (d, *J*=11.3 Hz, 1H, –CH_2Ph), 4.07 (dd, *J*=9.8, 8.0 Hz, 1H, 2-H), 4.00 (dd, *J*=2.8, 0.9 Hz, 1H, 4-H), 3.80 (s, 3H, –OCH_3), 3.77–3.71 (m, 1H, 5-H), 3.63 (dd, *J*=9.8, 2.8 Hz, 1H, 3-H), 3.69–3.55 (m, 2H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.7, 159.3, 138.3, 137.9, 137.7, 129.64, 129.63, 128.4, 128.3, 128.3, 128.2, 128.0, 127.8, 127.73, 127.71, 127.5, 113.8, 98.5 (C-1), 89.4 (–CCl_3), 81.9 (C-3), 77.5 (C-2), 75.4 (–CH_2Ph), 74.83 (–CH_2Ph), 74.77 (C-5), 73.1 (–CH_2Ph), 73.0 (C-4), 72.9 (–CH_2Ph), 67.4 (C-6), 55.2 (–OCH_3). IR (NaCl) cm^{-1} ν: 2870.5, 1777.1, 1612.2, 1512.9, 1454.1, 1246.8, 1100.2, 1027.0; HR-MS (FAB-pos, NBA matrix) *m*/*z* 739.1431 [M+Na]$^+$, calcd for $C_{37}H_{37}O_8Cl_3Na$: 739.1426 [M+Na].

*4.4.7. 2,3,4-Tri-O-benzyl-α-D-galactopyranosyl trichloroacetate (**20α**).* To a solution of **19α** (128.5 mg, 0.180 mmol) in CH_2Cl_2 (1.8 mL) and H_2O (100 μL) at ambient temperature was added DDQ (62.8 mg, 0.270 mmol) in one portion. The reaction mixture was stirred at ambient temperature for 1 h. After this mixture was diluted with CH_2Cl_2 (20 mL), the resultant mixture was filtered through Celite pad, and rinsed with CH_2Cl_2. The resultant mixture was washed with satd aq $NaHCO_3$. This satd aq $NaHCO_3$ layer was extracted with CH_2Cl_2. The combined organic layer was dried with sodium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (hexane/AcOEt=5/1) afforded **20α** (90.3 mg,

0.152 mmol, 84%) as a colorless oil; R_f=0.35 (hexane/AcOEt=2/1); $[\alpha]_D^{25}$ +72.8 (*c* 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.40–7.27 (m, 15H, Ph–*H*), 6.41 (d, *J*=3.4 Hz, 1H, 1-H), 5.00 (d, *J*=11.6 Hz, 1H, –C*H*$_2$Ph), 4.85 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.77 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.76 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.73 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.67 (d, *J*=11.6 Hz, 1H, –C*H*$_2$Ph), 4.25 (dd, *J*=9.8, 3.4 Hz, 1H, 2-H), 3.97 (dd, *J*=2.8, 1.3 Hz, 1H, 4-H), 3.93 (dd, *J*=9.8, 2.8 Hz, 1H, 3-H), 3.98–3.88 (m, 1H, 5-H), 3.73 (dd, *J*=11.4, 6.3 Hz, 1H, 6-H), 3.52 (dd, *J*=11.4, 5.4 Hz, 1H, 6-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 160.28, 138.05, 137.81, 137.73, 128.59, 128.58, 128.45, 128.37, 128.19, 127.80, 127.79, 127.75, 96.45 (C-1), 89.89 (–CCl_3), 77.68 (C-3), 75.40 (C-2), 74.62 (–CH_2Ph), 74.30 (C-5), 73.97 (C-4), 73.57 (–CH_2Ph), 73.32 (–CH_2Ph), 61.81 (C-6); IR (NaCl) cm^{-1} ν: 3444.2, 3030.6, 2911.0, 1759.4, 1496.5, 1454.1, 1241.0, 1132.0; HR-MS (FAB-pos, NBA matrix) *m*/*z* 617.0861 $[M]^+$, calcd for $C_{29}H_{29}O_7Cl_3$: 617.0877 [M].

*4.4.8. Methyl 2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-O-benzyl-α-D-galactopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-α-D-galactopyranoside (**22αα**) (Table 7, entry 1).* To a stirred suspension of MS 5 Å (123.6 mg, MS 5 Å/acceptor=3 g/1 mmol), **15** (30.1 mg, 0.0412 mmol), and acceptor **20α** (40.5 mg, 0.0618 mmol) in dry Et_2O (1.5 mL) was added TMSOTf (12 μL, 0.0618 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h. A solution of the acceptor **13** (41.7 mg, 0.0824 μmol) in Et_2O was added, and then reaction temperature was allowed to raise up to ambient temperature. The reaction mixture was stirred for 2 h at ambient temperature and, quenched by adding satd $NaHCO_3$ solution and, filtered through Celite pad. The filtrate was extracted with AcOEt, and the combined organic extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by preparative TLC (hexane/AcOEt=2/1), (toluene/AcOEt=8/1) to afford trisaccharide **22** (40.9 mg, 68%, αα/αβ/βα/ββ=44/22/23/11, two steps) as colorless oil. The anomeric ratio was determined by HPLC analysis [Senshu Pak PEGASIL silica SP 100 (4.6ø×250 mm), hexane/AcOEt=4/1, UV at 254 nm, flow rate; 1.0 mL/min, rt].

Compound **22αα**; R_f=0.43 (hexane/AcOEt=2/1); $[\alpha]_D^{31}$ +52.7 (*c* 0.62, $CHCl_3$); ^{1}H NMR (600 MHz, C_6D_6) δ: 8.30–8.26 (m, 2H, Ph–*H*), 8.26–8.22 (m, 2H, Ph–*H*), 8.10–8.07 (m, 2H, Ph–*H*), 7.54–7.37 (m, 15H, Ph–*H*), 7.36–7.17 (m, 21H, Ph–*H*), 7.16–7.12 (m, 2H, Ph–*H*), 7.07–7.02 (m, 2H, Ph–*H*), 6.99–6.94 (m, 2H, Ph–*H*), 6.88–6.83 (m, 2H, Ph–*H*), 6.48 (dd, *J*=10.5, 3.5 Hz, 1H, 3-H), 6.37 (dd, *J*=3.5, 1.0 Hz, 1H, 4-H), 6.28 (dd, *J*=10.5, 3.5 Hz, 1H, 2-H), 5.58 (d, *J*=3.5 Hz, 1H, 1-H), 5.20 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 5.19 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 5.18 (d, *J*=3.5 Hz, 1H, 1″-H), 5.00 (d, *J*=3.5 Hz, 1H, 1′-H), 4.85 (d, *J*=11.5 Hz, 2H, –C*H*$_2$Ph), 4.78 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.75 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.74 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.74 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 4.63 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.62 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.59 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 4.55 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.54 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.44 (d, *J*=11.5 Hz, 1H, –C*H*$_2$Ph), 4.44 (ddd, *J*=7.0, 6.0, 1.0 Hz, 1H, 5″-H), 4.43 (ddd, *J*=7.0, 6.0, 1.0 Hz, 1H, 5′-H), 4.39 (dd, *J*=10.0, 3.5 Hz, 1H, 2″-H), 4.38 (dt, *J*=6.0, 1.0 Hz, 1H, 5-H), 4.33 (dd, *J*=10.0, 3.5 Hz, 1H, 2′-H), 4.32 (dd, *J*=10.0, 3.5 Hz, 1H, 3″-H), 4.31 (dd, *J*=9.0, 6.0 Hz, 1H, 6′-H), 4.22 (dd, *J*=3.5, 1.0 Hz, 1H, 4″-H), 4.21 (dd, *J*=3.5, 1.0 Hz, 1H, 4′-H), 4.16 (dd, *J*=10.5, 6.0 Hz, 1H, 6-H), 4.13 (dd, *J*=10.0, 3.5 Hz, 1H, 3′-H), 4.03 (dd, *J*=9.0, 7.0 Hz, 1H, 6′-H), 4.00 (dd, *J*=9.0, 7.0 Hz, 1H, 6″-H), 3.88 (dd, *J*=10.5, 6.0 Hz, 1H, 6-H), 3.87 (dd, *J*=9.0, 6.0 Hz, 1H, 6″-H), 3.22 (s, 3H, –OC*H*$_3$); ^{13}C NMR (150 MHz, C_6D_6) δ: 166.70 (–O*C*OPh), 166.31 (–O*C*OPh), 166.15 (–O*C*OPh), 140.13, 140.06, 139.93, 139.86, 139.78, 139.36, 133.59, 133.33, 130.63, 130.55, 130.50, 130.35, 130.20, 129.18, 128.97, 128.95, 128.93, 128.89, 128.85, 128.36, 128.82, 128.78, 128.70, 128.64, 128.56, 128.50, 128.48, 128.40, 128.34, 128.32, 128.24, 128.14, 128.12, 128.03, 128.01, 128.00, 127.99, 127.98, 127.93, 127.91, 99.16 (C-1″), 99.13 (C-1′), 98.45 (C-1), 80.15 (C-3″), 79.34 (C-3′), 77.81 (C-2′), 77.80 (C-2″), 76.47 (C-4″), 76.25 (C-4′), 75.69 (–CH_2Ph), 75.59 (–CH_2Ph), 74.06 (–CH_2Ph), 73.96 (–CH_2Ph), 73.64 (–CH_2Ph), 73.37 (–CH_2Ph), 73.36 (–CH_2Ph), 70.75 (C-4), 70.73 (C-2), 70.65 (C-5′), 70.64 (C-5″), 69.45 (C-6″), 69.68 (C-3), 68.57 (C-5), 67.60 (C-6), 67.99 (C-6′), 55.76 (–OCH_3); IR (NaCl) cm^{-1} ν: 3030.6, 2924.5, 1727.9, 1601.6, 1495.5, 1453.1, 1283.4, 1097.3, 1056.8; HR-MS (FAB-pos, NBA matrix) *m*/*z* 1483.5828 $[M]^+$, calcd for $C_{29}H_{29}O_7Cl_3$: 1483.5818 [M].

4.5. Sequential one-pot glycosylation with mannose

*4.5.1. Glycosylation with mannosyl carbamate **24**: methyl 2,3,4-tri-O-benzoyl-6-O-(2,3,4,6-tetra-O-benzyl-α,β-D-mannopyranosyl)-α-D-mannopyranoside (**26**) (Table 8, entry 3).* The glycosylation was performed according to the typical procedure employing carbamate donor **24** (30.0 mg, 0.051 mmol), acceptor **25** (21.3 mg, 0.042 mmol), and TMSOTf (7 μL, 0.050 mmol) at 0 °C for 2 h. The anomeric mixture of a disaccharide **26** (31.7 mg, 0.0316 mmol, 75%, α/β=75/25) was obtained as a colorless oil after purification by preparative TLC (hexane/AcOEt=2/1).

Compound **26α**; R_f=0.40 (hexane/AcOEt=2/1); $[\alpha]_D^{32}$ +50.0 (*c* 1.03, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10–8.06 (m, 2H, Ph–*H*), 7.94–7.90 (m, 2H, Ph–*H*), 7.85–7.81 (m, 2H, Ph–*H*), 7.56–7.50 (m, 1H, Ph–*H*), 7.48–7.38 (m, 4H, Ph–*H*), 7.36–7.21 (m, 22H, Ph–*H*), 7.18–7.13 (m, 2H, Ph–*H*), 5.92 (t, *J*=9.9 Hz, 1H, 4-H), 5.86 (dd, *J*=9.9, 3.2 Hz, 1H, 3-H), 5.63 (dd, *J*=3.2, 1.6 Hz, 1H, 2-H), 4.97 (d, *J*=1.6 Hz, 1H, 1′-H), 4.94 (d, *J*=1.6 Hz, 1H, 1-H), 4.85 (d, *J*=10.8 Hz, 1H, –C*H*$_2$Ph), 4.65 (d, *J*=12.4 Hz, 1H, –C*H*$_2$Ph), 4.61 (d, *J*=12.4 Hz, 1H, –C*H*$_2$Ph), 4.57 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.47 (d, *J*=10.8 Hz, 1H, –C*H*$_2$Ph), 4.41 (d, *J*=12.0 Hz, 2H, –C*H*$_2$Ph), 4.36 (d, *J*=12.0 Hz, 1H, –C*H*$_2$Ph), 4.21–4.15 (m, 1H, 5-H), 3.97 (t, *J*=9.5 Hz, 1H, 4′-H), 3.95 (br d, *J*=10.8 Hz, 1H, 6-Ha), 3.85 (dd, *J*=9.5, 3.2 Hz, 1H, 3′-H), 3.72 (ddd, *J*=10.8, 4.7, 1.4 Hz, 1H, 5′-H), 3.71 (dd, *J*=3.2, 1.6 Hz, 1H, 2′-H), 3.70–3.68 (m, 1H, 6-Hb), 3.67 (dd, *J*=10.8, 4.7 Hz, 1H, 6′-Ha), 3.58 (dd, *J*=10.8, 1.4 Hz, 1H, 6′-Hb), 3.44 (s, 3H, –OC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.5 (–O*C*OPh), 165.44 (–O*C*OPh), 165.35 (–O*C*OPh), 138.6, 138.53, 138.46, 138.4, 133.5, 133.3, 133.1, 129.8, 129.7, 129.4, 129.2, 129.1, 128.6, 128.4, 128.3, 128.2, 128.2, 127.9, 127.7, 127.5, 127.42, 127.36, 98.5 ($^1J_{C,H}$=172.0 Hz, C-1), 98.1 ($^1J_{C,H}$=168.0 Hz, C-1′), 80.1 (C-3′), 75.0 (–CH_2Ph), 74.74 (C-2′), 74.70 (C-4′), 73.2 (–CH_2Ph), 72.5 (–CH_2Ph), 71.9 (C-5′), 71.8 (–CH_2Ph), 70.6 (C-2), 69.9 (C-3), 69.1 (C-5), 69.0 (C-6′), 67.9 (C-4), 66.7 (C-6), 55.4 (–OCH_3); IR (NaCl) cm^{-1} ν: 2914.9, 1729.8, 1601.6, 1452.1, 1264.1, 1097.3; HR-MS (FAB-pos, NBA matrix) *m*/*z* 1051.3881 $[M+Na]^+$, calcd for $C_{62}H_{60}O_{14}Na$: 1051.3884 [M+Na].

Compound **26β**; R_f=0.40 (hexane/AcOEt=2/1); $[\alpha]_D^{30}$ –101.8 (*c* 0.28, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07–8.03 (m, 2H, Ph–*H*), 7.95–7.90 (m, 2H, Ph–*H*), 7.85–7.81 (m, 2H, Ph–*H*), 7.57–7.21 (m, 27H, Ph–*H*), 7.18–7.13 (m, 2H, Ph–*H*), 5.89 (dd, *J*=10.0, 3.1 Hz, 1H, 3-H), 5.83 (dd, *J*=10.0, 9.8 Hz, 1H, 4-H), 5.66 (dd, *J*=3.1, 1.8 Hz, 1H, 2-H), 5.01 (d, *J*=12.3 Hz, 1H, –C*H*$_2$Ph), 5.00 (d, *J*=1.8 Hz, 1H, 1-H), 4.87 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.84 (d, *J*=12.3 Hz, 1H, –C*H*$_2$Ph), 4.52 (d, *J*=12.3 Hz, 1H, –C*H*$_2$Ph), 4.49 (d, *J*=11.0 Hz, 1H, –C*H*$_2$Ph), 4.46 (d, *J*=12.3 Hz, 1H, –C*H*$_2$Ph), 4.44 (d, *J*=12.1 Hz, 1H, –C*H*$_2$Ph), 4.43 (br s, 1H, 1′-H), 4.40 (d, *J*=12.1 Hz, 1H, –C*H*$_2$Ph), 4.35 (ddd, *J*=9.8, 7.2, 1.8 Hz, 1H, 5-H), 4.23 (dd, *J*=11.0, 1.8 Hz, 1H, 6-Ha), 4.03 (br d, *J*=2.9 Hz, 1H, 2′-H), 3.85 (t, *J*=9.6 Hz, 1H, 4′-H), 3.74 (dd, *J*=11.0, 7.2 Hz, 1H, 6-Hb), 3.70 (dd, *J*=11.0, 2.0 Hz, 1H, 6′-Ha), 3.66 (dd, *J*=11.0, 5.5 Hz, 1H, 6′-Hb), 3.48 (s, 3H, –OC*H*$_3$), 3.47 (dd, *J*=9.6, 2.9 Hz, 1H, 3′-H), 3.38 (ddd, *J*=9.6, 5.5, 2.0 Hz, 1H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.7 (–O*C*OPh), 165.6 (–O*C*OPh), 165.4 (–O*C*OPh), 138.7, 138.3, 138.2, 138.1, 133.4, 133.1, 129.8, 129.6, 129.3, 129.1, 128.9, 128.5, 128.4, 128.28, 128.25, 128.1, 128.0, 127.8, 127.60, 127.55, 127.5, 127.4, 102.4 ($^1J_{C,H}$=152.6 Hz, C-1′), 98.4 (C-1), 81.9 (C-3′), 76.0 (C-5′), 75.1 (–CH_2Ph), 74.6 (C-4′), 74.2 (–CH_2Ph), 74.0 (C-2′), 73.4 (–CH_2Ph), 71.2 (–CH_2Ph), 70.6 (C-2), 70.0 (C-3), 69.9 (C-5), 69.4 (C-6′), 69.0 (C-6), 67.2 (C-4), 55.3 (–OCH_3); IR (NaCl)

cm^{-1} ν: 2865.7, 1729.8, 1601.6, 1452.1, 1278.6, 1262.2, 1107.9; HR-MS (FAB-pos, NBA matrix) m/z 1051.3881 [M+Na]$^+$, calcd for $C_{62}H_{60}O_{14}Na$: 1051.3877 [M+Na].

*4.5.2. 2,3,4,6-Tetra-O-benzyl-α,β-D-mannoopyranosyl trichloroacetate (**27**).* To a stirred solution of 2,3,4,6-tetra-*O*-benzyl-D-mannopyranose (**23**) (199.1 mg, 0.370 mmol) in dry CH_2Cl_2 (4 mL) were added trichloroacetyl chloride (60.7 μL, 0.555 mmol) and pyridine (59.5 μL, 0.740 mmol). After the reaction mixture was stirred at room temperature for 1.5 h, the solvent was evaporated in vacuo with toluene as an azeotropic solvent. The crude product was purified by column chromatography (hexane/AcOEt=7/1) to give **27** (227.0 mg, 0.382 mmol, quant, α/β=76/24) as yellow oil. The anomeric ratio was determined by ^{1}H NMR(400 MHz).

Compound **27α**; R_f=0.67 (hexane/AcOEt=3/1); $[\alpha]_D^{23}$ +43.1 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46–7.17 (m, 20H, Ph–H), 6.26 (d, *J*=2.1 Hz, 1H, 1-H), 4.90 (d, *J*=10.6 Hz, 1H, –CH_2Ph), 4.81 (d, *J*=12.2 Hz, 1H, –CH_2Ph), 4.76 (d, *J*=12.2 Hz, 1H, –CH_2Ph), 4.69 (d, *J*=12.0 Hz, 1H, –CH_2Ph), 4.68 (d, *J*=12.0 Hz, 1H, –CH_2Ph), 4.62 (d, *J*=12.0 Hz, 1H, –CH_2Ph), 4.57 (d, *J*=10.6 Hz, 1H, –CH_2Ph), 4.54 (d, *J*=12.0 Hz, 1H, –CH_2Ph), 4.18 (dd, *J*=9.7, 9.4 Hz, 1H, 4-H), 3.92 (ddd, *J*=9.7, 4.4, 1.6 Hz, 1H, 5-H), 3.89 (dd, *J*=9.4, 3.2 Hz, 1H, 3-H), 3.83 (dd, *J*=11.3, 4.4 Hz, 1H, 6-Ha), 3.78 (dd, *J*=3.2, 2.1 Hz, 1H, 2-H), 3.73 (dd, *J*=10.8, 1.4 Hz, 1H, 6-Hb); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.9 (–$OCOCCl_3$), 138.1, 138.0, 137.8, 137.4, 128.44, 128.39, 128.3, 128.2, 128.0, 127.92, 127.89, 127.82, 127.77, 127.6, 96.9 ($^1J_{C,H}$=178.8 Hz, C-1), 89.5 (–$OCOCCl_3$), 78.3 (C-3), 75.3 (2C, C-5, –CH_2Ph), 73.9 (C-4), 73.7 (C-2), 73.4 (–CH_2Ph), 73.0 (–CH_2Ph), 72.6 (–CH_2Ph), 68.4 (C-6).; IR (NaCl) cm^{-1} ν: 3030.6, 2904.3, 2867.6, 1773.2, 1496.5, 1454.1, 1361.5, 1235.2, 1099.2; HR-MS (FAB-pos, NBA matrix) m/z 709.1325 [M+Na]$^+$, calcd for $C_{36}H_{35}O_7{}^{35}Cl_2{}^{37}ClNa$: 709.1323 [M+Na].

Compound **27β**; R_f=0.56 (hexane/AcOEt=3/1); $[\alpha]_D^{24}$ –8.26 (*c* 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.45–7.15 (m, 20H, Ph–H), 5.85 (d, *J*=1.6 Hz, 1H, 1-H), 4.92 (d, *J*=11.9 Hz, 1H, –CH_2Ph), 4.80 (d, *J*=11.2 Hz, 1H, –CH_2Ph), 4.79 (d, *J*=11.9 Hz, 1H, –CH_2Ph), 4.63 (d, *J*=11.9 Hz, 1H, –CH_2Ph), 4.61 (d, *J*=12.1 Hz, 1H, –CH_2Ph), 4.58 (d, *J*=11.2 Hz, 1H, –CH_2Ph), 4.57 (d, *J*=11.9 Hz, 1H, –CH_2Ph), 4.55 (d, *J*=12.1 Hz, 1H, –CH_2Ph), 4.08 (dd, *J*=2.9, 1.6 Hz, 1H, 2-H), 4.03 (t, *J*=7.8 Hz, 1H, 4-H), 3.88 (dd, *J*=10.6, 2.7 Hz, 1H, 6-Ha), 3.79 (dd, *J*=10.6, 5.1 Hz, 1H, 6-Hb), 3.77 (ddd, *J*=7.8, 5.1, 2.7 Hz, 1H, 5-H), 3.71 (dd, *J*=7.8, 2.9 Hz, 1H, 3-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.6 (–$OCOCCl_3$), 138.0, 137.9, 137.83, 137.79, 128.5, 128.39, 128.39, 128.35, 128.32, 128.30, 128.04, 127.99, 127.95, 127.9, 127.83, 127.78, 127.75, 127.74, 127.65, 127.60, 127.56, 96.6 ($^1J_{C,H}$=165.3 Hz, C-1), 89.5 (–$OCOCCl_3$), 79.7 (C-3), 76.6 (C-5), 74.4 (–CH_2Ph), 73.9 (C-4), 73.8 (–CH_2Ph), 73.4 (–CH_2Ph), 73.0 (C-2), 72.3 (–CH_2Ph), 68.9 (C-6); IR (NaCl) cm^{-1} ν: 3030.6, 2921.6, 2868.6, 1777.1, 1496.5, 1454.1, 1363.4, 1228.4, 1096.3; HR-MS (FAB-pos, NBA matrix) m/z 709.1325 [M+Na]$^+$, calcd for $C_{36}H_{35}O_7{}^{35}Cl_2{}^{37}ClNa$: 709.1327 [M+Na].

*4.5.3. Glycosylation with mannosyl trichloroacetate **27**: methyl 2,3,4-tri-O-benzoyl-6-O-(2,3,4,6-tetra-O-benzyl-α,β-D-mannopyranosyl)-α-D-mannopyranoside (**26**) (Table 8, entry 7).* The glycosylation was performed according to the typical procedure employing trichloroacetate donor **27** (29.9 mg, 0.050 mmol), acceptor **25** (25.9 mg, 0.050 mmol), and TMSOTf (11 μL, 0.061 mmol) at room temperature t. for 1 h. The anomeric mixture of the disaccharide **26** (46.7 mg, 0.0453 mmol, 91%, α/β=91/9) was obtained as a colorless oil after purification by preparative TLC (hexane/AcOEt=2/1).

*4.5.4. Phenyl 2,3,4-tri-O-benzyl-6-O-p-methoxybenzyl-1-thio-α-D-mannopyranoside (**29α**).* To a solution of phenyl 2,3,4-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (**28**) (13.6 g, 25.0 mmol) in DMF (85 mL) was added NaH (1.30 g, 30.0 mmol, 55% disp.) followed by PMBCl (3.73 mL, 27.5 mmol). The reaction mixture was stirred at 0 °C for 2 h, and quenched with H_2O. The resultant mixture was extracted with AcOEt. The combined extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by flash column chromatography (hexane/AcOEt=8/1→4/1→3/1), followed by recrystallization from EtOH to give **29α** (13.4 g, 20.7 mmol, 83%) as a yellow oil. The anomeric ratio was determined by ^{1}H NMR analysis.

Compound **29α**: R_f=0.49 (hexane/AcOEt=2/1); $[\alpha]_D^{23}$ +70.4 (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47–7.42 (m, 2H, Ph–H), 7.38–7.21 (m, 18H, Ph–H), 7.21–7.16 (m, 2H, Ph–H), 6.86–6.79 (m, 2H, Ph–H), 5.61 (d, *J*=1.7 Hz, 1H, 1-H), 4.89 (d, *J*=10.7 Hz, 1H, –CH_2Ph), 4.74 (d, *J*=12.4 Hz, 1H, –CH_2Ph), 4.63 (d, *J*=12.4 Hz, 1H, –CH_2Ph), 4.62 (d, *J*=12.6 Hz, 1H, –CH_2Ph), 4.60 (d, *J*=11.4 Hz, 1H, –CH_2Ph), 4.58 (d, *J*=12.6 Hz, 1H, –CH_2Ph), 4.50 (d, *J*=10.7 Hz, 1H, –CH_2Ph), 4.41 (d, *J*=11.4 Hz, 1H, –CH_2Ph), 4.26 (ddd, *J*=9.8, 5.0, 1.7 Hz, 1H, 5-H), 4.06 (t, *J*=9.8 Hz, 1H, 4-H), 3.99 (dd, *J*=3.1, 1.7 Hz, 1H, 2-H), 3.85 (dd, *J*=9.8, 3.1 Hz, 1H, 3-H), 3.82 (dd, *J*=11.0, 5.0 Hz, 1H, 6-H), 3.77 (s, 3H, –OCH_3), 3.70 (dd, *J*=11.0, 1.7 Hz, 1H, 6-H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 159.1, 138.4, 138.2, 137.88, 137.87, 131.6, 130.8, 130.4, 129.9, 129.5, 129.1, 129.0, 128.5, 128.39, 128.36, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6, 127.3, 113.6, 85.7 ($^1J_{C,H}$=166.8 Hz, C-1), 80.2 (C-3), 76.2 (C-2), 75.2 (–CH_2Ph), 74.9 (C-4), 72.9 (–CH_2Ph), 72.7 (C-5), 72.1 (–CH_2Ph), 71.9 (–CH_2Ph), 68.7 (C-6), 55.2 (–OCH_3); IR (NaCl) cm^{-1} ν: 3029.6, 2905.2, 2865.7, 1612.2, 1512.9, 1247.7, 1098.3; HR-MS (FAB-pos, NBA matrix) m/z 685.2606 [M+Na]$^+$, calcd for $C_{41}H_{42}O_6SNa$: 685.2600 [M+Na].

*4.5.5. 2,3,4-Tri-O-benzyl-6-O-p-methoxybenzyl-α-D-mannopyranose (**30α**).* To a solution of **29α** (13.3 g, 20.6 mmol) in acetone (96 mL) and H_2O (4 mL) was added NBS (5.49 g, 30.8 mmol) at –15 °C. The reaction mixture was stirred at –15 °C for 1 h 30 min, and diluted with AcOEt to stop the reaction. The resultant mixture was extracted with AcOEt, washed with H_2O, brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by flash column chromatography (hexane/AcOEt=3/1→1/1) to afford **30α** (9.95 g, 17.4 mmol, 85%, α only) as white solid; R_f=0.24 (hexane/AcOEt=2/1); $[\alpha]_D^{31}$ +15.7 (*c* 0.82, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40–7.22 (m, 15H, Ph–*H*), 7.18–7.13 (m, 2H, Ph–*H*), 6.86–6.80 (m, 2H, Ph–*H*), 5.25 (dd, *J*=3.3, 2.0 Hz, 1H, 1-H), 4.88 (d, *J*=10.8 Hz, 1H, –C*H*$_2$Ph), 4.75 (d, *J*=12.5 Hz, 1H, –C*H*$_2$Ph), 4.72 (d, *J*=12.5 Hz, 1H, –C*H*$_2$Ph), 4.63–4.60 (m, 2H, –C*H*$_2$Ph), 4.52 (d, *J*=11.9 Hz, 1H, –C*H*$_2$Ph), 4.48 (d, *J*=10.8 Hz, 1H, –C*H*$_2$Ph), 4.46 (d, *J*=11.9 Hz, 1H, –C*H*$_2$Ph), 4.02 (ddd, *J*=9.6, 6.5, 2.2 Hz, 1H, 5-H), 3.96 (dd, *J*=9.6, 3.1 Hz, 1H, 3-H), 3.84 (t, *J*=9.6 Hz, 1H, 4-H), 3.80 (dd, *J*=3.1, 2.0 Hz, 1H, 2-H), 3.77 (s, 3H, –OC*H*$_3$), 3.69 (dd, *J*=10.4, 2.2 Hz, 1H, 6-H), 3.64 (dd, *J*=10.4, 6.5 Hz, 1H, 6-H), 3.48–3.27 (m, 1H, –O*H*): ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.1, 138.5, 138.3, 129.9, 129.7, 128.30, 128.28, 128.2, 127.9, 127.8, 127.6, 127.54, 127.48, 113.7, 92.6 ($^1J_{C,H}$=169.0 Hz, C-1), 79.7 (C-3), 75.3 (C-4), 75.0 (–C*H*$_2$Ph), 74.8 (C-2), 72.8 (–C*H*$_2$Ph), 74.6 (–C*H*$_2$Ph), 72.1 (–C*H*$_2$Ph), 71.3 (C-5), 69.1 (C-6), 55.1 (–OCH_3); IR (NaCl) cm^{-1} ν: 3398.9, 2910.1, 1612.2, 1512.9, 1454.1, 1247.7, 1096.3; HR-MS (FAB-pos, NBA matrix) m/z 593.2524 [M+Na]$^+$, calcd for $C_{35}H_{38}O_7Na$: 593.2515 [M+Na].

*4.5.6. 2,3,4-Tri-O-benzyl-6-O-p-methoxybenzyl-α,β-D-mannopyranosyl trichloroacetate (**31**).* To a stirred solution of 2,3,4-tri-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-mannopyranose (**30α**) (50.0 mg, 0.088 mmol) in dry CH_2Cl_2 (0.9 mL) were added trichloroacetyl chloride (19.1 μL, 0.175 mmol) and pyridine (21.2 μL, 0.263 mmol). After the reaction mixture was stirred at room temperature for 3 h, the solvent was evaporated in vacuo with toluene as an azeotropic solvent. The crude product was purified by flash column chromatography (hexane/AcOEt=7/1) to afford **31** (55.7 mg, 0.078 mmol, 89%, α/β=88/12) as a yellow syrup.

Compound **31α**: R_f=0.59 (hexane/AcOEt=2/1); $[\alpha]_D^{31}$ +45.1 (*c* 0.62, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38–7.33 (m, 2H, Ph–H),

7.33–7.19 (m, 13H, Ph–H), 7.16–7.11 (m, 2H, Ph–H), 6.81–6.76 (m, 2H, Ph–H), 6.20 (d, *J*=2.1 Hz, 1H, 1-H), 4.82 (d, *J*=10.6 Hz, 1H, $-CH_2Ph$), 4.74 (d, *J*=12.1 Hz, 1H, $-CH_2Ph$), 4.70 (d, *J*=12.1 Hz, 1H, $-CH_2Ph$), 4.62 (d, *J*=11.8 Hz, 1H, $-CH_2Ph$), 4.57 (d, *J*=11.8 Hz, 1H, $-CH_2Ph$), 4.55 (d, *J*=11.8 Hz, 1H, $-CH_2Ph$), 4.48 (d, *J*=10.6 Hz, 1H, $-CH_2Ph$), 4.40 (d, *J*=11.8 Hz, 1H, $-CH_2Ph$), 4.10 (t, *J*=9.5 Hz, 1H, 4-H), 3.84 (ddd, *J*=9.5, 4.2, 1.8 Hz, 1H, 5-H), 3.82 (dd, *J*=9.5, 3.2 Hz, 1H, 3-H), 3.74 (dd, *J*=11.4, 4.2 Hz, 1H, 6-H), 3.73 (s, 3H, $-OCH_3$), 3.71 (dd, *J*=3.2, 2.1 Hz, 1H, 2-H), 3.63 (dd, *J*=11.4, 1.8 Hz, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 159.91, 159.16, 137.98, 137.83, 137.45, 130.10, 129.52, 128.45, 128.38, 128.12, 127.94, 127.87, 127.82, 127.54, 113.71, 96.95 (C-1), 89.49 (-CCl_3), 78.36 (C-3), 75.35 (C-5), 75.32 ($-CH_2Ph$), 73.87 (C-4), 73.70 (C-2), 73.05 ($-CH_2Ph$), 73.05 ($-CH_2Ph$), 72.58 ($-CH_2Ph$), 67.92 (C-6), 55.20 ($-OCH_3$); IR (NaCl) cm^{-1} *ν*: 3030.6, 2908.1, 2868.6, 1771.3, 1512.9, 1246.8, 1097.3; HR-MS (FAB-pos, NBA matrix) *m*/*z* 737.1465[M]$^+$, calcd for $C_{37}H_{37}O_8Cl_3$: 737.1452 [M].

*4.5.7. 2,3,4-Tri-O-benzyl-α,β-D-mannopyranosyl trichloroacetate (**32**).* To a solution of **31** (29.5 mg, 0.038 mmol) in CH_2Cl_2 (722 μL) and H_2O (40 μL) at ambient temperature was added DDQ (17.3 mg, 0.076 mmol) in one portion. The reaction mixture was stirred at ambient temperature for 1.5 h. To this mixture was added anhydrous Na_2SO_4 followed by filtration to remove hydrated Na_2SO_4, the resultant mixture was filtered over Celite and silica gel pad rinsed with AcOEt. The resultant filtrate was concentrated under reduced pressure. Flash column chromatography ($CHCl_3$/MeOH=40/1) afforded **32** (17.8 mg, 0.027 mmol, 71%, α/β=94/6) as a colorless oil.

Compound **32α**: R_f=0.43 (hexane/AcOEt=2/1); R_f=0.35 ($CHCl_3$/MeOH=20/1); $[\alpha]_D^{27}$ +38.2 (*c* 1.03, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) *δ*: 7.43–7.27 (m, 15H, Ph–H), 6.15 (d, *J*=2.1 Hz, 1H, 1-H), 4.94 (d, *J*=10.6 Hz, 1H, $-CH_2Ph$), 4.80 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.71 (d, *J*=12.0 Hz, 2H, $-CH_2Ph$), 4.68 (d, *J*=10.6 Hz, 1H, $-CH_2Ph$), 4.63 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.11 (dd, *J*=9.2 Hz, 1H, 4-H), 3.89 (dd, *J*=9.2, 3.0 Hz, 1H, 3-H), 3.84 (dd, *J*=13.4, 4.2 Hz, 1H, 6-H), 3.81–3.76 (m, 1H, 5-H), 3.80–3.76 (m, 1H, 6-H), 3.75 (dd, *J*=3.0, 2.1 Hz, 1H, 2-H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ*: 159.96, 137.86, 138.76, 137.38, 128.54, 128.51, 128.34, 128.24, 128.08, 128.02, 127.96, 127.91, 96.75 (C-1), 89.41 (-CCl_3), 78.35 (C-3), 75.71 (C-5), 75.42 ($-CH_2Ph$), 73.88 (C-2), 73.55 (C-4), 73.35 ($-CH_2Ph$), 72.75 ($-CH_2Ph$), 61.63 (C-6); IR (NaCl) cm^{-1} *ν*: 3398.9, 3030.6, 2928.4, 1767.4, 1454.1, 1236.2, 1093.4; HR-MS (FAB-pos, NBA matrix), *m*/*z* 619.0848[M]$^+$, calcd for $C_{29}H_{29}O_7Cl_3$: 619.0853 [M].

4.5.8. Methyl 2,3,4,6-tetra-O-benzyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-O-benzyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-O-benzoyl-α-D-mannopyranoside (34αα) (Table 9, entry 1). To a stirred suspension of MS 5 Å (127.5 mg, MS 5 Å/acceptor=3 g/1 mmol), **24** (31.3 mg, 0.0429 mmol), and acceptor **32** (37.4 mg, 0.0630 mmol) in dry Et_2O (1.5 mL) was added TMSOTf (8 μL, 0.0412 mmol) at 0 °C. The reaction mixture was stirred at −20 °C for 2 h. A solution of the acceptor **25** (43.6 mg, 0.0860 mmol) in Et_2O was added, and then reaction temperature was allowed to raise up to ambient temperature. The reaction mixture was stirred for 2 h at ambient temperature and, quenched by adding satd $NaHCO_3$ solution, and filtered through Celite pad. The filtrate was extracted with AcOEt, and the combined organic extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by preparative TLC (hexane/AcOEt=2/1), (toluene/AcOEt=10/1×4) to afford mannosyl trisaccharide **34** (32.6 mg, 52%, αα/αβ/βα/ββ=71/14/13/2, two steps) as colorless oil. The anomeric ratio was determined by HPLC analysis [Senshu Pak PEGASIL silica SP 100 (4.6ø×250 mm), hexane/AcOEt=4/1, UV at 254 nm, flow rate; 0.5 mL/min, rt].

Compound **34αα**; R_f=0.43 (hexane/AcOEt=2/1); $[\alpha]_D^{30}$ −13.1 (*c* 1.06, $CHCl_3$); ^1H NMR (600 MHz, C_6D_6) *δ*: 7.54–7.10 (m, 38H, Ph–*H*), 7.08–7.02 (m, 2H, Ph–*H*), 6.99–6.90 (m, 6H, Ph–*H*), 6.86–6.80 (m, 4H, Ph–*H*), 6.67 (t, *J*=10.0 Hz, 1H, 4-H), 6.42 (dd, *J*=10.0, 3.0 Hz, 1H, 3-H), 6.18 (dd, *J*=3.0, 1.5 Hz, 1H, 2-H), 5.33 (d, *J*=1.5 Hz, 1H, 1″-H), 5.18 (d, *J*=11.5 Hz, 1H, $-CH_2Ph$), 5.11 (d, *J*=11.5 Hz, 1H, $-CH_2Ph$), 5.09 (d, *J*=1.5 Hz, 1H, 1′-H), 4.87 (d, *J*=3.5 Hz, 1H, 1-H), 4.74 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.72 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.70 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.72–4.68 (m, 2H, $-CH_2Ph$), 4.69 (d, *J*=11.5 Hz, 1H, $-CH_2Ph$), 4.64 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.64 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.63 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.60 (d, *J*=11.5 Hz, 1H, $-CH_2Ph$), 4.55 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.52 (d, *J*=12.0 Hz, 1H, $-CH_2Ph$), 4.46 (t, *J*=9.5 Hz, 1H, 4″-H), 4.41 (t, *J*=9.5 Hz, 1H, 4′-H), 4.36 (dd, *J*=9.5, 3.0 Hz, 1H, 3′-H), 4.35 (dt, *J*=10.0, 3.0 Hz, 1H, 5-H), 4.26 (dd, *J*=9.5, 3.0 Hz, 1H, 3″-H), 4.13 (dd, *J*=11.0, 3.0 Hz, 1H, 6-H), 4.12 (ddd, *J*=9.5, 5.0, 1.5 Hz, 1H, 5″-H), 4.11 (dd, *J*=12.0, 4.0 Hz, 1H, 6′-H), 4.05 (dd, *J*=3.0, 1.5 Hz, 1H, 2″-H), 4.00 (dd, *J*=3.0, 1.5 Hz, 1H, 2′-H), 3.99 (ddd, *J*=9.5, 4.0, 1.5 Hz, 1H, 5′-H), 3.92 (dd, *J*=11.5, 5.0 Hz, 1H, 6″-H), 3.78 (dd, *J*=11.0, 3.0 Hz, 1H, 6-H), 3.77 (dd, *J*=12.0, 1.5 Hz, 1H, 6′-H), 3.76 (dd, *J*=11.5, 1.5 Hz, 1H, 6″-H), 3.14 (s, 3H, $-OCH_3$); ^{13}C NMR (150 MHz, C_6D_6) *δ*: 166.70 (−*O*COPh), 166.31 (−*O*COPh), 166.15 (−*O*COPh), 140.14, 139.96, 139.95, 139.91, 139.67, 139.62, 139.46, 133.86, 133.70, 133.40, 130.55, 130.51, 130.36, 130.21, 130.18, 129.28, 129.02, 129.01, 128.92, 128.84, 128.83, 128.80, 128.72, 128.69, 128.56, 128.56, 128.40, 128.32, 128.31, 128.24, 128.20, 128.17, 128.13, 128.11, 128.04, 127.87, 127.76, 127.70, 99.50 (C-1), 99.25 ($^1J_{C,H}$=168.7 Hz, C-1′), 99.17 ($^1J_{C,H}$=168.7 Hz, C-1″), 81.41 (C-3′), 80.39 (C-3″), 76.64 (C-2′), 76.34 (C-2″), 75.86 (C-4″), 75.65 ($-CH_2Ph$), 75.51 ($-CH_2Ph$), 75.45 (C-4′), 3.85 ($-CH_2Ph$), 73.59 ($-CH_2Ph$), 73.36 (C-5″), 73.25 ($-CH_2Ph$), 73.03 (C-5′), 72.72 ($-CH_2Ph$), 71.88 ($-CH_2Ph$), 71.58 (C-2), 71.23 (C-3), 70.30 (C-5), 70.28 (C-6″), 68.23 (C-4), 67.07 (C-6), 66.63 (C-6′), 55.46 ($-OCH_3$); IR (NaCl) cm^{-1} *ν*: 3030.6, 2924.5, 1729.8, 1601.6, 1495.5, 1453.1, 1278.6, 1106.9; HR-MS (FAB-pos, NBA matrix) *m*/*z* 1483.5817 [M]$^+$, calcd for $C_{29}H_{29}O_7Cl_3$: 1483.5818 [M].

4.6. One-pot dehydrative sequential glycosylation

4.6.1. Glucose. To a stirred solution of 2,3,4,6-tetra-*O*-benzyl-D-gulucopyranose (**1**) (20.3 mg, 0.0370 mmol) in dry CH_2Cl_2 (0.25 mL) was added trichloroacetyl isocyanate (6.0 μL, 0.0381 mmol) at room temperature. The reaction mixture was stirred at room temperature for 1 h. To the resultant mixture was added MS 5 Å (111.2 mg, MS 5 Å/acceptor=3 g/1 mmol) and a solution of **6** (37.4 mg, 0.0555 mmol) in dry Et_2O (1.3 mL), followed by cooling to 0 °C. To the stirred suspension was added TMSOTf (14 μL, 0.0555 mmol). The reaction mixture was stirred at 0 °C for 4 h. Acceptor **3** (38.0 mg, 0.0740 mmol) was added, and then reaction temperature was allowed to raise up to ambient temperature. The reaction mixture was stirred at that temperature and warmed up to 40 °C, and stirred for 24 h. The reaction mixture was quenched by adding satd $NaHCO_3$ solution, and filtered through Celite pad. The filtrate was extracted with AcOEt, and the combined organic extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by preparative TLC (hexane/AcOEt=2/1), (toluene/AcOEt=10/1×4) to afford glucosyl trisaccharide **8** (29.7 mg, 0.0203 mmol, 55%, αα/αβ/βα/ββ=71/14/13/2, three steps) as colorless oil. The anomeric ratio was determined by HPLC analysis [Senshu Pak PEGASIL Silica 60–5 (4.6ø×250 mm), hexane/AcOEt=3/2, UV at 254 nm, flow rate; 0.2 mL/min, 0 °C].

4.6.2. Galactose. To a stirred solution of 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose (**11**) (20.1 mg, 0.0372 mmol) in dry CH_2Cl_2 (0.25 mL) was added trichloroacetyl isocyanate (4.5 μL, 0.0553 mmol) at room temperature. The reaction mixture was stirred at room temperature for 1 h. To the resultant mixture was added MS 5 Å (111.0 mg, MS 5 Å/acceptor=3 g/1 mmol) and a solution of acceptor **20α** (33.0 mg, 0.0555 mmol) in dry Et_2O (1.3 mL), followed by cooling to −20 °C. To the stirred suspension was added TMSOTf (10 μL, 0.0555 mmol). The reaction mixture was stirred at

−20 °C for 2 h. Acceptor **13** (37.9 mg, 0.0740 mmol) was added, and then reaction temperature was allowed to raise up to ambient temperature. The reaction mixture was stirred at that temperature for 2 h. The reaction mixture was quenched by adding satd $NaHCO_3$ solution and, filtered through Celite pad. The filtrate was extracted with AcOEt, and the combined organic extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by preparative TLC (hexane/AcOEt=2/1) to afford trisaccharide **22** (38.5 mg, 0.0243 mmol, 71%, αα/αβ/βα/ββ=43/24/21/12, three steps) as a colorless oil. The anomeric ratio was determined by HPLC analysis [Senshu Pak PEGASIL silica SP 100 (4.6ø×250 mm), hexane/AcOEt=4/1, UV at 254 nm, flow rate; 1.0 mL/min, rt].

4.6.3. Mannose. To a stirred solution of 2,3,4,6-tetra-*O*-benzyl-D-mannnopyranose (**23**) (20.3 mg, 0.0375 mmol) in dry CH_2Cl_2 (0.25 mL) was added trichloroacetyl isocyanate (4.5 μL, 0.0553 mmol) at room temperature. The reaction mixture was stirred at room temperature for 2 h. To the resultant mixture was added MS 5 Å (112.5 mg, MS 5 Å/acceptor=3 g/1 mmol) and a solution of acceptor **32** (20.3 mg, 0.0375 mmol) in dry Et_2O (1.3 mL), followed by cooling to −20 °C. To the stirred suspension was added TMSOTf (7 μL, 0.0370 mmol). The reaction mixture was stirred at −20 °C for 2 h. Acceptor **25** (38.0 mg, 0.0740 mmol) was added, and then reaction temperature was allowed to raise up to ambient temperature. The reaction mixture was stirred at that temperature for 2 h. The reaction mixture was quenched by adding satd $NaHCO_3$ solution and, filtered through Celite pad. The filtrate was extracted with AcOEt, and the combined organic extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by preparative TLC (hexane/AcOEt=2/1) to afford trisaccharide **34** (38.4 mg, 0.0243 mmol, 71%, αα/αβ/βα/ββ=75/11/11/3, three steps) as a colorless oil. The anomeric ratio was determined by HPLC analysis [Senshu Pak PEGASIL silica SP 100 (4.6ø×250 mm), hexane/AcOEt=4/1, UV at 254 nm, flow rate; 0.5 mL/min, rt].

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