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Iron(III) chloride modulated selective 1,2-*trans* glycosylation based on glycosyl trichloroacetimidate donors and its application in orthogonal glycosylation†

Mana Mohan Mukherjee, Nabamita Basu‡ and Rina Ghosh*

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The development of a new glycosylation method for efficient stereoselective synthesis of β-gluco- and galactosides from their corresponding armed trichloroacetimidate donors mediated by 10 mole% of $FeCl_3$ has been focused. $FeCl_3$ has also been applied to a number of glucose, galactose, mannose and rhamnose based trichloroacetimidate donors with various protecting groups incorporated at the C-2-position to prepare a variety of disaccharides and trisaccharides with excellent 1,2-*trans* selectivity. $FeCl_3$ can also modulate the 1,2-*trans* selectivity of the reaction of 2-*O*-alkylated gluco- and galacto-pyranosyl trichloroacetimidates with phenolic compounds leading to the generation of the corresponding β-*O*-aryl glycosides in excellent yield and selectivity. Apart from these the present methodology has been successfully utilized for double glycosylation and orthogonal glycosylation reactions along with its application in one-pot three component orthogonal glycosylation reactions for synthesis of a trisaccharide.

Introduction

Beyond their traditionally accepted roles as energy sources and structural polymers, oligosaccharides and glycoconjugates serve critical roles in a wide range of biological processes like viral and bacterial infection, angiogenesis and tumour cell metastasis, toxin interaction, inflammation and immune response, cell growth and proliferation, and many other cell–cell communications.[1] However, such carbohydrates are difficult to isolate from natural sources with acceptable purity and in satisfactory quantities. The key step in the synthesis of oligosaccharides is the formation of the glycosidic linkages between monosaccharide units. The anomeric stereoselectivity can be controlled by the use of protecting groups that are capable of neighbouring group participation. For example, esters at the C-2 position of a glycosyl donor typically provide high selectivity for the 1,2-*trans* glycoside product. Occasionally, however, it suffers from several drawbacks too, such as low reactivity of the ester protected glycosyl donor prolonging reaction time and lowering of yield,[2] competitive formation of 1,2-*ortho* ester[3] and migration of C-2 ester functionality to other positions.[4]

Stereocontrol in the absence of usual neighbouring *O*-acyl group participation is considerably more challenging. Many factors, such as steric hindrance of protecting groups, reaction solvent, and temperature can affect the stereochemical outcome of a glycosylation reaction, and these effects are typically difficult to predict for any given donor–acceptor pair. So, better methods to control stereoselectivity in the absence of neighbouring ester group participation are also needed.

On the other hand, β-*O*-aryl glycosides have been recently found to exhibit anti tumour, anti HIV and anti bacterial activities. β-*O*-Aryl glycoside formation is considered as a difficult task due to electron withdrawing power of the aromatic ring, the facile rearrangement of the resulting *O*-aryl glycosides to their corresponding C-aryl glycosides and steric hindrance from substituents on phenolic glycosyl acceptors;[5] hence their stereo-controlled synthesis has become a challenging job.[6] Glycosyl acetates, halides and trichloroacetimidates (TCA) have been used as donors in the formation of β-*O*-aryl glycosides.[6] Glycosyl acetates usually provide the β-*O*-aryl glycosides with lower yields than trichloroacetimidates due to anomerization of both the glycosyl donor and the coupling product.[6] The β-*O*-aryl glycosides can be formed in the glycosylation reaction by employing ester functionalities as the directing group at the C-2 position of glycosyl donors. In some cases, formation of orthoester side products and migration of the C-2-*O*-acyl functionality are also observed in the reaction.[3,7]

Since the first paper on Schmidt's glycosylation method was published in 1980,[8a,b] till date trichloroacetimidates have been among the most widely used glycosyl donors.[8c] Their popularity

Department of Chemistry, Jadavpur University, Jadavpur, Kolkata 700032, West Bengal, India. E-mail: ghoshrina@yahoo.com

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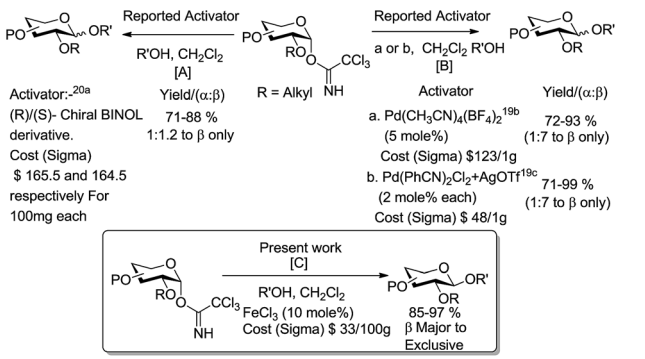
‡ At present: Department of Organic Chemistry, IACS, Jadavpur, Kolkata 700032, India.

comes from their relative ease of synthesis by base-catalyzed addition of trichloroacetonitrile to the anomeric hydroxy group[9] and their easy activation; it also opens up the scope for orthogonal glycosylation. The glycosyl trichloroacetimidate donors are generally activated by strong Lewis acids such as $BF_3 \cdot OEt_2$,[8a] TMSOTf,[9a] Tf_2O,[10] $ZnBr_2$,[11] $NOBF_4$,[12] $Sm(OTf)_3$,[13a] $LiClO_4$,[14] LiOTf,[15] or other systems like I_2/Et_3SiH,[13b] acid washed 4 Å molecular sieves,[13c,d] $HClO_4/SiO_2$,[16] Amberlyst 15,[17] $AuCl_3$–phenylacetylene,[18] *etc.*; many of these are however not without limitations.

Results and discussion

Recently Nguyen *et al.*[19] have reported trichloroacetimidate (TCA, containing 2-*O*-alkyl group) activation in high to excellent 1,2-*trans* selectivity utilizing second row transition metal complexes involving Pd in low catalyst loading. In another report chiral Brønsted acid has been utilized for such purpose.[20] In a more recent report by Schmidt *et al.* it has been demonstrated that β-glycosylation based on armed trichloroacetimidate donors using Au(III) or Au(I) chloride catalyst *via* formation of catalyst-glycosyl acceptor adduct permits glycosyl donor activation with concomitant glycosyl acceptor anion transfer to the anomeric carbon.[21] But the reported catalysts are very much expensive, and sometimes toxic for the living body as well as environment. In continuation of our research work on glycoscience,[22] we report herein a 1,2-*trans* glycosylation protocol using $FeCl_3$ as a green catalyst. Unlike all other reported glycosylation methods (except the reports made by Nguyen *et al.*[19] and by Schmidt *et al.*[21]) based on armed trichloroacetimidate glycosyl donors the present one generated the corresponding glycosides in excellent yields and 1,2-*trans* selectivity (Scheme 1). The acceptable catalyst load and low cost (Scheme 1) of $FeCl_3$ together with its greenness particularly in respect of the scope of its future utilization for large scale ramification make this procedure very attractive.



Scheme 1 Comparison of the recent works with the present one (inset).

In the last decade $FeCl_3$ has drawn much attention of the researchers worldwide for its wide range of application in organic synthesis.[23] Our strategy for 1,2-*trans* glycosylation was to exploit the ability of this first row transition metal-Lewis acids to direct glycosylation of trichloroacetimidate donor. The choice of $FeCl_3$ was based on the presumption that, for glucose and galactose donors, like Pd a seven member cyclic chelate[19,24] (b) may be the possibility involving electronically vacant metal center (Fe), α-imidate nitrogen and C-2-oxygen of glycosyl trichloroacetimidate donor (a) which in effect would block the α-face of the proposed TS (c) for the attacking incoming nucleophilic acceptor, so that ultimately it can result in β-glycoside (d), vide Fig. 1.

Our initial study was performed with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl trichloroacetimidate, **1** as the armed glycosyl donor and methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside **2** as the acceptor. Upon treatment of these coupling partners in 1.2 : 1 molar ratio with 30 mole% $FeCl_3$ at −5 °C to room temperature for 1 hour, the desired disaccharide **3** was isolated in 67% yield as a single β isomer. ^{1}H-NMR spectrum showed one anomeric proton appearing at δ 4.55 ppm with J 8.0 Hz corresponding to the H'_1 indicating 1,2-*trans* glycosylation. This was also corroborated by the appearance of peaks at δ 101.9 and 104.0 ppm, corresponding to the anomeric carbons C'_1 and C_1, respectively. Higher δ value of the reducing anomeric carbon, in spite of it having an α-stereochemistry is attributed to the deshielding caused by three benzoyl protections on this pyranoside ring. The result, as we presumed, was indeed interesting and encouraging too, as this was clearly implying the ability of $FeCl_3$ to activate trichloroacetimidate stereoselectively in the presence of apparently silent spectator protecting group like *O*-benzyl or without assistance by the solvent.

As an initial effort for optimization of a standard procedure for glycosylation we applied different catalyst loading (of $FeCl_3$)

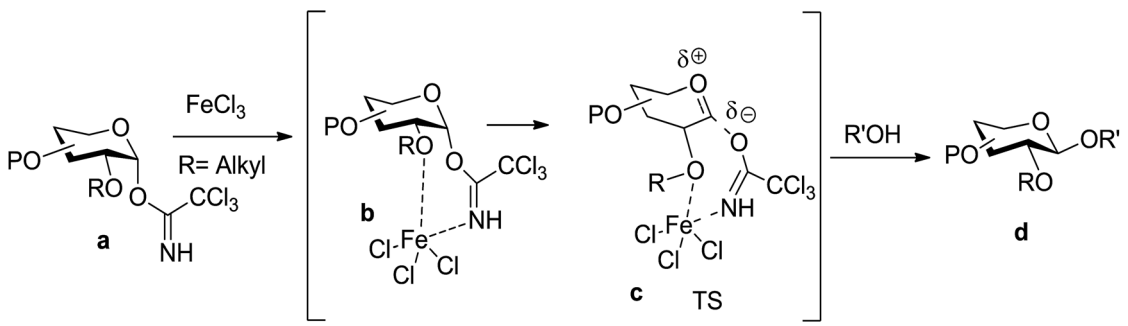


Fig. 1 Anticipated transition states for $FeCl_3$ catalyzed glucose and galactose based armed donors.

with variation in temperature and solvent, as well as few other catalysts too (Table 1). Finally we selected the most economically acceptable and efficient reaction condition as 10 mole% $FeCl_3$ at −60 °C to room temperature and used the process for further studies.

With an optimized reaction condition in hand we then set out to explore the scope of $FeCl_3$ catalyzed 1,2-*trans* selective glycosylations. A variety of nucleophilic glycosyl acceptors incorporating various protecting groups like ether, isopropylidene ketals and benzylidene acetals were exemplified with glycosyl donor **1** (Table 2). Glycosyl acceptors with least reactive 4-OH, hindered tertiary alcohol like 1-adamentanol and sensitive diisopropylidene protection (**4**, **6** and **8**, respectively) in reaction with **1** generated the corresponding disaccharides **5**, **7** and **9** in excellent yields (entries 2, 3 and 4, Table 2), with notable β selectivity compared to the reported ones.[13a,19b,c] The structure of compound **7** (CCDC no. 1501233) was confirmed by its X-ray structure (Fig. 2).

The efficacy of the present procedure was further established when we examined this chemistry with 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl trichloroacetimidate **12**; the armed donor is well known for its α-directive effect for 4 axial –OH group. Compared to other reported methods,[25,26] we observed remarkable β selectivity when glycosylation reactions of **12** were performed with carbohydrate acceptors **2**, **4**, **15** and **17** having nucleophilic hydroxy group on C-6, C-4, C-3 and C-2 positions, respectively; irrespective of their position and reactivity, the corresponding desired disaccharides (**13**, **14**, **16** and **18**) were obtained in excellent yield and β selectivity (entries 6 to 9, Table 2).

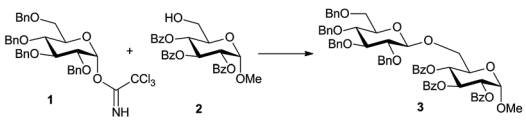
The present method also responded efficiently under a scale-up (∼30 fold) condition when applied for preparation of **3** from reaction of **1** and **2** (entry 1, Table 2), thus opening up scope to apply this method for preparative purpose also. When 4,6-*O*-benzylidene-2,3-di-*O*-benzyl-α-D-glucopyranosyl trichloroacetimidate donor, **10** reacted with acceptor **8** the desired disaccharide **11** was obtained in 87% yield as β isomer; the reaction of it's galactose analogue **21** with acceptor **22** gave the β-disaccharide **23** in 92% yield (entries 5 and 11, respectively, Table 2). When armed D-mannopyranosyl trichloroacetimidate donor **19** was allowed to react with nucleophilic acceptor **4**, the corresponding α-disaccharide **20** was obtained in high yield (entry 10, Table 2).

The other glycosyl trichloroacetimidate donor systems that needed to be exercised in $FeCl_3$ catalyzed glycosylation protocol were those with C-2-*O*-acyl protecting donors. It is expected that ester functionality from C-2 position might control the formation of 1,2-*trans* through the usual neighbouring group participation. Glycosylation of donors **24**, **27**, **29**, **32**, **34**, and **36** with a variety of glycosyl acceptors like **25**, **30** and **2** separately (entries 1 to 6, Table 3) provided the corresponding 1,2-*trans* selective products **26**, **28**, **31**, **33**, **35** and **37**.

To further demonstrate the efficacy of the glycosylation protocol, we set out to pursue a glycosylation reaction of donor **1** with a disaccharide acceptor **38**, where we get the trisaccharide, **39** in 89% yield and as β anomer. It is to be noted here that the reported method using $Pd(PhCN)_2Cl_2$ + AgOTf produces the trisaccharide **39** in 71% yield with β : α = 12 : 1 anomeric ratio.[19c] Then we turned to a couple of double glycosylation of carbohydrate diol. Pair up of 4,6-glucopyranosyl diol **41** and phthalimide protected glucosamine donor **40**, resulted with the desired trisaccharide **42** in 83% yield where as the same diol acceptor **41** reacted with the rhamnosyl donor **27** affording 81% of the desired trisaccharide **43** (Scheme 2).

Next, we turned our attention to apply the present protocol for the synthesis of β-aryl glycosides. $FeCl_3$ catalyzed β-selective

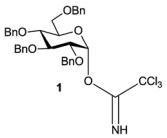
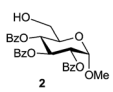
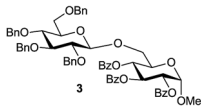
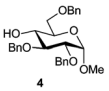
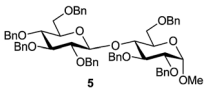
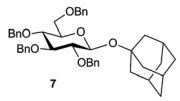
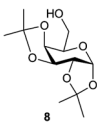
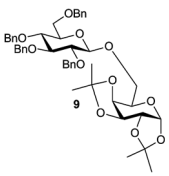
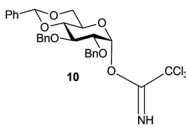
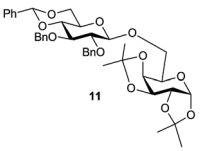
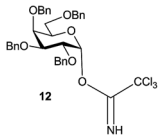
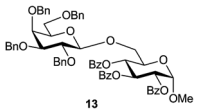
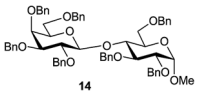
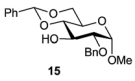
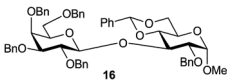
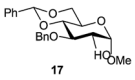
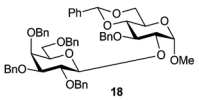
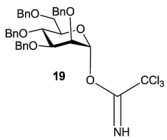
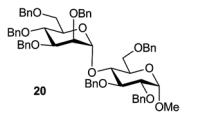
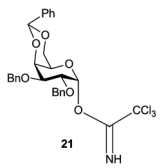
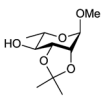
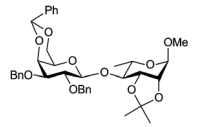
Table 1 Standardization of optimum reaction condition[a]



Entry	Catalyst (mole%)	Reaction temperature	Time	Yield[b]	(α/β ratio)[c]
1	$FeCl_3$ (30)	−5 °C to rt	1 h	67%	(β only)
2	$FeCl_3$ (20)	−30 °C to rt	45 min	72%	(β only)
3	$FeCl_3$ (30)	−60 °C to rt	45 min	83%	(β only)
4	$FeCl_3$ (20)	−60 °C to rt	45 min	90%	(β only)
5	**$FeCl_3$ (10)**	**−60 °C to rt**	**45 min**	**96%**	**(β only)**
6	$FeCl_3$ (5)	−60 °C to rt	45 min	92%	(β only)
7	$FeCl_3$ (10)	−80 °C to rt	45 min	94%	(β only)
8	$FeCl_3$ (10)	−60 °C to rt	45 min	94%	(β only)[d]
9	$FeCl_3$ (10)	−60 °C to rt	45 min	93%	(2 : 3)[e]
10	$FeCl_3$ (10)	−60 °C to rt	45 min	94%	(β only)[f]
11	$FeCl_3$ (10)	−60 °C to rt	35 min	93%	(β only)[g]
12	$FeBr_3$ (30)	−50 °C to rt	45 min	59%	(1 : 9)
13	$In(OTf)_3$ (30)	−50 °C to rt	45 min	62%	(β only)

[a] All reactions were carried out in DCM with 1.2 equiv. of donor. [b] Isolated yield. [c] ^1H NMR ratio. [d] Using MeCN : DCM (1 : 2). [e] Using Et_2O : DCM (1 : 1). [f] Using 99.99% $FeCl_3$ of Sigma Aldrich. [g] Using β anomer of **1** as donor.

Table 2 Glycosylation with C-2 alkyl donors[a]

Entry	Donor	Acceptor	Product	Yield[b] (α : β)
1				96% β (89%)[c]
2	**1**			93% β
3	**1**			94% β
4	**1**			85% β
5	 **8**			87% β
6		**2**		95% β
7	**12**	**4**		88% β
8	**12**			89% β
9	**12**			90% β
10		**4**		87% α[d]
11				92% β

[a] All reactions were carried out in dry DCM with 1.2 equiv. of donor at −60 °C to rt. [b] Isolated yield. [c] Use of glycosyl donor in 1.5 g scale. [d] Reaction was carried out at −5 °C to rt.

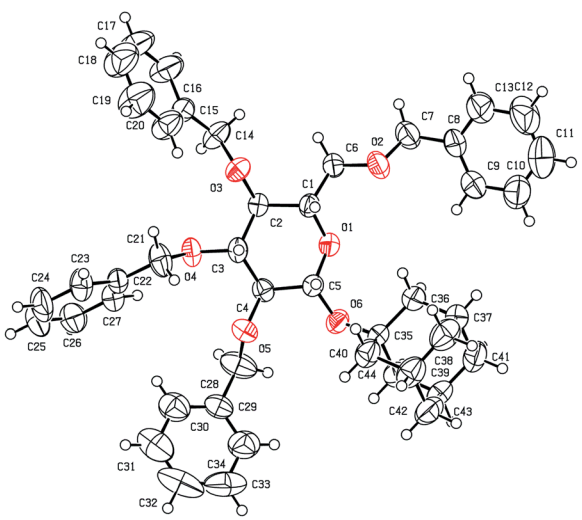


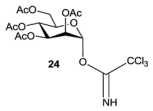
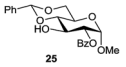
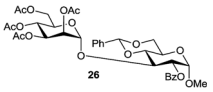
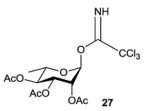
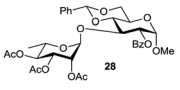
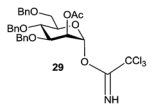
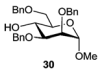
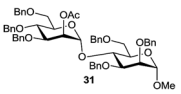
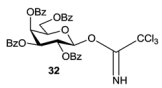
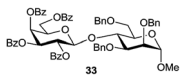
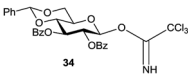
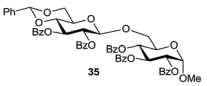
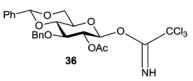
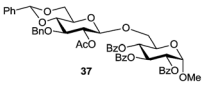
Fig. 2 ORTEP diagram of compound 7.

arylation was found effective for D-glucopyranosyl trichloroacetimidate donor **1** with a variety of electron-rich phenols (**44**, **46** and **50**), and the corresponding desired glycosides **45**, **47** and **51** were isolated in excellent yield and β-selectivity (entries 1, 2 and 4, Table 4). Similarly, tetra-*O*-benzyl-D-galactopyranosyl trichloroacetimidate substrate **12** was also examined under the standardized condition to react with different phenols **44**, **53**, and **55**; in each case we found the corresponding desired β-*O*-aryl galactoside **52**, **54** and **56** to be formed with promising result on the ground of yield and selectivity (entries 5 to 7, Table 4).

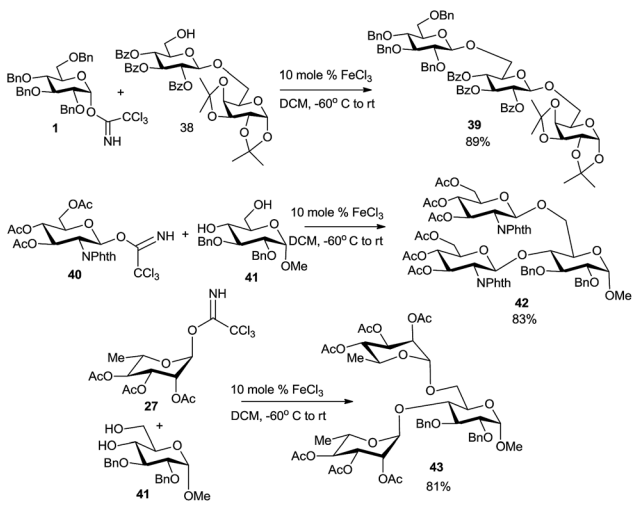
To explore further the applicability of this procedure we then chose a sterically hindered 2,6-dimethylphenol **48**. Gratifyingly, this phenol acceptor **48** was able to couple with both donors **1** and **12** to provide the corresponding *O*-aryl glycosides **49** and **57**, respectively with excellent yield and anomeric selectivity (entries 3 and 8, Table 4). It may be mentioned here that the reported coupling between phenol **48** and tetra-*O*-benzyl-D-glucothioglycoside donor affords the desired product **49** with excellent yield (90%) albeit with low selectivity (α : β = 2.6 : 1),[27a] whereas the sulfoxide approach gave 70% yield as a 2 : 1 mixture of α- and β-anomer.[27b]

After achieving a convenient synthetic route for 1,2-*trans* selective glycosylation with trichloroacetemidate donors, we also sought to verify the efficiency of the Lewis acidity of $FeCl_3$ to promote thioglycoside activation in combination with NIS. For

Table 3 Glycosylation with C-2 ester protected sugar[a]

Entry	Donor	Acceptor	Product	Yield[b] (α : β)
1				90% α only
2		**25**		89% α only
3				91% β only
4		**30**		91% β only
5		**2**		88% β only
6		**2**		90% β only

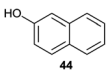
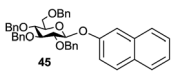
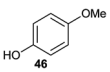
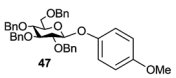
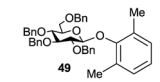
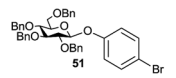
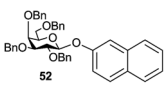
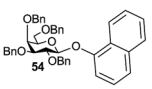
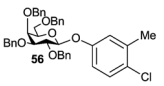
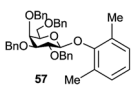
[a] All reactions were performed in dry DCM with 1.2 equiv. of donor and 10 mole% of $FeCl_3$ at −60 °C to rt. [b] Isolated yield.



Scheme 2 Glycosylation with disaccharide acceptor and double glycosylations.

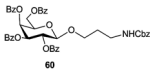
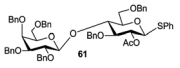
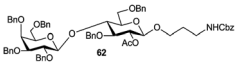
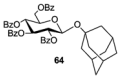
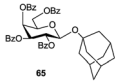
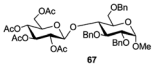
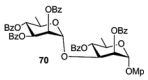
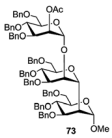
this purpose thioglycoside donors **58**, **61**, **63** and **66** were allowed to couple with benzyl *N*-(3-hydroxypropyl) carbamate **59** (entries 1 and 2, Table 5), 1-adamentanol **6** (entries 3 and 4, Table 5) and carbohydrate acceptor like **4** (entry 5, Table 5) to produce the corresponding glycosides **60**, **62**, **64**, **65** and **67** in excellent respective yield and expected β-steroselectivity due to C-2 neighbouring group participation. A rare sugar derivative of D-rhamnose donor **68** was allowed to couple with similar acceptor **69** to give stereoselectively the desired disaccharide **70**

Table 4 Glycosylation with different phenol[a]

Entry	Donor	Acceptor	Product	Yield[b] (α : β)
1	**1**			97% β
2	**1**			97% β
3	**1**			90% β
4	**1**			92% β
5	**12**	**44**		97% β
6	**12**			95% β
7	**12**			94% β
8	**12**	**48**		91% β

[a] All reactions were performed in dry DCM with 1.2 equiv. of donor and 10 mole% of $FeCl_3$ at −5 °C to rt. [b] Isolated yield.

Table 5 Glycosylatin reaction based on thioglycosides[a]

Entry	Donor	Acceptor	Product	Yield[b] (α : β)
1	 58	 59	 60	88% β only
2	 61	**59**	 62	92% β only
3	 63	**6**	 64	94% β only
4	**58**	**6**	 65	89% β only
5	 66	**4**	 67	91% β only
6	 68	 69	 70	91% α only
7	 71	 72	 73	90% α only

[a] All reactions were performed in dry DCM with 1.2 equiv. of donor 1 equiv. NIS and 20 mole% of $FeCl_3$ at −5 °C to rt. [b] Isolated yield.

in 91% yield (entry 6, Table 5). Reaction of mannosyl donor **71** with di-mannoside acceptor **72** produces the mannose trisaccharide **73** in 90% yield (entry 7, Table 5). These reactions thus prove the ability of $FeCl_3$ to catalyse thioglycoside activation too, in combination with NIS and opens up the gateway for its further elaboration in orthogonal glycosylations.

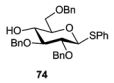
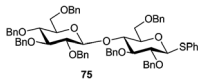
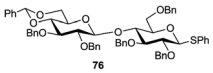
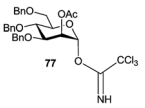
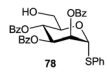
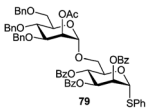
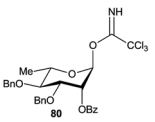
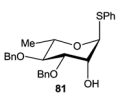
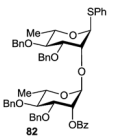
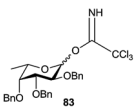
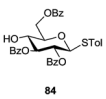
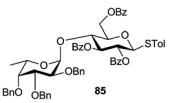
Orthogonal glycosylation of trichloroacetimidate donors with thioglycosides pave the way for efficient streamline oligosaccharide assemblies.[28] Activity of $FeCl_3$ towards orthogonal glycosylation of trichloroacetimidate donors with thio glycoside acceptors have also been investigated there after (Table 6). Glycosylation with orthogonal trichloroacetimidate donor **1** and the glycosyl acceptor **74** bearing thiophenyl group at its anomeric position produced the corresponding β disaccharide **75** in 85% yield (entry 1, Table 6). Similar reaction between 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl trichloroacetimidate donor **10** and phenyl 2,3,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside **74** generated the desired β disaccharide **76** in 94% yield (entry 2, Table 6). Coupling of trichloroacetimidate donors **77**, **80** and **83** separately with the thioglycoside acceptors **78** (entry 3, Table 6), **81** (entry 4, Table 6) and **84** (entry 5, Table 6), respectively produced the corresponding glycosides **79**, **82** and **85** in 94%, 92% and 88% yield. Unexpectedly, the armed fucosyl TCA donor **83** produced selectively the corresponding α-glycoside, **85**. This could be due to much high reactivity of **83**, for which here the glycosylation reaction probably proceeds *via* formation of the corresponding oxonium ion intermediate rather than *via* the corresponding Fe-chelated TS. This might cause the anomeric selectivity in favour of the thermodynamic product, α-glycoside (**85**). All the reactions under Tables 1–6 clearly represent the applicability of $FeCl_3$ in stereoselective glycosylation *via* trichloroacetemidate activation, thioglycoside activation in combination with NIS and also orthogonal glycosylation of the former in the presence of the thioglycoside acceptor.

Now, finally the efficacy of $FeCl_3$ was exemplified for chain elongation, essential for oligosaccharide synthesis[29] by one pot sequential glycosylation with trichloroacetimidate donor followed by thioglycoside activation (Scheme 3).

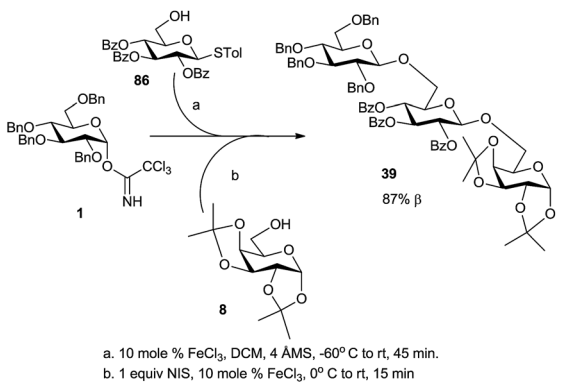
For this trichloroacetimidate donor **1** was allowed to react with 4-methylphenyl 2,3,4-tri-*O*-benzoyl-1-thio-β-D-glucopyranoside **86** at −60 °C to room temperature in the presence of 10 mole% $FeCl_3$; after consumption of both of the starting materials (checked by TLC) and after an increase of the reaction temperature to 0 °C the acceptor **8** was injected followed by addition of NIS along with additional 10 mole% $FeCl_3$. The reaction was complete within 15 minutes giving the trisaccharide **39** in 87% yield as β anomer (Scheme 3).

So far we have observed that glucose and galactose based trichloroacetimidate armed donors are activated by $FeCl_3$ generating selectively 1,2-*trans* glycosides in reaction with a variety of glycosyl acceptors (Tables 2, 4 and 6). It is also interesting to note that the reaction of β-TCA donor with **2** under similar condition also produced the same product **3** in comparable yield and selectivity (entry 11, Table 1). Moreover, *in situ* anomerisation of each of α- or β-TCA in the presence of $FeCl_3$ in CH_2Cl_2 solution could not also be established. These facts preclude the possibility of these reactions to proceed

Table 6 Orthogonal glycosylations[a]

Entry	Donor	Acceptor	Product	Yield[b] (α : β)
1	**1**	 74	 75	85% β
2	**10**	**74**	 76	94% β
3	 77	 78	 79	94% α
4	 80	 81	 82	92% α
5	 83	 84	 85	88% α

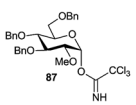
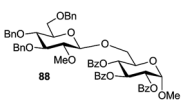
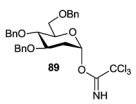
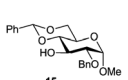
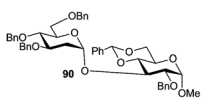
[a] All reactions were performed in dry DCM with 1.2 equiv. of donor and 10 mole% of $FeCl_3$ at −60 °C to rt. [b] Isolated yield.



Scheme 3 Application in one-pot sequential glycosylation reaction.

following S_N2 like pathway. All these thus support our initial proposition of the reaction proceeding *via* a S_N1 type mechanistic pathway through probably an initial formation of a 7-membered chelate in each case of the α- and β-TCA donor. Whereas the former chelate is attacked from the β-side of the carbocation intermediate by the incoming glycosyl acceptor (α-side being blocked, Fig. 1), but, for the more reactive β-TCA probably there is sufficient time lag between breaking of the β-C_1–O bond of the donor and formation of the β-glycosidic bond so that the approach of the incoming nucleophile can be accommodated at the β-side, since the α-side is still blocked by the bulky pendant C_2–O–[Fe]$NCOCCl_3$ group. In the case of mannosyl donor (entry 10, Table 2) possibility of chelation of catalyst with C-1 and C-2 substituents in the reactant donor does not arise due to their 1,2-*trans* diaxial orientation. So here probably the reaction proceeds *via* usual intermediate oxo-carbenium ion.[30] It has already been reported that with greater number of degrees of freedom, a direct steric interaction between the 6-benzyloxy group and the aglycon is possible, and this interaction will predominate the formation of α-anomer over the β one.[31] Moreover, the bulk of benzyloxy group at 4-

Table 7 Glycosylation reactions in support of anticipated mechanistic pathway

Entry	Donor	Acceptor	Product	Yield[a] α : β ratio
1	 87	**2**	 88	93% 0 : 1
2	 89	 15	 90	87% 1 : 0

[a] Isolated yield.

position also restricts the conformational space allotted for 3-*O*-benzyl ether, which in turn might impinge on the conformation of 2-*O*-benzyl ether destabilizing the β anomer over the α one.[31]

To corroborate with the above we further planned to perform $FeCl_3$ mediated glycosylation reactions (Table 7) using two other armed donors. Like the armed trichloroacetimidate donor **1** bearing C-2–OBn (Table 1), the first trichloroacetimidate donor having a C-2–OMe group **87** (entry 1, Table 7) in reaction with the glycosyl acceptor **2**, generated the corresponding disaccharide **88** (entry 1, Table 7) with exclusive 1,2-*trans* or β-anomeric selectivity. This observation precludes the take part of the phenyl ring of the 2-*O*-benzyl protection during formation of the proposed TS (b or c, Fig. 1). Additional indirect endorsement in favour of the projected mechanistic pathway (Fig. 1) came from a glycosylation reaction of acceptor **15** utilising 2-deoxy glycosyl donor **89** (entry 2, Table 7) which afforded the corresponding glycoside **90** in 87% yield but with α-anomeric selectivity, as evidenced by NMR[32] (^{1}H- and ^{13}C-) spectra. In the absence of 2-oxygen formation of TS (b) or (c) (Fig. 1) does not arise here. With the deoxy donor the reaction probably proceeds *via* formation of the usual oxonium ion intermediate.

Conclusion

In summary, we have demonstrated an efficient general glycosylation reaction condition catalyzed by $FeCl_3$ based on armed and disarmed trichloroacetimidate donors for the synthesis of 1,2-*trans* glycosides, and its use as a promoter in combination with NIS in thioglycoside activation. Advantages of this protocol include operational simplicity, general excellent yield, use of a catalytic amount of commercially available inexpensive, green catalyst for the activation of trichloroacetimidate, and formation of 1,2-*trans* glycoside in preparative scale (g) also. The applicability of this method to a broader scope of phenol nucleophiles as well as a wide variety of sugar nucleophiles and its excellent 1,2-*trans* selectivity both in the presence or absence of predesigned auxiliary protecting group. Its application in orthogonal glycosylation using trichloroacetimidate donor with thioglycoside acceptor, synthesis of a trisaccharide based on one-pot sequential glycosylation reactions, make this general protocol a promising one. We believe it will definitely find immense application in glyco-chemistry. Ramification of the present methodology including the orthogonal glycosylation leading to oligosaccharide synthesis are underway for future publication.

Experimental

General procedures

All reactions were performed in flamed-dried flasks fitted with rubber septa under a positive pressure of argon, unless otherwise stated. Dichloromethane was refluxed with P_2O_5 and distilled before use and stored over 4 Å molecular sieves. $FeCl_3$ was purchased from (Merck, India). Traces of water in the donor and acceptor glycosides were removed by co-evaporation with toluene. Molecular sieves (4 Å) were flame dried before use. Flash column chromatography was performed employing silica gel 60 sorbent (40–63 μm, 230–400 mesh). Thin-layer chromatography (analytical and preparative) was performed using Merck silica gel plates (60-F254) to monitor the reactions and visualized under UV (254 nm) and/or by charring with 5% ethanolic solution of sulfuric acid. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 (300 MHz), a Bruker DPX-400 (400 MHz), a Bruker DPX-500 (500 MHz), or a Bruker DPX-600 (600 MHz) spectrometer at ambient temperature in $CDCl_3$, and assigned using 2D-methods (COSY, HSQC). Optical rotations were measured using Jasco P-1020 digital polarimeter. High Resolution Mass Spectra (HRMS) were measured in a QTOF I (quadrupole-hexapole-TOF) mass spectrometer with an orthogonal Z-spray-electrospray interface on micro (YA-263) mass spectrometer (Manchester, UK). All the known compounds were characterised by NMR spectroscopic analysis and comparing those with their previously reported literature values.

Materials

All glycosydic donors **1**, **10**, **12**, **19**, **21**, **24**, **27**, **29**, **32**, **34**, **36**, **40**, **58**, **61**, **63**, **66**, **68**, **71**, **77**, **80**, **83**, **87**, **89** and **91** acceptors **2**, **4**, **8**, **15**, **17**, **22**, **25**, **30**, **38**, **41**, **69**, **72**, **74**, **78**, **81**, **84** and **86** were prepared according to standard literate procedures. Adamentanol (**6**), long chain alcohol (**59**) and arometic nucleophilic phenols **44**, **46**, **50**, **53** and **55** were purchased at the highest possible purity from Alfa Aesar and Sigma-Aldrich and used as received.

General procedure for glycosylation with carbohydrate acceptors

A 10 mL oven-dried round bottom flask was charged with trichloroacetimidate donor (1.2 equiv.), glycosyl acceptor (1 equiv.), and CH_2Cl_2 (3 mL). The resulting solution was stirred on freshly dried 4 Å molecular sieves for 40 min at room temperature under argon atmosphere. Then this mixture was cooled to −60 °C, $FeCl_3$ (0.1 equiv.) was added, and the reaction mass was allowed to achieve room temperature. After the acceptor was consumed completely (checked by TLC) molecular sieves were filtered off through celite bed. The filtrate was diluted with CH_2Cl_2 and washed subsequently with saturated $NaHCO_3$ solution and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated to afford the glycosylated product. The crude mass was purified by silica gel column chromatography and collected as pure product.

General procedure for glycosylation with phenol acceptors

A 10 mL oven-dried round bottom flask was charged with trichloroacetimidate donor (1.2 equiv.), phenol acceptor (1 equiv.), and CH_2Cl_2 (3 mL). The resulting solution was stirred on freshly dried 4 Å molecular sieves for 40 min at room temperature under argon atmosphere. Then this mixture was cooled to −5 °C, $FeCl_3$ (0.1 equiv.) was added, and the reaction mass was allowed to achieve room temperature. After the acceptor was consumed completely (checked by TLC) molecular sieves were filtered off through celite bed. The filtrate was diluted with CH_2Cl_2 and washed subsequently with saturated $NaHCO_3$

solution and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated to afford the glycosylated product. The crude mass was purified by silica gel column chromatography (60–120 mesh) and collected as pure product.

General procedure for glycosylation with thioglycoside donors

To a mixture of thioglycoside donor (1.1 equiv.) and acceptor (1 equiv.) in dry CH_2Cl_2 (5 mL), flame activated molecular sieves (4 Å) were added. It was stirred at room temperature under argon atmosphere. After 40 min the mixture was cooled to −5 °C, and NIS (1 equiv.) was added to it. Then $FeCl_3$ (0.2 equiv.) was added. After the acceptor was consumed completely (checked by TLC) reaction mixture was filtered off through Celite bed. The filtrate was diluted with CH_2Cl_2 and washed subsequently with saturated sodium thio sulphate, $NaHCO_3$ solution and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated to afford the glycosylated product. The crude mass was purified by silica gel column chromatography (60–120 mesh).

Methyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (3)[33]

A 10 mL oven-dried round bottom flask was charged with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl trichloroacetimidate donor **1** (48.5 mg, 0.071 mmol, 1.2 equiv.), methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside **2** (30 mg, 0.06 mmol, 1 equiv.), and CH_2Cl_2 (3 mL). The resulting solution was stirred on freshly dried 4 Å molecular sieves for 40 min at room temperature under argon atmosphere. Then this mixture was cooled to −60 °C, $FeCl_3$ (1.2 mg, 0.007 mmol, 0.1 equiv.) was added, and the reaction mass was allowed to achieve room temperature. After the acceptor was consumed completely (checked by TLC) molecular sieves were filtered off through celite bed. The filtrate was diluted with CH_2Cl_2 and washed subsequently with saturated $NaHCO_3$ solution and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated to afford the glycosylated product. The crude mass was purified by silica gel column chromatography (60–120 mesh) and collected as colorless syrup (**3**, 59.38 mg, 96%).[33]

Scale-up (∼30 fold) experimental procedure for preparation of 3

The scale-up experiment was done following the above reaction procedure using **1** (1.47 g, 2.16 mmol), **2** (0.92 g, 1.8 mmol), 4 Å molecular sieves, $FeCl_3$ (35 mg, 0.022 mmol) in dry CH_2Cl_2 (45 mL). Pure chromatographed product (**3**, 1.65 g) was obtained in 89% yield. $R_f = 0.18$ (hexane/ethyl acetate, 6/1); $[\alpha]_D^{20}$ +3.2 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.31 (s, 3H, OCH_3), 3.33–3.37 (m, 2H), 3.50–3.58 (m, 4H), 3.81 (dd, 1H, $J = 8.5$, 11.5 Hz), 4.00 (m, 2H), 4.35 (d, 1H, $J = 12.0$ Hz, Bn*H*), 4.41–4.48 (m, 3H, Bn*H*), 4.55 (d, 1H, $J = 8.0$ Hz, H'_1), 4.64–4.72 (m, 3H, Bn*H*, H_1), 4.83 (d, 1H, $J = 11.0$ Hz, Bn*H*), 4.90 (d, 1H, $J = 11.0$ Hz, Bn*H*), 5.32 (t, 1H, $J = 9.5$ Hz, H_4), 5.39 (app t, 1H, $J = 8.5$, 9.0 Hz, H_2), 5.79 (t, 1H, $J = 9.5$ Hz, H_3), 7.06 (bd, 2H, $J = 5.5$ Hz, Ar*H*), 7.16–7.34 (m, 25H, Ar*H*) 7.42 (app t, 2H, $J = 7.0$, 7.5 Hz, Ar*H*), 7.72 (d, 2H, $J = 8.0$ Hz, Ar*H*), 7.84 (d, 2H, $J = 7.5$ Hz, Ar*H*), 7.87 (d, 2H, $J =$ 7.5 Hz, Ar*H*). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 57.1, 68.7, 68.8, 70.1, 71.9, 73.1, 73.5, 74.4, 74.7, 74.8, 74.9, 75.6, 76.6, 82.2, 101.9 (C'_1), 104.0 (C_1), 127.6, 127.7, 127.8, 127.9, 128.2, 128.3, 128.9, 129.4, 129.7, 129.8, 133.2, 133.5, 138.2, 138.6, 165.12 (*C*=O), 165.5 (*C*=O), 165.8 (*C*=O). HRMS (ESI-TOF): calculated for $C_{62}H_{60}O_{14}Na$ (M + Na) 1051.3881 found 1051.3882.

Methyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (5)[33]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 4 : 1) to afford the compound **5** in 93% β only as white solid,[33] R_f 0.33 (80% CH_2Cl_2 in hexane); mp 84–85 °C (from hexane), lit.[33] mp 88–89 °C, mp 79–81 °C (ether–hexane); $[\alpha]_D^{24}$ +22.8 (*c* 1.15, $CHCl_3$); lit.[33] $[\alpha]_D^{24}$ +22 (*c* 0.4 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.34–3.38 (m, 2H), 3.41 (s, 3H, OCH_3), 3.49–3.56 (m, 3H), 3.60–3.65 (m, 3H), 3.77 (bd, 1H, $J = 10.9$ Hz, Bn*H*), 3.88–3.94 (m, 2H), 4.02 (t, 1H, $J = 9.7$ Hz), 4.41–4.48 (m, 4H, Bn*H*), 4.59–4.68 (m, 4H, Bn*H*), 4.77–4.95 (m, 7H, Bn*H*, H_1, H'_1), 5.14 (d, 1H, $J =$ 11.3 Hz, Bn*H*), 7.23–7.49 (m, 35H, Ar*H*). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 55.3, 67.9, 69.1, 70.1, 73.4, 73.7, 74.8, 74.9, 75.2, 75.4, 75.6, 78.1, 78.9, 80.4, 82.8, 84.9, 98.5 (C'_1), 102.5 (C_1), 127.1, 127.3, 127.5, 127.6, 127.7, 127.8, 127.82, 128.02, 128.04, 128.08, 128.1, 128.3, 128.4, 128.5, 137.9, 138.3, 138.4, 138.6, 138.62, 138.7, 139.6. HRMS (ESI-TOF): calculated for $C_{63}H_{70}O_{11}Na$ (M + Na) 1025.4816 and found 1025.4814.

Adamentyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (7)[19c]

A mixture of **1** (75 mg, 0.11 mmol), **6** (14 mg, 0.088 mmol) and flame activated 4 Å molecular sieves were stirred in dry solvent (4 mL) for 40 min at room temperature under argon atmosphere. The mixture was cooled to −5 °C, and $FeCl_3$ (1.8 mg, 0.011 mmol) was added to it. After the acceptor was consumed completely (checked by TLC) molecular sieves were filtered off through celite bed. The filtrate was diluted with CH_2Cl_2 and washed subsequently with saturated $NaHCO_3$ solution and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated to afford the glycosylated product. The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 9 : 1) to afford the compound **7** (62.3 mg) in 94% β as white solid.[19c] $R_f = 0.72$ (hexane/ethyl acetate, 4/1). Mp 118–120 °C (from ethyl acetate, pet-ether), $[\alpha]_D^{24}$ +14.2 (*c* 0.96, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.65 (bs, 6H), 1.83–1.93 (m, 6H), 2.17 (bs, 3H), 3.58 (dd, 1H, $J = 3.6$, 9.7 Hz), 3.60–3.72 (m, 2H), 3.80 (dd, 1H, $J =$ 3.5, 10.5 Hz), 4.03–4.09 (m, 2H), 4.49 (d, 1H, $J = 12.1$ Hz, Bn*H*), 4.51 (d, 1H, $J = 9.6$ Hz, Bn*H*), 4.68 (t, 1H, $J = 12.1$ Hz, Bn*H*), 4.73 (m, 2H, Bn*H*), 4.83–4.89 (app t, 2H, $J = 9.5$, 10.5 Hz, Bn*H*), 5.03 (d, 1H, $J = 10.9$ Hz, Bn*H*), 5.32 (d, 1H, $J = 3.5$ Hz, H_1), 7.17–7.38 (m, 20H, Ar*H*). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 30.7, 36.3, 42.5, 68.8, 69.7, 72.8, 73.4, 74.5, 75.1, 75.5, 78.2, 80.1, 82.1, 89.9 (C_1), 127.5, 127.6, 127.7, 127.76, 127.8, 127.9, 128.0, 128.1, 128.3, 138.36, 138.1, 138.4, 138.42, 139.1. HRMS (ESI-TOF): calculated for $C_{44}H_{50}O_6$ Na (M + Na) 697.3575, found 697.3507.

2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (9)[19b]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 9 : 1) to afford the compound **9** in 85% β as colorless syrup.[19b] $R_f = 0.36$ (hexane/ethyl acetate, 4/1); $[\alpha]_D^{22}$ −24 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 1.33 (s, 6H, CH_3), 1.52 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 3.45–3.50 (m, 2H), 3.59–3.69 (m, 2H), 3.72–3.78 (m, 2H), 4.11 (m, 1H, H_5), 4.18 (dd, 1H, $J = 3.3$, 10.5 Hz, H_6), 4.26 (bd, 1H, $J = 7.9$ Hz, H_4), 4.33 (dd, 1H, $J = 2.0$, 4.5 Hz, H_2), 4.46–4.65 (m, 5H, BnH, H'_1, H_3, H_6), 4.71–4.84 (m, 4H, Bn*H*), 4.97 (d, 1H, $J = 10.9$ Hz, Bn*H*), 5.07 (d, 1H, $J = 11.0$ Hz, *Bn*H), 5.58 (d, 1H, $J = 4.9$ Hz, H_1), 7.14–7.44 (m, 20H, Ar*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 24.5, 25.1, 26.1, 26.1, 67.4, 68.9, 69.8, 70.6, 70.9, 71.5, 73.6, 74.4, 74.9, 75.1, 75.7, 77.8, 81.7, 84.6, 96.5 (C'_1), 104.5 (C_1), 108.6 (*C*Me$_2$), 109.4 (*C*Me$_2$), 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.3, 128.4, 128.7, 138.2, 138.8. HRMS (ESI-TOF): calculated for $C_{46}H_{54}O_{11}Na$ (M + Na) 805.3558 found 805.3559.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl-(1→6)-1,2:3,4-(di-*O*-isopropylidene)-α-D-galactopyranose (11)[38]

The crude residue was purified by silica gel column chromatography (60–120 mesh) and collected as colorless syrup (87%). $R_f = 0.49$ (hexane/ethyl acetate, 3/1); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.33 (s, 6H, CH_3), 1.46 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 3.40–3.50 (m, 2H), 3.63–3.81 (m, 4H), 4.08–4.13 (m, 2H), 4.24 (bd, 1H, $J = 7.8$ Hz, H_4), 4.31–4.37 (m, 2H), 4.57–4.61 (m, 2H, H_3, H'_1), 4.73–4.92 (m, 3H, Bn*H*), 5.01 (d, 1H, $J = 11.0$ Hz, Bn*H*), 5.56 (s, 1H, PhC*H*), 5.57 (d, 1H, $J = 6.3$ Hz, H_1), 7.26–7.48 (m, 15H, Ar*H*). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.5, 24.9, 26.0, 26.1, 66.0, 67.2, 68.8, 70.0, 70.5, 70.8, 71.4, 74.8, 75.1, 77.2, 80.7, 81.4, 81.4, 81.6, 96.4 (C_1), 101.1 (Ph*C*H), 104.9 (C'_1), 108.6 (*C*Me$_2$), 109.4 (*C*Me$_2$), 126.0, 127.5, 128.0, 128.2, 128.3, 128.5, 128.9, 137.3, 138.6. HRMS (ESI-TOF): calculated for $C_{38}H_{43}O_{11}Na$ (M + Na) 698.2703 and found 698.2781.

Methyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (13)[35]

The crude mass was purified by silica gel column chromatography (60–120 mesh) and collected as colorless syrup (95%).[35] $R_f = 0.28$ (hexane/ethyl acetate, 6/1); ^1H NMR ($CDCl_3$, 300 MHz): δ 3.38 (s, 3H, OCH_3), 3.46–3.52 (m, 4H), 3.79–3.96 (m, 3H), 4.06–4.09 (m, 2H), 4.31–4.41 (m, 2H), 4.49 (d, 1H, $J = 7.6$ Hz, H'_1), 4.58–4.63 (m, 2H), 4.63–4.79 (m, 3H, Bn*H*, H_1), 4.92 (d, 1H, $J = 11.7$ Hz, Bn*H*), 4.98 (d, 1H, $J = 11.0$ Hz, Bn*H*), 5.38 (app t, 1H, $J = 9.6$, 9.9 Hz, H_4), 5.47 (t, 1H, $J = 9.6$ Hz, H_2), 5.87 (t, 1H, $J = 9.6$ Hz, H_3), 7.24–7.40 (m, 27H, Ar*H*), 7.47–7.51 (m, 2H, Ar*H*), 7.80–7.83 (d, 2H, $J = 7.1$ Hz, Ar*H*), 7.89–7.92 (d, 2H, $J = 8.0$ Hz, Ar*H*), 7.96–7.98 (d, 2H, $J = 6.6$ Hz, Ar*H*). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 57.3, 68.7, 68.8, 70.2, 72.1, 73.1, 73.2, 73.4, 73.5, 73.56, 73.61, 74.5, 74.6, 75.1, 79.6, 82.1, 101.9 (C'_1), 104.3 (C_1), 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 128.42, 128.48, 128.5, 128.9, 129.0, 129.8, 129.9, 133.2, 137.9, 129.5, 138.5, 138.7, 138.9, 165.3 (*C*=O), 165.6 (*C*=O), 165.9 (*C*=O). HRMS (ESI-TOF): calculated for $C_{62}H_{60}O_{14}Na$ (M + Na) 1051.3881 found 1051.3880.

Methyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (14)[34,36]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 4 : 1) to afford the compound **14** in 88% β as white foam[36] $R_f = 0.52$ (hexane/ethyl acetate, 3/1); ^1H NMR ($CDCl_3$, 300 MHz): δ 3.38–3.43 (m, 3H), 3.43 (s, 3H, OCH_3), 3.51–3.68 (m, 4H), 3.77–4.00 (m, 5H), 4.29 (d, 1H, $J = 11.8$ Hz, Bn*H*), 4.36–4.45 (m, 2H), 4.37 (d, 1H, $J = 7.5$ Hz, H'_1), 4.57–4.76 (m, 6H, Bn*H*, H_1), 4.80–4.90 (m, 4H), 5.03 (d, 1H, $J = 11.4$ Hz, Bn*H*), 5.10 (d, 1H, $J = 11.7$ Hz, Bn*H*), 7.19–7.44 (m, 35H, Ar*H*). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 55.3, 68.1, 68.3, 70.1, 72.6, 73.2, 73.5, 73.7, 73.8, 74.8, 75.3, 75.5, 77.3, 79.0, 80.1, 80.3, 82.5, 98.5 (C'_1), 102.9 (C_1), 127.0, 127.3, 127.4, 127.5, 127.53, 127.6, 127.67, 127.7, 127.8, 127.9, 128.1, 128.16, 128.2, 128.3, 128.4, 138.2, 138.3, 138.6, 138.7, 139.0, 139.1, 139.5. HRMS (ESI-TOF): calculated for $C_{62}H_{66}O_{11}Na$ (M + Na) 1009.4501 found 1009.4503.

Methyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (16)[37]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 4 : 1) to afford the compound **16** in 89% β as colorless syrup. $R_f = 0.35$ (hexane/ethyl acetate, 4.5/1); ^1H NMR ($CDCl_3$, 300 MHz): δ 3.35 (s, 3H, OCH_3), 3.36–3.43 (m, 2H), 3.49 (dd, 1H, $J = 2.6$, 9.7 Hz), 3.59–3.72 (m, 4H), 3.76–3.88 (m, 3H), 4.19–4.37 (m, 4H), 4.46 (d, 1H, $J = 3.7$ Hz, H_1), 4.52 (d, 1H, $J = 12.1$ Hz, Bn*H*), 4.61 (d, 1H, $J = 11.4$ Hz, Bn*H*), 4.70 (bs, 2H, Bn*H*), 4.74–4.82 (m, 3H, Bn*H*, H'_1), 4.94 (d, 1H, $J = 11.6$ Hz, Bn*H*), 5.04 (d, 1H, $J = 11.0$ Hz, Bn*H*), 5.51 (s, 1H, PhC*H*), 7.19–7.48 (m, 30H, Ar*H*). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 55.2, 63.2, 68.7, 70.2, 70.7, 73.3, 73.5, 73.6, 74.7, 75.0, 78.9, 79.5, 82.4, 98.2 (C'_1), 103.90 (C_1), 103.91 (Ph*C*H) 127.4, 127.7, 127.8, 127.9, 128.0, 128.04, 128.13, 1228.26, 128.39, 128.42, 128.50, 128.55, 129.1, 129.8, 134.5, 136.6, 137.8, 138.4, 138.5, 138.6, 139.0. HRMS (ESI-TOF): calculated for $C_{55}H_{58}O_{11}Na$ (M + Na) 917.3878 found 917.3877.

Methyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (18)[38]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 4 : 1) to afford the compound **18** in 90% β as colorless syrup.[38] $R_f = 0.35$ (hexane/ethyl acetate, 4.5/1); ^1H NMR ($CDCl_3$, 300 MHz): δ 3.45–3.47 (m, 6H, OCH_3), 3.57–3.61 (m, 2H), 3.73–3.78 (m, 2H), 3.79–3.85 (m, 3H), 3.81 (d, 1H, $J = 2.3$ Hz), 4.36 (dd, 1H, $J = 4.9$, 10.4 Hz, H_6), 4.42 (bs, 2H), 4.51 (d, 1H, $J = 6.5$ Hz, H'_1), 4.62 (d, 1H, $J = 11.6$ Hz, Bn*H*), 4.67–4.76 (m, 4H, Bn*H*), 4.80 (d, 1H, $J = 4.8$ Hz, H_1), 4.83 (d, 1H, $J = 7.9$ Hz, Bn*H*), 4.94 (d, 1H, $J = 10.8$ Hz, Bn*H*), 4.95 (d, 1H, $J = 11.6$ Hz, Bn*H*), 5.56 (s, 1H, PhC*H*), 7.16–7.38 (m, 30H, Ar*H*). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 56.7, 65.6, 68.7, 68.9, 72.9, 73.4, 73.5, 73.7, 74.6, 74.9, 75.1, 79.3, 79.9, 81.3, 81.5, 82.5, 101.1 (Ph*C*H), 102.8 (C'_1), 103.4 (C_1), 126.0, 127.3, 127.5, 127.6, 127.7, 127.8, 128.0, 128.1, 128.2, 128.23, 128.3, 128.37, 128.4, 128.9, 137.4, 137.9, 138.4, 138.5, 138.7, 138.9. HRMS (ESI-TOF): calculated for $C_{55}H_{58}O_{11}Na$ (M + Na) 917.3878, found 917.3877.

Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (20)[22b]

The crude mass was purified by silica gel column chromatography (60–120 mesh) and collected as colorless syrup (88%). R_f = 0.48 (hexane/ethyl acetate, 3/1); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.32 (bs, 3H, OCH_3), 3.45–3.50 (m, 2H), 3.58 (dd, 1H, J = 5.0, 11.0 Hz), 3.64–3.65 (m, 5H), 3.72–3.79 (m, 2H), 3.89 (t, 1H, J = 9.5 Hz), 4.13 (d, 1H, J = 12.0 Hz, BnH), 4.23 (d, 1H, J = 12.0 Hz, BnH), 4.34 (d, 1H, J = 12.5 Hz, BnH), 3.35 (d, 1H, J = 12.5 Hz, BnH), 4.42 (app t, 1H, J = 9.0, 11.0 Hz, BnH), 4.47–4.54 (m, 7H, BnH, H'_1), 4.60 (d, 1H, J = 12.0 Hz, BnH), 4.76 (d, 1H, J = 10.5 Hz, BnH), 5.01 (d, 1H, J = 11.5 Hz, BnH), 5.21 (d, 1H, J = 2.0 Hz, H_1), 7.11–7.23 (m, 35H, ArH). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 55.2, 69.3, 69.8, 72.0, 72.2, 72.9, 73.1, 73.2, 73.3, 74.8, 74.9, 75.0, 76.2, 77.7, 79.9, 81.5, 97.6 (C'_1), 100.5 (C_1), 126.7, 127.1, 127.2, 127.3, 127.5, 127.6, 127.7, 127.96, 127.98, 128.0, 128.1, 128.25, 128.27, 128.34, 128.38, 128.4, 137.8, 138.3, 138.4, 138.6, 138.7, 138.8. HRMS (ESI-TOF): calculated for $C_{63}H_{70}O_{11}Na$ (M + Na) 1025.4816 and found 1025.4815.

Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (23)[39]

The crude residue was purified by silica gel column chromatography (60–120 mesh) and collected as white foam (92%). R_f = 0.49 (hexane/ethyl acetate, 3/1); $[\alpha]_D^{25}$ = +8.0 (c, 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.33 (s, 3H, CH_3), 1.37 (d, 3H, J = 5.5 Hz, CH_3), 1.41 (s, 3H, CH_3), 3.29 (bs, 1H, H_2), 3.39 (s, 3H, OCH_3), 3.58 (dd, 1H, J = 3.6, 9.7 Hz), 3.65–3.74 (m, 2H), 3.78 (m, 1H), 4.00 (bd, 1H, J = 12.1 Hz), 4.05–4.10 (m, 2H), 4.23–4.33 (m, 2H), 4.70–4.93 (m, 6H, BnH, H_1, H'_1), 5.48 (s, 1H, PhCH), 7.26–7.56 (m, 15H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 17.9, 26.3, 27.8, 54.8, 66.3, 68.5, 69.2, 71.7, 73.5, 75.2, 76.2, 81.0, 98.1 (C'_1), 100.8 (C_1), 101.3 (PhCH), 109.1 (CMe$_2$), 126.1, 127.6, 127.9, 128.2, 128.5, 128.9, 137.4, 137.8, 137.9. HRMS (ESI-TOF): calculated for $C_{37}H_{44}O_{10}Na$ (M + Na) 671.2832 found 671.2861.

Methyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (26)[22b]

The crude residue was purified by column chromatography on silica gel (60–120 mesh) using PE/ethyl acetate 4 : 1 to afford **26** in 90% as white solid.[22b] R_f = 0.29 (25% ethyl acetate in hexane). $[\alpha]_D^{26}$ +28.2 (c 1.0, $CHCl_3$); ^{1}H (300 MHz, $CDCl_3$): δ 1.72 (s, 3H, COCH_3), 1.92 (s, 3H, COCH_3), 2.04 (s, 3H, COCH_3), 2.07 (s, 3H, COCH_3), 3.41 (s, 3H, OCH_3), 3.78–3.96 (m, 6H, H_3, H_4, H_5, H'_5, H_6, H_6), 4.34 (dd, 1H, J = 3.9, 9.9 Hz, H'_6), 4.45 (app t, 1H, J = 9.2, 9.6 Hz, H'_6), 5.01 (d, 1H, J = 5.9 Hz, H_1), 5.07–5.18 (m, 2H, H'_1, H'_4), 5.22 (dd, 1H, J = 3.7, 9.8 Hz, H'_3), 5.34–5.36 (m, 2H, H_2, H'_2), 5.60 (s, 1H, CHPh), 7.27–7.60 (m, 8H, ArH), 8.08 (d, 2H, J = 6.5 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.4, 20.6, 20.7, 55.5, 61.8, 62.1, 65.4, 68.3, 68.8, 69.0, 69.1, 71.7, 72.7, 77.4, 82.2, 97.8, 101.3 (PhCH), 126.0, 128.1, 128.5, 128.9, 129.4, 129.8, 133.5, 136.8, 165.5 (C=O), 169.4 (C=O), 169.6 (C=O), 169.7 (C=O), 170.6 (C=O). HRMS (ESI-TOF): calculated for $C_{35}H_{40}O_{16}Na$ [M + Na]$^+$ 716.2316, found 716.2317.

Methyl 2,3,4-tri-*O*-acetyl-α-L-rhamanopyranosyl-(1→3)-2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (28)[22b]

The crude product was purified by silica gel (60–120 mesh) column chromatography (PE/ethyl acetate 5 : 1) to afford **28** in 89% as white solid.[22b] R_f = 0.38 (hexane/ethyl acetate, 4/1); mp 162–164 °C (from ethyl acetate–hexane); $[\alpha]_D^{25}$ +44 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.75 (d, 3H, J = 6.2 Hz, CH_3), 1.89 (s, 3H, COCH_3), 1.91 (s, 3H, COCH_3), 1.93 (s, 3H, COCH_3), 3.38 (s, 3H, OCH_3), 3.72 (t, 1H, J = 9.4 Hz), 3.82 (t, 1H, J = 10.2 Hz), 3.94 (dt, 1H, J = 4.6, 9.9 Hz, H_5), 4.16 (m, 1H, H'_5), 4.34 (dd, 1H, J = 4.5, 10.0 Hz, H_6), 4.42 (app t, 1H, J = 9.3, 11.6 Hz, H_6), 4.89 (t, 1H, J = 10.0 Hz, H'_4), 5.00 (s, 1H, H'_1), 5.04–5.09 (m, 3H, H_1, H_2, H'_2), 5.22 (dd, 1H, J = 3.5, 10.0 Hz, H'_3), 5.59 (s, 1H, CHPh), 7.29–7.59 (m, 8H, ArH), 7.98–8.01 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 16.6, 20.4, 20.5, 20.6, 29.6, 55.4, 62.6, 66.2, 68.8, 68.9, 69.4, 70.9, 73.2, 74.7, 79.5, 97.7, 98.0, 101.9 (PhCH) 126.3, 128.0, 128.3, 129.1, 129.8, 133.3, 137.1, 165.6 (C=O), 169.2 (C=O), 169.8 (C=O). HRMS (ESI-TOF): calculated for $C_{33}H_{38}O_{14}Na$ (M + Na) 658.2262 found 658.2261.

Methyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (31)[22d]

The crude residue was directly purified by silica gel flash column chromatography (hexane/ethyl acetate, 4 : 1) to afford **31** (91%) as a white foam.[22d] R_f = 0.28 (25% ethyl acetate in hexane). $[\alpha]_D^{26}$ +28.2 (c 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.01 (s, 3H, COCH_3), 3.35 (s, 3H, OCH_3), 3.43 (d, 1H, J = 10.8 Hz), 3.63 (dd, 1H, J = 3.0, 10.8 Hz), 3.70–3.77 (m, 5H), 3.84–3.85 (m, 3H), 4.16 (t, 1H, J = 9.0 Hz), 4.35 (d, 1H, J = 12.0 Hz), 4.41 (brs, 1H), 4.43 (brs, 1H), 4.53–4.58 (m, 3H), 4.60–4.65 (m, 4H), 4.67 (d, 1H, J = 10.8 Hz), 4.76 (s, 1H, H_1), 4.80 (d, 1H, J = 10.8 Hz), 5.42 (brs, 1H, H'_1), 5.47 (brs, 1H), 7.13–7.34 (m, 30H, ArH). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.0, 54.9, 68.5, 68.6, 69.9, 71.4, 71.1, 71.7, 72.3, 72.5, 73.2, 73.4, 73.9, 74.0, 75.0, 78.4, 80.1, 98.7 (C_1), 99.4 (C'_1), 127.3, 127.4, 127.45, 127.5, 127.57, 127.6, 127.7, 127.8, 127.9, 128.0, 128.2, 128.27, 128.3, 137.9, 138.1, 138.2, 138.3, 138.4, 138.5, 169.9 (C=O); HRMS (ESI-TOF) : calculated for $C_{57}H_{62}O_{12}Na$ [M + Na]$^+$ 961.4139 found 961.4131.

Methyl 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-mannopyranoside (33)

The crude product was purified by silica gel flash column chromatography (hexane/ethyl acetate, 4 : 1) to afford **33** (91%) as a white foam. R_f = 0.21 (25% ethyl acetate in hexane). $[\alpha]_D^{26}$ +59.5 (c 1.06, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.25 (s, 3H, OCH_3), 3.39 (d, 1H, J = 9.6 Hz), 3.60–3.64 (m, 2H), 3.76 (t, 1H, J = 2.4 Hz), 3.90 (d, 1H, J = 3.0 Hz), 3.94 (t, 1H, J = 6.6 Hz), 4.26 (dd, 1H, J = 8.0, 12.0 Hz), 4.37 (apparent t, 2H, J = 9.0, 9.6 Hz), 4.40 (apparent t, 2H, J = 4.8, 6.0 Hz), 4.61 (d, 1H, J = 12.0 Hz), 4.67–4.73 (m, 3H, H_1), 4.92 (d, 1H, J = 12.0 Hz), 4.99 (d, 1H, J = 8.4 Hz, H'_1), 5.40 (dd, 1H, J = 3.6, 10.8 Hz), 5.72 (dd, 1H, J = 8.4, 10.2 Hz), 5.87 (d, 1H, J = 3.6 Hz), 7.17–7.57 (m, 27H, ArH), 7.76 (d, 2H, J = 7.2 Hz, ArH), 7.89 (d, 2H, J = 7.8 Hz, ArH), 7.94 (d, 2H, J = 7.8 Hz, ArH), 7.97 (d, 2H, J = 7.2 Hz, ArH). ^{13}C NMR (150 MHz, $CDCl_3$): δ 54.9, 61.8, 68.8, 70.7, 71.2, 72.1, 72.7, 73.0, 73.5, 75.6, 78.5, 99.5 (C_1)

101.2 (C'_1), 127.0, 127.4, 127.6, 127.9, 128.0, 128.4, 128.5, 128.6, 128.7, 129.0, 129.3, 129.4, 129.7, 129.9, 130.0, 133.26, 133.30, 133.4, 133.5, 138.6, 139.3, 165.3 (*C*=O), 165.6 (*C*=O), 165.7 (*C*=O), 166.0 (*C*=O). HRMS (ESI-TOF): calculated for $C_{62}H_{58}O_{15}Na$ $[M + Na]^+$ 1065.3673, found 1065.3665.

Methyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (35)[22b]

The crude mass was purified by silica gel column chromatography (60–120 mesh) (PE/EtOAc 5 : 1) to get pure product **35** in 88% yield. It was crystallized from PE/EtOAc; mp 232–234 °C. $[\alpha]_D^{25}$ +38.8 (*c* 1.39, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 3.12 (s, 3H, OCH_3), 3.66–3.83 (m, 3H), 3.90 (app t, 1H, J = 9.4, 9.7 Hz), 4.08 (bd, 1H, J = 10.9 Hz), 4.21 (app t, 1H, J = 8.0, 9.3 Hz, H_6), 4.42 (dd, 1H, J = 4.6, 10.2 Hz, H_6), 4.91 (d, 1H, J = 4.1 Hz, H_1), 4.93 (d, 1H, J = 7.3 Hz, H'_1), 5.11 (dd, 1H, J = 3.3, 10.2 Hz, H_2), 5.33 (ABq, 1H, J = 9.7 Hz, H_3), 5.48–5.58 (m, 2H, CHPh, H'_2), 5.81 (t, 1H, J = 9.5 Hz, H'_3), 6.08 (t, 1H, J = 9.8 Hz, H_4), 7.27–7.50 (m, 20H, ArH), 7.90 (d, 2H, J = 8.5 Hz, ArH), 7.89–7.99 (m, 8H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.0, 66.6, 68.5, 68.6, 69.6, 70.3, 71.9, 72.0, 72.4, 78.7, 96.4 (C'_1), 101.4 (Ph*C*H), 102.0 (C_1) 126.1, 128.19, 128.16, 128.26, 128.29, 128.33, 128.4, 129.0, 129.3, 129.6, 129.77, 129.84, 133.0, 133.1, 133.2, 133.4, 136.7, 165.3 (*C*=O), 165.4 (*C*=O), 165.6 (*C*=O), 165.7 (*C*=O). HRMS *m*/*z* calculated for ($C_{55}H_{48}O_{16}Na^+$) $[M + Na]^+$ 987.2840, found: 987.2841.

Methyl 2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (37)[22d]

The crude residue was purified by silica gel flash column chromatography (hexane/EtOAc, 3 : 1) to afford **37** (90%) as a white solid. R_f 0.30 (25% EtOAc in hexane); mp 185–186 °C (from PE–ethyl acetate); $[\alpha]_D^{26}$ +29.6 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 2.07 (s, 3H, COCH_3), 3.42 (m, 1H), 3.46 (s, 3H, OCH_3), 3.68 (dd, 1H, J = 6.7, 10.8 Hz), 3.71–3.77 (m, 3H), 4.05 (dd, 1H J = 1.5, 10.8 Hz), 4.25 (m, 1H), 4.31 (dd, 1H, J = 4.9, 10.5 Hz), 4.54 (d, 1H, J = 7.9 Hz, H'$_1$), 4.69 (d, 1H, J = 12.1 Hz, BnH), 4.88 (d, 1H, J = 12.1 Hz, BnH), 5.08 (dt, 1H, J = 2.4, 7.6 Hz, H'$_1$), 5.23–5.27 (m, 2H, H_1, H_2), 5.45 (t, 1H, J = 9.8 Hz, H_3), 5.55 (s, 1H, PhCH), 6.15 (t, 1H, J = 9.3 Hz, H_4), 7.26–7.31 (m, 7H, ArH), 7.35–7.42 (m, 8H, ArH), 7.49–7.54 (m, 4H, ArH), 7.85–7.88 (m, 2H, ArH), 7.94–7.99 (m, 4H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9, 55.4, 66.2, 68.3, 68.5, 69.4, 70.5, 72.0, 72.6, 74.1, 78.4, 81.4, 96.7, 101.2 (C_1), (Ph*C*H), 101.8 (C_1), 126.0, 127.6, 127.8, 128.2, 128.3, 128.40, 128.43, 128.87, 128.99, 129.03, 129.6, 129.8, 129.9, 133.0, 133.3, 133.5, 137.1, 138.2, 165.3 (*C*=O), 165.7 (*C*=O), 165.8 (*C*=O), 169.4 (*C*=O); HRMS (ESI-TOF) calculated for $C_{50}H_{48}O_{15}Na$ $[M + Na]^+$ 911.2891, found 911.2889.

2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (39)[19c]

The crude residue was purified by silica gel flash column chromatography (hexane/EtOAc, 3 : 1) to afford **39** (89%) as a white foam. R_f 0.30 (20% EtOAc in hexane); ^1H NMR ($CDCl_3$, 300 MHz): δ 1.33 (s, 4H), 1.69 (s, 8H), 3.43 (d, 2H, J = 3.43 Hz), 3.54–3.66 (m, 5H), 3.75–3.87 (m, 4H), 3.94–4.01 (m, 2H), 4.05–4.19 (m, 3H), 4.36 (m, 1H), 4.41–4.54 (m, 2H), 4.91 (d, 1H, J = 8.3 Hz), 4.59 (m, 1H), 4.66–4.84 (m, 3H), 4.91 (d, 1H, J = 8.3 Hz, H''_1), 5.38 (m, 1H), 5.44–5.53 (m, 2H), 5.87 (t, 1H, J = 9.5 Hz), 7.15–7.49 (m, 29H, ArH), 7.81 (d, 2H, J = 7.7 Hz, ArH), 7.92 (d, 2H, J = 7.4 Hz, ArH), 7.97 (d, 2H, J = 7.5 Hz, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.1, 24.8, 25.7, 25.9, 67.4, 68.6, 68.7, 68.8, 70.3, 70.4, 70.5, 70.8, 71.8, 73.2, 73.5, 74.0, 74.7, 74.8, 74.9, 75.6, 77.7, 82.1, 84.6, 96.1 (C_1), 101.3 (C''_1), 103.9 (C'_1), 108.3 (CMe_2), 109.2 (CMe_2), 127.5, 127.6, 127.7, 127.8, 127.91, 127.97, 128.15, 128.19, 128.24, 128.3, 128.4, 128.5, 128.7, 128.9, 129.7, 129.8, 130.0, 132.9, 133.1, 133.3, 133.4, 138.0, 138.2, 138.7, 165.2 (*C*=O), 165.4 (*C*=O), 165.8 (*C*=O); HRMS (ESI): calculated for $C_{73}H_{76}O_{19}Na$ (M + Na) 1279.4879 found 1279.4870.

Methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phathalimido-β-D-glucopyranosyl-(1→4)-[3,4,6-tri-*O*-acetyl-2-deoxy-2-phathalimido-β-D-glucopyranosyl-(1→6)]-2,3-di-*O*-benzyl-α-D-glucopyranoside (42)[22d]

The crude residue was purified by silica gel flash column chromatography (hexane/EtOAc, 1 : 2) to afford **42** (83%) as a white foam. R_f 0.31 (60% EtOAc in hexane). $[\alpha]_D^{24}$ +24.6 (*c* 1.0, $CHCl_3$); lit.[22d] $[\alpha]_D^{20}$ +23.9 (*c* 0.8, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.80 (s, 3H, COCH_3), 1.84 (s, 3H, COCH_3), 1.97 (s, 3H, COCH_3), 2.03 (s, 3H, COCH_3), 1.99 (s, 3H, COCH_3), 2.12 (s, 3H, COCH_3), 3.06 (s, 3H, OCH_3), 3.17–3.19 (m, 2H), 3.40 (app t, 1H, J = 9.0, 10.0 Hz), 3.52–3.59 (m, 2H), 3.66–3.68 (m, 2H), 3.76 (app t, 1H, J = 8.5, 9.5 Hz), 3.84 (dd, 1H, J = 2.5, 12.5 Hz), 4.08 (dd, 1H, J = 4.0, 12.5 Hz), 4.11–4.20 (m, 4H), 4.34 (dd, 1H, J = 5.0, 12.5 Hz), 4.41 and 4.53 (d, each 1H, J = 12.0 Hz, BnH), 4.82 and 4.90 (d, J = 12.0 Hz, each 1H, BnH), 5.05–5.12 (m, 3H), 5.47 (d, 1H, J = 8.5 Hz), 5.52 (dd, 1H, J = 9.5, 10.5 Hz), 5.69 (dd, 1H, J = 9.5, 10.5 Hz), 7.15–7.16 (m, 2H, ArH), 7.21–7.26 (m, 4H, ArH), 7.32–7.33 (m, 4H, ArH), 7.65–7.67 (m, 2H, ArH), 7.75–7.79 (m, 4H, ArH), 7.87–7.88 (m, 2H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.4, 20.5, 20.7, 20.8, 20.9, 54.58, 55.0, 55.4, 61.8, 62.2, 68.7, 68.8, 69.2, 69.3, 70.8, 70.85, 71.8, 73.3, 74.5, 77.3, 79.5, 79.8, 97.5, 97.6, 99.0, 123.5, 123.9, 126.8, 127.2, 127.9, 128.0, 128.3, 128.4, 131.4, 131.7, 134.2, 134.7, 138.1, 139.5, 169.5 (*C*=O), 170.2 (*C*=O), 170.8 (*C*=O), 170.9 (*C*=O). HRMS (ESI-TOF) calcd for $C_{50}H_{48}O_{15}Na$ $[M + Na]^+$ 911.2891, found 911.2889.

Methyl 2,3,4-tri-*O*-acetyl-α-L-rhamanopyranosyl-(1→4)-[2,3,4-tri-*O*-acetyl-α-L-rhamanopyranosyl-(1→6)]-2,3-di-*O*-benzyl-α-D-glucopyranoside (43)[22b]

The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using PE/EtOAc 2 : 1 to afford **43** in 81% as white foam. ^1H NMR (300 MHz, $CDCl_3$): δ 0.79 (d, 3H, J = 6.2 Hz, CH_3), 1.20 (d, 3H, J = 6.2 Hz, CH_3), 1.97 (s, 3H, COCH_3), 1.98 (s, 3H, COCH_3), 1.99 (s, 3H, COCH_3), 2.04 (s, 3H, COCH_3), 2.09 (s, 3H, COCH_3), 2.12 (s, 3H, COCH_3), 3.39 (s, 3H, OCH_3), 3.60 (dd, 1H, J = 3.6, 9.4 Hz), 3.65–3.78 (m, 4H), 3.83–3.95 (m, 3H), 4.00 (m, 1H), 4.57 (d, 1H, J = 3.5 Hz, H_1), 4.59 (d, 1H, J = 12.0 Hz, BnH), 4.62 (d, 1H, J = 12.0 Hz, BnH), 4.72 (app t, 1H, J = 5.1, 5.7 Hz), 4.74 (d, 1H, J = 11.9 Hz, BnH), 4.80

(d, 1H, J = 1.5 Hz, H'_1/H''_1), 4.88 (d, 1H, J = 1.5 Hz, H''_1/H'_1), 4.97 (d, 1H, J = 10.1 Hz, BnH), 4.99–5.0 (m, 1H), 5.08 (d, 1H, J = 11.2 Hz, BnH), 5.13 (dd, 1H, J = 1.7, 3.5 Hz), 5.22 (dd, 1H, J = 3.5, 10.2 Hz), 5.27 (dd, 1H, J = 3.6, 6.5 Hz), 7.25–7.39 (m, 10H, ArH).

2′-Napthyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (45)[40]

A mixture of **1** (57 mg, 0.083 mmol), **44** (10 mg, 0.07 mmol) and flame activated 4 Å molecular sieves were stirred in dry solvent (4 mL) for 40 min at room temperature under argon atmosphere. The mixture was cooled to −5 °C and $FeCl_3$ (1.3 mg, 0.0083 mmol) was added to it. After the acceptor was consumed completely (checked by TLC) molecular sieves were filtered off through celite bed. The filtrate was diluted with CH_2Cl_2 and washed subsequently with saturated $NaHCO_3$ solution and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated to afford the glycosylated product. The crude residue was directly purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 8 : 1) to afford the compound **45** (44.86 mg) in 97% β as white foam.[40] R_f = 0.42 (hexane/ethyl acetate, 4/1); ^{1}H (300 MHz, $CDCl_3$): δ 3.72–3.86 (m, 6H), 4.52–4.62 (m, 3H, BnH), 4.82–4.89 (m, 3H, BnH), 4.97 (d, 1H, J = 10.8 Hz, BnH), 5.11 (d, 1H, J = 10.8 Hz, BnH), 5.16 (d, 1H, J = 6.7 Hz, H_1), 7.23–7.45 (m, 24H, ArH), 7.66 (d, 1H, J = 7.7 Hz, ArH), 7.76–7.80 (m, 2H, ArH).

4′-Methoxyphenyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (47)[41]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 9.5 : 0.5) to afford the compound **47** in 97% β as white solid.[41] R_f = 0.54 (hexane/ethyl acetate, 9/1); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.60 (m, 1H), 3.68–3.76 (m, 4H), 3.80 (s, 3H, OCH_3), 3.83 (dd, 1H, J = 1.0, 10.0 Hz), 4.55–4.64 (m, 3H, BnH, H_1), 4.84–4.93 (m, 4H, BnH), 4.98 (d, 1H, J = 11.0 Hz, BnH), 5.08 (d, 1H, J = 11.0 Hz, BnH), 6.84 (d, 2H, J = 9.0 Hz, ArH), 7.06 (d, 2H, J = 12.5 Hz, ArH), 7.22 (d, 2H, J = 10.0 Hz, ArH), 7.27–7.38 (m, 18H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 55.8, 69.1, 73.6, 75.1, 75.2, 75.9, 76.7, 77.9, 82.2, 84.8, 102.9 (C_1) 114.7, 118.6, 127.7, 127.7, 127.8, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 138.2, 138.3, 138.4, 138.7, 151.7, 155.4. HRMS (ESI-TOF): calculated for $C_{41}H_{42}O_7$ Na (M + Na) 669.2823 found 669.2841.

2′,6′-Dimethylphenyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (49)[40]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 9.5 : 0.5) to afford the compound **49** in 90% β as white solid.[40] R_f = 0.52 (hexane/ethyl acetate, 9/1); $[\alpha]_D^{27}$ +96.4 (c 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.39 (s, 6H, 2 × CH_3), 3.32 (m, 1H, H_5), 3.65–3.77 (m, 5H), 4.46 (d, 1H, J = 12.4 Hz, BnH), 4.54 (d, 1H, J = 12.0 Hz, BnH), 4.62 (d, 1H, J = 10.8 Hz, BnH), 4.79–4.89 (m, 4H, BnH, H_1), 5.01 (d, 1H, J = 10.8 Hz, BnH), 5.16 (d, 1H, J = 10.8 Hz, BnH), 6.98–7.04 (m, 3H, ArH), 7.20 (d, 1H, J = 1.2 Hz, ArH), 7.21 (d, 1H, J = 2.0 Hz, ArH), 7.25–7.33 (m, 16H, ArH), 7.38–7.40 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 17.3, 69.1, 73.6, 75.10, 75.17, 75.4, 75.8, 78.0, 83.0, 84.9, 104.3 (C_1) 124.6, 127.5, 127.6, 127.7, 127.8, 128.1, 128.2, 128.3, 128.4, 128.5, 128.9, 132.0, 138.3, 138.4, 138.8, 153.4. HRMS (ESI-TOF): calculated for $C_{42}H_{44}O_6$Na (M + Na) 667.3729, found 667.3731.

4′-Bromophenyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (51)[41]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 9.5 : 0.5) to afford the compound **51** in 92% β as white solid.[41] R_f = 0.54 (hexane/ethyl acetate, 9/1); ^{1}H NMR ($CDCl_3$, 500 MHz): 3.59–3.79 (m, 6H), 4.52 (d, 1H, J = 12.5 Hz, BnH), 4.56–4.60 (m, 2H, BnH), 4.82–4.87 (m, 3H, BnH), 4.94–4.98 (m, 2H, BnH, H_1), 5.00 (d, 1H, J = 11.0 Hz, BnH), 6.95–6.97 (d, 2H, J = 8.5 Hz, ArH), 7.19–7.39 (m, 22H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 68.8, 73.5, 75.1, 75.3, 75.8, 77.7, 81.9, 84.7, 101.7 (C_1) 127.8, 127.9, 128.0, 128.2, 128.4, 128.5, 132.4, 137.9, 138.1, 138.2, 138.5, 156.5.

2′-Napthyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside (52)[40]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 8 : 1) to afford the compound **52** in 97% β as white foam.[40] R_f = 0.42 (hexane/ethyl acetate, 4/1); ^{1}H (300 MHz, $CDCl_3$): δ 3.60–3.71 (m, 3H), 3.77 (t, 1H, J = 5.9 Hz), 3.98 (d, 1H, J = 2.4 Hz), 4.19 (app t, 1H, J = 8.0 Hz), 4.45 (ABq, 2H, J = 11.6 Hz, BnH), 4.66 (d, 1H, J = 11.6 Hz, BnH), 4.76 (d, 1H, J = 11.9 Hz, BnH), 4.81 (d, 1H, J = 11.9 Hz, BnH), 4.89 (d, 1H, J = 11.8 Hz, BnH), 4.98–5.06 (app t, 2H, J = 11.3, 13.2 Hz, BnH), 5.14 (d, 1H, J = 7.6 Hz, H_1), 7.26–7.37 (m, 22H, ArH), 7.42 (d, 2H, J = 2.4 Hz, ArH), 7.64 (d, 1H, J = 7.9 Hz, ArH), 7.33–7.79 (m, 2H, ArH).

1′-Napthyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside (54)[40]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 9 : 1) to afford compound **54** in 95% β as white foam.[40] R_f = 0.62 (hexane/ethyl acetate, 4/1); ^{1}H (300 MHz, $CDCl_3$): δ 3.61–3.69 (m, 2H), 3.71–3.78 (m, 2H), 4.00 (d, 1H, J = 2.3 Hz), 4.32 (app t, 1H, J = 7.8, 9.4 Hz), 4.40 (d, 1H, J = 11.6 Hz, BnH), 4.47 (d, 1H, J = 11.7 Hz, BnH), 4.69 (d, 1H, J = 11.6 Hz, BnH), 4.79 (s, 2H, BnH), 4.97 (d, 1H, J = 10.6 Hz, BnH), 5.02 (d, 1H, J = 11.6 Hz, BnH), 5.12 (d, 1H, J = 10.6 Hz, BnH), 5.19 (d, 1H, J = 7.7 Hz, H_1), 7.13 (d, 1H, J = 7.6 Hz, ArH), 7.23–7.41 (m, 22H, ArH), 7.46 (d, 1H, J = 8.4 Hz, ArH), 7.52 (d, 1H, J = 8.2 Hz, ArH), 7.80 (d, 1H, J = 7.7 Hz, ArH), 8.32 (d, 1H, J = 8.1 Hz, ArH).

4′-Chloro-3′-methylphenyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside (56)

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 9 : 1) to afford the compound **56** in 94% β as white solid. R_f = 0.62 (hexane/ethyl acetate, 4/1); $[\alpha]_D^{25}$ −20.84 (c 1.9, $CHCl_3$); ^{1}H (300 MHz, $CDCl_3$): δ 2.28 (s, 3H, CH_3), 3.59–3.67 (m, 4H), 3.94 (bd, 1H, J = 2.6 Hz), 4.09 (dd, 1H, J = 7.8, 9.5 Hz), 4.37–4.48 (2d, 2H, J = 11.0 Hz, BnH), 4.63 (d, 1H, J = 11.6 Hz, BnH), 4.71–4.80 (2d, 2H, J = 11.0 Hz, BnH), 4.85 (d, 1H, J = 10.9 Hz, BnH), 4.91 (d, 1H, J = 7.7 Hz, H_1), 4.96 (d, 1H, J = 10.8 Hz, BnH), 4.98 (d, 1H, J

= 11.6 Hz, BnH), 6.83–7.36 (m, 23H, ArH). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 20.4, 69.1, 73.3, 73.5, 73.8, 74.1, 74.7, 75.6, 79.3, 82.2, 102.3 (C_1), 115.9, 119.7, 127.72, 127.78, 127.8, 127.9, 127.98, 128.3, 128.4, 128.5, 128.6, 129.7, 137.1, 137.9, 138.5, 138.6, 156.1. HRMS (ESI): calculated for $C_{41}H_{41}ClO_6Na$ (M + Na) 664.2592, found 664.2491.

2′,6′-Dimethylphenyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside (57)[41]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 9.5 : 0.5) to afford the compound **57** in 91% β as white solid.[41] R_f = 0.52 (hexane/ethyl acetate, 9/1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.35 (s, 6H, 2 × CH_3), 3.41–3.52 (m, 2H), 3.57–3.65 (m, 2H), 3.93 (bd, 1H, J = 2.5 Hz), 4.11 (dd, 1H, J = 7.7, 9.7 Hz), 4.35 (bs, 2H, BnH), 4.64 (d, 1H, J = 11.7 Hz, BnH), 4.72–4.82 (m, 3H, BnH, H_1), 4.89 (d, 1H, J = 10.9 Hz, BnH), 5.00 (d, 1H, J = 11.7 Hz, BnH), 5.10 (d, 1H, J = 10.9 Hz, BnH), 6.93–7.02 (m, 2H, ArH), 7.16–7.19 (m, 2H, ArH), 7.26–7.29 (m, 19H, ArH).

3-(*N*-Benzyloxycarbonyl)propyl 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranoside (60)[22b]

The crude product was purified by column chromatography on silica gel (60–120 mesh) using PE/EtOAc 6 : 1 to give **60** in 88% as white foam; $[\alpha]_D^{25}$ +60.05 (c 1.28, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.77–1.88 (m, 2H, CH_2), 3.15–3.27 (m, 2H, NCH_2), 3.67 (m, 1H, OCH), 4.03 (m, 1H, H_5), 4.32 (t, 1H, J = 6.5 Hz, OCH), 4.42 (dd, 1H, J = 6.8, 11.8 Hz, H_6), 4.67 (dd, 1H, J = 6.5, 11.5 Hz, H_6), 4.81 (d, 1H, J = 7.5 Hz, H_1), 5.00 (m, 1H, NH), 5.05 (s, 2H, BnH), 5.62 (dd, 1H, J = 3.8, 10.3 Hz, H_3), 5.78 (dd, 1H, J = 8.3, 10.3 Hz, H_2), 5.99 (d, 1H, J = 3.5 Hz, H_4), 7.21–7.26 (m, 2H, ArH), 7.29 (m, 1H, ArH), 7.33–7.36 (m, 6H, ArH), 7.41–7.44 (m, 3H, ArH), 7.46–7.51 (m, 3H, ArH), 7.55 (t, 1H, J = 7.5 Hz, ArH), 7.62 (t, 1H, J = 7.5 Hz, ArH), 7.77–7.79 (d, 2H, J = 8.0 Hz, ArH), 7.94–7.95 (d, 2H, J = 8.0 Hz, ArH), 8.00–8.02 (m, 2H, ArH), 8.08–8.09 (d, 2H, J = 8.0 Hz, ArH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 29.7, 38.3, 62.2, 66.6, 68.3, 70.0, 71.6, 71.7, 101.8 (C_1), 128.1, 128.4, 128.6, 128.8, 128.9, 129.2, 129.4, 129.6, 129.8, 129.9, 130.2, 133.4, 133.5, 133.7, 156.6 (C=O), 165.7 (C=O), 166.2 (C=O); HRMS m/z calcd for $C_{45}H_{41}NO_{12}Na^+$ calcd: 810.2527, found: 810.2526.

3-(*N*-Benzyloxycarbonyl)propyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl-(1→4) 2-*O*-acetyl-3,6-di-*O*-benzyl-β-D-glucopyranoside (62)[22e]

The crude mass was purified by silica gel column chromatography (60–120 mesh) (PE/EtOAc 3 : 1) to get pure product (**62**) as colourless syrup in 92% yield. $[\alpha]_D^{29}$ −2.57 (c 7.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.68–1.76 (m, 2H, CH_2), 1.97 (s, 3H, $COCH_3$), 3.23 (m, 1H, NCH), 3.33–3.37 (m, 3H), 3.38–3.43 (m, 2H), 3.46 (m, 1H), 3.55–3.59 (m, 2H), 3.69 (d, 1H, J = 10.0 Hz), 3.74–3.77 (m, 2H), 3.85 (m, 1H), 3.9 (d, 1H, J = 2.5 Hz), 3.95 (t, 1H, J = 9.0 Hz), 4.23 (d, 1H, J = 12.0 Hz), 4.29–4.34 (app t, 2H, J = 10.5, 11.5 Hz), 4.36–4.38 (dd, 2H, J = 1.5, 9.0 Hz), 4.48 (d, 1H, J = 12.0 Hz, BnH), 4.54 (d, 1H, J = 11.0 Hz, BnH), 4.58 (d, 1H, J = 11.0 Hz, BnH), 4.68 (d, 1H, J = 12.0 Hz, BnH), 4.72 (d, 1H, J = 12.0 Hz, BnH), 4.75 (d, 1H, J = 11.0 Hz, BnH), 4.82 (d, 1H, J = 11.0 Hz, BnH), 4.94–4.98 (m, 3H, H_1, H'_1, H_2), 5.08 (bs, 2H, BnH), 5.29 (bs, 1H, NH), 7.19–7.36 (m, 35H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9, 29.5, 38.2, 66.5, 66.7, 68.1, 68.3, 72.5, 72.6, 73.1, 73.5, 73.7, 74.3, 74.7, 75.3, 79.9, 80.8, 82.5, 100.8 (C_1), 102.9 (C'_1), 127.2, 127.4, 127.5, 127.57, 127.62, 127.7, 127.9, 128.0, 128.1, 128.2, 128.3, 128.3, 128.4, 128.5, 136.9, 138.1, 128.2, 138.5, 138.8, 139.0, 139.1, 156.6 (C=O), 169.6 (C=O). HRMS (TOF): calc. for (M + Na)$^+$ $C_{67}H_{73}NO_{14}Na$ 1138.4929, found 1138.4932.

Adamentyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside (64)[42]

The crude mass was purified by silica gel column chromatography (60–120 mesh) (PE/EtOAc 5 : 1) to get pure product (**64**) as colourless syrup in 94% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.49–1.61 (m, 6H), 1.66–1.70 (m, 3H), 1.83–1.87 (m, 3H), 2.04 (s, 3H), 4.22 (m, 1H, H_5), 4.52–4.60 (m, 2H, H_6, H_6), 5.16 (d, 1H, J = 7.9 Hz, H_1), 5.49–5.62 (m, 2H, H_2, H_4), 5.95 (t, 1H, J = 9.6 Hz, H_3), 7.28–7.55 (m, 12H, ArH), 7.85–8.06 (m, 8H, ArH).

Adamentyl 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranoside (65)

The crude mass was purified by silica gel column chromatography (60–120 mesh) (PE/EtOAc 5 : 1) to get pure product (**65**) as colourless syrup in 89% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.49–1.56 (m, 6H), 1.64–1.71 (m, 3H), 1.84–1.87 (m, 3H), 2.04 (s, 3H), 4.34 (m, 1H, H_5), 4.46 (dd, 1H, J = 5.9, 11.0 Hz, H_6), 4.59 (dd, 1H, J = 3.1, 10.8 Hz, H_6), 5.09 (d, 1H, J = 7.9 Hz, H_1), 5.60 (dd, 1H, J = 3.1, 10.2 Hz, H_3), 5.78 (app t, 1H, J = 8.2, 9.8 Hz, H_2), 5.97 (bs, 1H, H_4), 7.23–7.59 (m, 12H, ArH), 7.78–7.80 (d, 2H, J = 7.7 Hz, ArH), 7.95–7.98 (d, 2H, J = 7.5 Hz, ArH), 8.03–8.06 (d, 2H, J = 7.6 Hz, ArH), 8.10–8.13 (d, 2H, J = 7.6 Hz, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 30.6, 36.1, 42.4, 62.5, 68.4, 69.9, 71.2, 72.2, 75.8, 94.6 (C_1) 128.3, 128.37, 128.42, 128.6, 128.9, 129.1, 129.67, 129.72, 129.8, 130.2, 133.1, 133.2, 133.5, 165.6, 165.8, 166.1.

Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (67)[22d]

The crude mass was purified by silica gel column chromatography (60–120 mesh) (PE/EtOAc 5 : 1) to get pure product (**67**) as colourless syrup in 91% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.92 (s, 6H, $COCH_3$), 1.95 (s, 3H, $COCH_3$), 1.97 (s, 3H, $COCH_3$), 3.28 (m, 1H), 3.34 (s, 3H, OCH_3), 3.44 (dd, 1H, J = 4.0, 9.0 Hz), 3.56–3.60 (m, 2H), 3.73 (dd, 1H, J = 3.5, 11.0 Hz), 3.81–3.86 (m, 3H), 4.11 (dd, 1H, J = 4.0, 12.0 Hz), 4.40 (d, 1H, J = 12.0 Hz, BnH), 4.48 (d, 1H, J = 8.0 Hz, H'_1), 4.55 (d, 1H, J = 3.5 Hz, H_1), 4.56 (d, 1H, J = 12.5 Hz, BnH), 4.71 (app t, 3H, J = 11.0, 12.0 Hz, BnH), 4.86 (app t, 1H, J = 8.0, 9.0 Hz, H'_2), 4.91–5.00 (m, 3H, BnH, H'_3, H'_4), 7.21–7.27 (m, 8H, ArH), 7.33–7.39 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.6 ($COCH_3$), 20.7 ($COCH_3$), 55.4, 67.6, 68.1, 69.7, 71.5, 71.9, 73.2, 73.5, 73.7, 75.2, 78.9, 79.9, 98.4 (C_1), 100.0 (C'_1), 127.2, 127.4, 127.8, 128.1, 128.2, 128.22, 128.4, 128.7, 137.7, 138.3, 139.4, 169.1 (C=O), 169.4 (C=O), 170.2 (C=O), 170.7 (C=O).

4-Methoxyphenyl 2,3,4-tri-*O*-benzoyl-α-D-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-D-rhamnopyranoside (70)[43]

The residue was purified by flash column chromatography (PE/EtOAc, 4 : 1) to afford the title compound **70** as colorless syrup (91%); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.20 (d, 3H, J = 5.7 Hz), 1.37 (d, 3H, J = 6.0 Hz, CH_3), 3.81 (s, 3H, OCH_3), 4.18–4.28 (m, 2H), 4.72 (bd, 1H, J = 9.6 Hz), 5.34 (bs, 2H), 5.54 (app t, 1H, J = 9.6, 10.0 Hz), 5.63–5.67 (m, 2H), 5.71–5.74 (m, 2H), 6.88–6.90 (d, 2H, J = 7.2 Hz, ArH), 7.09–7.11 (m, 2H, ArH), 7.20–7.25 (t, 1H, J = 7.2 Hz, ArH), 7.28–7.37 (m, 3H, ArH), 7.39–7.51 (m, 7H, ArH), 7.61–7.63 (m, 3H, ArH), 7.68 (d, 1H, J = 6.2 Hz, ArH), 7.72–7.78 (app t, 4H, J = 8.1, 8.5 Hz, ArH), 7.94–7.96 (d, 2H, J = 6.2 Hz, ArH), 8.15–8.18 (d, 2H, J = 7.8 Hz, ArH), 8.28–8.31 (d, 2H, J = 7.8 Hz, ArH).

Methyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (73)[22f]

The residue was purified by flash column chromatography (PE/EtOAc, 4 : 1) to afford the title compound **73** as colorless syrup (90%); $[\alpha]_D^{25}$ +10.2 (c 1.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.14 (s, 3H, COCH_3), 3.23 (s, 3H, OCH_3), 3.53 (d, 1H, J = 10.5 Hz) 3.65–3.84 (m, 9H), 3.87–3.93 (m, 4H), 3.95–3.99 (m, 2H), 4.11 (bs, 1H), 4.32 (d, 1H, J = 12.1 Hz, BnH), 4.41–4.47 (m, 2H), 4.51–4.67 (m, 11H), 4.70 (d, 1H, J = 3.3 Hz), 4.81–4.87 (m, 4H), 5.06 (brs, 1H), 5.21 (brs, 1H), 5.55 (bs, 1H, H''_2), 7.15–7.36 (m, 45H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.2 (COCH_3), 54.7 (OCH_3), 68.8, 69.6, 71.7, 71.9, 72.1, 72.2, 73.3, 73.4, 74.3, 74.9, 75.0, 75.1, 78.1, 79.3, 79.5, 99.4, 99.8, 100.6, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.16, 128.23, 128.3, 128.4, 138.1, 138.2, 138.4, 138.5, 138.6, 170.1 (C=O).

Phenyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (75)[33c]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 4 : 1) to afford the compound **75** in 85% β only as white solid,[33c] R_f 0.33 (20% EA in hexane); mp 146–148 °C (from MeOH), lit.[33c] mp 147–148 °C, $[\alpha]_D^{25}$ +11.8 (c 1.05, $CHCl_3$); lit.[33c] $[\alpha]_D^{24}$ +10.4 (c 1.08, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.37–3.52 (m, 4H), 3.57–3.92 (m, 7H), 4.08 (appatent t, 1H, J = 9.2, 9.5 Hz), 4.43 (bs, 2H), 4.48–4.68 (m, 5H), 4.72–4.86 (m, 7H), 4.93 (d, 1H, J = 10.8 Hz, BnH), 5.17 (d, 1H, J = 11.1 Hz, BnH), 7.19–7.34 (m, 38H, ArH), 7.58–7.61 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 68.3, 68.9, 73.2, 73.3, 74.8, 75.0, 75.5, 75.7, 76.4, 78.1, 80.2, 82.8, 85.0, 87.5 (C_1), 102.6 (C'_1), 127.3, 127.4, 127.5, 127.6, 127.7, 127.9, 128.0, 128.1, 128.2, 128.3, 128.33, 128.4, 128.9, 132.1, 133.8, 138.2, 138.3, 138.4, 138.5, 138.6, 139.2. HRMS (ESI-TOF): calculated for $C_{67}H_{68}O_{10}$SNa (M + Na) 1087.4431 and found 1087.4414.

Phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzyledene-β-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (76)[33d]

The crude residue was purified by silica gel (230–400 mesh) flash column chromatography (hexane/ethyl acetate, 3 : 1) to afford the compound **76** in 94% β as colourless syrup.[33d] R_f 0.35 (25% EA in hexane); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.24 (m, 1H), 3.38–3.54 (m, 4H), 3.60–3.78 (m, 4H), 3.90 (dd, 1H, J = 3.2, 10.9 Hz), 4.04 (t, 1H, J = 9.5 Hz), 4.23 (dd, 1H, J = 4.9, 10.4 Hz), 4.45 (d, 1H, J = 11.9 Hz), 4.58–4.67 (m, 3H), 4.74–4.87 (m, 6H), 4.94 (d, 1H, J = 11.3 Hz), 5.01 (d, 1H, J = 10.7 Hz), 5.53 (s, 1H, PhCH), 7.27–7.61 (m, 35H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 62.4, 68.2, 70.7, 73.4, 74.9, 75.3, 75.5, 75.6, 76.6, 79.3, 82.5, 84.8, 87.5 (C_1), 101.4 (PhCH), 102.6 (C'_1), 126.1, 127.3, 127.5, 127.6, 127.7, 127.8, 127.9, 127.98, 128.2, 128.3, 128.4, 128.6, 128.9, 129.0, 129.7, 132.1, 138.2, 138.5. HRMS (ESI-TOF): calculated for $C_{60}H_{60}O_{10}$SNa (M + Na) 995.3805 and found 995.3810.

Phenyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-1-thio-α-D-mannopyranoside (79)[22d]

The crude residue was purified by silica gel flash column chromatography (hexane/ethyl acetate, 3 : 1) to afford **79** (94%) as a white foam.[22d] R_f = 0.25 (30% ethyl acetate in hexane); $[\alpha]_D^{26}$ +16.3 (c 1.34, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.10 (s, 3H, COCH_3), 3.53 (d, 1H, J = 9.6 Hz), 3.68 (m, 1H), 3.69 (m, 1H), 3.75 (dd, 1H, J = 3.0, 10.2 Hz), 3.87 (t, 1H, J = 9.6 Hz), 3.95 (dd, 1H, J = 3.6, 9.6 Hz), 4.00 (dd, 1H, J = 5.4, 10.8 Hz), 4.32 (d, 1H, J = 10.8 Hz), 4.36 (d, 1H, J = 12.0 Hz), 4.44 (d, 1H, J = 10.8 Hz), 4.50 (d, 1H, J = 10.8 Hz), 4.58 (d, 1H, J = 12.0 Hz), 4.81 (m, 1H), 4.84 (d, 1H, J = 10.8 Hz), 4.87 (d, 1H, J = 1.3 Hz, H'_1), 5.36 (dd, 1H, J = 1.8, 3.0 Hz), 5.73 (d, 1H, J = 1.2 Hz, H_1), 5.81 (dd, 1H, J = 3.0, 9.6 Hz), 5.94 (m, 1H), 5.99 (t, 1H, J = 10.2 Hz), 7.13–7.16 (m, 3H, ArH), 7.22–7.35 (m, 17H, ArH), 7.41–7.57 (m, 9H, ArH), 7.85 (d, 2H, J = 7.2 Hz, ArH), 8.00 (d, 2H, J = 7.2 Hz, ArH), 8.07 (d, 2H, J = 7.2 Hz, ArH). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.0, 66.6, 67.3, 68.44, 68.46, 70.45, 70.48, 71.5, 71.8, 72.0, 73.2, 74.0, 75.1, 78.4, 86.0 (C_1) 98.0 (C'_1) 127.50, 127.51, 127.7, 127.88, 127.90, 128.0, 128.18, 128.23, 128.27, 128.32, 128.4, 128.47, 128.54, 128.6, 128.9, 129.2, 129.3, 129.4, 129.71, 129.8, 129.74, 129.89, 129.9, 131.5, 132.1, 133.22, 133.25, 133.5, 133.6, 137.9, 138.0, 138.5, 165.3 (C=O), 165.4 (C=O), 170.3 (C=O); HRMS (ESI-TOF): calculated for $C_{62}H_{58}O_{14}$SNa $[M + Na]^+$ 1081.3445 found 1081.3441.

Phenyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-1-thio-α-L-rhamnopyranoside (82)

The crude residue was purified by silica gel flash column chromatography (hexane/ethyl acetate, 9 : 1) to afford **82** (92%) as a white foam. R_f = 0.25 (10% ethyl acetate in hexane); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32 (d, 3H, J = 5.8 Hz, CH_3), 1.36 (d, 3H, J = 6.1 Hz, CH_3), 3.53–3.61 (m, 2H, H_4, H'_4), 3.89–3.93 (m, 2H, H_3, H'_5), 4.11–4.19 (m, 2H, H_5, H'_3), 4.25 (bs, 1H, H_2), 4.62–4.69 (m, 3H, BnH), 4.73–4.76 (m, 2H, BnH), 4.85–4.99 (m, 3H, BnH), 5.12 (bs, 1H, H_1), 5.51 (bs, 1H, H'_1), 5.80 (bs, 1H, H'_2), 7.24–7.64 (m, 28H, ArH), 8.13–8.15 (d, 2H, J = 7.1 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.0 (CH_3), 18.1 (CH_3), 68.5, 69.4, 69.5, 71.7, 74.4, 75.4, 77.8, 80.7, 80.1, 80.2, 87.3 (C_1), 99.7 (C'_1), 127.3, 127.6, 127.7, 127.8, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 129.1, 129.9, 130.1, 131.3, 133.2, 134.6, 138.1, 138.1, 138.4, 138.5, 165.6 (C=O).

p-Methylphenyl 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-1-thio-β-D-glucopyranoside (85)[44]

The product was purified by flash chromatography (PE/EtOAc 5 : 1) on silica gel (230–400 mesh) to give **85** in 88% yield as colorless syrup. $[\alpha]_D^{27}$ −10.5 (*c* 1.2, $CHCl_3$); lit.[44] $[\alpha]_D^{24}$ −8.2 (*c* 0.98, $CHCl_3$); ^{1}H (300 MHz, $CDCl_3$): δ 0.59 (d, 3H, J = 6.4 Hz, CH_3), 2.23 (s, 3H, PhCH_3), 3.45 (bs, 1H, H'_4), 3.70 (m, 1H, H'_5), 3.86–3.98 (m, 4H, H_4, H_5, H'_2, H'_3), 4.50 (d, 1H, J = 11.5 Hz, BnH), 4.61–4.86 (m, 8H, 5BnH, H_1, H_6, H'_1), 5.06 (d, 1H, J = 10.9 Hz, H_6), 5.23 (t, 1H, J = 9.7 Hz, H_2), 5.69 (t, 1H, J = 8.9 Hz, H_3), 6.86 (d, 2H, J = 8.0 Hz, ArH), 7.21–7.23 (m, 7H, ArH), 7.25–7.35 (m, 11H, ArH), 7.38–7.44 (m, 4H, ArH), 7.47–7.53 (m, 3H, ArH), 7.62–7.64 (m, 1H, ArH), 7.83–7.85 (d, 2H, J = 7.4 Hz, ArH), 7.88–7.91 (d, 2H, J = 7.3 Hz, ArH), 8.06–8.09 (d, 2H, J = 7.3 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.9, 21.1, 63.1, 67.7, 70.9, 72.7, 74.3, 74.8, 75.6, 75.7, 76.3, 77.2, 77.6, 77.8, 79.2, 85.5 (C_1), 100.5 (C'_1), 127.4, 127.5, 127.7, 128.1, 128.2, 128.3, 128.4, 128.41, 129.3, 129.5, 129.8, 129.9, 130.1, 133.0, 133.1, 133.9, 138.1, 138.3, 138.4, 138.6.

Preparation of trisaccharide 2,3,4.6-tetra-*O*-benzyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (39)[19c]

***Via* sequential one-pot glycosylation technique.** A 25 mL oven-dried round bottom flask was charged with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl trichloroacetimidate donor **1** (155 mg, 0.227 mmol, 1.2 equiv.), 4′-methyl phenyl 2,3,4-tri-*O*-benzoyl-1-thio-α-D-glucopyranoside **86** (100 mg, 0.189 mmol, 1 equiv.), and CH_2Cl_2 (5 mL). The resulting solution was stirred on freshly dried 4 Å molecular sieves for 40 min at room temperature under argon atmosphere. Then this mixture was cooled to −60 °C, $FeCl_3$ (3.4 mg, 0.024 mmol, 0.1 equiv.) was added, and the reaction mass was allowed to achieve room temperature. After the acceptor was consumed completely (checked by TLC), to the reaction mass 1,2:3,4-diisopropyl-α-D-galactopyranoside **8** (40 mg, 0.151 mmol, 0.8 equiv.) was injected and was cooled on ice bath NIS (45 mg, 0.227 mmol, 1 equiv.) and $FeCl_3$ (4 mg, 0.024 mmol, 0.1 equiv.) was added one by one. After 15 min TLC was checked and the acceptor was consumed completely. Then molecular sieves were filtered off through celite bed. The filtrate was diluted with CH_2Cl_2 and washed subsequently with saturated $NaHCO_3$ solution and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated to afford the glycosylated product. The crude residue was purified by silica gel flash column chromatography (hexane/EtOAc, 3 : 1) to afford **39** (196 mg, 87.3%) as a white foam. Spectroscopic data match with previous one and reported one.

Methyl 3,4,6-tri-*O*-benzyl-2-*O*-methyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (88)

The residue was purified by flash column chromatography (PE/EA, 4 : 1) to afford the title compound **88** as colorless syrup (93%); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.19 (app t, 1H, J = 7.9, 9.1 Hz, H'_2), 3.46 (m, 1H, H'_5), 3.61 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3) 3.56–3.72 (m, 4H, H'_3, H'_4, H'_6, H'_6), 3.90 (dd, 1H, J = 8.4, 11.5 Hz, H_6), 4.14–4.18 (m, 2H, H_5, H_6), 4.46 (d, 1H, J = 7.9 Hz, H'_1), 4.52–4.62 (m, 3H, 3 × BnH), 4.78–4.97 (m, 4H, 3Bn × H, H_1), 5.49 (t, 1H, J = 9.6 Hz, H_4), 5.56 (t, 1H, J = 7.9 Hz, H_2), 5.96 (t, 1H, J = 9.6 Hz, H_3), 7.20–7.23 (m, 2H, ArH), 7.28–7.45 (m, 20H, ArH), 7.52–7.57 (t, 2H, J = 7.3 Hz, ArH), 7.86–7.88 (t, 2H, J = 7.6 Hz, ArH), 7.97–8.04 (m, 4H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 57.2, 60.5, 70.1, 72.0, 73.1, 73.5, 74.2, 74.8, 75.0, 75.6, 77.5, 84.2, 84.7, 102.0 ($J_{C\text{-}H}$ = 155.9 Hz, C'_1) 104.1 ($J_{C\text{-}H}$ = 157.1 Hz, C_1), 127.6, 127.7, 127.77, 127.82, 127.98, 128.01, 128.3, 128.39, 128.42, 128.5, 128.9, 129.4, 129.8, 129.9, 133.2, 133.5, 138.1, 138.2, 138.8, 165.2 (C=O), 165.4 (C=O), 165.9 (C=O).

Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl-(1→3)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (90)[32]

The product was purified by flash chromatography (PE/EA 4 : 1) on silica gel (100–200 mesh) to give **90** in 87% yield as colourless syrup. ^{1}H (500 MHz, $CDCl_3$): δ 1.60 (dt, 1H, J = 3.5, 12.5 Hz, H'_{2a}), 2.23 (dd, 1H, J = 4.5, 12.5 Hz, H'_{2e}), 3.29 (s, 3H, OCH_3), 3.36 (dd, 1H, J = 3.5, 9.5 Hz), 3.45–3.49 (m, 2H), 3.54–3.62 (m, 3H), 3.71 (m, 1H), 3.91 (m, 1H), 4.01 (d, 1H, J = 9.5 Hz), 4.14–4.19 (m, 2H), 4.29 (d, 1H, J = 12.0 Hz, BnH), 4.42 (d, 1H, J = 11.0 Hz, BnH), 4.44 (d, 1H, J = 11 Hz, BnH), 4.51–4.60 (m, 5H, 4 × BnH, H'_1), 4.79 (d, 1H, J = 11.0 Hz, BnH), 5.41 (d, 1H, J = 4.5 Hz, H1), 5.42 (s, 1H, PhCH) 7.07–7.37 (m, 25H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 35.4, 55.3, 61.9, 68.6, 70.7, 71.6, 72.7, 73.4, 73.7, 74.7, 77.4, 78.1, 78.3, 82.9, 97.6, 98.8, 101.4, 126.0, 127.3, 127.4, 127.5, 127.6, 127.7, 127.9, 128.1, 128.15, 128.2, 128.3, 128.4, 128.6, 129.0, 129.8, 134.5, 137.3, 137.7, 138.3, 138.9, 139.1.

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