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A Mild Glycosylation Protocol with Glycosyl 1-Methylimidazole-2-carboxylates as Donors

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A mild glycosylation protocol is developed by using glycosyl 1-methylimidazole-2-carboxylates. Such a glycosylation can be promoted by a series of metal triflates and triflimides, especially $Cu(OTf)_2$. The reaction is initiated by activation of the glycosyl ester donor via coordination with the metal cation assisted by the adjacent 1-methylimidazole chelating group.

Introduction

The design, synthesis, and glycosylation reactivity evaluation of glycosyl donors bearing novel anomeric leaving groups constitute an active area of research in glycoscience, and new glycosylation donors are continuously being developed.[1,2] Of the various glycosylation donors developed, glycosyl carboxylates type donors have occupied an important position due to their convenience of preparation, shelf stability, ease of activation, and high glycosylation efficiency.[3–5] The activation mode of these ester type donors can be classified into three types (Figure 1). Type I involves direct activation of the carbonyl group by a Lewis acid. Donors falling into this category include glycosyl 1-*O*-acetates and formates, and the Lewis acid promoters include $BF_3{\cdot}Et_2O$, TMSOTf, $ZnCl_2$, and $Sc(OTf)_3$.[3] Type II is activation of the carbonyl group via a transient carbocation or vinyl cation generated through electrophilic activation of an adjacent alkenyl or alkynyl group by an electrophilic reagent or a transition metal catalyst. Donors belonging to this category include glycosyl 1-*O*-4-hexynoate (Figure 1, **A**),[6] glycosyl *o*-alkynylbenzoates (**B**),[7] alkynyl glycosyl carbonates (**C**),[8] phenylpropiolate glycosides (**D**),[5f] glycosyl ynolates (**E**),[5d] glycosyl *ortho*-(1-phenylvinyl)benzoates (**F**),[5b] etc. The electrophilic reagents or transition metal catalysts employed for the activation of this type of donors include NIS/TMSOTf,[5b,h] HgX_2 (X=OTf or NTf_2),[6] R_3PAuX (X=OTf, NTf_2).[7–10] Type III is activation of the carbonyl group via coordination with a metal cation assisted by an adjacent chelating group, donors falling into this category are relatively limited so far.[11,12] In 1991, Kobayashi et al. reported the first example of chelation assisted glycosyl donor, i.e., glycosyl 2-pyridinecarboxylate (**G**) which can be activated by $Cu(OTf)_2$ or $Sn(OTf)_2$.[13] In 2016, Salamone, Jensen, and coworkers disclosed another chelation assisted donor, i.e., glycosyl *ortho*-methoxybenzoate (**H**) which can be catalytically activated by a range of promoters including $Bi(OTf)_3$, $Fe(OTf)_3$, TMSOTf, and triflic acid.[14] In 2017, Tang et al. further developed glycosyl isoquinoline-1-carboxylate (**I**),[15] which can be effectively activated by $Cu(OTf)_2$ and can avoid a troublesome transesterification side reaction observed in the glycosyl pyridine-2-carboxylates glycosylation system.

In fact, the use of glycosylation donors bearing heterocyclic anomeric leaving groups are pioneered by Mukaiyama et al., who employed 2-glycosyl 3-ethylbenzoxazolium salt for the construction of *N*-glycosides,[16] and Hanessian et al., who developed pyridine-2-yl 1-thioglycoside as donor for the construction of *O*-glycosyl linkages.[17] Ever since, a series of heterocycle-containing donors have been developed and successfully applied in glycoside synthesis.[18,19] Most of these donors contain *N*-heterocycles, particularly pyridine rings. The nitrogen atom usually plays a critical role that act as a coordinating site. It is noted that imidazole skeleton, an important class of *N*-heterocycle, has rarely been applied in glycosyl donor design.[20] The basicity of imidazole nitrogen is about two orders of magnitude stronger than pyridine nitrogen,[21] thus, the coordinating ability of the imidazole ring acting as a *N*-donor is expected to be stronger than the pyridine ring, and glycosyl donors bearing imidazole ring as the leaving group are expected to exhibit better leaving abilities. With this consideration in mind, a series of potential imidazole ring containing leaving groups were carefully surveyed and glycosyl 1-methylimidazole-2-carboxylates (i.e., **J**) attracted our attention. This type of donors might be prepared from 1-methyl-2-imidazolecarboxylic acid **1**, a commercially available shelf-stable reagent, and is expected to exhibit good glycosylation reactivity under the promotion of metal promoters. In this article, we report the preparation and evaluation of glycosyl 1-methylimidazole-2-carboxylates as a new type of glycosyl donors.

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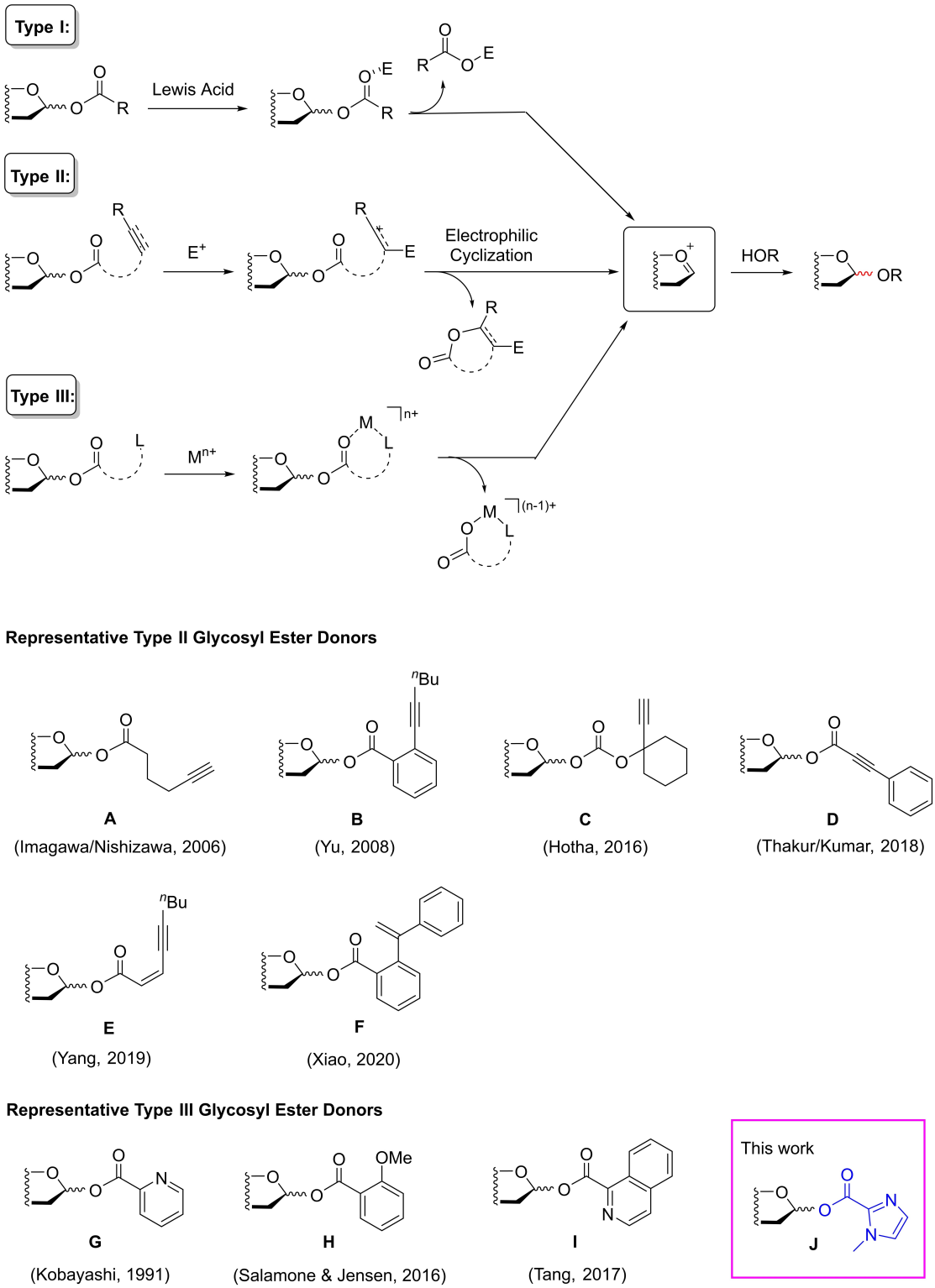


Figure 1. Activation modes of ester type glycosyl donors, representative examples, and the present work.

Results and Discussion

To test the glycosylation reactivity of glycosyl 1-methylimidazole-2-carboxylates, the first problem to address is how to prepare this type of compounds conveniently in high yields. Of the various possible preparation routes, the direct condensation of 1-methyl-2-imidazolecarboxylic acid with glycosyl hemiacetal derivatives is the most straightforward and convenient route.[22] Thus, we selected the condensation of 2,3,4,6-tetra-*O*-benzoyl-D-glucopyranose **2a** and 1-methyl-2-imidazolecarbox-

ylic acid **1** as a model reaction and studied a series of condensation conditions (Table 1). The condensation of **2a** (1 equiv.) and **1** (1.5 equiv.) in the presence of DCC (1.6 equiv.) and a catalytic amount of DMAP (0.2 equiv.) in CH_2Cl_2 afforded the desired 2,3,4,6-tetra-*O*-benzoyl-D-glucopyranosyl 1-methylimidazole-2-carboxylates **3a** in 71% yield with the β anomer as the major product (β/α = 3/1, entry 1). Switching the condensation agent from DCC to EDCI led to a diminished yield (entry 2). These unsatisfactory results were attributable to the poor solubility of 1-methyl-2-imidazolecarboxylic acid **1** in CH_2Cl_2. A screening of solvents revealed that acid **1** dissolved well in DMF. Indeed, the condensation of **2a** (1 equiv.) and **1** (1.5 equiv.) in the presence of EDCI (1.6 equiv.) and DMAP (1.6 equiv.) in DMF afforded the desired product **3a** in 80% yield with β/α ratio 3.5/1 (entry 4). Switching the condensation agent from EDCI to DCC led to a diminished yield (entry 3). Thus, the optimal conditions were established as either performing the condensation of glycosyl hemiacetal **2** (1.0 equiv.) with acid **1** (1.5 equiv.) in DMF in the presence of EDCI (1.6 equiv.) and DMAP (1.6 equiv.) (Conditions A) or in CH_2Cl_2 in the presence of DCC (1.6 equiv.) and DMAP (0.2 equiv.) (Conditions B).

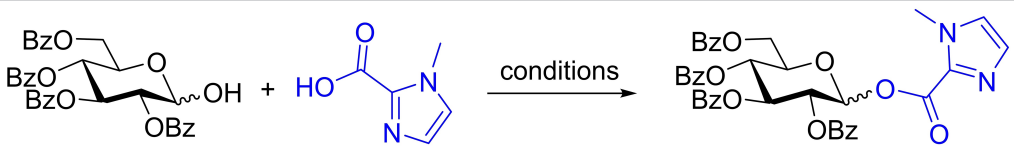
Under the optimal condensation reaction conditions, a series of glycosyl 1-methylimidazole-2-carboxylates were prepared (Scheme 1). Benzoylated glycosyl hemiacetals, including glucopyranosyl hemiacetal **2a**, mannopyranosyl hemiacetal **2c**, rhamnopyranosyl hemiacetal **2d**, xylopyranosyl hemiacetal **2e**, ribopyranosyl hemiacetal **2f**, ribofuranosyl hemiacetal **2g**, and benzylated glucopyranosyl hemiacetal **2b** all underwent smoothly condensation with acid **1** in the optimal reaction conditions, delivering the desired glycosyl 1-methylimidazole-2-carboxylates **3a**–**3g** in satisfactory 74–94% yields. All these products are shelf-stable solids which can be stored under ambient atmosphere for at least three months without decomposition. The structures of xylopyranosyl carboxylates **3eβ** (CCDC 2064548), ribopyranosyl **3fβ** (CCDC 2064549), and ribofuranosyl **3gβ** (CCDC 2064547) were ambiguously confirmed by single crystal X-ray analysis. Interestingly, the pyranosyl donors **3eβ** and **3fβ** crystallize in $^1C_4 \rightarrow {}^5H_O$ forms. In $CDCl_3$ solutions, these two donors appeared to retain the $^1C_4$ conformation, as evidenced by NMR analysis. Similar phenomenon was observed in the crystal structures of perbenzoylated β-D-xylopyranose, which also adopts a $^1C_4$ chair conformation slightly distorted toward the ^5H_O half-chair form.[23]

Apart from direct condensation, alternative methods for the preparation of glycosyl 1-methylimidazole-2-carboxylate **3a** were also tested (Scheme 2). The reaction of glycosyl hemiacetal **2a** with the corresponding 1-methyl-1-H-imidazole-2-carboxylic acid chloride **4** in the presence of Et_3N (2.0 equiv.) and DMAP (0.1 equiv.) provided the desired product **3a** in 72% yield with the α anomer predominantly (α/β = 5.5/1). In addition, pure β anomer of product **3a** could be prepared in 66% yield from the corresponding glucosyl bromide **5** and acid **1** in the presence of Ag_2CO_3 (0.6 equiv.) in dry DMF (0.2 M).

Having established convenient methods for the preparation of glycosyl 1-methylimidazole-2-carboxylates, the glycosylation reactivity of this type of donors were next tested. The glycosylation reaction between glycosyl donor **3a** and glycoside acceptor **6a** under the promotion of a metal salt bearing a weakly coordinating counteranion (1.5 equiv.) in CH_2Cl_2 in the presences of 4 Å molecular sieves were selected as a model reaction system, and a series of commercially available metal triflates and triflimides were evaluated. The results are depicted in Table 2. To our delight, several of these tested metal complexes, including $Cu(OTf)_2$, $Cu(NTf_2)_2$, $Zn(NTf_2)_2$, $In(OTf)_3$, $Bi(OTf)_3$, and $Sn(OTf)_2$, were effective promoters, delivering the desired 1→4-linked disaccharide **7a** in 78–87% yields. Of these promoters $Cu(OTf)_2$ is the most cost-effective and the most efficient one, the optimal conditions were thus established employing $Cu(OTf)_2$ as the glycosylation promoter.

The scope of the present glycosylation conditions was next explored, and the results are illustrated in Scheme 3. With respect to glycosyl donor scope, disarmed perbenzoylated donors, including glucopyranosyl donor **3a**, mannopyranosyl donor **3c**, rhamnopyranosyl donor **3d**, xylopyranosyl donor **3e**, ribopyranosyl donor **3f**, ribofuranosyl donor **3g**, and armed benzylated glucopyranosyl donor **3b** all underwent glycosylation smoothly, affording the glycosylated products **7a**–**7z** in 73–99% yields. With respect to glycosyl acceptor scope, primary aliphatic alcohol (**6g**), secondary aliphatic alcohols (**6e**, **6h**, and **6i**), tertiary aliphatic alcohol (**6c**), primary sugar alcohols (**6b**, **6d**) and secondary sugar alcohol (**6a**) were all suitable glycosyl acceptors. It is noteworthy that the glycosylation of acceptors bearing basic tertiary amine moieties, namely 2-(morpholin-4-yl)

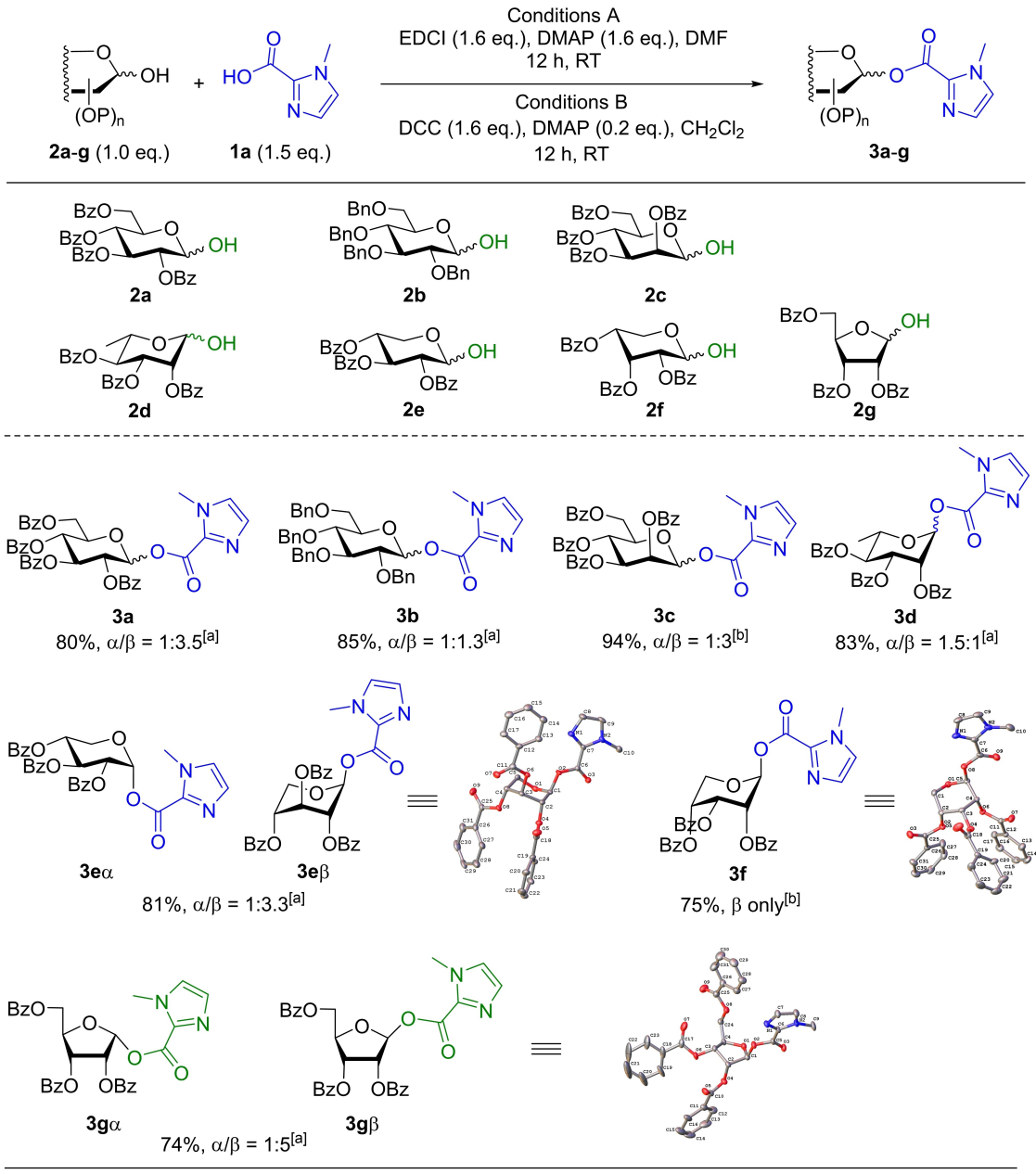
Table 1. Optimization of the condensation reaction of lactol **2a** and acid **1**.



2a **1** **3a**

Entry	Conditions	Yield[a]	β/α[b]
1	**1** (1.5 eq.), DCC (1.6 eq.), DMAP (0.2 eq.), CH_2Cl_2, 12 h, RT	71%	3:1
2	**1** (1.5 eq.), EDCI (1.6 eq.), DIPEA (2.3 eq.), DMAP (1.5 eq.), CH_2Cl_2, 12 h, RT	57%	3:1
3	**1** (1.5 eq.), DCC (1.6 eq.), DMAP (1.6 eq.), DMF, 12 h, RT	47%	–
4	**1** (1.5 eq.), EDCI (1.6 eq.), DMAP (1.6 eq.), DMF, 12 h, RT	80%	3.5:1

[a] Isolated yield. [b] The β/α ratio was determined by ^1H NMR analysis.



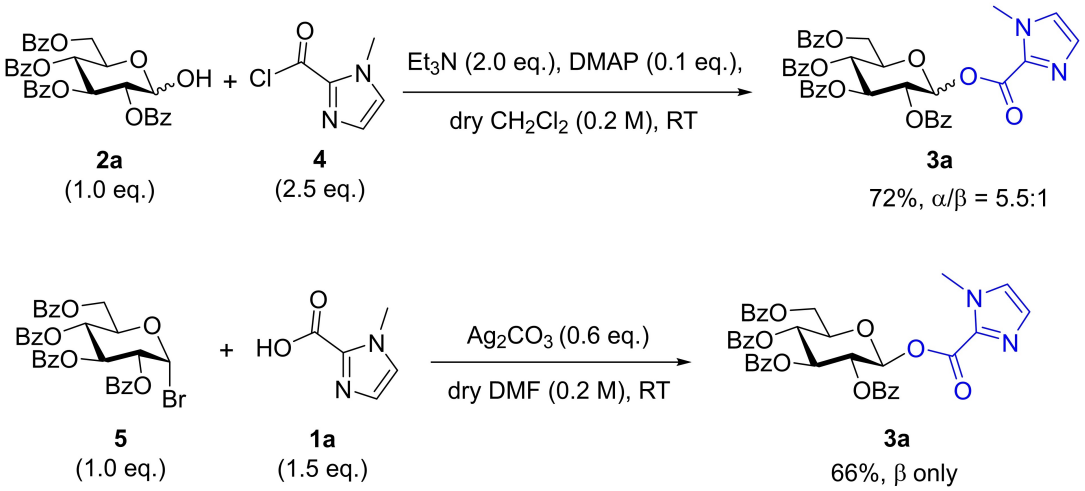
[a] The β/α ratio was determined by ^{1}H NMR analysis. [b] The β/α ratio was determined based on isolated yields.

Scheme 1. [a] Conditions A. [b] Conditions B. The α/β ratio was determined by ^{1}H NMR analysis.

ethanol **6g** and *pseudo* tropine **6h**, proceeded smoothly in high yield with α anomer predominantly under mild conditions, in sharp contrast to the previous reports for the glycosylation of acceptors bearing tertiary amine moieties, which always required harsh conditions (excess Lewis acid promoters) and the yields were only moderate.[24,25]

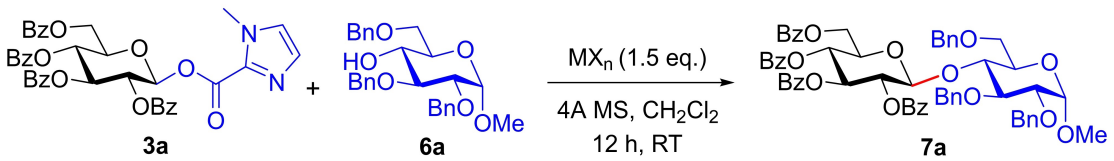
The mechanism of the present glycosylation reaction was briefly studied. The relationship between the equivalents of $Cu(OTf)_2$ and glycosylation yield was first investigated. The glycosylation reaction between benzoylated ribopyranosyl 1-methylimidazole-2-carboxylates donor **3fβ** and L-menthol **6e** under the promotion of $Cu(OTf)_2$ in CH_2Cl_2 in the presence of 4 Å molecular sieves was selected as a model reaction, and the results are shown in Figure 2. In the presence of 1.0 equiv. of $Cu(OTf)_2$ the glycosylation yield reached 84%; a further increase of $Cu(OTf)_2$ to 1.4 equiv. led to a slightly increase of the yield to 97%. These results demonstrated that for this glycosylation system, more than equal equivalent of Cu(II) promoter is needed to promote the glycosylation reaction to get complete conversion.

In order to compare the relative glycosylation reactivity of the α and β anomers of the glycosyl 1-methylimidazole-2-carboxylates donors, a competition experiment was next preformed (Scheme 4). Thus, a 1:1 mixture of the α and β



Scheme 2. Alternative methods for the preparation of glycosyl 1-methylimidazole-2-carboxylate **3a**.

Table 2. Screening of promoters for the glycosylation of sugar alcohol **6a** with donor **3a**.

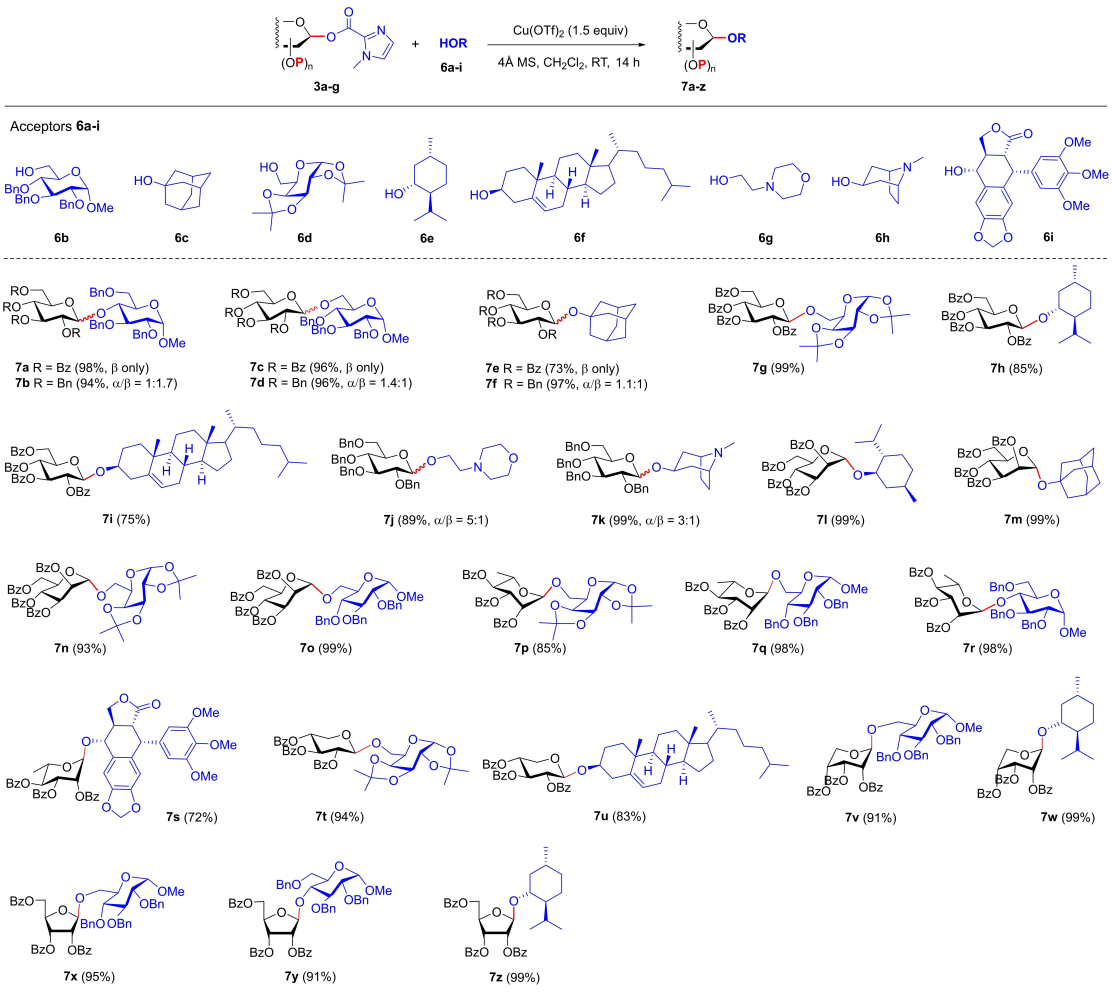


Entry	MX_n	Yield[a]
1	$Cu(OTf)_2$	87%
2	$Cu(NTf_2)_2$	86%
3	AgOTf	N.R.
4	$Zn(OTf)_2$	25%[b]
5	$Zn(NTf_2)_2$	79%
6	$In(OTf)_3$	78%
7	$Bi(OTf)_3$	85%
8	$Fe(OTf)_2$	65%
9	$Sn(OTf)_2$	81%
10	$Ni(OTf)_2$	<10%
11	$Sc(OTf)_3$	56%[b]
12	$La(OTf)_3$	<10%

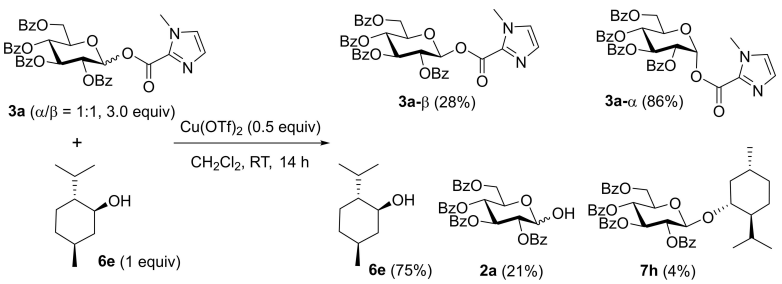
[a] Isolated yields. [b] Yield determined by ^{1}H NMR analysis using 2-cyanopyrimidine as internal standard.

anomers of donor **3a** (1.5 equiv. each relative to the acceptor) was competitively reacted with 1.0 equiv. of acceptor **6e** in CH_2Cl_2 at room temperature for 14 h in the presence of 0.5 equiv. of $Cu(OTf)_2$. After the reaction, the β anomer of donor **3a** was recovered in 28% yield while the α anomer was recovered in 86% yield, indicating that the β anomer is much more reactive than the α anomer.

During the reaction process a blue precipitate gradually formed, the composition of the precipitate was assumed to be a Cu(II) complex with 1-methylimidazole-2-carboxylate anion (L_N) as ligand. Three possible structures of this complex were assumed, namely, $Cu(L_N)_2$ (**K**), $[Cu(LN)]^+ \cdot TfO^-$ (**L**), and $[Cu(HL_N)_2]^{2+} \cdot 2TfO^-$ (**M**; Figure 3). The actual structure of this complex was deduced via elemental analysis, in that the measured elemental composition (including C, H, N, and Cu) well matched that of structure **K**. This structure was also supported by ESI-MS analysis, in that a peak at 336.76 corresponding to the $[M+Na]^+$ ion was observed. The ligand structure in this complex was further confirmed by NMR analysis. Due to the paramagnetic character and rather low solubility of Cu(II) complex, direct NMR analysis was not successful. Thus, the free ligand was released through a chemical transformation, namely, through reduction of this complex by I^- ion in acidic conditions, then, the aqueous solution was filtered and directly analyzed by NMR. The ^{1}H NMR signals corresponding to free 1-methylimidazole-2-carboxylate ligand were observed. Thus, the leaving species of this glycosylation was confirmed to be the Cu(II) complex with two 1-methylimidazole-2-carboxylate as ligands,[26] providing a strong support for the proposed chelation assisted activation mechanism of this type of donors.



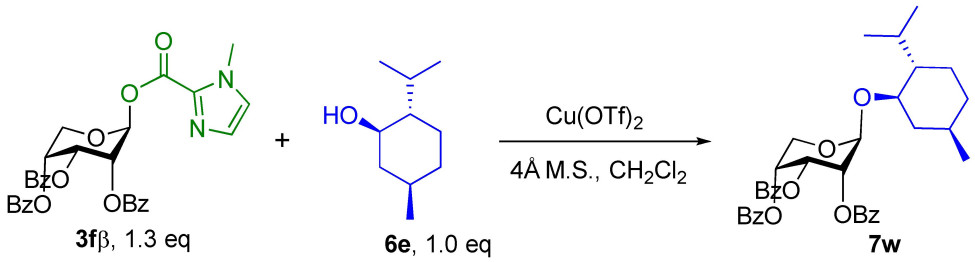
Scheme 3. Scope of the glycosylation using glycosyl 1-methylimidazole-2-carboxylates as donors under the promotion of $Cu(OTf)_2$.



Scheme 4. Competition experiment between the α and β anomers of glucosyl 1-methylimidazole-2-carboxylate donor **3**.

Conclusion

In conclusion, we have developed a mild glycosylation protocol using glycosyl 1-methylimidazole-2-carboxylates as donors, which can be promoted by a series of metal triflates and triflimides, especially $Cu(OTf)_2$. The glycosyl 1-methylimidazole-2-carboxylates donors employed in this protocol can be conveniently prepared in high yields from the corresponding glycosyl hemiacetals and commercially available 1-methyl-2-imidazolecarboxylic acid (**1**) via direct condensation. The reaction initiates from activation of the glycosyl ester donor via coordination with a metal cation assisted by the adjacent 1-methylimidazole chelating group, followed by a classic glycosylation mechanism via glycosyl oxocarbenium ion intermediate. The reaction enjoys a broad scope and especially suitable for acceptors bearing tertiary amine moieties. With these salient features, this glycosylation protocol is expected to find applications in the construction of glycosidic linkages.



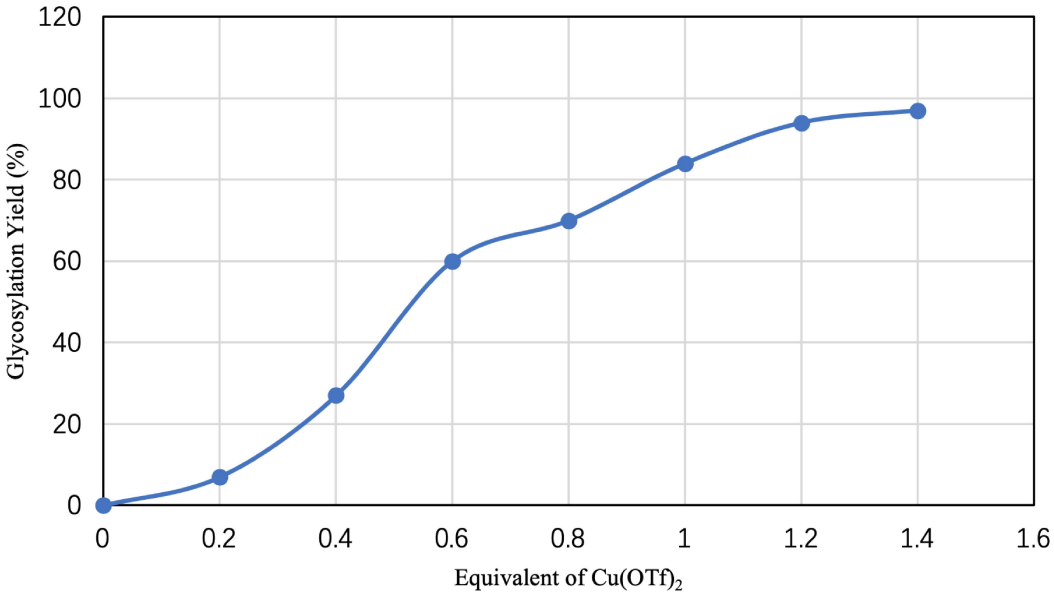
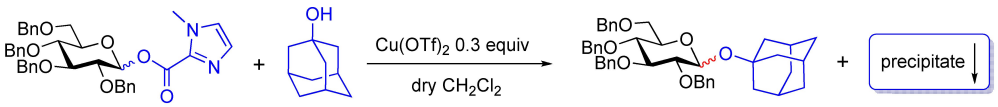
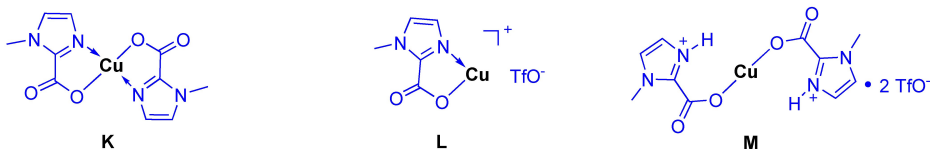


Figure 2. The dependence of glycosylation yields on the equivalents of $Cu(OTf)_2$.

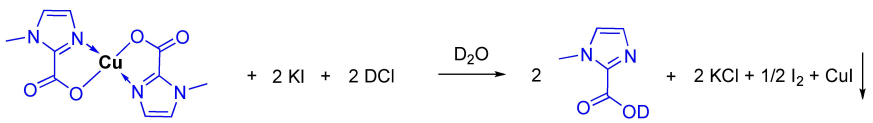


Plausible composition of the precipitate



Calculated: C 38.28, H 3.21, N 17.86, Cu 20.25 — C 21.34, H 1.49, N 8.30, Cu 18.82 — C 23.48, H 1.97, N 9.13, Cu 10.35
Molecular Weight: 313.00

Found: C 37.88, H 3.59, N 17.78, Cu 21.09
ESI-MS, m/z: 336.76, $[M+Na]^+$



Confirmed by NMR

Figure 3. Identification of the precipitate formed during the glycosylation process.

Experimental Section

General Information. Commercial reagents were used without further purification unless specialized. Crushed 4 Å molecular sieves were activated through flame-drying under high vacuum immediately prior to use. Dry CH_2Cl_2 were obtained by refluxing with CaH_2 (5%, w/v) under argon. Flash column chromatography was performed on silica gel SiliaFlash P60 (40–63 μm, Silicycle). The TLC plates were visualized with UV light and/or by staining with EtOH/H_2SO_4 (8%, v/v). Flash column chromatography was performed on Silica Gel 60 (40–64 μm, Fluka, Canada). NMR spectra were measured on Bruker AM 400, Agilent 500 or 600 MHz NMR spectrometer at 25 °C. ^{1}H and ^{13}C NMR signals were calibrated to the residual proton and carbon resonance of the solvent ($CDCl_3$: δH = 7.26 ppm; δC = 77.31 ppm). High-resolution mass spectra were recorded with IonSpec 4.7 Tesla FTMS or APEXIII 7.0 Tesla FTMS. Elemental analysis was obtained on a Vario EL III elemental analyzer. Optical rotations were measured on an Anton Paar MCP5500 polarimeter. Single crystal X-ray data were collected on a Bruker Apex II CCD diffractometer operating at 50 kV and 30 mA using Mo Kα radiation (λ = 0.71073 Å) at 133 K.

General Procedure A for the Preparation of Glycosyl 1-Methylimidazole-2-carboxylates. To a solution of glycosyl hemiacetals **2** (1.0 eq.) in dry DMF (0.20 M) were added 1-methyl-2-imidazolecarboxylic acid **1** (1.5 eq.), EDCI (1.6 eq.), and DMAP (1.6 eq.). The mixture was stirred at room temperature and monitored by TLC. After stirring for 8 h, the mixture was diluted with CH_2Cl_2, and was then washed with water and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to afford the desired esterification product.

General Procedure B for the Preparation of Glycosyl 1-Methylimidazole-2-carboxylates. To a solution of glycosyl hemiacetals **2** (1.0 eq.) in dry CH_2Cl_2 (0.20 M) were added 1-methyl-2-imidazolecarboxylic acid **1a** (1.5 eq.), DCC (1.6 eq.), and DMAP (0.2 eq.). The mixture was stirred at room temperature and monitored by TLC. After stirring for 8 h, the reaction mixture was filtered through a pad of Celite and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to afford the esterification product.

*2,3,4,6-Tetra-O-benzoyl-D-glucopyranosyl-1-methylimidazole-2-carboxylate (**3a**)* Esterification of hemiacetal **2a** (100 mg, 0.17 mmol) with acid **1** (32 mg, 0.25 mmol) employing General Procedure A afforded **3a** (94 mg, 80%, α/β = 1:3.5) as a white solid. Alternatively, esterification of hemiacetal **2a** (1.0 g, 1.8 mmol) with acid **1** (0.33 g, 2.6 mmol) with General Procedure B afforded **3a** (0.90 g, 71%, α/β = 1:3) as a white solid. **3aα**: [α]25 D = 113.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.99–7.91 (m, 4H), 7.89–7.85 (m, 2H), 7.57–7.53 (m, 1H), 7.51–7.45 (m, 2H), 7.45–7.40 (m, 3H), 7.38–7.26 (m, 7H), 7.08 (d, *J* = 1.0 Hz, 1H), 6.90 (d, *J* = 3.8 Hz, 1H), 6.39 (t, *J* = 10.0 Hz, 1H), 5.90 (t, *J* = 10.0 Hz, 1H), 5.64 (dd, *J* = 10.2, 3.8 Hz, 1H), 4.85 (dt, *J* = 10.3, 3.3 Hz, 1H), 4.66 (dd, *J* = 12.5, 2.8 Hz, 1H), 4.49 (dd, *J* = 12.5, 3.7 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.06, 165.57, 165.49, 165.15, 157.13, 135.26, 133.4, 133.44, 133.21, 133.09, 130.01, 129.92, 129.81, 129.72, 129.59, 128.94, 128.70, 128.69, 128.41, 128.38, 128.37, 128.30, 127.15, 90.27, 70.80, 70.67, 70.32, 68.52, 62.16, 35.94. **3aβ**: [α]25 D = 26.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.95–7.88 (m, 4H), 7.88–7.84 (m, 2H), 7.55–7.45 (m, 3H), 7.45–7.37 (m, 3H), 7.36–7.31 (m, 4H), 7.31–7.26 (m, 2H), 7.18 (s, 1H), 7.01 (s, 1H), 6.40 (d, *J* = 7.8 Hz, 1H), 6.02 (t, *J* = 9.3 Hz, 1H), 5.89–5.75 (m, 2H), 4.65 (dd, *J* = 12.3, 3.1 Hz, 1H), 4.53 (dd, *J* = 12.3, 5.0 Hz, 1H), 4.40 (ddd, *J* = 9.6, 5.0, 3.1 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.04, 165.65, 165.05, 164.85, 156.44, 135.02, 133.52, 133.45, 133.33, 133.11, 130.03, 129.89, 129.84, 129.83, 129.79, 129.45, 128.72, 128.63, 128.62, 128.42, 128.38, 128.33, 128.32, 127.10, 92.58, 73.31, 72.71, 70.87, 68.84, 62.69, 36.23; HRMS (ESI) calcd for $C_{39}H_{32}N_2O_{11}Na$ $[M+Na]^+$ 727.1898, found 727.1901.

*2,3,4,6-Tetra-O-benzyl-D-glucopyranosyl-1-methylimidazole-2-carboxylate (**3b**)* Esterification of hemiacetal **2b** (5.0 g, 9.3 mmol) with acid **1** (1.8 g, 14 mmol) employing the General Procedure A afforded donor **3b** (5.1 g, 85%, α/β = 1:1.3) as a colorless syrup: [α]25 D = 36.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.26 (m, 23.1H), 7.25–7.21 (m, 3.3H), 7.21–7.17 (m, 3.70H), 7.06 (d, *J* = 0.9 Hz, 1H), 7.04 (d, *J* = 0.9 Hz, 0.67H), 6.57 (d, *J* = 3.6 Hz, 0.7H), 5.85 (d, *J* = 7.9 Hz, 1H), 5.02 (d, *J* = 6.0 Hz, 0.7H), 4.99 (d, *J* = 5.9 Hz, 1H), 4.97 (d, *J* = 10.9 Hz, 1H), 4.89 (s, 0.74H), 4.88–4.84 (m, 3.55H), 4.80–4.71 (m, 1.52H), 4.64–4.60 (m, 1.75H), 4.59–4.54 (m, 1.61H), 4.51 (d, *J* = 12.1 Hz, 1H), 4.47 (d, *J* = 12.1 Hz, 0.77H), 4.23 (t, *J* = 9.4 Hz, 0.78H), 4.13 (dt, *J* = 10.0, 2.6 Hz, 0.80H), 3.97 (d, *J* = 1.0 Hz, 4.64H), 3.89–3.83 (m, 1.16H), 3.83–3.75 (m, 5.46H), 3.72–3.64 (m, 1.72H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.55, 138.68, 138.37, 138.23, 138.18, 138.05, 138.01, 137.78, 137.66, 135.94, 135.66, 129.88, 129.65, 128.39, 128.37, 128.33, 128.29, 128.18, 128.01, 128.00, 127.93, 127.90, 127.89, 127.87, 127.85, 127.76, 127.73, 127.68, 127.67, 127.58, 127.55, 127.53, 126.85, 126.61, 94.97, 91.20, 84.59, 81.61, 81.08, 78.76, 77.26, 76.96, 75.90, 75.72, 75.70, 75.09, 75.07, 75.04, 73.47, 73.43, 73.21, 73.09, 68.43, 68.02, 36.02, 35.91; HRMS (ESI) calcd for $C_{39}H_{40}N_2O_7Na$ $[M+Na]^+$ 671.2728, found 671.2732.

*2,3,4,6-Tetra-O-benzoyl-D-mannopyranosyl-1-methylimidazole-2-carboxylate (**3c**)* Esterification of mannopyranosyl hemiacetal **2c** (1.0 g, 1.7 mmol) with acid **1a** (0.32 g, 2.5 mmol) employing general procedure B afforded donor **3c** (1.1 g, 94%, α/β = 1:3.3) as a white solid. Alternatively, esterification of mannopyranosyl hemiacetal **2c** (100 mg, 0.17 mmol) with acid **1a** (32 mg, 0.25 mmol) using the General Procedure A afforded donor **3c** (90 mg, 76%, α/β = 1/1.5) as a white solid: [α]25 D = −21.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15–8.05 (m, 5.81H), 8.01–7.97 (m, 2H), 7.97–7.93 (m, 1.25H), 7.90–7.87 (m, 1.21H), 7.87–7.82 (m, 2H), 7.62–7.54 (m, 3H), 7.52–7.46 (m, 1.65H), 7.46–7.33 (m, 10.65H), 7.31–7.21 (m, 4H), 7.14 (d, *J* = 0.9 Hz, 1H), 7.11–7.08 (m, 0.65H), 6.94 (s, 0.63H), 6.64 (d, *J* = 2.0 Hz, 1H), 6.49 (d, *J* = 1.3 Hz, 0.63H), 6.35 (t, *J* = 10.2 Hz, 1H), 6.16 (td, *J* = 6.3, 3.0 Hz, 2H), 5.96 (dd, *J* = 3.3, 2.0 Hz, 1H), 5.83 (dd, *J* = 9.6, 3.2 Hz, 0.72H), 4.83 (d, *J* = 10.1 Hz, 1H), 4.79 (dd, *J* = 12.2, 2.9 Hz, 0.67H), 4.75 (dd, *J* = 12.5, 2.5 Hz, 1H), 4.61 (dd, *J* = 12.3, 4.6 Hz, 0.70H), 4.52 (dd, *J* = 12.5, 3.2 Hz, 1H), 4.40 (ddd, *J* = 9.3, 4.5, 2.9 Hz, 0.70H), 4.03 (s, 3H), 3.79 (s, 1.85H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.94, 165.39, 165.32, 165.28, 165.15, 165.05, 156.47, 156.32, 135.31, 135.01, 133.57, 133.52, 133.46, 133.42, 133.33, 133.16, 133.02, 132.98, 130.29, 129.91, 129.87, 129.84, 129.80, 129.71, 129.66, 129.12, 128.94, 128.87, 128.78, 128.67, 128.57, 128.52, 128.42, 128.38, 128.36, 128.28, 128.24, 127.36, 126.87, 91.69, 91.34, 73.38, 71.30, 71.27, 69.92, 69.35, 68.79, 66.35, 65.97, 62.59, 62.10, 36.06, 35.94; HRMS (ESI) calcd for $C_{39}H_{32}N_2O_{11}Na$ $[M+Na]^+$ 727.1898, found 727.1902.

*2,3,4-Tri-O-benzoyl-L-rhamnopyranosyl-1-methylimidazole-2-carboxylate (**3d**)* Esterification of rhamnopyranosyl hemiacetal **2d** (1.0 g, 2.1 mmol) with acid **1a** (0.40 g, 3.2 mmol) employing General Procedure A afforded donor **3d** (0.99 g, 81%, α/β = 1.5:1) as a white solid: [α]25 D = 97.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14–8.07 (m, 3.40H), 8.02 (dt, *J* = 8.4, 1.3 Hz, 2.11H), 7.98–7.93 (m, 1.34H), 7.81 (m, 3.20H), 7.62 (m, 1.61H), 7.50 (qt, *J* = 7.4, 6.5 Hz, 5.29H), 7.45–7.36 (m, 5.26H), 7.34–7.32 (m, 1.15H), 7.29–7.21 (m, 3.20H), 7.20–7.17 (m, 1.22H), 7.13 (t, *J* = 1.2 Hz, 0.61H), 6.98 (d, *J* = 1.1 Hz, 0.59H), 6.56 (d, *J* = 1.9 Hz, 1H), 6.37 (d, *J* = 1.3 Hz, 0.65H), 6.10 (dt, *J* = 2.9, 1.4 Hz, 1H), 6.08 (dd, *J* = 3.6, 1.7 Hz, 0.63H), 5.89 (dd, *J* = 3.5, 1.9 Hz, 1H), 5.80 (t, *J* = 10.0 Hz, 1H), 5.72–5.68 (m, 1.21H), 4.71–4.56 (m, 1H), 4.08 (d, *J* = 2.5 Hz, 3.70H), 3.83 (s, 1.88H), 1.47 (d, *J* = 6.1 Hz, 1.95H), 1.40 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.81, 165.64, 165.57, 165.42, 165.36, 165.33, 156.23, 135.43,

133.64, 133.53, 133.48, 133.38, 133.30, 133.14, 130.17, 130.00, 129.98, 129.86, 129.77, 129.72, 129.69, 129.22, 129.10, 129.04, 129.03, 128.99, 128.74, 128.62, 128.59, 128.48, 128.44, 128.30, 128.26, 127.25, 126.83, 92.01, 91.51, 71.99, 71.41, 71.07, 69.81, 69.69, 69.20, 36.30, 36.12, 17.75, 17.64; HRMS (ESI) calcd for $C_{32}H_{28}N_2O_9Na$ $[M+Na]^+$ 607.1687, found 607.1691.

*2,3,4-Tri-O-benzoyl-D-xylopyranosyl-1-methylimidazole-2-carboxylate (**3e**)* Esterification of xylopyranosyl hemiacetal **2e** (1.0 g, 2.2 mmol) with acid **1a** (0.42 g, 3.3 mmol) employing General Procedure A afforded donor **3e** (1.0 g, 83%, $\alpha/\beta = 1:3.3$) as a white solid: $[\alpha]25\ D = -22.4$ (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.36–8.28 (m, 2H), 8.04 (ddt, *J* = 14.0, 6.9, 1.4 Hz, 4H), 8.00–7.97 (m, 0.53H), 7.93 (dd, *J* = 6.6, 5.1 Hz, 1.19H), 7.60–7.51 (m, 3.11H), 7.48–7.45 (m, 0.25H), 7.45–7.38 (m, 2.58H), 7.38–7.29 (m, 5.28H), 7.27 (dd, *J* = 5.4, 1.0 Hz, 1.35H), 7.10 (d, *J* = 0.9 Hz, 1H), 7.08 (d, *J* = 1.0 Hz, 0.27H), 6.81 (d, *J* = 3.8 Hz, 0.27H), 6.50 (d, *J* = 2.8 Hz, 1H), 6.35 (t, *J* = 9.9 Hz, 0.30H), 5.80 (tt, *J* = 4.5, 1.1 Hz, 1H), 5.59 (dd, *J* = 10.1, 3.8 Hz, 0.28H), 5.54 (td, *J* = 9.4, 7.4 Hz, 0.26H), 5.51–5.49 (m, 1H), 5.29 (q, *J* = 3.5 Hz, 1H), 4.71 (dd, *J* = 13.1, 2.8 Hz, 1H), 4.30–4.23 (m, 0.56H), 4.07 (dd, *J* = 13.0, 3.5 Hz, 1H), 4.00 (s, 3H), 3.85 (s, 0.81H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.59, 165.52, 165.47, 164.97, 157.27, 157.21, 135.57, 135.27, 133.52, 133.48, 133.47, 133.43, 133.39, 133.23, 130.61, 130.06, 129.99, 129.92, 129.85, 129.72, 129.30, 129.09, 128.88, 128.87, 128.82, 128.72, 128.44, 128.40, 128.39, 128.34, 127.12, 127.09, 91.70, 90.53, 70.65, 69.84, 69.47, 67.84, 67.23, 67.02, 61.37, 61.09, 36.04, 36.01; HRMS (MALDI) calcd for $C_{31}H_{26}N_2O_9K$ $[M+K]^+$ 609.1245, found 609.1270.

*2,3,4-Tri-O-benzoyl-D-ribopyranosyl-1-methylimidazole-2-carboxylate (**3f**)* Esterification of ribopyranosyl hemiacetal **2f** (1.0 g, 2.2 mmol) with acid **1a** (0.42 g, 3.3 mmol) employing General Procedure A afforded donor **3f** (0.92 g, 75%, β only) as a white solid: $[\alpha]25\ D = -98.5$ (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 9.4, 8.1 Hz, 4H), 7.89–7.83 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 2H), 7.52–7.46 (m, 1H), 7.35–7.26 (m, 6H), 7.23 (s, 1H), 7.12 (s, 1H), 6.64 (d, *J* = 2.6 Hz, 1H), 6.10 (t, *J* = 3.9 Hz, 1H), 5.75 (dt, *J* = 4.2, 2.3 Hz, 2H), 4.58 (dd, *J* = 13.3, 2.1 Hz, 1H), 4.27 (dd, *J* = 13.1, 3.0 Hz, 1H), 4.03 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.03, 165.70, 165.00, 156.82, 135.18, 133.38, 133.25, 133.20, 130.04, 129.94, 129.88, 129.73, 129.69, 129.28, 129.25, 128.38, 128.36, 128.35, 127.34, 92.44, 67.64, 67.22, 66.07, 63.45, 36.08; HRMS (ESI) calcd for $C_{31}H_{26}N_2O_9Na$ $[M+Na]^+$ 593.1531, found 593.1533.

*2,3,5-Tri-O-benzoyl-D-ribofuranosyl-1-methylimidazole-2-carboxylate (**3g**)* Esterification of ribofuranosyl hemiacetal **2g** (0.32 g, 0.68 mmol) with acid **1a** (0.13 g, 1.0 mmol) according to General Procedure B afforded donor **3g** (0.28 g, 74%, $\alpha/\beta = 1/5$) as a white solid. **3gα**: $[\alpha]25\ D = 78.3$ (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.35–8.23 (m, 2H), 8.17–8.08 (m, 2H), 7.83–7.79 (m, 2H), 7.62–7.57 (m, 1H), 7.57–7.53 (m, 1H), 7.49 (dd, *J* = 8.3, 7.2 Hz, 2H), 7.44 (tt, *J* = 7.5, 1.3 Hz, 1H), 7.41–7.36 (m, 2H), 7.29–7.17 (m, 3H), 7.04 (d, *J* = 1.0 Hz, 1H), 6.94 (d, *J* = 4.4 Hz, 1H), 5.94 (dd, *J* = 6.5, 2.4 Hz, 1H), 5.78 (dd, *J* = 6.6, 4.4 Hz, 1H), 5.02 (q, *J* = 3.2 Hz, 1H), 4.75 (dd, *J* = 12.2, 3.2 Hz, 1H), 4.64 (dd, *J* = 12.2, 3.6 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.07, 166.05, 164.97, 157.97, 135.89, 133.38, 133.36, 130.51, 129.78, 129.76, 129.72, 129.40, 129.20, 128.72, 128.61, 128.34, 128.28, 126.74, 95.51, 82.72, 71.25, 70.31, 63.97, 35.78. **3gβ**: $[\alpha]25\ D = 11.5$ (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (ddd, *J* = 7.7, 6.3, 1.3 Hz, 4H), 7.91–7.85 (m, 2H), 7.63–7.55 (m, 1H), 7.52–7.39 (m, 4H), 7.30 (q, *J* = 7.6 Hz, 4H), 7.21 (s, 1H), 7.07 (s, 1H), 6.61 (s, 1H), 6.09 (dd, *J* = 7.1, 4.9 Hz, 1H), 6.04 (d, *J* = 5.0 Hz, 1H), 4.84 (dt, *J* = 7.1, 4.4 Hz, 1H), 4.74 (dd, *J* = 12.2, 4.0 Hz, 1H), 4.63 (dd, *J* = 12.1, 4.9 Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.14, 165.07, 164.96, 157.29, 135.27, 133.65, 133.46, 132.98, 129.85, 129.79, 129.76, 129.59, 129.40, 128.87, 128.71, 128.54, 128.37, 128.28, 127.09, 99.38, 80.51, 75.26, 71.36, 63.95, 36.02; HRMS (ESI) calcd for $C_{31}H_{26}N_2O_9Na$ $[M+Na]^+$ 593.1531, found 593.1532.

General Glycosylation Procedure. A solution of glycosyl donor **3** (1.3 eq.) and acceptor **6** (1.0 eq.) in dry CH_2Cl_2 (0.15 M) was stirred at room temperature in the presence of activated 4 Å M.S. (3.0 g/mmol) under argon atmosphere for 30 mins, to which $Cu(OTf)_2$ (1.5 eq.) was added. The mixture was stirred at room temperature and monitored by TLC. After completion (~3 h), the reaction mixture was filtered through a pad of Celite and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to afford the glycosylated product.

*Methyl 2,3,6-Tri-O-benzyl-4-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**7a**)*. Glycosylation of acceptor **6a** (40 mg, 0.086 mmol) with donor **3aβ** (79 mg, 0.11 mmol) using the General Glycosylation Procedure afforded glycoside **7a** (petroleum ether/ethyl acetate = 5/1; 78 mg, 87%) as a white solid. The ^1H NMR spectral data of **7a** are identical with the literature data.[27]

*Methyl 2,3,6-Tri-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-α/β-D-glucopyranosyl)-α-D-glucopyranoside (**7b**)*. Glycosylation of acceptor **6a** (40 mg, 0.086 mmol) with donor **3b** (77 mg, 0.12 mmol) using the General Glycosylation Procedure afforded glycoside **7b** (petroleum ether/ethyl acetate = 5/1; 80 mg, 94%, $\alpha/\beta = 1/1.7$) as a colorless syrup. The ^1H NMR spectral data of **7b** are identical with the literature data.[27]

*Methyl 2,3,4-Tri-O-benzyl-6-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**7c**)*. Glycosylation of acceptor **6b** (40 mg, 0.086 mmol) with donor **3aβ** (79 mg, 0.11 mmol) using the General Glycosylation Procedure afforded glycoside **7c** (petroleum ether/ethyl acetate = 5/1; 86 mg, 96%) as a white solid. The ^1H NMR spectral data of **7c** are identical with the literature data.[27]

*Methyl 2,3,4-Tri-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-αβ-D-glucopyranosyl)-α-D-glucopyranoside (**7d**)*. Glycosylation of acceptor **6b** (42 mg, 0.090 mmol) with donor **3b** (75 mg, 0.12 mmol) using the General Glycosylation Procedure afforded glycoside **7d** (petroleum ether/ethyl acetate = 5/1; 86 mg, 96%, $\alpha/\beta = 1.4/1$) as colorless syrup. The ^1H NMR spectral data of **7d** are identical with the literature data.[27]

*1-Adamantanyl 2,3,4,6-tetra-O-benzoyl-β-D-glucopyranoside (**7e**)*. Glycosylation of acceptor **6c** (14 mg, 0.092 mmol) with donor **3aβ** (85 mg, 0.12 mmol) using the General Glycosylation Procedure afforded glycoside **7e** (petroleum ether/ethyl acetate = 6/1; 49 mg, 73%) as a white solid. The ^1H NMR spectral data of **7e** are identical with the literature data.[27]

*1-Adamantanyl 2,3,4,6-tetra-O-benzyl-α,β-D-glucopyranoside (**7f**)*. Glycosylation of acceptor **6c** (14 mg, 0.092 mmol) with donor **3b** (79 mg, 0.12 mmol) using the General Glycosylation Procedure afforded glycoside **7f** (petroleum ether/ethyl acetate = 5/1; 60 mg, 97%, $\alpha/\beta = 1.1:1$) as a white solid. The ^1H NMR spectral data of **7f** are identical with the literature data.[27]

*6-O-(2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**7g**)*. Glycosylation of acceptor **6d** (28 mg, 0.11 mmol) with donor **3aβ** (95 mg, 0.13 mmol) using the General Glycosylation Procedure afforded glycoside **7g** (petroleum ether/ethyl acetate = 3/1; 84 mg, 95%) as colorless syrup. The ^1H NMR spectral data of **7g** are identical with the literature data.[27]

*(1S,2R,5S)-(+)-1-Menthyl 2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranoside (**7h**)*. Glycosylation of acceptor **6e** (10 mg, 0.064 mmol) with donor **3a** (59 mg, 0.084 mmol) using the General Glycosylation Procedure afforded glycoside **7h** (petroleum ether/ethyl acetate = 6/1; 40 mg, 85%) as colorless syrup. The ^1H NMR spectral data of **7h** are identical with the literature data.[27]

*Cholesteryl 2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranoside (**7i**)*. Glycosylation of acceptor **6f** (36 mg, 0.093 mmol) with donor **3aβ** (85 mg,

0.12 mmol) using the General Glycosylation Procedure afforded glycoside **7i** (petroleum ether/ethyl acetate = 6/1; 67 mg, 75%) as colorless syrup. The ^{1}H NMR spectral data of **7i** are identical with the literature data.[27]

*2-(N-morpholino)ethyl 2,3,4,6-Tetra-O-benzyl-αβ-D-glucopyranoside (**7j**).* Glycosylation of acceptor **6g** (10 μL, 0.083 mmol) with donor **3b** (74 mg, 0.11 mmol) using the General Glycosylation Procedure afforded glycoside **7j** (petroleum ether/ethyl acetate = 10/1; 48 mg, 89%, α/β = 5/1) as brown syrup: [α]25 D = 28.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.21 (m, 17.43H), 7.17–7.09 (m, 2.56H), 4.97 (d, *J* = 10.9 Hz, 1H), 4.94 (d, *J* = 6.6 Hz, 0.21H), 4.91 (d, *J* = 6.2 Hz, 0.22H), 4.82 (m, 3.65H), 4.76 (s, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.62–4.56 (m, 1.23H), 4.54 (d, *J* = 4.1 Hz, 0.24H), 4.51 (d, *J* = 2.7 Hz, 0.17H), 4.50–4.44 (m, 2H), 4.42 (d, *J* = 7.8 Hz, 0.22H), 4.08 (dt, *J* = 10.9, 5.6 Hz, 0.19H), 3.98 (t, *J* = 9.3 Hz, 1H), 3.84–3.53 (m, 13.30H), 3.49–3.41 (m, 0.43H), 2.65 (dq, *J* = 11.6, 5.8 Hz, 2.77H), 2.51 (q, *J* = 5.2 Hz, 5.37H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.73, 138.49, 138.44, 138.13, 138.04, 138.00, 137.82, 128.42, 128.36, 128.34, 127.94, 127.91, 127.89, 127.87, 127.84, 127.81, 127.75, 127.70, 127.62, 127.57, 103.57, 97.06, 84.65, 82.06, 81.90, 79.91, 77.78, 77.63, 75.66, 75.06, 74.99, 74.80, 74.66, 73.48, 73.13, 70.28, 68.86, 68.49, 67.22, 66.70, 64.81, 58.14, 57.95, 53.97, 53.91; HRMS (ESI) calcd for $C_{40}H_{48}NO_7$ $[M+H]^+$ 654.3425, found 654.3429.

*3-Exo-tropinyl 2,3,4,6-Tetra-O-benzyl-α/β-D-glucopyranoside (**7k**).* Glycosylation of acceptor **6h** (13 mg, 0.092 mmol) with donor **3b** (83 mg, 0.13 mmol) using the General Glycosylation Procedure afforded glycoside **7k** (petroleum ether/ethyl acetate = 10/1; 61 mg, 99%, α/β = 3:1) as brown syrup: [α]25 D = 32.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.24 (m, 20.92H), 7.19 (dd, *J* = 7.3, 2.2 Hz, 0.79H), 7.15 (dd, *J* = 7.3, 2.3 Hz, 2H), 5.00 (d, *J* = 10.9 Hz, 1H), 4.96 (d, *J* = 8.5 Hz, 0.34H), 4.93 (d, *J* = 8.4 Hz, 0.46H), 4.88 (d, *J* = 3.7 Hz, 1H), 4.86–4.79 (m, 2.64H), 4.76 (d, *J* = 12.2 Hz, 1.20H), 4.71 (d, *J* = 11.0 Hz, 0.40H), 4.64 (d, *J* = 4.2 Hz, 1.13H), 4.61 (d, *J* = 4.2 Hz, 1.27H), 4.59–4.53 (m, 0.78H), 4.50–4.44 (m, 2.37H), 4.04–3.94 (m, 1.40H), 3.90–3.76 (m, 2.23H), 3.73 (dd, *J* = 10.5, 4.0 Hz, 1.26H), 3.70–3.60 (m, 2.60H), 3.60–3.52 (m, 1.66H), 3.48 (dt, *J* = 6.4, 3.2 Hz, 0.34H), 3.43 (dd, *J* = 9.1, 7.8 Hz, 0.45H), 3.24 (dt, *J* = 6.1, 2.7 Hz, 1.73H), 3.19 (m, 1H), 2.37 (s, 4.10H), 2.06–1.68 (m, 8.72H), 1.63–1.45 (m, 2.89H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.86, 138.56, 138.36, 138.28, 138.20, 138.14, 138.02, 137.88, 128.37, 128.34, 128.32, 128.29, 128.17, 128.02, 127.97, 127.90, 127.88, 127.82, 127.78, 127.73, 127.68, 127.63, 127.61, 127.54, 127.49, 101.91, 95.18, 84.68, 82.09, 81.88, 80.06, 77.88, 77.79, 75.64, 75.58, 75.05, 74.96, 74.77, 74.73, 73.39, 73.34, 72.95, 71.63, 70.11, 69.68, 69.11, 68.60, 60.20, 60.11, 59.85, 59.80, 37.56, 37.45, 36.07, 35.74, 34.45, 26.99, 26.95, 26.70, 26.67; HRMS (ESI) calcd for $C_{42}H_{50}NO_6$ $[M+H]^+$ 664.3633, found 664.3635.

*(1S,2R,5S)-(+)-1-Menthyl 2,3,4,6-Tetra-O-benzoyl-α-D-mannopyranoside (**7l**).* Glycosylation of acceptor **6e** (16 mg, 0.10 mmol) with donor **3c** (92 mg, 0.13 mmol) using the General Glycosylation Procedure afforded glycoside **7l** (petroleum ether/ethyl acetate = 4/1; 73 mg, 99%) as a white solid: [α]25 D = −51.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18–8.03 (m, 4H), 8.05–7.95 (m, 2H), 7.90–7.81 (m, 2H), 7.62–7.54 (m, 2H), 7.54–7.49 (m, 1H), 7.46–7.34 (m, 7H), 7.30–7.24 (m, 2H), 6.07 (t, *J* = 10.1 Hz, 1H), 5.94 (dd, *J* = 10.1, 3.2 Hz, 1H), 5.63 (dd, *J* = 3.3, 1.9 Hz, 1H), 5.20 (d, *J* = 1.8 Hz, 1H), 4.67 (dd, *J* = 12.0, 2.4 Hz, 1H), 4.59 (ddd, *J* = 10.1, 5.2, 2.3 Hz, 1H), 4.49 (dd, *J* = 12.0, 5.2 Hz, 1H), 3.50 (td, *J* = 10.6, 4.4 Hz, 1H), 2.35–2.15 (m, 2H), 1.74–1.55 (m, 3H), 1.46–1.35 (m, 2H), 1.19 (q, *J* = 11.8 Hz, 1H), 1.07–0.94 (m, 4H), 0.84 (dd, *J* = 15.9, 6.7 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.22, 164.54, 164.50, 164.48, 132.39, 132.11, 132.03, 128.84, 128.81, 128.72, 128.70, 128.43, 128.13, 127.99, 127.55, 127.39, 127.37, 127.26, 98.25, 81.83, 70.00, 69.04, 68.00, 66.19, 62.28, 47.45, 41.78, 33.23, 30.66, 24.85, 22.22, 21.11, 20.05, 15.24; HRMS (ESI) calcd for $C_{44}H_{46}O_{10}Na$ $[M+Na]^+$ 757.2983, found 757.2986.

*1-Adamantanyl 2,3,4,6-tetra-O-benzoyl-α-D-mannopyranoside (**7m**).* Glycosylation of acceptor **6c** (15 mg, 0.10 mmol) with donor **3c** (93 mg, 0.13 mmol) using the General Glycosylation Procedure afforded glycoside **7m** (petroleum ether/ethyl acetate = 4/1; 73 mg, 99%) as a white solid. The ^{1}H NMR spectral data of **7m** are identical with the literature data.[28]

*6-O-(2,3,4,6-Tetra-O-benzoyl-α-D-mannopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**7n**).* Glycosylation of acceptor **6d** (20 mg, 0.077 mmol) with donor **3c** (75 mg, 0.11 mmol) using the General Glycosylation Procedure afforded glycoside **7n** (petroleum ether/ethyl acetate = 3/1; 60 mg, 93%) as colorless syrup. The ^{1}H NMR spectral data of **7n** are identical with the literature data.[29]

*Methyl 2,3,4-Tri-O-benzyl-6-O-(2,3,4,6-tetra-O-benzoyl-α-D-mannopyranosyl)-α-D-glucopyranoside (**7o**).* Glycosylation of acceptor **6b** (38 mg, 0.082 mmol) with donor **3c** (77 mg, 0.11 mmol) using the General Glycosylation Procedure afforded glycoside **7o** (petroleum ether/ethyl acetate = 5/1; 86 mg, 99%) as colorless syrup. The ^{1}H NMR spectral data of **7o** are identical with the literature data.[29]

*6-O-(2,3,4-Tri-O-benzoyl-α-L-rhamnopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**7p**).* Glycosylation of acceptor **6d** (20 mg, 0.077 mmol) with donor **3d** (59 mg, 0.10 mmol) using the General Glycosylation Procedure afforded glycoside **7p** (petroleum ether/ethyl acetate = 4/1; 47 mg, 85%) as colorless syrup. The ^{1}H NMR spectral data of **7p** are identical with the literature data.[5d]

*Methyl 2,3,4-Tri-O-benzyl-6-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-α-D-glucopyranoside (**7q**).* Glycosylation of acceptor **6b** (41 mg, 0.088 mmol) with donor **3d** (68 mg, 0.12 mmol) using the General Glycosylation Procedure afforded glycoside **7q** (petroleum ether/ethyl acetate = 5/1; 80 mg, 98%) as colorless syrup. The ^{1}H NMR spectral data of **7q** are identical with the literature data.[27]

*Methyl 2,3,6-Tri-O-benzyl-4-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-α-D-glucopyranoside (**7r**).* Glycosylation of acceptor **6a** (42 mg, 0.090 mmol) with donor **3d** (69 mg, 0.12 mmol) using the General Glycosylation Procedure afforded glycoside **7r** (petroleum ether/ethyl acetate = 5/1; 82 mg, 98%) as colorless syrup. The ^{1}H NMR spectral data of **7r** are identical with the literature data.[27]

*4-O-(2'',3'',4''-Tri-O-benzoyl-α-L-rhamnopyranosyl) podophyllotoxin (**7s**).* Glycosylation of acceptor **6i** (37 mg, 0.089 mmol) with donor **3d** (78 mg, 0.13 mmol) using the General Glycosylation Procedure afforded glycoside **7s** (petroleum ether/ethyl acetate = 5/1; 56 mg, 72%) as a white solid. The ^{1}H NMR spectral data of **7s** are identical with the literature data.[30]

*6-O-(2,3,4-tri-O-benzoyl-β-D-xylopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**7t**).* Glycosylation of acceptor **6d** (20 mg, 0.077 mmol) with donor **3e** (58 mg, 0.10 mmol) using the General Glycosylation Procedure afforded glycoside **7t** (petroleum ether/ethyl acetate = 3/1, 51 mg, 94%) as colorless syrup. The ^{1}H NMR spectral data of **7t** are identical with the literature data.[27]

*Cholesteryl-2,3,4-tri-O-benzoyl-β-D-xylopyranose (**7u**).* Glycosylation of acceptor **6f** (36 mg, 0.093 mmol) with donor **3e** (69 mg, 0.12 mmol) using the General Glycosylation Procedure afforded glycoside **7u** (petroleum ether/ethyl acetate = 6/1; 64 mg, 83%) as colorless syrup. The ^{1}H NMR spectral data of **7u** are identical with the literature data.[27]

*Methyl 2,3,4-Tri-O-benzyl-6-O-(2,3,4-tri-O-benzoyl-β-D-ribopyranosyl)-α-D-glucopyranoside (**7v**).* Glycosylation of acceptor **6b** (52 mg, 0.11 mmol) with donor **3f** (84 mg, 0.15 mmol) using the General Glycosylation Procedure afforded glycoside **7v** (petroleum ether/ethyl acetate = 3/1; 93 mg, 91%) as colorless syrup: [α]25 D = −16.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (ddd, *J* = 9.8, 8.2, 1.4 Hz, 4H), 7.95–7.87 (m, 2H), 7.60–7.48 (m, 3H), 7.42–7.19 (m, 21H),

5.83 (t, J = 3.8 Hz, 1H), 5.60 (d, J = 3.3 Hz, 1H), 5.49 (t, J = 3.3 Hz, 1H), 5.04 (d, J = 2.9 Hz, 1H), 5.01 (d, J = 10.9 Hz, 1H), 4.89 (d, J = 11.2 Hz, 1H), 4.84 (d, J = 9.0 Hz, 1H), 4.82 (d, J = 10.3 Hz, 1H), 4.70 (d, J = 12.1 Hz, 1H), 4.65 (d, J = 3.5 Hz, 1H), 4.61 (d, J = 11.2 Hz, 1H), 4.27 (dd, J = 12.9, 2.5 Hz, 1H), 4.06–3.98 (m, 3H), 3.82 (ddd, J = 10.1, 4.6, 1.7 Hz, 1H), 3.71 (dd, J = 10.8, 4.6 Hz, 1H), 3.61–3.54 (m, 2H), 3.41 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.09, 165.72, 165.18, 138.75, 138.23, 138.16, 133.20, 133.17, 133.10, 129.97, 129.92, 129.80, 129.72, 129.63, 129.46, 128.48, 128.41, 128.37, 128.34, 128.30, 128.12, 127.91, 127.86, 127.72, 127.55, 98.65, 98.05, 82.12, 80.11, 77.50, 75.71, 75.05, 73.48, 69.78, 68.70, 67.65, 66.92, 66.50, 61.20, 55.29; HRMS (ESI) calcd for $C_{54}H_{52}O_{13}Na$ $[M+Na]^+$ 931.3300, found 931.3294.

*(1S,2R,5S)-(+)-1-Menthyl 2,3,4-Tri-O-benzoyl-β-D-ribopyranoside (**7w**).* Glycosylation of acceptor **6e** (15 mg, 0.096 mmol) with donor **3f** (72 mg, 0.13 mmol) using the General Glycosylation Procedure afforded glycoside **7w** (petroleum ether/ethyl acetate = 6/1; 59 mg, 99%) as colorless syrup: [α]25 D = −89.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07–8.04 (m, 2H), 8.04–8.00 (m, 2H), 7.89 (dd, J = 8.4, 1.4 Hz, 2H), 7.58–7.50 (m, 2H), 7.49 (td, J = 7.4, 1.3 Hz, 1H), 7.36–7.27 (m, 6H), 5.83 (t, J = 3.8 Hz, 1H), 5.63 (q, J = 3.0 Hz, 1H), 5.45–5.40 (m, 1H), 5.31 (d, J = 2.5 Hz, 1H), 4.33 (dd, J = 13.0, 2.3 Hz, 1H), 4.08 (dd, J = 13.0, 3.0 Hz, 1H), 3.56 (td, J = 10.6, 4.1 Hz, 1H), 2.33 (pd, J = 6.9, 2.6 Hz, 1H), 2.20–2.11 (m, 1H), 1.74–1.65 (m, 2H), 1.45–1.31 (m, 2H), 1.08–0.82 (m, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.24, 166.06, 165.27, 133.17, 133.14, 133.05, 130.00, 129.94, 129.78, 129.73, 129.48, 128.34, 128.31, 128.30, 95.02, 76.64, 69.73, 67.89, 66.46, 61.43, 47.83, 39.79, 34.33, 31.44, 25.47, 22.83, 22.26, 21.22, 15.47; HRMS (ESI) calcd for $C_{36}H_{40}O_8Na$ $[M+Na]^+$ 623.2615, found 623.2617.

*Methyl 2,3,4-Tri-O-benzyl-6-O-(2,3,4-tri-O-benzoyl-β-D-ribofuranosyl)-α-D-glucopyranoside (**7x**).* Glycosylation of acceptor **6b** (42 mg, 0.090 mmol) with donor **3gβ** (68 mg, 0.12 mmol) using the General Glycosylation Procedure afforded glycoside **7x** (Eluent: petroleum ether/ethyl acetate = 3/1 v/v, 78 mg, 95% yield) as colorless syrup. The ^{1}H NMR spectral data of **7x** are identical with the literature data.[31]

*Methyl 2,3,6-Tri-O-benzyl-4-O-(2,3,4-tri-O-benzoyl-β-D-ribofuranosyl)-α-D-glucopyranoside (**7y**).* Glycosylation of acceptor **6a** (40 mg, 0.086 mmol) with donor **3g** (68 mg, 0.11 mmol) using the General Glycosylation Procedure afforded glycoside **7y** (petroleum ether/ethyl acetate = 3/1; 71 mg, 91%) as colorless syrup. The ^{1}H NMR spectral data of **7y** are identical with the literature data.[31]

*(1S,2R,5S)-(+)-1-Menthyl 2,3,4-Tri-O-benzoyl-β-D-ribofuranoside (**7z**).* Glycosylation of acceptor **6e** (14 mg, 0.089 mmol) with donor **3gβ** (68 mg, 0.11 mmol) using the General Glycosylation Procedure afforded glycoside **7z** (petroleum ether/ethyl acetate = 6/1; 55 mg, 99%) as a colorless syrup. The ^{1}H NMR spectral data of **7z** are identical with the literature data.[27]

Deposition Numbers 2064548 (for **3eβ**), 2064549 (for **3fβ**), and 2064547 (for **3gβ**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

Supporting Information

Supporting Information (see footnote on the first page of this article): Compound characterization and NMR spectra.

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Conflict of Interest

The authors declare no conflict of interest.

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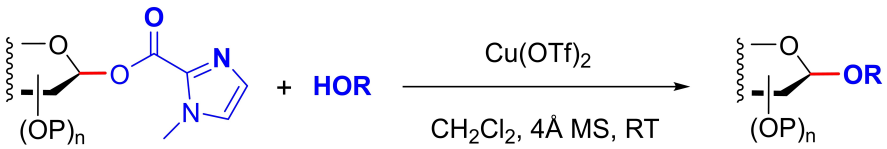

A mild glycosylation protocol is developed by using glycosyl 1-methylimidazole-2-carboxylates as donors. Such a glycosylation can be promoted by a series of metal triflates and triflimides, especially $Cu(OTf)_2$.

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A Mild Glycosylation Protocol with Glycosyl 1-Methylimidazole-2-carboxylates as Donors