Copper-Catalyzed Stereoselective Synthesis of 2-Deoxygalactosides

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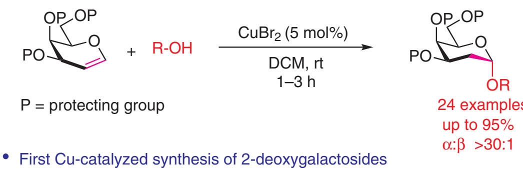


- First Cu-catalyzed synthesis of 2-deoxygalactosides
- Mild reaction conditions
- Affordable copper catalyst without additional ligand
- Broad substrate scope with high yields and excellent α-selectivity
- Gram scale and synthesis of trisaccharide

Received: 14.01.2020
Accepted after revision: 03.04.2020
Published online: 05.05.2020
DOI: 10.1055/s-0040-1707098; Art ID: st-2020-b0025-l

Abstract An efficient glycosylation method to synthesize 2-deoxy-*O*-galactosides based on a Cu(II)-catalyzed reaction without additional ligand has been developed. The glycosylation was amenable to different protected glycal donors and a wide range of acceptors including alcohols, amino acids, sugars, and phenol, and proceeds with excellent yield and high α-selectivity under mild conditions. The reaction proceeds readily on a gram scale, and its versatility is exemplified in the synthesis of oligosaccharides.

Key words copper catalyst, 2-deoxygalactosides, glycosylation, glycals, stereoselectivity

Deoxyglycosides are common components of a wide range of bioactive natural products (Figure 1),[1] and they often display antibiotic, anticancer, or cardiotonic activities.[2] As a result, many methods have been developed for the synthesis of 2-deoxyglycosides.[3] However, unlike fully oxygenated glycosides, the lack of substituents at C-2 to direct the nucleophilic approach presents an additional synthetic challenge that has piqued the interest of researchers for many decades.[4] To overcome these problems, many indirect approaches have been developed for the synthesis of 2-deoxyglycosides, usually by installing a temporary directing group at the C-2 position, which makes this methodology inherently inefficient.[4b,c,5] Thus, several direct approaches have been formulated to achieve the stereoselective synthesis of these compounds.[6] Among them, it is still the most atom-efficient route to synthesize 2-deoxyglycosides by adding an alcohol to a glycal directly in a catalyzed process.[7–10]

Recently, many methodologies using glycal to synthesis 2-deoxyglycosides have been reported, including organocatalysis,[11–13] Lewis acid catalysis,[14–16] and Brønsted acid catalysis[8a,17] (Scheme 1). For instance, Galan et al.[7] in 2012, reported the selective synthesis of 2-deoxy-*O*-galactosides using thiourea as an organocatalyst. Subsequently, in 2105, Galan et al.[12a] used pyridinium cations as novel organocatalyst to synthesize 2-deoxyglycosides efficiently. Since 2017, Galan's group[7–10] have developed several practical methods by using Lewis acids, such as Au(I) in combination with AgOTf, and Pd(II) in combination with a monodentate phosphine ligand and $B(C_6F_5)_3$. Meanwhile, Wang[11] reported the selective synthesis of 2-deoxy-*O*-glycosides catalyzed by photoacid. Despite the great efforts that have been made in this area, noble metals or expensive ligands are still re-

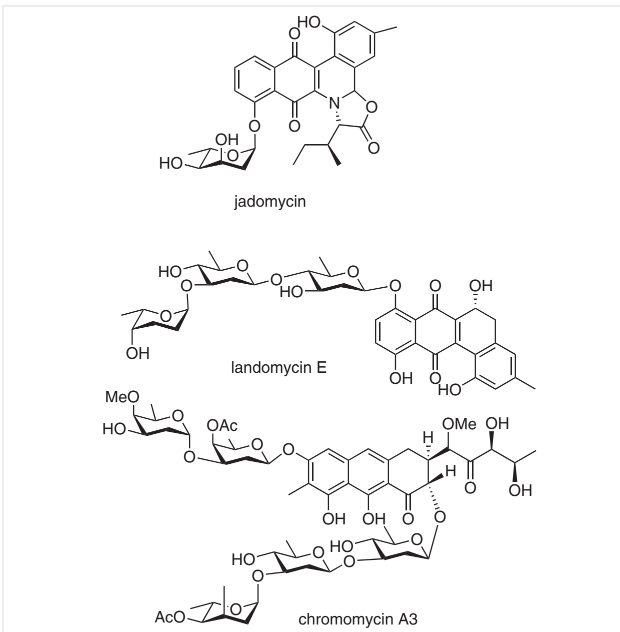
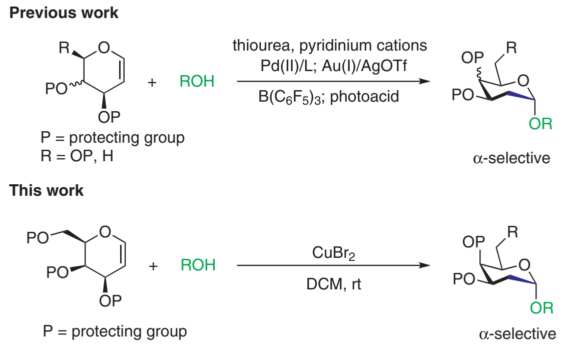


Figure 1 Representative deoxyglycoside-containing natural products

quired as catalysts in the reaction. Thus, there is a need to find improved and more general catalysts to access these high-value glycosides.

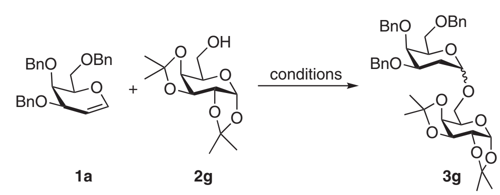


Scheme 1 Representative strategies for the synthesis of deoxyglycosides from glycals

In recent years, copper catalysts have been widely employed in organic chemistry because of its abundance, ready availability, and low toxicity.[18] For example, Debaraj et al. reported $Cu(OTf)_2$ mediated stereoselective synthesis of C-glycosides from unactivated alkynes.[18b] A recent reaction was developed by Tang et al., in which glycosyl isoquinoline-1-carboxylate was used as glycosyl donor, promoted by the $Cu(OTf)_2$ salt under mild reaction conditions.[18e] More recently, Messaoudi et al. reported $Cu(OAc)_2{\cdot}H_2O$ catalyzed anomeric O-arylation of carbohydrate derivatives at room temperature.[18f] However, copper salts have not been applied to the stereoselective synthesis of 2-deoxyglycosides. Based on our continuing interest in 2-deoxyglycosides,[15] we hoped to apply copper salts to the synthesis of 2-deoxyglycosides. Fortunately, we found that when $CuBr_2$ was used as the catalyst, 2-deoxy-*O*-glycosides could be successfully obtained with α-selectivity. Herein, we described an unprecedented Cu(II) direct activation of glycals to yield 2-deoxygalactosides under mild conditions (Scheme 1).

We started our studies with galactal **1a** and galactoside acceptor **2g** as model substrates. Initially, we examined a series of iron(III) catalysts: $FeCl_3{\cdot}6H_2O$/C, $FeCl_3$/C, Fe_3O_4@C@Fe(III), which have been widely used as efficient catalysts in glycosylation reactions.[19–21] As shown in Table 1, product **3g** was gained with poor yield, with the formation of more 2,3-unsaturated Ferrier product (yield 42–60%; entries 1–3). Next, a series of commercial Lewis catalysts were screened (entries 4–9). To our delight, when $CuBr_2$ was used as catalyst, the addition product **3g** could be obtained with 77% yield and α:β stereocontrol of >30:1 (entry 9).[9] Subsequently, other copper salts were further tested as catalysts (entries 10–15). The results indicated $CuBr_2$ was the best catalyst among copper salt catalysts. Solvent effect was also evaluated. Reactions in DMF, 1,4-dioxane, or DMSO did not proceed (entries 19–21), whereas reactions in DCE, CH_3CN and THF gave lower yields than in DCM (entries 16–18). When the reaction was carried out at 0 or 40 °C, product **3g** was obtained in 71 and 75% yield, respectively (entry 22 and 23). Further optimization studies of catalyst loadings were conducted that revealed that 0.05 equivalent $CuBr_2$ provided the highest yield (82%; entry 25). Increasing the number of equivalents of $CuBr_2$ to 0.1 or decreasing it to 0.025, both led to decreased yields of **3g** (en-

Table 1 Optimization of the Reaction Conditions[a]



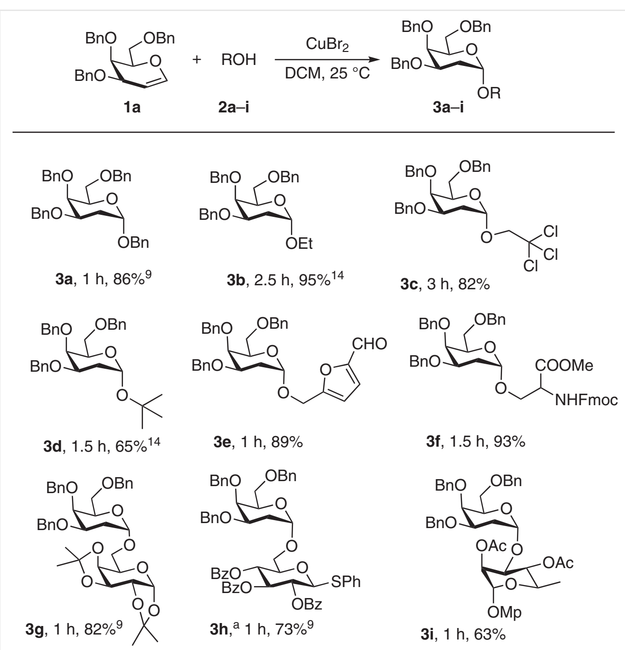
Entry	Catalyst	Cat. (equiv.)	Solvent	Time (h)	Yield (%)[b]	α:β
1	$FeCl_3{\cdot}6H_2O$/C	0.2	DCM	4	22	–
2	$FeCl_3$/C	0.2	DCM	3	30	–
3	Fe_3O_4@C@Fe(III)	0.2	DCM	2	45	–
4	$PdCl_2$	0.2	DCM	6	48	–
5	$CuCl_2$	0.2	DCM	12	N.R	–
6	$CoCl_2$	0.2	DCM	12	N.R	–
7	$CoBr_2$	0.2	DCM	12	N.R	–
8	$ZnCl_2$	0.2	DCM	0.5	5	–
9	$CuBr_2$	0.2	DCM	0.5	77	>30:1
10	$CuNO_3{\cdot}3H_2O$	0.2	DCM	12	N.R	–
11	$CuSO_4$	0.2	DCM	12	N.R	–
12	$Cu(OTf)_2$	0.2	DCM	12	71	–
13	$Cu(OAc)_2$	0.2	DCM	12	N.R	–
14	CuBr	0.2	DCM	12	5	–
15	CuI	0.2	DCM	12	N.R	–
16	$CuBr_2$	0.2	DCE	1.5	68	–
17	$CuBr_2$	0.2	CH_3CN	0.5	72	–
18	$CuBr_2$	0.2	THF	0.5	70	–
19	$CuBr_2$	0.2	DMF	2	N.R	–
20	$CuBr_2$	0.2	dioxane	2	N.R	–
21	$CuBr_2$	0.2	DMSO	2	N.R	–
22[c]	$CuBr_2$	0.2	DCM	4	71	>30:1
23[d]	$CuBr_2$	0.2	DCM	0.5	75	>30:1
24	$CuBr_2$	0.1	DCM	1	80	>30:1
25	$CuBr_2$	0.05	DCM	1	82	>30:1
26	$CuBr_2$	0.025	DCM	3	79	>30:1

[a] Reaction conditions: glycal donor **1a** (0.1 mmol), acceptor **2g** (0.12 mmol), catalyst (0.02 mmol), solvent (1.0 mL), 25 °C, N_2.
[b] Isolated yield.
[c] The reaction was conducted at 0 °C.
[d] The reaction was conducted at 40 °C.

tries 24 and 26). Therefore, the optimized reaction conditions were: 1.0 equiv donor, 1.2 equiv acceptor and 0.05 equiv $CuBr_2$ as catalyst in DCM at 25 °C.

Having established the optimum reaction conditions, our attention then turned to expanding the substrate scope of the glycosyl acceptors to other alcohols (Scheme 2; **2a–i**). Fortunately, in all cases, deoxy products **3a–i** could be obtained within three hours in good to excellent yields with high stereoselectivities (α:β >30:1). When simple primary alcohols such as benzyl alcohol **2a** and ethanol **2b** were used as nucleophilic acceptors, products **3a** and **3b** were obtained in yields of 86% and 95%, respectively. Additionally, trichloroethanol **2c**, an electron-deficient alcohol, reacted with glycal donor **1a** smoothly in 82% yield, albeit with longer time (3 h) due to the presence of a strong electron-withdrawing group. Notably, when *tert*-butanol was used as nucleophile, the expected product **3d** was also obtained in good yield (65%), despite its greater steric hindrance. 5-Hydroxymethylfurfural (HMF) **2e**, which is an important biofuel, and its sugar derivatives, shows antitumor activity in our previous research,[22] was also applied in this catalytic system with 89% yield.

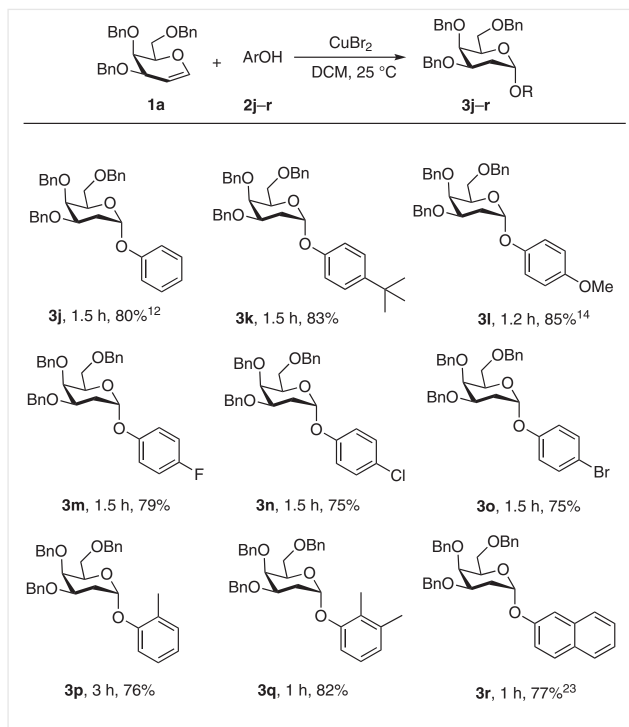
The catalytic system was also suitable for use with amino acid acceptors. For example, Fmoc-protected serine **2f** afforded the corresponding glycoside product **3f** in 93% yield within 1.5 h (Scheme 2). Moreover, sugar acceptors,



Scheme 2 Alcoholic acceptor scope of glycosylation reactions with galactal **1a**. *Reagents and conditions*: donor (0.1 mmol), acceptor (0.12 mmol), $CuBr_2$ (5 mol%), stirred in DCM (1.0 mL), 25 °C, nitrogen atmosphere. All yields are isolated yields; α:β ratio of all products was >30:1 and was determined based on the ^{1}H NMR spectra. [a] $CuBr_2$ (0.1 equiv) was used.

for instance, galactoside **2g**, glucoside **2h**, and rhamnoside **2i** also afforded the desired 2-deoxy products in good yields (63–82%) and with high α-selectivities. The results showed that aliphatic acceptors including simple alcohols, amino acids, and sugars could be used to obtain glycosides in excellent yields with high α-selectivities.

Encouraged by these results, the substrate scope of this reaction was further extended to phenol acceptors, which are scarcely studied.[15a,24] As illustrated in Scheme 3, reactions involving phenol acceptors **2j–r** were complete within 3 h in excellent yields (75–85%) and very high anomeric selectivities (α:β >30:1). The glycosylation of phenols with electron-donating substituents at the *para*-position such as *p*-*tert*-butyl and *p*-methoxy groups proceeded smoothly, giving the desired products **3k** and **3l** with excellent yields. In addition, phenols with electron-withdrawing substituents at the *para*-position such as *p*-fluoro, *p*-chloro and *p*-bromo were also employed to afford the desired products **3m–o** in satisfactory yields. Moreover, coupling of glycal donor **1a** with the relatively hindered acceptors **2p–q** also proceeded successfully. In earlier reports,[23,24] the synthesis of naphthol 2-deoxygalactoside **3r** usually involves 2-thioglycosides, which is a difficult donor to obtain; furthermore, the selectivity of the product was not very high. To

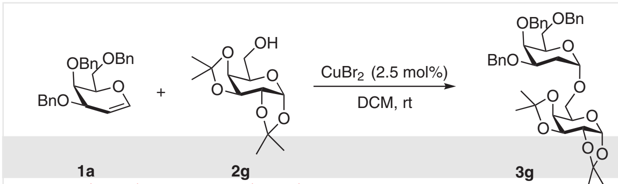


Scheme 3 Phenolic acceptor scope of glycosylation reactions with galactal **1a**. *Reagents and conditions*: donor (0.1 mmol), acceptor (0.12 mmol), $CuBr_2$ (5 mol%), stirred in DCM (1.0 mL), 25 °C, nitrogen atmosphere. All yields are isolated yields; α:β ratio of all products was >30:1 based on the ^{1}H NMR spectra.

our delight, 2-naphthol could also be directly applied in the catalytic system with excellent yield (77%) and pure α-selectivity.

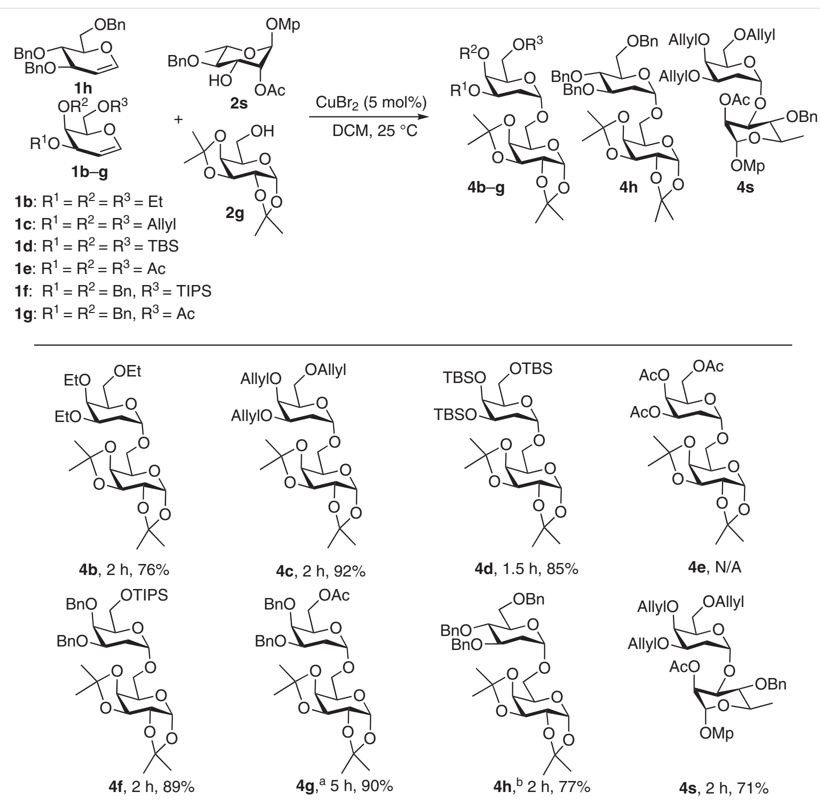
We then further investigated the donor scope of this glycosylation. A series of differentially protected galactals **1b–g** were prepared and reacted with **2g** as a model nucleophile under standard conditions (Scheme 4). Pleasingly, excellent yields (76–92%) and high selectivities (α:β >30:1) for the α-linked disaccharides were obtained in all cases except when **1e** was employed as glycal donor. The reason was postulated as the low activity of the disarmed peracetylated galactal.[9] Encouragingly, the reaction was also applicable to glycosylation with glycal donors **1f** and **1g**, which possess a readily removable protecting group at the 6-position. In addition, galactal donor **1c** could react with secondary alcohol **2s** with 71% yield. These results demonstrate that our reaction is tolerant of most protecting groups used in galactals, including benzyl, ethyl, allyl, and silyl ethers. The reaction was also amenable to glycosylation with perbenzylated glucal **1h**, affording the glycoside products in 77% yields with similarly high α-stereocontrol. However, ^{1}H NMR analysis showed that the product **4h** was a mixture of addition product and Ferrier rearrangement product with 8:1 ratio. The structure and stereochemistry of all glycosidation products were determined through spectroscopic analysis and by comparison with the reported data.[7]

It should be noted that this novel reaction could be readily scaled up. A gram-scale reaction of 2 mmol of **1a** (0.83 g) and 2.4 mmol of **2g** (0.63 g) was carried out with 2.5 mol% $CuBr_2$ at room temperature (Scheme 5). To our delight, the reaction finished within 1 h and 1.73 g of **3g** was obtained with 78% isolated yield and pure stereocontrol (α:β >30:1).



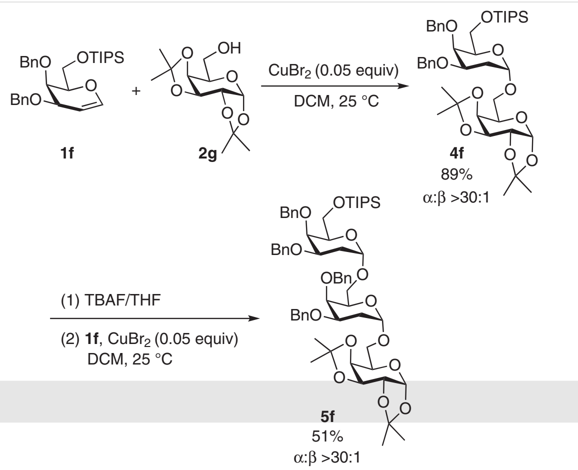
Scheme 5 Gram scale-up reaction

In addition, we extended the methodology to synthesize oligosaccharides **5f** (Scheme 6). Firstly, galactal **1f** was reacted with **2g** under the optimized condition, in which



Scheme 4 Glycals scope of glycosylation reactions with acceptor **2g**. *Reagents and conditions*: donor (0.1 mmol), acceptor (0.12 mmol) and $CuBr_2$ (5 mol%), stirred DCM (1.0 mL) at 25 °C, nitrogen atmosphere. [a] $CuBr_2$ (0.1 equiv) was used. [b] Product **4h** was obtained as a mixture of addition product and Ferrier rearrangement product with 8:1 ratio. All yields are isolated yields; α/β ratio of all products was >30:1 based on the ^{1}H NMR spectra. N/A = not applicable.

disaccharide **4f** was obtained in a yield of 89%. Considering that the silyl protecting group at the 6′-position of **4f** could be selectively removed using TBAF/THF solution, disaccharide **4f** could act as a new glycosyl acceptor for further glycosylation. Thus, we tried to synthesize trisaccharide **5f** by using our strategy. To our delight, deoxygalactose-containing trisaccharide **5f** was successfully obtained in two steps with 51% yield and high α-selectivity.



Scheme 6 Synthetic applications

In conclusion, we have demonstrated a direct and stereoselective synthesis of 2-deoxygalactosides catalyzed by ligand-free Cu(II) catalyst. Moreover, the new method is widely applicable to a range of differentially protected galactal donors and nucleophile acceptors. The reaction proceeds with excellent yields and high selectivities for the α-anomer in short time. In addition, its synthetic potential was successfully demonstrated in gram-scale reaction and by a simple synthesis of oligosaccharides. It should be pointed out that the reaction may result from various processes:[25,26] Cu-alcohol-complexes that lower the pK_a of the alcohol components is the most likely, but 'hidden acid catalysis' (i.e., hydrolysis/alcoholysis of the salt), acid impurities in the salt used, or bromine formation from $CuBr_2$ may also be operating.

Funding Information

The project was financially supported by Natural Science Foundation of Shanghai (11ZR1410400) and by the Large Instruments Open Foundation of East China Normal University (20162015).

Acknowledgment

We are thankful to the analytical centre of East China Normal University for data measurements. The authors express sincere gratitude for helpful discussions with Mr Zekun Ding.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1707098.

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(27) **6-*O*-(3',4',6'-Tri-O-benzyl-2'-deoxy-α-D-galactopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (3g)**
Under a nitrogen atmosphere, glycal donor **1a** (0.10 mmol, 41.6 mg) and nucleophile acceptor **2g** (0.12 mmol, 31.2 mg) were dissolved in anhydrous DCM (1.0 mL). Meanwhile $CuBr_2$ (0.005 mmol, 1.3 mg) was added to the system quickly. The reaction mixture was stirred at 25 °C until the reaction was determined to be complete by TLC. The reaction was then quenched with sat. aq. $NaHCO_3$, and the mixture was extracted with DCM. The combined organic phases were washed with sat. aq. $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (PE/EtOAc = 6:1) to give a yellow syrup. Yield: 55.4 mg (82%), α:β >30:1.
Trichloroethyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (3c)
Yield: 46.2 mg (82%); colorless syrup; α:β >30:1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.26 (m, 15 H), 5.24 (d, *J* = 2.3 Hz, 1 H), 4.95 (d, *J* = 11.6 Hz, 1 H), 4.62 (d, *J* = 11.4 Hz, 3 H), 4.51 (d, *J* = 11.8 Hz, 1 H), 4.44 (d, *J* = 11.8 Hz, 1 H), 4.19 (d, *J* = 11.5 Hz, 1 H), 4.07 (d, *J* = 11.5 Hz, 1 H), 4.04–3.98 (m, 2 H), 3.96 (s, 1 H), 3.59 (d, *J* = 6.3 Hz, 2 H), 2.29 (td, *J* = 12.5, 3.4 Hz, 1 H), 2.16 (dd, *J* = 12.7, 4.2 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.81, 138.39, 138.09, 128.52, 128.50, 128.34, 128.34, 127.82, 127.70, 127.68, 127.53, 98.87, 96.85, 79.15, 74.43, 73.55, 72.90, 71.03, 70.69, 69.46, 30.73. HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{31}Cl_3NaO_5$: 587.1129; found: 587.1110.
Furfuraldehyde-5-methyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (3e)
Yield: 48.2 mg (89%); yellow syrup; α:β >30:1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.61 (s, 1 H), 7.36–7.26 (m, 15 H), 7.17 (d, *J* = 3.5 Hz, 1 H), 6.48 (d, *J* = 3.5 Hz, 1 H), 5.08 (d, *J* = 3.1 Hz, 1 H), 4.94 (d, *J* = 11.6 Hz, 1 H), 4.66–4.58 (m, 4 H), 4.56–4.42 (m, 3 H), 3.96–3.90 (m, 3 H), 3.61–3.54 (m, 2 H), 2.26 (td, *J* = 12.6, 3.6 Hz, 1 H), 2.04 (dd, *J* = 12.8, 4.3 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.84, 157.96, 152.84, 138.85, 138.51, 138.11, 128.49, 128.31, 127.88, 127.81, 127.63, 127.37, 111.63, 97.69, 74.60, 74.39, 73.58, 72.93, 70.58, 70.48, 69.59, 60.96, 30.93. HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{34}NaO_7$: 565.2197; found: 565.2196.
***N*-(9-fluorenylmethoxycarbonyl)-L-serine methyl ester-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (3f)**
Yield: 70.4 mg (93%); yellow syrup; α:β >30:1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 7.6 Hz, 2 H), 7.58 (d, *J* = 7.4 Hz, 2 H), 7.41–7.26 (m, 19 H), 5.91 (d, *J* = 8.7 Hz, 1 H), 4.94 (dd, *J* = 14.2, 7.0 Hz, 2 H), 4.64–4.56 (m, 3 H), 4.56–4.45 (m, 2 H), 4.43–4.32 (m, 3 H), 4.21 (t, *J* = 7.1 Hz, 1 H), 3.99 (dd, *J* = 10.8, 3.7 Hz, 1 H), 3.93–3.83 (m, 4 H), 3.75 (s, 3 H), 3.62–3.57 (m, 1 H), 3.56–3.51 (m, 1 H), 2.23 (td, *J* = 12.4, 3.4 Hz, 1 H), 1.96 (dd, *J* = 12.5, 3.9 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.81, 156.09, 143.91, 141.36, 138.79, 138.40, 138.03, 128.60, 128.21, 128.05, 127.53, 127.46, 127.13, 125.19, 120.04, 99.22, 74.38, 73.49, 72.82, 70.55, 69.58, 68.77, 67.18, 54.56, 52.63, 47.19, 31.12. HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{46}H_{47}NNaO_9$: 780.3143; found: 780.3127.
4-*t*-Butyl-Phenyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (3k)
Yield: 47.0 mg (83%); yellow syrup; α:β >30:1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.26 (m, 15 H), 7.24 (d, *J* = 7.2 Hz, 2 H), 7.00 (d, *J* = 8.7 Hz, 2 H), 5.69 (d, *J* = 2.9 Hz, 1 H), 4.98 (d, *J* = 11.5 Hz, 1 H), 4.70–4.64 (m, 3 H), 4.43 (d, *J* = 11.6 Hz, 1 H), 4.37 (d, *J* = 11.6 Hz, 1 H), 4.15 (dd, *J* = 11.1, 3.2 Hz, 1 H), 4.09 (t, *J* = 6.5 Hz, 1 H), 4.03 (s, 1 H), 3.70–3.64 (m, 1 H), 3.56 (dd, *J* = 9.3, 5.7 Hz, 1 H), 2.40 (td, *J* = 12.4, 3.6 Hz, 1 H), 2.21 (dd, *J* = 12.7, 4.4 Hz, 1 H), 1.30 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.83, 144.65, 138.92, 138.57, 138.15, 128.52, 128.39, 128.3, 127.85, 127.69, 127.66, 127.62, 127.43, 126.26, 116.15, 96.82, 74.73, 74.51, 73.42, 72.98, 70.65, 69.32, 34.21, 31.59, 31.43. HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{37}H_{42}NaO_5$: 589.2924; found: 589.2916.
4-Fluoro-Phenyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (3m)
Yield: 41.7 mg (79%); colorless syrup; α:β >30:1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.19 (m, 15 H), 7.01 (dd, *J* = 8.7, 4.4 Hz, 2 H), 6.93 (t, *J* = 8.5 Hz, 2 H), 5.62 (s, 1 H), 4.97 (d, *J* = 11.5 Hz, 1 H), 4.71–4.61 (m, 3 H), 4.43 (d, *J* = 11.6 Hz, 1 H), 4.37 (d, *J* = 11.6 Hz, 1 H), 4.12 (d, *J* = 11.6 Hz, 1 H), 4.04 (dd, *J* = 15.5, 9.2 Hz, 2 H), 3.67–3.60 (m, 1 H), 3.55 (dd, *J* = 9.2, 6.1 Hz, 1 H), 2.39 (dd, *J* = 12.4, 3.1 Hz, 1 H), 2.20 (dd, *J* = 12.7, 4.1 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.05, 157.14, 153.08, 138.83, 138.48, 138.06, 128.55, 128.43, 128.36, 128.32, 127.79, 127.77, 127.72, 127.68, 127.44, 118.14, 118.08, 115.94, 115.76, 97.36, 74.56, 74.51, 73.45, 72.93, 70.80, 70.66, 69.40, 31.31. HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{33}FNaO_5$: 551.2204; found: 551.2194.
4-Chloro-Phenyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (3n)
Yield: 45.8 mg (75%); colorless syrup; α:β >30:1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.19 (m, 17 H), 6.99 (t, *J* = 6.1 Hz, 2 H), 5.66 (d, *J* = 3.0 Hz, 1 H), 4.97 (d, *J* = 11.5 Hz, 1 H), 4.70–4.62 (m, 3 H), 4.41 (d, *J* = 11.6 Hz, 1 H), 4.36 (d, *J* = 11.6 Hz, 1 H), 4.10 (ddd, *J* = 11.9, 4.3, 2.3 Hz, 1 H), 4.03–3.97 (m, 2 H), 3.63 (dd, *J* = 9.3, 7.2 Hz, 1 H), 3.52 (dd, *J* = 9.4, 5.8 Hz, 1 H), 2.40 (td, *J* = 12.5, 3.6 Hz, 1 H), 2.20 (dd, *J* = 12.8, 4.5 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.51, 138.81, 138.45, 138.01, 129.40, 128.56, 128.44, 128.36, 128.31, 127.81, 127.78, 127.74, 127.69, 127.44, 126.94, 118.05, 96.86, 74.53, 74.50, 73.44, 72.86, 70.87, 70.67,

69.29, 31.20, 29.79. HRMS (ESI): m/z[M + Na]+ calcd for $C_{33}H_{33}ClNaO_5$: 567.1909; found: 567.1895.

2-Methyl-Phenyl-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-galactopyranoside (3p)

Yield: 39.8 mg (76%); colorless syrup; α:β >30:1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.20 (m, 15 H), 7.15–7.08 (m, 3 H), 6.94–6.86 (m, 1 H), 5.71 (d, *J* = 1.9 Hz, 1 H), 4.99 (d, *J* = 11.5 Hz, 1 H), 4.73–4.62 (m, 3 H), 4.42 (d, *J* = 11.6 Hz, 1 H), 4.36 (d, *J* = 11.6 Hz, 1 H), 4.18–4.11 (m, 1 H), 4.03 (d, *J* = 7.6 Hz, 2 H), 3.67 (t, *J* = 8.4 Hz, 1 H), 3.53 (dd, *J* = 9.2, 5.5 Hz, 1 H), 2.42 (td, *J* = 12.5, 3.4 Hz, 1 H), 2.22–2.18 (m, 1 H), 2.17 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.98, 138.92, 138.37, 138.05, 130.69, 128.53, 128.41, 128.33, 128.30, 127.89, 127.74, 127.73, 127.62, 127.15, 126.95, 121.58, 114.24, 96.28, 74.51, 74.28, 73.47, 72.96, 70.78, 70.53, 69.18, 31.50, 16.3. HRMS (ESI): *m*/*z* [M + Na]+ calcd for $C_{34}H_{36}NaO_5$: 547.2455; found: 547.2441.