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Glycosylation

Stereodirecting Effect of C3-Ester Groups on the Glycosylation Stereochemistry of L-Rhamnopyranose Thioglycoside Donors: Stereoselective Synthesis of α- and β-L-Rhamnopyranosides

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Abstract: The tuning effect of C3-ester groups on the glycosylation stereochemistry of L-rhamnopyranose (L-Rha) ethyl thioglycoside donors is described. On one hand, the L-Rha thioglycoside donors carrying 3-*O*-arylcarbonyl or levulinoyl group undergo highly α-selective glycosylation to afford a wide variety of α-L-rhamnoside products in high chemical yields. On the other hand, the glycosylation of the 3-*O*-4-nitropicoloyl and 2-pyrazinecarbonyl group substituted L-Rha thioglycosides displays β-stereoselectivity. Only or predominant β anomeric products are obtained when these L-Rha donors couple with the primary or reactive secondary acceptors, while the β-selectivity may decrease significantly when these donors react with less reactive secondary alcohols. The synthetic utility of the newly developed α- and β-directing L-Rha donors **1h** and **1e** has been demonstrated by the efficient synthesis of a structurally unique trisaccharide **9**, which is derived from the cell wall polysaccharide of *Sphaerotilus natans*.

Introduction

L-Rhamnopyranose (L-Rha) is widespread in nature and is a very common component of numerous natural carbohydrates.[1] Synthesis of α-L-rhamnopyranoside can be achieved in a straightforward manner through classic neighboring group participating (NGP) approach. But highly stereoselective construction of β-L-rhamnoside, usually found in the cell wall polysaccharides of pathogenic bacteria, poses a great challenge.[2] This is because, in the L-Rha system with a standard $^1C_4$ chair conformation, the steric hindrance between the β-rhamnosidic bond and the axial C2-hydroxy group disfavors formation of β-anomer. Up to now, a variety of L-rhamnosyl donors,[3] such as the 3,4-*O*-carbonate or 2-*O*-sulfonate substituted thioglycoside or bromide derivatives discovered by Crich[3d,3e] as well as the 2-alkynyl-4-nitro-benzoate donor reported by Yu,[3g] have been developed to achieve the direct β-L-rhamnosylation. But some of them suffer from disadvantages such as limited β-selectivity, low stability or harsh conditions for the cleavage of the stereodirecting groups. Meanwhile, among the indirect methods,[4] the 2-naphthylmethyl (Nap) ether-mediated intramolecular aglycon delivery (IAD) strategy reported by Ito et al.[4a] was effective in the synthesis of β-L-rhamnosides, but the mixed acetal intermediates need further converting to the desired glycoside products, which lowered the total synthetic efficiency. Recently, an elegant β-L-rhamnosylation protocol using 1,2-anhydro-L-rhamnosyl donors and mono-ol or diol acceptors in the presence of borinic/boronic acid promoters was reported by the Toshima group.[5] Although stereospecific β-selectivity was obtained, the chemical yields in the glycosylations of the secondary glycosyl acceptors were strongly affected by the steric effects of the acceptors. Therefore, there has been a continuous pursuit of a more practical approach for the preparation of β-L-rhamnoside.

Recently, based on the hydrogen-bond-mediated aglycon delivery (HAD) concept first put forward by Demchenko,[6] our laboratory developed a novel 2-quinolinecarbonyl (Quin)-assisted glycosylation approach for stereocontrolled synthesis of various difficult-to-obtain glycosidic linkages including β-arabino-[7a] and α-galactofuranosides[7b] and β-3-deoxy-D-*manno*-oct-2-ulosonic acid (Kdo) glycoside.[7c] The Quin group, serving as a hydrogen-bond acceptor, exhibits powerful stereodirecting ability in the condensation of furanosyl or Kdo thioglycoside donors with a wide range of alcohols. In this paper, we planned to apply the Quin-directed stereoselective glycosylation method to the preparation of the β-L-rhamnoside. As shown by Scheme 1, we considered that, in a typical glycosylation reaction of a 3-*O*-Quin substituted Rha donor, the temporary hydrogen bond tether formed between the Quin group and the acceptor is capable of guiding the nucleophilic attack of the acceptor from the β-side of the pyranose ring, which would be likely to form a β-glycoside product.

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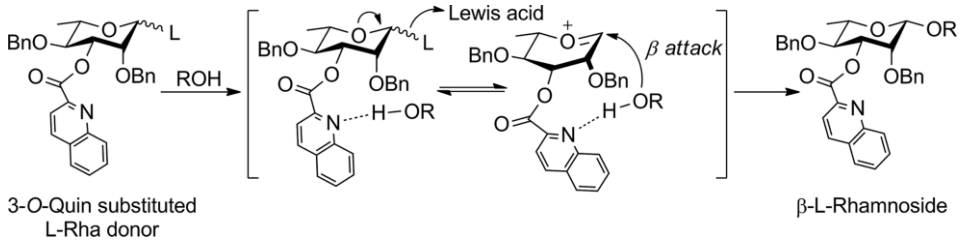


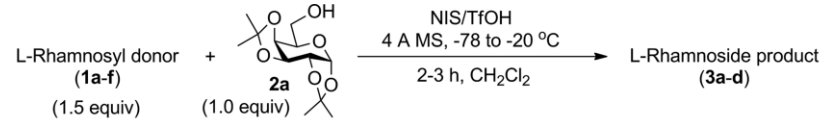
Scheme 1. 2-Quinolinecarbonyl-directed synthesis of β-L-rhamnopyranoside.

Results and Discussion

We first examined the effectiveness of hydrogen bond as a stereocontrolling factor on the formation of β-L-rhamnopyranoside. A series of L-rhamnosyl thioglycosides **1a**–**f** bearing Quin, 2-pyridinecarbonyl (Pico), 4-nitropicoloyl, and 2-pyrazinecarbonyl group, respectively, on the C3 position (Table 1) were prepared (see the Supporting Information) and their glycosylation behaviors were evaluated by reaction with model galactose (Gal) derivative **2a**.[8] We conducted all the reactions by employing 1.5 equiv. of the donor (50 mM) and 1 equiv. of the acceptor in the presence of the *N*-iodosuccinimide (NIS)/trifluoromethanesulfonic acid (TfOH) system in dry dichloromethane (CH_2Cl_2). The anomeric configuration of the product was assigned on the basis of the anomeric $^1J_{CH}$ coupling constants.[9] For the α-anomer, $^1J_{CH}$ is 167.2–172.3 Hz, while, for the β-anomer, $^1J_{CH}$ is 152.3–159.8 Hz.

As summarized in Table 1, entries 1–6, the couplings of all the donors **1a**–**f** with acceptor **2a** furnished the corresponding glycosides **3a**-**d** in good 72–85 % yields but with varying degree of anomeric selectivity. The reaction of 3-*O*-Quin substi-

Table 1. β-Selective glycosylation between donors **1a**–**f** and acceptor **2a**.[a]



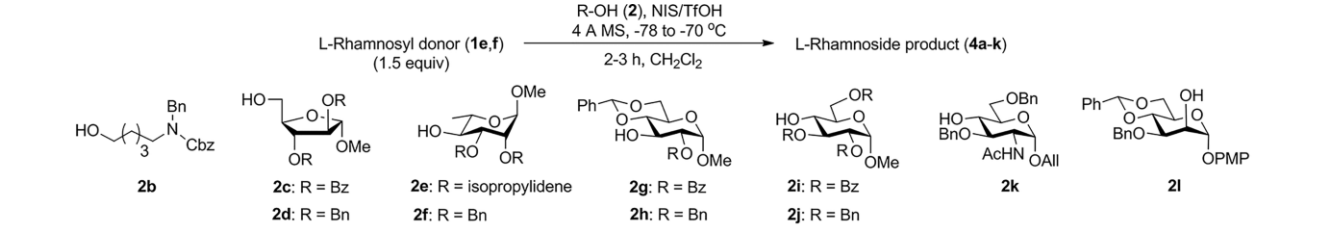
Entry	Donor	Product	Yield[b] (α/β)[c]
1	**1a**: R^1 = SEt, R^2 = H	**3a**	72% (1:4)
2	**1b**: R^1 = H, R^2 = SEt	**3a**	85% (1:4)
3	**1c**: R^1 = SEt, R^2 = H	**3b**	82% (1:6)
4	**1d**: R^1 = H, R^2 = SEt	**3b**	80% (1:10)
5	**1e**	**3c**	75% (1:14)
6	**1f**	**3d**	83% (1:8)

[a] Glycosylations were carried out with L-Rha thioglycoside donor (1.5 equiv.), acceptor (1 equiv.), NIS (1.5 equiv.)/TfOH (0.1 equiv.), 4 Å MS in anhydrous CH_2Cl_2. [b] Isolated yield based on the acceptor. [c] Determined by ^{1}H NMR of the corresponding isomer mixture.

tuted α- and β-thioglycosides **1a**, **b** showed poor β-selectivity (α/β 1:4, entries 1 and 2). In the cases of the 3-*O*-Pico substituted donors, the α-anomer **1c** showed a lower β-selectivity than its β-counterpart **1d** (α/β 1:6, entry 3 vs. α/β 1:10, entry 4). Gratifyingly, the 3-*O*-4-nitropicoloyl donor **1e** displayed a strong stereocontrolling ability in the reaction with **2a** and excellent β-selectivity was obtained for the product **3c** (75 % yield, α/β 1:14, entry 5). Moreover, the glycosylation between the 3-*O*-2-pyrazinecarbonyl donor **1f** and **2a** also proceeded in high yield with good β-selectivity (83 % yield, α/β 1:8, entry 6).

In order to broaden the substrate scope, we further investigated the glycosylations between Rha donors **1e**,**f** and a series of acceptors **2b**-**l** (Table 2). The reactions of **1e** with the primary alcohols including the linear molecule **2b**,[10] the disarmed and armed carbohydrate alcohols **2c**,[11] **d**[12] gave the corresponding glycoside products **4a**–**c** in high chemical yields and with good β-stereoselectivity (Table 2, entries 1–3). Nevertheless, for the reactions of **1e** with the secondary glycosyl acceptors, the yields were good but the stereochemical outcome was markedly influenced by the protecting group pattern of the acceptor (Table 2, entries 4–12). For instance, rhamnosylation of **1e** with Rha 4-OH alcohol **2e**[13] bearing a cyclic 2,3-*O*-isopropylidene acetal protection yielded the β-L-Rha-(1→4)-L-Rha disaccharide **4d** as a disappointing anomeric mixture (α/β 1:1.3, entry 4) but the rhamnosylation with 2,3-di-*O*-benzyl (Bn) protected Rha alcohol **2f**[14] showed excellent β-stereoselectivity (α/β 1:15, entry 5). We also assessed the electronic effect of the acceptor on the glycosylation selectivity. The condensation between **1e** and the 2-*O*-benzoyl (Bz)-4,6-*O*-benzylidene substituted D-glucose (Glc) acceptor **2g**[15] was non-stereoselective, whereas the coupling between **1e** and the 2-*O*-Bn-4,6-*O*-benzylidene blocked Glc alcohol **2h**[16] was highly β-selective (α/β 1:1, entry 6 vs. α/β 1:15, entry 7). A similar dramatic change in selectivity was also observed between the glycosylation of **1e** with the 2,3,6-tri-*O*-Bz protected Glc 4-OH substrate **2i**[17] and the glycosylation of **1e** with the 2,3,6-tri-*O*-Bn protected Glc alcohol **2j**[18] (α/β 1:2, entry 8 vs. α/β 1:15, entry 9). These results reveal that the electron-donating substituent on the acceptor is beneficial to the β-anomeric product formation. Other secondary acceptors such as the *N*-acetyl-D-glucosamine (GlcNAc, **2k**[19]) and D-mannose (Man, **2l**) alcohols were examined as well. As a result, the reaction of the former **2k** containing an electron-withdrawing acetyl (Ac) group at C2 position brought a moderate β-stereoselectivity (Table 2, entry 10) while the reaction of the latter **2l**,[20] having an axial 2-OH group, gave poor β-selectivity (entry 11) and no significant enhancement in β-selectivity was detected

Table 2. Glycosylation of donors **1e**,**f** with various acceptors.[a]



Entry	Donor	Acceptor	Product	Yield[b] (α/β)[c]
1	**1e**	**2b**	**4a**	73% (1:7)
2	**1e**	**2c**	**4b**: R = Bz	86% (1:11)
3	**1e**	**2d**	**4c**: R = Bn	81% (1:12)
4	**1e**	**2e**	**4d**: R = isopropylidene	87% (1:1.3)
5	**1e**	**2f**	**4e**: R = Bn	83% (1:15)
6	**1e**	**2g**	**4f**: R = Bz	91% (1:1)
7	**1e**	**2h**	**4g**: R = Bn	91% (1:15)
8	**1e**	**2i**	**4h**: R = Bz	88% (1:2)
9	**1e**	**2j**	**4i**: R = Bn	88% (1:15)
10	**1e**	**2k**	**4j**	53% (1:6)
11	**1e**	**2l**	**4k**	77% (1:2)
12	**1f**	**2l**	**4l**	57% (1:3)

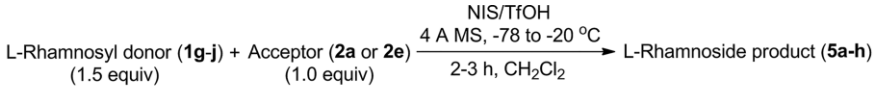
[a] Glycosylations were carried out with L-rhamnosyl thioglycoside donor (1.5 equiv.), acceptor (1 equiv.), NIS (1.5 equiv.)/TfOH (0.1 equiv.), 4 Å MS in anhydrous CH_2Cl_2. [b] Isolated yield based on the acceptor. [c] Determined by ^1H NMR of the corresponding isomer mixture.

upon switching the donor to the 3-*O*-2-pyrazinecarbonylated **1f** (entry 12).

Overall, the experimental outcomes above indicate that (1) in the couplings of **1e** with the primary or reactive secondary sugar alcohols, the hydrogen bond interaction between the 4-nitropicoloyl group and the acceptors is strong enough to achieve high β-selectivity; but (2) in the condensation between **1e** and the secondary alcohols with relatively low nucleophilicity, there is no or little hydrogen bond interaction, which leads to the dramatic loss of β-selectivity. Conversely, in these glycosylations, the increase in α-linked product was probably caused by the remote participating effect of the carbonyl of the 3-*O*-4-nitropicoloyl moiety on the anomeric center. Indeed, the remote participating phenomenon of a carbonyl protection has been reported in the literatures. For examples, Boons et al. described that the remote participation of the axial C4-carboxylate ester group in Gal donors was able to enforce facile α-galactosylation reaction. Recently, our group also reported a highly α-stereoselective glycosylation of Kdo thioglycoside donors enabled by the remote participation of 5-*O*-carbonyl function.

So, we further probed the possible remote participating effect of the C3-carbonyl functionality of thiorhamnosides on the stereoselectivity of glycosylation. Several 3-*O*-levulinoyl (Lev) or arylcarbonyl-substituted Rha thioglycoside substrates **1g–j** were synthesized and glycosylated with model compounds **2a** and **2e** under the activation of NIS/TfOH (cat.) in CH_2Cl_2 (Table 3). These donors showed good-to-excellent α-selectivity in all reactions with both primary (**2a**) and secondary (**2e**) sugar alcohols, giving predominantly or solely the corresponding α-linked disaccharide glycosides **5a–h** in satisfactory yields (Table 3, entries 1–8). These results obviously indicate the strong stereocontrolling ability of the C3-acyl substitution of thiorhamnosides to promote the α-glycosylation reaction. In the condensations of the 3-*O*-arylcarbonylated donors **1h–j** with the primary acceptor **2a**, the electron density of the carbonyl function affects the stereochemical outcome. For instance, compared to the Bz (**1h**) and the more electron-rich *p*-methoxybenzoyl (**1i**) moieties, the electron-deficient *p*-nitrobenzoyl (**1j**) substituent led to a relatively lower stereocontrol (α only, entries 2 and 3 vs. α/β 8.5:1, entry 4).

Table 3. α-Selective glycosylation of 3-*O*-acylated L-Rha donors (**1g–j**).[a]



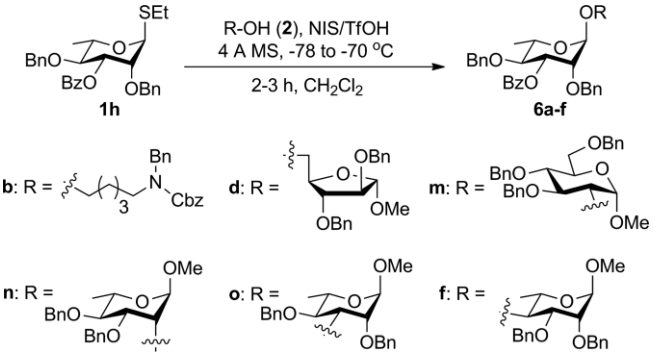
Entry	Donor	Acceptor	Product	Yield[b] (α/β)[c]
1	**1g**: R = Lev	**2a**	**5a**: R = Lev	87% (α only)
2	**1h**: R = Bz	**2a**	**5b**: R = Bz	89% (α only)
3	**1i**: R = OMe	**2a**	**5c**: R = OMe	76% (α only)
4	**1j**: R = NO_2	**2a**	**5d**: R = NO_2	76% (8.5:1)
5	**1g**: R = Lev	**2e**	**5e**: R = Lev	88% (α only)
6	**1h**: R = Bz	**2e**	**5f**: R = Bz	91% (α only)
7	**1i**: R = OMe	**2e**	**5g**: R = OMe	75% (α only)
8	**1j**: R = NO_2	**2e**	**5h**: R = NO_2	74% (α only)

[a] Glycosylations were carried out with L-rhamnosyl thioglycoside donor (1.5 equiv.), acceptor (1 equiv.), NIS (1.5 equiv.)/TfOH (0.1 equiv.), 4 Å MS in anhydrous CH_2Cl_2. [b] Isolated yield based on the acceptor. [c] Determined by ^1H NMR of the corresponding isomer mixture.

The reaction scope of the 3-*O*-Bz substituted thiorhamnoside donor **1h** was further studied. The couplings of this donor with the primary alcohols **2b** and **2d** proceeded in an α-selective and high-yielding manner, affording exclusively the α-linked glycoside products **6a**,**b** in good yield (Table 4, entries 1–2). Moreover, in the NIS/TfOH (cat.)-catalyzed condensation with sterically demanding secondary Glc 2-OH (**2m**[21]), Rha 2-, 3-, and 4-OH (**2n**[22]–**o**[23], and **2f**) acceptors, **1h** was also observed to be an efficient glycosyl donor and both the yields and α-selectivity in these coupling reactions were generally high (Table 4, entries 3–6).

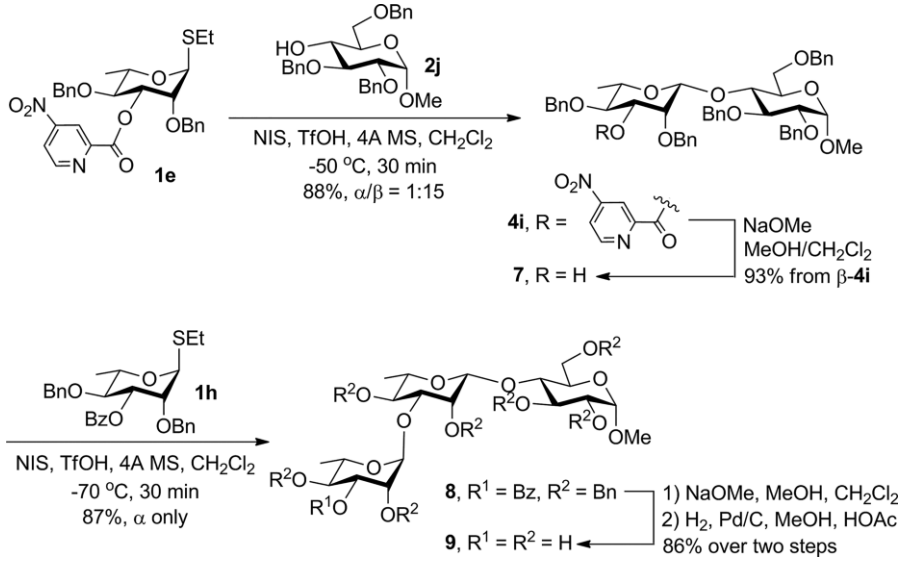
To demonstrate the usefulness of these approaches in the synthesis of α- and β-L-Rha-containing oligosaccharides, we targeted the production of trisaccharide glycoside **9** (Scheme 2). This trisaccharide motif, possessing a linear α-L-Rha-(1→3)-β-L-Rha-(1→4)-α-D-Glc framework, is isolated from the cell wall polysaccharide of *Sphaerotilus natans*.[24] The unique structural feature of **9** is that it comprises both α- and β-L-rhamnosyl bonds. Previously, a trisaccharide with identical sugar sequence was made by Ito and co-workers. In their preparation, the challenging β-L-Rha unit was constructed through the indirect C2-Nap-mediated IAD protocol. In this study, we decided to employ our newly developed **1e** and **1h** as the key building blocks for the assembly of the corresponding β- and α-L-rhamnosidic linkages, respectively. In Scheme 2, the synthesis started with the coupling of the effective β-L-rhamnosylating agent **1e** with methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (**2j**), which generated disaccharide **4i** in a satisfactory 88 % yield with excellent anomeric ratio (α/β 1:15). Pure β-**4i** was in turn selectively deprotected by treatment with sodium methoxide (NaOMe) in methanol to furnish the 3′-OH disaccharide alcohol **7** (93 %), thus ready for further glycosylation. Then, this material was subjected to condense with the α-directing donor **1h** upon activation with NIS/TfOH (cat.) in CH_2Cl_2 at –70 °C for 0.5 h, giving rise to the corresponding trisaccharide glycoside **8** in 87 % yield as a single α diastereomer. Finally, the global deprotection of **8** was readily carried out in the following order: removal of the benzoate ester groups with NaOMe in MeOH and then cleavage of all the Bn ethers by hydrogenolysis over Pd/C, which cleanly produced the desired **9** in 86 % yield over two steps. Compared to the existing synthetic route, our procedure is more practical for the preparation of the target molecule as it not only pro-

Table 4. α-Selective glycosylation of 3-*O*-benzoylated L-Rha donor **1h** with various acceptors.[a]



Entry	Donor	Acceptor	Product	Yield[b] (α/β)[c]
1	**1h**	**2b**	**6a**	80% (α only)
2	**1h**	**2d**	**6b**	77% (α only)
3	**1h**	**2m**	**6c**	83% (α only)
4	**1h**	**2n**[22]	**6d**	73% (α only)
5	**1h**	**2o**[23]	**6e**	91% (α only)
6	**1h**	**2f**	**6f**	86% (α only)

[a] Glycosylations were carried out with L-rhamnosyl thioglycoside donor **1h** (1.5 equiv.), acceptor (1 equiv.), NIS (1.5 equiv.)/TfOH (0.1 equiv.), 4 Å MS in anhydrous CH_2Cl_2. [b] Isolated yield based on the acceptor. [c] Determined by ^1H NMR of the corresponding isomer mixture.



Scheme 2. Synthesis of α-L-Rha-(1→3)-β-L-Rha-(1→4)-α-D-Glc trisaccharide **9**.

vides a direct β-glycosylation method for the installation of the key β-L-Rha unit but also facilitates the assembly of the α-L-Rha-(1→3)-L-Rha intersaccharidic linkage.

Conclusions

In conclusion, two stereoselective L-rhamnopyranosylation methods have been developed. One is an α-selective rhamnosylation reaction in which the 3-*O*-arylcarbonyl or Lev carrying L-Rha thioglycosides are used as glycosyl donors to couple with a variety of carbohydrate alcohols, forming the α-L-rhamnosides in high chemical yields with complete α-selectivity. The other is a β-rhamnosylation means adopting the 3-*O*-4-nitropicoloyl or 2-pyrazinecarbonyl-substituted L-Rha thioglycosides as donors. The glycosylation stereochemistry of these donors is found to mainly depend on the stereoelectronic nature of the acceptors. High β-stereocontrol is obtained when these donors glycosylate with the primary or reactive secondary acceptors, while the β-selectivity may greatly drop in the couplings with less reactive secondary carbohydrate nucleophiles. Utility of the present methods allowed a concise and stereocontrolled synthesis of a structurally unique trisaccharide **9** having both α- and β-L-rhamnoside substructures. Further application of the methods for the generation of biologically active L-Rha-containing glycoconjugates is currently underway.

Experimental Section

General glycosylation between donors and acceptors under the promotion of NIS/TfOH: A mixture of glycosyl donor (1.5 equiv.), glycosyl acceptor (1.0 equiv.), and freshly activated 4 Å molecular sieves in CH_2Cl_2 (50 mM) was stirred under nitrogen for 1 hour at room temperature. The reaction was cooled to −78 °C, then NIS (1.5 equiv.) and TfOH (0.1 equiv.) were added. The reaction mixture was gradually warmed to −20 °C and stirred for 2 to 3 hours at the same temperature. The reaction was quenched with Et_3N, diluted with CH_2Cl_2 and filtered. The filtrate was concentrated in vacuo. The resulting residue was purified by silica gel column chromatography to afford the glycoside product.

Conflicts of interest

The authors declare no competing financial interest.

Acknowledgments

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Keywords: Carbohydrates · Glycosides · Glycosylation · Stereoselective synthesis · Synthetic methods

[1] a) C. Kinnaert, M. Daugaard, F. Nami, M. H. Clausen, *Chem. Rev.* **2017**, *117*, 11337–11405; b) A. J. Griffiths, D. B. Davies, *Carbohydr. Polym.* **1991**, *14*, 241–279.
[2] a) H. Paulsen, *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 155–173; *Angew. Chem.* **1982**, *94*, 184; b) E. S. H. El Ashry, N. Rashed, E. S. I. Ibrahim, *Tetrahedron* **2008**, *64*, 10631–10648; c) S. S. Nigudkar, A. V. Demchenko, *Chem. Sci.* **2015**, *6*, 2687–2704; d) D. Crich, *Acc. Chem. Res.* **2010**, *43*, 1144–1153.
[3] a) L. V. Backinovsky, N. F. Balan, A. S. Shashkov, N. K. Kochetkov, *Carbohydr. Res.* **1980**, *84*, 225–235; b) T. Iversen, D. R. Bundle, *Carbohydr. Res.* **1980**, *84*, C13–C15; c) G. Hodosi, P. Kovác, *J. Am. Chem. Soc.* **1997**, *119*, 2335–2336; d) D. Crich, A. U. Vinod, J. Picione, *J. Org. Chem.* **2003**, *68*, 8453–8458; e) D. Crich, J. Picione, *Org. Lett.* **2003**, *5*, 781–784; f) F. W. Lichtenthaler, T. Metz, *Eur. J. Org. Chem.* **2003**, 3081–3093; g) Y.-G. Zhu, Z.-N. Shen, W. Li, B. Yu, *Org. Biomol. Chem.* **2016**, *14*, 1536–1539.
[4] a) Y. J. Lee, A. Ishiwata, Y. Ito, *J. Am. Chem. Soc.* **2008**, *130*, 6330–6331; b) I. Cumpstey, A. J. Fairbanks, A. J. Redgrave, *Tetrahedron* **2004**, *60*, 9061–9074.
[5] N. Nishi, K. Sueoka, K. Iijima, R. Sawa, D. Takahashi, K. Toshima, *Angew. Chem. Int. Ed.* **2018**, *57*, 13858–13862; *Angew. Chem.* **2018**, *130*, 14054.
[6] a) J. P. Yasomanee, A. V. Demchenko, *J. Am. Chem. Soc.* **2012**, *134*, 20097–20102; b) J. P. Yasomanee, A. V. Demchenko, *Angew. Chem. Int. Ed.* **2014**, *53*, 10453–10456; *Angew. Chem.* **2014**, *126*, 10621; c) S. G. Pistorio, J. P. Yasomanee, A. V. Demchenko, *Org. Lett.* **2014**, *16*, 716–719; d) J. P. Yasomanee, A. V. Demchenko, *Chem. Eur. J.* **2015**, *21*, 6572–6581; e) A. K. Kayastha, X.-G. Jia, J. P. Yasomanee, A. V. Demchenko, *Org. Lett.* **2015**, *17*, 4448–4451.
[7] a) Q.-W. Liu, H.-C. Bin, J.-S. Yang, *Org. Lett.* **2013**, *15*, 3974–3977; b) P.-C. Gao, S.-Y. Zhu, H. Cao, J.-S. Yang, *J. Am. Chem. Soc.* **2016**, *138*, 1684–1688; c) W. Huang, Y.-Y. Zhou, X.-L. Pan, X.-Y. Zhou, J.-C. Lei, D.-M. Liu, Y. Chu, J.-S. Yang, *J. Am. Chem. Soc.* **2018**, *140*, 3574–3582; d) K. Zhu, J.-S. Yang, *Tetrahedron* **2016**, *72*, 3113–3123; e) Y. Xu, H.-C. Bin, F. Su, J.-S. Yang, *Tetrahedron Lett.* **2017**, *58*, 1548–1552.
[8] F. G. Braga, E. S. Coimbra, M. de O. Matos, A. M. L. Carmo, M. D. Cancio, A. D. da Silva, *Eur. J. Med. Chem.* **2007**, *42*, 530–537.
[9] K. Bock, C. Pedersen, *J. Chem. Soc., Perkin Trans. 2* **1974**, 293–297.
[10] S. S. Mandal, N. V. Ganesh, J. M. Sadowska, D. R. Bundle, *Org. Biomol. Chem.* **2017**, *15*, 3874–3883.
[11] F. W. D'Souza, J. D. Ayers, P. R. McCarren, T. L. Lowary, *J. Am. Chem. Soc.* **2000**, *122*, 1251–1260.
[12] J. A. Montgomery, A. T. Shortnacy, H. J. Thomas, *J. Med. Chem.* **1974**, *17*, 1197–1207.
[13] T. G. Frihed, M. Heuckendorff, C. M. Pedersen, M. Bols, *Angew. Chem. Int. Ed.* **2012**, *51*, 12285–12288; *Angew. Chem.* **2012**, *124*, 12451.
[14] S. Rana, J. J. Barlow, K. L. Matta, *Carbohydr. Res.* **1980**, *85*, 313–317.
[15] M. L. Tong, F. Huber, E. S. T. Kaptouom, T. Cellnik, S. F. Kirsch, *Chem. Commun.* **2017**, *53*, 3086–3089.
[16] J. Xue, J. Wu, Z.-W. Guo, *Org. Lett.* **2004**, *6*, 1365–1368.
[17] O. Renaudet, P. Dumy, *Tetrahedron* **2002**, *58*, 2127–2135.
[18] M.-J. Xia, W. Yao, X.-B. Meng, Q.-H. Lou, Z.-J. Li, *Tetrahedron Lett.* **2017**, *58*, 2389–2392.
[19] F. Feng, K. Okuyama, K. Niikura, T. Ohta, R. Sadamoto, K. Monde, T. Noguchi, S.-I. Nishimura, *Org. Biomol. Chem.* **2004**, *2*, 1617–1623.
[20] S. S. Shivatare, S.-H. Chang, T.-I. Tsai, C.-T. Ren, H.-Y. Chuang, L. Hsu, C.-W. Lin, S.-T. Li, C.-Y. Wu, C.-H. Wong, *J. Am. Chem. Soc.* **2013**, *135*, 15382–15391.
[21] M. Sollogoub, S. K. Das, J. M. Mallet, P. Sinaÿ, *C. R. Seances Acad. Sci., Ser. 2* **1999**, *2*, 441–448.
[22] N. Pravdić, D. Keglević, *Tetrahedron* **1965**, *21*, 1897–1901.
[23] W. B. Severn, J. C. Richards, *J. Am. Chem. Soc.* **1993**, *115*, 1114–1120.
[24] M. Takeda, S. Nomoto, J.-I. Koizumi, *Biosci. Biotechnol. Biochem.* **2002**, *66*, 1546–1551.

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