Additive-Controlled Stereoselective Glycosylations of Oxazolidinone-Protected Glucosamine and Galactosamine Thioglycoside Donors Based on Preactivation Protocol

Yiqun Geng, Xin-Shan Ye*

State Key Laboratory of Natural and Biomimetic Drugs, Peking University, and School of Pharmaceutical Sciences, Peking University, Xue Yuan Rd No.38, Beijing 100191, P. R. of China
Fax +86(10)82802724; E-mail: xinshan@bjmu.edu.cn

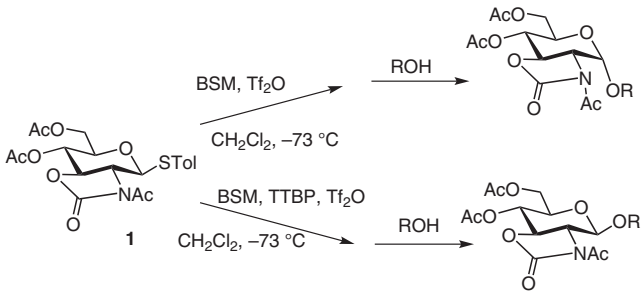
Received 1 June 2010

Abstract: Based on a pre-activation protocol, the stereoselectivity of oxazolidinone-protected amino sugar thioglycoside donors towards glycosylations can be controlled by additives. Either α- or β-selectivity could be obtained by changing additives. 2,4,6-Tri-*tert*-butylpyrimidine (TTBP) was the best β-directing additive, while thiophene worked as the best α-directing additive. The bifunctional additives such as tetrabutyl ammonium iodide (TBAI) afforded either α- or β-selectivity depending on the amount added. Poor α-selectivity of some glycosylations without any additives was greatly improved by adding TBAI or thiophene.

Key words: glycosylation, stereoselectivity, preactivation, additive, carbohydrate

Anomeric control in glycosylations is one of the major challenges in the synthesis of complex oligosaccharides and glycoconjugates with biological importance.[1,2] Generally, the 1,2-*trans*-linked glycosides are constructed by means of a participating neighboring group at the C-2 position of a glycosyl donor, while the formation of 1,2-*cis*-linked glycosides remains a difficult task.[3] Introduction of a nonparticipating neighboring group at C-2 is insufficient to guarantee stereoselective *cis*-glycosylation reactions and often leads to mixtures of anomers. Recently, 2,3-*trans*-oxazolidinone developed first by Kerns as a special nonparticipating group for glucosamine donors attract particular attention.[4] It is a good stereodirecting group for the formation of either α- or β-glycosidic linkages. In our own work,[4d] the hindered base 2,4,6-tri-*tert*-butylpyrimidine (TTBP)[5] was found to be a crucial factor in the stereoselectivity-controllable glycosylations of 4,6-di-*O*-acetyl-*N*-acetyl oxazolidinone protected donor **1** (Scheme 1). Based on a pre-activation protocol,[6,7] either excellent α- or β-stereoselectivity was obtained by means of the addition of TTBP or the absence of it.

These results open a new avenue to modulate the stereoselectivity by changing additives in glycosylation reactions. To investigate the effect of other additives on the stereochemistry outcomes of glucosamine donor **1** and to further extend the stereoselectivity-controllable pattern to the galactosamine case, our attention was paid to exploring additives in glycosylations of amino sugar donors **1**



Scheme 1 Stereoselectivity-controllable glycosylation of donor **1**[4d]

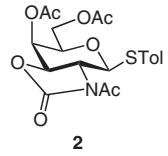


Figure 1 Galactosamine donor **2**

and **2** (Figure 1) under pre-activation conditions, and our findings are reported herein.

Enlightened by the mechanistic studies done by Kerns,[8a] Oscarson,[8b] and Ito,[8c] a reasonable explanation for the controllable stereoselectivity is as follows: after pre-activation by the combination of benzenesulfinyl morpholine (BSM) and triflic anhydride (Tf_2O)[9] donor **1** is converted into α-triflate intermediate,[10] and the glycosyl acceptor attacks in a S_N2-like fashion to form the β-glycoside; in situ anomerization of the β-glycoside under acidic conditions leads to formation of the α-glycoside. TTBP functions as an acid scavenger to hinder the anomerization and make the stereoselectivity controllable. According to this postulation, based on the pre-activation protocol, the good β-anomeric selectivity seems to arise from the triflate anion. To testify it and find other ways to control the stereoselectivity, we choose some molecules which might influence or change the status of intermediate as new potential additives.[11] On the one hand, the nature of the counterion in the promoter system was found to have an influence on the stereoselectivity in some glycosylations,[12] so we wanted to examine the effect of other types of anion. Because of the similarity of halide anion,[13] such as I^- to triflate anion, quaternary ammonium salts which are soluble in organic solvents were chosen as the alternative of triflate anion. On the other hand, since it was reported that thio-

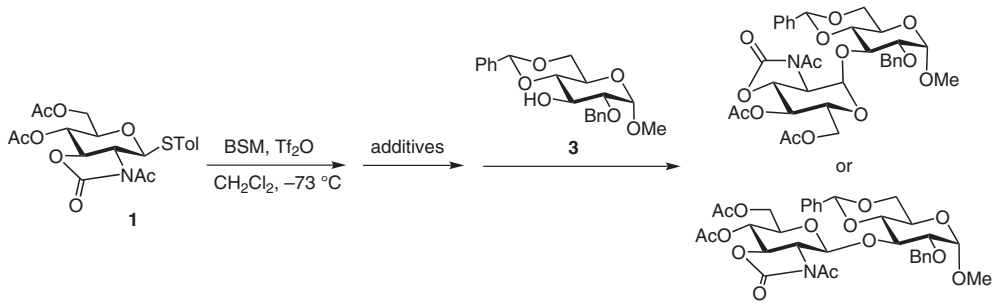
SYNLETT 2010, No. 16, pp 2506–2512
Advanced online publication: 03.09.2010
DOI: 10.1055/s-0030-1258557; Art ID: W08710ST

ethers could improve α-selectivity in the glycosylation reactions of 2-azido-2-deoxyglucosyl trichloroacetimidates[14] via the β-sulfonium ion intermediate,[15] we decided to check if thioethers have a similar effect on the oxazolidinone protected thioglycoside donors.

Firstly, four additives, tetrabutyl ammonium iodide (TBAI),[16] tetrabutyl ammonium bromide (TBAB),[13] dimethyl sulfide, and thiophene, were examined in the glycosylations of donor **1** with acceptor **3**, which were carried out in the pre-activation manner.[17] Donor **1** was pre-activated at –73 °C in anhydrous dichloromethane using BSM–Tf_2O. After disappearance of donor **1** by TLC detection, the additive and acceptor were added separately to the reaction mixture, with a time interval of 15 minutes. The reaction was then warmed to room temperature to furnish the glycosidic bond formation, and the results are listed in Table 1. The yields were high and all the glycosylations proceeded with excellent stereoselectivity (only α-anomer or only β-anomer). Both the α- and β-products are known compounds, and the NMR data of them are identical to those reported previously.[4d] As it was shown, TTBP (entry 2) was a good β-directing additive, both TBAB (entries 7–10) and thiophene (entries 15–18) were good α-directing additives. However, the effects of TBAI and dimethyl sulfide depended on the amounts added to the reaction system. Hence, adding 1 equivalent of TBAI gave rise to β-selectivity (entry 4), while adding 0.5 or even 0.1 equivalent of TBAI afforded α-selectivity (entries 5 and 6). Dimethyl sulfide showed similar effects (entries 11–14). In addition, the amount of TBAI and TBAB should not be more than 1 equivalent, because an excess of them resulted in a lower yield, and only trace amount of products were obtained when 2 equivalents of additives were used (entries 3 and 7). These interesting results gave us an important hint that other additives besides TTBP could dramatically control the stereoselectivity of donor **1** towards glycosylations.

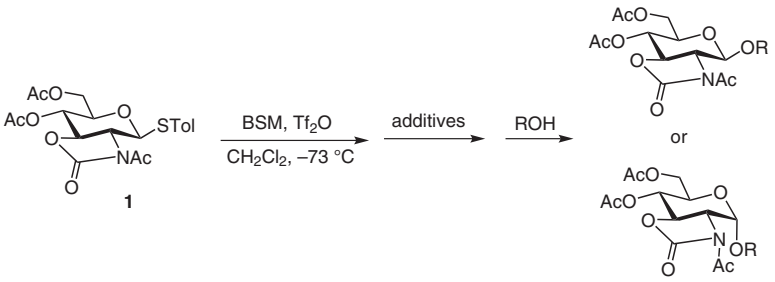
Since in the absence of any additives the glycosylation of donor **1** with acceptor **3** was also α-selective (entry 1, Table 1), it was important to know if the good α-selectivity really comes from the effect of additives. For the model reaction, there is no evidence to testify whether the additives lead to α-selectivity or they just have no effect at all. So we next checked the effect of these additives on two glycosylations with poor α-selectivity reported in our previous work (entries 1–20, Table 2).[4d] As displayed in Table 2, glycosylation of donor **1** with acceptor **4** under pre-activation conditions without any additives provided a mixture of α- and β-anomers, the anomeric ratio (α/β) was 3:1 (entry 1). Adding the α-directing additives such as

Table 1 Effect of Additives on the Stereoselective Glycosylation of Donor **1** with Acceptor **3**



Entry	Additive	Equiv	Isolated yield (%)	Anomeric ratio (α/β)
1	none		82	α only
2	TTBP	2	85	β only
3	TBAI	2	trace	–
4	TBAI	1	87	β only
5	TBAI	0.5	87	α only
6	TBAI	0.1	95	α only
7	TBAB	2	trace	–
8	TBAB	1	78	α only
9	TBAB	0.5	81	α only
10	TBAB	0.1	90	α only
11	Me_2S	2	86	β only
12	Me_2S	1	95	β only
13	Me_2S	0.5	94	α only
14	Me_2S	0.1	94	α only
15	thiophene	2	81	α only
16	thiophene	1	85	α only
17	thiophene	0.5	83	α only
18	thiophene	0.1	83	α only

Table 2 Additive-Controlled Stereoselective Glycosylations of Donor **1** with Acceptors **4–6**



Entry	ROH	Additive	Equiv	Yield (%)	α/β Ratio
1		none	–	81	3:1
2		TTBP	2	87	β only
3		TBAI	1	87	β only
4		TBAI	0.1	85	α only
5		TBAB	1	98	β only
6		TBAB	0.1	88	α only
7		Me_2S	1	96	β only
8	**4**	Me_2S	0.1	95	α only
9		thiophene	1	84	α only
10		thiophene	0.1	81	α only
11		none		87	1.5:1
12		TTBP	2	98	β only
13		TBAI	1	96	1:8
14		TBAI	0.1	82	α only
15		TBAB	1	50	1:5
16		TBAB	0.1	84	α only
17		Me_2S	1	87	1:5
18	**5**	Me_2S	0.1	79	α only
19		thiophene	1	82	α only
20		thiophene	0.1	80	α only
21		none		84	α only
22		TTBP	2	87	1:5
23		TBAI	1	96	1:3
24		TBAI	0.1	87	α only
25		TBAB	1	70	1:3
26		TBAB	0.1	73	α only
27	**6**	Me_2S	1	87	1:3
28		Me_2S	0.1	85	α only
29		thiophene	1	75	α only
30		thiophene	0.1	80	α only

thiophene (entries 9 and 10) greatly improved the α-selectivity. Other additives, like 0.1 equivalents of TBAI (entry 4), TBAB (entry 6), or dimethyl sulfide (entry 8) were able to improve the α-selectivity too. Thus, these α-directing additives did have an effect on the stereochemical outcome.

Meanwhile, the β-selectivity was obtained not only by adding TTBP (entry 2), but also by the addition of 1 equivalent of TBAI (entry 3), TBAB (entry 5), or dimethyl sulfide (entry 7). It is noteworthy that the effect of TBAB on this reaction was not consistent with the glycosyl coupling of donor **1** and acceptor **3** (entries 5 and 6, Table 2 vs. entries 8 and 10, Table 1). Another glycosylation of donor **1** with acceptor **5** with poor α-selectivity was also checked. Again, the poor anomeric ratio of 1.5:1 (entry 11) was significantly improved by adding thiophene (entries 19 and 20), or 0.1 equivalents of TBAI (entry 14), TBAB (entry 16), or dimethyl sulfide (entry 18). On the other hand, in this reaction, although the addition of 1 equivalent of TBAI (entry 13), TBAB (entry 15), or dimethyl sulfide (entry 17) increased the β-selectivity, TTBP was the best β-directing additive (entry 12). Then the effects of these additives on glycosylation of donor **1** with acceptor **6** (entries 21–30), which was the only reaction with moderate β-selectivity in our previous work, were checked. The similar results were obtained. These new β-directing additives improved the β-stereoselectivity, but none of them exceeded TTBP. The addition of TTBP afforded an anomeric ratio of 1:5 (entry 22), whereas the addition of 1 equivalent of TBAI (entry 23), TBAB (entry 25), or dimethyl sulfide (entry 27) only afforded the α/β ratio of 1:3.

After the above-mentioned investigations, the conclusion about the effects of the additives was summarized. Among them, TTBP was the best β-directing additive and thiophene was the best α-directing additive, while TBAI

and dimethyl sulfide were the bifunctional additives, catalytic amount of TBAI or dimethyl sulfide led to α-selectivity, stoichiometric amount of them led to β-selectivity. These interesting findings drove us to conduct some mechanism studies. To investigate the effects of different additives on changing the status of the intermediates during glycosylation reactions, we did some low-temperature ^{1}H NMR experiments[18] to detect the intermediate upon activation of donor **1** and addition of different additives (Figure 2). As shown, in the case of TTBP as the additive, ^{1}H NMR signals demonstrated that donor **1** was converted into α-triflate [^{1}H NMR (400 MHz, CD_2Cl_2): δ = 6.97 (s, H-1)] immediately upon activation. While in the case of no additives, donor **1** turned into both α-glucosamine thioglycoside [^{1}H NMR (400 MHz, CD_2Cl_2): δ = 6.08 (d, H-1, J = 4.4 Hz)] through anomerization and α-triflate intermediate [δ = 6.94 (d, H-1, J = 2.4 Hz)]. A similar phenomenon was observed when TBAI or thiophene was added after activation of donor **1**, and unexpectedly, none of other intermediates, such as glycosyl iodide or sulfonium ion, was detected. However, when TBAB was used as the additive, proportionate signal attributed to β-triflate [^{1}H NMR (400 MHz, CD_2Cl_2): δ = 6.52 (d, H-1, J = 7.6 Hz)] also appeared, indicating that TBAB can change the status of the intermediate. When dimethyl sulfide was added, no signals for triflates were detected, instead, the signal of β-sulfonium ion [^{1}H NMR (400 MHz, CD_2Cl_2): δ = 5.91 (d, H-1, J = 8.8 Hz)] appeared. Based on these observations, it seems that a conclusion about the influences of different additives on the stereochemistry outcomes in the glycosylation reactions of donor **1** can be deduced. In the case of no additives or when TTBP, thiophene, or TBAI was used as the additive, the intermediate after activation is α-triflate, leading to β-glycosides at first; subsequent anomerization of the β-glycosides could give rise to the α-glycosides. Different even opposite stereoselectivities conducted by these additives might arise from their effects on the anomerization course. To be sure, TTBP as an acid scavenger suppresses anomerization and gives rise to good β-selectivity. On the other hand, TBAB or dimethyl sulfide can change the intermediates in the glycosylations, different stereoselectivities might arise from different intermediates.

To further investigate the generality of these rules, the glycosylation of galactosamine donor **2** was checked. Donor **2** was synthesized following the preparative route of donor **1**[4d,8b] (see Supporting Information). It was glycosylated with four representative acceptors **3**, **4**, **7**, and **8**, affording α-glycosides **9**,[19] **11**, **13**, **15** and/or β-glycosides **10**,[20] **12**, **14**, **16** (Table 3). Additives TTBP, thiophene, and TBAI were separately added to the glycosylation reactions under the pre-activation conditions, and the results are listed in Table 3. Generally, the yields were high, and the rules of the additive-controlled stereoselectivity were well kept, either excellent α-selectivity or moderate to good β-selectivity could be obtained simply by modulating the additives.[21] The α-directing additive thiophene afforded good to excellent α-selectivity in all glycosylations (entries 5, 10, 15, and 20). The β-directing additive TTBP afforded good β-selectivity in glycosylations with acceptors **3**, **4**, and **7** (entries 2, 7, and 12), but poor β-selectivity in the glycosylation with acceptor **8** (entry 17). The bifunctional additive TBAI afforded either α- (entries 3, 8, 13, and 18) or β-selectivity (entries 4, 9, 14, and 19) by virtue of its amount added into the reactions, but its α-selectivity was not superior to that of thiophene and the

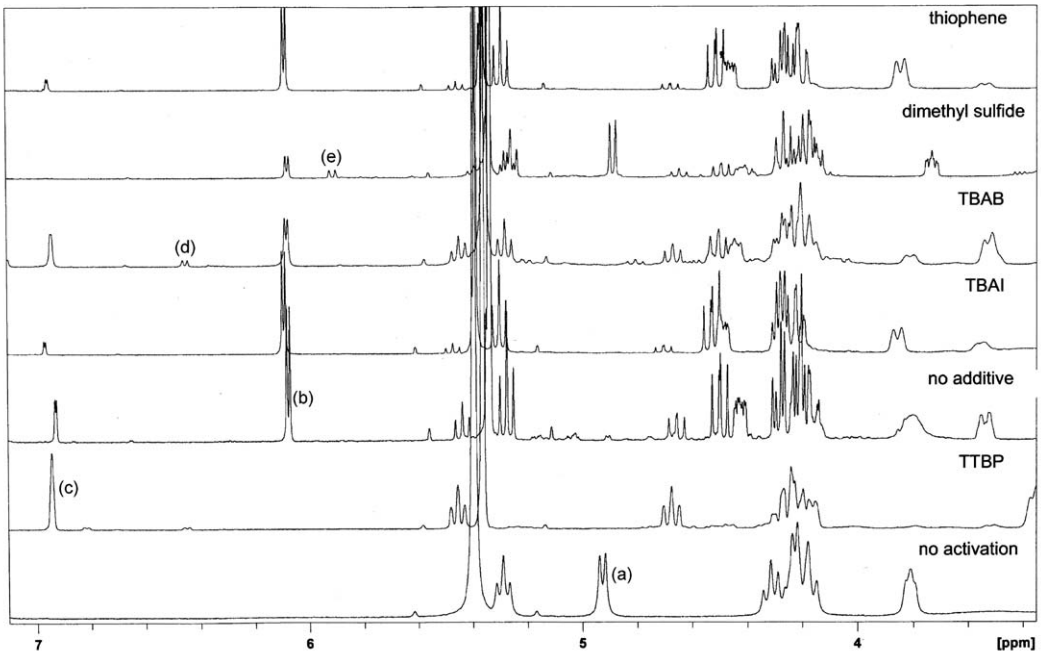
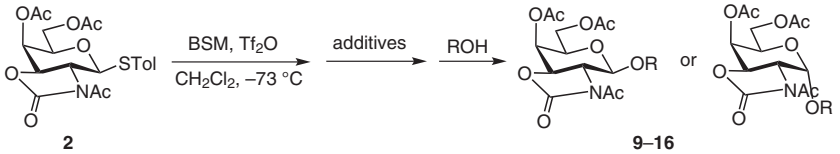


Figure 2 Investigations to the status of intermediates after activation of donor **1** and addition of different additives by low temperature NMR spectroscopy. The anomeric protons of β-thioglycoside (a), α-thioglycoside (b), α-triflate (c), β-triflate (d), and β-sulfonium ion (e) are assigned.

β-selectivity was not superior to that of TTBP. It is noteworthy that couplings of donor **2** with acceptors **4**, **7**, and **8** in the absence of any additives provided a mixture of α- and β-anomers (entries 6, 11, and 16). The poor selectivities were greatly changed by adding either the α-directing additive thiophene or the β-directing additive TTBP.

Table 3 Additive-controlled stereoselective glycosylations of donor **2** with acceptors **3, 4, 7** and **8**



2 **9–16**

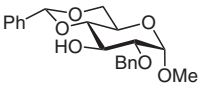
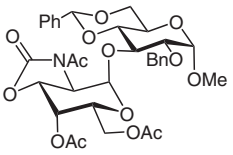
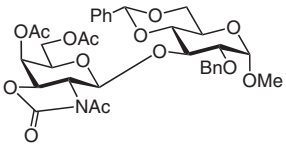
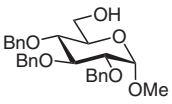
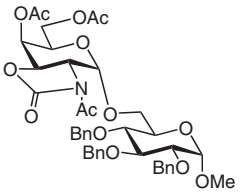
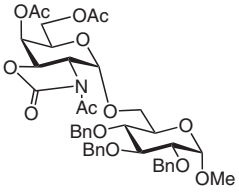
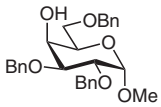
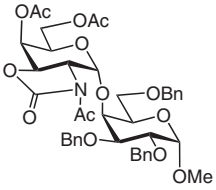
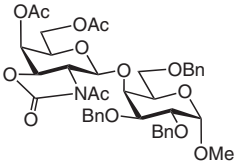
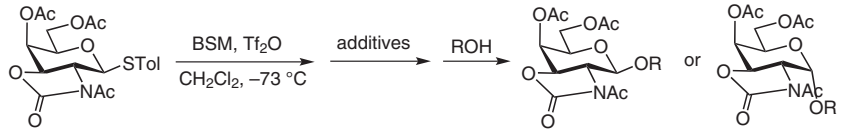
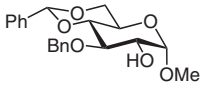
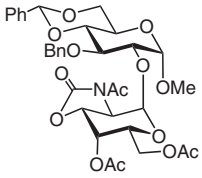
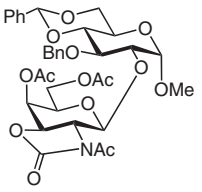
Entry	ROH	Additive	Product	Isolated yield (%)	Anomeric ratio (α/β)
1	 **3**	no	 **9**	76	α only
2		TTBP		87	1:9
3		TBAI (0.1 equiv)		75	α only
4		TBAI (1 equiv)		87	1:7
5		thiophene	 **10**	75	α only
6	 **4**	no	 **11**	75	2:1
7		TTBP		78	β only
8		TBAI (0.1 equiv)		75	α only
9		TBAI (1 equiv)		77	1:20
10		thiophene	 **12**	77	α only
11	 **7**	no	 **13**	90	1.5:1
12		TTBP		87	1:5
13		TBAI (0.1 equiv)		84	2:1
14		TBAI (1 equiv)		85	1:4
15		thiophene	 **14**	77	> 20:1

Table 3 Additive-controlled stereoselective glycosylations of donor **2** with acceptors **3, 4, 7** and **8** (continued)



2 **9–16**

Entry	ROH	Additive	Product	Isolated yield (%)	Anomeric ratio (α/β)
16		no		83	3:1
17		TTBP		84	1:1.5
18		TBAI (0.1 equiv)	**15**	85	3:1
19		TBAI (1 equiv)		87	1:1
20	**8**	thiophene		83	4:1
			16		

In summary, based on pre-activation protocol, not only hindered base TTBP but also some other additives can significantly influence the stereochemistry outcomes of glycosylations of 4,6-di-*O*-acetyl-*N*-acetyl oxazolidinone protected glucosamine donor **1** and galactosamine donor **2**. Generally, good to excellent β-anomeric selectivity was obtained by adding TTBP, whereas excellent α-anomeric selectivity was obtained by adding thiophene. The amount of bifunctional additives such as TBAI gave rise to completely different stereoselectivity, catalytic amount afforded α-selectivity while stoichiometric amount led to β-selectivity. The additive-controlled stereoselective glycoslylations may find wide applications to the oligosaccharide assembly. Further exploration of new additives which may modulate the stereoselectivity of glycosylations and extension of this protocol to other sugars are under investigation.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

Acknowledgment

This work was financially supported by the National Natural Science Foundation of China (Grant No. 20732001) and the grant (2009ZX09501-011) from the Ministry of Science and Technology of China.

References and Notes

(1) Boltje, T. J.; Buskas, T.; Boons, G. J. *Nat. Chem.* **2009**, *1*, 611.
(2) Zhu, X. M.; Schmidt, R. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 1900.
(3) Demchenko, A. V. *Synlett* **2003**, 1225.
(4) (a) Benakli, K.; Zha, C.; Kerns, R. J. *J. Am. Chem. Soc.* **2001**, *123*, 9461. (b) Boysen, M.; Gemma, E.; Lahmann, M.; Oscarson, S. *Chem. Commun.* **2005**, 3044. (c) Manabe, S.; Ishii, K.; Ito, Y. *J. Am. Chem. Soc.* **2006**, *128*, 10666. (d) Geng, Y.; Zhang, L.-H.; Ye, X.-S. *Chem. Commun.* **2008**, 597.
(5) (a) van der Plas, H. C.; Koudijs, A. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 159. (b) Crich, D.; Smith, M.; Yao, Q.; Picione, J. *Synthesis* **2001**, 323.
(6) (a) Huang, X.; Huang, L.; Wang, H.; Ye, X.-S. *Angew. Chem. Int. Ed.* **2004**, *43*, 5221. (b) Huang, L.; Wang, Z.; Li, X.; Ye, X.-S.; Huang, X. *Carbohydr. Res.* **2006**, *341*, 1669. (c) Huang, L.; Huang, X. *Chem. Eur. J.* **2007**, *13*, 529. (d) Wang, Y.; Ye, X.-S.; Zhang, L.-H. *Org. Biomol. Chem.* **2007**, *5*, 2189.
(7) (a) Crich, D.; Sun, S. *J. Org. Chem.* **1996**, *61*, 4506. (b) Crich, D.; Sun, S. *J. Org. Chem.* **1997**, *62*, 1198. (c) Codée, J. D. C.; Van den Bos, L. J.; Litjens, R. E. J. N.; Overkleeft, H. S.; Van Boom, J. H.; Van der Marel, G. A. *Org. Lett.* **2003**, *5*, 1947. (d) Yamago, S.; Yamada, T.; Maruyama, T.; Yoshida, J.-I. *Angew. Chem. Int. Ed.* **2004**, *43*, 2145. (e) Nguyen, H. M.; Poole, J. L.; Gin, D. Y. *Angew. Chem. Int. Ed.* **2001**, *40*, 414.
(8) (a) Wei, P.; Kerns, R. J. *J. Org. Chem.* **2005**, *70*, 4195. (b) Olsson, J. D.; Eriksson, L.; Lahmann, M.; Oscarson, S. *J. Org. Chem.* **2008**, *73*, 7181. (c) Manabe, S.; Ishii, K.; Hashizume, D.; Koshino, H.; Ito, Y. *Chem. Eur. J.* **2009**, *15*, 6894.
(9) Wang, C.; Wang, H.; Huang, X.; Zhang, L.-H.; Ye, X.-S. *Synlett* **2006**, 2846.
(10) (a) Crich, D.; Sun, S. *J. Am. Chem. Soc.* **1997**, *119*, 11217. (b) Crich, D.; Cai, W. *J. Org. Chem.* **1999**, *64*, 4926. (c) Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015.
(11) Although participating solvents such as Et_2O or MeCN can influence the intermediate of glycosylations, they cannot be used as additives because a large excess of them are needed. About the solvent effect, see: (a) Wulff, G.; Rohle, G. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 157. (b) Vankar, D.; Vankar, P. S.; Behrendt, M.; Schmidt, R. R. *Tetrahedron* **1992**, *47*, 9985; and references cited therein.

(12) Mukaiyama, T. *Angew. Chem. Int. Ed.* **2004**, *43*, 5590; and references cited therein.
(13) Lemieux, R. U.; Hendriks, K. B.; Stick, R. V.; James, K. *J. Am. Chem. Soc.* **1975**, *97*, 4056; and references cited therein.
(14) Park, J.; Kawatkar, S.; Kim, J. H.; Boons, G. J. *Org. Lett.* **2007**, *9*, 1959.
(15) Sulfonium ion observation: (a) West, A. C.; Schuerch, C. *J. Am. Chem. Soc.* **1973**, *95*, 1333. (b) Kim, J. H.; Yang, H.; Park, J.; Boons, G. J. *J. Am. Chem. Soc.* **2005**, *127*, 12090. (c) Nokami, T.; Shibuya, A.; Manabe, S.; Ito, Y.; Yoshida, J. *Chem. Eur. J.* **2009**, *15*, 2252.
(16) Hadd, M. J.; Gervay, J. *Carbohydr. Res.* **1999**, *320*, 61.
(17) **General Procedures for Glycosylations of Donors 1 or 2 with Acceptors 3–8**
Tf_2O (8.7 μL, 0.052 mmol, 1.3 equiv) was added to a stirred mixture of donors **1** or **2** (21.2 mg, 0.048 mmol, 1.2 equiv), BSM (11.1 mg, 0.052 mmol, 1.3 equiv), and activated 4 Å MS (300 mg, powder) in CH_2Cl_2 (3 mL) at –73 °C under nitrogen atmosphere. The reaction mixture was stirred for 5 min, after loss of the donor detected by TLC, the additive (0.1–2.0 equiv) was added to the mixture. After stirring for 15 min, a solution of the acceptor **3** (15.0 mg, 0.040 mmol, 1.0 equiv) or other acceptors in CH_2Cl_2 (0.2 mL) was added dropwise to the reaction mixture. The mixture was stirred and warmed up to r.t. slowly, quenched by Et_3N (0.1 mL). The precipitate was filtered off, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel to give the products.
(18) **Representative Procedures for Detecting Intermediates after Activation of Donor 1 by Variable Temperature NMR Spectroscopy**
To a solution of donor **1** (8.7 mg, 0.02 mmol), BSM (5.1 mg, 0.024 mmol) in CD_2Cl_2 (0.5 mL) in a NMR tube at –60 °C, under an argon atmosphere, was added 1.2 equiv of Tf_2O (0.024 mmol, 4.1 μL). The NMR tube was immediately transferred to the pre-cooled NMR probe (–60 °C), and ^1H NMR was recorded. Subsequently the temperature of the probe was raised in 10 °C steps with monitoring by ^1H NMR.
(19) Product **9** was purified by column chromatography on silica gel (PE–EtOAc, 3:1); R_f = 0.3 (PE–EtOAc, 1.5:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.61 (m, 2 H), 7.33–7.40 (m, 8 H), 6.25 (d, 1 H, *J* = 2.8 Hz, H-1′), 5.55 (s, 1 H), 5.30 (s, 1 H), 4.70 (d, 1 H, *J* = 3.6 Hz, H-1), 4.64 (d, 1 H, *J* = 11.6 Hz), 4.53 (d, 1 H, *J* = 11.6 Hz), 4.11–4.34 (m, 6 H), 3.77–3.84 (m, 2 H), 3.72 (t, 1 H, *J* = 10.0 Hz), 3.51–3.56 (m, 2 H), 3.37 (s, 3 H), 2.40 (s, 3 H), 2.08 (s, 3 H), 2.04 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.38 (2 C), 169.35, 152.90, 137.54, 137.11, 128.80, 128.62, 128.54, 128.47, 128.05, 126.29, 126.20, 101.14, 97.94, 95.01, 82.39, 78.38, 72.98, 72.07, 72.00, 68.87, 68.03, 65.80, 61.77, 61.54, 56.06, 55.17, 23.80, 20.58, 20.54. ESI-MS: *m/z* = 686 $[M + H]^+$, 703 $[M + NH_4]^+$, 708 $[M + Na]^+$. Anal. Calcd for $C_{34}H_{39}NO_{14}$: C, 59.56; H, 5.73; N, 2.04. Found: C, 59.30; H, 5.69; N, 1.97.
(20) Product **10** was purified by column chromatography on silica gel (PE–EtOAc, 1.5:1); R_f = 0.1 (PE–EtOAc, 1.5:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.50 (m, 2 H), 7.31–7.38 (m, 8 H), 5.59 (s, 1 H), 5.56 (s, 1 H), 5.08 (d, 1 H, *J* = 7.6 Hz, H-1′), 4.64 (d, 1 H, *J* = 11.8 Hz), 4.54 (d, 1 H, *J* = 3.6 Hz, H-1), 4.52 (d, 1 H, *J* = 12.0 Hz), 4.32 (dd, 1 H, *J* = 7.6, 12.0 Hz), 4.15–4.24 (m, 3 H), 3.95–4.08 (m, 3 H), 3.63–3.79 (m, 4 H), 3.30 (s, 3 H), 2.38 (s, 3 H), 2.10 (s, 3 H), 1.98 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.25, 170.28, 169.33, 153.54, 137.91, 137.35, 128.86, 128.56, 128.18, 128.03, 127.45, 126.04, 103.01, 100.85, 98.25, 80.63, 78.79, 77.23, 76.33, 72.98, 72.23, 68.84, 64.06, 62.53, 61.33, 57.55, 55.22, 25.08, 20.59, 20.56. ESI-MS: *m/z* = 686 $[M + H]^+$, 703 $[M + NH_4]^+$, 708 $[M + Na]^+$, 724 $[M + K]^+$. Anal. Calcd for $C_{34}H_{39}NO_{14}$: C, 59.56; H, 5.73; N, 2.04. Found: C, 59.34; H, 5.67; N, 1.96.
(21) The α-anomers and β-anomers were identified by their ^1H NMR coupling constants for anomeric protons. For α-anomers, $J_{1,2}$ = 2.4–2.8 Hz; for β-anomers, $J_{1,2}$ = 7.2–7.6 Hz.