A Catalytic and Stereoselective Glycosylation with Glucopyranosyl Fluoride by Using Various Protic Acids

Hideki Jona, Hiroki Mandai, and Teruaki Mukaiyama
Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162-8601

(Received February 13, 2001; CL-010124)

A catalytic and stereoselective glycosylation with glucosyl fluoride was effectively performed by using a catalytic amount of various protic acids. When the glycosylation was carried out, for example, using perchloric acid ($HClO_4$) in diethyl ether (Et_2O), the major products were α-glycosides while β-stereoselectivity was observed when tetrakis(pentafluorophenyl)boric acid [$HB(C_6F_5)_4$] was used in a mixed solvent of trifluoromethylbenzene (BTF)–pivalonitrile (^{t}BuCN) = (5:1). The stereoselectivity was controlled by not only the effect of solvent but also by the nature of counter anion of the catalyst such as $B(C_6F_5)_4^-$ or ClO_4^-.

To develop a new method for stereoselective glycosylation is one of the most important and fundamental topics in carbohydrate chemistry.[1] It was shown in our preceding report on catalytic glycosylation with glycosyl fluoride[2] by using carbocationic species paired with various counter anions[3] that the role of counter anion as well as an effect of solvent was quite important for the control of stereoselectivity. The above result prompted us to study on this topic concerning stereoselection in glycosylation in further detail by using various protic acids.[4] In this communication, we would like to report on an effective method for catalytic and stereoselective glycosylation of various glycosyl acceptors with glucosyl fluoride using $HClO_4$ in Et_2O or $HB(C_6F_5)_4$ in BTF–^{t}BuCN (5:1), which afforded the corresponding disaccharides in high yields with good to high α- or β-stereoselectivity. Further, the effects of the nature of counter anion as well as that of the solvent in controlling the stereoselectivities by using various protic acids in the glycosylation are shown.

In the first place, in-situ generation of strong protic acids was studied according to the modified procedure of Kevill[5] or Kato[6] by taking the reaction of various silver salts and ^{t}BuCl or ^{t}BuBr. As a result, the protic acids shown in Table 1 were effectively generated along with rapid precipitation of AgCl or AgBr. The generated catalyst in supernatant was used for glycosylation reaction of glycosyl acceptor **2** with glucosyl fluoride **1** in Et_2O at room temperature for 4 h, or in BTF–^{t}BuCN (5:1)[7] at 0 °C for 2 h to afford the corresponding α- or β-disaccharides in high yield. Furthermore, it was clearly recognized that the stereoselectivities of resulted glycosides varied depending on the combination of a catalyst and a solvent. For example, when the glycosylation was carried out in Et_2O, α-glycoside was obtained as a major product by using a catalytic amount of TfOH, $HClO_4$ or nonafluorobutanesulfonic acid (Entries 1–4). On the other hand, β-stereoselectivity was observed when a catalytic amount of $HNTf_2$, $HSbF_6$ or $HB(C_6F_5)_4$ in BTF–^{t}BuCN (5:1)[7] was used (Entries 5–8). It is interesting to note that the stereoselectivities of the formed disaccharides decreased considerably when combinations of the catalyst and solvent system were reversed.[3] After performing this stereoselectivity, the counter anions of the catalysts turned out to be as influential as the well-known effect of solvent[8] although how these counter anions work has not yet been made clear so far. Moreover, formation of α-glycoside by using $HClO_4$ in Et_2O took place in better stereoselectivity compared to the case by using TfOH in Et_2O. On the other hand, β-glycoside was best obtained when a catalytic amount of $HB(C_6F_5)_4$ was used in BTF–^{t}BuCN (5:1).

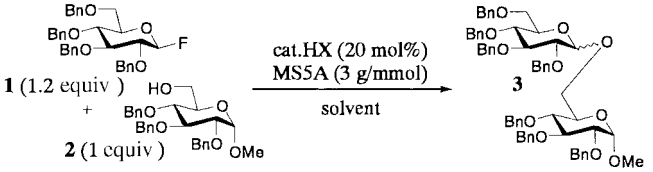


Table 1. Effect of the solvent and the counter anion of protic acid[a]

Entry	Cat.	Yield /% (α / β) (Et_2O, rt, 4 h)	Yield /% (α / β) (BTF–^{t}BuCN (5:1), 0 °C, 2 h)
1	HOTf[b]	98 (88 / 12)	>99 (47 / 53)
2	HOTf[c]	96 (88 / 12)	99 (49 / 51)
3	**$HClO_4$[c]**	**98 (92 / 8)**	>99 (60 / 40)
4	$HOSO_2C_4F_9$[d]	99 (88 / 12)	96 (47 / 53)
5	$HNTf_2$[b]	>99 (49 / 51)	99 (9 / 91)
6	$HNTf_2$[d]	>99 (50 / 50)	>99 (9 / 91)
7	$HSbF_6$[d]	99 (56 / 44)	>99 (12 / 88)
8	**$HB(C_6F_5)_4$[e]**	95 (55 / 45)	**99 (7 / 93)**

[a]In the case of using HBF_4–OMe_2, HOTs, HOMs or TFA as a catalyst, almost no reaction was observed. [b]Commercial substrate. [c]Protic acid was generated from silver salt and ^{t}BuCl in toluene, and the supernatant was used. [d]Protic acid was generated from silver salt and ^{t}BuBr in toluene, and the supernatant was used. [e]Protic acid was generated from $AgB(C_6F_5)_4$[9] and ^{t}BuBr in toluene–Et_2O (1:1), and the supernatant was used.

Next, glycosylations with other glucosyl donors such as thioglycoside, 1-hydroxy- and 1-*O*-acetyl sugars, and glycosyl trichloroacetimidate[10] using $HClO_4$ or $HB(C_6F_5)_4$ were tried in order to examine the effects of counter anions and solvents (Table 2). Surprisingly, in every case, the glycosylation reaction proceeded smoothly to afford the corresponding disaccharide in high yield. Further addition of 1.2 equivalent of *N*-iodosuccinimide was essential in the case of using thioglycoside.[11] Moreover, in the case of using $HClO_4$ in Et_2O, all glucosyl donors examined gave high α-selectivities. On the contrary, β-glycosides were predominantly obtained in high yields in the case of using $HB(C_6F_5)_4$ as a catalyst in BTF–^{t}BuCN (5:1) (Entries 1–5). And also, poor stereoselectivity was observed as in the glycosylation with glycosyl trichloroacetimidate under the conditions of $HB(C_6F_5)_4$ in Et_2O or $HClO_4$ in BTF–^{t}BuCN (5:1) (Entry 6). Next, various cationic species paired with the counter anions such as ClO_4^- or $B(C_6F_5)_4^-$ in Et_2O or BTF–^{t}BuCN (5:1) or vice versa with glucosyl fluoride were examined (Table 3).

As a result, every catalyst having ClO_4^- anion in Et_2O and that having $B(C_6F_5)_4^-$ anion in BTF–^{t}BuCN (5:1) gave almost the same α- or β-stereoselectivities, respectively, whereas poor selectivity was observed when the combinations were reversed. These results shown in Table 2 and 3 also indicate that the nature of counter anion is very influential in controlling the stereoselectivity.

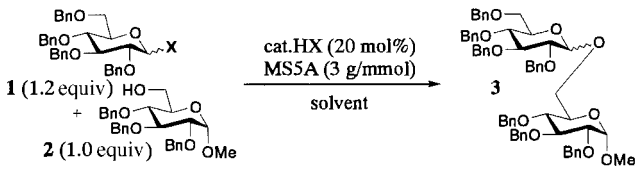


Table 2. Glycosylation with various donors

Entry	Donor	Yield /% (α / β) cat. $HClO_4$[a], rt Et_2O, 4 h	Yield /% (α / β) cat.$HB(C_6F_5)_4$[b], 0 °C BTF–^{t}BuCN (5:1), 2 h
1	SEt (β)	trace (-)	9 (11 / 89)
2	SEt (β)[c]	89 (90 / 10)	95 (11 / 89)
3	OH (mix)	93 (92 / 8)	93 (8 / 92)
4	OAc (α)	93 (92 / 8)	89 (9 / 91)
5	OC=N(H)CCl_3 (β)	99 (91 / 9)	97 (10 / 90)
6	OC=N(H)CCl_3 (β)	97 (43 / 57)[d]	95 (54 / 46)[e]

[a]Protic acid was generated from $AgClO_4$ and ^{t}BuCl in toluene, and the supernatant was used. [b]Protic acid was generated from $AgB(C_6F_5)_4$[9] and ^{t}BuBr in toluene–Et_2O (1:1), and the supernatant was used. [c]In this reaction, 1.2 equiv of NIS was added and stirred for 15 minutes. [d]The reaction was carried out by using $HB(C_6F_5)_4$ as a catalyst. [e]The reaction was carried out by using $HClO_4$ as a catalyst.

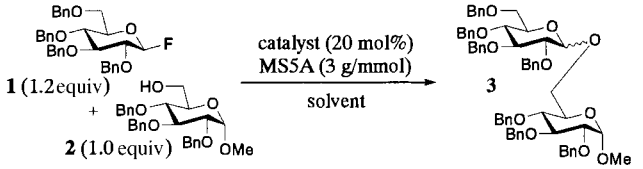


Table 3. Glycosylation using various catalysts

Entry	Catalyst	Yield /% (α / β) Et_2O rt, 4 h	Yield /% (α / β) BTF–^{t}BuCN (5:1) 0 °C, 2 h
1	$TrClO_4$[12]	94 (93 / 7)	91 (58 / 42)
2	$TrB(C_6F_5)_4$[7]	85 (47 / 53)	88 (4 / 96)
3	$SnCl_2$–$AgClO_4$[13]	97 (92 / 8)	94 (57 / 43)
4	$SnCl_2$–$AgB(C_6F_5)_4$[9]	90 (43 / 57)	95 (8 / 92)

Finally, in order to extend the scope of the present glycosylation using protic acids, glycosylation of various glycosyl acceptors were tried in Et_2O at 0 °C or in BTF–^{t}BuCN (5:1) at –20 °C (Table 4). In all cases, the desired disaccharides were obtained in high yields with high stereoselectivityies even when an acceptor having thioglycosidic linkage was used.

Thus, α- or β-stereoselective glycosylation with a glucosyl fluoride was achieved by using a catalytic amount of protic acids in appropriate solvents such as $HClO_4$ in Et_2O or $HB(C_6F_5)_4$ in BTF–^{t}BuCN (5:1), respectively. It should be noted again that the role of counter anion as well as the effect of solvent is quite important for the control of stereoselectivity in glycosylation.

Further studies on the control of stereoselectivity in glycosylaion using various glycosyl donors and acceptors, and one-pot sequential synthesis of trisaccharides are now in progress.

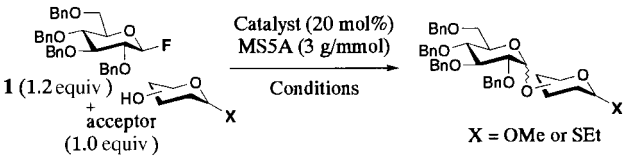
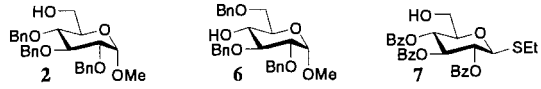


Table 4. Glycosylation using $HClO_4$ or $HB(C_6F_5)_4$ as a catalyst

Entry	Acceptor	Catalyst	Conditions	Time	Yield /% (α / β)
1	**2**	$HClO_4$	A[a]	6	94 (**93** / 7)
2	**2**	$HB(C_6F_5)_4$	B[b]	6	97 (4 / **96**)
3	**6**	$HClO_4$	A[a]	7	93 (**83** / 17)
4	**6**	$HB(C_6F_5)_4$	B[b]	11	95 (8 / **92**)
5	**7**	$HClO_4$	A[a]	4	92 (**89** / 11)
6	**7**	$HB(C_6F_5)_4$	B[b]	2	89 (5 / **95**)

[a]The reaction was carried out in **Et_2O** at 0 °C. [b]The reaction was carried out in **BTF–^{t}BuCN (5:1)** at –20 °C.



The present research is partially supported by Grant-in-Aids for Scientific Research from Ministry of Education, Science, Sports and Culture.

References and Notes

1 Reviews: K. Toshima and K. Tatsuta, *Chem. Rev.*, **93**, 1503 (1993); K. Suzuki and T. Nagasawa, *J. Synth. Org. Chem. Jpn.*, **50**, 378 (1992).
2 Reviews on glycosyl fluoride: M. Shimizu, H. Togo, and M. Yokoyama, *Synthesis*, **1998**, 799; K. Toshima, *Carbohydr. Res.*, **327**, 15 (2000).
3 M. Yanagisawa and T. Mukaiyama, *Chem. Lett.*, **2001**, 224.
4 T. Mukaiyama, K. Takeuchi, H. Jona, H. Maeshima, and T. Saitoh, *Helv. Chim. Acta*, **83**, 1901 (2000); T. Mukaiyama, H. Jona, and K. Takeuchi, *Chem. Lett.*, **2000**, 696; H. Jona, K. Takeuchi, and T. Mukaiyama, *Chem. Lett.*, **2000**, 1278.
5 D. N. Kevill and R. F. Sutthoff, *J. Chem. Soc., Perkin Trans 2*, **1977**, 201.
6 T. Kato, M. Tanaka, M. Hoshikawa, and M. Yagi, *Tetrahedron Lett.*, **39**, 7553 (1998).
7 Since the melting point of pivalonitrile is 15 °C, the reaction was carried out in the mixed solvent of pivalonitrile and trifluoromethylbenzene at 0 °C; K. Takeuchi and T. Mukaiyama, *Chem. Lett.*, **1998**, 555.
8 G. H. Veeneman, in "Carbohydrate Chemistry," ed. by G. -J. Boons, Blackie Academic & Professional, London (1998), p. 105.
9 T. Mukaiyama, H. Maeshima, and H. Jona, *Chem. Lett.*, **2001**, 388.
10 R. R. Schmidt and J. Michel, *Angew. Chem., Int. Ed. Engl.*, **19**, 731 (1980).
11 G. H. Veeneman, S. H. van Leeuwen, and J. H. van Boom, *Tetrahedron Lett.*, **31**, 1331 (1990); P. Konradsson, D. R. Mootoo, R. E. McDevitt, and B. Fraser-Reid, *J. Chem. Soc., Chem. Commun.*, **1990**, 270.
12 T. Mukaiyama, S. Kobayashi, and S. Shoda, *Chem. Lett.*, **1984**, 907.
13 T. Mukaiyama, Y. Murai, and S. Shoda, *Chem. Lett.*, **1981**, 431.