Catalytic and Stereoselective Glycosylation with Glycosyl Fluoride Using Active Carbocationic Species Paired with Tetrakis(pentafluorophenyl)borate or Trifluoromethanesulfonate

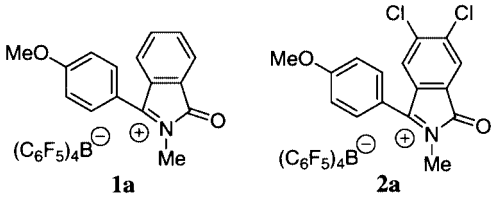
Manabu Yanagisawa and Teruaki Mukaiyama*
Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162-8601

(Received December 19, 2000; CL-001143)

Catalytic and stereoselective glycosylation with glycosyl fluoride using carbocationic species paired with tetrakis(pentafluorophenyl)borate [$B(C_6F_5)_4^-$] or trifluoromethanesulfonate (TfO^-) is investigated. When the glycosylation is carried out using the former catalyst in dichloromethane containing ^{t}BuCN, the major product is β-glycoside while α-selectivity is observed when the latter catalyst in dichloromethane containing Et_2O is used. In addition to the characteristic properties of the solvent, the nature of the counter anion such as $B(C_6F_5)_4^-$ or TfO^- plays important roles in controlling the selectivity. Thus, an appropriate combination of catalyst and solvent leads to the formation of disaccharides.

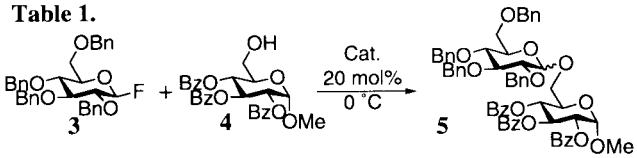
Development of stereoselective glycosylation reaction is one of the most fundamental topics in carbohydrate chemistry and various combinations of glycosyl donors and activators have been studied[1] in these two decades to establish efficient glycosylation methods. Among them, the use of glycosyl fluoride proved to be quite effective as it is a donor more stable than the corresponding chloride or bromide, and has widely been used in the synthesis of many complex oligosaccharides after our publication in 1981.[2] Activation of glycosyl fluoride was successfully achieved by using stoichiometric amounts of various Lewis acids most of which had ClO_4^- or TfO^- anions.[3] However, only a few examples of catalytic glycosylation using trimethylsilylated donors have been reported. In 1998, the first example[3] of catalytic glycosylation between glycosyl fluoride and alcohols was presented in the glycosylation of several alcohols and glucosides with glycosyl fluoride using a catalytic amount of trityl tetrakis(pentafluorophenyl)borate [$TrB(C_6F_5)_4$][4] affording the corresponding disaccharides in high yields with β-selectivities in dichloromethane containing ^{t}BuCN. However, α-selective catalytic glycosylation was not achieved by using the carbocationic species such as $TrB(C_6F_5)_4$.[5]

On the other hand, it was recently reported that the carbocationic species paired with $B(C_6F_5)_4^-$ (**1a** and **2a**) smoothly catalyzed the aldol reaction of aldehydes with silyl enol ethers[6a] or enol esters[6b] similar to the case using a trityl cation. There was also shown that the aldol reaction was promoted more effectively by the electron-deficient cationic species **2a** compared with that of **1a**. In this communication, we would like to report on catalytic and stereoselective glycosylation with glycosyl fluoride by using carbocationic species either **1a** or **2a** and its derivatives. It was recognized that the factors controlling the α- and β-selectivities were influenced both by characteristic properties of the solvent and the nature of counter anion of the catalysts.



In the first place, the catalytic glycosylation of methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (**4**) with 2,3,4,6-tetra-*O*-benzyl-β-D-glucosyl fluoride (**3**) was examined by using a catalytic amount of carbocationic species **1a**, **2a** or $TrB(C_6F_5)_4$ (see Table 1).

Table 1.



Entry	Solvent	Cat.[a]	Additive	Time /h	Yield /%[b]
1		**1a**		2	46 (8/92)
2		**2a**	Drierite	**2**	**86 (9/91)**
3	^{t}BuCN:CH_2Cl_2	**Tr**		2	86 (8/92)
4	(5:1)	**1a**		2	11[c] (3/97)
5		**2a**	MS 5Å	**1**	**85 (9/91)**
6		**Tr**		2	72 (10/90)
7		**1a**		2	51[d] (46/54)
8		**2a**	Drierite	2	59 (46/54)
9	Et_2O	**Tr**		2	81 (43/57)
10		**1a**		2	98 (47/53)
11		**2a**	MS 5Å	2	89 (45/55)
12		**Tr**		2	92 (47/53)

[a]Tr = $TrB(C_6F_5)_4$. [b]The values in parentheses indicate the ratio of α/β. [c]When the reaction was continued for 24 h, the yield was 23% (α/β=6/94). [d]When the reaction was continued for 13 h, the yield was 80% (α/β=47/53).

A typical experimental procedure is described for the reaction of **3** with **4** using **2a** as a catalyst in the co-existence of MS 5Å (Table 1; Entry 5): to a suspension of **2a** (12.0 mg, 0.012 mmol) and powdered MS 5Å (60 mg) in a solvent (pivalonitrile/dichloromethane = 5/1, 0.5 mL) was added 2,3,4,6-tetra-*O*-benzyl-β-D-glucosyl fluoride **3** (42.3 mg, 0.078 mmol) and methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside **4** (30.4 mg, 0.060 mmol) in the above solvent (2.5 mL) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, then was quenched by the addition of saturated aqueous sodium hydrogencarbonate (3 mL). The mixture was filtered through Celite pad and extracted with ethyl acetate. The combined organic layer was washed successively with water and brine and dried over $MgSO_4$. After filtration and evaporation, the resulting residue was purified by preparative TLC, and methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl)-D-glucopyranoside **5** (52.6 mg, 85% yield) was thus isolated. The ratio of anomers was determined by ^{1}H NMR analysis. Other examples of the glyco-

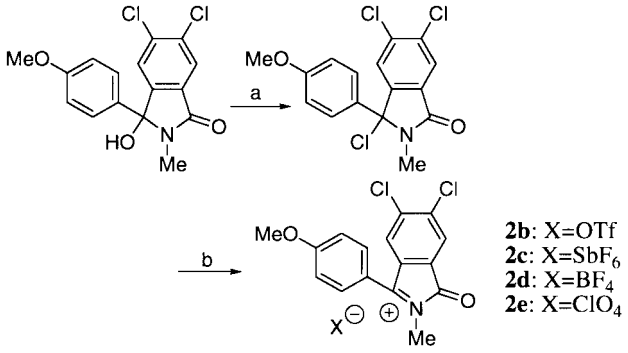
sylations with glycosyl fluoride by using different additives, solvents and catalysts are shown in Table 1.

When the glycosylation was carried out in dichloromethane containing ^{t}BuCN, disaccharide **5** was obtained with high β-selectivity (Entry 1–6). Cationic species **2a**, a more active one,[6b] exhibited higher catalytic activity than **1a** did (Entry 1 vs 2 and Entry 4 vs 5) and the activity was also slightly higher than that of $TrB(C_6F_5)_4$ (Entry 5 vs 6) when the catalyst was used together with MS 5Å. On the other hand, α-selectivity was not observed at all when the preparation of α-disaccharide was tried in the solvent containing Et_2O expecting its solvent effect,[7] (Entries 7–12).

In order to examine the effect of counter anions of the catalyst, the carbocationic species **2b**–**2e** were prepared by the following procedure as shown in Scheme 1, and were further examined their effects on the stereoselectivities in detail.

It was clearly recognized that the resulting glycosides were obtained with high stereoselectivities if the appropriate combinations of catalyst and solvent system were chosen. For example, when the reaction was carried out in dichloromethane containing ^{t}BuCN, β-glycoside was obtained by using the catalyst such as **2a**, **2c** or **2d**. On the other hand, disaccharide with α-selectivity was obtained in dichloromethane containing Et_2O by using a catalyst either **2b** or **2e**. Interestingly, the stereoselectivity of the produced glycosides decreased considerably when reversed combinations of the catalyst and solvent system were employed. The formation of α-glycoside was best achieved when **2b** and MS 5Å were used in dichloromethane containing Et_2O while β-glycoside was best obtained with **2a** and MS 5Å in dichloromethane containing ^{t}BuCN.

Some examples of the present glycosylation reaction are illustrated in Table 3. In every case, the desired glycosides were obtained in high yields and selectivities when the appropriate catalyst and solvent were combined.



Reagents and conditions: a. $SOCl_2$ / CH_2Cl_2; b. AgX / CH_2Cl_2: **2b**–**2e** was used as stock solution in CH_2Cl_2 without purification.

Scheme 1.

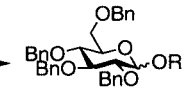
Table 2.

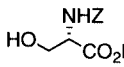
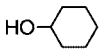
2a–**2e** (20 mol%), Additive, Solvent, rt.: **3** + **4** → **5**

			^{t}BuCN:CH_2Cl_2 (5:1)		Et_2O:CH_2Cl_2 (4:1)	
Entry	Cat.	Additive	Time /h	Yield /%[a]	Time /h	Yield /%[a]
1	**2a**	Drierite	2[b]	**86 (9/91)**	2[b]	59 (46/54)
2		MS 5Å	1[b]	**85 (9/91)**	2[b]	89 (45/55)
3	**2c**	Drierite	20	**79 (17/83)**	24	64 (59/41)
4		MS 5Å	25	2 (-)	3	99 (59/41)
5	**2d**	Drierite	1	77 (25/75)	32	46 (58/42)
6		MS 5Å	1	94 (21/79)	32	48 (58/42)
7	**2b**	Drierite	3	87 (48/52)	24	**60 (87/13)**
8		MS 5Å	16	60 (46/54)	2	**97 (88/12)**
9	**2e**	Drierite	3	73 (34/66)	30	**64 (88/12)**
10		MS 5Å	24	3 (32/68)	32	**7 (86/14)**

[a]The values in parentheses indicate the ratio of α/β. [b]The reaction was carried out at 0 °C.

Table 3.

2a or **2b** (20 mol%), MS 5Å: **3** + ROH → 

Entry	ROH	Cat.	Conditions	Time/h	Yield/%[a]
1		**2a**	A[b]	3	95 (17/83)
2		**2b**	B[c]	24	95 (83/17)
3		**2a**	A	2	97 (8/92)
4		**2b**	B	3	90 (83/17)

[a]The values in parentheses indicate the ratio of α/β. [b]Solvent: ^{t}BuCN/CH_2Cl_2=5/1, Temp: 0 °C. [c]Solvent: Et_2O/CH_2Cl_2=4/1; Temp: rt.

It is noted that the catalytic and stereoselective glycosylation with glycosyl fluoride was carried out effectively by using several cationic species paired with either $B(C_6F_5)_4^-$ or TfO^- in the coexistence of MS 5Å or Drierite as a dehydrating agent. When the reaction was performed in the solvent (^{t}BuCN:CH_2Cl_2=5:1) by using a catalytic amount of carbocationic species paired with a counter anion as $B(C_6F_5)_4^-$, the major product was β-glycoside. Contrary to the above result, α-glycoside was produced as a major product when the same reaction was carried out in the solvent containing Et_2O using a catalytic amount of carbocationic species paired with TfO^-. These results suggest that the stereoselectivity of the glycosylation is highly controlled by both the nature of a solvent and that of a counter anion of the catalyst. And the study on this topic is now in progress.

References and Notes

1 K. Toshima and K. Tatsuta, *Chem. Rev.*, **93**, 1503 (1993); K. Suzuki and T. Nagasawa, *J. Synth. Org. Chem. Jpn.*, **50**, 378 (1992); G-J. Boons, *Tetrahedron*, **52**, 1095 (1996).

2 T. Mukaiyama, Y. Murai, and S. Shoda, *Chem. Lett.*, **1981**, 431.

3 K. Takeuchi and T. Mukaiyama, *Chem. Lett.*, **1998**, 555, and references cited therein.

4 J. C. W. Chien, W-M. Tsai, and M. D. Rausch, *J. Am. Chem. Soc.*, **113**, 8570 (1991).

5 Recently, the α-selective catalytic glycosylation using a protic acid such as TfOH was performed in our laboratory: H. Jona, K. Takeuchi, and T. Mukaiyama, *Chem. Lett.*, **2000**, 1278.

6 a) T. Mukaiyama, M. Yanagisawa, D. Iida, and I. Hachiya, *Chem. Lett.*, **2000**, 606. b) M. Yanagisawa, T. Shimamura, D. Iida, J. Matsuo, and T. Mukaiyama, *Chem. Pharm. Bull.*, **48**, 1838 (2000).

7 G. Wulff and G. Röhle, *Angew. Chem., Int. Ed. Engl.*, **13**, 157 (1974)