Catalytic and Stereoselective Glycosylation with Disarmed Glycosyl Fluoride by Using a Combination of Stannous(II) Chloride ($SnCl_2$) and Silver Tetrakis(pentafluorophenyl)borate [$AgB(C_6F_5)_4$] as a Catalyst

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A catalytic and stereoselective glycosylation of various glycosyl acceptors with disarmed glycosyl fluorides is successfully carried out by using a combination of stannous(II) chloride ($SnCl_2$) and silver tetrakis(pentafluorophenyl)borate [$AgB(C_6F_5)_4$] as a catalyst in the coexistence of MS5A in toluene and the corresponding 1,2-*trans* di- or trisaccharides were obtained in high yields.

To develop a new and useful method for stereoselective glycosylation is one of the most fundamental research targets in carbohydrate chemistry.[1] In the synthesis of complex oligosaccharides chains, glycosyl fluorides are one of the most frequently used donors as they are quite stable compared with the corresponding other 1-halogenated sugars. Although many activating reagents for glycosyl fluorides had been studied[2] after our publication in 1981,[3] only five examples were reported for activation of 'disarmed' glycosyl fluorides by using stoichiometric amounts of activators such as $SnCl_2$–$AgClO_4$,[4] Cp_2ZrCl_2–$AgClO_4$,[5] Cp_2HfCl_2–AgOTf,[6] $BF_3{\cdot}OEt_2$,[7] or rare earth metal salts.[8] As for catalytic glycosylation, there is an example which uses trimethylsilylated acceptors catalyzed by 30 mol% of $La(ClO_4)_3{\cdot}nH_2O$.[9] Then, an efficient method for the reaction of various free hydroxy groups containing glycosyl acceptors with disarmed glycosyl fluorides was tried. Recently, it was reported from our laboratory that several catalysts containing soft and weakly-coordinating counter anions such as $B(C_6F_5)_4^-$ could effectively be employed in glycosylation[10] and aldol reactions.[11] It was then considered that the facile generation of active Sn(II) cationic species would take place by the combined use of $SnCl_2$ and $AgB(C_6F_5)_4$[12] to work as an effective catalyst for the activation of 'disarmed' glycosyl fluorides. In this communication, we would like to report an improved method for activation of 'disarmed' glycosyl fluorides by the combined use of catalytic amounts of the respective $SnCl_2$ and $AgB(C_6F_5)_4$, which afford the corresponding β-D-di- or tri-saccharides in excellent yields on treatment with several glycosyl acceptors.

In the first place, 1.2 equivalents of $SnCl_2$ and $AgClO_4$ were used together with MS4A in Et_2O by taking up the reaction of 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl fluoride (**1**), disarmed glycosyl fluoride, with methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (**2**) according to our previous procedure[3] (Table 1, Entry 4). As a result, it was observed that the desired disaccharide was obtained in only 13% yield and a large amount of starting material was recovered. Then, various additives and silver salts were examined to improve the yields of the desired disaccharides (Table 1). Among additives, MS5A proved to be most effective while almost no reaction took place in the absence of additives (Entries from 1 to 5).[13] It was noted

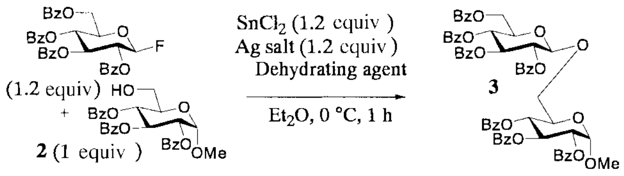


Table 1. Effect of silver salts and dehydrating agents

Entry	Ag salt	Dehydrating agent	Yield /%
1	$AgClO_4$	None	trace
2	$AgClO_4$	Drierite 1 g/mmol	8
3	$AgClO_4$	MS3A 1 g/mmol	12
4	$AgClO_4$	MS4A 1 g/mmol	13
5	$AgClO_4$	MS5A 1 g/mmol	16
6	AgOTf	MS5A 1 g/mmol	40
7	$AgBF_4$	MS5A 1 g/mmol	5
8	$AgB(C_6F_5)_4$	MS5A 1 g/mmol	78
9	**$AgB(C_6F_5)_4$**	**MS5A 3 g/mmol**	**quant.**
10	$AgB(C_6F_5)_4$	MS5A 5 g/mmol	88
11[a]	$AgB(C_6F_5)_4$	MS5A 1 g/mmol	0
12	None	MS5A 1 g/mmol	0

[a]The reaction was carried out in the absence of $SnCl_2$.

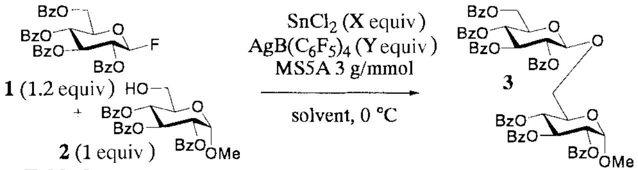


Table 2.

Entry	X	Y	Time /h	Solvent	Yield /%
1	1.2	1.2	1	Et_2O	quant.
2	0.2	0.2	1	Et_2O	90
3	0.2	0.2	2	Et_2O	91
4	0.1	0.1	1	Et_2O	20
5	0.1	0.1	12	Et_2O	18
6	0.1	0.2	1	Et_2O	trace
7[a]	0.1+0.1	0.2	1	Et_2O	92
8	**0.2**	**0.2**	**2**	**toluene**	**quant.**
9	0.2	0.2	2	CH_2Cl_2	92
10	0.2	0.2	2	CCl_4	87
11	0.2	0.2	2	fluorobenzene	86
12	0.2	0.2	2	BTF	80
13	0.2	0.2	2	THF	0
14	0.2	0.2	2	MeCN	0

[a]The glycosylation was carried out by using the catalyst prepared from succeeding addition of 0.1 equiv of $SnCl_2$ to the preprepared solution of 0.1 equiv of $SnCl_2$ and 0.2 equiv of $AgB(C_6F_5)_4$.

that $AgB(C_6F_5)_4$,[12] a useful reagent neither hydroscopic nor explosive, generated an active catalyst more effectively than any other silver salts on treatment with $SnCl_2$: that is, a catalyst generated by using the silver borate smoothly promoted the glycosylation and the desired disaccharide was obtained in higher yield (Entries from 5 to 8). The optimized reaction conditions were demonstrated in Entry 9 ($AgB(C_6F_5)_4$, MS5A = 3 g/mmol, quant.). No reaction took place when $SnCl_2$ or silver salt was used alone (Entries 11 and 12).

Next, in order to achieve the catalytic process of this glycosylation, both the amount of catalyst and the effect of solvents were examined to find the best conditions (Table 2). As a result, the combined use of 20 mol% each of $SnCl_2$ and $AgB(C_6F_5)_4$ effectively activated disarmed glycosyl fluoride and the corresponding disaccharide was obtained in 91% (Entry 3). When 10 mol% of $SnCl_2$ and 20 mol% of $AgB(C_6F_5)_4$ were treated, ca. 20 mol% of AgCl precipitated, which suggested the formation of $Sn[B(C_6F_5)_4]_2$ (Entry 6). On the other hand, only a trace amount of disaccharide was obtained when glycosyl donor **1** and acceptor **2** were allowed to react in the above solution while the desired disaccharide was smoothly afforded in 92% yield by further addition of 10 mol% of $SnCl_2$ to the solution (Entry 7). These results consequently indicate that $ClSnB(C_6F_5)_4$ might be the important active species generated from equimolar amounts of $SnCl_2$ and $AgB(C_6F_5)_4$. Therefore, $Sn[B(C_6F_5)_4]_2$ which was possibly generated from $ClSnB(C_6F_5)_4$ together with $SnCl_2$ by disproportionation would not behave as an effective catalyst for this glycosylation. Concerning the solvent, toluene gave the best result (Entry 8) while no reaction took place in polar solvents such as THF and MeCN (Entries 13 and 14), which is probably due to deactivation of the Lewis Acid by their strong coordination to stannous cation

Finally, glycosylation using various donors and acceptors were examined in order to extend the scope of the present method (Table 3). As a result, glycosylation reaction smoothly proceeded to afford the corresponding β-D-disaccharides in excellent yields even in the cases of using acceptors having secondary alcohol, **6** and **7**. In addition, glycosylation using disaccharide[14] having disarmed glycosyl fluoride as a donor also gave the corresponding β-D-trisaccharide in good yield.

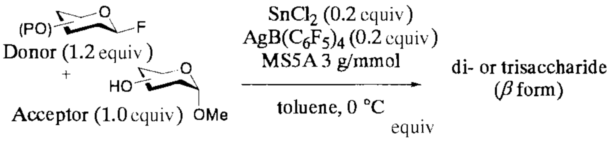
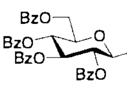


Table 3. Glycosylation using various glycosyl donors and acceptors

Entry	Donor	Acceptor	Time /h	Yield /%
1	**1**	**5**	1	quant.
2	**1**	**6**	1.5	90
3	**1**	**7**	1	quant.
4[a]	**4**	**2**	1	87

[a]The reaction was carried out in toluene–CH_2Cl_2 (3:1).



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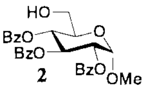

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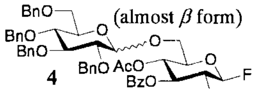

(almost β form)

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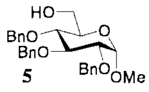

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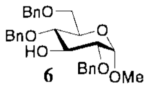

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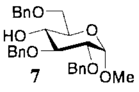

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The typical experimental procedure is as follows: to a stirred suspension of MS5A (150 mg), $SnCl_2$ (1.9 mg, 10 μmol) and $AgB(C_6F_5)_4$ (7.9 mg, 10 μmol) in toluene (1.0 mL) was added **1** (35.9 mg, 60.0 μmol) and **2** (25.3 mg, 50.0 μmol) in toluene (1.0 mL) at 0 °C. After the reaction mixture was stirred for 2 h, it was quenched by adding saturated aqueous $NaHCO_3$. The mixture was filtered through Celite and extracted with CH_2Cl_2 (× 3). The combined organic layer was washed with H_2O and brine, and dried over Na_2SO_4. After being filtered and evaporated, the resulting residue was purified by preparative TLC (silica gel) to give the desired product **3** (54.2 mg, 99.9%).[15]

Thus, a catalytic and stereoselective glycosylation using 'disarmed' glycosyl donor, the fluoride, was efficiently performed by using 20 mol% each of $SnCl_2$ and $AgB(C_6F_5)_4$ in the coexistence of MS5A in toluene. Further study on this glycosylation using various donors and acceptors including amino sugars, and the mechanistic study on the catalytic cycle is now in progress.

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