Catalytic and Stereoselective Glycosylation with Disarmed Glycosyl Fluoride Having Phthaloyl or Dichlorophthaloyl Protected Amino Function Using a 1:2 Combination of Stannic Chloride and Silver Tetrakis(pentafluorophenyl)borate

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

(Received April 18, 2001; CL-010355)

A catalytic and stereoselective glycosylation of various glycosyl acceptors with disarmed glycosyl fluorides having phthaloyl or dichlorophthaloyl protected amino function is successfully carried out by using a combination of stannic chloride ($SnCl_4$) and silver tetrakis(pentafluorophenyl)borate [$AgB(C_6F_5)_4$] in the coexistence of MS 5A, and the corresponding 1,2-*trans* disaccharides are obtained in high yields.

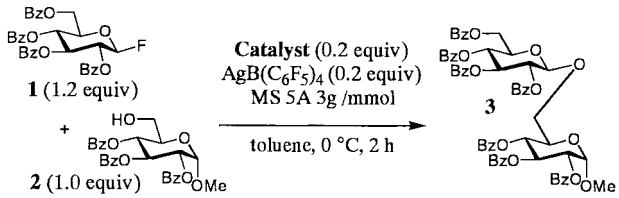
It was previously reported[1] that the combined use of catalytic amounts of $SnCl_2$ and silver tetrakis(pentafluorophenyl)borate $AgB(C_6F_5)_4$ was effective for glycosylation using disarmed glycosyl fluorides as donors. In this reaction, $B(C_6F_5)_4^-$ anion, a weakly coordinating counter anion,[2] considered to play an important role in generating active cationic species.

It is well known that 2-deoxy-2-amino sugars[3] are often found in naturally occurring oligosaccharides, glycoproteins, glycolipids and other glycoconjugates, which work as cell signaling molecules such as cancer associated antigens.[4] However, no catalytic glycosylation of various glycosyl acceptors with disarmed glycosyl fluorides[5] having a protected amino function has been reported as of today. In this communication, we would like to report an efficient glycosylation method including activation of disarmed glycosyl fluorides having phthaloyl(Phth) or 4,5-dichlorophthaloyl(DCPhth)[6] protected amino function[7] by the use of catalytic amounts of $SnCl_4$ and $AgB(C_6F_5)_4$ in 1:2 ratio from which the corresponding disaccharides were formed in high yields.

In the first place, 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**) was tried according to our previous procedure[1] using a combination of various Lewis acids and $AgB(C_6F_5)_4$ in 20 mol% each in order to estimate the activity of the combined catalysts (Table 1). The desired disaccharide was obtained in high yield when $SnCl_2$, $SnCl_4$, Cp_2ZrCl_2,[8] or $SiCl_4$ was used as a Lewis acid (Entries 1–4) while the yield remained moderate in the cases of using Cp_2HfCl_2,[8] Ph_3SiCl[9] and $TiCl_2$ (Entries 5–7). On the other hand, almost no glycosylation reaction took place when $HB(C_6F_5)_4$[10] or $TrB(C_6F_5)_4$,[11] useful activators for armed glycosyl fluorides, was used.

Then, glycosylation with disarmed glycosyl fluoride **4** having a DCPhth-protected amino function[6] was further tried by using $SnCl_2$ or $SnCl_4$ under the same conditions (Table 2). The combined use of $SnCl_2$ or $SnCl_4$ and $AgB(C_6F_5)_4$ in 20 mol% each was tried in toluene at 0 °C by taking the reaction of glycopyranosyl fluoride **4**, disarmed glycosyl fluoride having DCPhth-protected amino function, with the acceptor **2** (Entry 1 and 2). It then turned out that almost no reaction took place in

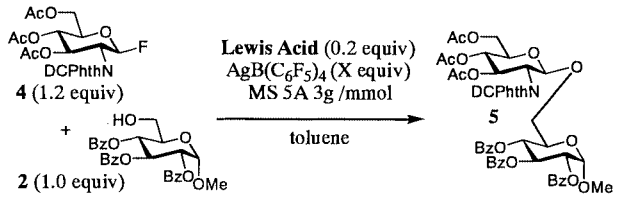
Table 1. Effect of catalyst



Entry	Catalyst	Yield /%	Entry	Catalyst	Yield /%
1	$SnCl_2$	quant	7	$TiCl_2$	46
2	$SnCl_4$	98	8	Cp_2TiCl_2	8
3	Cp_2ZrCl_2	95	9[a,b]	$HB(C_6F_5)_4$	7
4	$SiCl_4$	83	10	$TiCl_4$	trace
5	Cp_2HfCl_2	61	11[a]	$TrB(C_6F_5)_4$	0
6	Ph_3SiCl	53	12	TMSCl	0

[a]The reaction was carried out in the absence of $AgB(C_6F_5)_4$. [b]$HB(C_6F_5)_4$ was generated from $AgB(C_6F_5)_4$ and ^{t}BuBr in toluene-Et_2O (1:1) and the supernatant was used.

Table 2.



Entry	Lewis acid	X (equiv)	Time /h	Temp /°C	Yield /%
1	$SnCl_2$	0.2	1.0	0	trace
2	$SnCl_4$	0.2	1.0	0	96
3	$SnCl_4$	0.2	1.7	–20	22
4	$SnCl_4$	0.4	1.7	–20	96
5	$SnCl_4$	0.6	1.7	–20	quant
6	$SnCl_4$	0.8	1.7	–20	98
7	$SnCl_4$	None	1.0	0	trace

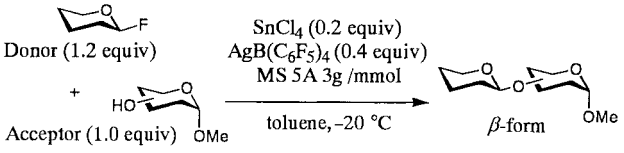
the case of using a combination of $SnCl_2$ and $AgB(C_6F_5)_4$[1] (Entry 1). On the other hand, the glycosyl fluoride **4** was effectively activated by the combined use of 20 mol% each of $SnCl_4$ and $AgB(C_6F_5)_4$ to afford the corresponding disaccharide in 96% yield (Entry 2). Therefore, $SnCl_4$ was chosen to further optimize the conditions of this glycosylation. Since the desired disaccharide was obtained in low yield when a combination of $SnCl_4$ and $AgB(C_6F_5)_4$ in 20 mol% each was employed at –20 °C for 1.7 h (Entry 3), the glycosylations using 40, 60 and 80 mol% of $AgB(C_6F_5)_4$ together with 20 mol% of $SnCl_4$ were

tried. Then it was found that those used more than 40 mol% of $AgB(C_6F_5)_4$ were effective for the present glycosylation to afford the desired disaccharide in high yield (Entries 4–7). This result indicated that the activity of the catalytic species formed under the above conditions depended on the ratios[12] of $SnCl_4$ and $AgB(C_6F_5)_4$.

Finally, glycosylation of the acceptors **2** and **7** with various donors using a combination of 20 mol% of $SnCl_4$ and 40 mol% of $AgB(C_6F_5)_4$ in toluene[13] was studied (Table 3). As a result, when the donor **1** and the acceptor **7** having a secondary alcohol were treated according to the above procedure, it took a long time to complete the reaction even if the glycosylation was carried out at 0 °C whereas the desired disaccharide was obtained in good yield (Entry 3). Concerning other donors **4** and **6**[14] having DCPhth or Phth protected amino function, the glycosylation reaction smoothly proceeded to afford the corresponding β-D-disaccharides in excellent yields even in the cases of using the acceptor **7** having secondary alcohol.

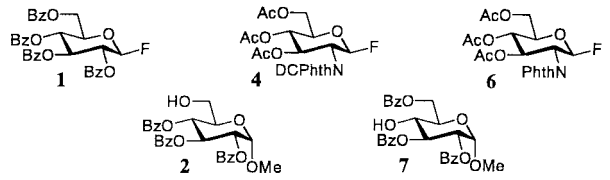
In the case of using the donor or acceptors having benzyl protected hydroxy groups, however, the desired disaccharides were obtained in moderate yields because of their partial deprotection of benzyl groups during the glycosylation.

Table 3. Glycosylation with various donors and acceptors



Entry	Donor	Acceptor	Time /h	Yield /%
1	**1**	**2**	2.0	96
2	**1**	**7**	20	38
3[a]	**1**	**7**	10	83
4	**4**	**2**	1.7	96
5	**4**	**7**	2.0	90
6	**6**	**2**	1.0	98
7	**6**	**7**	1.0	91

[a]The reaction was carried out at 0 °C.



The typical experimental procedure is as follows: to a stirred suspension of MS5A (150 mg), $AgB(C_6F_5)_4$ (15.7 mg, 20 μmol), **4** (30.4 mg, 60.0 μmol) and **2** (25.3 mg, 50.0 μmol) in toluene (1.8 mL) was added $SnCl_4$ (2.6 mg, 10 μmol, 0.2 mL in toluene) at –20 °C. After the reaction mixture was stirred for 1.7 h, it was quenched by addition of 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 resulted residue was purified by preparative TLC (silica gel) to give the desired product **5** (47.4 mg, 95.5%).

Thus, a catalytic and stereoselective glycosylation with 'disarmed' glycosyl donors, glycosyl fluorides having phthaloyl or dichlorophthaloyl protected amino function, was efficiently performed by using a combination of 20 mol% of $SnCl_4$ and 40 mol% of $AgB(C_6F_5)_4$ in the coexistence of MS 5A[15].

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

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