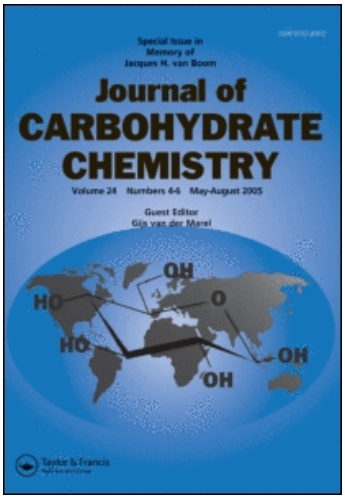

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Takashi Yamanoi[a]; Yoshihiro Iwai[a]; Toshiyuki Inazu[a]
[a] The Noguchi Institute, Tokyo, Japan

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COMMUNICATION

BF_3•OEt_2 ENHANCED $Yb(OTf)_3$-PROMOTED GLYCOSIDATION OF 1-*O*-ACYL-D-GLUCOPYRANOSE[1]

Takashi Yamanoi, Yoshihiro Iwai and Toshiyuki Inazu*

The Noguchi Institute, 1-8-1, Kaga, Itabashi-ku, Tokyo 173, Japan

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Much attention has been paid to the synthesis of glycosides and oligosaccharides for the preparation of natural products and their analogues to investigate biological functions.[2] Most known glycosidation methods are based on the activation of a leaving group at the anomeric center of a glycosyl donor.[3] In some cases alcohol derivatives such as $ROSnBu_3$ and $ROSiMe_3$ are used to increase the reactivity of glycosyl acceptors.[3]

Several glycosidations using 1-*O*-acyl sugars were investigated[4a-e] because they are stable, easy to prepare, and can be stored for a long time. The acetoxy, methoxyacetoxy, and other acyloxy groups have been used as leaving groups. It was reported that lanthanide triflates, especially ytterbium triflate ($Yb(OTf)_3$) was effective for the activation of several glycosyl donors such as 1-*O*-methoxyacetyl-D-glucopyranose[4d] and 1-*O*-acetyl-D-ribofuranose.[4e]

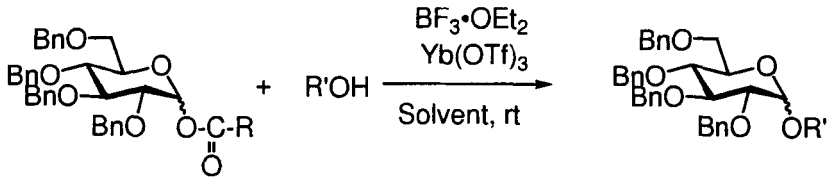
However it seems difficult to activate stable 1-*O*-acetyl glucopyranose. It was reported that no glucoside was obtained by the reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl acetate (**1**) with an alcohol using lanthanide triflates as activators.[4d] We examined the glucosidation of **1** with 3β-cholestanol in dichloromethane using $Yb(OTf)_3$

under several conditions, and suprisingly, found that by adding only a 3 mol% amount of BF_3•OEt_2, the above reaction system smoothly gave the corresponding 3β-cholestanyl glucopyranoside in 82% yield.

Although it was reported that the reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl methoxyacetate (**2**) with 1-octanol in the presence of a 30 mol% $Yb(OTf)_3$ in dichloromethane at room temperature for 16 hours gave the corresponding *n*-octyl glucopyranoside in 65% yield,[4d] we found that the addition of a 3 mol% BF_3•OEt_2 greatly facilitated the reaction and the chemical yield of the glucoside rose to 88% in a reaction time of only 2 hours. It is possible that the formation of unknown active species is occurring on addition of BF_3•OEt_2 and $Yb(OTf)_3$, however, we postulate that their acetoxy groups would be activated by $Yb(OTf)_3$, and the reactivity of the alcohol enhanced by the formation of a BF_3•OEt_2-ROH complex.[5] We have found that the reaction of **1** with several borates in the presence of $Yb(OTf)_3$ gave the corresponding alkyl glucosides in good yields.[6] These results show that compounds including a B-OR bond are likely to be highly reactive glycosyl acceptors.

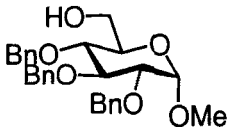
A 20 mol% excess amount of **1** improved the yield of the glucoside to 92%. Dichloromethane, benzene and acetonitrile were effective as the reaction solvents, and the reaction using acetonitrile increased β-selectivity of the glucoside. The disaccharide was similarly obtained in 89% yield by the reaction of **1** with methyl 2,3,4-tri-*O*-benzyl-D-glucopyranoside.

A typical experimental procedure was as follows: A 0.04 M (1 M=1 mol•dm^{-3}) dichloromethane solution of BF_3•OEt_2 (0.2 mL, 0.008 mmol) was added to a solution of compound **1** (anomer ratio;α/β=9/1, 0.31 mmol), alcohol (0.26 mmol), and $Yb(OTf)_3$ (0.26 mmol) in dichloromethane (4 mL). The resulting mixture was stirred for a few hours. The reaction was quenched by a saturated sodium hydrogen carbonate (5 mL). The mixture was extracted with chloroform, and the organic layer was washed with water and a saturated NaCl solution. After the organic layer was dried over sodium sulfate, the



1; R=CH_3-
2; R=CH_3OCH_2-

Table. Syntheses of Glucopyranosides by the Reaction of **1** (or **2**) with Alcohols[a)]

Entry	Donor	Alcohol	Solvent	Time/h	Yield/%	α/β
1	**1**	3β-Cholestanol[b)]	CH_2Cl_2	1	83	58/42
2[c)]	**2**	1-Octanol	CH_2Cl_2	16	65	47/53
3[d)]	**2**	1-Octanol	CH_2Cl_2	2	88	49/51
4	**1**	3β-Cholestanol[e)]	CH_2Cl_2	1	82	65/35
5	**1**	3β-Cholestanol	CH_2Cl_2	1	92	64/36
6	**1**	3β-Cholestanol	PhH	2	82	53/47
7	**1**	3β-Cholestanol	Et_2O	2.5	55	51/49
8	**1**	3β-Cholestanol	CH_3CN/CH_2Cl_2 =1/1	1	76	36/64
9	**1**		CH_2Cl_2	1	89	64/36

Molar ratio; a) **1**:ROH:$Yb(OTf)_3$:BF_3•OEt_2 =1.2:1:1:0.03; b) **1**:ROH:$Yb(OTf)_3$:BF_3•OEt_2 =1:1:1:0.03; c) The reported conditions in the absence of BF_3•OEt_2; **2**:ROH:$Yb(OTf)_3$= 1:1.3:0.3; d) **2**:ROH:$Yb(OTf)_3$:BF_3•OEt_2 =1:1.3:0.3:0.03; e) **1**:ROH:$Yb(OTf)_3$:BF_3•OEt_2 =1:1.2:0.3:0.03.

solvent was evaporated under reduced pressure. The crude product was purified by silica-gel thin-layer chromatography (hexane/ethyl acetate=6/1) to give the corresponding glucosides in the yields shown in the Table.

To conclude, we have found that a catalytic amount of $BF_3 \cdot OEt_2$ enhanced the $Yb(OTf)_3$-promoted glycosidation of 1-*O*-acyl sugars. Application of this method to the glycosidations of other glycosyl donors and acceptors is now in progress.

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