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# A Novel Method for Stereoselective Glycosidation with Thioglycosides: Promotion by Hypervalent Iodine Reagents Prepared from PhIO and Various Acids.[1]

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***Abstract:*** Combinations of iodosobenzene (PhIO) and various acids effectively promote glycosidation using thioglycosides as glycosyl donors. β-Selective glucosidation was effected by use of TfOH, $Tf_2O$, TMSOTf, $Sn(OTf)_2$, and $Yb(OTf)_3$ as catalysts with 2-*O*-benzoylated or 2-*O*-benzylated donors by virtue of either the neighboring group participation or the solvent effect of acetonitrile, respectively. Combinations of PhIO with $SnCl_2$-$AgClO_4$, $SnCl_4$-$AgClO_4$, $BiCl_3$-$AgClO_4$, and $SbCl_3$-$AgClO_4$ in ether were advantageous for α-glucosidation, where 2,2,2-trichloroethoxycarbonyl group introduced at the 6-position of a 2-*O*-benzylated donor remarkably increased α-selectivity.

Synthesis of oligosaccharides and glycoconjugates plays more and more important role for elucidation of their biological functions. Thioglycosides have attracted much attention as versatile glycosyl donors particularly for synthesis of complex carbohydrates since they are stable under a variety of reaction conditions but can be activated with appropriate thiophilic reagents.[2] We recently described a novel method for mild and stereoselective glycosidation with thioglycosides by combinations of *N*-bromosuccinimide (NBS) with a catalytic amount of various strong acid salts as promoters.[3,4] In that work, α-selective glucosidation was effected with *O*-benzylated thioglycosides in ether by use of $LiClO_4$ or $LiNO_3$ as catalysts. Under those conditions, however, glycosylation of an acceptor **6** with phenyl thioglycoside **3** possessing 6-*O*-trichloroethoxycarbonyl (Troc) group afforded disaccharide **10** only in a low yield owing to reduced reactivity of the donor. We, therefore, attempted to find more potent activation of thioglycosides with high, particularly α-oriented, stereoselectivity.

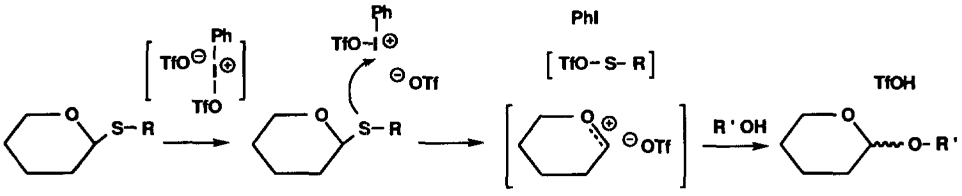
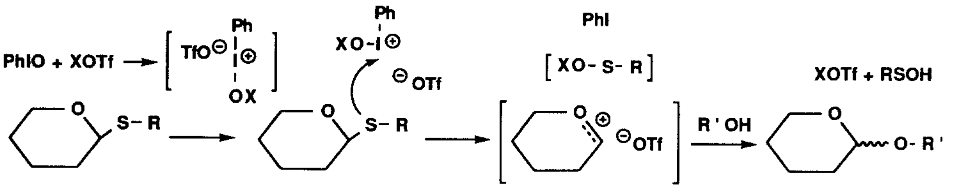


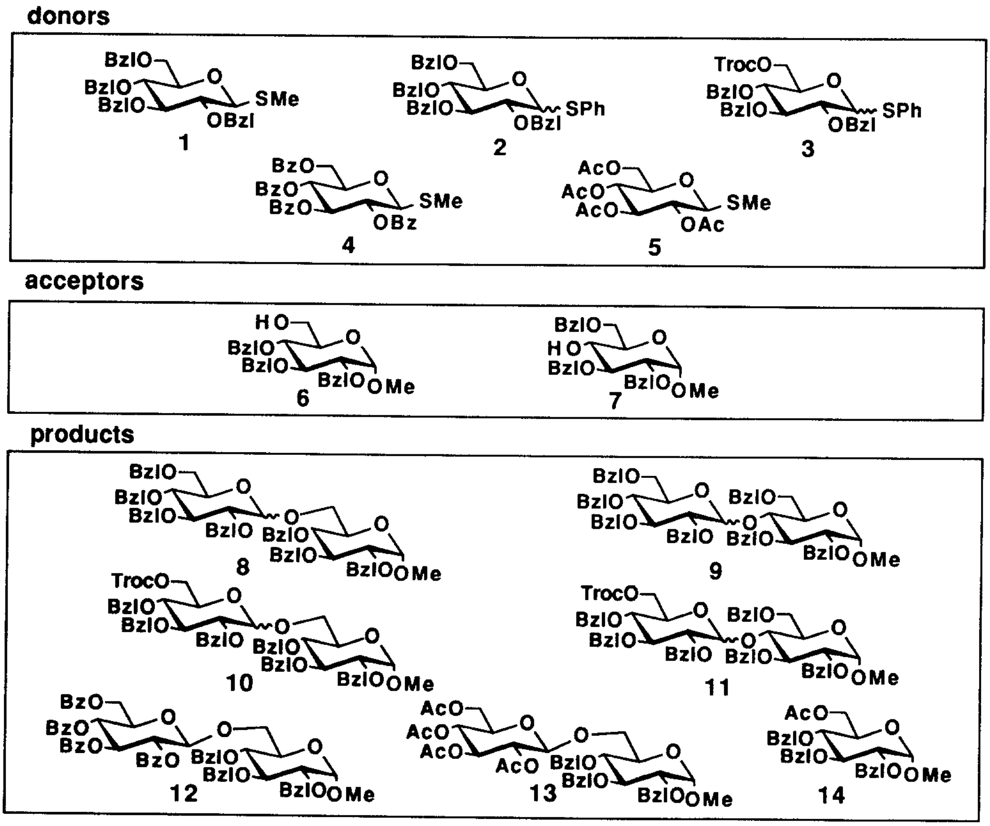
Fig. 1. A plausible reaction mechanism of the glycosidation by using [PhIO-$Tf_2O$ (1:1)].

We previously reported a hypervalent iodine reagent[5] prepared from iodosobenzene (PhIO) and triflic anhydride ($Tf_2O$) (1:1) effectively promotes glycosidation with thioglycosides.[6,7] The reagent, hereafter abbreviated as [PhIO-$Tf_2O$ (1:1)], showed very strong reactivity but was not effective for α-selective glucosidation. Besides, the reagent was prepared separately in another flask prior to glycosidation, which made the procedure troublesome. In the previous paper, we discussed its possible reaction mechanism as shown in Fig. 1. We anticipated that $Tf_2O$ should be regenerated from TfO-S-R and TfOH after each reaction cycle and hence work as a catalyst. We expected various other Lewis acids and TfOH also work as catalysts via similar reaction pathway as shown in Fig. 2. In the present study, we thus extended our approach in the following two points: 1) hypervalent iodine reagents were generated *in situ*, 2) less than stoichiometric amounts of Lewis acids (and TfOH) were examined, in particular crystalline Lewis acids in view of the experimental simplicity. Both high yield and stereoselectivity were achieved by selecting suitable combinations of solvents and acids as described below.



XOTf: $Tf_2O$, TMSOTf, $Sn(OTf)_2$, $Sc(OTf)_3$, $Yb(OTf)_3$, $Lu(OTf)_3$, HOTf

Fig. 2. A plausible reaction mechanism of the glycosidation by combinations of PhIO and acid catalysts.



Glycosidation reactions were carried out by use of 1.3 eq. of PhIO, 0.6 eq. of an acid, and 1.2 eq. of a donor against an acceptor under $\mathrm{N_2}$ atmosphere at -20 °C in 1,2-dichloroethane,[8] acetonitrile, or ether.

We first examined β-selective glycosidation with 2-*O*-benzylated or 2-*O*-acylated donors by use of $\mathrm{Tf_2O}$, TMSOTf, $\mathrm{Sn(OTf)_2}$, $\mathrm{Sc(OTf)_3}$, $\mathrm{Yb(OTf)_3}$, $\mathrm{Lu(OTf)_3}$, and TfOH as catalysts.[9,10] The results are summarized in Table 1. The glycosylation of acceptor **6** with methyl 2,3,4,6-tetra-*O*-benzyl thioglucoside **1** proceeded smoothly with high β-selectivity by virtue of known solvent effect of acetonitrile (entries 1-7). The glucosylation of acceptor **7** possessing a more hindered 4-hydroxyl group also proceeded smoothly to give disaccharide **9** though the β-orienting solvent effect of acetonitrile was suppressed (entries 8-11). β-Selectivity by the present procedure was generally better than those by the previous procedure using either [PhIO-$\mathrm{Tf_2O}$ (1:1)] or NBS-strong acid salts.

Table 1. Reaction conditions and products of β-selective glycosidation.

| entry | D[a] | A[b] | catalyst | solvent | time[c] | P[d] | yield(%) | α : β[e] |
|---|---|---|---|---|---|---|---|---|
| 1 | **1** | **6** | TMSOTf | $\mathrm{CH_3CN}$ | 8 min | **8** | 77 | 6 : 94 |
| 2 | **1** | **6** | $\mathrm{Tf_2O}$ | $\mathrm{CH_3CN}$ | <5 min | **8** | 73 | 9 : 91 |
| 3 | **1** | **6** | TfOH | $\mathrm{CH_3CN}$ | <5 min | **8** | 74 | 5 : 95 |
| 4 | **1** | **6** | $\mathrm{Sn(OTf)_2}$ | $\mathrm{CH_3CN}$ | <5 min | **8** | 81 | 6 : 94 |
| 5 | **1** | **6** | $\mathrm{Sc(OTf)_3}$ | $\mathrm{CH_3CN}$ | <5 min | **8** | 82 | 6 : 94 |
| 6 | **1** | **6** | $\mathrm{Yb(OTf)_3}$ | $\mathrm{CH_3CN}$ | 20 min | **8** | 87 | 7 : 93 |
| 7 | **1** | **6** | $\mathrm{Lu(OTf)_3}$ | $\mathrm{CH_3CN}$ | 15 min | **8** | 83 | 6 : 94 |
| 8 | **1** | **7** | TMSOTf | $\mathrm{CH_3CN}$ | <5 min | **9** | 91 | 12 : 88 |
| 9 | **1** | **7** | TfOH | $\mathrm{CH_3CN}$ | <5 min | **9** | 75 | 14 : 86 |
| 10[f] | **1** | **7** | $\mathrm{Sn(OTf)_2}$ | $\mathrm{CH_3CN}$ | <5 min | **9** | 88 | 20 : 80 |
| 11[f] | **1** | **7** | $\mathrm{Yb(OTf)_3}$ | $\mathrm{CH_3CN}$ | 5 min | **9** | 82 | 19 : 81 |
| 12 | **4** | **6** | $\mathrm{Tf_2O}$ | $\mathrm{(CH_2Cl)_2}$ | <5 min | **12** | 76 | 0 : 100 |
| 13 | **4** | **6** | $\mathrm{Sn(OTf)_2}$ | $\mathrm{(CH_2Cl)_2}$ | 40 min | **12** | 78 | 0 : 100 |
| 14 | **4** | **6** | TMSOTf | $\mathrm{(CH_2Cl)_2}$ | <5 min | **12** | 64 | 0 : 100 |
| 15 | **4** | **6** | $\mathrm{Yb(OTf)_3}$ | $\mathrm{(CH_2Cl)_2}$ | 24 h | **12** | 45 | 0 : 100 |
| 16 | **5** | **6** | $\mathrm{Sn(OTf)_2}$ | $\mathrm{(CH_2Cl)_2}$ | 5 h | **13, 14** | 39, 26 | 0 : 100 |
| 17 | **5** | **6** | $\mathrm{Tf_2O}$ | $\mathrm{(CH_2Cl)_2}$ | <5 min | **14** | 21 | — |

[a] D = donor. [b] A = acceptor. [c] The time required until the glycosyl donor disappeared as estimated by TLC analysis on silica gel. [d] P = product. [e] The anomer ratios of compounds **8** and **9** were determined by comparison of the intensities of methyl signals in $^1$H NMR, since the complete separation of the anomers was difficult by silica-gel column chromatography. [f] The reaction was carried out by use of 1.5 eq. of the donor.

More reliable β-selective glycosidation can be effected by use of a 2-*O*-benzoylated thioglucoside. The present hypervalent iodine reagents generated *in situ* from PhIO with $\mathrm{Tf_2O}$ or $\mathrm{Sn(OTf)_2}$ promoted the glycosidation with 2,3,4,6-tetra-*O*-benzoylthioglucoside **4** to give 1,2-*trans*-β-glucoside **12** in practical yields (entry 12, 13). The yield dropped by use of TMSOTf or $\mathrm{Yb(OTf)_3}$ (entry 14, 15). The use of TfOH caused many undesired side-reactions (data not shown). The present method, however, was not appropriate for the glycosidation with acetylated thioglycoside **5**: PhIO-$\mathrm{Sn(OTf)_2}$ gave **13** only in a low yield (entry 16) and PhIO-$\mathrm{Tf_2O}$ gave almost no glycoside either (entry 17). 6-*O*-Acetylated acceptor **14** was formed in a comparable amount or obtained predominantly in each case.

In our previous work where the separately prepared reagent [PhIO-$Tf_2O$ (1:1)] was used, the reaction of the acetylated donor **5** gave also a low yield (42%) of the disaccharide **13** and substantial amount (24%) of the same side product **14**. In that reaction, addition of silica gel to the reaction mixture suppressed the side reaction and gave higher yield (77%) of **13**. By contrast no such positive effect of silica gel was observed under the present reaction conditions. Either the reaction pathway or relevant active species might thus different under the two conditions though the same pair of reagents are employed.

Stereoselective formation of 1,2-*cis*-glycosides is generally a difficult issue where no assisting effect such as participation of a neighboring group is available. Among various methods reported for selective α-glucosidation in recent years, the combinations of ether as a solvent and perchlorates as a source of counter anion against oxocarbenium ion have been frequently used.[2g,11,12] In the glycosidation reaction, however, not only counter anions against oxocarbenium ion but also cations in the reaction medium proved to manifest important influence on the stereoselectivity. In fact, better α-selective glucosidation was effected with 2-*O*-benzylated thioglycosides by combined use of NBS with $LiClO_4$ or $LiNO_3$ as a catalyst in ether than with other perchlorates in our previous study.[4] In the present study, α-glycosidation was, therefore, examined of 6-OH free acceptor **6** and 2,3,4,6-tetra-*O*-benzyl thioglycoside **1** with PhIO and various acids; TfOH, TMSOTf, $Tf_2O$, $Sn(OTf)_2$, $Zn(OTf)_2$, $Cu(OTf)_2$, $Sc(OTf)_3$, $La(OTf)_3$, $Yb(OTf)_3$, $Lu(OTf)_3$, and Lewis acids generated *in situ* from $SnCl_2$-$AgClO_4$,[11] $SnCl_4$-$AgClO_4$,[12] $Cp_2ZrCl_2$-$AgClO_4$,[13] $SbCl_3$-$AgClO_4$, and $BiCl_3$-$AgClO_4$.[14] All the reactions were carried out at -20 °C in ether. The results are summarized in Table 2.

The presence of perchlorate anion was crucial for α-selective glycosidation in the present method although the glycosidation proceeded smoothly with most of the acids tested except $Zn(OTf)_2$, $Cu(OTf)_2$, and $La(OTf)_3$ to give the corresponding disaccharide **8** in good yields. Poor or no anomeric selectivity was observed by using TfOH, TMSOTf, and $Tf_2O$, $Sc(OTf)_3$, $Yb(OTf)_3$, $Lu(OTf)_3$ (data not shown), and $Sn(OTf)_2$ (entry 1). Addition of $LiClO_4$ (0.3 or 0.6 eq.) to $Sn(OTf)_2$ increased α-selectivity to some extent (entry 2, 3), but the selectivity decreased when a higher amount (1.2 or 2.4 eq.) of $LiClO_4$ was added (entry 4, 5). Most of the Lewis acids generated *in situ* from metal chlorides with $AgClO_4$ promoted the glycosidation in good total yields to give the α-glucoside **8** preferentially (entries 6-15) though the selectivities are not sufficiently high. The reaction rates seem to vary depending on the acidity of the catalysts. $SnCl_4$-$AgClO_4$ and $SbCl_3$-$AgClO_4$ are most reactive among the Lewis acids generated *in situ* (entries 7-10). In the case of $BiCl_3$-$AgClO_4$, both the yield and the reactivity were improved by increasing the amount of $AgClO_4$ (entries 11-13) as the acidity increased,[14] whereas those were not so affected in the case of $SbCl_3$-$AgClO_4$ (entries 8-10). $SnCl_2$-$AgClO_4$ also catalyzed the present glycosidation with more moderate activation (entry 6). The latter three metal chlorides, $SnCl_2$, $SbCl_3$, and $BiCl_3$ are crystalline, not strongly hygroscopic, and easy to handle. $Cp_2ZrCl_2$-$AgClO_4$ did not give particular advantage for the present method (entry 14, 15).

In our previous study for stereoselective glycosidation using thioglycosides,[4] we found α-selectivity was increased by use of less reactive phenyl thioglycoside **2** (α:β=2:1) as a glycosyl donor. We also found α-selectivity was enhanced by virtue of the influence of the trichloroethoxycarbonyl (Troc) function introduced at 6-*O*-group.[1b,1c,15] However, strong activation was required for glycosidation in the latter case to obtain good yields because the 6-*O*-Troc group reduces the reactivity of donors.[4] We expected highly reactive hypervalent iodine reagents would effectively activate 6-*O*-Troc phenyl thioglycoside **3** (α:β=2:1). The presence of 6-*O*-Troc group would thereby improve the α-selectivity. We then examined the α-glycosidation with **2** and **3** by using combinations of PhIO and various salts listed in Table 2 (entries 16-27), which showed better selectivity among those tested as described above. All the combinations effectively activates both **2** and **3** to give disaccharide **8** and **10** in good yields, respectively, as we expected. High $\alpha$-selectivity was achieved with the 6-*O*-Troc donor by using $SnCl_2$-$AgClO_4$, $SnCl_4$-$AgClO_4$, $SbCl_3$-$AgClO_4$, and $BiCl_3$-$AgClO_4$ (entries 23-27). Decreasing the amount of catalyst ($SbCl_3$-$AgClO_4$) did not affect the yield and selectivity but retarded the reaction (entry 20, 26).

The glycosidation of acceptor **7** possessing a more hindered 4-hydroxyl group also proceeded smoothly by use of 6-*O*-Troc phenyl thioglycoside **3** as a donor and $SbCl_3$-$AgClO_4$ as a catalyst to give disaccharide **11** with high $\alpha$-selectivity (entry 28).

Table 2. Reaction conditions and products of $\alpha$-selective glycosidation.

| entry | D[a] | A[b] | catalyst | time[c] | P[d] | yield(%) | $\alpha : \beta$[e] |
|---|---|---|---|---|---|---|---|
| 1 | **1** | **6** | $Sn(OTf)_2$ (0.6 eq.) | <5 min | **8** | 88 | 69 : 31 |
| 2 | **1** | **6** | $Sn(OTf)_2$ (0.6 eq.) - $LiClO_4$ (0.3 eq.) | <5 min | **8** | 87 | 75 : 25 |
| 3 | **1** | **6** | $Sn(OTf)_2$ (0.6 eq.) - $LiClO_4$ (0.6 eq.) | <5 min | **8** | 78 | 76 : 24 |
| 4 | **1** | **6** | $Sn(OTf)_2$ (0.6 eq.) - $LiClO_4$ (1.2 eq.) | <5 min | **8** | 85 | 62 : 38 |
| 5 | **1** | **6** | $Sn(OTf)_2$ (0.6 eq.) - $LiClO_4$ (2.4 eq.) | <5 min | **8** | 77 | 62 : 38 |
| 6 | **1** | **6** | $SnCl_2$ (0.6 eq.) - $AgClO_4$ (0.6 eq.) | 45 min | **8** | 74 | 76 : 24 |
| 7 | **1** | **6** | $SnCl_4$ (0.6 eq.) - $AgClO_4$ (0.6 eq.) | <5 min | **8** | 75 | 80 : 20 |
| 8 | **1** | **6** | $SbCl_3$ (0.6 eq.) - $AgClO_4$ (0.6 eq.) | <5 min | **8** | 83 | 78 : 22 |
| 9 | **1** | **6** | $SbCl_3$ (0.6 eq.) - $AgClO_4$ (1.2 eq.) | <5 min | **8** | 79 | 81 : 19 |
| 10 | **1** | **6** | $SbCl_3$ (0.6 eq.) - $AgClO_4$ (2.4 eq.) | <5 min | **8** | 79 | 83 : 17 |
| 11 | **1** | **6** | $BiCl_3$ (0.6 eq.) - $AgClO_4$ (0.6 eq.) | 1 h | **8** | 67 | 63 : 37 |
| 12 | **1** | **6** | $BiCl_3$ (0.6 eq.) - $AgClO_4$ (1.2 eq.) | 9 min | **8** | 72 | 81 : 19 |
| 13 | **1** | **6** | $BiCl_3$ (0.6 eq.) - $AgClO_4$ (2.4 eq.) | <5 min | **8** | 75 | 81 : 19 |
| 14 | **1** | **6** | $Cp_2ZrCl_2$ (0.6 eq.) - $AgClO_4$ (0.6 eq.) | 2 h | **8** | 73 | 81 : 19 |
| 15 | **1** | **6** | $Cp_2ZrCl_2$ (0.6 eq.) - $AgClO_4$ (1.2 eq.) | 2.5 h | **8** | 45 | 77 : 23 |
| 16 | **2** | **6** | $Sn(OTf)_2$ (0.6 eq.) - $LiClO_4$ (0.3 eq.) | <5 min | **8** | 86 | 78 : 22 |
| 17 | **2** | **6** | $SnCl_2$ (0.6 eq.) - $AgClO_4$ (0.6 eq.) | 8 min | **8** | 74 | 83 : 17 |
| 18 | **2** | **6** | $SnCl_4$ (0.6 eq.) - $AgClO_4$ (0.6 eq.) | <5 min | **8** | 80 | 92 : 8 |
| 19 | **2** | **6** | $SbCl_3$ (0.6 eq.) - $AgClO_4$ (2.4 eq.) | <5 min | **8** | 79 | 85 : 15 |
| 20 | **2** | **6** | $SbCl_3$ (0.1 eq.) - $AgClO_4$ (0.4 eq.) | 8 min | **8** | 77 | 88 : 12 |
| 21 | **2** | **6** | $BiCl_3$ (0.6 eq.) - $AgClO_4$ (2.4 eq.) | <5 min | **8** | 71 | 83 : 17 |
| 22 | **3** | **6** | $Sn(OTf)_2$ (0.6 eq.) - $LiClO_4$ (0.3 eq.) | <5 min | **10** | 79 | 88 : 12 |
| 23 | **3** | **6** | $SnCl_2$ (0.6 eq.) - $AgClO_4$ (0.6 eq.) | 30 min | **10** | 82 | 97 : 3 |
| 24 | **3** | **6** | $SnCl_4$ (0.6 eq.) - $AgClO_4$ (0.6 eq.) | <5 min | **10** | 98 | 96 : 4 |
| 25 | **3** | **6** | $SbCl_3$ (0.6 eq.) - $AgClO_4$ (2.4 eq.) | <5 min | **10** | 78 | 94 : 6 |
| 26 | **3** | **6** | $SbCl_3$ (0.1 eq.) - $AgClO_4$ (0.4 eq.) | 2 h | **10** | 80 | 94 : 6 |
| 27 | **3** | **6** | $BiCl_3$ (0.6 eq.) - $AgClO_4$ (2.4 eq.) | <5 min | **10** | 72 | 93 : 7 |
| 28[f] | **3** | **7** | $SbCl_3$ (0.6 eq.) - $AgClO_4$ (2.4 eq.) | <5 min | **11** | 70 | 91 : 9 |

a-d, f: see the legend of Table 1. [e] The anomer ratios of compounds **8**, **10**, and **11** were determined by comparison of the intensities of methyl signals in $^1H$ NMR, since the complete separation of the anomers was difficult by silica-gel column chromatography.

Hypervalent iodine reagents prepared from PhIO and various acids effectively promote glycosidation with thioglycosides to give high yields of glycosides. TMSOTf and $Sn(OTf)_2$ are suitable as catalysts for β-selective glucosidation with 2-*O*-benzylated donors in acetonitrile from the standpoint of yield, anomeric selectivity, operational simplicity, and cost. β-Glucosidation with acylated donors was also effected by [PhIO-$Tf_2O$ (1:1)] prepared prior to glycosidation in the presence of silica gel as previously reported, but the present hypervalent iodine reagents prepared *in situ* from PhIO with $Tf_2O$ or $Sn(OTf)_2$ enables simpler operation. From the practical point of view, $Sn(OTf)_2$ is concluded the best choice among the acids tested for β-glucosidation. It is a commercially available, not expensive and crystalline compound which is stable, not hygroscopic, and hence easy to handle. Selective α-glucosidation was effected by combinations of PhIO with $SnCl_2$-$AgClO_4$, $SnCl_4$-$AgClO_4$, $BiCl_3$-$AgClO_4$, or $SbCl_3$-$AgClO_4$ with 2-*O*-benzylated donors in ether. The Troc group introduced at 6-position of a 2-*O*-benzylated donor again proved to increase α-selectivity. The combinations of PhIO with both $SnCl_4$-$AgClO_4$ and $SbCl_3$-$AgClO_4$ showed particularly strong reactivity under the conditions for α-selective glycosidation. In fact, in our recent study of a bioactive radio-labeled lipid A analogue, the glycosylation of (*p*-methoxybenzyl)oxyethanol with a disaccharide 2-azidothioglycoside possessing many long fatty acids was effected only by use of a hypervalent iodine reagent, PhIO-$SnCl_4$-$AgClO_4$, among the activating methods of thioglycosides so far tested (NBS-$LiClO_4$, NIS-TfOH, NBS-$AgClO_4$, and so on).[16] Acid-catalyzed glycosidation must be carried out at low temperature during a short reaction period in order to prevent undesired acid-catalyzed anomerization. From this point of view, the present method is advantageous because of its high reaction rate, simple experimental procedure, and high stereoselectivity.

## EXPERIMENTAL

$^1H$ NMR spectra were measured on JEOL JNM-EX 270 or LA 500 spectrometers for $CDCl_3$ solutions. The chemical shifts are given in δ values with tetramethylsilane (TMS) as the internal standards. Silica-gel column chromatography was carried out using Merck Kieselgel 60 (0.040 - 0.063 mm) at medium-pressure (2 - 4 kg $cm^{-2}$). Silica-gel TLC was carried out using Merck Kieselgel 60 $F_{254}$. Silica gel used for glycosidation was dried at 200 °C under reduced pressure overnight. Organic solutions were dried over $MgSO_4$ and evaporated *in vacuo*.

**A Typical Procedure for β-Glycosidation.** To a solution of methyl 2,3,4,6-tetra-*O*-benzyl-β-D-thioglucopyranoside (**1**) (103 mg, 180 μmol) and methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**6**) (70.5 mg, 152 μmol) in dry $CH_3CN$ (2.0 ml) were added Molecular Sieves 4A (200 mg) and PhIO (42.1 mg, 191 μmol) under $N_2$ atmosphere. To the mixture was added $Sn(OTf)_2$ (37.8 mg, 91 μmol) at -20 °C, and the mixture was stirred at -20 °C until the reaction was completed. Ethyl acetate and a saturated aqueous $NaHCO_3$ solution were added and Molecular Sieves 4A was removed by filtration. The organic layer was washed with brine, dried, and concentrated. The product was purified by silica-gel column chromatography (20 g, toluene-AcOEt=12:1) to give **8** as a colorless solid: yield 121 mg (81%).

**A Typical Procedure for α-Glycosidation.** To a solution of phenyl 2,3,4-tri-*O*-benzyl-6-*O*-trichloroethoxycarbonyl-D-thioglucopyranoside (**3**) (130 mg, 181 μmol) and methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**6**) (69.5 mg, 150 μmol) in dry ether (2.0 ml) were added Molecular Sieves 4A (200 mg), PhIO (41.5 mg, 189 μmol), and $AgClO_4$ (76.4 mg, 369 μmol) under $N_2$ atmosphere. To the mixture were added $SbCl_3$ (21.3 mg, 93 μmol) at -20 °C, and the mixture was stirred at -20 °C until the reaction was completed. Ethyl acetate and a saturated aqueous $NaHCO_3$ solution were added and Molecular Sieves 4A was removed by filtration. The organic layer was washed with brine, dried, and concentrated. The product was purified by silica-gel column chromatography (20 g, toluene-AcOEt=12:1) to give **10** as colorless oil: yield 125 mg (78%).

Physical data of following compounds are shown in reference 4: methyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**8**), methyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (**9**), methyl 2,3,4-tri-*O*-benzyl-6-*O*-trichloroethoxycarbonyl-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**10**), methyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**12**), methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**13**).

**Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-trichloroethoxycarbonyl-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (11).** $^1H$ NMR, α-anomer: δ=7.35-7.19 (m, 30H, Ph x 6), 5.58 (d, 1H, $J_{1',2'}$=3.63 Hz, H-1'), 5.03-4.51 (m, 14H, $PhC\underline{H}_2$ x 6, $OC\underline{H}_2CCl_3$), 4.60 (d, 1H, $J_{1,2}$=3.63 Hz, H-1), 4.18 (d, 2H, $J_{5',6'}$ = 2.97 Hz, H-6'), 4.05 (dd, 1H, $J_{2,3}$=$J_{3,4}$=9.24 Hz, H-3), 3.93 (dd, 1H, $J_{2',3'}$=$J_{3',4'}$=9.24 Hz, H-3'), 3.85 (m, 1H, H-5'), 3.58 (dd, 1H, $J_{1,2}$= 3.63 Hz, $J_{2,3}$= 9.24 Hz, H-2), 3.51 (dd, 1H, $J_{3',4'}$=9.24 Hz, $J_{4',5'}$= 7.26 Hz, H-4'), 3.45 (dd, 1H, $J_{1',2'}$=3.63 Hz, $J_{2',3'}$=9.24 Hz, H-2'), 3.38 (s, 3H, OMe); β-anomer: δ=7.42-7.15 (m, 30H, Ph x 6), 5.03-4.51 (m, 14H, $PhC\underline{H}_2$ x 6, $OC\underline{H}_2CCl_3$), 4.59 (d, 1H, $J_{1',2'}$=7.92 Hz, H-1'), 4.57 (d, 1H, $J_{1,2}$=3.96 Hz, H-1), 4.29 (d, 2H, $J_{5',6'}$ = 3,30 Hz, H-6'), 4.07 (dd, 1H, $J_{2',3'}$=$J_{3',4'}$=9.24 Hz, H-3'), 3.83 (dd, 1H, $J_{2,3}$=$J_{3,4}$=9.24 Hz, H-3), 3.66 (dd, 1H, $J_{3,4}$=$J_{4,5}$=9.24 Hz, H-4), 3.56 (m, 1H, H-2'), 3.50 (dd, 1H, $J_{1,2}$=3.96 Hz, $J_{2,3}$=9.24 Hz, H-2), 3.36 (s, 3H, OMe). Found: C, 63.81; H, 5.72. Calcd for $C_{58}H_{61}O_{13}Cl_3{\cdot}1H_2O$: C, 63.88; H, 5.82.

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