A Stereoselective One-stage α-Glucosylation with 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranose and a Mixture of Methanesulfonic Acid, Cobalt(II) Bromide, and Tetraethylammonium Perchlorate

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A one-stage procedure for the stereoselective α-glucosylation of alcohol with 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose and a mixture of methanesulfonic acid, cobalt(II) bromide, and tetraethylammonium perchlorate is described. The mechanism of the glucosylation reaction is discussed.

Continuing effort has been dedicated to developing a variety of stereoselective α-glucosylation methods.[1] The methods employing various kinds of glucosyl halides and equivalents with a non-participating benzyloxyl group at C-2 are most often used for the synthesis of α-glucosides.[2] However, they always require the preparation of the moisture-sensitive glucosylating precursors. Even the one-pot method starting from the stable glucosylating precursor, 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**), involves a two-stage treatment of activation and condensation.[2e]

The glucosylation of alcohol with **1** readily proceeds in one-stage fashion in the presence of methanesulfonic acid ($MeSO_3H$) and $CoBr_2$ in CH_2Cl_2 at 25 °C.[3a] The later improvement[3b] of the stereoselectivity of this reaction using the additive tetraethylammonium perchlorate (Et_4NClO_4) enabled us to develop a simple method for the highly stereoselective α-glucosylation of alcohol with **1** (In Eq. 1, G denotes the 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl group).

$$\alpha\text{GOH} + \text{ROH} \xrightarrow{MeSO_3H/CoBr_2/Et_4NClO_4} \alpha\text{GOR}\ (+\beta\text{GOR}) \quad (1)$$

The method is as handy as the modified Fischer method[4] and is practically free from the moisture problem often encountered in the usual glucosylation, since $CoBr_2$ is a strong desiccant.

Results and Discussion

Glucosylation with $MeSO_3H$ and $CoBr_2$.[3a] When an equimolar mixture of **1**, cyclohexylmethanol, and $CoBr_2$ in CH_2Cl_2 was treated with $MeSO_3H$ at 25 °C, the glucosylation reaction (In Eq. 2, R=cyclohexylmethyl, X=$MeSO_3$) was found to proceed smoothly to give the anomeric glucosides (**2a** and **2b**)

$$\alpha\text{GOH} + \text{ROH} \xrightarrow{HX/CoBr_2} \alpha\text{GOR} + \beta\text{GOR} \quad (2)$$

(Table 1). The yield of the glucosides **2a** and **2b** was maximized at 0.5 h (Runs 1—6). The yield was very dependent on the amount of $MeSO_3H$ (Runs 1, 3, and 5) and moderately dependent on that of $CoBr_2$ (Runs 2, 3, and 4) and of the alcohol (Runs 3 and 6). Too much use of $MeSO_3H$ and the alcohol decreased yields of the glucosides (Runs 5 and 6). No other salts examined so far showed such acceleration effects.[5] Acid such as *p*-toluenesulfonic acid and 2,4,6-trimethylbenzenesulfonic acid were of use, but trifluoroacetic acid was not. As for the solvent, benzene was useful for the reaction. Nitromethane ($MeNO_2$) brought about the stereoselective formation of the α-glucoside **2a**, but the yield was not satisfactory because de-*O*-benzylation reactions occurred concurrently. Even in the use of CH_2Cl_2, trace amounts of by-products such as the de-*O*-benzylation products, cyclohexylmethyl 3,4,6-tri-*O*-benzyl-α- and -β-D-gluco-

Table 1. Results of glucosylation of cyclohexylmethanol (CmOH) with 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**), $MeSO_3H$, and $CoBr_2$ at 25 °C

Run	$MeSO_3H$ equiv.	$CoBr_2$ equiv.	CmOH equiv.	Solvent	Time / h	Yield of the glucosides **2a** and **2b**/%(α/β)	Recovery of **1**/%
1	0.1	1.0	1.0	CH_2Cl_2	0.5	27 (44/56)	68
2	0.3	0.5	1.0	CH_2Cl_2	0.5	29 (55/45)	67
3	0.3	1.0	1.0	CH_2Cl_2	0.5	72 (49/51)	14
4	0.3	2.0	1.0	CH_2Cl_2	0.5	72 (47/53)	15
5	1.0	1.0	1.0	CH_2Cl_2	0.5	51 (59/41)	25
6	0.3	1.0	2.0	CH_2Cl_2	0.5	64 (59/41)	14
7	0.3	1.0	1.0	CH_2Cl_2	2.0	85 (52/48)	1
8	0.3	1.0	1.0	C_6H_6	2.0	82 (54/46)	—[d]
9	0.3	1.0	1.0	CH_3NO_2	2.0	60 (72/28)	—[d]
10[a]	0.3	1.0	1.0	CH_2Cl_2	2.0	75 (53/47)	—[d]
11[b]	0.3	1.0	1.0	CH_2Cl_2	2.0	71 (51/49)	—[d]
12[c]	0.3	1.0	1.0	CH_2Cl_2	2.0	13 (46/54)	39

a) *p*-Toluenesulfonic acid (0.3 equiv.) used instead of $MeSO_3H$. b) 2,4,6-Trimethylbenzenesulfonic acid (0.3 equiv.) used instead of $MeSO_3H$. c) CF_3CO_2H (0.3 equiv.) used instead of $MeSO_3H$. d) Not determined.

Table 2. Results of glucosylation of cyclohexylmethanol with 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**), $MeSO_3H$, $CoBr_2$, and an additive in CH_2Cl_2[a]

Run	Additive	Equiv.	Time / h	Yield of the glucosides, **2a** and **2b**/%(α/β)	Recovery of **1**/%
13[b]	Bu_4NBr	0.5	2.0	65 (52/48)	—
14[b]	Bu_4NBr	1.0	2.0	62 (74/26)	27
15[b]	Bu_4NBr	1.0	4.0	62 (77/23)	30
16[b]	Bu_4NBr	2.0	2.0	5 (80/20)	88
17[b]	$BnEt_3NBr$[e]	1.0	2.0	69 (61/39)	20
18[b]	EtPyBr[e]	1.0	2.0	76 (55/45)	14
19[b]	KBr	1.0	2.0	70 (59/41)	—
20[c]	Et_4NClO_4	0.5	2.0	87 (75/25)	—
21[b]	Et_4NClO_4	1.0	2.0	75 (76/24)	—
22[d]	Et_4NClO_4	1.3	2.0	83 (76/24)	—
23[b]	$LiClO_4$	1.0	2.0	75 (53/47)	—
24[b]	$Et_4NCF_3SO_3$	1.0	2.0	50 (61/39)	—
25[b]	Et_4NBF_4	1.0	2.0	69 (60/40)	—

a) The reaction was conducted at 25 °C. Yields are based on the weight of glucosides obtained compared to the weight of alcohol charged. b) The mole ratio of **1**, $MeSO_3H$, and $CoBr_2$ to alcohol was 1.0, 0.3, and 1.0, respectively. c) The mole ratio of **1**, $MeSO_3H$, and $CoBr_2$ to alcohol was 1.3, 0.3, and 1.0, respectively. d) The mole ratio of **1**, $MeSO_3H$, and $CoBr_2$ to alcohol was 1.3, 0.4, and 1.3, respectively. e) Bn denotes benzyl group and EtPy means *N*-ethylpyridinium ion.

pyranosides (**3a** and **3b**), and the self-condensation products (**4a** and **4b**) of **1**[6a] were isolated from the reaction mixture.[6b]

When the glucosylation of methanol (MeOH) with **1** was carried out at 0 °C, the transient accumulation of the glucosyl bromide (**5**) was observed by means of TLC at the beginning of the reaction (<0.5 h). The ^1H NMR spectrum of the filtrate of the mixture of **1**, $MeSO_3H$, and $CoBr_2$ in CH_2Cl_2 was essentially superimposable with that of the authentic **5** in CH_2Cl_2. Therefore, **5** evidently intervenes in the glucosylation reaction.

The IR spectrum of the solid material recovered from the glucosylation mixture had the characteristic absorption of the salt of $MeSO_3H$ at ν=1180 and 1060 cm^{-1} and the ^1H NMR spectrum of the supernatant of the glucosylation mixture did not show the signal of the methyl group of $MeSO_3H$ near at δ 3.2. Moreover, it was found that $MeSO_3H$ and $CoBr_2$ reacted to afford the solid material whose composition was $CoBr_{2-x}(CH_3SO_3)_x$. Consequently, $MeSO_3H$ surely reacts with $CoBr_2$ to generate HBr (Eq. 3) during the glucosylation reaction.

$$CoBr_2 + xMeSO_3H \longrightarrow CoBr_{2-x}(MeSO_3)_x + xHBr \quad (3)$$

It was then confirmed that the glucosylation of MeOH with **1** proceeds well in the presence of $CoBr_2$ and HBr (In Eq. 2, R=Me, X=Br) and $CoBr_2$ accelerates the alcoholysis of **5** with cyclohexylmethanol.[7a] It is concluded that HBr generated *in situ* cooperates with $CoBr_2$ to convert **1** efficiently into **5** (Eq. 4a), which then undergoes alcoholysis (Eq. 4b). Figure 1 presents a summarized scheme for the one-stage glucosylation of alcohol using **1** and the mixture of $MeSO_3H$ and $CoBr_2$.[7b]

$$\alpha GOH \xrightarrow[-H_2O]{\text{a) HBr/CoBr}_2} \alpha GBr \xrightarrow[-HBr]{\text{b) ROH/CoBr}_2} \alpha GOR + \beta GOR \quad (4)$$

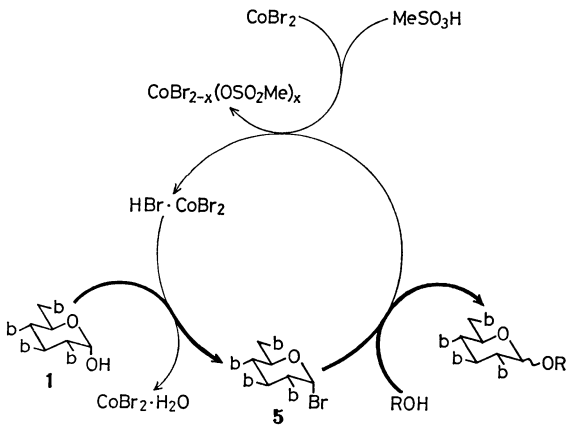


Fig. 1. Summarized scheme of the glucosylation reaction of alcohol with 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose using the mixture of methanesulfonic acid and cobalt(II) bromide.

Improvement of the Stereoselectivity of the Glucosylation.[3b] Since the glucosyl bromide **5** intervenes in the glucosylation reaction (Fig. 1), tetrabutylammonium bromide (Bu_4NBr) and relatives were added into the reaction mixture, because it was anticipated that they cause the bromide ion-catalyzed stereoselective α-glucosylation[2c] (Table 2). The addition of Bu_4NBr caused the predominant formation of the α-glucoside **2a**, but with a decrease of the yields of **2a** and **2b** (Runs 13—15). Excessive use of Bu_4NBr sharply decreased the yield of glucosides; two molar amounts of Bu_4NBr almost inhibited the reaction (Run 16). This is attributable to the fact that two molar amounts of Bu_4NBr interrupts the formation of **5** from **1**, because the bromide anion strongly coordinates with $CoBr_2$ to form $[CoBr_3]^-$ and/or $[CoBr_4]^{2-}$, in competition with $MeSO_3H$ (*cf.* Eq. 2).[8] Other bromides showed simi-

lar tendencies, but the effects were weaker than for Bu_4NBr.

Next, effects of Et_4NClO_4 and related substances on the selectivity of the glucosylation were examined, because the perchlorate anion has poor coordinating ability to $CoBr_2$[9] and the glucosyl perchlorates with a benzyloxyl group at C-2 undergo the stereoselective α-glucosylation[2b] (Runs 20—25). Among the salts used, Et_4NClO_4 sharply increased the proportion of the α-anomer **2a** without serious decrease of the yield of the glucosides. The difference in the coordinating ability to $CoBr_2$ between perchlorate anion (weaker) and bromide anion (stronger)[7b] promotes the formation of the glucosyl perchlorate as in Eq. 5, so that the perchlorate anion does not interrupt the whole reaction. The effect of other salts was similar but feeble (Runs 23—25).

$$\alpha GOH + Et_4N^+//ClO_4^- + CoBr_2 \longrightarrow G^+//ClO_4^- + Et_4N^+//[CoBr_3]^- \quad (5)$$

Finally, the extent of the anomerization of the β-glucoside **2b** was determined under the three glucosylation conditions described above (Table 3). Because **2b** did not anomerize into **2a** so much in the presence of $MeSO_3H$, $CoBr_2$, and Bu_4NBr (Run 27), most of **2a** seems to be formed *via* the bromide ion-catalyzed alcoholysis of **5**, in the glucosylation (Run 14) of cyclohexylmethanol with **1** and this reagent mixture. In contrast to this, the mixture of $MeSO_3H$, $CoBr_2$, and Et_4NClO_4 in CH_2Cl_2 anomerized **2b** into **2a** efficiently (Run 28) (Eq. 6). The composition of the anomeric glucosides of the anomerization mixture was almost identical with that of the glucosylation mixture of the alcohol with **1** and this ternary mixture (Run 21). Therefore, this glucosylation furnishes an equilibrium mixture of the anomeric glucosides like the Fischer glucosylation does. It is noted that the mixture of $MeSO_3H$ and $CoBr_2$ in $MeNO_2$ smoothly anomerized **2b** and the composition of the anomeric glucosides was equal to that of the glucosylation mixture in $MeNO_2$ containing this binary mixture (Run 9). In this case, the high solubility of $CoBr_2$ in $MeNO_2$ may greatly enhance the polarity of the medium. This promotes the formation of the glucosyl cation G^+ to attain the anomerization of **2b** with $MeSO_3H$. Based on the results described so far, the mechanism of the stereoselective α-glucosylation affording the equilibrium mixture of the anomeric glucosides is postulated in Fig. 2.

$$\beta GOR \xrightarrow{MeSO_3H/CoBr_2/Et_4NClO_4} \alpha GOR \quad (6)$$

Table 3. Anomerization of cyclohexylmethyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (**2b**) in various conditions[a]

Run	Additive, equiv.	Solvent	Yield of glucosides (**2a**, **2b**) %	(α/β)
26	None	CH_3NO_2	54	(74/26)
27	Bu_4NBr, 1.0	CH_2Cl_2	74	(12/88)
28	Et_4NClO_4, 1.0	CH_2Cl_2	74	(78/22)

a) The reaction was conducted for 2 h at 25 °C. The mole ratios of $MeSO_3H$ and $CoBr_2$ to the glucoside **2b** were 0.3 and 1.0.

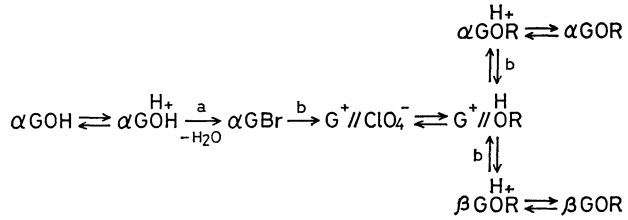


Fig. 2. Scheme of the stereoselective α-glucosylation of alcohol with 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose using the mixture of methanesulfonic acid, cobalt(II) bromide, and tetraethylammonium perchlorate (**a** denotes the step which may be assisted by $CoBr_2$ and **b** does the one which may be promoted be $CoBr_2$ and ClO_4^-).

Table 4. Results of glucosylation of various alcohols through the ternary system[a]

Alcohol	Glucosides obtained	Yield of glucosides %	(α/β)
1-Hexanol[b]	**7a, 7b**	83	(73/27)
1-Octanol[b]	**8a, 8b**	82	(75/25)
1-Dodecanol[b]	**9a, 9b**	80	(77/23)
Cyclohexylmethanol[b,d]	**2a, 2b**	83	(76/24)
6-(2,4-Dinitroanilino)-1-hexanol[b,d]	**10a, 10b**	88	(71/29)
Cyclopentanol[c]	**11a, 11b**	85	(72/28)
Cyclohexanol[c,d]	**12a, 12b**	83	(80/20)
Cyclooctanol[d]	**13a, 13b**	78	(77/23)
Cyclododecanol[c]	**14a, 14b**	80	(74/26)
5α-Cholestan-3β-ol[c,d]	**15a, 15b**	63	(79/21)

a) The reaction was conducted on a 0.5 mmol scale in CH_2Cl_2 for 2 h at 25 °C. Yields were based on the weight of glucosides compared to the weight of alcohol charged. b) Mole ratios of **1**, $MeSO_3H$, $CoBr_2$, and Et_4NClO_4 to alcohol were 1.3, 0.4, 1.3, and 1.3. c) Mole ratios of **1**, $MeSO_3H$, $CoBr_2$, and Et_4NClO_4 to alcohol were 1.3, 0.3, 1.3, and 0.5. d) Anomeric glucosides obtained were identified with the samples prepared by alternative methods (Ref. 11).

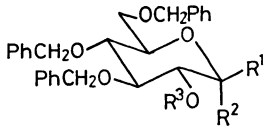
This one-stage stereoselective α-glucosylation was applied to several alcohols to give the results summarized in Table 4. For practical use, slightly excess amounts of **1**, $CoBr_2$, and Et_4NClO_4 were charged in the case of primary alcohols (Runs 22, 29—32). Because of the high susceptibility of the glucoside of secondary alcohols to the anomerization,[10] smaller amounts of Et_4NClO_4 was used in the glucosylation of such alcohols (Runs 33—37).

Experimental

Instruments used are identical with those described previously.[6a] Green-colored anhydrous $CoBr_2$ (Wako) was stored over P_2O_5. The acid $MeSO_3H$ (Tokyo Kasei) was used without any pretreatments. The additives Et_4NClO_4 (Tokyo Kasei) and Bu_4NBr (Tokyo Kasei), recrystallized from acetonitrile containing hexane, were used after being stored *in vacuo* over P_2O_5 for several days. The pre-distilled

Table 5. Physical and analytical data of alkyl D-glucoside derivatives

Compd	Mp θ_m/°C	$[\alpha]_D^{20}$/° (c, $CHCl_2$)	Found (%) C	Found (%) H	Molecular formula	Calcd (%) C	Calcd (%) H
7a	—	+32 (0.5)	76.71	7.76	$C_{40}H_{48}O_6$	76.89	7.74
7b	35—37	+6 (0.6)	76.97	7.68			
8a	—	+32 (0.7)	77.24	8.01	$C_{42}H_{52}O_6$	77.27	8.03
8b	30—32	+8 (0.9)	77.43	8.13			
9a	—	+30 (0.6)	77.82	8.63	$C_{46}H_{60}O_6$	77.93	8.53
9b	—	+5 (0.5)	77.79	8.70			
11a	—	+41 (1.8)	76.76	7.33	$C_{39}H_{44}O_6$	76.94	7.29
11b	102—103	+9 (0.6)	76.72	7.29			
13a	—	+50 (2.0)	77.39	7.72	$C_{42}H_{50}O_6$	77.51	7.74
13b	87—88	+6 (0.7)	77.46	7.81			
14a	—	+49 (2.0)	78.05	8.40	$C_{46}H_{58}O_6$	78.15	8.27
14b	96—97	+3 (1.0)	78.13	8.21			



Compd	R^1	R^2	R^3	Compd	R^1	R^2	R^3
1	H	OH	Bn	**9a**	H	ODd	Bn
2a	H	OCm	Bn	**9b**	ODd	H	Bn
2b	OCm	H	Bn	**10a**	H	ODh	Bn
3a	H	OCm	H	**10b**	ODh	H	Bn
3b	OCm	H	H	**11a**	H	OCp	Bn
4a	H	OαG	Bn	**11b**	OCp	H	Bn
4b	OαG	H	Bn	**12a**	H	OCh	Bn
5	H	Br	Bn	**12b**	OCh	H	Bn
6a	H	OMe	Bn	**13a**	H	OCoc	Bn
6b	OMe	H	Bn	**13b**	OCoc	H	Bn
7a	H	OHx	Bn	**14a**	H	OCdd	Bn
7b	OHx	H	Bn	**14b**	OCdd	H	Bn
8a	H	OOc	Bn	**15a**	H	OCt	Bn
8b	OOc	H	Bn	**15b**	OCt	H	Bn

Bn = benzyl, Ch = cyclohexyl, Cm = cyclohexylmethyl, Coc = cyclooctyl, Cp = cyclopentyl, Ct = 5α-cholestan-3β-yl, Dd = dodecyl, Dh = 6-(2,4-dinitroanilino)-1-hexyl, αG = 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl, Hx = hexyl, Me = methyl, Oc = octyl.

solvents were stored over Molecular Sieve (Linde 3A). Tetraethylammonium trifluoromethanesulfonate and tetrafluoroborate were prepared by the treatment of Et_4NBr with CF_3SO_3Ag (Alpha) and with $AgBF_4$ (Wako), respectively, in dry MeOH followed by evaporation *in vacuo*. Compound **1**, 6-(2,4-dinitroanilino)-1-hexanol, 5α-cholestan-3β-ol (Tokyo Kasei) were stored *in vacuo* over P_2O_5. Column chromatography of the pre-processed mixture of products was done on silica gel (Kanto Kagaku) using the solvent system of hexane and ethyl acetate, unless otherwise stated; each fraction was examined by TLC on silica gel (Merck, 7731). Evaporation was carried out under reduced pressure at 35—40 °C, unless otherwise stated. Table 5 summarized the physical and analytical data of newly synthesized compounds.

The Procedure for the Glucosylation with 2,3,4,6-Tetra-O-benzyl-α-D-glucopyranose (1), $MeSO_3H$, and $CoBr_2$. The acid $MeSO_3H$ (3.2 μl, 0.05 mmol) was added to a stirred mixture of **1** (90 mg, 0.17 mmol), $CoBr_2$ (36.5 mg, 0.17 mmol) and cyclohexylmethanol (20.5 μl, 0.17 mmol) in CH_2Cl_2 (0.45 ml). After being vigorously stirred at 25 °C for 2 h, the mixture was diluted with benzene, followed by the addition of powdered $NaHCO_3$ with agitation. The filtrate was evaporated and chromatographed to give cyclohexylmethyl 2,3,4,6-tetra-*O*-benzyl-α- and -β-D-glucopyranoside (**2a** and **2b**) and the by-products.[6] The glucosides (**2a** and **2b**) and the self-condensation products (**4a** and **4b**) were identified by comparison with those reported.[6a,11] Yields are based on the weight of products obtained, with reference to the weight of **1** charged. The results are summarized in Table 1.

The Glucosylation of MeOH with the Benzylated Glucose 1, $MeSO_3H$, and HBr. A cooled saturated solution of HBr in CH_2Cl_2 (0.64 M, 0.28 ml) was added into a stirred mixture of **1** (90 mg, 0.17 mmol), $CoBr_2$ (36.5 mg, 0.17 mmol), and MeOH (7 μl, 0.17 mmol) in CH_2Cl_2 (0.45 ml). After being agitated for 2 h at 25 °C, the mixture was processed as above to afford methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (**6a**) (30 mg, 33%) and the β-anomer **6b** (26 mg, 28%), identified with those reported.[6a] Some unchanged **1** was recovered (21 mg, 23%).

Without $CoBr_2$, the anomeric mixture of **6a** and **6b** was obtained in 15% yield (α/β = 70/30) and **1** was recovered (83%).

The Formation of 2,3,4,6-Tetra-O-benzyl-α-D-glucopyranosyl Bromide (5) from the Benzylated Glucose 1 with $MeSO_3H$ and $CoBr_2$. A mixture of **1** (90 mg, 0.17 mmol), $MeSO_3H$ (11 μl, 0.17 mmol), and $CoBr_2$ (36.5 mg, 0.17 mmol) in CH_2Cl_2 (0.45 ml) was stirred for 1 h at 25 °C. The insoluble material was filtered, washed with CH_2Cl_2, and ignited at 110 °C *in vacuo*; IR (KBr) 1345 (Me), 1180, 1060 cm^{-1} (SO_3). Found: C, 7.07; H, 2.08; Br, 18.07%. Calcd for $CoBr_{0.55}(CH_3SO_3)_{1.45}$: C, 7.23; H, 1.82; Br, 18.25%. The ^1H NMR of the filtrate was essentially the same as that of **5** prepared *via* the treatment of ethyl 2,3,4,6-tetra-*O*-benzyl-1-thio-α-D-glucopyranoside[12] (49 mg, 0.083 mmol) in CH_2Cl_2 (0.5 ml) with a solution of Br_2 in CH_2Cl_2 (60% w/v, 27 μl) for 10 min in the dark, followed by the quick evaporation at 60 °C; δ = 6.59 (d, *J* = 4.0 Hz, H-1 of **5**).

When Bu_4NBr (107 mg, 0.33 mmol) was added to the reaction mixture prior to the addition of $MeSO_3H$, ^1H NMR of the filtrate indicated that **5** did not form (the signal at δ 6.59 was absent).

The Procedure for the Glucosylation with the Benzylated Glucose 1, $MeSO_3H$, $CoBr_2$, and Additive. To a mixture of **1** (90 mg, 0.17 mmol), $CoBr_2$ (36.5 mg, 0.17 mmol), an additive, and an alcohol (0.17 mmol) in a solvent (0.45 ml), $MeSO_3H$ (3.3 μl, 0.050 mmol) was added under stirring. After agitation for 2 h at 25 °C, the mixture was processed

and then chromatographed as described above. The results are summarized in Tables 2 and 4.

*Synthesis of Cyclohexylmethyl 3,4,6-Tri-O-benzyl-α- and -β-D-glucopyranose(**3a** and **3b**), Which Were Isolated from the Reaction Mixture of the Glucosylation of Cyclohexylmethanol with the Benzylated Glucose **1**.* 3,4,6-Tri-*O*-benzyl-α-D-glucopyranose[13] (450 mg, 1.0 mmol) was condensed with cyclohexylmethanol (124 μl, 1.0 mmol) in CH_2Cl_2 (2.5 ml) in the presence of $MeSO_2H$ (20 μl, 0.3 mmol) and $CoBr_2$ (219 mg, 1.0 mmol) at 25 °C for 2 h. After processing, the mixture was chromatographed (benzene–2-butanone, gradient, 100:1→10:1) to afford the β-anomer **3b** (107.5 mg, 20%); colorless needles, mp 89.5—91 °C, $[\alpha]_D^{20}$ −8° (*c* 1.0, $CHCl_3$), and then the α-anomer **3a** (199.5 mg, 37%); $[\alpha]_D^{20}$ +84° (*c* 1.0, $CHCl_3$). Found: (**3a**) C, 74.03; H, 7.74%. (**3b**) C, 75.00; H, 7.83%. Calcd for $C_{34}H_{42}O_6$: C, 74.70; H, 7.74%.

The Reaction of $CoBr_2$ with $MeSO_3H$ in CH_2Cl_2. A suspension of $CoBr_2$ (43.6 mg, 0.2 mmol) in CH_2Cl_2 (0.54 ml) was treated with $MeSO_3H$ (0.2—0.4 mmol) at 25 °C for 1 h under vigorous stirring. The solid material was collected, washed with dry CH_2Cl_2 (0.3 ml×7), and ignited *in vacuo* at 110 °C over P_2O_5. In each case, the evolution of HBr was seen at the removal of the stopper of the vessel and the filtrate precipitated AgBr on addition of aq $AgNO_3$. The solid material obtained was analyzed to afford the following data [the amount of $MeSO_3H$ (mmol), analysis]: 13 μl (0.2). Found: C, 5.08; H, 1.36; Br, 30.37%. Calcd for $CoBr_{0.92}(CH_3SO_3)_{1.08}$: C, 5.52; H, 1.39; Br, 31.29%. 26 μl (0.4). Found: C, 7.47; H, 2.14; Br, 17.19%. Calcd for $CoBr_{0.50}(CH_3SO_3)_{1.50}$: C, 7.46; H, 1.89; Br, 16.54%.

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5) The following salts gave **2a** and **2b** in, at best, poor yields (<10%) when the equimolar mixture of **1**, $MeSO_3H$, a salt, and cyclohexylmethanol in CH_2Cl_2 was stirred for 2 h at 25 °C: $CoCl_2$, $CoSO_4$, $Co(MeSO_3)_2$, $NiBr_2$, $CuBr_2$, $HgBr_2$, $CdBr_2$, $ZnBr_2$, $CaBr_2$, $MnBr_2$, $MgSO_4$, and $CaSO_4$.

6) a) S. Koto, N. Morishima, and S. Zen, *Bull. Chem. Soc. Jpn.*, **52**, 784 (1979); b) For example, the isolated by-products of Run 7 were **4a**(5%), **4b**(2.6%), **3a**(3.8%), and **3b**(0.8%).

7) a) Stirring the equimolar mixture of $CoBr_2$, cyclohexylmethanol, and the glucosyl bromide **5** in CH_2Cl_2 for 2 h at 25 °C gave **2a** and **2b** in a 70% yield (α/β=54/46) and the de-*O*-benzylation products; b) The fact that $CoBr_2$ coordinates reversibly with alcohol but irreversibly with H_2O [K. Sone, T. Fukuda, J. Mizusaki, and K. Moriyama, *Monatsh. Chem.*, **107**, 271 (1976)] and selectively coordinates with Br^- in the presence of alcohol [D. L. Wertz and R. F. Kruh, *Inorg. Chem.*, **9**, 595 (1970); S. Buffagni and R. M. Dunn, *J. Chem. Soc.*, **1961**, 5105] appears important for the glucosylation to proceed. The order of the affinity of nucleophiles to $CoBr_2$ in CH_2Cl_2 may be: $H_2O \gg Br^- > ROH > ClO_4^-$.

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