A New Efficient Method for Catalytic Hydrolysis of Thioglycoside

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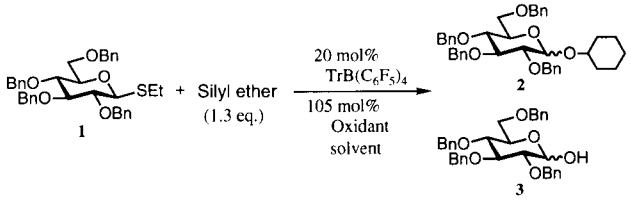
A new and efficient method for catalytic hydrolysis of thioglycosides was successfully developed. Various thioglycosides were smoothly hydrolyzed to afford the corresponding 1-hydroxy sugars in high yields. The hydrolysis of disaccharides was took place smoothly without accompanying no anomerization of existing glycosidic bond.

Suitable selection of anomeric protective group is one of the most important problems in planning a strategy for synthesizing complex saccharide chains. Of various protecting groups, thioglycoside linkages have widely been used because of their availability and stability under various reaction conditions such as in protection or deprotection steps of hydroxyl groups of saccharide molecules.[1] Thioglycosides are also effectively employed as glycosyl donors in many stereoselective glycosylation reactions.[2] Recently, thioglycosides were applied in solid phase saccharide synthesis for binding a saccharide molecule to polymer chain.[3] Therefore, thioglycosides are expected to contribute a great deal when used as anomeric protective group. Conventional methods for effective deprotection (hydrolysis) of thioglycosides are carried out using a stoichiometric amount of thiophilic reagent such as heavy metal salts[4] or *N*-bromosuccinimide[5] where yields are not always high enough under the above conditions. Therefore, the method for deprotection of thioglycosides needs to be improved to proceed under milder reaction condition. In this communication, we would like to report a new and efficient method for catalytic and high-yielding hydrolysis of various thioglycosides.

In the previous paper, a new and efficient method for catalytic and stereoselective glycosylation of thioglycosides with various glycosyl acceptors was reported.[6] In the reaction, various 1,2-*trans*-glycosides were obtained in high yields with high stereoselectivities from simple alkylthioglycosides by the combined use of a catalytic amount of trityl tetrakis(pentafluoro phenyl)borate, a Lewis acid catalyst, and sodium periodate, an oxidant. This new catalytic system enabled catalytic and irriversible activation of thioglycosides to afford the desired glycosides smoothly. During the continued study of this reaction, a very interesting result was observed: that is, the desired glycosylation of trimethylsilyl ether of cyclohexanol with ethyl 1-thio-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside **1** did not proceed at all when tetra-*n*-butylammonium periodate[7] was used as an oxidant instead of sodium periodate. On the other hand, 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose **3** was exclusively obtained in good yield unexpectedly (Table 1). Next, hexamethyldisiloxane was used instead of trimethylsilyl ether of cyclohexanol, and then hydrolysis of thioglycoside **1** was found also to proceed smoothly in acetonitrile at 0 °C and the corresponding 1-hydroxy sugar **3** was obtained in high yield. The above observation led us to study of a new method for catalytic hydrolysis of thioglycosides.

Table 1. Discovery of new condition for hydrolysis of thioglycoside



Oxidant	Silyl ether	Solvent	Temp.	Time /min.	Yield 2/%	3/%
$NaIO_4$	Me_3SiO-⬡	^{t}BuCN	r.t.	120	80[a,b]	5
$^n Bu_4NIO_4$	Me_3SiO-⬡	^{t}BuCN	r.t.	20	0	81
$^n Bu_4NIO_4$	$Me_3SiOSiMe_3$	MeCN	0 °C	20	-	90

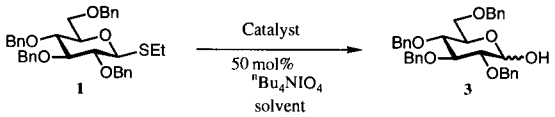
[a] This reaction condition is not optimized one for the glycosylation (see reference 6). [b] α / β = 14 / 86.

In the first place, several reaction conditions were screened (Table 2). In the absence of hexamethyldisiloxane, yellow color of the reaction mixture changed to brown rather rapidly probably because the trityl cation scavenged by iodine generated from tetra-*n*-butylammonium periodate and thus the yield of 1-hydroxy sugar significantly lowered. When more bulky nitrile solvent such as propionitrile and a mixture of pivalonitrile-dichloromethane (3/1) gave only poor yield. These results indicated that this hydrolysis proceeded via stabilized nitrilium-nitrile conjugate-type intermediate[8] which was in turn hydrolyzed on aqueous quenching. The concentration of substrate and reaction temperature were very influential to the yield and the best result was obtained when 0.011M of thioglycoside hydrolyzed at -10 °C. Several catalysts were also screened and the use of 30 mol% of trityl tetrakis(pentafluorophenyl)borate gave the best yield in non-aqueous condition. On the other hand, 70% aqueous solution of superacids such as trifluoromethanesulfonic acid and perchloric acid were also effective for the above hydrolysis. Such aqueous conditions are more desireble because the hydrolyzed product was obtained in high yield without using hexamethyldisiloxane with easy operation.

Next, optimization of reaction conditions using the aqueous acid catalyst was tried (Table 3). The best result was obtained when 20 mol% of catalyst was used, and the amount of tetra-*n*-butylammonium periodate could be reduced down to 40 mol%.

Several examples of the present hydrolysis of thioglycoside are demonstrated in Table 4. In every case, the corresponding 1-hydroxy sugar was obtained in high yield. It is noted that, several thioglycosides of disaccharide were hydrolyzed in high yields without accompanying the anomerization of existing glycoside bonds.

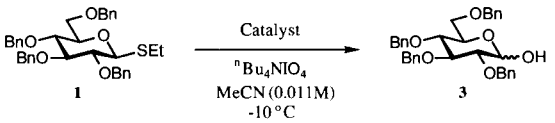
Table 2. Screening of reaction conditions



Catalyst (mol%)	$(Me_3Si)_2O$ /eq.	Solvent	Conc. /M	Temp. /°C	Time /min.	Yield /%
$TrB(C_6F_5)_4$ (30)	3.0	MeCN	0.011	-10	30	**93**
$TrB(C_6F_5)_4$ (30)	2.0	MeCN	0.011	-10	55	82
$TrB(C_6F_5)_4$ (30)	None	MeCN	0.011	-10	120	38
$TrB(C_6F_5)_4$ (30)	3.0	EtCN	0.011	-10	60	52
$TrB(C_6F_5)_4$ (30)	3.0	Mix.[a]	0.011	-10	80	56
$TrB(C_6F_5)_4$ (30)	3.0	MeCN	0.010	-10	80	87
$TrB(C_6F_5)_4$ (30)	3.0	MeCN	0.013	-10	80	86
$TrB(C_6F_5)_4$ (30)	3.0	MeCN	0.013	0	35	77
$TrB(C_6F_5)_4$ (30)	3.0	MeCN	0.013	-20	60	82
$TrB(C_6F_5)_4$ (20)	3.0	MeCN	0.011	0	120	74
$TrSbCl_6$ (30)	3.0	MeCN	0.011	-10	70	64
Me_3SiOTf (30)	3.0	MeCN	0.011	-10	60	62
TfOH (30)	3.0	MeCN	0.011	-10	35	78
70% TfOH[b] (30)	None	MeCN	0.011	-10	65	**91**
70% $HClO_4$[b] (30)	None	MeCN	0.011	-10	75	**95**

[a] Mix. = ^{t}BuCN - CH_2Cl_2 (v/v = 3/1).
[b] Aqueous solution.

Table 3. Optimization of reaction condition

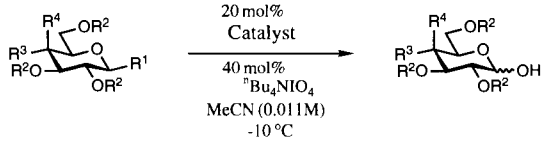


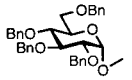
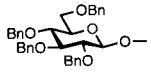
Catalyst (mol%)	$^nBu_4NIO_4$/mol%	Time/min.	Yield/%
TfOH (70% aq.) (10)	50	120	63
TfOH (70% aq.) (20)	50	70	**95**
TfOH (70% aq.) (30)	50	65	91
TfOH (70% aq.) (20)	40	75	**97**
TfOH (70% aq.) (20)	30	80	83
$HClO_4$ (70% aq.) (30)	50	75	**95**
$HClO_4$ (70% aq.) (20)	40	75	**94**

A typical experimental procedure is as follows: a stirred mixture of ethyl 1-thio-2,3,4,6-tetra-*O*-benzyl-β-D-gluco pyranoside (58.5 mg, 0.10 mmol) and 70% aqueous solution of trifluoromethanesulfonic acid (4.29 mg, 0.02 mmol) in acetonitrile (8.0 ml) was cooled down to -10 °C. An acetonitrile (1.0 ml) solution of tetra-*n*-butylammonium periodate (17.3 mg, 0.04 mmol) was rapidly added to the above mixture and stirred for 75 min at -10 °C. Then the mixture was quenched by adding saturated aqueous sodium hydrogen carbonate (5 ml). The mixture was extracted with dichloromethane (30 ml), and the organic layer was separated, which was successively washed with 10% aqueous sodium thiosulfate, water and brine (each of 20 ml). After drying and evaporation, the resulting residue was purified by preparative TLC (silica gel), 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (52.3 mg, 97% yield) was isolated.

Thus, a new and efficient method for catalytic and high-yielding hydrolysis of thioglycosides was successfully developed. It is noted that this new hydrolysis condition has great advantages over the conventional methods in its efficiency and easy operation.

Table 4. Hydrolysis of various thioglycosides



R^1	R^2	R^3	R^4	Catalyst	Yield/%
SEt	Bn	OBn	H	A	97
SEt	Bn	OBn	H	B	94
SMe	Bn	OBn	H	A	92
SPh	Bn	OBn	H	A	93
	Bn	OBn	H	A	93
SEt	Bn	H	OBn	A[a,b]	87
SEt	Bn	H	OBn	B[a,b,d]	94
SEt	Bz	OBz	H	A[a,b]	87
SEt	Bz	OBz	H	B[a,b,d]	94
SEt	Ac	OAc	H	B	94
SEt	Bn		H	A[b]	91
SEt	Bn		H	A[a,c,d]	95

Catalyst A: TfOH (70% aq.), Catalyst B: $HClO_4$ (70% aq.)
[a] The reaction was carried out at 0 °C.
[b] 30 mol% of catalyst was used.
[c] The reaction was carried out at 0.009M.
[d] A solution of the catalyst was finally added to the reaction mixture.

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References and Notes

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