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AN EFFICIENT GLUCOSYLATION OF ALCOHOL USING 1-THIOGLUCOSIDE DERIVATIVE

Teruaki MUKAIYAMA, Takashi NAKATSUKA, and Shin-ichiro SHODA
Department of Chemistry, Faculty of Science
The University of Tokyo, Hongo, Tokyo 113

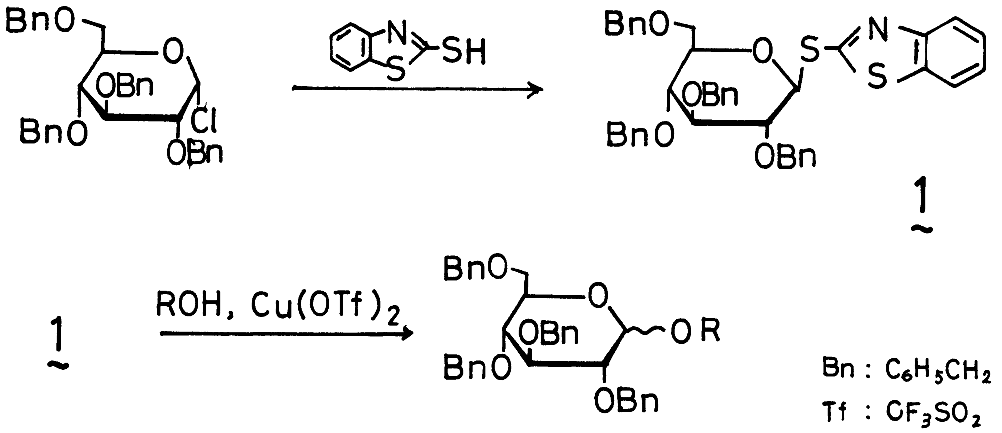
Glucosides and disaccharides were prepared in good yields from 2-benzothiazolyl 2,3,4,6-tetra-O-benzyl-1-thio-D-glucopyranoside and alcohols including sterically hindered secondary alcohols in the presence of cupric triflate. α-Glucosides were obtained predominantly by this method.

In recent years, glycosides especially di- and oligo-saccharides became to be interesting substances owing to their biochemical and pharmacological importance as antibiotics and antigens etc., and there appeared many reports$^{1)}$ on the synthesis of these complex compounds. While synthetic method of 1,2-trans-glycosides is established as Koenigs-Knorr reaction or its modifications, highly stereochemically controlled synthesis of 1,2-cis-glycosides still remains unresolved, and an efficient condensation reaction is strongly desired.

Recently we have shown that the onium salts of azaaromatics such as 1-alkyl-2-halopyridinium salts$^{2a)}$ or 3-ethyl-2-chlorobenzoxazolium salt$^{2b)}$ react with alcohols to afford 2-alkoxy-1-alkylpyridinium salts or 2-alkoxy-3-ethylbenzoxazolium salts and these active intermediates react with various nucleophiles to give the corresponding condensation products in high yields. It may be assumed that the active intermediates, similar to the onium salt, can be generated from alkoxyazaaromatics themselves by interaction of proton$^{3a)}$ or metal salts$^{3b)}$ with the ring nitrogen atom.

Taking these results into consideration, we investigated a new glycosylation reaction, and in the present communication we report an efficient method for the preparation of D-glucosides from 2-benzothiazolyl 2,3,4,6-tetra-O-benzyl-1-thio-β-

D-glucopyranoside(1) and various alcohols including sterically hindered secondary alcohols in the presence of cupric triflate[4,5)] as a metal salt as shown in the following equation.



Cupric triflate was used to promote the reaction and to scavenge 2-mercaptobenzothiazole formed in the course of the reaction.

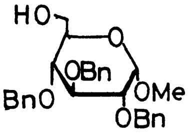
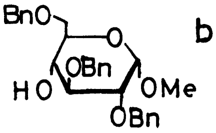
Compound 1 was prepared by the following procedure; to a dry dichloromethane solution of 2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl chloride[6)] (1 equiv) and 2-mercaptobenzothiazole (1.8 equiv) was added a dichloromethane solution of 1,8-bis-(dimethylamino)naphthalene (1.2 equiv) and stirred for 24 h under argon. The resulting solution was successively treated with dilute hydrochloric acid (5%), 2 N sodium hydroxide solution, and then water, and dried over sodium sulfate. After evaporation of the solvent, the residue was purified by column chromatography (silica gel) to afford a crystalline substance 1[7)] (80%, m.p. 91.5-93.0°, recrystallized from ethanol, $[\alpha]_D^{20}$ -23°(c 1.0, $CHCl_3$)). This material was stable under argon at room temperature.

A typical procedure is described for the reaction of 1 with 3β-cholestanol. To a dry ether solution of 1 (0.29 mmol) and 3β-cholestanol (0.26 mmol) were added cupric triflate (0.30 mmol), cupric oxide, and 4 A molecular sieves under argon, agitated for 16 h at room temperature,and neutralized with triethylamine. After insoluble materials[8)] were removed by filtration, the filtrate was evaporated and the residue was purified by column chromatography (silica gel)to give 3β-cholestanyl 2,3,4,6-tetra-O-benzyl-α-D-glucopyranoside (65%, m.p. 117.5-119.0°, $[\alpha]_D^{26}$+65.1° (c 1.06, $CHCl_3$)), and β-D-anomer (14%, m.p. 93.5°, $[\alpha]_D^{23}$+20.2° (c 1.04, $CHCl_3$)).

In a similar manner, three glucosides were obtained in good yields as shown in Table.

Table

Glucosylasion of Various Alcohols Using 1-Thioglucoside Derivative 1

Alcohol	Time	Yield (%)	α/β a)
MeOH	3 h	93	70/30
 b)	24 h	92	80c)/20
Cholestanol	24 h	79	83d)/17
 b)	24 h	73	67c)/33

a) These compounds were purified by column chromatography and were identified by ^{1}H-NMR spectra.

b) J. M. Kuster and I. Dyong, Justus Liebigs Ann. Chem., 1975, 2179.

c) These compounds were identified by physical constants reported by P.Sinaÿ et al.1)

d) The structure of this compound was confirmed by ^{13}C-NMR spectrum.

It is noted that, according to the present procedure, α-glucosides were obtained predominantly from alcohols and 1-thioglucoside 1, easily prepared from 2-mercaptobenzothiazole and glucopyranosyl chloride derivative.

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References and Notes

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2) a) T. Mukaiyama and M. Imaoka, Chem. Lett., 1978, 413; and references cited therein.

b) T. Mukaiyama, S. Shoda, and Y. Watanabe, Chem. Lett., 1977, 383.

3) a) Y. Watanabe and T. Mukaiyama, Chem. Lett., 1978, 349.

b) T. Mukaiyama, M. Yamaguchi, and K. Narasaka, Chem. Lett., 1978, 689.

4) C. L. Jenkins and J. K. Kochi, J. Am. Chem. Soc., 94, 843 (1972).

5) Good results could not be obtained when other copper salts, such as cupric acetate, cupric tosylate, cupric chloride, and cupric tetrafluoroborate were used.

6) P. W. Austin, F. H. Hardy, J. G. Buchanan, and J. Baddiley, J. Chem. Soc., 1964, 2128.

7) The structure of this compound was determined according to elemental analysis and spectroscopic data (^{1}H-, ^{13}C-NMR, IR, UV). The configuration of anomeric carbon was tentatively determined by ^{1}H-NMR [($CDCl_3$) 5.22 ppm (J=8 Hz)].

8) These materials were cupric oxide, copper-mercaptobenzothiazole complex,and molecular sieves.

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