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DIRECT GLUCOSIDATION OF TETRA-O-BENZYL-α-D-GLUCOPYRANOSE BY SYSTEM OF METHANESULFONIC ACID AND COBALT(II) BROMIDE

Shinkiti KOTO, Naohiko MORISHIMA, and Shonosuke ZEN
School of Pharmaceutical Sciences, Kitasato University
Shirokane, Minato-ku, Tokyo 108

A novel method for glucosidation of 2,3,4,6-tetra-O-benzyl-α-D-glucopyranose by a system of methanesulfonic acid and cobalt(II) bromide in dichloromethane at a room temperature is described.

Poly-O-benzyl-glycose has been one of the important synthetic intermediates in the glycoside synthesis.[1] Recently, several reports on the direct method for the glucosidation of 2,3,4,6-tetra-O-benzyl-α-D-glucopyranose (I) have appeared.[2,3] We now wish to present a new system suitable for the direct glucosidation of I, consisting of methanesulfonic acid and cobalt(II) bromide, formulated as (1).

$$\alpha\text{GOH} + \text{ROH} \xrightarrow[CH_2Cl_2]{MsOH/CoBr_2} \alpha\text{GOR} + \beta\text{GOR}; \quad \alpha(\beta)\text{G} = \text{Tetra-O-benzyl-}\alpha(\beta)\text{-D-glucosyl} \quad (1)$$

After extensively plotting the yields of cyclohexylmethyl 2,3,4,6-tetra-O-benzyl-D-glucopyranosides (R = cyclohexylmethyl) as shown in Fig. 1 and 2,[4] the optimum reaction conditions were found out: a mixture of I (0.167 mmol), an alcohol (0.167 mmol), and cobalt(II) bromide (0.167 mmol) in dichloromethane (0.5 ml) was stirred with methanesulfonic acid (0.05 mmol) at 25°C for 2 h under anhydrous conditions to give the corresponding glucosides in good yields (Table 1). The ratio of the anomers formed (α/β) varied between 0.8 and 1.4.

This glucosidation is considered to be an acid-catalyzed reaction.[5] During the course of the reaction, methanesulfonic acid has been exhausted by $CoBr_2$ with generating hydrogen bromide.[6] The fact that $CoBr_2$ has become reddish-purple at the end of the reaction indicates its coordination with water.[7] Diminution of the yields of glucosides caused by excessive amounts of methanesulfonic acid could be explained by the spoilage of the dehydration function of $CoBr_2$.[8] The excessive use of $CoBr_2$ was of no advantage possibly due to its complexation with alcohols indicated by a permanently blue coloration of the reaction mixture.[7,9] A little excess of alcohol was favorable to diminishing the extent of self-condensation as shown in Fig. 3.

In the absence of alcohols, 2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl bromide[10] was generated rather than the self-condensed products.[11] Furthermore, when the reaction was conducted at 0°C, the accumulation of the glucosyl bromide was observed in the early stage of the reaction. Thus, it is postulated that the reaction proceeds by way of the glucosyl bromide as illustrated in (2).[12,13]

$$\alpha\text{GOH} \xrightarrow[-H_2O]{CoBr_2/H^+} \alpha\text{GBr} \xrightarrow{\text{ROH}} \alpha\text{GOR} + \beta\text{GOR} \quad (2)$$

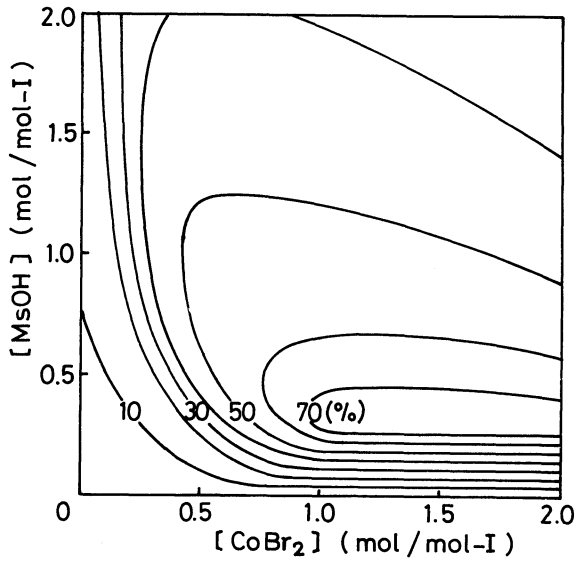
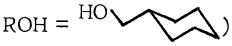


Fig. 1 Two Dimensional Plot of Yields (at 25°C for 0.5 h, ROH = )

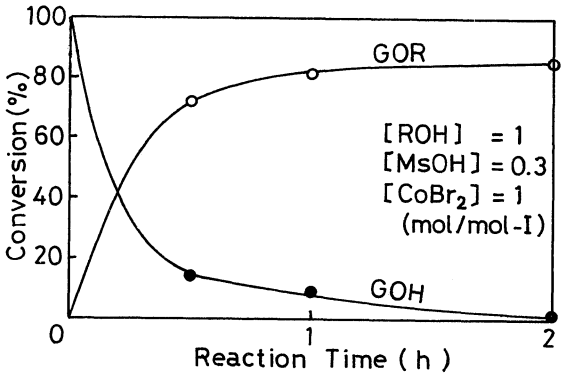


Fig. 2 Time Dependence of Reaction at 25°C (ROH = )

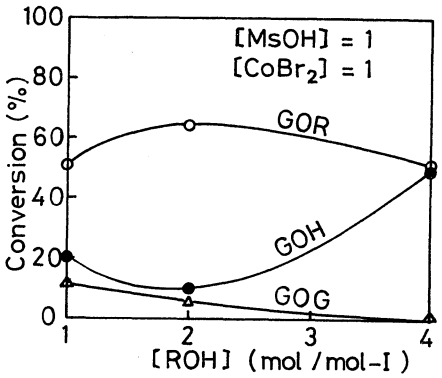


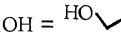
Fig. 3 Effect of Excessive Alcohol (at 25°C for 0.5 h, ROH = )

Table 1 Yields of Glucosides (at 25°C for 2 h)

ROH	Yields of GOR(α/β) (%)
Cyclohexylmethanol	85 (44/41)
Cyclohexanol	75 (44/31)
Methyl 2,3,4-tri-O-benzyl-α-D-glucoside	65 (31/34)

References and Notes

1) R.J.Ferrier, Fortschr. Natl. Forsch., 14, 389 (1970), G.Wulff and G.Röhle, Angew. Chem., 86, 173 (1974).

2) S.Koto, Y.Hamada, and S.Zen, Chem. Lett., 1975, 587, S.Koto, N.Morishima, and S.Zen, ibid., 1976, 61.

3) J.Leroux and A.S.Perlin, Carbohydrate Res., 47, C8 (1976).

4) In the absence of the acid, no glucosidation proceeded. Formation of partially de-O-benzylated products was observed especially when the amount of the acid exceeded 1.0 eq. to I.

5) A.Klemer and R.Kutz, Tetrahedron Lett., 1969, 1693, F.Micheel and E.-D. Pick, ibid., 1695, A.Klemer and B.Kraska, Carbohydrate Res., 32, 400 (1974).

6) The solid recovered from the reaction mixture showed a characteristic absorption of νS=O. The liberation of hydrogen bromide was checked by titrations with aq. sodium hydroxide and aq. silver nitrate. A system of hydrogen bromide and $CoBr_2$ was also found to be effective, though less convenient.

7) D.C.Wertz and R.F.Kruh, Inorg. Chem., 9, 595 (1970).

8) Plausibly by the displacement of Br with CH_3SO_3.

9) K.Sone, T.Fukuda, J.Mizusaki, and K.Moriyama, Monatosch. Chem., 107, 271 (1970).

10) F.Weygand and H.Ziemann, Ann., 657, 179 (1962).

11) Confirmed by tlc and pmr of the supernatant, the latter showing no signal of CH_3.

12) The proposal was substantiated by the observation of a facile condensation of the glucosyl bromide with an alcohol (1 eq.) in the presence of $CoBr_2$ in CH_2Cl_2.

13) When other salts such as $CoCl_2$, KBr, $NiBr_2$, $CuBr_2$, $HgBr_2$ and $MgSO_4$ (excess) instead of $CoBr_2$ were used, the yields of glucosides were quite poor.

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