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# A RAPID ANOMERIZATION OF ALKYL PER-O-BENZYL-β-D-GLUCOPYRANOSIDES BY TITANIUM TETRACHLORIDE

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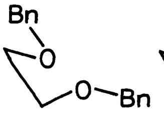
Alkyl per-O-benzyl-β-D-glucopyranosides are rapidly anomerized into the corresponding α-anomer by $TiCl_4$ in $CH_2Cl_2$ at 25 °C. Replacement of the benzyl group at O-6 by acetyl one dramatically slows the reaction but those of other benzyl groups at O-2, O-3, and O-4 do not. A plausible scheme for the reaction in which benzyloxymethylene group and ring oxygen play an important role is presented.

Anomerization1) of per-O-acetyl-β-D-glucopyranosides is one of the practical methods for preparing the α-glucosides.2) However, such reaction of per-O-benzyl-β-D-glucopyranosides and similar compounds has rarely been investigated.3) Continuing synthetic studies using carbohydrate protected by benzyl group,4) it has been found that $TiCl_4$ rapidly anomerized alkyl per-O-benzyl-β-D-glucopyranosides in $CH_2Cl_2$ into the corresponding α-anomers. The reaction finished within a few seconds at 25 °C as shown in Table 1.

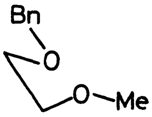
Replacement of the benzyl group at O-6 by acetyl one has been found to retard the anomerization considerably, but those of other benzyl groups at O-2, O-3, and O-4 did not show such effect as the data in Table 1 show.

1,2-Dibenzyloxyethane (**1**) and 1-benzyloxy-2-methoxyethane (**2**) which have $C_6H_5CH_2\text{-O-}CH_2\text{-}\overset{|}{\underset{|}{C}}\text{-O-}$ moiety structurally corresponding to the benzyloxymethylene group and the ring oxygen of methyl per-O-benzyl-β-D-glucopyranoside significantly impeded its anomerization, but 1,2-dibenzyloxycyclohexane (**3**) having only benzyloxymethine groups moderately5) and 1-acetoxy-2-benzyloxyethane (**4**) hardly showed such effect; the order of ligating ability of the additives toward $TiCl_4$ is **1** = **2** > **3** > **4**.

Based on these findings, a plausible scheme for anomerization of alkyl per-O-benzyl-β-D-glucopyranosides is postulated as illustrated in Fig. 1.



**1**



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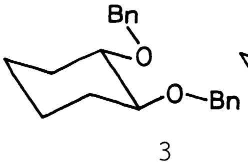

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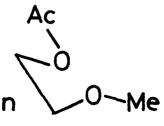

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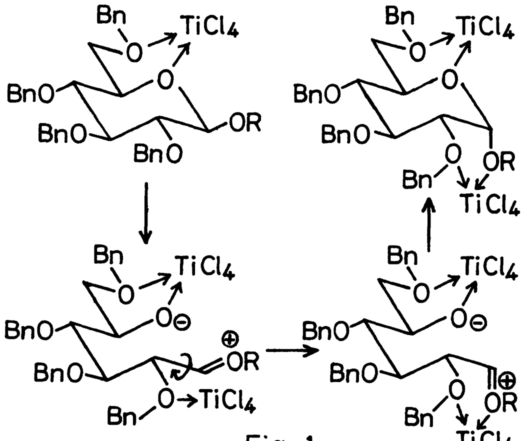
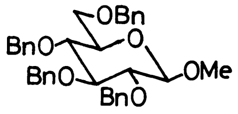


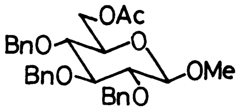
Fig. 1

Table 1. Results of Experiments[a,b]

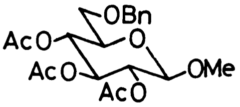
| β-Glucosides | [$TiCl_4$][c] | Additives[d] | Reaction Time | α-Cont.[e] | Recov.[f] |
|---|---|---|---|---|---|
| **5** | 0.2 | -- | 300 s | 42% | 96% |
| | 0.5 | -- | 300 | 89 | 93 |
| | 1.0 | -- | 2[a1] | 68[i] | 78[g] |
| | 1.0 | -- | 4[a1] | 90[i] | 78[g] |
| | 1.0 | -- | 10 | 96[i] | 78[g] |
| | 1.0 | -- | 300 | 96 | 77[g] |
| | 1.0 | **1** | 4[a1] | 7 | 87 |
| | 1.0 | **2** | 4[a1] | 8 | 86 |
| | 1.0 | **3** | 4[a1] | 21 | 84 |
| | 1.0 | **4** | 4[a1] | 57 | 84 |
| **6** | 1.0 | -- | 300 | 4 | 70[h] |
| **7** | 1.0 | -- | 300 | 98 | 87 |
| **8** | 1.0 | -- | 2[a1] | 100[i] | 87 |



**5**



**6**



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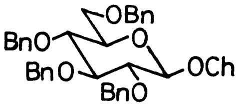

**8**

a) The reaction (0.1 mmol/1 ml-solv.) was quenched with excess iced aq $NaHCO_3$, followed by extraction with benzene and chromatography on silica gel.[4] a1) Short reactions were done as follows: the solvent (and an additive) was injected into a stoppered vial containing a starting material and then $TiCl_4$ in a syringe was shot quickly into a stirring solution at removal of the stopper, followed by pouring a large excess of iced aq $NaHCO_3$ into the reaction mixture. The values in 'α-Cont.' and 'Recov.' are based on the weight of fractions containing the glucosides after chromatography of the reaction mixture. b) Ac = acetyl, Bn = benzyl, Ch = cyclohexyl, Me = methyl. c) Molar ratio of $TiCl_4$ to the starting β-glucoside. d) The amount of additives was equimolar to β-glucoside. e) Mol% of the α-anomer in a mixture of the unchanged β-glucoside and the anomerized α-one. f) Sum of the recovery of the unchanged β-glucoside and the yield of the anomerized α-one. g) De-O-benzylation products such as 3,4,6-tri-O-benzyl-α-D-glucopyranoside were isolated. h) Unidentified de-O-benzylation products were formed. i) Based on these data, effects of moisture on 'α-Cont.' is regarded as negligible in short reactions (⩽ 4s).

## References and Footnote.

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5) Apparently because benzyloxymethine groups inlaid in cyclohexane have less freedom in their bidentate ligation with $TiCl_4$ than benzyloxymethylene ones do.

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