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# DIBROMINATION OF BENZYLOXY-GROUPS: GLYCOSYL BROMIDES FROM BENZYL GLYCOSIDES

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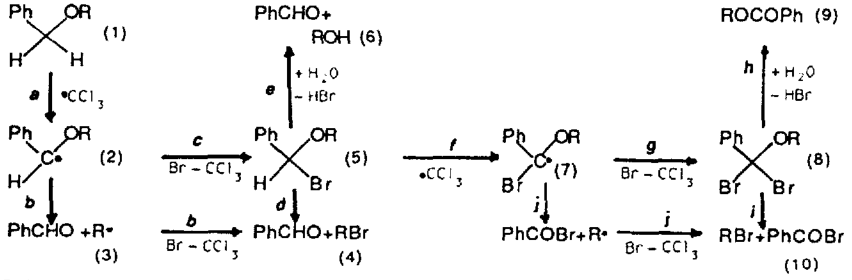
**ABSTRACT**
*Bromination of benzyloxy groups in sugar derivatives with bromotrichloromethane and ultraviolet light rapidly gives α-bromobenzyloxy sugars. On further irradiation α,α-dibromobenzyloxy derivatives are formed from benzyl sugar ethers, whereas glycosyl bromides are produced from benzyl furanosides and pyranosides.*

Free radical monobromination of alkyl benzyl ethers (1) yields alkly bromides (4) and benzaldehyde either by β-siccision of radical (2) and subsequent bromination of (3) (path *a*→*b* in Scheme) or by heterolytic decomposition of the unstable α-bromobenzyl ether (5) (path *a*→ *c*→*d*).[1] Carbohydrate benzyl ethers on the other hand yield α-bromobenzyl ether derivatives (5)[2] presumably by the later pathway. We now report that these monobromobenzyl sugar derivatives (5) may be further brominated to give α,α-dibromobenzyl derivatives (8) which when they are derived from benzyl glycosides readily decompose to give glycosyl bromides. Thus benzyl glycosides are shown to be valuable masked glycosylating agents suitable for use in block synthesis of oligosaccharides.[3]

Brominations were induced in $CCl_4$ solutions usually by irradiating bromotrichloromethane (BTM) or occasionally by heating NBS. The course of the bromination is illustrated by 6-*O*-benzyl-α-D-galacto-pyranose diacetonide (1, R=Gal). Upon irradiation with BTM (1 mol equiv.) it gave the monobromide (5, R=Gal) which hydrolysed to diacetonegalactose (6, R=Gal) (84%) and benzaldehyde according to route *a*→*c*→*e*. On longer irradiation with BTM (2.2 mol. equiv.) the methine pmr signal (PHC*H*BrO) of the monobromide disappeared but signals assignable to 6-bromo-6-deoxygalactose diacetonide (4, R=Gal) were not observed, therefore it was concluded that the α,α-dibromobenzyl ether (8, R=Gal) was formed, since the addition of water produced 91% of 6-O-benzoyl galactose diacetonide (9, R=Gal) by route *a*→ *c*→*f*→ *g*→*h*.

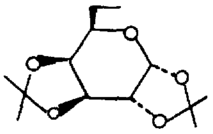


Scheme

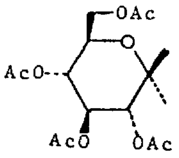
With benzyl glycosides the intial stages of the reaction are similar. Thus benzyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside (1, R=βGlc) (1g) in $CCl_4$ (10 ml) containing BTM (2.5 mol. equiv.) gave, after 4 min. irradiation, a solution which revealed a PhC*H*BrO signal at $\delta_H$ 6.89 ppm for the monobromide (5, R=βGlc). However, after a further 65 min. irradiation, the signal was replaced by two signals for the anomeric protons of α-and β-tetra-*O*-acetyl-D-glucopyranosyl bromides. It appears therefore that the dibromide (8, R=βGlc) is heterolytically transformed by nucleophilic attack at its reactive anomeric carbon atom (i.e. route *a→c→f→g→i* is followed).[4] For synthetic purposes the β-bromide (10, R=βGlc) in the solution was anomerised[5], diethylamine (2.1 mol. equiv.) was added, and after 2h at 0° the diethylbenzamide was filtered off. The solution was evaporated and the relevant alcohol and Hg(II)CN added. With methanol, for example, methyl tetra-*O*-acetyl-β-D-glucopyranoside was isolated in 80% overall yield. Several similar transformations have been carried out with other pyranosides[6], some of which are protected with isopropylidene groups that would be incompatible with the usual acid conditions employed to make glycosyl bromides.

The method has also been successful with furanosides. Thus when the α- and β-benzyl mannofuranoside (13) and (14) were sequentially brominated and treated with methanol they afforded the β-methyl glycoside (15) in 75% and 73% yields respectively.

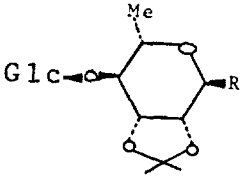
Preparation of trisaccharide (12) illustrates the scope of the reaction in oligosaccharide synthesis. The benzyl group, which initially protected the isopropylidene rhamnoside aglycone employed in the Koenigs Knorr synthesis of disaccharide (11, R=PhCH$_2$O), was brominated in the usual way and the bromodisaccharide (11, R=Br) was then chain elongated at its head with diacetone galactose to give (12) in 60% yield.



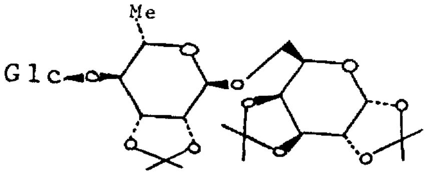
Gal



Glc



(11)



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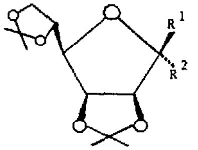

(13) R$^1$=H, R$^2$=PhCH$_2$O

(14) R$^1$=PhCH$_2$O, R$^2$=H

(15) R$^1$=MeO, R$^2$=H

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**References and Footnotes**

1. R. E. Lovine, L. J. Andrews and R. M. Keefer *J. Org. Chem*, 1965, *30*, 4150; R. L. Huang and K. H. Lee, *J. Chem. Soc.*, 1966, 932.
2. J. N. BeMiller and H. L. Muenchow, *Carbohydr. Res.*, 1973, *28*, 253.
3. H. Paulsen, *Angew. Chem .Int. Ed. Engl.*, 1982, *21*, 156.
4. Alternatively, radical (7, R=βGlc) could cleave to give the pyranosyl radical which would subsequently brominate as shown in pathway *j*.
5. R. U. Lemieux, K. B. Hendriks, R. V. Stick and K. James, *J. Amer. Chem. Soc.*, 1975, *97*, 4056.
6. Methyl β-glycosides have been prepared in better than 70% yield from the following benzyl pyranosides: α-glycoside tetra-accetate,α- and β- galactoside tetra acetates, 4-*O*-acetyl-2,3-*O*-isopropylidene-α-L--rhamnoside,and 4,6-di-*O*-acetyl-2,3-*O*-isopropylidene-α-D-mannoside.

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