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Note

Synthesis of methyl 4,6-*O*-benzylidene-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranoside by the Tipson–Cohen reaction[1]

TATSUMI YAMAZAKI, HIROSHI SUGIYAMA*, NAOTAKA YAMAOKA†, KAZUO MATSUDA,
AND SHUICHI SETO*

Department of Agricultural Chemistry and Chemical Research Institute of Non-Aqueous Solutions, Tohoku University, Sendai, 980 (Japan)

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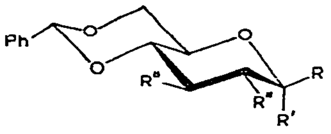
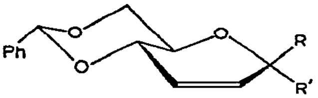
In connection with other work[2] in our laboratory, direct elimination of the C-2 and C-3 sulfonyloxy groups from simple pyranosides has aroused much interest. Horton *et al.*[3] showed a convenient route for the preparation of methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (5) from corresponding 2,3-sulfonates (3) using the Tipson–Cohen reaction (sodium iodide–zinc in *N*,*N*-dimethylformamide). However, Lemieux *et al.*[4] stated that the β-anomer (1) of 3 was not converted into the unsaturated sugar (4) under the same conditions, and Ferrier concluded in his review[5] that this reaction is apparently of less value as a general route to unsaturated sugars than the reaction involving iodohydrins, as it does not give the appropriate alkenes from methyl 4,6-*O*-benzylidene-2,3-di-*O*-*p*-tolylsulfonyl-β-D-glucopyranoside or the α-D-*galacto* isomer. More recently, Horton and Meshreki presented a successful example in the application of this reaction to a β-xylan derivative[6], and Tsuchiya *et al.* have applied this reaction to sugar antibiotics[7]. As yet, no complete proof has been given for the reaction mechanism. We describe here surprising results of the reaction of the β-glucopyranosides (1 or 2) with the Tipson–Cohen reagents.



1 R = OMe, R' = H, R'' = OTs
2 R = OMe, R' = H, R'' = OMs
3 R = H, R' = OMe, R'' = OTs



4 R = OMe, R' = H
5 R = H, R' = OMe

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*Chemical Research Institute of Non-Aqueous Solutions.
†Faculty of Pharmaceutical Science, Kitazato University, Tokyo, 108 Japan.

Methyl 4,6-*O*-benzylidene-2,3-di-*O*-*p*-tolylsulfonyl-β-D-glucopyranoside[8] (**1**) and a 20-fold excess sodium iodide and zinc dust[9] were suspended in dry *N*,*N*-dimethylformamide. The mixture was stirred under reflux. After 5 min, the spot (R_F 0.4) of the starting material had disappeared completely and only one spot (R_F 0.58) appeared on t.l.c. with 10:1 benzene–ethyl acetate as the developing solvent. The mixture was then diluted with water and extracted with chloroform. The chloroform solution of the product was evaporated to low volume and crystallization began upon addition of methanol. The unsaturated product, methyl 4,6-*O*-benzylidene-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranoside (**4**), was obtained in a yield over 85%, m.p. 94–95°, $[\alpha]_D^{12}$ +43° (*c* 1.0, chloroform)[4].

In the same manner, methyl 4,6-*O*-benzylidene-2,3-di-*O*-methylsulfonyl-β-D-glucopyranoside[10] (**2**) was converted into the unsaturated sugar **4** in 81% yield by refluxing the mixture for 30 min. As the *p*-tolylsulfonyloxy group is, in general, more readily eliminated than the methylsulfonyloxy group[3], this result is as anticipated. For these two reactions, sodium iodide and zinc were essential.

On the other hand, with the α-anomer, methyl 4,6-*O*-benzylidene-2,3-di-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside[11] (**3**), the spot (R_F 0.6) of the starting material on t.l.c. (the same system) remained even after 10 hr under the same conditions, and the unsaturated sugar (**5**), m.p. 117–118°, $[\alpha]_D^{12}$ +120° (*c* 1.0, chloroform), was obtained in the same yield (55%) as reported before[3].

Thus, in contrast to Lemieux's assertion[4], our experiments showed that the β-anomer is very rapidly changed into the unsaturated sugar in high yield by the Tipson–Cohen reaction.

EXPERIMENTAL

All compounds reported in this work are known and afforded i.r. and n.m.r. spectra that were in accord with their structures. Melting points are uncorrected and analyses were acceptable.

General procedure for the unsaturation reaction. — Dried methyl 4,6-*O*-benzylidene-2,3-di-*O*-methyl(or *p*-tolyl)sulfonyl-D-glucopyranoside (2 mmol), freshly prepared and dried zinc dust[9] (2.6 g, 40 mmol), and dried sodium iodide (6.0 g, 40 mmol) were suspended in 30 ml of freshly dried and distilled *N*,*N*-dimethylformamide. The mixture was refluxed for the appropriate time with stirring. After cooling, the mixture was diluted with 30 ml of water and extracted with three 20-ml portions of chloroform. The insoluble material in the chloroform solution was filtered off, and the solution was washed with two 20-ml portions of water and dried over sodium sulfate. After evaporation of the chloroform under diminished pressure, the residue was treated with a small amount of methanol for crystallization.

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