Preparation of 6-*O*-Acetyl-D-glucose

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Received December 21, 1970

The communication describes a simple procedure for the preparation of 6-*O*-acetyl-D-glucose by esterification of D-glucose with diluted acetic acid. Unchanged D-glucose is removed from the reaction mixture by crystallization and suceeding yeast fermentation. By-products are extracted with ethyl acetate and 6-*O*-acetyl-D-glucose is finally obtained by crystallization.

Greater reactivity of the primary hydroxyl group of D-glucose in esterification with diluted acetic acid was employed for the preparation of 6-*O*-acetyl-D-glucose by *Duff* [1]. *Frohwein* and *Leibowitz* [2] prepared the compound by partial alkaline hydrolysis of penta-*O*-acetyl-*β*,D-glucose at low temperatures when the ester bond of the primary hydroxyl group is relatively stable. The other procedures [3, 4] are more complicated since they involve a blocking of the secondary hydroxyl groups of D-glucose before acetylation of the primary hydroxyl group (6-*O*-acetyl-3,5-boric ester-1,2-isopropylidene-D-glucose and 6-*O*-acetyl-1,2 : 3,5-di-*O*-isopropylidene-D-glucose, respectively). The desired product is obtained in lower yields after removal of blocking groups by hydrolysis. The isolation of crystalline 6-*O*-acetyl-D-glucose required in all examples [1, 2, 4] chromatographic resolution of the reaction mixtures which is complicated from the preparative point of view.

A simple method convenient particularly for the preparation of 6-*O*-acetyl-D-glucose in larger quantities is presented in this paper. The method is based on partial acetylation of D-glucose with diluted acetic acid. Crystallization of the reaction mixture from ethanol recovered 55—65% of unaltered D-glucose and its rest was fermented by yeast. Di- and tri-*O*-acetyl-D-glucose (traces) were removed by extraction with ethyl acetate. Finally, crystallization from ethanol gave 6-*O*-acetyl-D-glucose in 20—25% yield based on the amount of unrecovered D-glucose.

Experimental

A solution of 400 g of D-glucose in 1000 ml of 75% acetic acid was kept at 100°C for 8 hours. The reaction mixture was then concentrated *in vacuo* to syrupy consistence and remnants of acetic acid were removed by two successive evaporations with water under reduced pressure. The syrupy residue was dissolved under heating in methanol (100 ml), diluted with 96% ethanol (1000 ml) and, after addition of crystalline D-glucose (*ca.* 0.5 g), stored at room temperature for 48 hours. Crystals of D-glucose formed (220—240 g) were filtered off and the filtrate was concentrated *in vacuo*. The residue was dissolved in tap water (2 litres), the resulting solution was adjusted to pH 7 with ammonia and mixed with a suspension of 50 g of baker's yeast in water. The mixture was then incubated (up to 3 days) until all D-glucose disappeared from the solution. This was followed by paper chromatography in the solvent system *n*-butanol—ethanol—water

(5 : 1 : 4 v/v). The yeast was filtered off and the filtrate was concentrated *in vacuo* at temperature below 50°C. The residue was dissolved in 96% ethanol (1000 ml), treated with charcoal, evaporated again and extracted twice with ethyl acetate (150 ml). The insoluble material was dissolved in 96% ethanol (300 ml), the solution was seeded with crystals of 6-*O*-acetyl-D-glucose (*ca.* 0.1 g) and crystallized for 48 hours at room temperature and after that for 48 hours at 5°C to give 40—50 g of crystalline product.

Recrystallization from 96% ethanol afforded chromatographically homogeneous 6-*O*-acetyl-D-glucose, m.p. 134—135°C (Kofler), $[\alpha]_D^{24}$ $+92 \pm 4°$ (10 minutes) → $+54 \pm 2°$ (4 hours) → $+49.5 \pm 1°$ (24 hours) (*c* 2, water). Ref. [1] m.p. 135°C, $[\alpha]_D^{20}$ +48 (*c* 4, water) and ref. [2] m.p. 146°C, $[\alpha]_D^{20}$ +90° → +53° (30 minutes).

References

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Translated by P. Biely