A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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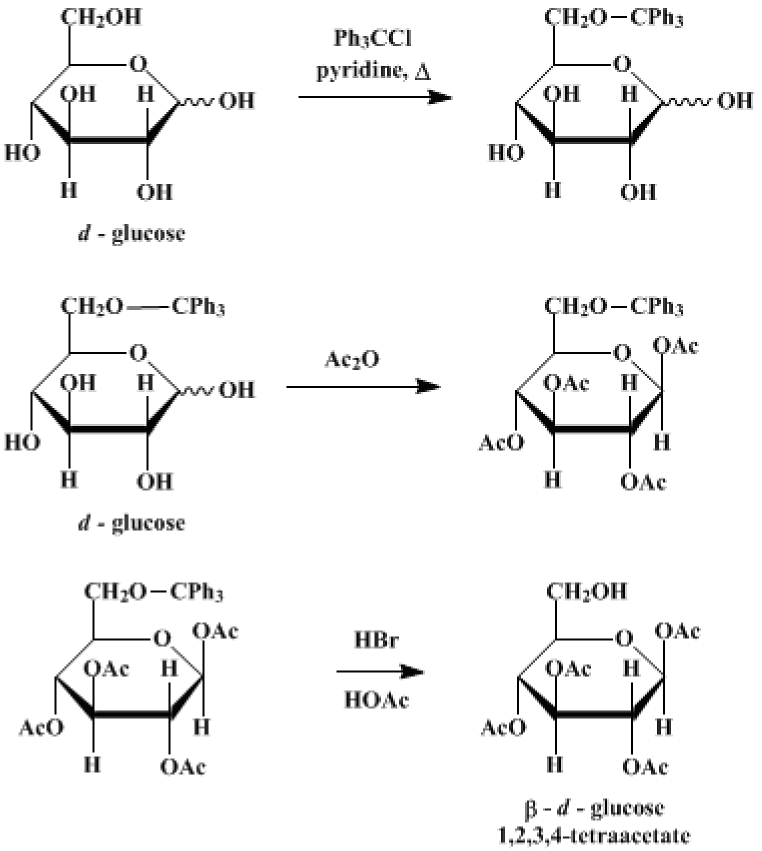
Organic Syntheses, Coll. Vol. 3, p.432 (1955); Vol. 22, p.56 (1942).

β-*d*-GLUCOSE-1,2,3,4-TETRAACETATE

[D-Glucose, β-1,2,3,4-tetraacetyl-]



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1. Procedure

A. 6-*Trityl*-β-*d*-*glucose*-1,2,3,4-*tetraacetate.* A mixture containing 120 g. (0.67 mole) of anhydrous glucose, 193.2 g. (0.7 mole) of trityl chloride, and 500 ml. of anhydrous pyridine [*Org. Syntheses* Coll. Vol. **1**, 100 (1941)], is heated on the steam cone until solution is complete (Note 1). Without cooling, 360 ml. of acetic anhydride is added in one portion (Note 2). After standing for 12 hours, the reaction mixture is poured slowly into 10 l. of ice water, to which 500 ml. of acetic acid has been added, and the resulting mixture is vigorously stirred mechanically for 2 hours (Note 3). The precipitate is filtered and is immediately stirred for a short time with 10 l. of ice water. The white, granular precipitate is filtered, washed well with cold water, and then air-dried (Note 4). The dried solid is digested with 500 ml. of ether (Note 5). The insoluble portion is dissolved in hot 95% ethanol (approximately 3 l.), and the solution is decolorized and filtered while hot. The filtrate, upon cooling, deposits fine needles of 6-trityl-β-*d*-glucose-1,2,3,4-tetraacetate of sufficient purity for further use. The yield at this point is about 169 g. (43%). Recrystallization from 95% ethanol gives the pure compound which melts at 166–166.5°. In pyridine, $[\alpha]_D^{19}$ is + 44.8°; $[\alpha]_D^{28}$, +45.3°. The yield of purified material is 137 g. (35%) (Note 6).

B. β-*d*-*Glucose-1,2,3,4-tetraacetate*. A solution of 46 g. (0.078 mole) of 6-trityl-β-*d*-glucose-1,2,3,4-tetraacetate in 200 ml. of acetic acid is prepared by warming on the steam bath. The solution is then cooled to approximately 10°, 18 ml. of a saturated solution of dry hydrogen bromide in acetic acid is added, and the reaction mixture is shaken for about 45 seconds. The trityl bromide formed during the reaction is removed *at once* by filtration, and the filtrate is poured *immediately* into 1 l. of cold water. The tetraacetate is extracted with 250 ml. of chloroform; the chloroform extract is washed four times with ice water and dried over anhydrous sodium sulfate. The drying agent is removed, and the chloroform is evaporated, under reduced pressure at room temperature. The remaining syrup is covered with 100 ml. of anhydrous ether and is rubbed with a glass rod. Crystallization takes place immediately. The product is removed and is purified by dissolving it in the minimum amount of chloroform and adding anhydrous ether until crystallization begins. The purified product melts at 128–129°. In chloroform, $[\alpha]_D^{20}$ is +12.1°. The yield is 15 g. (55%).

2. Notes

1. The materials and apparatus used for this reaction must be strictly anhydrous in order to prevent hydrolysis of the trityl chloride.
2. Higher temperatures favor formation of the β-isomer.
3. The stirring must be unusually rapid, and the solution must be added to the water slowly and in a fine stream. If this is not done, the precipitate will not be granular and will be extremely difficult to filter.
4. If the material warms up to room temperature during the time required for drying, it becomes exceedingly sticky, and mechanical difficulties in manipulation result. This behavior appears to be due to the presence of traces of pyridine. The checkers found that the pure product, m.p., 166–166.5°, when recrystallized from pyridine, gave a sticky material.
5. The α-isomer is soluble in ether, whereas the β-isomer is insoluble. In some cases the entire product dissolves, but the β-isomer separates when the solution is allowed to stand.
6. The submitters state that the yield of purified product varies from 148 g. to 180 g.

3. Discussion

These directions are modifications of the methods used by Helferich and Klein for the original preparation of the substance,[1] although it had apparently previously been obtained by Oldham by hydrolysis of tetraacetylglucose-6-mononitrate.[2]

References and Notes

1. Helferich and Klein, *Ann.*, **450**, 219 (1926); Helferich, Moog, and Junger, *Ber.*, **58**, 877 (1925).
2. Oldham, *J. Chem. Soc.*, **127**, 2840 (1925).

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

D-Glucose, β-1,2,3,4-tetraacetyl-

ethanol (64-17-5)

acetic acid (64-19-7)

ether (60-29-7)

acetic anhydride (108-24-7)

chloroform (67-66-3)

hydrogen bromide (10035-10-6)

sodium sulfate (7757-82-6)

pyridine (110-86-1)

glucose (492-62-6)

trityl chloride (76-83-5)

trityl bromide (596-43-0)

tetraacetylglucose-6-mononitrate

β-D-Glucose-1,2,3,4-tetraacetate (13100-46-4)

6-trityl-β-d-glucose-1,2,3,4-tetraacetate