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.

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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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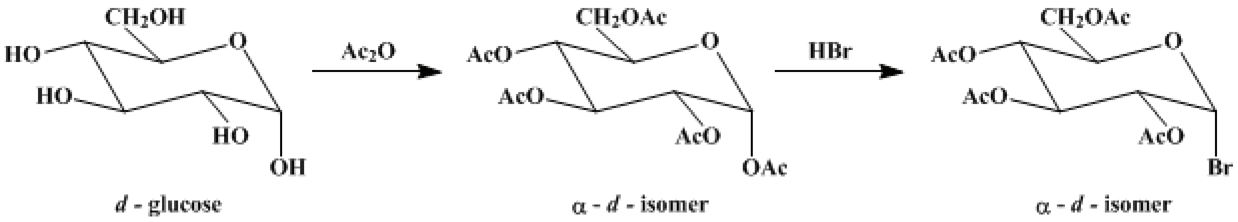
Organic Syntheses, Coll. Vol. 3, p.11 (1955); Vol. 22, p.1 (1942).

ACETOBROMOGLUCOSE

[2,3,4,6-Tetraacetyl-α-*d*-glucopyranosyl bromide]



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1. Procedure

In a 1-l. round-bottomed flask are placed 66 g. (0.33 mole) of *d*-glucose monohydrate (Note 1) and 302 g. of 95% acetic anhydride (280 ml., 2.81 moles). To this mixture 3 small drops of concentrated sulfuric acid are added *from a medicine dropper* (Note 2). The glucose is kept in partial suspension by shaking the flask with a swirling motion; the reaction starts almost immediately. If the temperature of the mixture approaches the boiling point, the flask is momentarily immersed in a pan of cold water. Within 10–15 minutes nearly all the glucose will have dissolved and the temperature of the reaction mixture will have risen nearly to 100°. The flask is loosely stoppered and is heated on a steam bath for 2 hours. Then about 200 ml. of mixed acetic acid and acetic anhydride is removed by distillation under reduced pressure (Note 3).

Sixty-five grams (60 ml., 0.64 mole) of acetic anhydride is added to the warm, viscous, light-yellow syrup; the mixture is warmed slightly and is mixed by imparting a swirling motion to the flask until the solution is homogeneous. The flask is then fitted with a two-holed rubber stopper bearing an inlet tube and an exit tube, the former reaching within 5 mm. of the bottom. Dry hydrogen bromide is passed into the mixture, while it is cooled in an ice bath, until the gain in weight is 140–160 g. (Note 4). The flask is then sealed with a rubber stopper and allowed to stand at 5° overnight.

The hydrogen bromide, acetic acid, and acetic anhydride are then removed from the straw-yellow solution by distillation under reduced pressure; a water bath whose temperature does not exceed 60° should be used to heat the mixture (Note 5). During the distillation the solution becomes slightly darker. When no further distillate comes over, or when the residue crystallizes, distillation is stopped, 250–300 ml. of dry isopropyl ether is added (Note 6), and the flask is warmed carefully on a water bath to hasten solution of the product (Note 7). The hot solution is transferred to a 1-l. Erlenmeyer flask and is cooled rapidly, with cold water, to about 45°. The mixture is then allowed to cool slowly to room temperature and is finally placed in a refrigerator at 5° for 2 or more hours. The acetobromoglucose is collected on a Büchner funnel, pressed into a firm cake, and washed with about 50 ml. of dry isopropyl ether. The white crystalline material, after being dried under reduced pressure over calcium (or sodium) hydroxide, weighs 110–120 g. (80–87%) (Note 8).

2. Notes

1. Ordinary commercial glucose monohydrate (Cerelose, Clintose, etc.) was used.
2. If any uncertainty exists about the size of the drops, it is better to add 2 drops at first and then to wait at least 10 minutes before adding the third drop. If too much sulfuric acid is added the reaction may become so vigorous that it cannot be controlled.
3. The lowest pressure attainable with a good aspirator is satisfactory. The acetic acid may be removed rapidly at bath temperatures up to 100°. Two hundred milliliters of distillate is collected in about 35 minutes. Complete removal of the acetic acid is not necessary; the only purpose of removing it is to

decrease the amount of hydrogen bromide required.

4. Hydrogen bromide may be generated by dropping liquid bromine into boiling tetrahydronaphthalene, or catalytically from hydrogen and bromine (*Org. Syntheses*, **15**, 35). Free bromine should be removed from the gas by passing it over red phosphorus. The hydrogen bromide may be passed in very rapidly at first, but as the solution becomes more concentrated the rate of introduction of the gas must be decreased. The absorption of 140 g. of hydrogen bromide requires about 2 hours if the solution is well stirred; otherwise a longer time is required.

5. This distillation is best conducted in the following manner: The hydrogen bromide is removed as completely as possible at a bath temperature of 40–50° under the pressure attainable with a good aspirator; this requires about 1 hour. The bath temperature is then slowly increased to 50–60° over a period of about 30 minutes, during which time considerable acetic acid and acetic anhydride are removed. The receiver is then emptied and the system is connected to a mechanical pump capable of maintaining a pressure of less than 5 mm. By keeping the temperature of the bath at 55–60°, sufficient acetic acid and anhydride are removed in 30–45 minutes. The mechanical pump must be adequately protected; the vapors should be passed through a trap cooled in carbon dioxide-ethanol, then through a 12- to 16-in. tower of flake sodium hydroxide, before they enter the pump. A somewhat higher bath temperature can be used with a good aspirator alone, but this will produce much darkening of the reaction mixture and will give a less desirable product.

6. Isopropyl ether which has been in contact with air for some time will contain peroxides. They should be removed by washing the ether, first with sodium bisulfite solution, then with sodium hydroxide solution, and finally with water. The ether is dried (24 hours over calcium chloride, then 24 hours over phosphorus pentoxide) and distilled.

7. Heating to effect solution should be as brief as possible. The water bath should be at a temperature near the boiling point, and the flask should be immersed for only short periods of time. The flask should be shaken continuously during this process.

8. The product, m.p. 87–88°, is satisfactory for most purposes. A single recrystallization from isopropyl ether gives a product having a melting point of 88–89°.

The product is best stored in a vacuum desiccator.

3. Discussion

α-Acetobromoglucose has been prepared by the action of acetyl bromide on anhydrous glucose;[1,2,3,4] by the action of hydrogen bromide in acetic acid upon β-pentaacetylglucose;[5,6,7,8] by the action of hydrogen bromide in acetic anhydride upon anhydrous glucose;[9,10] and by the action of hydrogen bromide in acetic anhydride upon starch or maltose.[11]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 434
- Org. Syn. Coll. Vol. 8, 148
- Org. Syn. Coll. Vol. 8, 583

References and Notes

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

red phosphorus

calcium (or sodium) hydroxide

acetic acid and anhydride

α-Acetobromoglucose

β-pentaacetylglucose;

ethanol (64-17-5)

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

acetic acid (64-19-7)

ether (60-29-7)

acetic anhydride (108-24-7)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

hydrogen bromide (10035-10-6)

bromine (7726-95-6)

sodium bisulfite (7631-90-5)

carbon dioxide (124-38-9)

glucose (492-62-6)

tetrahydronaphthalene (119-64-2)

Acetobromoglucose (572-09-8)

isopropyl ether (108-20-3)

glucose monohydrate,
d-glucose monohydrate (14431-43-7)

acetyl bromide (506-96-7)

maltose

phosphorus pentoxide (1314-56-3)

2,3,4,6-Tetraacetyl-α-d-glucopyranosyl bromide