Organic Syntheses

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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β-GENTIOBIOSE OCTAACETATE

[Gentiobiose, β-octaacetyl-]

$$2C_6H_{12}O_6 \xrightarrow{\text{Emulsin}} C_{12}H_{22}O_{11} + H_2O$$

$$C_{12}H_{22}O_{11} + 8(CH_3CO)_2O \longrightarrow C_{12}H_{14}O_3(OCOCH_3)_8 + 8CH_3CO_2H$$

Submitted by B. Helferich and J. F. Leete.
Checked by Homer Adkins and E. E. Bowden.

1. Procedure

A solution of 1.65 kg. of crystallized glucose or 1.5 kg. of anhydrous glucose (8.3 moles) is prepared by heating the solid on a steam bath with 1.35 l. of distilled water. The solution is cooled and placed in a 2.5-1. glass-stoppered bottle. Fifteen grams of emulsin (Note 1) is added, then 20 ml. of toluene, and the flask is closed and allowed to stand at room temperature, with occasional shaking, for 5 weeks. The solution is then boiled, diluted with 8.5 l. of water, and filtered. To the filtrate is added 56 g. of baker's yeast in 650 ml. of water, and the temperature of the mixture is maintained at 28–32° for 12–14 days (Note 2). The mixture is then boiled for 30 minutes with an excess of powdered calcium carbonate and filtered.

The filtrate is evaporated under a pressure of 20–30 mm. to as thick a syrup as possible. For this operation the solution is placed in a 12-l. flask set in a steam bath and connected by a goose-neck to a condenser, which in turn is connected to a suction or distilling flask. A very fine capillary inlet tube into the 12-l. flask prevents any violent ebullition (Note 3) and (Note 4).

To the thick syrup (170–185 g.) are added 100 g. of anhydrous sodium acetate and 1.125 l. of acetic anhydride. The mixture is carefully heated to the boiling point with provision for cooling the flask with wet cloths should the acetylation become too violent. When the reaction is complete (about 20 minutes is required) the solution is poured into 10 l. of ice water. The water is decanted and renewed twice at 24-hour intervals in order to render the acetylated sugar filterable.

The dark brown product is filtered and, after drying in the air, is extracted with ether in a Soxhlet apparatus. The ether is removed by evaporation, and the light-colored residue (170 g.) is recrystallized from 1.65 l. of hot methanol. The crystals are washed on a Büchner funnel with methanol until free from colored impurities. The yield is 77–87 g. of material which melts at 187–190°. A second recrystallization from methanol (1.25 ml. per g. of product) gives pure βoctaacetylgentiobiose, with about 10% loss. The pure substance melts at 196° (cor.).

2. Notes

1. A commercial sample of emulsin was purchased from Merck and Company. If freshly prepared emulsin of good quality is available, the quantity may be reduced to one-tenth or less of the specified amount.
2. The yeast, by fermentation, removes the glucose which has not been transformed into gentiobiose. Fleischmann's and "Red Star" yeast have been used. The flask should be stoppered and protected with the conventional trap for the escape of carbon dioxide.
3. The submitters suggest a more complicated apparatus (Note 4) for this operation. However, the checkers have had no trouble with foaming or bumping when using the simple apparatus described above. Very little water condenses in the receiver, which serves as a safety trap in case foaming or bumping should occur.
4. The submitters used quantities four times as large as those stated above. They give the following directions for the distillation:

"The solution is drawn slowly through a glass tube provided with a stopcock into a 3-l. distillation flask standing in a bath of rapidly boiling water. The small portion which foams over is collected and evaporated in a second 3-l. distillation flask, likewise standing in rapidly boiling water. The distillate is passed through an efficient condenser and is collected in a thick-walled bottle or flask to which the vacuum pump or water pump is connected. A high vacuum is essential. The tube connecting the condenser and the receiver is provided with a stopcock so that the distillate may be poured out without interrupting the vacuum to any extent."

3. Discussion

The chief methods for the preparation of gentiobiose and its octa-acetate are discussed in a paper by Reynolds and Evans.[1,2] These methods involve isolation of the substance from gentian root;[3,4] the action of emulsin on glucose;[5,6] the catalytic hydrogenolysis of amygdalin;[7] separation from the mother liquors ("Hydrol") obtained in the manufacture of glucose;[8] and the condensation of acetobromoglucose with β-*d*-glucose-1,2,3,4-tetraacetate.[1,9,10] Reynolds and Evans recommend the last-mentioned method.

The method given above is a modification of those originally described by Bourguelot[3] and Zemplén.[11]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 8, 332

References and Notes

1. Reynolds and Evans, *J. Am. Chem. Soc.*, **60**, 2559 (1938).
2. Haworth and Wylam, *J. Chem. Soc.*, **1923**, 123.
3. Bourquelot and Hérissey, *Compt. rend.*, **132**, 571 (1901).
4. Bourquelot and Hérissey, *Bull. soc. chim. France*, (3) **29**, 363 (1903).
5. Bourquelot and Hérissey, *Compt. rend.*, **157**, 732 (1913).
6. J. F. Leete, Ph.D. dissertation, Univ. of Greifswald, 1929.
7. Bergmann and Freudenberg, *Ber.*, **62**, 2783 (1929).
8. Berlin, *J. Am. Chem. Soc.*, **48**, 2627 (1926).
9. Helferich and Klein, *Ann.*, **450**, 219 (1926).
10. Gilbert, Smith, and Stacey, *J. Chem. Soc.*, **1946**, 622.
11. Zemplén, *Ber.*, **48**, 232 (1915).

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

amygdalin

Gentiobiose, β-octaacetyl-

gentiobiose and its octa-acetate

methanol (67-56-1)

ether (60-29-7)

acetic anhydride (108-24-7)

sodium acetate (127-09-3)

carbon dioxide (124-38-9)

calcium carbonate (471-34-1)

toluene (108-88-3)

glucose (492-62-6)

Acetobromoglucose (572-09-8)

β-Gentiobiose octaacetate (4613-78-9)

Gentiobiose (554-91-6)

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