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.541 (1955); Vol. 22, p.86 (1942).

D-MANNOSE

$$C_6H_{11}O_5OCH_3 + H_2O \longrightarrow C_6H_{12}O_6 + CH_3OH$$

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1. Procedure

A solution of 200 g. (1.03 moles) of α-methyl-*d*-mannoside [*Org. Syntheses* Coll. Vol. **1**, 362 (1932), 371 (1941)] in 3.2 l. of 2 *N* sulfuric acid (178 ml. concentrated sulfuric acid diluted to 3.2 l.) is steamdistilled from a 5-l. flask for 1 hour. The flask is heated externally during this time so that the volume of the solution remains constant. The mixture is transferred to a 2- or 3-gal. crock, 10 g. of decolorizing charcoal (Norit) is added, and the solution is rapidly stirred while it is neutralized (litmus) by the addition of barium carbonate (Note 1).

The mixture is filtered with suction through an asbestos mat supported on a filter paper in a 25-cm. Büchner funnel, and the barium sulfate is washed with two 100-ml. portions of water. The filtrate and washings are combined, and the clear colorless solution of the sugar is concentrated to about 300 ml. under reduced pressure (water pump) on a water bath whose temperature does not exceed 60°. The mixture is filtered, and the solid is washed on the filter with a little water. The combined filtrate and washings are then concentrated to a volume of 100 ml. under the conditions described above. The warm, slightly tan-colored syrup is poured into a 500-ml. Erlenmeyer flask. The transfer is completed by rinsing the distilling flask five times with 40-ml. portions of glacial acetic acid, each portion of the acetic acid being warmed to 50° in the bath before it is transferred. The acetic acid solution of the sugar is seeded with crystalline D-mannose (Note 2), and, after standing overnight at room temperature, the solution is placed in a refrigerator for a day or two.

The crystalline D-mannose is filtered and washed successively with two 20-ml. portions of cold glacial acetic acid, two 20-ml. portions of cold dry ethanol, and three 30-ml. portions of cold, dry ether (Note 3). After drying in the air for 3 days, the product weighs 112 to 115 g. (60%) (Note 4) and melts at 126.5–127.5° (Note 5).

2. Notes

1. The calculated quantity of pure barium carbonate required to neutralize the sulfuric acid is 630 g. However, the checkers found that the mixture was still acid after stirring it for 2–3 hours with 780 g. of carbonate. An additional 100 g. of carbonate was required to bring the mixture to the neutral point. The checkers found that it was preferable to add 975 g. of barium hydroxide [$Ba(OH)_2 \cdot 8H_2O$], stir for 30 minutes, and then to complete the neutralization by stirring with 75 g. of barium carbonate.
2. Crystallization may be induced by scratching with a glass rod if crystalline D-mannose is not available.
3. The sugar should be ground with each portion of the wash liquid, if the maximum purification with the minimum amount of solvent is to be obtained.
4. The submitters obtained 18–19 g. of crystalline D-mannose from the mother liquors, which increased the yield to about 70% of the theoretical amount.
5. The sugar so prepared is said to be predominately α-D-mannose. If a purer product is desired, the substance may be recrystallized from 80% ethanol. This procedure gives a product which melts at 131–132°; α_D^{23} + 15°. The recovery in this crystallization is about 80%.

3. Discussion

D-Mannose has been prepared by hydrolysis of the mannan in vegetable ivory,[1,2,3] but the crystalline sugar is apparently best obtained from mannan through the isolation of α-methyl-*d*-mannoside.[4] The method described above is similar to that of Hudson and Jackson[4] except that sulfuric acid, rather than hydrochloric acid, is used for hydrolysis of the α-methyl-*d*-mannoside. Levene[5] has described what is probably the best method for the conversion of mannan to D-mannose without the isolation of α-methyl mannoside. The D-mannose obtained by Levene was predominately the β-isomer.

The electrolytic reduction of D-mannonic lactone to D-mannose has been described.[6]

References and Notes

1. Hudson and Sawyer, *J. Am. Chem. Soc.*, **39**, 470 (1917).
2. Narayanan, *Indian J. Med. Research*, **29**, 1 (1941).
3. Isbell, *J. Research Natl. Bur. Standards*, **26**, 47 (1941).
4. Hudson and Jackson, *J. Am. Chem. Soc.*, **56**, 958 (1934).
5. Levene, *J. Biol. Chem.*, **108**, 419 (1935).
6. Sato, *J. Chem. Soc. Japan, Pure Chem. Sect.*, **71**, 194 (1950).

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

α-METHYL MANNOSIDE

α-methyl-d-mannoside

ethanol (64-17-5)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

barium sulfate (7727-43-7)

decolorizing charcoal (Norit) (7782-42-5)

barium hydroxide (17194-00-2)

barium carbonate (513-77-9)

D-Mannose

α-d-mannose

d-mannonic lactone