



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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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.

Organic Syntheses, Coll. Vol. 3, p.690 (1955); Vol. 20, p.74 (1940).

PENTAACETYL *d*-GLUCONONITRILE

[Gluconitrile, D-, pentaacetate]



Submitted by H. T. Clarke and S. M. Nagy.

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1. Procedure

To 350 ml. of anhydrous [methanol](#) contained in a 1-l. three-necked round-bottomed flask, to which is attached a reflux condenser protected by a drying tube, is added 20 g. (0.87 gram atom) of [sodium](#) ([Note 1](#)) in large pieces. The reaction is kept under control by cooling the flask in a pan of ice water. To the resulting solution of [sodium methoxide](#) is added a solution ([Note 2](#)) of 61 g. of [hydroxylamine hydrochloride](#) (0.88 mole) in 20 ml. of water; during the addition the mixture is swirled in order to avoid spattering. After 20 minutes the mixture is cooled to 0° and filtered with suction. The [sodium chloride](#) is washed with 350 ml. of anhydrous [methanol](#). The combined filtrate and washings are warmed to 65° in a 3-l. round-bottomed flask, and a solution of 100 g. of finely powdered commercial crystalline [glucose monohydrate](#) (0.50 mole) in 200 ml. of warm 25% aqueous [methanol](#) is added, with stirring. The resulting solution is held at 65° for 2 hours and then concentrated under reduced pressure until no further distillate is obtained; the residue weighs 155–160 g. The resulting syrup ([Note 3](#)) is diluted with 300 ml. of [methanol](#) and again distilled, and this process is repeated once ([Note 4](#)).

A mixture of 100 g. of powdered, anhydrous [sodium acetate](#) and 677 ml. of 90% [acetic anhydride](#) ([Note 5](#)) is heated on a steam bath in a 3-l. round-bottomed flask under an efficient reflux condenser. Without interrupting the heating a solution of the syrupy [glucose oxime](#) in 50 ml. of glacial [acetic acid](#) and 100 ml. of cold [acetic anhydride](#) is added through a dropping funnel to the hot mixture ([Note 6](#)); this requires about 1 hour ([Note 7](#)). Heating is continued for another hour, and the bulk (380–420 ml.) of the [acetic acid](#) and any unchanged [acetic anhydride](#) is distilled under reduced pressure from a water bath. The residue is immediately stirred into 2 l. of cold water, stirred occasionally during the first 3 hours, and allowed to stand overnight.

After the mixture has been chilled to 0°, the brown, crystalline mass is filtered with suction and washed with 500 ml. of water. The solid is dissolved in 300 ml. of hot 95% [ethanol](#), and the solution is heated with 10–15 g. of [Norit](#) for 5 minutes and filtered with suction. The filtrate is gradually cooled to 0°; the crystals are filtered with suction and washed with 20 ml. of cold [ethanol](#). The weight of the first crop is 90–93 g. A second crop is obtained by concentrating the mother liquor under reduced pressure to 25 ml., boiling the solution with [Norit](#), filtering, and chilling the filtrate to 0°. The total yield of colorless [pentaacetyl *d*-gluconitrile](#) melting at 82.5–83.5° is 95–96 g. (50%).

2. Notes

1. In preparing free [hydroxylamine](#), a little less than the theoretical amount of [sodium](#) is employed to avoid the presence of free alkali in the reaction mixture.
2. The [hydroxylamine hydrochloride](#) dissolves in the small amount of water when the mixture is warmed to about 125°.
3. The isolation of [glucose oxime](#) is unnecessary in this preparation.
4. The distillation with [methanol](#) serves to remove water almost completely.
5. If [acetic anhydride](#) of a higher concentration is available, correspondingly smaller quantities may be employed.
6. The viscous, syrupy [glucose oxime](#) dissolves with difficulty, and it may be necessary to warm the mixture slightly. If this is done, a pan of ice water should be at hand in order to cool the mixture should the temperature begin to rise rapidly.
7. In the process described in the literature, the oxime, [sodium acetate](#), and [acetic anhydride](#) are allowed

to react without dilution, a condition which frequently leads to an uncontrollably violent reaction.

3. Discussion

The above method for preparing [glucose oxime](#) is the modification of that of Jacobi¹ developed by Wohl,² who first converted the oxime into the [pentaacetyl glucononitrile](#) by means of [acetic anhydride](#). The latter reaction was later employed for the same purpose by Zemplén and Kiss.³

[Pentaacetyl glucononitrile](#) has also been prepared by dehydration of [pentaacetyl gluconamide](#) with [phosphorus oxychloride](#).⁴

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 101](#)

References and Notes

1. Jacobi, *Ber.*, **24**, 696 (1891).
 2. Wohl, *Ber.*, **26**, 730 (1893).
 3. Zemplén and Kiss, *Ber.*, **60**, 165 (1927).
 4. Ladenburg, Tischler, Wellman, and Babson, *J. Am. Chem. Soc.*, **66**, 1217 (1944).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

[ethanol](#) (64-17-5)

[acetic acid](#) (64-19-7)

[methanol](#) (67-56-1)

[acetic anhydride](#) (108-24-7)

[sodium acetate](#) (127-09-3)

[sodium chloride](#) (7647-14-5)

[sodium methoxide](#) (124-41-4)

[Norit](#) (7782-42-5)

[Phosphorus Oxychloride](#) (21295-50-1)

[sodium](#) (13966-32-0)

[Hydroxylamine hydrochloride](#) (5470-11-1)

[hydroxylamine](#) (7803-49-8)

glucose monohydrate (14431-43-7)

pentaacetyl glucononitrile,
PENTAACETYL d-GLUCONONITRILE

Glucononitrile, D-, pentaacetate (6272-51-1)

glucose oxime

pentaacetyl gluconamide