



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.

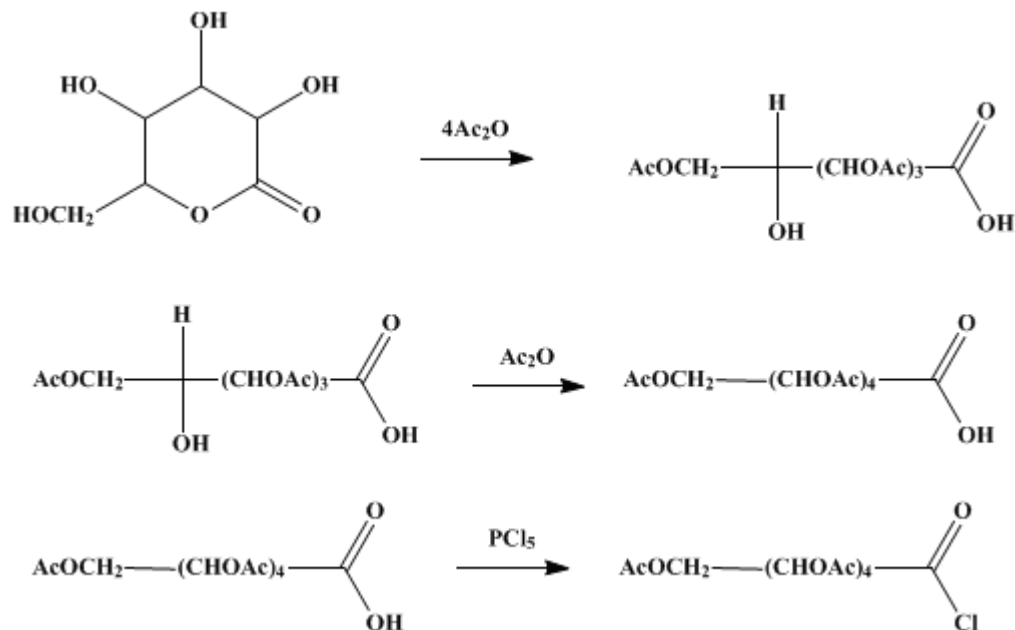
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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2,3,4,5,6-PENTA-O-ACETYL-D-GLUCONIC ACID AND 2,3,4,5,6-PENTA-O-ACETYL-D-GLUCONYL CHLORIDE

[Gluconic acid, pentaacetyl-,D-, and Gluconyl chloride, pentaacetyl-, D-]



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1. Procedure

A. *2,3,4,6-Tetra-O-acetyl-D-gluconic acid monohydrate*. Crushed, fused zinc chloride (20 g.) is shaken with 250 ml. of acetic anhydride in a 1-l. three-necked flask until most of the solid dissolves. The flask is then equipped with mechanical stirrer, thermometer reaching into the liquid, and a dropping funnel. As the flask is cooled in an ice bath, 50 g. (0.28 mole) of D-glucono- δ -lactone (Note 1) is added slowly with vigorous stirring. During the addition, the temperature should be kept below 65°. After an hour in the ice bath, the solution is kept at room temperature for 24 hours and is then poured into 1 l. of water and stirred until the hydrolysis of the acetic anhydride is complete (about an hour). The mixture is placed in a refrigerator until the product crystallizes completely (Note 2). The crude material is removed by filtration and washed with a small amount of ice water. The 2,3,4,6-tetra-O-acetyl-D-gluconic acid monohydrate thus obtained melts at 113–117°. The yield is 79–84 g. (74–79%).

B. *2,3,4,5,6-Penta-O-acetyl-D-gluconic acid*. Tetra-O-acetyl-D-gluconic acid monohydrate (50 g., 0.13 mole) is slowly added to a chilled (0–5°) solution of 18 g. of fused zinc chloride in 190 ml. of acetic anhydride contained in a 1-l. Erlenmeyer flask. The solution is kept in an ice bath for an hour and then allowed to stand at room temperature for 24 hours. After dilution with 1 l. of water, the solution is extracted with four 100-ml. portions of chloroform. In order to remove the chloroform, 200 ml. is distilled, 250 ml. of toluene is added, and 250 ml. of this solution is distilled. Another 250 ml. of toluene is then added and the volume is reduced to 300 ml. The product crystallizes on standing at 0° (Note 2). The solid is removed by filtration, washed with toluene and then with petroleum ether (b.p. 35–55°). A yield of 44–45 g. (83–84%) of anhydrous 2,3,4,5,6-penta-O-acetyl-D-gluconic acid, melting at 110–111°, is obtained; $[\alpha]_D^{23} +11.5^\circ$ ($c = 4.0$ in ethanol-free chloroform).

C. *2,3,4,5,6-Penta-O-acetyl-D-gluconyl chloride*. Anhydrous 2,3,4,5,6-penta-O-acetyl-D-gluconic acid (25 g., 0.062 mole) is shaken with 185 ml. of anhydrous ethyl ether in a 1-l. round-bottomed flask

until most of the solid dissolves. Then 15 g. (0.072 mole) of [phosphorus pentachloride](#) is added with shaking. The flask is fitted with a calcium chloride drying tube and stored overnight at room temperature. Any solid material is removed by filtration through a fritted-glass funnel into a 1-l. round-bottomed flask, and the ethereal solution is concentrated to about one-half volume under reduced pressure at room temperature. The concentrated solution is allowed to stand overnight at 0° or below. The mother liquor is decanted from the crystals, which are then broken up, transferred to a fritted-glass funnel, washed quickly with petroleum ether (b.p. 35–55°), and dried in a vacuum desiccator. The mother liquor is again concentrated to one-half its volume under reduced pressure and a second crop of crystals collected. The total yield of [2,3,4,5,6-penta-O-acetyl-D-gluconyl chloride](#), melting at 68–71° ([Note 3](#)), is 21–24 g. (80–92%), depending on the temperature of crystallization ([Note 4](#)) and ([Note 5](#)).

2. Notes

1. The [D-glucono- \$\delta\$ -lactone](#) (m.p. 153–155°; assay > 99%, Pfizer specification; water content < 0.2%, Karl Fischer titration) is obtained from Charles Pfizer & Co., Inc., 630 Flushing Avenue, Brooklyn 6, New York. Material having a water content greatly in excess of 0.2% may be dried for 48 hours at 100°. Drying at higher temperatures has in some samples produced decomposition. Independent experience with many preparations in the laboratories of one of the editors (Max Tishler, Merck Sharp & Dohme Research Laboratories) has indicated that drying is generally not necessary.
2. As long as 48 hours may be required.
3. The checkers found m.p. 69.5–74°.
4. Since [2,3,4,5,6-penta-O-acetyl-D-gluconyl chloride](#) is appreciably soluble in [ethyl ether](#) at 0°, the yield can be improved by carrying out the crystallization at lower temperatures.
5. The submitters report $[\alpha]_D^{23} = +2.2$ ($c = 4.0$ in ethanol-free [chloroform](#)). The checkers found $[\alpha]_D^{25} = +2.5$.

3. Discussion

The method followed for the preparation of the two acids is a modification of that of Major and Cook.² The preparation for [penta-O-acetyl-D-gluconyl chloride](#) is that of Braun and coworkers.³ A slightly different technique has also been described.⁴

References and Notes

1. University of Vermont, Burlington, Vt.
2. R. T. Major and E. W. Cook, *J. Am. Chem. Soc.*, **58**, 2475, 2477 (1936).
3. C. E. Braun, S. H. Nichols, Jr., J. L. Cohen, and T. E. Aitken, *J. Am. Chem. Soc.*, **62**, 1619 (1940).
4. R. T. Major, and E. W. Cook, U.S. pat. 2,368,557 [*C.A.*, **40**, 3549 (1946)].

Appendix

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

petroleum ether

[ethyl ether](#) (60-29-7)

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

[phosphorus pentachloride](#) (10026-13-8)

chloroform (67-66-3)

toluene (108-88-3)

zinc chloride (7646-85-7)

D-glucono- δ -lactone (90-80-2)

2,3,4,5,6-PENTA-O-ACETYL-D-GLUCONIC ACID (17430-71-6)

2,3,4,5,6-PENTA-O-ACETYL-D-GLUCONYL CHLORIDE,
penta-O-acetyl-D-gluconyl chloride (53555-69-4)

Gluconic acid, pentaacetyl-,D-

Tetra-O-acetyl-D-gluconic acid monohydrate

2,3,4,6-Tetra-O-acetyl-D-gluconic acid monohydrate

Gluconyl chloride, pentaacetyl-, D-