



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.

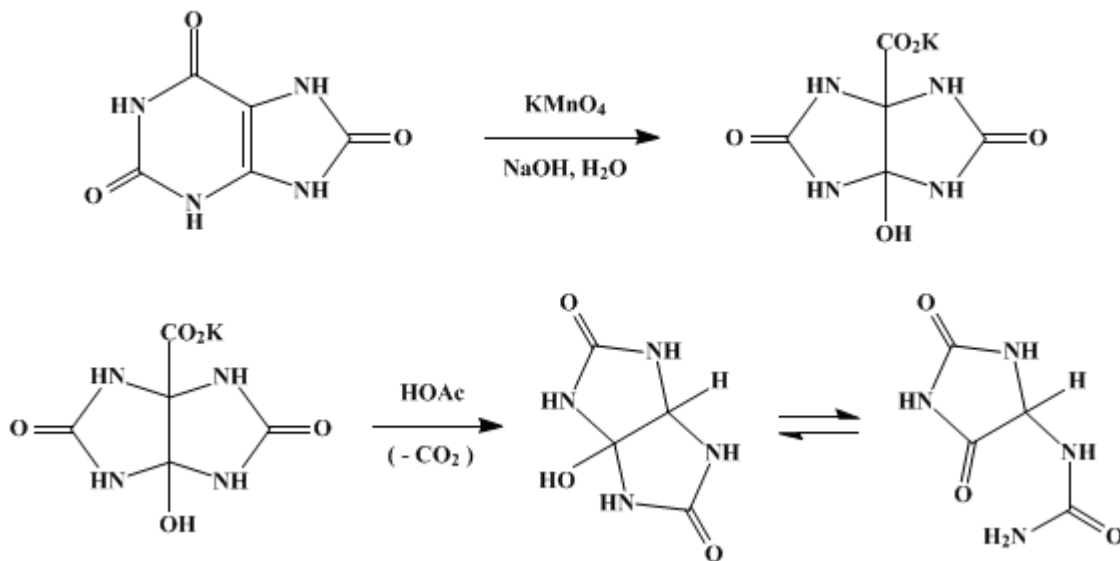
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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. 2, p.21 (1943); Vol. 13, p.1 (1933).

ALLANTOIN



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1. Procedure

One hundred grams of [uric acid](#) (0.595 mole) and 4.5 l. of hot ($70\text{--}85^\circ$) water are placed in a 12-l. round-bottomed flask equipped with a mechanical stirrer. The stirrer is started, and a solution of 80 g. (2 moles) ([Note 1](#)) of commercial [sodium hydroxide](#) in 120 cc. of water is added. Stirring is continued until the [uric acid](#) is in solution ([Note 2](#)), after which the solution is cooled by means of a stream of water directed against the flask. When the temperature has fallen to $25\text{--}30^\circ$, 50 g. (0.32 mole) ([Note 3](#)) of [potassium permanganate](#) is added all at once ([Note 4](#)) to the vigorously stirred solution. Stirring is continued for fifteen to twenty minutes ([Note 5](#)), and the mixture is filtered ([Note 6](#)) at once through a 19-cm. Büchner funnel. The first fraction of the filtrate contains a small amount of [manganese dioxide](#). This fraction must be collected separately and returned to the funnel. As soon as the filtrate becomes clear it is collected in a 12-l. round-bottomed flask which contains 130 cc. (137 g., 2.2 moles) of glacial [acetic acid](#). The filtrate is tested with litmus to be sure that it is acid, and evaporated to a volume of 1.5–2 l. on a steam bath under reduced pressure (20–30 mm.). The solution thus obtained is allowed to stand in a cool place overnight, and the [allantoin](#) which crystallizes is filtered on a 9-cm. Büchner funnel ([Note 7](#)). The [allantoin](#) is dissolved in 800–900 cc. of boiling water, treated with 5 g. of [Norite](#), and filtered rapidly through a fluted filter paper in a steam funnel. The filtrate is allowed to stand in a cool place overnight ([Note 8](#)), and the white crystals of [allantoin](#) are separated by filtration with suction. The yield of product melting at $230\text{--}231^\circ$ ([Note 9](#)) is 60–71 g. (64–75 per cent of the theoretical amount). If the filtrate from the purification liquors is concentrated to 100 cc., there is obtained an additional 3–5 g. of [allantoin](#).

2. Notes

1. The use of more than 80 g. of [sodium hydroxide](#) does not increase the yield, but, if not neutralized immediately upon completion of the reaction, it causes decomposition of some [allantoin](#).
2. It is essential that the [uric acid](#) be completely in solution; otherwise not all of it will be oxidized. When the solution is cooled a small amount of white precipitate sometimes separates, but this does not affect the yield.
3. The amount of [potassium permanganate](#) can be varied between 50 and 62 g. (0.32–0.39 mole) without changing the yield.

4. The [potassium permanganate](#) must be added rapidly (one to five minutes).
5. If the period of stirring is reduced to ten minutes, some unchanged [uric acid](#) is recovered. The period can be extended slightly beyond twenty minutes without decreasing the yield of [allantoin](#), but if it is extended beyond one hour the yield is appreciably decreased.
6. Filtration must be as rapid as possible; this necessitates the use of a large Büchner funnel.
7. The filtrate is discarded since the amount of [allantoin](#) is not sufficient to repay attempts to separate it from the various other compounds present.
8. Crystallization can be hastened by stirring in an ice bath.
9. The melting point appears to depend somewhat on the rate of heating. The melting point 228–230° is observed in a capillary tube in a bath heated slowly from room temperature. If the capillary is placed in a bath already heated to 228°, the specimen melts at 233–234°. On a copper block still higher melting points are obtained.

3. Discussion

[Allantoin](#) has been prepared by the oxidation of [uric acid](#) with [potassium permanganate](#),¹ [lead dioxide](#),² [potassium ferricyanide](#),³ [oxygen](#),⁴ [manganese dioxide](#),⁵ [ozone](#),⁶ or [hydrogen peroxide](#),⁷ and by the electrolytic oxidation of lithium urate.⁸ It is also formed by heating [urea](#) with [glyoxylic acid](#)⁹ or with any one of a number of disubstituted acetic acids such as, for instance, [dichloroacetic acid](#).¹⁰

References and Notes

1. Claus, Ber. 7, 226 (1874); Sundwik, Z. physiol. Chem. 41, 343 (1904); Behrend, Ann. 333, 141 (1904); Biltz, Ber. 43, 1999 (1910); Biltz and Giesler, ibid. 46, 3410 (1913); Biltz and Max, ibid. 54, 2451 (1921); Neubauer, Ann. 99, 206 (1856).
2. Wöhler and Liebig, ibid. 26, 241 (1838); Mulder, ibid. 159, 349 (1871).
3. Schlieper, ibid. 67, 214 (1848).
4. Biltz and Max, Ber. 54, 2451 (1921).
5. Wheeler, Zeit. für Chem. 1866, 746.
6. Gorup-Besanez, Ann. 110, 94 (1859).
7. Venable, J. Am. Chem. Soc. 40, 1099 (1918).
8. Fichter and Kern, Helv. Chim. Acta 9, 429 (1926).
9. Grimaux, Ann. chim. phys. (5) 11, 389 (1877).
10. Merck and Company, Inc., U. S. pat. 2,158,098 [C. A. 33, 6350 (1939)].

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

[lithium urate](#)

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

[sodium hydroxide](#) (1310-73-2)

[potassium permanganate](#) (7722-64-7)

[oxygen](#) (7782-44-7)

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

urea (57-13-6)

hydrogen peroxide (7722-84-1)

manganese dioxide (1313-13-9)

Allantoin (97-59-6)

uric acid

potassium ferricyanide (13746-66-2)

ozone (10028-15-6)

glyoxylic acid (298-12-4)

dichloroacetic acid (79-43-6)

lead dioxide