



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.

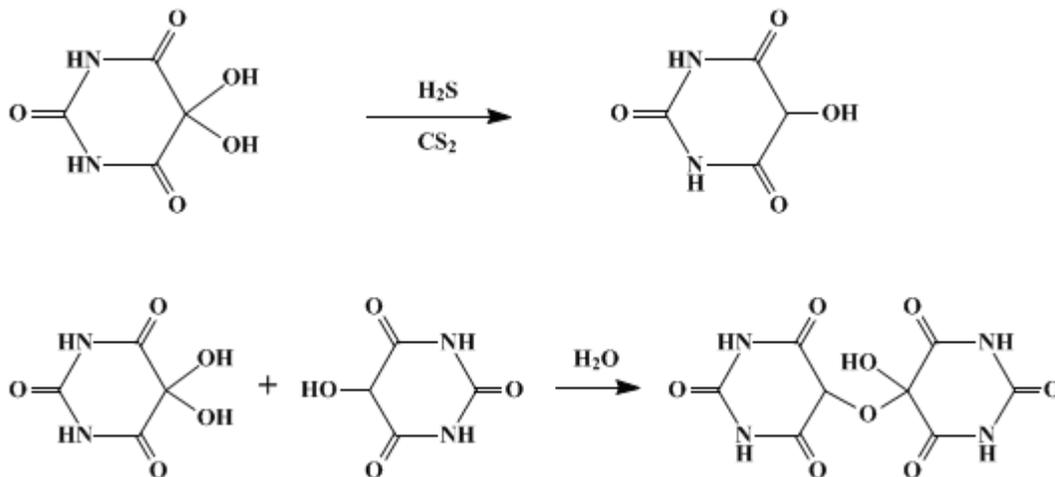
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

Organic Syntheses, Coll. Vol. 4, p.25 (1963); Vol. 33, p.3 (1953).

ALLOXANTIN DIHYDRATE

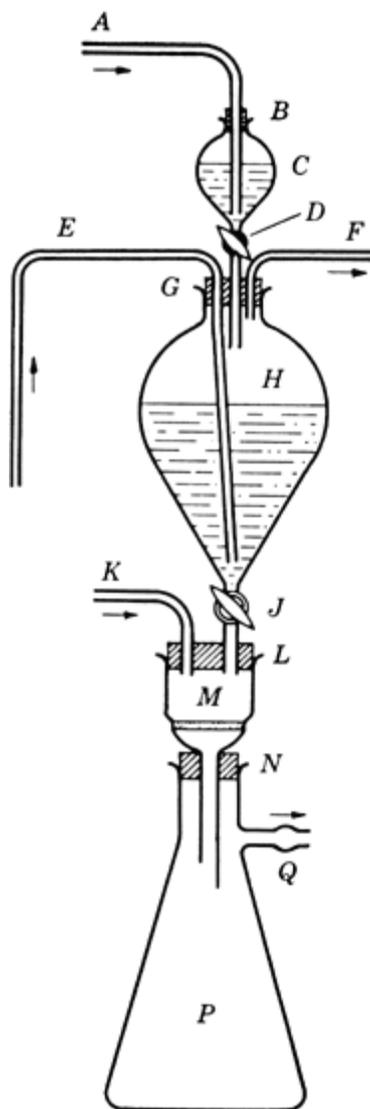


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1. Procedure

An apparatus is assembled in the hood, as shown in Fig. 1. In the 2-l. globe-shaped separatory funnel *H* (stopcock *J* closed) is placed 1.3 l. of deaerated water (Note 1). Three-holed rubber stopper *G* (bearing the stem of a 125-ml. separatory funnel *C* with stopcock *D* closed, a long inlet tube *E*, and a short outlet tube *F*) is inserted in the neck of *H*. In the neck of *C*, a rubber stopper *B*, provided with an inlet tube *A*, is inserted. *H* is flushed with nitrogen (Note 2) admitted at *E*. To the water is added 16.0 g. (0.1 mole) of alloxan monohydrate (Note 3), and the mixture is stirred by the flow of nitrogen through *E* until the alloxan monohydrate has dissolved. The nitrogen flow is discontinued, and hydrogen sulfide (Note 4) is passed in at *E* until the mixture is saturated with this gas and the aqueous solution is free from opalescence (about 2 hours). Carbon disulfide (100 ml.) is now added, and the mixture is agitated for 5 minutes by means of the hydrogen sulfide gas stream. The carbon disulfide layer is then cautiously withdrawn through *J* and discarded, and the aqueous solution is washed once more with 100 ml. of carbon disulfide which is separated and discarded. The hydrogen sulfide flow is discontinued, and nitrogen is passed in at *E* for about 2 hours or until the gas emerging at *F* gives no more than a faint test for hydrogen sulfide with lead acetate paper.

Fig. 1. Apparatus for preparation of alloxantin dihydrate.



Tubes *E* and *F* are now closed, stopper *B* is loosened, and *C* is flushed out with **nitrogen** admitted through tube *A*. Deaerated water (100 ml.) is placed in *C*, which is then flushed with **nitrogen**. To this water is added **alloxan monohydrate** (16.0 g.; 0.1 mole), and the mixture is stirred with *A*, while the **nitrogen** stream is continued, until the solid has dissolved. *B* is now pushed down to give a tight fit, a slight pressure of **nitrogen** is applied (at *A*), *F* and *D* are opened, and the solution is allowed to pass from *C* into *H*. To wash out traces of **alloxan**, a further 10 ml. of water is placed in *C* and run into *H*. *D* is closed, and **nitrogen** is passed in at *E* and out of *F* until the solutions are thoroughly mixed. *E* and *F* are now closed, and the mixture in *H* is allowed to stand until crystallization is complete (overnight). In the meantime, the stem of funnel *H* is inserted in one hole of the two-holed rubber stopper *L* (also bearing inlet tube *K*); *L* is inserted in the mouth of *M* (a 150-ml., Pyrex Büchner funnel with coarse, fritted-glass septum); and the stem of *M* is inserted in the rubber stopper *N* placed in the neck of a 2-liter Büchner flask *P* (side arm, *Q*). To flush out *M* and *P*, **nitrogen** is passed in at *K* and out of *Q*. *K* and *Q* are now closed, *F* is opened, and a slight pressure of **nitrogen** is applied at *F*. *Q* and *J* are opened, and, if necessary, slight suction is applied at *Q*. When all the suspension has passed out of *H*, the **nitrogen** stream is continued for a few minutes, to remove as much as possible of the liquid clinging to the precipitate in *M*. Then *F*, *J*, and *Q* are closed. The Büchner funnel *M* and its contents are quickly removed, placed in a vacuum desiccator (preflushed with **nitrogen**), and dried to constant weight, at room temperature, over **phosphorus pentoxide** and soda-lime. The yield is 27–27.5 g. (84–85%) (**Note 5**), (**Note 6**), and (**Note 7**).

2. Notes

1. Deaerated water is prepared as follows. A boiling stone is added to distilled water which is then boiled under reflux for at least 5 minutes; it is cooled in ice to room temperature under an atmosphere of oxygen-free [nitrogen](#).
2. For preparation of moist, oxygen-free [nitrogen](#), the commercial gas is passed through (a) a 500-ml. Drechsel bottle containing a fresh solution of 25 g. of [sodium hydroxide](#) plus 5 g. of [pyrogallol](#) in 250 ml. of deaerated water, (b) a reversed, empty 500-ml. bottle, and (c) a 500-ml. bottle containing 250 ml. of deaerated water.
3. [Alloxan monohydrate](#) from Eastman Kodak Company is satisfactory. It is dried to constant weight over soda-lime and [phosphorus pentoxide](#) in the vacuum desiccator at room temperature. It should be colorless, and readily and completely soluble in 5 volumes of cold water. The sample employed assayed 99–100% [alloxan monohydrate](#) (p. 23) by Tipson and Cretcher's method.²
4. Commercial [hydrogen sulfide](#) is passed through a (reversed) empty 500-ml. Drechsel gas-washing bottle and then through 250 ml. of deaerated water in a similar bottle (not reversed).
5. The solubility of [alloxantin dihydrate](#) in water at room temperature is about 0.29 g. per 100 ml. of solution.³ An additional 4 g. of product may be obtained by evaporation of the mother liquor to dryness at 25° under reduced pressure ([nitrogen](#) atmosphere).
6. The yield is slightly less if traces of crystals are left adhering to the inner walls of funnel *H*. The [alloxantin](#) obtained by dehydration of the product at 120–150° under reduced pressure for 2 hours melts with decomposition in 0.5 to 1 minute when placed in a block heated to 245°.⁴
7. The submitter reports that with minor modification the above [hydrogen sulfide](#) reduction procedure can be applied to the preparation of the [dialuric acid monohydrate](#) intermediate. The apparatus is assembled as in [Fig. 1](#) with the exception that funnel *C* and its accessories are deleted. The above reduction procedure is followed initially, employing 500 ml. of deaerated water and 50 g. of [alloxan monohydrate](#) instead of the quantities shown above. After the saturation with [hydrogen sulfide](#) (determined by weighing) and the first agitation with [carbon disulfide](#) have been conducted as above, the funnel is assembled for filtration in an atmosphere of [hydrogen sulfide](#) (rather than [nitrogen](#)), and the suspension in *H* is filtered through *M* by manipulations analogous to those described. The colorless crystals of [dialuric acid monohydrate](#) are washed on the filter with an additional 100 ml. of [carbon disulfide](#) added portionwise via *H*, and, while wet with [carbon disulfide](#) and [hydrogen sulfide](#), the crystals and funnel *M* are transferred to a shielded vacuum desiccator and dried over soda-lime and [phosphorus pentoxide](#) under high vacuum (Dry Ice-cooled trap). The yield is 44–44.5 g. (87–88%). Even at 300°, the compound exhibits no true melting or gas evolution. Heated at 2° per minute in an aluminum block (initial temperature, 150°) it appears unchanged at 200°, turns faintly pink at 203–206°, and gradually becomes reddish brown (229–232°) and then purplish black at about 270°.

3. Discussion

Methods of Preparation are reviewed in *Org. Syntheses Coll. Vol. 3*, 42 (1955).

This preparation is referenced from:

- *Org. Syn. Coll. Vol. 3*, 42

References and Notes

1. Mellon Institute of Industrial Research, Pittsburg, Pennsylvania.
 2. Tipson and Cretcher, *Anal. Chem.*, **22**, 822 (1950).
 3. Thunberg, *Skand. Arch. Physiol.*, **33**, 217 (1916) [*C. A.*, **11**, 456 (1917)]; Biilmann and Bentzon, *Ber.*, **51**, 522 (1918).
 4. *Org. Syntheses Coll. Vol. 3*, 42 (1955).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

soda-lime

sodium hydroxide (1310-73-2)

hydrogen sulfide (7783-06-4)

nitrogen (7727-37-9)

carbon disulfide (75-15-0)

pyrogallol (87-66-1)

alloxantin (76-24-4)

Alloxan monohydrate (2244-11-3)

Alloxan (50-71-5)

Alloxantin dihydrate (6011-27-4)

phosphorus pentoxide (1314-56-3)

dialuric acid monohydrate (444-15-5)