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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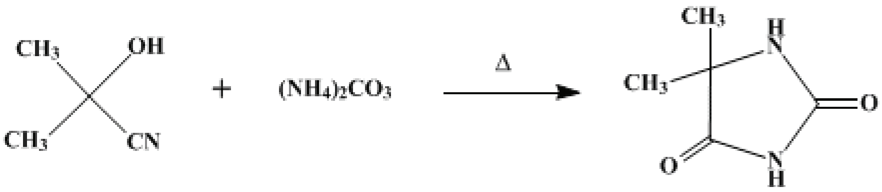
5,5-DIMETHYLHYDANTOIN

[Hydantoin, 5,5-dimethyl-]



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1. Procedure

In a 600-ml. beaker are mixed 85 g. (1 mole) of acetone cyanohydrin (Note 1) and 150 g. (1.31 moles) of freshly powdered ammonium carbonate. The mixture is warmed on a steam bath, preferably in a hood (Note 2), and stirred with a thermometer (Note 3). Gentle action begins around 50° and continues during about 3 hours at 68–80°. To complete the reaction and to decompose excess ammonium carbonate, the temperature is finally raised to 90° and maintained at this point until the liquid mixture is quiescent (30 minutes). The residue is colorless or pale yellow (Note 1) and solidifies on cooling. It is dissolved in 100 ml. of hot water, digested with Norit, and filtered rapidly through a heated filter. The filtrate is evaporated on a hot plate until crystals appear at the surface of the liquid, which is then chilled in an ice bath. The white crystals are filtered with suction; the filter cake is pressed and sucked dry and then washed twice with small portions (5–7 ml.) of ether, each portion being well incorporated with the crystals and then drawn through with suction. The mother liquor is concentrated as before to a volume of 25 ml. or less and chilled, and a further crop of crystals is obtained by repetition of the operations outlined (Note 4). The yield is 65–72 g. (51–56%). The first crop is nearly pure and melts at 173°; the second crop melts at about 164°.

The dimethylhydantoin is dissolved in the least boiling water (about 65 ml.) and digested with charcoal, and the hot solution is filtered through a heated filter. The filtrate is chilled, and the separated crystals are filtered with suction and washed sparingly with cold water. The recovery is about 80–85% of the crude weight. The recrystallized product melts at 174–175° (178° cor.). A further crop of less pure material (m.p. 171–172°) may be obtained by concentration of the mother liquor to small volume (Note 5).

2. Notes

1. Acetone cyanohydrin [*Org. Syntheses* Coll. Vol. **2**, 7 (1943)] is entirely satisfactory. For immediate use, a less pure cyanohydrin will serve; this is readily made as follows.[1] A solution of 165 g. (pure basis) of sodium bisulfite in 300 ml. of cold water is transferred to a 1-l. flask, which is cooled in an ice bath, while 87 g. of acetone is dropped in slowly with rotation of the flask. A solution of 100 g. (pure basis) of potassium or 75 g. of sodium cyanide in 300 ml. of cold water is then added gradually. The cyanohydrin separates as an upper layer; when sodium cyanide is used, this separation is slower and is not complete until the mixture has come to room temperature. It is drawn off and dried for several hours over sodium sulfate in a stoppered flask kept in the dark. The yield is about 90 g. (70%); it may be somewhat increased by ether extraction of the aqueous liquid. Acetone cyanohydrin so prepared is colorless, or nearly so, and if used promptly is satisfactory for the preparation of dimethylhydantoin. If it is kept more than a day or two, the cyanohydrin may become deep red and will then impart a red color to the dimethylhydantoin which is difficult to remove.
2. The reaction mixture evolves ammonia slowly in amounts which are unpleasant though tolerable in a well-ventilated room.
3. During most of the reaction, the mixture is partly solid or very viscous and cannot be stirred properly

by a mechanically operated stirrer of the usual type. A Hershberg stirrer is unsatisfactory.
4. Dimethylhydantoin is highly soluble in hot water, and its solubility in cold water is considerable. Several crops may be removed by successive concentrations of the mother liquors, taken finally to very small volume. The conversion of acetone cyanohydrin to dimethylhydantoin is said to be practically quantitative.[2]
5. The method described serves for the preparation of various 5-substituted or 5,5-disubstituted hydantoins, using appropriate cyanohydrins. With methylethylketone cyanohydrin there was obtained a 75% yield of 5-methyl-5-ethylhydantoin, m.p. 141.5°.

3. Discussion

Hydantoins with one or two substituents in the 5 position have been prepared by heating cyanohydrins with urea and treating this reaction mixture with moderately concentrated hydrochloric acid;[3] by heating alanine sulfate with potassium cyanate;[4] by the action of phosgene or oxalyl chloride[5] or carbonic esters[6] on C-substituted aminoacetamides; by the fusion of amino acids with urea;[7] by the action of potassium cyanate on α-aminonitrile hydrochlorides, and heating the resulting ureido-nitriles with dilute hydrochloric acid;[8] by heating aldehydes or ketones with alkali cyanide and ammonium carbonate under pressure of several atmospheres of carbon dioxide;[9] by warming cyanohydrins with ammonium carbonate;[2] by the interaction of ketone or aldehyde and ammonium carbonate with hydrogen cyanide or alkali cyanide, in ligroin or in 50% ethanol, at room temperature or at 50–80°;[10] or by the interaction of ketone or aldehyde bisulfite compounds with cyanide and ammonium carbonate.[10] The procedure described[11] is that of Bucherer and Steiner.[2] In a more recent method, an equimolecular mixture of acetone and hydrogen cyanide is treated with ammonia and carbon dioxide.[12]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 7

References and Notes

1. Houben, *Die Methoden der organischen Chemie*, 3rd Ed., Vol. III, p. 568, Verlag Georg Thieme, Leipzig, 1930.
2. Bucherer and Steiner, *J. prakt. Chem.*, **140**, 291 (1934).
3. Pinner, *Ber.*, **20**, 2355 (1887); **21**, 2320 (1888).
4. Urech, *Ann.*, **165**, 99 (1873).
5. Ger. pat. 310,427 [*Frdl.*, **13**, 803 (1923–1924)].
6. Read, *J. Am. Chem. Soc.*, **44**, 1749 (1922).
7. Griess, *Ber.*, **2**, 47 (1869); Halpern, *Monatsh.*, **17**, 243 (1896).
8. Herbst and Johnson, *J. Am. Chem. Soc.*, **54**, 2465 (1932).
9. Bergs, Ger. pat. 566,094 (1929) [*C. A.*, **27**, 1001 (1933)].
10. Bucherer and Lieb, *J. prakt. Chem.*, **141**, 5 (1934).
11. Wagner and Simons, *J. Chem. Education*, **13**, 266 (1936).
12. U. S. pat. 2,391,799 [*C. A.*, **40**, 1876 (1946)].

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

cyanohydrin

cyanohydrins

α-aminonitrile hydrochlorides

ureido-nitriles

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

ammonium carbonate (506-87-6)

ammonia (7664-41-7)

ether (60-29-7)

sodium cyanide (143-33-9)

hydrogen cyanide (74-90-8)

sodium sulfate (7757-82-6)

cyanide (57-12-5)

sodium bisulfite (7631-90-5)

carbon dioxide (124-38-9)

acetone (67-64-1)

Norit,
charcoal (7782-42-5)

phosgene (75-44-5)

urea (57-13-6)

potassium (7440-09-7)

potassium cyanate (590-28-3)

Acetone cyanohydrin (75-86-5)

oxalyl chloride (79-37-8)

5,5-Dimethylhydantoin,
Hydantoin, 5,5-dimethyl-,
dimethylhydantoin (77-71-4)

methylethylketone cyanohydrin

5-methyl-5-ethylhydantoin (16820-12-5)

alanine sulfate