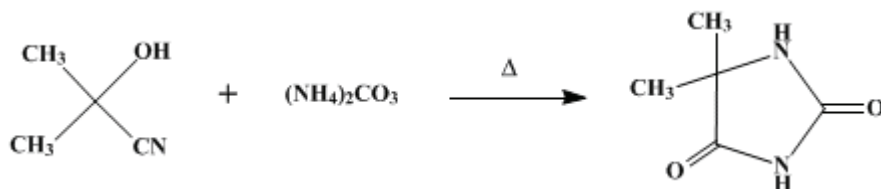


5,5-DIMETHYLHYDANTOIN

[Hydantoin, 5,5-dimethyl-]



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Checked by C. F. H. Allen and G. F. Frame.

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 hydantoin, using appropriate cyanohydrins. With **methylethylketone cyanohydrin** there was obtained a 75% yield of **5-methyl-5-ethylhydantoin**, m.p. 141.5°.

3. Discussion

Hydantoin 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 esters⁶ 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 described¹¹ 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

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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).
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10. Bucherer and Lieb, *J. prakt. Chem.*, **141**, 5 (1934).
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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

