Organic Syntheses

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.

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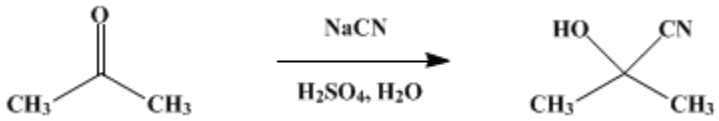
Organic Syntheses, Coll. Vol. 2, p.7 (1943); Vol. 15, p.1 (1935).

ACETONE CYANOHYDRIN

[Isobutyronitrile, α-hydroxy-]



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1. Procedure

In a 5-l. three-necked, round-bottomed flask fitted with an efficient stirrer (Note 1), a separatory funnel, and a thermometer in a well is placed a solution of 500 g. (9.7 moles) of powdered 95 per cent sodium cyanide in 1.2 l. of water and 900 cc. (713 g., 12.3 moles) of acetone. The flask is surrounded by an ice bath, and the solution is stirred vigorously. When the temperature falls to 15°, 2.1 l. (8.5 moles) of 40 per cent sulfuric acid (Note 2) is added over a period of three hours, the temperature being kept between 10° and 20°. After all the acid has been added the stirring is continued for fifteen minutes and then the flask is set aside for the salt to settle. Usually a layer of acetone cyanohydrin forms and is decanted and separated from the aqueous layer. The sodium bisulfate is removed by filtration and washed with three 50-cc. portions of acetone. The combined filtrate and acetone washings are added to the aqueous solution, which is then extracted three times with 250-cc. portions of ether (Note 3). The extracts are combined with the cyanohydrin previously separated and dried with anhydrous sodium sulfate. The ether and acetone are removed by distillation from a water bath, and the residue is distilled under reduced pressure. The low-boiling portion is discarded, and acetone cyanohydrin is collected at 78–82°/15 mm. The yield is 640–650 g. (77–78 per cent of the theoretical amount) (Note 4).

2. Notes

1. It is advantageous to use a heavy metal stirrer because of the increased viscosity of the mixture toward the end of the reaction. Since some hydrogen cyanide may escape from the reaction mixture, the stopper carrying the stirrer should be fitted with a tube for leading off the gas or the reaction should be carried out under a hood.
2. The 40 per cent sulfuric acid is prepared by adding 650 cc. of concentrated sulfuric acid (sp. gr. 1.84) to 1.8 l. of water.
3. Extraction and distillation should be started as soon as possible after the completion of the reaction, and the distillation should be done as rapidly as possible to avoid decomposition.
4. The preparation of acetone cyanohydrin from potassium cyanide and the bisulfite addition product of acetone is described in Org. Syn. **20**, 43. The procedure given there furnishes a less pure cyanohydrin which, however, is suitable for some synthetic uses.

3. Discussion

Acetone cyanohydrin has been prepared from acetone and anhydrous hydrogen cyanide in the presence of a basic catalyst such as potassium carbonate, potassium hydroxide, or potassium cyanide;[1] by the reaction of potassium cyanide on the sodium bisulfite addition product of acetone;[2] and by the action of hydrogen cyanide, prepared directly in the reaction mixture, on an aqueous solution of acetone.[3] More modern industrial procedures employ acetone, liquid hydrogen cyanide, and a basic catalyst.[4]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 323

- Org. Syn. Coll. Vol. 3, 560
- Org. Syn. Coll. Vol. 5, 839

References and Notes

1. Urech, Ann. **164**, 256 (1872); Ultée, Ber. **39**, 1857 (1906); Rec. trav. chim. **28**, 7 (1909).
2. Bucherer and Grolée, Ber. **39**, 1225 (1906); Ger. pat. 141,509 (Chem. Zentr. **1903**, I, 1244); Org. Syn. **20**, 43.
3. Welch and Clemo, J. Chem. Soc. **1928**, 2629.
4. Triplex Safety Glass Company Ltd., Brit. pat. 416,007 [C. A. **29**, 814 (1935)]; 452,285 [C. A. **31**, 417 (1937)]; I. G. Farbenind. A.-G., Fr. pat. 804,124 [C. A. **31**, 2615 (1937)]; Deutsche Gold- und Silber-Scheideanstalt vorm. Roessler, Fr. pat. 812,366 [C. A. **32**, 958 (1938)].

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

sodium bisulfite addition product of acetone

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

ether (60-29-7)

sodium cyanide (143-33-9)

hydrogen cyanide (74-90-8)

sodium sulfate (7757-82-6)

potassium cyanide (151-50-8)

acetone (67-64-1)

potassium hydroxide (1310-58-3)

sodium bisulfate (7681-38-1)

Acetone cyanohydrin,
Isobutyronitrile, α-hydroxy- (75-86-5)