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.

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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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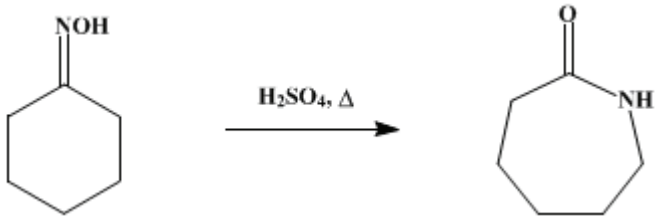
Organic Syntheses, Coll. Vol. 2, p.371 (1943); Vol. 17, p.60 (1937).

2-KETOHEXAMETHYLENIMINE

[Hexamethylenimine, 2-oxo-]



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1. Procedure

The rearrangement of 120 g. (1.06 moles) of pure cyclohexanone oxime (Note 1) is carried out in twelve 10-g. portions according to the procedure given in the first eight lines of (*B*), p. 77.

The acid solutions of ε-caprolactam from the twelve runs are combined in a 3-l. round-bottomed flask which is fitted with a mechanical stirrer and a separatory funnel and packed in an ice-salt mixture. The solution is cooled to 0° and carefully made faintly alkaline to litmus by the addition of 24 per cent potassium hydroxide solution, added very slowly (five to six hours) with good cooling (Note 2). Usually about 1550 cc. of the alkaline solution is needed. The temperature must be kept below 10° to avoid hydrolysis during this stage of the preparation.

The potassium sulfate which has separated is then removed by filtration and washed with two 100-cc. portions of chloroform. The faintly alkaline aqueous solution is extracted with about five 200-cc. portions (Note 3) of chloroform, and the combined chloroform solutions are washed once with 50 cc. of water to remove any alkali. The chloroform is then distilled and the product fractionated under reduced pressure. The yield of 2-ketohexamethylenimine, boiling at 127–133°/7 mm. and melting at 65–68°, amounts to 71–78 g. (59–65 per cent of the theoretical amount) (Note 4).

2. Notes

1. Pure cyclohexanone oxime, m.p. 86–88° (pp. 76 and 314), must be used since poorer grades char badly when treated with sulfuric acid.
2. Potassium hydroxide gives better results than sodium hydroxide, since the large amount of hydrated sodium sulfate which separates from the solution if sodium hydroxide is used prevents efficient cooling.
3. The extraction is continued until no appreciable amount of product is obtained in the chloroform layer.
4. The boiling point is reported in the literature as 139–140°/12 mm.; the melting point is reported at various temperatures from 65° to 70°.

3. Discussion

2-Ketohexamethylenimine, ε-caprolactam, has been obtained by heating ε-aminocaproic acid or its ethyl ester[1] and by the rearrangement of cyclohexanone oxime.[2], [3], [4] The method[4] described above is Ruzicka's[3] modification of Wallach's[2] original directions for the rearrangement of the oxime. This rearrangement can also be run as a continuous process.[5]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 28
- Org. Syn. Coll. Vol. 2, 76

- Org. Syn. Coll. Vol. 4, 588
- Org. Syn. Coll. Vol. 10, 207

References and Notes

1. Gabriel and Maass, Ber. **32**, 1271 (1899); von Braun, ibid. **40**, 1840 (1907); Carothers and Berchet, J. Am. Chem. Soc. **52**, 5289 (1930).
2. Wallach, Ann. **312**, 187 (1900); **343**, 43 (1905).
3. Ruzicka, Seidel, and Hugoson, Helv. Chim. Acta **4**, 477 (1921).
4. Eck and Marvel, J. Biol. Chem. **106**, 387 (1934).
5. E. I. du Pont de Nemours and Company, U. S. pat. 2,234,566 [C. A. **35**, 3650 (1941)]; I. G. Farbenind. A.-G., U. S. pat. 2,249,177 [C. A. **35**, 6599 (1941)].

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

sulfuric acid (7664-93-9)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

potassium sulfate (37222-66-5)

sodium sulfate (7757-82-6)

potassium hydroxide (1310-58-3)

ε-AMINOCAPROIC ACID (60-32-2)

2-Ketohexamethylenimine,
ε-caprolactam,
Hexamethylenimine, 2-oxo- (105-60-2)

Cyclohexanone oxime (100-64-1)