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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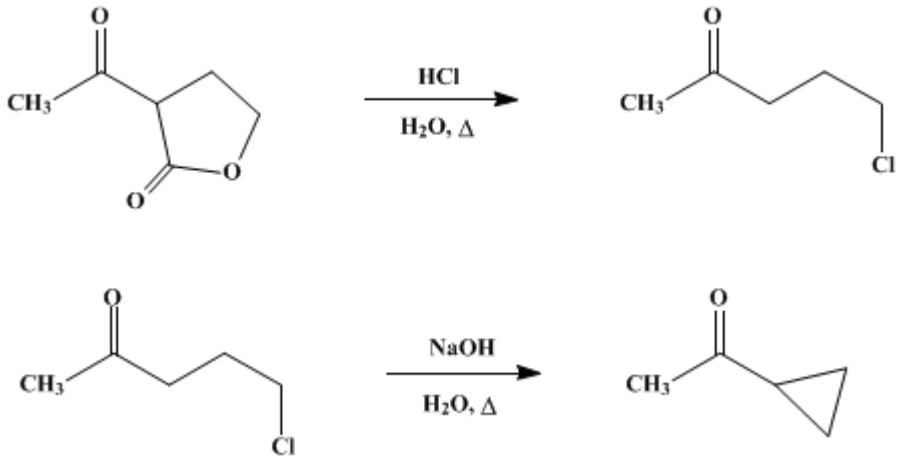
METHYL CYCLOPROPYL KETONE

[Ketone, cyclopropyl methyl]



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1. Procedure

A. *5-Chloro-2-pentanone*. A mixture of 450 ml. of concentrated hydrochloric acid, 525 ml. of water, and 384. g. (3 moles) of α-acetyl-γ-butyrolactone (Note 1) and a boiling chip are placed in a 2-l. distilling flask fitted with a 90-cm. bulb-type condenser and a receiver immersed in an ice water bath (Note 2). Carbon dioxide is evolved immediately. Heating of the reaction mixture is begun at once, and the temperature is raised at such a rate that the reaction mixture does not foam into the condenser. In about 10 minutes the color changes from yellow to orange to black, the effervescence begins to subside, and distillation commences. The distillation is continued as rapidly as possible (Note 3). After 900 ml. of distillate has been collected, 450 ml. of water is added to the distilling flask and another 300 ml. of distillate is collected.

The yellow organic layer in the distillate is separated (Note 4), and the aqueous layer is extracted with three 150-ml. portions of ether. The ether extracts are combined with the organic layer and dried for 1 hour over 25 g. of calcium chloride. A saturated calcium chloride layer forms in the bottom. The ether solution is decanted and dried with an additional 25 g. of calcium chloride. The ether is removed by distillation through a 30-cm. column packed with glass helices and fitted with a total condensation, variable take-off head. The residual crude 5-chloro-2-pentanone weighs 287–325 g. (79–90%) (Note 5). When 290 g. of this material is fractionated through a wrapped 12-in. Vigreux column, the major portion boils at 70–72°/20 mm., n_D^{25} 1.4371, and weighs 258–264 g. (89–91%).

B. *Methyl cyclopropyl ketone*. A 2-l. three-necked flask is fitted with a sweep-type stirrer made from ¼-in. iron rod (Note 6), a reflux condenser, and a 500-ml. dropping funnel. In the flask is placed a solution of 180 g. (4.5 moles) of sodium hydroxide pellets in 180 ml. of water. To this solution is added over a period of 15–20 minutes 361.5 g. (342 ml., approximately 3 moles) of the crude 5-chloro-2-pentanone (Note 7). If the reaction mixture does not begin to boil during the addition, boiling is initiated by slight heating of the flask and is continued for 1 hour. Three hundred and seventy milliliters of water is then added slowly to the reaction mixture over a 20-minute period, and the mixture is heated under reflux for an additional hour.

The condenser is arranged for distillation, and a water-ketone mixture is distilled until all the organic layer is removed from the reaction mixture. The aqueous layer of the distillate is saturated with potassium carbonate, and the upper layer of methyl cyclopropyl ketone is separated. The aqueous layer

is extraced with two 150-ml. portions of ether. The ether extracts and the ketone layer are combined and dried over 25 g. of calcium chloride for 1 hour. The ether solution is decanted and dried with an additional 25 g. of calcium chloride. The dried ether solution is fractionated through the 30-cm. column described in Part A (Note 8). The yield of methyl cyclopropyl ketone, b.p. 110–112°, n_D^{25} 1.4226, is 193–210 g. (77–83%).

2. Notes

1. Available from U. S. Industrial Chemicals, Inc. Its preparation has been described by several workers.[2,3,4]
2. Efficient condensation is important; otherwise some of the product is swept out by the carbon dioxide, and the yield of the chloride is decreased.
3. Any delay in distilling the chloride results in a decrease in yield. If the reaction mixture is allowed to stand overnight before removal of the chloride, the yield is less than 50%.
4. The chloride is usually the bottom layer. However, occasionally some of it also will be found on top. If so, the addition of 50–100 ml. of ether will cause all the chloride to be in the upper layer and will facilitate separation.
5. Corresponding runs beginning with 128 g. (1 mole) of α-acetyl-γ-butyrolactone gave 107–112 g. (89–93%) of crude 5-chloro-2-pentanone. The checkers consistently obtained yields of 79–81% using U. S. Industrial Chemicals, Inc., lactone.
6. A Hershberg stirrer constructed with a ¼-in. iron or stainless-steel shaft is also satisfactory. Glass stirrers are not recommended because they may break.
7. The use of distilled chloride does not result in better over-all yields.
8. A fractionating column is necessary for the separation of the ether-ketone solution. With an ordinary distilling flask, a ketone-ether mixture, b.p. 41°, is obtained with a resultant decrease in the yield of pure ketone. A well-insulated or preferably heated column is necessary for good fractionation.

3. Discussion

Methyl cyclopropyl ketone has been prepared from ethyl acetoacetate and ethylene bromide,[5] and by the action of methylmagnesium bromide on cyclopropyl cyanide.[6,7] The procedure described for its preparation from 5-chloro-2-pentanone is similar to that of Zelinsky and Dengin[8] and has been employed by Smith and Rogier.[9] Methyl cyclopropyl ketone also has been obtained by heating trimethyl-γ-acetopropylammonium bromide[10] or 5-bromo-2-pentanone with potassium hydroxide.[11]

5-Chloro-2-pentanone has been prepared by a number of methods,[12] including treatment of acetopropyl alcohol with gaseous hydrogen chloride.[13] The procedure given is essentially that of Boon[14] and of Forman.[15] A similar procedure has been used for the preparation of the corresponding bromo-and iodoketones.[14]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 278

References and Notes

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

calcium chloride (10043-52-4)

potassium carbonate (584-08-7)

hydrogen chloride,
hydrochloric acid (7647-01-0)

ether (60-29-7)

sodium hydroxide (1310-73-2)

carbon dioxide (124-38-9)

potassium hydroxide (1310-58-3)

ethylene bromide (106-93-4)

Ethyl acetoacetate (141-97-9)

α-acetyl-γ-butyrolactone (517-23-7)

methylmagnesium bromide (75-16-1)

Cyclopropyl cyanide (5500-21-0)

Methyl cyclopropyl ketone,
Ketone, cyclopropyl methyl (765-43-5)

acetopropyl alcohol (1071-73-4)

5-Chloro-2-pentanone (5891-21-4)

trimethyl-γ-acetopropylammonium bromide

5-bromo-2-pentanone