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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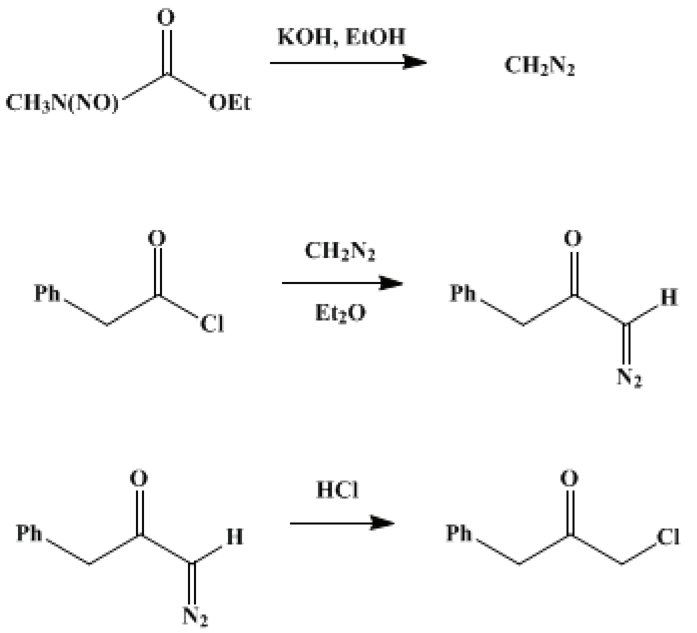
Organic Syntheses, Coll. Vol. 3, p.119 (1955); Vol. 26, p.13 (1946).

BENZYL CHLOROMETHYL KETONE

[2-Propanone, 1-chloro-3-phenyl-]



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1. Procedure

Warning: Diazomethane is poisonous and explosive.

Twelve grams (0.18 mole) of ground potassium hydroxide is dissolved in 45 ml. of *n*-propyl alcohol in a three-necked 500-ml. flask set on a steam bath so that the mixture can be warmed. Two necks of the flask are fitted with dropping funnels. A Vigreux fractionating column (25 cm. in length and 12 mm. in diameter) is inserted in the third neck of the flask. The column is connected, through a condenser and adapter, to a filter flask set in ice as the receiver. The side arm of the receiver is fitted with a drying tube. About 1.5 hours is required to dissolve the hydroxide, whereupon an additional amount of alcohol is added to bring the total volume to 50 ml. The solution is then cooled, and 100 ml. of absolute ether is added. Through one dropping funnel is added dropwise 20 ml. of nitrosomethylurethan[1] (equivalent to 0.10 mole of diazomethane; (Note 1)). The flask is warmed on a steam bath so that diazomethane distils over with ether while the nitrosomethylurethan is being added. The addition requires about 20 minutes. During this operation more dry ether is added as needed, through the second dropping funnel, until the total volume of ether distillate is 250 ml. When the ether distilling over is colorless, the distillate is transferred to another three-necked 500-ml. flask, equipped with a mechanical stirrer, a dropping funnel, and a condenser. To the stirred solution is added, over a period of 15 minutes, a solution of 6.6 ml. (7.7 g., 0.050 mole) of phenylacetyl chloride in 10 ml. of absolute ether. A copious evolution of nitrogen accompanies this operation.

After standing for 2 hours, the solution of diazoketone is cooled in ice and treated with dry gaseous hydrogen chloride until the passage of the gas no longer causes evolution of nitrogen (Note 2). At the end of this time, the original yellow color of the solution has changed to an orange-red. About 100 ml. of water is slowly and cautiously added to the ether solution in order to cause a separation into two layers. An additional 50 ml. of water is then added to give a more complete separation. The ether layer is then washed with two 50-ml. portions of a 5% solution of sodium carbonate in water. The ether solution is dried with anhydrous calcium chloride or calcium sulfate, the solvent evaporated, and the product distilled. The yield of benzyl chloromethyl ketone, b.p. 133–135°/19 mm. or 96–98°/1 mm., is 7.0–7.1 g. (83–85%) (Note 3) and (Note 4).

2. Notes

1. The yield of diazomethane from nitrosomethylurethan is usually given as 0.005 mole per ml.[2] Another method for the preparation of diazomethane has been described.[3]
2. This usually requires about 25 minutes. In certain runs, the hydrogen chloride caused the deposition of a dark red flocculent solid, which was removed by filtration. The yield was then 5–10% lower. This can apparently be avoided by waiting 2 hours, as directed, and by cooling the solution before the hydrogen chloride treatment.
3. This method is general for chloromethyl ketones. Yields of 75–85% may be obtained using hydrocinnamoyl chloride or diphenylacetyl chloride.
4. *Diazomethane is poisonous and explosive.*[4] *The preparation should be carried out in a good hood.*

3. Discussion

Benzyl chloromethyl ketone has been prepared by the reaction of diazomethane with phenylacetyl chloride. The method of Clibbens and Nierenstein,[5] in which one equivalent of diazomethane is added to the acyl chloride and the chloromethyl ketone obtained directly, could not be duplicated by Bradley and Schwarzenbach[6] or by the submitters.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 250
- Org. Syn. Coll. Vol. 5, 351

References and Notes

1. *Org. Syntheses* Coll. Vol. **2**, 464 (1943).
2. Fieser, *Experiments in Organic Chemistry*, 2nd ed., p. **377**, D. C. Heath & Company, Boston, 1941.
3. *Org. Syntheses*, **25**, 28 (1945).
4. Bachmann, *Organic Reactions*, **1**, 47 (1942), John Wiley & Sons, New York.
5. Clibbens and Nierenstein, *J. Chem. Soc.*, **107**, 1491 (1915).
6. Bradley and Schwarzenbach, *J. Chem. Soc.*, **1928**, 2904.

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

calcium chloride (10043-52-4)

hydrogen chloride (7647-01-0)

ether (60-29-7)

sodium carbonate (497-19-8)

nitrogen (7727-37-9)

calcium sulfate (7778-18-9)

potassium hydroxide (1310-58-3)

n-propyl alcohol (71-23-8)

phenylacetyl chloride (103-80-0)

Diazomethane (334-88-3)

nitrosomethylurethan

hydrocinnamoyl chloride (645-45-4)

BENZYL CHLOROMETHYL KETONE,
2-Propanone, 1-chloro-3-phenyl- (937-38-2)

Diphenylacetyl chloride (1871-76-7)