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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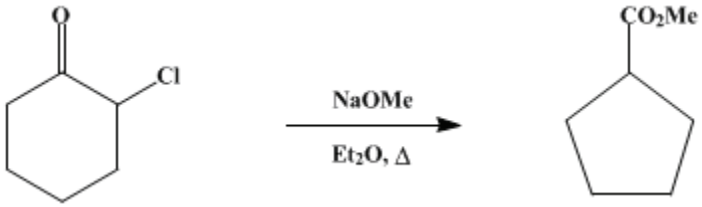
METHYL CYCLOPENTANECARBOXYLATE

[Cyclopentanecarboxylic acid, methyl ester]



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1. Procedure

A dry 1-l. three-necked, round-bottomed flask is equipped with an efficient stirrer (Note 1), a spiral reflux condenser, and a dropping funnel, and all openings are protected by calcium chloride drying tubes. A suspension of 58 g. (1.07 moles) of sodium methoxide (Note 2) and (Note 3) in 330 ml. of anhydrous ether (Note 4) is added, and stirring is begun. To the stirred suspension is added dropwise a solution of 133 g. (1 mole) of 2-chlorocyclohexanone[2] (Note 5) and (Note 6) diluted with 30 ml. of dry ether. The exothermic reaction is regulated by the rate of addition of the chloroketone; about 40 minutes is required for the addition. After the addition of the chloroketone is complete, the mixture is stirred and heated under reflux for 2 hours (Note 7) and is then cooled. Water is added until the salts are dissolved (Note 8). The ether layer is separated, and the aqueous layer is saturated with sodium chloride. After extraction of the aqueous layer two 50-ml. portions of ether, the ethereal solutions are combined and washed successively with 100-ml. portions of 5% hydrochloric acid, 5% aqueous sodium bicarbonate solution, and saturated sodium chloride solution. The ether solution is dried over magnesium sulfate, and the magnesium sulfate is removed by filtration and washed with ether. Removal of the ether by distillation at atmospheric pressure leaves the crude ester, which is distilled, with fractionation (Note 9), at 70–73°/48 mm., n_D^{25} 1.4341. The yield of methyl cyclopentanecarboxylate is 72–78 g. (56–61%) (Note 10).

2. Notes

1. A mercury seal and a Hershberg stirrer made from tantalum wire are suitable.
2. Commercial (Matheson Co., Inc.) sodium methoxide is most convenient. The reaction can be run using sodium methoxide prepared from sodium and methanol, but this procedure is more tedious since it requires the removal of a considerable amount of methanol.
3. A slight excess of sodium methoxide should always be used. When an equivalent amount is employed, slightly lower yields are obtained.
4. Commercial anhydrous analytical reagent ether, from sealed cans, was employed by the checkers without further drying.
5. The 2-chlorocyclohexanone[2] employed by the checkers had b.p. 98–99°/14.5 mm., n_D^{25} 1.4826. Purity is critical in determining the yield of methyl cyclopentanecarboxylate.
6. Chlorocyclohexanone is added to the sodium methoxide, since the reverse mode of addition results in lower yields through increased formation of high-boiling condensation products.
7. The submitters report that equivalent yields are obtained when the mixture is allowed to stand overnight after the addition of the chloroketone is complete.
8. The checkers found that approximately 175 ml. of water is required.
9. The checkers employed a Podbielniak column, 0.8 × 125 cm., with tantalum wire spiral and partial reflux head.[3]
10. The residue of higher-boiling material arises from the condensation of both the starting material and the product under the influence of sodium methoxide.

3. Discussion

Methyl cyclopentanecarboxylate has been prepared by the Favorskii rearrangement of 2-chlorocyclohexanone with sodium methoxide.[4] Other alkyl esters of cyclopentanecarboxylic acid have been prepared by employing the corresponding alkoxides with 2-chlorocyclohexanone.[4,5,6] The Favorskii reaction has been reviewed elsewhere.[7]

The methyl ester has also been obtained by esterification of cyclopentanecarboxylic acid.[8] The acid in turn, has been prepared by the Favorskii rearrangement,[6,7,9,10,11] by the reaction of cyclopentyl Grignard reagent with carbon dioxide,[12] by the carbonylation of cyclopentyl alcohol with nickel carbonyl[13] or with formic acid in the presence of sulfuric acid,[14] by the hydrogenation of cyclopentene-1-carboxylic acid prepared from ethyl cyclopentanone-2-carboxylate[15] or from cyclopentanone cyanohydrin,[16] and from cyclopentene and carbon monoxide in the presence of sulfuric acid.[17]

References and Notes

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

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

methanol (67-56-1)

ether (60-29-7)

carbon monoxide (630-08-0)

sodium bicarbonate (144-55-8)

sodium chloride (7647-14-5)

formic acid (64-18-6)

carbon dioxide (124-38-9)

sodium methoxide (124-41-4)

sodium (13966-32-0)

magnesium sulfate (7487-88-9)

ethyl cyclopentanone-2-carboxylate (611-10-9)

cyclopentyl alcohol (96-41-3)

Cyclopentene (142-29-0)

nickel carbonyl

2-Chlorocyclohexanone,
chlorocyclohexanone (822-87-7)

Methyl cyclopentanecarboxylate,
Cyclopentanecarboxylic acid, methyl ester (4630-80-2)

cyclopentanecarboxylic acid (3400-45-1)

cyclopentene-1-carboxylic acid

cyclopentanone cyanohydrin