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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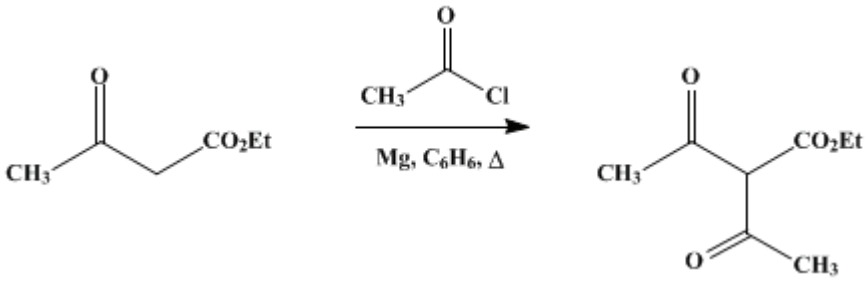
ETHYL DIACETYLACETATE



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1. Procedure

A mixture of 12 g. (0.50 gram atom) of magnesium turnings, 130 g. (1.0 mole) of ethyl acetoacetate, 200 g. of benzene (dried over sodium), and 120 g. (1.50 moles) of acetyl chloride is heated under reflux for 2 hours in a 1-l. round-bottomed flask provided with a condenser closed by a calcium chloride tube and supported in an oil bath (85–90°) (Note 1). The yellow reaction mixture is cooled in an ice bath, and the liquid portion is decanted into a separatory funnel. The residue in the flask is washed twice with 50-ml. portions of ether, and the ethereal solution is poured over ice. The ether-water mixture is then added to the benzene solution in the separatory funnel, and the mixture is shaken thoroughly (Note 2); the aqueous layer is drawn off and discarded. The benzene-ether solution is washed once with 500 ml. of 5% sodium bicarbonate solution and once with 50 ml. of water, and finally is dried over calcium chloride. The ether and most of the benzene are removed by distillation from a water bath, and the remainder of the benzene is driven off at 50°/50 mm. The ethyl diacetylacetate is then precipitated from the residue as the copper derivative by the addition of 1.2 l. of a saturated aqueous solution of copper acetate (Note 3). After addition of the copper acetate solution, the contents of the flask are shaken vigorously now and then and allowed to stand for an hour to ensure complete precipitation of the copper derivative. The blue copper derivative is filtered on a Büchner funnel, washed with two 50-ml. portions of water, and transferred directly to a separatory funnel where it is mixed with 600 ml. of ether.

Four hundred milliliters of 25% sulfuric acid is added, and the contents of the funnel are shaken continually until the copper derivative has disappeared (5–10 minutes). After separation of the ethereal layer, the aqueous layer is extracted twice with 100-ml. portions of ether, and the combined ethereal extracts are dried over calcium chloride. The ether is removed on the steam bath and the residual ester distilled under diminished pressure. A few drops come over up to 90°, but the bulk of the material distils at 92–98°/12 mm. Redistillation yields pure ethyl diacetylacetate boiling at 95–97°/12 mm. The yield is 80–90 g. (46–52%).

2. Notes

1. Hydrogen and hydrogen chloride are evolved; this operation must be conducted in a hood.
2. The greater part of the magnesium remains unchanged. It should be removed by filtering the solution through a plug of *fine* glass wool in an ordinary funnel.
3. The saturated solution of copper acetate is prepared by dissolving 100 g. of finely pulverized copper acetate in 1.2 l. of boiling water. If the preparation contains basic salt, a few milliliters of acetic acid is added, and the solution is filtered. The solution is cooled to 35° before use.

3. Discussion

Ethyl diacetylacetate has been prepared by Claisen from the sodium derivative of acetylacetone and

ethyl chloroformate.[1] It has also been prepared from the sodium derivative of ethyl acetoacetate and acetyl chloride,[2,3,4] from ethyl acetoacetate and acetyl chloride in the presence of magnesium,[5] and from ethyl acetoacetate and ketene.[6]

References and Notes

1. Claisen, *Ann.*, **277**, 171 (1893).
2. James, *Ann.*, **226**, 211 (1884).
3. Elion, *Rec. trav. chim.*, **3**, 250 (1884).
4. Michael, *Ber.*, **38**, 2088 (1905).
5. Ogata, Nosaki, and Takagi, *J. Pharm. Soc. Japan*, **59**, 105 (1939) [*C. A.*, **33**, 4230 (1939)].
6. U. S. pat. 2,417,381 [*C. A.*, **41**, 4169 (1947)].

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

sodium derivative of ethyl acetoacetate

sodium derivative of acetylacetone

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

hydrogen chloride (7647-01-0)

acetic acid (64-19-7)

Benzene (71-43-2)

ether (60-29-7)

hydrogen (1333-74-0)

acetyl chloride (75-36-5)

sodium bicarbonate (144-55-8)

magnesium,
magnesium turnings (7439-95-4)

sodium (13966-32-0)

copper acetate (142-71-2)

Ethyl acetoacetate (141-97-9)

Ketene (463-51-4)

ethyl chloroformate (541-41-3)

Ethyl diacetylacetate (603-69-0)