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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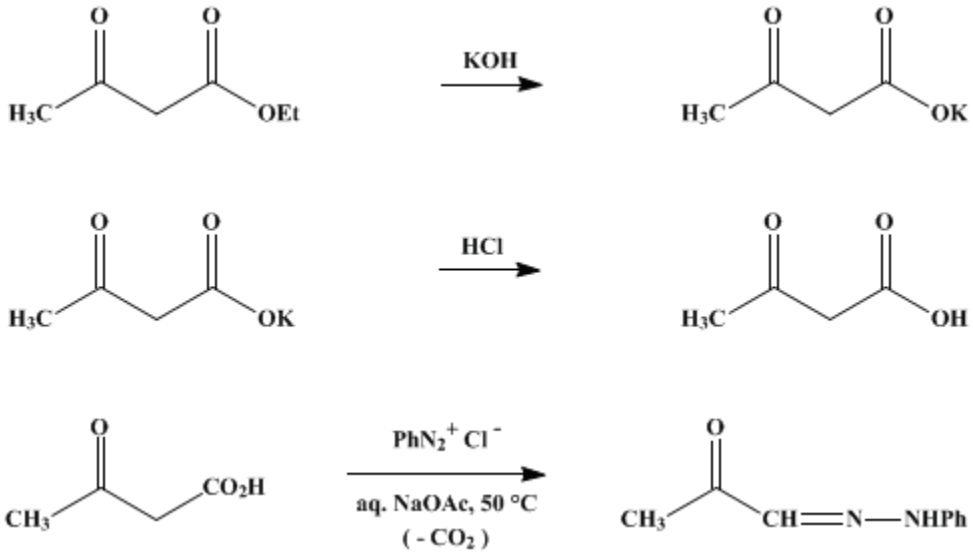
METHYLGLYOXAL-ω-PHENYLHYDRAZONE

[Pyruvaldehyde, 1-phenylhydrazone]



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1. Procedure

In a 4-l. beaker equipped with a mechanical stirrer is placed a solution of 35 g. (0.53 mole) of 85% potassium hydroxide in 1120 ml. of water. To the solution is added, with stirring, 65 g. (64 ml., 0.5 mole) of ethyl acetoacetate (Note 1). The mixture is allowed to stand at room temperature for 24 hours.

Forty-seven grams (48 ml., 0.5 mole) of aniline is dissolved in 200 ml. of aqueous hydrochloric acid (prepared from equal volumes of concentrated acid and water) in a 2-l. beaker. The beaker is equipped with a mechanical stirrer and immersed in an ice-salt bath. After the solution has cooled to ±5°, 36 g. (0.52 mole) of sodium nitrite dissolved in 1 l. of water is added slowly, with stirring, from a separatory funnel. The tip of the stem of the separatory funnel should dip well below the surface of the liquid. The rate of addition is adjusted to maintain the temperature below 10°. A drop of the reaction mixture is tested from time to time with starch-iodide paper (Note 2). The sodium nitrite solution is added until nitrous acid persists in the solution during a 5-minute interval.

The solution of potassium acetoacetate is cooled to 0°, and 45 ml. of concentrated hydrochloric acid in 150 ml. of ice water is added slowly with stirring (Note 3). The diazonium salt solution is then added over a period of 20 minutes, and the mixture is made basic by the addition of 82 g. of sodium acetate dissolved in 300 ml. of water (Note 4). The temperature of the reaction mixture is raised slowly to 50° and maintained at this value for 2 hours; the solid that separates is collected on a filter and dried. The yield of crude product is 72–77 g. (89–95%). Purification can be effected by recrystallization from 200 ml. of toluene. The purified product weights 59–66 g. (73–82%) (Note 5) and (Note 6); m.p. 148–150°.

2. Notes

1. Commercial ethyl acetoacetate was used.
2. The test is made by diluting the test drop on a watch glass with about 1 ml. of water and then placing a drop of this solution on the starch-iodide paper.
3. The solution is neutralized slowly in order to keep it cold so that the acetoacetic acid will not be decomposed.

4. The reaction proceeds much more rapidly in basic solution.
5. An additional 4–6 g. of product separates slowly from the filtrate.
6. This general procedure is effective for the preparation of many types of phenylhydrazones. For example, a substituted diazo compound can be employed.[2] Alkylated acetoacetic esters[3] and ethyl benzoylacetate[4] may be used. For the higher homologs, the α-formyl derivatives of ketones may be used in place of ethyl acetoacetate.[5,6] Ethyl pyridylacetates may also be substituted for ethyl acetoacetate.[7] The products in these cases are the phenylhydrazones of 2-acylpyridines.

3. Discussion

The procedure described is essentially that of Japp and Klingemann.[3] Methylglyoxal-ω-phenylhydrazone may also be prepared by heating phenylazoacetoacetic acid at 170–180°[8,9] or by warming ethyl phenylazoacetoacetate with a solution of sodium hydroxide in dilute ethanol.[8,9]

References and Notes

1. Eastman Kodak Company, Rochester, New York.
2. Stierlin, *Ber.*, **21**, 2124 (1888).
3. Japp and Klingemann, *Ann.*, **247**, 218 (1888).
4. Bamberger and Schmidt, *Ber.*, **34**, 2009 (1901).
5. Benary, *Ber.*, **59**, 2198 (1926).
6. Benary, Meyer, and Charisius, *Ber.*, **59**, 108, 600 (1926).
7. Frank and Phillips, *J. Am. Chem. Soc.*, **71**, 2804 (1949).
8. Richter and Munzer, *Ber.*, **17**, 1928 (1884).
9. Japp and Klingemann, *Ann.*, **247**, 198 (1888).

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

METHYLGLYOXAL-ω-PHENYLHYDRAZONE

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

sodium acetate (127-09-3)

aniline (62-53-3)

sodium hydroxide (1310-73-2)

sodium nitrite (7632-00-0)

nitrous acid (7782-77-6)

potassium hydroxide (1310-58-3)

toluene (108-88-3)

Ethyl acetoacetate (141-97-9)

Ethyl benzoylacetate (94-02-0)

Pyruvaldehyde, 1-phenylhydrazone (5391-74-2)

potassium acetoacetate

acetoacetic acid (541-50-4)

phenylazoacetoacetic acid

ethyl phenylazoacetoacetate