



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.

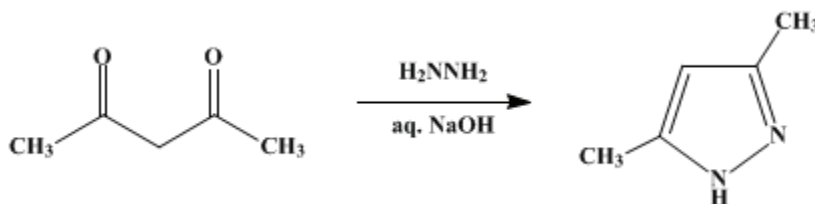
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.351 (1963); Vol. 31, p.43 (1951).

3,5-DIMETHYLPYRAZOLE

[Pyrazole, 3,5-dimethyl-]



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1. Procedure

Sixty-five grams (0.50 mole) of hydrazine sulfate (Note 1) is dissolved in 400 ml. of 10% sodium hydroxide in a 1-l. round-bottomed flask, fitted with a separatory funnel, a thermometer, and a stirrer. The flask is immersed in an ice bath and cooled. When the temperature of the mixture reaches 15° (Note 2), 50 g. (0.50 mole) of acetylacetone (Note 3) is added dropwise with stirring while the temperature is maintained at about 15°. The addition requires about 30 minutes to complete, and the mixture is stirred for 1 hour at 15° (Note 4). The contents of the flask are diluted with 200 ml. of water to dissolve precipitated inorganic salts, transferred to a 1-l. separatory funnel, and shaken with 125 ml. of ether. The layers are separated, and the aqueous layer is extracted with four 40-ml. portions of ether. The ether extracts are combined, washed once with saturated sodium chloride solution, and dried over anhydrous potassium carbonate. The ether is removed by distillation, and the slightly yellow residue of crystalline 3,5-dimethylpyrazole obtained by drying at reduced pressure (approximately 20 mm.) weighs 37–39 g. (77–81%), m.p. 107–108°. This product, which is of good quality, can be recrystallized from about 250 ml. of 90–100° petroleum ether without significant change in appearance or melting point. The yield after drying in a vacuum desiccator containing paraffin chips is 35–37 g. (73–77%) (Note 5).

2. Notes

1. Hydrazine sulfate supplied by the Eastman Kodak Company is satisfactory, or it may be prepared by a previously described procedure.²
2. A precipitate of sodium sulfate may form at this point.
3. Union Carbide and Carbon Corporation technical 2,4-pentanedione was used without purification.
4. The 3,5-dimethylpyrazole precipitates during this period.
5. Recrystallization from methanol or ethanol gives practically colorless material of the same melting point, but it is more difficult to obtain good recovery owing to the high solubility of the pyrazole in these solvents.

3. Discussion

3,5-Dimethylpyrazole has been prepared from acetylacetone and hydrazine hydrate in ethanol³ or hydrazine sulfate in aqueous alkali.^{4,5,6} The latter method is preferred, because the reaction with hydrazine hydrate is sometimes violent.^{3,4} 3,5-Dimethylpyrazole also has been prepared by hydrolysis and decarboxylation of the 1-carbamido- or 1-carboxamidine derivatives, obtained by reaction of semicarbazide⁷ or aminoguanidine⁸ with acetylacetone, and from 1,2-pentadien-4-one and hydrazine hydrate.⁹

References and Notes

1. University of Louisville, Louisville, Kentucky.
 2. *Org. Syntheses Coll. Vol. 1*, 309 (1941).
 3. Rothenberg, *J. Prakt. Chem.*, [2] **52**, 50 (1895); *Ber.*, **27**, 1097 (1894).
 4. Rosengarten, *Ann.*, **279**, 237 (1894).
 5. Morgan and Ackerman, *J. Chem. Soc.*, **123**, 1308 (1923).
 6. Zimmerman and Lochte, *J. Am. Chem. Soc.*, **60**, 2456 (1938).
 7. Posner, *Ber.*, **34**, 3980 (1901).
 8. Thiele and Dralle, *Ann.*, **302**, 294 (1898).
 9. Bertrand, *Compt. rend.*, **245**, 2306 (1957).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

petroleum ether

ethanol (64-17-5)

potassium carbonate (584-08-7)

methanol (67-56-1)

ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

sodium sulfate (7757-82-6)

hydrazine hydrate (7803-57-8)

Hydrazine sulfate (10034-93-2)

semicarbazide (57-56-7)

Acetylacetone,
2,4-pentanedione (123-54-6)

aminoguanidine

3,5-Dimethylpyrazole,
Pyrazole, 3,5-dimethyl- (67-51-6)

pyrazole (288-13-1)

1,2-pentadien-4-one (2200-53-5)