



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](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.

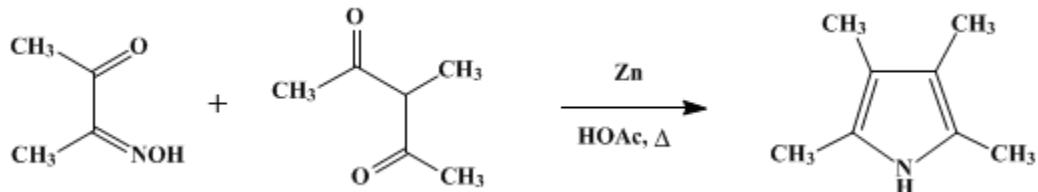
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

Organic Syntheses, Coll. Vol. 5, p.1022 (1973); Vol. 42, p.92 (1962).

## 2,3,4,5-TETRAMETHYLPYRROLE

### [Pyrrole, 2,3,4,5-tetramethyl-]



Submitted by A. W. Johnson and R. Price<sup>1</sup>.

Checked by Virgil Boekelheide and M. Kunstmann.

### 1. Procedure

In a 2-l. three-necked flask fitted with a stirrer, thermometer, and reflux condenser are placed 250 ml. of glacial acetic acid, 54.5 g. (0.84 g. atom) of zinc dust, and 52.5 g. (0.46 mole) of 3-methylpentane-2,4-dione (Note 1). The contents of the flask are stirred vigorously (Note 2), and a solution of 42 g. (0.415 mole) of diacetyl monoxime<sup>2</sup> in 150 ml. of glacial acetic acid is added from a separatory funnel at a rate to maintain the temperature of the mixture at 65–70°. The addition takes 1 hour. When the addition is complete, the mixture is refluxed with stirring for an additional 30 minutes. The flask is then fitted for distillation with steam under nitrogen; 500 ml. of water is added and steam is introduced. Steam distillation (Note 3) is continued until no more tetramethylpyrrole comes over. This takes 1–2 hours and the distillate amounts to 1–2 l. The tetramethylpyrrole crystallizes from the steam distillate and is collected by filtration, washed with water, and dried over phosphorus pentoxide in a vacuum desiccator. There is obtained 15–18 g. of white plates, m.p. 110–111° (lit.<sup>3</sup> m.p. 112°).

By neutralizing the filtrate with sodium hydroxide solution, a second crop of 4–5 g. of tetramethylpyrrole, m.p. 109–110°, is obtained. The total yield is 20.5–22.5 g. (40–44%) (Note 4).

### 2. Notes

1. 3-Methylpentane-2,4-dione is prepared by the methylation of acetacetone.<sup>4,5</sup>
2. It is essential that the zinc dust be stirred effectively or the reaction may become violent.
3. Tetramethylpyrrole must be prevented from blocking the condenser. From time to time the condenser is cleared by turning off the coolant water.
4. 2,3,4,5-Tetramethylpyrrole is very readily oxidized in the air to a green resinous substance. If it is not used immediately, it should be stored under nitrogen or sealed in a glass vial under vacuum.

### 3. Discussion

2,3,4,5-Tetramethylpyrrole has been prepared by the action of sodium methoxide on 2,3,5-trimethylpyrrole,<sup>6</sup> by the reduction of 2,3,5-trimethylpyrrole-4-aldehyde semicarbazone with sodium ethoxide,<sup>7</sup> by the reduction of 2,3,4-trimethylpyrrole-5-aldehyde with sodium ethoxide and hydrazine hydrate,<sup>8</sup> and by the reduction of 2,4-dimethylpyrrole-3,5-dicarboxylic acid with lithium aluminum hydride.<sup>9</sup> Direct ring synthesis by the condensation of 3-aminobutan-2-one and butan-2-one in alkaline solution gave very poor yields, the principal product being 2,3,5,6-tetramethylpyrazine.<sup>3</sup> The above modification of direct ring synthesis avoids this side reaction.<sup>10</sup>

### 4. Merits of Preparation

The present method possesses these advantages over those reported earlier:<sup>5,6,7,8</sup> it is less laborious, in that it is a single-stage preparation, and it gives a better over-all yield.

This preparation is referenced from:

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## References and Notes

1. Department of Chemistry, The University of Nottingham, Nottingham, England.
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3. H. Fischer and B. Walach, *Ann.*, **447**, 38 (1926).
4. A. W. Johnson, E. Markham, and R. Price, this volume, p. 785.
5. K. von Auwers and H. Jacobsen, *Ann.*, **426**, 161 (1921).
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7. H. Fischer and W. Zerweck, *Ber.*, **56**, 519 (1923).
8. M. Dennstedt, *Ber.*, **22**, 1924 (1889).
9. A. Treibs and H. Derra-Scherer, *Ann.*, **589**, 188 (1954).
10. A. W. Johnson, E. Markham, R. Price, and K. B. Shaw, *J. Chem. Soc.*, 4254 (1958).

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

diacetyl monoxime

acetic acid (64-19-7)

sodium hydroxide (1310-73-2)

nitrogen (7727-37-9)

sodium methoxide (124-41-4)

zinc (7440-66-6)

sodium ethoxide (141-52-6)

hydrazine hydrate (7803-57-8)

butan-2-one (78-93-3)

Acetylacetone (123-54-6)

lithium aluminum hydride (16853-85-3)

tetramethylpyrrole,  
2,3,4,5-Tetramethylpyrrole,  
Pyrrole, 2,3,4,5-tetramethyl- (1003-90-3)

3-Methylpentane-2,4-dione (815-57-6)

2,3,5-trimethylpyrrole

2,3,5-trimethylpyrrole-4-aldehyde semicarbazone

2,3,4-trimethylpyrrole-5-aldehyde

2,4-dimethylpyrrole-3,5-dicarboxylic acid

3-aminobutan-2-one

2,3,5,6-tetramethylpyrazine (1124-11-4)

phosphorus pentoxide (1314-56-3)

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