



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.

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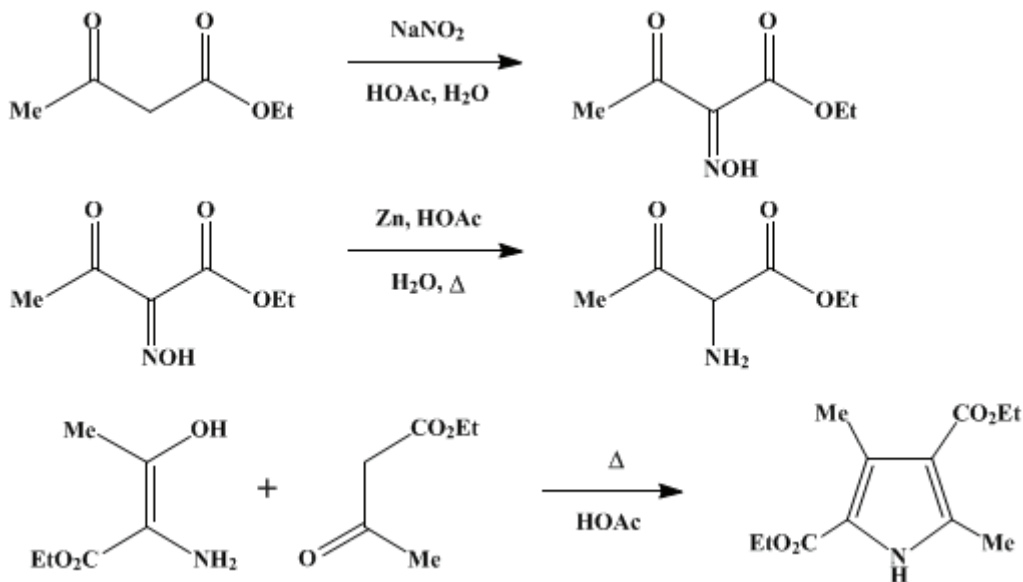
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.202 (1943); Vol. 15, p.17 (1935).

2,4-DIMETHYL-3,5-DICARBETHOXYPYRROLE

[2,4-Pyrroledicarboxylic acid, 3,5-dimethyl-, diethyl ester]



Submitted by Hans Fischer
Checked by C. R. Noller

1. Procedure

In a 3-l. three-necked, round-bottomed flask, fitted with a liquid-sealed mechanical stirrer and dropping funnel, are placed 390 g. (3 moles) of ethyl acetoacetate (*Org. Syn. Coll. Vol. I, 1941, 235*) and 900 cc. of glacial acetic acid. The solution is cooled in an efficient freezing mixture to 5° , and a cold solution of 107 g. (1.47 moles) of 95 per cent sodium nitrite in 150 cc. of water is added dropwise with vigorous stirring at such a rate that the temperature remains between 5° and 7° . With efficient cooling about one-half hour is required to add the nitrite. The mixture is stirred for one-half hour longer and then allowed to stand for four hours, during which time it warms up to room temperature.

The separatory funnel is replaced by a wide-bore condenser, and the third neck of the flask is fitted with a stopper. The solution is stirred and portions of 196 g. (3 gram atoms) of zinc dust (*Note 1*) are added quickly through the third neck of the flask until the liquid boils and then frequently enough to keep it boiling (*Note 2*). After the addition has been completed, the mixture is heated by a burner and refluxed for one hour (*Note 3*) and (*Note 4*). While still hot the contents of the flask are decanted from the remaining zinc into a crock containing 10 l. of water which is being vigorously stirred. The zinc residue is washed with two 50-cc. portions of hot glacial acetic acid which are also decanted into the water. After standing overnight, the crude product is filtered by suction, washed on the filter with two 500-cc. portions of water, and dried in air to constant weight. The yield is 205–230 g. (57–64 per cent of the theoretical amount) of material melting at $126\text{--}130^\circ$. On recrystallizing a 50-g. portion from 100 cc. of 95 per cent alcohol and washing twice with 20-cc. portions of cold alcohol, there is obtained 38.5 g. of pale yellow crystals melting at $136\text{--}137^\circ$ (*Note 5*).

2. Notes

1. The zinc dust should be at least 80 per cent pure, and an amount equivalent to 196 g. of 100 per cent material should be used. An excess of zinc dust up to 3.5 gram atoms has been used without changing the yield.
2. Four portions of approximately 15 g. each are required to bring the solution to the boiling point, after

which the remainder is added in about 5-g. portions over a period of three-quarters of an hour. Great care must be taken not to add too much [zinc](#) dust at first as the mixture foams badly. It is well to have a bath of ice and water and wet towels handy in order to control the reaction if it should become too violent.

3. For reasons unknown some runs behave entirely differently from others. Occasionally the foaming suddenly stops after about half of the [zinc](#) has been added and the remainder can be added much more rapidly, causing the solution to boil vigorously. During the period of external heating of the solution the mixture becomes thick and gummy and as much as 300 cc. of [acetic acid](#) must be added before stirring can be continued. The lower yields reported are obtained when this occurs.

4. It is reported that the yield is increased to 75 per cent by adding [sodium acetate](#) to the [zinc](#) dust reduction mixture to form a complex with the [zinc acetate](#) and so increase its solubility, and by adding the solution of the nitroso compound to the mixture of [zinc](#) dust, [sodium acetate](#), [ethyl acetoacetate](#), and glacial [acetic acid](#), instead of adding the [zinc](#) dust last.¹

5. The crude product turns pink when exposed to light whereas the recrystallized product is quite stable. A somewhat lighter product is obtained if 2 g. of [decolorizing carbon](#) is used during the crystallization, but this has no effect on the melting point.

3. Discussion

The above method, which has always been used for the preparation of [2,4-dimethyl-3,5-dicarbethoxypyrrole](#), is essentially that of Knorr.²

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 2, 217](#)

References and Notes

1. Corwin and Quattlebaum, Jr., *J. Am. Chem. Soc.* **58**, 1083 (1936).
2. Knorr, *Ann.* **236**, 318 (1886).

Appendix

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

[alcohol](#) (64-17-5)

[acetic acid](#) (64-19-7)

[sodium acetate](#) (127-09-3)

[sodium nitrite](#) (7632-00-0)

[decolorizing carbon](#) (7782-42-5)

[zinc](#) (7440-66-6)

[Ethyl acetoacetate](#) (141-97-9)

[2,4-Dimethyl-3,5-dicarbethoxypyrrole](#),

2,4-Pyrroledicarboxylic acid, 3,5-dimethyl-, diethyl ester (2436-79-5)

zinc acetate (557-34-6)

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