



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.

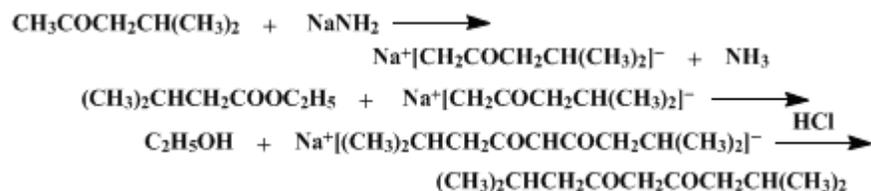
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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. 3, p.291 (1955); Vol. 28, p.44 (1948).

DIISOVALERYLMETHANE

[4,6-Nonanedione, 2,8-dimethyl-]



Submitted by C. R. Hauser, J. T. Adams, and R. Levine.

Checked by Arthur C. Cope and Frank S. Fawcett.

1. Procedure

Approximately 300 ml. of commercial anhydrous liquid ammonia is added to a 500-ml. three-necked round-bottomed flask equipped with a mercury-sealed stirrer and a reflux condenser connected to a soda-lime drying tube (Note 1). The drying tube is attached to a gas-absorption trap, or the apparatus is assembled in a well-ventilated hood. The third neck of the flask is closed with a stopper. Freshly cut sodium (13.8 g., 0.6 gram atom) is weighed under xylene or kerosene, and a small amount is added to the liquid ammonia, with stirring, until a permanent blue color is produced. A few small crystals of ferric nitrate are added to catalyze the conversion of sodium to sodium amide (Note 2), and when the blue color has disappeared the remainder of the sodium is added in small pieces. When the sodium is converted completely to sodium amide, as indicated by change of the blue solution to a gray suspension, the ammonia is evaporated by warming the flask on a steam bath. During this operation sufficient dry ether is added through a dropping funnel (attached to the third neck of the flask) so that the volume of the liquid remains approximately 300 ml. After practically all the ammonia has been evaporated, as indicated by refluxing of the ether, the sodium amide suspension is stirred and heated under reflux for a few minutes and then cooled to room temperature. The procedure to this point requires approximately 1 hour.

A solution of 30 g. (0.3 mole) of redistilled methyl isobutyl ketone in 50 ml. of absolute ether is added to the stirred suspension of sodium amide during 5–10 minutes. After an additional 5 minutes, a solution of 78 g. (0.6 mole) of redistilled ethyl isovalerate in 50 ml. of dry ether is added during about 15 minutes. Stirring is continued for 2 hours while the mixture is heated under reflux on the steam bath. The gelatinous suspension of the sodium salt of diisovalerylmethane is poured into 300 ml. of water, made neutral to litmus by dilute hydrochloric acid, and extracted with three 100-ml. portions of ether. The solvent is removed by distillation under reduced pressure, and the residue is dissolved in an equal volume of methanol. A solution prepared from 44 g. of cupric acetate monohydrate and 350 ml. of water is heated nearly to the boiling point, filtered, and added to the methanol solution. The resulting mixture is allowed to stand until it has cooled to room temperature. The blue copper salt of diisovalerylmethane is collected on a Büchner funnel, pressed as dry as possible, washed on the funnel with 100 ml. of petroleum ether (b.p. 30–60°), and again sucked dry. The yield of the copper salt after air drying is 44–51 g. (69–79%); it melts in the range 150–155° (Note 3).

The diisovalerylmethane is regenerated by shaking the copper salt vigorously with 500 ml. of 10% sulfuric acid and 200 ml. of ether until all the salt has dissolved. The aqueous acid layer is extracted with two 100-ml. portions of ether, and the combined ether solutions are dried over anhydrous sodium sulfate. The solvent is removed, and the residue is distilled under reduced pressure. The yield of diisovalerylmethane is 32–42 g. (58–76%, based on methyl isobutyl ketone), b.p. 115–116°/20 mm., n_D^{25} 1.4565 (Note 4) and (Note 5).

2. Notes

1. Apparatus fitted with standard-taper ground-glass joints is convenient for this preparation.
2. It may be helpful to provide additional catalysis of the conversion to [sodium amide](#) of the small amount of [sodium](#) added initially by bubbling dry air through the solution.¹
3. After recrystallization from [methanol](#) or 95% [ethanol](#) the fluffy light blue copper salt melts at 157–158°.
4. The submitters state that the reaction may be conducted with equal success by using 0.6 mole each of [sodium amide](#) and [methyl isobutyl ketone](#), and 0.3 mole of [ethyl isovalerate](#) (yield 75% based on the ester).^{2,3}
5. [Acetone](#) may be acylated with [ethyl laurate](#) by either procedure (with excess ester or excess ketone). [Lauroylacetone](#) (m.p. 31.5–32°) is obtained in 75% yield³ by either procedure.

3. Discussion

[Diisovalerylmethane](#) has been prepared by the method described^{2,3} and by the use of [sodium hydride](#)⁴ as the condensing agent.

References and Notes

1. Leffler, *Org. Reactions*, **1**, 99, John Wiley & Sons, New York, 1942; Vaughn, Vogt, and Nieuwland, *J. Am. Chem. Soc.*, **56**, 2120 (1934).
2. Adams and Hauser, *J. Am. Chem. Soc.*, **66**, 1220 (1944).
3. Levine, Conroy, Adams, and Hauser, *J. Am. Chem. Soc.*, **67**, 1510 (1945).
4. Swamer and Hauser, *J. Am. Chem. Soc.*, **72**, 1352 (1950).

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

petroleum ether

kerosene

sodium salt of diisovalerylmethane

copper salt of diisovalerylmethane

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

[sulfuric acid](#) (7664-93-9)

[hydrochloric acid](#) (7647-01-0)

[ammonia](#) (7664-41-7)

[methanol](#) (67-56-1)

[ether](#) (60-29-7)

[sodium sulfate](#) (7757-82-6)

acetone (67-64-1)

sodium (13966-32-0)

xylene (106-42-3)

Methyl isobutyl ketone (108-10-1)

ethyl laurate (106-33-2)

sodium amide (7782-92-5)

ferric nitrate

Diisovalerylmethane,
4,6-Nonanedione, 2,8-dimethyl- (7307-08-6)

ethyl isovalerate (108-64-5)

cupric acetate monohydrate (6046-93-1)

Lauroylacetone

sodium hydride (7646-69-7)