



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.

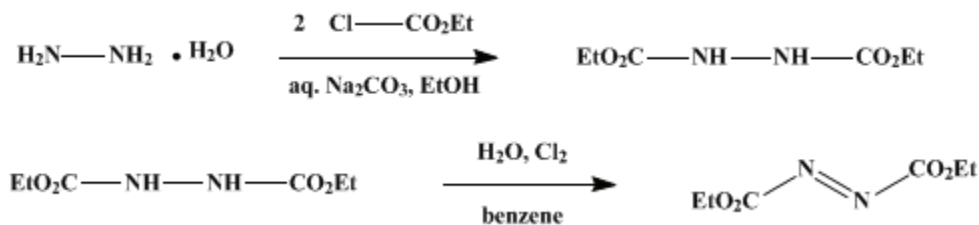
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.375 (1955); Vol. 28, p.58 (1948).

ETHYL AZODICARBOXYLATE

[Formic acid, azodi-, diethyl ester]



Submitted by Norman Rabjohn

Checked by H. J. Sampson and R. S. Schreiber.

1. Procedure

A report has been received that a sample of ethyl azodicarboxylate decomposed upon attempted distillation with sufficient violence to shatter the distillation apparatus. It is possible that the explosion may have been due to over chlorination or to insufficient washing of the product with sodium bicarbonate solution. It is recommended that ethyl azodicarboxylate be distilled only behind a safety shield, and protected from direct sources of light.

A. *Ethyl hydrazodicarboxylate.* In a 2-l. three-necked flask, equipped with a mechanical stirrer, two 500-ml. dropping funnels, and a thermometer (Note 1), is placed a solution of 59 g. (1 mole) of 85% hydrazine hydrate in 500 ml. of 95% ethanol. The reaction flask is cooled by means of an ice bath. When the temperature of the solution has dropped to 10°, 217 g. (2 moles) of ethyl chloroformate is added dropwise with stirring at a rate sufficient to maintain the temperature between 15° and 20°. After one-half of the ethyl chloroformate has been introduced, a solution of 106 g. (1 mole) of sodium carbonate in 500 ml. of water is added dropwise simultaneously with the remaining ethyl chloroformate. The addition of these two reactants is regulated so that the temperature does not rise above 20° and so that the addition of the chloroformate is completed slightly in advance of the sodium carbonate in order to ensure a slight excess of ethyl chloroformate in the reaction mixture at all times.

After all the reactants have been added, the precipitate on the upper walls of the flask is washed down with 200 ml. of water and the reaction mixture is allowed to stir for an additional 30-minute period. The precipitate is then collected on a Büchner funnel, washed well with a total of 800 ml. of water, and dried in an oven at 80°. There is obtained 145–150 g. (82–85%) of ethyl hydrazodicarboxylate which melts at 131–133°. It is sufficiently pure (Note 2) for the preparation of ethyl azodicarboxylate.

B. *Ethyl azodicarboxylate.* A mixture of 100 g. (0.57 mole) of ethyl hydrazodicarboxylate, 500 ml. of benzene, and 500 ml. of water is placed in a 2-l. three-necked flask equipped with a mechanical stirrer and a gas inlet tube. The flask and contents are tared, the flask is placed in an ice bath, and a slow stream of chlorine is bubbled into the mixture with stirring. The temperature is maintained below 15°, and chlorine is introduced until the increase in weight amounts to 50–55 g. (Note 3). The flow of chlorine is stopped, and the reaction mixture is stirred until a clear, orange-colored benzene layer forms when the mixture is allowed to settle.

The layers are separated, and the water layer is extracted once with benzene. The benzene solutions are combined and washed twice with 100-ml. portions of water, then with 100-ml. portions of 10% sodium bicarbonate solution until neutral (usually four to six washes are required), and twice more with water, and then are dried over anhydrous sodium sulfate. The benzene is removed under reduced pressure on a steam bath, and the residue is distilled in vacuum through a short indented column. After a

small fore-run, the main fraction is collected at 107–111° /15 mm. There is obtained 80–82 g. (81–83%) of ethyl azodicarboxylate.

2. Notes

1. The thermometer and one of the funnels are fitted to a two-necked adapter; the thermometer scale must be such that the range between 10° and 20° is easily visible, preferably outside the flask, when the bulb is inserted in the liquid.
2. Ethyl hydrazodicarboxylate may be purified by crystallization from dilute ethanol; m.p. 134–135°
3. A larger excess of chlorine causes the formation of higher-boiling materials and lowers the yield of ethyl azodicarboxylate.

3. Discussion

Ethyl hydrazodicarboxylate can be prepared by the reaction of ethyl chloroformate with hydrazine hydrate¹ or hydrazine sulfate in the presence of potassium hydroxide.² It can be prepared also by the treatment of symmetrical hydrazinedicarboxylic acid diazide with ethanol.³

Ethyl azodicarboxylate can be prepared by treating ethyl hydrazodicarboxylate with concentrated nitric acid² or a mixture of concentrated and fuming nitric acid.^{4,5}

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 411
- Org. Syn. Coll. Vol. 5, 96
- Org. Syn. Coll. Vol. 3, 58
- Org. Syn. Coll. Vol. 5, 544

References and Notes

1. Curtius and Heidenreich, *J. prakt. Chem.*, **52**, 476 (1895); Vogelesang, *Rec. trav. chim.*, **65**, 789 (1946).
 2. Ingold and Weaver, *J. Chem. Soc.*, **127**, 381 (1925).
 3. Stolle, *Ber.*, **43**, 2470 (1910).
 4. Curtius and Heidenreich, *Ber.*, **27**, 774 (1894).
 5. Diels and Fritzsche, *Ber.*, **44**, 3018 (1911).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

symmetrical hydrazinedicarboxylic acid diazide

ethanol (64-17-5)

Benzene (71-43-2)

sodium bicarbonate (144-55-8)

nitric acid (7697-37-2)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

chlorine (7782-50-5)

potassium hydroxide (1310-58-3)

hydrazine hydrate (7803-57-8)

Hydrazine sulfate (10034-93-2)

ethyl chloroformate (541-41-3)

Ethyl azodicarboxylate

Formic acid, azodi-, diethyl ester (1972-28-7)

Ethyl hydrazodicarboxylate