Organic Syntheses

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.

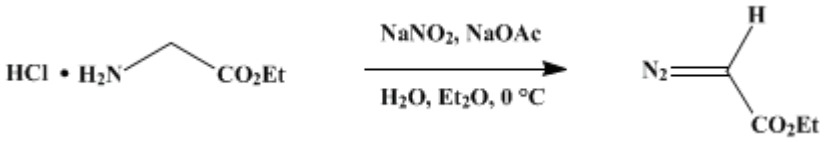
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.024.0056

Organic Syntheses, Coll. Vol. 3, p.392 (1955); Vol. 24, p.56 (1944).

ETHYL DIAZOACETATE

[Acetic acid, diazo-, ethyl ester]



Submitted by Ennis B. Womack and A. B. Nelson.
Checked by R. L. Shriner and C. H. Tilford.

1. Procedure

A 1-l. three-necked round-bottomed flask is fitted with a 50-ml. separatory funnel and a mechanical stirrer sealed with a well-lubricated rubber collar. A stopper in the third neck of the flask carries a glass tube that reaches to the bottom of the flask, enters the top of a 1-l. separatory funnel, and extends down to the stopcock.

A solution of 140 g. (1 mole) of glycine ethyl ester hydrochloride and 3 g. of sodium acetate in 150 ml. of water is added to the flask and cooled to 2° by means of an ice-salt bath. A cold solution of 80 g. (1.15 moles) of sodium nitrite in 100 ml. of water is added, and the mixture is stirred until the temperature has fallen to 0°. The temperature is maintained below 2°, and stirring is continued throughout all the following operations. To the cold mixture are added 80 ml. of cold, ethanol-free ethyl ether (Note 1) and 3 ml. of cold 10% sulfuric acid. After 5 minutes, the reaction mixture is blown over into the 1-l. separatory funnel by application of air pressure. The lower aqueous layer is *quickly* sucked back into the reaction flask. The ether layer is removed and immediately washed with 50 ml. of cold 10% sodium carbonate solution. This ether solution should be neutral to moist litmus paper; if not, the washing with sodium carbonate is repeated. The ether solution is finally dried over 10 g. of anhydrous sodium sulfate.

A second portion of 80 ml. of ethanol-free ether is then added to the reaction mixture with stirring, followed by 15 ml. of cold 10% sulfuric acid over a period of 5 minutes. After 3 minutes' contact (Note 2), the ether layer is removed as before, washed immediately with 50 ml. of fresh 10% sodium carbonate solution, and dried over 10 g. of sodium sulfate. This procedure is repeated (about 6 or 7 times) until the ether layer is no longer yellow.

The combined ether solutions are then subjected to distillation at 20°or below under the vacuum obtainable from a water pump until all the ether is removed. Prolonged distillation results in decomposition of the diazo ester and in a decreased yield. The yellow residual oil is practically pure ethyl diazoacetate and is satisfactory for most synthetic purposes (Note 3). The yield is about 98 g. (85%) (Note 4) and (Note 5).

2. Notes

1. The ethanol is removed from 600 ml. of commercial ethyl ether by thorough washing with 75 ml. of a saturated calcium chloride solution.
2. The ether layer should be removed as rapidly as possible from the aqueous layer, because ethyl diazoacetate is rapidly decomposed by acid.
3. Ethyl diazoacetate may be purified, but with considerable loss, by steam distillation under reduced pressure.[1]
4. The submitters have carried out preparations using twice the amounts stated.
5. The product should be placed in dark brown bottles and kept in a cool place. It should be used as soon as possible. *Distillation, even under reduced pressure, is dangerous, for the substance is explosive.*

3. Discussion

Ethyl diazoacetate has been prepared by the action of sodium nitrite on glycine ethyl ester hydrochloride.[1,2,3] A modification of this method, which is reported to give better yields than those described here, has been published.[4]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 424
- Org. Syn. Coll. Vol. 5, 258

References and Notes

1. Gattermann, *Laboratory Methods of Organic Chemistry*, p. 277, The Macmillan Company, New York, 1948.
2. Curtius, *J. prakt. Chem.*, (2) **38**, 396 (1888); Silberrad, *J. Chem. Soc.*, 81, 600 (1902).
3. U. S. pat. 2,490,714 [*C. A.*, **44**, 3519 (1950)].
4. La Forge, Gersdorff, Green, and Schechter, *J. Org. Chem.*, **17**, 381 (1952).

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

ethanol (64-17-5)

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

ether,
ethyl ether (60-29-7)

sodium acetate (127-09-3)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

sodium nitrite (7632-00-0)

ethyl diazoacetate,
Acetic acid, diazo-, ethyl ester (623-73-4)

Glycine ethyl ester hydrochloride (623-33-6)