



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.

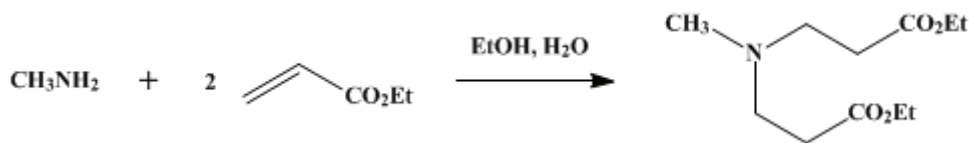
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.258 (1955); Vol. 20, p.35 (1940).

DI- β -CARBETHOXYETHYLMETHYLAMINE

[Propionic acid, β,β' -(methylimino)di-, diethyl ester]



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1. Procedure

In a 2-l. flask, fitted with a rubber stopper carrying a soda-lime drying tube and a glass tube reaching almost to the bottom, is placed 325 g. (420 ml.) of absolute [ethanol](#). The whole is then tared and placed in an ice bath, and the inlet tube is connected to a source of dry methylamine.

The methylamine generator consists of a 1-l. flask fitted with a dropping funnel and outlet tube, which in turn is connected to a 25-cm. drying tower containing soda-lime, followed by a 1-l. safety trap ([Note 1](#)). In the flask is placed 200 g. of technical [sodium hydroxide](#) flakes, and 263 g. of a 33–35% solution of [methylamine](#) in water ([Note 2](#)) is dropped in slowly at such a rate that an even current of gas is evolved. When the addition has been completed and the gas bubbles very slowly into the [ethanol](#), the flask and contents are removed and weighed; the increase should be 84–86 g. (2.71–2.77 moles) ([Note 3](#)).

The flask is reimmersed in the ice bath, and 900–925 g. (5.4–5.5 moles), depending upon the weight of [methylamine](#), of a 60% solution of [ethyl acrylate](#) in [ethanol](#) ([Note 4](#)) is added in portions of about 100 ml. at such a rate that the temperature of the mixture does not rise above 40°; this requires about 10 minutes. After each addition the flask is stoppered to exclude moisture. When all the ester has been added the flask is closed by a rubber stopper and allowed to stand 6 days ([Note 5](#)).

Most of the [ethanol](#) is removed by distillation (1.5 hours) on a steam bath, and the residue is transferred to a modified Claisen flask and distilled. The fraction boiling below 50°/20 mm. ([Note 6](#)) is removed with the aid of a water pump, and the residue is distilled using an oil pump (at 3 mm. pressure) ([Note 7](#)). The portion boiling at 105–108°/3 mm. ([Note 8](#)) is collected as [di- \$\beta\$ -carbethoxyethylmethylamine](#) ([Note 9](#)); it amounts to 519–550 g. (83–86%) ([Note 10](#)).

2. Notes

1. The safety trap is important, since the [ethanol](#) tends to suck back easily.
2. Solutions of [methylamine](#) in water are obtainable from Eastman Kodak Company (33%) and Rohm and Haas Company (35%).
3. It is much more convenient to use the amount of [methylamine](#) secured than to try to collect a predetermined weight.
4. The [ethyl acrylate](#) (60% solution in [ethanol](#)) is available from the Rohm and Haas Company. The solution, containing a polymerization inhibitor, is used without treatment. The inhibitor must not be removed.
5. If the time is shortened, the yield is correspondingly decreased.
6. Most of this distillate comes over with the oil-bath temperature at 75°; the temperature is finally raised to 150°. The fractionating arm of the Claisen flask used was wrapped with asbestos cord.
7. Any [ethyl N-methyl- \$\beta\$ -aminopropionate](#) formed comes over in the first or middle fraction (6–8 ml.). The middle fraction is obtained as the fraction boiling up to 105°/3 mm., on changing from the water pump to an oil pump. The oil bath is cooled to 100° before applying the higher vacuum.
8. The observed boiling points vary with the particular apparatus used.

9. Since the ester decomposes very slightly during distillation, the oil pump should be protected from ethyl acrylate and methylamine by a Dry Ice trap. The distillation should not be interrupted.
10. Di- β -carbomethoxyethylmethylamine may be prepared in a similar yield by substituting an equivalent quantity of methyl acrylate in methanol in the above procedure.

3. Discussion

This ester has been prepared by the action of ethyl β -bromopropionate on methylamine hydrochloride in the presence of silver oxide,¹ by the addition of methylamine to ethyl acrylate,² and by heating ethyl β -chloropropionate, methylamine, and benzene in an autoclave.³

References and Notes

1. McElvain, *J. Am. Chem. Soc.*, **46**, 1724 (1924).
 2. Morsch, *Monatsh.*, **63**, 229 (1933).
 3. Ger. pat. 491,877 [*Frdl.*, **16**, 2908 (1931)] [*C. A.*, **24**, 2468 (1930)].
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

ethyl β -chloropropionate

ethanol (64-17-5)

Benzene (71-43-2)

methanol (67-56-1)

sodium hydroxide (1310-73-2)

silver oxide (20667-12-3)

Ethyl β -bromopropionate (539-74-2)

ethyl acrylate (140-88-5)

Methylamine hydrochloride (593-51-1)

methylamine (74-89-5)

methyl acrylate (96-33-3)

DI- β -CARBETHOXYETHYLMETHYLAMINE,
Propionic acid, β,β' -(methylimino)di-, diethyl ester (6315-60-2)

ethyl N-methyl- β -aminopropionate

Di- β -carbomethoxyethylmethylamine

