



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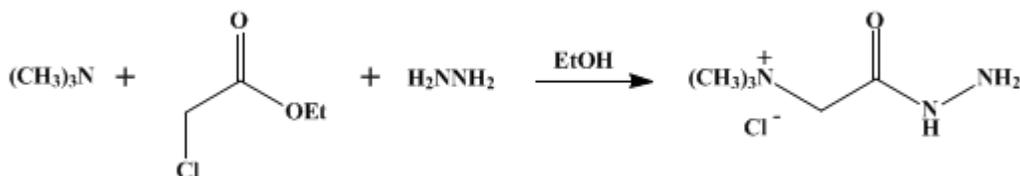
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.85 (1943); Vol. 18, p.10 (1938).

BETAINE HYDRAZIDE HYDROCHLORIDE

[Girard's Reagent]

[Ammonium compounds, substituted. (Carboxymethyl)trimethyl— chloride, hydrazide]



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1. Procedure

In a 1-l. three-necked flask fitted with a stirrer, a thermometer, and an ice-cooled spiral condenser (*Org. Syn. Coll. Vol. I, 1941, 529*) is placed a solution of 98 g. (84.5 cc., 0.8 mole) of [ethyl chloroacetate](#) (*Note 2, p. 263*) in 200 cc. of absolute [alcohol](#). The solution is cooled to 0° by stirring in a salt-ice bath; and, after the stirrer is stopped, 74 cc. (49 g., 0.83 mole) of [trimethylamine](#), measured after precooling to -5°, is added all at once. The exothermic reaction is controlled sufficiently by cooling so that the temperature of the mixture rises to 60° in the course of about one hour (*Note 1*). When there is no longer any heat effect, the mixture is allowed to stand at room temperature for twenty hours (without replenishment of the condenser ice).

The condenser is removed, the thermometer replaced by a dropping funnel, and 40 g. (0.8 mole) of 100 per cent [hydrazine hydrate](#) (*Note 2*) added, with stirring, in the course of ten to fifteen minutes. After being stirred for forty-five minutes longer, the solution is cooled slightly, and, unless crystallization of the reaction product starts spontaneously, the walls of the vessel are scratched with a glass rod to induce crystallization (*Note 3*). The product separates in fine, colorless needles. After being thoroughly cooled in an ice bath, the highly hygroscopic salt is collected quickly on a Büchner funnel, washed with 150 cc. of cold absolute [alcohol](#), and pressed dry under a rubber dam. Dried in a vacuum desiccator over concentrated [sulfuric acid](#), this material weighs 100–108 g. A further crop can be obtained after distilling 200–300 cc. of solvent from the mother liquor and washings at the pressure of the water pump. The total yield of salt, m.p. 175–180°, with decomposition, is 112–120 g. (83.5–89.5 per cent of the theoretical amount) (*Note 4*), (*Note 5*), and (*Note 6*).

2. Notes

1. Without external cooling the temperature rises to about 75° and it is difficult to avoid some loss of amine.

2. [Hydrazine hydrate](#) may be prepared by the ammonolysis of [hydrazine sulfate](#) (*Org. Syn. Coll. Vol. I, 1941, 309*) as described in *Org. Syn. 21, 70*.

The 42 per cent [hydrazine hydrate](#) solution supplied by the Eastman Kodak Company is too dilute for use as such, but may be concentrated by distillation with [xylene](#).¹ A mixture of 144 cc. (150 g.) of the 42 per cent solution and 230 cc. of [xylene](#) is distilled from a 500-cc. flask through a 17-cm. Hempel column fitted into a cork covered with tin foil. After distillation of the [xylene](#), with about 85 cc. of water, the residue yields on distillation 45–50 g. of 80–85 per cent [hydrazine hydrate](#). This material, assayed best by titration with standard acid using [methyl orange](#) as indicator, may be used as such or concentrated further (see (*Note 6*)).

3. When more dilute [hydrazine hydrate](#) is used, the crystallization is slower, but it is not advisable to cool the solution thoroughly until crystals have begun to appear.

4. Although this material contains a small amount of the symmetrical dihydrazide, which is not easily eliminated on crystallization, it is entirely satisfactory as a reagent for the isolation of ketones. A purer product, m.p. 192°, with decomposition, can be obtained by adding the solution prepared from [ethyl chloroacetate](#) and [trimethylamine](#) to an alcoholic solution containing a considerable excess of [hydrazine hydrate](#).
5. When stored in a dry, tightly stoppered container the reagent can be kept for long periods without deteriorating (odor), but samples withdrawn after some time are best recrystallized from absolute [alcohol](#) before use.
6. The yields obtained by the checkers when using 75 per cent and 50 per cent [hydrazine hydrate](#) were 78 per cent and 66 per cent, respectively, of the theoretical amount.

3. Discussion

The above procedure is essentially that of Girard and Sandulesco.²

References and Notes

1. Hurd and Bennett, J. Am. Chem. Soc. **51**, 265 (1929).
2. Girard and Sandulesco, Helv. Chim. Acta **19**, 1095 (1936).

Appendix

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

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

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

[Ethyl chloroacetate](#) (105-39-5)

[xylene](#) (106-42-3)

[hydrazine hydrate](#) (7803-57-8)

[Hydrazine sulfate](#) (10034-93-2)

[Trimethylamine](#) (75-50-3)

[BETAINES HYDRAZIDE HYDROCHLORIDE](#) (123-46-6)

[methyl orange](#) (547-58-0)