



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.

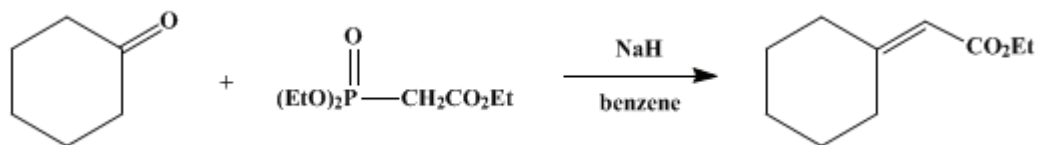
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 5, p.547 (1973); Vol. 45, p.44 (1965).

ETHYL CYCLOHEXYLIDENEACETATE

[Δ^1 - α -Cyclohexaneacetic acid, ethyl ester]



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Checked by William E. Parham, R. M. Dodson, W. L. Salo, and J. N. Wemple.

1. Procedure

A dry, 500-ml., three-necked flask equipped with stirrer, thermometer, condenser, and dropping funnel is purged with dry nitrogen and charged with 16 g. (0.33 mole) of a 50% dispersion of sodium hydride in mineral oil (Note 1) and 100 ml. of dry benzene (Note 2). To this stirred mixture is added dropwise over a 45–50 minute period 74.7 g. (0.33 mole) of triethyl phosphonoacetate (Note 3). During the addition period the temperature is maintained at 30–35°, and cooling is employed if necessary (Note 4). Vigorous evolution of hydrogen is noted during this portion of the reaction. After addition of triethyl phosphonoacetate is completed, the mixture is stirred for 1 hour at room temperature to ensure complete reaction (Note 5). To this nearly clear solution is added dropwise over a 30–40 minute period 32.7 g. (0.33 mole) of cyclohexanone (Note 6). During the addition the temperature is maintained at 20–30° by appropriate cooling with an ice bath. After approximately one-half of the ketone is added, a gummy precipitate of sodium diethyl phosphate forms, which in some instances makes agitation difficult. The mixture is then heated at 60–65° for 15 minutes, during which time it is stirred without difficulty. The resulting product is cooled to 15–20°, and the mother liquor is decanted from the precipitate. This gummy precipitate is washed well by mixing it at 60° with several 25-ml. portions of benzene and decanting at 20° (Note 7). Benzene is distilled from the combined mother and wash liquors at atmospheric pressure. The product is distilled through a 20-cm. Vigreux column, and the mineral oil remains as pot residue after distillation is completed. Ethyl cyclohexylideneacetate (37–43 g., 67–77% yield) is collected at 48–49° (0.02 mm.), n_D^{25} 1.4755 (Note 8).

2. Notes

1. Sodium hydride, 50–51% in mineral oil, was supplied by Metal Hydrides Inc., Beverly, Massachusetts.
2. Reagent grade benzene is filtered from sodium hydride just before use.
3. Triethylphosphonoacetate may be obtained from the Aldrich Chemical Company and is distilled before use; b.p. 140° (10 mm.).
4. Temperatures above 40–50° are detrimental to the anion and must be avoided.
5. Approximately the stoichiometric quantity of hydrogen (7.4 l.) is evolved during preparation of the anion.
6. The cyclohexanone was obtained from Eastman Organic Chemicals and redistilled before use.
7. The submitters obtained the yields indicated by washing the gummy precipitate with two 25-ml. portions of benzene; the checkers observed that additional extraction at this point is required, and they recommend extraction with a total of four 25-ml. portions of warm benzene.
8. If an excess of sodium hydride has been used, the product contains varying amounts of the β,γ -isomer, ethyl cyclohexenylacetate. To ensure against the occurrence of this side reaction, a 5–10% excess of the phosphonate ester can be used.

3. Discussion

Esters of cyclohexylideneacetic acid have been prepared by the Reformatsky reaction followed by

acylation and pyrolysis,² a laborious procedure giving low yields. The phosphonate carbanion procedure would appear to be the method of choice for preparation of these esters.

4. Merits of the Preparation

The phosphonate carbanion method is generally applicable to the synthesis of a wide variety of olefins.³ The synthesis complements the Wittig reaction in that the latter procedure is often unsatisfactory for preparation of olefins having an electron-withdrawing group adjacent to the double bond.⁴ Generally, any ketone or aldehyde can be used in the phosphonate carbanion synthesis, and yields of olefins comparable to that obtained with [cyclohexanone](#) are obtained. Although a variety of alkyl phosphonates can be employed, the present procedure is specific for phosphonates containing an electron-withdrawing group. The synthesis can be performed at room temperature or below, and product isolation is facilitated by simplified removal of the by-products, virtues which make this procedure of practical value.

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 5, 509](#)
- [Org. Syn. Coll. Vol. 5, 642](#)

References and Notes

1. Rohm and Haas Company, Philadelphia, Pennsylvania.
2. H. Schmid and P. Karrer, *Helv. Chim. Acta*, **31**, 1067 (1948).
3. W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1961). Other workers have investigated modifications of this reaction: L. Horner, H. Hoffman, H. G. Wippel, and G. Klahre, *Ber.*, **92**, 2499 (1959); H. Pommer, *Angew. Chem.*, **72**, 911 (1960); E. J. Seus and C. V. Wilson, *J. Org. Chem.*, **26**, 5243 (1961); J. Wolinsky and K. L. Erickson, *J. Org. Chem.*, **30**, 2208 (1965); H. Takahashi, K. Fujiwara, and M. Ohta, *Bull. Chem. Soc. Japan*, **35**, 1498 (1962).
4. G. Wittig and W. Haag, *Ber.*, **88**, 1654 (1955).

Appendix

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

Δ^1 - α -Cyclohexaneacetic acid, ethyl ester

[Benzene](#) (71-43-2)

[hydrogen](#) (1333-74-0)

[Cyclohexanone](#) (108-94-1)

[nitrogen](#) (7727-37-9)

[sodium hydride](#) (7646-69-7)

[cyclohexylideneacetic acid](#)

[triethyl phosphonoacetate](#) (867-13-0)

Ethyl cyclohexylideneacetate (1552-92-7)

sodium diethyl phosphate

Triethylphosphonoacetate

ethyl cyclohexenylacetate