



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.

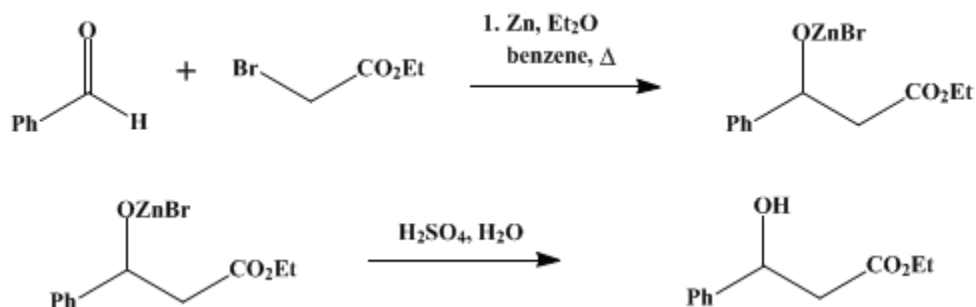
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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ETHYL β -PHENYL- β -HYDROXYPROPIONATE

[Hydracrylic acid, β -phenyl-, ethyl ester]



Submitted by Charles R. Hauser and David S. Breslow.

Checked by R. L. Shriner, W. M. Hoehn, and Vera A Patterson..

1. Procedure

In a clean, dry, 500-ml. three-necked flask, fitted with a mechanical stirrer, a 250-ml. separatory funnel, and a reflux condenser (Note 1), the upper end of which is protected by a calcium chloride drying tube, is placed 40 g. (0.62 gram atom) of powdered zinc (Note 2).

A solution of 83.5 g. (0.50 mole) of ethyl bromoacetate (Note 3) and 65 g. (0.61 mole) of benzaldehyde (Note 4) in 80 ml. of dry benzene and 20 ml. of absolute ether is placed in the separatory funnel. About 10 ml. of this solution is added to the zinc, and the flask is warmed until the reaction starts (Note 5). The mixture is then stirred and the rest of the solution added at such a rate that the reaction mixture refluxes, care being taken that the reaction does not become too vigorous. The addition should take about an hour. The reaction mixture is refluxed for 30 minutes on a water bath after the addition of the solution is complete.

The flask is then cooled in an ice bath and the reaction mixture hydrolyzed by the addition of 200 ml. of cold 10% sulfuric acid with vigorous stirring during the addition. The acid layer is drawn off and the benzene solution extracted twice with 50-ml. portions of 5% sulfuric acid. The benzene solution is washed once with 25 ml. of 10% sodium carbonate solution, then with 25 ml. of 5% sulfuric acid (Note 6), and finally with two 25-ml. portions of water. The combined acid solutions are extracted with two 50-ml. portions of ether, and the combined ether and benzene solutions are dried with 5 g. of magnesium sulfate or Drierite. The solution is filtered, the solvent removed by distillation at atmospheric pressure from a steam bath, and the residue fractionated under reduced pressure. The ester is collected at 151–154°/11–12 mm. (128–132°/5–7 mm.). The total yield is 59–62 g. (61–64%) (Note 7).

2. Notes

1. An efficient reflux condenser is necessary to prevent loss of solvent. The same precautions as to cleanliness of apparatus and absence of moisture should be observed in carrying out Reformatsky reactions as in reactions involving the Grignard reagent.
2. The zinc dust is purified by washing it rapidly with dilute sodium hydroxide solution, water, dilute acetic acid, water, ethanol, acetone, and ether. It is then dried in a vacuum oven at 100°.
3. Ethyl bromoacetate is a powerful lachrymator, and care should be exercised in handling it. A 10% solution of ammonium hydroxide should be kept available to neutralize any of the bromo ester which may be spilled.
4. The benzaldehyde should be washed with two 50-ml. portions of 10% sodium bicarbonate solution, dried, and distilled.
5. It is essential that the reaction start before any additional ethyl bromoacetate and benzaldehyde are

added.

6. The acid extraction should be continued until no white precipitate of [zinc hydroxide](#) is formed on extraction with [sodium carbonate](#). This step is important, since the zinc complex hydrolyzes much less readily than the corresponding magnesium complex. A small amount of unhydrolyzed complex forms at the interface of the [benzene](#) and acid solutions. It is most readily separated during the first alkaline extraction.

7. [Ethyl \$\alpha,\alpha\$ -dimethyl- \$\beta\$ -phenyl- \$\beta\$ -hydroxypropionate](#) may be prepared in a similar manner. For instance, from 100 g. of [ethyl \$\alpha\$ -bromoisobutyrate](#) and 65 g. of [benzaldehyde](#), 82.5 g. (73%) of [ethyl \$\alpha,\alpha\$ -dimethyl- \$\beta\$ -phenyl- \$\beta\$ -hydroxypropionate](#), boiling at 153–158°/11 mm., is obtained. It may be recrystallized by dissolving it at 30° in 100 ml. of ligroin (30–60°), chilling the solution for several days, and decanting the clear liquid from the precipitate; m.p. 38.5–39°.

3. Discussion

[Ethyl \$\beta\$ -phenyl- \$\beta\$ -hydroxypropionate](#) has been prepared by esterification of [\$\beta\$ -phenyl- \$\beta\$ -hydroxypropionic acid](#)^{1,2} obtained in turn by the addition of [hydrogen bromide](#) to [cinnamic acid](#) and hydrolysis; by catalytic reduction of [ethyl benzoylacetate](#) in aqueous [acetic acid](#) or aqueous [ethanol](#);³ by catalytic reduction of [ethyl \$\alpha\$ -anilino- \$\beta\$ -phenyl- \$\beta\$ -hydroxypropionate](#);⁴ and by the procedure described.^{5,6,7}

References and Notes

1. Findlay and Hickmans, *J. Chem. Soc.*, **1909**, 1004.
2. Fittig and Binder, *Ann.*, **195**, 131 (1877).
3. Kindler and Blaas, *Ber.*, **76B**, 1211 (1943).
4. Fourneau and Billeter, *Bull. soc. chim. France*, **7**, 593 (1940).
5. Andrijewski, *J. Russ. Phys. Chem. Soc.*, **40**, 1635 (1908).
6. Blaise and Herman, *Ann. chim. phys.*, [8] **23**, 532 (1911).
7. Gaudini, *Gazz. chim. ital.*, **73**, 263 (1943).

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

ligroin

Drierite

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

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

[acetic acid](#) (64-19-7)

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

[ether](#) (60-29-7)

[sodium hydroxide](#) (1310-73-2)

[sodium bicarbonate](#) (144-55-8)

hydrogen bromide (10035-10-6)

sodium carbonate (497-19-8)

benzaldehyde (100-52-7)

acetone (67-64-1)

zinc (7440-66-6)

ammonium hydroxide (1336-21-6)

cinnamic acid (621-82-9)

magnesium sulfate (7487-88-9)

Ethyl benzoylacetate (94-02-0)

Ethyl bromoacetate (105-36-2)

zinc hydroxide (20427-58-1)

Ethyl β -phenyl- β -hydroxypropionate,
Hydracrylic acid, β -phenyl-, ethyl ester (5764-85-2)

Ethyl α,α -dimethyl- β -phenyl- β -hydroxypropionate

β -phenyl- β -hydroxypropionic acid

ethyl α -anilino- β -phenyl- β -hydroxypropionate

ethyl α -bromoisobutyrate (600-00-0)