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.

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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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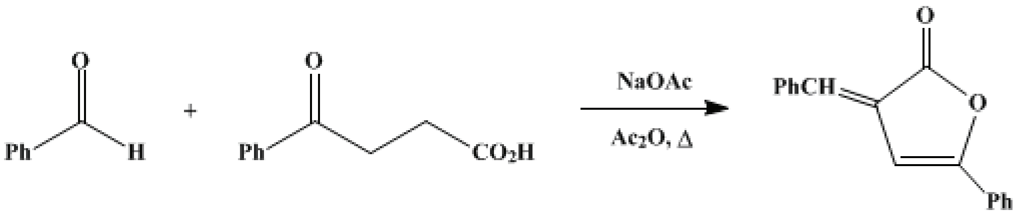
α-BENZYLIDENE-γ-PHENYL-Δ$^{\beta,\gamma}$-BUTENOLIDE

[Cinnamic acid, α-(β-hydroxystyryl)-, γ-lactone]



Submitted by Robert Filler, Edmund J. Piasek, and Hans A. Leipold[1].
Checked by S. Trofimenko and B. C. McKusick.

1. Procedure

The apparatus consists of a 200-ml., three-necked, round-bottomed flask fitted with thermometer, reflux condenser, and gas-inlet tube. The flask is charged with 17.8 g. (0.10 mole) of 3-benzoylpropionic acid (Note 1), 10.6 g. (10.6 ml., 0.10 mole) of benzaldehyde, 61.3 g. (57 ml., 0.60 mole) of acetic anhydride, and 8.2 g. (0.10 mole) of powdered anhydrous sodium acetate (freshly fused). The flask is placed in an oil bath maintained at a temperature of 95–100° and is kept there for 2 hours while dry oxygen-free nitrogen is passed through the reaction mixture (Note 2). At the end of this time the flask is removed from the oil bath, and the hot solution is decanted from the sodium acetate into a 250-ml. Erlenmeyer flask. The solution is kept at 0–5° in a refrigerator for 1 hour, during which time α-benzylidene-γ-phenyl-Δ$^{\beta,\gamma}$-butenolide separates as an orange solid.

About 40 ml. of 95% ethanol is added to the contents of the flask, and the butenolide is brought into suspension by thoroughly breaking up all lumps with a spatula. The suspension is filtered with suction, and the filter cake is washed with 30 ml. of cold 95% ethanol and then with 100 ml. of boiling water to remove any sodium acetate present. The butenolide is obtained as a yellow solid, m.p. 149–154°, weight 11.1–12.4 g. (45–50%), after being dried overnight in a vacuum desiccator. This product, which is pure enough for most purposes, may be further purified by crystallization from 95% ethanol (Note 3).

2. Notes

1. 3-Benzoylpropionic acid[2] is available from Aldrich Chemical Co., Milwaukee, Wisconsin.
2. Oxygen is removed from the nitrogen gas by passing the latter through Brady solution, which consists of zinc amalgam, sodium hydroxide, and sodium anthraquinone-β-sulfonate.[3] It has been shown that oxidizing agents induce formation of a Pechmann dye, a deep red substance which is difficult to remove from the butenolide.[4]
3. About 75 ml. of ethanol is used for every gram of butenolide to be dissolved. Clarification of the solution with charcoal should be avoided because the butenolide tends to separate from solution during filtration and clogs the steam-jacketed funnel. The crystallized butenolide melts at 150–152°.

3. Discussion

α-Benzylidene-γ-phenyl-Δ$^{\beta,\gamma}$-butenolide has been prepared by the condensation of benzaldehyde with 3-benzoylpropionic acid in the presence of acetic anhydride and sodium acetate[5,6] or in the presence of a mixture of dimethylformamide and sulfur trioxide.[7] The butenolide has also been obtained by reaction of α-chloromethylene-γ-phenyl-Δ$^{\beta,\gamma}$-butenolide with benzene in the presence of anhydrous aluminum chloride.[8]

The method described above may be used for the preparation of a wide variety of butenolides substituted in the arylidene ring with either electron-withdrawing or electron-releasing substituents. γ-Lactones such as α-benzylidene-γ-phenyl-Δ$^{\beta,\gamma}$-butenolide are isoelectronic with azlactones, but have received much less attention. Like the azlactone ring, the butenolide ring may be opened readily by water, alcohols, or amines to form keto acids, keto esters, or keto amides.[9] α-Benzylidene-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide is smoothly isomerized by aluminum chloride to 4-phenyl-2-naphthoic acid[10] in 70% yield via intramolecular alkylation. Grignard reagents add 1,4 to the α,β-unsaturated carbonyl system, with the lactone ring remaining intact,[11] while phenyllithium leads to ring opening and the formation of 1,1-diphenyl-2-phenacylcinnamyl alcohol.[11] The butenolide gives reduced dilactones, on treatment with lithium aluminum hydride.[12]

References and Notes

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

α-Benzylidene-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide

α-chloromethylene-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide

benzylidene-γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide

1,4 to the α,β-unsaturated carbonyl

ethanol (64-17-5)

Benzene (71-43-2)

acetic anhydride (108-24-7)

sodium acetate (127-09-3)

sodium hydroxide (1310-73-2)

sulfur trioxide (7446-11-9)

oxygen (7782-44-7)

nitrogen (7727-37-9)

benzaldehyde (100-52-7)

aluminum chloride (3495-54-3)

zinc (7440-66-6)

Phenyllithium (591-51-5)

3-benzoylpropionic acid (2051-95-8)

lithium aluminum hydride (16853-85-3)

dimethylformamide (68-12-2)

sodium anthraquinone-β-sulfonate (131-08-8)

4-phenyl-2-naphthoic acid

1,1-diphenyl-2-phenacylcinnamyl alcohol

Cinnamic acid, α-(β-hydroxystyryl)-, γ-lactone (4361-96-0)