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.

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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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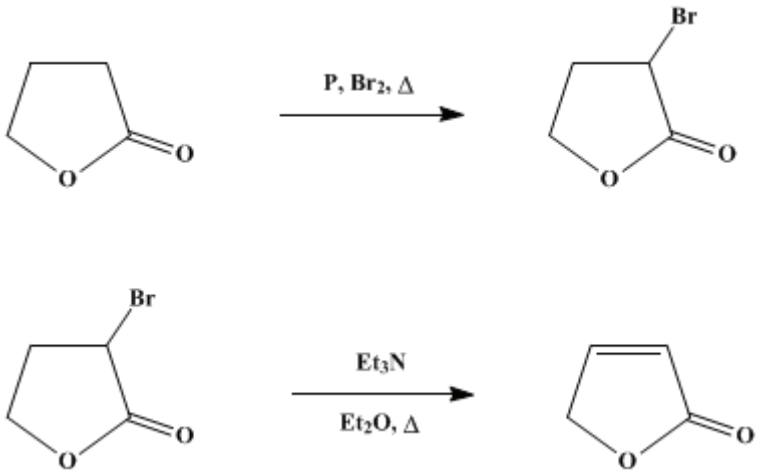
γ-CROTONOLACTONE

[Δ$^{\alpha,\beta}$-Butenolide]



Submitted by Charles C. Price and Joseph M. Judge[1].
Checked by Richard F. Atkinson and E. J. Corey.

1. Procedure

Caution! Contact with α-bromo-γ-butyrolactone can cause severe eye and skin irritation. This preparation should be carried out in a good hood, and the operator should wear protective goggles and rubber gloves.

A. *α-Bromo-γ-butyrolactone*. In a 1-l., three-necked, round-bottomed flask equipped with a dropping funnel, sealed stirrer, and an efficient reflux condenser (Note 1) are placed 100 g. (1.16 moles) of redistilled γ-butyrolactone and 13.4 g. (0.43 g. atom) of red phosphorus. Over a half-hour interval, 195 g. (66.5 ml., 1.22 moles) of bromine is added, the mixture being stirred moderately and cooled by an ice bath.

This mixture is heated to 70° and an additional 195 g. (66.5 ml., 1.22 moles) of bromine added over a half-hour interval. After the bromine addition, the temperature is raised to 80° and the mixture held at that temperature for 3 hours. Air is blown into the cooled reaction until the excess bromine and hydrogen bromide are removed (Note 1). This process usually requires one hour (Note 2).

The aerated reaction mixture is heated to 80° and 25 ml. of water is added cautiously, with stirring. A vigorous reaction ensues, and upon cessation of the reaction an additional 300 ml. of water is added.

The reaction mixture of two layers and some solid residue is heated under reflux for 4 hours. Upon cooling, two layers again appear. The product is extracted with two portions of ether (200 ml. each), and the extracts are dried over magnesium sulfate (Note 3). *Care should be taken since the α-bromolactone is a vesicant.*

The dried crude material is distilled, b.p. 125–127° (13 mm.), n^{25}D 1.5030, yield 105 g. (55%).

B. Δ$^{\alpha,\beta}$-*Butenolide*. In a 500-ml. three-necked flask fitted with a mechanical stirrer, a reflux condenser, and a 250-ml. dropping funnel containing a solution of 61 g. (84.5 ml., 0.6 mole) of triethylamine in 70 ml. of dry diethyl ether, a solution of 83 g. (0.5 mole) of α-bromo-γ-butyrolactone and 200 ml. of dry diethyl ether is heated to reflux, with stirring. The amine solution is added, slowly, during 5 hours and the stirring under reflux continued for an additional 24 hours. The brown precipitate

(40 g.) is removed by filtration. Most of the solvent is removed from the filtrate by evaporation, and the additional precipitate (8 g.) is removed. This precipitate is predominantly triethylamine hydrobromide. The liquid residue is distilled under reduced pressure and the $\Delta^{\alpha,\beta}$-butenolide is collected at 107–109° (24 mm.); yield 25 g. (60%, 33% overall), m.p. 5°[2,3,4] (Note 4).

2. Notes

1. A trap to catch the resulting bromine-hydrogen bromide vapors is desirable.
2. Plieninger[5] reports that the product at this stage is α,γ-dibromobutyryl bromide.
3. Extraction with ether is necessary to separate the bromolactone efficiently.
4. The infrared spectrum of γ-crotonolactone shows two bands in the carbonyl region at 5.60 and 5.71 μ in carbon tetrachloride (5%) [shifted to 5.61 and 5.71 μ. in chloroform (5%)] and carbon-carbon stretching absorption at 6.23 μ. The nuclear magnetic resonance spectrum shows olefinic peaks centered at 2.15τ (pair of triplets) and 3.85τ (pair of triplets), each due to one proton, and a two-proton triplet centered at 5.03τ (in CCl_4).
In the ultraviolet, γ-crotonolactone shows end absorption at 205 mμ (ε *ca.* 11,000) and no maximum at higher wavelength.
Oxidation of this product by potassium permanganate affords 2,3-dihydroxy-4-butyrolactone.[2]

3. Discussion

The original preparation of γ-crotonolactone by Lespieau involved a five-step sequence from epichlorohydrin and sodium cyanide.[2] A recent detailed study of this procedure reported an overall yield of 25% for the lactone.[3] Glattfeld[4] used a shorter route from glycerol chlorohydrin and sodium cyanide; hydrolysis and distillation of the intermediate dihydroxy acid yielded γ-crotonolactone in 23% yield and β-hydroxy-γ-butyrolactone in 28% yield.[4] The formation of γ-crotonolactone in 15% yield has also been reported from pyrolysis of 2,5-diacetoxy-2,5-dihydrofuran at 480–500°.[6] The lactone has been prepared in 37% overall yield from propynol by carboxylation and hydrogenation.[7]

The formation of α-bromo-γ-butyrolactone has been reported in 70% yield by uncatalyzed reaction of bromine at 160–170°,[8] as well as by the catalyzed procedure used here.[3]

4. Merits of the Preparation

γ-Crotonolactone is the simplest example of the butenolide ring system, which occurs in many natural products. In view of the availability of butyrolactone, the present procedure represents the most convenient method of synthesis of the unsaturated lactone.

The dehydrohalogenation by a tertiary amine illustrates the utility of such amines for dehydrohalogenations which produce a double bond normally activated for attack by many bases.[9]

References and Notes

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

bromolactone

$\Delta^{\alpha,\beta}$-Butenolide

α-bromolactone

bromine-hydrogen bromide

glycerol chlorohydrin

ether,
diethyl ether (60-29-7)

chloroform (67-66-3)

Epichlorohydrin (106-89-8)

potassium permanganate (7722-64-7)

sodium cyanide (143-33-9)

hydrogen bromide (10035-10-6)

bromine (7726-95-6)

PHOSPHORUS (7723-14-0)

carbon tetrachloride (56-23-5)

γ-butyrolactone,
Butyrolactone (96-48-0)

magnesium sulfate (7487-88-9)

triethylamine (121-44-8)

γ-Crotonolactone (497-23-4)

α-Bromo-γ-butyrolactone (5061-21-2)

triethylamine hydrobromide (636-70-4)

α,γ-dibromobutyryl bromide

2,3-dihydroxy-4-butyrolactone (15667-21-7)

β-hydroxy-γ-butyrolactone (7331-52-4)

2,5-diacetoxy-2,5-dihydrofuran

propynol