



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.

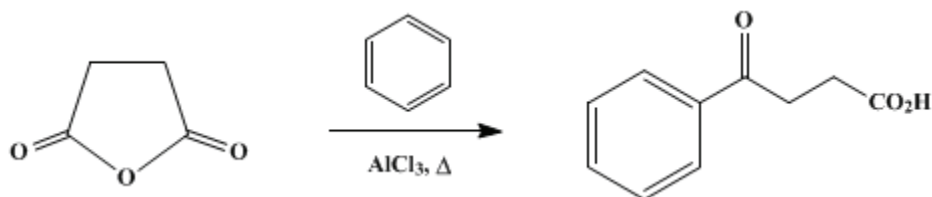
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.81 (1943); Vol. 13, p.12 (1933).

β -BENZOYLPROPIONIC ACID

[Propionic acid, β -benzoyl-]



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1. Procedure

In a 2-l. three-necked, round-bottomed flask fitted with a mechanical stirrer and two reflux condensers are placed 68 g. (0.68 mole) of succinic anhydride (p. 560) and 350 g. (4.5 moles) of dry, thiophene-free benzene (Note 1). The stirrer is started, and 200 g. (1.5 moles) of powdered, anhydrous aluminum chloride is added all at once. Hydrogen chloride is evolved and the mixture becomes hot (Note 2). It is heated in an oil bath and refluxed, with continued stirring, for half an hour (Note 3). The flask is then surrounded by cold water, and 300 cc. of water is slowly added from a dropping funnel inserted in the top of one of the condensers (Note 4). The excess benzene is removed by steam distillation, and the hot solution is at once poured into a 2-l. beaker. After the mixture is cold the liquid is decanted from the precipitated solid and acidified with concentrated hydrochloric acid (about 20 cc. is required); 5 to 15 g. of benzoylpropionic acid separates and is filtered (Note 5). The residual suspension in the beaker is boiled for five hours with 1.5 l. of water containing 360 g. of commercial soda ash; the resulting solution is filtered with suction, the filter cake washed with hot water, and the filtrate acidified with concentrated hydrochloric acid; about 300 cc. is required (Note 6). The precipitated benzoylpropionic acid is filtered and washed with hot water (Note 7). After drying for a day it weighs 95–100 g. (77–82 per cent of the theoretical amount) and melts at 111–113° (Note 8).

If the first, colored, precipitate (weight, 5–15 g.) is separated as suggested it is unnecessary to purify the remainder. The acid may be further purified, if desired, by dissolving in dilute sodium hydroxide and precipitating with concentrated hydrochloric acid, the first portion of the precipitate being collected separately. The pure product melts at 116° (Note 9).

2. Notes

- Commercial benzene is shaken with concentrated sulfuric acid, then with water and dried, first with anhydrous calcium chloride and then over metallic sodium.
- If the reaction does not start at once it is initiated by gentle heating.
- The yield is not increased by longer heating.
- The procedure from this point on can be simplified and improved as follows. After the addition of water to the aluminum chloride complex, 100 cc. of concentrated hydrochloric acid (sp. gr. 1.18) is added and the benzene is removed by steam distillation. The hot mixture is transferred to a 1-l. beaker, and the β -benzoylpropionic acid separates as a colorless oil which soon solidifies. After cooling to 0°, it is collected, washed with a cold mixture of 50 cc. of concentrated hydrochloric acid and 150 cc. of water, and then with 200 cc. of cold water. The crude acid is dissolved in a solution of 75 g. of anhydrous sodium carbonate in 500 cc. of water by boiling for fifteen minutes. The solution is filtered by suction and the small amount of aluminum hydroxide washed twice with 50-cc. portions of hot water. Four grams of charcoal is added to the hot filtrate; the solution is stirred for three to four minutes and then filtered with suction. The clear, colorless filtrate is transferred to a 2-l. beaker, cooled to 50–60°, and carefully acidified with 130 cc. of concentrated hydrochloric acid. After cooling to 0° in an ice-salt bath the acid is filtered, washed well with water, dried overnight at room temperature, and finally

dried to constant weight at 40–50°. The yield is 110–115 g. (92–95 per cent of the theoretical amount). It melts at 114–115° and needs no further purification. (E. L. Martin and Louis F. Fieser, private communication.)

5. The amount of acid isolated at this point varies according to the length of time the solution is allowed to stand before acidification.

6. The first portion of the precipitated acid is usually colored; it is best to filter it separately. The remaining acid will then be colorless and very nearly pure (m.p. 114–115°).

7. By evaporating the filtrate to a small volume and extracting with ether, a further 3 g. of acid may be obtained.

8. The acid tenaciously retains traces of water to which apparently higher yields may be due. The weights given were obtained on material that had been dried overnight in a vacuum desiccator.

9. γ -Benzoylbutyric acid may also be prepared by this method. Glutaric anhydride (0.68 mole) dissolved in part of 350 g. of benzene is added to the rest of the benzene, in which the aluminum chloride is suspended; the temperature is kept below 15° for one and one-half hours, including the time of addition; an 80–85 per cent yield of γ -benzoylbutyric acid melting at 125–126° is obtained.

3. Discussion

β -Benzoylpropionic acid can be prepared from succinic anhydride, benzene, and aluminum chloride,¹ or from succinic anhydride and phenyl-magnesium bromide.² It has also been obtained by prolonged heating of cinnamic aldehyde, hydrocyanic acid, hydrochloric acid, and water;³ by reduction of benzoylacrylic acid;⁴ by the ketonic hydrolysis of benzoylsuccinic ester;⁵ by heating phenylbromoparaconic, phenylbromoisoparaconic, or γ -phenyl- β,γ -dibromobutyric acids with water;⁶ by the hydrolysis of phenacylbenzoylacetic ester;⁷ and by heating phenacylmalonic acid.⁸

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 499
- Org. Syn. Coll. Vol. 5, 80

References and Notes

1. Burcker, Ann. chim. phys. (5) **26**, 435 (1882); Kohler and Engelbrecht, J. Am. Chem. Soc. **41**, 768 (1919).
2. Komppa and Rohrmann, Ann. **509**, 263 (1934).
3. Matsmoto, Ber. **8**, 1145 (1875); Peine, ibid. **17**, 2114 (1884).
4. von Pechmann, ibid. **15**, 889 (1882).
5. Perkin, J. Chem. Soc. **47**, 276 (1885).
6. Fittig and Leoni, Ann. **256**, 81 (1890); Fittig, Obermüller, and Schiffer, ibid. **268**, 74 (1892).
7. Kapf and Paal, Ber. **21**, 1487 (1888).
8. Kues and Paal, ibid. **18**, 3325 (1885).

Appendix

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

soda ash

benzoylsuccinic ester

phenylbromoparaconic, phenylbromoisoparaconic, or γ -phenyl- β,γ -dibromobutyric acids

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

hydrogen chloride,
hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

sodium hydroxide (1310-73-2)

hydrocyanic acid (74-90-8)

sodium carbonate (497-19-8)

aluminum chloride (3495-54-3)

metallic sodium (13966-32-0)

phenyl-magnesium bromide (100-58-3)

cinnamic aldehyde

Thiophene (110-02-1)

β -Benzoylpropionic acid,
Propionic acid, β -benzoyl-,
benzoylpropionic acid (2051-95-8)

Succinic anhydride (108-30-5)

aluminum hydroxide

γ -Benzoylbutyric acid (1501-05-9)

Glutaric anhydride (108-55-4)

benzoylacrylic acid (583-06-2)

phenacylmalonic acid