



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](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.

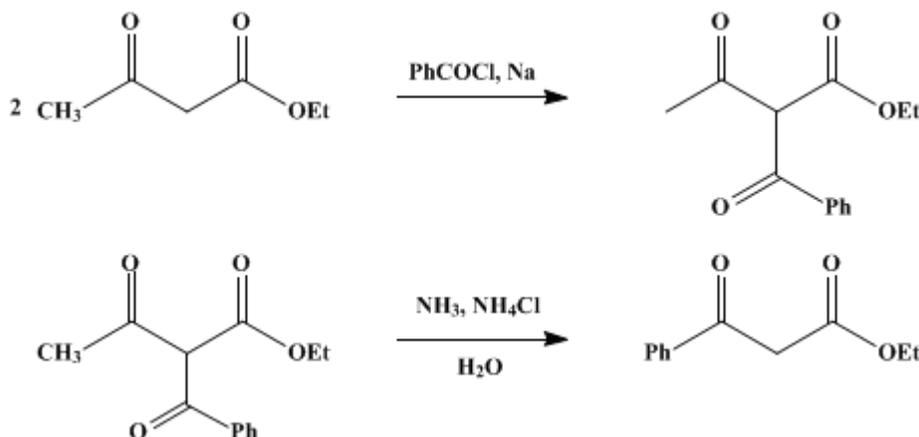
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

*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.266 (1943); Vol. 18, p.33 (1938).*

## ETHYL BENZOYLACETATE

[Acetic acid, benzoyl-, ethyl ester]



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### 1. Procedure

(A) *Preparation of Ethyl Benzoylacetoacetate.*—In a 5-l. three-necked flask, fitted with a liquid-sealed mechanical stirrer and a reflux condenser, are placed 3.4 l. of dry benzene (Note 1), 195 g. (1.5 moles) of ethyl acetoacetate (Org. Syn. Coll. Vol. I, 1941, 235), and 34.5 g. (1.5 gram atoms) of clean sodium. The mixture is heated on a steam cone with stirring and allowed to reflux gently for twenty-four hours. After the suspension of the sodioacetoacetic ester has been cooled slightly, 263 g. (218 cc., 1.9 moles) of benzoyl chloride is added over a period of three hours. The mixture is refluxed with stirring for an additional eight hours. It is then cooled to room temperature, and 375 g. of cracked ice is added. After thorough shaking, the benzene layer, which contains the ethyl benzoylacetoacetate, is separated, washed with 75 cc. of 5 per cent sodium bicarbonate solution, dried with sodium sulfate, and the benzene distilled (Note 2). The residue is distilled *in vacuo* from a 500-cc. Claisen flask with a 50-cm. fractionating side arm. After a small fore-run of benzoyl chloride, the fraction boiling at 142–148°/6 mm., or 177–181°/20 mm., is collected. The yield is 223–263 g. (63–75 per cent of the theoretical amount).

(B) *Hydrolysis of Ethyl Benzoylacetoacetate.*—Thirty-two grams (0.6 mole) of ammonium chloride is dissolved in 150 cc. (8.3 moles) of water in a 500-cc. Erlenmeyer flask, and 10 cc. (0.15 mole) of ammonia (sp. gr. 0.9) is added. The solution is warmed to 42°, 58.5 g. (0.25 mole) of ethyl benzoylacetoacetate at 20° is added quickly, and the mixture is shaken (Note 3). The flask is placed in a water bath at 42° for exactly ten minutes and then cooled rapidly by placing it in an ice bath. The solution is extracted twice with 100-cc. portions of ether, and the ether solution is dried with anhydrous magnesium sulfate. The ether is distilled, and the residue distilled *in vacuo*; the yield is 37.0–37.5 g. (77–78 per cent of the theoretical amount) of ethyl benzoylacetate boiling at 132–137°/4 mm., or 165–169°/20 mm.

### 2. Notes

1. The benzene was dried by distillation, the first portion of the distillate being discarded.
2. It is essential that these steps in the isolation be carried through as rapidly as possible.
3. Larger amounts gave lower yields. The exact procedure must be followed as to time, temperature, and amounts of reagents, and the procedure must be completed without interruption.

### 3. Discussion

Ethyl benzoylacetate has been prepared by the condensation (by means of sodium ethoxide) of ethyl acetate with ethyl benzoate,<sup>1</sup> acetophenone with ethyl carbonate,<sup>2</sup> and acetophenone with ethyl oxalate, with subsequent heating;<sup>3</sup> by treatment of ethyl phenylpropionate<sup>4</sup> or  $\alpha$ -bromocinnamic acid<sup>5</sup> with concentrated sulfuric acid, and of ethyl diazoacetate with benzaldehyde;<sup>6</sup> by the condensation of benzene with the monoethyl ester of malonyl monoacid chloride and aluminum chloride,<sup>7</sup> of benzoyl chloride with the product of the reaction of magnesium and ethyl chloroacetate in ether;<sup>8</sup> by the action of alcohol on benzoylacetimino ethyl ether hydrochloride;<sup>9</sup> and by the hydrolysis of ethyl benzoylacetate.<sup>10</sup>

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 379
- Org. Syn. Coll. Vol. 4, 415
- Org. Syn. Coll. Vol. 7, 359

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### References and Notes

1. Claisen and Lowman, Ber. **20**, 651 (1887).
2. Claisen, *ibid.* **20**, 655 (1887).
3. Wislicenus, *ibid.* **28**, 811 (1895).
4. Baeyer, *ibid.* **15**, 2705 (1882).
5. Michael and Browne, *ibid.* **19**, 1392 (1886).
6. Buchner and Curtius, *ibid.* **18**, 2371 (1885).
7. Marguery, Bull. soc. chim. (3) **33**, 549 (1905).
8. Meyer and Tögel, Ann. **347**, 76 (1906).
9. Haller, Bull. soc. chim. (2) **48**, 23 (1887).
10. Claisen, Ann. **291**, 71 (1896); Shriner and Schmidt, J. Am. Chem. Soc. **51**, 3636 (1929).

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### Appendix

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

sodioacetoacetic ester

monoethyl ester of malonyl monoacid chloride

sulfuric acid (7664-93-9)

ammonia (7664-41-7)

Benzene (71-43-2)

ethyl acetate (141-78-6)

ether (60-29-7)

ammonium chloride (12125-02-9)

sodium bicarbonate (144-55-8)  
magnesium (7439-95-4)  
sodium sulfate (7757-82-6)  
benzaldehyde (100-52-7)  
Acetophenone (98-86-2)  
benzoyl chloride (98-88-4)  
aluminum chloride (3495-54-3)  
sodium (13966-32-0)  
sodium ethoxide (141-52-6)  
Ethyl chloroacetate (105-39-5)  
ethyl benzoate (93-89-0)  
Ethyl acetoacetate (141-97-9)  
Ethyl oxalate  
magnesium sulfate (7487-88-9)  
Ethyl benzoylacetate,  
Acetic acid, benzoyl-, ethyl ester (94-02-0)  
Ethyl benzoylacetoacetate (569-37-9)  
ethyl carbonate  
ethyl phenylpropiolate (2216-94-6)  
 $\alpha$ -bromocinnamic acid  
ethyl diazoacetate (623-73-4)  
benzoylacetimino ethyl ether hydrochloride