



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.

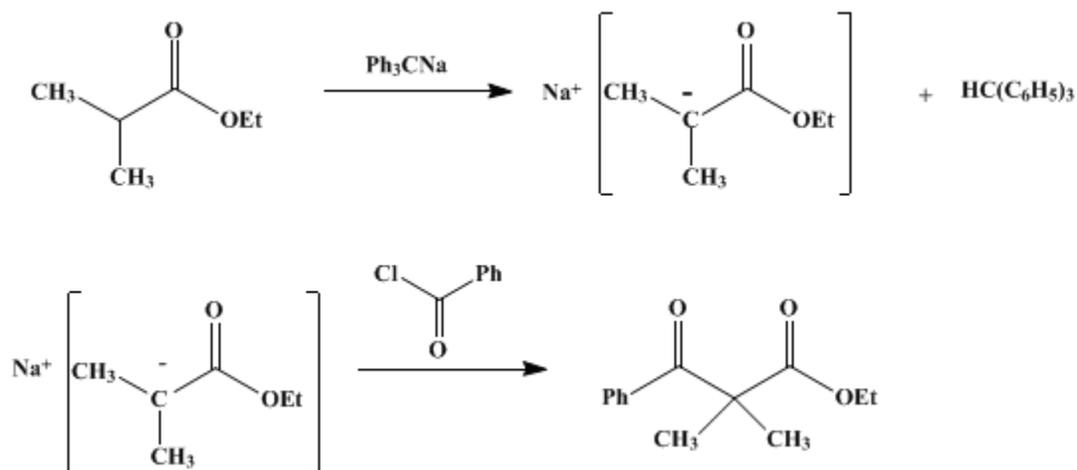
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries 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.268 (1943); Vol. 19, p.43 (1939).*

## ETHYL BENZOYLDIMETHYLACETATE

[Isobutyric acid,  $\alpha$ -benzoyl-, ethyl ester]



Submitted by C. R. Hauser and W. B. Renfrow, Jr.  
Checked by Lee Irvin Smith and E. C. Ballard.

### 1. Procedure

To a freshly prepared solution of 0.187 mole of [triphenylmethylsodium](#) (p. 607), contained in the flask into which it was transferred after preparation, is added 21.7 g. (25 cc., 0.187 mole) of pure [ethyl isobutyrate](#) ([Note 1](#)). The mixture is shaken, and, after it has stood at room temperature for ten minutes, a solution of 26 g. (21.5 cc., 0.186 mole) of pure [benzoyl chloride](#) in 50 cc. of dry [ether](#) is added, with shaking. The mixture becomes warm, and a white precipitate of [sodium chloride](#) separates immediately. After standing at room temperature for several hours the mixture is heated on a water bath and [ether](#) is distilled until the volume is reduced to 300–400 cc. A solution of 5 cc. of [acetic acid](#) in 300 cc. of water is added, and the mixture is shaken in a separatory funnel until two homogeneous layers separate on standing. The aqueous layer is drawn off and discarded; the ethereal layer is shaken with 10 per cent [sodium carbonate](#) solution and dried over [calcium chloride](#) or Drierite. The solution is filtered from the drying agent and distilled on a water bath until most of the [ether](#) is removed. The residue is cooled in a refrigerator, and the [triphenylmethane](#) which crystallizes is filtered with suction and washed with several small portions of dry [ether](#). The filtrate, after removal of [ether](#), is distilled under reduced pressure and all material boiling up to 180° at 15 mm. collected. The distillate is redistilled and the fraction boiling up to 160° at 15 mm. is subjected to a final redistillation. There is obtained 20.5–22.5 g. (50–55 per cent of the theoretical amount) of [ethyl benzoyldimethylacetate](#), b.p. 146–148° at 15 mm. or 133–135° at 9 mm ([Note 2](#)) and ([Note 3](#)).

### 2. Notes

1. It is essential to use pure reagents. Commercial [ethyl isobutyrate](#) may be purified satisfactorily by washing with 10 per cent [sodium carbonate](#) solution, drying over Drierite for several days, and fractionating through an effective column; material boiling over a one-degree range (110–111°) is recommended for this preparation. [Benzoyl chloride](#) was purified by distillation under reduced pressure, and a fraction collected over less than a two-degree range was used.

2. If the more concentrated solution of [triphenylmethylsodium](#), prepared as described in [Note 3](#), p. 609, is employed, approximately 120 g. of [ethyl benzoyldimethylacetate](#) can be prepared in a single experiment.

The bottle containing an [ether](#) solution of 0.85 mole of [triphenylmethylsodium](#) is immersed to two-thirds of its depth in an ice bath. When the bottle is thoroughly cold, the stopper is removed while a tube

delivering a rapid stream of dry **nitrogen** is held at the mouth of the bottle. The bottle is quickly fitted with a three-holed rubber stopper carrying a mechanical stirrer (with open shaft), a dropping funnel, and a bent tube which extends into the bottle for a distance of 1 cm. below the neck. A slow stream of dry **nitrogen** passes through the bent tube; the **nitrogen** supply is also connected to the top of the dropping funnel. One hundred two grams (0.875 mole) of **ethyl isobutyrate** is added rapidly to the vigorously stirred contents of the bottle. After five minutes, 123 g. (101 cc., 0.875 mole) of **benzoyl chloride** is added through the dropping funnel at such a rate that the mixture does not reflux too vigorously (the addition takes about five minutes). Stirring is continued for two or three minutes after the addition is complete. The bottle is then removed from the ice bath, stoppered, shaken, and allowed to stand for half an hour. The reaction mixture is transferred to a 2.5-l. separatory funnel and the **mercury** drained off. The remaining mixture is extracted with 300 cc. of water, any sludge formed being collected separately. The sludge is extracted with a little **ether**, the extract being added to the **ether** layer in the funnel. The **ether** solution is washed with two 100-cc. portions of 10 per cent **sodium carbonate** solution, and dried by shaking with 50 g. of anhydrous sodium or magnesium sulfate and by standing with 50 g. of Drierite in a stoppered 2-l. Erlenmeyer flask. The solution is filtered into a 2-l. round-bottomed flask and the **ether** removed by distillation. The residue is transferred to a 1-l. Claisen flask and distilled in vacuum, using a metal or oil bath and collecting all the material boiling below 175° at 15 mm. The distillate is transferred to a 200-cc. round-bottomed flask fitted with a 6-inch Widmer fractionating column and redistilled from a metal bath. The **ethyl benzoyldimethylacetate** boils at 146–148°/15 mm. and weighs 115–125 g. (61–67 per cent of the theoretical amount based on the quantity of **triphenylmethylsodium** used). (Charles R. Hauser and Boyd E. Hudson, Jr., private communication.)

3. The submitters report that **ethyl isobutyrylisobutyrate** (**ethyl  $\alpha,\alpha,\gamma,\gamma$ -tetramethylacetoacetate**) may be prepared in a similar manner, using **isobutyryl chloride** instead of **benzoyl chloride**. The yield of this ester, b.p. 94.5–95.5°/18 mm., is about 55 per cent of the theoretical amount. Several other examples of the acylation of esters by this procedure are given by Hudson, Jr., and Hauser.<sup>1</sup>

### 3. Discussion

**Ethyl benzoyldimethylacetate** has been prepared by the condensation of **ethyl isobutyrate** with **ethyl benzoate**,<sup>2</sup> **phenyl benzoate**, **benzoic anhydride**, or **benzoyl chloride**.<sup>3</sup> The procedure described above<sup>3</sup> is a modification of the method of Scheibler and Stein.<sup>4</sup>

This preparation is referenced from:

- **Org. Syn. Coll. Vol. 2, 607**

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### References and Notes

1. Hudson, Jr., and Hauser, *J. Am. Chem. Soc.* **63**, 3159 (1941).
2. Renfrow, Jr., and Hauser, *ibid.* **60**, 464 (1938).
3. Hudson, Jr., Dick, and Hauser, *ibid.* **60**, 1961 (1938).
4. Scheibler and Stein, *J. prakt. Chem. (2)* **139**, 111 (1934).

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### Appendix

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

Drierite

sodium or magnesium sulfate

calcium chloride (10043-52-4)

acetic acid (64-19-7)

ether (60-29-7)

sodium chloride (7647-14-5)

sodium carbonate (497-19-8)

nitrogen (7727-37-9)

mercury (7439-97-6)

benzoyl chloride (98-88-4)

Benzoic anhydride (93-97-0)

ethyl benzoate (93-89-0)

Triphenylmethane (519-73-3)

Ethyl benzoyldimethylacetate (25491-42-3)

Isobutyric acid,  $\alpha$ -benzoyl-, ethyl ester

Triphenylmethylsodium (4303-71-3)

ethyl isobutyrate (97-62-1)

Ethyl isobutyrylisobutyrate

isobutyryl chloride (79-30-1)

phenyl benzoate (93-99-2)

ethyl  $\alpha,\alpha,\gamma,\gamma$ -tetramethylacetoacetate