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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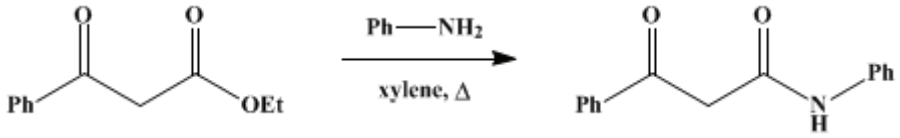
Organic Syntheses, Coll. Vol. 3, p.108 (1955); Vol. 25, p.7 (1945).

BENZOYLACETANILIDE

[Acetanilide, α-benzoyl-]



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1. Procedure

A 250-ml. three-necked round-bottomed flask is fitted with a dropping funnel, a mechanical stirrer, and a steam-jacketed column (15–20 cm. long) terminating in a still head. The still head carries a thermometer and is connected to a condenser set for downward distillation. In the flask are placed 42.2 g. (0.22 mole) of ethyl benzoylacetate (Note 1) and 50 ml. of dry xylene, and the flask is immersed in an oil bath. The bath is heated to 145–150°, stirring is begun, and 18.2 ml. (18.6 g., 0.20 mole) of aniline is added dropwise during 30 minutes. About 5 minutes after the addition has begun, the temperature in the still head rises to 75–78° as ethanol begins to distil. Approximately 12–14 ml. of distillate (Note 2) is collected in a 25-ml. graduate in about 1 hour; the end of the reaction is indicated by the fall of the temperature in the still head.

The reaction flask is removed from the oil bath, and the solution is poured into a 250-ml. beaker to crystallize; 10 ml. of benzene is used to rinse out the flask. When crystallization sets in, 50 ml. of petroleum ether (b.p. 35–55°) is added to the warm mixture with manual stirring. After the mixture has been chilled in an ice bath, the product is filtered by suction and washed with 100 ml. of a 1:1 petroleum ether-benzene mixture. It is then removed from the funnel, stirred into a slurry with 100 ml. of the mixed solvent, filtered, and again washed with 50 ml. of the solvent. These washings remove the bulk of the color, and a powdery white product remains. After standing overnight in a warm place, the product weighs 35.5–36.5 g. (74–76%) and melts at 104–105°. It may be purified further by recrystallization from benzene (3.7 ml. per g.). The yield of colorless benzoylacetanilide melting at 106–106.5° cor, is 32–34 g.

2. Notes

1. The ethyl benzoylacetate, aniline, and xylene should be redistilled before use. It is necessary that the flask and reagents be free from moisture. Impure starting materials and particularly traces of acids lower the yields. The submitters obtained 82–83% yields of benzoylacetanilide by using Eastman xylene (histological).
2. The distillate consists of a mixture of xylene and ethanol. By adding 100 ml. of water, the xylene layer can be separated and measured. Of 14 ml. of distillate, about 3.5 ml. is xylene and the balance, 10.5 ml. (89% of the theoretical amount), is ethanol.

3. Discussion

Benzoylacetanilide has been made by heating aniline and methyl benzoylacetate in an autoclave at 150°[1] and by heating the anil $C_6H_5NHCOCH_2(C{=}NC_6H_5)C_6H_5$ with dilute acid.[1]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 80

References and Notes

1. Knorr, *Ann.*, **245**, 372 (1888).

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

petroleum ether

ethanol (64-17-5)

Benzene (71-43-2)

aniline (62-53-3)

xylene (106-42-3)

Ethyl benzoylacetate (94-02-0)

Benzoylacetanilide,
Acetanilide, α-benzoyl- (85-99-4)

methyl benzoylacetate