



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.

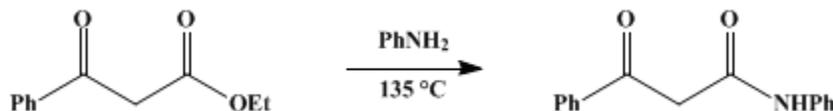
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.80 (1963); Vol. 37, p.2 (1957).

BENZOYLACETANILIDE

[Acetanilide, 2-benzoyl-]



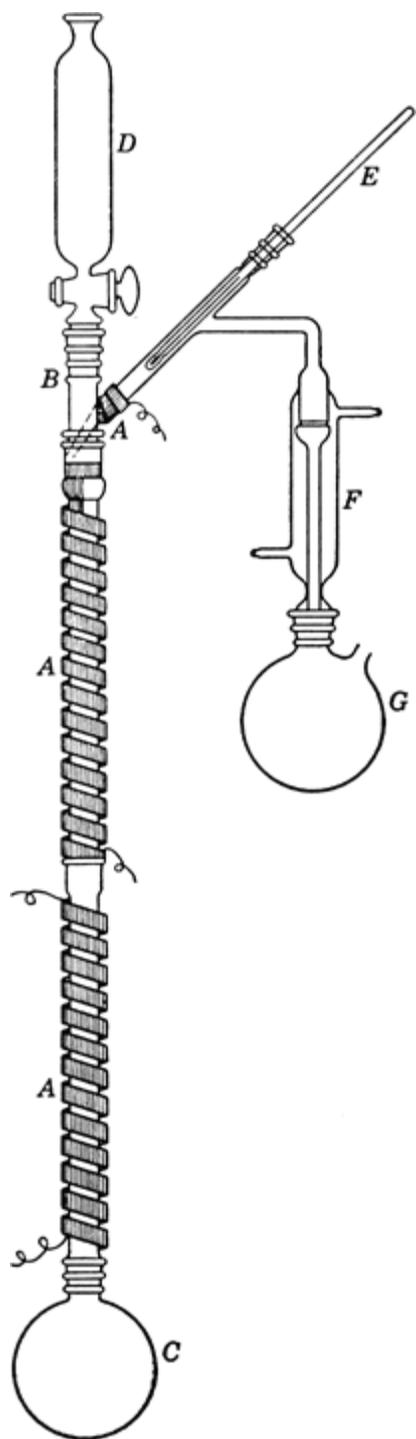
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Checked by Max Tishler and R. Connell.

1. Procedure

A mixture of 105.7 g. (0.55 mole) of ethyl benzoylacetate and 46.6 g. (0.5 mole) of aniline (Note 1) is placed in the dropping funnel *D* (Fig.4) at the top of the continuous reactor (Note 2) and (Note 3) after the column has been heated to 135° (transformer set at 80 volts) (Note 4) and (Note 5). The reactants are then admitted to the column during about 15 minutes (this corresponds to a rate of amide formation of 396–400 g. per hour). Alcohol distills (Note 5) noticeably from the column during the addition and collects in flask *G*. At the completion of the reaction, 100 ml. of xylene is passed through the hot column to rinse out the residual amide (Note 6). An additional 200 ml. of xylene is added to the receiver *C*, and solution is effected by warming. After the solution has been cooled enough to induce crystallization, 100 ml. of petroleum ether (b.p. 35–60°) is added with manual stirring. The mixture is chilled to 15°, then the crystalline product is separated by suction filtration and washed 300–400 ml. of petroleum ether. The yield is 99–100 g. (83–84%), m.p. 106–106.5° (Note 7). The melting point of this product is not altered by recrystallization from benzene (Note 8),(Note 9),(Note 10).

Fig. 4.



2. Notes

1. Commercial grades of [ethyl benzoylacetate](#) and [aniline](#) were freshly redistilled before use.
2. The continuous reactor shown in [Fig. 4](#) is of general utility for reactions that proceed at a rapid rate. Optimum conditions must be determined by experiment for each new product, but a high yield may often be secured. To determine a yield, it is necessary to run a given weight of the components through, rinse the column, and work up the combined products.
3. The reactor is built from stock pieces of glassware having 29/42 and 24/40 standard taper joints. It consists of a column 100 cm. long, of 2 cm. inside diameter, in two 50-cm. sections. The column is packed with 1/8-in. glass helices such as are used for packing distillation columns. The column is heated

by two 275-watt flexible heating tapes *A*, 6 ft. long and ½ in. wide, with lead wires connected to variable transformers, which are attached to a source of 110-volt power. The heating elements may be covered with asbestos tape if desired. At the bottom of the column is a 500-ml. flask *C* for receiving the product. At the top of the column is a 250-ml. addition funnel *D* (a cylindrical shape is convenient for calibration of volume or for winding with heating tape in instances where melting a solid or heating a solution is required). The addition funnel is connected to the column through a section *B* having a side arm provided with a thermometer *E* and a downward condenser *F* leading to a 500-ml. flask *G*, which has an outlet to the atmosphere for effluent gas.

4. It is always desirable to use a "wet" column; once a column has been used, this condition prevails. It is advantageous to admit a little [xylene](#) while regulating the heater, before addition of the reactants.

5. With two 275-watt heating tapes, the required temperature inside the column is secured at a voltage setting of about 80. If alcohol does not distil noticeably during the reaction, the internal temperature is not high enough and the transformer should be adjusted, or more time should be allowed for preheating the column.

6. Part of the product solidifies in the receiver.

7. This compares with 74–76% yield by the batch process.²

8. Recrystallization from [benzene](#) produces a whiter product in 92% recovery.

9. This procedure may be used to prepare other substituted anilides. If one of the components is a solid, it can be dissolved in an excess of the other. For instance, 46 g. of [2-amino-5-nitroanisole](#) in 285 ml. of hot [ethyl benzoylacetate](#) is passed through in 30 minutes, with a transformer setting of 70 volts; then the column is rinsed with 50 ml. of the ester. The product crystallizes in the receiver and is separated by filtration; the filtrate is used to make up more of the reacting component mixture. The work-up yields 75–76 g. (89%) of amide with the correct melting point (178.5–180°) and color. When the same amide is made by a batch procedure, the yield is only 81% of a product melting at 130–150°. This illustrates the advantage of short time of exposure to heat in the continuous reactor.

10. This reactor has also been used with other types of reactions.

	Voltage	Time, hr.	Mole Ester	Yield, %
Ethyl benzalmalonate (batch) (cont.) ³		18	0.63	90.8
	65	0.5	0.69	82
3-Carboxy-4-hydroxyquinoline ⁴	90	0.66		35
4-Benzal-2-phenyl-5-oxazolone (batch) (an azlactone) (cont.) ⁵				64
	60	0.25	>	73

3. Discussion

This preparation and [oleoyl chloride](#) (p.739) illustrate the use of the general form of a laboratory-sized continuous reactor.⁶ This device has many advantages over the commonly used flasks (batch procedure). In particular, the short time of exposure to heat results in a better quality of product, as shown by less color, fewer side reactions, and better melting point, often unchanged by recrystallization. Furthermore, the unlimited capacity, very short reaction time, and use of concentrated solutions permit a larger output with no increase in size of apparatus and less delay required for removal of solvents.

The continuous reactor is most useful with reactions that take place at a relatively rapid rate. Its wide versatility enables it to be used in many types of reactions. [Benzoylacetanilide](#) was selected as an example because it has previously appeared in *Organic Syntheses*.²

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 4, 739](#)

References and Notes

1. Eastman Kodak Company, Rochester, New York.
 2. *Org. Syntheses Coll. Vol. 3*, 108 (1955).
 3. *Org. Syntheses Coll. Vol. 3*, 377 (1955).
 4. Gould and Jacobs, *J. Am. Chem. Soc.*, **61**, 2893 (1939).
 5. *Org. Syntheses Coll. Vol. 2*, 490 (1943).
 6. Allen, Byers, Humphlett, and Reynolds, *J. Chem. Educ.*, **32**, 394 (1955).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

petroleum ether

Benzene (71-43-2)

aniline (62-53-3)

xylene (106-42-3)

Ethyl benzalmalonate

Ethyl benzoylacetate (94-02-0)

Benzoylacetanilide,
Acetanilide, 2-benzoyl- (85-99-4)

2-amino-5-nitroanisole (97-52-9)

3-Carboxy-4-hydroxyquinoline

4-Benzal-2-phenyl-5-oxazolone (842-74-0)

Oleoyl chloride (112-77-6)