



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.

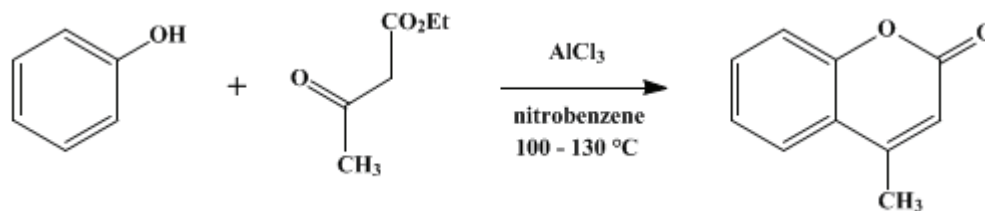
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.581 (1955); Vol. 24, p.69 (1944).

4-METHYLCOUMARIN

[Coumarin, 4-methyl-]



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1. Procedure

In a 5-l. three-necked round-bottomed flask, fitted with a sealed stirrer, dropping funnel, and air condenser, the open end of which is connected to a gas-absorption trap, are placed 188 g. (2 moles) of phenol and 268 g. (2 moles) of ethyl acetoacetate in 300 ml. of dry nitrobenzene (Note 1) and (Note 2). The mixture is heated to 100° by means of an oil bath, stirring is started, and 532 g. (4 moles) of anhydrous aluminum chloride dissolved in 2.1 l. of dry nitrobenzene is added over a period of 30–45 minutes (Note 3). The dropping funnel is then replaced by a thermometer, and the temperature of the solution is raised to 130° and held there 3 hours (Note 4). By this time the evolution of hydrogen chloride will have practically ceased.

The solution is cooled until its temperature is approximately that of the room, and 500 ml. of a mixture of equal parts of concentrated hydrochloric acid and water is added with stirring. The flask is then arranged for steam distillation and heated with a free flame while steam is passed into the reaction mixture until about 200 ml. of distillate is collected (Note 5). While hot, the mixture is placed in a large separatory funnel and the lower aqueous layer removed; the nitrobenzene layer is filtered through a Büchner funnel (Note 6) and (Note 7).

The nitrobenzene is then removed by vacuum distillation using a 2-l. Claisen flask, and the residue in the flask is distilled under diminished pressure; the fraction boiling at 180–195°/15 mm. is collected (Note 8) and (Note 9). The red-yellow oil, which solidifies on cooling, amounts to 128–176 g. (40–55%) and is sufficiently pure for some purposes (Note 10). A nearly white product can be obtained by dissolving the crude product in ether, shaking the ether solution with portions of 5% sodium hydroxide solution until no color appears in the aqueous layer, evaporating the ether, and recrystallizing the residue from a mixture of petroleum ether (b.p. 60–90°, Skellysolve B) and benzene (Note 11). The recrystallized product melts at 83–84°; the recovery is 80–85%.

2. Notes

1. Methyl acetoacetate has been used but insufficient data have been obtained as to the yield produced.
2. Commercial nitrobenzene is dried by distillation under reduced pressure until the distillate is clear. The residue is suitable for use without other treatment.
3. The aluminum chloride is added in 25- to 50-g. portions to the 2.1 l. of dry nitrobenzene contained in a 5-l. round-bottomed flask with stirring after each addition. The temperature may rise to 80–90° during the addition; occasional cooling of the flask under running water is necessary. After all the aluminum chloride has been added, the solution is cooled to room temperature. A small amount of aluminum chloride may settle to the bottom.

In one instance when the final cooling was omitted the temperature continued to rise and a large amount of hydrogen chloride was evolved. The residue in the flask was a thick paste. Addition of a portion of the paste to water caused nitrobenzene to separate. However, this batch was not suitable for condensation.

4. Below 100° the condensation does not take place; at 150° tar is formed and no coumarin can be isolated.
5. Some unchanged ester distills before the [nitrobenzene](#); its removal aids in the subsequent separation of the two layers.
6. If a sufficiently large funnel is not available the separation may be done by dividing the solution in portions to suit the funnel available. If too much steam has condensed during the distillation, the aqueous layer may appear on top.
7. The tarry by-products clog filter paper immediately; a small quantity of filter aid may be used to promote the filtration. If the condensation has been satisfactory only a small amount of material will be retained, and this step may be omitted. Occasionally a considerable amount of lumpy, tarry material is removed; filtration is then more difficult, and the yield is lower. The tar, on distillation, yields no coumarin.
8. The recovered [nitrobenzene](#), after being washed with water and dried as in (Note 2), may be used again. The loss is from 400 to 700 ml.
9. Considerable tar remains in the distillation flask. The tar is best poured immediately into a flat pan of water or a sink, where it solidifies to a hard brittle mass; that adhering to the walls of the flask is easily removed by adding 100–200 ml. of [nitrobenzene](#) to the flask and heating the solvent to boiling under atmospheric pressure.
10. According to the submitter, when quantities 3 times this size are used, the yield of distilled material is 38–50%.
11. The ratio of petroleum ether to [benzene](#) should be 8 to 2.

3. Discussion

[4-Methylcoumarin](#) is prepared by the condensation of [phenol](#) and acetoacetic ester. Concentrated [sulfuric acid](#)^{1,2} and 73% [sulfuric acid](#) have been used.^{3,4} The method given here was mentioned by Sethna, Shah, and Shah,⁵ and the procedure is adapted from that of the same authors⁶ for another coumarin derivative.

References and Notes

1. Von Pechmann and Duisberg, *Ber.*, **16**, 2127 (1883).
2. Von Pechmann and Kraft, *Ber.*, **34**, 421 (1901).
3. Peters and Simonis, *Ber.*, **41**, 831 (1908).
4. Fries and Volk, *Ann.*, **379**, 94, footnote 1 (1911).
5. Sethna, Shah, and Shah, *Current Sci.*, **6**, 93 (1937) [*C. A.*, **32**, 549 (1938)].
6. Sethna, Shah, and Shah, *J. Chem. Soc.*, **1938**, 228.

Appendix

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

petroleum ether

acetoacetic ester

[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)

phenol (108-95-2)

aluminum chloride (3495-54-3)

Nitrobenzene (98-95-3)

Ethyl acetoacetate (141-97-9)

4-Methylcoumarin,
Coumarin, 4-methyl- (607-71-6)

Methyl acetoacetate (105-45-3)