



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.

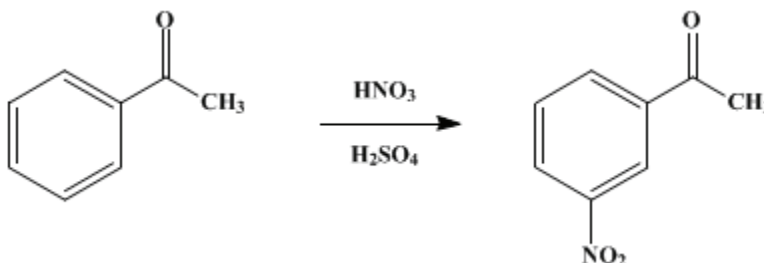
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 2, p.434 (1943); Vol. 10, p.74 (1930).*

## ***m*-NITROACETOPHENONE**

[Acetophenone, *m*-nitro-]



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### 1. Procedure

In a 1-l. wide-mouthed Erlenmeyer flask, immersed in an ice-salt bath contained in a 2-gal. earthenware crock, is placed 150 cc. of concentrated [sulfuric acid](#). The flask is equipped with an efficient mechanical stirrer, a small dropping funnel, and a thermometer reaching almost to the bottom of the flask ([Note 1](#)). The stirrer is started, and, when the [sulfuric acid](#) has cooled to ice temperature or below, 60 g. (0.5 mole) of pure [acetophenone](#) is slowly dropped in from the dropping funnel at such a rate (about ten minutes for the addition) that the temperature does not rise above 5° ([Note 2](#)). After the reaction mixture has cooled, this time to about -7°, the cooled (15–20°) nitrating mixture, consisting of 40 cc. (0.65 mole) of [nitric acid](#) (sp. gr. 1.42 at 15.5°) ([Note 3](#)) and 60 cc. of concentrated [sulfuric acid](#), is added through the dropping funnel at such a rate (100–120 drops per minute) that the temperature of the reaction mixture remains at 0° or lower ([Note 4](#)). After the nitrating acid has been added, stirring is continued for ten minutes longer and the contents of the flask are poured ([Note 5](#)), with vigorous manual stirring, into a mixture of 750 g. of cracked ice and 1.5 l. of water. The product separates as a yellow flocculent solid.

After the ice has melted, the product is filtered by suction and the somewhat sticky mass pressed as dry as possible. It is transferred to a mortar and triturated with three successive 300-cc. portions of cold water (to remove acid); it is then stirred to a mush with two successive 25-cc. portions of ice-cold [ethyl alcohol](#) (to remove adhering oil); the solid is pressed dry on the suction filter after each of the five washings. The product is pressed on a porous plate and, when fairly dry (about one hour), is dissolved in 100–120 cc. of hot [ethyl alcohol](#) ([Note 6](#)). The dark solution is filtered quickly through a small suction funnel ([Note 7](#)), and the hot filtrate is poured slowly into 1 l. of cold water which is stirred vigorously ([Note 8](#)) with a stirring rod during the addition and for several minutes afterward. After standing a few minutes the yellow solid is filtered by suction, washed with 200 cc. of cold water, sucked dry, and pressed out on a porous clay plate.

When the reprecipitated [m](#)-nitroacetophenone (50–55 g.) is dry it is dissolved in 100 cc. of hot [alcohol](#) in a 300-cc. Erlenmeyer flask. The flask is then immersed in an ice bath and shaken vigorously while crystallization is taking place. Because of the great change in solubility between 60° and 50° the agitation of the liquid must be vigorous during this temperature interval, or large clumps of crystals will be formed instead of the purer and more easily dried mush. After the temperature has reached 20° (about one hour) the mixture is filtered by suction ([Note 9](#)). The solid ([Note 10](#)) is washed with 10 cc. of ice-cold [alcohol](#) and pressed dry on a clay plate. The product is light yellow; it softens at 74° and melts at 76–78°. The total yield is 45 g. (55 per cent of the theoretical amount) ([Note 11](#)).

### 2. Notes

1. The only flask found suitable for this preparation is the 1-l. wide-mouthed Erlenmeyer. A large flask

is necessary to ensure rapid cooling. A propeller with long, wide blades agitates the viscous liquid much more efficiently than a stirrer of the centrifugal type. The blades should be as long as allowed by the wide mouth of the flask. The thermometer which is to record the temperature of the reaction mixture should enter at an angle and reach almost to the bottom of the flask, since the amount of liquid is small. The thermometer should have the zero point at least 15 cm. from the bulb in order to facilitate reading the temperature. It is essential that the temperature be watched throughout the experiment. A smaller ice-salt bath than that contained in a 2-gal. earthenware crock is inadequate.

2. The same dropping funnel can be used, without washing, for the addition of the concentrated [sulfuric acid](#), the [acetophenone](#), and the nitrating mixture. With rapid stirring the [acetophenone](#) can be easily added in seven minutes without raising the temperature of the reaction mixture above 3°.

3. [Nitric acid](#) of lower specific gravity than 1.42 at 15.5° yields an impure product. Ordinary concentrated [nitric acid](#) usually has to be strengthened by the addition of fuming [nitric acid](#).

4. Two conditions are necessary for a good nitration: low temperature (0° or below) and rapidity of addition of the nitrating mixture (not longer than forty-five minutes). With efficient cooling the temperature can be held between -5 and 0°. If the temperature should rise once or twice to 3° no harm is done provided that the reaction mixture is quickly cooled back to the correct temperature. In order to avoid local heating the delivery tube of the dropping funnel should be so directed as to deliver the nitrating acid near the site of greatest agitation.

The rate of stirring must be rapid. The optimum speed will be different for different stirrers, depending on the shape and size of the blades. For the stirrer described the speed is 1600 r.p.m. During the addition of [acetophenone](#) this high speed is not necessary; in fact, it cannot be maintained on account of excessive splashing. However, during the addition of the nitrating acid the reaction mixture thickens and high-speed stirring becomes possible. The ice-salt mixture must be stirred repeatedly with a stick, and fresh ice and salt must be added from time to time. The temperature of the bath should be around -16°. Enough liquid should be present in the cooling bath so that the lower half of the flask is immersed in brine. If no especial care is exercised, the addition of the nitrating acid requires from two to three hours in order to maintain the temperature at 0° or below. This long exposure to the mixture of sulfuric and nitric acids is as harmful as a rise of temperature; the product is of poor quality and the yield drops from 55 to 15 per cent or less.

By using solid [carbon dioxide](#) as the cooling medium and also adding it directly to the reaction mixture, a temperature of -20° can be maintained during the nitration.<sup>1</sup> According to W. W. Hartman, private communication, the use of solid [carbon dioxide](#) in this way permits larger runs of [m-nitroacetophenone](#) to be made.

5. The experiment should not be stopped until the product has been poured into ice water.

6. Although 55° suffices to dissolve the [m-nitroacetophenone](#) it is desirable to bring the alcoholic solution to a boil to avoid crystallization during filtration.

7. Excessive frothing in the filter flask is easily checked by pinching off the suction tube from time to time.

8. Vigorous stirring and slow pouring are absolutely necessary. In the absence of either, the product will be lumpy rather than flocculent.

9. Since the solubility curve is so flat in the vicinity of room temperature it is not necessary to cool very low before filtering. The difference in solubility between 20° and 10° amounts to only 1 g. per 100 cc. of solution. The solubility of [m-nitroacetophenone](#) in 96 per cent [alcohol](#) is as follows:

Temperature	Weight in 10 cc.	Temperature	Weight in 10 cc.
8°	0.16	48°	1.88
17	0.25	50	2.38
22	0.31	52	3.08
23	0.34	53.5	4.05
27	0.41	56	5.46
28	0.45	57	8.05
32	0.64	59	11.00
39	0.97	60	15.60
42	1.22		

10. A small additional yield (about 5 g.) may be obtained from the mother liquor by concentrating to 20 cc. and then cooling in ice.
11. This work was aided by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

### 3. Discussion

*m*-Nitroacetophenone has usually been prepared by the nitration of acetophenone;<sup>1, 2</sup> it has been made also by the hydrolysis of *m*-nitrobenzoylacetoacetic ester.<sup>3</sup> The procedure given above has been modified by Morgan and Watson; the modified procedure is reported to increase the yield of *m*-nitroacetophenone to 83 per cent of the theoretical amount.<sup>4</sup>

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 7, 393](#)

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### References and Notes

1. Barkenbus and Clements, *J. Am. Chem. Soc.* **56**, 1369 (1934).
2. Emmerling and Engler, *Ber.* **3**, 886 (1870); Buchka, *ibid.* **10**, 1714 (1877); Engler, *ibid.* **18**, 2238 (1885); v. Kostanecki and Tambor, *ibid.* **34**, 1691 (1901); Rupe, Braun, and v. Zembruski, *ibid.* **34**, 3522 (1901); Camps, *Arch. Pharm.* **240**, 5 (1902).
3. Gevekoht, *Ann.* **221**, 334 (1883).
4. Morgan and Watson, *J. Soc. Chem. Ind.* **55**, 29T (1936).

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### Appendix

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

sulfuric and nitric acids

*m*-nitrobenzoylacetoacetic ester

ethyl alcohol,  
alcohol (64-17-5)

sulfuric acid (7664-93-9)

nitric acid (7697-37-2)

carbon dioxide (124-38-9)

Acetophenone (98-86-2)

*m*-Nitroacetophenone,  
Acetophenone, *m*-nitro- (121-89-1)