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.

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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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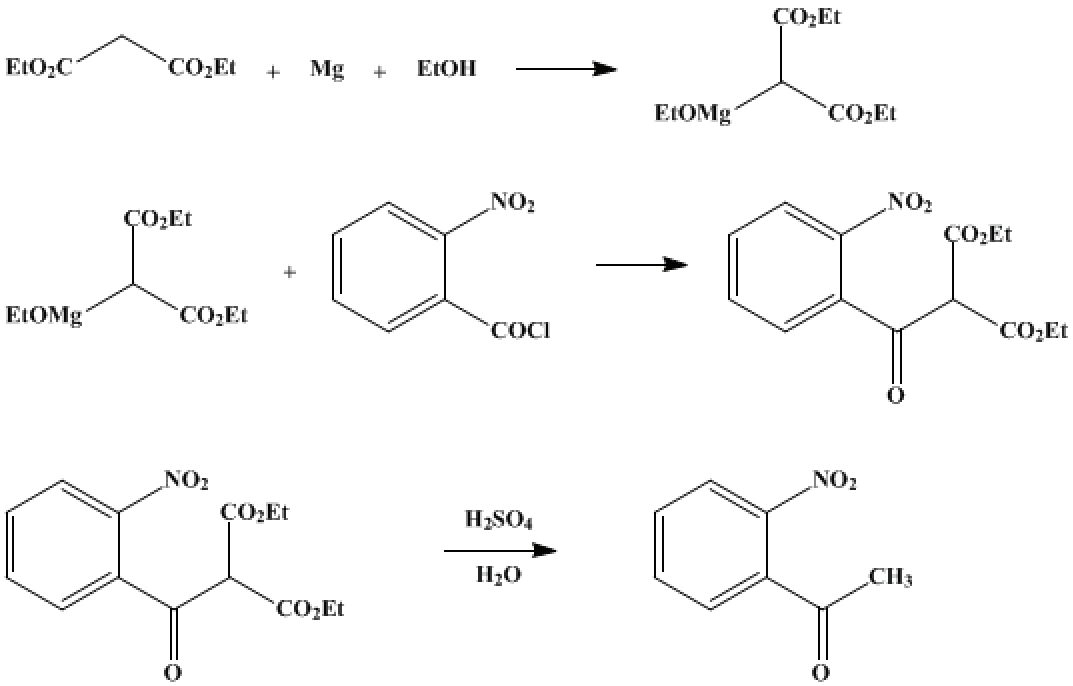
o-NITROACETOPHENONE

[Acetophenone, 2'-nitro-]



Submitted by George A. Reynolds and Charles R. Hauser[1].
Checked by Cliff S. Hamilton and Yao-Hua Wu.

1. Procedure

In a 500-ml. three-necked round-bottomed flask equipped with a mercury-sealed stirrer, a dropping funnel, and a reflux condenser (protected by a drying tube) is placed 5.4 g. (0.22 g. atom) of magnesium turnings. Five milliliters (0.085 mole) of absolute ethanol and 0.5 ml. of carbon tetrachloride are added. If the reaction does not start immediately, the flask is heated for a short time on a steam bath. After the reaction has proceeded for several minutes, 150 ml. of absolute ether is added cautiously with stirring. A solution of 35.2 g. (0.22 mole) of diethyl malonate (Note 1), 20 ml. (0.34 mole) of absolute ethanol, and 25 ml. of absolute ether is added with stirring at such a rate that rapid boiling is maintained; heat is supplied when necessary. The mixture is heated under reflux on a steam bath for 3 hours, at which time most of the magnesium has dissolved. To the gray solution is added 37 g. (0.2 mole) of *o*-nitrobenzoyl chloride (Note 2), dissolved in 50 ml. of ether, in a period of 15 minutes. Heating under reflux on the steam bath is continued throughout the addition of the *o*-nitrobenzoyl chloride and until the green solution becomes too viscous to stir. The reaction mixture is cooled and shaken with dilute sulfuric acid (25 g. of concentrated sulfuric acid in 200 ml. of water) until all the solid has dissolved (Note 3).

The ether phase is separated and the aqueous layer extracted with 75 ml. of ether. The ether extracts are combined and washed with water, and the solvent is removed by distillation.

To the crude diethyl *o*-nitrobenzoylmalonate is added a solution of 60 ml. of glacial acetic acid, 7.6 ml. of concentrated sulfuric acid, and 40 ml. of water, and the mixture is heated under reflux for 4 hours (Note 4) or until no more carbon dioxide is evolved. The reaction mixture is chilled in an ice bath, made alkaline with 20% sodium hydroxide solution, and extracted with several portions of ether. The combined ethereal extracts are washed with water and dried with anhydrous sodium sulfate followed by Drierite, and the solvent is removed by distillation. On fractional distillation of the residue, 27.0–27.4 g. (82–83%) of light-yellow *o*-nitroacetophenone boiling at 158–159° /16 mm. is obtained (n_D^{25} 1.548,

n_D^{20} 1.551, d_4^{25} 1.236) (Note 5).

2. Notes

1. The checkers found that the yield of final product was cut in half unless the commercial grade of diethyl malonate was purified by distillation.
2. The *o*-nitrobenzoyl chloride can be prepared from the commercially available acid and thionyl chloride. It has been reported[2] that, when a particularly pure sample of *o*-nitrobenzoyl chloride was used, no difficulty was encountered in stirring the reaction mixture, and that the precipitate formed in a granular state. As a consequence, the subsequent decomposition with sulfuric acid was simple and rapid. The final product boiled at 107° /0.5 mm., and melted at 26.8°; the supercooled liquid had n_D^{25} 1.5499.
3. The solution of the magnesium complex, which is difficult to decompose, is facilitated by mechanical shaking of the mixture for 30 minutes.
4. The decarboxylation is almost complete within 2 to 3 hours.
5. *p*-Nitroacetophenone may be prepared in 73% yield by a similar procedure. Various other methyl ketones have been prepared by this procedure.[3] It has been reported[2] that *o*-chloroacetophenone was obtained in 82% yield by this method; the product possessed the following physical properties; b.p. 70° /1.5 mm., n_D^{25} 1.5404; it did not solidify at −50°.

3. Discussion

This procedure is an adaptation of one described by Walker and Hauser.[3] Schofield and Swain[4] state that, in their opinion, for both convenience and economy, this method[3] is the best yet described for the preparation of *o*-nitroacetophenone.

o-Nitroacetophenone has also been prepared by the treatment of ethyl *o*-nitrobenzoylacetoacetate with sulfuric acid in ethanol,[5] by the direct nitration of acetophenone,[6,7] by the reaction of *o*-nitrobenzaldehyde with diazomethane,[8] by the oxidation of *o*-nitroethylbenzene with potassium permanganate,[9] by the hydrolysis of *o*-nitroacetophenone oxime (obtained by the nitrosation of *o*-nitroethylbenzene with amyl nitrate),[10] and by the oxidation of *o*-nitrophenylmethylcarbinol with chromic acid.[10]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 285
- Org. Syn. Coll. Vol. 8, 247

References and Notes

1. Duke University, Durham, North Carolina.
2. Ford-Moore, Private communication.
3. Walker and Hauser, *J. Am. Chem. Soc.*, **68**, 1386 (1946).
4. Schofield and Swain, *J. Chem. Soc.*, **1948**, 384.
5. Kermack and Smith, *J. Chem. Soc.*, **1929**, 814.
6. Morgan and Moss, *J. Soc. Chem. Ind. (London)*, **42**, 461 (1923).
7. Elson, Gibson, and Johnson, *J. Chem. Soc.*, **1930**, 1128.
8. Arndt, *Z. angew. Chem.*, **40**, 1099 (1927).
9. Kochergin, Tilkova, Zasosov, and Grigorovskii, *Zhur. Priklad. Khim.*, **32**, 1806 (1959) [*C. A.*, **54**, 4458 (1960)].
10. Ford-Moore and Rydon, *J. Chem. Soc.*, **1946**, 679.

Appendix

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

Drierite

ethanol (64-17-5)

sulfuric acid (7664-93-9)

acetic acid (64-19-7)

ether (60-29-7)

sodium hydroxide (1310-73-2)

thionyl chloride (7719-09-7)

magnesium,
magnesium turnings (7439-95-4)

potassium permanganate (7722-64-7)

sodium sulfate (7757-82-6)

carbon tetrachloride (56-23-5)

carbon dioxide (124-38-9)

Acetophenone (98-86-2)

chromic acid (7738-94-5)

diethyl malonate (105-53-3)

o-Nitrobenzaldehyde (552-89-6)

Diazomethane (334-88-3)

amyl nitrate (1002-16-0)

o-Nitroacetophenone,
Acetophenone, 2'-nitro- (577-59-3)

o-nitrobenzoyl chloride (610-14-0)

diethyl o-nitrobenzoylmalonate

p-Nitroacetophenone (100-19-6)

o-chloroacetophenone (2142-68-9)

ethyl o-nitrobenzoylacetoacetate

o-nitroethylbenzene (6125-24-2)

o-nitroacetophenone oxime

o-nitrophenylmethylcarbinol (15121-84-3)