



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.

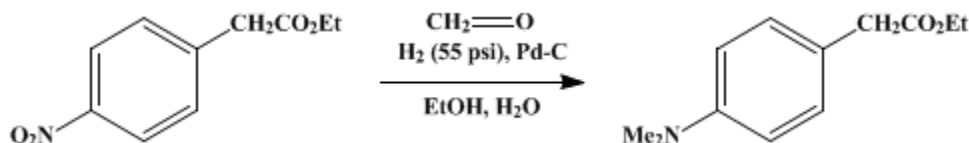
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 5, p.552 (1973); Vol. 47, p.69 (1967).

ETHYL *p*-DIMETHYLAMINOPHENYLACETATE

[Acetic acid, *p*-dimethylaminophenyl-, ethyl ester]



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1. Procedure

In a 400-ml. Parr bottle are placed 41.8 g. (0.20 mole) of ethyl *p*-nitrophenylacetate, 40 ml. of 40% aqueous formaldehyde solution, 200 ml. of 95% ethanol, and 2.0 g. of 10% palladium on charcoal (Note 1). The bottle is then placed on a Parr hydrogenation apparatus. The sample is evacuated and filled with hydrogen, this process being repeated three times. The tank and bottle are then filled with hydrogen to 55 p.s.i. The shaker is started, and the hydrogenation is allowed to proceed until the pressure drop corresponds to 1.0 mole of hydrogen (Note 2), (Note 3). The time required for hydrogenation is approximately 2.5 hours (Note 4). After venting the hydrogen from the bottle safely (Note 1), the ethanol solution is filtered and the catalyst washed carefully (Note 5) with 20 ml. of ethanol.

The filtrate is transferred to a flask which is placed on a rotary evaporator. The ethanol is then removed under reduced pressure on a steam bath. Using ether as a washing solvent, the residue is transferred to a small distilling flask and the ether distilled. The ethyl *p*-dimethylaminophenylacetate is then distilled (Note 6), (Note 7) at reduced pressure, affording 27.7–31.8 g. (67–77%) of colorless product, b.p. 122–124° (0.4 mm.), n_D^{23} 1.5358.

2. Notes

- Care must be taken in weighing out and transferring the catalyst as it can ignite mixtures of air and flammable vapors. The operation of the Parr apparatus and appropriate safety precautions in its use have been described in detail.²
- The hydrogenation is exothermic, and care must be taken in order to prevent the reaction from getting out of control. The submitters have not experienced this difficulty, but exothermic hydrogenations require supervision.
- With the apparatus used, a pressure drop of 85 lb. corresponds to 1.0 mole of hydrogen. Either the particular apparatus used can be calibrated or the hydrogenation allowed to proceed until the pressure ceases to drop.²
- The time required for the hydrogenation will depend on several factors, such as the speed of shaking, activity and particle size of the catalyst. In the experiments run on ethyl *p*-nitrophenylacetate the submitters have found that the time required varied from about 2 to 4 hours.
- The filtration was by suction. The catalyst must not be allowed to dry out with a stream of air passing through it, as it can then readily ignite.
- Before the actual distillation could be carried out, the flask was heated to approximately 95° and the residual formaldehyde removed at the aspirator. Only after the formaldehyde was removed could the pressure be reduced to that required for the distillation.
- The checkers observed that rather rapid decomposition of the product occurs unless precautions were taken. A short path distillation using a 50-ml. distilling flask equipped with a capillary nitrogen bubbler was employed.

3. Discussion

Ethyl *p*-dimethylaminophenylacetate has been previously prepared in this laboratory by Fischer

esterification of *p*-dimethylaminophenylacetic acid, the acid in turn being prepared by the reductive hydrolysis of *p*-dimethylaminomandelonitrile.³

4. Merits of the Preparation

Besides being a convenient preparation for ethyl *p*-dimethylaminophenylacetate, the procedure for reductive alkylation can be generalized.^{4,5} Table I lists the results obtained by the submitters.

TABLE I REDUCTIVE
ALKYLATION OF NITRO
COMPOUNDS"

| Nitro Compound | % Yield" |
|----------------------------------|----------|
| <i>p</i> -Nitrophenylacetic acid | 84–91" |
| <i>p</i> -Nitrobenzoic acid | 87" |
| <i>m</i> -Nitrobenzoic acid | 95" |
| <i>p</i> -Nitrotoluene | 90" |
| <i>o</i> -Nitrotoluene | 76" |

References and Notes

- 1 Department of Chemistry, University of Massachusetts, Boston, Massachusetts. This work was carried out at the Polytechnic Institute of Brooklyn, Brooklyn, New York.
- 2 R. Adams and V. Voorhees, *Org. Syntheses, Coll. Vol. 1*, 61 (1941).
- 3 Celal Tüzün and E. I. Becker, unpublished results.
- 4 R. E. Bowman and H. H. Stroud, *J. Chem. Soc.*, 1342 (1950).
- 5 W. S. Emerson, *Org. Reactions*, **4**, 174 (1948).

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

palladium on charcoal ethanol (64-17-5)

ether (60-29-7)

hydrogen (1333-74-0)

formaldehyde (50-00-0)

nitrogen (7727-37-9)

o-nitrotoluene (88-72-2)

m-Nitrobenzoic acid (121-92-6)

p-NITROBENZOIC ACID (62-23-7)

p-Nitrophenylacetic acid (104-03-0)

p-nitrotoluene (99-99-0)

Ethyl p-dimethylaminophenylacetate,
Acetic acid, p-dimethylaminophenyl-, ethyl ester (17078-29-4)

ethyl p-nitrophenylacetate (5445-26-1)

p-dimethylaminophenylacetic acid (17078-28-3)

p-dimethylaminomandelonitrile