



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.

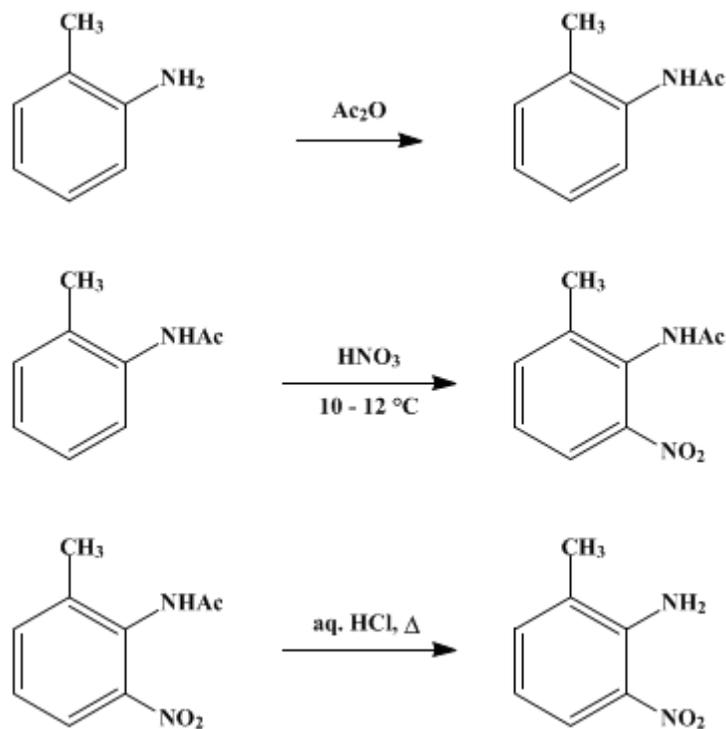
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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.42 (1963); Vol. 35, p.3 (1955).

2-AMINO-3-NITROTOLUENE

[*o*-Toluidine, 6-nitro-]



Submitted by John C. Howard¹

Checked by Charles C. Price and Joseph D. Berman.

1. Procedure

A 1-l. three-necked flask is fitted with a sealed Hershberg stirrer, a reflux condenser, and a dropping funnel. The flask is charged with 650 ml. of **acetic anhydride**, and 107 g. (107 ml., 1 mole) of *o*-toluidine (**Note 1**) is introduced from the dropping funnel. The mixture becomes very warm. After the amine has been completely added, the solution is cooled to 12–13° in an ice-salt bath (**Note 2**). During the cooling, the dropping funnel and condenser are replaced by another dropping funnel containing 126 ml. (2 moles) of 70% **nitric acid** and a thermometer which can be read to within 0.5° in the range from 10° to 20° (**Note 3**).

The **nitric acid** is added drop by drop to the cold slurry at a rate which maintains the temperature carefully within the limits of 10–12° (**Note 4**). If the temperature persists in dropping, the addition is stopped after about 5 minutes. The ice bath is removed until the temperature rises 0.5°, the ice-salt bath is replaced, and addition is continued. As the reaction progresses, the **acetotoluide** which may have precipitated redissolves, and the solution becomes deeply colored. The addition is complete in 1–2 hours, and the nitro compounds may start to separate.

The solution is poured, with stirring, into 3 l. of ice water. The mixture of 4- and 6-nitroacetotoluides precipitates as a cream-colored solid which is collected on a large Büchner funnel. After thorough washing with four 500-ml. portions of ice water, the precipitate is partly dried by suction (**Note 5**). The moist product is then placed in a steam-distillation apparatus (**Note 6**), covered with 300 ml. of concentrated **hydrochloric acid**, and heated until the mixture boils. The acetotoluides are rapidly hydrolyzed, and the solution becomes dark red. Steam is then introduced, and the distillation is thus continued until 36 l. of distillate has been collected (**Note 7**) and (**Note 8**). The 2-amino-3-nitrotoluene,

which separates as bright orange needles when the distillate is cooled, is collected on a large Büchner funnel. The dried product amounts to 75–84 g. (49–55%), m.p. 92–94°. The product may be further purified by a second steam distillation. Ten grams of the amine is distilled from 150 ml. of water, and 3 l. of distillate is collected, yielding 8.7 g. of **2-amino-3-nitrotoluene**, m.p. 95–96° (cor.).

2. Notes

1. Commercially available **o-toluidine**, b.p. 75–77°/10 mm., is suitable. Redistillation of this material gave no significantly better results. The checkers obtained a 42% yield of **2-amino-3-nitrotoluene** using practical grade **o-toluidine** directly, and a 57% yield after redistillation.
2. The flask should be immersed up to the neck in the slurry of ice and salt. During the cooling, the **acetotoluide** may suddenly precipitate, immobilizing the stirrer; a few turns manually break up the mass of crystals and allow the stirring to be continued.
3. A low-temperature thermometer with a range from –15° to +50° is suitable.
4. If the temperature is allowed to rise above 18°, violent if not explosive decomposition may ensue.
5. The precipitate can be air-dried to a constant weight of 150–160 g.
6. An efficient steam-distillation apparatus such as that described by Fieser² is recommended. A 12-l. round-bottomed flask cooled in a tub of ice serves as the receiver, which is equipped with an auxiliary vertical condenser attached to a gas absorption trap³ to accommodate the **hydrogen chloride** which distils first.
7. The third 12-l. portion yields about 20 g. of **2-amino-3-nitrotoluene**. The residue in the steam-distillation flask, about 20 g. of crude **2-amino-5-nitrotoluene**, solidifies when cooled and may be separated by filtration. It can be recrystallized from 2 l. of hot water, yielding 14–15 g. of yellow plates, m.p. 130–131° (cor.).
8. Instead of separating the mixture of isomers by the slow steam distillation, one may employ the procedure of Wepster and Verkade.⁴ In the latter, the product from the nitration of **o-methylacetanilide** is treated with the Witt-Utermann solution,⁵ which consists of a **water-alcohol** solution of **potassium hydroxide**. **2-Acetylamino-5-nitrotoluene** is insoluble in this solution, while the 3-nitro isomer is soluble and may be recovered in high yield and a good state of purity by acidification of the red filtrate. Hydrolysis of the acetyl derivatives affords 2-amino-5-nitro- and 2-amino-3-nitrotoluene.

3. Discussion

2-Amino-3-nitrotoluene has been prepared by the nitration of oxalotoluide⁶ and by the nitration of **o-acetotoluide** in **acetic acid** with fuming **nitric acid**,⁷ with a mixture of nitric and sulfuric acid,⁸ or with metal nitrates.⁹

This preparation is referenced from:

- *Org. Syn. Coll. Vol. 4*, 291
- *Org. Syn. Coll. Vol. 9*, 573

References and Notes

1. Cornell University, Ithaca, New York.
2. Fieser, *Experiments in Organic Chemistry*, 3rd ed., p 257 (Figs. 45.4 and 45.5), D. C. Heath and Company, Boston, Massachusetts, 1955.
3. *Org. Syntheses Coll. Vol. 2*, 4 (1943).
4. Wepster and Verkade, *Rec. trav. chim.*, **68**, 77 (1949).
5. Witt and Utermann, *Ber.*, **39**, 3901 (1906).
6. Hadfield and Kenner, *Proc. Chem. Soc.*, **30**, 253 (1914).
7. Cohen and Dakin, *J. Chem. Soc.*, **79**, 1127 (1901).
8. McGookin and Swift, *J. Soc. Chem. Ind.*, **58**, 152 (1939).
9. Kyriacos and Schultz, *J. Am. Chem. Soc.*, **75**, 3597 (1953).

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

4- and 6-nitroacetotoluides

2-amino-5-nitro-and 2-amino-3-nitrotoluene

nitric and sulfuric acid

hydrogen chloride,
hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

acetic anhydride (108-24-7)

nitric acid (7697-37-2)

potassium hydroxide (1310-58-3)

2-amino-5-nitrotoluene (99-52-5)

2-Amino-3-nitrotoluene,
o-Toluidine, 6-nitro- (570-24-1)

acetotoluide (103-89-9)

water-alcohol

2-Acetylamino-5-nitrotoluene

o-toluidine (95-53-4)

o-methylacetanilide,
o-acetotoluide (120-66-1)