



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.

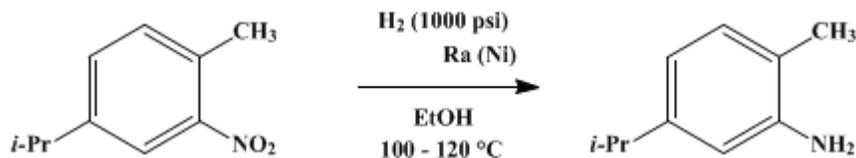
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.63 (1955); Vol. 22, p.9 (1942).

2-AMINO-*p*-CYMENE

[Carvacrylamine]



Submitted by C. F. H. Allen and James VanAllan.

Checked by Homer Adkins

1. Procedure

A mixture of 179 g. (167 ml., 1 mole) of 2-nitro-*p*-cymene (p. 653), 300 ml. of absolute ethanol, and 3–5 g. of Raney nickel (p. 181) is placed in the steel reaction vessel of a high-pressure hydrogenation apparatus.¹ The bomb is then closed, and hydrogen is admitted until the pressure, at 25°, is about 1000 lb. While the bomb is shaken, the temperature is rapidly raised to 80–90°, and then the heater is shut off (Note 1). Owing to the strong exothermic reaction, the temperature continues to rise, reaching about 120°, while the pressure drops rapidly. The pressure in the reaction vessel is maintained at 700–1500 lb., by the introduction of hydrogen from a tank, until the rapid reaction is over (15 minutes). The reaction mixture is kept at 100–120° for 30 minutes after there is no further drop in the pressure of hydrogen. After the bomb has cooled, the hydrogen is slowly released and the catalyst is separated from the reaction mixture by centrifuging, or by filtration through a sintered-glass or Büchner funnel (Note 2). The alcohol and water are removed by distillation, and the product is fractionated in a suitable apparatus (Note 3), (Note 4), (Note 5), (Note 6), (Note 7).

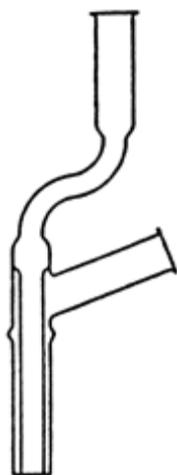
The amine distils at 239–240°/740 mm., 242° (cor.)/760 mm., 110°/10 mm., or 92–94°/2 mm. In the first distillation the portion boiling below 225°/740 mm. (or below 100°/9 mm.) is discarded. The yield is 130–135 g. (87–90%).

2. Notes

1. The hydrogenation of nitro compounds liberates so much heat, and the reaction may proceed so rapidly, that precautions must be taken against excessive reaction temperatures. Temperatures of 150–200° may bring about the formation of secondary amines, and at higher temperatures decomposition reactions may occur with explosive violence. These dangers may be avoided by the use of small amounts of catalyst and by having an insufficient amount of hydrogen in the reaction vessel at the beginning of the reaction. After sufficient hydrogen for the hydrogenation of half of the nitro compound has been taken up there need be no fear that the reaction will proceed too rapidly. It is always desirable, however, to complete the hydrogenation as rapidly as possible while avoiding temperatures above about 120°. The use of ethanol as a solvent prevents the separation of a water layer, which would cover most of the catalyst and thus give rise to a slow and perhaps incomplete hydrogenation.

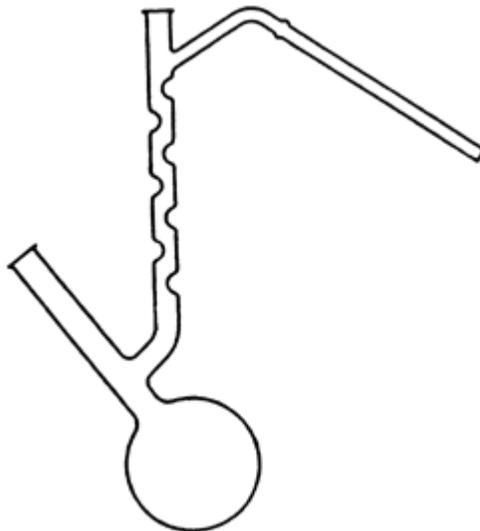
2. If the sample of nitrocymene is impure, or if the catalyst is of poor quality, the hydrogenation may not proceed to completion and a solution of the product in hydrochloric acid will be turbid. In this event, the mixture of products (after separation of the spent catalyst) may again be submitted to hydrogenation. An alternative procedure involves removal of the non-basic material by steam distillation of a mixture of the product with 350 ml. of water and 90 ml. of concentrated hydrochloric acid. The amine is then liberated from its salt by the addition of 45 g. of sodium hydroxide and is extracted with 500 ml. of ether. The ether layer may be siphoned from the water layer. The ether is removed by distillation, and the residue is fractionated as described in the procedure. For steam distillations, the submitters employ the adapter shown in Fig. 3. With this adapter the apparatus is much more compact than in the usual arrangement, for the receiver may serve as a partial condenser, as in distillation under reduced pressure.

Fig. 3.



3. The apparatus may consist of a modified Claisen flask, or of an ordinary flask connected to a Vigreux, Widmer, modified Widmer, or other column. The checker used a modified Widmer column and a distillation at 9 mm. pressure. The submitters conducted the distillation at atmospheric pressure, in the type of flask shown in Fig. 4. This type of flask, as well as the adapter described in (Note 2), has been used in the laboratories of the Eastman Kodak Company for some time. In comparison with the standard Claisen flask, this flask has several advantages. It has a longer column; liquids seldom bump over, and consequently more material may be handled in a flask of given size; and material that has come into contact with the rubber stopper cannot contaminate the distillate. No dimensions are given for the flask, or for the adapter described in (Note 2) above; these pieces may be constructed in various sizes to suit individual needs.

Fig. 4.



4. Nitrocymene usually contains about 8% of *p*-nitrotoluene. The complete separation of the resulting *p*-toluidine from the 2-amino-*p*-cymene requires a rather careful fractionation.
5. If air comes in contact with the hot amine vapor, the product will be colored. However, a product distilled at 9 mm. with a capillary ebullition tube was only faintly yellow.
6. The reduction may also be carried out at lower pressures in the usual laboratory apparatus [*Org. Syntheses Coll. Vol. 1, 53 (1932); 63 (1941)*]. A mixture of 50 g. of nitrocymene, 200 ml. of 95% ethanol, and 5 g. of Raney nickel is reduced at 85–90°, at an initial pressure of 55–60 lb.; the time required is 6 hours. The product is processed as described above. The yield is 33–36 g. (80–85%).
7. Nitrocymene may also be reduced by the use of iron powder, essentially as described under 2,4-diaminotoluene (*Org. Syntheses, 11, 32; Coll. Vol. 2, 160*) (Kenneth A. Kobe, private communication).²

3. Discussion

Because of the accessibility of *p*-cymene, reduction of the nitroderivative constitutes the only practical method for preparation of 2-aminocymene. Tin^{3,4,5,6} and iron,^{7,8} together with hydrochloric acid, have been used for this purpose. A patent⁷ mentions the use of hydrogen in the presence of a nickel catalyst.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 59
- Org. Syn. Coll. Vol. 3, 140
- Org. Syn. Coll. Vol. 3, 159
- Org. Syn. Coll. Vol. 3, 438

References and Notes

1. American Instrument Company, Silver Springs, Maryland, or Parr Instrument Company, Moline, Illinois.
2. Doumani and Kobe, *J. Am. Chem. Soc.*, **62**, 563 (1940).
3. Soderbaum and Widman, *Ber.*, **21**, 2127 (1888).
4. Wheeler and Smithey, *J. Am. Chem. Soc.*, **43**, 2613 (1921).
5. Demonbreun and Kremers, *J. Am. Pharm. Assoc.*, **12**, 296 (1923) [*C. A.*, **17**, 3906 (1923)].
6. Straneo, *Ann. chim. appl.*, **31**, 116 (1941).
7. U. S. pat. 1,314,920 [*C. A.*, **13**, 2765 (1919)].
8. Doumani and Kobe, *Ind. Eng. Chem.*, **31**, 264 (1939).

Appendix

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

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

ether (60-29-7)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

iron (7439-89-6)

tin (7440-31-5)

nickel (7440-02-0)

p-cymene (99-87-6)

2,4-Diaminotoluene (95-80-7)

Carvacrylamine,
2-aminocymene,
2-Amino-p-cymene (2051-53-8)

nitrocymene

p-toluidine (106-49-0)

p-nitrotoluene (99-99-0)

2-Nitro-p-cymene (943-15-7)