



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.

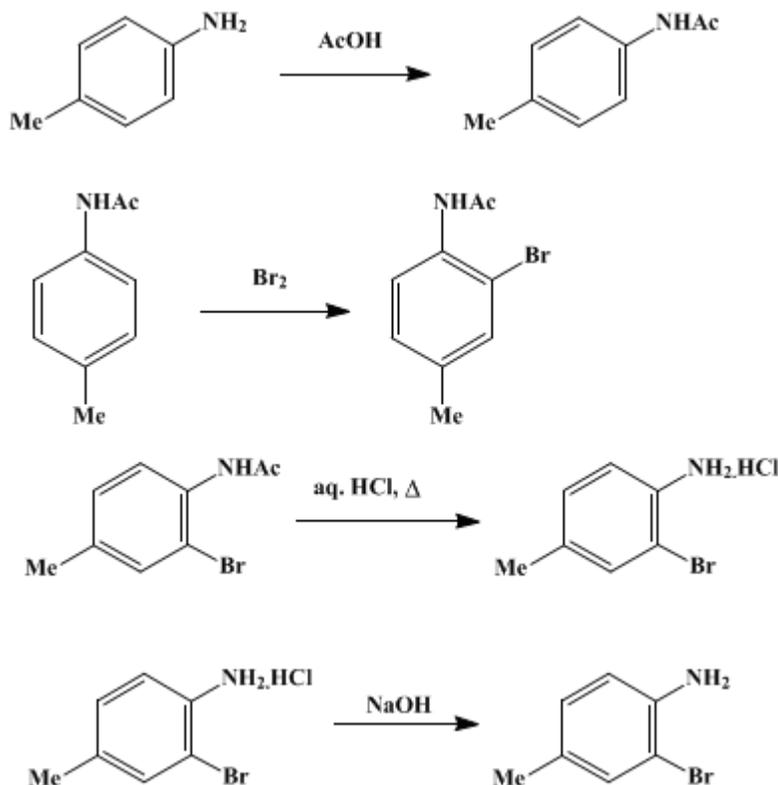
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 1, p.111 (1941); Vol. 6, p.8 (1926).

3-BROMO-4-AMINOTOLUENE

[*p*-Toluidine, 2-bromo-]



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1. Procedure

p-Acetotoluene is prepared by refluxing 214 g. (2 moles) of commercial *p*-toluidine with 800 cc. of glacial acetic acid in a 2-l. round-bottomed flask for two hours. The reflux condenser is replaced by a mechanical stirrer and the mixture is stirred and cooled to 45°. Part of the product may separate in small crystalline flakes. The mixture is thoroughly stirred and 325 g. (102 cc., 2.03 moles) of bromine is added slowly from a separatory funnel at such a rate that the temperature of the mixture is maintained at 50–55°. During the course of this addition, which requires about forty minutes, a precipitate may separate; this later dissolves. The mixture is stirred one-half hour after the bromine has been added, and is then poured in a thin stream (Note 1) with efficient stirring into 10 l. of cold water to which has been added 25 g. of sodium bisulfite (Note 2).

The 3-bromo-4-acetaminotoluene separates in crystalline flocks. It is filtered by suction and washed well with water and pressed dry. The wet crude material is dried until its weight does not exceed 500 g. before proceeding with the hydrolysis (Note 3).

The partially dried 3-bromo-4-acetaminotoluene is refluxed with 500 cc. of 95 per cent ethyl alcohol in a 3-l. round-bottomed flask. To the boiling solution is added 500 cc. of concentrated hydrochloric acid and the refluxing is continued for three hours. During this time, crystals of the hydrochloride of 3-bromo-4-aminotoluene separate. The hot mixture is poured into a 2-l. beaker and cooled thoroughly in running water. The hydrochloride is filtered by suction and washed rapidly with two 100-cc. portions of chilled alcohol. The weight of the hydrochloride is 250–300 g. (Note 4).

The hydrochloride is suspended in 800 cc. of water in a 2-l. beaker provided with a mechanical stirrer. The base is liberated by the addition of a solution of 140 g. of technical [sodium hydroxide](#) in 700 cc. of water, and settles as a heavy brownish oil. After cooling to room temperature, the oil is separated and weighed. The yield of the crude base is 225–250 g. (60–67 per cent of the theoretical amount based on the amount of [p-toluidine](#) used). The crude material may be used directly for the preparation of [m-bromotoluene](#) (p. 133).

The base may be purified by steam distillation but distillation under reduced pressure is more satisfactory. The oil is dried over 5 g. of solid [sodium hydroxide](#) and distilled under reduced pressure. The first portion of the distillate may contain [p-toluidine](#) and must be carefully separated, as it causes rapid discoloration. The [3-bromo-4-aminotoluene](#) is obtained as a colorless liquid of b.p. 120–122°/30 mm. or 92–94°/3 mm. It solidifies on cooling and melts at 16–18°. The loss on purification is about 15 per cent of the weight of the crude base.

2. Notes

1. The [bromine](#) compound often separates at first as a heavy oil. To avoid the formation of lumps, this material should be seeded or allowed to crystallize spontaneously before the main portion is poured into water.
2. If the color of [bromine](#) persists, more [sodium bisulfite](#) should be added.
3. If the material is not partly dried before hydrolysis, the yield of the hydrochloride is diminished because of its solubility. If pure [3-bromo-4-acetaminotoluene](#) is desired, the crude material may be crystallized from 50 per cent [alcohol](#) with the addition of [decolorizing carbon \(Norite\)](#) as almost colorless needles, m.p. 116–117°. The yield is 360 g. (79 per cent of the theoretical amount). This purification has no advantage when the acetamino compound is to be hydrolyzed to the amine.
4. The dark filtrate from the hydrochloride does not contain enough dissolved salt to justify recovery unless the acetamino compound is insufficiently dried before the hydrolysis.

3. Discussion

[3-Bromo-4-aminotoluene](#) can be prepared by the bromination of [p-acetotoluide](#), followed by hydrolysis of the resulting [bromoacetotoluidide](#).¹ The procedure described is a modification of Feitler's method.¹

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 1, 133](#)
- [Org. Syn. Coll. Vol. 2, 480](#)
- [Org. Syn. Coll. Vol. 3, 130](#)
- [Org. Syn. Coll. Vol. 3, 791](#)
- [Org. Syn. Coll. Vol. 5, 139](#)

References and Notes

1. [Wroblevsky, Ann. 168, 153 \(1873\); Feitler, Z. physik. Chem. 4, 77 \(1889\).](#)
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Appendix

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

hydrochloride of 3-bromo-4-aminotoluene

ethyl alcohol,
alcohol (64-17-5)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

sodium hydroxide (1310-73-2)

bromine (7726-95-6)

sodium bisulfite (7631-90-5)

decolorizing carbon (Norite) (7782-42-5)

3-Bromo-4-aminotoluene,
p-Toluidine, 2-bromo- (583-68-6)

3-Bromo-4-acetaminotoluene (614-83-5)

bromoacetotoluidide

p-toluidine (106-49-0)

p-Acetotoluide (103-89-9)

m-Bromotoluene (591-17-3)