



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.

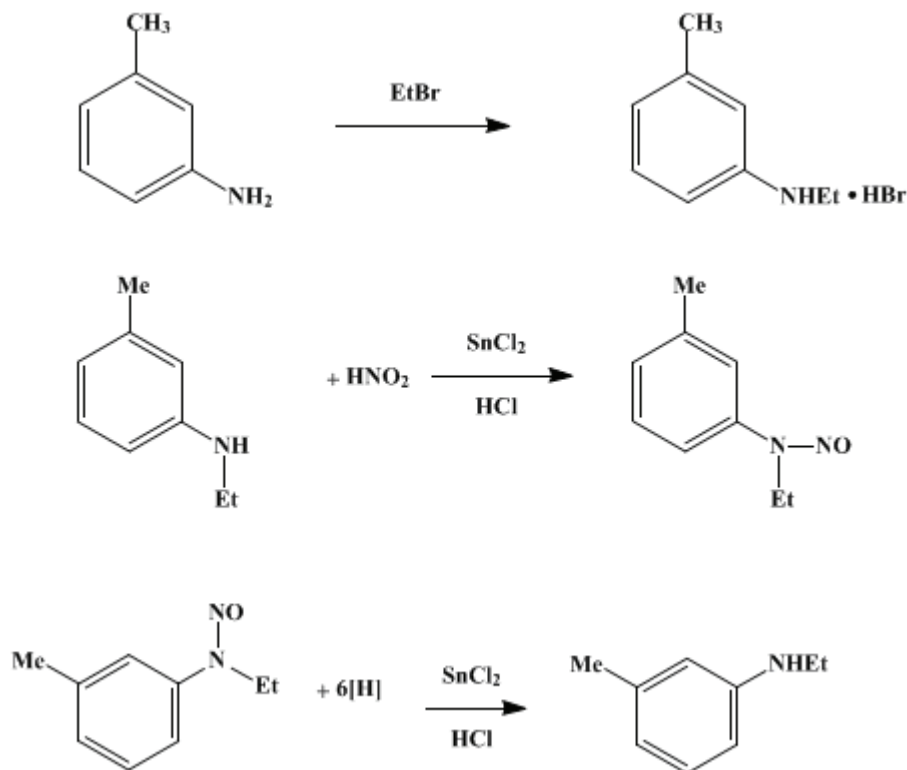
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 2, p.290 (1943); Vol. 18, p.40 (1938).

N-ETHYL-*m*TOLUIDINE

[*m*-Toluidine, N-ethyl-]



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1. Procedure

In each of two ordinary 250-cc. (8-oz.) narrow-mouthed bottles are placed 32.1 g. (0.3 mole) of *m*-toluidine and 33 g. (23 cc., 0.3 mole) of ethyl bromide (Note 1). The bottles are sealed with rubber stoppers wired tightly in place and then allowed to stand for twenty-four hours in a 2-l. beaker filled with water at room temperature (Note 2). The white crystalline mass in each bottle is broken up and the amine is liberated by shaking with 150 cc. of 10 per cent sodium hydroxide solution and 50 cc. of ether. The contents of the two flasks are combined, the lower aqueous layer is separated and discarded, and the ether solution of the amine is washed with 150 cc. of water. When the ether is distilled from a steam bath, the crude amine (90–92 g.) is obtained.

This crude amine is added, with cooling, to a solution of 100 cc. of concentrated hydrochloric acid (sp. gr. 1.18) in 350 cc. of water. The solution of the hydrochloride is cooled in an ice bath, and stirred rapidly, while a solution of 41.5 g. (0.6 mole) of sodium nitrite in 150 cc. of water is added slowly. During this addition the temperature should not be allowed to rise above 12°. After all the nitrite has been added, the mixture is allowed to stand for ten minutes and is then extracted with three 100-cc. portions of ether. The ether is evaporated from the extract by warming gently on a steam bath and blowing a stream of air over the surface. Care must be taken to keep the temperature as low as possible during the evaporation (Note 3).

The crude nitroso compound is added gradually, with continuous shaking, to a solution of 407 g. (1.8 moles) of stannous chloride dihydrate in 420 cc. (4.8 moles) of concentrated hydrochloric acid (sp. gr. 1.18) contained in a 3-l. flask. The reaction is exothermic, and cooling is applied, if necessary, to

keep the temperature below 60°. After standing for at least an hour (Note 4), the mixture is made strongly alkaline by the cautious addition of a cold solution of 520 g. (13 moles) of sodium hydroxide in about 800 cc. of water. During the addition of the alkali the mixture is agitated vigorously and cooled in running water.

The resulting milky suspension is distilled with steam until about 2 l. of distillate has collected. The distillate is saturated with sodium chloride and extracted with three 100-cc. portions of benzene. The extract is dried thoroughly overnight with flaked potassium hydroxide and decanted from the spent drying agent. After removal of the solvent by distillation, the amine is distilled under reduced pressure. Practically all the material distils at 111–112°/20 mm., or 115.5–117°/26 mm. The pure amine forms a practically colorless, highly refringent liquid and weighs 51–53 g. (63–66 per cent of the theoretical amount) (Note 5). It develops color rapidly on standing.

2. Notes

1. A pure grade of *m*-toluidine was used. A "practical" grade of ethyl bromide gave satisfactory results.
2. If the initial reaction is allowed to proceed too rapidly, considerable pressure may be developed in the bottles. As a safeguard against explosions it is advisable to enclose the bottles in wire mesh shields.
3. The nitroso compound decomposes on warming or on standing. It should not be stored but treated at once with the reducing agent.
4. The mixture may be allowed to stand for a longer period (overnight) without harm. Frequently a granular precipitate of a tin complex of the amine separates.
5. Other N-alkyl-*m*-toluidines may be prepared by practically the same procedure. The submitters report that *n*-propyl, isopropyl, and *n*-butyl derivatives are obtained readily from *m*-toluidine and the appropriate alkyl iodides (rather than the bromides). With these halides the alkylation is effected by placing the sealed bottle in a beaker of water which is warmed gradually to 70–80° and kept in a warm place until the reaction is completed; usually several days are required.

3. Discussion

N-Ethyl-*m*-toluidine has been obtained by passing *m*-toluidine and ethyl alcohol over a catalyst at high temperatures,¹ and by the use of ethyl *p*-toluenesulfonate² as an alkylating agent. The present method of purification is a modification of a general procedure for secondary amines developed by Diepolder.³

References and Notes

1. Mailhe and de Godon, Compt. rend. **172**, 1417 (1921); Mailhe, Fr. pat. 23,891 (Chem. Zentr. **1922**, IV, 760).
2. Finzi, Ann. chim. applicata **15**, 41 (1925) [C. A. **19**, 2647 (1925)].
3. Diepolder, Ber. **32**, 3514 (1899).

Appendix

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

amine

ethyl alcohol (64-17-5)

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

Ethyl bromide (74-96-4)

sodium nitrite (7632-00-0)

potassium hydroxide (1310-58-3)

stannous chloride dihydrate (10025-69-1)

m-toluidine (108-44-1)

ethyl p-toluenesulfonate (80-40-0)

N-ETHYL-mTOLUIDINE,
m-Toluidine, N-ethyl-,
N-Ethyl-m-toluidine (102-27-2)