



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.

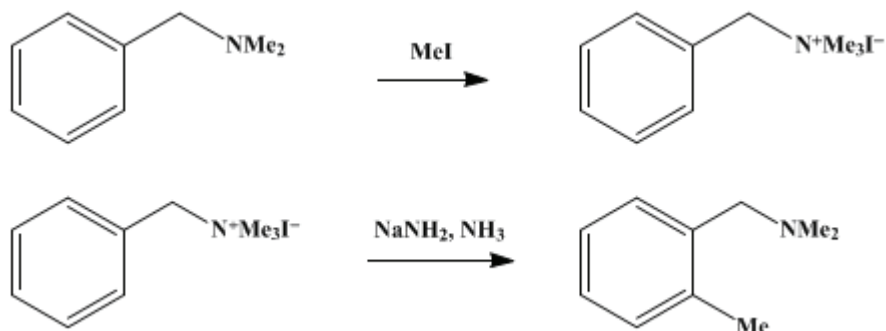
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries 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.585 (1963); Vol. 34, p.61 (1954).

2-METHYLBENZYL DIMETHYLAMINE

[Benzylamine, N,N,*o*-trimethyl-]



Submitted by W. R. Brasen and C. R. Hauser¹.

Checked by William S. Johnson, Mary E. Mills, and A. L. Wilds.

1. Procedure

A. *Benzyltrimethylammonium iodide*. A solution of 135 g. (1 mole) of *N,N*-dimethylbenzylamine (Note 1) in 200 ml. of commercial absolute ethanol (Note 2) is placed in a three-necked flask fitted with a 125-ml. dropping funnel, a reflux condenser, and a rubber slip-sleeve-sealed stirrer. The openings of the dropping funnel and condenser are protected from atmospheric moisture with drying tubes. While the solution is stirred rapidly, 190 g. (1.34 moles) of methyl iodide contained in the dropping funnel is added slowly at first, then at such a rate as to cause gentle refluxing of the solution. After the addition is complete (30 minutes), the solution is boiled under reflux on the steam bath for 30 minutes more and transferred to a 2-l. Erlenmeyer flask with the aid of an additional 25-ml. of absolute ethanol for rinsing. On cooling to room temperature a large portion of the methiodide crystallizes, and the remaining material is then precipitated by the addition of 1 l. of anhydrous ether with stirring (Note 3). The product is separated by suction filtration, washed with two 100-ml. portions of anhydrous ether (Note 4), and dried in air at room temperature. The yield of *benzyltrimethylammonium iodide*, m.p. 178–179° (dec.), is 260–274 g. (94–99%), and is pure enough for most purposes (Note 5).

B. *2-Methylbenzyl dimethylamine*. (*Caution! This preparation should be conducted in a good hood to avoid exposure to ammonia*). To 800 ml. of liquid ammonia contained in a 2-l. three-necked flask fitted with a rubber slip-sleeve-sealed wire stirrer and an air-cooled reflux condenser, sodium is added in small pieces until the blue color persists (Note 6). At this point 0.5 g. of granulated ferric nitrate is added, and then 27.8 g. (1.2 g. atoms) of sodium (cut into approximately 0.5-g. pieces), is introduced at such a rate that stirring is not hindered. After all the sodium has been added (about 15 minutes), the mixture is stirred until the blue color disappears and the grayish-black suspension of sodium amide remains (15–20 minutes). Stirring is discontinued, and the mixture is swirled to wash down the mirror of sodium which forms on the upper walls of the flask (Note 7).

A 500-ml. Erlenmeyer flask is charged with 277 g. (1 mole) of *benzyltrimethylammonium iodide* (prepared as described in Part A) and is connected with a short section of large-diameter rubber tubing to the third neck of the flask containing the sodium amide. Stirring is started, and the salt is shaken in at a steady rate and as rapidly as possible without serious loss of material through the condenser. This operation requires about 10–15 minutes (Note 8). The greenish-violet color, which is first produced by addition of the salt, persists for about 15 minutes after all the material has been added. During this and the subsequent reaction period, more ammonia is added as necessary to maintain the original volume. The mixture is stirred for an additional 2 hours, and then 27 g. (0.5 mole) of ammonium chloride is added cautiously to destroy excess sodium amide.

The flask is fitted with a dropping funnel, and enough (about 100 ml.) water is added, dropwise at

first, to bring all the solid material into solution. The mixture is stirred until it reaches room temperature, 70 ml. of ether is added, and the organic layer is separated. The water layer is extracted with two 70-ml. portions of ether, and the combined ether solutions are washed with two 50-ml. portions of saturated salt solution and dried over anhydrous potassium carbonate. After filtration and removal of the ether by distillation, the amine is distilled through a 10-cm. Vigreux column. The fraction, b.p. 72–73°/9 mm., 97–99°/13 mm., or 197–198°/atm., amounts to 134–141.5 g. (90–95% yield), n_D^{20} 1.5050–1.5060 (Note 8). On redistillation all but about 5% of the material is recovered, b.p. 78–79°/12 mm., n_D^{20} 1.5049–1.5052.

2. Notes

1. N,N-Dimethylbenzylamine supplied by the Rohm and Haas Company was used without purification.
 2. Methanol may be substituted in the preparation of this as well as other quaternary salts, which, however, are generally more soluble in this medium and therefore require a larger volume of ether for complete precipitation.
 3. This isolation procedure produces a granular product which is more desirable for use in the rearrangement reaction than the fluffy material obtained on rapid cooling.
 4. The ether should be free of peroxides; otherwise iodine will be liberated from the salt and will color the product.
 5. This procedure is suitable for the preparation of the following quaternary salts with changes only in the proportion of ethanol employed: 2-methylbenzyltrimethylammonium iodide, using 350 ml. of ethanol per mole of amine (yield 98–99%), and 2,3-dimethylbenzyltrimethylammonium iodide, using 500 ml. of ethanol per mole of amine (yield 98–99%).
 6. Only about 0.05 g. of sodium is required unless the ammonia is quite wet.
 7. The complete removal of sodium is indicated by the lack of formation of blue coloration when the solution is swirled over the upper walls of the flask.
 8. Essentially the same procedure may be used for the preparation of 2,3-dimethylbenzyl dimethylamine from 2-methylbenzyltrimethylammonium iodide except that the time of addition of the latter to the sodium amide is increased to 75 minutes. The checkers found it necessary also to use a larger volume of ammonia. Thus, on a 0.3-mole scale, 1 l. of ammonia was employed, and a total of 600 ml. more ammonia was added during the reaction to maintain the volume at 800–1000 ml.
- Owing to the formation of neutral side products, the reaction mixture is extracted with excess 4*N* hydrochloric acid, and the mixture of amines is liberated from the acid solution by neutralization with sodium hydroxide. The amine fraction is taken up in ether and dried over anhydrous sodium sulfate or solid sodium hydroxide. After removal of the ether, the 2,3-dimethylbenzyl dimethylamine distils at 101–102°/15 mm., 107–109°/19 mm., n_D^{23} 1.5100–1.5102. The yield is 60–70%.

3. Discussion

This procedure is based on the method of Kantor and Hauser.² 2-Methylbenzyl dimethylamine has also been prepared from *o*-xylyl bromide and hexamethylenetetramine.²

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 508
- Org. Syn. Coll. Vol. 4, 582

References and Notes

1. Duke University, Durham, North Carolina. Work supported by the Office of Ordnance Research.
 2. Kantor and Hauser, *J. Am. Chem. Soc.*, **73**, 4122 (1951).
-

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

ethanol (64-17-5)

potassium carbonate (584-08-7)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

methanol (67-56-1)

ether (60-29-7)

ammonium chloride (12125-02-9)

sodium hydroxide (1310-73-2)

sodium sulfate (7757-82-6)

iodine (7553-56-2)

sodium (13966-32-0)

Methyl iodide (74-88-4)

hexamethylenetetramine (100-97-0)

sodium amide (7782-92-5)

ferric nitrate

2,3-dimethylbenzyltrimethylammonium iodide

2,3-dimethylbenzyl dimethylamine (15848-75-6)

2-Methylbenzyl dimethylamine,
Benzylamine, N,N,o-trimethyl- (4525-48-8)

N,N-dimethylbenzylamine (103-83-3)

benzyltrimethylammonium iodide

2-methylbenzyltrimethylammonium iodide

o-xylyl bromide (576-23-8)