



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.

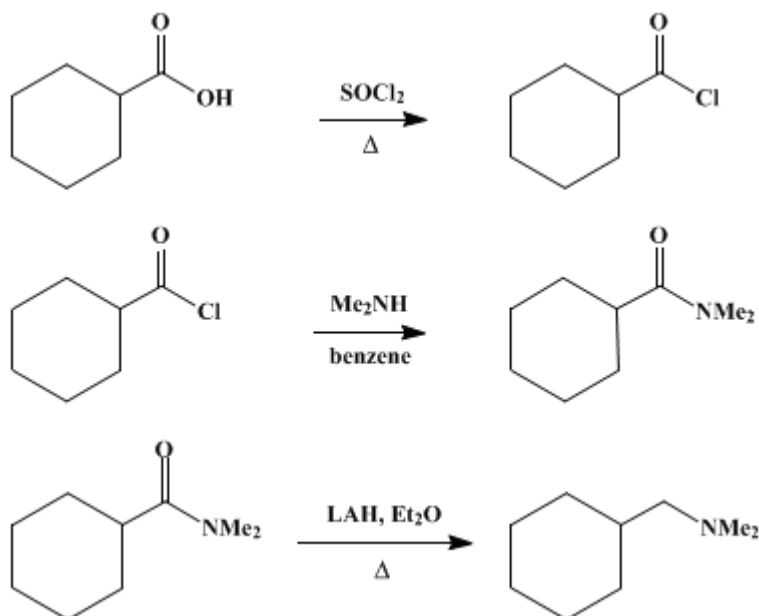
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.339 (1963); Vol. 39, p.19 (1959).

N,N-DIMETHYLCYCLOHEXYLMETHYLAMINE

[Cyclohexanemethylamine, N,N-dimethyl-]



Submitted by Arthur C. Cope and Engelbert Ciganek¹.
Checked by William E. Parham and Robert Koncos.

1. Procedure

A. *N,N-Dimethylcyclohexanecarboxamide*. In a 1-l. three-necked flask equipped with a reflux condenser and a dropping funnel, both carrying drying tubes, is placed 128 g. (1.0 mole) of cyclohexanecarboxylic acid (Note 1). Thionyl chloride (179 g., 1.5 moles) (Note 1) is added during 5 minutes to the acid, with stirring by a magnetic stirrer. The flask is placed in an oil bath and heated at a bath temperature of 150° for 1 hour. The reflux condenser is then replaced by a distillation head (Note 2), 200 ml. of anhydrous benzene is added, and the mixture is distilled until the temperature of the vapors reaches 95°. The mixture is cooled, another 200 ml. of anhydrous benzene is added, and the distillation is continued until the temperature of the vapors again reaches 95°. The cooled residual acid chloride is transferred with a little benzene to a dropping funnel which is attached to a 2-l. three-necked flask. The flask is fitted with an efficient mechanical stirrer and a drying tube and is immersed in an ice bath. A solution of 135 g. (3.0 moles) of anhydrous dimethylamine (Note 1) in 150 ml. of anhydrous benzene is introduced into the flask. The acid chloride is added very slowly from the dropping funnel to the vigorously stirred solution, the addition taking about 2 hours. The mixture is then stirred at room temperature overnight. Two hundred milliliters of water is added, the layers are separated, and the aqueous phase is extracted with two 100-ml. portions of ether. The extracts are combined with the benzene layer, washed with saturated sodium chloride solution, and dried over 100 g. of anhydrous magnesium sulfate. Most of the solvent is removed by distillation through a 20-cm. Vigreux column at atmospheric pressure, and the residual liquid is distilled through the column under reduced pressure. The fraction boiling at 85–86°/1.5 mm. is collected (Note 3). The yield of *N,N*-dimethylcyclohexanecarboxamide is 133–138 g. (86–89%), n_D^{25} 1.4800–1.4807.

B. *N,N-Dimethylcyclohexylmethylamine*. In a 3-l. three-necked flask equipped with a reflux condenser and a dropping funnel, both protected by drying tubes, is placed a suspension of 32 g. (0.85 mole) of lithium aluminum hydride (Note 4) in 400 ml. of anhydrous ether (Note 5). The mixture is stirred with a magnetic stirrer using a 40-mm. Teflon-covered stirring bar. A solution of 133 g. (0.86 mole) of *N,N*-dimethylcyclohexanecarboxamide in 300 ml. of anhydrous ether (Note 5) is added at such

a rate as to maintain gentle reflux. The addition requires about 1 hour. The flask is then placed in an electric heating mantle, and the mixture is stirred and heated under reflux for 15 hours. The heating mantle is replaced by an ice bath, and the flask is fitted with an efficient mechanical, sealed stirrer. Water (70 ml.) is added slowly with vigorous stirring. Stirring is continued for 30 minutes after the addition of water is complete. A cold solution of 200 g. of sodium hydroxide in 500 ml. of water is added at once, and the flask is fitted for steam distillation. The mixture is steam-distilled until the distillate is neutral; about 1.5 l. is collected. The distillate is acidified by careful addition, with water cooling, of 95 ml. of concentrated hydrochloric acid. The two layers are separated and the ether layer washed with 50 ml. of 10% hydrochloric acid. The combined acidic solutions are concentrated until no more distillate comes over at steam bath temperature and 20 mm. pressure. The residue is dissolved in 200 ml. of water, the solution cooled, and 110 g. of sodium hydroxide pellets is added slowly, with stirring and external cooling with ice. The two layers are separated, and the aqueous phase is extracted with three 100-ml. portions of ether (Note 6). The combined amine layer and ether extracts are dried over 40 g. of potassium hydroxide pellets for 3 hours. The drying agent is separated by decantation, and the solvent is removed by distillation through a 20-cm. Vigreux column. The residue, on distillation under reduced pressure, yields 106–107 g. (88%) of N,N-dimethylcyclohexylmethylamine, b.p. 76°/29 mm., n_D^{25} 1.4462–1.4463.

2. Notes

1. The material as supplied by the Eastman Kodak Company (white label grade) may be used without further purification.
2. No fractionating column was used.
3. In some runs, small amounts of sulfur-containing compounds distilled together with the amide. These impurities did not affect the yield and purity of the N,N-dimethylcyclohexylmethylamine obtained in the subsequent reduction with lithium aluminum hydride.
4. Lithium aluminum hydride as supplied by Metal Hydrides Inc., Beverly, Massachusetts, may be used without prior pulverization.
5. Mallinckrodt absolute ethyl ether (reagent grade) may be used without further drying.
6. The checkers added enough water to dissolve most of the solid before the second and third ether extractions.

3. Discussion

N,N-Dimethylcyclohexylmethylamine has been prepared by reduction of N,N-dimethylcyclohexanecarboxamide with lithium aluminum hydride;^{2,3} by the action of dimethylformamide on cyclohexanecarboxaldehyde;⁴ by methylation of cyclohexylmethylamine^{3,5} and of N-methylcyclohexylmethylamine by the Clarke-Eschweiler method (treatment with formaldehyde and formic acid) and by the action of dimethylamine on cyclohexylmethyl bromide.⁶

N,N-Dimethylcyclohexanecarboxamide has been prepared by the action of dimethylamine on cyclohexanecarbonyl chloride.^{2,3,7}

The experimental procedure described is a modification of the method reported by Mousseron, Jacquier, Mousseron-Canet, and Zagdoun² and by Baumgarten, Bower, and Okamoto.³

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 492
- Org. Syn. Coll. Vol. 9, 559

References and Notes

1. Massachusetts Institute of Technology, Cambridge 39, Massachusetts. Supported by the Office of Ordnance Research, U. S. Army, under Contract No. DA-19-020-ORD-4542.
2. Mousseron, Jacquier, Mousseron-Canet, and Zagdoun, *Bull. soc. chim. France*, **1952**, 1042.

3. Baumgarten, Bower, and Okamoto, *J. Am. Chem. Soc.*, **79**, 3145 (1957).
 4. Mousseron, Jacquier, and Zagdoun, *Bull. soc. chim. France*, **1952**, 197.
 5. Cope, Bumgardner, and Schweizer, *J. Am. Chem. Soc.*, **79**, 4729 (1957).
 6. Dunn and Stevens, *J. Chem. Soc.*, **1934**, 279.
 7. Bernhard, *Z. physiol. Chem.*, **248**, 256 (1937).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether,
ethyl ether (60-29-7)

sodium hydroxide (1310-73-2)

formaldehyde (50-00-0)

thionyl chloride (7719-09-7)

sodium chloride (7647-14-5)

formic acid (64-18-6)

potassium hydroxide (1310-58-3)

dimethylamine (124-40-3)

Cyclohexanecarboxylic acid (98-89-5)

magnesium sulfate (7487-88-9)

lithium aluminum hydride (16853-85-3)

dimethylformamide (68-12-2)

cyclohexylmethylamine (3218-02-8)

N,N-Dimethylcyclohexylmethylamine,
Cyclohexanemethylamine, N,N-dimethyl- (16607-80-0)

N,N-Dimethylcyclohexanecarboxamide (17566-51-7)

Cyclohexanecarboxaldehyde (2043-61-0)

N-methylcyclohexylmethylamine

cyclohexylmethyl bromide (2550-36-9)

cyclohexanecarbonyl chloride (2719-27-9)

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