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.*
METHYLENECYCLOHEXANE AND N,N-DIMETHYLHYDROXYLAMINE HYDROCHLORIDE

[Cyclohexane, methylene-]

[Hydroxylamine, N,N-dimethyl-, hydrochloride]

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

1. Procedure

In a carefully cleaned 500-ml. Erlenmeyer flask, covered with a watch glass, are placed 49.4 g. (0.35 mole) of N,N-dimethylcyclohexylmethylamine (Note 1), 39.5 g. (0.35 mole) of 30% hydrogen peroxide, and 45 ml. of methanol. The homogeneous solution is allowed to stand at room temperature for 36 hours. After 2 and 5 hours hydrogen peroxide (39.5-g. portions each time) is added (Note 2), (Note 3). The excess hydrogen peroxide is destroyed by stirring the mixture with a small amount of platinum black (Note 4) until the evolution of oxygen ceases. The solution is filtered into a 500-ml. round-bottomed flask and concentrated at a bath temperature of 50–60° (Note 5), a water aspirator being used initially and an oil pump finally, until the amine oxide hydrate solidifies. A Teflon-covered stirring bar is introduced into the flask, which is then connected by a 20-cm. column to a trap (reversed to avoid plugging) cooled in Dry Ice-acetone. The flask is heated in an oil bath to 90–100°, and the apparatus is evacuated to a pressure of ca. 10 mm. with stirring of the liquefied amine oxide hydrate. When the content of the flask resolidifies, the temperature of the oil bath is raised to 160°. The amine oxide decomposes completely within about 2 hours at this temperature. Water (100 ml.) is added to the contents of the trap. The olefin layer is removed with a pipette and washed with two 5-ml. portions of water, two 5-ml. portions of ice-cold 10% hydrochloric acid (Note 6), (Note 7), and one 5-ml. portion of 5% sodium bicarbonate solution. The olefin is cooled in a Dry Ice-acetone bath and filtered through glass wool (Note 8). Distillation over a small piece of sodium through a semimicro column yields 26.6–29.6 g. (79–88%) of methylenecyclohexane, b.p. 100–102°, nD25 1.4474 (Note 10).

The aqueous layer is combined with the two neutral aqueous extracts and acidified by addition of 45 ml. of concentrated hydrochloric acid. The solution is concentrated under reduced pressure at 60–70° until no more distillate comes over. The residue, which solidifies on cooling, is dried in a vacuum desiccator over potassium hydroxide pellets to yield 30.7–32.7 g. (90–96%) of crude N,N-dimethylhydroxylamine hydrochloride, m.p. 103–106° (sealed tube). Crystallization from 40 ml. of isopropyl alcohol gives 26.6–30.7 g. (78–90%) of the pure hydrochloride, m.p. 106–108° (sealed tube).

2. Notes

1. The preparation of N,N-dimethylcyclohexylmethylamine is described on p.339.
2. Many amines are oxidized much more rapidly than the one used in this preparation, and it is often necessary to cool such reaction mixtures in order to avoid decomposition of the amine oxide or a...
vigorousexothermic reaction.
3. The completion of the oxidation should be tested by adding 1 drop of an alcoholic phenolphthalein
solution and 3 drops of water to 1 drop of the oxidation mixture on a porcelain spot plate. Amine oxides
give no color with phenolphthalein.
4. Prepared by the procedure of Feulgen, *Ber.*, **54**, 360 (1921), and added as an aqueous suspension.
5. Some amine oxides decompose at slightly elevated temperatures. In these cases, removal of the
solvents should be carried out at room temperature. It is convenient to use a rotary evaporator for
removal of the solvents.
6. Methylene cyclohexane does not rearrange to 1-methylocyclohexene under these conditions. In
preparations of those olefins which are more sensitive to acid, washing with acid should be omitted.
7. By making the acid extracts strongly alkaline, extracting the basic material with ether, and distilling the
ether extracts, 1.0–2.5 g. (2–5%) of N,N-dimethylethylcyclohexylmethylamine containing a small
amount of a higher-boiling base compound of unknown structure may be recovered.
8. The material obtained in this manner is of high purity before distillation; it has the same refractive
index as the distilled methylenecyclohexane, and no impurities could be detected by gas
chromatographic analysis on two different columns.
9. Most of the material boils at 101–102°C; the small fore-run has the same refractive index as the main
fraction.
10. 1-Methylocyclohexene is completely absent, as shown by gas chromatography on a column packed
with 30% by weight of a 52% solution of silver nitrate in tetraethylene glycol (Dow Chemical
Company) on 48–100 mesh "firebrick" at 60°C. It is estimated that the presence of less than 0.01% of this
isomer could have been detected.

3. Discussion

The present preparation of methylenecyclohexane is an example of an amine oxide pyrolysis. This
route from amines to olefins in many cases yields pure olefins where the alternative method, the
Hofmann exhaustive methylation reaction, is accompanied by some rearrangement to more stable
isomeric olefins.

Methylene cyclohexane has been prepared by treatment of cyclohexylmethyl iodide with alcoholic
potassium hydroxide solution,1 by thermal decarboxylation of cyclohexylidenacetic acid and of
cyclohexane-1-acetic acid,4,5,6 and of cyclohexane-1,1-diacetic acid;7 by pyrolysis of the xanthate,8 the
acetate,9,10,11,12,13 and the stearate14 of cyclohexanemethanol; by the action of triphenylphosphine-
methylene on cyclohexanone;15 by the pyrolysis of N,N-dimethylethylcyclohexylmethylamine
methohydroxide16,17 and of N,N-dimethylethylcyclohexylmethylamine N-oxide;16,17 and by treatment of
benzylhexahydrobenzyldimethylammonium bromide with sodium amide in liquid ammonia.18

N,N-Dimethylhydroxylamine has been prepared by the action of methylmagnesium iodide on ethyl
nitrate.19

References and Notes

1. Massachusetts Institute of Technology, Cambridge 39, Massachusetts. Supported by the Office of

---

**Appendix**

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

platinum black

N,N-dimethylcyclohexylmethylamine methohydroxide

- hydrochloric acid (7647-01-0)
- ammonia (7664-41-7)
- methanol (67-56-1)
- ether (60-29-7)
- sodium bicarbonate (144-55-8)
- Cyclohexanone (108-94-1)
- silver nitrate (7761-88-8)
- oxygen (7782-44-7)
- potassium hydroxide, potassium hydroxide pellets (1310-58-3)
- sodium (13966-32-0)
- isopropyl alcohol (67-63-0)
- hydrogen peroxide (7722-84-1)
- cyclohexanemethanol (100-49-2)
- methylmagnesium iodide (917-64-6)
- phenolphthalein (77-09-8)
- sodium amide (7782-92-5)
ethyl nitrate (625-58-1)

1-methylocyclohexene

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

Methylene cyclohexane,
Cyclohexane, methylene- (1192-37-6)

N,N-DIMETHYLHYDROXYLAMINE HYDROCHLORIDE,
Hydroxylamine, N,N-dimethyl-, hydrochloride (16645-06-0)

tetraethylene glycol (112-60-7)
cyclohexylmethyl iodide
cyclohexylideneacetic acid
cyclohexane-1-acetic acid (5292-21-7)
cyclohexane-1,1-diacetic acid (4355-11-7)
triphenylphosphine-methylene

N,N-dimethylcyclohexylmethylamine N-oxide

benzylhexahydrobenzylidimethylammonium bromide

N,N-Dimethylhydroxylamine (5725-96-2)