



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.

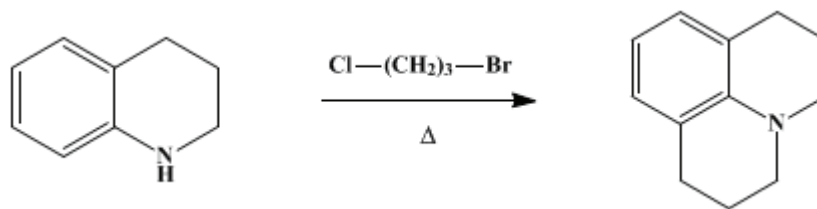
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.504 (1955); Vol. 26, p.40 (1946).

JULOLIDINE

[Benzo[*ij*]quinolizine, 1,2,3,5,6,7-hexahydro-]



Submitted by D. B. Glass and A. Weissberger.

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1. Procedure

A mixture of 66.5 g (0.5 mole) of tetrahydroquinoline and 400 g. of trimethylene chlorobromide (Note 1) is placed in a 1-l. round-bottomed flask attached to a reflux condenser, and heated in an oil bath held at 150–160° for 20 hours (Note 2). The reaction mixture is cooled, a solution of 50 ml. of concentrated hydrochloric acid in 500 ml. of water is added, and the excess trimethylene chlorobromide is removed by distillation with steam (Note 3). The acid residue from the steam distillation is made alkaline with a 40% solution of sodium hydroxide (about 75 ml.), and the julolidine is extracted with two 150-ml. portions of ether. The ethereal solution is washed with 150 ml. of water and dried over sodium hydroxide pellets. The ether is evaporated and the residue distilled under reduced pressure. The portion that boils at 105–110°/1 mm. is collected (Note 4) and (Note 5). The yield is 67–70 g. (77–81%).

2. Notes

1. The tetrahydroquinoline and trimethylene chlorobromide were Eastman grade materials of the Eastman Kodak Company.
2. The heating should be carried out in a hood, or a gas trap should be used to remove the hydrogen halides that are evolved.
3. The trimethylene chlorobromide recovered may be dried over calcium chloride and used in a subsequent run.
4. The julolidine solidifies in the receiver, m.p. 39–40°.
5. After standing in contact with air for several weeks, the julolidine may become colored by the formation of a red compound. This red compound may be removed by distillation or by dissolving the amine in 2 or 3 volumes of hexane, treating the hexane solution with Norit or Darco, and filtering. The julolidine is crystallized from the hexane solution by cooling in an acetone-Dry Ice bath. The resulting product melts at 39–40° and amounts to 85–90% of the original.

3. Discussion

Julolidine has been prepared by the reaction of trimethylene chlorobromide with formanilide,¹ aniline,¹ methylaniline,¹ and tetrahydroquinoline;^{1,2} by the reduction of 8,10-diketojulolidine;¹ by the intra-molecular condensation of N-(γ -bromopropyl) tetrahydroquinoline;³ and by dehydration of N-(γ -hydroxypropyl) tetrahydroquinoline or di-(γ -hydroxypropyl) aniline with phosphorus pentoxide.⁴

References and Notes

1. Pinkus, *Ber.*, **25**, 2802 (1892).
2. von Braun, Heider, and Wyczałkowska, *Ber.*, **51**, 1219 (1918).

3. Jones and Dunlop, *J. Chem. Soc.*, **101**, 1752 (1912).
 4. Rindfusz and Harnack, *J. Am. Chem. Soc.*, **42**, 1724 (1920).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

Darco

calcium chloride (10043-52-4)

hydrochloric acid (7647-01-0)

ether (60-29-7)

aniline (62-53-3)

sodium hydroxide,
sodium hydroxide pellets (1310-73-2)

Norit (7782-42-5)

Trimethylene chlorobromide (109-70-6)

methylaniline (100-61-8)

Julolidine,
Benzo[*ij*]quinolizine, 1,2,3,5,6,7-hexahydro- (479-59-4)

tetrahydroquinoline (635-46-1)

hexane (110-54-3)

formanilide (103-70-8)

8,10-diketojulolidine

N-(γ -bromopropyl) tetrahydroquinoline

N-(γ -hydroxypropyl) tetrahydroquinoline

di-(γ -hydroxypropyl) aniline

phosphorus pentoxide (1314-56-3)