Organic Syntheses

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.

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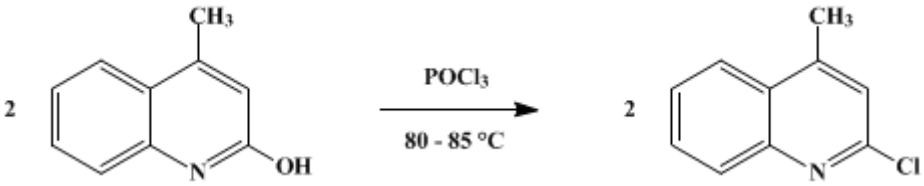
2-CHLOROLEPIDINE

[Lepidine, 2-chloro-]



Submitted by C. E. Kaslow and W. M. Lauer.
Checked by C. F. H. Allen and H. W. J. Cressman.

1. Procedure

In a 500-ml. flask, to which is attached an air condenser whose open end is protected by absorbent cotton or calcium chloride in a drying tube, are mixed 119 g. (0.75 mole) of 4-methylcarbostyril (p. 580) and 138 g. (82.5 ml., 0.9 mole) of freshly distilled phosphorus oxychloride. The mixture is maintained at 80–85° in a water bath for about 15 minutes until most of the solid has dissolved, and then it is warmed carefully for an additional 15 minutes on a wire gauze until solution is complete. The hot reaction mixture is poured into 1 l. of water containing 1 kg. of cracked ice.

The 2-chlorolepidine is extracted, using two 750-ml. portions of ether (Note 1). The extract is shaken with two 200-ml. portions of water and then dried over 50 g. of potassium carbonate. After removal of the ether, the residual oil is distilled from a 200-ml. modified Claisen flask. The colorless distillate boils at 132–135°/3 mm. and weighs 118–122 g. (89–92%). The distillate is melted if necessary and poured into 250 ml. of petroleum ether (b.p. 40–50°); the solution is then chilled in a freezing mixture; the crystals are filtered by suction and dried in a vacuum desiccator over paraffin. The snow-white 2-chlorolepidine melts at 58–59° and weighs 114–118 g. (86–89%).

2. Notes

1. An additional 5–8 g. of slightly colored material can be secured by neutralizing the aqueous solution with 200 g. of sodium carbonate, extracting with 500 ml. of ether, and distilling. The total yield of distilled product then amounts to 125–130 g. (95–97%).

3. Discussion

The preparation described is based on the method of Knorr[1] and has been used by Mikhailov,[2] Krahler and Burger,[3] and Mizuno.[4] 2-Chlorolepidine has also been prepared by the action of benzoyl chloride on 4-methylcarbostyril.[5]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 519
- Org. Syn. Coll. Vol. 3, 580

References and Notes

1. Knorr, *Ann.*, **236**, 98 (1886).
2. Mikhailov, *J. Gen. Chem. U.S.S.R.*, **6**, 511 (1936) [*C. A.*, **30**, 6372 (1936)].
3. Krahler and Burger, *J. Am. Chem. Soc.*, **63**, 2368 (1941).
4. Mizuno, *J. Pharm. Soc. Japan*, **69**, 126 (1949) [*C. A.*, **44**, 1985 (1950)].

5. Ellinger and Reisser, *Ber.*, **42**, 3338 (1909).

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

petroleum ether

potassium carbonate (584-08-7)

ether (60-29-7)

sodium carbonate (497-19-8)

benzoyl chloride (98-88-4)

Phosphorus Oxychloride (21295-50-1)

2-Chlorolepidine,
Lepidine, 2-chloro- (634-47-9)

4-Methylcarbostyril (607-66-9)