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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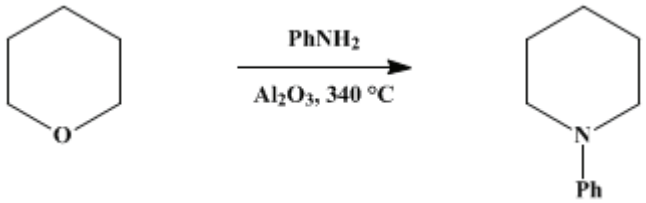
1-PHENYLPIPERIDINE

[Piperidine, 1-phenyl]



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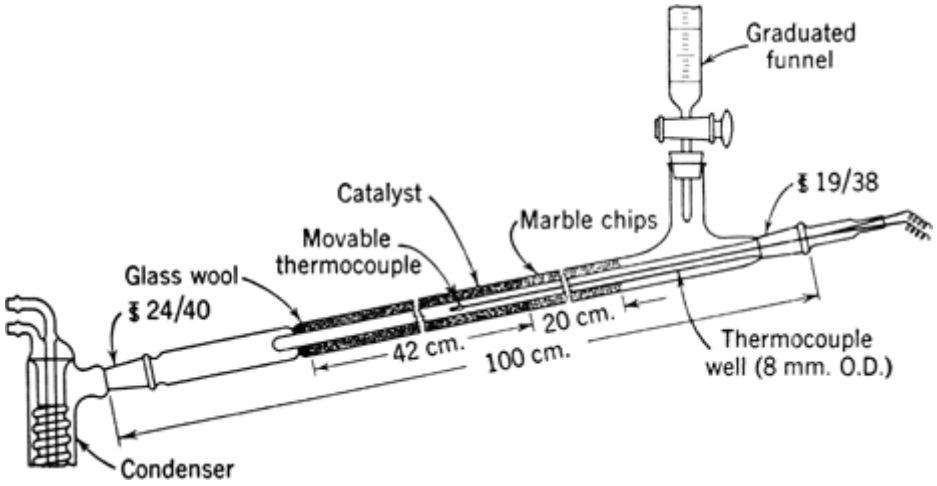
Checked by R. T. Arnold, William E. Parham, and Carl Serres.

1. Procedure

The apparatus (Fig. 15) consists of a reaction tube, 100 cm. long and 3 cm. in diameter, provided with an inlet tube to which a graduated dropping funnel is connected. The lower end of the reaction tube is fitted with a Friedrichs condenser and receiver. A thermocouple well, concentric with the reaction tube, is passed through the upper end by means of a standard ground-glass joint. The tube is packed with 200 ml. of 4- to 8-mesh alumina (Note 1) held in place by a plug of glass wool supported by indentations in the tube, followed by 100 ml. of marble chips which serve as a vaporizer and preheater for the reactants. The reaction tube is supported in an electrically heated furnace (Note 2) extending from the inlet tube to the joint connecting the condenser.

Fig. 15.



The reaction tube is heated to 330–340° (Note 3) and is swept out with a stream of nitrogen gas. A solution of 258 g. (3 mole) of tetrahydropyran (Note 4) and 559 g. (6 mole) of aniline is then placed in the graduated funnel and introduced into the reaction tube at a rate of 90–100 ml. per hour. The product, which is collected in a 1-l. flask containing 10 g. of sodium chloride, consists of a light-yellow oil and a lower aqueous layer. After the addition of the reactants is complete, a slow stream of nitrogen is passed through the reaction tube for 20–30 minutes to remove any product adsorbed on the catalyst. The lower aqueous layer is separated and discarded, and the upper organic layer is dried over sodium hydroxide pellets. The product is fractionated under reduced pressure using a Whitmore-Lux column[2] (Note 5) only to remove the small amount of unchanged tetrahydropyran and excess aniline. The column is permitted to drain, and the residue is distilled from an ordinary Claisen flask under reduced pressure. 1-Phenylpiperidine is obtained as a colorless or very light-yellow liquid, b.p. 123–126°/12.5 mm., 133–136°/21 mm., n_D^{25} 1.5603. The yield is 403–435 g. (83–90% based on tetrahydropyran) (Note 6).

2. Notes

1. The catalyst employed was Alcoa Activated Alumina (Grade F-1, 4- to 8-mesh) from the Aluminum Company of America. A fresh catalyst is brought to a condition of maximum activity by passing a slow stream of air through the catalyst bed for 94 hours at 390–405°. Without this pretreatment, yields are 5–10% lower than those reported here. The catalyst is reactivated after each run by passing air through it for 39 hours at 390–405°.
2. The furnace may be of the construction described in a previous volume.[3] It is desirable, although not essential, to provide separately controlled heating elements for each of the two packed zones of the reaction tube.
3. The temperature of the furnace is measured by a thermocouple which can be moved to various positions in the thermocouple well. The catalyst temperature should be maintained at 325–345°, although it may be as low as 320° at the ends of the catalyst zone, depending unon the construction of the furnace.
4. Eastman Kodak Company practical grade tetrahydropyran may be used without purification.
5. A column of equivalent efficiency may be employed.
6. 1-*m*-Tolylpiperidine (b.p. 141–143°/16 mm., n_D^{25} 1.5535) and 1-*p*-tolylpiperidine (b.p. 140–143°/15 mm., n_D^{25} 1.5509) may be prepared in 85–90% yield by a similar procedure. 1-*o*-Tolylpiperidine (b.p. 123–125°/15 mm., n_D^{25} 1.5391) is obtained in 60% yield under similar reaction conditions, but it is necessary to fractionate the product in order to obtain pure material.

3. Discussion

1-Phenylpiperidine has been prepared by warming aniline with 1,5-dibromopentane;[4,5] heating 5-anilino-1-bromopentane;[6] the dehydration of 5-anilino-1-pentanol over alumina;[7] the electrolytic reduction of N-phenylglutarimide;[8] the catalytic hydrogenation of 1-phenyl-3-hydroxypyridinium chloride;[9] the action of bromobenzene on piperidine in the presence of lithium[10] or sodium amide;[11] the reaction of fluorobenzene, 1-methylpiperidine, and phenyllithium;[12] the action of diphenylsulfone on piperidine in the presence of sodamide;[13] the diazotization and deamination of 1-(2-aminophenyl) piperidine[14] and of 1-(4-aminophenyl)piperidine;[15] the reduction of N-phenylglutarimide with lithium aluminum hydride;[16] the reaction of pentamethylene glycol dibenzenesulfonate with aniline;[17] the action of lithium piperidide on chlorobenzene;[18] and the present method.[19]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 746

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

alumina

lithium piperidide

aniline (62-53-3)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

chlorobenzene (108-90-7)

diphenylsulfone (127-63-9)

piperidine (110-89-4)

1,5-dibromopentane (111-24-0)

bromobenzene (108-86-1)

Tetrahydropyran (142-68-7)

Phenyllithium (591-51-5)

Fluorobenzene (462-06-6)

sodamide (7782-92-5)

lithium aluminum hydride (16853-85-3)

1-Phenylpiperidine,
Piperidine, 1-phenyl (4096-20-2)

5-anilino-1-bromopentane

5-anilino-1-pentanol

N-phenylglutarimide

1-phenyl-3-hydroxypyridinium chloride

1-methylpiperidine (626-67-5)

1-(2-aminophenyl)piperidine (39643-31-7)

1-(4-aminophenyl)piperidine (2359-60-6)

pentamethylene glycol dibenzenesulfonate

1-m-Tolylpiperidine

1-p-tolylpiperidine

1-o-Tolylpiperidine (7250-70-6)