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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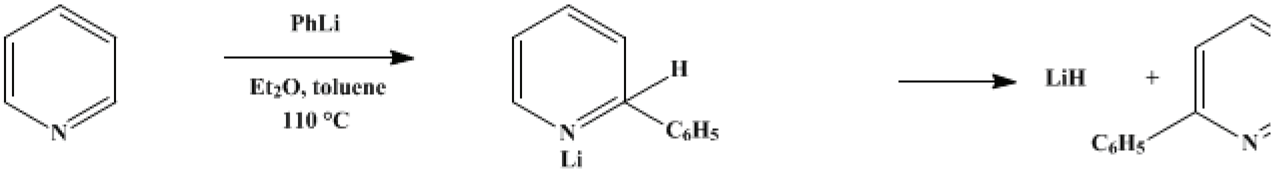
*Organic Syntheses, Coll. Vol. 2, p.517 (1943); Vol. 18, p.70 (1938).*

# 2-PHENYLPYRIDINE

## [Pyridine, 2-phenyl-]

$$C_6H_5Br + Li \longrightarrow C_6H_5Li + LiBr$$



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## 1. Procedure

In a 1-l. three-necked flask, fitted with a dropping funnel, a thermometer, mechanical stirrer, and reflux condenser protected from moisture (Note 1), the whole being swept with dry nitrogen, are placed 3.5 g. (0.5 gram atom) of lithium, cut into pieces the size of a pea, and 100 cc. of dry ether. The stirrer is started, and about 10 cc. of a mixture of 40 g. of bromobenzene (0.25 mole) in 50 cc. of dry ether is admitted from the dropping funnel; a vigorous reaction usually takes place (Note 2). The remainder of the mixture is added gradually over a half-hour period, when the metal should have largely disappeared (Note 3).

From the dropping funnel is next slowly introduced, with stirring, 40 g. (0.5 mole) of dry pyridine (Note 4) in 100 cc. of dry toluene. The ether is then distilled (Note 5) and the residual suspension stirred at 110° (inside temperature) for eight hours. It is then cooled to about 40°, 35 cc. of water cautiously added, and the liquids filtered if necessary (Note 6). The lower layer is separated and discarded. The toluene layer is dried for an hour with 20 g. of pulverized potassium hydroxide and carefully distilled, using a modified Claisen flask with a fractionating column attached. The material boiling up to 150° is removed at ordinary pressure and the residue distilled *in vacuo*; after two fractional distillations, the yield of 2-phenylpyridine, b.p. 140°/12 mm., is 15.5–19 g. (40–49 per cent of the theoretical amount).

## 2. Notes

1. The apparatus and reagents must be dried as for the Grignard reaction.
2. Occasionally the reaction will not start without the application of heat; as soon as the reaction begins, however, the source of heat is removed.
3. The yield of phenyllithium is approximately 75 per cent. It can be determined by allowing the phenyllithium to react with an excess of benzophenone and weighing the triphenylcarbinol formed. It is assumed that the carbinol is formed quantitatively.[1]
4. The success of the preparation depends on the dryness of the pyridine. The pyridine was refluxed for eight hours over fresh quicklime and distilled, and then a similar treatment with pulverized potassium hydroxide followed. None of the available barium oxide gave as good results. Merck's medicinal pyridine gave the highest yields.
5. This is easily accomplished by running the water out of the condenser, while heating to 110°.
6. The small particles of unused metal that usually remain hinder the separation into layers.

## 3. Discussion

2-Phenylpyridine has been prepared from pyridine and phenyllithium[2] or benzenediazonium chloride.[3] In the procedure described above, replacing ether as a solvent by toluene avoids the necessity of using a sealed tube.[4]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 757

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## References and Notes

1. Gilman, Zoellner, and Selby, J. Am. Chem. Soc. **54**, 1957 (1932).
2. Ziegler and Zeiser, Ber. **63**, 1847 (1930).
3. Haworth, Heilbron, and Hey, J. Chem. Soc. **1940**, 352.
4. Walters and McElvain, J. Am. Chem. Soc. **55**, 4625 (1933).

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

quicklime

ether (60-29-7)

barium oxide

nitrogen (7727-37-9)

benzenediazonium chloride

pyridine (110-86-1)

potassium hydroxide (1310-58-3)

toluene (108-88-3)

Benzophenone (119-61-9)

bromobenzene (108-86-1)

Triphenylcarbinol (76-84-6)

Phenyllithium (591-51-5)

lithium (7439-93-2)

2-Phenylpyridine,

Pyridine, 2-phenyl- (1008-89-5)