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.

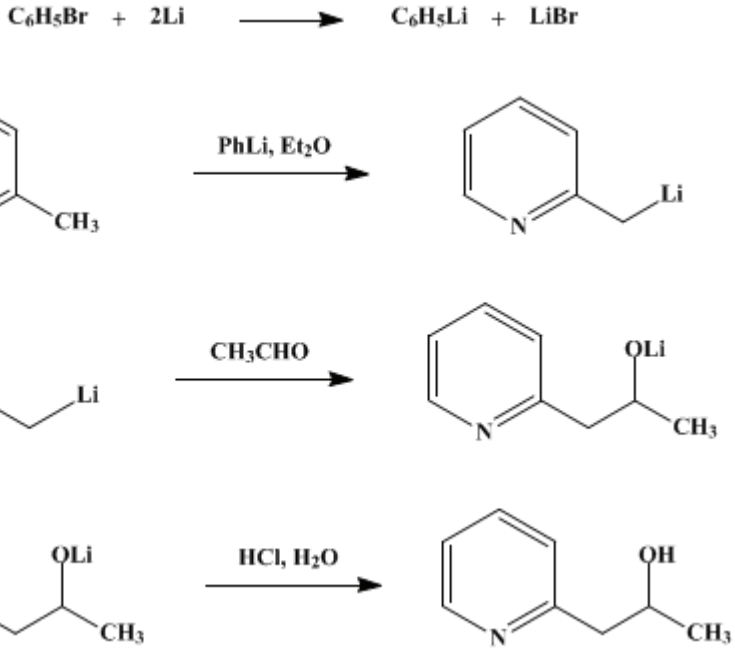
*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

DOI:10.15227/orgsyn.023.0083

*Organic Syntheses, Coll. Vol. 3, p.757 (1955); Vol. 23, p.83 (1943).*

# 1-(α-PYRIDYL)-2-PROPANOL

## [2-(β-Hydroxypropyl)pyridine]




Submitted by L. A. Walter
Checked by C. F. H. Allen and James VanAllan.

## 1. Procedure

While a current of dry nitrogen is passed through the apparatus, 400 ml. of dry ether and 6.9 g. (1 gram atom) of lithium (in small pieces) (Note 1) are placed in a 1-l. three-necked flask fitted with a dropping funnel, mechanical stirrer, and reflux condenser protected from moisture. The stirrer is started, and 10–15 ml. of a solution of 79 g. (0.5 mole) of dry bromobenzene in 100 ml. of dry ether is added from the dropping funnel. The reaction usually starts immediately; if not, the flask may be warmed, and the remainder of the mixture is then added at such a rate that the ether refluxes gently. The mixture is stirred until the lithium disappears (Note 2).

Forty-six grams (0.5 mole) of α-picoline (Note 3) is then added, and the mixture is stirred at room temperature for 1 hour, during which time the dark red solution of picolyllithium is formed. The flask is then immersed in an ice-salt bath, and when the mixture is thoroughly chilled the nitrogen train is disconnected. Then 20 g. of dry acetaldehyde in 50 ml. of dry ether (Note 4) is slowly dropped into the mixture over a period of 20 minutes. The red color entirely disappears. After 15 minutes, 100 ml. of water is slowly added and then 100 ml. of concentrated hydrochloric acid (sp. gr. 1.2). The aqueous layer is removed and poured, with stirring, into a warm solution of 300 g. of sodium carbonate decahydrate in 100 ml. of water (Note 5). The crude reaction product separates as an oil and is taken up in 300 ml. of chloroform. The precipitated lithium carbonate is filtered, transferred to a beaker, and stirred with four 200-ml. portions of chloroform. The chloroform extracts are decanted or filtered, and all the chloroform solutions are combined (Note 6). The chloroform is removed by distillation, and the residue is fractionated under reduced pressure through a good column. The 1-(α-pyridyl)-2-propanol boils sharply at 116–117°/17 mm. (124–125°/20 mm.). A small fore-run and a considerable amount of high-boiling residue are discarded. The yield is 30–34 g. (44–50% based on the α-picoline) (Note 7) and (Note 8). This product darkens on exposure to light, and it should be preserved in a brown glass bottle.

## 2. Notes

1. The most unsatisfactory operation of this preparation is cutting the lithium. It may be finely divided by rubbing the metal against a coarse wood rasp and allowing the filings to drop through a large paper funnel directly into the ether while a rapid stream of dry nitrogen is passed through the flask. This procedure is most convenient when a large piece of lithium is available and the amount of filings can be determined by the loss in weight. Larger pieces, cut with a knife [*Org. Syntheses* Coll. Vol. 2, 518 (1943)], can be used equally well (Note 2). Bartlett, Swain, and Woodward[1] have published a convenient method for the preparation of lithium sand.
2. The time depends upon the size of the pieces; the solution may be stirred for 24 hours without affecting the yield.
3. The submitters used α-picoline, b.p. 128–130°, obtained from the Barrett Company. The checkers used practical α-picoline, b.p. 128–134°, freshly distilled under reduced pressure. Samples of picoline containing water should be carefully fractionated to remove the water as the α-picoline-water azeotrope, b.p. 93°.
4. Alternatively, the acetaldehyde may be distilled into the flask through the nitrogen inlet. During this operation, the outlet must be kept well above the surface, to prevent clogging. The introduction of aldehyde is stopped when the red color has disappeared.
5. A solution of 111 g. of anhydrous sodium carbonate in 150 ml. of water may be substituted.
6. If sodium hydroxide is used to liberate the amino alcohol from its salt, extraction with chloroform produces unworkable emulsions.
7. Equally good yields of 1-(α-pyridyl)-3-propanol, b.p. 116–118°/4 mm., may be obtained by using ethylene oxide in place of acetaldehyde.
8. The submitters obtained yields as high as 43 g. (60%).

## 3. Discussion

This procedure is based upon that of Ziegler.[2] 1-(α-Pyridyl)-2-propanol has also been prepared in poor yields (4–6 per cent) by heating α-picoline with aqueous acetaldehyde in sealed tubes.[3,4]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 641

---

## References and Notes


1. Bartlett, Swain, and Woodward, *J. Am. Chem. Soc.*, **63**, 3230 (1941).
2. Ziegler and Zeiser, *Ann.*, **485**, 174 (1931).
3. Ladenburg, *Ann.*, **301**, 140 (1898).
4. Meisenheimer and Mahler, *Ann.*, **462**, 308 (1928).


---

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

acetaldehyde (75-07-0)

hydrochloric acid (7647-01-0)

ether (60-29-7)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

sodium carbonate (497-19-8)

nitrogen (7727-37-9)

bromobenzene (108-86-1)

Ethylene oxide (75-21-8)

sodium carbonate decahydrate (6132-02-1)

lithium (7439-93-2)

picolyllithium

picoline,
α-picoline (109-06-8)

1-(α-PYRIDYL)-2-PROPANOL,
2-(β-Hydroxypropyl)pyridine (5307-19-7)

lithium carbonate (554-13-2)

1-(α-pyridyl)-3-propanol (2859-68-9)