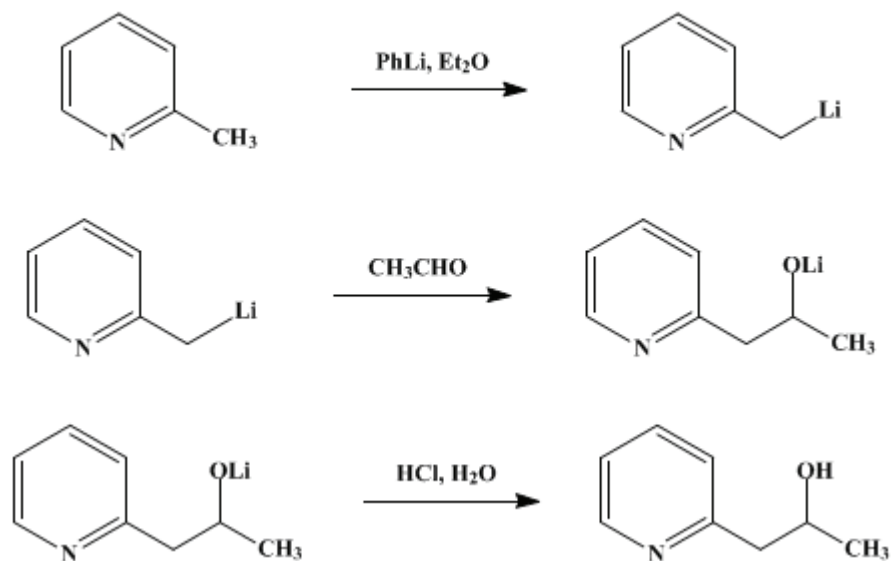


## 1-( $\alpha$ -PYRIDYL)-2-PROPANOL

### [2-( $\beta$ -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  $\alpha$ -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 picolylithium 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-( $\alpha$ -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  $\alpha$ -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<sup>1</sup> 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.<sup>2</sup> [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.<sup>3,4</sup>

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 4, 641](#)

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## 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).

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## 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)

picolylithium

picoline,  
 $\alpha$ -picoline (109-06-8)

1-( $\alpha$ -PYRIDYL)-2-PROPANOL,  
2-( $\beta$ -Hydroxypropyl)pyridine (5307-19-7)

lithium carbonate (554-13-2)

1-( $\alpha$ -pyridyl)-3-propanol (2859-68-9)