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.

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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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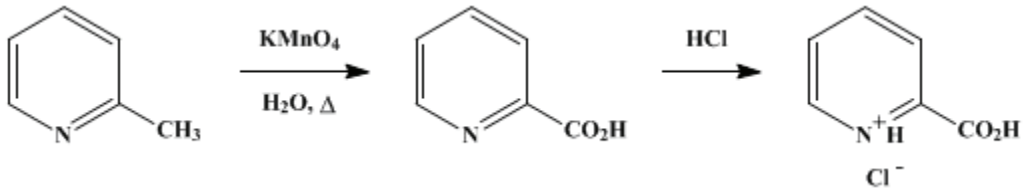
PICOLINIC ACID HYDROCHLORIDE



Submitted by Alvin W. Singer and S. M. McElvain.
Checked by C. F. H. Allen and Alan Bell.

1. Procedure

In a 5-l. three-necked flask, fitted with a reflux condenser and stirrer, are placed 2500 ml. of water and 50 g. of α-picoline (0.54 mole) (Note 1). Ninety grams (0.57 mole) of potassium permanganate is added, and the solution is heated on a steam bath until the purple color has practically disappeared (about 1 hour). A second 90-g. portion of permanganate is then introduced, followed by 500 ml. of water, and the heating is continued until the purple color is destroyed (2–2.5 hours). The reaction mixture is allowed to cool slightly, and the precipitated oxides of manganese are filtered and washed well with 1 l. of hot water (Note 2). The filtrate is concentrated under reduced pressure to 150–200 ml., filtered, if necessary, and acidified to Congo red with concentrated hydrochloric acid (65–70 ml., sp. gr. 1.19). This acid solution is then evaporated to dryness under reduced pressure. The solid residue is refluxed for one hour with 250 ml. of 95% ethanol and filtered, and the extraction is repeated with 150 ml. of 95% ethanol. Dry hydrogen chloride is passed into the combined ethanolic filtrates until crystals begin to separate. The solution is then chilled to about 10° in a freezing mixture, the addition of hydrogen chloride being continued until the solution is saturated. The crystals of picolinic acid hydrochloride which separate are filtered and air-dried. The yield is 43–44 g. (50–51%), m.p. 228–230° (Note 3).

This hydrochloride may contain traces of potassium chloride, which can be removed by dissolving the hydrochloride in hot absolute ethanol (50 g. requires 1 l.) and filtering from insoluble material. An equal volume of dry ether is then added to the warm ethanolic solution, and, after cooling, the crystallized product is filtered. The recovery is 40–43 g., m.p. 210–212° (230°) (Note 3) and (Note 4).

2. Notes

1. The submitters used a picoline fraction, b.p. 128–132°, whereas the checkers used the practical product, Eastman Kodak Company, b.p. 128–134°. The same yield was obtained with a carefully fractionated picoline, boiling over the 1° range 128–129°.
2. The washed manganese dioxide does not contain an appreciable amount of acid.
3. When the melting point is determined in the ordinary manner, it is found to be 228–230° with decomposition. If, on approaching the melting point, the rate of heating is reduced to 1° in 5 minutes, the value 210–212° can be observed.
4. About 2 g. of potassium chloride is removed by this procedure. The unpurified material can be used for most purposes.

3. Discussion

Picolinic acid has been generally prepared by the permanganate oxidation of α-picoline and isolated through the copper salt.[1,2,3,4,5] In one instance,[6] it was isolated directly as in the present procedure. It has also been secured by the hydrolysis of ω-trichloropicoline,[7,8] and by the nitric acid oxidation of α-picoline.[9]

References and Notes

1. Weidel, *Ber.*, **12**, 1992 (1879).
2. Pinner, *Ber.*, **33**, 1226 (1900).
3. Camps, *Arch. Pharm.*, **240**, 345 (1902).
4. Ley and Ficken, *Ber.*, **50**, 1132 (1917).
5. Clemo and Ramage, *J. Chem. Soc.*, **1931**, 440.
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8. Ochiai and Okuda, *J. Pharm. Soc. Japan*, **70**, 156 (1950) [*C. A.*, **44**, 5878 (1950)].
9. U. S. pat. 2,505,568 [*C. A.*, **44**, 6443 (1950)].

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

oxides of manganese

ω-trichloropicoline

ethanol (64-17-5)

hydrogen chloride,
hydrochloric acid (7647-01-0)

ether (60-29-7)

nitric acid (7697-37-2)

potassium permanganate (7722-64-7)

manganese dioxide (1313-13-9)

permanganate

potassium chloride (7447-40-7)

Picolinic acid hydrochloride (636-80-6)

picoline,
α-picoline (109-06-8)

Picolinic acid (98-98-6)