



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.

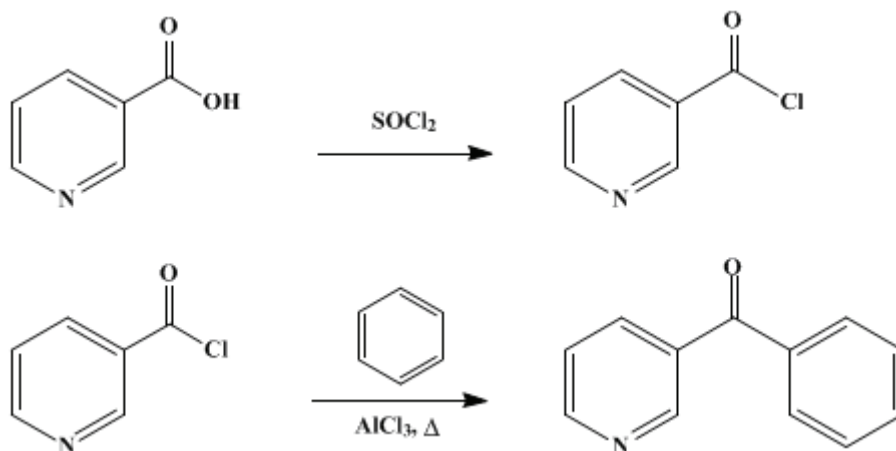
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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3-BENZOYLPYRIDINE

[Ketone, phenyl 3-pyridyl]



Submitted by Frank J. Villani and Mary S. King¹.
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1. Procedure

In a 2-l. three-necked flask, fitted with a sealed mechanical stirrer (Note 1), a reflux condenser protected with a calcium chloride tube, and a dropping funnel, is placed 123 g. (1 mole) of nicotinic acid (Note 2). The stirrer is started, and 500 ml. (818 g., 6.9 moles) of distilled thionyl chloride is added in a slow stream over a period of 15–20 minutes (Note 3). After the addition is complete, the mixture is heated on the steam bath with continuous stirring for 1 hour; then the reflux condenser is replaced by one set for downward distillation, and the excess thionyl chloride is removed by distillation at reduced pressure as heating on the steam bath is continued (Note 1) and (Note 3). After most of the thionyl chloride has been distilled, 200 ml. of anhydrous benzene is added, and the benzene is distilled at reduced pressure. An additional 500 ml. of anhydrous benzene is added; then the flask is fitted with a thermometer and a reflux condenser and is placed in an ice-salt bath. The stirrer is started, and 330 g. (2.5 moles) of anhydrous aluminum chloride is added in portions over a period of 1 hour as the internal temperature is held between 5° and 10°. The ice bath is removed, and the flask is permitted to warm to room temperature and is finally heated under reflux for 6 hours.

The dark red-brown reaction mixture is cautiously poured onto a mixture of 2 kg. of ice and 200 ml. of concentrated hydrochloric acid. The organic layer is separated and discarded. The acid solution is extracted with three 500-ml. portions of ether (Note 4), which are discarded; then it is treated with 50% aqueous sodium hydroxide until the aluminum hydroxide which first forms redissolves (Note 5). After cooling, the organic material is extracted with five 300-ml. portions of chloroform. The combined chloroform extracts are washed with water, the solvent is removed by distillation on the steam bath, and the product is distilled. The yield of 3-benzoylpyridine (Note 6), b.p. 107–110°/0.3 mm. or 141–145°/4 mm., is 165–175 g. (90–96%), n_D^{26} 1.6088.

2. Notes

1. It is convenient to use a sealed stirrer, such as the Tubore stirrer, which may be left in the flask during the distillation of thionyl chloride and benzene at reduced pressure; however, the stirrer cannot be left running during this distillation, for it is stopped by the cake of acid chloride hydrochloride. The distillations are accomplished most conveniently if the dropping funnel is removed and replaced by a capillary and the stirrer is left in place but not running during the distillations.
2. Satisfactory results were obtained with nicotinic acid from either Eastman Organic Chemicals or

Matheson, Coleman and Bell.

3. The submitters used [thionyl chloride](#) from Hooker Electrochemical Company. It was distilled and collected over a 1° range (78–79°). The first few drops of [thionyl chloride](#) are added cautiously as the initial reaction may be quite vigorous. Recovered [thionyl chloride](#) may be used for subsequent runs.

4. The [ether](#) extractions remove any [diphenyl sulfoxide](#) that is formed.

5. About 800–1000 ml. of 50% [sodium hydroxide](#) is required.

6. [4-Benzoylpyridine](#) can be obtained by this procedure from [isonicotinic acid](#) in yields of 87–90%. This product is recrystallized from [hexane](#), m.p. 72–73°.

3. Discussion

The described method of preparing [3-benzoylpyridine](#) is a modification of that of Wolffenstein and Hartwich.² Other methods of preparing this compound are by the addition of [phenylmagnesium bromide](#) to [3-cyanopyridine](#),³ the addition of [3-pyridyllithium](#) to [benzonitrile](#),⁴ the [chromic acid](#) oxidation of [phenyl-3-pyridylcarbinol](#),⁵ and the decarboxylation of [β-benzoylpicolinic acid](#) obtained from [quinolinic acid anhydride](#) and [benzene](#).⁶

References and Notes

1. Schering Corporation, Bloomfield, New Jersey.
 2. Wolffenstein and Hartwich, *Ber.*, **48**, 2043 (1915).
 3. LaForge, *J. Am. Chem. Soc.*, **50**, 2486 (1928).
 4. French and Sears, *J. Am. Chem. Soc.*, **73**, 469 (1951); Wibaut, deJonge, van der Voort, and Otto, *Rec. trav. chim.*, **70**, 1054 (1951).
 5. Kleipool and Wibaut, *Rec. trav. chim.*, **69**, 1041 (1950).
 6. Bernthsen and Mettegang, *Ber.*, **20**, 1209 (1887).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

[hydrochloric acid](#) (7647-01-0)

[Benzene](#) (71-43-2)

[ether](#) (60-29-7)

[benzonitrile](#) (100-47-0)

[sodium hydroxide](#) (1310-73-2)

[thionyl chloride](#) (7719-09-7)

[chloroform](#) (67-66-3)

[aluminum chloride](#) (3495-54-3)

[chromic acid](#) (7738-94-5)

[Phenylmagnesium bromide](#) (100-58-3)

Nicotinic acid (59-67-6)

aluminum hydroxide

hexane (110-54-3)

3-Benzoylpyridine,
Ketone, phenyl 3-pyridyl (5424-19-1)

diphenyl sulfoxide (945-51-7)

4-Benzoylpyridine (14548-46-0)

3-cyanopyridine (100-54-9)

3-pyridyllithium

phenyl-3-pyridylcarbinol

β -benzoylpicolinic acid

quinolinic acid anhydride

isonicotinic acid (55-22-1)