



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.

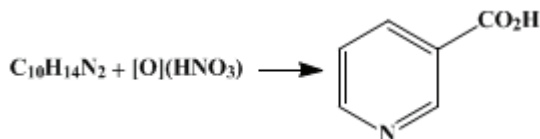
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 1, p.385 (1941); Vol. 4, p.49 (1925).

NICOTINIC ACID



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1. Procedure

In a 5-l. round-bottomed flask is placed 4 kg. (2816 cc.) of c.p. concentrated **nitric acid** (sp. gr. 1.42) (**Note 1**). To this is added, in 25-cc. portions, 210 g. (1.23 moles) of **nicotine** (**Note 2**). The addition should be made carefully in order that local heating may not occur and material be lost. After each addition of **nicotine**, the flask should be shaken in order to insure a homogeneous solution. The addition of the **nicotine** causes the temperature of the liquid to rise somewhat but not sufficiently to cause evolution of **nitrogen dioxide**. The flask is placed on a steam bath under a hood and heated until the liquid reaches a temperature of 70°. It is then removed and the reaction allowed to continue spontaneously (**Note 3**), sufficient heat being evolved to cause the liquid to boil. The boiling ceases after one hour, but the flask is replaced upon the steam bath for ten to twelve hours, during which time there is a more or less continuous evolution of oxides of nitrogen.

The contents of the flask are then poured into an evaporating dish and evaporated almost to dryness on the steam bath (about ten hours). The purification which follows is best carried out with the product of two runs such as have been described above.

After the evaporation of most of the liquid, the **nicotinic acid nitrate** from two runs is transferred to a 1.5-l. beaker, 400 cc. of distilled water is added (**Note 4**), and the mixture is heated until complete solution results. On cooling, the **nicotinic acid nitrate** separates as yellow granular crystals and is filtered off. To obtain it absolutely pure, it may be recrystallized in a way similar to that just described but with the use of animal charcoal. It contains one molecule of water of crystallization and has a melting point of 190–192° (corr.). The yield is 420–460 g. 83–91 per cent of the theoretical amount).

The 420–460 g. of crude **nicotinic acid nitrate** from two runs (not necessarily dry) is dissolved in 900 cc. of boiling water in a 3-l. beaker, and 800 g. of crystalline disodium phosphate ($\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$) is added with constant stirring. The resulting thick mixture is stirred and heated almost to boiling for five minutes and then allowed to cool. The mixture is finally chilled to 0° by an ice bath. It is well to stir occasionally during the crystallization to prevent the formation of too solid a cake of crystalline material. The **nicotinic acid** is filtered off upon a 15-cm. Büchner funnel and washed with three 100-cc. portions of cold water.

The yield is 260–300 g. of material containing a small amount of mineral salts but otherwise nearly pure. It can be purified further by recrystallization from 2.5 to 3.5 l. (**Note 4**) of hot water, 150–180 g. of material, which melts at 230–232° (corr.), being obtained. The yield of recrystallized material is 50–60 per cent of the theoretical amount, based upon the **nicotine** employed.

The recrystallization is the least satisfactory part of this procedure and involves the greatest apparent loss of material; the product before recrystallization is sufficiently pure for most purposes. By evaporation of the mother liquors, 40–45 g. of pure **nicotinic acid** may be obtained, making the total yield of pure material 190–225 g. (63–74 per cent of the theoretical amount); in addition, a small amount of somewhat less pure material is recovered (**Note 5**).

2. Notes

1. Fuming **nitric acid**, the use of which is advised in the literature, is not so convenient and gives no

better results than concentrated [nitric acid](#).

2. A product of 100 per cent purity gives no better results than does the crude 95 per cent material used in this experiment.

Care should be exercised in handling [nicotine](#) because of its high toxicity.

3. If the [nicotine](#) and [nitric acid](#) mixture is merely placed on a steam bath and allowed to heat without control of the temperature, an occasional run will react violently, with loss of material.

4. The amounts of solvent given for the various recrystallizations are those which result in the best yields, and it is advisable to follow them as closely as possible.

5. [Nicotinic acid hydrochloride](#) may be obtained directly from the nitrate by heating on a steam bath 460 g. of crude nitrate with 1 l. of concentrated [hydrochloric acid](#) (sp. gr. 1.19). After six to eight hours, the evolution of gas ceases and the liquid is evaporated under diminished pressure. The dry salt is again treated with 500 cc. of [hydrochloric acid](#) and heated for five hours and then evaporated as before.

After the salt has been obtained again, it is dissolved in 400 cc. of hot water and the solution diluted with four times its volume of 95 per cent [alcohol](#). Upon cooling and stirring, the hydrochloride, melting at 273–274°, is obtained in a yield of 245–250 g. (63–65 per cent of the theoretical amount). An additional quantity of 75–80 g. may be obtained from the mother liquors.

3. Discussion

[Nicotinic acid](#) can be prepared by oxidation of [nicotine](#) with [nitric acid](#),¹ [potassium permanganate](#)² or [chromic acid](#),³ and by carbonation of the lithium derivative made from 3-bromopyridine.⁴

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 334](#)

References and Notes

1. Weidel, Ann. **165**, 330 (1873); Pictet and Rotschy, Ber. **34**, 702 (1901); Pictet and Sussdorff, Arch. sci. phys. nat. (4) **5**, 113 (1898) [Chem. Zentr. I, 677 (1898)]; McElvain and Adams, J. Am. Chem. Soc. **45**, 2738 (1923).
2. Laiblin, Ann. **196**, 134 (1879); Ber. **10**, 2136 (1877); Späth and Spitzer, Ber. **59**, 1482 (1926).
3. Hoogewerff and van Dorp, Rec. trav. chim. **1**, 121 (1882); Camps, Arch. Pharm. **240**, 353 (1902).
4. Gilman and Spatz, J. Am. Chem. Soc. **62**, 446 (1940).

Appendix

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

oxides of nitrogen

disodium phosphate ($\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$)

lithium derivative made from 3-bromopyridine

[alcohol](#) (64-17-5)

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

[nitric acid](#) (7697-37-2)

potassium permanganate (7722-64-7)

chromic acid (7738-94-5)

nitrogen dioxide (10102-44-0)

Nicotinic acid (59-67-6)

nicotine (22083-74-5)

nicotinic acid nitrate

Nicotinic acid hydrochloride (636-79-3)