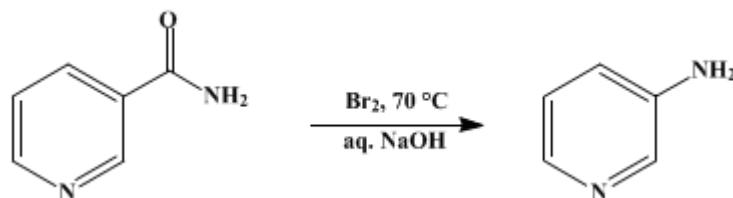


## 3-AMINOPYRIDINE

### [Pyridine, 3-amino-]



Submitted by C. F. H. Allen and Calvin N. Wolf<sup>1</sup>.

Checked by Cliff S. Hamilton and Marjorie Debrunner.

### 1. Procedure

In a 2-l. beaker equipped with a mechanical stirrer and immersed in an ice-salt bath is placed a solution of 75 g. (1.87 moles) of sodium hydroxide in 800 ml. of water. To the solution is added, with stirring, 95.8 g. (30.7 ml., 0.6 mole) of bromine. When the temperature of the solution reaches 0°, 60 g. (0.49 mole) of nicotinamide (Note 1) is added all at once with vigorous stirring. After being stirred for 15 minutes, the solution is clear. The ice-salt bath is replaced by a bath containing water at 75°, and the solution is stirred and heated at 70–75° for 45 minutes.

The solution is cooled to room temperature, saturated with sodium chloride (about 170 g. is required), and extracted with ether in a continuous extractor (Note 2). The extraction time is 15–20 hours. The ether extract is adjusted to a volume of 1 l., dried over 4–5 g. of sodium hydroxide pellets, and filtered, and the ether is removed by distillation from a steam bath. The residue crystallizes on cooling. The yield of dark red crystals melting at 61–63° is 39–41 g. (85–89%).

The crude product is dissolved in a mixture of 320 ml. of benzene and 80 ml. of ligroin (b.p. 60–90°) and heated on a steam bath with 5 g. of Norit and 2 g. of sodium hydrosulfite for 20 minutes. The hot solution is filtered by gravity, allowed to cool slowly to room temperature, and then chilled overnight in a refrigerator. The product is isolated by gravity filtration (Note 3), washed on the filter with 25 ml. of ligroin, and dried in a vacuum desiccator. The yield of white crystals melting at 63–64° amounts to 28–30 g. (61–65%). By concentrating the combined filtrate and washings to a volume of 150 ml., an additional 2–3 g. of pale yellow crystals melting at 62–64° can be obtained. The total yield of 3-aminopyridine is 30–33 g. (65–71%).

### 2. Notes

1. The nicotinamide should be finely powdered to facilitate rapid solution.
2. The continuous extractor described by Pearl<sup>2</sup> was used. If the material is extracted in a separatory funnel, four 800-ml. portions and ten 500-ml. portions of ether are required to give the above yield.
3. Since 3-aminopyridine is somewhat hygroscopic, it tends to liquefy if collected on a suction filter.

### 3. Discussion

3-Aminopyridine has been prepared by heating nicotinamide in an alkaline potassium hypobromite solution at 70°;<sup>3,4</sup> by hydrolysis of β-pyridylurethane with oleum;<sup>5</sup> by heating 3-aminopyridine-2-carboxylic acid at 250°;<sup>6</sup> by reduction of 3-nitropyridine with zinc and hydrochloric acid;<sup>7</sup> by heating 3-bromopyridine with ammonia and copper sulfate in a sealed tube;<sup>8,9</sup> and by the hydrolysis of benzyl 3-pyridylcarbamate, prepared from nicotinic acid hydrazide through the corresponding azide.<sup>10</sup>

This preparation is referenced from:

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## References and Notes

1. Eastman Kodak Company, Rochester, New York.
  2. Pearl, *Ind. Eng. Chem., Anal. Ed.*, **16**, 62 (1944).
  3. Camps, *Arch. Pharm.*, **240**, 354 (1902).
  4. Philips, *Ann.*, **288**, 263 (1895).
  5. Curtius and Mohr, *Ber.*, **31**, 2494 (1898).
  6. Gabriel and Colman, *Ber.*, **35**, 2833 (1902).
  7. Binz and Räth, *Ann.*, **486**, 95 (1931).
  8. Maier-Bode, *Ber.*, **69**, 1534 (1936).
  9. Gitsels and Wibaut, *Rec. trav. chim.*, **60**, 176 (1941).
  10. Sugasawa, Akahoshi, Toda, and Tomisawa, *J. Pharm. Soc. Japan*, **72**, 192 (1952) [*C. A.*, **47**, 6418 (1953)].
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## Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

ligroin

$\beta$ -pyridylurethane

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

Benzene (71-43-2)

ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

bromine (7726-95-6)

copper sulfate (7758-98-7)

sodium hydrosulfite (7775-14-6)

Norit (7782-42-5)

zinc (7440-66-6)

potassium hypobromite

3-Aminopyridine,

[Pyridine, 3-amino-](#) (462-08-8)

[nicotinamide](#) (98-92-0)

[3-aminopyridine-2-carboxylic acid](#)

[3-nitropyridine](#) (2530-26-9)

[3-bromopyridine](#) (626-55-1)

[benzyl 3-pyridylcarbamate](#)

[nicotinic acid hydrazide](#) (553-53-7)

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