Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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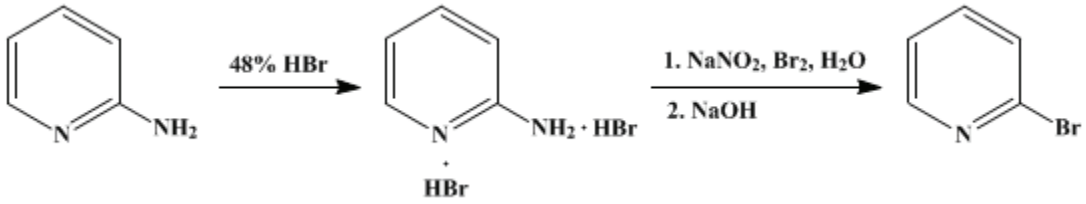
2-BROMOPYRIDINE

[Pyridine, 2-bromo-]



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1. Procedure

In a 5-l. three-necked flask fitted with a mechanical stirrer (Note 1), a dropping funnel, and a thermometer for reading low temperatures is placed 790 ml. (7 moles) of 48% hydrobromic acid. The flask and contents are cooled to 10–20° in an ice-salt bath, and 150 g. (1.59 moles) of 2-aminopyridine (Note 2) is added over a period of about 10 minutes. While the temperature is kept at 0° or lower, 240 ml. (4.7 moles) of bromine is added dropwise (Note 3). A solution of 275 g. (4 moles) of sodium nitrite in 400 ml. of water is added dropwise over a period of 2 hours, the temperature being carefully maintained at 0° or lower (Note 4). After an additional 30 minutes of stirring, a solution of 600 g. (15 moles) of sodium hydroxide in 600 ml. of water is added at such a rate that the temperature does not rise above 20–25° (Note 5). The nearly colorless reaction mixture is extracted with four 250-ml. portions of ether (Note 6). The extract is dried for 1 hour over 100 g. of solid potassium hydroxide and is then distilled through a Vigreux column 15 cm. in length. 2-Bromopyridine distils at 74–75°/13 mm., and the yield is 216–230 g. (86–92%) (Note 7).

2. Notes

1. A stirrer which gives efficient stirring near the walls of the flask is advisable. The fittings should not be gas tight since oxides of nitrogen and bromine are evolved during the reaction. It is advisable to work in a hood or out-of-doors.
2. The checkers used Eastman Kodak Company's practical grade of 2-aminopyridine.
3. The reaction mixture thickens, owing to formation of a yellow-orange perbromide during the addition of about one-half of the bromine; the first half of the bromine is added over a period of 30 minutes; the second half, over a period of 15 minutes.
4. The ice-salt bath is renewed before the sodium nitrite is added and once during the addition.
5. The color of the reaction mixture darkens during the addition of the alkali but becomes light yellow toward the end.
6. The separation into layers may not take place readily. The use of a "lily" may be helpful in separating the ether layer. A "lily"[1] is essentially a U-tube having unequal legs, the shorter of which has a flared top. It is easily prepared from a thistle or funnel tube by making a U bend just below the funnel. In use, a suction flask to act as a receiver is attached by means of rubber tubing. With this device it is a simple matter to draw off the upper layer when making separations, in any wide-mouth bottle or open jar. It may be necessary to filter the intermediate layer before attempting the separation.
7. This procedure can be used with 7 times the above amounts in a 22-l. flask, cooled in a half-barrel. A "Lightnin" stirrer is required (Model C-2).

3. Discussion

2-Bromopyridine has been made by direct bromination of pyridine;[2] from N-methyl-2-pyridone with phosphorus pentabromide and phosphorus oxybromide;[3] from 2-aminopyridine by diazotization

with amyl nitrite in 20% hydrobromic acid;[4] from sodium 2-pyridinediazotate by solution in concentrated hydrobromic acid;[5] from 2-aminopyridine by diazotization in the presence of bromine and concentrated hydrobromic acid;[6] and from 2-aminopyridine by diazotization with nitrogen trioxide in 40% hydrobromic acid.[7] The method described here is essentially that of Craig.[6]

References and Notes

1. Private communication, Emil J. Rahrs, Eastman Kodak Company.
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3. Fischer, *Ber.*, **32**, 1303 (1899).
4. Tschitschibabin and Rjasanzew, *J. Russ. Phys. Chem. Soc.*, **47**, 1571 (1915) (*Chem. Zentr.*, **1916**, II, 228); *J. Chem. Soc.*, **110**, I, 224 (1916) [*C. A.*, **10**, 2898 (1916)].
5. Tschitschibabin and Tjashelowa, *J. Russ. Phys. Chem. Soc.*, **50**, 495 (1918) (*Chem. Zentr.*, **1923**, III, 1021).
6. Craig, *J. Am. Chem. Soc.*, **56**, 232 (1934).
7. Newman and Fones, *J. Am. Chem. Soc.*, **69**, 1221 (1947).

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

oxides of nitrogen

sodium 2-pyridinediazotate

ether (60-29-7)

sodium hydroxide (1310-73-2)

HYDROBROMIC ACID (10035-10-6)

bromine (7726-95-6)

sodium nitrite (7632-00-0)

pyridine (110-86-1)

potassium hydroxide (1310-58-3)

amyl nitrite (463-04-7)

phosphorus oxybromide

phosphorus pentabromide (7789-69-7)

2-aminopyridine (504-29-0)

N-methyl-2-pyridone (694-85-9)

2-Bromopyridine,
Pyridine, 2-bromo- (109-04-6)

nitrogen trioxide

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