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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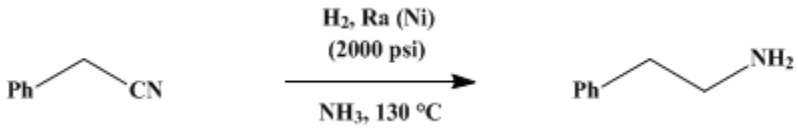
β-PHENYLETHYLAMINE

[Phenylethylamine]



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1. Procedure

In a 2-l. bomb are placed 1 kg. (8.55 moles) of pure (Note 1) benzyl cyanide and 1 tablespoon of Raney nickel catalyst (p. 181). After the cap is securely fastened down, 150 ml. of liquid ammonia is introduced (Note 2). Hydrogen is introduced until the pressure is about 2000 lb. The bomb is then heated to 120–130° and shaking is begun. The reduction is complete well within an hour (Note 1). The bomb is cooled and opened, and the contents are removed. The bomb is rinsed with a little ether, and the combined liquids are filtered from the catalyst. The ether is removed, and the residue is fractionated under reduced pressure. The yield is 860–890 g. (83–87%) of β-phenylethylamine, b.p. 90–93°/15 mm. (Note 3), (Note 4), (Note 5).

2. Notes

1. Benzyl cyanide, prepared according to *Org. Syntheses* Coll. Vol. 1, 107 (1941), should be distilled from Raney nickel. Minute traces of halide have a strong poisoning effect on the catalyst. If the reduction does not occur within an hour, the contents of the bomb should be removed and filtered. New catalyst is then added and the process is repeated.
2. The presence of ammonia in the reduction mixture reduces the amount of secondary amine formed. For directions for introducing the liquid ammonia, see Note 1 to the preparation of α-phenylethylamine (p. 718).
3. If several runs are made, a small amount of the secondary amine may be recovered from the combined residues. Di-(β-phenylethyl)-amine boils at 155–157°/4 mm.
4. Similarly *n*-amyl cyanide has been converted to *n*-hexylamine, b.p. 128–130°, in 67–70% yields.
5. It has been reported (R. N. Icke and C. E. Redemann, private communication) that β-phenylethylamine, as well as several substituted β-phenylethylamines, may be prepared in excellent yields by catalytic reduction of the corresponding cyanides in 10 *N* methanolic ammonia. An example of this procedure follows. Commercial anhydrous methanol is saturated with ammonia gas at 0°; this solution is approximately 10 *N*. A solution of 58.5 g. (0.5 mole) of benzyl cyanide in 300 ml. of 10 *N* methanolic ammonia (the ratio of ammonia to benzyl cyanide should be at least 5:1 in order to minimize the formation of the secondary amine) is placed in a high-pressure hydrogenation bomb, 5–10 ml. of settled Raney nickel catalyst (p. 181) is added, the bomb is closed, and hydrogen is introduced until the pressure is 500–1000 lb. The bomb is shaken and heated to 100–125° until absorption of hydrogen ceases (about 2 hours). The bomb is cooled and opened, and the contents are removed. The bomb is rinsed with two or three 100-ml. portions of methanol, and the combined liquids are poured through a fluted filter to remove the catalyst. (*Caution! If the catalyst becomes dry, it is likely to ignite.*) The solvent and the ammonia are removed by distillation, and the residue is fractionated through a short column. The yield of β-phenylethylamine boiling at 92–93°/19 mm. (62–63°/4 mm.) is 51–54.5 g. (84–90%). The hydrochloride, after crystallization from dry ethanol, melts at 218–219°. This procedure has also been used for preparation of the following β-phenylethylamines from the cyanides; the yields of amines were uniformly high: 3,4-dimethoxyphenylethylamine, b.p. 119–119.5°/1 mm.; *o*-methylphenylethylamine, b.p. 67°/0.5 mm.; *m*-methylphenylethylamine, b.p. 68°/2 mm.; *p*-methylphenylethylamine, b.p. 71°/2 mm.; and 3,4-methylenedioxyphenylethylamine, b.p. 109°/2 mm.

3. Discussion

β-Phenylethylamine has been made by a number of reactions, many of which are unsuitable for preparative purposes. Only the most important methods, from a preparative point of view, are given here. The present method is adapted from that of Adkins,[1] which in turn was based upon those of Mignonac,[2] von Braun and coworkers,[3] and Mailhe.[4] Benzyl cyanide has been converted to the amine by catalytic reduction with palladium on charcoal,[5] with palladium on barium sulfate,[6] and with Adams' catalyst;[7] by chemical reduction with sodium and ethanol,[8] and with zinc dust and mineral acids.[9] Hydrocinnamic acid has been converted to the azide and thence by the Curtius rearrangement to β-phenylethylamine;[10] also the Hofmann degradation of hydrocinnamide has been used successfully.[11] β-Nitrostyrene,[12] phenylthioacetamide,[13] and the benzoyl derivative of mandelonitrile[14] all yield β-phenylethylamine upon reduction. The amine has also been prepared by cleavage of N-(β-phenylethyl) phthalimide[15] with hydrazine; by the Delépine synthesis from β-phenylethyl iodide and hexamethylenetetramine;[16] by the hydrolysis of the corresponding urethan and urea;[17] by reduction of phenylacetaldoxamine;[18] and by catalytic reduction of O-carbethoxymandelonitrile in the presence of acids.[19]

More recent methods for preparation of the amine include the lithium aluminum hydride reduction of β-nitrostyrene[20] and of phenylacetamide.[21]

The Raney nickel reduction of the nitrile in the presence of formamide is reported to give an 87% yield of the formylated primary amine.[22]

References and Notes

1. Adkins, *The Reaction of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts*, University of Wisconsin Press, Madison, Wisconsin, 1937, pp. 53–54.
2. Mignonac, French pat. 638,550 [*C. A.*, **23**, 154 (1929)]; Brit. pat. 282,038 [*C. A.*, **22**, 3668 (1928)].
3. von Braun, Blessing, and Zobel, *Ber.*, **56**, 1988 (1923).
4. Mailhe, *Bull. soc. chim. France*, (4) **23**, 237 (1918).
5. Strack and Schwaneberg, *Ber.*, **65**, 710 (1932).
6. Rosenmund and Pfannkuch, *Ber.*, **56**, 2258 (1923).
7. Carothers and Jones, *J. Am. Chem. Soc.*, **47**, 3051 (1925).
8. Wohl and Berthold, *Ber.*, **43**, 2184 (1910).
9. Bernthsen, *Ann.*, **184**, 304 (1877).
10. Sah and Kao, *Science Repts. Natl. Tsing Hua Univ., Ser. A*, **3**, 525 (1936) [*C. A.*, **31**, 3889 (1937)].
11. McRae and Vining, *Can. J. Research*, **6**, 409 (1932).
12. Kindler, Brandt, and Gehlhaar, *Ann.*, **511**, 209 (1934).
13. Kindler, *Ber.*, **57**, 775 (1924).
14. Hartung, *J. Am. Chem. Soc.*, **50**, 3373 (1928).
15. Ing and Manske, *J. Chem. Soc.*, **1926**, 2348.
16. Galat and Elion, *J. Am. Chem. Soc.*, **61**, 3585 (1939).
17. Curtius and Jordan, *J. prakt. Chem.*, (2) **64**, 308 (1901).
18. Bischler and Napieralski, *Ber.*, **26**, 1905 (1893).
19. Indler and Schrader, *Ann.*, **564**, 49 (1949).
20. Nystrom and Brown, *J. Am. Chem. Soc.*, **70**, 3738 (1948).
21. Uffer and Schlittler, *Helv. Chim. Acta*, **31**, 1397 (1948).
22. Sekiya, *J. Pharm. Soc. Japan*, **70**, 520 (1950).

Appendix

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

benzoyl derivative of mandelonitrile

phenylacetaldoxamine

ethanol (64-17-5)

ammonia (7664-41-7)

methanol (67-56-1)

ether (60-29-7)

formamide (75-12-7)

hydrogen (1333-74-0)

nickel,
Raney nickel (7440-02-0)

barium sulfate (7727-43-7)

zinc (7440-66-6)

sodium (13966-32-0)

palladium (7440-05-3)

Benzyl cyanide (140-29-4)

urea (57-13-6)

hydrazine (302-01-2)

Hydrocinnamic acid (501-52-0)

hexamethylenetetramine (100-97-0)

β-Nitrostyrene (102-96-5)

α-Phenylethylamine (3886-69-9)

Phenylethylamine,
β-Phenylethylamine (64-04-0)

lithium aluminum hydride (16853-85-3)

n-amyl cyanide (628-73-9)

Di-(β-phenylethyl)-amine

3,4-dimethoxyphenylethylamine (120-20-7)

3,4-methylenedioxyphenylethylamine (1484-85-1)

hydrocinnamide (102-93-2)

phenylthioacetamide (645-54-5)

N-(β-phenylethyl) phthalimide

β-phenylethyl iodide (17376-04-4)

O-carbethoxymandelonitrile

Phenylacetamide (103-81-1)

n-hexylamine (111-26-2)

o-methylphenylethylamine

m-methylphenylethylamine

p-methylphenylethylamine (3261-62-9)