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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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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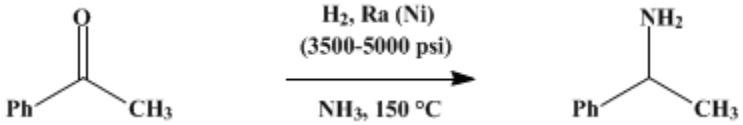
Organic Syntheses, Coll. Vol. 3, p.717 (1955); Vol. 23, p.68 (1943).

α-PHENYLETHYLAMINE

[Benzylamine, α-methyl-]



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1. Procedure

In a 2-l. bomb are placed 720 g. (6 moles) of pure acetophenone and 1 tablespoon of Raney nickel catalyst (p. 181). After the cap and gauge block are securely fastened, 700 ml. (30 moles) of liquid ammonia is introduced (Note 1). The mixture is hydrogenated at 150° under 5000–3500 lb. (Note 2). The reaction is allowed to continue as long as hydrogen is absorbed, generally 4–6 hours. The bomb is cooled, the excess ammonia is allowed to escape, and the contents are filtered from the catalyst. The mixture is cooled in an ice bath, acidified to Congo red with concentrated hydrochloric acid (200–300 ml.), and steam-distilled for 10–12 hours to remove excess acetophenone (Note 3). The residue is then cooled and added slowly to 200 g. of solid sodium hydroxide in a flask surrounded by an ice bath. The amine is separated, and the aqueous layer is extracted with three 150-ml. portions of benzene. The extracts and amine are combined and dried over solid sodium hydroxide. After removal of the benzene, the residue is fractionated under diminished pressure. The yield of α-phenylethylamine (Note 4), b.p. 80–81°/18 mm., is 320–380 g. (Note 5) (44ndash;52%).

2. Notes

1. Liquid ammonia is introduced into the large bomb as follows: The cap and gauge block of the large bomb are tightened in place. The inner gas inlet tube is removed from the cap assembly of a smaller bomb (capacity about 250 ml.). This bomb is equipped with a test-tube-type liner which is kept chilled in a bath of Dry Ice while it is filled with liquid ammonia. This test tube is then placed in the small bomb, and the cap and gauge block are quickly (15–30 seconds) tightened. The bomb is then filled with hydrogen under high pressure and connected with the larger bomb by means of a short length of the conventional steel pressure tubing. The smaller bomb is inverted, and the valves are opened. This operation will introduce about 150 ml. of liquid ammonia at one time and may be repeated as often as necessary.
2. A booster pump is required, for it is quite important to keep the pressure above the minimum value of about 3500 lb. The temperature of the reduction is above the critical temperature of ammonia, and the pressure will not fall much below 3500 lb. At this point hydrogen must be pumped into the bomb until the pressure is about 5000 lb.; this process is repeated until the reaction is complete. If a safety disk is to be incorporated into the line, it *must not* be made of *copper*, as ammonia, even under 2–3 atm., rapidly attacks copper. A *special* disk of steel, nickel, or other suitable material is required.
3. It is necessary to heat the flask externally with a flame or the volume of the solution will greatly increase during the lengthy steam distillation.
4. According to the submitters, methyl amyl ketone (800 g.) and ammonia (600 ml.) have been converted to 2-aminoheptane, b.p. 139–141°, in exactly the same manner, in 50–55% yields. A slightly modified procedure was used in the preparation of *n*-heptylamine and furfurylamine. Heptaldehyde (320 g.) was dissolved in 500 ml. of methanol, and 150 ml. of liquid ammonia was added; the reduction was conducted as above. *n*-Heptylamine, b.p. 57–58°/23 mm., was obtained in yields of 53–63%. Freshly distilled furfural (290 g.) was dissolved in 500 ml. of methanol, 150 ml. of liquid ammonia was introduced, and the reduction carried out as usual. The product was removed, filtered, and fractionated directly. Furfurylamine, b.p. 144–146°, was obtained in 50% yield.
5. The yields are based upon the amount of acetophenone initially used and do not make allowances for

the material recovered from the steam distillation. A small amount of di-(α-phenylethyl) amine, b.p. 61–62°/2 mm., may be recovered from the residues.

3. Discussion

α-Phenylethylamine has been prepared by reducing acetophenone with hydrogen at high pressures over nickel catalysts in the presence of ammonia;[1,2] with hydrogen at low pressures over a nickel catalyst in the presence of ammonia-saturated ethanol;[3] and with hydrogen at low pressures over a platinum catalyst in the presence of ammonia-saturated methanol containing ammonium chloride (69% yield).[4]

l-α-Phenylethylamine has been prepared through the oxime of *d*-α-phenylethyl methyl ketone by the Beckmann rearrangement;[5] from *d*-phenylmethylacethydroxamic acid by the Lossen rearrangement;[5] from *d*-hydratropic azide;[6,7] from *d*-hydratropic acid by the Schmidt reaction;[5] from *d*-hydratropamide by treatment with alkaline hypobromite;[8] and by the reduction of acetophenone oxime with lithium aluminum hydride.[9]

Other methods of preparing α-phenylethylamine are reviewed in *Org. Syntheses* Coll. Vol. 2, 503 (1943), where detailed directions are given for the preparation of this amine from acetophenone and ammonium formate. The procedure given above was based upon that of Schwoegler and Adkins.[2]

Methods of preparing *d*- and *l*-α-phenylethylamine, based on the resolution of *dl*-α-phenylethylamine, are reviewed in *Org. Syntheses* Coll. Vol. 2, 506 (1943), where detailed directions are given for the resolution of this amine by *l*-malic and *d*-tartaric acids.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 50
- Org. Syn. Coll. Vol. 3, 229
- Org. Syn. Coll. Vol. 3, 720
- Org. Syn. Coll. Vol. 5, 909

References and Notes

1. Couturier, *Ann. chim.*, (11) **10**, 610 (1938).
2. Schwoegler and Adkins, *J. Am. Chem. Soc.*, **61**, 3499 (1939).
3. Mignonac, *Compt. rend.*, **172**, 223 (1921).
4. Alexander and Misegades, *J. Am. Chem. Soc.*, **70**, 1315 (1948).
5. Campbell and Kenyon, *J. Chem. Soc.*, **1946**, 25.
6. Bernstein and Whitmore, *J. Am. Chem. Soc.*, **61**, 1324 (1939).
7. Kenyon and Young, *J. Chem. Soc.*, **1941**, 263.
8. Arcus and Kenyon, *J. Chem. Soc.*, **1939**, 916.
9. Larsson, *Trans. Chalmers Univ. Technol., Gothenburg*, **94**, 15 (1950) [*C. A.*, **45**, 1494 (1951)].

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

D- and L-α-Phenylethylamine

oxime of d-α-phenylethyl methyl ketone

l-malic and d-tartaric acids

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

Benzene (71-43-2)

methanol (67-56-1)

ammonium chloride (12125-02-9)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

platinum (7440-06-4)

copper (7440-50-8)

nickel (7440-02-0)

Acetophenone (98-86-2)

hypobromite

Furfural (98-01-1)

Methyl amyl ketone (110-43-0)

α-Phenylethylamine,
Benzylamine, α-methyl-,
dl-α-phenylethylamine,
l-α-Phenylethylamine (3886-69-9)

ammonium formate (540-69-2)

di-(α-phenylethyl) amine

acetophenone oxime

lithium aluminum hydride (16853-85-3)

2-aminoheptane (123-82-0)

furfurylamine (617-89-0)

d-hydratropic acid (492-37-5)

heptaldehyde (111-71-7)

n-heptylamine (111-68-2)

d-phenylmethylacethydroxamic acid

d-hydratropic azide

d-hydratropamide