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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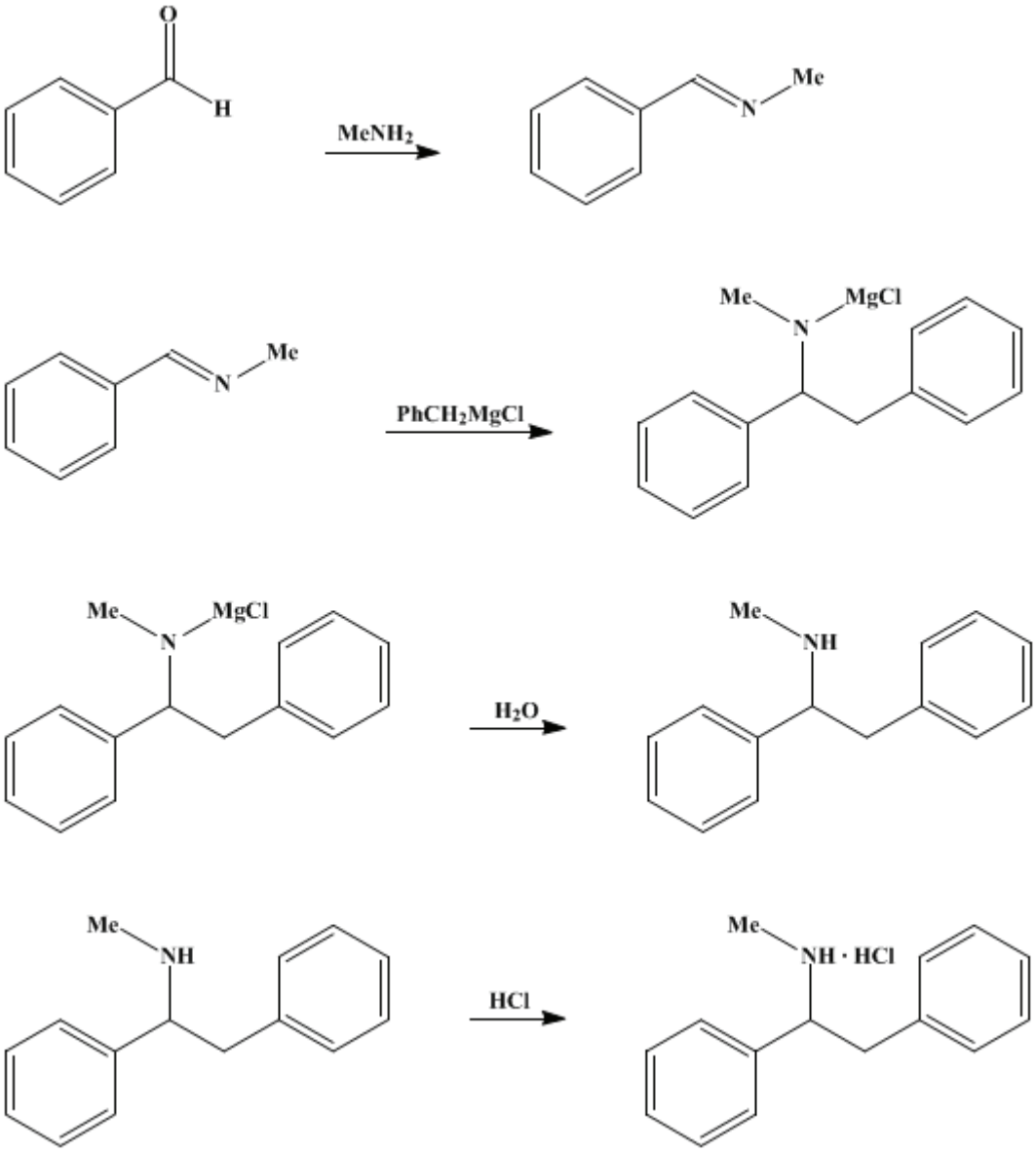
N-METHYL-1,2-DIPHENYLETHYLAMINE AND HYDROCHLORIDE

[Ethylamine, 1,2-diphenyl-N-methyl-]



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1. Procedure

A. *N-Benzylidenemethylamine*. A solution of 31.9 g. (0.3 mole) of benzaldehyde in 80 ml. of benzene contained in a 300-ml. round-bottomed flask is cooled to approximately 10°. To this is added a solution of 14 g. (0.45 mole) of anhydrous methylamine in 50 ml. of benzene (Note 1). On standing, the solution becomes warm and turns milky. After 1 hour the flask is connected to a DeanStark water separator[2] which is attached to a reflux condenser, and the solvent is caused to reflux until no more water separates (Note 2). The water separator is then replaced by an 8-in. Vigreux column (Note 3), and

the solution is distilled under reduced pressure. After removal of the solvent, the product distils at 92–93°/34 mm. The yield is 31–34 g. (87–95%) of colorless liquid, n_D^{25} 1.5497, n_D^{20} 1.5528.

B. *N-Methyl-1,2-diphenylethylamine*. Benzylmagnesium chloride is prepared in a 1-l. three-necked flask as described previously,[3] using 19.5 g. (0.8 g. atom) of magnesium, 92 ml. (102 g., 0.8 mole) of benzyl chloride, and 300 ml. of anhydrous ether. From the dropping funnel a solution of 24.0 g. (0.2 mole) of N-benzylidenemethylamine in 50 ml. of anhydrous ether or benzene (Note 3) is added slowly to the Grignard reagent with stirring. After being stirred at reflux temperature for 2 hours, the mixture is cooled and poured slowly into a mixture of ice and 200 ml. of concentrated hydrochloric acid. The layers are separated, the ether layer is extracted with 100 ml. of water, and the ether solution is discarded. The aqueous layer and water extract are combined, washed with 100 ml. of ether, and made strongly basic with about 600 ml. of 20% aqueous sodium hydroxide solution. The aqueous suspension of magnesium hydroxide is extracted with 800 ml. of ether in a continuous extractor for 48 hours. The ether extract is washed with about 150 ml. of water and dried over anhydrous potassium carbonate. The solution is filtered from the drying agent, the solvent is removed by distillation on a steam bath, and the residue is distilled from a Claisen flask under reduced pressure. The product distils at 83–90°/0.04 mm., 90–93°/0.2 mm., 94–97°/0.3 mm. The yield is 38.4–40.5 g. (91–96%) of colorless liquid, n_D^{25} 1.5640,n_D^{20} 1.5667.

C. *N-Methyl-1,2-diphenylethylamine hydrochloride*. Hydrogen chloride gas (Note 4) is passed into a stirred solution of 30 g. (0.14 mole) of N-methyl-1,2-diphenylethylamine in 500 ml. of anhydrous ether until saturated or until a drop of the ether on moistened pH test paper indicates that it is strongly acid. The hydrochloride separates as a colorless crystalline precipitate. It is collected on a suction filter, washed with ether, and dried. The yield is 34.2–35.1 g. (97–100%), and the product is practically pure, m.p. 184–186°. If desired it can be recrystallized by dissolution in a little methanol followed by addition of absolute ether.

2. Notes

1. Methylamine is most conveniently obtained commercially in cylinders. However, it can be generated by adding 50% aqueous sodium hydroxide solution dropwise to a flask containing the hydrochloride, and allowing the amine to distil. It can also be generated by allowing an aqueous solution of methylamine to drop into a flask containing solid sodium or potassium hydroxide. The methylamine is distilled directly below the surface of a weighed quantity of benzene kept just above its freezing point. The resulting solution is reweighed to determine the concentration, or an aliquot can be titrated with standard acid.
2. The collection of the theoretical amount of water (about 5.4 ml.) requires approximately 3 hours.
3. For the preparation of N-methyl-1,2-diphenylethylamine it is not absolutely necessary to distil the N-benzylidenemethylamine. The dried benzene solution can be used directly.
4. Hydrogen chloride gas is most conveniently obtained in a cylinder which should be connected to the outlet tube through a safety trap. It can be generated if desired.[4]

3. Discussion

The only practical method for preparing N-benzylidenemethylamine is by the reaction of benzaldehyde with methylamine.[5,6,7]

N-Methyl-1,2-diphenylethylamine has been prepared in 8% yield by the Leuckart reaction from deoxybenzoin and methylammonium formate[8] and by the present method.[9]

References and Notes

1. The Upjohn Company, Kalamazoo, Michigan.
2. *Org. Syntheses Coll. Vol.* **3**, 382 (1955).
3. *Org. Syntheses Coll. Vol.* **1**, 471 (1941).
4. *Org. Syntheses Coll. Vol.* **1**, 293, 534 (1941).

5. Zaunschirm, *Ann.*, **245**, 279 (1888).
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7. Campbell, Helbing, Florkowski, and Campbell, *J. Am. Chem. Soc.*, **70**, 3868 (1948).
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9. Moffett and Hoehn, *J. Am. Chem. Soc.*, **69**, 1792 (1947).

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

N-METHYL-1,2-DIPHENYLETHYLAMINE AND HYDROCHLORIDE

potassium carbonate (584-08-7)

hydrogen chloride,
hydrochloric acid (7647-01-0)

Benzene (71-43-2)

methanol (67-56-1)

ether (60-29-7)

sodium hydroxide (1310-73-2)

magnesium (7439-95-4)

benzaldehyde (100-52-7)

potassium hydroxide (1310-58-3)

sodium (13966-32-0)

benzyl chloride (100-44-7)

benzylmagnesium chloride (6921-34-2)

magnesium hydroxide

methylamine (74-89-5)

N-Methyl-1,2-diphenylethylamine,
Ethylamine, 1,2-diphenyl-N-methyl- (53663-25-5)

N-benzylidenemethylamine (622-29-7)

N-Methyl-1,2-diphenylethylamine hydrochloride (7400-77-3)

deoxybenzoin (451-40-1)

methylammonium formate