



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.

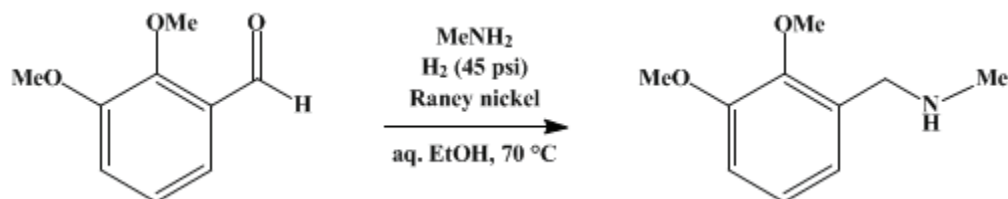
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.603 (1963); Vol. 30, p.59 (1950).

N-METHYL-2,3-DIMETHOXYBENZYLAMINE

[Benzylamine, 2,3-dimethoxy-N-methyl-]



Submitted by Don M. Balcom and C. R. Noller¹.
Checked by Homer Adkins and Walter W. Gilbert.

1. Procedure

To a solution of 41.6 g. (0.25 mole) of purified 2,3-dimethoxybenzaldehyde (Note 1) in 150 ml. of 95% ethanol is added 23.4 g. (0.75 mole) of methylamine in 50 to 75 ml. of water (Note 2). The mixture is heated to boiling and placed in a 500-ml. heavywalled bottle (Note 3), and 6 g. of Raney nickel catalyst is added (Note 4). The bottle is connected to a low-pressure hydrogenation apparatus,² the system is flushed with hydrogen, and the mixture is shaken with hydrogen at an initial pressure of 45 lb. until 0.25 mole of hydrogen is absorbed and the absorption ceases (Note 5).

After the completion of the reduction the catalyst is removed by filtration and the alcohol is evaporated on the steam bath. To the resulting syrupy solution is added about 85 ml. of 3*N* hydrochloric acid (sufficient to make the solution acid to Congo red paper). The solution is extracted with three 50-ml. portions of ether. The aqueous layer is made alkaline with 50 ml. of 6*N* sodium hydroxide, and the amine layer is separated. The aqueous layer is extracted with three 50-ml. portions of ether, and the extracts are combined with the amine layer. The ether solution is dried overnight with solid potassium hydroxide and is filtered to remove suspended matter; the flask is rinsed with 25 ml. of ether. The ether is removed on a steam bath, and the amine is distilled under reduced pressure from a modified Claisen flask having a 15-cm. indented column. The *N*-methyl-2,3-dimethoxybenzylamine distils at 120–124°/8 mm. and is obtained in a yield of 39–42 g. (86–93%) (Note 6) and (Note 7).

2. Notes

1. The 2,3-dimethoxybenzaldehyde employed was a darkcolored product supplied by the Monsanto Chemical Company or Eastman Kodak Company. It was purified by distilling at reduced pressure and crystallizing from methanol, after which it was colorless and melted at 52–54°.
2. The submitters used 72 g. of a 33% water solution of methylamine; the checkers used 100 g. of a 23% solution.
3. The submitters used a pint hydrogenation bottle wound with 30 ft. of No. 24 Nichrome wire insulated with asbestos paper. Before the reaction the current was adjusted by means of a variable transformer so that the solution was maintained at approximately 70° during the reaction. The checkers used a 500-ml. centrifuge bottle without provision for heating.
4. The submitters used Raney nickel catalyst prepared as described by Mozingo.³ The checkers used W-6 Raney nickel catalyst.⁴
5. The time required depends upon the activity of the catalyst and the temperature of reaction. The submitters reported that 90–95% of the calculated amount of hydrogen was taken up in 90 minutes at 70° whereas 20 hours was required at room temperature. The checkers found the reaction to be complete after 36 to 41 minutes, the temperature dropping during the period from 70° to 30° since no provision was made for heating. When the whole hydrogenation was carried out at room temperature the period of reaction was 90 minutes with the W-6 Raney nickel catalyst.
6. The submitters state that with a 1:1 mole ratio of aldehyde to amine the yield dropped to 75%, presumably because more of the aldehyde was reduced.

7. The submitters report that similar yields of methylarylamines were obtained from [benzaldehyde](#), [anisaldehyde](#), [veratraldehyde](#), and [piperonal](#).

3. Discussion

N-Methyl-2,3-dimethoxybenzylamine has been prepared by the reaction of 2,3-dimethoxybenzyl chloride with [methylamine](#)⁵ and by the catalytic reduction of a mixture of 2,3-dimethoxybenzaldehyde and [methylamine](#) using Adams' [platinum](#) catalyst.⁶

References and Notes

1. Stanford University, Stanford, California.
 2. *Org. Syntheses Coll. Vol. 1*, 61 (1941).
 3. *Org. Syntheses Coll. Vol. 3*, 181 (1955).
 4. Adkins and Billica, *J. Am. Chem. Soc.*, **70**, 695 (1948); *Org. Syntheses Coll. Vol. 3*, 176 (1955).
 5. Douetteau, *Bull. soc. chim. France*, [4] **11**, 655 (1912); Ishii and Mariani, *Anales asoc. quím. argentina*, **33**, 167 (1945) [*C. A.*, **41**, 2399 (1947)].
 6. Sapp, Dissertation, Stanford University, 1940.
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

W-6 Raney nickel

[ethanol](#) (64-17-5)

[hydrochloric acid](#) (7647-01-0)

[methanol](#) (67-56-1)

[ether](#) (60-29-7)

[hydrogen](#) (1333-74-0)

[sodium hydroxide](#) (1310-73-2)

[platinum](#) (7440-06-4)

[benzaldehyde](#) (100-52-7)

[Raney nickel](#) (7440-02-0)

[potassium hydroxide](#) (1310-58-3)

[methylamine](#) (74-89-5)

[Veratraldehyde](#) (120-14-9)

[piperonal](#) (120-57-0)

2,3-dimethoxybenzaldehyde (86-51-1)

N-Methyl-2,3-dimethoxybenzylamine,
Benzylamine, 2,3-dimethoxy-N-methyl- (53663-28-8)

2,3-dimethoxybenzyl chloride

anisaldehyde (123-11-5)