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.

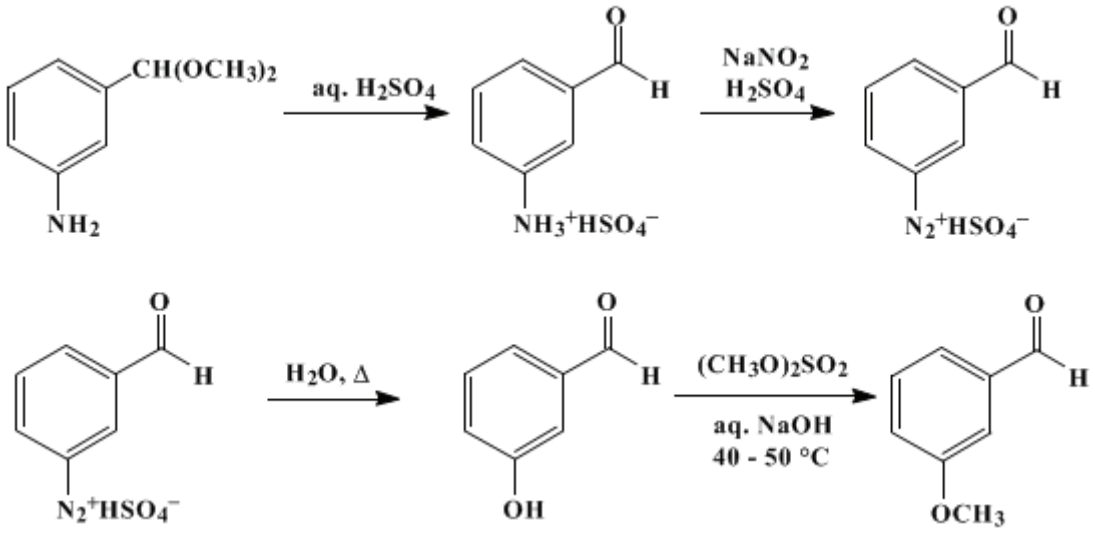
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.029.0063

Organic Syntheses, Coll. Vol. 3, p.564 (1955); Vol. 29, p.63 (1949).

m-METHOXYBENZALDEHYDE

[Benzaldehyde, *m*-methoxy-]



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1. Procedure

A. *m-Hydroxybenzaldehyde*. In a 2-l. three-necked flask, equipped with a mechanical stirrer, a thermometer, and a 250-ml. dropping funnel, 575 ml. of 6 *N* sulfuric acid is cooled to 0° by means of a salt-ice bath. The acid is stirred and maintained at 0° or below while 167 g. (1 mole) of *m*-aminobenzaldehyde dimethylacetal (p. 59) is added dropwise. The solution becomes deep orange or red. When the addition of the amino compound is complete, a solution of 71 g. (1 mole) of 97% sodium nitrite in about 175 ml. of water is introduced slowly while the temperature of the acid solution is maintained at 5°. Stirring at 5° is continued for 1 hour to complete the reaction.

In each of two 4-l. beakers are placed 450 ml. of water and 50 ml. of concentrated sulfuric acid, and the solutions are heated to boiling with large burners. The cold diazonium solution is divided into two approximately equal portions which are placed in 500-ml. separatory funnels suspended above the beakers containing the boiling acid. The two portions of the diazonium solution are run dropwise into the strongly heated acid at such a rate that boiling continues. The solutions are boiled for 5 minutes after the additions are complete. They are then allowed to cool to room temperature and are finally stored overnight in a refrigerator. The crude product separates as a dark oil which crystallizes (Note 1) and becomes lighter in color upon standing. It is collected on a Büchner funnel and used in part B without purification (Note 2).

Methyl sulfate is quite toxic. Caution! The methylation should be carried out in a good hood.

B. *m-Methoxybenzaldehyde*. The crude *m*-hydroxybenzaldehyde is dissolved in about 550 ml. of 2 *N* sodium hydroxide in a 2-l. three-necked flask equipped with a mechanical stirrer, a thermometer, and a 125-ml. dropping funnel. The dark-colored solution is stirred while 126 g. (95 ml., 1 mole) of methyl sulfate (Note 3) is added dropwise and the temperature is maintained at 40–45°. When the addition is complete the mixture is stirred for 5 minutes. A 275-ml. portion of 2 *N* sodium hydroxide (Note 4) is added in one lot, and then 63 g. (47.5 ml.) of methyl sulfate is added as before, except that the temperature is allowed to rise to 50°. Stirring at 50° is continued for 30 minutes, the mixture is cooled, and the organic layer is extracted with ether (Note 5). The ether solution is dried over anhydrous sodium sulfate for 8 hours, then filtered and concentrated by distillation. The residue is distilled under reduced

pressure. The yield of *m*-methoxybenzaldehyde, a pale yellow liquid boiling at 88–90° /3 mm., is 86–98 g. (63–72%) (Note 6).

2. Notes

1. Seeding the mixture helps to initiate crystallization.
2. If *m*-hydroxybenzaldehyde is desired, the crude product may be purified as described elsewhere (p. 453).
3. A good technical grade of methyl sulfate was used.
4. The optimum amount of sodium hydroxide solution apparently varies according to the amount of acid remaining in the crude, wet hydroxybenzaldehyde employed in the methylation. The checkers found it advisable to increase the amount added at this point to 345 ml. It is wise to test the reaction mixture with litmus paper occasionally during the final heating period and to add alkali as necessary to keep the solution from becoming acid.
5. If the methylation is not complete, some *m*-hydroxybenzaldehyde will remain dissolved in the aqueous phase. This may be recovered by acidifying the alkaline solution and collecting any crystalline solid which separates.
6. As with other aromatic aldehydes, *m*-methoxybenzaldehyde is susceptible to air oxidation and should be stored in a bottle which will just hold the product, so that air space above the liquid is minimized.

3. Discussion

m-Methoxybenzaldehyde has been prepared by the reduction of *m*-methoxybenzoic acid,[1] by the reaction of diazotized *m*-aminobenzaldehyde with methanol,[2] by an acid hydrolysis of the phenylhydrazone which was obtained by oxidation of the hydrazine analog,[3] and by the methylation of *m*-hydroxybenzaldehyde, with methyl iodide,[4,5,6,7] and with methyl sulfate.[2,7,8,9]

References and Notes

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

phenylhydrazone

sulfuric acid (7664-93-9)

methanol (67-56-1)

ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium sulfate (7757-82-6)

sodium nitrite (7632-00-0)

hydroxybenzaldehyde (90-02-8)

Methyl iodide (74-88-4)

methyl sulfate (75-93-4)

m-Hydroxybenzaldehyde (100-83-4)

m-aminobenzaldehyde (1709-44-0)

m-Aminobenzaldehyde dimethylacetal (53663-37-9)

m-Methoxybenzaldehyde,
Benzaldehyde, m-methoxy- (591-31-1)

m-methoxybenzoic acid (586-38-9)