



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](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.

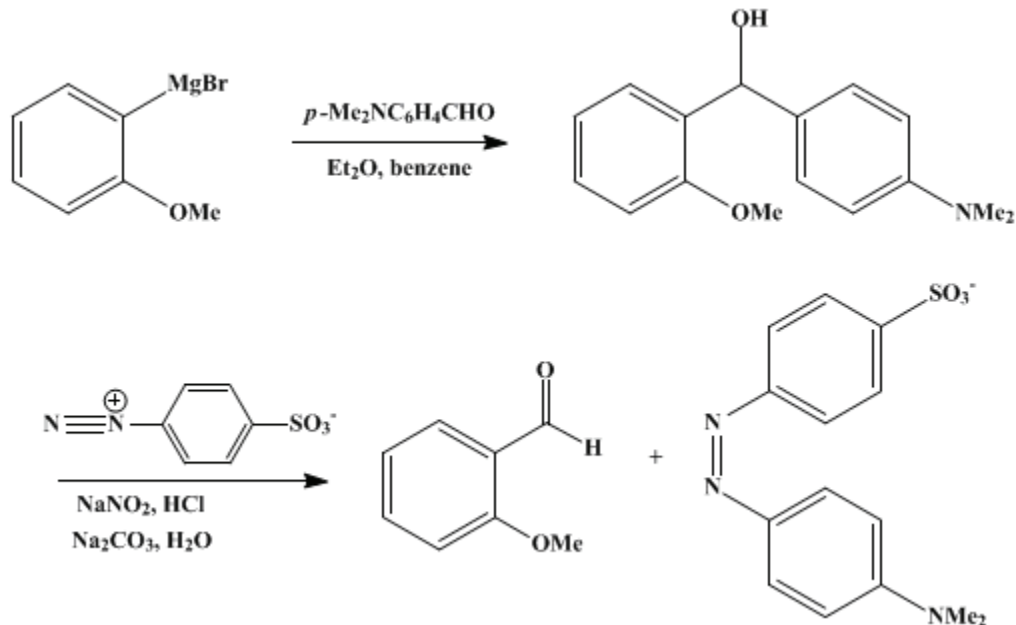
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.*

*Organic Syntheses, Coll. Vol. 5, p.46 (1973); Vol. 44, p.4 (1964).*

## *o*-ANISALDEHYDE



Submitted by A. J. Sisti<sup>1</sup>

Checked by G. L. Walford and Peter Yates.

### 1. Procedure

A. *4-Dimethylamino-2'-methoxybenzhydrol*. An ethereal solution of *o*-methoxyphenylmagnesium bromide is prepared in the usual manner<sup>2</sup> with 250 ml. of anhydrous ether, 14.5 g. (0.60 g. atom) of magnesium, and 100 g. (0.53 mole) of *o*-bromoanisoie (Note 1). A solution of 60 g. (0.40 mole) of *p*-dimethylaminobenzaldehyde (Note 2) in 200 ml. of anhydrous benzene is added dropwise to the Grignard reagent (Note 3). After the addition is completed, the reaction mixture is stirred for 10 hours at room temperature. The magnesium complex, which forms a very thick suspension, is decomposed with a solution of 75 g. of ammonium chloride in 450 ml. of water. The ether-benzene layer is separated, washed with 100 ml. of water, and dried over calcium sulfate (Note 4). The solvent is removed under reduced pressure, and the residue is induced to crystallize by trituration with a little petroleum ether (30–60°). Recrystallization of the solid from benzene-petroleum ether (30–60°) gives 4-dimethylamino-2'-methoxybenzhydrol (59–60 g., 57–58%), m.p. 75–80°.

B. *o*-Anisaldehyde. In a 3-l. three-necked flask fitted with a mechanical stirrer and a nitrogen inlet tube are placed 60 g. (0.35 mole) of sulfanilic acid (Note 5), 18 g. (0.17 mole) of anhydrous sodium carbonate, and 400 ml. of water. Stirring is started, and the resulting solution is cooled to 0–5° in an ice bath. Nitrogen is passed into the reaction flask, and a nitrogen atmosphere is maintained throughout the reaction. To the cooled solution is added three-quarters of a solution of 24.2 g. (0.35 mole) of sodium nitrite in 75 ml. of water, followed by 32 ml. of concentrated hydrochloric acid. During the diazotization the temperature of the solution is maintained below 5° by the addition of ice in small pieces. After a few minutes another 32 ml. of acid is added. Further additions of the sodium nitrite solution are made slowly until a positive test for excess nitrous acid is observed (Note 6). The diazonium solution is buffered to pH ~6 by the addition of a cooled solution of 50 g. of sodium acetate in 125 ml. of water. A solution of 52 g. (0.20 mole) of 4-dimethylamino-2'-methoxybenzhydrol in 500 ml. of acetone is added rapidly, followed by an additional 500 ml. of acetone. The reaction mixture becomes red almost immediately, and stirring is continued for 30 minutes. at 0–5°. The cooling bath is replaced by a warm water bath (50–60°), and stirring is continued for an additional 30 minutes. The reaction mixture is diluted with an equal volume of water and extracted with three 750-ml. portions of ether. The combined ethereal

extracts are washed with water until all the dissolved **methyl orange** is removed, then dried over **calcium sulfate**. The **ether** is removed under reduced pressure, and the residue is distilled to yield 19–20.5 g. (69–75%) of colorless liquid, b.p. 79–80° (1.5 mm.),  $n_{D}^{25}$  1.5586 (**Note 7**).

## 2. Notes

1. ***o*-Bromoanisole** obtained from Eastman Kodak Company was used without further purification.
2. A good commercial grade (Matheson, Coleman and Bell) of ***p*-dimethylaminobenzaldehyde** was used without further purification.
3. In one run the checkers cooled the reaction mixture in an ice bath throughout the addition. In another run only initial cooling was used. There was no difference in yield.
4. The checkers found that separation of the aqueous and organic phases is very difficult if the mixture is shaken. In one run shaking and washing were omitted without affecting the yield or purity of the product.
5. Eastman white label **sulfanilic acid** was used without purification.
6. Excess **nitrous acid** causes an *immediate* blue color at the point of contact with starch-iodide test paper. At all times there must be an excess of mineral acid (Congo red test paper).
7. The submitters found for the 2,4-dinitrophenylhydrazone m.p. 252–254° (lit.<sup>2</sup> m.p. 249–250°). The checkers found m.p. 34–36° for ***o*-anisaldehyde** (lit.<sup>3</sup> m.p. 37°) and m.p. 249–251° for the 2,4-dinitrophenylhydrazone.

## 3. Discussion

***o*-Anisaldehyde** is commercially available. However, this procedure illustrates a method of general applicability<sup>4,5,6</sup> for the preparation of aromatic, aliphatic, and unsaturated aldehydes and ketones.

---

## References and Notes

1. Department of Chemistry, Adelphi University, Garden City, Long Island, New York.
2. E. K. Harvill and R. M. Herbst, *J. Org. Chem.*, **9**, 21 (1944).
3. F. B. Garner and S. Sugden, *J. Chem. Soc.*, **2877** (1927).
4. M. Stiles and A. J. Sisti, *J. Org. Chem.*, **25**, 1691 (1960).
5. A. Sisti, J. Burgmaster, and M. Fudim, *J. Org. Chem.*, **27**, 279 (1962).
6. A. J. Sisti, J. Sawinski, and R. Stout, *J. Chem. Eng. Data*, **9**, 108 (1964).

---

## Appendix

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

petroleum ether

2,4-dinitrophenylhydrazone

**hydrochloric acid** (7647-01-0)

**Benzene** (71-43-2)

**ether** (60-29-7)

**ammonium chloride** (12125-02-9)

sodium acetate (127-09-3)  
magnesium (7439-95-4)  
sodium carbonate (497-19-8)  
nitrogen (7727-37-9)  
sodium nitrite (7632-00-0)  
nitrous acid (7782-77-6)  
calcium sulfate (7778-18-9)  
acetone (67-64-1)  
sulfanilic acid (121-57-3)  
o-Anisaldehyde (135-02-4)  
p-Dimethylaminobenzaldehyde (100-10-7)  
o-methoxyphenylmagnesium bromide  
o-bromoanisole (578-57-4)  
methyl orange (547-58-0)  
4-Dimethylamino-2'-methoxybenzhydrol