



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.

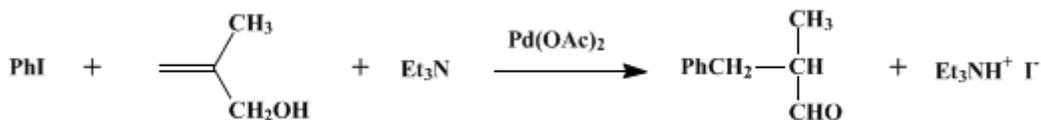
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 7, p.361 (1990); Vol. 61, p.82 (1983).

2-METHYL-3-PHENYLPROPANAL

[Benzenepropanal, α -methyl-]



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Checked by C. M. Tice and C. H. Heathcock.

1. Procedure

A 250-mL, three-necked, round-bottomed flask, equipped with a mechanical stirrer and a reflux condenser, is charged with 0.49 g (2.2 mmol) of palladium acetate (Note 1), 20.4 g (100 mmol) of iodobenzene, 9.0 g (125 mmol) of 2-methyl-2-propen-1-ol, 12.6 g (125 mmol) of triethylamine, and 32.5 mL of acetonitrile (Note 2). The reaction vessel is placed in an oil bath at 100°C and the solution is heated to reflux for 11 hr under a nitrogen atmosphere. The reaction mixture is allowed to cool to room temperature and transferred to a 500-mL separatory funnel with the aid of 100 mL of ether and 100 mL of water. The organic layer is washed five times with 100 mL portions of water. The combined aqueous layers are reextracted with 100 mL of ether. The organic layers are combined, dried over anhydrous sodium carbonate, and filtered. The organic layer is concentrated and distilled under reduced pressure. The product, 2-methyl-3-phenylpropanal, 12.05 g (82%), has a boiling range of 52–58°C at 0.40 mm (Note 3).

2. Notes

1. Palladium acetate was prepared by the method of Stephenson et al.² A suitable material is also available from the Strem Chemical Company or Alfa Inorganics.
2. Iodobenzene, 2-methyl-2-propen-1-ol, and triethylamine were obtained from the Aldrich Chemical Company, Inc. Acetonitrile was obtained from the J. T. Baker Chemical Company. All these reagents were used as received.
3. The 2-methyl-3-phenylpropanal is 90% pure by GLC. The product mixture contains 6% of another isomer, 2-methyl-2-phenylpropanal, and a small amount of 2-phenyl-2-propen-1-ol. A completely pure sample of the aldehyde is readily obtained by stirring the crude aldehyde with excess saturated aqueous sodium bisulfite solution for several hours, filtering the solid bisulfite adduct, washing with ether, and liberating the aldehyde with excess aqueous sodium bicarbonate. Redistillation gives the completely pure aldehyde in about 60% yield.

3. Discussion

The reaction of allylic alcohols and aryl halides in the presence of a palladium catalyst has been used in the past to prepare various β -arylaldehydes. The procedure described here is essentially that of Heck and Melpolder.³ A similar reaction has been carried out with bromobenzene and 2-methyl-2-propen-1-ol in hexamethylphosphoric triamide (HMPT) as solvent with sodium bicarbonate as base. A variety of other bases have also been used.⁴ 2-Methyl-3-phenylpropanal has been prepared by reacting palladium acetate and phenylmercuric acetate with 2-methyl-2-propen-1-ol.⁵

The aldehyde is also obtained by the hydroformylation of allylbenzene.⁶ An alternative method involves benzylation of 2-ethylthiazoline followed by reduction with aluminum amalgam and cleavage with mercuric chloride.⁷ A sixth method of preparation is the phenylation of 2-vinyl-5,6-dihydro-1,3-oxazine with phenylmagnesium bromide followed by methylation and hydrolysis.⁸ Finally, arylation of 2-methyl-2-propen-1-ol with phenyldiazonium salts catalyzed by zero-valent palladium complexes gives the title aldehyde.⁹

References and Notes

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Appendix

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

ether (60-29-7)

acetonitrile (75-05-8)

sodium bicarbonate (144-55-8)

sodium carbonate (497-19-8)

nitrogen (7727-37-9)

aluminum (7429-90-5)

sodium bisulfite (7631-90-5)

palladium (7440-05-3)

bromobenzene (108-86-1)

mercuric chloride (7487-94-7)

Phenylmagnesium bromide (100-58-3)

phenylmercuric acetate

Iodobenzene (591-50-4)

2-methyl-2-propen-1-ol (513-42-8)

triethylamine (121-44-8)

allylbenzene (300-57-2)

hexamethylphosphoric triamide (680-31-9)

palladium acetate (3375-31-3)

Benzenepropanal, α -methyl-,
2-Methyl-3-phenylpropanal,
2-methyl-3-phenyl-propanal (5445-77-2)

2-ethylthiazoline

2-vinyl-5,6-dihydro-1,3-oxazine

2-methyl-2-phenylpropanal

2-phenyl-2-propen-1-ol