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.

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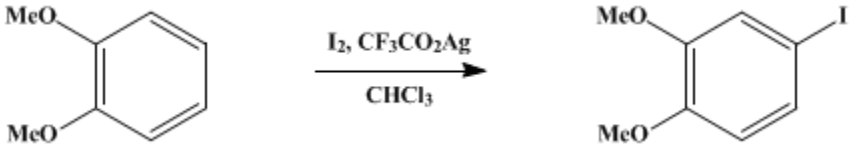
Organic Syntheses, Coll. Vol. 4, p.547 (1963); Vol. 36, p.46 (1956).

4-IODOVERATROLE

[Veratrole, 4-iodo-]



Submitted by Donald E. Janssen and C. V. Wilson[1].
Checked by Max Tishler and George Purdue.

1. Procedure

A. *Silver trifluoroacetate.* To a suspension of 187 g. (0.81 mole) of silver oxide (Note 1) in 200 ml. of water is added 177 g. (1.55 moles) of trifluoroacetic acid (Note 2). The resulting solution is filtered, and the filtrate is evaporated to dryness under reduced pressure. The dry silver trifluoroacetate thus obtained is purified by placing it in a Soxhlet thimble and extracting with ether, or by dissolving the salt in 1.2 l. of ether, filtering through a thin layer of activated carbon, and evaporating the filtered ether solution to dryness. The yield of colorless crystalline salt obtained after removal of the ether is 300 g. (88%).

B. *4-Iodoveratrole.* In a 3-l. three-necked round-bottomed flask, fitted with a sealed stirrer, a dropping funnel, and a reflux condenser protected with a drying tube, is placed 110 g. (0.5 mole) of dry silver trifluoroacetate (Note 3). The flask is flamed to remove all moisture, and 69 g. (0.5 mole) of dry veratrole is added (Note 2). To the stirred suspension a solution of 127 g. (0.5 mole) of iodine in 1.6 l. of chloroform is added through the dropping funnel over a period of 2 hours. After stirring an additional hour, the mixture is filtered and the precipitated silver iodide is washed with 100 ml. of chloroform. The solvent is removed from the filtrate and washings under vacuum, and the residue is distilled through an 8-in. Vigreux column. The fraction boiling at 152–155°/15 mm. weighs 112–120 g. and constitutes a yield of 85–91% (Note 4) and (Note 5).

2. Notes

1. The silver oxide was prepared by adding, with manual stirring, 66 g. of 98% sodium hydroxide (1.62 moles) in 2 l. of water to a solution of 274 g. (1.62 moles) of silver nitrate in 500 ml. of water. The precipitate was collected by filtration and washed with water until free from alkali. The wet cake can be dried or preferably used moist for reaction with trifluoroacetic acid.
2. The trifluoroacetic acid and veratrole used were Eastman Kodak Company white label grade.
3. Commercially available silver acetate may be used in place of the silver trifluoroacetate, but the yield is somewhat lower (75–80%).
4. The product, n_D^{25} 1.612, solidifies on chilling. Recrystallization from ethanol gives solid of melting point 34–35°.
5. Iodination in the presence of mercuric oxide[2,3,4,5,6] gives yields of about 40–55%, and even after careful distillation the product is contaminated with mercury salts.

3. Discussion

4-Iodoveratrole has been prepared by iodination of veratrole in the presence of mercuric oxide[2,3,4,5,6] and by methylation of 4-iodoguaiacol with methyl iodide in alcoholic sodium ethoxide solution.[7]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 8, 71
- Org. Syn. Coll. Vol. 8, 586

References and Notes

1. Eastman Kodak Company, Rochester 17, New York.
2. Ritchie, *J. Proc. Roy. Soc. N. S. Wales*, **78**, 134 (1945) [*C. A.*, **40**, 876 (1946)].
3. Jurd, *Australian J. Sci. Research*, **2A**, 246 (1949) [*C. A.*, **45**, 2887 (1951)].
4. Seer and Karl, *Monatsh.*, **34**, 647 (1913).
5. Bruce and Sutcliffe, *J. Chem. Soc.*, **1955**, 4435.
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

ethanol (64-17-5)

ether (60-29-7)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

silver oxide (20667-12-3)

silver nitrate (7761-88-8)

mercuric oxide (21908-53-2)

iodine (7553-56-2)

activated carbon (7782-42-5)

sodium ethoxide (141-52-6)

Methyl iodide (74-88-4)

silver acetate (563-63-3)

veratrole (91-16-7)

silver iodide (7783-96-2)

4-IODOVERATROLE,
Veratrole, 4-iodo- (5460-32-2)

trifluoroacetic acid (76-05-1)

silver trifluoroacetate (2966-50-9)

4-iodoguaiacol