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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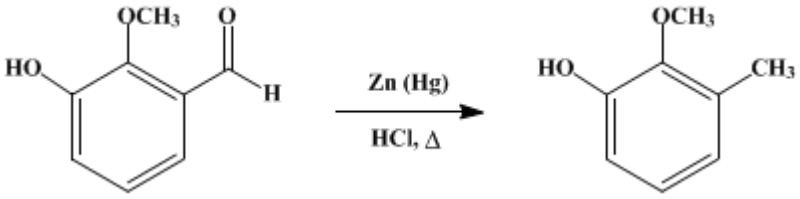
CREOSOL



Submitted by R. Schwarz and H. Hering[1].
Checked by R. L. Shriner and C. L. Furrow, Jr..

1. Procedure

In a 5-l. three-necked flask fitted with a stopper, a reflux condenser, and a 250-ml. dropping funnel are placed 1.5 kg. (22.9 g. atoms) of amalgamated zinc (Note 1) and 800 ml. of concentrated hydrochloric acid. The flask is heated to cause gentle refluxing to occur. A solution of 152 g. (1.0 mole) of vanillin in 450 ml. of 95% ethanol and 1.5 l. of concentrated hydrochloric acid (Note 2) is added dropwise through the dropping funnel over an 8-hour period (Note 3). After the addition of the vanillin is complete the mixture is refluxed for 30 minutes more. The liquid, consisting of two layers, is decanted from the zinc (Note 4) into a 4-l. separatory funnel. The aqueous layer is removed and washed three times with 200-ml. portions of benzene, and the benzene extracts are combined with the crude creosol separated initially. The residual amalgamated zinc is washed twice with 100-ml. portions of benzene, and this benzene solution is added to the combined extracts. The extracts are washed twice with 200-ml. portions of 5% sodium bicarbonate solution, and the resultant precipitate of metallic salts is removed by filtration. The solution is washed once with 200 ml. of water.

The benzene is removed under reduced pressure by distillation on a steam bath. The residue is distilled under reduced pressure, the fraction boiling at 78–79°/4 mm., at 104–105°/15 mm., or at 219–222.5°/760 mm. being collected. A yield of 83–92.5 g. (60–67%) of colorless or pale yellow creosol is obtained, d_4^{25} , 1.092; n_D^{20} 1.5354 (Note 5) and (Note 6).

2. Notes

1. The amalgamated zinc may be prepared by adding 1500 g. of clean granulated zinc to 600 ml. of 5% mercuric chloride solution. After standing for 2 hours with occasional shaking, the liquid is decanted and the zinc is used immediately.
Alternatively,[2] 1500 g. of granulated zinc is added to a solution of 62.5 g. of mercuric chloride and 62.5 ml. of concentrated hydrochloric acid in 1875 ml. of water. The mixture is shaken for about 5 minutes, the liquid decanted, and the zinc used immediately.
2. The vanillin is first dissolved in ethanol by warming gently, and then 1.5 l. of concentrated hydrochloric acid (d = 1.19) is added. A clear yellow solution is obtained, which soon becomes blue-green.
3. It is advisable to avoid overheating the upper parts of the flask to prevent some brown-red tarry masses from forming.
4. The recovered zinc (900–950 g.) can be used for further preparations by adding more zinc and renewing amalgamation.
5. The submitters report yields up to 103 g. (75%), but this yield could not be consistently obtained by the checkers.
6. The reduction of vanillin by the Clemmensen method using toluene as an auxiliary solvent has been reported.[3] By following these directions, a yield of 49% of creosol was obtained with large amounts of tar.

3. Discussion

creosol (also called 2-methoxy-*p*-cresol, 4-methylguaiacol, and 3-methoxy-4-hydroxytoluene) has been obtained by the fractionation of beach creosote tar,[4] by the reduction of vanillin by electrolytic methods,[5,6] by hydrogen and palladium on charcoal or barium sulfate,[7,8] with hydrazine,[9] and by amalgamated zinc and hydrochloric acid.[3,10,11] It has also been prepared by methylation of 4-methylcatechol with methyl iodide[12,13] or with methyl sulfate[14] and is reported to be formed by the distillation of the calcium salt of 3-methoxy-4-hydroxyphenylacetic acid.[15]

References and Notes

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

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

hydrogen (1333-74-0)

sodium bicarbonate (144-55-8)

barium sulfate (7727-43-7)

toluene (108-88-3)

zinc (7440-66-6)

palladium (7440-05-3)

mercuric chloride (7487-94-7)

Methyl iodide (74-88-4)

methyl sulfate (75-93-4)

hydrazine (302-01-2)

vanillin (121-33-5)

3-methoxy-4-hydroxytoluene (93-51-6)

4-methylcatechol (452-86-8)

2-methoxy-p-cresol, 4-methylguaiacol

Creosol (93-51-6)

calcium salt of 3-methoxy-4-hydroxyphenylacetic acid