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.

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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.

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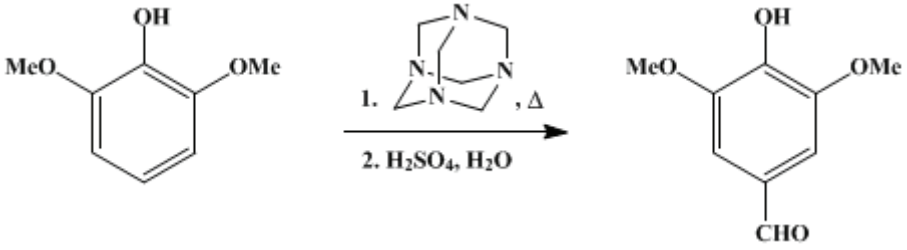
SYRINGIC ALDEHYDE

[Syringaldehyde]



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1. Procedure

A well-stirred (Note 1) and (Note 2) mixture of 740 ml. of glycerol and 216 g. of boric acid, in a 2-l. three-necked round-bottomed flask fitted with a thermometer and a condenser for downward distillation, is dehydrated by heating in an oil bath to *exactly* 170°. This temperature is maintained for 30 minutes and then allowed to drop. When the temperature has fallen to 150°, a mixture of 154 g. (1 mole) of pyrogallol-1,3-dimethyl ether and 154 g. (1.1 moles) of hexamethylenetetramine (Note 3) is added as rapidly as possible through the neck holding the thermometer. The temperature drops to approximately 125°. Rapid heating is immediately started but is slowed down when the temperature begins to reach 145° and stopped at 148°. The reaction must be watched and controlled *very carefully* when this temperature is reached, since the reaction becomes exothermic at this point (Note 4), (Note 5), and (Note 6). The temperature is maintained at 150–160° for approximately 6 minutes (Note 7). At the end of this reaction time the mixture is cooled to 110° as rapidly as possible (Note 6) and (Note 8), and a previously prepared solution of 184 ml. of concentrated sulfuric acid in 620 ml. of water is added to the reaction mixture. After being stirred for 1 hour, the mixture is cooled to 25° in an ice bath. The boric acid, which separates from the solution, is removed by filtration (Note 9) and washed free of mother liquor with 400 ml. of water. The filtrate and washings are combined and extracted with three 500-ml. portions of chloroform (Note 10), (Note 11), and (Note 12).

The chloroform solution is then extracted with a filtered solution of 180 g. of sodium bisulfite in 720 ml. of water (Note 13) by stirring rapidly with a Hershberg stirrer for 1 hour. The separated bisulfite solution is washed twice with chloroform, filtered, and acidified in a hood with a solution of 55 ml. of concentrated sulfuric acid in 55 ml. of water. After careful heating on a steam bath for a short time, air is bubbled through the hot solution until all the sulfur dioxide has been expelled. The product, which separates as a mixture of crystals and oil, readily solidifies upon cooling (Note 14). The syringic aldehyde is collected by filtration, washed with cold water, and dried in an oven at 40° to give 62.5–66 g. of light-tan material, melting at 110.5–111°, which still contains a small amount of foreign material that does not melt at 300°. Recrystallization of the crude product from aqueous methanol using 30 ml. of water and 3 ml. of methanol for each 10 g. of aldehyde gives 56–59 g. (31–32%) of product melting clear at 111–112° (uncor.). A second extraction of the chloroform solution with a filtered solution of 60 g. of sodium bisulfite in 240 ml. of water gives an additional 3–4 g. of product.

2. Notes

1. The use of a Hershberg[2] stirrer is recommended.
2. It is desirable to conduct this preparation in a hood because of the large volume of ammonia liberated in the second step.
3. Eastman Kodak Company white label grade pyrogallol-1,3-dimethyl ether was used. A larger excess of hexamethylenetetramine in a small trial run did not improve the yield.

4. The reaction mixture darkens rapidly, and there is a vigorous evolution of ammonia.
5. The temperature usually rises to 160° within 5 minutes, and cooling is necessary.
6. Cooling is accomplished by playing a stream of cold water over the outside of the flask.
7. There is undoubtedly some leeway in these conditions. The same yields were obtained when the temperature was maintained at 150–160° for periods of 5 to 9 minutes. Longer reaction times, without rapid cooling after the heating period, lowered the yield. Reaction times of 15 minutes, 30 minutes, and 1 hour gave yields of 20.8%, 10.0%, and 6.5%, respectively. Liggett and Diehl,[3] after having run a large number of other Duff reactions, have come to the conclusion that the temperature may vary between 145° and 175° without detriment to the yield.
8. About 3 to 5 minutes is required for cooling.
9. If not removed, the boric acid makes extraction of the product impossible or very difficult. Since the boric acid is finely divided, filtration is extremely slow unless large Büchner funnels, preferably with large holes, are employed. The checkers avoided the difficulty by using a filter cloth at this point.
10. The product cannot be isolated by steam distillation of the reaction mixture.
11. Syringic aldehyde is much more soluble in chloroform than in ether. Extraction is essentially complete since a fourth extraction gave only a 0.3–0.7% increase in yield.
12. If the aldehyde is isolated directly by concentration of the chloroform solution, the color is darker, and the melting point and yield are lower.
13. This represents a large excess of sodium bisulfite, but smaller amounts remove a smaller percentage of the syringic aldehyde from the chloroform solution. When larger amounts of bisulfite are employed, extraction of the product is still incomplete.
14. The product should be cooled to just 15° and filtered immediately. Longer and further cooling causes sodium sulfate to crystallize from the mixture. Very little product remains in the filtrate.

3. Discussion

This procedure is a modification of the method described by Manske and co-workers.[4] Syringic aldehyde has also been obtained by numerous other procedures from pyrogallol-1,3-dimethyl ether[5,6,7,8] from gallic acid,[9,10,11] and from vanillin.[12]

References and Notes

1. Eastman Kodak Company, Rochester, New York.
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3. Liggett and Diehl, *Proc. Iowa Acad. Sci.*, **52**, 191 (1945).
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9. Mauthner, *J. prakt. Chem.*, **142**, 26 (1935).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

sulfuric acid (7664-93-9)

ammonia (7664-41-7)

methanol (67-56-1)

ether (60-29-7)

chloroform (67-66-3)

glycerol (56-81-5)

sulfur dioxide (7446-09-5)

sodium sulfate (7757-82-6)

sodium bisulfite (7631-90-5)

hexamethylenetetramine (100-97-0)

boric acid (10043-35-3)

vanillin (121-33-5)

Syringic aldehyde,
Syringaldehyde (134-96-3)

pyrogallol-1,3-dimethyl ether