



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.

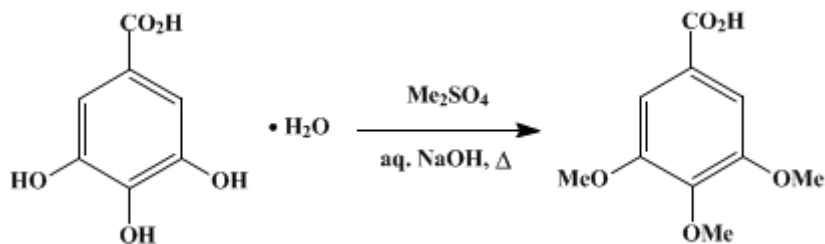
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 1, p.537 (1941); Vol. 6, p.96 (1926).

TRIMETHYLGALLIC ACID

[Benzoic acid, 3,4,5-trimethoxy-]



Submitted by F. Mauthner
Checked by H. T. Clarke

1. Procedure

To a cold solution of 80 g. (2 moles) of sodium hydroxide in 500 cc. of water in a 1-l. flask is added 50 g. (0.266 mole) of gallic acid. The flask is immediately tightly stoppered (Note 1), and the mixture shaken occasionally until all the acid has dissolved; 89 g. (67 cc.) of dimethyl sulfate (0.71 mole) is then added (Note 2) and the flask is shaken for twenty minutes, being cooled by means of cold water in order that the temperature does not rise above 30–35°. Occasionally the stopper is raised to release any pressure. A second portion of 89 g. of dimethyl sulfate is then added and shaking continued for ten minutes longer. During this second addition the temperature may rise to 40–45°.

The flask is then fitted with a reflux condenser and the contents boiled for two hours. In order to saponify the small amount of ester which is produced, a solution of 20 g. of sodium hydroxide in 30 cc. of water is then added and boiling continued for two additional hours. The reaction mixture is then cooled and acidified with dilute hydrochloric acid; the precipitated trimethylgallic acid is filtered with suction and washed well with cold water. The product, which melts at 157–160°, is sufficiently pure for many purposes. It weighs 50–52 g. (89–92 per cent of the theoretical amount). It may be purified by recrystallization from 2 l. of boiling water with the use of decolorizing carbon, the filtration being carried out in a steam-jacketed funnel. In this way 41–43 g. (Note 3) of colorless needles melting at 167° is obtained.

2. Notes

1. The alkaline solution immediately darkens somewhat, owing to the presence of dissolved air; further oxidation must be limited by preventing access of air to the mixture. This is particularly necessary during the early stages; with increasing methylation the tendency to absorb oxygen falls off rapidly. Sodium bisulfite has been recommended to prevent oxidation during methylation.¹

Access of air may be prevented in an apparatus that permits of mechanical stirring. For this purpose a three-necked flask is provided with a mechanical stirrer, separatory funnel, and Bunsen valve. The valve is made by cutting a vertical slit in a piece of rubber tubing, closed at one end by a solid glass plug or pinchcock and attached at the other end to a piece of glass tubing contained in a stopper. Such a valve acts in one direction, permitting release of gas pressure. A guard tube filled with sodium hyposulfite has been used to exclude oxygen.¹

2. The toxic nature of methyl sulfate must always be borne in mind. Ammonia is a specific antidote for methyl sulfate and should be kept at hand to destroy any of the ester accidentally spilled.

3. A further quantity can be recovered by concentrating the mother liquor. The residue of decolorizing carbon is also likely to contain an appreciable proportion of trimethylgallic acid, which can be extracted by boiling it with the mother liquor.

3. Discussion

Trimethylgallic acid can be prepared by methylating gallic acid with dimethyl sulfate,² and by methylating methyl gallate and saponifying the product.³

References and Notes

1. Bogert and Coyne, J. Am. Chem. Soc. **51**, 571 (1929).
 2. Graebe and Martz, Ann. **340**, 219 (1905); Perkin and Weizmann, J. Chem. Soc. **89**, 1655 (1906); Fischer and Freudenberg, Ber. **45**, 2718 (1912); Bogert and Isham, J. Am. Chem. Soc. **36**, 517 (1914); Nierenstein, J. Chem. Soc. **111**, 7 (1917); Overmyer, J. Am. Chem. Soc. **49**, 503 (1927); Bogert and Coyne, *ibid.* **51**, 571 (1929).
 3. Will, Ber. **21**, 2022 (1888).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

sodium hydroxide (1310-73-2)

oxygen (7782-44-7)

sodium bisulfite (7631-90-5)

dimethyl sulfate (77-78-1)

decolorizing carbon (7782-42-5)

methyl sulfate (75-93-4)

Trimethylgallic acid

Benzoic acid, 3,4,5-trimethoxy- (118-41-2)

gallic acid (149-91-7)

methyl gallate (99-24-1)