

A Rapid Synthesis of 3-O-Methylgallic Acid

RONALD R. SCHELIN

Department of Pharmacology, University of Bergen, Bergen, Norway

The synthesis of 3-O-methylgallic acid from gallic acid or its methyl ester is carried out by blocking two vicinal hydroxyl groups prior to methylation and subsequent hydrolysis. An early but rather laborious example of this was described by Fischer and Freudenberg.¹ The method of Bradley *et al.*² simplified the synthesis by reacting methyl gallate with dichlorodiphenylmethane to give methyl 3-hydroxy-4,5-diphenylmethylenedioxybenzoate. It appears that this procedure using dichlorodiphenylmethane to block the hydroxyl groups has been the method usually used to prepare 3-O-methylgallic acid and it has been recently improved by Jurd.³ Nevertheless, the synthesis has the drawbacks of using fairly expensive reagents, of being time-consuming and of giving only moderately good yields, a fact which results partly from the need for isolating the intermediates methyl 3-hydroxy-4,5-diphenylmethylenedioxybenzoate and its 3-methoxy derivative.

Shimizu and Ohta⁴ have shown that sodium borate can be used to protect vicinal hydroxyl groups and they were able to partially methylate the flavonoids rutin and quercetin in this way. This method was also used successfully by Jain *et al.*⁵ and Anand *et al.*⁶ for the synthesis of partial methyl ethers of some flavonols. The present report shows that this approach can also be used for the preparation of 3-O-methylgallic acid in good yield and it has the further advantages over earlier

methods of being inexpensive and fairly rapid.

Procedure. Methyl gallate (10 g) was dissolved in 5 % aqueous borax solution (800 ml). Dimethyl sulfate (30 ml) and a solution of sodium hydroxide (13 g in 50 ml of distilled water) were each added dropwise to the stirred solution at room temperature during 3 h. After standing overnight the solution was acidified with sulfuric acid and continuously extracted with ethyl acetate. After partially decolorizing with charcoal the extract was concentrated to a orange-brown syrup and heated on a steam bath for 1 h with 20 % aqueous sodium hydroxide solution (100 ml). This was acidified with hydrochloric acid and continuously extracted with ether. The residue after evaporation of the ether was crystallized once from water (charcoal) and gave crude 3-O-methylgallic acid (7.5 g, m.p. 214–216°). Further crystallization from water and then from benzene-methanol gave colourless needles which were dried *in vacuo* over silica gel (m.p. 218.5–219°, uncorr., lit. 220°). The infrared spectrum (Hilger H 900, KBr disc) of this material was identical to that of authentic 3-O-methylgallic acid and is shown in Fig. 1.

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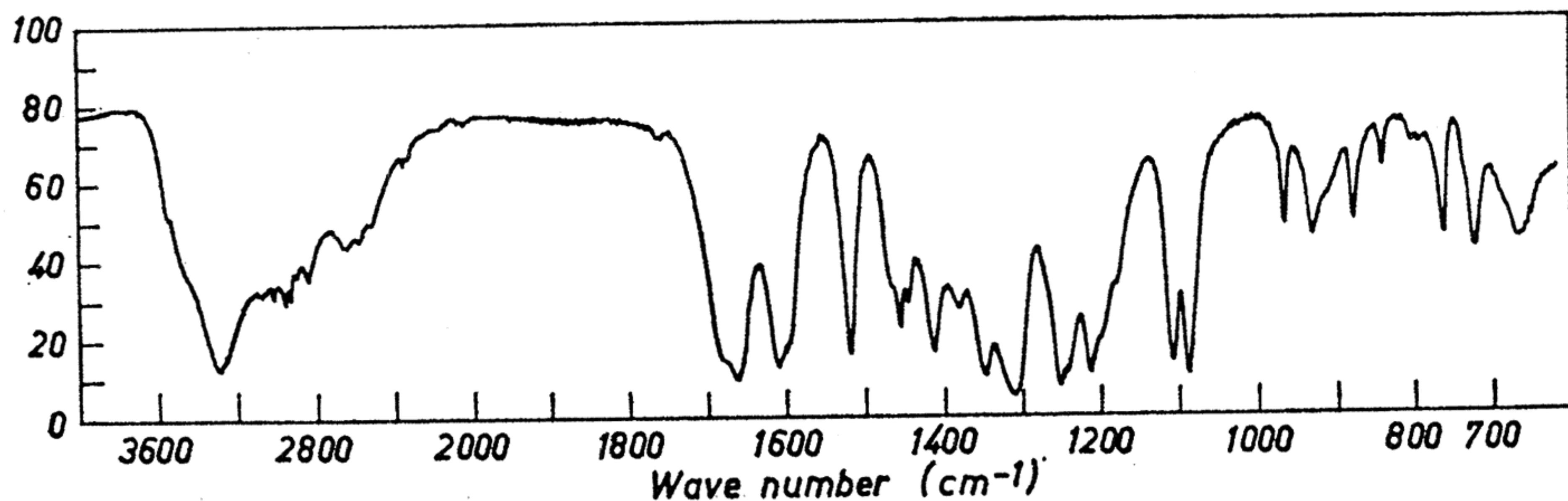


Fig. 1. Infrared spectrum of 3-O-methylgallic acid (KBr disc).