

## ELABORATION OF A METHOD FOR SYNTHESIS FOR METHYL P-HIDROXYLBENZOATE, A FOOD PRESERVATIVE

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### **Abstract**

*Esters of p-hydroxybenzoic acid have many practical uses, the most important being preservatives for food, cosmetics and medicinal products. In this paper we present the study of the synthesis of the methyl ester of p-hydroxybenzoic acid called methylparaben. The optimal ratio of reactants was established to obtain good yield. If the molar ratio of p-hydroxybenzoic: methanol is of 1: 3, the synthesis yield was 86%.*

**Key words:** preservatives, parabens, ester synthesis

### **INTRODUCTION**

P-Hydroxybenzoic acid and its esters are well known and have been studied because of their multiple uses and their biological activity (Ullmann, 2004; Kirk-Othmer, 2010; <http://www.chem.elte.hu/w/gpch/tasks/gpch2003-synt-oc.pdf>).

Foods, cosmetics, and pharmaceuticals, with their nutrient rich composition are exposed to time degradation. Their damage cannot be stopped but the rate of degradation can be reduced by controlling their composition, processing conditions, packaging, storage and handling. The end result of their degradation is the impossibility of capitalizing on them. Of the degradation mechanisms, those of a microbial nature are most often involved because microorganisms are ubiquitous, making it almost impossible to exclude them from human products. The use of chemical methods to reduce the degradation phenomenon has been, is and will remain a viable alternative that reduces industry losses (Endo, Imamura, 1998; Suzuki, Mokiko, 1989).

The first description of antimicrobial properties of benzoic acid was made in 1875. It was more frequently used for its antimicrobial properties after 1900. It is found in varying quantities in some fruits, vegetables, spices, fermented products, green tea, coffee beans, tobacco, where it exerts its antimicrobial effect and where it can be extracted from.

Its antimicrobial action exerts primarily on yeasts and in a lower proportion in micettes and lactic bacteria being a preservative that can be

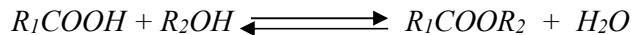
used in products obtained by bacterial fermentation. It prevents the synthesis of mycotoxins of *Aspergillus*, *Penicillium*, *Fusarium*. Parahydroxybenzoates and their salts (E 214 - E 219) are esters of parahydroxybenzoic acid with organic fatty acids. The first notice of the antimicrobial effect of these compounds dates from 1920 due to the structural similarities with phenol (Enda, Imamura, 1991; Luck, Jager, 2010).

In Europe, methyl, ethyl and propyl parabens are used, but in other countries, butylparaben and heptyl paraben are also used. They are noted for their ability to be active in neutral pH environments, have an optimal pH between 3 and 8. Their solubility in water is inversely proportional to the alkyl chain length, however, the solubility in oils is directly proportional. Also, the antimicrobial action increases with the length of the alkyl chain.

They manifest the antimicrobial action in the undissociated form. They have intense antimicrobial action on yeasts and micettes and less on bacteria (especially Gram positive). The antimicrobial action is the consequence of inhibiting enzymes involved in cellular respiration, inhibition of spore germination, blocking of protein synthesis and DNA or bacterial RNA (Kazumi, Takeshi, 1986; Akoshi et al., 1972).

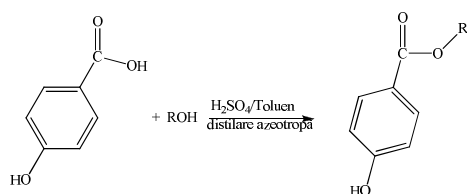
They are used in foods, in mixtures with each other (methyl: propyl in a ratio of 3: 1) or with sorbic acid or benzoic acid and their salts. They are used for preservation in: meat products, snacks, sweets in quantities up to 0.3g/kg (Bourke, Breheton, 2014; Brian, Binghua, 2007; <http://www.inchem.org/documents/sids/sids/99967.pdf>; [https://ec.europa.eu/health/scientific\\_committees/docs/citizens\\_parabens\\_en.pdf](https://ec.europa.eu/health/scientific_committees/docs/citizens_parabens_en.pdf)).

The classical method of ester synthesis is Fischer esterification. It consists of the reaction of a carboxylic acid and an alcohol in a solvent, which may actually be the reactant alcohol:



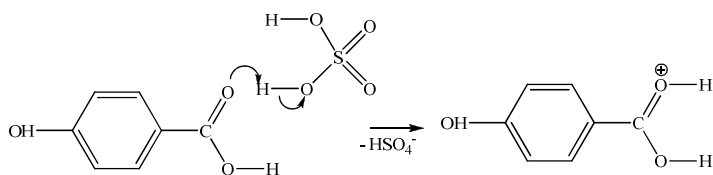
A strong acid, usually sulfuric acid, is used as a catalyst. The esterification reaction is an equilibrium reaction. In order to displace of the balance to form a larger amount of ester and the increase in yield, it is operated with excess of alcohol and/or the elimination of a reaction product, usually the water formed as a by-product of the reaction. The sulfuric acid introduced into the reaction acts as a catalyst but it can also be a desiccant (Suzuki, Jiri, 1993; Hirao, 1970; Citron, Samuels, 1997). Azeotrope distillation is a unitary operation much used in esterification reactions. The advantages of using azeotropic distillation to separate a compound from the esterification reaction mass is displacement of the reaction equilibrium to ester synthesis and operation under milder conditions, avoiding the handling

of a large amount of sulfuric acid (Hanri, Clay, 1965; Narbad et al., 2003). Synthesis of p-hydroxybenzoic acid esters by azeotropic distillation technique, using toluene as azeotropic agent and in the presence of catalytic amounts of sulfuric acid is an efficient and economical method to produce pure products.

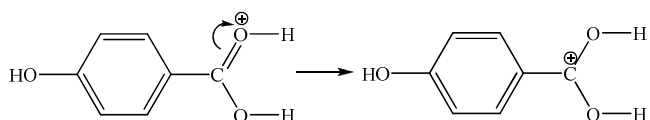


The most important way to obtain carboxylic acid esters is the reaction of free acids with alcohol, direct esterification of carboxylic acids. Carboxylic acids generally react very slowly with alcohols. By adding strong acids, esterification can be accelerated considerably (Ullmann, 2004; Kirk-Othmer, 2010).

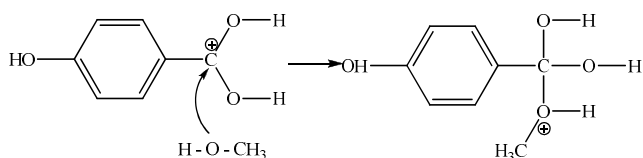
In the first step, a hydrogen atom is attached to the carbonyl oxygen atom.



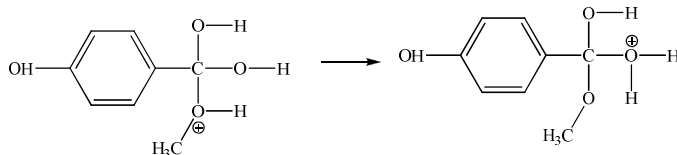
The transfer of protons to oxygen leads to a positive charge to this atom that is delocalized by the transfer of the  $\pi$  electrons of the double bond  $C = O$ .



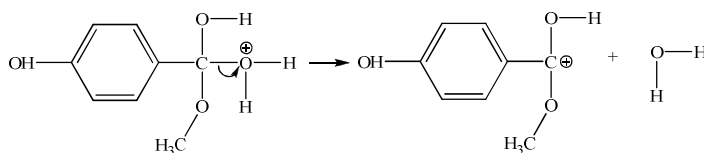
In a next step, occurs the nucleophilic attack of the hydroxyl oxygen with the pair of non-participating electrons.



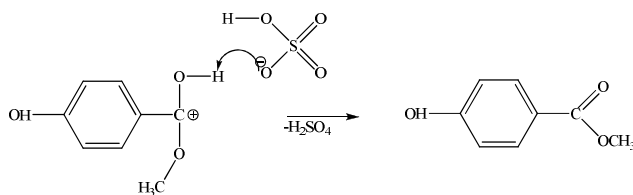
In the third step, there occurs a proton transfer from the positive oxygen atom.



A molecule of water is removed from the formed ion, resulting in a new carbocation that is stabilized through resonance.



In the last step of this mechanism, a proton from the carbocation formed in reaction with the hydrogen-sulfate ion is removed:



Steric conditions have a great influence on esterification. The rate of esterification is lower if the alkyl bonded to the carboxyl group and the esterified alcohol have larger volume.

## MATERIAL AND METHOD

*Reagents and Materials:* P-Hydroxybenzoic Acid, Methyl Alcohol, Toluene, Merck Sulfuric Acid.

*Method:* In a 3-necked flask placed in a heating bath, the amount of p-hydroxybenzoic acid, methyl alcohol and catalytic amounts of concentrated sulfuric acid and toluene are introduced. Heat the mixture to reflux, leave for 1 hour. The flame temperature is 100°C and the vapor temperature is 90 ° C. Cool the reaction mass to 80 ° C and place the water separator and heat to reflux. The flame temperature is 90-95°C. After 10 minutes, the separation of the aqueous phase begins. The refluxing is continued by recording the amount of collected aqueous phase. A toluene-methanol-water ternary azeotrope is distilled until further water is removed from the system when the reaction is considered to be complete. The reaction mixture is cooled to 5°C when the methyl paraben crystallizes and it is then separated by vacuum filtration and dried.

## RESULTS AND DISCUSSION

For the reagent and product Table 1 synthesis of methyl paraben, there were used the amounts of reagents indicated in Table 1.

Table 1

No	Amount of reagent and product							
	P-hydroxybenzoic acid		Methanol		Toluene	H <sub>2</sub> SO <sub>4</sub>	Ester quantity (g)	Yield (%)
	Mass (g)	Mole	Masa (g)	Mole	Volume (ml)	Volume (ml)		
1	50	0,36	30,5	0,95	100	2	47	86,1
2	50	0,36	11,6	0,36	100	2	22	40,2

If the synthesis was performed using a molar ratio of p-hydroxybenzoic acid: methanol 1: 1, the synthesis yield was low, 40.2%. When a synthesis using a methanol excess was performed, the yield was higher, 86.1%. 47 g of p-hydroxybenzoic acid methyl ester are obtained in this case (Mp. 121-123°C).

Verification of the structure of the synthesized compound was performed by IR spectroscopy. Figure 1 shows the spectrum obtained.

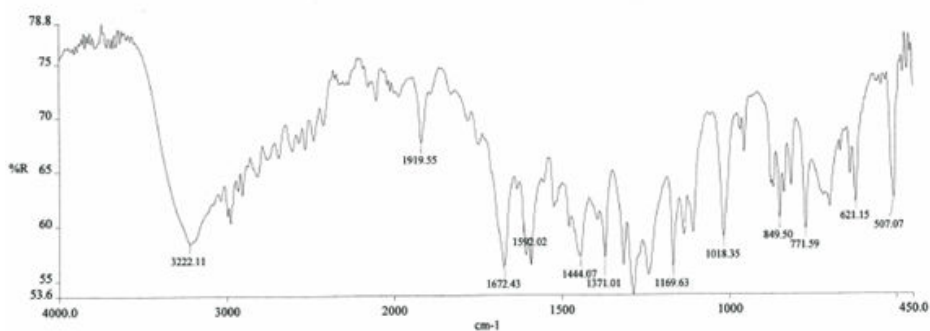


Fig. 1. IR spectrum of the synthesized ester

The maximum absorption at 3222 cm<sup>-1</sup> corresponds to the phenolic OH bond. The presence of the aromatic ring is demonstrated by the maximum absorption in the range of 1592-1449 cm<sup>-1</sup> (C-H) aromatic and the ester group 1672 (C = O), 1169 (C-O).

## CONCLUSION

An efficient method for synthesis methyl paraben was developed. The optimal ratio of reactants was established to obtain good yield. If the molar ratio of p-hydroxybenzoic: methanol is of 1: 3, the synthesis yield was 86%. The product was characterized by IR spectroscopy.

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