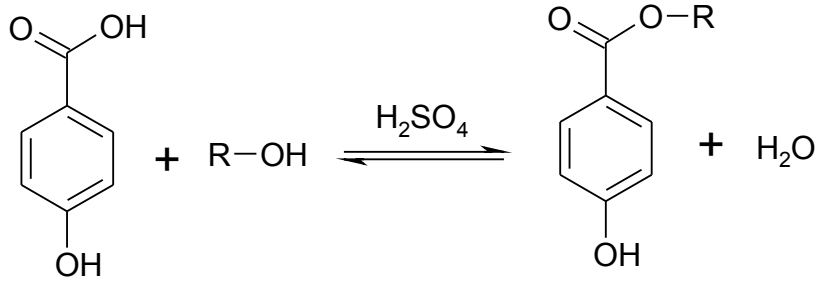
5. 4-hydroxybenzoic acid esters - parabens

Systematic names: 4-hydroxybenzoic acid alkyl ester; alkyl 4-hydroxybenzoate; alkyl 4-hydroxybenzenecarboxylate

Parabens are prepared by esterification of the 4-hydroxybenzoic acid in presence of concentrated sulfuric acid which acts as both catalyst and dehydrating reagent.

Scheme of preparation::



Chemicals:
4-hydroxybenzoic acid 1.38 g (0.01 mol)
appropriate alcohol 25 ml
sulfuric acid 0.4 g (*Calculate and measure **volume** of sulfuric acid; data for the particular concentration can be found on bottle label, if not, see a laboratory chemicals catalogue.*)

Procedure: 4-hydroxybenzoic acid is dissolved or suspended in an appropriate aliphatic alcohol in a flask equipped with a condenser. Sulfuric acid is then added and the mixture is refluxed under stirring on a magnetic stirrer for 4 hours. If an alcohol with boiling point above 100°C (e.g. propanol, 2-methylpropanol = isobutylalcohol) is used the temperature in the oil bath is kept at approx. 110°C. After cooling, the reaction mixture is neutralized with diluted ammonia solution and the excessive alcohol together with a portion of water are distilled off at a vacuum rotary evaporator. The syrupy evaporation residue is then suspended in water .The formed precipitate is then isolated by suction and, if needed, recrystallized from a suitable solvent (hot water, aqueous ethanol or, after perfect drying, from heptane or petroleum ether. If a hydrocarbon is used the crystallisation must proceed in an oil bath under reflux.) This procedure is suitable for synthesis of methyl, ethyl, propyl, propan-2-yl and 2-methylpropyl (= isobutyl)parabens. *Longer-chain alcohols have higher boiling points, it is difficult to distil them off on an evaporator and they are limitedly miscible with water.* **Thin layer chromatography (TLC)** for coarse confirmation of purity of a given product is performed on a silica gel plate with a mobile phase consisted of ethyl acetate and petroleum ether in a suitable ratio. A solution of starting 4-hydroxybenzoic acid is used as the comparison solution. The identity of the well dried product is confirmed by **melting point** determination and by **^{1}H-NMR spectroscopy.** *Weigh 10-15 mg of the product into a plastic test tube with lid and consult your lecturer. Samples of several pairs are usually measured together.*

Melting points of selected parabens and boiling points of alcohols used for their preparation

Compound	m.p. [°C]	b.p. of alcohol [°C]
Methylparaben	131	64.7
Ethylparaben	116 - 118	78.3
Propylparaben	96 - 98	97.2
Isopropylparaben (2-propylparaben)	86	82.3
Isobutylparaben (2-methylpropylparaben)	72 - 73	107.7

Usage
Parabens are frequently used as antimicrobial preservatives of medicinal and cosmetic preparations. Despite of their weak local anaesthetic activity which leads to attenuation of taste, parabens are also used in food and beverages. They are less toxic and are effective in broader range of pH than benzoic acid and

its salts, which are predominantly used here. Parabens are official in many pharmacopoeias as free phenolic compounds as well as sodium salts (phenolates), which are freely soluble in water. Esters with branched alcohols are used namely in cosmetic preparations.