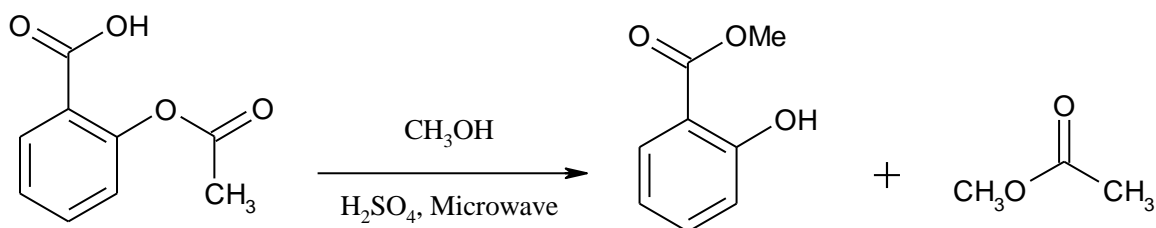


Transesterification and Fischer Esterification of Aspirin using Microwave Heating

Esters, like most carboxylic acid derivatives, typically undergo acyl substitution reactions when treated with nucleophiles under acidic conditions. When an alcohol is the nucleophile, the reaction is called a transesterification. In this experiment, an ester (aspirin) will be transesterified to produce methyl acetate and salicylic acid. This carboxylic acid will then be reacted with acidic methanol to produce a methyl ester (methyl salicylate) via Fischer esterification. This ester is used commercially as a flavoring and is known as oil of wintergreen.

The use of microwave energy in place of conventional heating for many processes has been shown to give faster reactions, higher yields, and reduced formation of by-products. In this experiment, you will use microwave heating to carry out the reaction, and use carbon nuclear magnetic resonance (^{13}C -NMR) to verify the identity of your product.



Required Reading:

Padias:

Carbon-13 NMR (pp. 96 – 101)

Safety:

- Sulfuric acid is a strong acid and can cause severe burns and damage to skin and eyes. **Handle with gloves!**
- Dichloromethane is a suspected carcinogen.

Procedure:

Preparation of the Reaction Mixture

Crush three aspirin tablets. Place 3.5 – 4.0 mL of methanol in a 5-mL conical vial and add the aspirin powder. Cap the vial and shake the mixture (**shake it hard!**) for *at least* 1 min. Filter the slightly cloudy mixture through a filter pipet (cotton only) into a 20-mL CEM reaction tube containing a “stir flea”, add 0.3 mL of concentrated sulfuric acid (**CAUTION! Sulfuric acid is very corrosive and can cause severe burns to skin and eyes! Handle with gloves!**) Using a magnetic stirrer, stir this reaction mixture for about 30 sec, then seal the reaction tube with the Teflon insert and screw top.

Microwave Heating of the Reaction Mixture

Place the reaction tube in the carousel, and place the carousel into the CEM MARS microwave reactor and insert the thermocouple in tube #1. Heat the reaction mass at 120 °C for 5 min using the following program:

Vessel Type = GlassChem	Control = Ramp to Temperature
Power = 800 W (100%)	Ramp = 5:00
PSI = 200	°C = 120
S (Stir) = 3	Hold = 5:00

After the heating time, the unit will cool the reaction tubes for 5 min. **CAUTION: Since the vessel temperature may still be above the boiling point of methanol, unscrewing the cap may cause an eruption. Cool the reaction tube in an ice-water bath for 5 min prior to unscrewing the cap.** Add 5 mL of saturated aqueous sodium bicarbonate to the reaction mixture in the reaction tube and mix well. Transfer the mixture to a small separatory funnel and extract the mixture with dichloromethane (2 x 5 mL). After completing both extractions, remove the aqueous layer from the separatory funnel. Place the combined organic layers back into the separatory funnel and wash with 5 mL of saturated aqueous sodium bicarbonate. Check the pH of this bicarbonate wash liquid with pH paper. If it is acidic, wash the organic layer with an additional 5 mL of saturated aqueous sodium bicarbonate. Drain the lower organic layer into a small Erlenmeyer flask and dry the solution over a small amount of anhydrous sodium sulfate for 5 minutes. Transfer the dried solution into a small pre-weighed beaker and evaporate the solvent with gentle heating on a hotplate. This process can be accelerated by directing a gentle air stream into the top of the beaker. Re-weigh the beaker to determine the mass of methyl salicylate and analyze by ^{13}C NMR spectroscopy.

Writing Your Report:

Interpret your NMR spectrum and explain how you determined the peak assignments. Calculate the overall percent yield for the synthesis of methyl salicylate from aspirin (assume each tablet contained 325 mg of aspirin).

Questions:

1. Look up the structure of triacetin (the simplest possible fat). What are the products of the acid-catalyzed transesterification of triacetin with ethanol?
2. Design a synthesis of methyl salicylate starting from aniline.
3. Why was an aqueous sodium bicarbonate solution used in the extraction? What would have happened if an aqueous NaOH solution was used instead?