

Honors Cup Proposal (231 III – Tu PM – W08)

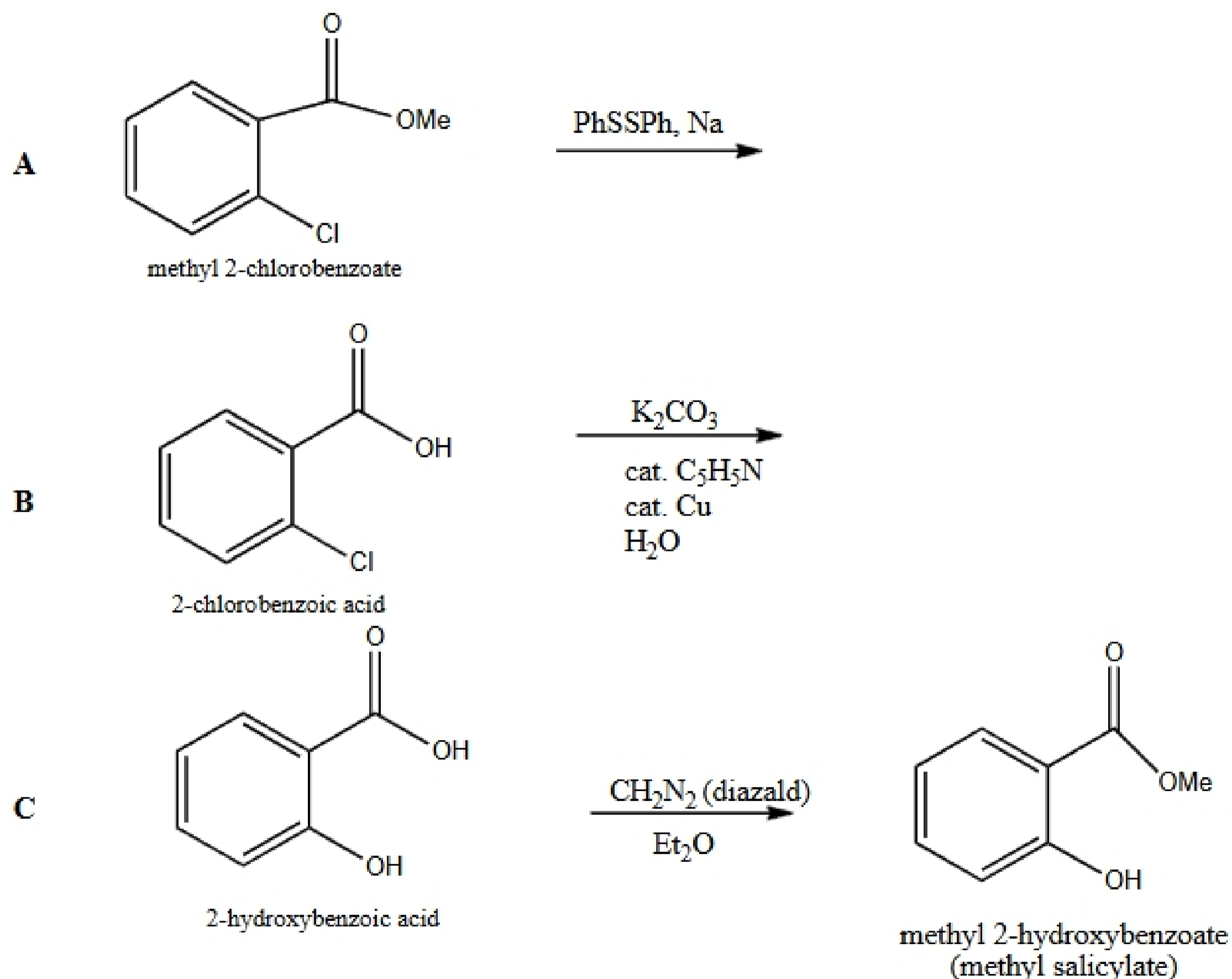
Section: 231

Group Members: Andy Cipa, Andrew Konishi, Kanya Sankar

TITLE: Synthesis of Glory (methyl 2-hydroxybenzoate from methyl 2-chlorobenzoate)

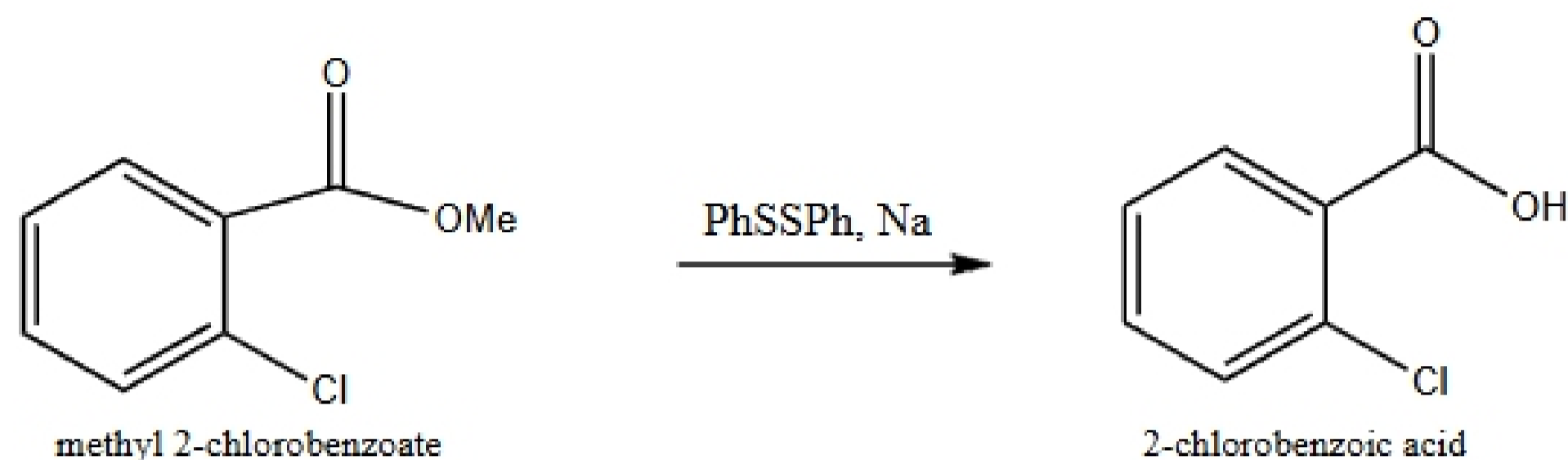
INTRODUCTION:

Methyl Salicylate (oil of wintergreen) is an organic molecule, which is thoroughly involved with several processes that maintain the biosphere. This molecule functions as a pheromone in certain plants and animals. It also proves beneficial to humans by providing a fragrant and glorious smell for use in deodorants and flavorings; however, it can be fatal in large doses.



STEP 1

Synthetic Transformation 1



Experimental 1

The reaction is carried out by treatment of Ph_2S_2 (0.6 equivalent) and Na (1.6 equivalent) for 15 minutes in 90°C in solvent NMP followed by the addition of the ester (methyl 2-chlorobenzoate). It is heated at 90°C for another 15 minutes.

Procedure:

Magnetically stirred solution of Ph_2S_2 (0.786 g – 0.0036 mol) in NMP (4.8 mL) is treated with Na (0.211 g – 0.0096 mol) under reflux for 15 minutes under N_2 . Methyl 2-chlorobenzoate (1.026 g – 0.006 mol) in NMP (7.2 mL) is added, and the mixture is heated under reflux for 30 minutes. The cooled mixture is made alkaline with 25 mL of 5% NaOH to separate any neutral component. The aqueous part is acidified in an ice bath with 6 N HCl and extracted with Et_2O (3 x 15 mL). The extracts are washed with 15 mL of brine, dried with sodium sulfate, and concentrated under a vacuum to obtain a brown solid. This is passed through a column of silica gel and elution with 5 % EtOAc-hexane (200 mL) results in predicted 100 % yield of the product.

Expected Yield:

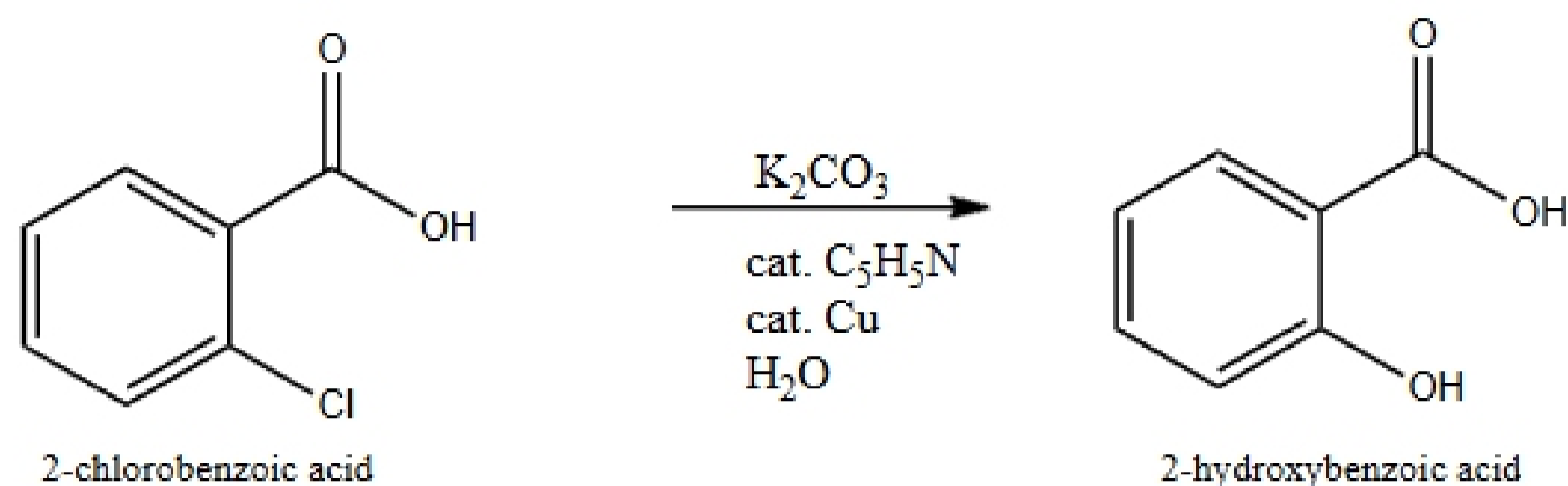
100 % 0.006 mol (0.936 g)

Safety Issues:

Diphenyl disulfide: Safety glasses, adequate ventilation. Irritating to eyes, respiratory system, skin.
NMP: Safety glasses, adequate ventilation. Irritating to eyes, respiratory system, skin
methyl 2-chlorobenzoate: Irritating to eyes and skin.
NaOH: Very corrosive, causes severe burns. Harmful by ingestion, skin contact or inhalation. Use safety glasses and adequate ventilation.
Diethyl Ether Can be ignited at a very low temperature and constitutes a serious fire risk. An explosion is possible when the volume of vapor in air is just 2% Harmful if breathed in May react with the oxygen in the air once a container is opened
Silica Gel: Wear safety glasses Work in a well ventilated area
Sodium: If the product is dusty, handle only in a fume cupboard Can cause serious permanent damage if it gets into the eyes. Reacts with moisture in the air to form sodium hydroxide and tarnishes quickly. Should always be stored under a protective material, normally an unreactive oil. Always wear safety glasses. When cutting, remove protective oil and cut cleanly with a knife. Return all traces of sodium to the storage vessel. Disposal can normally be done by carefully dissolving small portions of sodium in dry isopropanol. Hydrogen is released during this process, so precautions must be taken to avoid any possibility of fire.

STEP 2

Synthetic Transformation 2



Experimental 2

The hydrolysis of 2-chlorobenzoic acid is performed using 3 equivalents of potassium carbonate, 2 moles of pyridine, and 3 % copper powder per mole of the acid using water, and 2 hours reaction time.

Procedure:

A mixture of 2-chlorobenzoic acid (0.006 mol – 0.936 g), anhydrous potassium carbonate (0.018 mol – 2.49 g), pyridine (0.012 mol – 0.949 g), copper powder (0.005 mol – 0.3 g) is refluxed in 37.5 mL of water for 2 hours. The reaction mixture is cooled and poured into water acidified with HCl (1:1) to pH = 3. The solid is filtered and crystallized with ethanol & water (1:2). This results in a 90% yield.

Note: If reaction time is reduced to 1.5 hours, the product reduces to 50 % yield.

Expected Yield:

90% 0.0054 mol (0.7452 g)

Safety Issues:

Potassium Carbonate: Irritating to the lungs if inhaled.

Pyridine: Harmful if breathed, swallowed, or if it is absorbed through the skin. Always wear safety glasses and use proper ventilation.

Copper: Irritating if inhaled.