Introductory remarks:

At all times while you are in the laboratory you should wear safety spectacles or your own spectacles if they have been approved. Eating of any kind of food is strictly prohibited in the laboratory.

Participants are expected to work safely, to behave socially and to keep equipment and work environment clean. Violation of these rules may result in penalty points. Do not hesitate to ask a laboratory assistant if you have any questions concerning safety issues.

For each experiment you will get two sort of papers:

- prescription of experiment
- report sheet.

Please read carefully text of the entire experimental task before you begin your experimental work. Check where instruments are located. You have 15 minutes to prepare yourself for the experimental tasks.

Work may only begin when the start signal is given At the end there will be a pre-warning 15 minutes before the end of your time. You must stop your work immediately after the stop command is given..

Write your name and personal identification code (posted at your work station) in the appropriate box of the protocol sheets.

Use the list of the R/S safety codes to protect yourself.

All results must be written in an appropriate places on the answer sheets. Data written elsewhere will not be marked. Do not write anything on the back of your answer sheets. If you need additional paper or a replacement answer sheet, request it from the laboratory assistant.

When you have finished the examination, you must put all papers into the envelope provided, then you must seal the envelope. Only papers in the sealed envelope will be marked.

Do not leave the laboratory until you have permission to do so.

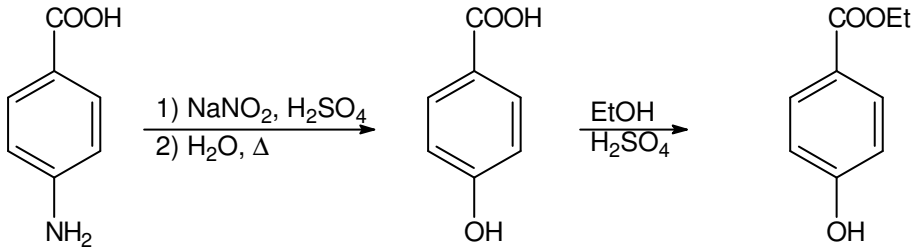
The number of significant figures in numerical answers must conform to the rules of evaluation of experimental error. The inability to perform calculations correctly will result in penalty points, even if your experimental technique is flawless.

An official English-language version is available only on request.

SYNTHESIS OF ETHYL 4-HYDROXYBENZOATE

The goal of this experiment is the preparation of ethyl ester of 4-hydroxybenzoic acid, starting from 4-aminobenzoic acid. The starting compound is first diazotized and the diazo group subsequently replaced by a hydroxy group. The product, 4-hydroxybenzoic acid, is in the second step esterified with ethanol and the resulting ester purified by recrystallization.

Reaction scheme



List of equipment

a) Personal equipment (located at the working place)

Item	Quantity	Location
beaker 25 mL	2	at your workplace
beaker, 50 mL	2	
beaker, 100 mL	1	
beaker, 250 mL	1	
beaker 400 mL	1	
round bottom flask, 100 mL NS 29/32	1	
Liebig condenser, NS 29/32	1	
measuring cylinder, 50 mL	1	
thermometer, Hg, –10 to +50 °C	1	
crystallizing dish, 10 cm	1	

separatory funnel 100 mL	1	
Erlenmeyer flask, 100 mL	1	
filtering funnel	1	
Büchner funnel	1	
filter flask	1	
TLC chamber	1	
vials	8	at your workplace
glass rod	1	
spatula	1	
filter paper	3 sheets	
Pasteur pipettes	5	
watch glass	1	
washing bottle with water	1	
washing bottle with ethanol	1	
capillaries for TLC		on the shelf
TLC plates		on the shelf

b) Equipment in common use

Item	Location
ultraviolet lamp for TLC	each laboratory
laboratory oven	each laboratory
rotary evaporator	each laboratory
water pump	on every bench
laboratory balance	on every bench

List of chemicals

Reagent	R codes	S codes	Location
4-aminobenzoic acid	36/37/38	26, 36	Ready weighed (1.37 g) on the work bench
sulfuric acid (concentrated)	35	26-30-45	in a hood
sodium chloride			supplied with ice
sodium nitrate(III)	8-25	45	on a shelf
ethanol (absolute)	11	7-16	in a hood
diethyl ether	12-19	9-16-29-33	in a hood
sodium hydrogen carbonate (solution)		22-24/25	on a shelf over the bench
sodium sulfate (anhydrous)		22-24/25	on a shelf over the bench
hexane ethyl acetate	11-48/20 11	9-16-24/25-29-51 16-23-29-33	mixture of hexane and ethyl acetate as a mobile phase. On a shelf.
methanol	11-23/24/25-39/23/24/25	7-16-36/37-45	in a hood
acetone	11	16-23-29-33	in a washing bottle at the end of the bench

Relative atomic masses:

H: 1.01	C: 12.01	N: 14.01
O: 16.00	Na: 22.99	S: 32.07

Procedure

Step 1

Place 10 mL of water into 50 mL beaker and add cautiously 3.0 mL of concentrated sulfuric acid from a small beaker. (CAUTION! Concentrated sulfuric acid is extremely hazardous and corrosive. Handle it with care! Upon mixing of concentrated sulfuric acid and water, a substantial amount of heat is evolved, the mixture may start boiling.) In the resulting solution disperse 1.37 g of 4-aminobenzoic acid and after that cool the reaction mixture in an ice-salt mixture to approx. 0 °C upon stirring with magnetic stirrer.

To the cooled suspension slowly add a solution of 0.72 g of sodium nitrate(III) in 2 mL of water, while stirring. Do not allow the temperature to rise above 5 °C! Upon the complete addition of sodium nitrate(III) leave the reaction mixture in the ice bath, removing the magnetic stirrer.

Prepare 40 mL of water in 250 mL beaker and bring it to boiling on magnetic stirrer hot plate. Pour the diazotized mixture slowly into a boiling water. This is accompanied with a development of a gas. After the addition is complete, let the solution to boil for 5 minutes, cool it to room temperature and subsequently in an ice-water bath. Filter the product with suction, wash with little ice-water, dry it on funnel for a few minutes and finally in an oven at 120 °C for 15 minutes, together with the filter paper. Scrape the dry product off the filter to a watch glass and weigh it in the presence of the supervisor.

Step 2

Place 30 mL of absolute ethanol in a 100 mL beaker, cool it in an ice bath and add cautiously upon stirring 3.0 mL of concentrated sulfuric acid. (CAUTION! Concentrated sulfuric acid is extremely hazardous and corrosive. Handle it with care! Upon mixing of concentrated sulfuric acid and ethanol, a substantial amount of heat is evolved, the mixture may start boiling.) Place the dry 4-hydroxybenzoic acid in 100 mL round bottom flask and add the ethanol solution of sulfuric acid. Equip the flask with a reflux condenser an heat it in a boiling water bath. Follow the progress of the reaction by means of thin-layer chromatography at approximately 30 minute intervals (see instructions at the end of text).

When there is no more starting compound in the reaction mixture (the corresponding spot on the chromatogram dissapears or becomes very weak), or the reaction time has reached 2

hours, cool the flask, transfer the contents into a separatory funnel, add 40 mL of a diethyl ether and wash with 50 mL of water. Separate the layers and wash the organic layer with 10 mL of saturated $NaHCO_3$ solution and again with a small quantity of water. Dry the ethereal solution with anhydrous sodium sulfate, filter to a weighed 100 mL round bottom flask and evaporate the solvent by a rotary evaporator. Weigh the flask with crude ester in the presence of the supervisor.

After evaporation is complete, recrystalize the residue from a mixture of methanol and water as follows: dissolve the product in little methanol in a 25 mL beaker, heat the solution to boiling and dilute it with water until it becomes turbid. Cool the solution and filter the crystals of ethyl 4-hydroxybenzoate with suction, dry the product for few minutes on filter and finally in an oven at 100 °C for 15 minutes, together with filter. Scrape the dry product off the filter to a watch glass and weigh it in the presence of the supervisor.

Procedure for analysis of the reaction mixture by thin-layer chromatography (esterification step) Lift the flask from the water bath, wait approx. 1 minute and then lift the condenser and shift it a bit aside. By means of a Pasteur pipette withdraw a little of a reaction mixture from the flask and place 1 drop into a vial. Reassemble the reaction apparatus.

Dilute the sample with 1 mL of ethanol and apply the solution to the TLC plate, along with a solution of 4-hydroxybenzoic acid as a standard. Develop the chromatogram in the given mobile phase (mixture of ethyl acetate : hexane, 1:3) and observe the plate under the UV lamp.