



GRAND PRIX CHIMIQUE

PETNICA SCIENCE CENTER, VALJEVO, SERBIA

9TH-14TH OCTOBER 2017

PREPARATIVE TASK

Preparation of *p*-nitroacetanilide

Preparation of vanillyl alcohol

SUPPORTED BY



**Serbian Chemical
Society**



**Ministry of Science, Education
and Technological
Development of the Republic of
Serbia**



Faculty of Chemistry, University of Belgrade

**Innovation Center of the Faculty of Chemistry,
University of Belgrade**



Faculty of Science, University of Kragujevac

Available equipment and chemicals

A list of glassware and laboratory equipment on each workbench

Item	Qty	Item	Qty
Beaker, 100 mL	2	Pipette, 5 mL	3
Beaker, 250 mL	1	Reagent bottle for liquids	1
Büchner funnel	1	Reflux condenser	1
Clamp	4	Ring stand	2
Cloth	1	Rod muff	4
Cork stand, larger	1	Round-bottom flask, 100 mL	2
Cork stand, smaller	1	Round-bottom flask, 50 mL	1
Developing chamber	1	Round-bottom flask, 500 mL	1
Dry-flash column	1	Rubber conical gasket	1
Erlenmeyer flask, 100 mL (with stopper)	1	Rubber tube	2
Erlenmeyer flask, 250 mL	1	Rubber-coated glass rod	1
Filter paper	1	Ruler	1
Filtration funnel	1	Scissors	1
Funnel, plastic	1	Separatory funnel, 250 mL	1
Glass rod	1	Separatory funnel, 50 mL	1
Graduated cylinder, 10 mL	1	Spatula	2
Graduated cylinder, 25 mL	1	Stir bar	2
Graduated cylinder, 50 mL	2	Test tube rack	1
Magnetic stirrer	1	Test tubes	20
Marker pen	1	Thermometer	1
Metal bath	2	TLC plate	5
Metal ring	1	Vacuum flask	1
Pencil	1	Wash bottle (distilled water)	1
Pipette filler	1	Wash bottle (ethanol)	1
Pipette, 2 mL	1	Watch glass	2

Two workbenches share a package of a universal pH indicator, capillary tubes, and a pair of tweezers. A hair dryer and a stir bar retriever to be shared among all contestants can be found on the weighing desk. Ice is available from several styrofoam containers.

A list of available chemicals and their locations

Chemical	Location	Chemical	Location
Acetanilide	weighing desk	NaBH ₄	weighing desk
Vanillin	weighing desk	Silica gel	weighing desk
Acetic acid, glacial	fume hood	H ₂ SO ₄ , concentrated	fume hood
HNO ₃ , concentrated	fume hood	Ethanol (in wash bottle)	each workbench
Methanol	shared by two workbenches	Acetone	shared by two workbenches
Na ₂ SO ₄ , anhydrous	shared by two workbenches	Iodine (in chamber)	shared by two workbenches
Hexane/ethyl acetate 3:2	shared by two workbenches	NaCl, solid	shared by two workbenches
NaCl, saturated solution	shared by two workbenches	NH ₄ Cl, saturated solution	shared by two workbenches
Toluene	shared by two workbenches	Ethyl acetate	shared by two workbenches

Safety considerations

A pair of protective goggles is provided on each workbench. Protective gloves can be found at the weighing desk. Each workplace is equipped with a fume extractor arm.

A list of risk (R) and safety (S) statements for chemicals which will be handled

Chemical	R statements	S statements
Acetanilide	22	36/37
Acetic acid, glacial	10-34-35-36/38-42	23-24/25-26-36/37/38-45
Acetone	11-39/23/24/25-36-66-67	7-9-16-26-36/37-45
Ammonium chloride	22-36-37/38-41	22-26-36
Ethanol	10-11-36/37/38-39/23/24/25-51/53-52/53-68/20/21/22	7-16-24/25-26-35-36/37-45-61
Ethyl acetate	10-11-36-39/23/24/25-66-67-68/20/21/22	7-16-25-26-33-36/37-45
H ₂ SO ₄ , concentrated	11-35-36/38-39/23/24/25	16-26-30-36/37-45
Hexane	11-36/36/38-48/20-50/53-51/53-62-65-67	9-16-26-29-33-36/37/39-45-53-60-61-62
HNO ₃ , concentrated	8-20-26/27-34-35-36/38-37/38-41	23-26-28-36/37/39-45-60
Iodine	11-19-20/21/22-36/37/38-40-50	16-23-25-26-36/37-61
Methanol	10-11-39/23/24/25-36/38-40-68/20/21/22	7-16-23-24/25-26-36/37-45
Na ₂ SO ₄ , anhydrous	–	22-24/25
NaBH ₄	15-19-21/22-23/24/25-34-35-36/38-42/43-49-50/53-51/53-60-61-62-63-68	22-26-36/37/39-43-43A-45-50-53-61
<i>p</i> -Nitroacetanilide	36/37/38	26-36
Silica gel	22-36/37-41-42/43-48/20-49-50/53-51/53-60-68	22-24/25-26-36/37-39-45-53-60-61
Sodium chloride	22-36/37/38	24/25-26-36
Toluene	11-38-39/23/24/25-48/20-63-65-67	7-16-36/37-45-46-62
Vanillin	22-36/37/38-36	22-24/25-26-37/39-36/37/38
Vanillyl alcohol	36/37/38	26-36

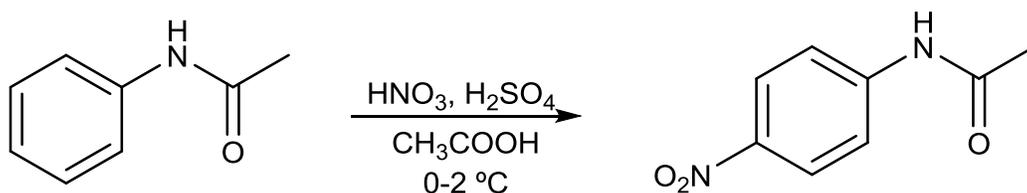
Problem 1: Preparation of *p*-nitroacetanilide

In this task, you will prepare *p*-nitroacetanilide by nitration of acetanilide, and purify the product by recrystallization. *p*-Nitroacetanilide is an intermediate in the synthesis of azo dyes and heterocyclic compounds.

The nitration of acetanilide is an exothermic reaction. Reaction temperature must be carefully controlled by cooling and stirring the reaction mixture, as well as by adding reagents slowly. Glacial acetic acid is used as a polar solvent capable of dissolving acetanilide when mixed with some concentrated sulfuric acid. Both the acetanilide solution and the nitrating mixture must be cooled prior to the reaction. The nitrating mixture is added in small portions to limit dinitration.

The reaction workup procedure entails the removal of excess acid and product crystallization. Excess acid is removed because hydrogen ions are capable of catalyzing the amide hydrolysis to *p*-nitroaniline or its protonated cation. Most of the acid is removed by pouring the crude product into ice, but it is also necessary to rinse the obtained crystals with water.

Reaction scheme



$$A_r(\text{C}) = 12, A_r(\text{H}) = 1, A_r(\text{N}) = 14, A_r(\text{O}) = 16$$

Procedure

1. Measure out 5 mL of glacial acetic acid and 0.037 mol of acetanilide into a 250-mL Erlenmeyer flask.

Note: Show your calculation for the mass of acetanilide to a jury member!

Calculation:

2. Carefully add 10 mL of concentrated sulfuric acid to the mixture of acetanilide and glacial acetic acid. The mixture becomes warm and clear.
3. Prepare an ice-salt bath and place the Erlenmeyer flask with the previously prepared mixture in it to cool.
4. Prepare the nitrating mixture in a graduated cylinder constantly cooled in a salt-ice bath by carefully adding 1.4 mL of concentrated sulfuric acid to 2.2 mL of concentrated nitric acid.
5. When the solution in the Erlenmeyer flask cools down to 0-2 °C, slowly add the nitrating mixture dropwise into it using a separatory funnel, taking care that the reaction mixture temperature does not rise above 10 °C. Gently stir the contents of the Erlenmeyer flask periodically throughout the course of the reaction. When the nitrating mixture addition is completed, remove the Erlenmeyer flask from the ice bath and allow it to stand at room temperature for the course of one hour, with periodic stirring.
6. After one hour, pour the obtained solution into a beaker filled with 50 g of ice, which causes the nitroacetanilide to precipitate out.
7. After 15 minutes, filter the mixture through a Büchner funnel and rinse with a significant quantity of water to remove the excess acid, and then place the crude product in a laboratory oven to dry.
8. The crude product is a mixture of *ortho*- and *para*-isomers which separate during crystallization from hot ethanol: *p*-nitroacetanilide crystallizes upon cooling while the yellow-colored *o*-nitroacetanilide remains in the filtrate.
9. Recrystallize the crude product from 96% ethanol using a properly placed reflux condenser and a water bath to heat the solution.
10. After cooling, filter the obtained *p*-nitroacetanilide through a Büchner funnel, and place it in a laboratory oven to dry.

11. Calculate the percent yield of *p*-nitroacetanilide.

Calculation:

Problem 2: Preparation of vanillyl alcohol

Vanillyl alcohol (4-(hydroxymethyl)-2-methoxyphenol) is a primary alcohol, that is obtained by reduction of vanillin (4-hydroxy-3-methoxybenzaldehyde). Vanillyl alcohol is used as a flavouring agent.

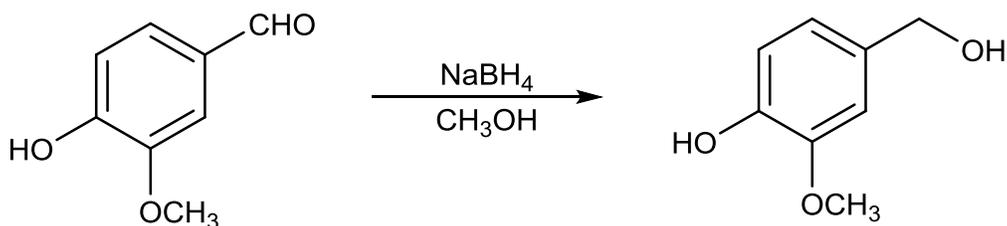
The most common method for preparing primary alcohols is the reduction of aldehydes with reduction agents such as NaBH_4 and LiAlH_4 . Although a milder reduction agent, the benefits of using NaBH_4 include compatibility with aqueous and alcohol solutions, and ease of handling.

In the majority of reduction reactions the aldehyde is dissolved in a solvent, and sodium borohydride is added slowly in multiple portions. The reasons behind this are:

- a side reaction with the protic solvent generates a certain quantity of hydrogen gas which causes the solution to bubble and foam, and
- the possibility of sodium borohydride decomposition at higher temperatures if added all at once (the reaction is exothermic).

It is necessary to wash the reaction mixture with a saturated aqueous solution of ammonium chloride to remove any basic borate products. Additionally, the saturated aqueous solution of salt stops supersaturated aqueous solutions of vanillyl alcohol from forming.

Reaction scheme



$$A_r(\text{C}) = 12, A_r(\text{H}) = 1, A_r(\text{O}) = 16$$

Procedure

1. Weigh 0.0066 mol of vanillin on a laboratory balance.

Note: Show your calculation for the mass of vanillin to a jury member!

Calculation:

2. Transfer the measured vanillin to a 100-mL round-bottom flask with a ground-glass joint and add 35 mL of methanol. Place the flask on a magnetic stirrer and equip it with a reflux condenser.
3. Slowly add 0.8 g of sodium borohydride to the reaction mixture with stirring and in small portions. Then stir the reaction at room temperature for one hour.
4. After one hour, dilute the reaction mixture with 50 mL of ethyl acetate and transfer to a separatory funnel.
5. In the separatory funnel, wash the mixture first with 50 mL of a saturated aqueous ammonium chloride solution, and then with 50 mL of a saturated aqueous sodium chloride solution. Dry the organic layer with anhydrous sodium sulfate.
6. After the solution is dried, filter the solution and remove the solvent by evaporation under reduced pressure. Measure the mass of the crude product. Record the mass. The residue in the flask will be purified by dry-column flash chromatography on silica gel.
7. Assemble the dry-column flash chromatography apparatus (a column and a separatory funnel with a ground-glass joint). Pour 15 g of dry silica gel into the column and gently tap the column walls (using a rubber-coated glass rod) to pack it compactly. Then apply the vacuum and press the surface firmly to obtain a well compacted bed.
8. Pass 15 mL of toluene twice through the column while applying vacuum. If the column was packed properly the solvent should descend as a horizontal line.
9. Dissolve the crude vanillyl alcohol in 4 mL of methanol and transfer it onto the column. When the sample is adsorbed onto the column, begin the dry-column flash chromatography using portions of 10 mL of toluene/ethyl acetate (9:1).
10. Transfer each fraction into a labelled test tube and monitor the dry-column flash chromatography progress with thin-layer chromatography.
11. Dissolve a small amount of vanillin and of vanillyl alcohol standard in ca. 1 mL of acetone in a dry and clean test tube.
12. Spot the standards and contents of the dry-column flash chromatography fractions onto a TLC plate (use multiple plates in order to spot all of the fractions).
13. Place an adequate volume of TLC eluent (hexane/ethyl acetate 3:2) in a developing chamber. Dry the developed plate using a hair dryer.
14. Visualization of the plate spots is to be performed in a iodine chamber. Place the dried plates in a iodine chamber and wait for spots to appear.

15. Determine the Rf values for the prepared vanillyl alcohol and vanillin.

Rf value for vanillyl alcohol _____

Rf value for vanillin _____

16. Continue the dry-column flash chromatography for as long as vanillyl alcohol is present in the fractions. Transfer the fractions that contain pure vanillyl alcohol from the test tubes into a round-bottom flask and remove the solvent from it by evaporation under reduced pressure. Calculate the percent yield of the obtained product.

Calculation:

Hand over the prepared vanillyl alcohol and developed TLC plates to a jury member.