

19th – 29th July, 2018
Bratislava, SLOVAKIA
Prague, CZECH REPUBLIC

www.50icho.eu

PREPARATORY PROBLEMS: PRACTICAL



50th IChO 2018

International Chemistry Olympiad
SLOVAKIA & CZECH REPUBLIC

BACK TO WHERE IT ALL BEGAN



Table of Contents

Contributing Authors.....	2
Fields of Advanced Difficulty	2
Safety.....	3
Problem P1. Determination of a metallic ore composition.....	4
Problem P2. Determination of a carbonate rock composition	8
Problem P3. Determination and identification of organic acids	11
Problem P4. A chemical oscillator and its activation energies.....	15
Problem P5. Kinetics of a chemical wave front propagation	19
Problem P6. Separation of acidic, basic and neutral organic compounds.....	22
Problem P7. Meerwein–Ponndorf–Verley reduction	26
Problem P8. Transformation of a drug to a sweetener.....	29



Contributing Authors

Ambroz Almásy	Comenius University in Bratislava
Iveta Kmentová	Comenius University in Bratislava
Elena Kulichová	Secondary Chemical School in Nováky
Pavel Májek	Slovak Technical University in Bratislava
Erik Szabó	Comenius University in Bratislava
Pavol Tarapčík	Slovak Technical University in Bratislava
Matej Žabka	Comenius University in Bratislava

Edited by

Petra Ménová	University of Chemistry and Technology, Prague
Martin Putala	Comenius University in Bratislava

Fields of Advanced Difficulty

1. *Techniques in organic synthesis*: thin layer chromatography, filtration and drying of precipitates
2. *Extraction* using immiscible solvents

Notes

During the practical exam, students WILL NOT be expected to:

- Determine melting points
- Use a rotary evaporator
- Use a spectrophotometer
- Handle and work up moisture sensitive compounds (using syringes and balloons)
- Perform column chromatography

Dedication of Problems P4 and P5 to the Belousov–Zhabotinsky (BZ) oscillating reaction is entirely commemorative. Students will not be expected to have received training specifically addressing this particular reaction or other chemical oscillators.



Safety

Participants in the Olympiad must be prepared to work in a chemical laboratory and be aware of all relevant rules and safety procedures. The organizers will strictly enforce the safety rules given in *Appendix A* of the IChO Regulations during the Olympiad.

The Preparatory Problems are designed to be carried out in properly equipped chemical laboratories under competent supervision **only**. We did not include specific and detailed safety and disposal instructions as regulations are different in each country. Mentors must carefully adapt the problems accordingly.

The GHS hazard statements (H-phrases) associated with the materials used are indicated in the problems. Their meanings are as follows.

Definition of GHS hazard statements

Physical hazards

- H225 Highly flammable liquid and vapour.
- H226 Flammable liquid and vapour.
- H228 Flammable solid.
- H271 May cause fire or explosion; strong oxidizer.
- H272 May intensify fire; oxidizer.
- H290 May be corrosive to metals.

Health hazards

- H301 Toxic if swallowed.
- H302 Harmful if swallowed.
- H304 May be fatal if swallowed and enters airways.
- H311 Toxic in contact with skin.
- H312 Harmful in contact with skin.
- H314 Causes severe skin burns and eye damage.
- H315 Causes skin irritation.
- H317 May cause an allergic skin reaction.
- H318 Causes serious eye damage.
- H319 Causes serious eye irritation.
- H331 Toxic if inhaled.
- H332 Harmful if inhaled.
- H333 May be harmful if inhaled.
- H334 May cause allergy or asthma symptoms or breathing difficulties if inhaled.
- H335 May cause respiratory irritation.
- H336 May cause drowsiness or dizziness.
- H351 Suspected of causing cancer.
- H361 Suspected of damaging fertility or the unborn child.
- H371 May cause damage to organs.
- H372 Causes damage to organs through prolonged or repeated exposure.
- H373 May cause damage to organs through prolonged or repeated exposure.

Environmental hazards

- H400 Very toxic to aquatic life.
- H402 Harmful to aquatic life.
- H410 Very toxic to aquatic life with long lasting effects.
- H411 Toxic to aquatic life with long lasting effects.
- H412 Harmful to aquatic life with long lasting effects.



Problem P1. Determination of a metallic ore composition

Slovakia has a rich history in mining. Since the Middle Ages, gold, silver and copper ores have been mined in Kremnica, Banská Bystrica and especially in Banská Štiavnica, where the remnant of the extinct stratovolcano is rich in mineral raw materials. Mining in Slovakia has provided notable technological advancements. In 1763, the Academy of Mining and Forestry was founded in Banská Štiavnica. It is one of the oldest technically-oriented educational institutions in all of Europe. One particularly extraordinary division at the Academy was the Department of Chemistry, which allowed students to experiment in real laboratories.

In this task, you will determine the concentration of copper and zinc ions in a solution obtained by the decomposition and proper modification of polymetallic ore.



Figure P1. Academy of Mining and Forestry in Banská Štiavnica.

Chemicals and Reagents

- Processed aqueous sample of the ore containing Zn^{2+} and Cu^{2+} , 50 cm³
- Strongly acidic cation exchange resin in hydrogen cycle, equivalent to Dowex 50, 15 cm³
- 0.1 M standard sodium hydroxide solution, 200 cm³
- 0.05 M standard Cu^{2+} solution, 50 cm³
- 2 M hydrochloric acid solution, 200 cm³
- 0.15 M standard EDTA disodium salt solution, 200 cm³
- 25% aqueous ammonia solution (w/w), 50 cm³
- 6% hydrogen peroxide solution (w/w), 1 cm³
- 0.25 M ammonium oxalate solution, 100 cm³
- Buffer solution (35 cm³ of 25% ammonia (w/w) and 5.4 g of ammonium chloride diluted to 100 cm³)
- Indicators: methyl red solution, universal pH indicator paper, murexide (solid indicator mixture), Eriochrome black T (solid indicator mixture)

Substance	Name	State	GHS Hazard Statement
NaOH	Sodium hydroxide	Aqueous solution	H314
HCl	Hydrochloric acid	Aqueous solution	H314, H318
$CuSO_4 \cdot 5H_2O$	Copper sulfate pentahydrate	Aqueous solution	H302, H315, H410
NH_3	Ammonia	Aqueous solution	H314, H400
$C_{10}H_{14}N_2O_8Na_2 \cdot 2H_2O$	Disodium ethylenediamine tetraacetate dihydrate	Aqueous solution	H302, H315, H319, H335
$(NH_4)_2C_2O_4$	Ammonium oxalate	Aqueous solution	H302, H312



NH ₄ Cl	Ammonium chloride	Solid	H302, H319
H ₂ O ₂	Hydrogen peroxide	Aqueous solution	H271, H302, H314, H333, H402
C ₂₀ H ₁₂ N ₃ O ₇ SNa	Eriochrome black T	Solid	H319
C ₈ H ₈ N ₆ O ₆	Murexide	Solid	Not classified
C ₁₅ H ₁₅ N ₃ O ₂	Methyl red	Solution	H225, H319, H371

Equipment and Glassware

- Laboratory stand with burette clamp
- Volumetric flasks, 250 cm³ (1) and 100 cm³ (4)
- Titration flasks, 250 cm³ (3)
- Burette, 25 cm³
- Pipettes, 5, 10, 25 and 50 cm³ with pipette filler
- Spectrophotometer with cuvettes (2, *l* = 1 cm)
- Ion exchange chromatography column (recommended diameter ca 1.5 cm)
- Hotplate

Procedure

I. Determination of the metal ion concentration by alkalimetry and photometry

When a solution of copper and zinc ions is passed through a column packed with a cation exchange resin, the ions are trapped on the resin, releasing an equivalent amount of H⁺ ions into the eluate. One of these ions forms a coloured species that enables its determination in the mixture by spectrophotometry.

1. Fill the column with the strongly acidic cation exchange resin. A suitable height for the resin in the column is 12–15 cm (recommended volume of the resin is 10–15 cm³).
2. Add 50 cm³ of 2 M hydrochloric acid solution to the column and let the solution pass through the column with a flow rate of 2 drops per second. Allow the level of the solution to fall just above the level of the resin. Discard the eluate. Wash the column at the same flow rate with deionised water until a neutral pH of the eluate is obtained. Check the pH of the dropping eluate using the pH indicator paper. Allow the level of water to fall just above the level of the resin. The column is now ready for use in the H⁺ cycle.
3. Add 10.00 cm³ (*V*) of a sample stock solution to the column and let the level of the solution drop just above the level of the resin. Then wash the column with deionised water at a flow rate of 2 drops per second and collect the eluate into a 250 cm³ (*V_{el}*) volumetric flask. After filling half of the flask, check the pH of the dropping eluate. If the pH = 7, the ion exchange is finished; if the pH < 7, continue washing the column. After a neutral pH has been reached, fill the flask up to the mark with deionised water.
4. Alkalimetric titration: Pipette 50.00 cm³ (*V_{1at}*) of the eluate stock solution into the titration flask and add methyl red indicator. Titrate with the standard sodium hydroxide solution until the first visible colour change of the indicator (*V_{2at}*). Repeat the titration as necessary.
5. Prepare two diluted standard Cu²⁺ solutions containing ammonia solution: pipette 5.00 cm³ of the standard Cu²⁺ solution into one 100 cm³ volumetric flask and 10.00 cm³ of standard Cu²⁺ solution into the second 100 cm³ volumetric flask. Add 10 cm³ of the ammonia solution into each flask and then fill each flask to the mark with deionised water. Label the flasks with the concentrations of the prepared solutions as *c_{min}* and *c_{max}*.



- Pipette 25.00 cm^3 (V_{orig}) of the sample stock solution into a 100 cm^3 (V_{dil}) volumetric flask and add deionised water to the mark. From this solution, pipette 5.00 cm^3 (V_{pip}) into another 100 cm^3 (V_x) volumetric flask. Add 10 cm^3 of the ammonia solution and add water to the mark.
- Measure the absorbance of the diluted standard solutions (A_{min} and A_{max}) and the sample solution (A_x) at proper wavelength, following the instructions given by the spectrophotometer manufacturer. Use deionized water as a blank solution.

Note: The Cu^{2+} cation forms a coordinate covalent complex with ammonia, $[\text{Cu}(\text{NH}_3)_4]^{2+}$. This complex species absorbs light strongly in the visible region 550–650 nm. The wavelength of maximum absorption lies between 600–620 nm, nominally at 610 nm.

II. Ion exchange separation and complexometric titration

Copper and zinc ions can be trapped from the solution by the ion exchange resin as described above in Part I. When ammonium oxalate is passed through the resin, an oxalate copper complex is released. The zinc ions remain fixed to the resin under these conditions. When a strong acid solution is passed through the column, the zinc cations are released. Both cations can then be determined separately by titration using EDTA.

- Follow steps 1, 2, and 3 from Part I.
- Releasing the Cu^{2+} ions: wash the column with 60 cm^3 of ammonium oxalate solution (eluate No. 1).
- Releasing the Zn^{2+} ions: wash the column with 50 cm^3 of hydrochloric acid solution (eluate No. 2).
- Determination of copper by EDTA complexometric titration: add 6–7 drops of hydrogen peroxide solution to eluate No. 1 and boil the solution for 10 minutes. After cooling, add murexide indicator, neutralize with ammonia solution and titrate with standard EDTA from yellow to purple. The indicator colour depends on the amount of murexide, copper ion concentration and pH. The neutralization must proceed carefully to keep the solution yellow. If the solution is greenish-yellow, dilute it and wait 1–2 minutes, until it turns yellow. If the solution is not clear yellow (rusty or grey) before the endpoint has been reached, add a few drops of ammonia solution and titrate from yellow to purple. The colour change at the endpoint of the titration is sharp if the titration is performed correctly.
- Determination of zinc by EDTA complexometric titration: neutralize acidic eluate No. 2 with ammonia solution. Titrate with standard EDTA solution using Eriochrome black T indicator from wine red to blue. If the colour turns violet before the endpoint is reached, heat it to 40–50 °C. If the colour turns to blue, the titration is finished (i.e. the endpoint has been reached), if not, continue to titrate until a blue colour is observed.

Data Analysis and Questions

I. Determination of the metal ion concentration by alkalimetry and photometry

P1.1 Write down the balanced chemical equations of the reactions which occur:

- In the cation exchange between the sample solution and the resin in the H^+ cycle (indicated by the symbol $\{\text{R-H}\}(\text{s})$, where (s) denotes the solid phase of the resin),
- At the endpoint of the titration (use HInd and Ind^- notation).

P1.2 Explain why the resin must be washed with deionised water before the ion exchange.



P1.3 Explain the role of ammonia in the spectrophotometric determination of copper.

P1.4 Explain why the selected standard concentrations of Cu^{2+} were used in the spectrophotometric experiment.

P1.5 Calculate the concentrations of both cations in the sample (in mol dm^{-3}).

II. Ion exchange separation and complexometric titration

P1.6 Write down the balanced chemical equations describing the release of the Cu^{2+} and Zn^{2+} ions from the ion exchange resin.

P1.7 Explain the role of hydrogen peroxide in step II.4.

P1.8 Calculate the number of moles of both cations in 10.00 cm^3 of the sample.



Problem P2. Determination of a carbonate rock composition

Slovakia is a landlocked Central European country with mountainous regions in the north and flat terrain in the south. The mountains are part of the Carpathian arch with a varied geological structure: ancient volcanic rock, granite in the alpine mountains and sedimentary rocks, mainly composed of calcite (CaCO_3), dolomite ($\text{CaMg}(\text{CO}_3)_2$) and an admixture of ankerite ($\text{CaFe}(\text{CO}_3)_2$). These carbonate minerals have a common formula of $\text{Ca}(\text{Fe},\text{Mg})(\text{CO}_3)_2$. Your sample comes from such a dolomite rock with dolomite as the main component, but containing also some calcite, ankerite and other inert components.



Figure P2. Krásnohorská Cave in the dolomite region of Slovak Karst is currently listed by the Guinness Book of Records as the cave containing the largest stalagmite in existence, generally accepted as being about 12 m in diameter and 32.7 m in height. There are more than 2 400 caves in Slovakia, of which to date more than 400 have been explored and 18 can be visited by tourists.

Chemicals and Reagents

- Powdered sample, ca 1 g (precise weight)
- 3 M hydrochloric acid solution, 10 cm³
- 2 M sodium hydroxide solution, 50 cm³
- 25% aqueous ammonia solution (w/w), 50 cm³
- 4 M ammonium chloride solution, 50 cm³
- 30% hydrogen peroxide solution (w/w), 5 cm³
- 5 mM standard EDTA disodium salt solution, 200 cm³
- Indicators: methyl red solution, sulfosalicylic acid solution (5%, w/w), Eriochrome black T (solid indicator mixture), murexide (solid indicator mixture), universal pH indicator paper

Substance	Name	State	GHS Hazard Statement
HCl	Hydrochloric acid	Aqueous solution	H314, H318
NaOH	Sodium hydroxide	Aqueous solution	H314
NH ₃	Ammonia	Aqueous solution	H314, H400
NH ₄ Cl	Ammonium chloride	Aqueous solution	H302, H319
H ₂ O ₂	Hydrogen peroxide	Aqueous solution	H271, H302, H314, H333, H402
C ₁₀ H ₁₄ N ₂ O ₈ Na ₂ · 2H ₂ O	Disodium ethylenediamine tetraacetate dihydrate	Aqueous solution	H302, H315, H319, H335
C ₂₀ H ₁₂ N ₃ O ₇ Na	Eriochrome black T	Solid	H319



$C_8H_8N_6O_6$	Murexide	Solid	Not classified
$C_7H_6O_6S$	Sulfosalicylic acid	Aqueous solution	H315, H319, H335
$C_7H_6O_3$	Salicylic acid	Aqueous solution	H302, H318
$C_{15}H_{15}N_3O_2$	Methyl red	Solution	H225, H319, H371

Equipment and Glassware

- Laboratory stand with burette clamp
- Volumetric flasks, 250 cm³ (2)
- Burette, 25 cm³
- Pipettes, 50 cm³ and 2 cm³, with pipette filler
- Graduated pipette, 1 cm³
- Graduated cylinders, 25 cm³ and 5 cm³
- Titration flasks, 250 cm³ (3)
- Beakers, 100 cm³ (2), 150 cm³ (1) and 250 cm³ (1)
- Watch glass
- Plastic Pasteur pipettes
- Filtration funnel
- Filter paper
- Hotplate

Procedure

1. Calculate the volume of 3 M HCl needed to decompose the rock sample. Assume the sample is pure mineral dolomite and you need 10% excess of the acid.
2. Decompose the powdered rock sample (m_0) in a 10% excess of HCl solution. Boil the solution for two minutes. After cooling, transfer the solution quantitatively to a 250 cm³ volumetric flask and add deionized water to the mark (V_0).
3. Pipette 50.00 cm³ of the sample solution (V_1), add 1 cm³ of the H₂O₂ solution and boil the resulting solution for two minutes. If necessary, adjust the pH with aqueous ammonia solution to ca 4 (indicator methyl red, red colour, pH = 4.4). Add a few drops (ca 0.5 cm³) of sulfosalicylic acid indicator and titrate with the standard EDTA solution from purple to yellowish (V_2). Repeat the titration as necessary.
4. Pipette 50.00 cm³ of the sample solution (V_3), add 1 cm³ of the H₂O₂ solution, adjust the pH to the range of 6 to 7 and boil the resulting solution for two minutes. After cooling, filter the precipitate, wash it with deionized water and collect the filtrate into a 250 cm³ volumetric flask (V_4). Then add deionized water to the mark.
5. Pipette a 20.00 cm³ aliquot of the sample solution obtained in step 4 (V_5) into the titration flask, dilute with deionized water and adjust the pH to ca 9. Titrate with the standard EDTA solution using Eriochrome black T indicator. The endpoint of the titration (V_6) is indicated by a sharp colour change from wine red to blue.
6. Pipette 20.00 cm³ of the sample solution obtained in step 4 (V_7) into the titration flask, dilute with water and adjust the pH to ca 12. Titrate with the standard EDTA solution using the murexide indicator until the colour changes from pink (red) to violet (V_8).



Data Analysis and Questions

- P2.1 Report the calculated volume of HCl needed to decompose the rock sample.
- P2.2 Estimate the pH of the solution prepared in step 2.
- P2.3 Explain why it is necessary to boil the mixture in step 2.
- P2.4 Explain why it is necessary to boil the mixture after the addition of the hydrogen peroxide solution in step 3.
- P2.5 Explain the role of the added hydrogen peroxide solution, the pH adjustment and boiling in step 4.
- P2.6 Calculate the content (% w/w) of dolomite, ankerite and calcite minerals and inert impurities in the sample.



Problem P3. Determination and identification of organic acids

Acid concentrations can be determined by iodometry by reaction with a mixture of iodate/iodide (IO_3^-/I^-). The reaction yields a proportional amount of iodine that can be determined by titration with thiosulfate. The rate of the reaction depends on the H^+ concentration, and is decreased as the reaction proceeds. Reliable results are obtained with strong acids when the reaction mixture is left to stand for about 15 minutes. For weak acids, the completeness of the reaction can be reached in hours (or, possibly, more quickly at elevated temperatures) but risks inaccuracies due to the volatility of the produced iodine. In special cases, the strength of an acid can be modified. For example, weak oxalic acid can be converted by CaCl_2 to an equivalent amount of the strong acid, HCl, and calcium oxalate which precipitates out, thus driving this reaction in the forward direction. Similarly, an increased acidity is observed for hydroxy substituted carboxylic acids due to the formation of calcium complexes.

Chemicals and Reagents

- Sample solutions of unknown acids labelled **A** and **B**, 150 cm³. Each solution contains just one acid from the following:
 - 0.1 M acetic acid solution
 - 0.1 M hydrochloric acid solution
 - Hydroxy carboxylic acid ($\text{R}(\text{OH})_x(\text{COOH})_y$) solution, i.e.:
 - 0.1 M lactic acid solution
 - 0.05 M tartaric acid solution or 0.05 M malic acid solution
 - 0.0333 M citric acid solution
- 0.05 M standard iodine solution in ca 0.1 M potassium iodide solution, 200 cm³
- 0.1 M standard sodium hydroxide solution, 25 cm³
- 0.1 M sodium thiosulfate solution, 500 cm³
- 1 M potassium iodide solution, 50 cm³
- 3% potassium iodate solution (w/w), 50 cm³
- Calcium chloride, 20 g
- Starch indicator solution

Substance	Name	State	GHS Hazard Statement
HCl	Hydrochloric acid	Aqueous solution	H314, H318
CH ₃ COOH	Acetic acid	Aqueous solution	H226, H314
NaOH	Sodium hydroxide	Aqueous solution	H314
Na ₂ S ₂ O ₃	Sodium thiosulfate	Aqueous solution	H315, H319, H335
I ₂	Iodine	Aqueous solution	H312, H332, H400
KI	Potassium iodide	Aqueous solution	H302, H315, H317, H319, H334, H335
KIO ₃	Potassium iodate	Aqueous solution	H272, H302, H315, H317, H319, H335
CaCl ₂	Calcium chloride	Solid	H312, H319
C ₆ H ₈ O ₇	Citric acid	Aqueous solution	H315, H319, H335
C ₃ H ₆ O ₃	Lactic acid	Aqueous solution	H315, H318
C ₄ H ₆ O ₅	Malic acid	Aqueous solution	H302, H315, H318, H319, H335
C ₄ H ₆ O ₆	Tartaric acid	Aqueous solution	H315, H318, H319, H335



Equipment and Glassware

- Laboratory stand equipped with a burette clamp
- Burette, 25 cm³
- Volumetric pipettes, 20 and 25 cm³, with pipette filler
- Iodine flasks (Erlenmeyer flask with stopper), 250 cm³ (2)
- Beakers, 100 cm³ (2) and 250 cm³ (1)
- Graduated cylinder, 25 cm³
- Plastic transfer pipettes, 3 cm³ (2) and 5 cm³ (2)
- pH-Meter, accuracy ± 0.01

Procedure

I. Determination of sodium thiosulfate concentration in solution

Pipette 20.00 cm³ of the standard iodine solution (V_1) into an Erlenmeyer flask, add 25 cm³ of distilled water and titrate with the thiosulfate solution until a colour change to a pale yellow colour is observed. Add 3 cm³ of the starch indicator and titrate the obtained blue coloured solution until the colour disappears (V_2). Repeat the titration as necessary.

II. Identification of an unknown acid in sample solutions A and B and determination of its concentration

For the analysis of the unknown acid samples, use the following procedures **a–c**. You can conduct these titration experiments in any order. Repeat the titrations as necessary.

Procedure **a**: Pipette 20.00 cm³ (V_{11}) of an unknown acid solution (sample **A** or **B**) into the iodine flask, add 5 cm³ of the KI solution and 5 cm³ of the KIO₃ solution using the plastic transfer pipettes. Stopper the flask, let it stand in the dark for 15 minutes and then titrate the produced iodine using the thiosulfate solution (V_3 , V_4 , respectively).

Procedure **b**: Pipette 20.00 cm³ (V_{12}) of an unknown acid solution (sample **A** or **B**) into the iodine flask, add 5 cm³ of the KI solution and 5 cm³ of the KIO₃ solution. Add 4 g of CaCl₂. Stopper the flask, let it stand in the dark for 15 minutes and then titrate the produced iodine using the thiosulfate solution (V_5 , V_6 , respectively).

Procedure **c**: Pipette 20.00 cm³ (V_{13}) of an unknown acid solution (sample **A** or **B**) into the iodine flask, add 5 cm³ of the KI solution and 5 cm³ of the KIO₃ solution, then 25.00 cm³ (V_{23}) of the thiosulfate solution. Stopper the flask and let it stand in the dark for 15 minutes. Add 20.00 cm³ (V_{33}) of the standard iodine solution and titrate the excess iodine in the flask using the thiosulfate solution (V_5 , V_7 , respectively).

III. Identification of an unknown hydroxy carboxylic acid in the sample

There is a possibility that the sample contains an unknown hydroxy carboxylic acid that can be determined using iodometry as described above. Differentiate the hydroxy carboxylic acids according to their acid-base properties (Table P3).

Table P3. pK_a values of selected hydroxy carboxylic acids.

Acid	pK_{a1}	pK_{a2}	pK_{a3}
Lactic	3.86	-	-
Malic	3.46	5.10	-
Tartaric	3.04	4.37	-
Citric	3.13	4.76	6.40



The acids can be identified by measuring the pH of the buffer prepared from the unknown acid and sodium hydroxide. The precise concentration of the hydroxy carboxylic acid is known from Part II. Calculate the volume of the NaOH standard solution needed to prepare the buffer, for example in the molar ratio 1 : 1. The pH of such solution can be determined using the available software (e.g., http://www.iq.usp.br/gutz/Curtipot_.html).

Prepare such buffers from sample **A** or **B** identified as hydroxy carboxylic acid and measure the pH.

Data Analysis and Questions

I. Determination of sodium thiosulfate concentration in solution

P3.1 Provide a balanced chemical equation for the standardization of the thiosulfate solution.

P3.2 Derive the formulae for calculating the molar concentration of the sodium thiosulfate in the solution.

P3.3 Calculate the molar concentration of the sodium thiosulfate in the solution.

II. Identification of an unknown acid in sample solutions A and B and determination of its concentration

P3.4 Based on the results obtained in Part II, fill in the table and identify the acids in the samples.

Procedure a	Volume of sample solution A or B added to the titration flask		$V_{11} =$
	Volumes read from the burette (perform only the necessary analyses)		
	Sample A	$V_{3a} =$	$V_{3b} =$
	<i>Note/observation:</i>		
	Sample B	$V_{4a} =$	$V_{4b} =$
<i>Note/observation:</i>			
	Accepted volumes	$V_3 =$	$V_4 =$
Procedure b	Volume of sample solution A or B added to the titration flask		$V_{12} =$
	Volumes read from burette (perform only the necessary analyses)		
	Sample A	$V_{5a} =$	$V_{5b} =$
	<i>Note/observation:</i>		
	Sample B	$V_{6a} =$	$V_{6b} =$
<i>Note/observation:</i>			



	Accepted volumes	$V_5 =$	$V_6 =$
Procedure c	Volume of sample solution A or B added to the titration flask $V_{13} =$		
	Volumes read from burette (perform only the necessary analyses)		
	Sample A	$V_{7a} =$	$V_{7b} =$
	<i>Note/Observation:</i>		
	Sample B	$V_{8a} =$	$V_{8b} =$
<i>Note/Observation:</i>			
	Accepted volumes	$V_7 =$	$V_8 =$
Indicate with a ✓ the identified component in sample A			
HCl	CH ₃ COOH	(R(OH) _x (COOH) _y)	
Indicate with a ✓ the identified component in sample B			
HCl	CH ₃ COOH	(R(OH) _x (COOH) _y)	

- P3.5 Provide reasons for your conclusions about the acids identified in the samples.
- P3.6 Write down the balanced chemical equations of the reactions necessary to calculate the result.
- P3.7 Derive the formulae for calculating the concentration of the strong acid when Procedure **a** was used.
- P3.8 Derive the formulae for calculating the concentration of the hydroxy acid when Procedure **b** was used.
- P3.9 Explain the role of the excess thiosulfate in Procedure **c**.
- P3.10 In an acid solution, thiosulfate undergoes an undesired side reaction. Write down the balanced chemical equation of this unwanted side reaction. Explain why it is possible to add an excess of thiosulfate to the acid sample in Procedure **c**.
- P3.11 Derive the formulae for calculating the concentration of the weak acid when Procedure **c** was used.
- P3.12 Calculate the molar concentration of the acid in each sample.

III. Identification of an unknown hydroxy carboxylic acid in the sample

- P3.13 Identify the unknown hydroxy carboxylic acid (if present) by comparing the measured and theoretical pH values of the buffer solution.



Problem P4. A chemical oscillator and its activation energies

In 2018, we celebrate the 50th anniversary of the International Chemistry Olympiad, which was first organized in 1968 in Czechoslovakia. By coincidence, it is also the 50th anniversary of an important breakthrough that began a new era in chemical kinetics.

In July 1968, Prague hosted an international conference called "Biological and Biochemical Oscillators", one of a few rare occasions that brought together Western scientists with the scientists from the Eastern Bloc. At this conference, a young Russian chemist Anatol Zhabotinsky introduced to the crowd a new, remarkable system, an oscillator based on nothing else but chemical reactions.

The oscillations were originally discovered in the early 1950s by Boris Belousov, who was looking for an inorganic analogue of the Krebs cycle. Unfortunately, at that time, his colleagues did not accept that a homogeneous chemical oscillator could exist. For many years, Belousov's recipe survived only as a bizarre chemical curiosity, passed on among a few Chemistry departments in Moscow.

It was the 1968 conference in Prague that marked the real turning point. Zhabotinsky's careful verifications and extensions of Belousov's work finally attracted the attention they deserved, and research groups studying oscillatory kinetics formed all throughout the Eastern Bloc, including Czechoslovakia, as well as in the West. The field of nonlinear chemical kinetics was born.

This famous oscillator became known as the Belousov-Zhabotinsky or, for short, the BZ reaction. In this task, your own observations of the oscillations will enable you to elucidate their core mechanism. Furthermore, you will explore a remarkable island of simplicity in the rather complex phenomenon. You will verify that the periods of the BZ oscillations still obey the Arrhenius law.

Chemicals and Reagents

- 1.50 M sulfuric acid solution, 150 cm³
- Malonic acid, 5.203 g
- Cerium(III) sulfate tetrahydrate, 0.801 g
- 7.5 mM ferroin sulfate solution, 20 cm³
- Sodium bromate(V), 7.545 g
- 0.05 M potassium bromide solution, 50 cm³

Substance	Name	State	GHS Hazard Statements
H ₂ SO ₄	Sulfuric acid	Aqueous solution	H290, H314
C ₃ H ₄ O ₄	Malonic acid	Solid ^a	H319
Ce ₂ (SO ₄) ₃ · 4 H ₂ O	Cerium(III) sulfate tetrahydrate ^b	Solid ^a	H315, H319, H335
[Fe(C ₁₂ H ₈ N ₂) ₃]SO ₄	Ferroin sulfate ^c	Aqueous solution	Not hazardous
NaBrO ₃	Sodium bromate(V)	Solid ^a	H272, H315, H319, H335
KBr	Potassium bromide	Aqueous solution	Not hazardous

^a It is recommended to start from solids if reproducible results are to be obtained. Stock solutions of these substances age quickly and results will drift as the solutions are stored, especially in the case of Ce₂(SO₄)₃.

^b Other hydrates of Ce₂(SO₄)₃ may be used. Anhydrous Ce₂(SO₄)₃ can be very difficult to dissolve.

^c The stock solution may also be prepared from FeSO₄ and *o*-phenanthroline, but the results may vary. Commercial ferroin sulfate indicator solution is preferred as starting material.



Equipment and Glassware

- Digital stop-watch capable of split timing
- Laboratory stand with clamps
- Jacketed beaker, 50 cm³
- Circulating thermostat bath
- Thermometer
- Magnetic stirrer and a PTFE-coated stir bar
- Graduated pipettes, 10 cm³, 5 cm³ and 1 cm³
- Volumetric flask, 50 cm³
- Bottles for stock solutions, 50 cm³ (3)
- Wash-bottle with deionized water
- Ultrasonic bath (if needed)

Procedure

I. Preparation of stock solutions

Note: This part may be omitted if reagents are supplied as solutions. It must be noted, however, that results will depend on storage time and conditions.

Mix solid cerium(III) sulfate with some water and transfer the suspension quantitatively into a volumetric flask charged with 1.5 cm³ of 1.50 M sulfuric acid solution. Add enough water to dissolve and, if needed, treat with ultrasound. Then, add water to the mark, transfer the solution into the stock bottle and wash the flask well. Repeat the procedure with bromate(V) and malonic acid, except adding any sulfuric acid.

II. Setting up and getting familiar with the BZ oscillator

1. Select pipettes of appropriate volumes, one for each stock solution plus one for water.
2. To assemble the apparatus, connect the jacketed beaker to the circulating thermostat and fix it on the magnetic stirrer with a clamp. Turn on the thermostat and set the temperature to 25.0 °C.
3. Charge the jacketed beaker with 10.0 cm³ water, 10.0 cm³ sulfuric acid solution, 3.0 cm³ malonic acid solution, 3.0 cm³ cerium(III) solution, and 1.0 cm³ ferroin solution.
4. If the stirring intensity is not set for you, you will need to find it. It should be as high as possible, but the vortex must not be so deep that bubbles of air get stirred into the solution. Once you set the right stirring intensity, maintain this setting during all your work.

Note: The results can vary significantly with stirring intensity, just as they depend on the overall geometry of the reactor vessel, of the stir bar etc. If the results are to be compared against benchmark values, all these parameters must be preset and fixed carefully.

5. Start the reaction by adding 3.0 cm³ of the bromate(V) solution. Initially, the solution will maintain one colour and then it will start changing gradually. At some point, there will be a sudden colour change that will restore the first colour. This colour cycle will be repeated. Note down the colour changes.

III. Determining the building blocks of the BZ chemistry

1. Prepare a BZ oscillator mixture with the same concentrations of sulfuric acid, malonic acid and bromate(V) as in Part II, but omit the metal catalysts – cerium(III) and ferroin. Instead, add 3.0 cm³ of the bromide stock solution and increase the volume of water accordingly to



keep the total volume at 30 cm³. Note the colour changes after you start the reaction by adding the bromate(V) solution.

2. Prepare a BZ oscillator mixture with the same concentrations of sulfuric acid, cerium(III), ferroin and bromate(V) as in Part II, but omit the malonic acid. Instead, add the same volume of the bromide stock solution. As indicated by a thermometer, wait until the solution temperature has stabilized, and record the reading. Finally, once you begin adding 3.0 cm³ of the bromate(V) solution, immediately start the stop-watch. Note how the colour of the reaction mixture develops, and record the time when the colour changes abruptly.

IV. Timing the oscillations for various amounts of cerium(III)

1. Prepare a BZ oscillator mixture with the same concentrations of sulfuric acid, malonic acid, ferroin and bromate(V) as in Part II, but only half of the volume of cerium(III) solution. Do not add any bromide solution, but increase the volume of water accordingly to keep the total volume of the mixture at 30 cm³. Wait until the solution temperature has stabilized and record the reading.
2. Finally, once you begin adding 3.0 cm³ of the bromate(V) solution, immediately start the stop-watch. Every time a sudden colour transition occurs, hence indicating a new colour cycle has begun, press the SPLIT button to read the exact time while continuing to time. In this way, record the times of the first four sudden colour transitions.
3. Repeat the same timing procedure with the original volume of cerium(III) solution, 3.0 cm³.

V. Temperature dependence

Repeat the same timing procedure with the same BZ oscillator that you observed in Part IV.3 at approximately 25 °C, with 3.0 cm³ of the cerium(III) solution, but increase the temperature setting on the thermostat to 27.0 °C, 29.0 °C, 31.0 °C and 33.0 °C. For each temperature, record the times of the first four sudden colour changes.

Data Analysis and Questions

- P4.1 Write a balanced ionic equation for the chemical reaction responsible for the colour observed when bromate(V) and bromide are mixed in an acidic solution. Write a balanced equation for the chemical reaction responsible for the disappearance of this colour in the presence of malonic acid. Sum the two equations appropriately to provide the overall reaction that has taken place in the mixture when the colour has disappeared.
- P4.2 Consider your observation in the reaction in which malonic acid (MA) was replaced with Br⁻. Provided that the recorded reaction time is proportional to [Br⁻], calculate the rate at which [Br⁻] is consumed. Using the average period of oscillation recorded in the BZ oscillator at 25 °C, calculate the concentration [Br⁻] consumed in each cycle of the BZ oscillator. How much [MA] does this consume? Where does the Br⁻ for each cycle come from?
- P4.3 The most concise version of the BZ oscillations mechanism consist of steps that are all in the form of redox reactions with a simple 1:1:*n* stoichiometry:

oxidizing-agent species + reducing-agent species + *n* H⁺ = products (*n* can be 0, 1, 2, ...)

Usually, only a single organic step (bromomalonic acid cleavage with Ce⁴⁺) is included, and the stoichiometry of its products is traditionally formulated as adjustable. In the inorganic subset, however, all steps are perfectly balanced, and stoichiometric coefficients



are always integers, even for all the products. Only the following bromine-containing species are considered: Br^- , Br_2 , HBrO , HBrO_2 , BrO_2 , BrO_3^- .

How many balanced equations that satisfy these criteria can you write for the step of Ce^{3+} oxidation to Ce^{4+} ? Which of your experimental observations can you combine with these equations to conclude that Ce^{3+} is oxidized by BrO_2 ? Write down the step producing BrO_2 . Which species can be eliminated in the combined equation for Ce^{3+} oxidation and BrO_2 production to show that this pair of reactions forms an autocatalytic cycle? Write down the step responsible for the inhibition of this autocatalytic cycle with Br^- .

- P4.4 Compare the BZ oscillations at the two different concentrations of cerium(III) catalyst. How is increased catalyst concentration reflected in the lengths of the induction periods, i.e. in the times taken until the first sudden colour changes, and how is it reflected in the average lengths of the first three periods of oscillation? What role does this suggest for cerium(III) in the oscillations?
- P4.5 Assuming that the induction periods and the average periods of oscillation directly reflect the rates of the rate-determining steps in the system, use your experimental data measured at various temperatures to plot their natural logarithms against $1/T$, and find the corresponding activation energies. Compare the results to the reference data, around 60 kJ mol^{-1} for cerium-catalyzed oscillations and around 75 kJ mol^{-1} for ferroin-catalyzed oscillations.



Problem P5. Kinetics of a chemical wave front propagation

We usually tend to think of synthesis as of making substances. In this task, however, you will use chemical reagents to synthesize *patterns*.

When a BZ oscillating reaction solution is poured onto a Petri dish, the interaction between an autocatalytic reaction and diffusion has the ability to transform the solution, initially homogeneous, into a beautifully self-ordered sea of chemical waves. This phenomenon is not only pretty, but the movement of the structures can also be used to study the kinetics of the underlying reactions.

If we have an autocatalytic reaction producing autocatalytic species **X**, the simplest form of autocatalysis is described by a simple reaction rate equation:

$$\frac{d[\mathbf{X}]}{dt} = k' [\mathbf{X}] \quad (1)$$

An interesting thing happens when we have a medium capable of undergoing such an autocatalytic reaction, but **X** is initially present only in a selected region. As expected from an autocatalytic reaction, wherever **X** is available, a burst of production of even more **X** occurs. In addition, if diffusion can take place, the diffused **X** can trigger the autocatalytic production of **X** in the adjacent regions, too. This spreads like fire and we observe a chemical trigger wave. If D is the diffusion coefficient of **X**, the velocity v of the trigger wave is:

$$v = 2\sqrt{k'D} \quad (2)$$

In the BZ oscillator the rate of the autocatalytic step was found to depend on acidity and on the concentration of bromate(V) in the following way:

$$k' = 20 \text{ M}^{-2} \text{ s}^{-1} [\text{H}^+][\text{BrO}_3^-] \quad (3)$$

Your task is to validate this relationship experimentally, by measuring the velocity of the wave fronts at various concentrations.

Chemicals and Reagents

- 1.50 M sulfuric acid solution, 150 cm³
- Malonic acid, 5.203 g
- Cerium(III) sulfate tetrahydrate, 0.801 g
- 25 mM ferroin sulfate solution, 25 cm³
- Sodium bromate(V), 7.545 g

Note: The chemicals and reagents are the same as in Problem P4, except that the ferroin sulfate solution is now more concentrated, 25 mM. All safety information and all notes regarding handling and storage apply as in Problem P4.

Equipment and Glassware

- Digital stop-watch
- Petri dish, 14 cm diameter, with lid
- Millimeter graph paper
- Beaker, 100 cm³
- Graduated pipettes, 10 cm³ and 5 cm³
- Wash-bottle with deionized water



Procedure

I. Preparation of stock solutions and equipment

1. The procedure for the preparation of the stock solutions is the same as in Problem P4.
2. Select pipettes of appropriate volumes, one for each stock solution plus one for water. Place the Petri dish on a sheet of millimeter graph paper.

Note: The benchtop for this experiment must be perfectly level. Leaning against the table while a measurement is in progress must be avoided. Since the temperature of the Petri dish is not controlled, the experiment must not be performed near a source of heat or a draught.

II. General procedure for finding the chemical wave front velocity

1. Prepare a BZ oscillator by charging the beaker with water and solutions of sulfuric acid, malonic acid, cerium(III) sulfate, and ferroin sulfate, using the volumes specified in Part III. Finally, start the reaction by adding the solution of bromate(V) and swirling the beaker with your hand.
2. Pour the oscillator solution from the beaker onto the Petri dish. Swirl the dish a few times to distribute the solution evenly over its entire surface, and cover the dish with its lid. Initially, the solution will change colour uniformly, but eventually, spots of a different colour will appear. The spots will grow into rings, and when a ring becomes large enough, a new spot will appear in its center. This leads to the formation of *target patterns* (Fig. P5).



Figure P5. The patterns to be formed in a Petri dish.

3. To find the wave front velocity, measure the time that it takes for a front, preferably *inside* a target pattern, to advance by 5 mm. This will not be possible immediately, as the outmost rings in each target pattern will be regularly annihilated. At some point, however, the patterns will become large enough to allow the fronts to be followed across a 5 mm long path, at least in one direction.

Note: Tracking the fronts along the left–right axis is preferred. To read the position of a front that is moving towards or away from the observer, it may be necessary to close one eye, or watch the pattern from another angle. Be careful not to perturb the dish!

4. To find the mean wave front velocity in the dish, repeat the reading of the time required to cover a 5 mm distance for three different fronts, preferably in three different places on the Petri dish.

III. Dependence of the chemical wave front velocity on concentrations

Using the procedure described above, find the average wave front velocities at four different concentration sets (Table P5). All contain 3.0 cm³ malonic acid solution, 3.0 cm³ cerium(III) sulfate solution and 2.0 cm³ ferroin sulfate solution. The first two sets will differ in the volumes of



sulfuric acid and the other two sets will differ in the volumes of bromate(V) solution. To make sure that your data is correct, replicate each concentration set twice. If the data disagree, add more replicates for verification.

Table P5. Concentration sets for finding the dependence of the chemical wave front velocity.

Set	Water	Sulfuric acid solution	Bromate(V) solution
#1	9.0 cm ³	10.0 cm ³	3.0 cm ³
#2	12.0 cm ³	7.0 cm ³	3.0 cm ³
#3	8.1 cm ³	10.0 cm ³	3.9 cm ³
#4	9.9 cm ³	10.0 cm ³	2.1 cm ³

Data Analysis and Questions

- P5.1 Assume that the total volumes of the reaction mixtures always add up to 30 cm³. Calculate the concentrations of sulfuric acid and bromate(V) in the four concentration sets examined. Using all time readings taken in accepted replicates, calculate one mean wave front velocity, expressed in mm min⁻¹, for each concentration set. $M(\text{NaBrO}_3) = 150.89 \text{ g mol}^{-1}$
- P5.2 Assume that instead of equation (3), the dependence of v^2 on $[\text{BrO}_3^-]$ is described as $v^2 = p [\text{BrO}_3^-] + q$. What would it suggest about the kinetics of the autocatalysis, if $q > 0$, and what would it suggest if $q < 0$? Use the results from Sets #3 and #4 to evaluate p and q . Calculate the percentage of the overall reaction rate that is contributed by q . Is this significant?
- P5.3 Assume that the wave front propagation velocity v is a power function of both, $[\text{H}_2\text{SO}_4]$ and $[\text{BrO}_3^-]$, i.e. $v = k [\text{H}_2\text{SO}_4]^a [\text{BrO}_3^-]^b$. Use the results from Sets #1 and #2 to calculate the exponent a , and the results from Sets #3 and #4 to calculate the exponent b . What assumption would allow us to deduce the reaction order with respect to $[\text{H}^+]$ from a ? Compare the results to the values that are expected based on equation (3). Are a and b roughly as expected or does any value suggest that, for the conditions studied, the rate equation (3) should be revised?
- P5.4 Assume that equation (3) applies, and that $[\text{H}^+] \approx [\text{H}_2\text{SO}_4]$. Using the reference value of the autocatalytic species diffusion coefficient $D = 2.0 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$, calculate what values are suggested for the autocatalytic reaction rate constant from your experimental data. Does any of the concentration sets come close to the reference value $20 \text{ M}^{-2} \text{ s}^{-1}$?



Problem P6. Separation of acidic, basic and neutral organic compounds

This task is designed to help you understand the chemical basis of separation of up to a four-component mixture using extraction techniques and visualizing the separation by checking the composition of the organic layer after each extraction. Extraction in an organic chemistry laboratory is most often used to isolate organic compounds from reaction mixtures after an aqueous work-up. Extraction is a particularly useful method for separating organic compounds if one compound in the mixture can be chemically converted to an ionic form. The ionic form is often more soluble in an aqueous layer and can be extracted into it. Non-ionic organic compounds in the mixture will remain dissolved in the organic layer. The separation of the two layers results in the separation of the compounds. The pK_a values of the acids provide a measure of the acidity of each compound. The extent to which an acid–base reaction proceeds to completion depends on the relative acidity of the reactants and products.

Chemicals and Reagents

- Unknown solid sample containing 3–4 of these compounds: benzoic acid, 4-nitroaniline, 2-naphthol, naphthalene; 750 mg
- Chloroform, 20 cm³
- 20% hydrochloric acid aqueous solution (w/w), 42 cm³
- 10% sodium bicarbonate aqueous solution (w/w), 24 cm³
- 10% sodium hydroxide aqueous solution (w/w), 24 cm³
- 20% potassium hydroxide aqueous solution (w/w), 30 cm³
- Anhydrous sodium sulfate, 2 tea spoons
- Hexanes/ethyl acetate 3:1 mixture (TLC eluent), 5 cm³

Substance	Name	State	GHS Hazard Statements
C ₇ H ₆ O ₂	Benzoic acid	Solid	H315, H318, H372
C ₆ H ₆ N ₂ O ₂	4-Nitroaniline	Solid	H301, H311, H331, H373, H412
C ₁₀ H ₈ O	2-Naphthol	Solid	H302, H332, H400
C ₁₀ H ₈	Naphthalene	Solid	H228, H302, H351, H410
CHCl ₃	Chloroform	Liquid	H302, H315, H319, H331, H336, H351, H361d, H372
HCl	Hydrochloric acid	Aqueous solution	H290, H314, H335
NaHCO ₃	Sodium bicarbonate	Aqueous solution	H319
NaOH	Sodium hydroxide	Aqueous solution	H290, H314
KOH	Potassium hydroxide	Aqueous solution	H290, H302, H314, H315, H319
C ₄ H ₈ O ₂	Ethyl acetate	Liquid	H225, H319, H336
C ₆ H ₁₄	Hexanes (mixture of isomers)	Liquid	H225, H304, H315, H336, H411
Na ₂ SO ₄	Sodium sulfate	Solid	Not hazardous

Equipment and Glassware

- Laboratory stand with clamps and metal ring
- Magnetic hotplate stirrer and a PTFE-coated stir bar
- Rotary evaporator
- Water aspirator (or other vacuum source for suction filtration and vacuum rotary evaporator)



- Measuring cylinders, 10 cm³ and 20 cm³
- Erlenmeyer flasks, 50 cm³ (2)
- Glass rod
- TLC chamber or a Petri dish covered small beaker
- TLC plates, silica gel 60 F₂₅₄ (4), and capillaries
- UV lamp (254 nm)
- Beakers, 50 cm³ (1) and 100 cm³ (3)
- Separatory funnel, 100 cm³
- pH indicator paper
- Büchner filter funnel
- Filter paper
- Suction flask, 100 cm³, with rubber adapter for filter funnel
- Round bottom flask, 50 cm³
- Spatula
- Tweezers
- Marker for glass

Procedure

Warning: Chloroform and naphthalene should be handled only in a well-ventilated fumehood.

I. Sample preparation

The sample weighing 750 mg contains three to four of these compounds: benzoic acid, 4-nitroaniline, naphthalene-2-ol and naphthalene. Dissolve this sample in 20 cm³ of chloroform in a 50 cm³ Erlenmeyer flask.

II. TLC analysis

Check the composition of the solution before extractions (Plate 1). Spot the chloroform solution on the TLC plate using a glass capillary spotter (mark the start line at a height of 1 cm, Figure P6). Take a 50 cm³ beaker, load it with 2 cm³ of the TLC eluent using a measuring cylinder. Insert the TLC plate upright into the TLC developing chamber. Ensure that the eluent level is below the start line. Cover the beaker with one of the Petri dishes. Wait until the solvent system reaches the pre-drawn eluent front line. Remove the TLC plate using tweezers and let the eluent dry in air. Place the TLC plate under a UV lamp. Mark the spots of the compounds with a pencil and calculate the R_f values.

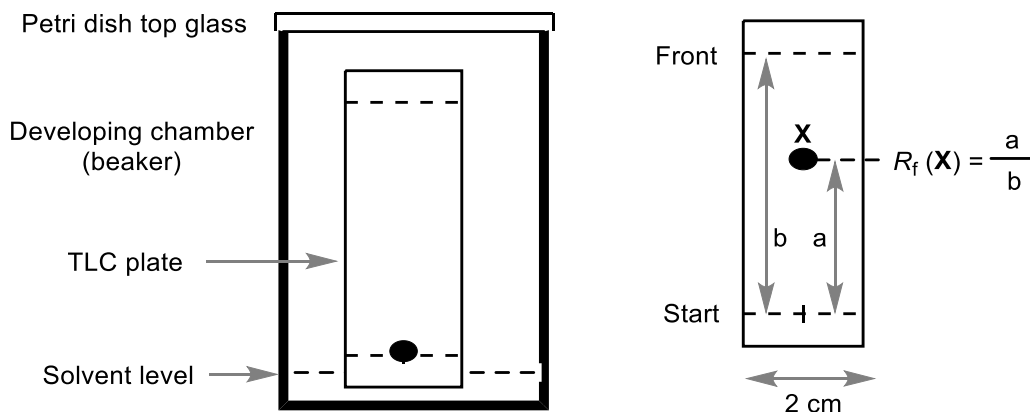


Figure P6. Developing a TLC plate (left), evaluation of R_f value (right).



III. Separation of the basic compound A

1. Place a separatory funnel with a closed stopcock into a metal ring and place a 50 cm³ Erlenmeyer flask under it. Using a glass filter funnel, pour the chloroform solution into the separatory funnel. Measure 6 cm³ of 20% solution of HCl using a measuring cylinder. Add it into the separatory funnel using a conic filter funnel. Hold the funnel around the top, lift it out of the supporting ring and swirl it gently (chloroform vapours may cause pressure build-up in the funnel). Return the separatory funnel to the ring and insert the stopper.
2. To perform the extraction, use both hands; hold the body of the funnel around stopcock with one and the stopper with the other. Take out the funnel from the support ring and invert it and vent it by opening the stopcock. Repeat the swirling-venting process until the pressure build-up diminishes. Then shake the funnel for 5 × 10 s. Make sure that the stopcock is closed and return the separatory funnel to the metal ring over the 50 cm³ Erlenmeyer flask and remove the stopper.
3. Allow the layers to separate and collect the organic layer by opening the stopcock and collecting the bottom layer into the 50 cm³ Erlenmeyer flask. Close the stopcock and pour the aqueous layer through the top neck and into the 100 cm³ beaker, using a glass filter funnel. Keep both phases.
4. Pour the organic phase back into separatory funnel and repeat the extraction with another 6 cm³ of the 20% solution of HCl. Combine the aqueous layers after both extractions, label the beaker as **A** and keep aside for subsequent isolation.
5. Check the composition of the organic solution after the extraction with the diluted HCl solution using TLC analysis (Plate 2).

IV. Separation of the acidic compounds B and C

1. Extract the organic layer twice with 12 cm³ of 10% solution of NaHCO₃ and combine the aqueous layers after both extractions in a 100 cm³ beaker. Label the beaker as **B** and keep aside for subsequent isolation.
2. Check the composition of your organic layer (Plate 3).
3. Then extract the organic layer twice with 12 cm³ of 10% solution of NaOH and combine the aqueous layers after both extractions in a 100 cm³ beaker. Label the beaker as **C** and keep aside for subsequent isolation.
4. Collect the organic phase into a 50 cm³ Erlenmeyer flask. Check the composition of the organic layer (Plate 4).

V. Isolation of organic compounds A, B and C from the aqueous layers

1. Basify the acidic aqueous layer in the beaker labelled **A** with a 20% solution of KOH (adjust the pH to 11, ca 12 cm³). Yellow precipitate **A** is formed.
2. Acidify the basic aqueous extracts in beakers labelled **B** and **C** with a 20% solution of HCl (to pH 1, ca 12 cm³). Watch out for the CO₂ evolution during the neutralization of the bicarbonate extract. White precipitate **B** and pink precipitate **C** are formed, respectively.
3. Isolate each of the precipitated compounds (**A**, **B**, **C**) by suction filtration using a Büchner funnel and filter paper. Dry all the products in air and then record the yields.

VI. Isolation of neutral organic compound D from organic layer

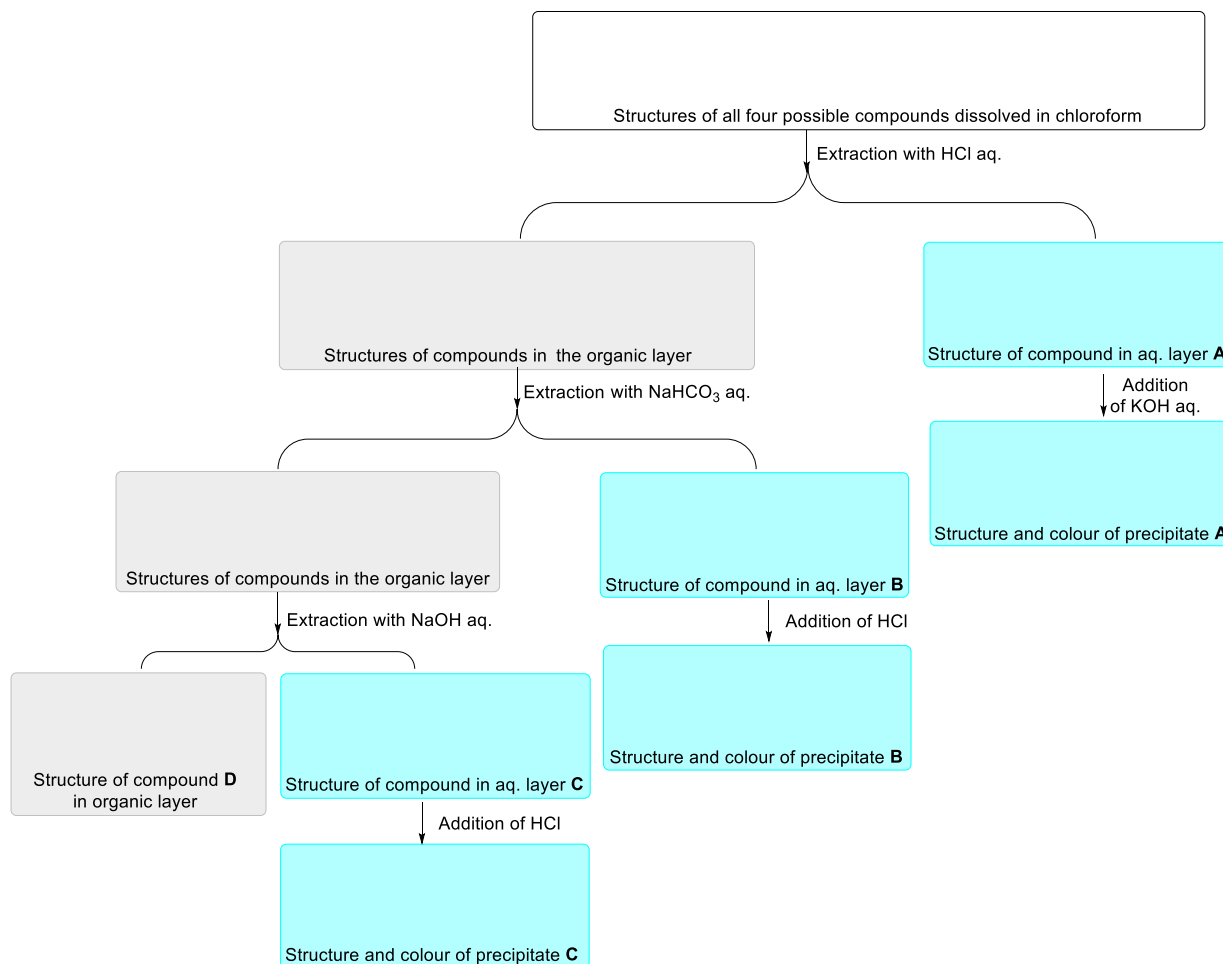
Dry the organic layer over anhydrous Na₂SO₄ for 10 min. Filter off the used drying agent through filter paper and collect the filtrate in a pre-weighed round bottom flask. Compound **D**



can be recovered from the filtrate by evaporating the solvent on a rotary evaporator. Record the yield.

Data Analysis and Questions

P6.1 Fill in the structures of all the missing compounds and the colour of the precipitates into the flow chart:



P6.2 Compare all four TLC plates from the task and explain your observation.

P6.3 Write the equations of the acid–base reactions for the separations and isolations.

P6.4 Explain why it is important to perform the second extraction (the first extraction using the basic aqueous solution) with NaHCO_3 and not with the NaOH solution.

P6.5 Fill in the following table and identify compounds **A–D**.

Compound	R_f	m (g)	Compound name
A			
B			
C			
D			

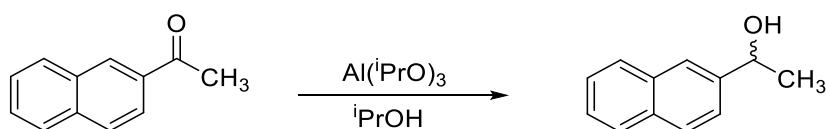
P6.6 Determine the ratio of the compounds in your sample and discuss the quantitative difference of the initial sample mass and the sum of the masses of the pure isolated compounds. Explain the difference.



Problem P7. Meerwein–Ponndorf–Verley reduction

The Meerwein–Ponndorf–Verley reduction is an aluminium(III)-catalyzed hydride transfer from the α -carbon of isopropyl alcohol to the carbonyl carbon of an aldehyde or ketone. The product of this reaction is the corresponding primary or secondary alcohol, respectively, while an equimolar amount of isopropyl alcohol (which is used as a solvent and is present in large excess) is oxidized to acetone. The advantages of this reduction lie in the high degree of chemoselectivity and use of a cheap, environmentally friendly metal catalyst.

In this task, you will perform the Meerwein–Ponndorf–Verley reduction on (2-naphthyl)ethanone (2-acetonaphthone).



Chemicals and Reagents

- 2-Acetonaphthone, 200 mg
- Aluminum isopropoxide, 300 mg
- Isopropyl alcohol, 4 cm³
- Ethyl acetate, 20 cm³
- Hexanes, 15 cm³
- Saturated ammonium chloride aqueous solution, 8 cm³
- Anhydrous sodium sulfate
- Inert gas (nitrogen or argon)

Substance	Name	State	GHS Hazard Statements
C ₁₂ H ₁₀ O	2-Acetonaphthone	Solid	H302, H315, H319, H335, H411
Al[OCH(CH ₃) ₂] ₃	Aluminum isopropoxide	Solid	H228
(CH ₃) ₂ CHOH	Isopropyl alcohol	Liquid	H225, H319, H336
CH ₃ COOC ₂ H ₅	Ethyl acetate	Liquid	H225, H319, H336
C ₆ H ₁₄	Hexanes (mixture of isomers)	Liquid	H225, H304, H315, H336, H411
NH ₄ Cl	Ammonium chloride	Aqueous solution	H302, H319
Na ₂ SO ₄	Anhydrous sodium sulfate	Solid	Not hazardous

Equipment and Glassware

- Laboratory stand with clamps
- Magnetic hotplate stirrer and a PTFE-coated stir bar
- Round-bottom flask, 25 cm³
- Reflux condenser
- Inert gas joint
- Inflatable balloon
- Water bath with paper clip
- Graduated cylinder, 10 cm³
- Separatory funnel, 50 cm³
- Erlenmeyer flask, 25 cm³
- Filtration funnel
- Paper filter



- Round bottom flask, 50 cm³
- TLC plates, silica gel 60 F₂₅₄ (2)
- TLC chamber or a Petri dish covered small beaker
- UV lamp (254 nm)
- Petri dish
- Spatula
- Capillary
- Vial
- Ice bath
- Teflon sleeves for tapered joints or vacuum grease
- Vacuum rotary evaporator with vacuum source
- Melting point apparatus

Procedure

I. Drying of isopropyl alcohol

Place 300 mg of aluminium isopropoxide into a 25 cm³ round-bottom flask equipped with a magnetic stir bar. Add 4 cm³ of isopropyl alcohol and fit the reflux condenser. Fix the apparatus at the laboratory stand over the magnetic stirrer (Figure P7). Attach an inflatable balloon filled with an inert gas (N₂ or Ar). Heat the water bath with a paper clip to 90 °C. Place the flask in the water bath and stir the reaction mixture under an inert atmosphere for 1 hour. At this stage, the excess aluminium isopropoxide is used to remove the moisture present in isopropyl alcohol ($w(\text{H}_2\text{O}) \leq 0.002$). Remove the flask from the water bath and let the reaction mixture cool under the inert atmosphere.

II. Meerwein–Ponndorf–Verley reduction of 2-acetonaphthone and isolation of the product

1. Add 2-acetonaphthone to the reaction mixture, leaving a small amount (on the tip of a spatula) in the vial as a standard for TLC analysis. Then, reattach the reflux condenser with an inflatable balloon and place the flask in the water bath heated to 90 °C. Stir the reaction mixture under an inert atmosphere for 2 hours. Remove the flask from the water bath and let the reaction mixture cool down. Add 8 cm³ of NH₄Cl saturated aqueous solution and stir the mixture at room temperature for 10 min.
2. Transfer the white suspension into the separatory funnel. Extract the aqueous phase 3 times with 5 cm³ of ethyl acetate. Collect the organic extracts in a 25 cm³ Erlenmeyer flask. Add one teaspoon of anhydrous Na₂SO₄, and let the organic phase stand over the drying agent for 20 min.
3. Prepare the standard solution of the starting material in a vial by dissolving a small amount of 2-acetonaphthone (set aside in step 1) in 0.5 cm³ of ethyl acetate. Prepare the eluent mixture hexanes/ethyl acetate 6:1 and pour it into the developing chamber and cover it with a Petri dish. Spot a sample of the starting material and a sample of the extract with a capillary tube on a TLC plate. Place the TLC plate into the developing chamber, close the lid and let the eluent evolve. Mark the solvent front and the position of the starting material and the product spots under a UV light. Calculate the retention factors of the starting material and the product.
4. After 20 minutes of drying have elapsed (step 2), filter the extract through filter paper into a 50 cm³ round-bottom flask. Remove the solvents using a vacuum rotary evaporator.

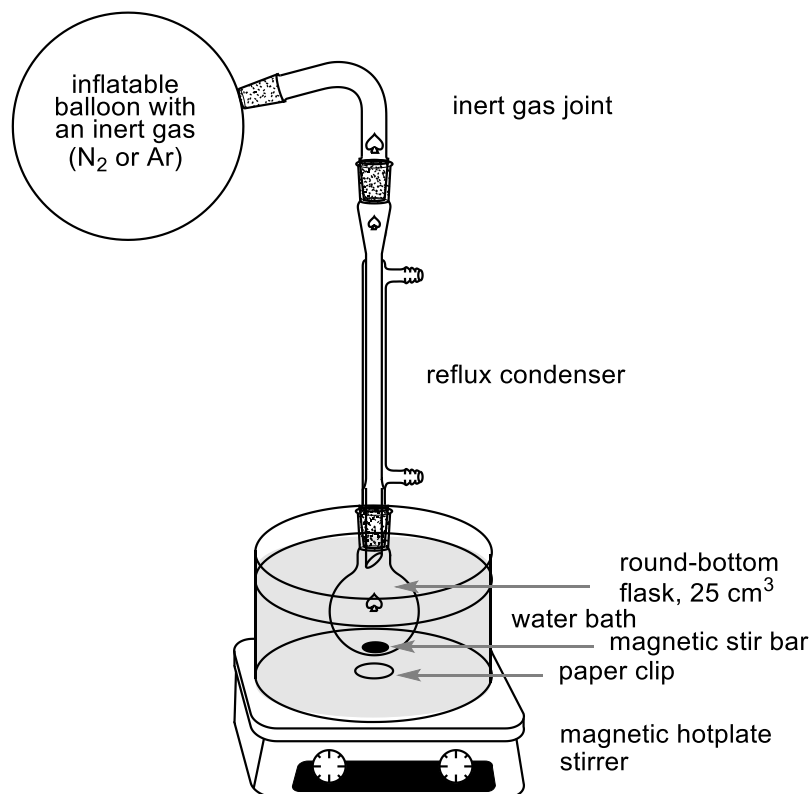


Figure P7. Apparatus for drying of isopropyl alcohol.

III. Crystallization of the product

Dilute the residue after the evaporation with 10 cm³ of hexanes. If the crude product precipitates, attach a reflux condenser and heat the solvent to the boiling point in the water bath heated to 90 °C until the solid material dissolves. Place the flask in the ice bath and let the product crystallize. Separate the crystals by filtration on filter paper and wash them with 5 cm³ of hexanes. Let the isolated product dry in air. Weigh the product and calculate the yield. Determine the melting point of the product. Compare the value with the reference data and draw a conclusion about the product purity.

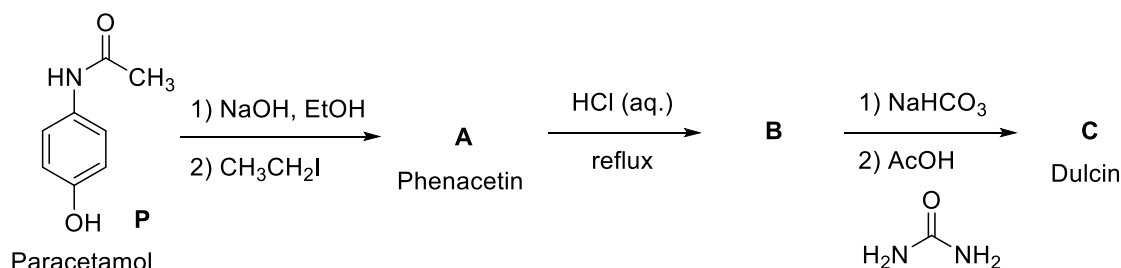
Data Analysis and Questions

- P7.1 Calculate the theoretical yield of the product in mg.
- P7.2 Calculate the experimental yield of the product in %.
- P7.3 Provide the melting point of the product.
- P7.4 Provide the R_f values of the starting material and the product.
- P7.5 Calculate the number of moles of water present in 4 cm³ of isopropyl alcohol ($w(\text{H}_2\text{O}) = 0.002$; $d(\text{iPrOH}) = 0.786 \text{ g}\cdot\text{cm}^{-3}$).
- P7.6 What is the final product of the aluminium isopropoxide hydrolysis in the final step of the synthesis?
- P7.7 Explain the difference in the retention factors of the starting 2-acetonaphthone and the obtained 1-(2-naphthyl)ethanol.
- P7.8 Propose an alternative synthetic method for the transformation of 2-acetonaphthone to 1-(2-naphthyl)ethanol.



Problem P8. Transformation of a drug to a sweetener

In this task, you will conduct a multistep synthesis of the artificial sweetener dulcin. You will start with paracetamol (acetaminophen) tablets, which can be bought, for example, in local drug stores as the well-known drug Paralen®.



Chemicals and Reagents

- Paracetamol tablets with paracetamol content 1.00 g (or pure paracetamol)
- 1.0 M sodium hydroxide solution in 95% ethanol, 8 cm³
- Iodoethane, 1 cm³
- 6.0 M hydrochloric acid solution (20% w/w), 5 cm³
- Sodium bicarbonate, 3.00 g
- Acetic acid, 2 drops
- Urea, 1.37 g
- Hexanes, 5 cm³
- 95% ethanol (w/w), 5 cm³
- Ethyl acetate, 5 cm³

Substance	Name	State	GHS Hazard Statements
C ₈ H ₉ NO ₂	Paracetamol	Tablets or pure solid	H302, H315, H317, H319
NaOH	Sodium hydroxide	Solution in 95% ethanol	H314
CH ₃ CH ₂ I	Iodoethane	Liquid (in a syringe)	H302, H315, H317, H319, H334, H335
HCl	Hydrochloric acid	Aqueous solution	H315
NaHCO ₃	Sodium bicarbonate	Solid	Not hazardous
NH ₂ CONH ₂	Urea	Solid	Not hazardous
CH ₃ COOH	Acetic acid	Liquid	H226, H314
C ₆ H ₁₄	Hexanes (mixture of isomers)	Liquid	H225, H304, H315, H336, H411
CH ₃ COOCH ₂ CH ₃	Ethyl acetate	Liquid	H225, H319, H336
CH ₃ CH ₂ OH	Ethanol	Liquid azeotropic mixture	H225, H319
CH ₃ COCH ₃	Acetone	Liquid (in a wash-bottle)	H225, H319, H336

Equipment and Glassware

- Laboratory stand with clamps
- Magnetic hotplate stirrer and a PTFE-coated stir bar
- Water aspirator (or other vacuum source for suction filtration)
- Two-neck round bottom flask, 50 cm³
- Round-bottom flask, 50 cm³ (2)



- Round-bottom flask, 25 cm³
- Reflux condenser with water hoses
- Suction flask, 100 cm³ (2), with rubber adapter
- Sintered glass filter funnel, porosity S2 (2)
- Graduated cylinder, 10 cm³ (2)
- TLC plates, silica gel 60 F₂₅₄ (2), and capillaries
- TLC chamber or a Petri dish covered small beaker
- UV lamp (254 nm)
- Erlenmeyer flask, 50 or 100 cm³ (2)
- Filtration funnel and filter paper
- Pasteur pipettes with rubber bulb
- Syringe, 1 cm³, with needle
- Rubber septum
- pH indicator paper
- Spatula
- Vials (3), labelled **P**, **A** and **C**
- Mortar with pestle
- Glass rod
- Wash-bottle
- Oil bath
- Ice bath
- Melting point apparatus

Procedure

I. Synthesis of phenacetine (A)

1. Grind the paracetamol tablets with the total paracetamol content of 1.0 g using a mortar and pestle. Transfer a small amount of the material (on the tip of a spatula) in vial **P** for TLC analysis. Transfer the remaining powder into a 50 cm³ two-neck round-bottom flask, equipped with a magnetic stir bar, via plastic funnel or by using a folded weighing paper.
2. Add 8 cm³ of 1 M NaOH solution in 95% ethanol into the flask using a Pasteur pipette. Stopper the side neck with a rubber septum and fold it over the neck. Equip the flask top neck with a reflux condenser, start running the cooling water in the condenser and immerse the flask in an oil bath. Turn the stirring on. Heat the mixture at reflux for 15 min after it has reached boiling point (the boiling point of ethanol is 78 °C).
3. Take the flask out of the oil bath (*Caution! Hot.*). Take 1.0 cm³ of iodoethane using a 1 cm³ syringe with a needle, pierce the septum with the needle and add the iodoethane dropwise to the hot solution (Figure P8). Remove the syringe, immerse the flask again to the oil bath and continue heating the mixture. Reflux for a further 15 min.
4. Prepare a suction filtration apparatus with a sintered glass funnel. The collector flask should contain approximately 25 cm³ of a mixture of water and ice. Lift the flask from the oil bath, disconnect the condenser and filter the hot mixture under vacuum. You will thus filter off the insoluble starch (used as a tablet filler). Let the collector flask stand for about 2 min. A precipitate will form. Prepare another suction filtration apparatus with a sintered glass funnel and filter the contents of the collector flask under vacuum. Rinse the flask with a small amount of ice-cold water (2 × 5 cm³). Leave a small amount of solid **A** (on the tip of a spatula) for TLC analysis in a vial labelled **A**.

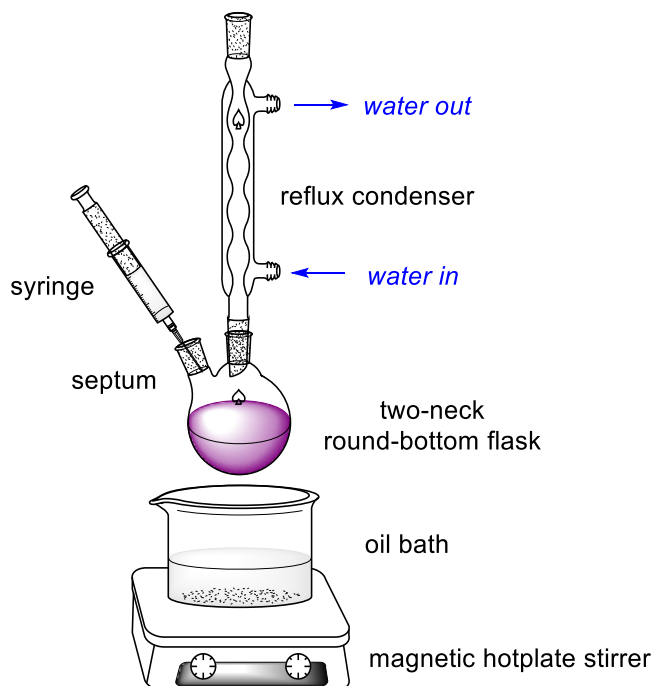


Figure P8. Adding iodoethane by syringe.

II. Synthesis of dulcin (C)

1. Transfer the filtered solid (product **A**) to a clean 50 cm³ round-bottom flask, equipped with a magnetic stir bar. Add 5 cm³ of 6 M HCl (aq.) by a Pasteur pipette. Equip the flask with a reflux condenser and turn on the stirring. Heat the mixture at reflux for 15 min.
2. Remove the flask from the oil bath and add solid NaHCO₃ to the hot mixture (3 g in 3–5 portions) for neutralization. Be careful, as CO₂ gas evolves. At the same time, stir the mixture vigorously and do not let it solidify. Check the pH of the mixture using glass rod and pH indicator paper. The final pH should be 6.0–6.5. If not, add more solid NaHCO₃. If the pH is higher, add diluted aq. HCl to adjust the final pH.
3. After neutralization, add 1.37 g of urea and two drops of acetic acid to the mixture using a Pasteur pipette. Immerse the flask fitted with the condenser in the oil bath. Heat the mixture under reflux for 60 min.
4. Remove the flask from the oil bath and let it cool down for 10 min. Then, immerse the flask in an ice bath. A solid will precipitate. Prepare a suction filtration apparatus with a sintered glass funnel. Filter product **C** under vacuum and wash it with ice-cold water (2 × 5 cm³).

III. Recrystallization of dulcin (C)

1. Transfer product **C** to a clean 50 cm³ round-bottom flask, equipped with a magnetic stir bar. Add 15 cm³ of water, attach a reflux condenser and immerse the flask in an oil bath. Heat the mixture under reflux until all the solid dissolves. If necessary, add more water (but not more than additional 15 cm³).
2. Remove the flask from the oil bath, filter the hot solution through filter paper into an Erlenmeyer flask and let it cool to room temperature. Then, cool the flask in an ice bath for 10 min. Crystals will start to form. Prepare a suction filtration apparatus with a sintered glass funnel. Filter the crystals of product **C** under vacuum and wash them with ice-cold water (2 × 5 cm³). Let them air dry on the funnel.



- If the product is not pure enough (brown colour persists), repeat the crystallization using organic solvents: Transfer the product into a 25 cm³ round-bottom flask equipped with a magnetic stir bar and add 5 cm³ of hexanes. Attach the reflux condenser and heat to reflux. At this point, add a few drops of ethanol by a Pasteur pipette, until all the solid dissolves. Remove the flask from the oil bath and filter the hot solution through filter paper into an Erlenmeyer flask. Let it cool for 5 min, then immerse the flask in an ice bath for 10 min. Collect the formed crystalline material using the suction filtration apparatus, as described before.
- Transfer the product to a *pre-weighed* Petri dish.
- Leave a small amount of the solid (**C**) for TLC analysis in a small vial labelled **C**.
- Weigh the product and determine the melting point of product **C**.
- Perform TLC analysis of the paracetamol standard (**P**) and your samples **A** and **C** (silica gel plate, eluent ethyl acetate).

Data Analysis and Questions

- P8.1 Draw the structures of compounds **A**, **B**, and **C**.
- P8.2 Calculate the theoretical yield of product **C** in mg, based on the amount of the starting material **P**.
- P8.3 Calculate the experimental yield of product **C** in %.
- P8.4 Provide the melting point of product **C**.
- P8.5 Provide the R_f values of compounds **P**, **A**, and **C**.
- P8.6 Select the correct statements, based on the observations and expected reactivity:
- NaOH deprotonates the OH group of paracetamol to give a coloured phenolate.
 - NaOH deprotonates the methyl protons of the acetamide.
 - NaOH does not react with paracetamol; it only reacts with H⁺, which is released after the addition of iodoethane.
 - The deprotonated, anionic substrate is much more reactive than the neutral paracetamol.
 - Nucleophilic substitutions with iododethane are usually S_N1 reactions (i.e., the rate is independent of the nucleophile concentration and reactivity).
 - Acetamide functional group is stable towards an aqueous acid (aq. HCl).
 - Acetamide functional group is stable towards a base (NaOH in 95% EtOH).
 - Aryl ethyl ether functional group is stable towards an aqueous acid (aq. HCl).
 - Product **B** is a salt (it contains a cation and an anion).
 - Product **C** is a salt.
- P8.7 In the last step of the process, urea and acetic acid react to form ammonium acetate and a reactive species:
- Hydrogen cyanide, H–C≡N,
 - Fulminic acid, ⁽⁻⁾O–N⁽⁺⁾≡C–H,
 - Hydrogen isocyanide, H–N⁽⁺⁾≡C⁽⁻⁾,
 - Isocyanic acid, H–N=C=O.