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Introduction

The laboratory work includes eight syntheses, the identification reactions of organic compounds as well as a two-component qualitative analysis. In the analytic part of the laboratory course, the student gets to separate the two components of an analytical mixture by active extraction and to identify them with the help of their physical properties and on basis of spectroscopical methods. After the completion of the analytical work, a work report has to be composed. The identification reactions can be done alongside with the syntheses. The analytical work can be started once the syntheses and the identification reactions have been approved by the assistant.

The theory and execution of the laboratory work is examined in the morning groupwise led by an assistant. It is therefore important to be present right from the start of the work session. The participants of the course are divided into groups in such a way, that every group works on a different synthesis. The members of the group carry out the same synthesis individually. The student receives a grade for every completed synthesis. This grade is based on the product yield and purity. During the synthetic lab work a test on work methods and laboratory safety will be held, which consists of questions related to safety at work. The examination has to be passed before the laboratory work can be continued and the pass mark influences the final mark. Once the syntheses, identification reactions, analysis and the final examination have been approved with a pass mark and appropriate fees have been payed (the receipt has to be presented to the student office), the course will be added to your transcript of studies. The final mark depends on the partial marks that have been achieved during the course. The test on work methods and laboratory safety and the final examination includes topics which can be found in the work hand-out and the following book (in Finnish): T. Simonen, Ogaanisen kemian synteettiset työmenetelmät.
Acetylsalisylic acid (Aspirin)

\[
\text{C}_9\text{H}_8\text{O}_4 + \text{H}_2\text{SO}_4 \rightarrow \text{C}_9\text{H}_7\text{O}_4\text{COOH} + \text{CO}_2
\]

Reagents

- 5.0 mL of acetic anhydride
- 2.8 g of salicylic acid
- 3-4 drops of conc. sulfuric acid

Safety Notes

Acetic anhydride is volatile and a strong irritant.

Equipment

- 100 mL round-bottomed flask (14/29)
- magnetic stirrer
- water and ice baths
- suction filtration apparatus
  - Büchner funnel
  - rubber stopper
  - 2 filter flasks
  - round-bottomed flask, condenser, oil bath

Procedure

Place 2.8 g of salicylic acid in a dry 100 mL round-bottomed flask, then add 5.0 mL of acetic anhydride and 3-4 drops of concentrated sulfuric acid. Mix the resulting white slurry with a magnetic stirrer, and place the flask in a warm water bath (45-50°C) for 15 min. Allow the flask to cool and add 50 mL of water and break up any lumps with a spatula.

Isolation and purification

Allow the mixture to stand for an additional five minutes, then chill the flask in an ice bath and remove the crystals by suction. Crystallize the crude aspirin from warm 30% ethanol - water mixture not exceeding 80°C (see experimental note). Allowing the mother liquor to stand overnight may produce a second crop of crystals. Air-dry the crystals and determine the per cent yield and melting point (mp. for aspirin is 135°C). The yield is 80%.

Experimental note: At temperatures exceeding 80°C, aspirin forms an oil that dissolves organic impurities from water; in this case it may be difficult to redisolve the aspirin in water.

Product characterization

Measure the melting point and run an IR-spectrum of the product.
Meso-1,2-dibromo-1,2-diphenylethane

Reaction mechanism is an electrophilic addition to the double bond

<table>
<thead>
<tr>
<th>Reagents</th>
<th>Safety notes</th>
<th>Equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 g of <em>trans</em>-stilbene</td>
<td>Bromine is extremely poisonous and corrosive. It has to be handled in a fume cupboard. Wear protective gloves. Additional information (in Finnish): T. Simonen Työtapamonista p. 53</td>
<td>50 ml round-bottomed flask (14/29) small graduated cylinder suction filtration apparatus watch glass</td>
</tr>
<tr>
<td>10 ml of dichloromethane</td>
<td></td>
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<tr>
<td>10 ml 10% (w/v) solution of bromine in dichloromethane</td>
<td></td>
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<tr>
<td>cyclohexene</td>
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</tbody>
</table>

**Procedure**

Dissolve 1.0 g of *trans*-stilbene in 10 ml of dichloromethane in a 50 ml round-bottomed flask. Stir the solution with magnetic stirrer and add 10 ml of a 10% solution of bromine in dichloromethane (0.10 g of bromine/1.0 ml). If the colour of bromine disappears completely, add bromine dichloromethane solution in 1 ml portions until the colour of the bromine stays permanently. The developing dibromocompound precipitates from the solution. Add to the reaction mixture cyclohexene in drops until the extra bromine is destroyed. Stop adding the cyclohexene when the colour of the bromine disappears. Cool the solution in an ice bath to complete the precipitation.

**Isolation**

Collect the product by suction filtration. Wash it in the funnel with 5 ml of ice cooled dichloromethane. Dry the product by sucking air through the funnel. Transfer the dry product to a watch glass and weight the dry product. The yield of the product is 75%.

**Product characterization**

Measure the melting point and run an IR-spectrum of the product. Check the purity of the product by TLC (1:2 dichloromethane:petroleum ether)
The reaction in question is an acid catalyzed esterification. Propanoic acid is protonated by the acid used as a catalyst. The emerging cation is resonance stabilized. Ethanol acts as a nucleophile as it attacks the cation. This is followed by the transfer of a proton and the loss of water. The reaction is a nucleophilic substitution.

### Reagents
- 10 mL abs. ethanol
- 14 mL propanoic acid
- conc. sulfuric acid
- 40 mL ether
- 2M NaHCO₃ solution
- MgSO₄

### Safety Notes
- Concentrated sulfuric acid is highly corrosive.
- Ether is a highly flammable and volatile liquid.
- Ethanol is a highly flammable and volatile liquid.

### Equipment
- reflux apparatus
- extraction/separation equipment
- apparatus for continuous feed distillation

### Procedure
In a 50 mL round-bottomed flask mix 10 mL of ethanol and 14 mL of propanoic acid. Carefully add 2-3 drops of concentrated sulfuric acid (catalyst) and mix the solution well. After addition of a few anti-bumping granules, reflux the mixture for one hour using an oil bath. Let the reaction mixture cool.

### Isolation and purification
Pour the cool reaction mixture into a separatory funnel filled with 40 mL of water. Add 40 mL of ether into the funnel, stopper, and shake it gently (wear safety glasses!). Release any pressure inside the separation funnel by turning the stoppered funnel upside down and opening the stopcock. Let the funnel rest (upright, stopcock closed) until the layers are separated. Let the aqueous layer (the lower one) drain from the funnel into a different vessel. Wash the ether layer that remains in the funnel with 20 mL of water (shake it with the added water). Once the layers have separated, the aqueous layer is drained. Wash the ether solution with 2 M NaHCO₃ solution to remove any unreacted acid. It is essential that you are especially careful at this stage since carbon dioxide is produced when the acid is
neutralized. The gas causes pressure inside the separatory funnel. The pressure is released as described above. The acid is now present in the aqueous layer as the Na salt. Finally wash the ether solution with 20 mL of water. Remove the aqueous layer as thoroughly as possible and then dry the ether solution with anhydrous magnesium sulfate. After 30 minutes of drying, filter the solution through a regular glass funnel fitted with a clean cotton plug into a dropping funnel. Part of the ether solution is poured into a round-bottomed flask and boiling stones are added. The ether is removed by a distillation procedure used for the removal of large amounts of solvent (bp. of ether = 35°C). The flask can be heated either in a water or oil bath. The product is purified by distillation. The boiling point of ethyl propanoate is 99°C (oil bath). The product yield is 60%.

**Product characterization**

Measure the refractive index and run an IR spectrum of the product.
Aromatic aldehydes when treated with an alkali cyanide, usually in aqueous solution, undergo condensation to the α-hydroxyketone or benzoin (called benzoin condensation). The best known example is the conversion of benzaldehyde to benzoin.


**Reagents**
- 2.5 mL of benzaldehyde
- 35 mL of techn. alcohol
- 0.25 g of potassium cyanide

**Safety Notes**
Potassium cyanide is a poisonous and corrosive solid. For the disposal of cyanide compounds see (in Finnish):


Benzaldehyde is an irritant.

**Equipment**
- reflux apparatus
- water bath
- Erlenmeyer flask
- suction filtration apparatus

**Procedure**

In a 50 mL round-bottomed flask place 5 mL alcohol, 2.5 mL purified benzaldehyde and 0.25 g potassium cyanide dissolved in 4ml of water(CARE! This preparation must be done in the hood! Assumed purity of KCN is 96-98%). Attach a reflux condenser and heat on a boiling water bath for 30 minutes. Cool the flask in ice-water, filter the crude benzoin and wash it with water and drain dry.

**Isolation and purification**

Recrystallize the crude product from ethanol; the benzoin is obtained as a white crystalline solid, m.p. 137 °C, the yield of the pure product being 2.1 g.

**Product characterization**

Measure the melting point and run an IR spectrum of the product.
Reduction of benzoin with sodium borohydride – 1,2-Diphenylethane-1,2-diol

The stereochemical course of ketone reductions can be influenced by the presence of hydroxyl groups close to the carbonyl function. This experiment illustrates the stereoselective reduction of benzoin using sodium borohydride as reducing agent. For the mechanism see the course folder *Orgaanisen kemian perustyöt* I in the assistant room.

### Reagents
- 2.00 g benzoin
- 0.40 g sodium borohydride
- ethanol
- hydrochloric acid (6 M)

### Safety Notes
- irritant
- corrosive, flammable
- flammable, toxic
- corrosive

### Equipment
- magnetic stirrer
- suction filtration apparatus
- recrystallization apparatus

### Procedure
Dissolve the benzoin in 20 mL of ethanol in a 100 mL Erlenmeyer flask.¹ Stir the solution magnetically and add the sodium borohydride in small portions over 5 min using a spatula.² If necessary, rinse in the last traces of sodium borohydride with 5 mL of ethanol. Stir the mixture at room temperature for a further 20 min. and then cool it in an ice bath whilst adding 30 mL of water followed by 1 mL of 6 M hydrochloric acid.³ Add a further 10 mL of water, and stir the mixture for a further 20 min.

1) Warming may be necessary; solution need not be complete. 2) Care! Exothermic 3) Foaming may occur!

### Isolation and purification
Collect the product by suction filtration, and wash it thoroughly with 100 ml water. Dry the product by suction for 30 min, and record the yield. Recrystallize from ethanol-water (1:1). Yield 90 %.

### Product characterization
Check the purity by tlc (silica plates; eluent ethyl acetate-hexane 1:1). Measure the melting point and run a IR spectrum of the product.
**p-Benzquinone**

![Chemical structure of p-Benzoquinone]

**Reagents**
- 2.5 g of hydroquinone
- 1.4 g of potassium bromate
- 1.2 mL of sulfuric acid (2 M)

**Safety Notes**
- harmful
- oxidative, explosive

**Equipment**
- 100 mL flask (14/29) + stopper
- suction filtration apparatus
- sublimation apparatus

**Procedure**

Place potassium bromate (1.4 g), 2 M sulfuric acid (1.2 mL), water (25 mL) and hydroquinone (2.5 g) into a 100 mL round-bottomed flask. Close the flask with a stopper and stir the mixture (by swirling) for about 30 minutes at room temperature. The reaction is over when the initially black mixture turns yellow (yellowish green).

**Isolation and purification**

Filter by suction filtration, wash with ice cold water and spread the product on filter paper until it is dry. Purify the obtained crude product by sublimation under vacuum. *p*-Benzoquinone gives a yield of 1.3 g and has its melting point at 115°C.

**Note:** The product is water soluble. This means that over eager washing will diminish the amount of product that is left in the funnel. The impure product in particular decomposes easily so that it is important that there is no delay in the isolation and purification of the compound.

**Product characterization**

Measure the melting point and run an IR spectrum of the product.
Protection of ketones as ethylene acetal (1,3-dioxolanes): ethyl acetoacetate ethylene acetal

In polyfunctional molecules it is often necessary to protect aldehyde and ketone carbonyl groups to stop undesirable side-reactions during a synthetic sequence, and then remove the protecting group at a later stage. One common protecting group for aldehydes and ketones is the ethylene acetal (1,3-dioxolane derivative) easily prepared from the carbonyl compound and ethane-1,2-diol (ethylene glycol) in the presence of an acid catalyst. The protecting group can be removed subsequently by treatment with aqueous acid.


**Reagents**
- 12.7 mL / 13.0 g ethyl acetoacetate
- 5.8 mL / 6.5 g ethane-1,2-diol
- 0.05 g toluene-4-sulfonic acid monohydrate
- 50 mL toluene
- sodium hydroxide solution (10%)
- anhydrous potassium carbonate

**Safety Notes**
- irritant
- corrosive, toxic
- flammable, irritant
- corrosive
- corrosive, hygroscopic

**Equipment**
- reflux with water removal (Dean and Stark apparatus)
- extraction/separation
- distillation under reduced pressure (water aspirator)


Set up a 100 mL round bottomed flask with a Dean and Stark water separator and reflux condenser. Add the ethyl acetoacetate, toluene, ethane-1,2-diol, toluene-4-sulfonic acid, and a few anti-bumping granules to the flask. Heat the flask so that the toluene refluxes vigorously.1 Continue to heat the mixture until no more water collects in the separator.2

**Isolation and purification**

Cool the mixture to room temperature, transfer it to a separatory funnel, and wash the solution with 15
mL sodium hydroxide solution followed by 2 x 20 mL portions of water.\textsuperscript{3} Dry the organic layer over anhydrous potassium carbonate.\textsuperscript{4} Filter off the drying agent by suction, evaporate the filtrate on the rotary evaporator,\textsuperscript{4} transfer the residue to a 25 mL flask and distil it under reduced pressure using water aspirator. Record the exact boiling point and the yield of the product. The pure compound boils at 99.5 -101°C/17 mm Hg and has the index of refraction 1.43262. Yield 64%.

1) Vapor should condense half way up condenser.

2) Takes about 45 min.

3) Check the pH with pH-paper. The final washing should be neutral.

4) May be interrupted at this stage.

**Product characterization**

Measure the refractive index and run an IR spectrum of the product.
**p-Methyl acetophenone**


<table>
<thead>
<tr>
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<tbody>
<tr>
<td>15 g AlCl₃</td>
<td>Aluminium chloride produces HCl when it comes into contact with dampness of the air and reacts violently with water. AlCl₃ dust is harmful when inhaled.</td>
<td>100 mL 3-necked round-bottomed flask</td>
</tr>
<tr>
<td>25 mL distilled toluene</td>
<td>Toluene: flammable.</td>
<td>dropping funnel</td>
</tr>
<tr>
<td>4.8 mL acetic anhydride</td>
<td>Acetic anhydride: lachrymator, corrosive.</td>
<td>CaCl₂-tube</td>
</tr>
<tr>
<td>anhydrous MgSO₄</td>
<td></td>
<td>mechanical stirrer</td>
</tr>
</tbody>
</table>


In a 100 mL 3-necked flask, equipped with a separatory funnel carrying a calcium chloride tube, a mechanical stirrer, and an efficient reflux condenser attached to a gas absorption device, place 15 g of finely-powdered, anhydrous aluminium chloride and 25 mL of toluene. Set the stirrer in motion and add 5.1 g (4.8 mL) of acetic anhydride slowly through the addition funnel; the addition requires 15 minutes, during which time the temperature rises to about 90°C and much hydrogen chloride is evolved. Heat the mixture on a water bath, with stirring, for 30 minutes or until there is practically no evolution of gas. Cool the reaction mixture to room temperature and pour it into a mixture of 30 g of crushed ice and 30 mL of concentrated hydrochloric acid: stir until the aluminium salts dissolve completely.
**Isolation and purification**

Separate the toluene layer, wash it with water, then with 10 per cent sodium hydroxide solution until the washings remain alkaline, and finally with water: dry over anhydrous magnesium sulphate. Distill the residue using a Claisen adapter at atmospheric pressure until the temperature rises to about 125°C, then allow to cool and distil under reduced pressure. Alternatively, toluene may be removed with a rotary evaporator. Collect the \( p \)-methylacetophenone at 93-94°C/7 mm (the b.p. at atmospheric pressure is 225°C); the yield is 5.8 g.

**Product characterization**

Measure the refractive index and run an IR spectrum of the product.