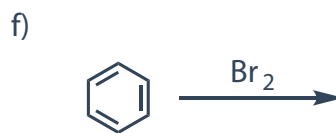
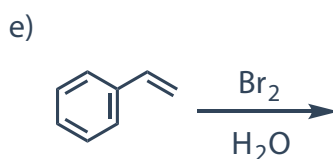
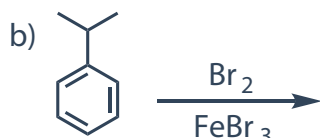
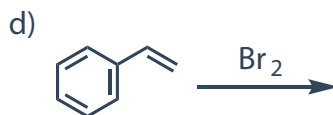
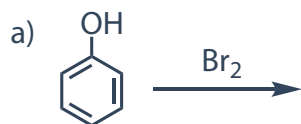


- d. If the available amount of benzaldehyde is at least two times higher than the amount of acetone and there is enough base, this reaction continues. Write down the net reaction (no detailed mechanism) if there is 1 mol of acetone, 2 mol of benzaldehyde, and an excess of sodium hydroxide in the system.
- e. What is a potential side reaction that can happen in this system?
- f. Briefly note whether, and why the reaction would be faster or slower if:
- i. *p*-nitrobenzaldehyde is used instead of benzaldehyde;
 - ii. *p*-ethoxybenzaldehyde is used instead of benzaldehyde;
 - iii. formaldehyde is used instead of benzaldehyde;
 - iv. 3-pentanone is used instead of acetone;
 - v. sodium carbonate is used instead of sodium hydroxide?

2. Bromine can react with organic compounds in many different ways depending on the reaction conditions. Consider the following reactions of aromatic compounds with bromine (there is 1 equivalent of bromine in each case). Give the structure of the major product (the product obtained in the highest yield) and state what is the type of the reaction that led to that product. Comment on regioselectivity where relevant (you don't have to comment on stereochemistry).



3. Ibuprofen is an anti-inflammatory drug used to relieve pain, fever and inflammation. It is widely used because it is usually available without prescription. Ibuprofen can be synthesized in many different ways and one of them is going to be analyzed in this exercise.



The starting compound in this sequence is benzene. In the first step it is treated with one equivalent of isobutyl chloride in presence of aluminium chloride to yield compound **A**. Compound **A** is then treated with acetic anhydride in presence of aluminium chloride to yield compound **B**.

- a. Show the structures of compounds **A** and **B**. What are the reaction mechanisms (just give the acronyms, no detailed mechanism) through which these two compounds were obtained? Comment on the regiochemistry where relevant.

Sodium borohydride (NaBH₄) is a reagent widely used in chemistry for reducing various compounds. One of the most common applications of sodium borohydride is for reduction of carbonyl compounds to yield the corresponding alcohols.

- b. Knowing that the role of sodium borohydride in this sequence is to provide a "hydride anion" (H⁻) precursor that acts as a nucleophile, give the structure of compound **C** (do not pay attention to stereochemistry).

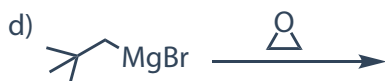
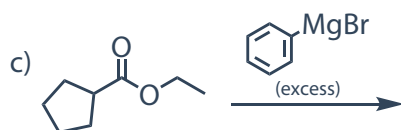
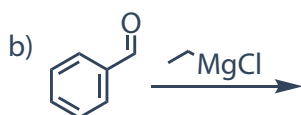
Compound **C** is treated with concentrated hydrochloric acid to yield compound **D** at low temperature. Compound **D** is then heated with elementary magnesium in an inert solvent to yield compound **E**.

- c. Give the structures of compounds **D** and **E**. What is the mechanistic pathway through which compound **D** is obtained? Explain your answer.

Finally, compound **E** is treated with carbon dioxide. After workup with hydrochloric acid, **ibuprofen** is obtained.

- d. Draw the structure of **ibuprofen**. What is type of reaction through which this compound is obtained? What is the role of hydrochloric acid during the workup?

4. Give the structures and IUPAC names of the major products of the following reactions with Grignard's reagents. Consider that there is an acidic aqueous workup after each reaction.



5. Transesterification is the reaction of an ester with an alcohol. This reaction is very useful in various organic synthetic strategies. It is especially useful in synthesis of polyesters (this will be discussed in much greater detail during the last chapter of the course). Transesterification is going to be discussed on the example of reaction of methyl acrylate (propenoate) and 1-butanol.

- a. Show the equation of the overall reaction between methyl acrylate and butanol. Give the IUPAC names of both products.

Transesterification is usually performed in presence of a catalyst. This process can be both acid- and base-catalyzed.

- b. Show the mechanism if the reaction is catalyzed with a Brønsted acid (that delivers H^+). What is the role of the mineral acid in this case?

- c. What is the potential side reaction that can occur if transesterification of *these* compounds is carried out in presence of mineral acid? Comment on why this is a side reaction and transesterification is the main one.

6. Xylene is a trivial name for dimethyl benzene. There are three isomers of xylene.
 - a. Draw structures of three isomers of xylene. What type of isomerism is this?

- b. These isomers significantly differ in reactivity in electrophilic aromatic substitution. If a mixture of **one** mol of each of these three isomers is treated with **one** mole of chlorine in presence of AlCl_3 , only one compound reacts. Which isomer reacts and why?
- c. How would the outcome differ if the same reaction was done with only *para*-xylene (1,4-dimethylbenzene) in absence of AlCl_3 and with constant irradiation of reaction mixture with UV light? Draw the structures of the product(s) and explain your answer.
- d. Show the overall reaction of phosgene (COCl_2) with an excess of toluene in presence of AlCl_3 .

Reading Suggestions:

Clayden, Greeves, Warren, *Oxford University Press*, **2012**.

Organic Chemistry, John McMurry, *Thomson Brooks/Cole*, **2008**.

Chimie Organique, Les Grands Principes, John McMurry, *Dunod Editeur*, **2009**.

Chimie Organique, Paul Arnaud, *Dunod Editeur*, **2009**.