

20th BChO, 2012, Riga, Latvia

Problem 1 – RADIO – Seasonal radioactivity

In some northern regions of Estonia, surface soil is enriched with uranium. Therefore, due to the high concentration of radioactive gas ^{222}Rn , it is not recommended to build houses in these regions. In the basement of a private house, the floor area equals 100 m^2 and the height is 2 m. The house is built in a potentially hazardous region. Radon concentration in the basement is low in the summertime, while during winter, radioactivity holds at 400 Bq m^{-3} level (Bq = decay per second).

- a) Why is the concentration of radon in the basement much greater during winter than in summertime?
 - i) The concentration of radon is higher at lower temperatures obeys $pV = nRT$.
 - ii) Soil under the basement does not freeze in winter, while the soil around the house does freeze. Consequently, radon gas leaks into the house through gaps and cracks inside the basement. In the summertime, gas escapes through the soil around the house.
 - iii) The rate of radon production from uranium is higher at lower temperatures. Therefore, a greater amount of radon enters the basement during winter.
- b) The half-life of ^{222}Rn is 3.82 days. Calculate the time needed for radon to decay, decreasing activity from 400 to 4 Bq m^{-3} . Assume that there is no entry of radon from the outside.
- c) Estimate the average radioactivity of radon in the basement during a year. Assume that the radon leaking rate is expressed as follows: $v_{\max} \cdot \cos^2(\pi d/365)$, where $v_{\max}$ is the maximal leaking rate, d is the day number from the beginning of the year.
- d) For comparison, calculate the total radioactivity (Bq m^{-3}) in an average banana (118 g, 124 cm^3). One banana contains 422 mg of potassium ions and 28 g of carbohydrates ($\text{C}_{12}\text{H}_{22}\text{O}_{11}$). Among potassium atoms, there are 0.0117% isotopes of radioactive ^{40}K ($T_{1/2} = 1.277 \cdot 10^9\text{ y}$). Among carbon atoms, $1.2 \cdot 10^{-10}\%$ isotopes of radioactive ^{14}C ($T_{1/2} = 5730\text{ y}$).
- e) What is more hazardous: ^{40}K and ^{14}C in bananas or ^{222}Rn in the air of the basement? Think of the total ionization energy released in a sequence of radioactive decay; the total rate of accumulation of radioactive isotopes and their daughter nuclei in a human body; and the calculated radioactivity per m^3 .

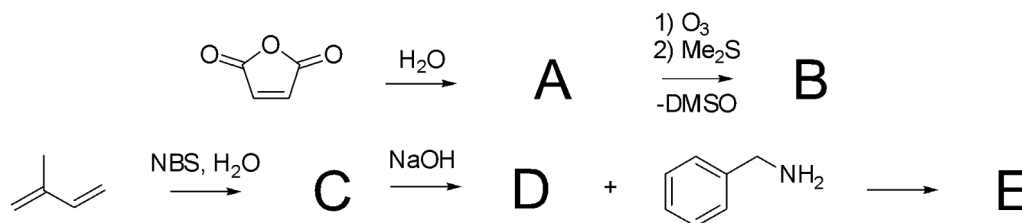
Problem 2 – EQUIL, THERMO – Ammonia

Nitrogen and hydrogen react to form ammonia: $\text{N}_2(\text{g}) + 3\text{H}_2(\text{g}) \rightleftharpoons 2\text{NH}_3(\text{g})$.

- a) Calculate the equilibrium constant at i) 298 K and ii) 450 K. Assume that enthalpy and entropy change of the reaction is constant for the given interval of temperatures. $\Delta G_f^\circ(\text{NH}_3) = -16.30\text{ kJ mol}^{-1}$, $\Delta H_f^\circ(\text{NH}_3) = -45.86\text{ kJ mol}^{-1}$.
- b) Express equilibrium partial pressure of N_2 , H_2 and NH_3 at pressure p assuming stoichiometric amounts of reactants.
- c) Stoichiometric amounts of reactants react at $10.0 \cdot 10^5\text{ Pa}$ pressure at 450 K. Calculate the percent of nitrogen that, in the course of the reaction, transforms into ammonia.
- d) At what pressure at 450 K nitrogen conversion into ammonium would be 25% (at stoichiometric amount of reactants)?

Problem 3 – MECH, SYNTH – The synthesis of proline

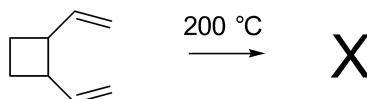
Proline is an α -amino acid, one of the twenty DNA-encoded amino acids. Its derivatives have shown to exhibit interesting biological activities, so a number of synthetic strategies have been utilized throughout the years to synthesize substituted proline derivatives, including this clever pericyclic reaction of a cationic intermediate.



NBS – *N*-bromosuccinimide, DMSO – dimethyl sulfoxide

- a) Draw the structural formulas of compounds **A–E**. *Hints: 2 moles of B are obtained from 1 mol of A; structures D and E each contain one monosubstituted double bond!*

Before going next to the main step in the synthesis of proline, consider a much simpler example of this type of transformation. Properly substituted cyclobutane under thermal conditions provides structure **X** in a single reaction. All double bonds in **X** have *Z*-configuration.



- b) Draw the structural formula of **X** and the starting cyclobutane, clearly indicating the stereochemical information that guides the formation of all *Z*-configuration in **X**.

X is used in the synthesis of the very popular reducing reagent 9-BBN (9-borabicyclo[3.3.1]nonane) by reacting with borane-dimethyl sulfide complex.

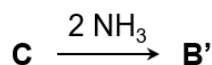
- c) Draw the structural formula structure of 9-BBN.

Completion of proline synthesis: **B** + **E** $\rightarrow$ [**F** $\rightarrow$ **G**] $\rightarrow$ **H**. Combining **B** and **E** initiates the two reaction sequences, the so-called domino reaction or cascade reaction, where the first reaction is similar to the one described above. Both **F** and **G** are iminium ions.

- d) Draw the structural formulas of compounds **F**, **G**, and **H**.
e) Provide the mechanisms of transformation **B** + **E** $\rightarrow$ **H**.

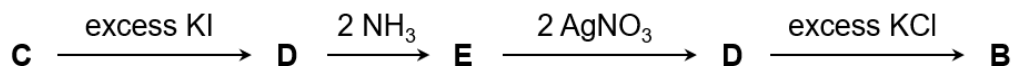
Problem 4 – ABC, INORG, STRUCT – Antitumor agent

In 1989, L. S. Hollis et al. discovered a new antitumor agent – a coordination compound **A** which contains transition metal **X** with an oxidation number of +2. It is synthesized from neutral inorganic compound **B**. Although the preparation of **B** may seem straightforward, it is actually done in multiple steps, as described by S. C. Dhara. A straightforward method for synthesis of **B** would be from potassium salt **C** in reaction with two equivalents of ammonia (Scheme 1). However, in this reaction, compound **B'** forms and, as a byproduct, potassium chloride solution is obtained. It is known that **C** consists of three chemical elements and the molecular mass ratio of compounds **C** : **B** is 1.383.



- a) Find out element **X** and molecular formulas of compounds **B**, **B'** and **C**.
b) Draw the structural formulas of **B** and **B'** with stereochemistry.

Synthesis of **B** is actually carried out as shown in scheme 2:



c) Draw the structural formulas of compounds **D–F** with stereochemistry.

A was prepared by heating an equimolar amount of **B** and pyridine (azabenzene, Py). In this reaction, no byproduct forms.

d) Draw the structural formula of compound **A** with stereochemistry.

e) Provide a method for how **A** can be isolated from the reaction mixture without **B**.

If metal **X** is replaced by nickel in compound **C** and nickel analogue of **B** is synthesized, by both straightforward (scheme 1) and provided method (scheme 2), the same product **G** is obtained.

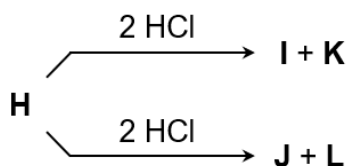
f) Explain this result and draw the structure of compound **G** with stereochemistry.

In 2008, USA scientists, using an analytical method, proved that compound **A** binds to DNA chains and found out the exact binding site and position of molecules in the formed product.

g) What type of binding is possible between compound **A** and a DNA chain?

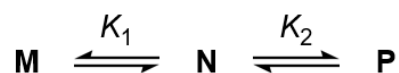
h) What analytical method is capable of identifying the exact binding site and position of molecules in a formed product?

If the reaction of **B'** is carried out with two equivalents of pyridine, compound **H** is obtained. If **H** reacts with two equivalents of hydrochloric acid, two compounds with the same stereochemistry, **I** and **J** may form giving byproducts **K** and **L**, respectively. The reaction scheme is as follows:



i) Write the structural formulas of compounds **H–L** with stereochemistry.

There are known reactions with coordination compounds where from arbitrary compound **N** only two isomers, **M** and **P**, are formed.



j) Calculate equilibrium concentrations of **N**, **M** and **P** if the initial concentration of **N** was α and equilibrium constants are K_1 and K_2 as shown in the scheme above.

Problem 5 – EQUIL – Aspirin absorption

When administered orally, a popular analgesic, Aspirin (2-acetoxybenzoic acid), passes through a membrane in the stomach to enter the bloodstream. To model this process two solutions representing the gastric acid and blood were prepared. To a flask containing some water, 10.00 cm³ of 85.0% H₃PO₄ and 50.00 cm³ of 4.00% NaOH solution were added. The mixture was diluted to 1.00 dm³ and is called the “Stomach” solution.

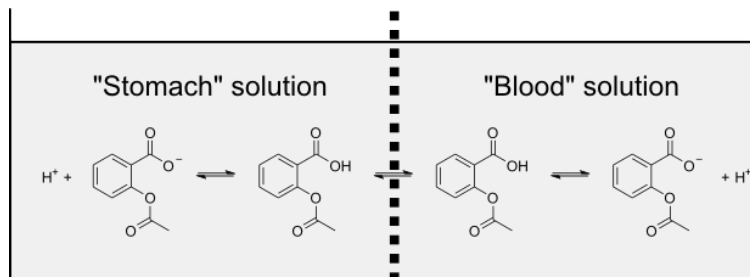
The data for 85.0% H₃PO₄: $\rho = 1.685 \text{ g cm}^{-3}$; $K_{a1} = 7.25 \cdot 10^{-3}$; $K_{a2} = 6.31 \cdot 10^{-8}$; $K_{a3} = 3.98 \cdot 10^{-13}$.

a) Calculate the pH of the “Stomach” solution.

To prepare 1.00 dm³ of the “Blood” solution, 10.00 cm³ of 85.0% H₃PO₄ was used.

- b) Calculate the volume of 4.00% NaOH solution one needs to add so the pH of the resulting "Blood" solution is 7.40.

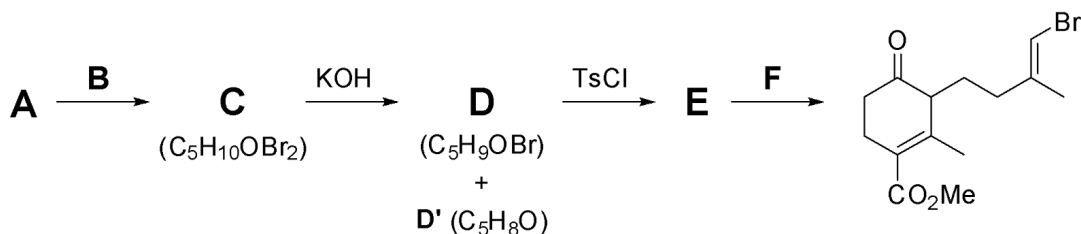
The "Stomach" and "Blood" solutions (1.00 dm³ of each) are separated by a membrane, which can be passed only by Aspirin in its neutral form. 1.00 g of aspirin is added to the "Stomach" solution. An equilibrium is considered to be reached when the concentrations of neutral Aspirin are equal in both solutions ([HA]_{stomach} = [HA]_{blood}). Aspirin $K_a = 3.02 \cdot 10^{-4}$.



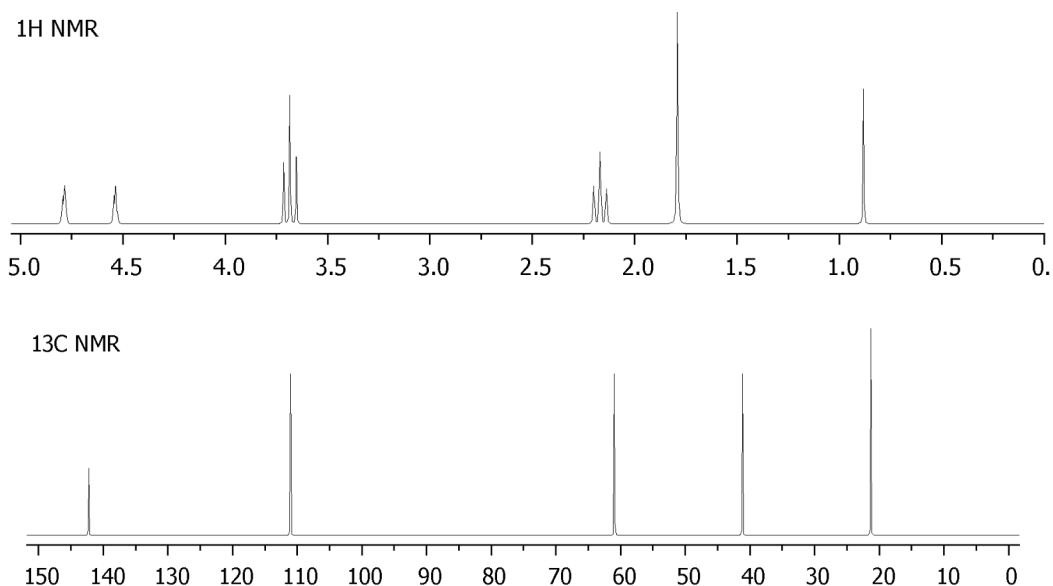
- c) Write the mass-balance equation for Aspirin.
- d) Calculate the concentrations for ionized and neutral Aspirin in both solutions (A^-_{stomach} , HA_{stomach} , HA_{blood} , A^-_{blood}) when equilibrium is reached.

Problem 6 - SPECTRA, SYNTH - Algae against cancer

Red algae from the genus *Laurencia* are known to produce a variety of bioactive compounds. Screening an extract from *Laurencia cartilaginea* led to the discovery of two closely related chamigranes that showed selective and potent cytotoxicity in anti-tumor tests, being particularly effective against colon cancer. Here is an attempt at a total synthesis of a chamigrane class compound majusculone.

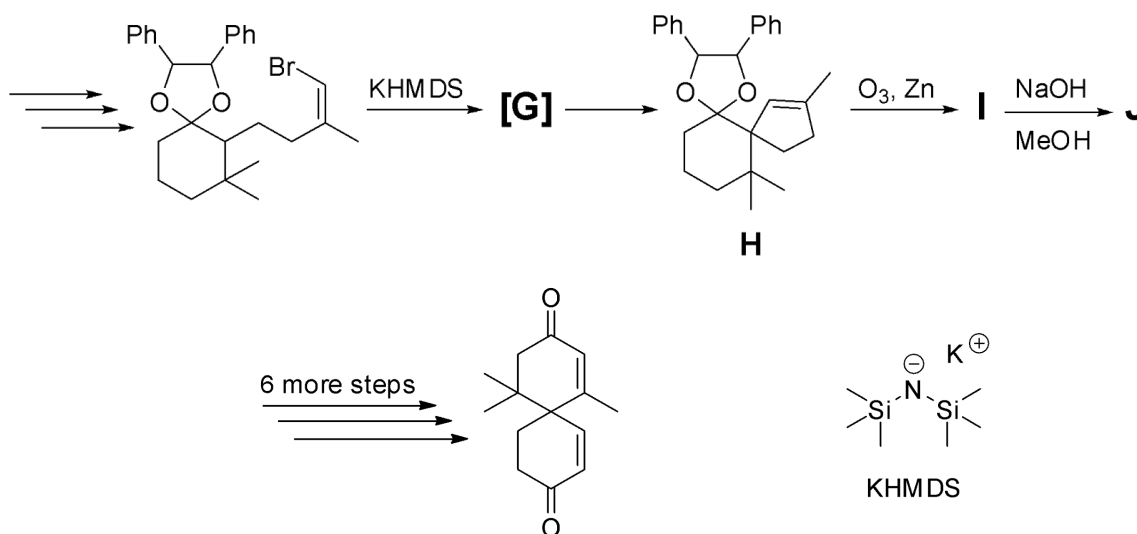


Compound A NMR spectra:



Notes: The ^1H NMR signal at 0.9 ppm disappears after the addition of some CD_3OD . Ratios of the areas below the ^1H NMR peaks are 1 : 1 : 2 : 2 : 3 : 1. The molecular mass of the compound **A** is 86.07 g mol^{-1} . **D'** is a side product of the reaction.

- Draw the structural formulas of compounds **A–E**.
- Provide reaction conditions and reagents needed for step **F**.



Notes: **G** is a reactive neutral intermediate formed during α -elimination reaction. It contains a carbon atom with only six valence electrons. KHMDS is a strong, hindered base.

- Draw structural formulas of the intermediate **G** and compounds **I** and **J**.
- Determine whether the final product is chiral or achiral. If it is chiral, provide the structure of one of its stereoisomers and specify absolute configurations for all stereogenic centers.
- Write the number of possible stereoisomers of **H**.
- Draw the mechanisms for the formation of **G** and transformation **I** $\rightarrow$ **J**.