22nd BChO, 2014, Vilnius, Lithuania

Problem 1 – EQUIL – Silver compounds

Silver forms sparingly soluble salts with chloride, bromide, iodine, and cyanide. Their K_{sp} values are $1.77 \cdot 10^{-10}$, $5.2 \cdot 10^{-13}$, $8.3 \cdot 10^{-17}$, and $5.97 \cdot 10^{-17}$, respectively.

a) Determine the order of precipitation of the anions in an equimolar solution. Assume that precipitation is the only reaction and that cyanide ions do not hydrolyze.

b) To what extent (in percent) have bromide ions precipitated by the time chloride ions start to precipitate?

c) Cyanide ions correspond to a weak acid hydrogen cyanide (pK_a = 9.21) and are, therefore, hydrolyzed to a different extent depending on the pH of the solution. If the pH of the solution is 7.0, what extent of the cyanide ions has been hydrolyzed?

d) Determine the order of precipitation of the chloride, bromide, iodine, and cyanide anions in the equimolar solution (pH = 7.0) while accounting for the hydrolyses of CN^- ions.

e) Is it possible to selectively (left into the solution less than 0.1% of the starting concentration) precipitate iodine so that other ions do not coprecipitate at pH = 7?

In the solutions with high halogen content, ammonia (pK_b = 4.75) is often added to avoid precipitation. In the solution, two possible complexes are formed:

$Ag^+ + NH_3 \rightleftharpoons Ag(NH_3)^+$ $\quad K_f[Ag(NH_3)^+] = 2.1 \cdot 10^3$

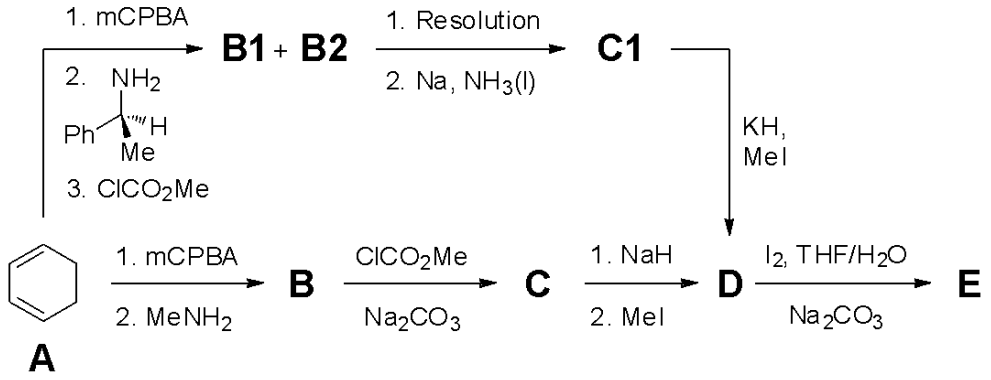
$Ag(NH_3)^+ + NH_3 \rightleftharpoons Ag(NH_3)_2^+$ $\quad K_f[Ag(NH_3)_2^+] = 1.7 \cdot 10^7$

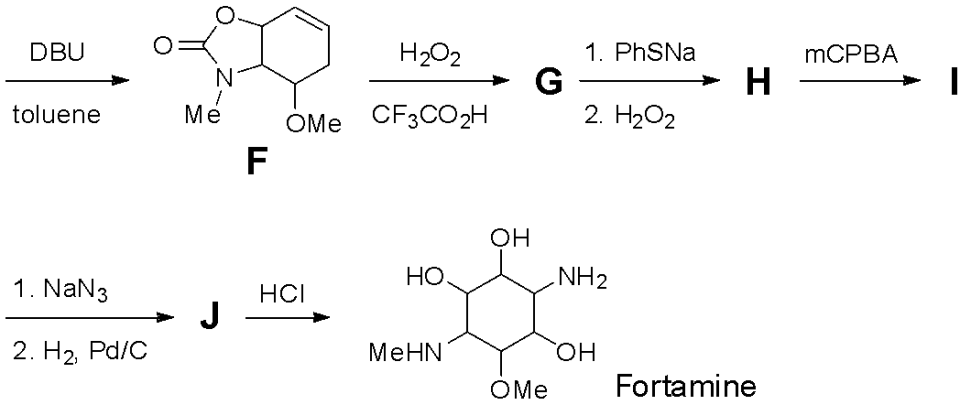
f) Determine how much silver is not bound to the complexes if the solution contains 0.10 M Ag^+, 0.50 M ammonia, and the pH of the solution is 7.0.

g) How much silver can be dissolved in 0.10 M chloride solution that also contains 0.50 M ammonia and the pH is 7.0?

Problem 2 – STEREO, SYNTH – Fortamine

Antibiotic Fortamine has an interesting structure – all of its cyclohexane carbon atoms are chiral. You must deduce the absolute configuration for all of them (besides the other questions). The stereochemical information must be shown unambiguously for all the compounds.





The starting material **A** was treated with *m*-chloroperoxybenzoic acid, followed by methylamine to produce compound **B**. The reaction of **B** with methyl chloroformate and then NaH/MeI yields racemic product **D**. Since Fortamine must be enantiomerically pure, an alternative method to access single enantiomer of **D** was proposed via intermediates **B1** and **B2** (which are diastereomers to each other). During the resolution of **B1** and **B2**, the (*S*,*S*,*S*)-compound was isolated and treated with sodium in liquid ammonia to produce enantiomerically pure **C1**.

a) Draw the structures of compounds **B**, **B1**, **B2**, **C**, and **C1**.

The conversion of **D** to **E** is a modification of a classical reaction, where a carboxylic acid is used instead of an ester. However, both the ester and acid would yield the same product **E**. The latter was treated with a non-nucleophilic base DBU to give an elimination product **F**.

b) Draw the structures of compounds **D** and **E**.

c) Show the mechanism for the reaction **D** → **E**.

Unlike *m*-CPBA and other peroxyacids, CF_3CO_3H is able to coordinate not only with hydrogen-bond donors but also to protect alcohols. In this case, it leads to a stereoselective reaction. Treatment of **G** with PhSNa followed by elimination gives compound **H**, which, after a few subsequent reactions, is transformed into enantiomerically pure Fortamine.

d) Show the structure of the intermediate molecular complex of reaction **F** → **G**.

e) Draw the structural formulas for compounds **G**–**J**.

f) Indicate the configuration of all the chiral carbons of Fortamine using *R*/*S* nomenclature.

Problem 3 – APPLIED, ELECTRO – Redox flow battery

A redox flow battery consists of two electrolyte tanks and two (usually carbon) electrodes, which are separated by a proton exchange membrane. One of the tanks contains an oxidizer aqueous solution and the other reducing agent aqueous solution. If the oxidation-reduction reactions are reversible, the system can be used as a rechargeable battery. Some high energy density flow battery systems are promising candidates as an energy source for an electric car.

In the case of the vanadium redox battery (VRB), both electrolytes contain vanadium redox species, which exist in oxidation states V, IV, III, and II. The cathode electrolyte with 1 M vanadium cation concentration was prepared by dissolving vanadium(V) oxide in 4 M sulfuric acid, yielding a hydrated cation with a molecular mass of 155 g mol^{-1}. The anode electrolyte was prepared by electrochemical reduction of the cathode electrolyte.

During VRB discharging, the cathode electrolyte changes from yellow to green and, finally, blue; the anode electrolyte turns from violet to green.

If ammonium vanadate(V) is reduced with zinc in a sulfuric acid solution, the following color changes can be seen: yellow → green → blue → green → violet.

a) Deduce the reactions taking place during ammonium vanadate(V) reduction with zinc.

b) Identify redox compounds and write **i)** anode, **ii)** cathode, and **iii)** overall reaction during discharging of VRB.

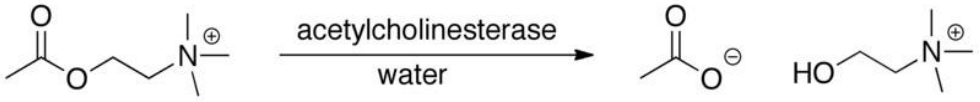
c) **i)** Write a formula for calculating the EMF of the VRB cell as a function of vanadium redox potentials and concentration of cations. **ii)** How much does the voltage of VRB change when pH is one unit lower?

d) The experimental voltage of VRB is 1.4 V. Calculate **i)** Gibbs energy and **ii)** equilibrium constant K.

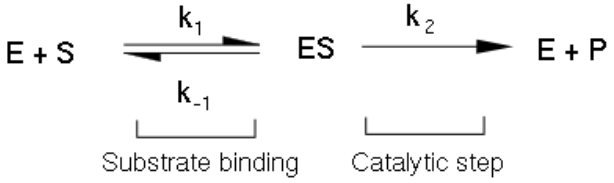
e) Calculate and compare the energy density of VRB with lead-acid battery (40 Wh kg^{-1}). For simplification, the volume of the VRB can be taken equal to the volume of electrolyte solutions with a density of 1.3 g cm^{-3}.

Problem 4 – BIO, KINETICS – Kinetics of neuromuscular enzyme

Acetylcholinesterase is the enzyme in the neuromuscular junction that catalyzes the degradation of acetylcholine – a neurotransmitter released by the parasympathetic nervous system. Inhibitors of this enzyme are used in medicine to treat glaucoma and postural tachycardia syndrome. In this problem, the kinetics of this enzyme is analyzed.



It is known that the first step of this enzymatic reaction is the reversible binding of the acetylcholine (substrate, S) to the acetylcholinesterase (enzyme, E), producing enzyme-substrate complex (ES). The second step is the reaction itself and the release of the products (P) and free enzyme (E), and it is known that this is the rate-determining step.



It is also known that this reaction obeys the Michaelis–Menten kinetics: $v = \frac{v_{max}[S]}{K_M + [S]}$, where v_{max} is the maximum rate of the reaction and K_M is Michaelis constant.

a) By assuming that the enzyme-substrate complex is in a steady state, derive the Michaelis–Menten equation.

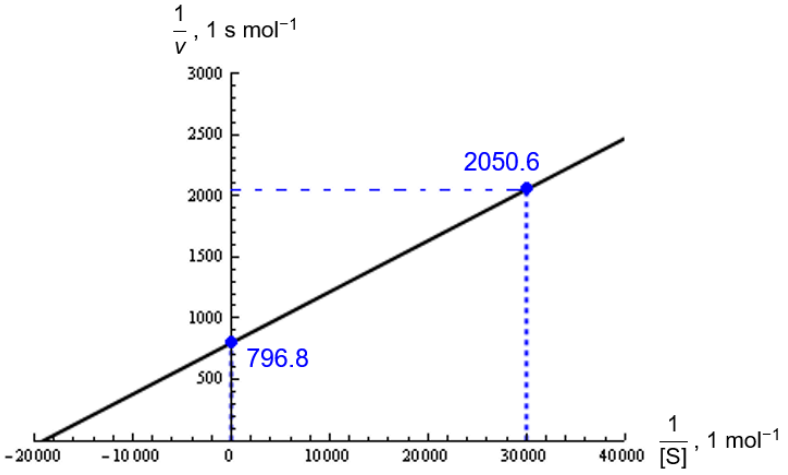
Using the Michaelis–Menten equation, determine reaction rate order with respect to the substrate in two cases: **i)** substrate concentration in solution is huge; **ii)** substrate concentration is very small.

b) Sketch the graph showing reaction rate dependence on the enzyme concentration.

The reaction rate is temperature-dependent.

c) Sketch two graphs showing reaction rate as a function of temperature in classical reaction (case **i**) and in enzymatic reaction (case **ii**).

In the experiment, the rate of this enzymatic reaction was measured at various acetylcholine concentrations. The results are shown as a plot of the inverse of the rate against the inverse of substrate (acetylcholine) concentration. Two data points are marked in the graph.



d) Which method is more suitable for investigating acetylcholine hydrolysis reaction: **i)** gasometry; **ii)** gravimetry; **iii)** conductometry; **iv)** titrimetry?

e) Linearize the Michaelis–Menten equation to obtain an equation consistent with the data presented in the Figure.

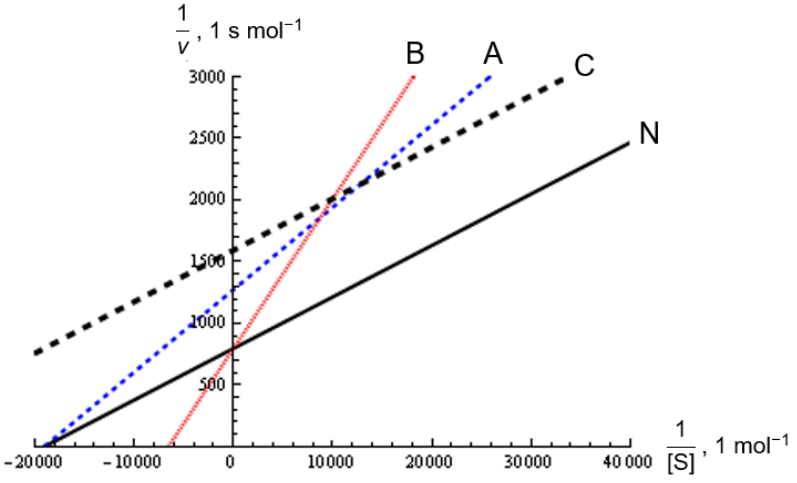
f) Calculate v_{max} and concentration of the substrate at which the reaction rate is half the maximum.

g) Calculate the rate constant k_2., if the total concentration of acetylcholinesterase in the experiment was $2.00 \cdot 10^{-5}$ M.

The activity of acetylcholinesterase was tested in the presence of 3 different inhibitors:

- Physostigmine – competitive inhibitor used in the treatment of glaucoma;
- Caffeine – non-competitive inhibitor, effects of coffee partly originate from this inhibition; Caffeine can bind with both free enzyme and enzyme-substrate complex, rate of both reactions is the same;
- A2435 – uncompetitive inhibitor which binds only to the enzyme-substrate complex.

The effects of these three inhibitors are shown in a plot of the inverse of rate against the inverse of substrate concentration with inhibitors (**A**, **B**, **C**) and without an inhibitor (**N**).



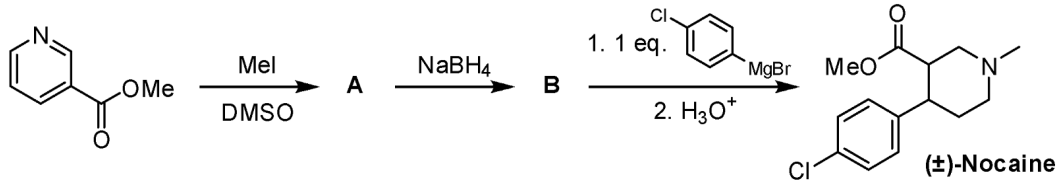
h) Which of the lines **A**, **B,** or **C** correspond to each of the inhibitors mentioned above?

There is another way of linearizing the Michaelis–Menten equation to a different form. In this form, plotting [S]/*v* against **X** gives a straight line.

i) Determine the variable **X**.

Problem 5 – SPECTRA, STEREO – Nocaine

Nocaine effects on CNS are similar to those of cocaine, but due to its less pronounced addictive effect, it has been used in cocaine addiction treatment. Some of its derivatives show enhanced activity, while others have an entirely different mode of action.



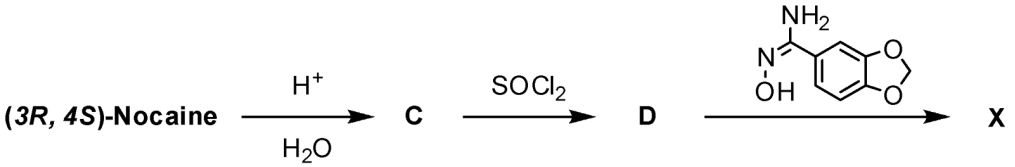
NMR spectra of compound **B**: ^{1}H NMR (500 MHz) δ: 2.37 (2H, dt, J = 6.0, 3.0 Hz), 2.41 (3H, s), 2.50 (2H, t, J = 6.0 Hz), 3.15 (2H, s), 3.74 (3H, s), 7.00 (1H, t, J = 4.0 Hz).

^{13}C NMR (125 MHz) δ: 26.5, 45.6, 50.7, 51.4, 53.2, 128.9, 137.5, 166.9.

a) Draw structures for compounds **A** and **B**.

b) Assign NMR signals to their respective atoms. It will be considered that some of the ^{13}C signals cannot be assigned unambiguously.

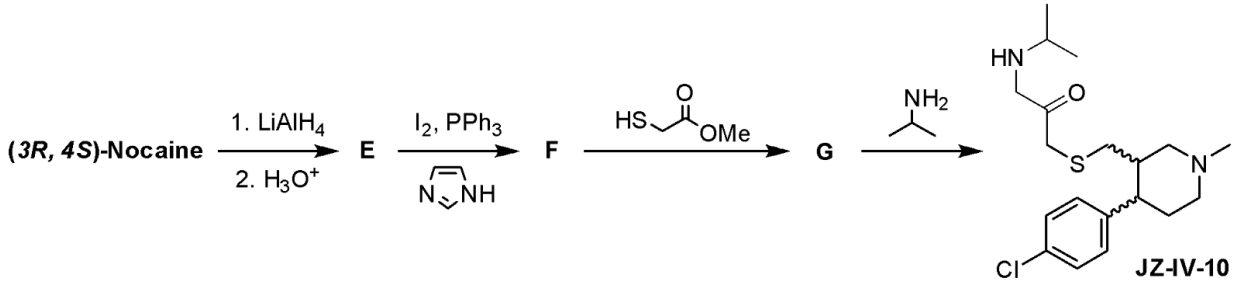
1,2,4-oxadiazoline derivative **X** is both more potent and more resistant to metabolism than nocaine, which means it can be used in lower doses.



c) Draw structural formulas of compounds **C**, **D**, and **X**.

d) Provide a mechanism for the formation of 1,2,4-oxadiazoline ring (**D** → **X**).

Another nocaine derivative, JZ-IV-10, does not display cocaine-like euphoric and stimulant effects; however, it does increase wakefulness and reduces the need for sleep.



e) Draw structures for compounds **E**–**G**.

f) The 3*R*,4*S* stereoisomer of the nocaine derivatives is usually the most active. Draw the JZ-IV-10 structure, indicating the correct absolute configuration.

g) Provide the mechanism for the **E** → **F** transformation. The reaction also produces triphenylphosphine oxide and imidazolium iodide.

h) Which method could theoretically be used to separate (3*R*,4*S*)-nocaine from (3*S*,4*R*)-nocaine?

Problem 6 – ABC, CALC, THERMO – Chemistry of superacids

According to the classical definition, a superacid is an acid with an acidity greater than that of 100% sulfuric acid. According to the modern definition, a superacid is a medium in which the chemical potential of the proton is higher than in pure sulfuric acid.

The simplest class of superacids is the Brønsted superacids. The first acid named accordingly was chlorine-containing **A** because of its ability to protonate aldehydes and ketones. Due to its explosive hazard, its use is partially limited. By adding anhydrous **A** to concentrated nitric acid, salt **B** can be obtained.

a) Draw the chemical formula for **A** and **B** and the Lewis structure formulas for ions in **B**. Draw all resonance structures of the cation in **B**.

A superacid **C** is considered to be the strongest among superacids known so far and is prepared in a simple reaction between a Lewis superacid **D** and Brønsted superacid **E**, both being binary compounds containing a common chemical element. The ratio of the weight fraction of this element in **D** and **E** is 2.1668. It is known that **C** is ionic and consists of two ions, $\mathbf{C}_+$ and $\mathbf{C}_-$.

b) Draw the chemical formulas and Lewis structures of **D** and **E**. What is the geometrical shape of **D**? Write equations of the described reactions.

c) Draw the chemical formula of **C**. Draw the Lewis structures of $\mathbf{C}_+$ and $\mathbf{C}_-$. What is the geometrical shape of these ions?

This extraordinarily strong acid is able to protonate nearly all organic compounds. It has been shown it removes H_2 from isobutane (2-methylpropane) and methane from 2,2-dimethyl-propane. Note that in this way, cation $\mathbf{K}_+$ is obtained.

d) Write the equations of these chemical reactions by showing the carbon atom that will be protonated. What considerations will determine which carbon atom gets protonated?

Recently, a group of scientists from Freiburg, Germany, reported the superacidity of **F**, which is prepared in a simple reaction between a Brønsted acid **G** and a Lewis acid **H**, both containing a common chemical element. It is known that the weight fraction of element **X** (not present in **G**) in **H** is 0.10117, and also that **F** is ionic and its anion can exist in two chemically distinct forms for which molecular weight ratio $\mathbf{F}_{-B} : \mathbf{F}_{-A}$ is 1.7695.

e) Draw the chemical formula of **F**, $\mathbf{F}_{-A}$, $\mathbf{F}_{-B}$, **G**, and **H**. Draw the Lewis structures and predict the geometry of $\mathbf{F}_{-A}$ and **H**. Draw the geometry of $\mathbf{F}_{-B}$.

F can protonate benzene by producing an ionic compound **J** containing anion $\mathbf{F}_{-B}$.

f) Write the chemical structure of **J**. How many signals will there be in the ^1H, ^{13}C and **X** NMR spectra of **J**?

Interestingly, the reaction between the Lewis acid **H** and 2-bromo-2-methylpropane produced an ionic compound **K** with the same anion $\mathbf{F}_{-B}$ and a cation $\mathbf{K}_+$.

g) Write the chemical structure of **K**. How many signals will there be in the ^1H, ^{13}C and **X** NMR spectra of **K**?

It has been shown that thermodynamic characteristics of ionic compounds similar to **K** can be calculated by the use of empiric equations. As input data, experimentally determined compound properties or those obtained from quantum chemical calculations can be used. Equations for calculation of vaporization, solvation (enthalpy for the transition from ions in the gas phase to ions in the liquid state), and lattice enthalpies are given below:

$$\Delta H_{vap} = aV_m^{2/3} + bH_g + c;\ \Delta H_{solv} = -\Delta H_{vap} - \Delta H_{diss};\ \Delta H_{latt} = d\Delta H_{solv} + e$$

a = –224 kJ mol^{-1} nm^{-2}, b = 0.0929, c = 194 kJ mol^{-1}, d = –0.685, and e = 172 kJ mol^{-1}

h) Use the provided equations (consistent with the Born–Haber cycle) to calculate the lattice enthalpy of **K**, if V_m of **K** is 0.4175 nm^3 (determined by single-crystal X-Ray diffraction), H_g = 394.9 kJ mol^{-1}, and ΔH_{diss} = 395.9 kJ mol^{-1} (both found by quantum chemical calculations).

The reaction between 0.100 mol of **H** and 0.100 mol of 2-bromo-2-methylpropane was performed in a calorimeter filled with $2.00 \cdot 10^2$ g of ethanol (specific heat capacity of 2.44 J g^{-1} K^{-1}). By performing the reaction at 0 °C it was found that the temperature of ethanol increased by 5.94 °C, while by performing the same reaction at 20 °C, the temperature of ethanol increased by 2.46 °C (assume the calorimeter constant to be 0 and enthalpy being temperature independent). It was determined that the melting point of **K** is 2 °C.

i) Calculate the reaction enthalpy at 0 °C and at 20 °C. Calculate the enthalpy of fusion of **K**.

j) Use the Born–Haber cycle to calculate the enthalpy of fusion of **K** from the results in question **h)**. Identify the main cause of errors for each of the approaches used to determine the enthalpy of fusion.

The experimental enthalpy of vaporization of 2-bromo-2-methylpropane (+32 kJ mol^{-1}) and the sublimation enthalpy of **H** (+85 kJ mol^{-1}) are tabulated in handbooks of physical chemistry.

k) Use the Born-Haber cycle to calculate the reaction enthalpy for the reaction between **H** and 2-bromo-2-methylpropane in the gas phase (where separated ions $\mathbf{F_{-B}}$ and $\mathbf{K_+}$ in the gaseous state are obtained).