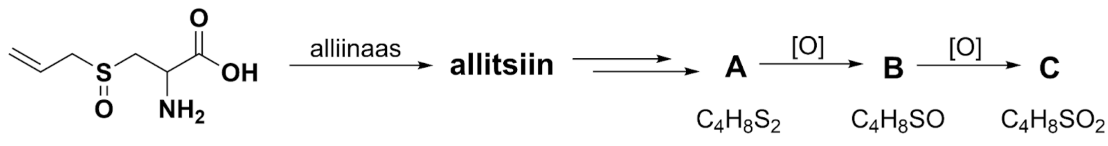
**Problems of the 2023/24 Open Chemistry Competition**
**Senior group (11th and 12th grade)**
**30th september 2023**

## 1. A noxious snack (8 p)

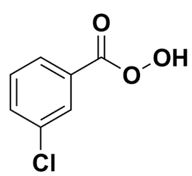
Consumption of garlic-containing food is followed by a rather unpleasant smell that lingers in the mouth for quite a while. This is caused by compounds formed upon degradation of the amino acid alliin that is found in garlic. Firstly, alliin is converted into allicin by the enzyme alliinase released upon intake of garlic. Allicin is subsequently converted into multiple compounds, out of which allylmethyldisulfide (compound **A**) – the main component of the unpleasant garlic smell – persists the longest in the human organism. Compound **A** degrades further, forming, for example, allylmethylsulfoxide (compound **B**) and allylmethylsulfone (compound **C**).




alliin

**a)** Draw the structure of **allicin** and compounds **A**-**C** if allicin contains two sulfur-bound allyl groups ($-CH_2CH=CH_2$) and a S–S bond between sulfur atoms in different oxidation states.
(3)

**b)** Determine the oxidation state of every sulfur atom in compounds **A**, **B** and **C**. (2)

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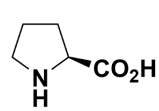


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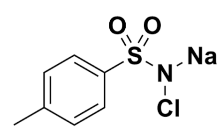


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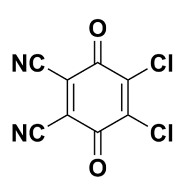


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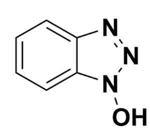



**5**

**c)** Select which of the reagents **1**-**5** could be used to synthesise **B** from **C**. (1)

Decrease of the concentration of compound **A** is described by the equation:

$$[\mathrm{A}] = [\mathrm{A}]_0 e^{-kt}$$

where [A] is the concentration of **A** at time $t$ and $[\mathrm{A}]_0$ is the initial concentration of **A**. The rate constant $k$ can be calculated by $k = \ln(2)/t_{½}$, where $t_{½}$ denotes the half-life.

**d)** Calculate the value of $k$ ($h^{-1}$) if the half-life of compound **A** is $t_{½}$ = 6.1 h. (1)

Garlic odour can be perceived until the concentration of **A** has not decreased below 20 µg $kg^{-1}$ in the body.

**e)** Calculate for how long the smell of garlic will remain in the mouth of an average person with a body mass $m$ = 62 kg, if 10 mg of **A** was formed upon degradation of allicin. (1)

## 2. Dragon chemistry (10 p)

Dragons are frequently encountered in the mythologies of many cultures. In legends of European countries, dragons are often depicted as fire-breathing flying lizard-like creatures. In this task, you will take a closer look at a particularly fascinating dragon species which use nitroglycerin ($C_3H_5N_3O_9$) as fuel for their fire. For this purpose, their organisms synthesise nitroglycerin via the reaction of glycerol (propane-1,2,3-triol) with nitric acid in the presence of sulfuric acid.

**a) i)** Write and balance the equation of nitroglycerin synthesis reaction and **ii)** select which compounds depicted on the scheme can be formed as by-products. (2)

Selected thermodynamic data relevant to dragon chemistry are brought in the table below.

| Reaction | $\Delta H$ (kJ mol$^{-1}$) |
|---|---|
| $0{,}5N_2 + O_2 \rightarrow NO_2$ | +34 |
| $H_2 + 0{,}5O_2 \rightarrow H_2O$ | −242 |
| $3C + 2{,}5H_2 + 1{,}5N_2 + 4{,}5O_2 \rightarrow C_3H_5N_3O_9$ | −145 |
| $C + O_2 \rightarrow CO_2$ | −394 |
| $C_3H_5N_3O_9 + 2{,}75O_2 \rightarrow 3CO_2 + 2{,}5H_2O + 3NO_2$ | $\Delta_c H$ |

**b)** Calculate the enthalpy change $\Delta_c H$ for the nitroglycerin combustion reaction. (3)

As dragons are rather large creatures, they require a lot of energy for their day-to-day activities. Thus, they need to eat a lot. As dragons are environmentally conscious animals, we can assume that they only consume plant material. In a day, an average dragon eats roughly $m$ = 600 kg of plants, which consists of 45% cellulose, of which about 92% is converted into glucose upon ingestion. Digestion of glucose releases $\Delta_r H$ = −2840 kJ mol$^{-1}$ of energy and it can be assumed this proceeds with complete efficiency. A dragon's average caloric need excluding the energy required to breathe fire is $E = 5\cdot10^5$ kcal. To release its fiery inferno, the dragon must overcome an energetic barrier of $E_a$ = 950 kJ mol$^{-1}$ (assume that all of the energy released in the reaction is converted into heat).

**c)** Find the time $t$ which the dragon could possibly spend during the day, spewing fire, if it uses up nitroglycerin at a conservative rate of $r$ = 3 dm$^3$ s$^{-1}$. The density and molar mass of liquid nitroglycerin are $\rho$ = 1.6 g cm$^{-3}$ and $M$ = 227 g mol$^{-1}$, respectively. (2)

Dragons can hold up to $V_1$ = 0.5 m$^3$ of liquid nitroglycerin in their bodies. To initiate the blaze, the dragon ignites nitroglycerin in its special organ and breathes out the combustion products at a temperature of $T_2$ = 500 $^0$C as a roughly conical $d$ = 30 m long jet of flame. Assume the pressure of gases exiting the dragon's jaws instantaneously equalises with the atmospheric pressure $p_0$ = 1 atm.

**d)** Approximate the maximal radius of the fire cone at distance $d$. (3)

## 3. Minerals (11 p)

Elements **X** and **Y** of the same group in the periodic table are in the composition of minerals antlerite and klebelsbergite. The empirical formulas of those minerals are $Cu_3\mathbf{XY}_8H_4$ and $Sb_4\mathbf{XY}_{10}H_2$, respectively. Unit cells of both minerals are rectangular cuboids. The unit cell is the smallest repeating unit of the crystal structure in which the empirical formula is contained χ times, where χ is a positive whole number. Knowing the chemical composition and dimensions of the unit cell, density of the bulk solid can be calculated:

$$\rho = \frac{\chi M}{N_A V},$$

where $M$ corresponds to the molar mass of the empirical formula, $N_A$ = 6.02·10$^{23}$ mol$^{-1}$ and $V$ is the unit cell volume. Crystallographic data regarding antlerite and klebelsbergite can be found in the table below.

| Mineral | Empirical formula | $\rho$ (g cm$^{-3}$) | χ | $\alpha$ (Å) | $\beta$ (Å) | $\gamma$ (Å) |
|---|---|---|---|---|---|---|
| Antlerite (**A**) | $Cu_3\mathbf{XY}_8H_4$ | 3.950 | 4 | 8.24 | 11.99 | 6.04 |
| Klebelsbergite (**B**) | $Sb_4\mathbf{XY}_{10}H_2$ | 4.664 | 4 | 11.28 | 14.91 | 5.77 |

**a)** Determine the elements **X** and **Y** by calculations. 1 Å = 10$^{-10}$ m. (4)

**b)** Determine the formulas of antlerite and klebelsbergite if **A** only contains $Cu^{2+}$ cations and **B** only contains $Sb^{3+}$ cations. (1)

Naturally occurring minerals are seldom perfect, i.e., other metal cations, also in different oxidation states, may be incorporated. Let us assume a fraction of $Cu^{2+}$ cations have been substituted by $M^{3+}$ cations in the antlerite lattice. The empirical formula of such antlerite can be expressed with the formula $(Cu^{2+})_a(M^{3+})_b\mathbf{XY}_8H_4$, where $a$ and $b$ are appropriate coefficients.

A chemical analysis was carried out to determine the precise chemical composition of an antlerite sample. The ground rock sample was dissolved in dilute sulfuric acid, transferred quantitatively into a 250,00 mL volumetric flask and filled with a buffer solution to the mark.

Titration I: A sample of $V_{\text{sample, I}}$ = 10,00 mL was taken from the volumetric flask, transferred into a conical flask and a few drops of an indicator solution were added. The resulting solution was titrated with a $c_{\text{EDTA}}$ = 0.0100 M solution of ethylenediaminetetraacetic acid (EDTA). The titration was repeated three times and on average, a volume of $V_{\text{EDTA, I}}$ = 14.56 mL EDTA solution was needed.

Titration II: A sample of $V_{\text{sample, II}}$ = 30.00 mL was taken from the volumetric flask, transferred into a conical flask and a solution of thioglycerol ($HSCH_2CH(OH)CH_2OH$) was added followed by a few drops of an indicator solution. The resulting solution was titrated with the EDTA solution. The titration was repeated three times and on average, a volume of $V_{\text{EDTA, II}}$ = 2.89 mL EDTA solution was needed.

**c)** Write a balanced reaction equation that describes the dissolution of antlerite with the formula $Cu_3\mathbf{XY}_8H_4$ in sulfuric acid. (1)

**d)** **i)** In which ratio does EDTA react with $Cu^{2+}$ and $M^{3+}$ cations? (0.5)

- ☐ 2:1
- ☐ 1:1
- ☐ 1:2
- ☐ in a different ratio depending on the charge of the cation

**ii)** why is thioglycerol added to the solution in the second titration? (0.5)

☐ for masking $Cu^{2+}$ to determine only the content of $M^{3+}$ in solution
☐ for masking $M^{3+}$ to determine only the content of $Cu^{2+}$ in solution
☐ for masking both $Cu^{2+}$ and $M^{3+}$ in the solution

**e)** **i)** The content of which ion(s) is determined in the first titration? (0.5)

☐ Both metal cations
☐ $Cu^{2+}$
☐ $M^{3+}$
☐ $H^+$

**ii)** The content of which ion(s) is/are determined in the second titration? (0.5)

☐ Both metal cations
☐ $Cu^{2+}$
☐ $M^{3+}$
☐ $H^+$

**f)** Determine the coefficients *a* and *b* for the analysed antlerite sample. (3)

**4. Methanol cycle (10 p)**

Robert noticed that during nighttime, the cost of electricity usually dropped significantly, and he sought a way to take advantage of it. He decided to store electrical energy in the form of methanol via electrolysis of carbon dioxide.

**a)** Choose the correct anode and cathode half-reactions and the correct balanced net equation, which describe the production of methanol from carbon dioxide in an acidic medium. Note that one mole of methanol is produced per mole of $CO_2$, and $O_2$ is formed at the anode. (3)

The Gibbs free energy change can be calculated using the formula:

$$\Delta G = -nFE,$$

where $n$ denotes the number of electrons partaking in the (half)-reaction, $E$ denotes the corresponding (half)-reaction potential and $F$ = 96485 C mol$^{-1}$. Reminder: 1 volt corresponds to the potential for which the electric field performs 1 joule worth of work on moving one coulomb of charge.

**b)** Calculate the standard potential of the electrolysis cell ($E^0_{cell}$) and the Gibbs free energy change for the net reaction if the anode and cathode standard potentials for reducing one mole of $CO_2$ are $E^0_{anode}$ = 1.23 V and $E^0_{cathode}$ = 0.05 V, respectively. (2)

Robert went for a hike and utilised his methanol to charge his phone. For this purpose, he constructed a fuel cell using a Pt-catalyst and a proton-permeable membrane.

**c)** Using the Gibbs free energy of methanol production, calculate the free energy change $\Delta G_{methanol}$ in units kJ g$^{-1}$. (1)

**d)** Calculate the volume (in mL) of fuel (80% solution of methanol in water) needed to fully charge a $q_{battery}$ = 5000 mA·h battery at a voltage of $U$ = 4.00 V. Density of an 80% solution of methanol is $\rho$ = 0.847 g cm$^{-3}$. Assume all of the methanol was oxidised into carbon dioxide, but only 40% of the energy stored in the form of methanol was converted into electrical energy. (2)

In addition to the desired four-electron oxygen reduction reaction (four electrons are consumed per molecule of oxygen), a two-electron reduction reaction may also proceed in Robert's fuel cell, yielding hydrogen peroxide by the equation:

$$O_2 + 2\ H^+ + 2e^- \rightleftharpoons H_2O_2\ (E^0_1 = ?).$$

Hydrogen peroxide can then be further reduced into water by the equation:

$$H_2O_2 + 2\ H^+ + 2e^- \rightleftharpoons 2\ H_2O\ (E^0_2 = 1.78\ V).$$

**e)** Choose the correct conversion of the six-electron reduction reaction determined in question **a)** into a four-electron reduction reaction. (1)

**f)** Using the standard potential of hydrogen peroxide reduction ($E^0_2$), the standard potential of the electrolyser's anode reaction ($E^0_{anood}$) and the equation for Gibbs free energy as a function of potential, calculate the standard reduction potential of the two-electron oxygen reduction reaction ($E^0_1$). Assume that the four-electron oxygen reduction reaction potential is the same for six-electron and four-electron reduction reactions. Reminder: 1 ampere is equal to a charge of 1 coulomb moving past a point in 1 second. (2)

## 5. A compound from Hell (9 p)

Gas **A** is an extremely strong oxidant capable of igniting even asbestos and water. Gas **A** is used in the semiconductor industry and in nuclear reprocessing. Although **A** was considered for use as rocket fuel oxidant, in flamethrowers and organic synthesis in the mid-20th century, those endeavours were eventually dismissed due to unreasonably high hazards posed by the gas. For instance, when **A** was being investigated for its potential use in propellants, some of the compound leaked onto the concrete surface below, which resulted in a more than a metre-deep hole being burned in the concrete and a layer of gravel below it. The binary compound **A** is composed of elements **X** and **Y** (mass percent of **X** in **A** is $w_X$(**A**) = 61.65%) and its vapours are 3.19 times as dense as air. The average molecular weight of air is 29.0 g mol$^{-1}$.

**a)** Determine the chemical formula of compound **A**. (2)

Compound **A** reacts with water to give two binary acids and one elementary substance. Upon the reaction of **A** and silicon dioxide, two elementary substances and compound **B** ($w_X$(**B**) = 73.01%) are formed, whereas upon reacting with silicon, a single elementary substance and compound **B** are formed.

**b)** Write balanced reaction equations for **i)** **A** + $H_2O$ → …, **ii)** **A** + $SiO_2$ → …, **iii)** **A** + Si → … (1,5)

Gas **A** is used in the semiconductor industry to etch surfaces and for plasma-free cleaning at low temperatures. The etching rate of silicon ($v_{etching}$, mol m$^{-2}$ s$^{-1}$) depends on the concentration of **A** ($C_A$, mol m$^{-3}$):

$$v_{etching} = k\cdot(C_{\mathbf{A}})^n,$$

where $k$ is the rate constant and $n$ is the reaction order. The etching rate of Si was investigated at different concentrations of **A** in a mixture with an inert gas. The following results were obtained:

| | | | | |
|---|---|---|---|---|
| Etching rate (µm min$^{-1}$) | 1.5 | 5.2 | 12.3 | 23.8 |
| Volume percent of **A** in gas (%) | 1 | 5 | 11 | 20 |

**c)** **i)** Determine the reaction order (exponent $n$), which fits the data the best (assume $n$ is a positive whole number.)

**ii)** Under certain conditions the etching rate was $v_{etching} = 6.5 \cdot 10^{-2}$ mol m$^{-2}$ s$^{-1}$. Calculate the etching rate in units μm min$^{-1}$, if the density of silicon is $\rho_{Si} = 2.33$ g cm$^{-3}$. (2)

Liquid compound **A** is usually stored in steel containers.

**d)** Why is it possible to store **A** in steel containers?

- ☐ In liquid form, the reactivity of **A** is much smaller than in its gaseous form.
- ☐ The steel surface is covered with a thin oxide layer which makes it very stable.
- ☐ The surface of steel is passivated by the formation of a thin layer inhibiting further oxidation as a result of coming into contact with **A**. (0,5)

Compound **A** reacts with strong Lewis acids **C** ($w_X$(**C**) = 43.82%) and **D** ($w_X$(**D**) = 55.91%), forming unusual compounds which contain the cation **E**$^+$ ($M$(**E**$^+$) = 73.45 g mol$^{-1}$).

**e)** Write the formulae of **C**, **D** and the cation **E**$^+$. (3)

## 6. Gold nanoparticles (10 p)

Nanoparticles are particles of solid-state material with dimensions 1-100 nm. Gold nanoparticles, for instance, are widely used in various fields due to their special properties: in catalysis, optics, electronics and even medicine. They are often synthesised via the so-called bottom-up method, in which atomic gold is initially dispersed in solution. Nanoparticle formation is triggered by nucleation, in which gold atoms spontaneously aggregate due to attractive forces. After nucleation, gradual nanoparticle growth proceeds. To create the atomic dispersion, metallic gold must first be dissolved. For this purpose, an especially strong mixture of acids is used: aqua regia, a 1:3 mixture of concentrated nitric and hydrochloric acids. Dissolution of gold in aqua regia follows the balanced equation:

$$Au(t) + 3HNO_3 + 4HCl \rightarrow \mathbf{X} + 3\mathbf{Y}\uparrow + 2H_2O$$

The gold-containing compound **X** is then added into a boiling solution of sodium citrate, in which the following reactions occur:

$$\mathbf{X} + C_6H_8O_7Na \rightarrow \mathbf{Z} + 2HCl + CO_2\uparrow + C_5H_6O_5$$

$$3\mathbf{Z} \rightarrow 2Au(atomic) + \mathbf{X} + 2HCl$$

Weight percentages of gold in chlorine-containing compounds **X** and **Z** are $w_{Au}$(**X**) = 57.97% and $w_{Au}$(**Z**) = 73.53%, respectively. Molar mass of gas **Y** is 46.01 g mol$^{-1}$.

**a)** Determine the formulae of **X**, **Y** and **Z**. (3)

A nucleation event can be considered successful only if the radius of the formed nanoparticle is greater than the critical radius $r_{crit}$. Otherwise, the nanoparticle will not be stable enough.

The free energy of a spherical nanoparticle has two components: internal free energy and the surface free energy. The former results from interactions between atoms of the bulk nanoparticle material. Internal free energy per unit volume is $-\Delta G^*$ (J m$^{-3}$). The surface free energy derives from the fact that surface atoms interact with less atoms than the bulk atoms. Surface free energy per unit area is denoted as $\gamma$ (J m$^{-2}$). The critical radius $r_{crit}$ is given by the equation:

$$r_{crit} = 2\gamma/\Delta G^*$$

The surface free energy for gold nanoparticles coated in citrate anions is $\gamma$ = 0,100 J m$^{-2}$.

**b)** Write the equation for calculating free energy of a spherical nanoparticle at the critical radius ($\Delta G_{crit}$) via $r_{crit}$ and $\gamma$ and find its value if $r_{crit}$ = 1,00 nm. *Hint: volume and surface area of a sphere are given by* $V_{sphere} = \frac{4}{3}\pi r^3$ *and* $S_{sphere} = 4\pi r^2$*, respectively.* (2)

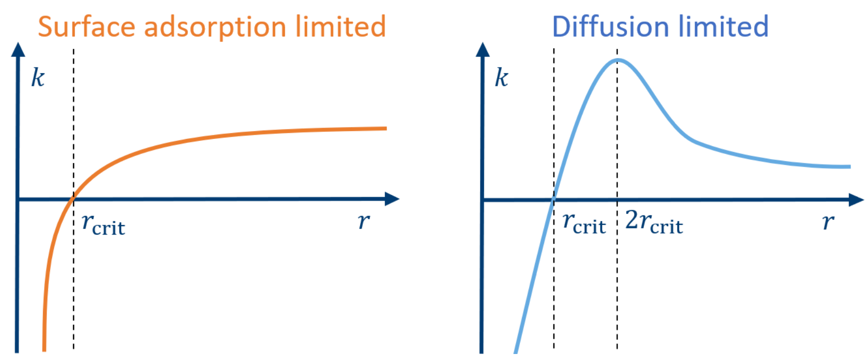
Nucleation rate is strongly concentration-dependent. When the concentration of gold atoms exceeds a certain threshold, nucleation proceeds seemingly instantaneously throughout the solution. Nucleation rate is linearly dependent on the Arrhenius factor $e^{-\Delta G_{piir}/k_B T}$. The critical radius can also be expressed as:

$$r_{crit} = 2\gamma v \, / \, [k_B T \ln (C \, / \, C_{sol})],$$

where $v$ is the volume of a single gold atom (17.0 Å$^3$), $T$ denotes temperature, $C$ is the concentration of atoms in solution and $C_{sol}$ is the solubility of atoms. 1 Å = $10^{-10}$ m.

**c)** Calculate the ratio of nucleation rates between the cases of $C = 2C_{sol}$ and $C = 3C_{sol}$ at room temperature ($T = 298$ K). (3)

After nucleation, formed nanoparticles start gradual growth. Rate of growth is dependent on how rapidly new atoms adsorb to the surface and how fast new atoms can diffuse to the surface. Usually one of those processes is significantly slower than the other and is the rate-limiting step of nanoparticle growth. The figures below depict the dependence of growth rate ($k$) on nanoparticle radius in the surface adsorption-limited and diffusion-limited cases.



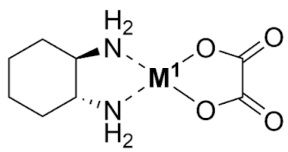

Nanoparticles with a wide range of radii are inevitably formed during the growth process. One of the key descriptors of a nanoparticle mixture is polydispersity, which describes how much the particle size in the mixture varies.

**d)** Choose the correct answers for a nanoparticle mixture, where the initial distribution of particle radii is symmetrical, with the average radius being $r_{avg}$. Assume that no new nucleation occurs. (2)

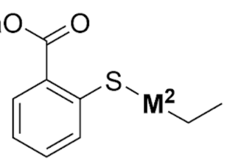
- ☐ Polydispersity decreases in the adsorption-limited case if $r_{avg} >> r_{crit}$.
- ☐ Polydispersity decreases in the diffusion-limited case if $r_{avg} >> 2r_{crit}$.
- ☐ If $r_{avg} = 2r_{crit}$ in the diffusion-limited case, polydispersity will not change after a long period of time.
- ☐ If $r_{avg} = r_{crit}$, the number of nanoparticles in solution will have decreased by half after a long period of time.

## 7. Unusual medicines (12 p)

Metals vital for a healthy life (Na, K, Ca, Mg, Fe, Zn and many others) can be obtained from balanced and varied meals or supplements, if necessary, yet we do not encounter most elements of the periodic table in remarkable quantities in our diets. Although most biologically less important elements and their compounds are in general harmful or downright poisonous to living organisms, a number of counterexamples can be brought to showcase how these elements can actually be quite useful for the human body. In this task, you will take a closer look at six medicines and their active ingredients, which contain quite unusual elements to be found in drug molecules.



**1**



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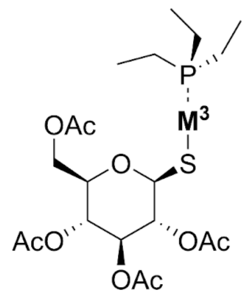

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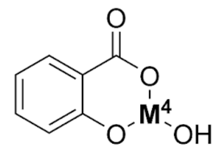

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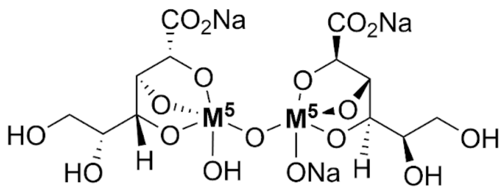

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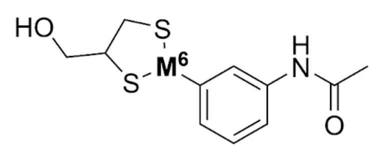


**6**

Active pharmaceutical ingredients (APIs) **1**–**6** contain elements $\mathbf{M^1}$–$\mathbf{M^6}$, which <u>in a random order</u> are: Sb, Bi, Hg, As, Au and Pt. The medication *Pepto-Bismol* is used to treat *heartburn*. The element which was used in chemical weapons in World War I, is found in the medication used to treat *endemic syphilis*. The oxalate complex of the element used in catalytic hydrogenation is the API in an *anticancer* drug. The API of an *antiseptic* and the drug *Pentostam* are sodium salts. The thioglycose derivative is the API of *Auranofin*. One of the heavy metal-containing drugs is used to treat *rheumatoid arthritis*. The API of *Arsthinol* contains a benzene ring. *Thiomersal* contains mercury. Only one of the salicylic acid derivatives contains a heavy metal. The antimony-containing drug is used to treat *parasitic diseases*. Element $\mathbf{M^5}$ has a higher atomic mass than $\mathbf{M^6}$, but smaller than the atomic mass of $\mathbf{M^4}$.

**a)** Determine the oxidation states of $\mathbf{M^1}$–$\mathbf{M^6}$ in compounds **1**–**6**. (3)

**b)** Fill in the table. Determine elements $\mathbf{M^1}$–$\mathbf{M^6}$ and match them with the appropriate medicinal use and commercial name of the drug. (9)

| API | Element **M** | Medicinal use | Commercial name |
|---|---|---|---|
| **1** | | | |
| **2** | | | |
| **3** | | | |
| **4** | | | |

| API | Element **M** | Medicinal use | Commercial name |
|---|---|---|---|
| **1** | | | |
| **5** | | | |
| **6** | | | |

## 8. Fluorescing bacteria (11)

Scientist Bac Illus wanted to explore a communication system within a population of *Geobacillus kaustophilus* bacteria. It usually flourishes in environments with extreme living conditions, for example, in the Mariana trench, and has subsequently developed a sophisticated signalisation system based on the population-wide diffusion of signalling molecules.

*Geobacillus* cells are producing proteins (Syn) by default that synthesise signalling molecules (Sig). These diffuse freely within and outside of the cells. At the same time, the cells are creating receptor proteins (Rec) that are continuously binding to Sig molecules. Once the bacterial population has grown dense enough, the concentration of Sig molecules between the cells reaches a certain threshold and Rec-Sig complexes associate with the bacterial genome, thus regulating gene expression and population behaviour.

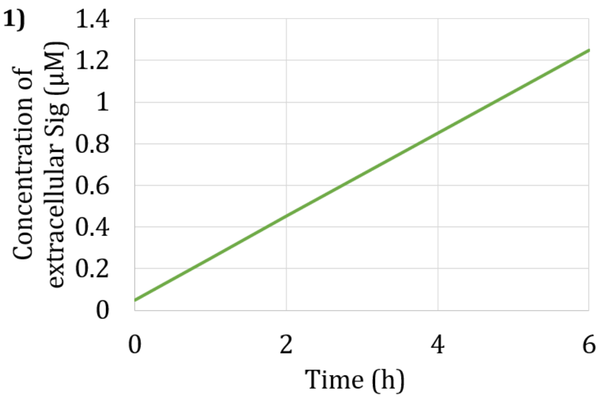
**The basics of the diffusion system**

Bac mutated natural *Geobacillus* in a way that Rec-Sig complexes would activate the production of a fluorescing pigment and started to grow it in a 50 mL culture. The *Geobacillus* culture grows at a rate $N_t = N_0 2^{kt}$, where $N_t$ is the number of cells in the culture after time $t$, $N_0$ is the number of cells at $t_0 = 0$ min and $k$ is the population growth constant ($k = 3\ \text{h}^{-1}$).

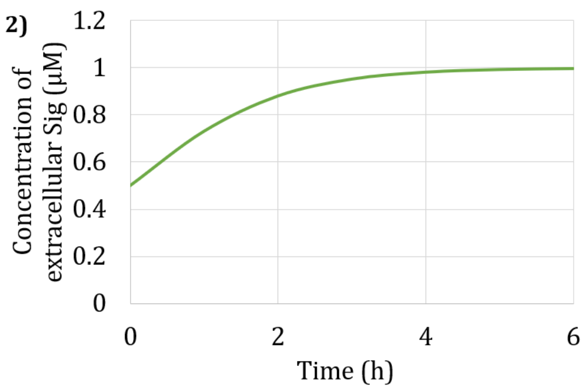
**a)** **i)** Calculate the density of Bac's culture after $t$ = 25 min, knowing that the volume of the culture is constant and the start concentration of cells is $N_0 = 1.5 \cdot 10^4$. (1)

**ii)** Choose the graph that best demonstrates the diffusion of Sig molecules into the extracellular space during culture growth. (1)

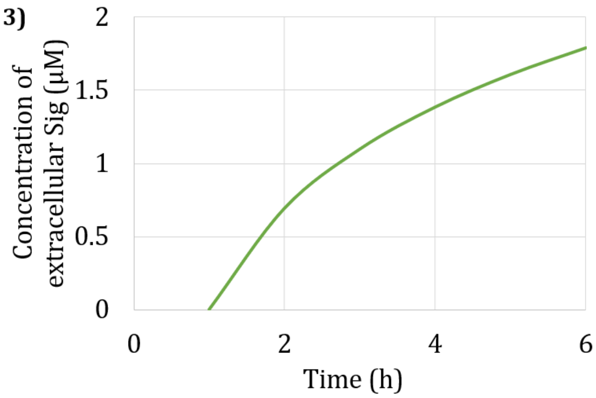
**1)**




**2)**

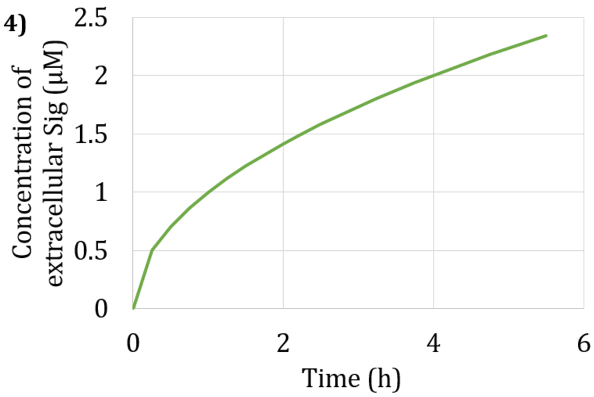


**3)**



Concentration of extracellular Sig (μM)
2
1.5
1
0.5
0
0
2
4
6
Time (h)


**4)**

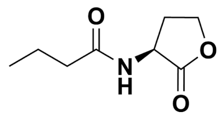


Concentration of extracellular Sig (μM)
2.5
2
1.5
1
0.5
0
0
2
4
6
Time (h)

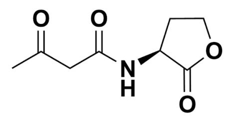
**Signalling molecules as messengers**

Natural signalling molecules produced by *Geobacillus* is *N*-butanoyl-homoserine lactone (C4-HSL) but the general spectrum of signalling molecules in the bacterial kingdom is wide, varying in structure and properties. Bac cleverly designed four variants of the *Geobacillus* protein Syn so that each one would produce a different Sig* molecule (see below).

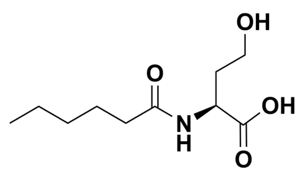
**b)** Taking into account that new Rec-Sig* complexes do not affect expression of the fluorescing pigment, place the following Sig/Sig* molecules in descending order, starting from the one which causes the fastest change of the colour of the culture. Consider that the diffusion rate of Sig molecules is affected by its structure. (2)



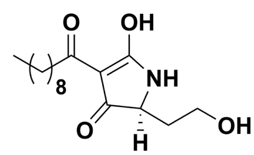
C4-HSL



3-oxo-C4-HSL



C6-HSL

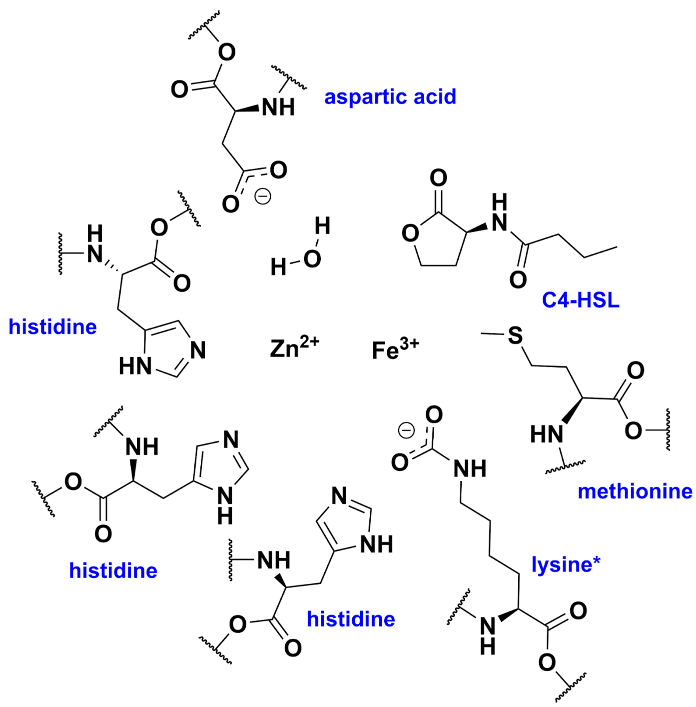


tetramic acid

**Lactonase as a communication inhibitor**

So that the balance within a population existed and bacterial cells would not intoxicate themselves, *Geobacillus* has developed multiple pathways for subsequent degradation of Sig molecules. One of such is carried out by lactonase, an enzyme catalysing the hydrolysis of a Sig molecule. Below is a scheme of lactonase reaction pocket that C4-HSL associates with.

**c)** Decide which role has each of the molecules and ions shown below inside the pocket. (3)




Options for roles: substrate or reactant, nucleophile, polarises the signalling molecule, stabilises metal ions (2x), creates hydrophobic environment, temporal acceptor of protons

| Molecule/Ion | Role |
|---|---|
| C4-HSL | |
| Aspartic acid | |
| $H_2O$ | |
| histidine (x3) | |
| methionine | |
| $Zn^{2+}$ and $Fe^{3+}$ | |
| lysine* | |

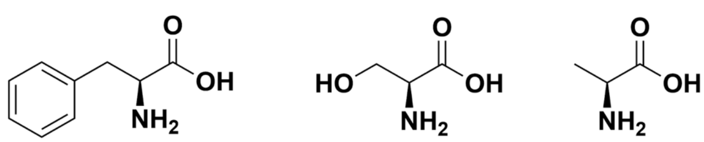
**Mutated lactonase**

As Bac was excited to see green *Geobacillus* cultures, he started with a next gene engineering experiment. So, he mutated the lactonase reaction pocket, replacing aspartic acid and methionine with other amino acids with an aim to change the catalytic rate of lactonase which is expressed as $k_{Sig}$. Unfortunately, as he was engagingly stargazing the last night and felt tired the next day, the kinetic data of mutated lactonases got mixed up. Below are listed a table with the generated mutations, structural formulae of relevant amino acids and kinetic data collected from the experiment.

**d) i)** Help out our stargazer and associate the mutations with right kinetic data and justify your choices. (3)

| Natural amino acid | Mutation |
|---|---|
| Aspartic acid | Alanine |
| Methionine | Serine |
| Methionine | Phenylalanine |

| Mutation number | $k_{Sig}$ ($s^{-1}$) |
|---|---|
| Natural | $10^5$ |
| 1 | $10^{-6}$ |
| 2 | $10^7$ |
| 3 | $10^2$ |




Justification options: creates a more hydrophobic environment, creates a more hydrophilic environment, stronger nucleophile, weaker nucleophile, stronger hydrolyser, weaker hydrolyser

| Mutation | Natural → mutated amino acid | Justification |
|---|---|---|
| **1** | __ → __ | |
| **2** | __ → __ | |
| **3** | __ → __ | |

**ii)** Choose which mutation would cause a slower change in colour inside the bacterial culture if compared to the natural lactonase reaction pocket.

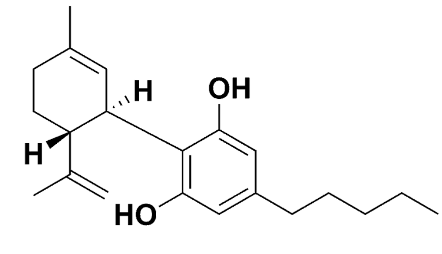
☐ 1

- ☐ 2
- ☐ 3

(1)

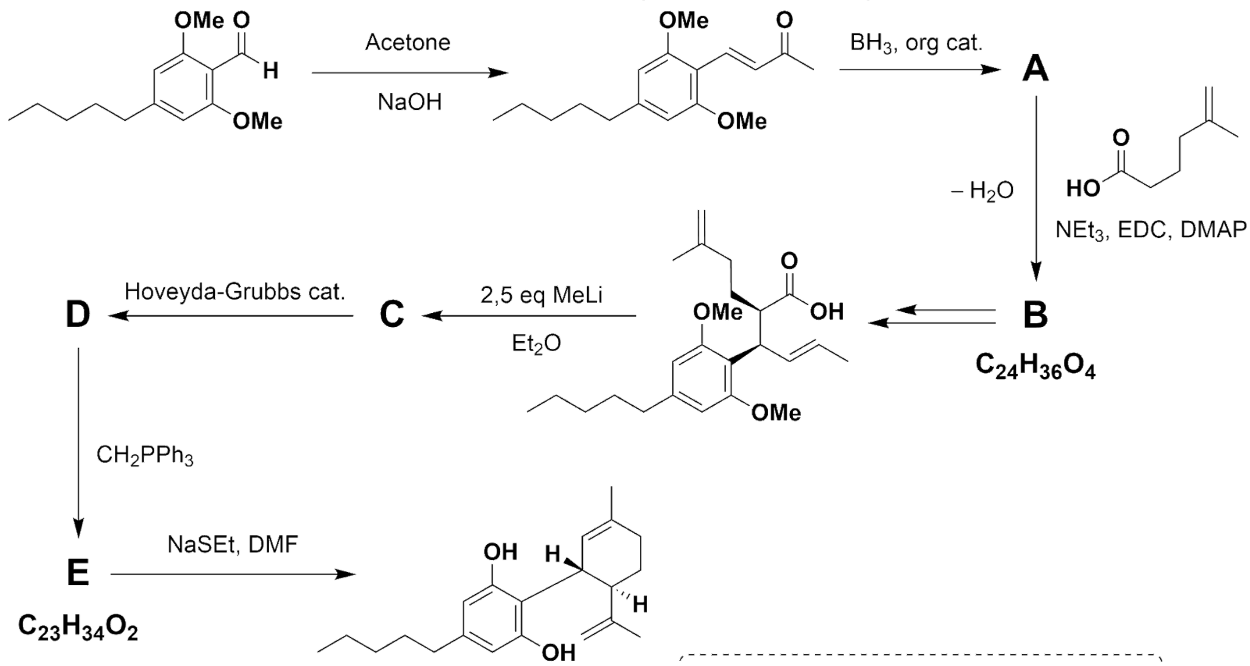
## 9. A chill synthesis (9 p)

Cannabis plants contain a plethora of interesting organic compounds, the most well-known of which are cannabinoids. Among these are Δ[9]-tetrahydrocannabinol (**THC**), which has a psychoactive effect on humans, and the non-psychoactive cannabidiol (**CBD**, see figure). Both **THC** and **CBD** are medicinally used as sedatives and analgesics. Some **CBD**-containing compounds are also used to alleviate epilepsy or depression. Furthermore, the **THC**-containing drug Dronabinol is used to alleviate side-effects of chemotherapy, such as nausea.

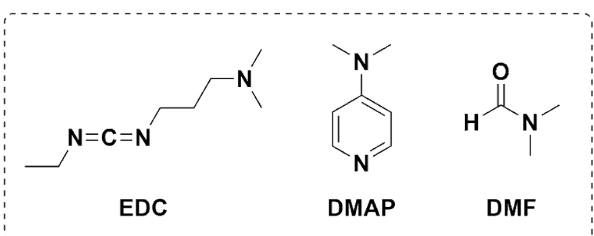


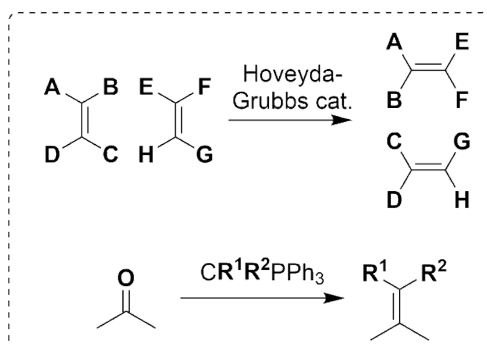

**CBD**

**a)** Select which functional groups are present in the **CBD** molecule: alkyne, benzene ring, epoxide, alkene, ester, ether, lactone, hydroxyl group, carboxyl group, amine, amide. (1,5)




**CBD**




**b)** What is the name of the first reaction in the sequence, in which acetone and sodium hydroxide are employed?

- ☐ Aldol condensation
- ☐ Diels-Alder reaction
- ☐ Friedel-Crafts alkylation
- ☐ Swern oxidation

☐ Ozonolysis (0,5)

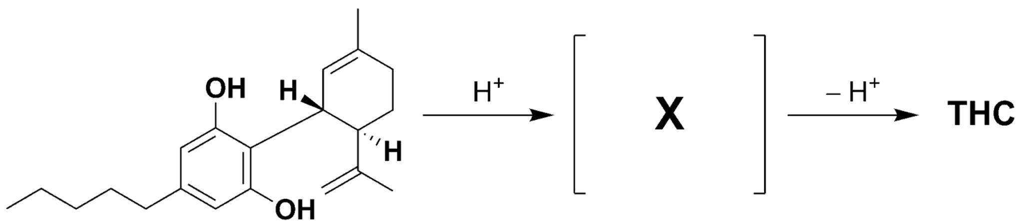
**c)** Why $NaBH_4$ or $LiAlH_4$ cannot be used to obtain compound **A**?

☐ $NaBH_4$ and $LiAlH_4$ are too weak as reducing agents for this purpose: they are incapable of reducing a ketone.

☐ $NaBH_4$ and $LiAlH_4$ are too strong as reducing agents for this purpose: unwanted by-products would be formed. (0,5)

**d)** Draw the structures of compounds **A-E**. *Hint: in the last step of the sequence, protecting groups are removed.* (5)

In an acidic medium, for instance in stomach acid, **CBD** cyclises into **THC**, however the major product is the non-psychoactive $\Delta^8$ isomer. The same transformation occurs during pyrolysis of **CBD**-containing tobacco, where roughly a quarter of **CBD** is converted into a mixture of $\Delta^8$- and $\Delta^9$-isomers of **THC**.




**CBD**

**e)** Draw the structures of intermediate **X** and **THC**. Assume only the $\Delta^9$-isomer is formed. (1,5)