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# Q1-1

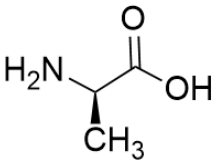
English (Official)

## Peptide Synthesis in the Lab (11.5 pts, 8%)

The way nature and a lab chemist approach a synthesis is very different: nature is likely to have specific enzymes for the very specific synthesis it wants to carry out, while the humble chemist is typically forced to work with an array of glasswares, reagents and other gizmos, only to then produce a few grams of the desired product (we're being optimistic).

Peptides are polymers formed by amino acids, so called due to the presence of an amino group and a carboxylic acid.

Most amino acids we know of are chiral, and nature seems to have picked a favourite enantiomeric configuration: the L configuration. Although nowadays we're used to absolute configuration labels such as *R* and *S*, some compounds are still commonly referred to using their L or D label, like amino acids and carbohydrates. Most L-amino acids would be labelled as *S* using Cahn-Ingold-Prelog rules, with one exception being L-cysteine.




**A**

**1.1** **Determine** the absolute configuration of the amino acid **A** and **label** it as either *R* or *S*. 0.5 pt

**SOLUTION:**

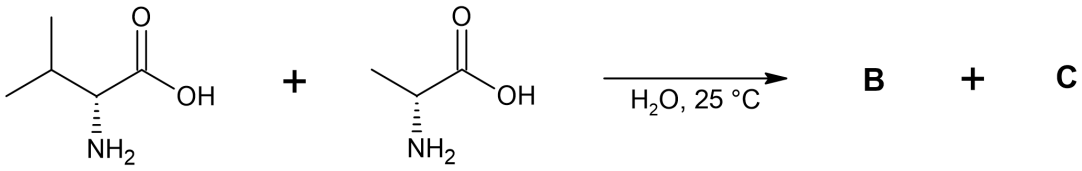
*R*

0.5 pts for configuration.

0.5 pts total.

In the lab, things immediately become trickier when we try coupling two amino acids. Jotting it down on a piece of paper it may seem like the amine group would readily add to the carboxylic acid via addition, as other good nucleophiles could, but this doesn't happen. In fact, an unwanted reaction occurs instead, yielding no desired peptide product.

When solutions of two different amino acids are mixed together, no coupling occurs. Instead, the two amino acids will be found in forms **B** and **C** in the solution.

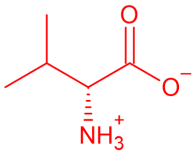



**1.2** **Draw** the structures of forms **B** and **C**. 1.0 pt
**Hint**: **Think** about other properties than nucleophilicity/electrophilicity.

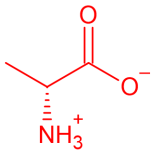
**B**:

**C**:

**SOLUTION:**
**B**:

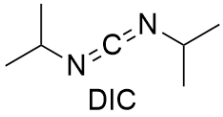



**C**:



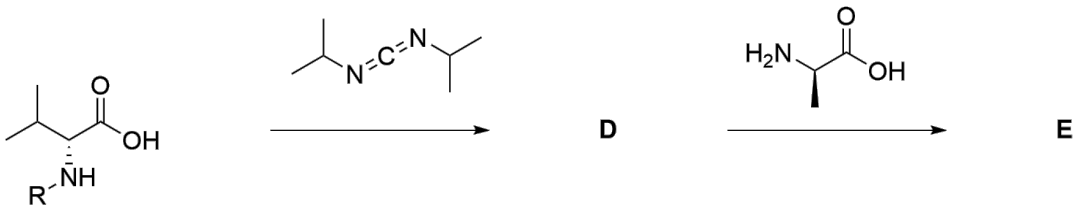

0.5 pts for each correct zwitterionic form.
1.0 pts total.

It is for this reason that coupling reagent are used in peptide synthesis; without them, the amino acids would typically not couple in a desirable manner.



DIC

A commonly used coupling reagent is diisopropylcarbodiimide (DIC). The coupling takes place via an *O*-acylisourea intermediate.

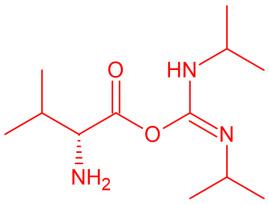



**1.3** **Draw** the structure of the intermediate **D** and of the final coupling product **E**. 3.0 pt
**Hint**: diisopropylurea is produced as a byproduct alongside **E**.

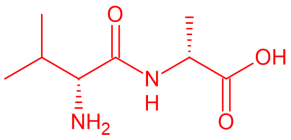
**D**:

**E**:

**SOLUTION:**
**D**:



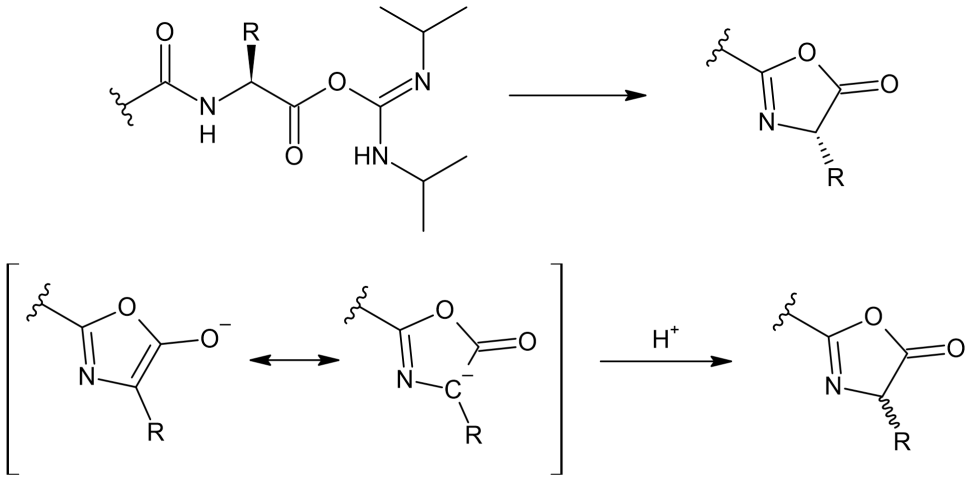

**E**:




The amine keeps the R and should be NHR for product and intermediate.
2.0 pts for correct product.
1.0 pts for correct intermediate.
3.0 pts total.

Running the coupling reactions with only a coupling reagent poses a risk of racemization, which can be circumvented by using an additives. Racemization can be detrimental to a peptide's biological activity, as most physiological processes are highly specific to one stereoisomer.

The main culprit is a cyclic and planar oxazolone intermediate. This intermediate is produced via a reaction between the carbonyl oxygen of the penultimate amino acid and the carbonyl carbon of the last amino acid (see figure below).




| | | |
|---|---|---|
| **1.4** | **State** two reasons why the oxazolone precursor is so easily deprotonated. | 1.0 pt |

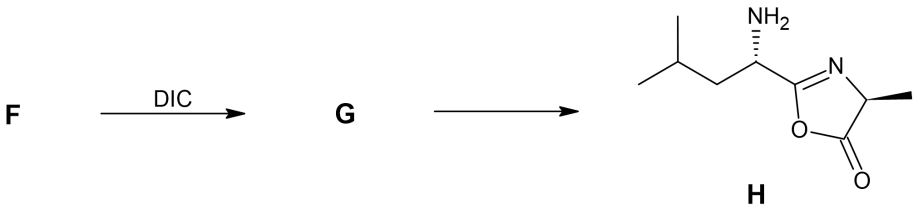
**SOLUTION:**

$\alpha$-carbons are very acidic.

Negative charge is stabilised by conjugated/aromatic system.

0.5 pts per reason.

1.0 pts total.



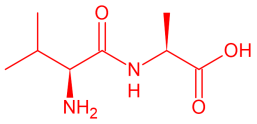

**1.5** **Draw** the structures of dipeptide **F** and intermediate **G** working backwards from oxazolone **H**. 4.0 pt

**F**:

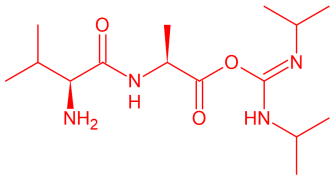
**G**:

**SOLUTION:**

**F**:



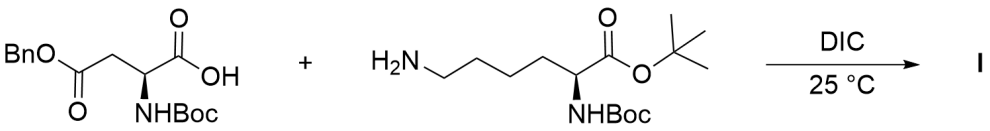

**G**:

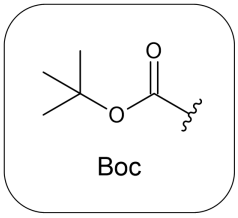


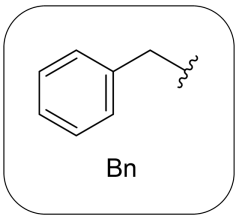

2.0 pts for correct intermediate.
2.0 pts for correct dipeptide.
4.0 pts total.

Protecting groups are also commonly employed to prevent self-coupling and unwanted side chain reactivity.

In liquid-phase peptide synthesis, a commonly seen scheme uses *tert*-butyloxycarbonyl (Boc) as a temporary N-terminal protecting group, and benzyl (Bn) as a permanent side chain carboxyl protecting group. This means Boc protecting groups are periodically added and cleaved to prevent unwanted reactivity at the N-terminus, while Bn is used to protect the side chains permanently throughout the synthesis.




**1.6** **Draw** the structure of product **I**. 2.0 pt

**SOLUTION:**


2.0 pts for the product.
2.0 pts total.

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# Q2-1

English (Official)

## Nonlinear Networks (19.0 pts, 12%)

Oscillating reactions are chemical reactions that show periodic changes in reaction rate and intermediate concentrations instead of progressing smoothly to equilibrium. This behavior arises from non-linear kinetics, where the rate of certain steps depends on the concentration of intermediates. Positive feedback (autocatalysis) accelerates the reaction, while negative feedback (inhibition) slows it down, producing repeating cycles.

***Autocatalysis*** occurs when a reaction product catalyzes its own formation, leading to positive feedback.

***Inhibition*** occurs when a species consumes or removes an autocatalytic reactant, preventing the autocatalytic cycle from starting.

The Belousov–Zhabotinsky (BZ) reaction is a classic example of a nonlinear chemical oscillator. It alternates between an inhibitory phase, characterized by a high concentration of bromide ions consuming bromous acid ($HBrO_2$), and an autocatalytic production of bromous acid that occurs once bromide levels fall below a critical treshold. The reaction is typically performed in an acidic medium, while using potassium bromate as the oxidant and malonic acid as the reductant, with cerium ions serving as a redox indicator. After an initial induction period, the solution undergoes periodic color changes between colorless ($Ce^{3+}$) and yellow ($Ce^{4+}$). When carried out in a Petri dish, these oscillations appear as expanding spirals as seen in the image below. The reaction continues until all reactants have been consumed.

There are multiple variations of the BZ reaction each characterised by its own set of colors.

Consider the following simplified reaction scheme focusing on the autocatalytic and inhibitory reactions. Assume all reaction steps to be elementary. The radical $BrO_2^\bullet$ is a short-lived intermediate.

| Reaction | Rate Constant |
|---|---|
| $R_1:\ BrO_3^- + Br^- + 2\,H^+ \rightarrow HBrO_2 + HOBr$ | $k_1 = 2.4\,L^3\,mol^{-3}\,s^{-1}$ |
| $R_2:\ HBrO_2 + Br^- + H^+ \rightarrow 2\,HOBr$ | $k_2 = 1 \times 10^6\,L^2\,mol^{-2}\,s^{-1}$ |
| $R_3:\ HOBr + Br^- + H^+ \rightarrow Br_2 + H_2O$ | $k_3 = 3.16 \times 10^8\,L^2\,mol^{-2}\,s^{-1}$ |
| $R_4:\ BrO_3^- + HBrO_2 + H^+ \rightarrow 2\,BrO_2^\bullet + H_2O$ | $k_4 = 10\,L^2\,mol^{-2}\,s^{-1}$ |
| $R_5:\ BrO_2^\bullet + Ce^{3+} + H^+ \rightarrow HBrO_2 + Ce^{4+}$ | $k_5 = 5 \times 10^5\,L^2\,mol^{-2}\,s^{-1}$ |

**2.1** **Explain** why $R_4$ and $R_5$ are an autocatalytic system and **identify** the catalytic species. **Show** why we see an increase in the reaction rate as the reaction progresses. 2.5 pt

**SOLUTION:**

In $R_4$ bromous acid ($HBrO_2$) is consumed to produce two $BrO_2^\bullet$ radicals. Each of these radicals only exists for a very short amount of time and subsequently reacts with $Ce^{3+}$ and $H^+$ in $R_5$ to regenerate one molecule of $HBrO_2$. Therefore, although one $HBrO_2$ molecule is initially consumed, two molecules are regenerated. The net effect of $R_4$ and $R_5$ is the conversion of one $HBrO_2$ molecule into two $HBrO_2$ molecules.

Because $HBrO_2$ participates in its own overall formation, the reaction sequence is autocatalytic. The rate of $R_4$ increases with increasing $HBrO_2$ concentration, since the rate law for $R_4$ depends on the $HBrO_2$ concentration ($rate_{R4} = k_4[BrO_3^-][HBrO_2][H^+]$). As more $HBrO_2$ is produced, the rate of its further production increases, creating positive feedback and leading to an accelerating reaction rate.

0.5 pts for identifying $HBrO_2$as the catalytic species.
1.0 pts for explaining the net $HBrO_2$ production.
1.0 pts for explaining that the rate of R4 depends on the concentration of $HBrO_2$, which is why we see an accelerating rate.
2.5 pts total.

**2.2** **Write** the differential rate law for $R_1$ and **indicate** the reaction order with respect to $HBrO_2$ and the overall reaction order. 3.0 pt

**SOLUTION:**

Rate Law $R_1$: $r_1 = k_1[BrO_3^-][Br^-][H^+]^2$
Reaction order with respect to $HBrO_2$: 0 ($HBrO_2$ is not a reactant in $R_1$)
Overall reaction order: 1 + 1 + 2 = 4 (addition of exponents)

1.0 pts per correct solution.
3.0 pts total.

For the following problems you may assume these concentrations:

$[BrO_3^-] = 0.3\,\text{mol L}^{-1}$ $[Ce^{3+}] = 0.005\,\text{mol L}^{-1}$ $[H^+] = 0.3\,\text{mol L}^{-1}$ $[HBrO_2] = 0.0001\,\text{mol L}^{-1}$

**2.3** **Calculate** the concentration of $BrO_2^\bullet$ in mol $L^{-1}$ using the steady-state approximation. 3.5 pt

**SOLUTION:**

rate of production = rate of consumption

$\frac{d[BrO_2^\bullet]}{dt} = 0$

$2k_4[BrO_3^-][HBrO_2][H^+] = k_5[BrO_2^\bullet][Ce^{3+}][H^+]$

$[BrO_2^\bullet] = \frac{2k_4[BrO_3^-][HBrO_2]}{k_5[Ce^{3+}]} = 2.4 \times 10^{-7}\ \text{mol}\,L^{-1}$

0.5 pts for $\frac{d[BrO_2^\bullet]}{dt} = 0$ (but still give full points if all else is correct and they didn't write this expression specifically).

1.0 pts for $2k_4[BrO_3^-][HBrO_2][H^+] = k_5[BrO_2^\bullet][Ce^{3+}][H^+]$.

-0.5 pts if they forget factor 2.

1.0 pts for the correct algebraic solution.

1.0 pts for the correct numerical solution.

3.5 pts total.

The oscillations in the BZ reaction depend on the bromide ion concentration. When the bromide concentration is high, the inhibitory reaction dominates. When the bromide concentration drops below a critical threshold $[Br^-]_{crit}$ the autocatalytic process takes over and the color change becomes visible.

**2.4** **Show** that $[Br^-]_{crit}(T) \propto \frac{k_5(T)}{k_2(T)}$. 5.0 pt

**Hint**: You only need to consider one autocatalytic and one inhibitory reaction for this.

**SOLUTION:**

Autocatalytic prodution of $HBrO_2$ : $r_{auto} = k_5[BrO_2^\bullet][Ce^{3+}][H^+]$

Inhibitory consumption of $HBrO_2$ : $r_{inhib} = k_2[HBrO_2][Br^-][H^+]$

$r_{autocatalytic} = r_{inhibitory}$

$k_5[BrO_2^\bullet][Ce^{3+}][H^+] = k_2[HBrO_2][Br^-][H^+]$

$[Br^-]_{crit} = \frac{k_5[BrO_2^\bullet][Ce^{3+}]}{k_2[HBrO_2]}$

Brief explanation of why $R_1$ and $R_4$ are not in this equation:

$R_1$ provides a background source of bromous acid but doesn't determine if autocatalysis can sustain itself (this depends on whether the bromous acid is being consumed by bromide in $R_2$).

Although $R_4$ consumes $HBrO_2$ it is part of the autocatalytic cycle and ultimately contributes to net $HBrO_2$ regeneration rather than inhibition. The radical intermediate is very short-lived.

1.5 pts each for identifying $r_{auto}$ and $r_{inhib}$.

1.0 pts for the equations $r_{auto} = r_{inhib}$.

1.0 pts for solving the equation for $[Br^-]_{crit}$.

5.0 pts total.

Finally we would like to calculate the temperature dependence of this reaction. Assume the $[Br^-]_{crit}$ is found to be $6 \times 10^{-6}$ mol L$^{-1}$ at $T_1 = 298$ K. Assume the following activation energies:

$E_a^{autocatalytic} = 45$ kJ mol$^{-1}$

$E_a^{inhibitory} = 20$ kJ mol$^{-1}$

**2.5** **Find** $[Br^-]_{crit}$ at $T_2 = 318$ K. 5.0 pt

**SOLUTION:**

Only the rate constants depend on temperature, the concentrations are assumed constant.

from the exercise description in 2.4 $\Longrightarrow [Br^-]_{crit}(T) \propto \frac{k_5(T)}{k_2(T)}$

$k(T) = Ae^{-E_a/(RT)}$

$\frac{k_5(T)}{k_2(T)} = e^{-\frac{\Delta Ea}{R}\left(\frac{1}{T_2}-\frac{1}{T_1}\right)}$

$\frac{[Br^-]_{crit}(T_2)}{[Br^-]_{crit}(T_1)} = e^{-\frac{\Delta Ea}{R}\left(\frac{1}{T2}-\frac{1}{T1}\right)} = e^{-\frac{25000}{8.314}\left(\frac{1}{318}-\frac{1}{298}\right)} \approx 1.88$

$[Br^-]_{crit}(T_2) = [Br^-]_{crit}(T_1) \times 1.88 = 1.13 \times 10^{-5}$ mol L$^{-1}$

1.0 pts for using the Arrhenius equation.
2.0 pts for rearranging the Arrhenius equation corresponding to $\frac{k_5(T)}{k_2(T)}$.
1.0 pts for finding the factor 1.88.
1.0 pts for the correct numerical result.
5.0 pts total.

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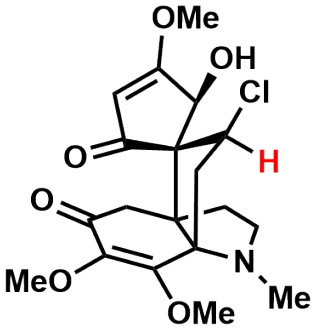
# Q3-1

English (Official)

## Total Synthesis of Acutumine (18.0 pts, 10%)

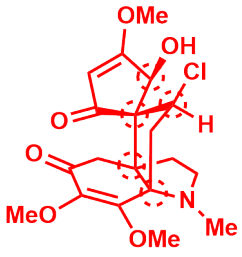
Acutumine belongs to a class of chlorinated aza-propellane tetracyclic alkaloids. It was first isolated in 1929 by Goto and Sudzuki from *Sinomenium acutum*. Later, Tomita obtained Acutumine from *Menispermum dauricum* and determined its structure by X-ray crystallography. The structure of Acutumine is shown below:




**3.1** **Circle** all the stereogenic centers of Acutumine. 2.5 pt

**SOLUTION:**

(a)




0.5 pt each
2.5 pt in total

If incorrect centre is circled then -1 pt per incorrect circle. Minimum score is 0 pt.

**3.2** **State** the expected splitting pattern of the highlighted hydrogen in $^{1}$H NMR. 1.0 pt

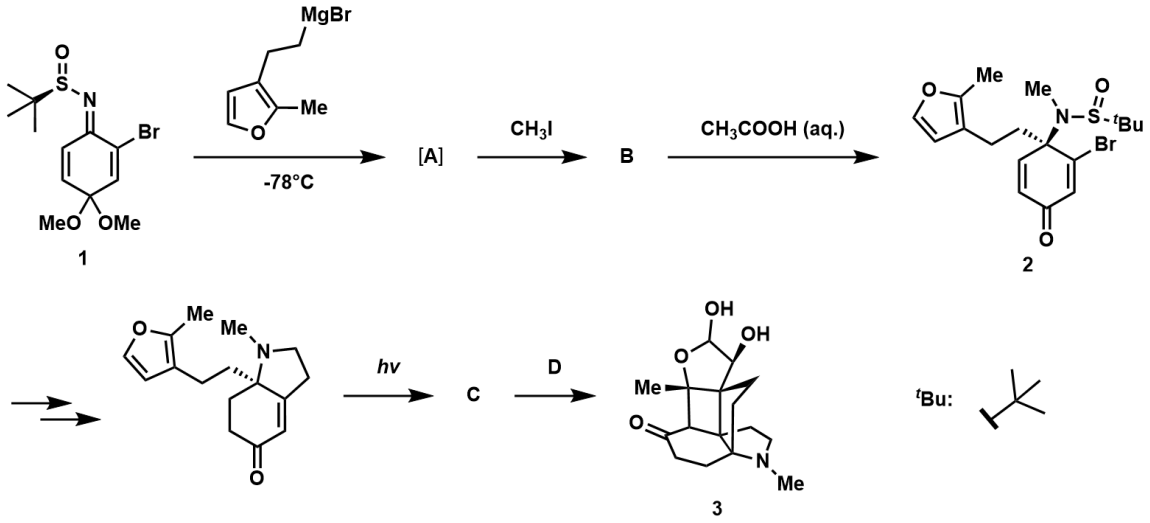
**SOLUTION:**

triplet / 3 / t / dd / doublet of doublet

1.0 pts for correct splitting.

1.0 pts total.

The molecule is highly functionalized and exhibits several notable biological activities. Due to its densely packed functional groups and structural complexity, the total synthesis of Acutumine remains exceptionally challenging and has aroused significant interest within the synthetic chemistry community. During the development of synthetic strategies towards the core skeleton of Acutumine, the following studies were carried out by Reisman's group in 2012:

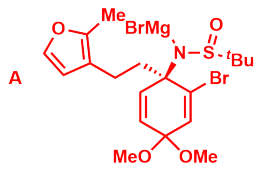



**3.3** **Draw** the structure of **A** and **B**, including stereochemistry. 4.0 pt

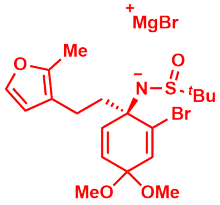
**SOLUTION:**

(a)

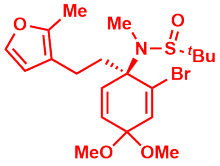
A




or




B



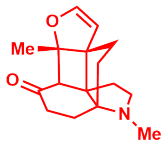

2 pt each
4 pt total
- 0.5 pt for wrong stereogenic center
1 pt if hydrolyzed product is drawn for A

The structure of **C** is formed by photo-induced [2+2] cycloaddition (*hv* means light), which is a reaction very similar to Diels-Alder cyclization (also known as [4+2] cycloaddition).

**3.4** Based on the structure of the product, **deduce** the structure of **C** and **provide** the reaction condition **D**. 3.0 pt

**SOLUTION:**

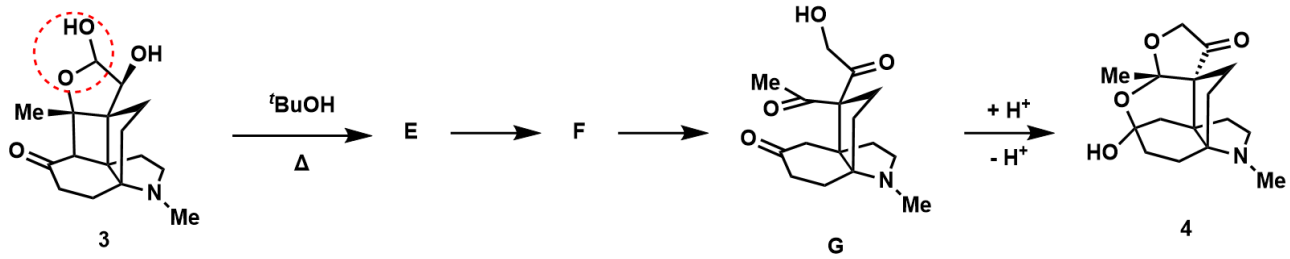
(b)

C 


D cold dilute alkaline $KMnO_4$ / $OsO_4$, $KHSO_3$ / $OsO_4$ (cat.), NMO

2 pt for C
- 0.5 pt for wrong stereogenic center
1 pt if the reaction condition is logical for D
0.5 pt if the answer is only $OsO_4$ (work up is needed!)
0 pt if cold / dilute / alkaline is missing for the answer of $KMnO_4$
3 pt total

The synthesis goes on with the following consequences:

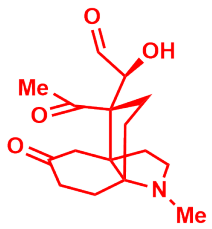



It is known that the highlighted part in **3** is prone to hydrolysis. The formation of **E** involves a retro-Aldol reaction (reverse of the Aldol reaction). **E** contains 3 carbonyl groups and **F** contains 2 carbonyl groups.

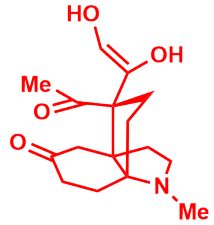
**3.5** **Draw** the structure of **E** and **F**. 4.0 pt

**SOLUTION:**

E



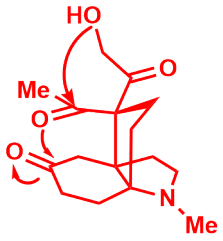

F




2 pt each
4 pt in total
- 0.5 mark for wrong stereogenic center

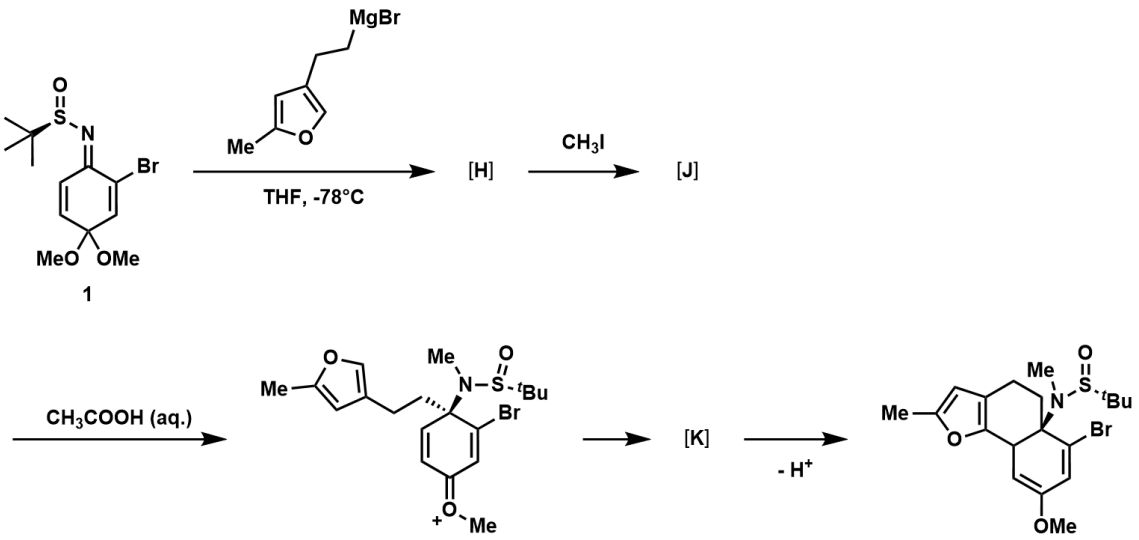
**3.6** **Draw** the curly-arrow mechanism indicating the electron flow for the formation of **4** from **G** in the structure below. 1.5 pt

**SOLUTION:**



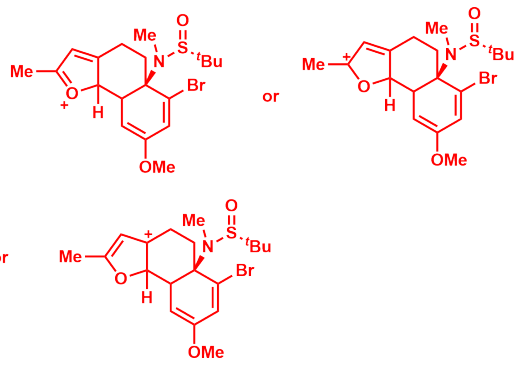

**0.5 pt each**
**1.5 pt in total**

If we use different Grignard reagent to react with **1**, the product changes:



**3.7** **Draw** the structure of the intermediate **K**. 2.0 pt

**SOLUTION:**




2 pt in total
- 0.5 pt for wrong stereogenic center

# Click Chemistry on Gold Nanoparticles (15.0 pts, 11%)

The nanoparticle ***nucleation rate*** (the rate at which stable particles of a new solid phase get formed in a given volume over time), $J$, can be expressed using the Arrhenius-style relationship:

$$J = A(S-1) \cdot \exp\left(-\frac{\Delta G_{\text{crit}}}{k_B T}\right) \tag{1}$$

$$\Delta G_{\text{crit}} = \frac{16\pi\gamma^3\nu^2}{3(k_B T \ln(S))^2} \tag{2}$$

The ***rate of particle growth*** ($r$) can be described as:

$$r = \frac{dR}{dt} = k_0 \cdot \exp\left(-\frac{\Delta G_g}{k_B T}\right) \cdot (S-1) \tag{3}$$

Where parameters are:

$A$ – Arrhenius constant

$\gamma$ – surface energy

$\nu$ – molecular (or atomic) volume of the phase being formed

$S$ – supersaturation (***not entropy***), defined as $S = \frac{c_\infty}{c_0}$, where: $c_\infty$ is actual concentration of the solute in the bulk solution and $c_0$ is the concentration of saturated solution

$\Delta G_g$ – activation energy for the growth process

$R$ – radius of the particle

$k_0$ – constant

Consider all parameters ($\gamma$, $\nu$, $c_\infty$, $c_0$, $k_0$, $\Delta G_g$) independent from each other and temperature.

To analyse how the temperature $T$ affects the particle size, the ratio of the nucleation rate to the growth rate $J/r$ needs to be analysed.

**4.1** **Analyse** how the ratio $J/r$ depends on $T$ and **simplify** the obtained equation, assuming $T \longrightarrow +\infty$. Based on this, **identify** whether bigger or smaller particles are formed at higher $T$. **Note:** $S$ remains constant and $S > 1$. 3.0 pt

**SOLUTION:**

After putting $\Delta G_{crit}$ in the equation of $J$, we get that $J$ depends on temperature as:$J = const \cdot \exp(-\frac{\text{const}}{T^3})$, while $r = const \cdot \exp(-\frac{\text{const}}{T})$ (1.0p - dependence of J on T calculated)

By dividing we get: $\frac{J}{r} = const \cdot e^{\frac{const}{T} - \frac{const}{T^3}} = const \cdot e^{\frac{const}{T}(const - \frac{const}{T^2})} = const \cdot e^{\frac{const}{T}}$ (0.5p - ratio calculated, 1.0p - approximation of high T used)

This means that with the increase of temperature, growth of particles outperforms nucleation as obtained ratio is decreasing with the increase of T and ***bigger particles*** will be formed. (0.5p - right conclusion)

Interestingly, this contradicts usually used conditions for nanoparticle synthesis, where higher temperature is used for smaller particles. One of the reasons of this is that sometimes function at reasonably high temperatures just doesn't reach extremum and factor $\frac{const}{T^3}$ still outperforms $\frac{const}{T}$.

1.0 pts for the calculation of J dependence on T.
0.5 pts for calculation the $\frac{J}{r}$ ratio.
1.0 pts for useing the high T approximation.
0.5 pts for for conclusion of bigger particles.
3.0 pts total.

**4.2** Among the four parameters $J$, $c_\infty$, $r$ and $\gamma$, **select** two that, when increased, lead to a larger final particle size. **Note:** **Assume** all other parameters remain constant in each case. 1.0 pt

**SOLUTION:**

$r$, $\gamma$ - increase particle size.

$J$ and $r$ determine which process is faster nucleation or growth. As a result, first decreases particles, second increases.

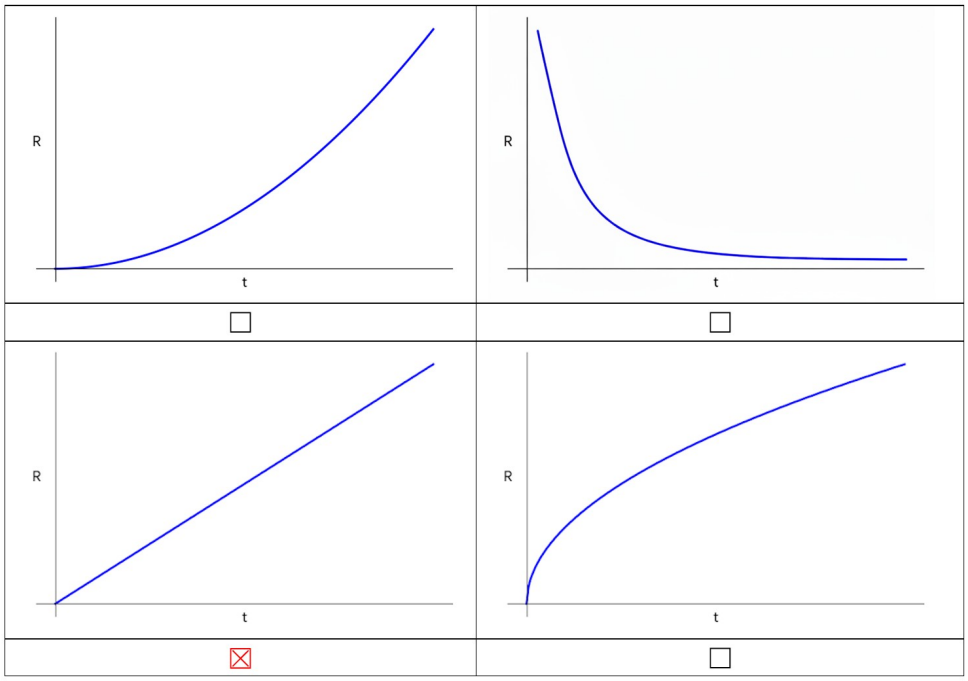
$\gamma$ - increases the barrier of nucleation, as a result, decreasing nucleation rate and increasing particle size.

$c_\infty$ increases S. As both, $J$ and $r$, have (S-1) factor in both equations, we only need to compare how S influences factor in exponent. So, S decreases barrier of nucleation and increases $J$ leading to a smaller particles.

0.5 pts per correct option.
0.0 pts if more than 2 boxes are ticked.
1.0 pts total.

**4.3** Assuming $S > 1$ remains constant over time, **select** the graph correctly representing the change in particle radius ($R$) as a function of time ($t$). 1.0 pt

**SOLUTION:**




☐ ☐ ☒ ☐

1.0 pts for correct answer.
1.0 pts total.

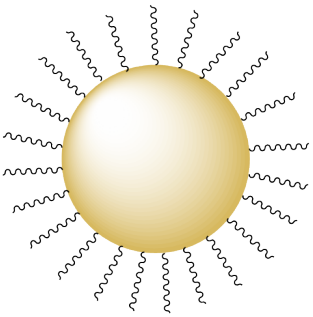
**4.4** **Suggest** the likely outcome of a nanoparticle synthesis attempt in the regime where $S < 1$. 1.0 pt

**SOLUTION:**

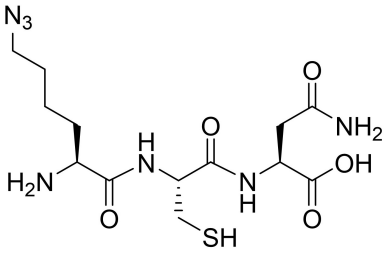
Under this conditions particles will not form, as their solubility is higher than their concentration in solution.

1.0 pts total.

To obtain particles of a desired size, the reaction is typically quenched after a certain amount of time to stop further growth. Following quenching, the nanoparticles are capped with a ligand to stabilize them and prevent aggregation. An obtained gold nanoparticle capped with the ligand can be represented schematically as follows:

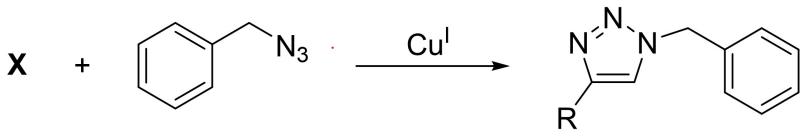


**4.5** **Circle** the functional group in the following ligand structure that binds most strongly to the gold surface during the capping of gold nanoparticles. **Note:** The ligand is monodentate. 1.0 pt



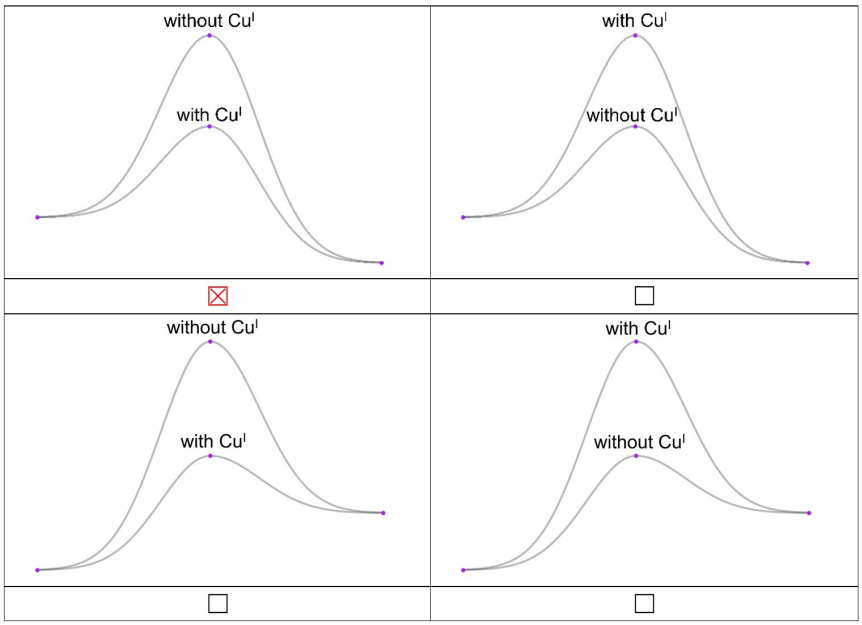

**SOLUTION:**
-SH group
1.0 pts for thiol.
1.0 pts total.

Capped gold nanoparticles can be further functionalized or labeled using CuAAC, a classic copper-catalyzed click chemistry reaction. This classic reaction is characterized by high efficiency and 100% atom economy, as all atoms of the reactants are incorporated into the final product:




**4.6** **Choose** the Gibbs free energy diagram that corresponds to the catalyzed and uncatalyzed labeling reaction (CuAAC). For simplicity, **assume** all intermediate states are omitted and the highest transition states in each case are shown. **Note:** Starting materials are located on the left side of the diagram, while the product on the right side. 1.0 pt

**SOLUTION:**




The correct answer is determined by two criteria: the catalyzed reaction has a lower overall activation energy than the uncatalyzed path, and the spontaneity of the process means a negative Gibbs free energy change.

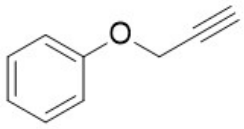
1.0 pts for correct answer.

1.0 pts total.

**4.7** **Identify** compound **X**, if: 2.0 pt

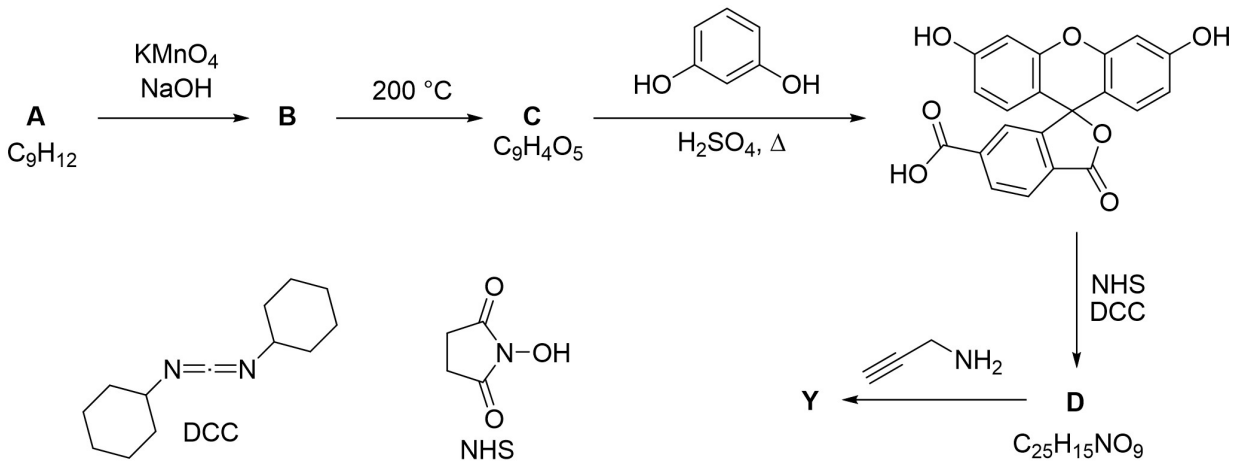
- its chemical formular is $C_9H_8O$
- its $^1$H NMR: 7.27 (t, 2H), 6.97 (d, 2H), 6.93 (t, 1H), 4.68 (s, 2H), 2.50 (s, 1H)
- **assume** that coupling in $^1$H NMR is only observed for hydrogens separated by at most three bonds

**SOLUTION:**



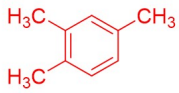
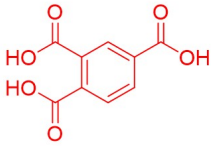
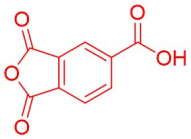
2.0 pts for correct structure.
1.5 pts for Benzyl ether (contradicts aromatic region, where the presence of EDG is evident).
2.0 pts total.

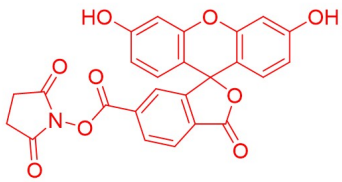
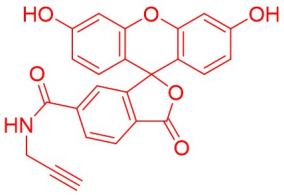
Fluorescein derivative **Y** was used for the labeling of capped gold nanoparticles via CuAAC. It was synthesized according to the following scheme:



**4.8** **Identify** compounds **A**–**D** and **Y** if **A** has 3 signals in aromatic region (each integrates to 1H) and 3 signals in aliphatic region (each integrates to 3H). 5.0 pt

**SOLUTION:**

| A | B | C |
|---|---|---|
|  |  |  |

| D | Y |
|---|---|
|  |  |

1.0 pts per structure.
5.0 pts total.

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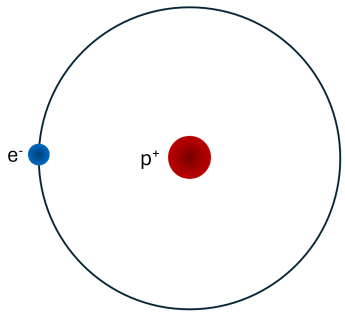
OLIMPIADI DELLA CHIMICA

# Q5-1

English (Official)

## Bohr Model and Energy Levels (16.5 pts, 10%)

Hydrogen-like atoms can be well approximated using the Bohr model. In this model, the electron is assumed to move in a circular orbit around the nucleus (see figure below). Apart from hydrogen, all atoms with just one electron are also considered hydrogen-like, e.g. $He^+$.




**5.1** **Give** the force that keeps the electron bound to the proton. **Show** that the kinetic energy of an electron in a hydrogen atom is given by $E_{\text{kin}} = -\frac{1}{8\pi\epsilon_0}\frac{q_1 q_2}{r}$. 1.5 pt

**Hint**: The centripetal force is given by $F_z = -\frac{mv^2}{r}$.

**SOLUTION:**

The force is the Coulomb Force given by $F_c = \frac{1}{4\pi\epsilon_0} \cdot \frac{q_1 q_2}{r^2}$.

It holds $F_c = F_z$ which gives an expression for $mv^2 = -\frac{1}{4\pi\epsilon_0} \cdot \frac{q_1 q_2}{r}$

We have $E_{kin} = \frac{1}{2}mv^2 = -\frac{1}{8\pi\epsilon_0} \cdot \frac{q_1 q_2}{r}$

0.5 pts for each step.

1.5 pts total.

The Bohr model assumes that the angular momentum $L$ of the electron is quantized:

$$L = m_e v r = \frac{nh}{2\pi} \text{ with } n = 1, 2, 3, \ldots \quad (1)$$

**5.2** **Show** that this condition leads to discrete energy levels for the electron given by $E(n) = -\frac{q_1^2 q_2^2 m_e}{8\epsilon_0^2 n^2 h^2}$. 2.0 pt

**SOLUTION:**

$mvr = \frac{nh}{2\pi} \Rightarrow v = \frac{nh}{2\pi mr}$

then we equate with the equation above for $mv^2$: $m \cdot \frac{n^2h^2}{2^2\pi^2 m^2 r^2} = -\frac{1}{4\pi\epsilon_0} \cdot \frac{q_1 q_2}{r} \Rightarrow$

$r_n = -\frac{n^2h^2}{m\pi} \cdot \frac{\epsilon_0}{q_1 q_2}$

which we then can plug in in the equation for the energy from above to get:

$E_n = -\frac{q_1^2 q_2^2 m_e}{8\epsilon_0^2 n^2 h^2}$

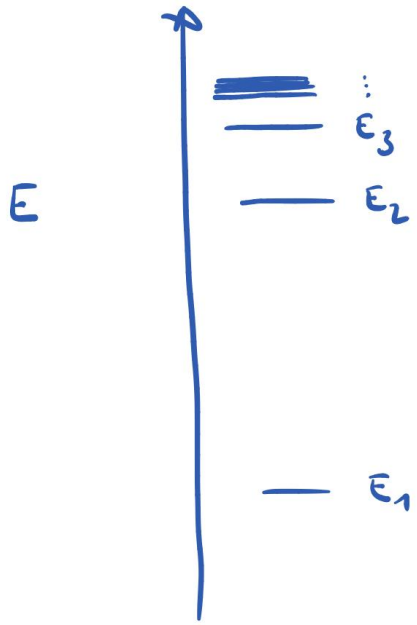
1.0 pts for equation of $r_n$

1.0 pts for getting to the final equation

2.0 pts total.

**5.3** Schematically **draw** a diagram of the electron energy levels $E(n)$. Is there a limit to how much energy a bound electron can absorb? **Explain** what happens when this value is exceeded. 2.0 pt

**SOLUTION:**




when the electrons have more energy than the highest energy level, the electron becomes unbound.

1.0 pts for diagram (- 0.5 pts if axis is not labeled).

1.0 pts for correct explanation.

2.0 pts total.

In 1888, Johannes Rydberg empirically found the formula now known as the Rydberg formula. It is given as follows, where $\lambda$ is the wavelength of light emitted by a transition from the energy level of $n_1$ to the energy level $n_2$. $R_\infty$ is a constant.

$$\frac{1}{\lambda} = R_\infty \left( \frac{1}{n_1^2} - \frac{1}{n_2^2} \right) \tag{2}$$

**5.4** Based on the Bohr model, **show** that it holds $R_\infty = \frac{q_1^2 q_2^2 m_e}{8\epsilon_0 h^3 c}$. 2.0 pt

**SOLUTION:**

it holds: $E = h\nu = \frac{hc}{\lambda} \Rightarrow \frac{1}{\lambda} = \frac{E}{hc}$

$\Delta E = E_2 - E_1 = \frac{q_1^2 q_2^2 m_e}{8\epsilon_0^2 h^2} \left( \frac{1}{n_1^2} - \frac{1}{n_1^2} \right)$ so we see it has the same form than the Rydberg formula.

to get $R_\infty$ we multiply the prefactor of our equation with $\frac{1}{hc}$ to get:

$R_\infty = \frac{q_1^2 q_2^2 m_e}{8\epsilon_0 h^3 c}$

0.5 pts for equation for $1/\lambda$.

0.5 pts for realizing $\Delta E$ has the same form than the Rydberg formula.

1.0 pts for correct reasoning to get to $R_\infty$.

2.0 pts total.

The Bohr model can also be applied to larger atoms. We now look at this in more detail.

**5.5** **Give** the full electron configuration of caesium. 1.0 pt

**SOLUTION:**

Cs: $1s^2 2s^2 2p^6 3s^2 3p^6 3d^{10} 4s^2 4p^6 4d^{10} 5s^2 5p^6 6s^1$

1.0 pts for correct electron configuration.

1.0 pts total.

Experimentally, it is observed that when a metal surface is irradiated with light, electrons are emitted only if the frequency of the incident light exceeds a well-defined threshold value. Increasing the light intensity below this threshold has no effect on electron emission, regardless of how intense the radiation is. This behavior is known as the photoelectric effect.

The minimum energy required to liberate an electron from the metal is called the work function $\Phi$. It is given as follows, where $h$ is Planck constant and $\nu_{\text{threshold}}$ is the threshold frequency.

$$\Phi = h\nu_{\text{threshold}} \tag{3}$$

**5.6** **Calculate** the work function $\Phi_{Cs}$ of Cs in eV. **Assume** you can apply the Bohr model. 3.0 pt

**Hint**: **Consider** only the outermost electron and **treat** the remaining electrons as part of the atomic core.

**SOLUTION:**

$\Phi = \Delta E = E_\infty - E_6 = -E_6 = \frac{e^4 m_e}{8\epsilon_0^2 6^2 h^2} = 6.055 \cdot 10^{-20} J = 0.378 eV$

1.0 pts for realizing $\Phi$ is equal to $\Delta E$.
1.0 pts for realizing $E_\infty$ = 0.
0.5 pts for correct final formula.
0.5 pts for correct numerical value.
3.0 pts total.

Experimentally, the work function $\Phi_{Cs}$ of Cs is measured to be 2.1 eV.

**5.7** **Give** one possible reason for the difference between the theoretical estimate and the experimental value. **Specify** the exact reason what the difference is between our model and what we measure in reality. 2.0 pt

**Note**: If you could not solve **5.6**, **assume** that the theoretical value is $\Phi_{Cs} = 0.832$ eV.

**SOLUTION:**

The Bohr model holds only for hydrogen like atoms.
Several possible reasons are correct:
In Cs the electrons interact with each other and the approximation that the valence electron "sees" only a single charged core does not hold. We say the electrons below the valence electron don't shield perfectly. Therefore the calculated value is lower than the experimentally measured.
The work function is a solid-state property, not purely an atomic property. The electrons in the metal don't belong to just one metal atom, but are bound to a collective potential of all metal cores.
0.5 pts for the reason.
1.5 pts for the specification.
give full points if one of the two reasons above is specified. Give max. 1 extra point if more than one specification is mentioned
2.0 pts total.

A hydrogen laser can be built using the $n = 4$ to $n = 2$ transition.

**5.8** If we irradiate Cs with this laser, **calculate** the speed of the emitted electrons. For the work function $\Phi_{Cs}$ of Cs, **use** the experimental measured value of 2.1 eV. 3.0 pt

**SOLUTION:**

from the Rydberg formula we get:

$\frac{1}{\lambda} \cdot hc = \Delta E = \frac{e^4 m_e}{8\epsilon_0^2 h^2}(\frac{1}{2^2} - \frac{1}{4^2}) = 2.55eV = 4.09 \cdot 10^{-19} J$ wich is the energy from the laser. The energy from the laser is higher than the work function of Cs, so the electrons get emitted.

The electrons have the energy of: $E_{electron} = E_{laser} - \Phi = E_{kin,\,electrons}$

$E_{kin} = \frac{1}{2}mv^2 \Rightarrow v = (\frac{2E_{kin}}{m})^{0.5} = (\frac{2(E_{laser}-\Phi)}{m_e})^{0.5} = 3.99 \cdot 10^5 \frac{m}{s}$

0.5 pts for applying the Rydberg formula

1.0 pts to get to correct value of $\Delta E$

1.0 pts for correct value of $\Delta E$

0.5 pts for correct final result

(if numerical values are incorrect but the formula is correct, give half the points for the corresponding step. Follow-up errors should be taken into account)

3.0 pts total.

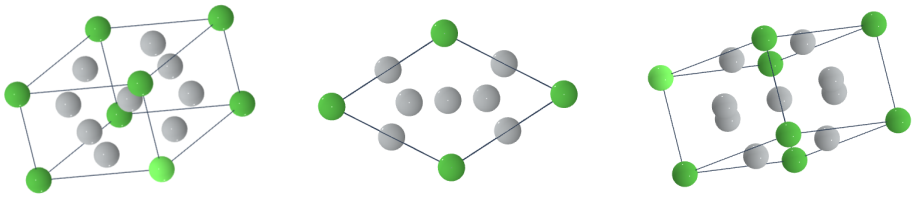
# Lanthanum's Momentum in Hydrogen Retention (18.5 pts, 9%)

Hydrogen is a promising energy carrier due to its high energy density and the fact that it produces water upon combustion, making it a potential sustainable fuel. However, further research is still needed to enable efficient and truly sustainable hydrogen production, since most of hydrogen is currently produced from hydrocarbons, which releases typically significant amounts of $CO_2$.

Additionally, hydrogen storage remains challenging because hydrogen has a very low density and is difficult to store as a gas or liquid, partly due to its low molar mass and tendency to escape from containment systems.

A possible hydrogen storage is lanthanum pentanickel $LaNi_5$. But just like all other hydrogen storage solutions it comes with a specific set of properties and challenges, which you decide to investigate.

**6.1** **Assign** nickel and lanthanum to their respective coloured atom in the crystal structure. 1.0 pt



**SOLUTION:**
Green Lanthanum
Grey Nickel
0.5 pts per correct assignment.
1.0 pts total.

During your research you find that the unit cell (uc) contains one lanthanum atom and five nickel atoms. You also discover that one unit cell can store up to 6 hydrogen atoms.

| | $r$/pm | $V$/pm$^3$ |
|---|---|---|
| $uc_{LaNi_5}$ | | $9.0 \times 10^7$ |
| $uc_{LaNi_5H_6}$ | | $1.1 \times 10^8$ |
| La | 195 | $3.1 \times 10^7$ |
| Ni | 135 | $1.0 \times 10^7$ |
| H | 53 | |

**6.2** **Calculate** the available volume for hydrogen in the unit cell ($V_a$) in pm$^3$ and the volume hydrogen requires ($V_H$) in pm$^3$. 2.0 pt

**SOLUTION:**

$V_a = V_{uc} - (V_{La} + 5 \times V_{Ni}) = (9.0 \times 10^7 - (3.1 \times 10^7 + 5(1.0 \times 10^7)))\text{pm}^3 = 9.0 \times 10^6 \text{pm}^3$

$V_H = 6 \times \frac{4}{3}\pi r^3 = 6 \times \frac{4}{3}\pi(53)^3 = 6 \times (6.2 \times 10^5)\text{pm}^3 = 3.7 \times 10^6 \text{pm}^3$

0.5 pts per formula/calculation ($V_H$ & $V_a$).
0.5 pts per numerical result.
2.0 pts total.

**6.3** **Calculate** the mass percentage of hydrogen (%wt.) in the saturated unit cell. 1.0 pt

**SOLUTION:**

Mass unit cell $= m_{\text{La}} + 5m_{\text{Ni}} + 6m_{\text{H}} = (138.91 + 5 \times 58.69 + 6 \times 1.01)\text{u} = 438.42$ u

Mass $\% = \frac{6m_{\text{H}}}{m_{uc}} = \frac{6.06 \text{ u}}{438.42 \text{ u}} = 1.38$ wt%

0.5 pts for calculation.
0.5 pts for numerical results.
1.0 pts total.

You decide to compare the hydrogen storage capacity of Lanthanum pentanickel to just liquid dihydrogen. You find that the density of liquid hydrogen is $\rho_{\text{H}_2(\text{l})} = 70.85\,\text{kg m}^{-3}$.

**6.4** **Calculate** the density of hydrogen ($\rho_{\text{H,LaNi}_5}$ in kg m$^{-3}$) when stored in lanthanum pentanickel. 3.0 pt

**SOLUTION:**

Volume unit cell (with hydrogen) $= 1.1 \times 10^8 \text{pm}^3$ (given above)

$\frac{1\text{m}^3}{V_{uc}} = \frac{1\text{m}^3}{1.1 \times 10^{-28}\text{m}^3} = 9.1 \times 10^{27}$ unit cells m$^{-3}$

H mass per unit cell $= \frac{6 \times m_H \times 10^{-3}}{N_A} = \frac{6 \times 1.008\text{g mol}^{-1} \times 10^{-3}\text{kg g}^{-1}}{6.022 \times 10^{23}\text{mol}^{-1}} = \frac{6.048 \times 10^{-3}\text{mol kg per unit cell}}{6.022 \times 10^{23}\text{mol}^{-1}} = 1.004 \times 10^{-26}\text{kg per unit cell}$

$d_H = uc\text{m}^{-3} \times m_H per\ uc = 9.09 \times 10^{27}\text{m}^{-3} \times 1.004 \times 10^{-26}\text{kg} per\ uc = 91.4\text{kg m}^{-3}$

2.0 pts for calculation.
1.0 pts for result.
3.0 pts total.

**6.5** **Comment** on the difference of hydrogen density between pure liquid hydrogen and hydrogen in $LaNi_5H_6$. **Propose** a reason for the difference. **Hint**: You may assume that $LaNi_5$ stores more hydrogen per volume. 2.0 pt

**SOLUTION:**

Tight packing in interstitial sites of $LaNi_5$ lattice stabilised by strong M-H bonds
Liquid hydrogen is only held by van der Wals (very weak)

1.0 pts for packing in interstitial sites.
1.0 pts for force difference (vdW vs M-H).
2.0 pts total.

Besides storage capacity an important hydrogen storage factor is the efficient adsorption (**Ad**) and desorption (**De**) of hydrogen. You look up the enthaply values of both processes in the literature.

| | $\Delta_r H\,(\mathrm{kJ\,mol^{-1}})$ |
|---|---|
| **Ad** | $-40 \pm 7$ |
| **De** | $29 \pm 1$ |

When running a test experiment in your reactor, you observe slow adsorption and desorption.

**6.6** **Propose** two things you could change to increase adsorption efficiency and two ways to increase desorption efficiency. **Explain** your choice. 4.0 pt

**SOLUTION:**

Increase adsorption: increase hydrogen pressure (deduced from hydrogen consumption during reaction) and decrease the temperature (deduced from negative enthalpy) pushes the equilibrium towards adsorption.

Increase desorption: decrease hydrogen pressure (deduced from hydrogen production during reaction) and increase the temperature (deduced from positive enthalpy) pushes the equilibrium towards desorption.

0.5 pts per reason per reaction.

4.0 pts total.

Another important consideration for hydrogen storage is efficient longevity, meaning little degradation over many cycles.

Repeated adsorption/desorption cycles cause several signs of wear in lanthanum pentanickel such as decrepitation (pulverisation), H trapping, amorphisation and disproportionation. All of which decrease hydrogen storage capacity over time.

Pulverisation means that the crystalline material cracks, eventually forming a powder. This changes the kinetics of adsorption/desorption. During the first few cycles, pulverisation accelerates adsorption until it reaches a maximum, after which pulverisation progressively slows down adsorption.

**6.7** **Explain** how cycling-induced pulverisation leads to the changes in the rate of hydrogen adsorption. **Note**: Desorption follows the same trend. 2.0 pt

**SOLUTION:**

Increase: The first cracks create additional surface area, which accelerates the reaction (they're surface reactions) and the hydrogen can diffuse into the cracks, which makes the required "intra compound diffusion distances" shorter.

Decrease: The surfaces oxidise, which hinders/inhibits reaction. Also hydrogen diffusion in powder is less efficient.

1.0 pts for a good increase reason (surface creation or hydrogen crack diffusion).

1.0 pts for a good decrease reason (surface oxidation or limited hydrogen diffusion in powder).

2.0 pts total.

**6.8** **Draw** an example of the atomic structure of amorphous $LaNi_5$. **Reason** how amorphisation has a negative effect on the hydrogen storage capacity of $LaNi_5$. 2.0 pt

**SOLUTION:**

Any amorphous (no long range symmetry) is acceptable.

The disorder "destroys" the interstitial sites hydrogen would/could occupy and hinders diffusion within the (not anymore) crystal.

1.0 pts for amorphous structure.

1.0 pts for one good reason about reduced strorage capacity.

2.0 pts total.

One possibility to reduce degration effects and increase the life time of $LaNi_5$ is doping it with aluminum, creating $LaNi_{4.5}Al_{0.5}$. The added aluminum reduces strain during adsorption/desorption and slightly changes the electronics of the compound.

During your experiments you are able to store 60 mol $H_2$ in 10 kg $LaNi_{4.5}Al_{0.5}$.

**6.9** **Complete** the sum formula of hydrogen saturated $LaNi_{4.5}Al_{0.5}$. 1.5 pt

**SOLUTION:**

Molar mass of $LaNi_{4.5}Al_{0.5} = m_{La} + 4.5m_{Ni} + 0.5m_{Al} = (138.91 + 5 \times 58.69 + 0.5 \times 26.98)\,u = 416.51$ u

$\frac{10\,kg}{416.51\,g\,mol^{-1}} = 24.009\,mol$

$60\,molH_2 = 120\,molH \cdot$

$\frac{120\,molH \cdot}{24.009\,molLaNi_{4.5}Al_{0.5}} = 5$ equivalents $\rightarrow LaNi_{4.5}Al_{0.5}H_5$

1.0 pts for calculation.

0.5 pts for sum formula.

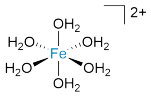
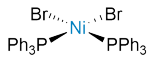
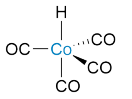
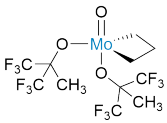
1.5 pts total.

# Radically Important Complexes (17.0 pts, 9%)

Transition metal complexes are some of the most important catalysts—both in the laboratory and in your body. Most transition metals strive to fulfil the so-called 18-electron rule, which is similar to the octet rule for non-transition metals. However, opposed to the octet rule, the 18-electron rule is more flexible, and complexes with lower and higher valence electron counts can exist.

**7.1** For the following compounds, **give** the oxidation state (OS), d-electron count ($d^n$), coordination number (CN) and total valence electron count (VEC) of the metal. 4.0 pt

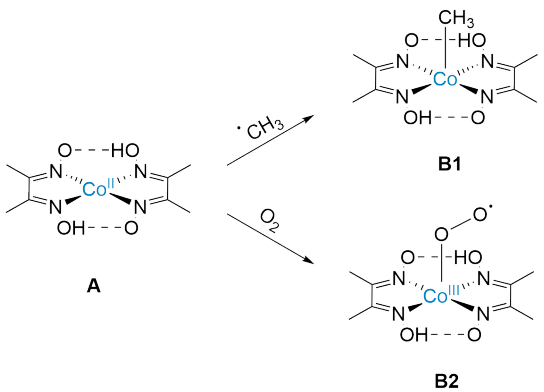
**SOLUTION:**

| Complex |  |  |  |  |
|---|---|---|---|---|
| OS | +II | +II | +I | +VI |
| $d^n$ | $d^6$ | $d^8$ | $d^8$ | $d^0$ |
| CN | 6 | 4 | 5 | 5 |
| VEC | 18 | 16 | 18 | 12 |

1.0 pt for each fully correct column.
0.5 pts for each column in which one mistake (account for double punishment/subsequent errors!) has been made. A missing entry also counts.
0.0 pts for each column in which more than one thing is incorrect.

4.0 pts total.

Let us now consider the following reactions where a Co(II) complex **A** encounters a methyl radical and reacts with it to form **B1** or where it encounters $O_2$, and forms **B2**.
**Note:** The $CH_3$ ligand in **B1** is formally a $CH_3^-$ anion.



**7.2** **Determine** $d^n$ for **A** and the OS of Co for **B1**. 1.0 pt

**SOLUTION:**

$d^n(\mathbf{A}) = d^7$ $\quad$ $\mathrm{OS}(\mathbf{B1}) = +\mathrm{III}$

0.5 pts for the correct $d^n(\mathbf{A})$.
0.5 pts for the correct $\mathrm{OS}(\mathbf{B1})$.

1.0 pts total.

**7.3** **Select** the correct electronic nature of the dioxygen ligand in **B2**. 0.5 pt

**SOLUTION:**

☐ $O_2^{2-}$ ☒ $O_2^{\bullet-}$ ☐ $O_2$ ☐ $O_2^{\bullet+}$ ☐ $O_2^{2+}$

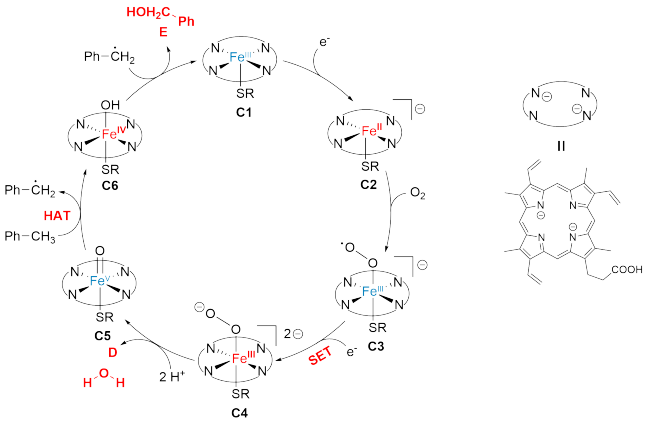
0.5 pts for the correct choice.
0.0 pts for the incorrect/multiple choice(s).

0.5 pts total.

Knowing this, let us look at two enzymes that involve both transition metals and radicals: Cytochrome P450 and Methyl CoM Reductase.

Cytochrome P450 is an enzyme that catalyses the mono-oxygenation (introduction of a single oxygen atom) of various compounds within your body, making them more water-soluble and more easy to excrete. A simplified catalytic cycle is shown below, where toluene ($H_3C{-}Ph$) functions as the substrate. The structure of the doubly negatively charged porphyrin ligand is given next to the catalytic cycle. The axial $R{-}S^-$ ligand is a thiolate. Neither of these ligands undergo any changes throughout the course of the catalytic cycle.

**SOLUTION:**



**7.4** **Determine** the OS of Fe in the following catalytic intermediates. 3.0 pt

**SOLUTION:**

| Intermediate | **C2** | **C4** | **C6** |
|---|---|---|---|
| OS of Fe | +II | +III | +IV |

1.0 pts per correct answer.

3.0 pts total.

**7.5** **Choose** the appropriate processes for **C3**→**C4** and **C5**→**C6**. 2.0 pt

**SOLUTION:**

| Step | Single-electron tranfer (SET) | Hydrogen-atom transfer (HAT) | Halogen-atom transfer (XAT) | Proton transfer (PT) | None of these options |
|---|---|---|---|---|---|
| **C3**→**C4** | ☒ | ☐ | ☐ | ☐ | ☐ |
| **C5**→**C6** | ☐ | ☒ | ☐ | ☐ | ☐ |

1.0 pt for each correct choice.
0.0 pts for incorrect/multiple choice(s).
**EXCEPTION:** 0.5 pts awarded for choosing SET + PT for **C5**→**C6** ($H^+ + e^- \longrightarrow H^\bullet$).

2.0 pts total.

**7.6** **Draw** the structure of **D** and **E**. 1.5 pt

**SOLUTION:**

**D**
$H_2O$, H–O–H, water (any reasonable option accepted)

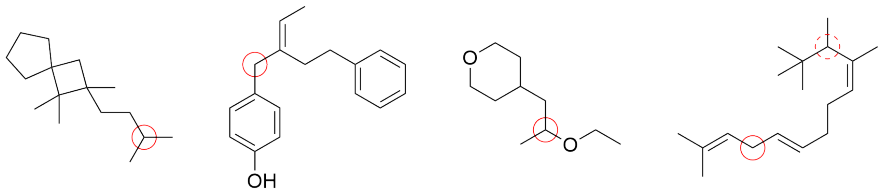
**E**
Benzyl alcohol, BnOH, Ph–$CH_2$–OH, $C_6H_5$–$CH_2$–OH, structural formula (any reasonable option accepted)

0.5 pts for water.
1.0 pts for benzyl alcohol.

1.5 pts total.

**7.7** For each of the following molecules, **circle** the carbon atom whose C–H bond is most readily oxidised by Cytochrome P450. 2.0 pt

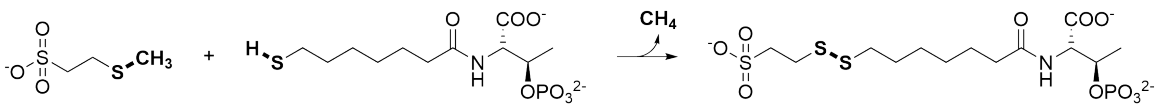
**SOLUTION:**




The key factor is radical stability. A position that yields a more stable radical will be more easily oxidised via the radical pathway.
Higher substitution 3° > 2° >> 1° carbons show higher radical stability.
Furthermore, conjugation (with hetereoatoms or $\pi$-systems) is even more strongly stabilising.
0.5 pts for each correctly circled carbon atom.
0.0 pts for each substrate, where none/more than one carbon atoms have been circled.
0.5 pts for the carbon atom circled with dashes. Although it is 3°, it is only singly allylic instead of 2° and doubly allylic. It is also in a neopentylic position, which inhibits reactivity. Still a totally reasonable choice, therefore full points awarded.
2.0 pts total.

Another enzyme that deals with radicals is Methyl CoM Reductase (MCR), the enzyme involved in the last step of methanogenesis in bacteria. MCR is responsible for the biological production of around 1 billion tonnes of methane per year.

The reaction involves a methyl donor ($H_3C–S–CoM$) and a hydrogen donor ($H–S–CoB$) that are formally coupled together like so, resulting in a disulfide bond between the two sulfurs:




The reaction is mediated using a Ni-containing active site. The ring structure containing four N is similar to the one in P450, however, it only carries a single negative charge. Let us now examine the catalytic steps one-by-one.

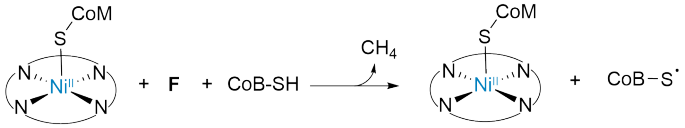

**7.8** **Draw** the structure of **F**. 0.5 pt

**SOLUTION:**

**F** is a methyl radical. Any correctly drawn structure counts.

0.5 pts for the correct structure.

0.5 pts total.



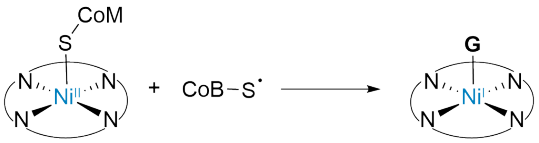

**7.9** **Name** the type of elementary step that is occurring in this reaction. 0.5 pt

**SOLUTION:**

Hydrogen atom transfer (HAT). Also accepted: radical abstraction or equivalent.

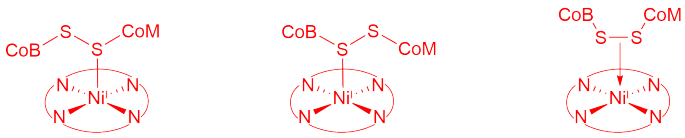
0.5 pts for any correct answer.

0.5 pts total.




**7.10** Given the OS of the nickel centre, **draw** the ligand **G** that is missing below. 1.0 pt

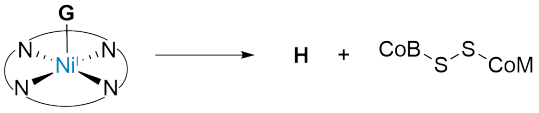
**SOLUTION:**




Any complex that obeys the correct Ni(I) oxidation state and accounts for both sulfides in one ligand is accepted.

1.0 pts for correct ligand.

1.0 pts total.




**7.11** **Draw H**, **indicating** the correct OS on Ni. 1.0 pt

**SOLUTION:**


As the full reaction has now taken place (disulfide and methane generated), the catalytic cycle must be over. This means that **H** is again the "first" state of the catalyst.
0.5 pts for correct OS on Ni.
0.5 pts for correct ligand.

1.0 pt total.

## 'Funky'-Block Elements (17.0 pts, 11%)

The f-block elements are rarely discussed in detail in high-school chemistry courses, yet they play important roles in redox chemistry, catalysis and material science. Among the lanthanides, the +III oxidation state is by far the most common because of formation of lanthanide ions.

Cerium is a notable exception: the oxidation of $Ce^{3+}$ to $Ce^{4+}$ is possible. $Ce^{4+}$ is a strong oxidising agent that reacts vigorously with water (hydrolysis) under neutral and basic conditions. However, under highly acidic conditions, free $Ce^{4+}$ can exist in solution.

**8.1** **Explain** why $Ce^{4+}$ exists, whereas other lanthanide ions usually occur only in their +III form. 1.0 pt

**SOLUTION:**

$Ce^{4+}$ has a noble gas electron configuration of [Xe]. This stabilises the cation, meaning the oxidation state is attainable.

1.0 pt for correct reasoning.

1.0 pt total.

The cumulative formation constant $\beta_n^{\mathrm{L}}$ of a complex $ML_n$ is given as the equilibrium constant for the formation of the complex from the free metal centre M with $n$ ligands L.

$Ce^{4+}$ is most well-known as its nitrate complex hexanitrocerate(IV) $[Ce(NO_3)_6]^{2-}$. Which is formed like so:

$$Ce^{4+} \overset{+NO_3^-}{\rightleftharpoons} [Ce(NO_3)]^{3+} \overset{+NO_3^-}{\rightleftharpoons} [Ce(NO_3)_2]^{2+} \overset{+NO_3^-}{\rightleftharpoons} [Ce(NO_3)_3]^{+} \overset{+NO_3^-}{\rightleftharpoons} \ldots$$

**8.2** **Give** $\beta_3^{NO_3^-}$ and $\beta_6^{NO_3^-}$ of the complex forming reaction between $Ce^{4+}$ with $NO_3^-$. 2.0 pt

**SOLUTION:**

$$\beta_3^{NO_3^-} = \frac{[Ce(NO_3)_3^+]}{[Ce^{4+}]\cdot[NO_3^-]^3}$$

$$\beta_6^{NO_3^-} = \frac{[Ce(NO_3)_6^{2-}]}{[Ce^{4+}]\cdot[NO_3^-]^6}$$

1.0 pt each.

2.0 pts total.

The aforementioned hydrolysis $Ce^{4+} + 4\,H_2O \longrightarrow Ce(OH)_4 + 4\,H^+$ has $\beta_1^{H_2O}$ through $\beta_4^{H_2O}$.

$$\beta_1^{H_2O} = \frac{[Ce(OH)^{3+}]\cdot[H^+]}{[Ce^{4+}]\cdot[H_2O]} \qquad \beta_2^{H_2O} = \frac{[Ce(OH)_2{}^{2+}]\cdot[H^+]^2}{[Ce^{4+}]\cdot[H_2O]^2} \qquad \beta_3^{H_2O} = \frac{[Ce(OH)_3{}^{+}]\cdot[H^+]^3}{[Ce^{4+}]\cdot[H_2O]^3} \qquad \beta_4^{H_2O} = \frac{[Ce(OH)_4]\cdot[H^+]^4}{[Ce^{4+}]\cdot[H_2O]^4}$$

For $\beta_n^{H_2O}$ of the hydrolysis products, the following values were obtained.

| $n$ | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| $\ln\left(\beta_n^{H_2O}\right)$ | 33.99 | 64.56 | 93.32 | 119.41 |

The standard molar Gibbs free energy of formation of some relevant substances, $\Delta_fG^\ominus(298.15\ K)$ is listed in the table below.

| Substance | $H_2O\,(l)$ | $OH^-(aq)$ | $H^+(aq)$ | $Ce^{4+}(aq)$ |
|---|---|---|---|---|
| $\Delta_fG^\ominus(298.15\ K)/kJ\ mol^{-1}$ | -237.10 | -157.20 | 0 | -503.80 |

**8.3** **Calculate** the $\Delta_fG^\ominus$ of $Ce(OH)^{3+}$ and $Ce(OH)_3{}^+$ in kJ $mol^{-1}$. 6.0 pt

**SOLUTION:**

Given that each hydrolysis reaction has $\Delta_rG^\ominus = -RT\ln\beta_n^{H_2O}$,
so $\Delta_fG^\ominus(Ce(OH)^{(3+)}) = -RT\ln\beta_1^{H_2O} + \Delta_fG^\ominus(Ce^{4+}) + \Delta_fG^\ominus(H_2O) - \Delta_fG^\ominus(H^+) = -RT\ln\beta_1^{H_2O} + \Delta_fG^\ominus(Ce^{4+}) + \Delta_fG^\ominus(H_2O)$
and
$\Delta_fG^\ominus(Ce(OH)_3^+) = -RT\ln\beta_3^{H_2O} + \Delta_fG^\ominus(Ce^{4+}) + 3\Delta_fG^\ominus(H_2O) - 3\Delta_fG^\ominus(H^+) = -RT\ln\beta_3^{H_2O} + \Delta_fG^\ominus(Ce^{4+}) + 3\Delta_fG^\ominus(H_2O)$
By substituting the values from the given table that and changing the bases of logarithm, we can get:
$Ce(OH)^{3+}$: -825.16 kJ $mol^{-1}$
$Ce(OH)_3^+$: -1299.36 kJ $mol^{-1}$
2.0 pts for $\Delta_rG^\ominus = -RT\ln\beta_n^{H_2O}$.
2.0 pts for the relationship to give $\Delta_fG$ of the complexes.
1.0 pts for each correct value for the hydroxides.

6.0 pts total.

Let us assume that only the non-complexed $Ce^{4+}$ is redox-active and can be reduced to $Ce^{3+}$. In this case, the observed reduction potential of the $Ce^{4+}|Ce^{3+}$ redox couple ($E^{red}_{Ce^{4+}|Ce^{3+}}$) is pH-dependent.

**8.4** **Explain** in both words and formulae why $E^{red}_{Ce^{4+}|Ce^{3+}}$ is pH-dependent. 4.0 pt
**Determine** whether $E^{red}_{Ce^{4+}|Ce^{3+}}$ increases or decreases, when the solution is acidified.

**SOLUTION:**

**Words**: using Le Châtelier's principle, we can see that decreasing the pH (increasing $[H^+]$), the hydroxide complex equilibria for cerium will shift towards the uncomplexed, redox-active $Ce^{4+}$. This will in turn give us more $Ce^{4+}$ to react in a redox reaction. Le Châtelier (again) will state, that by increasing the oxidant, the reaction will move towards the side of the products, thereby INCREASING $E^{red}_{Ce^{4+}|Ce^{3+}}$.

**Equations**:

Nernst equation: $E = E^{\ominus} - \frac{RT}{zF} \ln\left(\frac{[Ce^{3+}]}{[Ce^{4+}]}\right)$

By increasing $[Ce^{4+}]$ (decrease pH), $E^{red}_{Ce^{4+}|Ce^{3+}}$ will increase.

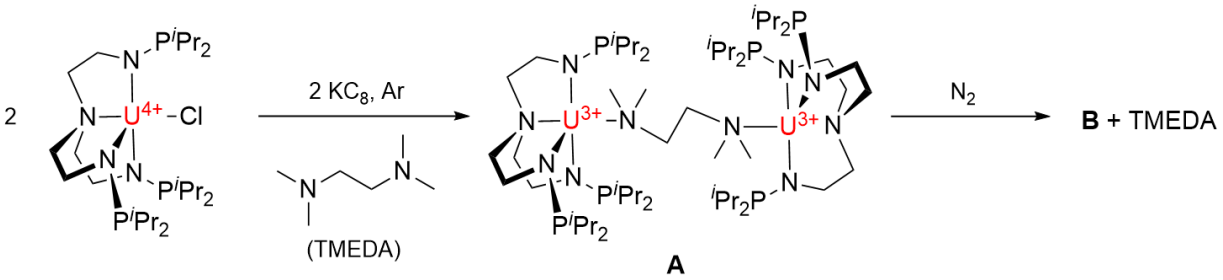
When acidified: ☒ $E^{red}_{Ce^{4+}|Ce^{3+}}$ increases ☐ $E^{red}_{Ce^{4+}|Ce^{3+}}$ decreases

1.0 pt for arguing that $[Ce^{4+}]$ increases, as $[H^+]$ increases.
2.0 pts for arguing with Le Châtelier in the redox OR the use of the Nernst equation.
1.0 pt for the correct choice based on their arguments (even if arguments were wrong but choice is consistent)
0.0 pts for choosing none/both boxes OR ticking a box without explanation.

4.0 pts total.

The redox chemistry of cerium illustrates how the stability of different oxidation states and their interactions with ligands influence chemical behavior in aqueous solution. Similar principles apply more broadly in f-block chemistry, where metal–ligand interactions can significantly modify electronic structure and reactivity. In addition to simple hydrolysis equilibria, f-block elements are also capable of forming complexes that activate small, and inert molecules. One important example is the coordination of dinitrogen ($N_2$) by uranium complexes, which weakens the strong N ≡ N bond and enables its chemical transformation.

Consider the following reaction:

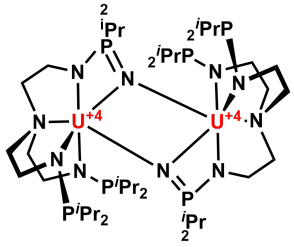



You are now working in a radioactive laboratory. The reaction was performed in a glovebox with argon atmosphere with water and oxygen level lower than 0.1 ppm. $KC_8$ is a super strong reducing agent that can reduce the metal by removing a chloride to form KCl and graphite as by-products.

The structure of product **B** could not be easily predicted from our knowledge. However, after single-crystal X-ray analysis (a technique used to determine how atoms are connected) and theoretical calculations, it was found that one molecule of $N_2$ reacts with complex **A**, and the strong N≡N triple bond is completely broken. The product **B** still contains two uranium atoms, but their oxidation states return to +IV. Each uranium atom is bonded to six nitrogen atoms and has an octahedral geometry. In addition, some phosphorus atoms in the ligands are oxidized, and the structure of **B** contains three four-membered rings.

**8.5** Based on the information above, **predict** the structure of **B**. 3.0 pt

**SOLUTION:**




3.0 pts for correct structure.
3.0 pts total.

Complex **B** undergoes hydrolysis readily in the presence of water to form two small molecules **X** with molar mass smaller than 20 g $mol^{-1}$.

**8.6** **Predict** the chemical formula of **X**. 1.0 pt

**SOLUTION:**

$NH_3$

1.0 pts for correct formula.
1.0 pts total.

CHEMISTRY.
OLYMPIAD.CH
CHEMIE-OLYMPIADE
OLYMPIADES DE CHIMIE
OLIMPIADI DELLA CHIMICA

# Q9-1

English (Official)

## Not Just Playing with Fire (16.5 pts, 12%)

Uzbekistan has large natural gas reserves. Natural gas mainly consists of methane, ethane, propane, and butane, as well as non-hydrocarbon impurities. The individual components are separated using cryogenic distillation, so that they can, for example, be used in a lighter.

The following table contains the standard enthalpy of formation $\Delta_f H^0$, standard enthalpy of vaporization $\Delta_{vap} H^0$, and the vapor pressure $p$ (at the temperature $T_{max}$ you will calculate in **9.5**) for several hydrocarbons and other molecules.

| Molecule | $\Delta_f H^0$ / kJ mol$^{-1}$ | $\Delta_{vap} H^0$ / kJ mol$^{-1}$ | $p$ / bar |
|---|---|---|---|
| Propane (g) | -104 | 18.8 | 24 |
| Butane (g) | -126 | 23.2 | 6.5 |
| $H_2O$ (g) | -242 | | |
| $CO_2$ (g) | -394 | | |

The following quantities may also prove useful for the task.

| | |
|---|---|
| Density of propane (l) | 0.58 g cm$^{-3}$ |
| Density of butane (l) | 0.60 g cm$^{-3}$ |

We have a lighter filled with 90 vol.% butane and 10 vol.% propane. Assume the lighter has a volume of 4 mL and that all the fuel is in the liquid phase due to the high pressure inside the lighter.

**9.1** **Write** the combustion reactions and **calculate** the standard enthalpy of combustion $\Delta_{comb}H^0$ in kJ mol$^{-1}$ for the complete fuel mixture, assuming that all of the fuel in the lighter is fully burned. 2.5 pt

**Note**: You do not need to take the vaporization of propane and butane into account.

**SOLUTION:**

$M(propane) = 44.10\,g\,mol^{-1}$, $M(butane) = 58.12\,g\,mol^{-1}$, $V_{propane} = 0.1 \cdot V_{tot} = 0.4\,ml$, $V_{butane} = 0.9 \cdot V_{tot} = 3.6\,ml$

reactions:

for butane: $C_4H_{10} + 6.5\,O_2 \longrightarrow 4\,CO_2 + 5\,H_2O$

for propane: $C_3H_8 + 5\,O_2 \longrightarrow 3\,CO_2 + 4\,H_2O$

$\Delta_{comb}H^0_{butane} = 4 \cdot \Delta_f H^0(CO_2) + 5 \cdot \Delta_f H^0(H_2O(g)) - \Delta_f H^0(butane) = -2660\,kJ\,mol^{-1}$

$\Delta_{comb}H^0_{propane} = 3 \cdot \Delta_f H^0(CO_2) + 4 \cdot \Delta_f H^0(H_2O(g)) - \Delta_f H^0(propane) = -2046\,kJ\,mol^{-1}$

$\Delta_{comb}H^0 = \frac{V_{butane} \cdot \rho_{butane}}{M(butane)} \cdot \Delta_{comb}H^0_{butane} + \frac{V_{propane} \cdot \rho_{butane}}{M(propane)} \cdot \Delta_{comb}H^0_{propane} = -109.6\,kJ\,mol^{-1}$

0.5 pts if both combustion reactions are correct, 0.0 pts if one reaction is incorrect.

0.5 pts for per calculations of $\Delta_{comb}H^0$.

0.5 pts for the correct final expression.

0.5 pts for the correct numerical solution.

2.5 pts total.

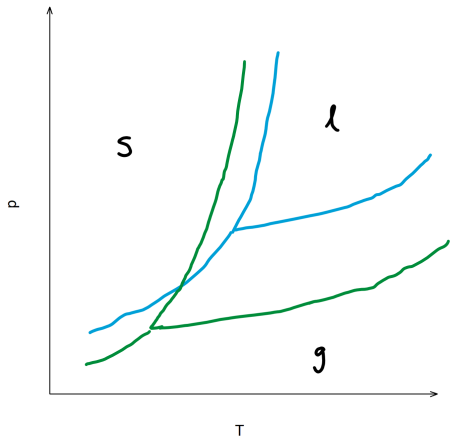
**9.2** **Draw** a qualitative phase diagram of butane in the grid below. **Label** all phases and **provide** a qualitative explanation of the slopes of the phase boundaries. 3.0 pt

**Hint:** The Clausius–Clapeyron equation can be rearranged as follows:

$$\frac{dp}{dT} = \frac{\Delta S_{\alpha \longrightarrow \beta}}{\Delta V_{\alpha \longrightarrow \beta}}$$

where $\frac{dp}{dT}$ is the slope of the coexistence line, $\Delta S_{\alpha \longrightarrow \beta}$ is the entropy change from phase $\alpha$ to phase $\beta$ (for example liquid to solid), $\Delta V_{\alpha \longrightarrow \beta}$ is the volume change associated with the phase transition from phase $\alpha$ to $\beta$.

**SOLUTION:**




in blue is the phase diagram of butane and in black the labeled phases.

slopes:
solid to gaseous: many more microstates possible which implies huge $\Delta S$, the volume change is big. In total we get a steep slope.
solid to liquid: more microstates possible, and a small, positive volume change. In total a very steep slope. The slope must be drawn steeper than the slope from solid to gaseous.
liquid to gaseous: more microstates possible and a big volume change. In total we get a gentle slope.
0.5 pt for each correct slope (so in total 1.5 pt for the correct diagram)
0.5 pt for each correct explanation.
3.0 pts total.

Now we add a small amount of ethanol.

| | | |
|---|---|---|
| **9.3** | **Draw** the coexistence curve of the butane-ethanol mixture into the phase diagram above. If the triple point shifts, **state** at which direction it shifts.<br>**Note**: **Assume** that ethanol has a much higher boiling point than butane. Further **assume** that the mixture freezes fast, so the ethanol gets trapped inside the butane crystal lattice.<br>**SOLUTION:**<br>the tripple point shifts left and under the solid --> gaseous coexistence line. The solution is drawn in green in the above diagram<br>1.0 pts for drawing the solid to liquid phase slope more on the left.<br>1.0 pts for drawing the liquid to gaesous phase slope lower.<br>0.5 pts for explanation of movement of tripple point.<br>2.5 pts total. | 2.5 pt |

Butane and propane originate from natural gas. To obtain the pure substances for use in a lighter, cryogenic distillation is carried out. For this purpose, the natural gas is cooled and compressed until it liquefies. The individual fractions are then separated.

Now all components of the natural gas except butane and propane were separated and another distillation is performed. For illustration, we consider a mole fraction versus pressure diagram (see **9.4**).

The dew line indicates the pressure at which the substance begins to condense. The bubble line describes the pressure at which the substance begins to boil. It can be derived that the following relations hold at the dew line and the bubble line.

The dew line is a function of $Y_B$ and it holds:

$$p = \frac{p_A^* p_B^*}{p_B^* - Y_B(p_B^* - p_A^*)} \tag{1}$$

The bubble line is a linear function of $x_B$ and it holds:

$$p = p_A^* + x_B(p_B^* - p_A^*) \tag{2}$$

where $p$ is the pressure, $p_i^*$ is the vapor pressure of substance $i$, $Y_B = \frac{p_B}{p}$ is the mole fraction of substance B in the vapor phase, and $x_B = \frac{p_B}{p_B^*}$ is the mole fraction of substance B in the liquid phase.

The mole fractions of a state (e.g. liquid) of all substances in a mixture add to 1. Mathematically speaking:

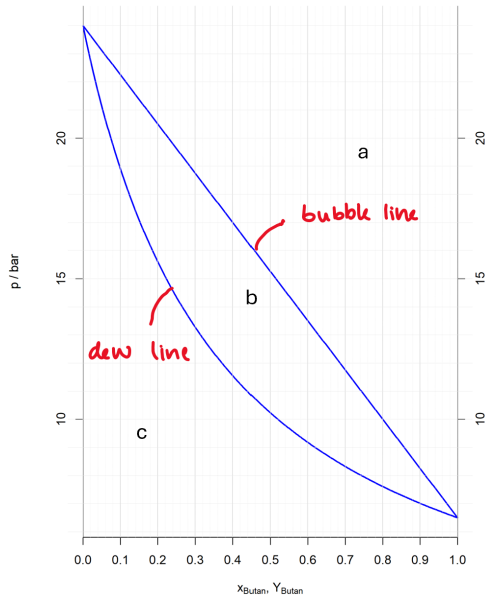
$$Y_A + Y_B + ... = 1 \tag{3}$$

$$x_A + x_B + ... = 1 \quad (4)$$

**9.4** **Label** the dew line and the bubble line in the below figure. **Give** the states of matter of propane and butane found in the three regions bounded by the dew and bubble lines (i.e., in regions a, b, and c). 2.5 pt

**Hint**: **Think** about what happens when you lower the pressure of just a single substance. In which state is it at high pressure? In which state is it at low pressure? For region b, think about the mole fraction in the vapor phase and the mole fraction in the liquid phase.

**SOLUTION:**




region a: both propane and butane are in liquid phase
region b: proportions of both propane and butane are in liquid phase and some proportions of both substances are in gaseous phase
region c: both propane and butane are in gaseous phase
0.5 pts each for identifying bubble and dew line.
0.5 pts each for correct answer in the regions a-c.
2.5 pts total.

Industrially, distillation is carried out by varying both temperature and pressure. For simplicity, however, we separate our propane–butane mixture using changes in pressure only.

**9.5** For a mole fraction $x_{\text{butane}} = 0.5$, **calculate** the maximum temperature $T_{\text{max}}$ in °C at which both substances are just only in the liquid phase. **Note**: The vapour pressure of the mixture at 20 °C is 8.0 bar. — 2.5 pt

**SOLUTION:**

read the pressure at the bubble line from the diagram at $x_{butane} = 0.5$ which gives roughly $p_1 = 15.2 \cdot 10^5\ Pa$.

we can rearrange the Clausius-Clapeyron equation to $T_1 = (\ln(\frac{p_2}{p_1}) + \frac{\Delta_{vap,tot}H}{R} \cdot \frac{1}{T_2})^{-1} \cdot \frac{\Delta_{vap,tot}H}{R}$ where $\Delta_{vap,tot}H = 0.5 \cdot \Delta_{vap}H_{butane} + 0.5 \cdot \Delta_{vap}H_{propane} = 21\ kJ\ mol^{-1}$, $T_2 = 293.15K$, $p_2 = 8.0 \cdot 10^5 Pa$

which gives $T_1 = 63°C = 336\ K$

1.0 pts for reading correct value of pressure.
1.0 pts for correct formula.
0.5 pts for correct numerical solution.
2.5 pts total.

Now we lower the pressure isothermally until it lies slightly below the upper, linear line and wait until thermal equilibrium is reached. We then separate the gas phase.

**9.6** **Read** the composition $Y_{\text{Butane}}$ of the separated gas phase from the diagram and **state** the molar fractions in the gas phase of butane $Y_{\text{Butane}}$ and propane $Y_{\text{Propane}}$. — 0.5 pt

**SOLUTION:**

approx $Y_{butane} = 0.21$ and therefore $Y_{\text{propane}} = 0.79$

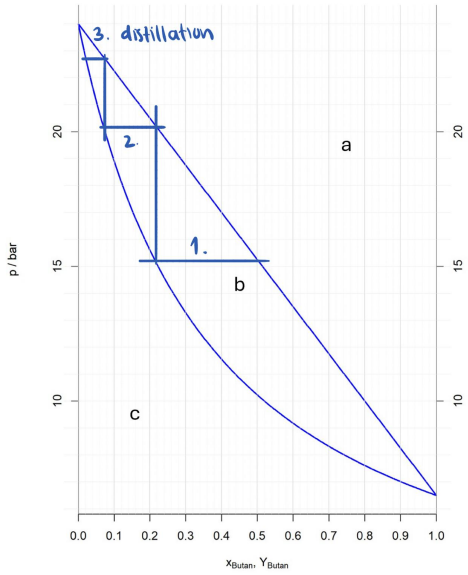
0.5 pts if both $Y_i$ are correct, 0.0 pts if one or both $Y_i$ are incorrect.
0.5 pts total.

Now we perform another distillation with the obtained gas and again collect the gas phase.

**9.7** **Find out** and **state** how many times we must repeat this procedure to obtain 95% pure propane. Include in your number also the first distillation starting at $x_{\text{Butane}} = 0.5$. **Give** the purity of propane after the last needed distillation. 2.0 pt

**SOLUTION:**

After the third distillation we get approx. 98% pure propane




0.5 pts for number of distillation steps.
0.5 pts for purity of propane.
1.0 pts if correct reasoning is being made (see figure in solutions, calculations or other ways of finding out). If both, number of distillation steps and purity of propane are correct give.
2.0 pts total.

Most lighters contain a mixture of butane and propane, with the relative proportions of each varying depending on how the lighter is used.

| | | |
|---|---|---|
| **9.8** | **Give** one reason why butane is used in lighters in addition to propane. **Give** one reason why butane is not used exlusively in lighters.<br>**SOLUTION:**<br>At low pressures and higher temperatures, butane ensures that the lighter does not explode. (+ butane is cheaper)<br>Propane on the other hand ensures, that the lighter also works at higher pressures and lower temperatures.<br><br>the calorific values are for both substances in the same region, so this is an incorrect answer<br>0.5 pts for each correct reason. Give 0.5 pts extra, if they give more than one correct reason of each question.<br>1.0 pts total. | 1.0 pt |

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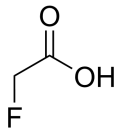
# Q10-1

English (Official)

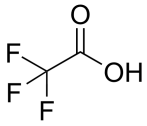
## Fluorines Activate Acetate (11.0 pts, 8%)

While fluorine is rare in biological organic molecules, it is heavly used in synthetic chemistry. Its applications range from the deprotection of alcohols by cleaving Si—O bonds to the modification of metabolic stability of drugs and alteration of the reaction charateristics of chemicals.

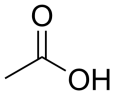
Trifluoroacetic acid (**TFA**) and monofluoroacetic acid (**MFA**) are fluorated derivatives of acetic acid (**AcOH**).




**MFA**




**TFA**




**AcOH**

**10.1** **Order** acetic acid, **TFA** and **MFA** by their acid strength ($pK_a$). **Explain** your choice of strongest and weakest acid (using text and/or drawings). 2.0 pt

**SOLUTION:**

pKa TFA < MFA < AcOH

Fluorine stabilises the deprotonated version by its electronegativity/electron-withdrawing properties (inductive effect), which is additive for multiple fluorines.

1.0 pts for correct order (no partial points).

1.0 pts for sensible reasoning.

2.0 pts total.

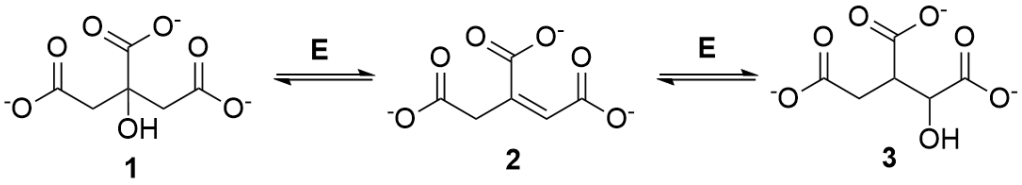
As a responsible chemist you check the safety data sheets of **TFA**, **MFA** and **AcOH** before doing any experiments. All three have warnings about severe skin burns and eye damage, which is typical for acids. **MFA** has the additional warning "fatal if swallowed" even at relatively low doses, which is absent in either **TFA** and **AcOH**. Surprised, you look into the mechanism of **MFA** toxicity.

You discover that intracellular **MFA** affects the citrate cycle, citrate transport in mitochondria and causes low bioavailability of calcium. The three mechanisms have various biological consequences such as ATP & metabolite depletion, heart failure and chaos in the nervous system.

After focusing on the chemical aspects, you discover that this is a case of lethal synthesis. This means not **MFA** (fluoroacetate in biological conditions) acts as the toxin, but rather a product, which is first synthesised via cell metabolism.

The responsible metabolic process is the citrate cycle, which is responsible for energy production and providing biosynthetic intermediates.

Under **MFA**-free conditions, the enzyme acetyl-CoA synthetase catalyses the formation of acetyl-CoA from acetate and cofactor A. Then acetyl-CoA is converted to citrate (**1**) via enzymatic reactions. The enzyme aconitase (**E**) converts citrate (**1**) to isocitrate (**3**) via the intermediate aconitate (**2**).




1 2 3

**10.2** **Name** the two reactions catalysed by aconitase (**E**). 1.0 pt

**SOLUTION:**

Dehydration & Hydration, but elimination/addition of water (to alkene) are accepted.

0.5 pts per reaction.

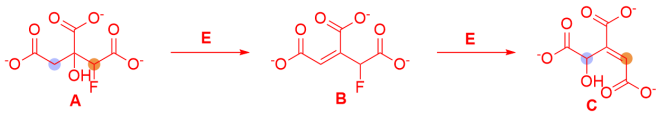
1.0 pts total.

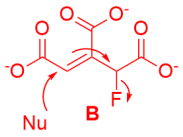
Upon entering the cells, fluoroacetate (deprotonated **MFA**) is mistaken for acetate by acetyl-CoA synthetase and used to produce fluoroacetyl-CoA. Fluoroacetyl-CoA is used by the enzymes of the citrate cycle to produce 2-fluorocitrate (**A**).

The enzyme aconitase (**E**) catalyses the reaction from **A** to 4-hydroxyaconitate (**C**). **C** binds the active site and fully inhibits enzymatic activity, halting the citrate cycle.

**10.3** **Draw** intermediate **B** and the reaction mechanism from intermediate **B** to **C**. 2.0 pt

**SOLUTION:**




1.0 pts for correct intermediate **B**.
1.0 pts for mechanism.
2.0 pts total.

You read that only one of the four possible stereoisomers of 4-hydroxyaconitate is able to inhibit the enzyme.

**10.4** **Assign** the two stereodescriptors of the inhibiting stereoisomer of 4-hydroxyaconitate. 1.0 pt

**SOLUTION:**

*R* and *E*/*trans*.
0.5 pts per correct assignment.
0.0 pts if both or the wrong answer is marked.
1.0 pts total.

When looking into the low calcium bioavailabilty (hypocalcaemia), you find the formation constant $K_{\text{cit}} = 2.76 \times 10^{-3}$ of this calcium citrate complex ($Ca(cit)^-$) under physiological conditions. Unfortunately you can not find any values for the calcium fluorocitrate complex ($Ca(Fcit)^-$). You decide to measure it yourself and get the following values.

| | mol dm$^{-3}$ |
|---|---|
| $[Ca^{2+}]$ | $2.083333 \times 10^{-2}$ |
| $[Fcit^{3-}]_{\text{total}}$ | $6.000000 \times 10^{-2}$ |
| $[Fcit^{3-}]$ | $5.999908 \times 10^{-2}$ |

**10.5** **Calculate** the formation constant $K_{\text{Fcit}}$ of calcium fluorocitrate ($Ca(Fcit)^-$). 1.0 pt

**SOLUTION:**

$K_{fcit} = \frac{[Fcit]_T - [Fcit^{3-}]}{[Ca^{2+}][Fcit^{3-}]} = \frac{6.000000\times10^{-2} - 5.999908\times10^{-2}}{2.083365\times10^{-2}\times5.999908\times10^{-2}} \times = \frac{9.2\times10^{-7}}{1.250019\times10^{-3}} = 7.3599\times10^{-4}$

The nominator serves to find the concentration of $Ca(Fcit)^-$.

Result can be rounded to $7.36\times10^{-4}$ for full points, but more rounding ($7.4\times10^{-4}$ and so forth) gives only half points for result.

0.5 pts for formula.

0.5 pts for result.

1.0 pts total.

**10.6** Given that $K_{\text{Fcit}}$ is lower than $K_{\text{cit}}$, **explain** how hypocalcaemia happens upon **MFA** exposure. 1.0 pt

**SOLUTION:**

Accumulating (due to inhibition of aconitase) "normal" citrate binds/chelates calcium.

The released fluorine during $S_N2'$ is not as relevent, due to formation constant relative to the concentration, but a good thought.

1.0 pts for **accumulated** normal citrate binding calcium.

0.5 pts for fluorine binding the calcium (in absence of citrate argument)

1.0 pts total.

When reading more about the toxicity of halogenated acetate derivatives, you find that many of them (iodoacetate, bromoacetate, dichloroacetate and others) are toxic to cell metabolism, all of them by inhibiting different enzymes.

Interestingly trifluoroacetate and difluoroacetate are not among them. The data suggests that both compounds enter the cell. While difluoroacetate can enter the citrate cycle, trifluoroacetate is not metabolised.

**10.7** **Speculate** why trifluoroacetate can not be metabolised and is therefore not toxic via the same mechanism as monofluoroacetate. 1.0 pt

**SOLUTION:**

Electronics/reactivity from acetate is too different to be processed by acetyl-CoA synthetase.

0.5 pts for pointing out the three fluorines change electronics/reactivity via their electron withdrawing properties.

0.5 pts for stating this likely means that the enzyme can not use it.

1.0 pts total.

**10.8** **Speculate** why difluoroacetate and its metabolites can not inhibit aconitase similarly to fluoroacetate and its metabolites. **State** the consequences. 2.0 pt

**SOLUTION:**

Difluoroacetate is metabolised less efficiently by the enzymes (Acetyl-CoA synthetase & citrate synthetase) due to the additional electronwithdrawing properties of the second fluorine (reactivity too different from acetate). This means less intermediates are available.

Aconitase can not process difluorocitrate to an inhibiting compound/metabolite, due to less binding to enzymes pocket (less likely to react) and simply to being able to produce the inhibitor (4-hydroxy-trans-aconitate). Without the inhibitor of aconitase, the citrate cycle and cell metabolims function as usual.

0.5 pts for stating that difluoroacetate and/or its metabolites are metabolised less (by the enzymes).

0.5 pts for stating this is due to the eletron withdrawing properties of second fluorine (can also be given for just mentioning that they are relevant).

0.5 pts for stating that inhibiting compound (4-hydroxyaconitase) is not formed.

0.5 pts for stating that its absence means citrate cycle without this inhibitor functions (mostly) normal (Energy production, no citrate accumulation and metabolism as ususal).

2.0 pts total.