**Theoretical Final Exam SwissChO 2021**

**INSTRUCTIONS**

- Write your name on each page and number these.

- You have three hours to solve the problems. Wait for the **START** signal before you begin.

- Use a new page for each problem.

- Write all necessary calculations legibly. Do not forget the units.

- Finish your work immediately when the **STOP** signal is given.

- Leave your seat only when allowed to do so.

- Only **answers written on the answer sheets** can be considered.

- This test has 27 pages.

**Viel Erfolg!**
**Bonne chance!**
**Buona fortuna!**
**Good luck!**

## CONSTANTS AND FORMULAE

| | | | |
|---|---|---|---|
| Avogadro constant | $N_A = 6.022 \cdot 10^{23} \ \text{mol}^{-1}$ | Ideal gas law | $pV = nRT$ |
| Universal gas constant | $R = 8.314 \ \text{J mol}^{-1} \ \text{K}^{-1}$ | Gibbs energy | $G = H - TS$ |
| Faraday constant | $F = 96\,485 \ \text{C mol}^{-1}$ | $\Delta_r G^0 = -RT \cdot \ln(K) = -nFE^0_{\text{Zelle}}$ | |
| Planck constant | $h = 6.626 \cdot 10^{-34} \ \text{J s}$ | Nernst equation | $E = E^0 + \dfrac{R \cdot T}{z \cdot F} \cdot \ln\left(\dfrac{c_{\text{ox}}}{c_{\text{red}}}\right)$ |
| Speed of light | $c = 2.998 \cdot 10^8 \ \text{m s}^{-1}$ | Energy of a photon | $E = \dfrac{h \cdot c}{\lambda}$ |
| Temperature | $0\,°\text{C} = 273.15 \ \text{K}$ | Lambert-Beer law | $A = \log\left(\dfrac{I_0}{I}\right) = \epsilon \cdot c \cdot L$ |

For the calculation of equilibrium constants all concentrations, refer to the standard concentration $1\,\text{mol dm}^{-3} = 1\,\text{mol L}^{-1}$. If not stated otherwise in a task, consider all gases ideal throughout this test.

## Periodic Table of Elements

| 1 H 1.008 | | | | | | | | | | | | | | | | | | 2 He 4.003 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3 Li 6.94 | 4 Be 9.01 | | | | | | | | | | | 5 B 10.81 | 6 C 12.01 | 7 N 14.01 | 8 O 16.00 | 9 F 19.00 | | 10 Ne 20.18 |
| 11 Na 22.99 | 12 Mg 24.31 | | | | | | | | | | | 13 Al 26.98 | 14 Si 28.09 | 15 P 30.97 | 16 S 32.06 | 17 Cl 35.45 | | 18 Ar 39.95 |
| 19 K 39.10 | 20 Ca 40.08 | 21 Sc 44.96 | 22 Ti 47.87 | 23 V 50.94 | 24 Cr 52.00 | 25 Mn 54.94 | 26 Fe 55.85 | 27 Co 58.93 | 28 Ni 58.69 | 29 Cu 63.55 | 30 Zn 65.38 | 31 Ga 69.72 | 32 Ge 72.63 | 33 As 74.92 | 34 Se 78.97 | 35 Br 79.90 | | 36 Kr 83.80 |
| 37 Rb 85.47 | 38 Sr 87.62 | 39 Y 88.91 | 40 Zr 91.22 | 41 Nb 92.91 | 42 Mo 95.95 | 43 Tc [98] | 44 Ru 101.07 | 45 Rh 102.91 | 46 Pd 106.42 | 47 Ag 107.87 | 48 Cd 112.41 | 49 In 114.82 | 50 Sn 118.71 | 51 Sb 121.76 | 52 Te 127.60 | 53 I 126.90 | | 54 Xe 131.29 |
| 55 Cs 132.91 | 56 Ba 137.33 | 57–71 | 72 Hf 178.49 | 73 Ta 180.95 | 74 W 183.84 | 75 Re 186.21 | 76 Os 190.23 | 77 Ir 192.22 | 78 Pt 195.08 | 79 Au 196.97 | 80 Hg 200.59 | 81 Tl 204.38 | 82 Pb 207.2 | 83 Bi 208.98 | 84 Po [209] | 85 At [210] | | 86 Rn [212] |
| 87 Fr [223] | 88 Ra [226] | 89–103 | 104 Rf [267] | 105 Db [268] | 106 Sg [269] | 107 Bh [270] | 108 Hs [270] | 109 Mt [278] | 110 Ds [281] | 111 Rg [282] | 112 Cn [285] | 113 Nh [286] | 114 Fl [289] | 115 Mc [290] | 116 Lv [293] | 117 Ts [294] | | 118 Og [294] |

| 57 La 138.91 | 58 Ce 140.12 | 59 Pr 140.91 | 60 Nd 140.24 | 61 Pm [145] | 62 Sm 150.36 | 63 Eu 151.96 | 64 Gd 157.25 | 65 Tb 158.93 | 66 Dy 162.50 | 67 Ho 164.93 | 68 Er 167.26 | 69 Tm 168.93 | 70 Yb 173.05 | 71 Lu 174.97 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 89 Ac [227] | 90 Th 232.04 | 91 Pa 231.04 | 92 U 238.03 | 93 Np [237] | 94 Pu [244] | 95 Am [243] | 96 Cm [247] | 97 Bk [247] | 98 Cf [251] | 99 Es [252] | 100 Fm [257] | 101 Md [258] | 102 No [259] | 103 Lr [266] |

## $^1$H Nuclear Magnetic Resonance Spectroscopy

### Chemical Shifts (in ppm / TMS)
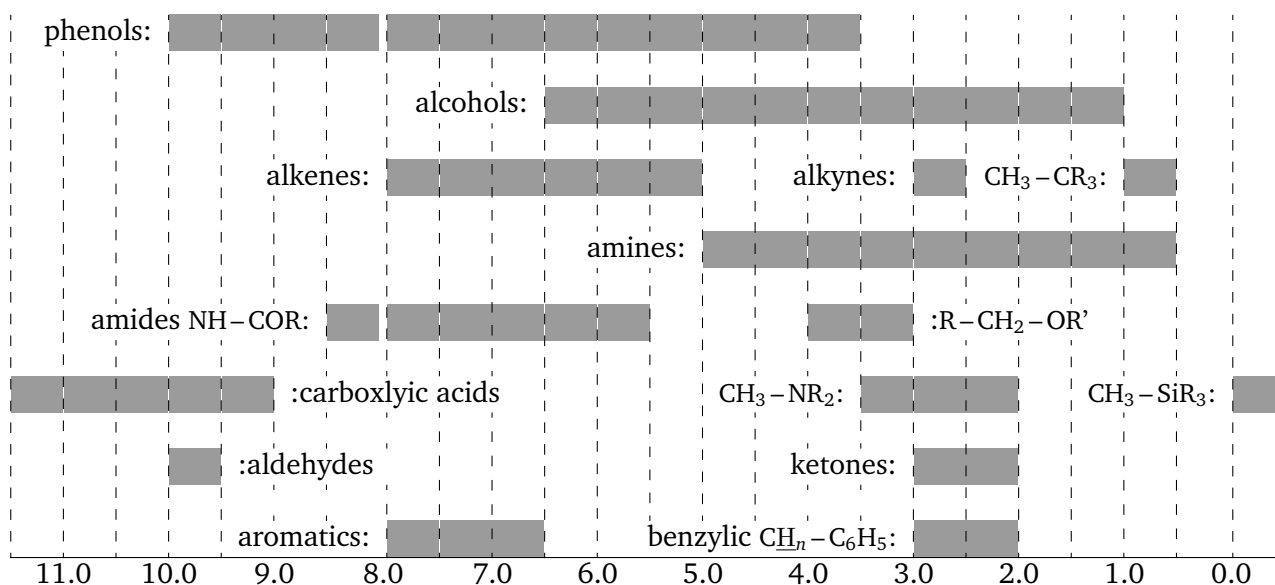


### H–H Coupling Constatns (in Hz)

| Connectivity | Specification | $|J_{ab}|$ |
|---|---|---|
| $R_2CH_aH_b$ | - | $4 - 20$ |
| $R_2CH_a - CR_2H_b$ | freely rotating | $6 - 8$ |
| | ax-ax in $C_6H_{12}$ | $10 - 12$ |
| | ax-eq in $C_6H_{12}$ | $3 - 5$ |
| | eq-eq in $C_6H_{12}$ | $2 - 3$ |
| $R_2CH_a - CR_2 - CR_2H_b$ | freely rotating | $< 0.1$ |
| | rigid | $1 - 8$ |
| $RCH_a = CRH_b$ | *cis* | $7 - 12$ |
| | *trans* | $12 - 18$ |
| $R_2C = CH_aH_b$ | - | $0.5 - 3$ |
| $H_a(CO) - CR_2H_b$ | - | $1 - 3$ |
| $RH_aC = CR - CR_2H_b$ | - | $0.5 - 2.5$ |

ax = axial, eq = equatorial

**IR Spectroscopy Table**

| Vibrational Mode | $\sigma\,/\,\mathrm{cm^{-1}}$ | Intensity |
|---|---|---|
| alcohol O–H (stretching) | $3600-3200$ | strong |
| carboxylic acid O–H (stretching) | $3600-2500$ | strong |
| amine; amide N–H (stretching) | $3500-3350$ | strong |
| alkyne $\equiv$C–H (stretching) | $3300$ | strong |
| alkene =C–H (stretching) | $3100-3000$ | weak |
| alkane –C–H (stretching) | $2950-2840$ | weak |
| aldehyde –(CO)–H (stretching) | $2900-2800$ | weak |
| nitrile C$\equiv$N (stretching) | $2250$ | strong |
| alkyne C$\equiv$C (stretching) | $2260-2100$ | variable |
| aldehyde C=O (stretching) | $1740-1720$ | strong |
| anhydride C=O (stretching 1) | $1840-1800$ | weak |
| anhydride C=O (stretching 2) | $1780-1740$ | strong |
| ester C=O (stretching) | $1750-1720$ | strong |
| ketone C=O (stretching) | $1750-1710$ | strong |
| amide C=O (stretching) | $1700-1500$ | strong |
| alkene C=C (stretching) | $1680-1600$ | weak |
| aromatic C=C (stretching) | $1600-1400$ | weak |
| amine N–H (bending) | $1800-1600$ | medium |
| aliphatic $CH_2$ (bending) | $1480-1440$ | medium |
| aliphatic $CH_3$ (bending 1) | $1470-1440$ | medium |
| aliphatic $CH_3$ (bending 2) | $1390-1360$ | medium |
| ester; ether C–O–C (stretching) | $1250-1050$ | strong |
| alcohol C–OH (stretching) | $1200-1020$ | strong |
| nitro $NO_2$ (stretching 1) | $1600-1500$ | strong |
| nitro $NO_2$ (stretching 2) | $1400-1300$ | strong |
| sulfonate S=O (stretching 1) | $1400-1200$ | strong |
| sulfonate S=O (stretching 2) | $1100-1000$ | strong |
| halide C–F (stretching) | $1400-1000$ | strong |
| halide C–Cl (stretching) | $800-600$ | strong |
| halide C–Br (stretching) | $600-500$ | strong |
| halide C–I (stretching) | $500$ | strong |

**PROBLEM 1 - MAKING MAGNETS GO NANO**                                    **15.0 POINTS**

Metallic iron and iron carbide nanoparticles, so called "nanomagnets", are rather unique materials. During their production in a sooty reductive flame, a few layers of graphite-like carbon get deposited on the magnetic core. After functionalization of the carbon coating such as the immobilization of an active catalyst or an antibody, the resulting nanopowders can be used for catalysis in lab-scale reactions or medical application. In any application, the advantage of the nanoparticles is their ease of separation due to their magnetism. In this task, you will produce and analyze nanomagnets theoretically.

Flame spray synthesis of iron and iron carbide nanoparticles is a scalable one-step process to obtain nanomagnets from a suitable iron precursor, Fe(2-ethylhexanoate)$_3$ ($C_{24}H_{45}FeO_6$, $MW = 485.46\,g/mol$). A precursor solution is dispersed by a nozzle and the spray is ignited by a secondary flame of premixed $CH_4$ and $O_2$. To obtain reducing conditions, the combustion of the spray thereby takes place in a $N_2$ atmosphere. A scheme of the process in shown in Fig. 1. Assume gases to be ideal and to be at $1 \times 10^5\,Pa$ and $298\,K$ throughout the problem.
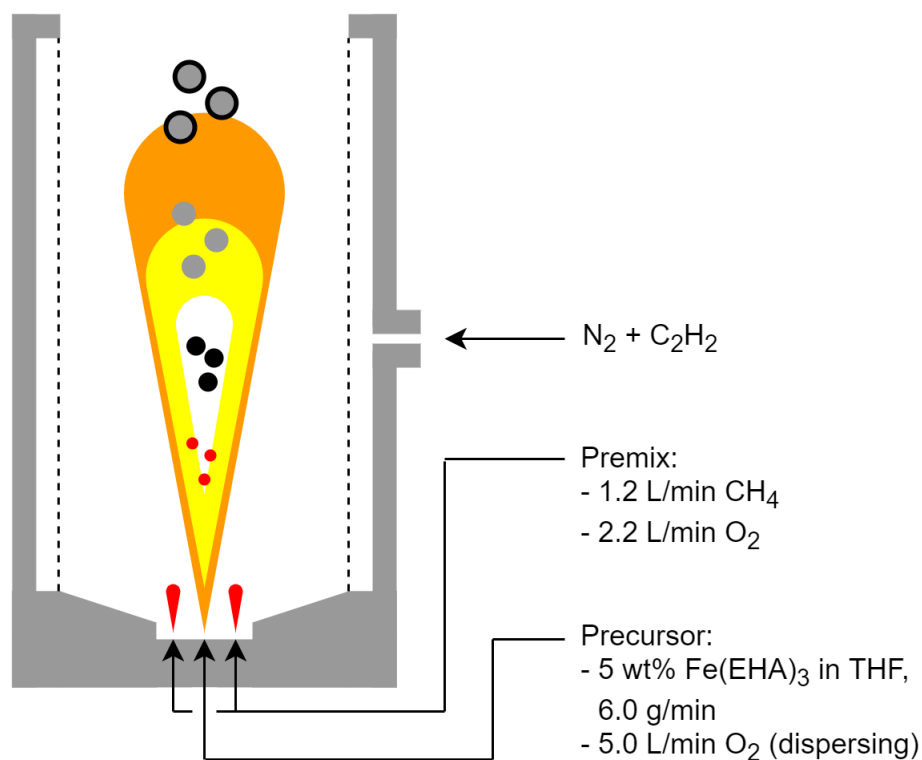


Figure 1: Scheme of reducing flame spray pyrolysis.

a) Draw the structure of the precursor complex. Assume it to be mononuclear.

b) Write the combustion equation of Fe(2-ethylhexanoate)$_3$, of tetrahydrofuran (THF, $C_4H_8O$, $MW = 72.11\,g/mol$) and of methane separately. Assume the conditions to be reducing, resulting in the formation of metallic iron.

c) The equivalence ratio $\phi$ of a combustion is defined by the ratio of moles of $O_2$ required for complete combustion to moles of $O_2$ actually available. From this definition, it can be seen that for fuel-rich mixtures $\phi > 1$. Calculate $\phi$ for the conditions shown in Fig. 1.

d) The following reaction summarizes the overall combustion process and is assumed to have the same oxygen equivalence ratio as calculated in c):

$$C_4H_8OFe_{0.07} \, (l) + n \, O_2 \, (g) \longrightarrow m \, CO_2 \, (g) + 4 \, H_2O \, (g) + 0.07 \, FeC_x \, (s) + c \, C \, (s)$$
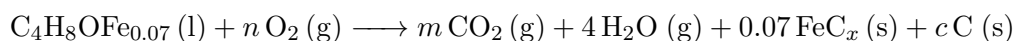
What is the mass fraction of carbon in the particles? Which phase(s) constitute(s) the produced particles if they are cooled down quickly? The binary phase diagram of iron and carbon is depicted in Fig. 2 below. You can assume that, first, all hydrogen gets converted to water and that, second, only $0.5\,\%$ of elemental carbon gets incorporated in nanomagnets whereas the rest becomes soot. If you could no solve c), assume $\phi = 2.00$ instead.
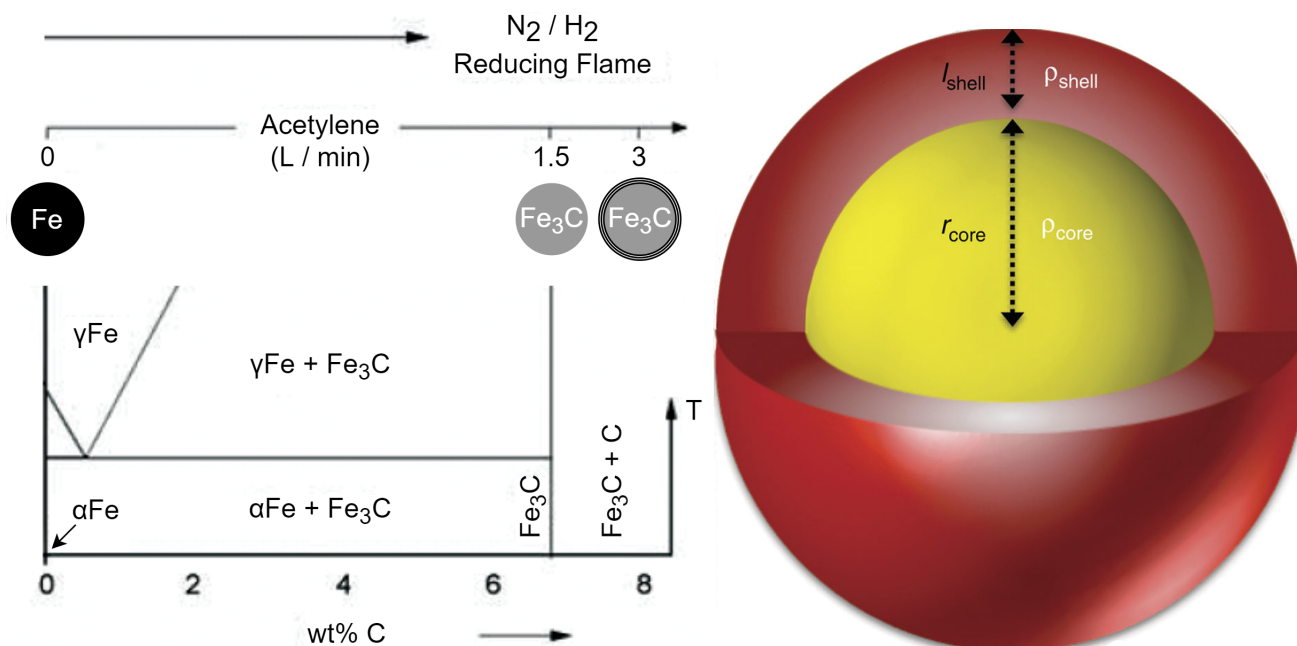


Figure 2: *Left*: Binary phase diagram of iron and carbon. *Right*: Simplified model for carbon-coated iron carbide nanoparticles.

e) Even stronger sooty conditions can be achieved by co-feeding acetylene ($C_2H_2$) to the combustion. Using $5\,L/min$ acetylene, you produced nanomagnets with a carbon mass fraction of $wt\%C = 9.4\,\%$ according to elemental microanalysis. Assuming monodisperse particles with a core radius of $30.00\,nm$, how many graphene layers were deposited on the nanoparticles on average? The density of $Fe_3C$ and C are 7.79 and $2.23\,g\,cm^{-3}$ respectively. In bulk graphite, the interplane distance is $0.335\,nm$.

f) The produced particles were functionalized in three separate reactions to carry amine, nitro or sulfonic acid groups respectively. Unfortunately, the labels of the three vials got mixed up. The IR spectra of all samples are shown below in Fig. 3. Assign structures **A – C** to spectra I – III.

g) Suggest two other methods which you could assign the particles with.

h) The amine particles are finally reacted with stearoyl chloride, $CH_3(CH_2)_{16}COCl$, to demonstrate their surface reactivity. Calculate the yield for this test reaction given elemental analysis before and after the reaction. Assume the mass change during the reaction to be negligible.
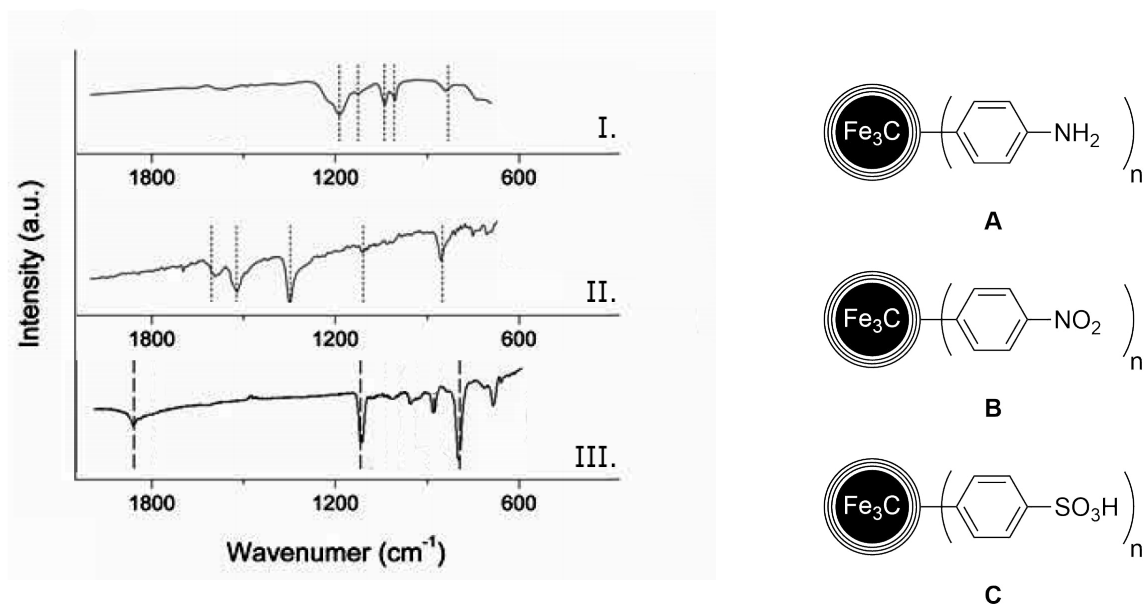
Figure 3: *Left*: Recorded IR spectra of particles **A** - **C**. *Right*: Structure of said functionalized particles.

Table 1: Elemental composition (by mass fraction) of amine functionalized nanomagnets before and
         after reaction.

| Element $i$ | $wt\%_{i,before}$ | $wt\%_{i,after}$ |
|---|---|---|
| C | 9.38 | 11.05 |
| H | 0.02 | 0.31 |
| N | 0.16 | 0.15 |

**PROBLEM 2 - EXCITING PHOTONS AND ELECTRONS**                         **9.0 POINTS**

If a metal plate is irradiated with light, emission of electrons can be detected. The energy needed for an electron to be emitted by a metal is called the work function. In the following exercise we will look at such metal plates and the events taking place as they are irradiated with light.

a) Assume that the energy from the light source is distributed equally on the atoms at the surface of the plate. The light source has an output $P = 1.3\,\mu\text{W}$. The surface of the metal plate is $1.0\,\text{m}^2$ and the ionisation energy of a single metal atom is $1.0\,\text{eV}$. Further, only the atoms on the surface are relevant and an electron per atom takes up a space of $1.3\,\text{Å}^2$.

   • Calculate the number of electrons at the surface of the plate.

   • Calculate the time it would take until the first emission of an electron can be expected. Assume that the energy taken up by the electrons is saved over time.

b) This does not represent what is really observed. Actually, emission of an electron can be observed immediately below a certain wavelength of the light and no emission is observed above this wavelength, regardless of how long the plate is irradiated. Explain this phenomenon briefly (keywords).

c) The work function of zinc, potassium and platinum are $4.34\,\text{eV}$, $2.25\,\text{eV}$ and $5.60\,\text{eV}$. From which wavelength on can emission of an electron be expected for each of these metals, such that they could be used as active material for a photodetector?

d) Calculate the velocity of an electron emitted from aluminium (work function of $4.20\,\text{eV}$) which has absorbed a photon of wavelength of I) $250\,\text{nm}$ and II) $310\,\text{nm}$?

An experiment was conducted to determine the work function of tungsten. A tungsten plate was placed into a vacuum tube and irradiated with light of different wavelengths. As an electron was emitted, an electric potential was applied inside the vacuum tube such that the electron was halted completely. This potential is called the stopping voltage.

Table 2: Experimentally determined stopping voltage for different irradiation wavelengths on a tungsten surface.

| $\lambda_x$ / nm | 134 | 181 | 192 | 223 | 236 | 261 |
|---|---|---|---|---|---|---|
| $V_{stopping}$ / eV | 4.7 | 2.3 | 1.9 | 1.0 | 0.7 | 0.2 |

e) Now the scientists need your help. They have done six measurements at six different wavelengths. Help them determine the work function of tungsten with the six measurements given in the table above.

f) An electron was emitted from a metal plate with a kinetic energy of $3.4\,\text{eV}$. How high of an electrical potential would need to be applied in order to halt the electron completely?

**PROBLEM 3 - ALL ABOUT ELECTROLYSIS**                                                 **18.0 POINTS**

Electrolysis has found application in manufacturing of many useful chemical compounds and revealed new interesting transformations. Sometimes it allows to perform reactions, which normally occur in a reverse way. For example, sodium (Na) reacts with chlorine ($Cl_2$) to form sodium chloride (NaCl), but the electrolysis of molten NaCl reverses this reaction:

$$2\,NaCl\,(l) \xrightarrow{\Delta V} 2\,Na\,(l) + Cl_2\,(g)\uparrow$$
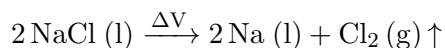
If the electrolysis of an aqueous solution of NaCl is performed, gases are released both on cathode and anode.

 a) Write down the reaction of electrolysis of a solution of NaCl, providing the reactions taking place on cathode and anode.

Imagine we conduct the electrolysis of cold and hot solutions of NaCl constantly mixing the reaction mixture. In both cases you will see that the gas evolution on one of the electrodes will stop.

 b) Rationalize the observation by corresponding chemical reactions (for cold and hot solutions, respectively).

 c) Propose a salt whose aqueous solution does not give any gaseous products when electrolysed. Write down the corresponding reaction of electrolysis.

$6.04\,g$ of some hydrate of copper(II) nitrate **A** were dissolved in $100\,mL$ of distilled water and the solution formed was subjected to electrolysis. The electric current of $1.96\,A$ was applied for $82\,min$ to get equal amounts of gases on the cathode and anode. Note that none of the gases contains nitrogen.

 d) Determine the formula of hydrate **A** and write down all the chemical reactions taking place during the experiment.
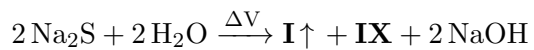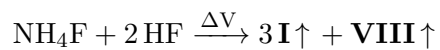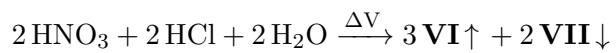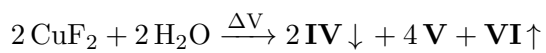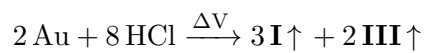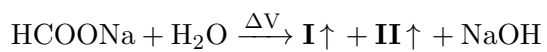
Thermal decomposition of coppe(II) nitrate hydrates occurs in 3 steps. On the first step, the blue copper hydroxy nitrate **B** is formed, which then decomposes to a black solid **C**. In both steps, the mixture of two gases is formed along with the formation of water vapours. If hexahydrate of copper(II) nitrate is decomposed, then the amount of gaseous mixture, including water vapours, on the first step is $57/11$ times higher than on the second. On the third step compound **C** loses $10.06\,\%$ of its mass and forms a red solid **D**.

 e) Determine the formulas of compounds **B–D** and write down all the reactions corresponding to the three steps of decomposition.

Electrolysis allows obtaining different peroxy compounds, which can act as strong oxidants. For instance, electrolysis of ammonium hydrosulfate ($NH_4HSO_4$) gives compound **E** with the same ratio of sulfur and oxygen in it as in $NH_4HSO_4$. The other example is compound **F**, which is formed by electrolysis of borax ($Na_2B_4O_7$) in alkaline solution. The mass percentages (in $wt\%$) of Na and B atoms in **F** are just near to their atomic masses rounded to integer values. The salt **F** has a doubly charged cyclic anion containing two peroxy groups. And the last example is a highly unstable salt **G**, formed by 2-electron oxidation of the carbonate ion during the electrolysis of lithium carbonate ($Li_2CO_3$).

 f) Provide the structural formulas of the anions present in compounds **E–G**.

g) Determine compounds **I–IX** and give their molecular formulas or if the compound is ionic – the formulas of its cation and anion separately (coefficients are already given):

$$HCOONa + H_2O \xrightarrow{\Delta V} \textbf{I}\uparrow + \textbf{II}\uparrow + NaOH$$

$$2\,Au + 8\,HCl \xrightarrow{\Delta V} 3\,\textbf{I}\uparrow + 2\,\textbf{III}\uparrow$$

$$2\,CuF_2 + 2\,H_2O \xrightarrow{\Delta V} 2\,\textbf{IV}\downarrow + 4\,\textbf{V} + \textbf{VI}\uparrow$$

$$2\,HNO_3 + 2\,HCl + 2\,H_2O \xrightarrow{\Delta V} 3\,\textbf{VI}\uparrow + 2\,\textbf{VII}\downarrow$$

$$NH_4F + 2\,HF \xrightarrow{\Delta V} 3\,\textbf{I}\uparrow + \textbf{VIII}\uparrow$$

$$2\,Na_2S + 2\,H_2O \xrightarrow{\Delta V} \textbf{I}\uparrow + \textbf{IX} + 2\,NaOH$$

**PROBLEM 4 - REDOX CHEMISTRY OF CHROMIUM**                                                **9.5 POINTS**

Latimer diagrams are the oldest and most compact way to represent the electrochemical stability of substances with several oxidation states. In the following Latimer diagram, the given values in V are the standard reduction potentials $E°$ at standard conditions of $1.0\,\text{atm}$, $25\,°\text{C}$ and all concentrations are $1.0\,\text{M}$.
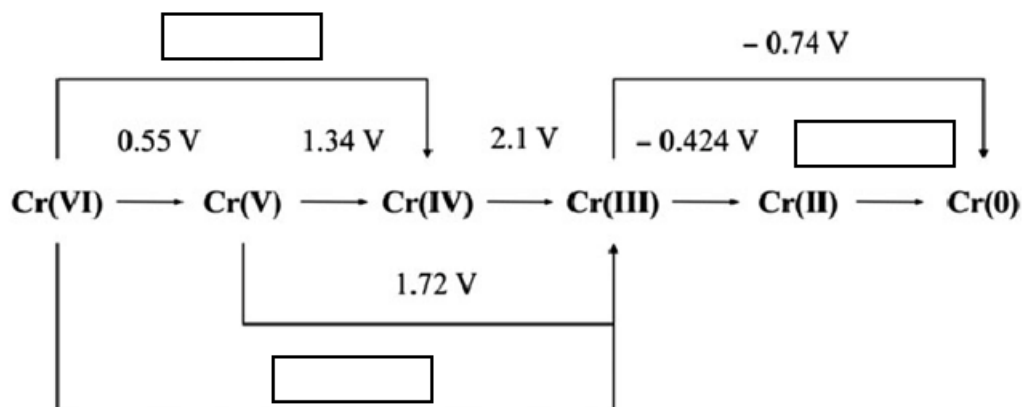


Figure 4: Latimer diagram for chromium at standard conditions.

a) Complete the Latimer diagram for chromium from above.

Another way to represent the electrochemical stability of a substance is the Frost diagram. For this diagram, the oxidation number is plotted against $-\Delta G/F$. Frost diagrams can be drawn for different standard conditions such as pH = 0 or pH = 14 and combined into one single diagram as can be seen down below for chromium. As the oxidation number increases from left to right, this corresponds to the oxidation of the substance. The opposite direction, right to left, accordingly corresponds to the reduction. The "valleys and hills" of the diagram give a hint which species are thermodynamically stable or not. (The Frost diagram below is based on the standard reduction potentials of Chromium at standard conditions and the red curve has the exception that $[\text{H}^+] = 1 \times 10^{-14}\,\text{M}$ whereas everything else conforms to the same standard conditions as the Latimer diagram above.)

b) Complete the two missing species in the Frost diagram: the one with oxidation number +6 at pH = 14, given that:
$$\text{Cr} + 8\,\text{OH}^- \longrightarrow \text{CrO}_4{}^{2-} + 4\,\text{H}_2\text{O} + 6\,\text{e}^-$$
at pH = 14 has $E = -0.73\,\text{V}$, and the one with oxidation number +3 at pH = 0.

c) Which are the most stable and instable species for each pH?

d) Even though standard reduction potentials are defined at pH = 0, they are not very realistic to consider for a biological system. Where in the Frost diagram would the species $\text{Cr}_2\text{O}_7{}^{2-}$ be situated at pH = 7? Hints: Use $E°$ from the Latimer diagram above and the reaction equation:
$$\text{Cr}_2\text{O}_7{}^{2-} + 14\,\text{H}^+ + 12\,\text{e}^- \longrightarrow 2\,\text{Cr}(0) + 7\,\text{H}_2\text{O}$$
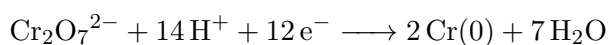
e) Write down the balanced equation for one comproportionation and one disproportionation from the Frost diagram above. (Take a look at the "hills and valleys" of the diagram.)

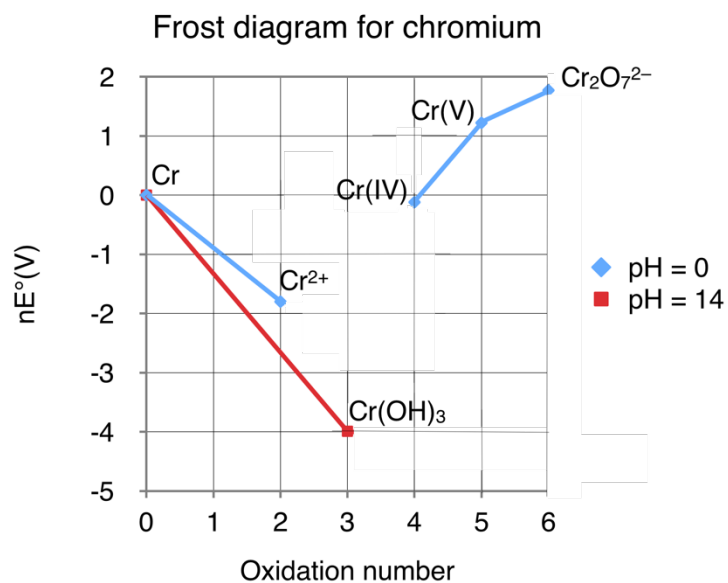In Fig. 6 the electrochemical properties from Ca to Cu are combined into one single Frost diagram.

Figure 5: Frost diagram for chromium at standard conditions and at pH $= 14$.

f) If we take a closer look at the diagram, we can see that the only lines that ever cross are the ones of Cr and Mn at the oxidation number $+2$. Suggest a reason for this. (Hint: Take into account their $d$-electron configuration.)
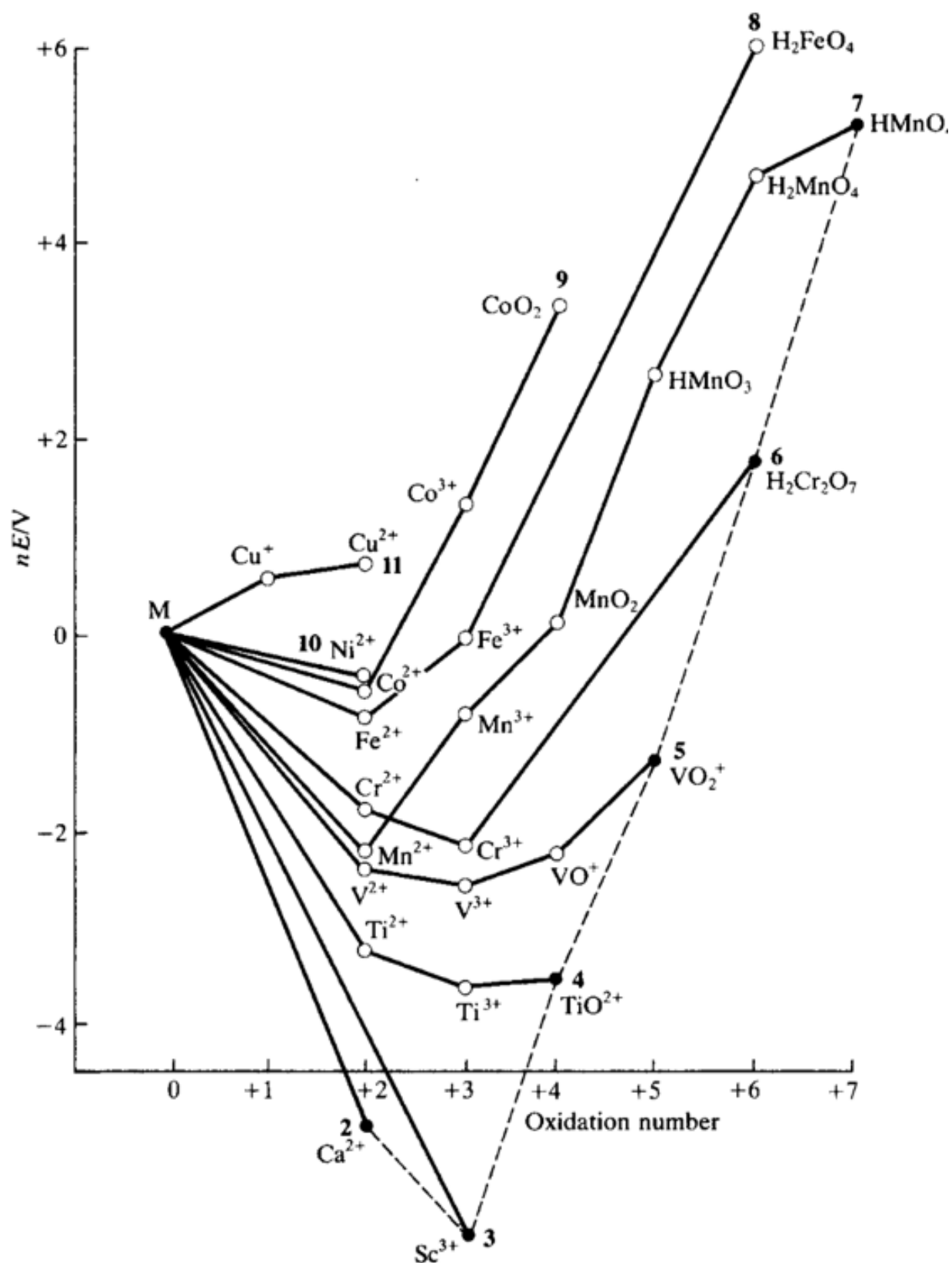
Figure 6: Combined Frost diagrams for $3s$ and $3d$ metals at standard conditions.

**PROBLEM 5 - ENZYME KINETICS**                                        **10.5 POINTS**

Enzymes are perhaps the most important biological molecules that maintain all the cellular cycles. They represent highly selective catalysts for almost every reaction in the human body, starting from digestion to synthesis of DNA.

To describe the mechanism of enzyme catalysis, the Michaelis-Menten mechanism (MM) was introduced in 1913. This mechanism describes the reaction of enzyme **E** with the substrate **S**. It gives the dependence of the maximal reaction rate $v_{max}$ as a function of the substrate concentration $[S]_0$. In a nutshell, the mechanism suggests that before the irreversible formation of the final product **P**, a reversible step involves the formation of an enzyme-substrate complex **ES**:

$$E + S \underset{k_2}{\overset{k_1}{\rightleftarrows}} ES \overset{k_3}{\longrightarrow} E + P$$
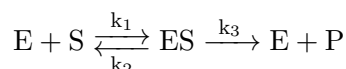
a) To describe an enzyme reaction using only easily measurable quantities such as the initial enzyme concentration $[E]_0$ and the substrate concentration S the following expression was derived:

$$v = \frac{k_3 [E]_0}{1 + K_M/[S]_0}$$

, where $K_M$ is defined as $(k_2 + k_3)/k_1$ and is the so-called Michaelis-constant. You are supposed to show this by following the outlined sub-questions:
- Write down the rate equation for the formation of product **P**.
- Do likewise for the formation of **ES**.
- Use the steady state approximation for **ES**.
- Use $[E]_0 = [E] + [ES]$

b) Write the equation for $v_{max}$ and sketch the graph of $v$ as a function of $[S]_0$.

c) The MM equation is more useful after linearization when assessing enzymatic activity. The so called Lineweaver-Burk plot is obtained by plotting $1/v$ vs. $1/[S]_0$. Linearize the MM equation derived in a). Sketch the obtained Lineweaver-Burk plot, denoting the slope and the intercept.

The catalytic efficiency $\epsilon$ of an enzyme, is defined as $\epsilon = k_3/K_M$ and describes how fast an enzyme can overall convert its substrate to product.

d) In which case does $\epsilon$ reach its maximum value? (Hint: consider the chemical problem at hand, not only the equation).

Carbonic anhydrase is an enzyme that catalyses the hydration of $CO_2$ in the red blood cells to give the bicarbonate ion and the reverse reaction in the lungs. Without this reaction, the bicarbonate buffer of the blood couldn't be sustained, leading to systematic acidosis and shut down of the respiratory system. For a reaction at pH = 7.1, T = $273.5\,$K and $[E]_0 = 2.3\,$nM the following data is obtained:

Table 3: Measured reaction rates $v$ for given $CO_2$ concentrations.

| $[CO_2]$ / mM | 1.25 | 2.50 | 5.00 | 20.0 |
|---|---|---|---|---|
| $v$ / mM/s | 0.0278 | 0.0500 | 0.0833 | 0.167 |

e) Determine the catalytic efficiency and the value of $K_M$ (either arithmetically or graphically) using the principles in the previous points, bearing in mind that the reaction was monitored according to MM.

**PROBLEM 6 - RADIOPHARMACEUTICAL TECHNETIUM**                              **12.5 POINTS**

Technetium is a very rarely encountered element of the periodic table and was the first element to be produced artificially. Several complexes of technetium have found their use in medicine, where they are employed as radioactive tracers (radiopharmaceuticals) for the diagnosis of various diseases.

The diagnostically relevant isotope of Tc is the so-called $^{99m}$Tc, a metastable $\gamma$-emitter nucleus. It is obtained from radioactive $^{99}$Mo (itself being a fission product of $^{235}$U) and ultimately decays to the stable isotope $^{99}$Ru.

a) Complete the equations below and indicate what type of radiation is accompanying these nuclear decay processes.

$$^{99}\text{Mo} \longrightarrow \ldots + \ldots$$
$$^{99m}\text{Tc} \longrightarrow \text{M} + \ldots$$
$$\text{M} \longrightarrow \ldots + \ldots$$
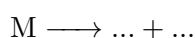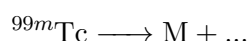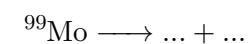
The particular form the $^{99m}$Tc is typically obtained as, is $TcO_4^-$ (the so-called pertechnetate ion **A**), which itself has found application as a radiopharmaceutical (in e.g. thyroid diagnostics). More typically however, the $TcO_4^-$ is being reduced with $SnCl_2$ and complexed by different ligands to give a variety of radiopharmaceuticals. One important example is $[Tc(MIBI)_6]^+$ **B**, a complex containing isonitrile ligands whose structure is shown in figure 7.
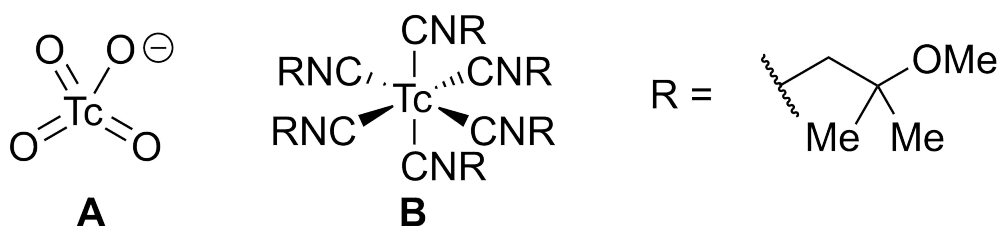


Figure 7: Structure of the pertechnetate anion **A** as well as the $[Tc(MIBI)_6]^+$ complex **B**.

b) Based on this information, what Mo-precursor is used for the synthesis of **A** and what would be a suitable way to separate remaining starting material from the product $TcO_4^-$?

c) Determine the oxidation numbers of the Tc-atoms in **A** and **B** and write a balanced redox-equation for the production of $[Tc(MIBI)_6]^+$ from $TcO_4^-$.

d) Based on the oxidation numbers of the two complexes, determine the $d$-electron count and draw ligand-field diagrams for the two complexes. Would you expect the complexes to be diamagnetic or paramagnetic? Justify why!

Radiopharmaceuticals are highly potent imaging agents and therefore only need to be administered in very low doses. $^{99m}$Tc has a physical half-life of $6.0\,\text{h}$ and a typical dose of $[Tc(MIBI)_6]^+$ has an initial activity of $500\,\text{MBq}$ ($1\,\text{Bq} = 1\,\text{s}^{-1} = 1\,\text{decay per second}$).

e) Calculate how many $^{99m}$Tc nuclei are required to achieve this activity and the mass of $[Tc(MIBI)_6]^+$ that needs to be administered.

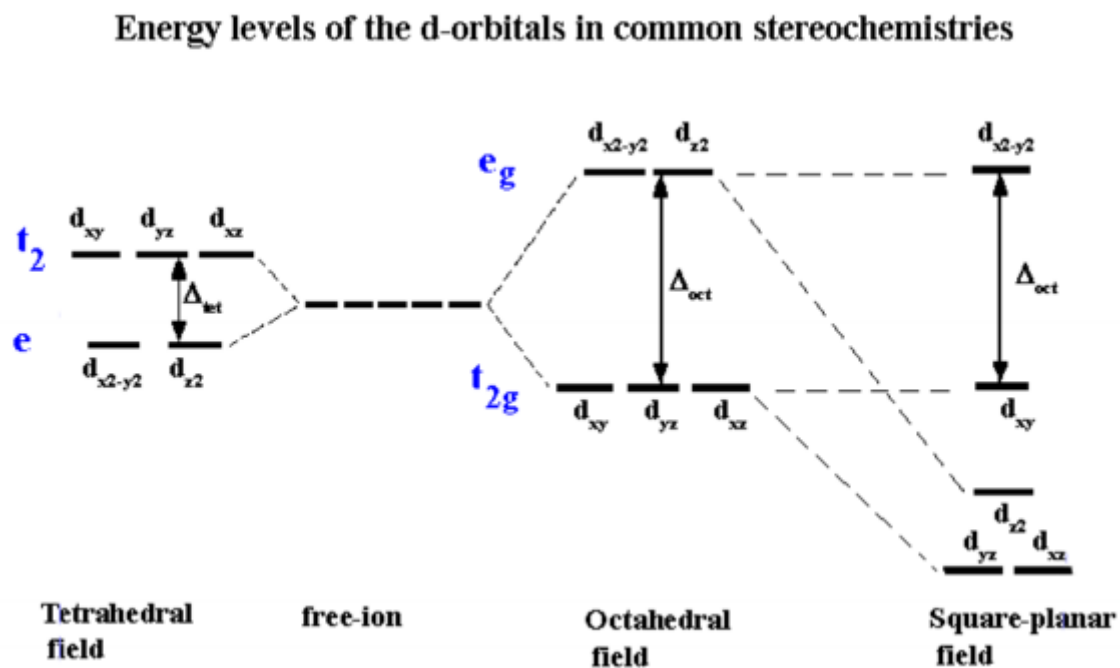## Energy levels of the d-orbitals in common stereochemistries



Figure 8: Crystal field splitting of different coordination geometries.

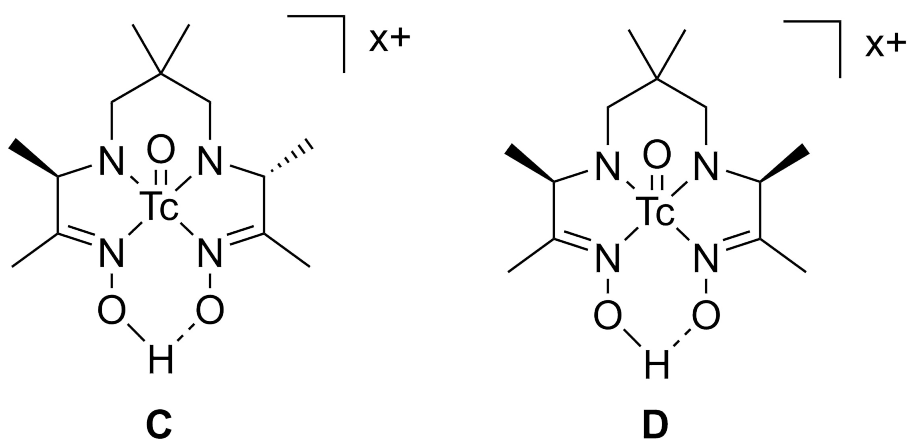Another very important Tc-Radiopharmaceutical is $^{99m}$Tc-HMPAO shown as two stereoisomers in figure 9.



Figure 9: Two stereoisomers of $[\text{Tc(HMPAO)}]^{x+}$.

f) Determine the overall charge x of this Tc-complex, given that the oxidation state on Tc is +5.

g) Based on the crystal-field splitting of an octahedral geometry, how would the crystal field splitting look like for such a complex?

h) Which of the two shown stereoisomers shown **C** and **D** are chiral? Justify your answer.

**PROBLEM 7 - AROMATICITY – LORD OF THE RINGS**                                    **13.0 POINTS**

Aromatic molecules have fascinated chemists ever since they were originally discovered. They are widespread in nature and have found a plethora of uses to mankind. In this task we will try to have look at the underlying principles of aromaticity of molecules based on their molecular-orbital (MO) diagrams.
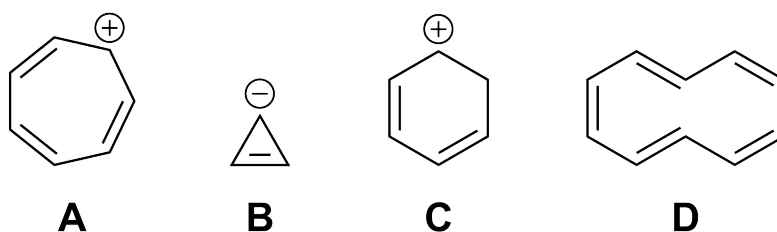


Figure 10: Stuctures of potentially aromatic compounds **A** - **D**.

   a) For the shown molecules **A** - **D**, denote whether these are considered aromatic, anti-aromatic or non-aromatic according to Hückel's rule.

In the following we will look deeper at the following series of molecules:
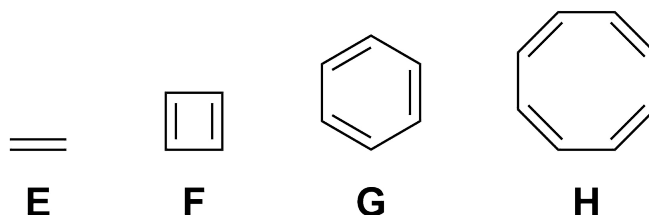


Figure 11: Structures from left to right: ethylene **E**, cyclobutadiene **F**, benzene **G**, cyclooctatetraene **H**.

Frost-Musulin diagrams are a useful aid for the construction of MO-diagrams of such cyclic $\pi$-systems and can easily be constructed as follows: Draw a circle with the arbitrary radius $2\beta$. Draw the shape of an equilateral polygon into the circle with one corner of the polygon facing straight down. Note that $\beta$ is typically considered as a negative factor by convention and the lowest point of the circle has therefore an energy of $\alpha + 2\beta$.
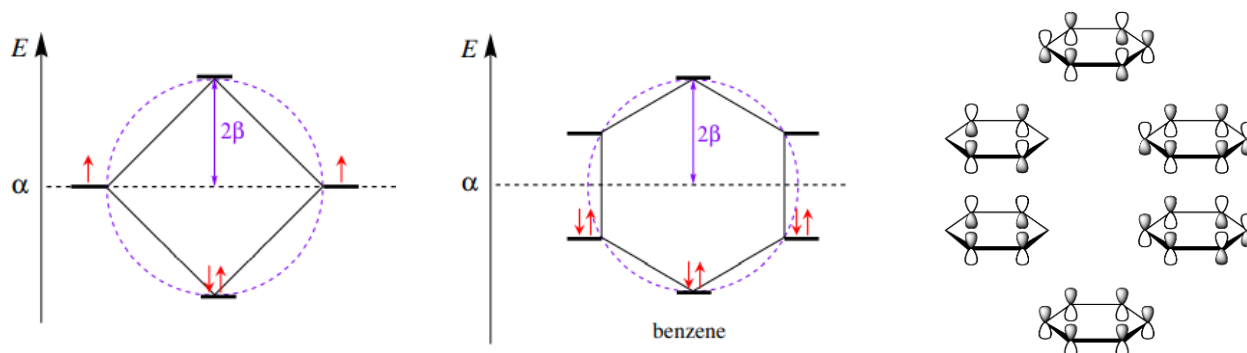


Figure 12: *Left*: Frost-Musulin diagram for cyclobutadiene. *Middle*: Frost-Musulin diagram for benzene. *Right*: Molecular orbitals for benzene.

To construct a Frost-Musulin diagram, everywhere the polygon touches the circle, draw a horizontal line which corresponds to the energy level of a MO. Above, the Frost-Musulin diagrams of cyclobutadiene **F** and benzene **G** are shown as an example.

b) Draw the Frost-Musulin diagram of cyclooctatetraene **H** and fill in the $\pi$-electrons. Estimate the energy levels (in terms of the factor $\beta$) based on your sketch.

c) In analogy to the shown MO-diagram of benzene draw all the molecular orbitals of flat cyclobutadiene **F** and flat cyclooctatetraene **H**. Hint: It is enough to show a projection of the molecule from the top to save time while drawing.

The factor $\beta$ used to draw the Frost-Musulin diagrams is related to the binding energy of ethylene. Given the MO-diagram of ethylene below, summation over all occupied orbitals for each filled-in electron yields an electronic energy of $2\alpha + 2\beta$ for ethylene.
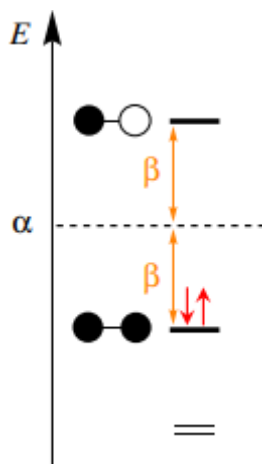


Figure 13: MO-diagram for ethylene.

d) Calculate the electronic energies of cyclobutadiene **F**, benzene **G** and cyclooctatetraene **H** based on their MO diagrams.

e) Compare the obtained values with the energy of the corresponding "localized structures", i.e. treating e.g. benzene as if it was a system of three non-interacting ethylene units (cyclohexatriene) and thereby effectively neglecting the effect of electron delocalization in the ring. Is this simple argument enough to explain why cyclobutadiene and cyclooctatetraene are antiaromatic?

Both, cyclobutadiene **F** and cyclooctatetraene **H** in the previously shown flat geometry are antiaromatic. They try to avoid this property in two different ways: Cyclooctatetraene is flexible enough to distort out of planarity, while cyclobutadiene undergoes an in-plane distortion and gets from a square to a more rectangular shape.

f) Draw the geometry of non-planar cyclooctatetraene **H** (keep in mind that all double-bonds in the ring still need to have cis-configuration).

g) Draw the Frost-Musulin diagram of a rectangular-distorted cyclobutadiene **F**. How do you expect the electron configuration to change?

**PROBLEM 8 - NMR DYNAMICS - FAST OR SLOW?**                    **14.0 POINTS**

Chlorocyclohexane, $C_6H_{11}Cl$, is a simple organic halide that finds limited application as a reagent in cross-coupling reactions or as a solvent slightly more polar than cyclohexane.

a) How many cyclic constitutional isomers of $C_6H_{11}Cl$ could theoretically exist? (Start by drawing the different C–H backbones and only then decide how many chloro regioisomers exist per backbone structure)

b) How many peaks do you expect in the $^1$H NMR spectra of the parent hydrocarbons?

Below, you can find a simulated $^1$H NMR spectrum of chlorocyclohexane in $CDCl_3$ at $300\,MHz$ at $298\,K$.
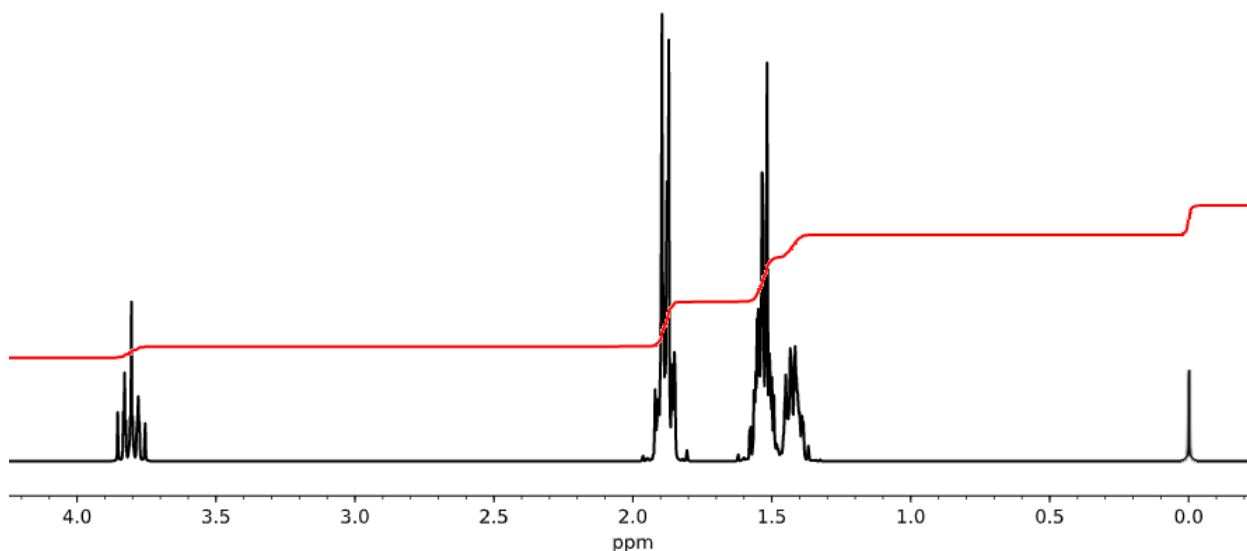


Figure 14: Simulated $^1$H NMR spectrum for chlorocyclohexane in $CDCl_3$ at $300\,MHz$ at $298\,K$.

c) Assign all peaks to the protons in the structure.

d) What is the peak at 0.00 ppm?

Experimentally, you record a $^1$H NMR spectrum for a chlorocyclohexane sample in $CDCl_3$ at $300\,MHz$ and both at $298\,K$ and at $192\,K$. To your surprise, you now find two peaks near $4.00\,ppm$ in the $192\,K$ spectrum.
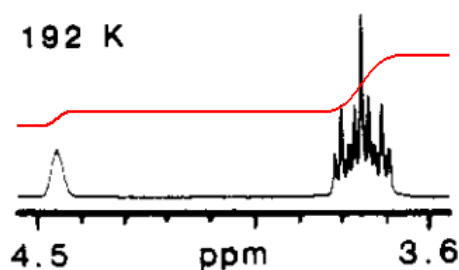


Figure 15: Recorded $^1$H NMR spectrum for chlorocyclohexane in $CDCl_3$ at $300\,MHz$ at $192\,K$ near $4.00\,ppm$.

e) Provide an explanation with structures for the observation of the splitting of the signal near $4.00\,ppm$.

f) What is the expected peak splitting for both peaks? Draw the splitting diagrams for both and label the type of expected patterns. Why is it experimentally only observed for one of the two peaks?

g) Calculate the change in $\Delta$G for a chloride substituent at $192\,\text{K}$ in kcal/mol.

h) Finally, you record even more spectra at different temperatures and the obtained fitted inter-conversion rates as shown below. Calculate the activation energy in kcal/mol for the observed interconversion. You can assume the activation energy is constant over the whole temperature range.
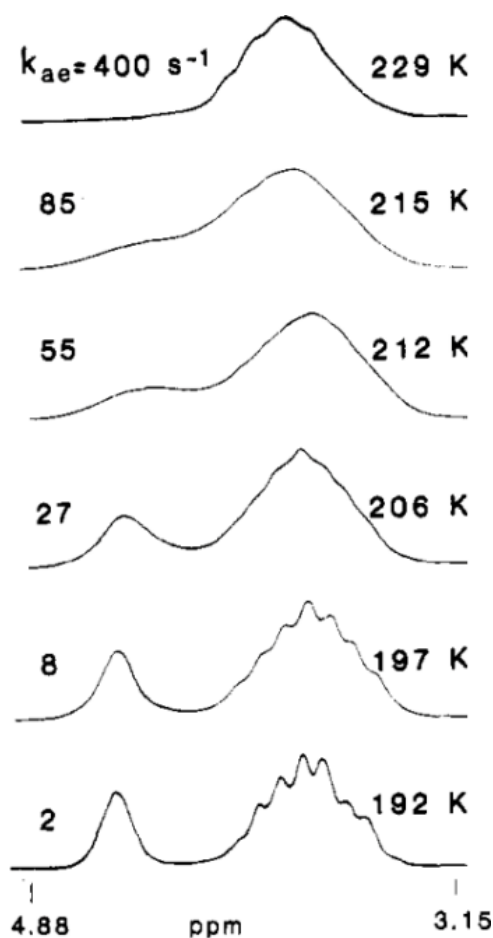


Figure 16: Series of $^1$H NMR spectra for chlorocyclohexane in CDCl$_3$ at $300\,\text{MHz}$ near $4.00\,\text{ppm}$ recorded at different temperatures. Fitted interconversion rates going from the axial to the equatorial conformer.

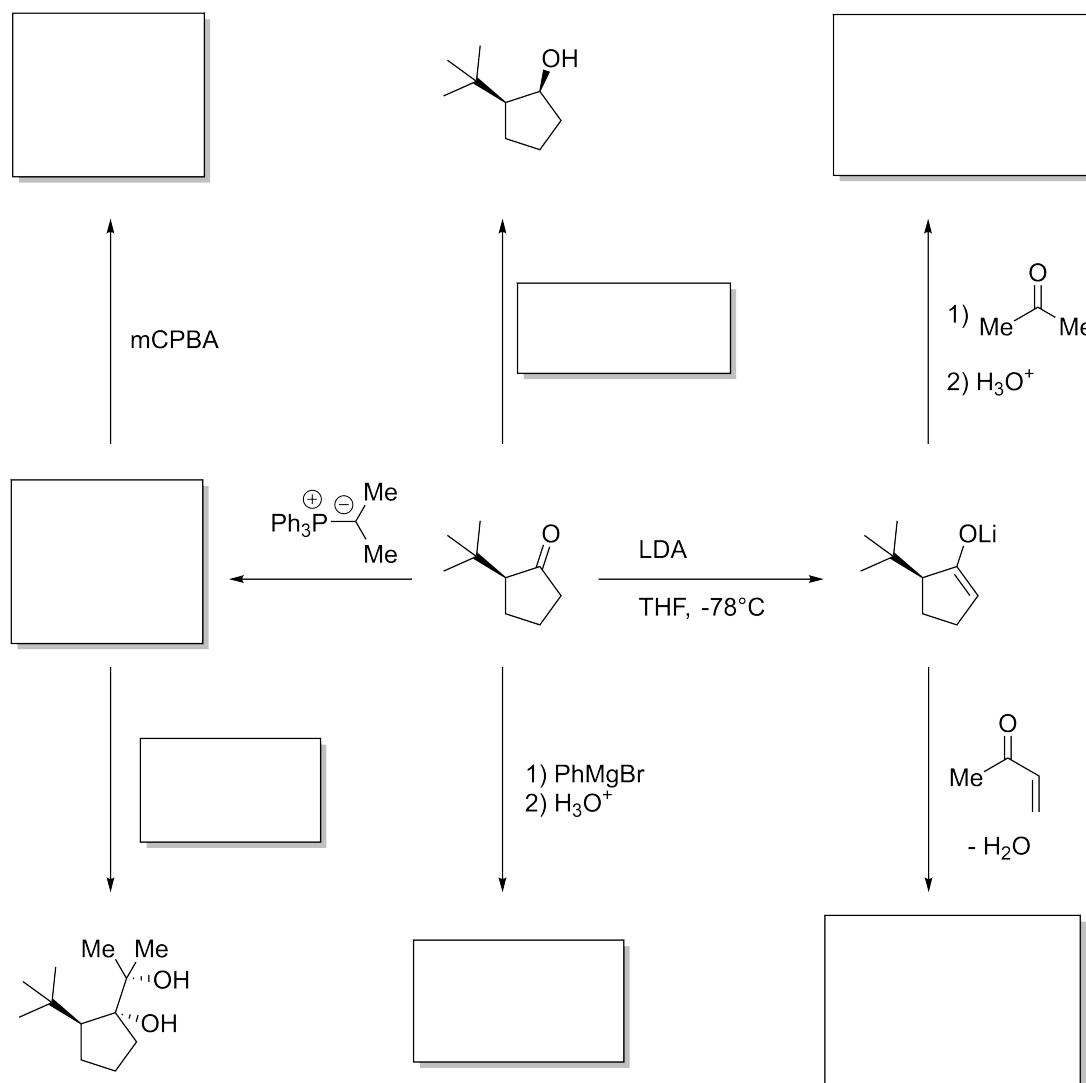**PROBLEM 9 - MIRROR, MIRROR ON THE WALL – CHIRALITY FAIRYTALES**          **11.5 POINTS**



Figure 17: Scheme involving 2-*tert*-butylcyclopentanone.

a) For the scheme shown above fill in all the boxes. Provide stereoinformation where necessary.

b) Determine the absolute configuration of the following molecules **A** containing a plane and **B** containing an axis of chirality. Justify your answer.
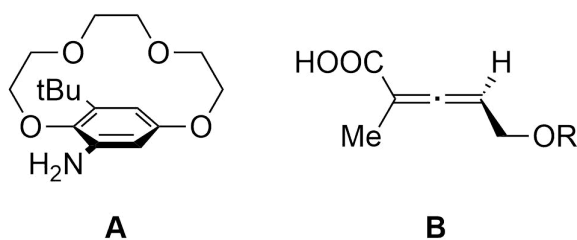


Figure 18: Two molecules showing planar or axial chirality.

c) For the two shown bis-helical systems **C** and **D**, determine the helicality for all helical elements. Which of these stereoisomers are chiral? How do the two stereoisomers relate to each other?
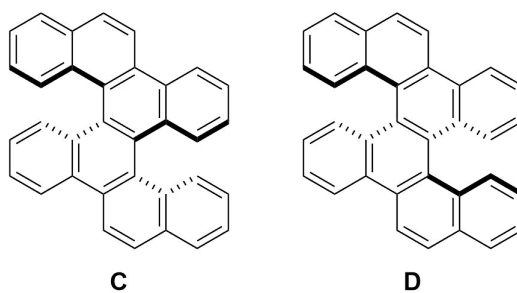


Figure 19: Two molecules **C** and **D** showing potential helical chirality.

## Problem 10 - Total Synthesis of Clavizepine

16.0 Points

(-)-Clavizepine (1) is an alkaloid isolated in 1986 from *Corydalis claviculata* and first synthesized as a racemic mixture by the Japanese organic chemist Hiroyuki Ishibashi. One intriguing feature is the presence of a pharmacologically attractive 1-aryl-3-benzazepine moiety as highly selective central D-1 dopamine receptor antagonists. The key step is of this synthesis a Pummerer rearrangement to form elegantly the 7-membered ring.
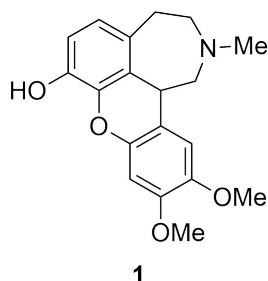


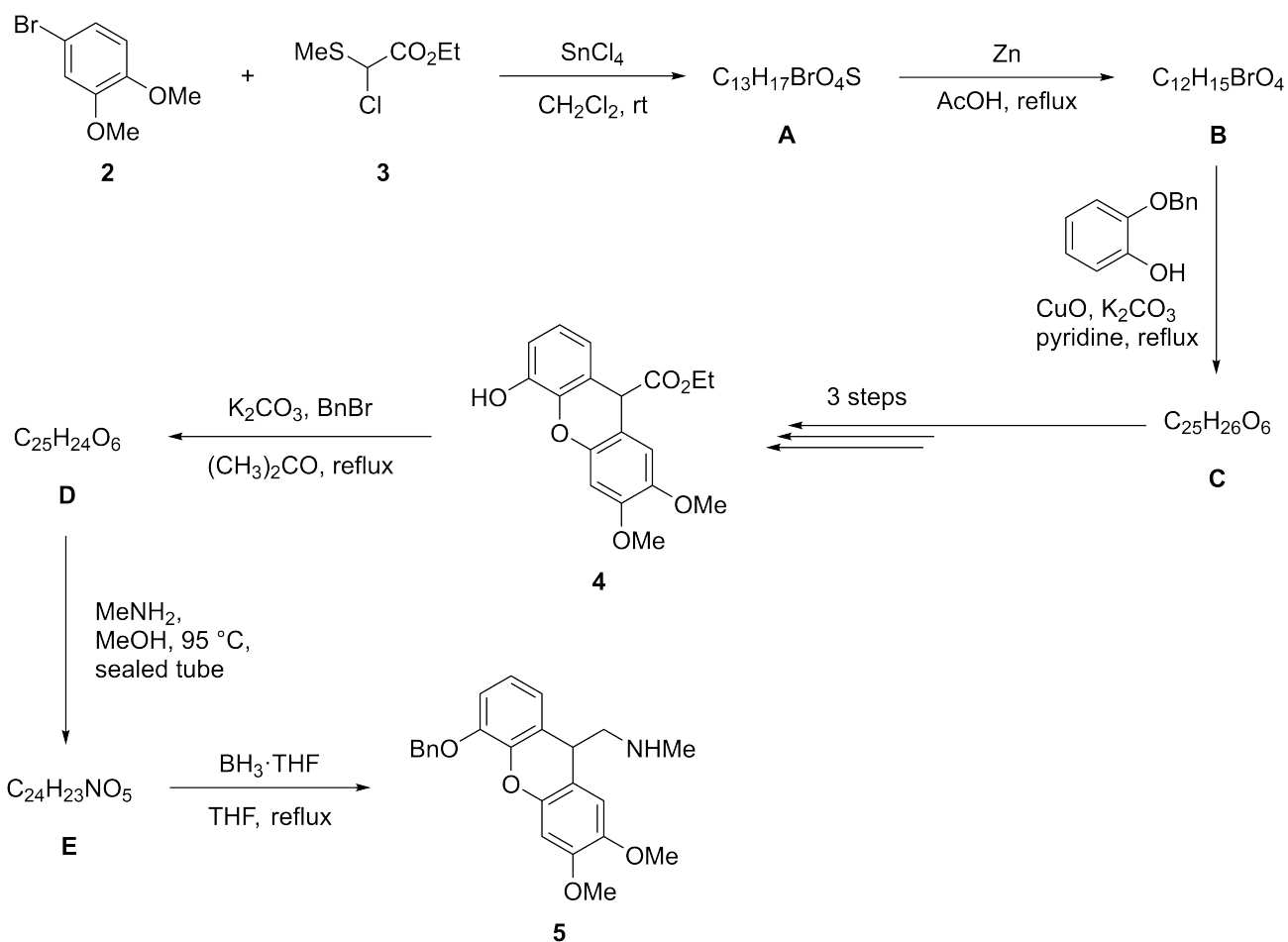Figure 20: Structure of clavizepine without stereoinformation.



Figure 21: First half of Ishibashi's route.

a) Draw the structures of compounds **A – E** without stereochemistry.
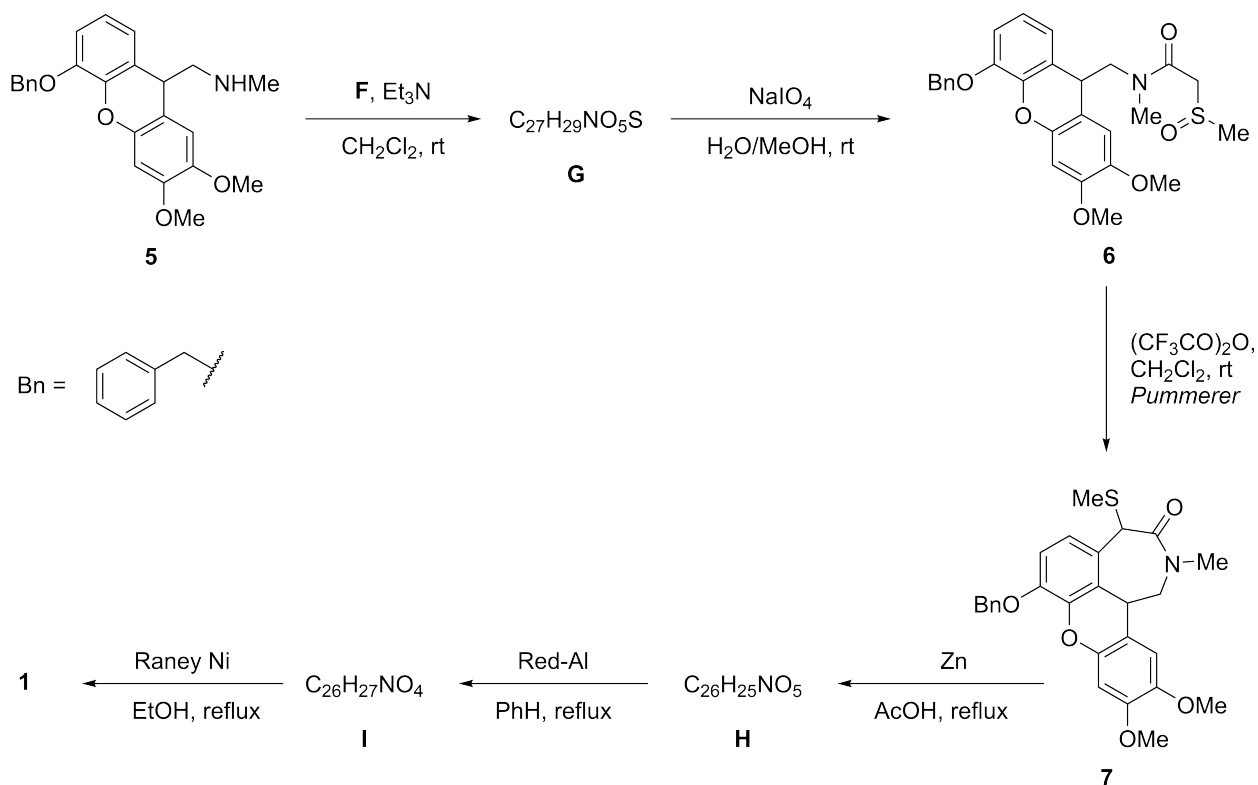
Figure 22: Second half of Ishibashi's route. rt = room temperature.

b) Suggest a suitable structure for reagent **F**.

c) Draw the structures of compounds **G** – **I** without stereochemistry.

d) (-)-Clavizepine (**1**) has S-configuration. Draw the natural production with its proper stereochemistry.

e) How would you prepare (-)-clavizepine based on Ishibashi's route?

Hints:

- Reducing agents:
    - Zn, selective for C–S bonds
    - BH$_3$·THF
    - Red-Al
    - Raney Ni, for removal of benzyl protecting groups

- Oxidizing agents:
    - NaIO$_4$, for vicinal diols and sulfides

An alternative route to obtain enantiopure 1-aryl-3-benzazepines is based on the racemic separation by camphor-10-sulfonic acid.
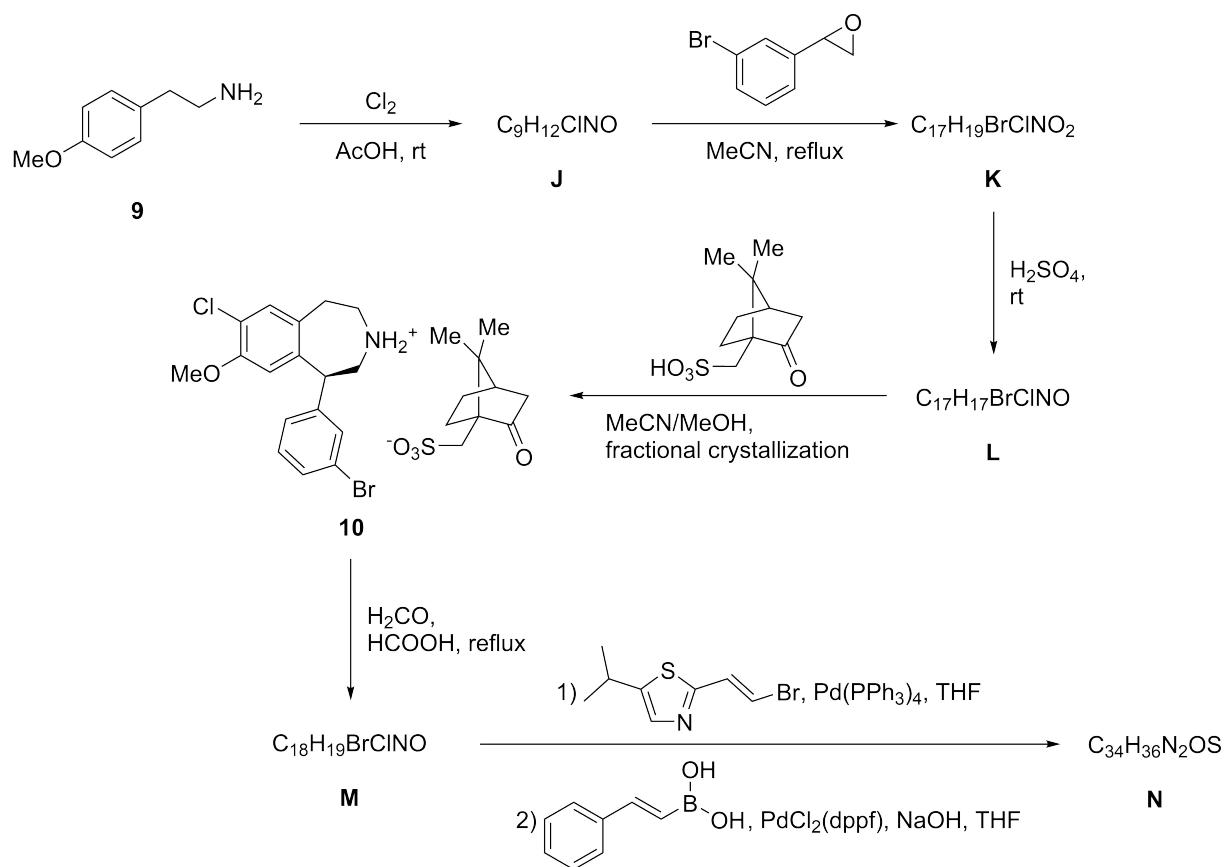


Figure 23: Alternative route for clavizepine derivatives. dppf = bis(diphenylphosphino)ferrocene.

f) Draw structures **J** – **N** including stereochemistry.