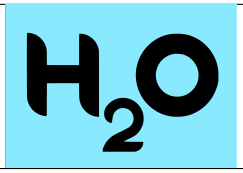
General Instructions

- This examination has **10 problems**.
- Each signal is given by the ringing of a cowbell.
- You may begin working as soon as the **START** command is given. You will then have **5 hours** to complete the exam.
- All results must be written in the appropriate answer boxes with pen on the **answer sheets**. Use the back of the question sheets if you need scratch paper. Remember that answers written outside the answer boxes will not be graded.
- Write relevant calculations in the appropriate boxes when necessary. Full marks will be given for correct answers only when your work is shown.
- For the multiple choice questions, **if you want to change your answer**, fill the tick box completely and then make a **new box next to it**.
- Use only the pen and calculator provided.
- The official English version of this examination is available on request for clarification only.
- The supervisors will announce a **30-minute** warning before the **STOP** command.
- You **must stop** working when the **STOP** command is given. Failure to stop writing can lead to the nullification of your examination.
- After the supervisor tells you to do so, put **all sheets with the cover sheet on top** back into the envelope. **Do not** seal the envelope.
- You are not allowed to leave your working place without permission. If you need any assistance, raise the corresponding nonverbal communication card (see table below for meanings).
- **Do not** draw anything into or close to the QR codes.

		
I need to use the toilet, grab a snack, or take a break	I need my water bottle refilled	I need to see the official English version for clarification

Meanings of the non-verbal communication cards.

GOOD LUCK!

Problems and Grading Information

	Title	Question Pages	Answer Pages	Total Score	Percentage
1	Molecular Imaging	3	4	**22**	5
2	Electrochemical CO_2 Reduction	4	5	**33**	5
3	Artificial Photosynthesis	4	6	**29**	6
4	Fluorinated and Hypervalent Compounds	6	4	**34**	6
5	Hydrodesulfurization	3	4	**34.5**	7
6	Direct Conversion of Methane to Methanol	3	5	**32**	7
7	Enzyme Kinetics	3	5	**34**	7
8	Nazarov Reaction	3	3	**31**	5
9	Electrolysis in Organic Synthesis	6	5	**29**	6
10	Switzerland - The Country of Pharmaceuticals	6	4	**39**	6
Total					**60**

Physical Constants and Equations

Constants

Planck constant	$h = 6.626 \cdot 10^{-34}\ \mathrm{J\ s}$
Boltzmann constant	$k_B = 1.381 \cdot 10^{-23}\ \mathrm{kg\ m^2\ s^{-2}\ K^{-1}}$
Speed of Light	$c = 2.998 \cdot 10^{8}\ \mathrm{m\ s^{-1}}$
Elementary charge	$e = 1.602 \cdot 10^{-19}\ \mathrm{C}$
Avogadro constant	$N_A = 6.022 \cdot 10^{23}\ \mathrm{mol^{-1}}$
Universal gas constant	$R = 8.314\ \mathrm{J\ mol^{-1}\ K^{-1}}$
Faraday constant	$F = 96485\ \mathrm{C\ mol^{-1}}$
Standard pressure	$p_0 = 1 \cdot 10^5\ \mathrm{Pa} = 1\ \mathrm{bar}$
SHE:	Standard Hydrogen Electrode ($p = 1\ \mathrm{bar}$)
Electronvolt	$1\ \mathrm{eV} = 1.602 \cdot 10^{-19}\ \mathrm{J}$
Electric Charge & Current	$1\ \mathrm{C} = 1\ \mathrm{A} \cdot 1\ \mathrm{s}$
Absolute zero	$0\ \mathrm{K} = -273.15\ ^\circ\mathrm{C}$
Ångstrom	$1\ \text{Å} = 10^{-10}\ \mathrm{m}$
pico (p)	10^{-12}
nano (n)	10^{-9}
micro (μ)	10^{-6}
milli (m)	10^{-3}
centi (c)	10^{-2}
deci (d)	10^{-1}
kilo (k)	10^{3}
mega (M)	10^{6}
giga (G)	10^{9}
tera (T)	10^{12}
Pi (π)	$\pi = 3.141592\ldots$
Euler's number	$e = 2.718281\ldots$

Equations

Ideal gas law	$pV = nRT = Nk_BT$
Gibbs free energy	$\Delta G = \Delta H - T\Delta S$ $\Delta G^\circ = -RT \ln K^\circ$ $\Delta_r G^\circ = -nFE^\circ_{cell}$ where n is the number of electrons $\Delta_r G = \Delta_r G^\circ + RT \ln Q$
Reaction quotient Q for reaction: $aA+bB \rightleftharpoons cC+dD$	$Q = \frac{[C]^c[D]^d}{[A]^a[B]^b}$
Nernst equation	$E = E_0 - \frac{RT}{nF} \ln Q$
Electric current	$I = Q/t$
Faraday equation	$I \cdot t = n \cdot z \cdot F$
Energy of charge q in electric field	$E = k\frac{q_1 q_2}{d}$
Arrhenius law	$k = A \exp\left(\frac{-E_A}{RT}\right)$
Lambert Beer equation	$A = \log(I_0/I_1) = \varepsilon \cdot l \cdot c$
Henderson-Hasselbalch equation	$\mathrm{pH} = \mathrm{pK_a} + \log(\frac{[A^-]}{[HA]})$
Energy of a photon	$E = h\nu = \frac{hc}{\lambda}$
Integrated rate laws for …	
… zeroth order	$[A] = [A]_0 - kt$
… first order	$\ln[A] = \ln[A]_0 - kt$
… second order	$\frac{1}{[A]} = \frac{1}{[A]_0} + kt$
Half life for a first order reaction	$t_{1/2} = \frac{\ln 2}{k}$
Half life for a second order process	$t_{1/2} = \frac{1}{[A]_0 k}$
Radioactivity	$A = k \cdot N$
Surface area of a sphere with radius R	$A = 4\pi R^2$
Volume of a sphere with radius R	$V = \frac{4\pi}{3} R^3$

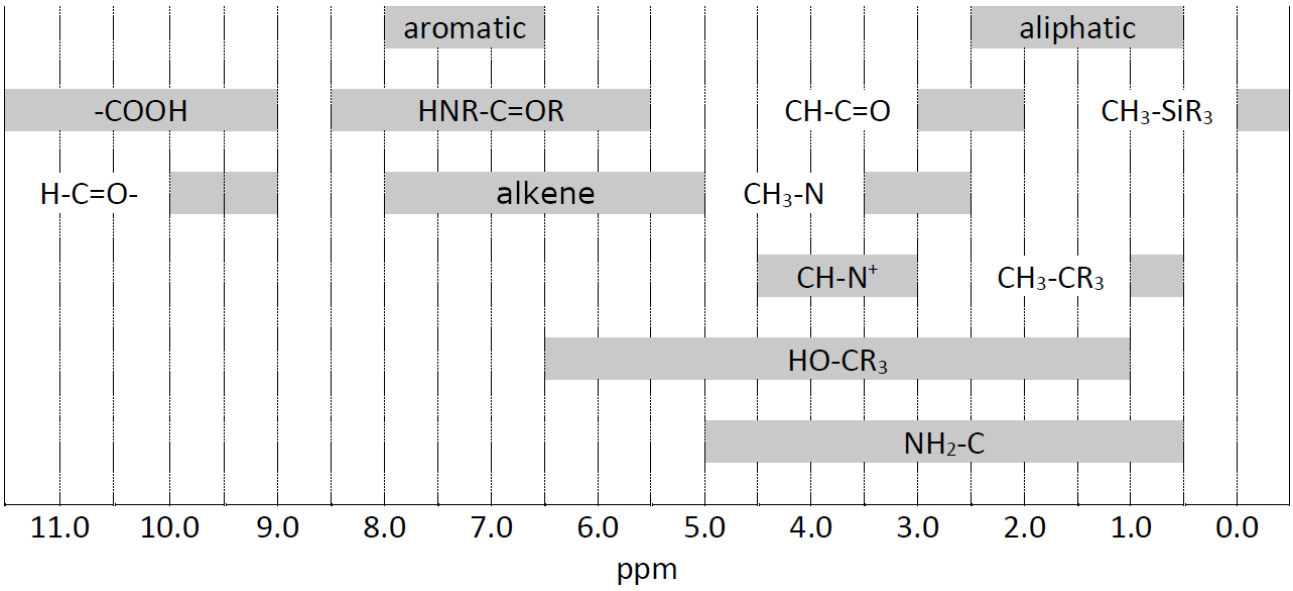
Periodic Table of the Elements

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]

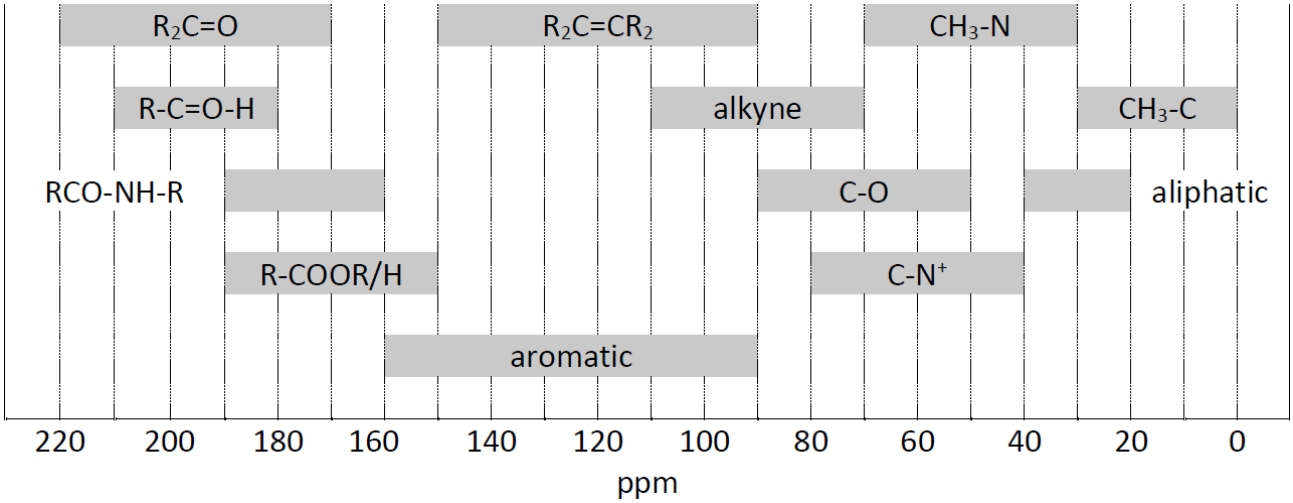
Table of NMR Chemical Shifts

^{1}H NMR Chemical Shifts



Possible translation for aromatic, aliphatic and alkyne

^{13}C NMR Chemical Shifts

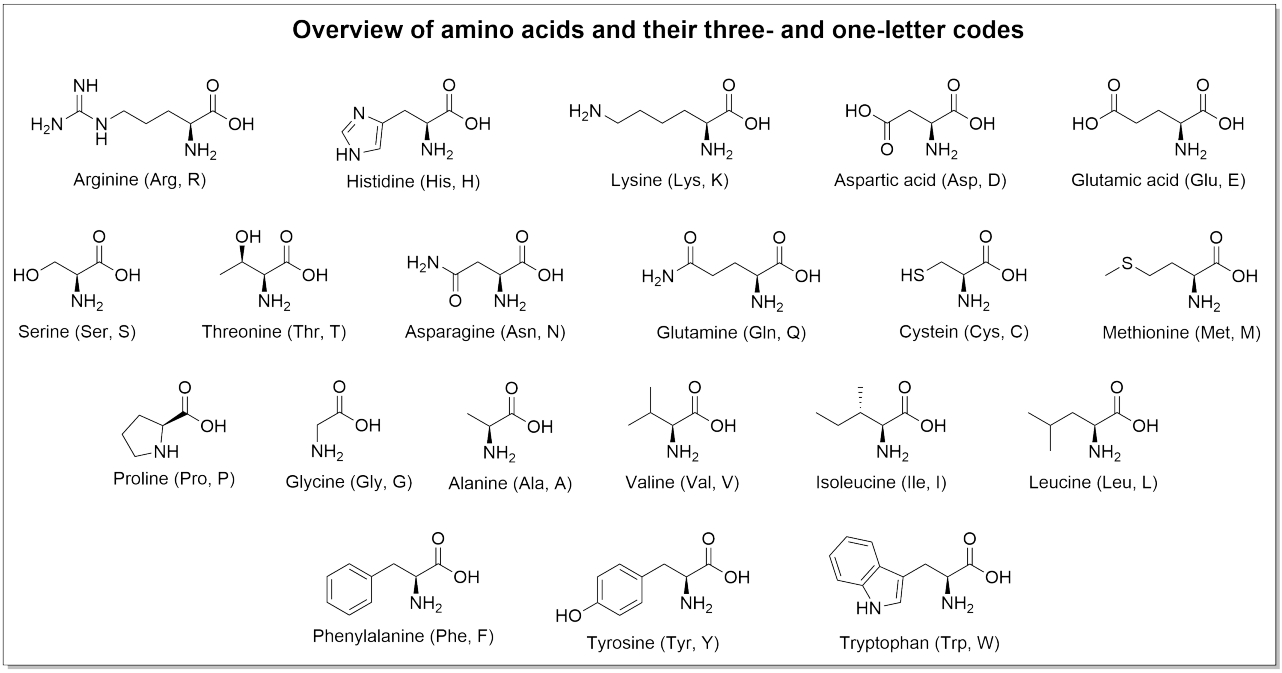


Possible translation for aromatic, aliphatic and alkyne

^{1}H NMR Coupling Constants

Type of hydrogen	$\lvert J_{ab} \rvert$ (Hz)
$R_2CH_aH_b$	4-20
R_2CH_a-CR_2H_b	2-12
R_2CH_a-CR_2-CR_2H_b	If rotation free: < 0.1 Otherwise (fixed): 1-8
RH_aC=CRH_b	*cis*: 7-12 *trans*: 12-18
R_2C=CH_aH_b	0.5-3
RH_aC=CR-CR_2H_b	0.5-2.5

List of Amino Acids



Possible translations for the English expressions in the figure above.

Molecular Imaging - Solutions

5% of total											
Question	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9	1.10	**Total**
Points	1	2	2	1	1	2	4	4	2	3	**22**
Score											

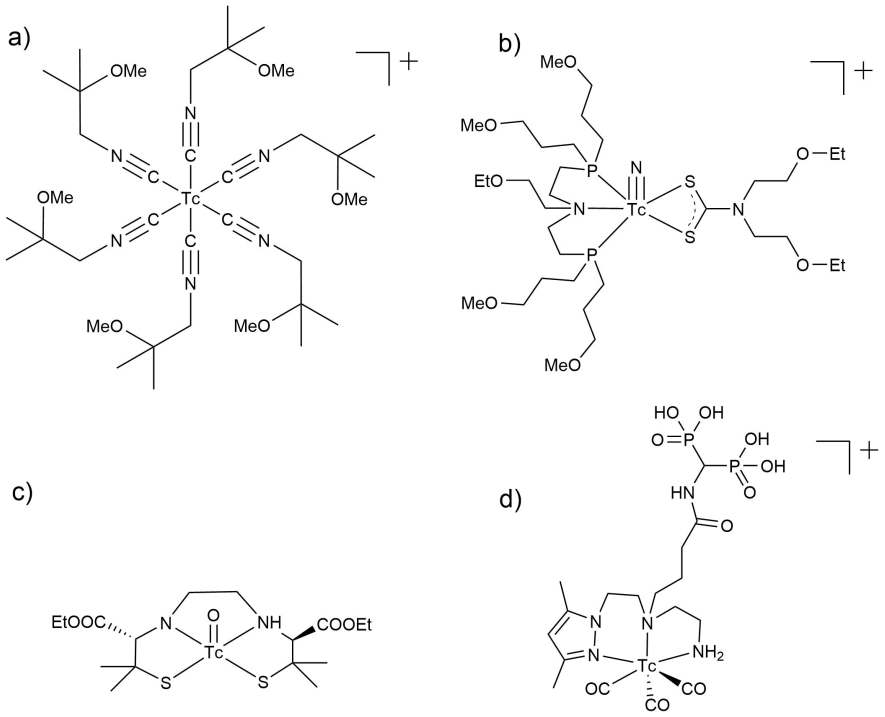
Molecular imaging is a powerful tool in medical diagnostics. The nuclear isomer ^{99m}Tc (m = metastable) of the isotope ^{99g}Tc (g = ground state) has excellent radiation properties (γ – emitter, $t_{1/2}$= 6.015 h) for radioimaging. ^{99m}Tc is obtained by β^- decay of a mother nuclide in a so-called technetium generator as ^{99m}Tc-pertechnetate [^{99m}TcO$_4$]$^-$.

1.1 **Identify** the mother nuclide (**A**) of ^{99m}Tc and and the emitted particle (**B**). 1.0pt

$$\mathbf{A} \longrightarrow {}^{99m}\mathrm{Tc} + \mathbf{B}$$

β^- decay: [^{99}MoO$_4$]$^{2-}$ $\longrightarrow$ [^{99m}TcO$_4$]$^-$ + e$^-$ + v
so A = ^{99}Mo and B = e$^-$
The students will not be penalized should the antineutrino not be mentioned.
1pt

1.2 **Provide** the oxidation states of the radiometal in the following ^{99m}Tc-probes **on the answer sheet**. 2.0pt



a) +I
b) +V
c) +V
d) +I
each 0.5 pt
no distinction will be made between arabic and roman numerals for the grading.

The redox potentials of the group seven elements manganese (**Mn**), technetium (**Tc**) and rhenium (**Re**) follow the general trend in the periodic tables (see **Figure 2** below).

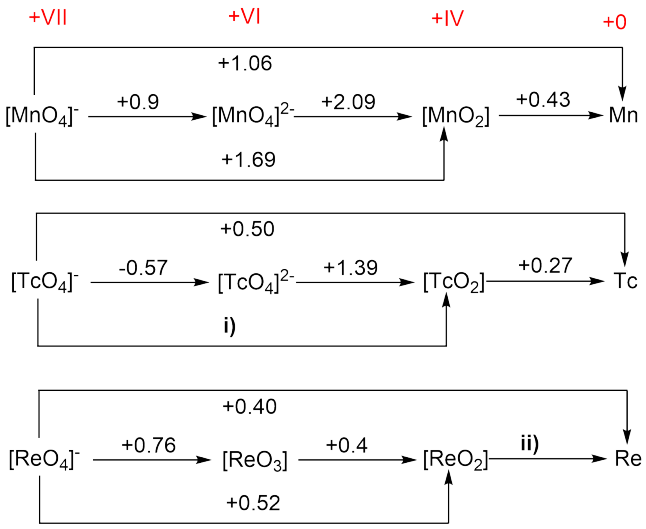


Figure 2

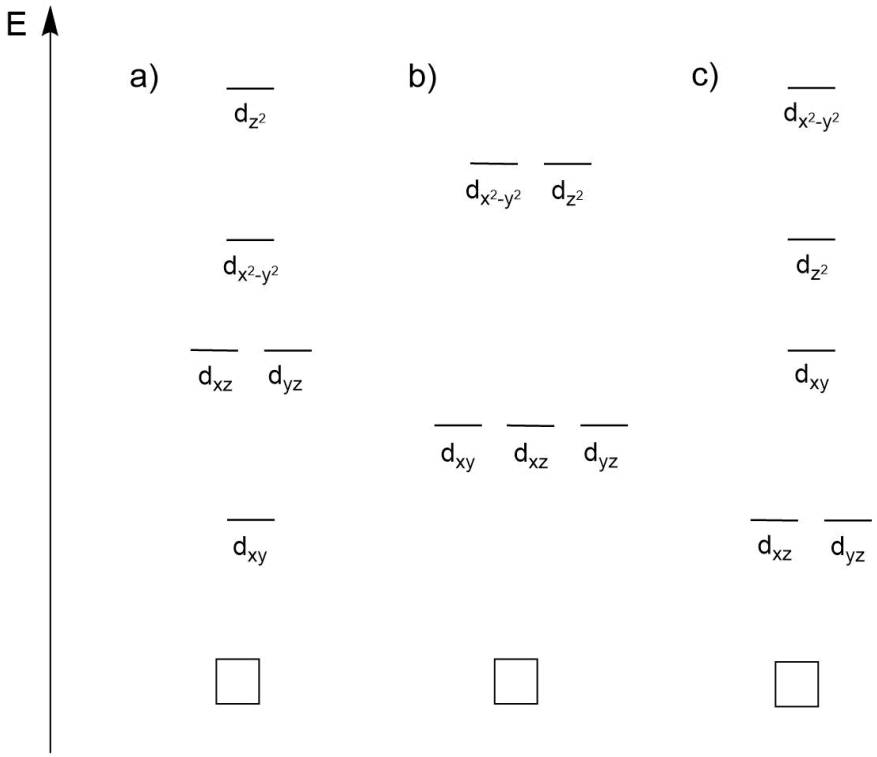
1.3	**Calculate** the two missing redox potentials. i) +0.74 ii) +0.31 each 1pt	2.0pt

1.4	Compare $[MnO_4]^-$, $[TcO_4]^-$ and $[ReO_4]^-$. **Choose** the strongest oxidizing agent and **tick** your answer. ☐ $[MnO_4]^-$ 1pt	1.0pt

1.5	Based on the values indicated by **Figure 2** in the question sheet, **select** if TcO_2 would disproportionate to Tc and TcO_4^{2-} under acidic conditions. The answer is no. 1pt	1.0pt

Tc and Re complexes at the oxidation state +V (d^2 systems) which contain a terminal oxo- (O=) or nitrido-ligand (N≡) are diamagnetic. The scheme on the answer sheet shows three possible molecular orbital energy diagrams.

1.6 **Choose** which orbital energy diagram explains the observed diamagnetism and **tick** your answer. **Draw** the corresponding electron configuration in the correct diagram. 2.0pt



The compressed version to the left.
correct orbital 1pt
correct electron confg 1pt

$((C_4H_9)_4N)[^{99g}TcO_4]$ is a colorless powder. By the addition of conc. HCl this common starting compound for ^{99g}Tc chemistry is converted into the green complex $((C_4H_9)_4N)[^{99g}TcOCl_4]$.

1.7 **Write** down both oxidation and reduction half-reactions using the formulas of ions or neutral molecules, and the complete redox reaction. 4.0pt

Red.: $((C_4H_9)_4N)[^{99g}TcO_4] + 2e^- + 6H^+ + 4Cl^- \longrightarrow ((C_4H_9)_4N)[^{99g}TcOCl_4] + 3H_2O$
2pt for the reduction
Ox.: $2Cl^- \longrightarrow Cl_2 + 2e^-$
1pt for the oxidation
$((C_4H_9)_4N)[^{99g}TcO_4] + 2e^- + 6H^+ + 6Cl^- \longrightarrow ((C_4H_9)_4N)[^{99g}TcOCl_4] + Cl_2 + 3H_2O + 2e^-$
or
$((C_4H_9)_4N)[^{99g}TcO_4] + 6HCl \longrightarrow ((C_4H_9)_4N)[^{99g}TcOCl_4] + Cl_2 + 3H_2O$
1pt for either equation

All ^{99m}Tc radiotracers in clinics are prepared in “one pot” reactions, applying commercialized

kits. Typically (^{99m}Tc t1/2= 6.015 h), an eluate of a ^{99m}Tc generator has an activity of $12.5\ \mathrm{GBq}$ ($\mathrm{GBq} = \text{giga Becquerel} = 10^9 \text{decays per second}$).

1.8 **Calculate** how many mol ^{99m}Tc are present in such samples. 4.0pt

$A = \lambda * N$ 1pt

$\lambda = \ln 2 / t_{1/2}$

$t_{1/2}$ = 6h = 21600 s 1pt

$\lambda = \ln 2 / 21600\ s = 3.209*10^{-5}\ s^{-1}$

$N = A/\lambda$

$N = (12.5*10^9 \text{ decays /s}) / 3.209*10^{-5}\ s^{-1}$

$N = 3.895*10^{14}$ atoms 1pt

$\text{Mol} = 3.895*10^{14} \text{ atoms} / 6.022*10^{23} \text{ atoms / Mol}$

$\text{Mol} = 0.647*10^{-9}$ Mol = 0.647 nMol 1pt

For standard imaging, around $200\ \mathrm{MBq}$ ^{99m}Tc are administered to the patient.

1.9 Assume that no activity is lost through excretion. **Calculate** how many hours the patient has to wait until the injected activity decreases to under 1% of the starting activity. 2.0pt

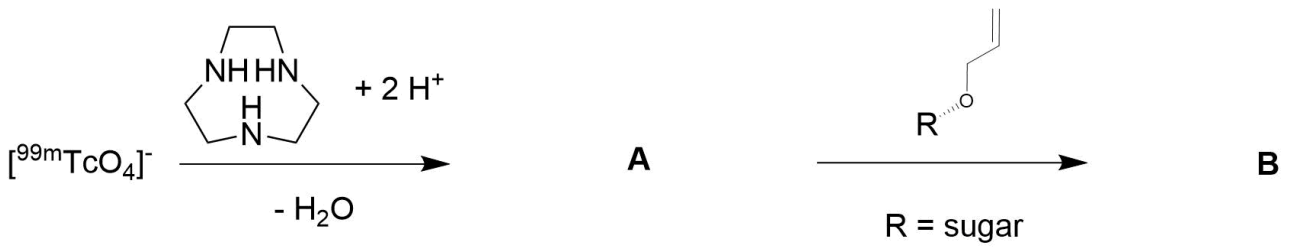
1% of 200 MBq = 2 MBq

$t = -\ln(A/A_0)/\lambda$

$t = -\ln(2\ \text{MBq}/200\ \text{MBq})/ 3.209*10^{-5}\ s^{-1}$ 1pt

t = 143507.95 s = 39.86 h 1pt

Bioconjugation of radiometals is a chemical challenge. A recent example is the (3+2) cycloaddition of $[^{99m}TcO_3(tacn)]^+$ (**A**) (tacn = 1,4,7-triazacyclononane) with alkenes. In this context (3 + 2) refers to the number of atoms involved and not to the numbers of electrons. The following scheme shows an example of this reaction by labeling a protected carbohydrate.

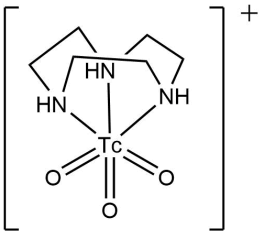


1.10 **Draw** the structures of compound **A** and **B.** Further, **state** the oxidation state of the technetium in these compounds. 3.0pt

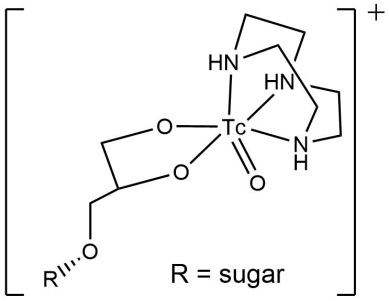
A oxidation state: + VII

B oxidation state: +V

1pt for a correct structure and 0.5pt for a right oxidation state



A)



B)

Electrochemical CO_2 Reduction - Solutions

5% of total								
Question	2.1	2.2	2.3	2.4	2.5	2.6	2.7	**Total**
Points	2	8	3	3	5	8	4	**33**
Score								

In recent years, the electrochemical conversion of CO_2 into higher value products has been considered a promising and technologically feasible approach to mitigate the negative climatic effects caused by its increasing levels in the atmosphere. Several technologies have been developed to achieve this goal. Among these, CO_2 reduction through electrochemical means (CO_2RR) warrants particular attention due to its ability to be powered by renewable energy to transform environmentally harmful CO_2 into platform chemicals.

Electrocatalysts are essential not only to accelerate the intrinsically slow CO_2RR but also to direct the electrolysis reaction towards the desired reaction products (product selectivity). In this context, it is not only the chemical nature of the catalyst itself which governs the resulting CO_2RR product distribution but also its morphological characteristics on various length scales. A new concept of CO_2RR catalyst design relies on the electrodeposition of foam-type materials, which offer a large surface area that is accessible to reactants (e.g. H_2O, H_2, and CO_2). Copper-based materials are the only known metallic CO_2RR catalysts that can produce hydrocarbons and alcohols in significant amounts from CO_2 electrolysis.

Given below are thermodynamic data of selected substances:

	$\triangle_f H^\ominus$ kJ mol^{-1}	$S^\ominus$, J mol^{-1} K^{-1}
H_2O (l)	-285.83	69.95
O_2 (g)	0	205.15
H_2 (g)	0	130.68
CO_2 (g)	-393.52	213.79
ethanol (l)	-276.00	159.86
***n*-propanol (l)**	-302.54	192.80

Table 1. Standard formation enthalpy $\triangle_f H^\ominus$ and standard entropy $S^\ominus$ for some substances under standard conditions ($T = 298.15$ K, $p = 1$ bar).

Cell reaction	E, V vs. SHE
$Cu^{2+} + 2e^- \longleftrightarrow Cu$	+0.34
$2H^+ + 2e^- \longleftrightarrow H_2$	0.00

Table 2. Selected half-cell reactions and corresponding standard potentials under the standard conditions.

2.1 **Write and balance** the chemical equation of the half-cell reactions for the following electrochemical reduction processes in acidic environment (i) CO_2 to ethanol; (ii) CO_2 to *n*-propanol. 2pt

- (i) Ethanol: $2CO_2 + 12H^+ + 12e^- \rightleftharpoons C_2H_5OH + 3H_2O$ 1pt
- (ii) Propanol: $3CO_2 + 18H^+ + 18e^- \rightleftharpoons C_3H_7OH + 5H_2O$ 1pt

2.2 **Combine** the half-cell of the reduction process with an $H_2/2H^+$ half-cell where the latter acts as anode. **Calculate** the value of the standard cell potential of the CO_2 to **ethanol** reduction. 8pt

Process a)
$2CO_2 + 12H^{(+)} + 12e^{(-)}. \longleftrightarrow C_2H_5OH + 3H_2O$ (R1) cathode. 1pt
$H_2 \cdot (-6) \longleftrightarrow 2\ H+ + 2\ e^-$ 1pt
$6\ H_2 \longleftrightarrow 12\ H^+ + 12\ e^-$ (R2) anode
Combining the two half cells we get:
$2\ CO_2 + 6\ H_2 \longleftrightarrow C_2H_5OH + 3\ H_2O$ (R3) 1pt
$\Delta H_{R3} = -276 + (-3\ 285.83) - 2\ (-\ 393.52) = -\ 346.45$ kJ / mol 1pt
$\Delta S_{R3} = 3 \cdot S_{H_2O} + S_{C_2H_5OH} - 2 \cdot S_{CO_2} + -6 \cdot S_{H_2} = -842$ J/(K · mol) = –0.842 kJ/(K · mol) 1pt
$\Delta G_{R3} = \Delta H_{R2} - T\Delta S_{R2} = -346.45$ kJ / mol – 298.15K · (–0.842 kJ / (K · mol)) = -95.53 kJ/mol 1pt
$\Delta E_{R3} = -\Delta G_{R3}/n_{R3}F = 95\ 530$ J / mol : (12 · 96485 C / mol) = **0.0825 V** 1pt
$\Delta E_{R3} = E_{cathode} - E_{anode.}$
$E_{cathode} = \Delta E(R3) + E_{anode.} = 0.0825$ V + 0.00 V =. **0.0825** V 1pt

2.3 **Write** all the reduction and oxidation half-cell reactions taking place at the cathode and the anode, respectively. 3pt

Anode reaction
Oxidative oxygen evolution reaction (OER): **$2H_2O \longrightarrow O_2 + 4H^+ + 4e^-$** 1pt
Cathode reaction
Reductive hydrogen evolution reaction (HER):
$2H^+ + 2e^- \longrightarrow H_2$ (proton reduction) 1pt
$2H_2O + 2e^- \longrightarrow H_2 + 2OH^-$ (water splitting)
Metal deposition / reduction of cupric ions: **$Cu^{2+} + 2e^- \longrightarrow Cu$** 1pt

Figure 1 shows the principle of dynamic hydrogen bubble-templated metal deposition.

Figure 2 displays top-down scanning electron microscopy (SEM) images of five different Cu foams obtained upon interruption of the metal deposition at different times: $5\ \mathrm{s}$, $20\ \mathrm{s}$ and $80\ \mathrm{s}$

Cu foam electrodeposition processes (see Figure 1) were carried out in an aqueous $1.5\ \mathrm{M}$ sulfuric acid solution containing $0.2\ \mathrm{M}$ copper sulfate ($CuSO_4 \cdot 5H_2O$) as the copper source. A Cu disk ($1\ \mathrm{cm}^2$) and a Pt foil served as the cathode and the anode, respectively.

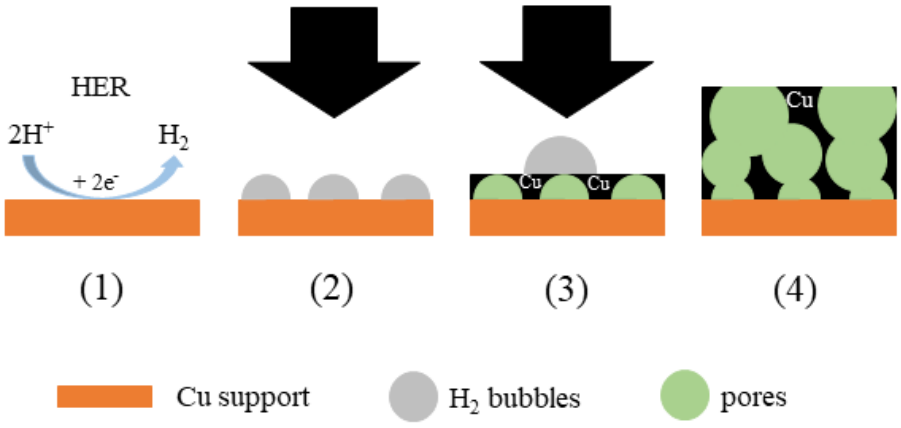


Figure 1. Depiction of the electrodeposition of foam-type materials. In the course of electrochemical metal deposition (black arrows) at high current densities in aqueous media, the Hydrogen Evolution Reaction (HER) takes place on the metallic (Cu) support (1). The surface becomes thus partially covered by H_2 bubbles (2). The H_2 bubbles act as a template for metal deposition (3). As a result a highly porous metal foam emerges (4).

2.4 3pt

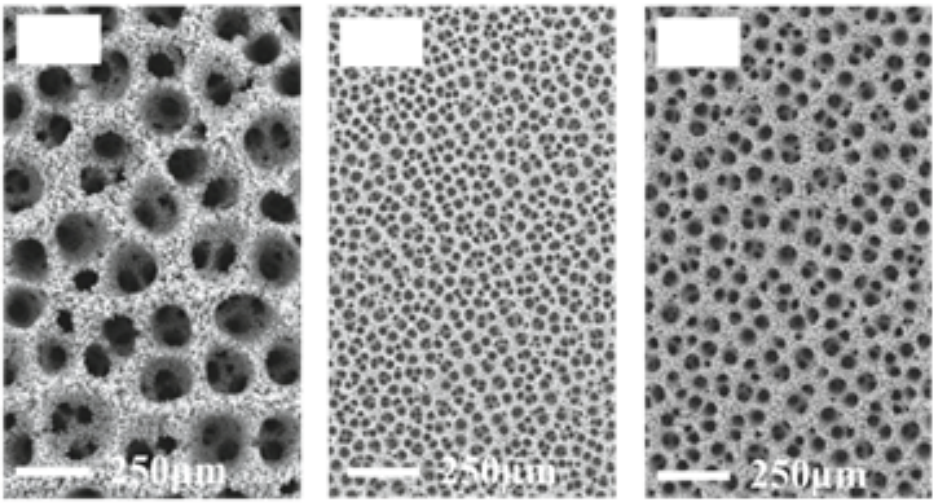


Figure 2. Cu foams obtained by galvanostatic Cu electrodeposition at a current density of $j = -3\ \mathrm{A\ cm^{-2}}$ The deposition was, in each case, interrupted at distinct elapsed duration: $5\ \mathrm{s}$, $20\ \mathrm{s}$ and $80\ \mathrm{s}$. The scale bar is the same in all panels.

Considering this mechanism, **assign** the correct deposition time to the Cu foams shown in **Figure 2 on the answer sheet (white boxes upper left corner)**.
all correct: 3pt one incorrect: 2pt, two incorrect: 0pt

Bimetallic CuAg systems are excellent catalysts for the electrosynthesis of alcohols from CO_2. $5.4\ \mathrm{mg}$ of a bimetallic Cu-Ag foam catalyst ($90\ \mathrm{wt.\%\ Cu}$, $M_{Cu} = 63.546\ \mathrm{g}\ mol^{-1}$; $10\ \mathrm{wt.\%\ Ag}$, M_{Ag}=$107.868\ \mathrm{g}\ mol^{-1}$) was galvanostatically deposited onto a Cu foil ($1\ \mathrm{cm^2}$) at a current density of $j = -3\ \mathrm{A\ cm^{-2}}$ applied for $20\ \mathrm{s}$ (the minus sign accounts for a reductive/cathodic process).

2.5 **Calculate** the Faradaic efficiency (FE in %) of this metal deposition process. FE is defined as $\frac{Q_{product}}{Q_{total}} \times 100$. Q denotes the charge. 5pt

m(Cu-Ag) = 0.0054 g ⟶ m(Cu) = 0.00486 g; m(Ag) = 0.00054 g 1pt
n = m/M ⟶ n(Cu) = $7.65 \cdot 10^{-5}$ mol; n(Ag) = $5.004 \cdot 10^{-6}$ mol 1pt
Q(Cu) = $2 \cdot 96485\ \mathrm{C\ mol^{-1}} \cdot 7.65 \cdot 10^{-5}$ mol = 14.7 C; 1pt
Q(Ag) = $96485\ \mathrm{C\ mol^{-1}} \cdot 5.004 \cdot 10^{-6}$ mol = 0.48 C 1pt
$Q_{Cu\text{-}Ag}$ = 14.7 C + 0.48 C = 15.18 C;

- Q_{tot} = 20s · 3A = 60 A·s = 60 C
- $FE_{Cu\text{-}Ag} = (Q_{Cu\text{-}Ag} / Q_{tot}) \cdot 100\% = (15.18\ \mathrm{C} / 60\ \mathrm{C}) \cdot 100\% =$ **25.3%** 1pt

We consider a CO_2 electrolysis experiment carried out in $35\ \mathrm{mL}$ CO_2-saturated $0.5\ \mathrm{M}$ $KHCO_3$ electrolyte solution over the bimetallic Cu-Ag foam catalyst ($90\ \mathrm{wt.\%\ Cu;\ 10\ wt.\%\ Ag}$). The CO_2 electrolysis was carried out at a constant (total) current density of $j(tot) = -30\ \mathrm{mA\ cm^{-2}}$ for $3600\ \mathrm{s}$ (note the current density is normalized to the geometric surface area of $1\ \mathrm{cm^2}$; the minus sign accounts for a reductive/cathodic pro-

cess). A product analysis, carried out after the electrolysis, revealed mass concentrations of $41.3\ \mathrm{mg\ L^{-1}}$ and $7.4\ \mathrm{mg\ L^{-1}}$ for ethanol and *n*-propanol, respectively. Both alcohols are liquid reaction products and accumulate in the electrolyte in the course of the electrolysis reaction. We assume that gaseous hydrogen (H_2) is formed as the only by-product of the process.

2.6 **Calculate** the current densities required for the formation of (a) ethanol ($MW_{\mathrm{ethanol}} = 46.08\ \mathrm{g\ mol^{-1}}$) and (b) n-propanol ($MW_{n\text{-propanol}} = 60.10\ \mathrm{g\ mol^{-1}}$) assuming that the current densities do not change with electrolysis time. 8pt

$Q_{Area} = 0.03\ \mathrm{A \cdot cm^{-2}} \cdot 3600s = 108\ \mathrm{C \cdot} cm^{-2}$; assuming a geometric surface area of $1\ \mathrm{cm^{-2}}$ (see X.4)$\rightarrow Q_{tot} = 108\ \mathrm{C}$ 1pt

$\mathrm{c(EtOH)} = 41.3\ \mathrm{mg \cdot L^{-1}} = 41.3\ \mu\mathrm{g \cdot mL^{-1}} \rightarrow \mathrm{m(EtOH)} = 41.3\ \mu\mathrm{g \cdot mL^{-1}} \cdot 35\ \mathrm{mL} = 1445.5\ \mu\mathrm{g} = 1.446\ \mathrm{mg}$ 1pt

$\mathrm{n(EtOH)} = \frac{1.4455mg}{46\ \mathrm{g\ mol^{-1}}} = 3.14 \cdot 10^{-5}\ \mathrm{mol}$; 1pt

$\mathrm{Q(EtOH)} = 3.14 \cdot 10^{-5}\ \mathrm{mol} \cdot 12 \cdot 96485\ \mathrm{C\ mol^{-1}} 36.355\ \mathrm{C}$, 1pt

$\mathrm{FE(EtOH)} = \frac{36.355\ \mathrm{C}}{108\ \mathrm{C}} \cdot 100\% = 33.6\%$;1pt

j(EtOH) = 0.336 · (-30 mA cm^{-2}) = **-10.09 mA cm^{-2}** 1pt

$\mathrm{FE(EtOH)} = \frac{36.355\ \mathrm{C}}{108\ \mathrm{C}} \cdot 100\% = 33.6\%$

$\mathrm{c(PrOH)} = 7.4\ \mathrm{mg \cdot L^{-1}} = 7.4\ \mu\mathrm{g \cdot mL^{-1}} \rightarrow \mathrm{m(EtOH)} = 7.4\ \mu\mathrm{g \cdot mL^{-1}} \cdot 35\ \mathrm{mL} = 2.59 \cdot 10^{-4}\ \mathrm{g}$

$\mathrm{n(PrOH)} = \frac{2.59 \cdot 10^{-4}\ \mathrm{g}}{60\ \mathrm{g\ mol^{-1}}} = 4.3 \cdot 10^{-6}\ \mathrm{mol}$; 1pt

$\mathrm{Q(PrOH)} = 4.3 \cdot 10^{-6}\ \mathrm{mol} \cdot 18 \cdot 96485\ \mathrm{C\ mol^{-1}} = 7.468\ \mathrm{C}$,

$\mathrm{FE(PrOH)} = \frac{7.468\ \mathrm{C}}{108\ \mathrm{C}} \cdot 100\% = 6.9\%$ 1pt

j(PrOH) = 0.069 · (-30 mA·cm^{-2}) = **-2.07 mA·cm^{-2}** 1pt

(note the current densities are normalized to geometric surface area of 1 cm^2).

2.7 **Calculate** the volume of the formed hydrogen on the 1 cm^2 catalyst area at 298.15 K and 1 bar, assuming ideal behavior of the formed hydrogen, and its complete release into the gas phase. 4pt

*If you did not get a result in **Task 2.6**, continue with $FE_{(EtOH)} = 45.1\%$ and $FE_{(PrOH)} = 4.8\%$.*

FE(H_2) = 100% - (33.6% + 6.9%) = 59.5% 1pt

$n(H_2) = \frac{1}{z \cdot F} \cdot Q_{H2} = \frac{1}{z \cdot F} \cdot Q_{tot} \cdot 0.595 = \frac{1}{z \cdot F} \cdot t \cdot 0.595$

(note I refers to the current passing through the geometric surface area of 1 cm^2) 1pt

$n(H_2) = (0.03A \cdot 3600s \cdot 0.595 \cdot mol)/(2 \cdot 96485A \cdot s) = 3.33 \cdot 10^{-4}\ mol$

Ideal behavior of the hydrogen gas: $p \cdot V = n \cdot R \cdot T; V = (n \cdot R \cdot T)/p$

$V_{H_2} = \frac{3.33 \cdot 10^{-4} mol \cdot 0.314\ kg \cdot m^2 \cdot 298.15\ K \cdot m \cdot s^2}{10^5\ kg \cdot s^2 \cdot mol \cdot K} = 8.25 \cdot 10^{-6} m^3 = 8.25\ cm^3 = 8.25\ ml$ 2pt

If you used FE(H_2) = 50.1%: $n(H_2)$ = 2.80 · 10^{-4} mol and V_{H2} = 7.00 ml

Artificial Photosynthesis - Solutions

6% of total									
Question	3.1	3.2	3.3	3.4	3.5	3.6	3.7	3.8	**Total**
Points	3	4	3	2	6	6	1	4	**29**
Score									

The field of artificial photosynthesis research aims at storing solar energy in chemical bonds. Photons are absorbed by exciting sensitizers, thereby producing a charge-separated state. The excited electron is transferred to a catalyst (hydrogen evolving catalyst, HER), which is reduced twice and then produces H_2. The photosensitizer or light absorber is often $[Ru(bpy)_3]^{2+}$ (bpy=2,2'-bipyridine), and the HERs are often cobalt complexes.

Energetics of Water Splitting

3.1 **Calculate** the enthalpy of the reaction $H_2 \longrightarrow 2H^+(aq) + 2e^-$. 3pt

Solvation enthalpy of proton: $\Delta H_{aq}(H^+) = -1190\ \text{kJ mol}^{-1}$

Ionization energy of hydrogen: $IE_1 = 13.6\ \text{eV}$

Dissociation enthalpy of H_2: $\Delta H_{diss}(H_2) = 432\ \text{kJ mol}^{-1}$

All correct: 3pt; 1 incorrect: 2pt; 2 incorrect: 0pt

Ideally, electrochemical water splitting into O_2 and H_2 runs at 1.23 V. Since $T\Delta S$ for this process is > 0, heat from the environment is needed. If additional voltage produces the heat required to compensate the decrease in temperature the process is called **thermoneutral**.

The enthalpy of H_2O formation $\Delta H^\circ_{H_2O}$ is -285 kJ/mol.

3.2 **Calculate** (a) the water splitting reaction entropy ΔS°_R at $25\ ^\circ C$ of 1 mol of H_2O and (b) the voltage at which water splitting is thermoneutral. 4pt

$-1.23\,V = +237\,kJ\,mol^{-1}$ ($\Delta G^\circ(H_2O)$) 1pt
$\Delta G^\circ(H_2O) = \Delta H^\circ - T\cdot\Delta S^\circ$

$-T\Delta S^\circ$ equals the lost heat that must be compensated
$-T\Delta S^\circ = (237-285)\,kJ\,mol^{-1} = -48\,kJ\,mol^{-1}$ and $\Delta S^\circ_R = 161\,J\,mol^{-1}\,K^{-1}$ 2pt

$\frac{-48000\,J\,mol^{-1}}{2\cdot 96500\,C\,mol^{-1}} = 0.25\,V$ 1pt

To be thermoneutral, the cell voltage needs to be $1.23\,V + 0.25\,V = 1.48\,V$ which corresponds to ΔH°_R.

Catalysts

Cobalt-salen (salcomin) type complexes are potential catalysts for H_2 formation from protons and electrons. The structure of salcomin is given below:

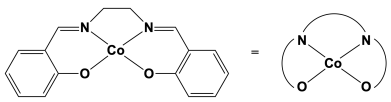


Figure 1. The structure of salcomin.

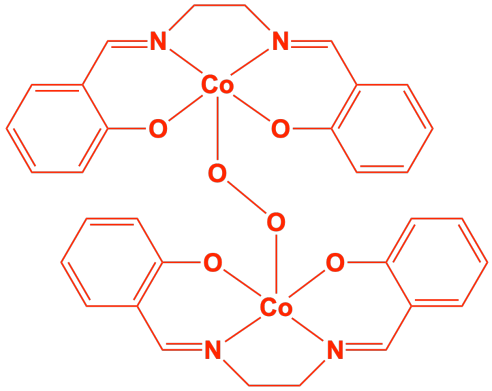
3.3
- **Determine** the oxidation state of the cobalt atom in salcomin.
- **Determine** the geometric structure around the cobalt center of salcomin, choosing from these three possibilities: tetrahedral, square planar or octahedral. **Fill in** the corresponding checkbox on the **answer sheet**.

3pt

Oxidation number: +II 1pt
Geometric structure: square planar (the ligand is a conjugated system) 2pt

In solution, salcomin can bind O_2; that links two salcomin moieties by coordinating to the two Co centres. The oxidation state of both Co centres is then +III.

3.4 **Draw** the resulting structure. 2pt



2pt

The H_2 formation takes place exclusively at the cobalt center. The reaction is described by a 4-step catalytic cycle starting with Co^{2+} using 2 H^+ and 2 electrons. During one step a hydride is formed by an intramolecular electron transfer.

3.5 **Write down** two possible variations of the catalytic cycle with charges of the complex and oxidations states of the Co center. The oxidation state on the Co center should not be larger than + III. **Mark** the hydride formation step with an asterisk and **label** H^+ uptake with **C** (chemical reaction), and electron uptake with **E** (electrochemical reaction), see example cycle in **Figure 2** below. [Co^{II}] stands for the Cobalt-salen complex. 6pt

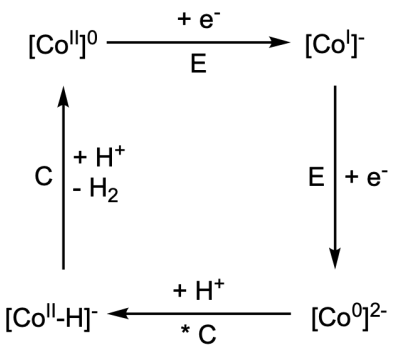
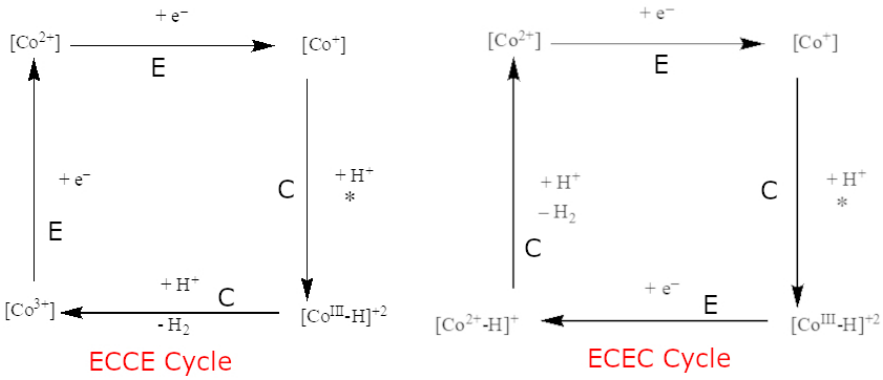


Figure 2. An example cycle for task 3.5.

Solution:



For **each** cycle:
All oxidation states correct: 2pt; one incorrect: 1pt; two incorrect: 0pt
Hydride formation correct: 1pt

Redox Potentials

3.6 6pt

- Using the redox potential values of different cobalt complexes given in **Table 1**, **write down** which complex is suitable for **a)** water oxidation at neutral pH **b)** water reduction at neutral pH.
- **Write down** the corresponding overall reaction for both processes (only for the complexes, capable of performing it) and **calculate** the cell potentials at neutral pH.
- The half-cell potential for the proton reduction at pH = 7, *T* = 298 K is -0.41 V.

Co(III/II) redox couple	E° vs normal hydrogen electrode
$[Co(H_2O)_6]^{3+/2+}$	+1.92 V
$[Co(C_2O_4)_3]^{3-/4-}$	+0.55 V
$[Co(EDTA)]^{1-/2-}$	+0.38 V
$[Co(NH_3)_6]^{3+/2+}$	+0.06 V
$[Co(en)_3]^{3+/2+}$	-0.18 V
$[Co(CN)_5]^{2-/3-}$	-0.6 V

Table 1. Possible redox couples for task 3.6. $[C_2O_4]^{2-}$ = oxalate, en = 1,2-ethylendiamine.

$H_2O \rightarrow \frac{1}{2}O_2 + 2H^+ + 2e^- \; \Delta E^\circ_{1/2} = 1.23\,V$ (standard conditions)
This potential is pH dependent. According to Nernst, the reduction potential $E_{1/2}$ at pH = 7 is thus $1.23\,V - 0.41\,V = +0.817\,V$ and, for the above reaction, -0.817 V. 1pt

To be able to oxidize water, the reduction potential must be larger than +0.817 V at pH = 7, which means that only the $[Co(H_2O)]_6^{3+/2+}$ couple is able to do this reaction.
Redox couple for oxidation: $[Co(H_2O)_6]^{3+} + e^- \rightarrow [Co(H_2O)_6]^{2+}$, $E^\circ_{1/2} = +1.92\,V$ 1pt

$H_2O \rightarrow \frac{1}{2}O_2 + 2H^+ + 2e^- \; \Delta E_{1/2} = -0.817\,V$ (pH = 7)
$2[Co(H_2O)_6]^{3+} + H_2O \rightarrow 2[Co(H_2O)_6]^{2+} + \frac{1}{2}O_2 + 2H^+$, $E = +1.1\,V$ 2pt

The reduction potential for the reduction of water at pH = 7 is -0.41 V. The $E^\circ_{1/2}$ of the redox couple must be smaller than -0.41 V:
Redox couple for reduction: $[Co(CN)_5]^{2-} + e^- \rightarrow [Co(CN)_5]^{3-}$, $E^\circ_{1/2} = -0.6\,V$ 1pt

$2[Co(CN)_5]^{3-} + H_2O \rightarrow 2[Co(CN)_5]^{2-} + H_2 + "O^{2-}"$, $E = +0.19\,V$ (pH = 7) 1pt

A Glimpse at the Natural Process

The natural storage of biological H_2 equivalents is NADPH, which is produced from $NADP^+$ through the

addition of a hydride ion. The structure of NADPH is shown in **Figure 3**.

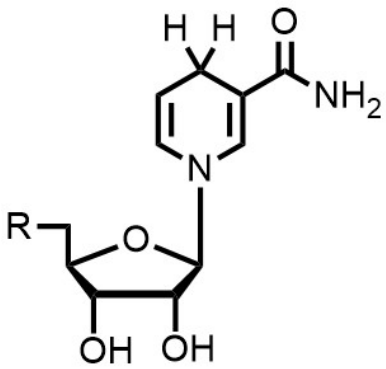
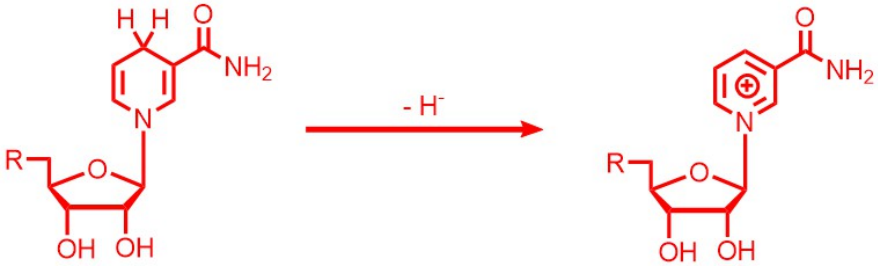


Figure 3. The structure of NADPH.

3.7 **Draw** the structure of $NADP^+$. 1pt



1pt. Only the structure on the right is required.

Chlorophyll has an extinction coefficient of about $\varepsilon = 8 \cdot 10^4$ $M^{-1}cm^{-1}$ at 680 nm.

3.8 Assuming an efficiency (photon to hydrogen H atom) of $\phi = 20\%$ at a 680 nm photon flux of $100\ \mathrm{nE\ s^{-1}\ cm^{-2}}$ ($1\ \mathrm{E} = 1\ \mathrm{mol\ of\ photons}$), **calculate** a) the number of photons per second and b) the concentration of chlorophyll in a 1x1x1 cm cell needed to get a turnover frequency of 1 nmol H_2/s. 4pt

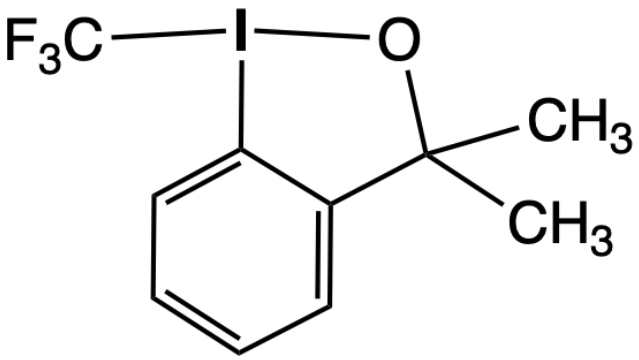
1 nmol H_2 per second corresponds to 2 nmol H atoms per second. This corresponds to $1.2 \cdot 10^{15}$ H atoms per second. Taking the efficiency into account, this would require $6 \cdot 10^{15}$ photons per second. 2pt
The Lambert-Beer law states $E_\lambda = \log(I_0/I_1) = \varepsilon \cdot c \cdot d$.
With $I_0 = 6 \cdot 10^{16}$ photons/s and $I_1 = 6 \cdot 10^{16} - 6 \cdot 10^{15}$ photons/s:
$\varepsilon \cdot c \cdot d = 0.045$ and $c = 5.7 \cdot 10^{-7}$ M. 2pt

Fluorinated and Hypervalent Compounds

6% of total										
Question	4.1	4.2	4.3	4.4	4.5	4.6	4.7	4.8	4.9	**Total**
Points	4	4	4	2	6	4	1	4	5	**34**
Score										

Introduction - Fluorine forms stable and isolable compounds with essentially all elements, including the noble gases Kr and Xe. Fluorine-containing molecules often feature uncommon structures. Thus, fluorine is frequently involved in the formation of compounds with elements of groups 14-18, which are defined as hypervalent. The synthesis of fluorinated organic compounds is nowadays heavily based on the availability of specifically designed reagents, compound **4** below being an example.

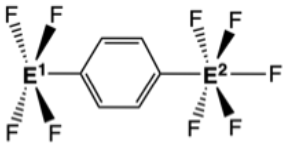
Hint: Any element E in the series ***E*^{1}-*E*^{8}** *may be represented more than once.*



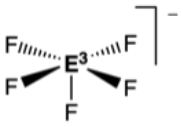
4

I Molecular Geometry

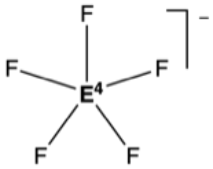
4.1 **Identify** elements $\mathbf{E^1}$, $\mathbf{E^2}$, $\mathbf{E^3}$, and $\mathbf{E^4}$ in the three species **1**, $[\mathbf{2}]^-$, and $[\mathbf{3}]^-$. **Write** the answer in the appropriate box on your answer sheet. 4.0pt



1



$[\mathbf{2}]^-$



$[\mathbf{3}]^-$

1: neutral, non-zwitterionic molecule, $\mathbf{E^1}$, square pyramidal; $\mathbf{E^2}$, octahedral,
av. d(E^1–F)=1.91Å; av. d(E^2–F)=1.58Å

$[\mathbf{2}]^-$:anion, square pyramidal
av. d(E^3–F)=1.96Å

$[\mathbf{3}]^-$: anion, pentagonal planar
av. d(E^4–F)=1.98Å

15	16	17	18
d(P–F), 1.50-1.68 Å	d(S–F) 1.52-1.60 Å	d(Cl–F), 1.63-1.85 Å	
d(As–F), 1.68-1.72 Å	d(Se–F), 1.75-1.80 Å	d(Br–F), 1.77-1.97 Å	d(Kr–F), 1.77-1.89 Å
d(Sb–F), 1.85-2.05 Å	d(Te–F), 1.80-2.00 Å	d(I–F), 1.90-2.00 Å	d(Xe–F), 1.77-2.00 Å

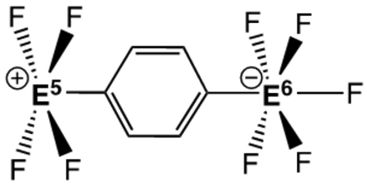
Table 1. Typical E–F bond distance ranges for a selection of elements in Groups 15 - 18

Hints:

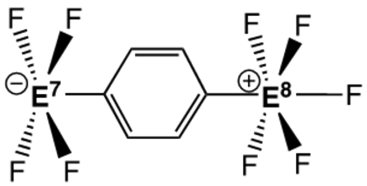
1. *The specified molecular geometries refer to the arrangement of atoms bonding to E^1-E^4*
2. *The elemental analysis of **1** gives a carbon content of 17.75 wt %*

E^1 = I, E^2 = S, E^3 = Te, E^4 = Xe
1pt each

4.2 **Choose** which elements **E^5 / E^6** and **E^7 / E^8**, respectively, would display the given molecular geometry, including E-F bond distances close to those in **1** (see table 1). **Write** the answer in the boxes provided on your answer sheet. 4.0pt



1'

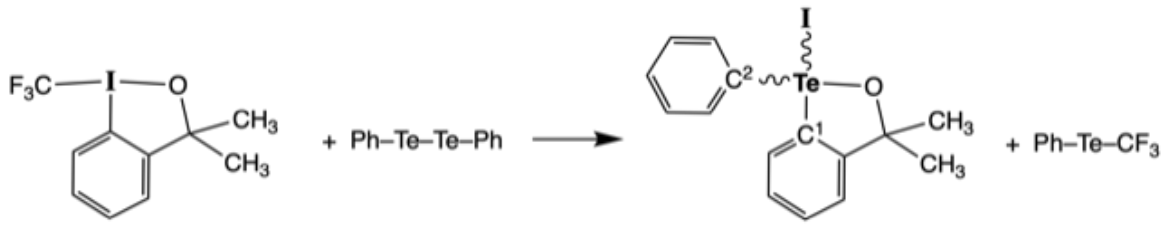


1"

E^5 = Xe, E^6 = P, E^7 = Te, E^8 = Cl
1pt each

II Reactivity and structure

Consider the reaction shown below:



4 5 6 7

4.3 4.0pt

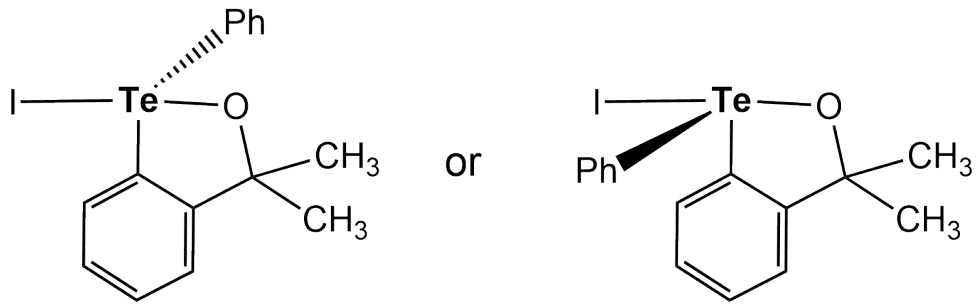
- **Specify** the ideal geometry of compound **6** in terms of the arrangement of the valence-shell electron-pair domains around the Te atom. **Tick** the right box on your answer sheet.
- **Provide** the expected ideal bond angles C^1-Te-I, C^2-Te-I, I-Te-O, and C^1-Te-C^2. **Write** the answer on your answer sheet in the respective box.

Ideal geometry (tick one)

☐ square planar
☒ trigonal bipyramidal
☐ tetrahedral
☐ square pyramidal
☐ octahedral

Trigonal bipyramidal
C^1-Te-I= 90°
C^2-Te-I= 90°
I-Te-O = 180°
C^1-Te-C^2 = 120°
2pt for the ideal geometry 0.5pt for each correct angle

any configuration having O and I trans to each other is considered correct (even if the geometry is wrong) and will be awarded 2 points in total



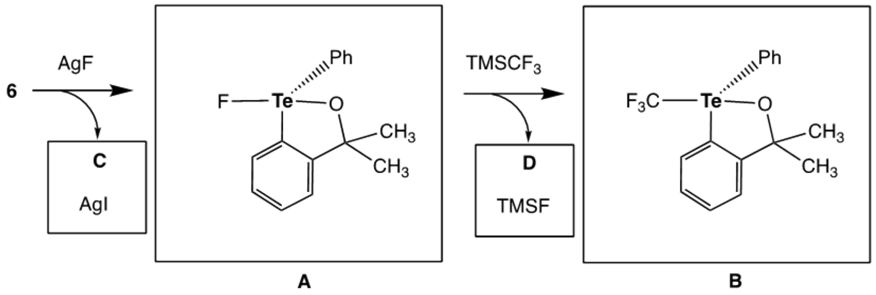
4.4 2.0pt

Write the number ^{1}H-NMR signals you expect for the two methyl groups in compounds **4** and **6** respectively on your answer sheet.

Compound 4: 1 Signal
Compound 6: 2 Signals
each correct answer: 1pt

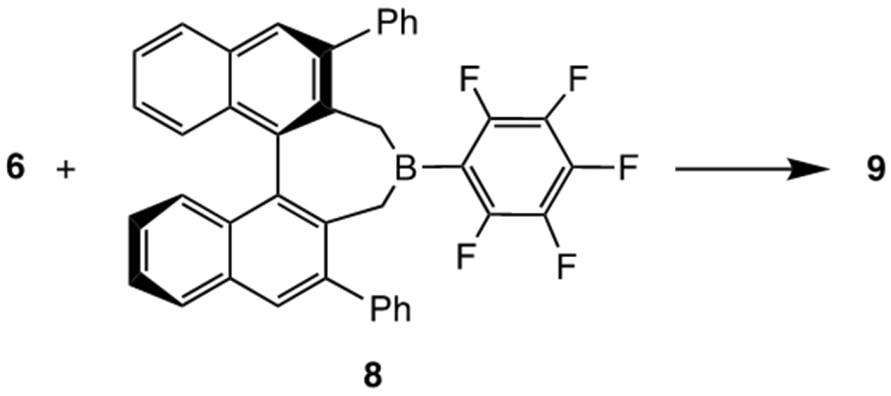
4.5 Compound **6** reacts consecutively with AgF and $(H_3C)_3SiCF_3$ ($TMSCF_3$). **Formulate** the Te-containing intermediate **A** and final product **B**, including their correct geometry, as well as the byproducts **C** and **D**. **Draw** **A** and **B** and **write** the by-products **C** and **D** on your answer sheet. 6.0pt

*Hint: MW of **D** is 92.08 g/mol.*



Points:
AgI = 1 pt
A = 2 pt
TMSF = 1 pt
B = 2 pt

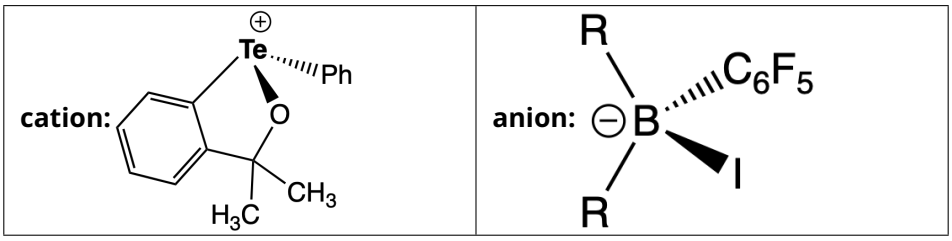
Assume that compound **6** reacts with a sterically bulky, chiral, enantiomerically pure Lewis acid, such as the known boron derivative **8**, as shown below. This reaction should lead to the formation of a new product **9** the composition of which corresponds to the sum of **6** and **8**. Further assume that **9** is a salt, in which the cation derives from **6** and the anion from **8**.

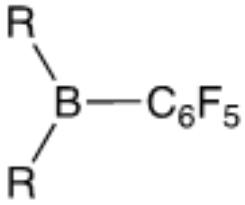


8

4.6 **Draw** the structure of both the Te-containing cation and the boron-containing anion and and **tick** the box corresponding to the ideal geometry of the cation in terms of the arrangement of the valence-shell electron-pair domains around the Te atom. **Draw** on your answer sheet. 4.0pt

*Hint: Use for compound **8** (chiral, enantiomerically pure) the following generic schematic representation:*





Tick the box containing the ideal molecular structure

- ☐ square-planar
- ☐ trigonal-planar
- ☐ tetrahedral
- ☐ trigonal-pyramidal
- ☐ trigonal-bipyramidal

Above is the correct structure
Correct configuration cation: 1pt
Correct configuration antion: 1pt
Correct drawn geometry of cation: 1pt

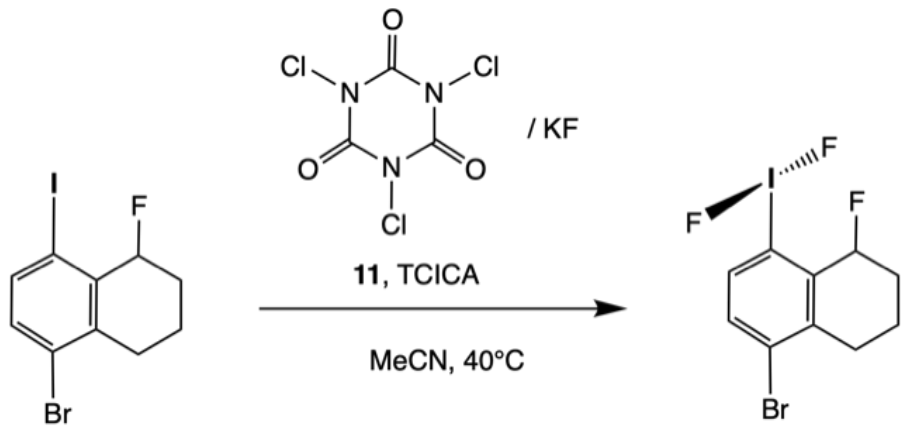
Correct ticked geometry of cation: 1pt

4.7 **Write** the number of possible stereochemically different salts **9** on your answer sheet. 1.0pt

Two diastereoisomeric salts (Number "Two" sufficient as an answer)

III Synthesis of a λ^3 -difluoroiodane and rotation around a single bond

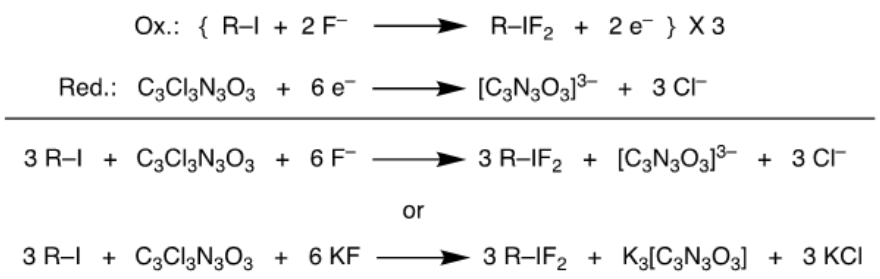
Compound **10** is prepared from starting material **8** by oxidation with trichloroisocyanuric acid (TCICA, **9**) in the presence of excess KF in dry acetonitrile as shown below.



10 12

4.8 **Formulate** balanced half-cell reactions and a balanced overall reaction for this process. **Write** the reactions on your answer sheet. 4.0pt

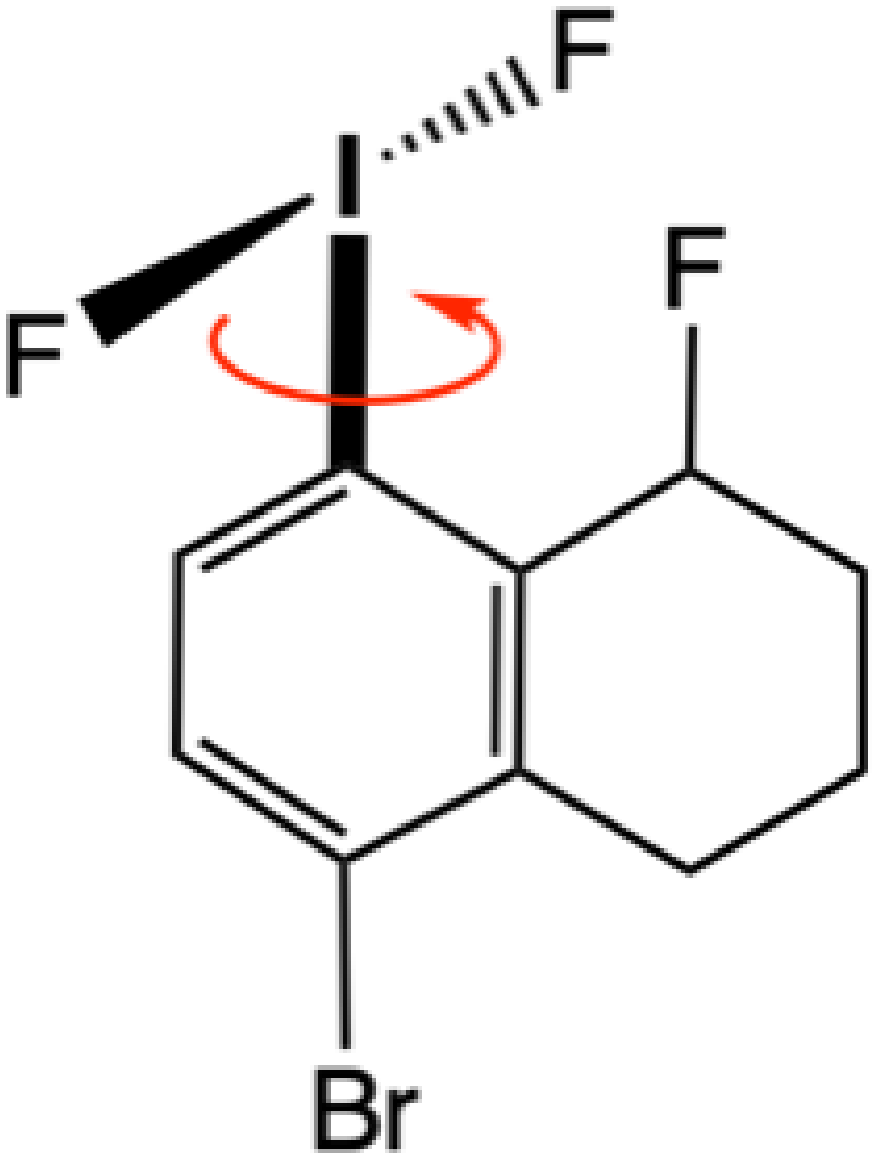
*Hint: Abbreviate **10** as R–I and **11** as R–IF_2 and TCICA as $C_3Cl_3N_3O_3$. The six-membered ring of TCICA stays intact upon reduction.*



Ox. reaction = 1pt Red. reaction = 2pt
Overall (either) = 1pt

Red. reactions involving one or two Cl per TCICA instead of three will also be considered correct. For the red. reaction, two consecutive two-electron reductions of TCICA (leading to the same product $K_3C_3N_3O_3$) are also considered correct.

The IF_2 group in **12** can rotate around the I-C bond (imagine a molecular propeller). The corresponding rotation barrier has been measured experimentally: E_a = 30 kJ·mol^{-1}. Furthermore, the rate constant for the rotation is k = 2500 s^{-1} at 228K.



12

4.9 **Determine** how fast the IF_2 group can in principle rotate at room temperature (298K). Consider this process as if it were a chemical reaction for which you are determining the rate constant. **Write** your answer on the answer sheet. The unit of the constant should be given in s^{-1}. 5.0pt

(1)

$\ln k_1 = -E_a/RT_1 + \ln A$ and $\ln k_2 = E_a/RT_2 + \ln A$ 1.0 pt
$\ln k_1 - \ln k_2 = E_a/R\,(1/T_2 - 1/T_1)$
$\ln k_2 = \ln k_1 - E_a/R\,(1/T_2 - 1/T_1)$ 2.0 pt
for $k_1 = 2500\ s^{-1}$, $T_1 = 228$ K, $T_2 = 298$ K, and $E_a = 30\ kJ{\cdot}mol^{-1}$: 1.0 pt
$k_2 = 1.03 \cdot 10^5\ s^{-1}$ 1.0 pt

- use of Arrhenius law +1.0 pt
- expression of k2/k1 as a function of temperature and activation (free) energy +2.0 pt
- correct assignment for k2 and k1 +1.0 pt
- numerical answer WITH correct unit +1.0 pt

only answers with the correct unit s^{-1} will be marked as correct.

Hydrodesulfurization

7% of total							
Question	5.1	5.2	5.3	5.4	5.5	5.6	**Total**
Points	2.5	3	3.5	5	8	12.5	**34.5**
Score							

The production of sulfur-free fuels is the general trend towards lowering the emission of sulfur-containing compounds that are toxic to the environment. To remove sulfur, the hydrogen-assisted hydrodesulfurization process is used at the refineries.

5.1 **Draw** the structure of products **A** to **E** of thiophene hydrodesulfurization, knowing that **A** and **B** are cyclic regioisomers and **C** is cyclic. 2.5pt

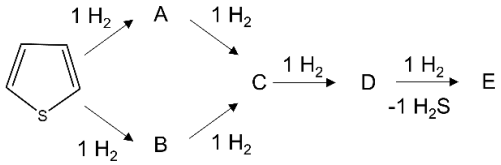
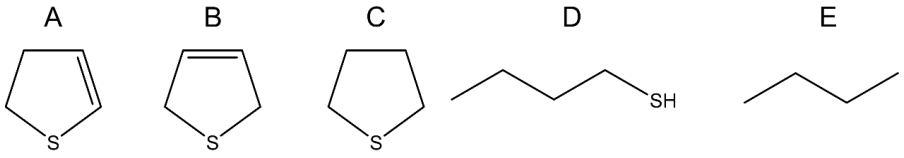


Figure 1. Thiophene hydrodesulfurization process.



0.5 pt for each structure, total 2.5 pt; A and B can be exchanged

Sulfur has two most common natural stable isotopes, ^{32}S and ^{34}S, with a relative molar abundance of $\chi(^{32}S)$ = 94.8% and $\chi(^{34}S)$ = 4.37%, respectively. For hydrogen, the stable natural isotopes are ^{1}H and ^{2}H(D), with a relative molar abundance of $\chi(^{1}H)$ = 99.986% and $\chi(^{2}H)$ = 0.014%, respectively.

5.2 Considering only the isotopes listed above, **list** all isotopologues of H_2S. 3pt

$^{1}H_2{}^{32}S$, $^{1}H_2{}^{34}S$, $^{1}H^{2}H^{32}S$, $^{1}H^{2}H^{34}S$, $^{2}H_2{}^{32}S$, $^{2}H_2{}^{34}S$

0.5pt each, total 3pt (use of D instead of ^{2}H is acceptable).

5.3 Considering only the isotopes listed above, **list** all isotopologue of H_2S containing simultaneously D and ^{34}S nuclei and for each **calculate** the respective relative molar abundance in %. 3.5pt

$\chi(D_2{}^{34}S) = (0.00014)^2 \cdot 0.0437 = 8.57 \cdot 10^{-10} = 8.57 \cdot 10^{-8}$ %. 1.5pt

$\chi(^{1}HD^{34}S) = 2 \cdot 0.00014 \cdot 0.99986 \cdot 0.0437 = 1.22 \cdot 10^{-5} = 1.22 \cdot 10^{-3}$ %. 2pt

The desulfurization is a catalytic process typically carried out over MoS_2 supported on SiO_2 (MoS_2/SiO_2) catalyst. To study the surface of the catalyst, isotope exchange methods can be employed. The isotope exchange reaction takes place at the gas-solid interface, resulting in the exchange of the surface atoms exclusively. In a first approximation, the bulk atoms do not participate in the exchange (**Figure 2**).

In the experiment, the isotope exchange between the MoS_2/SiO_2 catalyst (Mo mass fraction w_{Mo} = 4.280 wt.%., initially containing only ^{32}S) and gaseous isotopically-labeled $H_2{}^{34}S$ was studied in a flow reactor (**Figure 2**). The MoS_2/SiO_2 catalyst (m_{cat} = 1.2350 g) was kept in a flow (p = 1.00 bar, v = 20.0 mL/min, T = 23.0 °C) of gas mixture containing $H_2{}^{34}S$ balanced with Ar (volume fraction $\phi_{H_2^{34}S}$ = 1.00 vol.% $H_2{}^{34}S$, ^{34}S isotopic purity α = 99.95 mol.%).

The experiment duration was t = 10.0 min and gas from the outlet was collected during the entire experiment. The measured fraction of ^{34}S isotope among the sulfur atoms (γ) in the collected gas phase was γ = 87.3 mol%. Assume ideal gas behavior, and that the elemental (not isotopic!) composition of MoS_2 on the surface and in the bulk are identical, and by the end of the experiment all sulfur atoms from the surface are exchanged with the gas phase.

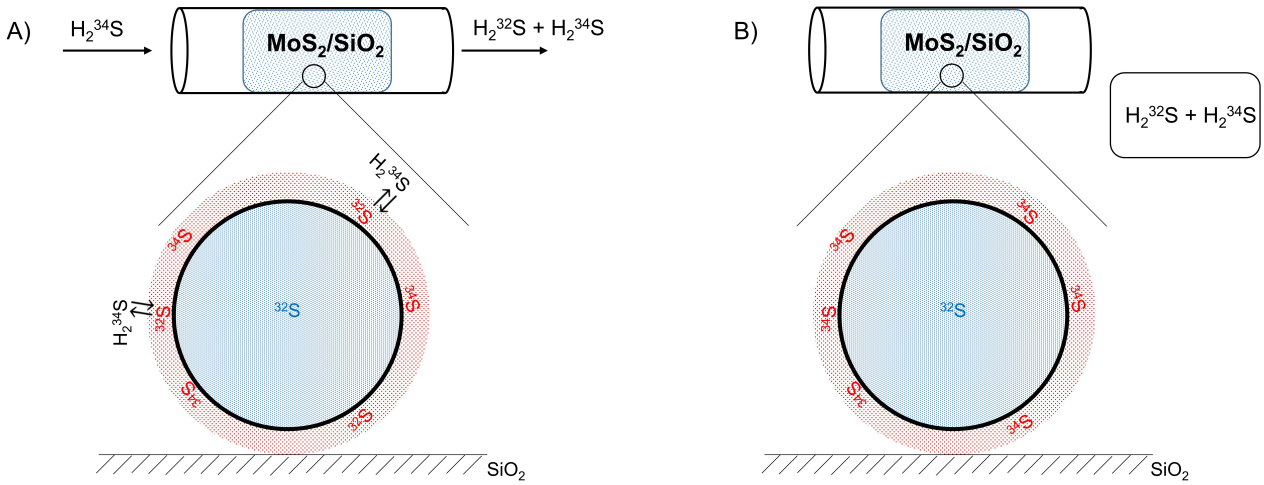


Figure 2. Schematic representation of the experiment in the course (**A**) and at the final stage (**B**). Sulfur atoms on the surface are shown in red, sulfur atoms in the bulk are shown in blue. Molybdenum atoms are not shown.

5.4 **Calculate** the number of exchanged sulfur atoms *n(S)$_{surface}$*, give your answer in mol. 5pt

All exchanged sulfur atoms are ^{32}S atoms which were initially on the catalyst surface and in the end of experiment appeared in the gas phase. The volume of $H_2{}^{32}S$ can be calculated as difference between volume of $H_2{}^{34}S$ supplied and collected. The volume of supplied $H_2{}^{34}S$ can be calculated as:

$V(H_2^{34}S)_{supplied} = v \cdot t \cdot \phi_{H_2^{34}S} \cdot \alpha = 20.0\,\frac{mL}{\text{min}} \cdot 10.0\ \text{min} \cdot 0.01 \cdot 0.9995 = 2.00 \cdot 10^{-3}\,L$

Applying the same formula, the volume of collected $H_2{}^{34}S$ can be calculated as:

$V(H_2^{34}S)_{collected} = v \cdot t \cdot \phi_{H_2^{34}S} \cdot \gamma = 20.0\,\frac{mL}{\text{min}} \cdot 10.0\,min \cdot 0.01 \cdot 0.873 = 1.75 \cdot 10^{-3} L$

0.5 pt for each correct formula, 0.5 for each calculation

The volume of $H_2{}^{32}S$ with ^{32}S atoms from the catalyst is the difference between the volume of supplied and collected $H_2{}^{34}S$:

$V(H_2^{32}S) = V(H_2^{34}S)_{supplied} - V(H_2^{34}S)_{collected} = (2.00 - 1.75) \cdot 10^{-3} L = 2.50 \cdot 10^{-4} L$

1 pt for correct formula, 0.5 for calculation

The number of exchanged sulfur atoms can be calculated from the ideal gas law:

$n(S)_{surface} = n(H_2^{32}S) = \frac{p \cdot V}{R \cdot T} = \frac{1.00 \cdot 10^5\ Pa \cdot 2.50 \cdot 10^{-7}\ m^3}{8.314472\ \frac{J}{mol\,K} \cdot 296.15\ K} = 1.02 \cdot 10^{-5}\ mol$

1 pt for correct formula, 0.5 for calculation

If you have been unable to calculate the number of total exchanged sulfur atoms, use the value $1.53 \cdot 10^{-5}$ mol *in all the following calculations.*

Assume that the MoS_2 phase consists of uniform spherical particles, and at the end of the experiment all sulfur atoms located on the surface are exchanged, while the bulk atoms did not participate in the exchange reaction. The density ρ of MoS_2 is ρ = 5.06 g·cm^{-3}, the average area occupied by S and Mo atoms on the surface is equal to A_S = $3.00 \cdot 10^{-19}$ m^2 and A_{Mo} = $5.00 \cdot 10^{-19}$ m^2, respectively. The area of a sphere with radius R can be calculated as $S = 4\pi R^2$, and its volume as $V = \frac{4}{3}\pi R^3$. Assume that isotopic composition does not affect the density of MoS_2.

5.5 **Calculate** the particle radius *R* of the MoS_2 particles, give your answer in nm. 8pt

Let N be the total number of MoS_2 spherical particles and R be the radius of each sphere. The total volume of all spheres is equal to the total volume of the MoS_2 phase:

$$V(MoS_2) = N\frac{4}{3}\pi R^3 = \frac{m(MoS_2)}{\rho(MoS_2)} = \frac{\frac{m_{cat}\cdot w_{Mo}}{MW(Mo)}\cdot MW(MoS_2)}{\rho(MoS_2)} = \frac{\frac{1.235\,g\cdot 0.0428}{95.95\,g}\cdot\frac{160.07\,g}{mol}\cdot\frac{10^{-3}kg}{g}}{5.06\cdot 10^3\,\frac{kg}{m^3}} = 1.74\cdot 10^{-8}\,m^3$$

1 pt for the formula of total volume being equal to the volume of all spheres, 1 pt for the formula for calculation of total volume as mass divided by density, 1 pt for correct calculations

The total number of sulfur atoms on the surface of all spheres is equal to the total number of exchanged sulfur atoms. Therefore, the total area of all MoS2 spheres can be calculated as follows:

$$A(MoS_2) = N4\pi R^2 = n(S)_{surface}\cdot N_A\cdot\frac{2\cdot A_S + A_{Mo}}{2} = 1.02\cdot 10^{-5}mol\cdot 6.022\cdot 10^{23}\cdot mol^{-1}\cdot\frac{(2\cdot 3.00 + 5.00)\cdot 10^{-19}m^2}{2} = 3.38\,m^2$$

1 pt for the formula of total surface area being equal to the surface of all spheres, 1 pt for the formula for calculation of total surface, 1 pt for correct calculations

The radius R can be calculated from the ratio of the total volume over the total surface area:

$$\frac{V(MoS_2)}{A(MoS_2)} = \frac{R}{3} = \frac{1.74\cdot 10^{-8}\,m^3}{3.38\,m^2} = 5.15\cdot 10^{-9}\,m$$

$$R = 3\cdot 5.15\cdot 10^{-9}\,m = 15.5\,nm$$

1 pt for the formula, 1 pt for correct calculations

If $n(S)_{surface} = 1.53\cdot 10^{-5}\,mol$ was used:
$A(MoS_2) = 5.07\,m^2$ and $R = 10.3\,nm$

In reality, the isotopically-labeled atoms from the surface diffuse into the bulk and the non-labeled atoms from the bulk travel to the surface, undergoing a gradual exchange (**Figure 3A**). Therefore, for a given moment, the fraction of the labeled atoms inside the particle decreases from the surface of the particle to its center. Simultaneously, with an increase in time of exchange, the involvement of bulk atoms to the exchange reaction increases, as sketched in **Figure 3B**.

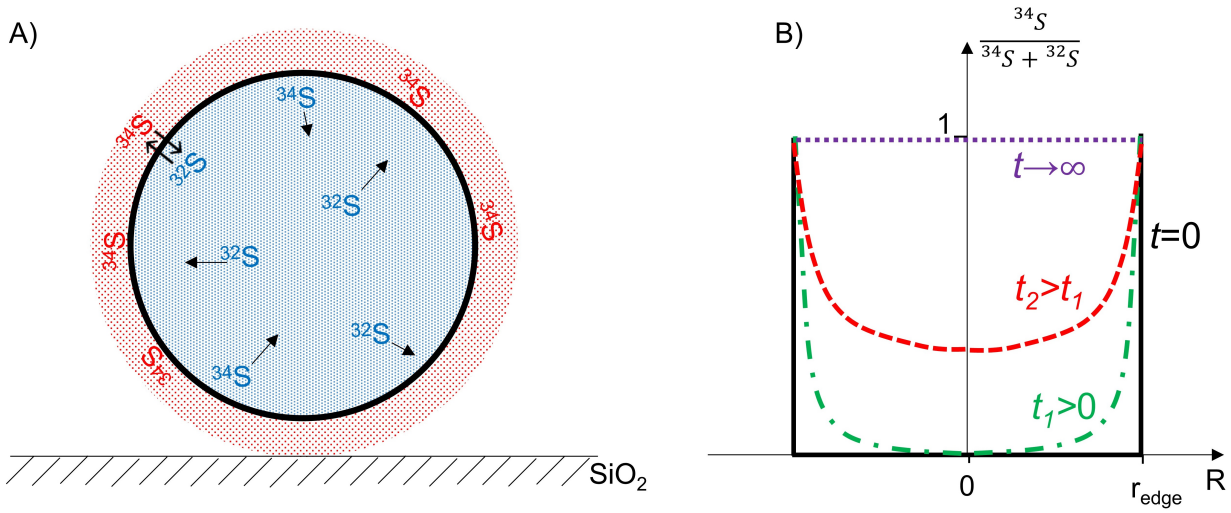


Figure 3. **A**) Schematic representation of the diffusion of sulfur isotopes from the surface to the bulk in MoS_2 particle. Sulfur atoms on the surface are shown in red, sulfur atoms in the bulk are shown in blue. Molybdenum atoms are not shown. **B**) The fraction of ^{34}S atoms in the bulk as function of time and distance from center of the particle. r_{edge} corresponds to the radius of MoS_2 particle.

At the end of the experiment, the surface atoms are completely exchanged, and additionally a fraction of the bulk is exchanged due to the diffusion. The fraction *F* of the exchanged bulk atoms ($n(S)^{ex}_{bulk}$) and the total bulk atoms of sulfur ($n(S)^{total}_{bulk}$) can be calculated as follows: $F = n(S)^{ex}_{bulk}/n(S)^{total}_{bulk} = 1-e^{-\frac{D\cdot t}{R^2}}$, where t is the time of exchange experiment (described above), R is the particle size (radius for a spherical shape particle) and D is the diffusion coefficient. The catalyst described above was independently studied by means of electron microscopy, which showed that the MoS_2 particles are uniformly distributed spheres with a radius of 35.0 nm.

5.6	Using *R* = 35.0 nm as the radius and the data of the exchange experiment described above, **<u>calculate</u>** the diffusion coefficient *D* for the diffusion of sulfur atoms in MoS_2, give your answer in $\frac{m^2}{s}$. In your calculations, use the following approximation: $e^x \approx 1 + x$ for $x \ll 1$.	12.5pt

The number of spherical particles N with R = 35 nm can be calculated from the total volume of the MoS_2 phase divided by the volume of one sphere:

$N = \frac{V(MoS_2)}{\frac{4}{3}\pi R^3} = \frac{1.74 \cdot 10^{-8}\, m^3}{\frac{4}{3}\pi \cdot (3.50 \cdot 10^{-8}\, m)^3} = 9.69 \cdot 10^{13}$

1.5 pt for the formula, 1 pt for the calculation

The total surface area A(MoS_2) for all spheres with a radius R = 35.0 nm:

$A(MoS_2) = N\, 4\,\pi\, R^2 = 9.69 \cdot 10^{13} \cdot 4\,\pi\,(3.50 \cdot 10^{-8}\, m)^2 = 1.49\, m^2$

1.5 pt for formula, 1 pt for the calculation

The number of sulfur atoms on the surface $n(\mathrm{S})_{\mathrm{surface}(R=35\,\mathrm{nm})}$ of all spheres can be calculated as:

$n(\mathrm{S})_{\mathrm{surface}(R=35\,\mathrm{nm})} = \frac{A(MoS_2)}{(2 \cdot A_S + A_{Mo}) \cdot N_A} \cdot 2 = \frac{2 \cdot 1.49\, m^2}{(2 \cdot 3.00 + 5.00) \cdot 10^{-19}\, m^2 \cdot 6.022 \cdot 10^{23}\, mol^{-1}} = 4.59 \cdot 10^{-6}\, mol$

1.5 pt for the formula, 1 pt for the calculation

The number of total sulfur $n(\mathrm{S})_{\mathrm{total}}$ atoms can be calculated as:

$n(S)_{total} = 2n(Mo) = 2 \cdot \frac{m_{cat} \cdot w_{Mo}}{MW(Mo)} = 2 \cdot \frac{1.235\, g \cdot 0.0428}{\frac{95.95\, g}{mol}} = 1.10 \cdot 10^{-3}\, mol$

The number of sulfur atoms in the bulk $n(S)^{total}_{bulk}$ can be calculated as the difference between the total number of atoms $n(\mathrm{S})_{\mathrm{total}}$ and the number of sulfur atoms on the surface $n(\mathrm{S})_{\mathrm{surface}(R=35\,\mathrm{nm})}$:

$n(S)^{total}_{bulk} = n(S)_{total} - n(\mathrm{S})_{\mathrm{surface}(R=35\,\mathrm{nm})}$

The number of sulfur atoms from the bulk that participated in the exchanged $n(S)^{ex}_{bulk}$ can be calculated as the difference between the total number of exchanged atoms $n(S)^{ex}_{total}$ and the number of sulfur atoms of the surface $n(\mathrm{S})_{\mathrm{surface}(R=35\,\mathrm{nm})}$ (all surface atoms got exchanged):

$n(S)^{ex}_{bulk} = n(S)^{ex}_{total} - n(\mathrm{S})_{\mathrm{surface}(R=35\,\mathrm{nm})}$

The fraction *F* of the exchanged bulk atoms ($n(S)^{ex}_{bulk}$) and the total bulk atoms of sulfur ($n(S)^{total}_{bulk}$) can be calculated as:

$F = \frac{n(\mathrm{S})^{\mathrm{ex}}_{\mathrm{bulk}}}{n(\mathrm{S})^{\mathrm{total}}_{\mathrm{bulk}}} = \frac{n(\mathrm{S})^{\mathrm{ex}}_{\mathrm{total}} - n(\mathrm{S})_{\mathrm{surface}(R=35\,\mathrm{nm})}}{n(\mathrm{S})_{\mathrm{total}} - n(\mathrm{S})_{\mathrm{surface}(R=35\,\mathrm{nm})}} = \frac{1.03 \cdot 10^{-5} - 4.5 \cdot 10^{-6}}{1.10 \cdot 10^{-3} - 4.5 \cdot 10^{-6}} = 5.26 \cdot 10^{-3}$

0.5 pt for each formula for $n(S)^{total}_{bulk}$, $n(S)^{ex}_{bulk}$ and F, 1 pt for the calculations

F<<1 indicates that the given approximation is valid:

$F = 1 - e^{-\frac{D \cdot t}{R^2}} \approx 1 - \left(1 - \frac{D \cdot t}{R^2}\right) = \frac{D \cdot t}{R^2}$

1 pt for the formula

$D = \frac{F \cdot R^2}{t} = \frac{5.26 \cdot 10^{-3} \cdot (3.50 \cdot 10^{-8}\,\mathrm{m})^2}{600\,\mathrm{s}} = 1.07 \cdot 10^{-20}\,\frac{\mathrm{m}^2}{\mathrm{s}}$

0.5 pt for the formula, 1 pt for the calculations

Calculations using $1.53 \cdot 10^{-5} mol$ for $n(S)^{ex}_{total}$:

$F = \frac{n(\mathrm{S})^{\mathrm{ex}}_{\mathrm{bulk}}}{n(\mathrm{S})^{\mathrm{total}}_{\mathrm{bulk}}} = \frac{n(\mathrm{S})^{\mathrm{ex}}_{\mathrm{total}} - n(\mathrm{S})_{\mathrm{surface}(R=35\,\mathrm{nm})}}{n(\mathrm{S})_{\mathrm{total}} - n(\mathrm{S})_{\mathrm{surface}(R=35\,\mathrm{nm})}} = \frac{1.53 \cdot 10^{-5} - 4.5 \cdot 10^{-6}}{1.10 \cdot 10^{-3} - 4.5 \cdot 10^{-6}} = 9.85 \cdot 10^{-3}$

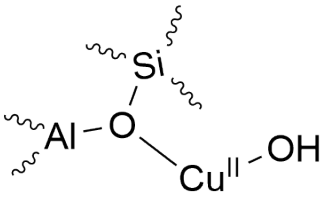
$D = \frac{F \cdot R^2}{t} = \frac{9.85 \cdot 10^{-3} \cdot (3.50 \cdot 10^{-8}\,\mathrm{m})^2}{600\,\mathrm{s}} = 2.01 \cdot 10^{-20}\,\frac{\mathrm{m}^2}{\mathrm{s}}$

Direct conversion of methane to methanol - Solutions

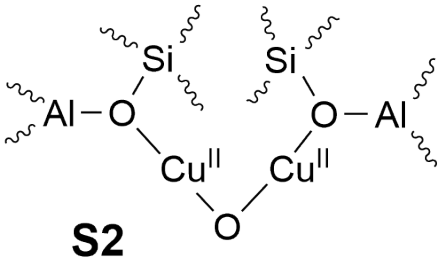
7% of total											
Question	6.1	6.2	6.3	6.4	6.5	6.6	6.7	6.8	6.9	6.10	**Total**
Points	2	4	1	2	4	3	3	3	4	6	**32**
Score											

Methane is widely available as natural gas making it an attractive feedstock for the chemical industry, such as for the production of methanol. However, control of this process is challenging as methanol is more easily oxidized than methane.

Overoxidation is avoided in a chemical looping process, where active sites of copper-exchanged zeolite catalysts provide only the single oxygen atom required for oxidation to methanol and are consumed. In a second step, the catalyst is regenerated with oxygen in the absence of methane. The scheme below shows two potential catalytic copper sites.



S1



S2

During the reaction, $Cu^{(II)}$ is reduced to $Cu^{(I)}$.

6.1 **Give** the number of **S1** sites and the number of **S2** sites required to oxidize one methane molecule to methanol. 2pt

Two S1 sites or one S2 site would be needed, since oxidation state changes by two units.

if both correct; reasoning not needed **2pt**

In the absence of oxygen, the formed methanol does not desorb from zeolite. If the reaction is performed in a container with constant volume and temperature (an autoclave), a pressure drop results only from the consumption of methane, which can be considered as an ideal gas. In a 1 L autoclave containing 200 mg of zeolite loaded with 4.3 wt.% copper, the initial methane pressure $p_0 = 933\ \mathrm{Pa}$ dropped to $p_\infty = 925\ \mathrm{Pa}$ after completion of the reaction at 528 K.

6.2 **Compute** the percentage of copper that reacted. 4pt

△ $n_{methane} = pV/(RT) = 8\ Pa \cdot 10^{-3}\ m^3/(8.314\ J \cdot mol^{-1} \cdot K^{-1} \cdot 528\ K) = 1.822 \cdot 10^{-6}$ mol

$n_{Cu} = 4.3 \cdot 10^{-2} \cdot 0.2\ g/(63.55\ g \cdot mol^{-1}) = 1.353 \cdot 10^{-4}$ mol.

Two copper are required per methane molecule. A fraction of 0.0269 (2.69%) of the copper has reacted. ($2 \cdot 1.822 \cdot 10^{-6}$ mol/$1.353 \cdot 10^{-4}$ mol)

for everything in the range of 2.6 to 2.8 %.; 4pt

if n_{Cu} was computed in the range 1.3 to $1.4 \cdot 10^{-4}$ mol, but not more; 2pt

if the answer given is in the range 1.3-1.4% due to forgetting that there are 2 Cu per methane; 3pt

if in the answer to 6.1, the ratio of S1 to S2 sites was 2:1 and the percentage is consistent with the number of sites in the answer to 6.1: 4pt

6.3 Experimental data is plotted in **Figure 1**. Based on this, **decide** on the (pseudo) order of the oxidation of CH_4. **Tick** the box with the correct statement **on the answer sheet**. 1pt

☐ The reaction is of (pseudo) zeroth order.

☒ The reaction is of (pseudo) first order.

☐ The reaction is of (pseudo) second order.

The semi-logarithmic plot is linear, which applies only to first-order reactions. Because the contributing elementary reactions are bimolecular (CH_4 and site **S1** as well as CH_4 and site **S2**), it is of pseudo first order.

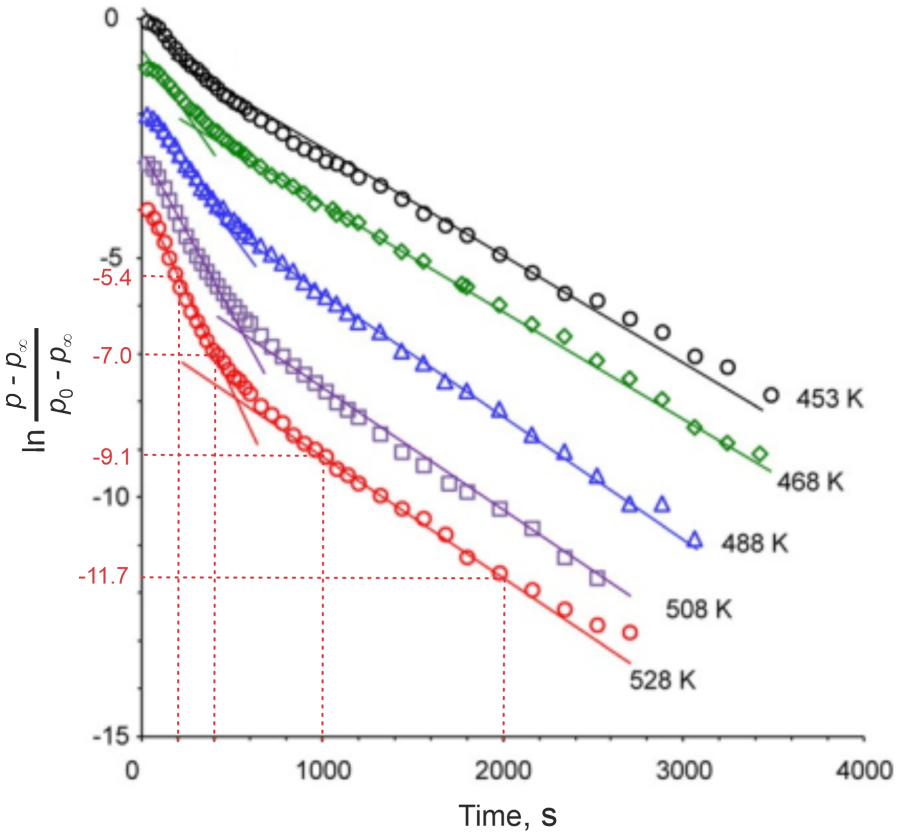


Figure 1: Semi-logarithmic graph of normalized methane pressure p versus time for the reaction with copper-loaded zeolite containing sites **S1** and **S2** in an autoclave at various temperatures. The symbols denote experimental data points. The solid lines are linear fits to appropriate time ranges. The dotted lines are guides to the eyes.

6.4 **Write** down the (pseudo) rate law for the oxidation of CH_4 that is consistent with the experimental data under the given conditions. Note that it may depend on the concentrations of CH_4 as well as of sites **S1** and **S2** and on the rate constants. 2pt

$v = -d[CH_4]/dt = k_{S1}\,[S1] + k_{S2}\,[S2]$

Because of the large excess of methane (small relative pressure drop), the concentration $[CH_4]$ does not feature in the rate law. It is not obvious from the plot, but the rate must of course depend on the concentration of the catalytic sites (they are consumed). As **S1** is visited sequentially, the **S1** rate should be proportional to [S1] and not $[S1]^2$.

if correct and two different rate constants are specified (with any reasonable notation); 2pt
if $v = -d[CH_4]/dt = k_{S1}\,[CH_4][S1] + k_{S2}\,[S2]\,[CH_4]$ is given 1pt
if both rate constants assumed to be equal or if only one term on right-hand-side is given or if $[S1]^2$ instead of [S1]; 1pt

Further clarification of marking scheme:
(k1+k2)[CH4] 0pt
two errors 0pt

6.5 **Tick** the boxes with correct statements **on the answer sheet**. 4pt

Two processes with different rates are observed. At least for the faster process (S2 sites), it is seen in Figure 1 that the slope increases with increasing temperature. What fraction of the copper sites reacts, cannot be determined from these plots.

☒ At least two types of copper sites react, each with a different rate constant.
☒ The overall methane oxidation by copper-loaded zeolite is faster at higher temperature.
☐ At higher temperature, a larger fraction of the copper sites will have reacted with methane after completion of the reaction.
☐ One of the reactions becomes slower at higher temperature.

if all correctly ticked/unticked 4pt
if only one error 2pt

Paramagnetic sites **S1** can be observed by electron paramagnetic resonance (EPR) spectroscopy, whereas diamagnetic sites **S2** do not give an EPR signal. EPR spectroscopy measures the number of electron spins. Thus, the number of **S1** sites is proportional to the double integral I_2 of the EPR spectrum, i.e. **[S1]** $\propto I_2$. Spectra were measured at different temperatures T and at each temperature at different times, t, after initiating the reaction.

6.6 **Derive** the equation linear in time that relates $I_2(t)$ to the rate constant for the loss of **S1** sites. 3pt

Since $I_2(t)$ is proportional to [S1](*t*), we can use the rate law -d[S1]/dt = k_{S1} [S1] and the time dependence of [S1] that follows from the rate law [S1](*t*) = [S1](0) exp(-$k_{S1}t$).
Hence, $I_2(t) = I_2(0)\exp(-k_{S1}t)$. By taking the logarithm, we linearize this equation, ln $I_2(t)$ = ln $I_2(0)$ - $k_{S1}t$ and find that k_{S1} is the negative of the slope of a plot of ln $I_2(t)$ against *t*.

for correct result 3pt
for stopping at $I_2(t) = I_2(0)\exp(-k_{S1}t)$ 2pt

Further clarification of marking scheme:
ln(I2(t)/I2(0) = -kt 3pt
ln(I2(0)/I2(t) = +kt 3pt
ln[S1](t) = ln[S1](0) - kt 2pt
d I2/dt = -k I2 1pt
correct equation for creation of product instead of loss of reactant 1pt
correct except for sign error 1pt
continuation error from 6.4 giving correct equations for 2nd-order process 2pt
(not full marks because it is clear that this does not match results of Fig 1)

6.7 **Tick** the boxes **on the answer sheet** for each measurement that needs to be calibrated with a known Cu(II) standard. 3pt

☒ Total number of paramagnetic Cu(II) sites in the sample
☒ Concentration of paramagnetic Cu(II) sites in the sample
☐ Rate constant
☐ Types of different paramagnetic Cu(II) species in the sample

For determining absolute number and concentration, we need to calibrate signal amplitude with respect to number of spins. The rate constant can be derived from relative amplitudes in spectra obtained at different times, which does not require calibration. The types of Cu(II) species can be inferred from the number of spectral components and this also does not require calibration.

if all correct 3pt
if one error 2pt

From EPR measurements, it is known that the rate constant for the reaction with **S1** sites at 528 K is 2.604×10^{-3} s^{-1}.

6.8 Considering **Figure 1** and **based on a calculation**, **decide** if methane reacts faster or slower with **S2** sites than with **S1** sites. 3pt

From the Figure, we can compute the two rate constants at 528 K. For each process, we have $p(CH_4) = p_0(CH_4)\exp(-k_i\,t)$.
It follows that $\ln p(CH_4,t_1) - \ln p(CH_4,t_2) = k_i\,(t_2 - t_1)$, i.e., the rate constants are the negative slopes in Figure 1. At short times, the fast process dominates, but at long times, only the slow process contributes. For the fast process, we find k_{fast} = [-5.4-(-7)]/(400 s – 200s) = $8\cdot10^{-3}$ s^{-1}. For the slow process, we have k_{slow} = = [-9.1-(-11.7)]/(2000 s – 1000 s) = $2.6\cdot10^{-3}$ s^{-1}. The latter value is very close to the value given in Table 1. Hence, the slower process can be assigned to **S1** sites, meaning that **S2** sites react faster.

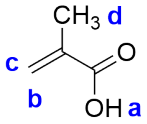
☐ Methane reacts faster with **S1**.
☐ Both reaction rates are the same.
☒ Methane reacts faster with **S2**.

for either fast rate between $7\cdot10^{-3}$ s^{-1} and $9\cdot10^{-3}$ s^{-1} or slow rate between $2\cdot10^{-3}$ s^{-1} and $3\cdot10^{-3}$ s^{-1} 1pt
for correct answer 2pt

further clarification:
it is OK to simply measure the slope (giving the -ve of the rate) for the 1pt

Methanol can be further converted into valuable olefins with different zeolite catalysts. In this process, one observes an intermediate product with molar mass 86.09 g mol^{-1}, elemental analysis (55.8 wt.% C, 7.0 wt.% H) and an ^{1}H NMR spectrum consisting of signals at four different chemical shifts (**a**: $12.2\ \mathrm{ppm}\ (1\mathrm{H},\ \mathrm{s})$, broad, disappears when D_2O is added; **b**: 6.3 ppm (1H, d); **c**: 5.7 ppm (1H, d); **d**: 2.0 ppm (3H, s)).

6.9 **Draw** the structure of the intermediate product and **assign** protons **a** and **d**. 4pt



The compound has 4 carbon atoms and 6 protons. This leaves 32.02 g/mol for other elements. From the chemical context, we can expect that this corresponds to two oxygen atoms. Each of the signals **a**, **b**, and **c** corresponds to a single proton, signal **d** corresponds to three protons. Together with the chemical shift, we can safely assign signal **d** to a methyl group. The very large chemical shift of proton **a** suggests an acidic proton. From the number of protons we can infer a carbon-carbon double bond or a cyclic structure. A cyclic structure cannot be constructed with the groups that we have already assigned. The relatively large chemical shift of the methyl protons suggests that the methyl group is next to the carboxylic acid group. The multiplet information safely excludes a structure with the methyl group on the other side of the C=C bond.

for any molecule with formula $C_4O_2H_6$ (or for stating this formula) 1pt
for identifying d as methyl group +1pt
for identifying a as acidic; +1pt
for exactly correct structure +1pt

Further clarification of marking scheme:
if neither a nor d is identified, but there are CH3 and COOH groups +1pt

The United States Department of Energy assigned 12 chemical compounds only containing C, H and O as platform chemicals. These are the most promising candidates, easy to prepare from renewable resources and with multiple target derivatives to be prepared from them.

One of them is compound **A**, that can either be further derivatized or used for example in medicinal applications or in detergents.

- ^{1}H NMR in DMSO: 7.81 ppm (**a,** s), 13.0 ppm (**b**, s, broad, disappears when D_2O is added), both signals have the same integral.
- ^{13}C NMR: 165.1 ppm (**1**), 150.6 ppm (**2**) and 120.6 ppm (**3**).
- MW: 156.03 g mol^{-1}. Elemental analysis (EA): 46.15 wt.% C, 2.56 wt.% H.

6.10 **Give** a possible structure of **A** and **assign** all protons and carbon **1**. 6pt

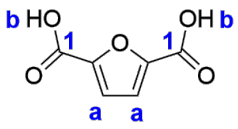
From the EA 100 wt % - 46.15 wt % - 2.56 wt % = 51.29 wt % remain for O.

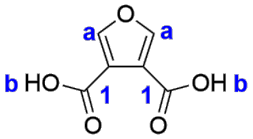
element	*Mol. mass*	*EA*	*EA/M_N*
C	12.000	46.15 %	3.85
H	1.008	2.56 %	2.56
O	15.999	??	

The empirical formula is $C_6H_4O_5$

From the NMR data one can conclude that **A** is a symmetrical molecule with one proton attached to an aromatic ring and one acidic proton in each moiety.

There are two possible products in line with this data, 2,5-furandicarboxylic acid (actual data and designated platform chemical) and 3,4-furandicarboxylic acid.





2 possible schemes (choose whichever gives higher grade):

EITHER

for any molecule with formula $C_6H_4O_5$ 1pt

if the molecule is symmetric and has COOH groups 1pt

if the NMR signals are assigned correctly 1pt

if they have won these 3 points and the molecule is not one of the molecules given above, but is "reasonable", i.e. has been reported in the literature +1pt

OR

if one of the two correct structures is given (or both) with correct assignments 6pt

but for each wrong structure -2pt

and for each wrong set of assignments (protons or carbons) for a correct structure a point is deducted, down to a minimum of zero.]

Enzyme Kinetics - Solutions

7% of total						
Question	7.1	7.2	7.3	7.4	7.5	**Total**
Points	3	4	2	8	17	**34**
Score						

The Michaelis–Menten (MM) mechanism was introduced in 1913 to describe the kinetics of enzyme catalysis. In this mechanism, enzyme **E** catalyzes the conversion of substrate **S** to the product **P**:

$$\mathbf{E} + \mathbf{S} \underset{k_2}{\overset{k_1}{\rightleftarrows}} \mathbf{ES} \xrightarrow{k_3} \mathbf{E} + \mathbf{P}$$

The initial rate for an enzymatic reaction following the MM mechanism is usually given as:

$$v_0 = \frac{v_{\max}[\mathbf{S}]_0}{[\mathbf{S}]_0 + K_M} \tag{1}$$

when the initial concentration of **E** is much lower than the initial concentration of **S** ($[\mathbf{E}]_0 \ll [\mathbf{S}]_0$). The Michaelis constant is defined as $K_M = \frac{k_2+k_3}{k_1}$. The initial rate can also be expressed as the product of the relative flow j and $[\mathbf{E}]_0$:

$$v_0 = j[\mathbf{E}]_0 \tag{2}$$

Note: *Questions **7.1** and **7.2** can have one, multiple, or no correct answer(s).*

7.1 **Choose** the correct alternative form(s) of the initial rate (v_0) expressions (1) and (2) **on the answer sheet**. $[\mathbf{ES}]_{\max}$ is the maximum concentration of the **ES** complex. 3pt

☒ $v_0 = \frac{k_3[\mathbf{E}]_0[\mathbf{S}]_0}{[\mathbf{S}]_0+K_M}$ ☐ $v_0 = \frac{k_3[\mathbf{E}]}{1+K_M/[\mathbf{S}]_0}$ ☒ $v_0 = j[\mathbf{ES}]_{\max}$

☐ $v_0 = \frac{k_3[\mathbf{E}]_0[\mathbf{ES}]_{\max}}{[\mathbf{S}]_0+K_M}$ ☒ $v_0 = \frac{k_3[\mathbf{E}]_0}{1+K_M/[\mathbf{S}]_0}$ ☐ $v_0 = \frac{j[\mathbf{E}]_0}{K_M+[\mathbf{S}]_0}$

The answers represent the same kinetic equation $v_0 = \frac{v_{max}[S]_0}{[S]_0+K_M} = \frac{k_3[E]_0[S]_0}{[S]_0+K_M} = j[E]_0$ expressed in different ways.
(1pt for each correct option, –1pt for each incorrect option until minimum 0pt is reached, 3pt in total)

7.2 **Choose** the pair(s) of axes (y vs. x) **on the answer sheet** that are expected to give a linear plot. 4pt

☐ v_0 vs. $1/[\mathbf{S}]_0$ ☒ v_0 vs. v_0/K_M ☐ v_0 vs. K_M/v_0

☐ $1/v_0$ vs. $v_0/[\mathbf{S}]_0$ ☐ $1/v_0$ vs. v_0/K_M ☒ $[\mathbf{S}]_0/v_0$ vs. $[\mathbf{S}]_0$

When the equation $v_0 = \frac{v_{max}[S]_0}{[S]_0+K_M}$ is inversed, the following equation is obtained: $\frac{1}{v_0} = \frac{[S]_0+K_M}{v_{max}[S]_0} = \frac{1}{v_{max}} + \frac{K_M}{v_{max}} \cdot \frac{1}{[S]_0}$. This equation matches the linear form $y = ax+b$ with $\frac{1}{v_0}$ vs. $\frac{1}{[S]_0}$ as y vs. x coordinates. Thus, options v_0 vs. $1/[S]_0$ and $1/v_0$ vs. $v_0/[S]_0$ are not correct. Option $[S]_0/v_0$ vs. $[S]_0$ can be checked if the reversed equation is multiplied by $[S]_0$: $\frac{[S]_0}{v_0} = \frac{[S]_0}{v_{max}} + \frac{K_M}{v_{max}}$, making it the correct answer. The other three options don't contain $[S]_0$ as a variable, thus, the MM equation is not needed to check them. Only option v_0 vs. v_0/K_M reflects the linear dependence $v_0 = K_M \frac{v_0}{K_M}$.
(2pt for each correct option, –2pt for each incorrect option until minimum 0pt is reached, 4pt in total)

Many enzymes catalyze multi- rather than single-substrate transformations. However, if the concentration of one of the substrates is much higher than that of the other substrate or it is kept constant, the MM kinetics is also valid. Here we will look at *two independent enzymatic systems* that follow the MM kinetics.

Enzymatic System I

Enzyme **E** converts substrates **A** and **B** to products $\mathbf{P_A}$ and $\mathbf{P_B}$. At rapid pre-equilibrium between the free enzyme and all enzyme-substrate complexes, the following v_0 equation applies:

$$v_0 = \frac{k[\mathbf{E}]_0[\mathbf{A}]_0[\mathbf{B}]_0}{(K+[\mathbf{A}]_0)(K+[\mathbf{B}]_0)} \quad (3)$$

k is the rate constant of one of the reactions. The same equilibrium constant K characterizes the dissociation of either substrate from the corresponding active site of **E**.

7.3 **Show** that equation (3) takes the MM form (1) if the concentration of substrate **B** is maintained at a constant value c_0. **Give** the expression for $v_{\max}$ in this case. 2pt

If the concentration of substrate **B** is maintained constant, c_0:

$$v_0 = \frac{k[E]_0[A]_0 c_0}{(K + [A]_0)(K + c_0)} = \frac{\frac{k[E]_0 c_0}{K + c_0}[A]_0}{K + [A]_0} = \frac{v_{max}[A]_0}{K_M + [A]_0}$$

Thus, the maximum rate v_{max} corresponds to the expression:

$$v_{max} = \frac{k[E]_0 c_0}{K + c_0}$$

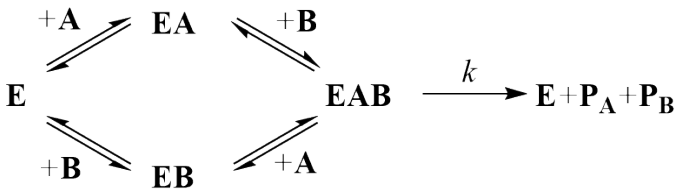
(1pt for the MM form, 1pt for v_{max}, 2pt in total)

7.4 **Propose** a kinetic scheme for the Enzymatic System I consistent with equation (3), showing all the intermediates and products. **Indicate** the reaction with a rate constant k. 8pt

One-substrate enzymatic reaction:

$$\mathbf{E} + \mathbf{S} \underset{k_2}{\overset{k_1}{\rightleftarrows}} \mathbf{ES} \xrightarrow{k_3} \mathbf{E} + \mathbf{P}$$

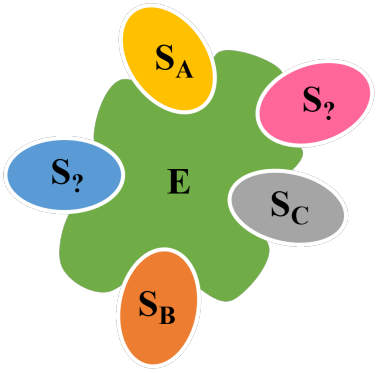
In the case of pre-equilibrium ($k_3 \ll k_2$), the equilibrium constant for the dissociation of a substrate from a catalyst active site is: $K = \frac{k_2}{k_1} = \frac{[E][S]}{[ES]}$. The initial rate for this enzymatic reaction is $v_0 = k_3[ES] = k_3\alpha_{ES}[E]_0$, where $\alpha_{ES} = \frac{[ES]}{[E]_0} = \frac{[ES]}{K[ES]/[S]+[ES]} = \frac{[S]}{K+[S]}$ is a fraction of catalyst in the form of enzyme–substrate complex **ES**. As the substrate concentration at the beginning of a reaction is much higher than the enzyme concentration, it can be considered equal to the initial concentration, thus $\alpha_{ES} = \frac{[S]_0}{K+[S]_0}$. This is how the initial rate equation takes the Michaelis–Menten form: $v_0 = k_3\alpha_{ES}[E]_0 = \frac{k_3[E]_0[S]_0}{K+[S]_0} = \frac{v_{max}[S]_0}{K_M+[S]_0}$ with $v_{max} = k_3[E]_0$ and $K_M = K$, which can be expected from the original expression $K_M = \frac{k_2+k_3}{k_1}$ with the pre-equilibrium condition $k_3 \ll k_2$.
Based on this analogy, the expression from the question $v_0 = \frac{k[E]_0[A]_0[B]_0}{(K+[A]_0)(K+[B]_0)}$ lets assuming that k corresponds to the rate constant for the step of formation of the products from that form of the enzyme, with a fraction $\alpha = \frac{[A]_0[B]_0}{(K+[A]_0)(K+[B]_0)} = \frac{[A]_0[B]_0}{K^2+K[A]_0+K[B]_0+[A]_0[B]_0}$. This expression corresponds to the case when four enzyme forms are present: free enzyme **E** and enzyme bound to one or two substrates **EA**, **EB**, and **EAB**. This mole fraction corresponds to **EAB**, meaning that the products are formed from this form, e.g., $\alpha = \frac{[EAB]}{[E]_0}$.
The mechanism is a random sequential reaction:



Case 1. Equilibria between **E**, **EAB**, **EA**, **EB**; product formation reaction is shown: 8pt. –2pt if $\mathbf{P_A}$ and $\mathbf{P_B}$ are formed not from **EAB**, but from **EA** and **EB**. –0.5pt each if k/**E**/$\mathbf{P_A}$/$\mathbf{P_B}$ are missing in the products formation reaction.
Case 2. Equilibria between **E**, **EAB** and **EA** or **EB**; product formation reaction from **EAB** is shown: 4pt. –0.5pt each if k/**E**/$\mathbf{P_A}$/$\mathbf{P_B}$ are missing in the products formation reaction.
Case 3. Equilibrium between **E** and **EAB**; neither **EA**, nor **EB** are present; product formation reaction from **EAB** is shown: 3pt. –0.5pt each if k/**E**/$\mathbf{P_A}$/$\mathbf{P_B}$ are missing in the products formation reaction.
Case 4. Equilibria between **E**, **EAB**, **EA**, **EB**; no product formation reaction: 2pt.
All other cases: 0pt.

Enzymatic System II

Enzyme **E** has five active sites, each of which is specific to one of the substrates $\mathbf{S_A}$, $\mathbf{S_B}$, or $\mathbf{S_C}$ that are selectively transformed to products $\mathbf{P_A}$, $\mathbf{P_B}$, or $\mathbf{P_C}$, respectively. There is at least one active site for each substrate. Each active site is independent of the others.



$$\mathbf{E} + \mathbf{S_A} \underset{k_{a2}}{\overset{k_{a1}}{\rightleftarrows}} \mathbf{ES_A} \xrightarrow{k_{a3}} \mathbf{E} + \mathbf{P_A}$$

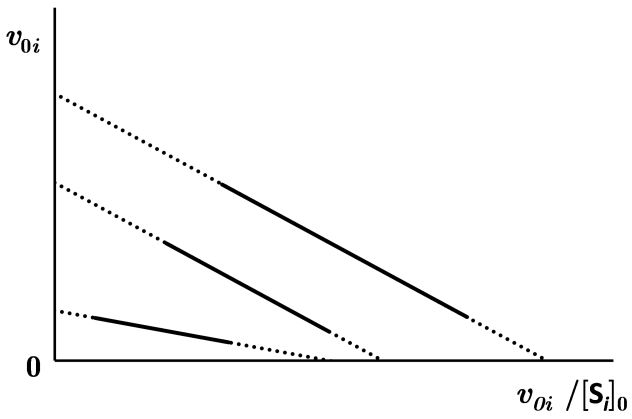
$$\mathbf{E} + \mathbf{S_B} \underset{k_{b2}}{\overset{k_{b1}}{\rightleftarrows}} \mathbf{ES_B} \xrightarrow{k_{b3}} \mathbf{E} + \mathbf{P_B}$$

$$\mathbf{E} + \mathbf{S_C} \underset{k_{c2}}{\overset{k_{c1}}{\rightleftarrows}} \mathbf{ES_C} \xrightarrow{k_{c3}} \mathbf{E} + \mathbf{P_C}$$

For **E**, it is known that:

1. The affinity for $\mathbf{S_C}$ is higher than for $\mathbf{S_B}$.

2. The plot of v_{0i} vs $v_{0i}/[\mathbf{S}_i]_0$, known as Eadie–Hofstee plot, for $\mathbf{S_A}$, $\mathbf{S_B}$, $\mathbf{S_C}$, with rate given per active site (v_{0i}), is shown below, but the scale and the legend are omitted.



3. When **E** is saturated with **S_A**, **S_B**, **S_C**, the catalytic turnover number (TON) for **S_C** per site is $10200\ \mathrm{min^{-1}}$, and 2023 **P_A**, **P_B**, **P_C** product molecules in total are synthesized per second. At the same time, no more than $5.94 \cdot 10^6$ molecules of **P_A** and **P_B** are detected to form per hour.

4. At equimolar concentrations of **S_A**, **S_B**, **S_C**, which are at least 1000 times lower than corresponding K_M values, the **P_A**, **P_B**, **P_C** concentrations become proportional to the catalytic efficiency ($\varepsilon_i = \frac{k_{i3}}{K_{M,i}}$), and their ratio is $3 : 2 : 5$, respectively.

5. Two **ES_i** complexes have equal rate constants for dissociation to **E** and **S_i**. The activation barrier for the reaction of **ES_C** into the initial compounds is $1266\ \mathrm{J\ mol^{-1}}$ higher than for the reaction into the final products. Assume that the pre-exponential factors are equal for both reactions and $T = 25\ ^\circ\mathrm{C}$.

6. For **E** + **S_i** reaction: $k_{c1} = 1.57 \cdot 10^7\ \mathrm{M^{-1}s^{-1}}$ and $k_{a1} = k_{b1}$.

7.5 **Fill in** the table **on the answer sheet** and **provide** your calculations. 17pt

Hints:

- Use information from 1. and 2. to find the relation between $K_{M,A}$, $K_{M,B}$ and $K_{M,C}$ ($<, >, =$).
- Information from 3. and 5. allows you to complete the first column (*number of active sites for each substrate*) and the last row *(all the constants for substrate **S_C**)* of the table. *Check that the sum of active sites is equal to 5.*

From the information given in **1.**, we get that $K_{M,C} < K_{M,B}$ (1pt), because the lower the constant is, the higher affinity is observed.

From **2.**, the slope of the Eadie–Hofstee plot is $-K_M$ as the corresponding linear form of the MM equation is $v_0 = v_{max} - K_M \frac{v_0}{[S]_0}$. We see two parallel lines on the plot, thus, two $K_{M,i}$ values are equal. The absolute value of the third slope is smaller, therefore, it corresponds to $K_{M,C}$, and univocally we obtain $K_{M,A} = K_{M,B}$ (1pt).

From the information given in **3.**, we obtain directly that $k_{c3} = 10200\ \mathrm{min^{-1}} = 170\ \mathrm{s^{-1}}$ (1pt) as the meaning of this constant is turnover number (TON) (when **E** is saturated by **S**), i.e., the formation of a given number of product molecules by one site per given time.Also, we could write the relation: $xk_{a3} + yk_{b3} + zk_{c3} = 2023\ \mathrm{s^{-1}} \implies xk_{a3} + yk_{b3} + z \cdot 170 = 2023$ (1pt), where x, y and z are the numbers of **S_A**, **S_B**, and **S_C** active sites, respectively, with the sum of 5. The other condition tells us that $xk_{a3} + yk_{b3} \leq 5.94 \cdot 10^6 / 3600\ \mathrm{s^{-1}} = 1650\ \mathrm{s^{-1}}$. From these two expressions, we get $z \geq \frac{2023 - 1650}{170} = 2.19$, i.e., there are 3 active sites for **S_C** ($z = 3$) (1pt) in enzyme **E**, and all joker active sites are responsible for the transformation of **S_C**. Consequently, there is just 1 active site for substrate **S_A** ($x = 1$) (1pt) and 1 active site for substrate **S_B** ($y = 1$) (1pt).

Analysis of the information given in **4.** gives the following. For low concentrations of **S_{A-C}**, we have $[S_i]_0 \ll K_{M,i}$ (i = A–C), and the rate equation (per active site) can be converted to: $v_0 = \frac{k_{i3}[E]_0[S_i]_0}{K_{M,i} + [S_i]_0} \approx \frac{k_{i3}}{K_{M,i}}[E]_0[S_i]_0$. As $[S_i]_0$ are all equal, and **E** is the same enzyme, we obtain that the concentration of a product **P_i** is directly proportional to the ratio $\varepsilon_i = \frac{k_{i3}}{K_{M,i}}$, known as catalytic efficiency. Considering the number of sites, we get the following:

7.5 (cont.)

$$1 \cdot \frac{k_{a3}}{K_{M,A}} : 1 \cdot \frac{k_{b3}}{K_{M,B}} : 3 \cdot \frac{k_{c3}}{K_{M,C}} = 3 : 2 : 5 \text{ (1pt)}$$

As $K_{M,A} = K_{M,B}$, also the following ratio of constants can be derived: $\frac{k_{a3}}{k_{b3}} = \frac{3}{2} \implies k_{a3} = 1.5 k_{b3}$.
In combination with the equation from the analysis of **3.**, we obtain the following expression:

$$1 \cdot k_{a3} + 1 \cdot k_{b3} + 3 \cdot 170 = 2023 \implies 2.5 k_{b3} = 1513 \implies k_{b3} = 605\ \text{s}^{-1} \text{(1pt)}$$

Therefore, $k_{a3} = 1.5 \cdot k_{b3} = 1.5 \cdot 605\ \text{s}^{-1} = 908\ \text{s}^{-1}$ (1pt).
Now we can also find the ratio between $K_{M,A} = K_{M,B}$ and $K_{M,C}$, which will be needed later:

$$\frac{k_{b3}}{K_{M,B}} : \frac{3k_{c3}}{K_{M,C}} = 2 : 5 \implies \frac{K_{M,B}}{K_{M,C}} = \frac{5 \cdot k_{b3}}{2 \cdot 3 \cdot k_{c3}} = \frac{5 \cdot 605}{6 \cdot 170} = 2.97$$

From the information given in **5.**, using the Arrhenius equation, the ratio between k_{c3} and k_{c2} can be found:

$$\frac{k_{c3}}{k_{c2}} = \frac{A_{c3} \cdot e^{-E_{c3}/RT}}{A_{c2} \cdot e^{-E_{c2}/RT}} = e^{\frac{E_{c2}-E_{c3}}{RT}} = e^{\frac{1266\ \text{J mol}^{-1}}{8.314\ \text{J mol}^{-1}\ \text{K}^{-1}\ 298\ \text{K}}} = 1.667 \text{ (1pt)}$$

As k_{c3} is known, the value of k_{c2} can be found: $k_{c2} = 170\ \text{s}^{-1}/1.667 = 102\ \text{s}^{-1}$ (1pt).
Since it is stated that two enzyme–substrate complexes dissociate back with the same rate constant, two k_{i2} are equal: $k_{a2} = k_{b2}, k_{a2} = k_{c2}$, or $k_{b2} = k_{c2}$. As $K_{M,A} = K_{M,B}$and $k_{a1} = k_{b1}$ (from the information given in **6.**), using the definition of a Michaelis constant $K_{M,i} = \frac{k_{i2}+k_{i3}}{k_{i1}}$, we get that $k_{a2} + k_{a3} = k_{b2} + k_{b3}$, i.e., $k_{a2} + 908\ \text{s}^{-1} = k_{b2} + 605\ \text{s}^{-1}$. This means that k_{a2} can't be equal to k_{b2}. Moreover, k_{b2} can't be equal to $k_{c2} = 102\ \text{s}^{-1}$, as in this case, k_{a2} will become negative. Therefore, the only option for equal k_{i2} is that $k_{a2} = k_{c2} = 102\ \text{s}^{-1}$ (1pt). Thus, k_{b2} is:

$$k_{b2} = k_{a2} + 908\ \text{s}^{-1} - 605\ \text{s}^{-1} = 102\ \text{s}^{-1} + 908\ \text{s}^{-1} - 605\ \text{s}^{-1} = 405\ \text{s}^{-1} \text{(1pt)}$$

All the rate constants for $\mathbf{S_C}$ are now known, thus, $K_{M,C}$ can be calculated:

$$K_{M,C} = \frac{k_{c2} + k_{c3}}{k_{c1}} = \frac{102\ \text{s}^{-1} + 170\ \text{s}^{-1}}{1.57 \cdot 10^7\ \text{M}^{-1}\text{s}^{-1}} = 1.73 \cdot 10^{-5}\ \text{M (1pt)}$$

The ratio between $K_{M,A} = K_{M,B}$ and $K_{M,C}$ was calculated during the analysis of **4.** Therefore:

$$K_{M,A} = K_{M,B} = 2.97 \cdot K_{M,C} = 2.97 \cdot 1.73 \cdot 10^{-5}\ \text{M} = 5.14 \cdot 10^{-5}\ \text{M (1pt)}$$

The only remaining constant is $k_{a1} = k_{b1}$:

$$k_{a1} = k_{b1} = \frac{k_{b2} + k_{b3}}{K_{M,B}} = \frac{405\ \text{s}^{-1} + 605\ \text{s}^{-1}}{5.14 \cdot 10^{-5}\ \text{M}} = 1.96 \cdot 10^7\ \text{M}^{-1}\text{s}^{-1} \text{ (1pt)}$$

7.5 (cont.)

The completed table:

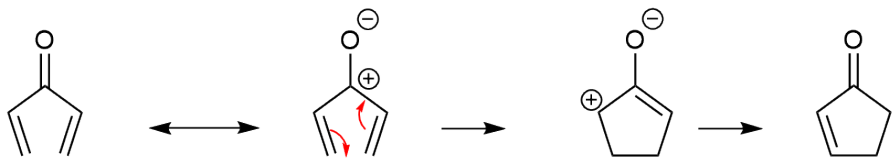
	Number of active sites	k_1	k_2	k_3	K_M
S_A	1	$1.96 \cdot 10^7$ $M^{-1}s^{-1}$	102 s^{-1}	908 s^{-1}	$5.14 \cdot 10^{-5}$ M
S_B	1		405 s^{-1}	605 s^{-1}	$5.14 \cdot 10^{-5}$ M
S_C	3	$1.57 \cdot 10^7$ $M^{-1}s^{-1}$	102 s^{-1}	170 s^{-1}	$1.73 \cdot 10^{-5}$ M

(1pt for each value in the table + 4pt for 4 intermediate expressions, 17pt in total. If a mistake is made at some step, all the other values are recalculated and awarded with full points if correct)

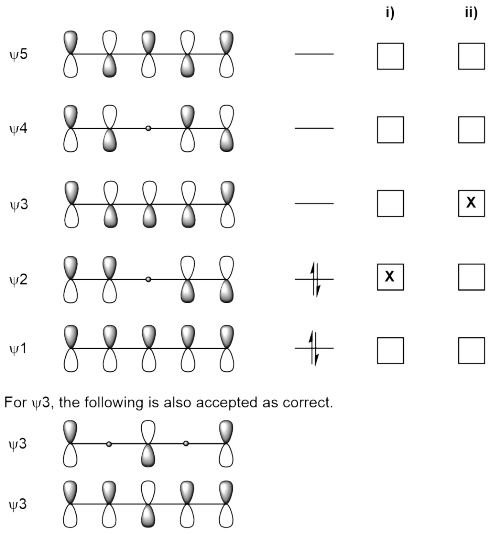
Nazarov Reaction - Solutions

5% of total							
Question	8.1	8.2	8.3	8.4	8.5	8.6	**Total**
Points	5	2	6	2	8	8	**31**
Score							

The Nazarov reaction is a frequently used reaction of divinyl ketones to give cyclopentenones. It proceeds either photochemically or via acid catalysis and is an electrocyclization, followed by a proton transfer.



8.1 **Draw** the pi molecular orbitals to describe the Nazarov reaction. **Fill in** the electrons into the respective energy levels. **Mark** with an X the **i)** HOMO (highest occupied molecular orbital) and **ii)** LUMO (lowest unoccupied molecular orbital). For this exercise, you can consider the divinyl ketone as a pentadienyl cation with five p-orbitals. 5pt



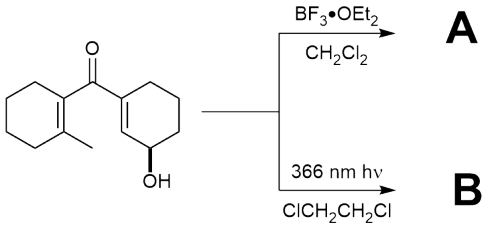
correct scheme with 5 correctly drawn MOs: 3pt, 3 or 4 correctly drawn MOs: 2pt, 1 or 2 correctly drawn MOs: 1pt;
correct electron distribution 1pt;
correct HOMO-LUMO each 0.5pt

8.2 From the pi molecular orbitals you derived in **Task 8.1**, **predict** under which conditions the Nazarov reaction of the divinyl ketone will proceed in a disrotatory or conrotatory fashion. In the **table on the answer sheet**, **mark** with an X the conditions under which the reaction is allowed. 2pt

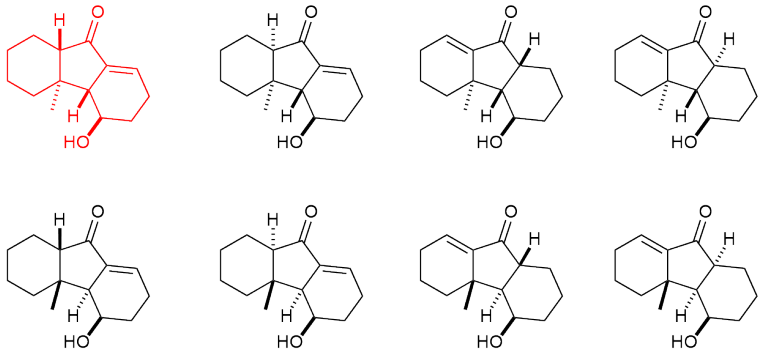
	disrotatory	conrotatory
thermal		**X**
photochemical	**X**	

Incorrect ticking: - 1pt down to zero

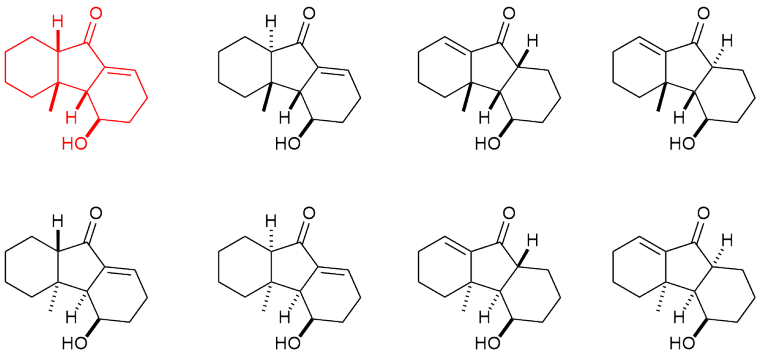
8.3 The Nazarov reaction was used as key reaction in a synthesis of Farnesin. For both conditions below, **draw** one possible structure for each of **A** and **B**, including stereochemistry. Note that the products of both reactions show a signal at 6.70 - 6.73 ppm in the ^{1}H NMR. 6pt



A: The red isomer is the one actually formed in the reaction, however all 8 possible combinations of olefin isomer, α-H and torque selectivity in the electrocyclization will be graded as correct.



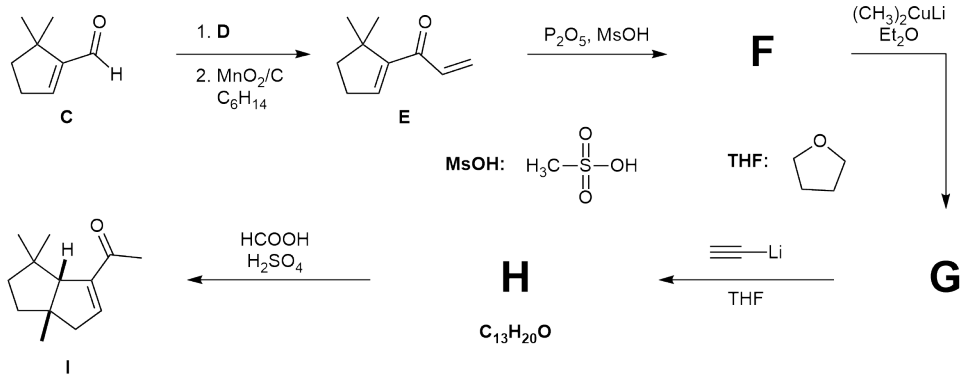
B: The red isomer is the one actually formed in the reaction, however all 8 possible combinations of olefin isomer, α-H and torque selectivity in the electrocyclization will be graded as correct.



each structure including connectivity and stereochemistry: 3pt
each structure with wrong/no stereochemistry but correct connectivity: 1pt

The synthesis of Capnellene commences with unsaturated aldehyde **C** shown below. Treatment with

conditions **D**, followed by reaction with MnO_2 supported on carbon gave divinyl ketone **E** shown below. Exposure to a mixture of P_2O_5 and MsOH yielded **F**, which was elaborated via a sequence of reactions to the unsaturated ketone **I**.

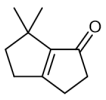
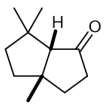
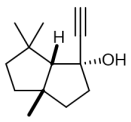


8.4 **Choose** the reagent(s) from the list **on the answer sheet** that would be suitable as **D.** 2pt

⊡ H_2C=CHMgBr
☐ 1. $NaBH_4$ 2. H_2C=CHLi
☐ H_2C=CHBr, $Pd(PPh_3)_4$
☐ H_2C=CHMgBr, CuI

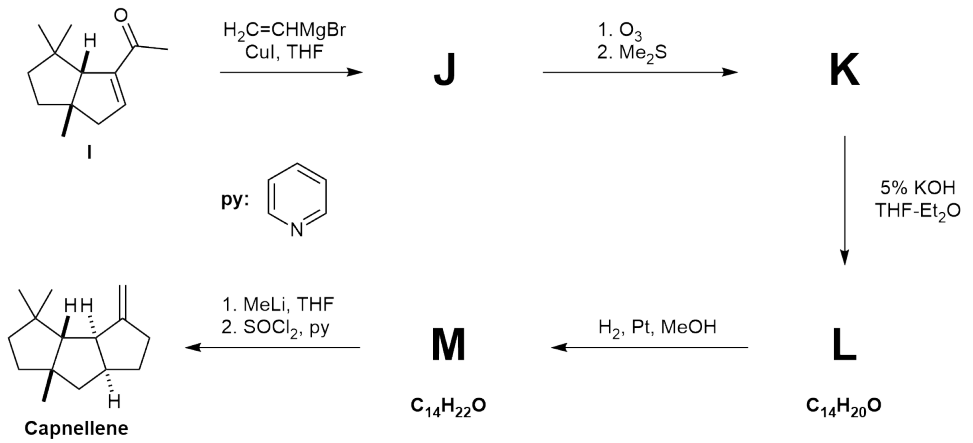
Incorrect ticking: - 1pt down to zero

8.5 **Give** the structures of intermediates **F**, **G**, and **H**, including their stereochemistry. 8pt

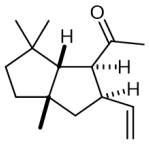
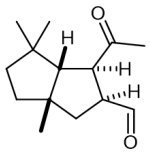
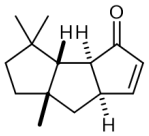
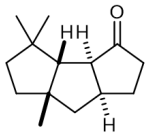
F	G	H
		

structure **F**: 2pt (1pt if the other regioisomer of the double bond is drawn)
structures **G** and **H** with correct stereochemistry and connectivity: 3pt
structures **G** and **H** with incorrect/no stereochemistry but correct connectivity: 1pt

Enone **I** was then subjected to H_2C=CHMgBr and CuI in THF to give intermediate **J**, followed by ozonolysis to yield intermediate **K**, which shows a signal at 9.61 ppm in the ^1H NMR. Treatment with 5% KOH in a mixture of THF and ether yielded intermediate **L**. Hydrogenation with a Pt-catalyst and under an atmosphere of H_2 yielded **M**, which finally gave rise to Capnellene.



8.6 **Give** the structures **J**, **K**, **L**, and **M**, including their stereochemistry. 8pt

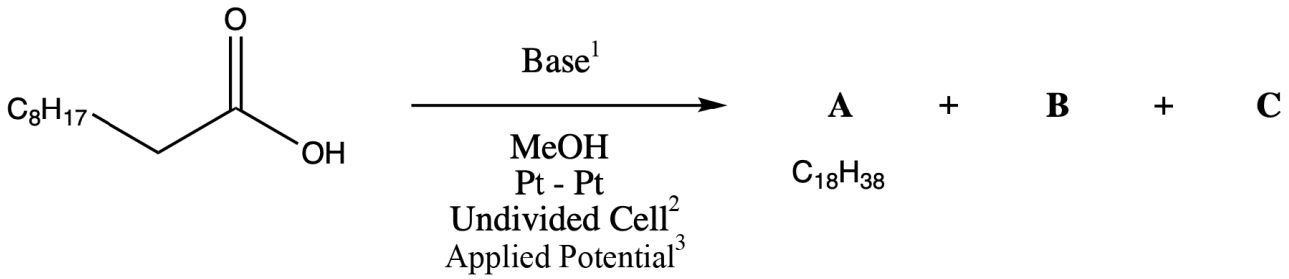
J 	**K** 
L 	**M** 

each structure with correct stereochemistry and connectivity: 2pt
each structure with either correct stereochemistry or correct connectivity: 1pt
The stereochemistry of the alpha-hydrogen of ketones **J** and **K** will also be considered correct if the epimer is drawn, as epimerization under the condensation conditions is conceivable.

Electrolysis in Organic Synthesis - Solutions

6% of total								
Question	9.1	9.2	9.3	9.4	9.5	9.6	9.7	**Total**
Points	3	3	2	5	5	2	9	**29**
Score								

The Kolbe electrolysis describes the decarboxylative dimerization of two carboxylic acids and only proceeds if the acid is deprotonated. The unbalanced equation is shown here.



Translations:

1:

2:

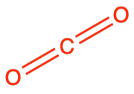
3:

Two gases (**B** and **C**) are produced during the reaction. **B** reacts with $Ca(OH)_2$, while **C** is highly flammable.

9.1 **Provide** the structural formulae of **A**, **B**, and **C**. 3pt

A

B



C

Each correct structure: 1pt (3pt total)
Full points only if B and C are in the correct order, half points if B and C are reversed

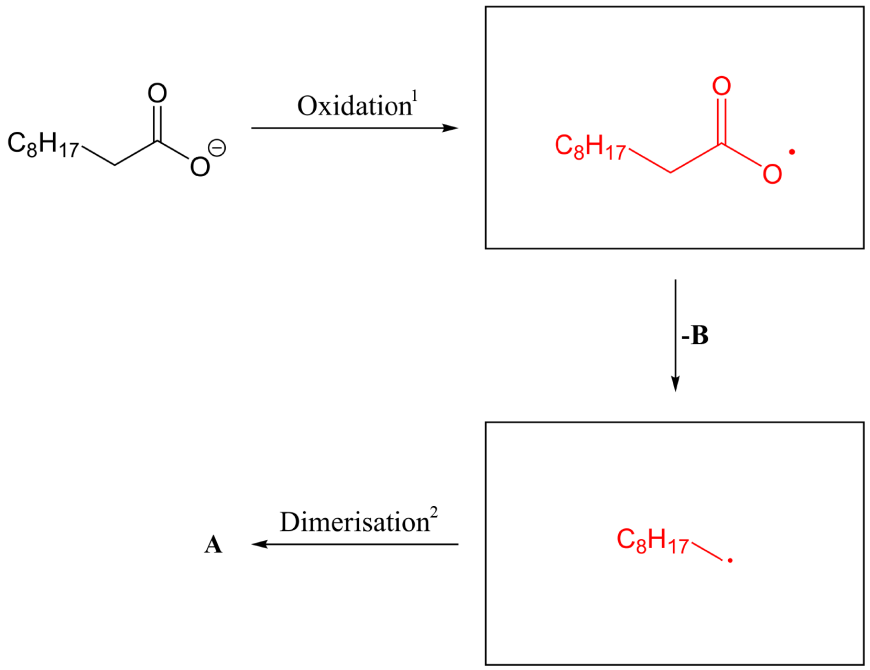
9.2 The synthesis is formally a redox reaction, where the carboxylate is oxidized and the solvent is reduced. **Formulate** the oxidative and reductive half reactions and the full redox reaction. 3pt

Reductive half reaction:
$2\ MeOH + 2\ e^- \longrightarrow 2\ MeO^- + H_2$ 1pt
Full points if specified H-Base$^+$, half points for H^+

Oxidative half reaction:
$2\ R\text{-}COO^- \longrightarrow R\text{-}R + 2\ CO_2 + 2\ e^-$ 1pt

Full redox reaction:
$2\ R\text{-}COO^- + 2\ MeOH \longrightarrow R\text{-}R + 2\ CO_2 + 2\ MeO^- + H_2$ 1pt

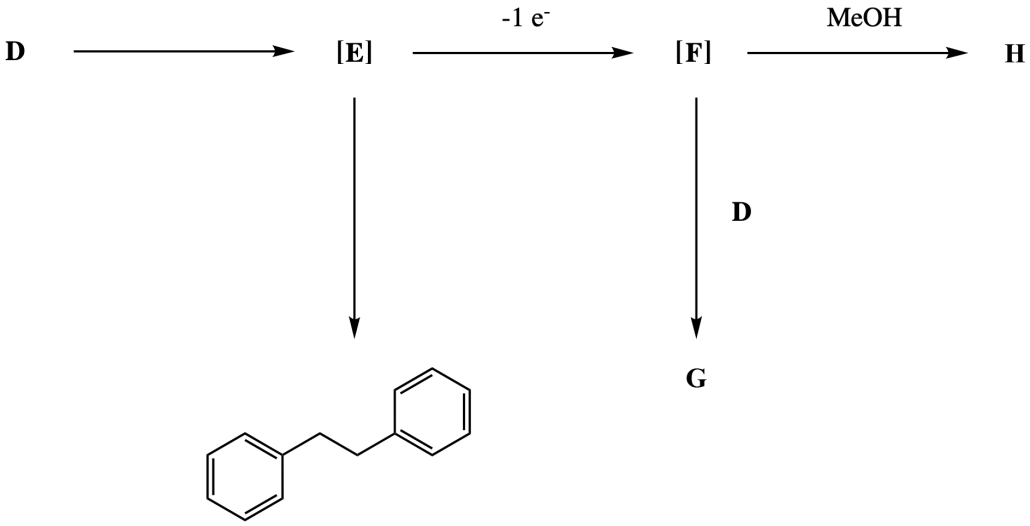
9.3 **Provide** the intermediates in the mechanism for the oxidative decarboxylation and formation of the product. 2pt



Translation:
1:
2:
First step: 1pt
Second step: 1pt

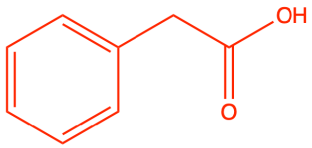
The Kolbe electrolysis is usually only efficient for long-chained saturated carboxylic acids and not for certain carboxylic acids, such as **D**. Here, the overoxidation of the radical intermediate **E** to a positively charged species **F** is facilitated.

Intermediate **F** can react with nucleophiles to form different side products, for example it reacts with **D** to form an ester **G**, and with MeOH to form **H**.

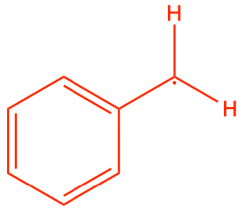

D
[E]
-1 e-
[F]
MeOH
H
D
G

9.4 **Provide** the structures of **D**-**H**. 5pt

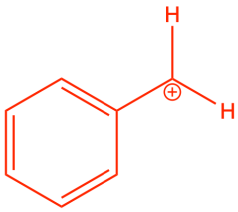
D



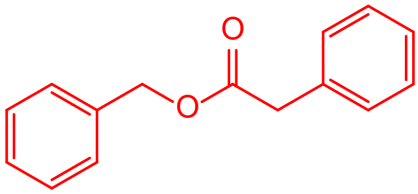
E



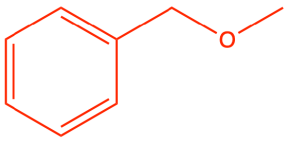
F



G



H



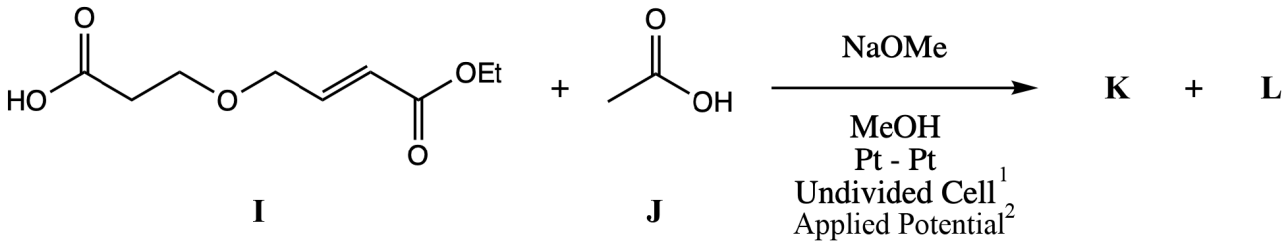
Each correct structure: 1pt (5pt total)

The electrolysis of carboxylic acid **I** in the presence of an excess of co-acid **J** yields two main products (by ^{1}H NMR analysis) that are inseparable by silica gel chromatography. Their spectroscopic data are almost identical. In the ^{1}H NMR spectrum, the two species are only distinguishable by two signals with small differences in chemical shifts. The spectrum looks as follows (1:1 mixture of products):

^{1}H NMR (**K** and **L**): 4.18-4.08 (m, 4 H), 3.95-3.60 (m, 6 H), 3.43 (dt, 2 H, *J* = 7.8, 2.2 Hz), 2.55-2.25 (m, 4 H), 2.20-1.95 (m, 2 H), 1.65-1.50 (m, 2 H)

Specific signals for **K**: 1.26 (t, 3 H, *J* = 7.2 Hz), 1.20 (d, 3 H, *J* = 6.6 Hz).

Specific signals for **L**: 1.24 (t, 3 H, *J* = 7.2 Hz), 1.15 (d, 3 H, *J* = 6.6 Hz).

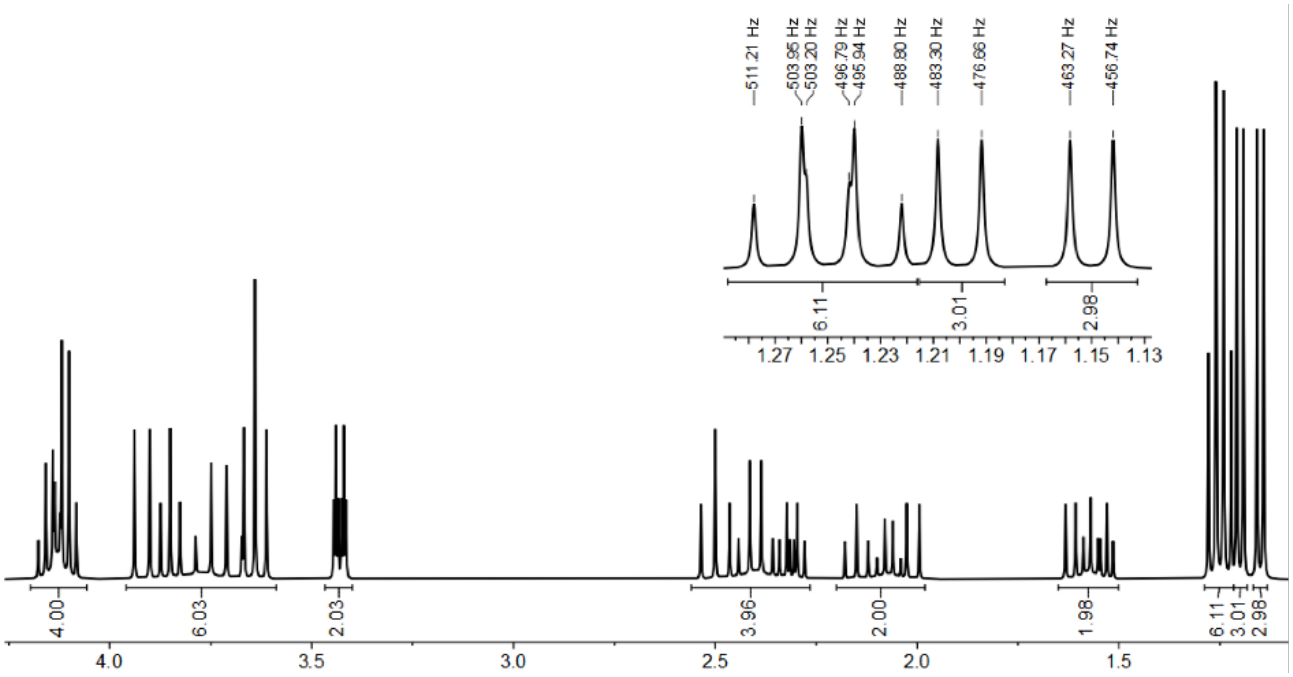


I **J**

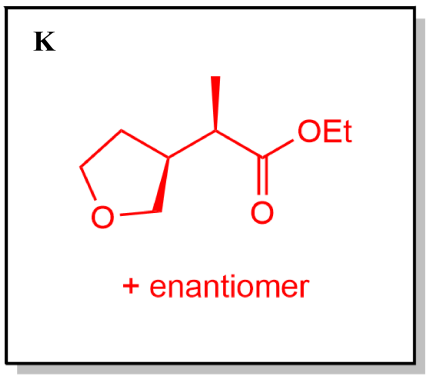
Translation:

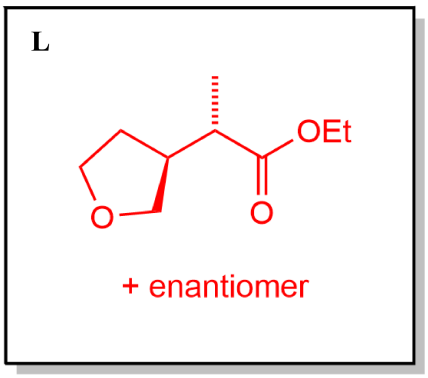
1:

2:



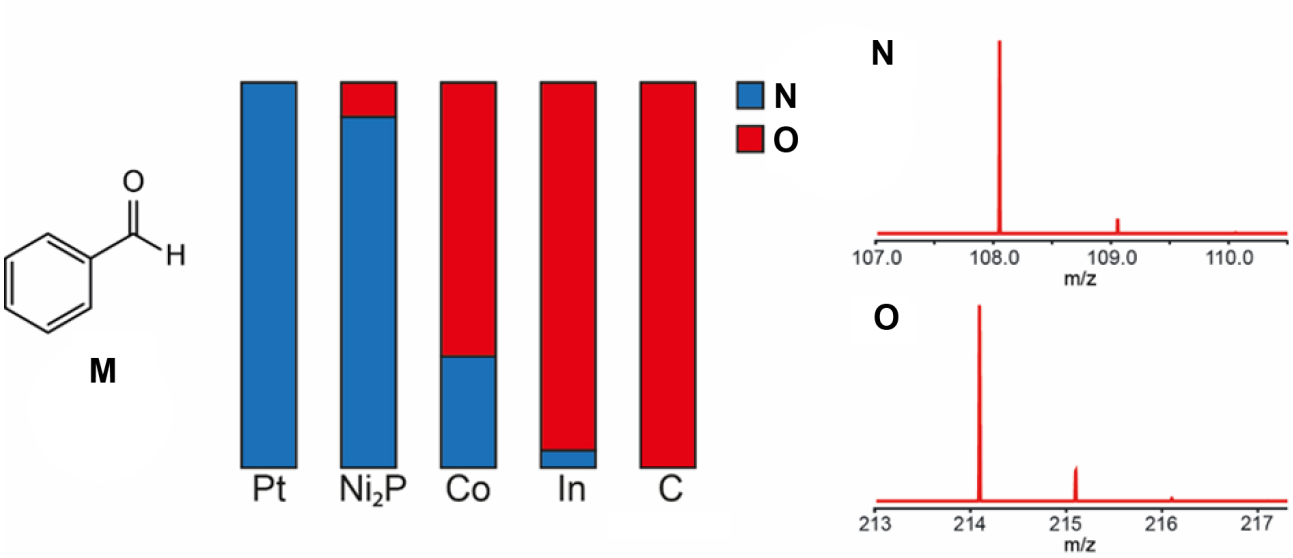
9.5 **Provide** the structures for both products **J** and **K**. **Indicate** how the two products are related. 5pt



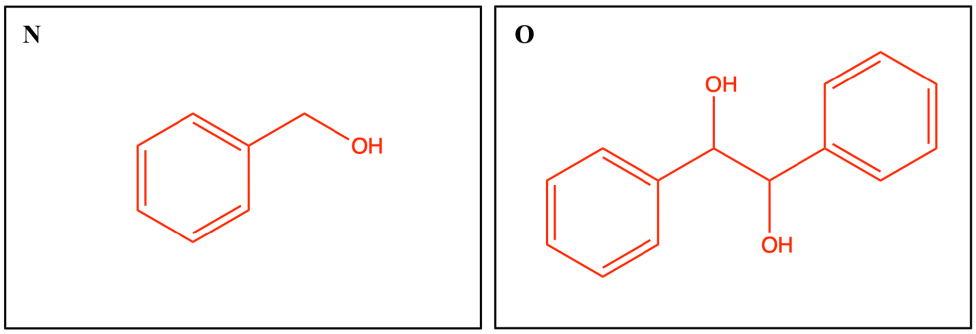


⊡ Epimer 0.5pt
⊡ Diastereomer 0.5pt
☐ Enantiomer
☐ Constitutional Isomer
0.5pt for each correct answer, 0.5 points deduction for each wrong answer
K; **L**:
Each correct structure: 2pt (4pt total)
Both enantiomers give full marks, specification "+ enantiomer" not necessary for full points, K and L can be in reverse order for full points

The choice of the electrode material can influence the selectivity of an organic electrosynthetic reaction. The reductive electrolysis of benzaldehyde (**M**) (16 mM in 1 M aqueous KOH, Pt anode, -1.3 V vs. Ag/AgCl) yields different products depending on the cathode material used. Strong binding to the surface favours intermolecular reactions. The figure below shows the product distribution for different cathode materials and the mass spectra of the products.

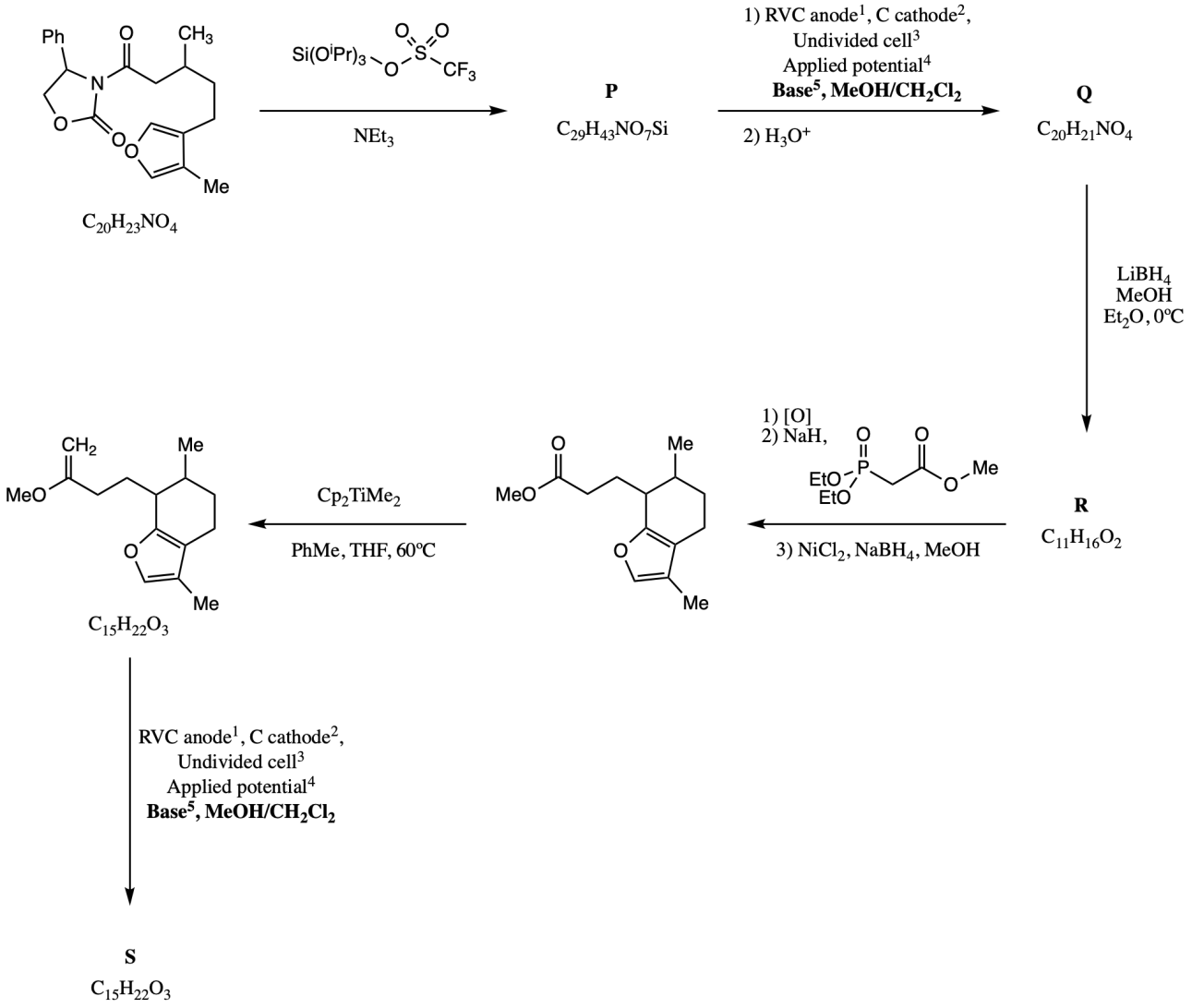


9.6 **Provide** the structure of **N** and **O**. 2pt



Each correct structure: 1pt (2pt total)

Alkenes, such as enol ethers, can be oxidatively coupled. This typically involves the anodic oxidation of the alkene fragment to yield a radical cation which can be intercepted by a nucleophile.



Translation:

1: RVC = glassy carbon

2:

3:

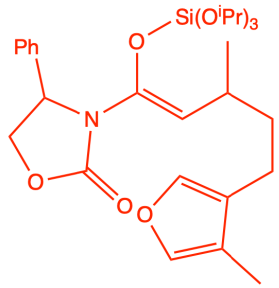
4:

5:

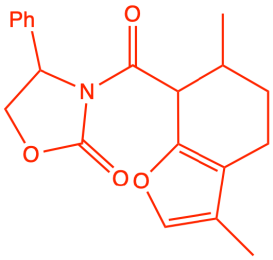
Cp = cyclopentadienyl

9.7 **Provide** the structural formulae of compounds **P**, **Q**, **R**, and **S**. Indicating stereochemistry is not required. *Hint:* **S** is a tricyclic product. 9pt

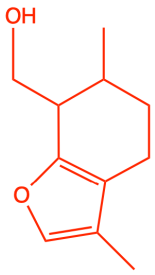
P



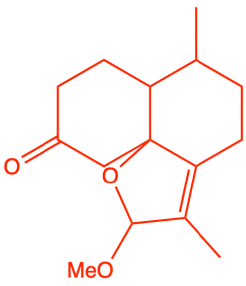
Q



R



S

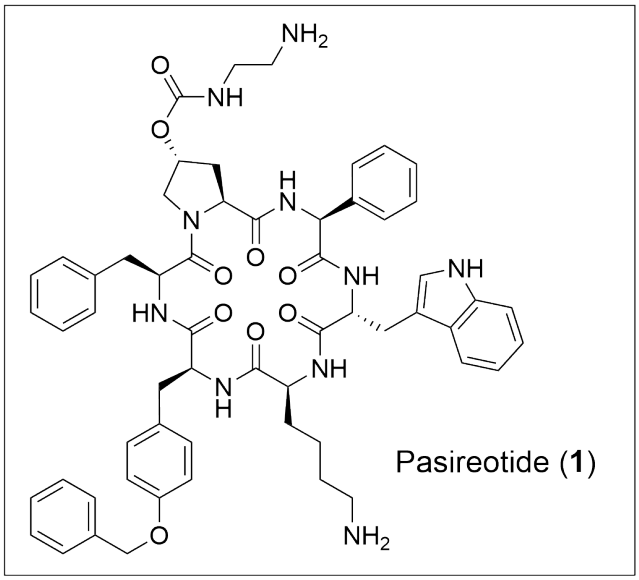


P: 2pt
Q: 2pt
R: 2pt
S: 3pt If OMe in wrong position 2pt

Switzerland - The Country of Pharmaceuticals - Solutions

6% of total								
Question	10.1	10.2	10.3	10.4	10.5	10.6	10.7	**Total**
Points	2	11	6	6	6	6	2	**39**
Score								

Pasireotide (**1**) is a peptide-based drug developed by the Swiss pharmaceutical company Novartis to treat the Cushing's disease.



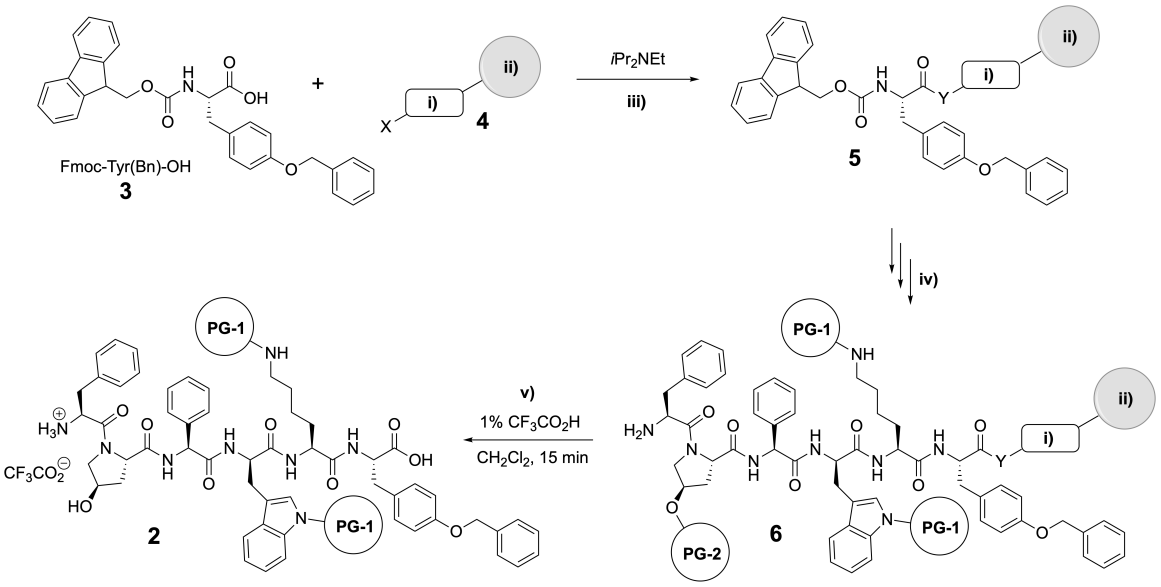
10.1 **Determine** the number of stereogenic centers (n) in Pasireotide (**1**). **Calculate** the total number of all possible stereoisomers (t) of Pasireotide (**1**). 2pt

Number of stereogenic centers: $n = 7$ **1 pt**

In total $t = 2^n = 2^7 = 128$ stereoisomers **1 pt**

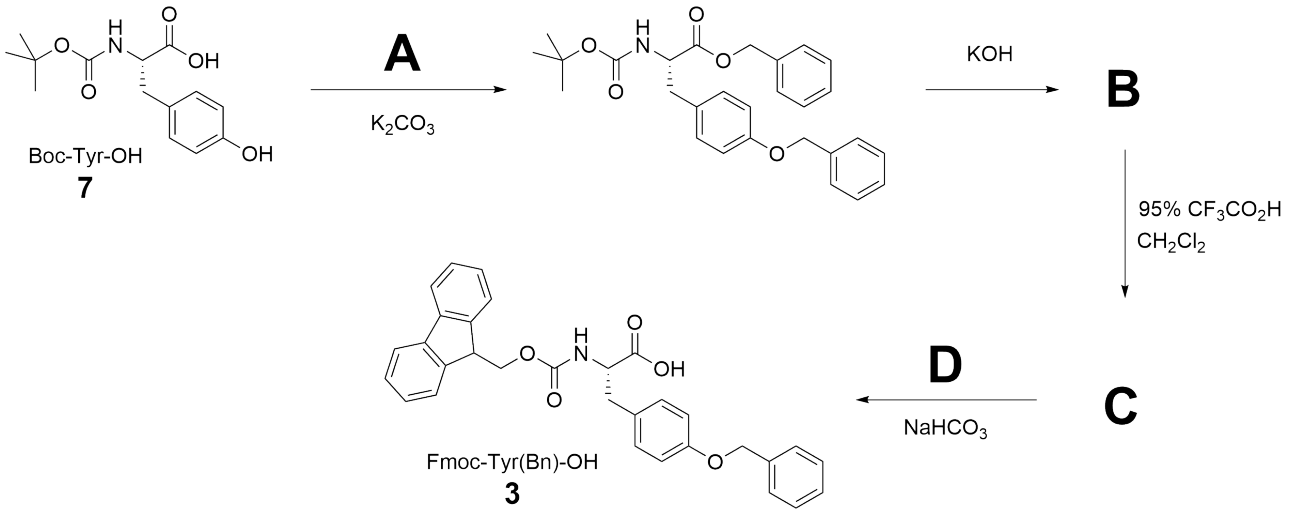
Full credits for a correct calculation of *t* using an incorrect number of *n* answered above.

Pasireotide (**1**) is a cyclic peptide. An advanced intermediate in its synthesis (linear peptide **2**) can be prepared by solid-phase peptide synthesis (SPPS) using the Fmoc/tBu strategy as shown in **Scheme 1**.



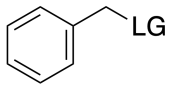
Scheme 1: SPPS of peptide **2**. i) Linker; ii) Resin; iii) Resin loading; iv) SPPS: repetition of 1. Fmoc deprotection 2. amino acid coupling + final Fmoc deprotection; v) Peptide cleavage from resin and deprotection of **PG-2**.

The synthesis starts with the preparation of Fmoc-Tyr(Bn)-OH (**3**) from Boc-Tyr-OH (**7**).



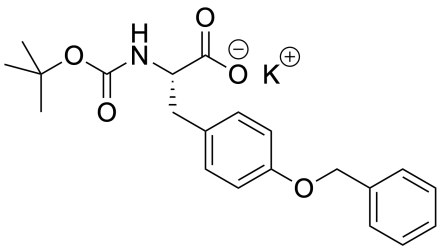
10.2 11pt

A

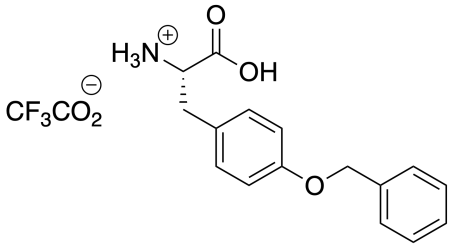


LG = Cl, Br, I, OTs, OMs, OTf…

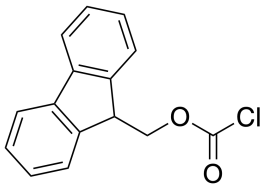
B



C

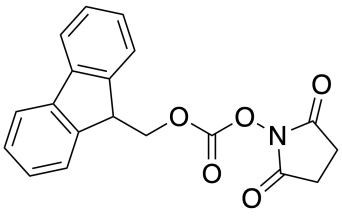


D

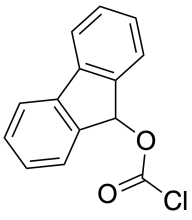


Fmoc-Cl

or



Fmoc-OSu

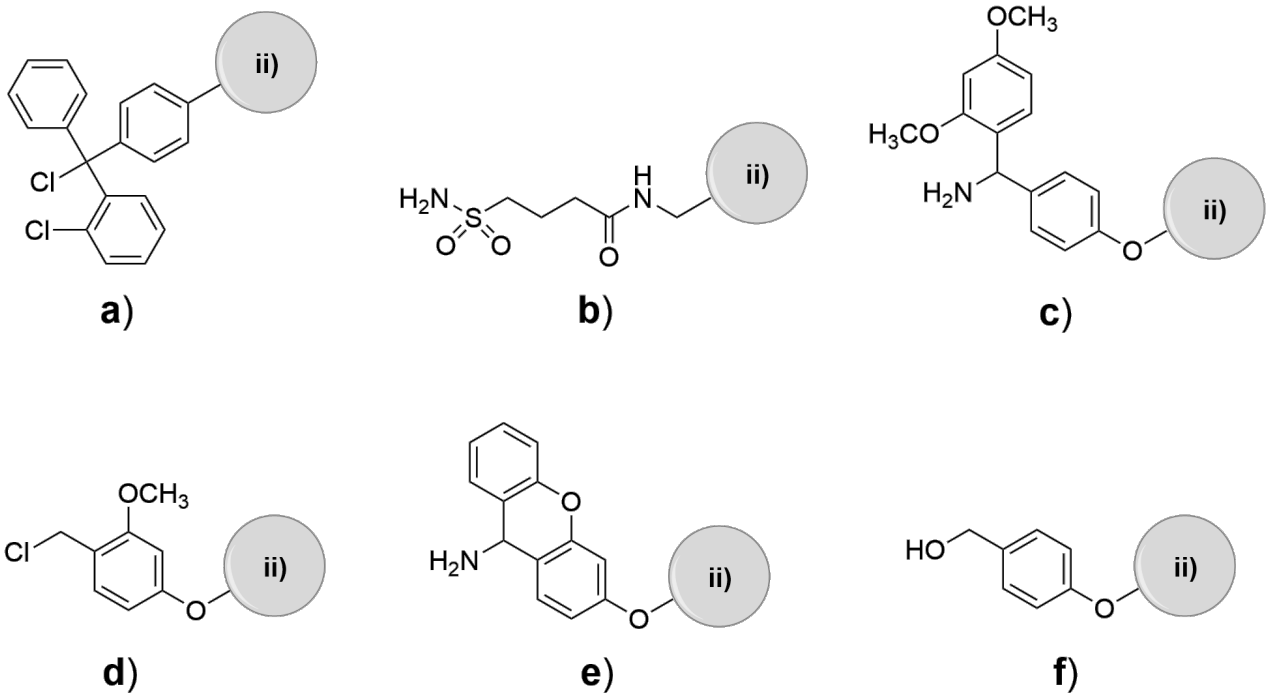


Draw reagents **A** and **D** and intermediates **B** and **C** in the synthesis of Fmoc-Tyr(Bn)-OH (**3**) as shown below.

1 pt for a missing methylene group (i.e. phenyl ether instead of benzyl ether)

The SPPS of intermediate **2** begins with attaching the Fmoc-Tyr(Bn)-OH (**3**) to a suitable resin-bound

linker.

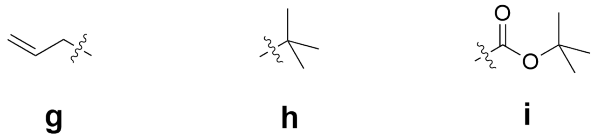


Scheme 2. ii) Resin; a) 2-Chlorotrityl-chloride linker; b) Safety-catch linker; c) Rink amide linker; d) SASRIN-chloride linker; e) Sieber amide linker; f) Wang linker.

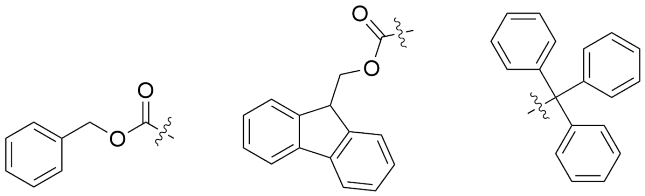
10.3 **Choose** the linker(s) **4** that are appropriate for SPPS of peptide **2** according to **Scheme 1** in the question sheet. Incorrect answers will result in deductions of points but the total score may not be negative. 6pt

- ☒ 2-Chlorotrityl-chloride linker (**a**)
- ☐ Safety-catch linker (**b**)
- ☐ Rink amide linker (**c**)
- ☒ SASRIN-chloride linker (**d**)
- ☐ Sieber amide linker (**e**)
- ☐ Wang linker (**f**)

3pt for ticking each correct answer
–3pt for each incorrect answer. The total score may not be negative.



g h i



j k l

10.4 **Choose** the most suitable side-chain protecting groups **PG-1** and **PG-2** for SPPS of **2** according to **Scheme 1** in the question sheet that can be orthogonally cleaved in the presence of all other functional groups present in Pasireotide. Only one answer is correct for each of the protecting groups. 6pt

PG-1

- ☐ **g**
- ☐ **h**
- ☒ **i**
- ☐ **j**
- ☐ **k**
- ☐ **l**

PG-2

- ☐ **g**
- ☐ **h**
- ☐ **i**
- ☐ **j**
- ☐ **k**
- ☒ **l**

3pt for ticking the correct answer for each PG-1 and PG-2
0pt if more than one or the wrong box is ticked.

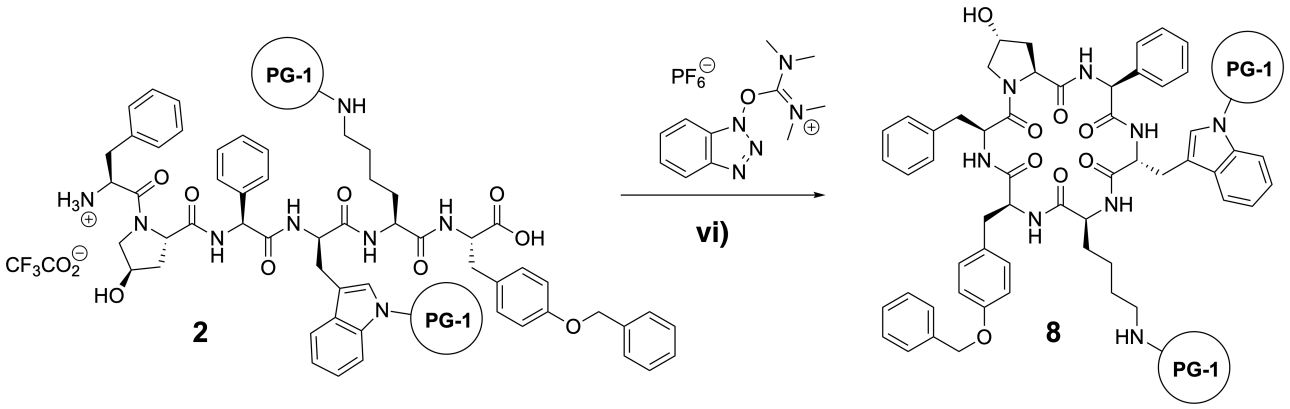
For PG-1:

• **PG-g** and **PG-h** lead to 2° amines in the peptide –not compatible with Fmoc and the coupling conditions
• **PG-i** is stable in 1% TFA in CH_2Cl_2 and the correct answer
• Deprotection conditions of **PG-j** are not orthogonal with Tyr(Bn) which is in the structure of peptide **1**
• **PG-k** not stable to SPPS deprotection conditions
• **PG-l** is not stable in 1% TFA in CH_2Cl_2

For PG-2:

• Only **PG-l** is cleavable in 1% TFA in CH_2Cl_2 and therefore the only correct answer

Next, linear peptide **2** undergoes an intramolecular coupling reaction to form cyclic peptide **8** according to the following scheme:



Scheme 3. vi) Base.

10.5 **Choose** the correct statement(s) about the cyclization of peptide **2** to **8**. Incorrect answers will result in deductions of points but the total score may not be negative. 6pt

☒ A possible side-product of the reaction is tetramethylguanidylation of the N-terminal phenylalanine residue resulting in compound **9** shown below.

☐ A possible side-product of the reaction is the cleavage of protecting group **PG-1** and cyclization via the amino group of the lysine residue to give compound **10** shown below.

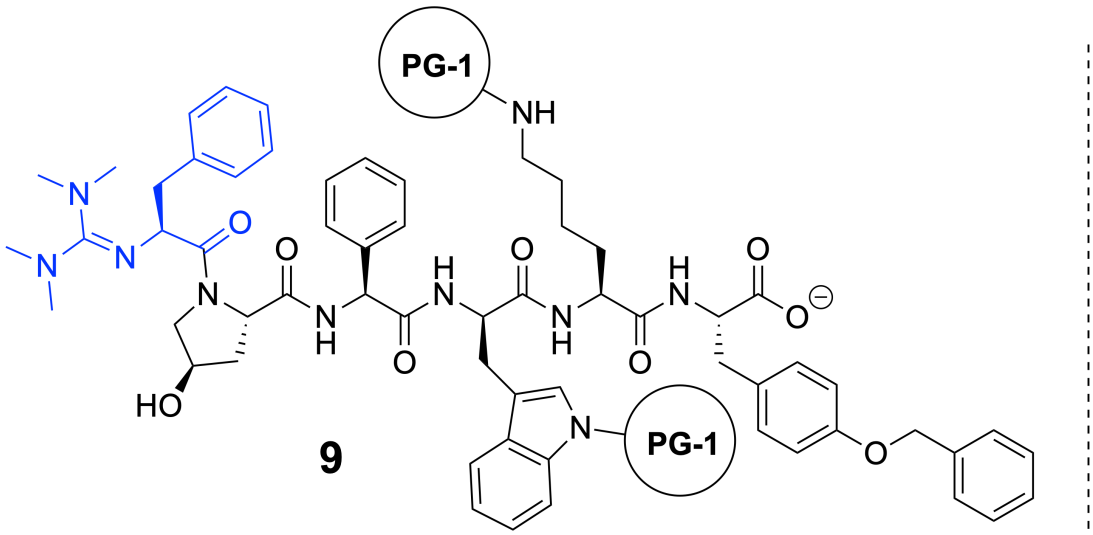
☐ The reaction must be carried out at a high peptide concentration to achieve a sufficient reaction rate.

☒ The reaction must be carried out at a low peptide concentration to prevent polycondensation.

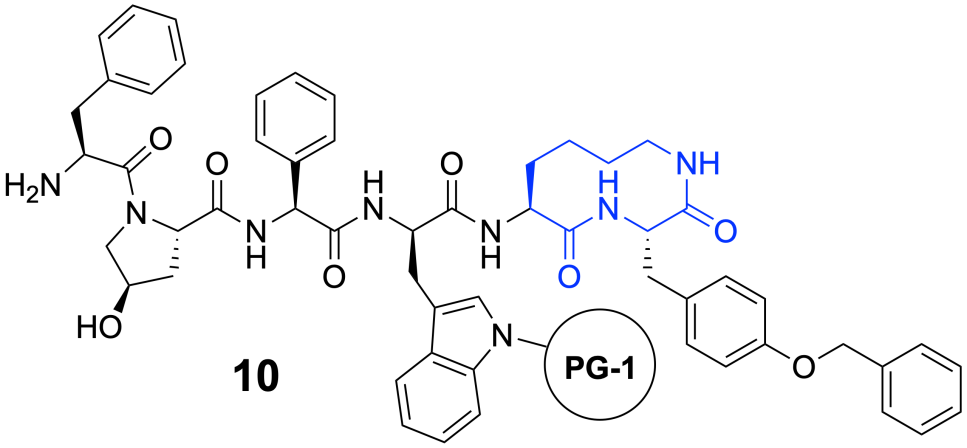
☐ Piperidine (**11**) below is a suitable base for the reaction.

3pt for ticking each correct answer
–3pt for ticking an incorrect box. The total score may not be negative.
Option 2 will be considered as correct (no negative points) if the student chose ***k*** as **PG-1**.

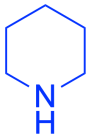
Explanations for incorrect options:
Second option:
PG-1 is stable under cyclization conditions and does not fall off
Third option:
At high concentrations, *inter*molecular reactions (undesired polycondensation) are favored over *intra*molecular reactions (desired cyclization)
Fifth option:
Piperidine is a nucleophilic base and would compete with the N-terminal amino group for amidation of the C-terminus



9

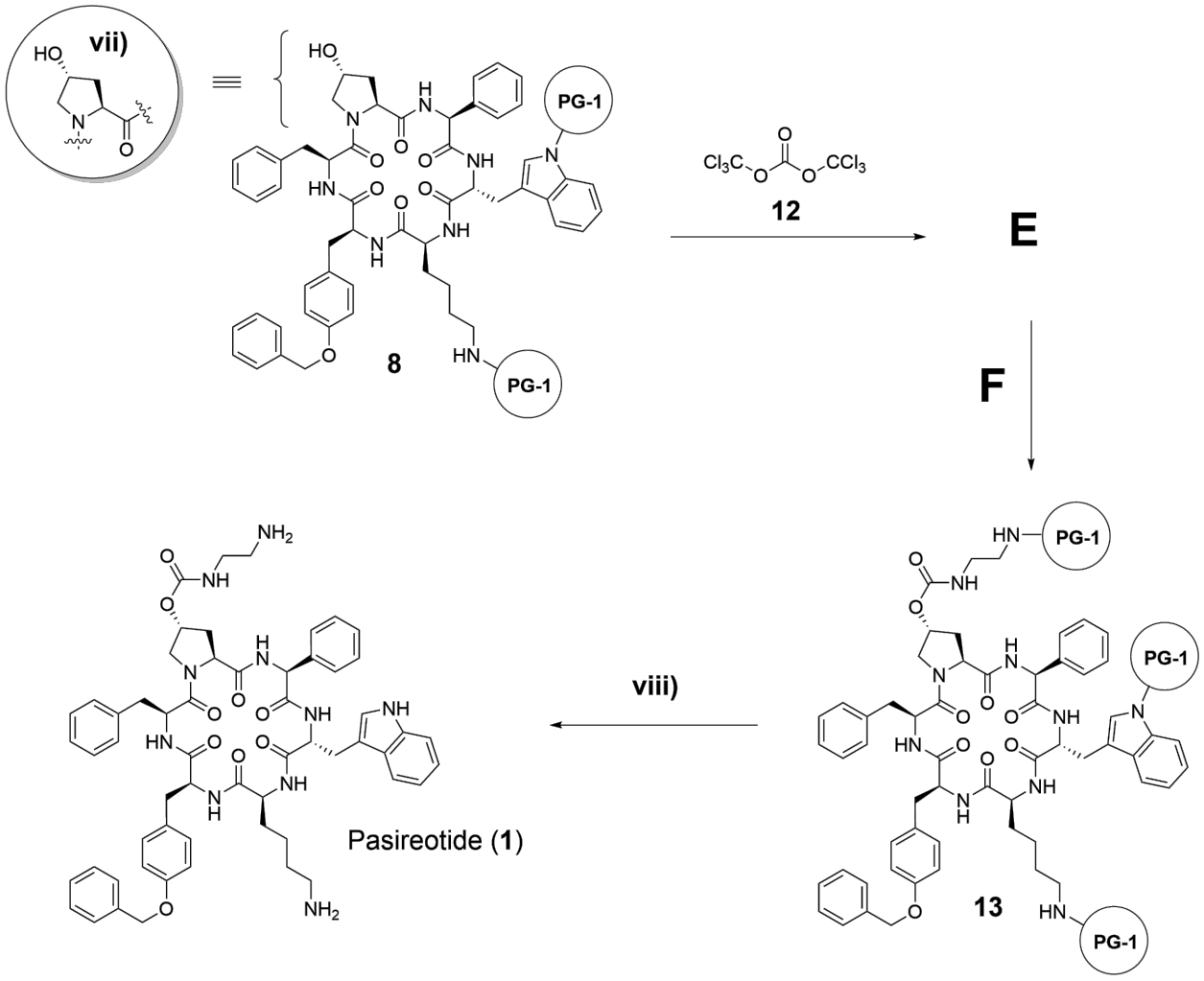


10



11

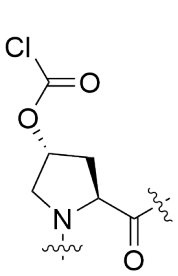
The last steps of the synthesis involve functionalization of the OH-group of the 4-hydroxyproline residue in **8**, followed by cleavage of all protecting groups to give Pasireotide (**1**).



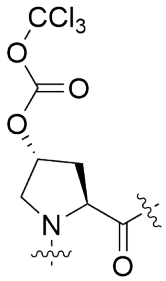
Scheme 4. vii) can be used as simplification of **8**; viii) Cleavage of protecting groups.

10.6 **Draw** the structures of intermediate **E** (including stereochemistry) and reagent **F**. Abbreviate intermediate **8** as (**vii**) and the protecting group as **PG-1** in structures **E** and **F** as depicted in **Scheme 5**. 6pt

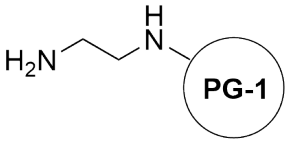
E



Full credit also for:



F



E: 3pt for the correct structure (any of the two will give full points).
–1pt for incorrect or non-specified stereochemistry.
– 1pt for wrong derivative of hydroxyproline (3- or 5-hydroxyproline instead of 4-hydroxyproline).
for the correct structure **F** 3pt

10.7 **Determine** the lowest possible molar equivalents of compound **12** that are necessary to enable full conversion of **8** to **13**. 2pt

1/3 equivalents, 0.3 equiv. are also accepted

2pt for either correct answer,
0pt for 1 equivalent

39pt in total. No fractional points will be given.