

**51<sup>st</sup>**



**International Chemistry Olympiad**

**PREPARATORY PROBLEMS**

**Edited by Anton Sirota**

**27 theoretical problems**

**6 practical problems**

**2019**

**THE PREPARATORY PROBLEMS FROM THE INTERNATIONAL CHEMISTRY OLYMPIADS, Series 4,  
THE PREPARATORY PROBLEMS FROM THE 51<sup>st</sup> IChO**

Edited by Anton Sirota

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International Chemistry Olympiad

International Information Centre

Director: Anton Sirota

IUVENTA

Karlovská 64, 84258 Bratislava 1, Slovakia

Phone: +421-907-473367

E-mail: anton.sirota@stuba.sk

Web: www.icho.sk

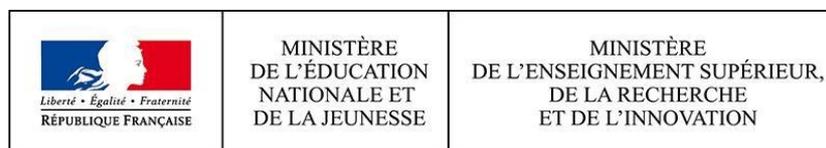
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# PREPARATORY PROBLEMS



**51st — International  
Chemistry Olympiad  
France — Paris — 2019**

Making science together!



**LA CHIMIE**  
de l'école à l'université  
**2019**

## Preface

We are happy to provide Preparatory Problems for the 51<sup>st</sup> International Chemistry Olympiad. These problems will be an opportunity for students to prepare for the Olympiad, but also to discover numerous topics in both modern and traditional chemistry. These problems should be solved using the topics covered in high school and some topics of advanced difficulty listed below (six for the theoretical part and two for the practical one).

This booklet contains 27 theoretical and 6 practical problems. Its length should not be seen as an indication of its difficulty: it merely reflects our commitment to write these problems in a spirit as similar as possible to the final problems. An additional theoretical task (*Back to 1990*) ends the first section. This problem should not be studied as thoroughly as the others, as it is an excerpt of the tasks proposed to the candidates during the last Olympiad held in France, in 1990.

The members of the Scientific Committee in charge of the preparatory problems:

- Didier Bourissou, *CNRS, Toulouse* Aurélien Moncomble, *Université de Lille* Élise Duboué-Dijon, *CNRS, Paris*
  - Clément Guibert, *Sorbonne Université, Paris*
  - Baptiste Haddou, *Lycée Darius Milhaud, Le Kremlin-Bicêtre*
  - Hakim Lakmini, *Lycée Saint Louis, Paris*
-

## Fields of advanced difficulty

### Theoretical

1. *Thermodynamics*: relation between equilibrium constants and standard reaction Gibbs free energy, relation between thermodynamic and electrochemical data.
2. *Kinetics*: orders of reaction, half-life, rates defined as time derivatives of concentrations, use of integrated rate laws, classic approximations.
3. *Basic quantum chemistry*: notion of wavefunction, expression of simple molecular orbitals, electronic energy levels, crystal field theory.
4. *Spectroscopy*: simple IR spectroscopy (identification of chemical groups only),  $^1\text{H}$  NMR spectroscopy (chemical shifts, integrals, couplings and multiplicity).
5. *Polymers*: block copolymers, polymerization, polydispersity, simple size exclusion chromatography (SEC).
6. *Stereochemistry*: stereoisomers in organic and inorganic chemistry, stereoselectivity in organic synthesis.

### Practical

- Techniques in organic synthesis (drying of a precipitate, recrystallization, TLC).
- Use of a spectrophotometer (mono-wavelength measurements).

**THE FIFTY-FIRST  
INTERNATIONAL CHEMISTRY OLYMPIAD  
21 – 30 JULY 2019, PARIS, FRANCE**

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**PREPARATORY PROBLEMS**

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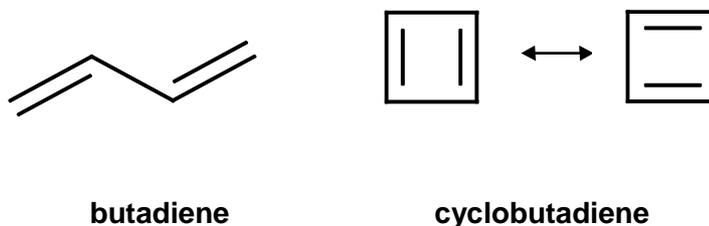


## THEORETICAL PREPARATORY PROBLEMS

### THEORETICAL PROBLEM 1

#### Butadiene $\pi$ -electron system

Buta-1,3-diene (simply called butadiene thereafter) is a diene of chemical formula  $C_4H_6$ , which was isolated for the first time in 1863 by the French chemist E. Caventou and identified in 1886 by the English chemist H. E. Armstrong. It is a key reagent in the production of synthetic rubber. Over 12.7 million tons of butadiene are produced every year. We will study here the properties of its  $\pi$ -electron system. We will then compare them to those of the hypothetical cyclobutadiene, which has never been isolated in its free form.



1.1 Give the number of  $\pi$ -electrons of butadiene.

The Molecular Orbitals (MO)  $\psi_i$  of the  $\pi$ -electron system can be written as a weighted sum (linear combination) of the  $2p_z$  atomic orbitals of each carbon atom,  $\varphi_j$ :

$$\psi_i = \sum_{j=1}^4 c_{ij} \varphi_j ; i = 1-4$$

We provide below an approximate expression for the MOs together with their associated energy. The energy of each MO is expressed as a function of two parameters,  $\alpha$  and  $\beta$ , both negative real numbers.  $\alpha$  represents the energy of an electron in an isolated  $2p_z$  orbital, and  $\beta$  is the interaction energy between two neighboring  $2p_z$  orbitals.

$$\psi_1 = 0.3717 \varphi_1 + 0.6015 \varphi_2 + 0.6015 \varphi_3 + 0.3717 \varphi_4 ; E_1 = \alpha + 1.62\beta$$

$$\psi_2 = 0.6015 \varphi_1 + 0.3717 \varphi_2 - 0.3717 \varphi_3 - 0.6015 \varphi_4 ; E_2 = \alpha + 0.62\beta$$

$$\psi_3 = 0.6015 \varphi_1 - 0.3717 \varphi_2 - 0.3717 \varphi_3 + 0.6015 \varphi_4 ; E_3 = \alpha - 0.62\beta$$

$$\Psi_4 = 0.3717\varphi_1 - 0.6015\varphi_2 + 0.6015\varphi_3 - 0.3717\varphi_4; \quad E_4 = \alpha - 1.62\beta$$

**1.2** Draw and fill in the MO diagram of butadiene. Draw schematically each MO and identify its nature (bonding or anti-bonding).

We consider the formation of the butadiene  $\pi$ -electron system, starting from four carbon atoms, each bringing an electron in a  $2p_z$  orbital of energy  $\alpha$ .

**1.3** Calculate the formation energy  $\Delta E_f$  associated with this transformation.

Here, the conjugation energy is defined as the difference between the total  $\pi$ -energy of the studied compound and that of two non-interacting ethylene molecules. The  $\pi$ -energy of ethylene is equal to  $2(\alpha + \beta)$ .

**1.4** Calculate the conjugation energy  $\Delta E_c$  of butadiene. Give its sign. Which system is the most stable? Choose the correct answer :

- butadiene
- 2 ethylene molecules
- both are equally stable

The net charge  $q_j$  on each carbon atom (*i.e.*, the charge gained or lost by the atom compared to its neutral state) can be calculated in the present case as:

$$q_j = 1 - \sum_{i=1}^{occ} n_i c_{ij}^2$$

where the sum runs over the occupied MOs,  $n_i$  is the number of electrons in the  $i$ th MO, and  $c_{ij}$  is the coefficient of the  $j$ th carbon atom in the  $i$ th MO.

**1.5** Calculate the net charges  $q_1$  and  $q_2$  of the butadiene carbon atoms 1 and 2. Deduce the values of  $q_3$  and  $q_4$ .

The bond order  $I$  is an estimate of the number of  $\pi$  chemical bonds between two atoms. For instance, a pure single bond would have a bond order  $I = 0$ , a pure double bond would correspond to  $I = 1$ , etc. The bond order  $I_{rs}$  between two neighboring atoms  $r$  and  $s$  can be obtained from the MOs as:

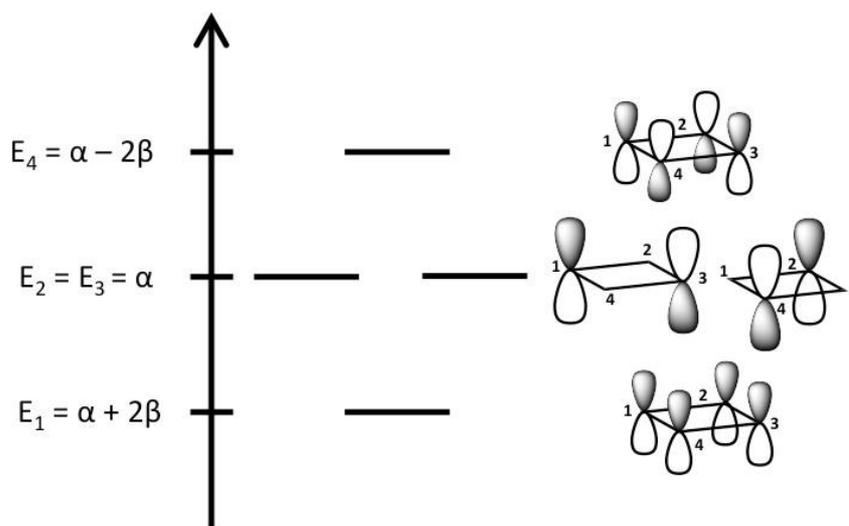
$$I_{rs} = \sum_{i=1}^{occ} n_i c_{ir} c_{is}$$

where  $I_{rs}$  is defined as the sum over the occupied MOs of the product of the number of electrons in the MO by the coefficient of each of the two atoms  $r$  and  $s$  in this MO.

**1.6** Calculate for each bond the associated bond order:  $I_{12}$ ,  $I_{23}$ , and  $I_{34}$ . Identify the bond(s) that has (have) the strongest double-bond character.

**1.7** Draw alternative Lewis structures of butadiene to reflect the previously obtained results (charges and bond orders).

The MO diagram of the hypothetical cyclobutadiene is provided below. The size of each atomic orbital is proportional to its coefficient in the considered MO, and its color (grey or white) reflects the sign of the wavefunction.



**1.8** Fill in the MO diagram of cyclobutadiene.

**1.9** Using the provided diagram and considering the symmetry of the molecule, determine the missing coefficients ( $c_{ij}$ ) in the following MO expressions.

$$\Psi_1 = 0.500 \varphi_1 + c_{12} \varphi_2 + c_{13} \varphi_3 + c_{14} \varphi_4$$

$$\Psi_2 = 0.707 \varphi_1 + c_{22} \varphi_2 + c_{23} \varphi_3 + c_{24} \varphi_4$$

$$\Psi_3 = c_{31} \varphi_1 + 0.707 \varphi_2 + c_{33} \varphi_3 + c_{34} \varphi_4$$

$$\Psi_4 = 0.500 \varphi_1 + c_{42} \varphi_2 + c_{43} \varphi_3 + c_{44} \varphi_4$$

**1.10** Calculate the formation and conjugation energies,  $\Delta E_f'$  and  $\Delta E_c'$ , for cyclobutadiene.

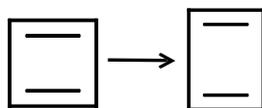
Which system is the most stable? Choose the correct answer :

- Cyclobutadiene  
 Two ethylene molecules  
 Both are equally stable

**1.11** Compare the formation energy of cyclobutadiene and that of butadiene. Which compound is the most stable? Choose the correct answer :

- Butadiene
- Cyclobutadiene
- Both are equally stable

We now consider a rectangular deformation of cyclobutadiene, with localization and shortening of the double bonds and elongation of the simple bonds compared to the square geometry.



**1.12** Choose the correct statement(s) from among the following :

- This deformation stabilizes C=C double bonds.
- This deformation weakens C=C double bonds.
- This deformation does not affect the stability of C=C double bonds.
- This deformation increases the stability due to electronic conjugation.
- This deformation diminishes the stability due to electronic conjugation.
- This deformation does not affect the stability due to electronic conjugation.

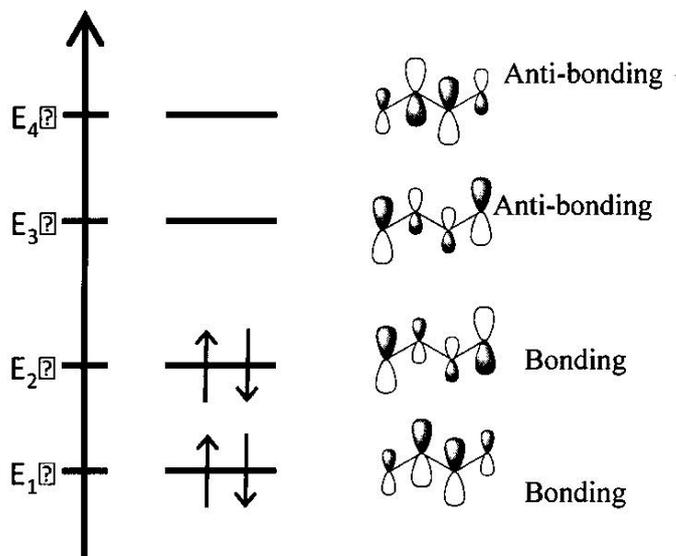
**1.13** Using your previous answers, choose the correct statement among the following.

The  $\pi$ -system after deformation is:

- More stable than the square cyclobutadiene.
- Less stable than the square cyclobutadiene.
- As stable as the square cyclobutadiene.

## SOLUTION OF PREPARATORY PROBLEM 1

1.1 Butadiene possesses 4  $\pi$ -electrons.



1.3  $\Delta E_i = 2 E_1 + 2 E_2 - 4 \alpha = 4.48 \beta$

1.4  $\Delta E_c = 2 E_1 + 2 E_2 - 2 \times 2(\alpha + \beta) = 0.48 \beta < 0$

Correct statement: Butadiene

1.5  $q_1 = q_2 = 0$ ;  $q_3 = q_4 = 0$  and  $q_1 = q_4 = 0$

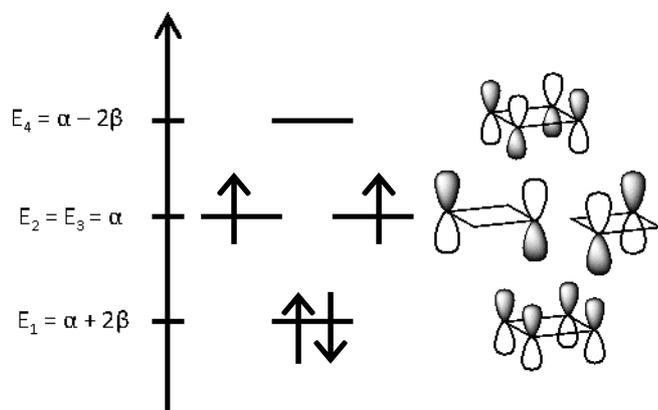
1.6  $l_{12} = 0.8943$ ;  $l_{23} = 0.4473$ ;  $l_{34} = 0.8943$

Strongest double-bond character: bonds  $C_1C_2$  and  $C_3C_4$ .

1.7



1.8



**1.9**  $c_{12} = c_{13} = c_{14} = 0.5$

$$c_{22} = c_{24} = 0; c_{23} = -0.707$$

$$c_{31} = c_{33} = 0;$$

$$c_{34} = -0.707$$

$$c_{42} = c_{44} = -0.5;$$

$$c_{43} = 0.5$$

**1.10**  $\Delta E_f' = 2 E_1 + 2 E_2 - 4 \alpha = 4 \beta$

$$\Delta E_c' = 2 E_1 + 2 E_2 - 2 \times 2(\alpha + \beta) = 0$$

Correct answer: Both are equally stable

**1.11**  $\Delta E_f$  (butadiene) <  $\Delta E_f'$  (cyclobutadiene)

Correct statement: Butadiene

**1.12** Correct statements:

This deformation stabilizes C=C double bonds. (shortening of the double bonds, stronger overlap of the  $2p_z$  orbitals)

This deformation does not affect the stability due to electronic conjugation. ( $\Delta E_c' = 0$  so there was no stabilization due to delocalization in the square geometry. Hence, localizing the double bonds does not affect the electronic conjugation)

**1.13** Correct statement:

More stable than the square cyclobutadiene.

---

## THEORETICAL PROBLEM 2

### Localization and delocalization in benzene

Historically, benzene was first isolated from benjoin (essence of the “Papier d’Arménie”). It was then synthesized by the French chemist M. Berthelot in the middle of the 19<sup>th</sup> century using acetylene trimerization. In this problem, the objective is to study the electronic properties of this compound, which is a representative of aromatic molecules. Let us start with benzene by referring to the carbon atoms as  $C_i$ ,  $i = 1 - 6$  in a clock-wise manner.

- 2.1 Write the reaction from acetylene  $C_2H_2$  generating benzene.
- 2.2 Draw a structure of benzene using three single bonds and three double bonds between carbon atoms. It is referred to as Kekulé’s benzene.
- 2.3 Draw a structure of benzene holding five single and two double bonds. This structure is called Dewar’s benzene.

Let us start with a Kekulé structure K1, holding a double bond between  $C_1$  and  $C_2$  atoms. A simple model to describe the  $\pi$  bond between  $C_1$  and  $C_2$  consists of characterizing the delocalization of a single electron by an energy  $t < 0$ .

- 2.4 Give the energy  $E_\pi$  of the  $\pi$ -system of this bond as a function of  $t$ .
- 2.5 In K1, double bonds are supposed to be fixed. For this structure K1, calculate the energy of the  $\pi$ -system  $E_{K1}$  as a function of  $t$ .
- 2.6 Write an analog to K1. It will be called K2.
- 2.7 Express the energy  $E_{K2}$  of this structure K2.

Mathematically, the benzene molecule is expressed as a mix between K1 and K2,  $K = c_1 K1 + c_2 K2$ , where  $c_1$  and  $c_2$  are real numbers<sup>3</sup> with  $c_1^2 + c_2^2 = 1$  and  $c_1 > 0$  and  $c_2 > 0$ . This expression stresses that a proper description of benzene cannot be restricted to K1 or K2.

- 2.8 In a scheme, show the displacement of the double bond localized between  $C_1$  and  $C_2$  and the movement of the other double bonds. These formulae are the resonance structures of benzene.

Starting from a localized view K1 or K2, the electronic delocalization over all the carbon atoms can be accounted for by the introduction of a supplementary energetic energy  $E_K$  of K is thus defined as:

$$E_K = c_1^2 E_{K1} + c_2^2 E_{K2} + 2 c_1 c_2 H_{12}$$

where  $H_{12}$  varies between  $t$  and 0, with  $t < 0$ . Therefore,  $E_K$  is a function of  $c_1$  and  $c_2$ .

**2.9** Express  $E_K$  as a function of  $c_1$  only.

It can be shown that  $E_K$  is minimal for  $c_1 = 1 / (2)^{1/2}$ . From now on, we assume that  $c_1 = 1 / (2)^{1/2}$ .

**2.10** If  $H_{12} = 0$ , what is the expression of  $E_K$ ? The resonance energy is defined as the difference  $\Delta E_1 = E_K(H_{12} = t) - E_K(H_{12} = 0)$ . Evaluate  $\Delta E_1$  as a function of  $t$ .

**2.11** Specify the sign of  $\Delta E_1$ . Choose the correct statement between:

- electronic delocalization contributes to stabilize the benzene molecule.
- electronic delocalization contributes to destabilize the benzene molecule.

Alternatively, the  $\pi$  energy of a  $n$  carbon atom-system can be evaluated from the occupations of the molecular orbitals (MOs). C. A. Coulson (C. A. Coulson, Proc. Roy Soc., 1939) showed that the MOs energies  $\varepsilon_k$  of a cyclic  $n$  carbon atom-system, not necessarily in energy order, read:

$$\varepsilon_k = 2 t \cos \frac{2k\pi}{n} ; k \in N, k \in [0; n-1]$$

**2.12** Draw the MOs diagram of the  $\pi$ -system of benzene ( $n = 6$ ) and calculate the corresponding energies for each MO.

**2.13** Fill the MOs diagram.

**2.14** Evaluate the  $\pi$ -system energy of benzene,  $E_{MO}$ , from the filling of the MOs in ascending order. Then, calculate the resonance energy  $\Delta E_2 = E_{MO} - E_K(H_{12} = 0)$ .

**2.15** Compare  $\Delta E_2$  and  $\Delta E_1$ .

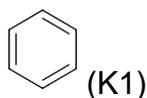
**2.16** From the previous results, choose one expression for the relation between the standard hydrogenation enthalpy of cyclohexene ( $\Delta_r H_c^\circ$ ) and that of benzene ( $\Delta_r H_b^\circ$ ).

- $|\Delta_r H_b^\circ| < 3 |\Delta_r H_c^\circ|$
- $|\Delta_r H_b^\circ| = 3 |\Delta_r H_c^\circ|$
- $|\Delta_r H_b^\circ| > 3 |\Delta_r H_c^\circ|$

**SOLUTION OF PREPARATORY PROBLEM 2**

2.1  $3 \text{ C}_2\text{H}_2 = \text{C}_6\text{H}_6$

2.2



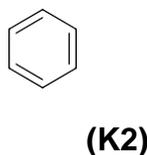
2.3



2.4  $E_\pi = 2t$

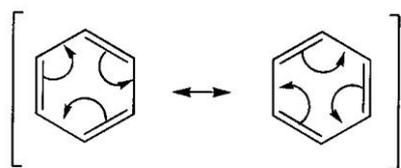
2.5  $E_{K1} = 3 \times 2t = 6t$

2.6



2.7  $E_{K2} = E_{K1} = 6t$

2.8



2.9 Using  $c_1^2 + c_2^2 = 1$ ,

$$c_2 = \sqrt{1 - c_1^2}$$

Hence  $E_K = E_{K2} + (E_{K1} - E_{K2})c_1^2 + 2c_1\sqrt{1 - c_1^2}H_{12}$

2.10  $E_K(H_{12} = 0) = (1 - c_1^2)E_{K2} + c_1^2E_{K1}$

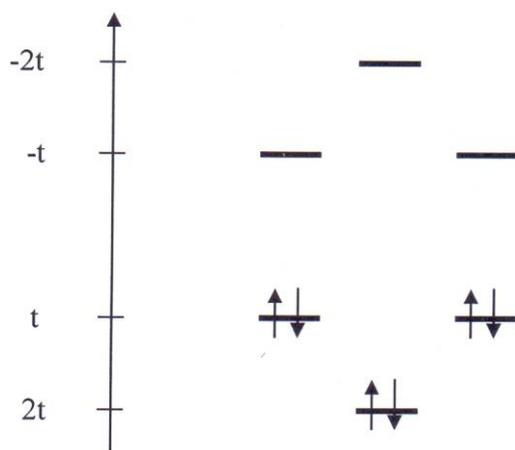
$$\Delta E_1 = 7t - 6t = t$$

..

2.11  $t < 0$ , so  $\Delta E_1 < 0$ : electronic delocalization contributes to stabilize the benzene molecule.

2.12 See answer 2.13.

2.13



2.14  $EMO = 2 \times 2t + 4t = 8t$  and  $\Delta E_2 = (2 \times 2t + 4t) - 6t = 2t$

2.15 Since  $t < 0$ ,  $\Delta E_2 = 2t < t = \Delta E_1$

2.16 Correct answer:  $|\Delta_r H b| < 3 |\Delta_r H c^\circ|$



**3.6** Complete this scheme by calculating the standard enthalpy of hydrogenation of benzene into cyclohexa-1,3-diene.

The sign of the standard enthalpy of this reaction differs from the sign of the other standard enthalpies of hydrogenation in scheme 1.

**3.7** What is the main reason for such a difference?

- All the double bonds are not equivalent in benzene: one is stronger than the others.
- The breaking of benzene aromaticity.
- The formation of a reaction intermediate (cyclohexa-1,3-diene) with a constrained geometry.

**3.8** Using only the values given in scheme 1, calculate the resonance energy of cyclohexa-1,3-diene and the resonance energy of benzene.

Data:

Standard combustion enthalpies  $\Delta_{\text{comb}}H^\circ$  at 298 K in  $\text{kJ mol}^{-1}$

Compound	C(graphite)	H <sub>2</sub> (g)	C <sub>6</sub> H <sub>6</sub> (l)
$\Delta_{\text{comb}}H^\circ$	-393.5	-285.6	-3268

Standard enthalpy of formation of cyclohexane at 298 K

$$\Delta_f H^\circ(\text{C}_6\text{H}_{12}(\text{l})) = -156.4 \text{ kJ mol}^{-1}$$

Standard bond enthalpies  $\Delta_d H^\circ$  at 298 K in  $\text{kJ mol}^{-1}$

Bond	C—H	C—C	C=C
$\Delta_d H^\circ$	414.8	346.9	614.5

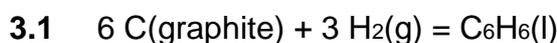
Standard enthalpies of dissociation  $D^\circ$  at 298 K in  $\text{kJ mol}^{-1}$

Bond	O=O	H—H
$D^\circ$	498.3	436.0

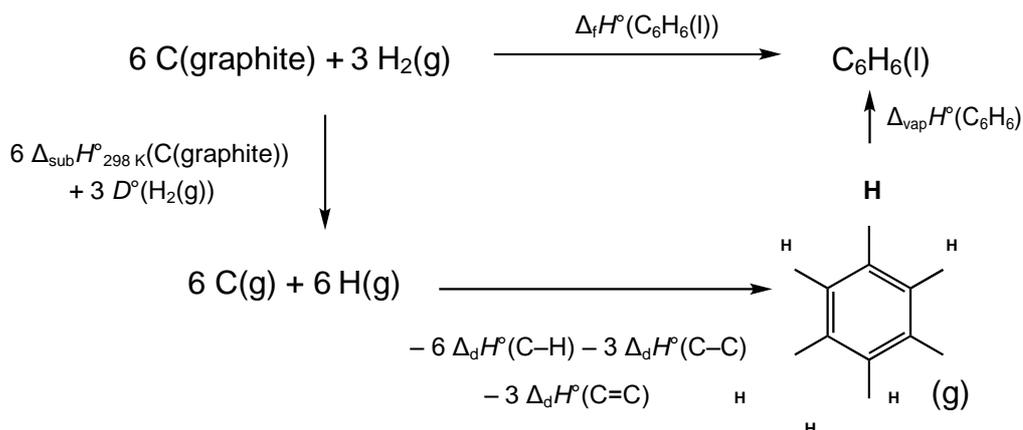
Standard latent heat at 298 K in  $\text{kJ mol}^{-1}$

$$\Delta_{\text{sub}}H^\circ(\text{C}(\text{graphite})) = 716.70 \text{ kJ mol}^{-1}$$

$$\Delta_{\text{vap}}H^\circ(\text{C}_6\text{H}_6) = 33.90 \text{ kJ mol}^{-1}$$

**SOLUTION OF PREPARATORY PROBLEM 3**

3.2



$$\begin{aligned}
 \Delta_f H^\circ(\text{C}_6\text{H}_6(\text{l})) &= 6 \Delta_{\text{sub}} H^\circ(\text{C(graphite)}) + 3 D^\circ(\text{H}_2(\text{g})) - 6 \Delta_d H^\circ(\text{C-H}) - 3 \Delta_d H^\circ(\text{C-C}) - \\
 &\quad - 3 \Delta_d H^\circ(\text{C=C}) - \Delta_{\text{vap}} H^\circ(\text{C}_6\text{H}_6(\text{l}))
 \end{aligned}$$

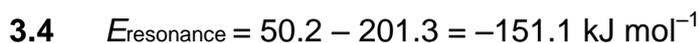
$$\Delta_f H^\circ(\text{C}_6\text{H}_6(\text{l})) = 6 \times 716.7 + 3 \times 436.0 - 6 \times 414.8 - 3 \times 346.9 - 3 \times 614.5 - 33.9$$

$$\Delta_f H^\circ(\text{C}_6\text{H}_6(\text{l})) = 201.3 \text{ kJ mol}^{-1}$$



$$\Delta_f H^\circ(\text{C}_6\text{H}_6(\text{l})) = -6 \times 393.5 - 3 \times 285.6 + 3268.0$$

$$\Delta_f H^\circ(\text{C}_6\text{H}_6(\text{l})) = 50.2 \text{ kJ mol}^{-1}$$



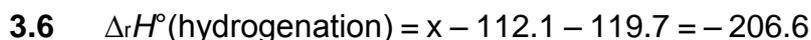
Correct statement:

The method used at question 2 does not take into account the nature of bonds in benzene.



$$\Delta_r H^\circ(\text{hydrogenation}) = - \Delta_f H^\circ(\text{C}_6\text{H}_6(\text{l})) - 3 \Delta_f H^\circ(\text{H}_2(\text{g})) + \Delta_f H^\circ(\text{C}_6\text{H}_{12}(\text{l}))$$

$$\Delta_r H^\circ = -50.2 - 3 \times 0.0 - 156.4 = -206.6 \text{ kJ mol}^{-1}$$

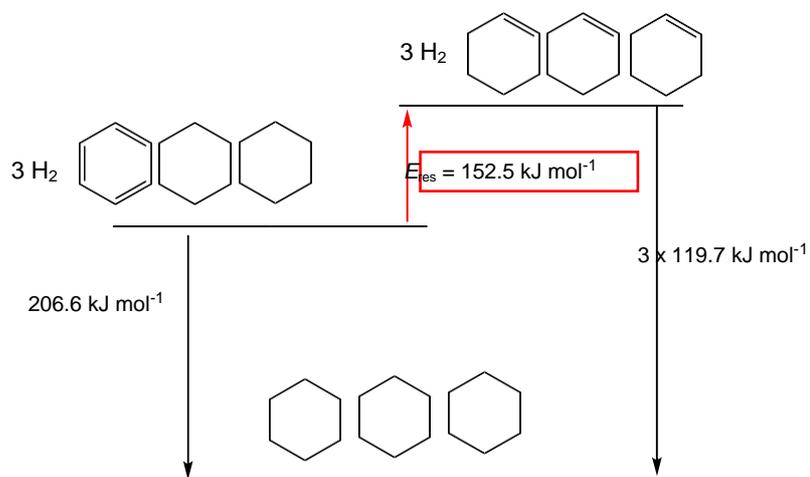
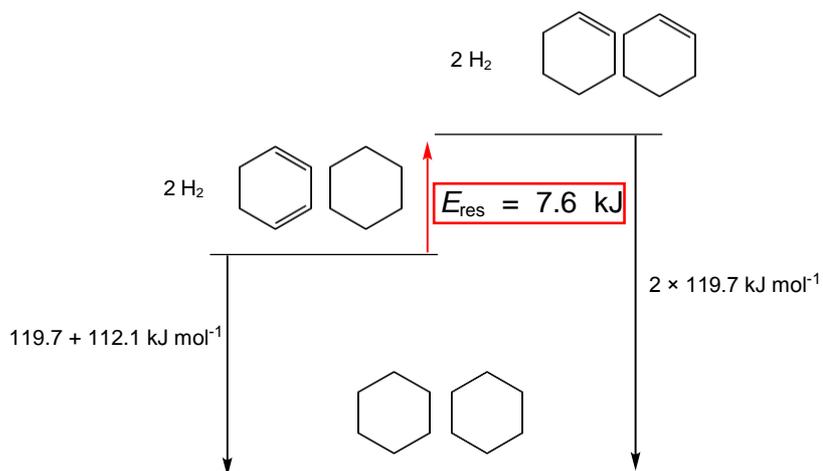


$$x = 25.2 \text{ kJ mol}^{-1}$$

3.7 Correct statement:

The breaking of benzene aromaticity.

### 3.8

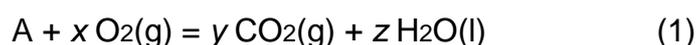


## THEORETICAL PROBLEM 4

### Use of dihydrogen: fuel cells

In order to generate electricity, the heat produced by fuel combustion (dihydrogen, methanol, etc.) can be used to evaporate liquid water. The produced steam turns a turbine, which drives a generator. In such a process, the chemical energy is first converted into thermal energy, then into mechanical energy and finally into electrical energy. Leaks occur at each conversion step (mainly by heat dissipation), which decreases the yield of the global process. On the contrary, fuel cells directly convert the chemical energy into electrical energy.

The balanced chemical equation for the combustion of one equivalent of fuel A is:



$\Delta_{\text{comb}}H^\circ(\text{A})$  and  $\Delta_{\text{comb}}G^\circ(\text{A})$  are respectively the standard enthalpy of reaction and the standard Gibbs free energy of reaction associated with reaction (1).

### The hydrogen fuel cell

The global reaction in the hydrogen fuel cell is the same as that of  $\text{H}_2$  combustion. In this problem, compounds of the hydrogen fuel cell will be considered in their standard state at 298 K.

- 4.1 Write down the redox half-reactions occurring at the anode and the cathode. Write down the balanced chemical equation for the global reaction, for one equivalent of dihydrogen.
- 4.2 Compute the open circuit voltage of such a cell.
- 4.3 Compute the theoretical maximum electrical energy recoverable by one mol of dihydrogen consumed.
- 4.4 Electric cars consume between 10 and 20 kWh / 100 km. Compute the volume of dihydrogen necessary to produce an electrical energy of 20 kWh at 1.0 bar.

The thermodynamic efficiency of a cell is defined as:

$$Y_{\text{thermo}} = \frac{\Delta_r G^\circ}{\Delta_r H^\circ}$$

where  $\Delta_r G^\circ$  and  $\Delta_r H^\circ$  are respectively the standard Gibbs free energy of reaction and the standard enthalpy of reaction associated with the global reaction of the running cell.

- 4.5 Calculate the standard enthalpy of the combustion reaction of gaseous dihydrogen

$\Delta_{\text{comb}}H^{\circ}_{298\text{K}}(\text{H}_2(\text{g}))$  at 298 K. Deduce the thermodynamic efficiency of the dihydrogen fuel cell.

The thermodynamic efficiency is smaller than 1 because there is a variation of the entropy of the system.

**4.6** Calculate the standard entropy of the dihydrogen combustion reaction  $\Delta_{\text{comb}}S^{\circ}_{298\text{K}}(\text{H}_2(\text{g}))$  at 298 K.

**4.7** Determine if the sign of this standard entropy is consistent with the balanced chemical equation for the reaction (Yes/No). Justify it by a short calculation using the stoichiometric coefficients.

### The liquid methanol cell

The low energy density of dihydrogen and the necessity of a large pressure for its storage have motivated the development of batteries using other fuels. In a cell using liquid methanol as a fuel, the global reaction is that of the combustion of liquid methanol.

**4.8** Determine the oxidation state of the carbon atom in methanol and in carbon dioxide.

**4.9** Write down the redox half-reactions occurring at the anode and the cathode. Write down the balanced chemical equation for the global reaction of the running cell for one equivalent of liquid methanol.

**4.10** Calculate the associated thermodynamic efficiency. Compare it to the efficiency of the dihydrogen fuel cell.

**4.11** Calculate the volume of liquid methanol required to produce 20 kWh. Compare this value to the previously calculated volume of gaseous dihydrogen.

**4.12** Assuming  $\text{H}_2$  is an ideal gas, determine the pressure to store the dihydrogen necessary to produce 20 kWh in the same volume as methanol (question 11).

#### Data:

Standard enthalpies of formation  $\Delta_f H^{\circ}$  at 298 K in  $\text{kJ mol}^{-1}$

Compound	$\text{O}_2(\text{g})$	$\text{CO}_2(\text{g})$	$\text{H}_2\text{O}(\text{g})$	$\text{CH}_3\text{OH}(\text{l})$
$\Delta_f H^{\circ}$	0.0	-394.0	-241.8	-239.0

Molar heat capacities at constant pressure  $C^{\circ}_P$  in  $\text{J mol}^{-1} \text{K}^{-1}$ . They are supposed to be independent of the temperature:

Compound	H <sub>2</sub> O(g)	H <sub>2</sub> O(l)
$C^{\circ}_P$	33.6	75.3

Standard latent heat of water at 373 K :

$$\Delta_{\text{vap}}H^{\circ}(\text{H}_2\text{O}) = 40.66 \text{ kJ mol}^{-1}$$

Standard potentials at 25 °C related to the standard hydrogen electrode (SHE) :

$$E^{\circ}(\text{O}_2(\text{g})/\text{H}_2\text{O}(\text{l})) = 1.23 \text{ V /SHE}$$

$$E^{\circ}(\text{CO}_2(\text{g})/\text{CH}_3\text{OH}(\text{l})) = 0.03 \text{ V /SHE}$$

Liquid methanol density :

$$\rho_{\text{methanol}} = 0.79 \text{ g cm}^{-3}$$

---

**SOLUTION OF PREPARATORY PROBLEM 4**

4.1 At the anode:  $\text{H}_2(\text{g}) = 2 \text{H}^+(\text{aq}) + 2 \text{e}^-$

At the cathode:  $1/2 \text{O}_2(\text{g}) + 2 \text{H}^+(\text{aq}) + 2 \text{e}^- = \text{H}_2\text{O}(\text{l})$

Global reaction:  $\text{H}_2(\text{g}) + 1/2 \text{O}_2(\text{g}) = \text{H}_2\text{O}(\text{l})$

4.2  $U = E^\circ(\text{O}_2(\text{g})/\text{H}_2\text{O}(\text{l})) - E^\circ(\text{H}^+(\text{aq})/\text{H}_2(\text{g})) = 1.23 \text{ V}$

4.3 The temperature and the pressure of the system are fixed. Hence, the maximum energy that can be recovered from a system is computed from Gibbs free energy.

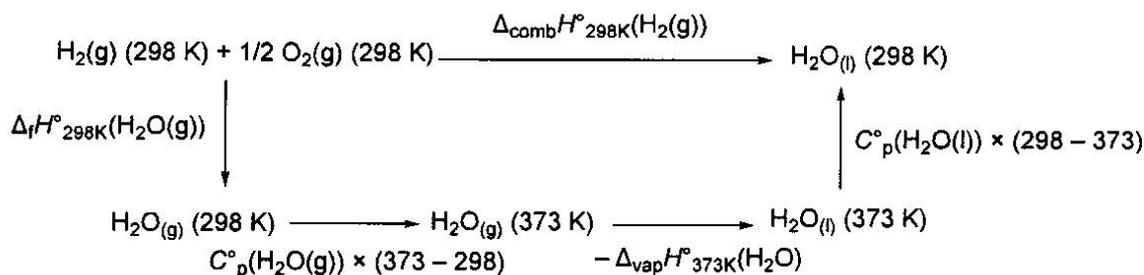
$$\Delta_{\text{comb}} G^\circ_{298\text{K}}(\text{H}_2(\text{g})) = -n F U = -2 \times 96485 \times 1.23 = -237 \text{ kJ mol}^{-1}$$

4.4  $E$  being the energy to be produced:

$$n(\text{H}_2(\text{g})) = \frac{E}{\Delta_{\text{comb}} G^\circ_{298\text{K}}(\text{H}_2(\text{g}))} = 3.0 \times 10^2 \text{ mol}$$

$$V = \frac{n(\text{H}_2(\text{g}))RT}{p} = \frac{3.0 \times 10^2 \times 8.31 \times 298}{1.0 \times 10^5} = 7.5 \text{ m}^3$$

4.5



$$\Delta_{\text{comb}} H^\circ_{298\text{K}}(\text{H}_2(\text{g})) = \Delta_f H^\circ_{298\text{K}}(\text{H}_2\text{O}(\text{g})) + C_p^\circ(\text{H}_2\text{O}(\text{g})) (373 - 298) - \Delta_{\text{vap}} H^\circ_{373\text{K}}(\text{H}_2\text{O}) + C_p^\circ(\text{H}_2\text{O}(\text{l})) (298 - 373)$$

$$\Delta_{\text{comb}} H^\circ_{298\text{K}}(\text{H}_2(\text{g})) = -241.8 + 33.6 \times 10^{-3} \times (373 - 298) - 40.66 + 75.3 \times 10^{-3} \times (298 - 373)$$

$$\Delta_{\text{comb}} H^\circ_{298\text{K}}(\text{H}_2(\text{g})) = -286 \text{ kJ mol}^{-1}$$

Thus, the thermodynamic efficiency of the dihydrogen fuel cell is:

$$\gamma_{\text{thermo}} = \frac{\Delta_{\text{comb}} G^\circ_{298\text{K}}(\text{H}_2(\text{g}))}{\Delta_{\text{comb}} H^\circ_{298\text{K}}(\text{H}_2(\text{g}))} = \frac{-237}{-287} = 0.83$$

**4.6**  $\Delta_{\text{comb}}G^{\circ}_{298\text{K}}(\text{H}_2(\text{g})) = \Delta_{\text{comb}}H^{\circ}_{298\text{K}}(\text{H}_2(\text{g})) - T\Delta_{\text{comb}}S^{\circ}_{298\text{K}}(\text{H}_2(\text{g}))$  with  $T = 298 \text{ K}$

$$\Delta_{\text{comb}}S^{\circ}_{298\text{K}}(\text{H}_2(\text{g})) = \frac{\Delta_{\text{comb}}H^{\circ}_{298\text{K}}(\text{H}_2(\text{g})) - \Delta_{\text{comb}}G^{\circ}_{298\text{K}}(\text{H}_2(\text{g}))}{T} = \frac{-286 + 237}{298}$$

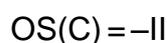
$$\Delta_{\text{comb}}S^{\circ}_{298\text{K}}(\text{H}_2(\text{g})) = -164 \text{ J mol}^{-1}\text{K}^{-1}$$

**4.7** The difference between the stoichiometric coefficients of the gaseous compounds in the balanced chemical equation for the reaction is:

$$0 - (1 + 1/2) = -3/2 < 0$$

This is consistent with a decrease of the disorder.

**4.8** In methanol:



in  $\text{CO}_2$ :



**4.9** At the anode:  $\text{CH}_3\text{OH}(\text{l}) + \text{H}_2\text{O}(\text{l}) = \text{CO}_2(\text{g}) + 6 \text{ H}^+(\text{aq}) + 6 \text{ e}^-$

at the cathode:  $3/2 \text{ O}_2(\text{g}) + 6 \text{ H}^+(\text{aq}) + 6 \text{ e}^- = 3 \text{ H}_2\text{O}(\text{l})$

Global reaction:  $\text{CH}_3\text{OH}(\text{l}) + 3/2 \text{ O}_2(\text{g}) = \text{CO}_2(\text{g}) + 2 \text{ H}_2\text{O}(\text{l})$

**4.10**  $\Delta_{\text{comb}}G^{\circ}_{298\text{K}}(\text{CH}_3\text{OH}(\text{l})) = -nF[E^{\circ}(\text{O}_2(\text{g})/\text{H}_2\text{O}(\text{l})) - E^{\circ}(\text{CH}_3\text{OH}(\text{l})/\text{CO}_2(\text{g}))]$

$$\Delta_{\text{comb}}G^{\circ}_{298\text{K}}(\text{CH}_3\text{OH}(\text{l})) = -6 \times 96485 \times (1.23 - 0.03)$$

$$\Delta_{\text{comb}}G^{\circ}_{298\text{K}}(\text{CH}_3\text{OH}(\text{l})) = -695 \text{ kJ mol}^{-1}$$

$$\Delta_{\text{comb}}H^{\circ}_{298\text{K}}(\text{CH}_3\text{OH}(\text{l})) = -\Delta_f H^{\circ}_{298\text{K}}(\text{CH}_3\text{OH}(\text{l})) + \Delta_f H^{\circ}_{298\text{K}}(\text{CO}_2(\text{g})) + 2\Delta_f H^{\circ}_{298\text{K}}(\text{H}_2\text{O}(\text{l}))$$

$\Delta_f H^{\circ}_{298\text{K}}(\text{H}_2\text{O}(\text{l})) = \Delta_{\text{comb}}H^{\circ}_{298\text{K}}(\text{H}_2(\text{g})) = -286 \text{ kJ mol}^{-1}$  (question 5). Hence:

$$\Delta_{\text{comb}}H^{\circ}_{298\text{K}}(\text{CH}_3\text{OH}(\text{l})) = -(-239) + (-394) + 2 \times (-286)$$

$$\Delta_{\text{comb}}H^{\circ}_{298\text{K}}(\text{CH}_3\text{OH}(\text{l})) = -727 \text{ kJ mol}^{-1}$$

$$Y_{\text{thermo}} = \frac{-695}{-727} = 0.96$$

**4.11**

$$n(\text{CH}_3\text{OH}(\text{l})) = \frac{E}{\Delta_{\text{comb}}G^{\circ}_{298\text{K}}(\text{CH}_3\text{OH}(\text{l}))} = \frac{-20 \times 3600}{-695} = 1.04 \times 10^2 \text{ mol}$$

$$V = \frac{n(\text{CH}_3\text{OH}, \text{l}) \times M}{\mu(\text{CH}_3\text{OH}, \text{l})} = \frac{104 \times 32}{0.79} = 4.2 \times 10^3 \text{ cm}^3 < V(\text{gaseous dihydrogen})$$

**4.12**

$E$  being the energy to be produced:

$$n(\text{H}_2(\text{g})) = \frac{E}{\Delta_{\text{comb}} G^{\circ}_{298 \text{ K}}(\text{H}_2(\text{g}))} = \frac{-20 \times 3600}{-237} = 3.04 \times 10^2 \text{ mol}$$

$$p = \frac{n(\text{H}_2, \text{g}) R T}{V} = \frac{3.04 \times 10^2 \times 8.31 \times 298}{4.2 \times 10^{-3}} = 1.8 \times 10^8 \text{ Pa}$$

---

## THEORETICAL PROBLEM 5

### Hydrogen storage

Dihydrogen is a promising fuel for the future, notably for power production or mobility purposes. It is an attractive alternative to the use of fossil fuels (hydrocarbons), which release carbon dioxide during their combustion, thus contributing to global warming. Unfortunately, storing efficiently large amounts of  $\text{H}_2$  is not easy. Dihydrogen has a low energy per unit volume at room temperature, is highly flammable and requires several technological advances to be competitive with fossil fuels. In this problem, we investigate the advantages and disadvantages of some hydrogen storing methods.

### Storing $\text{H}_2$ as a gas

Compressing dihydrogen is one of the methods commonly used to store it. The gas is stored in containers at a pressure kept between 350 and 700 bars.

**5.1** Calculate the density of an ideal dihydrogen gas at a pressure of 500 bar and at room temperature (293 K).

### Storing $\text{H}_2$ as a liquid

Dihydrogen gas is liquefied and kept in a Dewar flask (a thermally insulated container) usually under a relatively low pressure (1 to 4 bar). However, the system needs to be kept at very low temperatures, because the melting point of  $\text{H}_2$  at a pressure  $p = 1$  atm is  $T_m = -259.2$  °C and its boiling point under the same pressure is  $T_v = -252.78$  °C. Its critical point is located at:  $p_c = 13.0$  bar,  $T_c = -240.01$  °C.

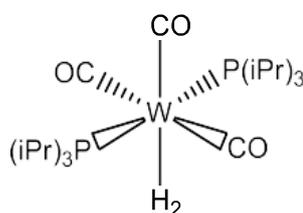
**5.2** At which temperatures can liquid hydrogen be observed?

- 16 K
- 25 K
- 77 K
- 293 K

**5.3** Using the Clausius-Clapeyron relation, calculate the pressure needed to liquefy ideal gaseous dihydrogen at 27.15 K.

### Storing dihydrogen as a complex

In 1984, using measurements obtained from neutron diffraction, G. J. Kubas and his collaborators (G. J. Kubas *et al.*, J. Am. Chem. Soc., 1984) identified a tungsten complex  $[\text{W}(\text{CO})_3(\text{P}(\text{iPr})_3)_2(\eta^2\text{-H}_2)]$  that possesses a H—H bond with a length of 0.82 Å, close to that of an isolated H<sub>2</sub> molecule (0.74 Å). ((iPr) = iso-propyl). This complex easily dissociates under partial vacuum or under argon atmosphere, and it can be regenerated in the presence of dihydrogen.

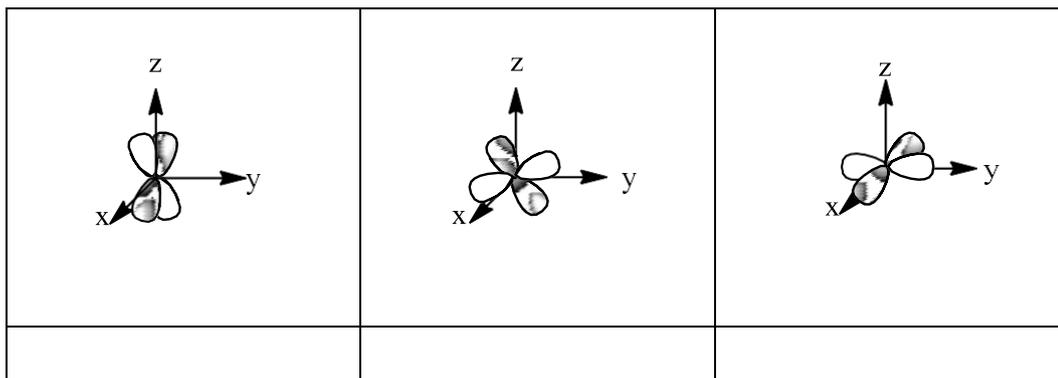


- 5.4** Calculate the mass of the dehydrogenated complex needed to store 1 kg of dihydrogen. Calculate  $\rho_{\text{H}}$  (the density of hydrogen in the complex, defined as the mass of hydrogen atoms per volume unit of complex).

The next section will study the binding of a H<sub>2</sub> molecule to the dehydrogenated complex within the field of other ligands. The dehydrogenated complex is assumed to be a square-based pyramid, which the dihydrogen molecule is added to.

### Metallic central atom

- 5.5** Give the electronic configuration of atomic tungsten. Specify the number of valence electrons.
- 5.6** Fill in the table with the name of each depicted atomic orbital ( $s$ ,  $d_{yz}$ ,  $d_{z^2}$ ,  $d_{(x^2-y^2)}$ ,  $d_{xz}$ ,  $d_{xy}$ ).

## Dihydrogen as a ligand

5.7 Draw and fill the molecular orbital diagram of dihydrogen.

### Kubas complex

Since the complex is considered as a square-based pyramid to which the  $H_2$  molecule is added, we have to take into account the influence of other ligands. The splitting thus obtained is given in the diagram below.

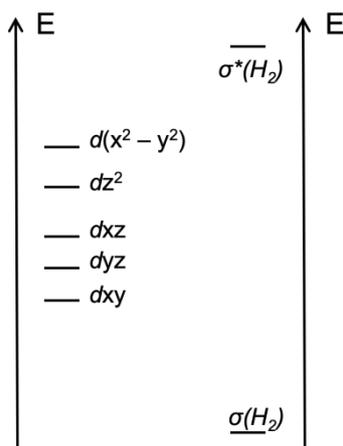
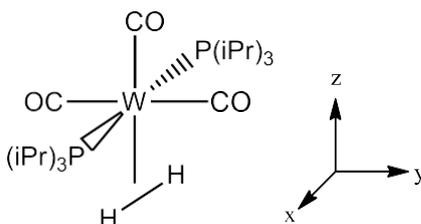


Figure 1: Simplified diagram of molecular orbitals of the Kubas complex

In order to build the molecular orbital diagram of the Kubas complex, we can study the interaction of the molecular orbitals of the complex ( $[W(CO)_3(P(iPr)_3)_2]$ ) — which will be merely considered as the  $d$  orbitals of the metallic central atom — with the  $H_2$  molecule orbitals.

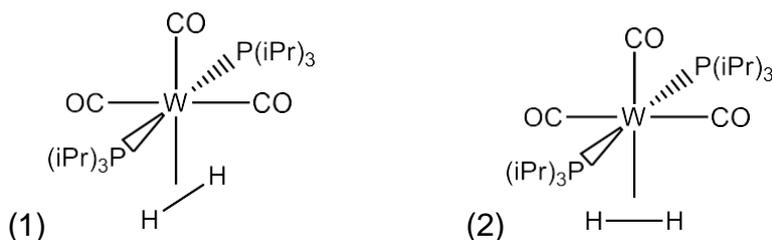
Figure 2: Kubas complex and reference axes



**5.8** Give the two planes of symmetry of the Kubas complex (using the axes of Figure 2).

**5.9** Indicate for each orbital  $d$  of the metallic central atom if they are symmetric or anti-symmetric with respect to each of the symmetry planes (using the axes of figure 2).

Two conformations have been proposed: (1) where  $H_2$  is parallel to the phosphine ligands  $P(iPr)_3$ , and (2) where  $H_2$  is parallel to the CO ligands. Even if steric effects favor conformation (2), conformation (1) is actually more stable.



**5.10** Fill in the diagram in figure 1 with electrons.

**5.11** Knowing that only orbitals with the same symmetry interact, enumerate the possible interactions for each conformation. Which conformation is the most stable one?

### Storing hydrogen in form of formic acid

In 2006, a research team of EPFL (Switzerland) (C. Fellay *et al.*, *Angew. Chem. Int. Ed.*, 2008) proposed to store  $H_2$  in form of formic acid. The main idea is to use formic acid as fuel that can be decomposed on a catalyst made of ruthenium to produce dihydrogen and carbon dioxide according to the following reaction:



**5.12** Calculate  $\rho_H$  (the density of hydrogen at 25 °C defined as the mass of hydrogen atoms per volume unit of formic acid). Compare this value to those obtained for gaseous dihydrogen at 500 bar and for liquid dihydrogen.

**5.13** Calculate the standard enthalpy and entropy of reaction at 20 °C for reaction (R1).

**5.14** Using the Ellingham approximation (that supposes enthalpy and entropy independent on temperature), calculate the equilibrium constant at 20 °C for reaction (R1).

Formic acid (2.3 g) is added to a 1 dm<sup>3</sup> container with 0.1 g of ruthenium catalyst, under constant atmospheric pressure and at an initial temperature of 25 °C. The container initially contains dinitrogen.

**5.15** Determine the final composition of the mixture.

### Storing hydrogen in metal hydrides

Metal hydrides have also been proposed to store dihydrogen. Compounds with a  $X_xY_yH_n$  formula can store large amounts of hydrogen in a compact way. Moreover, the adsorption-desorption properties of hydrogen can be tailored by choosing an element X from light elements (Li, Mg, B,...) or other electropositive elements (lanthanides) that have a good affinity with hydride ligands, and an element Y from transition metals that have a low affinity with hydride ligands. Among the numerous existing metal hydrides, two of them will be studied in their operating conditions:  $\text{LaNi}_5\text{H}_6$  (300 K, 2 bar) and  $\text{Mg}_2\text{NiH}_4$  (550 K, 4 bar).

**5.16** Determine  $\rho_{\text{H}}$  (the density of hydrogen, which is defined as the mass of hydrogen atoms per volume for these two compounds in their operating conditions).

The adsorption-desorption equilibrium can be described as a phase change  $\text{A}(\text{g}) \rightarrow \text{A}(\text{ads})$ . Hence, dihydrogen is considered as an ideal gas and the Clausius-Clapeyron relation for a phase transformation from an ideal gas is a rather good approximation. The latent heat can be assimilated, in this case, to the adsorption enthalpy. In the following tables, the pressure (MPa) is given as a function of the temperature (K).

$\text{LaNi}_5\text{H}_6$

$p$ (MPa)	2.15	0.68	0.10	0.07
$T$ (K)	370	333	285	278

$\text{Mg}_2\text{NiH}_4$

$p$ (MPa)	1.94	0.71	0.26	0.10
$T$ (K)	667	625	588	555

Table 1: Van't Hoff plot data (pressure (MPa) as a function of the temperature (K)) of several metal hydrides (A. Züttel, Naturwissenschaften, 2004)

**5.17** Using table 1, determine the adsorption enthalpies of  $\text{LaNi}_5\text{H}_6$  and  $\text{Mg}_2\text{NiH}_4$ .

**Data:**

Van der Waals gas equation:

$$\left(p + \frac{n^2 a}{V^2}\right)(V - nb) = nRT$$

Van der Waals coefficients for dihydrogen:

$$a = 0.2476 \text{ L}^2 \text{ bar mol}^{-2}$$

$$b = 0.02661 \text{ L mol}^{-1}$$

Specific latent heat of fusion (at standard pressure):  $\Delta_{\text{fus}}H^{\circ}_m = 58.089 \text{ kJ kg}^{-1}$

Specific latent heat of vaporization (at standard pressure):  $\Delta_{\text{vap}}H^{\circ}_m = 448.69 \text{ kJ kg}^{-1}$

### Densities

Gaseous dihydrogen, standard conditions:  $0.08988 \text{ g L}^{-1}$

Liquid dihydrogen,  $-252.78 \text{ }^{\circ}\text{C}$ :  $70.849 \text{ g dm}^{-3}$

compound	Kubas complex	formic acid	LaNi <sub>5</sub> H <sub>6</sub>	Mg <sub>2</sub> NiH <sub>4</sub>
conditions	--	25 °C	300 K	550 K
$\rho$	$1.94 \text{ g cm}^{-3}$	$1.22 \text{ kg dm}^{-3}$	$8620 \text{ kg m}^{-3}$	$2643 \text{ kg m}^{-3}$

### Thermodynamic data at normal conditions of temperature and pressure

(20 °C, 1 atm)

compound	HCOOH(g)	HCOOH(l)	CO <sub>2</sub> (g)	H <sub>2</sub> (g)	N <sub>2</sub> (g)
$\Delta_f H^{\circ} \text{ kJ mol}^{-1}$	-378.60	-425.09	-393.51	0.00	0.00
$S_m^{\circ} \text{ J mol}^{-1} \text{ K}^{-1}$	248.70	131.84	213.79	130.68	191.61

**SOLUTION OF PREPARATORY PROBLEM 5****5.1**

$$pV = nRT \Leftrightarrow \frac{p}{RT} = \frac{\rho}{M}$$

$$\rho = \frac{Mp}{RT} = \frac{2.0 \times 10^{-3} \times 500 \times 10^5}{8.314 \times 293} = 41.1 \text{ kg m}^{-3}$$

**5.2** Correct statements :

16 K, 25 K

**5.3** Using the Clausius-Clapeyron relation and the boiling point under a pressure of 1 atm:

$$\ln\left(\frac{p_2}{p_1}\right) = \frac{\Delta_{\text{vap}}H^\circ}{R} \left(\frac{1}{T_1} - \frac{1}{T_2}\right)$$

$$p_{27.15 \text{ K}} = p_{\text{atm}} \exp\left[\frac{\Delta_{\text{vap}}H^\circ}{R} \left(\frac{1}{T_v} - \frac{1}{T_{27.15 \text{ K}}}\right)\right]$$

$\Delta_{\text{vap}}H^\circ_m = 448.69 \text{ kJ kg}^{-1}$ , so that  $\Delta_{\text{vap}}H^\circ = 897.38 \text{ J mol}^{-1}$

$$p_{27.15 \text{ K}} = 1.0 \times 10^5 \exp\left[\frac{897.38}{8.314} \left(\frac{1}{20.37} - \frac{1}{27.15}\right)\right] = 0.380 \text{ MPa} = 3.75 \text{ atm}$$

**5.4** Dehydrogenated complex:  $W(\text{CO})_3(\text{P}(i\text{Pr})_3)_2 = \text{WC}_{21}\text{O}_3\text{P}_2\text{H}_{42}$   $M = 588.4 \text{ g mol}^{-1}$ 

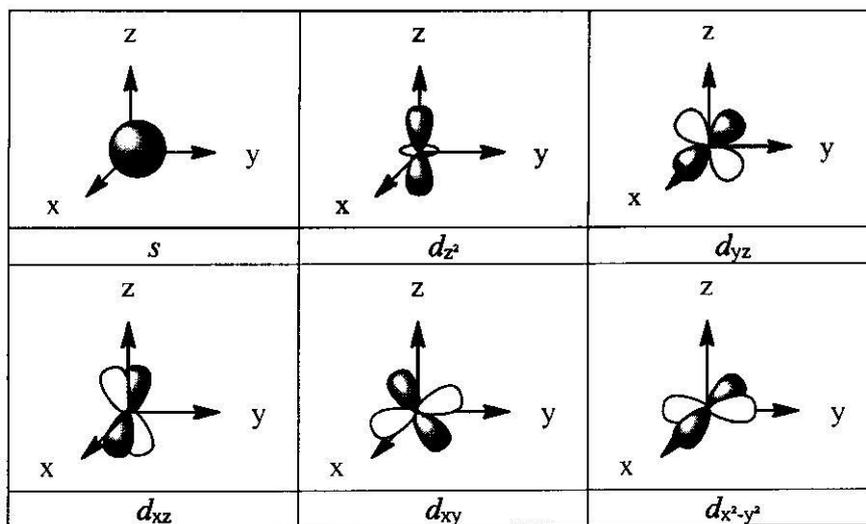
Each complex can store one molecule of dihydrogen. In 1 kg of dihydrogen, there are 500 mol of dihydrogen. Hence,  $m = 294.2 \text{ kg}$  of dehydrogenated complex are needed to store 1 kg of dihydrogen.

Once bound to 1 kg of  $\text{H}_2$ , the complex thus weighs  $m_{\text{Kubas}} = 295.2 \text{ kg}$

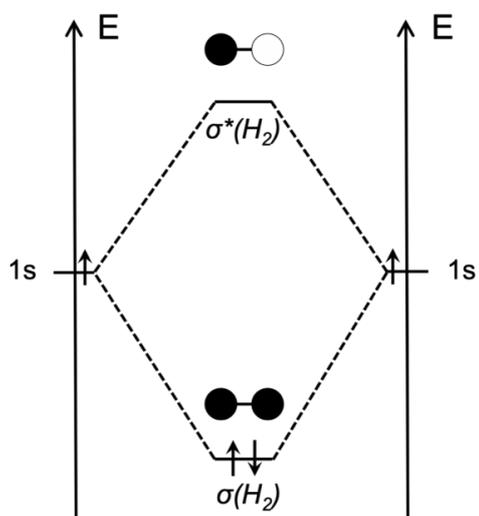
$$\rho_{\text{H}} = \frac{m_{\text{H}} \rho_{\text{Kubas}}}{m_{\text{Kubas}}} \quad \text{hence } \rho_{\text{H}} = 6.6 \times 10^{-6} \text{ kg m}^{-3}$$

**5.5**  $[\text{Xe}] (6s)^2(4f)^{14}(5d)^4$  so 6 valence electrons (4f layer is full)

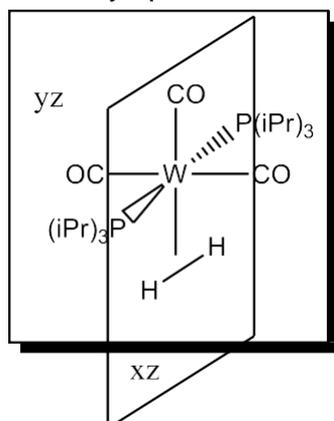
5.6



5.7



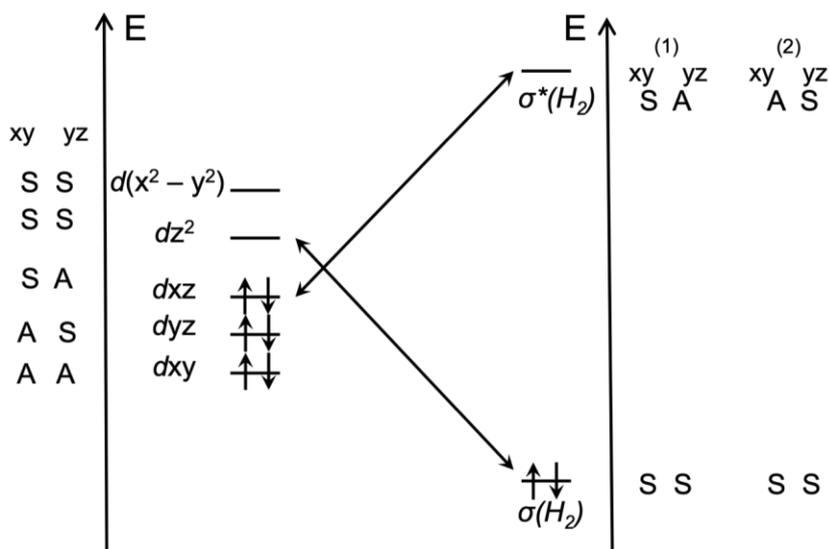
5.8 xz and yz planes



**5.9** An orbital is symmetric with respect to a symmetry element if it remains the same when the symmetry operation is applied. An orbital is antisymmetric with respect to a symmetry element if it changes to its opposite when the symmetry operation is applied. The results are gathered in the diagram below.

**5.10** As a general rule, interactions between two orbitals implying two electrons with the same symmetry lead to a stabilization inversely proportional to the difference of energy between the two orbitals. On the contrary, an interaction between two orbitals implying four electrons destabilizes the complex. Two orbitals have the same symmetry if all the symmetry elements are the same for each of the fragments. Moreover, all valence electrons have to be considered for tungsten to fill the d orbitals. Thus, 6 electrons for the metallic core and 2 electrons for hydrogen molecules are considered. One has to use Aufbau and Pauli principles. The result is depicted on the diagram below.

**5.11** For all conformations,  $d_{z^2}$  and  $d_{x^2-y^2}$  interacts with  $\sigma_{H_2}$ .  
For conformation (1), only  $d_{xz}$  interacts with  $\sigma^*_{H_2}$ .  
For conformation (2), only  $d_{yz}$  interacts with  $\sigma^*_{H_2}$ .



In conformation (1),  $\sigma^*$  is SA (symmetric for xz plane and antisymmetric for yz plane) and in conformation (2),  $\sigma^*$  is AS. So in conformation (1),  $\sigma^*$  interacts with  $d_{xz}$  (same symmetry SA), while in conformation (2) it interacts with  $d_{yz}$ . In conformation (1), the energies of the two interacting parts are the closest, thus leading to an enhanced stabilization.

### 5.12

$$\rho_H = \frac{m_H}{V} = \frac{n_H M_H}{V} = \frac{2 n_{\text{HCOOH}} M_H}{V} = \frac{2 m_{\text{HCOOH}} M_H}{M_{\text{HCOOH}} V} = \frac{2 \rho_{\text{HCOOH}} M_H}{M_{\text{HCOOH}}}$$

$$\rho_H = \frac{2 \times 1.22 \times 10^3}{(2 + 12 + 32)} = 53.0 \text{ kg m}^{-3}$$

The hydrogen density is higher in formic acid than for high pressure (500 bars) dihydrogen ( $31 \text{ kg m}^{-3}$ ) but lower than for cryogenic liquid hydrogen ( $70.85 \text{ kg m}^{-3}$ ). If one can extract efficiently  $\text{H}_2$  molecule from formic acid, it constitutes a good alternative to pure  $\text{H}_2$  storage.

### 5.13

$$\Delta_r H^\circ = \sum_{i=1}^N \nu_i \Delta_r H_i^\circ$$

$$\Delta_r H^\circ = -(-425.09) + (-393.51) + 0 = 31.58 \text{ kJ mol}^{-1}$$

$$\Delta_r S^\circ = \sum_{i=1}^N \nu_i S_{i,m}^\circ$$

$$\Delta_r S^\circ = -131.84 + 213.79 + 130.68 = 212.63 \text{ J mol}^{-1} \text{ K}^{-1}$$

### 5.14

$$\Delta_r G^\circ(T) = \Delta_r H^\circ - T \Delta_r S^\circ$$

$$\Delta_r G^\circ(T) = 31.58 - 0.213 \times 293 = -30.8 \text{ kJ mol}^{-1}$$

$$K^\circ = e^{-\frac{\Delta_r G^\circ}{RT}}$$

$$\text{Thus: } K^\circ = 3.1 \times 10^5$$

### 5.15

$$n(\text{N}_2) = n(\text{N}_2\text{O}) = pV / RT$$

$$n(\text{N}_2) = (1.013 \times 10^5 \times 1.0 \times 10^{-3}) / (8.314 \times 298.15) = 0.04 \text{ mol}$$

### 5.16

$$\text{LaNi}_5\text{H}_6: \rho_H = 118 \text{ kg m}^{-3} \quad \text{Mg}_2\text{NiH}_4: \rho_H = 95 \text{ kg m}^{-3}$$

## THEORETICAL PROBLEM 6

### Deacidification and desulfurization of natural gas

95% of dihydrogen is produced by steam reforming from natural gas. The corresponding reaction is analogous to the reaction with methane (reaction (1)), which is carried out at about 900 °C in presence of a catalyst.



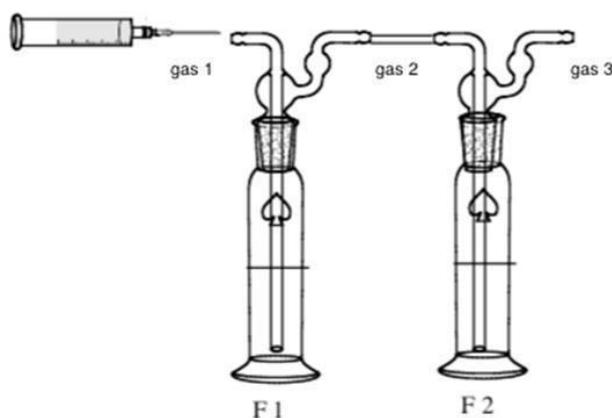
35% to 40% of the dihydrogen thus obtained is used in ammonia synthesis. However, one sulfur atom per 1000 nickel atoms is sufficient to poison the nickel-based catalyst. Since acidic gases ( $\text{H}_2\text{S}$  and  $\text{CO}_2$ ) contained in natural gas can also damage the pipelines, natural gas must be deacidified and desulfurized.

### Steam reforming from natural gas

- 6.1 Give the chemical reaction of steam reforming for an alkane  $\text{C}_n\text{H}_{2n+2}$ .  
 6.2 Calculate the equilibrium constant  $K^\circ$  of reaction (1) at 900 °C.

### Removal of acidic gases

A common method to remove acidic gases from natural gas is to use an amine solution. Some amine solutions can solubilize all the acidic gases, whereas others are selective due to kinetic differences between  $\text{H}_2\text{S}$  and  $\text{CO}_2$ . This process is modeled below, replacing the hydrocarbons by  $\text{N}_2$ . The following experiments aim to study deacidification with two different amines: monoethanolamine (MEA) and methyl-diethanolamine (MDEA), using the apparatus depicted below.



Flask F1 initially contains  $100 \text{ cm}^3$  of a  $0.5 \text{ mol dm}^{-3}$  amine solution ( $n_0 = 50 \text{ mmol}$ : large excess).

Flask F2 initially contains  $100 \text{ cm}^3$  of a  $0.5 \text{ mol dm}^{-3}$  NaOH solution (large excess too).

**Step. 1:** A gas sample (gas 1) is driven by  $\text{N}_2$  into a flask containing an amine solution; the outgoing gas (gas 2) bubbles in a second flask containing a NaOH solution; the final gas (gas 3) no longer contains acidic gas.

**Step. 2:** The liquid contents of each flask are titrated by an HCl solution ( $c_{\text{HCl}} = 1.0 \text{ mol dm}^{-3}$ ). Both pH and conductivity are recorded along the titration, so that two curves are obtained for each experiment (see below).

The sample of gas 1 contains  $n_1 \text{ mmol}$  of  $\text{CO}_2$ ,  $n_2 \text{ mmol}$  of  $\text{H}_2\text{S}$  and  $n_3 \text{ mmol}$  of  $\text{CH}_3\text{SH}$ . The first experiment is carried out with the primary amine MEA; the second one with the tertiary amine MDEA.

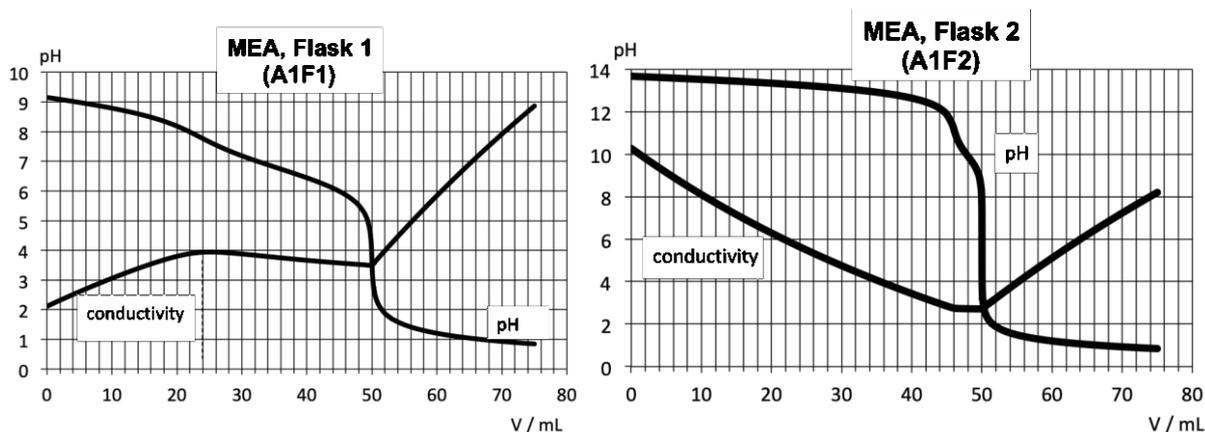
**6.3** Write down the thermodynamic quantitative ( $K^\circ \gg 1$ ) reactions between the different gases and (i) the amine solution and (ii) the NaOH solution.

We first study the experiment with MEA. There is no kinetic blockage with this amine.

**6.4** Determine the amount of each species in the solution (as a function of  $n_1$ ,  $n_2$  and  $n_3$ ) in the flask F1 before titration.

**6.5** Which chemical species is/are present in gas 2?

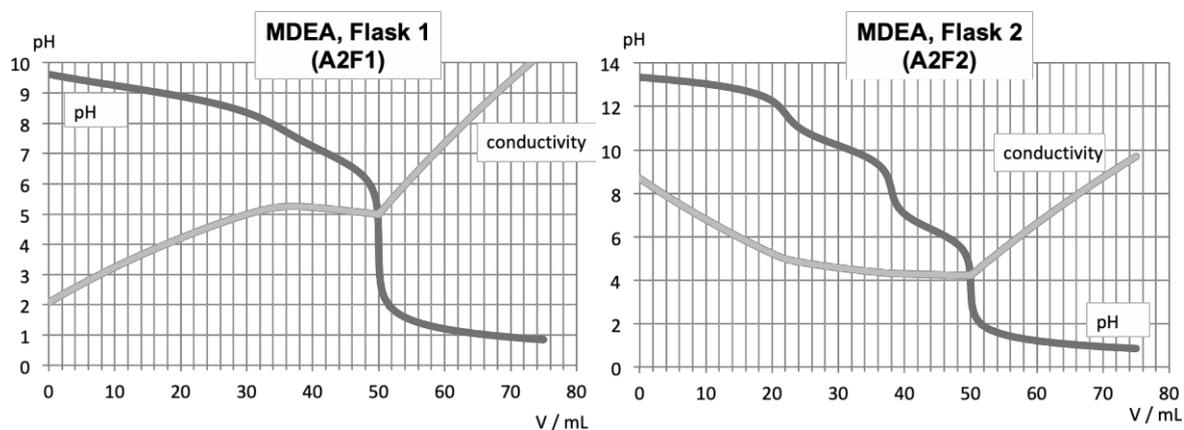
**6.6** Using the curves A1F1 and A1F2, determine (i)  $n_3$  and (ii) a relation between  $n_1$  and  $n_2$ .



MDEA reacts with only one of the acid species, the other reaction being kinetically blocked.

**6.7** Determine the amount of the reacting species using curve A2F1.

6.8 Using curve A2F2, determine if MDEA selectively reacts with  $\text{CO}_2$  or with  $\text{H}_2\text{S}$ . Calculate the two remaining  $n_1$  and  $n_2$ .



Data at 298 K:

	$\text{CO}_2(\text{g})$	$\text{H}_2\text{O}(\text{g})$	$\text{CH}_4(\text{g})$	$\text{C}_5\text{H}_{12}(\text{l})$	$\text{CO}(\text{g})$	$\text{CH}_3\text{CH}_3(\text{g})$	$\text{H}_2(\text{g})$
$\Delta_f H^\circ$ ( $\text{kJ mol}^{-1}$ )	-393.5	-241.8	-74.6	-178.4	-110.5	-84.0	0.0
$S_m^\circ$ ( $\text{JK}^{-1} \text{mol}^{-1}$ )	213.8	188.8	186.3	260.4	197.7	229.2	130.7

$\text{p}K_a$

Amines:  $\text{MEA}^+/\text{MEA}$ ;  $\text{MDEA}^+/\text{MDEA}$

$\text{p}K_a = 9.5$

$\text{CO}_2(\text{aq})$

$\text{p}K_{a1} = 6.4$ ;  $\text{p}K_{a2} = 10.3$

$\text{H}_2\text{S}$

$\text{p}K_{a1} = 7.0$ ;  $\text{p}K_{a2} = 13.0$

$\text{CH}_3\text{SH}$

$\text{p}K_a = 10.3$

**SOLUTION OF PREPARATORY PROBLEM 6**

6.2  $\Delta_r H^\circ = 205.9 \text{ kJ mol}^{-1}$ ;  $\Delta_r S^\circ = 214.7 \text{ J K}^{-1} \text{ mol}^{-1}$ ;  
 $\Delta_r G^\circ = -46 \text{ kJ mol}^{-1} = -RT \ln(K^\circ)$  then  $K^\circ = 112$

6.3 pH > 7:  $HCO_3^-$  and  $CO_3^{2-}$  can be encountered in solution

(i) with amine:

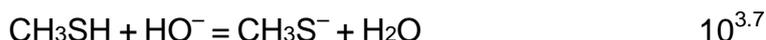


(ii) with NaOH:

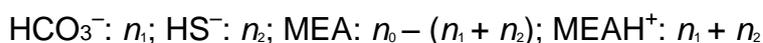
If, for kinetic reasons,  $CO_2$  and/or  $H_2S$  do not react with the amine:



in all cases:



6.4 With MEA, case (i) of question 5:



6.5  $CH_3SH$

6.6 A1F1, titration by  $H^+$  first:

$$V_{eq} = 24 \text{ cm}^3 \text{ hence } 24 \text{ mmol } n_0 - (n_1 + n_2) \text{ so: } n_1 + n_2 = 26 \text{ mmol}$$

A1F2:

between  $V_1$  and  $V_2$  ( $4 \text{ cm}^3$ ): titration of  $CH_3S^-$  ( $n_3$ )  $\rightarrow n_3 = 4 \text{ mmol}$

6.7 A2F1, titration by  $H^+$  first:

$$V_{eq} = 36 \text{ cm}^3 \text{ so } 36 \text{ mmol} = n_0 - n_i \quad (i = 1 \text{ or } i = 2) \text{ so: } n_i = 14 \text{ mmol}$$

6.8 Two possibilities:

- at half-equivalence of last step of A2F2, pH = 6.4. Hence gas 2 contains  $CO_2$ , so  $H_2S$  has reacted.

$$n_1 = 12 \text{ mmol et } n_2 = 14 \text{ mmol}$$

- more complete, considering both hypotheses:

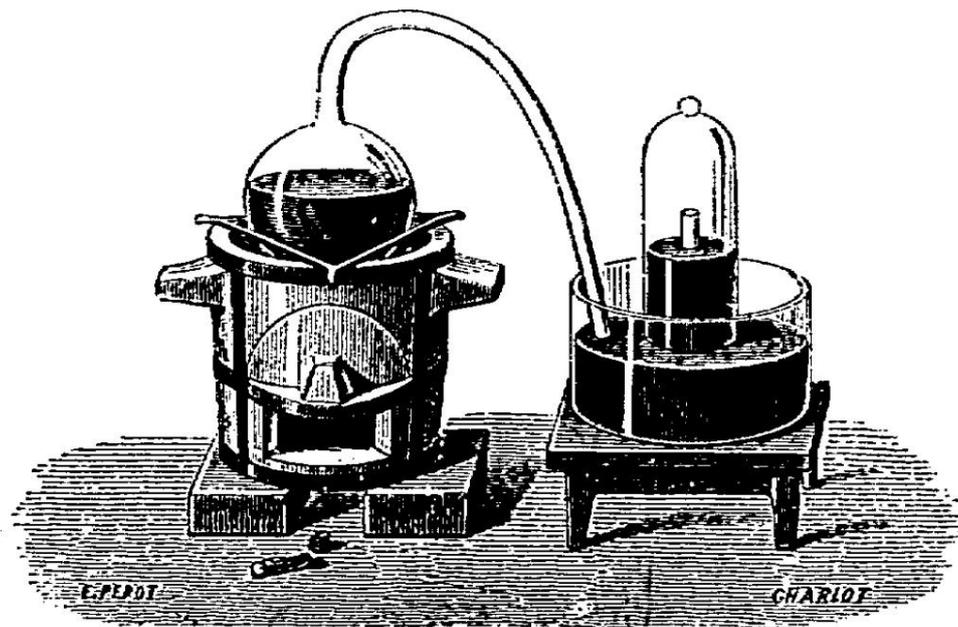
$CO_2 - H_2S - CH_3S$	Gas 1	$CO_2 - H_2S - CH_3S$
<b><math>CO_2</math> has reacted with MDEA</b>	<b>hypothesis</b>	<b><math>H_2S</math> has reacted with MDEA</b>
MDEA – MDEAH <sup>+</sup> – HCO <sub>3</sub> <sup>-</sup>	F1	MDEA – MDEAH <sup>+</sup> – HS <sup>-</sup>

CH <sub>3</sub> SH (4 mmol) – H <sub>2</sub> S (12 mmol)	Gas 2	CH <sub>3</sub> SH (4 mmol) – CO <sub>2</sub> (12 mmol)
HO <sup>-</sup> (22 mmol) – CH <sub>3</sub> S <sup>-</sup> (4 mmol)S <sup>2-</sup> (12 mmol)	F <sub>2</sub>	HO <sup>-</sup> (22 mmol) – CH <sub>3</sub> S <sup>-</sup> (4 mmol) CO <sub>3</sub> <sup>2-</sup> (12 mmol)
pK <sub>a</sub> = 14.0; 13.0; 10.3; 7.0 so V <sub>eq</sub> should be 34 – 38 – 50 cm <sup>3</sup>	V <sub>eq</sub>	pK <sub>a</sub> = 14.0; 10.3; 10.3; 6.4 so V <sub>eq</sub> should be 22 – 38 – 50 cm <sup>3</sup>
<b>22 cm<sup>3</sup> is lacking → false</b>	<b>validity of the hypothesis</b>	<b>22 cm<sup>3</sup> is present → true</b>

## THEORETICAL PROBLEM 7

### Lavoisier's experiment

In 1775, the French chemist A L de Lavoisier, father of modern chemistry, showed by an experiment that oxygen is one of the constituents of air.



Lavoisier's experiment (Bussard and Dubois, *Leçons élémentaires de chimie*, 1897)

The experiment he performed can be summarized as follows:

- he first introduced 122 g of mercury into a retort, the end of which was inside a cloche (see illustration above) containing 0.80 dm<sup>3</sup> of air and placed upside down on a tank containing mercury,
- then he heated the retort in such a way as to keep the mercury boiling for several days,
- after two days, the surface of the mercury began to get covered with red particles,
- after twelve days, the calcination of mercury seemed to have finished because the thickness of the particle layer was no longer increasing, he then stopped heating,
- after cooling, he observed the following:
  - only 0.66 dm<sup>3</sup> of “air” subsisted under the cloche,
  - this remaining “air” could extinguish a candle or kill a mouse,

- 2.3 g of red particles had been formed. He called them “rust of mercury”.

The table below shows thermodynamic data at 298 K of some mercury-based compounds and dioxygen.

Compound	$\Delta_f H^\circ$ (kJ mol <sup>-1</sup> )	$S_m^\circ$ (J K <sup>-1</sup> mol <sup>-1</sup> )
HgO(s) (red)	-90	70
HgO(s) (yellow)	-87	70
Hg <sub>2</sub> O(s)	-90	
Hg(l)		75
Hg(g)	60	175
O <sub>2</sub> (g)		200

**7.1** Standard molar entropy  $S_m^\circ$  of mercurous oxide Hg<sub>2</sub>O has not been experimentally determined. Choose the value that seems closest to reality:

- 0 J K<sup>-1</sup> mol<sup>-1</sup>
- 100 J K<sup>-1</sup> mol<sup>-1</sup>
- 200 J K<sup>-1</sup> mol<sup>-1</sup>
- 300 J K<sup>-1</sup> mol<sup>-1</sup>

**7.2** Write down equations for the formation of HgO(s) and Hg<sub>2</sub>O(s).

**7.3** It is assumed that only the liquid state of mercury reacts, and that either red or yellow HgO can be formed. Using the value chosen in 1, calculate the equilibrium constants  $K^\circ$  at 298 K for a) red HgO, b) yellow HgO and c) Hg<sub>2</sub>O.

The red and yellow forms of the mercury (II) oxide have, in particular, very similar standard potentials and quasi-equal magnetic susceptibilities. However, the yellow form has larger structural defects than the red form. The red mercury oxide can be obtained by a slow pyrolysis of Hg(NO<sub>3</sub>)<sub>2</sub>, while the yellow oxide can be obtained by precipitation of aqueous mercury (II) ions in an alkaline medium.

**7.4** Write the chemical equations of these processes.

Lavoisier's experiment is similar to pyrolysis because of the use of heating and the absence of an aqueous medium, which may explain the formation of red oxide. In the following, we will consider this one as the only product of the reaction.

- 7.5** Calculate the theoretical amount of each species in the final state of Lavoisier's reaction.
- 7.6** Calculate the theoretical mass of mercury (II) oxide in the final state.
- 7.7** Choose an explanation to the difference from the mass obtained by Lavoisier.
- Other oxides of the type  $\text{HgO}_x$  ( $x > 1$ ) are obtained.
  - The yield is not maximum.
  - Lavoisier measured volumes at  $T < 25$  °C.
  - Mercury rust also contains nitride  $\text{Hg}_x\text{N}_y$ .
-

**SOLUTION OF PREPARATORY PROBLEM 7**

7.1 Correct statement:  $100 \text{ J K}^{-1} \text{ mol}^{-1}$

Since  $\text{Hg}_2\text{O}$  is a solid, its  $S_m^\circ$  should be smaller than that of gases like  $\text{O}_2$  ( $200 \text{ J K}^{-1} \text{ mol}^{-1}$ ). In addition, the standard molar entropy of a compound can be  $0 \text{ J K}^{-1} \text{ mol}^{-1}$  only in a perfect crystalline state at  $0 \text{ K}$ , which is not the case here ( $298 \text{ K}$ ).

7.2  $\text{HgO}$  formation:  $\text{Hg(l)} + 1/2 \text{ O}_2(\text{g}) = \text{HgO(s)}$

$\text{Hg}_2\text{O}$  formation:  $2 \text{ Hg(l)} + 1/2 \text{ O}_2(\text{g}) = \text{Hg}_2\text{O(s)}$

7.3 a)  $\text{HgO}$  (red)

Calculation:

$$\Delta_r H^\circ = \Delta_f H^\circ(\text{HgO(s)}) = -90 \text{ kJ mol}^{-1} \text{ (because } \Delta_f H^\circ(\text{Hg(l)}) = 0 \text{ kJ mol}^{-1}\text{)}$$

$$\Delta_r S^\circ = S_m^\circ(\text{HgO(s)}) - S_m^\circ(\text{Hg(l)}) - 1/2 S_m^\circ(\text{O}_2(\text{g})) = -105 \text{ J K}^{-1} \text{ mol}^{-1}$$

$$\Delta_r G^\circ = \Delta_r H^\circ - 298 \times \Delta_r S^\circ = -58.7 \times 10^3 \text{ J mol}^{-1}$$

$$K^\circ = \exp(-\Delta_r G^\circ / RT) = 1.95 \times 10^{10}$$

b)  $\text{HgO}$  (yellow)

Calculation:

$$\Delta_r H^\circ = \Delta_f H^\circ(\text{HgO(s)}) = -87 \text{ kJ mol}^{-1}$$

$$\Delta_r S^\circ = S_m^\circ(\text{HgO(s)}) - S_m^\circ(\text{Hg(l)}) - 1/2 S_m^\circ(\text{O}_2(\text{g})) = -105 \text{ J K}^{-1} \text{ mol}^{-1}$$

$$\Delta_r G^\circ = \Delta_r H^\circ - 298 \times \Delta_r S^\circ = -55.7 \times 10^3 \text{ J mol}^{-1}$$

$$K^\circ = 5.83 \times 10^9$$

c)  $\text{Hg}_2\text{O}$

Calculation:

$$\Delta_r H^\circ = \Delta_f H^\circ(\text{Hg}_2\text{O(s)}) = -90 \text{ kJ mol}^{-1}$$

$$\Delta_r S^\circ = S_m^\circ(\text{Hg}_2\text{O(s)}) - 2 \times S_m^\circ(\text{Hg(l)}) - 1/2 S_m^\circ(\text{O}_2(\text{g})) = -150 \text{ J K}^{-1} \text{ mol}^{-1}$$

$$\Delta_r G^\circ = \Delta_r H^\circ - 298 \times \Delta_r S^\circ = -45.3 \times 10^3 \text{ J mol}^{-1}$$

$$K^\circ = 8.72 \times 10^7$$

7.4  $\text{HgO}$  (red):  $\text{Hg(NO}_3)_2(\text{s}) = \text{HgO(s)} + 2 \text{ NO}_2(\text{g}) + \text{O}_2(\text{g})$

$\text{HgO}$  (yellow):  $\text{Hg}^{2+}(\text{aq}) + 2 \text{ HO}^-(\text{aq}) = \text{HgO(s)} + \text{H}_2\text{O(l)}$

7.5  $n(\text{Hg,i}) = 122 / 200.6 = 6.08 \times 10^{-1} \text{ mol}$

At 25 °C,  $V_m = 24 \text{ dm}^3 \text{ mol}^{-1}$  so  $0.80 \text{ dm}^3$  of air corresponds to  $0.0333 \text{ mol}$  of gas molecules.  $\text{O}_2$  constitutes 20% of air, so:

$$n(\text{O}_2) = 0.0333 \times 0.20 = 6.7 \times 10^{-3} \text{ mol}$$

The reaction is quantitative and  $\text{O}_2$  is the limiting reagent therefore  $\xi_{\max} = 6.7 \times 10^{-3} \text{ mol}$ .

$$n(\text{Hg}) = n(\text{Hg},i) - 2 \xi_{\max} = 6.08 \times 10^{-1} - (2 \times 6.7 \times 10^{-3}) = 5.95 \times 10^{-1} \text{ mol}$$

$$n(\text{O}_2) = 0 \text{ mol (limiting)}$$

$$n(\text{HgO}) = 2 \xi_{\max} = 1.3 \times 10^{-2} \text{ mol}$$

**7.6**  $M(\text{HgO}) = 200.6 + 16.0 = 216.6 \text{ g mol}^{-1}$

$$m(\text{HgO}) = n(\text{HgO}) \times M(\text{HgO}) = 2.8 \text{ g}$$

**7.7** Correct statement: The yield is not maximum.

Relative difference:  $(2.8 - 2.3) / 2.8 = 18\%$ , which is a rather high discrepancy.

Lavoisier did not reach the maximum yield (maybe for kinetic reasons?).

The other statements are not satisfactory as they would explain an apparent yield higher than expected.

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## THEORETICAL PROBLEM 8

### Which wine is it? Blind tasting challenge

Fermentation of grape juice is a crucial step in the production of wine. During this biochemical process, sugars accumulated in grapes are converted into ethanol. This process is performed by microorganisms that are naturally present in the environment, and in particular, on the surface of fruits. One of the sugars converted by microorganisms is glucose. Action of the microorganisms will not be considered in the rest of the problem.

- 8.1** Write a balanced equation for the transformation of solid glucose ( $C_6H_{12}O_6(s)$ ) into liquid ethanol ( $C_2H_6O(l)$ ) and gaseous carbon dioxide. Does this reaction require the presence of dioxygen? (Yes/No)
- 8.2** Calculate the standard enthalpy, the standard entropy and the standard Gibbs free energy associated with this reaction at 298 K. Does this reaction generate heat? (Yes/No)

Conversion of glucose into carbon dioxide and water is called cellular respiration.

- 8.3** Write a balanced equation for the transformation of glucose into carbon dioxide and water. Does this reaction require the presence of dioxygen? (Yes/No)

The concentration of ethanol can vary a lot from one wine to another. Some Riesling wines from Germany (named “kabinett”) only contain 7–8 vol% of ethanol, while Châteauneuf du Pape wines (Rhône Valley, France) usually contain about 14 vol% of ethanol (“vol %” means “percent of alcohol by volume” and is defined as the ratio between the volume of ethanol contained in wine and the total volume of wine, multiplied by 100, at 298 K). It is thus very important to control the concentration of ethanol in grape juice during fermentation. To determine the concentration of ethanol in a wine, the following protocol was used: wine X is diluted 50 times with distilled water. The aqueous solution of wine is added dropwise to a  $100\text{ cm}^3$  aqueous solution of potassium dichromate ( $5.0 \times 10^{-3}\text{ mol dm}^{-3}$ ) containing sulfuric acid ( $0.1\text{ mol dm}^{-3}$ ). The volume at the equivalence point is  $15\text{ cm}^3$ .

- 8.4** Write a balanced equation for the oxidation reaction of ethanol by dichromate anions.
- 8.5** Calculate the equilibrium constant of this reaction. Can it be used to determine the concentration of ethanol in wine? (Yes/No)
- 8.6** Calculate the pH of the solution of potassium dichromate and sulfuric acid before starting the titration. Here, sulfuric acid can be treated as a strong monoacid.

- 8.7** Calculate the pH of the solution of potassium dichromate and sulfuric acid at the equivalence point (sulfuric acid is still considered to be a strong monoacid). Is it possible to determine the equivalence point using the pH change of the solution? (Yes/No)
- 8.8** Calculate the concentration (in % vol) of ethanol contained in wine X. Is this wine a German Riesling or a French Châteauneuf du Pape?

**Data:**

Thermodynamic data (at 298 K):

	CO <sub>2</sub> (g)	Glucose(s)	Ethanol(l)
$\Delta_f H^\circ$ (kJ mol <sup>-1</sup> )	-393.5	-1274	-277.0
$S^\circ_m$ (J mol <sup>-1</sup> K <sup>-1</sup> )	213.6	212.1	160.7

	Cr <sub>2</sub> O <sub>7</sub> <sup>2-</sup> /Cr <sup>3+</sup>	CH <sub>3</sub> COOH/CH <sub>3</sub> CH <sub>2</sub> OH
$E^\circ$ (V)	1.33	0.19

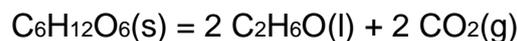
Density of ethanol at 293 K: 0.79 g cm<sup>-3</sup>

**SOLUTION OF PREPARATORY PROBLEM 8**

8.1 Half-reactions:



Hence:



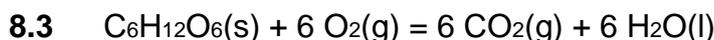
No, this reaction does not require the presence of dioxygen.

$$\begin{aligned} 8.2 \quad \Delta_r H^\circ(298 \text{ K}) &= 2 \Delta_f H^\circ(\text{C}_2\text{H}_6\text{O}(\text{l})) + 2 \Delta_f H^\circ(\text{CO}_2(\text{g})) - \Delta_f H^\circ(\text{C}_6\text{H}_{12}\text{O}_6(\text{s})) = \\ &= -67.0 \text{ kJ mol}^{-1} \end{aligned}$$

$$\begin{aligned} \Delta_r S^\circ(298 \text{ K}) &= 2 S^\circ_m(\text{C}_2\text{H}_6\text{O}(\text{l})) + 2 S^\circ_m(\text{CO}_2(\text{g})) - S^\circ_m(\text{C}_6\text{H}_{12}\text{O}_6(\text{s})) = \\ &= 536.5 \text{ J mol}^{-1} \text{ K}^{-1} \end{aligned}$$

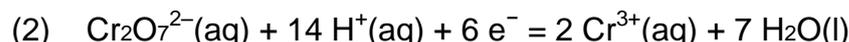
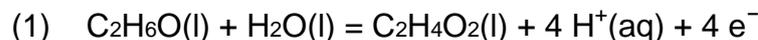
$$\Delta_r G^\circ(298 \text{ K}) = \Delta_r H^\circ(298 \text{ K}) - T \Delta_r S^\circ(298 \text{ K}) = -226.9 \text{ kJ mol}^{-1}$$

Yes, this reaction generates heat because  $\Delta_r H^\circ < 0$ .



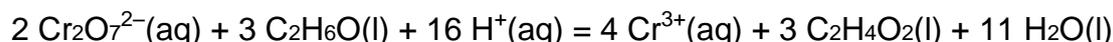
Yes, this reaction requires the presence of dioxygen.

8.4 Half-reactions:



Hence:

$$2 \times (2) + 3 \times (1):$$



$$8.5 \quad \Delta_r G^\circ(\text{Cr}_2\text{O}_7^{2-}/\text{Cr}^{3+}) = -6 FE^\circ(\text{Cr}_2\text{O}_7^{2-}/\text{Cr}^{3+})$$

$$\Delta_r G^\circ(\text{C}_2\text{H}_4\text{O}_2/\text{C}_2\text{H}_6\text{O}) = -4 FE^\circ(\text{C}_2\text{H}_4\text{O}_2/\text{C}_2\text{H}_6\text{O})$$

$$\text{Hence } \Delta_r G^\circ = 12F (E^\circ(\text{C}_2\text{H}_4\text{O}_2/\text{C}_2\text{H}_6\text{O}) - E^\circ(\text{Cr}_2\text{O}_7^{2-}/\text{Cr}^{3+})) = -RT \ln K^\circ$$

$$\text{And } K^\circ = 10^{231}$$

$K^\circ \gg 1$ , so the reaction can be used to determine the concentration of alcohol in wine.

$$8.6 \quad \text{pH} = -\log[\text{H}_3\text{O}^+] = 1$$

$$\begin{aligned} 8.7 \quad \text{At the equivalence point, } n(\text{H}_3\text{O}^+) &= n_0(\text{H}_3\text{O}^+) - 8 V_0 \times [\text{Cr}_2\text{O}_7^{2-}] = \\ &= 1 \times 10^{-2} - 8 \times 1.00 \times 10^{-1} \times 5 \times 10^{-3} = 6 \times 10^{-3} \text{ mol.} \end{aligned}$$

Hence,  $\text{pH} = -\log[\text{H}_3\text{O}^+] = 1.3$  taking into account the dilution.

No, because the pH does not change significantly along the reaction course.

**8.8** At the equivalence point,

$$\frac{n(\text{C}_2\text{H}_6\text{O})}{3} = \frac{n(\text{Cr}_2\text{O}_7^{2-})}{2}, \text{ i. e. } \frac{c(\text{C}_2\text{H}_6\text{O}) \times V_e}{3} = \frac{c(\text{Cr}_2\text{O}_7^{2-}) \times V(\text{Cr}_2\text{O}_7^{2-})}{2}$$

where  $c(\text{C}_2\text{H}_6\text{O})$  is the concentration of alcohol in the diluted wine.

$c(\text{C}_2\text{H}_6\text{O}) = 0.05 \text{ mol dm}^{-3}$  so the concentration of ethanol in the non-diluted wine is  $2.5 \text{ mol dm}^{-3}$ .

In terms of mass concentration:  $c_m(\text{C}_2\text{H}_6\text{O}) = c(\text{C}_2\text{H}_6\text{O}) \times M(\text{C}_2\text{H}_6\text{O}) = 115 \text{ g dm}^{-3}$ .

The percentage of alcohol per volume of this wine is thus:

$$\frac{c_m(\text{C}_2\text{H}_6\text{O})}{\rho(\text{etanol})} \times 100 = \frac{115}{0.79 \times 10^3} \times 100 = 14.6 \%$$

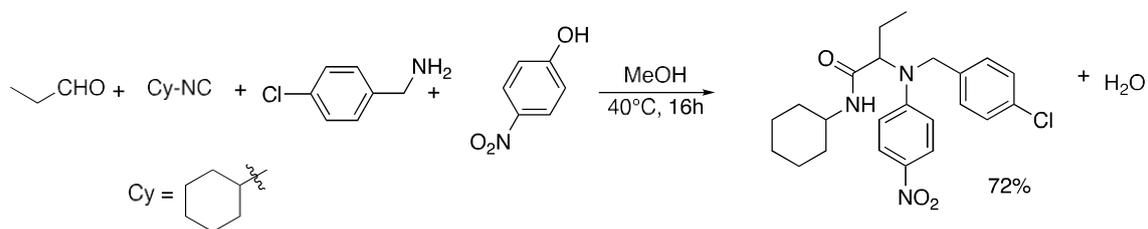
Wine X is thus a Châteauneuf du Pape.

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## THEORETICAL PROBLEM 9

### Nitrophenols: synthesis and physical properties

A multicomponent reaction is a reaction where three or more reactants react together to form a product involving all the reactants. For instance, the Ugi-Smiles coupling has been studied by the French duo L. El-Kaïm and L. Grimaud in 2005. During the past decade, this coupling has been used for the synthesis of various heterocyclic compounds using various post-condensations. This reaction involves an aldehyde, an amine, an isocyanide, and activated phenols, such as nitrophenols.

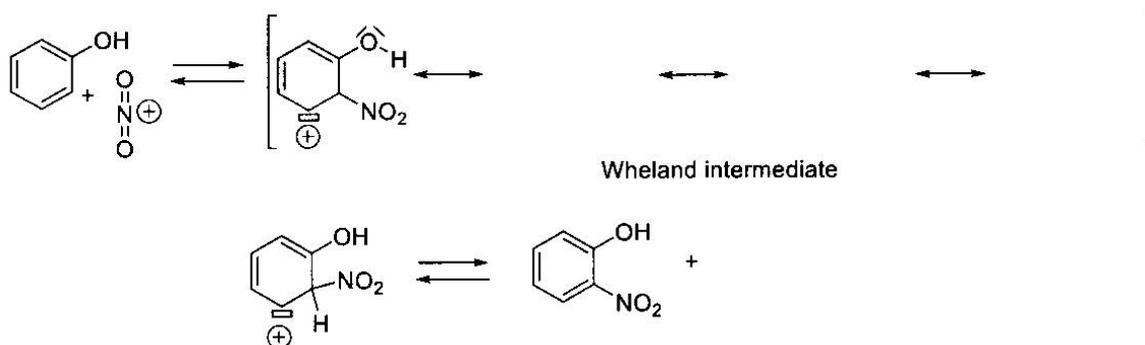


In this problem, the synthesis of nitrophenols is examined and some physical properties of the 4-nitrophenol are studied.

### Synthesis of nitrophenols

In a three-neck reaction flask, sodium nitrate (20.0 g, 235 mmol) is dissolved in water (50.0 cm<sup>3</sup>). After cooling the solution in an ice bath, concentrated sulfuric acid (H<sub>2</sub>SO<sub>4</sub>, 14.5 cm<sup>3</sup>) is added in small portions. A solution of phenol (12.5 g in 5.00 cm<sup>3</sup> of water, 133 mmol) is then added slowly under vigorous stirring. The temperature is kept below 20 °C and the solution is stirred for 2 hours. The liquor is then distilled and a first yellow compound, the 2-nitrophenol, is obtained (46.5 mmol). The residue in the distillation flask is cooled and a 2.00 mol dm<sup>-3</sup> solution of sodium hydroxide (NaOH) is used to adjust the pH to 8-9 and charcoal is added (2.00 g). The mixture is then warmed to reflux for 5 minutes and immediately filtered. After distillation of 30 cm<sup>3</sup> of water, the concentrated mixture is cooled down in an iced bath. The obtained crystals are then dissolved and boiled into 50.0 cm<sup>3</sup> of hydrochloric acid (HCl, 3.7%) before filtration. The 4-nitrophenol is then obtained (20.0 mmol).

**9.1** A partial scheme for the formation of the 2-nitrophenol starting from the nitronium ion NO<sub>2</sub><sup>+</sup> is proposed below. Draw the missing intermediates and products.



**9.2** Give at least two products other than 2-nitrophenol and 4-nitrophenol that could explain the low yield.

Various characterizations of the 2-nitrophenol and 4-nitrophenol were performed:  $^1\text{H}$  NMR, and measurement of their melting point, boiling point and solubility. The results were attributed anonymously with two labels: **A** and **B**.

$^1\text{H}$  NMR of **A** and **B**:

**A** ( $\delta$ , ppm in  $\text{CDCl}_3$ ): 10.6 (large s, 1H), 8.1 (d,  $J = 8.4$  Hz, 1H), 7.6 (dd,  $J = 8.5, 8.4$  Hz, 1H), 7.2 (d,  $J = 8.4$  Hz, 1H), 7.0 (dd,  $J = 8.5, 8.4$  Hz, 1H)

**B** ( $\delta$ , ppm in  $\text{DMSO-d}^6$ ): 11.1 (large s, 1H), 8.1 (d,  $J = 9.1$  Hz, 2H), 7.0 (d,  $J = 9.1$  Hz, 2H)

Properties	m.p.	b.p.	Solubility in water (298 K)
<b>A</b>	44 °C	214 °C	2 g dm <sup>-3</sup>
<b>B</b>	113 - 115 °C	--	15 dm <sup>-3</sup>

**9.3** Using the NMR data, determine which product (2-nitrophenol or 4-nitrophenol) corresponds to **A** and **B**. To justify your answer, interpret the NMR chemical shifts of the products.

**9.4** Which interaction(s) between B and water can explain the higher solubility in comparison to A? Choose the correct answer(s).

- Intermolecular hydrogen bonds
- Intramolecular hydrogen bond
- Electrostatic interaction
- Van der Waals interactions
- Covalent bond

To check the purity of **A** and **B**, a Thin Layer Chromatography (TLC) on silica was performed. The eluent is a mixture of pentane/diethylether (7:3 in volume). After visualization of the TLC using a UV light, the retention factor was calculated for the two spots (0.4 and 0.9).

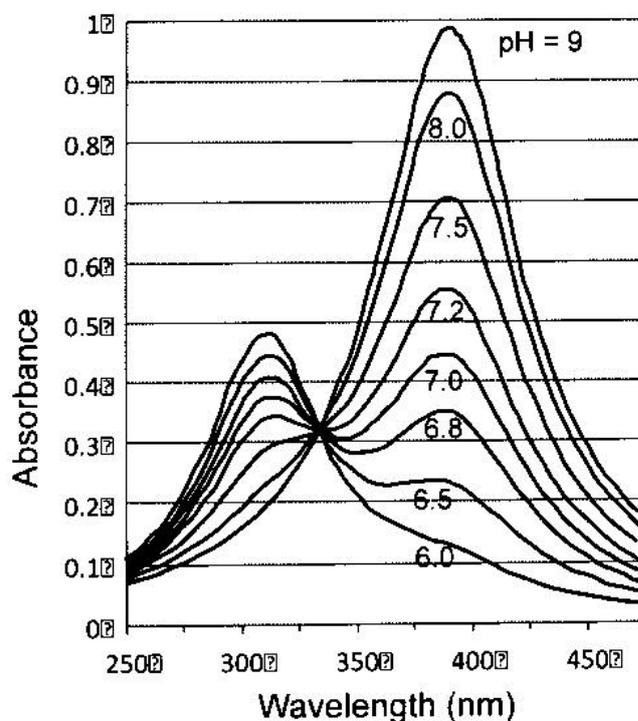
**9.5** Choose the correct statement(s).

A has a  lower or  higher retardation factor ( $R_f$ ) than B on the TLC because:

- A develops intermolecular hydrogen bonds with the silica.
- A develops an intramolecular hydrogen bond.
- B develops intermolecular hydrogen bonds with the silica.
- B develops an intramolecular hydrogen bond.

### Characterization of the 4-nitrophenol

**Absorbance.** The absorbance (A) versus the wavelength at various pH is given in the figure below. Absorbance beyond 450 nm is negligible. The two maxima of the absorbance are at 310 nm and 390 nm, respectively.



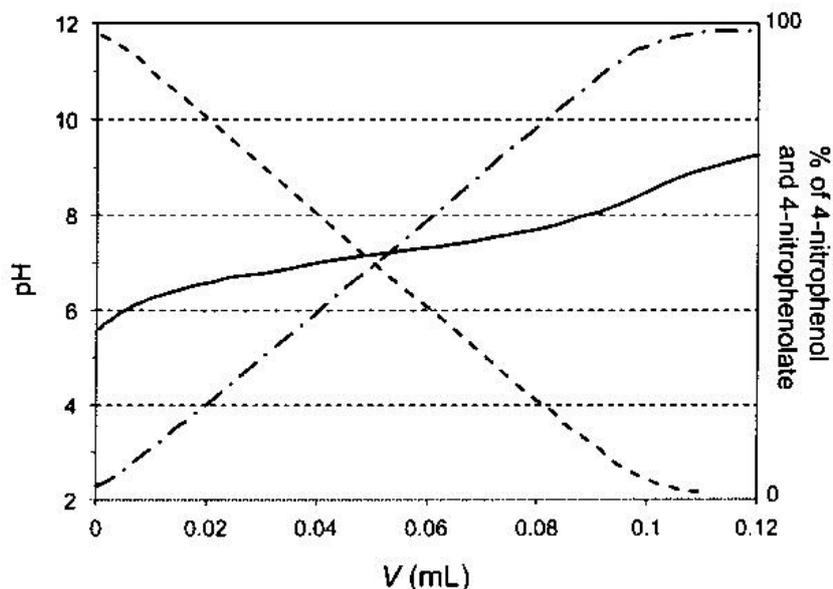
**9.6** Which is the color of a solution of 4-nitrophenol in neutral water? Choose the correct answer.

- Blue     Green     Pink     Purple     Red     Yellow

9.7 Choose the correct answer.

- 4-nitrophenol has a longer absorption wavelength than its conjugated base because its conjugation is more important.
- 4-nitrophenol has a longer absorption wavelength than its conjugated base because its conjugation is less important.
- 4-nitrophenol has a shorter absorption wavelength than its conjugated base because its conjugation is more important.
- 4-nitrophenol has a shorter absorption wavelength than its conjugated base because its conjugation is less important.

**Determination of the  $pK_a$ .** A solution of  $10 \text{ cm}^3$  of 4-nitrophenol at  $c = 1.00 \cdot 10^{-4} \text{ mol dm}^{-3}$  was titrated by a solution of sodium hydroxide ( $\text{NaOH}$ ,  $c = 1.00 \cdot 10^{-2} \text{ mol dm}^{-3}$ ). The variation of the pH as a function of the volume of  $\text{NaOH}$  is calculated and given in the figure below. Dashed curves represent the fraction of 4-nitrophenol and 4-nitrophenolate, expressed in percentage on the right side. The pH is indicated as a solid line (scale on the left side).



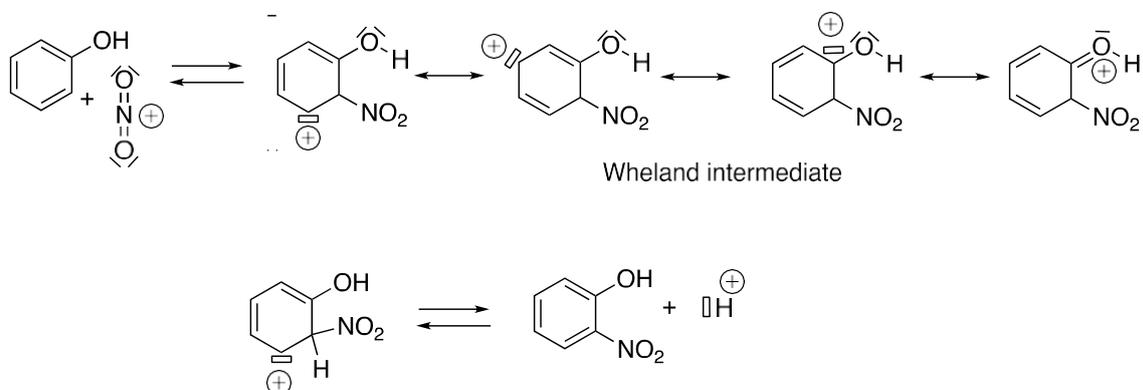
9.8 Assign each curve to 4-nitrophenol or 4-nitrophenolate.

9.9 Estimate the  $pK_a$  of the 4-nitrophenol.

According to the theoretical curve, the pH jump is expected to be small, which makes the experimental titration data difficult to analyze.

**9.10** Which alternative method(s) can be used for the titration of 4-nitrophenol? Choose the correct answer(s).

- UV-Visible spectroscopy
  - Potentiometry
  - NMR
  - Conductometry
-

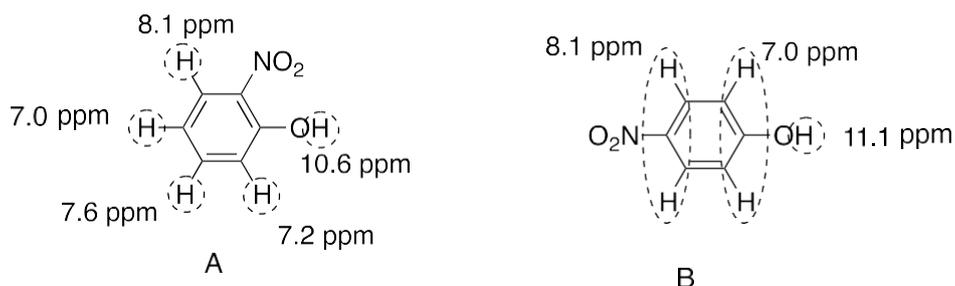
**SOLUTION OF PREPARATORY PROBLEM 9****9.1**

**9.2** 2,6-dinitrophenol, 2,4-dinitrophenol, 2,4,6-trinitrophenol are possible products due to polynitration. 3-nitrophenol is also a possible side-product but it is not favored because the corresponding Wheland intermediate is less stable.

**9.3 A:** 2-nitrophenol, **B:** 4-nitrophenol

The easiest assignment is for the 4-nitrophenol **B**. Indeed, due to the symmetry of the molecule, it presents two doublets with an integration of 2 protons. To assign the shifts, we have to keep in mind that the OH group is an electro-donating group and increases the density in ortho position, which explains a lower shift. On the contrary, NO<sub>2</sub> is an electron-withdrawing group, which explains a higher shift.

For **A**, the hydrogens will all have a different shift. The two singlets correspond to hydrogens in ortho position of OH and NO<sub>2</sub> groups. The assignment can be explained using the same argument as before. Other protons are also assigned using the electronic effects too. In para position of the OH (NO<sub>2</sub>) group, the density is more (less) important, which decreases (increases) the NMR displacement of the corresponding proton.



**9.4** Correct answer: Intermolecular hydrogen bonds

**B** can develop hydrogen bonds with water molecules, which increases its solubility, while **A** develops more intramolecular hydrogen bonds.

**9.5** Correct statements:

**A** has a higher retardation factor ( $R_f$ ) than **B** on the TLC because:

**A** develops an intramolecular hydrogen bond.

**B** develops intermolecular hydrogen bonds with the silica.

Due to its intramolecular hydrogen bond, the 2-nitrophenol exhibits a higher migration because fewer interactions are developed with the silica. On the contrary, **B** develops hydrogen bonds with the silica and is retained.

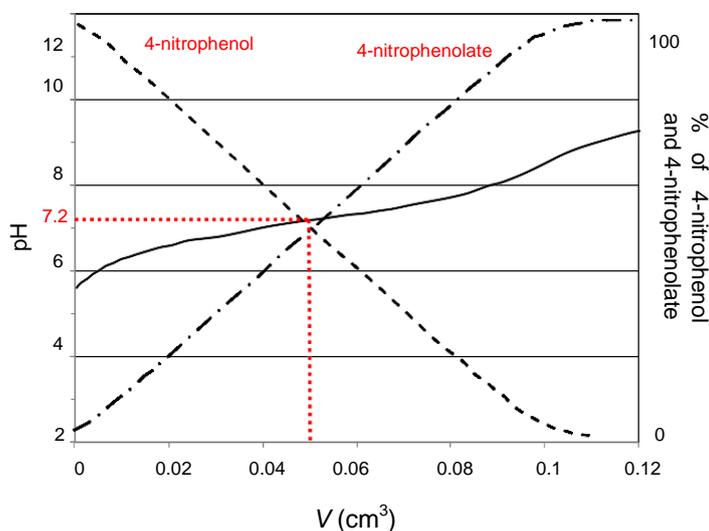
**9.6** Correct answer: Yellow

At  $\text{pH} = 7$ , the absorbance in the visible light is important around 390 nm, which corresponds to purple. The complementary color is yellow.

**9.7** Correct answer:

4-nitrophenol has a shorter absorption wavelength than its conjugated base because its conjugation is less important.

**9.8** Assignment of spectra on figure:



**9.9**  $\text{pH} = \text{p}K_a$  when  $[\text{acid}] = [\text{basis}]$ . Using the figure above, we find  $\text{p}K_a = 7.2$ .

**9.10** Correct answers:

UV-Visible spectroscopy, NMR, conductometry.

## THEORETICAL PROBLEM 10

### French stone flower

Laumontite is a natural zeolite, a hydrated calcium aluminosilicate of formula  $(\text{CaO})_x(\text{A})_y(\text{B})_z \cdot y\text{H}_2\text{O}$ , where **A** and **B** are oxides. It dehydrates in dry air and becomes then very brittle. Due to this property, it was first called *zéolithe efflorescente* (stone flower). But then the mineral was named after the French mineralogist Gillet de Laumont who discovered it in 1785.



*Laumontite from Espira-de-l'Agly deposit, France (© Christian Berbain)*

Laumontite crystallizes into a monoclinic crystal system of parameters:  $a = 1.49 \text{ nm}$ ,  $b = 1.37 \text{ nm}$ ,  $c = 0.76 \text{ nm}$ ,  $\alpha = \gamma = 90^\circ$ ,  $\beta = 112^\circ$ ,  $Z = 4$ . Its density is  $\rho = 2.17 \text{ g cm}^{-3}$ . After heating in dry air, the mineral loses 15.3% of its mass, and no further mass change is then observed.

**10.1** Calculate the stoichiometry  $y$  of the water crystallized in laumontite.

*Hint 1:* The volume of a monoclinic unit cell is  $V = abc \times \sin \beta$ .

*Hint 2:* The mass  $m$  of  $4 (\text{CaO})_x(\text{A})_y(\text{B})_z \cdot y \text{H}_2\text{O}$  in one unit cell is:  $m = 4 M/N_A$ , where  $M$  is the molar mass of the mineral and  $N_A$  Avogadro's constant. Also,  $m = \rho V$ , where  $\rho$  is the density and  $V$  the volume of a unit cell.

To determine the composition of this mineral, 0.500 g of laumontite was placed in a crucible and  $2 \text{ cm}^3$  of concentrated hydrochloric acid were then added to it and heated up to  $90^\circ \text{C}$ . The sample was then washed with distilled water and dried at  $120^\circ \text{C}$  for a few hours. The insoluble residue was placed in another crucible ( $m_0 = 14.375 \text{ g}$ ). It was then calcined at a temperature of  $900^\circ \text{C}$  to constant weight. The final mass of the crucible and its content was found to be  $m_1 = 14.630 \text{ g}$ . The residue is a pure binary compound that does not contain chlorine atoms.

**10.2** Determine the nature of **A** and **B** and the values of  $x$  and  $z$ .

Some samples of laumontite are orange. This coloration is caused by the presence of an impurity, an element E that partly substitutes calcium, yielding the compound of formula:



The dissolution of a 0.500 g sample in nitric acid led to the formation of the same precipitate as before. The filtrate was separated. When a few drops of  $\text{NH}_4\text{SCN}$  are added to the filtrate, the solution turns bright red. The filtrate was then neutralized with an excess of a concentrated aqueous solution of ammonia ( $\text{NH}_3$ ) until complete formation of a precipitate. The latter was filtered, washed with water and redissolved in sulfuric acid ( $\text{H}_2\text{SO}_4$ ,  $c = 1 \text{ mol dm}^{-3}$ ) followed by the addition of an excess of zinc powder. The excess of metallic zinc was removed by filtration and the solution was then transferred to a  $100.0 \text{ cm}^3$  volumetric flask and brought up to volume with distilled water. A  $20.0 \text{ cm}^3$  aliquot was transferred into a titration flask and potentiometrically titrated (using a saturated calomel electrode (SCE) as a reference) by  $5.15 \text{ cm}^3$  of a solution of  $\text{Ce}(\text{SO}_4)_2$  ( $c = 2.00 \text{ mmol dm}^{-3}$ ) prepared by a solution of  $\text{Ce}(\text{SO}_4)_2$  in  $\text{H}_2\text{SO}_4$  with a concentration of  $1 \text{ mol dm}^{-3}$ .

**10.3** Identify the impurity **E**.

**10.4** Write the equations of the reactions corresponding to the aliquot preparation and titration.

**10.5** Determine the amount of impurity **E** (mol. % compared to Ca).

**10.6** Show that the potential at the equivalence point  $E_{\text{e.p.}}$  can be expressed as:

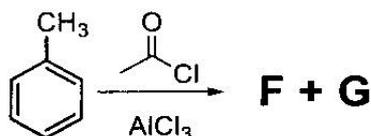
$$E_{\text{e.p.}} = \frac{1}{2} [(E^\circ(\text{E}^{3+}/\text{E}^{2+}) + (E^\circ(\text{Ce}^{4+}/\text{Ce}^{3+}))]$$

**10.7** According to the following table, determine which compounds would be the two best indicators in this titration.

Indicator	$E^\circ$ (V /SCE)	Color	
		Oxidized form	Reduced form
diphenylamine-4-sulfonic acid, sodium salt	0.60	blue	colorless
5,6-dimethyl,10-phenanthroline	0.73	yellow	red
3,3'-dimethoxybenzidine	0.54	red	colorless
safranin T	0.00	purple	colorless
4-ethoxychrysoidine hydrochloride	0.76	red	yellow
1,2-benzanthracene	1.00	colorless	colorless

Zeolites are widely used as materials in heterogeneous catalysis because of their large specific surface area, their structural framework and their large number of acid sites. The structured porous system of zeolites provides a molecular sieve effect. This effect leads to an increase of the selectivity of some reactions in which the reactants and products have a kinetic diameter (the typical length under which the corresponding molecule will collide with an obstacle) similar to the pore size of the zeolite. For laumontite, the largest pores present a diameter  $d_{\max} = 0.604$  nm. As a comparison, the kinetic diameter of benzene, 1,4-dimethylbenzene and toluene is 0.585 nm and that of 1,2-dimethylbenzene is  $d = 0.680$  nm.

Let us study the following reaction:



**10.8** Draw the two main products **F** and **G**.

**10.9** This reaction can also be catalyzed by laumontite. Determine which product will mainly be formed in the pore system of the mineral.

**Data at T = 298 K:**

$$E^{\circ}(\mathbf{E}^{3+}/\mathbf{E}^{2+}) = 0.53 \text{ V /SCE}$$

$$E^{\circ}(\text{NO}_3^-/\text{NO}_2) = 0.56 \text{ V /SCE}$$

$$E^{\circ}(\text{Zn}^{2+}/\text{Zn}) = -1.00 \text{ V /SCE}$$

$$E^{\circ}(\text{Ce}^{4+}/\text{Ce}^{3+}) = 1.09 \text{ V /SCE}$$

$$E(\text{SCE}) = 0.24 \text{ V}$$

$$E^{\circ}(\text{Ox/Red}) (\text{V /SCE}) = E^{\circ}(\text{Ox/Red})(\text{V /SHE}) - E(\text{SCE}) (\text{V})$$

## SOLUTION OF PREPARATORY PROBLEM 10

**10.1** To determine the stoichiometry of crystallized water  $y$ , the molar mass of laumontite needs first to be calculated:

$$\rho = \frac{m}{V} = \frac{m}{abc \sin\beta} \quad \text{and} \quad n = \frac{m}{M} = \frac{Z}{N_A} \quad \text{i.e.} \quad m = \frac{MZ}{N_A} \quad \text{then}$$

$$M = \frac{\rho N_A \times abc \sin\beta}{Z} = 470 \text{ g mol}^{-1}$$

In dry air the crystallized water is removed: we can then deduce it corresponds to 15.3% of the total mass as a further heat treatment does not make the mass of the sample vary. 15.3% corresponds to  $72 \text{ g mol}^{-1}$  and then  $y = 72/18 = 4$ .

According to the laumontite formula, this number corresponds also to the stoichiometry of the oxide **A**.

**10.2** The mass of the residue can be calculated as the difference of masses of the crucible before and after the calcination. A mass of 0.255 g is obtained: it corresponds to a molar mass for the binary compound of  $470 \times 0.255 / 0.500 = 240 \text{ g mol}^{-1}$ .

This binary compound is either the oxide **A** or **B**.

Knowing that  $y = 4$  we obtain  $M_A = 60 \text{ g mol}^{-1}$  which is univocally  $\text{SiO}_2$  ( $\text{ScO}$  and  $\text{CO}_3$  are not relevant): the addition of  $\text{HCl}$  yielded a  $\text{SiO}_2 \cdot n\text{H}_2\text{O}$  precipitate which lost its water molecules during calcination.

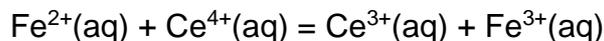
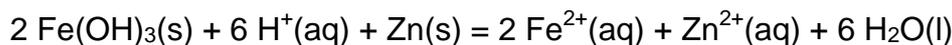
The hypothesis that precipitate is **B** with possible values of  $z = 1, 2, 3, 5$ , etc. does not lead to satisfying results.

The unknown part  $(\text{CaO})_x(\text{B})_z$  still needs to be elucidated. Its molar mass can be calculated as:  $M_{(\text{CaO})_x(\text{B})_z} = (470 - 72 - 240) = 158 \text{ g mol}^{-1}$ . It can then be deduced that the value of  $x$  cannot exceed 2. If  $x = 2$ ,  $\text{B}_z$  has a molar mass  $M = 46 \text{ g mol}^{-1}$ , which is not possible, since there is no oxide with this molar mass. So,  $x = 1$  and the molar mass of  $\text{B}_z$  is  $102 \text{ g mol}^{-1}$ . For  $z = 1$ , we find **B** =  $\text{Al}_2\text{O}_3$ .

**10.3** From the qualitative data (formation of a  $\text{FeSCN}^{2+}$  red complex) we can deduce that **E** is Fe ( $\text{Fe}^{3+}$  when oxidized and  $\text{Fe}^{2+}$  in the crystal).

**10.4**  $\text{Fe}^{3+}(\text{aq}) + \text{SCN}^-(\text{aq}) = \text{Fe}(\text{SCN})^{2+}(\text{aq})$





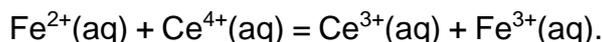
(several answers and notations are acceptable)

**10.5** Using the titration reaction  $\text{Fe}^{2+}(\text{aq}) + \text{Ce}^{4+}(\text{aq}) = \text{Ce}^{3+}(\text{aq}) + \text{Fe}^{3+}(\text{aq})$  we find that:

$n(\text{Fe}^{3+}) = 5.15 \cdot 10^{-3} \times 2.00 \cdot 10^{-3} = 1.03 \cdot 10^{-5}$  mol in the titrated solution and thus:

$n(\text{Fe}^{3+}) = 1.03 \cdot 10^{-5} \times 100.0/20.0 = 5.15 \cdot 10^{-5}$  mol in the initial solution which corresponds to  $n(\text{Fe}^{2+}) = 5.15 \cdot 10^{-5}$  mol in 0.500 g of the solid. In 0.500 g of the pure crystal,  $n(\text{Ca}^{2+}) = 0.500 / 471 = 1.06 \cdot 10^{-3}$  mol, so the molar percentage of the impurity compared to calcium is  $5.15 \cdot 10^{-5} / 1.06 \cdot 10^{-3} = 4.86\%$ .

**10.6** The titration reaction is:



Then, at the equivalence point,  $\text{Fe}^{2+}$  and  $\text{Ce}^{4+}$  have been introduced in equivalent quantities. When the reaction occurs, equal quantities of  $\text{Fe}^{2+}$  and  $\text{Ce}^{4+}$  are consumed and equal quantities of  $\text{Fe}^{3+}$  and  $\text{Ce}^{3+}$  are produced. Thus, at equilibrium, the following relationships can be written:  $[\text{Fe}^{2+}] = [\text{Ce}^{4+}]$  and  $[\text{Fe}^{3+}] = [\text{Ce}^{3+}]$ .

At equilibrium, the potential  $E_{e.p.}$  of the solution can be expressed as a function of each of the redox couples:

$$E_{e.p.} = E^\circ(\text{Fe}^{3+}/\text{Fe}^{2+}) - \frac{RT}{F} \ln\left(\frac{[\text{Fe}^{2+}]}{[\text{Fe}^{3+}]}\right) = E^\circ(\text{Ce}^{4+}/\text{Ce}^{3+}) - \frac{RT}{F} \ln\left(\frac{[\text{Ce}^{3+}]}{[\text{Ce}^{4+}]}\right)$$

The combination of these two expressions leads to:

$$E_{e.p.} = \frac{1}{2} \left( E^\circ(\text{Fe}^{3+}/\text{Fe}^{2+}) - \frac{RT}{F} \ln\left(\frac{[\text{Fe}^{2+}]}{[\text{Fe}^{3+}]}\right) + E^\circ(\text{Ce}^{4+}/\text{Ce}^{3+}) - \frac{RT}{F} \ln\left(\frac{[\text{Ce}^{3+}]}{[\text{Ce}^{4+}]}\right) \right)$$

*Note:* such a formula WILL NOT be expected to be known by heart for the competition exam but the simple use of Nernst equation as it is demonstrated here could be required.

**10.7** According to the value of the potential at the equivalence point (0.81 V /SCE), we can use the following indicators that exhibit the standard potential the closest to this value: 5,6- dimethyl-1,10-phenanthroline and 4-ethoxychrysoidine hydrochloride.



## THEORETICAL PROBLEM 11

The mineral pyromorphite (from Greek *pyro*–fire and *morpho*–form) has the following formula:  $A_5(PO_4)_3B$ . It was named after its property to recrystallize after melting. Therefore, it is also sometimes called *mineral of winners*. In France, deposits of this mineral are found in the Centre region.



The mineral of winners *Pyromorphite* from Chaillac Mine, Centre, France  
(© Didier Descouens)

Pyromorphite crystallizes into a hexagonal crystal system of parameters:  $a = b = 0.999 \text{ nm}$ ,  $c = 0.733 \text{ nm}$ ,  $\alpha = \gamma = 90^\circ$ ,  $\beta = 120^\circ$ ,  $Z = 2$ . Its density is  $\rho = 7.111 \text{ g cm}^{-3}$ .

After complete dissolution of 1.000 g of pyromorphite in concentrated nitric acid, the solution was neutralized with potassium hydroxide up to  $\text{pH} \approx 5$ . An addition of 1.224 g of KI was needed to form 1.700 g of a bright yellow precipitate.

### 11.1 Determine the formula of pyromorphite.

Hint 1: The volume of a hexagonal unit cell is  $V = abc \times \sin \beta$ .

Hint 2: The mass  $m$  of  $2 A_5(PO_4)_3B$  in one unit cell is:  $m = 2M / N_A$ , where  $M$  is the molar mass of the mineral and  $N_A$  Avogadro's constant. Also,  $m = \rho V$ , where  $\rho$  is the density and  $V$  the volume of a unit cell.

### 11.2 Write an equation for a reaction that could occur if the KI was added in excess.

In some cases, A is replaced by the impurity C in a significant proportion. The atomic mass of A is 3.98 times more than that of C. To determine the amount of the impurity, 1.00 g of the mineral was dissolved in  $\text{HNO}_3$ . After addition of  $\text{Na}_2\text{SO}_4$  to the solution, a white precipitate was formed. The precipitate was filtered out and the filtrate was added to an aqueous solution of ammonia ( $\text{NH}_3$ ). Then,  $\text{C}(\text{OH})_n$  was separated and dissolved in a sulfuric acid ( $\text{H}_2\text{SO}_4$ ) solution. To proceed to the titration of  $\text{C}(+n)$ , this impurity should be pre-oxidized into  $\text{C}(+m)$ . For this purpose, the solution of  $\text{C}(+n)$  in  $\text{H}_2\text{SO}_4$  was heated in the presence of  $\text{Ag}_2\text{S}_2\text{O}_8$  ( $\text{Ag}^+$  was used as a catalyst). The solution

was then transferred to a 100.0 mL volumetric flask and brought up to volume with distilled water. A 10.0 cm<sup>3</sup> aliquot was then transferred to a titration flask. Then, 10.0 cm<sup>3</sup> of an acidic solution of Fe(NH<sub>4</sub>)<sub>2</sub>(SO<sub>4</sub>)<sub>2</sub> were added. The obtained mixture was finally titrated by 15.0 cm<sup>3</sup> of an aqueous solution of KMnO<sub>4</sub> solution of concentration 9.44×10<sup>-3</sup> mol dm<sup>-3</sup>.

- 11.3** Identify the impurity C. Write an equation for each reaction mentioned in the text.
- 11.4** Calculate the percentage of C in the studied pyromorphite (w. %).
- 11.5** Calculate the equilibrium constant of the titration reaction, for one equivalent of permanganate ions, at 298 K.

Mn<sup>2+</sup> can be added to the solution to indicate the completeness of the C(+*n*) pre-oxidation reaction.

- 11.6** Write the equation of the reaction that indicates the completeness of the C(+*n*) pre-oxidation reaction. Underline the species that allows the detection of the completeness of the reaction.
- 11.7** Why is Fe(NH<sub>4</sub>)<sub>2</sub>(SO<sub>4</sub>)<sub>2</sub> often used in redox titrations instead of FeSO<sub>4</sub>? Choose the correct answer:
- FeSO<sub>4</sub> is not stable and get quickly oxidized by the oxygen in the air.
  - Fe(NH<sub>4</sub>)<sub>2</sub>(SO<sub>4</sub>)<sub>2</sub> is more soluble than FeSO<sub>4</sub>.
  - Fe(NH<sub>4</sub>)<sub>2</sub>(SO<sub>4</sub>)<sub>2</sub> is a cheaper reagent than FeSO<sub>4</sub>.

**Data at 298 K:**

$$E^\circ(\text{MnO}_4^-/\text{Mn}^{2+}) = 1.51 \text{ V /SHE}$$

$$E^\circ(\text{Fe}^{3+}/\text{Fe}^{2+}) = 0.77 \text{ V /SHE}$$

$$E^\circ(\text{C}(+m)/\text{C}(+n)) = 1.33 \text{ V /SHE}$$

**SOLUTION OF PREPARATORY PROBLEM 11**

11.1 To determine the formula of pyromorphite, its molar mass needs first to be calculated:

$$\rho = \frac{m}{V} = \frac{m}{abc \times \sin\beta} \text{ and } n = \frac{m}{M} = \frac{Z}{N_A} \text{ i.e. } m = \frac{MZ}{N_A} \text{ then:}$$

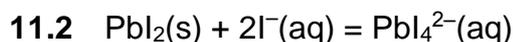
$$M = \frac{\rho N_A \times abc \times \sin\beta}{Z} = 1356 \text{ g mol}^{-1}$$

The cation **A** can be identified from the reaction with potassium iodide. Using the problem data and the molar mass of the mineral, the number of moles of the mineral in solution can be calculated: in 1.000 g of solid, there is  $1 / 1356 = 7.375 \times 10^{-4}$  mol of pyromorphite. 1.224 g of KI, that is  $1.224 / 166 = 7.37 \times 10^{-3}$  mol. Hence, the ratio between both reagents is  $7.37 \times 10^{-4} \times 5 / 7.375 \times 10^{-3} = 0.500$  and the reaction between both reads:

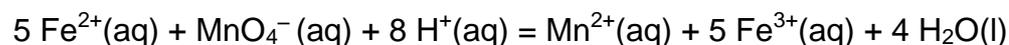
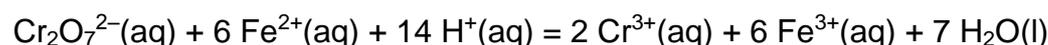
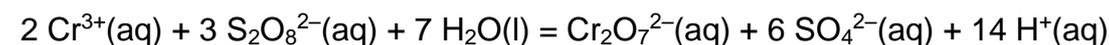
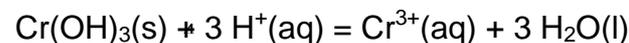
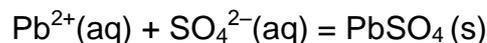


The molar mass of the precipitate is then  $1.700 / 3.688 \times 10^{-3} \text{ mol} = 461 \text{ g mol}^{-1}$  and we can finally calculate the molar mass of **A**:  $M(\mathbf{A}) = 461 - (2 \times M(\mathbf{I})) = 207 \text{ g mol}^{-1}$ . We can deduce: **A** = Pb.

To determine **B**:  $M(\mathbf{B}) = 1356 - (5 \times 207) - (3 \times 95) = 36 \text{ g mol}^{-1}$ . Therefore, **B** = Cl and the formula of pyromorphite is **Pb<sub>5</sub>(PO<sub>4</sub>)<sub>3</sub>Cl**.

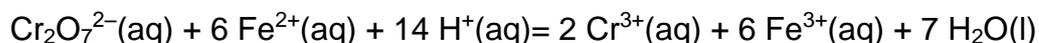


11.3  $M(\mathbf{C}) = 207 / 3.98 = 52 \text{ g mol}^{-1}$ . Therefore, **C** = Cr.

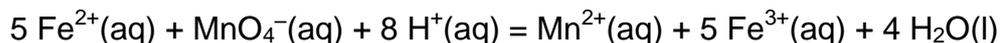


*(several notations are acceptable)*

**11.4** The method described here is a back titration. Indeed, after the following reaction:



The excess iron (II) is titrated by a solution of potassium permanganate:



According to the last reaction, the amount of iron titrated by potassium permanganate:

$$n_{\text{excess}}(\text{Fe}^{2+}) = 5 \times c(\text{MnO}_4^-) \times V(\text{MnO}_4^-) = 7.08 \times 10^{-4} \text{ mol}$$

We can then deduce that, in the 10.0 cm<sup>3</sup> aliquot,

$10.0 \times 10^{-3} \times 0.100 - 7.08 \times 10^{-4} = 2.92 \times 10^{-4}$  mol of Fe<sup>2+</sup> reacted with Cr<sub>2</sub>O<sub>7</sub><sup>2-</sup>. In the aliquot:

$$m_{\text{al}}(\text{Cr}) = (2.92 \times 10^{-4} \times 2 \times M(\text{Cr})) / 6 = 5.1 \text{ mg}$$

For 1.00 g of the mineral, we find then:  $m(\text{Cr}) = m_{\text{al}}(\text{Cr}) \times V_{\text{vol.fl.}} / V_{\text{al.}} = 51 \text{ mg}$

Hence, the weight content of chromium in the mineral is equal to:  $0.051 / 1.00 = 5.1 \text{ w\%}$

**11.5**  $5 \text{Fe}^{2+}(\text{aq}) + \text{MnO}_4^-(\text{aq}) + 8 \text{H}^+(\text{aq}) = \text{Mn}^{2+}(\text{aq}) + 5 \text{Fe}^{3+}(\text{aq}) + 4 \text{H}_2\text{O}(\text{l})$

$$\Delta_r G^\circ = -5 \times F E^\circ(\text{MnO}_4^-/\text{Mn}^{2+}) - 5 \times (-F E^\circ(\text{Fe}^{3+}/\text{Fe}^{2+}))$$

$$K^\circ = \exp(-\Delta_r G^\circ / RT) = \exp(-5F(E^\circ(\text{Fe}^{3+}/\text{Fe}^{2+}) - E^\circ(\text{MnO}_4^-/\text{Mn}^{2+})) / RT) = 3.8 \cdot 10^{62}$$

**11.6**  $2 \text{Mn}^{2+}(\text{aq}) + 5 \text{S}_2\text{O}_8^{2-}(\text{aq}) + 8 \text{H}_2\text{O}(\text{l}) = 2 \text{MnO}_4^-(\text{aq}) + 10 \text{SO}_4^{2-}(\text{aq}) + 16 \text{H}^+(\text{aq})$

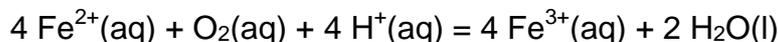
Mn<sup>2+</sup> is oxidized only after the complete oxidation of Cr<sup>3+</sup>

$$(E^\circ(\text{MnO}_4^-/\text{Mn}^{2+}) > E^\circ(\text{C}(+m)/\text{C}(+n))).$$

The solution will then turn pink.

**11.7** Correct answer:

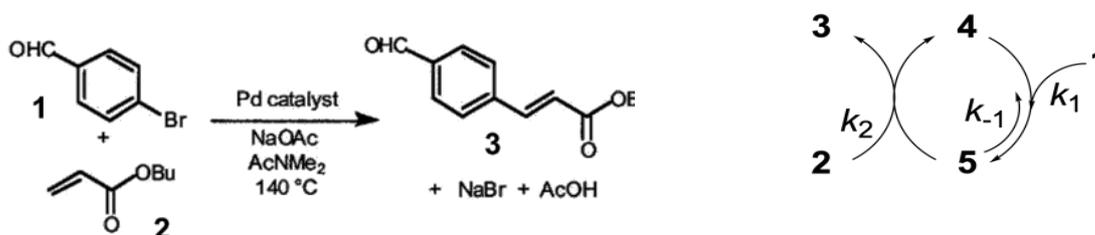
FeSO<sub>4</sub> is not stable and get quickly oxidized by the oxygen in the air.



## THEORETICAL PROBLEM 12

### Reaction progress kinetics

Kinetic investigations of multistep organic reactions are crucial for fundamental mechanistic studies and are also necessary for practical applications of organic synthesis. Reaction progress kinetic analysis is a methodology that makes use of the voluminous data sets that are now readily obtained from continuous monitoring of reactions. The figure below shows a Heck transformation catalyzed by a palladium complex together with the sequence of steps in a typical catalytic cycle where the substrate 1 reacts with the catalyst 4 to form an intermediate 5 (rate constant  $k_1$ ). The reverse reaction is associated with a rate constant  $k_{-1}$ . Further reaction of this intermediate with a second substrate 2 delivers the product 3 and regenerates the catalyst 4 (rate constant  $k_2$ ). The exact nature of the palladium complexes 4 and 5 is unknown.



- 12.1** Express the rate  $r$  of the reaction as a function of the rate constant  $k_2$  and the instantaneous concentrations of 2 and 5 ( $[2]$  and  $[5]$ , respectively).
- 12.2** Express the total concentration in catalyst  $[4]_{\text{tot}}$  as a function of  $[4]$  and  $[5]$ .
- 12.3** Assuming that intermediate 5 is in a steady-state regime, show that the rate  $r$  of the reaction can be written as:

$$r = \frac{k_1 k_2 [1][2][4]_{\text{tot}}}{k_{-1} + k_1[1] + k_2[2]}$$

Let us define a parameter called [“excess”], which is equal to the difference in the initial concentrations of the two substrates:

$$\text{[“excess”]} = [2]_0 - [1]_0$$

Hence we can write:

$$[2] = [2]_0 - [1]_0 + [1] = \text{[“excess”]} + [1]$$

12.4 Show that the rate can now be written as:

$$r = a \frac{[\text{"excess"}][1] + [1]^2}{1 + b[1]} [4]_{\text{tot}}$$

where

$$a = \frac{k_1 k_2}{k_{-1} + k_2[\text{"excess"}]}$$

and

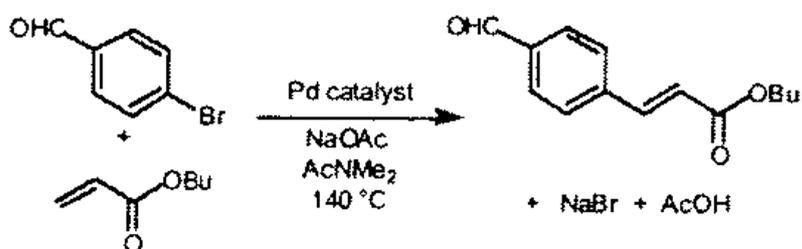
$$b = \frac{k_1 + k_2}{k_{-1} + k_2[\text{"excess"}]}$$

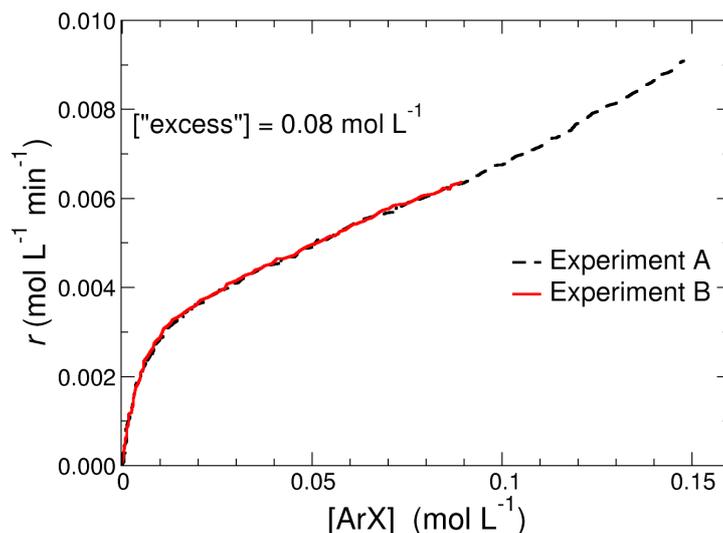
For a given set of conditions, the values  $[4]_{\text{tot}}$  and  $[\text{"excess"}]$  are constant, thus leaving  $[1]$  as the only variable. Hence, there is a direct relationship between the rate of the reaction  $r$  and the instantaneous concentration of one reactant  $[1]$ , which can be easily accessed, for instance by absorbance measurements.

Reaction calorimetry is a technique that can also be used. The heat flowing in or out of the reactor is measured over time, while the temperature is controlled and kept constant. Let us assume that only one transformation  $1 + 2 \rightarrow 3$  is occurring in the reactor.

12.5 Express the relationship between the heat flow  $dq(t)$  at a given time  $t$  evaluated during the period  $dt$ , the volume  $V$  of the reactor, the reaction enthalpy  $\Delta_r H$  and the rate  $r$ .

By combining the results from these different experimental procedures, it is possible to construct reaction progress analysis graphs where the rate  $r$  is expressed as a function of the concentration of 1. The figure below shows experimental results for the relation between the rate  $r$  of the Heck reaction as a function of substrate concentration, ArX. Two different initial conditions with the same total catalyst concentration and  $[\text{"excess"}]$  values has been considered.





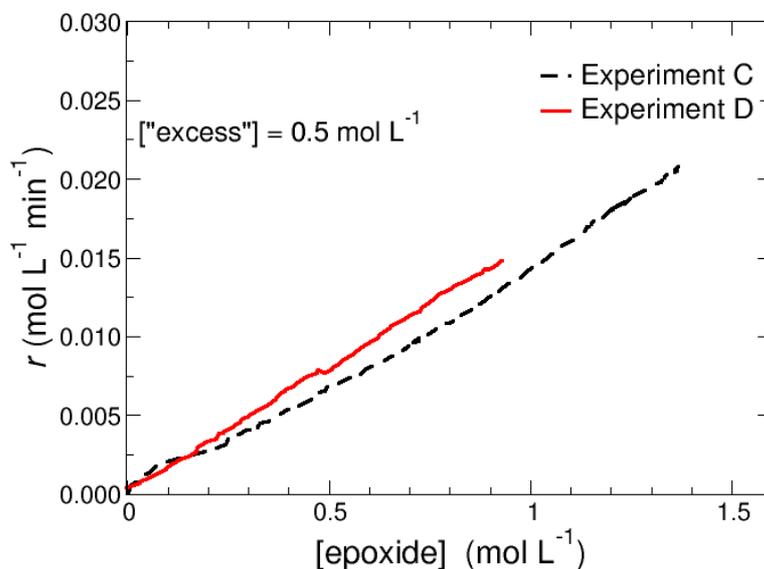
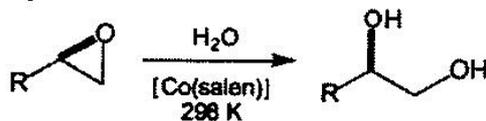
Experiment A:  $[\text{ArX}]_0 = 0.16 \text{ mol dm}^{-3}$  ( $\text{mol L}^{-1}$ ) and  $[\text{alkene}]_0 = 0.24 \text{ mol dm}^{-3}$

Experiment B:  $[\text{ArX}]_0 = 0.12 \text{ mol dm}^{-3}$  and  $[\text{alkene}]_0 = 0.20 \text{ mol dm}^{-3}$

- 12.6** For a given concentration  $[\text{ArX}]$  on the plot, which experiment yielded more product? (Experiment A / Experiment B)
- 12.7** For a given concentration  $[\text{ArX}]$  on the plot, which is the reaction in which the catalyst has completed the more turnovers? (Experiment A / Experiment B)
- In the following questions, choose the correct answer (True / False).
- 12.8** Product inhibition would reduce more the rate of the reaction in which more product is formed. (True / False)
- 12.9** Catalyst deactivation would reduce the rate of the reaction where the catalyst has one more turnovers. (True / False)
- 12.10** Neither catalyst deactivation nor product inhibition is a factor in the Heck reaction shown. (True / False)

Experimental results for the reaction progress kinetic analysis in the case of cobalt-catalyzed epoxide ring-opening are shown below. This reaction tells a different story. For a given epoxide concentration, a slightly higher rate was observed in Experiment D (lower initial concentration) compared to that shown in Experiment C (higher initial concentration).

This result suggests that either product inhibition or catalyst deactivation influences the reaction.



Experiment C:  $[\text{epoxide}]_0 = 1.5 \text{ mol dm}^{-3}$  ( $\text{mol L}^{-1}$ ) and  $[\text{H}_2\text{O}]_0 = 2.0 \text{ mol dm}^{-3}$

Experiment D:  $[\text{epoxide}]_0 = 1.0 \text{ mol dm}^{-3}$  and  $[\text{H}_2\text{O}]_0 = 1.5 \text{ mol dm}^{-3}$

Let us assume that a new experiment, Experiment E, is performed with the same initial conditions as in Experiment D but with some product of the reaction added right from the beginning.

**12.11** If the curve obtained for the reaction progress kinetic analysis is identical to that observed for Experiment D, then catalyst deactivation is the factor responsible for the behavior shown on the figure above. (True / False)

**SOLUTION OF PREPARATORY PROBLEM 12**

**12.1**  $r = k_2[2][5]$

**12.2**  $[4]_{\text{tot}} = [4] + [5]$

**12.3** Steady state approximation for **5**:  $k_{-1}[5] + k_2[2][5] = k_1[1][4]$

$$[5] = \frac{k_1 [4] [1]}{k_{-1} + k_2 [2]}$$

With result from question 3, one obtains

$$[5] = \frac{k_1 [4]_{\text{tot}} [1]}{k_{-1} + k_2 [2]} - \frac{k_1 [5] [1]}{k_{-1} + k_2 [2]}$$

This allows writing

$$[5] = \frac{k_1 [1] + k_{-1} + k_2 [2]}{k_{-1} + k_2 [2]} = \frac{k_1 [4]_{\text{tot}} [1]}{k_{-1} + k_2 [2]}$$

Finally using result from question one obtains:

$$r = \frac{k_1 k_2 [1] [2] [4]_{\text{tot}}}{k_{-1} + k_1 [1] + k_2 [2]}$$

**12.4** Replace [2] in the above equation by [1] + ["excess"] and the relation is found.

$$r = \frac{k_1 k_2 [1] ([1] + [\text{"excess"}])}{k_{-1} + k_1 [1] + k_2 [1] + k_2 [\text{"excess"}]} [4]_{\text{tot}}$$

It is easy to show that

$$\frac{a}{1 + b[1]} = \frac{k_1 k_2}{k_{-1} + k_1 [1] + k_2 [1] + k_2 [\text{"excess"}]} [4]_{\text{tot}}$$

**12.5** The rate of the reaction is expressed as  $r = 1 / V \times (dn / dt)$  where  $dn$  is the amount of matter that has been transformed in the reaction with molar heat  $\Delta_r H$  during the time  $dt$ . Consequently, the heat flow during time  $dt$  is  $dq = dn \Delta_r H = \Delta_r H V r dt$ .

**12.6** Correct answer: Experiment A because the initial concentration in reactant was higher.

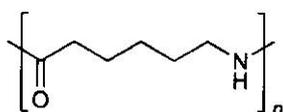
**12.7** Correct answer: Experiment A because if more product has been formed, it implies that more catalyst turnovers have been achieved.

- 12.8** Correct answer: True because in the case of product inhibition, the formation of the product would hamper the reaction and thus the more product the less efficient the reaction.
- 12.9** Correct answer: True because catalyst deactivation is occurring with time and therefore the more turnovers have been achieved the more likely catalyst deactivation is to happen. Moreover, catalyst deactivation implies that less catalyst is present and thus the rate decreases.
- 12.10** Correct answer: True because the rates of the two reactions with same excess but different initial concentration do overlap.
- 12.11** Correct answer: True; in that case, the reaction of Experiment C with the same excess but larger initial concentration has a rate lower rate than that of Experiment D. Therefore, either catalyst deactivation or product inhibition is taking place. If product inhibition is the reason for the observed behavior, then setting an experiment for Experiment D where more product is present right from the start would create a situation similar to that observed in Experiment C and thus the curves should overlap. If the curve obtained remains similar to that observed for Experiment D then product inhibition is not the investigated factor and catalyst deactivation is.
-

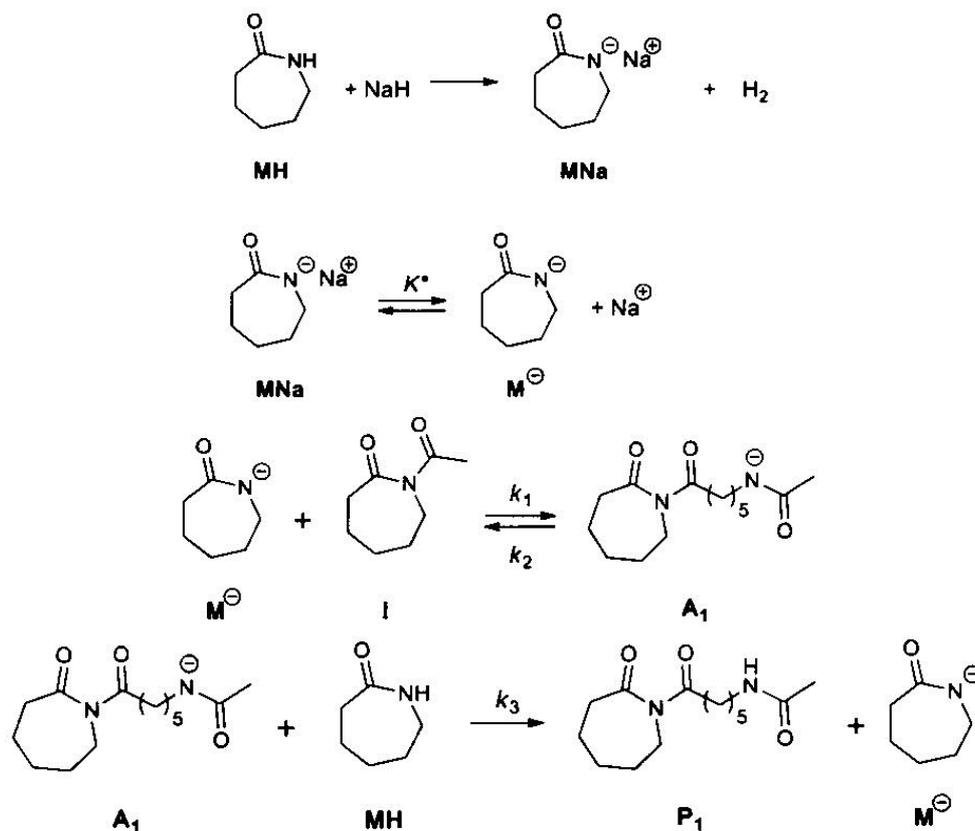
## THEORETICAL PROBLEM 13

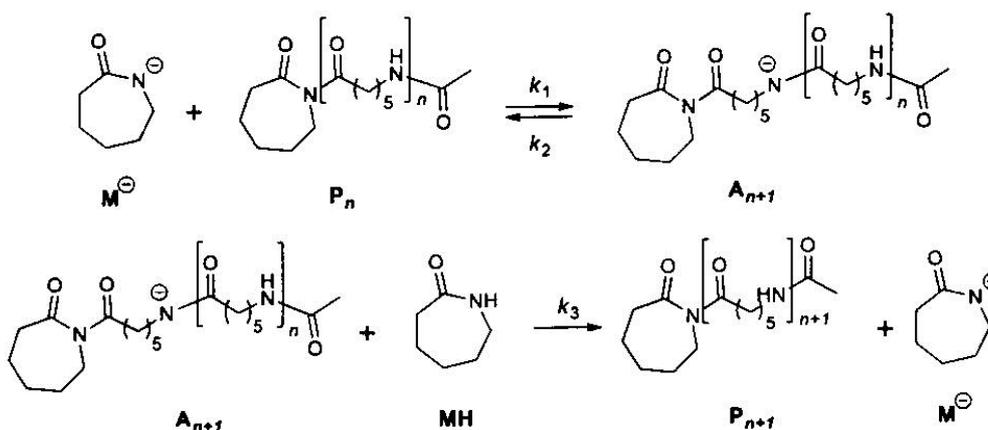
### Nylon 6

Nylon 6 is a synthetic linear polyamide. Its repeating unit contains six carbon atoms, as shown in the figure below. This polymer was first synthesized by P. Schlack at IG Farben. Most nylon 6 polymers tend to be semi-crystalline and are produced in the form of fiber yarns. Nylon is a tough material with good thermal and chemical resistance.



Nylon 6 can be prepared from  $\epsilon$ -caprolactam *via* a catalyzed anionic ring opening polymerization. The polymerization can be accelerated by an acylated lactam named I. One of the postulated mechanism for this reaction is shown below:





The first acid base reaction will not be considered in the following study. We further assume that no reaction other than those listed above occurs.

**13.1** Determine the relationship between the following concentrations  $[I]_0$  (initial concentration of **I**),  $[I]$ ,

$$\sum_{i=1}^n [A_i] \text{ and } \sum_{i=1}^n [P_i]$$

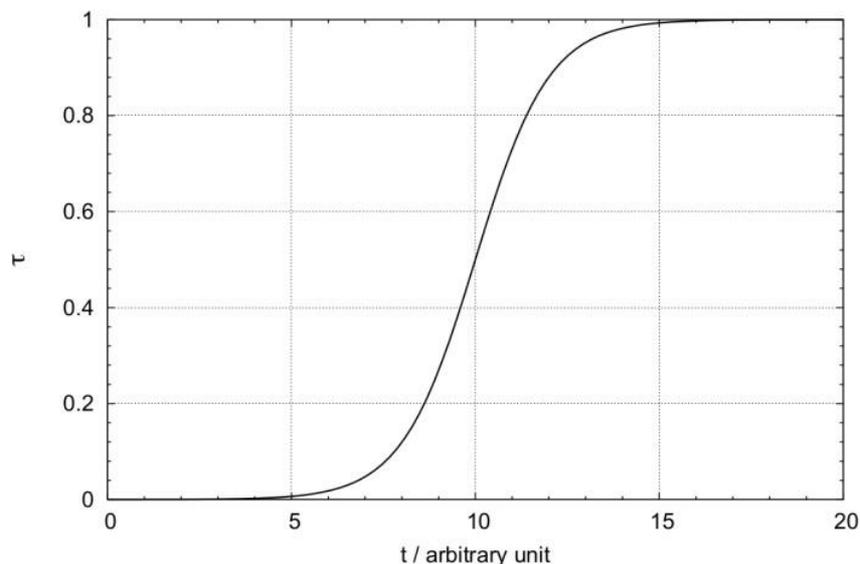
**13.2** Apply the steady state approximation to all **An** intermediates.

**13.3** Derive the rate of disappearance of the monomer **MH** as a function of the reactant concentrations  $[I]_0$ ,  $[MNa]$ ,  $[MH]$ ,  $k_i$  and  $K^\circ$ .

**13.4** Show that, depending on the rate-limiting step, the partial order with respect to the monomer **MH** is 0 or 1 and express the conversion  $\tau$ , fraction of the initial monomer concentration that has been consumed.

**13.5** In the two limit cases studied in the previous question, draw the conversion of monomer **MH** versus time curve.

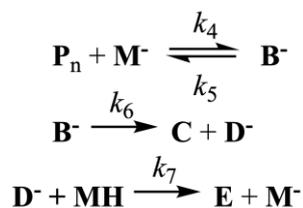
The monomer conversion  $\tau$  vs time curve obtained by Macosco *et al.* is the following:



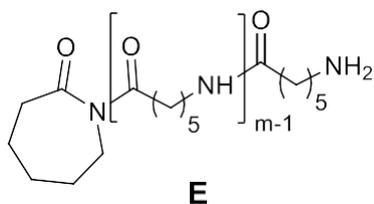
**13.6** What does the shape of the monomer conversion vs time curve stress out? Choose the correct answer(s).

- An inhibition effect of the monomer
- An oscillatory reaction
- A second order reaction
- An autocatalytic process
- A catalyzed reaction

To explain the experimental kinetic data, a competing mechanism was suggested. This side reaction decreases the degree of polymerization of nylon:



The chemical structure of E is:



- 13.7** Draw possible structures of **B<sup>-</sup>**, **C** and **D<sup>-</sup>**.
- 13.8** Considering only this mechanism, the disappearance rate of the monomer **MH** is proportional to  $[MH]([MH]_0 - [MH])$ . Plot the disappearance rate of the monomer **MH** versus the monomer concentration **[MH]**. Find the monomer concentration at which the rate is the highest.
-

## SOLUTION OF PREPARATORY PROBLEM 13

**13.1** The initial initiator concentration is equal to the sum of the concentrations of the remaining initiator in solution and of the initiator in the ionic or neutral polymer chain:

$$[I]_0 = [I] + \sum_{i=1}^n [P_i] + \sum_{i=1}^n [A_i]$$

**13.2** If we apply the steady state approximation to all the  $A_i$  we obtain:

$$\begin{aligned} k_1 [I] [M^-] &= k_2 [A_1] + k_3 [MH] [A_1] \\ k_1 [P_1] [M^-] &= k_2 [A_2] + k_3 [MH] [A_2] \\ &\dots \\ k_1 [P_{n-1}] [M^-] &= k_2 [A_n] + k_3 [MH] [A_n] \end{aligned}$$

**13.3** The rate of disappearance of the monomer **MH** is:

$$-\frac{d[MH]}{dt} = k_3 [MH] \sum_{i=1}^n [A_i]$$

From the previous question, we have:

$$(k_2 + k_3 [MH]) \left( \sum_{i=1}^n [A_i] \right) = k_1 [M^-] \left( [I] + \sum_{i=1}^n [P_i] \right)$$

□

hence, from the relation obtained at question 1:

$$\sum_{i=1}^n [A_i] = \frac{k_1 [M^-] [I]_0}{(k_1 [M^-] + k_2 + k_3 [MH])}$$

The concentration of  $[M^-]$  is related to the ion pair  $[MNa]$  via the equilibrium constant

$$K^o = \frac{[Na^+] [M^-]}{[MNa]}$$

If we neglect the concentration of the intermediates **A**, the electroneutrality condition imposes  $[Na^+] = [M^-]$ . Hence:

$$[M^-] = \sqrt{K^o [MNa]}$$

Finally, the disappearance rate of monomer **MH** is:

$$-\frac{d[\text{MH}]}{dt} = \frac{k_1 k_3 [\text{MH}] \sqrt{K^\circ [\text{MNa}]} [\text{I}]_0}{k_1 \sqrt{K^\circ [\text{MNa}]} + k_2 + k_3 [\text{MH}]}$$

**13.4** If we assume that the acid base reaction between **A**<sub>1</sub> and **MH** is the rate determining step, then  $k_2 \gg k_3[\text{MH}]$  and  $k_1(K^\circ[\text{MNa}])^{1/2} \gg k_3[\text{MH}]$ , so the rate expression can be simplified as:

$$-\frac{d[\text{MH}]}{dt} = \frac{k_1 k_3 \sqrt{K^\circ [\text{MNa}]} [\text{I}]_0 [\text{MH}]}{k_1 \sqrt{K^\circ [\text{MNa}]} + k_2}$$

In this case, the monomer reaction order is equal to 1 and the conversion rate of the monomer is:

$$\tau = \frac{[\text{MH}]_0 - [\text{MH}]}{[\text{MH}]_0} = 1 - \exp\left(-\frac{k_1 k_3 \sqrt{K^\circ [\text{MNa}]} [\text{I}]_0 t}{k_1 \sqrt{K^\circ [\text{MNa}]} + k_2}\right)$$

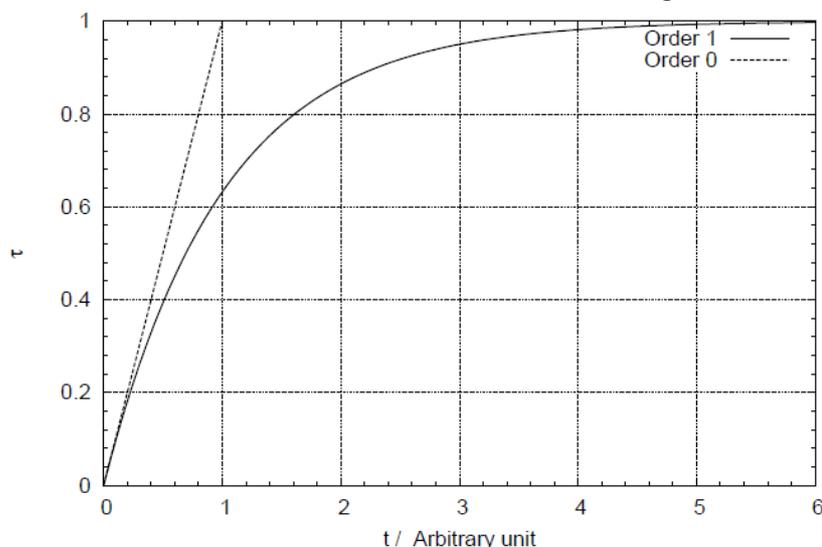
On the contrary, if we assume that  $k_2 \ll k_3[\text{MH}]$  and  $k_1(K^\circ[\text{MNa}])^{1/2} \ll k_3[\text{MH}]$ , the rate can be rewritten as:

$$-\frac{d[\text{MH}]}{dt} = k_1 \sqrt{K^\circ [\text{MNa}]} [\text{I}]_0$$

The monomer reaction order is then equal to 0 and the conversion rate of the monomer is:

$$\tau = \frac{[\text{MH}]_0 - [\text{MH}]}{[\text{MH}]_0} = \frac{k_1 \sqrt{K^\circ [\text{MNa}]} [\text{I}]_0 t}{[\text{MH}]_0}$$

**13.5** The conversion of monomer versus time of the two limiting cases is thus:

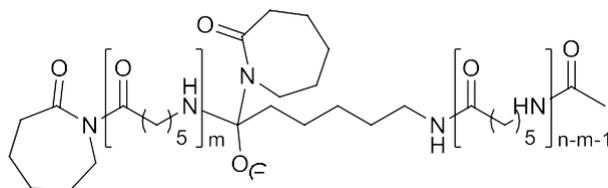


**13.6** Correct answers: An autocatalytic process, A catalyzed reaction

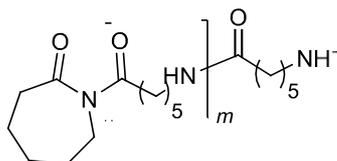
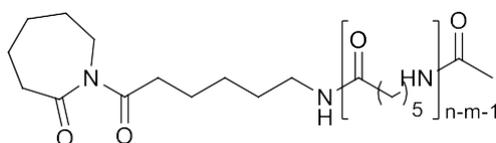
The sigmoid curve stresses out that the polymerization reaction is an autocatalytic process.

13.7 The structures of the intermediates are the following:

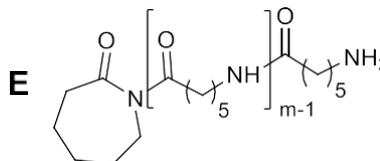
**B<sup>-</sup>**



**C**

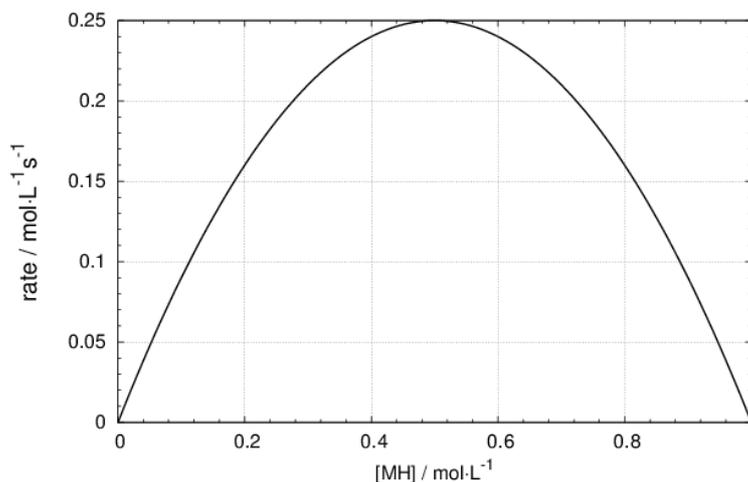


**D<sup>-</sup>**



13.8

$$-\frac{d[\text{MH}]}{dt} \sim ([\text{MH}] ([\text{MH}_0] - [\text{MH}]))$$



The disappearance rate of the monomer **MH** increases until the monomer concentration reaches  $[\text{MH}]_0 / 2$  and then decreases. The rate is then the highest for

$[MH] = [MH]_0 / 2$ . It means that the conversion versus time curve of the monomer slowly increases (induction time), then the conversion changes rapidly and then slowly increases. This degradation mechanism can explain the sigmoid curve observed by Macosco.

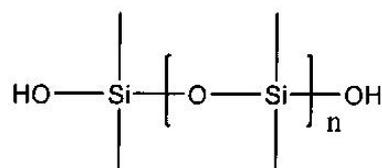
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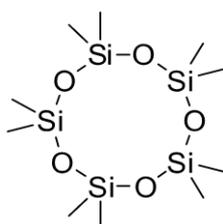


### Synthesis of Polydimethylsiloxane (PDMS)

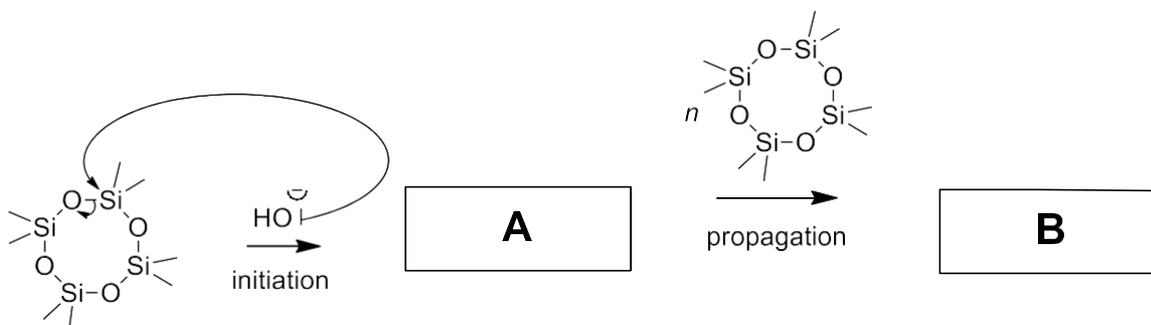
We now examine the synthesis of polydimethylsiloxane (figure below), also known as silicone. These polymers are usually used in sealants, adhesives, lubricants, medicine, cooking utensils, and thermal insulation.



We will also consider cyclic and short polydimethylsiloxane molecules written  $D_n$  with  $n$  the number of Si atoms. For example,  $D_5$  is pictured below.



**14.9** We consider a reaction medium with  $D_4$  and hydroxide ions. Give the structures of **A** and **B** in the mechanism below, leading to the formation of PDMS.

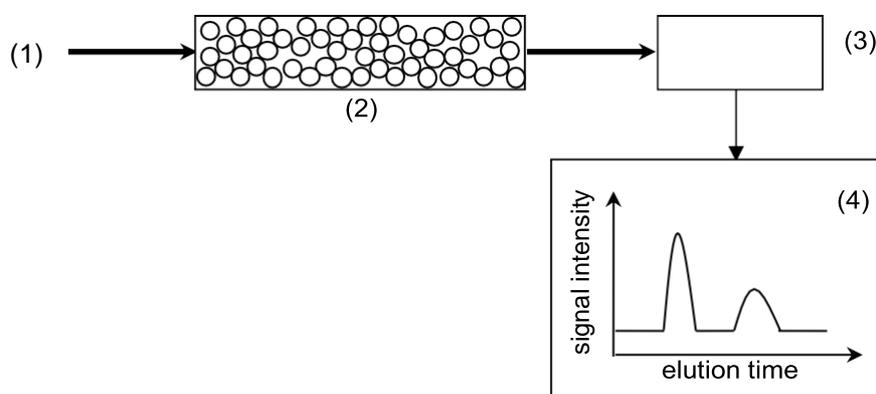


**14.10** During this reaction the synthesis of macrocycles is observed. Draw a mechanism or a pattern to explain the formation of such macrocycles.

**14.11** Transfer reactions are also observed. Draw a mechanism showing what a transfer reaction in such a reaction medium could be.

### Size-exclusion chromatography and synthesis of a block copolymer

The copolymer is studied by size-exclusion chromatography (SEC), also called gel permeation chromatography (GPC). The principles of the method are represented in the figure below: (1) the sample is introduced on a column filled with a microporous packing material (millions of highly porous and rigid particles tightly packed together in a column). This material (2) does not react with polymers. Molecules of various sizes elute from the column at different rates. The column retains the molecules with low hydrodynamic volume (*i.e.* the smaller molecules) for a longer time than the molecules with high hydrodynamic volume. A detector (3), such as a refractive index detector or an infrared absorption detector, detects molecules at the end of the column. For a single species, the intensity of the measured signal (4) is proportional to the concentration of the molecules detected. The experimental curve (4) can be translated into a curve giving the mass fraction of polymer chains in the sample as a function of their molar mass. This translation is done using monodisperse polymer standards.



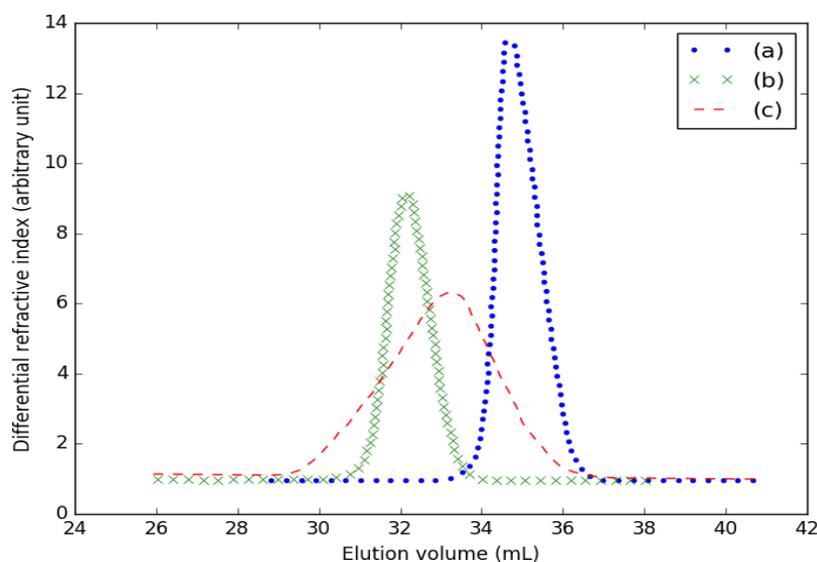
PDMS synthesis is performed in THF, starting with  $\text{D}_3$  and  $n\text{-BuLi}$  at the concentration  $[\text{BuLi}]_0$ . Variations of temperature of the reaction medium and/or of  $[\text{BuLi}]_0$  have consequences on the product obtained. We introduce the polydispersity index denoted  $I_p = M_w/M_n$ , where  $M_w$  is the average molecular weight and  $M_n$  is the number average molecular weight.

**14.12** In order to better understand the meaning of the polydispersity index, fill in the gaps in the following sentence with the word “low” or “high”:

*“ $M_n$  is more sensitive to molecules of \_\_\_\_\_ molecular mass while  $M_w$  is more sensitive to molecules of \_\_\_\_\_ molecular mass. Therefore the more the polymer chains approach uniform chain length, the more  $I_p$  is close to 1.”*

Three experiments (V. Bellas *et al.*, *Macromolecules*, 2000) in different reaction conditions are performed and the polydispersity index  $I_p$  is determined in each case.

- (I) 25 °C until 50% conversion is reached. The SEC analysis gives  $I_p = 1.06$ .
- (II) conditions (I) followed by polymerization at –20 °C for 8 days.
- (III) 25 °C until 100% conversion is reached. The SEC analysis gives  $I_p = 1.3$ . The SEC analysis of the three experiments is represented in the figure below.



**14.13** A qualitative analysis of the experimental curves obtained with SEC allows to associate which reaction conditions lead to the highest  $M_n$ . Which of the 3 curves is related to the highest  $M_n$ ?

**14.14** Match each curve with reaction conditions (I, II or III with (a), (b) or (c)).

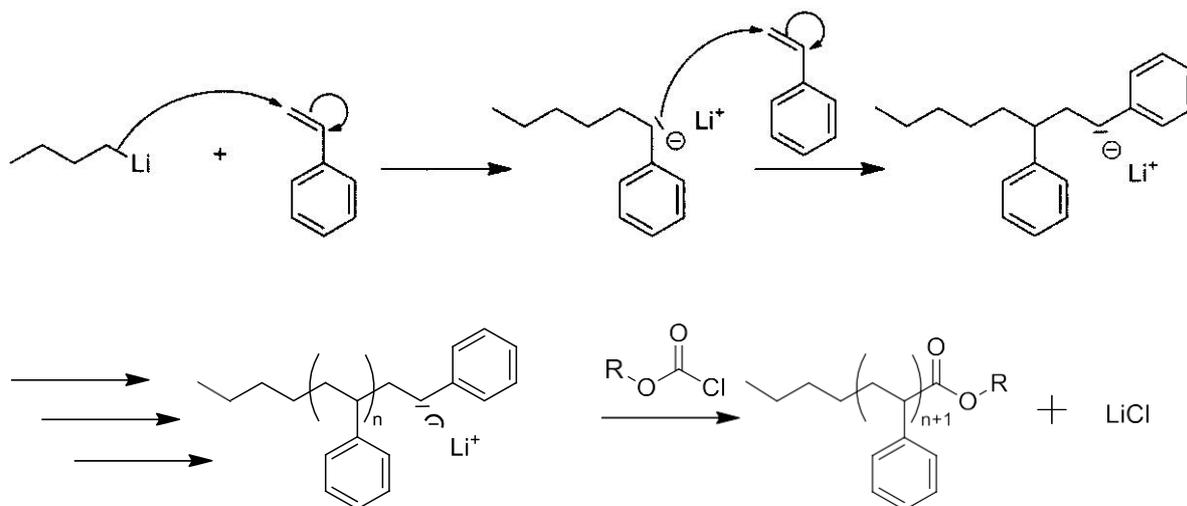
We (finally!) synthesize the block copolymer following the procedure depicted below, and monitor the reaction by SEC.



## SOLUTION OF PREPARATORY PROBLEM 14

14.1 Correct answer: *n*-Butyllithium (*n*-BuLi)

14.2



14.3  $k_a \gg k_p$

14.4 The rate of disappearance of the monomer corresponds to  $-d[M]/dt$ , and M is consumed at each polymerization step  $i$ . Therefore:

$$-\frac{d[M]}{dt} = k_p \sum_i [AM_i^-] [M]$$

14.5 The active species concentration is constant and equal to C, thus

$$\sum_i [AM_i^-] = C$$

Therefore,

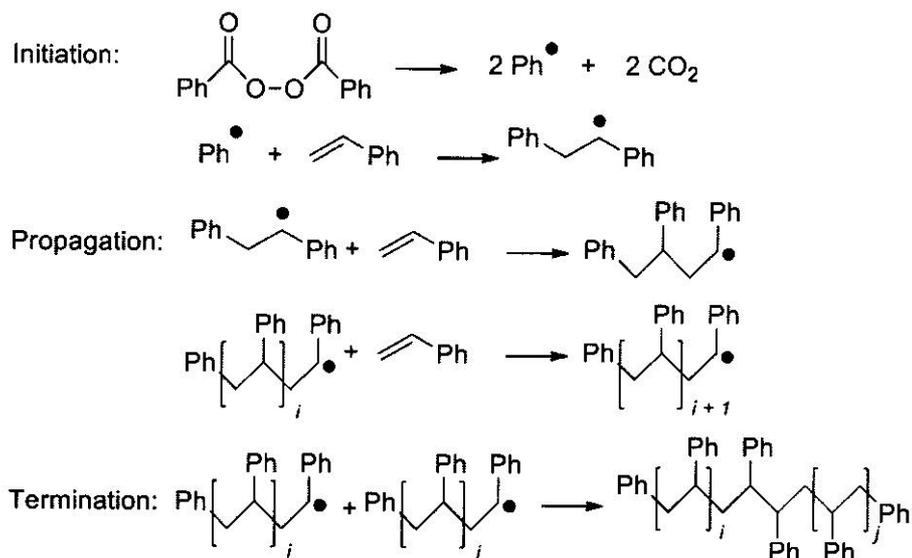
$$-\frac{d[MH]}{dt} = k_p [M] C$$

14.6

$$[M](t) = [M](t=0) e^{-\frac{t}{k_p C}}$$

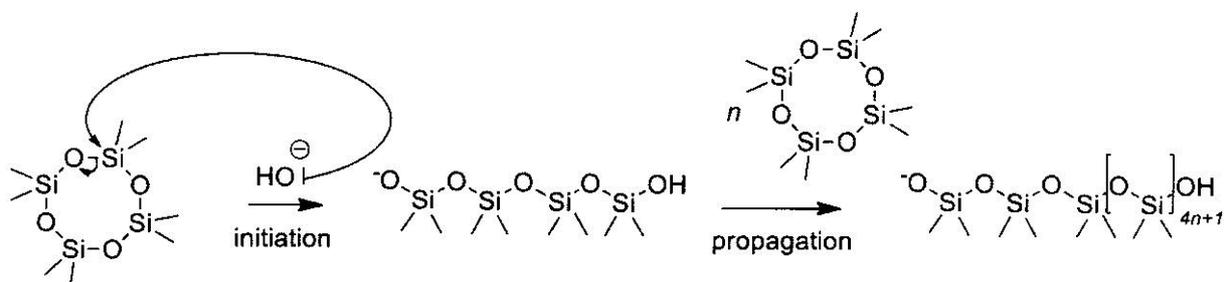
The half-time is thus:  $t_{1/2} = \ln 2 / (k_p C)$

## 14.7

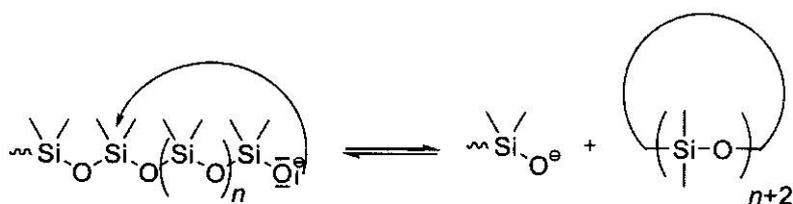


**14.8** Correct answer: Yes, because of the preferential formation of one product over another (the reaction selectively generates one constitutional isomer over the other). Radicals add to the terminal carbon atom of styrene to form a benzyl-type radical.

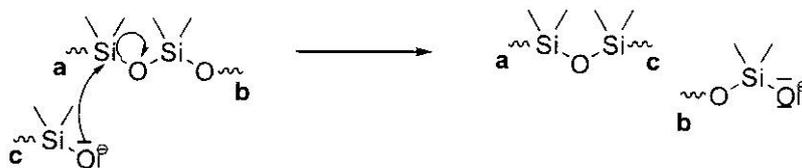
## 14.9



## 14.10



## 14.11



**14.12**  $M_n$  is more sensitive to molecules of **low** molecular mass while  $M_w$  is more sensitive to molecules of **high** molecular mass. Therefore, the more the polymer chains approach uniform chain length, the more  $I_p$  is close to 1.

**14.13** Curve (b) (the shorter the polymer, the higher the elution volume).

**14.14** The full width half maximum of the SEC signal is related to the  $I_p$  value: the closer to 1 the  $I_p$ , the thinner the SEC curve. Curves (a) and (b) correspond then to similar  $I_p$  values, whereas curves (c) corresponds to a larger one. Since sample (II) was prepared at a low temperature, starting from (I), are likely to display similar polydispersities and then we can state: (I)  $\rightarrow$  (a), (II)  $\rightarrow$  (b) and (III)  $\rightarrow$  (c).

**14.15** PS-PDMS- $O(CH_3)_2SiCH_2CH_2Si-(CH_3)_2O$ -PDMS-PS or in a more condensed form PS- PDMS-PS (as the linkage is chemically close to PDMS).

**14.16 PS**  $\rightarrow$  **3** (because it is the shortest molecule of the list)

**PS-PDMS precursor**  $\rightarrow$  **2** (because it is a molecule that is bigger than PS, but smaller than the final product)

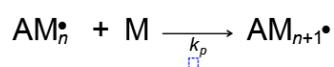
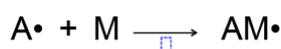
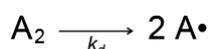
**unfractionated product**  $\rightarrow$  **1** (because we observe that there are two SEC curves that reach the lowest elution volume, therefore they could be the final product. But as we suggest an unfractionated product, it should correspond to the curve with 2 signals i.e. 2 products with the desired and the unwanted product)

**fractionated product**  $\rightarrow$  **4**

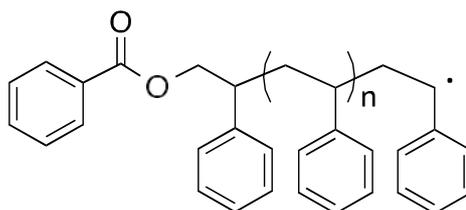
## THEORETICAL PROBLEM 15

### Radical polymerization

Radical polymerization is a method of choice for polymer synthesis. Easy to implement and compatible with a wide range of functional monomers, this process can be carried out under various experimental conditions, including in the presence of water. Typically, radical polymerization is composed of three steps: (i) initiation, (ii) propagation and (iii) termination. The initiation step consists of the thermal decomposition of an organic compound according to a radical mechanism (first step of the kinetic scheme below). This leads to a radical species that further initiates radical polymerization.



- 15.1 Considering a symmetric unimolecular initiator, give the chemical structures of the initiator and the monomer used for the synthesis of the polymer **P1**.



P1

At a given temperature, the half-life of the initiator  $t_{1/2}$  can be determined experimentally by following the evolution of the concentration of the initiator vs time.

- 15.2 The table below gives the evolution of  $A_2$  concentration over time at 82 °C in chlorobenzene. Determine graphically the value of  $t_{1/2}$  for the initiator  $A_2$  at 82 °C in chlorobenzene.

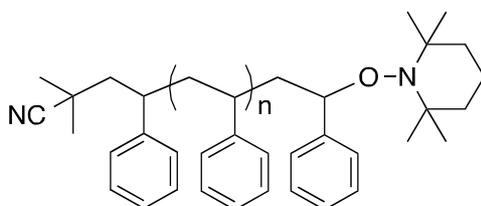
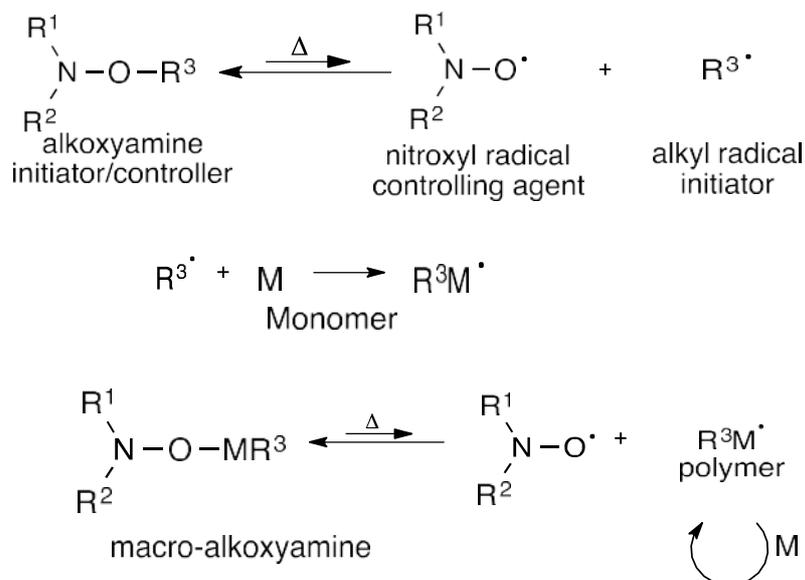
$[A_2]$ (mmol dm <sup>-3</sup> )	1.00	0.81	0.66	0.54	0.44	0.24	0.06
time (h)	0.0	0.3	0.6	0.9	1.2	3.0	6.0

**15.3** Calculate the rate constant for the dissociation of the initiator **A<sub>2</sub>**, denoted  $k_d$ , at 82 °C in chlorobenzene.

Despite its many advantages, radical polymerization presents some drawbacks mainly related to the occurrence of irreversible termination reactions (combination, disproportionation, transfer reactions), which limit the possibilities of obtaining polymers with controlled architectures and compositions.

**15.4** Among the possible termination reactions of **P<sub>1</sub>**, write its self-combination reaction.

New techniques such as Reversible-Deactivation Radical Polymerization (RDRP) have been developed to limit the irreversible termination of the propagating radical chains. RDRP conducted in the presence of a nitroxide, known as Nitroxide Mediated Polymerization (NMP), consists of using an alkoxyamine as initiator, as shown in the scheme below. These alkoxyamines dissociate homolytically under heating to form an alkyl radical that acts as an initiator and a nitroxyl radical that end-caps reversibly the polymer chain end during the polymerization process.



**15.5** Give the chemical structure of the alkoxyamine that will be written **ALK1** and is used to obtain the polymer **P2**.

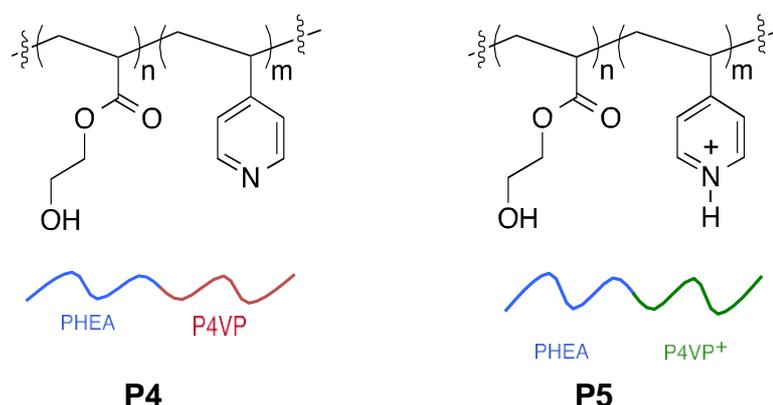
In the following *conv* represent the monomer conversion (% of consumed monomer), *m* is the mass of styrene, *n* the number of moles of initiator, and *f* is the efficiency factor (in the case of alkoamine, *f* = 1).

**15.6** Knowing that the number average molar mass  $M_n$  can be expressed as

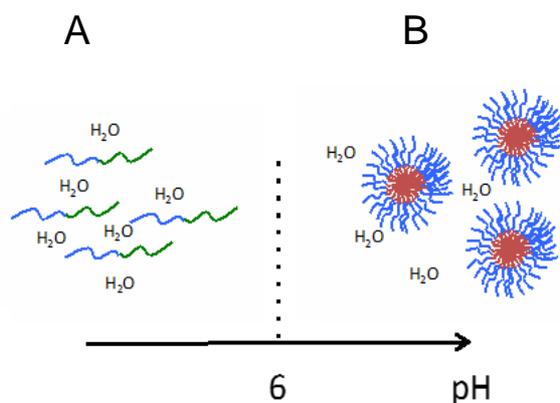
$$M_n = conv \times \frac{m}{f \times n}$$

give the number of moles and the mass of **ALK1** required to obtain 10 g of a polystyrene sample exhibiting  $M_n = 20000 \text{ g mol}^{-1}$  at 100% conversion of styrene.

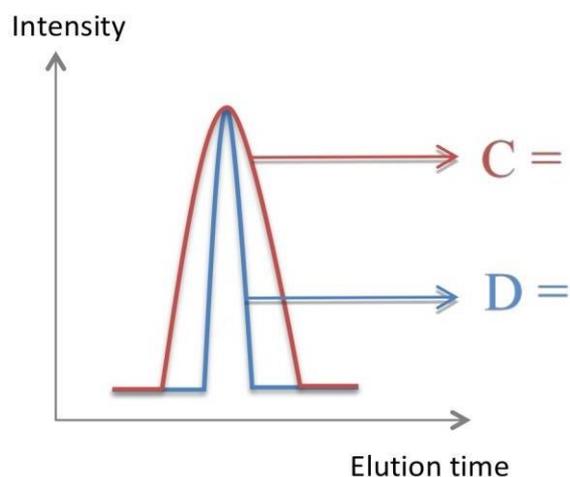
Thanks to RDRP techniques, access to block copolymers became easier. These copolymers are composed of at least two blocks of homopolymer linked together by a covalent bond. They combine the properties of homopolymers presenting different characteristics (e.g. combination of a hydrophilic block and a hydrophobic block). For instance, the poly(hydroxyethyl acrylate)-*b*-poly(4-vinylpyridine) diblock copolymer (PHEA-*b*-P4VP, P4) behaves as a surfactant. Poly(hydroxyethyl acrylate) is hydrophilic, and poly(4-vinylpyridine) is soluble in water for pH < 6 (protonation of pyridine) and insoluble in water for pH > 6.



**15.7** In the figure below, assign the state (P4 or P5) of the PHEA-*b*-P4VP block copolymer in aqueous solution according to the pH values.

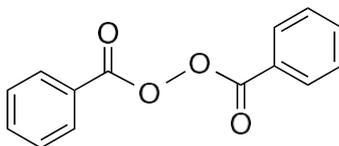


- 15.8** Give the expected number of  $^1\text{H}$  NMR signals with their splitting pattern for the  $\text{C}(=\text{O})\text{OCH}_2\text{CH}_2\text{OH}$  side chains of the copolymer P4 dissolved in deuterated tetrahydrofuran. In this solvent, the copolymer P4 is perfectly soluble. (Note: No coupling will be considered with the terminal OH group).
- 15.9** Assign on the following chromatogram obtained by Size Exclusion Chromatography (SEC, see question 12 in problem 14) which curve corresponds to a polystyrene sample prepared by conventional free radical polymerization (**P6**) and which one corresponds to polystyrene prepared by NMP (**P7**).

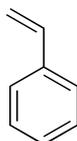


## SOLUTION OF PREPARATORY PROBLEM 15

15.1 The initiator is benzoyl peroxide.

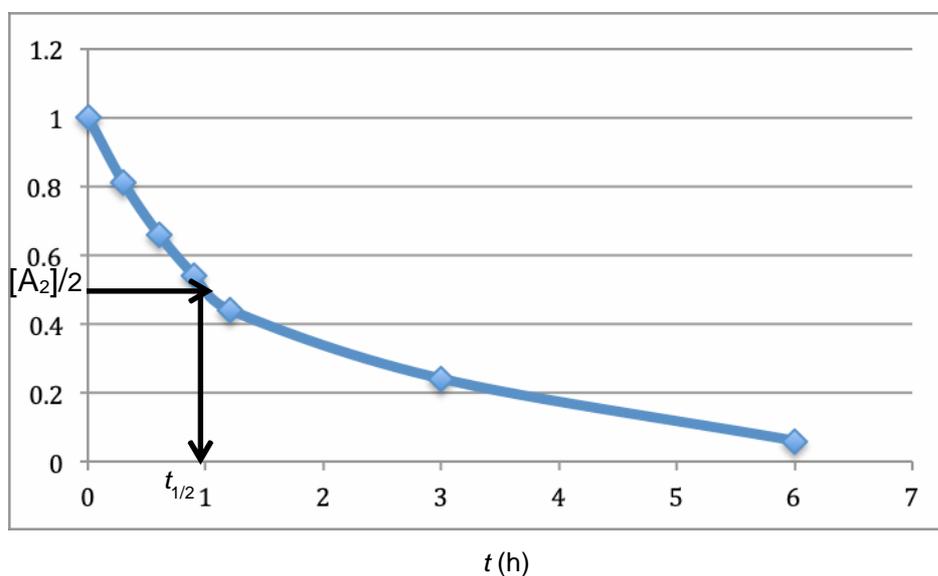


The monomer used is styrene.



15.2 The half-life is the time required to consume 50% of the reactants.

$[A_2] \cdot 10^3 \text{ mol dm}^{-3}$



We can graphically determine  $t_{1/2}$  as roughly 1 h.

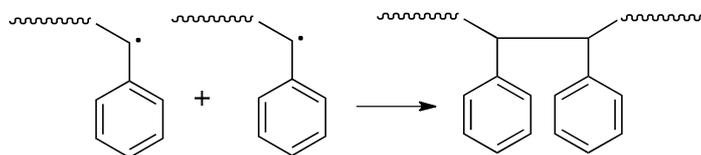
15.3  $A_2$  is a unimolecular initiator, and its decomposition follows a first order kinetic.

In this case the half-life is:

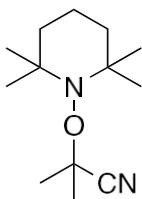
$$k_d = \frac{\ln 2}{t_{1/2}}$$

Given the half-life estimate from question 2:  $k_d = 1.9 \cdot 10^{-4} \text{ s}^{-1}$

## 15.4 Self-combination



## 15.5 ALK1:



## 15.6 By substituting the provided data in the following equation:

$$M_n = conv \times \frac{m}{f + n}$$

we obtain:

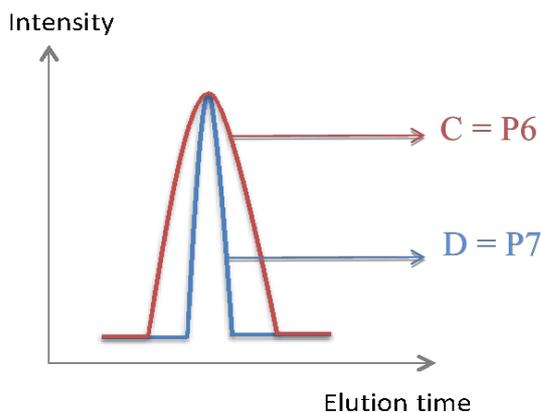
$$n = 5 \times 10^{-4} \text{ mol}$$

$$m(\text{ALK1}) = n \times M(\text{ALK1}) = 0.112 \text{ g}$$

15.7 When the pyridine is protonated, the block copolymer is fully soluble in water so **A = P5**. When the pyridine is not protonated the block copolymer is amphiphilic. In water, the block copolymer thus self-organizes as a micelle. The core is composed of the hydrophobic block (P4VP). The outside of the micelle is composed of the hydrophilic PHEA block. Hence **B = P4**.

15.8 2 signals (triplet) for the two non-equivalent  $\text{CH}_2$  groups, 1 signal (singlet) for OH.

15.9 Contrary to a conventional radical polymerization, RDRP techniques limit the occurrence of irreversible termination reactions of the propagating radical chains. Ideally, all the chains are created and grow at the same time. Narrow molecular weight distributions are obtained, hence the following answer.



## THEORETICAL PROBLEM 16

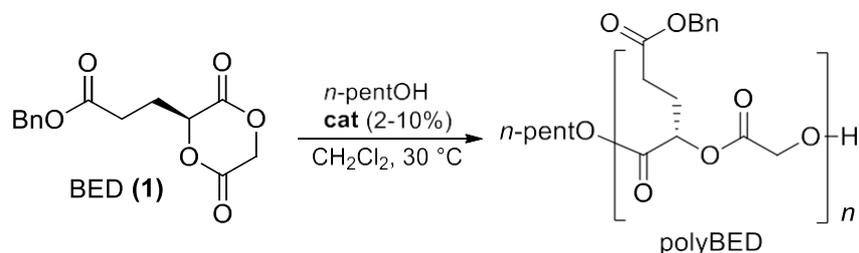
### Biodegradable polyesters

Replacing conventional polymer materials, sources of pollution, by biodegradable polymers is a major industrial challenge. The synthesis and characterization of such a biodegradable polymer is studied here.

**16.1** What is a biodegradable polymer? Choose the correct answer(s).

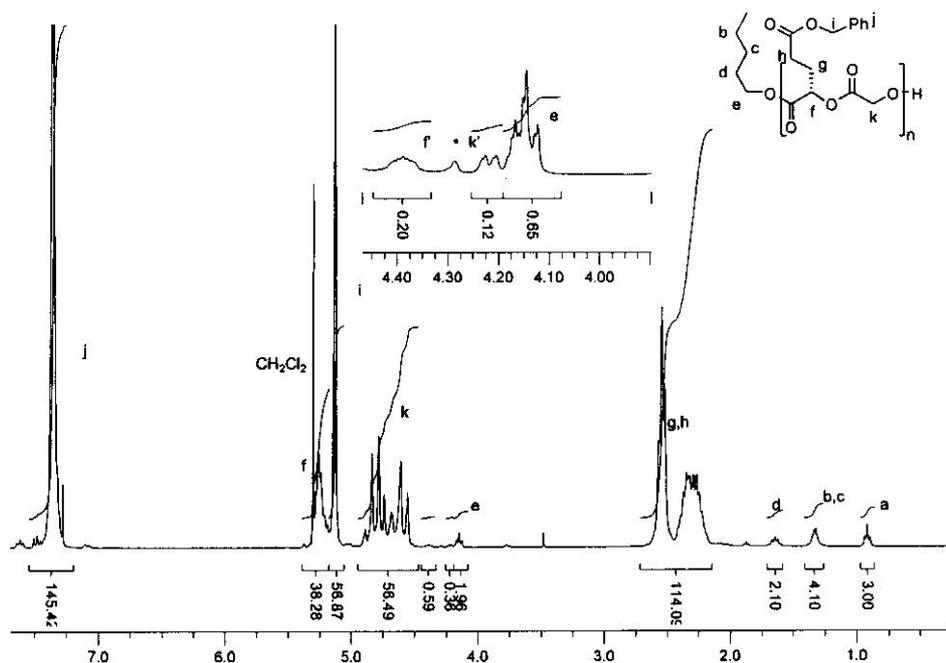
- A polymer available in native form in nature.
- A polymer made from biobased compounds.
- A polymer transformable by microorganisms into less polluting molecules.

A polymer functionalized by an ester side-chain is prepared by polymerization of the corresponding monomer (BED) in the presence of a catalyst. The polymerization is initiated by pentan-1-ol (denoted *n*-pentOH in the following scheme). Bn corresponds to the benzyl group *i.e.* C<sub>6</sub>H<sub>5</sub>–CH<sub>2</sub>–).



**16.2** Give chemical function(s) that can explain the biodegradability of this polymer.

The polymer is first characterized by NMR spectroscopy. The obtained <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>, 300 MHz) is given in the figure below:



**16.3** Give the definition of the number average degree of polymerization  $X_n$ .

NMR provides access to the average degree of polymerization  $X_{n,NMR}$  and to the number averaged molecular weight  $M_{n,NMR}$ . For that, we compare the integrations of the protons at the end of the chains with those of protons of the main chain.

**16.4** By integration of appropriate peaks, determine  $X_{n,NMR}$ .

**16.5** Calculate  $M_{n,NMR}$  from this value knowing that the molar mass of the monomer unit and end chain are equal to 278 and 88 g mol<sup>-1</sup>, respectively.

**16.6** In general, <sup>1</sup>H NMR spectroscopy is an effective method to determine  $M_n$ . However, it remains limited for very large polymers. Why? Choose the correct answer(s).

- The peaks at the ends of the chains are not sufficiently resolved compared to the peaks of the main chain.
- The integration of the different peaks observed may be distorted due to the observed peak broadening for high mass polymers.
- The number of protons will be too high to be properly analyzed.

The polymer is then analyzed by size exclusion chromatography (SEC, see question 12 in problem 14). The measured elution volumes can be related to the molar mass of the polymer obtained by, for example, the prior injection of a range of polystyrene samples of known masses (standard polymers). The obtained value for  $M_{n,SEC}$  is equal to 8950 g mol<sup>-1</sup>.

**16.7** Compare  $M_{n,NMR}$  and  $M_{n,SEC}$ . How to explain this difference? Choose the correct answer(s).

- SEC is not a sufficiently precise analytical method.
- Polystyrene has a larger hydrodynamic volume than that of polyBED.
- Polystyrene has a smaller hydrodynamic volume than that of polyBED.

**16.8** Cite a property of polymers, not accessible by NMR, that SEC can provide.

---

## SOLUTION OF PREPARATORY PROBLEM 16

**16.1** Correct answer:

A polymer transformable by microorganisms into less polluting molecules.

**16.2** The ester function can be easily degraded (hydrolyzed) by enzymatic processes.

**16.3**  $X_n = (M_n - M_{\text{end chain}})/M_0$  with  $M_0$  the molecular weight of the monomer (= average number of monomer unit),  $M_n$  its number averaged molecular weight, and  $M_{\text{endchain}}$  the molar mass of the chain end.

**16.4**

Therefore :  $X_{n,\text{NMR}} = (I_j/5)/(I_a/3) = 29$  Peaks from benzyl (j) and methyl (a) groups were chosen because these peaks are isolated and well defined. The first one *corresponds* to 5 protons, the second one to 3. If the polymerization degree was equal to 1 then the ratio  $(I_j/5)/(I_a/3)$  should be also equal to 1, with  $I_j$  and  $I_a$  the integration value of  $j$  and  $a$  peaks.

**16.5**  $M_{n,\text{NMR}} = X_{n,\text{NMR}} \times M_0 + M_{\text{end chain}} = 29 \times 278 + 88 = 8150 \text{ g mol}^{-1}$

**16.6** Determining  $M_n$  thanks to NMR spectroscopy requires to measure accurately integration value of peaks related to the end group and to the monomer. When the size of the polymer increases, the relative intensity of the peak from the end group decreases. In addition, peaks are broadened due to relaxation issues. Therefore, the correct statements are:

The peaks at the ends of the chains are not sufficiently resolved compared to the peaks of the main chain.

The integration of the different peaks observed may be distorted due to the observed peak broadening for high mass polymers.

**16.7** Here  $M_{n,\text{SEC}} (8950 \text{ g mol}^{-1})$  is larger than  $M_{n,\text{NMR}} (8150 \text{ g mol}^{-1})$  so the value of  $M_n$  is overestimated by SEC therefore the polystyrene used for calibration has not the same hydrodynamic radius than polyBED. More precisely, it means that a polystyrene of  $8950 \text{ g mol}^{-1}$  has the same hydrodynamic radius as a polyBED of  $8150 \text{ g mol}^{-1}$ . Therefore, the correct statement is:

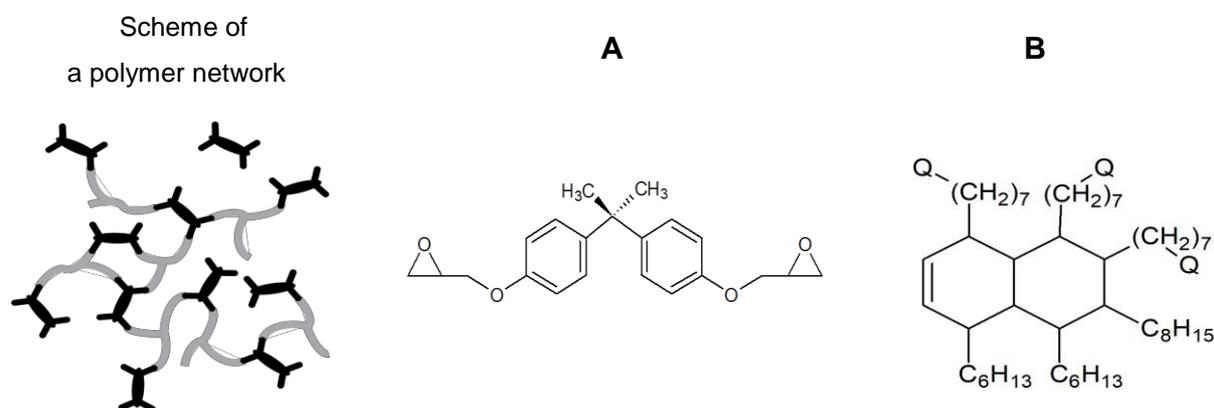
Polystyrene has a smaller hydrodynamic volume than that of polyBED.

**16.8** Mass average molecular weight  $M_w$  or dispersity which is the ratio  $M_w / M_n$ .

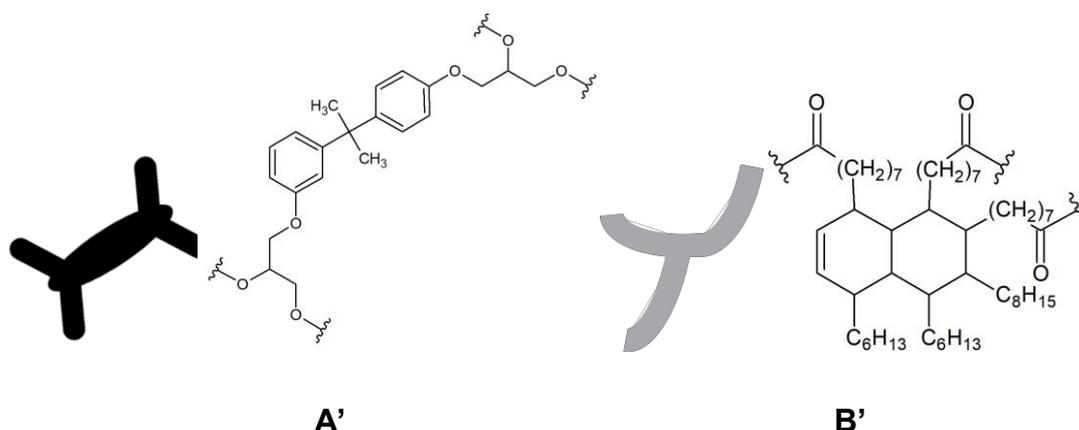
## THEORETICAL PROBLEM 17

### Vitrimers

Vitrimers are a new type of material, in which chemical bonds are constantly exchanged. It has been developed in France by L. Leibler *et al.* in the early 2010s. These polymers can be easily processed at high temperature, which is used in self-healing materials. Here, we will examine an early example of vitrimer. The polymer network below was made using **A** and **B** under acidic conditions.



**17.1** Write a structure for the reactive group **Q** in **B**, taking into account that the network above is composed of **A'** and **B'**, interlinked by ester bonds (wiggly lines).



Each epoxy group in **A** reacts with two **Q** groups from **B** molecules, to form two esters. **A** has two epoxy groups and **B** has three **Q** groups. **A** is added to **B** in a 3 : 4 ratio. Of all the reactive groups (epoxy and **Q** groups), a fraction  $\zeta$  reacts (conversion =  $\zeta \times 100$ ), such that at 100% conversion ( $\zeta = 1.0$ ), all epoxy groups in **A** and all **Q** groups in **B** have reacted.

17.2 Express the average number of ester bonds formed per molecule of **A**,  $n_{EA}$ , as a function of  $\zeta$ .

17.3 Express the average number of ester bonds formed by a molecule **B**,  $n_{EB}$ , as a function of  $\zeta$ .

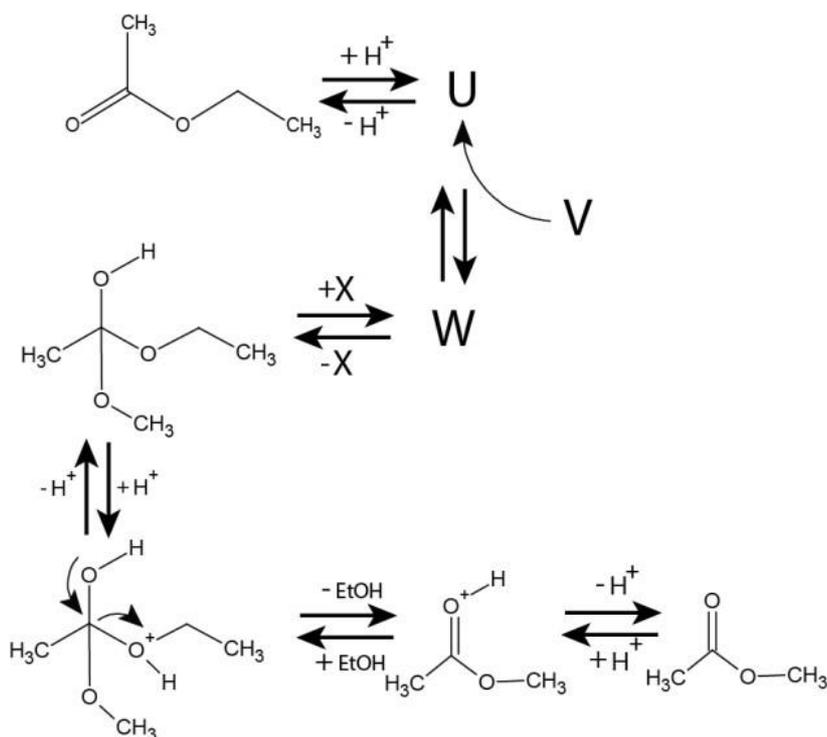
The total number of molecules **A** and **B** is given by  $N = N_A + N_B$ .

17.4 Calculate the total number of formed ester bonds,  $N_E$ , expressed as a function of  $N_A$ ,  $N_B$ ,  $n_{EA}$ , and  $n_{EB}$ .

17.5 Calculate the average number of ester bonds attached to a molecule,  $\underline{n}$ , as a function of  $\zeta$  (e.g. **A** has four ester bonds attached to it).

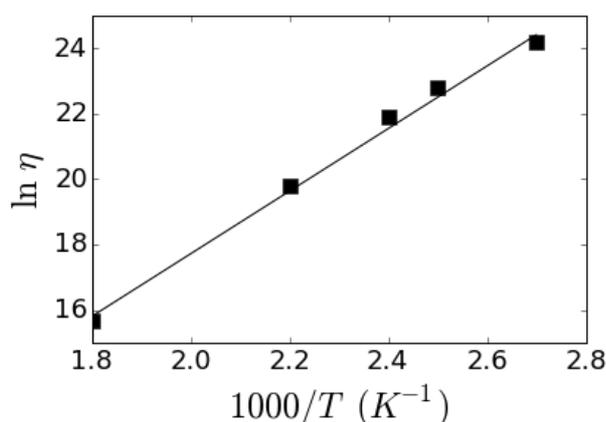
17.6 Calculate the value of  $\zeta$  for which a crosslinked network starts to form.

The network becomes dynamic when the chemical bonds interchange constantly. In order to reach this state, esterification reactions are essential. The reaction mechanism for acid catalyzed-transesterification of ethyl acetate ( $\text{CH}_3\text{COOEt}$ ) with an unknown alcohol **V** is provided below.



17.7 Draw the missing structures **U**, **V**, **W**, **X**.

If transesterification reactions are rapid enough, a vitrimer can easily be deformed. The resistance to flow  $\eta$  (viscosity) was measured and  $1/\eta$  was shown to follow an Arrhenius law. Viscosity  $\eta$  is proportional to the time needed for a material to adjust itself, which is inversely proportional to the transesterification reaction rate constant  $k$ :  $\eta \propto 1/k$ . The plot and table below show that  $1/\eta$  follows an Arrhenius law.



$\eta$ (Pa s)	$6.310 \times 10^5$	$3.981 \times 10^7$	$3.162 \times 10^9$	$7.943 \times 10^9$	$3.134 \times 10^{10}$
$\ln \eta$	15.66	19.80	21.87	22.80	24.17
$1000/T$ ( $K^{-1}$ )	1.8	2.2	2.4	2.5	2.7

**17.8** Using the data provided in the table, determine the activation energy  $EA$  for transesterification in  $\text{kJ mol}^{-1}$ .

The viscosity  $\eta$  of the material can be controlled by changing the reaction conditions.

**17.9** For the following statements, choose the correct answer:

I) When a transesterification catalyst is added to the material

- $\eta$  increases        $\eta$  remains constant        $\eta$  decreases

II) When the temperature is decreased

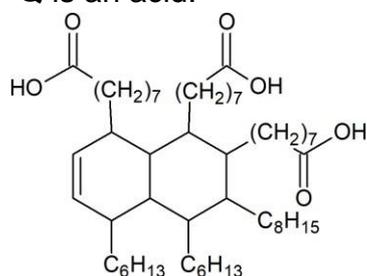
- $\eta$  increases        $\eta$  remains constant        $\eta$  decreases

III) When the pH is lowered from neutral to acidic

- $\eta$  increases        $\eta$  remains constant        $\eta$  decreases

## SOLUTION OF PREPARATORY PROBLEM 17

17.1 **Q** is an acid:



(Other acceptable answers possible, e.g. **Q** can be an ester)

17.2 Each epoxy group in **A** reacts with two reactive groups from **B**, thus forming two esters. Since there are 2 epoxy groups, there can be at most 4 esters formed by a molecule of **A**. If the conversion is  $\zeta$ , it follows that  $n_{EA} = 4\zeta$ .

17.3 Each reactive group in **B** can form one ester. Since there are three reactive groups per **B** molecule, a **B** molecule can form three ester bonds at most. Therefore,  $n_{EB} = 3\zeta$ .

17.4 Every **A** molecule forms on average  $n_{EA}$  ester bonds, every **B** molecule forms on average  $n_{EB}$  ester bonds. Since these bonds are shared, we find for the total number of formed esters:

$$N_E = \frac{1}{2} N_A n_{EA} + \frac{1}{2} N_B n_{EB}$$

17.5 The number of attached ester groups  $n_E$  counts every ester bond twice (once per attachment). Consequently, we have:

$$n_E = \frac{2 N_E}{N} = \frac{N_A}{N} n_{EA} + \frac{N_B}{N} n_{EB}$$

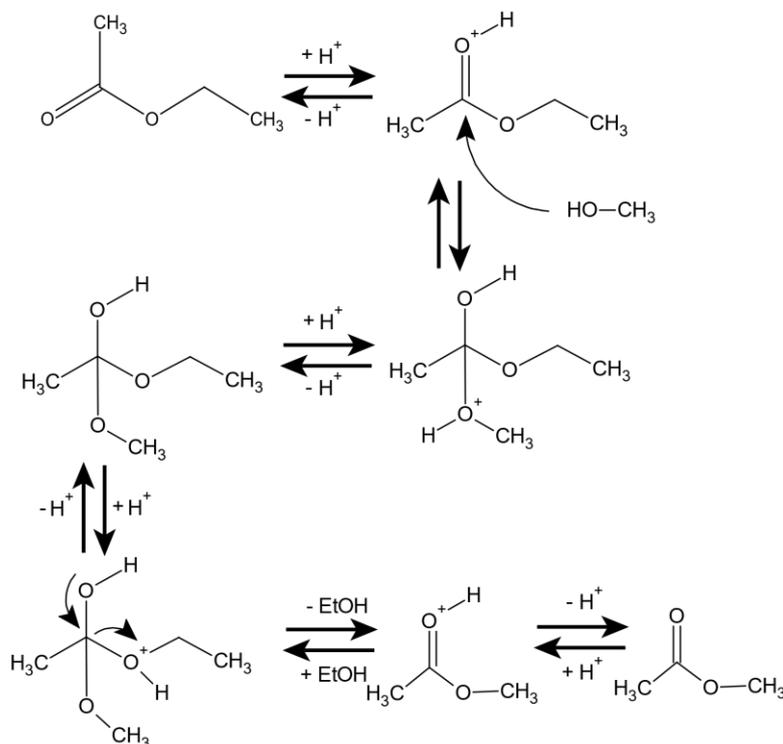
**A** and **B** are mixed in a 3 : 4 ratio. So 3 out of 7 molecules are **A** molecules- ( $N_A/N = 3/7$ ) and 4 out of 7 molecules are **B** molecules ( $N_B/N = 4/7$ )

Therefore, the number of formed ester bonds per a molecule can be expressed as:

$$n = (3/7) 4 \zeta + (4/7) 3 \zeta = 24/7 \zeta$$

17.6 To obtain a crosslinked network, a molecule should on average have more than two links to a neighbor. Then,  $n > 2$ , which means  $\zeta > 7/12$ .

## 17.7



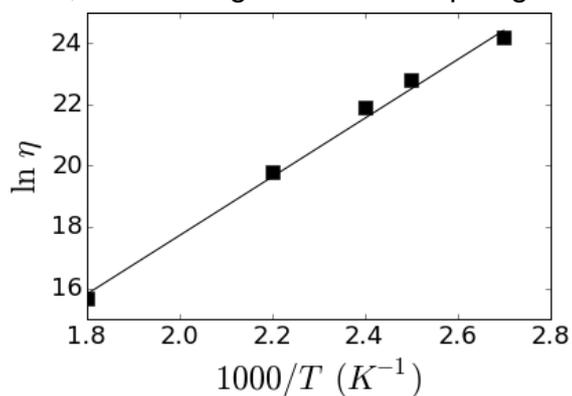
**U, W** are protonated intermediates, given in above figure

**V** = methanol ( $\text{HOCH}_3$ ), **X** =  $\text{H}^+$  see also the above figure.

## 17.8

$$\eta(T) \propto \frac{1}{k} = \frac{1}{A} \exp\left(\frac{E_A}{RT}\right) \text{ hence } \ln(\eta) = \frac{E_A}{R} \times \frac{1}{T} + C \text{ is a constant}$$

Then, a linear regression of the plot gives:



$$y = 9.65x - 1.54$$

$$r^2 = 0.994$$

From which we estimate  $E_A = R \times 1000 \times 9.65 = 80.2 \text{ kJ mol}^{-1}$ .

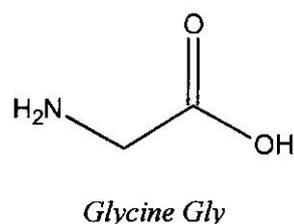
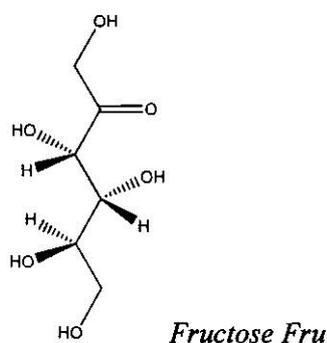
**17.9** Correct answers: Anything that makes  $k$  increase, makes also  $\eta$  decrease, so:

- I)  $\eta$  **decreases** (transesterification catalyst increases  $k$ )
  - II)  $\eta$  **increases** (lower temperature decreases  $k$ , see Arrhenius)
  - III)  $\eta$  **decreases** (transesterification can be base-catalyzed or acid- catalyzed)
-

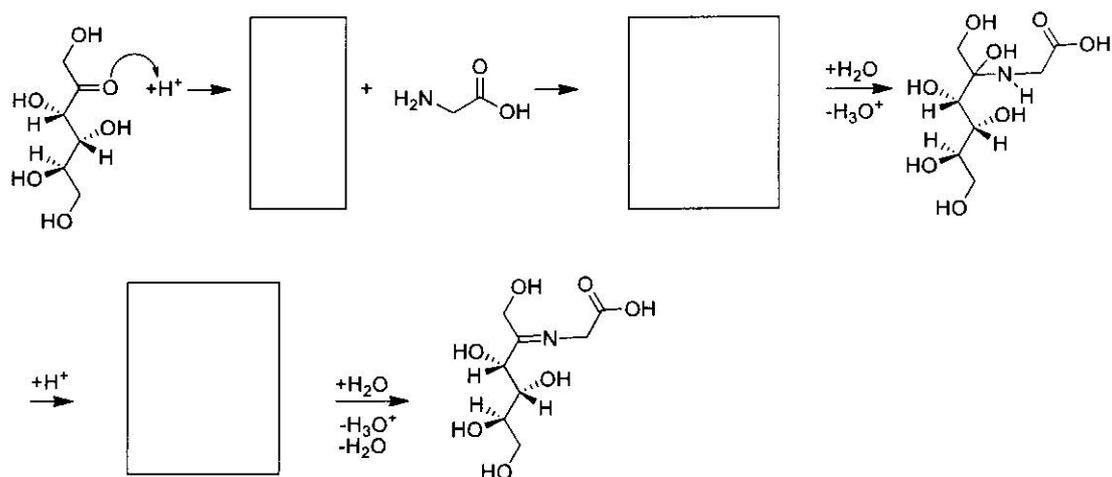
## THEORETICAL PROBLEM 18

### A kinetic study of the Maillard reaction

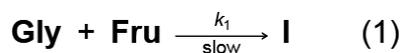
The Maillard reaction is a chemical reaction that involves aminoacids and reducing sugars. It leads to brown molecules (melanoidin polymers) without enzymatic catalysis. Many other products can be formed through the different steps of its complex mechanism. These products can notably enhance taste and flavors. The Maillard reaction was first described by the French chemist L C Maillard in 1912 (L. C. Maillard, *Compt. Rend.*, 1912). This reaction is observed during roasting and toasting processes of meat, bread, coffee, etc. (S. Martins *et al.*, *Trends in Food Science & Technology*, 2001). In the first attempt to describe the Maillard reaction, a reactive model with glycine amino-acid ( $\text{H}_2\text{NCH}_2\text{COOH}$ ) and fructose reducing sugar ( $\text{C}_6\text{H}_{12}\text{O}_6$ ) is considered.



- 18.1** Fill in the proposed mechanism for the first step of addition of glycine on fructose that leads to an imine (acidic conditions).

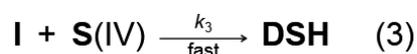


In order to describe the formation of melanoidin products, the following mechanism has been proposed (S. Mundt *et al.*, J. Agric. Food Chem., 2003):



where **Gly** stands for glycine, Fru for fructose, I an unknown intermediate and M the melanoidin product.

Previous kinetic studies showed that step (1) exhibits a zero kinetic order for glycine Gly and step (2) a first kinetic order for the intermediate I. We will now determine the rate constants  $k_1$  and  $k_2$  as well as the kinetic order (named  $\alpha$ ) for the fructose during step (1). We consider the reaction of the intermediate product I with sodium metabisulphite, S(IV). This reaction is known to be thermodynamically and kinetically favorable and leads to a stable product DSH (3,4-dideoxy-4-sulfohexosone), which does not react with other compounds of the reaction medium. This reaction strongly favors products and is fast.



Sodium metabisulphite reacts with Ellman's reagent (5,5'-dithiobis-(2-nitrobenzoic acid)). It produces a colored compound, the concentration of which can be spectrophotometrically determined at 412 nm. Sodium metabisulphite does not interact with other reactants or products. The melanoidin product M absorbs at 470 nm and its absorption coefficient in these conditions is  $\epsilon_M = 478 \text{ L mol}^{-1} \text{ cm}^{-1}$ . All other compounds are considered colorless in the range of the UV- visible wavelengths.

1 dm<sup>3</sup> of solution was prepared with a sodium acetate/acetic acid buffer (pH = 5.5). All the experiments were carried out at 55 °C. The length of the cell was  $l = 1 \text{ cm}$  for the spectrophotometric measurements.

**18.2** Write down the rates of disappearance of Fru and I.

**18.3** Controlling the pH and temperature of the chemical mixture is compelling in this study case. Choose the correct answer(s).

- Equilibrium constants can depend on pH.
- Equilibrium constants can depend on temperature.
- Rate constants can depend on equilibrium constants.
- Rate constants can depend on pH.
- Rate constants can depend on temperature.

The first experiment (A) was carried out by adding  $n_{\text{Fru},A,0} = 1$  mol of fructose,  $n_{\text{Gly},A,0} = 0.5$  mol of glycine and  $n_{\text{S(IV)},A,0} = 0.02$  mol of S(IV) at the same time to  $1 \text{ dm}^3$  sodium acetate/acetic acid buffer. Every 15 hours (roughly), an aliquot of  $1 \text{ cm}^3$  was extracted from the reactive medium, put in a cell of  $l = 1 \text{ cm}$  and a drop of Ellman's reagent was added. The absorbance was measured after stirring. Results obtained from this experiment are shown in figure 1.

**18.4** Choose a wavelength to measure the absorbance of the aliquots of experiment (A).

**18.5** Demonstrate that the concentration  $[\text{Fru}]$  of fructose at time  $t$  can be deduced from the concentration  $[\text{S(IV)}]$  at time  $t$  and the initial concentrations  $[\text{S(IV)}]_0$  and  $[\text{Fru}]_0$  as:

$$[\text{Fru}] = [\text{Fru}]_0 - [\text{S(IV)}]_0 + [\text{S(IV)}]$$

**18.6** Using the following graph and the rate equations determined in question 2, determine the kinetic order  $\alpha$  of fructose in step (1) of the mechanism. It can be equal to 0, 1 or 2.

**18.7** Determine the kinetic rate constant  $k_1$ .

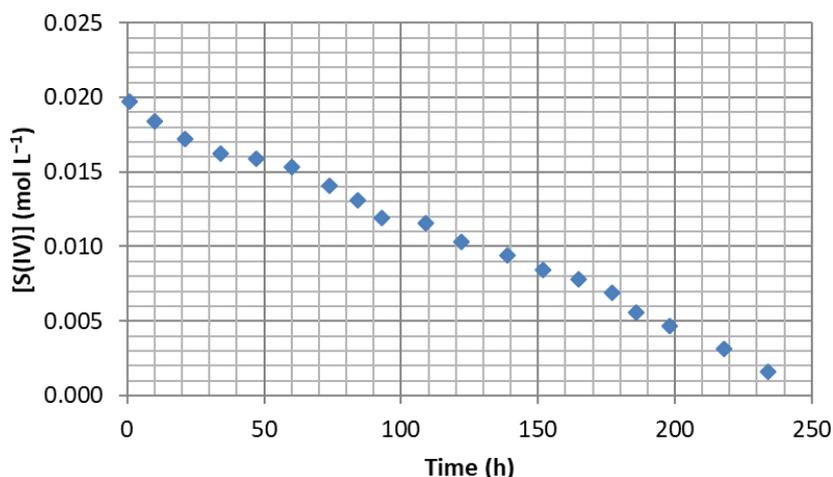


Figure 1:  $[\text{S(IV)}]$  as a function of time for the fructose - glycine - sodium metabisulphite S(IV) reaction

A second experiment (B) was carried out by adding  $n_{\text{Fru},B,0} = 1$  mol of fructose and  $n_{\text{Gly},B,0} = 0.5$  mol of glycine without sodium metabisulphite to a  $1 \text{ dm}^3$  sodium acetate/acetic acid buffer. A magnetic stirrer was used all along the experiment. Every 6 hours, the absorbance of an aliquot of  $1 \text{ cm}^3$  was directly measured at  $470 \text{ nm}$  in a cell of

$l = 1$  cm. The obtained data is shown in figure 2. Given the steps (1) and (2), the concentration of the melanoidin product  $[M]$  can be written as:

$$[M] = k_1 t - \frac{k_1}{k_2} (1 - e^{-k_2 t})$$

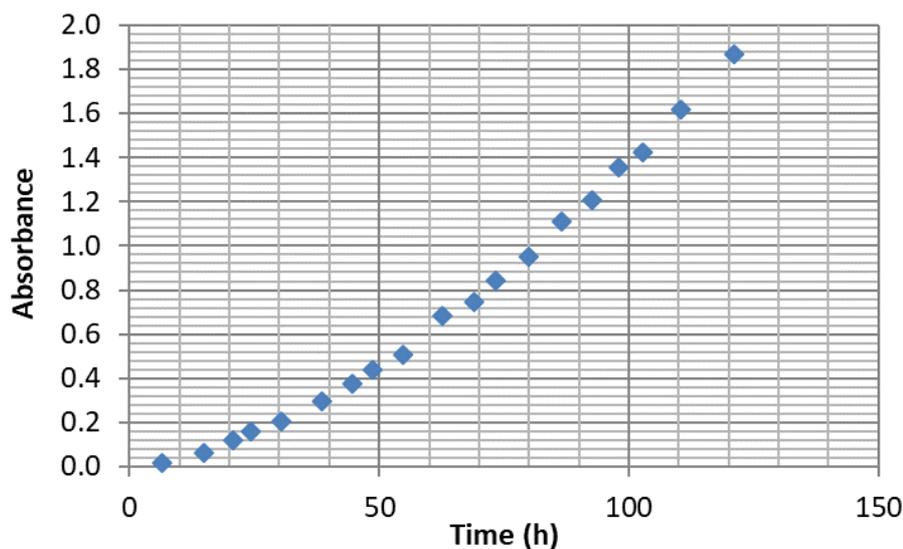


Figure 2:  $A_{470}$  (absorbance at 470 nm) as a function of time for the fructose - glycine reaction

**18.8** Determine graphically the value of  $dA_{470}/dt$  ( $t = 80$  h) (derivative of  $A_{470}$  absorbance at  $t = 80$  h) based on Fig. 2.

$t$ (h)	15.0	30.5	44.6	62.7	80.0
$dA_{470}/dt$ ( $\text{h}^{-1}$ )	$6.95 \times 10^{-3}$	$9.22 \times 10^{-3}$	$1.35 \times 10^{-2}$	$1.82 \times 10^{-2}$	

*Derivative of  $A_{470}$  as a function of time data for the fructose – glycine reaction*

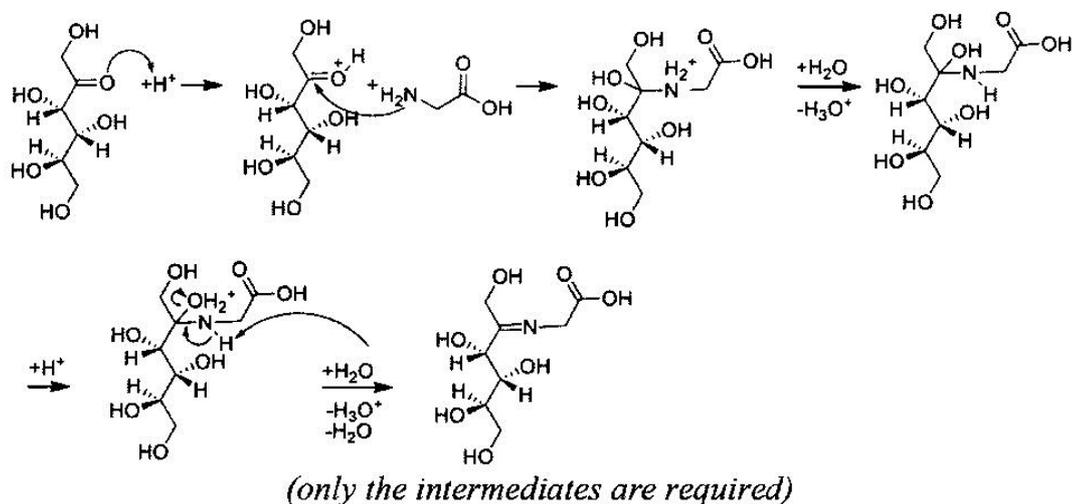
**18.9** Assuming that :

$$\ln \left[ 1 - \frac{1}{\epsilon_M l k_1} \frac{dA_{470}}{dt} \right] = -k_2 t$$

determine the rate constant  $k_2$ .

## SOLUTION OF PREPARATORY PROBLEM 18

### 18.1



18.2 The rate equations can be written:

$$-\frac{d[\text{Fru}]}{dt} = k_1 [\text{Fru}]^{\alpha}$$

$$-\frac{d[\text{I}]}{dt} = -k_1 [\text{Fru}]^{\alpha} + k_2 [\text{I}]$$

18.3 Correct answers:

Equilibrium constants can depend on temperature. Rate constants can depend on pH. Rate constants can depend on temperature.

18.4 **S(IV)** is known to react with Ellmann's reagent to form a colored compound with an absorbance maximum at 412 nm. Hence, 412 nm is an appropriate wavelength to work at as **S(IV)** reacts completely and quickly with the intermediate **I**. Thus, no melanoidin is likely to be formed.

18.5 Reaction (2) is hindered by the faster reaction (3) between **I** and **S(IV)**, thus, reaction (1) gives:  $[\text{I}] = [\text{Fru}]_0 - [\text{Fru}]$ .

Reaction (3) between **I** and **S(IV)** is fast and complete. Knowing what remains of **S(IV)** in the presence of Ellman's reagent, the concentration of **I** at a time  $t$  can be deduced:  $[\text{I}] = [\text{S(IV)}]_0 - [\text{S(IV)}]$ .

It can thus be shown that:  $[\text{Fru}] = [\text{Fru}]_0 - [\text{S(IV)}]_0 + [\text{S(IV)}]$ .

18.6 According to question 2:  $d[\text{Fru}]/dt = k_1 [\text{Fru}]^{\alpha}$

As no **M** is produced, the reaction can be followed by a kinetic order analysis.

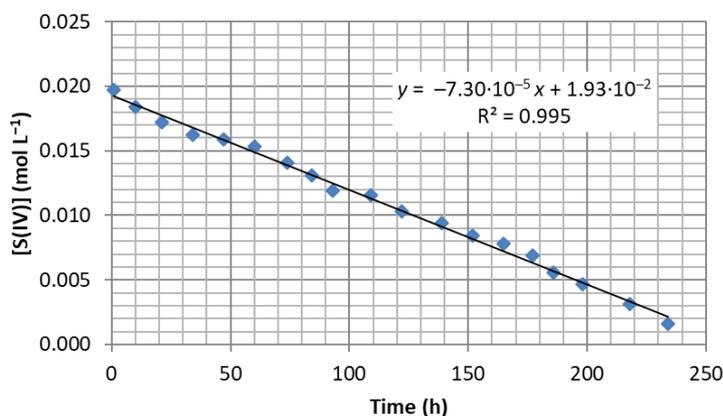
Case  $\alpha = 0$ :  $[\text{Fru}] = [\text{Fru}]_0 - k_1 t$

Case  $\alpha = 1$ :  $\ln[\text{Fru}] = \ln[\text{Fru}]_0 - k_1 t$

Case  $\alpha = 2$ :  $\frac{1}{[\text{Fru}]} = \frac{1}{[\text{Fru}]_0} + k_1 t$

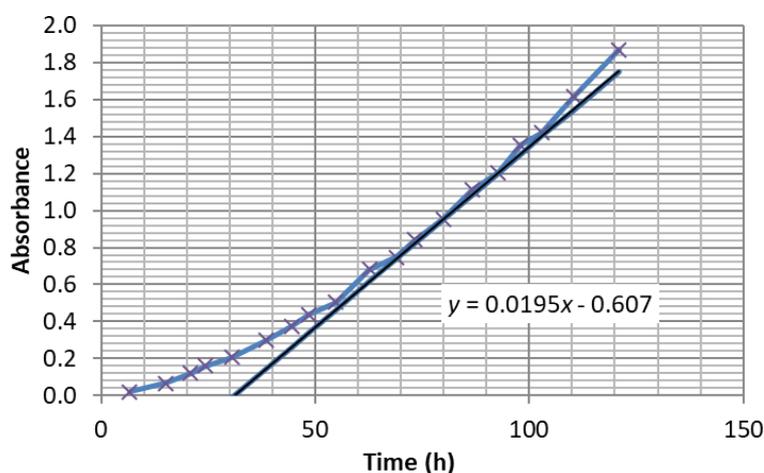
The following plot is a straight line: the assumption  $\alpha = 0$  is the correct one.

**18.7** By graphical calculation of the slope:



$$k_1 = 7.3 \times 10^{-5} \text{ mol L}^{-1} \text{ h}^{-1}$$

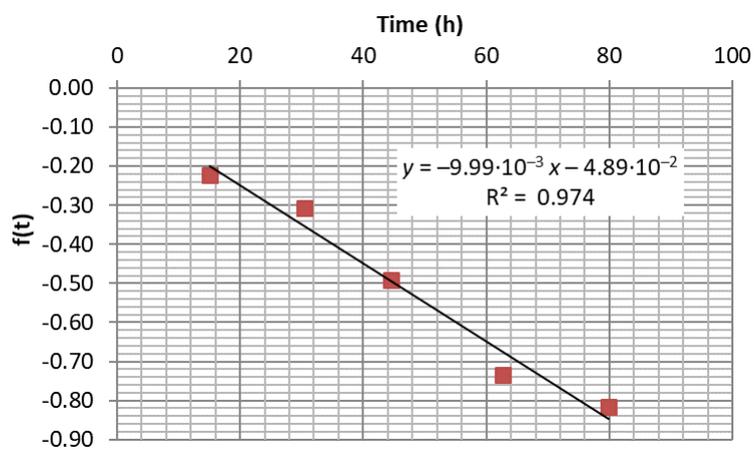
**18.8** By graphical measurement of the slope:



$$dA_{470}/dt \Big|_{t=80 \text{ h}} = 0.019 \text{ h}^{-1}$$

**18.9** The following function can be plotted versus time:

$$\ln \left[ 1 - \frac{1}{\epsilon_M l k_1} \frac{dA_{470}}{dt} \right] = f(t)$$

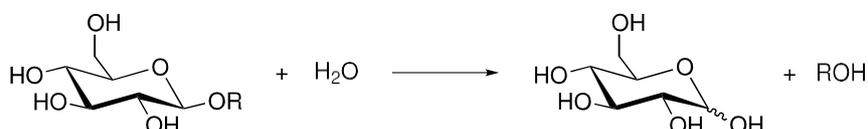


$$k_2 = 9.99 \times 10^{-3} \text{ h}^{-1}$$

## THEORETICAL PROBLEM 19

### Glycosidases and inhibitors

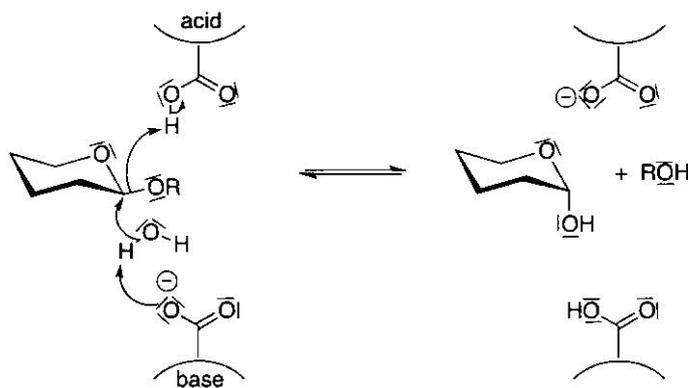
The glycosidic bond is one of the most stable bonds among biological polymers. This bond is found in DNA, in glycoproteins and in polysaccharides. Glycosidases, also called glycoside hydrolases, are enzymes that catalyze this reaction (scheme 1). They are the most abundant and most efficient enzymes in nature: they can increase the speed of the C—O bond cleavage reaction by a factor of  $10^{17}$ .



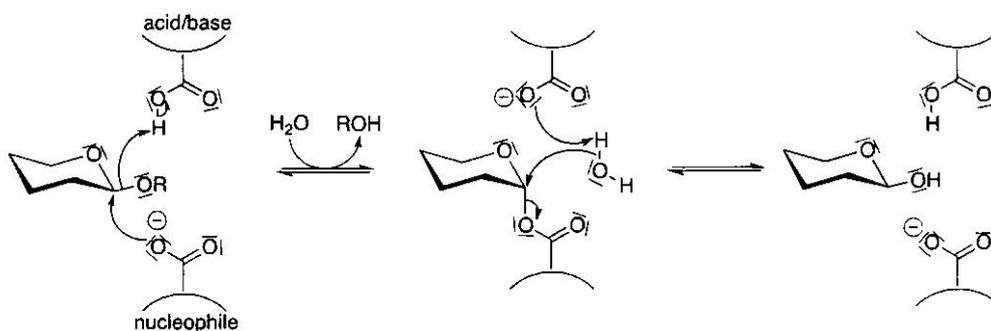
Scheme 1: Hydrolysis of the glycosidic bond

### Mechanism of hydrolysis catalyzed by glycosidase

The hydrolysis of the glycosidic bond can occur with inversion (scheme 2) or with retention of the configuration (scheme 3).

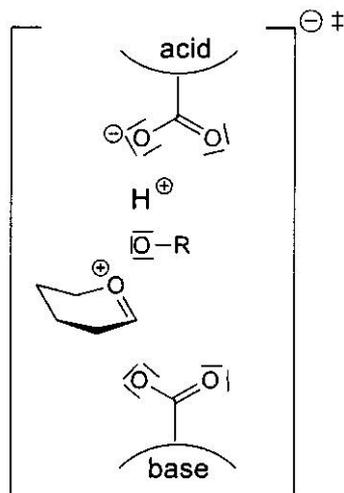


Scheme 2: Mechanism with inversion of configuration



Scheme 3: Mechanism with retention of configuration

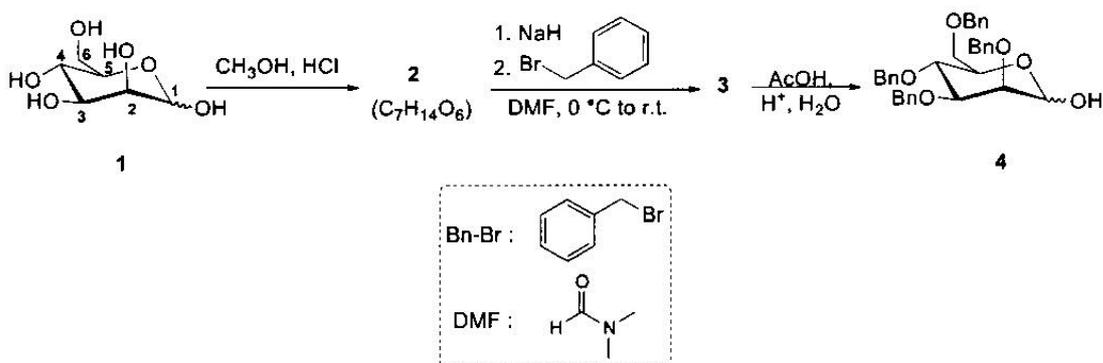
- 19.1 Complete the structure of the transition state (scheme 4) for the mechanism with retention of configuration (step 1), with forming and breaking bonds symbolized by dashed lines (---).



Scheme 4: Structure of the transition state of the first step of the mechanism with retention of configuration

### Synthesis of a glycosidase inhibitor

Given the essential role of glycosidases, glycosidase inhibitors are of great interest for researchers: they allow a better understanding of the enzymatic mechanisms of hydrolysis of the glycosidic bond, but they are also important for therapeutic applications because of the large number of diseases involving this type of enzymes (diabetes, influenza, cystic fibrosis, etc.). One way to obtain carbohydrate mimics that could act as inhibitors is to replace the endocyclic oxygen atom with a nitrogen atom. These inhibitors mimic reaction intermediates or transition states of glycosidic hydrolysis. In this part, we study the synthesis of a mannoimidazole-type  $\beta$ -mannosidase inhibitor.



Scheme 5

In the first step, compound **2** is formed from a natural carbohydrate **1**, which reacts in an acidic environment with methanol.

**19.2** Give the number of the most electrophilic carbon of **1**. Draw a tautomeric form in acidic environment to justify your answer.

**19.3** Compound **2** is  $C_7H_{14}O_6$ . Draw its topological formula.

Compound **2** reacts with sodium hydride NaH and benzyl bromide Bn-Br, to give compound **3**.

**19.4** Chose the correct statement indicating the reactivity of sodium hydride:

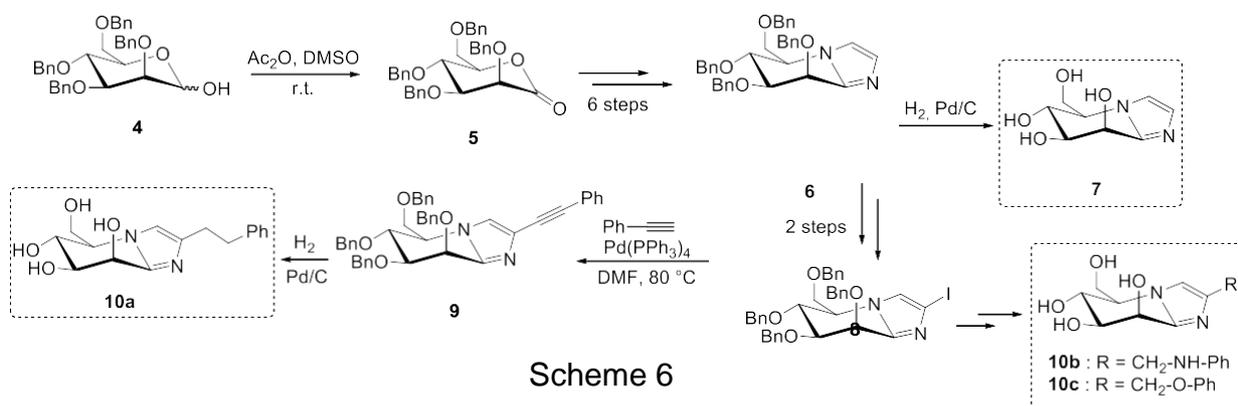
- base  
 acid  
 nucleophile  
 electrophile

**19.5** Chose the correct statement indicating the reaction that occurs in a second step:

- nucleophilic addition  
 nucleophilic substitution  
 elimination  
 electron transfer

**19.6** Draw the structure of compound **3**.

Compound **4** is obtained after hydrolysis of the acetal function of **3** to get a hemiacetal function.



Compound **4** yields lactone **5**. A bicyclic structure is then obtained in **6** steps, not detailed here. From there, product **7** is obtained after deprotection of the alcohol functions of **6** with dihydrogen in the presence of Pd/C. Three analogs of **7** are then synthesized from **6** in **4** steps (**10a**, **10b**, **10c**).

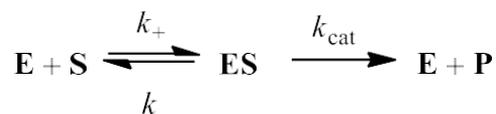
**19.7** Write down the redox half-reaction between **4** and **5**.

**19.8** Using the structure given in question 1, draw a scheme explaining the mode of action for the mimic 7.

A library of potential glycosidase inhibitors has thus been obtained. It is now necessary to know if the synthesized glycosidase inhibitors are true mimics of the transition state. To do so, we have to characterize the affinity of each inhibitor with the active site. A kinetic study based on a classical model in enzymatic kinetics, called the Michaelis-Menten model, is presented here.

### Michaelis-Menten kinetics

The following mechanism is often used to rationalize the early stages of enzymatic catalysis processes. In the first step, the enzyme **E** associates with the substrate **S** to give an enzyme- substrate complex denoted **ES**. This equilibrium is fast. The enzyme-substrate complex dissociates in a second step to give the product **P** and the regenerated catalyst **E**.



**19.9** Demonstrate that the reaction rate  $r$  is:

$$r = \frac{R_{\text{max}}[\text{S}]}{[\text{S}] + K_m} \text{ with } K_m = \frac{k_- + k_{\text{cat}}}{k_+} \text{ and } R_{\text{max}} = k_{\text{cat}}[\text{E}]_{\text{tot}}$$

and  $[\text{E}]_{\text{tot}}$  the total concentration of enzyme introduced in the solution.

**19.10** We consider the two cases where  $[\text{S}] \gg K_m$  and  $[\text{S}] \ll K_m$ . In both cases, determine the reaction rate  $r$  and draw the shape of the evolution of  $r$  as a function of  $[\text{S}]$ .

$k_{\text{cat}}$  is the rate constant of the transformation reaction of the enzyme-substrate complex into the product.  $K_m$  is called the Michaelis constant.

**19.11** In the case of  $k_- \gg k_{\text{cat}}$ , write the expression of  $K_m$ .

**19.12** Tick the right boxes to indicate the link between  $K_m$  and the affinity of the enzyme for the substrate:

	$K_m$ low	$K_m$ high
High affinity		
Low affinity		

In the presence of a competitive inhibitor, the inhibition constant  $K_i$  is the constant of the equilibrium:



where I is the inhibitor.

The concentration of inhibition  $\alpha$ , a typical concentration for which half of the enzymatic sites are occupied, can be measured. The following  $\alpha$  values were obtained for the different mimics studied on *Bacteroides thetaiotaomicron*  $\beta$ -mannosidase:

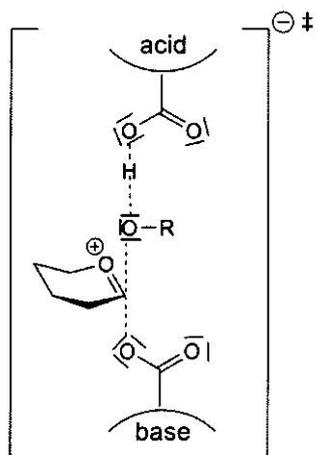
Mimic	7	10a	10b	10c	11	12
$\alpha$ (mol dm <sup>-3</sup> )	400	57	72	401	1000	975

**19.13** Write the relation between  $\alpha$  and  $K_i$ . Choose the best mimic, *i.e.* the mimic that exhibits the highest affinity with the enzyme.

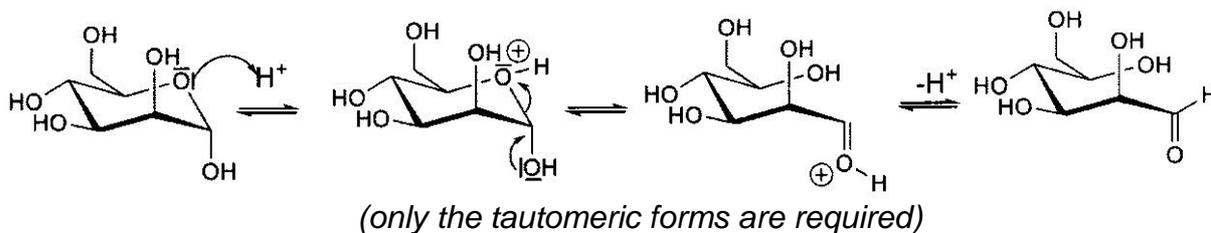
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## SOLUTION OF PREPARATORY PROBLEM 19

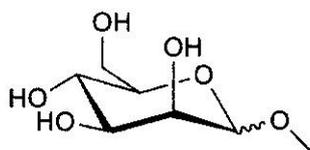
19.1 Structure of the transition state of the first step of the mechanism with retention of configuration:



19.2 Carbon 1



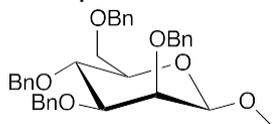
19.3 Compound 2:



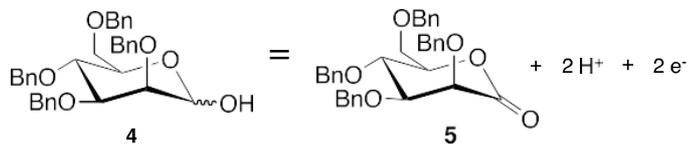
19.4 Correct statement: base

19.5 Correct statement: nucleophilic substitution

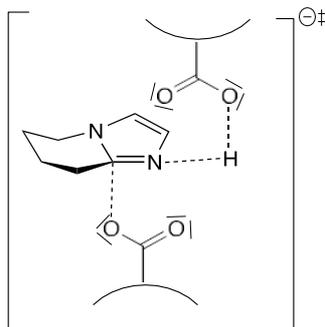
19.6 Compound 3:



## 19.7 Half-reaction between 4 and 5:



## 19.8 Mode of action for the mimic 7:



## 19.9 The first equilibrium is fast, then:

$$d[\text{ES}]/dt = k_+ [\text{E}][\text{S}] - k_- [\text{ES}] - k_{\text{cat}} [\text{ES}] = 0 \quad \text{and} \quad r = k_{\text{cat}}[\text{ES}]$$

Conservation of matter:

$$[\text{E}]_{\text{tot}} = [\text{E}] + [\text{ES}] \quad \text{thus} \quad [\text{E}] = [\text{E}]_{\text{tot}} - [\text{ES}]$$

If we replace [E] in the first expression, we get:

$$k_+([\text{E}]_{\text{tot}} - [\text{ES}])[\text{S}] - k_-[\text{ES}] - k_{\text{cat}}[\text{ES}] = 0$$

$$\text{thus} \quad [\text{ES}](k_+[\text{S}] + k_- + k_{\text{cat}}) = k_+[\text{S}][\text{E}]_{\text{tot}}$$

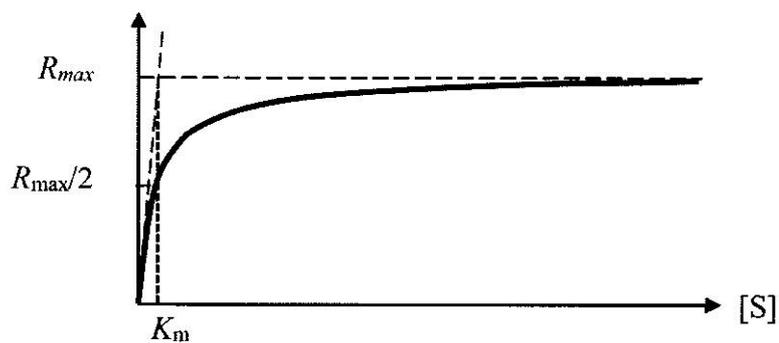
$$\Leftrightarrow [\text{ES}] = \frac{k_+[\text{E}]_{\text{tot}}[\text{S}]}{k_+[\text{S}] + k_- + k_{\text{cat}}}$$

As  $r = k_{\text{cat}}[\text{ES}]$  we deduce the expression:

$$r = \frac{k_{\text{cat}} [\text{E}]_{\text{tot}} [\text{S}]}{[\text{S}] + \frac{k_- + k_{\text{cat}}}{k_+}}$$

19.10 1<sup>st</sup> case:  $[\text{S}] \gg K_m$ :  $r = R_{\text{max}} = k_{\text{cat}} [\text{E}]_{\text{tot}}$

2<sup>nd</sup> case:  $[\text{S}] \ll K_m$ :  $r = R_{\text{max}}[\text{S}] / K_m$


 $[S] \ll K_m$ 
 $[S] \gg K_m$ 

**19.11** If  $k_{-1} \gg k_{cat}$ ,  $K_m = k_{-1} / k_1$ . It is the dissociation constant (affinity between enzyme and substrate).

**19.12**

	$K_m$ low	$K_m$ high
High affinity	x	
Low affinity		x

**19.13** At the equilibrium:  $K_i = ([E][I]) / ([EI])$  and for  $[I] = c_i$ ,  $[EI] = [E]$ , so  $c_i = K_i$ .

The mimic that seems to be the best is the one that displays the smallest dissociation constant  $K_i$ , that is the smallest value of  $c_i$ . It is thus 10a.

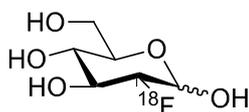
## THEORETICAL PROBLEM 20

### Fluoro-deoxyglucose and PET imaging

Positron Emission Tomography (PET) is a nuclear imaging method allowing *in vivo* investigations of the distribution of an isotope emitting positrons ( $\beta^+$ ) upon radioactive decay. Among the  $\beta^+$  emitters,  $^{18}\text{F}$  has found numerous applications due to its particular properties: ( $t_{1/2} = 109.74$  min; decay by  $\beta^+$  emission; specific activity of  $^{18}\text{F} = 6.336 \times 10^{19}$  Bq mol $^{-1}$ ).  $^{18}\text{F}$  can be introduced via a nucleophilic process using  $^{18}\text{F}^-$  obtained in water, after desolvation of the fluoride.

*N.B.:* Bq stands for the Becquerel unit. It is a unit of radioactivity corresponding to one disintegration per second.

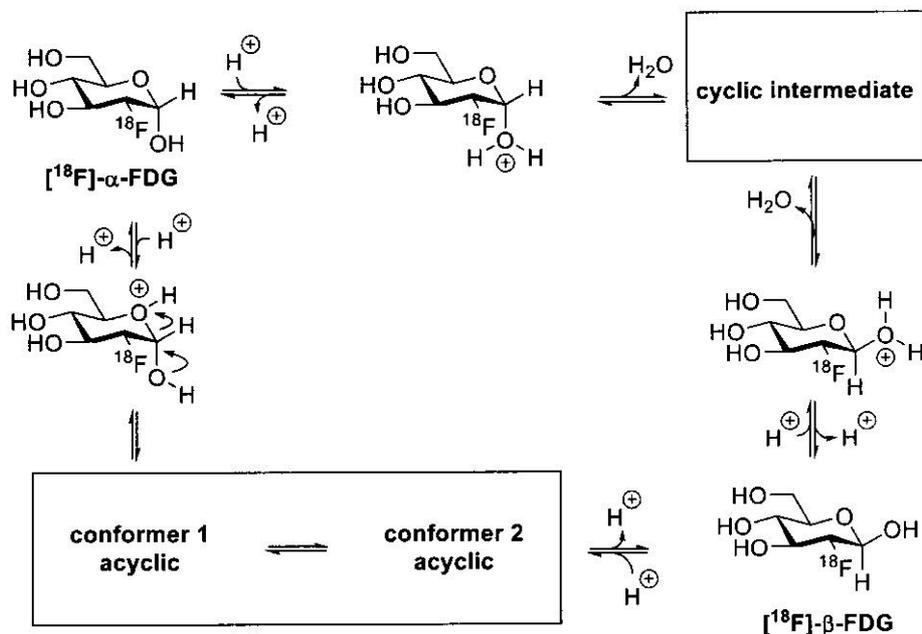
Among the very few radiolabelled molecules commercialized worldwide for PET imaging, 2- deoxy-2- $^{18}\text{F}$ fluoro-glucose ( $^{18}\text{F}$ -FDG) is the most widely used. This problem examines the formation of  $^{18}\text{F}$ -FDG from organic compounds and  $^{18}\text{F}^-$ .



$^{18}\text{F}$ -FDG

### Reactivity and stereochemistry at C<sup>1</sup>

The isomerization from the  $\alpha$  to the  $\beta$  form of  $^{18}\text{F}$ -FDG can occur according to two different mechanisms in protic media.



- 20.1** The endocyclic bond cleavage path makes use of the equilibrium between two acyclic forms that can recyclize to yield both compounds  $[^{18}\text{F}]\text{-}\alpha\text{-FDG}$  and  $[^{18}\text{F}]\text{-}\beta\text{-FDG}$ . Draw the two conformers of the acyclic form that lead to the formation of  $[^{18}\text{F}]\text{-}\alpha\text{-FDG}$  and  $[^{18}\text{F}]\text{-}\beta\text{-FDG}$ , respectively.
- 20.2** Choose the correct structural relationship(s) between  $[^{18}\text{F}]\text{-}\alpha\text{-FDG}$  and  $[^{18}\text{F}]\text{-}\beta\text{-FDG}$ .
- $[^{18}\text{F}]\text{-}\alpha\text{-FDG}$  and  $[^{18}\text{F}]\text{-}\beta\text{-FDG}$  are enantiomers.
- $[^{18}\text{F}]\text{-}\alpha\text{-FDG}$  and  $[^{18}\text{F}]\text{-}\beta\text{-FDG}$  are epimers.
- $[^{18}\text{F}]\text{-}\alpha\text{-FDG}$  and  $[^{18}\text{F}]\text{-}\beta\text{-FDG}$  are diastereoisomers.
- $[^{18}\text{F}]\text{-}\alpha\text{-FDG}$  and  $[^{18}\text{F}]\text{-}\beta\text{-FDG}$  are atropoisomers.
- 20.3** Draw the structure of the missing cyclic intermediate.

### Evolution of $^{18}\text{F}$ and molecular consequences of isotopic distribution and decay

$^{18}\text{F}$  is a radioactive isotope that decays by the emission of a positron  $0\beta^+$ .

- 20.4** Write down the nuclear equation for the radioactive decay of  $^{18}\text{F}$ .
- 20.5** Draw the molecular structure of the hexose arising from the decay of  $[^{18}\text{F}]\text{-FDG}$ .
- 20.6** Establish the equation of the radioactive decay as a function of time and determine the value of the radioactive constant ( $\lambda$ , that corresponds to the kinetic constant associated with the radioactive disintegration reaction).

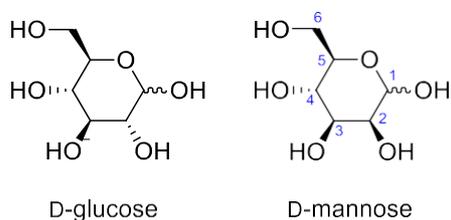
**20.7** Given that one injection to a human requires 370 MBq for imaging purposes and that the patient needs to rest for one hour before imaging is processed, calculate the remaining radioactivity (i) at the imaging processing time, (ii) after 4 h.

### 2-deoxy-2-[<sup>18</sup>F]fluoro-glucose by nucleophilic radiofluorination

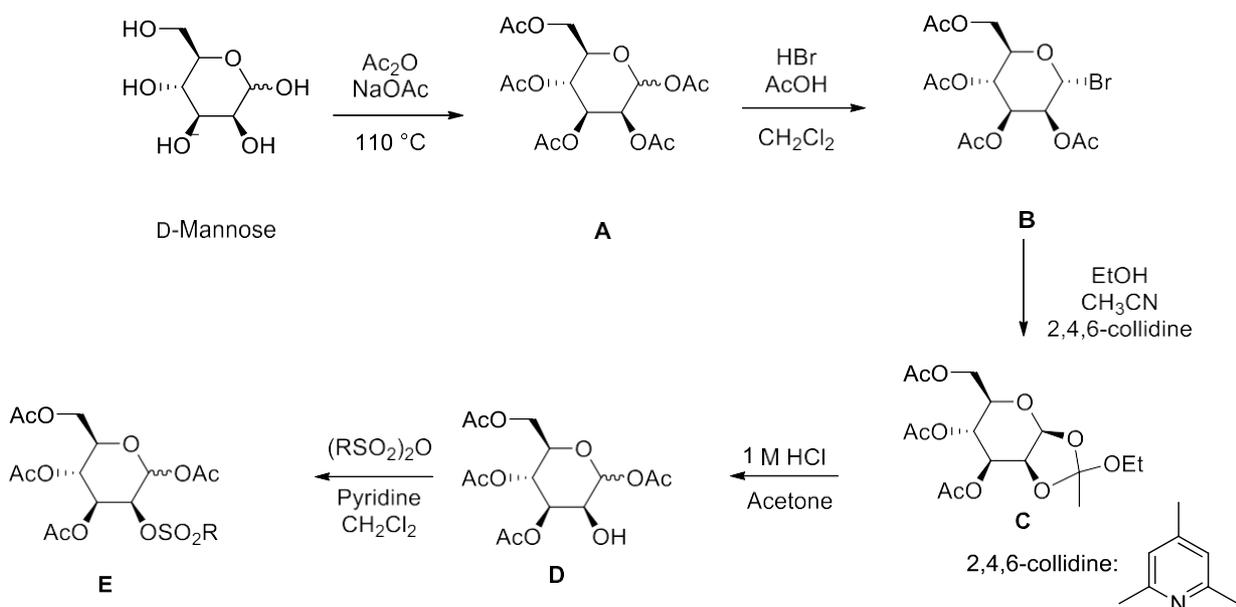
D-Mannose is the required starting material to achieve the synthesis of 2-deoxy-2-[<sup>18</sup>F]fluoro- glucose by nucleophilic radiofluorination.

**20.8** Among the following, choose what type of reaction can be used to convert a compound from the mannose class to a compound of the glucose class with complete stereocontrol:

- second-order nucleophilic substitution
- first-order nucleophilic substitution
- elimination-addition mechanism



The synthesis of the required peracetylated mannose sulfonate **E** is described below. **E** is the precursor for the radiofluorination reaction.



**20.9** The first step is a peracetylation of D-mannose yielding **A**. Represent the tetrahedral intermediate involved in the acetylation of alcohols under the used conditions.

**20.10** The transformation **A** → **B** favors the substitution of the acetate in  $\alpha$  position of the endocyclic oxygen atom. Draw the carbocationic intermediate involved in this transformation and represent the electronic effect responsible for the observed selectivity.

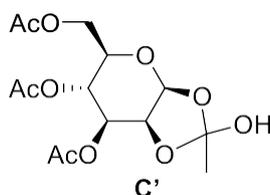
**20.11**  nucleophile In the transformation from **B** to **C**, choose the reactivity of ethanol among the following:

- electrophile  
 inert solvent

**20.12** In the same transformation, choose the reactivity of 2,4,6-collidine among the following:

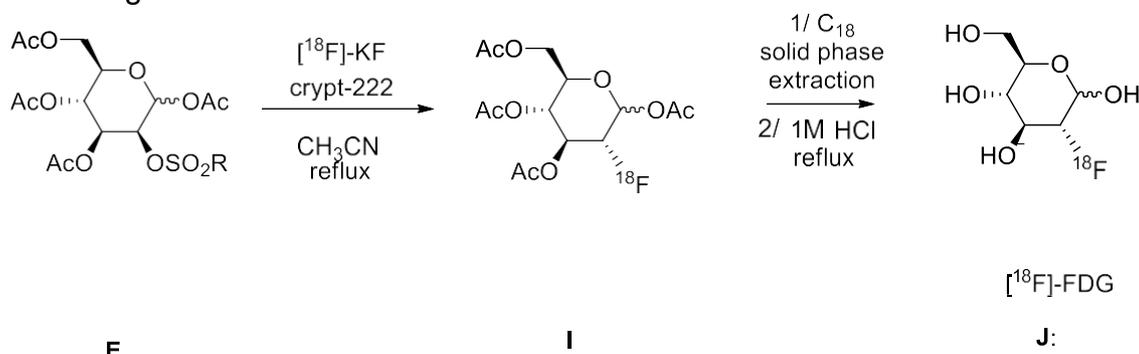
- nucleophilic catalyst  
 base  
 co-solvent

One of the intermediates in the transformation from **C** to **D** is **C'**.

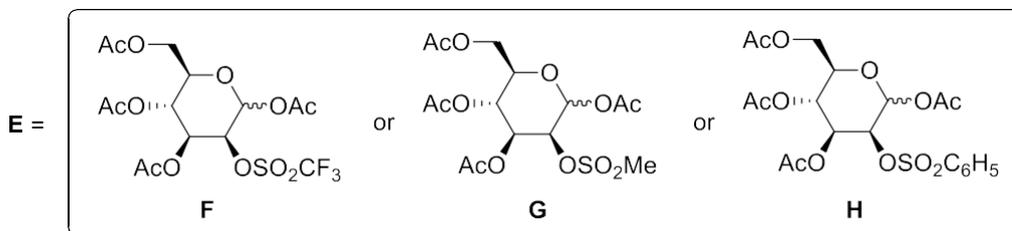


**20.13** Draw the structure of the ionic reaction intermediate between **C** and **C'**.

The formation of [ $^{18}\text{F}$ ]-FDG is finally achieved as follows. The compound of general formula **E** given above, can be either **F**, **G** or **H** as shown in the following scheme.

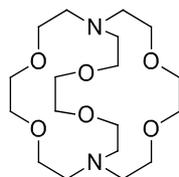


**20.14** Identify which of these three compounds **F**, **G** or **H** is the most reactive toward the



nucleophilic substitution leading to **I**.

Crypt-222 has the following structure:



**20.15** Why is the use of crypt-222 a way to increase fluoride nucleophilicity?

Choose the correct answer:

- Crypt-222 provides a chelation of potassium ion enhancing the fluoride nucleophilicity.
- Crypt-222 provides a chelation of fluoride ion enhancing its nucleophilicity.
- Crypt-222 selectively traps  $^{18}\text{F}^-$  and enhances the radiofluorination yield.
- Crypt-222 chelates E, promoting the substitution by a fluoride.

C18 solid phase extraction is a purification process that allows for the separation of polar compounds and non-polar compounds, the latter being first retained on a cartridge when carried out with water. The non-polar compounds are then eluted with an organic solvent.

**20.16** In the process of  $[^{18}\text{F}]$ -FDG production, the first wash (or elution) is carried out with a slightly acidic aqueous phase (pH around 3) followed by the second wash with acetonitrile. Choose the correct statement among the following (a list of  $pK_a$  values is given at the end of the problem):

- Crypt-222 is eluted in first place, then  $[^{18}\text{F}]$ -FDG.

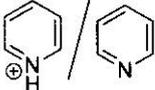
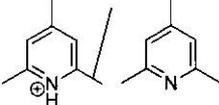
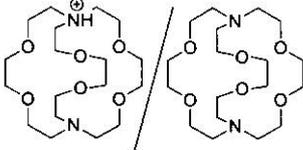
- [ $^{18}\text{F}$ ]-FDG is eluted in first place, then Crypt-222.
- Crypt-222 is retained in the  $\text{C}_{18}$  column, meanwhile glucose derivatives can be eluted.

**20.17** Considering that  $^{18}\text{F}^-$  is the limiting reagent, both [ $^{18}\text{F}$ ]-FDG and a monosaccharide are obtained after acid hydrolysis. Draw the structure of this monosaccharide. Why is there no need to separate this monosaccharide from [ $^{18}\text{F}$ ]-FDG before injection for *in vivo* imaging?

The whole process from the selected form of E to J takes 30 minutes and a 75% chemical yield.

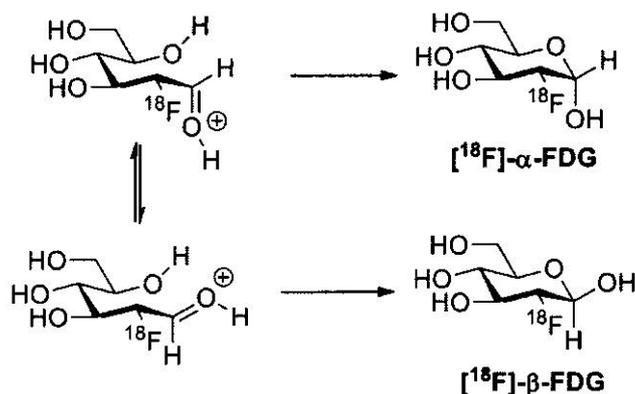
**20.18** Calculate the minimal molar amount of  $^{18}\text{F}^-$  required at the beginning of the process to allow one injection to human for imaging purposes.

**Data at 298 K:**

	<b><math>\text{p}K_{\text{a}}</math> values</b>
AcOH/AcO $^-$	4.8
ROH/RO $^-$	15.5 – 17
 <i>pyridinium/pyridine</i>	5.23
 <i>2,4,6-collidinium/2,4,6-collidine</i>	7.43
 <i>monoprotonated Crypt-222/Crypt-222</i>	8.5

## SOLUTION OF PREPARATORY PROBLEM 20

### 20.1

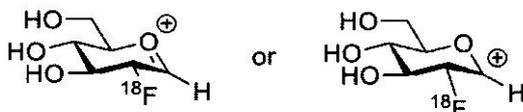


### 20.2 Correct statements:

$[^{18}\text{F}]\text{-}\alpha\text{-FDG}$  and  $[^{18}\text{F}]\text{-}\beta\text{-FDG}$  are epimers.

$[^{18}\text{F}]\text{-}\alpha\text{-FDG}$  and  $[^{18}\text{F}]\text{-}\beta\text{-FDG}$  are diastereoisomers.

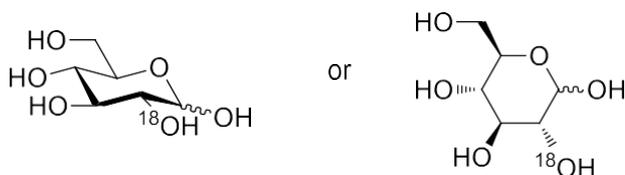
### 20.3



### 20.4



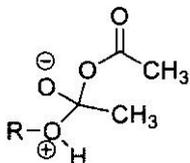
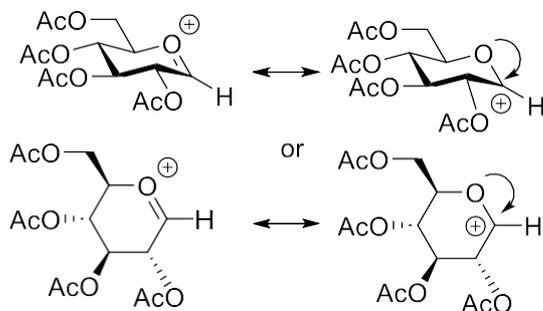
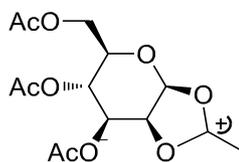
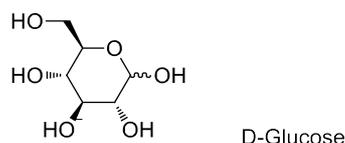
### 20.5



**20.6**  $N(t) = N(0) \times e^{-\lambda t}$ , hence  $\lambda = \ln(2) / t_{1/2} = 0.0063 \text{ min}^{-1}$

**20.7** (i) One hour (60 min) is required between injection and imaging, and  $N(0) = 370$  MBq so the remaining activity at the time of imaging is  $N(60) = N(0) \times \exp(-0.0063 \times 60) = 254$  MBq (ii) Similarly after 4 h (240 min),  $N(240) = 370 \times \exp(-0.0063 \times 240) =$

81.5 MBq

**20.8** Correct answer: second-order nucleophilic substitution**20.9****20.10****20.11** Correct answer: nucleophile**20.12** Correct answer: base**20.13** Mesomeric structures featuring the positive charge on both oxygens are also acceptable.**20.14** Correct answer: F**20.15** Correct answer: Crypt-222 provides a chelation of potassium ion enhancing the fluoride nucleophilicity.**20.16** Correct answer: Crypt-222 is eluted in first place, then [<sup>18</sup>F]-FDG.**20.17**

Glucose is not a toxic compound and can be injected together with FDG.

**20.18**  $370 \times 10^6$  Bq are required for one injection, the transformation and process from **E** to **J** take 30 min.

So  $N(0) = N(t) \times e^{\lambda t}$  with  $t = 30$  min and  $\lambda = 0.0063 \text{ min}^{-1}$  (according to question 6), thus  $N(0) = 447 \times 10^6$  Bq.

Chemical yield of 75%:  $n = N(0) / 0.75 = 447 \times 10^6 / 0.75 = 596 \times 10^6$  Bq are initially required. The determination of the amount of  $^{18}\text{F}^-$  is obtained by considering the specific activity of  $^{18}\text{F}$ .  $\text{SA} = 6.336 \cdot 10^{19} \text{ Bq mol}^{-1}$ :

$$\frac{596 \times 10^6}{6.336 \times 10^{19}} = 9.41 \times 10^{-12} \text{ mol (9.41 pmol)}$$

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## THEORETICAL PROBLEM 21

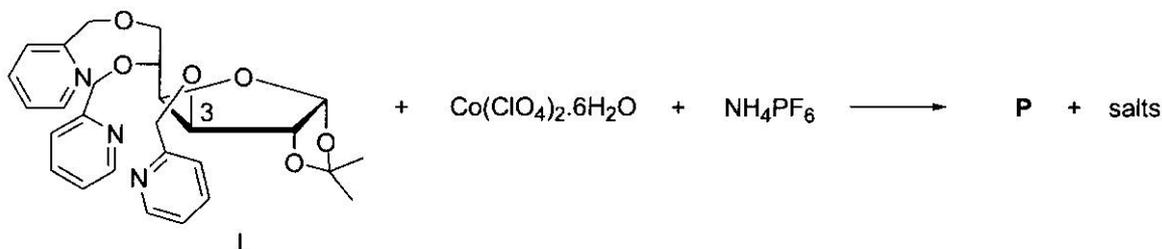
### Catalysis and stereoselective synthesis of cobalt glycoconjugates

Stereoselective synthesis of coordination compounds with chiral ligands is a blossoming field. This is mainly due to their potential applications in asymmetric catalysis and drug design. One strategy takes advantage of the sugar scaffold diversity by appending Lewis bases at selected positions around the sugar cycle (F. Cisnetti *et al.*, Dalton Trans., 2007 and F. Bellot *et al.*, Chem. Commun., 2005).

### Stereoselective synthesis of cobalt complexes

Glycoligand **L** and its epimer **L'** (on the C3 carbon) were first synthesized. Then, their corresponding cobalt complexes **P** and **P'** were prepared:

Below are gathered some results concerning physical and chemical studies on **P** and **P'** complexes.



Elemental analysis of a neutral salt of **P**

C: 38.50%; H: 3.71%; N: 4.99%;

Co: 7.00 %; P: 7.35 %.

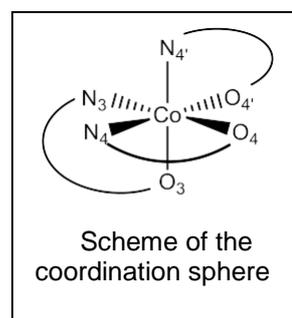
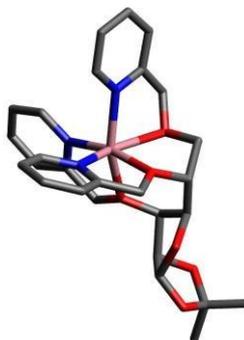
Visible spectrum of **P** (\*)

$\lambda_{\max} = 515 \text{ nm}$  ( $\epsilon = 50 \text{ L mol}^{-1} \text{ cm}^{-1}$ )  
 (\*)  $c_P = 10^{-2} \text{ mol L}^{-1}$  in an ethanol/acetone  
 (1/1) mixture

Spin state of **P**

$S = 3/2$

Crystal structure of **P** (X-ray diffraction).  
 Counter-ions have been deleted.

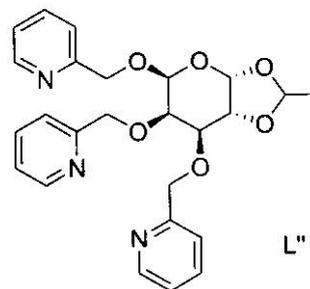
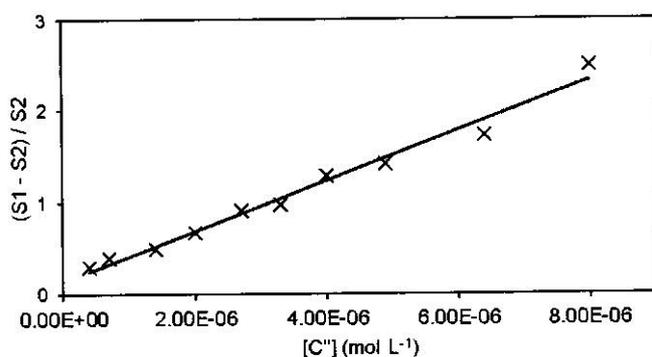


- 21.1** Draw  $L'$ , the epimer of glycoligand  $L$  on C3, using the Cram representation.
- 21.2** Thanks to the elemental analysis of a neutral salt of  $P$ , give the oxidation number of cobalt in  $P$ . Deduce the electronic configuration of the corresponding free ion.
- 21.3** Name the type of transition observed in the visible spectra of  $P$ .
- 21.4** Draw and fill the d orbital diagram of  $P$  consistent with the measured spin state. Name the type of field created by the ligand  $L$  (Low field/High field).
- 21.5** Draw the coordination sphere of  $P'$  (as shown in the inset).

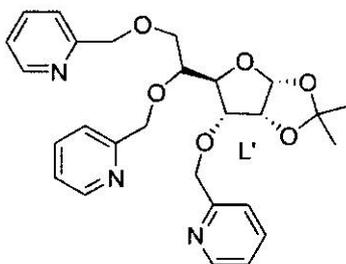
### SOD-like activity

Cobalt complex  $C''$  synthesized from glycoligand  $L''$  was tested for its potential superoxide dismutase-like (SOD-like) activity as this activity presents a pharmaceutical interest to protect against oxidative stress. A modified McCord-Fridovich assay was performed based on the kinetic competition for the reaction of superoxide with  $C''$  or ferricytochrome-C.

$S_1$  is the slope of the kinetic plot for the  $\text{cytcFe}^{\text{III}}$  reduction before the introduction of the complex and  $S_2$  is the slope recorded after the addition of putative SOD-mimic.



- 21.6** Draw the Lewis structure of superoxide radical anion  $\text{O}_2^{\cdot-}$ .
- 21.7** Write the redox reaction for the dismutation of superoxide radical that yields dioxygen and hydrogen peroxide.
- 21.8** Determine the half maximal inhibitory concentration,  $IC_{50}$ , of  $C''$  that corresponds to the inhibitor concentration needed to inhibit half of the response without inhibitor.

**SOLUTION OF PREPARATORY PROBLEM 21****21.1**

**21.2** Molecular formula of **L**:  $C_{27}H_{31}N_3O_6$  and  $M = 493.548 \text{ g mol}^{-1}$

Molecular formula of **P**:  $C_xH_yN_zO_aCo_bP_cF_d$

$$12x + y + 14z + 16a + 58.9b + 31c + 19d = M$$

Hypothesis:

- 1 ligand for 1 Co then  $x = 27$ ,  $y = 31$ ,  $z = 3$ ,  $a = 6$

- Co(II) or (III) then  $2 \text{ PF}_6^-$  or  $3 \text{ PF}_6^-$  then  $c = 2$ ,  $d = 12$  or  $c = 3$ ,  $d = 18$

Test with Co(II):  $493.548 + 58.93 + 2 \times 30.98 + 12 \times 19.00 = M = 842.438 \text{ g mol}^{-1}$

$$\%C: 27 \times 12.01 / 842.438 = 38.49\%$$

$$\%H: 31 \times 1.008 / 842.438 = 3.71\%$$

$$\%N: 3 \times 14.01 / 842.438 = 4.99\%$$

$$\%Co: 1 \times 58.93 / 842.438 = 7.00\%$$

$$\%P: 2 \times 30.98 / 842.438 = 7.35\%$$

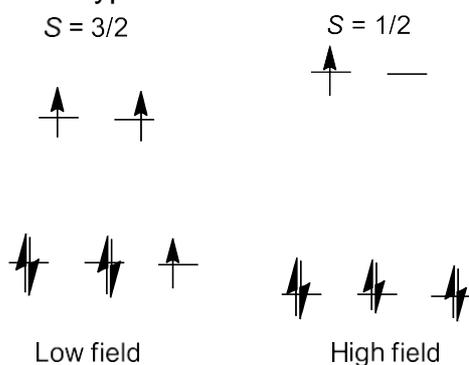
$$\%F: 12 \times 19.00 / 842.438 = 27.06\%$$

The result is consistent with the experimental data:

$$\text{Co(II): } Z = 27 \quad (1s)^2(2s)^2(2p)^6(3s)^2(3p)^6(4s)^0(3d)^7$$

**21.3**  $\lambda_{\text{max}} = 515 \text{ nm}$  ( $\epsilon = 50 \text{ L mol}^{-1} \text{ cm}^{-1}$ )  $\Rightarrow$  d-d band

## 22.4 Two hypotheses:

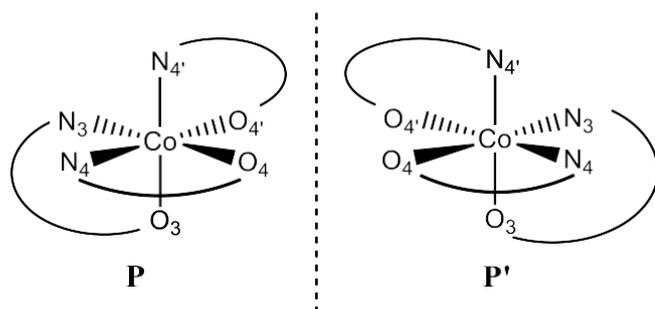


If the ligand is associated with a “Low field”, the resulting complex is “High spin”, while if the ligand is associated with a “High field”, the resulting complex is “Low spin”.

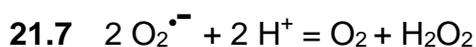
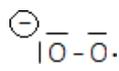
By comparison with the experimental data, a “High spin” complex is evidenced. Therefore,

L is a “**Low field**” ligand.

## 21.5 P' is a quasi-enantiomer that is formed simultaneously.



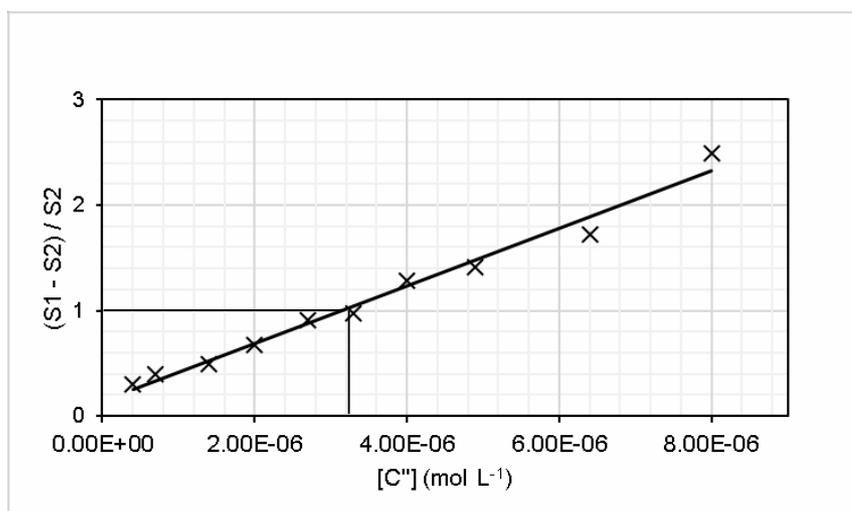
## 21.6

21.8 IC50 is obtained when  $S_2 = S_1 / 2$ 

$$\text{i.e. } (S_1 - S_2) / S_2 = 1$$

$$\text{IC50} = 3.2 \mu\text{mol dm}^{-3} \text{ (accepted values } 3.1 - 3.3 \mu\text{mol dm}^{-3}\text{)}$$

(in the graph as  $\mu\text{mol L}^{-1}$ )



## THEORETICAL PROBLEM 22

### Structural study of copper (II) complexes

#### Stoichiometry and molecular formula

The stoichiometry of a complex can be determined by various methods. One of them is Job's method, also known as the method of continuous variation. This method will be used to find the formula of the amine aqua copper (II) complex Z.

**22.1** Copper sulfate ( $\text{CuSO}_4$ ) in aqueous solution is blue. Write down the formula of the complex responsible for the color of the solution and the approximate wavelength  $\lambda_1$  at which this complex absorbs.

We consider the reaction between the hexaqua copper complex and ammonia in water. Its equilibrium constant is  $K^\circ$ . Let us assume that  $n$  ammonia ligands replace water in the coordination sphere of the metal ion. The corresponding reaction equation is then:



Several solutions were prepared by mixing a copper sulfate solution ( $c_0 = 0.044 \text{ mol dm}^{-3}$ ), an ammonia solution ( $c_0 = 0.044 \text{ mol dm}^{-3}$ ) and 2.0 g of ammonium nitrate  $\text{NH}_4\text{NO}_3$ . The absorbance of each solution was measured at  $\lambda_1$ . The blank solution contained  $\text{NH}_4\text{NO}_3$  in water.

Solution	1	2	3	4	5	6
$\text{Cu}^{2+}$ : $x \text{ cm}^3$	2.50	3.00	3.50	3.75	4.00	4.25
$\text{NH}_3$ : $(20-x) \text{ cm}^3$	17.50	17.00	16.50	16.25	16.00	15.75
A	0.224	0.262	0.305	0.327	0.329	0.326
Solution	7	8	9	10	11	12
$\text{Cu}^{2+}$ : $x \text{ cm}^3$	4.50	5.00	5.50	6.00	12.0	20.0
$\text{NH}_3$ : $(20-x) \text{ cm}^3$	15.50	15.00	14.50	14.00	8.00	0.00
A	0.319	0.309	0.295	0.275	0.134	0.080

**22.2** Show that, if the absorbance of ammonia and sulfate ion can be neglected at  $\lambda_1$ , the corrected absorbance  $A'$  can be written:

$$A' = A - x/20 \quad A_{12} = (\varepsilon_Z - \varepsilon_{\text{Cu}}) \times [Z] \times l$$

where  $A_{12}$  is the absorbance of the 12th solution,  $\varepsilon_Z$  the molar absorption coefficient of the amine aqua copper (II) complex Z,  $\varepsilon_{\text{Cu}}$  the molar absorption coefficient of free copper ion and  $[Z]$  the amine aqua copper (II) complex Z concentration, and  $l$  the cuvette path length.

**22.3** Plot the corrected absorbance  $A'$  with respect to  $x$ .

- 22.4** Assuming that the copper ion is the limiting reagent, determine the corrected absorbance  $A'$  with respect to  $x$ .
- 2.5** Assuming that the ligand is the limiting reagent, determine the corrected absorbance  $A'$  with respect to  $x$ .
- 22.6** Show that the intersection of the two straight lines occurs when  $x_{\max} = 20/(1+n)$ .
- 22.7** Deduce the molecular formula of the amine aqua copper (II) complex Z.

### Electronic study of the complexes

- 22.8** Assuming a regular octahedral frame of the ligands around the copper center, draw and fill the electronic levels of the d orbitals along an energetic axis.
- 22.9** Draw and fill the diagram if a manganese (II) ion is used instead of a copper (II) ion ( $\text{Mn}(\text{H}_2\text{O})_6^{2+}$  complex). Give the maximum value of the spin for this complex.
- 22.10** Draw and fill the diagram if cyano ligands are used instead of water ligands ( $\text{Mn}(\text{CN})_6^{4-}$  complex). Give the maximum value of the spin for this complex.
- 22.11** Using arrows, illustrate the evolution of the electronic levels of the copper (II) complex when water is replaced by ammonia during the transformation studied in question 1. The involved ligands will be taken on the z axis.
-

## SOLUTION OF PREPARATORY PROBLEM 22

**22.1** The complex responsible for the color of the solution is the hexaaquacopper(II) complex  $\text{Cu}(\text{H}_2\text{O})_6^{2+}$ . This compound absorbs light mainly in the orange region, which is the complementary color of blue, *i.e.*  $\lambda_1 = 620 \text{ nm}$ .

**22.2** Using the Beer Lambert law:

$$A = l (\epsilon_Z [\text{Z}] + \epsilon_{\text{Cu}} [\text{Cu}^{2+}])$$

The conservation of copper in the solution leads to:  $(x/20)[\text{Cu}^{2+}]_0 = [\text{Z}] + [\text{Cu}^{2+}]$

Hence:

$$A = l (\epsilon_Z [\text{Z}] + \epsilon_{\text{Cu}} [\text{Cu}^{2+}])$$

$$A = l (\epsilon_Z [\text{Z}] + \epsilon_{\text{Cu}} ((x/20)[\text{Cu}^{2+}]_0 - [\text{Z}])))$$

$$A = l \epsilon_{\text{Cu}} ((x/20)[\text{Cu}^{2+}]_0 + l$$

$$(\epsilon_Z - \epsilon_{\text{Cu}})[\text{Z}] \text{ As } A_{12} = l \epsilon_{\text{Cu}}$$

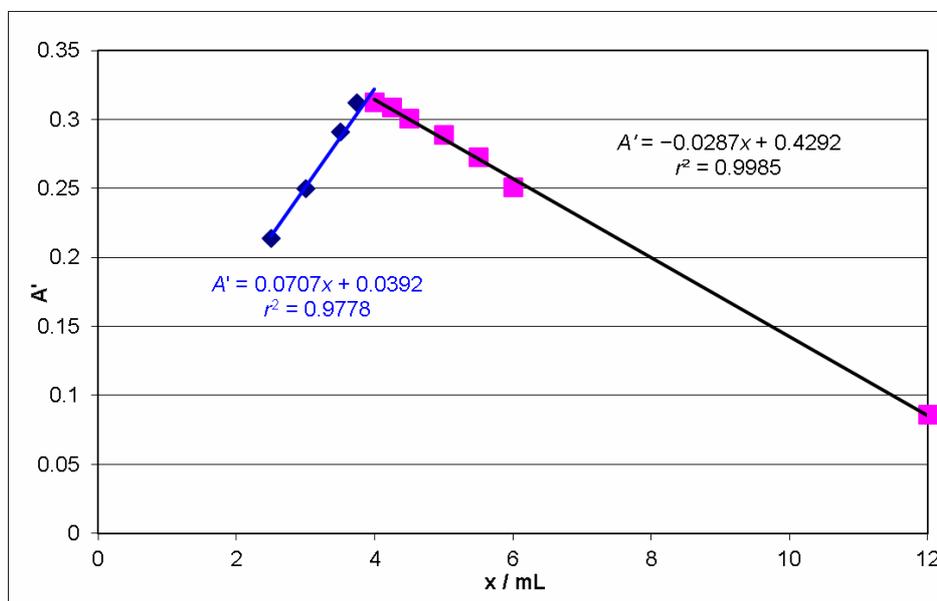
$$[\text{Cu}^{2+}]_0$$

$$A - x/20 A_{12} = l (\epsilon_Z - \epsilon_{\text{Cu}})[\text{Z}]$$

**22.3** The corrected absorbances for each solution are:

	$x / \text{cm}^3$	$(20-x) / \text{cm}^3$	$A$	$A'$
1	2.50	17.50	0.224	0.214
2	3.00	17.00	0.262	0.250
3	3.50	16.50	0.305	0.291
4	3.75	16.25	0.327	0.312
5	4.00	16.00	0.329	0.313
6	4.25	15.75	0.326	0.309
7	4.50	15.50	0.319	0.301
8	5.00	15.00	0.309	0.289
9	5.50	14.50	0.295	0.273
10	6.00	14.00	0.275	0.251
11	12.00	8.00	0.134	0.086
12	20.00	0.00	0.080	0.000

And the graph of the corrected absorbance with respect to the volume of copper solution added is:



**22.4** If the copper ion is the limiting reagent, the concentration of the complex is equal to  $(x/20)[\text{Cu}^{2+}]_0$  so the corrected absorbance increases with  $x$ :

$$A' = l(\epsilon_Z - \epsilon_{\text{Cu}}) (x/20)[\text{Cu}^{2+}]_0$$

**22.5** If the ligand is the limiting reagent, the complex concentration is equal to  $(20 - x/(20n))[\text{Cu}^{2+}]_0$  so the corrected absorbance decreases with  $x$ :

$$A' = l(\epsilon_Z - \epsilon_{\text{Cu}}) [\text{Cu}^{2+}]_0/n - l(\epsilon_Z - \epsilon_{\text{Cu}}) x [\text{Cu}^{2+}]_0/(20n)$$

**22.6** The two lines intersect when  $A'_{\text{question 4}} = A'_{\text{question 5}}$

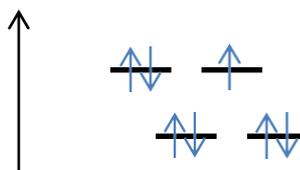
$$\text{Thus: } x_{\text{max}} = 20/(1 + n).$$

**22.7** The two curves plotted in question 3 intersect at  $x_{\text{max}} = 3.92$  which gives  $n = 4.10 \approx 4$

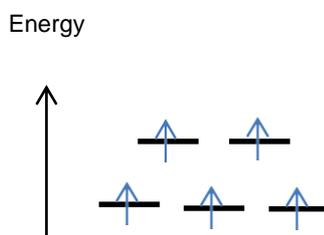
The molecular formula of the complex is then:  $[\text{Cu}(\text{H}_2\text{O})_2(\text{NH}_3)_4]^{2+}$

**22.8**  $\text{Cu}^{\text{II}}$  possesses 9 d electrons and water is a low-field ligand so the filled diagram in a hypothetical regular octahedral field would be:

Energy

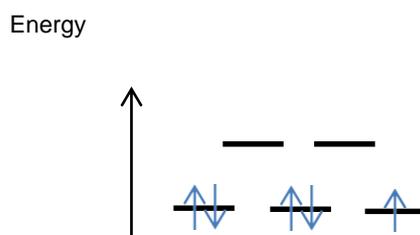


22.9  $\text{Mn}^{\text{II}}$  possesses 5 d electrons, and water is still a low-field ligand so the filled diagram in an octahedral field is:

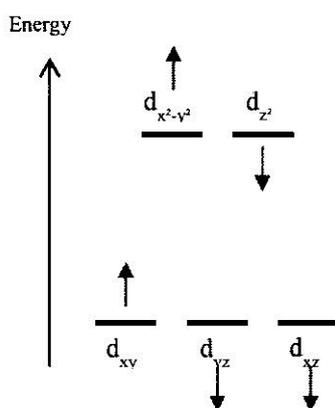


The maximum value for the spin in this configuration is thus  $5/2$ .

22.10 The cyano ligand is a high-field ligand so the electrons are located on the low-energy levels. The maximum value for the spin in this configuration is thus  $1/2$ .



22.11 Let us assume that the  $\text{NH}_3$  ligands are located in the  $xy$  plane. A stronger crystal field is applied to the orbitals by these ligands than by  $\text{H}_2\text{O}$  (located along the  $z$  axis). Thus, the splitting will be enforced for the orbitals lying in the  $xy$  plane. The result is depicted on the scheme below.

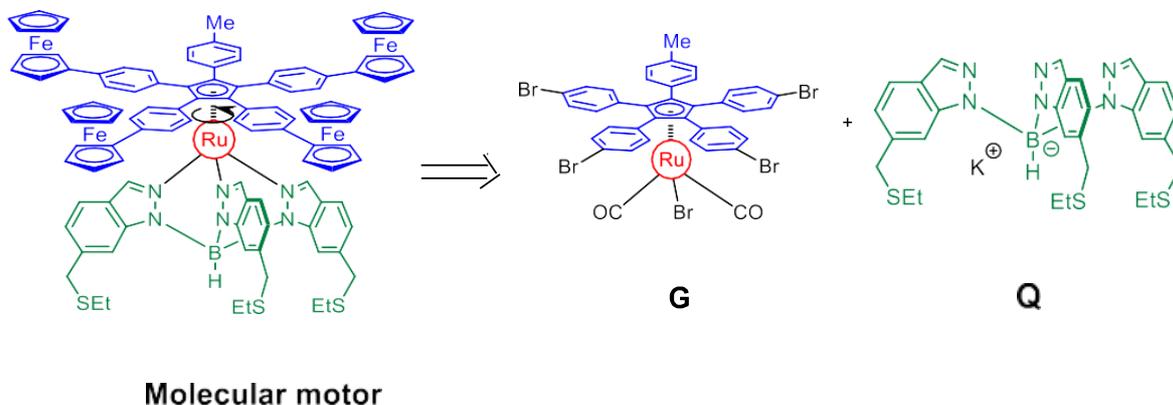


The potential crossing of the  $d_{xy}$  and  $d_{z^2}$  levels is beyond the scope of this problem.

## THEORETICAL PROBLEM 23

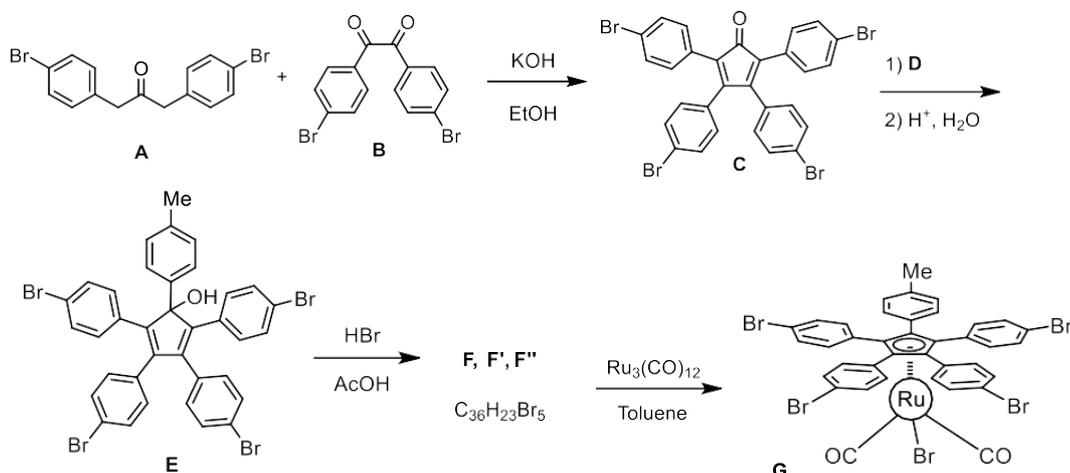
### Synthesis and study of a molecular motor

In 2016, the Nobel Prize in Chemistry was jointly awarded to J.-P. Sauvage, J. F. Stoddart and B. L. Feringa for the “*design and synthesis of molecular machines*”. Within this area, the synthesis of a new type of molecular motor which allows the conversion of an electron flow into a controlled unidirectional rotary motion was reported in 2008 (G. Vives *et al.*, *Tetrahedron*, 2008).



The structure of this molecular motor is based on a ruthenium (II) complex featuring a cyclopentadienyl ligand (the rotating subunit called a rotor, in blue) and a tris(indazolyl)borate ligand (motionless subunit called a stator, in green) functionalized with thioether groups, which provide a tight anchor on gold surfaces. In this problem, the preparation of the ruthenium complex G, the key intermediate of the synthesis, will first be examined. The synthetic sequence leading to tris(indazolyl)borate ligand Q will then be detailed and the redox properties of the whole molecular motor will finally be addressed.

### Synthesis of the intermediate ruthenium complex G



- 23.1** Draw the structure of the first reaction intermediate resulting from the action of KOH on compound **A**.
- 23.2** In these types of reactions, can KOH be used in catalytic amounts? (Yes/No)
- 23.3** Draw the structure of a possible reagent **D** that would lead to the formation of the alcohol **E** from **C**.

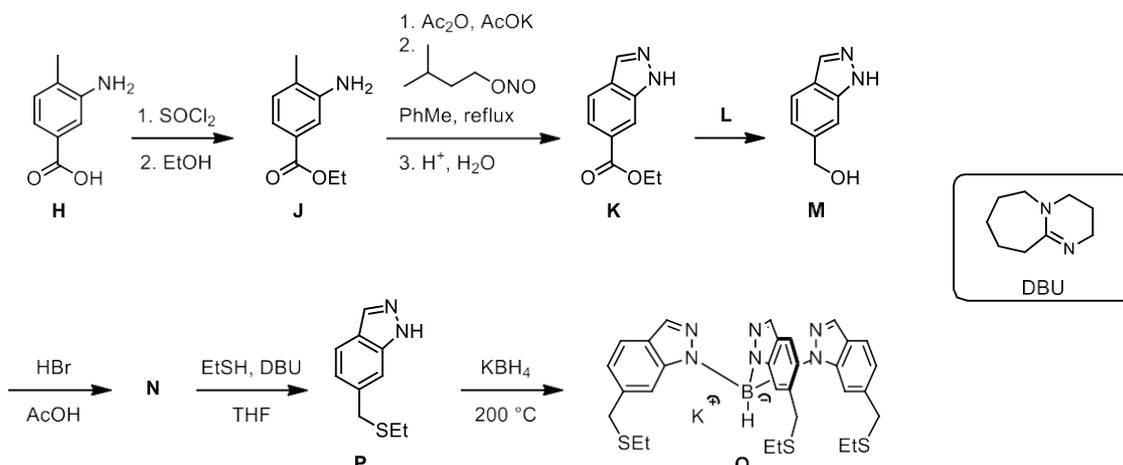
In the third step ( $\mathbf{E} \rightarrow \mathbf{F} + \mathbf{F}' + \mathbf{F}''$ ), compound **E** is treated with HBr in glacial acetic acid to give the corresponding product as a mixture of three regioisomers (and their enantiomers) **F**, **F'** and **F''** (molecular formula:  $\text{C}_{36}\text{H}_{23}\text{Br}_5$ ).

- 23.4** Select the appropriate type of mechanism involved in the step  $\mathbf{E} \rightarrow \mathbf{F} + \mathbf{F}' + \mathbf{F}''$  among the following choices:
- Electrophilic aromatic substitution
  - Nucleophilic aromatic substitution
  - Unimolecular nucleophilic substitution  $\text{S}_{\text{N}}1$
  - Bimolecular nucleophilic substitution  $\text{S}_{\text{N}}2$
- 23.5** Give the structure of the reaction intermediate accounting for the formation of these three regioisomers.
- 23.6** Draw the structure of the three isomers **F**, **F'** and **F''**.

In the fourth step ( $\mathbf{F} + \mathbf{F}' + \mathbf{F}'' \rightarrow \mathbf{G}$ ), the three regioisomers are reacted with the ruthenium cluster  $\text{Ru}_3(\text{CO})_{12}$  to give the ruthenium (II) complex **G**, the key intermediate in the synthesis of the molecular motor. The evolution of a gas is observed during this reaction.

- 23.7** A metallic cluster is a structure involving at least three metal atoms linked via metal-metal bonds. Give the oxidation state of the ruthenium atoms in the cluster  $\text{Ru}_3(\text{CO})_{12}$ .
- 23.8** Write the electronic configuration of ruthenium in the free ion corresponding to **G**.
- 23.9** Write a balanced equation for the formation of complex **G** starting from **F** and  $\text{Ru}_3(\text{CO})_{12}$ .

### Synthesis of the tris(indazolyl)borate ligand



**23.10** Draw the compound which is formed as an intermediate in the first step (H → J).

**23.11** Draw the Lewis structure of the 3-methylbutyl nitrite reagent involved in the second step (J → K).

**23.12** Select appropriate experimental conditions for the third step (K → M).

- NaBH<sub>4</sub> in ethanol/water (vol. 50/50)
- LiAlH<sub>4</sub> in diethyl ether
- CrO<sub>3</sub>, H<sub>2</sub>SO<sub>4</sub> in water
- PTSA in toluene
- (COCl)<sub>2</sub>, DMSO, NEt<sub>3</sub> in dichloromethane

**23.13** Draw the structure of compound N.

Alternatively, alcohol **M** may have been converted into a mesylate by the reaction of **M** with methanesulfonyl chloride CH<sub>3</sub>SO<sub>2</sub>Cl in the presence of pyridine. However, the efficiency of this reaction is limited by the formation of a by-product having the molecular formula C<sub>10</sub>H<sub>12</sub>N<sub>2</sub>O<sub>5</sub>S<sub>2</sub>.

**23.14** Draw the structure of this by-product.

In the fifth step (N → P), the nucleophilic substitution is carried out in the presence of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene).

**23.15** What is the role of DBU in this reaction? Choose the appropriate answer from the following list:

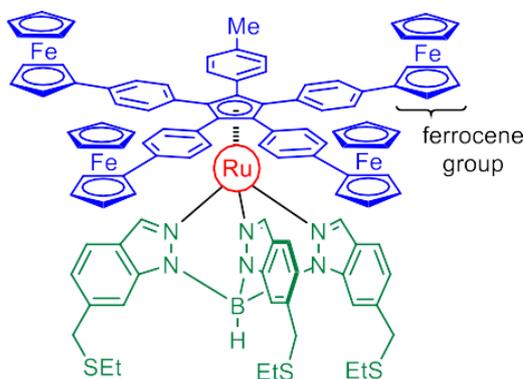
- nucleophile
- electrophile

- Brønsted base
- Brønsted acid
- oxidizing agent
- reducing agent

**23.16** Write a balanced equation of the reaction accounting for the formation of potassium tris(indazolyl)borate **Q** starting from functionalized indazole **P** and potassium borohydride.

### Redox properties of the molecular motor

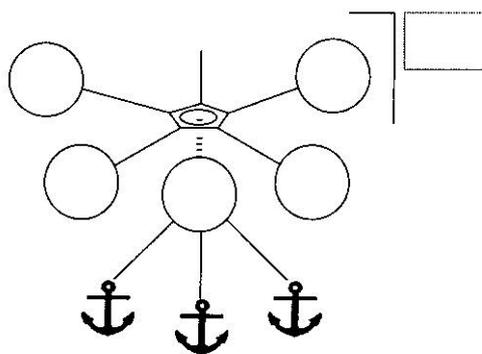
The design of the molecular motor involves electroactive groups such as ferrocenes, positioned at the extremities of four of the rotors arms. These ferrocene groups play an important role in the control of the rotary motion when the motor is submitted to an electron flow. Cyclic voltammetry studies of this molecular motor showed that the redox potential of ruthenium is higher than the redox potential of the iron centers.



**23.17** Give the oxidation state of the iron center in each of the ferrocene groups.

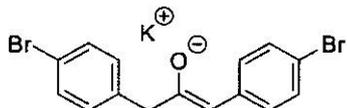
**23.18** The four iron centers should be oxidized selectively. Order the standard potential of an appropriate oxidant (named "Ox") regarding to the ones of the ruthenium and iron ions.

**23.19** Fill in the scheme given below with the oxidation state of each metallic center and the charge of the complex after selective oxidation of the four iron centers.



**SOLUTION OF PREPARATORY PROBLEM 23**

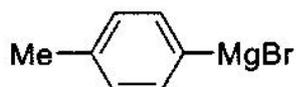
23.1



or any of the resonance structures of this enolate species

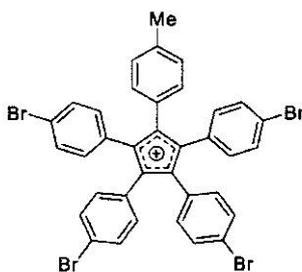
23.2 Correct answer: Yes: the base is regenerated after each aldol condensation sequence. However, an excess of KOH is usually used in such reactions.

23.3 The addition of an organolithium reagent or a Grignard reagent, such as:

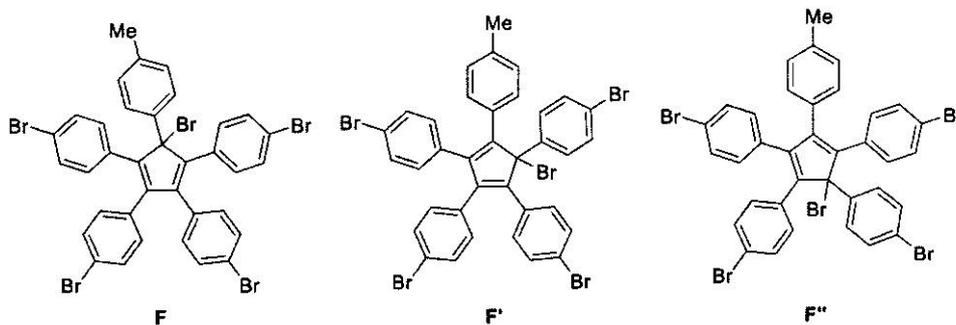


23.4 Correct statement: Unimolecular nucleophilic substitution  $S_N1$ .

23.5



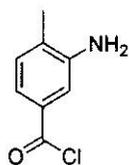
23.6

23.7  $Ru^0$ 

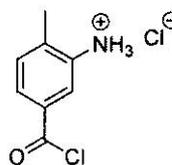
23.8  $Ru^{2+}$ :  $(1s)^2(2s)^2(2p)^6(3s)^2(3p)^6(4s)^2(3d)^{10}(4p)^6(5s)^0(4d)^6$  i.e.  $[Kr](5s)^0(4d)^6$



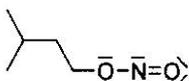
23.10



can be accepted but formally the actual intermediate is

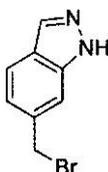


23.11



23.12 Correct statement:  $\text{LiAlH}_4$  in diethyl ether

23.13 In the fourth step ( $\mathbf{M} \rightarrow \mathbf{N}$ ), the hydroxy group is converted into a better leaving group in view of the nucleophilic substitution step ( $\mathbf{N} \rightarrow \mathbf{P}$ ). Alcohol  $\mathbf{M}$  is thus treated with  $\text{HBr}$  in acetic acid.



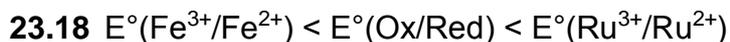
23.14



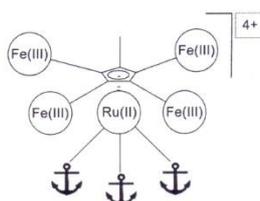
23.15 Correct statement: Brønsted base



23.17  $\text{Fe}^{\text{II}}$



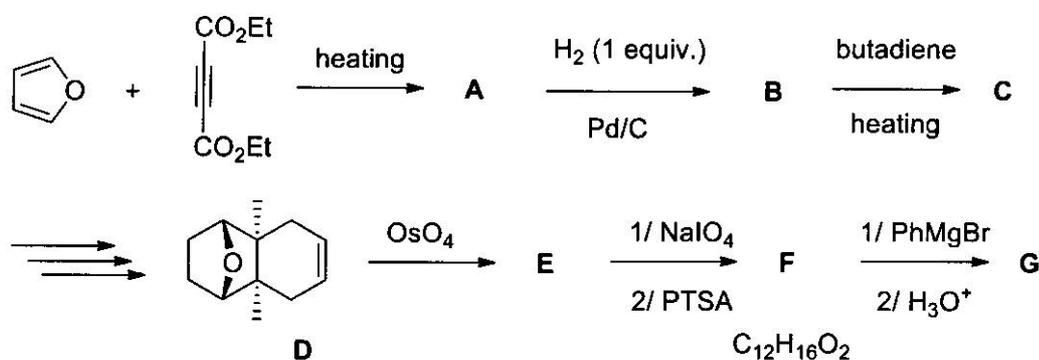
23.19



## THEORETICAL PROBLEM 24

### Some steps of a synthesis of cantharidin

Cantharidin is a terpenoid that some beetles secrete. Several medicinal uses have been known since the ancient times, but its isolation by the French chemist P Robiquet in 1810 was a milestone in its rigorous study. It is now recognized to be a strong poison, especially for horses, and incidentally as a medication to remove warts. Some steps of the synthesis achieved in 1951 by the Belgium chemist G Stork are studied in this problem.



*PTSA = para-toluene sulfonic acid*

- 24.1 Draw the structures of **A** and **B**.
- 24.2 Is **A** optically active?
- Yes
- No
- 24.3 Draw the most stable conformation of butadiene.
- 24.4 Draw the 3D structure of **C** (obtained as a single diastereomer).
- 24.5 Draw the 3D structure of the transition state yielding product **C**.

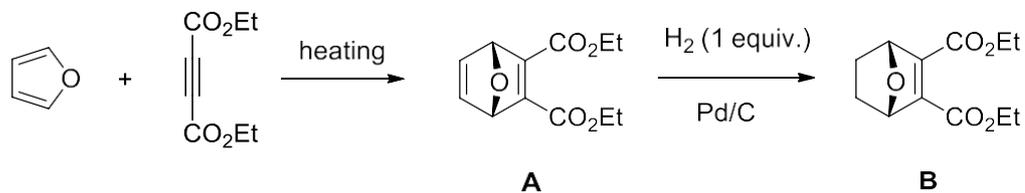
Several steps convert **C** to **D**, but they are not studied in this problem.

- 24.6 Draw the structure of **E** and **F** as a mixture of isomers.
- 24.7 How could we thermodynamically favor the formation of **F**?
- by heating
- by using anhydrous magnesium sulfate.
- by cooling down
- by using an oxidizing agent

- 24.8 Draw the structure of **G** as a mixture of isomers.

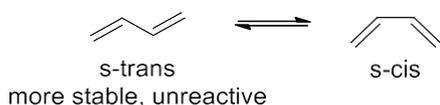
**SOLUTION OF PREPARATORY PROBLEM 24**

24.1

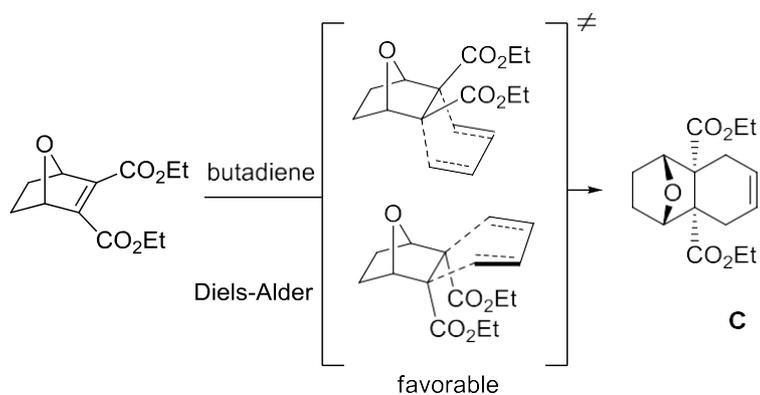


24.2 Correct answer: no.

24.3

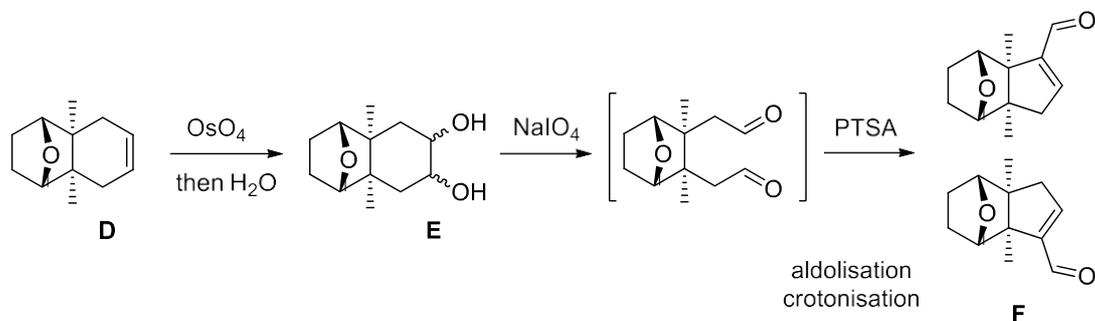


24.4

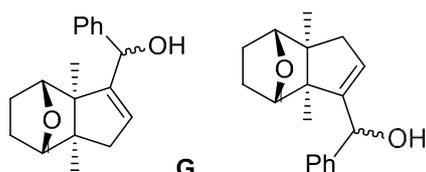


24.5 See question 4

24.6

24.7 Correct answers: by heating, by using anhydrous magnesium sulfate.

24.8



## THEORETICAL PROBLEM 25

### Study of ricinoleic acid

Ricinus seeds contain about 50 to 70% of triglyceride whose fatty acid chains are composed of nearly 90% of ricinoleic acid. Oleic and linoleic acids are also present in smaller amounts (respectively around 4 and 3% of fatty acid chains). Fatty acids are carboxylic acids with long aliphatic chains. There are two main classes of fatty acids: saturated fatty acids and mono- or polyunsaturated fatty acids. When one or more double bonds are present, their position on the chain and their configuration are specified according to the IUPAC rules.

**25.1** Give the general formula of a saturated fatty acid.

Ricinoleic acid is a fatty acid of formula  $C_{18}H_{34}O_3$ . Its carbon chain is unbranched. It has a  $C_9=C_{10}$  unsaturation and a stereogenic center at  $C_{12}$  with *R* configuration.

Partial spectroscopic data:

$^1H$  NMR ( $CDCl_3$ , 300 MHz): the coupling constant measured between the two ethylenic protons at 5.53 and 5.40 ppm is 7.8 Hz.

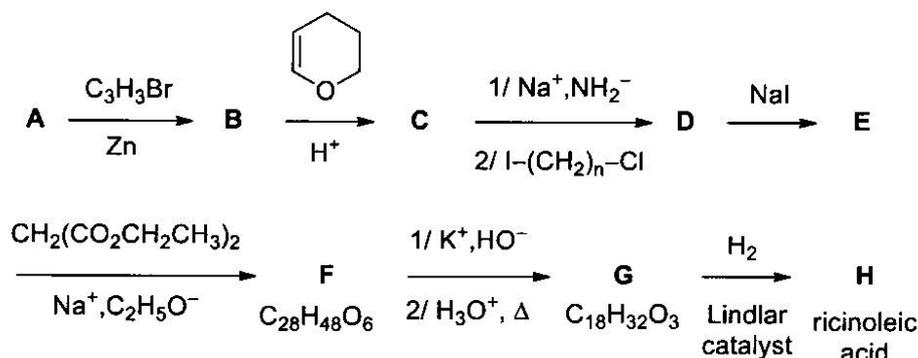
IR ( $\sigma$ ,  $cm^{-1}$ ): 1711; 3406.

**25.2** Draw the structure of ricinoleic acid based on the spectroscopic data.

**25.3** Give the number of stereoisomers of ricinoleic acid.

**25.4** Justify the attribution of the stereodescriptor *R* to  $C_{12}$  by classifying the substituents in order of their priority.

A total synthesis of racemic ricinoleic acid has been published in 1955 by L. Crombie and A. G. Jacklin according to this scheme. The synthesis of **B** from **A** can be done by a Reformatskii reaction (R-Br with zinc).



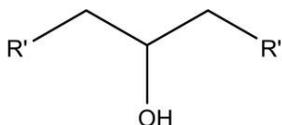
Some data about used compounds:

**A:**

- mass composition of A: %C = 74%; %H = 12%; %O = 14%
- $^1\text{H}$  NMR ( $\delta$ , ppm in  $\text{CDCl}_3$ , 300 MHz): 9.7 (s, 1H), 2.1 (m, 2H), 1.6 (m, 2H), 1.3 (m, 6H), 0.9 (t, 3H)

**B:**

- general structure:



$\text{I}-(\text{CH}_2)_n\text{-Cl}$ : %I = 52 ; %C = 29; %Cl = 14; %H = 5.

**25.5** Give the structures of **A** and **B**.

**25.6** Choose the correct sentences.

- the mixture obtained while forming B would rotate light
- the mixture obtained while forming B would not rotate light
- B contains one stereogenic carbon
- B contains two stereogenic carbons
- the reaction is stereoselective
- a 50/50 R/S mixture is obtained

**25.7** Choose the reactants that could have been used in this sequence as an alternative to 3,4- dihydro-2*H*-pyran:

- benzyl bromide  $\text{PhCH}_2\text{Br}$
- ethyl iodide  $\text{C}_2\text{H}_5\text{I}$
- trimethylsilyl chloride  $\text{Me}_3\text{SiCl}$
- thionyl chloride  $\text{SOCl}_2$
- hex-1-ene  $n\text{-BuCH}=\text{CH}_2$

**25.8** Draw the structure of an oxonium involved as a reaction intermediate in the step **B**  $\rightarrow$  **C**.

**25.9** Draw the structure of **C**.

**25.10** Write the chemical equation for the reaction **C** +  $\text{Na}^+$ ,  $\text{NH}_2^-$ .

**25.11** Draw the structure of the transition state involved in the step **D** → **E**. The main carbon chain can be represented as an **R** group. Give, in the transition state, the geometry of the carbon atom at which the reaction takes place.

**25.12** Draw the structures of **D**, **E**, **F**, and **G**.

**25.13** Write the balanced equation of the first step of **F** → **G** transformation. During a later step of this transformation, a gas molecule is produced. Write the formula of this molecule.

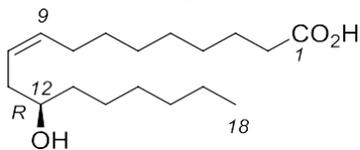
**25.14** What are the stereochemical characteristics the step **G** → **H**?

- Stereospecific
  - Stereoselective
  - Enantiospecific
  - Diastereoselective
-

**SOLUTION OF PREPARATORY PROBLEM 25**

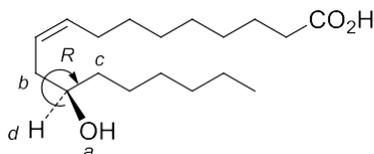
25.1  $\text{H}_3\text{C}-[\text{CH}_2]_n-\text{COOH}$  or  $\text{C}_n\text{H}_{2n}\text{O}_2$

25.2 The *cis* configuration of the double bond is obtained from the NMR data.

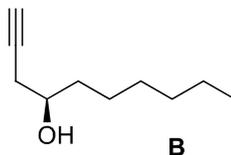
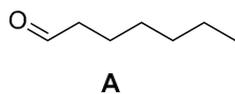


25.3 Ricinoleic acid has one stereogenic carbon and one double bond so  $2^2 = 4$ ; stereoisomers.

25.4 Using usual rules, the priority of the groups is  $a > b > c > d$ , leading to a *R* configuration.



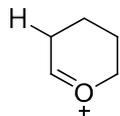
25.5



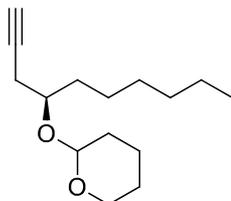
25.6 Correct answers: the mixture obtained while forming **B** is not optically active, **B** contains one stereogenic carbon, **B** is obtained as a 50/50 *R/S* mixture.

25.7 Correct answers: benzyl bromide  $\text{PhCH}_2\text{Br}$ , trimethylsilyl chloride  $\text{Me}_3\text{SiCl}$ .

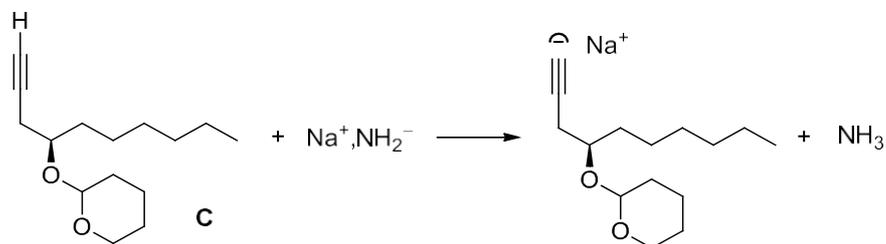
25.8



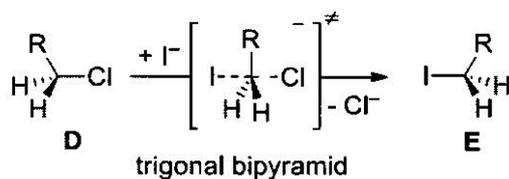
25.9



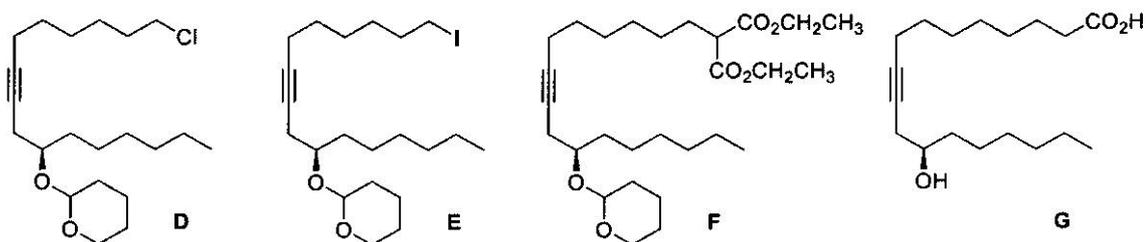
## 25.10



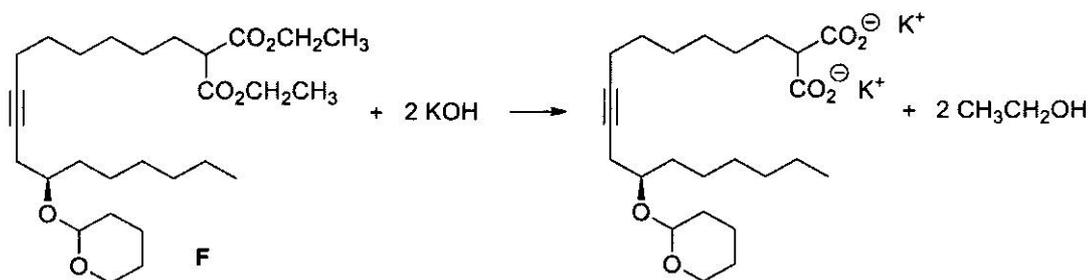
## 25.11



## 25.12



## 25.13



The preparation of **G** from **E** corresponds to the first stages of a malonic synthesis, a set of reactions for synthesizing carboxylic acids from diethyl malonate. During the

step **F** → **G**, the compound **F** (C<sub>28</sub>H<sub>48</sub>O<sub>6</sub>), which possesses two ester functions, is transformed into compound **G** (C<sub>18</sub>H<sub>32</sub>O<sub>3</sub>) with one carboxylic acid function. The gas that is produced latter in the synthesis is **carbon dioxide (CO<sub>2</sub>)**.

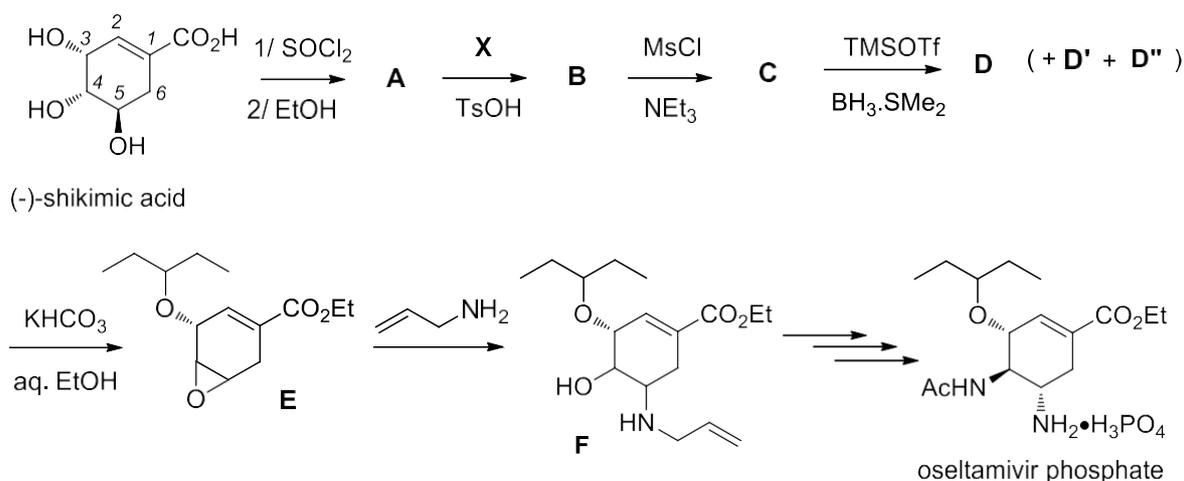
**25.14** Correct answers: Stereoselective, diastereoselective.

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## THEORETICAL PROBLEM 26

### Synthesis of oseltamivir

Oseltamivir is the active ingredient in an antiviral drug (Tamiflu®) used for the prevention and treatment of influenza A and B. There are several ways to synthesize oseltamivir. The route proposed below (Karpf-Trussardi synthesis) is based on (–)-shikimic acid, a stereoisomer of 3,4,5-trihydroxycyclohex-1-ene-1-carboxylic acid, that is a precursor for many syntheses in plants. The first steps are studied in this problem. A series of reactions (not shown) follows the opening of the epoxide E, and finally lead to the formation of oseltamivir.



notes: Ms = mesyl =  $\text{CH}_3\text{SO}_2$  / Ts = tosyl = *para*- $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2$   
 Tf = triflyl =  $\text{CF}_3\text{SO}_2$  / TMS = trimethylsilyl =  $\text{Me}_3\text{Si}$

**26.1** Give the number of stereoisomers of (–)-shikimic acid.

**26.2** Give the meaning of the symbol (–) in (–)-shikimic acid.

- It is the sign of the specific rotatory power of shikimic acid.
- Shikimic acid is levorotatory.
- Shikimic acid is dextrorotatory.
- Shikimic acid rotates the polarization plane to the right when the observer faces the source.
- Shikimic acid rotates the polarization plane to the left when the observer faces the source.
- It gives the absolute configuration of the carboxylic acid function of shikimic acid.

**26.3** Give the structure of **A**.

**26.4** Draw the structure of a chlorinated compound involved as a reaction intermediate in the formation of **A**.

The  $^1\text{H}$  NMR spectrum of compound **A** is partly described below (the OH signals have not been reported). The two hydrogen atoms linked to C6 are diastereotopic and appear as two different signals.

**A** ( $\delta$ , ppm in  $\text{CDCl}_3$ , 400 MHz): 6.78 (1H, m), 4.37 (1H, m), 4.20 (2H, q, 7.3), 4.00 (1H, dt, 7.2 and 5.2), 3.69 (1H, dd, 7.2 and 4.0), 2.70 (1H, dd, 18.4 and 5.2), 2.21 (1H, dd, 18.4 and 5.2), 1.28 (3H, t, 7.3)

**26.5** Assign all the  $^1\text{H}$  NMR signals to the corresponding hydrogen atom(s) of **A**.

Data about compound **X**:

- Mass composition: %C = 70; %H = 12; %O = 18
- $^1\text{H}$  NMR ( $\delta$ , ppm in  $\text{CDCl}_3$ , 300 MHz): 2.42 (q, 2H), 1.05 (t, 3H)
- Partial IR spectroscopic data: intense absorption at  $1715\text{ cm}^{-1}$

**26.6** Identify **X**, draw its structure and draw the structure of **B**.

**26.7** Draw the structure of a hemiacetal involved as a reaction intermediate in the formation of **B**.

**26.8** Indicate the synthetic interest(s) of the transformation  $\text{A} \rightarrow \text{B}$ :

- Protect the C3 hydroxy group
- Protect the C3 and C4 hydroxy groups
- Hinder one face of the six-membered ring by a bulky group
- Prepare the derivatization of the C3 hydroxy group
- Increase the reactivity of the C5 hydroxy group
- Differentiate chemically the 3 hydroxy groups

**26.9** Draw the structure of **C**.

The opening of the ketal **C** produces a mixture of mesylates (**D**, **D'** and **D''** in proportion 10/1/1) among which only one, **D**, will serve for the next part of the synthesis. **D** ( $\text{C}_{15}\text{H}_{26}\text{O}_7\text{S}$ ) has a vibration band around  $3300\text{ cm}^{-1}$ . The by-product **D'** is an isomer of **D**.

It also has a vibration band around  $3300\text{ cm}^{-1}$  but does not lead to an epoxide under the proposed conditions. **D''** is not an isomer of **D** but has also a vibration band around  $3300\text{ cm}^{-1}$ . Unlike **D'**, it can undergo epoxidation under the proposed conditions. The product then obtained, **E''**, has also a vibration band around  $3300\text{ cm}^{-1}$ .

**26.10** Draw **E** with the stereochemistry of all stereochemical centers.

**26.11** Using the given information and a retrosynthetic analysis, draw the structures of **D**, **D'**, **D''**, and **E''** (including their stereochemistry).

**26.12** Draw **F** with the stereochemistry of all stereochemical centers.

**26.13** Give the stereochemical descriptors of the stereogenic centers of oseltamivir.

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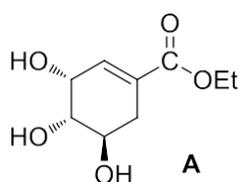
## SOLUTION OF PREPARATORY PROBLEM 26

**26.1** Three independent stereogenic centers (no particular symmetry) so  $2^3 = 8$  stereoisomers.

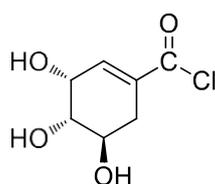
**26.2** Correct statements:

It is the sign of the specific rotatory power of shikimic acid. Shikimic acid is levorotatory. Shikimic acid rotates the polarization plane to the left when the observer faces the source.

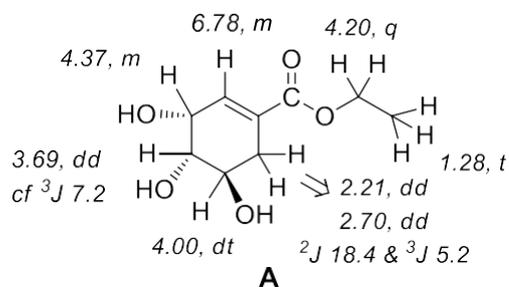
**26.3**



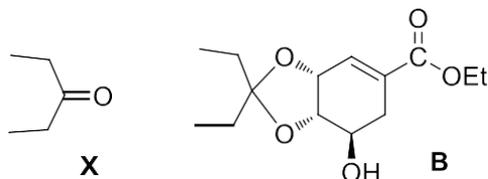
**26.4**



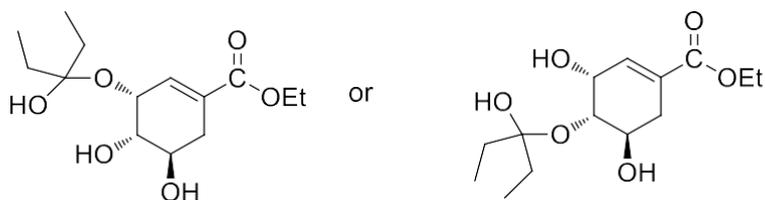
**26.5**



**26.6**



26.7

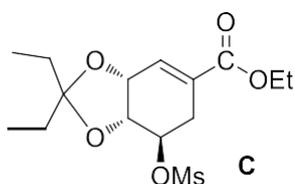


26.8 Correct statements:

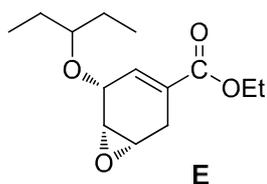
Protect the C3 and C4 hydroxy groups

Prepare the derivatization of the C3 hydroxy group Differentiate chemically the 3 hydroxy groups

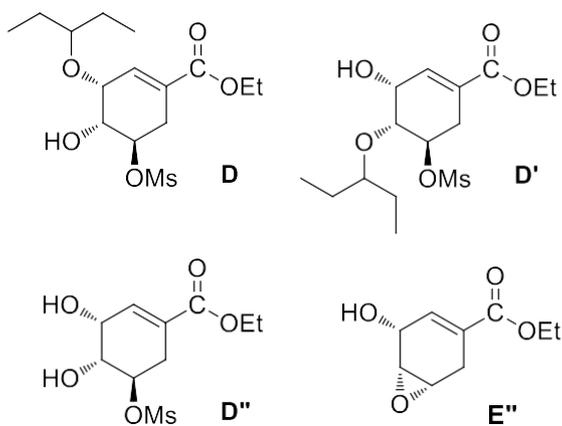
26.9



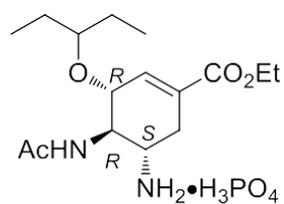
26.10



26.11



26.12



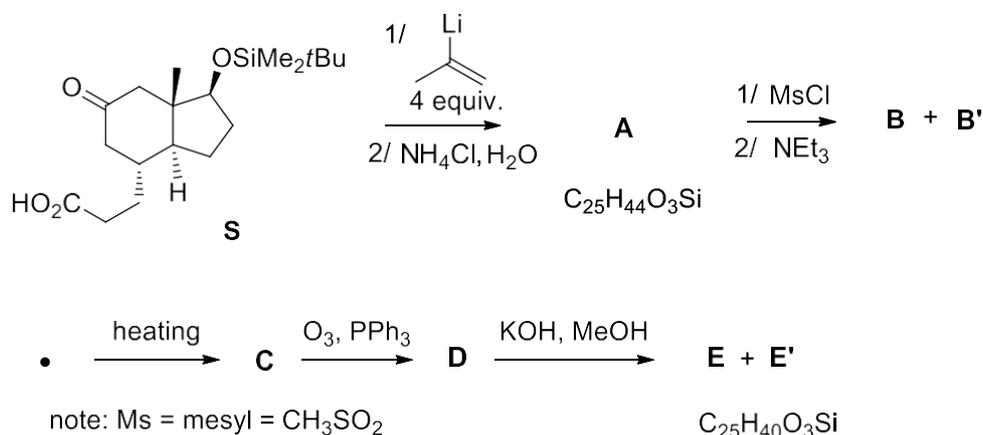
oseltamivir

of ring-opening of the epoxide by an  $S_N2$  mechanism

## THEORETICAL PROBLEM 27

### Formal synthesis of testosterone

Testosterone is a hormone, which is a biologically active substance that has signaling properties, and is produced in a living organism. It is observed in most vertebrates, both in female and male organism. Its effects on health are so important that testosterone is included in the World Health Organization's list of essential medicines. Some steps of a formal synthesis of this molecule are studied in this problem.

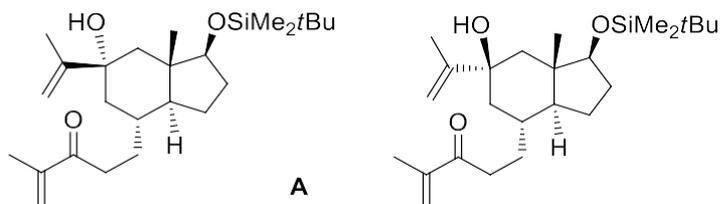


- 27.1** Is **S** optically active? (Yes/No)
- 27.2** Draw the structure of **A** (two diastereomers).
- 27.3** Draw the structure of the non-isolated intermediate obtained after the addition of MsCl on **A**.
- 27.4** Draw the structure of **B** and **B'**.
- 27.5** Draw the 3D structure of **C** and the structure of the transition state yielding **C** (only **B** is reactive).
- 27.6** Draw the structure of **D**.
- 27.7** Circle the most acidic protons of **D**.
- In a mixture of KOH in MeOH, **D** yields two products. **E** is the thermodynamic product and **E'** the kinetic one. **E** has three 6-membered rings and one 5-membered ring, while **E'** has two 6-membered rings and two 5-membered rings.
- 27.8** Draw the structure of these two products.

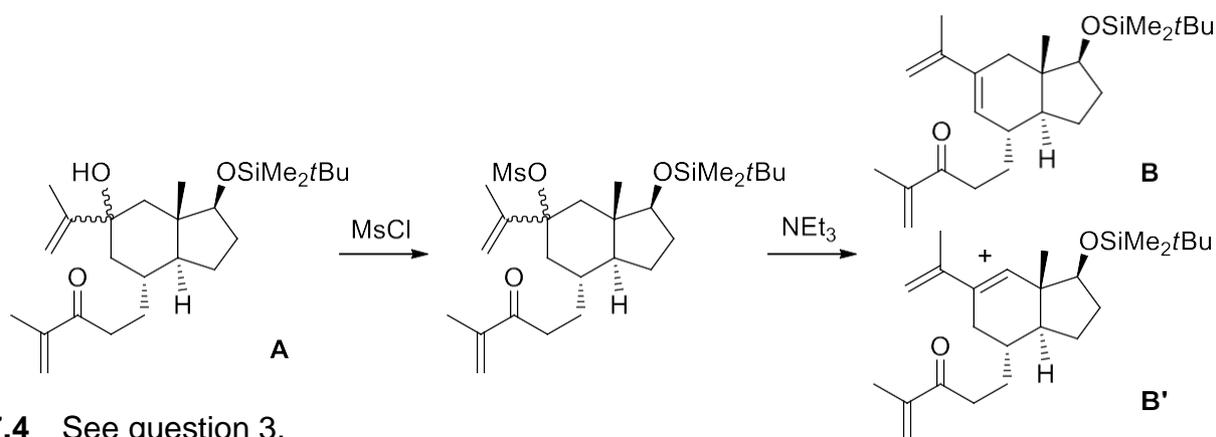
## SOLUTION OF PREPARATORY PROBLEM 27

27.1 Correct answer: Yes.

27.2 After quenching of the reaction:

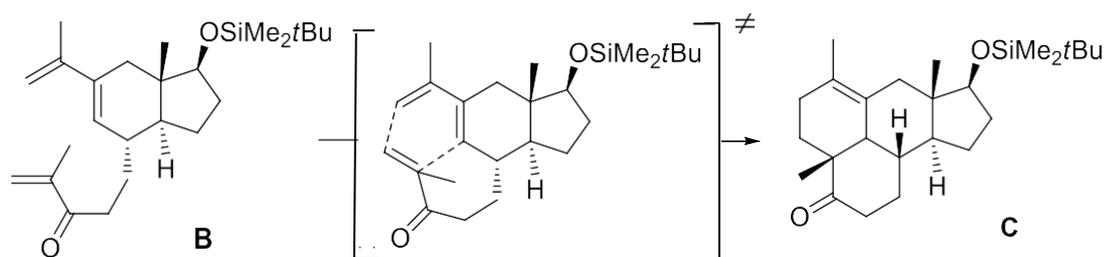


27.3

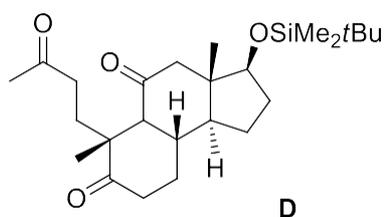


27.4 See question 3.

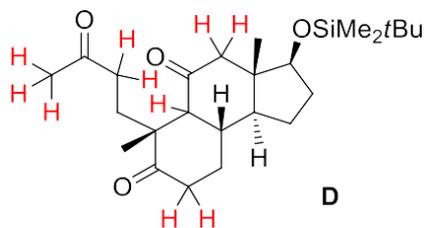
27.5 **B** reacts because the reaction involving **B'** would lead to a too stretched transition state for the reaction to occur.



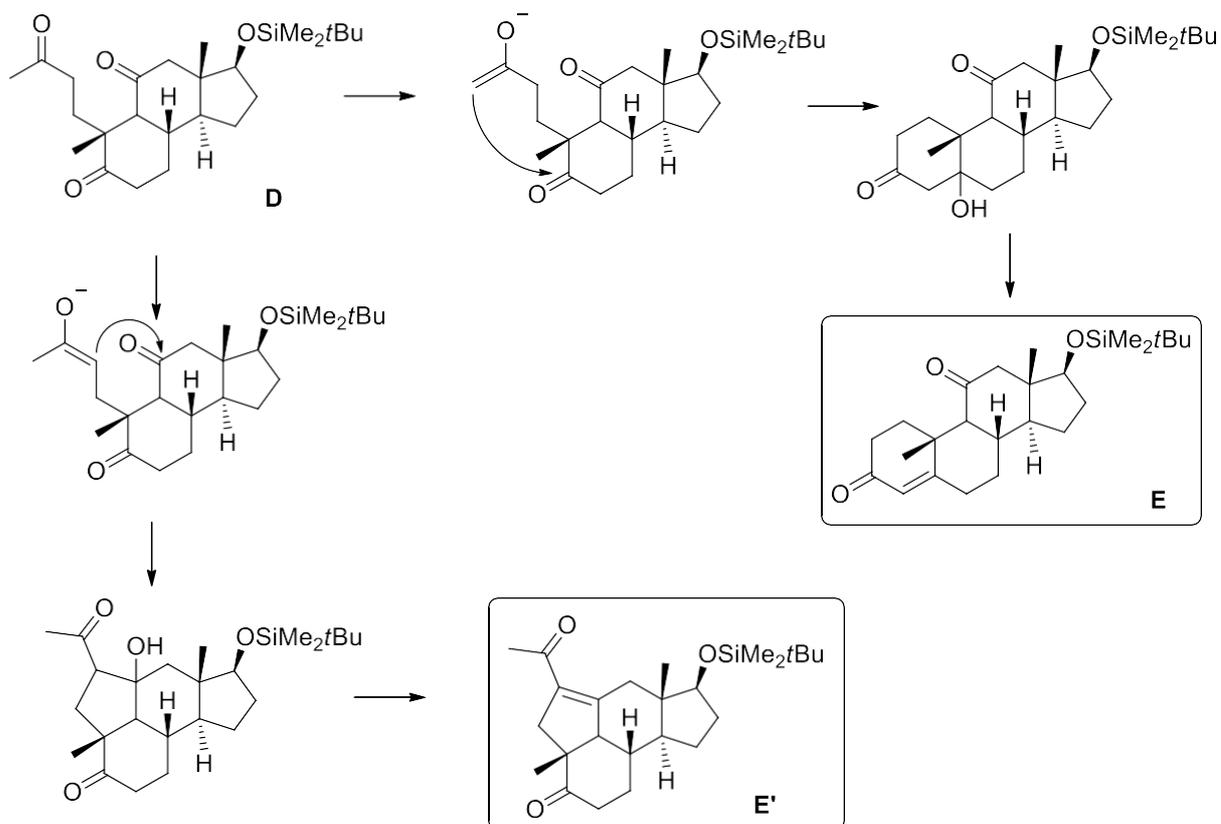
27.6



27.7 The protons in  $\alpha$  position from a C=O double bond are more acidic than the others.



27.8



**Back to 1990:****THEORETICAL PROBLEM 28****Aqueous solutions of copper salts**

This problem derives from the 22nd IChO that took place in Paris in 1990. It is not a preparatory problem, but it is reported here as a reminiscence of the last IChO organized in France.

**About the acidity of the hydrated  $\text{Cu}^{2+}$  ion and the precipitation of the hydroxide**

Consider solution of copper (II) nitrate with a concentration of a  $1.00 \times 10^{-2} \text{ mol dm}^{-3}$ . The pH of the solution is 4.65.

- 28.1** Give the equation for the formation of the conjugate base of the hydrated  $\text{Cu}^{2+}$  ion.
- 28.2** Calculate the  $\text{p}K_{\text{a}}$  of the corresponding acid-base pair.
- 28.3** The solubility product of copper (II) hydroxide is  $K_{\text{sp}} = 1 \times 10^{-20}$ . Calculate the pH of precipitation of  $\text{Cu}(\text{OH})_2$  in the solution under consideration. Justify your calculation, showing that the conjugate base of this hydrated  $\text{Cu}^{2+}$  ion is present in negligible quantity.

**Disproportionation of copper (I) ions**

The  $\text{Cu}^+$  ion is involved in two redox couples:

- couple (1):  $\text{Cu}^+(\text{aq}) + \text{e}^- = \text{Cu}(\text{s})$                       standard potential  $E_1^\circ = 0.52 \text{ V}$
- couple (2):  $\text{Cu}^{2+}(\text{aq}) + \text{e}^- = \text{Cu}^+(\text{aq})$                       standard potential  $E_2^\circ = 0.16 \text{ V}$

- 28.4** Write down the equation for the disproportionation of copper (I) ions and calculate the corresponding equilibrium constant.
- 28.5** Calculate the composition in  $\text{mol dm}^{-3}$  of the solution obtained on dissolving  $1.00 \times 10^{-2}$  mol of copper (I) in  $1.0 \text{ dm}^3$  of water.
- 28.6** Name two chemical species other than  $\text{Cu}^+$  which disproportionate in aqueous solution; write down the equations of the reactions involved and describe the experimental conditions under which disproportionation is observed.

We now examine the stability of copper (I) oxide  $\text{Cu}_2\text{O}$  in contact with a  $1.00 \times 10^{-2} \text{ mol dm}^{-3}$  solution of  $\text{Cu}^{2+}$  ions. The solubility product of copper (I) oxide is:

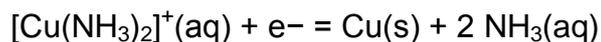
$$K_{\text{sp}} = [\text{Cu}^+][\text{OH}^-] = 1 \times 10^{-15}$$

- 28.7** Calculate the pH at which  $\text{Cu}_2\text{O}$  becomes stable.

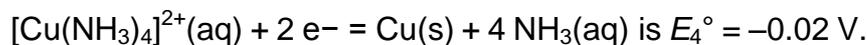
**28.8** Quote a simple experiment allowing the observation of  $\text{Cu}_2\text{O}$  precipitation.

**Complex formation involving  $\text{Cu}^+$  and  $\text{Cu}^{2+}$  ions**

**28.9** The dissociation constant of the complex ion  $[\text{Cu}(\text{NH}_3)_2]^+$  is  $K_{\text{D}1} = 1 \times 10^{-11}$ . Calculate the standard electrode potential  $E_3^\circ$  of the couple:



**28.10** The standard electrode potential of the couple:



Calculate the dissociation constant  $K_{\text{D}2}$  of the complex ion  $[\text{Cu}(\text{NH}_3)_4]^{2+}$ .

**28.11** Deduce the standard electrode potential  $E_5^\circ$  of the couple:



**28.12** Does the disproportionation of the cation  $[\text{Cu}(\text{NH}_3)_2]^+$  take place? (Yes/No)

---

## SOLUTION OF PREPARATORY PROBLEM 28

### Back to 1990: Aqueous solutions of copper salts

**28.1** The acidity measured through the pH can be explained by the following reaction: Simplified equation:  $\text{Cu}^{2+}(\text{aq}) + \text{H}_2\text{O}(\text{l}) = \text{CuOH}^+(\text{aq}) + \text{H}^+(\text{aq})$

Full equation:  $\text{Cu}(\text{H}_2\text{O})_4^{2+}(\text{aq}) + \text{H}_2\text{O}(\text{l}) = [\text{Cu}(\text{OH})(\text{H}_2\text{O})_3]^+(\text{aq}) + \text{H}_3\text{O}^+(\text{aq})$

**28.2**  $\text{pH} = \frac{1}{2} \text{p}K_a - \frac{1}{2} \log c$  thus  $\text{p}K_a = 2 \text{pH} + \log c = 9.30 - 2.00 = 7.30$

**28.3**  $K_{\text{sp}} = [\text{Cu}^{2+}][\text{OH}^-]^2 = 10^{-20}$

At the beginning of the precipitation,  $[\text{Cu}^{2+}] = 1.00 \cdot 10^{-2} \text{ mol dm}^{-3}$  thus  $[\text{OH}^-]^2 = 10^{-18}$ , and  $\text{pH} = 5$ .

$\text{pH} \ll \text{p}K_a$  and  $[\text{CuOH}^+]$  is negligible.

**28.4** Disproportionation: redox reaction of a chemical species with itself.



$$K^\circ = \frac{[\text{Cu}^{2+}]}{[\text{Cu}^+]^2}$$

$E_{\text{Cu}^{2+}/\text{Cu}} - E_{\text{Cu}^+/\text{Cu}} = 0.52 - 0.16 = 0.36 = 0.06 = \log K^\circ$ , thus  $K^\circ = 10^6$

**28.5** Two equivalents of  $\text{Cu}^+$  yield one equivalent of  $\text{Cu}^{2+}$  and one equivalent of Cu. Then:  $[\text{Cu}^+] + 2[\text{Cu}^{2+}] = 10^{-2} \text{ mol dm}^{-3}$

And at equilibrium:  $K^\circ = 10^6 = [\text{Cu}^{2+}] / [\text{Cu}^+]^2$ , thus:  $[\text{Cu}^+] + 2 \times 10^6 [\text{Cu}^+]^2 = 10^{-2}$

$$[\text{Cu}^+] = \frac{\sqrt{2}}{2} \times 10^{-4} = 7.07 \times 10^{-5}$$

$$[\text{Cu}^{2+}] = \frac{993}{2} \times 10^{-5} = 4.96 \times 10^{-3}$$

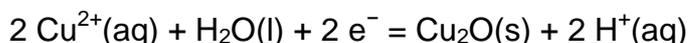
**28.6**  $\text{H}_2\text{O}_2$  and dihalogens  $\text{X}_2$  disproportionate.

In the case of  $\text{H}_2\text{O}_2 = 2 \text{H}_2\text{O} + \text{O}_2$ , catalytic conditions are required.

In the case of dihalogens:  $2 \text{X}_2 + 2 \text{OH}^- = 2 \text{HX} + 2 \text{XO}^-$ , basic conditions are required.

**28.7**  $\text{Cu}_2\text{O}(\text{s}) + 2 \text{H}^+(\text{aq}) + 2 \text{e}^- = 2 \text{Cu}(\text{s}) + \text{H}_2\text{O}(\text{l})$

$$E_1 = E_1^\circ + 0.06 \log [\text{Cu}^+] = 0.52 + 0.06 \log \frac{1 \times 10^{-15}}{[\text{OH}^-]} = 0.46 + 0.06 \text{pH}$$



$$E_2 = E_2^\circ + 0.06 \log \frac{[\text{Cu}^{2+}]}{[\text{Cu}^+]} = 0.16 + 0.06 \log \frac{1.00 \times 10^{-2}}{1.00 \times 10^{-15}} [\text{OH}^-] = 0.10 + 0.06 \text{ pH}$$

$\text{Cu}_2\text{O}$  is stable if  $E_2 > E_1$  i.e.  $\text{pH} > 3$

**28.8**  $\text{Cu}_2\text{O}$  can be obtained by the reduction of  $\text{Cu}^{2+}$  or of copper (II) complexes in slightly acidic or basic media, e.g. Fehling's solution or reducing sugars.

**28.9**  $[\text{Cu}(\text{NH}_3)_2]^+$ :  $\text{p}K_{D1} = 11$

At the equilibrium, the following relationships can be written:

$$E_3 = E_3^\circ + 0.06 \log \frac{[[\text{Cu}(\text{NH}_3)_2]^+]}{[\text{NH}_3]^2}$$

$$\text{and } E_1^\circ + 0.06 \log [\text{Cu}^+] = E_1^\circ + 0.06 \log \frac{[[\text{Cu}(\text{NH}_3)_2]^+]}{[\text{NH}_3]^2} \times \frac{1}{K_{D1}}$$

Since the electrode potential of a solution is unique,  $E_1 = E_3$  and then:

$$E_3^\circ = 0.52 - 0.06 \text{ p}K_{D1} = -0.14 \text{ V}$$

**28.10** Standard electrode potential of  $\text{Cu}^{2+}/\text{Cu}$ :  $(0.52 + 0.16) / 2 = 0.34 \text{ V}$

$[\text{Cu}(\text{NH}_3)_4]^{2+} / \text{Cu}$ :  $E_4^\circ = 0.34 - 0.03 \text{ p}K_{D2} = -0.02 \text{ V}$  so  $\text{p}K_{D2} = 12$

**28.11**  $[\text{Cu}(\text{NH}_3)_4]^{2+} / [\text{Cu}(\text{NH}_3)_2]^+$ :  $E_5^\circ = 0.16 - 0.06 (\text{p}K_{D2} - \text{p}K_{D1}) = 0.10 \text{ V}$

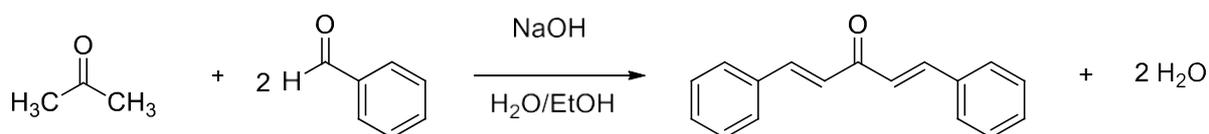
**28.12** Conclusion: No, since  $E_5^\circ > E_4^\circ$ , the  $[\text{Cu}(\text{NH}_3)_2]^+$  ion does not disproportionate in standard conditions.

## PREPARATORY PRACTICAL PROBLEMS

### PRACTICAL PROBLEM P1

#### Synthesis of dibenzylideneacetone

In this task, you will synthesize dibenzylideneacetone (DBA) through an aldol condensation, starting from acetone and benzaldehyde.



DBA synthesis through aldol condensation

#### Chemicals

- Sodium hydroxide
- Benzaldehyde
- Acetone
- 95% Ethanol
- Ethyl Acetate
- TLC Eluent (Cyclohexane/Ethyl acetate 3:1)

#### Glassware and equipment

- 1 Two-neck round-bottom flask, 250 cm<sup>3</sup>
- 1 Graduated cylinder, 10 cm<sup>3</sup>
- 1 Graduated cylinder, 100 cm<sup>3</sup>
- 1 Erlenmeyer flask, 50 cm<sup>3</sup>
- 1 Erlenmeyer flask, 100 cm<sup>3</sup>
- 1 Büchner flask, 500 cm<sup>3</sup>
- 1 Dropping funnel
- 1 Weighing dish
- 1 Petri dish

- 1 Weighing balance (0.01 g)
- 1 Condenser
- 1 Large Büchner funnel
- 1 Crystallizing dish
- 1 Transfer funnel
- 1 Thermometer
- 1 Magnetic stirrer
- 1 Magnetic rod
- 1 Laboratory stand
- 3 TLC sampling vials
- 1 TLC chamber
- 1 TLC sheet (with fluorescence indicator)

Filter paper

Pasteur pipettes

Spatula

TLC capillaries Bossheads and clamps

UV lamp (for TLC)

Laboratory oven (80 °C)

### Procedure

1. Clamp the 250 cm<sup>3</sup> two-neck round bottom flask and add 35 cm<sup>3</sup> of deionized water to the flask. Insert the magnetic rod and transfer ca. 3.2 g of sodium hydroxide to the flask. Stir vigorously.
2. Once the dissolution is complete, add 30 cm<sup>3</sup> of 95% ethanol. Let the flask cool down to 20-25 °C using an ice-water bath. Place an ice filled crystallizer beneath the flask and keep the stirring on until temperature goes down between 20-25 °C.
3. Assemble the condenser on the main neck of the round-bottom flask and the dropping funnel on the side neck. Be careful that the tap of the dropping funnel is closed.
4. Prepare a solution by mixing 7.6 cm<sup>3</sup> (7.9 g) of benzaldehyde and 2.8 cm<sup>3</sup> (2.2 g) of acetone in a 50 cm<sup>3</sup> Erlenmeyer flask.
5. Once the mixture is homogenous, transfer it to the dropping funnel. Gently pour half of it in the round-bottom flask. After a few minutes, a yellow blurring appears followed by a yellow puffy precipitate.

6. After 15 minutes of stirring, add the second half of the benzaldehyde-acetone mixture **dropwise**.
  7. **Keep the reaction medium under stirring for 15 minutes.**
  8. Collect the product by filtration using a Büchner funnel and wash the yellow solid with three 50 cm<sup>3</sup> portions of (cold) distilled water. Let the solid dry for 5 minutes.
  9. Recrystallize the crude product in ethyl acetate (*ca.* 20-25 cm<sup>3</sup> are needed) in the 100 cm<sup>3</sup> Erlenmeyer flask.
  10. Collect the recrystallized product by filtration. Let the product dry on the Büchner funnel for 5 minutes.
  11. Weigh a Petri dish and record the value. Transfer the recrystallized product to the Petri dish and let it dry in a laboratory oven (80 °C).
  12. Weigh the dried product and calculate the yield.
  13. Perform a thin layer chromatography using the recrystallized product and the given references for benzaldehyde and DBA. The eluent is a cyclohexane/ethyl acetate mixture (3:1). Report the  $R_f$  values of each compound and check the purity of the recrystallized DBA.
-

**SOLUTION OF PRACTICAL PROBLEM P1****P1.12** Reactant quantities:

$$n(\text{acetone}) = \frac{m(\text{acetone})}{M(\text{acetone})} = \frac{2.2 \text{ g}}{58.1 \text{ g mol}^{-1}} = 38 \text{ mmol}$$

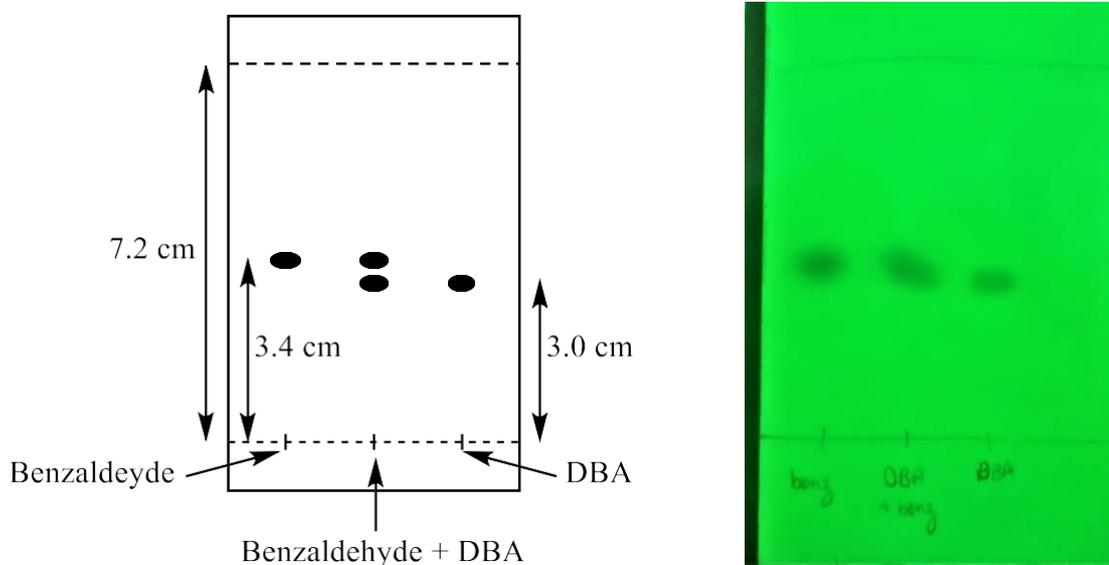
$$n(\text{benzaldehyde}) = \frac{m(\text{benzaldehyde})}{M(\text{benzaldehyde})} = \frac{7.9 \text{ g}}{106.1 \text{ g mol}^{-1}} = 74 \text{ mmol}$$

Given that 2 benzaldehyde molecules react with 1 acetone molecule, the maximum quantity expected for DBA is:  $n_{\text{max}} = 37 \text{ mmol}$ .

Expected mass (if 100% yield):

$$m_{\text{max, DBA}} = M_{\text{DBA}} \times n_{\text{max, DBA}} = 234.3 \text{ g mol}^{-1} \times 37 \text{ mmol} = 8.7 \text{ g}$$

The yield is:  $y(\%) = (m / m_{\text{max, DBA}}) \times 100$

**P1.13** TLC obtained: $R_f$  calculations:

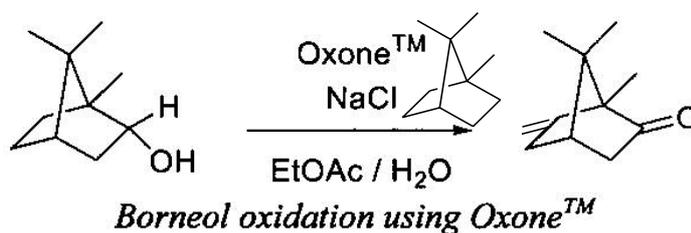
– Benzaldehyde:  $R_f = 3.4 \text{ cm} / 7.2 \text{ cm} = 0.47$

– DBA :  $R_f = 3.0 \text{ cm} / 7.2 \text{ cm} = 0.42$

## PRACTICAL PROBLEM P2

### Oxidation of (–)-borneol to (–)-camphor

In this task you will perform the synthesis of (–)-camphor by oxidation of (–)-borneol, using potassium monopersulfate (MPS) and sodium chloride. MPS, commercialized as Oxone™, has been chosen as it is both a strong oxidizing reagent and a stable solid quite easy to handle. Furthermore, the produced sulfate salts are non-toxic.



### Chemicals

- Deionized water
- (–)-borneol (2.0 g, 13 mmol)
- Sodium chloride (NaCl, 0.2 g)
- Oxone (potassium monopersulfate, MPS) (4.8 g)
- Sodium sulfite
- Anhydrous magnesium (or sodium) sulfate
- Ethyl acetate (50 cm<sup>3</sup>)
- Starch iodide paper

### Glassware and equipment

- 1 Round-bottom flask (or Erlenmeyer flask), 100 cm<sup>3</sup>
- 1 Pear-shaped round-bottom flask
- 1 Magnetic rod
- 1 Magnetic stirrer
- 1 Transfer funnel Filter paper
- 1 Glass rod
- 1 Graduated cylinder, 50 cm<sup>3</sup>
- 1 Graduated cylinder, 10 cm<sup>3</sup>
- 3 Erlenmeyer flasks, 100 cm<sup>3</sup>
- 1 Separatory funnel + stopper, 125 cm<sup>3</sup>

- 1 Sublimation apparatus
- 1 Laboratory stand Weighing dishes
- 1 Petri dish Spatula
- Bossheads, ring and clamps Rotary evaporator
- Melting point apparatus

### Procedure

1. Clamp the 100 cm<sup>3</sup> round-bottom flask. Add 2.0 g of (–)-borneol and 10 cm<sup>3</sup> of ethyl acetate. Insert the magnetic rod and stir to dissolve.
2. With continued stirring, add 4.8 g of Oxone™ to the flask, and then 0.16 g of sodium chloride and 3 cm<sup>3</sup> of deionized water.
3. Stir vigorously the reaction at room temperature for 50 minutes. Add 0.06 g more of NaCl and keep stirring 10 minutes more. *Reaction should be complete and excess oxidant has to be reduced before the extraction of camphor.*
4. Add 30 cm<sup>3</sup> of deionized water into the flask and two spatula tips of sodium sulfite. Keep stirring until most of the salts are dissolved. Test aqueous phase with starch iodide paper (dip a glass rod into the aqueous phase and touch the starch paper; a black color reveals the presence of remaining oxidant). *If the test is positive, add another spatula tip of sodium sulfite and repeat starch iodide paper test, until no color appears.;*
5. Transfer all the content of the reaction flask in a separatory funnel and separate the phases. Extract (three times) the aqueous phase with 10 cm<sup>3</sup> of ethyl acetate.
6. Dry the combined organic phases over anhydrous magnesium (or sodium) sulfate. Filter by gravity into a pre-weighed evaporating round-bottom flask and remove the solvent with a rotary evaporator. Record the mass and the melting point of the crude white solid.
7. Purify the crude solid by sublimation. Record mass and melting point of purified camphor.
8. Calculate the yield of the synthesis.

### Note

The following skills will not be asked during the competition: use a separatory funnel and perform extraction using immiscible solvents; use a rotary evaporator; sublimation; use a melting point apparatus.

**SOLUTION OF PRACTICAL PROBLEM P2**

**P2.8** Reactant quantities:

$$n(\text{borneol}) = \frac{m(\text{borneol})}{M(\text{borneol})} = \frac{2.0 \text{ g}}{154.2 \text{ g mol}^{-1}} = 13 \text{ mmol}$$

$$n(\text{oxone}) = \frac{m(\text{oxone})}{M(\text{oxone})} = \frac{4.8 \text{ g}}{614.8 \text{ g mol}^{-1}} = 7.8 \text{ mmol}$$

With Oxone<sup>TM</sup> as the triple salt  $2 \text{ KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$ .

each Oxone formula gives 2  $\text{HSO}_5^-$  ions.

The limiting reactant is (as expected) borneol:  $n_{\text{max}} = 13 \text{ mmol}$ .

Expected mass (if 100% yield):

$$m_{\text{max, camphor}} = M_{\text{camphor}} \times n_{\text{max}} = 152.2 \text{ g mol}^{-1} \times 13 \text{ mmol} = 2.0 \text{ g}$$

The yield is:

$$y(\%) = (m / m_{\text{max, camphor}}) \times 100$$

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## PRACTICAL PROBLEM P3

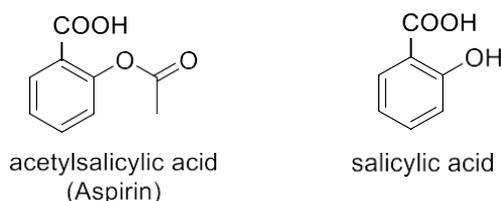
### Aspirin<sup>®</sup> tablet

Acetylsalicylic acid has been used as a drug since ancient Egypt. It has been synthesized for the first time in 1853 by the French chemist C Gerhardt from sodium salicylate and acetyl chloride, but the compound thus obtained was unstable and not pure enough. The preparation method was improved in the following years and in the end F Hoffman, a German chemist and employee of Bayer, succeeded in the total synthesis of the pure compound.

This compound was then marketed under the name Aspirin<sup>®</sup>, now worldwide known, by Bayer. The patent and the trademark were deposited 120 years ago, in 1899. It is used to treat pain, fever, or inflammation, and is as well an antiplatelet drug.

For its 120<sup>th</sup> anniversary, Aspirin<sup>®</sup> is still one of the most widely used medications, with an estimated 44 000 tons produced and 120 billion pills consumed each year. Bayer is still responsible for 85% of this production.

It is on the World Health Organization's List of Essential Medicines as one of the safest and most effective medicines needed in a health system.



The proposed task aims to determine the amount of aspirin contained in a commercial tablet thanks to a back titration, using sodium hydroxide solution. A saponification reaction is first performed and the excess of sodium hydroxide is titrated with hydrochloric acid.

The second part of the task consists of the optimization of TLC eluent in order to monitor this saponification reaction.

### Chemicals

- Deionized water
- Acetylsalicylic acid
- Salicylic acid
- Eluent A (Pure cyclohexane)

- Eluent B (Pure ethyl acetate)
- Eluent C (mixture 65:30:5 of cyclohexane : ethyl acetate : acetic acid)
- Aspirin<sup>®</sup> tablets (500 mg of acetylsalicylic acid)
- Phenolphthalein solution, indicator
- Standardized hydrochloric acid solution ( $c = 0.200 \text{ mol dm}^{-3}$ )
- Sodium hydroxide, (pellets)
- Acetone

### **Glassware and equipment**

- 1 Volumetric flask (with stopper),  $100 \text{ cm}^3$
- 1 Weighing dish
- 1 Spatula
- 1 Weighing balance (0.1 mg)
- 1 Transfer funnel
- 1 Volumetric pipette,  $20 \text{ cm}^3$
- 1 Volumetric pipette,  $10 \text{ cm}^3$
- 1 Pipetting bulb
- 1 Hotplate (with magnetic stirring)
- 1 Erlenmeyer flask,  $100 \text{ cm}^3$
- 1 Air condenser
- 1 Magnetic rod
- 1 Burette,  $25 \text{ cm}^3$
- 1 Laboratory stand with burette clamp Bossheads and clamps
- 2 Titration flasks,  $100 \text{ cm}^3$
- 1 Titration flask,  $250 \text{ cm}^3$
- 1 Stopwatch
- 2 TLC vials (for sampling) TLC capillaries
- 1 TLC chamber
- 3 TLC sheets (with fluorescence indicator) Beakers (for transfers)

### **Procedure for back titration**

1. Prepare  $100 \text{ cm}^3$  of a sodium hydroxide solution (*ca.*  $0.4 \text{ mol dm}^{-3}$ ), using *ca.* 1.6 g of solid sodium hydroxide. This solution is called SB.

2. Clamp the 100 cm<sup>3</sup> Erlenmeyer flask to the laboratory stand. Insert the aspirin tablet and add 20.00 cm<sup>3</sup> of the sodium hydroxide solution SB prepared. Insert the magnetic rod and heat the reaction mixture under reflux with stirring for 15 min.
3. During the reflux, fill the burette with the hydrochloric solution provided ( $c = 0.200 \text{ mol dm}^{-3}$ ).
4. Transfer 10.00 cm<sup>3</sup> of solution SB in the 100 cm<sup>3</sup> titration flask, add a few drops of the phenolphthalein indicator solution and titrate it with the hydrochloric acid solution. Record the volume  $V_1$  and repeat the titration as necessary.
5. After the 15 minutes of reflux, let the Erlenmeyer flask cool down to room temperature. Transfer the whole content of the Erlenmeyer flask to a 250 cm<sup>3</sup> titration flask and rinse with deionized water (pour the rinsing water in the titration flask).
6. Add a few drops of the phenolphthalein indicator solution and titrate it with with the hydrochloric acid solution ( $c = 0.200 \text{ mol dm}^{-3}$ ). Record the volume  $V_2$ .
7. Repeat the procedure (1., 2., 5. and 6.) with another aspirin tablet.
8. Calculate the concentration of the sodium hydroxide in the solution SB.
9. Calculate the amount (in mg) of aspirin in one tablet.

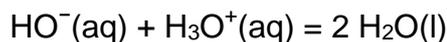
### TLC Optimization

10. Prepare TLC samples of acetylsalicylic acid and salicylic acid in acetone.
  11. Prepare a TLC sheet by spotting the acetylsalicylic acid and the salicylic acid samples.
  12. Let the TLC sheet elute with eluent A.
  13. Visualize the TLC sheet with the UV lamp.
  14. Repeat the procedure (11., 12., 13.) with eluents B and C.
  15. Analyze the TLC sheets and identify which of the eluents is the most appropriate to monitor aspirin saponification.
-

**SOLUTION P3**

**P3.8** Let us take  $V_1 = 19.80 \text{ cm}^3$  as a typical value for  $V_1$ .

The reaction equation for the standardization of the sodium hydroxide solution is:



At the equivalence point:

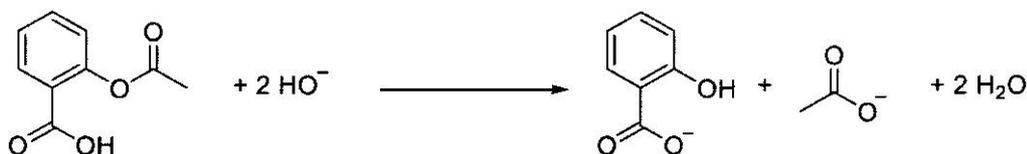
$$n_{\text{HO}^-} = n_{\text{H}_3\text{O}^+}$$

$$c_{\text{HO}^-} \times V_{\text{HO}^-} = c_{\text{H}_3\text{O}^+} \times V_1$$

$$c_{\text{HO}^-} = (19.80 \text{ cm}^3 \times 0.200 \text{ mol dm}^{-3}) / 10 \text{ cm}^3$$

$$c_{\text{HO}^-} = 0.396 \text{ mol dm}^{-3}$$

**P3.9** During step 2, two equivalents of hydroxide ions react with acetylsalicylic acid (1 equivalent for the saponification and 1 equivalent for the reaction with the carboxylic acid).



With phenolphthalein as indicator, salicylate and acetate ions are not titrated. Let us take  $V_2 = 11.75 \text{ mL}$  as a typical value for  $V_2$ .

In the titration flask:

$$n_{\text{remaining HO}^-} = c_{\text{H}_3\text{O}^+} \times V_2$$

$$n_{\text{remaining HO}^-} = 0.200 \text{ mol dm}^{-3} \times 11.75 \text{ cm}^3$$

$$n_{\text{remaining HO}^-} = 2.35 \text{ mmol}$$

Therefore:

$$n_{\text{remaining HO}^-} = n_{\text{added HO}^-} - 2 n_{\text{acetylsalicylic acid}}$$

$$n_{\text{acetylsalicylic acid}} = \frac{n_{\text{added HO}^-} - n_{\text{remaining HO}^-}}{2}$$

$$n_{\text{acetylsalicylic acid}} = \frac{20.00 \text{ cm}^3 \times 0.396 \text{ mol dm}^{-3} - 2.35 \text{ mmol}}{2}$$

$$n_{\text{acetylsalicylic acid}} = 2.79 \text{ mmol}$$

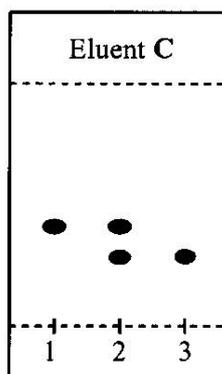
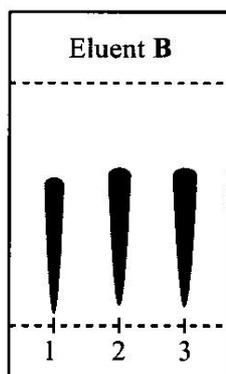
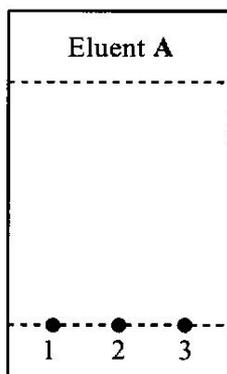
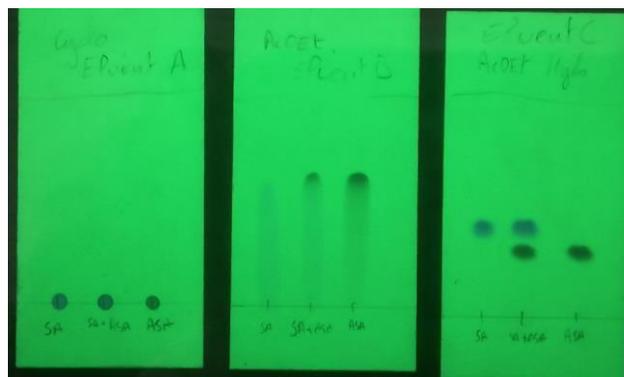
The mass amount is derived directly:

$$m_{\text{acetylsalicylic acid}} = M_{\text{acetylsalicylic acid}} \times n_{\text{acetylsalicylic acid}}$$

$$m_{\text{acetylsalicylic acid}} = 180.2 \text{ g mol}^{-1} \times 2.79 \text{ mmol}$$

$$m_{\text{acetylsalicylic acid}} = 503 \text{ mg}$$

**P3.15** TLC obtained:



- 1 : Salicylic acid (SA)  
 2 : Co-deposition (SA + ASA)  
 3 : Acetylsalicylic acid (ASA)

With eluent **A**, all spots are on the start line.

With eluent **B**, the spots are in the middle of the TLC sheet, but they are tailing a lot and the separation between salicylic acid and acetylsalicylic acid is poor.

With eluent **C**, the separation of salicylic acid and the acetylsalicylic acid is clear, and the spots are well defined.

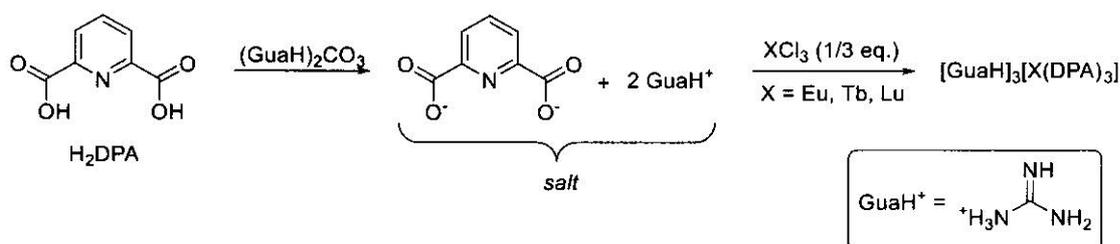
Eluent **C** is the best to monitor the reaction.

## PRACTICAL PROBLEM P4

### Illuminated Europe

In this task you will perform a two-step synthesis of lanthanide complexes. In the first step an acid base reaction occurs between the 2,6-pyridinedicarboxylic acid and guanidinium carbonate, leading to a salt. Then, this salt reacts with a lanthanide salt ( $XCl_3$ ) to give the lanthanide complex. The scheme below shows the reactions.

These lanthanide complexes are used in Euro banknotes, as they emit a specific light under UV irradiation.



### Chemicals

- Deionized water
- 2,6-pyridinedicarboxylic acid ( $H_2DPA$ );  $M = 167.1 \text{ g mol}^{-1}$
- Guanidinium carbonate  $(GuaH)_2CO_3$ ;  $M = 180.2 \text{ g mol}^{-1}$
- Europium(III) chloride hexahydrate;  $M = 366.4 \text{ g mol}^{-1}$
- Lutetium(III) chloride hexahydrate;  $M = 389.4 \text{ g mol}^{-1}$
- Terbium(III) chloride hexahydrate;  $M = 373.4 \text{ g mol}^{-1}$

### Glassware and equipment

- 1 Erlenmeyer flask,  $50 \text{ cm}^3$
- 1 Graduated cylinder,  $25 \text{ cm}^3$
- 1 Büchner flask
- 1 Büchner funnel
- 1 Crystallizer
- 1 Magnetic stirrer
- 1 Magnetic rod
- 1 Petri dish

1 Laboratory stand  
1 Weighing balance (0.1 mg)  
Laboratory oven (80 °C)  
Bossheads and clamps  
Weighing dishes  
UV lamp (365 nm) for banknotes  
€50 banknote (a copy is provided below)  
Filter paper  
Spatula  
Stopwatch

### Procedure

1. Clamp the 50 cm<sup>3</sup> Erlenmeyer flask. Add 0.70 g of 2,6-pyridinedicarboxylic acid and 20 cm<sup>3</sup> of de-ionized water to the flask. Add 0.75 g of guanidinium carbonate and swirl the flask until dissolution of both solids.
2. Insert the magnetic rod and transfer a stoichiometric amount of lanthanide salt into the flask (1 molar equivalent of XCl<sub>3</sub> for 3 molar equivalents of 2,6-pyridinedicarboxylic acid). Stir the flask at room temperature for 1 hour.
3. Cool the mixture in an ice bath for five to ten minutes before filtering.
4. Collect the product by filtration using a Büchner funnel and wash the crystals with small portions of ice-cold water. Allow the crystals to dry in Büchner funnel for five minutes.
5. Transfer the solid to the pre-weighed Petri dish and let it dry in a laboratory oven (80 °C).
6. Weigh the complex and calculate the percentage yield.
7. Look at the three complexes under the UV lamp. Record the fluorescence color of each complex.
8. Observe the €50 banknote under the UV lamp. Identify which of the previous complexes might be used in the ink of the banknote.



*€50 banknote under UV irradiation*

**Note**

This problem is dedicated to Europe. No specific knowledge on the lanthanide chemistry nor the fluorescence properties of such complexes is needed for the competition.

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**SOLUTION OF PRACTICAL PROBLEM P4**

**P4.2** The reaction is performed with stoichiometric amounts of reactants.

$$n(2,6\text{-pyridinedicarboxylic acid}) = \frac{m}{M} = \frac{0.70\text{ g}}{167.1\text{ g mol}^{-1}} = 4.2\text{ mmol}$$

Three equivalents of 2,6-pyridinedicarboxylic acid react with one equivalent of lanthanide salt:

$$n_{\text{max, complex}} = \frac{4.2\text{ mmol}}{3} = 1.4\text{ mmol}$$

Required mass for the particular lanthanide salts:

- $\text{EuCl}_3 \times 6\text{ H}_2\text{O}$ :  $m = 1.4\text{ mmol} \times 366.4\text{ g mol}^{-1} = 0.51\text{ g}$
- $\text{LuCl}_3 \times 6\text{ H}_2\text{O}$ :  $m = 1.4\text{ mmol} \times 389.4\text{ g mol}^{-1} = 0.55\text{ g}$
- $\text{TbCl}_3 \times 6\text{ H}_2\text{O}$ :  $m = 1.4\text{ mmol} \times 373.4\text{ g mol}^{-1} = 0.52\text{ g}$

**P4.5** Expected mass (if 100% yield):

$$m_{\text{max, Eu complex}} = M_{\text{Eu complex}} \times n_{\text{max, complex}} = 827.5\text{ g mol}^{-1} \times 1.4\text{ mol} = 1.16\text{ g}$$

$$m_{\text{max, Lu complex}} = M_{\text{Lu complex}} \times n_{\text{max, complex}} = 850.5\text{ g mol}^{-1} \times 1.4\text{ mol} = 1.19\text{ g}$$

$$m_{\text{max, Tb complex}} = M_{\text{Tb complex}} \times n_{\text{max, complex}} = 834.5\text{ g mol}^{-1} \times 1.4\text{ mol} = 1.17\text{ g}$$

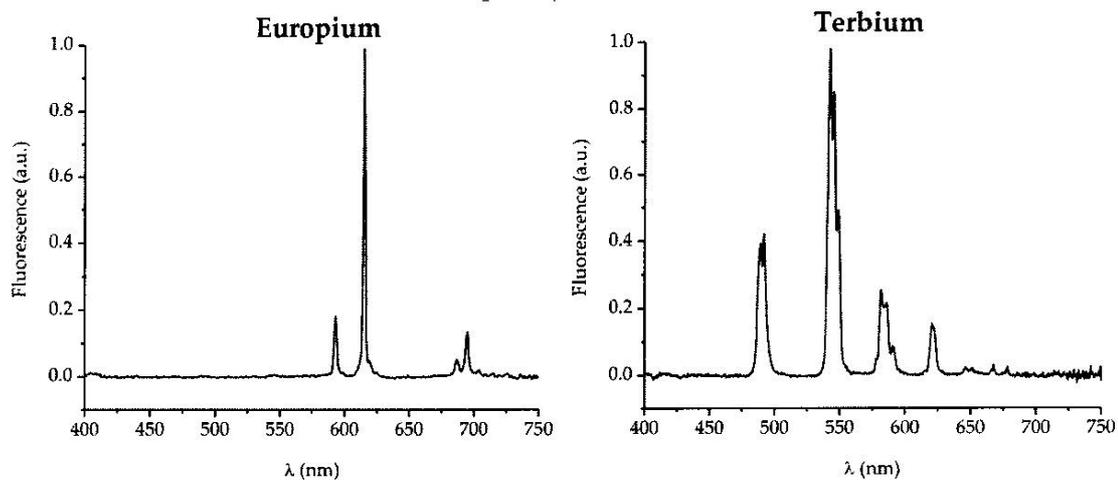
$$\text{The yield is: } y(\%) = (m / m_{\text{max, complex}}) \times 100$$

**P4.6** Europium complex: red fluorescence (see the fluorescence spectrum below)

Lutetium complex: no fluorescence

Terbium complex: green fluorescence (see the fluorescence spectrum below)

Mixture of europium and terbium complex: yellow fluorescence



- P4.7**
- Red dots, red stars and red door on the banknote : Europium complex
  - Green stars, green background and green flag: Terbium complex
  - Yellow stars on the little flag: mixture of Europium and Terbium complexes

## PRACTICAL PROBLEM P5

### Protecting the vineyard

In order to protect grapes against the mildew, French wine-growers in the area of Bordeaux (south- west of France) developed the so-called “Bordeaux mixture”, which they spread around the vines. The Bordeaux mixture is composed of copper (II) sulfate  $\text{CuSO}_4$  and slacked lime  $\text{Ca(OH)}_2$ . The goal of this problem is to determine the copper content of the Bordeaux mixture provided.



*Vineyard treated with the “Bordeaux mixture”*

*Picture from Pg1945, under CC BY-SA 3.0 license (Wikipedia page “Bordeaux mixture”)*

### Chemicals

- Bordeaux mixture
- Standardized potassium iodate ( $\text{KIO}_3$ ) solution,  $c = 0.001600 \text{ mol dm}^{-3}$
- Sodium thiosulfate ( $\text{Na}_2\text{S}_2\text{O}_3$ ) solution,  $c = 0.0200 \text{ mol dm}^{-3}$
- Potassium iodide (KI)
- Sulfuric acid ( $\text{H}_2\text{SO}_4$ ),  $c = 1 \text{ mol dm}^{-3}$
- Ammonia ( $\text{NH}_3$ ) solution,  $c = 1 \text{ mol dm}^{-3}$
- Standardized copper (II) sulfate ( $\text{CuSO}_4$ ) solution,  $c = 0.02000 \text{ mol dm}^{-3}$
- Deionized water

### Glassware and equipment

- 1 Laboratory stand with burette clamp
- 1 Erlenmeyer flask,  $250 \text{ cm}^3$
- 1 Filter paper
- 1 Transfer funnel

- 3 Titration flasks, 250 cm<sup>3</sup>
- 1 Weighing balance (0.1 mg)
- 1 Burette, 25 cm<sup>3</sup>
- 1 Volumetric flask (with stopper), 250 cm<sup>3</sup>
- 1 Volumetric pipette, 20 cm<sup>3</sup>
- 3 Graduated pipettes, 5 cm<sup>3</sup>
- 1 Graduated cylinder, 50 cm<sup>3</sup>
- 1 Graduated cylinder, 10 cm<sup>3</sup>
- 3 Weighing dishes
- 1 Spatula
- Aluminum foil
- Beakers, 100 cm<sup>3</sup> (for transfers)
- 1 Spectrophotometer (calibrated at 610 nm)
- 1 UV-vis plastic absorption cuvette ( $l = 1.0$  cm)
- 1 Test tube stand
- 7 Test tubes, 15 cm<sup>3</sup>
- 7 Plastic Pasteur pipettes, 2 - 3 cm<sup>3</sup>
- 1 Pipetting bulb Beakers (for transfers)

### Procedure for the iodometric titration of copper

1. Weigh accurately *ca.* 1 g of Bordeaux mixture (record the mass). Transfer it to the 250 cm<sup>3</sup> Erlenmeyer flask. Add *ca.* 50 cm<sup>3</sup> of deionized water and 5 cm<sup>3</sup> of sulfuric acid ( $c = 1$  mol dm<sup>-3</sup>). Swirl the Erlenmeyer flask for 5 minutes (the color of the solution does not change anymore).
2. Using a filter paper and a transfer funnel, transfer the solution into the 250 cm<sup>3</sup> volumetric flask. Carefully rinse the Erlenmeyer flask and the filter paper into the volumetric flask. Fill the flask with deionized water. Homogenize the solution, which is called SBM.
3. Fill the burette with the sodium thiosulfate solution ( $c = 0.0200$  mol dm<sup>-3</sup>).
4. Transfer 20.00 cm<sup>3</sup> of the standardized potassium iodate solution ( $c = 0.001600$  mol dm<sup>-3</sup>) to a 250 cm<sup>3</sup> titration flask. Add 2 g of potassium iodide, 25 cm<sup>3</sup> of deionized water and 10 cm<sup>3</sup> of sulfuric acid solution ( $c = 1$  mol dm<sup>-3</sup>). Swirl until all potassium

iodide gets dissolved. Stopper the titration flask and let it stand in the dark (using aluminum foil or in a cabinet) for 5 minutes.

5. Titrate using the sodium thiosulfate solution ( $0.0200 \text{ mol dm}^{-3}$ ). Record the titration volume  $V_1$ . Repeat the titration as needed.
6. Using a  $20 \text{ cm}^3$  volumetric pipette, transfer  $20 \text{ cm}^3$  of solution SBM into a  $250 \text{ cm}^3$  titration flask. Add  $5 \text{ cm}^3$  of sulfuric acid solution ( $c = 1 \text{ mol dm}^{-3}$ ) and 5 g of potassium iodide. Swirl until all potassium iodide gets dissolved. Stopper the titration flask and let it stand in the dark (using aluminum foil or in a cabinet) for 5 minutes.
7. Titrate using the sodium thiosulfate solution ( $c = 0.0200 \text{ mol dm}^{-3}$ ). Record the titration volume  $V_2$ .

### Analysis

8. Write down the equations for all the reactions occurring during the standardization of sodium thiosulfate.
9. Calculate the exact molar concentration of the sodium thiosulfate solution.
10. Write down the equations for all the reactions occurring during the iodometric titration of copper (preparation and titration) in solution SBM.
11. Determine the molar concentration of copper in the solution SBM.
12. Calculate the mass percentage of copper in the Bordeaux mixture.

### Spectrophotometric determination of copper

To confirm the results obtained by iodometry, a spectrophotometric determination of copper as its ammine complex is performed. A known amount of copper is mixed with an excess of ammonia solution.

Tube #	0	1	2	3	4	5	Bordeaux
copper (II) sulfate solution ( $c = 0.0200 \text{ mol dm}^{-3}$ )	$0.0 \text{ cm}^3$						$0.0 \text{ cm}^3$
ammonia solution ( $c = 1 \text{ mol dm}^{-3}$ )	$5.0 \text{ cm}^3$						$5.0 \text{ cm}^3$

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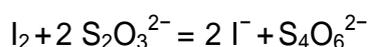
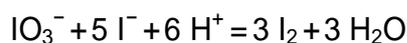
Deionized water	5.0 cm <sup>3</sup>						0.0 cm <sup>3</sup>
Solution SBM	0.0 cm <sup>3</sup>	5.0 cm <sup>3</sup>					

13. Using the calculated concentration for the solution SBM (question 11), fill the previous table with volumes that can be used to create a calibration scale for copper.
  14. Prepare all these solutions (0 to 5 and "Bordeaux") in test tubes, using graduated pipettes for transfers.
  15. Record the absorbance value  $A$  for each solution, at 610 nm.
  16. Plot the absorbance value  $A$  versus the molar concentration of copper in each tube (0 to 5).
  17. Using this plot, determine the molar concentration of copper in the solution SBM.
  18. Calculate the mass percentage of copper in the Bordeaux mixture. Compare with the iodometric determination.
-

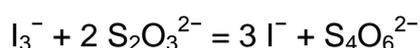
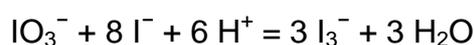
**SOLUTION OF PRACTICAL PROBLEM P5**

A fake Bordeaux mixture can be prepared by mixing the same mass of anhydrous copper sulfate  $\text{CuSO}_4$  and calcium hydroxide  $\text{Ca}(\text{OH})_2$ . The weight percentage of copper in this solid mixture is around 20 %.

**P5.8** Standardization of sodium thiosulfate:



or



Further calculations will be performed considering  $\text{I}_2$ .

**P5.9** Iodate  $\text{IO}_3^-$  is the limiting reactant in the comproportionation leading to iodine.

$$n(\text{I}_2) = 3 n(\text{IO}_3^-)$$

$$n(\text{I}_2) = 3 c(\text{IO}_3^-) \times V(\text{IO}_3^-)$$

$$n(\text{I}_2) = 3 \times 0.001600 \text{ mol dm}^{-3} \times 20.00 \text{ cm}^3$$

$$n(\text{I}_2) = 0.09600 \text{ mmol}$$

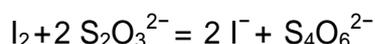
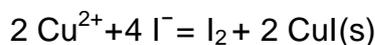
Let us take  $V_1 = 9.80 \text{ cm}^3$  as a typical value for  $V_1$ . At the equivalence point:

$$n(\text{S}_2\text{O}_3^{2-}) = 2 n(\text{I}_2)$$

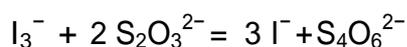
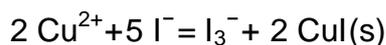
$$c(\text{S}_2\text{O}_3^{2-}) \times V_1 = 2 n(\text{I}_2)$$

$$c(\text{S}_2\text{O}_3^{2-}) = 2 n(\text{I}_2) / V_1 = (2 \times 0.09600 \text{ mmol}) / 9.80 \text{ cm}^3 = 0.0196 \text{ mol dm}^{-3}$$

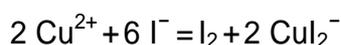
**P5.10** Iodometric titration of copper in **S<sub>BM</sub>**.

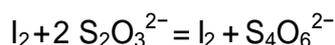


or

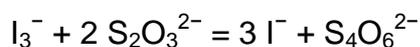
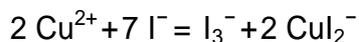


or





or



With high iodide concentration copper(I) iodide  $CuI$  is dissolved as  $CuI_2^-$ .

Further calculations will be performed considering  $I_2$ .

**P5.11** The reduction of copper(II) is quantitative:

$$n(Cu^{2+}) = 2 n(I_2)$$

Let us take  $V_2 = 12.45 \text{ cm}^3$  as a typical value for  $V_2$ . At the equivalence point:

$$2 n(I_2) = n(S_2O_3^{2-})$$

$$n(Cu^{2+}) = n(S_2O_3^{2-})$$

$$c(Cu^{2+}) \times V(Cu^{2+}) = c(S_2O_3^{2-}) \times V_2$$

$$c(Cu^{2+}) = \frac{c(S_2O_3^{2-}) \times V_2}{V(Cu^{2+})} = \frac{0.0196 \text{ mol dm}^{-3} \times 12.45 \text{ cm}^3}{20.00 \text{ cm}^3}$$

$$c(Cu^{2+}) = 0.0122 \text{ mol dm}^{-3}$$

**P5.12** The mass  $m_{Cu}$  of copper in the  $250 \text{ cm}^3$  of  $S_{BM}$  solution is:

$$m(Cu) = c(Cu^{2+}) \times M(Cu) \times V_{S_{BM}}$$

$$m(Cu) = 0.0122 \text{ mol dm}^{-3} \times 63.55 \text{ g mol}^{-1} \times 250 \text{ cm}^3$$

$$m(Cu) = 194 \text{ mg}$$

Assuming that  $m_{BM} = 1.000 \text{ g}$  of Bordeaux Mixture was weighed in step 1., the mass percentage %Cu is:

$$\%Cu = 100 \times [m(Cu) / m_{MB}]$$

$$\%Cu = 100 \times [194 \text{ mg} / 1.000 \text{ g}]$$

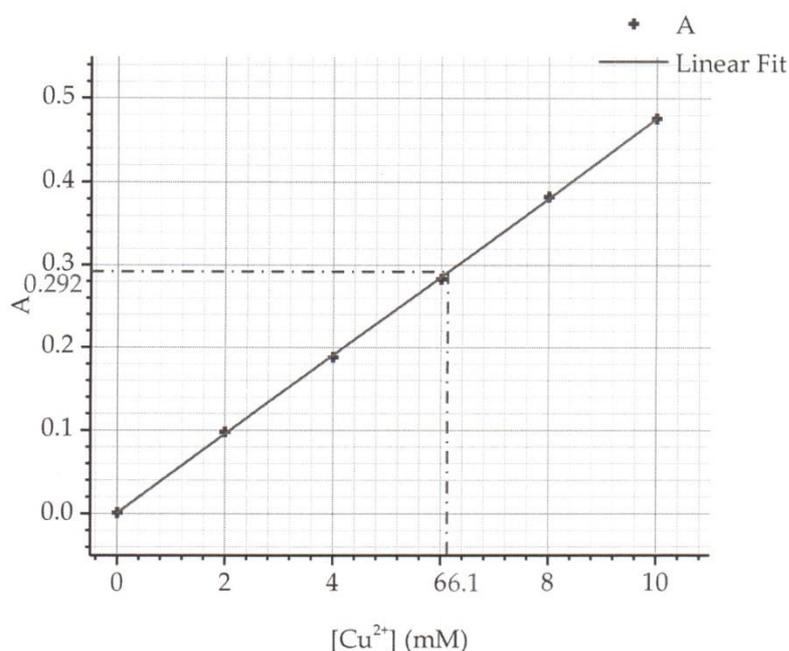
$$\%Cu = 19.4$$

**P5.13** Copper(II) concentration in  $S_{BM}$  was found to be  $c(Cu^{2+}) = 0.0122 \text{ mol dm}^{-3}$ . A standardized copper(II) solution ( $0.0200 \text{ mol dm}^{-3}$ ) is provided. In order to have absorbance values around the one of "Bordeaux" test tube, the following volumes may be used:

Tube #	0	1	2	3	4	5	Bordeaux
copper sulfate solution ( $c = 0.0200 \text{ mol dm}^{-3}$ )	$0 \text{ cm}^3$	$1.0 \text{ cm}^3$	$2.0 \text{ cm}^3$	$3.0 \text{ cm}^3$	$4.0 \text{ cm}^3$	$5.0 \text{ cm}^3$	$0 \text{ cm}^3$
ammonia solution ( $c = 1 \text{ mol dm}^{-3}$ )	$5.0 \text{ cm}^3$						
Deionized water	$5.0 \text{ cm}^3$	$4.0 \text{ cm}^3$	$3.0 \text{ cm}^3$	$2.0 \text{ cm}^3$	$1.0 \text{ cm}^3$	$0 \text{ cm}^3$	$0 \text{ cm}^3$
Solution <b>SBM</b>	$0 \text{ cm}^3$	$5.0 \text{ cm}^3$					
Copper(II) concentration in the tube in $\text{mmol} \cdot \text{dm}^{-3}$	0	2.0	4.0	6.0	8.0	10.0	6.1 (estimated)
Absorbance (at 610 nm)	0.001	0.098	0.188	0.283	0.383	0.476	0.292

**P5.17** The plot  $A = f([\text{Cu}^{2+}])$  is shown hereafter.

The plot  $A = f([\text{Cu}^{2+}])$  is linear. The determination of  $[\text{Cu}^{2+}]$  concentration in the tube **Bordeaux** is performed by reporting the absorbance value of 0.292 on the linear fit. We found that  $[\text{Cu}^{2+}] = 6.1 \text{ mmol dm}^{-3}$  in the tube **Bordeaux**. Given that the tube is obtained by dilution with a factor of 2 from the **SBM** solution, we find that:  $[\text{Cu}^{2+}]_{\text{SBM}}^{\text{spectro}} = 0.0122 \text{ mol dm}^{-3}$



**P5.18** Using the calculation as in question 12., we found:

$$m_{\text{Cu}}^{\text{spectro}} = c_{\text{Cu}^{2+}} \times M_{\text{Cu}} \times V_{\text{S}_{\text{BM}}}$$

$$m_{\text{Cu}}^{\text{spectro}} = 0.0122 \text{ mol dm}^{-3} \times 63.55 \text{ g mol}^{-1} \times 250 \text{ cm}^3$$

$$m_{\text{Cu}}^{\text{spectro}} = 194 \text{ mg}$$

Assuming that  $m_{\text{BM}} = 1.000 \text{ g}$  of Bordeaux Mixture was weighed in step 1, the mass percentage  $\% \text{Cu}^{\text{spectro}}$  is:

$$\% \text{Cu}^{\text{spectro}} = 100 \times (m_{\text{Cu}} / m_{\text{BM}}) = 100 \times (194 \text{ mg} / 1.000 \text{ g}) = 19.4$$

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## PRACTICAL PROBLEM P6

### Equilibrium constant determination

pH indicators are often used in colorimetric titrations of acids and bases. The key point when choosing an indicator is to find one having a  $pK_a$  close to the pH at the equivalence point. Therefore, it is very important to know accurately the  $pK_a$  of such acid/base couples.

Fortunately, pH indicators have very high absorption coefficients (usually  $\epsilon > 10^4 \text{ cm}^{-1} \text{ dm}^3 \text{ mol}^{-1}$ ). UV-visible spectroscopy can be used to determine such constants.



*Various pH indicators*

*Picture from TheChimist, under CC BY-SA 3.0 license  
(Wikipedia page "Potentiel hydrogène")*

The goal of this task is to determine the  $pK_a$  of bromophenol blue (BPB) using UV-vis spectroscopy.

### Chemicals

- Bromophenol blue (BPB)
- mixed solution of hydrochloric acid ( $c = 0.2 \text{ mol dm}^{-3}$ ) and acetic acid ( $c = 1 \text{ mol dm}^{-3}$ ) (called HCl/CH<sub>3</sub>COOH mixture)
- sodium acetate solution ( $c = 1 \text{ mol dm}^{-3}$ )
- Ethanol, 95 %
- Deionized water

### Glassware and equipment

- 1 Weighing balance (0.1 mg)

- 2 Volumetric flasks (with stopper), 250 cm<sup>3</sup>
- 1 Volumetric flask (with stopper), 100 cm<sup>3</sup>
- 1 Volumetric pipette, 5 cm<sup>3</sup>
- 1 Graduated pipette, 10 cm<sup>3</sup>
- 1 Weighing dish
- 1 Spatula
- Beakers, 100 cm<sup>3</sup> (for transfers)
- 1 Spectrophotometer (calibrated at 590 nm)
- 1 UV-vis plastic absorption cuvette ( $l = 1.0$  cm)
- 1 Test tube stand
- 7 Test tubes, 15 cm<sup>3</sup>
- 7 Plastic Pasteur pipettes, 2 - 3 cm<sup>3</sup>
- 1 Pipetting bulb
- 1 pH-meter with pH-probe (calibrated in the acidic domain)
- Beakers (for transfers)

### Procedure

1. Weigh ca. 0.100 g of Bromophenol Blue. Transfer it to a 100 cm<sup>3</sup> volumetric flask using 95% ethanol. Dissolve the Bromophenol Blue with 95% ethanol. Homogenize the solution, which is called S0,BPB.
2. Using a volumetric pipette, transfer 5.00 cm<sup>3</sup> of S0,BPB into a 250 cm<sup>3</sup> volumetric flask. Fill the flask with the mixture of hydrochloric acid and acetic acid provided. Homogenize the solution, which is called SA,BPB.
3. Using a volumetric pipette, transfer 5.00 cm<sup>3</sup> of S0,BPB into a 250 cm<sup>3</sup> volumetric flask. Fill the flask with the sodium acetate solution ( $c = 1$  mol dm<sup>-3</sup>). Homogenize the solution, which is called SB,BPB.
4. For each column in the following table, prepare the solution in a test tube using the volumes reported in the table. The stock solutions are to be transferred with graduated pipettes.

Tube #	1	2	3	4	5	6	7
SA,BPB	0.0 cm <sup>3</sup>	5.0 cm <sup>3</sup>	6.0 cm <sup>3</sup>	7.0 cm <sup>3</sup>	8.0 cm <sup>3</sup>	8.5 cm <sup>3</sup>	10.0 cm <sup>3</sup>
SB,BPB	10.0 cm <sup>3</sup>	5.0 cm <sup>3</sup>	4.0 cm <sup>3</sup>	3.0 cm <sup>3</sup>	2.0 cm <sup>3</sup>	1.5 cm <sup>3</sup>	0.0 cm <sup>3</sup>
pH							
Absorbance <i>A</i> (at 590 nm)							

- Using the pH-meter, record the pH of each tube.
- Record the absorbance value *A* for each solution (1 to 7) at 590 nm.

### Analysis

- Explain why the analytical concentration of BPB is identical in all tubes. This concentration will be referred to as (BPB).
- Draw the plot of the absorbance *A* with respect to the pH.
- Using the plot and assuming hypothesis to be verified, determine the molar absorption coefficients ( $\epsilon(\text{HInd})$  and  $\epsilon(\text{Ind}^-)$ ) of the acidic form HInd and the basic form Ind of BPB as function of  $c(\text{BPB})$ .
- Derive the equation giving the absorbance *A* of the solution as a function of the  $\epsilon(\text{HInd})$ ,  $\epsilon(\text{Ind}^-)$ ,  $c(\text{BPB})$  and the molar concentrations  $[\text{HInd}]$  and  $[\text{Ind}^-]$ .
- Using the Henderson-Hasselbalch equation, derive the equation of the absorbance *A* for  $\text{pH} = \text{p}K_a$ .
- Using the plot of  $A = f(\text{pH})$ , determine the value of the  $\text{p}K_a$  of BPB.

## SOLUTION OF PRACTICAL PROBLEM P6

**P6.7** Solutions  $\mathbf{S}_{A,BPB}$  and  $\mathbf{S}_{B,BPB}$  are both prepared by the same dilution of  $\mathbf{S}_{0,BPB}$  (dilution factor of 50). Therefore, the analytical concentration of BPB in  $\mathbf{S}_{A,BPB}$  and in  $\mathbf{S}_{B,BPB}$  are the same. Each tube is prepared by mixing only  $\mathbf{S}_{A,BPB}$  and  $\mathbf{S}_{B,BPB}$ . Therefore, the analytical concentration of BPB in each tube is the same as its value in  $\mathbf{S}_{A,BPB}$  and  $\mathbf{S}_{B,BPB}$ :  $c_{BPB}$ .

**P6.8** The results are presented in the following table.

Tube #	1	2	3	4	5	6	7
$\mathbf{S}_{A,BPB}$	0.0 cm <sup>3</sup>	5.0 cm <sup>3</sup>	6.0 cm <sup>3</sup>	7.0 cm <sup>3</sup>	8.0 cm <sup>3</sup>	8.5 cm <sup>3</sup>	10.0 cm <sup>3</sup>
$\mathbf{S}_{B,BPB}$	10.0 cm <sup>3</sup>	5.0 cm <sup>3</sup>	4.0 cm <sup>3</sup>	3.0 cm <sup>3</sup>	2.0 cm <sup>3</sup>	1.5 cm <sup>3</sup>	0.0 cm <sup>3</sup>
pH	8.48	4.43	4.21	4.00	3.63	3.39	1.44
Absorbance A (at 590 nm)	2.33	1.92	1.72	1.40	0.89	0.59	0.01

The data are presented in the following graphs.

**P6.9** In tube 1, the mixture is basic enough to exhibit only the absorption of  $\text{Ind}^-$ :

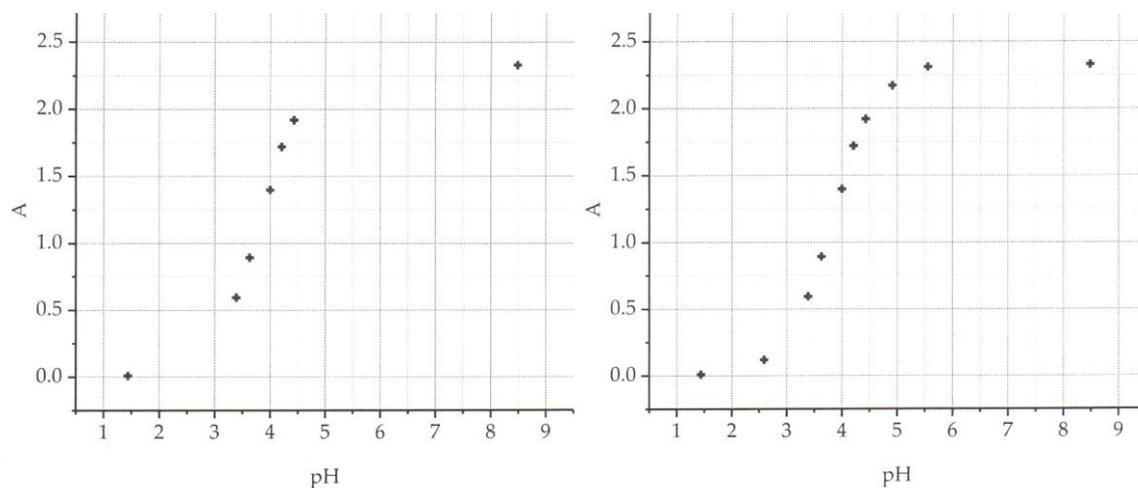
$[\text{Ind}^-] \approx c_{BPB}$  and  $[\text{HInd}]$  is negligible.

Therefore:  $A_1 \approx \varepsilon_{\text{Ind}^-} \cdot l \cdot c_{BPB}$ .

In tube 7, the mixture is acidic enough to exhibit only the absorption of  $\text{HInd}$ :

$[\text{HInd}] \approx c_{BPB}$  and  $[\text{Ind}^-]$  is negligible. Therefore:  $A_7 \approx \varepsilon_{\text{HInd}} \cdot l \cdot c_{BPB}$ .

At the end of the problem, one should compare the  $pK_a$  value to the pH value in tube 1 and tube 7 to check these hypotheses.



Left: Data obtained from tube 1 to 7. Right: with extra points using different ratio of  $S_{A,BPB}$  and  $S_{B,BPB}$

**P6.10** At any pH:

$$A = \epsilon_{\text{HInd}} l [\text{HInd}] + \epsilon_{\text{Ind}^-} l [\text{Ind}^-]$$

$$A = \epsilon_{\text{HInd}} l c_{\text{BPB}} \times \frac{[\text{HInd}]}{c_{\text{BPB}}} + \epsilon_{\text{Ind}^-} l c_{\text{BPB}} \times \frac{[\text{Ind}^-]}{c_{\text{BPB}}}$$

$$A = A_7 \times \frac{[\text{HInd}]}{c_{\text{BPB}}} + A_1 \times \frac{[\text{Ind}^-]}{c_{\text{BPB}}}$$

**P6.11** The Henderson-Hasselbalch equation is:

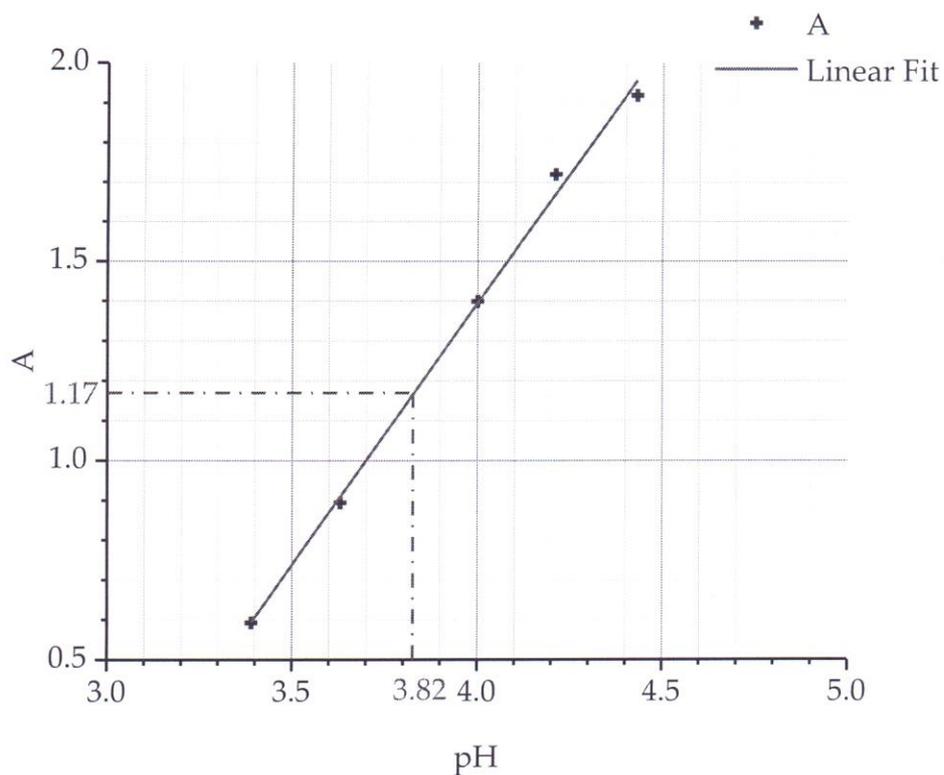
$$\text{pH} = \text{p}K_a + \log \frac{[\text{Ind}^-]}{[\text{HInd}]}$$

At  $\text{pH} = \text{p}K_a$ :  $[\text{Ind}^-] = [\text{HInd}] = \frac{1}{2} c_{\text{BPB}}$

Therefore:

$$A_{\text{pH} = \text{p}K_a} = \frac{A_1 + A_7}{2} = \frac{0.01 + 2.33}{2} = 1.17$$

**P6.12** To get a better graphical determination, the following graph shows a close-up in the central values.



The graphical determination leads to a  $pK_a$  value of 3.82. The literature data report a value around 3.85 at 25 °C.

Given that the pH in tube 1 and 7 is at least two units far from the  $pK_a$ , the hypotheses in question 9 are valid.