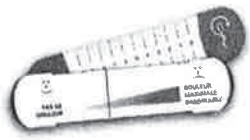
CHEMISTRY 1

Final exam (3 hours)

Caution: marking is for information only: 40 points + 1 bonus point



No document allowed. Only « collège » type calculators are authorized.
The four different problems are independent. Every answer must be justified.

A pain killer exam !!

Morphine is a potent analgesic, used in acute or chronic pain syndromes. It was discovered simultaneously in 1804 by Seguin and Courtois. Later, Sertürner, a young German pharmacist, discovered that this isolated crystalline substance was an alkaloid. He named it morphium because its biological effects reminded him the god of dreams of the ancient Greeks, Morpheus. Such as morphine, codeine (or methylmorphine) is one of the alkaloids present in opium poppy (*Papaver somniferum*). It is used as an analgesic and as an antitussive agent. It was isolated for the first time in 1832 by the French chemist Robiquet and was named after the Greek name of the poppy flower head: kôdé.

Data: $e = 1.602 \times 10^{-19}$ C $c = 2.998 \times 10^{8}$ m.s^{-1} $h = 6.626 \times 10^{-34}$ J.s
$N_A = 6.022 \times 10^{23}$ mol^{-1} $R_H = 109678.8$ cm^{-1} $m_e = 9.11 \times 10^{-31}$ kg
Rydberg constant will be considered as valid for any hydrogen-like ions.

Atom	H	C	N	O	S	K	Mn	Fe	Ni	Cu	Zn	Ga	Br
Z	1	6	7	8	16	19	25	26	28	29	30	31	35
M (g.mol^{-1})	1.000	12.00	14.00	16.00	32.00	39.00	54.90	55.85	58.70	63.50	65.40	69.72	79.90
χ	2.1	2.5	3.0	3.5	2.5	0.8	1.5	1.8	1.8	1.9	1.6	1.6	2.8

	Fe	Ni	Cu	Zn	Ga
E_K (eV)	-7112	-8333	-8979	-9659	-10368
$E_{L2,3}$ (eV)	-715.8				-1137
$E_{M2,3}$ (eV)	-52.70	-66.70	-77.50	-89.60	-111.7

I) Crystal structure of morphine

This compound was studied by X-ray scattering at 173 K using an X-ray beam with a wavelength of λ=1.542 Å, corresponding to the $KL_{2,3}$ ray of the anticathode.

I.A - Production of X-rays *(5 points)*

Three elements can be used as anticathode: nickel (Ni), copper (Cu) or zinc (Zn). At first, we wish to study the X-ray beam used to analyze the crystalline structure of morphine.

1) Compute the $KL_{2,3}$ wavelengths emitted by anticathodes made of either nickel, copper or zinc. Deduce the element used as anticathode in this scattering experiment.
2) Give the electronic configuration of the element constituting the anticathode.
3) A nickel foil is placed in the path of the beam arising from the anticathode. Give the thickness of the nickel foil in microns that leads to an attenuation rate of 99.9% of the $KM_{2,3}$ line. For the anticathode's $KM_{2,3}$ line, the linear absorption coefficient of nickel is μ_{Ni}=2447.5 cm^{-1}.
4) The study of morphine crystals requires a monochromatized beam. How can we get it? Justify your answer using a scheme.

5) What electrical potential difference needs to be applied to observe the $KL_{2,3}$ line of nickel? Same question for the $KM_{2,3}$ line of nickel?

I.B – Cristalline structure of Zinc *(3.75 points)*

Zinc (Zn) crystallizes in a hexagonal close packed structure where atoms are tangent along the edges of the base. An additional atom is inserted into the cell at the reduced coordinates (2/3, 1/3, 1/2) associated with this cell. This atom is tangent with 3 atoms of the diamond base ("base losange"). Its atomic radius is 1.390 Å.

1) Give the Bravais lattice of this system and the composition of the motif.
2) Give the definition of the coordination number of an atom. Give its value for a Zinc atom in this particular crystal structure.
3) Determine the hexagonal unit-cell parameters (to within 10^{-3} Å) knowing that the c/a ratio equals $2\sqrt{2/3}$ for such structure.
4) One of the tetrahedral holes has (2/3, 1/3, 1/8) as reduced coordinates. **Compute** the $\frac{r_X}{R_{Zn}}$ ratio in which r_X is theoretically maximum value for the radius of the X atom to be inserted in such holes without distortion of the parent lattice.

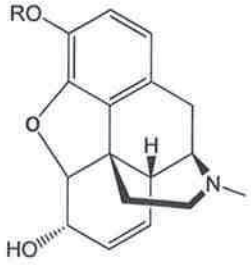
I.C – Study of the cristalline structure of morphine *(9 points)*

Morphine (see scheme in part II) possesses the following brut formula: $C_{17}H_{19}NO_3$. It crystallizes in the orthorhombic system. A crystallographic analysis allowed us to identify some diffraction lines:

d (Å)	6,5888	4,5800	5,9410	3,7068	3,2036	2,4746	2,9425
h, k, l	1 1 0	0 0 3	1 1 1	2 0 1	2 2 1	3 1 1	1 4 0

1) Give the possible Bravais lattices for this system.
   For each of them, give the existing conditions related to the Miller indices.
2) What are the symmetry axes which characterize the orthorhombic system? Draw them on a scheme.
3) Using the above table, compute to within 10^{-3} Å the a, b and c cell parameters of the orthorhombic unit-cell.
4) Give the diffraction angle corresponding to the (005) family.
5) Knowing that the orthorhombic unit-cell contains 4 molecules of morphine, compute the density of the crystal (to within 10^{-2} g.cm^{-3}).
6) Give the Bravais lattice of morphine and the composition of the motif.
7) On two different schemes representing the unit-cell, draw the first planes of the following families: (110) and (221).

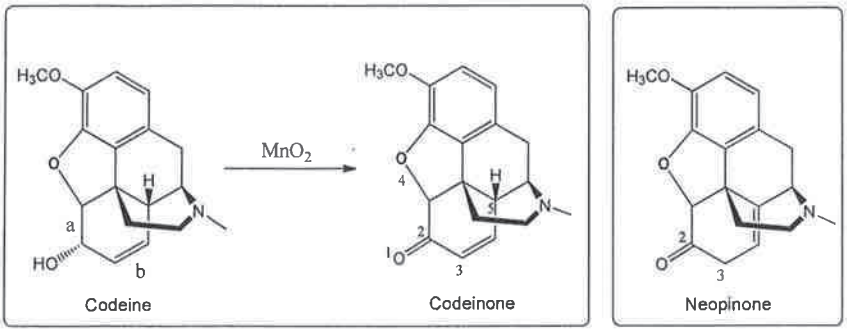
II) Morphine, codeine and derivatives



R = H Morphine
R = CH_3 Codeine

II.A Synthesis of codeinone from codeine

Many molecules derived from **morphine** and **codeine** have been synthesized in order to evaluate their analgesic properties. **Codeinone** is a key-intermediate for preparing the corresponding derivatives, and can be prepared from **codeine** through reaction with manganese dioxide **MnO_2**. In poppy plant, it has been demonstrated that an enzyme catalyses the biosynthesis of **codeine** starting from **neopinone**, an isomer of **codeinone**. The chemical structures of codeine, codeinone and neopinone are presentated below.



II.A.1 Preparation of MnO_2 *(7.25 points)*

MnO_2 can be prepared by the reaction of potassium permanganate (K^+, MnO_4^-) with manganese sulfate hydrated ((Mn^{2+}, SO_4^{2-}.)H_2O) in acidic medium.

1) Give the electronic structure of manganese (Mn).
2) Which period, group and block of the periodic table of elements does manganese belong to?
3) With the help of the oxidation number of the appropriate elements, specify the oxidized form and the reduced form for each couple involved in the following global redox reaction:
   $Mn^{2+} + MnO_4^- \rightarrow MnO_2$ (not well-balanced).
   Write the two-half reactions and then correctly balance the redox reaction above in acidic medium.
   The oxidation number of oxygen in each species equals –II.
4) Potassium permanganate is among the strongest oxidants used in chemistry. Nitric acid (HNO_3) and bromic acid ($HBrO_3$) are also oxidant acids or oxoacids.
   a) Write the Lewis structure for MnO_4^-, NO_3^- and BrO_3^-. Compare the N-O bond lengths together in the NO_3^- ion.
   b) Give the oxidation number of the central atom for all three ions.
   c) Give the geometry and the angle of the bonds around the central atom in the three cases.

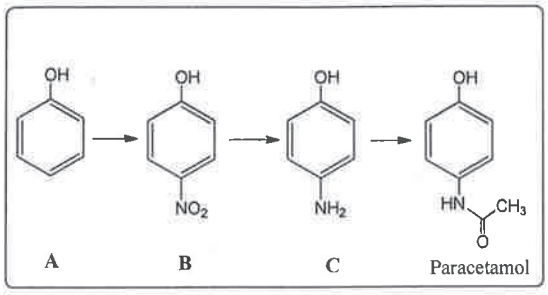
II.A.2 Reaction with codeine *(7 points)*

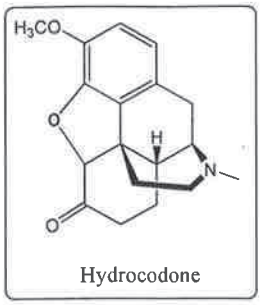
1) Represent on your copy the structure of **codeinone** including the non-bonding pairs of electrons.
2) Give the hybridization state of the atoms numbered from 1 to 5.
3) What is the approximate value of the bond angles around atoms 2 and 5, respectively?
4) In **codeine**, what are the type of bonds (σ and/or π) noted as "a" and "b" on the scheme? Specify the atomic orbitals involved in the formation of the corresponding bonds.
5) Qualifying your answer, compare together the lengths of the bond between carbon 2 and carbon 3 in **neopinone** and **codeinone**.
6) What is the name of the transformation leading from **codeinone** to **codeine**? And from **neopinone** to **codeinone**?

II.B Hydrocodone and paracetamol *(4 points)*

Oral **hydrocodone** is considered as less potent than oral **morphine**, but combining **paracetamol** with **hydrocodone** produce synergistic effect that strongly enforce the analgesic effect of the Vicodin® drug.

The chemical structures of the molecules formed as intermediates along the synthesis of **paracetamol** when starting from phenol (A) are presented below, as well as the structure of **hydrocodone**.





Phenol (A) is a weak acid. The pKa of the corresponding acid/base couple is pKa= 10.0.

1) Write the ionization reaction of **A** in water; define and express the acidity constant Ka.
2) Considering the acidity of the phenol group (i.e. aromatic alcohol), rank the acids **A**, **B**, **C** with respect to their pKa. Qualify your answer while using their mesomeric structures.
3) Identify the acid/base couple associated to **paracetamol** (pKa = 9.5). What is the major form for **paracetamol** (pKa = 9.5) when dissolved in pure water?

III) Hydrogen-like ions *(5 points)*

A hydrogen-like ion is excited by a photon, the energy of which is 852.6 eV. This excitation induces an electronic transition to the level n = 7.

1) To which phenomenon is related this experiment: absorption or emission? Give the departure and arrival levels of this transition.
2) Identify the hydrogen-like ion (explain your approach). Represent it under the form $_ZX^{n+}$.
3) Calculate the energy of the seven first levels corresponding to this hydrogen-like ion (to within 10^{-1}eV).
4) Represent these levels on a Grotrian's diagram.
5) Once this excitation is done, the hydrogen-like ion comes back to its fundamental state while emitting one or more photons. Give the number of possible transitions that are associated to the emitted photons, and represent them on the Grotrian's diagram.

FORM

Bragg's law : $2\,d_{hkl}\sin\theta = \lambda$ **Beer Lambert's law** : $I = I_0 \exp(-\mu x)$

Moseley's law : $\sqrt{\nu} = a(Z-b)$

Reticular distance :

$$\frac{1}{d_{hkl}^2} = \frac{\frac{h^2}{a^2}\sin^2\alpha + \frac{k^2}{b^2}\sin^2\beta + \frac{l^2}{c^2}\sin^2\gamma + \frac{2hk}{ab}(\cos\alpha\cdot\cos\beta - \cos\gamma)}{1-\cos^2\alpha-\cos^2\beta-\cos^2\gamma+2\cos\alpha\cdot\cos\beta\cdot\cos\gamma} + \frac{\frac{2kl}{bc}(\cos\beta\cdot\cos\gamma-\cos\alpha)+\frac{2lh}{ca}(\cos\gamma\cdot\cos\alpha-\cos\beta)}{1-\cos^2\alpha-\cos^2\beta-\cos^2\gamma+2\cos\alpha\cdot\cos\beta\cdot\cos\gamma}$$

Relation between E and λ : E(eV) = 12400 / λ (Å)

Slater's rule: contribution of the electrons localized in the n' orbital on the screen constant which applies on an electron localized in the orbital n are gathered in the following table:

Orbital of the electron	*n'<n*-1	*n'=n*-1	*n'=n*	*n'>n*
1s	-	-	0.30	0
ns,np	1.00	0.85	0.35	0
nd	1.00	1.00	1.00 for *s* and *p* 0.35 for *d*	0