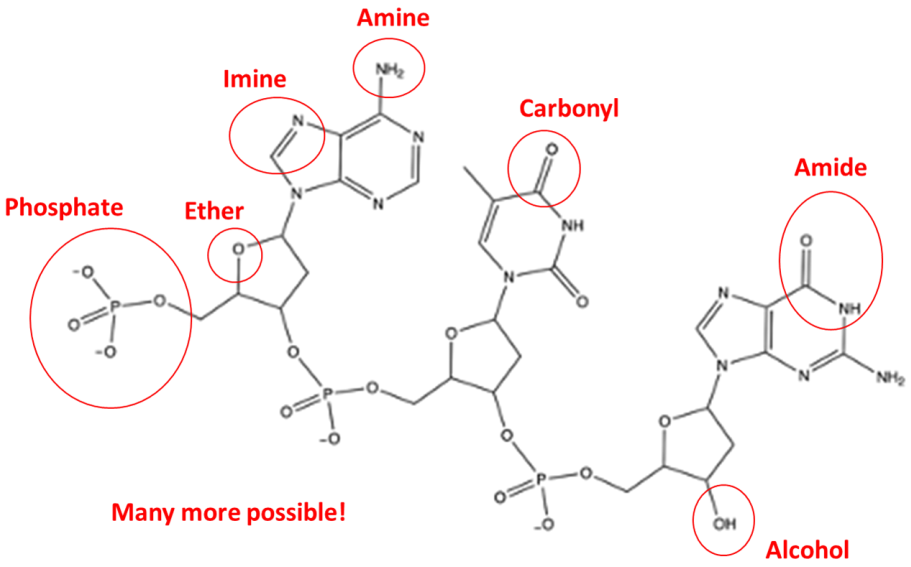
1.1. Functional Groups (2 points)

The 'start' codon ATG in DNA, which signals the beginning of protein translation - is shown below. Circle at least 4 unique functional groups and name them.

Le codon « start » ATG de l'ADN, qui signale le début de la traduction des protéines, est montré ci-dessous. Entourez au moins 4 groupes fonctionnels uniques et nommez-les.

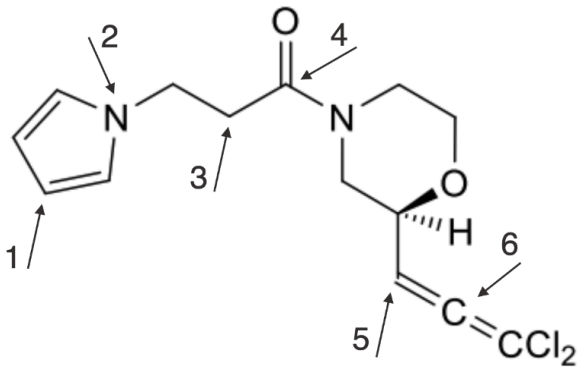


1.2. Hybridization (3 points)

Indicate the hybridization of all atoms marked by arrows.

Indiquez l'hybridation de tous les atomes marqués par des flèches.

0.5 points for each correct hybridization



1 sp2

2 sp2

3 sp3

4 sp2

5 sp2

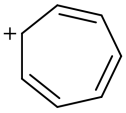
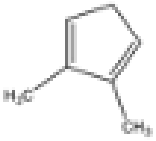
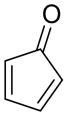
6 sp

1.3 Aromaticity (6 points)

Indicate for the following molecules whether they are aromatic, non-aromatic or antiaromatic according to the Hückel rule.

Indiquez pour les molécules suivantes si elles sont aromatiques, non-aromatiques ou antiaromatiques selon la règle de Hückel.

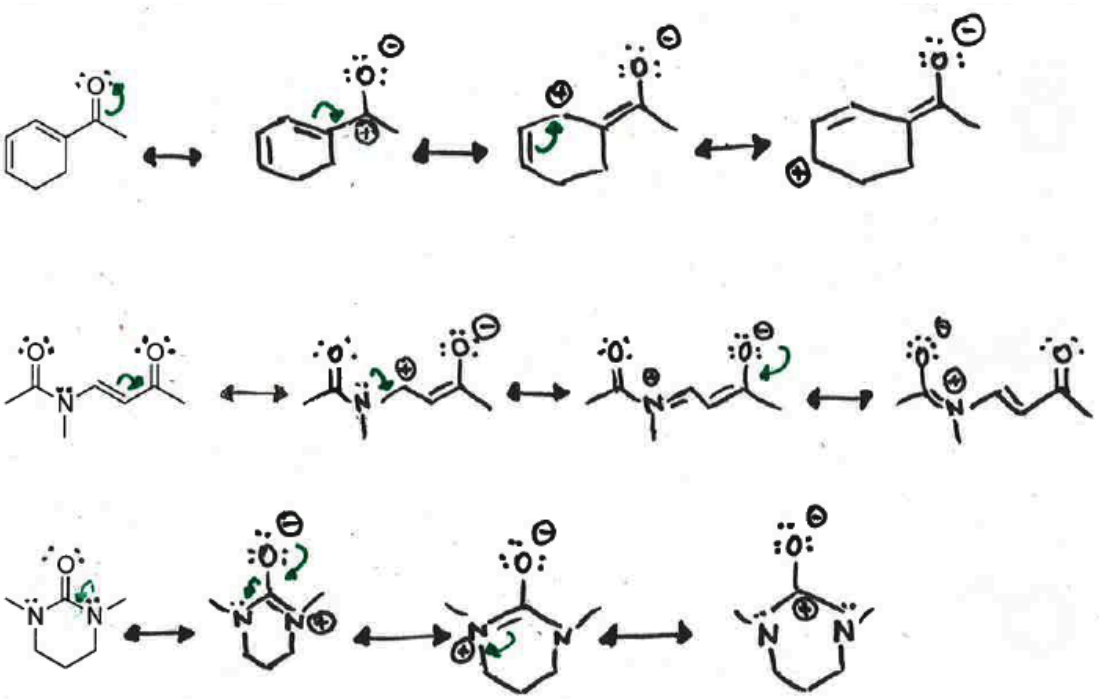
0.5 points per correct molecule

Molecule	Aromaticity?
	aromatic
	aromatic
	non-aromatic
	non-aromatic
	antiaromatic
	antiaromatic

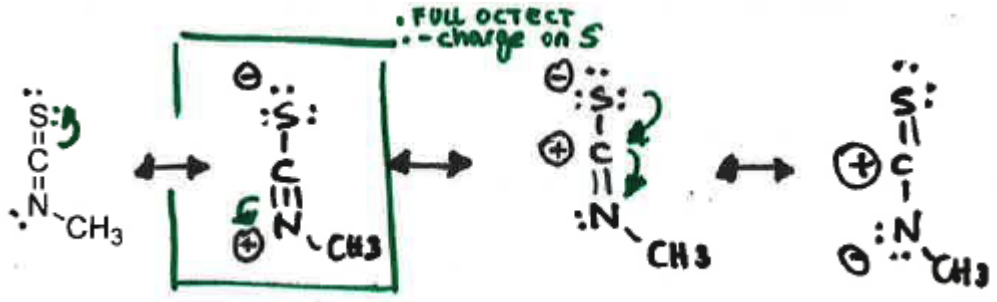
2. Resonance

2.1 Resonance structures (6 points)

a) Provide three additional reasonable resonance structures for the following compounds. *Proposez trois structures de résonance supplémentaires raisonnables pour les composés suivants.* (3 points)



b) Draw the Lewis structure of each resonance contributor for the following molecule and indicate the ones that contributes more to the resonance hybrid. *Dessinez la structure de Lewis de chaque contributeur de résonance pour la molécule suivante et indiquez ceux qui contribuent le plus à l'hybride de résonance.* (1.5 points)



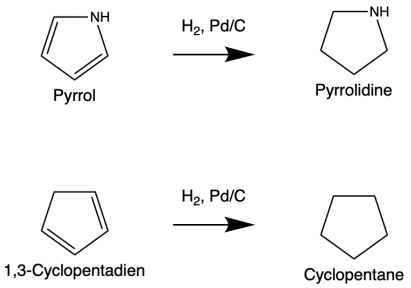
c) Create two reasonable resonance drawings for this molecule. Of the three which one contributes the least to the hybrid structure? *Créez deux dessins de résonance raisonnables pour cette molécule. Parmi les trois, lequel contribue le moins à la structure hybride ?* (1.5 points)

2.2 Resonance stabilization

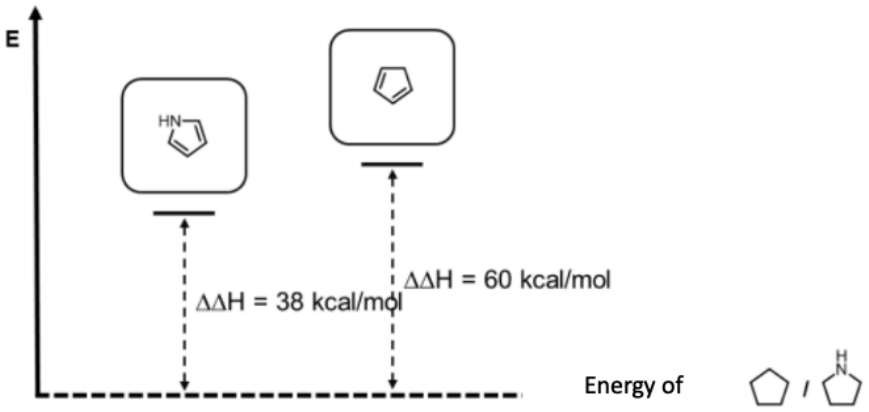
Describe an experiment that would be suitable to quantify the contribution of aromaticity to the energy (Enthalpy H) of a compound of your choice. Assume you can use calorimetry to measure the heat development of a reaction ΔH. Clearly state with a formula how you would derive the aromatic contribution to the enthalpy from your measurements.

Décrivez une expérience qui serait appropriée pour quantifier la contribution de l'aromaticité à l'énergie (enthalpie H) d'un composé de votre choix. Supposez que vous pouvez utiliser la calorimétrie pour mesurer la chaleur dégagée lors d'une réaction ΔH. Indiquez clairement avec une formule comment vous dériveriez la contribution aromatique à l'enthalpie à partir de vos mesures.

Hint: Recall the hydrogenation of Pyrrole and 1,3-Cyclopentadiene with Hydrogen (H_2) using Palladium on Carbon (Pd/C) as a catalyst:
Indice: Rappelez-vous de l'hydrogénation du pyrrole et du 1,3-cyclopentadiène avec de l'hydrogène (H_2) en utilisant le palladium sur carbone (Pd/C) comme catalyseur :



Estimate the heat development (ΔH) of these hydrogenations. Explain which factors you have taken into account and complete the diagram below.



Pyrrol:

ΔH

= + (2 x ΔH(C=C)) + (2 x ΔH(Hp//-H)) + aromatic stabilizaton – (4 x ΔH(C-H)) H

= + 2 x 66 kcal/mol + 2 x 104 kcal/mol + 22 kcal/mol – 4 x 100 kcal/mol

= – 38 kcal/mol

1,3-Cyclopentadien:

ΔH

= + (2 x ΔH(C=C)) + (2 x ΔH(H-H)) – (4 x ΔH(C-H)) H

= + 2 x 66 kcal/mol + 2 x 104 kcal/mol – 4 x 100 kcal/mol

= – 60 kcal/mol

ΔΔH = -60 kcal/mol - (-38 kcal/mol) = 22 kcal/mol = aromatic stabilizaton

3. Conformation & Stereochemistry

3.1. Stereochemistry (4 points)

a) What type of Isomers are the following compounds from one another? *Quel type d'isomères sont les composés suivants les uns par rapport aux autres?* (3 points)

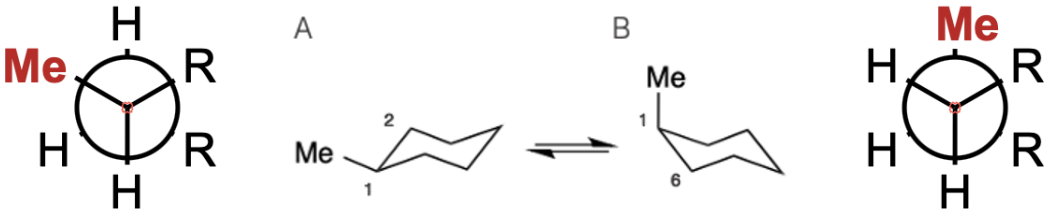
I) Enantiomers. The stereocenter on the right changes from R to S.
II) Diastereomers cis/trans isomers to be specific.
III) No isomers, these are the same compound.

b) Give the number of possible diastereomers of this compound. *Donnez le nombre de diastéréoisomères possibles de ce composé.* (1 point)

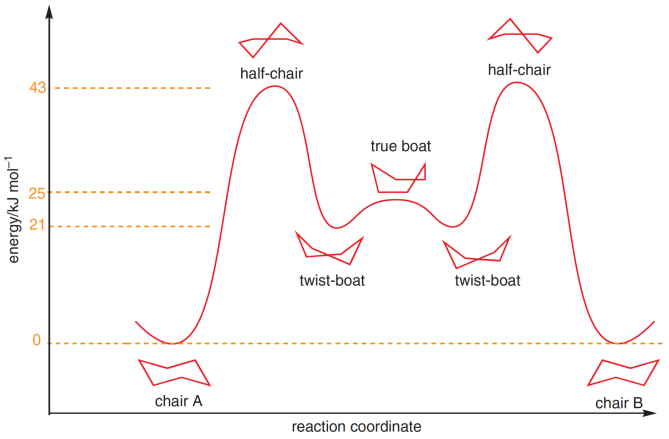
2 there is only one cis/trans isomer (center double bond).

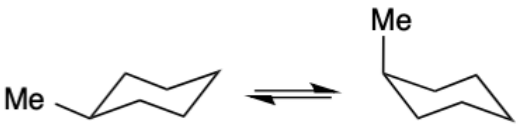
3.1 Conformation of cyclic organic molecules

a) Draw the Newman projections of both conformations of 1-methylcyclohexane along the bond (A: C1-C2, B: C6-C1). *Dessinez les projections de Newman des deux conformations de la 1-méthylcyclohexane le long des liaisons (A : C1-C2, B : C6-C1).* (2 points)



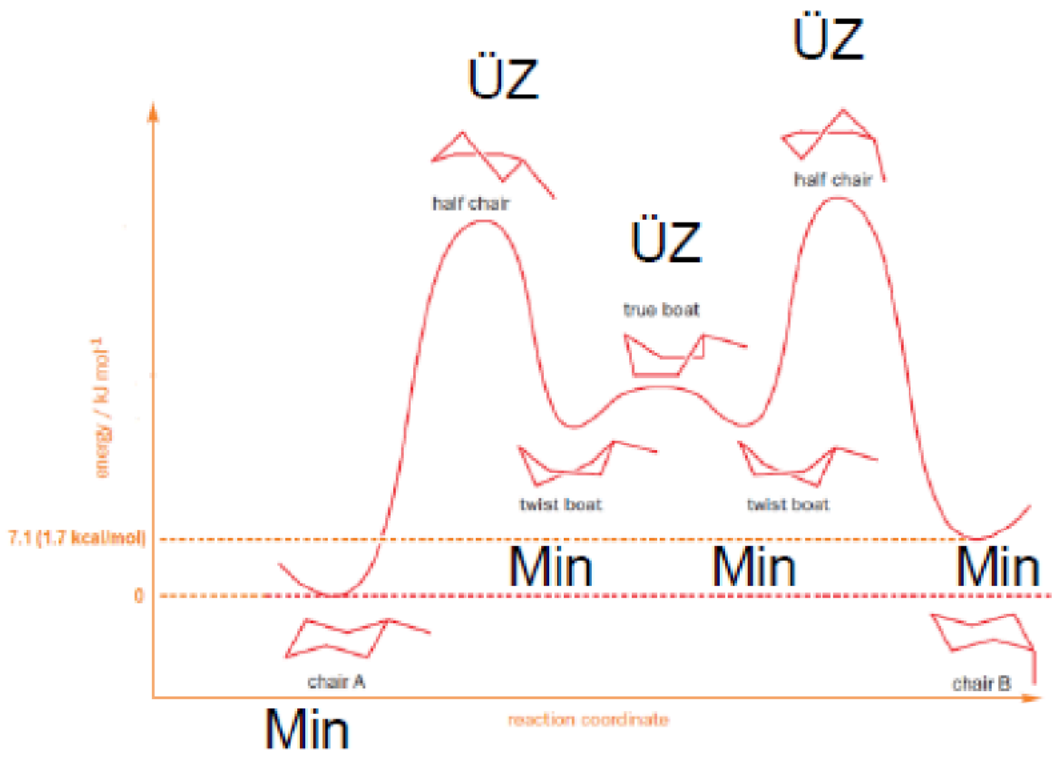
b) The energy diagram provided illustrates the "ring flip" process in cyclohexane. If we were to examine 1-methylcyclohexane instead, how would the energy levels of the two endpoints ‘chair A’ and ‘chair B’ differ? Sketch the energy diagram for 1-methylcyclohexene, paying particular attention to the two chair conformations, and discuss the key energy contributions that arise.
Le diagramme d'énergie fourni illustre le processus de "changement de chaise" dans le cyclohexane. Si nous devions examiner la 1-méthylcyclohexane à la place, comment les niveaux d'énergie des deux extrémités 'chaise A' et 'chaise B' différeraient-ils ? Esquissez le diagramme d'énergie pour la 1-méthylcyclohexane, en accordant une attention particulière aux deux conformations en chaise, et discutez des principales contributions énergétiques qui en découlent. (2 points)





The most stable conformation of methylcyclohexane is the chair conformation in which the methyl group is equatorial.

The conformer with the methyl group axial is 7.3 kJ mol−1 higher in energy than the conformer with the methyl group equatorial. This energy difference corresponds to a 20:1 ratio of equatorial:axial conformers at 25 °C.
There are two reasons why the axial conformer is higher in energy than the equatorial conformer. The first is that the axial conformer is destabilized by the repulsion between the axial group X and the two axial hydrogen atoms on the same side of the ring. This interaction is known as the 1,3-diaxial interaction. As the group X gets larger, this interaction becomes more severe and there is less of the conformer with the group axial. The second reason is that in the equatorial conformer the C–X bond is anti-periplanar to two C–C bonds, while, for the axial conformer, the C–X bond is synclinal (gauche) to two C–C bonds.



4. IR & NMR & MS

4.1. Mass Spectrometry (3.5 points)

a) From the spectra below indicate the m/z number corresponding to the base peak, the parent peak and the M+2 peak.
À partir des spectres ci-dessous, indiquez le numéro m/z correspondant au pic de base, au pic parent et au pic M+2 (1.5 points)

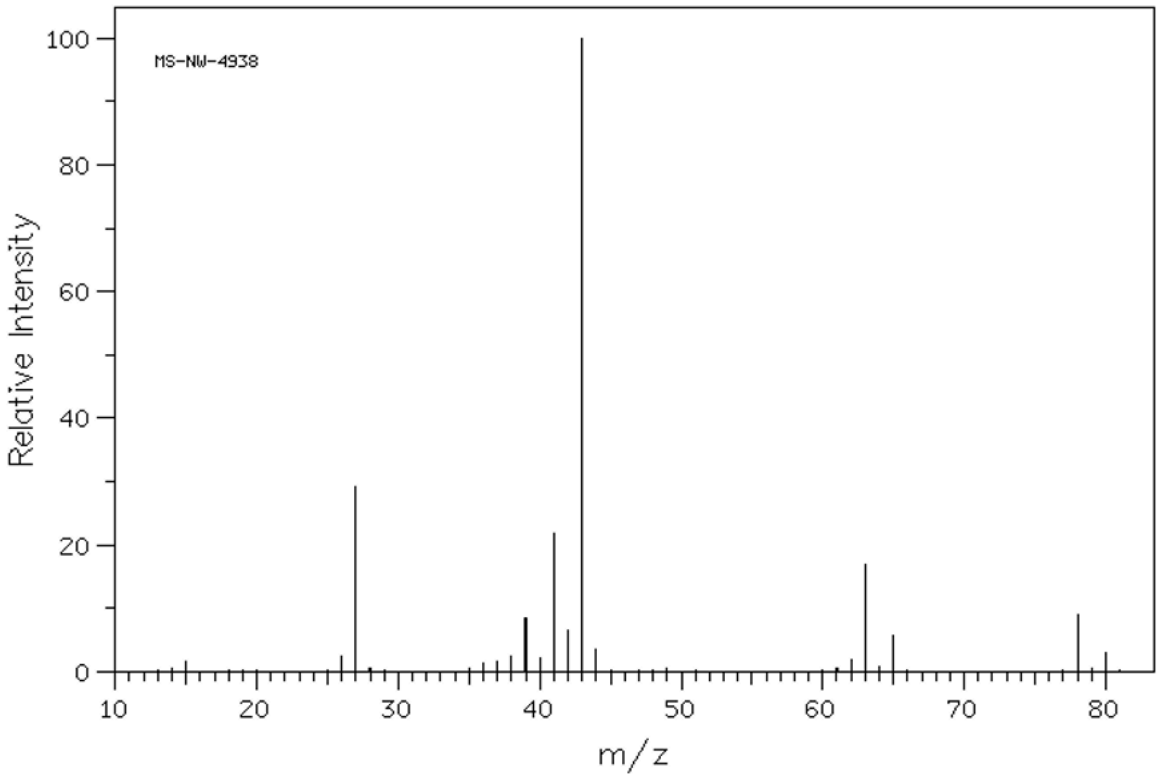
Base peak: 43 m/z

Parent peak: 78 m/z

M+2 peak: 80 m/z

b) Does the molecule corresponding to the spectra below contain Br or Cl? If yes, explain how you see that in the spectra. *Est-ce que la molécule correspondant aux spectres ci-dessous contient du Br ou du Cl ? Si oui, expliquez comment vous le voyez dans les spectres*. (1 points)

The molecule contains Cl.
This is visible, as the M+2 peak is a third of the M peak which mirrors the natural occurrence to the two Cl isotopes (The natural occurrence of ^{35}Cl is 3 times higher than ^{37}Cl.



c) The two molecules below have the same molecular weight. Explain why you are nonetheless able to distinguish them from their MS spectra?
Les deux molécules ci-dessous ont le même poids moléculaire. Expliquez pourquoi vous pouvez néanmoins les distinguer à partir de leur spectre de spectrométrie de masse. (1 point)

Due to different placement of the imine, the two compounds will **fragment** differently. Therefore while the parent peak will be the same for the two compounds but the **base peak** and fragment peaks will differ.

4.2 UV and IR (4 points)

a) Which of the following molecules absorbs at a longer wavelength in UV-Vis, A or B? *Lequel des deux molécules suivantes absorbe à une longueur d'onde plus longue en UV-Vis, A ou B ?* (1 point)

A) B)

In general the longer the system of conjugated system the longer the wavelength it absorbs, as the energetic HOMO-LUMO gap shrinks. A has the longer conjugated system, therefore it will absorb at a longer wavelength.

b) In the IR-spectra of molecule A we see a peak at a wavenumber 1700 cm^{-1} for the C=O double bond, whereas for molecule B there is a peak for the C=C double bond at around 1640 cm^{-1}. Indicate if the following statements are right or wrong? *Dans les spectres IR de la molécule A, nous voyons un pic à un nombre d'onde de 1700 cm^{-1} pour la double liaison C=O, tandis que pour la molécule B, il y a un pic pour la double liaison C=C autour de 1640 cm^{-1}. Indiquez si les déclarations suivantes sont vraies ou fausses.* (3 points, no negative points).

Statements:

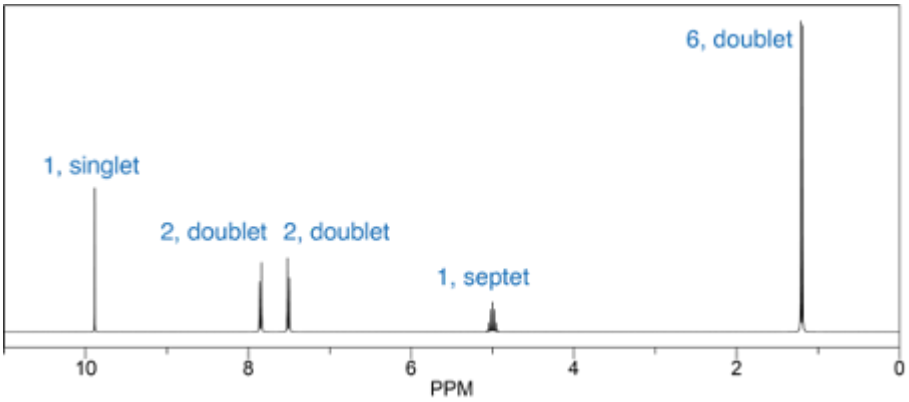
A) The C=O double bond has higher energy than the C=C double bond. *Right* *Wrong*

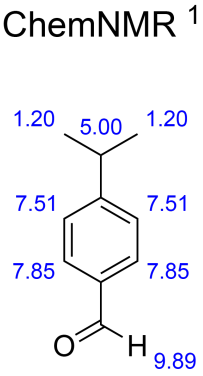
B) The C=O double bond absorbs at a lower wavelength than the C=C bond. *Right* *Wrong*

C) Both bonds absorb at the same wavelength, as they are both double bonds *Right* *Wrong*

4.3 NMR (2.5 points)

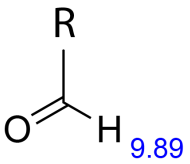
You have obtained a compound with the chemical formula of $C_{10}H_{12}O$. To make sure the chemical structure is what you had in mind, you decide to perform an NMR experiment. Reconstruct the structure with the 1H-NMR spectrum given below.
Vous avez obtenu un composé de formule chimique $C_{10}H_{12}O$. Pour vous assurer que la structure chimique correspond à ce que vous aviez en tête, vous décidez de réaliser une expérience de RMN. Reconstituez la structure à partir du spectre de RMN du proton (1H) donné ci-dessous.



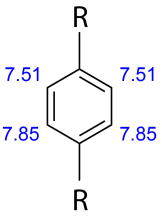


Answer:

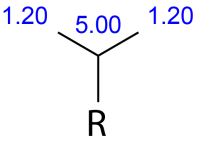
- 1 singlet around 10 PPM indicates the presence of an aldehyde group.



- Two 2, doublets around 8 PPM is characteristic for a symmetric aromatic ring with 4 protons.



- 1, septet indicates a single proton with 6 neighbors



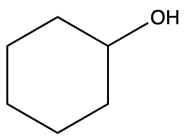
- 6, doublet indicates six protons with one neighbor.
  From this we can conclude there must be a three carbon alkyl group present.

There is only one way how to assemble these groups into a molecule, which should give you the following structure:

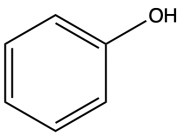
5. Organic Reactivity

5.1 Acidity

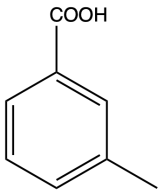
Order the following compounds from least to most acidic.



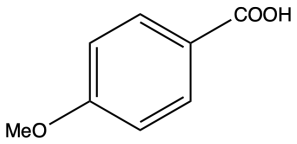
1



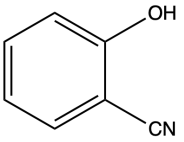
2



3



4



5

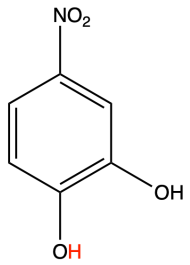
Order:

1 < 2 < 5 < 4 < 3

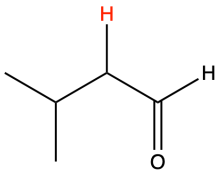
1 point for getting right that COOH > OH
0.5 points for getting OH ordering right
0.5 points for getting COOH ordering right

-Carbonic Acids are more acidic then alcohols
-Acids, where the resulting negative charge can be delocalized are more acidic
-sigma/pi effects can stabilize anions/cations (e.g. sigma donors can stabilize cations, acceptors anions)
1-ACOC2-2018-W-Chen-L.pdf

Mark the most acidic proton in each of the three compounds below.



1



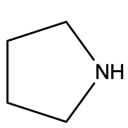
2

3

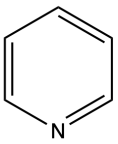
0.5 points for each correctly marked proton

5.2 Basicity

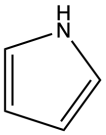
Order the following compounds from least to most basic.



1



2



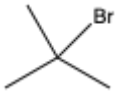
3

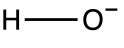
Order:

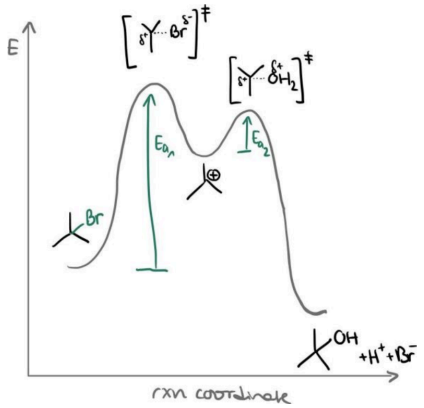
6. Nucleophilic substitutions (8 points)

a) Sketch the reaction diagram for the S_N1 reaction of the molecule 2-bromo-2-methylpropane (A) with a Hydroxide ion (B) in the diagram below. Pay attention to the axis labeling and state the energy levels of the reactants, any intermediates and products. Label the activation energy of the rate-determining step in the graph. (4 points)

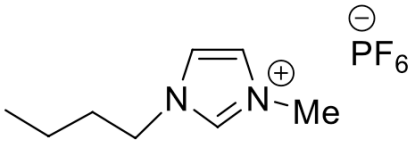
1p product lower than educt
1p for rate determining Activation energy
1p for clear intermediate
1p for axis labelling

A: 

B: 



b) The ionic solvent BMIM (1-butyl-3-methylimidazolium) hexafluorophosphate is shown below. Ionic solvents are liquid at room temperature, although they are salts, and can dissolve organic and inorganic substances. Is [BMIM]PF_6 polar or apolar, and is it protic or aprotic? (2 P.)



Strongly polar (ionic salt) (1 P.) and aprotic (has no hydrogen atoms bound to electronegative atoms) (1 P.), therefore cannot form H-bridges.

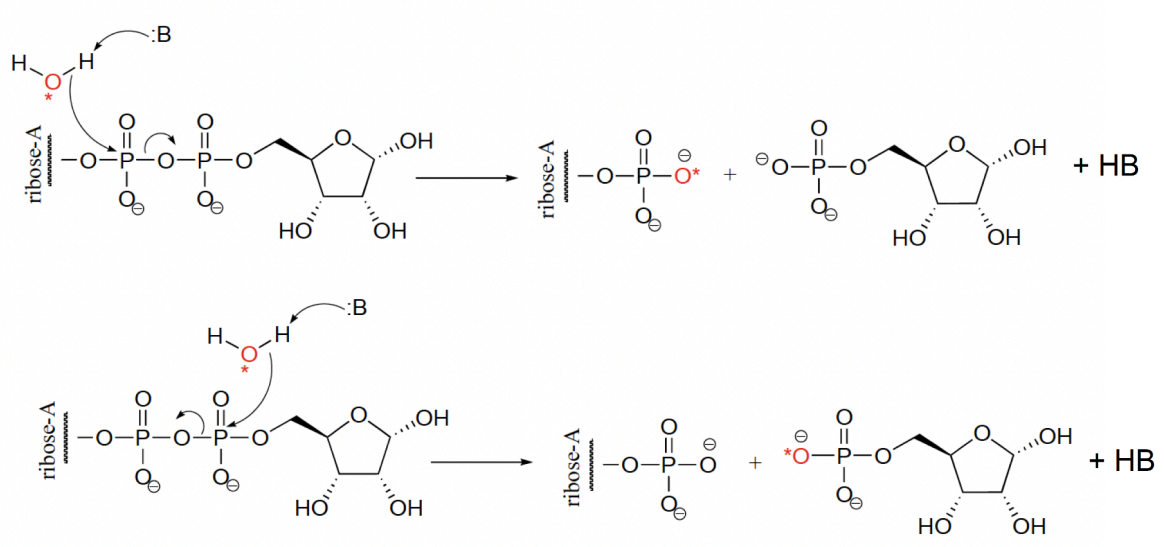
c) Would [BMIM]PF_6 as a solvent speed up or slow down an S_N2 reaction compared to water? Give brief reasons. (2 P.)

S_N2 reaction, thus BMIM (polar, aprotic) accelerates the reaction. (1P) Aprotic solvent raises reactivity of nucleophile. (1P.)

6. Phosphate Transfer Reactions

6.1 Exercise

Using 18O-labelled water, we could determine the course of the reaction. In the first case, the AMP would contain the label, in the second case the sugar would contain the label. The authors of the study above, working with an enzyme from E. coli, found that the reaction proceeded by the top mechanism (attack by water at the adenosyl phosphate).



8. Carbonyl Chemistry

8.1 Protective Groups (3 points)

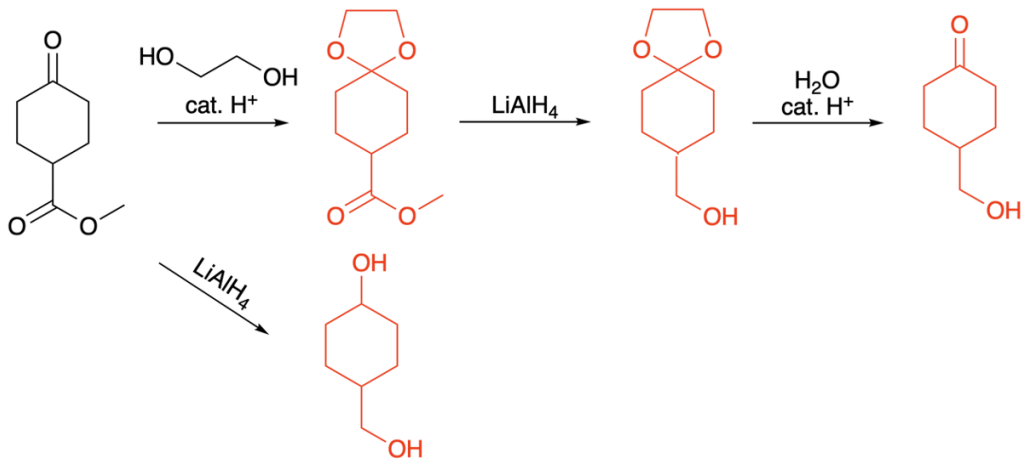
Lithium aluminum hydride is a strong reducing agent with the molecular formula LiAlH4. It is a highly reactive reagent that usefully reduces esters to alcohols. However, It always reacts with carbonyl groups, and cannot be discouraged by any means. Therefore, chemists have developed strategies to selectively reduce carbonyl groups.

As an example, Ethylene Glycol can be used as a protective reagent for carbonyl groups. Fill the gaps of the following reaction scheme to showcase the effect of the protective group in comparison to the “normal” reaction.

(Hint: Recall acetal formation)

Le lithium aluminium hydride est un agent réducteur puissant de formule moléculaire $LiAlH_4$. C'est un réactif hautement réactif qui réduit efficacement les esters en alcools. Cependant, il réagit toujours avec les groupes carbonyle et ne peut pas être inhibé par aucun moyen. Par conséquent, les chimistes ont développé des stratégies pour réduire sélectivement les groupes carbonyle. À titre d'exemple, l'éthylène glycol peut être utilisé comme réactif protecteur pour les groupes carbonyle. Complétez les espaces vides du schéma de réaction suivant pour illustrer l'effet du groupe protecteur par rapport à la réaction "normale". (Indice : Rappelez-vous la formation d'acétal.)

(Indice : Rappelez-vous la formation d'acétal.)



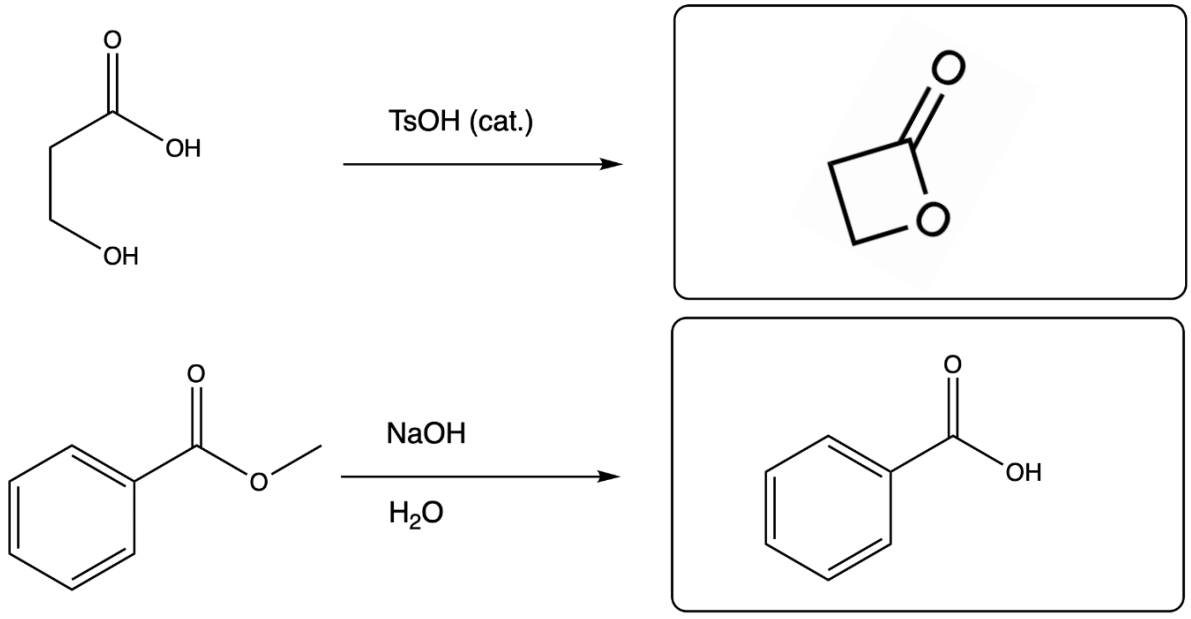
1 point for the normal LiAlH4 pathway. 0.5 points for each of the protected structures plus 0.5 points if the full acetal is shown.

8.2 Esterification (2 points)

Draw the main product(s) for each of the following reactions in the corresponding empty box.

Tracez le(s) produit(s) principal(s) pour chacune des réactions suivantes dans la case vide correspondante. (2 points) 1 Point each for correct product

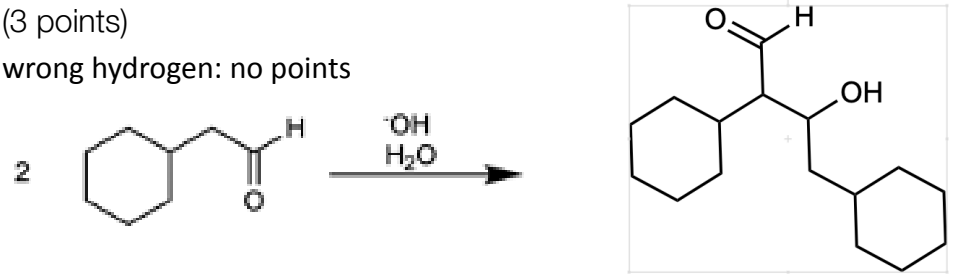
one carbon too much 0.5



8.3 Aldol Reactions (5 points)

a) Draw the product formed in the aldol reactions below. If multiple products are possible, explain why your choice is the preferred product.
Dessinez le produit formé dans les réactions d'aldol ci-dessous. Si plusieurs produits sont possibles, expliquez pourquoi votre choix est le produit préféré.
(3 points)

wrong hydrogen: no points



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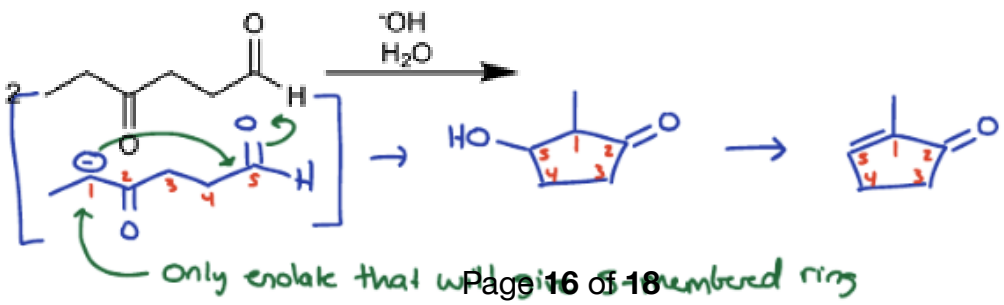
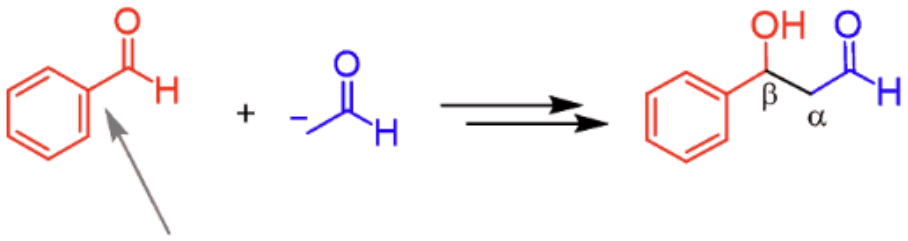


b) Crossed aldol reactions (aldol reactions with multiple compounds) usually lead to a mixture of products. However, in the following reaction, chemists don't need to worry about multiple products. Draw the product and explain why only one aldol product is possible.
Les réactions d'aldol croisées (réactions d'aldol avec plusieurs composés) conduisent généralement à un mélange de produits. Cependant, dans la réaction suivante, les chimistes n'ont pas à se soucier de multiples produits. Dessinez le produit et expliquez pourquoi un seul produit d'aldol est possible. (2 points)



no α H – cannot form an enolate

1.1. Reaction Control

Answer the following questions by ticking the corresponding correct answers. Wrong answers will result in a deduction of points, no less than 0 points can be achieved.

a) Tick the factors that clearly favor the **E2** mechanism over the **E1** mechanism:
- i) good leaving group
- ii) Presence of a strong base
- iii) good nucleophile
- iv) high ambient temperature
- v) strong π-acceptor substituents close to the reactive center
- vi) high steric demand of the substrate

b) Tick the factors that clearly favor the **E1** mechanism over the **S_N1** elimination mechanism:
- i) good leaving group
- ii) Presence of a strong base
- iii) Basic leaving group
- iv) high ambient temperature
- v) good nucleophile
- vi) high steric demand of the substrate

c) Where do you see problems with the following reaction? What reaction conditions would you choose or how would you design the substrate so that the desired product is formed?