CHEMISTRY 12A FALL 2020

EXAM 2 13 October 2020

Name: Key

Student ID: _____

As a member of the UC Berkeley community, I act with honesty, integrity, and respect for others. This exam represents my own original work.

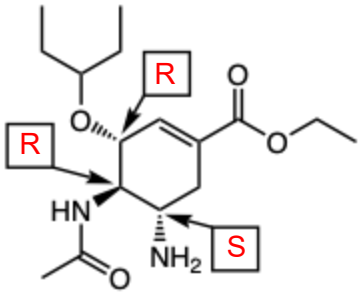
Please sign: _____

- You have 80 minutes to complete this exam. Gradescope will not accept submissions after the 80-minute mark, so please submit your exam before this point even if you are not done.
- Only those answers located within or very close to the answer boxes will be graded.
- You may refer to your notes, the textbook, the answer guide, and any documents that have been uploaded to the 2020 Chem 12A bCourses website. You may use molecular models. You may not consult any website, or collaborate or consult with any other person. Piazza will be disabled during the exam.

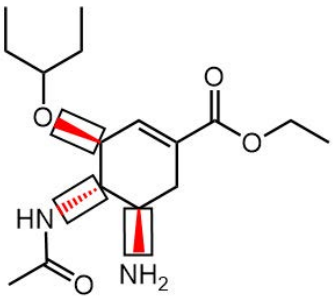
This exam consists of six questions spread over eight pages. If you are printing the exam, please make sure the pages are in the correct order when you scan your completed exam. The pages are numbered in the bottom right corner.

Good luck!!!

1. (14 points) Oseltamivir is the active ingredient in Tamiflu®. It was discovered by researchers at Gilead and is prescribed to 3 million people every year for the treatment of influenza.



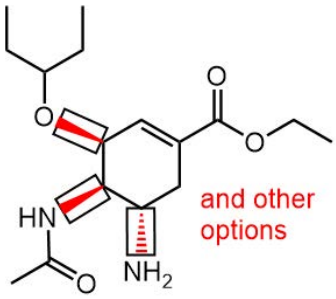
(a) The structure of oseltamivir is shown at left. It contains 3 stereocenters. Please assign the stereochemistry of each stereocenter by writing "R" or "S" in each of the boxes provided.



Enantiomer

(b) Using the diagram at **left**, draw wedged and/or dashed bonds to illustrate the structure of the **enantiomer** of oseltamivir.

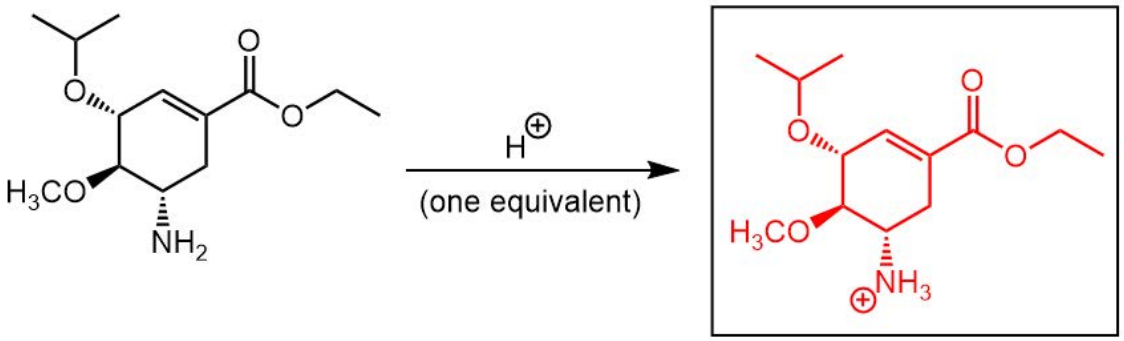
(c) Using the diagram at **right**, draw wedged and/or dashed bonds to illustrate the structure of a **diastereomer** of oseltamivir.



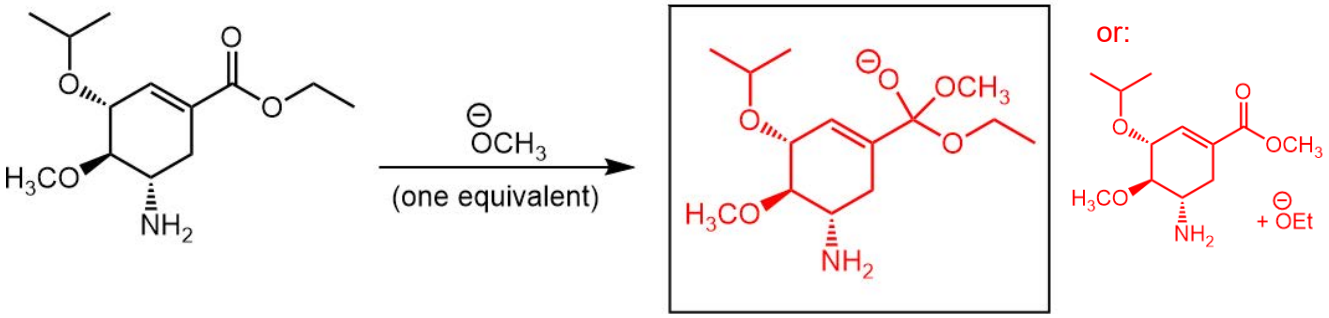
Diastereomer

(d) In the boxes below, predict the products of the following reactions with a derivative of Oseltamivir. Hint: Recall that -OCH_3 can act as a nucleophile.

i.

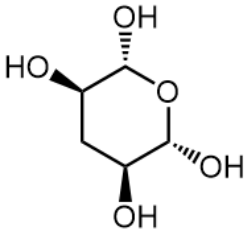


ii.

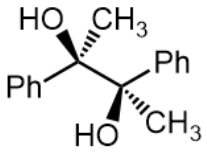


2. (10 points) A little more about stereochemistry.

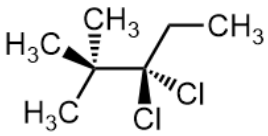
(a) Consider the three molecules below. For each one, fill in the bubble to indicate whether you believe the molecule shown is simply **achiral**, **achiral and meso**, or **chiral**.



○ achiral
● achiral and meso
○ chiral



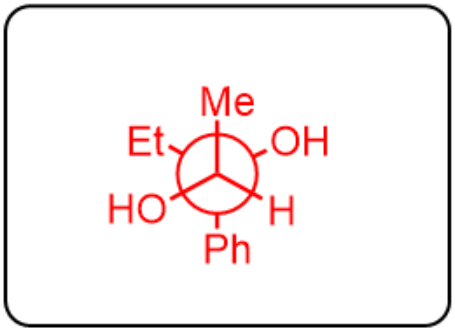
○ achiral
○ achiral and meso
● chiral



● achiral
○ achiral and meso
○ chiral

(b) Please draw a Newman projection that sights along the central C-C bond in the direction indicated by the arrow and corresponds to the line drawing shown.

Newman Projection



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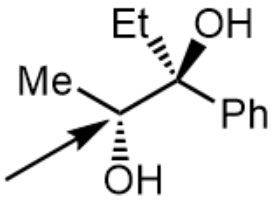
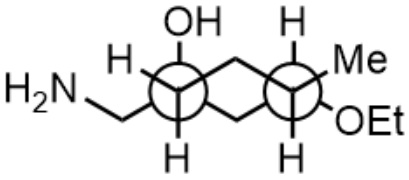
Line Drawing



(c) Please draw a line drawing that corresponds to the Newman projection shown.

Newman Projection



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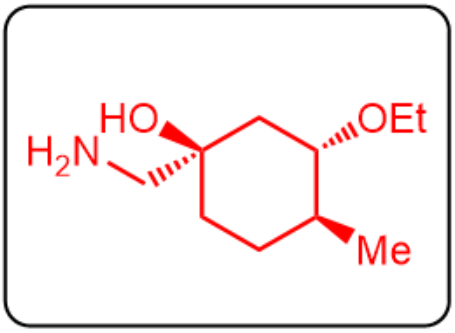
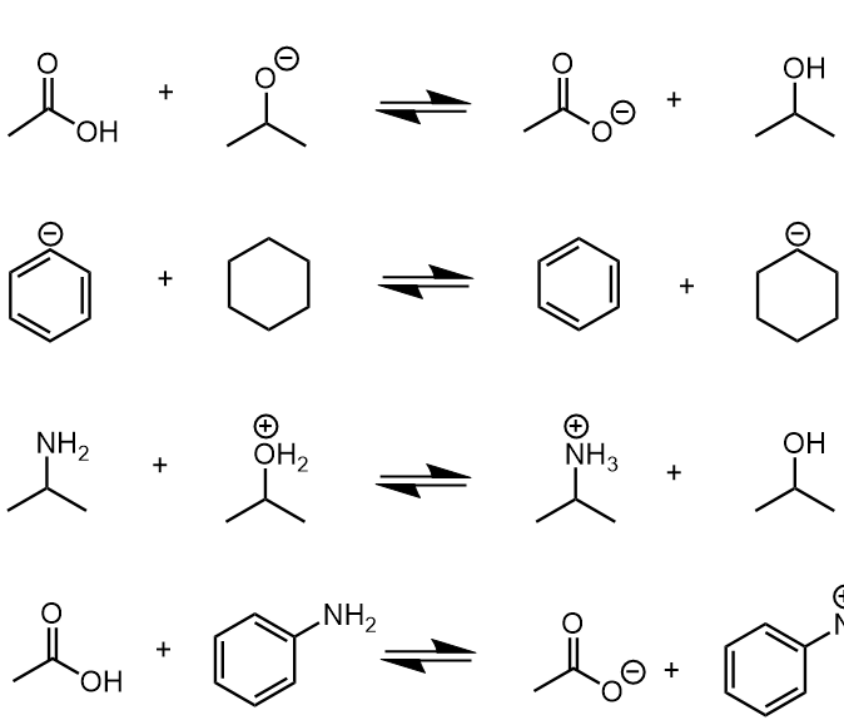
Line Drawing

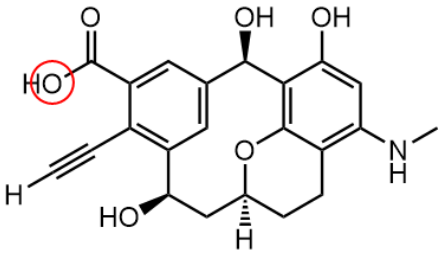


3. (22 points) All about acidity!

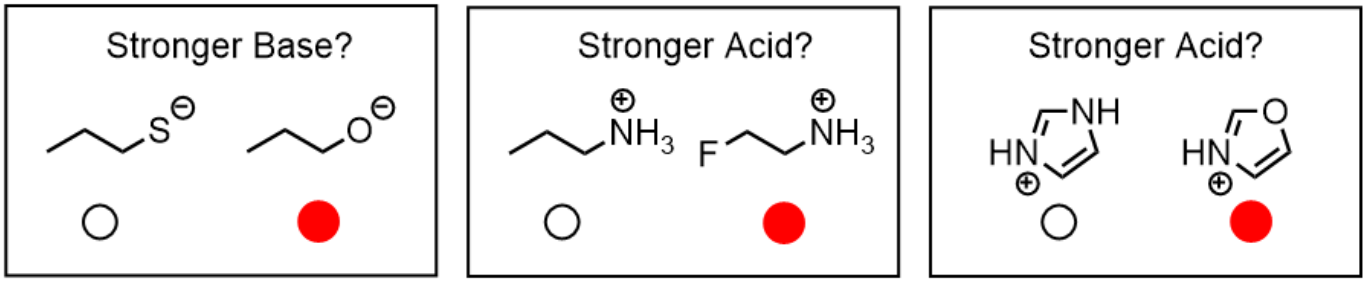
(a) Consider the four acid-base equilibria shown below. In each case, indicate which side of the equilibrium is favored. If neither side is especially favored, please choose “neither”.



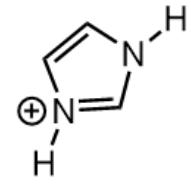
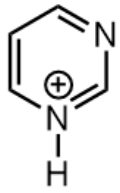
(b) Circle the atom that becomes deprotonated when the molecule shown at right is treated with one equivalent of NaOH.



(c) Please compare the pair of molecules in each of the boxes below. Use the bubble to identify which molecule correctly answers the question that is posed.



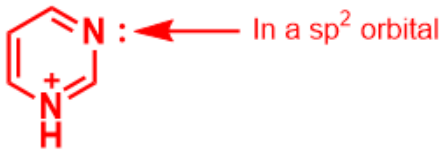
(d) Consider Molecules A and B. Molecule A has a pK_a of 7.0 whereas Molecule B has a pK_a of 1.3. Which molecule is more acidic? Please fill in the appropriate bubble.

Molecule A ○   Molecule B ●

(e) Use resonance structures and words to rationalize the difference in acidity between Molecules A and B.

The lone pairs of the uncharged nitrogen atom in molecule A is in a p orbital. As a result, the positive charge of the acid can be stabilized by resonance (see structures on right).

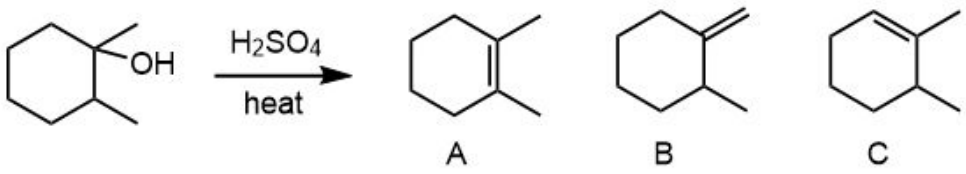
However, in molecule B, the lone pair of the uncharged nitrogen atom is in a sp^2 orbital and thus cannot stabilize the positive charge on the other nitrogen atom through resonance.



Because molecule A can better stabilize the positive charge, it is the weaker acid and has a higher pKa than molecule B.

4. (20 points) All about alkenes!

(a) Three different alkene isomers can be produced during the reaction drawn below. Please rank the three isomers in terms of their heat of combustion.



Which alkene has the **largest** (**most negative**) heat of combustion?

B

C

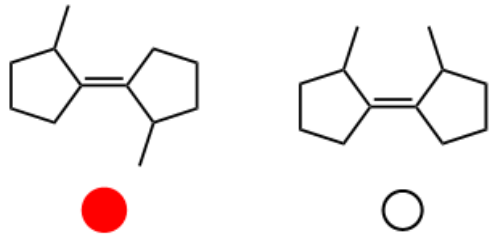
Which alkene has the **smallest** (**least negative**) heat of combustion?

A

(b) Assuming this reaction favors the most stable product, which isomer do you believe would represent the major product of this reaction? Fill in the bubble corresponding to your choice.

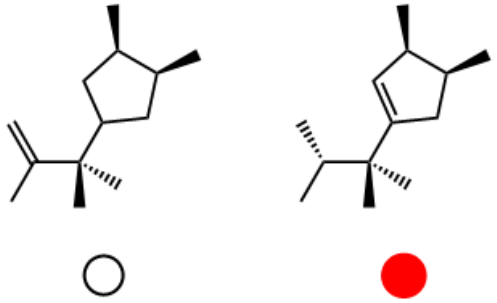
● Molecule A ○ Molecule B ○ Molecule C

(c) Consider each of the pairs of molecules shown below. In each case, fill in the bubble that identifies the more stable alkene and explain your choice in the box.



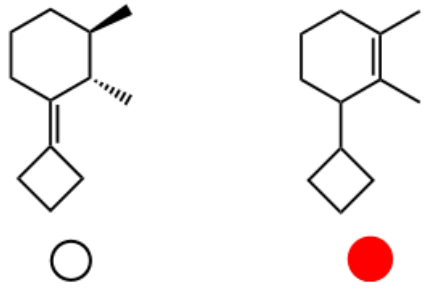
● ○

The alkene on the left is more stable because the large groups are trans to each other, avoiding steric interactions between the methyl groups.



○ ●

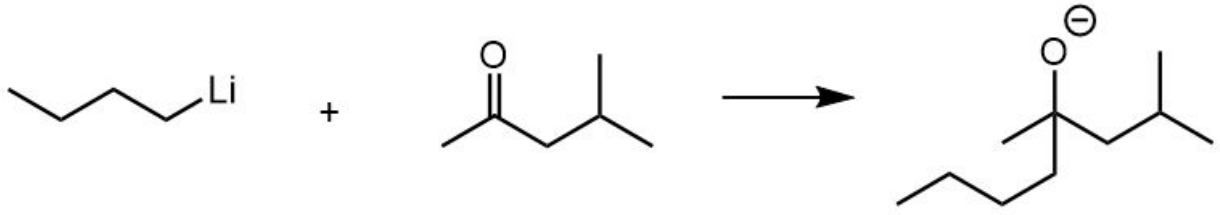
The alkene on the right is more stable because it is more substituted than the alkene on the left (trisubstituted = more stable than disubstituted)



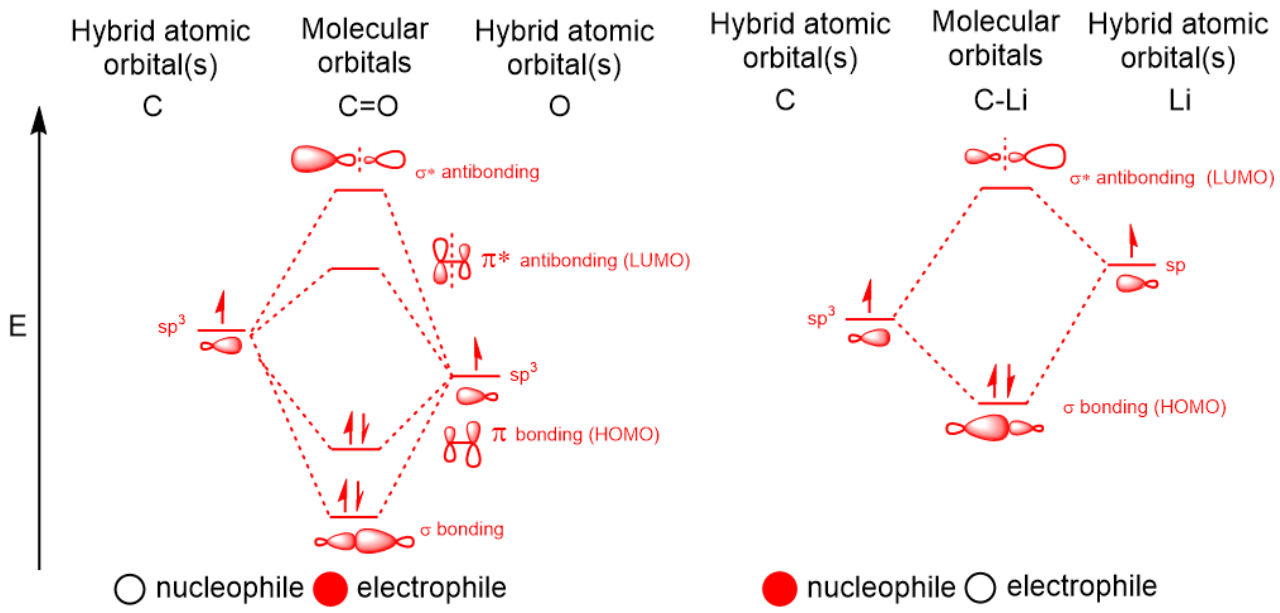
○ ●

The alkene on the right is more stable Both alkenes are tetrasubstituted, but the alkene on the left induces more ring strain due to the presence of an sp^2-hybridized carbon in a four-membered ring.

5. (20 points) Consider the reaction below.



(a) On the following page, draw molecular orbital diagrams illustrating the bonding and antibonding molecular orbitals associated with the C=O double bond and C_{sp3}-Li_{sp} single bond. Sketch and label all atomic and molecular orbitals, indicate whether they are occupied (and by how many electrons) and identify which MO represents the HOMO and LUMO in each case.



(b) Use the bubbles above to indicate which molecule acts as the nucleophile and the electrophile in this reaction.

(c) Which molecular orbital contributes the electrons to form the new C-C bond?

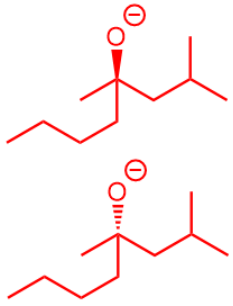
C-Li σ bonding (HOMO)

(d) Which molecular orbital receives the electrons to form the new C-C bond?

C-O π* antibonding (LUMO)

(e) This reaction produces two stereoisomers in roughly equal amounts. Draw them in the box at right.

Draw both stereoisomeric products



(f) Are these stereoisomers enantiomers or diastereomers? Please fill in the bubble that represents your choice.

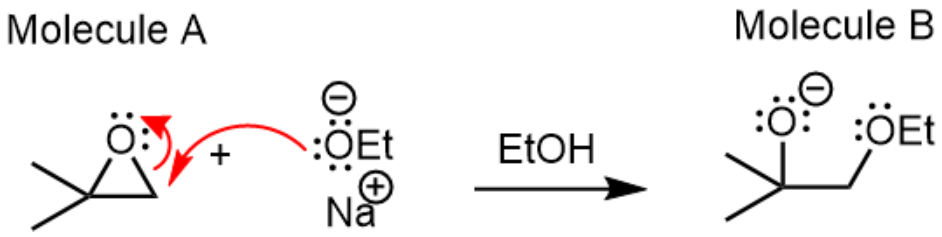
● enantiomers ○ diastereomers

(g) Draw the LUMO for the C=O bond in the box below. Based on your drawing, explain why the two stereoisomers are produced in roughly equal amounts.

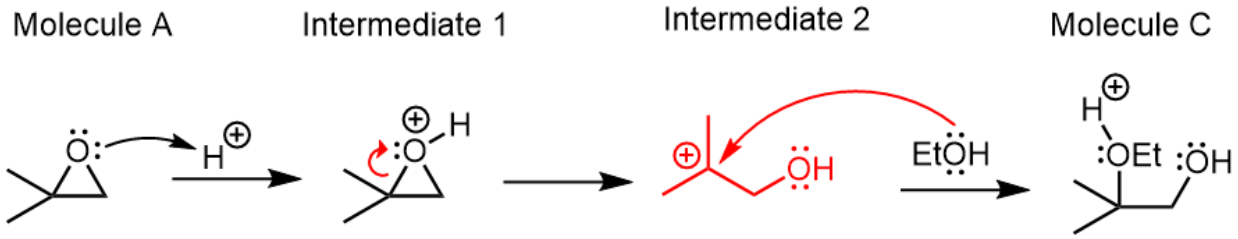
The bond forming reaction involves the interaction of the C-Li σ (HOMO) with the C-O π* (LUMO). The π* orbital has positive and negative lobes on carbon that are equal in magnitude. This means the nucleophile can attack the electrophile from either face of this planar carbon (see arrows) to generate the products, resulting in roughly equal amounts of each enantiomer.

6. (14 points) Arrows, arrows, and more arrows!

(a) Draw curved arrows on the structures below to illustrate how electrons flow during this chemical reaction to form the product, Molecule B.



(b) Now consider the multi-step reaction shown below, in which Molecule A reacts under acidic conditions. The first step in the mechanism (formation of Intermediate 1) has been provided for you. Please draw the structure of intermediate 2. Note that **no reagents are needed to convert Intermediate 1 into Intermediate 2**.



(c) Draw arrows that illustrate how Intermediate 1 is converted into Intermediate 2.

(d) Draw arrows that illustrate how Intermediate 2 is converted into the product, Molecule C.

(e) Why does Molecule A react to generate Molecule B under basic conditions and Molecule C under acidic conditions?

Under basic conditions, the epoxide group on Molecule A will not be protonated. As RO- is a poor leaving group, the epoxide will not open until it is attacked by the nucleophile -OEt. The nucleophile will attack the less hindered side of Molecule A, resulting in Molecule B.

Under acidic conditions, the epoxide group on Molecule A can be protonated. As ROH is a good leaving group, the epoxide can then open to generate the most stable carbocation (Intermediate 2). EtOH can then attack this carbocation to generate Molecule C.