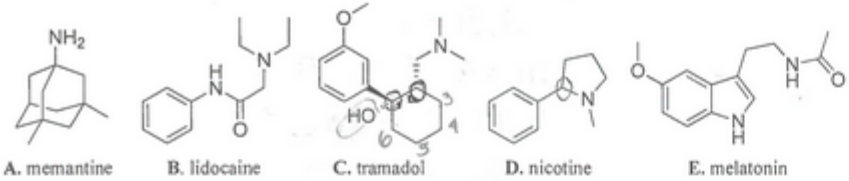
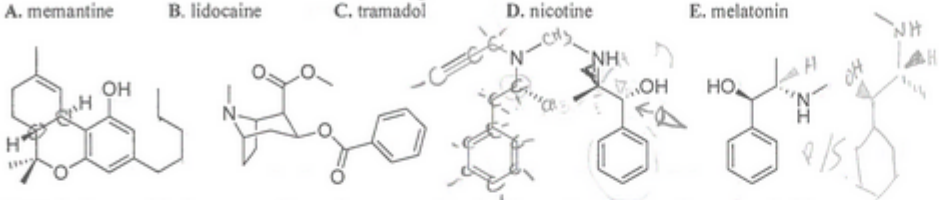
1. The molecules below all have effects on the nervous system:



A. memantine B. lidocaine C. tramadol D. nicotine E. melatonin



F. tetrahydrocannabinol G. cocaine H. selegiline I. ephedrin J. pseudoephedrine

a. The list below contains vocabulary terms that can be used to describe molecules or portions of molecules. For each term, identify one corresponding example above and write the letter (A-J) in the box to the right of each term. Place only one letter per box (several boxes have more than one correct answer). (2 pt each, 30 pt)

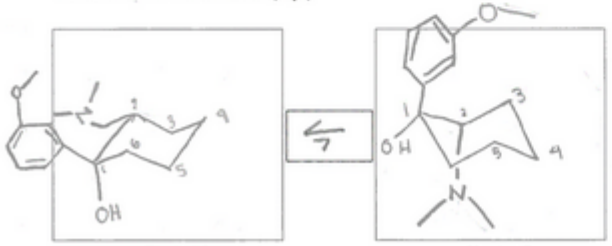
methoxy group	C	cyclohexane ring	A	amide	E
N,N-diethylamino group	B	cyclohexene ring	F	ester	G
hydroxyl group	J	cycloheptane ring	G	ether	C
pentyl group	F	meso compound	F	tertiary alcohol	C
aromatic alcohol (phenol)	F	sp-hybridized atoms	H	primary amine	A

b. What is the molecular formula of selegiline? (3 pt) $C_{13}H_{18}N$

c. Are ephedrine and pseudoephendrine conformers, enantiomers or diastereomers? (circle your answer) (3 pt)

d. List the letters corresponding to three achiral molecules. (6 pt) B, E, F

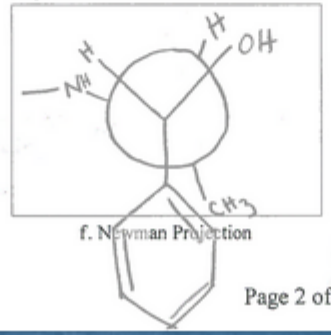
e. Draw two different chair conformations of tramadol in the boxes below. Add an equilibrium arrow between the boxes to indicate which chair is more stable. (8 pt)



e. Chair #1

e. Chair #2

f. Draw a Newman projection showing an eclipsing interaction between the methyl group and the phenyl group in ephedrine. (4 pt)



f. Newman Projection

between questions.

Grading Rubric

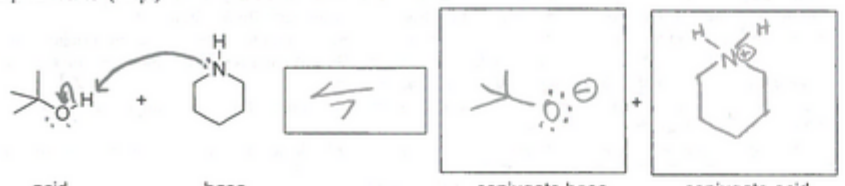
- +0.0 for no answer
- +2.0 for Correct: A
- +2.0 for Correct: B
- +2.0 for Correct: E
- +0.0 for No credit

Meso should be A

Mol. formula should be C13H17N

Correct answer= diastereomers

2. a. Draw curved arrows for this single-step reaction. Draw the structures of the products. Fill in the pKa boxes for the acid and conjugate acid, and add an equilibrium arrow that clearly shows which direction the reaction favors based on those pKa values. (12 pt)



acid | base | conjugate base | conjugate acid

15 (pKa) | 10 (pKa)

b. Calculate Keq for this reaction. Show your work. Your answer will be graded based on whether it matches the information you provided in part a. (3 pt)

$15 - 10 = 5$ Keq should be small b/c rxn favors reverse direction

$K_{eq} = 10^{-5}$

c. Set up an equation showing how to calculate ΔG (in kcal/mol) for this reaction at room temperature using data from parts a and b of this question. (3 pt)

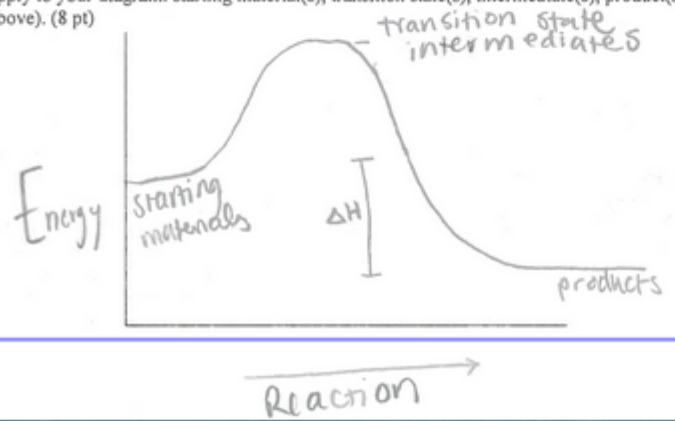
$K_{eq} = 10^{-\Delta G/1.36}$ $10^{-5} = 10^{-\Delta G/1.36}$

$-5 = -\Delta G/1.36$ $\Delta G = 5(1.36)$ kcal/mol

d. Estimate the value of ΔG (kcal/mol) (circle one of the answer ranges below). (2 pt)

- Less than -10
- Between -10 and -5
- Between -5 and -2
- Between -2 and +2
- Between +2 and +5
- Between +5 and +10
- Greater than +10

e. Sketch a reaction coordinate diagram for this reaction on the axes below. Label each axis. Add any of the following labels that apply to your diagram: starting material(s), transition state(s), intermediate(s), product(s), ΔG (calculated in part c/d above). (8 pt)

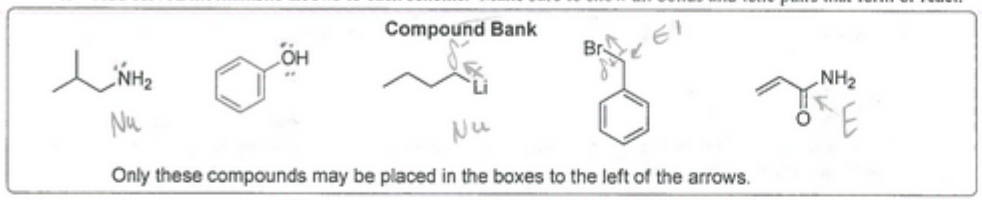


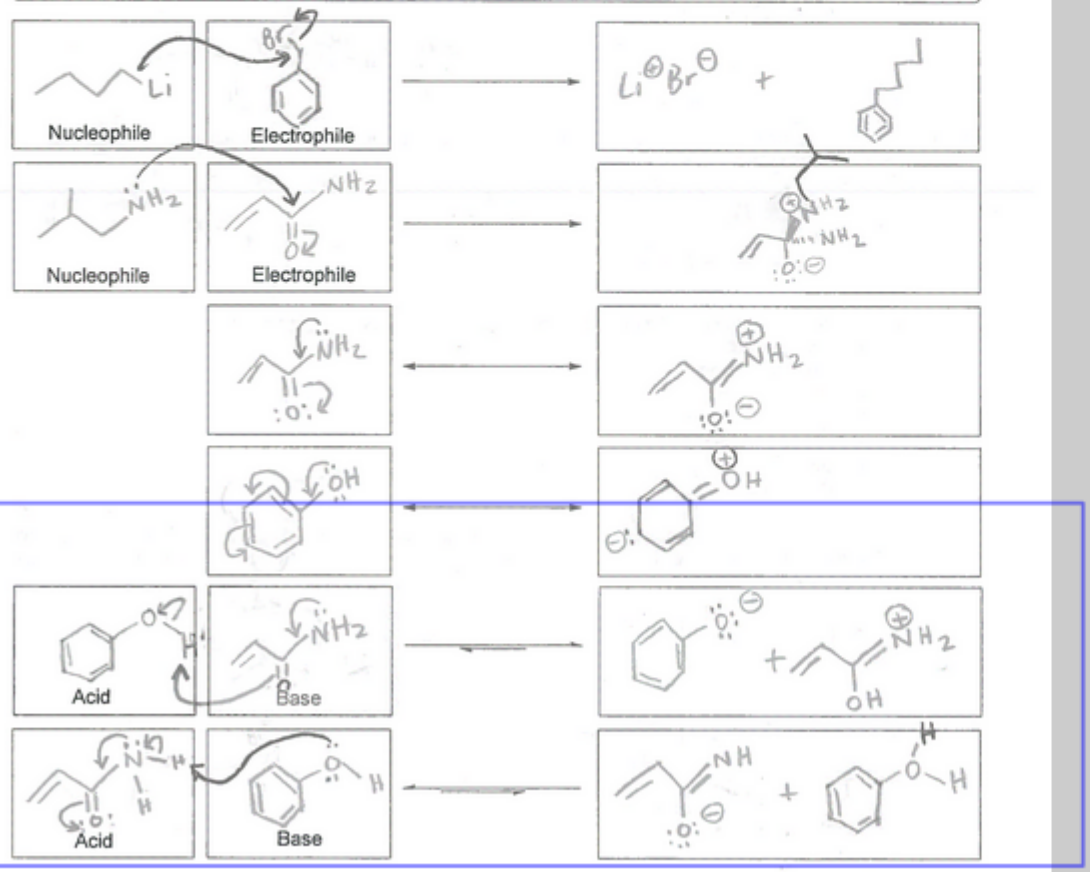
between questions.

Grading Rubric

- +0.0 for No answer
- +1.0 for The axes are labeled (y-axis is G (or E or H), X-axis is reaction coordinate)
- +1.0 for Starting material position is drawn and labeled on the left side.
- +1.0 for A curve is drawn from starting materials to products, and at least one point in the curve is higher energy than the starting materials.
- +1.0 for Transition is state labeled (if multiple steps, at least one transition state is labeled)
- +1.0 for Only one step is shown (no intermediates).
- +1.0 for Product position is drawn and labeled on the right side of the diagram.
- +1.0 for deltaG(rxn) (energy difference between starting material and product) is labeled. (Credit may be earned if some variation of this energy label is used, as long as it is clear that this corresponds to the value from part d of this question)
- +1.0 for deltaG(rxn) direction matches the value circled in part d (positive vs. negative).

3. Six blank organic schemes are shown below. For each scheme, your job is to provide an example of a plausible organic reaction/expression based on the type of arrow shown. Some of the schemes have the same arrow type. Please provide different examples in each case. Read all three steps below before beginning the problem. (6 pt per scheme, 36 pt)
   a. On the left side of each arrow, choose compounds from the "Compound Bank" (below) to use as the reagents/starting compounds for your proposed reactions/schemes. You will need to use the structures more than once. Notice that reagent roles are provided in some boxes. **Do not use the same reagent in the same role more than once.** There is not a single correct choice for each scheme.
   b. Based on the type of the arrow in the scheme, provide appropriate product(s) or structure(s) to the right of the arrow. These will NOT come from the compound bank.
   c. Add curved/mechanistic arrows to each scheme. Make sure to show all bonds and lone pairs that form or react.





between questions.

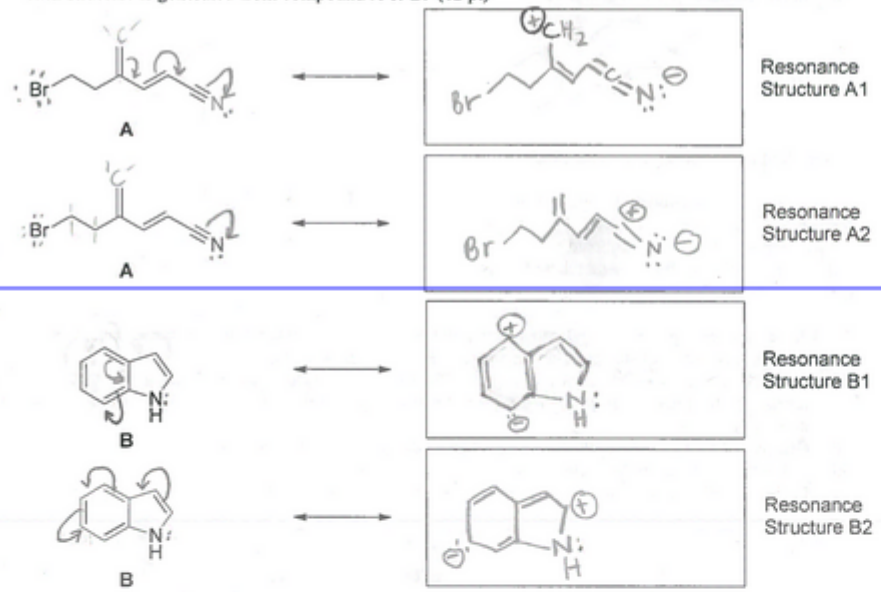
Grading Rubric

- +0.0 for No answer
- +1.0 for The structure drawn in the acid box is from the compound bank, and is being used as a Bronsted acid (a source of a proton)
- +1.0 for The structure drawn in the base box is from the compound bank, and is being used as a Bronsted base (a proton acceptor)
- +1.0 for Valid curved arrows are shown for the proton transfer (an arrow from the base to the H, and an arrow from the H-X sigma bond to the X atom.)
- +1.0 for The acid-base reaction shown is favorable (consistent with the equilibrium arrow provided)
- +1.0 for All atoms/bonds are accounted for in the product box.
- +1.0 for All formal charges are correct in the product box, structures are valid (not breaking octet rule, etc.)
- +1.0 for An answer is drawn but is insufficient to earn credit.

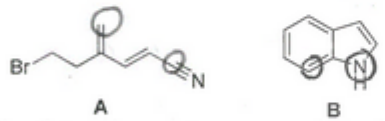
O should have a + charge

4. Many molecules have multiple sites of reactivity. Minor resonance structures can reveal additional reactive sites.

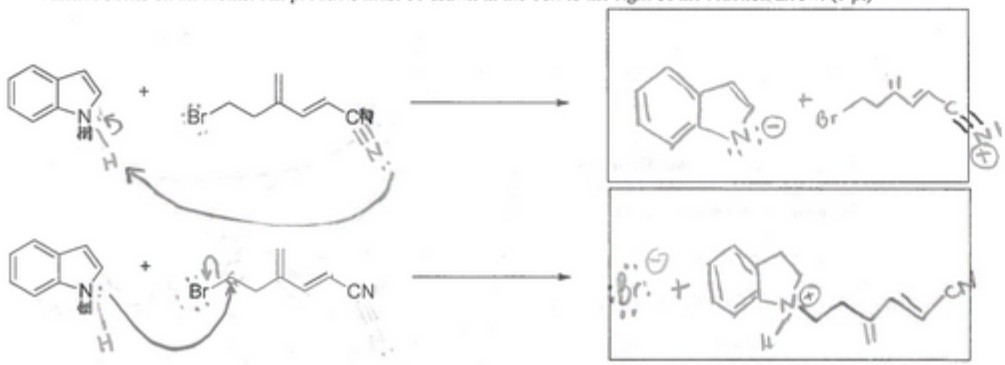
a. Draw two, non-identical, reasonable resonance structures of each compound (A and B) in the spaces provided. These resonance structures may have an unfilled valence shell on up to one atom. Add curved arrows to show how each structure is generated from compound A or B. (12 pt)



b. Identify two **electrophilic sites** on compound **A**, and two **nucleophilic sites** on compound **B**. Circle these four sites on the structures below. Be sure not to include extraneous atoms within your circles. (8 pt)



c. Propose two possible, 1-step reactions that could occur between compounds A and B. Use curved arrow notation to show the mechanism of each proposed reaction. Your proposed products may be charged, but must have filled valence shells on all atoms. All products must be drawn in the box to the right of the reaction arrow. (6 pt)



between questions.

Grading Rubric

- +0.0 for No answer
- +2.0 for A valid resonance structure of A is drawn, including all charges/bonds/atoms etc. Octet rule is obeyed (no overfilled octets; No unfilled octets on heteroatoms)
- +1.0 for Curved arrows and structure are consistent with each other.
- +0.0 for An answer is drawn, but it is insufficient to earn credit.
- +1.0 for Partial credit for curved arrow (curved arrow is correct, resulting structure is incorrect)

5. Cycloaddition reactions can be used to create complex cyclic products containing a large number of stereocenters in a single step.

a. An example of a [4+2] cycloaddition reaction leading to a 6-membered ring is shown below. Add **curved arrows** to show the mechanism of this reaction. (2 pt)

b. Circle all of the stereocenters on the product above. (4 pt)

c. In some cases, four-membered rings can also be formed in a cycloaddition reaction. Provide an explanation for why four membered rings are more difficult to synthesize than six-membered rings. (limit: 10 words) (4 pt)

- more bond angle strain
- atoms won't line up to bond

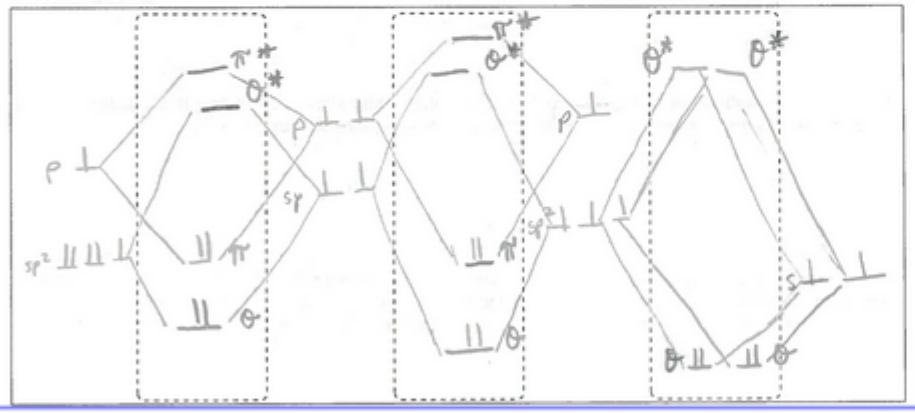
d. The ketene functional group can undergo a cycloaddition reaction generate a four membered ring. Construct an MO diagram to describe the valence bonding in the ketene shown below. (18 pt)

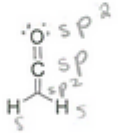
i. Atom labels are provided below the diagram. Place the (hybridized) atomic orbitals at the appropriate energy levels directly above these atom labels. Place the molecular orbitals in the regions of the diagram outlined by dotted-line boxes.

ii. Clearly indicate which atomic orbitals are being combined to make each molecular orbital.

iii. Fill in the electrons in the molecular orbitals.

iv. Places a label next to each atomic or molecular orbital that accurately describes it (s, p, sp^3, nb, σ, etc)





Ketene

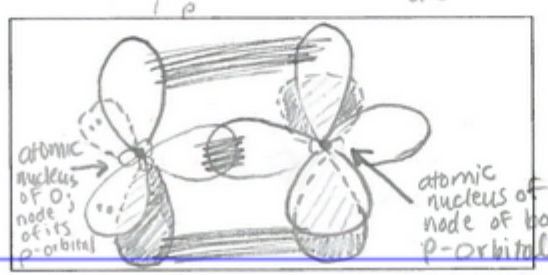
O C C 2xH

e. Choose one of the molecular orbitals in the ketene molecule. Sketch a picture, including orbital shading. (6 pt)

State which orbital you have chosen.

Label the location of each atomic nucleus.

Label any nodes that are present.



C-O bond

between questions.

Grading Rubric

- +0.0 for No answer
- +2.0 for A valid molecular orbital sketch is drawn, including orbital shading. Sketch matches the orbital label.
- +2.0 for atomic nuclei are labeled
- +1.0 for At least one of the node(s) are labeled correctly, if this orbital contains any nodes (partial credit)
- +2.0 for All node(s) are labeled correctly, if this orbital contains any nodes
- +0.0 for An answer is drawn but is insufficient to earn credit.

Point Adjustment

-1.0

Comments

What MO does your drawing represent?

For MO diagram (not sketch) sp2 carbon should be lower than s carbon

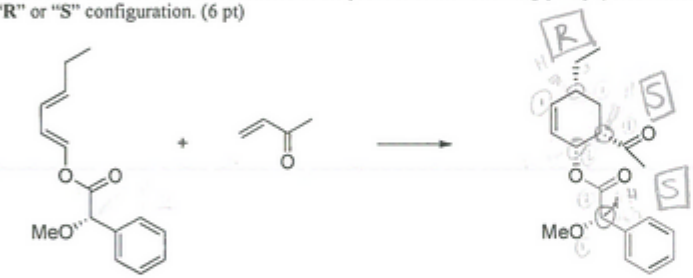
f. Provide curved arrows to explain the mechanism of this [2+2] cycloaddition reaction involving a more complex ketene. (2 pt)

g. Name three functional groups (compound classes) that are present in the product of the above reaction. (6 pt)

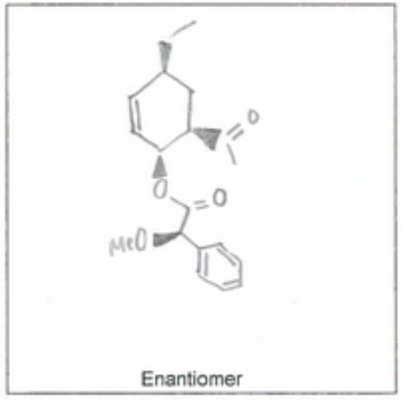
ketone	ether	halide (cyclobutyl)

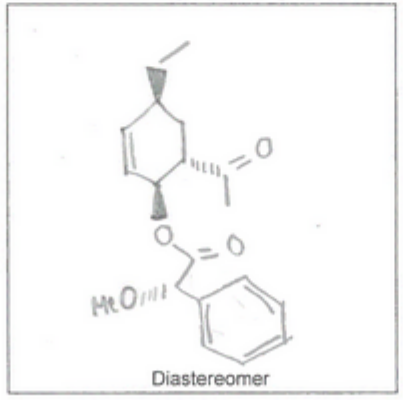
h. How many stereoisomers are possible of the product above? (2 pt) 8

i. Amazingly, under the correct conditions, cycloaddition reactions can proceed and give only a single stereoisomer of the product. **Choose three of the stereocenters** in the product of the following [4+2] cycloaddition and label each one as "**R**" or "**S**" configuration. (6 pt)



j. Provide the structure of an enantiomer and a diastereomer of the product of the reaction in part i. (6 pt)





Select a question to show how it was graded. You can also use the left and right arrow keys to switch between questions.

Grading Rubric

- +0.0 for No answer
- +2.0 for Correct
- +0.0 for Incorrect