Final Exam

Chem 3B, Fall 2016
Monday, Dec 12, 2016
3-6 pm

Name ___Answer Key_____

Student ID _____

If you are making up an incomplete, list the semester here:_____

You have 180 minutes to complete this exam.

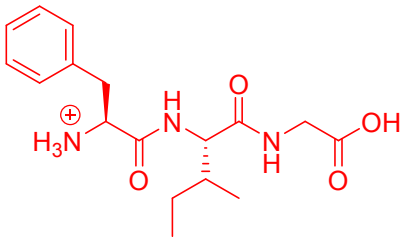
Please provide all answers in the space provided. Work drawn in the margins may not be picked up by the scanner and therefore will not be graded.

The last page of the exam is scratch paper. Please tear it off before you begin. It will not be collected, scanned, or graded, so make sure your answers are copied into the appropriate location on your exam.

Point values are listed within each question. The exam is worth 300 points total.

1. Nomenclature and Functional Groups

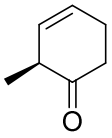
A. Draw a structure to match the prompt. (14 pt)



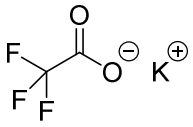
The tripeptide Phe-Ile-Gly (Phe R = benzyl; Ile R= s-Bu, Gly R = H), in the protonation state that would be expected at low pH (in the presence of excess strong acid)

(note: include stereochemistry at the alpha carbons.

B. Provide a systematic name for each of the following structures. (2x8 pt = 16 pt)



(*S*)-2-methylcyclohex-3-en-1-one



potassium trifluoroacetate

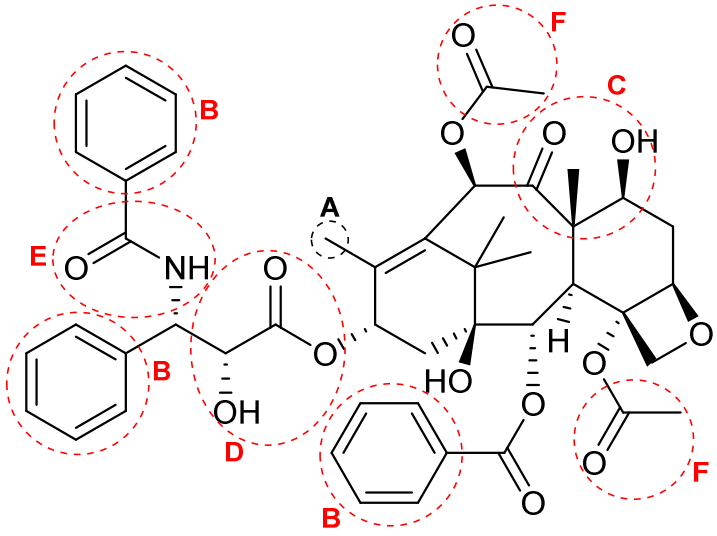
potassium 2,2,2-trifluoroacetate

potassium 2,2,2-trifluoroethanoate

C. For each term in the following list, **circle an example** in the structure at the right, and **label the circle with the letter** corresponding to that term. An example (A = methyl) is completed for you. (5x4 pt = 20 pt)

Note: For some terms, there may be more than one possible correct site – you should only circle and label one of them. Use each label once and only once.

A. methyl (*example already completed*)
B. phenyl
C. β - hydroxy ketone
D. α - hydroxy ester
E. amide
F. acetyl group



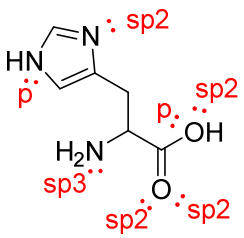
paclitaxel (Taxol), an anticancer drug

2. **Histidine**

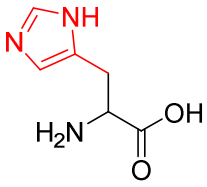
The amino acid histidine, shown below with all functional groups in their neutral protonation state, often acts as a base in the catalytic site of enzymes.

A. On the structure in the left box, draw all "lone pair" electrons on each heteroatom, and label the type of orbital (s, p sp, sp^2, or sp^3) occupied by each pair. (10 pt)

B. The histidine side chain contains a heterocycle known as an imidazole. There is a second tautomer of the imidazole that is approximately equal in stability to the one shown. Draw this tautomer in the box on the right. (4 pt)



"neutral" histidine structure
(add lone pairs with orbital labels)



A tautomer of histidine
(finish the structure)

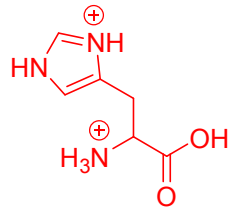
C. Explain why the imidazole ring in histidine is considered aromatic (your answer must address multiple criteria to earn full credit). (4 pt)

explanation

cyclic, planar, conjugated pi system
6 electrons (4n+2) (2 pi bonds and one nitrogen lone pair)

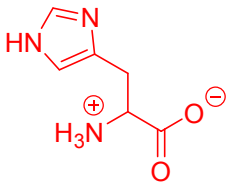
D. The conjugate acid of imidazole has a pKa of 6. With this information in mind, draw the major protonation state of histidine at each pKa listed in the boxes below. (6 pt)

(either resonance structure)



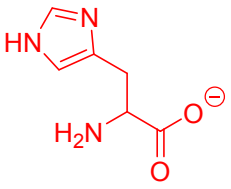
histidine at pH = 1

(either tautomer)



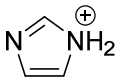
histidine at pH =7

(either tautomer)



histidine at pH = 13

E. Structure X is NOT a major structure observed when imidazole is dissolved in water with excess HCl. Explain why, then circle one choice describing the pKa of structure X. (6 pt)



X

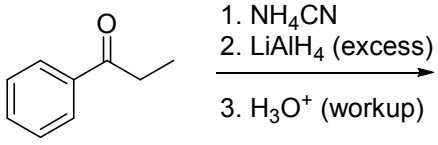
NOT observed in HCl, H_2O

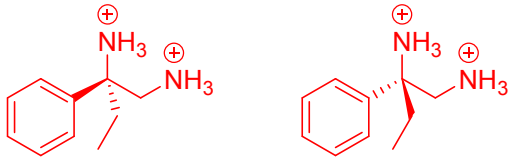
Why X is not observed:

not aromatic
(protonation at this site breaks aromaticity, vs.
protonation at other site does not affect aromaticity)

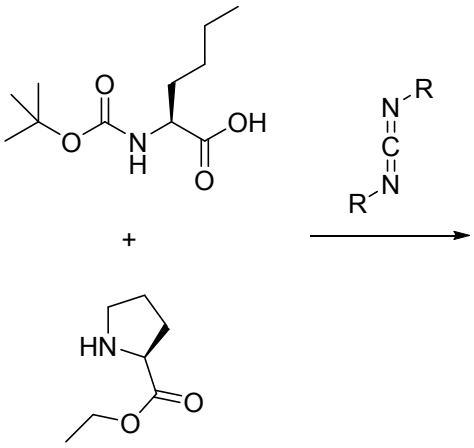
pKa of X (circle one): (lower than 6) (approximately 6) (higher than 6)

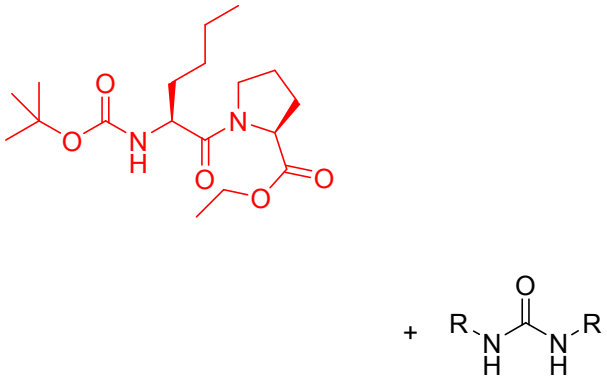
3. Predict the product(s) from the following reactions. Pay attention to any information given in the product boxes. (3x8 = 24 pt)



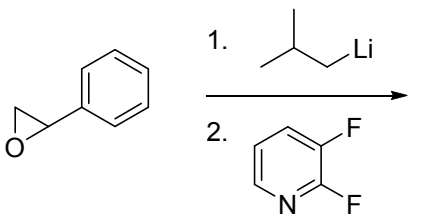


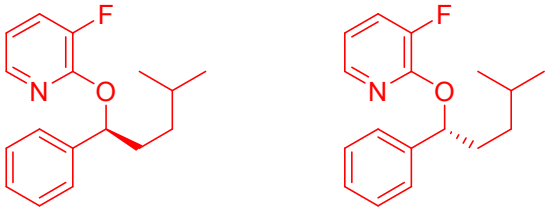
major product (including stereoisomer(s) if relevant)





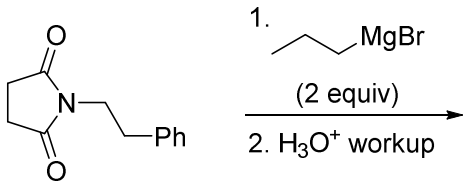
major product (including stereoisomer(s) if relevant)



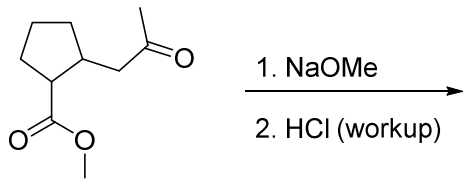


major product (including stereoisomer(s) if relevant) + LiF

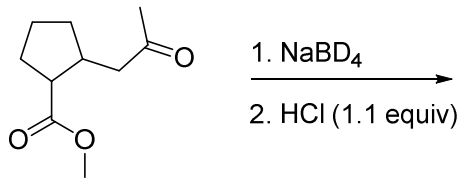
4. Predict the product(s) from the following reactions. Pay attention to any information given in the product boxes. (3x8 = 24 pt)



major product (including stereoisomer(s) if relevant)

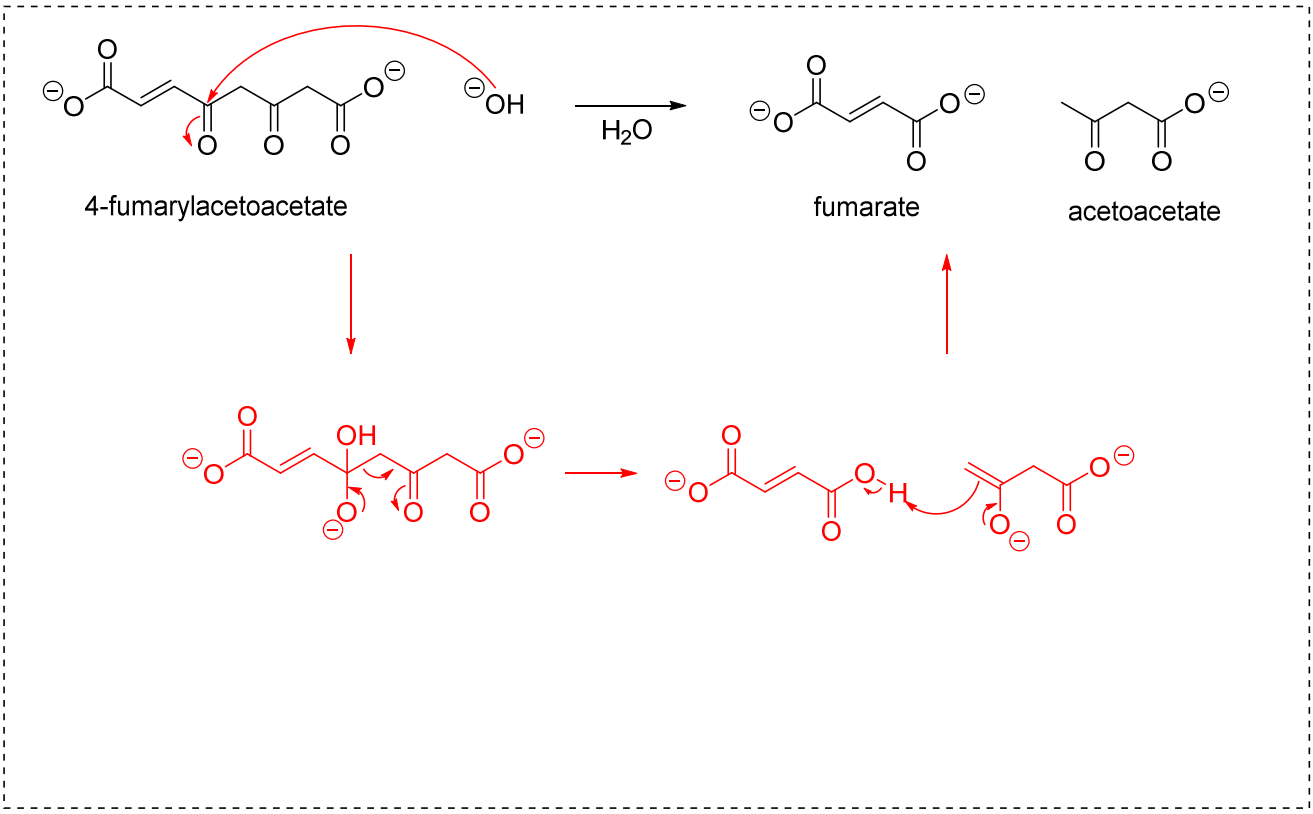


major bicyclic product (ignore sterochemistry) + 2 MeOH + 2 NaCl

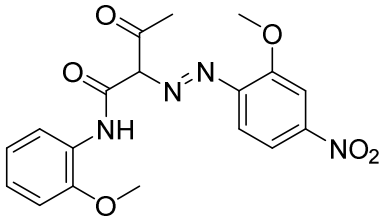


major bicyclic product (ignore sterochemistry) + MeOH

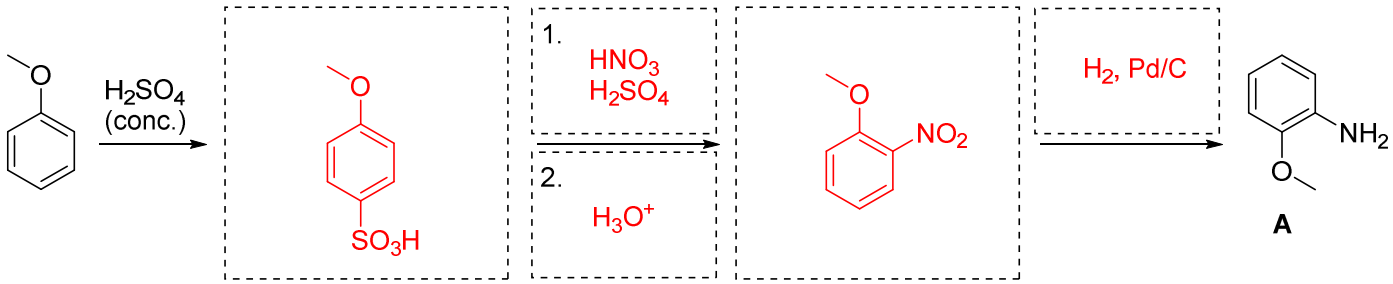
5. The enzyme-catalyzed reaction below is one of the steps in the degradation of the aromatic amino acids tyrosine and phenylalanine. Draw a curved arrow mechanism for this reaction. (8 pt)



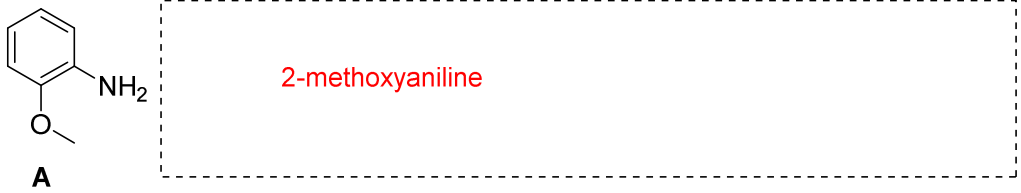
6. **Multistep Synthesis of an Azo Dye, "Pigment Yellow 74".**
The following series of questions examines the multistep synthesis of "Pigment Yellow 74", an azo dye with a greenish-yellow hue used primarily in printing inks and coatings.



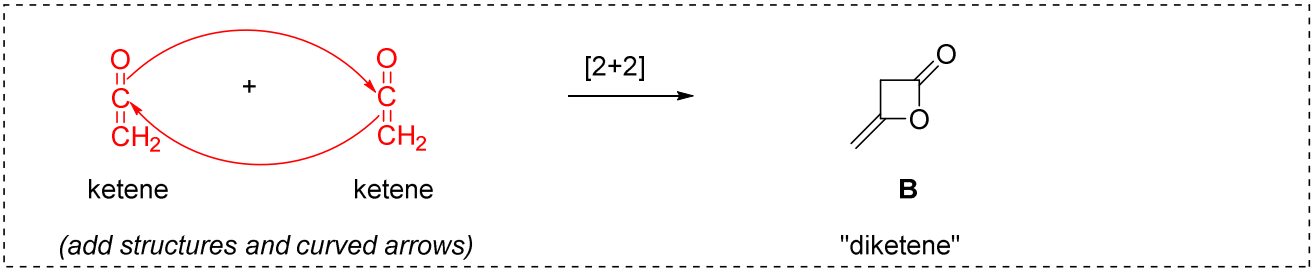
A. Fill in the boxes in the multistep synthesis of compound **A**. (20 pt)



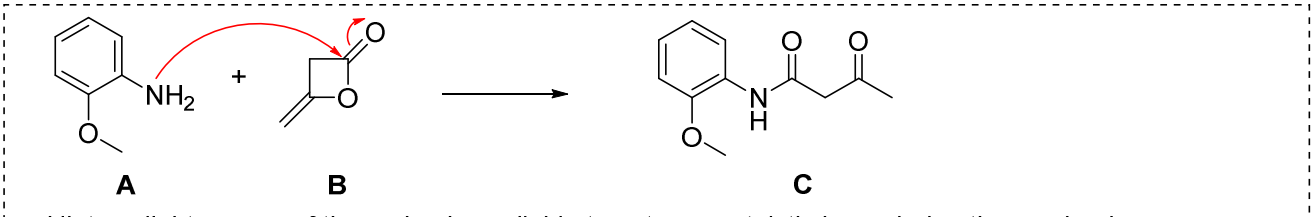
Provide a systematic name for compound **A**. (6 pt)



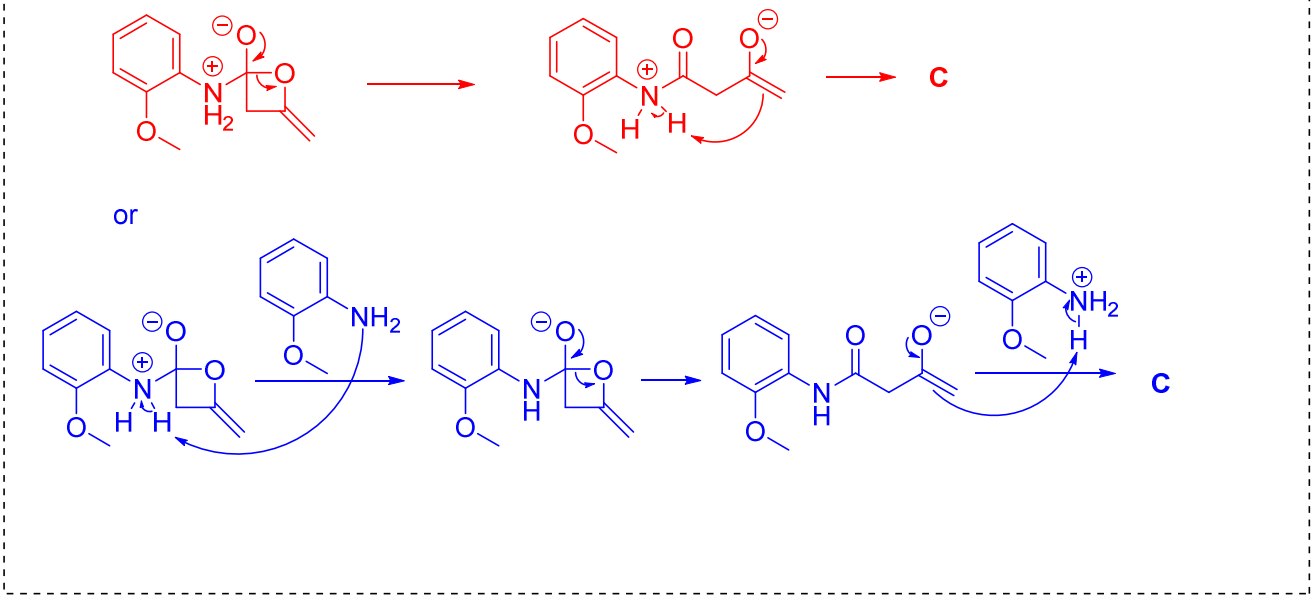
B. Compound **B** is commonly called "diketene", because it is synthesized by a 2+2 cycloaddition (dimerization) of a compound known as "ketene". Draw the starting materials and curved arrows for this reaction. (8 pt)



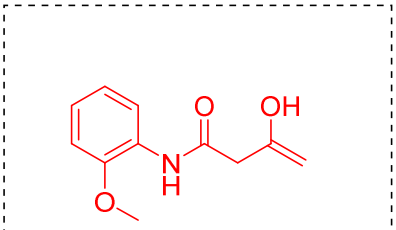
C. Draw a curved arrow mechanism for the reaction of shown below. You can abbreviate the aromatic ring as "Ar" in this mechanism. (8 pt)

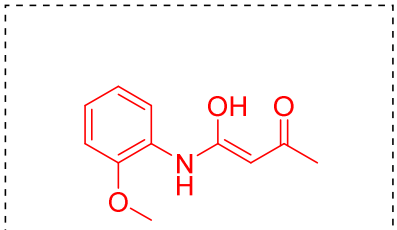


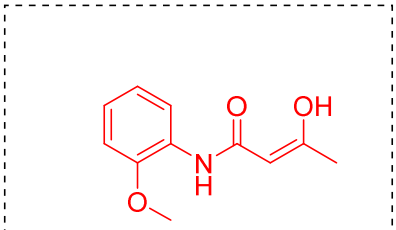
Hint: a slight excess of the amine is available to act as a catalytic base during the mechanism



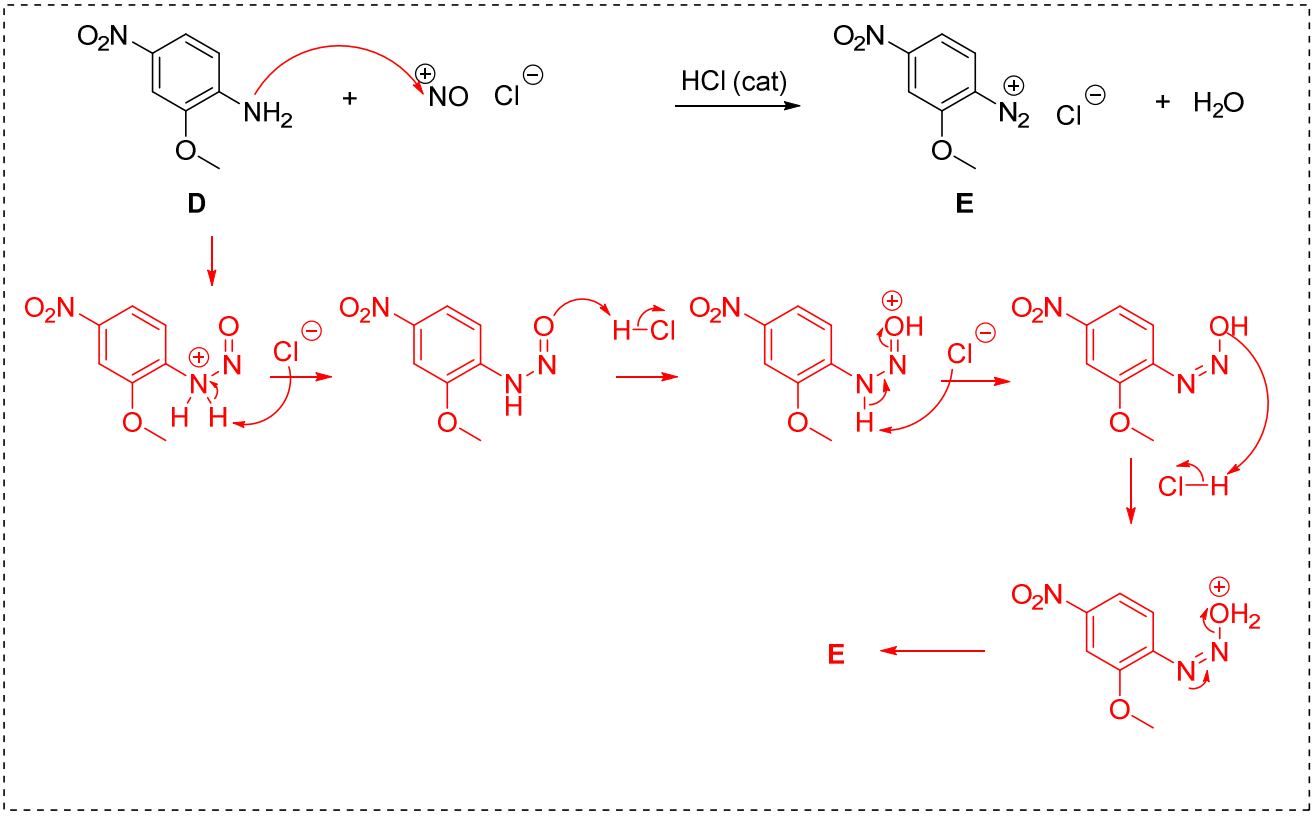
D. Three enol tautomers of product **C** are possible. Draw them below in order of increasing stability (do not include stereoisomers). You can abbreviate the aromatic ring as "Ar" in these structures. (12 pt)

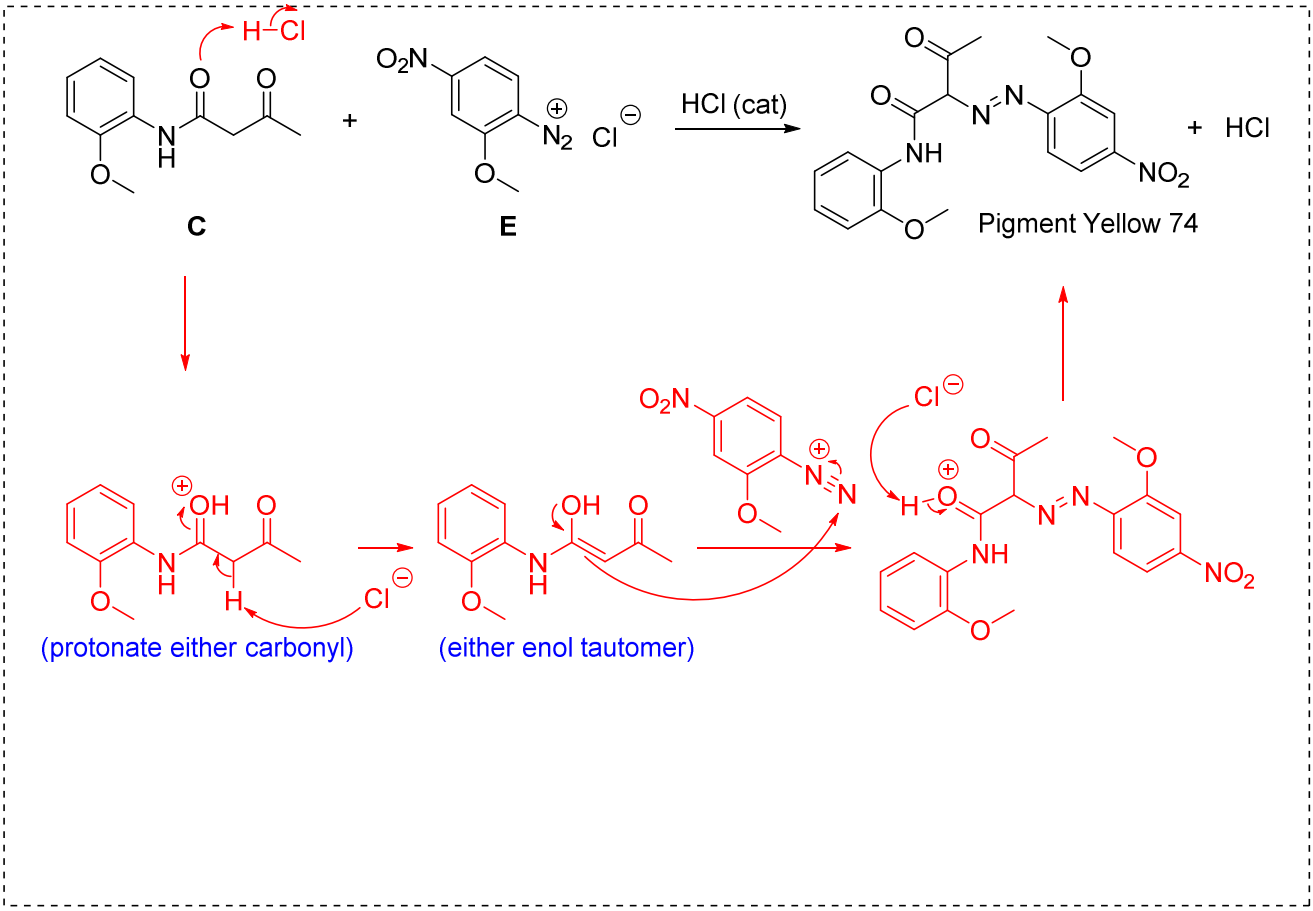






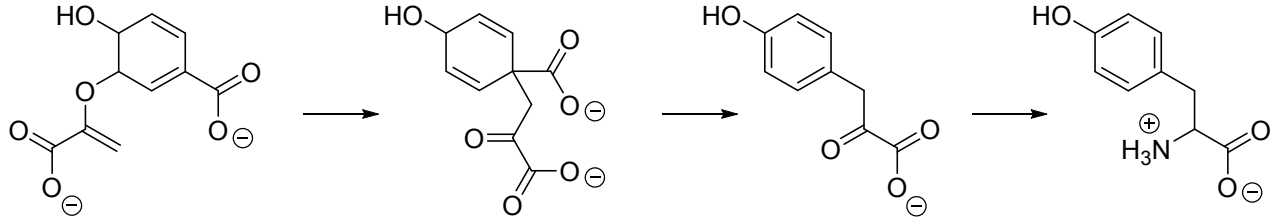
E. Draw a curved arrow mechanism for each reaction shown below. You can abbreviate the aromatic rings in these mechanisms, but you must unambiguously define your abbreviations (circle and label parts of the structures) so that it is clear which ring is which if you abbreviate both. (2 x 8 = 16 pt)





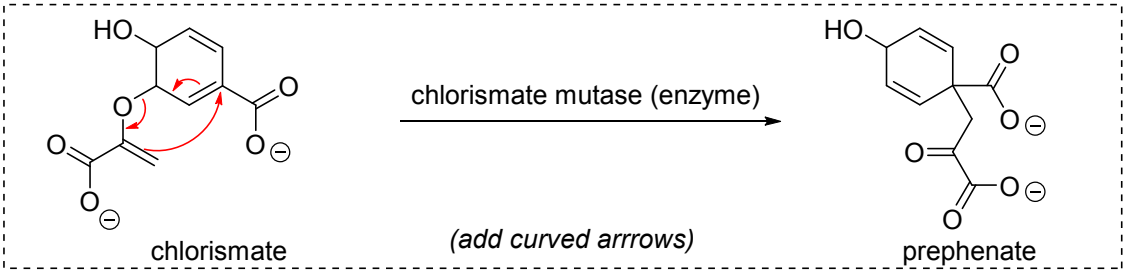
7. **Biosynthesis of Aromatic Amino Acids from Chlorismate**

The biosynthetic pathways leading to two amino acids, tryptophan and tyrosine, share a common starting material, chlorismate. This question examine the synthesis of tyrosine, while a later question will examine steps toward the synthesis of tryptophan.

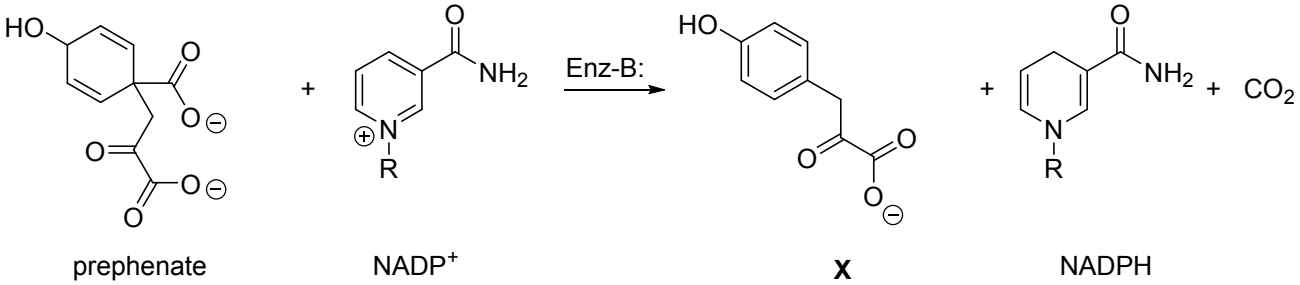


chlorismate prephanate **X** tyrosine

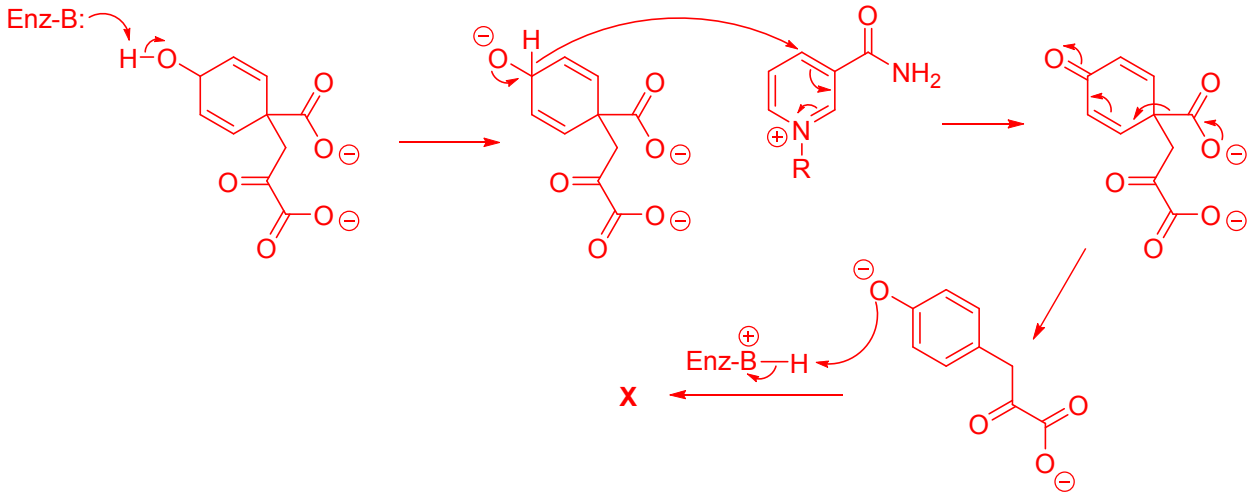
A. The rearrangement of chlorismate to prephenate is a concerted reaction with a 6-membered ring transition state. Add curved arrows to complete this mechanism. (8 pt)



B. Draw a mechanism for the enzyme-catalyzed reaction below, using Enz-B: as a generic catalytic base. (8 pt)



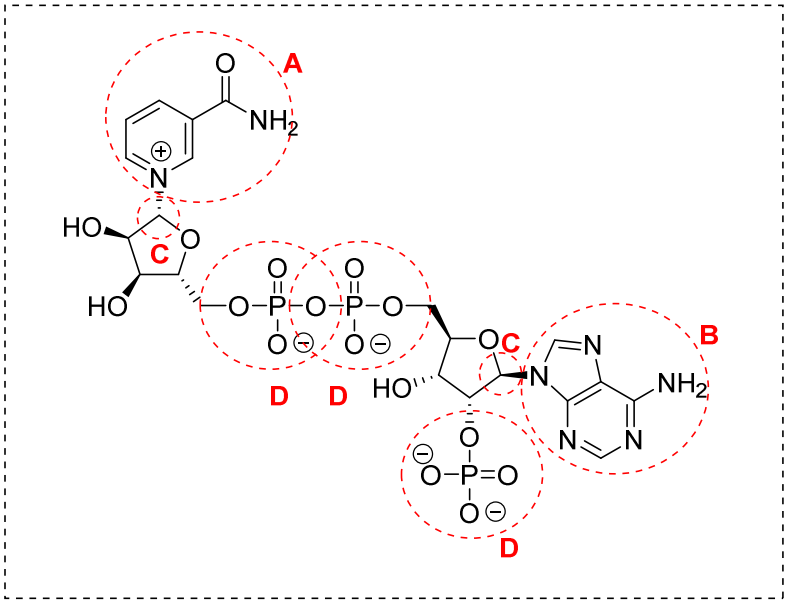
Hints: Start by deprotonating the hydroxyl group.
This mechanism contains a conjugated ketone intermediate.



C. One of the reactants in part B was **N**icotinamide **A**denine **D**inucleotide **P**hosphate ($NADP^+$), shown below.

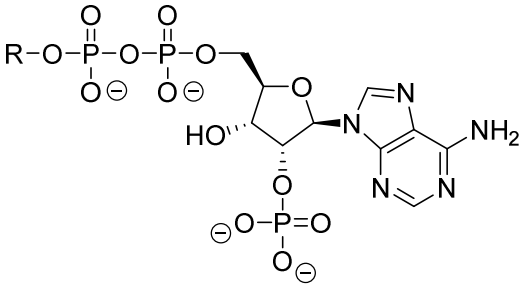
i. For each term in the following list, **circle each group** in the structure at the right, and **label the circle with the letter** corresponding to that term. (15 pt)

A. Nicotinamide *(hint: has an amide substituent)*
B. Adenine *(an aromatic nucleotide base)*
C. All anomeric carbons *(there are more than one)*
D. All phosphate groups

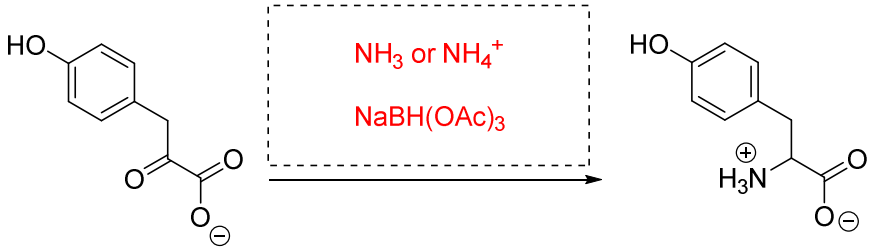


ii. The structure below is the right half of the NADP+ structure. Classify the sugar in the structure below by circling the appropriate term out of each pair of choices below. (15 pt)

A. D or L
B. α or β
C. aldose or ketose
D. furanose or pyranose
E. pentose or hexose

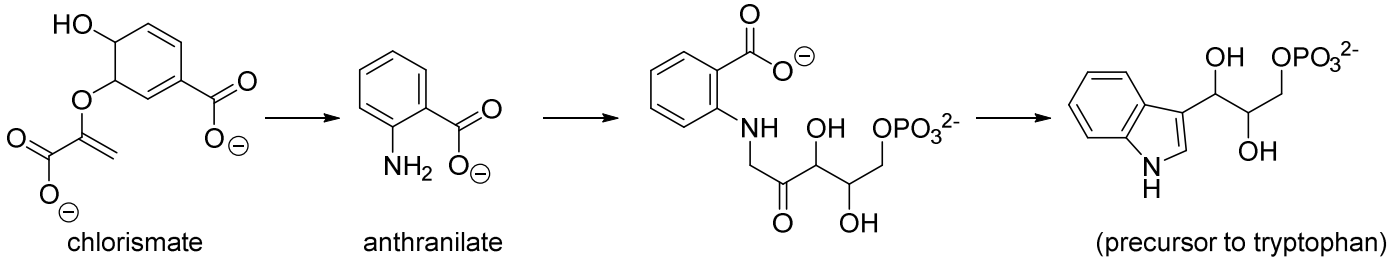


D. Amino acids can be synthesized from α-keto carboxylic acids, both in biosynthetic (enzyme catalyzed) sequences and in the chemistry lab. **Propose reaction conditions/reagents that can be used to accomplish the following synthesis of tyrosine from X in a single reaction in the chemistry lab.** (4 pt)



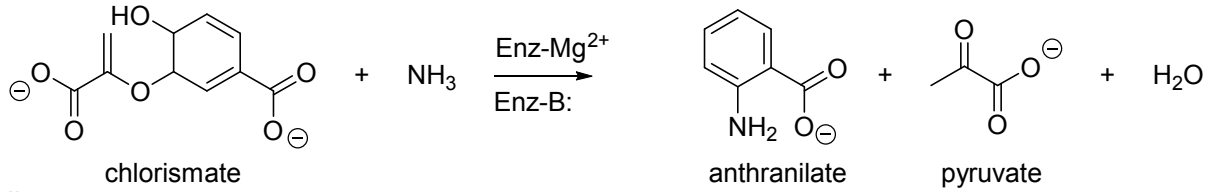
X **tyrosine**

8. Biosynthesis of Tryptophan

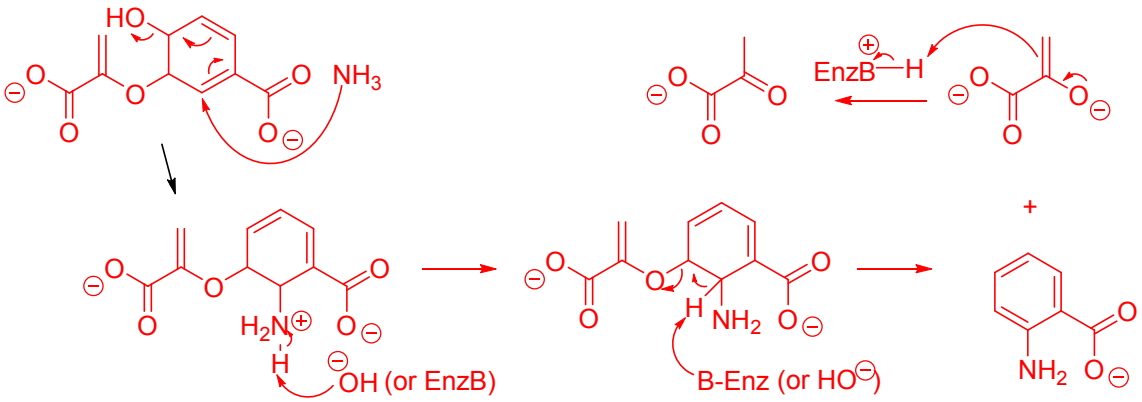


A. The synthesis of tryptophan from chlorismate begins with the synthesis of anthranilate.

i. Draw a mechanism for the enzyme-catalyzed reaction, taking into account the following information. (8 pt)

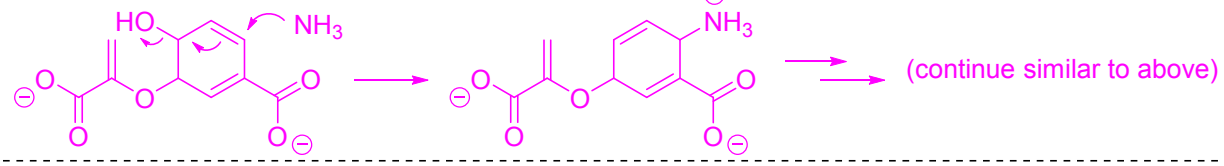


Hints:
The first step is a concerted nucleophilic substitution, in which ammonia acts as a nucleophile and hydroxide acts as a leaving group.
A later step is an E2 reaction.



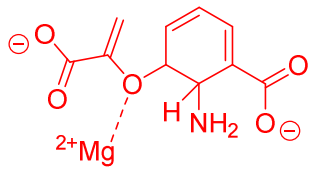
(these two deprotonations can be in either order with either base)

alternative site of substitution:



ii. The enzyme contains a Mg^{2+} ion in the active site which has been demonstrated to be essential for reactivity. Draw a figure clearly showing the **role of the Mg^{2+} ion** in the **E2 step of the mechanism**, and explain (in 10 words or fewer) how it speeds up this step of the reaction. (4 pt)

Drawing (role of Mg^{2+} in E2 step):

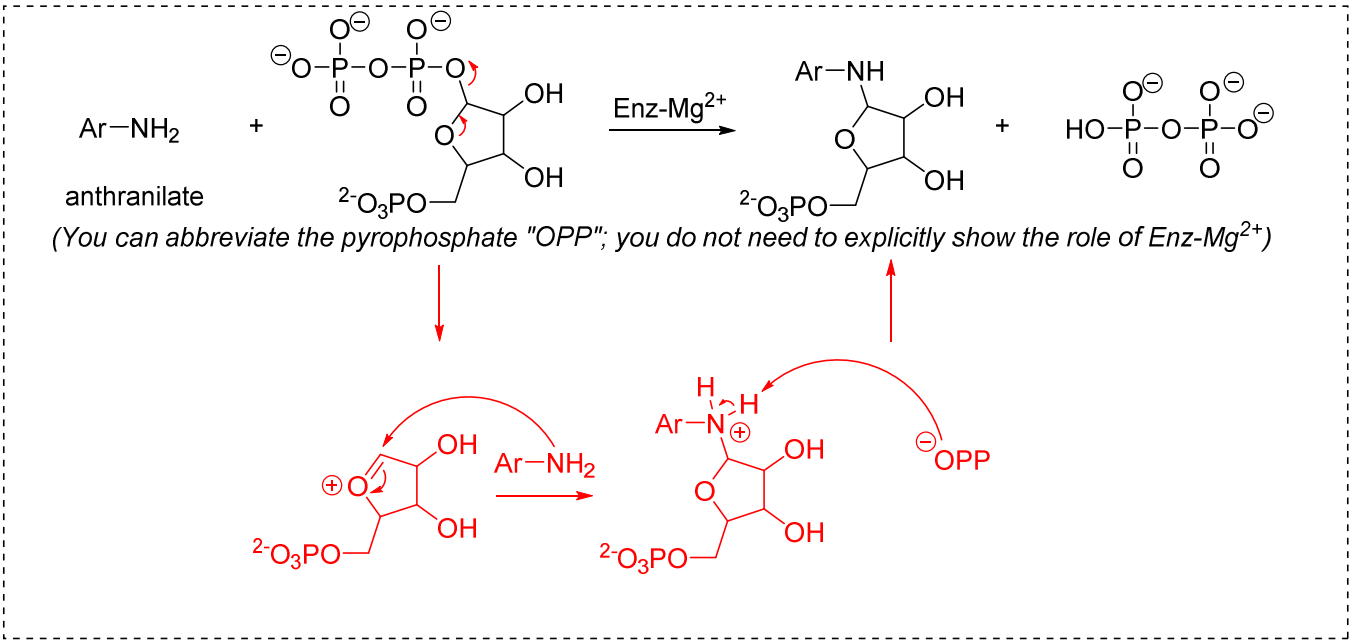


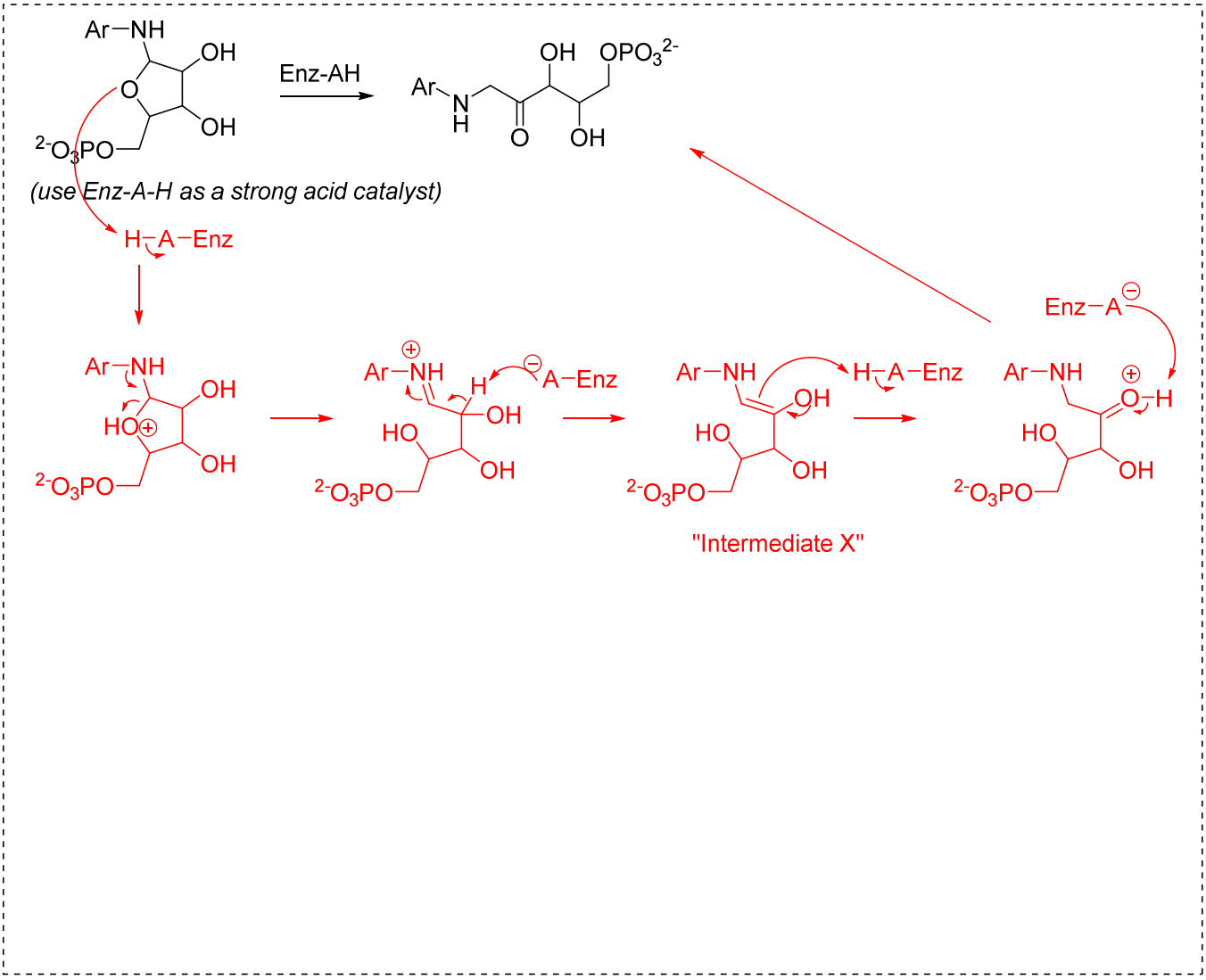
(any drawing showing interaction between Mg and the enolate leaving group)

Explanation:

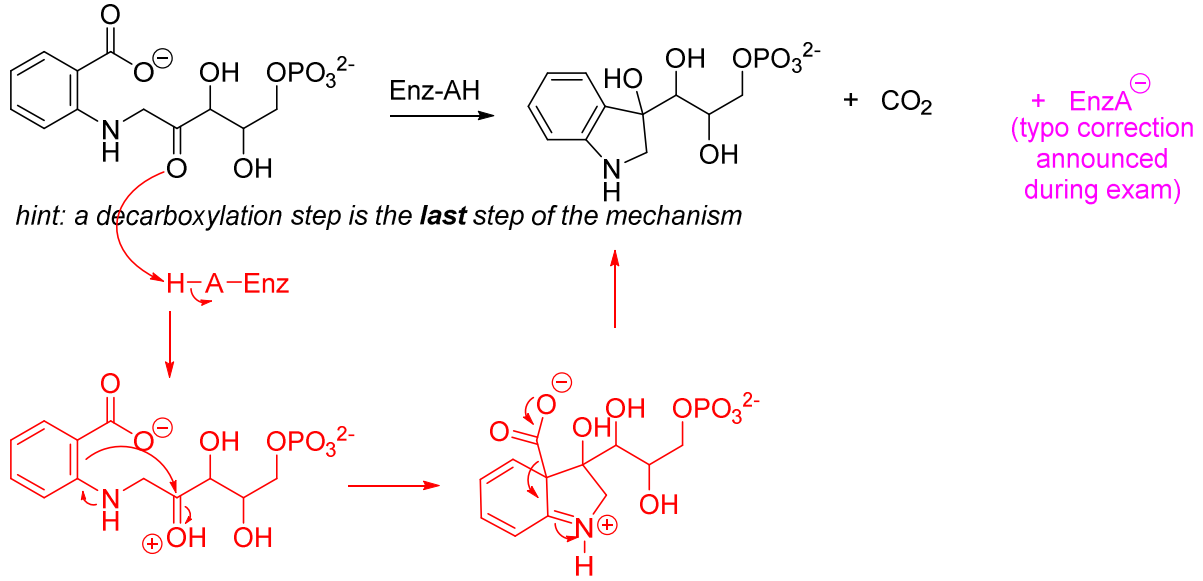
Lewis acid activation makes enolate a better leaving group

B. Draw a mechanism for each of the two sequential reactions below (the aromatic ring in anthraniliate is abbreviated "Ar"). (2 x 8 = 16 pt)

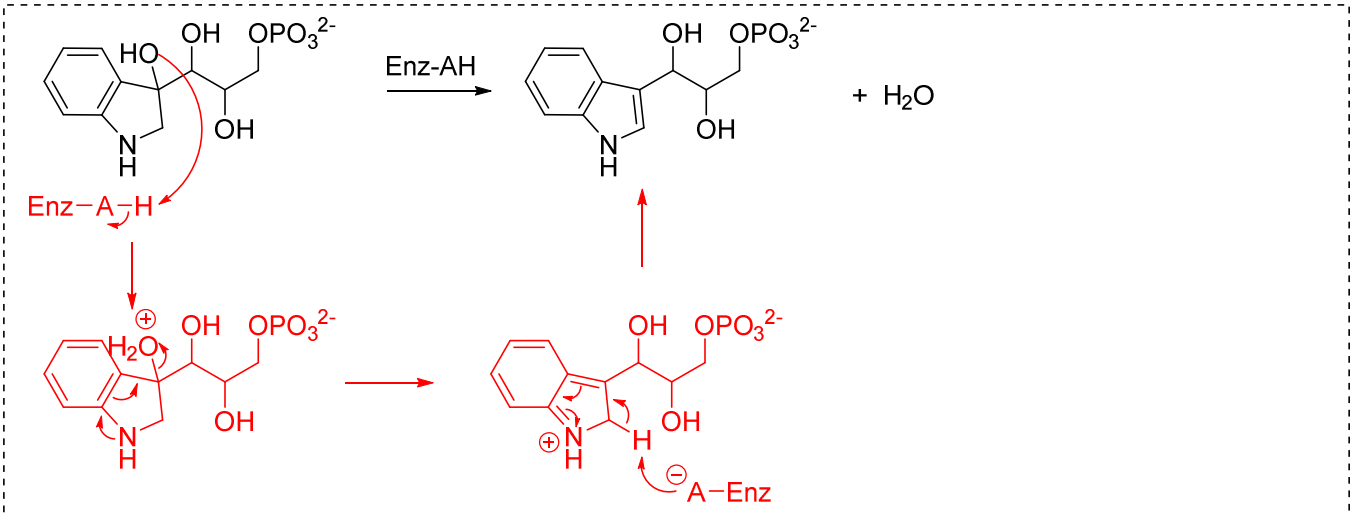




C. The two sequential reaction below are catalyzed by a single enzyme. Draw a mechanism for each, using Enz-AH as a generic **strong acid catalyst**. Make sure that each mechanism includes **major resonance contributors of the intermediates**. (2 x 8 = 16 pt)
(You may abbreviate a portion of the molecule "R" throughout the mechanisms. If you do, circle and label it "R" on the first structure to define your abbreviation)



reminder: all intermediates must be drawn as the major resonance contributors to earn full credit



reminder: all intermediates must be drawn as the major resonance contributors to earn full credit

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