

Midterm Exam 1

Chem 3B, Fall 2016
Thursday, September 29, 2016
7:00 – 9:00 pm

Name _____ **Answer Key** _____

Student ID _____

You have 120 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 200 points total.

Partial Periodic Table							
I	II	III	IV	V	VI	VII	VIII
H							He
Li	Be	B	C	N	O	F	Ne
Na	Mg	Al	Si	P	S	Cl	Ar
K	Ca	Ga	Ge	As	Se	Br	Kr
Rb	Sr	In	Sn	Sb	Te	I	Xe

1. Nomenclature and Vocabulary

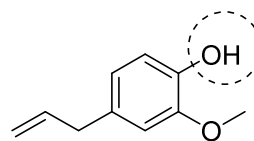
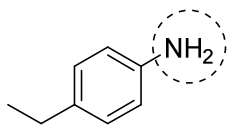
A. Draw a structure to match each prompt. (3x5 = 15 pt)

<i>ortho</i> -diisobutylbenzene	a benzylic anion	a heterocyclic molecule that is NOT aromatic

R group is optional, could be any substituent including just hydrogen

(many other answers possible)

B. Provide systematic name for each of the following structures. In each name, use a “base chain” name that INCLUDES the circled group. (2x5 = 10 pt)



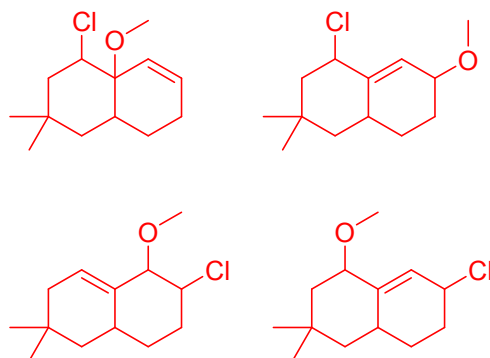
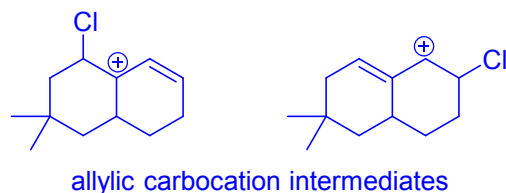
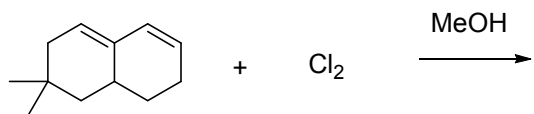
(eugenol)

4-ethyl aniline or para-ethyl aniline	4-allyl-2-methoxyphenol
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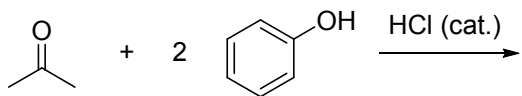
2. Draw a π energy level diagram for each of the four molecules below. Fill in the electrons. Circle the aromatic structure(s). (20 pt)

				circle the aromatic structure(s)
				π MO energy level diagrams, with electrons

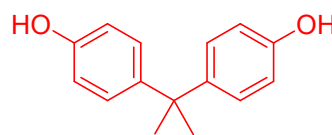
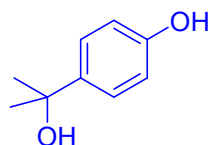
3. Predict the possible organic product(s) from the following reactions. Pay attention to any information given in the product boxes. (3x10 = 30 pt)



include all expected regioisomers ($\text{C}_{13}\text{H}_{21}\text{ClO}$), but do not include stereochemistry + HCl

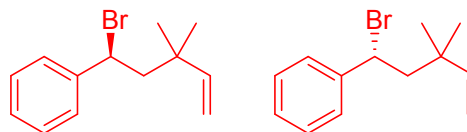
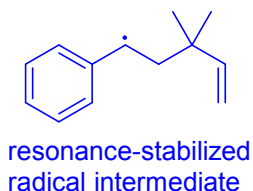
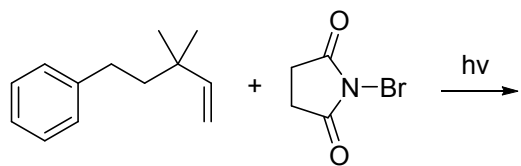


hint: two sequential EAS reactions

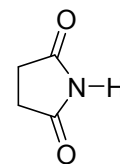


This is BPA (bisphenol A, the A refers to acetone), a plasticizer that has been removed from many consumer products in the recent past due to concerns about its endocrine effects

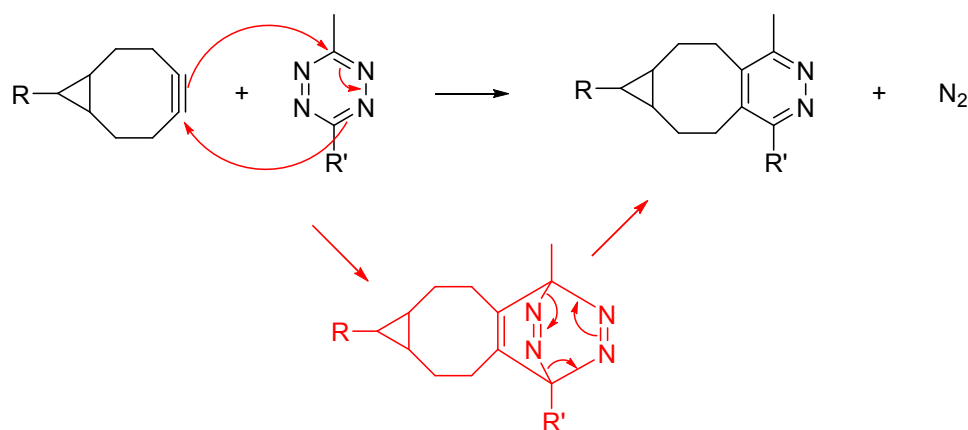
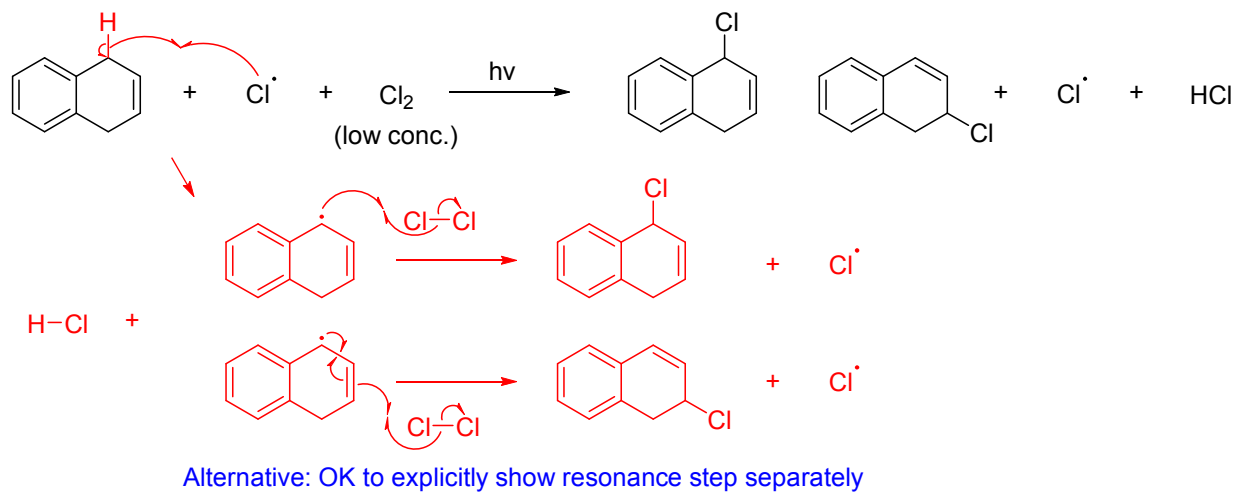
one major product + H_2O



include all expected regioisomer(s)/stereoisomer(s)



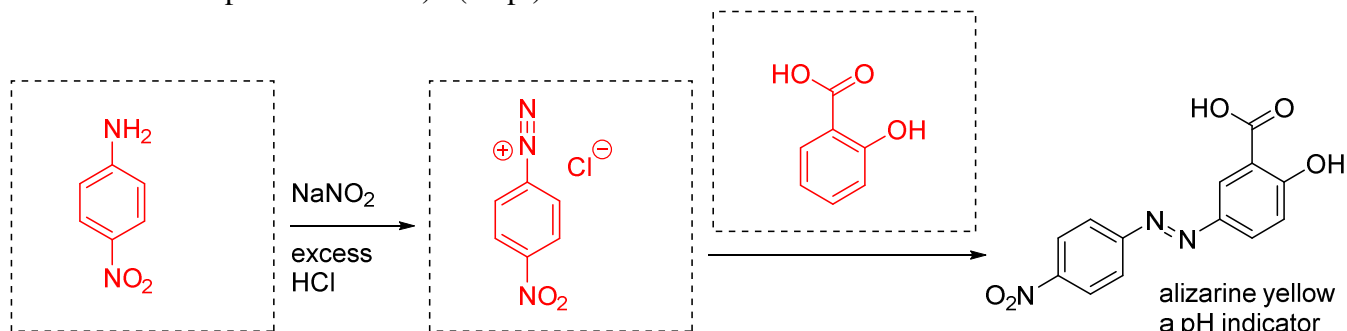
4. Draw a curved arrow mechanism for each of the reactions shown below. Your mechanism must account for all product(s) shown. (Note: For some of these reactions, there may be other possible products that are not shown. You only need to explain the product(s) pictured in the scheme) (2x10 = 20 pt)



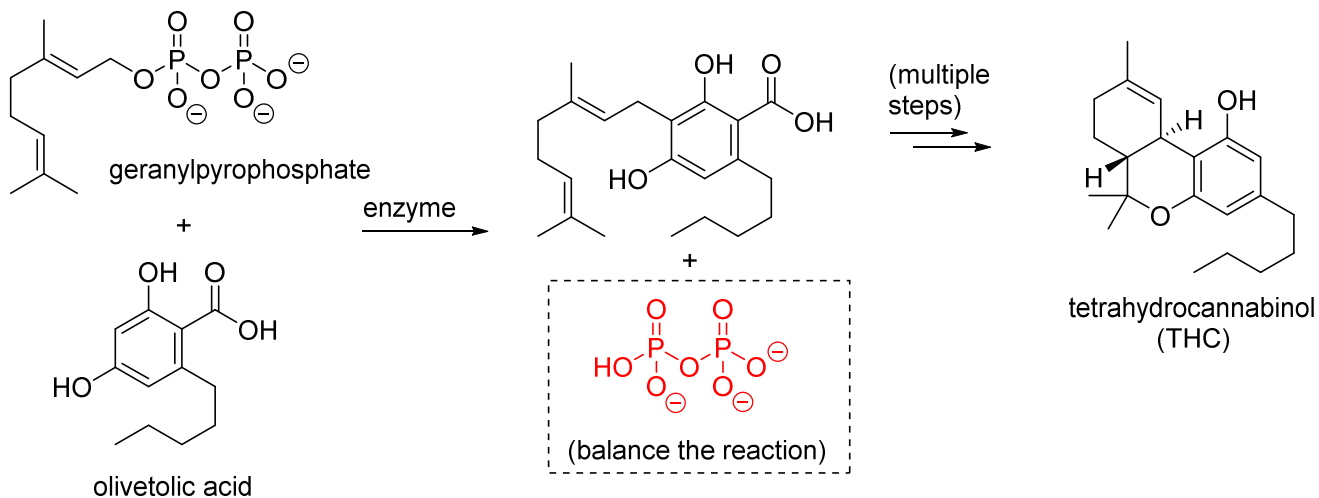
Literature example from Lecture D

Agarwal, P., Beahm, B. J., Shieh, P. and Bertozzi, C. R. (2015), Systemic Fluorescence Imaging of Zebrafish Glycans with Bioorthogonal Chemistry. *Angew. Chem. Int. Ed.*, 54: 11504-11510.

5. Fill in the missing reagents and structures in the following synthesis scheme. Assume that only one major product forms in each reaction. Do not combine multiple reaction steps in a single box (no numbered steps within a box). (15 pt)



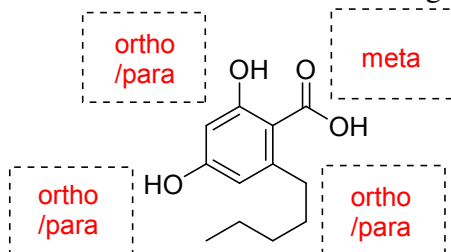
6. The biosynthesis pathway in marijuana (*Cannabis sativa*) plants that leads to the psychoactive compound tetrahydrocannabinol (THC) includes the enzyme-catalyzed electrophilic aromatic substitution reaction shown below. ¹



- A. Fill in the box in the scheme above to balance the EAS reaction scheme. (5 pt)
 B. Provide a systematic name for olivetolic acid. (5 pt)

2,4-dihydroxy-6-pentylbenzoic acid

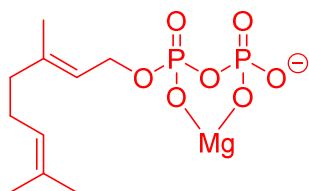
- C. Olivetolic acid has substituents that should affect the regioselectivity of an EAS reaction. Fill in the boxes below to indicate the “directing effect” that would be expected for each substituent. (6 pt)



expected directing effects of substituents

- D. The enzyme’s catalytic activity was found to require the presence of Mg^{2+} . Show how the Mg^{2+} in the enzyme active site interacts with the starting material(s) to catalyze reaction. (4 pt)
 (Use at least one picture/scheme and ≤ 5 words)

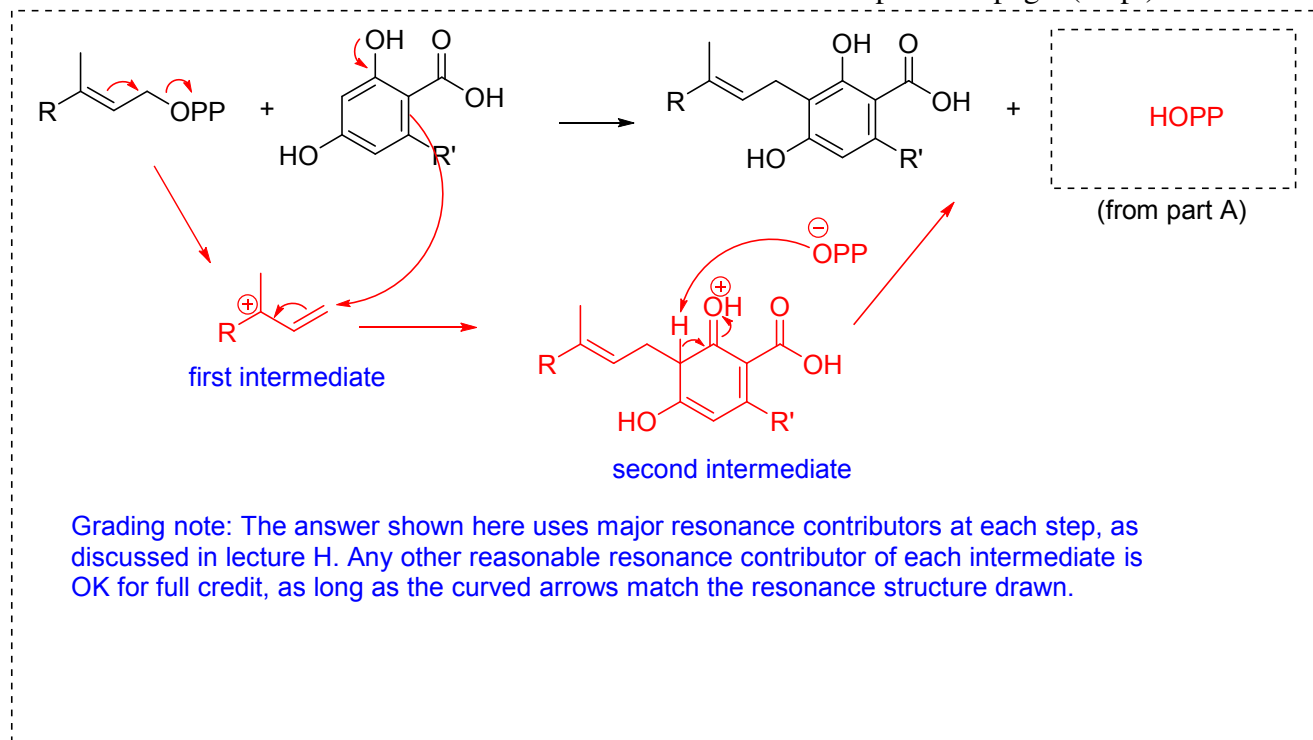
Mg^{2+} is a Lewis acid for activation of leaving group



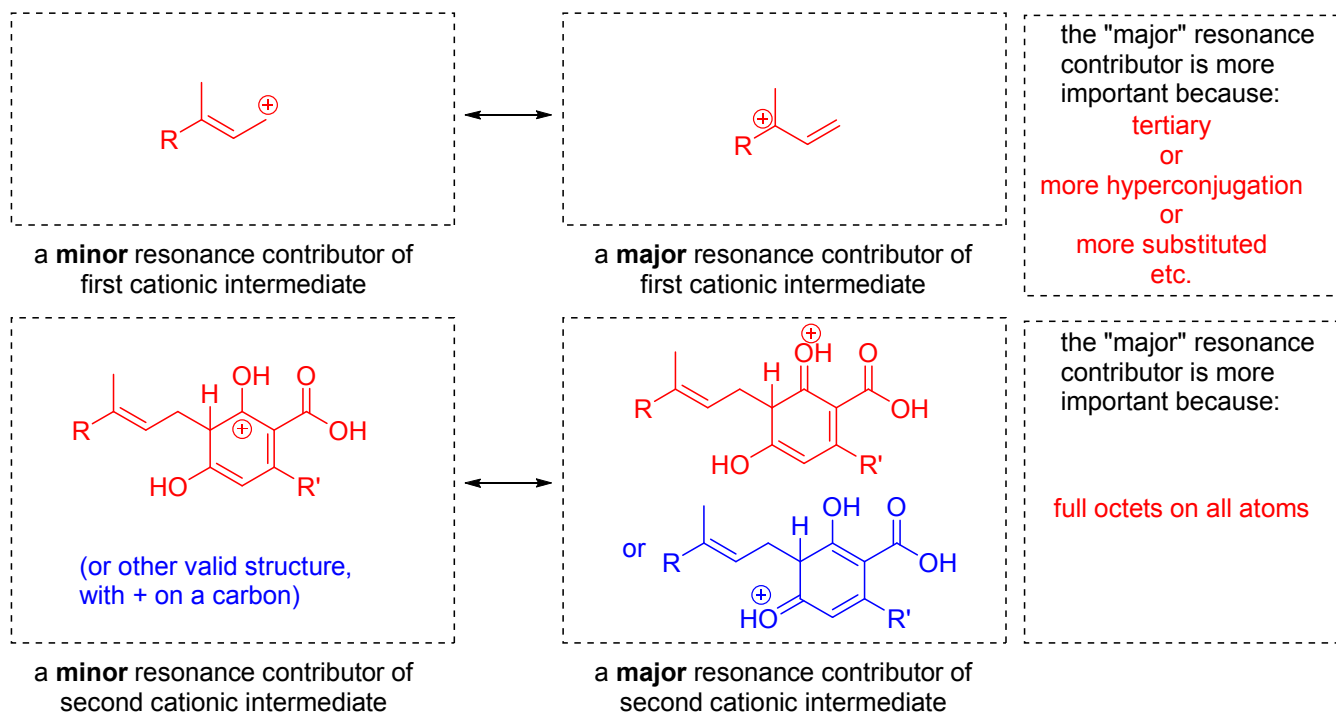
(this is one acceptable picture. Also OK to show coordination to just one O, at ANY oxygen site.)

¹ Fellermeier, M.; Zenk, M. H. “Prenylation of olivetolate by a hemp transferase yields cannabigerolic acid, the precursor of tetrahydrocannabinol” *FEBS Letters*, **1998**, 427(2), 283-285.

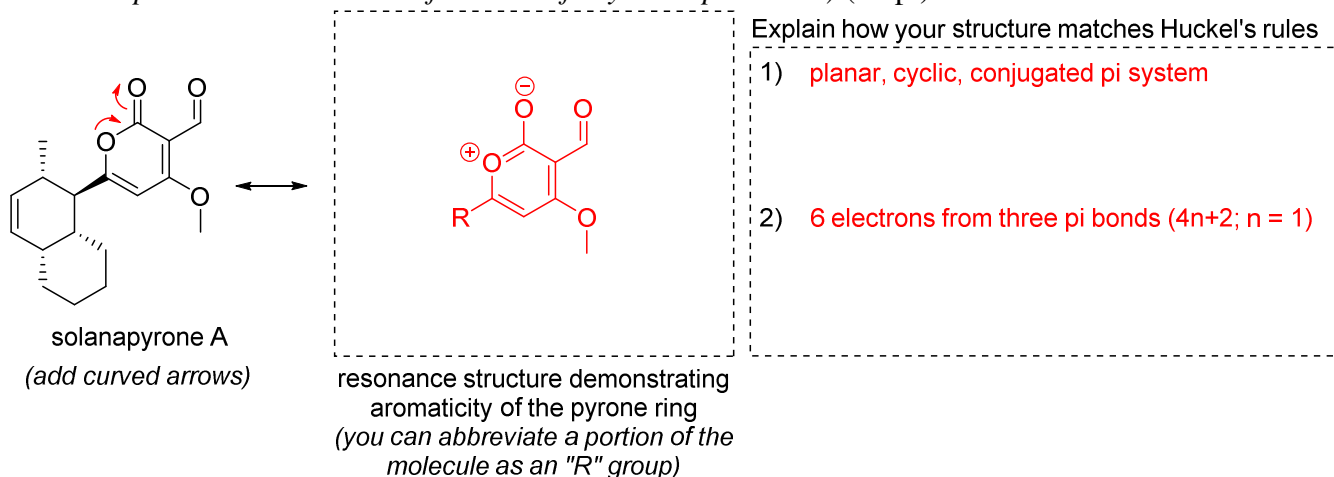
E. Draw a curved arrow mechanism for the EAS reaction from the previous page. (10 pt)



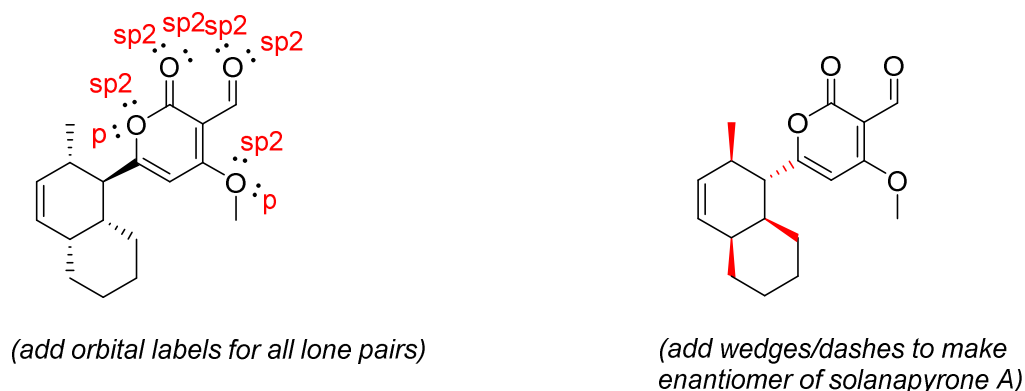
F. Your mechanism above should include **two sequential resonance-stabilized cation intermediates**. For each one, draw both a minor and a major resonance contributor in the spaces provided, and indicate why the major resonance contributor is more important than the minor one. (*A few words is sufficient, complete sentences are not required.*) (10 pt)



7. Solanapyrone A is a fungal toxin that inhibits the activity of mammalian DNA polymerase enzymes.²
- A. Solanapyrone A contains a heteroaromatic ring known as a “pyrone”. Draw curved arrows and the resulting resonance contributor which clearly demonstrate why this pyrone ring is considered aromatic, and explain how Huckel’s rules apply to the structure you drew. (*Hint: you must address two separate criteria to earn full credit for your explanation*) (10 pt)



- B. On the structure of solanapyrone A below (left), draw all oxygen lone pairs, and clearly label the type of orbital (s, p, sp², sp³) occupied by each one. (5 pt)



- C. Solanapyrone A is chiral molecule that is produced both enantioselectively and diastereoselectively by the fungus that it was isolated from.

- Add wedged/dashed lines to the template above (right) to draw the enantiomer of solanapyrone A. (5 pt)
- Define “enantioselective” in 10 words or fewer (5 pt)

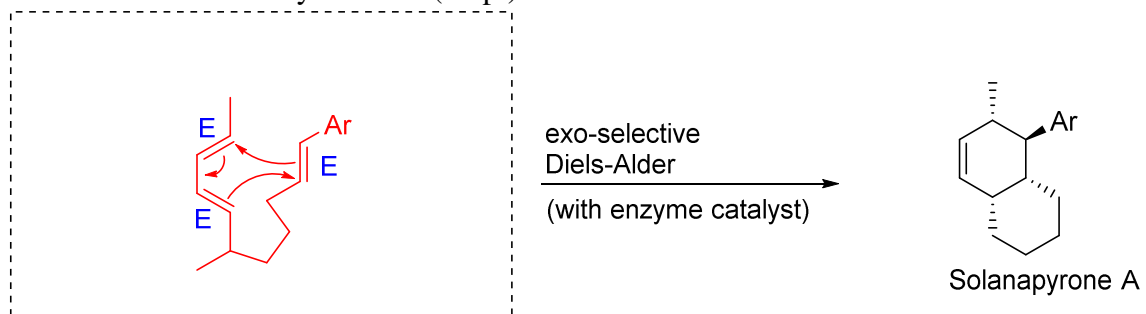
"enantioselective" means

more of one enantiomer formed than the other enantiomer
(or only one enantiomer forms)

² Mizushima, Y. *et al.* “A Plant Phytotoxin, Solanapyrone A, Is an Inhibitor of DNA Polymerase β and λ ”, *J. Biol. Chem.* **2002**, 27(1), 630-638.

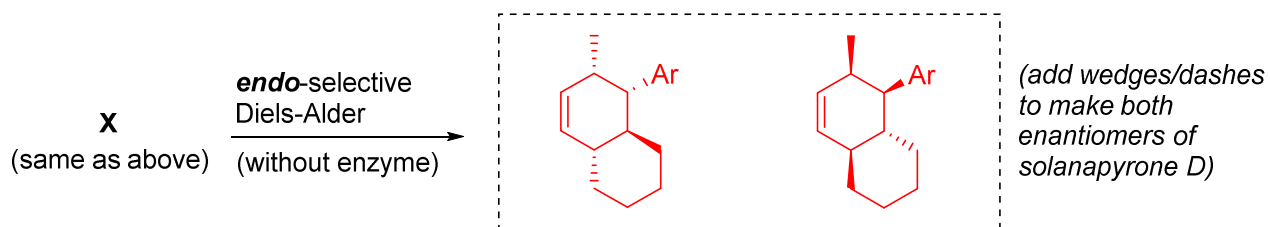
D. The final step in the biosynthesis of solanapyrone A has been referred to (by researchers who isolated and characterized the enzyme involved) as an “enzyme-catalyzed **exo-selective** Diels-Alder reaction”.³ Their use of “**exo/endo**” terminology in this reaction focuses on the relative position of the **aromatic pyrone ring**, which is abbreviated “Ar” throughout this whole page of the exam.

- i. Draw the starting material **X** (in the reactive conformation) that would lead to solanapyrone A by a Diels-Alder reaction. Add curved arrows. Label the stereochemistry (E or Z) of each alkene in the structure you drew. (15 pt)

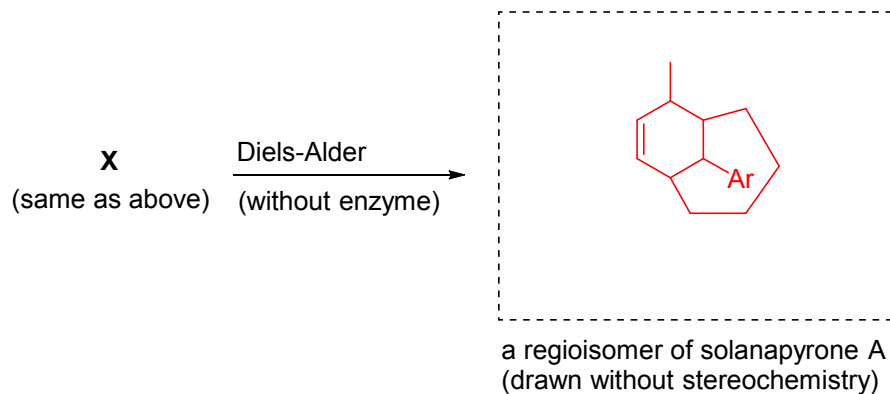


- structure of **X** (in reactive conformation)
- curved arrows
- E/Z labels for each alkene

- ii. In the absence of the enzyme catalyst, researchers found that the major product resulting from reaction of starting material **X** was the **endo diastereomer**, named solanopyrone D. Add wedges/dashes to the templates below to show both enantiomers of this endo diastereomer. (5 pt)



- iii. Since both the diene and the dienophile are asymmetric, the uncatalyzed Diels-Alder reaction could theoretically also form a set of products that are regioisomers of solanapyrone A. Draw this regioisomer (**without** any stereochemistry). (5 pt)



³ Oikawa, H.; Katayama, K.; Suzuki, Y.; Ichihara, A. “Enzymatic Activity Catalysing Exo-selective Diels-Alder Reaction in Solanapyrone Biosynthesis”, *J. Chem Soc. Chem Commun.* **1995**, 1321-1322.