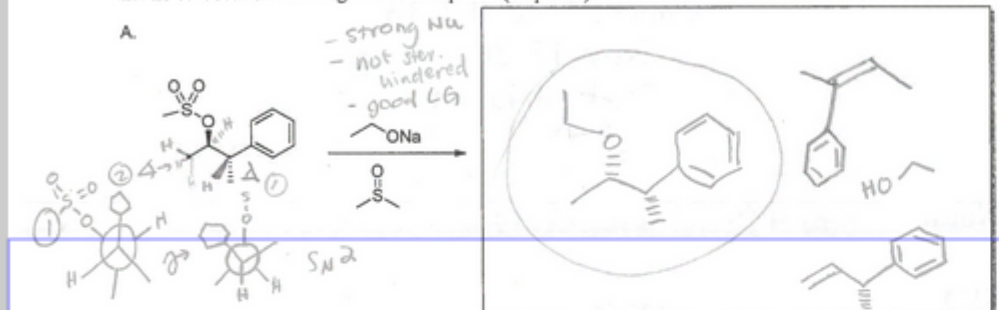
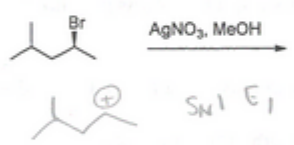
1. Predict the product(s) from the following reactions, paying careful attention to any instructions provided in the answer boxes. Unless otherwise instructed, show **all possible organic products, including stereoisomers**. Each redundant or wrong answer cancels one correct answer within any given box. Assume that no carbocation rearrangements take place. (56 points)

A.



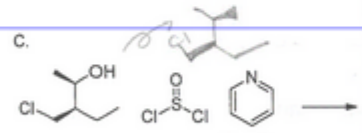
Substitution **and** elimination products - **circle the major product**

B.

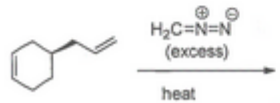


Substitution **and** elimination products

C.



D.



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

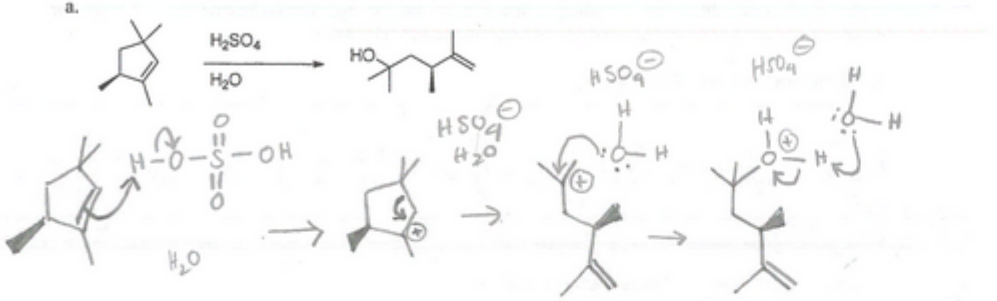
Grading Rubric

- +20.0 for Correct - full credit
- +4.0 for Partial credit: (R)-2-methoxy-4-methylpentane
- +4.0 for Partial credit: (S)-2-methoxy-4-methylpentane
- +4.0 for Partial credit: 4-methyl-1-pentene
- +4.0 for Partial credit: trans-4-methyl-2-pentene
- +4.0 for Partial credit: cis-4-methyl-2-pentene
- +-2.0 for Point deduction: Redundant/extra answer(s)
- +0.0 for No answer

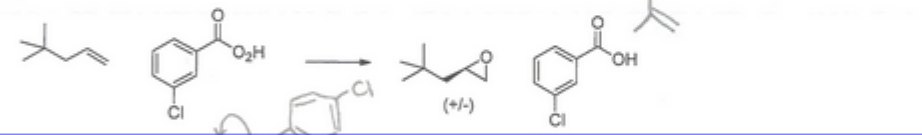
Points were also deducted for duplicate stereoisomers <-----

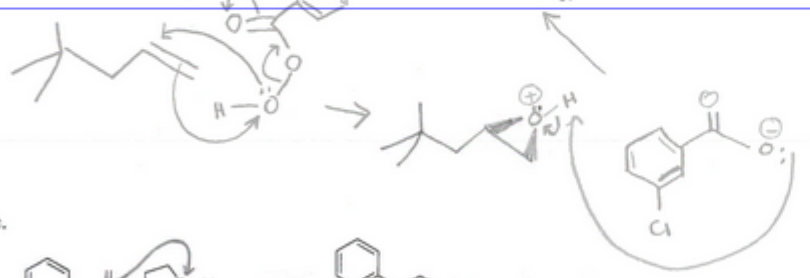
2. Write logical curved-arrow mechanisms for the following reactions. Make sure that each answer clearly shows the number of steps and the order of steps and accounts for all products shown. **If necessary, redraw reagents in order to clearly show all electrons that move in the reaction.** (24 points)

a.

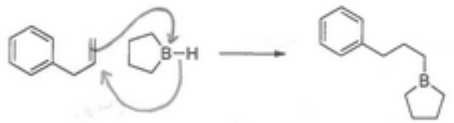


b.





c.



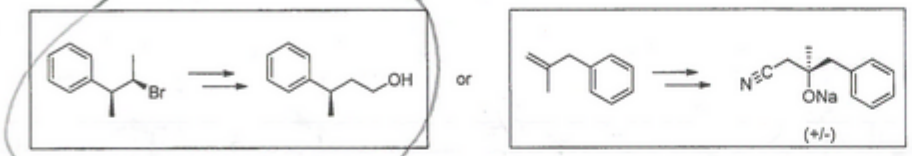
Select a question to show how it was graded. You can also use the left and right arrow keys to switch between questions.

Grading Rubric

- +6.0 for Correct - full credit
- +3.0 for Partial credit - curved arrows demonstrate concerted formation of both C-O bonds
- +3.0 for Partial credit - valid curved arrows account for every bond that is broken and every bond that is formed. If any intermediates are drawn, they have appropriate formal charges based on the curved arrows.
- +0.0 for No credit.

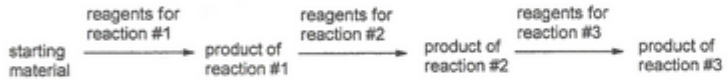
3. Choose one of the two synthesis problems on this page. **Propose the reagents needed to accomplish the synthesis shown in three or fewer synthetic steps.** It is fine to include additional work on the page, but for your final route, draw a linear sequence with the reagents for each step above a reaction arrow leading to the isolatable organic product of that step (see the example format below). *Note: You do not need to draw curved arrow mechanisms for these reactions.* (15 points)

Circle the problem you choose to answer:

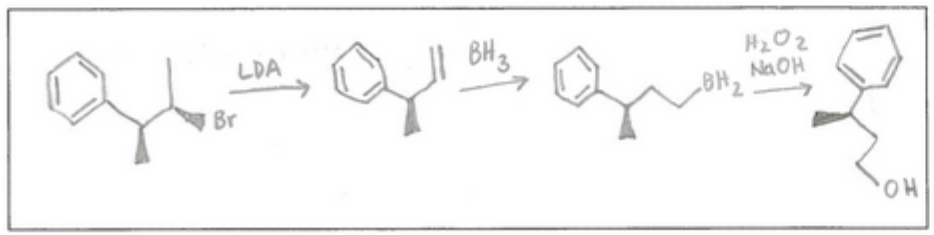


or

Example format for answer if three steps are required:



Final Answer (formatted as in the example)

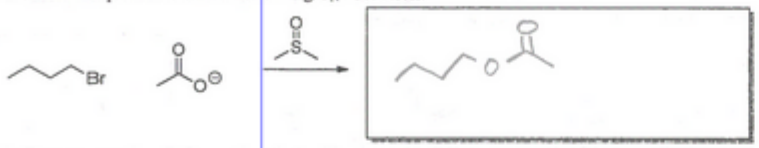


Select a question to show how it was graded. You can also use the left and right arrow keys to switch between questions.

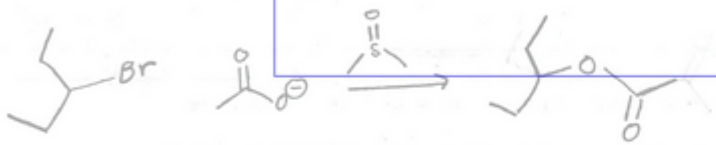
Grading Rubric

- +15.0 for Correct - full credit
- +6.0 for Partial credit - A viable intermediate was identified, addressing the change in location and identity of the functional groups from starting material to product. (For example, a terminal alkene for scheme A or epoxide for scheme B)
- +6.0 for Partial credit - at least one of the reaction steps has the correct reagents listed to accomplish the indicated reaction (with the correct regiose/ectivity if applicable).
- +0.0 for No credit.

4. Reaction rates and reaction coordinate diagrams. (20 points)
a. Draw the products of the following S_N2 reaction.



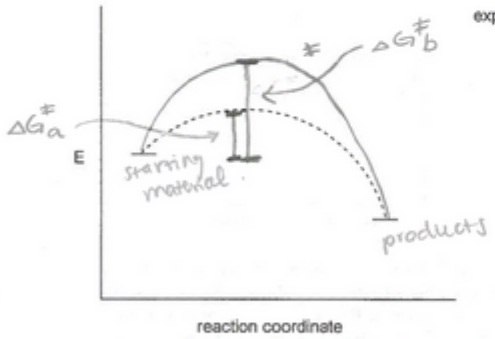
b. Propose another S_N2 reaction that will occur at a **different rate** than the reaction in part A. Draw all starting materials and products for your proposed reaction.



c. Will the reaction you proposed in part b occur at a faster or slower rate than the reaction in part A? Circle your answer:

faster slower

d. Explain your reasoning for part c in 2-3 sentences. As part of your answer, include the following:
i. Add a reaction coordinate curve for your proposed reaction to the reaction coordinate diagram below, which already shows the reaction from part a.
ii. Label any relevant energy differences on the diagram and explain them as part of your answer.



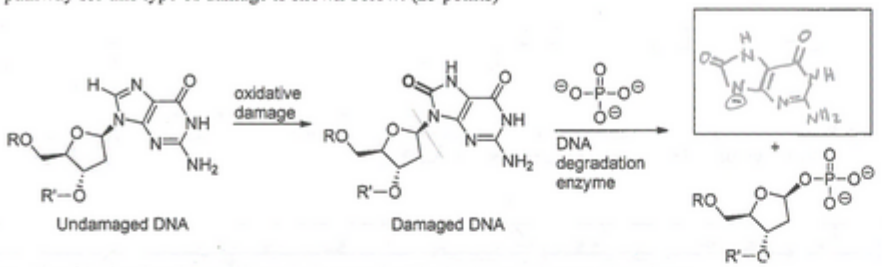
explanation: The bromine in a is attached a primary carbon, but the bromine in b is attached a secondary carbon. The steric hinderance of the two ethyl groups slows the backside attack of the S_N2 reaction and raises the energy required to attain the transition state ($\Delta G^{\ddagger}_b > \Delta G^{\ddagger}_a$).

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

- +4.0 for Correct
- +4.0 for Partial credit: ester is drawn correctly
- +1.0 for Partial credit: bromide ion is included
- +0.0 for Incorrect - no credit.

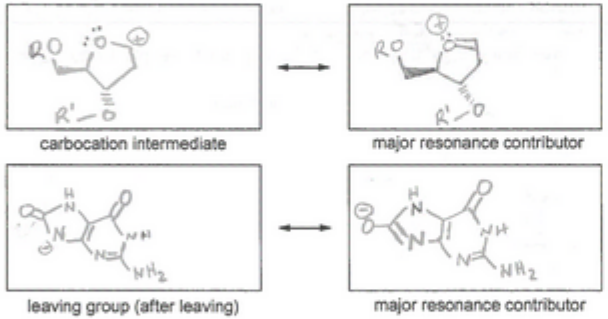
5. When DNA becomes damaged, it must be degraded quickly to prevent incorrect genetic material from being used or copied into new cells. One type of DNA damage that can occur and the first step in a degradation pathway for this type of damage is shown below: (25 points)



a. Provide the **structure of the missing product** in the degradation reaction above.

b. Is this degradation reaction an **addition, substitution, or elimination**? (circle one)

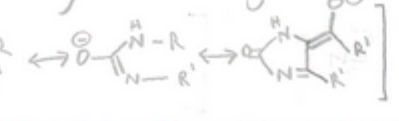
c. **This degradation reaction proceeds through a carbocation intermediate.** Both the leaving group (after leaving) and the carbocation are resonance stabilized. Draw the structure of the **carbocation intermediate** and the **leaving group** after they have dissociated. Then, draw one **major resonance contributor of each to explain their stability.**



d. Damaged DNA degrades more quickly than undamaged DNA. **Propose an explanation for this difference in reaction rates. As a reminder, the structure of undamaged DNA is shown at the top of the page.** In your explanation, be specific about the **energy difference (think about reaction coordinate diagrams)** that leads to the rate difference. Draw **at least one relevant organic structure** as part of your answer (abbreviate parts of the structure with "R" groups as needed).

The carbonyl group added to the DNA due to oxidative dama forms part of a major resonance contributor that help Stabilize the negative charge on N after the leaving group leaves. This makes damaged DNA have a better leaving group, allowing it to degrade more quickly.

damaged: can delocalize ⊖ charge to either of 2 O atoms



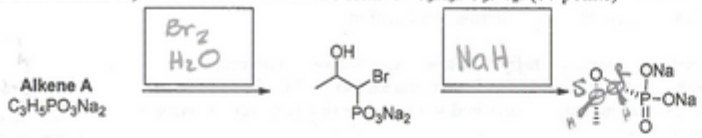
- LG on undamaged DNA can only delocalize ⊖ charge to one O atom. → less stable

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

- +2.0 for Damaged DNA contains a better leaving group due to resonance
- +1.0 for Resonance stabilization of leaving group in undamaged DNA exists, but is worse than the resonance stabilization of the leaving group in the damaged DNA
- +1.0 for At least one relevant organic structure is drawn. This structure contributes significantly to the explanation.
- +2.0 for Explanation specifically addresses how either the activation energy or transition state energy is affected by the change, rather than discussing only product stability
- +0.0 for No credit.

6. Fosfomycin is an epoxide-containing antibiotic. It can be synthesized from **bromohydrin B**, whose structure is drawn without the relevant stereochemistry in the scheme below. This bromohydrin can be synthesized from **alkene A**, which has the molecular formula $C_3H_5PO_3Na_2$. (60 points)

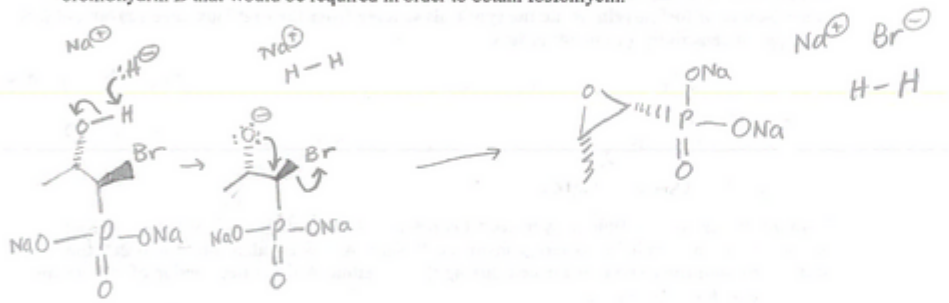


Alkene A $C_3H_5PO_3Na_2$ — **Bromohydrin B** — **fosfomycin**

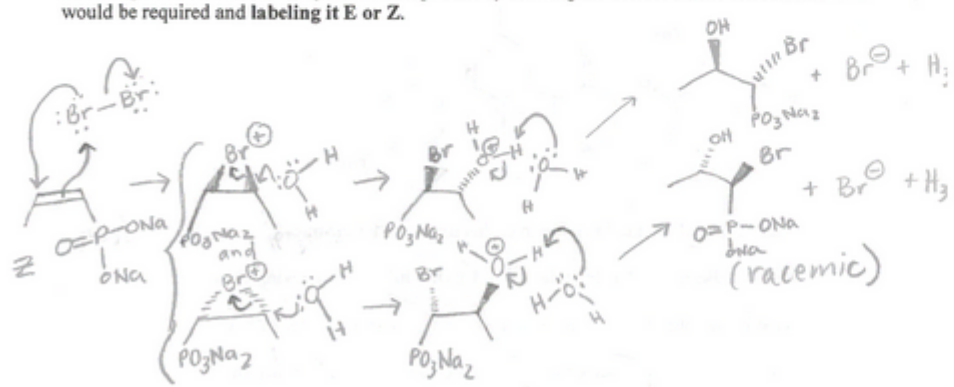
a. **Fill in the boxes** with the reagents that would be needed for each of the two reaction steps in the scheme above.

b. Label the **configuration of each stereocenter** in fosfomycin in the scheme above (R or S).

c. In the space below, draw a **curved-arrow mechanism** for the reaction of **bromohydrin B** to **fosfomycin**. Make sure that your mechanism clearly shows the number of steps, order of steps, and **correct, unambiguous stereochemistry in each step**. Start by drawing the correct stereoisomer of bromohydrin B that would be required in order to obtain fosfomycin.



d. In the space below, draw a **curved-arrow mechanism** for the reaction of **alkene A** to **bromohydrin B**. Make sure that your mechanism clearly shows the number of steps, order of steps, and **correct, unambiguous stereochemistry in each step**. Start by drawing the correct alkene stereoisomer that would be required and **labeling it E or Z**.

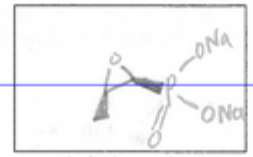


between questions.

Grading Rubric

- +8.0 for Correct - full credit
- +4.0 for Partial credit - Correct reagents are shown for the first reaction (Br2, H2O)
- +4.0 for Partial credit - Correct reagents are shown for the second reaction (any base strong enough to deprotonate the hydroxyl group - for example, hydroxide, NaH, KH, LDA)
- +0.0 for No credit.

e. The synthesis scheme on the previous page produces a racemic mixture (two stereoisomers) of fosfomycin. **Draw the undesired stereoisomer** of fosfomycin that forms during this reaction.



undesired stereoisomer of fosfomycin that forms during reaction

f. What is the name of the type of selectivity that would describe a reaction producing only the desired stereoisomer of fosfomycin, without producing the undesired stereoisomer that you drew in part e ? (circle one).

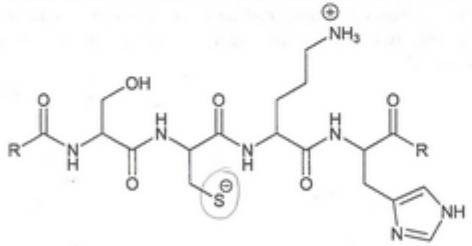
regioselectivity (diastereoselectivity) enantioselectivity

g. One method that has been used to selectively synthesize only the desired stereoisomer of fosfomycin from this alkene starting material is carry out a "bacterial fermentation" in which particular types of bacteria are grown in the presence of the alkene and they produce the fosfomycin product via enzyme-catalyzed reactions.
Explain why the enzymatic reaction(s) are capable of selectively producing only the desired stereoisomer of fosfomycin, while the synthesis scheme from the previous page cannot achieve this type of selectivity. (15 words or less)

Enzymes = chiral, can catalyze stereospecific reactions; our reagents = achiral, Br_2/H_2O addition = not diastereoselective.

h. Fosfomycin acts as an antibiotic by irreversibly reacting with the amino acid side chains of an important enzyme that helps bacteria construct cell walls. **A new covalent bond between the fosfomycin and the enzyme is formed during this reaction.** A simplified version of the enzyme active site is shown below.

i. **Circle the atom** within this active site that would be most likely to react with fosfomycin.



ii. What is the role of the fosfomycin in this reaction? (circle one)

Acid Base Nucleophile (Electrophile) Leaving Group

iii. What is the role of the enzyme side chain in this reaction? (circle one)

Acid Base (Nucleophile) Electrophile Leaving Group

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

- +3.0 for Correct (enantioselectivity if the enantiomer was drawn, diastereoselectivity if a diastereomer was drawn)
- +0.0 for Incorrect