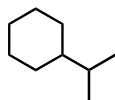


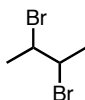
Problem Set 9

Question 1.

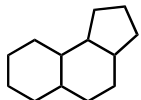
- a. Rank in order of increasing number of chirality centers (1 = fewest chirality centers; 5 = most chirality).



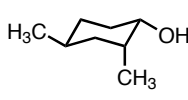
1



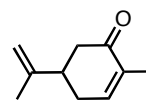
3



5



4



2

- b. Rank in order of increasing rate of S_N2 substitution (1 = slowest rate; 5 = fastest rate).



1



3



4

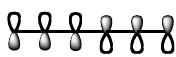


2

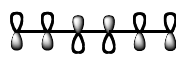


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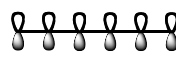
- c. Rank the following molecular orbitals in order of decreasing energy (1 = highest energy; 4 = lowest energy)



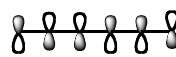
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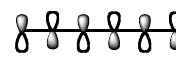
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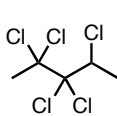


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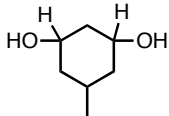


1

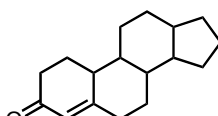
- d. Rank in order of increasing number of chirality centers (1 = fewest chirality centers; 5 = most chirality centers).



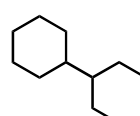
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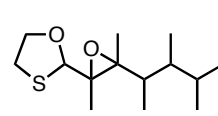
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4



1

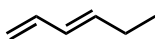


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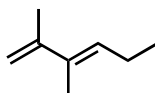
- e. Rank in order of increasing heat of hydrogenation (ΔH_{hydrog}) (1 = lowest ΔH_{hydrog} , least exothermic; 5 = highest ΔH_{hydrog} , most exothermic).



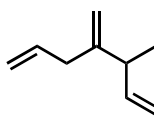
1



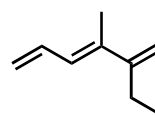
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3



6

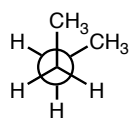


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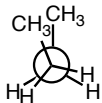


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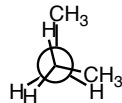
f. Rank in order increasing stability (1 = least stable, highest energy; 4 = most stable, lowest energy).



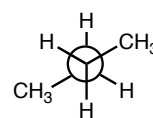
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1

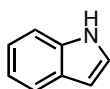


2



4

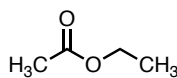
h. Rank in order of increasing index of hydrogen deficiency (IHD) (1 = lowest IHD; 5 = highest IHD).



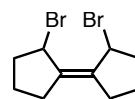
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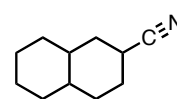
2



1

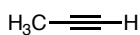


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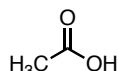


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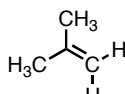
i. Considering only the most acidic proton in each molecule, rank in order of increasing acidity. (1 = least acidic, highest pKa; 5 = most acidic, lowest pKa).



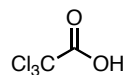
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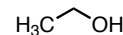
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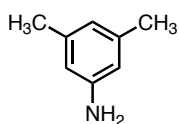


1

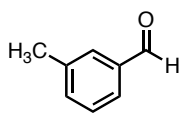


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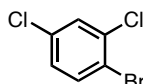
j. Rank in order of increasing rate of electrophilic aromatic substitution (S_EAr) (1 = slowest rate; 5 = fastest rate).



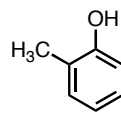
1



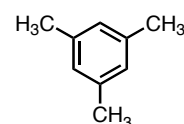
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4



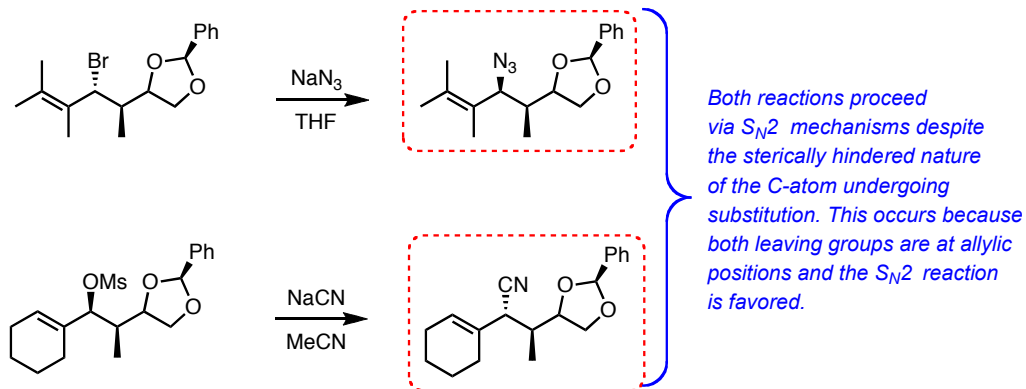
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3

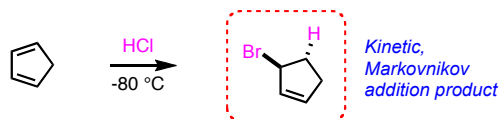
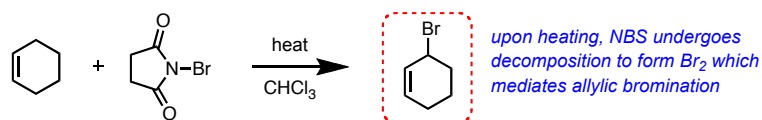
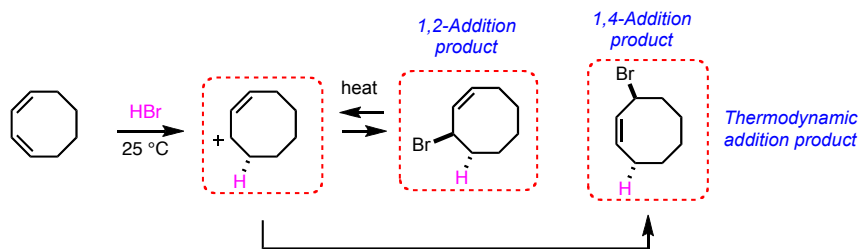
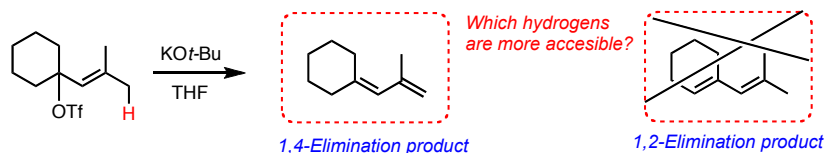
Question 2

Draw the major organic product in the boxes provided for each reaction scheme below. If the reaction is regioselective, only draw the major product. Be sure to indicate the correct relative stereochemistry (i.e. dashes & wedges or axial & equatorial bonds) where appropriate.



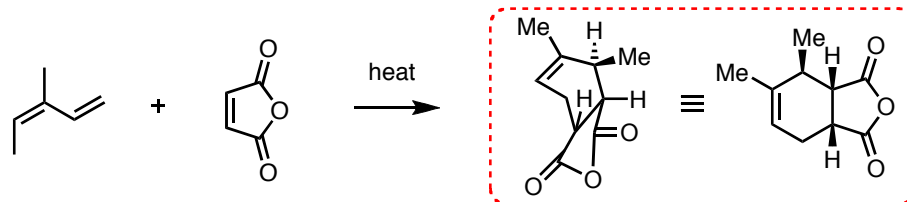
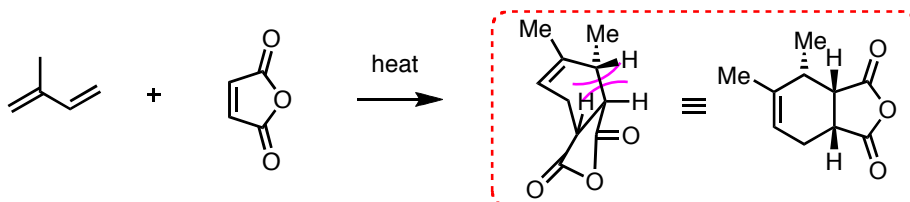
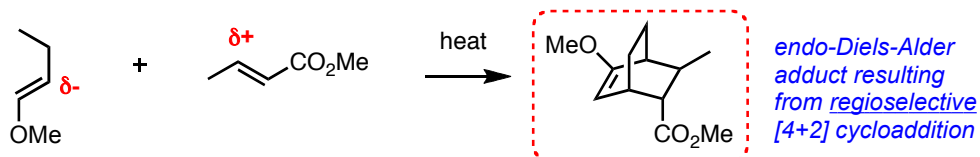
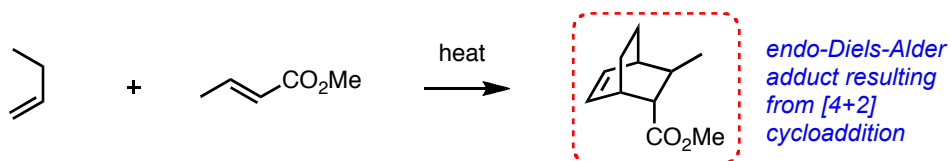
For each of the transformations shown above, by what mechanism is product formed? (S_N1 , S_N2 , E1, or E2)
If the solvent was changed from THF to DMF would the mechanism or rate of reaction change?

The use of DMF, a polar non-protic solvent would increase the nucleophilicity of cyanide and increase the rate of S_N2 reaction.

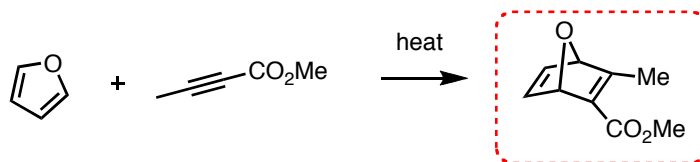


Question 3

Draw the major Diels-Alder adducts in the boxes provided for each reaction scheme below. If the reaction is regioselective, only draw the major product. Be sure to indicate the correct relative stereochemistry (i.e. dashes & wedges or axial & equatorial bonds) where appropriate.

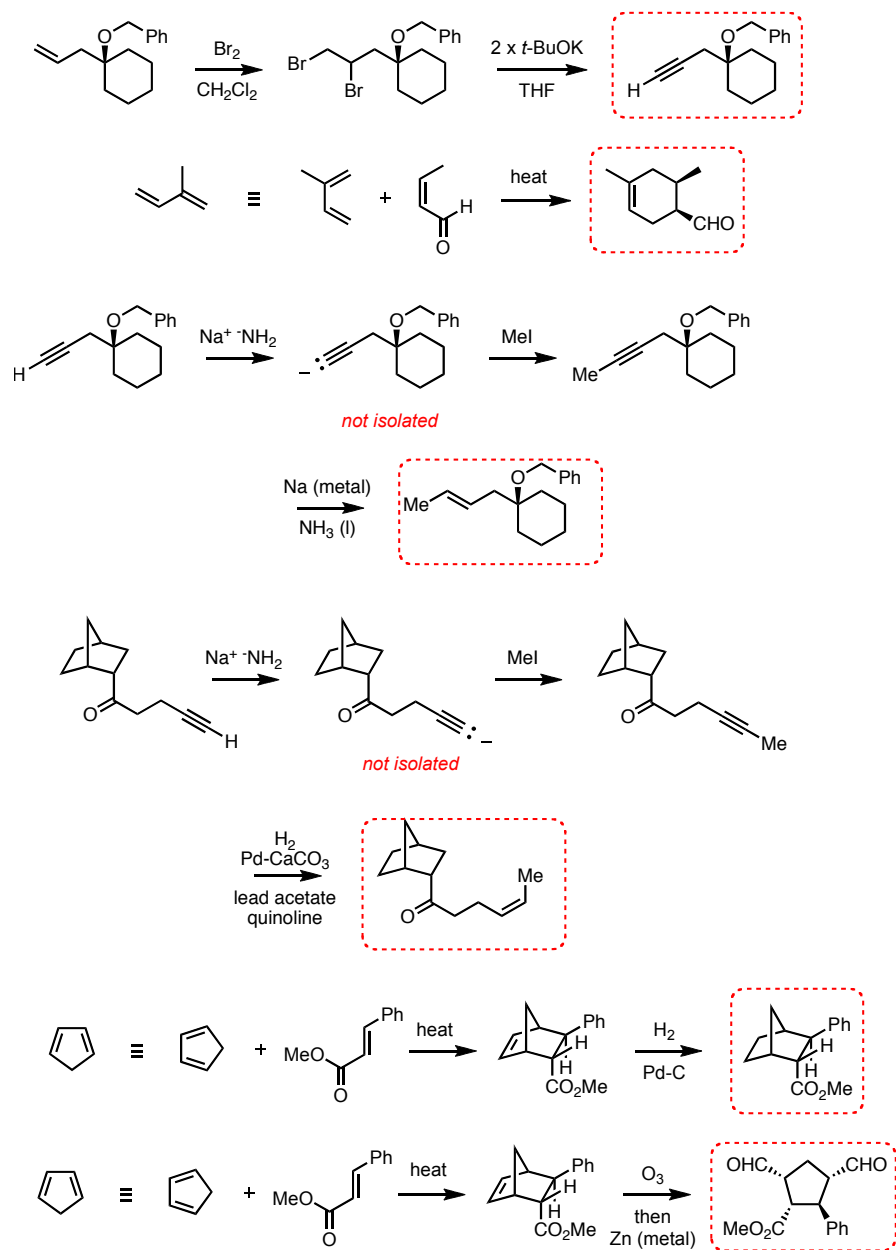


this substrate pair will react faster since there is less compression in TS



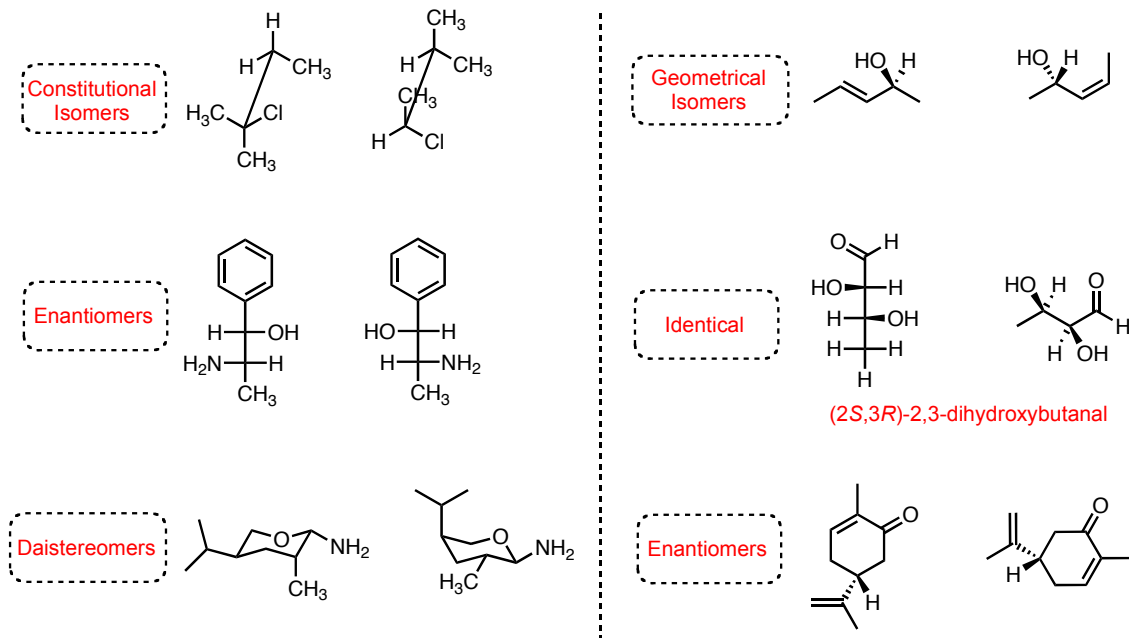
Question 4

Devise a synthesis for each of the target molecules (products) below. Write the forward synthesis from the reactant. Include all necessary conditions above/below the reaction arrow for each transformation. Write out the product for each transformation in your synthesis separately.

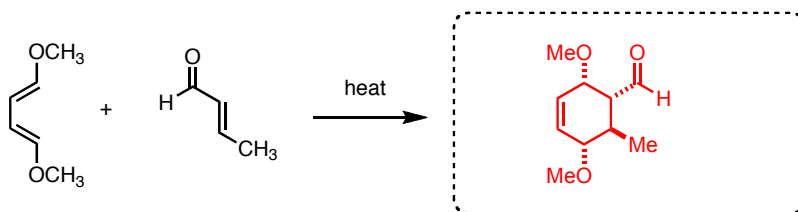


Question 5

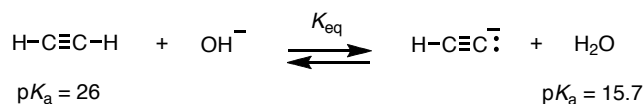
- a. Label each pair of molecules as one of the following: identical, conformational isomers, constitutional isomers, enantiomers, diastereomers, or geometrical isomers.



- b. Diels-Alder reactions are both regioselective and stereoselective. Use the **Out-Endo-Cis** rule to draw the endo regioisomeric product of the Diels-Alder reaction below. Hint: the electron withdrawing group on the dienophile is the endo group; the methyl groups on the diene are both out.

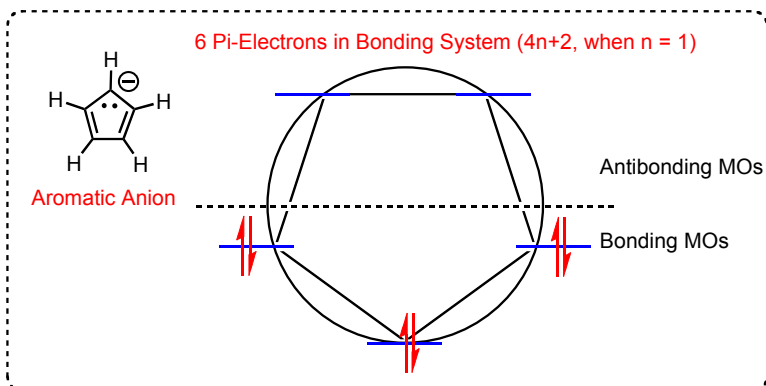


- c. Determine whether hydroxide is a strong enough base to fully deprotonate the alkyne shown by calculating the K_{eq} for the reaction. Show all work. Write the equation being used.

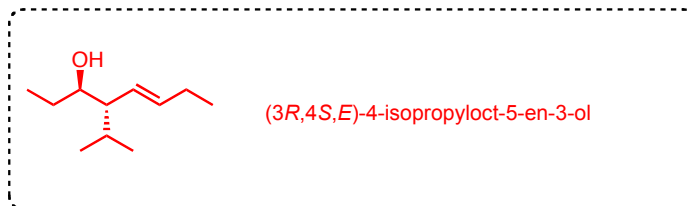


See Lecture 19, Slide 23

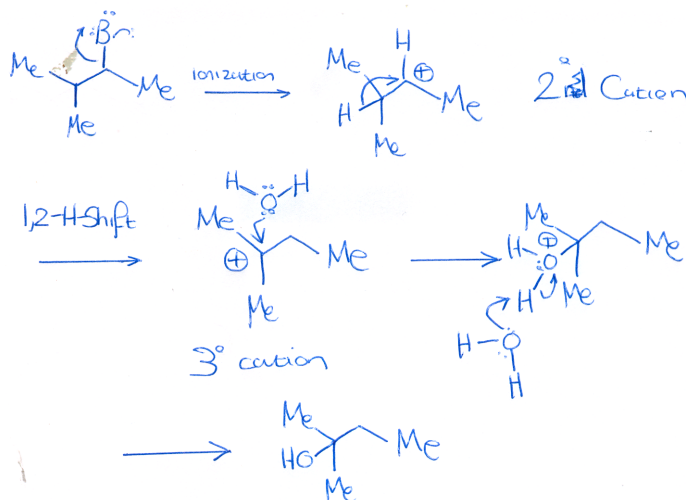
- d. Using the Frost Circle mnemonic, draw the molecular orbital diagram for a cyclopentadienyl carbanion (energy levels only). Indicate which MOs are bonding, non-bonding and anti-bonding. Use up and down arrows to represent the electrons present in each orbital. State whether a cyclopentadienyl carbanion is aromatic, anti-aromatic or neither. Use your diagram to explain.



- e. Write the IUPAC name for the molecule below.



- f. Draw a mechanism that accounts for the formation of 2-methyl-2-butanol from the hydrolysis (S_N1) of 2-bromo-3-methylbutane.

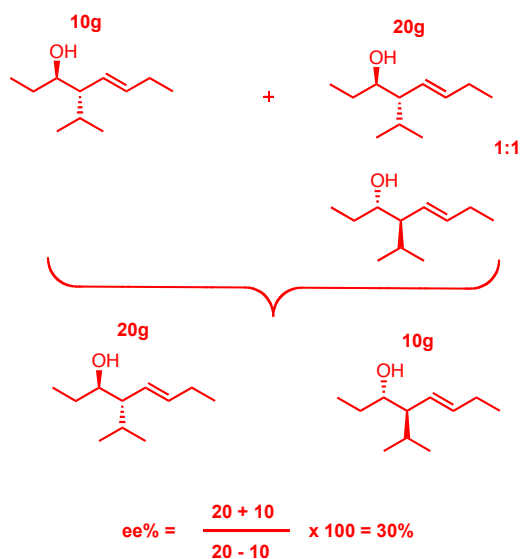


- h. An aqueous solution containing 10 g of optically pure (2*S*,3*R*)-2-chloro-5-hexyne-3-ol was diluted to 5 dL with CHCl₃ and placed in a polarimeter tube 5 cm long. The measured rotation was -5.50°. Using the equation below, determine the specific rotation ([α]_D). Hint: all values have been given with the correct units for use in the equation below.

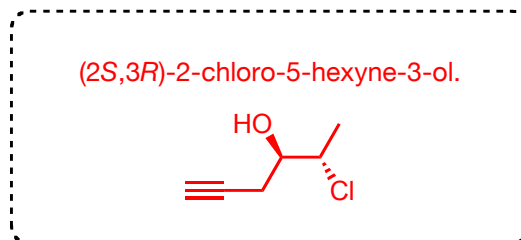
$$100 \times -5.50 / 2 \times 5 = -55.$$

$$[\alpha]_D^{25} = \frac{(100)(\alpha)}{(c)(l)}$$

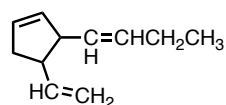
- h. The solution above was mixed with 5 dL of a solution containing 20 g of racemic 2-chloro-5-hexyne-3-ol. Calculate the enantiomeric excess (ee) (optical purity) of this solution.



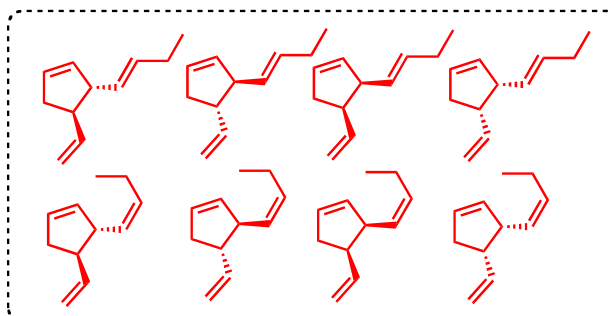
- i. Draw the stereochemical structural formula for (2*S*,3*R*)-2-chloro-5-hexyne-3-ol.



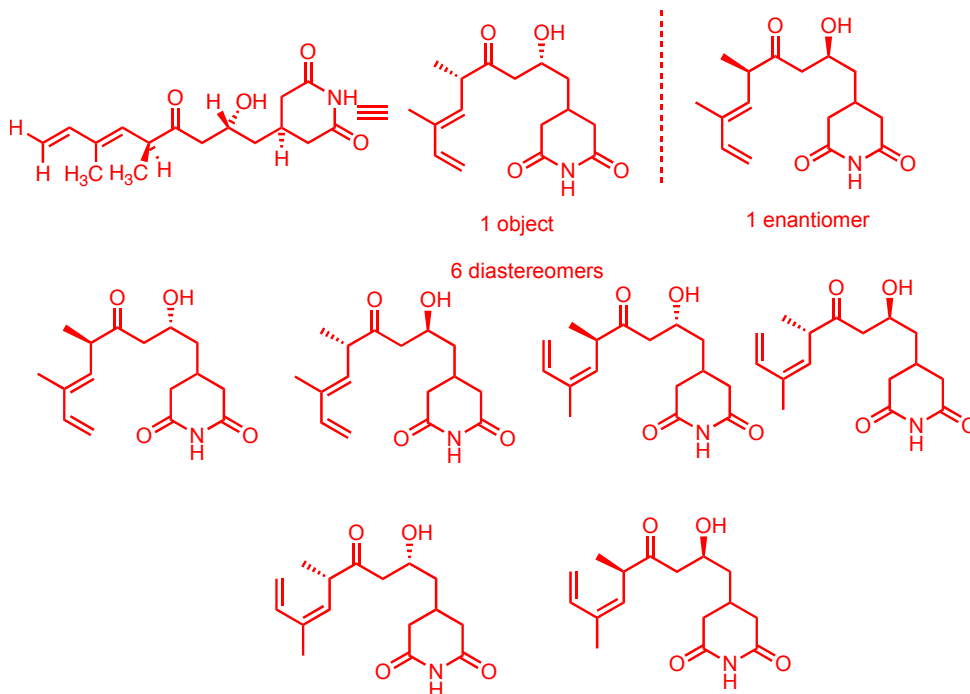
- I. How many total stereoisomers are possible for the structure below. Show your work for credit.



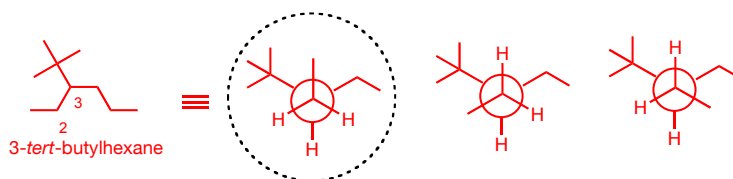
2 stereocenters
1 disubstituted alkene
total number of isomers = $2^3 = 8$



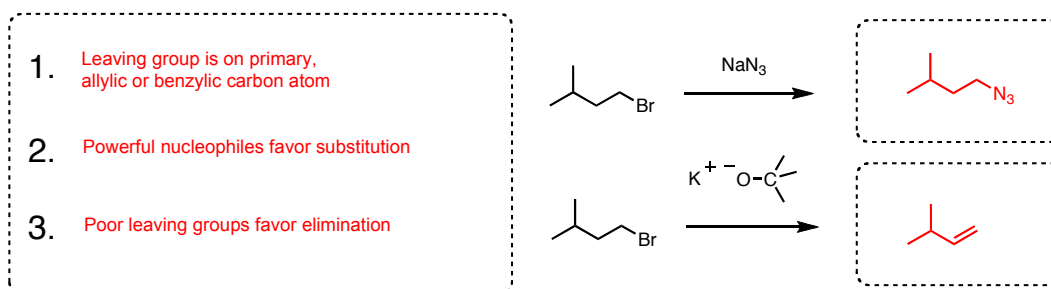
- m. Streptimidone is an antibiotic and has the structure shown below. How many diastereomers of streptimidone are possible? How many enantiomers? Using the *E-Z* and *R-S* descriptors, specify all essential elements of stereochemistry of streptimidone.



- n. Draw Newman projections that sight down the C2-C3 bond for the three gauche conformations of 3-*tert*-butylhexane. Circle the most stable of those three conformations. Draw a square around the least stable of those three conformations.

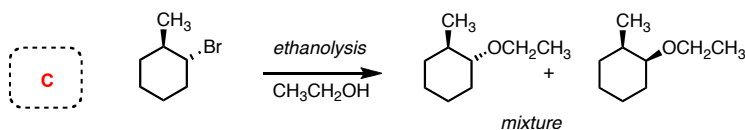
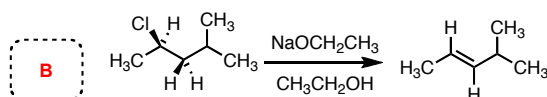
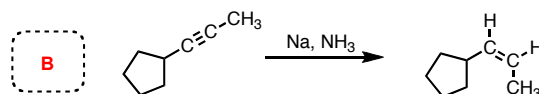
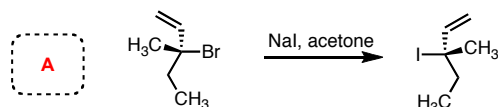


- o. Substitution of alkyl halides can compete with elimination as shown in the figure below. Clearly state three conditions (or circumstances) that favor substitution over elimination. Based on those conditions, draw the expected major product for the two reactions below.



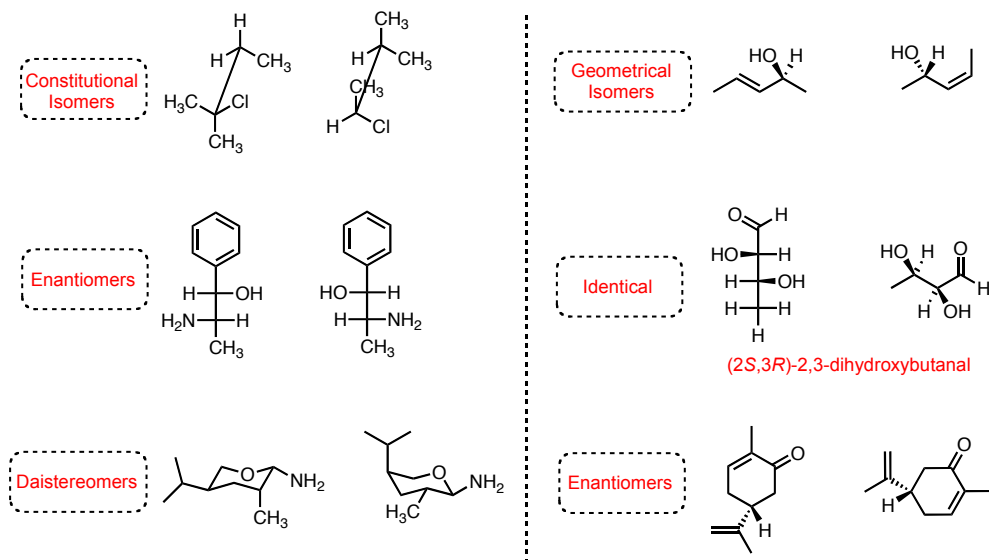
Question 6

Classify each of the reactions below as stereospecific (**A**), only stereoselective (**B**) or not stereoselective (**C**). Write the appropriate letter in the boxes next to each reaction. Only one letter should be written in each box. Only the actual products isolated in each reaction is shown. In other words, if a product isn't drawn, it isn't obtained by that reaction.

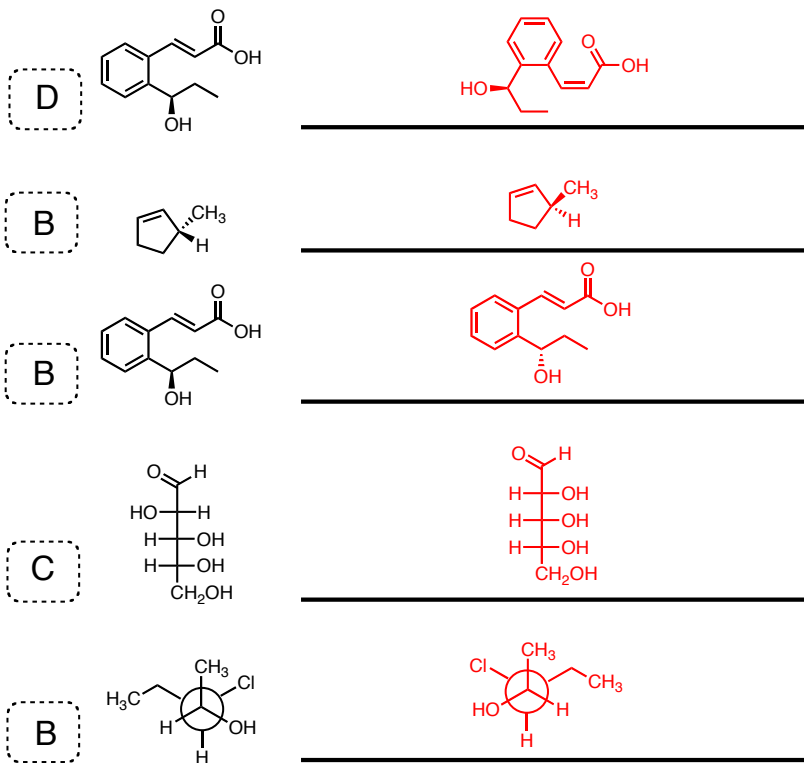


Question 6 (contd)

Determine the relationship between each of the following six pairs of molecules. Classify them as constitutional isomers (**A**), enantiomers (**B**), diastereomers (**C**), geometrical isomers (**D**), or not isomers (**E**). Write the letter corresponding to each classification in the boxes next to each pair. Only one letter should be written in each box.

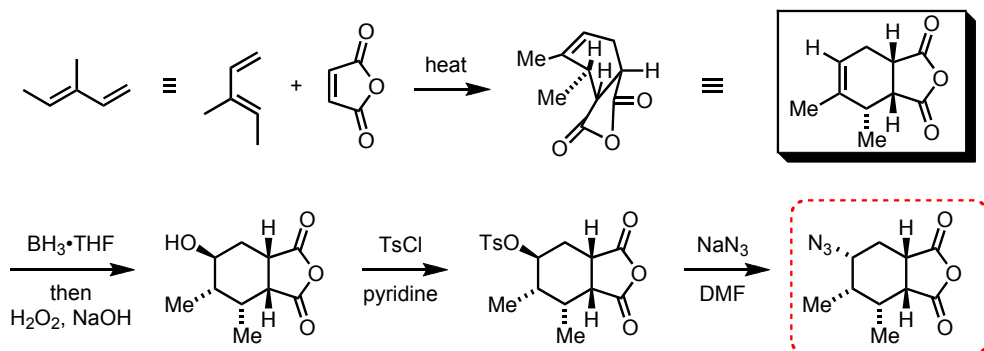
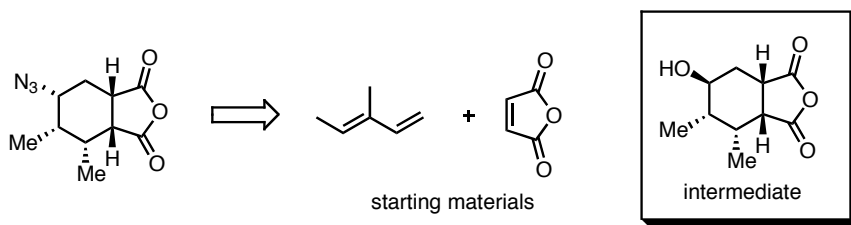
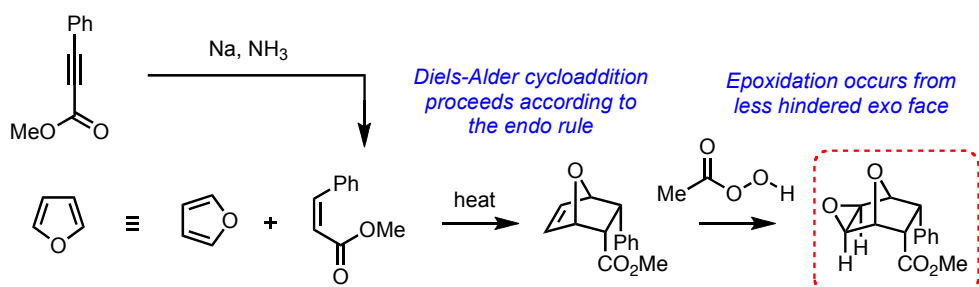
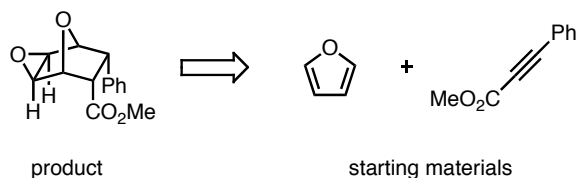


In the right column, draw the stereoisomer indicated by the letter in each box. It may be helpful to determine *R* or *S* for each chirality center to check your classification.



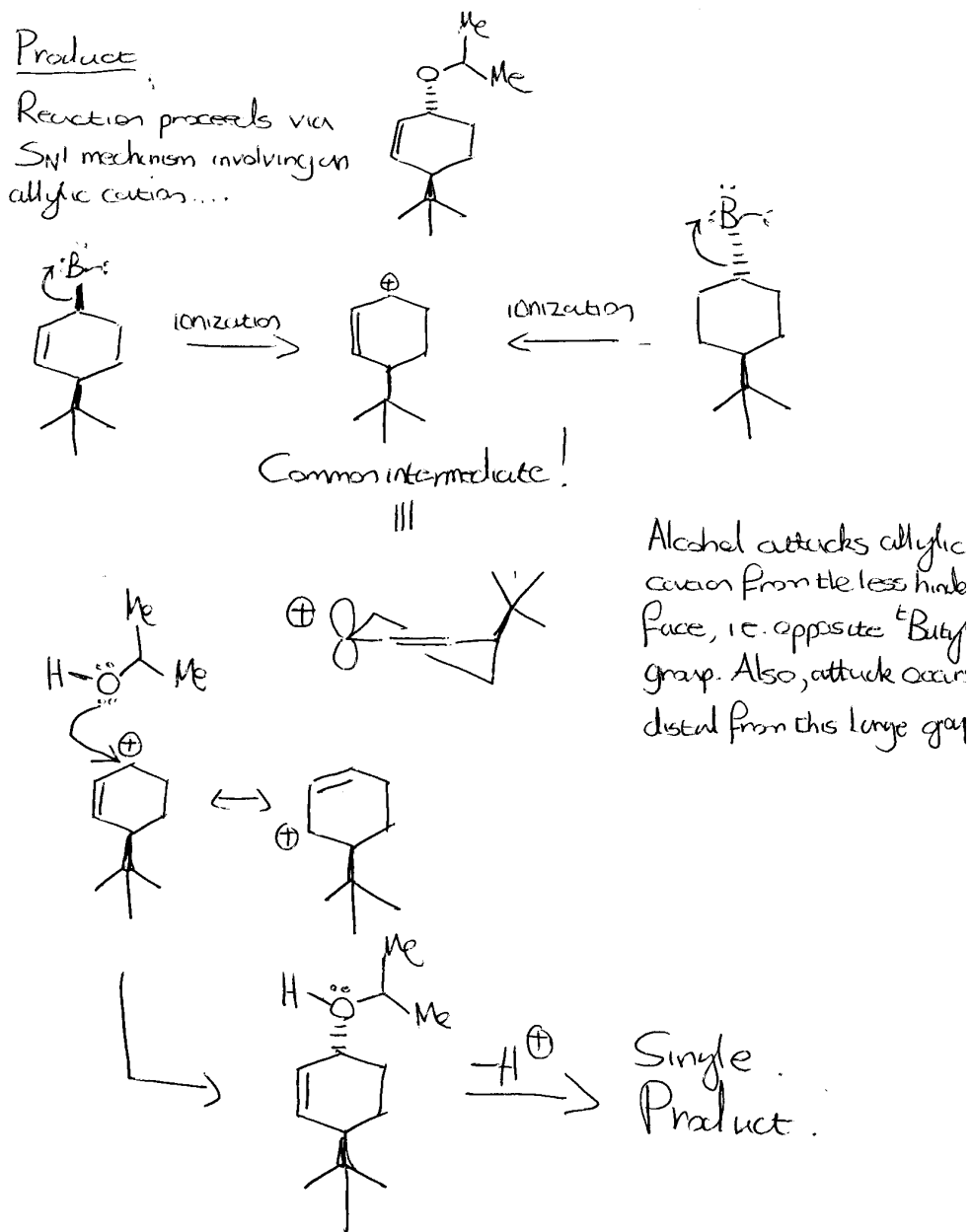
Question 7

Devise a synthesis for each of the target molecules (products) below. Write the forward synthesis from the reactant. Include all necessary conditions above/below the reaction arrow for each transformation. Write out the product for each transformation in your synthesis separately.

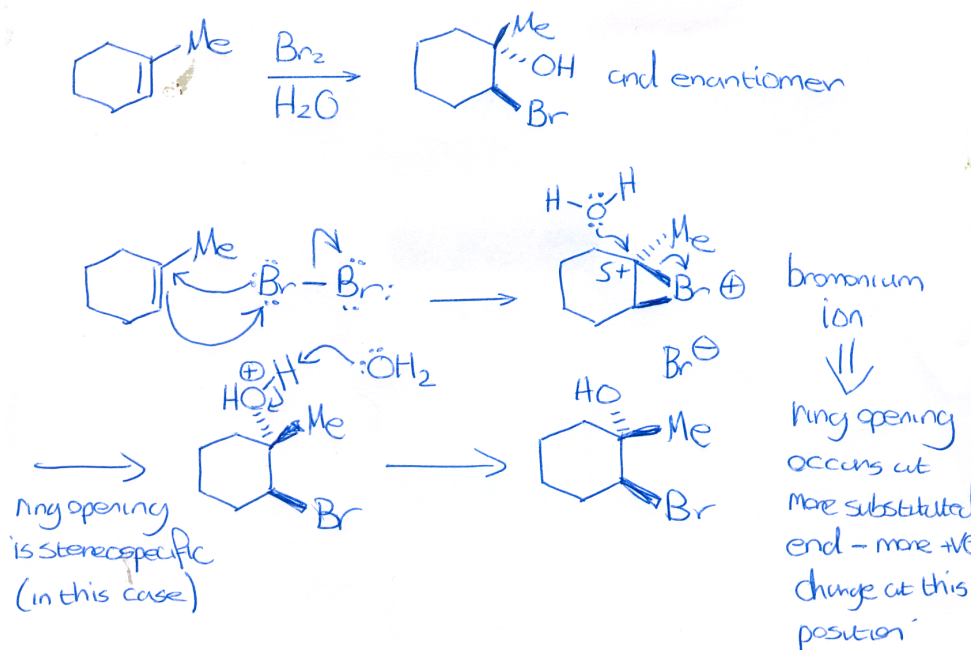


Question 8

A mixture containing both allylic bromides **1** and **2** undergoes solvolysis upon heating with isopropanol to provide a single product. The reaction is both regioselective and stereoselective. First, draw the product of solvolysis including the correct stereochemical notation. Then, draw a complete mechanism, beginning with **1**, that includes curved arrow notation to show electron flow, shows all electron pairs being used in your mechanism and indicates charges where appropriate. Your mechanism should account for the fact that this reaction is both stereoselective and regioselective.



Methylcyclohexene (**3**) reacts with Br_2 and H_2O to form a vicinal halohydrin. The reaction is both stereospecific and regioselective. First, draw the major product you would expect including correct regiochemistry and stereochemical notation (i.e. dashes and wedges). Then, draw a complete mechanism that includes curved arrow notation to show electron flow, shows all electron pairs being used in your mechanism and indicates charges where appropriate. Your mechanism should account for the fact that this reaction is both stereospecific and regioselective. Hint: show the correct stereochemistry of the bromonium ion intermediate.



The following bromination reaction was carried out by as part of a study to prepare analogs of the cytotoxic microtubulin inhibitor, lavendustin A. In this case, substrate **4** undergoes benzylic bromination when heated with *N*-bromosuccinamide. In this case, NBS reacts to form bromine radicals ($\text{Br}\cdot$) and diatomic bromine (Br_2) before bromination takes place. Draw a mechanism for the conversion of **4** to **5**, which includes the formation of bromine and bromine radicals.

See Problem Set 7, Question 2 Key For Answer

tert-Butyl benzene (**6**) undergoes Friedel-Crafts acylation in the presence of AlCl_3 . Not surprisingly, this reaction is highly regioselective and provides the para isomer as the major product. First, draw the major product for this reaction. Second, draw the mechanism for the formation of the acylium ion when propanoyl chloride (**7**) reacts with AlCl_3 ; show both resonance structures for the acylium ion. Finally, draw the mechanism for the reaction of toluene with the acylium ion to give the final product.

