Chemistry 3A – Spring 2011
Second Midterm – April 1, 2011

Professor Carolyn Bertozzi **Page 1 of 20**

Your full signature__Key____

Print your full name____

(Last Name, First Name, Middle)

Your SID____

GSI's name or section number______________________________________

This exam has **20** pages; **make sure that you have them all**. We will only grade answers that are in the designated spaces; please do your scratch work on the last page or the backs of pages. Write only **one** answer to each problem; multiple answers will receive **no** credit, even if one of them is correct.

Note: This examination runs for a total of 120 minutes. Please write legibly; ambiguous or illegible answers will receive **no credit**.

Do Not Write in this Box:

1.________(16)

2.________(8)

3.________(18)

4.________(9)

5.________(12)

6.________(12)

7.________(8)

8.________(12)

9.________(5)

Total______(100)

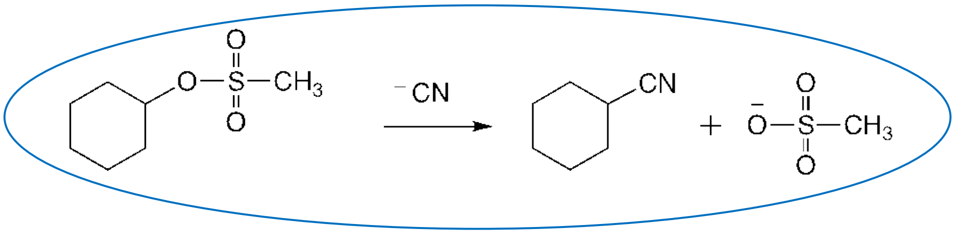
Partial Periodic Table

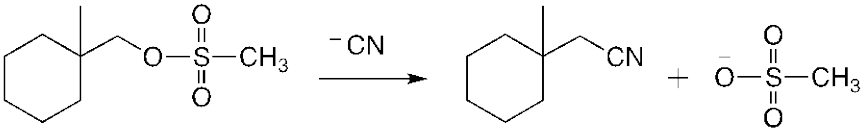
I	II	III	IV	V	VI	VII	VIII
H							He
Li	Be	B	C	N	O	F	Ne
Na	Mg	Al	Si	P	S	Cl	Ar
K	Ca	Ga	Ge	As	Se	Br	Kr
Rb	Sr	In	Sn	Sb	Te	I	Xe

1. [16 points]

For each pair of reactions, <u>circle the one that will proceed fastest and provide a brief explanation for your choice in the space below the pair</u>. <u>Your explanation must include the reaction type</u> (i.e., S_N2, S_N1, E1 or E2).

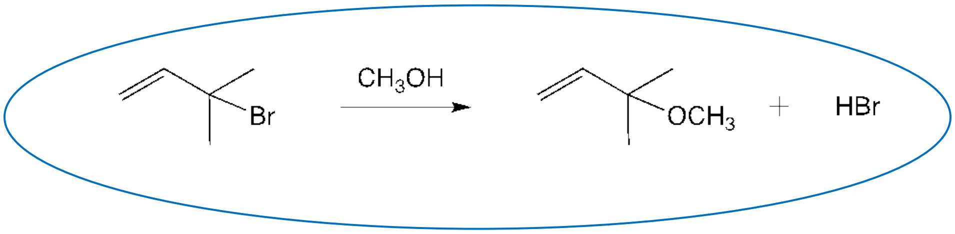
a.





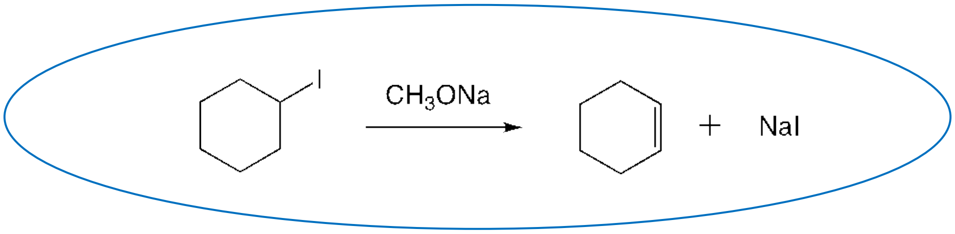
Explanation:
Neopentyl electrophiles are more sterically encumbered than secondary electrophiles and are slower in S_N2 reactions.

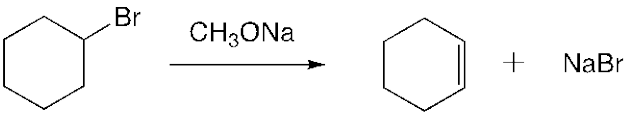
b.



Explanation:
The carbocation character in the transition state of the S_N1 reaction is stabilized by resonance, lowering the activation energy, and resulting in a faster reaction rate.

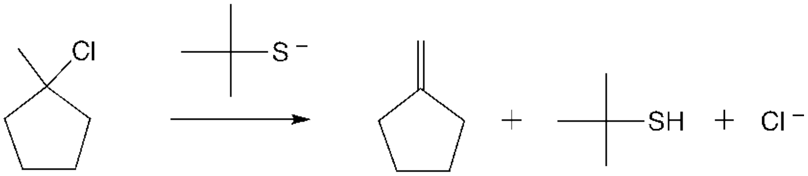
c.

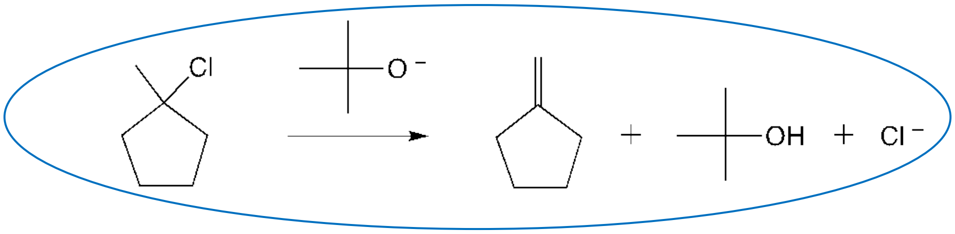




Explanation:
Iodide ion is a better leaving group than a bromide ion and consequently the electrophile with the better leaving group will react faster in the E2 reaction.

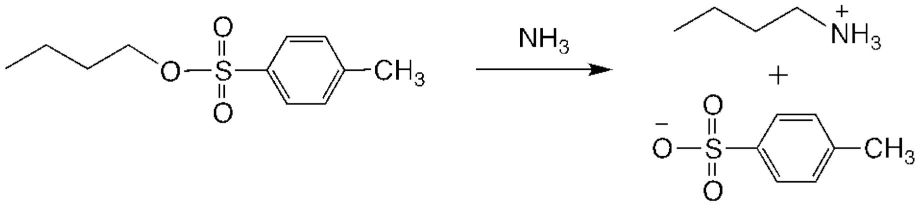
d.

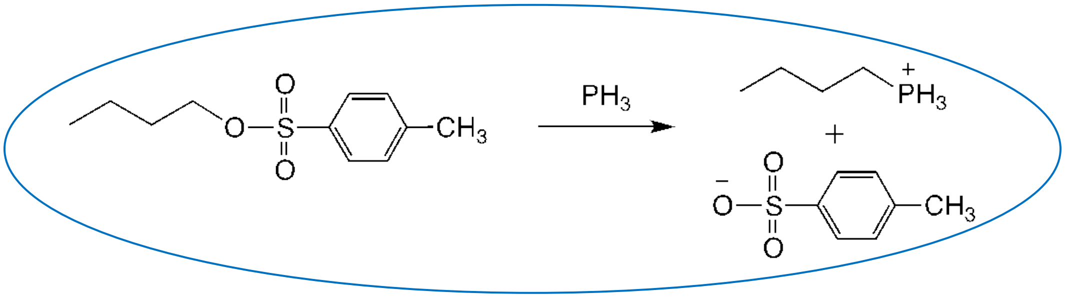




Explanation:
The strength of the base affects the rate of E2 reaction, and basicity decreases going down a column of the periodic table.

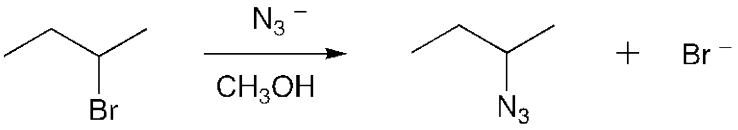
e.

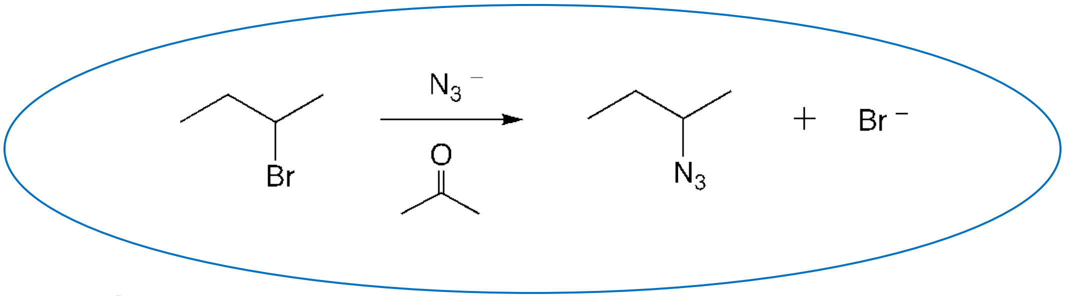




Explanation:
Nucleophilicity increases going down a column of the periodic table due to the increasing polarizability of the atoms. Therefore, the bottom S_N2 reaction is faster.

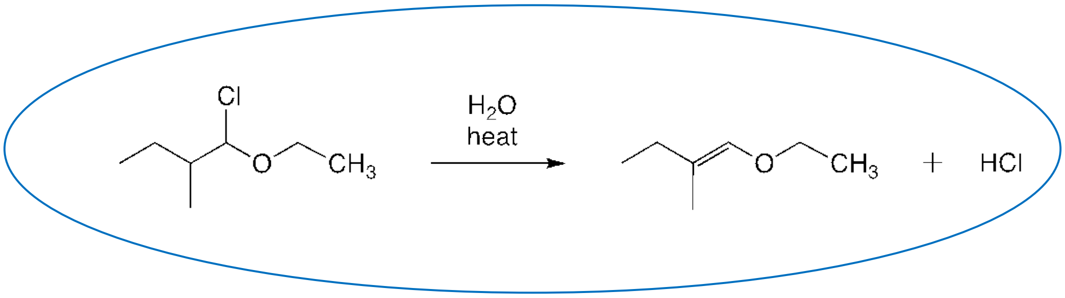
f.

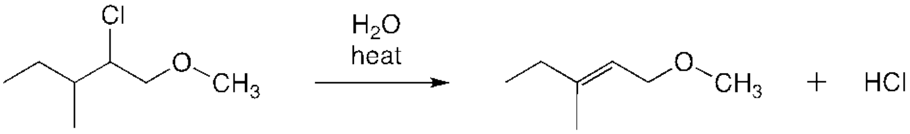




Explanation:
Azide anion is better solvated in methanol than in acetone, and is therefore more reactive in acetone. The leads to the bottom S_N2 reaction being faster.

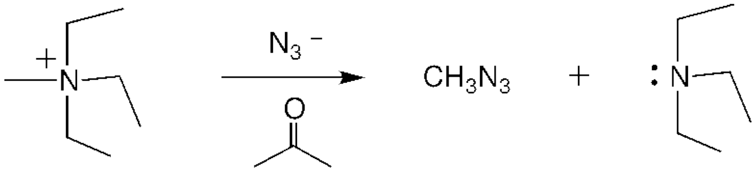
g.

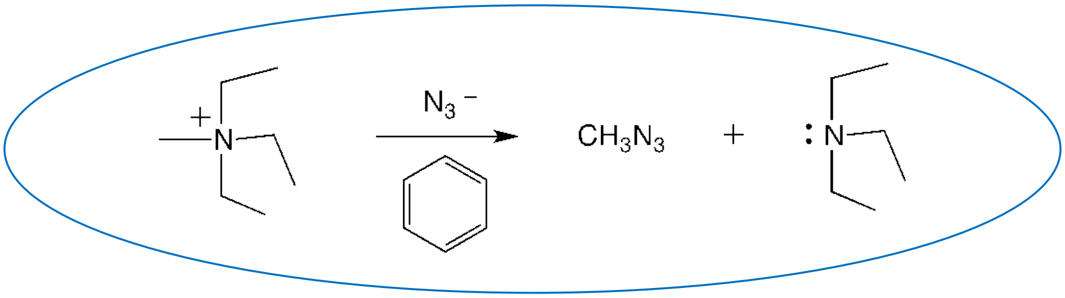




Explanation:
The carbocation character in the transition of this E1 reaction will be stabilized by resonance from the adjacent oxygen’s lone pairs.

h.



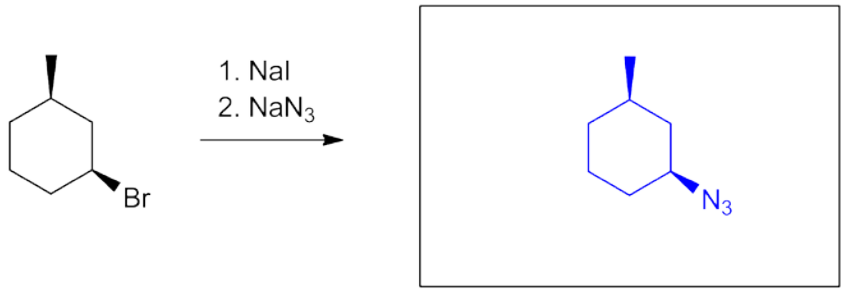


Explanation:
Both reactants are charged but the transition state is not. The more polar solvent will be able to better stabilize the reactants than the less polar solvent, which leads to a higher activation energy and slower reaction rate in acetone.

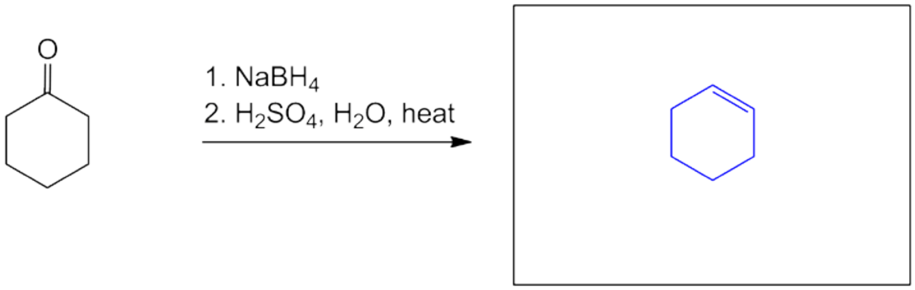
2. [8 points]

In each box, fill in the major organic product or reactant that completes the synthesis scheme. Assume workup steps are included in reactions that normally require them; they are not shown explicitly. Be sure to clearly indicate the stereochemistry of the product where relevant.

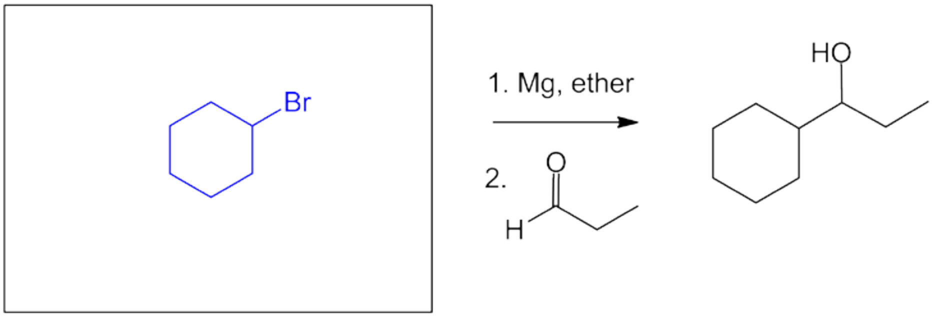
a.



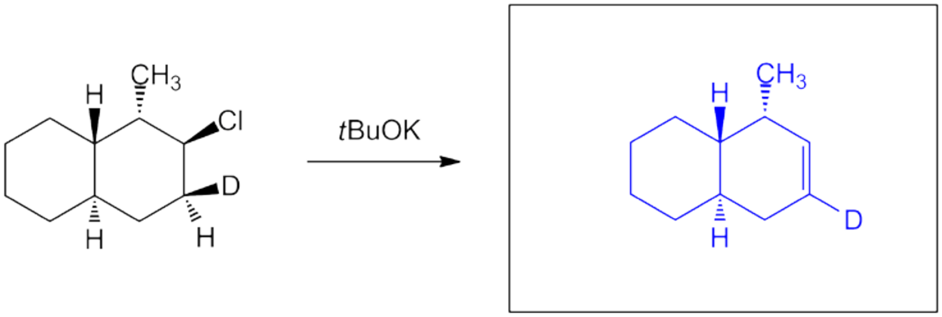
b.



c.



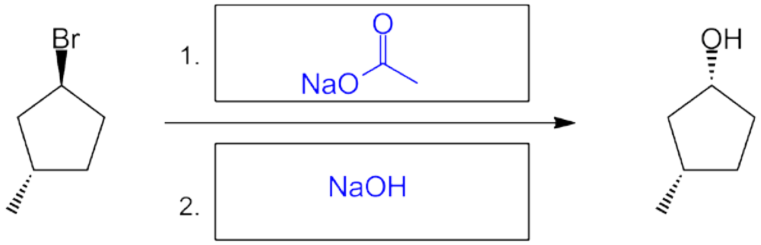
d.



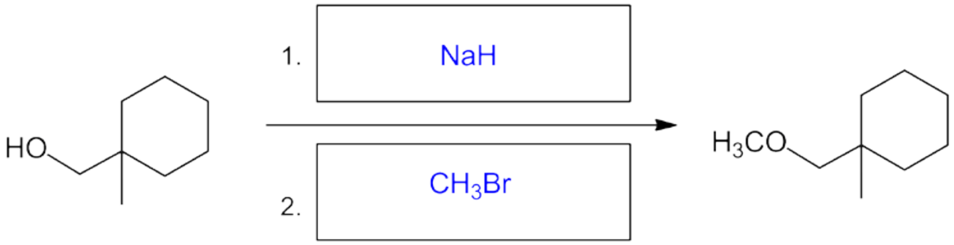
3. [18 points]

For each synthetic scheme below, <u>add reagents to the boxes above and below each arrow</u> that are required to convert the starting material to the given product. <u>Each box should include reagents for just one synthetic step</u>. <u>Workup steps are implied and should **not** be shown in boxes</u>.

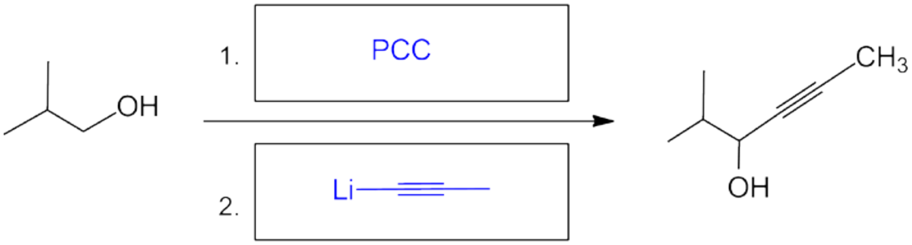
a.



b.



c.

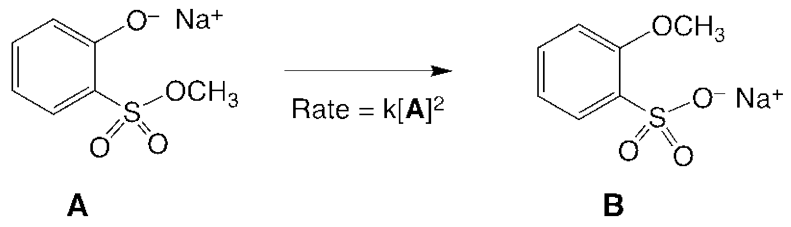


d.

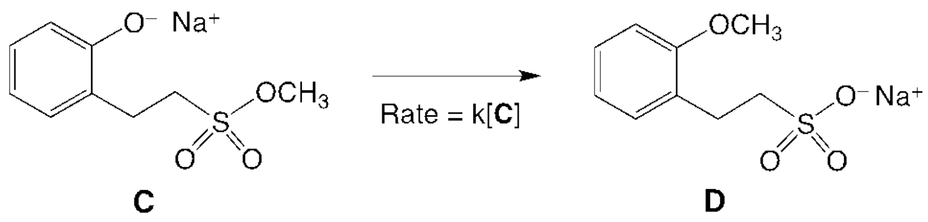
4. [9 points]

The two related reactions below display different experimental rate laws, as indicated below the arrows.

Reaction 1

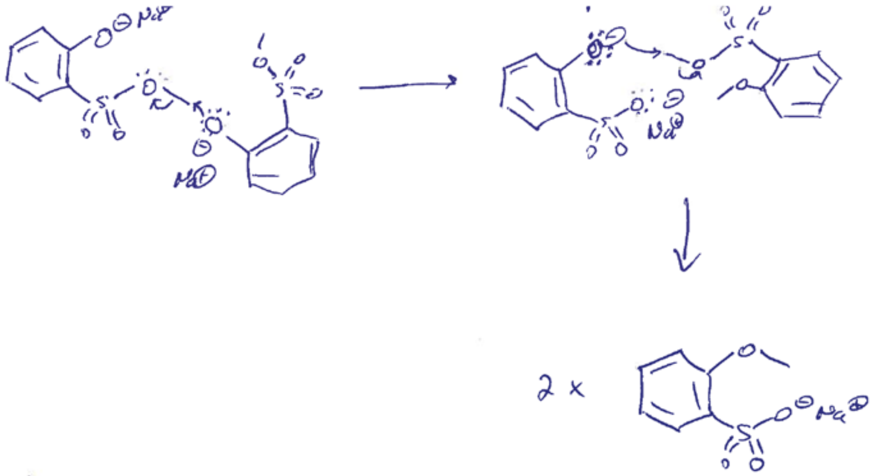


Reaction 2



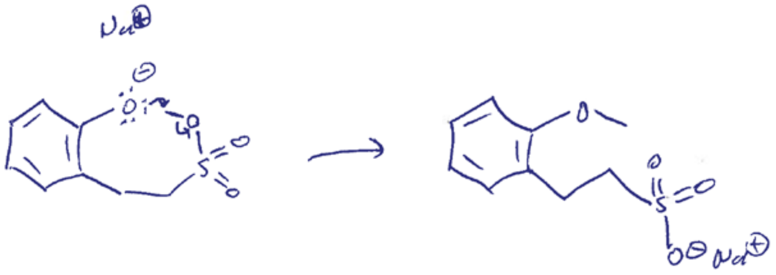
a. Using the curved-arrow notation, show a step-wise mechanism for each reaction that is consistent with its observed rate law. Be sure to show all steps leading from reactants to products.

Mechanism of Reaction 1:



The second order rate law above indicates that two starting material molecules are involved in the transition state for the rate-determining step.

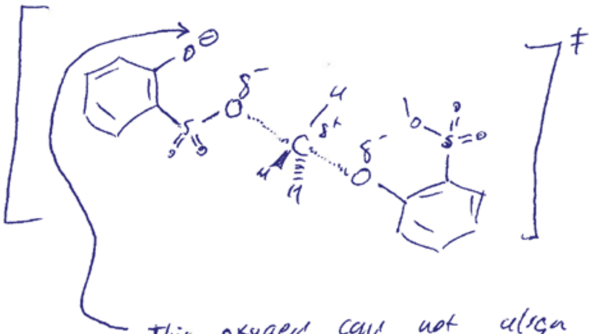
Mechanism of Reaction 2:



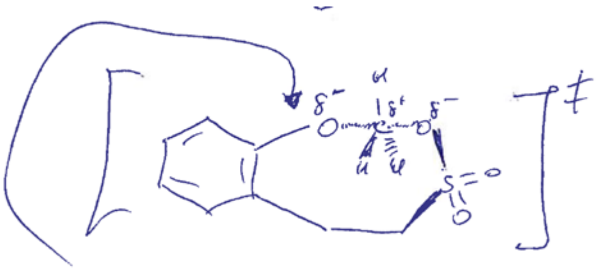
In the rate law expression for this transformation, it is first order with respect to the starting material, demonstrating that the transition state only involves one starting material molecule.

b. Provide a rationale for any differences in the two mechanisms you proposed above (Hint: Draw the transition states for the rate-determining step in each reaction).

1:



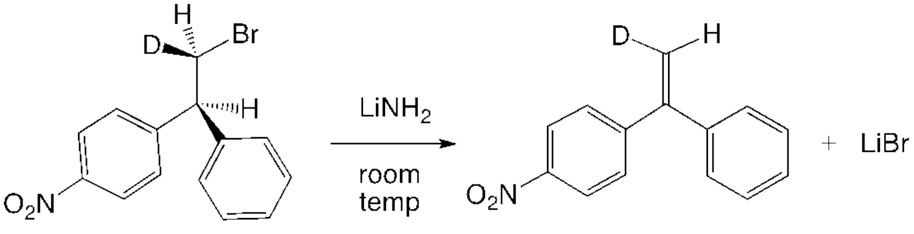
This oxygen can not align coplanar w/ the methyl on the same molecule ∴ a bimolecular SN2 rxn takes place



Oxygen on same molecule can align itself for backside attack on the methyl group, permitting the intramolecular SN2 rxn.

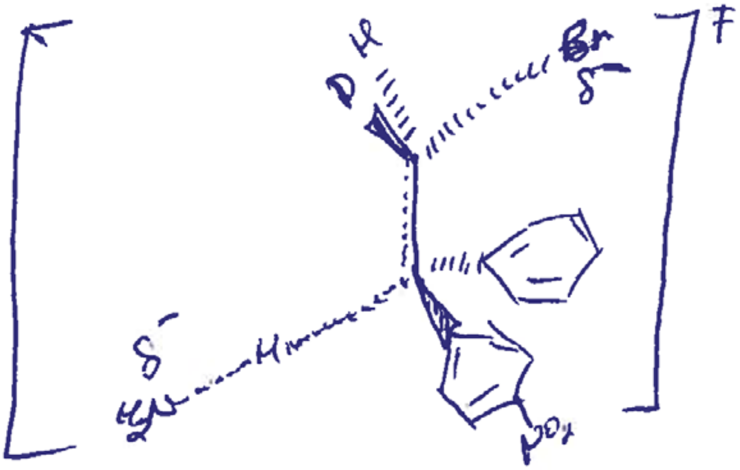
5. [12 points]

a. Reactant **A** below undergoes an E2 reaction in the presence of $LiNH_2$ to give a single alkene product **B**.



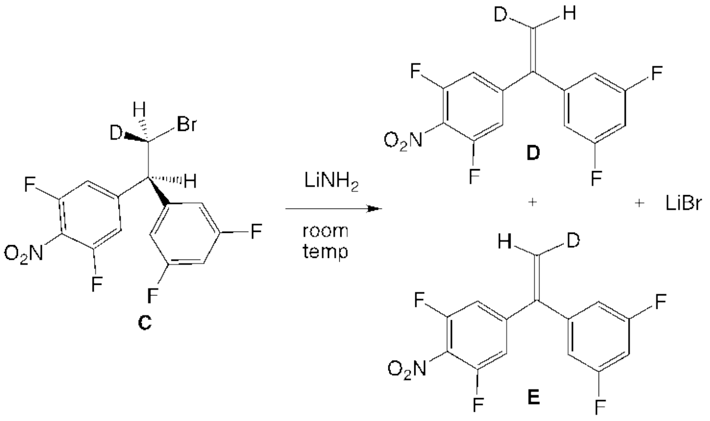
A **B**

Draw a three-dimensional structure of the transition state for the reaction that clearly indicates the relative orientations of substituents around the α– and β–carbon atoms. Explain how the stereochemistry of reactant **A** determines the stereochemistry of product **B**?

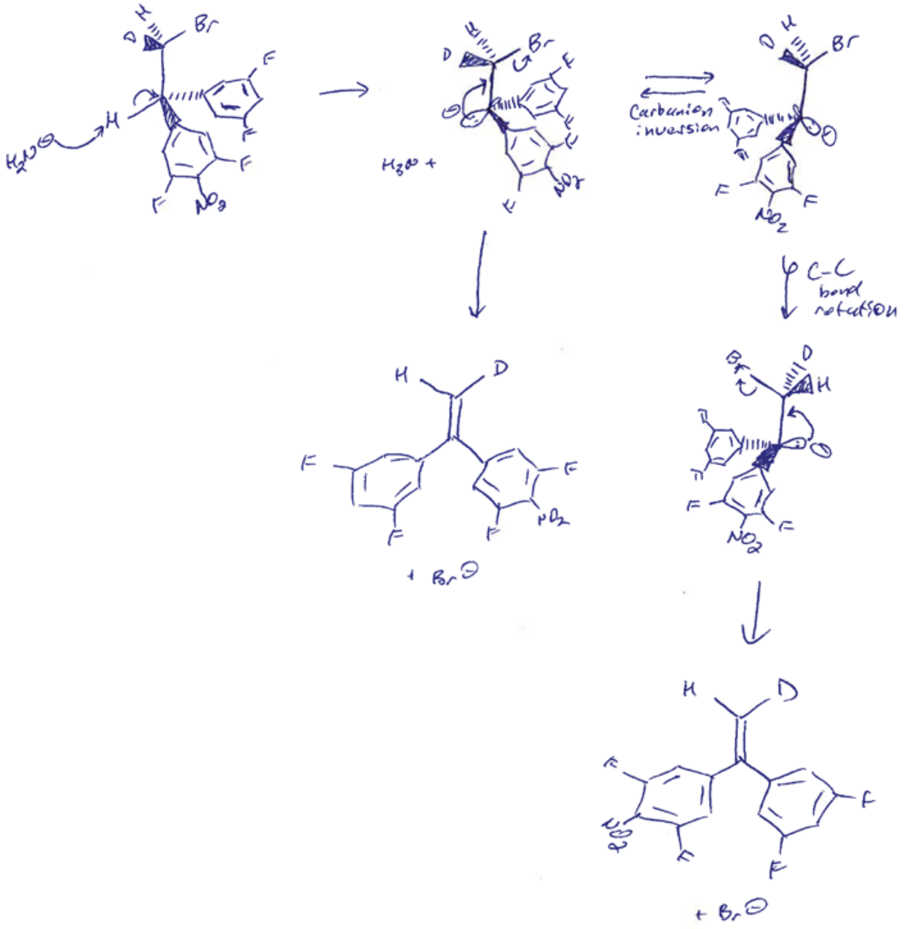


The transition state has the hydrogen that is being abstracted antiperiplanar to the leaving group, in this case a bromide ion. In this conformation, the deuterium is on the same side of the molecule as the nitrophenyl group, which explains the stereochemical outcome of the product.

b. Compound **C** also undergoes a kind of elimination reaction in the presence of $LiNH_2$, but in this case two alkene diastereomers, **D** and **E**, are formed in roughly equal amounts.



Using the curved arrow notation, <u>provide a step-wise mechanism for this reaction that explains how **C** reacts to form both products **D** and **E**</u>.



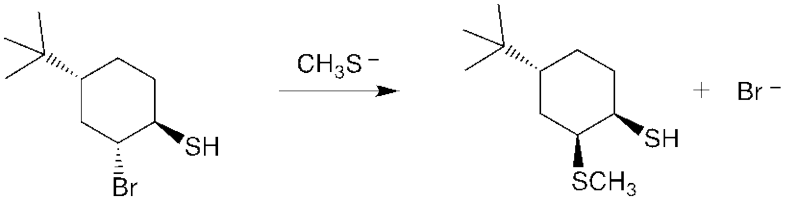
c. Why does reaction (**b**) proceed via a mechanism that is different from the conventional E2 mechanism observed in (**a**)?

In the second example, the aromatic rings are functionalized with electronegative fluorine atoms. These added inductive groups stabilize the formation of a negative charge on the carbon (carbanion) in addition to the resonance delocalization provided by the aromatic rings. This carbanion can undergo pyramidal inversion before forming the alkene product, resulting in the mixture of stereoisomers.

6. [12 points]

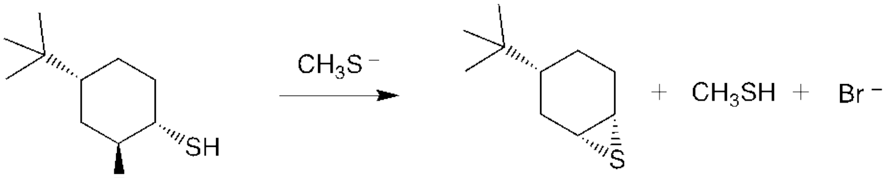
In reactions **1** and **2** below, diastereomers **A** and **C** react with CH_3S^- to give different products, **B** and **D**, respectively.

Reaction 1



A **B**

Reaction 2

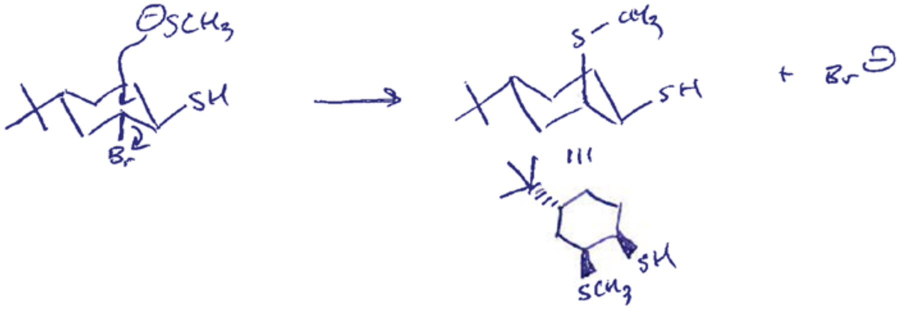


C **D**

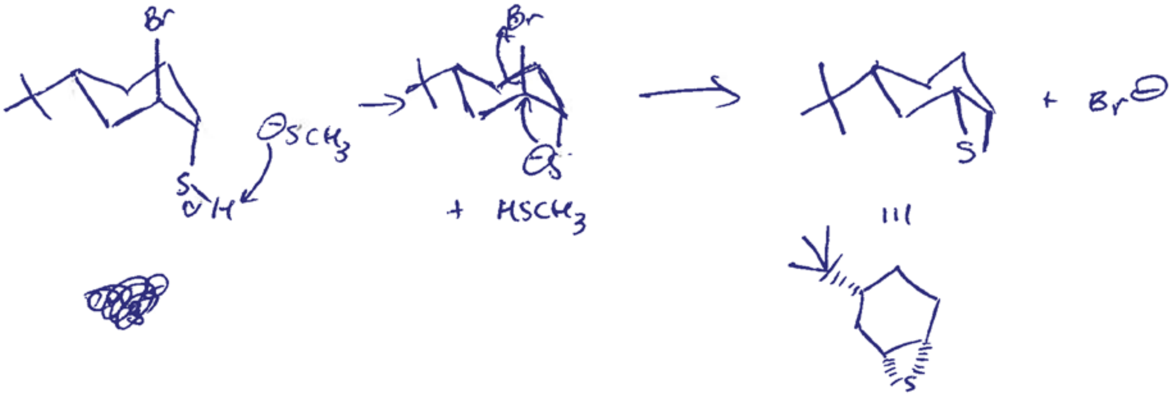
a. In the spaces provided, show step-wise mechanisms for these two transformations using the curved-arrow notation.

Mechanism of Reaction 1:

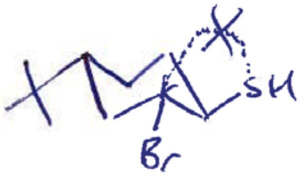
6) a) 1:



Mechanism of Reaction 2:



b. Using three-dimensional structural representations, explain why **A** and **C** give different products under these conditions.

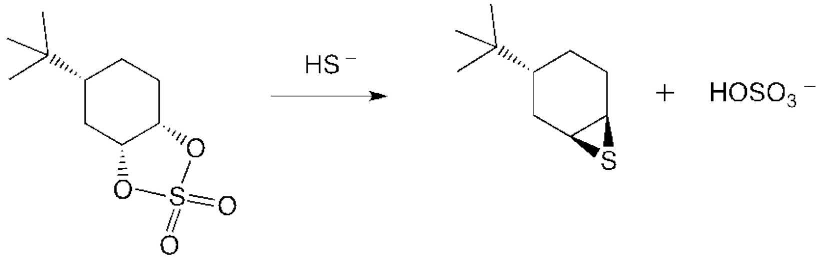


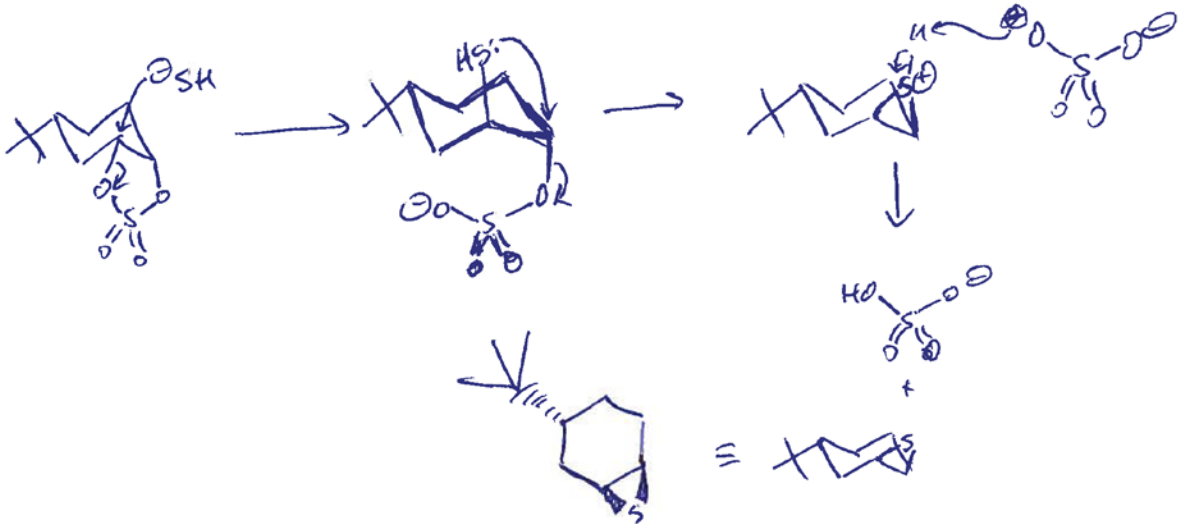
backside attack not possible in equatorial positions

vs.

backside attack is possible from axial positions.

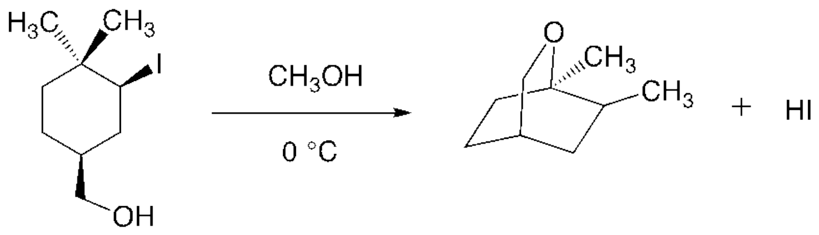
c. Based on your above analysis, show the best step-wise mechanism for the following reaction using the curved-arrow notation.

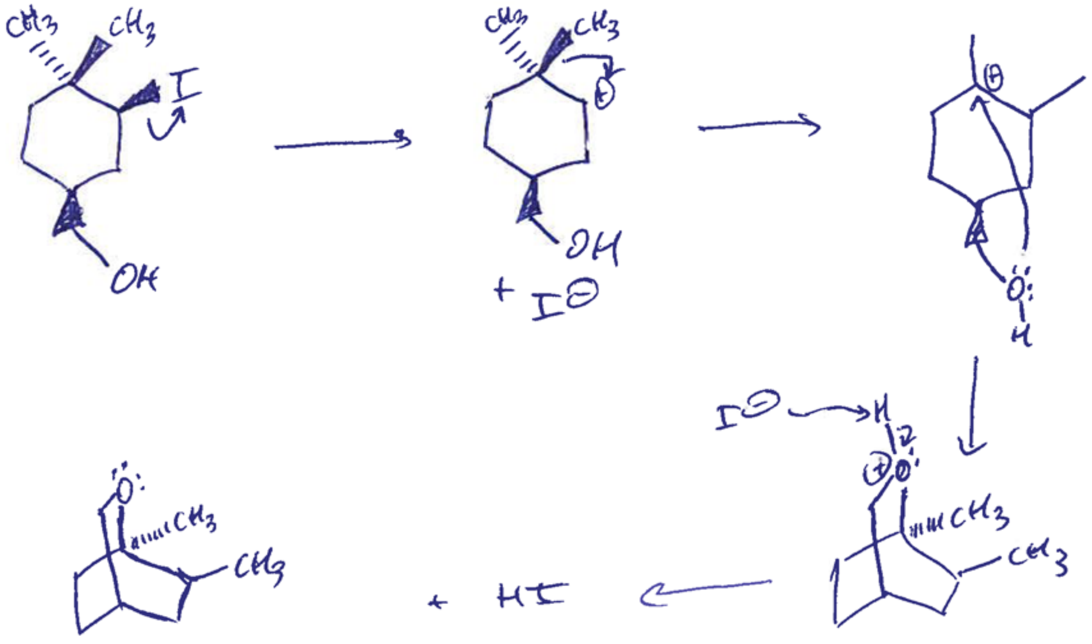




7. [8 points]

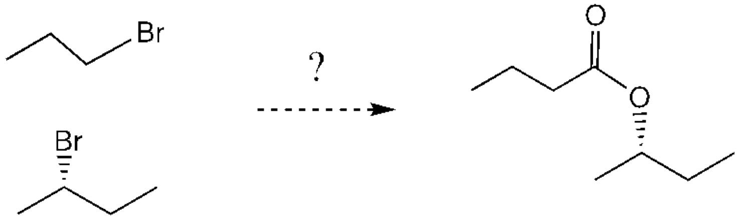
Provide a step-wise mechanism for the reaction below using the curved arrow notation:

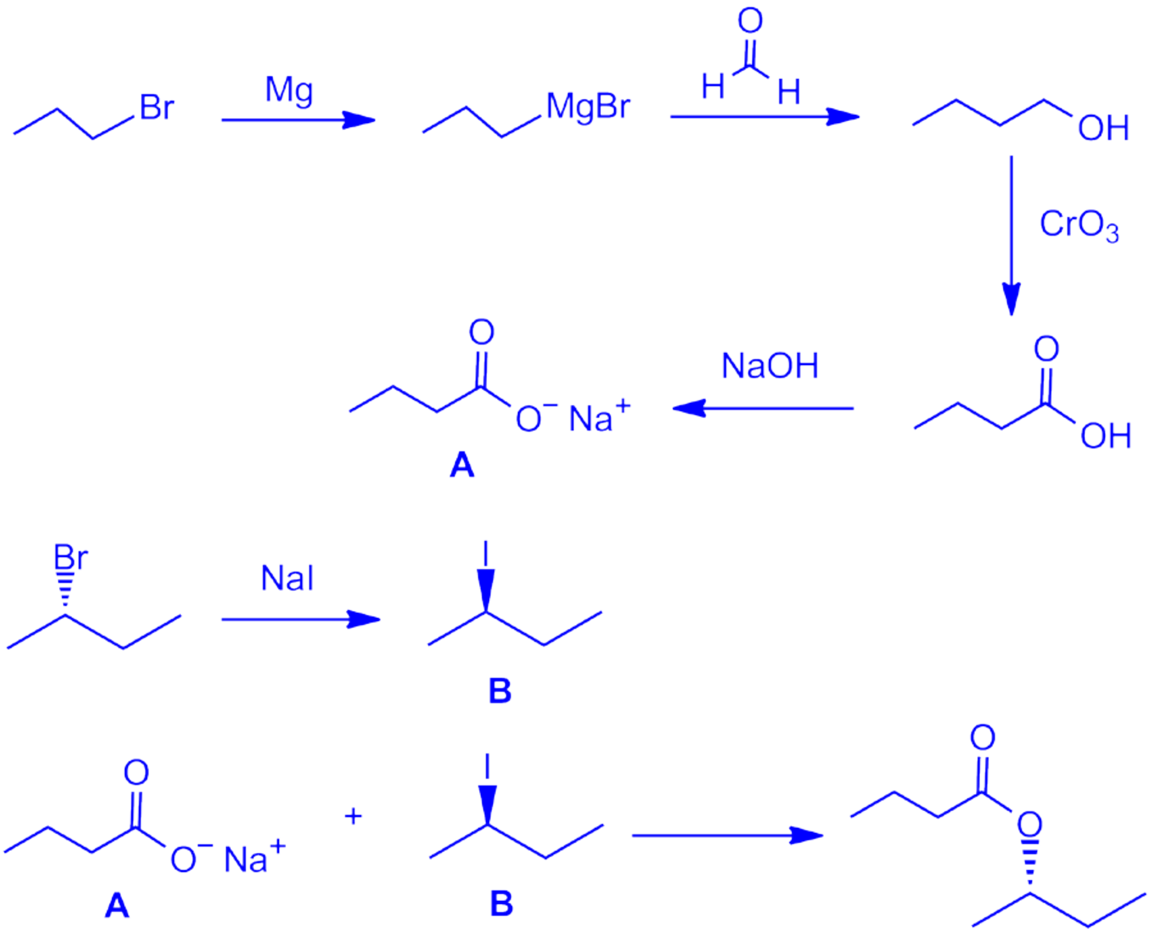




8. [12 points]

Propose a synthesis of the compound on the right starting with the reagents on the left as well as any other necessary reagents. Be sure to show each individual step of your synthesis, the required reagents (above the arrow), and the intermediate product obtained from each step. Workup steps are implied and need not be shown explicitly.





9. [5 points]

For each of the following multiple choice questions, mark the single best answer with an **X**.

a. The Swern oxidation is often preferred to the use of PCC because:

A. ____ PCC tends to over-oxidize 1° alcohols to carboxylic acids.

B. X___ Cr^{VI} is toxic to humans and the environment.

C. ____ DMSO is a good solvent for S_N2 reactions.

D. ____ PCC reacts with water to form a flammable gas.

b. Which reagent is Nature's equivalent of $NaBH_4$?

A. X___ NADH

B. ____ $LiAlH_4$

C. ____ SAM

D. ____ NaH

c. The E1 reaction can be favored over a competing S_N1 reaction by using:

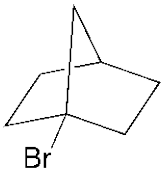
A. ____ an excellent leaving group

B. ____ a polar protic solvent

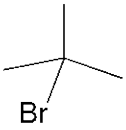
C. ____ a strong nucleophile

D. X___ high temperatures

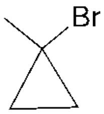
e. Which substrate undergoes the fastest solvolysis reaction in H_2O?



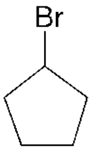
A



B



C



D

A. _____

B. X___

C. _____

D. _____

f. Which of the following reactions is stereospecific?

A. _____ S_N1

B. _____ Formation of an alkyllithium reagent at room temperature

C. _____ Free radical halogenation

D. X___ None of the above

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