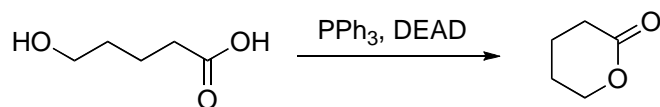


Chemistry 35

Exam 2 Answers - April 9, 2007

Problem 1. (14 points) Provide the products for the reactions shown below. If stereochemistry is important, be sure to indicate stereochemistry clearly. If no reaction would occur, write NO REACTION.

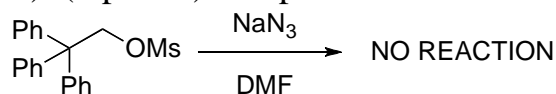
A) (2 points) No partial credit



Intramolecular Mitsunobu reaction.

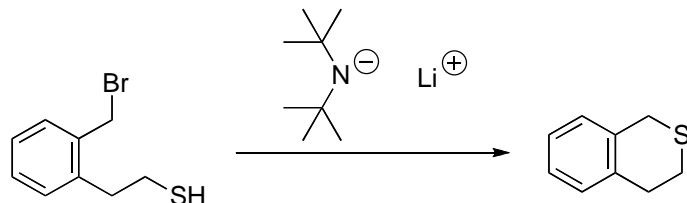
B) (2 points) No partial credit

MUST PROVIDE EXPLANATION!!!



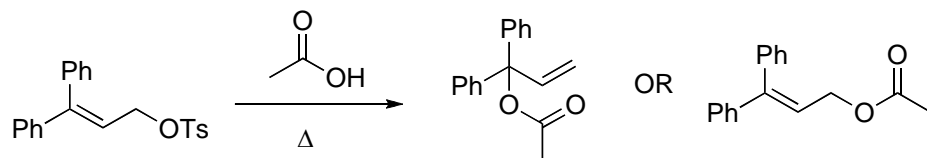
This is similar to a neopentyl system. Beta branching does not allow an $\text{S}_\text{N}2$ reaction to occur.

C) (2 points) No partial credit



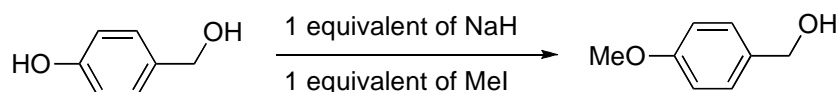
The base is very strong, with a pK_a around 35. However, it is a poor nucleophile because it is very sterically hindered due to the two tBu groups. This base deprotonates the thiol to generate a thiolate, which is a strong nucleophile. The thiolate initiates an intramolecular $\text{S}_\text{N}2$ reaction with the benzyl bromide to give the cyclic thioether.

D) (2 points) 2 points for either answer, but 2 points total. No partial credit.



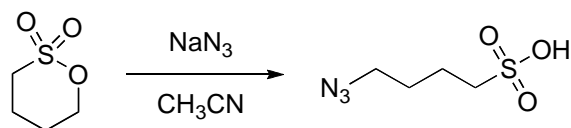
This is an SN1 reaction. The tosylate leaves to generate a carbocation. Resonance distributes the positive charge over two different carbon atoms, either of which can be attacked by acetic acid to generate the indicated products.

E) (2 points) No partial credit.



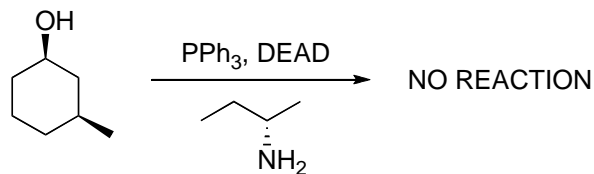
NaH deprotonates the most acidic position, which is the phenolic OH rather than the benzylic OH. The resulting phenoxide ion does an SN2 reaction with MeI (Williamson ether synthesis) to generate the methyl ether product.

F) (2 points) No partial credit. OK to show the Na salt of the product.



The starting material is an internal sulfonic ester, and behaves just like a tosylate or mesylate. Azide is a strong nucleophile, and it attacks the sulfonic ester (SN2 reaction) to give the ring opened product.

G) (2 points) No partial credit



The Mitsunobu reaction only works with nucleophiles that have a conjugate acid with a pKa between 3 and 12. The primary amine in this reaction has a pKa of approximately 35, which is outside of this range.

Problem 2 (14 points)

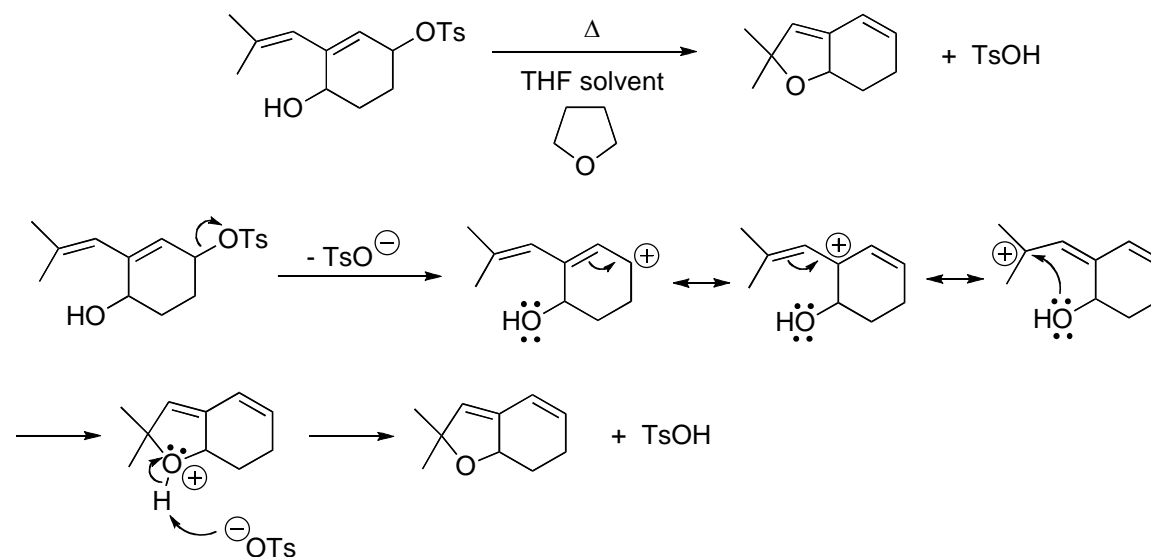
A) (12 points) Provide a detailed, step-by-step mechanism for the following reaction. In this question, we provide the reactant and reaction conditions. **YOUR JOB IS TO:**

1) Show the individual chemical steps and all intermediates formed in the process of converting the reactant to the product.

2) Use curved arrows to show all changes in bonding and lone pair electrons.

3) Show all formal charges and all contributing resonance structures.

Remember, the sequence of steps you propose must convert the reactant into the product using only the starting material provided. You may not use additional acids or bases, since they are not present in the reaction mixture. The solvent for the reaction is THF, the structure of which is provided below.



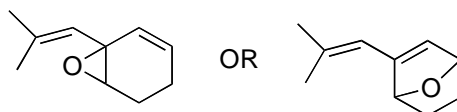
Arrows (4 points): 1 point for each of the four arrows shown in the 1st, 4th, and 5th structures. The arrows must clearly start and end in the proper place (bond or atom).

Formal charge (4 points): 1 point for each of the + formal charges shown in the 2nd, 3rd, 4th and 5th structures.

Resonance structures (3 points): 1 point for each resonance structure that is completely correct. They do not have to show the arrows in the 2nd and 3rd structures that show movement of electrons to interconvert resonance structures.

Deprotonation (1 point): 1 point if the deprotonation step is drawn completely right: deprotonation occurs **AFTER the alcohol reacts** with the carbocation. No point if the student shows deprotonation of the alcohol **BEFORE reaction** with the carbocation. They do not have to show the lone pair on oxygen. It is OK if they use THF rather than tosylate as the base during the deprotonation.

B) (2 points) Based on your mechanism, predict one other ether that might be formed as a product during this reaction.

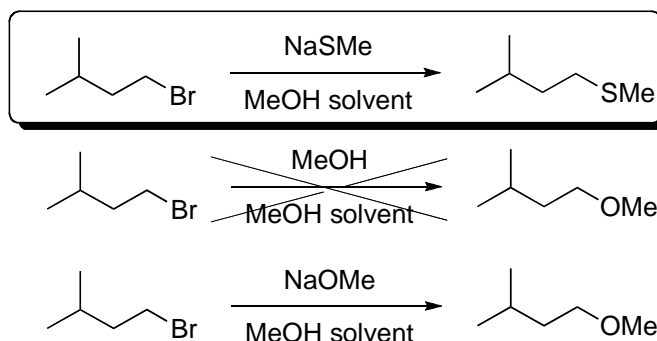


2 points for either answer, but 2 points total. No partial credit.

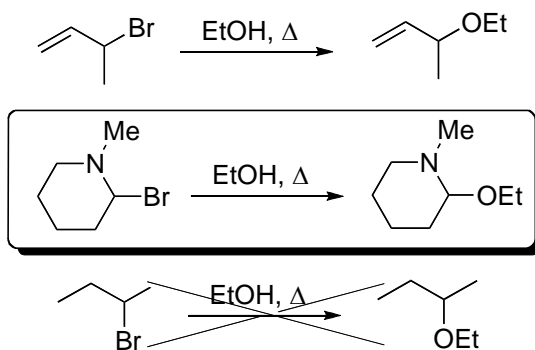
Problem 3. (14 points) For each set of reactions shown below, circle the reaction that is fastest, and cross out the reaction that is slowest.

Grading: 1 point for each correct circled reaction, and 1 point for each correct crossed out reaction.

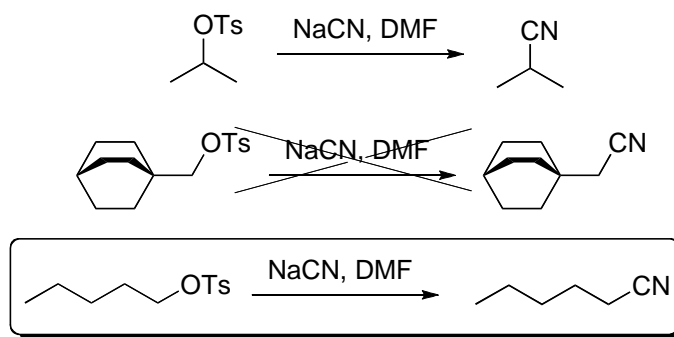
A) (2 points)



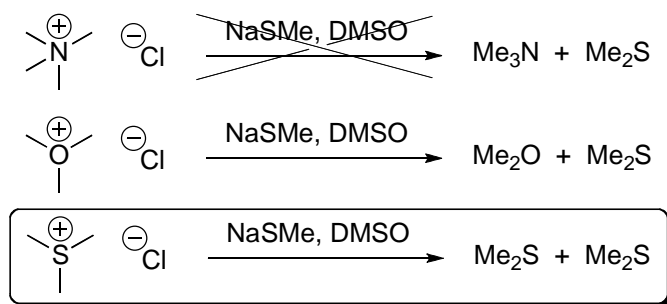
B) (2 points)



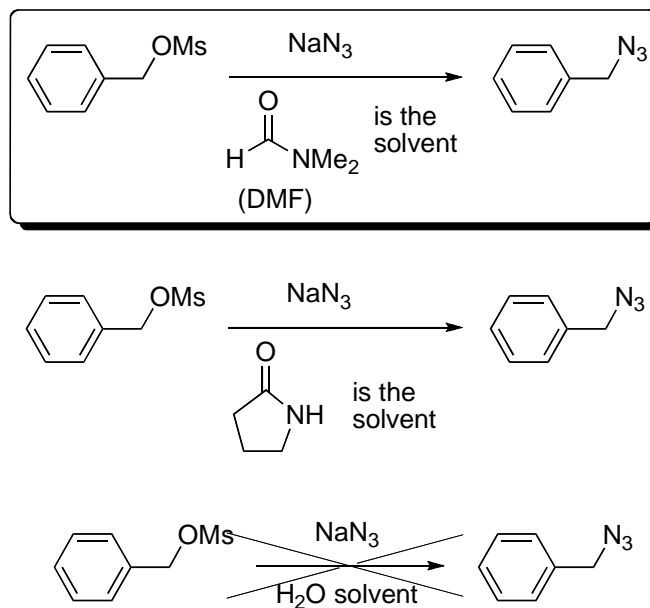
C) (2 points)



D) (2 points)



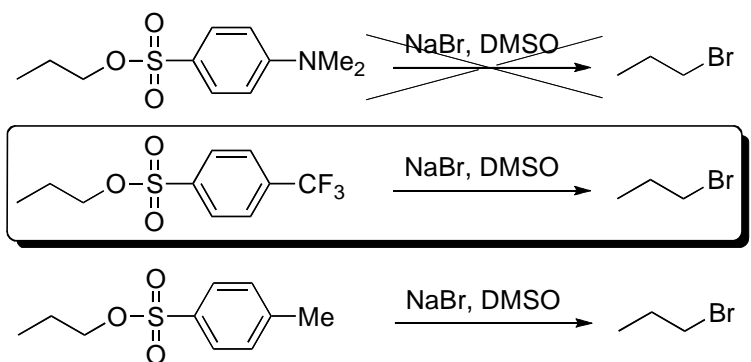
E) (2 points)



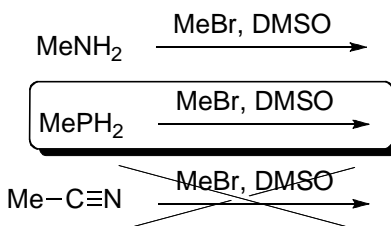
Name _____

SISD _____

F) (2 points)

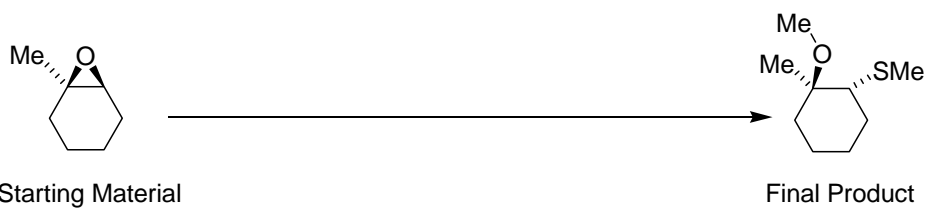


G) (2 points) The products for these three reactions are intentionally not provided.



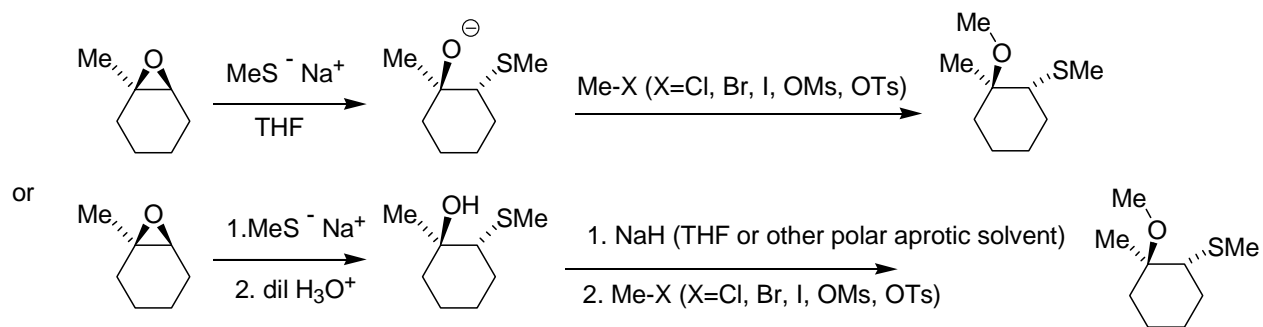
Problem 4.

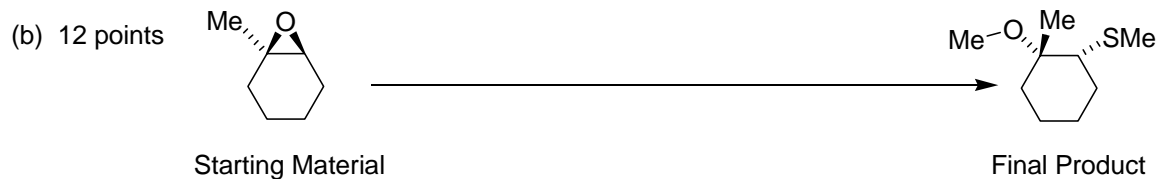
(a) 8 points



Requires - substitution (MeS^-) with inversion at less substituted epoxide carbon, producing alkoxide at more substituted epoxide carbon **(4 points properly completed)**

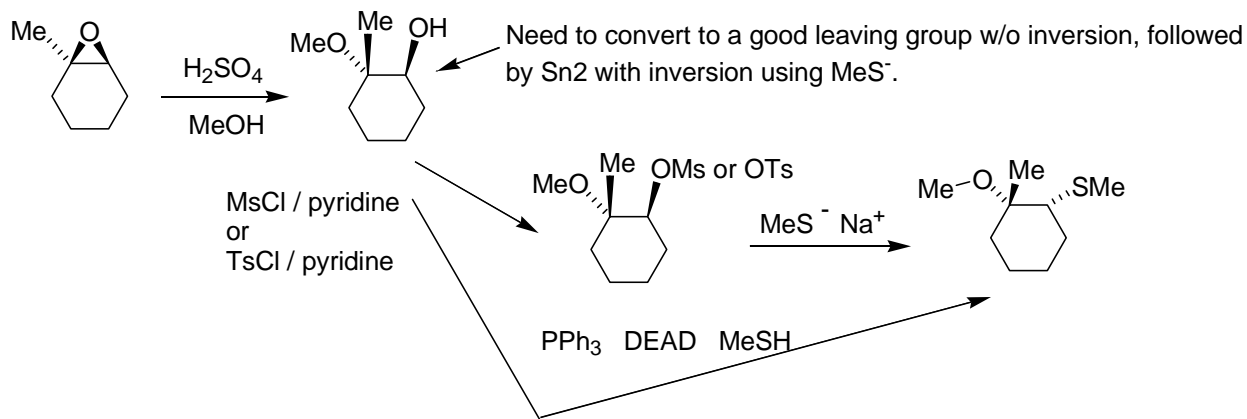
- ether formation (Me-X electrophile) at 3° alkoxide (or alcohol) **(4 points properly completed)**





Requires - substitution with inversion (MeS^-) at less substituted epoxide carbon
 - substitution with inversion (MeO^- ??) at more substituted epoxide carbon

SUBSTITUTION WITH INVERSION AT 3° epoxide carbon only possible using H_2SO_4 / MeOH



4 points proper epoxide ring opening,
AND 4 pts proper OMs or OTs, 4 points proper MeS^-
OR 8 points proper Mitsunobu

silly errors

H_2SO_4 / MeO^- 2 pts - reaction works but MeO^- is protonated by H_2SO_4

MsCl / TsCl without pyridine 2 pts - pyridine prevents formation of HCl which will open epoxide

0 points if use SOCl_2 or PBr_3 to convert alcohol into good leaving group - inversion, not retention

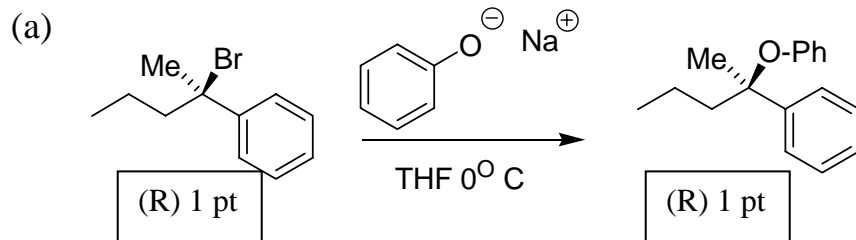
Problem 5. (20 points) For the following reactions,

(1) Give the absolute configuration, (R) or (S), of all stereocenters in the reactants and products PROVIDED BY US.

(2) If the reaction is 100% correct as written, write “CORRECT” in the box.

If the reaction product(s) provided are not entirely correct, draw **ALL THE CORRECT PRODUCTS** in the box and **SPECIFY THE SUBSTITUTION MECHANISM(S)**.

If no reaction occurs, write “NO REACTION” in the box.



Sn2 will not occur at a tertiary carbon.

The solution temperature (0° C) greatly slows Sn1 carbocation formation.

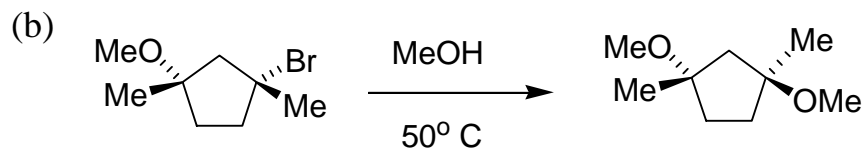
If one waits long enough, **Sn1 racemic product forms.**

NO REACTION - 2 pts (must explain that Sn1 is slow because THF is not very polar)

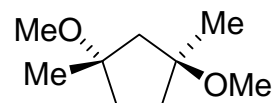
or

RACEMIC PRODUCT 2pts (1 pt each enantiomer or 2 pts squiggly line)

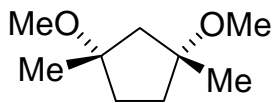
4 pts total for part (A)



(S) (R) 1 pt each center (S) (S)



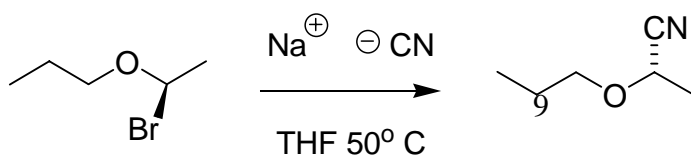
1 pt



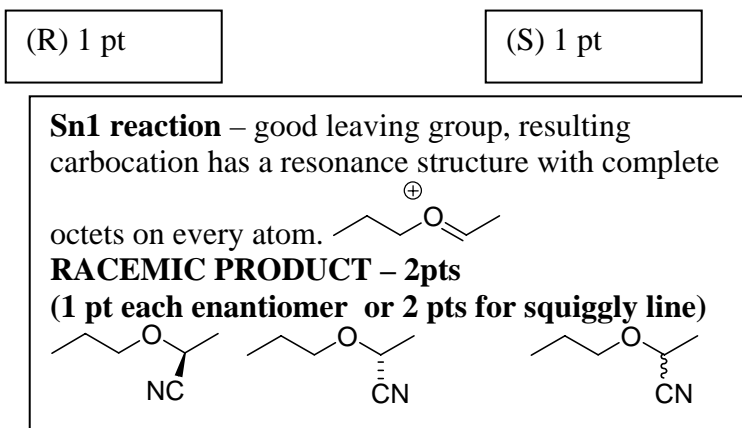
1 pt

Sn1 reaction: obtain both absolute configurations at reacting C (NOT RACEMIC – left stereocenter (S)) (squiggly line okay for right stereocenter)

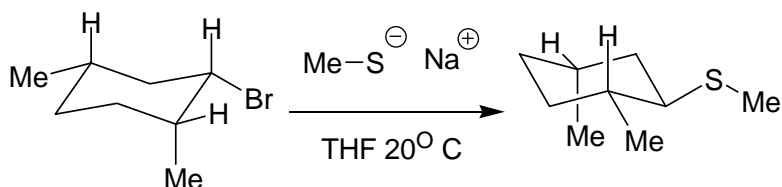
6 pts total for part (B)



(c)

4 pts total for part C

(d)



_____ (S) (R) (S) 1 pt for labeled 4 () () (R)

Slow Sn2 – inversion of configuration, Sn2 at cyclohexane requires axial bromide (WHY ? when the Br is equatorial, the axial hydrogens on the C-Br backside block backside access. When the Br is axial, the molecule acts as a normal 2° halide.)

“CORRECT” – 2pts

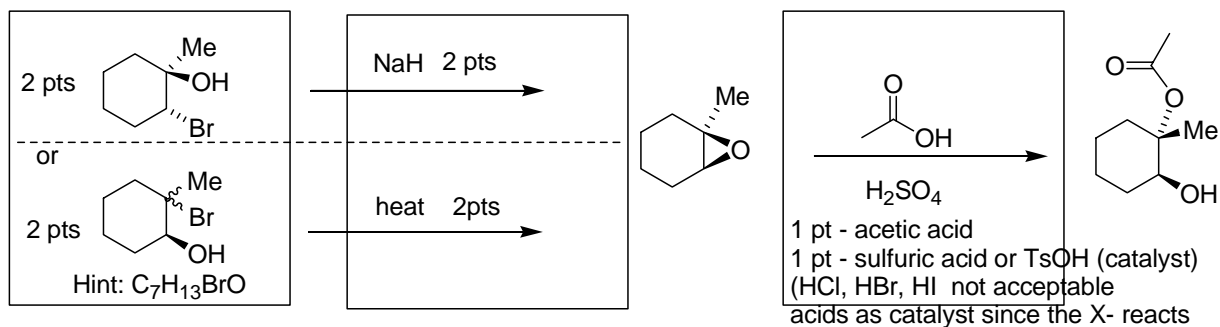
Or

“NO REACTION” – 2 pts if student states that this reaction required extensive heating in lab (No points if student does not give explanation)

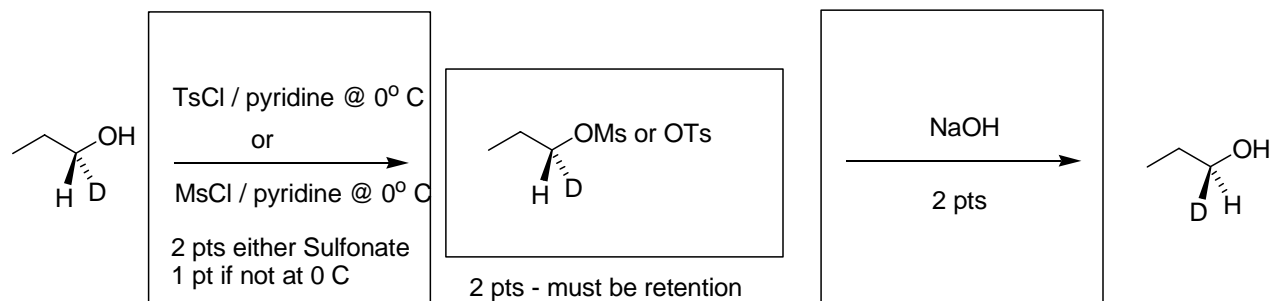
6 pts total for part D

Problem 6. (18 points) Provide the missing starting materials (left box), reagents (box around arrow), product of first reaction (middle box) or product of second reaction (right box) that complete the following reaction sequences.

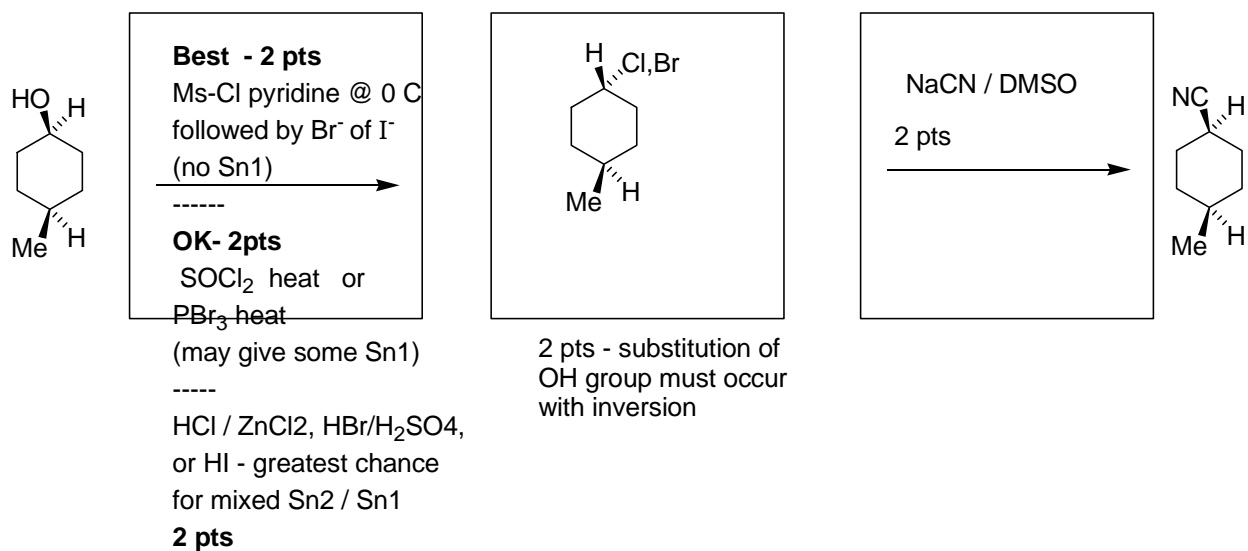
(a) 6 pts total



(b) 6 pts total



(c) 6 pts total



0 pts for H₂SO₄ + NaCN