

Chemistry 261: Organic Chemistry

Examination #3

November 4, 2013

Name: *ANSWER KEY*

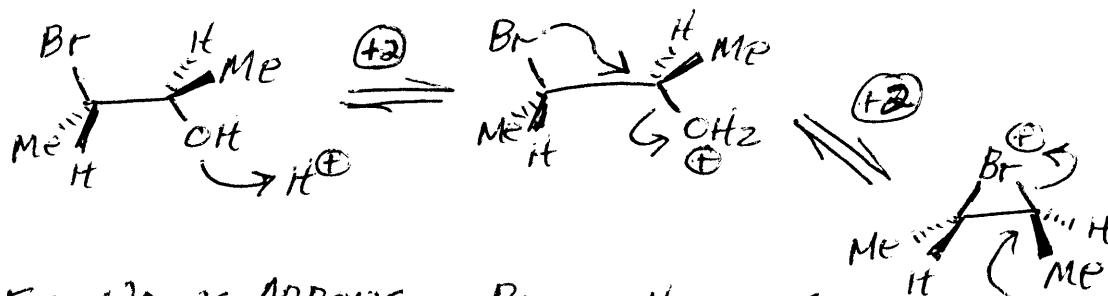
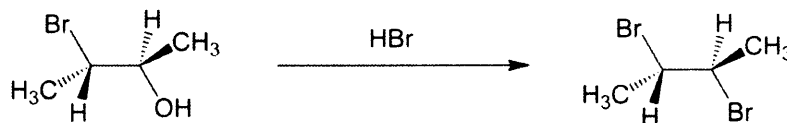
Student ID Number:

Exams will be returned via the Chem 261 wall-mount racks outside Lab Sci 300.

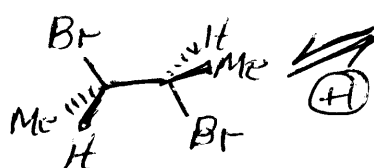
Please check the box if you would prefer to pick up your graded examination directly from Prof. Ponder during office hours.

Problem 1 (10 points; A & B = 5 points each) For each reaction, rationalize the product by writing the mechanism. Be sure to note key intermediates leading to the observed regiochemistry or stereochemistry.

(A)

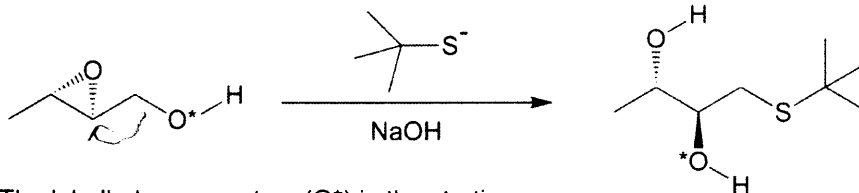


(-i) FOR WRONG ARROWS & FORMAL CHARGES

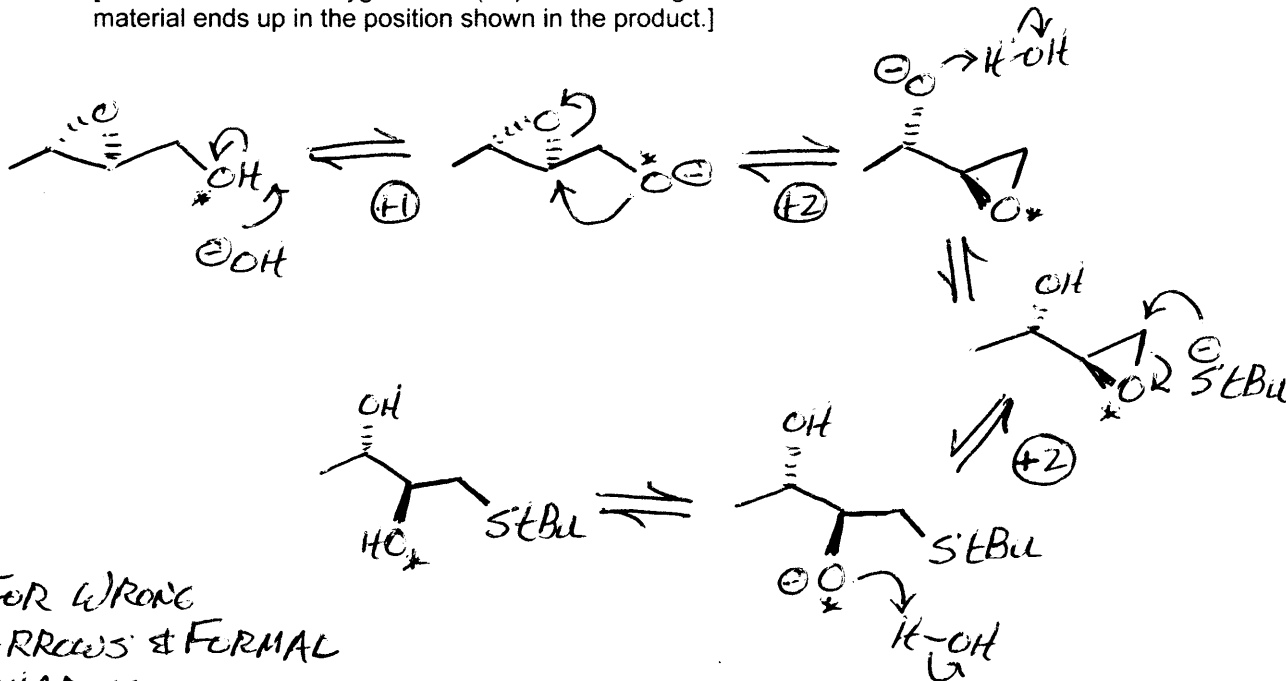


• ATTACK AT OTHER SIDE GIVES THE SAME PRODUCT

(B)



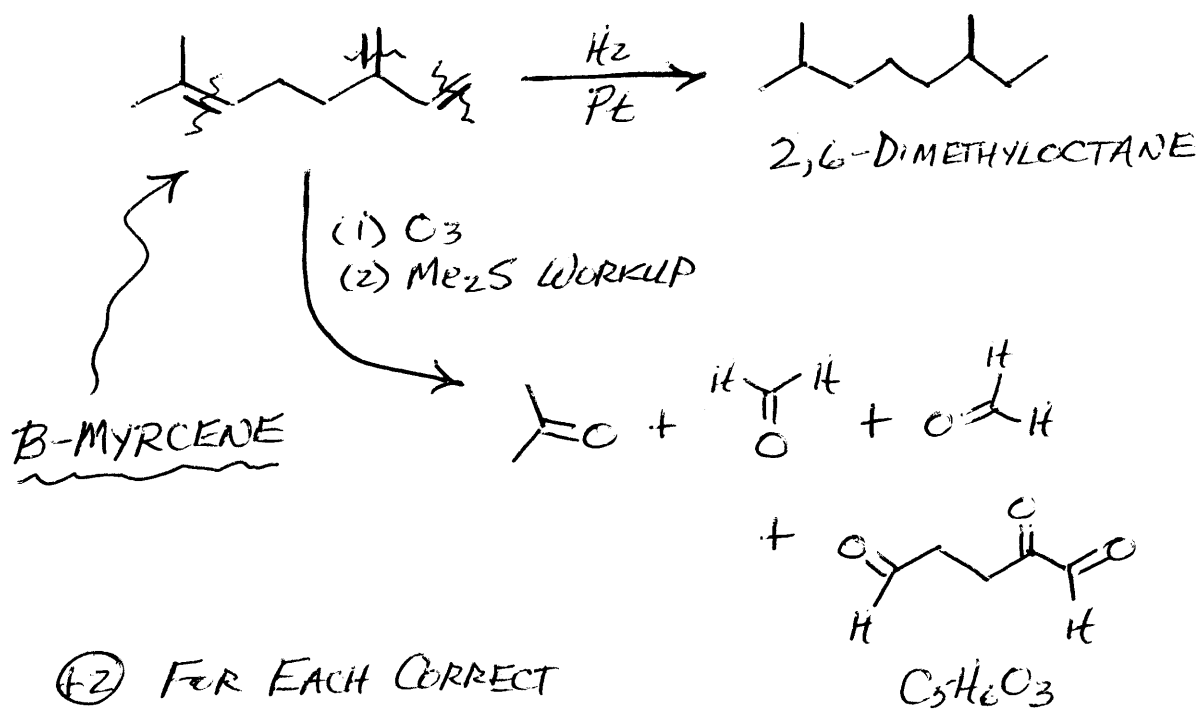
[Note: The labelled oxygen atom (O*) in the starting material ends up in the position shown in the product.]



(-i) FOR WRONG ARROWS & FORMAL CHARGES

Problem 2 (8 points)

β -Myrcene is produced naturally by the herbs thyme and parsley. It has a pleasant odor, and is a much-used intermediate in the perfume industry. Reaction of β -myrcene in the presence of finely divided platinum catalyst and an excess of hydrogen gas results in 2,6-dimethyloctane. Ozonolysis of β -myrcene followed by workup with dimethyl sulfide produces two equivalents of formaldehyde (HCHO), one equivalent of acetone (CH₃COCH₃), and another molecule of formula C₅H₆O₃. Based upon this information, deduce the structure of β -myrcene.



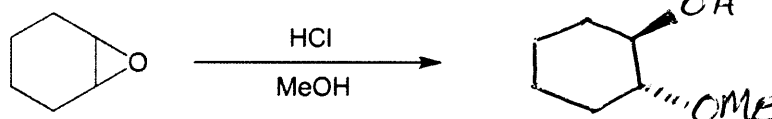
(+2) FOR EACH CORRECT

DOUBLE BOND THAT
GIVES ACETONE OR FORMALDEHYDE
(UP TO 1 >C=O AND 2 H₂C=O)

(+2) FOR HAVING CORRECT CARBON BACKBONE
(2,6-DIMETHYLOCTANE) PRESENT IN FINAL ANSWER

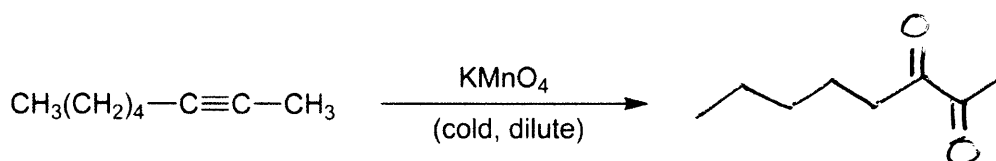
Problem 3 (12 points; A–D = 3 points each) Predict the major product resulting from each of the following reactions. Pay attention to stereochemistry when appropriate. You need not show mechanisms, intermediates or minor products.

(A)



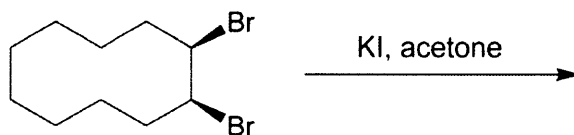
WITH EITHER OMe OR Cl
 (+1) IF WRONG STEREOCHEM
 (+2) FOR

(B)



(+1) FOR ACIDS

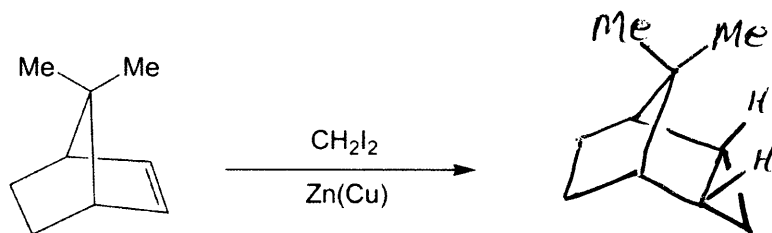
(C)



trans

(+2) FOR CIS

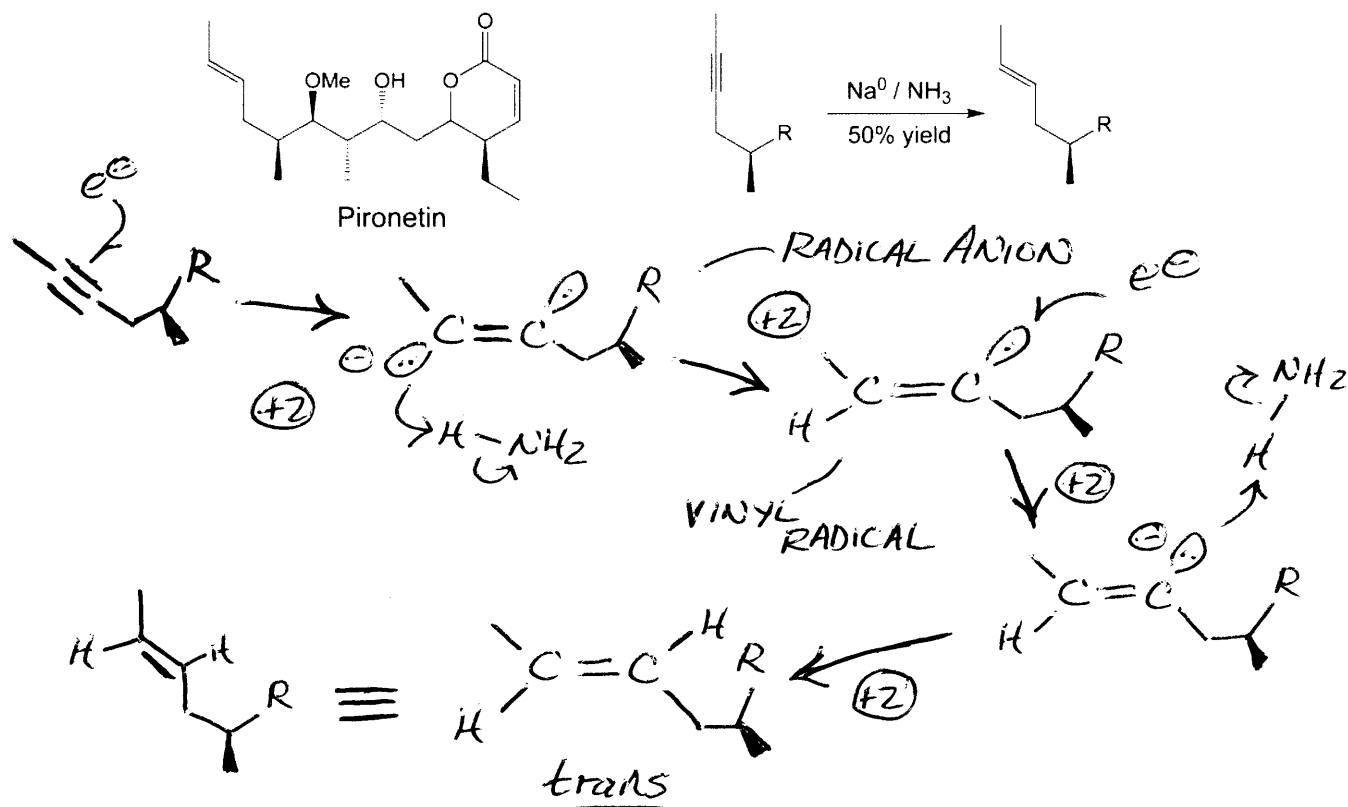
(D)



(+2) FOR ATTACK AT MORE HINDERED FACE

Problem 4 (12 points; A = 8 points, B & C = 2 points each)

- (A) Pironetin is a naturally occurring anticancer agent. It is a potent inhibitor of tubulin assembly and arrests the cell cycle at M phase. The metal-ammonia (Birch) reduction shown is a key step in a pironetin synthesis. Write the mechanism.



+2 FOR EACH STEP, -1 FOR MISSING/WRONG ARROWS & CHARGES

- (B) What orbital of the starting alkyne is involved in the first step of the reduction?

(+2) ALKYNE π^* ORBITAL ALL-OR-NONE

- (C) Terminal alkynes (an alkyne bond at the end of a carbon chain) often give a poor yield of alkene product under Birch conditions. Adding ammonium sulfate to the metal-ammonia solution prior to addition of the terminal alkyne can dramatically increase the yield. Explain these observations.

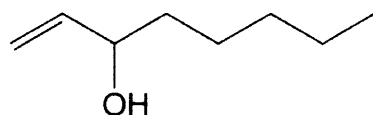
(+2) FORMATION OF ACETYLIDE FROM TERMINAL ALKYNE INHIBITS RXN SINCE IT ALREADY HAS A NEGATIVE CHARGE

(+1) FOR ONLY SAYING THAT "ACID" OR PROTON SOURCE HELPS DRIVE RXN FORWARD

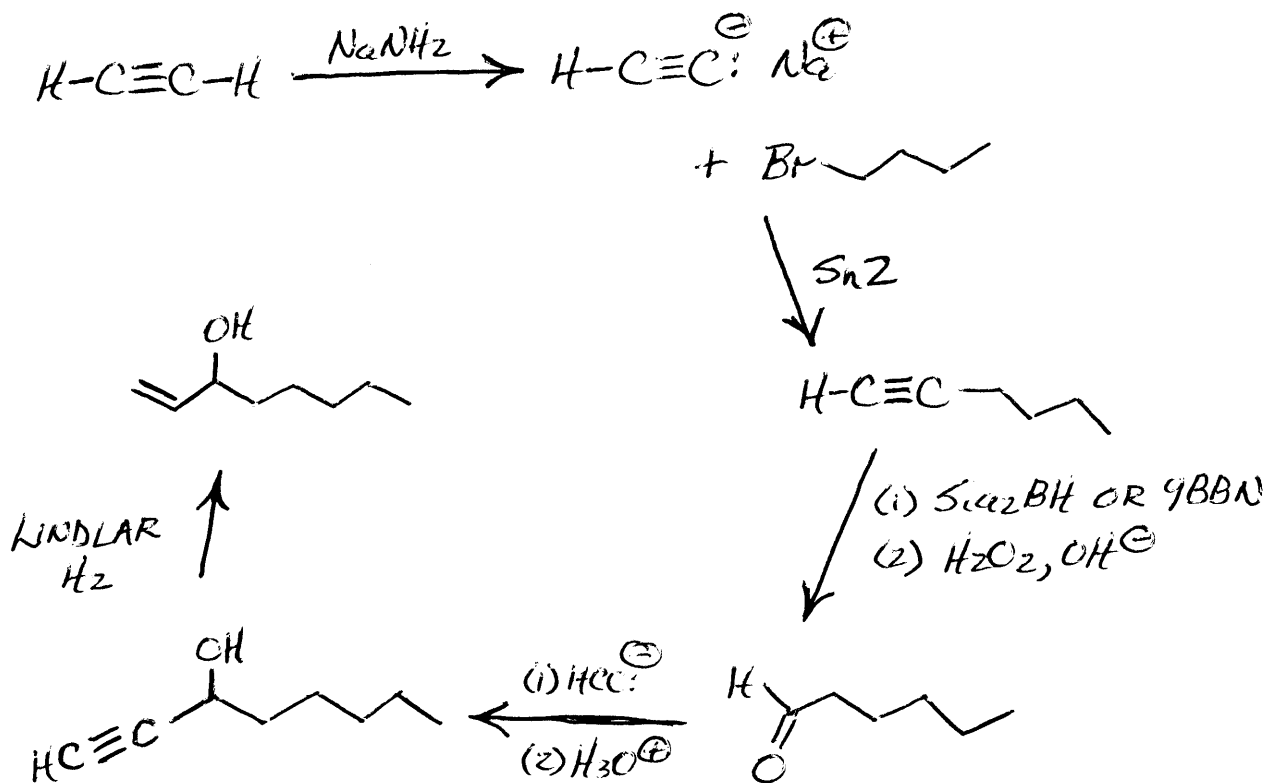
Problem 5 (10 points)

(*R*)-Oct-1-en-3-ol is known as mushroom alcohol, as this specific enantiomer can be isolated from the caps of several mushroom species. It is a potent chemical attractant for various "biting" insects. For example, a few milliliters of this substance placed on a dish in the open air will attract mosquitos from a 1-acre area.

Starting from any neutral organic species containing four carbons or less, and any needed inorganic reagents, propose a synthetic route to racemic oct-1-en-3-ol. Your synthesis will be evaluated on the total number of steps, the yield of the individual steps, and their selectivity.

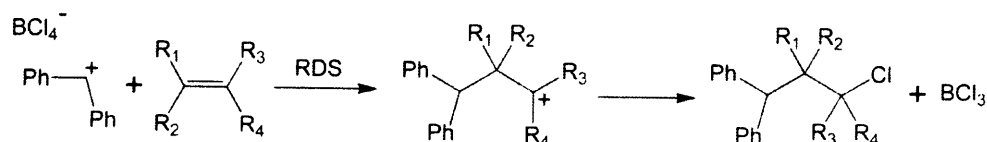


Oct-1-en-3-ol



Problem 6 (10 points; A = 4 points, B = 6 points)

A variety of alkenes react with diphenylmethyl tetrachloroborate ($\text{Ph}_2\text{CH}^+ \text{BCl}_4^-$) via the process shown below. The first step is found to be rate determining step (RDS).



The heat of hydrogenation, HOMO energy, and relative rate of reaction with diphenylmethyl cation is given in the following table for several alkenes.

Alkene	$\Delta H_{\text{hydrogenation}}$ (KJ/mol)	HOMO Energy (eV)	Relative Reaction Rate (Propene=1)
Propene	-125.1	-9.7	1
(E)-2-Butene	-114.8	-9.3	1.3
2-Methylpropene	-116.3	-9.4	25000
2-Methyl-2-butene	-112.6	-8.9	260000
2,3-Dimethyl-2-butene	-107.5	-8.6	6000
(E)-PhHC=CHMe	-114.4	-8.2	4100
PhMeC=CH ₂	-109.6	-8.5	1500000

- (A) We have used the heat of hydrogenation as a measure of alkene π -bond stability. By this measure, which alkene is least "stable"? Based upon only the HOMO energies, and ignoring steric effects, which alkene should be most nucleophilic?

(+2) LEAST STABLE: PROPENE (LARGEST ΔH_{HYDR})

(+2) MOST NUCLEOPHILIC: (E)-PhHC=CHMe (HIGHEST ENERGY HOMO)

- (B) The hydrogenation data and HOMO energies do not correlate well with the relative reaction rates. What does appear to correlate well with the reaction rates? Based on the data provided, do you think the first step is endothermic or exothermic? Is the transition state "early" or "late"? Explain using a reaction coordinate diagram.

(+1) FIRST STEP IS ENDOOTHERMIC

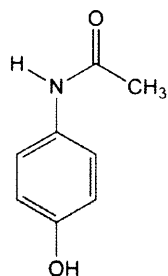
(+1) TRANSITION STATE IS "LATE" ALONG RXN COORDINATE

(+2) RXN RATE CORRELATES STABILITY OF THE PRODUCT CATION

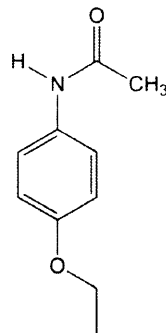
(+2) FOR RXN COORDINATE DIAGRAM CONSISTENT
w/ ENDO/EXO & EARLY/LATE ANSWERS GIVEN
BY THE STUDENT

Problem 7 (8 points; A = 5 points, B = 3 points)

- (A) Phenacetin was widely used as an analgesic until 1983, when it was banned due to kidney toxicity and other adverse effects. Starting with acetaminophen and any other organic or inorganic compounds, show how you can synthesize phenacetin.

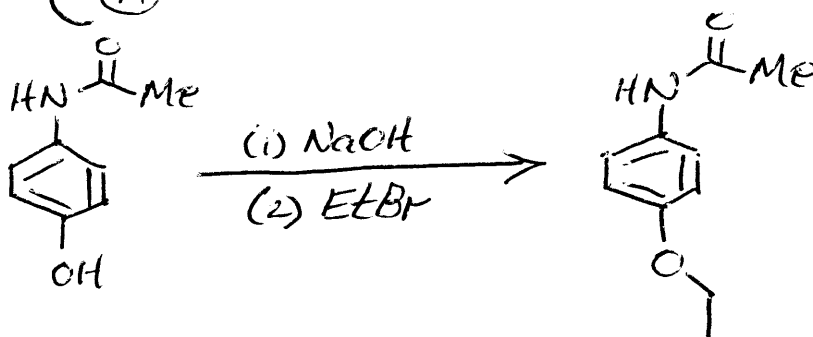


Acetaminophen



Phenacetin

{ (+2) FOR $Et-X$, $X=I, Br, Cl$
(+2) FOR $NaOH$ OR APPROPRIATE BASE
(+1) TWO SEPARATE STEPS

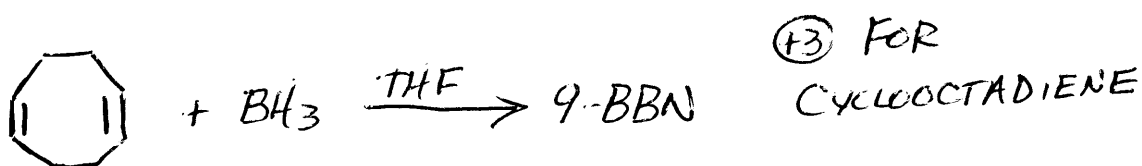
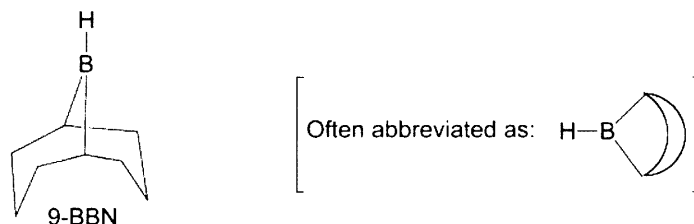


- (B) At the end of the reaction, what method could be used to determine if any starting material remains in the product?

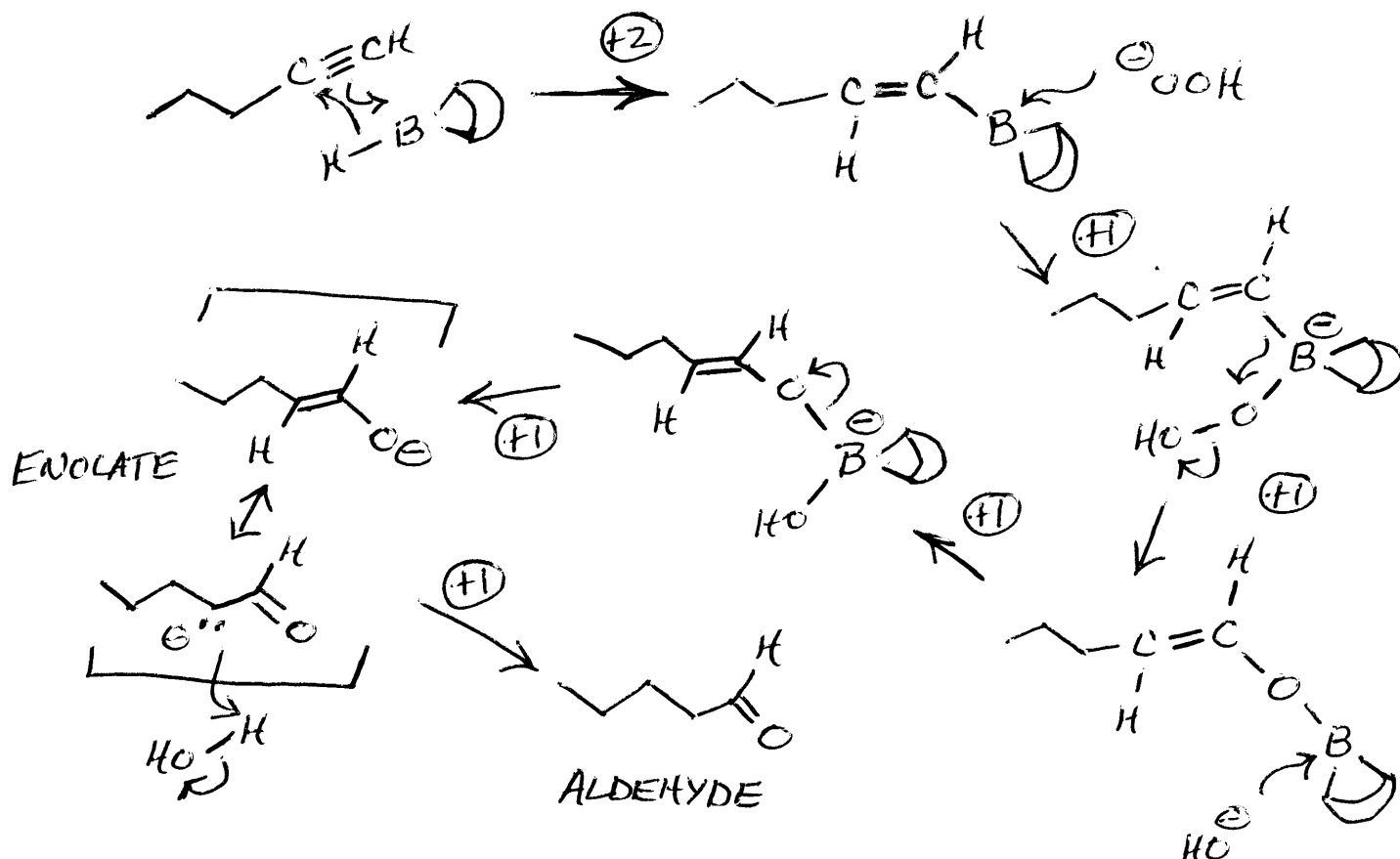
TLC (+3)
THIN-LAYER CHROMATOGRAPHY

Problem 8 (10 points; A = 3 points, B = 7 points)

- (A) 9-Borabicyclo[3.3.1]nonane, known as 9-BBN, is a useful reagent in organic synthesis. It is a stable white solid, first reported by Brown and co-workers. Herbert C. Brown received the 1979 Nobel Prize in Chemistry for work in organoboron chemistry. What molecule(s) would you react with borane (BH_3) to make 9-BBN?

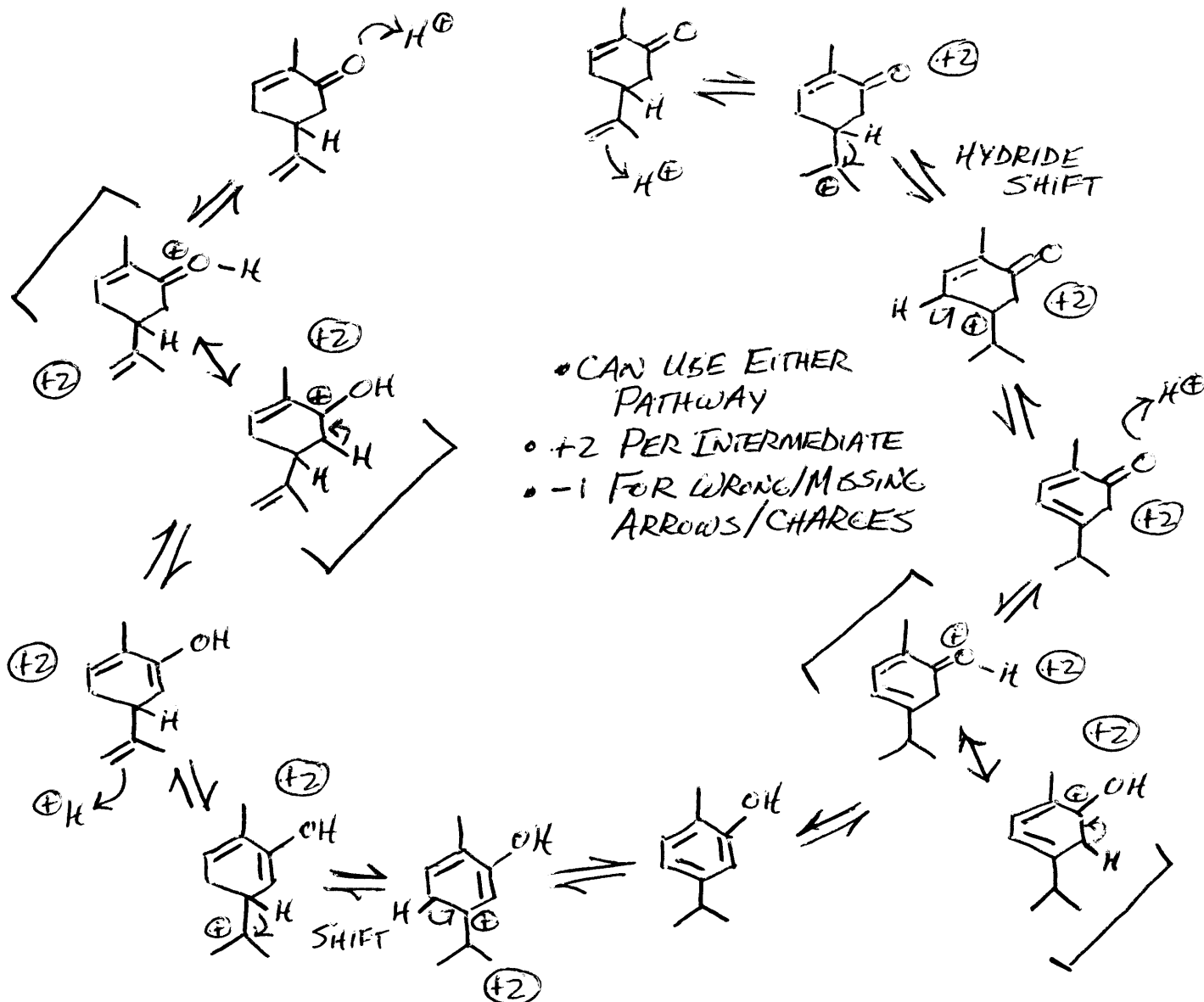
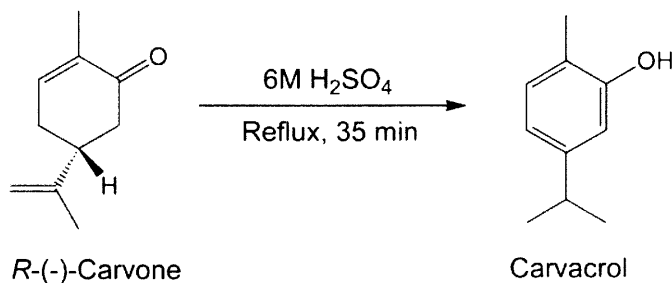


- (B) Write the full mechanism for reaction of 1-pentyne with a solution of 9-BBN in tetrahydrofuran (THF), followed by treatment with basic peroxide. What is the major product derived from the alkyne? What other organic molecule is produced?



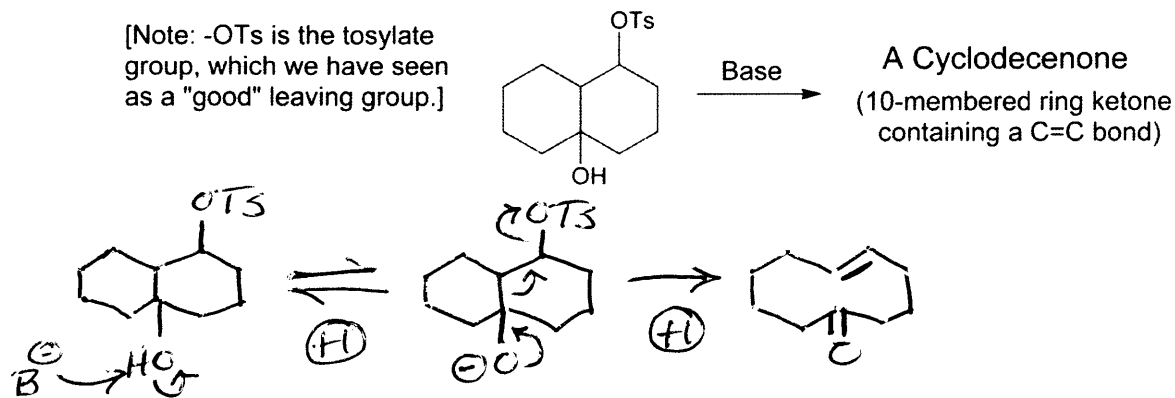
Problem 9 (10 points)

The *R*-enantiomer of carvone comprises 50-80% of spearmint oil, derived from *Mentha spicata*. Provide a complete, detailed mechanism for the acid-catalyzed conversion of *R*-(-)-carvone to carvacrol. Include all intermediates, and show important resonance structures as appropriate.

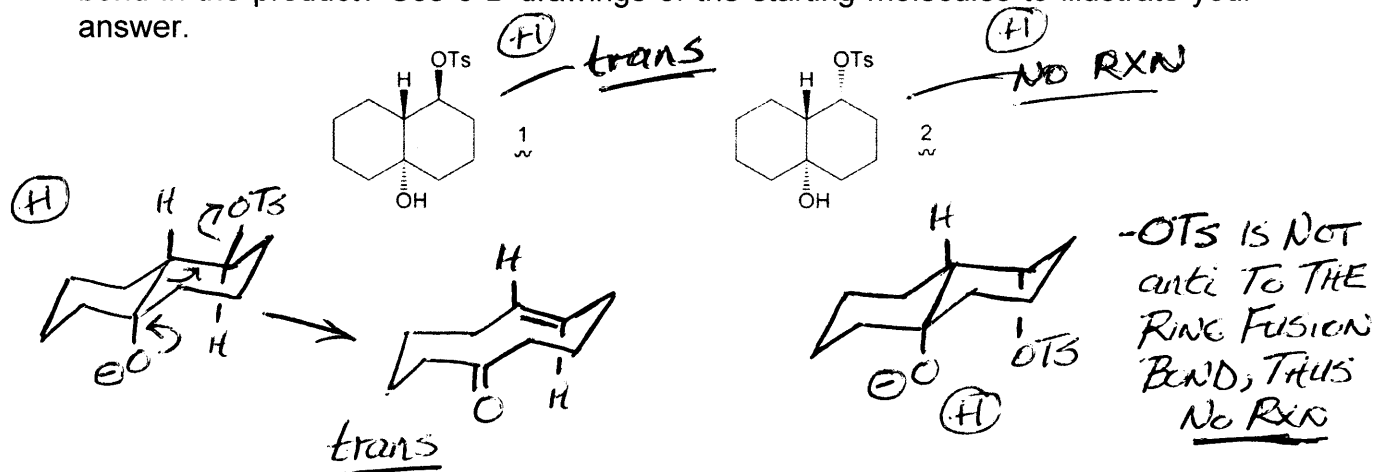


Problem 10 (10 points; A = 2 points, B & C = 4 points each)

- (A) Some isomers of the molecule shown below react under basic conditions to form a ketone containing a 10-membered ring with a C=C bond. Without regard to stereochemistry, draw the "arrow pushing" mechanism leading to the product.



- (B) Consider the mechanism in part (A) for each of the stereoisomers shown. Will these particular isomers react, and if so, what is the stereochemistry of the C=C bond in the product? Use 3-D drawings of the starting molecules to illustrate your answer.



- (C) Repeat part (B) for the two stereoisomers shown below.

