Last Name ANSWER

First Name KEY

MI

Student ID Number:

Total Score

230

/ 200

Chem 30A Spring 2005

FINAL

(180 Min)

Thurs June 16th

Course Grade

A+

****DO NOT OPEN THIS EXAM UNTIL INSTRUCTED TO DO SO****

ONLY ANSWERS WRITTEN IN THE BOXES PROVIDED WILL BE GRADED

INTERPRETATION OF THE QUESTIONS IS PART OF THE EXAM – DO NOT ASK FOR THE QUESTIONS TO BE EXPLAINED TO YOU

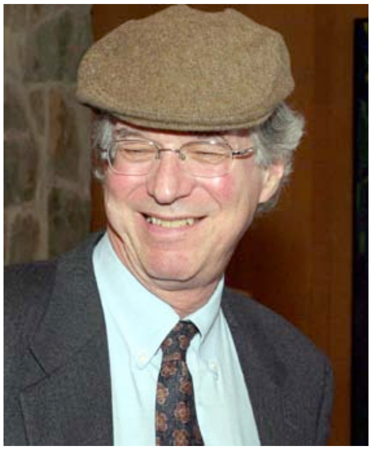
Q1	24 **/ 24**	**Q4**	16 **/ 16**	**Q7**	30 **/ 30**
Q2	30 **/ 30**	**Q5**	32 **/ 32**	**Q8**	20 **/ 20**
Q3	18 **/ 18**	**Q6**	40 **/ 40**	**Q9**	20 **/ 20**
				Total	230 **/ 200**

"A professor is one who talks in someone else's sleep." - W H Auden

"I cannot teach anybody anything, I can only make them think." - Socrates

"I fully realize that I have not succeeded in answering all of your questions...Indeed, I feel I have not answered any of them completely. The answers I have found only serve to raise a whole new set of questions, which only lead to more problems, some of which we weren't even aware were problems. To sum it all up...In some ways I feel we are confused as ever, but I believe we are confused on a higher level, and about more important things." - Unknown

In Memoriam

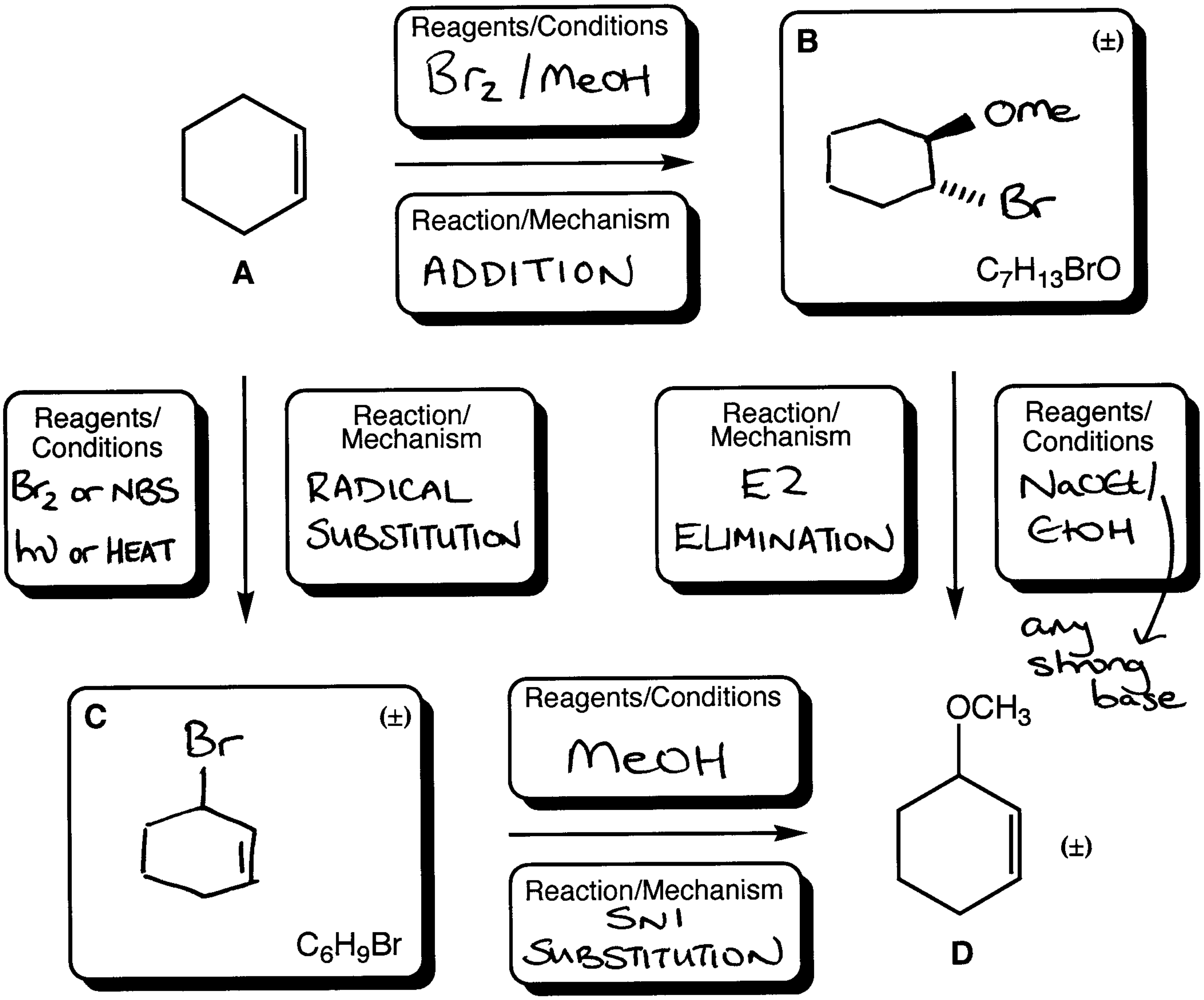


Christopher Spencer Foote

Scholar, Teacher, Professor & Author

(6/5/1935 – 6/13/2005)

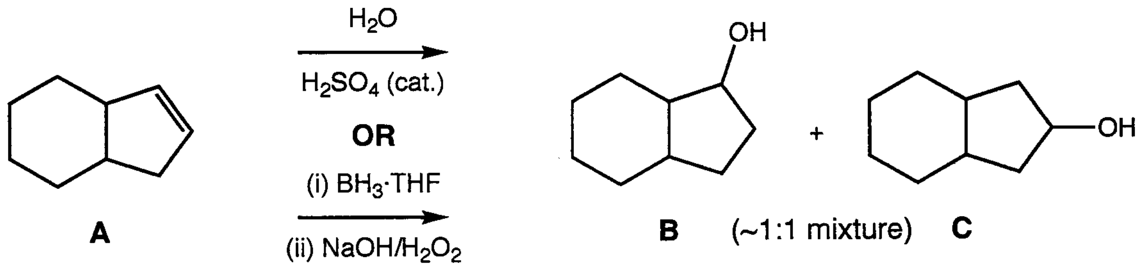
Q1. Cyclohexene **A** can be converted into 3-methoxycyclohexene **D** in a number of ways. One pathway involves the reaction of **A** to give intermediate **B**, which has the formula $C_7H_{13}BrO$, followed by a second reaction to give the desired product **D**. Alternatively, cyclohexane can be reacted to give intermediate **C**, which has the formula C_6H_9Br, followed by a second reaction to give the desired product **D**. Intermediates **B** and **C**, as well as the final product **D**, are formed as racemic mixtures. Suggest possible structures for **B** and **C** in the appropriate boxes below. For each reaction (**A** → **B**, **B** → **D** and **A** → **C**, **C** → **D**), provide the necessary reagents/conditions in the appropriate box AND indicate what kind of reaction is happening – in the case of substitution and elimination reactions, indicate which mechanism is most likely operating (your choices are listed in the box at the bottom of this page). (24 points)



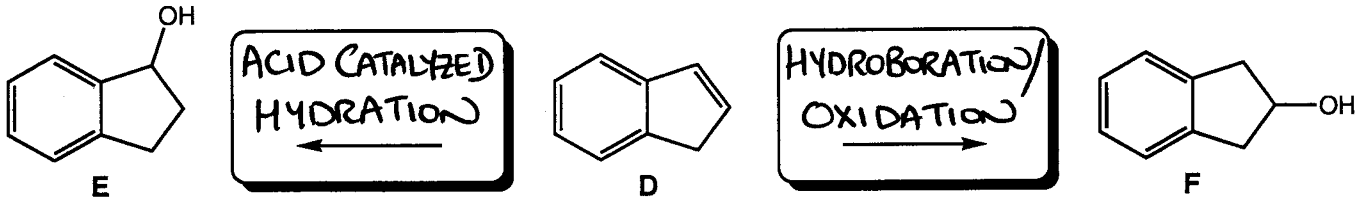
Reaction Types / Mechanisms to choose from –

Addition / Elimination (E1 or E2?) / Substitution (Radical, S_N1, S_N2?) / Rearrangment

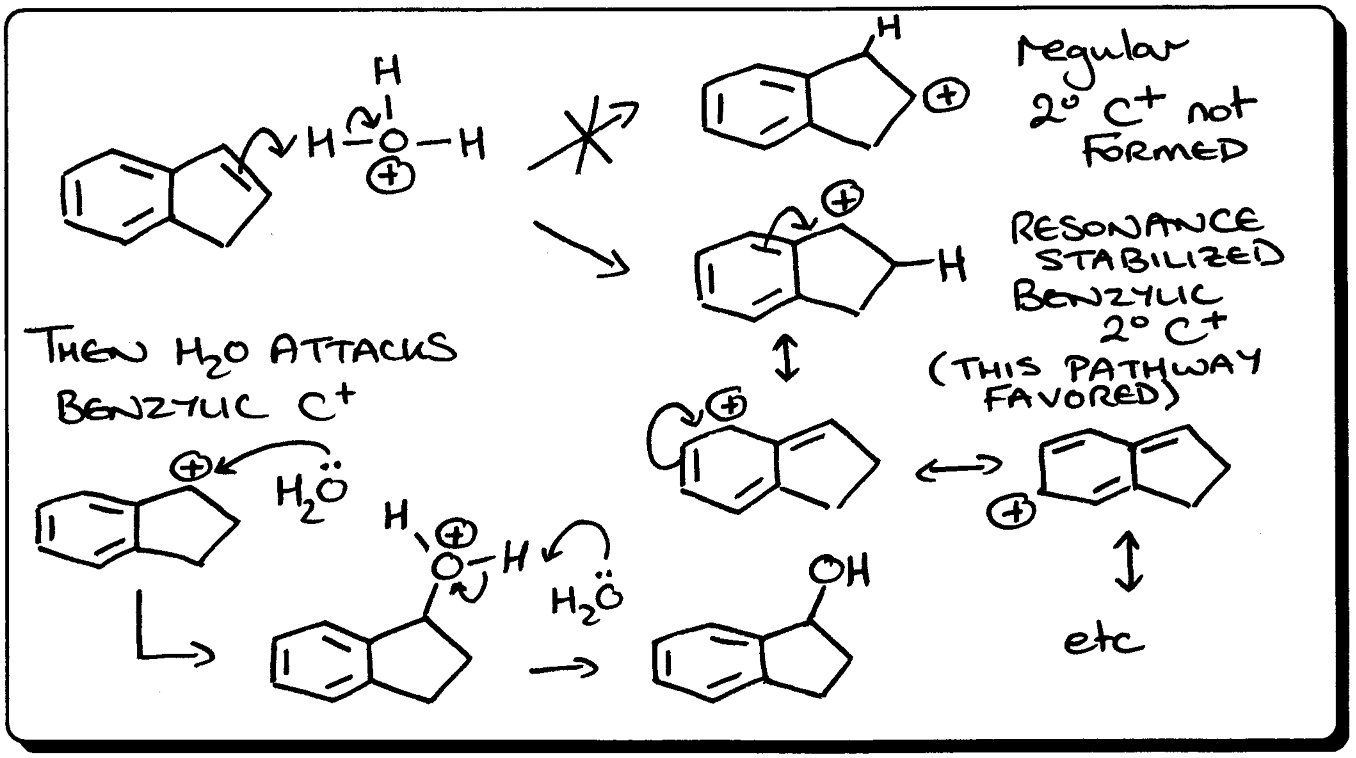
Q2. When alkene **A** is hydrated using EITHER acid catalyzed hydration (H_2O/H_2SO_4 cat.) OR hydroboration/oxidation ($BH_3 \cdot THF$ followed by $NaOH/H_2O_2$), an approximately 1:1 mixture of the secondary alcohols **B** and **C** is obtained, i.e., neither set of reagents gives any regioselectivity.



(a) In contrast, however, when alkene **D** is hydrated separately under these two sets of conditions, one reaction gives secondary alcohol **E** as the MAJOR product (>98%), whereas the other gives the secondary alcohol **F** as the MAJOR product (>98%). Indicate which set of conditions gives which product, by writing the words **'HYDROBORATION/OXIDATION'** in one arrowed box, and **'ACID CATALYZED HYDRATION'** in the other. (You may want to answer parts (b) and (c) first...) (4 points)



(b) In the box below, draw the mechanism for the acid catalyzed hydration (H_2O/H_2SO_4 cat.) of alkene **D** and explain why the reaction is regioselective. (8 points)



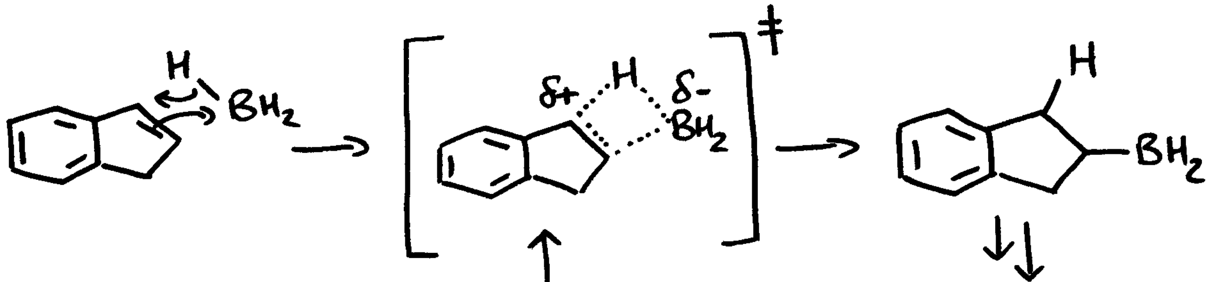
Regular 2° C+ not FORMED

RESONANCE STABILIZED BENZYLIC 2° C+ (THIS PATHWAY FAVORED)

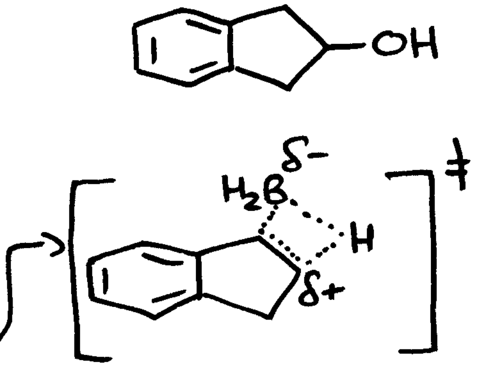
THEN H₂O ATTACKS BENZYLIC C+

Question 2 is continued on the next page...

(c) In the box below, draw the mechanism for the VERY FIRST STEP of the hydroboration/oxidation reaction of alkene **D** (i.e., just show the mechanism for the first addition of alkene **D** to BH_3). Draw the transition state for this step, and explain why the addition is regioselective. (8 points)

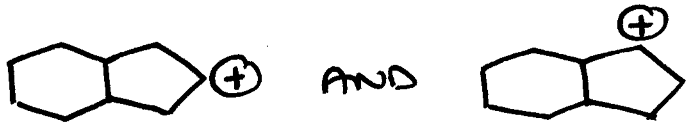


ADDITION OF BH_3
THIS WAY AROUND PLACES THE
δ+ IN THE TRANSITION STATE ON
THE CARBON ATOM MOST ABLE
TO STABILIZE A POSITIVE CHARGE,
i.e., THE BENZYLIC POSITION,
MAKING THIS A LOWER ENERGY
REACTION PATHWAY THAN THIS



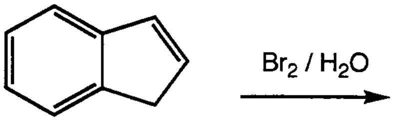
(d) Suggest a reason why no regioselectivity is observed in the hydration of alkene **A**, no matter what conditions are chosen. (4 points)

THERE IS LITTLE OR NO DIFFERENCE IN ENERGY
BETWEEN THESE TWO CATIONS:

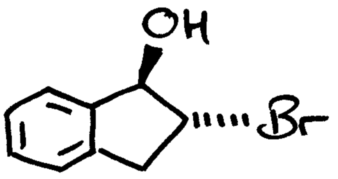


SO NO REGIOSELECTIVITY
IS OBSERVED AS NO ONE
PATHWAY IS STABILIZED

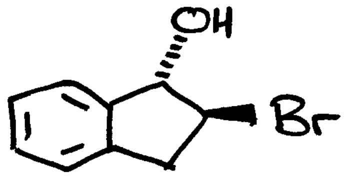
(e) The reaction of alkene **D** with Br_2 in water gives a racemic mixture of two bromohydrins – draw the structures of these two bromohydrins below. (6 points)



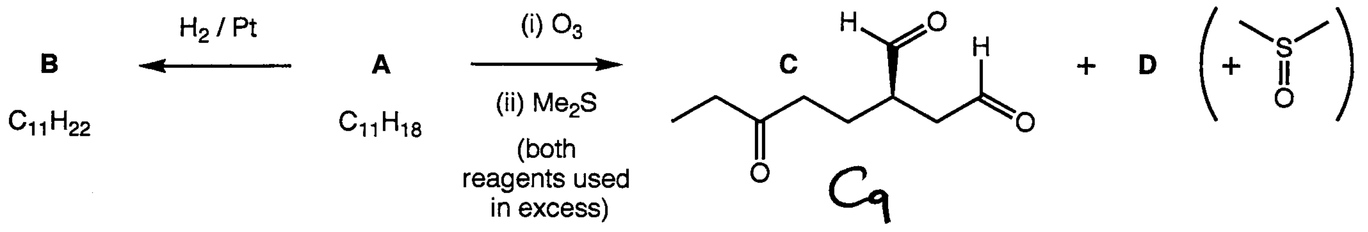
D



+

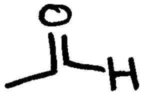


Q3. An optically active (chiral) compound **A** ($C_{11}H_{18}$) reacts with hydrogen in the presence of a platinum (Pt) catalyst to give one SINGLE compound **B**, with the formula $C_{11}H_{22}$. Compound **B** is optically inactive (achiral). When **A** undergoes an ozonolysis reaction (O_3/Me_2S), two new compounds are formed; the ketodialdehyde (**C**) shown below, and compound **D** (in addition to the byproduct $Me_2S{=}O$). Draw the structures of compounds **A**, **B**, and **D**, in the boxes at the bottom of this page, including any relevant stereochemistry. (7 points each **A** and **B**, 4 points for **D**)

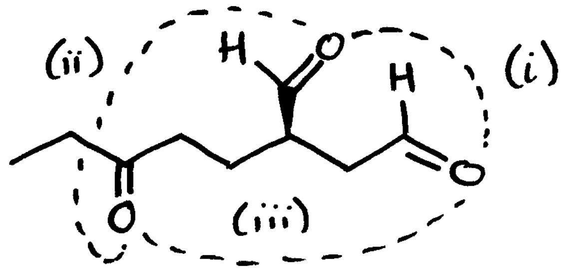


Space for working...

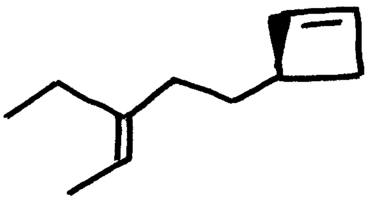
SINCE A IS BROKEN APART BY OZONOLYSIS INTO A C9 and a C2 FRAGMENT, D MUST BE



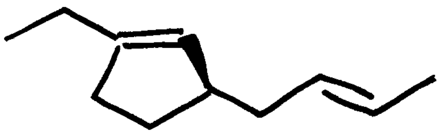
THE OTHER TWO C=O GROUPS IN C MUST HAVE FORMED A RING, SO WHICH ONE IS IT?



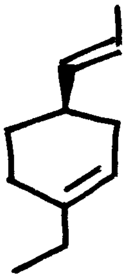
(i)



(ii)

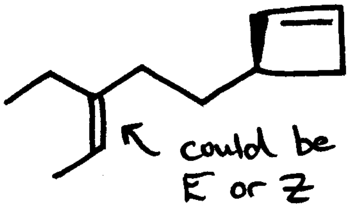


(iii)



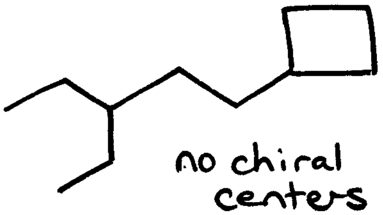
AND ONLY THE COMPOUND FROM (i) GIVES A SINGLE ACHIRAL COMPOUND WHEN HYDROGENATED

A



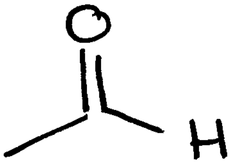
could be E or Z

B

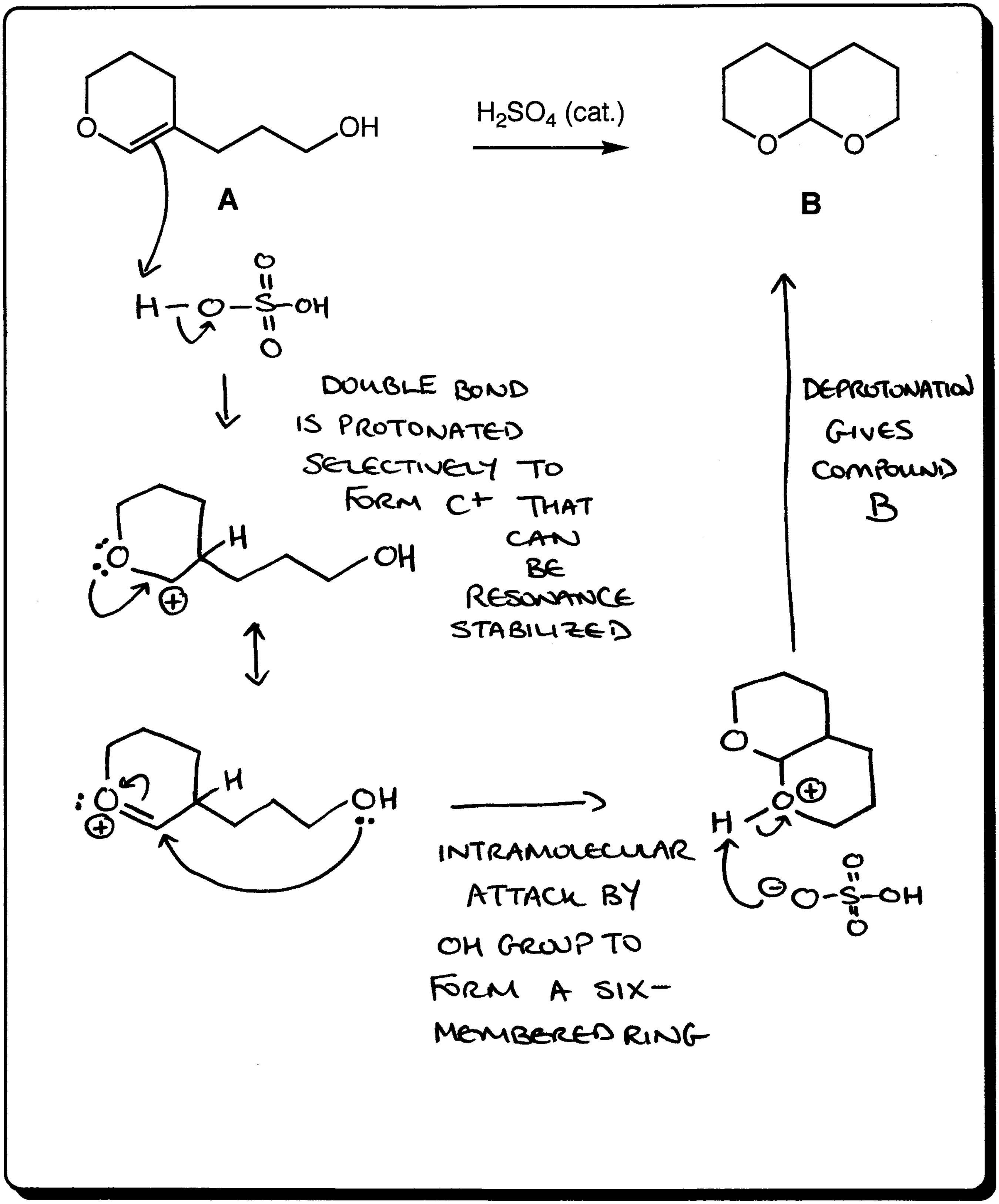


no chiral centers

D



Q4. Propose a reasonable mechanism that accounts for the transformation of compound **A** into compound **B** shown below – (show all intermediates, all appropriate lone pairs, formal charges, significant resonance forms, and curly arrows). Explain each step with a few words. (16 points)

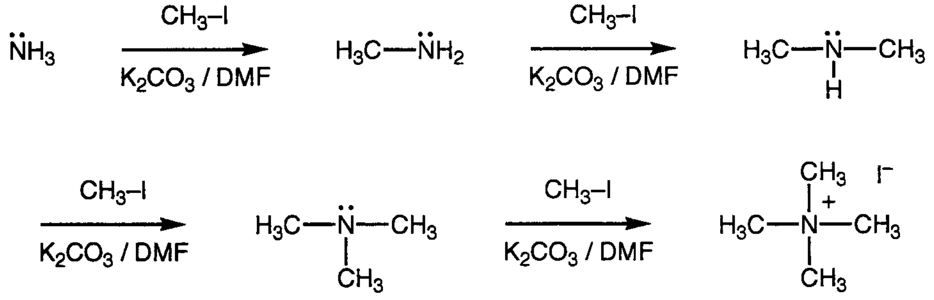


DOUBLE BOND IS PROTONATED SELECTIVELY TO FORM C+ THAT CAN BE RESONANCE STABILIZED

INTRAMOLECULAR ATTACK BY OH GROUP TO FORM A SIX-MEMBERED RING

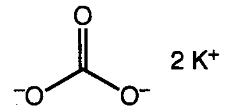
DEPROTONATION GIVES COMPOUND B

Q5. Ammonia (NH_3) undergoes an S_N2 reaction with methyl iodide (CH_3–I) in the presence of a base such as potassium carbonate (K_2CO_3) to give methylamine (CH_3–NH_2). Methylamine is still a good nucleophile, and will react with another equivalent of CH_3–I under the same conditions to give dimethylamine. In turn, dimethylamine will continue to react to form trimethylamine, and finally trimethylamine will react to form tetramethylammonium iodide.

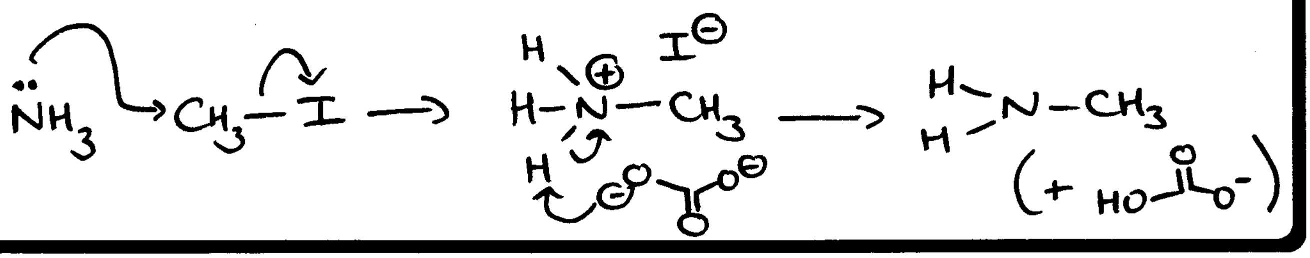


Structure of K_2CO_3

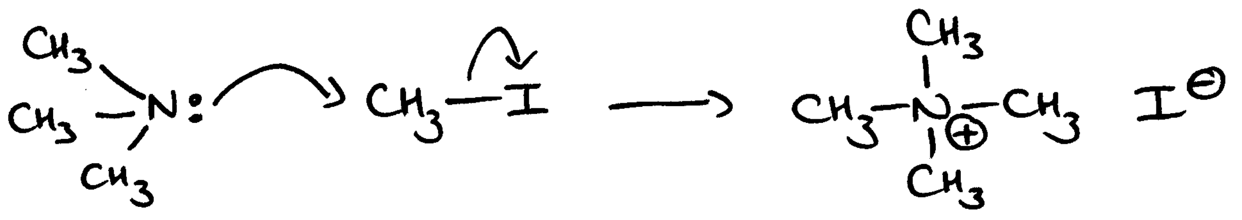
(Potassium carbonate)



(a) In the box below draw the mechanism showing how NH_3 reacts with CH_3–I in the presence of a carbonate base to give methylamine (CH_3–NH_2), i.e., the FIRST step of the sequence shown above – (show all intermediates, all appropriate lone pairs, formal charges, and curly arrows). (6 points)



(b) In the box below draw the mechanism showing how trimethylamine $(CH_3)_3N$ reacts with CH_3–I to give tetramethylammonium iodide $(CH_3)_4N^+I^-$, i.e., the LAST step of the sequence shown above – (show all intermediates, all appropriate lone pairs, formal charges, and curly arrows). (3 points)

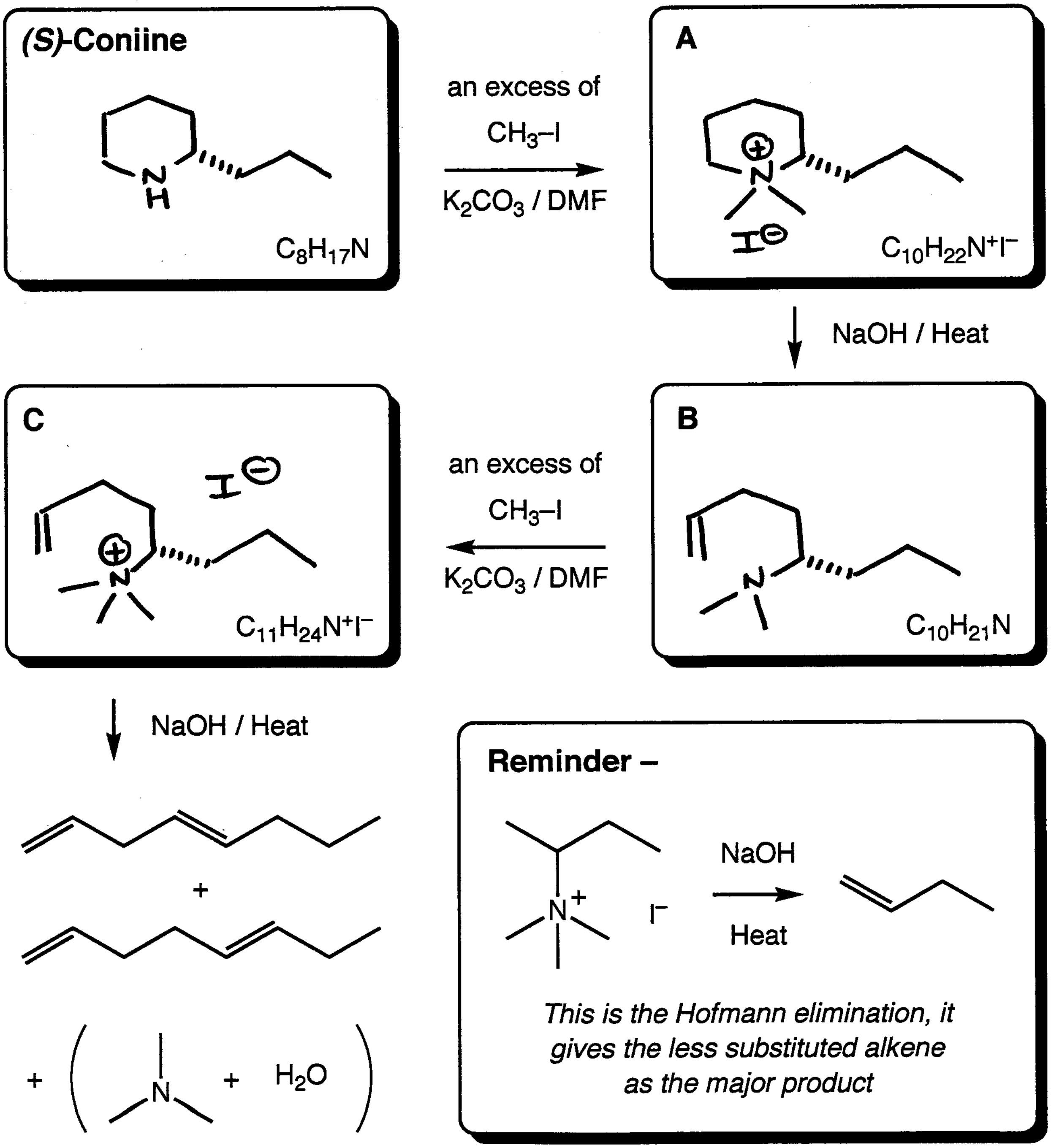


(c) Briefly comment upon the role of the carbonate base in the reaction – and suggest why it does not participate in the final step? (3 points)

CARBONATE BASE WILL REMOVE ANY ACIDIC PROTONS FROM THE NITROGEN ATOM, ALLOWING IT TO ACT FURTHER AS A NUCLEOPHILE. IN THE LAST STEP, THERE IS NO ACIDIC H ON N FOR THE CARBONATE TO ATTACK

Question 5 is continued on the next page...

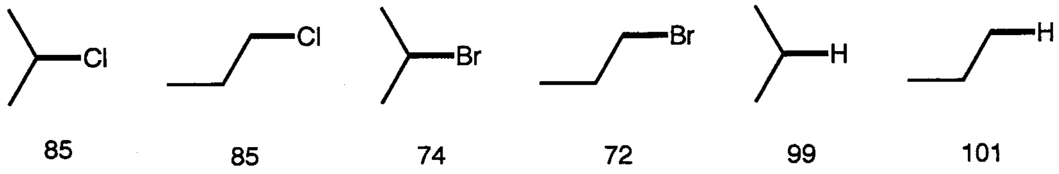
(d) *(S)*-Coniine is a toxic alkaloid found in the hemlock plant, and is most infamously associated with the death of Socrates – he was sentenced to death in 399 BC and made to drink a cup of hemlock juice. (*You can ignore this bit of trivia inside these parentheses if you wish... In man, 3 mg of coniine is said to have produced symptoms, but 15 mg have been tolerated without discomfort. Perhaps 30-60 mg is dangerous and death may occur with doses greater than 100 mg. It has been reported that a lethal dose may be 6 to 8 fresh leaves.*) When ***(S)*-coniine** ($C_8H_{17}N$) is treated with an excess of CH_3–I, a compound **A**, with the formula $C_{10}H_{22}N^+I^-$, is formed. When **A** is heated with NaOH, a Hofmann elimination occurs, giving A SINGLE COMPOUND (**B**), which has the formula $C_{10}H_{21}N$. When reacted with an excess of CH_3–I, **B** can be turned into compound **C**, with the formula $C_{11}H_{24}N^+I^-$. Finally, when **C** is heated with NaOH, a 1:1 mixture of 1,4-octadiene and 1,5-octadiene is produced, as well as the byproducts water and trimethylamine. Suggest structures for compounds **A**, **B**, and **C**, as well as for ***(S)*-coniine** – HINT: coniine contains only ONE stereocenter. (5 points each structure)



This is the Hofmann elimination, it gives the less substituted alkene as the major product

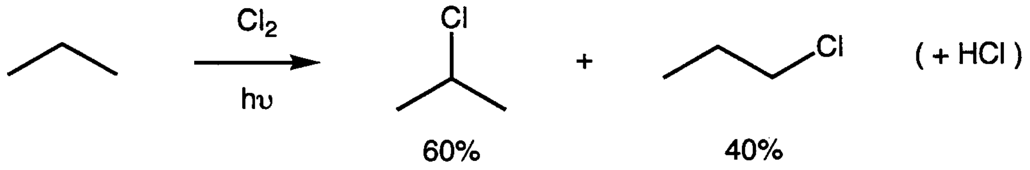
Q6. You may find the following bond dissociation values useful for answering this question –

Cl—Cl	H—Cl	Br—Br	H—Br
59	103	46	88

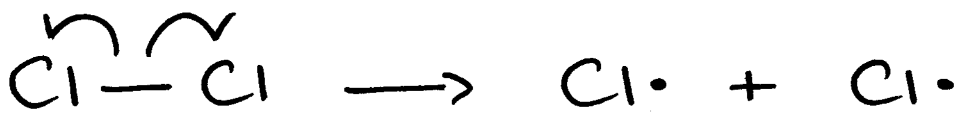


Numbers correspond to the Bond Dissociation Energy (BDE) in kcal/mol for the thicker bond in each structure

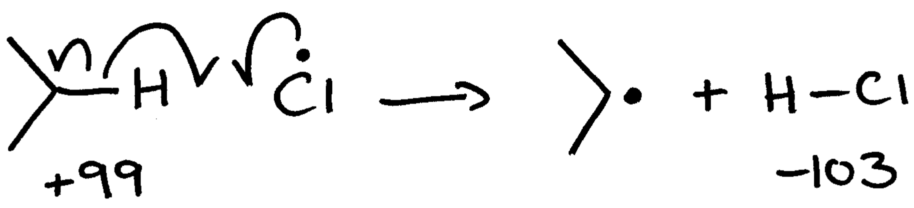
(a) The radical chlorination of propane (shown below) gives a mixture of 2-chloro- and 1-chloropropane. **IMPORTANT**: *The following questions about the mechanism of this reaction concern the MAJOR product (i.e., 2-chloropropane) of the reaction.*



This reaction begins with a CHAIN INITIATION STEP that creates radical species – in the box below, write down the mechanism for this first step of the reaction. (2 points)



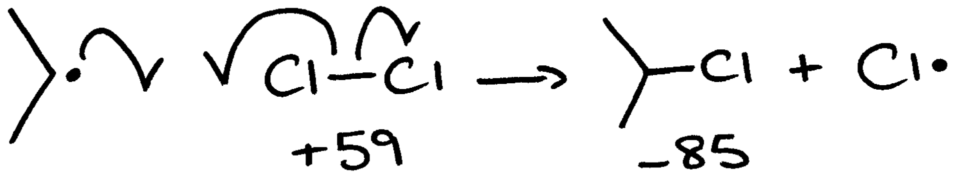
(b) After initiation, there are two CHAIN PROPAGATION steps that can happen many times over before a termination reaction occurs. The first chain propagation step is one in which a halogen radical abstracts an H atom from the alkane – this is the rate determining step (RDS) for the whole reaction. Write down the mechanism for this first PROPAGATION step, and using the values given at the top of this page, calculate the ΔH value for this process. (4 points mechanism, 2 points ΔH)



ΔH =
−4
kcal/mol

Question 6 is continued on the next page...

(c) The second CHAIN PROPAGATION step produces a molecule of the product, and regenerates a halogen radical. Write down the mechanism for this second PROPAGATION step, and using the values given at the top of this page, calculate the ΔH value for this process. (4 points mechanism, 2 points ΔH)



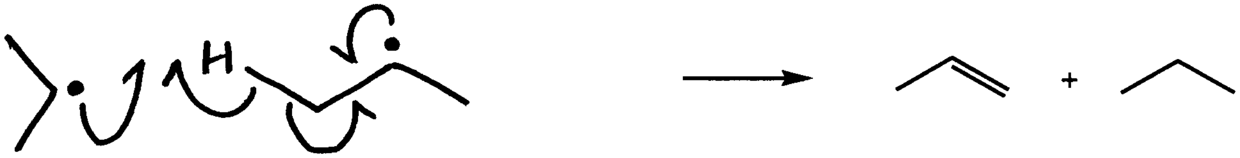
ΔH =
−26
kcal/mol

(d) The CHAIN REACTION continues until a CHAIN TERMINATION reaction occurs, in which radicals are consumed. Show the mechanisms for the TERMINATION reactions that lead to the three sets of products below. (2 points each)

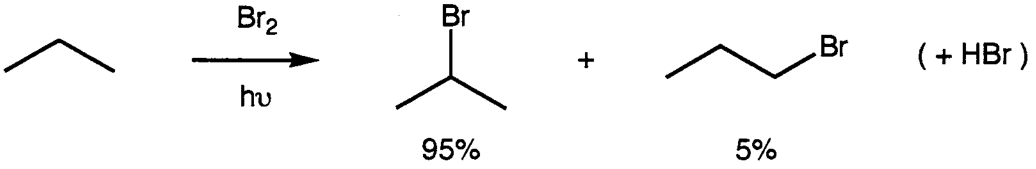
Termination mechanism #1

Termination mechanism #2

Termination mechanism #3

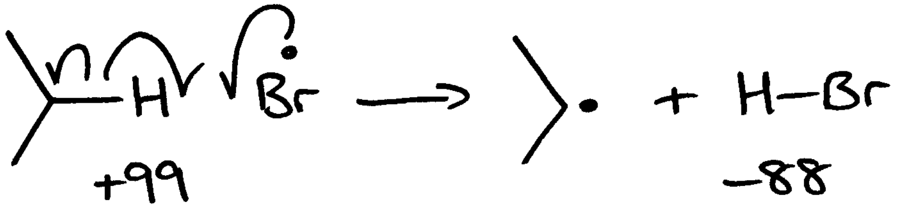


(e) The radical bromination of propane (shown below) gives a mixture of 2-bromo- and 1-brompropane. In this case, the regioselectivity is much more pronounced that in the case of chlorination, as 2-bromopropane is produced in over 95% yield.



Question 6 is continued on the next page...

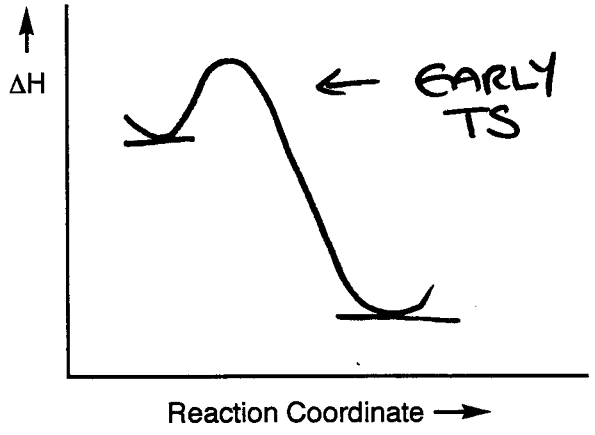
IMPORTANT: *The following questions about the mechanism of this reaction concern the MAJOR product (i.e., 2-bromopropane) of the reaction.* Just as you did in part (b) of this question for the analogous chlorination reaction, write down the mechanism for the first PROPAGATION step of this bromination reaction (the rate determing step), and using the values given at the beginning of this question, calculate the ΔH value for this process. (4 points mechanism, 2 points ΔH)



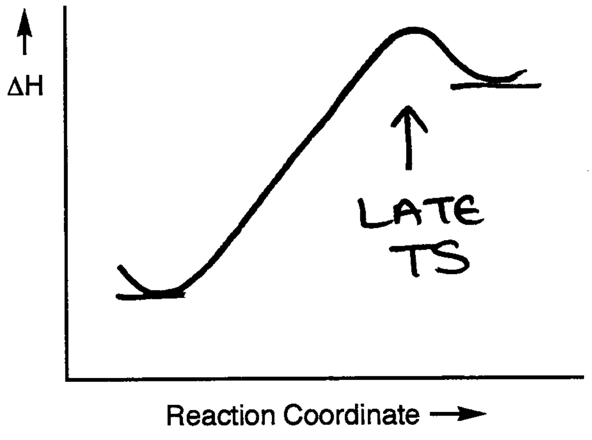
ΔH = +11 kcal/mol

(f) If you calculated everything correctly, you should notice that the ΔH change for the RDS of the bromination reaction is a POSITIVE number, whereas for the chlorination reaction it is a NEGATIVE number, i.e., it is an endothermic process for bromination, but an exothermic process for chlorination. Using your knowledge of the HAMMOND postulate, draw energy profiles for the rate determing steps of the chlorination and bromination reactions (*Note: don't draw profiles for the whole reaction, just for the RDS in each case*). In each case, label the transition state as either EARLY or LATE, and draw what you think the actual TS structure looks like in the box below. Finally, in the last box on this page, use your previous answers to explain why the regioselectivity is more significant for bromination. (14 points)

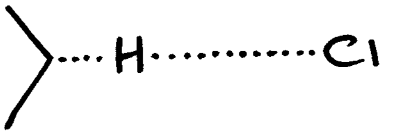
Chlorination



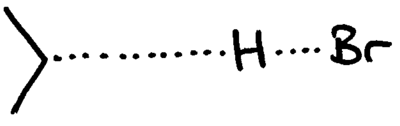
Bromination



Chlorination TS structure



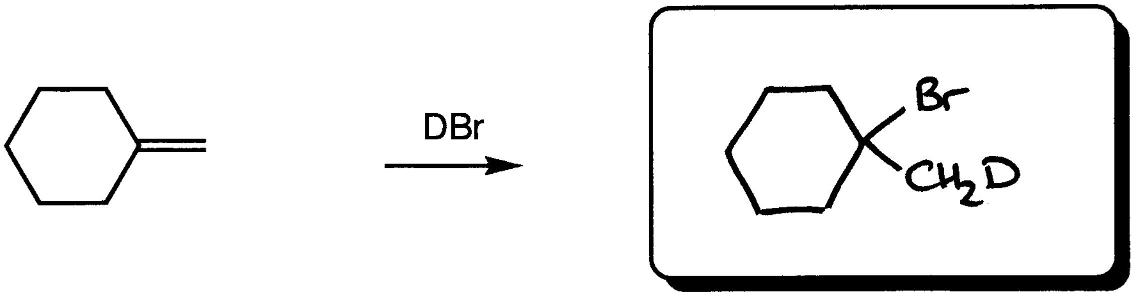
Bromination TS structure



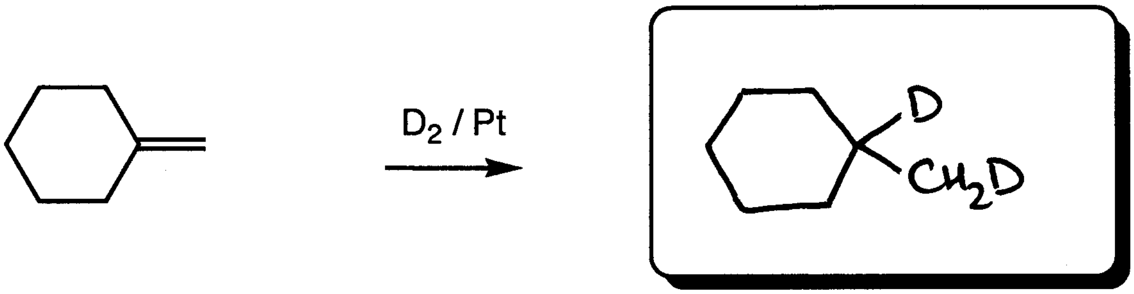
Regioselectivity? THE STABILITY OF THE RADICAL IS MUCH MORE REFLECTED IN THE BROMINATION TS THAN IN THE CASE OF CHLORINATION, SO GREATER STABILITY OF 2° VS 1° RADICALS IS REFLECTED IN PRODUCT DISTRIBUTION FOR Br_2

Q7. For each of the reactions shown below draw the MAJOR PRODUCT (paying particular attention to any appropriate stereochemical relationships) in the boxes provided. Note: for two-step reactions, just give the final product, DO NOT draw intermediates. (3 points each)

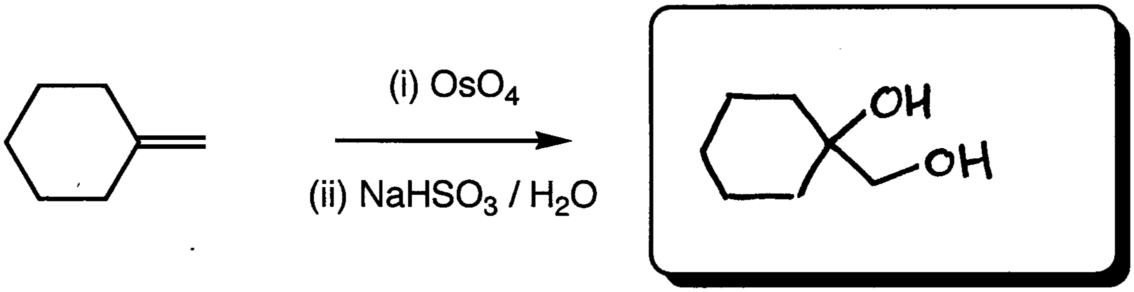
(a)



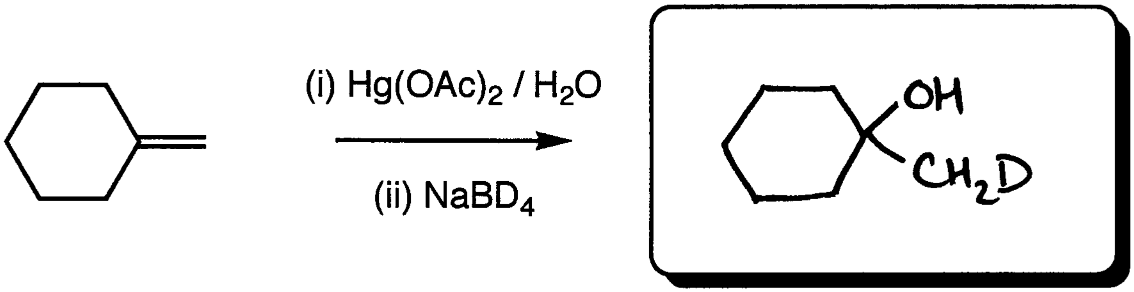
(b)



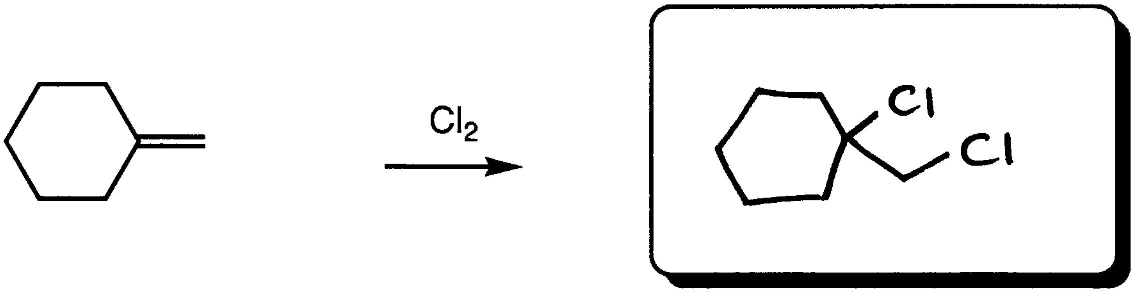
(c)



(d)

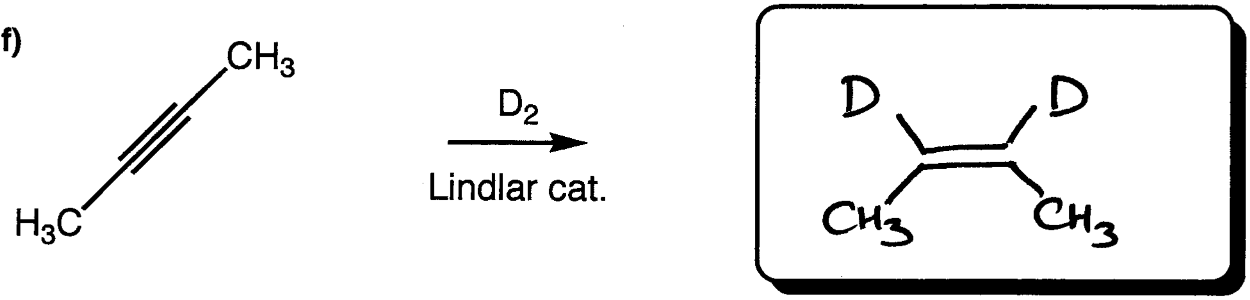


(e)

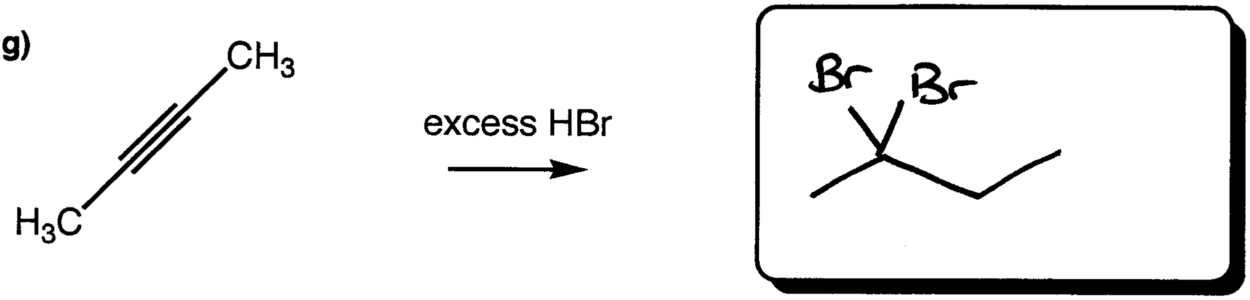


Question 7 is continued on the next page...

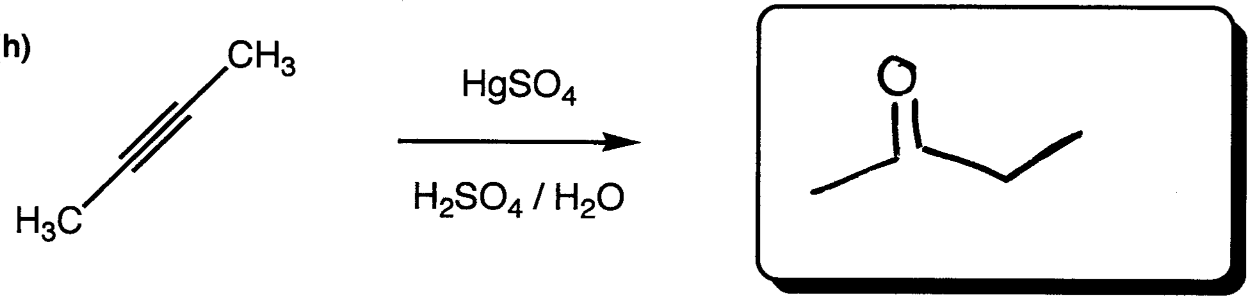
(f)


CH3
H3C
D2
Lindlar cat.
D
D
CH3
CH3

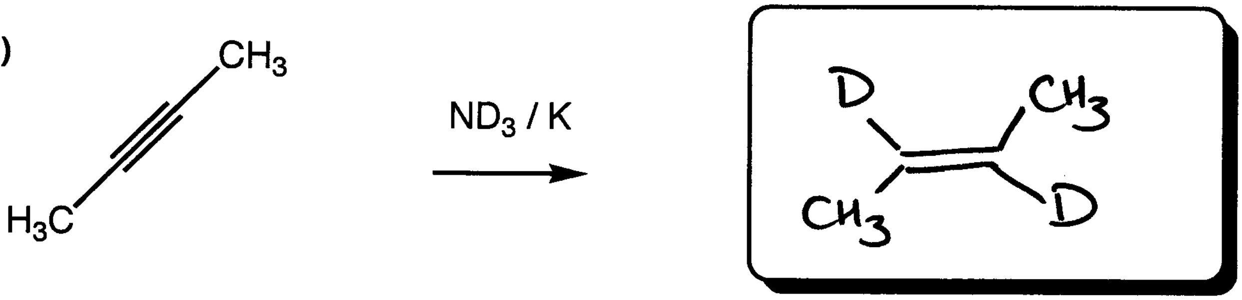
(g)


CH3
H3C
excess HBr
Br
Br

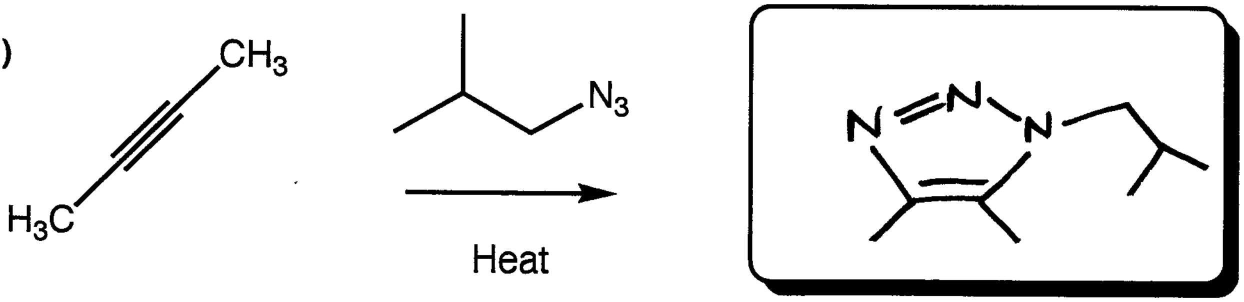
(h)


CH3
H3C
HgSO4
H2SO4 / H2O
O

(i)


CH3
H3C
ND3 / K
D
CH3
CH3
D

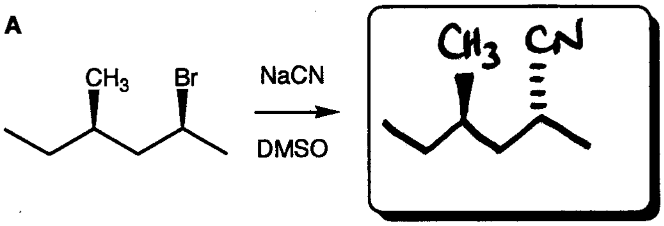
(j)


CH3
H3C
N3
Heat
N
N
N

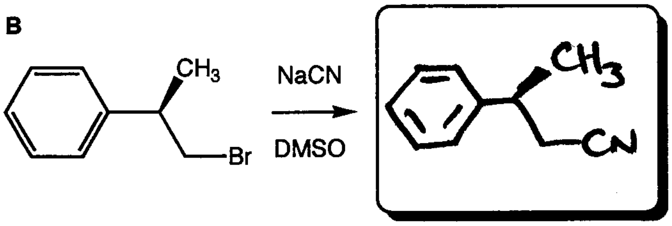
Q8. Answer the following questions about nucleophilic substitution reactions –

(a) Predict the products of the following S_N2 reactions – (3 points each)

A

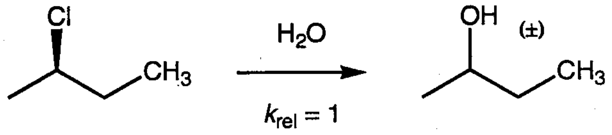


B

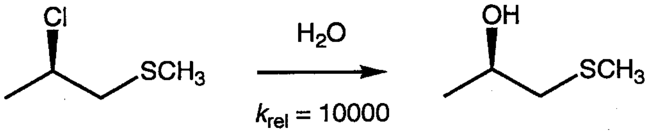


Consider the two reactions shown below, and then answer the following questions:

C



D

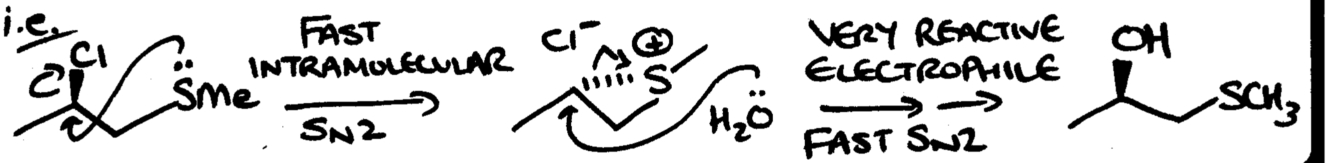


(b) Why is reaction **D** so much faster than reaction **C**? (4 points)

RXN C is a SLOW S_N1 REACTION ON A 2° SUBSTRATE

RXN D: NEIGHBORING GROUP PARTICIPATION – TWO FAST S_N2s

i.e.



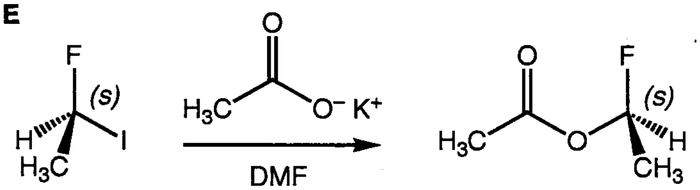
(c) Reaction **D** appears to proceed with retention (rather than inversion) of configuration – explain what is actually happening, and why does reaction **C** give a mixture of stereoisomers? (6 points)

C goes via CARBOCATION which is PLANAR → RACEMIZATION

D is actually a sequence of TWO S_N2 REACTIONS (see above), and so INVERSION FOLLOWED BY INVERSION = RETENTION

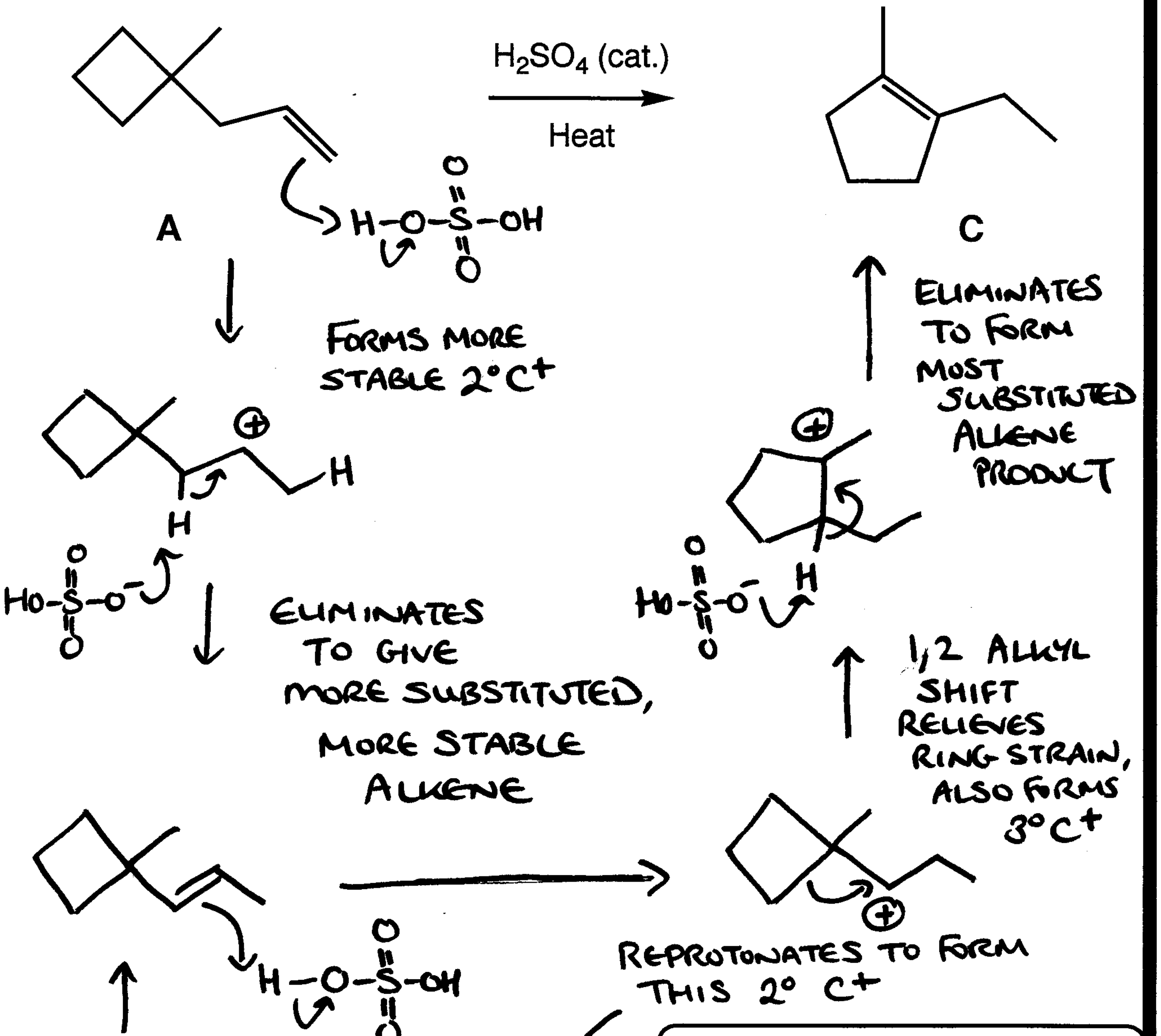
(d) Reaction **E** (below) also appears to proceed with retention (rather than inversion) of configuration – explain what is actually happening... (4 points)

E



INVERSION DOES OCCUR, BUT THE PRIORITIES ARE DIFFERENT IN THE PRODUCT, AND IT JUST HAPPENS TO BE (S) AS WELL!!

Q9. If heated with a catalytic amount of sulfuric acid, the cyclobutane derivative **A** rearranges into the cyclopentene derivative **C**. Propose a reasonable mechanism for this transformation and briefly explain each step with a few words – (show all intermediates, all appropriate lone pairs, formal charges, and curly arrows). HINT: An intermediate (**B**), with the same molecular formula as both **A** and **C**, is formed en route from **A** to **C**. *Your mechanism may NOT involve ANY 1,2-hydride shifts.* (20 points)



FORMS MORE STABLE 2° C+

ELIMINATES TO GIVE MORE SUBSTITUTED, MORE STABLE ALKENE

THIS IS B

REPROTONATES TO FORM THIS 2° C+

1,2 ALKYL SHIFT RELIEVES RING STRAIN, ALSO FORMS 3° C+

ELIMINATES TO FORM MOST SUBSTITUTED ALLENE PRODUCT

COULD FORM OTHER 2° C+, BUT YOU WOULD JUST GET BACK THE 1ST C+ YOU FORMED

Intermediate B