Last Name ANSWER	**First Name** KEY	**MI**	

Student ID Number:

Total Score 230 **/ 200**

Chem 30A Fall 2004

FINAL

(180 Min)

Fri Dec 17th

Course Grade A+

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

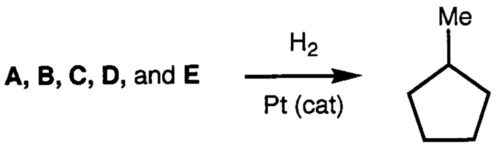
ONLY ANSWERS WRITTEN IN THE BOXES PROVIDED WILL BE GRADED

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

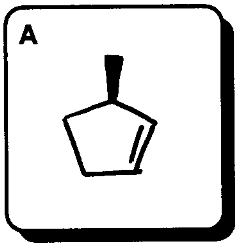
Q1	20 / 20	**Q4**	30 / 30	**Q7**	40 / 40
Q2	20 / 20	**Q5**	20 / 20	**Q8** **BONUS**	15 / 15
Q3	40 / 40	**Q6**	30 / 30	**Q9** **BONUS**	15 / 15
				Total	230 / 200

"ATTEMPTED murder, what is that!? Do they give a Nobel Prize for ATTEMPTED chemistry? Well, do they?!" - Sideshow Bob

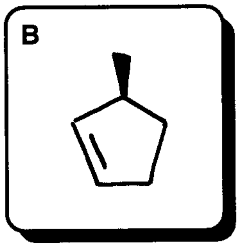
Q1. Five different cycloalkenes (**A–E**), each with the molecular formula C_6H_{10}, will yield methylcyclopentane when subjected to catalytic hydrogenation (H_2/Pt catalyst) – as shown below.



(**a**) Two of these cycloalkenes constitute a pair of enantiomers; the absolute configuration of the stereogenic center in compound **A** is (*R*) and in **B** it is (*S*). Draw these compounds below. (2 points each)



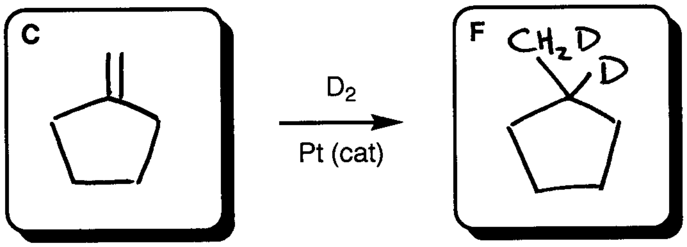
(R)-Isomer



(S)-Isomer

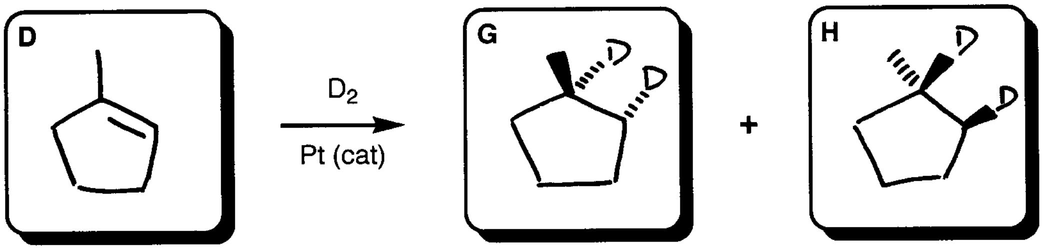
(**b**) The other three cycloalkenes (**C**, **D**, and **E**) are achiral, but when hydrogen gas (H_2) is replaced by deuterium gas (D_2), different results are observed. (2 points for each structure **C–J**)

(i) Compound **C** reacts to form a single product (**F**) – draw these compounds below:



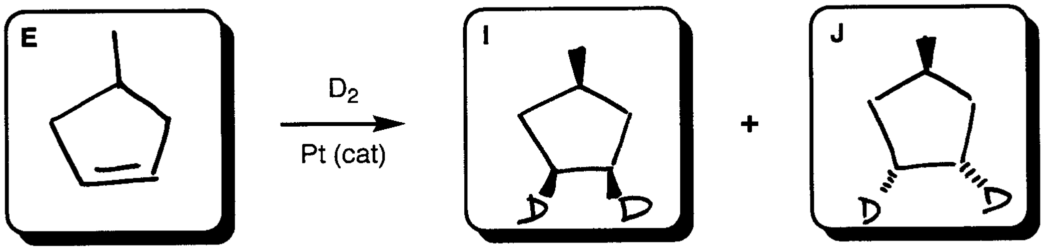
Single Compound

(ii) Compound **D** reacts to form a pair of enantiomers (**G** & **H**) – draw these compounds below:



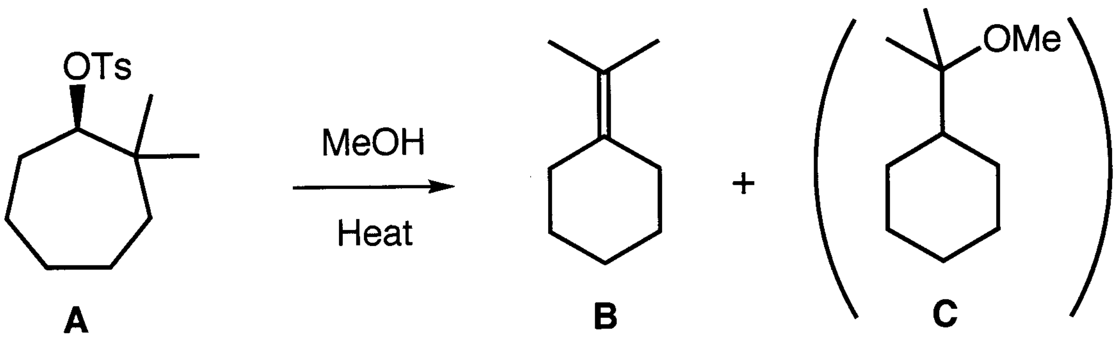
Enantiomers

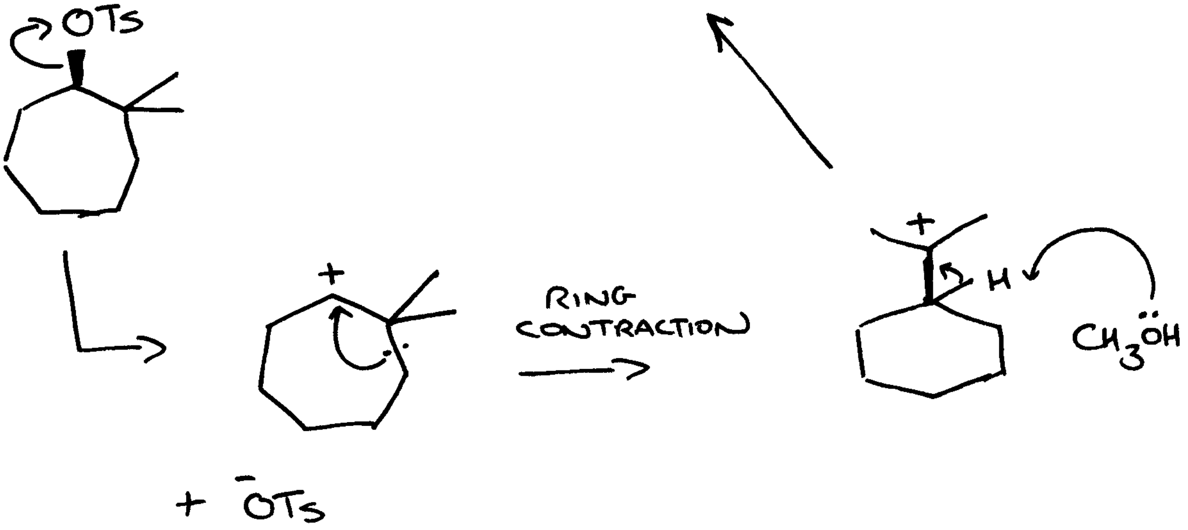
(iii) Compound **E** reacts to form a pair of diastereoisomers (**I** & **J**) – draw these compounds below:



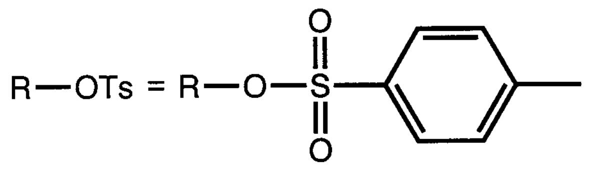
Diastereoisomers

Q2. **(a)** When the tosylate derivative **A** is heated in a methanol solution, compounds **B** and **C** are formed. Propose a reasonable mechanism that accounts for the transformation of compound **A** into compound **B** – SHOW ALL STEPS. (10 points)





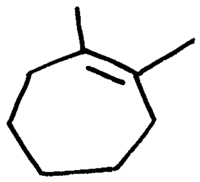
(E1 MECHANISM,
SN1 COMPETES)



Question 2 is continued on the next page...

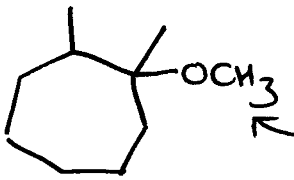
(b) This reaction also yields many compounds that retain seven-membered ring structures. (i) Draw the structure of the MOST ABUNDANT seven-membered ring-containing alkene (**D**) formed in this reaction, and circle the mechanism responsible for forming this product. (ii) Draw the structure of the MOST ABUNDANT seven-membered ring-containing methyl ether (**E**) formed in this reaction, and circle the mechanism responsible for forming this product. (2 + 1/2 points each)

D



Mechanism: S_N1 [✓ E1] S_N2 E2

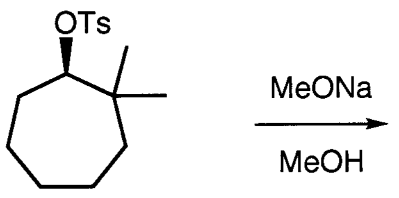
E



mixture of four stereoisomers

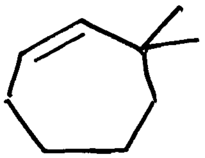
Mechanism: [✓ S_N1] E1 S_N2 E2

(c) When the reaction conditions are changed, and tosylate **A** is reacted with sodium methoxide in methanol, yet another different product (F) is formed. Draw the structure of this product, and circle the mechanism responsible for its formation? (2 + 1/2 points)



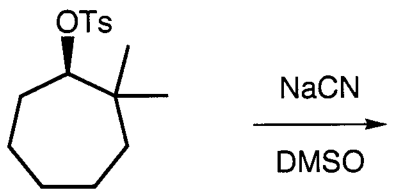
A

F



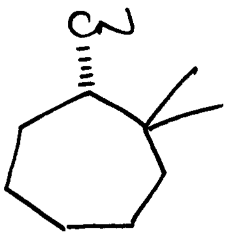
Mechanism: S_N1 E1 S_N2 [✓ E2]

(d) When tosylate **A** is reacted with sodium cyanide in dimethyl sulfoxide (DMSO), product **G** is formed. Draw the structure of this product, and circle the mechanism responsible for its formation? (2 + 1/2 points)



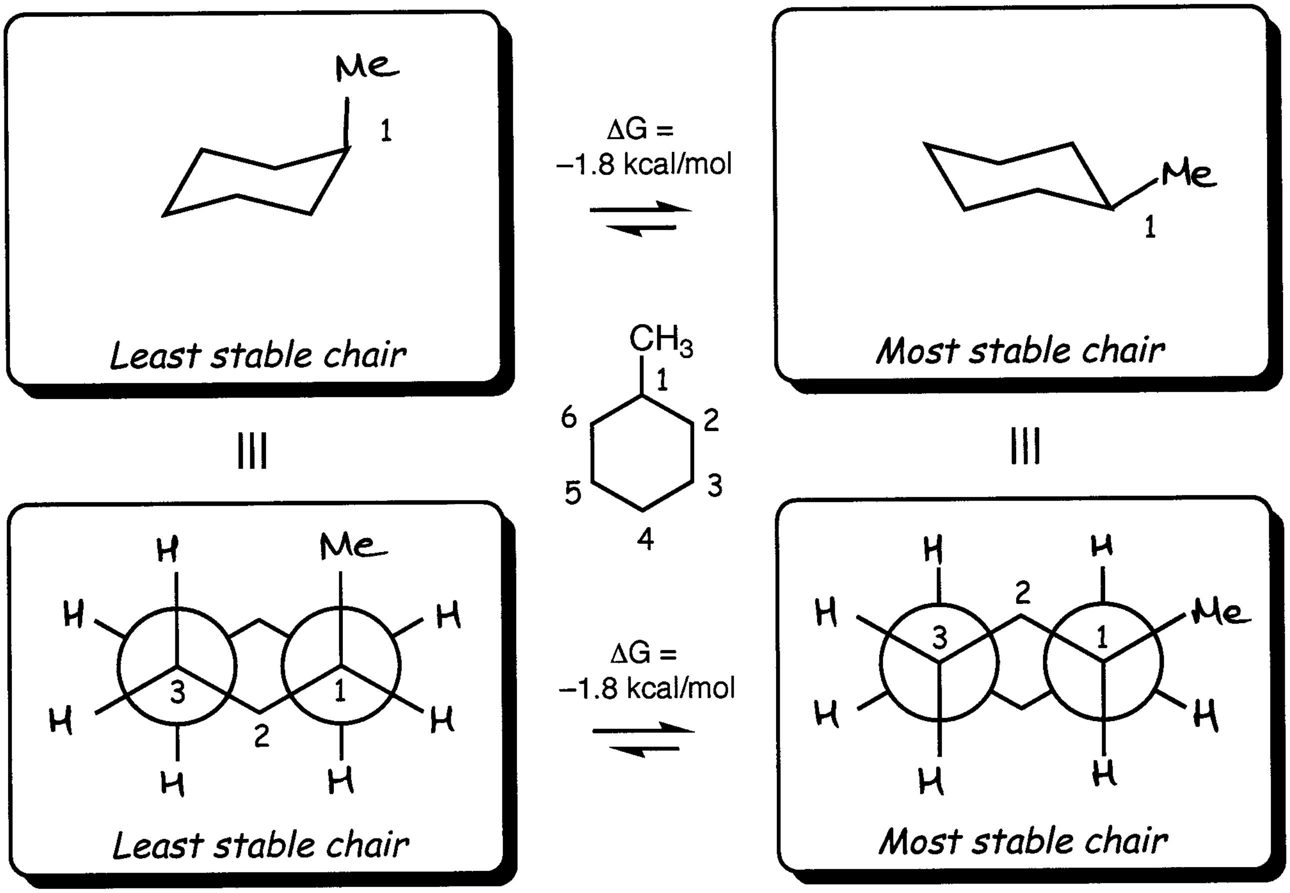
A

G

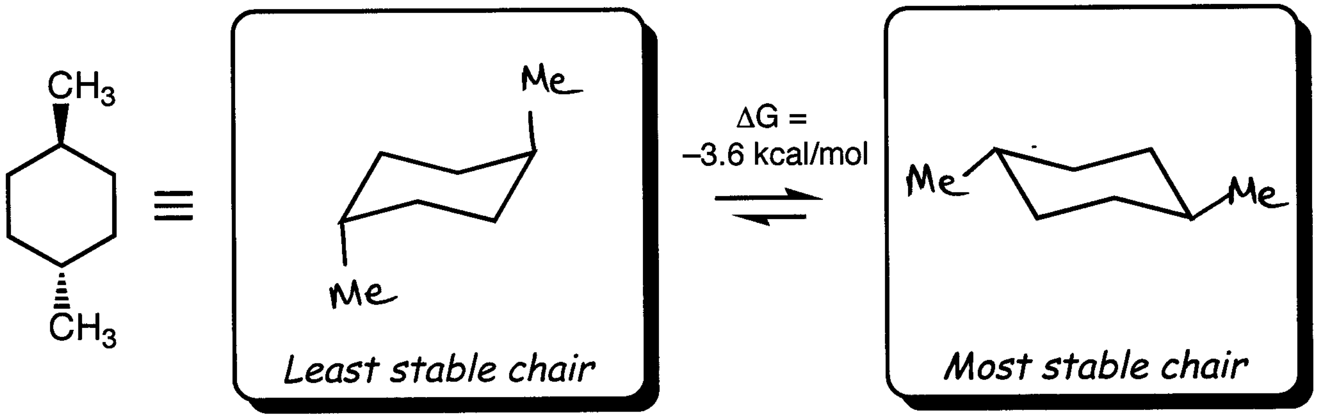


Mechanism: S_N1 E1 [✓ S_N2] E2

Q3. **(a)** Methylcyclohexane (shown in the middle below) can exist in two different chair conformations, one of which is 1.8 kcal/mol more stable than the other. In each of the top two boxes below, draw in a bond to one methyl (Me) group in the appropriate position. In the bottom two boxes, complete the Newman projections by filling in methyl (Me) groups AND hydrogen atoms (H) where appropriate. (4 points)

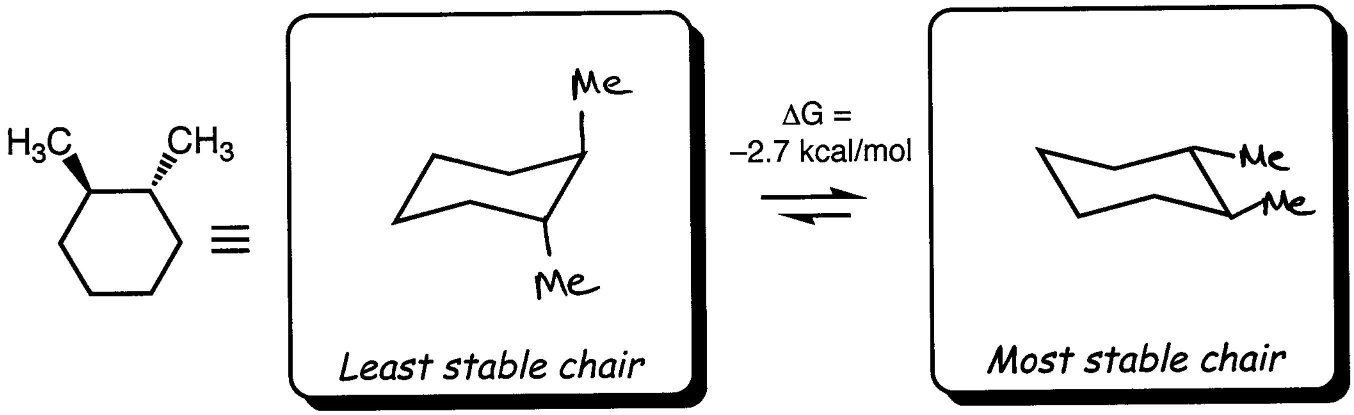


(b) *trans*-1,4-Dimethylcyclohexane (shown below) also exists in two different chair conformations, one of which is **3.6 kcal/mol** more stable than the other. In each of the boxes below, draw in methyl (Me) groups in the appropriate positions. (4 points)



Question 3 is continued on the next page...

(c) *trans*-1,2-Dimethylcyclohexane (shown below) also exists in two different chair conformations, one of which is **2.7 kcal/mol** more stable than the other. In each of the boxes below, draw in methyl (Me) groups in the appropriate positions. (4 points)

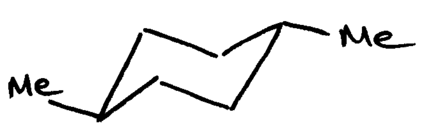


(d) In the box below, explain (using appropriate diagrams if you wish), why the difference in energy between the two chair conformations of *trans*-1,2-dimethylcyclohexane is **0.9 kcal/mol** LESS than the difference in energy between the two chair conformations of *trans*-1,4-dimethylcyclohexane. (8 points)

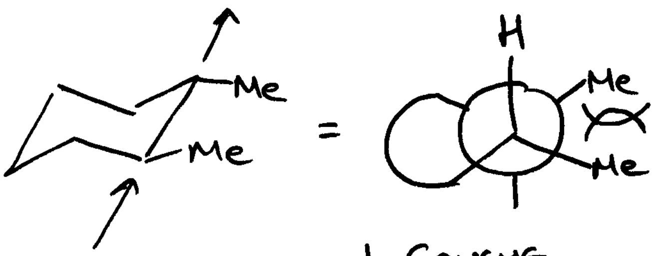
THE DIAXIAL CONFORMERS OF THE 1,2 AND 1,4 ISOMERS ARE EQUALLY BAD - EACH HAS TWO AXIAL METHYL GROUPS, HENCE THERE ARE 4 BUTANE GAUCHE INTERACTIONS.

NOW CONSIDER THE DIEQUATORIAL CONFORMERS:

1,4



BUT



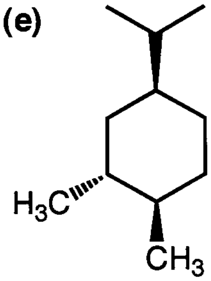
NO GAUCHE INTERACTIONS,

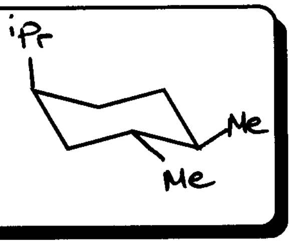
1 GAUCHE INTERACTION, SO DESTABILIZES BY 0.9 KCAL/MOL.

Question 3 is continued on the next page...

For each of the questions below (**e–h**) draw the most stable chair conformation for each compound, and in each case give a succinct reason for your choice. (*Hint: the answers aren't perhaps as easy as you may think they are...*) (2 + 2 points each)

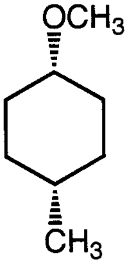
(e)

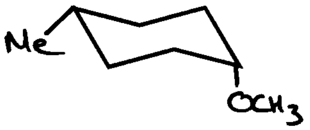




reason:
'A' value for ^{i}Pr, is not much larger than for Me, so better to have two methyls equatorial and one ^{i}Pr axial than vice-versa

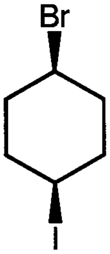
(f)

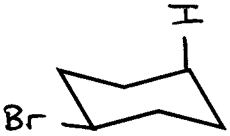




reason:
OCH_3 group can swing away from the ring, and so has less diaxial interactions than an Me group. 'Lone pair vs 'H' into ring

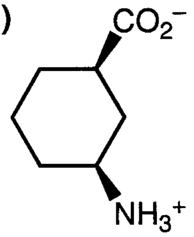
(g)

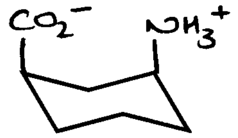




reason:
'I' is bigger than 'Br', but the C–I bond is longer, and so there are less 1,3 diaxial interactions with C–I than C–Br.

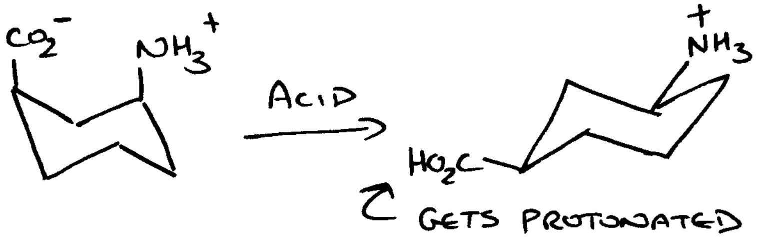
(h)





reason:
The diaxial interactions are bad, but the electrostatic attraction of opposite charges are enough to overcome this.

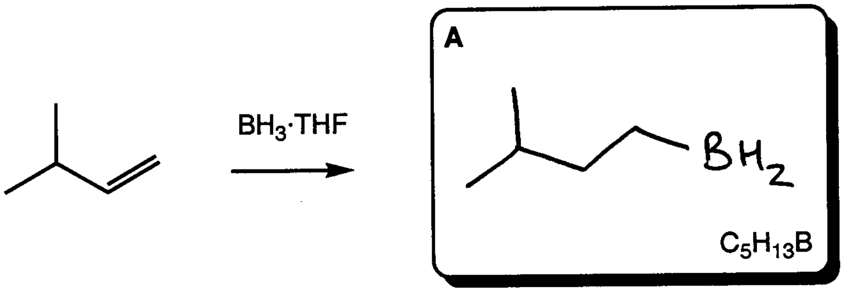
(**i**) When the compound in part (**h**) is treated with a strong acid, a new compound is formed. Draw the most stable chair conformation of this new product and justify your choice (4 points)



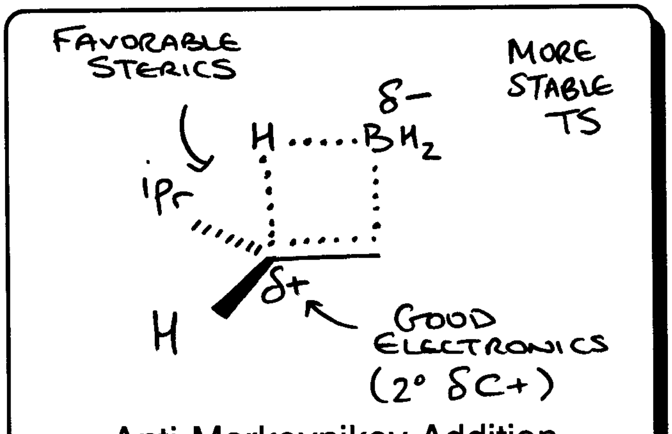
NO LONGER ANY ELECTROSTATIC ATTRACTION TO OVERCOME BAD STERICS - DIEQUATORIAL IS FAVORED

Q4. Consider the reaction of 3-methyl-1-butene with borane·THF (BH_3·THF):

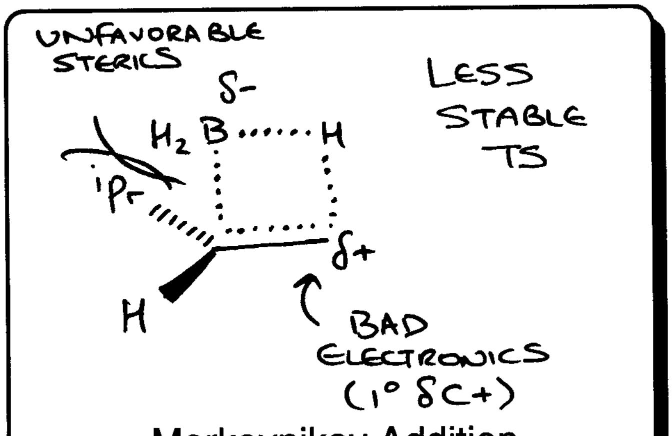
(**a**) The very first step of the reaction proceeds regioselectively to give one major product (**A**) with the molecular formula $C_5H_{13}B$. Draw the structure of **A** in the box below. (2 points)



(**b**) Draw and briefly annotate (with a few words) the transition states that would lead to Markovnikov and anti-Markovnikov addition of BH_3 in the reaction shown above. Indicate how both steric and electronic effects influence the observed regioselectivity in the hydroboration of such unsymmetrical alkenes. Note: Just drawing the transition states WILL NOT earn you full credit, you must indicate how the electronics and/or sterics either stabilize or destabilize each transition state structure. (10 points)

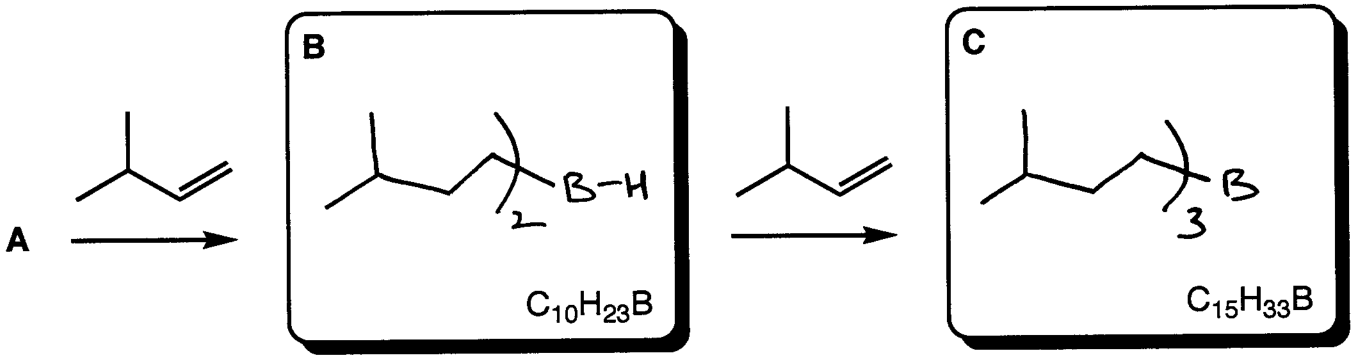


Anti-Markovnikov Addition



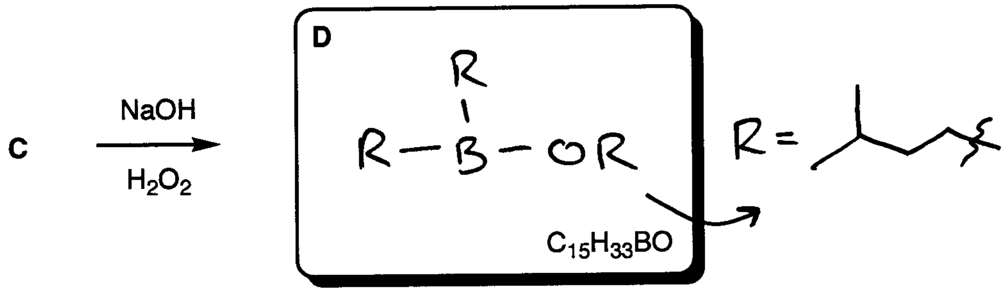
Markovnikov Addition

(**c**) Compound **A** can react with another equivalent of 3-methyl-1-butene to give compound **B**, which can also react with another equivalent of 3-methyl-1-butene to give compound **C**. Draw compounds **B** and **C** in the boxes below (their molecular formulas are given to you). (4 points)

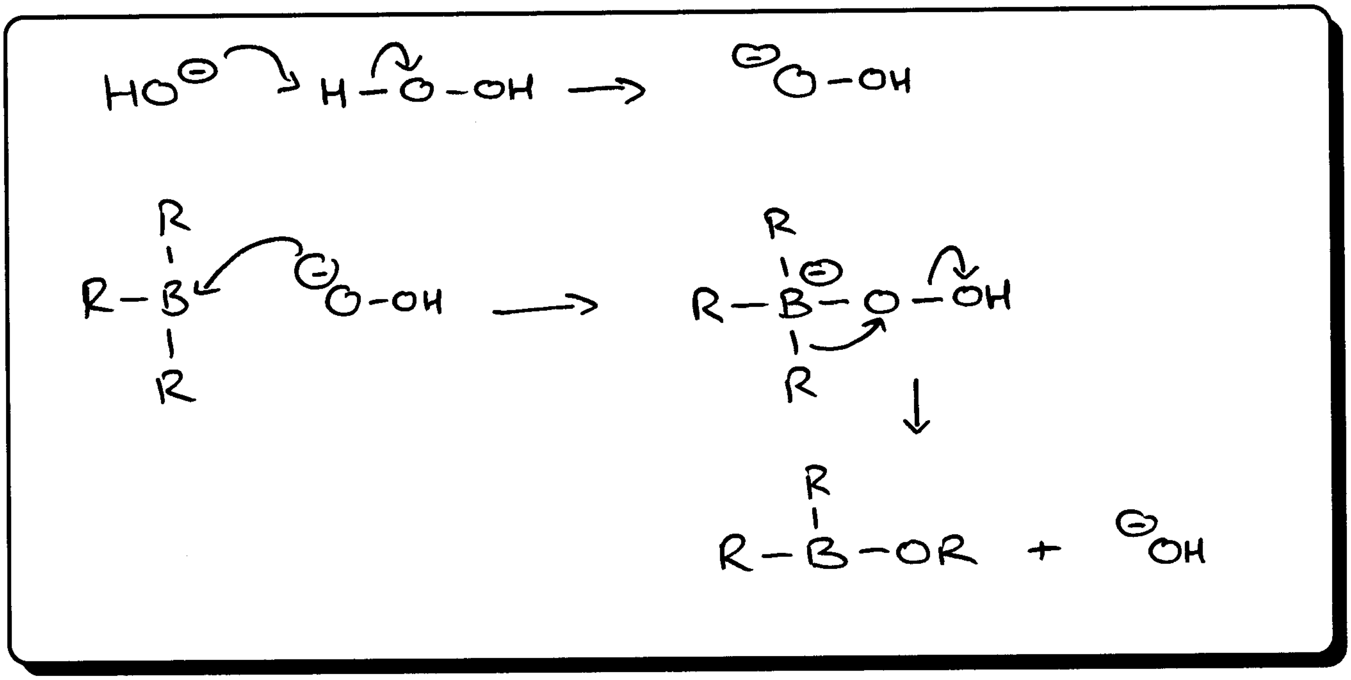


Question 4 is continued on the next page...

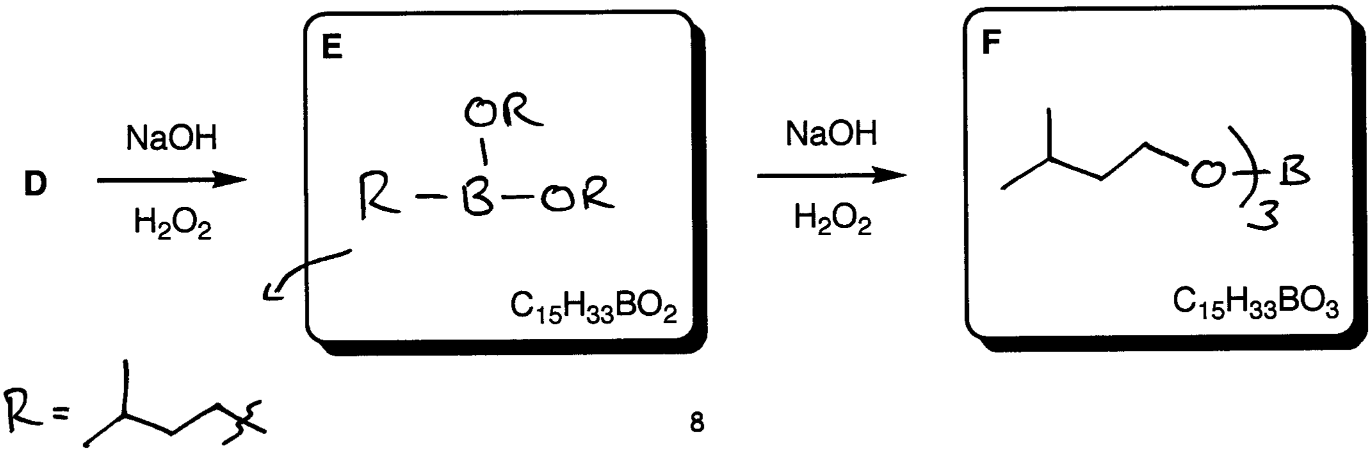
(d) When compound C is reacted with sodium hydroxide and hydrogen peroxide, the first product to be formed (**D**) is one in which ONE oxygen atom has been inserted into the structure. Draw compound **D** in the box below: (2 points)



(e) In the box below, propose a reasonable mechanism that accounts for the transformation of compound **C** into compound **D**: (8 points)

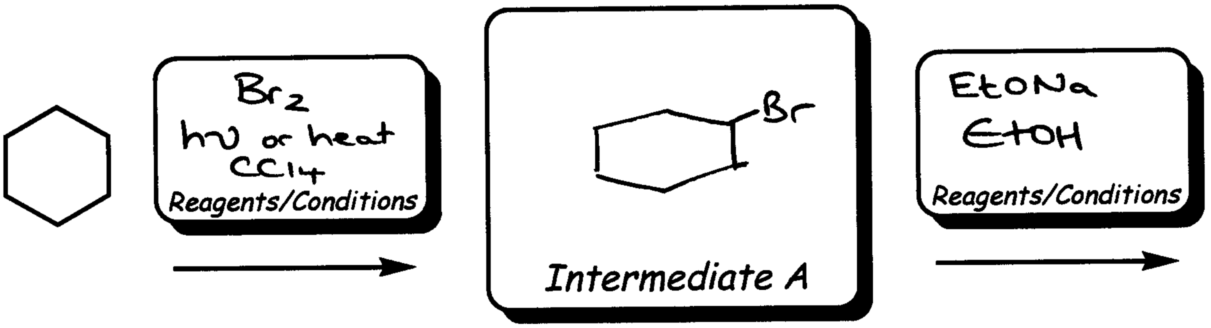


(f) Compound **D** can react further with NaOH/H_2O_2 to give compound **E**, which can also react again to give compound **F**. Draw compounds **E** and **F** in the boxes below (their molecular formulas are given to you). (4 points)

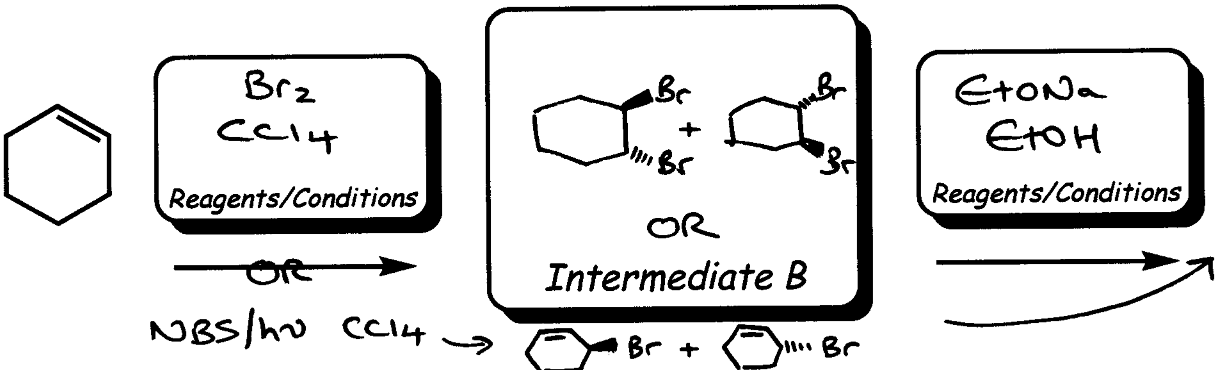


Q5. Shown below is a stepwise synthesis that could be used to turn cyclohexane into benzene (in reality you can do it in one step with chemistry you have not learned yet, but what fun would that be?). In each case, identify the intermediate(s) and the reagents/conditions necessary to bring about each transformation.

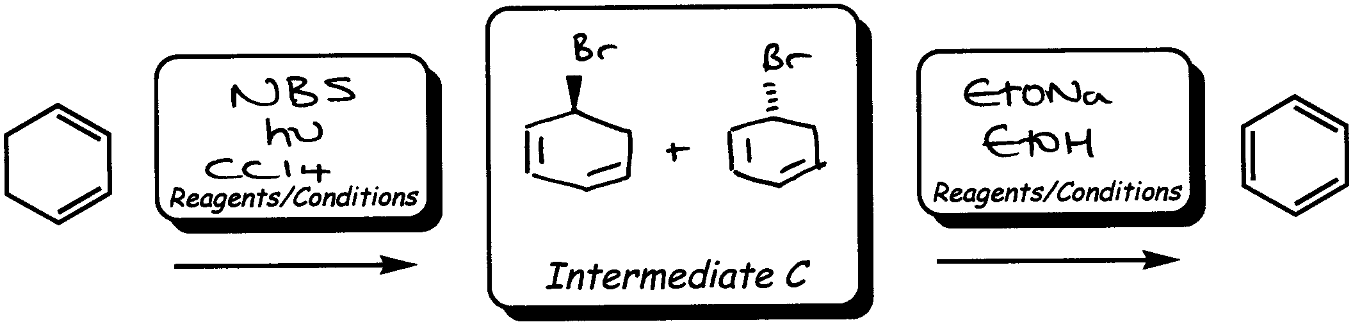
(a) Cyclohexane can be reacted to give an intermediate compound **A**, which can then undergo a reaction to form cyclohexene. In the middle box below, draw the structure of **A**, and show what reagents and conditions are necessary to achieve each of the two transformations. (6 points)



(b) Cyclohexene can be reacted to give an intermediate compound **B** (as a racemic mixture), both enantiomers of which can then undergo a reaction to form 1,3-cyclohexadiene. In the middle box below, draw **BOTH** enantiomers of **B**, and show what reagents and conditions are necessary to achieve each of the two transformations. (7 points)



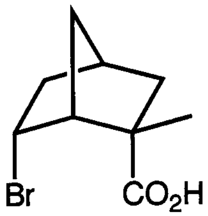
(c) 1,3-Cyclohexadiene can be reacted to give an intermediate compound **C** (as a racemic mixture), both enantiomers of which can then undergo a reaction to form benzene. In the middle box below, draw **BOTH** enantiomers of **C**, and show what reagents and conditions are necessary to achieve each of the two transformations. (7 points)



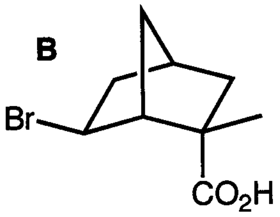
* OTHER STRONG BASES WOULD WORK IN EACH SECOND STEP ABOVE.

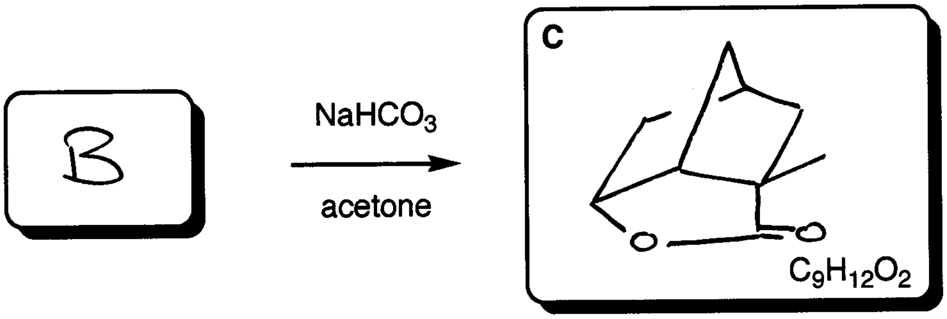
Q6. **(a)** Shown below are two diastereoisomeric compounds, **A** and **B**. When treated with a weak base such as sodium hydrogen carbonate ($NaHCO_3$), only one of them will react to form a new product (**C**). Draw the structure of **C** (you are given its molecular formula), and in the small box to the left, indicate which compound (**A** or **B**) undergoes the reaction. (1 + 4 points)

A

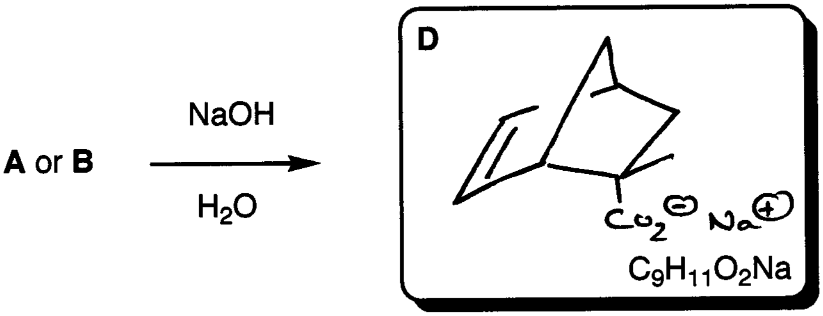


B





(b) In contrast, however, both compounds **A** and **B** will react with aqueous sodium hydroxide to give the SAME PRODUCT (**D**). Draw the structure of **D** in the box below – you are given its molecular formula. (3 points)

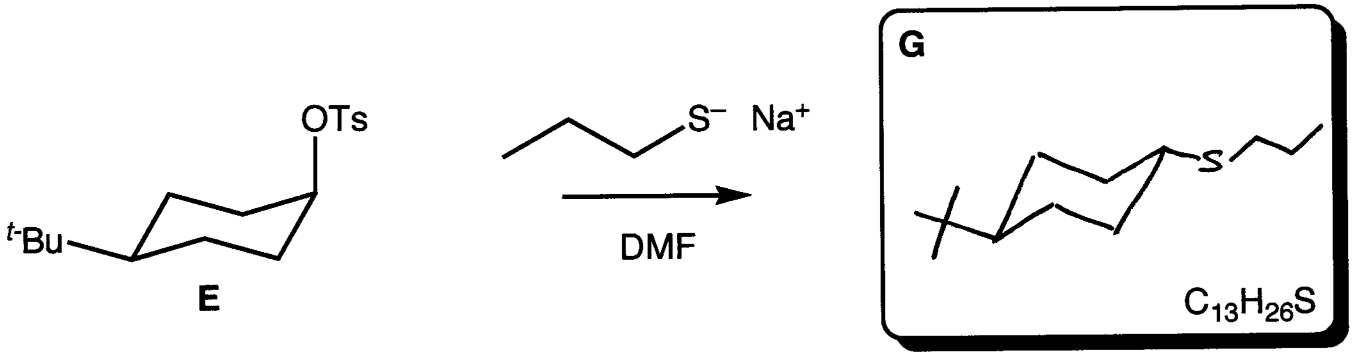


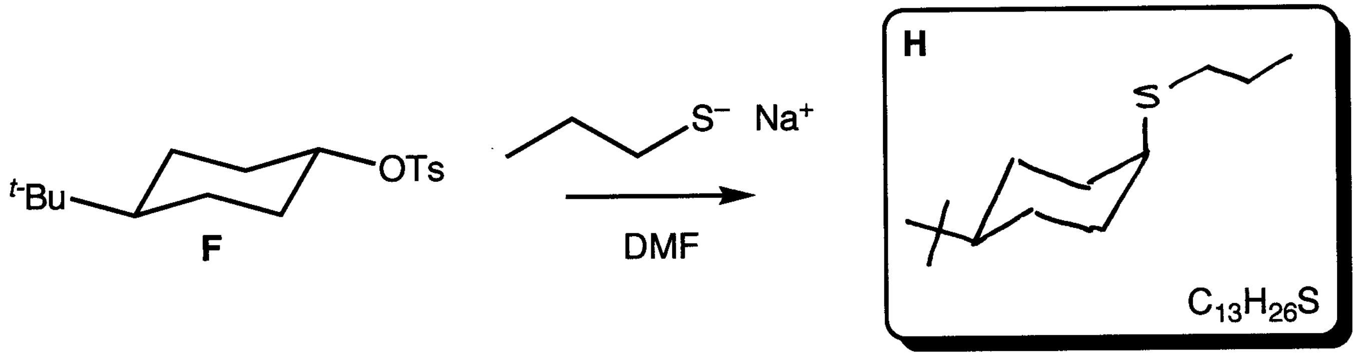
(c) Explain, in no more than two sentences, your answers to parts **(a)** and **(b)** of this question. (6 points)

- ONLY S_N2 will happen with B, as backside attack is required (if it was an S_N1 mechanism, both A and B would have reacted)
- BOTH A and B will eliminate in the presence of a STRONG BASE to give the NON-BRIDGEHEAD ALKENE (probably an E2 SYN ELIMINATION)

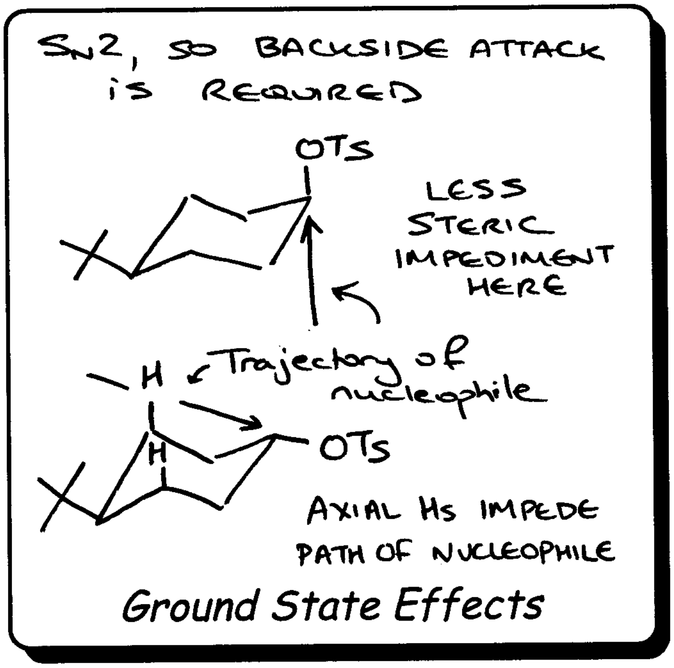
Question 6 is continued on the next page...

(d) The reaction of the *cis*-4-*t*-butylcyclohexytosylate (**E**) with the sodium salt of propanethiol in dimethylformamide (DMF) yields a compound (**G**) with the molecular formula $C_{13}H_{26}S$. Similarly, the reaction of the *trans*-4-*t*-butylcyclohexytosylate (**F**) results in a different compound (**H**) with the molecular formula $C_{13}H_{26}S$. Draw the structures of compounds **G** and **H** in the appropriate boxes below. (6 points)





(e) The reaction of **E** to give **G** is over 30 times faster than the reaction of **F** to give **H**. Rationalise this observation in terms of both ground state considerations (how the reactants interact) and transition state geometries. (10 points)



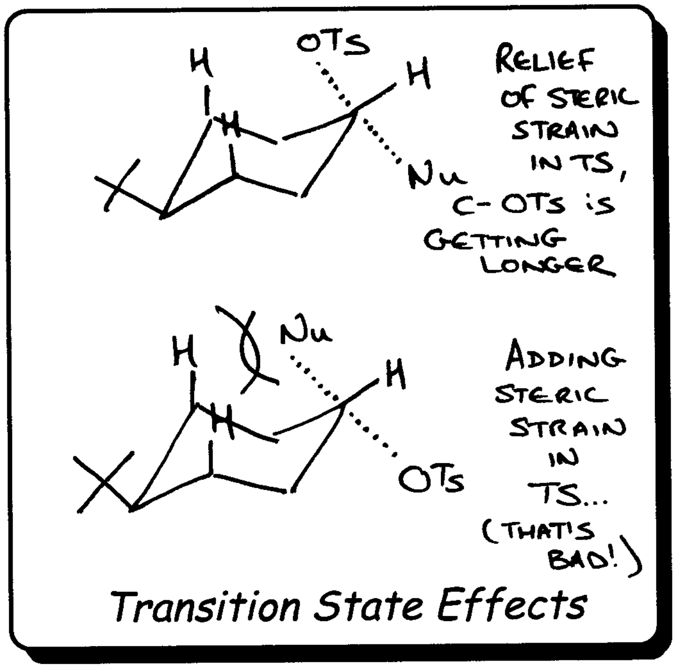
S_N2, SO BACKSIDE ATTACK IS REQUIRED

LESS STERIC IMPEDIMENT HERE

Trajectory of nucleophile

AXIAL Hs IMPEDE PATH OF NUCLEOPHILE

Ground State Effects



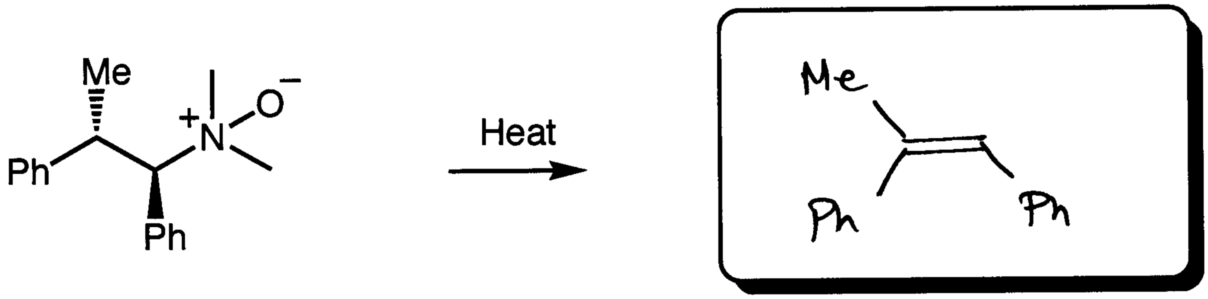
RELIEF OF STERIC STRAIN IN TS, C-OTs IS GETTING LONGER

ADDING STERIC STRAIN IN TS... (THAT'S BAD!)

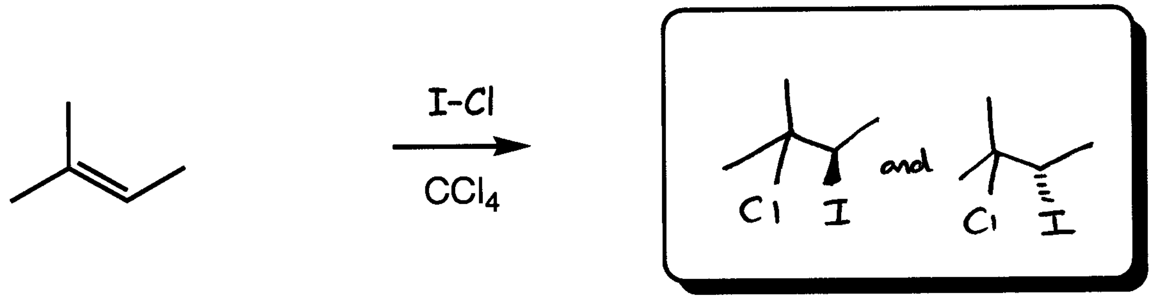
Transition State Effects

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. Some of these reactions yield a pair of enantiomers, and in these cases, draw both of them. (40 points)

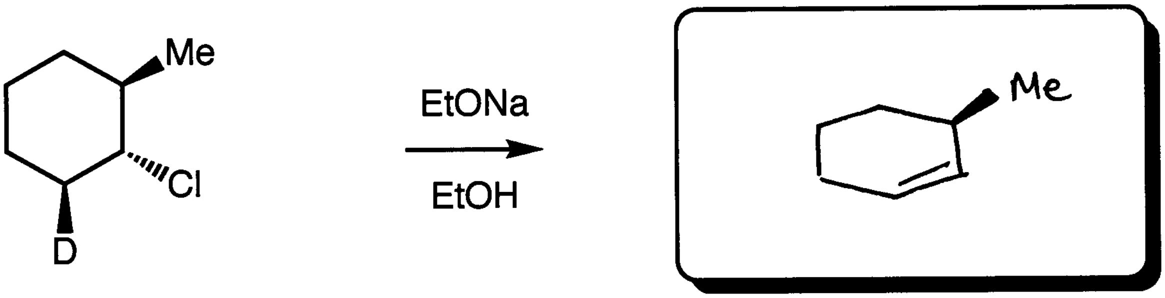
(a)



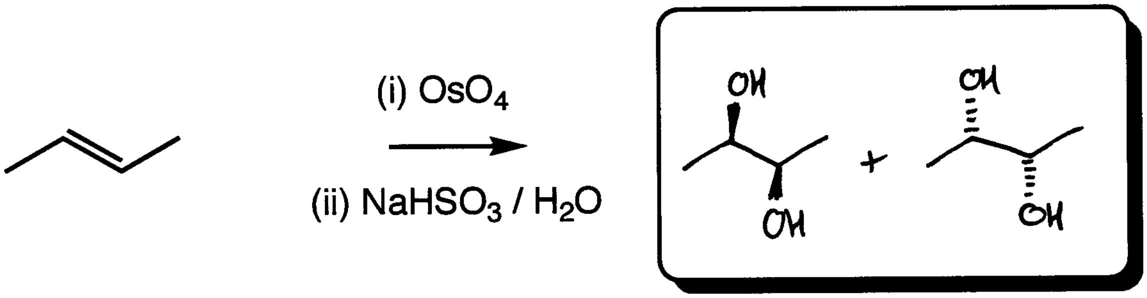
(b)



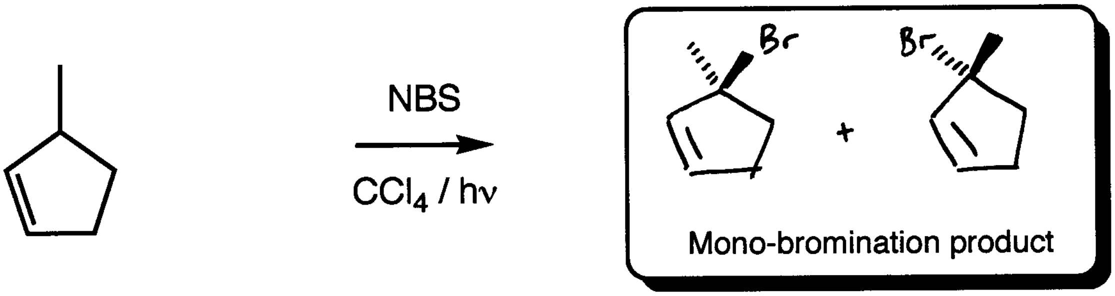
(c)



(d)

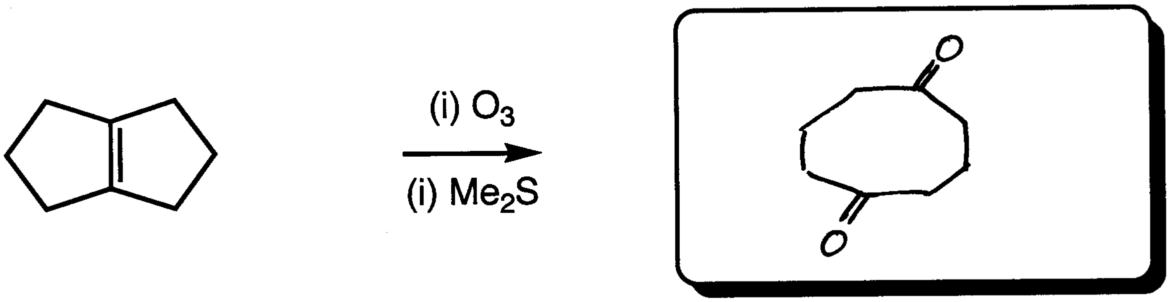


(e)

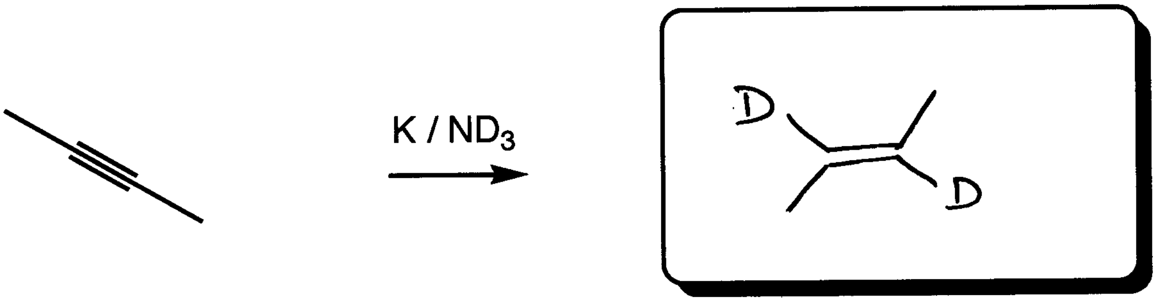


Question 7 is continued on the next page...

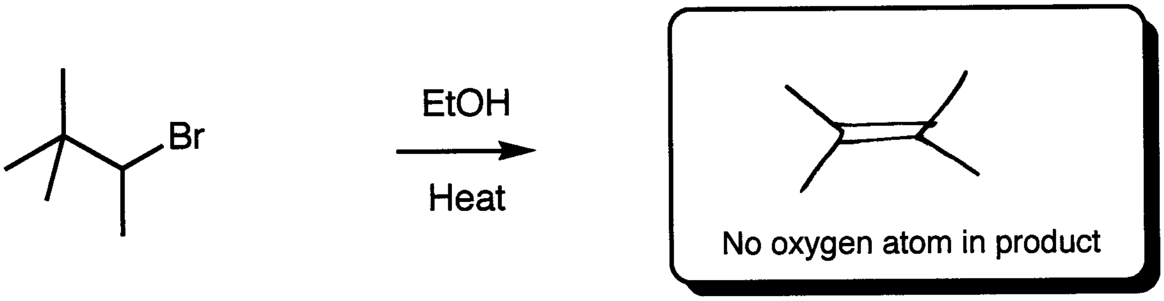
(f)



(g)

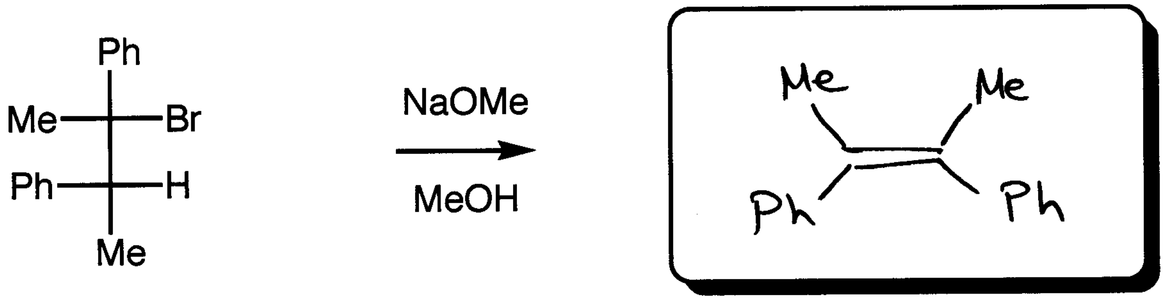


(h)

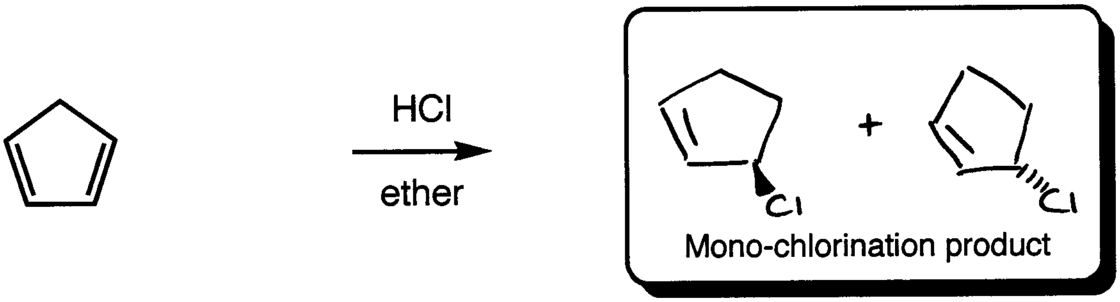


No oxygen atom in product

(i)

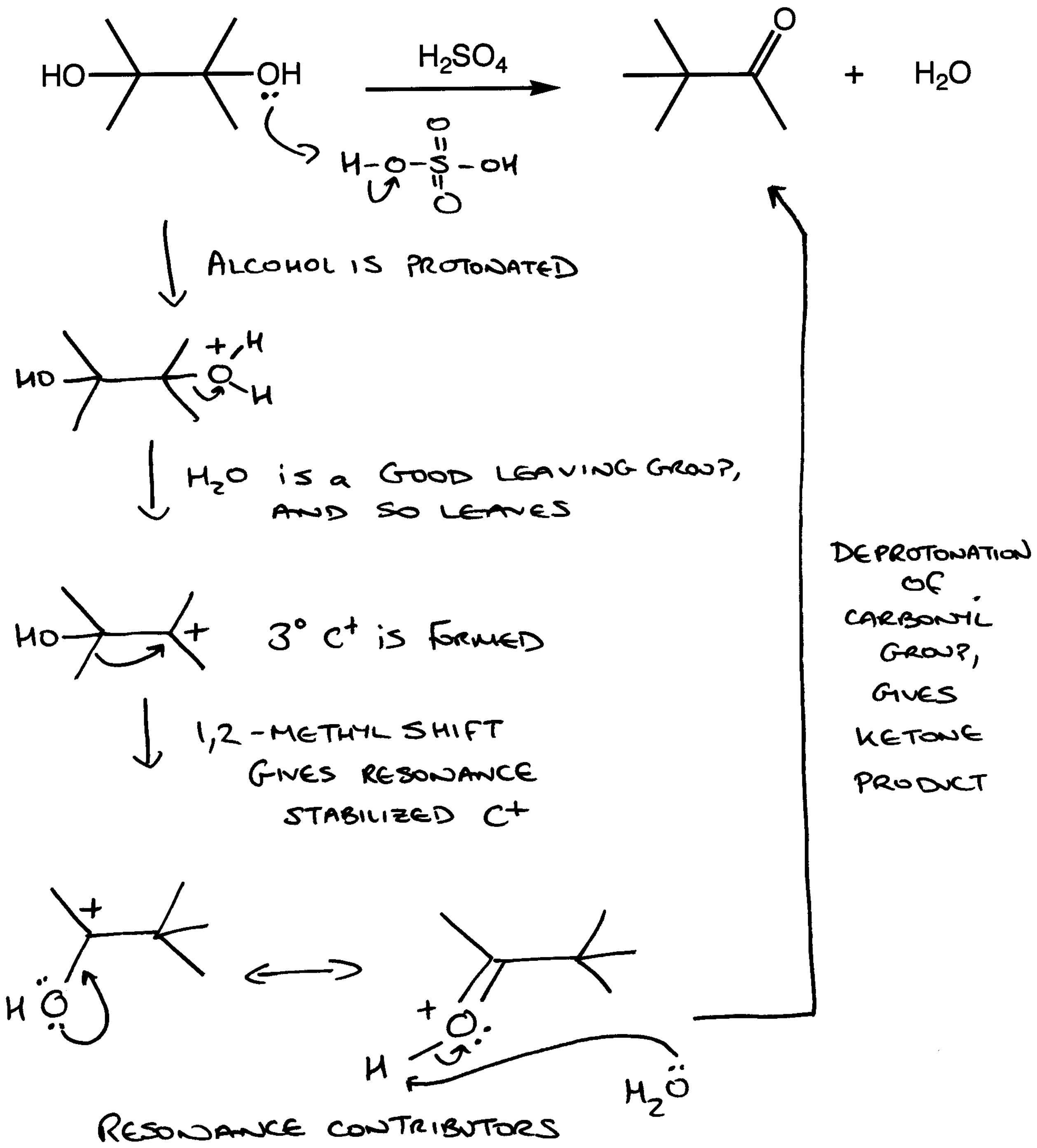


(j)



Mono-chlorination product

Q8. (BONUS). Shown below is a reaction you have probably not seen before. It is called the Pinacol rearrangement. In Chem 30A you have been presented with all of the chemical information and concepts necessary for you to be able to work out the mechanism of this reaction, so... propose a reasonable mechanism that accounts for the transformation shown in the box below – SHOW ALL STEPS AND EXPLAIN EACH ONE WITH A FEW WORDS. (15 points)



ALCOHOL IS PROTONATED

H_2O IS A GOOD LEAVING GROUP, AND SO LEAVES

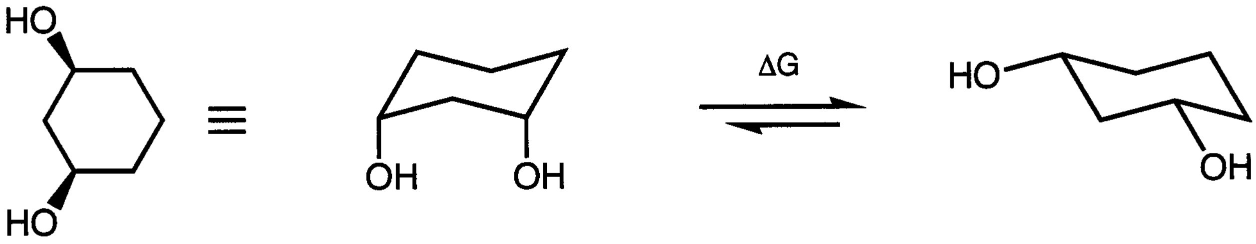
3° C^+ IS FORMED

1,2-METHYL SHIFT GIVES RESONANCE STABILIZED C^+

RESONANCE CONTRIBUTORS

DEPROTONATION OF CARBONYL GROUP, GIVES KETONE PRODUCT

Q9. (BONUS). The conformational equilibrium between the diaxial and diequatorial chair forms of *cis*-1,3-cyclohexanediol (shown below) is affected dramatically by the solvent in which the compound is dissolved. In water, there is an overwhelming preference (99:1) for the diequatorial conformer, but in carbon tetrachloride, this bias is barely evident (diequatorial:diaxial ratio of 55:45). Explain this phenomenon. (15 points)

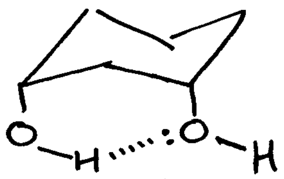


Least stable chair *Most stable chair*

ΔG (H_2O) = −2.7 kcal/mol *BUT* ΔG (CCl_4) = −0.1 kcal/mol

BOTH CONFORMERS ARE WELL-SOLVATED IN H_2O, BECAUSE OF INTERMOLECULAR HYDROGEN BONDING BETWEEN THE −OH GROUPS AND THE SOLVENT, SO IN H_2O, THE DIEQUATORIAL CONFORMER IS FAVORED AS A CONSEQUENCE OF STERIC ARGUMENTS (AND OHS ARE MORE ACCESIBLE IN EQUATORIAL POSITIONS, SO ARE BETTER SOLVATED, i.e., MORE STABLE)

IN CCl_4 ON THE OTHER HAND, WHICH IS A SOLVENT THAT IS NON-POLAR AND INCAPABLE OF HYDROGEN BONDING, THE DIAXIAL CONFORMER IS STABILIZED BY AN INTRAMOLECULAR HYDROGEN BOND, AS SHOWN BELOW:



NO SUCH STABILIZATION IN THE DIEQUATORIAL CONFORMER IN CCl_4.

STABLE 6-MEMBERED RING SYSTEM