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

Student ID Number:

Total Score	230 /200
Course Grade	A+

Chem 30A Winter 2005

FINAL

(180 Min)

Mon March 21st

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

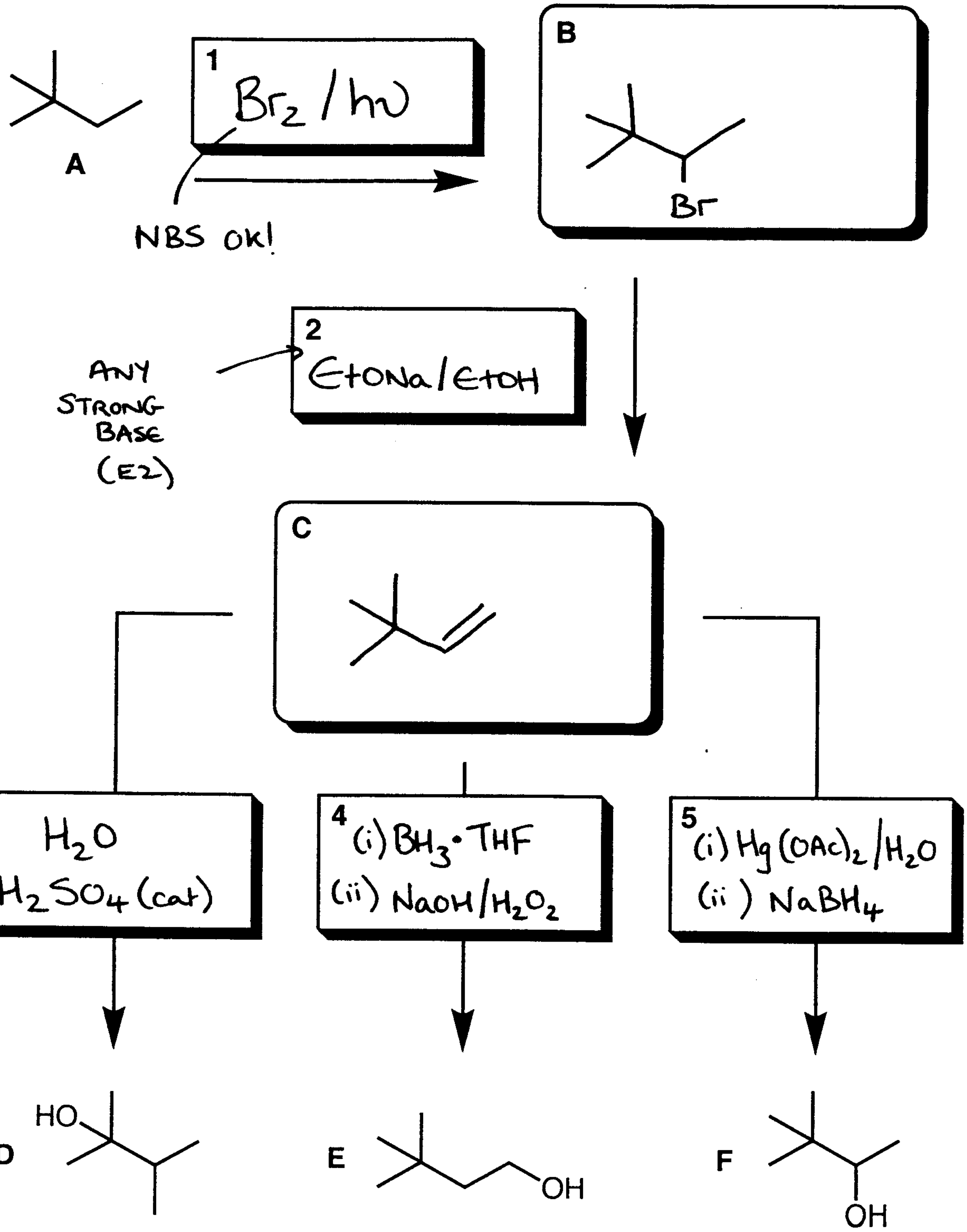
ONLY ANSWERS WRITTEN IN THE BOXES PROVIDED WILL BE GRADED

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

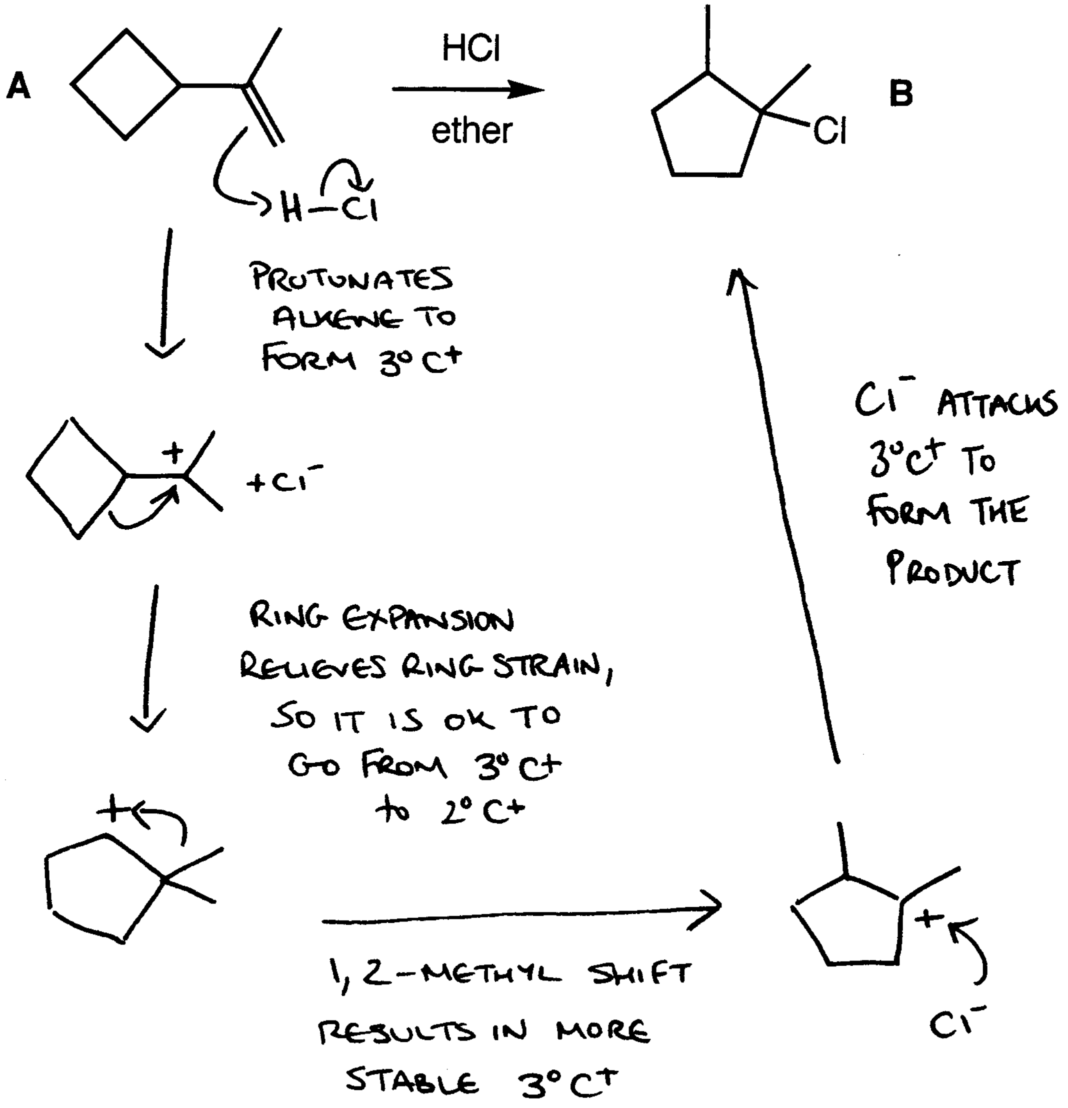
Q1	20 /20	**Q5**	20 /20	**Q9** BONUS	15 /15
Q2	15 /15	**Q6**	40 /40	**Q10** BONUS	15 /15
Q3	30 /30	**Q7**	30 /30	**Total**	230 /200
Q4	25 /25	**Q8**	20 /20		

"Organic chemistry just now is enough to drive one mad. It gives me the impression of a primeval forest full of the most remarkable things, a monstrous and boundless thicket, with no way of escape, into which one may well dread to enter." - Friedrich Wöhler (1835)

Q1. Using the appropriate reagents and conditions, 2,2-dimethylbutane (**A**) can be transformed into compound **B**, which, in turn, can be converted into compound **C**. Three constitutionally isomeric alcohols (**D**, **E**, and **F**) can then be made separately from compound **C**, depending upon what reaction conditions are chosen. Draw appropriate structures for compounds **B** and **C**, and suggest the reagents and conditions that are necessary for each transformation shown on the page (boxes **1** through **5**). Note: some boxes require two-step reactions, and the reagents and conditions you choose must yield the desired compound as the MAJOR product. (20 points)



Q2. Propose a reasonable mechanism that accounts for the transformation of 2-cyclobutylpropene (**A**) into 1-chloro-1,2-dimethylcyclopentane (**B**) as depicted in the box below – SHOW ALL STEPS AND EXPLAIN EACH ONE WITH A FEW WORDS. (15 points)



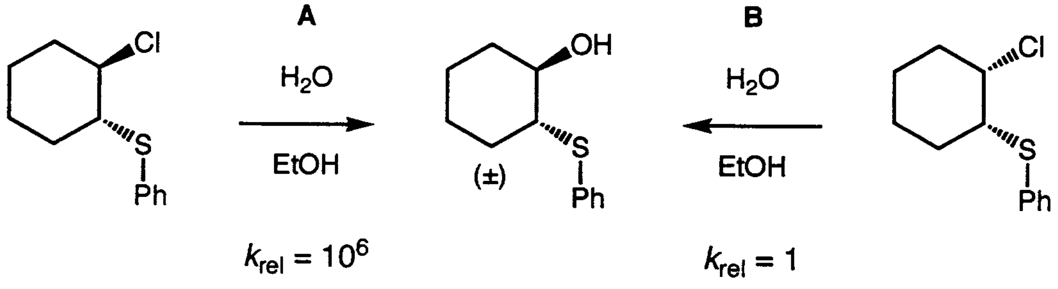
PROTONATES ALKENE TO FORM 3° C+

RING EXPANSION RELIEVES RING STRAIN, SO IT IS OK TO GO FROM 3° C+ to 2° C+

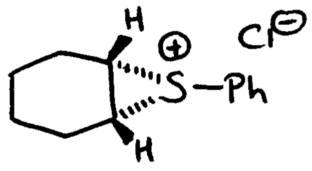
1, 2-METHYL SHIFT RESULTS IN MORE STABLE 3° C+

Cl⁻ ATTACKS 3°C+ TO FORM THE PRODUCT

Q3. Consider the reactions (**A** and **B**) of *trans*- and *cis*-1-chloro-2-thiophenylcyclohexane with water in ethanolic solution. The reaction (**A**) of the *trans* isomer is a million times faster than the reaction (**B**) of the *cis* isomer, and perhaps somewhat surprisingly, both reactions give the same product, namely a racemic mixture of the *trans*-diastereoisomer of 1-thiophenylcyclohexan-2-ol – in neither reaction is any of the *cis*-diastereoisomer formed.

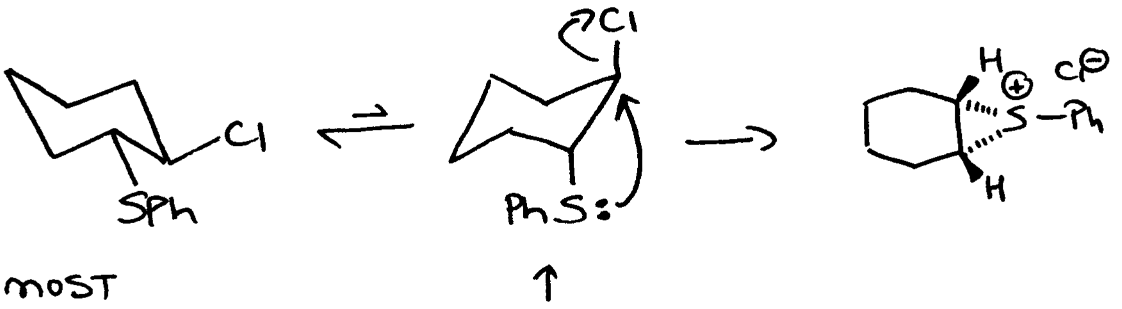


(a) From the significant difference in reaction rate, it is apparent that reactions **A** and **B** proceed through different mechanisms, DESPITE THE FACT THAT THEY SHARE A COMMON INTERMEDIATE. In the box to the right, draw the structure of the intermediate that is common to both pathways. (3 points)



Common Intermediate

(b) Starting from the MOST STABLE CHAIR CONFORMATION of *trans*-1-chloro-2-thiophenylcyclohexane, draw a mechanism showing how reaction **A** arrives at the reaction intermediate you drew above. Briefly explain each step with a few words. (8 points)

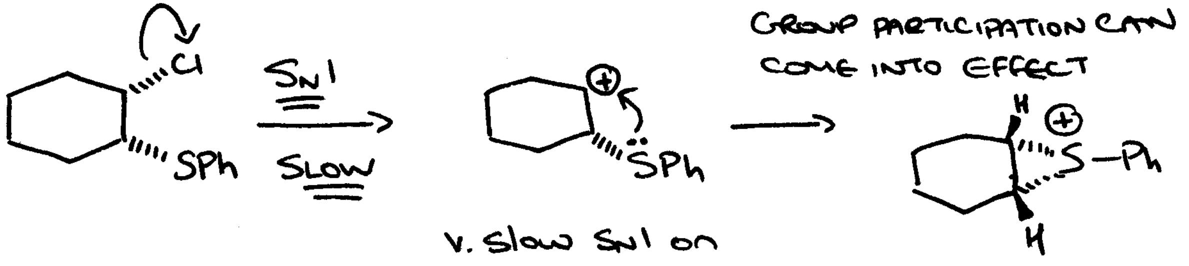


MOST STABLE CHAIR

THIS IS THE LESS STABLE CHAIR, BUT NOW, NEIGHBORING GROUP PARTICIPATION CAN COME INTO EFFECT, AS AN INTRAMOLECULAR S_N2 REACTION (FAST) IS NOW POSSIBLE (BACKSIDE ATTACK REQUIRED)

Question 3 is continued on the next page...

(c) Starting from a simple flat representation of *cis*-1-chloro-2-thiophenylcyclohexane (as drawn in the reactions at the top of the previous page), draw a mechanism showing how reaction **B** arrives at the reaction intermediate you drew above. Briefly explain each step with a few words. (8 points)

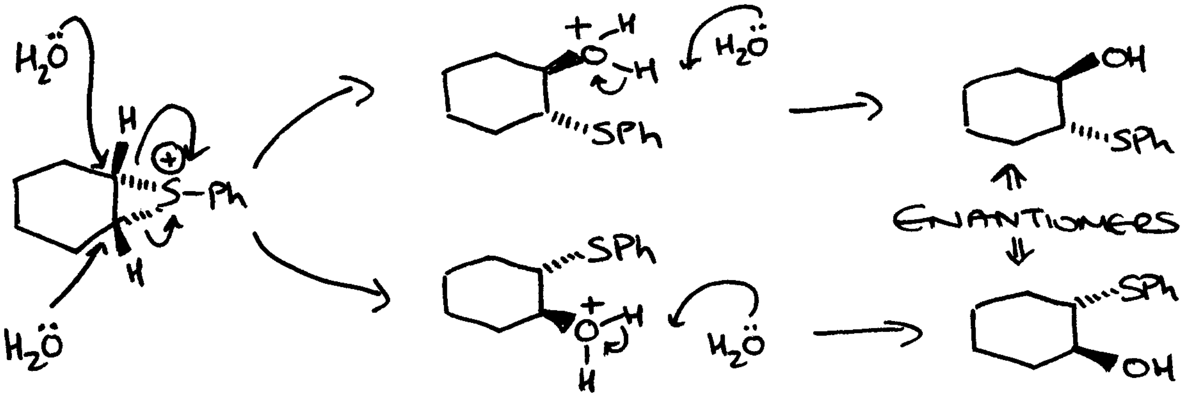


NOW, NEIGHBORING GROUP PARTICIPATION CAN COME INTO EFFECT

V. SLOW S_N1 ON 2° SUBSTRATE GIVES C^+

MORE STABLE CATION

(d) Draw a mechanism showing how the intermediate common to reactions **A** and **B** is converted into a racemic mixture of *trans*-1-thiophenylcyclohexan-2-ol. (6 points)



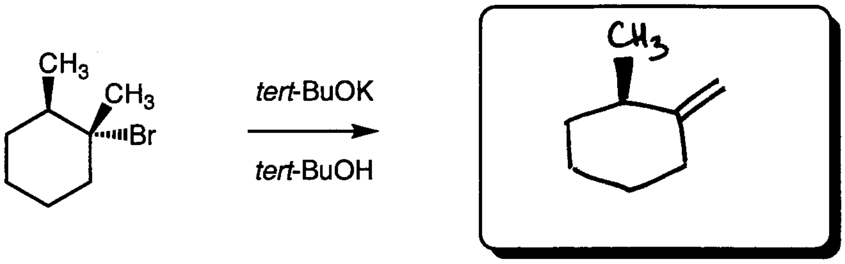
(e) Using words and illustrations as appropriate, explain why reaction **A** is a million times faster than reaction **B**, i.e., why can't the *cis*-isomer of the starting material react via the same mechanism as the *trans*-isomer? (5 points)

IN REACTION <u>A</u>, THE FIRST STEP IS A VERY RAPID INTRA-MOLECULAR S_N2 REACTION, AS THE CORRECT GEOMETRY FOR BACK-SIDE ATTACK EXISTS IN THE TRANS-DIAXIAL CHAIR CONFORMER, RESULTING IN THE FORMATION OF THE SULFONIUM INTERMEDIATE. IN REACTION <u>B</u>, NEIGHBORING GROUP PARTICIPATION IS NOT POSSIBLE INITIALLY, (NO BACKSIDE ATTACK POSSIBLE IN ANY CHAIR CONFORMATION OF THE CIS ISOMER), SO THE FIRST STEP IS A VERY SLOW S_N1 REACTION, TO GIVE THE SULFONIUM ION.

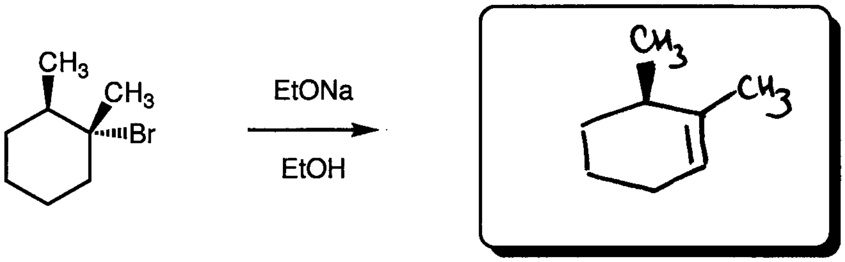
NOTE: THE SECOND STEP IN EACH REACTION IS EXACTLY THE SAME!

Q4. Answer the following questions about ELIMINATION REACTIONS: (4 + 1 points each)

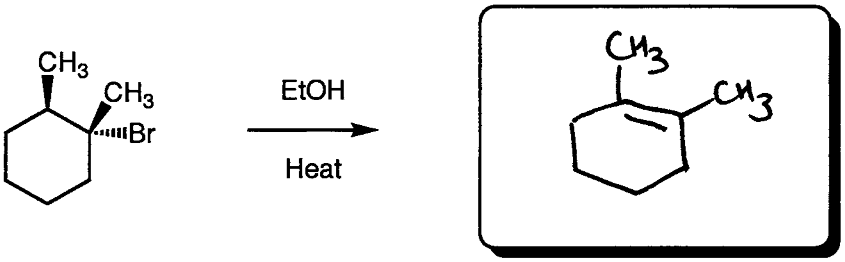
(a) For each of the three reactions shown below, predict the MAJOR ELIMINATION PRODUCT. In each case, indicate if the reaction proceeds via an **E1** or **E2** mechanism in the small box to the right.



E2

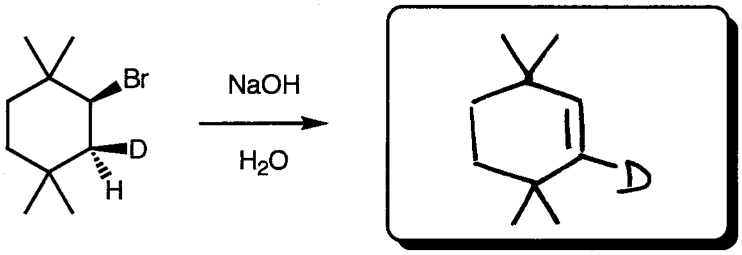


E2

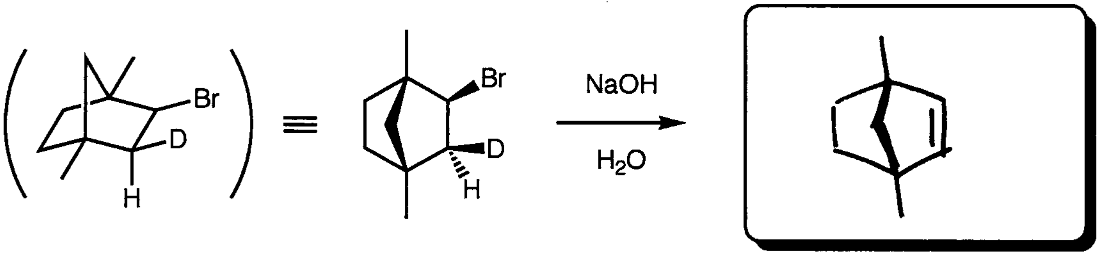


E1

(b) For both of the reactions shown below, predict the MAJOR ELIMINATION PRODUCT – carefully indicating the position of the deuterium atom (if present). In each case, indicate if the reaction proceeds with **SYN**, **ANTI**, or **NO** stereospecificity in the small box to the right.



ANTI



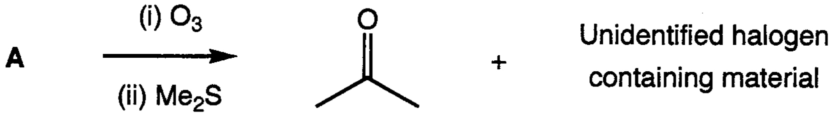
SYN

Q5. You are given a sample vial that is labeled "achiral alkyl halide **A**" and are told to determine the identity of the compound and some of its derivatives. A combustion analysis of **A** shows the molecular formula to be $C_{10}H_{17}Br$. (20 points)

— Treatment of **A** with ethanolic potassium hydroxide gives two different compounds (**B** and **C**) each with the formula $C_{10}H_{16}$.

$$\underset{C_{10}H_{17}Br}{\mathbf{A}} \xrightarrow[\text{EtOH}]{\text{KOH}} \underset{C_{10}H_{16}}{\mathbf{B}} + \underset{C_{10}H_{16}}{\mathbf{C}}$$

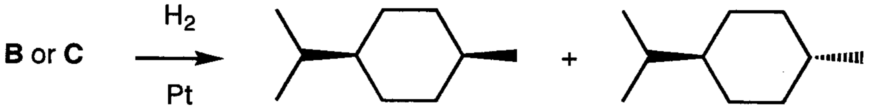
— Ozonolysis of **A** gives a product mixture containing some 2-propanone (acetone)



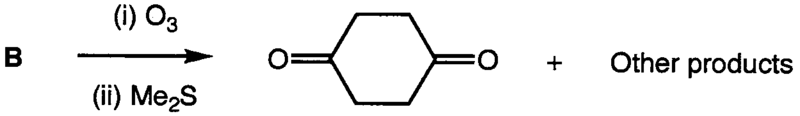
— Dissolving **A** in H_2O/EtOH rapidly gives an acidic solution that contains bromide ions (AgBr precipitates upon addition of $AgNO_3$)

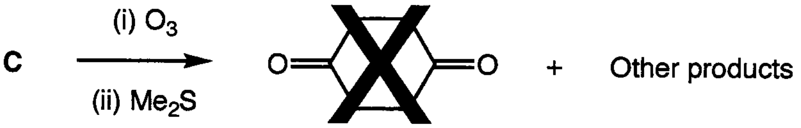
— Bromination of **A** (Br_2/CCl_4) gives two compounds (**D** and **E**) that can be separated, and each shown to be achiral

— Catalytic hydrogenation of either **B** or **C**, results in a mixture of *cis*- and *trans*-1-methyl-4-isopropylcyclohexane



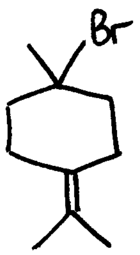
— Ozonolysis of **B** gives a product mixture containing some 1,4-cyclohexanedione, but ozonolysis of **C** gives a mixture of products that DOES NOT contain any of this compound



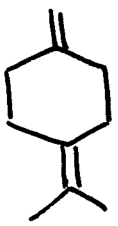


— What are the structures of compounds **A**, **B**, **C**, **D**, and **E**?

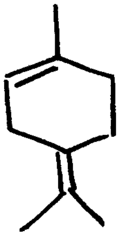
A



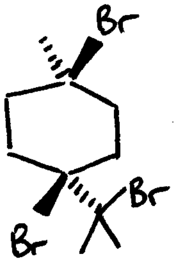
B



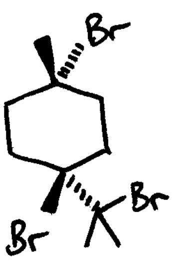
C



D

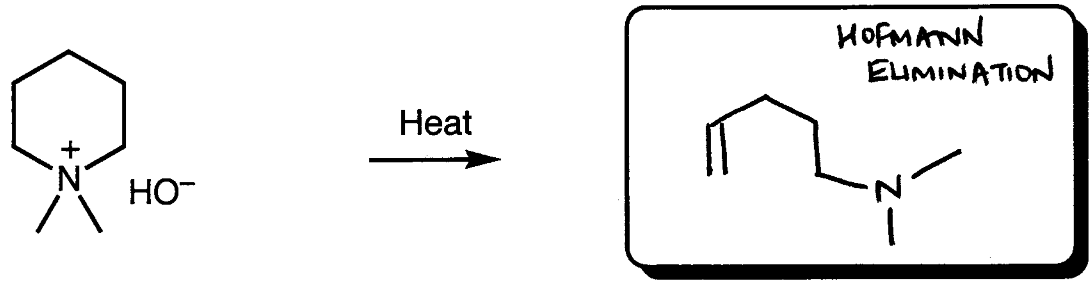


E

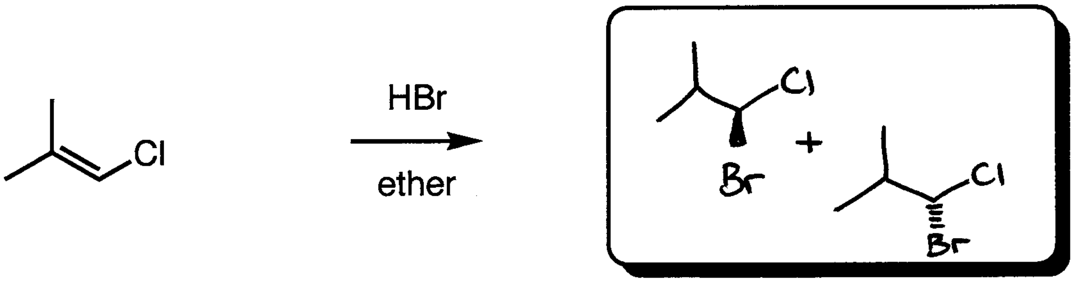


Q6. For each of the reactions shown below draw the MAJOR PRODUCT (paying particular attention to any appropriate stereochemical relationships) in the boxes provided. Note: for two-step reactions, just give the final product, DO NOT draw intermediates. Some of these reactions may yield a pair of enantiomers, and in these cases, draw both of them. If a reaction produces a single enantiomer, assign its configuration as either **R** or **S**, depending upon which enantiomer is formed. (40 points)

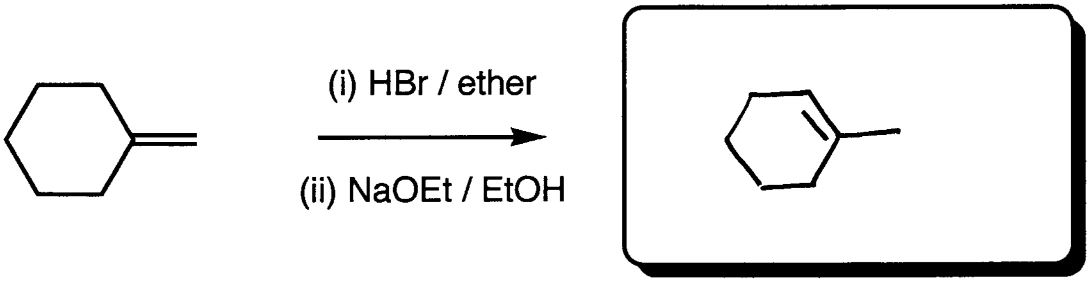
(a)



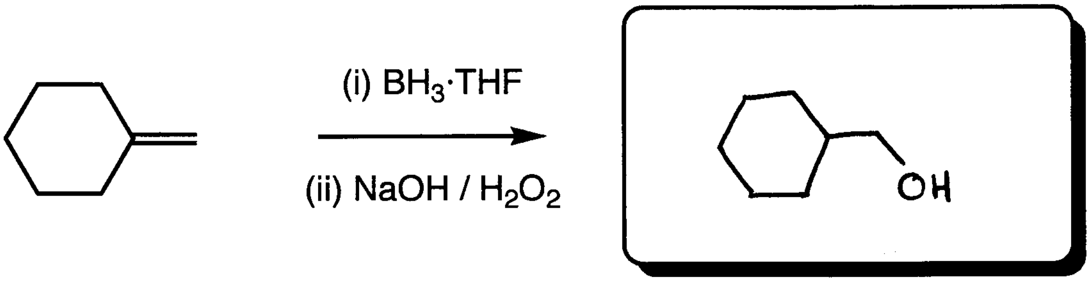
(b)



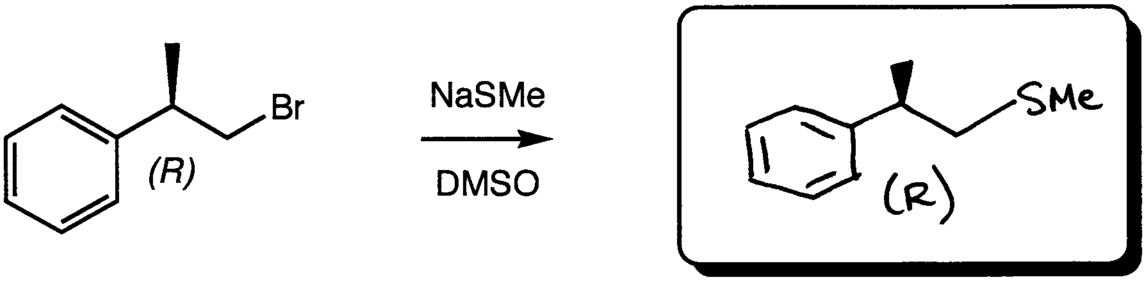
(c)



(d)

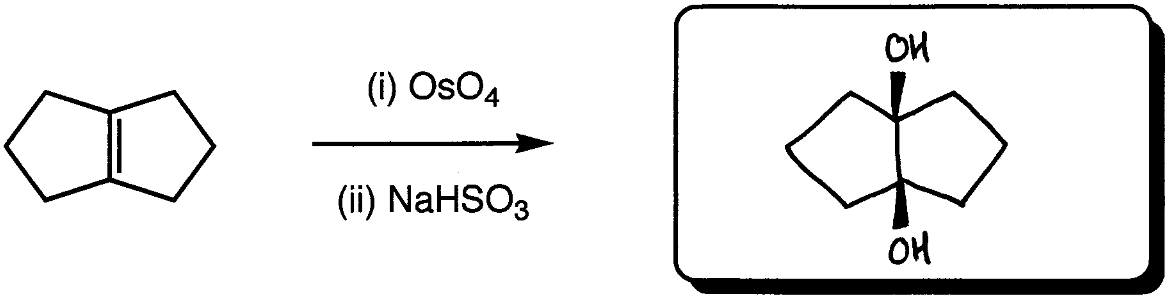


(e)

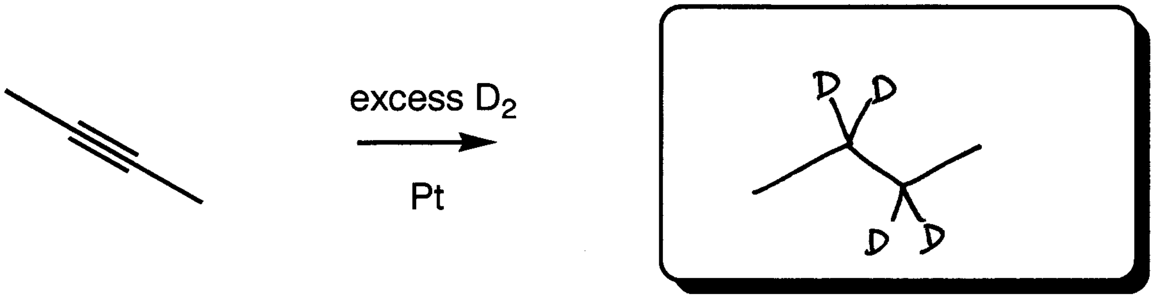


Question 6 is continued on the next page...

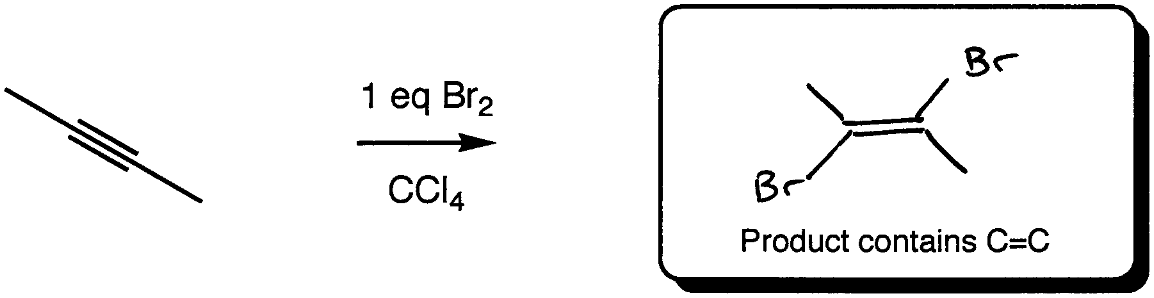
(f)


(i) OsO$_4$
(ii) NaHSO$_3$
OH
OH

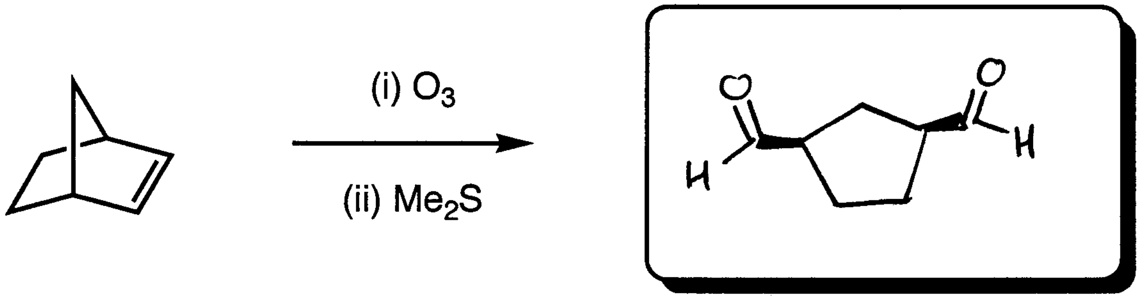
(g)


excess D$_2$
Pt
D
D
D
D

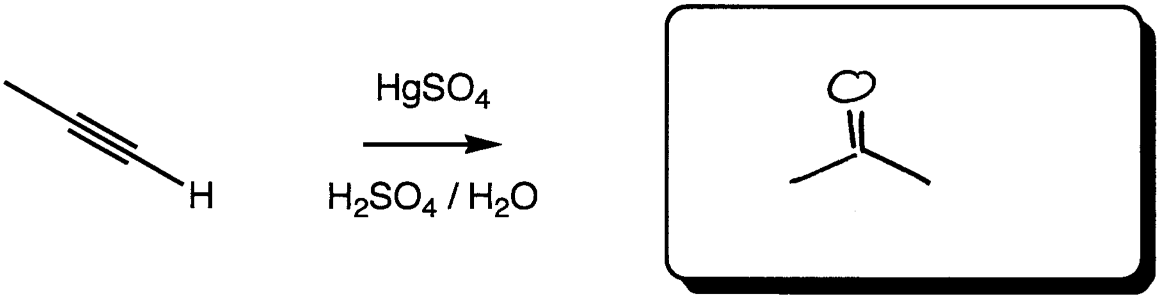
(h)


1 eq Br$_2$
CCl$_4$
Br
Br
Product contains C=C

(i)


(i) O$_3$
(ii) Me$_2$S
O
O
H
H

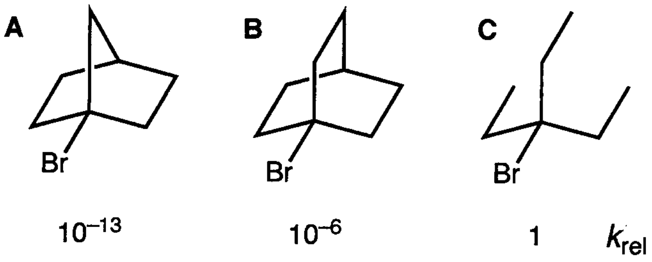
(j)


H
HgSO$_4$
H$_2$SO$_4$ / H$_2$O
O

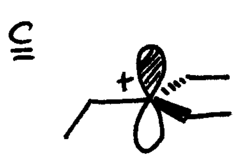
Q7. Answer the following questions about SUBSTITUTION REACTIONS: (30 points)

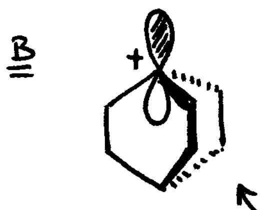
(a) The rates of the S_N1 solvolysis reactions of the three alkyl bromides shown below (**A**, **B**, and **C**) differ dramatically – **C** reacts a million times faster than **B**, which, in turn, reacts a million times faster than **A** (which reacts so slowly, it essentially doesn't happen at all). Explain this trend in the box below.

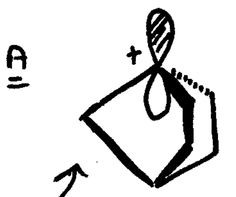
$$R{-}Br \xrightarrow[EtOH]{H_2O} R{-}OH$$



RDS INVOLVES THE FORMATION OF A CARBOCATION —





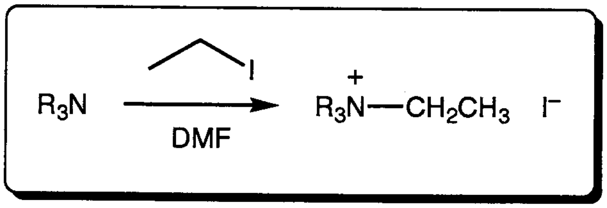


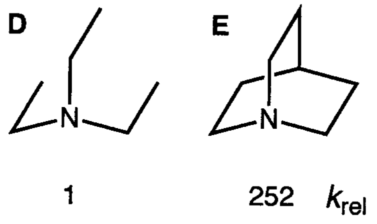
THERE IS A BIT MORE FLEXIBILITY IN B THAN IN A, SO B CAN GET CLOSER TO PLANARITY => MORE STABLE

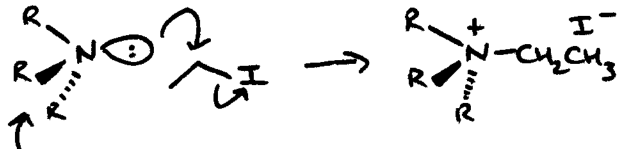
THIS C+ CAN BE PLANAR, AND THEREFORE STABILIZED BY HYPER-CONJUGATION OF ADJACENT BONDS

BECAUSE OF THE CAGE STRUCTURES, CARBOCATIONS ARE NOT PLANAR, SO THERE IS LESS HYPERCONJUGATIVE STABILISATION

(b) Tertiary amines (R_3N) react with ethyl iodide in S_N2 reactions to form quaternary ammonium iodide salts. The two tertiary amines shown below (**D** and **E**) react at substantially different rates – **E** reacts about 250 times faster than **D**. Explain this trend in the box below.







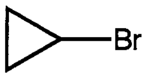
IN D, THE R GROUPS ARE FREE TO MOVE IN SPACE, AND WILL OCCASIONALLY SWING AROUND AND HINDER THE APPROACH OF THE NITROGEN LONE PAIR TOWARD THE ETHYL IODIDE. IN E, HOWEVER, THE R GROUPS ARE CONVENIENTLY TIED BACK, SO THE N LONE PAIR IS UNHINDERED IN ITS ATTACK ON ETHYL IODIDE.

Question 7 is continued on the next page...

(c) The rates of the S_N2 reactions of certain cycloalkyl bromides with NaCN in DMSO are shown below – cyclopropyl bromide reacts 100 times slower than cyclobutyl bromide, which in turn reacts 100 times slower than cyclopentyl bromide. Explain this trend in the box below.

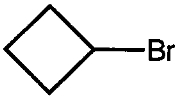
$$R{-}Br \xrightarrow[DMSO]{NaCN} R{-}CN$$

F



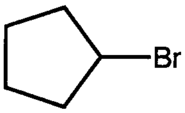
10^{-4}

G



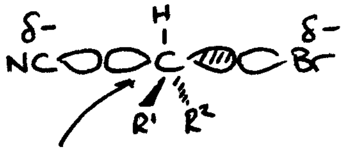
10^{-2}

H



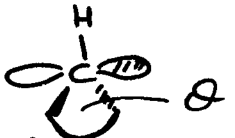
1 k_{rel}

CONSIDER THE TRANSITION STATE FOR AN S_N2 REACTION



THIS IS AN sp^2 HYBRIDISED CARBON, AND SO THE THREE SUBSTITUENTS (H, R¹ & R²) WANT TO BE 120° APART AS THEY ARE ALL IN THE SAME PLANE

So, in F, G and H, we ARE ESSENTIALLY TYING R¹ AND R² TOGETHER AND STOPPING THEM FROM BEING 120° APART, i.e

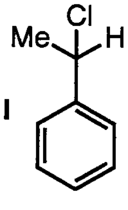


IN CYCLOPROPYL, θ = 60°, FURTHEST AWAY FROM 120°, SO IT'S A HIGH ENERGY TS, CYCLOBUTYL NOT SO BAD (90°), AND CYCLOPENTYL EVEN BETTER (~108°)

(d) The rates of the S_N1 solvolysis reactions of the four benzyl chlorides shown below (I, J, K, and L) differ significantly – as the steric bulk of the alkyl side chain increases (methyl, ethyl, isopropyl, *tert*-butyl), the rate of the reaction decreases. Explain this trend in the box below. (Note: the inductive effect of each of these four alkyl groups is approximately the same).

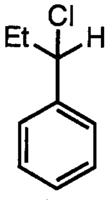
$$R{-}Br \xrightarrow[EtOH]{H_2O} R{-}OH$$

I



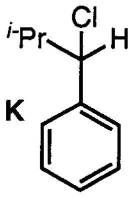
540

J



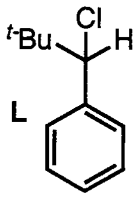
125

K



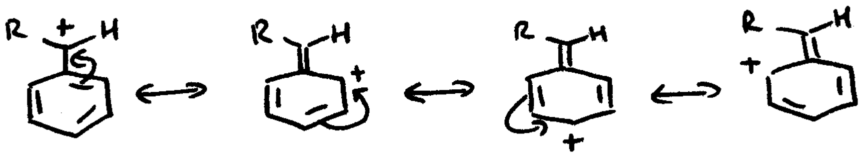
27

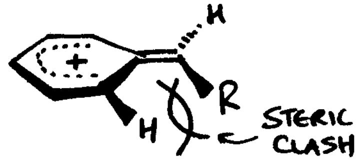
L



1 k_{rel}

WHEN Cl⁻ LEAVES, WE FORM A BENZYL CARBOCATION IN EACH CASE, WHICH CAN BE RESONANCE STABILIZED:



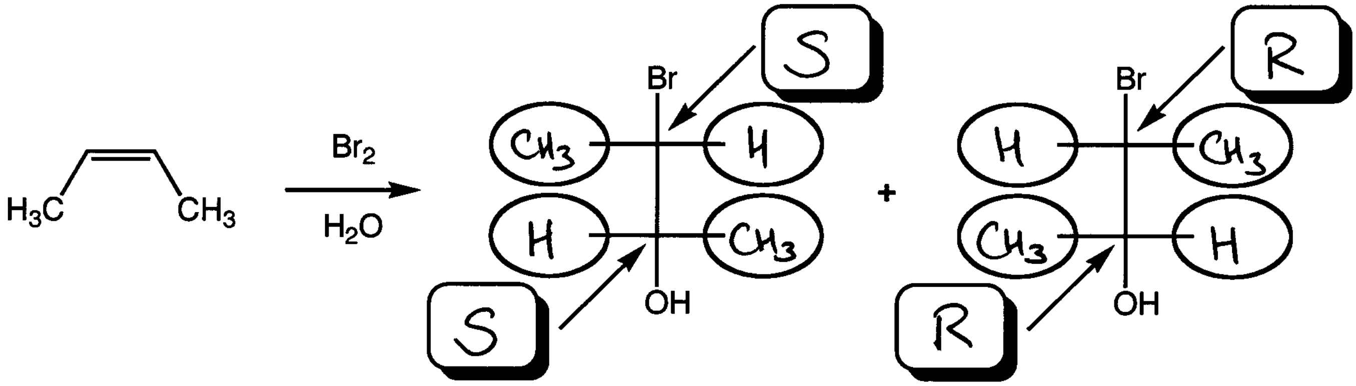


TO CONJUGATE INTO THE RING HOWEVER, THE R GROUP MUST LIE IN THE SAME PLANE AS ALL OF THE RING ATOMS, AND AS R GETS BIGGER, THERE ARE WORSE STERIC INTERACTIONS, WHICH ACTUALLY DESTABILISE SLIGHTLY ALL OF THE RING RESONANCE FORMS

WORSE AS R GETS BIGGER.

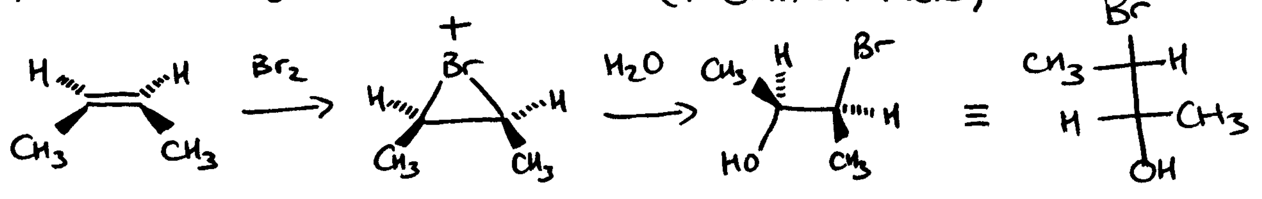
Q8. Consider the reactions of *cis*- and *trans*-2-butene with Br_2 in water. (20 points)

(a) The reaction of *cis*-2-butene with Br_2 in water results in the formation of TWO stereoisomeric bromohydrins. Complete the Fischer projections that have been provided for you by filling in the circles with the necessary groups (**CH_3** or **H**). Each stereocenter in each compound is labeled with a shaded box in which you should denote the configuration (**R** or **S**) of that particular stereocenter.

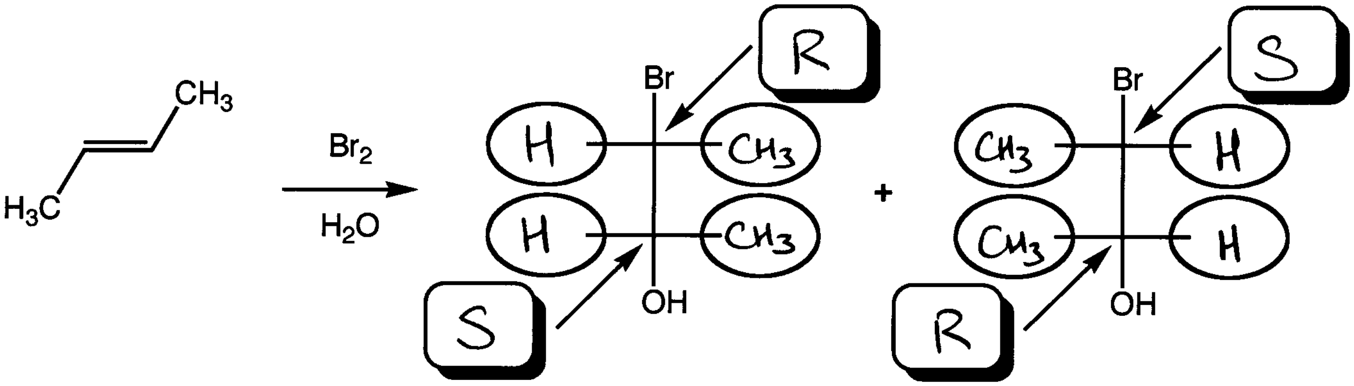


space for working...

(+ ENANTIOMER)



(b) The reaction of *trans*-2-butene with Br_2 in water results in the formation of TWO stereoisomeric bromohydrins. Complete the Fischer projections that have been provided for you by filling in the circles with the necessary groups (**CH_3** or **H**). Each stereocenter in each compound is labeled with a shaded box in which you should denote the configuration (**R** or **S**) of that particular stereocenter.



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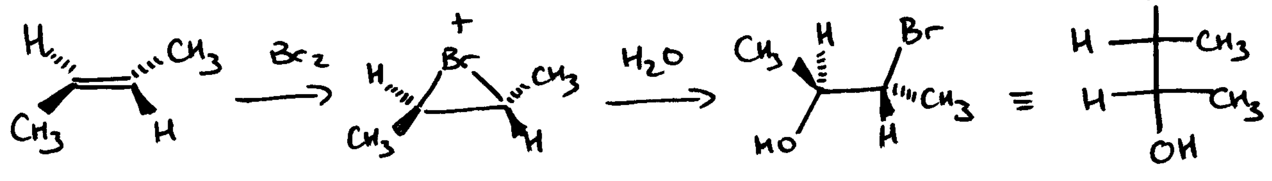
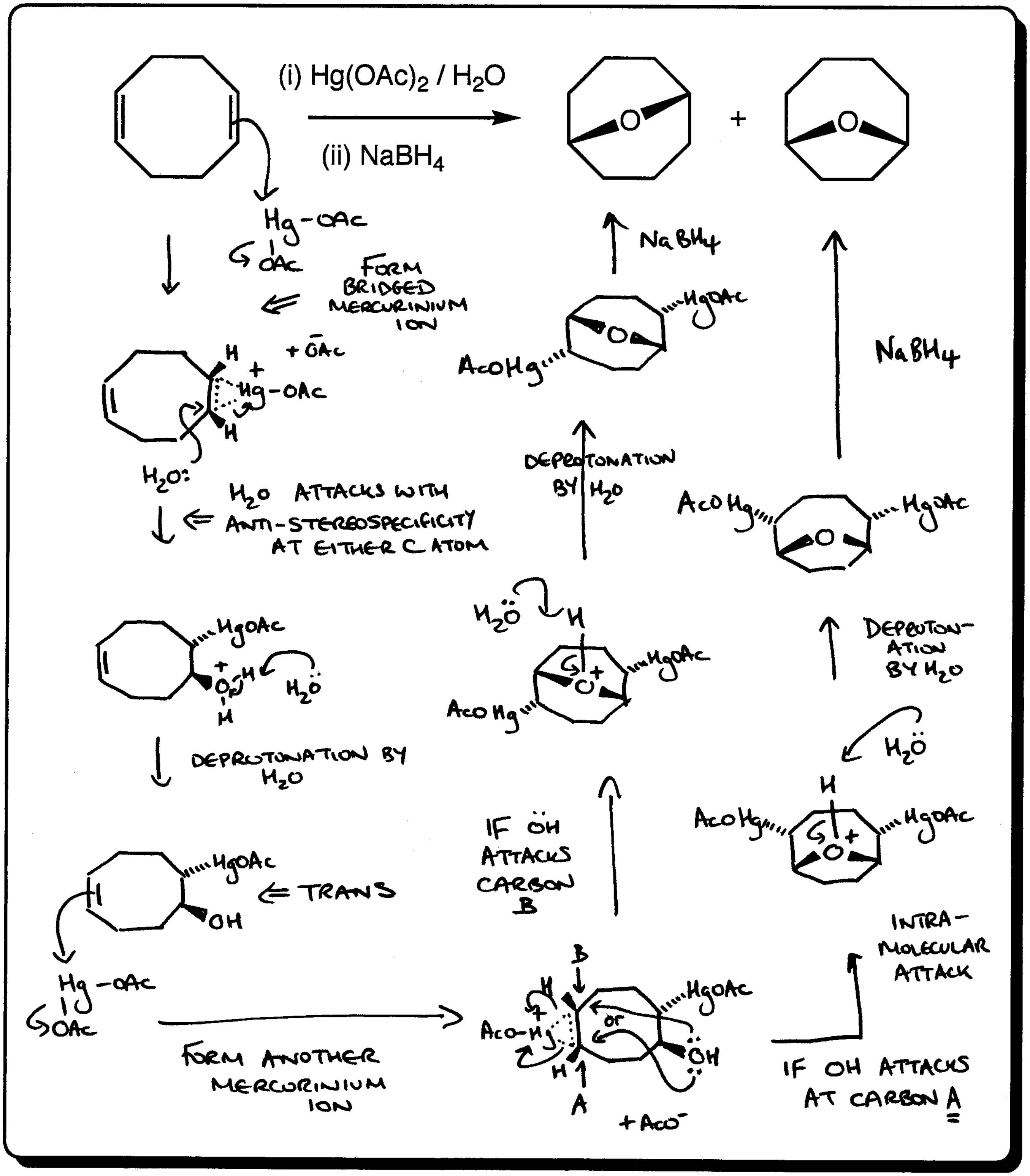
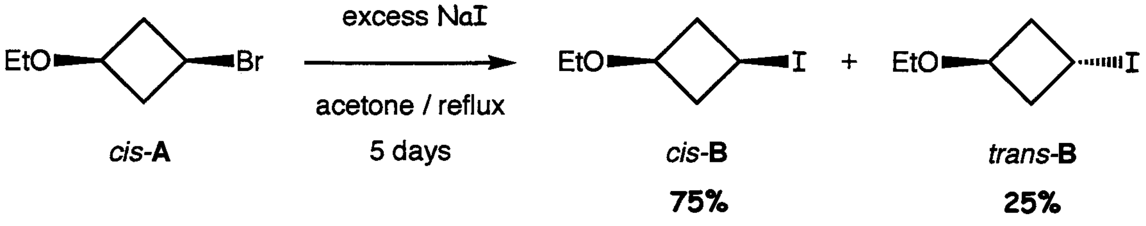


Q9. (BONUS). The oxymercuration/reduction reaction sequence when applied to 1,5-cyclooctadiene results in the formation of two isomeric bicyclic ether compounds. Propose a reasonable mechanism that accounts for this transformation – SHOW ALL NECESSARY STEPS AND EXPLAIN EACH ONE WITH A FEW WORDS. Note: you do not need to show any arrow pushing for the sodium borohydride reduction, i.e., step (ii) – just draw an arrow and write "NaBH$_4$" above it when you get to that point in the mechanism. (15 points)



Q10. (BONUS). In 1975, it was reported in the chemical literature that the reaction of *cis*-1-bromo-4-ethoxy-cyclobutane (*cis*-**A**) with sodium iodide in acetone gives a mixture of the *cis*- and *trans*-iodo products (*cis*-**B** and *trans*-**B**), with the MAJOR PRODUCT observed to be *cis*-**B**. (15 points)



(a) This reaction caused quite a stir at the time, and seemed to challenge many years of accepted wisdom – briefly explain why.

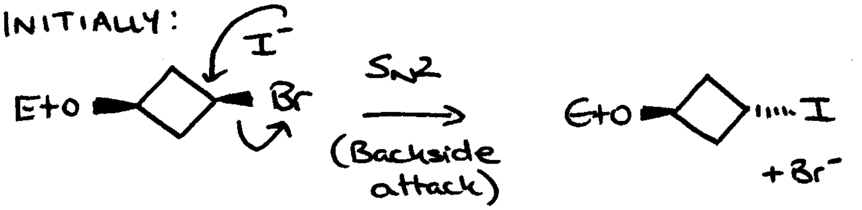
IT EITHER SUGGESTS THAT:

(i) THE REACTION DID NOT PROCEED VIA AN S_N2 REACTION, EVEN THOUGH S_N2 CONDITIONS WERE USED, OR:

(ii) AN S_N2 REACTION OCCURRED, BUT DID NOT PROCEED WITH INVERSION, RATHER IT HAPPENED WITH RETENTION OF CONFIGURATION.

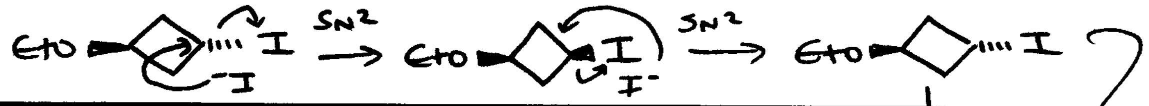
(b) The result was so controversial, it was soon reinvestigated by other research groups. When the reaction mixture was sampled after only 10 hours, it was discovered that the product was almost entirely *trans*-**B**, and that samples taken over the next four days, showed the amount of *trans*-**B** present in the reaction mixture to be dwindling, with a concomitant increase in the amount of *cis*-**B**, until after five days, the 25:75 ratio is reached, which does not change any further. Moreover, when the reaction of *trans*-**A** was investigated using the same conditions, it was found that after 10 hours, the product was almost entirely *cis*-**B**, but after 5 days, the same 75:25 ratio of *cis*-**B** to *trans*-**B** was observed. It does not matter which isomer you start with, the product distribution after five days is the same! Using words and illustrations as necessary, explain what is going on.

INITIALLY:



PROCEEDS WITH INVERSION AS EXPECTED

BUT SINCE AN EXCESS OF NaI IS USED, AND BECAUSE I⁻ IS A GOOD LEAVING GROUP AS WELL AS A GOOD NUCLEOPHILE, THE FOLLOWING REACTIONS ARE POSSIBLE...

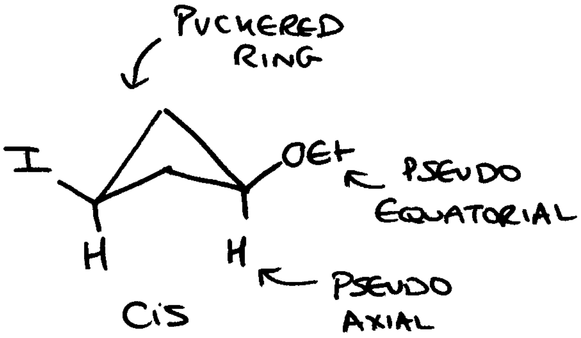


So, the configuration at the C–I C ATOM is constantly being SCRAMBLED.

Question 10 is continued on the next page...

(c) Suggest why *cis*-**B** is the MAJOR product – i.e., why is its formation favored over *trans*-**B**?

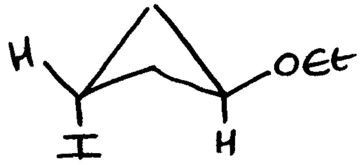
Cis is more stable than trans because:



Cis

VS

trans



BOTH LARGE GROUPS "EQUATORIAL"

ALWAYS ONE LARGE GROUP WILL BE IN AN "AXIAL" POSITION

***************End of Exam***************

SO, IN THE EQUILIBRATING REACTION MIXTURE, EVENTUALLY A STABLE EQUILIBRIUM IS REACHED (NO MATTER WHAT THE STARTING POINT), WHERE WE GET 75% OF THE MORE STABLE CIS ISOMER, AND 25% OF THE LESS STABLE TRANS ISOMER...