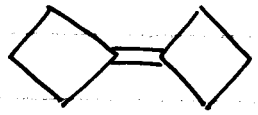
CHEM 30A FALL 2004

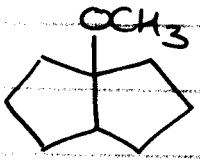
MIDTERM 2 "HOW-TO" GUIDE

Q1)



CH_3OH

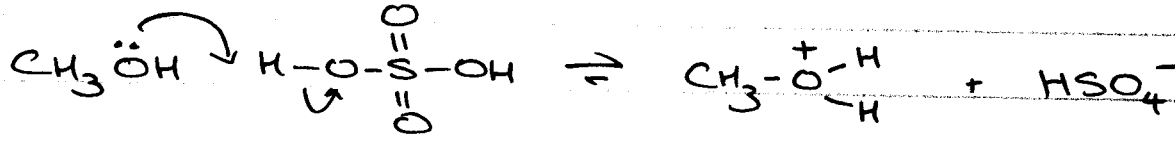
H_2SO_4 (cat)



What is the mechanism of this reaction?

Well, we have an alkene, and the reaction is acid catalysed, so protonation of the alkene seems like a good first step... but what do we protonate with?

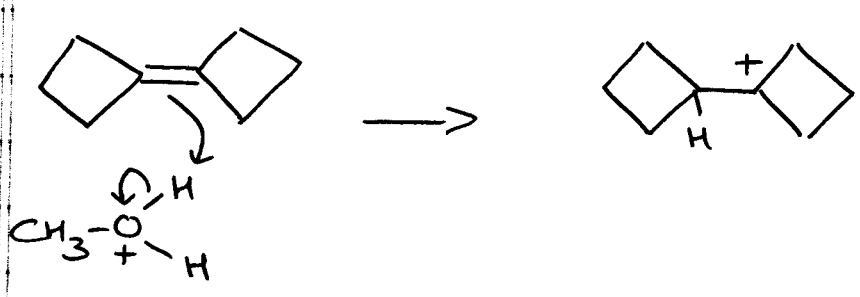
H_2SO_4 (sulfuric acid) is a very strong acid, and in methanol, it will only exist in its ionized form, i.e.,



So, the species that will protonate the alkene is $CH_3\overset{+}{O}H_2$ — the protonated form of methanol (Note: this is similar to the hydronium ion that you get when you protonate water, i.e., $H_2O + H_2SO_4 \longrightarrow H_3O^+ + HSO_4^-$)

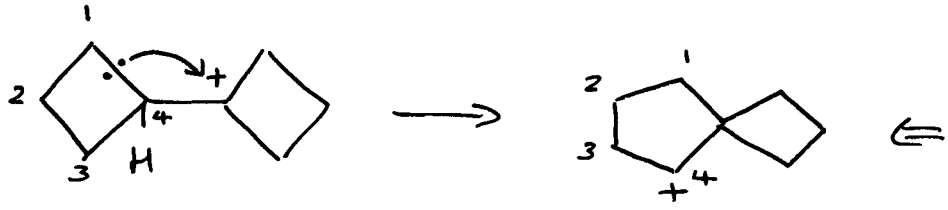
DO NOT PROTONATE WITH CH_3OH, YOU WILL NOT FORM $CH_3O^\ominus$ IN ACIDIC CONDITIONS

So,



So, we form a 3° C+ (it doesn't matter which alkene C atom we choose, as reactant is symmetric)

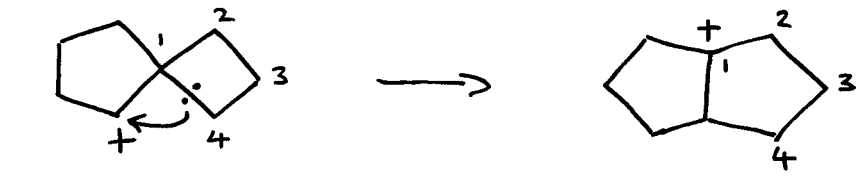
A 3° C+ is quite stable, but this one finds itself as part of a 4-membered ring, which is quite strained, so can we do a rearrangement that can relieve this strain? The answer, is of course, yes!



ALKYL SHIFT

This is a 2° C+

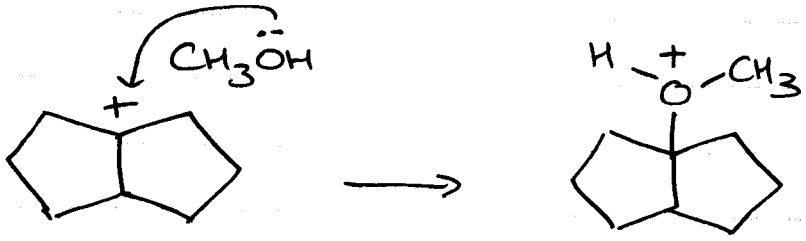
So, even though we form a 2°C+, we have relieved a lot of ring strain to compensate, and we still have a four-membered ring, and so we can do another ring expansion:



ALKYL SHIFT

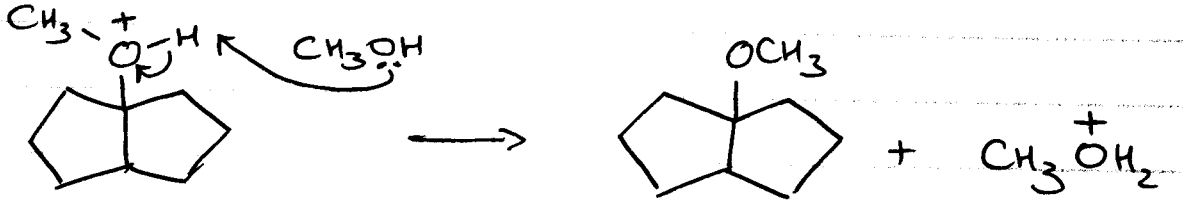
This is once more, a stable 3°C+

At this point, the final step is pretty obvious, the CH_3OH attacks this newly rearranged C^+:



This is the intial product, but...

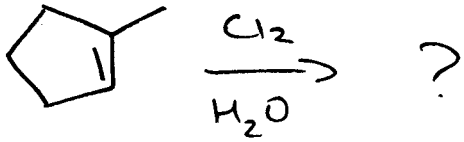
$CH_3\ddot{O}H$ will come along and remove the extra proton:



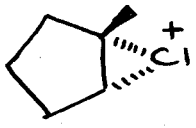
In doing so, we have completed the mechanism, and notice that we have regenerated $CH_3\overset{+}{O}H_2$, the species that protonated the alkene in the first place. So, we have consumed one molecule of CH_3OH, but the "H^+" is truly catalytic, it does not get used up in the reaction.

<u>NOTE</u>: There was <u>NO</u> water (H_2O) in the reaction, sulfuric acid (when in its concentrated form) is just H_2SO_4, there is NO water present.

Q2) a)

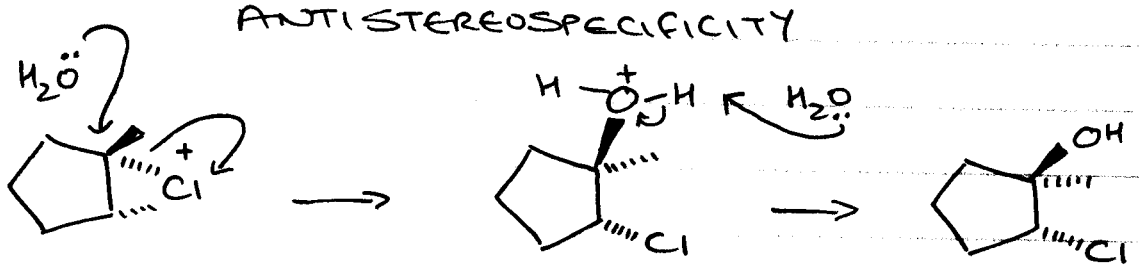


First step is formation of the chloronium ion



and in the second step, the nucleophile is water (H_2O) and it will attack regioselectively at the most substituted position with ANTISTEREOSPECIFICITY

i.e. -

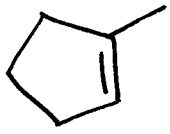
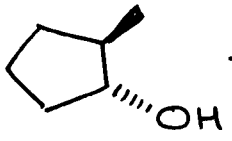


So, the Cl ends up on the least substituted alkene C atom, and the OH ends up on the most substituted, and the OH and Cl groups must be <u>TRANS</u>

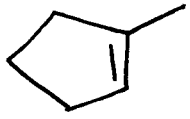
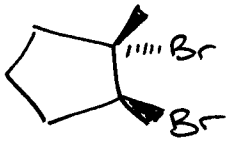
The reaction forms both enantiomers, i.e.,

because the initial formation of the chloronium ion can occur from either face of the alkene, resulting in enantiomeric chloronium ions.

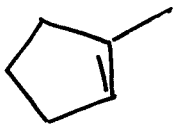
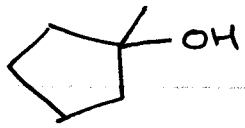
I'm not going to go into so much detail for the rest of this question, but I will point out the important features.

b)  (i) $BH_3 \cdot THF$ (ii) $NaOH/H_2O_2$  + enantiomer

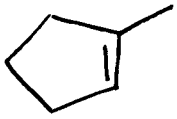
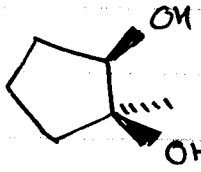
- hydroboration/oxidation
- initial addition of BH_3 goes SYN, and so in product, the OH and H will be cis, so the -OH and methyl group will be TRANS.
- product formed as a racemic mixture, as BH_3 can initially add to either face of the alkene (i.e., top or bottom)
- anti Markovnikov selectivity → B adds to least substituted C atom of alkene

c)  Br_2 CCl_4  + enantiomer

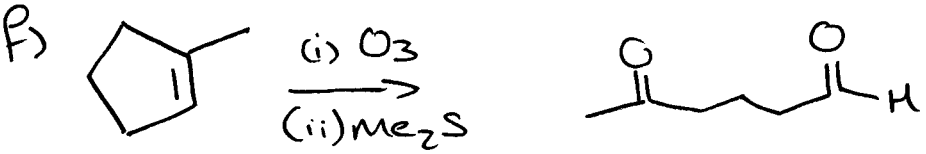
- CCl_4 is an inert solvent
- Br atoms must be TRANS in the product (ANTISTEREOSPECIFICITY)
- no regioselectivity issues, you get one Br on each alkene C atom
- product formed as a racemic mixture, as initial bromonium ion can form on either face of the alkene.

d)  (i) $Hg(OAc)_2 / H_2O$ → (ii) $NaBH_4$ 

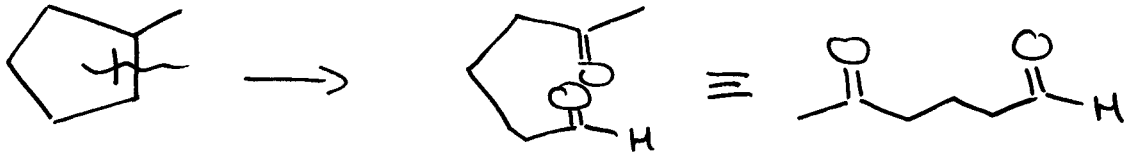
- oxymercuration / reduction
- only one single product (not enantiomers) as the product is achiral (NO STEREOCENTRES)
- reaction proceeds with MARKOVNIKOV regioselectivity, and so -OH ends up on most substituted alkene C atom
- No C^+ intermediate, reaction proceeds through a cyclic mercurinium ion, so no rearrangement is possible.

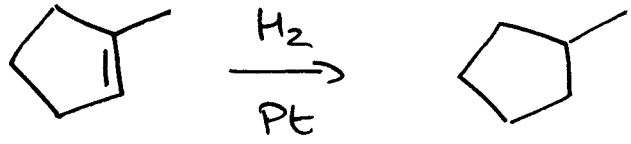
e)  (i) OsO_4 → (ii) $NaHSO_3$ / H_2O  + enantiomer

- dihydroxylation reaction
- reaction proceeds with SYN stereospecificity, and so -OH groups both end up on the same side of the ring, i.e., the CIS 1,2 DIOL
- reaction results in a racemic mixture of products, as initial reaction with OsO_4 can result in the osmate ester forming on either face of the alkene, resulting in enantiomeric intermediates.

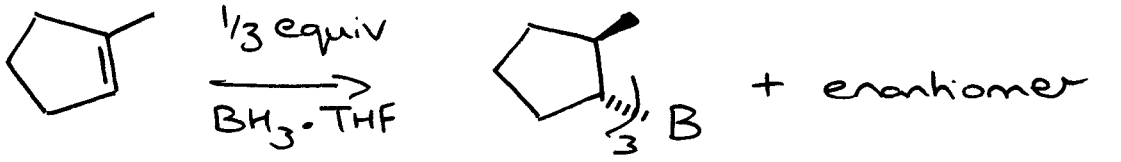
f) 

- ozonolysis cleavage of C=C
- Me_2S work-up gives carbonyl groups
- no stereochemistry issues for product (product is ACHIRAL)



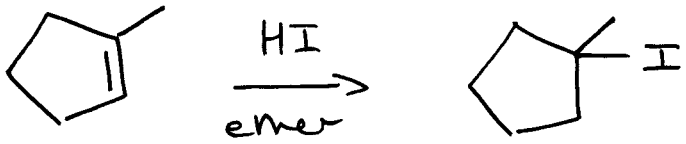
g) 

- catalytic hydrogeration (add H_2 across C=C)
- product is ACHIRAL, addition of H_2 is a SYN addition, but in this case has no stereochemical consequences for the product.

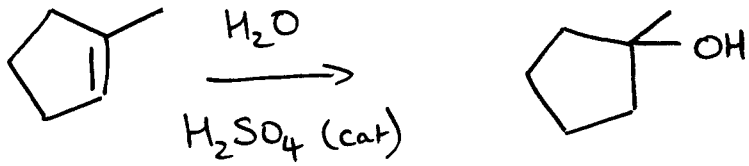
h) 

- hydroboration (NO OXIDATION STEP)
- syn addition of BH_3, results in B and methyl group being TRANS
- alkenes add across each B–H bond, leading to a TRIALKYLBORANE
- either face of each alkene can add across the B–H bonds, resulting in STEREOISOMERS

... technically, the product is not formed as a racemic mixture, there will be different DIASTEREOISOMERS formed, but pairs of enantiomers will be formed, so credit was given for an 'E' in the box.

i) 

- acidic conditions, reaction proceeds via most stable carbocation (3° vs 2°)
- ether is an inert solvent, so nucleophile in second step is I^-
- product is ACHIRAL, so no stereochemistry issues.

j) 

- acid catalysed hydration
- proceeds via most stable C^+ (3° vs 2°) leading to MARKOVNIKOV regioselectivity i.e., -OH ends up on most substituted alkene C atom
- product is ACHIRAL, so no stereochemistry issues.

Q3

a) $W \xrightarrow{k_1} X \qquad Y \xrightarrow{k_2} Z$

If the reaction of Y to give Z is 100 times faster (under the same conditions) than the reaction of W to give X, then the reaction with the highest activation energy barrier must be $W \rightarrow X$, i.e., the slowest reaction.

b) Simple mathematics → below is the answer from the KEY:

$k_1 = Ae^{q_1}$

$k_2 = Ae^{q_2}$ So, if $k_2/k_1 = 100$, $\dfrac{Ae^{q_2}}{Ae^{q_1}} = 100$

A is the same for both reactions, so that cancels to give

$$\frac{e^{q_2}}{e^{q_1}} = 100$$, so take natural log of both sides

$$\ln\left(\frac{e^{q_2}}{e^{q_1}}\right) = \ln 100$$

and we know that

$\ln N = 2.3 \log_{10} N$, so $\ln 100 = 2.3 \log_{10} 100$

and $\log_{10} 100 = 2$, so $\ln 100 = 4.6$

So, $\ln\left(\frac{e^{q_2}}{e^{q_1}}\right) = \ln e^{q_2} - \ln e^{q_1} = 4.6$

$= q^2 - q^1 = 4.6$

Since

$$q = \frac{-\Delta G^{\ddagger}}{RT}$$

$$\frac{-\Delta G_2^{\ddagger}}{RT} - \left(\frac{-\Delta G_1^{\ddagger}}{RT}\right) = 4.6$$

So, $\Delta G_1^{\ddagger} - \Delta G_2^{\ddagger} = 4.6\,RT$

$RT = 0.2 \times 500$

$= 1000$ cal/mol

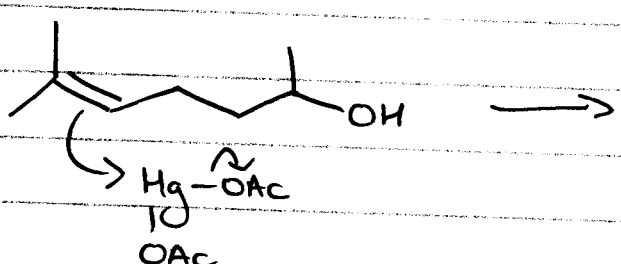
$= 1$ kcal/mol

So, $\Delta G_1^{\ddagger} - \Delta G_2^{\ddagger} = 4.6 \times 1$ kcal/mol

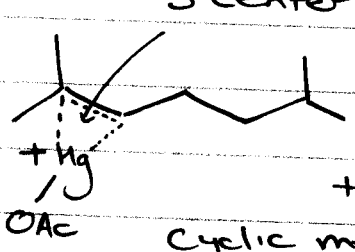
$= 4.6$ kcal/mol

Q4) So, perhaps the best way to answer this question is to do the mechanism first, and that will lead you (hopefully) to the correct product...

1ST STEP:



3 center, 2e⁻ BOND



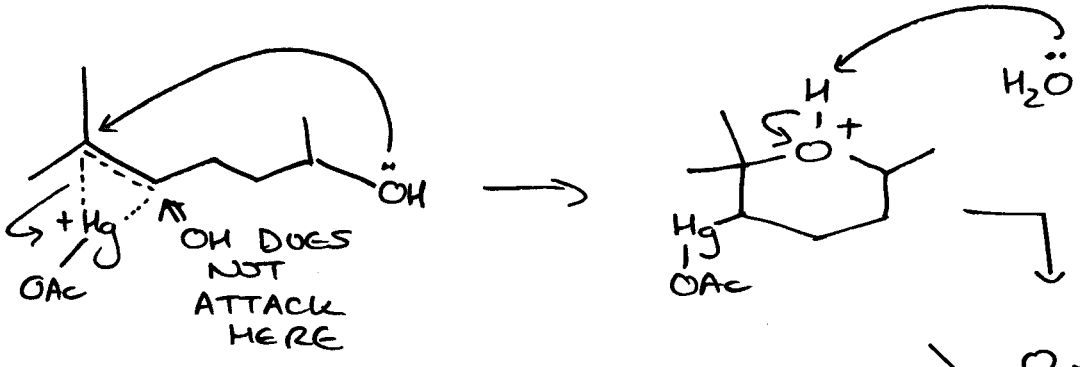
Cyclic mercurinium ion

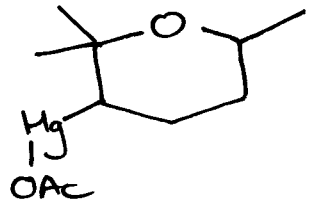
The second step of the reaction is where a nucleophile attacks the cyclic mercurinium ion, and there are TWO CHOICES

(i) H_2O or (ii) the OH group already in the molecule

The first (H_2O) would be an INTERMOLECULAR reaction, whereas the 2nd option would be a much faster INTRAMOLECULAR reaction. MORE IMPORTANTLY HOWEVER, IS THAT IF YOU CHOOSE H_2O TO BE THE NUCLEOPHILE IN THE SECOND STEP, IT WILL GIVE YOU A COMPOUND WITH THE WRONG MOLECULAR FORMULA – because I told you that the final product was $C_8H_{16}O$ i.e., it only contains <u>ONE</u> oxygen atom.

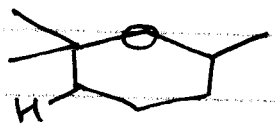
So, the nucleophile is the internal -OH group, and it attacks with MARKOVNIKOV selectivity at the more substituted C atom of the mercurinium ion, i.e.,





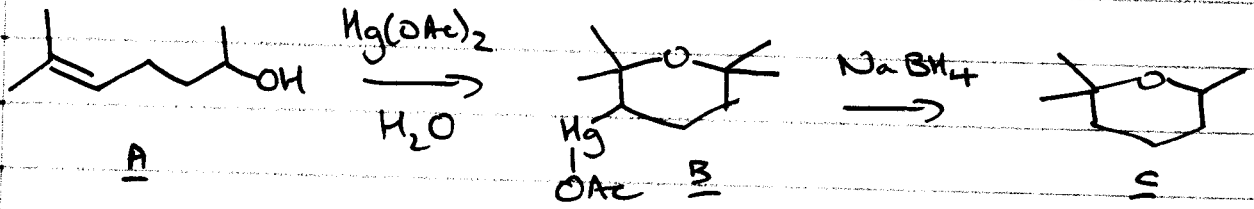
SO, THIS IS B, The Product of OXYMERCURATION

The organomercury compound is then treated with $NaBH_4$, which replaces the $-HgOAc$ group with a -H atom (YOU DON'T NEED TO KNOW THE MECHANISM FOR THIS STEP - it involves radicals)

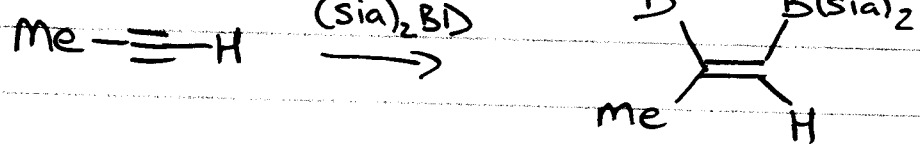
So, C is  which is $C_8H_{16}O$

IF you drew ANY compound that did not have the formula $C_8H_{16}O$, do NOT EXPECT any partial credit, as the answer is obviously wrong.

So, the overall reaction scheme looks like:

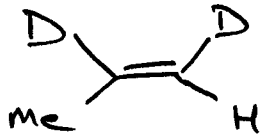


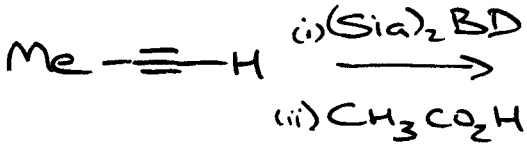
Q5 So, this question tests your understanding of some alkyne chemistry

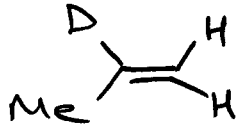
a) 

1ST STEP, B ADDS TO TERMINAL CARBON ATOM

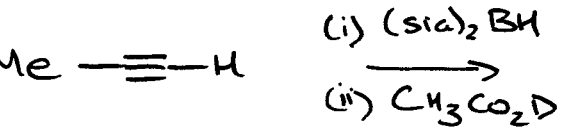
Then in STEP 2, we use CH_3CO_2D, which replaces the $B(sia)_2$ group for a D atom, so the product is

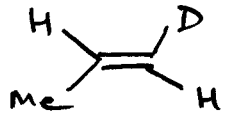


b) 

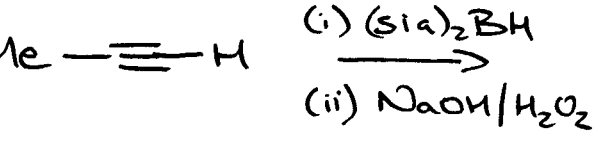


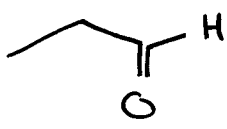
same as part (a), but by using CH_3CO_2H instead of CH_3CO_2D, we replace the $(sia)_2B$ group for H and not D.

c) 

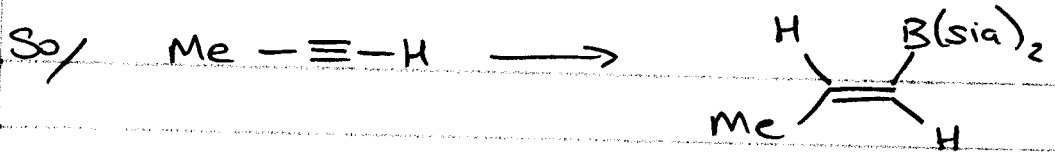


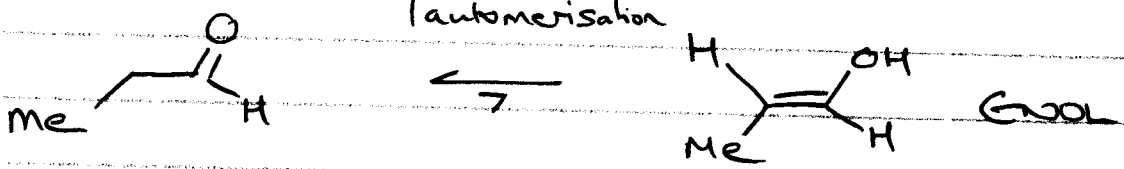
Similar to parts (a) and (b), but we add an H from $(sia)_2B$-H to the non-terminal carbon atom of the alkyne, and the $B(sia)_2$ group is replaced by a D atom from CH_3CO_2D

d) 



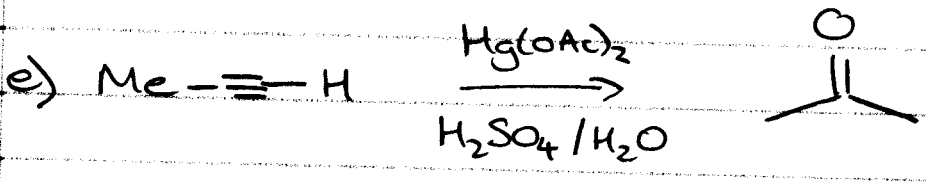
HYDROBORATION/OXIDATION OF A TERMINAL ALKYNE
$\Rightarrow$ ANTIMARKOVNIKOV SELECTIVITY (REGIO)

So/ 



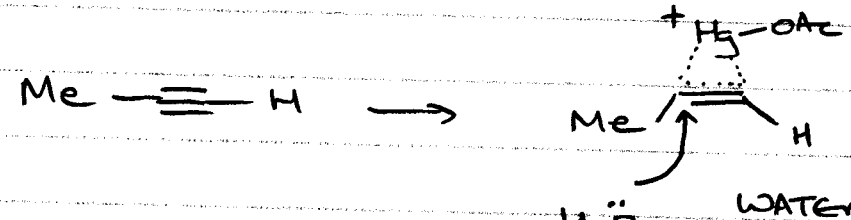
KETO (aldehyde)

ENOL

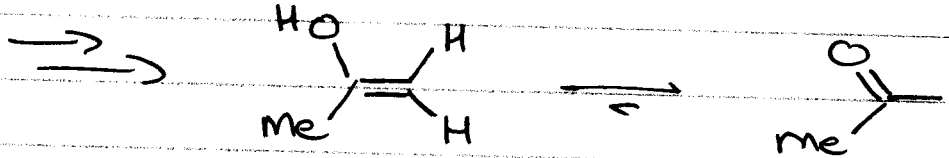
e) 

OXYMERCURATION/HYDRATION

=> MARKOVNIKOV REGIOSELECTIVITY



WATER ATTACKS AT MOST SUBSTITUTED C ATOM



See Lecture notes for mechanism

ENOL

KETO

FOR EXTRA CREDIT QUESTION, A DETAILED EXPLANATION CAN BE FOUND IN THE ANSWER KEY.