Organic Chemistry Peer Tutoring Department
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Chem 51B
Professor Pronin
https://sites.uci.edu/ochemtutors/

Midterm 2 Review Packet

Evaluation form: https://forms.gle/aiMLtZL8U3zBjUUR7

Topics to review:

Chapter 9: Alcohols, Ethers, and Related Compounds

- Synthesis of alcohols, ethers, and epoxides
- Rank alcohols by reactivity in various reactions
- Recognize carbocation rearrangements and draw the resulting products
- Draw the mechanism and products of alcohol dehydration for 1°, 2°, and 3° alcohols
    - Including dehydration with $POCl_3$ and pyridine
- Convert alcohols to alkyl halides using HX, $SOCl_2$ and pyridine, or PBr_3
- Generate alkyl tosylates from alcohols
- Predict products of reactions of epoxides with strong nucleophiles or strong acid

Chapter 10: Alkenes

- Predict the products and draw the mechanisms for the 5 major alkene addition reactions:
    - Hydrohalogenation
    - Hydration
    - Halogenation
    - Halohydrin formation
    - Hydroboration-oxidation
- Use Markovnikov's Rule to determine regioselectivity
- Recognize the stereochemistry of each alkene reaction

Chapter 11: Alkenes

- Predict the products and draw the mechanisms for the 4 major alkyne addition reactions:
    - Hydrohalogenation
    - Halogenation
    - Hydration
    - Hydroboration-oxidation
- Recognize keto-enol tautomerization
- Devise a synthesis for organic compounds

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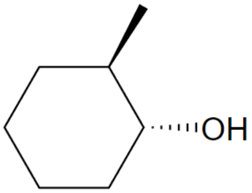
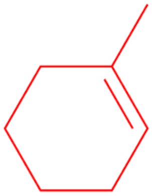
Chapter 9:

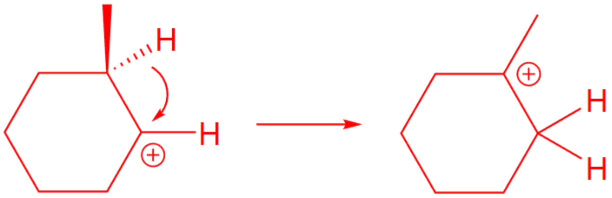
1.

a. What is the major alkene formed when the compound below is dehydrated with H_2SO_4? (9.47)



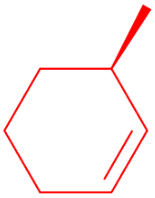


The reaction of a 2° alcohol with H_2SO_4 proceeds by E1. Therefore, a carbocation forms, and a 1,2-hydride shift occurs to go from a 2° carbocation to a more stable 3° carbocation (shown below).

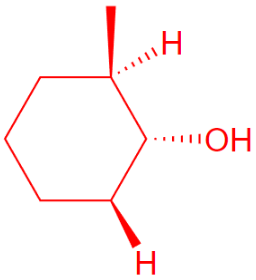


After a beta hydrogen is removed, a trisubstituted alkene forms.

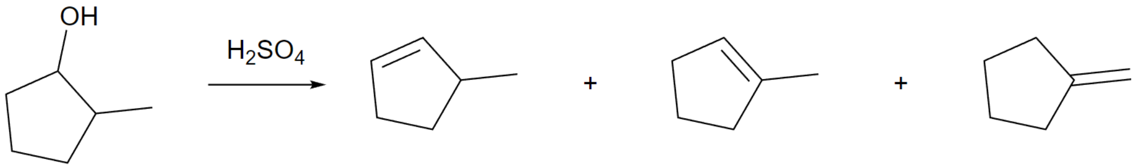
b. What is the major alkene formed when this compound is treated with $POCl_3$ and pyridine? Explain why the major product is different in these reactions.

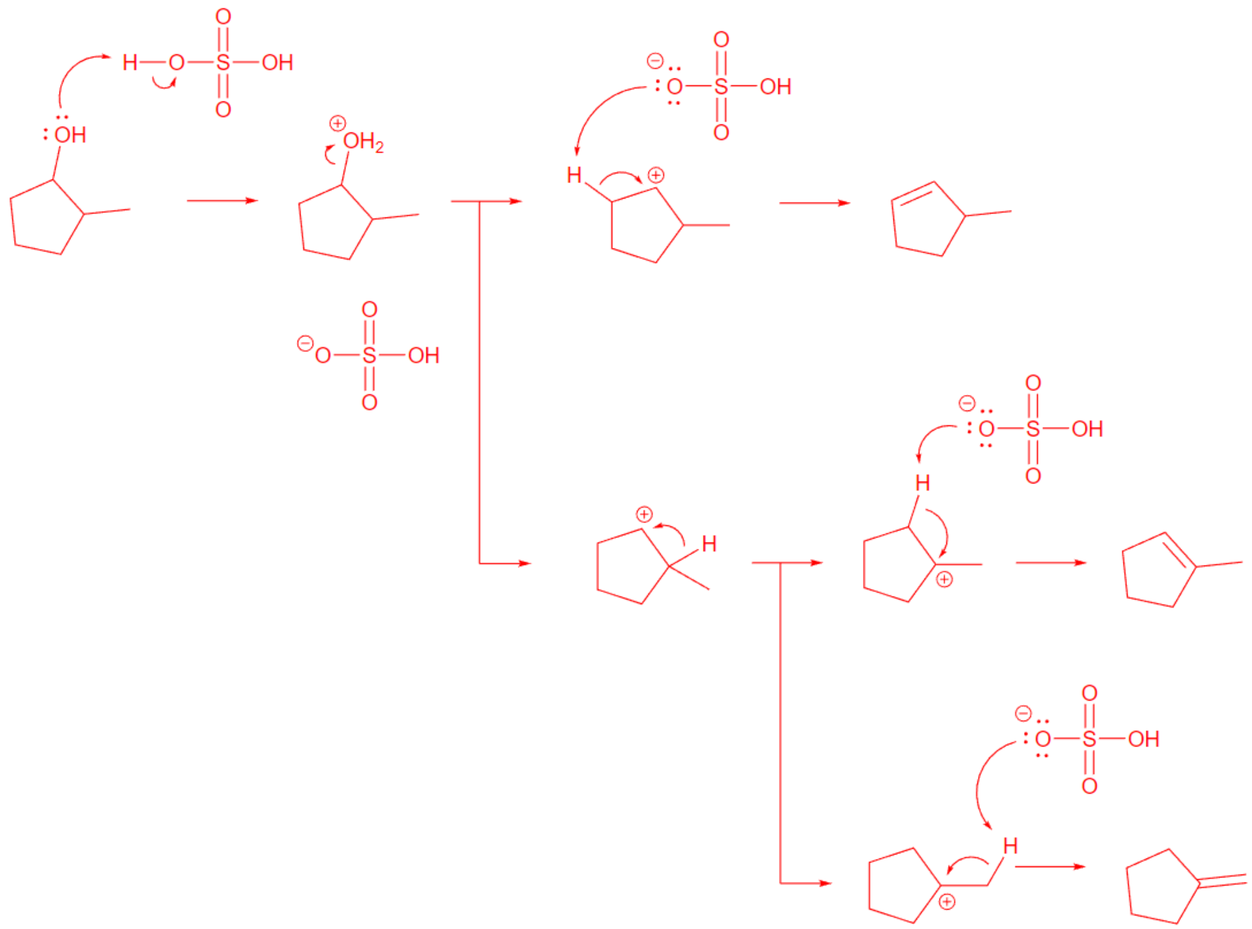


The reaction of $POCl_3$ and pyridine with an alcohol always proceeds by E2. Since no carbocation is formed, there is no carbocation rearrangement. Therefore, the only available beta hydrogen to remove is on the side *away* from the methyl – this is because E2 requires the beta hydrogen and leaving group to be antiperiplanar (and therefore trans). The only hydrogen on the more substituted side is cis to the leaving group, as shown below.



2. Draw a stepwise mechanism for the following reaction. (9.49)

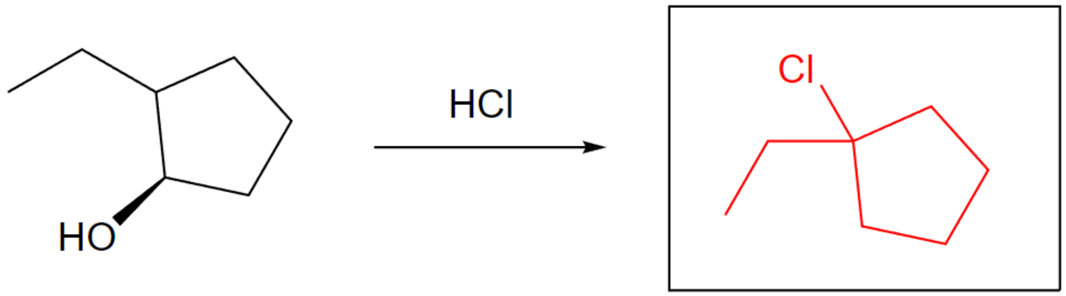




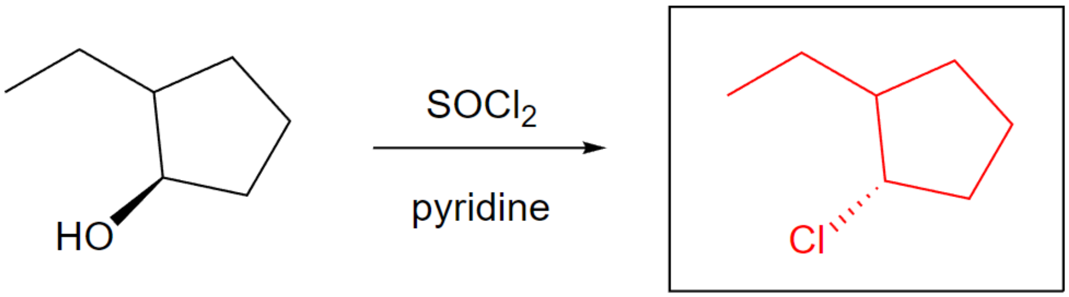
Since this is a 2° alcohol, the dehydration reaction with strong acid proceeds by E1. As typical of such a reaction, H_2SO_4 first protonates the alcohol OH group to turn it into a good leaving group. As H2O leaves, a carbocation forms. A disubstituted alkene can be formed here.

However, a carbocation rearrangement can also occur through a 1,2-hydride shift. There are then two different beta hydrogens that can be removed to complete the reaction and form two different possible alkene products. The second product shown could also be created without a carbocation rearrangement.

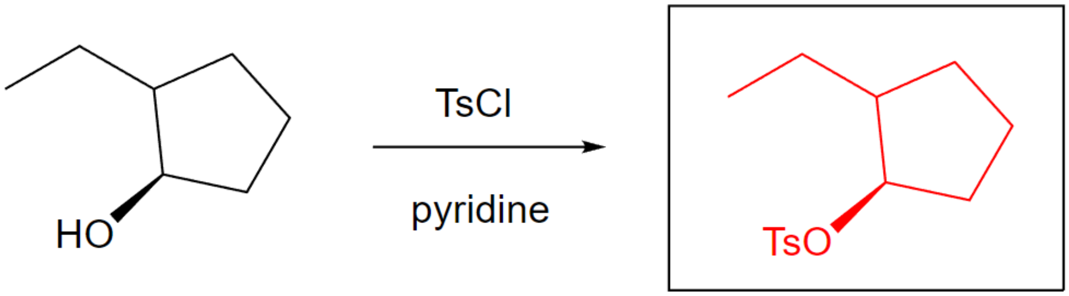
3. Draw the major product formed (including stereochemistry) when the given compound is treated with each reagent. (9.37)



HCl protonates the alcohol OH group, which leaves as H_2O and forms a carbocation. A carbocation rearrangement moves the carbocation to the 3° carbon, where Cl- then attacks.

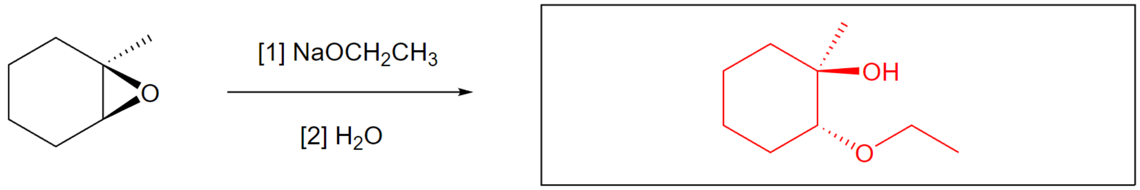


$SOCl_2$ reacts with alcohols by S_N2 to turn them into an alkyl chloride. Therefore, the nucleophile performs backside attack and the newly installed Cl has opposite stereochemistry to the original OH leaving group.

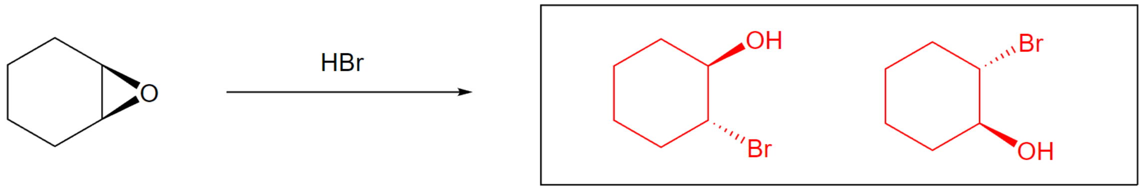


TsCl reacts with alcohols to replace the OH group with a tosylate group (TsO). Since the mechanism of this process does not even involve the carbon stereocenter, the stereochemistry is unchanged.

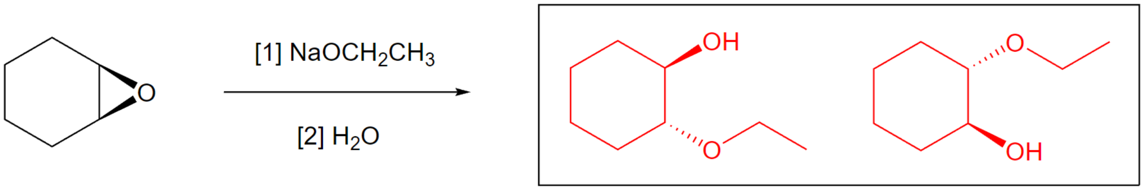
4. Draw all products of the following reactions. (9.60, 9.64)



Since there is no strong acid to protonate the epoxide and the nucleophile present is a strong nucleophile, the reaction will proceed by S_N2. Therefore, -OCH2CH3 will perform backside attack at the *least* substituted carbon. The negatively charged O left behind as the ring opens is then neutralized by water.



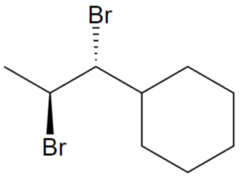
HBr protonates the epoxide O. Since the epoxide has equivalent groups bonded to either of its carbons, Br- does not favor attacking either side. Br- will perform backside attack. Therefore, two different products form with Br always pointing into the page and OH pointing out of the page. Note that these two are enantiomers.



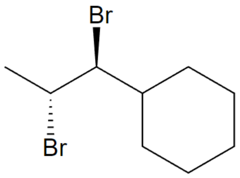
Since the epoxide has equivalent groups bonded to either of its carbons, its reaction with a strong nucleophile works the same way as the previous reaction above (with a strong acid HBr present). -OCH2CH3 performs backside attack to form two different products, which again are enantiomers.

Chapter 10: Alkenes

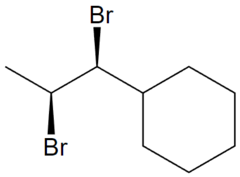
5. What alkene yields A and B when it is treated with Br_2? What alkene yields C and D under the same conditions? (10.54)



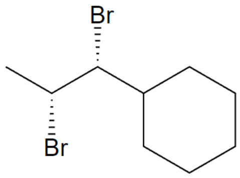
A



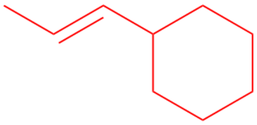
B



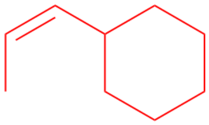
C



D

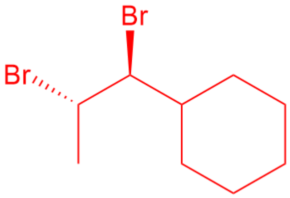


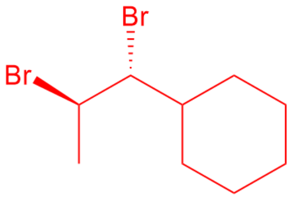
A and B



C and D

The reaction of Br_2 and alkenes is anti addition (the Br atoms end up on the opposite sides of the alkene). Rotate the bonds in C and D to find a conformation where the bromines are pointing in opposite directions:

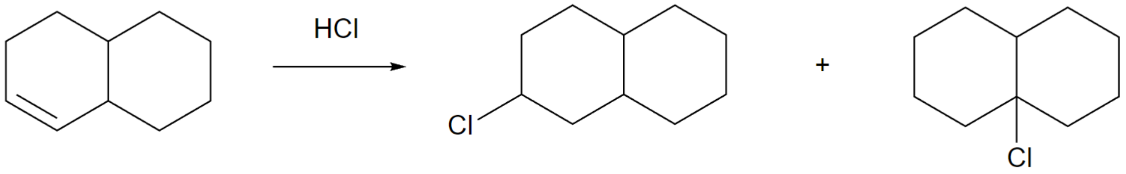


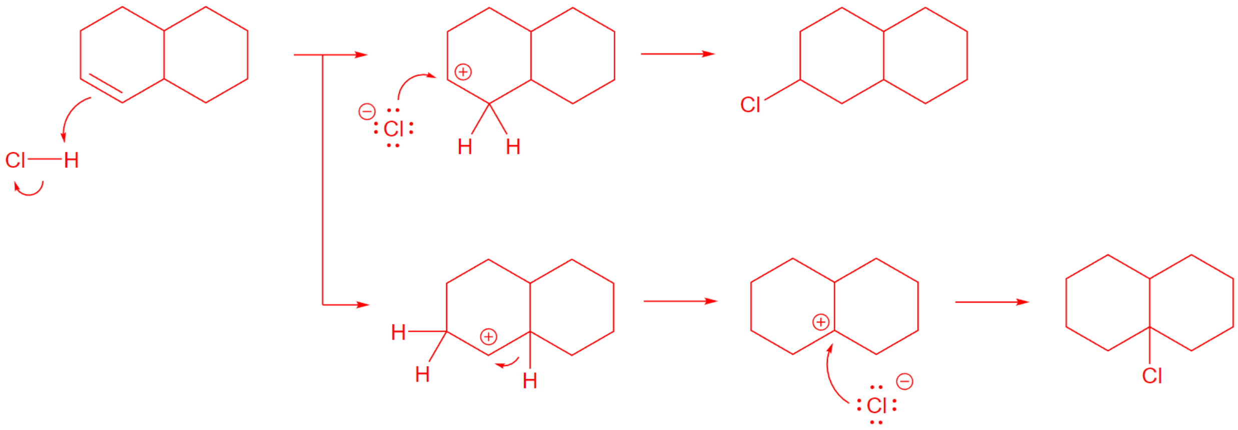


Then draw in the alkene with the carbon skeleton in this conformation. Since the bromines must end up on opposite sides after the addition, this must be the starting alkene.

A and B are already in a conformation where the bromines are on opposite sides, so that is the stereochemistry of the carbon skeleton in the starting alkene.

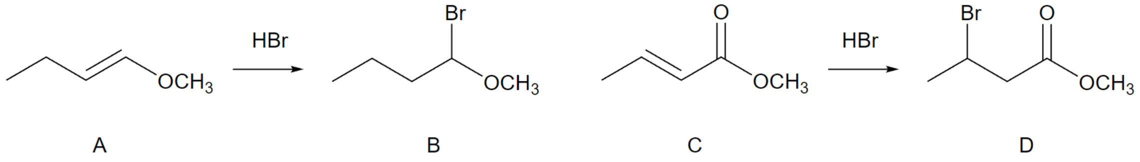
6. Draw a stepwise mechanism for the following reaction. (10.55)



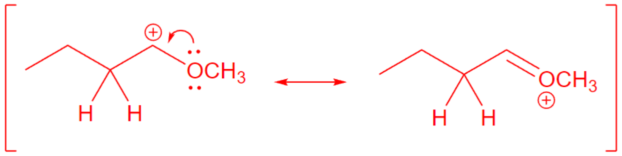


In the first step of hydrohalogenation, H adds to the alkene, resulting in a carbocation. Since the two sides of the alkene are equally substituted, there is no preference for which side H will add to. Therefore, two different carbocations can form. If the carbocation forms on the carbon on the left side of the alkene, Cl- can attack it and form the first product. However, if the carbocation forms on the right carbon, a carbocation rearrangement can occur to form a more stable 3° carbocation, which Cl- attack to form the second possible product.

7. Explain why the addition of HBr to alkenes A and C is regioselective, forming addition products B and D, respectively. (10.61)

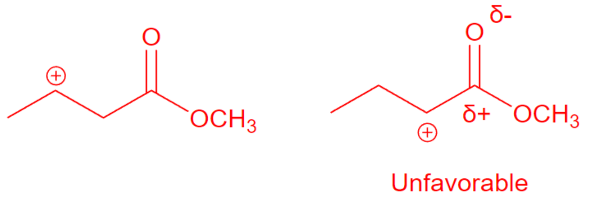


For the addition of H to alkene A, it is preferred to form the carbocation on the right side, since this allows for stabilizing resonance due to the lone pairs on the adjacent O. The resonance structures are shown below.

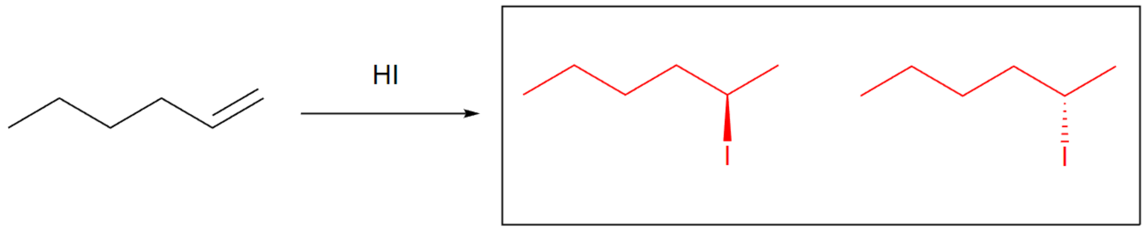


Therefore Br- will attack on the right side and form alkene B.

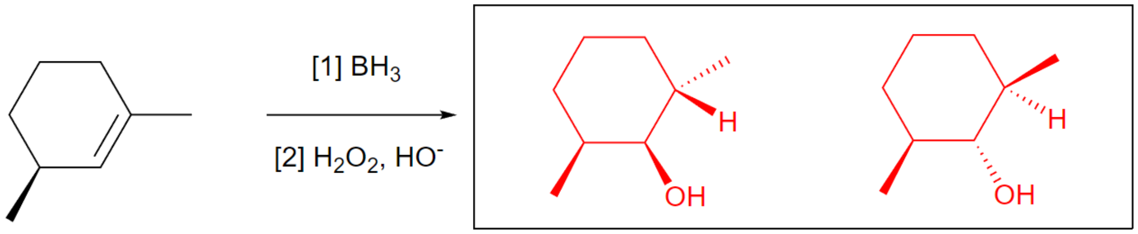
The carbonyl on alkene C causes the carbonyl carbon to have a partial positive charge due to resonance. It is unfavorable to form the carbocation on the right side of the alkene since there will be a positively charged carbon adjacent to a partial positive carbon. Therefore H adds to the right side to form the carbocation on the left side, and Br- attacks on the left side.



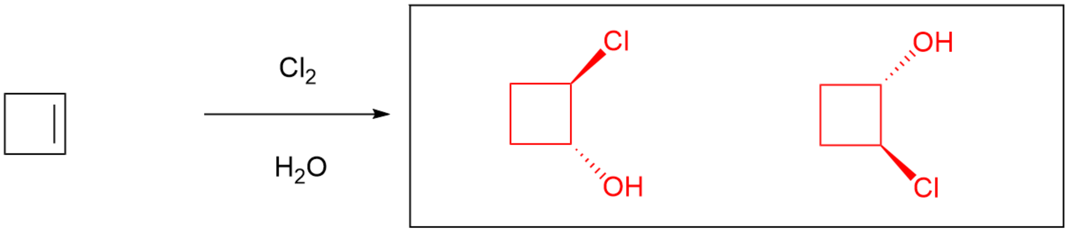
8. Draw the products of each reaction, including stereoisomers. (10.52)



Since hydrohalogenation involves a halide attacking a carbocation, the halide can come in from either side of the alkene. This produces two different alkyl iodides depending on which side HI addition occurred.



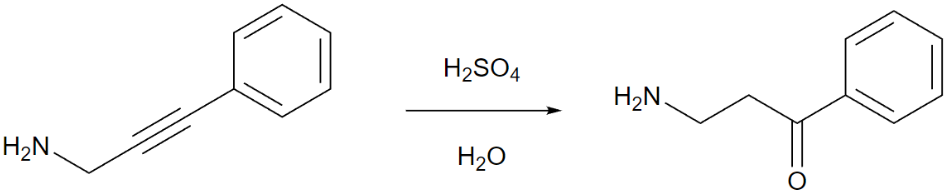
Hydroboration-oxidation involves syn addition. OH and H are added to the same side of the alkene. If both come in from the side of the alkene facing out of the page, the methyl on the top carbon is pushed back and ends up pointing into the page. If both come in from the side of the alkene facing into the page, the same methyl is pushed forward and ends up pointing out of the page.

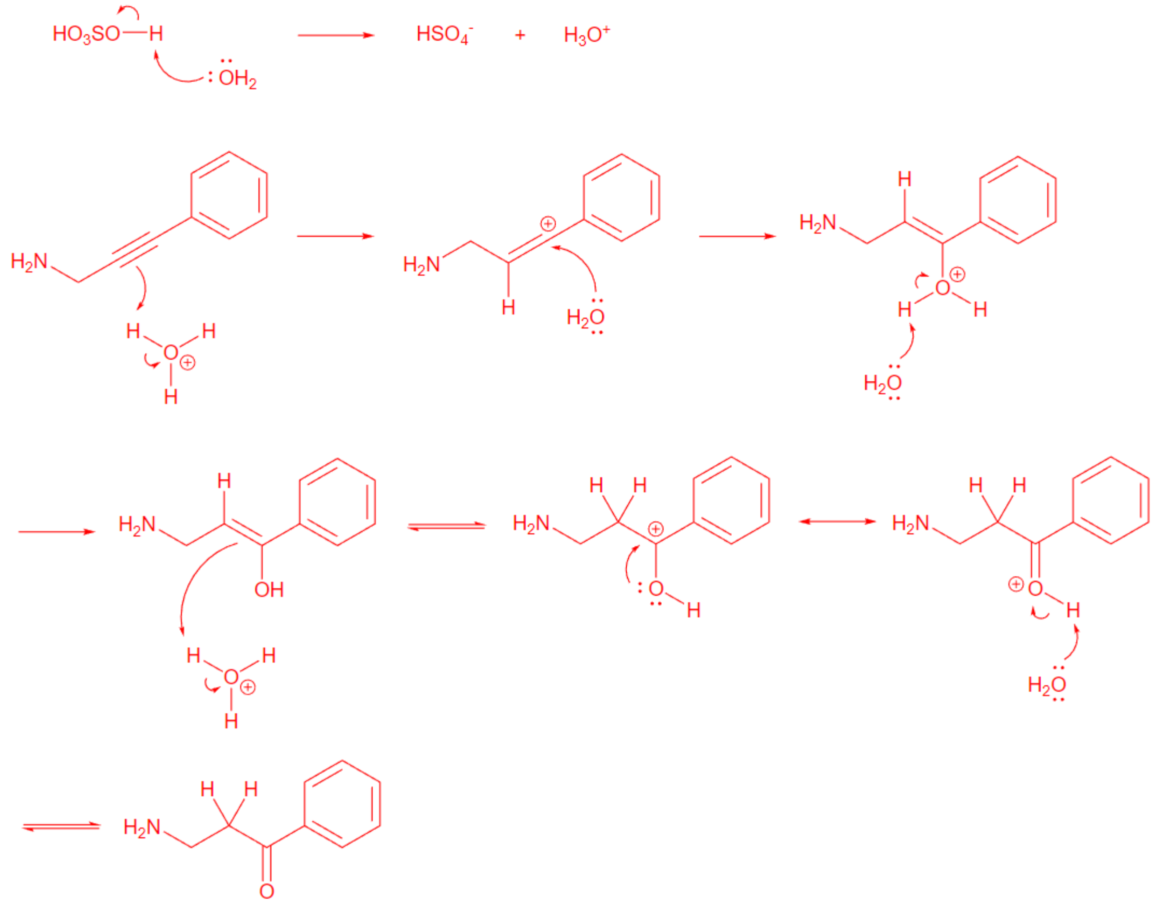


Halohydrin formation involves anti addition. Cl and OH must end up trans to each other on the 4-member ring, so there are only two possible products.

Chapter 11: Alkynes

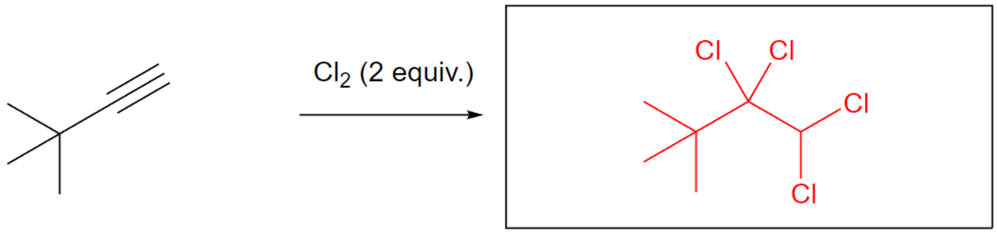
9. Draw a stepwise mechanism for this reaction and explain why only this ketone forms. (11.43)



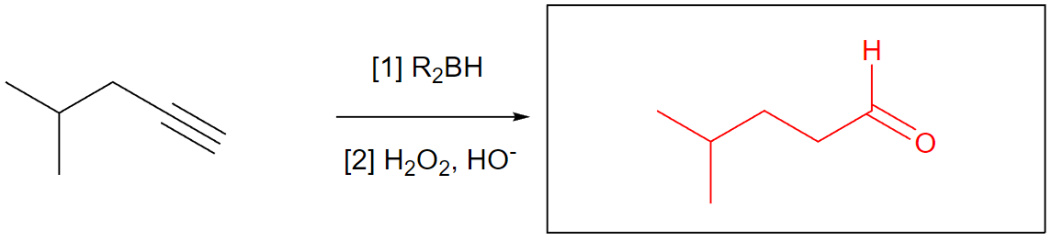


Since water is present as a solvent, it is protonated first by H_2SO_4. Acid-catalyzed hydration of an alkyne starts with addition of an H and formation of a carbocation. It is favorable for the carbocation to form at the carbon on the right since the nearby benzene stabilizes it by resonance. The N on the left is two bonds away from the alkyne so it would not be able to donate electrons to form resonance structures. Therefore, only this ketone can form, as there would be no carbocation on the left side of the alkyne for the water to attack.

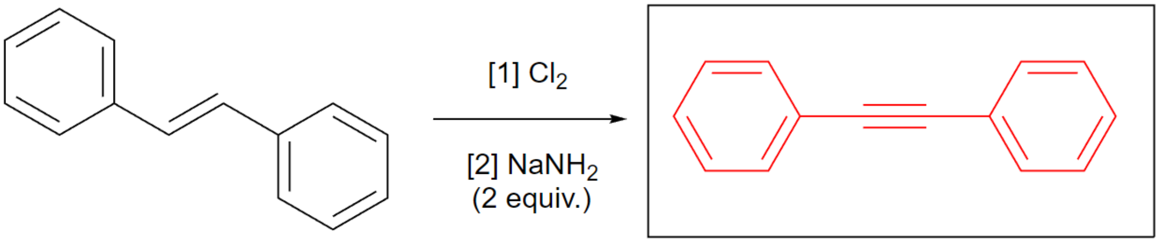
10. Draw the organic products formed in each reaction. (11.38)



The result of halogenation of an alkyne is that each equivalent of Cl_2 effectively breaks a pi bond and installs a Cl at either end of the former pi bond. Two equivalents turn the alkyne into an alkane and install four chlorines.

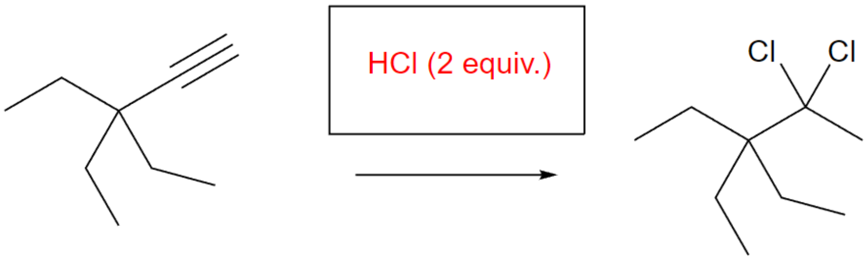


Hydroboration-oxidation of an alkyne is similar to hydroboration-oxidation of an alkene. For both, the new C-OH bond is on the carbon with *less* substitution or that participates less in resonance. In this case, that is the right side of the alkyne, so that's where the C-OH bond forms, which then becomes a carbonyl after tautomerization.

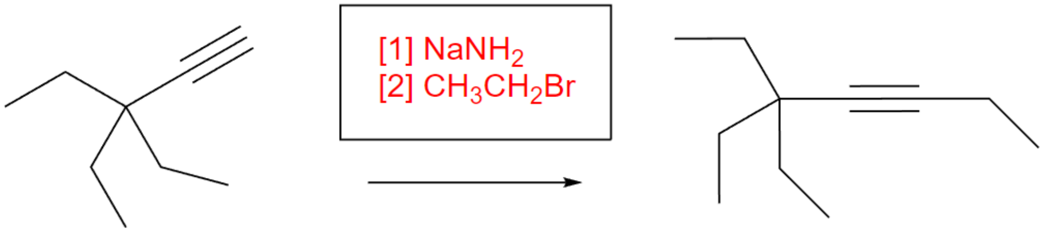


Halogenation of an alkene with Cl_2 forms a vicinal dihalide. Adding two equivalents of a very strong base like NH_2^- causes two successive elimination reactions that remove both chlorines and form 2 pi bonds, resulting in an alkyne.

11. What reagents are needed to convert the starting material to each compound? (10.34)

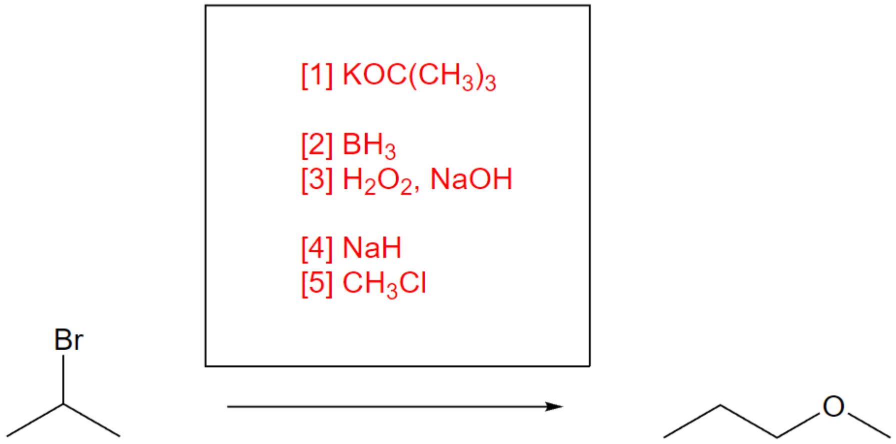


The reaction involves an alkyne turning into a geminal dihalide (two halogens on the same carbon). The halogens are also on the *more* substituted carbon. This is characteristic of hydrohalogenation, so the reagent needed is HCl. Since the alkyne was reacted all the way to an alkane and two chlorines are added, we need two equivalents of HCl.



Note that the structure of the entire starting material is retained. The only new part is an ethyl group attached to the alkyne. One way to achieve this is to deprotonate the alkyne using a very strong base like $NaNH_2$ or NaH to turn the alkyne into a nucleophile, which can then perform a nucleophilic substitution reaction with ethyl bromide. This must be done in two separate steps because if added together, NH_2^- would attack ethyl bromide directly.

12. Devise a synthesis of each compound using the given starting material. You may use any other organic compounds or inorganic reagents. (10.63b, 11.49c)

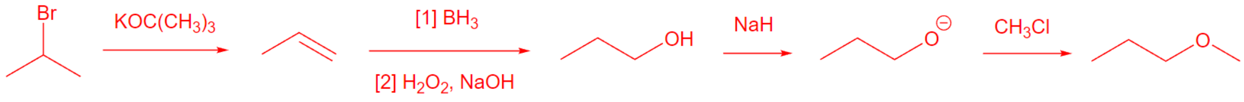


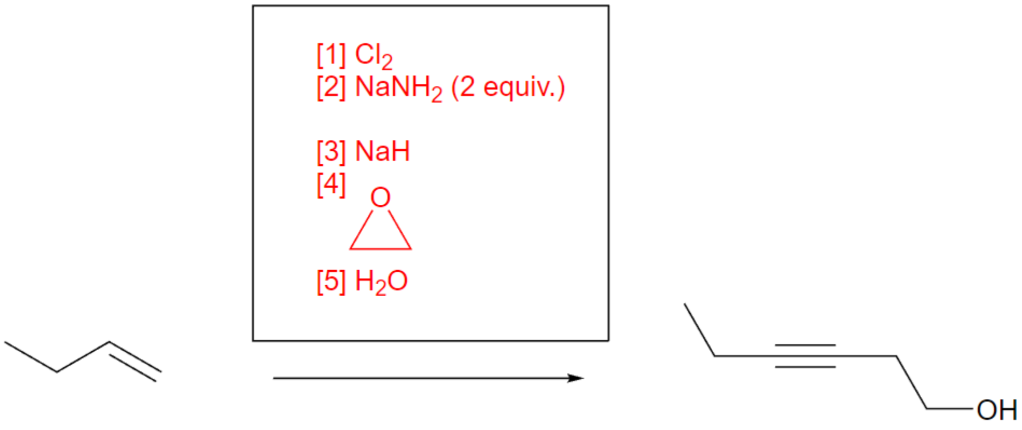
With synthesis problems, try working forward from the starting material or working backward from the product or both at once.

One way to get the product would be nucleophilic substitution, which means that in the previous step the compound was either a nucleophile or alkyl halide. Let's say it was the nucleophile and the reaction was S_N2. So in the previous step, it was an alkoxide. To be deprotonated, it would have started as a 1° alcohol and gotten deprotonated by a strong base like NaH.

Now we work forward from the starting 2° alkyl halide to get the 1° alcohol that we need. Since the OH group is on a different carbon than Br, this can't just be nucleophilic substitution. Instead, we can do an elimination reaction using a bulky base like tert-butoxide to form an alkene. Then hydroboration-oxidation will install OH on the less substituted carbon to form a 1° alcohol.

Now stitch these two lines of thinking together to get one full list of steps.





Use a similar thought process here. The product has a R-C-C-OH pattern that is characteristic of an epoxide ring opening. Since the starting material has four carbons, epoxide was an added reagent and the acetylide nucleophile is what we're working with. This would have needed to be deprotonated by a very strong base like NaNH2 or NaH.

To turn the starting alkene into an alkyne, do halogenation to add two halides. This can then undergo double elimination using two equivalents of a very strong base like NaNH2 or NaH to form the alkyne.