Midterm 2 Review Answer Key

Concepts Covered:

Ch. 9
- Alcohols and Ethers
- Epoxide Formation
  - Rxns with Epoxides
- Dehydration
- Carbocation Rearrangement
- Conversion of Alcohols to Alkyl Halides

Ch. 10
- Physical Properties of Alkenes
- E and Z isomerism
- Synthesis of alkenes via elimination
  - Commonly used reagents
- Alkene Addition Reactions
  - Hydrohalogenation
    - Carbocation Rearrangement
  - Halohydrin formation
  - Hydroboration–Oxidation
  - Synthesis
- Markovnikov’s Rule

Ch. 11
- Alkyne Reactions
  - Addition
    - Hydrohalogenation
    - Halogenation
      - Geminal
      - Vicinal
    - Hydration
    - Hydroboration–Oxidation
1. Draw a stepwise mechanism for each reaction.

\[ \text{OH} \quad \xrightarrow{\text{H}_2\text{SO}_4} \quad \text{Cyclic Compound} \]

\[ \text{Cyclic Compound} \quad \xrightarrow{\text{H}_2\text{SO}_4} \quad \text{OH} \]
Dehydration of secondary alcohols will undergo via an E1 mechanism and thus will produce carbocation intermediates. These carbocation intermediates can rearrange to form more stable intermediates and is SOMETHING YOU SHOULD LOOK FOR ALWAYS with these types of reactions. Both reactions above had carbocation rearrangements within their mechanism and from there the different Beta Hydrogens led to different alkene products in both instances.
2. Draw the products of each reaction and indicate stereochemistry around stereogenic centers.

Remember that SOCl\(_2\) with pyridine or PBr\(_3\) change the alcohol to an alkyl halide via inversion and alkyl tosylate conversely changes the alcohol to a tosylate leaving group with retention of the original stereochemistry of the alcohol. Hydrogen Halide acids can react via sn2 if the alcohol is primary or sn1 if the alcohol is either tertiary or secondary resulting in inversion or racemization, respectively.
3. Write the reagents needed to complete the indicated reaction with the only product form being the one drawn:

\[
\text{OH} \quad \xrightarrow{1. \text{SOCl}_2, \text{pyridine or PBr}_3} \quad \text{CN} \\
\text{2. NaCN}
\]

Note that for the stereochemistry to be retained in two steps the most likely way for this to occur is with double inversion. We must introduce a good leaving group without forming carbocations and this is usually done via sn2 reactions. To do this we can use either SOCl$_2$ with pyridine or PBr$_3$ which changes the alcohol to an alkyl halide via exactly sn2 inversion. From here we can do an sn2 reaction again using NaCN which will revert the stereochemistry back.
4. Draw the products of the following reactions. Show stereochemistry where necessary.

A. 1. \( \text{NaOCH}_2\text{CH}_3 \)
    2. \( \text{H}_2\text{O} \)

B. 1. \( \text{CH}_3\text{CH}_2\text{OH} \)
    2. \( \text{H}_2\text{SO}_4 \)
Note that epoxide opening via strong nucleophiles occurs via nucleophilic attack of least substituted carbon of the epoxide ring while acid-catalyzed epoxide ring opening occurs via attack at the most substituted carbon. Note also that regardless of the route the nucleophile performs a backside attack and thus be on opposite sides of the alcohol formed following epoxide opening.
5. (i) Draw two different routes to each of the following ethers using a Williamson ether synthesis. Indicate the preferred route (if there is one). (ii) Draw the products formed when molecule b is treated with two equivalents of HBr.

Solution (i):

Solution (ii):
Note how the products of 2 equivalents of H-Br (The same occurs with use of 2 equiv of HI as well) are just the carbon skeletons on each respective side of the epoxide drawn as alkyl halide.
6. Prepare an alkene from each starting material by adding appropriate reagents. Then, if applicable, decide whether each alkene is E or Z.

a. All the above reagents can lead to the product alkene via E2 elimination. The product is neither E nor Z because all the substituents are the same. Note: POCl₃ must be used with pyridine.

b. Any bulky base would do well in making an alkene. Elimination leads to 3 products: a monosubstituted alkene and an E (trans) and Z (cis) disubstituted alkene.

c. Much like part a, the above reagents allow the formation of an alkene via E2 elimination from an alcohol. The product is neither E nor Z because both sides house the same substituents (one side has 2 methyl groups and the other 2 hydrogens). Note: POCl₃ must be used with pyridine.
7. Draw out the electron-pushing mechanism of the following reaction. Draw out the individual stereoisomers of the product in your mechanism, if applicable.

In step 1, we form a bromonium ion either via an attack from the top or bottom, leading to 2 enantiomers as intermediates. In step 2, note that the Br⁻ always attacks the more substituted carbon in halogenation of alkenes, leading to enantiomeric products.
8. (10.26) Which alkylborane is formed from hydroboration of each alkene?

A.

B.

Solution:
Hydroboration involves addition of BH₂ and H to the alkene, forming an alkylborane.
Hydroboration is regioselective: when the alkene is unsymmetrical, the boron atom bonds to the less substituted carbon atom.

A. The given alkene is unsymmetrical, meaning that both sides of the double bond are not equivalent. Thus, boron is added to the less substituted carbon of the double bond.

B. The given alkene is unsymmetrical, meaning that both sides of the double bond are not equivalent. Thus, boron is added to the less substituted carbon of the double bond.
9. (10.14) Draw out the missing structures A and B.

Solution: This is a reaction of a conversion of BH$_3$ to a trialkylborane with 3 equivalents of CH$_2$=CH$_2$. 
10. Complete the following reactions by adding missing components.

a. BH$_3$ performs a syn-addition on the alkene, adding the BH$_2$ group to the less substituted carbon and the H to the more substituted carbon. This addition may occur via the top or bottom of the molecule, leading to enantiomers. H$_2$O$_2$ + NaOH are reaction conditions that allow the substitution of BH$_2$ for OH (oxidation) with a retention of stereochemistry, unlike Sn2 which causes inversion.

b. This is a typical halohydrin formation reaction. The reaction proceeds with the corresponding diatomic halogen (Cl$_2$) and H$_2$O.
c. This is a hydrohalogenation reaction. Be careful and note that in hydrohalogenation, a carbocation is formed as an intermediate. This secondary carbocation can undergo a 1,2-hydride shift to form a more stable tertiary carbocation (see mechanism below). The bromide then adds to the C+ position, leading to the final product.

11. (11.5) Draw the products of the following reactions when but-1-yne is placed in such conditions. Let X be Br for this question.
A.

\[
\text{2 HX} \\
\text{(X = Cl, Br, I)}
\]

B.

\[
\text{2 X}_2 \\
\text{(X = Cl, Br)}
\]
Solution:
First, we must draw out the correct structure for but-1-yne. The structure is as such: remember that but- means the structure must have 4 carbons. The suffix -yne means that there is an alkyne at the C1 position.

\[
\text{but-1-yne}
\]

A. A hydrohalogenation addition reaction occurred. In this reaction, 2 H’s and 2 Br’s are added.
B. A halogenation addition reaction occurred. In this reaction, 4 Br’s are added.
C. A hydration addition reaction occurred. In this reaction, 2 H’s and 1 O are added.

The first couple steps (the first three arrows) are the addition of H2O to form an enol. The remaining 3 arrows are the tautomerization step, which involves converting the enol into a keto form.

D. A hydroboration-oxidation reaction occurred. In this reaction, 2 H’s and 1 O are added. Professor Pronin never went over the mechanism of hydroboration-oxidation in class, so I doubt that you will get tested on the specific mechanism. However, what is important is to know that there are 3 steps in this reaction: hydroboration, which is the addition of BH3, oxidation, which is the conversion from BH2 to an OH, and finally tautomerization, which is a conversion from enol to a keto form. I have attached the hydroboration portion of this reaction, as you can see, it is complex.
and will not be tested on the midterm, given the time restraint.

After this, tautomerization proceeds. Which forms the bottom structure.

12. (11.3) Show the mechanism and product of this tautomerization of the given molecule.

Solution:
Tautomerization is the reaction of converting an enol form structure to a keto form. Thus, for every tautomerization, we MUST start off with an alcohol, and MUST end with a carbonyl group. In a tautomerization, first, we have protonation of the double bond, then, after a resonance-stabilization step, the positive charge is allocated to the oxygen, finally, the oxygen is deprotonated to regenerate
13. (11.7) Draw the organic products formed when each alkyne is treated with two equivalents of HBr.

A.

B.

Solution: the addition of 2 HBr follows the Markovnikov’s Rule when it is a terminal alkyne.
14. (11.14) Draw the products formed when the following alkynes are treated with each set of reagents: [1] H2O, H2SO4, HgSO4; or [2] R2BH followed by H2O2, –OH.
Solution:

Condition 1: H2O, H2SO4, HgSO4, which is an addition of water reaction. Therefore, there should be a net gain of 2 H’s and 1 O.
The hydration reaction of an alkyne involves an addition and tautomeration portions.

Product:

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\[ \text{Product} \]
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Mechanism:

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\[ \text{Mechanism} \]
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Condition 2: This is a hydroboration oxidation

Product:

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\[ \text{Product} \]
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Steps:

15. (11.11) Draw the keto tautomer of each enol.
A.

B.

C.

Solution:
A.

B.
C.