Chemistry 310
Spring 2009
Prof. B. Hanson

Name: KEY

Exam #1

1. _____ 15 points

2. _____ 15 points

3. _____ 15 points

4. _____ 10 points

5. _____ 15 points

6. _____ 15 points

7. _____ 15 points

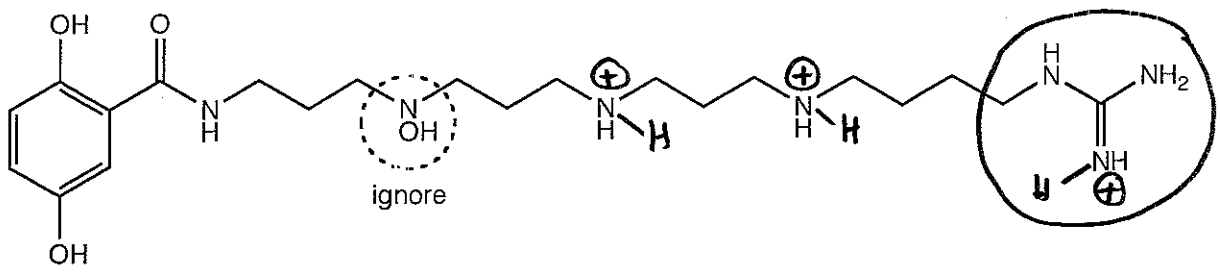
100 points

"Molecular interactions and chemical transformations are at the heart of biology, and all biological phenomenon that we can analyze today can be traced back to chemical processes: biology is molecular."

"This insight, on the one hand, makes clear that chemistry may turn out to be the central science in the quest for understanding the molecular basis of life. This is so because the study of interactions between molecules, be they large or small, and the methodology to prepare them and to prepare new compounds with a predetermined set of properties are at the heart of chemistry and constituted the key expertise of chemists. On the other hand, it demands from chemistry to devote a major part of its undisputed powers to addressing the problems unravelled by the research in the biological sciences."

H. Waldman
"At the Crossroads of Chemistry and Biology"
Biorganic & Medicinal Chemistry 11 (2003) 3045-3051

1. (15 points). The following molecule was isolated from the venom of a spider in the genus *Agelenopsis*.



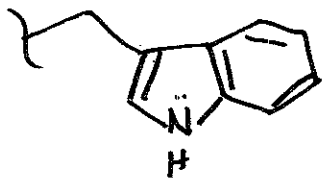
5 pts each

a. Modify the structure above carefully to show its protonation state at pH 7.

b. On your structure from question (a), circle the least acidic group and give its approximate pKa.

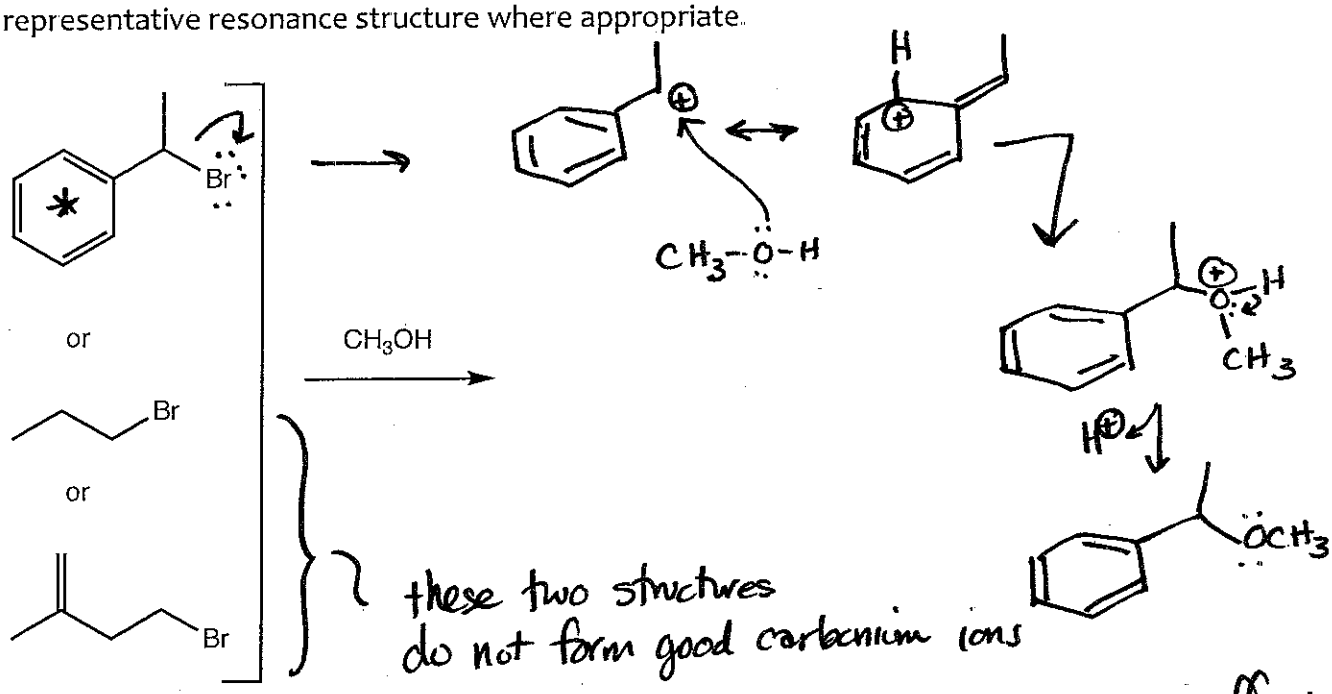
~12.5 (guanidinium group, compare to arg)

c. The side chain of the amino acid tryptophan is not very basic. Draw the structure of the side chain, and explain why it is not basic.



The lone pair on trp (the N) is in a 2p orbital and "busy" w/resonance. Therefore it is not very basic (not even remotely)

2. (15 points). Choose an appropriate structure from the list below, and draw out an S_N1 mechanism showing it reacting with methanol (you will be predicting the product in the process). Be sure all lone pairs, all formal charges, and all mechanistic arrows are shown. Include a representative resonance structure where appropriate.

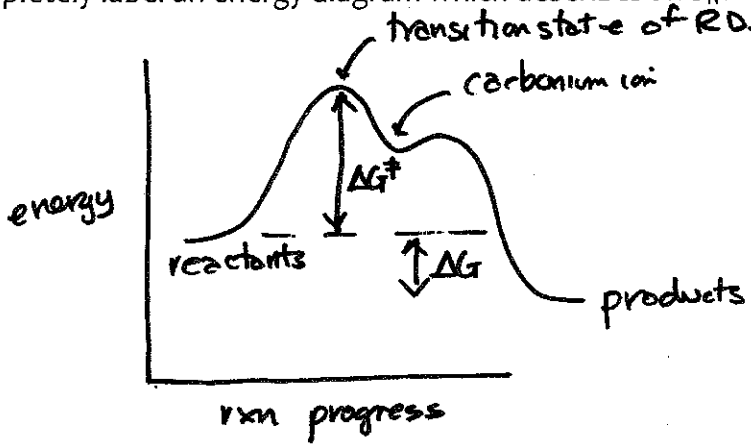


these two structures do not form good carbocation ions

* best candidate for SN1 due to resonance and inductive effects.

3. (15 points)

a. Draw and completely label an energy diagram which describes an S_N1 mechanism.



discussed in class

b. If a better leaving group is used, what happens to the energy profile? Annotate your answer to part (a) to show any changes. If you predict there is no change, state so.

Transition state energy and $\Delta G^{\ddagger}$ decrease (same $c^{\oplus}$ is produced)

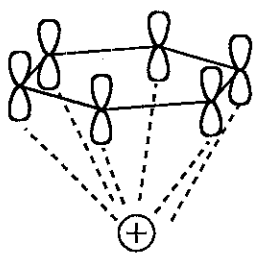
c. Draw and completely label an energy diagram for an Ad_E reaction.

This is identical to the one in part (a), since the slow step would be the protonation of an alkene to produce a carbonium ion.

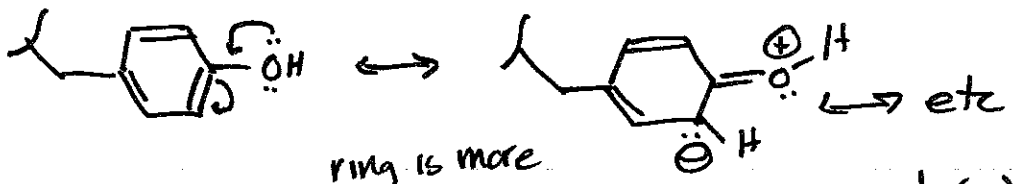
this one was not discussed in class

5 pts each

4. (10 points). We have seen several examples of a cation-π interaction in which an aromatic ring "sits" on a positive charge, as shown below. For example, phe can participate in this type of interaction, as can tyr. Would the interaction between tyr and an ion be stronger, about the same, or weaker than phe? Explain clearly.

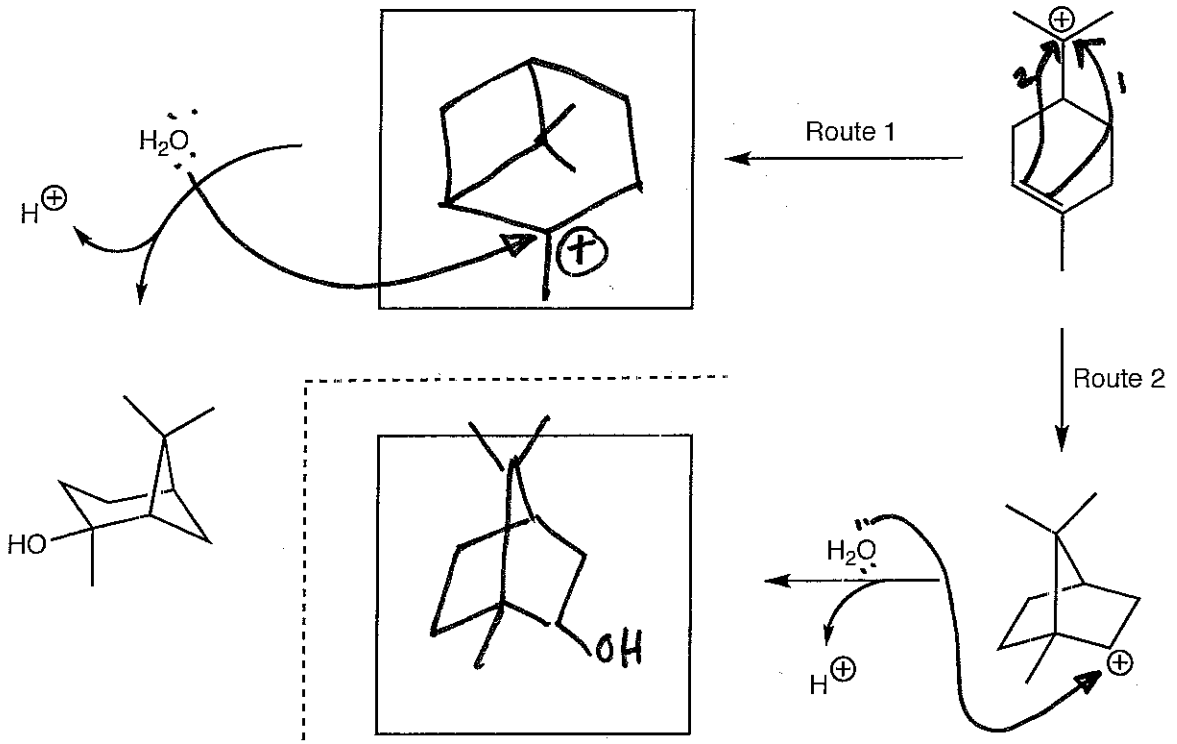


tyr, w/ the OH on the aromatic ring, is a better e^- donor / more e^- rich ring, so the interaction between tyr + (+) should be stronger



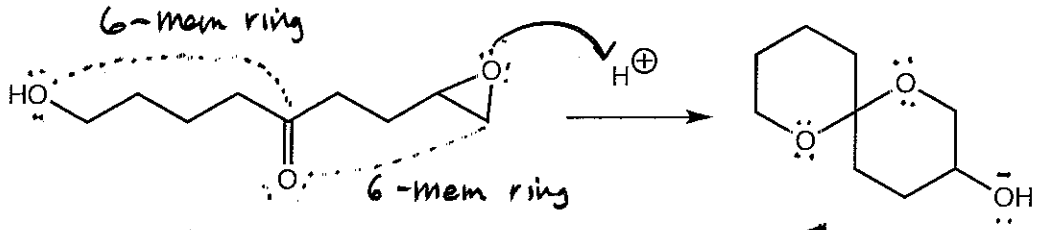
ring is more e^- rich, better able to interact w/ (+)

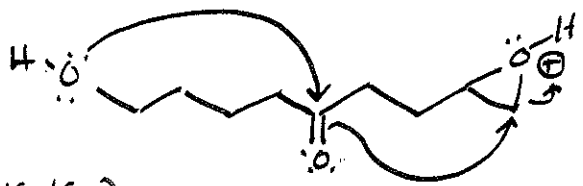
5. (15 points). As we discussed in class, a carbonium ion can be difficult creature to corral. We've seen the ion below before, but here are some other tricks it can do! Fill in the missing structures, add needed arrows and of course lone pairs where needed to complete this mechanistic scheme.



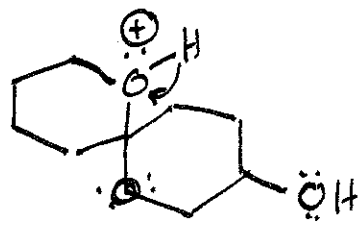
In comparison to Route 2, what factors favor Route 1? What factors disfavor Route 1? Answer succinctly. Route 1 creates a 3° carbonium ion (good), but also a 4-membered ring (bad). Route 1 creates a chair, but Route 2 generates a boat.

6. (15 points). Here is a reaction that blends aspects of several mechanisms we have studied. Draw a mechanism for this reaction occurring under acid catalysis.





This is a "concerted" mechanism

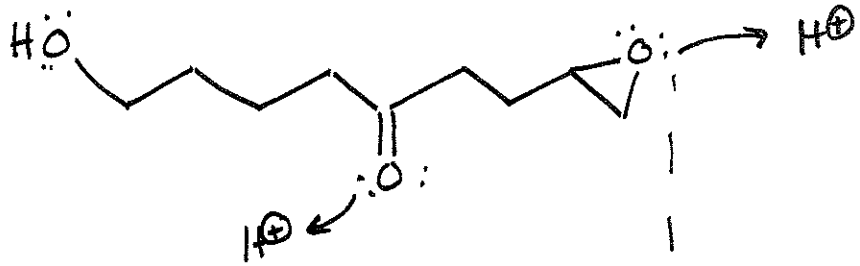


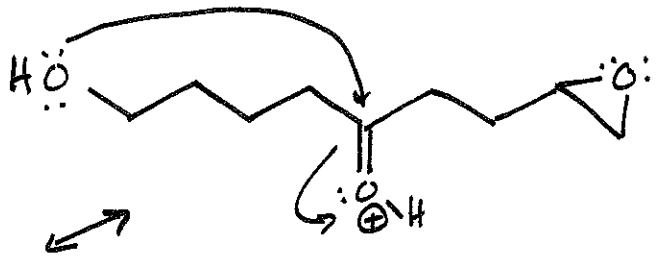
This dual cyclization in one step is similar to the formation of lanosterol and monensin

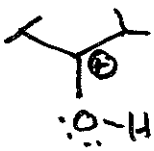
Other mechanisms are possible + reasonable. For instance, one might proceed through the hemi-ketal

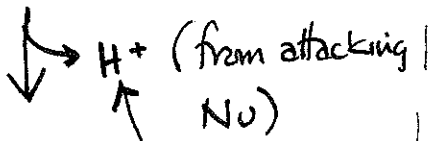
See next page

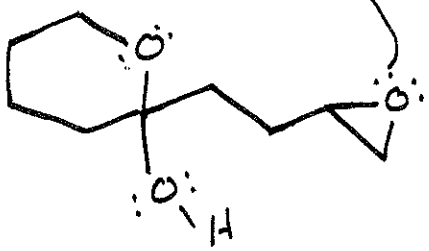
Stepwise mechanisms (alternate answers)

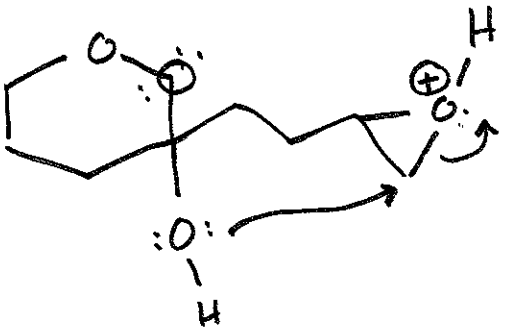


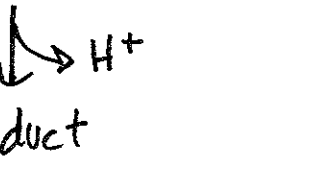






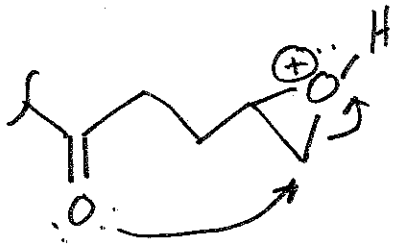


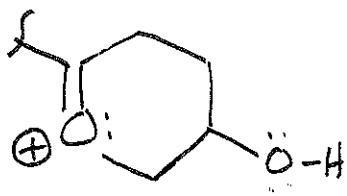


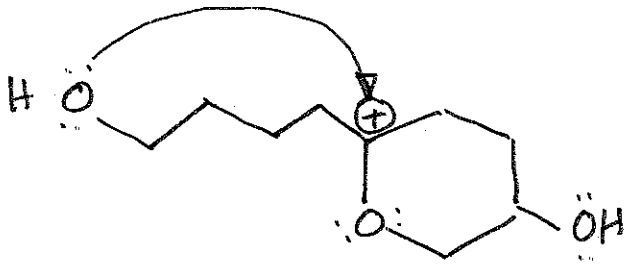


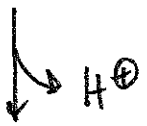
another option...

Q6 can't

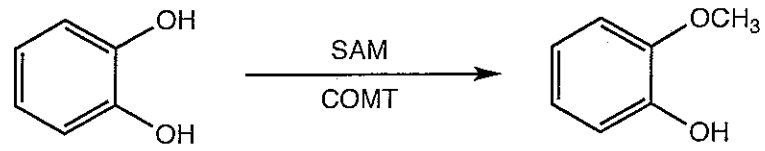








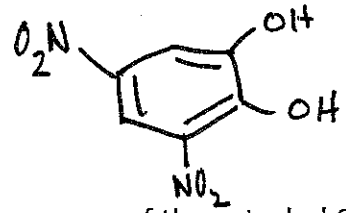
7. (15 points). Catechol *O*-methyl transferase (COMT) catalyzes the addition of a methyl group (from SAM) to catechol (and many endogenous phenolic compounds, like neurotransmitters). The general reaction is shown below.



2 pts each (1 free pt for everyone!) catechol

Call up the structure of COMT found in pdb file 3bwm.pdb and answer the following questions using Chimera. Go to **Presets → Interactive 1** to begin.

a. Give the structure of the catechol analog that is present at the active site of this structure.



$-NO_2$ or $-N^{+}(=O)-O^{-}$

know the nitro group!

b. How far is the oxygen of the catechol OH from the electrophilic CH3 of SAM?

2.714 Å

c. What is the metal ion at the active site?

Mg^{2+}

d. Give the name and number of each amino acid side chain that is coordinated to this metal.

asp 169.A asn 170.A asp 141.A

e. Besides the amino acid side chains, there is another species coordinated to the metal. What is it?

water (also the O of the catechol analog)

f. What amino acid side chain is positioned over the adenine ring (name and number)? What kind of force is acting between the two groups?

Ile 91.A London forces

g. What amino acid side chain is positioned near the hydroxyls of the ribose (name and number)? What kind of force is acting between the two groups? Sketch the arrangement below.

glu 90.A hydrogen bonding