Exam 1 - Key

1. (15 pts) For each of the following hypothetical equilibration reactions below, circle the side of the equilibrium which you expect to be more stable, either all the starting materials or all the products.
   a. \( \text{O} + \text{NH} \rightleftharpoons \text{O} + \text{NH}_2 \)
   b. \( \text{NH} + \text{NH} \rightleftharpoons \text{NH} + \text{NH}_2 \)
   c. \( +\text{NH} + +\text{N} \rightleftharpoons +\text{NH} + +\text{N} \)
   d. \( +\text{C}_6\text{H}_5 \rightleftharpoons +\text{C}_6\text{H}_5 \)
   e. \( +\text{C}_3\text{H}_5 \rightleftharpoons +\text{C}_3\text{H}_5 \)

2. (10 pts) Suggest a plausible arrow-pushing mechanism for the following reaction.

Answer:
I like this best neighboring group participation

For a cyclopropylcarbinyl system, I would accept this:
3. (12 pts) The following reaction generates a single racemic product.

**Circle the diastereomer** (A or B) that would be favored in the following solvolysis reaction. Suggest a plausible arrow-pushing mechanism for the reaction.

\[
\text{TsO} \rightarrow \text{AcOH} \quad 119 \, ^\circ C \quad \text{A} \quad \text{OAc} \quad \text{vs.} \quad \text{B} \quad \text{OAc}
\]

**Answer:**

\[
\text{Tso} \quad \rightarrow
\]

4. (15 pts) Suggest a plausible arrow-pushing mechanism for the following reaction of lactone 1 in boiling methanol. Under similar conditions, the related lactone 2 is recovered un-changed.

\[
\text{Br} \quad \rightarrow \quad \text{CH}_3\text{OH} \quad 65 \, ^\circ C, 18 \, h \quad \text{80%} \quad \text{HO} \quad \text{80%} \quad \text{Br} \quad \rightarrow \quad \text{2}
\]

**Answer:**
5. (15 pts) Suggest a plausible arrow-pushing mechanism for the following reaction.

\[
\begin{align*}
\text{H}_3\text{C}_\text{O}_2\text{Na} & \quad \text{CH}_3\text{CO}_2\text{H} \\
\text{CH}_3\text{CO}_2\text{H} & \quad \text{Ts} \\
\downarrow & \quad 120^\circ C, 4 \text{ h} \\
\text{90\%} & \quad \text{OAc} \\
\end{align*}
\]

Answer:

\[
\begin{align*}
\text{not subject to neighboring group assistance} & \\
\text{attack with} \pi_{\text{cc}}, \text{ not} \sigma_{\text{cc}} &
\end{align*}
\]

6. (10 pts) Consider the following equilibrium.

\[
\text{aldehyde starting material} \rightleftharpoons \text{alcohol product}
\]

a. Using bond dissociation energies (BDEs), estimate the enthalpy change going from aldehyde starting material to alcohol product.

b. Estimate the equilibrium constant for the reaction.

Answers:

a.

\[
\begin{align*}
\text{Bonds Broken} & \\
C-H & 98 \\
C-H & 98 \\
\pi_{\text{C-O}} & 94 \\
\hline & 290 \text{ kcal/mol}
\end{align*}
\]

\[
\begin{align*}
\text{Bonds Formed} & \\
C-H & 98 \\
O-H & 110 \\
\pi_{\text{C=C}} & 64 \\
\hline & 272 \text{ kcal/mol}
\end{align*}
\]

\[
\Delta H = H(\text{bonds broken}) - H(\text{bonds formed}) = +18 \text{ kcal/mol}
\]

b. There is no change in molecularity (one molecule goes to one molecule) and the starting material and product will exhibit similar conformations. Therefore the entropy change (-T\Delta S) will be small and \Delta G will be about the same as \Delta H. If \Delta G > 0 \text{ kcal/mol} then the equilibrium favors reactants and \( K_{\text{eq}} < 1 \) (way less than one.

\[
18 \text{ kcal/mol} + 1.4 \text{ kcal/mol} = 12.9 \text{ factors of ten}
\]

\[
K_{\text{eq}} \approx 10^{-13}
\]
7. (15 pts) The reaction below is proposed to account for the DNA damage induced by a range of α-halo-enones in the presence of thiols. Importantly, no reaction occurs in the absence of the thiol. Suggest a plausible arrow-pushing mechanism for the reaction. Assume the reaction is catalyzed by base and use the symbol B: in your mechanism.

$$\text{RSH} + \text{BrC}O \rightarrow \text{H}_2\text{NNNNHHOOH} \rightarrow \text{H}_2\text{NNNNHHOOH}$$

Answer:

8. (10 pts) Suggest a plausible arrow-pushing mechanism for the following reaction.

$$\text{MsO} + \text{H}_2\text{NNNNHHOOH} \rightarrow \text{H}_2\text{NNNNHHOOH}$$

Answer:

The stereochemical consequences of aziridinium formation are kind of hard to envision. That's why I didn't ask you to predict the stereochemistry.
References

1 These types of hypothetic reactions are referred to as isodesmic reactions. Ponomarev, D.A.; Tahkistov, V.V. “What are Isodesmic Reactions?” J. Chem. Educ. 1997, 74, 201-203.


