Problem Set 2: Reactions of Carbocations - KEY

Due Tuesday, 10/11/16

1. a. Formation of 1° and 2° silyl ethers is always high-yielding, but selective silylation of a single hydroxyl group can be challenging. Suggest a plausible arrow-pushing mechanism for the formation of the primary silyl ether in the presence pyridine under kinetic conditions. 

Answer: I would accept either of these two mechanisms…

for soluble bases like pyridine:

for insoluble bases: where [B] is low

b. The secondary silyl ether is obtained exclusively under thermodynamic conditions (in the absence of base). Draw a reaction coordinate-free energy diagram for the reaction under kinetic conditions. Graphically indicate the difference in free energies between the starting materials and products, between the 1° and 2° products, and between the two transition states leading to each product.

Inorganic salt bases have low solubility in CH₂Cl₂ and lead to the same result as adding no base at all.
2. Suggest a plausible arrow-pushing mechanism for the following reaction.\(^2\)

\[
\begin{align*}
\text{cat. } \text{H}_2\text{SO}_4 & \quad \text{Ac}_2\text{O} \\
\text{23 } ^\circ\text{C}, 5 \text{ min} & \quad \text{63%}
\end{align*}
\]

Answer:

3. Suggest a plausible arrow-pushing mechanism for the following transformation.\(^3\)

\[
\begin{align*}
\text{cat. } \text{ArCO}_2\text{H} & \quad \text{CH}_2\text{Cl}_2 \\
\text{23 } ^\circ\text{C}, 45 \text{ min} & \quad \text{23 } ^\circ\text{C}, 45 \text{ min}
\end{align*}
\]

Answer:

4. Suggest a plausible arrow-pushing mechanism for the following reaction.\(^4\)

\[
\begin{align*}
\text{conc. } \text{HCl} & \quad \text{H}_2\text{O} \\
\text{110 } ^\circ\text{C}, 3 \text{ h} & \quad \text{76%}
\end{align*}
\]

Answer:
5. Chloride A undergoes solvolysis ($S_N1$) 60 times faster than bicyclic chloride B. However, ketal C undergoes solvolysis $10,000,000,000,000$ times faster than bicyclic ketal D. Explain these results using appropriate drawings.

**Answer:**
The carbocation formed by B is not quite planar, so the transition state leading to it is higher in energy than that of A. However, this effect is small compared to the difference between C and D.

The oxygen in C has a lone pair of electrons which is perfectly aligned with $\sigma^*_{CO}$, making C more readily ionized. The carbocation formed from C is stabilized by overlap with the lone pair on oxygen (an oxocarbenium ion), so the transition state leading to this cation is lower in energy. In D, there is no alignment between the lone pairs of oxygen and $\sigma^*_{CO}$. Also, the carbocation formed by D does not have effective overlap with the lone pairs of oxygen (drawing D as an oxocarbenium ion would violate Bredt’s rule). For these reasons, the transition state to form a carbocation from D is much higher in energy than that of C.

6. The introduction of a cyano group slows the solvolysis of the tosylates below. Explain (using appropriate drawings) why an $\alpha$–cyano group slows the reaction less than a $\beta$–cyano group.

**Answer:**
The cyano group is electron-withdrawing, so it makes the transition state to form a carbocation higher in energy. However, the $\alpha$–cyano group has a filled $\pi$-orbital which overlaps with the empty p-orbital in the carbocation, stabilizing it and making the transition state lower in energy. The molecular orbitals for this
system are like the allyl cation, but the stabilization is somewhat less due to the electronegativity of nitrogen. A resonance structure can be drawn for this carbocation; while it is not a very good resonance structure, it still contributes to the structure of the carbocation.

7. Suggest a plausible arrow-pushing mechanism for this enzyme-catalyzed reaction of farnesyl diphosphate. Note: the enzyme acts as an acid catalyst and controls the conformation of the substrate.

Answer:

**Practice Problems**

The following problems demonstrate important concepts. They will not be graded, but you are expected to complete them. We will cover some of these in discussion section.

8. Suggest a plausible arrow-pushing mechanism for the following reaction.
9. Suggest a plausible arrow-pushing mechanism for the following reaction.\(^9\)

\[
\text{OTs} \quad \xrightarrow{\text{4:1 acetone/water}} \quad \text{H}_2\text{O}\quad 99\%
\]

**Answer:**
Note that water attacks the exo face due to the nonclassical carbocation.

10. Suggest a plausible arrow-pushing mechanism for the following reaction.\(^{10}\)

\[
\text{Cl} \quad \xrightarrow{\text{6 M HCl}} \quad H_2\text{O}\quad 60\%
\]

**Answer:**

11. Suggest a plausible arrow-pushing mechanism for the following reaction.\(^{11}\) Don’t worry about the enantioselectivity.
12. Suggest an arrow-pushing mechanism for the following reaction.\textsuperscript{12}

\begin{equation}
\text{HO} - \text{CH} = \text{CH} - \text{CH} = \text{CH} - \text{CH} = \text{CH} \quad \xrightarrow{\text{HCO}_2\text{H} / \text{pentane}} \quad \text{84%}
\end{equation}

Answer:

\begin{equation}
\text{HO} - \text{CH} = \text{CH} - \text{CH} = \text{CH} - \text{CH} = \text{CH} \quad \xrightarrow{\text{HCO}_2\text{H} / \text{pentane}} \quad \text{84%}
\end{equation}
13. Suggest a plausible arrow-pushing mechanism for the following transformation. The first step involves double bond isomerization catalyzed by protic species, HA.

Answer:
The alkene could be isomerized before or after the cyclization. If you do it before, you get to draw a cyclopropylcarbinyl carbocation resonance structure. Ah…

References

3 John E. Baldwin, Samuel Bonacorsi Jr., Robert G. Carlson, Forest D. Graber “Cyclohexyl(2-methylenecyclopropyl)carbinyl carbocationic rearrangements” *J. Org. Chem.* **1993**, *58*, 981-984. The epoxide was produced in situ using mCPBA.


