Problem Set 8.1

1. Give the product or products of the following reactions:

   a. \[
   \text{Br} \quad \text{Na} \quad \text{CN} \quad \text{acetonitrile} \quad \text{CH}_3 \quad \text{CN} \quad \text{CH}_3
   \]

   b. \[
   (\text{CH}_3)_2\text{CHBr} \quad \text{Na} \quad \text{OCH}_3 \quad \text{DMSO} \quad (\text{CH}_3)_2\text{CHOCH}_3
   \]

2. Supply the following reactions with starting materials which would give the observed products:

   a. \[
   \text{CH}_3\text{CH}_2\text{CH}_2\text{L.G.} \quad \text{H} \quad \text{Na} \quad \text{SCH}_3 \quad \text{acetone} \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{SCH}_3
   \]

   a. L.G.=any "good" leaving group of your choice

   b. \[
   \text{CH}_3\text{CH}_2\text{OH} \quad \text{L.G.} \quad \text{Na} \quad (\text{CH}_3)_2\text{NH} \quad \text{DMSO} \quad (\text{CH}_3)_2\text{NHCH}_2\text{CH}_2\text{CH}_3
   \]

   b. L.G.=any "good" leaving group of your choice

   c. \[
   \text{CH}_3\text{CH}_2\text{CH}_3 \quad \text{K} \quad \text{I} \quad \text{DMF} \quad \text{CH}_3\text{CH}_2\text{CH}_3 \quad \text{CH}_3
   \]

   c. L.G.=any "good" leaving group of your choice
3. Give the reagents over the arrow that would give the following products from the following starting materials (don't forget solvents!):

a. \[
\text{Br} \quad \xrightarrow{\text{KOH}} \quad \text{HO}
\]

\[
\text{your favorite SN2 solvent}
\]

b. \[
\text{O} \quad \xrightarrow{\text{P(CH}_3)_3} \quad \text{P(CH}_3)_3
\]

\[
\text{your favorite SN2 solvent}
\]

c. \[
\text{H} \quad \xrightarrow{\text{NaCN (2 eq.)}} \quad \text{NC}
\]

\[
\text{your favorite SN2 solvent}
\]
Problem Set 8.2

1. Give the product or products of the following substitution reactions: (E1 also included!)

   a. \[ \text{CH}_3 \text{CH}_2 \text{CH}_2 \text{OH} \xrightarrow{\Delta} \text{CH}_3\text{SO}_2\text{CH}_3 \]

   b. \[ \text{(CH}_3\text{)}_2\text{CHBr} \xrightarrow{\Delta} \text{(CH}_3\text{)}_2\text{CH} \]

   c. \[ \text{Br} \xrightarrow{\Delta} \text{CH}_3\text{CH}_2\text{OH} \]

2. Supply the following reactions with starting materials which would give the observed products:

   a. \[ \text{OTs}^* \xrightarrow{\Delta} \text{CH}_3\text{CH}_2\text{OH} \]

   b. \[ \text{H}_2\text{SO}_4, \Delta \xrightarrow{(\text{CH}_3)_2\text{CHOH}} \]

   "extra carbon (sorry)"
3. Give the reagents over the arrow that would give the following products from the following starting materials (don’t forget solvents!):

*** a. \[ \text{CH}_3\text{CH}_2\text{CH}_3\text{OH, } \Delta \rightarrow \text{OCH}_2\text{CH}_2\text{CH}_3 \]

b. \[ \text{Br}_2 \rightarrow \text{C}_6\text{H}_5\text{CO}_2\text{H, } \Delta \rightarrow \text{C}_6\text{H}_5\text{CO}_2\text{H} + \text{C}_6\text{H}_5\text{CO}_2\text{H} \]

4. Give the mechanisms for the starred transformations above.

1c. 

\[ \text{SN}_1 \text{ Part:} \]

\[ \text{E1 Part:} \]
2a.

(either starting compound will give the same intermediate!)

3a.

(continued on the next page)
Additional problems:

1. Predict all the products from the following reactions. If more than one of a particular kind of product (substitution or elimination) is formed, label them major or minor.

   a. 1-iodo-1-isopropylcyclopentane

   b. 

   c. 

   d. 

   e.
2. Supply starting materials that would give the observed products under the conditions shown:

a. *any good L. G. okay

b. (only E1 products shown, S_N1 possible but not shown)

d. *any good L. G. okay

3. Supply reagents which will perform the conversion of the following starting materials to the products shown. Don’t forget solvents!

a. (can you draw a mechanism to account for both of these E1 products?)

b. * any good S_N2 solvent
4. a. In comparing the nucleophilicity of MeONa and MeCO₂Na, it was found that MeONa was the stronger nucleophile, why is this?

MeONa has all the negative charge on a single oxygen, MeCO₂Na has the negative charge resonance stabilized between two oxygens. This stabilization makes the negative charge less “reactive,” which in turn makes the MeCO₂Na less nucleophilic. The MeONa is more “reactive” (more interested in making a bond), and is a “better” nucleophile.

b. Which of the following two alcohols will undergo dehydration (elimination) faster under acidic conditions? Why?

\[
\text{or } \quad \text{OH} \quad \text{OH}
\]

The alcohol on the left is primary, the alcohol on the right is secondary. A secondary carbocation is possible, whereas a primary carbocation is not. The secondary carbocation is more reactive toward elimination in an E1 sense (or substitution for that matter), where the primary protonated alcohol would have to go through an E2 type of reaction. There is no strong base possible in this reaction pathway (no strong bases in the presence of strong acid!), so the E2 pathway will be very slow.

c. Ethers can be made by the reaction of alkyl halides and sodium or potassium alkoxides (see equation below). Using this method, outline all steps in two conceivable alternative routes to tert-butyl ethyl ether (t-Bu-O-Et). One of these routes gives excellent yields, the other is worthless. Which is the worthless route, and why? Explain using the mechanisms you outlined in your routes.

\[
R-X + R'ONa \rightarrow R-O-R' + NaX
\]

alkyl sodium ether
halide alkoxide
The tert-butoxide must be the nucleophile, the Et must have the leaving group on it. You cannot use an SN2 reaction on a tertiary center (too much steric hindrance). The only way to make this ether is using sodium tert-butoxide, and even then, we get competing elimination!

5. The following are reactions which are not obvious, they are a little tricky. Look carefully and predict products based one what can happen (i.e. look at the mechanisms!). PS- something CAN happen, I’m not being that tricky!

a.  
\[
\begin{align*}
\text{Br} & \quad \text{CH}_3\text{CO}_2\text{Na} \\
\text{EtOH, } & \Delta \\
\text{as major products}
\end{align*}
\]

\[
\begin{align*}
\text{SN1 conditions. No SN1 next to two quaternary C’s and no E1 (no } & \beta \text{ hydrogens), so there is a RAR to give a more stable carbocation, then the SN1 and E1 from that carbocation.}
\end{align*}
\]

b.  
\[
\begin{align*}
\text{2-methyl-2-butene} & \quad 1) \text{HBr} \\
& \quad 2) \text{Na}^{+}\text{OCCCH}_3 \\
& \text{DMSO} \\
& \text{major} + \text{minor}
\end{align*}
\]

\[
\begin{align*}
\text{SN2 conditions, but you can’t do SN2 reactions on a tertiary center. So, the only possible thing to do is use the nucleophile as a base giving E2 products.}
\end{align*}
\]

c.  
\[
\begin{align*}
\text{MeOH, } & \Delta \\
\text{OMe}
\end{align*}
\]

\[
\begin{align*}
\text{This is an SN2 reaction under SN1 conditions because you cannot make a primary carbocation. The protonated intermediate is a good leaving group, allowing the solvent (methanol) to behave as a nucleophile even though it is not a particularly good one!}
\end{align*}
\]