**HANDOUT on ORGANIC SYNTHESSES**

**Purpose:** Figuring out the ways that molecules react is the province of the mechanistic chemist. By understanding the mechanisms of reactions, the chemist can manipulate the experimental variables to favor one product over another. This element of control is the province of the synthetic organic chemist. This workshop continues to explore how we know how molecules react and how this knowledge leads to control of the products.

**Purpose:** Organic chemists make molecules. They make molecules that occur in nature. They also invent and make molecules that are the products of the chemist’ imagination and curiosity (i.e. molecules that do not occur in nature). The first step in synthesizing (making) a more complicated molecule from simpler molecules is to design a plan. One of the primary reasons to learn the chemical reactions of the functional groups is because the reactions are the tools of organic synthesis. We can group the reactions into two general types: functional group interchanges and bond-making (or –breaking) reactions. We will be specially interested in ways to make carbon-carbon bonds, because doing that is central to making larger molecules from smaller building blocks.

Synthesis is fun because it is a creative act. This workshop will give you opportunities to apply the chemical reactions you have learned to the synthesis of organic molecules. The problems are challenging because the goal is to get the desired constitutional isomer and the desired stereoisomer. Ultimately, we will explore retrosynthetic analysis, a step-by-step procedure for constructing a rational design of a synthetic plan. This takes practice because we tend to learn reactions in the forward direction A to B to C.

**Expectations:** You need to have a mastered starting materials, reagents, conditions, and products for the fundamental organic reactions of alkenes, alkyl halides, and alkynes in order to be able to use these reactions in synthesis. It will help to organize the reactions into functional group interchanges and bond-making reactions and to group together reactions that give products with well-defined stereochemistry. You should review the meaning of cis, trans, (E), (Z), chiral, achiral, and racemic mixture.

1. Propose methods for accomplishing the functional group interchanges in Chart 1. More than one step may be required. Specify reagents and reaction conditions for each step.

Working together as a brainstorming team, simplify Chart 1 by identifying compounds that can serve as branch points to make several target molecules.
Do this by thinking “backwards” to identify the branch points. For example, work your way around the perimeter of the molecule, considering the target molecules one by one. For each target, identify a precursor molecule that you could convert to the target in one step, using a reaction that you know. After you have done this for several target molecules, you will begin to see that there are common precursors (branch points) from which you can prepare several target molecules. Now the problem simplifies to preparing the precursors from chlorobutane. (The arrow symbol identifies a retrosynthetic step; it means that the target can be made from the precursor by a known reaction).

Chart 1

2. Identify the target molecules in Chart 1 that will be formed as racemic mixtures. Explain why a racemic mixture is formed in some cases but not in others.
3. Propose methods for synthesizing the target molecules in Chart 2 from acetylene.

4. Identify all of the target molecules in Chart 2 that will be formed as racemic mixtures.

5. Propose synthetic plans to carry out the transformations that follow. Specify necessary reagents and reaction conditions. Each transformation requires at least two steps. Start by brainstorming the problem to diagnose the major chemical challenge (e.g., make a C-C bond, control stereochemistry, control regiochemistry, etc.). Then “back the problem up” by asking:
a. What could be the penultimate (next-to-last) compound in the synthetic sequence?
b. How could you convert the penultimate compound to the ultimate compound?
c. If you can not answer b, then recycle to a and try another precursor to the final product.
d. When you get a good final step, figure out how to make the penultimate compound, following the same logic until you get back to the starting material.

e.

i. \[
\begin{align*}
\text{H}_3\text{C}-\text{C}-\text{CH}_3 & \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{-Br} \\
\end{align*}
\]

ii. 

iii. \[
\begin{align*}
\text{CH}_2\text{CH}_3\text{C}≡\text{CCH}_2\text{CH}_3 & \rightarrow \text{H}_2\text{CH}_3\text{C} & \text{H}_2\text{CO}_2\text{H} \\
\text{racemic mixture} & & \\
\end{align*}
\]

iv. \[
\begin{align*}
\text{(CH}_3\text{)}_3\text{CH} & \rightarrow \text{(CH}_3\text{)}_3\text{C} & \text{CO}_2\text{H} \\
\end{align*}
\]

v. \[
\begin{align*}
\text{(CH}_3\text{)}_2\text{CHCH}_2\text{CH}_2\text{CH}_2\text{Cl} & \rightarrow \text{(CH}_3\text{)}_2\text{CHCH}_2\text{CH}_2\text{CH}_2\text{OH} \\
\end{align*}
\]

**Reflection:** Work with your colleagues to construct a stepwise flowchart for solving a synthesis problem.