Chemistry 41c: Organic Chemistry

Spring 2011-In Class Activity #2 “Retrosynthetic Analysis”

Answer the following questions using any and all resources available in 153 Noyes. You have 40 minutes, so use your team’s resources wisely. Most questions will seem simple, while some may be challenging and will require your creativity. Do your best! Also, remember that in organic chemistry, pictures often speak louder than words! You may not have time to finish this activity, but you can continue to think about these concepts and questions. We will return to synthesis in about a week. (this exercise is worth 20 points)

Who was on your team (limit to 3 people)?

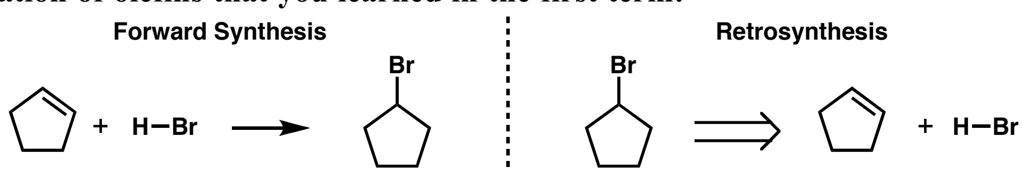
This year you have learned many reactions. When reactions are strung together in a sequence to produce or construct a more complicated molecule from simple starting materials, this is referred to as a synthesis. Shown below is a simple schematic example of *synthesis*.

$$\mathbf{A} + \mathbf{B} \longrightarrow \mathbf{C} \longrightarrow \mathbf{D} \longrightarrow \mathbf{E}$$

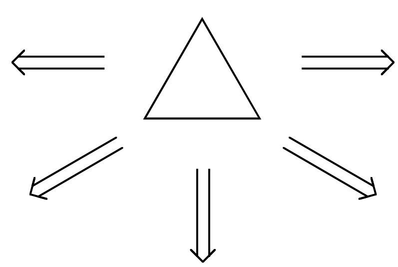
***Retrosynthesis* is the process of deconstructing a “target” molecule (the molecule that you ultimately want to make) into constituent simpler pieces. This is accomplished by imagining the last reaction used to prepare a certain material and taking the molecule backward through a retrosynthetic a scheme. An example of a retrosynthetic sequence is shown below (notice the special type of arrow that is used):**

$$\mathbf{E} \Longrightarrow \mathbf{D} \Longrightarrow \mathbf{C} \Longrightarrow \mathbf{B} + \mathbf{A}$$

This means that you will benefit from learning organic reactions “forward and backward.” Take the hydrobromination of olefins that you learned in the first term:

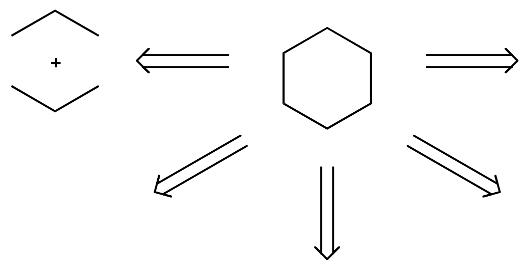


Retrosynthetic analysis is particularly powerful because there are many possible pathways that one can intellectually pursue. In other words, there are many possible solutions to any synthetic problem (possibly an infinite number). One can carry out a retrosynthesis on things beyond chemistry. For instance, a triangle! With your team, provide as many retrosyntheses for a triangle (i.e., not a cyclopropane) as you can (try to devise at least 5)

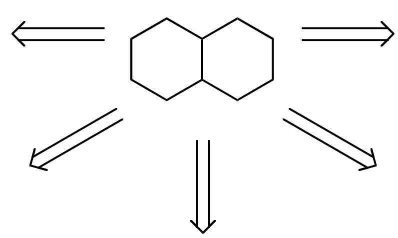


Now treat the triangle as a cyclopropane (i.e., with C and H atoms and bonds). How many of your routes apply (circle them)? Which would you imagine to be most strategic?

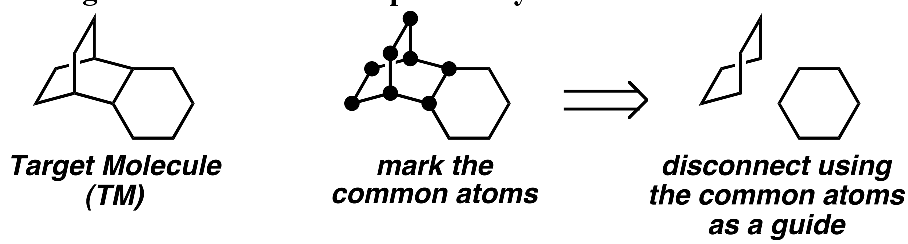
Another powerful utility of retrosynthesis is that one can envision strategic bond disconnections without knowing particular forward reaction details. For instance, you currently only know a fraction of the many C–C bond forming reactions that exist, yet you successfully disconnected a cyclopropane! Furthermore, you can gain insight into possible constructions that have yet to be discovered or invented! Provide as many strategic bond disconnections for cyclohexane as you can (like the one shown). Use the back of the sheet if you need more space.



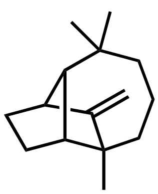
Now try a decalin system:



Retrosynthesis of polycyclic compounds is aided by a technique called the "common atom" approach. For instance, in the following bicycle the atoms common to more than one ring are marked, and the most strategic disconnections occur by retrosynthetically cleaving those bonds linking two or more of the common atoms. Disconnections involving rupture of other bonds are typically not as strategically relevant (they do not lead to significant simplification of the target structure). Show an example of a non-strategic disconnection and prove to yourselves that this is the case.



Longifolene is a naturally occurring hydrocarbon extracted from in pine resins. Using the common atom approach (and your creativity) provide a retrosynthesis (or a few) for the following target molecule, Longifolene.



Longifolene

Did you learn anything from this exercise? (Was it fun, useful, or a waste of time?)