**Chemistry 2301** Friday, April 3

# Workshop 21
# Retrosynthetic Analysis

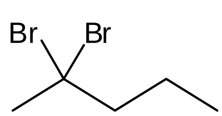
Sometimes it is easier to think about organic synthesis in reverse, by "disconnecting" a complex molecule into simple parts that you know how to reconnect synthetically. Organic chemists call this approach *retrosynthetic analysis*, and E.J. Corey won the Nobel Prize in Chemistry in 1990 for introducing the concept.[1] In the case of complex pharmaceuticals, this kind of approach is essential. In this problem, we will mimic the retrosynthetic approach of pharmaceutical chemists by designing multistep syntheses using hydrocarbons—alkanes, alkenes or alkynes, but no functional groups—containing **four carbons or less** as starting materials.[2] (You may also use organic solvents, like $CH_3OH$, without making them from scratch.)

For each of the molecules on the next page, propose a multistep synthesis. As you look at each molecule and think backwards (retrosynthetically), you might ask yourself the following questions:

1. Do I know a single reaction that would allow me to put together this complicated molecule from two simpler parts, as it is?

2. If not, do I know a simple functional group transformation that I could use to make this molecule from another, similar molecule, for which I might be able to answer question (1)?

**Example:**

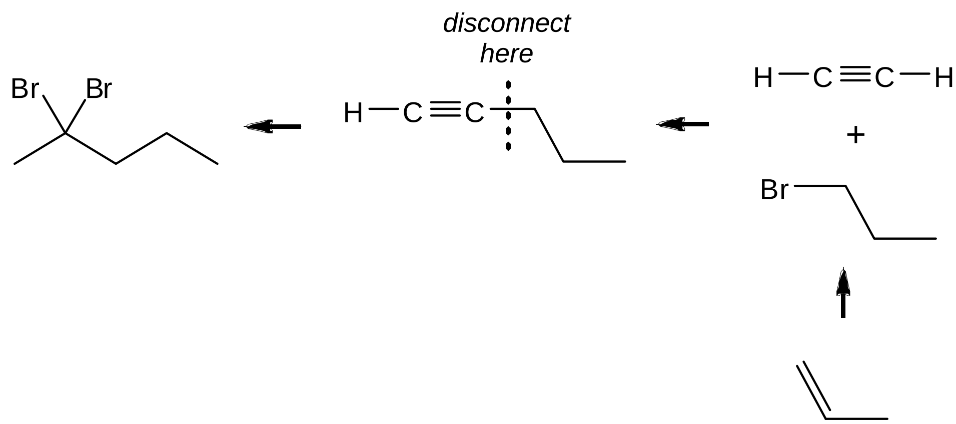



This molecule has five carbons, so we'll need to construct it from pieces smaller than four carbons by making a C-C bond somewhere. We know how to do this using alkynyl anions, but it's not clear where to do that with this molecule yet. We do know that two Br atoms can be added to an alkyne by sequential Markovnikov additions to the triple bond.

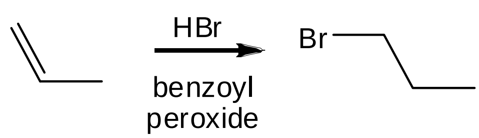
Can you imagine the synthetic route already? If so, plot it out (before turning over this sheet of paper). If not, written in the reverse direction (next page):

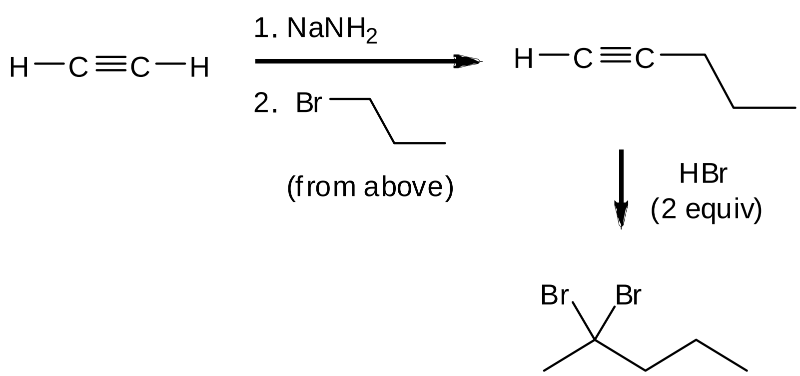
[1] http://nobelprize.org/nobel_prizes/chemistry/laureates/1990/

[2] Chemical companies like Milwaukee's Sigma-Aldrich (http://www.sigma-aldrich.com) sell tens of thousands of chemical starting materials, most with more than four carbons, and most with functional groups useful to synthetic chemists. So your syntheses will be more complicated than they would be if you had all commercially available starting materials available to you. Nevertheless, this is a good way to introduce the concept of disconnections in multistep synthesis.

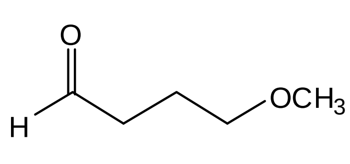


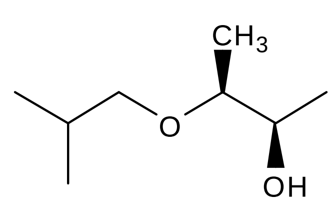

In the forward direction:




Okay, now it’s your turn. Design syntheses of:




(+ *enantiomer*)