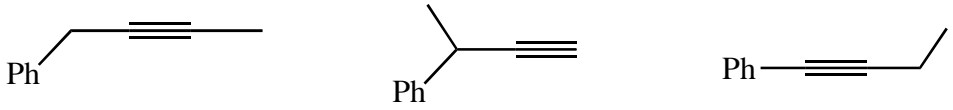
Name _____

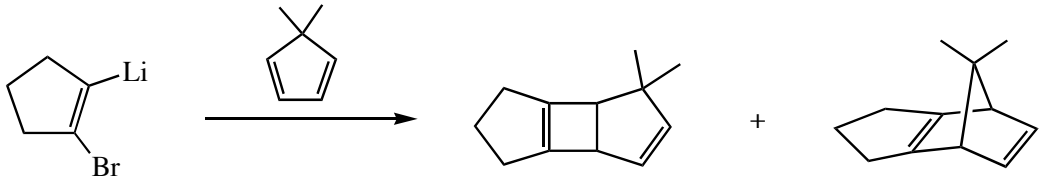
1 Like alkenes, alkynes are stabilized by alkyl groups, so internal alkynes (i.e. disubstituted alkynes) are generally more stable than terminal alkynes (i.e. monosubstituted alkynes). With this in mind, as well as another factor you already know about, rank the following isomeric alkynes in order of stability, with 1 being least stable, and 3 being the most stable.



2 With acyclic alkenes, we saw that *cis* substituents can clash, destabilizing the *cis* isomer relative to the *trans*. Do you think this might also be an issue for alkynes? Explain.

3 The smallest cyclic alkyne that is stable at room temperature is cyclooctyne. Smaller cycloalkynes have only a fleeting existence at best. Draw cyclooctyne and cyclopentyne, and explain why the former is stable but the latter is not.

4 Evidence for the existence of cyclopentyne comes from experiments such as the following. When the bromo-lithio-alkene below (a C–Li bond is a rare example of a covalent bond to an alkali metal) decomposes in the presence of 5,5-dimethylcyclopentadiene, the two products shown are formed. The rate of loss of the Br-Li-alkene is first-order and independent of the concentration of the dimethylcyclopentadiene, ruling out a direct reaction between these two. Write the mechanism for formation of the first product below — use curved arrows to show how the intermediate cyclopentyne is produced, and to show how it might react with the cyclopentadiene to make the first product.



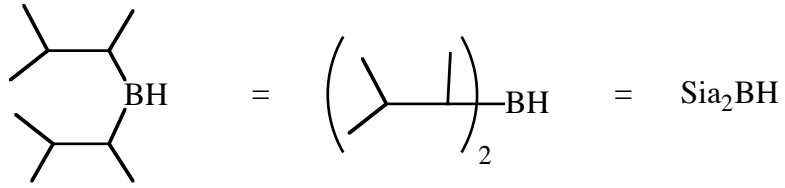
Lecture outline

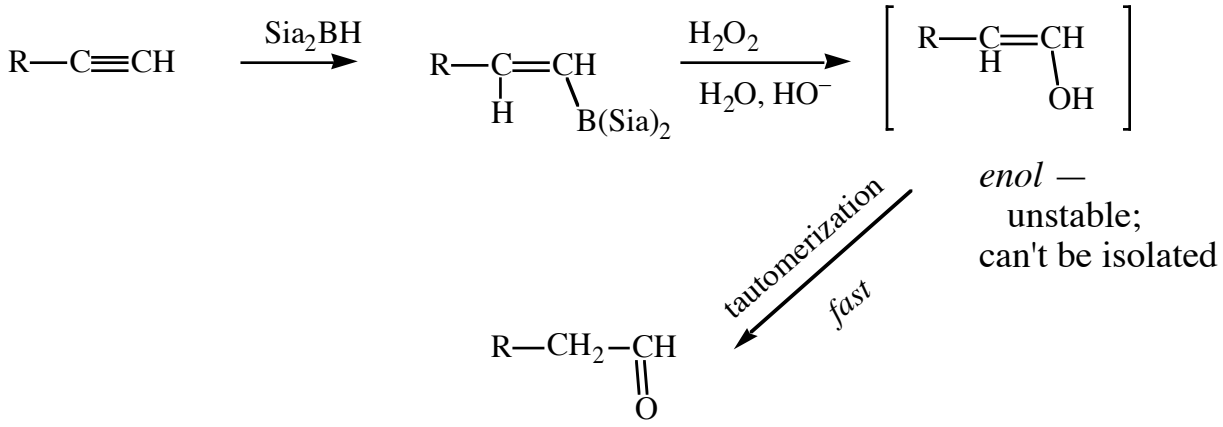
A few more reactions of alkynes —

4. Hydroboration
— overall anti-Markovnikov add'n of 2 Hs and O to triple bond

Add'n of BH_3 to a terminal alkyne makes a mess. (2 B–H bonds can add to the two π-bonds of a triple bond, eh?) With a sterically hindered borane, one B–H adds and that's it. Clean 'n' simple.

One such borane is di-*sec*-isopentylborane, aka "disiamylborane", $Sia_2B–H$.
(Q: Huh? A: the old name for pentyl is amyl, so **s**ec-**i**so**amyl** => "siamyl".)

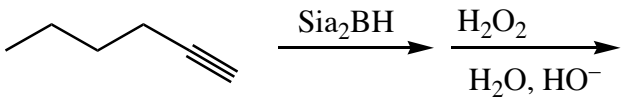




What becomes of the "siamyl" groups? Draw the byproduct produced from
this alkyl group in the alkaline hydrogen peroxide step.
— tautomerization occurs under basic conditions in this case... write the mechanism.

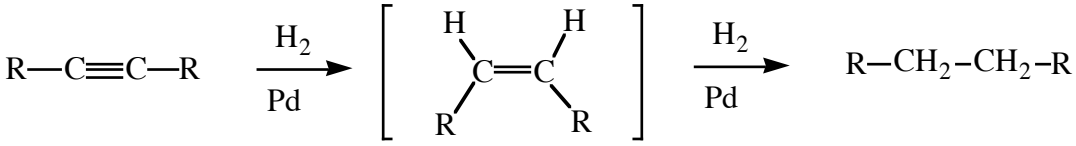
— Basic soln, *HO^- and H_2O* ***only***; *NO H^+ !!!*
— Notice also that intermediates formed under basic conditions
are generally neg(–)-charged.

Draw the product of the following reaction.



5. Reduction — addition of 2 Hs across one π-bond (or both)

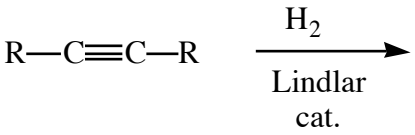
a. (both) Hydrogenation with standard (Pd, Pt, Ni) catalysts



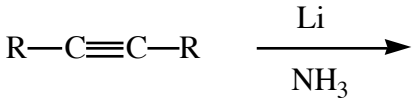
— rxn can't be stopped at the alkene stage...

... unless a poisoned (deactivated) catalyst,
like Lindlar's catalyst is used...

b. (one) Hydrogenation with Lindlar's catalyst (Pd, PbO, $CaCO_3$)

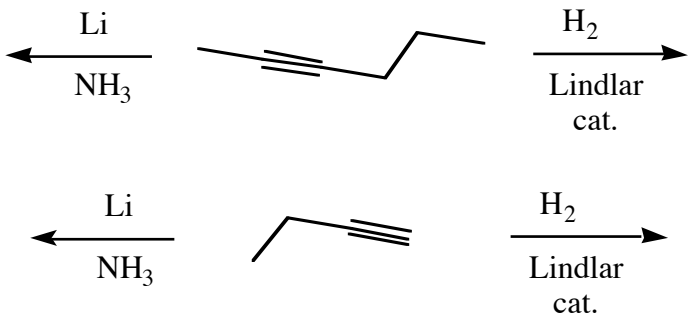


c. (one) Reduction with Li (or Na) in liquid ammonia (NH_3)



(This rxn goes via an interesting mechanism —add'n of (1) an e^- from Li, (2) an H^+ from NH_3, (3) an e^- from Li, and (4) an H^+ from NH_3, thus, 2 Hs overall.)

Draw products —



6. Recall that acetylide ions can be made by deprotonation of terminal alkynes with a strong base like H_2N^-. Acetylide ions are good S_N2 nucleophiles.

Synthesis —

By now we've learned enough reactions to do some substantive syntheses. Here's some general advice that will be helpful —

(1) It's often easiest to work backward, as least part way this is called "retrosynthetic analysis". This is the way synthetic organic chemists mentally "dissect" complex molecules to figure out how they can be made from starting materials that can be bought.

(2) Always look for the route that gives the highest possible yield of the desired product.

(3) Only propose reagents that you might find on the shelf of a lab. For example, if you want to add a methyl group to an alkoxide ($R–O^-$), don't suggest using H_3C^+! Where are you going to get methyl cation?! (I call this "cave man chemistry" — get minus rock, get plus rock, bang rocks together, bang bang, try not get head in way... ow.) That's the correct polarity, but certainly we can find a more reasonable source of a ("positive", or partially positive) methyl group... how about an S_N2 reaction with $CH_3–I$?

(4) If you're asked to write a synthesis, don't write reaction mechanisms, and don't try to do chemistry with unstable intermediates like enols or carbocations — these will do whatever they'll do as soon as they're formed. They're not going to sit around and wait for you to work up the reaction mixture or add different reagents. For example, if you generate a carbocation, it will find something already in the solution to react with — whatever that is must already be there waiting for it (e.g., Br^- or EtOH). If you generate an enol, it will tautomerize faster than you can say "enol". If you'd like to hydrogenate it, too bad, it's already gone.

Keep in mind that a mechanism is a proposed pathway that explains how reactants are converted to products. Mechanisms do not provide handles by which you can grab high-energy intermediates and prevent them from reacting or steer them uphill in energy or in any other direction. When you propose reactants and reagents, they are going to react however they react, and you'll have to deal with the end result.

You can stay out of this trap by not even writing mechanisms when you're asked to write a synthetic sequence — draw the starting cmpd, the reagents, and the final organic product of each reaction in the sequence.

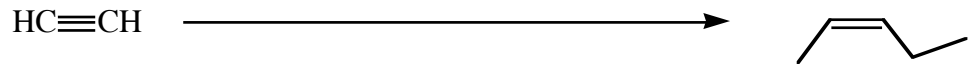
(5) An important corollary to this is that when you're asked to write a mechanism, don't write a synthesis. A mechanism is an explanation of how reactants get converted to products under the conditions specified. Don't propose that other compounds and reagents magically appear! (That includes resisting the temptation to propose HO^- in acidic solutions and H^+ in basic solutions.)

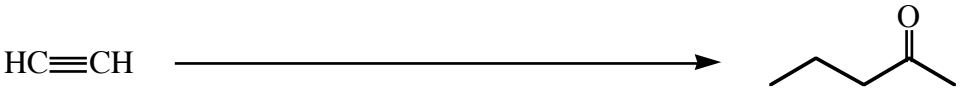
Now for a little specific advice for syntheses involving alkyne chem:

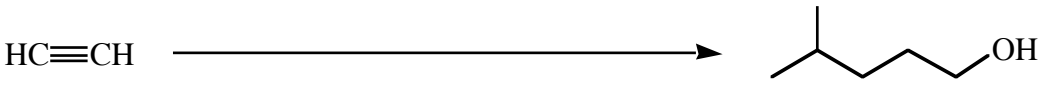
— use acetylide + R–X rxn to make new CC bonds

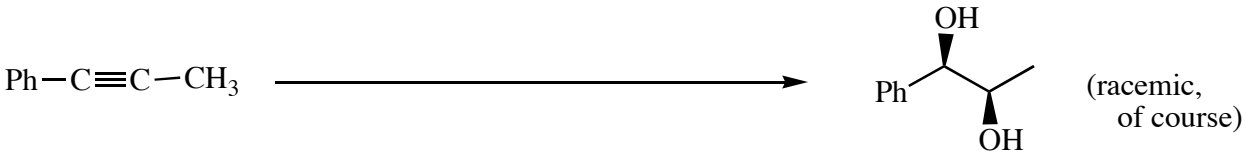
— use the triple bond to introduce new functional groups and control regiochemistry and stereochemistry

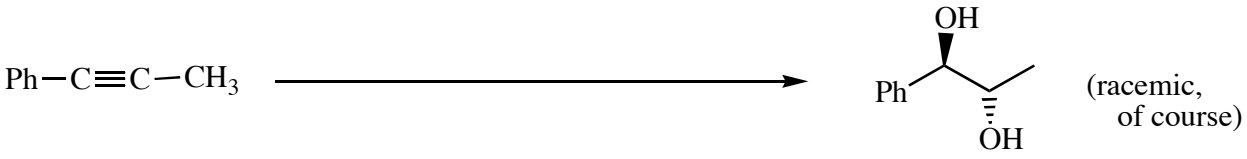
How would you carry out the following syntheses?






HC≡CH
OH


Ph−C≡C−CH3
OH
Ph
OH
(racemic,
of course)


Ph−C≡C−CH3
OH
Ph
OH
(racemic,
of course)