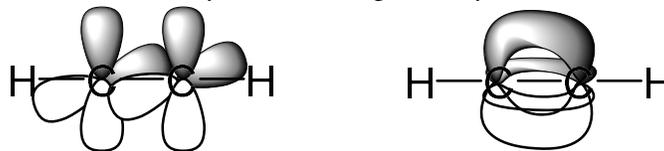


# Loudon Chapter 14 Review: Reactions of Alkynes

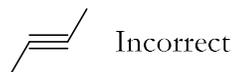
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An alkyne is any molecule with a triple bond between two carbon atoms. This triple bond consists of one  $\sigma$  bond and two  $\pi$  bonds: the  $\sigma$  bond exists on a straight line between carbon atoms, while one  $\pi$  bond is above/below this line and the other is behind/in front of this line. This particular molecule is acetylene, the simplest alkyne.

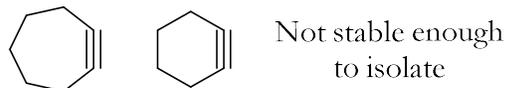
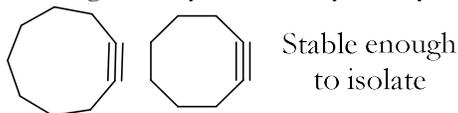


2 p orbitals on each C  $\rightarrow$  2  $\pi$  bonding orbitals

Since each alkyne carbon is  $sp$ -hybridized, the geometry around each of them is linear. This means that in line-bond/skeletal structures, the two bonds to the alkyne carbon should be straight, not zigzagged.

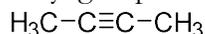
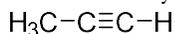


Since the geometry is linear, cycloalkynes have to be at least 8-membered rings or larger.



## Nomenclature

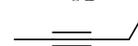
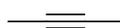
Nomenclature can go by either common, nonsystematic names, or by IUPAC. Common naming involves identifying the two alkyl groups attached to either side of acetylene:



or

or

or

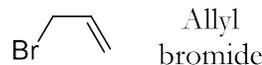


Methylacetylene

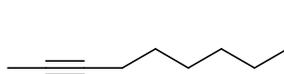
Dimethylacetylene

Ethylmethylacetylene

The substituent group “propargyl” also shows up in common names. It’s the same as the allyl group, but with a triple bond instead of a double.



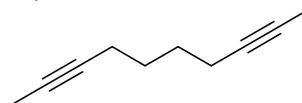
IUPAC naming for alkynes is very similar to alkenes – start numbering from the end closest to the first triple bond. The ending of the name changes to “yne” instead of “ene”. If there are multiple triple bonds then ending changes to “diyne”, “triyne”, etc.



2-nonyne



5,5-dimethyl-2-hexyne



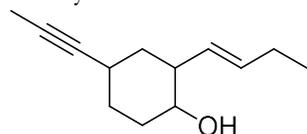
2,8-decadiyne

If a substituent group has an alkyne in it, the group is named by replacing the final “e” from the alkyne’s name with an “yl”, the same as alkene-containing groups. (If there’s more than one possible location for the double/triple bond within the substituent, give the location number and put the whole group’s name in parentheses. Numbering within the group starts from its point of attachment to the parent chain/ring.) Substituents with multiple bonds

# Loudon Chapter 14 Review: Reactions of Alkynes

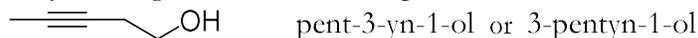
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follow the same rules for priority as any other group – if all else is equal, the group that comes first alphabetically wins.



2-(1-butenyl)-4-(1-propynyl)cyclohexanol

If the molecule contains a principal functional group (alcohols and thiols are the only examples we've seen of these so far), then the ending contains "yn" followed by the ending for the principal group. The location of the principal group goes right before the end, but the location of the alkyne can go either before the parent chain, or before the "yn".

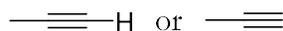


For molecules with both alkenes and alkynes, numbering should still start at the end closest to the first double/triple bond. If both ends are equally close, the double bond takes priority.

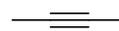


## Addition Reactions of Alkynes

For all these reactions, we'll show them occurring on a terminal alkyne: one which has an R group on one side and an H on the other. This is so you can tell what prefers to add where (the regiochemistry). For internal alkynes, though, there are R groups on both ends. This means that there is no regiochemical preference, since both ends are equally substituted and Markovnikov and anti-Markovnikov cease to have any meaning.



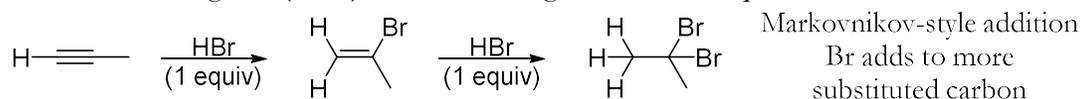
Terminal alkyne



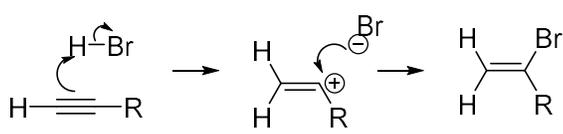
Internal alkyne

The addition reactions that Loudon covers in this chapter fall into three categories.

- Hydrogen halide addition:** Most of the reactions that alkynes do are directly analogous to the things that alkenes do in Ch. 4 & 5. The main difference is that an alkene can only react once, turning it from a double bond to a single bond. An alkyne can react up to two times: once to make it go from triple to double, and again to make it go from double to single. (The first reaction is usually a little faster). So the outcome of the reaction will often depend on how many equivalents of reagents you add to it. This particular reaction involves adding HX across the bond, with Markovnikov-style regiochemistry. If you want to make absolutely sure that the reaction stops after a single addition, you can include something like  $(C_2H_5)_4N^+ Br^-$ , although this is not required.



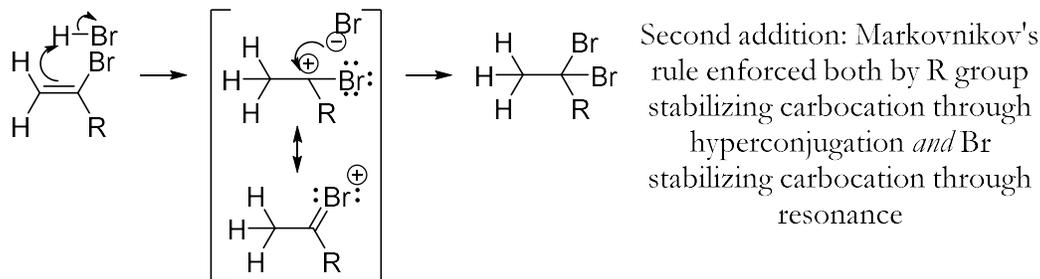
Markovnikov's rule is reinforced by the fact that not only is the carbocation stabilized by more R-group substituents, it's also stabilized by the first Br to get added. This means that the two bromine atoms will prefer to add to the same carbon atom, even when both ends of the alkyne are the same.



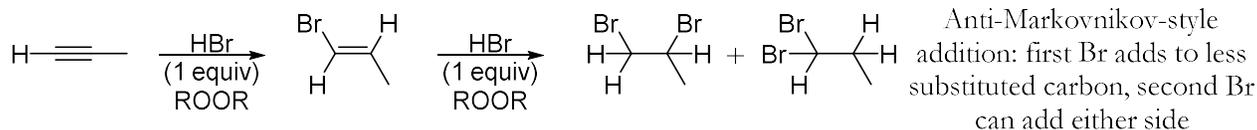
First addition: Markovnikov's rule enforced by R group stabilizing carbocation through hyperconjugation

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What about radical addition of HBr and peroxides? This adds anti-Markovnikov the first time, but it turns out to be more complicated the second time because now either the first Br or the R group can stabilize the radical. So the second addition gives a mixture of products.

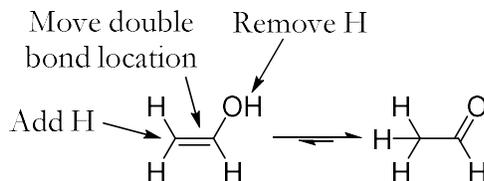


- Hydration:** Just like for alkenes, this involves adding a molecule of water across the bond, by adding an H to one carbon and an OH to the other. However, there's a complication: keto-enol tautomerism. Molecules with hydroxyl groups (OHs) connected directly to alkene carbons are called enols (from **alkene** + **alcohol**). Except in a few cases, enols will always rearrange immediately to form carbonyl compounds instead (molecules with C=O double bonds). This is mostly because the C=O double bond is a lot stronger than the C=C double bond.

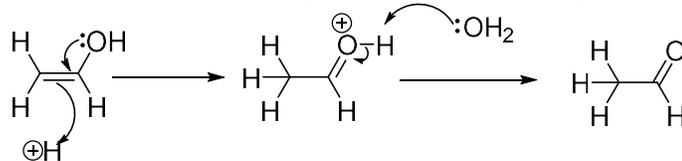


Keto-enol tautomerism

There are three steps involved in this rearrangement: the location of the double bond needs to move, an H (proton) needs to add to the alkene carbon without an OH, and an H needs to be removed from the oxygen. The reaction can happen in acidic or basic conditions. The same three steps will happen either way, it's just a question of what order they occur.



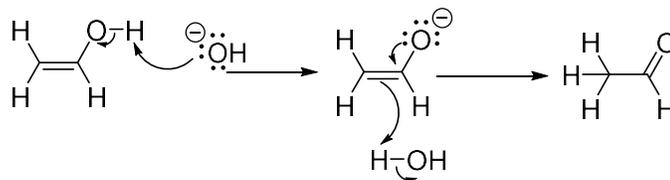
In acidic conditions, there's an excess of protons, so the add-a-proton step happens first:



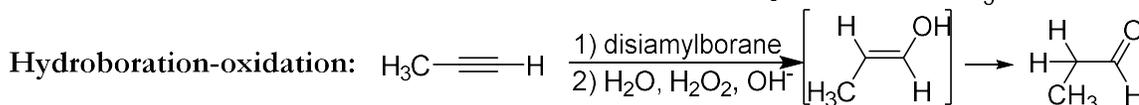
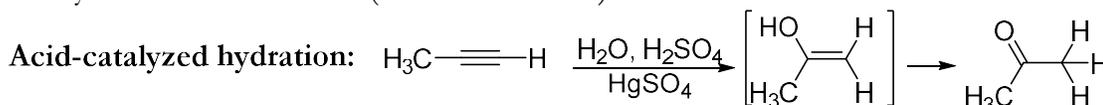
In base, there's a shortage of protons, so the remove-a-proton step happens first.

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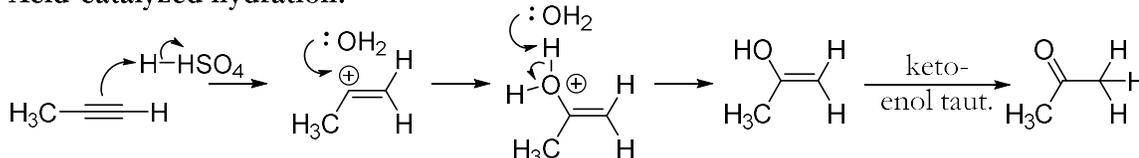


Note that for both these possible mechanisms, there's never a positive or negative charge on a carbon atom. The oxygen atom always carries the charge because it's better equipped to do so, thanks to its lone pairs and higher electronegativity. Now we can plug this tautomerization into the mechanism for hydration. We know three mechanisms for hydration of alkenes: acid-catalyzed and oxymercuration-reduction (both Markovnikov), and hydroboration-oxidation (anti-Markovnikov).



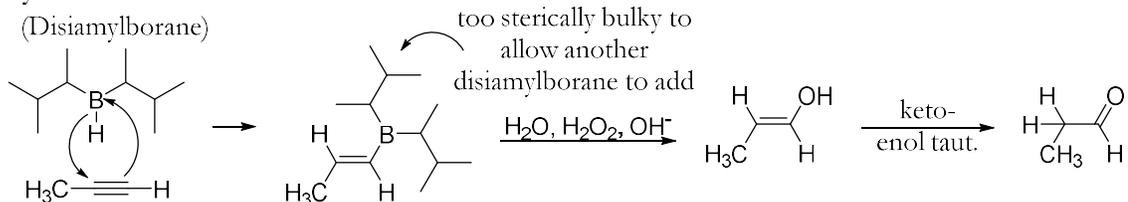
For acid-catalyzed hydration, some form of mercury (II), such as  $\text{HgSO}_4$ , is often added as a catalyst. The OH adds Markovnikov-style first. As soon as it forms, the enol will rearrange to the ketone. And since it's already in acidic conditions, it will follow the acidic mechanism for keto-enol tautomerism.

**Acid-catalyzed hydration:**



For hydroboration-oxidation, we can use either  $\text{BH}_3$ ,  $\text{BH}_3\cdot\text{THF}$  or  $\text{B}_2\text{H}_6$  (like we did for alkenes) or a bulkier version of these, disiamylborane. This is useful to force stereochemistry to be more selectively anti-Markovnikov and to make sure that only one addition occurs to each alkyne. Once the OH is added anti-Markovnikov style, it will tautomerize to the carbonyl compound – in this case, the aldehyde. Since we're already using basic conditions to make the enol, the mechanism will be base-catalyzed tautomerization.

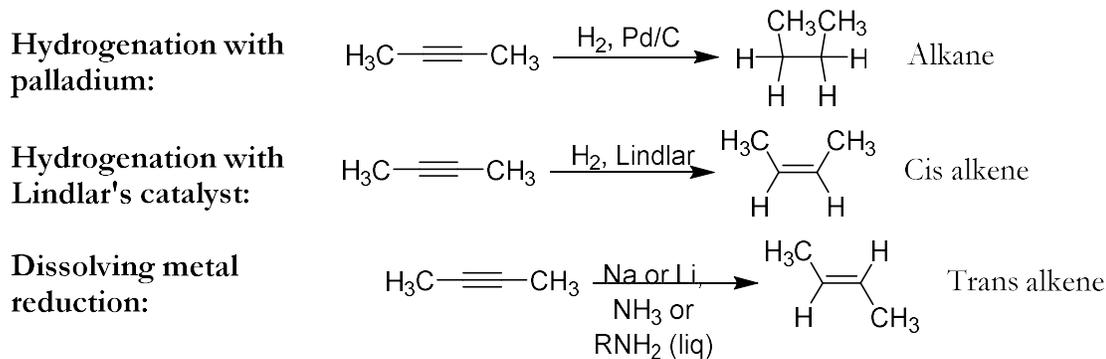
**Hydroboration-oxidation:**



- Reduction:** When we were looking at alkene additions, there was only one reaction in this category:  $\text{H}_2$  and Pd/C. But like with HBr addition, we can add either once or twice.

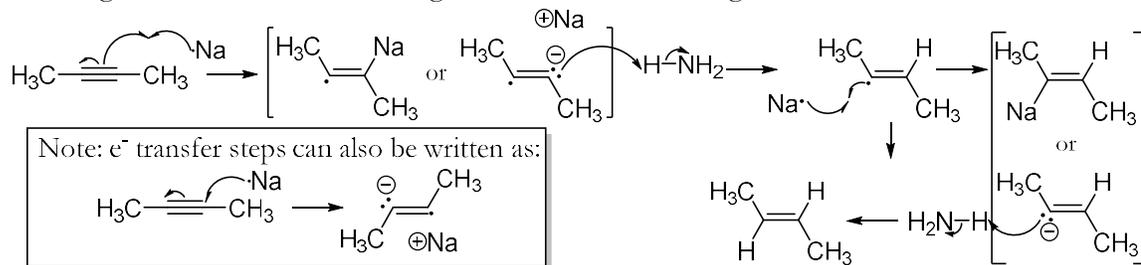
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Palladium will add as many hydrogen atoms as it can, to make the alkane. To make it stop partway at the alkene, we have to “poison” the catalyst with some form of lead, pyridine or quinoline. This poisoned catalyst is called “Lindlar’s Catalyst”. We don’t cover the mechanism for either of these solid-phase reactions, but they’re about the same: it’s a concerted addition, so each pair of Hs always adds to the same face. That’s why Lindlar’s catalyst will always give the cis alkene.

For the trans alkene, we need totally different conditions. This reaction takes place in liquid ammonia or amine, with solid sodium or lithium metal mixed in with it. This is called a “dissolving metal reduction,” since the metal becomes  $\text{Li}^+$  or  $\text{Na}^+$  ions and dissolves as the reaction proceeds. The mechanism has four steps: Add an electron, add a proton, add an electron, add a proton. It may seem odd that sodium will just give an electron up to the molecule entirely, but remember: any organometallic species can be depicted as an ionic bond or a covalent bond – both are two extremes of the same spectrum. So in the first step, you could show sodium contributing an electron to form a bond to the molecule, just like the bromine radical did when we were looking at radical halogenation. But in the next step, just like any organometallic, the molecule will be primarily interested in pulling an H from whatever protic source is available. In terms of why it makes the trans form specifically, you should know already that trans alkenes are more stable due to lower sterics. Since this molecule has the opportunity to get itself to either the cis or trans form at any step in the mechanism, it will end up being trans most of the time. As a side note: don’t get  $\text{Na}/\text{NH}_3$  confused with  $\text{NaNH}_2$  (from the next set of reactions). They look similar, but in  $\text{Na}/\text{NH}_3$ , sodium has a single electron which it can donate to the molecule. In  $\text{NaNH}_2$ , sodium already has a positive charge, so it won’t be doing much.  $\text{NH}_2^-$  will be doing all the work, as a strong base.



## Acetylates as Nucleophiles

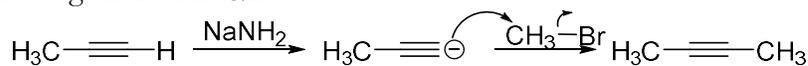
This is something unique to alkynes - alkenes did not do this. An H next to a triple bond (in a terminal alkyne) has a very low  $\text{pK}_a$  for a C-H bond; carbon with a triple bond is much more stable with a minus charge than carbon with a single or double bond. The  $\text{pK}_a$  value

# Loudon Chapter 14 Review: Reactions of Alkynes

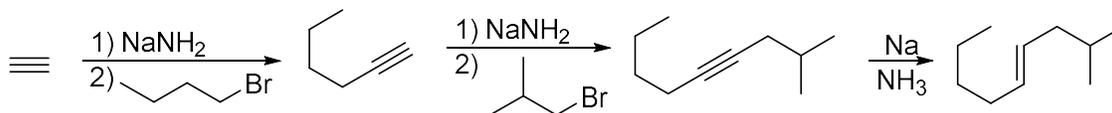
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for these acetylides (the conjugate base of an acetylene) is typically in the mid-twenties, instead of the forties and up. This means we can deprotonate with a sufficiently strong base, typically  $\text{NaNH}_2$  (sodium amide), but Grignard reagents can be used as well.

This makes an acetylide anion, which is a strong base/good nucleophile. If you remember chapter 9, things in this category will do  $\text{S}_{\text{N}}2$  on methyl, primary and maybe secondary, and  $\text{E}2$  on tertiary. So if we take the acetylide and react it with a suitable alkyl halide, we can stick the two molecules together with  $\text{S}_{\text{N}}2$ .

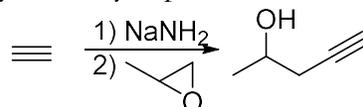


This is a great way to form new carbon-carbon bonds, and is very useful in syntheses for putting big sections of the carbon skeleton together. The alkyne can act as the lynchpin that holds the two halves of the molecule together, although it doesn't have to stay an alkyne afterwards – it can be converted to other functional groups, following the addition reactions shown above.



Note that we have to do each addition as two separate steps – first we deprotonate the alkyne with  $\text{NaNH}_2$ , and *then* we add the alkyl halide. If we added them both at once, the  $\text{NaNH}_2$  would react with the alkyl halide by doing  $\text{S}_{\text{N}}2$  and/or  $\text{E}2$  on it. Also note that we can only alkylate one side at a time, since otherwise we would be making a species where both triple-bonded Cs have negative charges at the same time – very unstable!

This acetylide reaction is useful because it makes new C-C bonds, similar to a reaction we saw in Ch. 11 – cuprates plus epoxides. In fact, you can also use acetylide to do the same kind of epoxide ring-opening as you did with cuprates! As before, the acetylide attacks the less-substituted carbon of the epoxide, because it's under basic conditions. Note, though, that this creates an alcohol group, so you can only do this once – if you tried to add anything to the other end of the alkyne, you'd only deprotonate the OH.

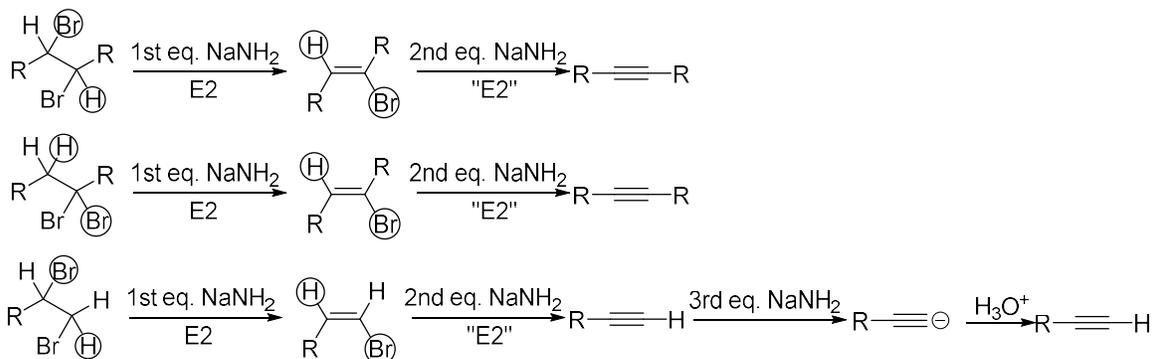


## Alkyne formation by elimination

(This reaction isn't covered in Loudon 6<sup>th</sup> edition until Ch. 18, but it's so useful for synthesis that I'm covering it a little early.) We haven't covered how to form a carbon-carbon triple bond in the first place. This is similar to the way you most often make alkenes: doing an elimination. You need to do it twice, though, once to make the double bond and once to make the triple bond. For each elimination, you need an H and a leaving group on adjacent carbons. Again, the base is normally sodium amide,  $\text{NaNH}_2$ . The groups that are about to leave in each step are circled. The two halogens can be either on the same or different carbons. Only the first elimination is truly  $\text{E}2$  (happening to an  $\text{sp}^3$ -hybridized carbon), although the second elimination is similar to  $\text{E}2$ .

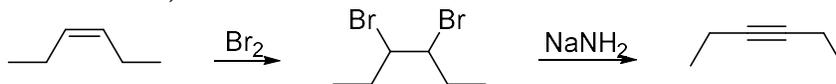
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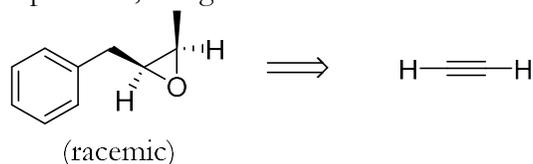
The important difference in outcomes is based on the difference between internal alkynes and terminal alkynes. In the case of terminal alkynes, the H will come off whether you want it to or not, because  $\text{NaNH}_2$  is a strong enough base to do this. This means a third equivalent of  $\text{NaNH}_2$  will automatically be used up. To put the proton back on at the end, you need a workup with  $\text{H}_2\text{O}$  or  $\text{H}_3\text{O}^+$ .

Now that we have this reaction, we can make alkynes from alkenes (the opposite of the reductions covered earlier).

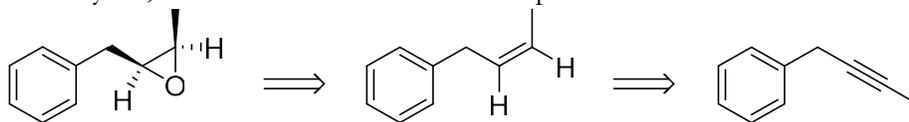


## Ch. 14 Synthesis Practice

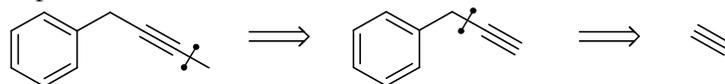
Here's a synthesis practice problem, using these new reactions.



Remember that the retrosynthesis arrow ( $\Rightarrow$ ) means we're working backwards, so we're trying to make the left molecule by starting with the right molecule. We know that the precursor to an epoxide is likely to be an alkene, so we can work backwards one step. (Note that the stereochem is conserved for this step – both R groups are cis on the epoxide, so they come from a cis alkene.) We also know that we can choose to make either cis or trans alkenes from alkynes, so let's use that as our next step backwards.



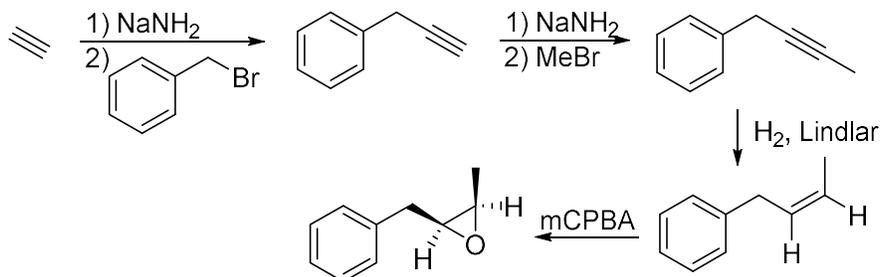
Now we have an alkyne, which is likely the alkyne from the starting material. Since we can attach R groups onto each side of the alkyne, let's reverse this process, one side at a time. Remember that the "cut here" line – the synthetic disconnect – shows where bonds were broken during a step. It doesn't matter which side we disconnect first.



Now we can put this together into a full synthesis by adding reagents for each step.

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Quick check: Does each step make sense? We know that the first two steps involve doing S<sub>N</sub>2 on an alkyl halide, so is each R group (the benzyl group and the methyl group) sterically unhindered enough to be S<sub>N</sub>2-capable? Yep! They're both primary or methyl.