At first glance the chemistry of alkynes looks as if it should be similar to that of alkenes, the reactions will be dominated by additions across the pi-bonds, and to a certain extent this is true. However, there are some very significant differences and reactivity that we will need to learn, and more importantly the chemistry of alkynes introduces us to some new and important concepts, these are:

- Many real organic molecules contain more than one functional group, how do we do chemistry of one functional group in the presence of others, i.e., how do we understand chemical reaction selectivity.

- Many reactions this semester will proceed via acid and base catalysis, this section of the notes gives us our first real introduction to these concepts.

- The construction of larger complex organic molecules out of smaller simpler ones requires making new carbon-carbon bonds to join together smaller organic fragments, here we will learn our first useful method for making new carbon-carbon bonds.

1 Nomenclature

- We must now learn how to name structures that contain more than one functional group. To handle this IUPAC has rules that determine the priorities of the various functional groups. Establishing functional group priority is necessary when naming a structure that contains more than one functional group, the structure then gets named as the highest priority group.

- IUPAC Functional Priority: alkenes = alkynes > halides, i.e. number the chain to give either the alkene OR the alkyne the lowest number, whichever wins.

- If there is a tie (and ONLY if there is a tie), give the alkene the lowest number (the alkene "wins").

- Suffix: -yne, if the structure contains BOTH an alkene and an alkyne, the -ene suffix comes before the -yne suffix

- IUPAC has TWO methods for naming alkynes (and alkenes). One puts number specifying the position of the triple bond at the beginning of the name, the second puts the number before the "-yne", which is much more useful when naming structures that contain more than one functional group, since it clearly establishes which number is associated with which functional group.

Examples:

- Above LEFT, the alkyne is #5 numbering from either end of the chain, the chain is thus numbered from the left to give the first substituent the lowest number, but this is ONLY done if the functional group numbering is the same from both directions, the alkyne numbering TAKES PRIORITY if possible. The configuration of the two chiral/asymmetric centers is not specified in the structure, and therefore cannot be specified in the name.

- Above RIGHT, the absolute configuration is specified in the structure, must be specified in the name.
Some common (non-IUPAC) names for alkynes:

- CH≡CH: acetylene
- CH≡C(CH₂)₂CH₃: ethyl acetylene
- Ph−C≡CH: phenylacetylene
- Ph−C≡C−Ph: diphenylacetylene

* you NEED to know this one

### 2 Structure and Properties

- First, some notation, alkynes with the triple bonds at the end of the chain (terminal alkynes) have enough different properties from those with the triple bonds in the middle of the chain (internal) alkynes, that terminology that distinguishes them is useful:

  \[
  \begin{align*}
  &\text{INTERNAL} & \quad &\text{TERMINAL} \\
  &\text{R−C≡C−R'} & &\text{R−C≡C−H} \\
  
  \end{align*}
  \]

- The sp hybridized carbons give alkynes distinct properties:

<table>
<thead>
<tr>
<th>Hybridization</th>
<th>C-C BDE (kcal/mol)</th>
<th>C-C Length (Å)</th>
<th>C-H BDE (kcal/mol)</th>
<th>C-H Length (Å)</th>
<th>Ionization Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>sp³</td>
<td>~90</td>
<td>1.53</td>
<td>~101</td>
<td>1.10</td>
<td>π</td>
</tr>
<tr>
<td>sp²</td>
<td>~174</td>
<td>1.33</td>
<td>~110</td>
<td>1.08</td>
<td>electrons note order</td>
</tr>
<tr>
<td>sp</td>
<td>~231</td>
<td>1.20</td>
<td>~117</td>
<td>1.00</td>
<td>lower energy</td>
</tr>
</tbody>
</table>

- Bonds to sp hybridized carbons are stronger and shorter bonds, **BOTH the C-H and the C-C bonds**.
- When the carbon atoms are sp hybridized, ALL of the electrons, in both the sigma- and the pi-bonds, are closer to the nuclei in smaller orbitals (sometimes the sp carbon is described as being more "electronnegative" than sp² and sp³ hybridized carbons)
- The **LARGER I.P. for the alkyne** compared to the alkene shows that the **energy of the electrons in the pi-bonds in the alkyne are LOWER than those in the pi-bonds of alkenes.**

- BOTH the pi- electrons and the sigma-bonding electrons in alkynes are **LOWER IN ENERGY** than the corresponding pi- and sigma-bonding electrons in alkenes (BUT, see further below!!)
2.1 Alkyne Acidities, Revisit Bronsted Acidity

- Alkynes are stronger Bronsted acids than alkenes and alkanes, although still overall weak, weaker even than conventional weak acids such as ethanol and water
- The ACETYLIDE anion (the conjugate base anion of a terminal alkyne) is RELATIVELY stable for a carbon anion

As discussed previously, Bronsted acidity increases as hybridization changes, with decreasing p character in the relevant orbital, i.e., sp3 to sp2 to sp when comparing an alkane, alkene and alkyne, above
- Recall, there are usually two competing factors that control Bronsted acidity, in this case it is the strength of the C-H bond (which gets larger with decreasing p character in the relevant hybrid orbital) versus the stability of the non-bonding electrons in the Bronsted base, which also increases with decreasing p character, it is the stability of the electrons in the conjugate base anion that "wins" in this case, rather than the bond strength argument, the species with the stronger bond is the stronger acid because the electrons in the base are more stable
- OR, simply look at the energy of the electrons in the conjugate base anion, the lower the energy of the electrons (because of resonance, electronegativity etc., or in this case, hybridization), the more stable the conjugate base anion, the stronger the Bronsted acid.

• Determining base (and therefore acid) strength based on the energy of the electrons in the conjugate base anion ALWAYS works EXCEPT when going down the periodic table (recall H-F, versus H-Cl versus H-I)

2.2 Alkyne Acidity in Water and in Ammonia

- Let's start by understanding alkyne acidity in water

• stronger acid wins, equilibrium lies on ALKYNE side
• From this learn that: OH is not strong enough base to deprotonate a terminal alkyne
• From this learn that: H2O will protonate an acetylide anion
• Now, alkyne acidity in ammonia

\[
\text{HC≡C=H} + \text{NH}_2^\text{=} \rightarrow \text{HC≡C}^\text{=} \text{Na} \rightarrow \text{HC≡C}^\text{=} \text{Na} + \text{NH}_3
\]

\[
\text{HC≡C}^\text{=} \text{Na} + \text{H}_2\text{O} \rightarrow \text{HC≡C=H} + \text{Na}^+ \text{OH}^-
\]

New reagent, stronger base:

• sodium amide (also sometimes called sodamide) is a stronger base because the non-bonding electrons are on the less electronegative nitrogen, are higher in energy, more reactive
• the number of pairs of non-bonding electrons is not important, they "keep out of each others way"

more than you really need to know….

sodium amide is made by reacting metallic sodium in liquid ammonia:

\[
\text{Na} + \text{NH}_3(\text{l}) \xrightarrow{\text{Fe(III) Catalyst}} \text{Na}^\text{=} \text{NH}_2/\text{NH}_3(\text{l}) \quad (+ \quad 1/2 \text{H}_2)
\]

it is usually used as a solution in liquid ammonia (low temperatures) and may be written as NaNH2/NaNH3(l) to emphasize that point, but it is usually just written simply as NaNH2

NaNH2 tends to act as a base rather than a nucleophile simply because it is such as strong base it overwhelms any nucleophilic substitution reactivity

3 Preparation of Alkynes

Recall:

Similarly:

But………………

needs a stronger base!!

• SN2 OR E2 is not possible at an sp2 hybridized carbon atom (using -OH as the base at least)
a VINYL bromide is less reactive than an alkyl bromide due to the stronger C-Br bond involving an sp2 hybridized carbon, compared to the Br to sp3 hybridized carbon in the alkyl halide. We saw this previously, vinyl bromides don’t do SN2 reactions for partially the same reason (the bond to leaving group is too strong).

To make this reaction USEFUL we need a STRONGER base than hydroxide, NaNH₂

- Luckily, we just learned about a stronger base than Na⁺ ‘OH, that is Na⁺ ‘NH₂

Note the use of the term "Excess" (XS) - means use more than 1 equivalent of the reagent (more than one mole of reagent per mole of reactant), usually much more than 1 equivalent (more than 2 in this case).
- why is water required in a second step?

Mechanism: for the example of a vicinal dibromide

- the mechanism shows why EXCESS NaNH₂ is needed, since we need TWO NaNH₂ to do the two deprotonations, and THEN, deprotonation of the terminal alkyne formed in the second E2 reaction is unavoidable
- therefore, we need the water to put the proton back after the amide anion removed it!
- this overall reaction is useful for making terminal alkynes

Example:

- this method for alkyne synthesis is really only useful for synthesis of TERMINAL alkynes, because of the following triple bond migration effect
• think about this apparently complex mechanism as a MECHANISM PROBLEM
• what bonds have to be made, what bonds have to be broken, how to we make/break these bonds in reasonable order using the Lewis/Bronsted acid base reactions that we know or could predict?
• need to both add and remove hydrogen atoms in the form of protons, in the presence of a base,
• In the presence of base, FIRST remove protons and then reprotonate using the acid that you just generated
• it is the irreversible formation of the terminal acetylide anion, the last step in the mechanism, that "traps" the terminal alkyne and prevents further migration
• the amide anion is a CATALYST, it never gets consumed, but it helps the reaction to "go"
• NOTE: This process isn't really a reaction that you can use in, for example, synthesis, in practice it is not possible to convert an internal alkyne into a terminal alkyne with high yield, it is given here purely as a MECHANISM problem

4 Reactions of Alkynes: Reactions of One Functional Group in the Presence of Another

• Here we start our discussion of the reactions of the alkyne functional group, but also do something much more important: We learn how to control reactions of one functional group IN THE PRESENCE of another.
• Organic molecules often have many functional groups, how do we do a reaction SELECTIVELY at one functional group and leave the others alone? Here is we start to find out how to do this.

4.1 Selective Syn-Addition of Hydrogen (Reduction)

Recall:

![Reaction diagram]

• This reaction is exothermic because it converts a sigma- and a pi-bond into a sigma- and a sigma-bond, sigma-bonds are stronger than pi-bonds, the electrons in sigma-bonds are lower in energy than those in pi-bonds

Similarly:

![Reaction diagram]

• The reaction can't be stopped after one addition of H₂, the alkene formed in the first step will be further reduced to the alkane, BUT, the two reactions are not the same, they don't have the same exothermicity:

![Energy diagram]

NOTE: Alkyne reactions are generally more exothermic than corresponding alkene reactions, even though they have lower energy electrons in their pi-bonds
• When considering chemical reactivity we have to think about ALL of the bonds that are broken AND formed.
The reaction exothermicity takes into account the energy of the electrons in the alkene and the alkyne pi-bonds, AND, the energy of the electrons in the PRODUCTS that are formed.

EVEN THOUGH alkynes have lower energy electrons in their pi-bonds, the two C(sp2)-H that are formed are STRONGER than the C(sp3)-H bonds that are formed when an alkene reacts, which is why the alkyne reactions are more exothermic.

THEREFORE, the reactions of alkynes and alkenes could, in principle, be distinguished or selected on the basis that the additions reactions have different THERMODYNAMICS, and as we will see, this works!

The two new sigma bonds that are made when the H₂ adds to the alkyne are C(sp2)-H, whereas the two new sigma bonds that are made when the H₂ adds to the alkene are C(sp3)-H. Therefore, the addition reaction of H₂ to the alkyne makes stronger sigma-bonds than the addition reaction of H₂ to an alkene. Now, a lot of other stuff also happens in these reactions, for example, when the H₂ adds, the existing C-H bonds in the alkyne change from C(sp)-H to C(sp2)-H, and, stronger pi-bonds are broken in the alkyne reaction, but it is the new sigma bonds that are formed that is the major difference between the two reactions, and is the main reason why addition of H₂ to an alkyne is more exothermic than addition to an alkene.

Compare: SYN-ADDITION of H₂ across the carbon-carbon triple bond of the alkyne

• syn-addition (same as to alkenes) leads to formation of cis-product
• poisoned catalyst = Pd on CaCO₃ with PbO₂ and quinoline to reduce activity = Lindlar’s catalyst (there are other recipes for the Lindlar catalyst, it can get confusing, and so we will just refer to the Lindlar catalyst using its name
• the alkyne reaction is MORE exothermic, which aids selectivity based on THERMODYNAMICS (although in reality it is a bit more complicated than this since the alkyne also adsorbs preferentially to the surface)
• the details about exactly how the catalyst works, and indeed its composition, are not worth the effort to learn
• HOWEVER, you DO need to know this method for synthesizing a cis-alkene from an alkyne

Example:
A stereospecific reaction of an alkyne in the presence of an alkene

Using the Lindlar catalyst, the alkyne can be made to react selectively, AND, a single alkene stereoisomer is formed as a result of this reaction!

The alkyne reacts preferentially to the alkene because the reactions have different exothermicities and the alkyne tends to adsorb PREFERENTIALLY to the catalyst

To get two hydrogen atoms from a hydrogen molecule, a way is needed to break the strong H-H bond, that is the role of the catalyst
4.2 Selective Anti-Addition of Hydrogen (Reduction)

- How DO we add $\text{H}_2$ specifically to make the TRANS-isomer (ANTI-ADDITION)?

\[
\text{H} + \text{H} = \text{H}_2
\]

- Formation of a trans-alkene from an alkyne requires a different New Reagent and a new MECHANISM.

\[
\begin{align*}
\text{Na} & \rightarrow \text{Na}^+ + e^{-} \\
\text{NH}_3 & \rightarrow \text{NH}_2^- + \text{H}^+ \\
\text{together} & \text{make H atom}
\end{align*}
\]

- A sodium atom can provide an electron and a hydrogen atom containing solvent ($\text{NH}_3$, ammonia in this case) can provide a proton, together they constitute a hydrogen atom AND a very different way of adding hydrogen atoms to an organic structure, via a very different mechanism to catalytic hydrogenation.
- A hydrogen atom is equivalent to a PROTON AND AN ELECTRON, adding a proton and an electron to a molecule is equivalent to adding a hydrogen atom.
- Mixing sodium metal and ammonia provides H atoms in the form of electrons and protons.

\[
\begin{align*}
\text{R} - \text{C} & \equiv \text{C} - \text{R}' \\
\text{Na}/\text{NH}_3(\text{l}) & \rightarrow \text{Na}^+ + e^{-} (\text{NH}_3)_n
\end{align*}
\]

- This reagent reduces (adds $\text{H}$ atoms) to an alkyne but not an alkene, the addition to the alkyne is ANTI-, a trans-alkene is produced.
- The sodium metal dissolves in the ammonia solvent (at low temperature) to generate an electron in the ammonia solvent, a solvated electron, $\text{Na}/\text{NH}_3(\text{l})$ is an example of a DISSOLVING METAL REDUCING AGENT (we will see these again later in the course).
- The solvated electron (in ammonia):

\[
\begin{align*}
\text{Na} + \text{NH}_3(\text{l}) & \leftrightarrow \text{Na}^+ + e^{-} (\text{NH}_3)_n
\end{align*}
\]

The Mechanism is not a conventional Lewis acid/base mechanism, and you are unlikely to be asked to reproduce it on an exam, the key intermediates are a TRANS-vinyl radical and a TRANS-vinyl anion.

\[
\begin{align*}
\text{R} - \text{C} & \equiv \text{C} - \text{R}' \\
\text{Na} / \text{NH}_3(\text{l}) & \rightarrow \text{trans-alkene}
\end{align*}
\]

- The intermediate vinyl radical and anion are more stable in the trans-form, which explains the overall stereochemistry of the reaction.

Alkenes : Page 8
Example:

\[
\text{Na/NH}_3(l) \quad \text{e}^- + \text{H}^+ \quad \text{Na/NH}_3(l) \quad \text{e}^- + \text{H}^+ \\
\]

• AGAIN, here we have reaction of one functional group (alkyne) in the presence of another (alkene) and with SPECIFIC stereochemistry.

4.3 Addition of H-Br, Br\textsubscript{2} etc.
Remember the Following Reactions:

\[
\text{H-Br} \quad \text{Br} \quad \text{Markovnikov} \\
\text{H-Br} \quad \text{ROOR} \quad \text{Anti-Markovnikov} \quad \text{(stereochemistry ignored)} \\
\text{Br-Br} \quad \text{anti-addition} \quad (\pm) \\
\]

Compare:

\[
\text{R-C≡C-H} \quad \text{H-Br:} \quad \text{LB} \quad \text{C≡C-H} \quad \text{sp} \quad \text{Br} \quad \text{Markovnikov} \\
\text{THIS reaction SLOWER than alkene reaction} \quad \text{THIS reaction SLOWER than alkene reaction} \quad \text{Markovnikov} \\
\]

• The second cation is resonance stabilized, which explains the second Markovnikov addition
• NOTE: the kinetics and thermodynamics of alkyne reactions compared to alkene reactions are tricky, alkyne reactions tend to be BOTH slower AND more exothermic!

Different types of pi-bond react at different rates with HBr:

\[
\text{alkene} \quad \text{faster than} \quad \text{alkyne} \quad \text{faster than} \quad \text{vinyl bromide} \\
\]

Alkynes : Page 9
Alkynes react slower than alkenes because of the stronger π-bond as a consequence of the carbon hybridization
- The vinyl bromide reacts slower than BOTH the alkyne and the alkene because of the electron energy lowering effect of having the bromine atom attached directly to the C=C double bond
- This reactivity order can't be predicted from first principles, but it is understandable and explains some important reactivity differences between alkynes and alkenes
- **THEREFORE, the reactions of alkynes and alkenes could, in principle, be distinguished or selected on the basis that the additions reactions have different KINETICS, and as we will see, this works!**
- This is a **SECOND WAY** in which alkenes and alkyne reactivity can be differentiated and selected
- We previously saw that reductions by adding hydrogen (hydrogenation) with catalysts such as the Lindlar catalyst, could distinguish alkenes and alkynes based on how exothermic the reactions are, i.e. based on THERMODYNAMICS.

**NOTE:** The Hammond postulate is NOT disobeyed, it works for EACH STEP of the mechanism (energy diagram below)
- The Hammond postulate can only be used to analyze single step reactions or a single step in a mechanism

---

**Example:** One Equivalent

- Addition of a single (1 Equivalent of) HBr to an alkyne is possible, the product of the first addition, the vinyl bromide, reacts slower than the reactant alkyne, and so some of the HBr does not also react with the vinyl bromide making a complex mess. **This is selectivity based on KINETICS!**
- Note that the intermediate **VINYL CATIONS** tend to rearrange SLOWLY due to a stereoelectronic effect associated with the relevant orbitals, therefore in this course we assume that they **DON'T REARRANGE**

---

**more than you really need to know…..**

Hydride transfer to a vinyl cation should produce a resonance stabilized allyl cation, however, the newly formed empty π A.O. is orthogonal to the π-system of the C=C double bond, there is no large energy gain associated with rearrangement until rotation, which makes rearrangement of vinyl cations slow.
Example: Two Equivalents

\[ \text{HBr} \text{Br} \rightarrow \text{Br} \text{Br} \]

Example: AlkENE versus AlkYNE

\[ \text{Br} \text{Br} \rightarrow \text{Br} \text{Br} \]

- reaction of 1 Equivalent of HBr with a structure that has both an alkene and an alkyne functional group results in reaction of the alkene and not the alkyne
- this is actually a pretty important point, this is our first example of preferential reaction of one functional group in the presence of another very similar one! The small change in hybridization is sufficient to allow this selectivity.

Similarly:

\[ \text{Br} \text{Br} \rightarrow \text{Br} \text{Br} \]

- again, we expect 1 equivalent of Br2 (or Cl2) to add to an alkyne without resulting in a complex mixture of single and double additions, as observed (although we DO get stereoisomers)
- again, we expect 1 equivalent of Br2 (or Cl2) to react preferentially with an alkene in the presence of an alkyne, as observed
And:

\[
\text{Ph--C\equiv C--H} \overset{\text{HBr}}{\longrightarrow} \text{Ph--C\equiv C--H} \overset{\text{Peroxides (ROOR)}}{\longrightarrow} \text{Ph--C=C--H} \overset{\text{sp}}{\longrightarrow} \text{H}^+ \text{C=C--C} \text{Ph} \text{Br}^+ \text{HBr} \]

- the complete radical chain mechanism is not shown here, it is the same as the reaction of alkenes with HBr in the presence of peroxides

\[
\text{C=C--C} \text{Ph} \text{Br}^+ \text{HBr} \]

4.4 Addition of Water

Recall:

\[
\text{Me--C=CD} \overset{1. \text{BH}_3, \text{THF}}{\longrightarrow} \text{Me--C=CD (t)} \overset{2. \text{OH/H}_2\text{O}_2}{\longrightarrow} \text{Me--C=C--D} \overset{\text{Anti-Markovnikov and syn-addition}}{\longrightarrow} \text{Me--C=C--D (t)}
\]

\[
\text{Me--C=CD} \overset{1. \text{Hg(OAc)}_2/\text{H}_2\text{O}}{\longrightarrow} \text{Me--C=C--D} \overset{2. \text{NaBH}_4}{\longrightarrow} \text{Me--C=C--D (t)} \overset{\text{Markovnikov and anti-addition}}{\longrightarrow} \text{Me--C=C--D (t)}
\]

\[\text{H}_3\text{O}^+ \text{also works, but not used in synthesis}\]

Analogously: Markovnikov addition of water to an alkyne:

\[
\text{R--C\equiv C--H} \overset{\text{HgSO}_4/\text{H}_2\text{SO}_4}{\longrightarrow} \text{R--C\equiv C--H} \overset{\text{enol}}{\longrightarrow} \text{R--C=CH} \overset{\text{Markovnikov}}{\longrightarrow} \text{we will need to explain this!}
\]

- aqueous acid actually reacts pretty slowly with alkenes, even slower than with alkenes, and the Hg\(^{2+}\) catalyst is usually required to allow water addition to the alkyne
- Hg(OAc)\(_2\) is not reactive enough as a catalyst to make the alkyne reaction go with a reasonable rate

\[
\text{Hg(OAc)}_2 \overset{\text{H}_2\text{O}}{\longrightarrow} \overset{\text{MONOcation, weaker Lewis acid}}{\longrightarrow} \overset{\text{HgSO}_4}{\overset{\text{H}_2\text{O}}{\longrightarrow}} \overset{\text{DIcation, stronger Lewis acid}}{\longrightarrow}
\]

- in reality, dissolving HgSO\(_4\) in water is more complicated than indicated here, but what we show here is sufficient to make the point that a MONOcation mercury catalyst is sufficient to allow the alkene/H\(_2\)O reaction to occur, but a DIcation Lewis acid is a stronger electrophile and needed for the alkyne/water reaction
- The alkyne mechanism can be broken down into two important parts
Mechanism part 1: formation of the enol

alkynes will not react with aqueous acid (alkynes are less reactive than alkenes) without a catalyst
the Hg$^{2+}$ cation is a stronger electrophile (works with alkynes) than Hg$^+$OAc (works with alkenes)

Mechanism part 2: tautomerization of the enol

- keto-enol tautomerization: equilibrium between proton shift isomers
- TAUTOMERIZATION is interconversion between isomers, where the only difference between the isomers is the position of on H atom and one double bond
- need to add (first) H and remove (second) H in presence of ACID (i.e., in the form of H$^+$)
- critical point - with ACID ADD proton FIRST, remove proton second
- the enol and the ketone are ISOMERS, in this case the reaction is a KETO-ENOL TAUTOMERIZATION
- equilibrium favors stronger C=O bond compared top weaker C=C bond in enol
- The acid is not overall consumed, the acid that used in the first step is regenerated in the second step, the acid acts as a true catalyst

Example

Example:

- OK with symmetrical or terminal alkynes, otherwise get a mess!!
Analogously: ANTI-Markovnikov addition of H\textsubscript{2}O to an alkyne:

\[
\text{R} = \text{C} = \text{C} = \text{H}
\]

alkyne

1. (Sia\textsubscript{2})BH \cdot \text{THF}
2. \cdot \text{OH}, H\textsubscript{2}O\textsubscript{2}

\[
\text{R} = \text{C} = \text{C} = \text{H}
\]

concerted or rapid 2-step reaction

\[
\text{R} = \text{C} = \text{C} = \text{H}
\]

Mechanism part 1: formation of the enol

\[
\text{R} = \text{C} = \text{C} = \text{H}
\]

Mechanism part 2: tautomerization of the enol

- This reaction is BASE CATALYZED, the base that is consumed in the first step of the mechanism is regenerated in the second step, the base is a true catalyst
- Need to add and remove "H" with BASE (i.e. remove first, a base will NOT provide protons)
- Treat this a mechanism PROBLEM, think about the order of making and breaking bonds and what the best order is given the provided reagents/condition, in this case BASE....

Example:

\[
\begin{array}{c}
\text{1. (Sia\textsubscript{2})BH \cdot THF} \\
\text{2. \cdot OH, H\textsubscript{2}O\textsubscript{2}}
\end{array}
\]

\[
\begin{array}{c}
\text{1. (Sia\textsubscript{2})BH \cdot THF} \\
\text{2. \cdot OH, H\textsubscript{2}O\textsubscript{2}}
\end{array}
\]
5 Acetylide Anions: Retrosynthesis and Carbon-Carbon Bonds

• suppose we want to make one of the C-C bonds in the structure shown
• consider the retrosynthetic analysis indicated by the disconnections A and B

```
  synths / \  A    B
  \   /   \  \  \  \ synths
 NOT a good synthon
```

• Generate the synthons that have the lowest energy electron energy
• Disconnection A generates a negative synthon with the charge on an sp3 hybrid carbon, very high energy electrons
• The MUCH better disconnection B generates a negative synthon with the negative charge in an sp hybridized carbon, much lower energy electrons, disconnection B is the better one!
• The negative synthon from B CAN be "put into a bottle" as a sodium salt, since the synthetic equivalent in this case is simply an ACETYLEIDE ANION
• The positive synthon is converted into a synthetic equivalent as a bromide, as usual
• Acetylide anions are by far the most useful carbon anion synthons, and are VERY IMPORTANT SYNTHETIC REAGENTS FOR CARBON-CARBON bond forming reactions

5.1 Addition to Alkyl Halides
• We KNOW how to make the acetylide anion, by deprotonation of a terminal alkyne using our new favorite strong base, sodium amide (NaNH$_2$)

```
NaNH$_2$

H-C≡C-H → H-C≡C:Na
```

sodium acetylide

• The acetylide anion reaction is simply an SN2 reaction AND, Makes a new C-C bond.
• It proceeds via the usual concerted backside attack mechanism, with a WALDEN inversion
• RECALL: SN2 reactions work best at primary and allylic carbons atoms

Examples:

```
NaNH$_2$

H≡H + CH$_3$CH$_2$Br → H≡H + (CH$_3$CH$_2$)Br
```

1. NaNH$_2$
2. EtBr

1. NaNH$_2$
2. BuBr

• IMPORTANT, Note 1:..... 2:..... notation, First NaNH2 then alkyl halide
• Works best with primary/allylic halides, otherwise you get the usual SN2/E2 elimination/substitution competition
• the acetylide anion is a STRONG BRONSTED BASE, does standard E2 elimination with a tertiary halide, cn NOT do SN2 (substitution) at a tertiary carbon atom.

5.2 Addition to Carboxyls and Epoxides
• The acetylide anion reacts with an alkyl halide via SN12, the carbon it attacks has a partial positive charge
• The acetylide anion can also attack other electrophilic carbons that have partial positive charges, e.g. the carbon in a carbonyl (C=O) bond

**Example with a carbonyl (C=O bond):**

```
HC≡CH  \[NaNH_2\]  \[\Theta\]  HC≡C:Na

\[\Theta\]  "carbonyl group"
```

• makes a C-C bond AND makes an alcohol
• the C=O pi-bond is the "leaving group" in this case
• H_3O^+ is required to add the proton to the oxygen with the negative charge in the second step
• Here we have a (slightly) more complex conversion of SYNTHON to SYNTHETIC EQUIVALENT, for the positive synthon, the synthetic equivalents are a carbonyl (aldehyde or ketone) AND the proton (H^+)
• the carbon involved in the new C-C bond has an oxygen atom "attached", this is addition to a C=O bond

```
CH_3
\[CH_2\cdot\cdot\cdotCH_3\]  \[H_3O^+\]  \[=\]  \[\Theta\]  \[\Theta\]

HC≡C\cdot\cdot\cdotCH_2\cdot\cdot\cdotCH_3

HC≡C\cdot\cdot\cdotCH_2\cdot\cdot\cdotCH_3
```

• Note 1...  2....  3.... notation, it is IMPORTANT!!

**Example with an epoxide:**

```
HC≡C:  \[\Theta\]  \[\Theta\]  NaNH_2

\[\Theta\]  epoxide

HC≡C\cdot\cdot\cdotCH_2\cdot\cdot\cdotCH_3  \[H_3O^+\]  \[=\]  \[\Theta\]  \[\Theta\]  \[\Theta\]  \[\Theta\]  \[\Theta\]  \[\Theta\]

HC≡C\cdot\cdot\cdotCH_2\cdot\cdot\cdotCH_3
```

• makes a C-C bond AND makes an alcohol
• the strained C-O sigma-bond is the "leaving group" in this case
• H3O+ is required to add the proton to the oxygen with the negative charge in the second step
• Here we have a (slightly) more complex conversion of SYNTHON to SYNTHETIC EQUIVALENT, for the positive synthon, the synthetic equivalents are an epoxide AND the proton (H+)
• the carbon involved in the new C-C bond has an oxygen atom on the ADJACENT carbon, this is addition to an epoxide
• the acetylide anion adds to least substituted side of epoxide for steric reasons
Compare:

- When the 3-membered ring has a **POSITIVE CHARGE**, a Lewis base attacks the **MOST SUBSTITUTED** carbon (electronic effect)
- When the 3-membered ring is **NEUTRAL**, a Lewis base attacks the **LEAST SUBSTITUTED** carbon (usual SN2 steric effect)

**Example:**

- Note 1... 2.... 3.... notation, it is **IMPORTANT**!!

### 5.3 Examples in Synthesis

As a simple example of a multi-step reaction that forms a new C-C bond followed by two different **functional group interconversions** (FGI or F.G.I.):

- **Synthesis Example 1:**
  1. Look for starting materials in product (circled)
  2. Any C-C bonds to make? (yes)
  3. **HEURISTICS**: The -OH on **SAME** carbon as new C-C bond, therefore, the reaction must be addition to a **CARBONYL** (C=O bond)
Synthesis Example 2:

1. Look for starting materials in product (circled)
2. HUERISTICS: The -OH is on a carbon that is ADJACENT to the carbon involved in making the new C-C bond, therefore, this must be addition to an EXPoxide

Synthesis Example 3: Synthesize target structure on the right from the starting alkyne on the left

- 1. NaNH$_2$ - make 2 bonds
- 2. EtI - Alkyne -> Alkene

Synthesis Example 4: Synthesize the target structure on the right from the starting alkyne on the left

- 1. NaNH$_2$
- 2. PrI

• there is only one good way of getting the bromine onto the required carbon in the last step in the synthesis
• Conversion of the alkyne to the alkene does not involve stereochemistry, therefore, Na/NH$_3$(l) could have been used equally well for this step
Synthesis Example 5: Synthesize the target structure on the right from the starting alkene on the left

- the order in which the two C-C bonds are made is important
- if we try to make bond A AFTER making bond B, then we will have a problem, the sodium amide (NaNH₂) will not deprotonate the terminal alkyne to make an acetylide anion, instead it will simply deprotonate the -OH alcohol group as shown above
- this is a common issue when dealing with organic structures that have multiple functional groups, we need to pay attention to all possible reactions
6 Alkynes : Summary of Reactions

Do NOT start studying by trying to memorize the reactions here!
Work as many problems as you can, with this list of reactions in front of you if necessary, so that you can get through as many problems as you can without getting stuck on the reagents/conditions, and so that you can learn and practice solving reaction problems. Use this list AFTER you have worked all of the problems, and just before an exam. By then you will have learned a lot of the reagents/conditions just by using them and you will only have to memorize what you haven't learned yet. Then do the following:
• Cover the entire page of reagents/conditions with a long vertical strip of paper, see if you can write down the reagents/conditions for each reaction, check to see which you get correct, if COMPLETELY correct, circle Y, if incorrect or even slightly incorrect, circle N. In this way you keep track of what you know and what you don't know.
• Keep coming back to this list and so the same thing only for those reactions you circled N, until all are circled Y.

Knowing the reagents/conditions on this page is INSUFFICIENT to do well on an exam since you will ALSO need to recognize how to use and solve reaction problems in different contexts, this page ONLY helps you to learn the reagents/conditions that you have not YET learned by working problems.

Obviously we like to minimize memorization in a class that is designed to help you understand organic chemistry, but you can’t work everything out from first principles, and there is nothing wrong with a little bit of memorization. There is a reason that it is useful to “just know” some material. Material that you just know can be used more quickly and accurately than material you have to "work out". This is why we memorize multiplication tables, for example.
Alkynes

\[
\text{HgSO}_4/\text{H}_2\text{SO}_4/\text{H}_2\text{O} \quad \text{Y/N}
\]
sometimes the \text{H}_2\text{O} will not be specified

\[
\text{Si}_2\text{BH} \cdot \text{THF} \quad \text{Y/N}
\]
1. \text{Si}_2\text{BH} \cdot \text{THF}

\[
\text{H}_2\text{O}_2 / \text{^\text{\text{-}}OH} \quad \text{Y/N}
\]
2. \text{H}_2\text{O}_2 / \text{^\text{-OH}}

\[
1 \text{ Equiv. Cl}_2
\]
1. Equiv. Cl\_2

\[
\text{Y/N}
\]
specifying an inert solvent is optional

\[
2 \text{ Br}_2
\]
2. Br\_2

\[
\text{Y/N}
\]
specifying an inert solvent is optional

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{C}≡\text{CH}
\]
1 equiv. HBr

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{C}≡\text{CH}
\]
2 HBr

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{C}≡\text{CH}
\]
2 HBr

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{C}≡\text{CH}
\]
t-BuOO\text{-}t-Bu

or \text{H}_2\text{O}_2, or a generic peroxide ROOR