Chapter 8
Alkynes: An Introduction to Organic Synthesis

Alkynes
- Hydrocarbons that contain carbon-carbon triple bonds
- Carbon-carbon triple bond result from sp orbital on each C forming a sigma bond and unhybridized px and py orbitals forming a π bond
- The remaining sp orbitals form bonds to other atoms at 180° to C-C triple bond.
- The bond is shorter and stronger than single or double
- The total bond dissociation energy for C≡C is 835 kJ/mol (200 kcal/mol)

IUPAC Naming Alkynes
- Find the longest continuous chain that contains the C≡C
- Take the alkane parent name, drop the -ane and add -yne
- Numbering of chain with triple bond is set so that the smallest number possible include the triple bond

CH₃CH₂CH=CHC≡CH₂CH₃

Begin numbering at the end nearer the triple bond.
IUPAC Nomenclature of Alkynes

- More than one triple bond are called diyne, triyne etc.
- Compounds containing both double and triple bond - enyne
- Numbering of an enyne chain starts from the end nearer the first multiple bond, whether double or triple
- If numbering is the same in either direction, the C=C gets the lower number

Alkyl, Alkenyl and Alkynyl groups

- Butyl (an alkyl group)
- 1-Butenyl (an alkenyl group)
- 1-Butynyl (an alkynyl group)

Examples

- 4-Propyl-2-heptyne
- 4-Bromo-2-hexyne
- 3-Penten-1-yne
- 1-Penten-4-yne
Synthesis of Alkynes by Elimination

- Just as dehydrohalogenation under strong basic conditions yields an alkene, so may an alkyne be formed.
- Either vicinal dihalides (halides on adjacent carbons) or geminal dihalides (halides on the same carbon) must be used.
- A two fold elimination.
- A strong base such as KOH or NaNH₂ is used.

\[ \text{Vicinal Dihalide} \]
\[ \text{Geminal Dihalide} \]

Synthesis of diphenyl acetylene

Reactions of Alkynes: Addition of HX

- Addition reactions of alkynes are similar to those of alkenes.
- Reaction can be stopped after the addition of one eq of HX.
- Intermediate alkene reacts further with excess HX.
- Regiospecificity according to Markovnikov. Geminal dihalide is formed.
Comparison Between Alkynes and Alkenes

Addition of HX to Alkynes

- HCl, HBr, and HI add across alkynes in the same way as alkenes
- Addition of HX to a terminal alkyne proceeds by Markovnikov addition

Addition of Bromine and Chlorine

- Initial addition gives a dihalide
- Product with excess reagent is tetrahalide
Addition of Halogens to Alkynes

• Br₂ and Cl₂ add to alkynes just as they did to alkenes
• The major difference is that no bromonium or chloronium ion intermediate is formed
• Because of this, both cis and trans alkenes can be formed
• Also, formation of tetrahalides can occur even when 1 mole of halogen is used

\[
\begin{align*}
\text{H}_3\text{C} & \text{C} \text{CH}_2 \text{CH}_3 + \text{Br}_2 & \rightarrow & \text{H}_3\text{C} & \text{C} \text{CH}_2 \text{CH}_3 & \cdot & \text{Br}^+ \text{Br}^- \\
\text{H}_3\text{C} & \text{C} \text{CH}_2 \text{CH}_2 \text{Br} & \rightarrow & \text{H}_3\text{C} & \text{C} \text{CH}_2 \text{CH}_3 & + & \text{Br}_2 \\
\end{align*}
\]

Write a series of equations showing how you could prepare 1,1-dichloroethane from ethylene

\[
\begin{align*}
\text{CH}_3 & \text{CH} & \rightarrow & \text{Cl} & \rightarrow & \text{CH}_3 & \text{C} & \text{H} & \text{Cl} \\
\text{CH}_3 & \text{C} & \text{H} & \rightarrow & \text{Br} & \rightarrow & \text{CH}_3 & \text{C} & \text{H} \\
\text{CH}_3 & \text{C} & \text{H} & \rightarrow & 2 \text{HCl} & & \text{NaNH}_2 & \rightarrow & \text{CH}_3 & \text{CH}_2 & \text{CH}_2 & \text{Cl} \\
\end{align*}
\]

Mercury(II)-Catalyzed Hydration of Alkynes

• Alkynes do not react with aqueous proton acids
• Mercuric ion (as the sulfate) is a Lewis acid catalyst that promotes addition of water in Markovnikov orientation
• The immediate product is a vinylic alcohol, or enol, which spontaneously transforms to a ketone

\[
\begin{align*}
\text{CH}_3 & \text{CH} & \rightarrow & \text{H}_2\text{O} & \rightarrow & \text{CH}_3 & \text{CH} = \text{CH}_2 & \rightarrow & \text{CH}_3 & \text{C} & \text{H}_2 & \text{C} & \text{H} & \rightarrow & \text{CH}_3 & \text{C} & \text{H}_2 & \text{C} & \text{O} \\
\end{align*}
\]
Keto-enol Tautomerism

- Isomeric compounds that can rapidly interconvert by the movement of a proton are called **tautomers** and the phenomenon is called **tautomerism**
- Enols rearrange to the isomeric **ketone** by the rapid transfer of a proton from the hydroxyl to the alkene carbon
- The **keto form** is usually **more stable** compared to the enol that only the keto form can be observed

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Keto tautomer
(less favored)

Enol tautomer
(thermodynamically favored)
```

Mechanism of Mercury(II)-Catalyzed Hydration of Alkynes

Hydration of Unsymmetrical Alkynes

- If the alkyl groups at either end of the C-C triple bond are not the same, both products can form and this is not normally useful
- If the triple bond is at the first carbon of the chain (then H is what is attached to one side) this is called a **terminal** alkyne
- Hydration of a terminal always gives the methyl ketone, which is useful

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\text{Terminal alkyne}
\text{Methyl ketone}
```
Summary of Mercury(II)-Catalyzed Hydration of Alkynes

- Acetylene
- Symmetrical Alkyne
- Unsymmetrical Alkyne
- Terminal Alkyne

\[
\text{Acetylene} \xrightarrow{\text{HgSO}_4, \text{H}_2\text{SO}_4, \text{H}_2\text{O}} \text{Acetaldehyde}
\]

\[
\text{Symmetrical Alkyne} \xrightarrow{\text{HgSO}_4, \text{H}_2\text{SO}_4, \text{H}_2\text{O}} \text{Ketone}
\]

\[
\text{Unsymmetrical Alkyne} \xrightarrow{\text{HgSO}_4, \text{H}_2\text{SO}_4, \text{H}_2\text{O}} \text{Ketone}
\]

\[
\text{Terminal Alkyne} \xrightarrow{\text{HgSO}_4, \text{H}_2\text{SO}_4, \text{H}_2\text{O}} \text{Methyl Ketone}
\]

Hydroboration/Oxidation of Alkynes

- BH₃ (borane) adds to alkynes to give a vinylic borane
- Oxidation with H₂O₂ produces an enol that converts to the ketone or aldehyde
- Process converts alkyne to ketone or aldehyde with orientation opposite to mercuric ion catalyzed hydration
Hydroboration/Oxidation

- Adds in a syn fashion just as with alkenes
- The mechanism occurs in an Anti-Markovnikov fashion with the Boron atom attacking at the least substituted carbon
- The intermediate formed is a vinyl borane which gives an enol when oxidized
- The enol intermediate rearranges to either an aldehyde or ketone
- Unlike hydroboration with alkenes, which use ordinary BH₃, now a hindered borane must be used
- This prevents a second hydroboration from occurring

\[ \text{Di(tert-butyl)borane} \]

Mechanism of Hydroboration

Comparison of Hydration of Terminal Alkynes

- Hydroboration/oxidation converts terminal alkynes to aldehydes because addition of water is non-Markovnikov
- The product from the mercury(II) catalyzed hydration converts terminal alkynes to methyl ketones
Synthetic Considerations

- When a terminal alkyne is used, an aldehyde is formed.
- When a symmetric internal alkyne is used, one ketone is formed.
- When an unsymmetrical internal alkyne is used, a mixture of isomeric ketones are formed.

\[ R\text{=C=CH}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{C=CH}_2 + \text{H}_2\text{O} \]

Comparison to Hg\(^{2+}\) Catalyzed Hydration v/s Hydroboration

\[ \text{CH}_3\text{CH}_2\text{C=CH}_2 \]  
\[ \text{H}_2\text{SO}_4, \text{H}_2\text{O} \]
\[ 1. (\text{Sia})_2\text{BH} \]
\[ 2. \text{H}_2\text{O}_2, \text{OH}^- \]

\[ \text{CH}_3\text{CH}_2\text{C=CH}_2 \]  
\[ \text{H}_2\text{SO}_4 \]
\[ 1. (\text{Sia})_2\text{BH} \]
\[ 2. \text{H}_2\text{O}_2, \text{OH}^- \]

Reduction of Alkynes

- Addition of \( \text{H}_2 \) over a metal catalyst (such as palladium on carbon, Pd/C) converts alkynes to alkanes (complete reduction).
- The addition of the first equivalent of \( \text{H}_2 \) produces an alkene, which is more reactive than the alkyne so the alkene is not observed.

\[ \text{H}_2\text{C=CH}_2 \]  
\[ \text{H}_2\text{C}=\text{CH}_2 \]  
\[ \Delta \text{H}_{\text{rxn}} = -136 \text{ kJ/mol} (-32 \text{ kcal/mol}) \]

\[ \text{CH}_3\text{CH}=\text{CH}_2 \]  
\[ \text{H}_2\text{C}=\text{CH}_2 \]  
\[ \Delta \text{H}_{\text{rxn}} = -137 \text{ kJ/mol} (-33 \text{ kcal/mol}) \]
Conversion of Alkynes to cis-Alkenes

- If we make the catalyst less active, the second H₂ addition might become less likely
- The catalyst surface must be partially deactivated or poisoned
- Lindlar’s Catalyst is Pd on CaCO₃ poisoned with lead acetate and quinoline.
- The two hydrogens add syn (from the same side of the triple bond)

Conversion of Alkynes to trans-Alkenes

- Anhydrous ammonia (NH₃) is a liquid below -33 °C
  - Alkali metals dissolve in liquid ammonia and function as reducing agents
- Alkynes are reduced to trans alkenes with sodium or lithium in liquid ammonia

Mechanism of Metal Reduction

The reaction involves a radical anion intermediate
Reduction of 2-Butyne

\[
\begin{align*}
\text{cis-2-butene} & \xrightarrow{\text{H}_2, \text{Lindlar catalyst}} \text{trans-2-butene} \\
\text{cis-2-butene} & \xrightarrow{\text{Na or Li, liq. NH}_3} \text{cis-2-butene} \\
\text{cis-2-butene} & \xrightarrow{\text{H}_2, \text{Pd/C}} \text{cyclohexane}
\end{align*}
\]

Oxidative Cleavage of Alkynes

- Strong oxidizing reagents (O_3 or KMnO_4) cleave internal alkynes, producing two carboxylic acids
- Terminal alkynes are oxidized to a carboxylic acid and carbon dioxide
- Neither process is useful in modern synthesis – were used to elucidate structures because the products indicate the structure of the alkyne precursor

Example

\[
\begin{align*}
\text{CH}_3\text{CHRR}_2\text{CH_3} & \xrightarrow{\text{O}_3} \text{CH}_3\text{CHRR}_2\text{COOH} + \text{CH}_3\text{CHRR}_2\text{COOH} \\
\text{CH}_3\text{CHRR}_2\text{COOH} & \xrightarrow{\text{KOH/THF}} \text{CH}_3\text{CHRR}_2\text{COOH} \\
\text{CH}_3\text{CHRR}_2\text{COOH} & \xrightarrow{\text{H}_2, \text{Pd/C}} \text{CH}_3\text{CHRR}_2\text{CH_3}
\end{align*}
\]
A certain hydrocarbon had the molecular formula $C_{16}H_{26}$ and contained two triple bonds. Oxidation using ozone gave $CH_3(CH_2)_4CO_2H$ and $HO_2C(CH_2)_2CO_2H$ as the only products. Suggest a reasonable structure for this hydrocarbon.

$C_{16}H_{26}$

16 Carbons, Two triple bonds

$CH_3(CH_2)_4CO_2H \quad HO_2C(CH_2)_2CO_2H \quad HO_2C(CH_2)_4CH_3$

$CH_3(CH_2)_4=CC(=C(CH_2)_3)=C(=C(CH_2)_3)CH_3$

**Alkyne Acidity**

Terminal alkynes are *weak Bronsted acids* (alkenes and alkanes are much less acidic ($pK_a \approx 25$. See Table 8.1 for comparisons)

<table>
<thead>
<tr>
<th>Alkyne Acidity: Formation of Acetylide Anions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reaction of strong anhydrous bases with a terminal acetylene produces an acetylide ion</td>
</tr>
</tbody>
</table>

$R=\overset{\text{H}}{\overset{\text{C}}{\text{C}}} \quad NH_2Na^+ \quad \rightarrow \quad R=\overset{\text{H}}{\overset{\text{C}}{\text{C}}}^{\text{Na}^+} \quad \text{Acetylide anion}$
Why is an acetylide anion more stable than vinyl of alkyl anions?

The sp-hydbridization at carbon holds negative charge relatively close to the positive nucleus (see figure 8-5).

Alkylation of Acetylide Anions

- Reaction with a primary alkyl halide produces a hydrocarbon that contains carbons from both partners, providing a general route to larger alkenes

\[
\text{HCCCH}_2\text{Na} + \text{HCCCH}_2\text{Na} \rightarrow \text{HCCCH}_2\text{CH}_2\text{CCH}_3
\]

- Acetylene

\[
\text{HC} = \text{CH} + \text{Na} \rightarrow \text{HC} = \text{CCH}_2\text{Na}
\]

A terminal alkyne

CH2=CH2 + NaCl → CH2=CHNaCl

An internal alkyne

- Limitations of Alkylation of Acetylide Ions

- Reactions only are efficient with 1º alkyl bromides and alkyl iodides
- Acetylide anions can behave as bases as well as nucleophiles
- Reactions with 2º and 3º alkyl halides gives dehydrohalogenation, converting alkyl halide to alkene

Limitations of Alkylation of Acetylide Ions

- Reactions only are efficient with 1º alkyl bromides and alkyl iodides
- Acetylide anions can behave as bases as well as nucleophiles
Organic Synthesis

- Organic synthesis creates molecules by design
- Synthesis can produce new molecules that are needed as drugs or materials
- A synthesis combines a series of proposed steps to go from a defined set of reactants to a specified product
- In order to propose a synthesis you must be familiar with reactions
  - What they begin with
  - What they lead to
  - How they are accomplished
  - What the limitations are

Strategies for Synthesis

- Compare the target and the starting material
- Consider reactions that efficiently produce the outcome. Look at the product and think of what can lead to it
- Example:
  - Problem: prepare octane from 1-pentyne
  - Strategy: use acetylide coupling

Planning a Synthesis

- Starting with acetylene, any alkyl halide, any reagents, and solvents, prepare the following compound

\[
\text{H}_\text{C} = \text{C} - \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3
\]
How could you prepare \( (E)-2\)-pentene from acetylene?

\[ \text{HCH}_2\text{C} \rightarrow \text{H} \quad ? \quad \text{CH}_2\text{CH}_3 \quad \text{H} \quad \text{C}=\text{C}^\cdots \text{H} \quad \text{HCH}_2\text{CH}_3 \quad (E)-2\text{-pentene} \]

\[ \text{CH}_3\text{CH}_2\text{H} \quad \text{C} \quad \text{C} \quad \text{H} \quad \text{CH}_3 \]

\[ \begin{array}{c}
\text{CH}_3\text{CH}_2\text{H} \\
\text{C} \\
\text{C} \\
\text{H} \\
\text{CH}_3
\end{array} \quad \xrightarrow{(1) \text{NaNH}_2} \quad \begin{array}{c}
\text{CH}_3\text{CH}_2\text{C} \\
\text{C} \\
\text{C} \\
\text{H} \\
\text{CH}_3
\end{array} \quad \xrightarrow{(2) \text{CH}_3\text{Br}} \quad \begin{array}{c}
\text{CH}_3\text{CH}_2\text{H} \\
\text{C} \\
\text{C} \\
\text{H} \\
\text{CH}_3
\end{array} \]

\[ \text{CH}_3\text{CH}_2\text{H} \quad \text{C} \quad \text{C} \quad \text{H} \quad \text{CH}_3 \]

\[ \begin{array}{c}
\text{CH}_3\text{CH}_2\text{H} \\
\text{C} \\
\text{C} \\
\text{H} \\
\text{CH}_3
\end{array} \quad \xrightarrow{(1) \text{NaNH}_2} \quad \begin{array}{c}
\text{CH}_3\text{CH}_2\text{C} \\
\text{C} \\
\text{C} \\
\text{H} \\
\text{CH}_3
\end{array} \quad \xrightarrow{(2) \text{CH}_3\text{Br}} \quad \begin{array}{c}
\text{CH}_3\text{CH}_2\text{H} \\
\text{C} \\
\text{C} \\
\text{H} \\
\text{CH}_3
\end{array} \]

\[ \text{CH}_3\text{CH}_2\text{H} \quad \text{C} \quad \text{C} \quad \text{H} \quad \text{CH}_3 \]