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 \( p_x \) and \( p_y \) orbitals forming two \( \pi \) bonds

- 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

\[
\text{CH}_3\text{CH}_2\text{CHCH}_2\text{C≡CCH}_2\text{CH}_3 \\
\text{CH}_3 \\
\text{6-Methyl-3-octyne}
\]

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

\[
\begin{align*}
\text{HC≡CCH}_2\text{CHCH}_2\text{CHCH}_2\text{CH}_3 & \quad \text{HC≡CCH}_2\text{CHCHCH}_2\text{CHCH}_3 \\
\text{1-Hepten-6-yne} & \quad \text{4-Methyl-7-nonen-1-yne}
\end{align*}
\]
Examples

4-Propyl-2-heptyne

4-Bromo-2-hexyne

3-Penten-1-yne

1-Penten-4-yne

Alkyl, Alkenyl and Alkynyl groups

Butyl
(an alkyl group)

1-Butenyl
(a vinylic group)

1-Butynyl
(an alkynyl group)
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 NaNH\(_2\) is used.

\[
\begin{align*}
\text{Vicinal Dihalide} & : \quad \text{Base} \quad \text{Fast} \quad \text{Base} \\
\text{Geminal Dihalide} & : \quad \text{Base} \quad \text{Fast} \quad \text{Base}
\end{align*}
\]

Synthesis of diphenyl acetylene

\[
\begin{align*}
\text{(a vicinal dibromide)} & : \quad 2\text{KOH} \quad \text{CH}_3\text{CH}_2\text{OH} \\
\text{1,2-Dibrom-1,2-diphenylethane} & : \quad + 2\text{KBr} + 2\text{H}_2\text{O}
\end{align*}
\]
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.

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
Comparison Between Alkynes and Alkenes

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.

$$\text{H}_3\text{C}\text{CH}_2\text{C}≡\text{C}\text{CH}_2\text{CH}_3 + \text{Br}_2 \rightarrow \text{H}_3\text{C}\text{CH}_2\text{C}≡\text{C}\text{CH}_2\text{CH}_3 + \cdot\text{Br}^2$$

$$\text{H}_3\text{C}\text{CH}_2\text{C}≡\text{C}\text{CH}_2\text{CH}_3 + \cdot\text{Br}^2 \rightarrow \text{H}_3\text{C}\text{CH}_2\text{C}≡\text{C}\text{CH}_2\text{CH}_3$$

$$\text{H}_3\text{C}\text{CH}_2\text{C}≡\text{C}\text{CH}_2\text{CH}_3$$

$$\text{H}_3\text{C}\text{CH}_2\text{C}≡\text{C}\text{CH}_2\text{CH}_3$$

Mercury(II)-Catalyzed Hydration of Alkynes

- Alkynes do not react with aqueous protic 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.

$$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}≡\text{CH} \xrightarrow{\text{H}_2\text{O}, \text{HSO}_4^-} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}≡\text{C}≡\text{CH} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}≡\text{C}≡\text{CH}_3$$

An enol

2-Hexanone (35%)
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

\[\text{Enol tautomer (less favored) } \xrightarrow{\text{Rapid}} \text{Keto tautomer (more favored)}\]

---

Mechanism of Mercury(II)-Catalyzed Hydration of Alkynes

The alkynes use a pair of electrons to attack the electrophilic mercury(II) ion, yielding a mercury-hydride intermediate.

Nucleophilic attack of water on the intermediate forms a C-O bond and yields a protenol mercury-containing enol.

Abstraction of H+ from the protonated enol by water gives an organomercury compound.

Replacement of R'OH by H+ occurs to give a neutral enol.

The enol undergoes tautomerization to give the final ketene product.
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.

\[
\text{R} \text{C≡C} \text{R}^' \xrightarrow{\text{H}_2\text{O}, \text{HgSO}_4} \text{R}^' \text{CHO} + \text{R} \text{CH}_2 \text{C}=\text{O}
\]

Hydroboration/Oxidation of Alkynes

- BH\(_3\) (borane) adds to alkynes to give a vinylic borane.

- Oxidation with H\(_2\)O\(_2\) 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 BH$_3$, now a hindered borane must be used
- This prevents a second hydroboration from occurring

\[ \text{Sia} = \text{Di(sec-isoamy1)borane} \]

Mechanism of Hydroboration
Comparison of Hg(II)catalyzed Hydration with Hydroboration/Oxidation

- 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

![Chemical reactions diagram showing hydration and hydroboration/oxidation processes.]

Reduction of Alkynes

- Addition of H₂ over a metal catalyst (such as palladium on carbon, Pd/C) converts alkynes to alkanes (complete reduction)
- The addition of the first equivalent of H₂ produces an alkene, which is more reactive than the alkyne so the alkene is not observed

![Chemical reactions diagram showing reduction processes.]

\[
\begin{align*}
\text{Hydration:} & \quad \text{H}_2 + \text{H}_2\text{O} \rightarrow 2\text{H}_2\text{O} \\
\text{Hydroboration:} & \quad \text{R} - \text{C} = \text{CH} + \text{BH}_3 \rightarrow \text{R} - \text{C} - \text{CH}_2 \text{CH}_3 \\
\text{Reduction:} & \quad \text{HC} = \text{CH} + \text{H}_2 \rightarrow \text{CH}_2 = \text{CH}_2 \\
\end{align*}
\]
Conversion of Alkynes to cis-Alkenes

- If we make the catalyst less active, the second \( \text{H}_2 \) addition might become less likely.
- The catalyst surface must be partially deactivated or poisoned.
- **Lindlar's Catalyst** is \( \text{Pd on CaCO}_3 \) poisoned with lead acetate and quinoline.
- The two hydrogens add **syn** (from the same side of the triple bond).

\[
\begin{align*}
\text{CH}_3(CH_2)_2C&=C(CH_2)_2CH_3 & \rightarrow & \text{CH}_3(CH_2)_3CH_3 \\
\text{Decane (96\%)} & & \\
\end{align*}
\]

Conversion of Alkynes to trans-Alkenes

- Anhydrous ammonia (NH\(_3\)) 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.

\[
\begin{align*}
\text{CH}_3CH_2CH_2CH_2C&=CCH_2CH_2CH_3 & \rightarrow & \text{CH}_3CH_2CH_2CH_3 \\
\text{trans-5-Decene (78\%)} & & \\
\end{align*}
\]
Mechanism of Metal Reduction

The reaction involves a **radical anion** intermediate.

\[
\begin{align*}
R-C\equiv C-R' &\rightarrow R-C\equiv C-R'\quad \text{alkyne} \\
R-C\equiv C-R' &\rightarrow R-C\equiv C-R'\quad \text{radical anion} \\
R-C\equiv C-R' &\rightarrow R-C\equiv C-R'\quad \text{vinyl radical} \\
R-C\equiv C-R' &\rightarrow R-C\equiv C-R'\quad \text{vinyl anion} \\
R-C\equiv C-R' &\rightarrow R-C\equiv C-R'\quad \text{trans alkene}
\end{align*}
\]

Reduction of 2-Butyne

\[
\begin{align*}
\text{cis-2-butyne} &\quad \text{H}_2,\text{Lindlar catalyst} \\
\text{2-Butyne} &\quad \text{Na or Li, liq. NH}_3 \\
\text{trans-2-butyne} &\quad \text{CH}_3-\text{CH} \equiv \text{CH}_2-\text{CH}_3 \\
\text{n-Butane} &\quad \text{H}_2,\text{Pd/C} \\
\text{cis-Alkene} &\quad \text{H}_2,\text{Lindlar catalyst} \\
\text{Alkyne} &\quad \text{Na or Li, liq. NH}_3 \\
\text{trans-Alkene} &\quad \text{H}_2,\text{Pd/C}
\end{align*}
\]
Oxidative Cleavage of Alkynes

- Strong oxidizing reagents (O₃ or KMnO₄) 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

\[
\text{An internal alkyne} \quad R\overset{\cdot}{\cong}\text{C}=\text{C}\overset{\cdot}{\cong}R' \xrightarrow{\text{KMnO}_4 \text{ or } \text{O}_3} \text{ROH} + \text{RCO}_2\text{H}
\]

\[
\text{A terminal alkyne} \quad R\overset{\cdot}{\cong}\text{C}=\text{C}\overset{\cdot}{\cong}H \xrightarrow{\text{KMnO}_4 \text{ or } \text{O}_3} \text{ROH} + \text{CO}_2
\]

Example

\[
\text{6-Octadeceynoic acid} \quad \text{(Turpentine acid)} \quad \xrightarrow{\text{KMnO}_4} \quad \text{Dodecanoic acid} \quad \text{(Lauric acid)} + \text{1,6-Hexanediol acid} \quad \text{(Adipic acid)}
\]
A certain hydrocarbon had the molecular formula $C_{16}H_{26}$ and contained two triple bonds. Oxidation using ozone gave $\text{CH}_3(\text{CH}_2)_4\text{CO}_2\text{H}$ and $\text{HO}_2\text{C}(\text{CH}_2)_2\text{CO}_2\text{H}$ as the only products. Suggest a reasonable structure for this hydrocarbon.

$$C_{16}H_{26}$$

16 Carbons, Two triple bonds:

\[
\begin{align*}
\text{CH}_3(\text{CH}_2)_4\text{CO}_2\text{H} & \quad \text{HO}_2\text{C}(\text{CH}_2)_2\text{CO}_2\text{H} & \quad \text{HO}_2\text{C}(\text{CH}_2)_4\text{CH}_3 \\
\text{CH}_3(\text{CH}_2)_4-C≡C-(\text{CH}_2)_2-C≡C-(\text{CH}_2)_4\text{CH}_3
\end{align*}
\]

**Alkyne Acidity**

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

<table>
<thead>
<tr>
<th>Type</th>
<th>Example</th>
<th>$K_a$</th>
<th>$pK_a$</th>
<th>Acidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkyne</td>
<td>$\text{HC}≡\text{CH}$</td>
<td>$10^{-25}$</td>
<td>25</td>
<td>Stronger acid</td>
</tr>
<tr>
<td>Alkene</td>
<td>$\text{H}_2\text{C}≡\text{CH}_3$</td>
<td>$10^{-44}$</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Alkane</td>
<td>$\text{CH}_4$</td>
<td>$10^{-60}$</td>
<td>60</td>
<td>Weaker acid</td>
</tr>
</tbody>
</table>

CH$_3$CH$_2$OH, \hspace{1cm} pKa = 16 \\
CH$_3$COOH, \hspace{1cm} pKa = 5 \\
HCl, \hspace{1cm} pKa = -7 \\
NH$_3$, \hspace{1cm} pKa = 35
Alkyne Acidity: Formation of Acetylide Anions

- Reaction of strong anhydrous bases with a terminal acetylene produces an acetylide ion

\[
\begin{align*}
R-C≡C-H + \text{NH}_2\text{Na}^+ & \rightarrow R-C≡C^-\text{Na}^+ + \text{NH}_3 \\
pK_a &= 25 & pK_a &= 35
\end{align*}
\]

Why is an acetylide anion more stable than vinylic alkyl anions?

The sp-hydbridization at carbon holds negative charge relatively close to the positive nucleus.
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 alkynes

\[
\begin{align*}
\text{H-C≡C}^\text{-Na}^+ + \text{H-C}^\text{-R} & \rightarrow \text{H-C≡C-C-H + NaBr} \\
\text{HC=CH} & \xrightarrow{\text{NaNH}_2} \text{HC=C}^\text{-Na}^+ \\
\text{RCH}_2\text{Br} & \rightarrow \text{RCH}_2\text{C≡CH}_2\text{R} \\
\text{RC=CH} & \xrightarrow{\text{NaNH}_2} \text{RC=C}^\text{-Na}^+ \\
\text{R'}\text{CH}_2\text{Br} & \rightarrow \text{RC=CCH}_2\text{R'}
\end{align*}
\]

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
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

\[ \text{CH}_2\text{CH}_2\text{CH}_3 \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \quad \text{Octane} \]

\[ \text{CH}_2\text{CH}_2\text{CH}_3 \quad \text{1-Pentyne} \]

\[ \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \quad \text{Octane} \]

\[ \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \quad \text{1-Pentyne} \]

\[ \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \quad \text{Octane} \]
Planning a Synthesis

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

```
\[
\begin{align*}
\text{HC=CH} & \quad + \quad \text{NaNH}_2 \\ & \quad \xrightarrow{\text{NH}_3 \,(l)} \\ \text{HC≡CH} & \quad \xrightarrow{\text{HgSO}_4, \text{H}_2\text{O}} \quad \text{BrCH}_2\text{CH}_2\text{CH}_2\text{CH}_3
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \quad \xrightarrow{\text{H}_2\text{SO}_4} \quad \text{HC≡CH} & \quad \xrightarrow{\text{HC=O}} \quad \text{H}_3\text{C} \\
& \quad \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 & \quad \xrightarrow{\text{HC=O}} \quad \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3
\end{align*}
\]