Chapter 9
Alkynes: An Introduction to Organic Synthesis
Hydrocarbons that contain carbon-carbon triple bonds

Acetylene, the simplest alkyne is produced industrially from methane and steam at high temperature

Our study of alkynes provides an introduction to organic synthesis, the preparation of organic molecules from simpler organic molecules
We will use alkyne chemistry to begin looking at general strategies used in organic synthesis.

H―C≡C―C≡C―C≡C―C≡C―C≡C―C≡C―C≡C―C≡C―C≡C―H

A polyyne detected in interstellar space
9.1 Naming Alkynes

- General hydrocarbon rules apply with “-yne” as a suffix indicating an alkyne.
- Numbering of chain with triple bond is set so that the smallest number possible is assigned to the first carbon of the triple bond.

**Examples:**

- **6-Methyl-3-octyne**
  - (New: 6-Methyloct-3-yne)

- **1-Hepten-6-yne**
  - (New: Hept-1-en-6-yne)

- **4-Methyl-7-non-1-yne**
  - (New: 4-Methylnon-7-en-1-yne)

- **Butyl** (an alkyl group)
  - (New: But-1-ethyl)

- **1-Butenyl** (a vinylic group)
  - (New: But-1-enyl)

- **1-Butynyl** (an alkynyl group)
  - (New: But-1-ynyl)
9.2 Preparation of Alkynes: Elimination Reactions of Dihalides

- Treatment of a 1,2-dihaloalkane with KOH or NaOH produces a two-fold elimination of HX
- Vicinal dihalides are available from addition of bromine or chlorine to an alkene
- Intermediate is a vinyl halide
Addition reactions of alkynes are similar to those of alkenes.

Intermediate alkene reacts further with excess reagent.

Regioselectivity according to Markovnikov.

\[
\begin{align*}
\text{1-Butyne} & \quad \text{CH}_3\text{CH}_2\text{C}≡\text{CH} & \quad \text{Br}_2 & \quad \text{CH}_2\text{Cl}_2 & \quad \text{CH}_3\text{CH}_2\text{C}≡\text{CH} & \quad \text{Br}_2 & \quad \text{CH}_2\text{Cl}_2 & \quad \text{CH}_3\text{CH}_2\text{C}≡\text{CH} \\
& & & & \text{CH}_3\text{CH}_2 & & \text{CH}_3\text{CH}_2 & \\
& & & & & & \text{Br} & & \text{Br} \\
& & & & & & \text{Br} & & \text{Br} \\
& & & & & & \text{H} & & \\
& & & & & & \text{Br} & & \text{Br} \\
& & & & & & \text{CH}_3\text{CH}_2 & & \text{CH} \\
& & & & & & \text{Br} & & \text{Br} \\
& & & & & & \text{Br} & & \text{Br} \\
& & & & & & \text{Br} & & \text{Br} \\
\end{align*}
\]

\(1\)-Butyne \quad (E)-1,2-Dibromo-1-butene \quad 1,1,2,2-Tetrabromobutane
Electronic Structure of Alkynes

- Carbon-carbon triple bond results from $sp$ orbital on each C forming a sigma bond and unhybridized $p_x$ and $p_y$ orbitals forming $\pi$ 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.
- Breaking a $\pi$ bond in acetylene (HCCH) requires 202 kJ/mole (in ethylene it is 269 kJ/mole)
Addition of Bromine and Chlorine

- Initial addition gives *trans* intermediate
- Product with excess reagent is tetrahalide

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{C}≡\text{CH} & \xrightarrow{\text{Br}_2/\text{CH}_2\text{Cl}_2} \quad \text{Br} & \quad \text{C}≡\text{C} & \xrightarrow{\text{Br}_2/\text{CH}_2\text{Cl}_2} \quad \text{CH}_3\text{CH}_2\text{C} – \text{CH} \\
1\text{-Butyne} & & (E)-1,2\text{-Dibromo-1-butene} & 1,1,2,2\text{-Tetrabromobutane}
\end{align*}
\]
Addition of H-X to alkynes should produce a vinylic carbocation intermediate.

- Secondary vinyl carbocations form less readily than primary alkyl carbocations.
- Primary vinyl carbocations probably do not form at all.

Nonetheless, H-Br can add to an alkyne to give a vinyl bromide if the Br does not end up on a primary carbon.
9.4 Hydration of Alkynes

- Addition of H-OH as in alkenes
  - Mercury (II) catalyzes Markovnikov oriented addition
  - Hydroboration-oxidation gives the anti-Markovnikov product

$$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}≡\text{CH} \xrightarrow{\text{H}_2\text{O}, \text{H}_2\text{SO}_4, \text{HgSO}_4} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}≡\text{CH}$$

1-Hexyne  \hspace{1cm} An enol  \hspace{1cm} 2-Hexanone (78%)
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 with Markovnikov orientation
- The immediate product is a vinylic alcohol, or *enol*, which spontaneously transforms to a ketone or to an aldehyde in the event that acetylene is employed.
Mechanism of Mercury(II)-Catalyzed Hydration of Alkynes

- Addition of Hg(II) to alkyne gives a vinylic cation
- Water adds and loses a proton
- A proton from aqueous acid replaces Hg(II)
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 so stable compared to the enol that only the keto form can be observed.

![Keto-enol Tautomerism](image-url)

Enol tautomer (less favored)  
Keto tautomer (more favored)
- 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 alkyne always gives the methyl ketone, which is useful.

**An internal alkyne**

\[
R\text{–C≡C–R}' \quad \xrightarrow{\text{H}_3\text{O}^+ / \text{HgSO}_4} \quad R\text{C(}\text{CH}_2\text{R}') + R\text{CH}_2\text{C(}\text{R}')
\]

**Mixture**

- **A terminal alkyne**

\[
R\text{–C≡C–H} \quad \xrightarrow{\text{H}_3\text{O}^+ / \text{HgSO}_4} \quad R\text{C(}\text{CH}_3)
\]

**A 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

An internal alkyne

\[
3 \text{CH}_3\text{CH}_2\text{C}≡\text{CCH}_2\text{CH}_3 \xrightarrow{\text{BH}_3/\text{THF}} \text{A vinylic borane} \xrightarrow{\text{H}_2\text{O}_2/\text{H}_2\text{O}, \text{NaOH}} \text{An enol} \xrightarrow{} 3 \text{CH}_3\text{CH}_2\text{CH}_2\text{CCH}_2\text{CH}_3
\]

3-Hexanone
Hydroboration/oxidation converts terminal alkynes to aldehydes because addition of water is anti-Markovnikov.

The product from the mercury(II) catalyzed hydration converts terminal alkynes to methyl ketones.
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

\[
\begin{align*}
\text{HC}≡\text{CH} &\xrightarrow{\text{H}_2/\text{Catalyst}} \text{H}_2\text{C}≡\text{CH}_2 & \Delta H^\circ_{\text{hydrog}} &= -176 \text{ kJ/mol} \ (-42 \text{ kcal/mol}) \\
\text{H}_2\text{C}≡\text{CH}_2 &\xrightarrow{\text{H}_2/\text{Catalyst}} \text{CH}_3−\text{CH}_3 & \Delta H^\circ_{\text{hydrog}} &= -137 \text{ kJ/mol} \ (-33 \text{ kcal/mol})
\end{align*}
\]
Conversion of Alkynes to cis-Alkenes

- Addition of $H_2$ using chemically deactivated palladium on calcium carbonate as a catalyst (the *Lindlar catalyst*) produces a *cis* alkene
- The two hydrogens add *syn* (from the same side of the triple bond)

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{C}≡\text{CCH}_2\text{CH}_2\text{CH}_3 & \xrightarrow{\text{H}_2, \text{Lindlar catalyst}} \xrightarrow[\text{H}_2, \text{Pd/C catalyst}]{\text{cis}} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \\
\text{4-Octyne} & \longrightarrow \text{Octane} \\
\end{align*}
\]
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
- The reaction involves a *radical anion* intermediate

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}≡\text{CCH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \xrightarrow{\text{Li, NH}_3} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}≡\text{CCH}_2\text{CH}_2\text{CH}_2\text{CH}_3
\]

5-Decyne  \hspace{2cm} \textit{trans}-5-Decene (78%)
Mechanism of Li/NH$_3$ Reduction of an Alkyne

1. Lithium metal donates an electron to the alkyne to give an anion radical . . .

   \[ R-\overset{\cdot}{C}=\overset{\cdot}{C}-R' \]

   \[ \overset{1}{\text{Li}} \]

2. . . which abstracts a proton from ammonia solvent to yield a vinylic radical.

   \[ R\overset{\cdot}{C}=\overset{\cdot}{C}-R' + \overset{2}{\text{H-NH}_2} \]

3. The vinylic radical accepts another electron from a second lithium atom to produce a vinylic anion . . .

   \[ R\overset{\cdot}{C}=\overset{\cdot}{C}-H + \overset{3}{\text{NH}_2^-} \]

4. . . which abstracts another proton from ammonia solvent to yield the final trans alkene product.

   \[ R\overset{\cdot}{C}=\overset{\cdot}{C}-H + \overset{4}{\text{H-NH}_2} \]

   A trans alkene
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.

An internal alkyne

$\text{R-C≡C-R'} \xrightarrow{KMnO_4 \text{ or } O_3} \text{R-COOH} + \text{HO-CR'}$

A terminal alkyne

$\text{R-C≡C-H} \xrightarrow{KMnO_4 \text{ or } O_3} \text{R-COOH} + \text{O=C=O}$
9.7 Alkyne Acidity: Formation of Acetylide Anions

- Terminal alkynes are weak Brønsted acids (alkenes and alkanes are much less acidic ($pK_a \sim 25$. See Table 9.1 for comparisons))
- Reaction of strong anhydrous bases with a terminal alkyne produces an **acetylide ion**
- The $sp$-hybridization at carbon holds negative charge relatively close to the positive nucleus (Figure 9.5 in text)

\[
\begin{align*}
R\text{C}=\text{C}=-\text{H} & \quad \xrightarrow{\text{NH}_2\text{Na}^+} \quad R\text{C}=\text{C}^-\text{Na}^+ \quad + \quad \cdot\text{NH}_3 \\
\text{A terminal alkyne} & \quad \text{An acetylide anion}
\end{align*}
\]
9.8 Alkylation of Acetylide Anions

- Acetylide ions can react as nucleophiles as well as bases (see Figure 9-6 for mechanism)
- Reaction with a primary alkyl halide produces a hydrocarbon that contains carbons from both partners, providing a general route to larger alkynes

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}≡\text{CH} & \xrightarrow{1. \text{NaNH}_2, \text{NH}_3} \xrightarrow{2. \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br}} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}≡\text{CCH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \\
\text{1-Hexyne} & \quad \text{5-Decyne (76%)} \\
\text{H}–\text{C}≡\text{C}–\text{H} & \xrightarrow{\text{NaNH}_2} \left[\text{H}–\text{C}≡\text{C}^- \quad \text{Na}^+\right] \xrightarrow{\text{RCH}_2\text{Br}} \text{H}–\text{C}≡\text{C}–\text{CH}_2\text{R} \\
\text{Acetylene} & \quad \text{A terminal alkyne} \\
\text{R}–\text{C}≡\text{C}–\text{H} & \xrightarrow{\text{NaNH}_2} \left[\text{R}–\text{C}≡\text{C}^- \quad \text{Na}^+\right] \xrightarrow{\text{R’CH}_2\text{Br}} \text{R}–\text{C}≡\text{C}–\text{CH}_2\text{R’} \\
\text{A terminal alkyne} & \quad \text{An internal alkyne}
\end{align*}
\]
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
9.9 An Introduction to Organic Synthesis

- Organic synthesis creates molecules by design
- Synthesis can produce new molecules that are needed as drugs or materials
- Syntheses can be designed and tested to improve efficiency and safety for making known molecules
- Highly advanced synthesis is used to test ideas and methods, answering challenges
- Chemists who engage in synthesis may see some work as *elegant* or *beautiful* when it uses novel ideas or combinations of steps – this is very subjective and not part of an introductory course
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

A synthesis combines a series of proposed steps to go from a defined set of reactants to a specified product:
- Questions related to synthesis can include partial information about a reaction of series that the student completes
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
- Read the practice problems in the text
Let’s Work a Problem

Prepare \( n \)-octane from 1-pentyne.

The best strategy to approach this problem is to use acetylide coupling:

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{C}≡\text{CH} \quad \xrightarrow{1. \text{NaNH}_2, \text{NH}_3, \text{2. BrCH}_2\text{CH}_2\text{CH}_3, \text{THF}} \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{C}≡\text{CCH}_2\text{CH}_2\text{CH}_3
\]

4-Octyne

\[
\xrightarrow{\text{H}_2/\text{Pd in ethanol}} \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{C}—\text{CCH}_2\text{CH}_2\text{CH}_3
\]

Octane