Organic Chemistry

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Chapter 10

Alkynes
IUPAC: use the infix \(-\textit{yn}\)- to show the presence of a carbon-carbon triple bond

3-Methyl-1-butyne

6,6-Dimethyl-3-heptyne
Nomenclature

Common names: prefix the substituents on the triple bond to the name “acetylene”

<table>
<thead>
<tr>
<th>IUPAC</th>
<th>Common</th>
<th>CH₃ C≡CH</th>
<th>CH₃ C≡CCH₃</th>
<th>CH₂ =CHC ≡ CH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propyne</td>
<td>Methylacetylene</td>
<td>2-Butyne</td>
<td>Dimethylacetylene</td>
<td>1-Buten-3-yne</td>
</tr>
<tr>
<td>Common:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The smallest cycloalkyne isolated is cyclononyne. In it, the C-C-C bond angle about the triple bond is approximately 156°.
Quite similar to alkanes and alkenes of comparable molecular weight and carbon skeleton
A major difference between the chemistry of alkynes and that of alkenes and alkanes is the acidity of the hydrogen bonded to a triply bonded carbon (Section 3.3C).

The $pK_a$ of acetylene is approximately 25, which makes it a stronger acid than ammonia.
## 10 Acidity

<table>
<thead>
<tr>
<th>Weak Acid</th>
<th>Example</th>
<th>Conjugate Base</th>
<th>$pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>water</td>
<td>$\text{H}^+\text{O}\cdot\text{H}$</td>
<td>$\text{HO}^-$</td>
<td>15.7</td>
</tr>
<tr>
<td>alkyne</td>
<td>$\text{HC}\equiv\text{C}\cdot\text{H}$</td>
<td>$\text{HC}\equiv\text{C}\cdot$</td>
<td>25</td>
</tr>
<tr>
<td>ammonia</td>
<td>$\text{H}_2\text{N}\cdot\text{H}$</td>
<td>$\text{H}_2\text{N}\cdot$</td>
<td>38</td>
</tr>
<tr>
<td>alkene</td>
<td>$\text{CH}_2=\text{CH}\cdot\text{H}$</td>
<td>$\text{CH}_2=\text{CH}\cdot$</td>
<td>44</td>
</tr>
<tr>
<td>alkane</td>
<td>$\text{CH}_3\text{CH}_2\cdot\text{H}$</td>
<td>$\text{CH}_3\text{CH}_2\cdot$</td>
<td>51</td>
</tr>
</tbody>
</table>
Acetylene reacts with sodium amide to form sodium acetylide.

\[
\begin{align*}
\text{HC} & \equiv \text{CH} + \cdot \text{NH}_2 \quad \xleftarrow{\text{K}_{\text{eq}} = 10^{13}} \quad \text{HC} & \equiv \text{C}^{\ddagger} - + \cdot \text{NH}_3 \\
pK_a & = 25 \quad \text{Stronger} & \quad \text{Stronger} & \quad \text{Weaker} & \quad \text{Weaker}
\end{align*}
\]

- It can also be converted to its metal salt by reaction with sodium hydride or lithium diisopropylamide (LDA).
Water is a stronger acid than acetylene; hydroxide ion is not a strong enough base to convert acetylene to its anion.

\[ \text{HC≡CH} + \text{OH}^- \rightleftharpoons \text{HC≡C}^- + \text{H}_2\text{O} \]

\[ K_{eq} = 10^{-9.3} \]

\( pK_a \ 25 \) weaker acid
\( pK_a \ 15.7 \) stronger acid

Weaker base
Stronger base
Alkylation of Acetylide

- Acetylide anions are both strong bases and good nucleophiles.

- They undergo $S_N$2 reactions with alkyl halides, tosylates, and mesylates to form new C-C bonds to alkyl groups; they undergo alkylation.

Alkylation: any reaction in which a new carbon-carbon bond to an alkyl group is formed.
Alkylation of acetylide anions is the most convenient method for the synthesis of terminal alkynes.

\[
\text{HC≡C}^- \text{Na}^+ + \text{CH}_3(\text{CH}_2)_2\text{CH}_2^-\text{Br} \xrightarrow{\text{SN2}} \text{HC≡CCH}_2(\text{CH}_2)_2\text{CH}_3 + \text{Na}^+\text{Br}^-
\]

- Sodium acetylide
- 1-Bromobutane
- 1-Hexyne
Alkylation of Acetylides

Alkylation can be repeated and a terminal alkyne can be converted to an internal alkyne.

\[
\text{CH}_3\text{CH}_2\text{C}≡\text{C}:\text{Na}^+ + \text{CH}_3\text{CH}_2\text{-Br} \xrightarrow{\text{SN}_2} \text{Na}^+\text{Br}^- \]

\[
\text{Sodium butynide} \quad \text{Bromoethane}
\]

\[
\text{CH}_3\text{CH}_2\text{C}≡\text{CCH}_2\text{CH}_3 + \text{Na}^+\text{Br}^- \quad \text{3-Hexyne}
\]
Because acetylide anions are also strong bases, alkylation is practical only with methyl and 1° halides. With 2° and 3° halides, E2 is the major reaction.
Alkylation of Acetylidnes

\[ \text{HC≡C}^- \text{Na}^+ + \text{Br}^- \xrightarrow{E2} \text{H} \quad \text{HC≡CH} + \text{Na}^+ \text{Br}^- \]

Sodium acetylide  Bromocyclohexane

Acetylene  Cyclohexene
Preparation

- Treatment of a vicinal dibromoalkane (from an alkene + bromine) with 2 mol of base, most commonly sodium amide, results in two successive E2 reactions and formation of an alkyne
A vicinal dibromide + 2 NaNH$_2$ $\xrightarrow{\text{-33$^\circ$C}}$ R-C=C-R + 2 NaBr + 2 NH$_3$

An alkyne
A side product may be an allene, a compound containing adjacent carbon-carbon double bonds, C=C=C.

A haloalkene (a vinylic halide)

\[
\text{RC-C=CR} \quad \xrightarrow{\text{NaNH}_2 \quad \text{-HBr}} \quad \text{C=C= C}
\]

An allene
Most allenes are less stable than their isomeric alkynes, and are generally only minor products in alkyne-forming dehydrohalogenation reactions.

\[ \text{CH}_2\equiv\text{C}=-\text{CH}_2 \rightarrow \text{CH}_3\equiv\text{C}=-\text{CH} \quad \Delta H^\circ = -1.6 \text{ kcal/mol} \]

\[ \text{CH}_2\equiv\text{C}=-\text{CHCH}_3 \rightarrow \text{CH}_3\equiv\text{C}=-\text{CCH}_3 \quad \Delta H^\circ = -4.0 \text{ kcal/mol} \]
Reduction

Treatment of an alkyne with hydrogen in the presence of a transition metal catalyst, most commonly Pd, Pt, or Ni, converts the alkyne to an alkane.

\[
\text{CH}_3\text{C}≡\text{CCH}_3 + 2\text{H}_2 \xrightarrow{\text{Pd, Pt, or Ni}} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3
\]

2-Butyne (3 atm) Butane
With the Lindlar catalyst, reduction stops at addition of 1 mol of H₂. This reduction shows syn stereoselectivity.

\[
\text{CH}_3\text{C}≡\text{CCH}_3 + \text{H}_2 \xrightarrow{\text{Lindlar catalyst}} \text{cis-2-Butene}
\]
Reduction of an alkyne with Na or Li in liquid ammonia converts an alkyne to an alkene with anti stereoselectivity.

\[ \text{RC≡CR'} + 2 \text{Na} + 2 \text{NH}_3 \xrightarrow{\text{NH}_3 (l)} \text{C}≡\text{C} + 2 \text{NaNH}_2 \]

An alkyne

A trans alkene
Step 1: a one-electron reduction of the alkyne to a radical anion

\[ \text{R-C}\equiv\text{C-R} + \cdot\text{Na} \rightarrow \text{R-}\dot{\text{C}}\equiv\dot{\text{C}}\text{-R} + \text{Na}^+ \]

An alkenyl radical anion
Step 2: an acid-base reaction to form an alkenyl radical and amide ion

\[ R-C\equiv\ddot{C}-R + H\cdot NH_2 \rightarrow \ddot{C}=C-R + NH_2^- \]

An alkenyl radical
Step 3: a second one-electron reduction to form an alkenyl anion. It is at this step that the configuration of the alkene is determined; a trans alkenyl radical is more stable than its cis isomer.

\[
\text{Na} \quad + \quad \text{C} \equiv \text{C} \quad \text{R} \quad \text{H} \quad \xrightarrow{\text{Na}^+} \quad \text{R} \quad \text{C} \equiv \text{C} \quad \text{H} \quad + \quad \text{Na}^+ \quad + \quad \text{C} \equiv \text{C} \quad \text{R} \quad \text{H}
\]

An alkenyl anion
Step 4: a second acid-base reaction to give the trans alkene

\[
\text{H}_2\text{NNH} + \text{R}C\equiv\text{C}R \rightarrow \text{NH}_2^- + \text{R}C\equiv\text{C}R
\]

A trans alkene
Hydroboration

Borane adds to internal alkynes to give a trialkenylborane

\[ 3 \text{CH}_3 \text{CH}_2 \text{C}≡\text{CCH}_2 \text{CH}_3 \xrightarrow{\text{BH}_3/\text{THF}} \]

A trialkenylborane
(R = cis-3-hexenyl group)
Hydroboration

Treatment of a trialkenylborane with acetic acid results in stereoselective replacement of B by H.

A trialkenylborane

\[
\text{cis-3-Hexene}
\]
To prevent dihydroboration with terminal alkynes, it is necessary to use a sterically hindered dialkylborane

\[
\text{di-sec-isoamylborane} \quad [(\text{sia})_2\text{BH}]
\]
Hydroboration

Treatment of a terminal alkyne with \((\text{sia})_2\text{BH}\) results and regioselective hydroboration

\[
\text{CH}_3(\text{CH}_2)_5\text{C≡CH} \xrightarrow{\text{\(\text{(sia)}_2\text{BH}\)}} \text{CH}_3(\text{CH}_2)_5\text{C≡C-CH} \text{B(sia)}_2
\]

1-Octyne

An alkenylborane
Hydroboration

Treatment of an alkenylborane with $\text{H}_2\text{O}_2$ in aqueous $\text{NaOH}$ gives a product which corresponds to hydration of the alkyne; addition of H to one carbon and -OH to the other. The product is called an enol.

$$\text{CH}_3\text{C}≡\text{CCH}_3 \xrightarrow{1. \text{BH}_3} \text{CH}_3\text{CH}=\text{CCH}_3 \xrightarrow{2. \text{H}_2\text{O}_2, \text{NaOH}} \text{CH}_3\text{CH}=\text{CCH}_3 \text{OH}$$

2-Butyne
2-Buten-2-ol (an enol)
Enol: a compound containing an OH group on one carbon of a C=C

The enol is in equilibrium with a compound formed by migration of a hydrogen atom from oxygen to carbon and the double bond from C=C to C=O

The enol and keto forms are tautomers and their interconversion is called tautomerism
The keto form generally predominates at equilibrium.

\[
\begin{align*}
\text{CH}_3 \text{CH}=\text{CCH}_3 & \quad \text{CH}_3 \text{CH-}\text{CCH}_3 \\
\text{2-Buten-2-ol (an enol)} & \quad \text{2-Butanone (a ketone)}
\end{align*}
\]

\[K_{eq} = 6.7 \times 10^6\]

We discuss keto-enol tautomerism in detail in Section 15.11
Hydroboration

Hydroboration/oxidation of an internal alkyne gives a ketone

\[
\text{CH}_3\text{CH}_2\text{C}≡\text{CCH}_2\text{CH}_3 \xrightarrow{1. \ BH_3} \xrightarrow{2. \ H_2O_2, \ NaOH} \text{CH}_3\text{CH}_2\text{CHCH}_2\text{CH}_2\text{CH}_3
\]

3-Hexyne → 3-Hexanone
Hydroboration/oxidation of a terminal alkyne gives an aldehyde.

$$\text{CH}_3(\text{CH}_2)_5\text{C}≡\text{CH} \xrightarrow{1. \text{(sia) } 2\text{BH}} \text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{CH}$$

1-Octyne

Octanal
Addition of $X_2$

Alkynes add one mol of bromine to give a dibromoalkane, predominantly with anti stereoselectivity.

$$\text{CH}_3\text{C}≡\text{CCH}_3 + \text{Br}_2 \xrightarrow{\text{CH}_3\text{CO}_2\text{H}, \text{LiBr}} \text{(E)-2,3-Dibromo-2-butene}$$
Addition of $X_2$

- The intermediate in bromination is a bridged bromonium ion.

![Chemical structures showing the addition of $X_2$ and the formation of a bridged bromonium ion intermediate.]

A bridged bromonium ion intermediate.
10 Addition of HX

Alkynes undergo regioselective addition of first one mol of HX and then a second mol to give a dibromoalkane.

\[
\begin{align*}
\text{CH}_3\text{C}≡\text{CH} & \overset{\text{HBr}}{\longrightarrow} \text{CH}_3\text{C}≡\text{CH}_2 & \overset{\text{HBr}}{\longrightarrow} \text{CH}_3\text{C}≡\text{CCH}_3 \\
\text{Propyne} & \quad \text{2-Bromo-propene} & \quad \text{2,2-Dibromo-propane}
\end{align*}
\]
Addition of HX

The intermediate in addition of HX is a 2° vinylic carbocation:

\[ \text{CH}_3\text{C}≡\text{CH} \rightarrow \text{CH}_3\text{C}=\text{CH}_2 \rightarrow \text{CH}_3\text{C}=\text{CH}_2 \]

A 2° vinylic carbocation

Addition of the 2nd mol of HX forms of a resonance-stabilized cation intermediate.
10 Addition of HX

CH₃C=CH₂ → CH₃C—CH₂

A resonance-stabilized cation intermediate
In the presence of sulfuric acid and Hg(II) salts, alkynes undergo addition of water.

\[ \text{CH}_3\text{C}≡\text{CH} + \text{H}_2\text{O} \xrightleftharpoons[\text{HgSO}_4]{\text{H}_2\text{SO}_4} \text{CH}_3\text{C}=\text{CH}_2 \ (\text{1-Propen-2-ol, an enol}) \rightarrow \text{CH}_3\text{CCH}_3 \ (\text{Propanone, Acetone}) \]
Step 1: attack of Hg$^{2+}$ on the triple bond to give a mercurinium ion intermediate, which contains a three-center, two-electron bond.
Step 2: attack of water on the bridged mercurinium ion intermediate from the side opposite the bridge.
10 Addition of $\text{H}_2\text{O}$: hydration

Step 3: proton transfer to solvent
Addition of $\text{H}_2\text{O}$: hydration

Step 4: cleavage of the C-Hg bond by water followed by keto-enol tautomerism
A successful synthesis must

- provide the desired product in maximum yield
- with the maximum control of stereochemistry
- and minimum damage to the environment (it must be a “green” synthesis)

Our strategy will be to work backwards from the target molecule
We analyze a target molecule in the following ways

- the carbon skeleton - how can we put it together. Our only methods to date for forming new C-C bonds are cross-coupling of Gilman reagents (Section 7.7C) and alkylation of acetylide anions (Section 10.5)
- the functional groups - what are they, how can they be used in forming the carbon-skeleton of the target molecule, and how can they be changed to give the functional groups of the target molecule
We use a method called a retrosynthesis and use an open arrow to symbolize a step in a retrosynthesis.

Retrosynthesis: a process of reasoning backwards from a target molecule to a set of suitable starting materials.
Target molecule: cis-3-hexene

\[ \text{cis-3-Hexene} \rightarrow \text{3-Hexyne} \]

\[ \text{Acetylide dianion} + \text{Bromoethane} \]
Starting materials are acetylene and bromoethane

\[
\begin{align*}
\text{HC}≡\text{CH} & \xrightarrow{1. \text{NaNH}_2} \text{CH}_3 \text{CH}_2 -\text{C}≡\text{CH} \\
\text{CH}_3 \text{CH}_2 -\text{C}≡\text{C}-\text{CH}_2 \text{CH}_3 & \xrightarrow{3. \text{NaNH}_2} \text{cis-3-Hexene} \\
\end{align*}
\]
Organic Synthesis

Target molecule: 2-heptanone

\[
\text{CH}_3\text{CCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \xrightarrow{\text{FGI}} \text{HC} \equiv \text{C} \equiv \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3
\]

2-Heptanone \quad \text{1-Heptyne}

\[
\xrightarrow{\text{FGI}} \text{HC} \equiv \text{C} : \equiv \text{CH}_3 + \text{CH}_3(\text{CH}_2)_3\text{CH}_2\text{Br}
\]

Acetylide anion \quad \text{1-Bromopentane}
Starting materials are acetylene and 1-bromopentane

1. NaNH₂

2. CH₃(CH₂)₃CH₂Br

3. H₂O

H₂SO₄, HgSO₄

1-Heptyne

2-Heptanone
Alkynes

End Chapter 10