1. NOMENCLATURE - Refer to section 9-2 of the textbook for IUPAC and common names, and to the chart of functional group order of precedence on page 2 of this manuscript.

2. ACID-BASE REACTIONS OF TERMINAL ALKYNES - Refer to section 9-6 of the textbook, including 9-6A and 9-6B.

![Acetylide ion reaction](image)

The acetylide ion can be used as a strong base or nucleophile.

3. USING ACETYLIDE IONS AS CARBON NUCLEOPHILES - Carbon nucleophiles are used for carbon chain expansion by creating new carbon-carbon bonds. In this chapter they are used in Sn2 reactions to make internal alkynes, and in reactions with carbonyl compounds to make alcohols.

   (a) SYNTHESIS OF INTERNAL ALKYNES BY Sn2 REACTIONS (Sect. 9-6A).

![Internal alkyne synthesis](image)

   (b) SYNTHESIS OF ALCOHOLS BY NUCLEOPHILIC ADDITION TO CARBONYL COMPOUNDS (Sect. 9-7B).

![Alcohol synthesis](image)

4. ADDITION OF ELECTROPHILES TO THE CARBON-CARBON TRIPLE BOND - Similar to addition of electrophiles to the carbon-carbon double bond, with some differences (Sect. 9-9A to 9-9F).

5. OXIDATION REACTIONS OF THE CARBON-CARBON TRIPLE BOND - Similar to oxidation reactions of the carbon-carbon double bond, with some differences (Sect. 9-10).
In the IUPAC nomenclature system, organic molecules are grouped into specific classes of compounds determined by the main functional group present in the structure. A system of priorities is used to determine the main functional group, which determines the identity of the compound. All other functional groups are treated as substituents. The following order of precedence refers to functional groups containing carbon as the central atom. As a rule of thumb, the higher the oxidation state of the central carbon, the higher the priority of the functional group. Thus, carboxylic acids have higher priority than alcohols, and so on (See also table 21-1 in your textbook).

1. CARBOXYLIC ACIDS (highest priority among carbon-containing functional groups).

2. CARBOXYLIC ACID DERIVATIVES
   - Anhydrides
   - Esters
   - Acid halides
   - Amides
   - Nitriles

3. OTHER GROUPS CONTAINING OXYGEN OR NITROGEN
   - Aldehydes
   - Ketones
   - Alcohols
   - Amines

4. ALKENES AND ALKYNES
   - Alkenes
   - Alkynes

   Note: substances containing double and triple bonds are called alkenynes. (notice that the name ends in yne). Chain numbering starts from the end closest to either group, unless they’re both equidistant from the chain ends, in which case the double bond takes priority and is given the lower number. See examples in the textbook.

5. LOWEST PRIORITY. These groups are usually considered substituents in the main chain.
   - Alkyl groups
   - Alkoxy groups
   - Halides
USE OF CARBON NUCLEOPHILES IN ORGANIC SYNTHESIS

Carbon nucleophiles are widely used in organic synthesis to create new carbon-carbon bonds when they react with electrophiles, and therefore expand a carbon chain. To be nucleophilic, the carbon atom must be bonded to a less electronegative atom to create a dipole favoring higher electron density on carbon. In most cases this atom is a metal, typically an alkali (group I) or alkaline earth (group II) metal. The difference in electronegativity between the carbon and the metal dictates the degree of nucleophilicity (or basicity) of the carbon atom. Some of the most commonly used metals are Li, Na, K, and Mg. Such species that contain a carbon-metal bond are known as organometallic reagents, or just organometallics, in organic chemistry. Examples are:

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2^-\text{Li} & \quad \text{CH}_3\text{CH}_2\text{CH}_3\text{CH}_2^-\text{Li} \\
\text{R}^-\text{C} \equiv \text{C} \quad \text{Na}^- & \quad \text{R}^-\text{C} \equiv \text{C}^-\text{Na} \\
\text{δ}^- & \quad \text{δ}^+ \\
\text{δ}^- & \quad \text{δ}^+ \\
\text{MgBr}^- & \quad \text{MgBr}^+
\end{align*}
\]

Organolithium reagents
Sodium acetylides
Organomagnesium halides (Grignard reagents)

Two important types of organometallics used as carbon nucleophiles are the acetylides (ch. 9) and the Grignard reagents (ch. 10). More specifically, we focus on the reactions between these substances and carbonyl compounds (aldehydes and ketones) to produce primary, secondary, and tertiary alcohols. Before we proceed, we must revisit the characteristics of electrophiles, since it is a reaction between a nucleophile and an electrophile that we are considering now.

CLASSIFICATION OF ELECTROPHILES BY THEIR CARBON HYBRIDIZATION

There are two major types of carbon electrophiles, those containing \( sp^3 \) carbon and those containing \( sp^2 \) carbon. We now look at the characteristics of each.

1. ELECTROPHILES CONTAINING \( sp^3 \) CARBON

To be of use in synthesis, the electrophilic center of substrates containing \( sp^3 \) carbon must be sterically accessible and contain a good leaving group. This is the type encountered in ch. 6 in Sn2 reactions. Examples are many primary and secondary halides. The outcome of the reaction between a nucleophile and this type of electrophile is a substitution product.
If the nucleophile used is a carbon nucleophile, the product has an expanded carbon chain because a new carbon-carbon bond has been created. For example, the acetylide ion is used as a carbon nucleophile to make internal alkynes from terminal alkynes. The complete sequence is shown below. This type of reaction is discussed in sections 9-6 and 9-7A of the textbook.

2. ELECTROPHILES CONTAINING \( sp^2 \) CARBON

To be of use in organic synthesis, electrophiles containing \( sp^2 \) carbon must contain a polarized \( C=X \) bond, where \( X \) can be O, N, or S. In this discussion we consider only carbonyl compounds, where \( X=O \). The polarization of the \( C=O \) bond leaves the carbon with low electron density. At the same time it enables the displacement of the \( \pi \)-electrons towards the oxygen to make room for the new carbon-carbon bond that forms when the nucleophile attacks. Examples of electrophiles containing \( sp^2 \) carbon are most aldehydes and ketones.
The outcome of the nucleophilic attack is an addition product. The $sp^2$ carbon changes hybridization to $sp^3$ (tetrahedral), and $\pi$-electrons are displaced towards the oxygen atom, resulting in formation of an alkoxide ion, which is the conjugate base of the alcohol. The last step in the sequence then calls for treatment of the alkoxide ion with water or dilute acid to convert it into the alcohol. As long as the alcohol is desired, this last protonation step is taken for granted and sometimes left out in reaction sequences shown in textbooks. This doesn’t mean that the step was actually omitted, but simply that the author assumes awareness on the reader’s part of such obvious step.

Abbreviated synthetic sequence, as shown in most textbooks
An interesting trend can be observed in regards to the type of alcohol obtained as a product. Carbon nucleophiles, when reacted with formaldehyde (as in the first example), yield primary alcohols. When reacted with any other aldehyde (acetaldehyde in the second example) they yield secondary alcohols. Finally, when reacted with ketones (acetone in the third example), they yield tertiary alcohols.

\[
\text{CARBON NUCLEOPHILE} + \text{FORMALDEHYDE} \rightarrow \text{PRIMARY ALCOHOL}
\]

\[
\text{CARBON NUCLEOPHILE} + \text{OTHER ALDEHYDES} \rightarrow \text{SECONDARY ALCOHOL}
\]

\[
\text{CARBON NUCLEOPHILE} + \text{KETONE} \rightarrow \text{TERTIARY ALCOHOL}
\]

Refer to pages 379 - 382 of the Wade textbook (5th ed.) for additional examples using alkynide ions as carbon nucleophiles, and to pages 422 - 429 for examples using Grignard reagents as carbon nucleophiles (including the summary on p. 429). Mention should be made that Grignard chemistry is an important topic that gets heavily emphasized in organic chemistry II.

**STRATEGY FOR ALCOHOL SYNTHESIS (RETROSYNTHETIC ANALYSIS)**

From the pattern outlined above, one can devise a synthesis for a primary, secondary, or tertiary alcohol by reversing the steps shown in the examples in the previous page. In other words, knowing the structure of the target molecule, one can reason backwards and arrive at the starting materials needed for the synthesis. This approach is called retrosynthetic analysis, and it is also highly emphasized in organic chemistry courses. An example will serve to illustrate this point.

**PROBLEM**: How can the following alcohol be synthesized from simpler starting materials?

![Alcohol structure](image)

**SOLUTION**: First, note that the alcohol is tertiary. Tertiary alcohols can be synthesized from carbon nucleophiles and ketones. Second, it is also an internal alkyne. This suggests that an alkynide ion can be used as the nucleophile that reacts with the ketone.

To arrive at the starting materials, first identify the carbon bearing the hydroxyl group. This is the electrophilic carbon in the ketone. Next, identify the sp-hybridized carbon bonded to the hydroxyl-bearing carbon. This is the nucleophilic carbon in the alkynide ion. This leads directly to the fragments that represent the starting materials.
The complete synthesis starting from a terminal alkyne could be written thus:

See problem 10-2 (p. 437 in your textbook) for a similar example using Grignard reagents as the carbon nucleophiles.
KETO-ENOL TAUTOMERISM

An organic structure that consists of a hydroxyl group (OH) attached to a carbon which is also part of a double bond is called an enol. This is because it consists of an alkene and an alcohol at the same time. Such arrangement is susceptible to a rearrangement called tautomerization.

Tautomerization is a shift of the hydroxyl hydrogen to carbon 2 of the alkene, and vice versa. This means that it is an equilibrium process which is either acid or base catalyzed. In the acid-catalyzed tautomerization, the alkene acts as a base and a proton from the acid is added to the $\pi$-bond with formation of the most stable carbocation.

EXAMPLE: Acid-catalyzed tautomerization

The second resonance structure shows what is essentially a protonated ketone. The positive charge on oxygen makes the proton highly acidic. It is readily lost to a base (water for example) to yield the free ketone.
The net equilibrium can be represented as in the example below. In the absence of special stabilizing factors, equilibrium usually favors the “*keto*” form (so called, even though it could be an aldehyde) over the enol form.

The tautomerization process can also be base-catalyzed. In this case the base takes up the acidic proton from the hydroxyl group, leading to formation of an *enolate ion*, which becomes reprotonated at the carbon atom.

**EXAMPLE: Base-catalyzed tautomerization**

The second resonance structure shows what is essentially a ketone. The highly basic negatively charged carbon captures a proton to form the free ketone.
The following examples show how an enol whose hydroxyl group is at the end of a carbon chain tautomerizes into an aldehyde, whereas an enol whose hydroxyl group is in the middle of a carbon chain tautomerizes into a ketone. In both cases the “keto form” is favored by equilibrium.

![Diagram of tautomerization](image)

Of course, when the hydroxyl group is attached to a cyclic structure, the “keto form” is always a ketone. The two forms in equilibrium constitute a tautomeric pair, and they are referred to as tautomers.

![Diagram of tautomeric pair](image)

Needless to say, tautomers are not resonance structures. They are independent species in equilibrim with each other. To be tautomers, the two species must feature a central carbon which in the enol form contains both the hydroxyl group and the alkene, and in the keto form contains the carbonyl group. In the above example that carbon is number 1. The example below shows species which are NOT tautomers. The carbon that contains the hydroxyl group (or the carbonyl group) is not the same as the carbon that contains the double bond.

![Not tautomers](image)

are NOT tautomers