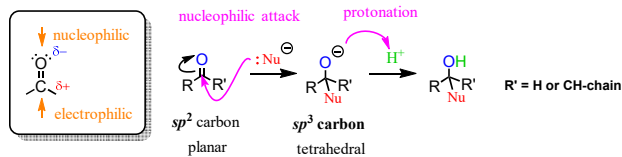


# Reactions of Aldehydes and Ketones

## Nucleophilic Additions to the Carbonyl Group

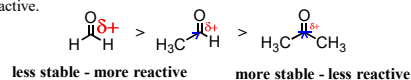
### Mechanism and Reactivity

For addition reactions, remember that the **Nucleophile attacks the carbon** because of the unequal electron density distribution between the carbon and oxygen.

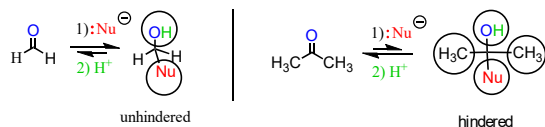


**Aldehydes are more reactive than ketones.** There are two reasons for this: **Electronic effect** and **Steric effect**. (This is not pertinent to aldehydes and ketones only; most organic reactions can be explained either by electronic or steric effects)

**1) Electronic effect:** The greater the partial positive charge on carbon (more electrophilic), the more reactive the carbonyl. Remember that alkyl groups are electron-donating, thus making ketones less reactive.

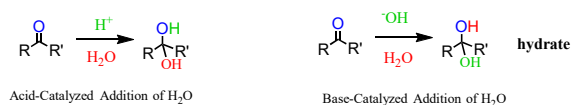


**2) Steric effect:** Most addition reactions are reversible and the equilibrium shifts based on the stability of the reactants and products. The tetrahedral product of the addition reaction is less crowded/bulky/sterically hindered and hence more stable in the case of aldehydes: Also, bulkier alkyl groups make the nucleophilic attack more difficult/slower.

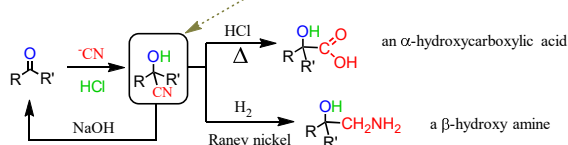


### Summary of Common Nucleophilic Addition Reactions

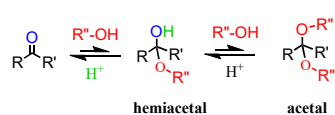
Reaction with **Water** produces a **Hydrate**:



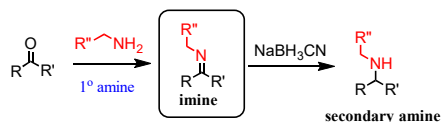
Reaction with **Cyanide ion** produces a **Cyanohydrin**:



Reaction with **Alcohols** produces a **Hemiacetal** or an **Acetal**:



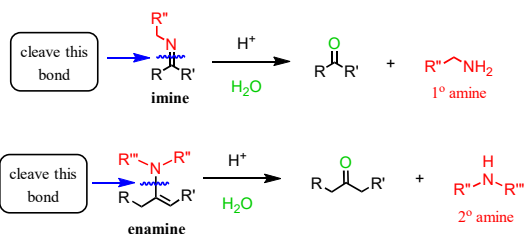
Reactions with **primary Amines** produce **Imines** which can further be reduced to amines. This is called **reductive amination**.



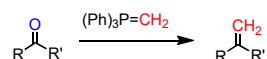
Reactions with **secondary amines** produce an **iminium ion**, which is reduced to a 3° amine.



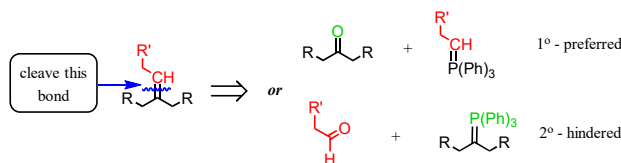
Imines and Enamines can be hydrolyzed back to the starting materials in presence of an acid. To predict the product of these reactions, just cleave the N-C bond and place a =O on the carbon:



The **Wittig Reaction** is used to convert **Aldehydes and Ketones** by a phosphorus ylide to **Alkenes**:

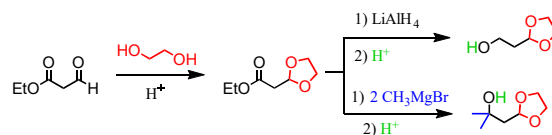


To predict the reactants of a Wittig reaction, cleave the C=C bond and place an oxygen on one and  $(\text{Ph})_3\text{P}$  on the other end. Less substituted ylides are easier to prepare.

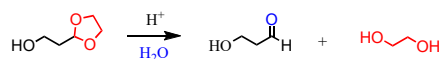


### Protecting Groups for Aldehydes and Ketones

Reactions with diols produce **cyclic acetals** which are **stable under neutral and basic conditions** and serve as **protecting groups** for aldehydes and ketones.

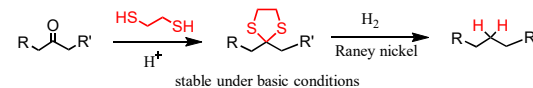


The **acetal protecting group** can then be **removed under acidic conditions**:



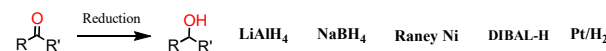
**Thiols** react with aldehydes and ketones similar to alcohols and form **Thioacetals** which are less stable compared to acetals.

**Dithiols**, on the other hand, form **cyclic thioacetals** which are stable and used in different reactions including conversion of the **carbonyl to C-H bonds**.



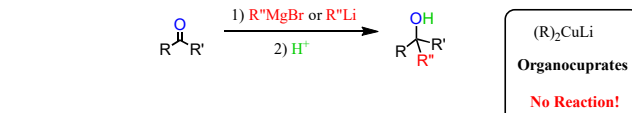
### Reduction of Aldehydes and Ketones by a Hydride Ion

Aldehydes and ketones can be reduced with all the standard reducing agents. Metal-catalyzed hydrogenation is not always effective though.

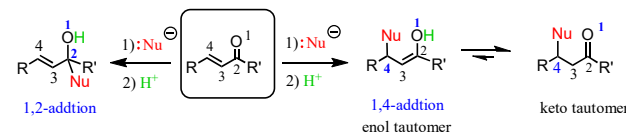


### Reactions with Organometallics

**Aldehydes and ketones** react with **Grignard reagents and Organolithiums** to form secondary and tertiary alcohols respectively.



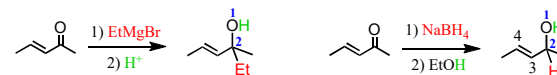
**1,2- and 1,4-Additions**  
 $\alpha, \beta$ -unsaturated carbonyl compounds can undergo a direct (1,2) or a conjugate (1,4) addition:



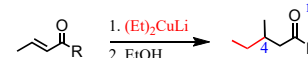
For relatively **weak nucleophiles** such as halides, a cyanide ion, a thiol, an alcohol, or an amine, the reaction is under thermodynamic control and **1,4-addition** occurs:



For **strong nucleophiles** such as Grignard reagents, Organolithiums (RLi), or hydride ion, the reaction is under kinetic control and **1,2-addition** occurs:



However, unlike Grignard reagents, **Organocuprates** also undergo a **1,4-addition**:



The **Baeyer-Villiger oxidation** uses peroxides for converting **aldehydes and ketones to carboxylic acids and esters** respectively:

