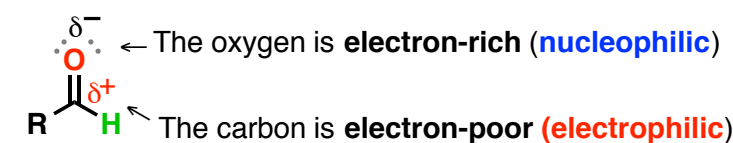


## A Simple "Formula" for Seven Key Reactions of Aldehydes & Ketones

## What factors affect the reactivity of aldehydes and ketones?

### 1. Electronic effects

In aldehydes and ketones, the C=O bond is polarized; due to the greater electronegativity of oxygen relative to carbon [3.4 vs. 2.5]; the carbon bears a partial positive charge and the oxygen bears a partial negative charge



Most of the reactions of aldehydes and ketones involve an electron-rich *nucleophile* forming a bond with the electron-poor *electrophile* that is the carbonyl carbon of the aldehyde or ketone.

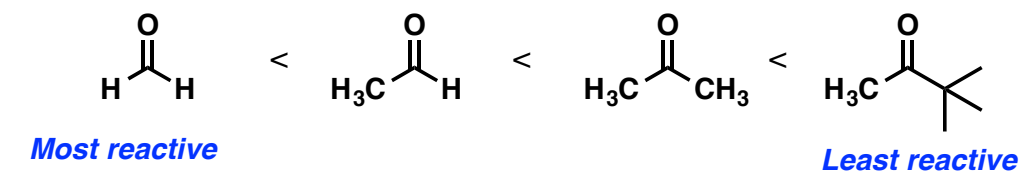
The more *electron-poor* the aldehyde or ketone, the more reactive it will be with nucleophiles



this aldehyde is more electron-poor than the aldehyde on the right due to the electron-withdrawing fluorines

### 2. Steric effects

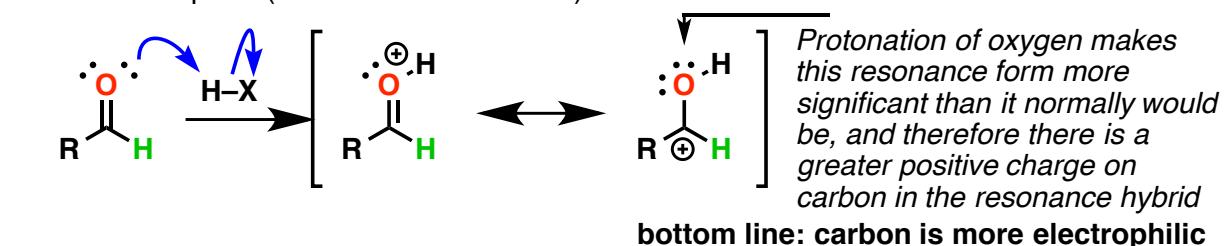
The larger the group adjacent to the carbonyl carbon, the more difficult it will be for nucleophiles to attack. This is referred to as *steric hindrance*.



Aldehydes are more reactive than ketones largely for this reason.

### 3. Acid catalysis

When acid ("HX" is added to an aldehyde or ketone it can make the carbonyl carbon more electrophilic (and thus more reactive)

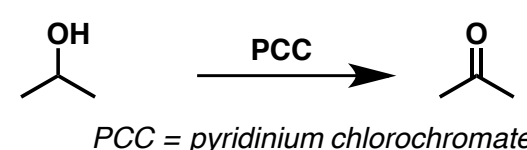


The only "catch" with using acid to accelerate a reaction is that it can't be used with strongly basic nucleophiles, because it will protonate them irreversibly. For instance using strong acid to accelerate a Grignard reaction would **not** work because Grignard reagents are strong bases; once protonated, they can't be regenerated.

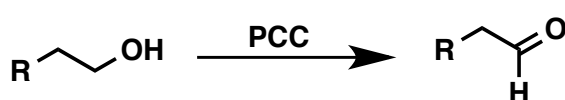
Acid catalysis works well with neutral nucleophiles like H<sub>2</sub>O, ROH, and amines, and also with weakly basic nucleophiles like <sup>-</sup>CN

## Synthesis of aldehydes and ketones

### Through oxidation of alcohols

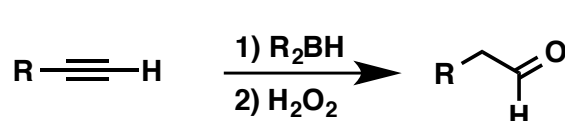


Secondary alcohols can also be oxidized to ketones with oxidizing agents such as H<sub>2</sub>CrO<sub>4</sub> and others.



PCC is a mild oxidant that does not oxidize the aldehyde further to the carboxylic acid

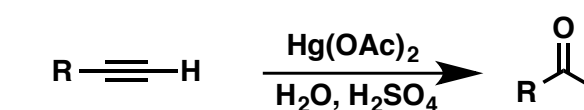
### Hydroboration of alkynes



This first forms the enol, which then tautomerizes to the aldehyde.

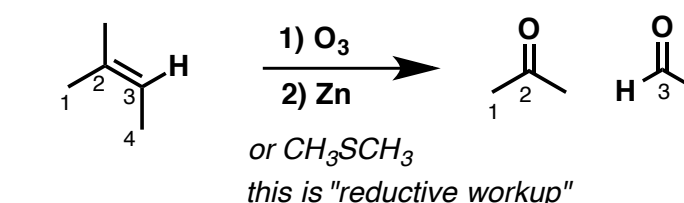
## Synthesis of Aldehydes and Ketones (continued)

### Oxymercuration of alkynes



This adds water to the more substituted end of the alkyne, forming an enol, which then tautomerizes to the ketone.

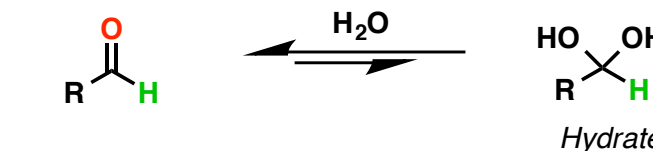
### Ozonolysis of alkenes



Ozonolysis cleaves C-C π bonds. If a "reductive workup" is used, C-H bonds attached to the alkene are preserved, leading to aldehydes.

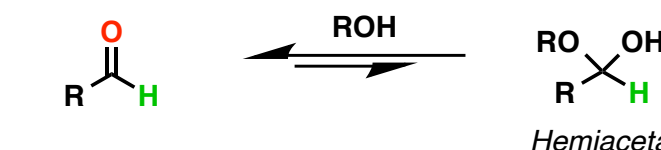
## Other Key Reactions of Aldehydes and Ketones

### Hydration



Water will add to aldehydes and ketones to give hydrates. Equilibrium favors the starting aldehyde/ketone. The reaction is made faster by acid.

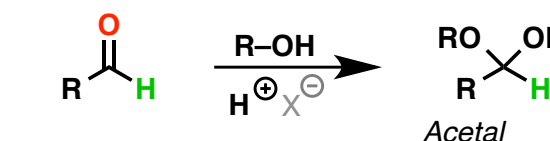
### Hemiacetal formation



Alcohols will add to aldehydes/ketones to give hemiacetals. Equilibrium usually favors the starting aldehyde/ketone, except in cases where a ring is formed.

The reaction is made faster by acid. Electron withdrawing groups on the aldehyde favor hemiacetal formation

### Acetal formation



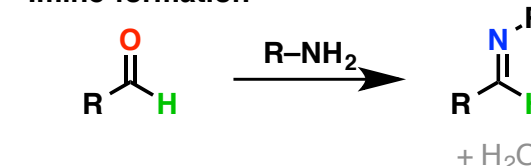
Treatment of an aldehyde or ketone with an alcohol in acid leads to an acetal. The acetal can be removed by heating with aqueous acid.

### Acetals as protecting groups



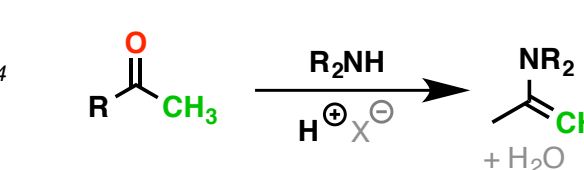
Acetals only react with aqueous acid. So forming an acetal is a method of "masking" a carbonyl group.

### Imine formation



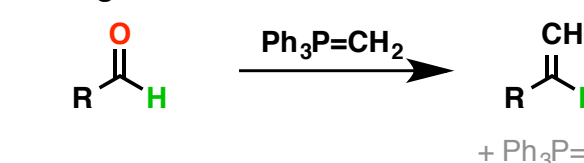
Aldehydes/ketones treated with a primary amine will give **imines**. Mild acid can be used to promote this reaction

### Enamine formation



Aldehydes/ketones treated with a **secondary** amine give **enamines**. Acid catalyzes their formation.

### Wittig Reaction



Treatment of an aldehyde/ketone with a phosphorus ylide leads to formation of an alkene. This is the Wittig Reaction.

Aldehyde (but also applies to ketones)

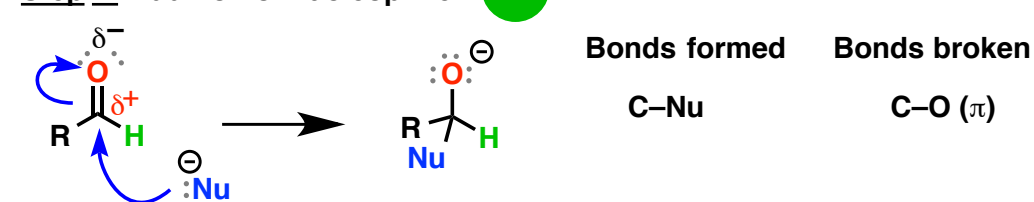
Reaction	Nucleophile	Product
Grignard Reaction	R-MgX	
Addition of Organolithiums	R-Li	
Reduction by sodium borohydride (NaBH <sub>4</sub> )	Na <sup>+</sup> H-BH <sub>3</sub> <sup>-</sup>	
Reduction by lithium aluminum hydride (LiAlH <sub>4</sub> )	Li <sup>+</sup> H-AlH <sub>3</sub> <sup>-</sup>	
Addition of cyanide ion to form cyanohydrins	<sup>-</sup> :CN	
Addition of hydroxide ion to form hydrates	<sup>-</sup> :OH	
Addition of alkoxide ions to form hemiacetals	<sup>-</sup> :OR	

Each of these reactions follows a "two-step" pattern: 1) addition 2) protonation

### How to draw the mechanism for this pattern:

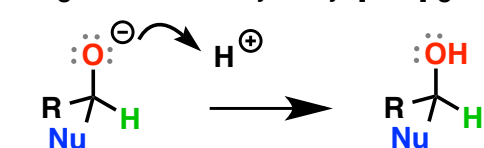
Step 1 is donation of a lone pair of electrons **from** the nucleophile **to** the carbonyl carbon, which bears a partial positive charge [oxygen is more electronegative than carbon]. A bond forms between the nucleophile and carbon, and the carbon-oxygen double bond [π bond] breaks. The oxygen then bears a negative charge.

#### Step 1: Addition of nucleophile



#### Step 2: Protonation of oxygen

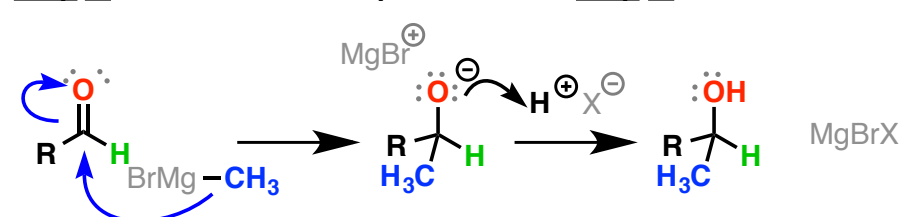
In the second step of this reaction, acid is added the oxygen is protonated to give a neutral hydroxyl [O-H] group:



### Specific example: Grignard addition

#### Step 1: Addition of nucleophile

#### Step 2: Protonation



draw the arrow as coming from the Mg-C bond