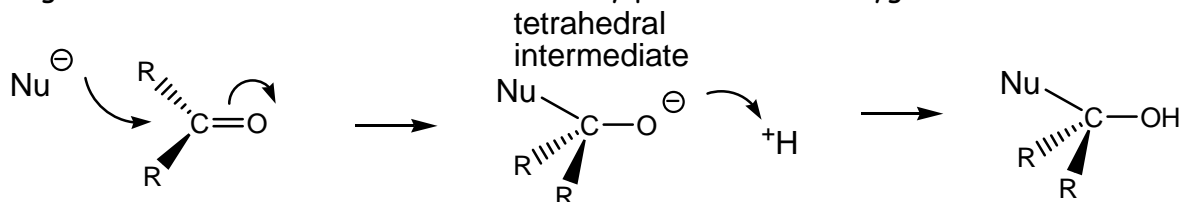




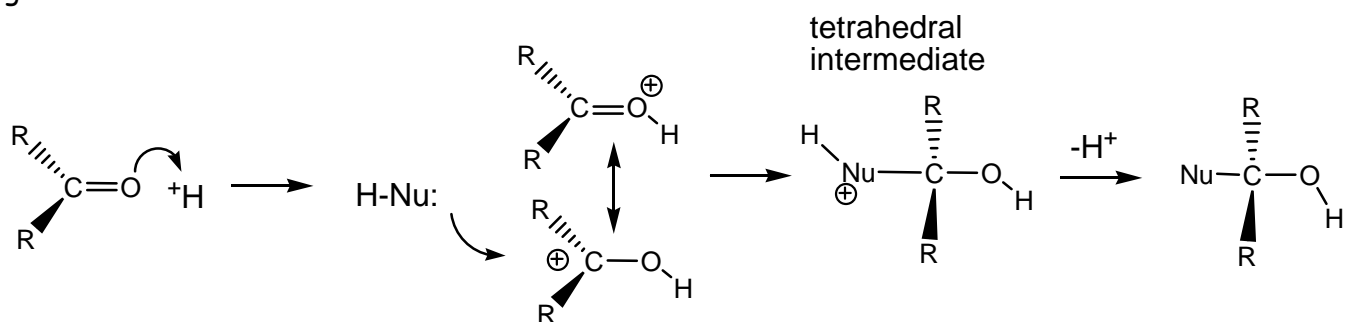
## Two modes of attack on a carbonyl group:

### A. Strong Nucleophiles attack carbon 1st

to give **tetrahedral intermediate** followed by protonation on oxygen:



### B. Weak Nucleophiles attack after oxygen is protonated 1<sup>st</sup> then nucleophile adds to carbon to give tetrahedral intermediate:



- The product is also tetrahedral in structure.
- The addition reaction is usually reversible, i.e., the tetrahedral product may eliminate a group to regenerate the carbonyl group.
- If the tetrahedral product is stable or not, a common subsequent step is elimination, especially dehydration.
- Aldehydes are more reactive towards addition than ketones (steric hindrance and electronics).

## The mode of attack is determined by nucleophile strength:

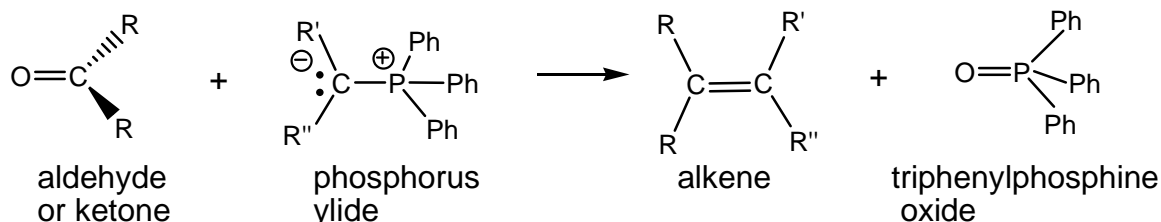
**A. Strong Nu:** attack at carbonyl carbon occurs first, then alkoxide intermediate gets protonated in a later step

**B. Weak Nu:** carbonyl oxygen gets protonated first, then nucleophile attack carbonyl carbon

## Addition Reactions of Aldehydes and Ketones

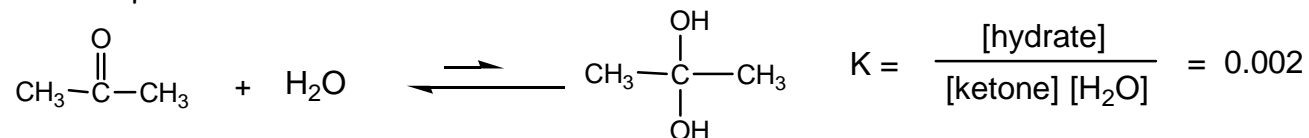
1. The Wittig Reaction- Addition of Ylides (Formation of Alkenes)
2. Hydrates- Addition of water
3. Acetal Formation- Addition of Alcohols
4. Addition of organometallics- Synthesis of 2° and 3° Alcohols
5. Cyanohydrin Formation- Addition of HCN
6. Addition of Ammonia Derivatives- Synthesis of Hydrazones, Semicarbazides and Oximes

### 1. The Wittig Reaction- Addition of Ylides- Synthesis of Alkenes

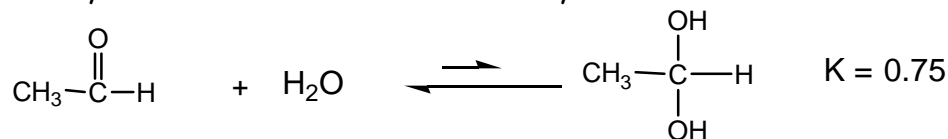


### 2. Hydrates- Addition of water across the double bond

Equilibrium favors the ketone:

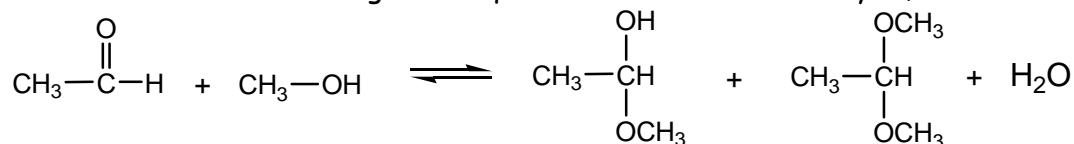


Aldehydes are more reactive but carbonyl is still favored:



### 3. Acetal Formation- Addition of Alcohol

Aldehydes react with alcohols to give an equilibrium mixture of aldehyde, hemiacetal and acetal.

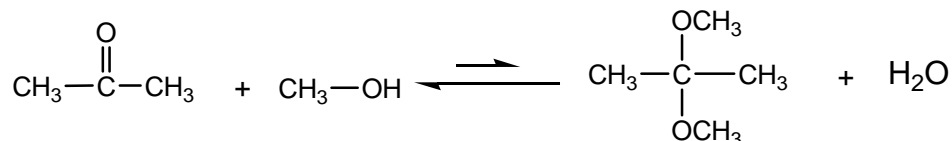


**Hemiacetal** has one alkoxy group and one hydroxy attached to the same carbon.

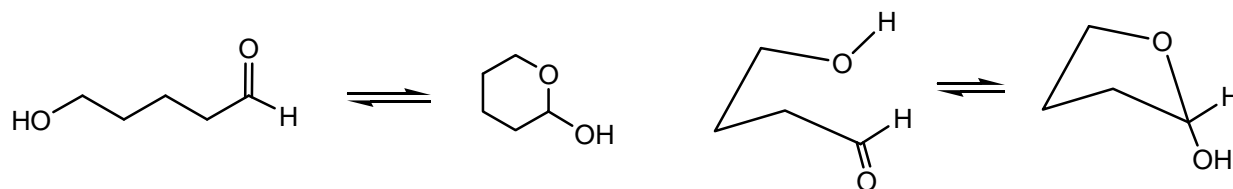
**Acetal** has two alkoxy groups attached to the same carbon.

Usually alcohol is in excess to drive reaction all the way to the acetal

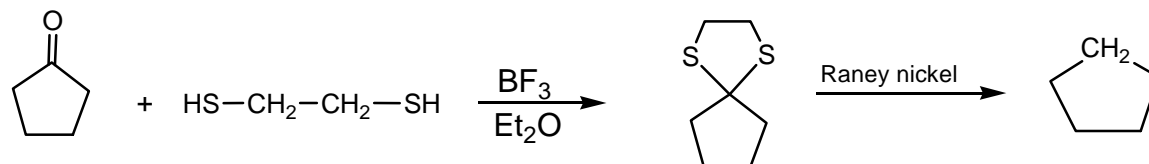
Ketones form acetals also but equilibrium favors the ketone; i.e., must drive reaction to acetal



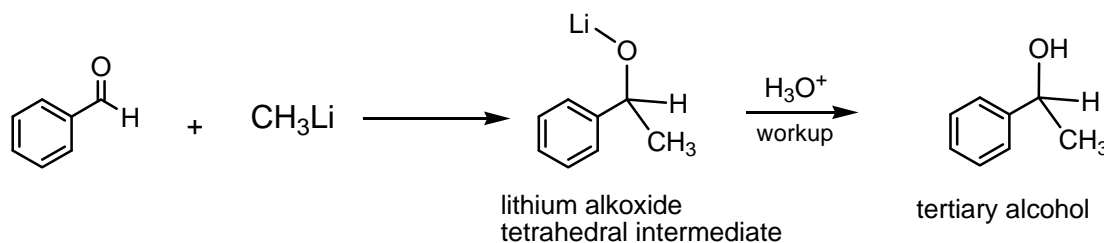
**Hemiacetals** are not stable but can be isolated if part of a 5-membered or 6-membered ring.



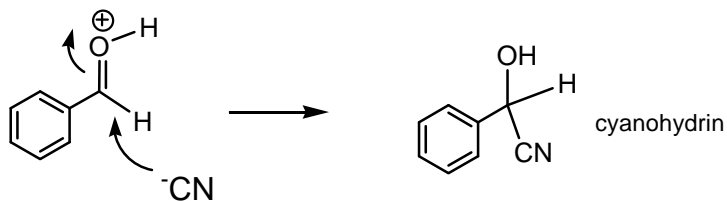
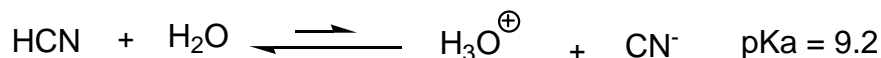
**Thioacetals** are easily reduced to the methylene compound using Raney nickel.



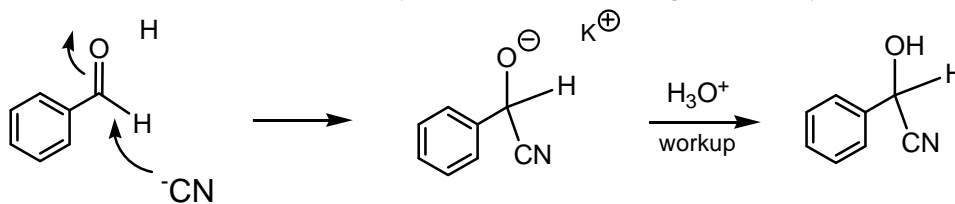
#### 4. Addition of Alkyl lithium reagents and Grignard reagents (strong nucleophiles)



#### 5. Cyanohydrins- Addition of HCN



Better to use KCN or NaCN since cyanide ion is a stronger nucleophile:

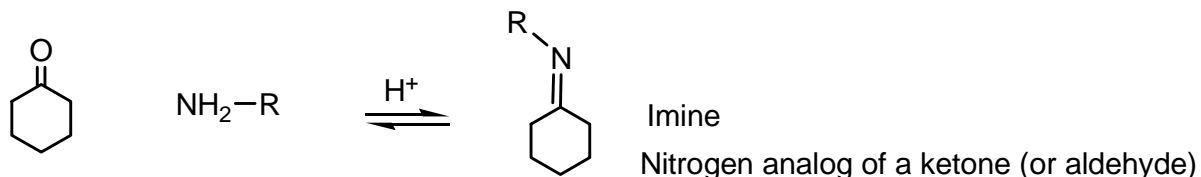


Use proton-donating solvents or acidic work-up

## 6. Addition of Ammonia and Ammonia Derivatives

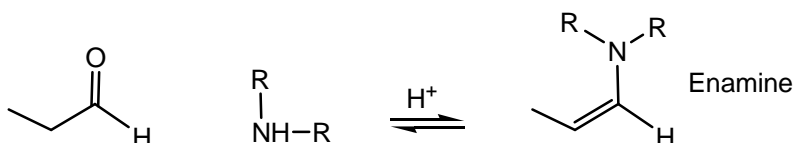
Aldehydes and ketones ... react with 1° amines to give imines  
 ... react with 2° amines to give enamines

### 1° amine



- The imine is also called a [Schiff base](#)
- These are also called condensation reactions- two compounds are joined and a small molecule is lost (usually water)

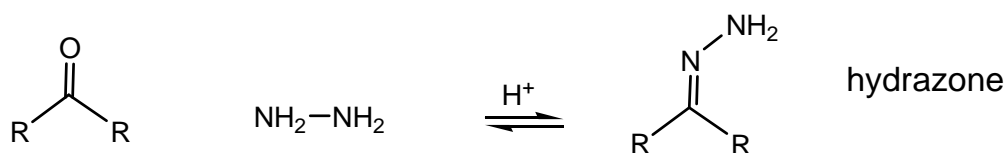
### 2° amine Enamine formation



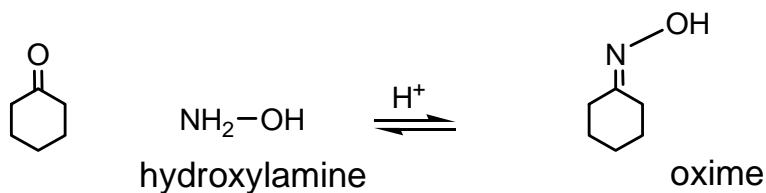
### Other Classes of Imines (Ammonia Derivatives)

- hydrazones
- oximes
- semicarbazones

#### a. Hydrazones- Condensation with hydrazine and hydrazine derivatives



#### b. Oximes- Condensation with hydroxyl amines



#### c. Semicarbazones- Condensations with semicarbazide

