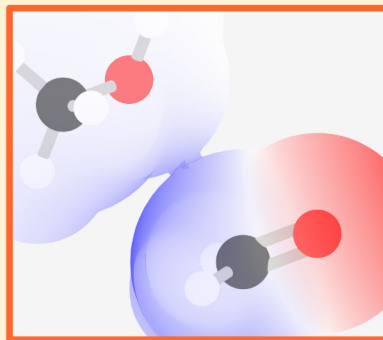


# HIGHLIGHTS

- Polarization of the carbonyl bond
- The two-step mechanism for nucleophilic addition to aldehydes and ketones
- What makes the reaction reversible or not
- Examples of irreversible addition
- Examples of reversible addition
- Simplified molecular orbital view of addition to aldehydes and ketones



Aldehydes & ketones contain a polarized carbonyl bond, and are good electrophiles. Nucleophilic addition proceeds by a two-step mechanism that delivers a tetrahedral product. The first step involved addition to the carbonyl, accompanied by breaking the  $\pi$  bond. The second step is proton transfer to quench the intermediate.

Addition can be irreversible, as seen with organometallic reagents & reducing reagents, if there is no suitable leaving group on the tetrahedral intermediate.

Alternatively, the reaction is reversible and an equilibrium between aldehyde/ketone and the product is established. This occurs when the nucleophile is a good leaving group (it is a weak base).

## CHEMISTRY CLASSICS

### ADDITION TO THE CARBONYL GROUP

#### NUCLEOPHILIC ADDITION TO ALDEHYDES & KETONES

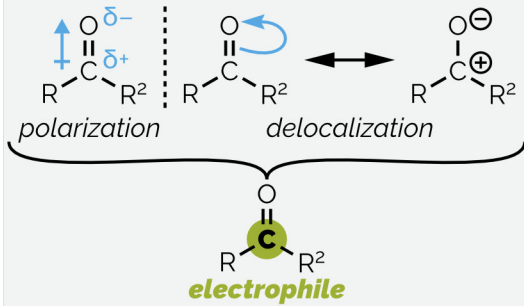


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# Nucleophilic addition

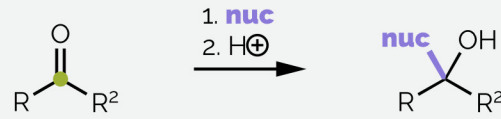
## 1. Carbonyl bond



Carbonyl is C=O  $\sigma$  +  $\pi$  bond; RC(O) = acyl  
 $R^2 = H$  (aldehyde);  $R^2 = C$  (ketone)

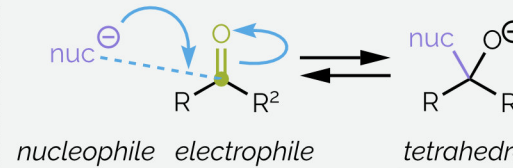
## 2. General reaction mechanism

overall reaction

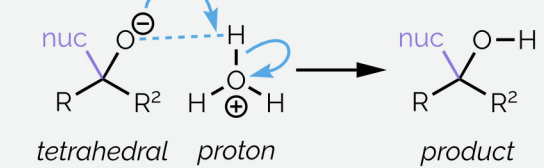


Reversible addition:  
**nuc** &  $H^+$  combined (1 + 2) or same molecule  
 Irreversible addition:  
**nuc** &  $H^+$  must be independent (1 then 2)

step 1: nucleophilic addition  
**make:**  $\sigma$  bond; **break:**  $\pi$  bond



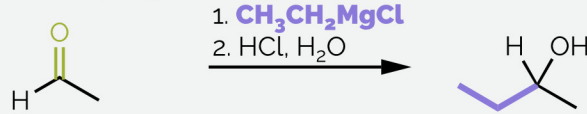
step 2: proton transfer  
 intermolecular (shown) or intramolecular



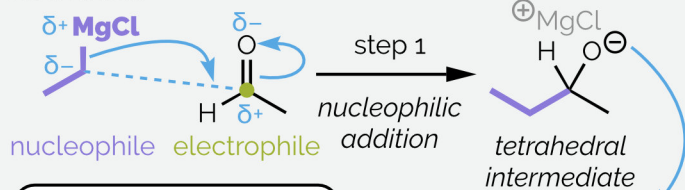
reversible: **nuc** = weak base ( $pK_a H < 20$ )  
 irreversible: **nuc** = strong base ( $pK_a H > 20$ )

## 3. Irreversible addition

Addition of Grignard reagent



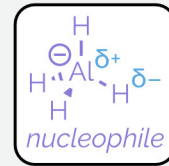
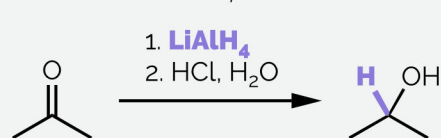
Mechanism



irreversible addition  
 no leaving group on tetrahedral intermediate

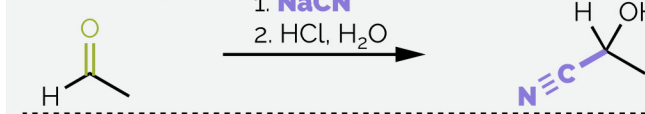
|              |               |
|--------------|---------------|
| $CH_3CH_3^-$ | $pK_a H = 48$ |
| $H^-$        | $pK_a H = 36$ |
| $CH_3^-$     | $pK_a H = 48$ |

Reduction with  $LiAlH_4$

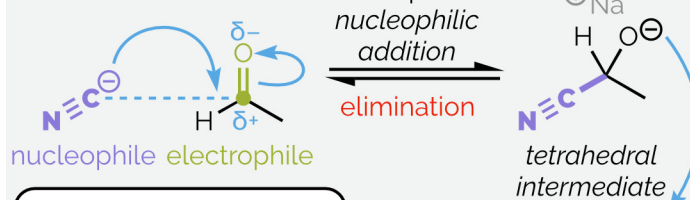


## 4. Reversible addition

Addition of cyanide



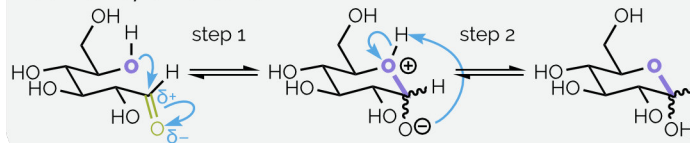
Mechanism



reversible addition  
 C=O formation possible as leaving group present

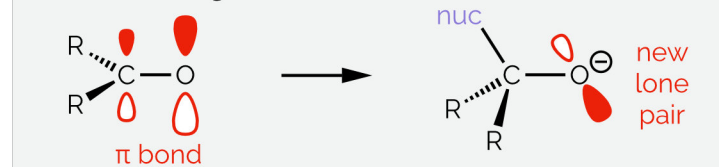
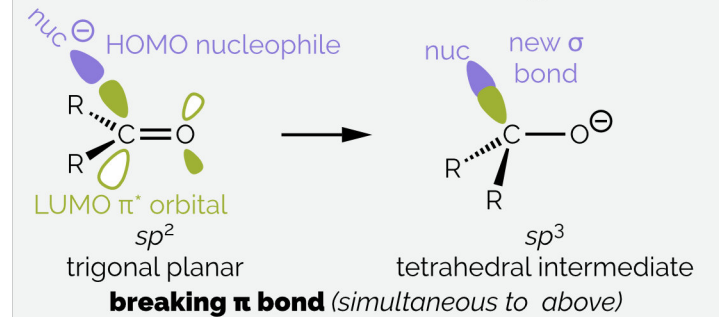
|          |                |
|----------|----------------|
| $NC^-$   | $pK_a H = 9.6$ |
| $H^-$    | $pK_a H = 36$  |
| $CH_3^-$ | $pK_a H = 48$  |

Addition of an alcohol



## 5. Orbitals & direction (taking it further)

HOMO & LUMO interaction forming  $\sigma$  bond



direction of attack

