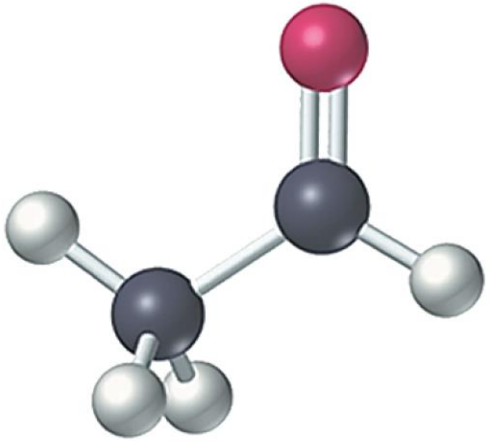
2302106 – Basic Organic Chemistry for ISE – Part II

Lecture 4-2

Aldehydes & Ketones – Nucleophilic addition-1



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Recommended Textbook:

Chapter 18 in *Organic Chemistry*, 8th Edition, L. G. Wade, Jr., **2010**, Prentice Hall (Pearson Education)

Reactions of Aldehydes and Ketones

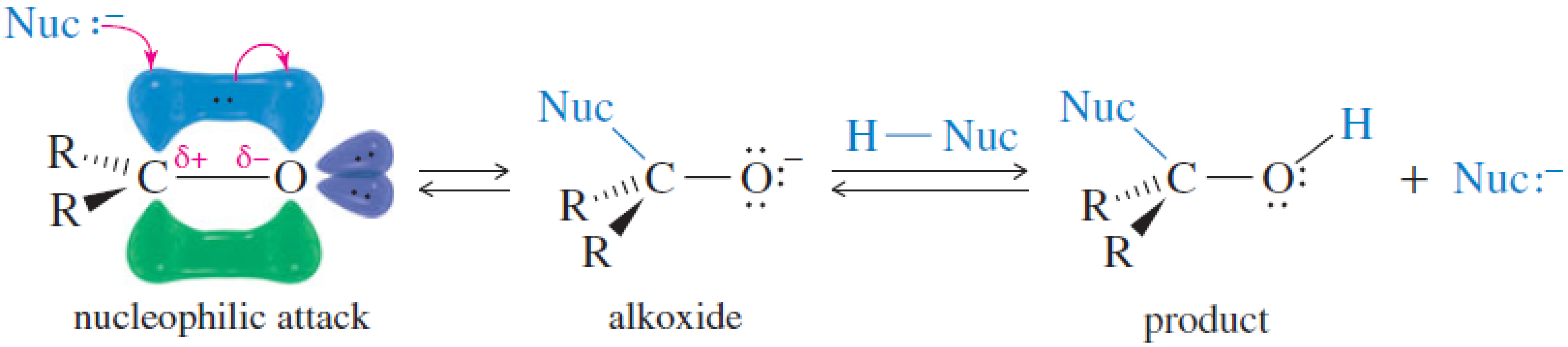
- The most common reaction is **nucleophilic addition**

  (addition of a nucleophile and a proton across the double bond)

- The reactivity of the carbonyl group arises from the **electronegativity** of the oxygen atom and the resulting **polarization** of the carbon–oxygen double bond

Reactions of Aldehydes and Ketones – Nucleophilic Addition

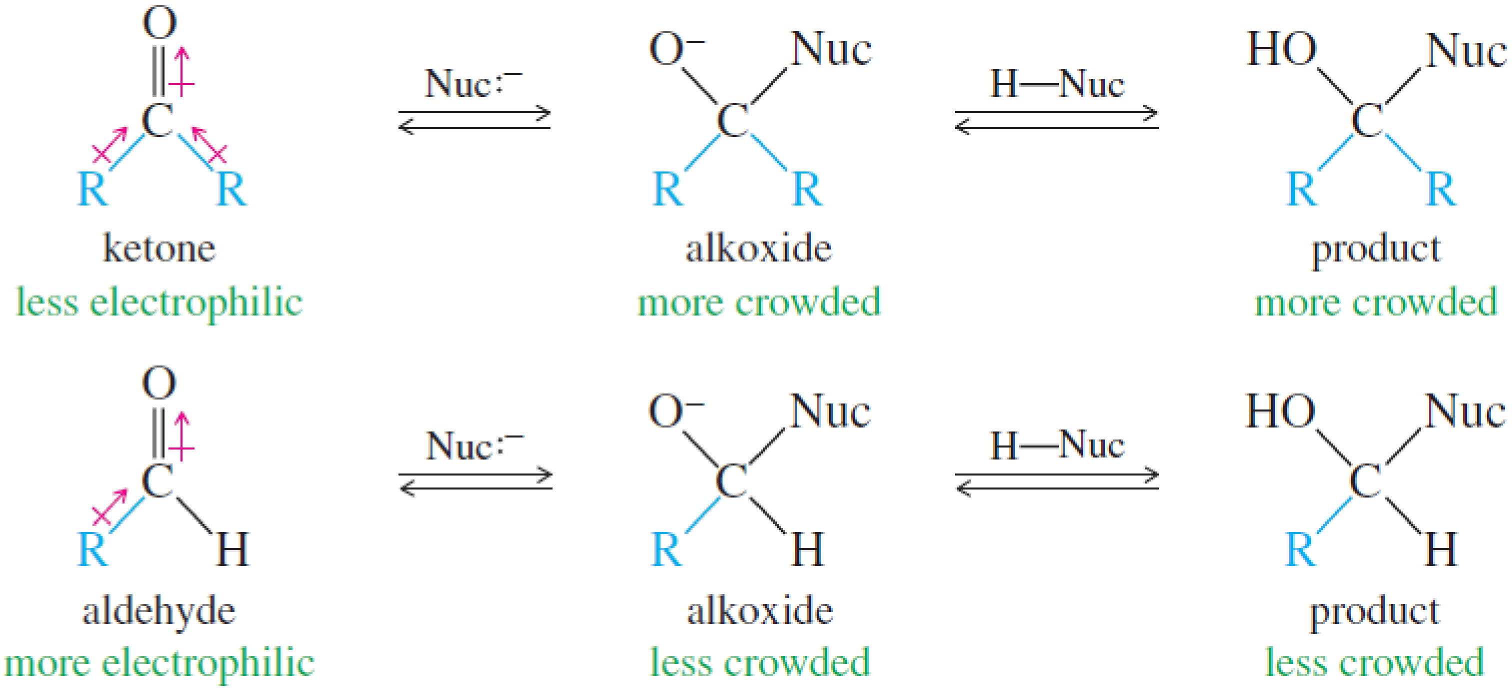
- The electrophilic carbonyl carbon atom is **sp^2** hybridized and **flat**, leaving it relatively **unhindered** and open to attack from either face of the double bond



- The carbon atom changes hybridization from **sp^2** to **sp^3**
- The electrons of the pi bond are forced out to the oxygen atom to form an **alkoxide** anion, which **protonates** to give the product of nucleophilic addition

Aldehydes vs. Ketones towards Nucleophilic Addition

- In most cases, aldehydes are **more reactive** than ketones; they usually react more quickly (**Kinetics**), and the position of the equilibrium usually lies more toward the products (**Thermodynamics**) than with ketones

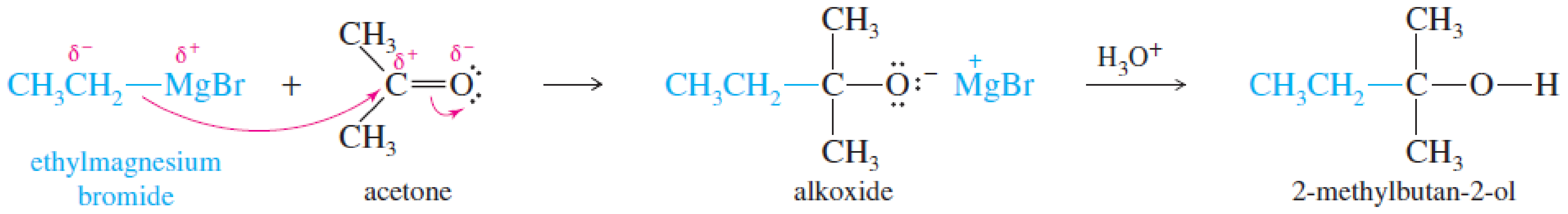


Electronic Effect

Steric Effect

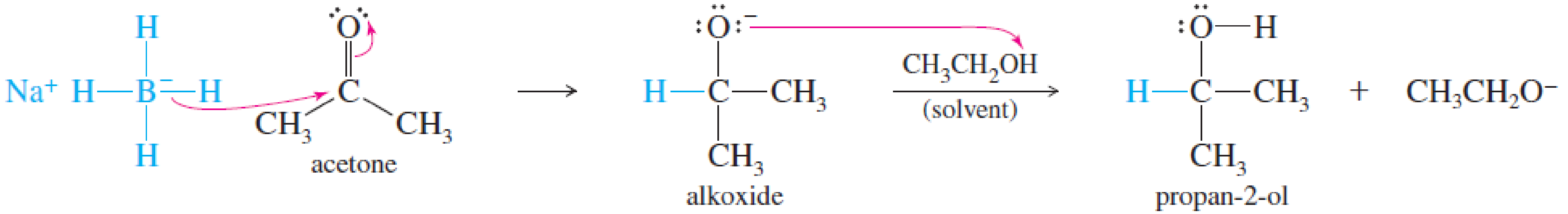
Nucleophilic Addition with Strong Nucleophiles

1) Reaction with Organometallic Reagents (carbanions, R^-)



- Attack by R^- gives an alkoxide that protonates to form an alcohol

2) Hydride Reductions (H^-)



- Attack by hydride gives an alkoxide that protonates to form an alcohol

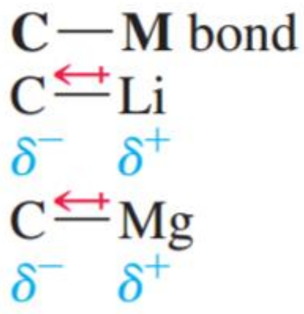
Nucleophilic Addition with **Strong Nucleophiles**

1) Reaction with **Organometallic Reagents** (carbanions, R^-)

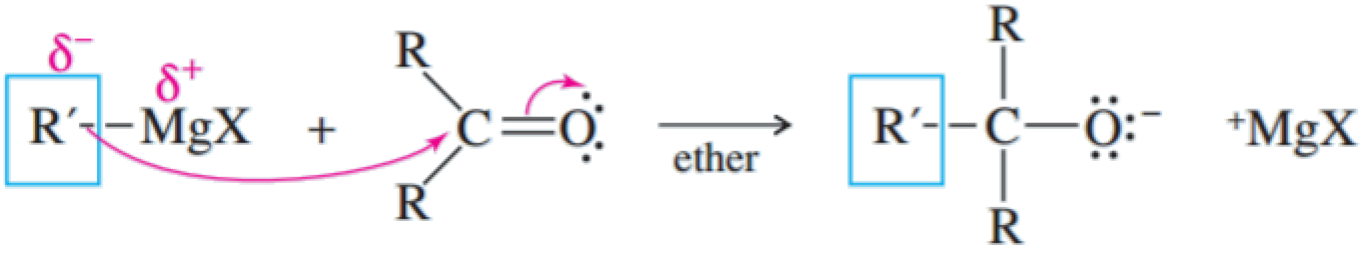
- Carbon which is bonded to a metal (eg. Li or Mg) is **negatively charged**

Electronegativities

Li	1.0					C	2.5
Na	0.9	Mg	1.3	Al	1.6		
K	0.8						



- It will attack a partially positive carbon (eg. C–X, C=O)
- Good for forming **carbon-carbon bonds**



1) Reaction with Organometallic Reagents (carbanions, R^-)

Grignard Reagents

- Formula: **R—Mg—X** (alkyl magnesium halide)
- May be formed from any **halides**

  (alkyl, vinyl or aryl halides)

$$R{-}X \xrightarrow{Mg} R{-}MgX$$

(**X = Cl, Br, or I**)

- Reacts like $R^{-}\ {}^{+}MgX$

Organolithium Reagents

- Formula: **R—Li** (alkyl lithium)
- May be formed from any **halides**

  (alkyl, vinyl or aryl halides)

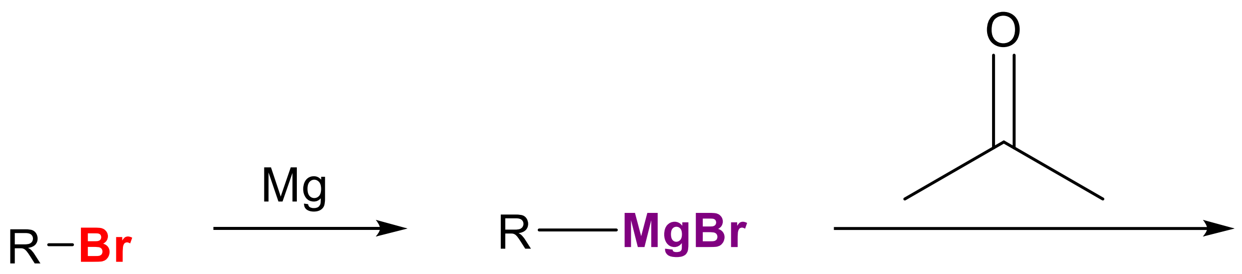
$$R{-}X \xrightarrow{Li} R{-}Li$$

(**X = Cl, Br, or I**)

- Reacts like $R^{-}\ {}^{+}Li$

1) Reaction with Organometallic Reagents (carbanions, R^-)

Mechanism



1) Reaction with Organometallic Reagents (carbanions, R⁻)

Examples:

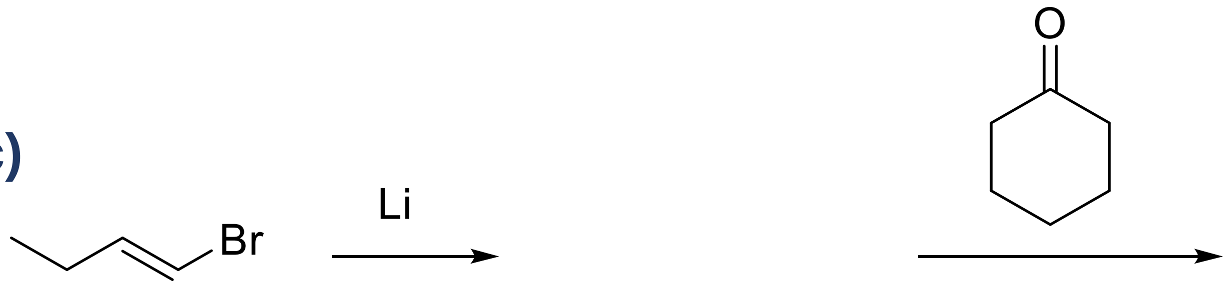
a) 

b) 

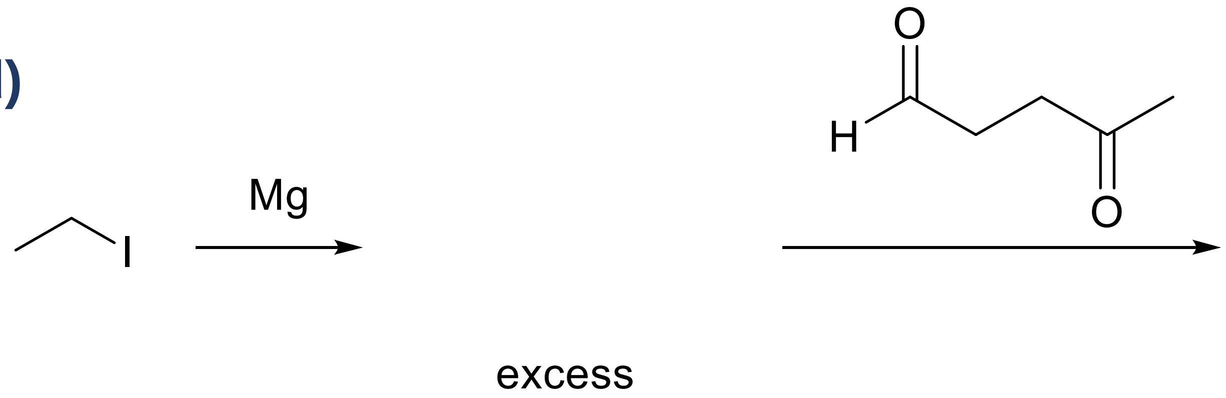
1) Reaction with Organometallic Reagents (carbanions, R⁻)

Examples:

c)

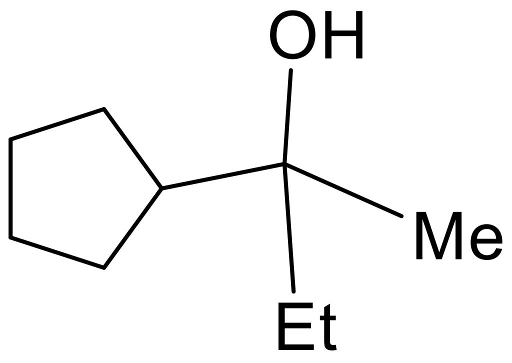


d)



1) Reaction with Organometallic Reagents (carbanions, R^-)

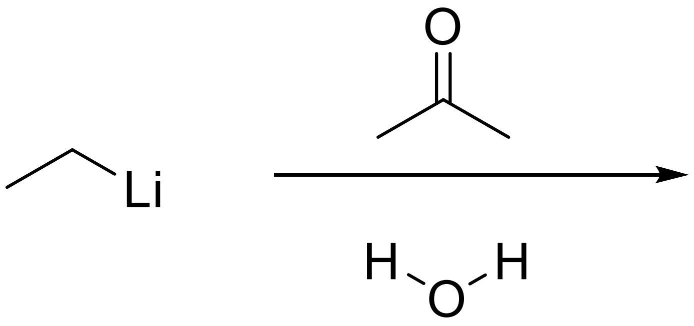
Examples: Show how you would synthesize the following alcohol from compounds containing **no more than five carbon atoms**



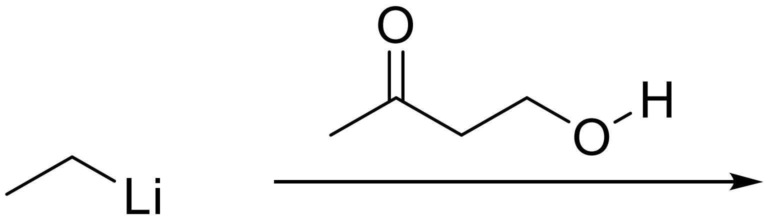
1) Reaction with **Organometallic Reagents** (carbanions, R^-)

Limitations !!

- Grignard and organolithium reagents **react vigorously and irreversibly with water**
  Therefore, all reagents and solvents used in these reactions must be **dry**



- **Acidic protons** like O—H, N—H, S—H, or terminal alkyne are not compatible

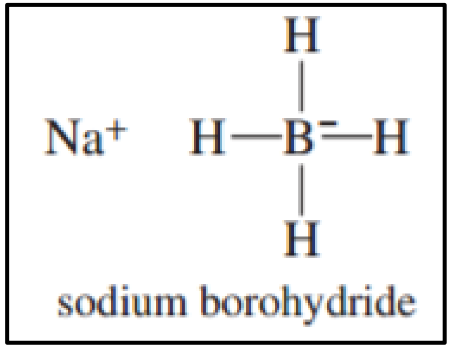


Nucleophilic Addition with Strong Nucleophiles

2) Hydride Reductions

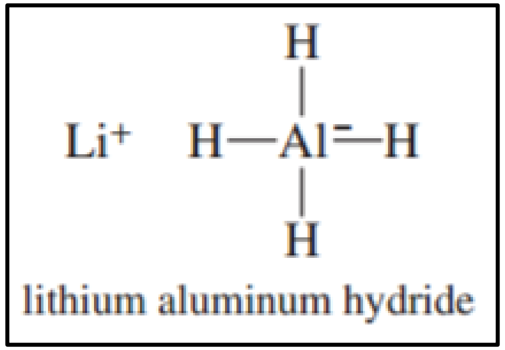
Common Reagents

#1: Sodium Borohydride ($NaBH_4$)



- **B** has higher EN than **Al**
- H^- of $NaBH_4$ is **less reactive**
- **More stable** (reaction with water)

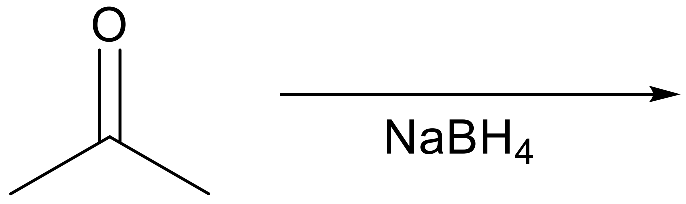
#2: Lithium Aluminium Hydride ($LiAlH_4$)



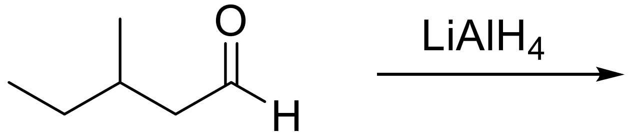
- **Al** has lower EN than **B**
- H^- of $LiAlH_4$ is **more reactive**
- **Less stable** (reaction with water)

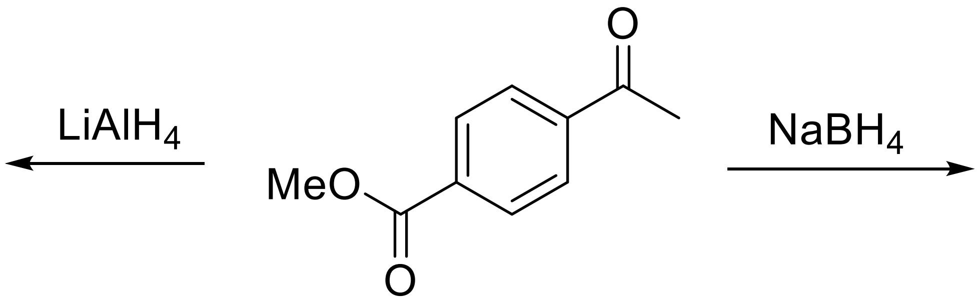
Nucleophilic Addition with Strong Nucleophiles

Mechanism:



Examples:





Nucleophilic Addition with Strong Nucleophiles

Examples: Suggest 4 different ways to synthesize this alcohol