

# **6. Substituição Nucleofílica Acíclica via Adição/ Eliminação**

**6.1. Ácidos carboxílicos e derivados: nomenclatura.**

**6.2. Acidez de ácidos carboxílicos**

**6.3. Reações de derivados de ácido carboxílicos: reatividade.**

**6.4. Reação de haletos de acila**

**6.5. Reação de anidridos de ácido carboxílicos**

**6.6. Reação de ésteres de ácido carboxílicos**

**6.7. Formação de ésteres de ácido carboxílicos**

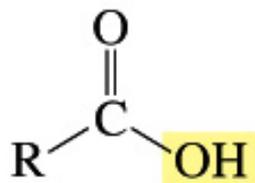
**6.8. Formação e Reações de Amidas**

**6.9. Ativação de Ácidos Carboxílicos**

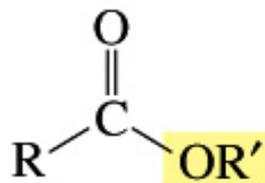
**6.10. Reações de Oxidação e Redução**

**6.11. Reações com Organometálicos**

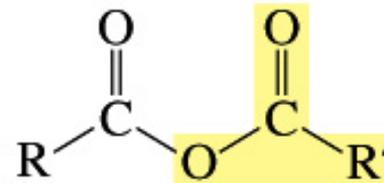
# 6. Compostos Carboxílicos: Ácidos Carboxílicos e Derivados



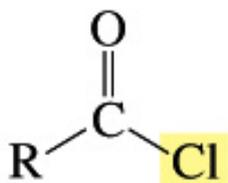
a carboxylic acid



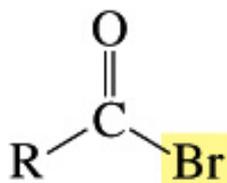
an ester



an acid anhydride

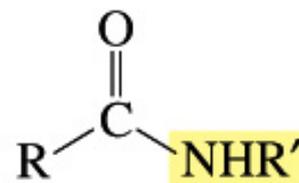
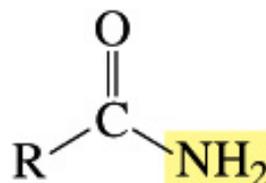


an acyl chloride

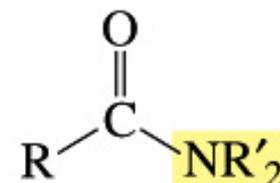


an acyl bromide

acyl halides



amides



Compostos carboxílicos são compostos carbonílicos contendo um bom grupo de partida (que pode ser substituídos por um nucleófilo)

# 6.1. Nomenclatura de Ácidos Carboxílicos



systematic name: methanoic acid  
common name: formic acid



ethanoic acid  
acetic acid



propanoic acid  
propionic acid



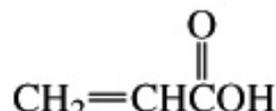
butanoic acid  
butyric acid



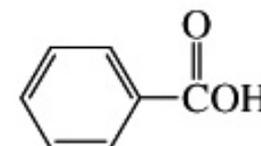
pentanoic acid  
valeric acid



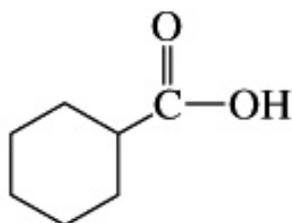
hexanoic acid  
caproic acid



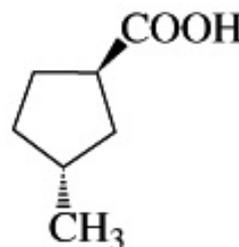
propenoic acid  
acrylic acid



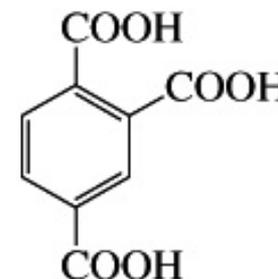
benzenecarboxylic acid  
benzoic acid



ácido ciclohexanocarboxílico

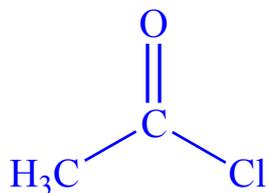


ácido trans-3-metilciclo-  
pentanocarboxílico

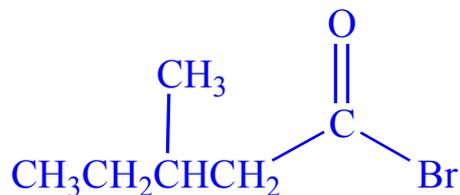


ácido 1,2,4-benzo-  
tricarboxílico

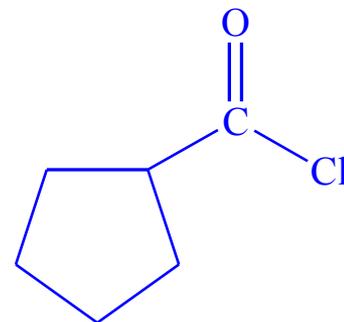
# Haletos de Acila



cloreto de etanoíla  
cloreto de acetila

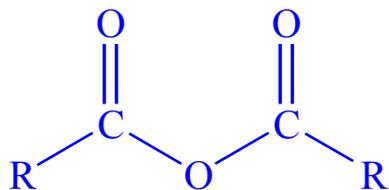


brometo de 3-metilpentanoíla  
brometo de β-metilvaleríla



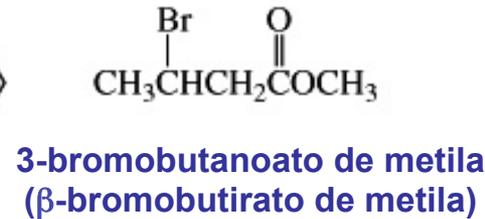
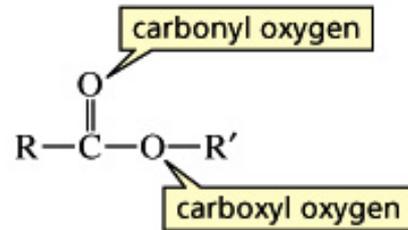
cloreto de  
ciclopentanocarboníla

# Anidridos de Ácido

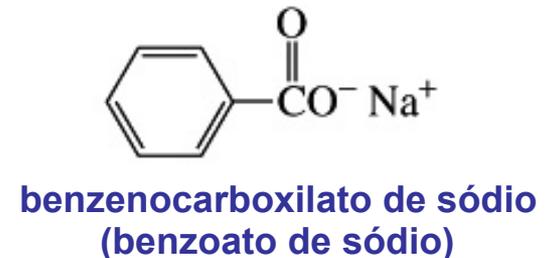


R = CH<sub>3</sub>: anidrido acético  
R = C<sub>2</sub>H<sub>5</sub>: anidrido propanoico  
R = C<sub>6</sub>H<sub>5</sub>: anidrido benzôico

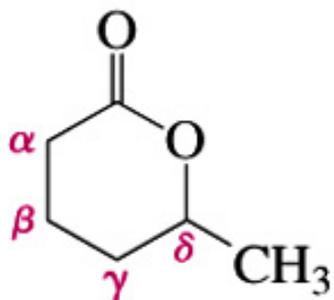
# Ésteres



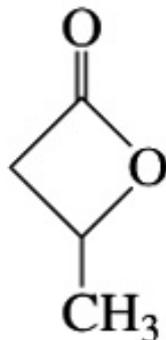
# Sais de Ácidos Carboxílicos



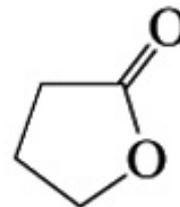
# Ésteres Cíclicos: Lactonas



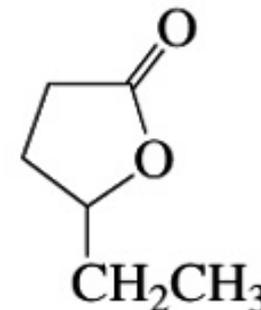
$\delta$ -caprolactona



$\beta$ -butirolactona



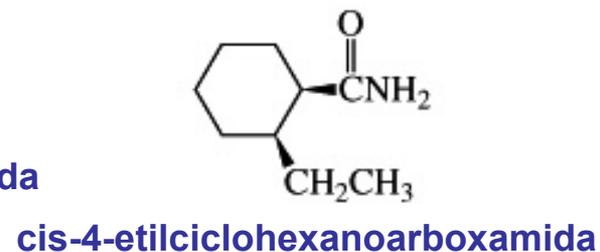
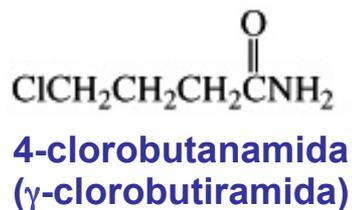
$\gamma$ -butirolactona



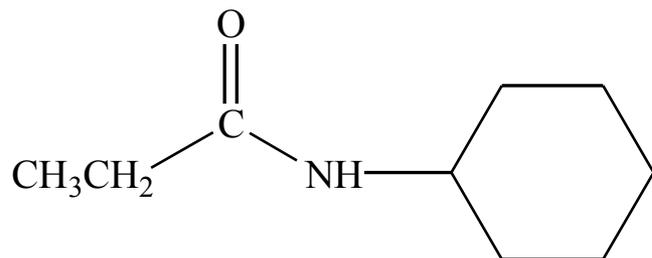
$\gamma$ -caprolactona

C-4: butirolactona; C-5: valerolactona; C-6: caprolactona;  
 $\beta$ ,  $\gamma$ ,  $\delta$ : posição do grupo funcional -O-.

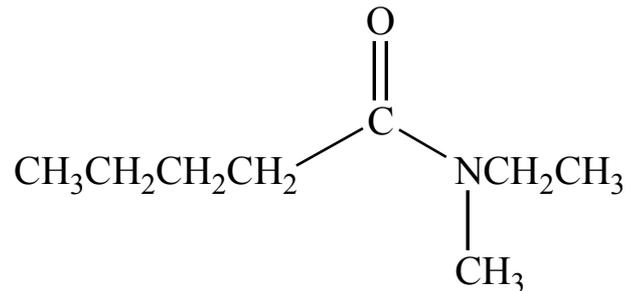
# Amidas



# Amidas substituídas no nitrogênio

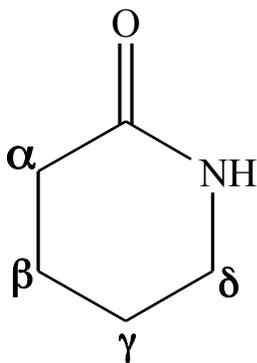


**N-ciclohexilpropanamida**

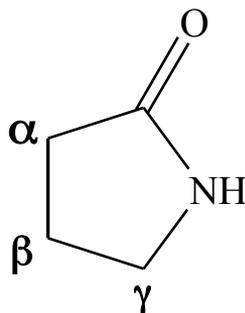


**N-etil-N-metilpentanamida**

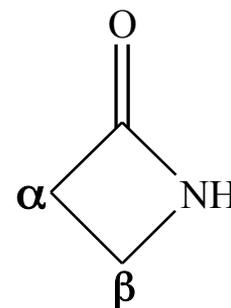
# Amidas Cíclicas: Lactamas



**2-azaciclohexanona**  
**δ-valerolactama**



**2-azaciclopanonona**  
**γ-butirolactama**

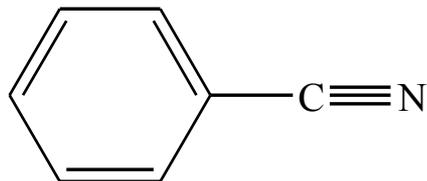


**2-azaciclobutanona**  
**β-propiolactama**

# Nitrilas



etanonitrila  
**acetonitrila**  
cianeto de metila



benzenocarbonitrile  
**benzonitrila**  
cianeto de fenila  
cianobenzeno



**5-metilhexanonitrila**  
 $\delta$ -metilcapronitrila  
cianeto de *iso*-hexila

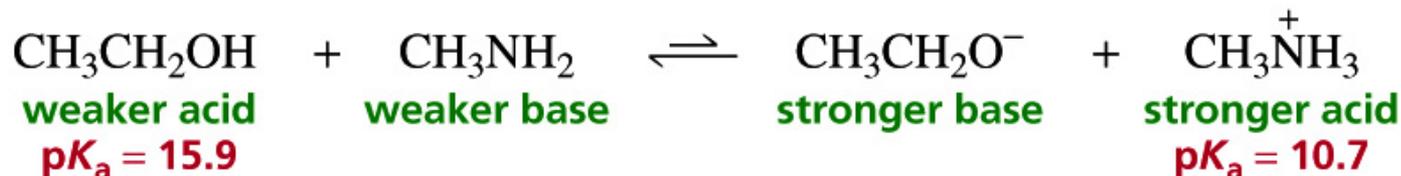
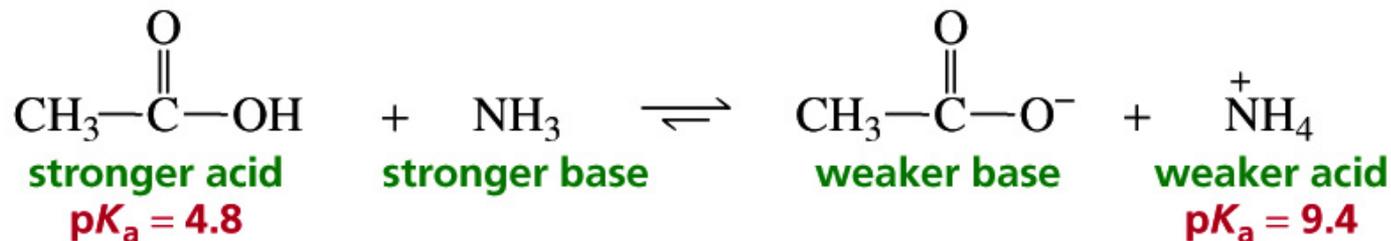


propenonitrila  
**acrilonitrila**

# 6.2. Acidez de Ácidos Carboxílicos

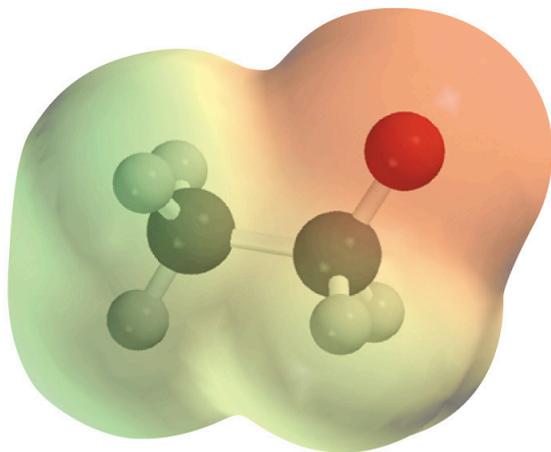
## Ácidos e Bases de Brønsted–Lowry

❖ Ácidos doam prótons e Bases recebem prótons



- “Fortes reagem para dar fracos”
- Quanto mais fraca a base, mais forte o ácido conjugado
- Ácidos (bases) estáveis são fracos

# Acidez de Ácidos Carboxílicos



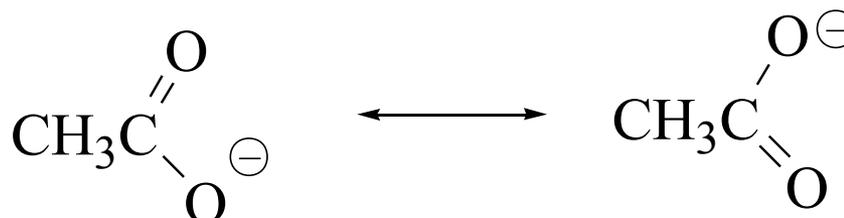
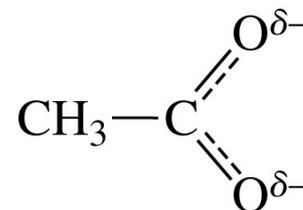
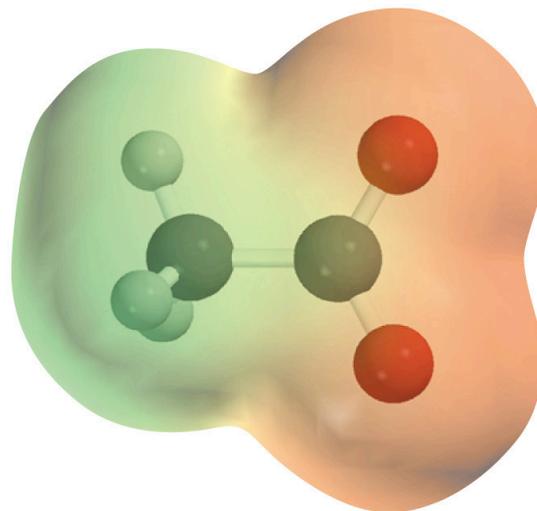
$\text{pK}_a = 4.76$

acetic acid

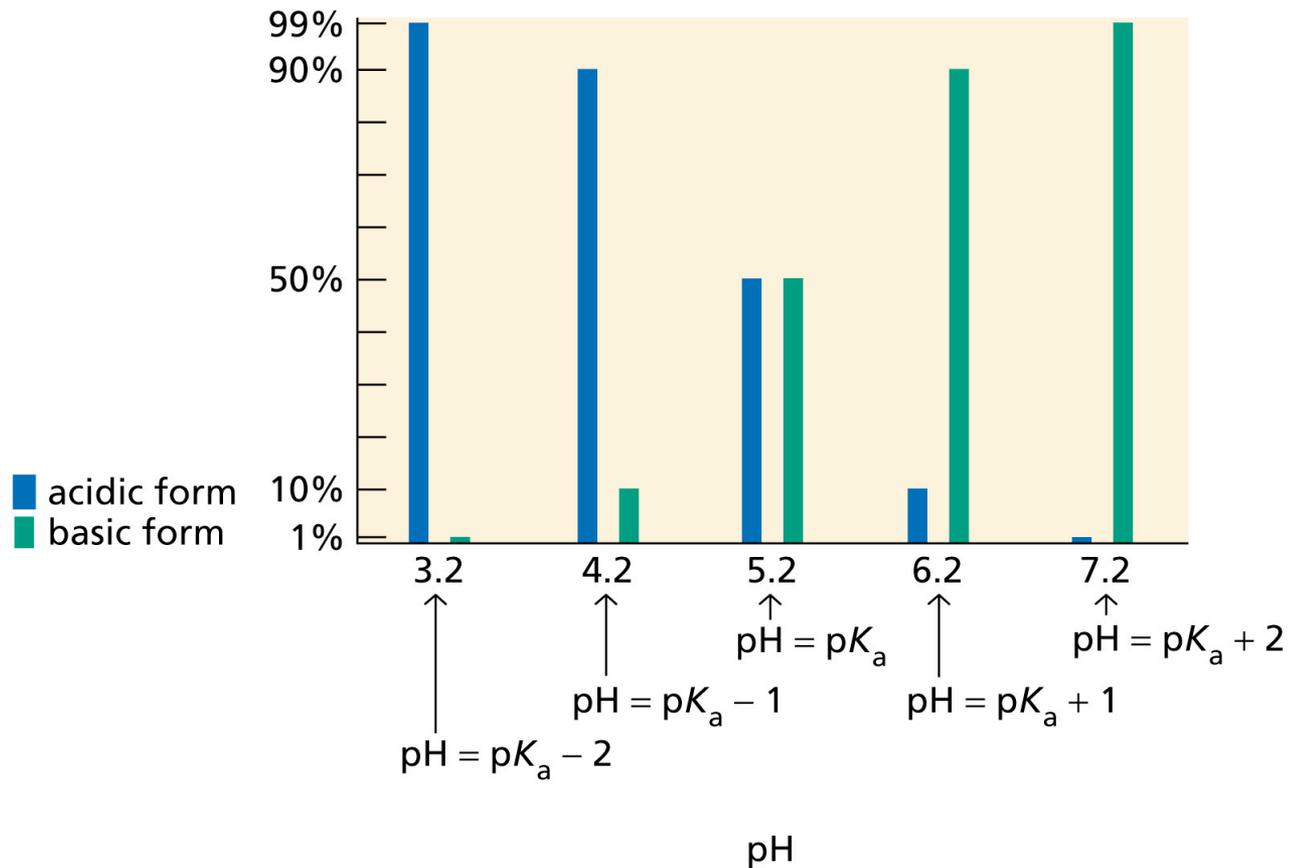


$\text{pK}_a = 15.9$

ethanol



# Acidez de Ácidos Carboxílicos



# Equilíbrio Ácido / Base



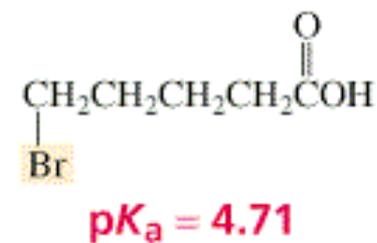
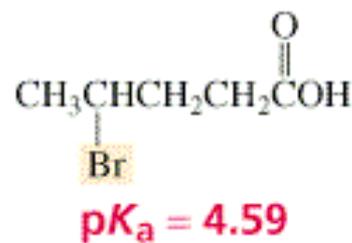
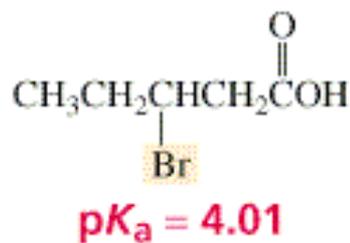
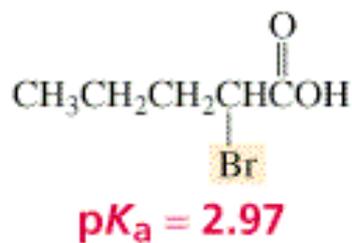
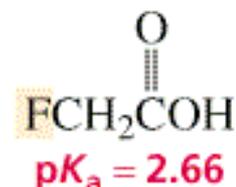
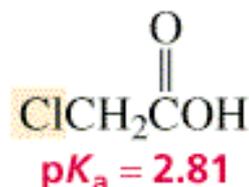
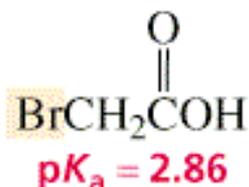
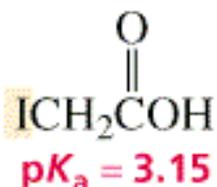
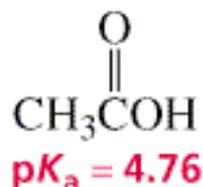
$$K = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{H}_2\text{O}][\text{HA}]} \quad K_a = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]}$$

$$\text{p}K_a = -\log K_a$$

$K$ : Constante de equilíbrio

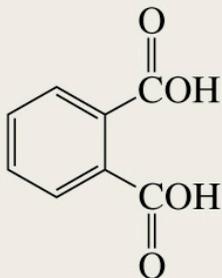
$K_a$ : Constante de dissociação do ácido HA

# Acidez de Ácidos Carboxílicos



- O efeito indutivo atraente de elétrons dos halogênios aumenta a acidez devido a estabilização da base conjugada;
- O efeito depende da eletronegatividade e da distância.

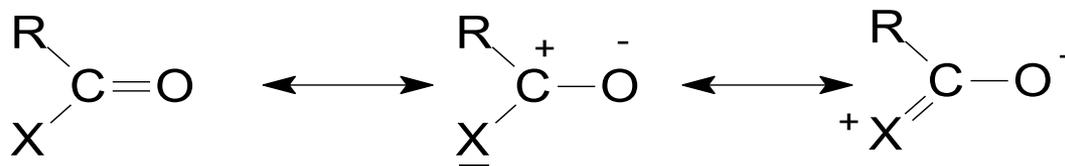
**Table 17.2 Structures, Names, and  $pK_a$  Values of Some Simple Dicarboxylic Acids**

Dicarboxylic acid	Common name	$pK_{a1}$	$pK_{a2}$
$\begin{array}{c} \text{O} \\ \parallel \\ \text{HO} \text{---} \text{COH} \end{array}$	Carbonic acid	3.58	6.35
$\begin{array}{c} \text{O} \quad \text{O} \\ \parallel \quad \parallel \\ \text{HO} \text{C} \text{---} \text{COH} \end{array}$	Oxalic acid	1.27	4.27
$\begin{array}{c} \text{O} \quad \text{O} \\ \parallel \quad \parallel \\ \text{HO} \text{C} \text{CH}_2 \text{COH} \end{array}$	Malonic acid	2.86	5.70
$\begin{array}{c} \text{O} \quad \quad \text{O} \\ \parallel \quad \quad \parallel \\ \text{HO} \text{C} \text{CH}_2 \text{CH}_2 \text{COH} \end{array}$	Succinic acid	4.21	5.64
$\begin{array}{c} \text{O} \quad \quad \quad \text{O} \\ \parallel \quad \quad \quad \parallel \\ \text{HO} \text{C} \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{COH} \end{array}$	Glutaric acid	4.34	5.27
$\begin{array}{c} \text{O} \quad \quad \quad \quad \text{O} \\ \parallel \quad \quad \quad \quad \parallel \\ \text{HO} \text{C} \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{COH} \end{array}$	Adipic acid	4.41	5.28
	Phthalic acid	2.95	5.41



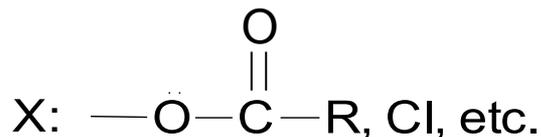
# Reatividade de Derivados de Ácidos Carboxílicos

- derivados de ácidos carboxílicos são geralmente menos reativos frente adição nucleofílica de que aldeídos e cetonas;
- Efeito estabilizador de substituintes em relação aos aldeídos e cetonas:



X: NH<sub>2</sub>, OR, OH :

estabilização  $\pi$  (+M) alta e efeito -I baixo:  
**mais estáveis**



estabilização  $\pi$  (+M) baixa e efeito -I alto:  
**menos estáveis**

relative reactivities of carbonyl compounds toward nucleophiles

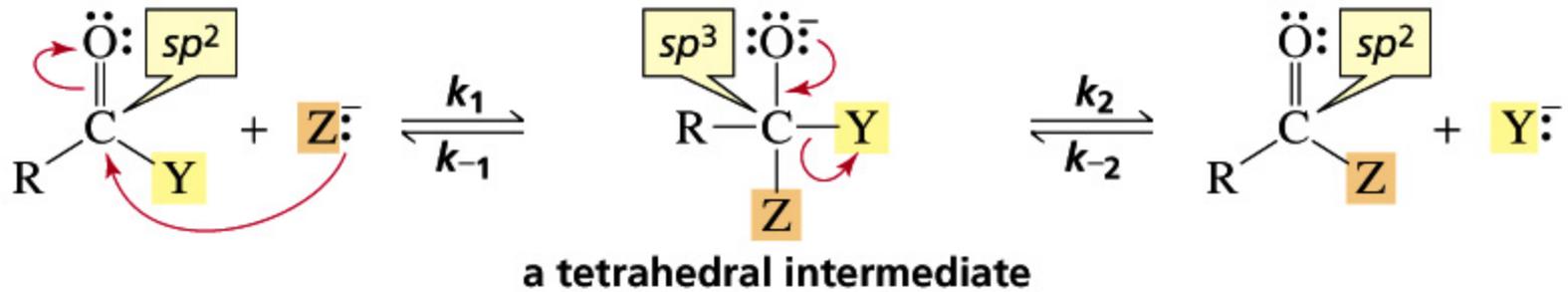
acyl halide > acid anhydride > aldehyde > ketone > ester ~ carboxylic acid > amide > carboxylate ion

most reactive

least reactive

# Reatividade de Derivados de Ácidos Carboxílicos

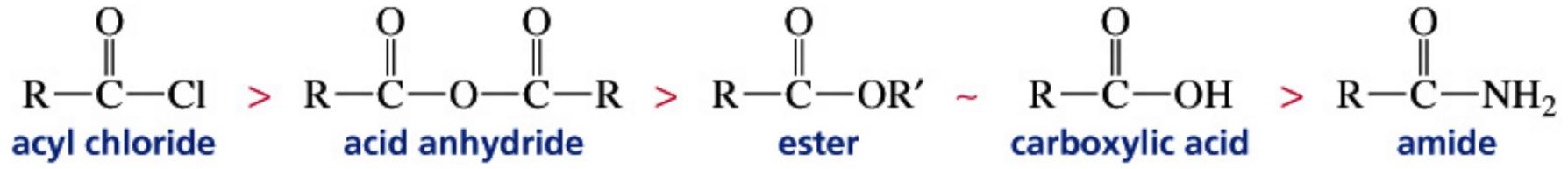
## Reação não catalisada ou catálise básica



Z<sup>-</sup> será expelido se for uma base mais fraca do que Y<sup>-</sup> ( $k_{-1} \gg k_2$ )

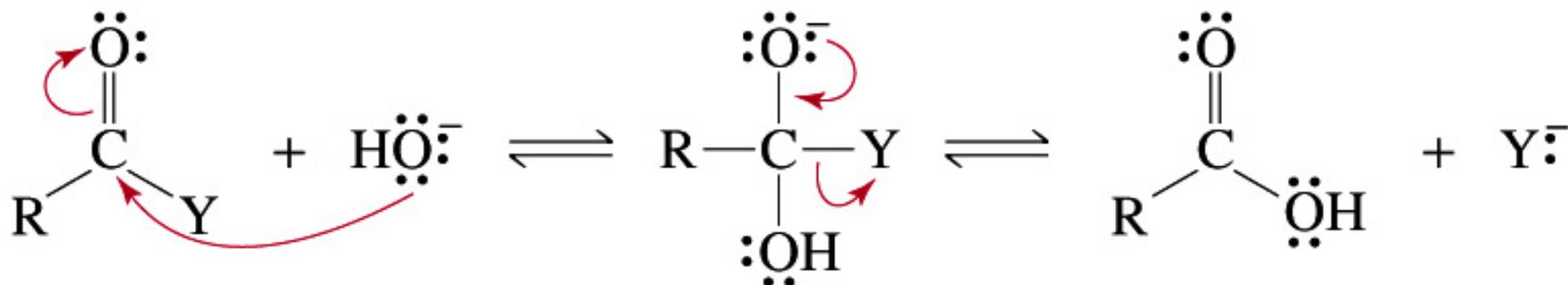
Y<sup>-</sup> será expelido se for uma base mais fraca do que Z<sup>-</sup> ( $k_2 \gg k_{-1}$ )

### relative reactivities of carboxylic acid derivatives



# Mecanismo geral de reação de derivados de ácidos carboxílicos: **Catálise Básica**

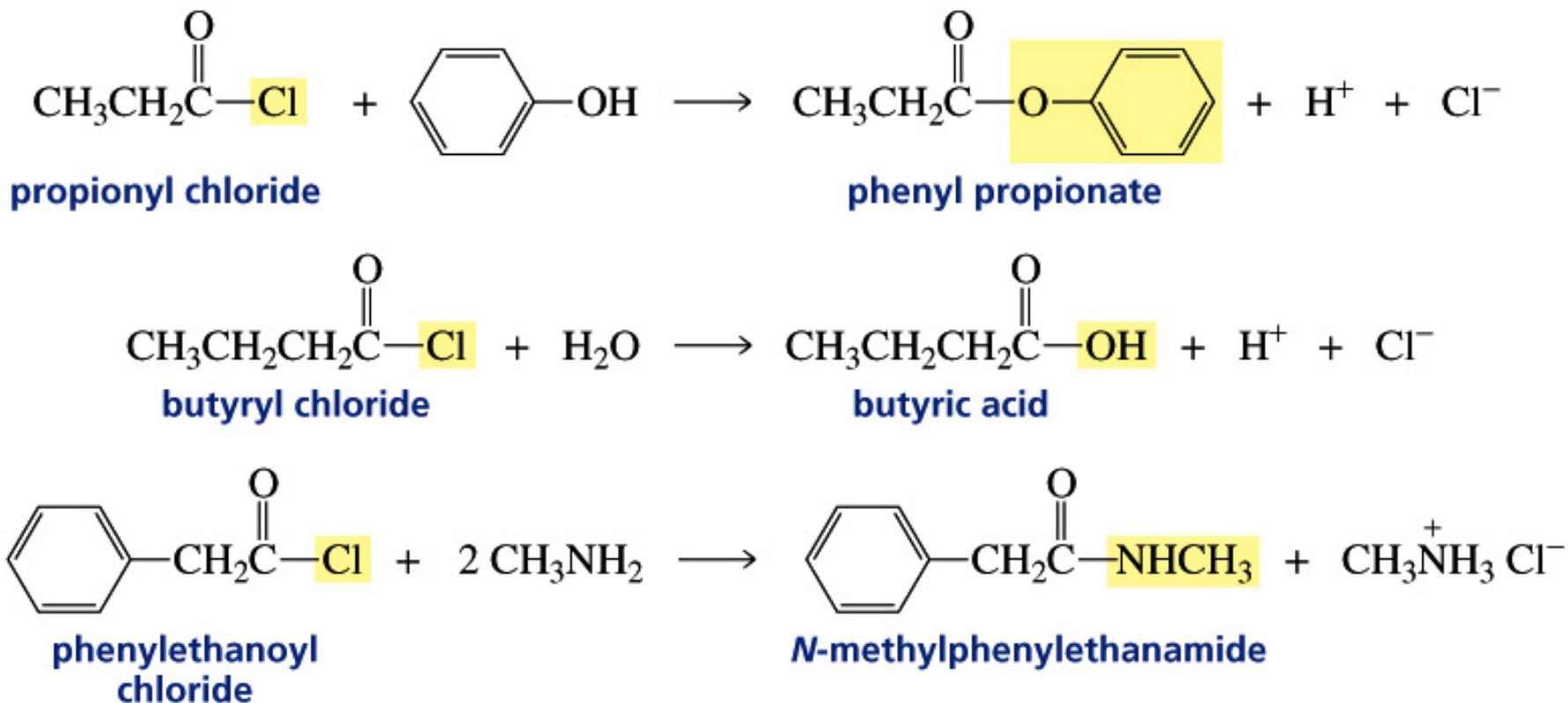
Todos compostos carboxílicos reagem pelo mesmo mecanismo



Mecanismo de Adição / Eliminação com um intermediário tetrahedral, do qual será eliminado o melhor grupo de partida (a base mais fraca).

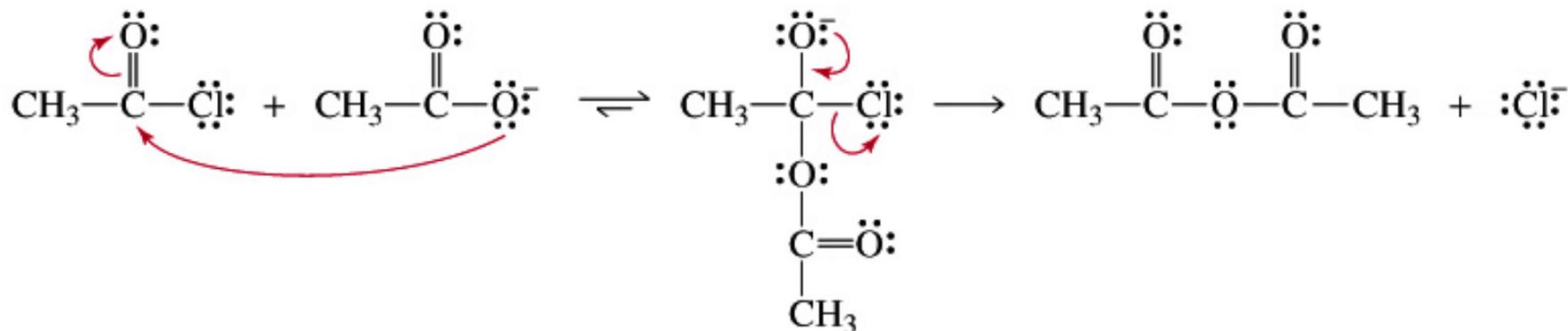
Formulado aqui para a **hidrólise por catálise básica**, porém com outro nucleófilo, o mecanismo é análogo.

## 6.4. Reações de Haletos de Acila

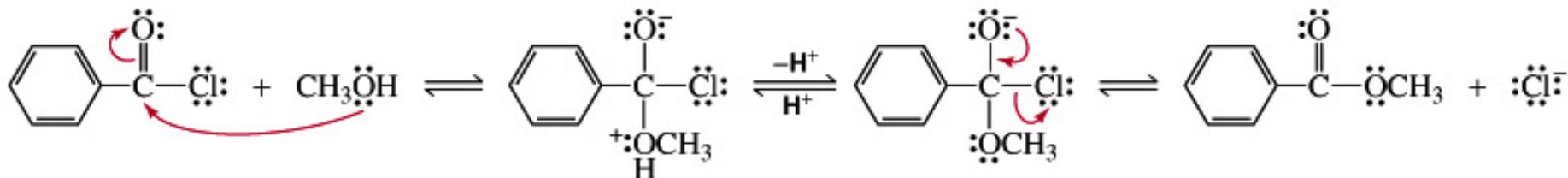


# Mecanismo da Reação de Haletos de Acila

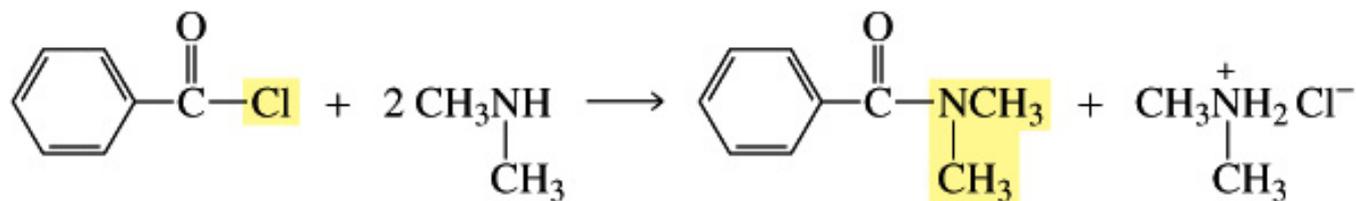
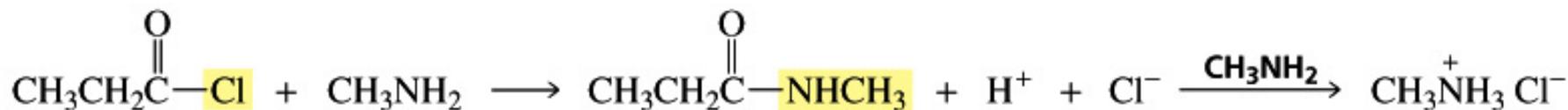
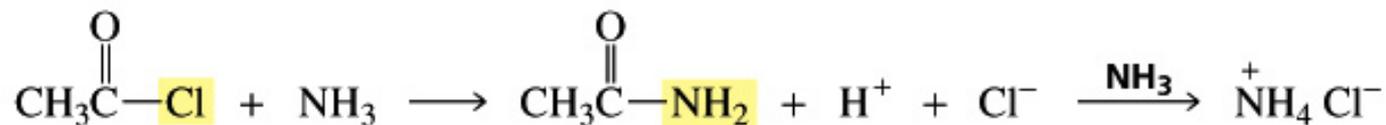
## Conversão em anidridos



## Conversão em ésteres

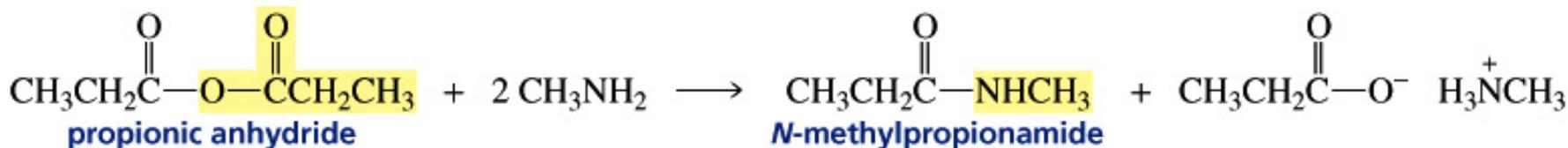
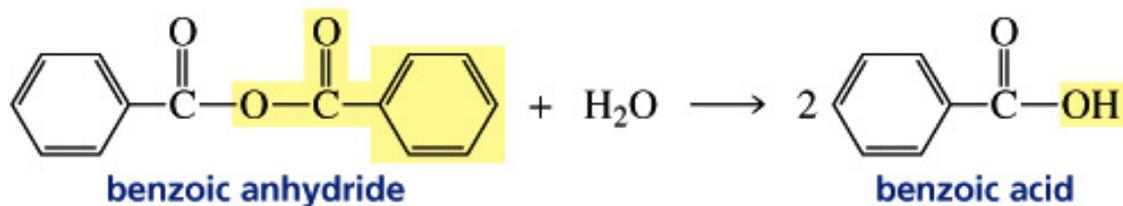
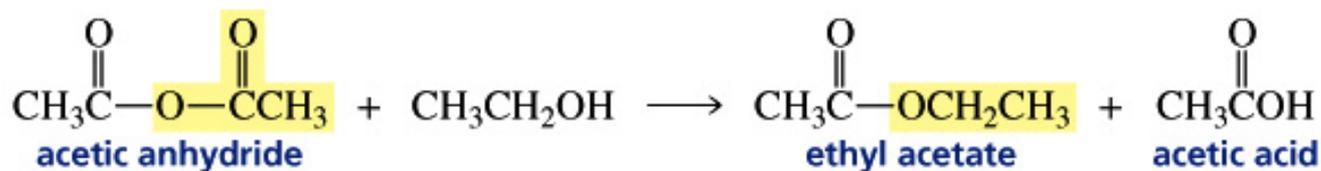


# Formação de Amidas a Partir de Haletos de Acila



Aminas terciárias não podem formar amidas:  
**Porque será??**

## 6.5. Reações de Anidridos de Ácido



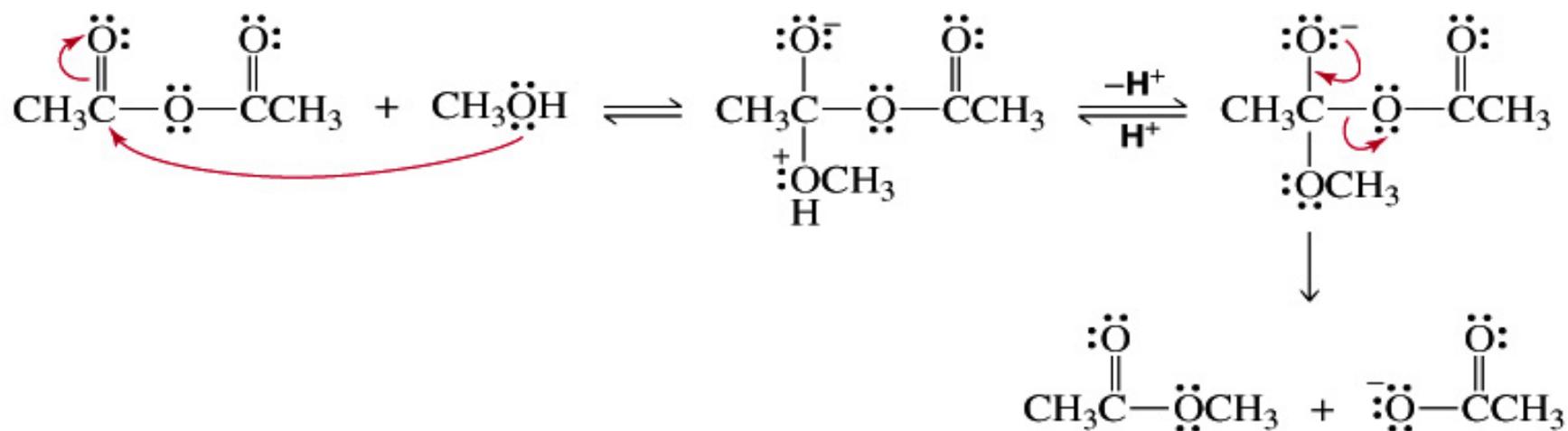
Anidridos não reagem com cloreto ou brometo de sódio

**Porque??**

**Qualidade do grupo de partida??**

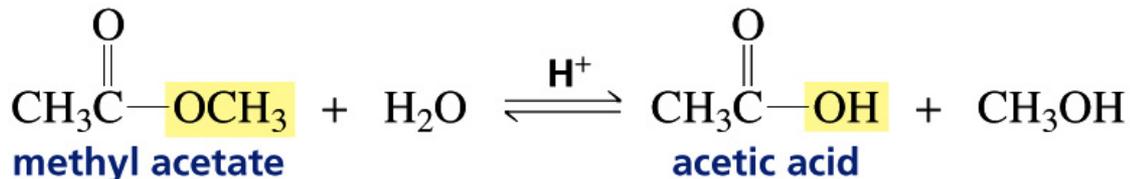
# Conversão de Anidridos em Ésteres

Mecanismo da conversão de um anidrido para um éster (e um ácido carboxílico):

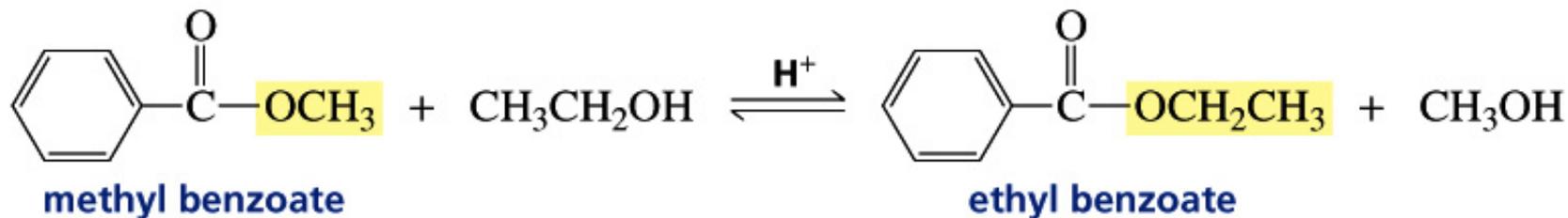


## 6.6. Reação de Ésteres: **Catálise Ácida**

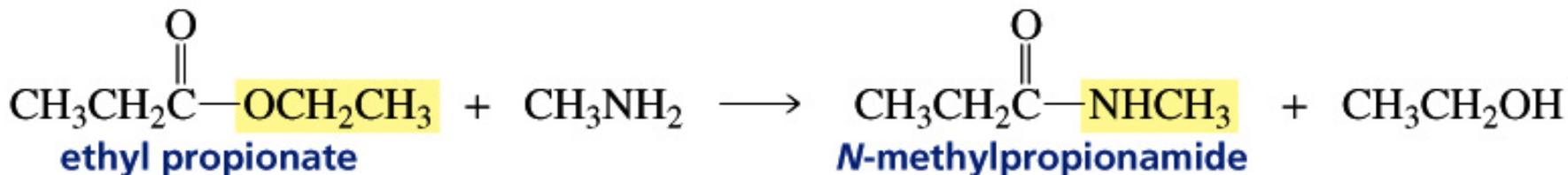
### Hidrólise



### Transesterificação

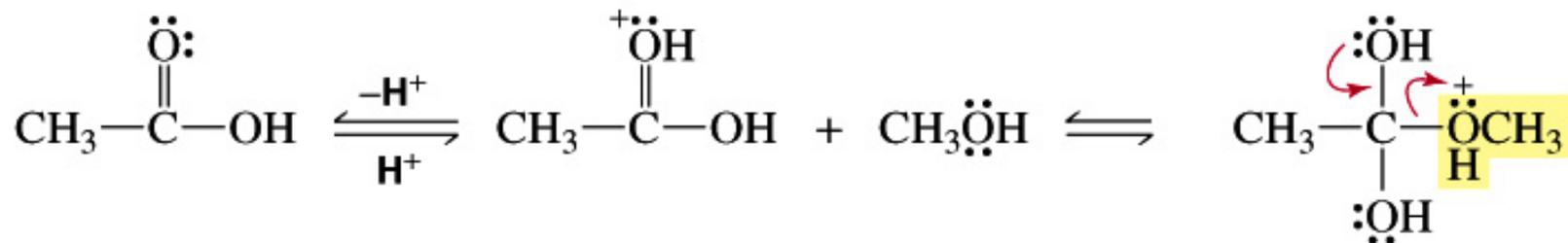
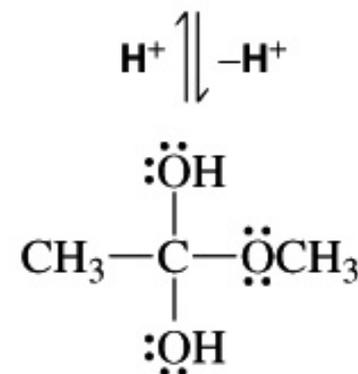
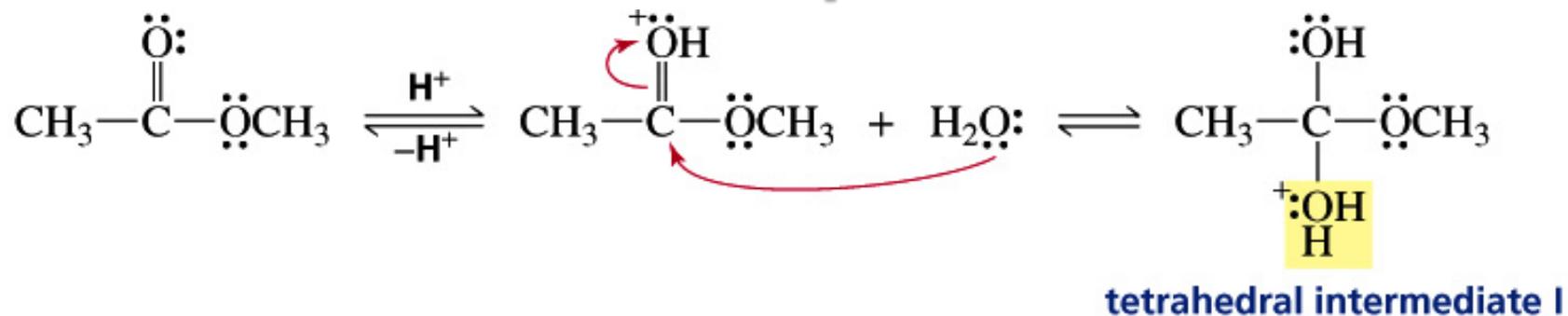


### Aminólise

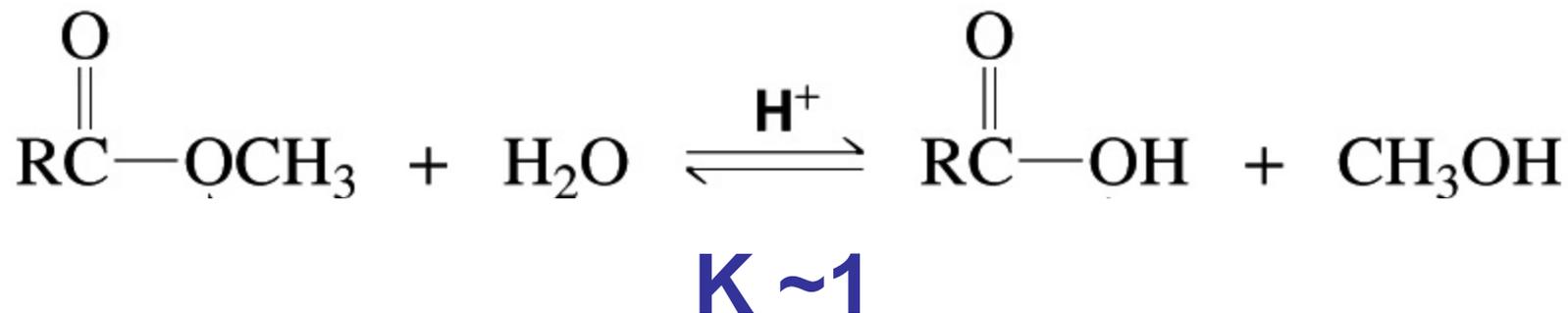


# Mecanismo da Hidrólise de Ésteres

## Catalisada por Ácido



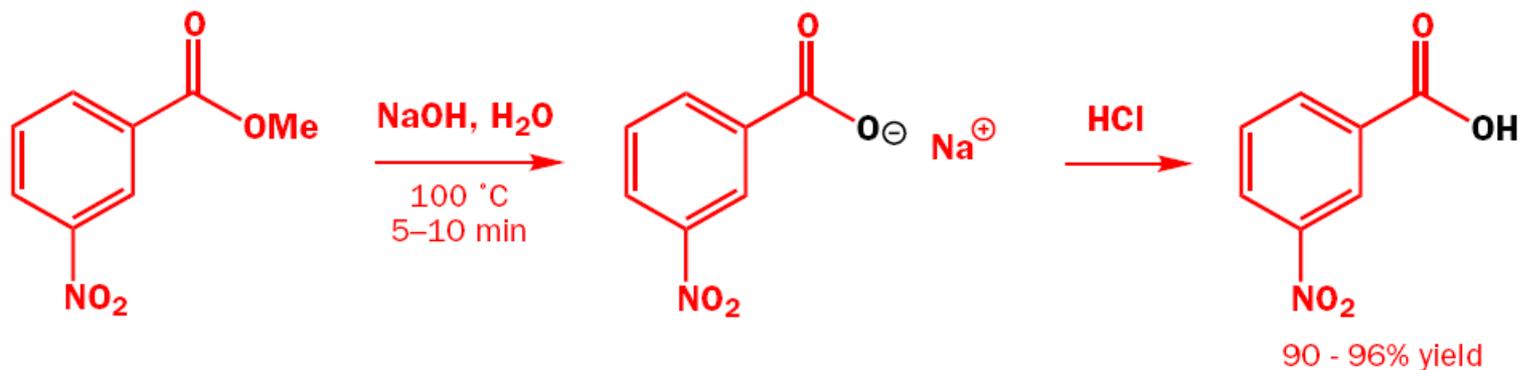
# Constante de Equilíbrio na Esterificação e Hidrólise de Ésteres



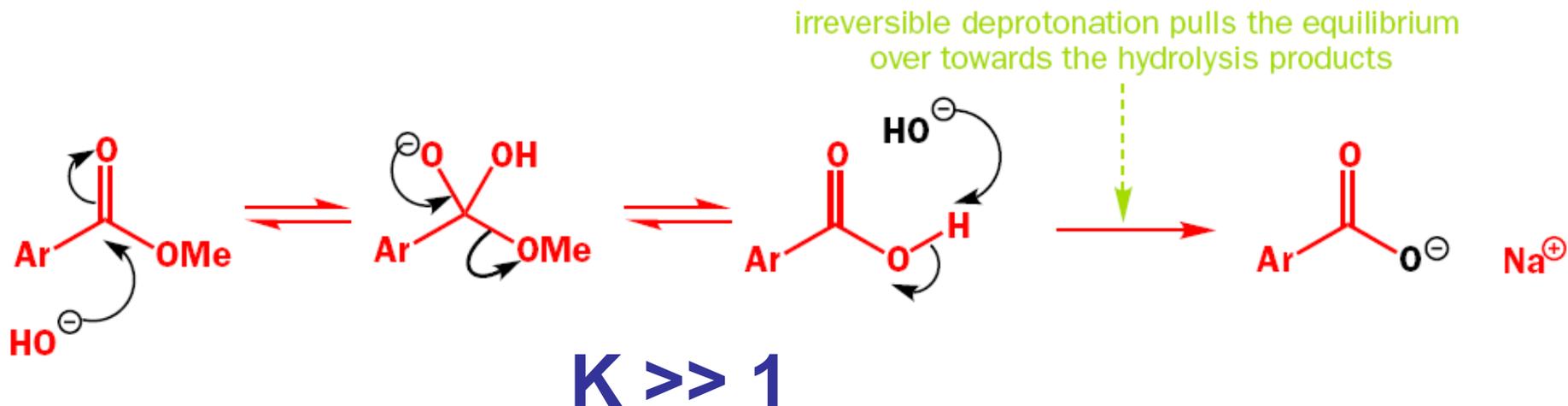
## Deslocar o equilíbrio:

- Excesso de água desloca o equilíbrio para o lado do ácido carboxílico;
- Excesso de álcool desloca o equilíbrio para o lado do éster;
- Remoção de água ou álcool desloca o equilíbrio para o lado do ácido carboxílico e éster, respectivamente.

# Hidrólise de Ésteres: Catalisada por Base

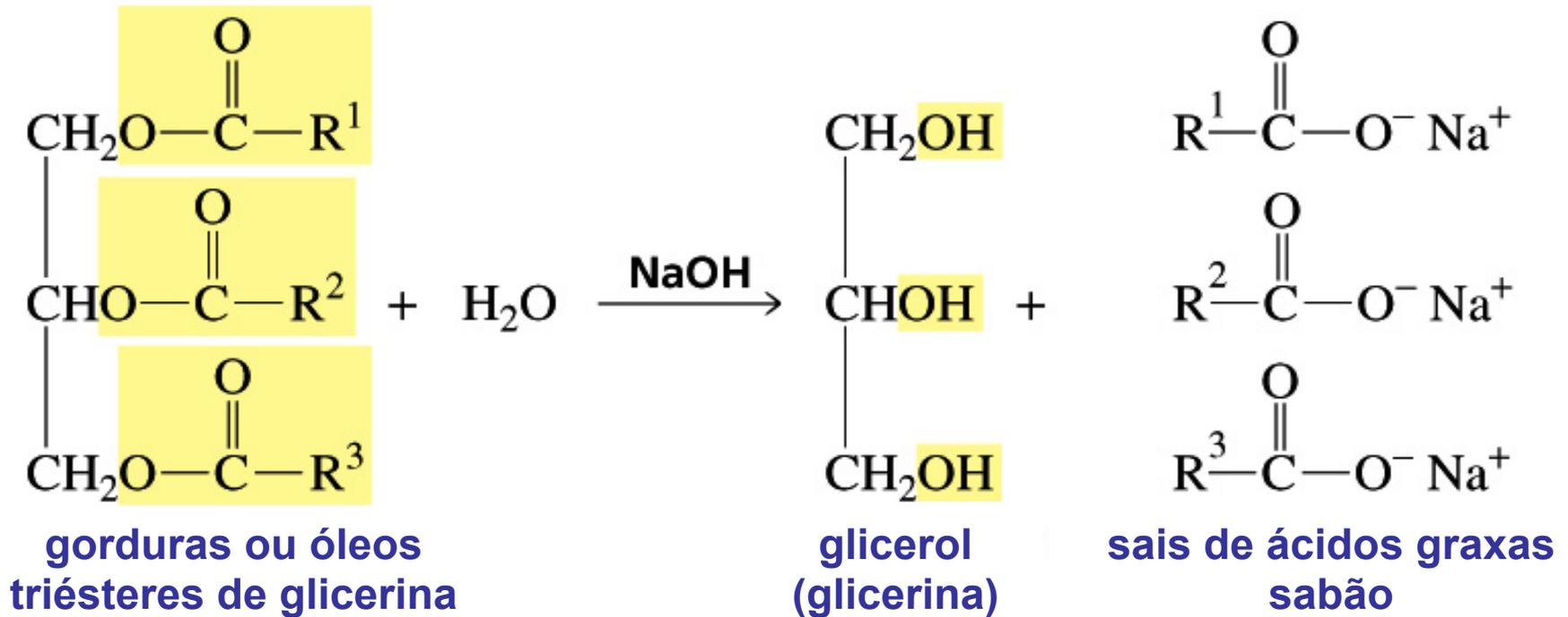


## Mecanismo:



# Hidrólise de Ésteres Catalisada por Base

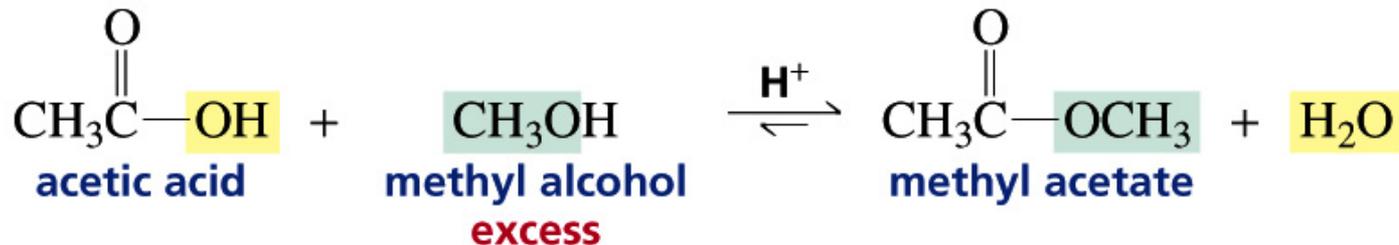
## Saponificação



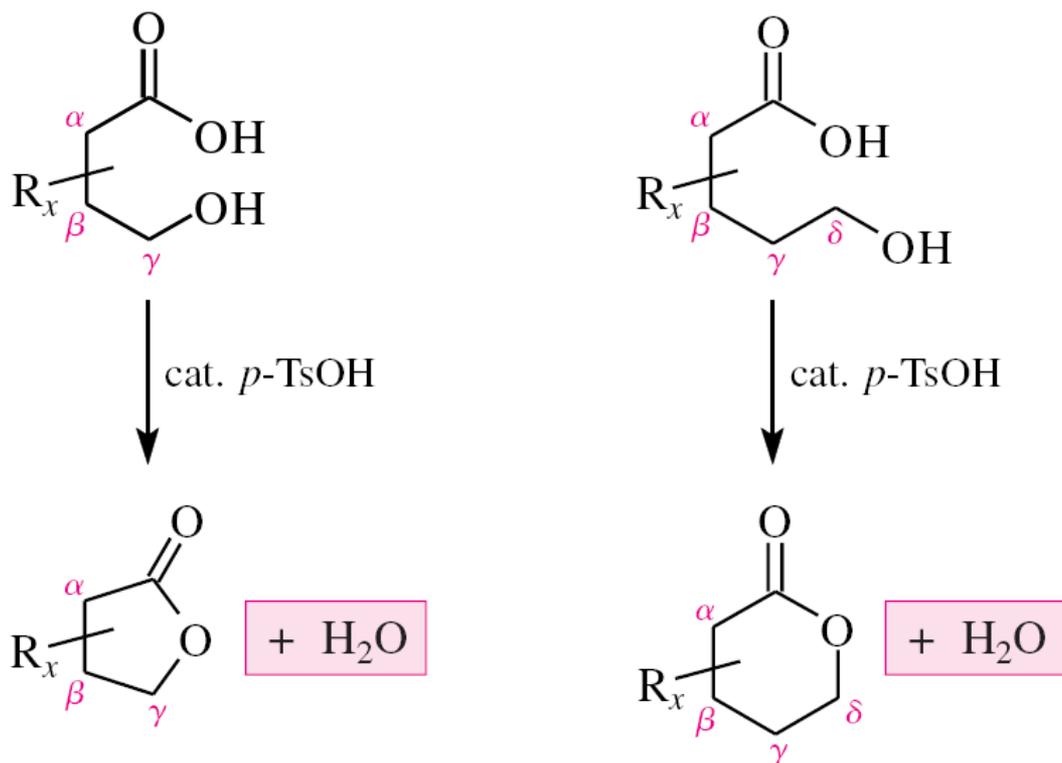
Reação correspondente com álcoois (transesterificação) muito importante para a obtenção de **biodiesel** (ésteres metílicos ou etílicos de ácidos graxas).

# 6.7. Formação de Ésteres: **Catalisada por Ácido**

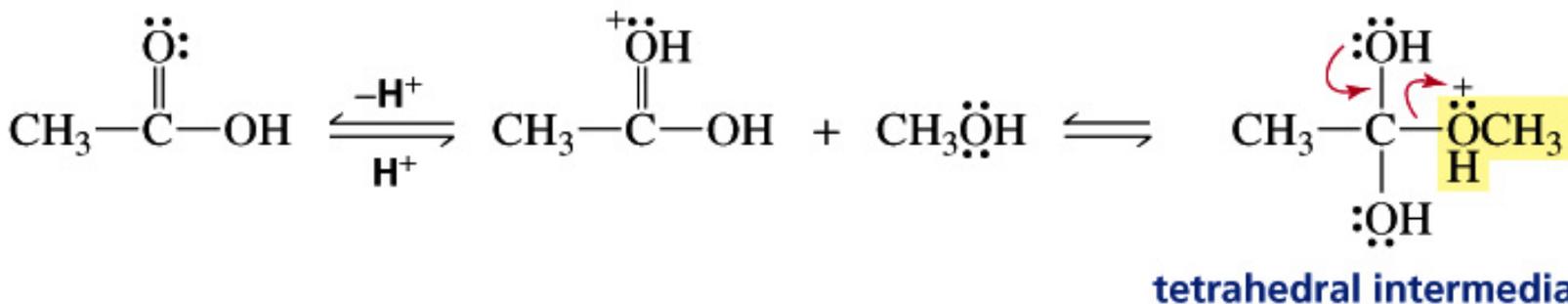
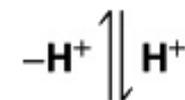
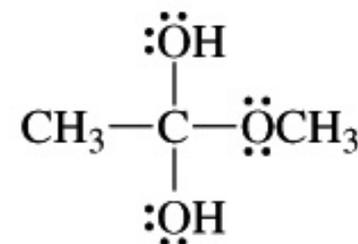
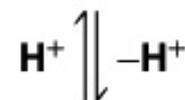
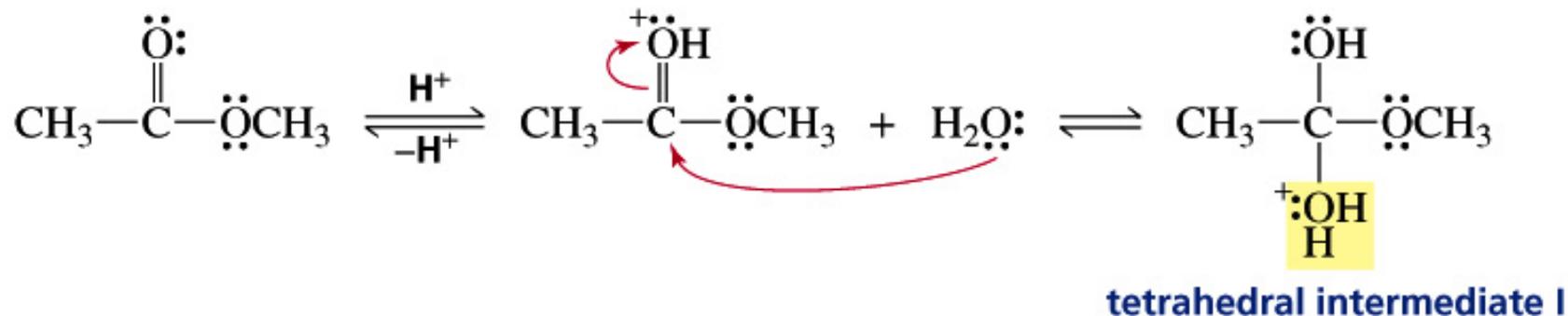
Esterificação de ácidos carboxílicos:



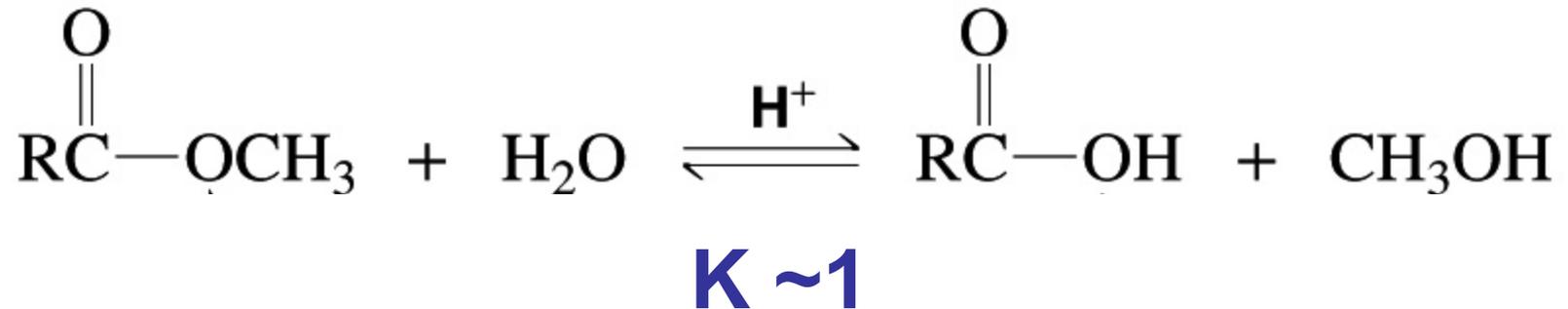
## Esterificação Intramolecular: Formação de Lactonas



# Mecanismo da Esterificação: Catalisada por Ácido



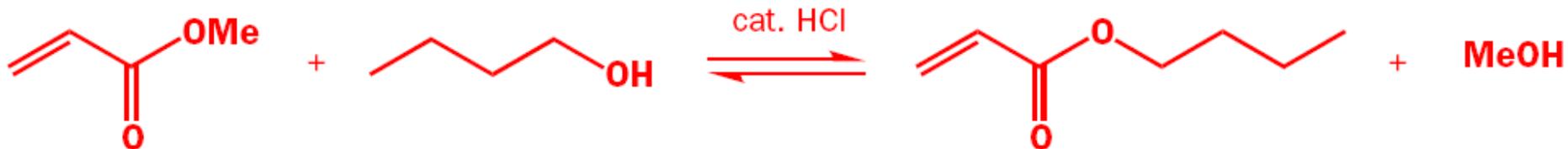
# Equilíbrio na Esterificação



**Deslocar o equilíbrio:**

- **Excesso de álcool** desloca o equilíbrio para o lado do **éster**;
- **Remoção de água** desloca o equilíbrio para o lado do **éster**.

# Reação de Transesterificação



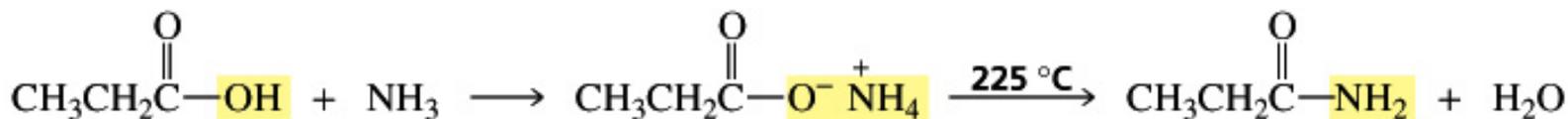
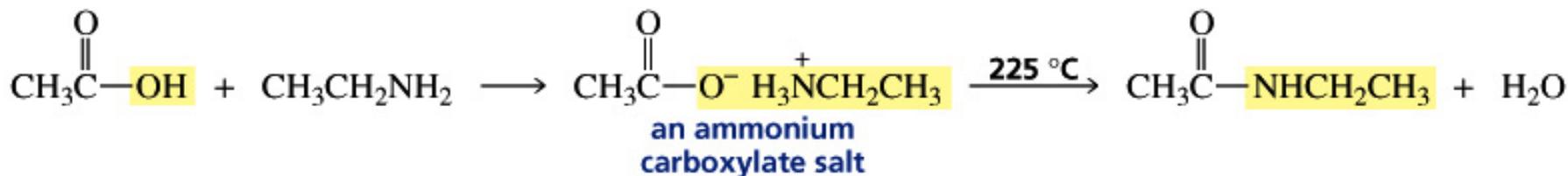
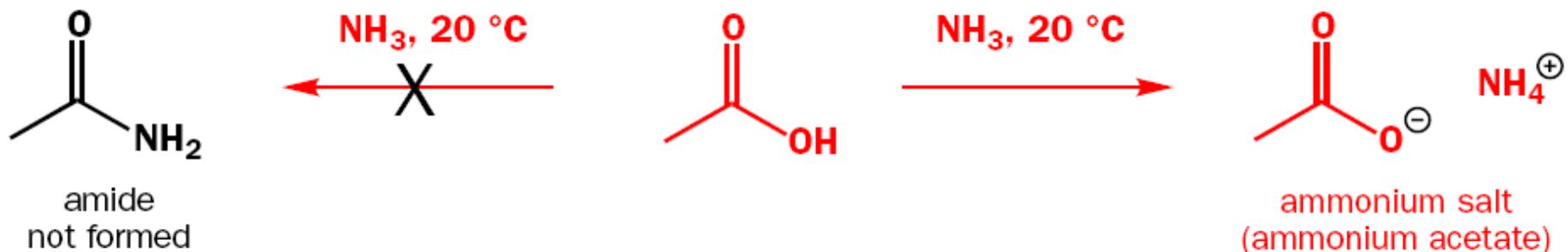
Transesterificações têm normalmente uma constante de equilíbrio cerca de 1, mas em alguns casos o equilíbrio pode ser deslocado.

Como isso poderia ser feito?

O mecanismo destas reações é análogo ao de hidrólise.

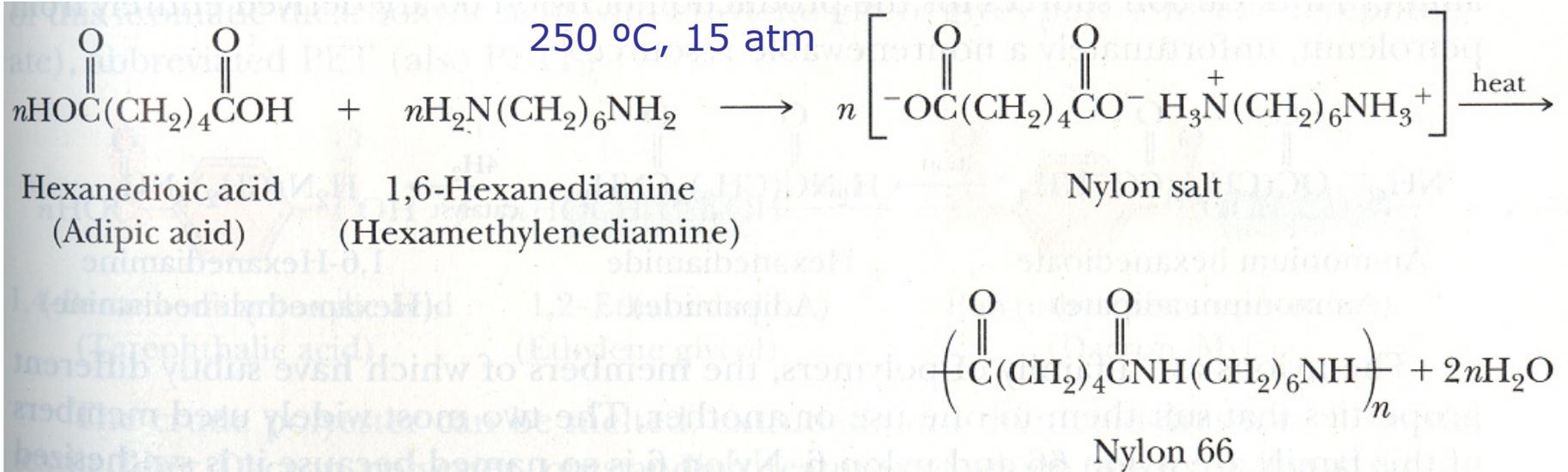
## 6.8. Formação e Reações de Amidas

Formação a partir de ácidos carboxílicos:

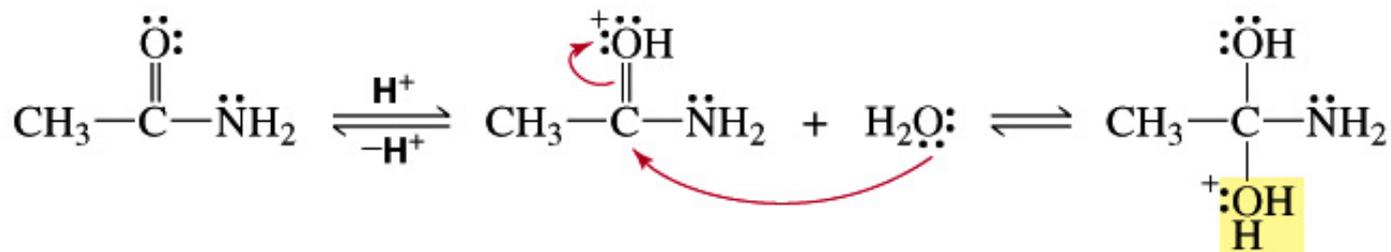


Ácidos carboxílicos não sofrem reações de substituição acílica **direta** com aminas. Reação ocorre via sal de amônio.

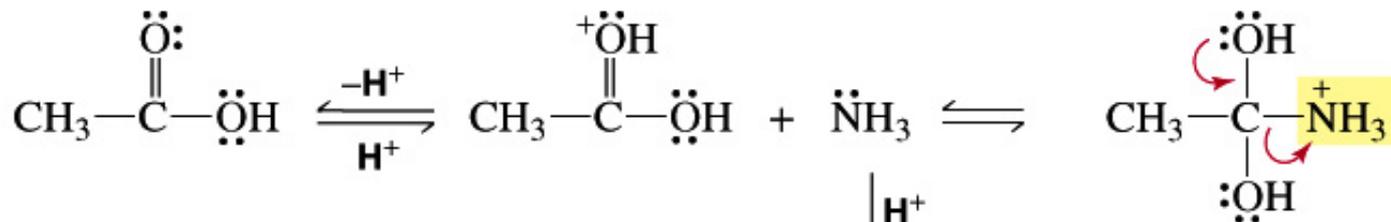
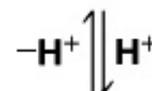
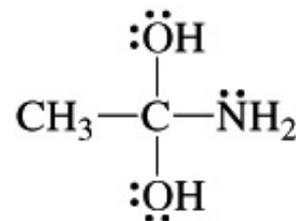
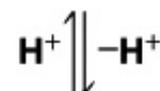
# Preparação de Amidas a partir de Ácidos Carboxílicos: Aplicação



# Mecanismo da Hidrólise de Amidas



tetrahedral intermediate I

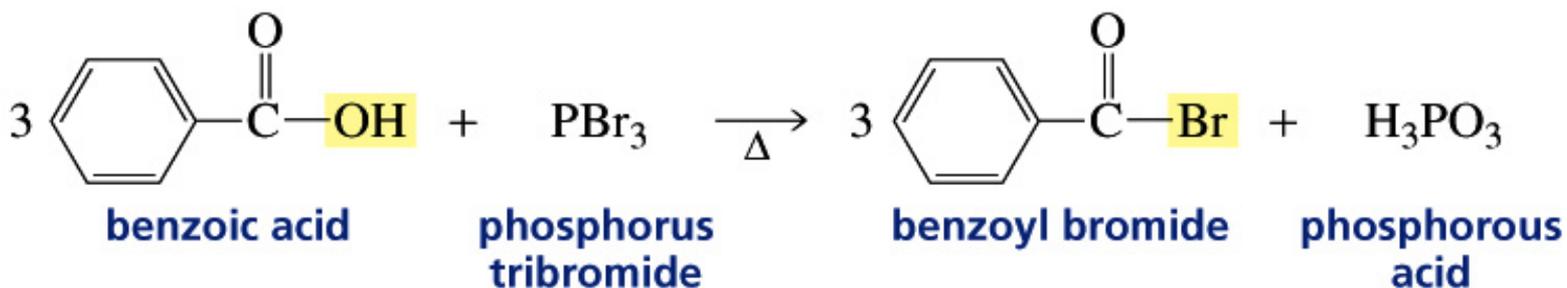
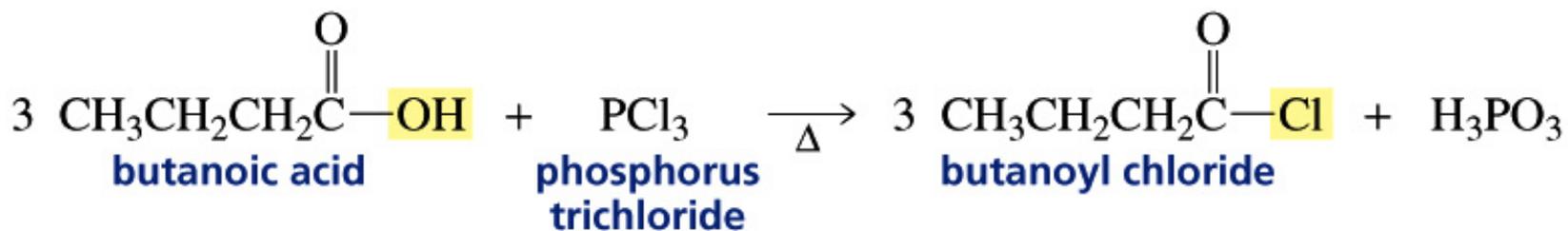
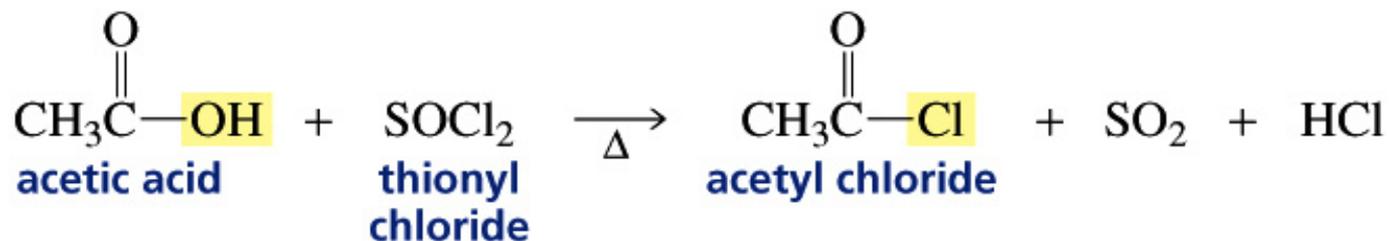


tetrahedral intermediate II

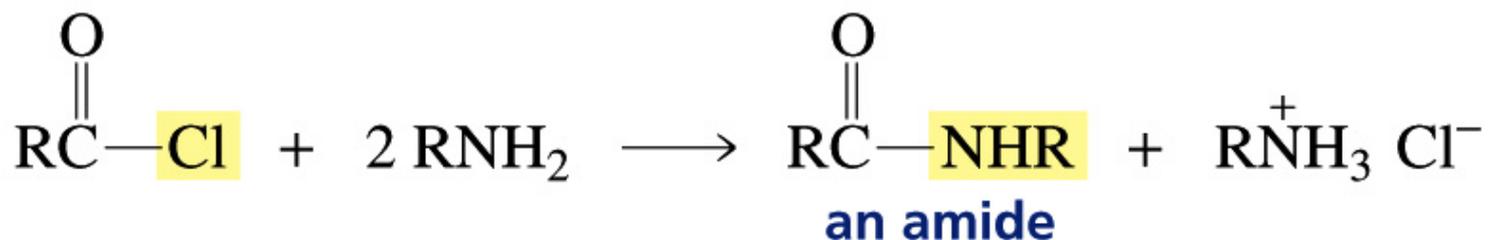
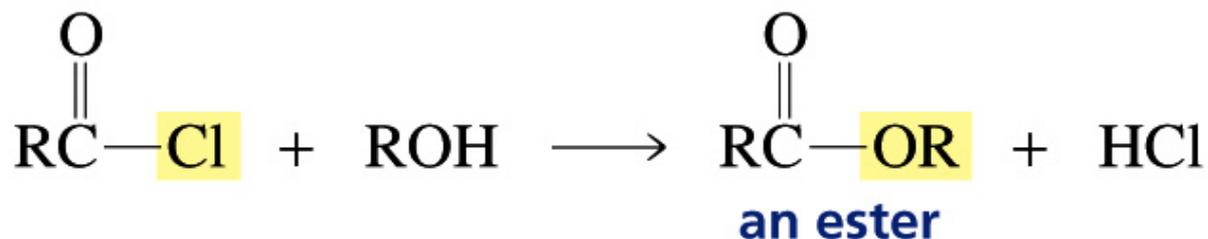
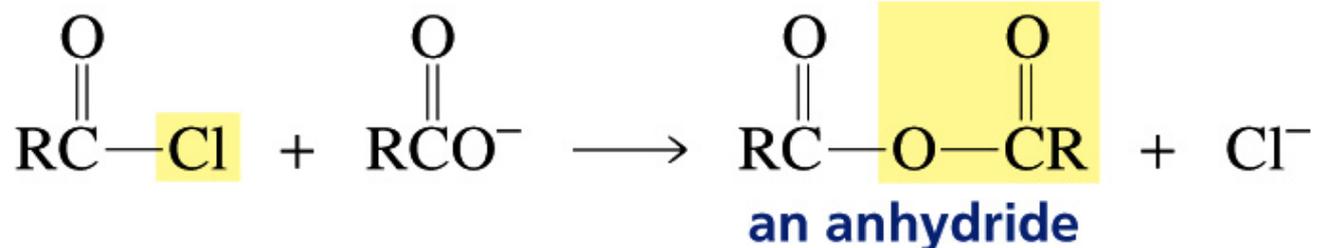


A reação ocorre melhor por catálise ácida:  
**Grupo de partida amônia é boa; amideto não é bom grupo de partida.**

## 6.9. Ativação de Ácidos Carboxílicos: Preparação de Haletos de Acila



# Haleto de Acila na Preparação de Derivados Carboxílicos



## **6.10. Reações de Oxidação e Redução de Compostos Orgânicos**

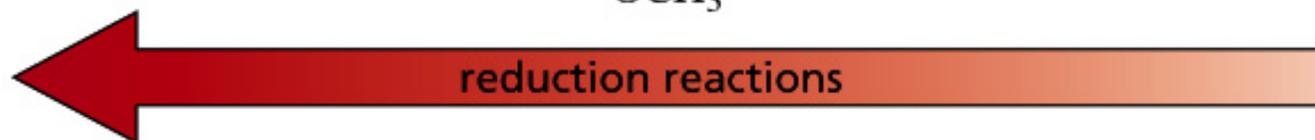
# Número de Oxidação 'Formal' de Compostos Orgânicos



## OXIDATION STATE

number of C-Z bonds  
(Z = O, N, or halogen)

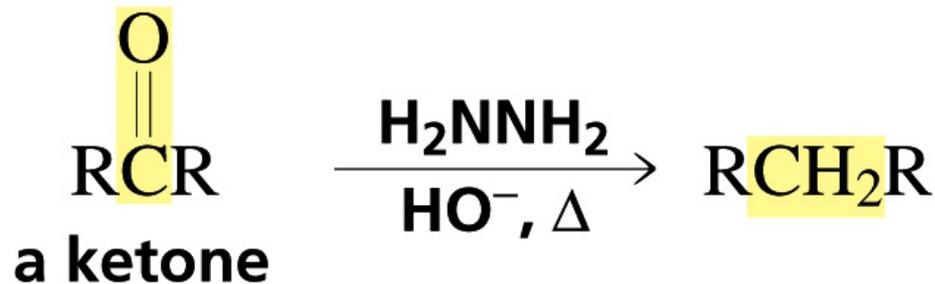
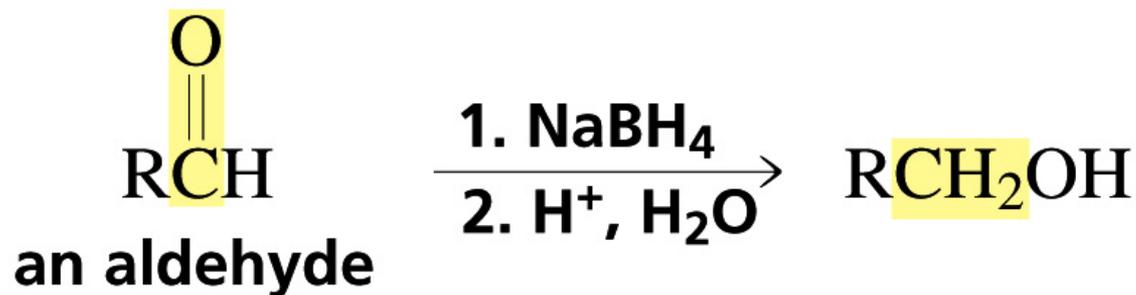
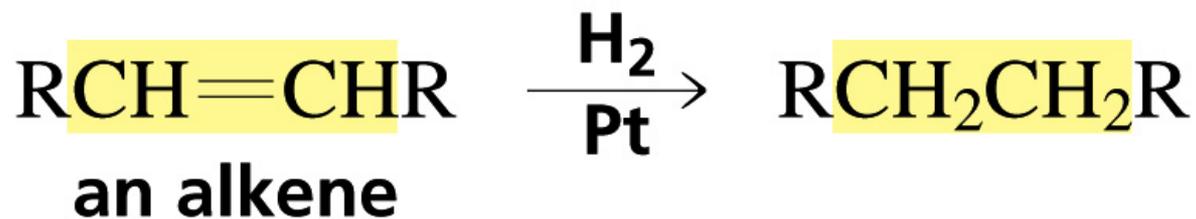
0	1	2	3	4
CH <sub>4</sub>	CH <sub>3</sub> OH	$\begin{array}{c} \text{O} \\    \\ \text{HCH} \end{array}$	$\begin{array}{c} \text{O} \\    \\ \text{HCOH} \end{array}$	O=C=O
	CH <sub>3</sub> OCH <sub>3</sub>	$\begin{array}{c} \text{O} \\    \\ \text{CH}_3\text{CCH}_3 \end{array}$	$\begin{array}{c} \text{O} \\    \\ \text{CH}_3\text{COCH}_3 \end{array}$	$\begin{array}{c} \text{O} \\    \\ \text{CH}_3\text{OCOCH}_3 \end{array}$
		$\begin{array}{c} \text{NCH}_3 \\    \\ \text{CH}_3\text{CCH}_3 \end{array}$	$\begin{array}{c} \text{O} \\    \\ \text{CH}_3\text{CNH}_2 \end{array}$	$\begin{array}{c} \text{O} \\    \\ \text{CH}_3\text{OCNHCH}_3 \end{array}$
		$\begin{array}{c} \text{OCH}_3 \\   \\ \text{CH}_3\text{CCH}_3(\text{H}) \\   \\ \text{OCH}_3 \end{array}$	$\begin{array}{c} \text{O} \\    \\ \text{CH}_3\text{CCl} \end{array}$	$\begin{array}{c} \text{O} \\    \\ \text{ClCCl} \end{array}$



**Porém:** existe outra escala para os números de oxidação formais que é mais adequada. Nesta escala o H é contado com polarização positiva.

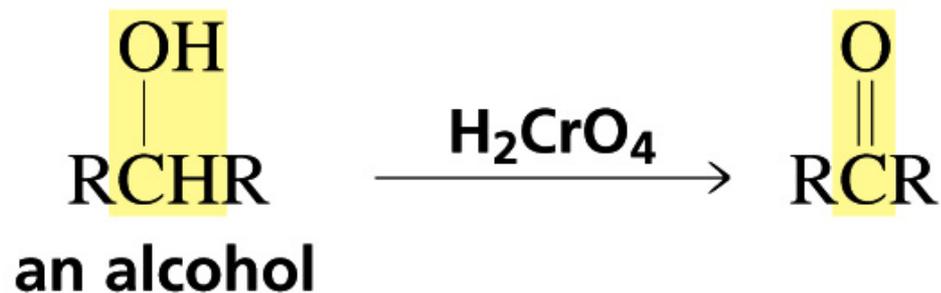
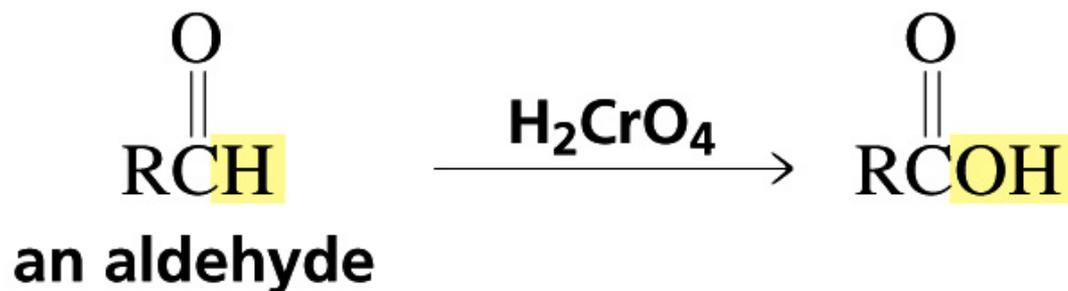
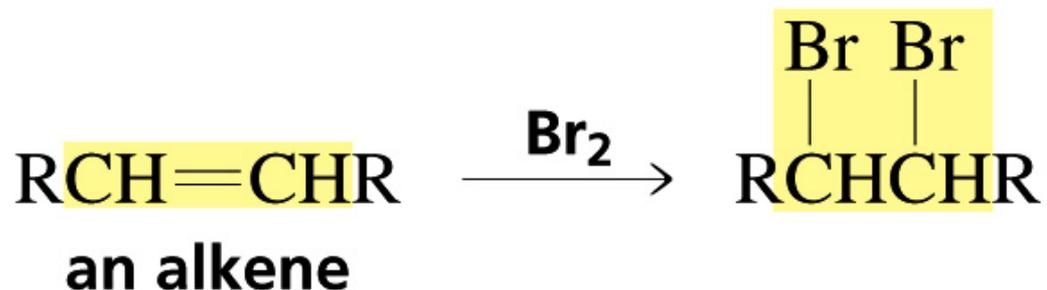
# Redução de Compostos Orgânicos:

Hidrogenação catalítica, hidretos complexos, Wolff-Kishner

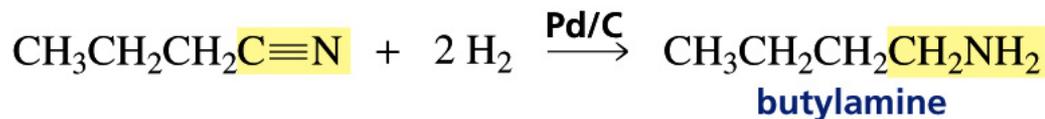
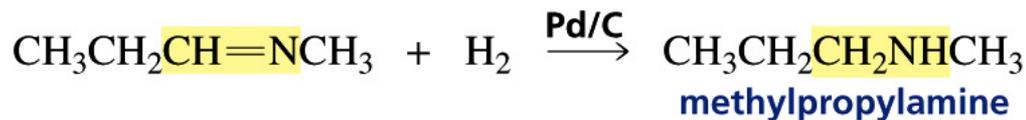
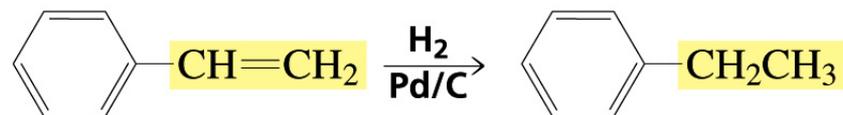
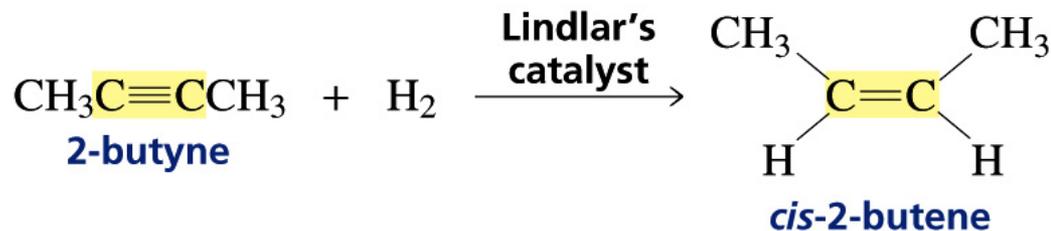
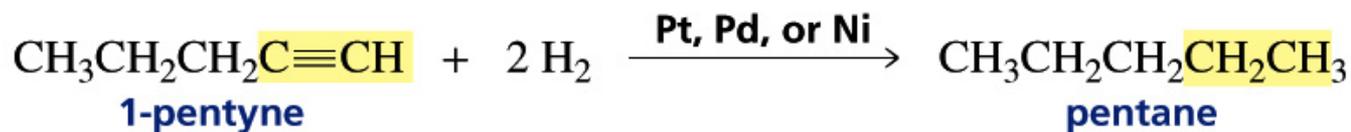


# Oxidação de Compostos Orgânicos:

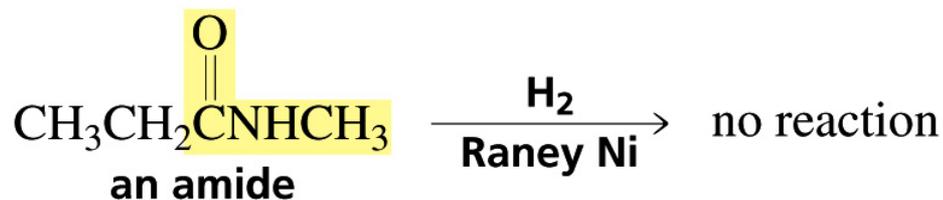
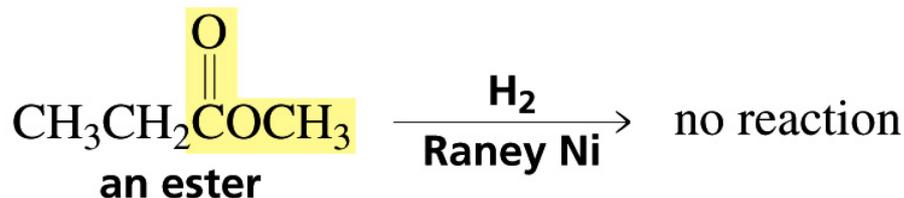
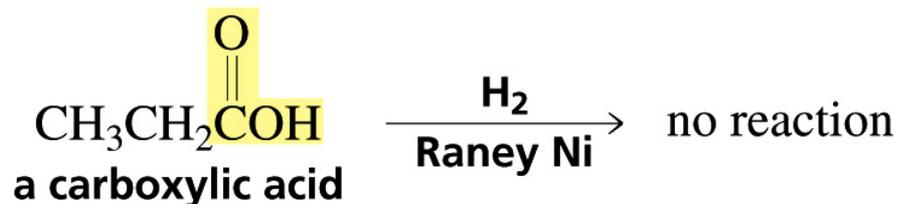
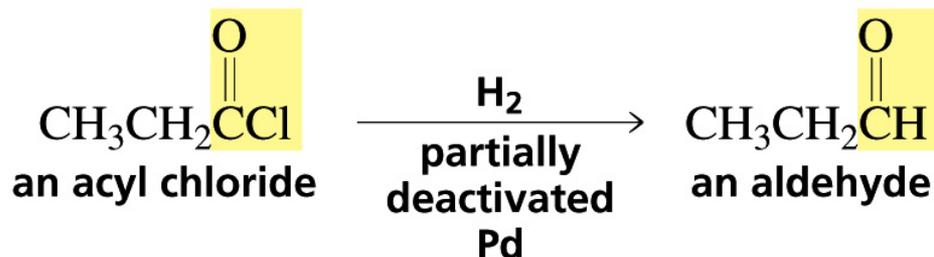
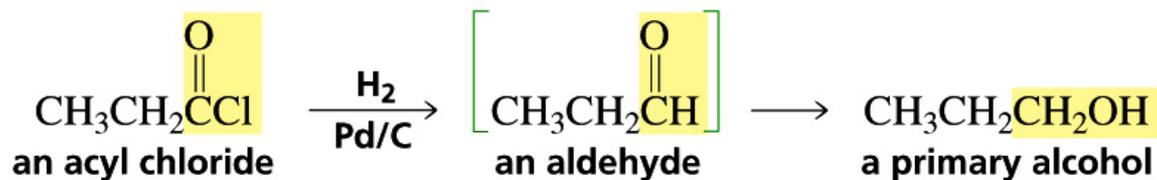
Bromo, ácido crômico



# Redução por Hidrogenação Catalítica

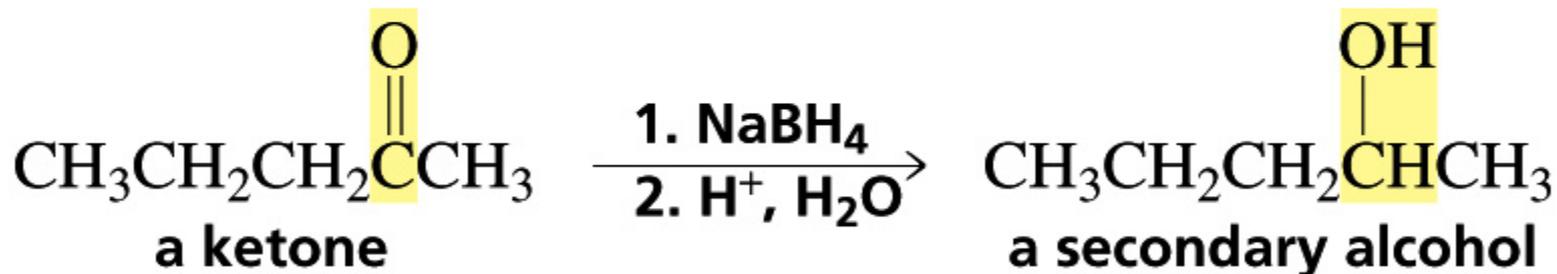
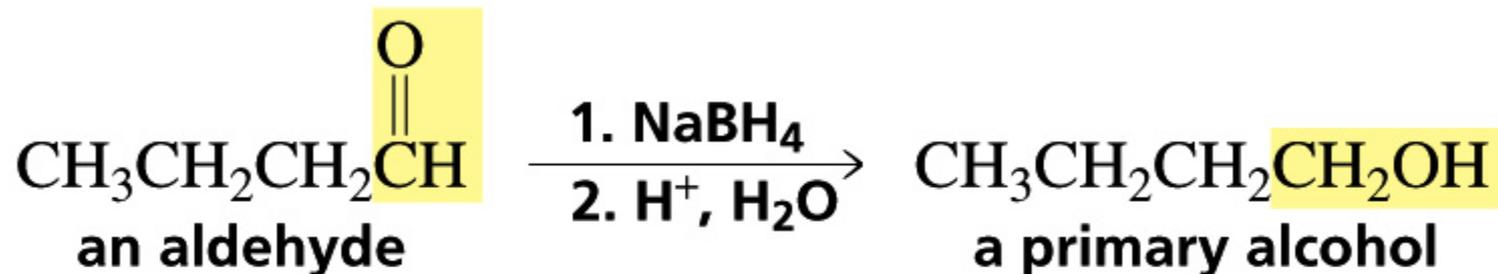


# Redução por Hidrogenação Catalítica



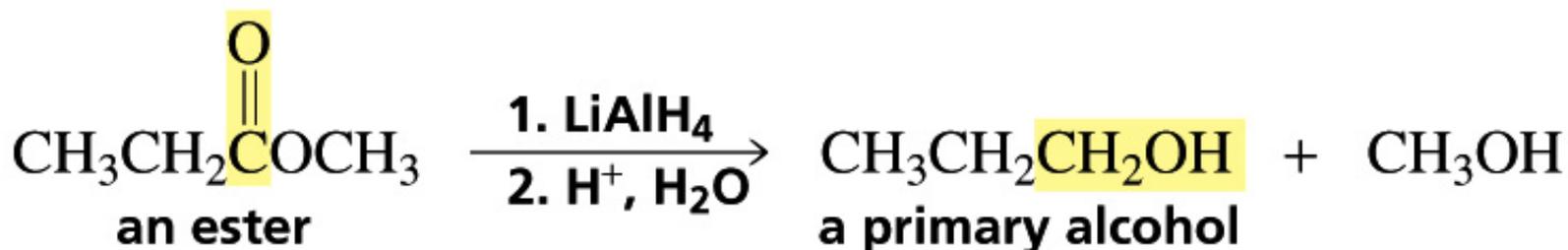
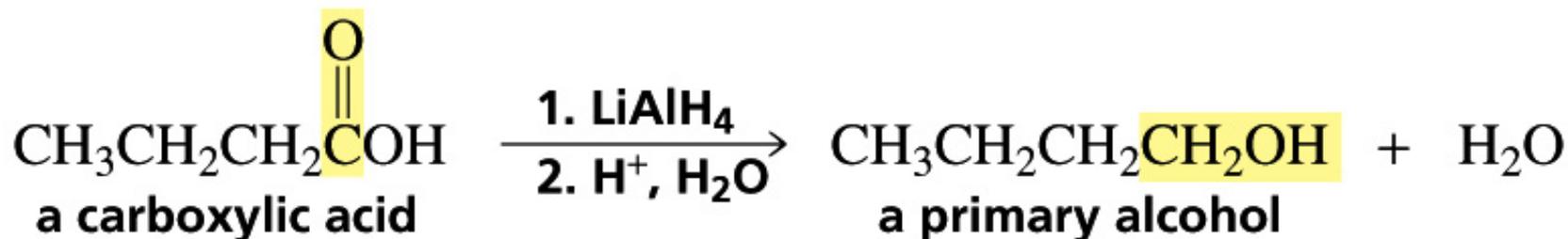
# Redução de Compostos Carbonílicos:

Adição de Íon Hidreto, seguido de protonação



# Redução de Compostos Carboxílicos:

## Utilizando-se Hidreto de Lítio Alumínio

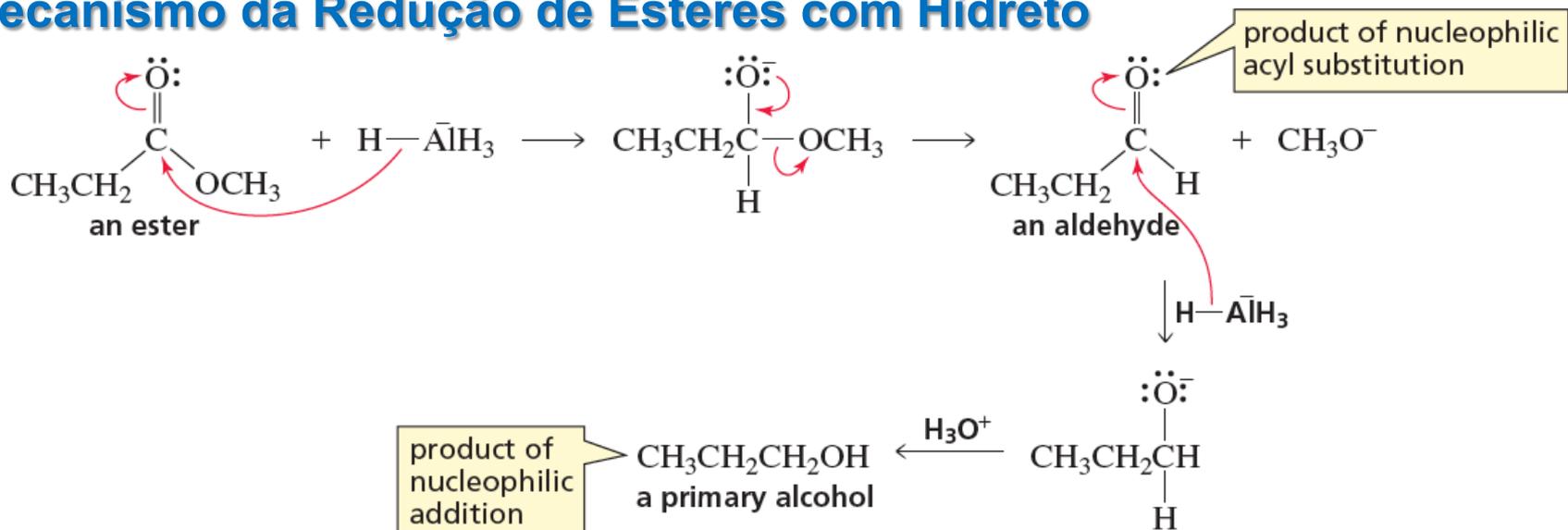


$\text{LiAlH}_4$  é agente redutor mais forte do que  $\text{NaBH}_4$ ;

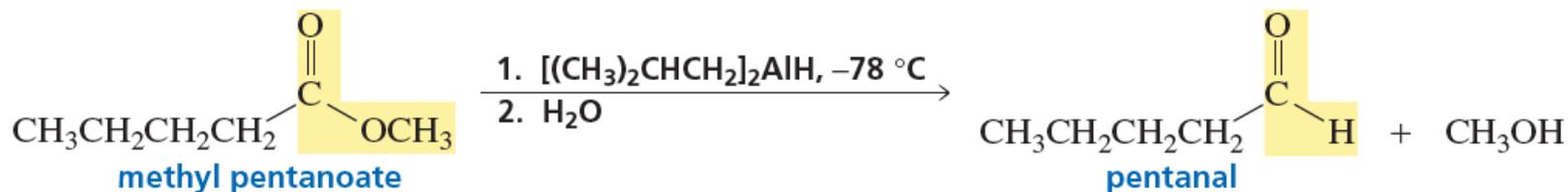
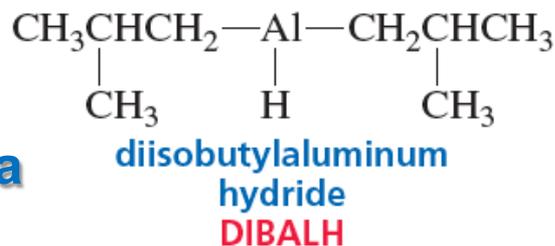
$\text{LiAlH}_4$  é usado para reduzir composto que não reagem com  $\text{NaBH}_4$  como ácidos carboxílicos.

# Redução de Derivados de Ácidos Carboxílicos

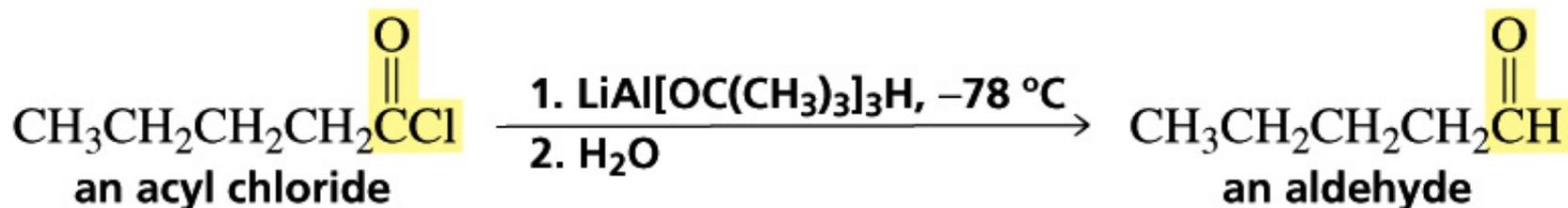
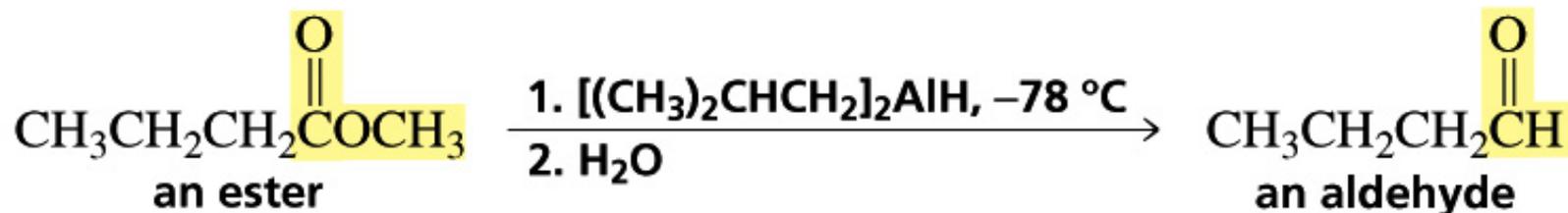
## Mecanismo da Redução de Ésteres com Hidreto



## Redução de Ésteres para Aldeídos: DIBALH



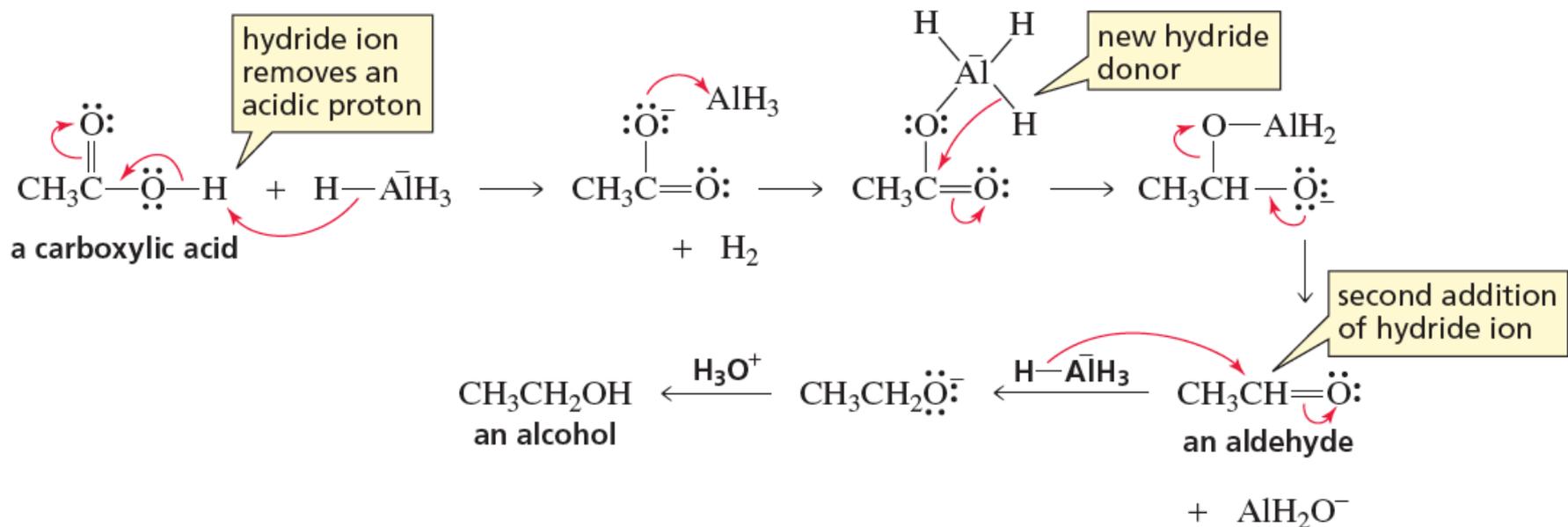
# Redução de Ésteres e Cloretos de Ácido para o Aldeído Correspondente com DIBAL



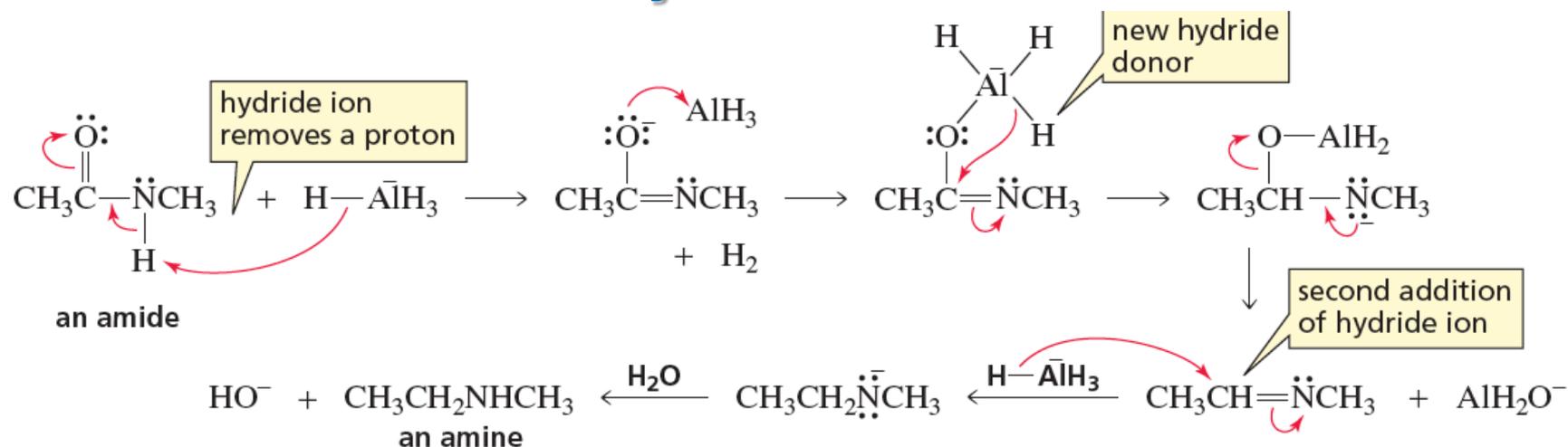
**DIBAL** permite a adição de somente um hidreto ao éster.

A substituição de hidrogênios do  $\text{LiAlH}_4$  por grupos OR leva a uma diminuição da reatividade do reagente.

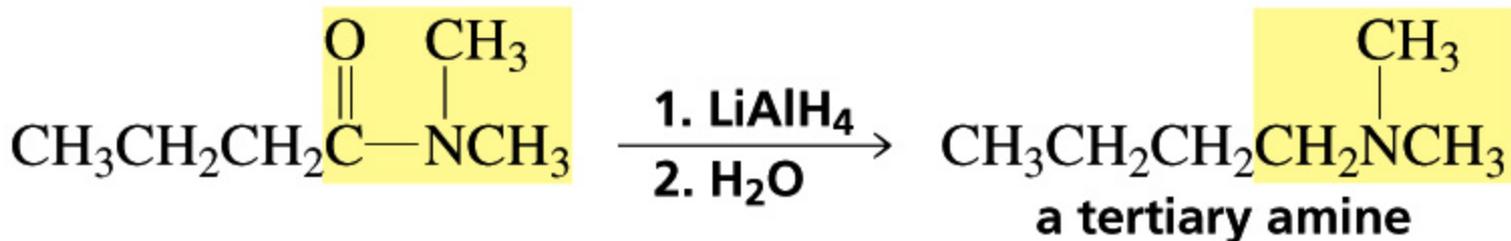
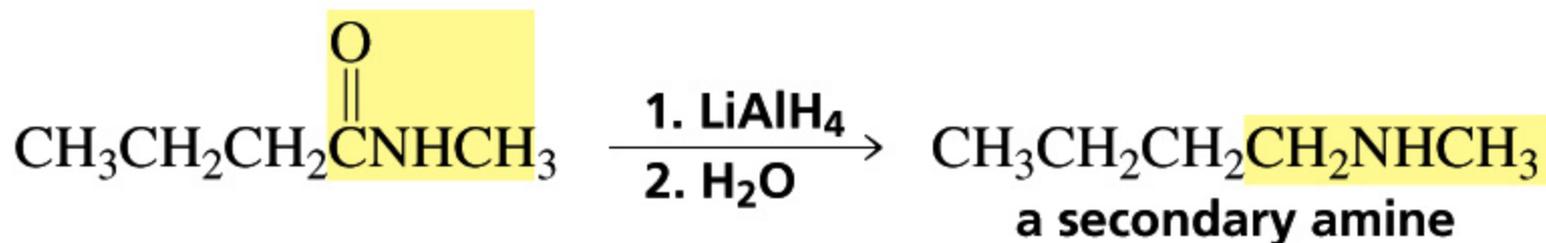
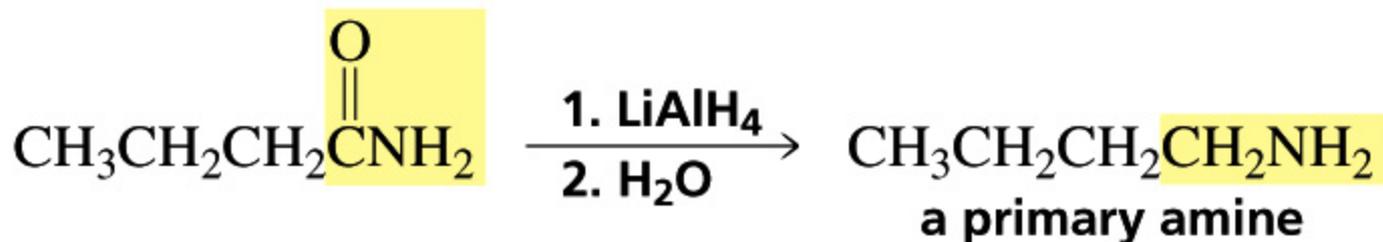
# Mecanismo da Redução de Ácidos Carboxílicos com Hidreto



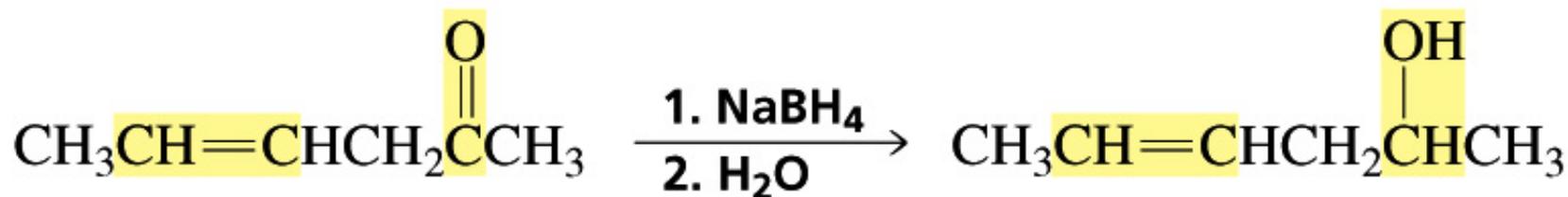
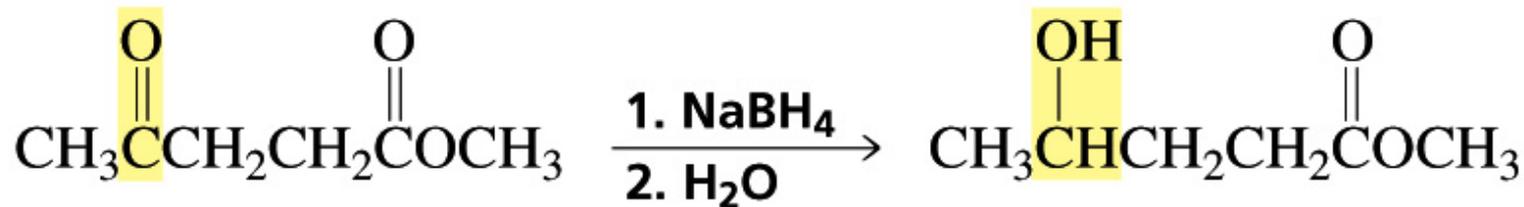
# Mecanismo da Redução de Amidas com Hidreto



# Formação de Aminas por Redução

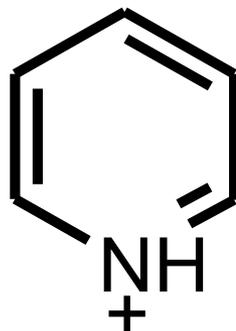
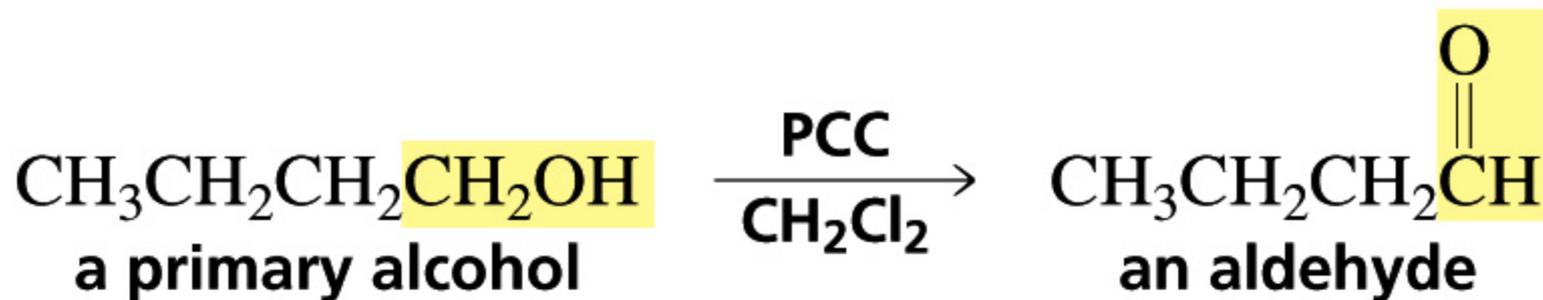


# Redução Seletiva de Aldeídos e Cetonas com $\text{NaBH}_4$



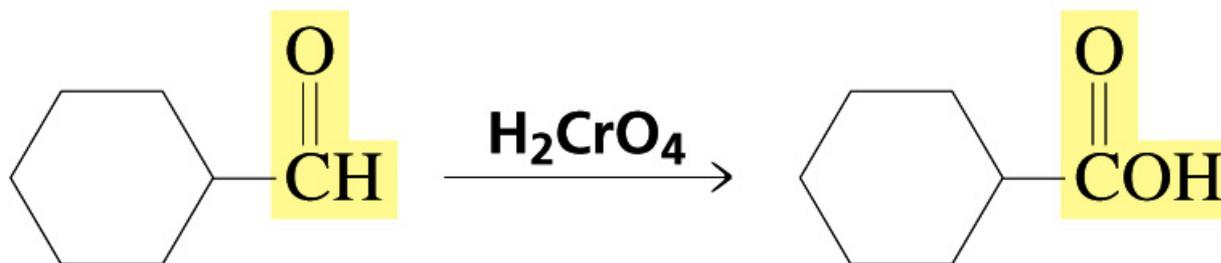
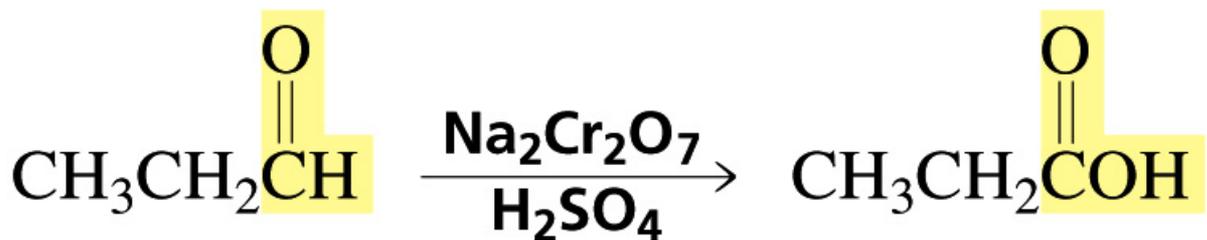


# Oxidação Seletiva de Alcóois Primários para Aldeídos com PCC



**A oxidação de um álcool primário pode ser interrompida no aldeído se piridínio clorocromato (PCC) for usado como agente de oxidação.**

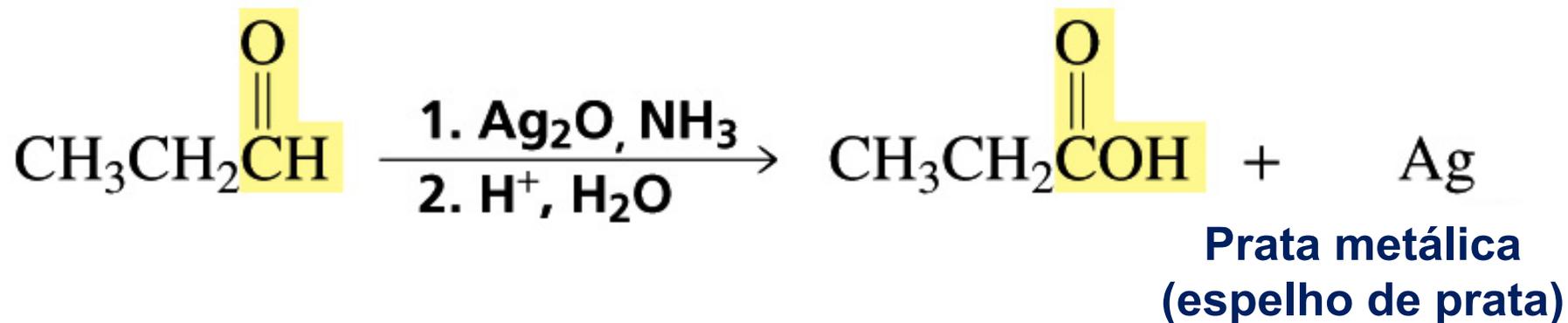
# Oxidação de Aldeídos



**aldehydes**

**carboxylic acids**

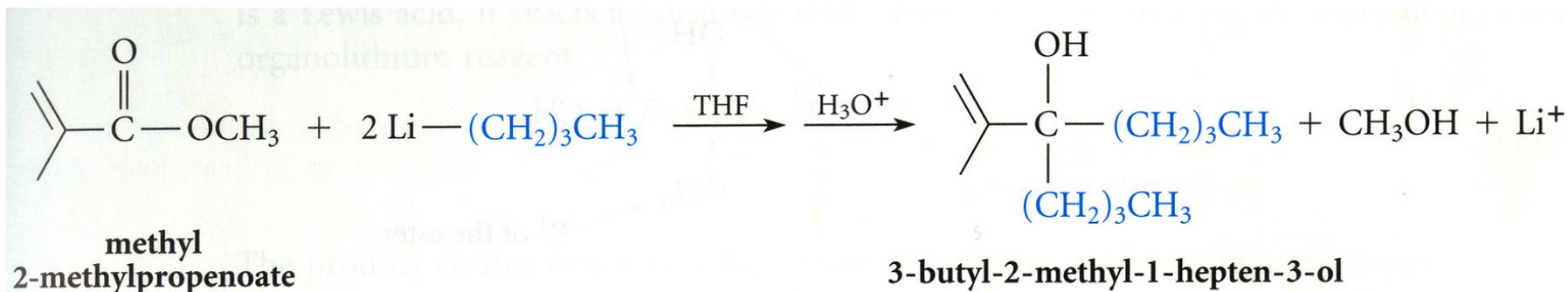
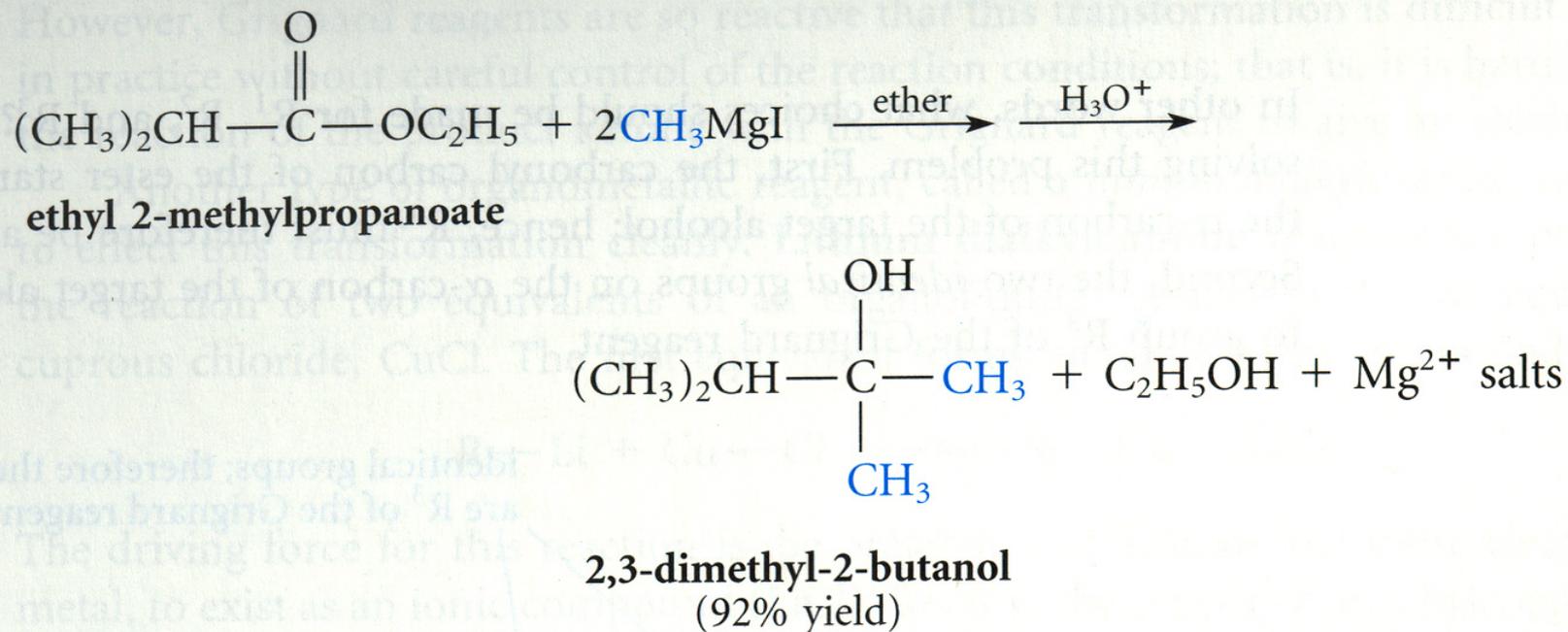
# Oxidação de Aldeídos



**O Reagente de Tollens é seletivo para a oxidação de aldeídos e usado como teste qualitativo para presença destes compostos.**

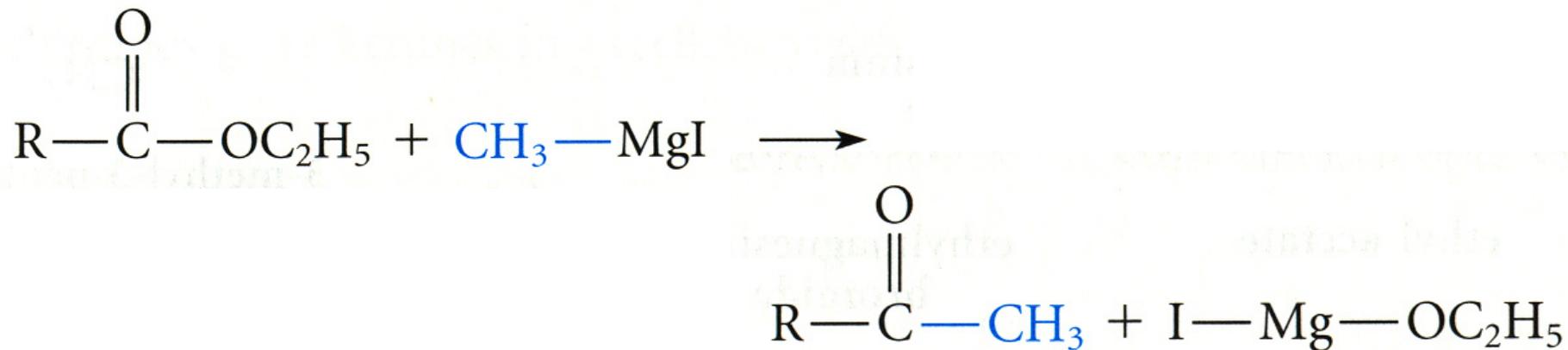
## 6.12. Reações com Organometálicos

### Reação de Ésteres com Organometálicos de Magnésio e de Lítio:

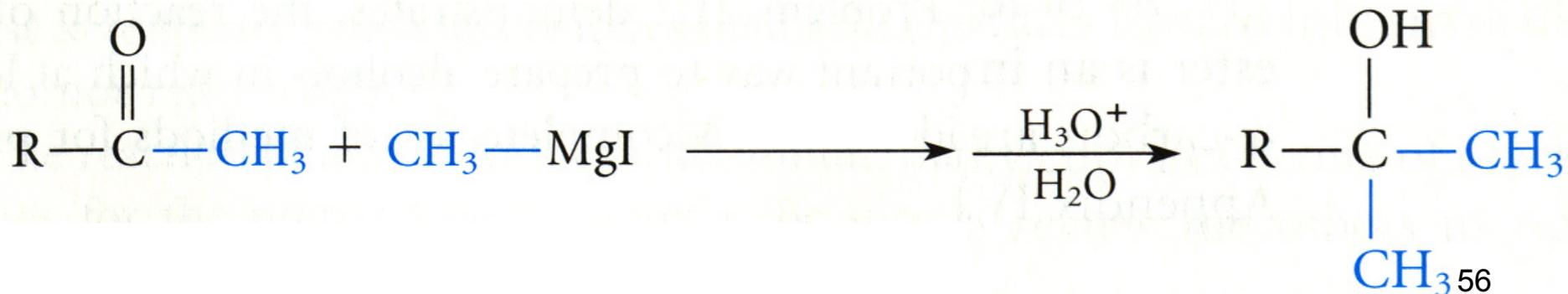


# Mecanismo da Reação de Ésteres com Organometálicos de Magnésio e de Lítio:

**Etapa 1:** Substituição Nucleofílica Acílica:



**Etapa 2:** Adição Nucleofílica:



# Preparação de Cetonas: Reação de Carboxilatos com Organolítio

