# 6. Substituição Nucleofílica Acílica 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

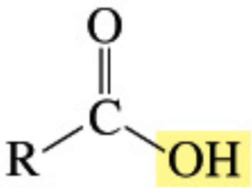
6.8. Formação e Reações de Amidas

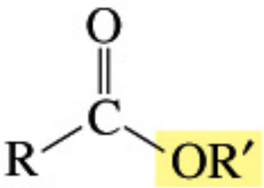
6.9. Ativação de Ácidos Carboxílicos

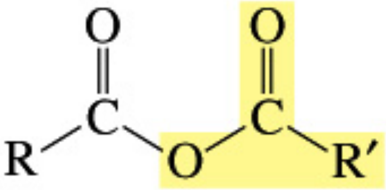
6.10. Reações de Oxidação e Redução

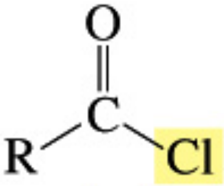
6.11. Reações com Organometálicos

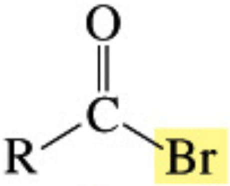
# 6. Compostos Carboxílicos: Ácidos Carboxílicos e Derivados


a carboxylic acid

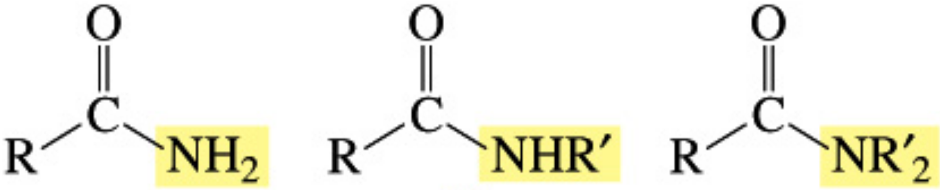

an ester


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

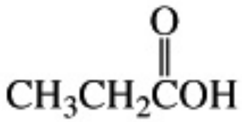
systematic name:
common name:

$HC(=O)OH$

methanoic acid
formic acid

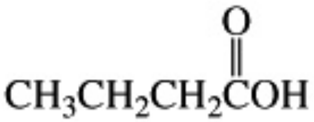
$CH_3C(=O)OH$

ethanoic acid
acetic acid



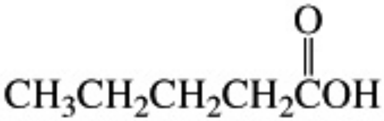
$CH_3CH_2C(=O)OH$

propanoic acid
propionic acid



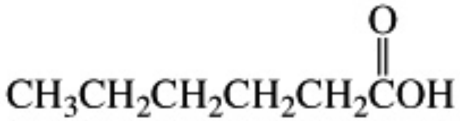
$CH_3CH_2CH_2C(=O)OH$

butanoic acid
butyric acid



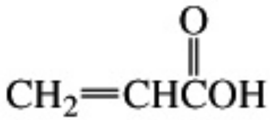
$CH_3CH_2CH_2CH_2C(=O)OH$

pentanoic acid
valeric acid



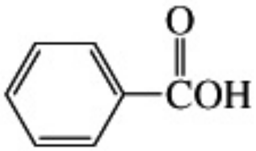
$CH_3CH_2CH_2CH_2CH_2C(=O)OH$

hexanoic acid
caproic acid

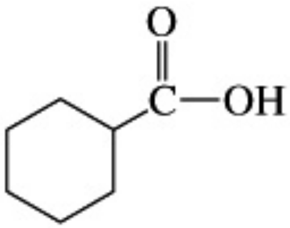


$CH_2{=}CHC(=O)OH$

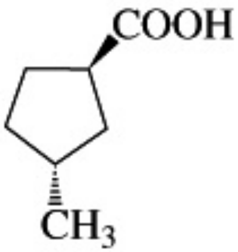
propenoic acid
acrylic acid



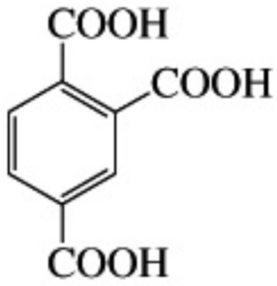
benzenecarboxylic acid
benzoic acid



ácido ciclohexanocarboxílico

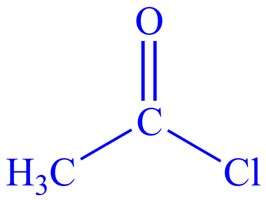


ácido trans-3-metilciclo-pentanocarboxílico

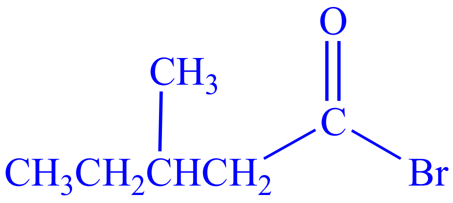


ácido 1,2,4-benzeno-tricarboxílico

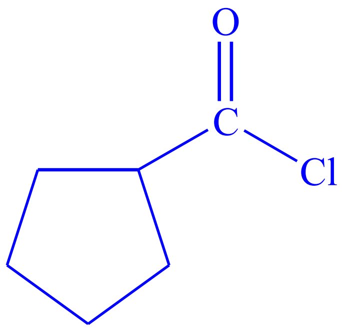
# Haletos de Acila



**cloreto de etanoíla**
**cloreto de acetila**

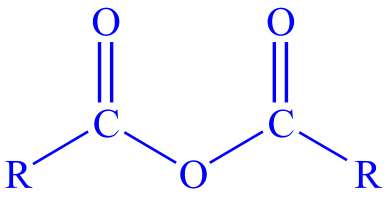


**brometo de 3-metilpentanoíla**
**brometo de β-metilvaleríla**



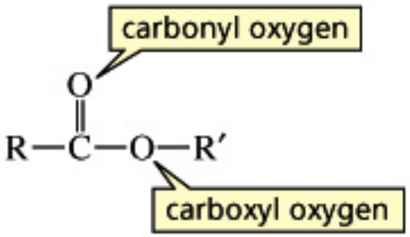
**cloreto de**
**ciclopentanocarbonila**

# Anidridos de Ácido



R = $CH_3$:  anidrido acético
R = $C_2H_5$: anidrido propanôico
R = $C_6H_5$: anidrido benzôico

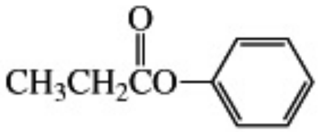
# Ésteres



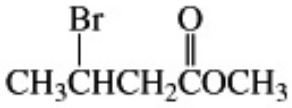
$$R-\overset{\displaystyle O}{\overset{\|}{C}}-O-R'$$

$$\mathrm{CH_3\overset{\displaystyle O}{\overset{\|}{C}}OCH_2CH_3}$$

etanoato de etila
(acetato de etila)

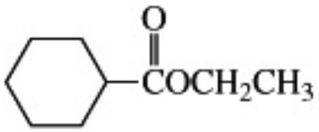


propanoato
e fenila



$$\mathrm{CH_3\overset{\displaystyle Br}{\overset{|}{C}}HCH_2\overset{\displaystyle O}{\overset{\|}{C}}OCH_3}$$

3-bromobutanoato de metila
(β-bromobutirato de metila)

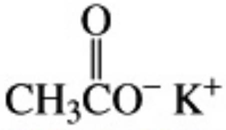


ciclohexanocarboxilato
de metila

# Sais de Ácidos Carboxílicos

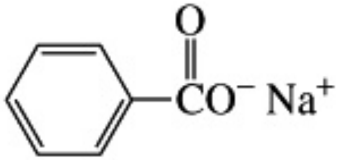
$$\mathrm{H\overset{\displaystyle O}{\overset{\|}{C}}O^-\ Na^+}$$

metanoato de sódio
(formiato de sódio)



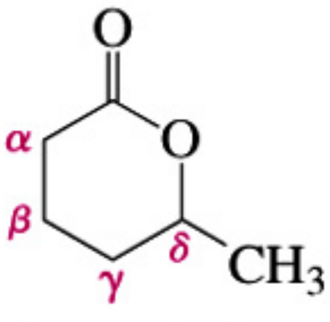
$$\mathrm{CH_3\overset{\displaystyle O}{\overset{\|}{C}}O^-\ K^+}$$

etanoato de potássio
(acetato de potássio)

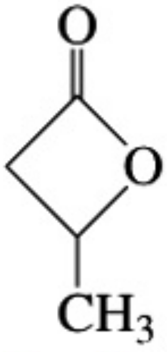


benzenocarboxilato de sódio
(benzoato de sódio)

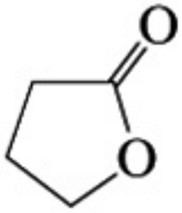
# Ésteres Cíclicos: Lactonas



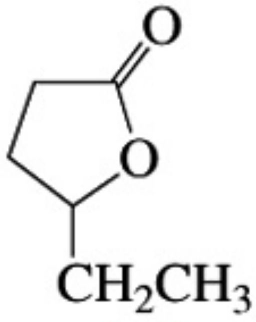
**δ-caprolactona**



**β-butirolactona**



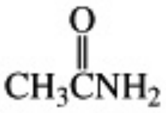
**γ-butirolactona**



**γ-caprolactona**

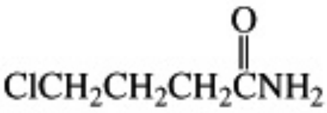
C-4: butirolactona; C-5: valerolactona; C-6: caprolactona;
β, γ, δ: posição do grupo funcional -O-.

# Amidas



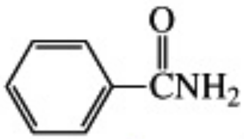
$CH_3\overset{O}{\overset{\|}{C}}NH_2$

**etanamida**
**(acetamida)**

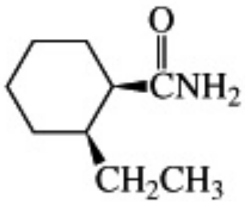


$ClCH_2CH_2CH_2\overset{O}{\overset{\|}{C}}NH_2$

**4-clorobutanamida**
**(γ-clorobutiramida)**

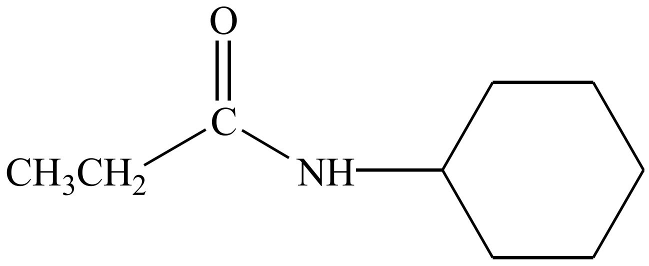


**benzenocarboxamida**
**(benzamida)**

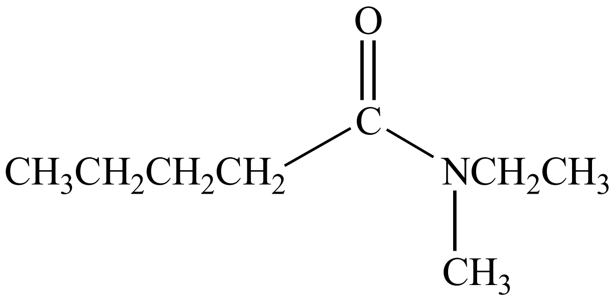


**cis-4-etilciclohexanoarboxamida**

# Amidas substituídas no nitrogênio

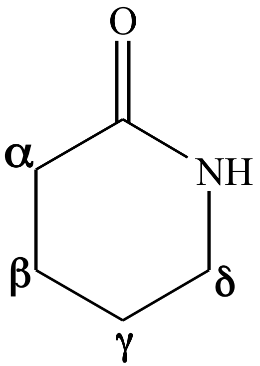


***N*-ciclohexilpropanamida**

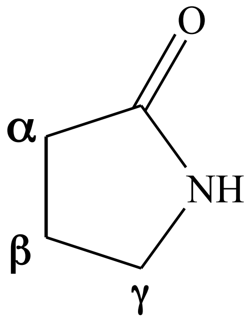


***N*-etil-*N*-metilpentanamida**

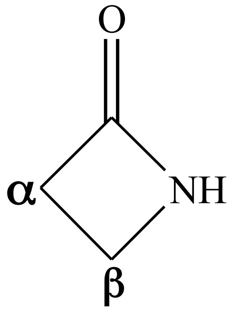
# Amidas Cíclicas: Lactamas



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



**2-azaciclopentanona**
**γ-butirolactama**

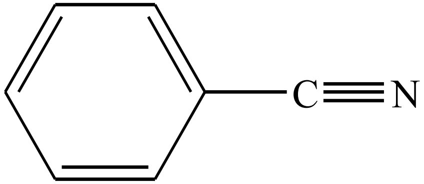


**2-azaciclobutanona**
**β-propiolactama**

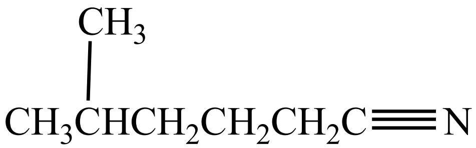
# Nitrilas

$CH_3C{\equiv}N$

etanonitrila
**acetonitrila**
cianeto de metila



benzenocarbonitrile
**benzonitrila**
cianeto de fenila
cianobenzeno



$CH_3\overset{\overset{\displaystyle CH_3}{|}}{C}HCH_2CH_2CH_2C{\equiv}N$

5-metilhexanonitrila
δ-metilcapronitrila
cianeto de *iso*-hexila

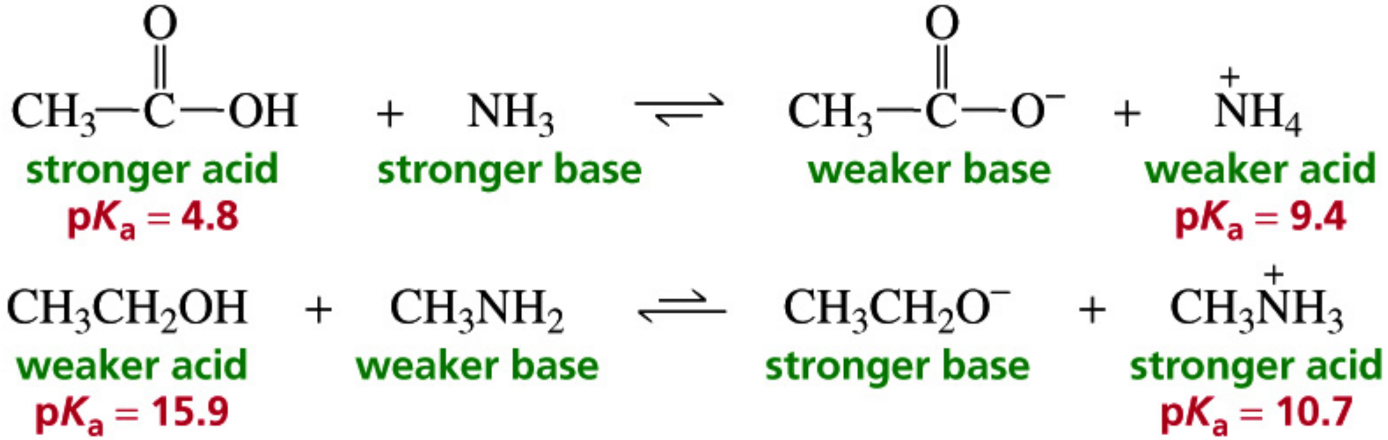
$CH_2{=}CHC{\equiv}N$

propenonitrila
**acrilonitrila**

# 6.2. Acidez de Ácidos Carboxílicos

## Ácidos e Bases de Brønsted–Lowry

- Ácidos doam prótons e Bases recebem prótons

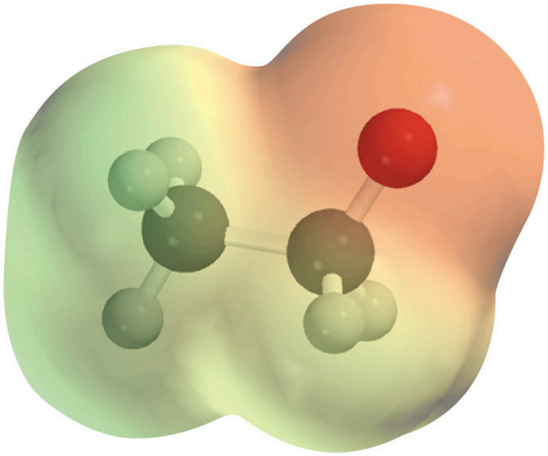


$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-OH + NH_3 \rightleftharpoons CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-O^- + \overset{+}{N}H_4$$

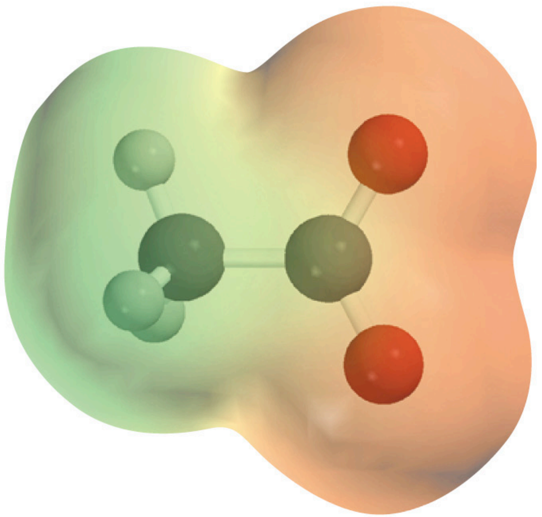
$$CH_3CH_2OH + CH_3NH_2 \rightleftharpoons CH_3CH_2O^- + CH_3\overset{+}{N}H_3$$

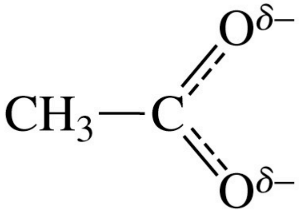
- “Fortes reagem para dar fracos”
- Quanto mais fraca a base, mais forte o ácido conjugado
- Ácidos (bases) estáveis são fracos

# Acidez de Ácidos Carboxílicos



$CH_3CH_2O^-$





$CH_3\overset{O}{\overset{\|}{C}}OH$

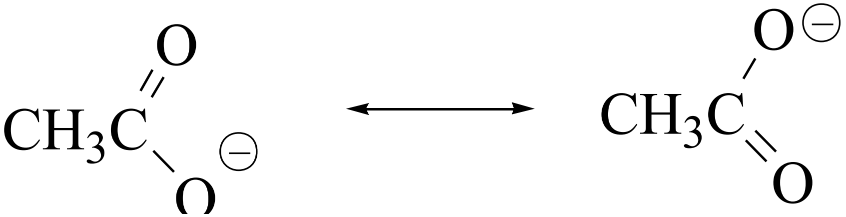
$pK_a = 4.76$

acetic acid

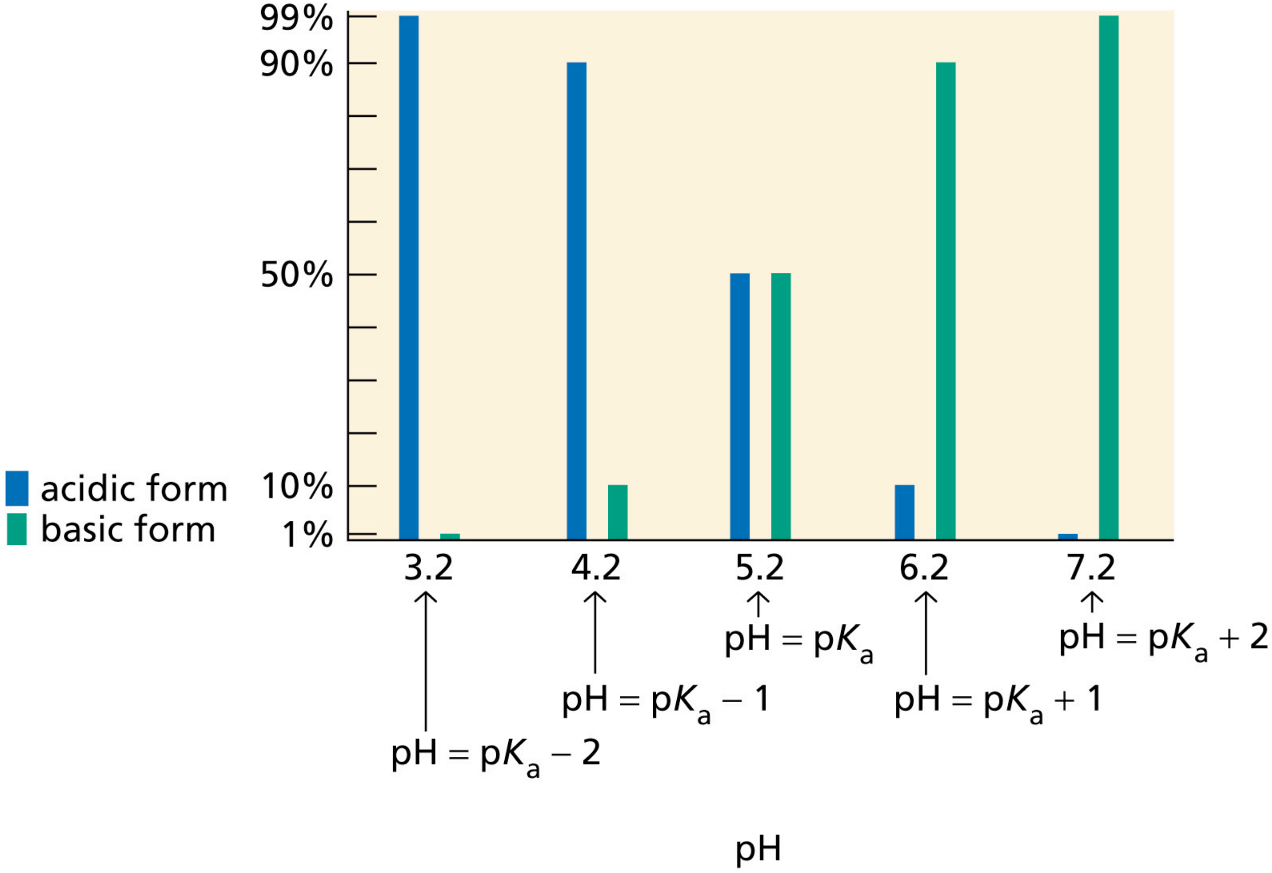
$CH_3CH_2OH$

$pK_a = 15.9$

ethanol



# Acidez de Ácidos Carboxílicos



# Equilíbrio Ácido / Base

$$H_2O + HA \rightleftharpoons H_3O^+ + A^-$$

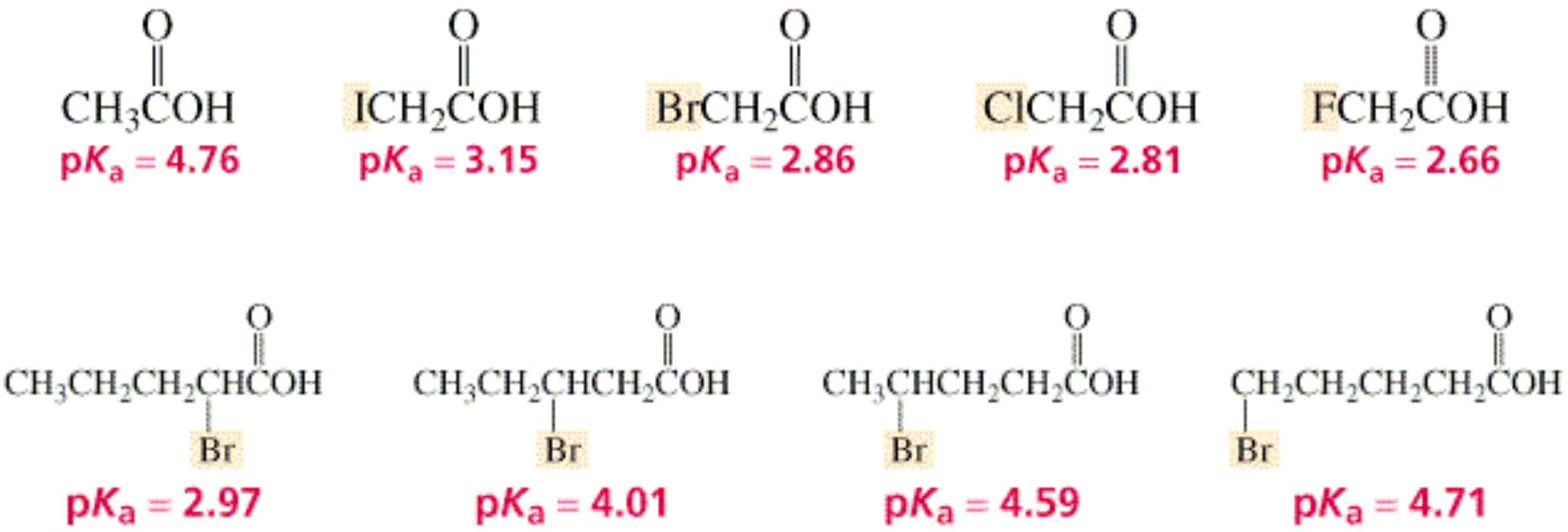
$$K = \frac{[H_3O^+][A^-]}{[H_2O][HA]} \qquad K_a = \frac{[H_3O^+][A^-]}{[HA]}$$

$$pK_a = -\log K_a$$

$K$: Constante de equilíbrio

$K_a$: Constante de dissociação do ácido HA

# Acidez de Ácidos Carboxílicos



$CH_3\overset{O}{\overset{\|}{C}}OH$ $pK_a = 4.76$

$ICH_2\overset{O}{\overset{\|}{C}}OH$ $pK_a = 3.15$

$BrCH_2\overset{O}{\overset{\|}{C}}OH$ $pK_a = 2.86$

$ClCH_2\overset{O}{\overset{\|}{C}}OH$ $pK_a = 2.81$

$FCH_2\overset{O}{\overset{\|}{C}}OH$ $pK_a = 2.66$

$CH_3CH_2CH_2\underset{Br}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}OH$ $pK_a = 2.97$

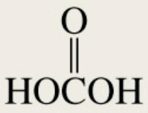
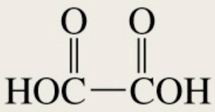
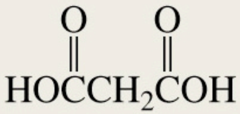
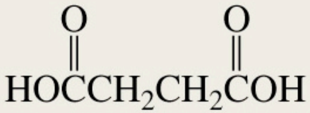
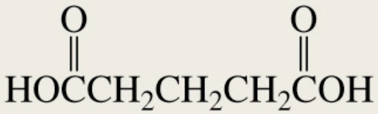
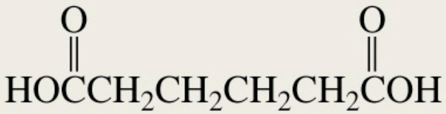
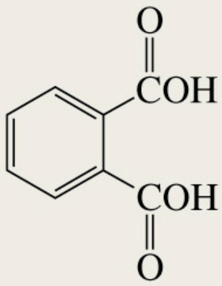
$CH_3CH_2\underset{Br}{\underset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}OH$ $pK_a = 4.01$

$CH_3\underset{Br}{\underset{|}{C}}HCH_2CH_2\overset{O}{\overset{\|}{C}}OH$ $pK_a = 4.59$

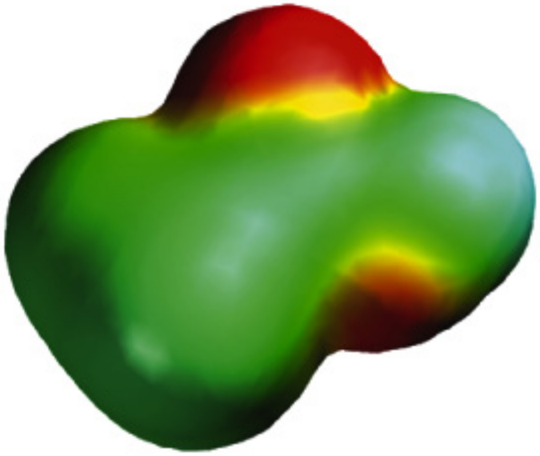
$\underset{Br}{\underset{|}{C}}H_2CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH$ $pK_a = 4.71$

- 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.

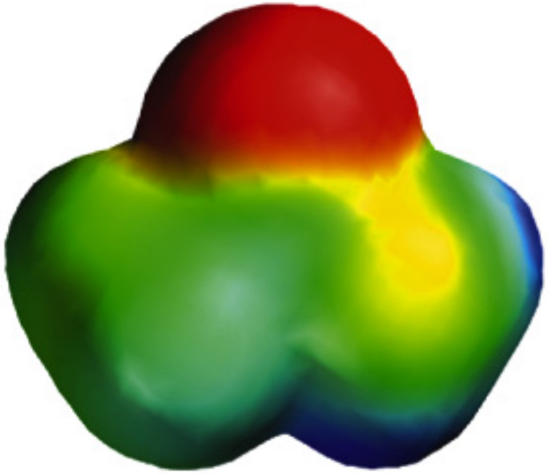
## Table 17.2 Structures, Names, and p$K_a$ Values of Some Simple Dicarboxylic Acids

| Dicarboxylic acid | Common name | p$K_{a1}$ | p$K_{a2}$ |
|---|---|---|---|
|  $\mathrm{HO}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$ | Carbonic acid | 3.58 | 6.35 |
|  $\mathrm{HO}\overset{O}{\overset{\|}{\mathrm{C}}}-\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$ | Oxalic acid | 1.27 | 4.27 |
|  $\mathrm{HO}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$ | Malonic acid | 2.86 | 5.70 |
|  $\mathrm{HO}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2CH_2}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$ | Succinic acid | 4.21 | 5.64 |
|  $\mathrm{HO}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2CH_2CH_2}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$ | Glutaric acid | 4.34 | 5.27 |
|  $\mathrm{HO}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2CH_2CH_2CH_2}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$ | Adipic acid | 4.41 | 5.28 |
|  | Phthalic acid | 2.95 | 5.41 |

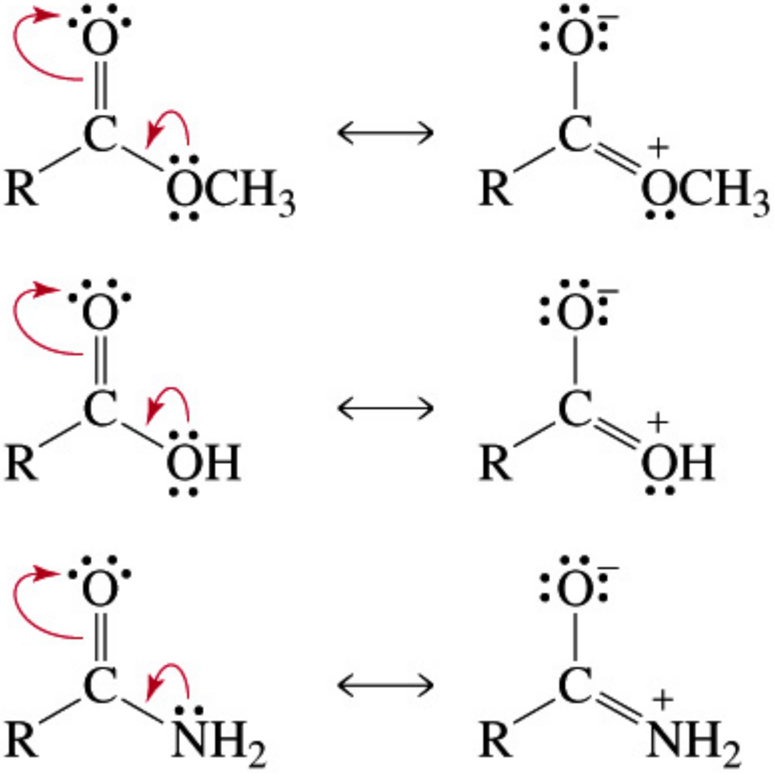
# 6.3. Reatividade de Derivados de Ácidos Carboxílicos



acetic acid



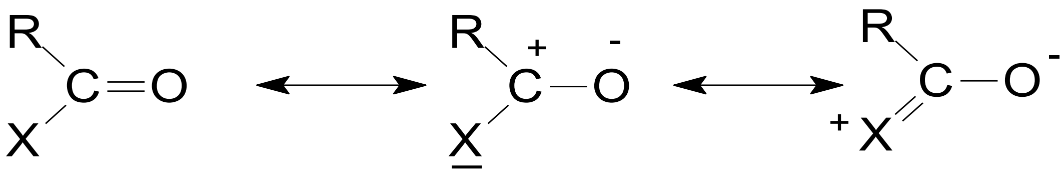
acetamide



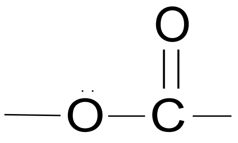
**Ressonância de Ésteres, Ácidos e Amidas**

# Reatividade de Derivados de Ácidos Carboxílicos

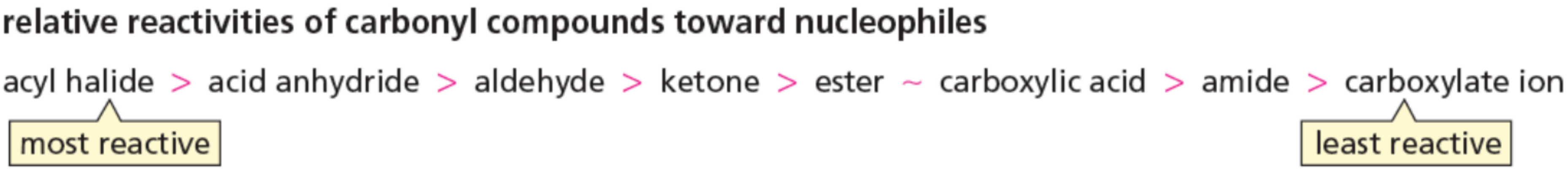
- derivados de ácidos carboxílicos são geralmente menos reativos frente adição nucleofílica de que aldeídos e cetonas;
- Efeito estabilizador de substituintes em relação aos aldeídos e cetonas:



X: $NH_2$, OR, OH : estabilização π (+M) alta e efeito -I baixo: **mais estáveis**



X: $-\ddot{O}-\overset{\overset{O}{\|}}{C}-R$, Cl, etc. estabilização π (+M) baixa e efeito -I alto: **menos estáveis**



**relative reactivities of carbonyl compounds toward nucleophiles**

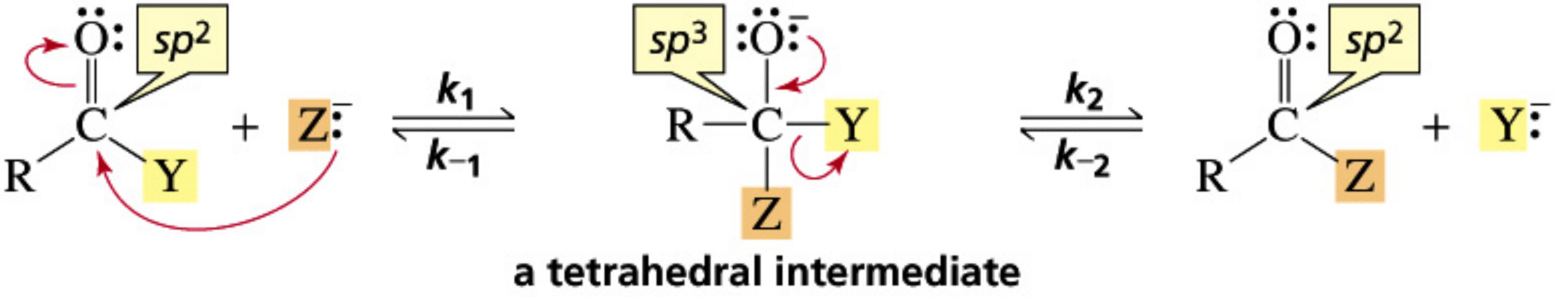
acyl halide > acid anhydride > aldehyde > ketone > ester ~ carboxylic acid > amide > carboxylate ion

most reactive

least reactive

# Reatividade de Derivados de Ácidos Carboxílicos

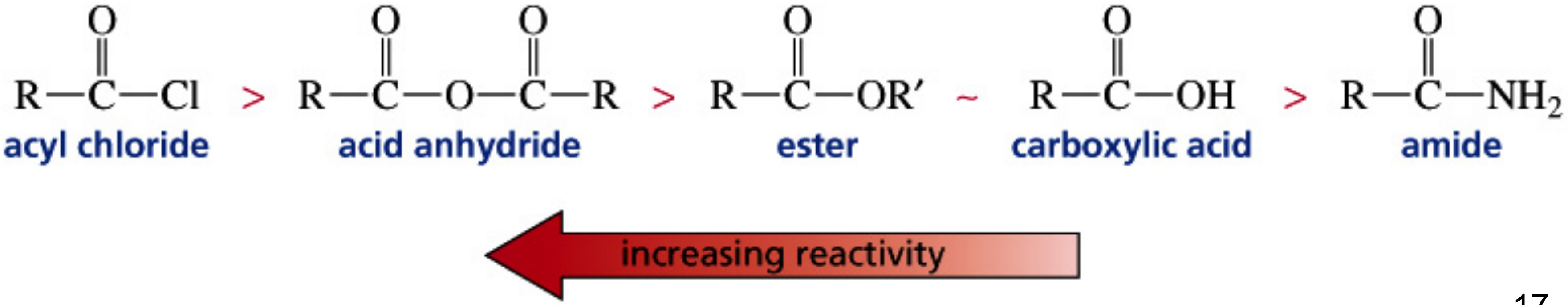
## Reação não catalisada ou catálise básica



Z⁻ será expelido se for uma base mais fraca do que Y⁻ ($k_{-1} >> k_2$)

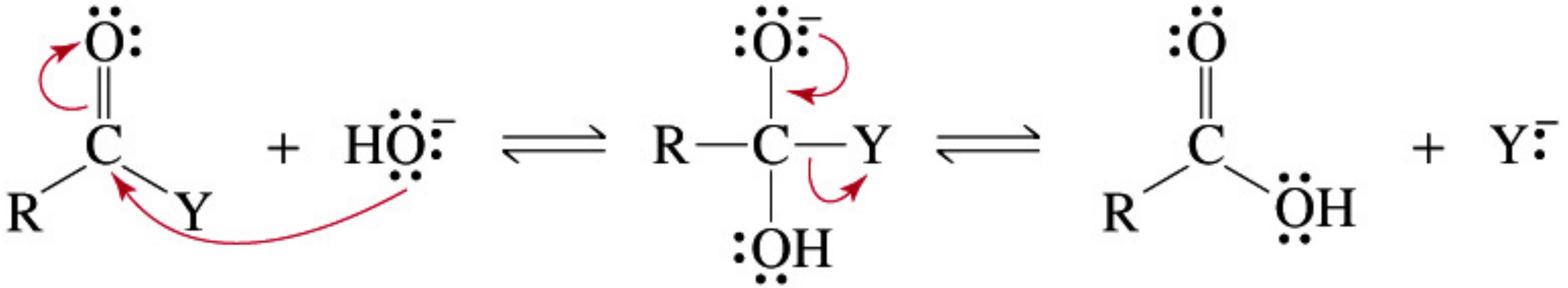
Y⁻ será expelido se for uma base mais fraca do que Z⁻ ($k_2 >> k_{-1}$)

**relative reactivities of carboxylic acid derivatives**



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

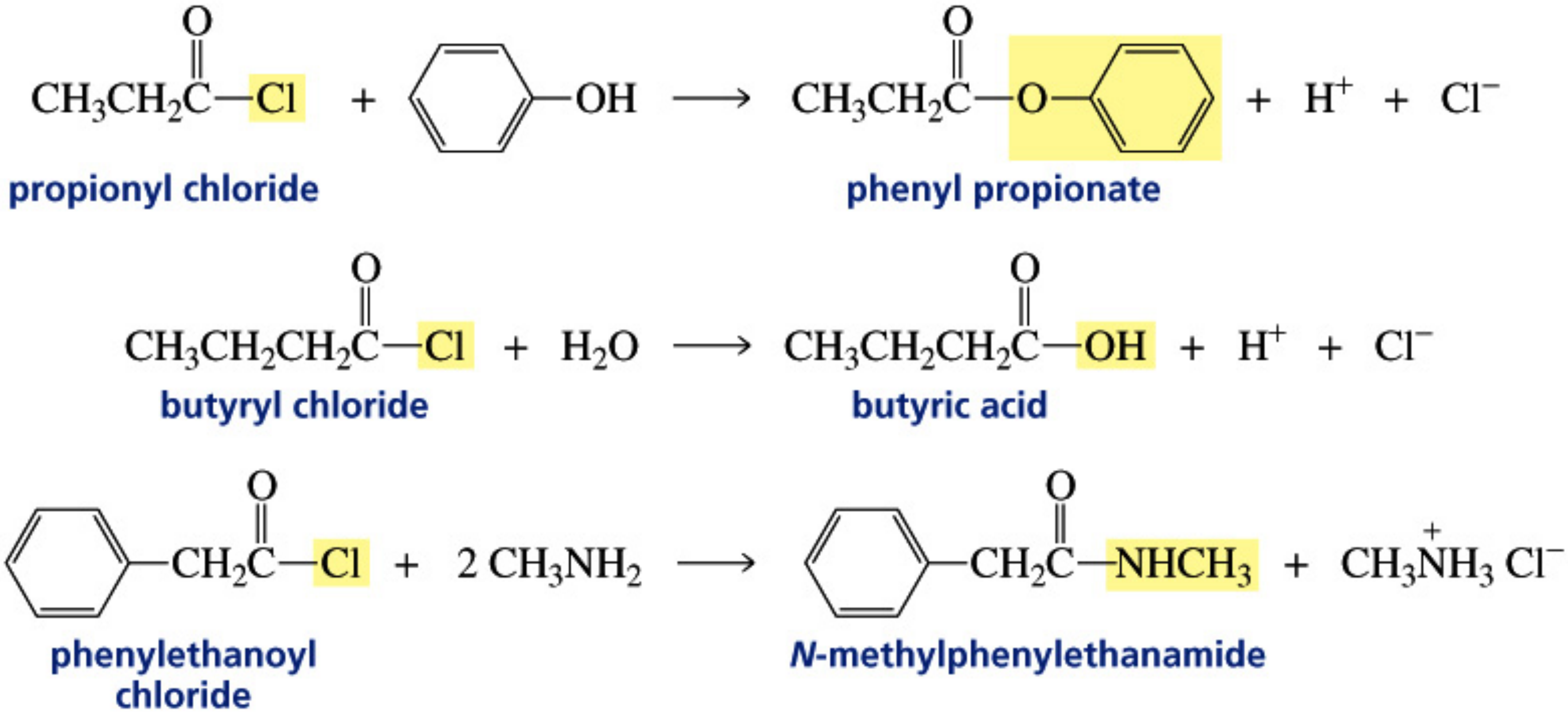
Todos compostos carboxílicos reagem pelo mesmo mecanismo



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

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

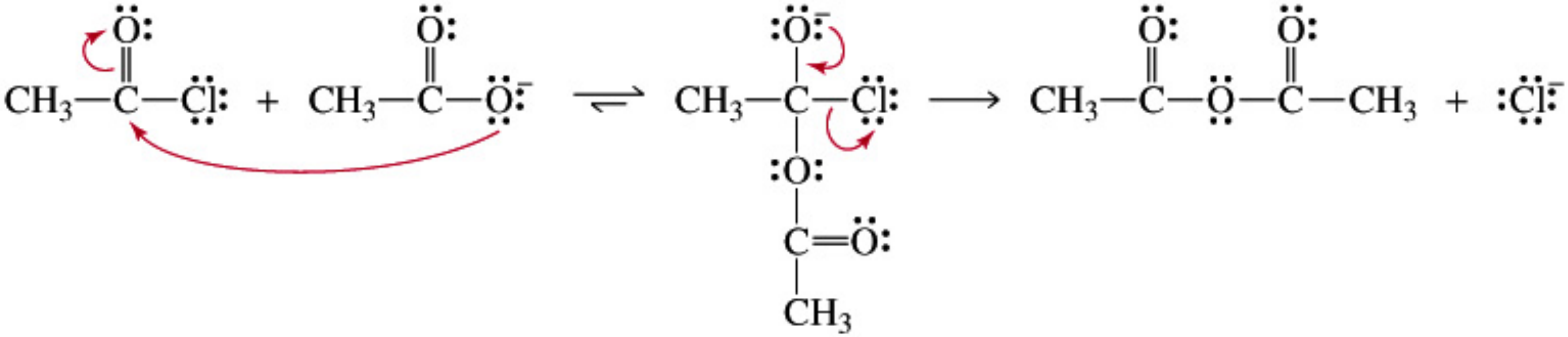
# 6.4. Reações de Haletos de Acila



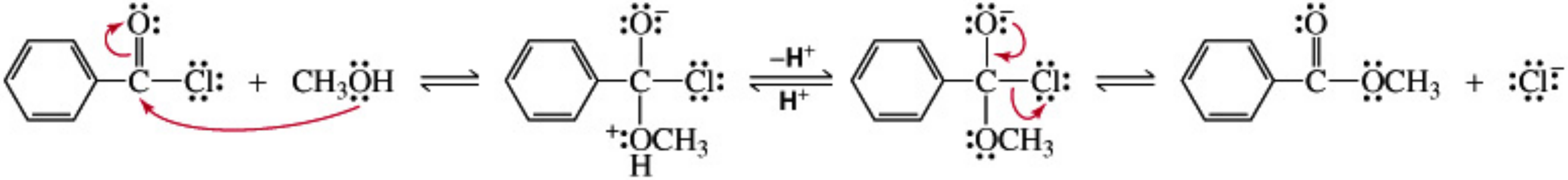
$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}-Cl + H_2O \longrightarrow CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}-OH + H^+ + Cl^-$$

# Mecanismo da Reação de Haletos de Acila

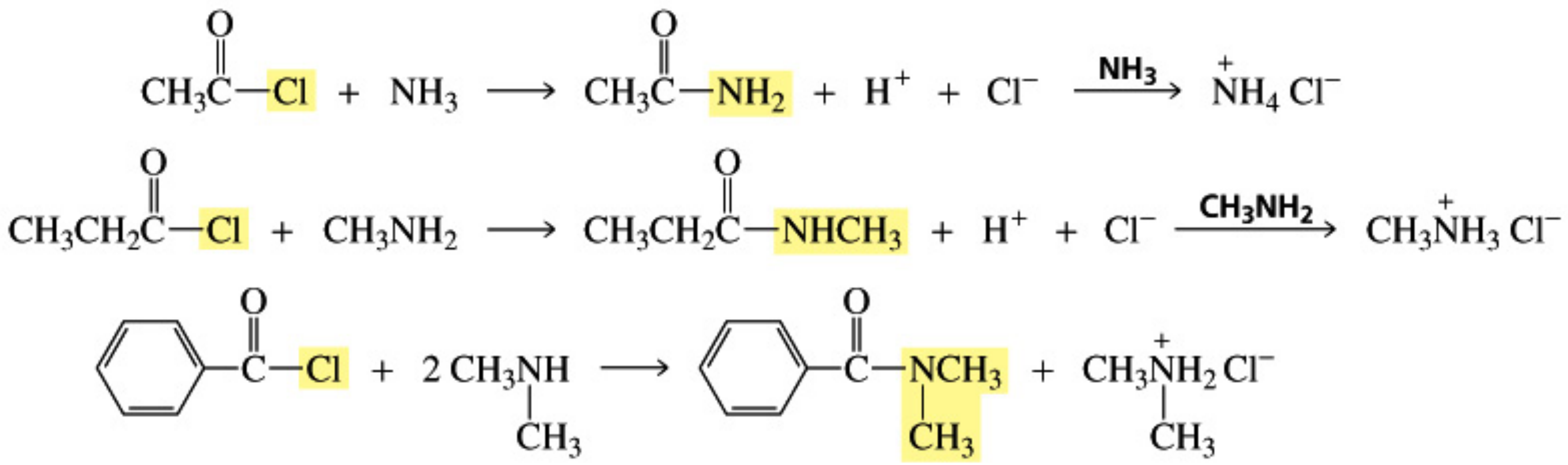
## Conversão em anidridos



## Conversão em ésteres



# Formação de Amidas a Partir de Haletos de Acila



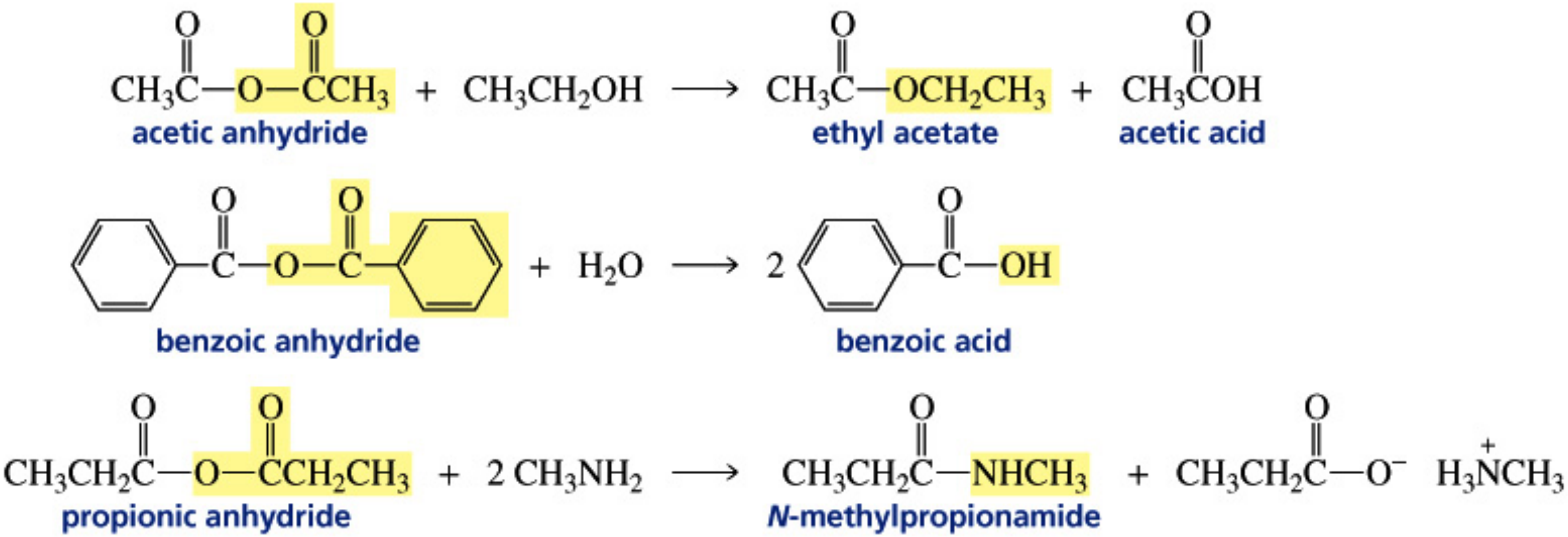
$$CH_3\overset{\overset{O}{\|}}{C}-Cl + NH_3 \longrightarrow CH_3\overset{\overset{O}{\|}}{C}-NH_2 + H^+ + Cl^- \xrightarrow{NH_3} \overset{+}{N}H_4\,Cl^-$$

$$CH_3CH_2\overset{\overset{O}{\|}}{C}-Cl + CH_3NH_2 \longrightarrow CH_3CH_2\overset{\overset{O}{\|}}{C}-NHCH_3 + H^+ + Cl^- \xrightarrow{CH_3NH_2} CH_3\overset{+}{N}H_3\,Cl^-$$

Aminas terciárias não podem formar amidas:

**Porque será??**

# 6.5. Reações de Anidridos de Ácido



$$CH_3\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}CH_3 + CH_3CH_2OH \longrightarrow CH_3\overset{O}{\overset{\|}{C}}-OCH_2CH_3 + CH_3\overset{O}{\overset{\|}{C}}OH$$

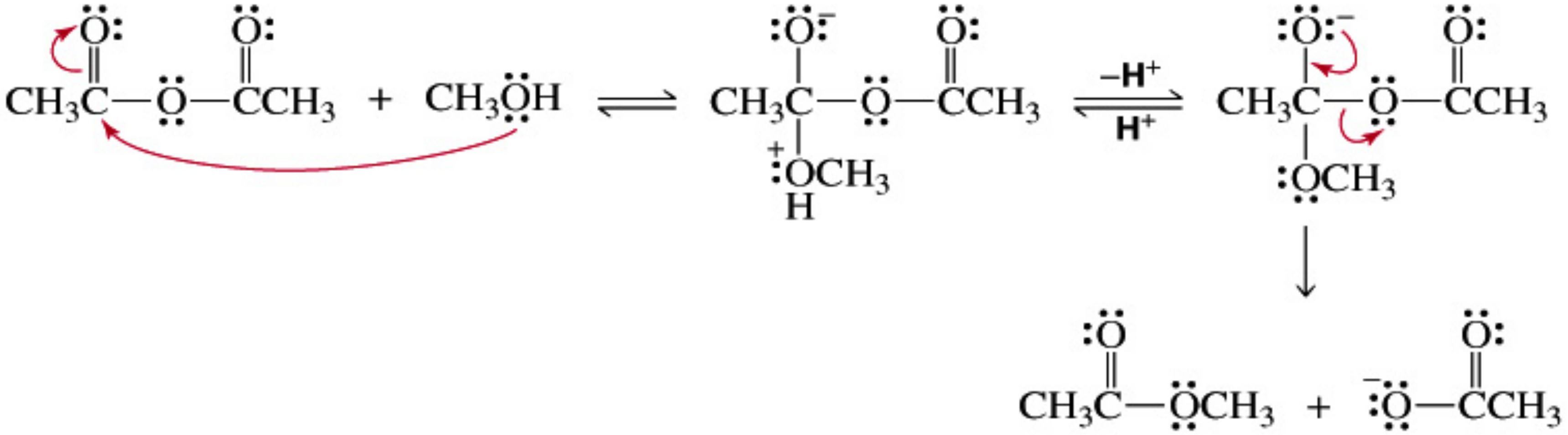
$$CH_3CH_2\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}CH_2CH_3 + 2\,CH_3NH_2 \longrightarrow CH_3CH_2\overset{O}{\overset{\|}{C}}-NHCH_3 + CH_3CH_2\overset{O}{\overset{\|}{C}}-O^- \; H_3\overset{+}{N}CH_3$$

Anidridos não reagem com cloreto ou brometo de sódio

**Porque??** **Qualidade do grupo de partida??**

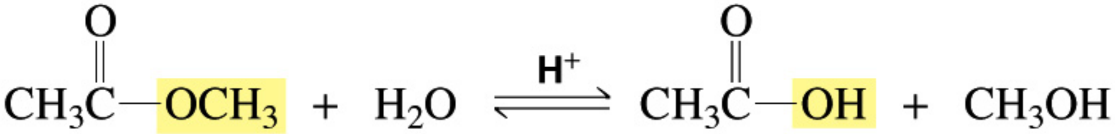
# Conversão de Anidridos em Ésteres

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



# 6.6. Reação de Ésteres: Catálise Ácida

## Hidrólise

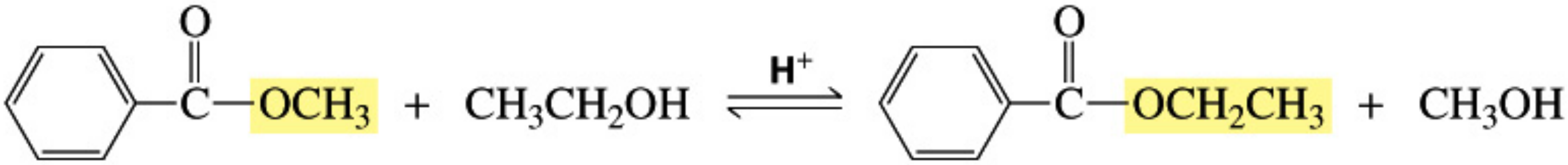


$$\mathrm{CH_3\overset{O}{\overset{\|}{C}}-OCH_3 + H_2O \xrightleftharpoons{H^+} CH_3\overset{O}{\overset{\|}{C}}-OH + CH_3OH}$$

methyl acetate

acetic acid

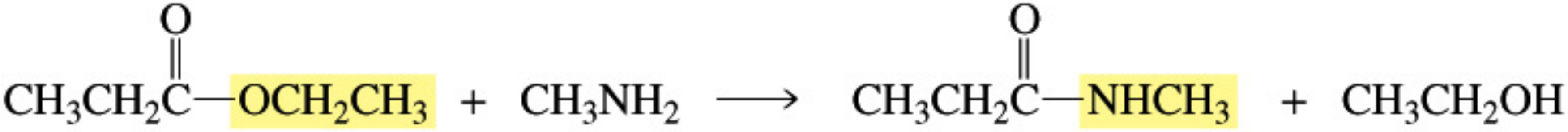
## Transesterificação



methyl benzoate

ethyl benzoate

## Aminólise

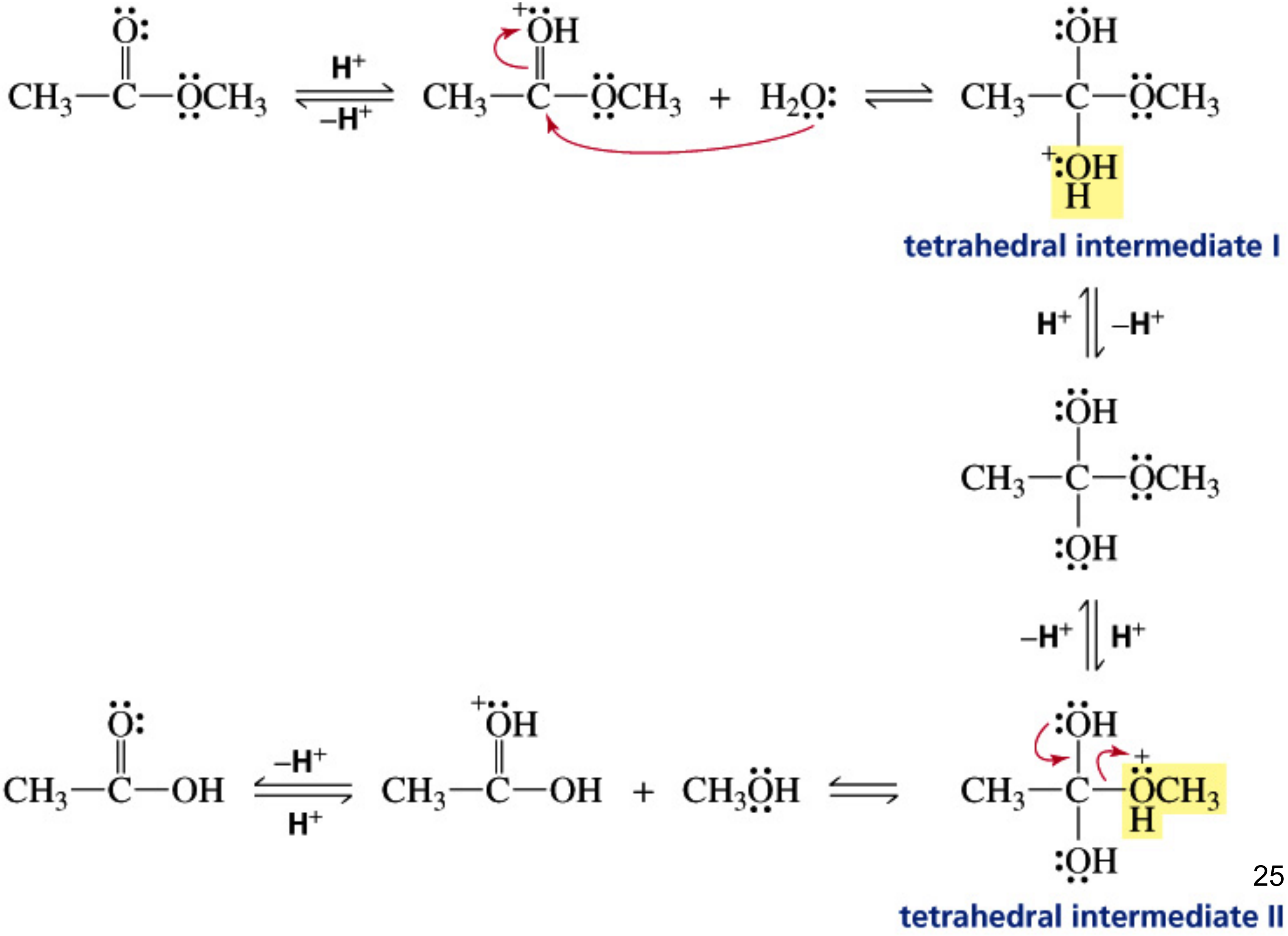


$$\mathrm{CH_3CH_2\overset{O}{\overset{\|}{C}}-OCH_2CH_3 + CH_3NH_2 \longrightarrow CH_3CH_2\overset{O}{\overset{\|}{C}}-NHCH_3 + CH_3CH_2OH}$$

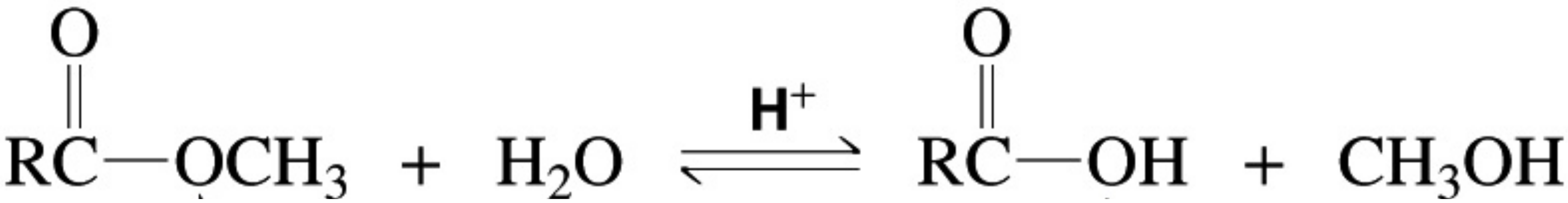
ethyl propionate

*N*-methylpropionamide

# Mecanismo da Hidrólise de Ésteres Catalisada por Ácido



# Constante de Equilíbrio na Esterificação e Hidrólise de Ésteres



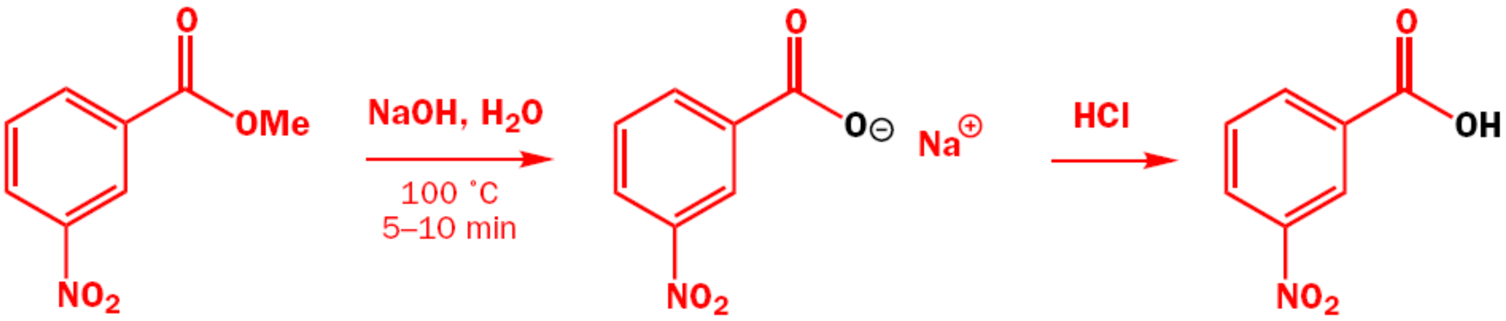
$$\overset{\overset{O}{\|}}{RC}-OCH_3 + H_2O \underset{}{\overset{H^+}{\rightleftharpoons}} \overset{\overset{O}{\|}}{RC}-OH + CH_3OH$$

**K ~1**

**Deslocar o equilíbrio**:

- Excesso de água desloca o equilíbrio para o lado do ácido carboxílica;
- 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.

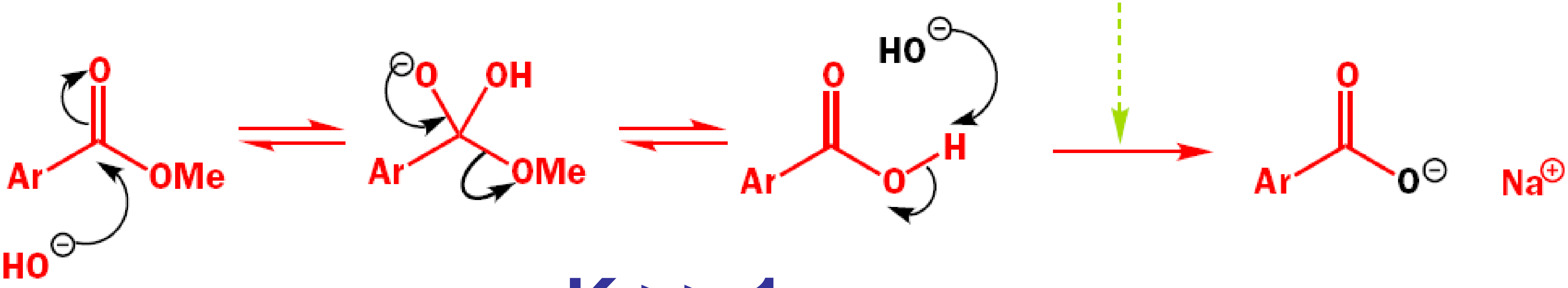
# Hidrólise de Ésteres: Catalisada por Base



90 - 96% yield

## Mecanismo:

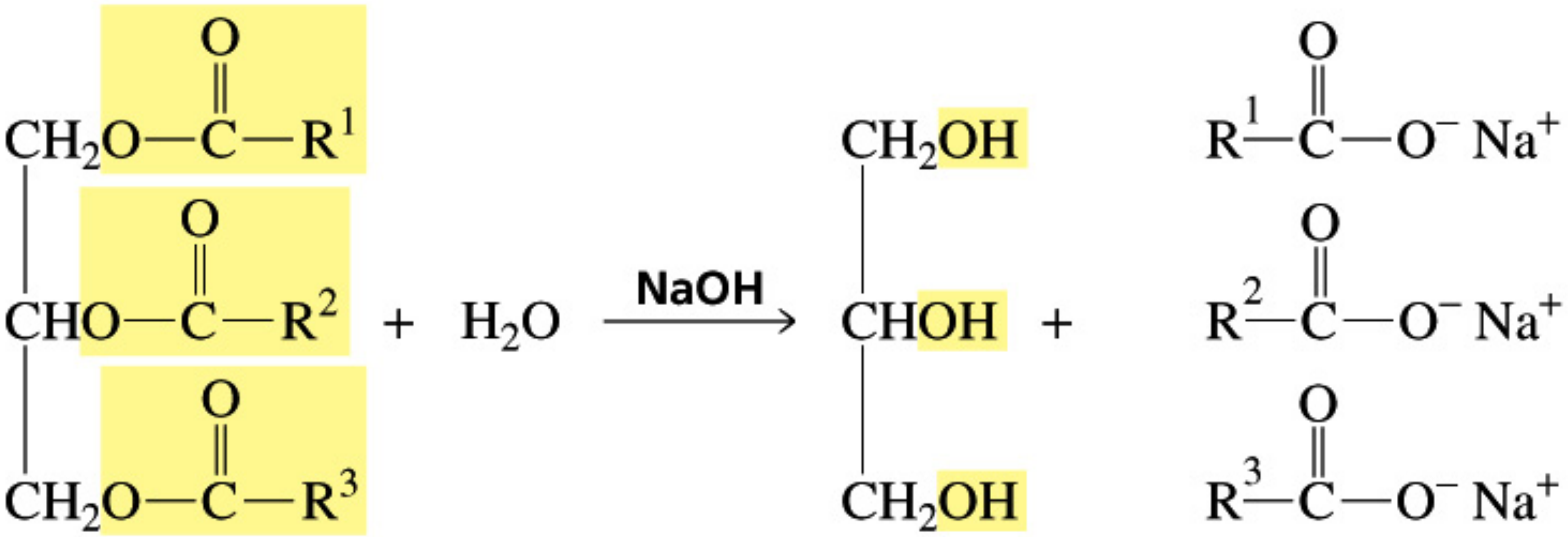
irreversible deprotonation pulls the equilibrium
over towards the hydrolysis products



K >> 1

# Hidrólise de Ésteres Catalisada por Base

## Saponificação



**gorduras ou óleos**
**triésteres de glicerina**

**gliceról**

**gliceról**

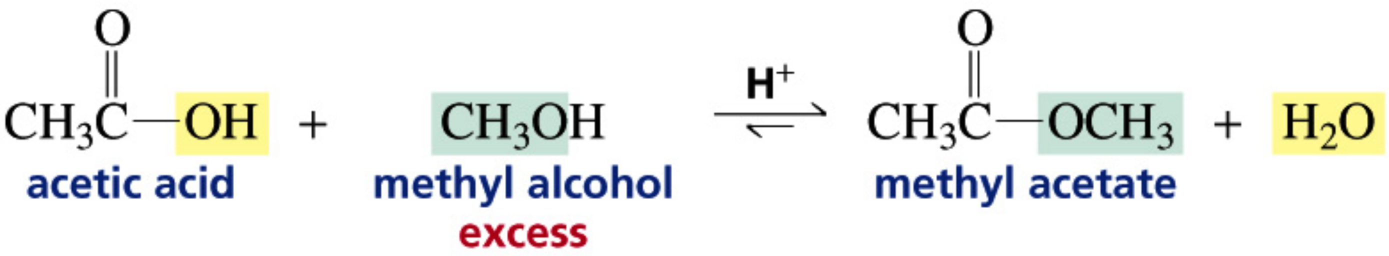
**(glicerina)**

**sais de ácidos graxas**
**sabão**

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

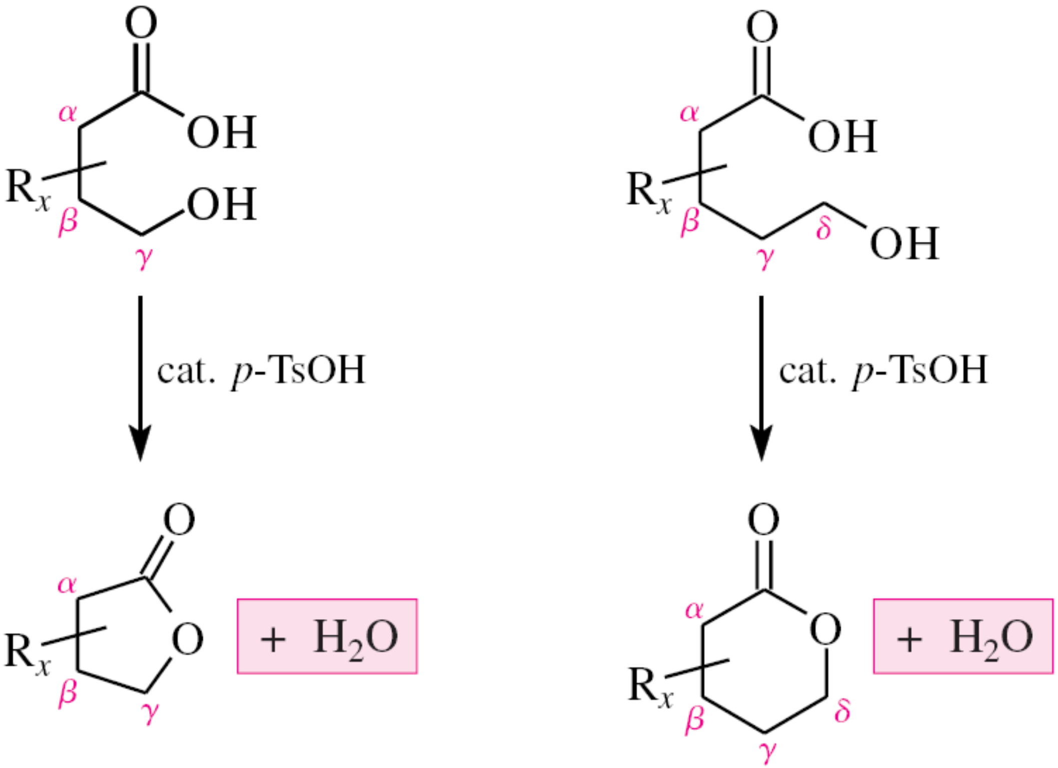
# 6.7. Formação de Ésteres: Catalisada por Ácido

## Esterificação de ácidos carboxílicos:

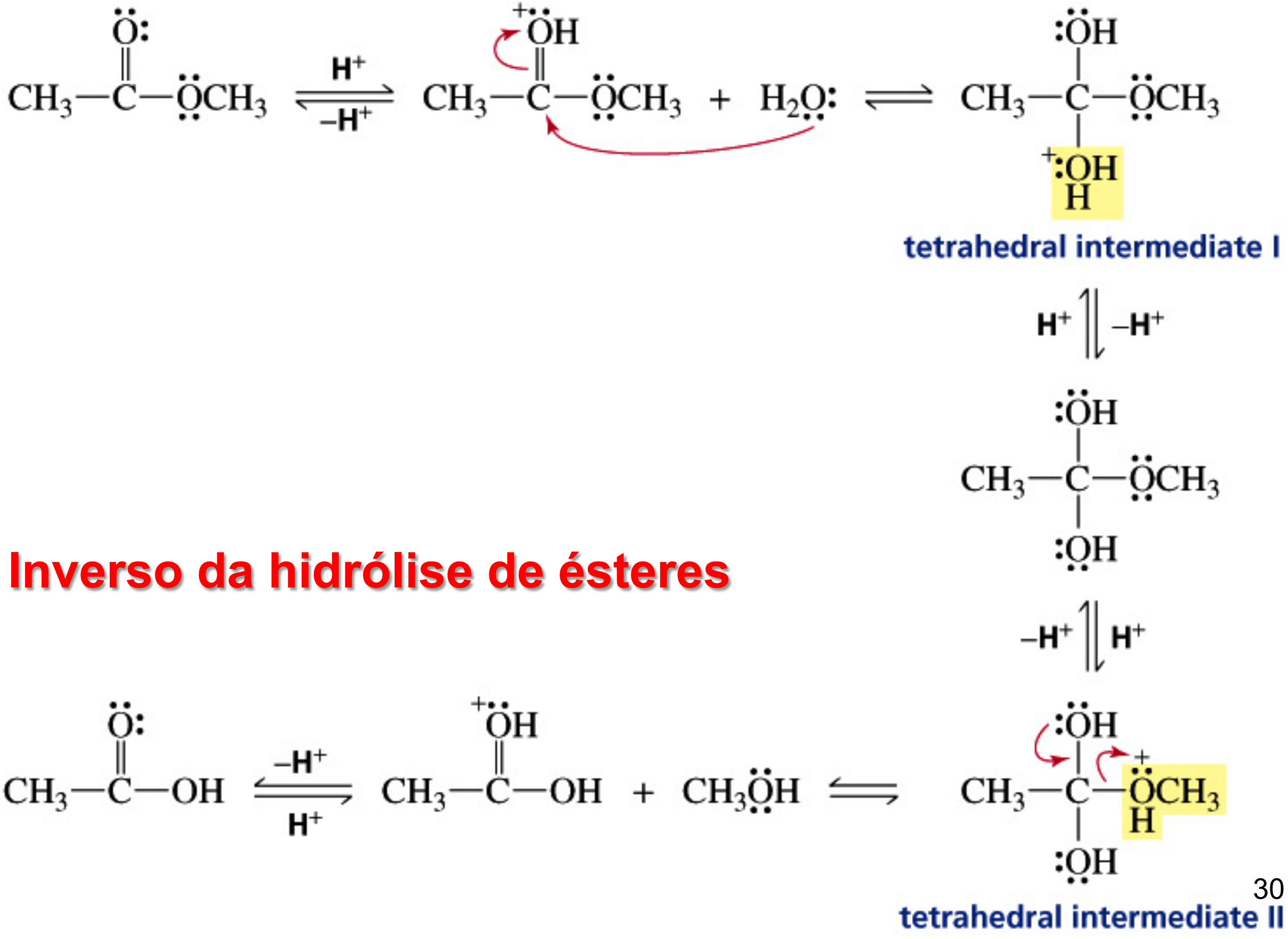


$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}{-}OH + CH_3OH \xrightleftharpoons{H^+} CH_3\overset{\overset{\displaystyle O}{\|}}{C}{-}OCH_3 + H_2O$$

## Esterificação Intramolecular: Formação de Lactonas

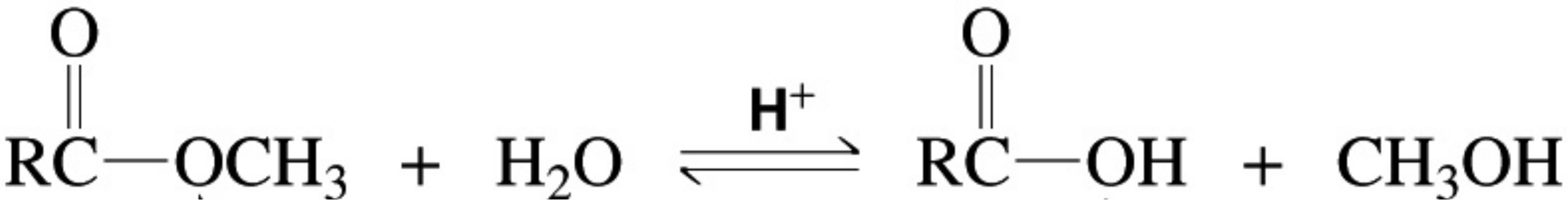


# Mecanismo da Esterificação: Catalisada por Ácido



Inverso da hidrólise de ésteres

# Equilíbrio na Esterificação



$$\mathrm{R\overset{\overset{O}{\|}}{C}{-}OCH_3 + H_2O \xrightleftharpoons{H^+} R\overset{\overset{O}{\|}}{C}{-}OH + CH_3OH}$$

**K ~1**

**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

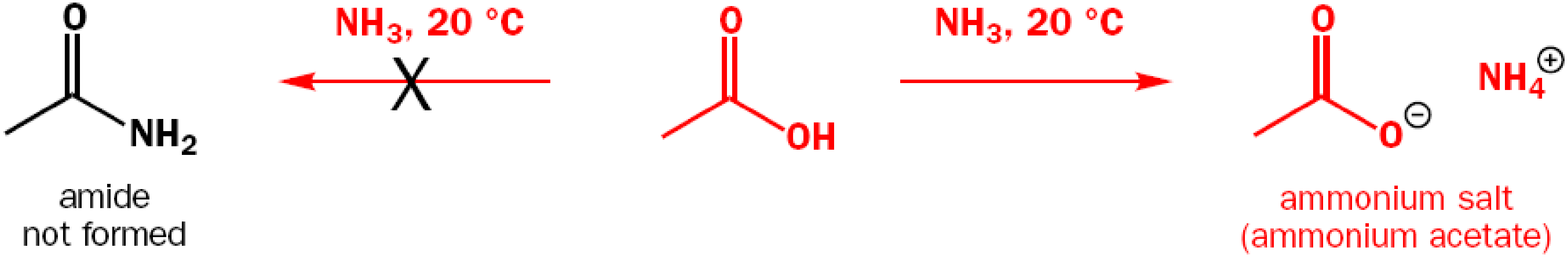
Transesterificações têm normalmente uma constante de equilíbrio cerca de 1, mas em alguns casos o equilíbrio pode ser deslocado.

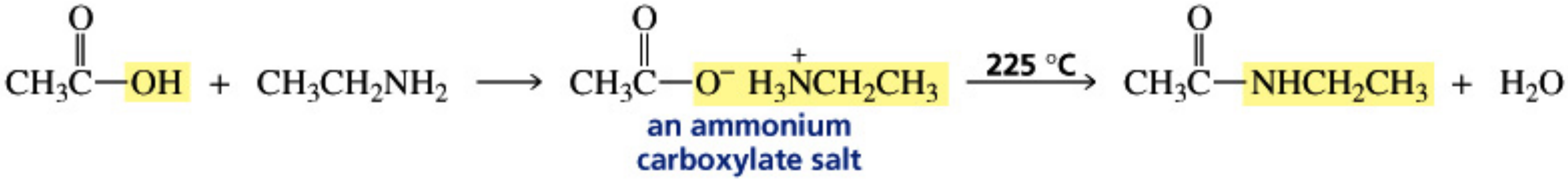
Como isso poderia ser feito?

O mecanismo destas reações é análogo ao de hidrólise.

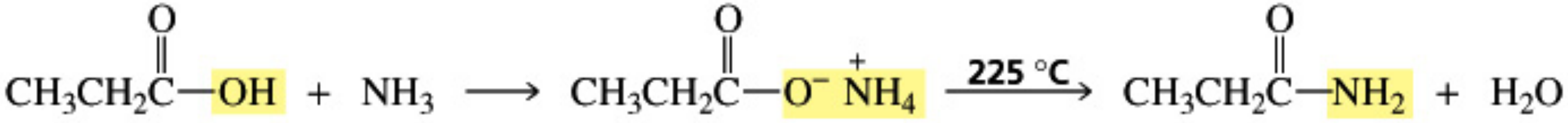
# 6.8. Formação e Reações de Amidas

## Formação a partir de ácidos carboxílicos:





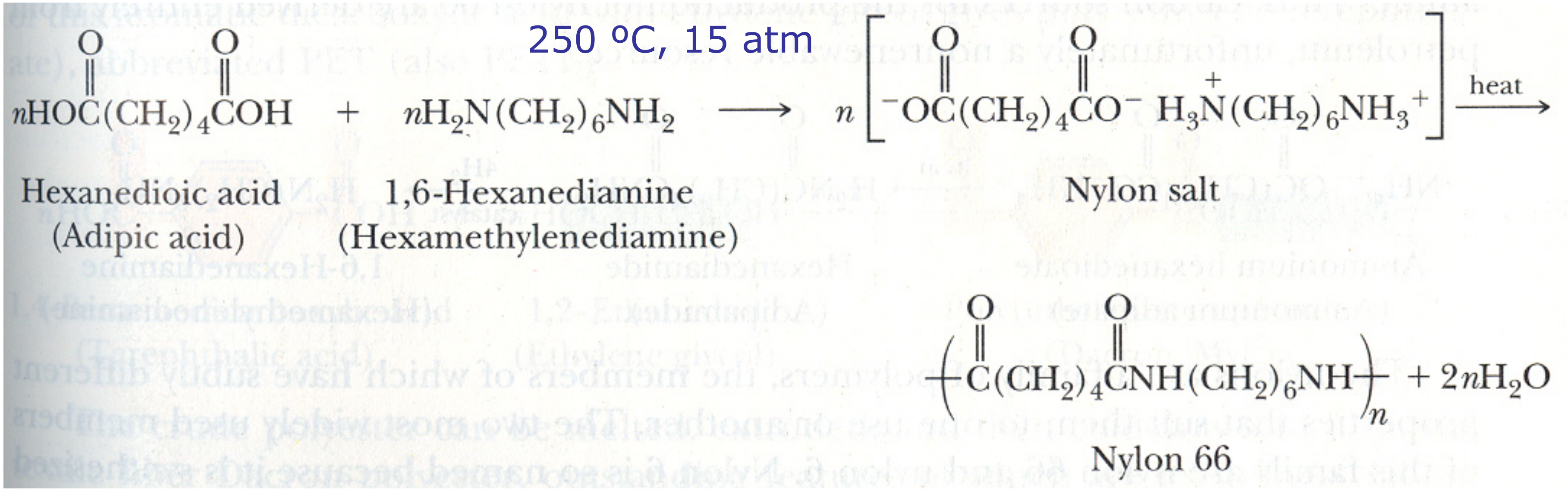
$$CH_3\overset{\overset{O}{\|}}{C}-OH + CH_3CH_2NH_2 \longrightarrow CH_3\overset{\overset{O}{\|}}{C}-O^- \ H_3\overset{+}{N}CH_2CH_3 \xrightarrow{225\ ^\circ C} CH_3\overset{\overset{O}{\|}}{C}-NHCH_2CH_3 + H_2O$$



$$CH_3CH_2\overset{\overset{O}{\|}}{C}-OH + NH_3 \longrightarrow CH_3CH_2\overset{\overset{O}{\|}}{C}-O^- \ \overset{+}{N}H_4 \xrightarrow{225\ ^\circ C} CH_3CH_2\overset{\overset{O}{\|}}{C}-NH_2 + H_2O$$

**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



$$n\mathrm{HO}\overset{O}{\overset{\|}{C}}(CH_2)_4\overset{O}{\overset{\|}{C}}OH + nH_2N(CH_2)_6NH_2 \xrightarrow{250\ ºC,\ 15\ atm} n\left[{}^{-}O\overset{O}{\overset{\|}{C}}(CH_2)_4\overset{O}{\overset{\|}{C}}O^{-}\ H_3\overset{+}{N}(CH_2)_6NH_3^{+}\right] \xrightarrow{heat}$$

$$\left(\overset{O}{\overset{\|}{C}}(CH_2)_4\overset{O}{\overset{\|}{C}}NH(CH_2)_6NH\right)_n + 2nH_2O$$

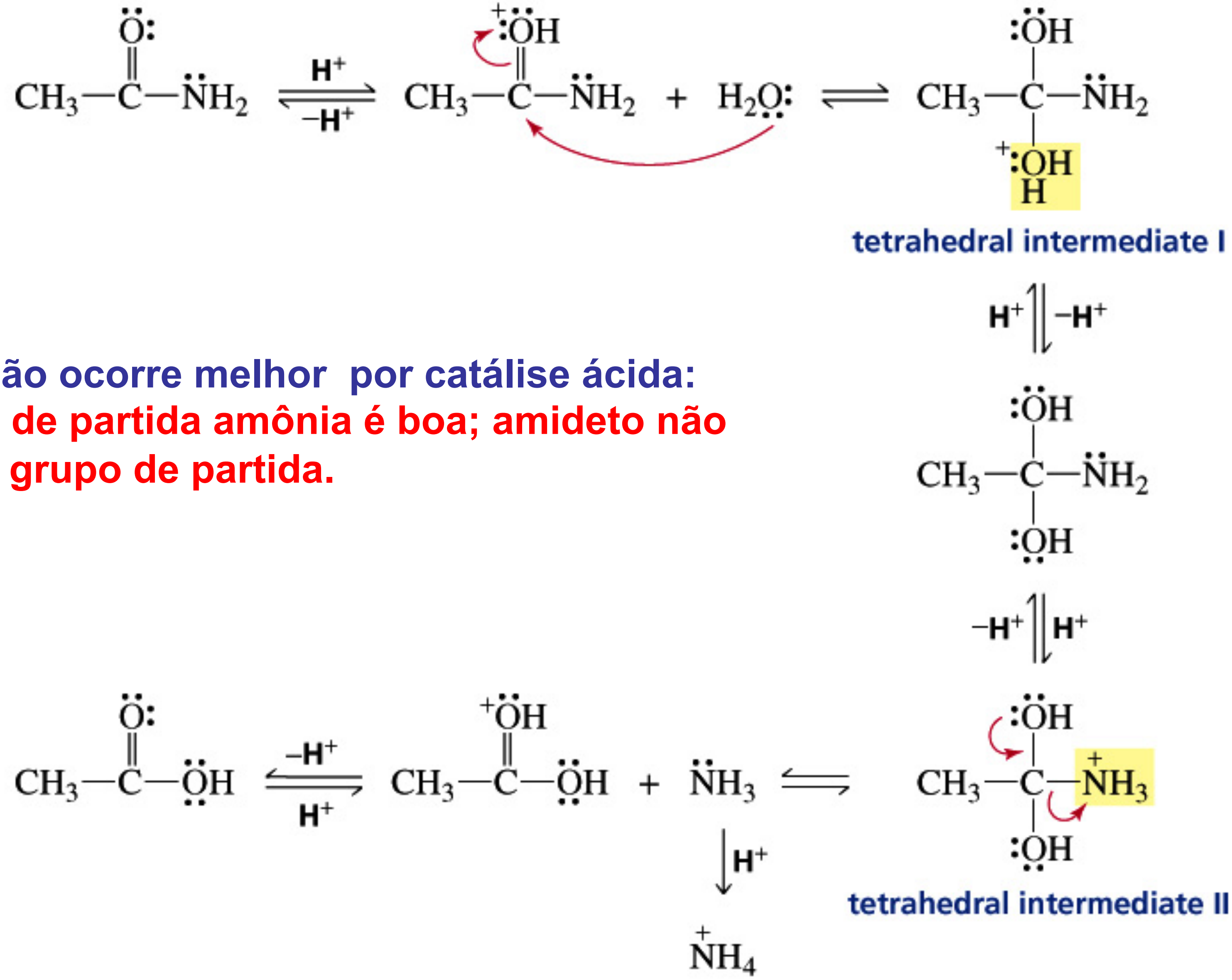
Hexanedioic acid
(Adipic acid)

1,6-Hexanediamine
(Hexamethylenediamine)

Nylon salt

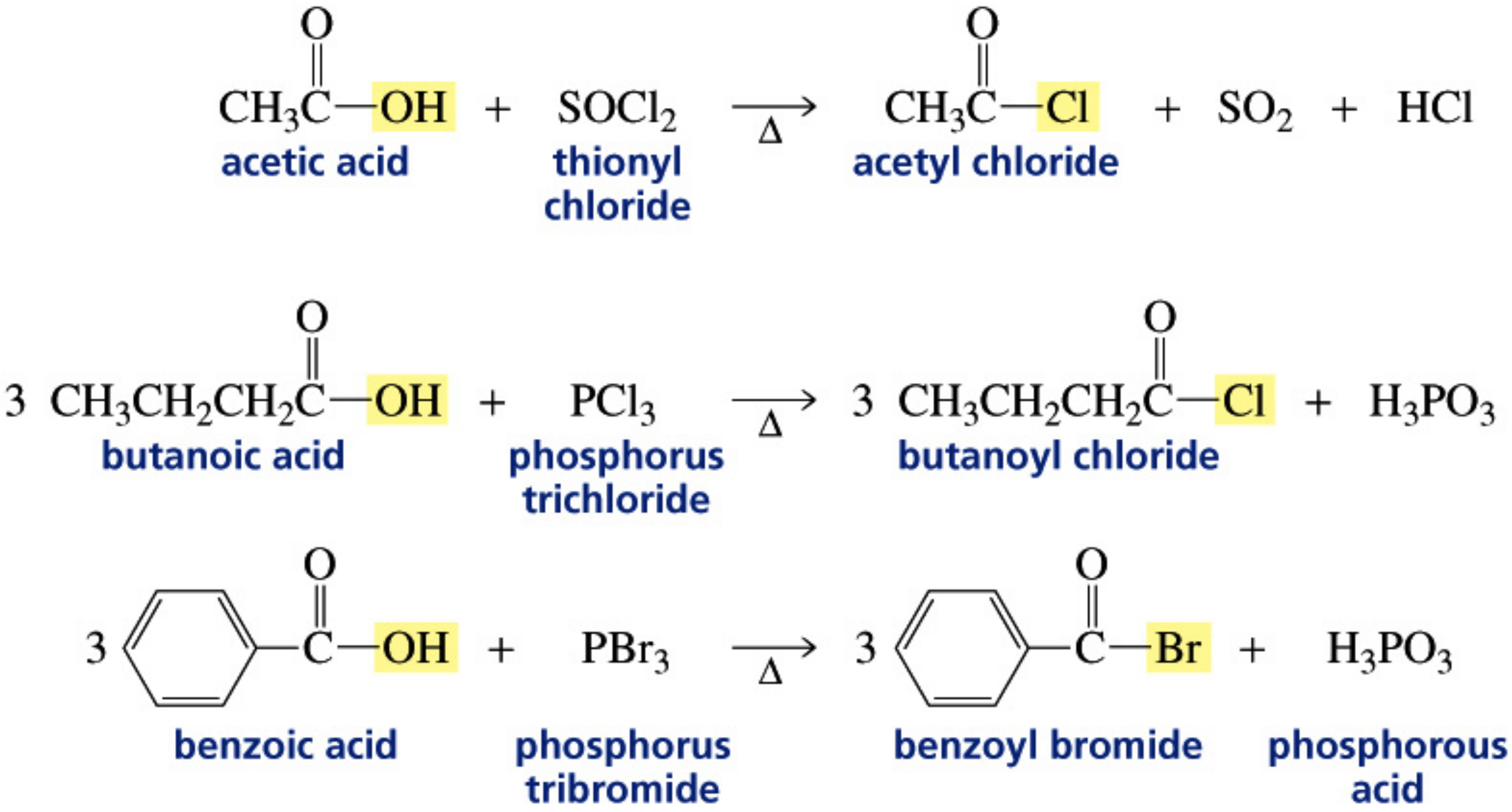
Nylon 66

# Mecanismo da Hidrólise de Amidas



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

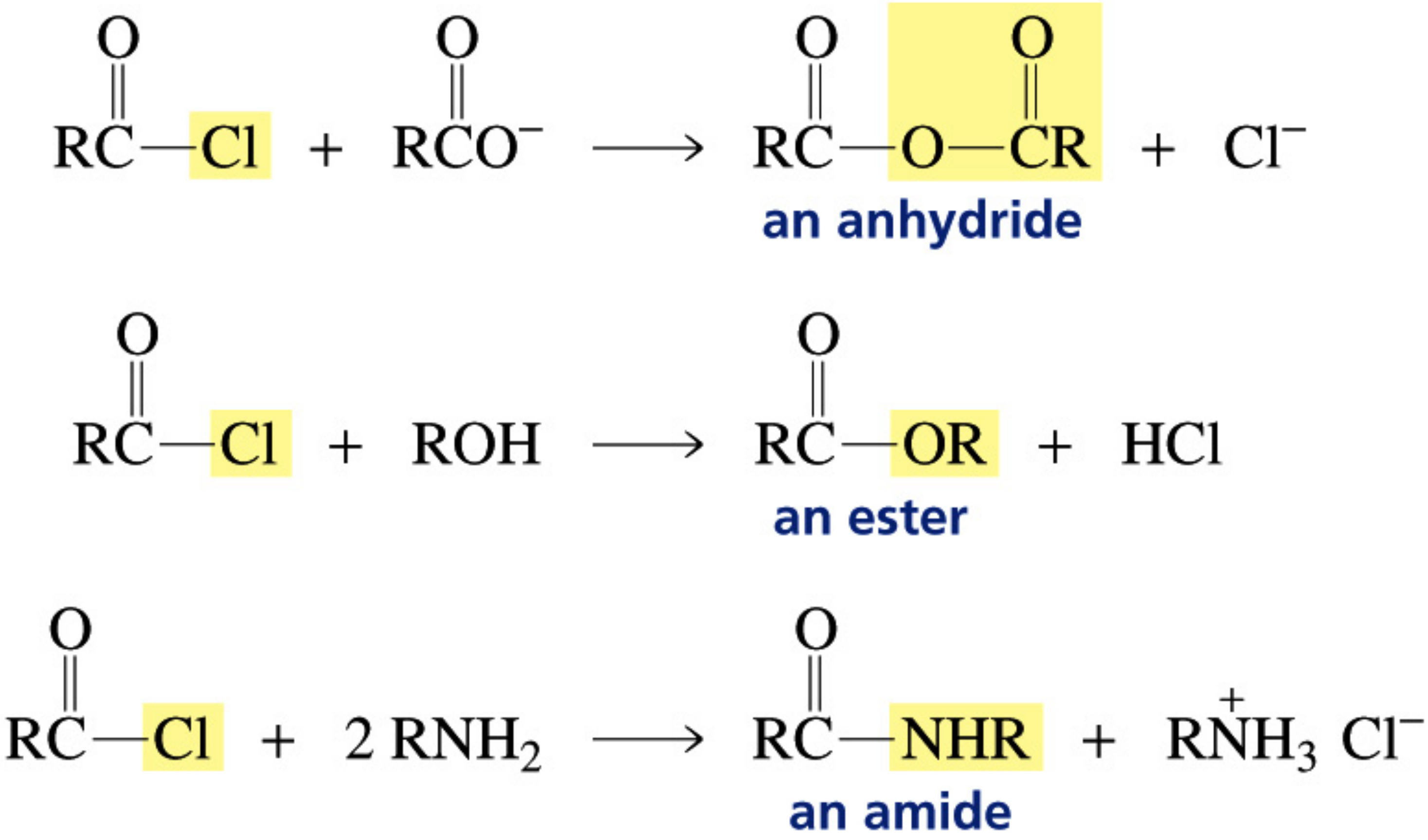
# 6.9. Ativação de Ácidos Carboxílicos: Preparação de Haletos de Acila



$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}-OH + SOCl_2 \xrightarrow[\Delta]{} CH_3\overset{\overset{\displaystyle O}{\|}}{C}-Cl + SO_2 + HCl$$

$$3\ CH_3CH_2CH_2\overset{\overset{\displaystyle O}{\|}}{C}-OH + PCl_3 \xrightarrow[\Delta]{} 3\ CH_3CH_2CH_2\overset{\overset{\displaystyle O}{\|}}{C}-Cl + H_3PO_3$$

# Haletos de Acila na Preparação de Derivados Carboxílicos



$$\mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{Cl} + \mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{O}^- \longrightarrow \mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{O}-\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{R} + \mathrm{Cl}^-$$

**an anhydride**

$$\mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{Cl} + \mathrm{ROH} \longrightarrow \mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{OR} + \mathrm{HCl}$$

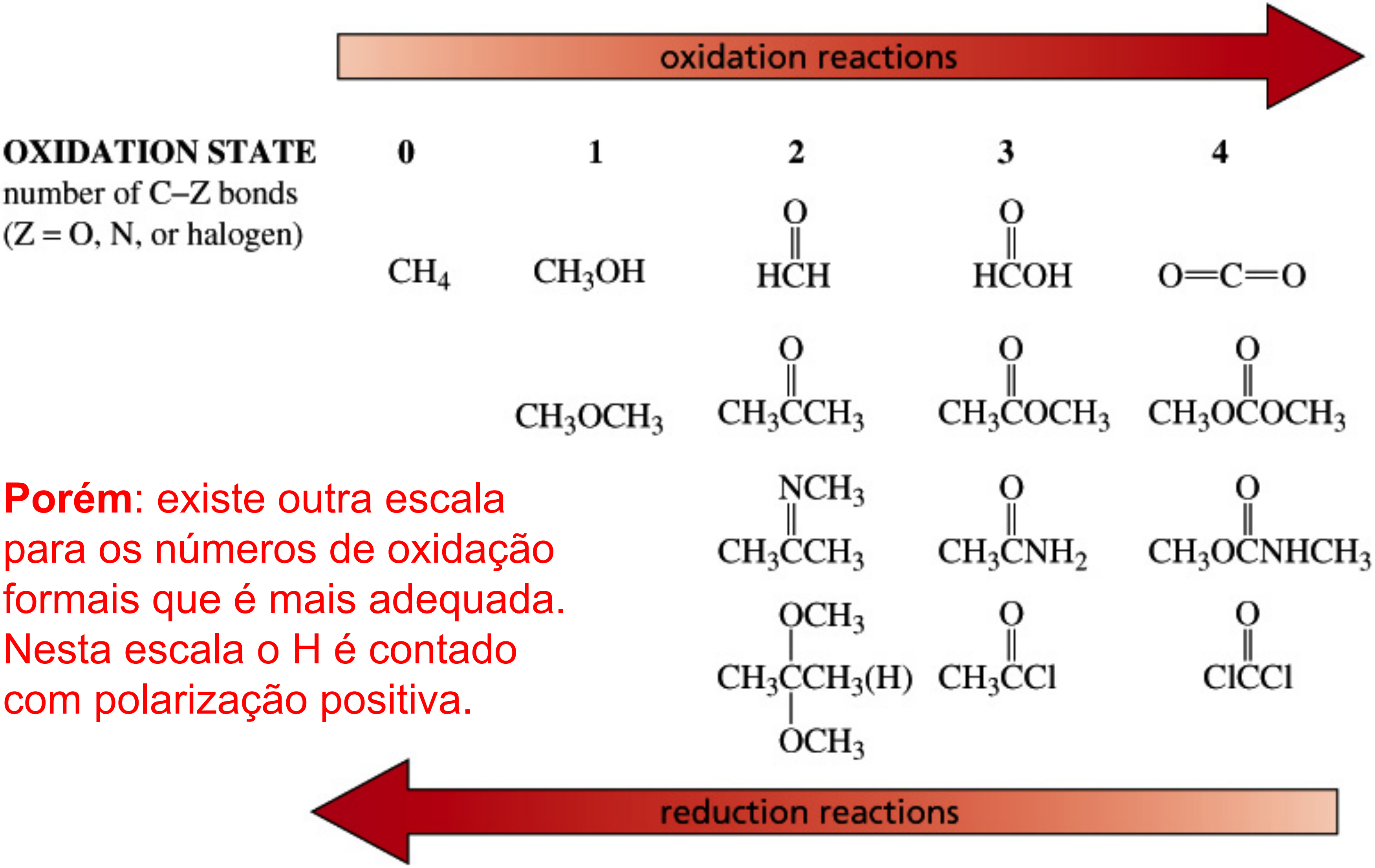
**an ester**

$$\mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{Cl} + 2\,\mathrm{RNH_2} \longrightarrow \mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{NHR} + \mathrm{R}\overset{+}{\mathrm{N}}\mathrm{H_3}\;\mathrm{Cl}^-$$

**an amide**

# 6.10. Reações de Oxidação e Redução de Compostos Orgânicos

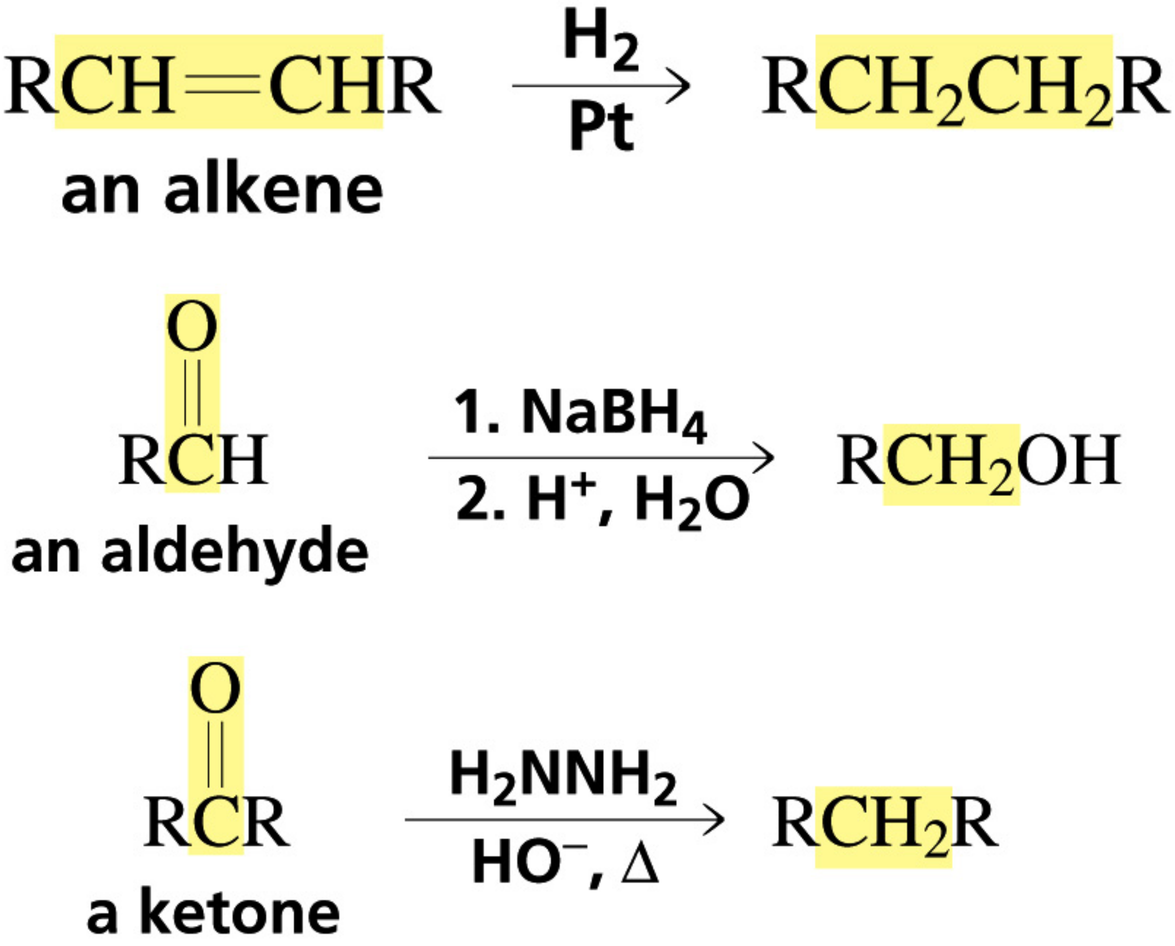
# Número de Oxidação ‘Formal’ de Compostos Orgânicos



**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



$$RCH{=}CHR \xrightarrow[\text{Pt}]{H_2} RCH_2CH_2R$$

an alkene

$$R\overset{\overset{\Large O}{\|}}{C}H \xrightarrow[2.\ H^+,\ H_2O]{1.\ NaBH_4} RCH_2OH$$

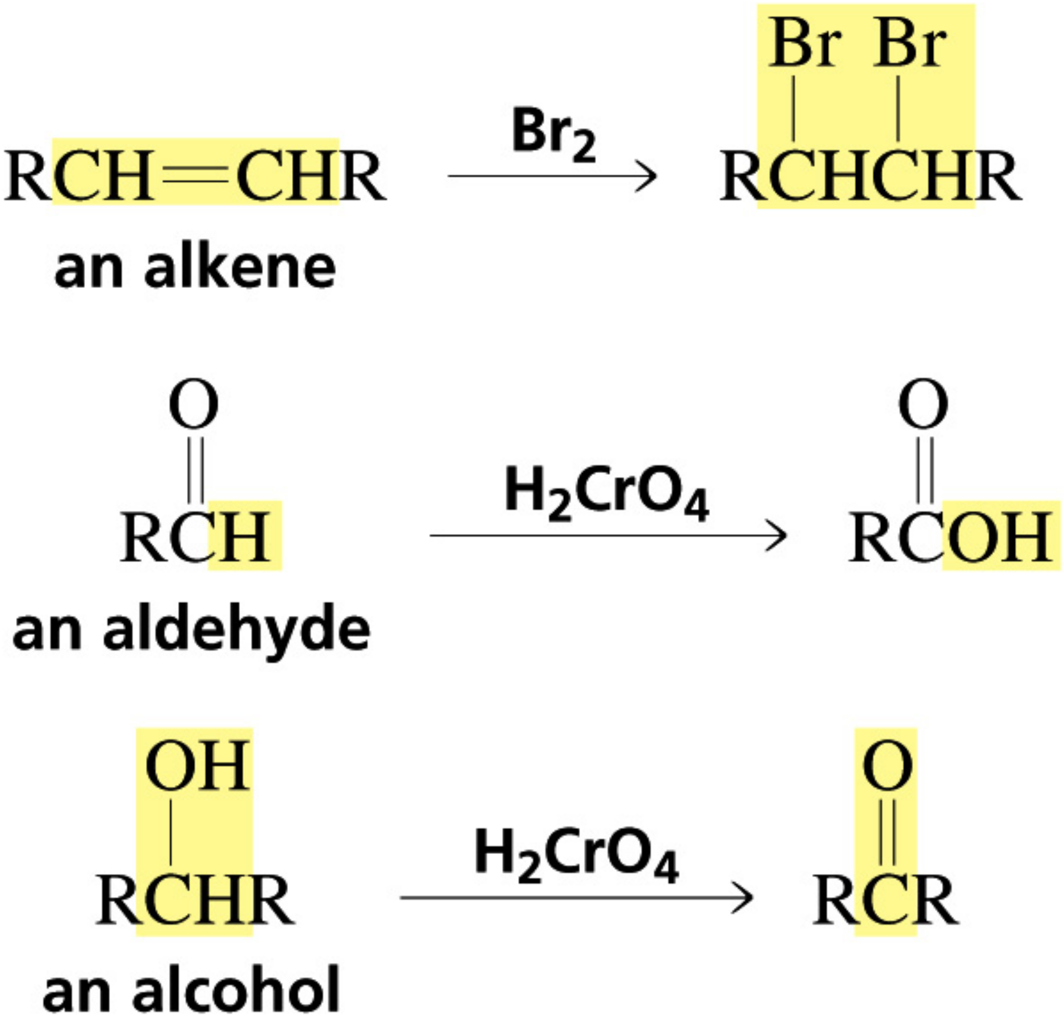
an aldehyde

$$R\overset{\overset{\Large O}{\|}}{C}R \xrightarrow[HO^-,\ \Delta]{H_2NNH_2} RCH_2R$$

a ketone

# Oxidação de Compostos Orgânicos:

## Bromo, ácido crômico



$$\mathrm{RCH{=}CHR} \xrightarrow{Br_2} \mathrm{R}\overset{Br}{\mathrm{C}}\mathrm{H}\overset{Br}{\mathrm{C}}\mathrm{HR}$$

$$\mathrm{R}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{H} \xrightarrow{H_2CrO_4} \mathrm{R}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$$

$$\mathrm{R}\overset{OH}{\overset{|}{\mathrm{C}}}\mathrm{HR} \xrightarrow{H_2CrO_4} \mathrm{R}\overset{O}{\overset{\|}{\mathrm{C}}}\mathrm{R}$$

# Redução por Hidrogenação Catalítica

$$CH_3CH_2CH{=}CH_2 + H_2 \xrightarrow{\text{Pt, Pd, or Ni}} CH_3CH_2CH_2CH_3$$

**1-butene** → **butane**

$$CH_3CH_2CH_2C{\equiv}CH + 2\,H_2 \xrightarrow{\text{Pt, Pd, or Ni}} CH_3CH_2CH_2CH_2CH_3$$

**1-pentyne** → **pentane**

$$CH_3C{\equiv}CCH_3 + H_2 \xrightarrow{\text{Lindlar's catalyst}}$$

**2-butyne**

***cis*-2-butene**

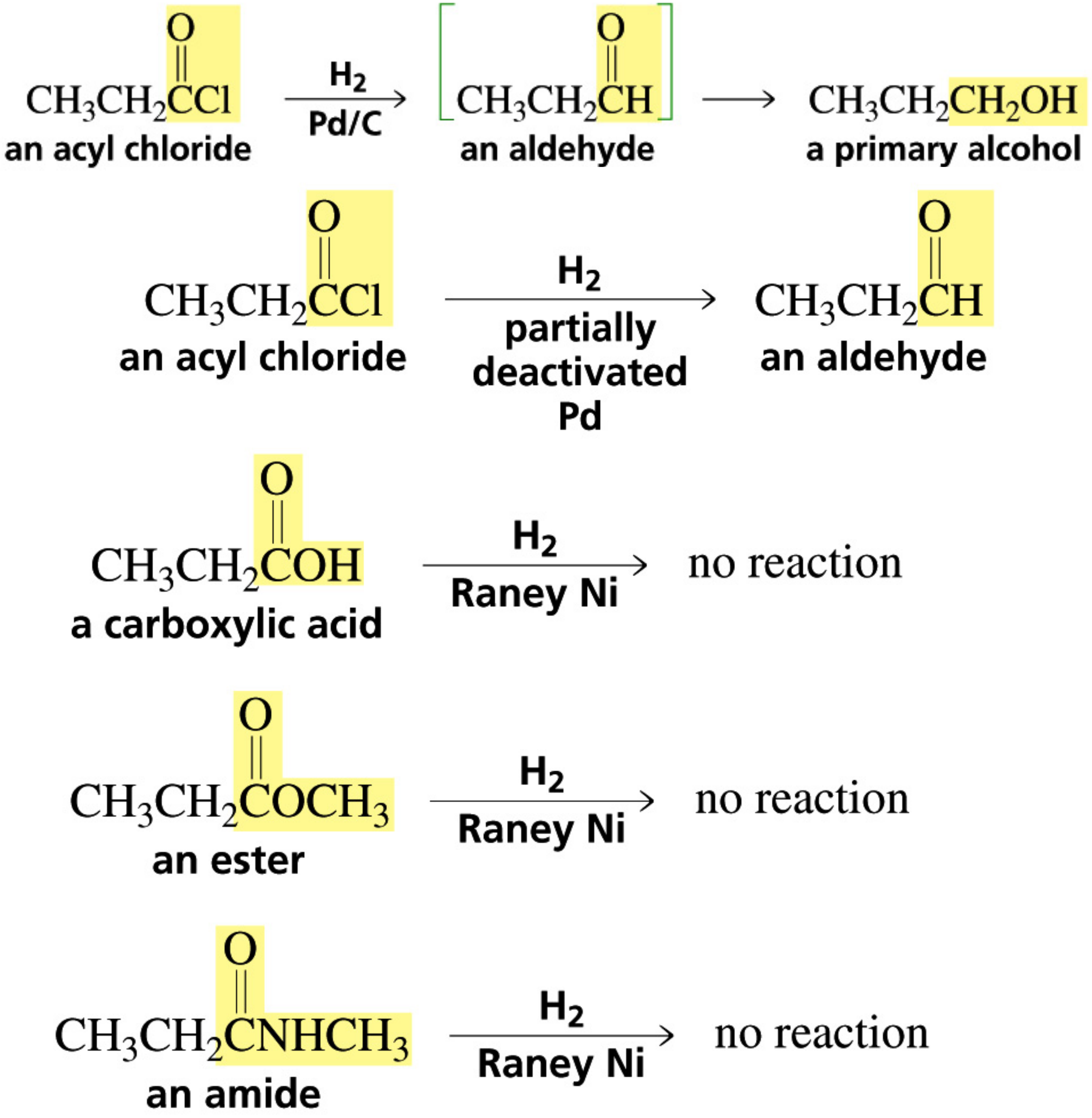
$$CH_3CH_2CH{=}NCH_3 + H_2 \xrightarrow{\text{Pd/C}} CH_3CH_2CH_2NHCH_3$$

**methylpropylamine**

$$CH_3CH_2CH_2C{\equiv}N + 2\,H_2 \xrightarrow{\text{Pd/C}} CH_3CH_2CH_2CH_2NH_2$$

**butylamine**

# Redução por Hidrogenação Catalítica



$$\mathrm{CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}Cl} \xrightarrow[\text{Pd/C}]{\text{H}_2} \left[\mathrm{CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}H}\right] \longrightarrow \mathrm{CH_3CH_2CH_2OH}$$

$$\mathrm{CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}Cl} \xrightarrow[\text{partially deactivated Pd}]{\text{H}_2} \mathrm{CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}H}$$

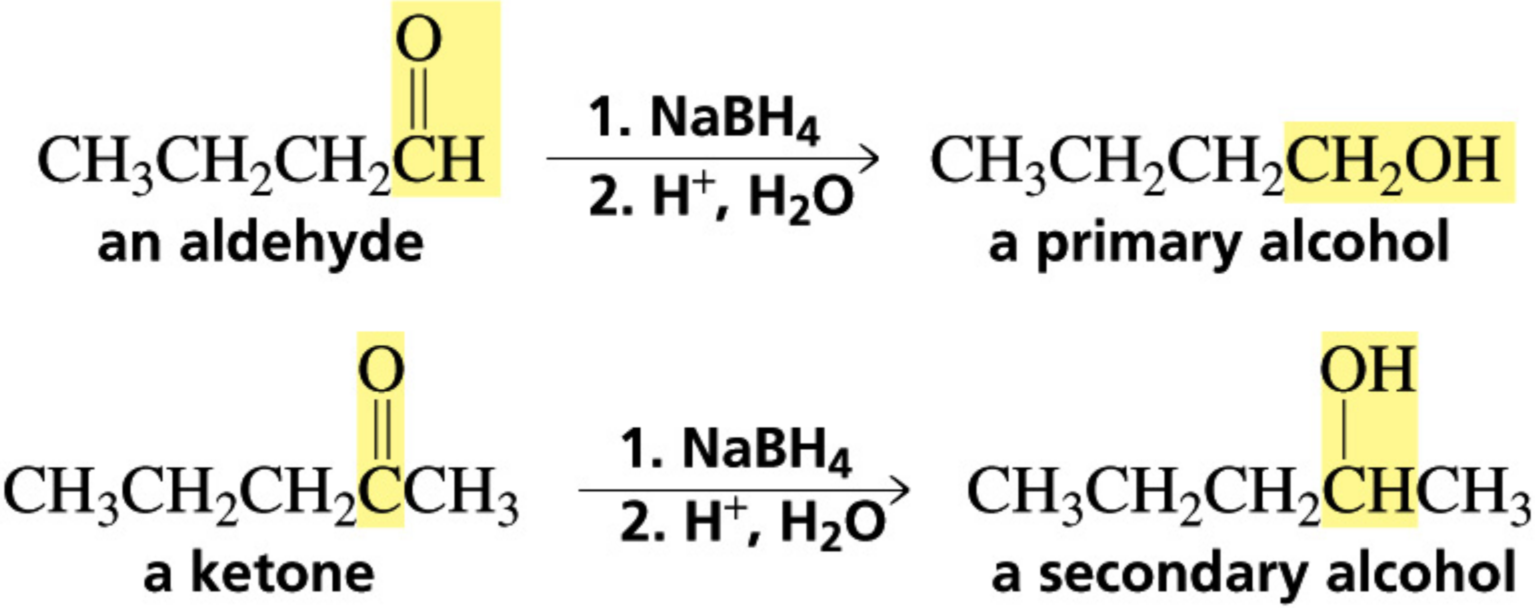
$$\mathrm{CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}OH} \xrightarrow[\text{Raney Ni}]{\text{H}_2} \text{no reaction}$$

$$\mathrm{CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}OCH_3} \xrightarrow[\text{Raney Ni}]{\text{H}_2} \text{no reaction}$$

$$\mathrm{CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}NHCH_3} \xrightarrow[\text{Raney Ni}]{\text{H}_2} \text{no reaction}$$

# Redução de Compostos Carbonílicos:

## Adição de Íon Hidreto, seguido de protonação



$$CH_3CH_2CH_2\overset{\overset{\displaystyle O}{\|}}{C}H \xrightarrow[\text{2. } H^+,\ H_2O]{\text{1. } NaBH_4} CH_3CH_2CH_2CH_2OH$$

an aldehyde

a primary alcohol

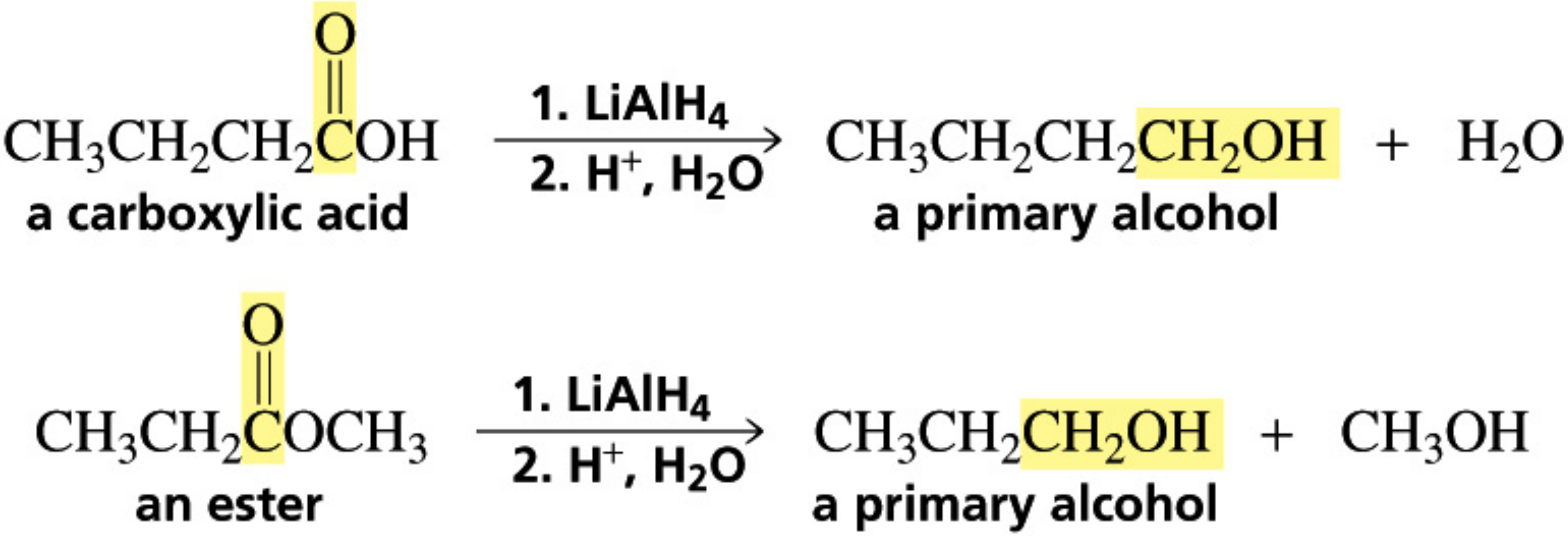
$$CH_3CH_2CH_2\overset{\overset{\displaystyle O}{\|}}{C}CH_3 \xrightarrow[\text{2. } H^+,\ H_2O]{\text{1. } NaBH_4} CH_3CH_2CH_2\overset{\overset{\displaystyle OH}{|}}{C}HCH_3$$

a ketone

a secondary alcohol

# Redução de Compostos Carboxílicos:

## Utilizando-se Hidreto de Lítio Alumínio



$$CH_3CH_2CH_2\overset{\overset{\displaystyle O}{\|}}{C}OH \xrightarrow[\text{2. } H^+,\ H_2O]{\text{1. } LiAlH_4} CH_3CH_2CH_2CH_2OH + H_2O$$

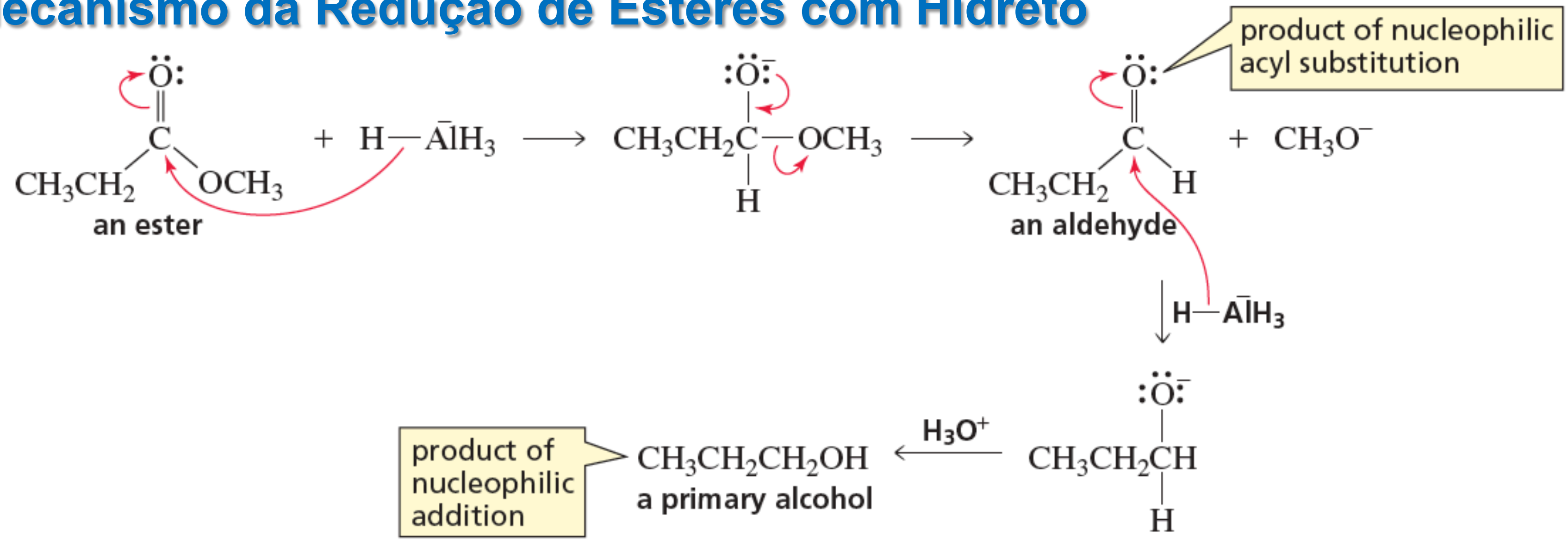
$$CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}OCH_3 \xrightarrow[\text{2. } H^+,\ H_2O]{\text{1. } LiAlH_4} CH_3CH_2CH_2OH + CH_3OH$$

$LiAlH_4$ é agente redutor mais forte do que $NaBH_4$;

$LiAlH_4$ é usado para reduzir composto que não reagem com $NaBH_4$ como ácidos carboxílicos.

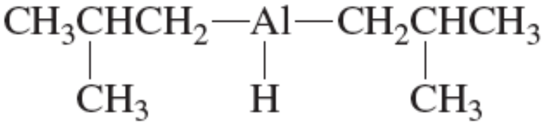
# Redução de Derivados de Ácidos Carboxílicos

## Mecanismo da Redução de Ésteres com Hidreto



product of nucleophilic acyl substitution

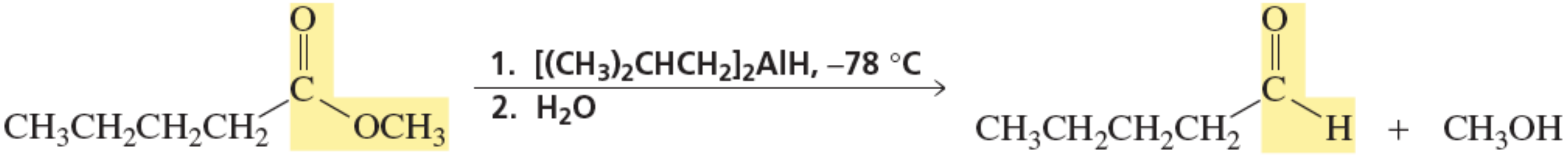
product of nucleophilic addition



$$\underset{CH_3}{CH_3CH}CH_2-\underset{H}{Al}-CH_2\underset{CH_3}{CH}CH_3$$

**diisobutylaluminum hydride**
**DIBALH**

## Redução de Ésteres para Aldeídos: DIBALH



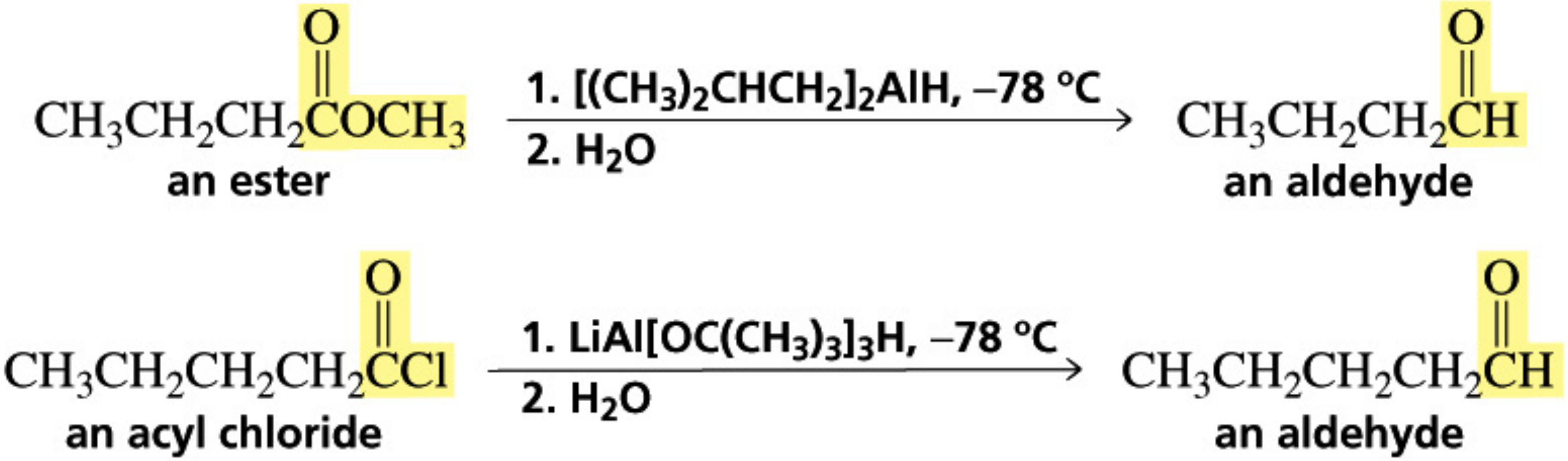
methyl pentanoate

1. $[(CH_3)_2CHCH_2]_2AlH$, –78 °C
2. $H_2O$

pentanal

$CH_3OH$

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



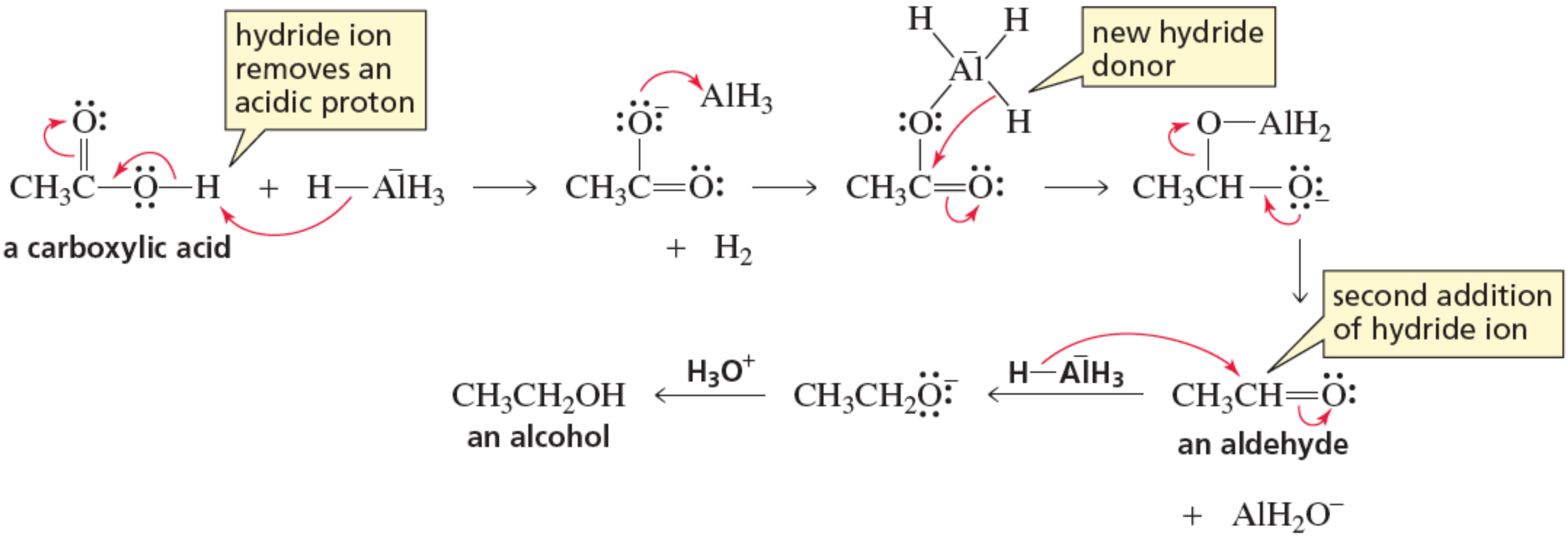
$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow[\text{2. } H_2O]{\text{1. } [(CH_3)_2CHCH_2]_2AlH,\ -78\ °C} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H$$

$$CH_3CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}Cl \xrightarrow[\text{2. } H_2O]{\text{1. } LiAl[OC(CH_3)_3]_3H,\ -78\ °C} CH_3CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}H$$

DIBAL permite a adição de somente um hidreto ao éster.

A substituição de hidrogênios do $LiAlH_4$ por grupos OR leva a uma diminuição da reatividade do reagente.

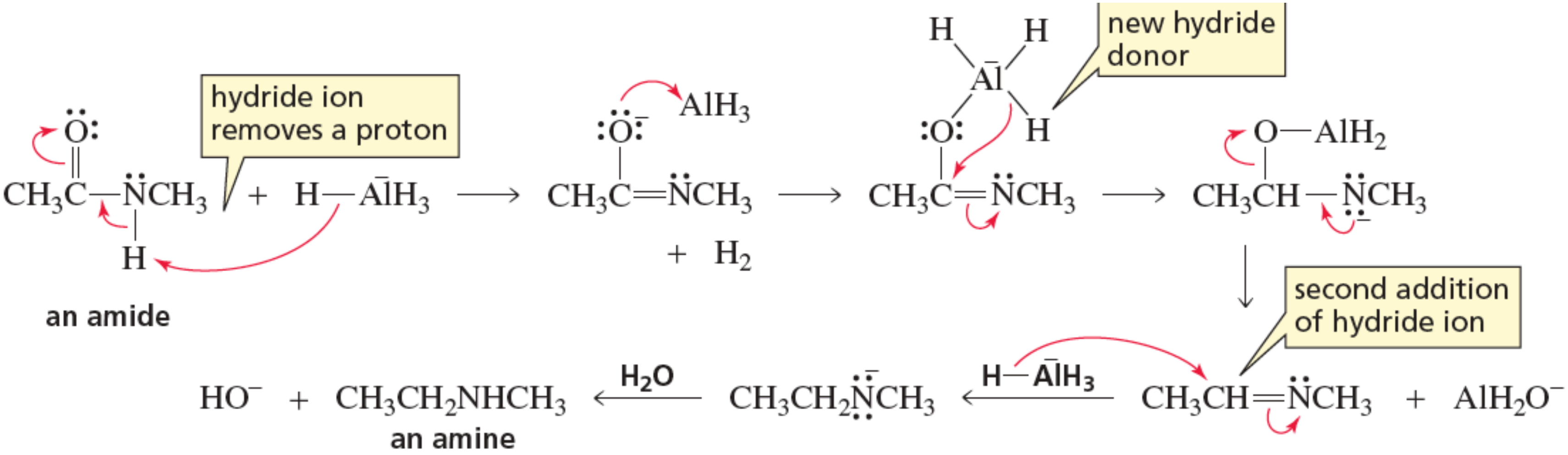
# Mecanismo da Redução de Ácidos Carboxílicos com Hidreto


hydride ion removes an acidic proton

new hydride donor

second addition of hydride ion

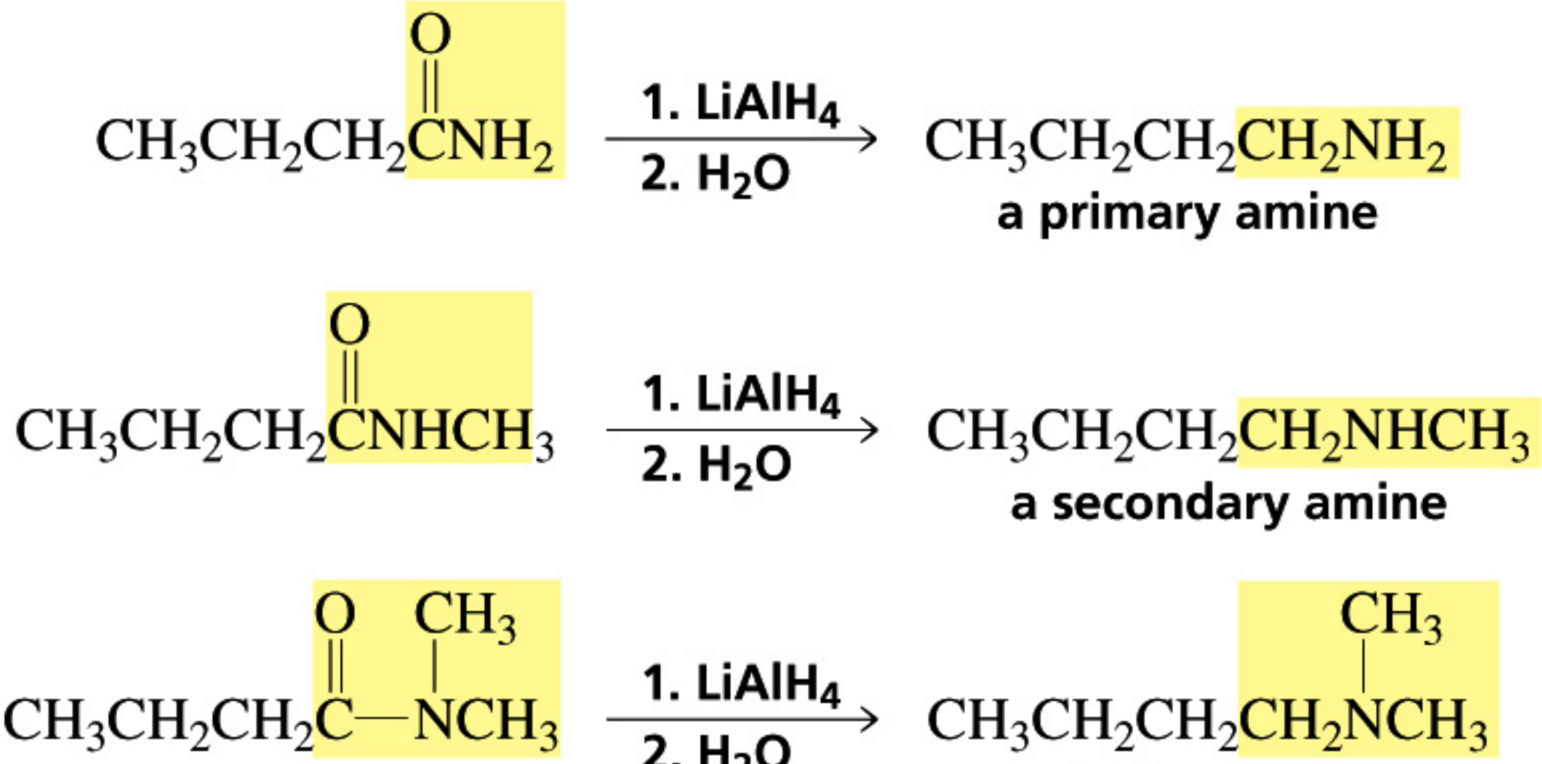
# Mecanismo da Redução de Amidas com Hidreto


hydride ion removes a proton

new hydride donor

second addition of hydride ion

# Formação de Aminas por Redução



$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}NH_2 \xrightarrow[2.\ H_2O]{1.\ LiAlH_4} CH_3CH_2CH_2CH_2NH_2$$

a primary amine

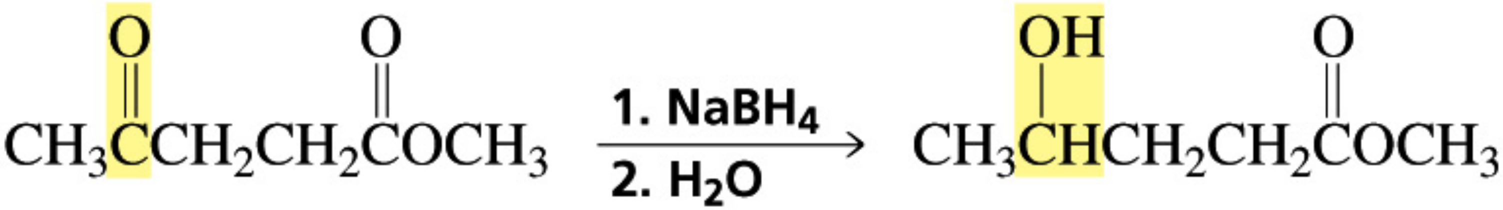
$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}NHCH_3 \xrightarrow[2.\ H_2O]{1.\ LiAlH_4} CH_3CH_2CH_2CH_2NHCH_3$$

a secondary amine

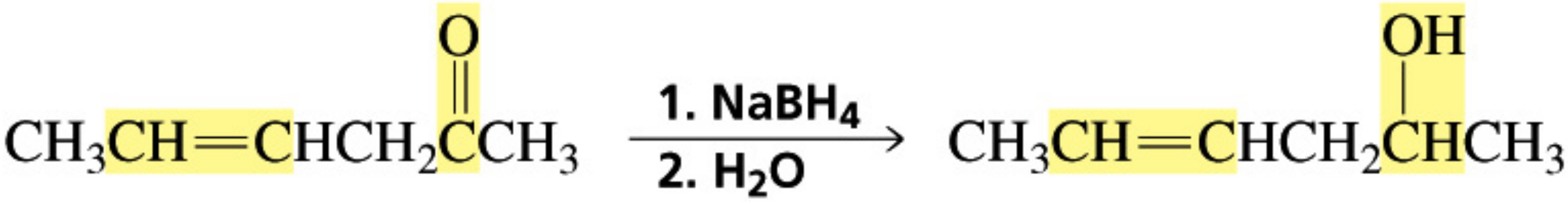
$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}-\overset{CH_3}{\overset{|}{N}}CH_3 \xrightarrow[2.\ H_2O]{1.\ LiAlH_4} CH_3CH_2CH_2CH_2\overset{CH_3}{\overset{|}{N}}CH_3$$

a tertiary amine

# Redução Seletiva de Aldeídos e Cetonas com $NaBH_4$

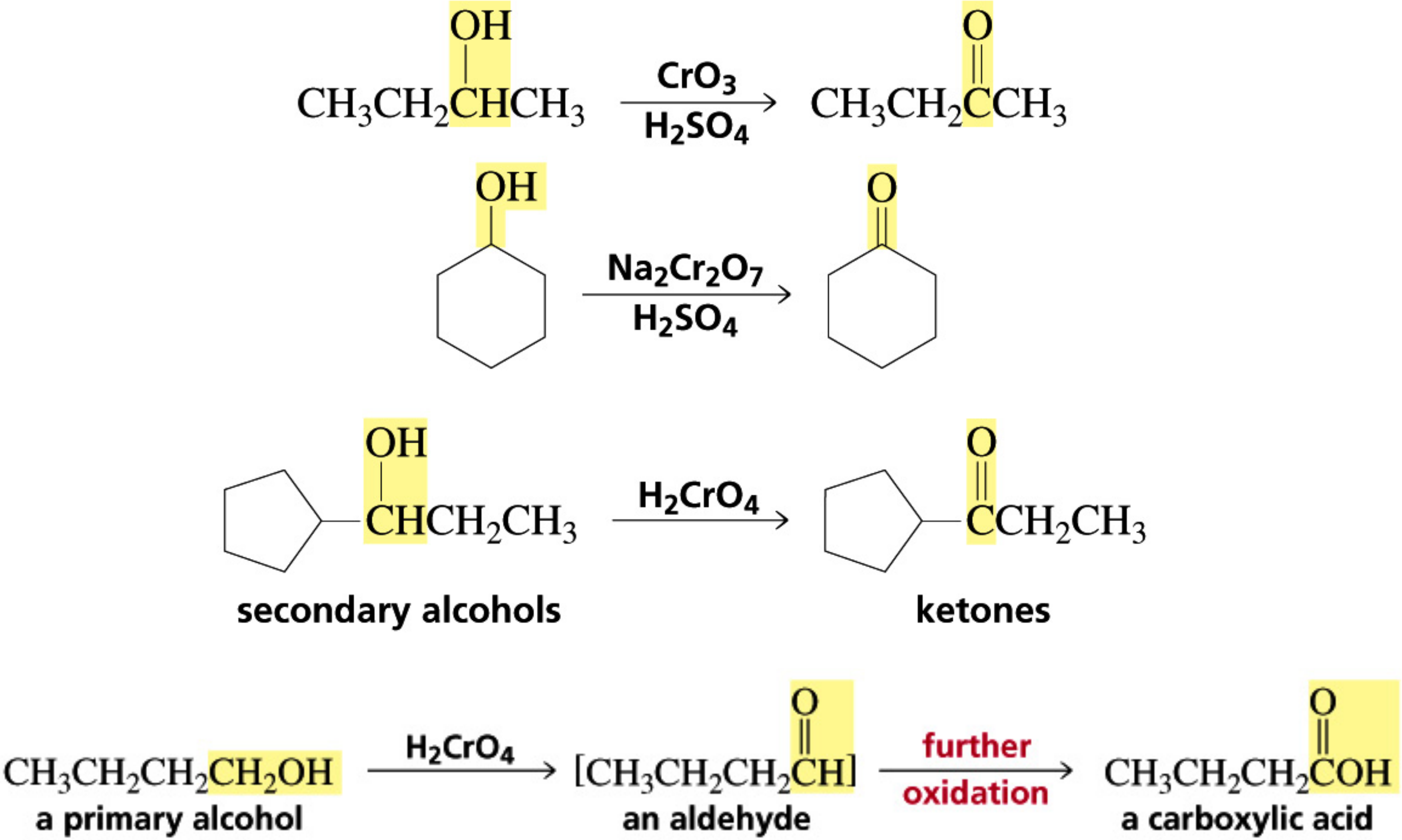


$$CH_3\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow[\text{2. } H_2O]{\text{1. } NaBH_4} CH_3\overset{OH}{\overset{|}{C}}HCH_2CH_2\overset{O}{\overset{\|}{C}}OCH_3$$



$$CH_3CH{=}CHCH_2\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[\text{2. } H_2O]{\text{1. } NaBH_4} CH_3CH{=}CHCH_2\overset{OH}{\overset{|}{C}}HCH_3$$

# Oxidação de Alcóois com Óxidos de Cromo



$$CH_3CH_2\overset{OH}{\overset{|}{C}}HCH_3 \xrightarrow[H_2SO_4]{CrO_3} CH_3CH_2\overset{O}{\overset{\|}{C}}CH_3$$

secondary alcohols

ketones

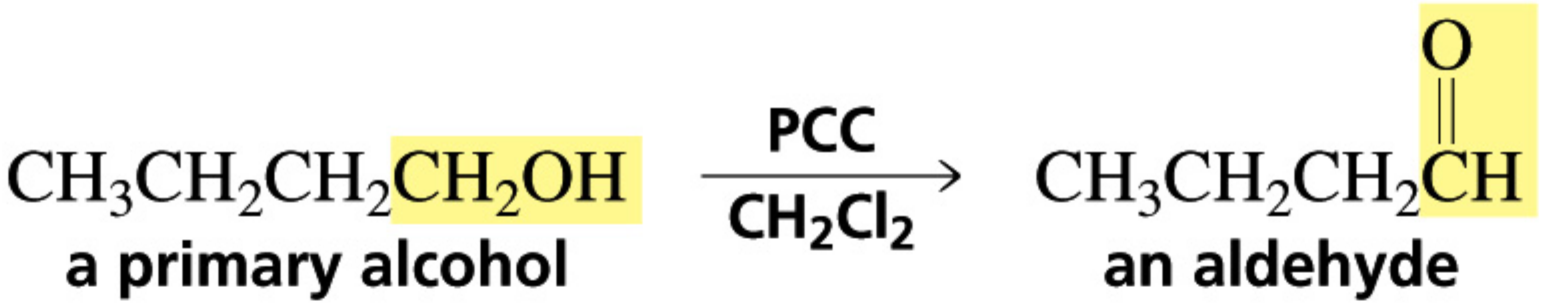
$$CH_3CH_2CH_2CH_2OH \xrightarrow{H_2CrO_4} [CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H] \xrightarrow[\text{oxidation}]{\text{further}} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH$$

a primary alcohol

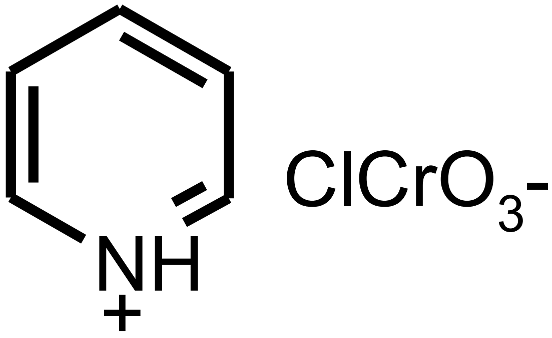
an aldehyde

a carboxylic acid

# Oxidação Seletiva de Alcóois Primários para Aldeídos com PCC

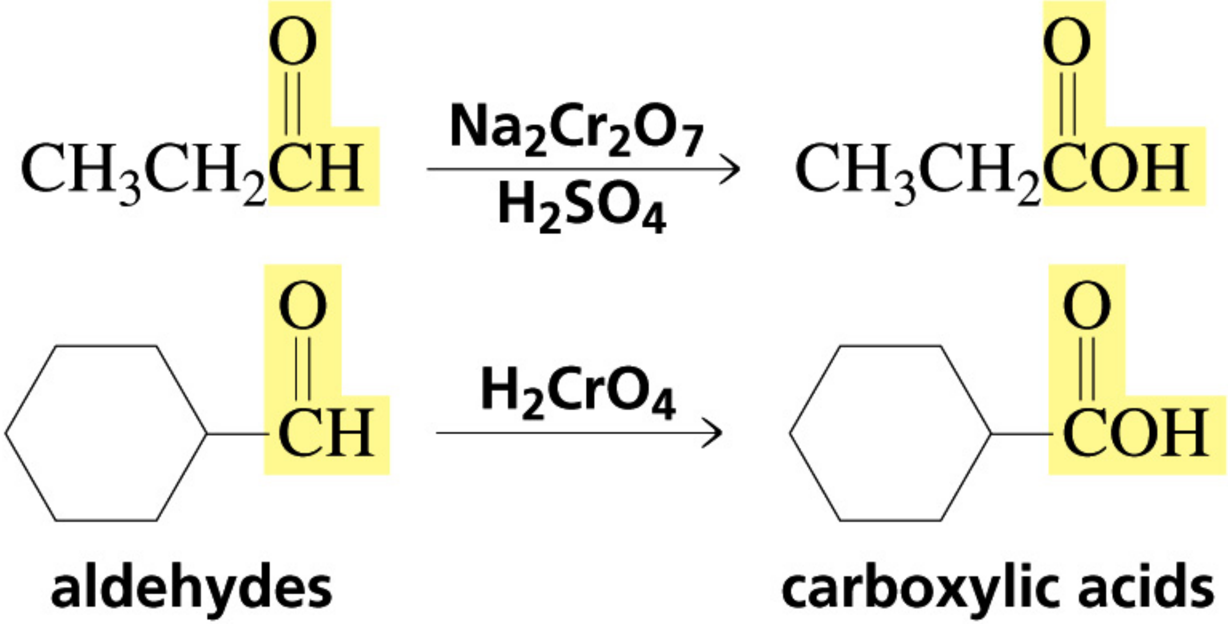


$$CH_3CH_2CH_2CH_2OH \xrightarrow[CH_2Cl_2]{PCC} CH_3CH_2CH_2\overset{\overset{\displaystyle O}{\|}}{C}H$$

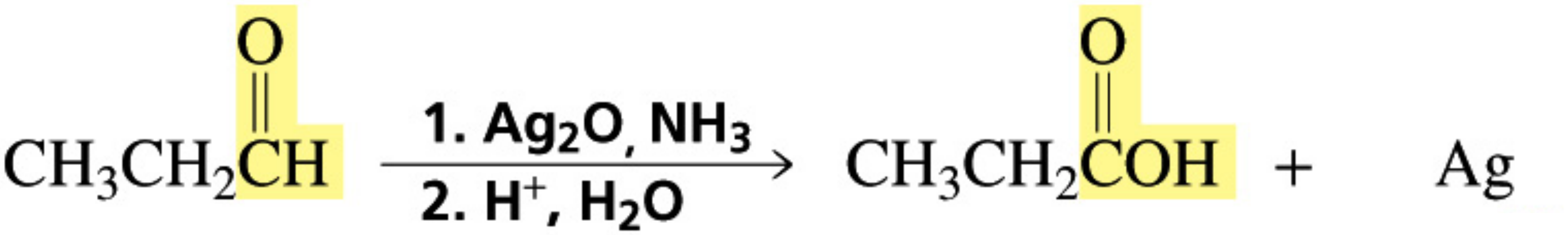


A oxidação de um álcool primário pode ser interrompida no aldeído se piridínio clorocromato (PCC) for usado como agente de oxidação.

# Oxidação de Aldeídos



# Oxidação de Aldeídos



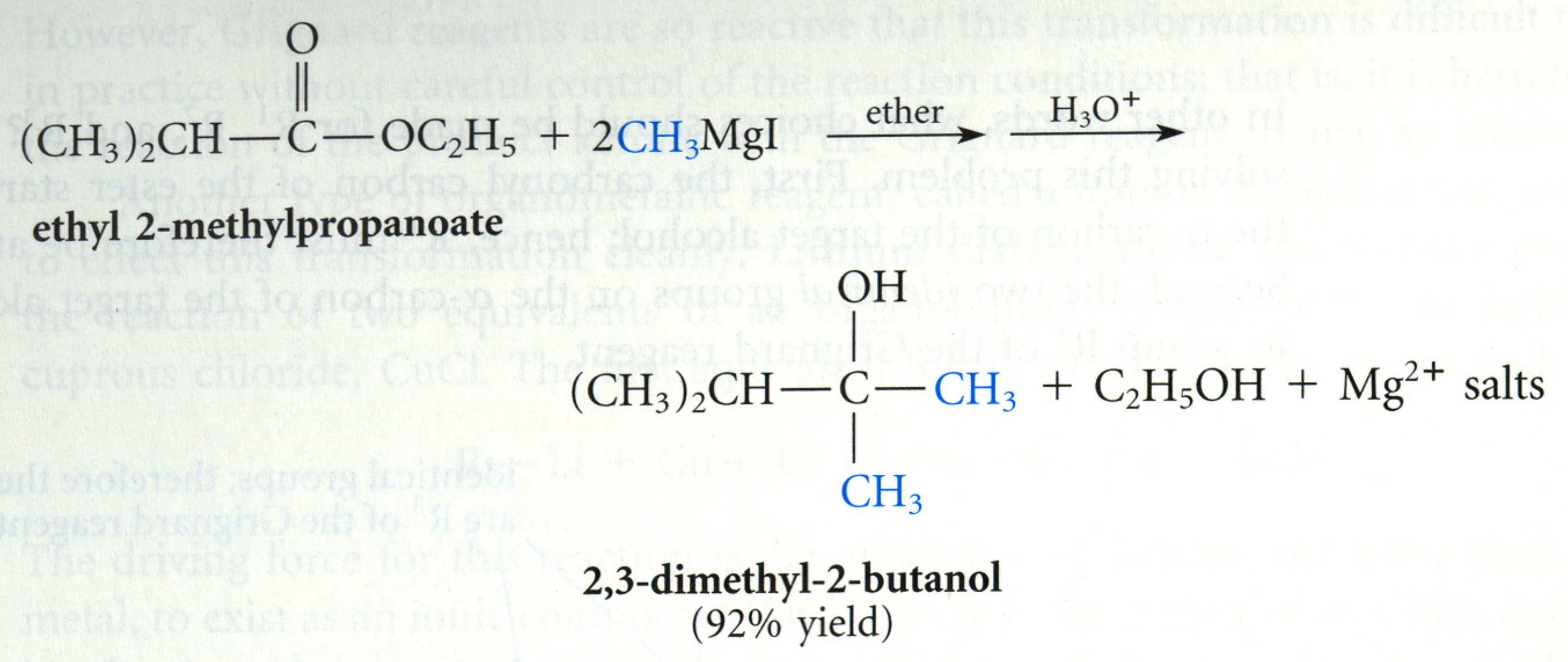
$$\mathrm{CH_3CH_2\overset{\overset{O}{\|}}{C}H} \xrightarrow[\text{2. } H^+,\ H_2O]{\text{1. } Ag_2O,\ NH_3} \mathrm{CH_3CH_2\overset{\overset{O}{\|}}{C}OH} + \mathrm{Ag}$$

**Prata metálica (espelho de prata)**

**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

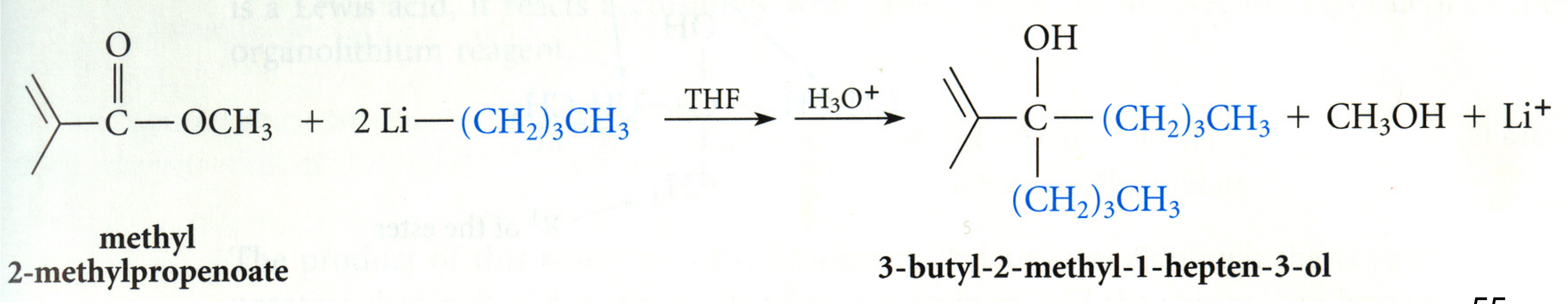
## Reação de Ésteres com Organometálicos de Magnésio e de Lítio:



$$(CH_3)_2CH-\overset{\overset{\displaystyle O}{\|}}{C}-OC_2H_5 + 2CH_3MgI \xrightarrow{ether} \xrightarrow{H_3O^+} (CH_3)_2CH-\underset{\underset{\displaystyle CH_3}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}-CH_3 + C_2H_5OH + Mg^{2+} \text{ salts}$$

**ethyl 2-methylpropanoate**

**2,3-dimethyl-2-butanol**
(92% yield)

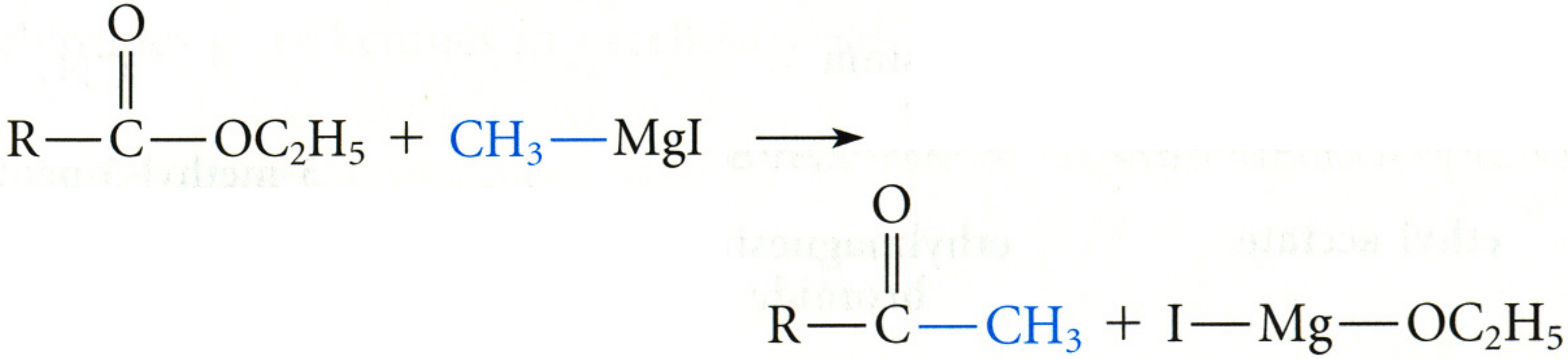


**methyl 2-methylpropenoate**

**3-butyl-2-methyl-1-hepten-3-ol**

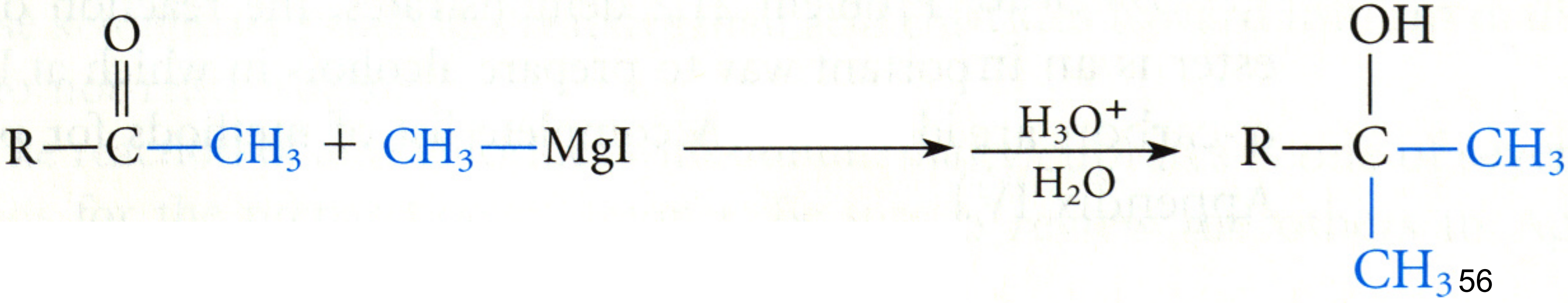
# Mecanismo da Reação de Ésteres com Organometálicos de Magnésio e de Lítio:

**Etapa 1:** Substituição Nucleofílica Acílica:



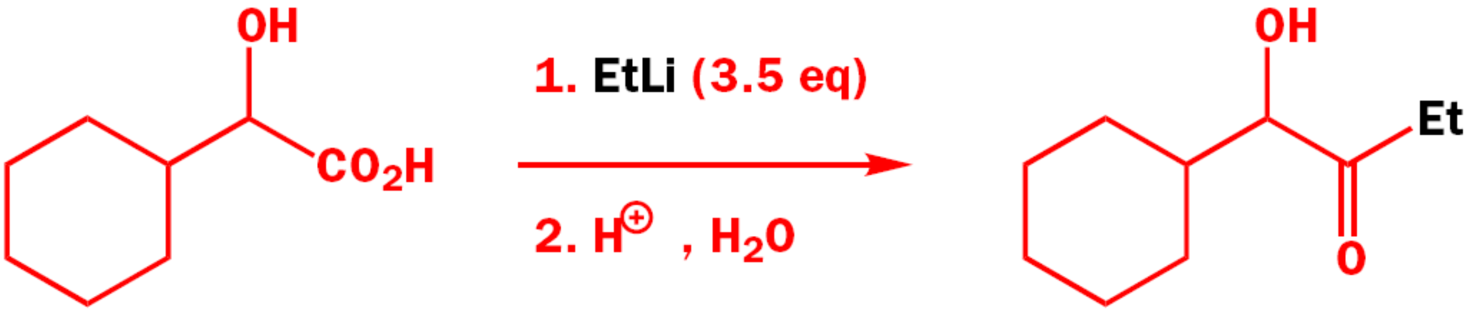
$$R-\overset{\overset{O}{\|}}{C}-OC_2H_5 + CH_3-MgI \longrightarrow R-\overset{\overset{O}{\|}}{C}-CH_3 + I-Mg-OC_2H_5$$

**Etapa 2:** Adição Nucleofílica:



$$R-\overset{\overset{O}{\|}}{C}-CH_3 + CH_3-MgI \longrightarrow \xrightarrow[H_2O]{H_3O^+} R-\underset{\underset{CH_3}{|}}{\overset{\overset{OH}{|}}{C}}-CH_3$$

# Preparação de Cetonas: Reação de Carboxilatos com Organolítio



65% yield