

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

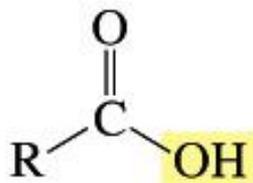
6.8. Formação e Reações de Amidas

6.9. Ativação de Ácidos Carboxílicos

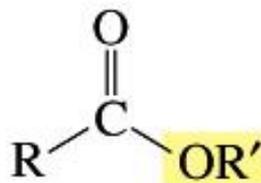
6.10. Reações de Oxidação e Redução

6.11. Reações com Organometálicos

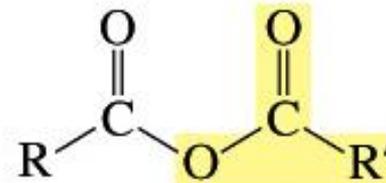
6. Compostos Carboxílicos: Ácidos Carboxílicos e Derivados



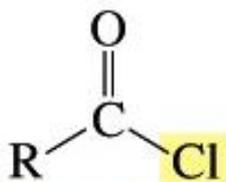
a carboxylic acid



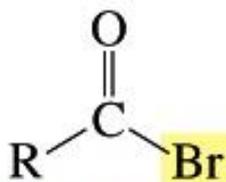
an ester



an acid anhydride

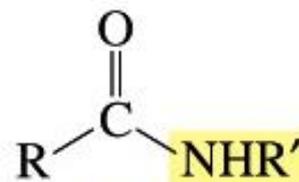
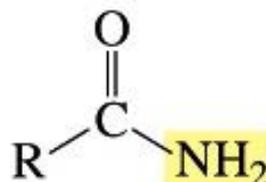


an acyl chloride

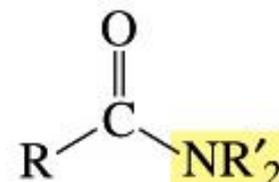


an acyl bromide

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



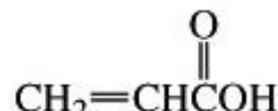
butanoic acid
butyric acid



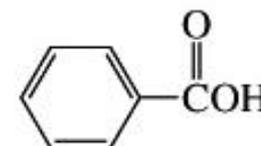
pentanoic acid
valeric acid



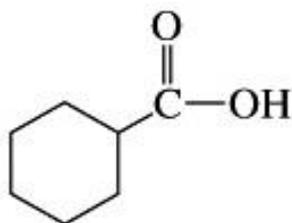
hexanoic acid
caproic acid



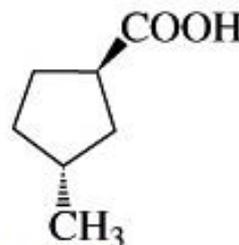
propenoic acid
acrylic acid



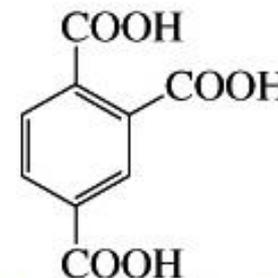
benzenecarboxylic acid
benzoic acid



ácido ciclohexanocarboxílico

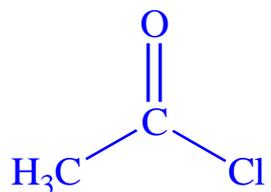


ácido trans-3-metilciclo-
pentanocarboxílico

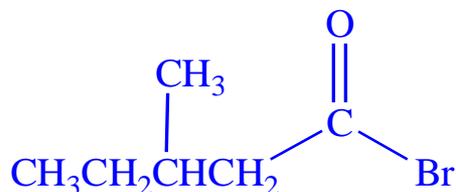


ácido 1,2,4-benzo-
tricarboxílico

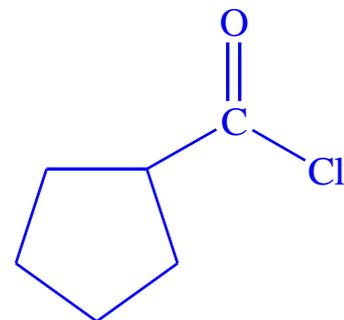
Haletos de Acila



cloreto de etanoíla
cloreto de acetila

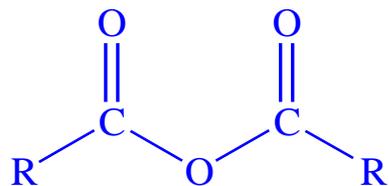


brometo de 3-metilpentanoíla
brometo de β-metilvaleríla



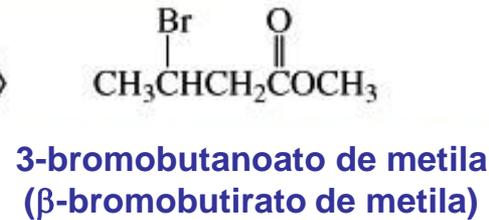
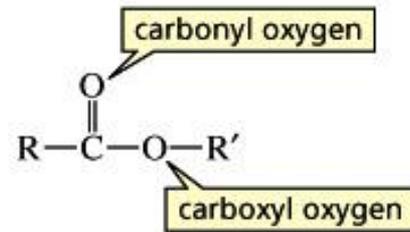
cloreto de
ciclopentanocarbonila

Anidridos de Ácido



R = CH₃: anidrido acético
R = C₂H₅: anidrido propanôico
R = C₆H₅: anidrido benzôico

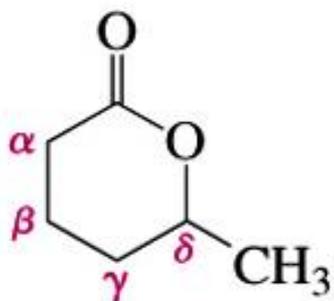
Ésteres



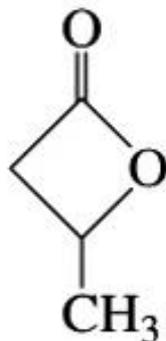
Sais de Ácidos Carboxílicos



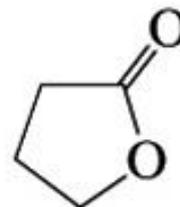
Ésteres Cíclicos: Lactonas



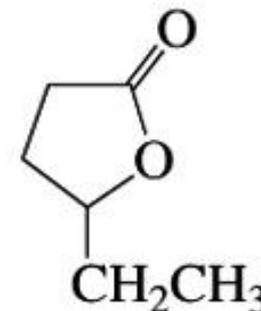
δ -caprolactona



β -butirolactona



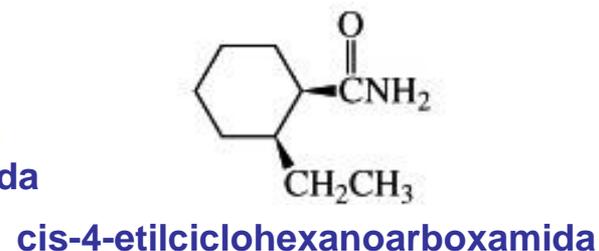
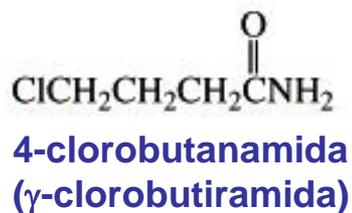
γ -butirolactona



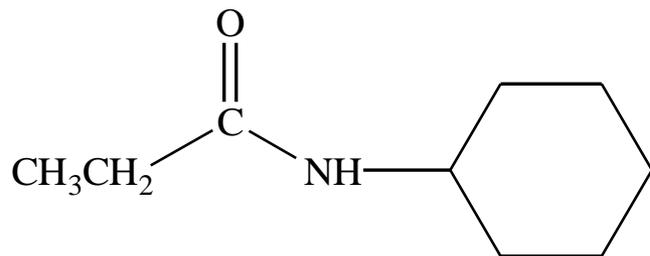
γ -caprolactona

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

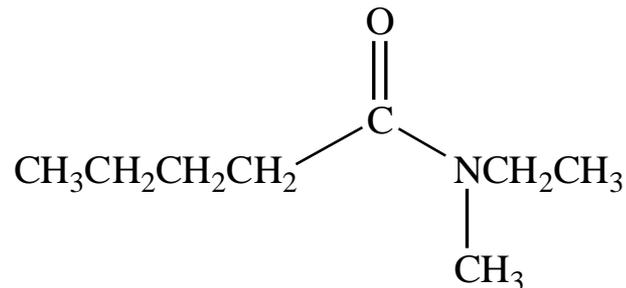
Amidas



Amidas substituídas no nitrogênio

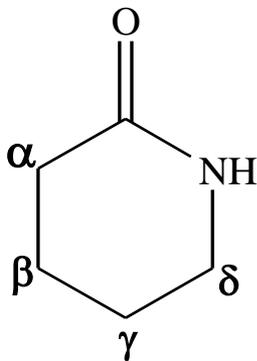


N-ciclohexilpropanamida

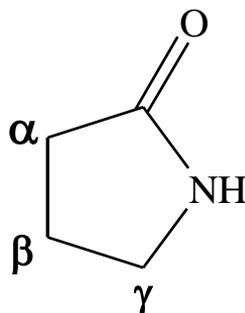


N-etil-N-metilpentanamida

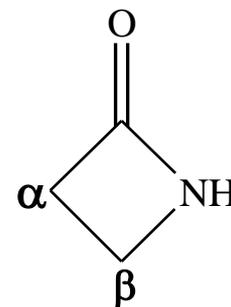
Amidas Cíclicas: Lactamas



2-azaciclohexanona
δ-valerolactama



2-azaciclopentanona
γ-butirolactama

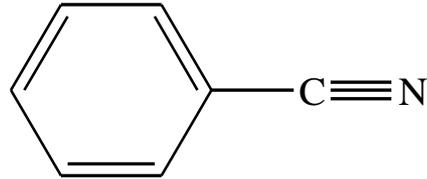


2-azaciclobutanona
β-propiolactama

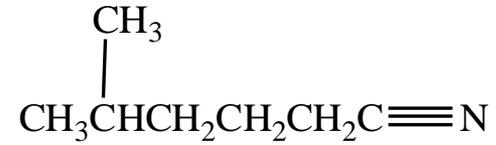
Nitrilas



etanonitrila
acetonitrila
cianeto de metila



benzenocarbonitrile
benzonitrila
cianeto de fenila
cianobenzeno



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

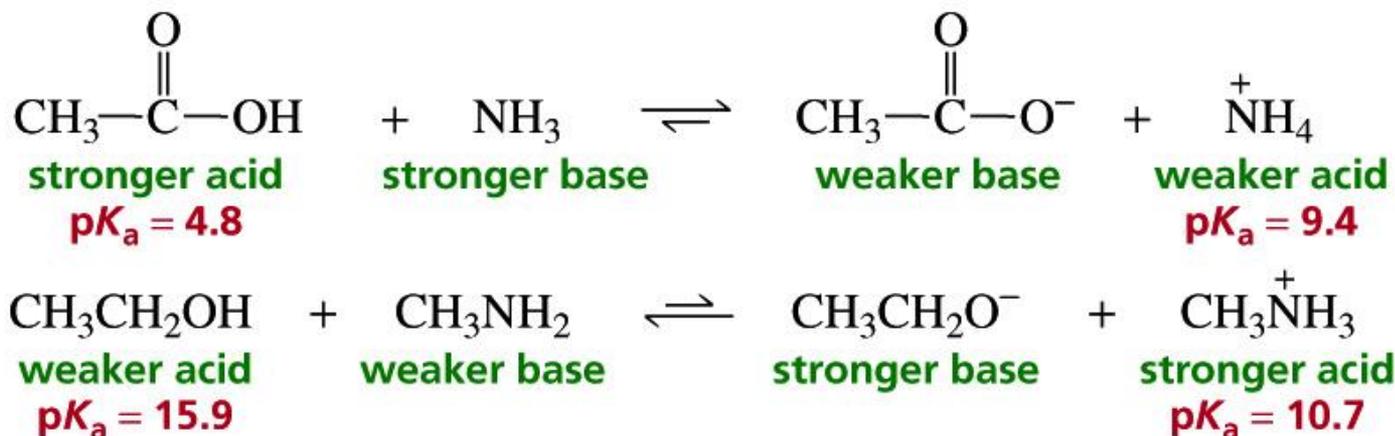


propenonitrila
acrilonitrila

6.2. Acidez de Ácidos Carboxílicos

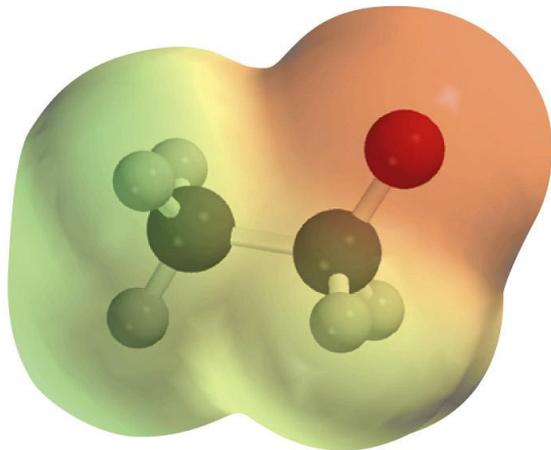
Ácidos e Bases de Brønsted–Lowry

❖ 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



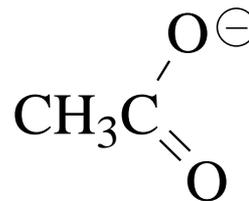
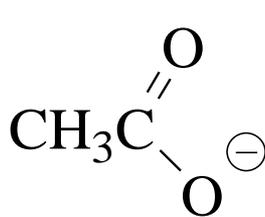
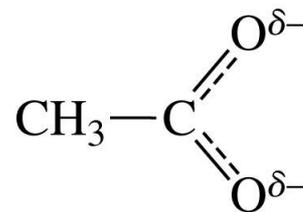
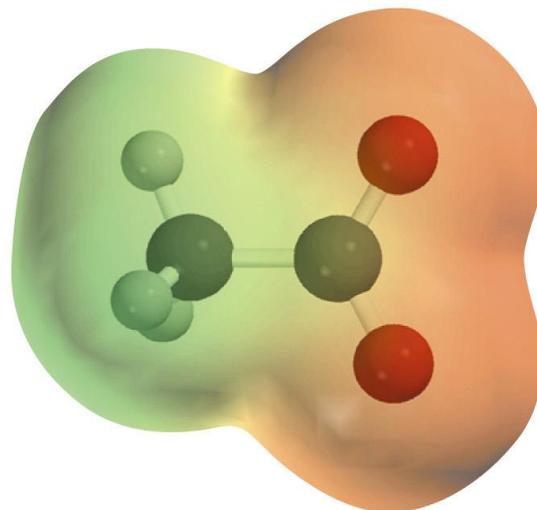
$\text{pK}_a = 4.76$

acetic acid

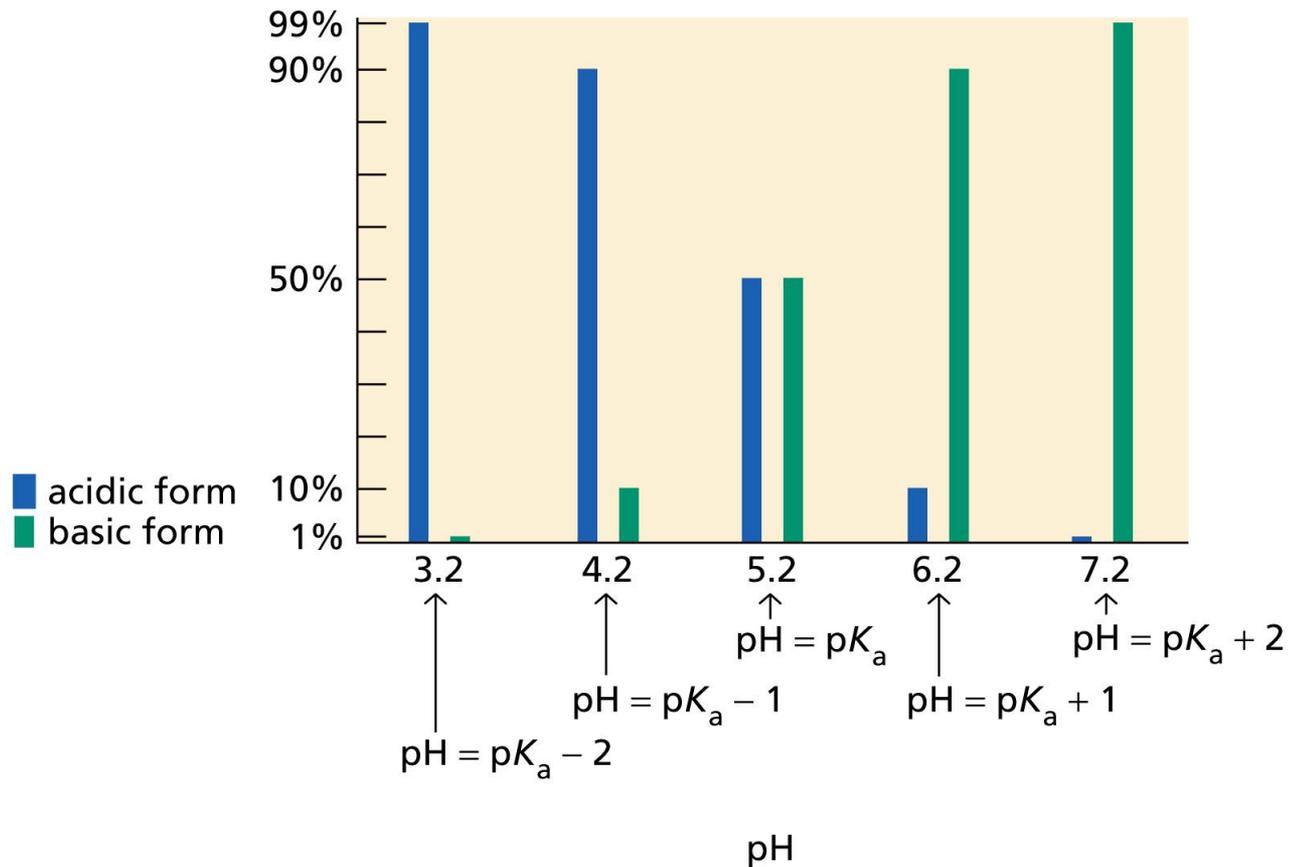


$\text{pK}_a = 15.9$

ethanol



Acidez de Ácidos Carboxílicos



Equilíbrio Ácido / Base



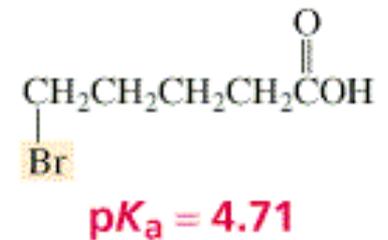
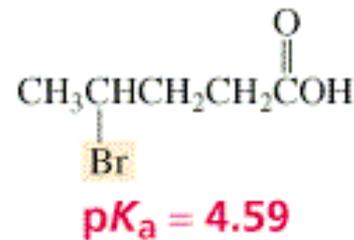
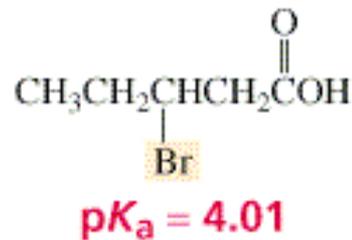
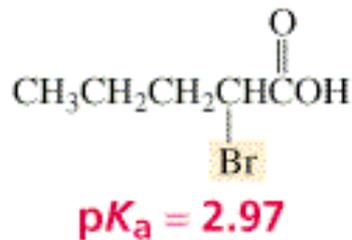
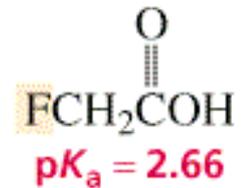
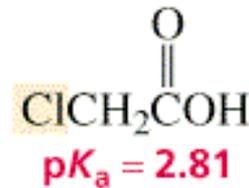
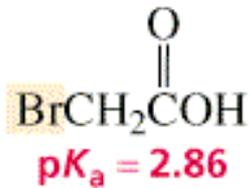
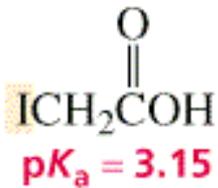
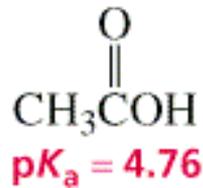
$$K = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{H}_2\text{O}][\text{HA}]} \quad K_a = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]}$$

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

K : Constante de equilíbrio

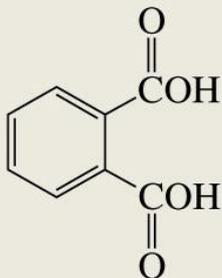
K_a : Constante de dissociação do ácido HA

Acidez de Ácidos Carboxílicos



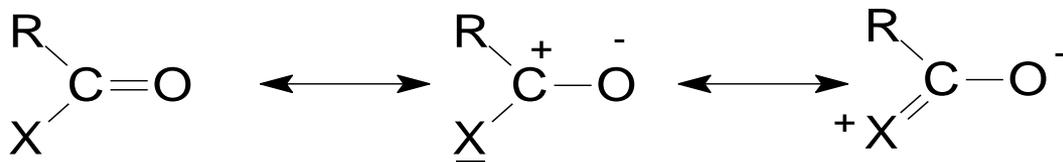
- O efeito indutivo atraente de elétrons dos halogênios aumenta a acidez devido a estabilização da base conjugada;
- O efeito depende da eletronegatividade e da distância.

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

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

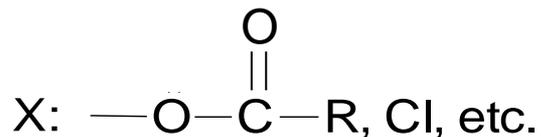
Reatividade de Derivados de Ácidos Carboxílicos

- 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: NH₂, OR, OH :

estabilização π (+M) alta e efeito -I baixo:
mais estáveis



estabilização π (+M) baixa e efeito -I alto:
menos estáveis

relative reactivities of carbonyl compounds toward nucleophiles

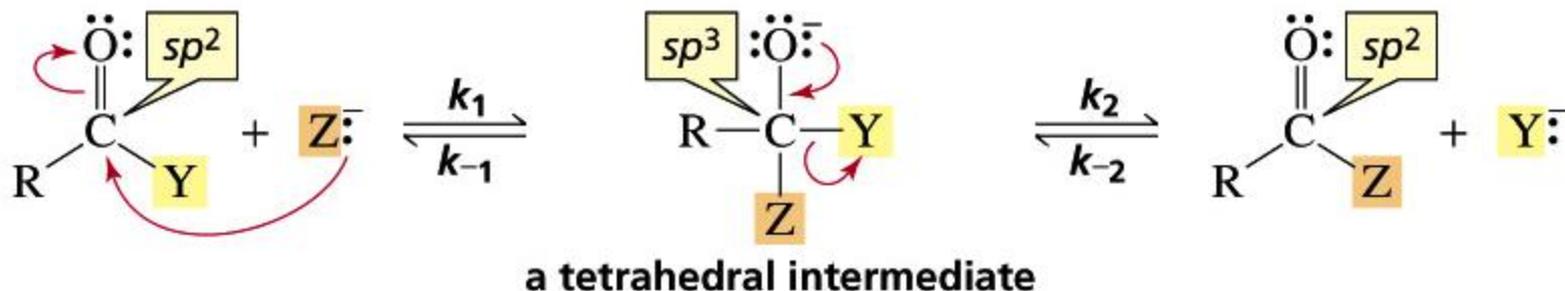
acyl halide > acid anhydride > aldehyde > ketone > ester ~ carboxylic acid > amide > carboxylate ion

most reactive

least reactive

Reatividade de Derivados de Ácidos Carboxílicos

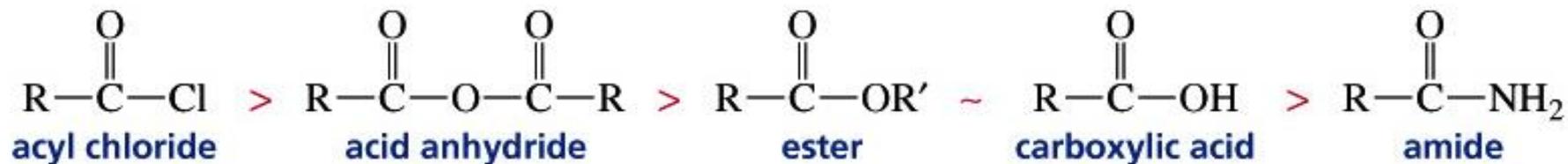
Reação não catalisada ou catálise básica



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

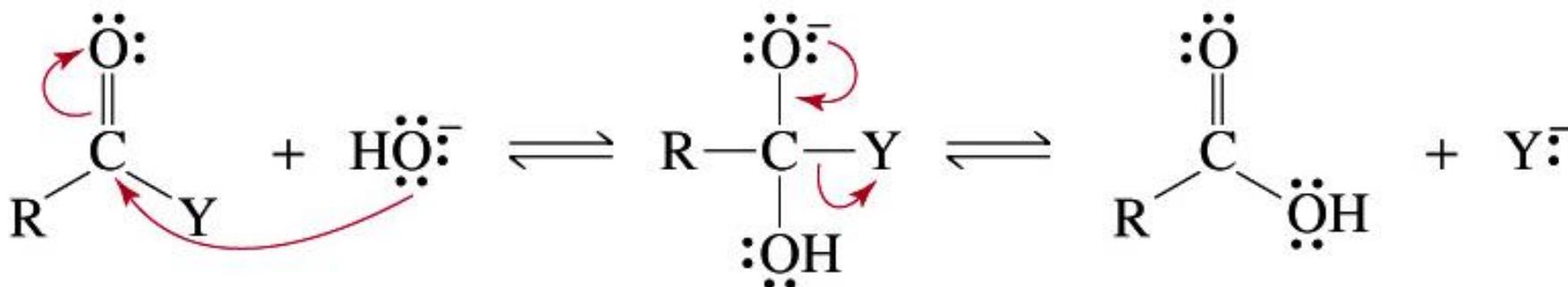
Y^- será expelido se for uma base mais fraca do que Z^- ($k_2 \gg k_{-1}$)

relative reactivities of carboxylic acid derivatives



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

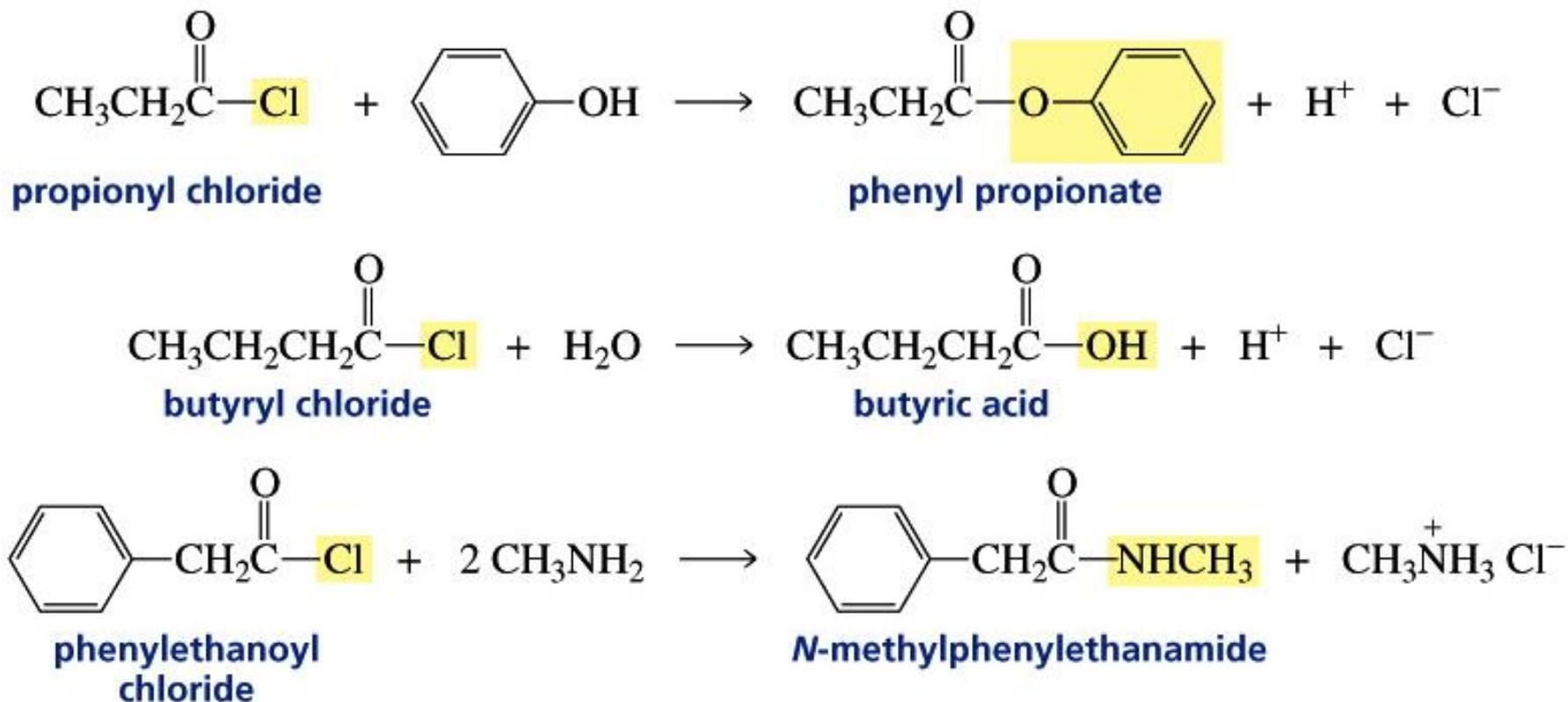
Todos compostos carboxílicos reagem pelo mesmo mecanismo



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

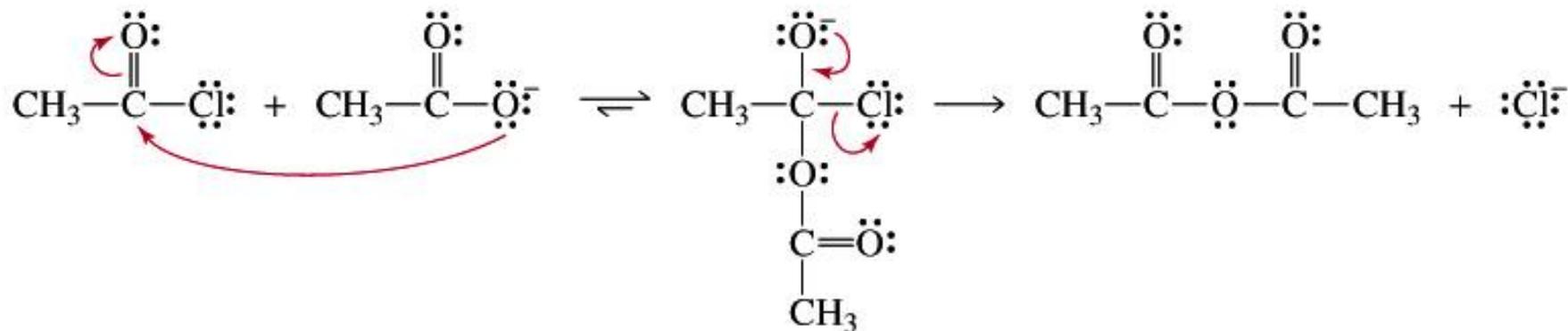
Formulado aqui para a **hidrólise por catálise básica**, porém com outro nucleófilo, o mecanismo é análogo.

6.4. Reações de Haletos de Acila

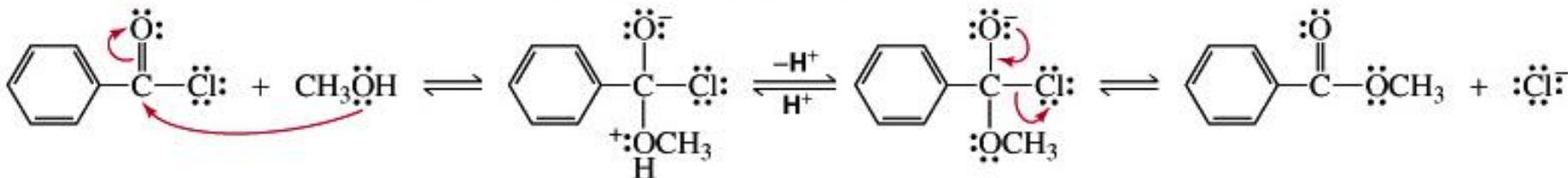


Mecanismo da Reação de Haletos de Acila

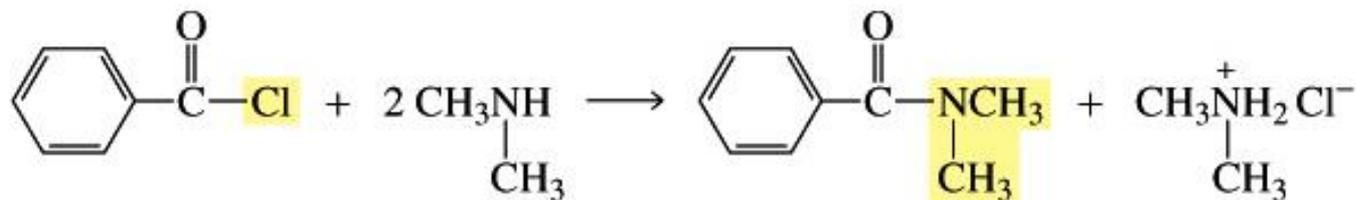
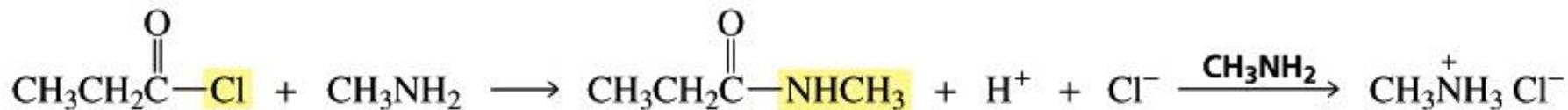
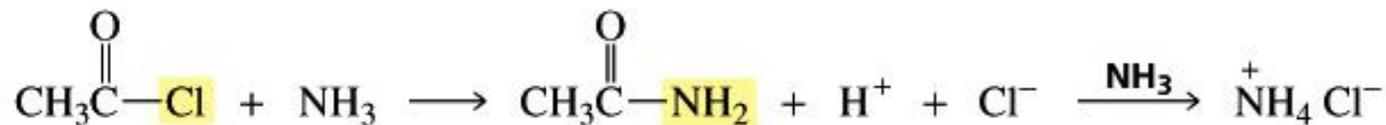
Conversão em anidridos



Conversão em ésteres

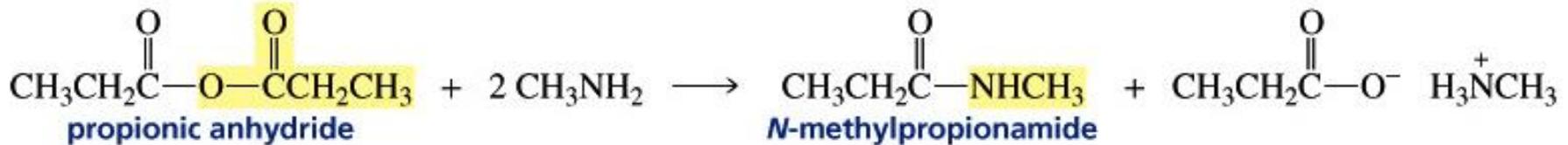
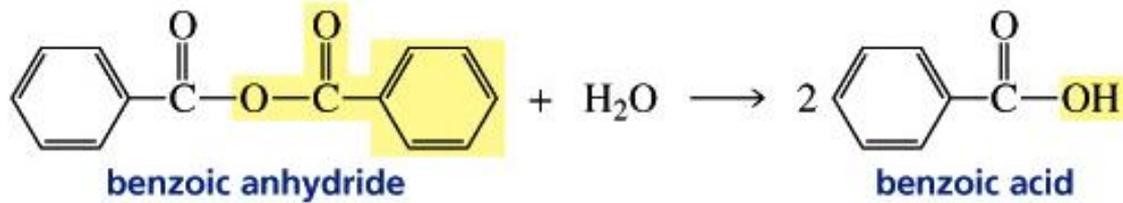
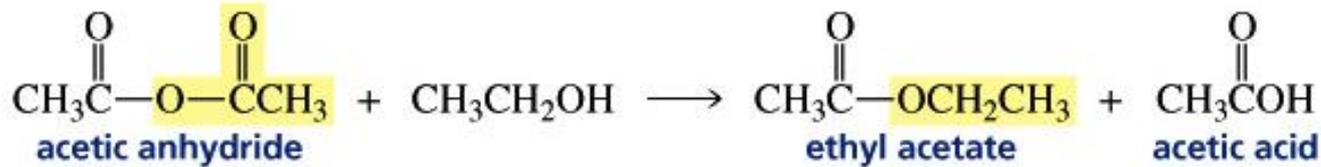


Formação de Amidas a Partir de Haletos de Acila



Aminas terciárias não podem formar amidas:
Porque será??

6.5. Reações de Anidridos de Ácido



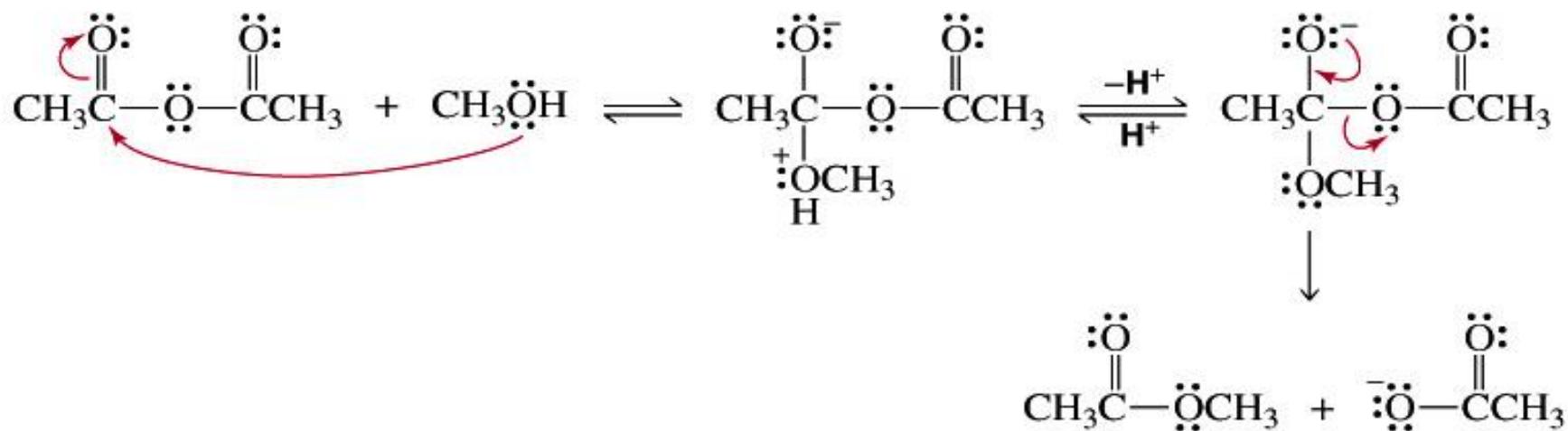
Anidridos não reagem com cloreto ou brometo de sódio

Porque??

Qualidade do grupo de partida??

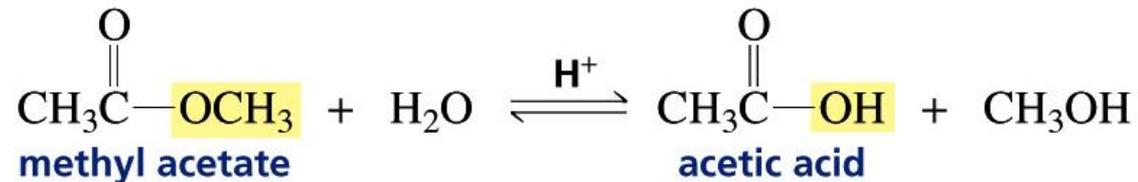
Conversão de Anidridos em Ésteres

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

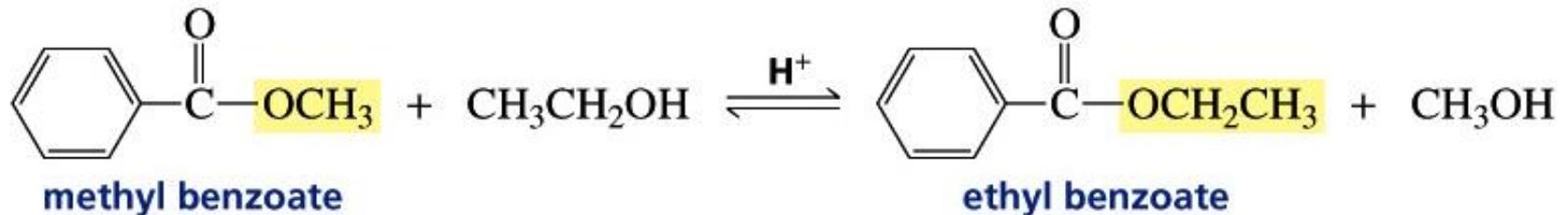


6.6. Reação de Ésteres: **Catálise Ácida**

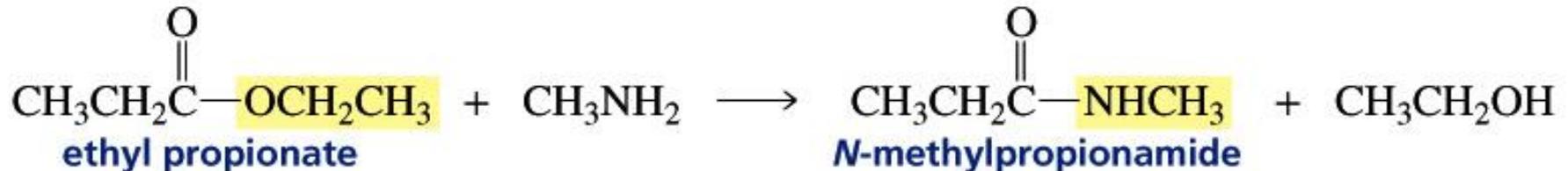
Hidrólise



Transesterificação

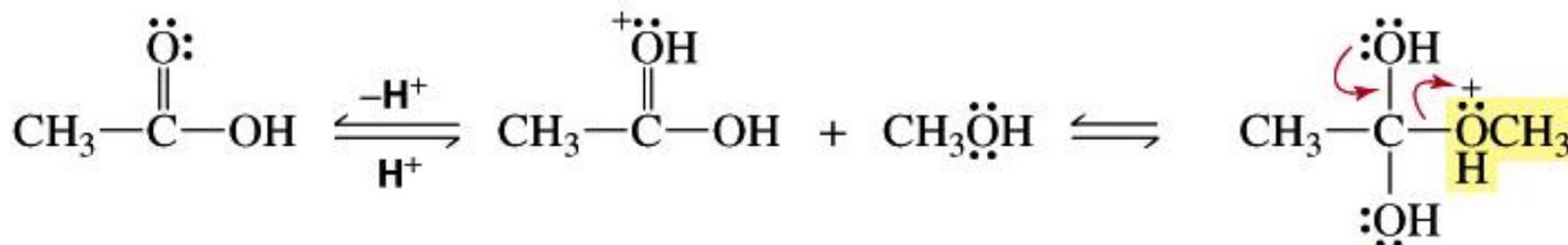
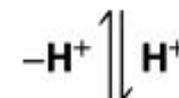
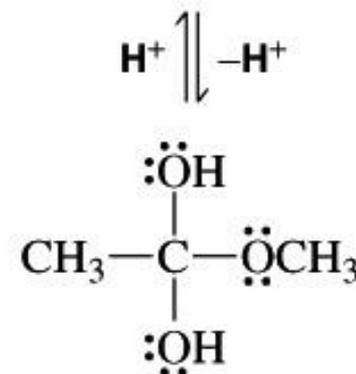
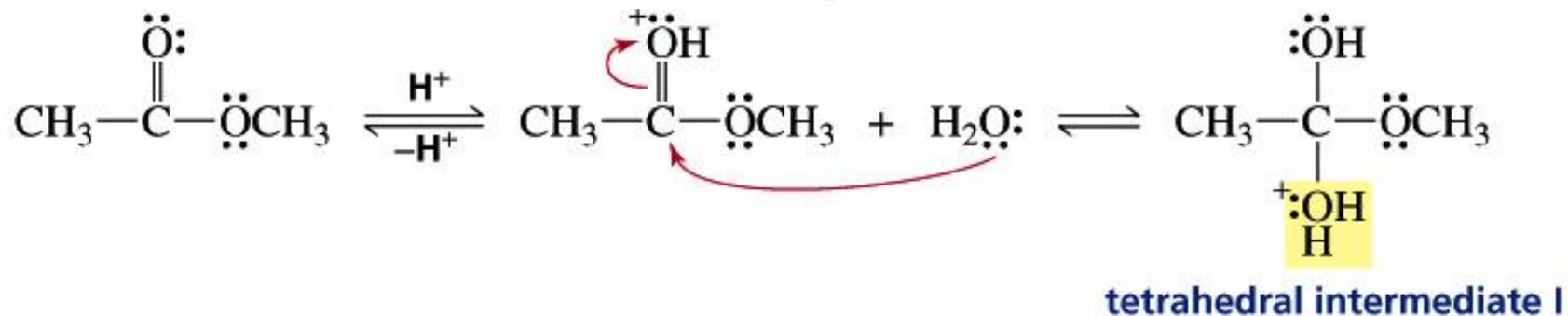


Aminólise

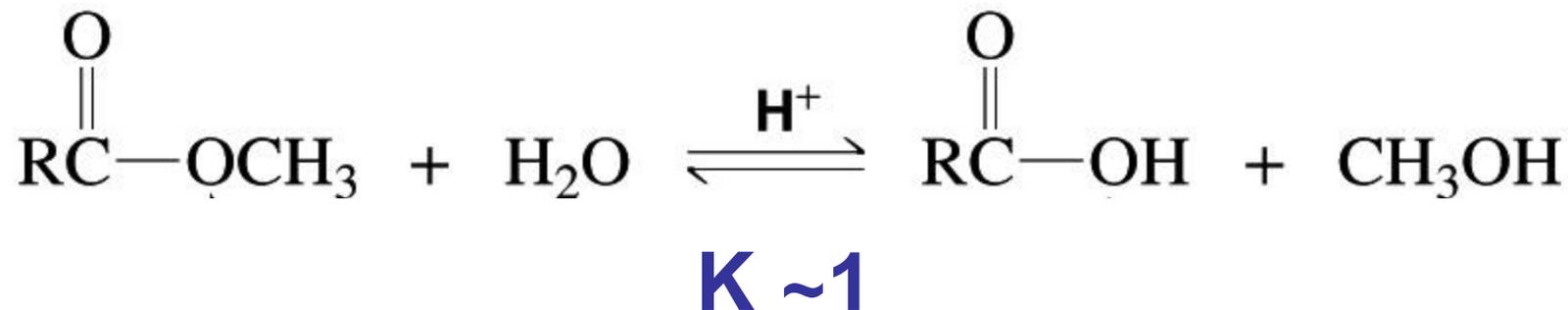


Mecanismo da Hidrólise de Ésteres

Catalisada por Ácido



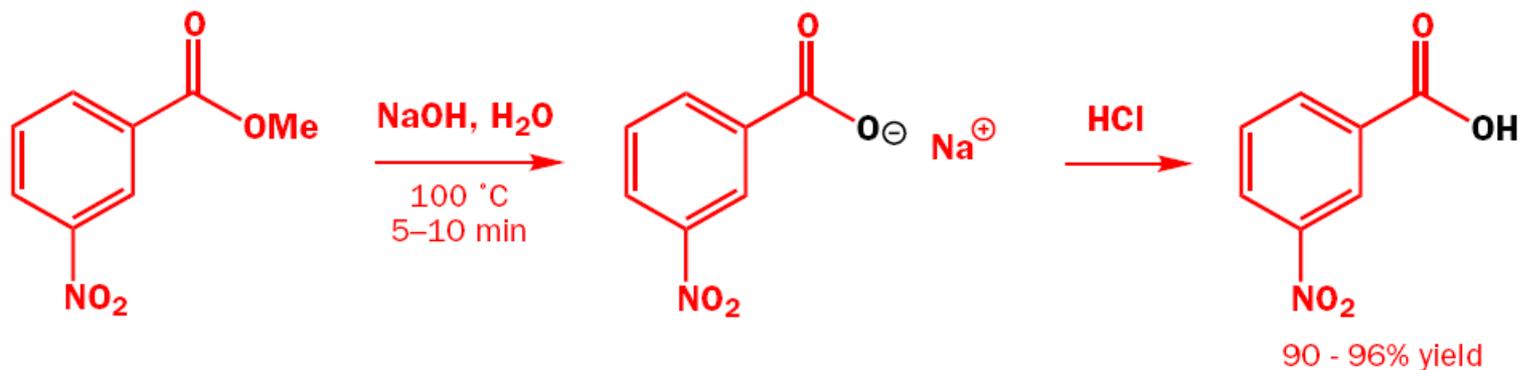
Constante de Equilíbrio na Esterificação e Hidrólise de Ésteres



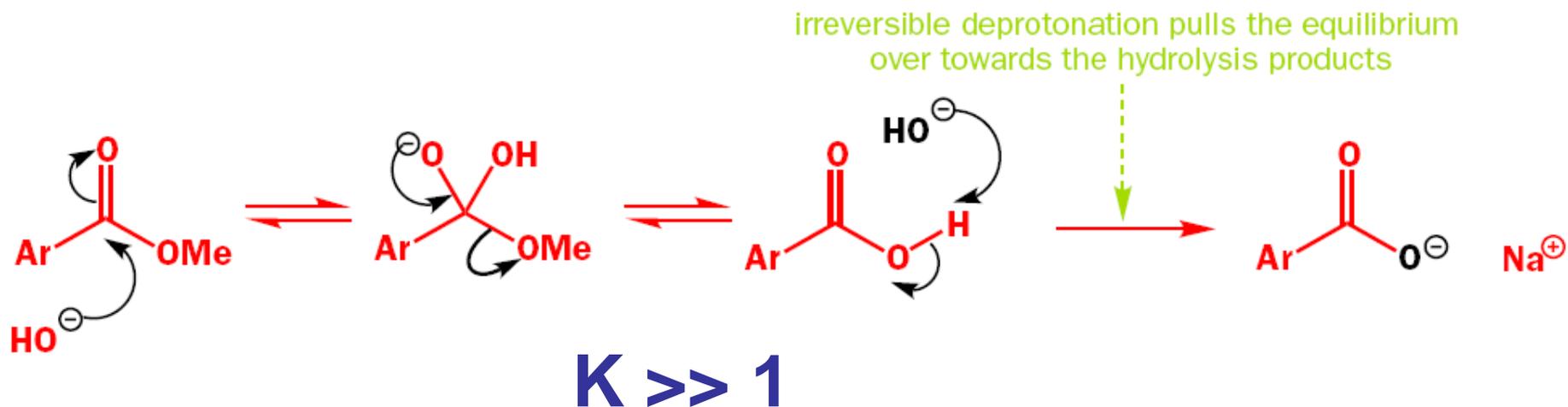
Deslocar o equilíbrio:

- 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

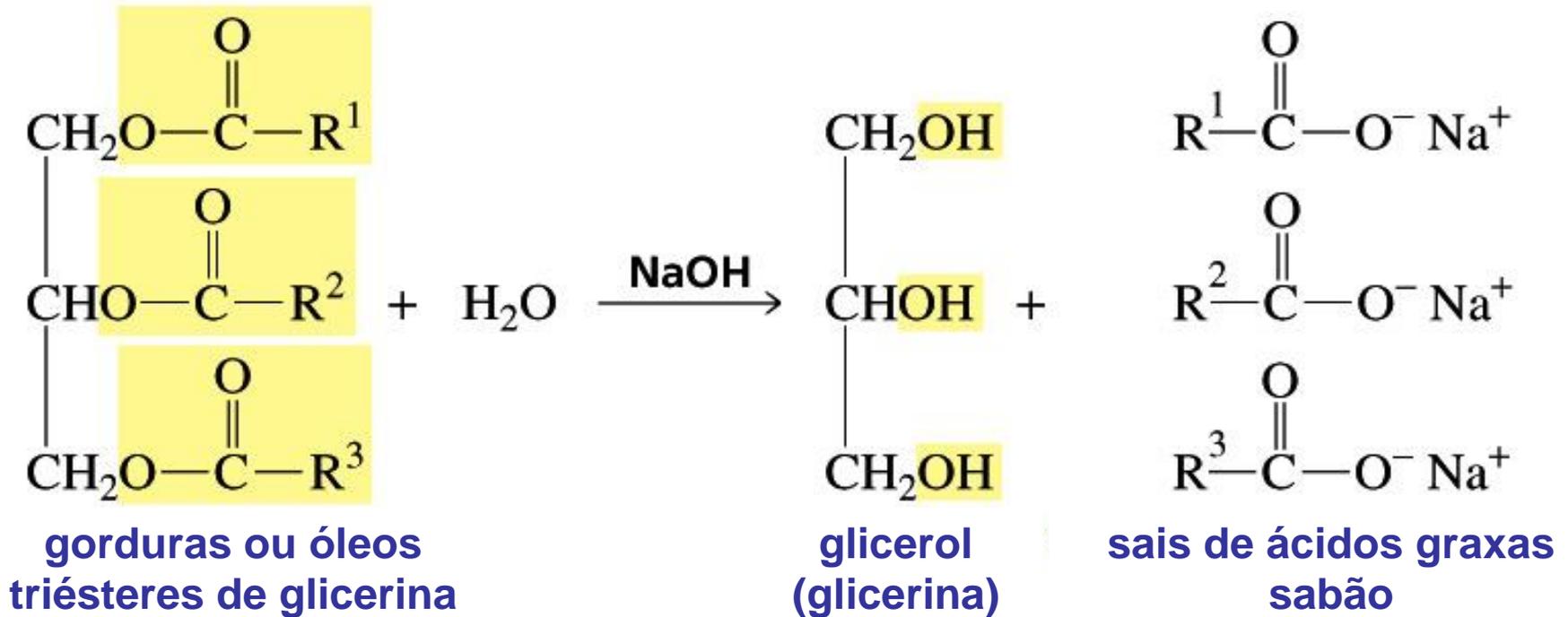


Mecanismo:



Hidrólise de Ésteres Catalisada por Base

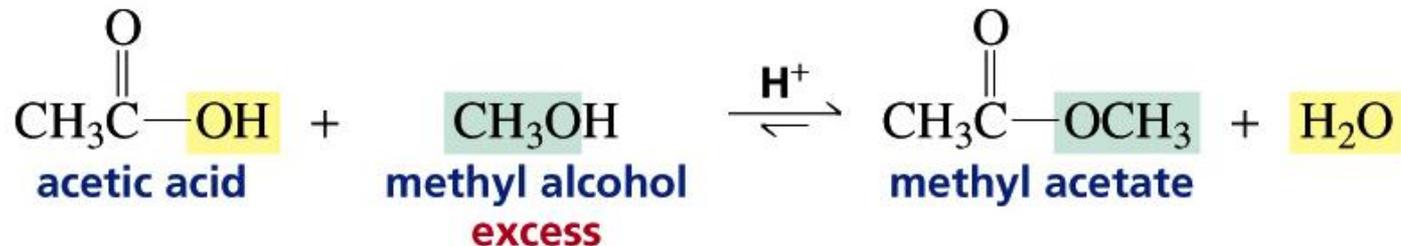
Saponificação



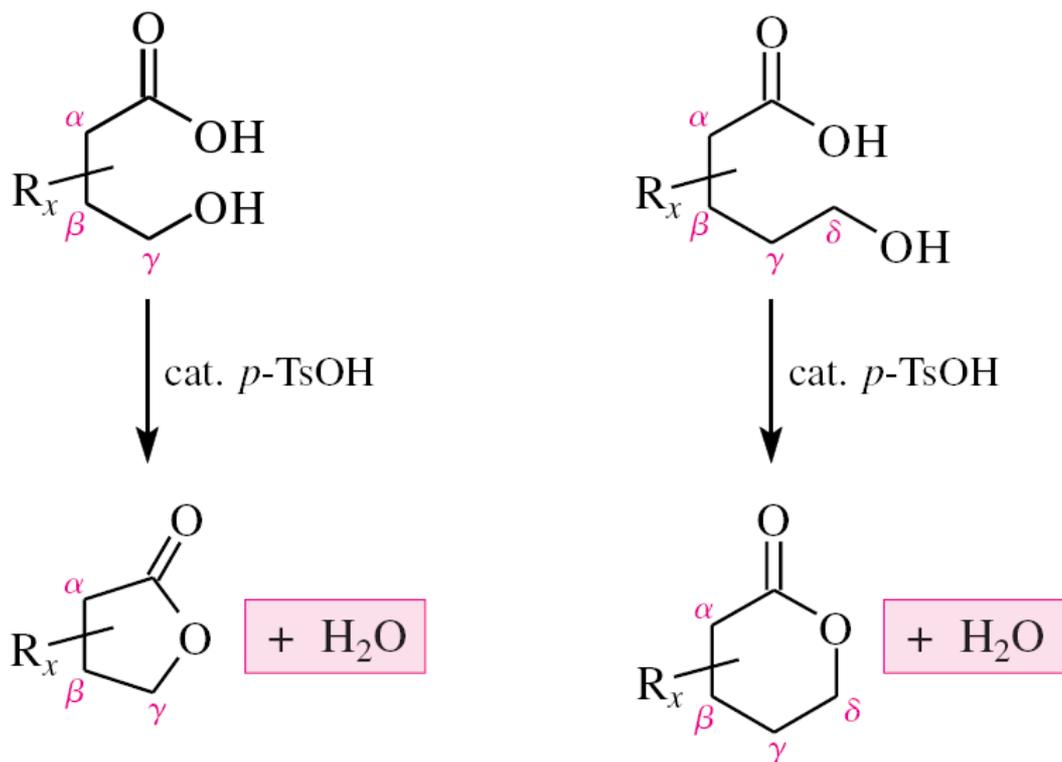
Reação correspondente com álcoois (transesterificação) muito importante para a obtenção de **biodiesel** (ésteres metílicos ou etílicos de ácidos graxas).

6.7. Formação de Ésteres: Catalisada por Ácido

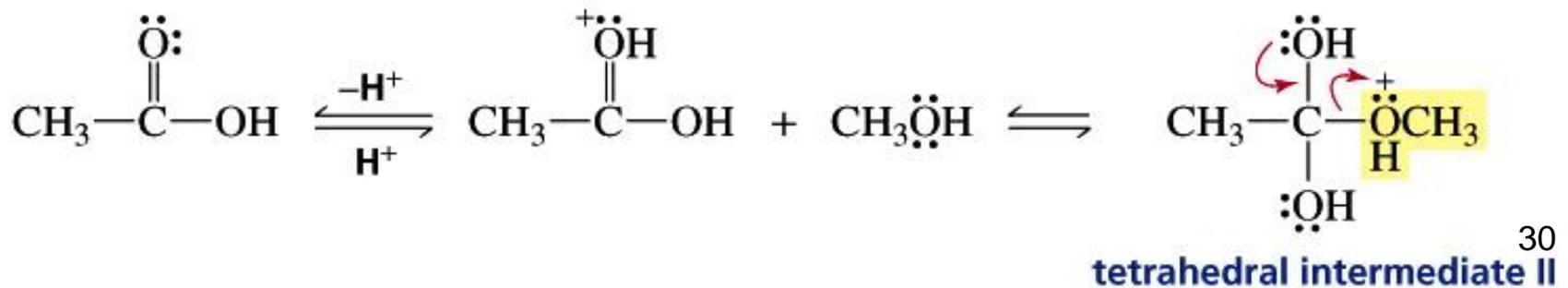
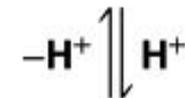
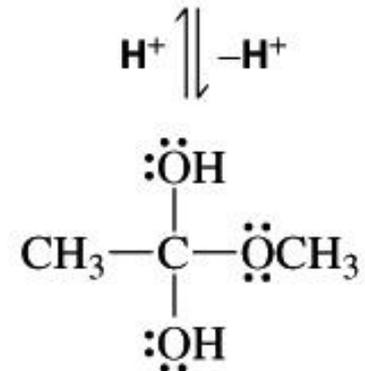
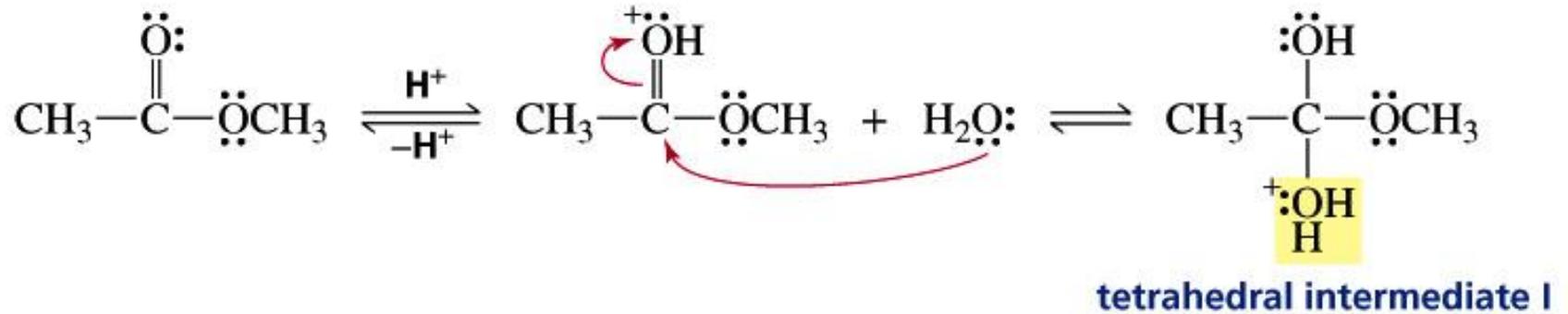
Esterificação de ácidos carboxílicos:



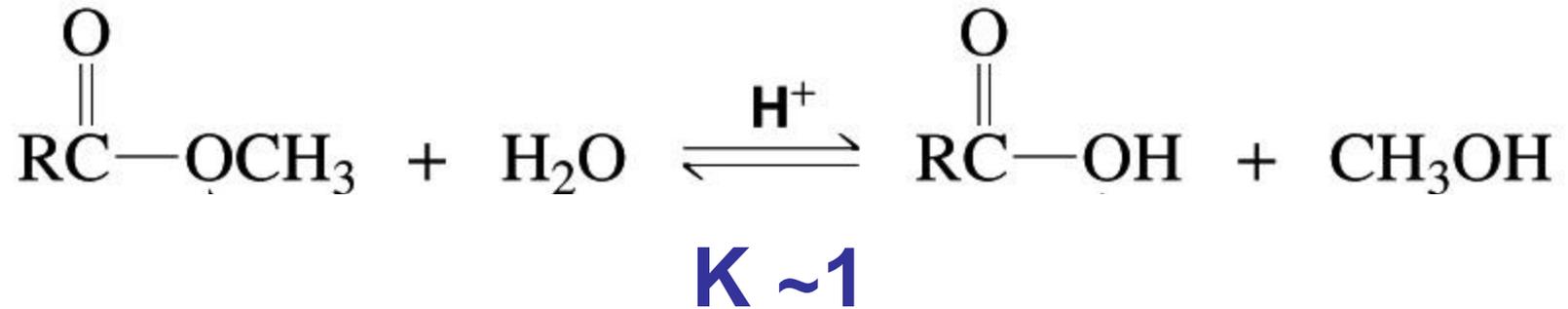
Esterificação Intramolecular: Formação de Lactonas



Mecanismo da Esterificação: Catalisada por Ácido



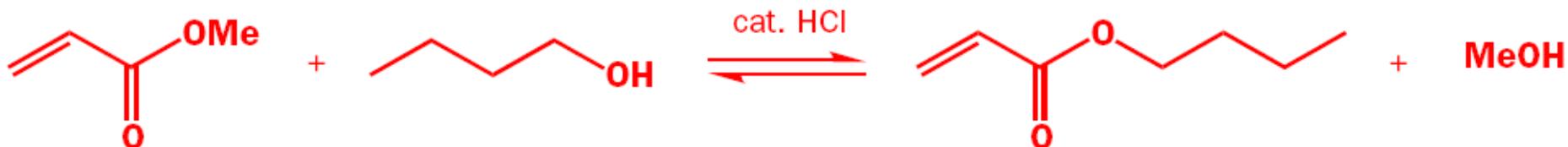
Equilíbrio na Esterificação



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



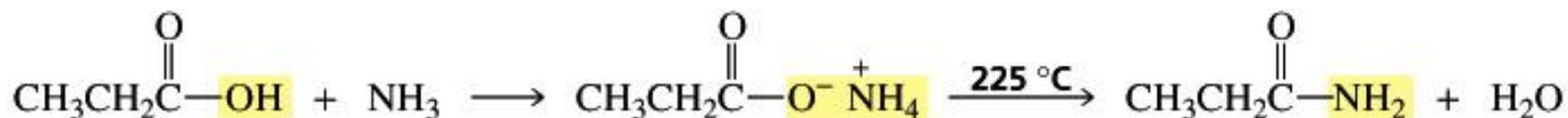
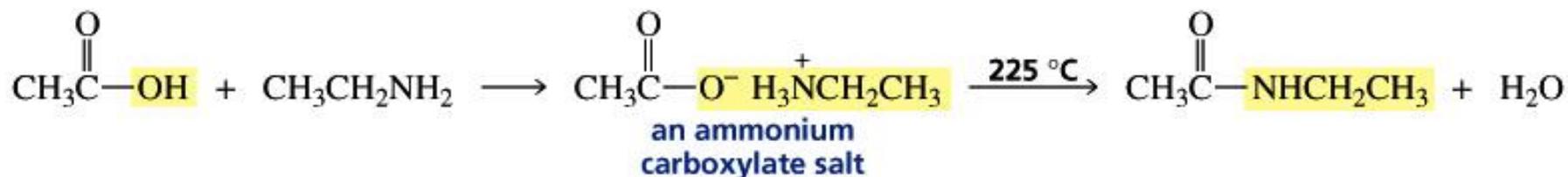
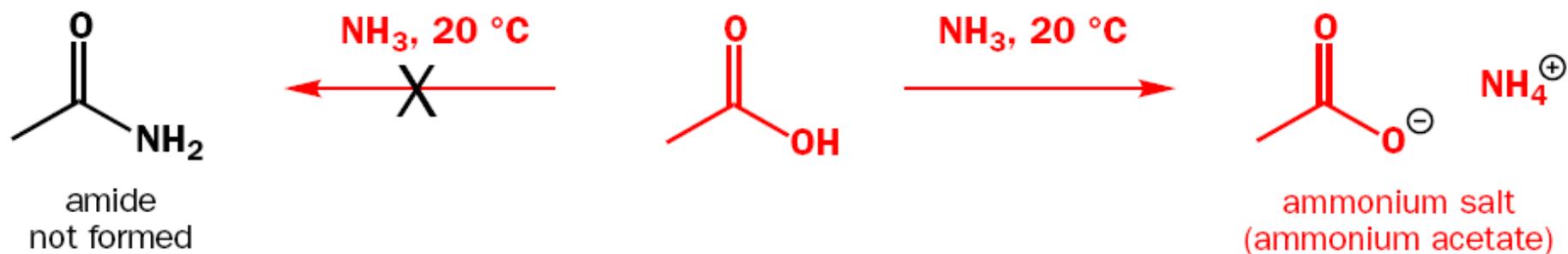
Transesterificações têm normalmente uma constante de equilíbrio cerca de 1, mas em alguns casos o equilíbrio pode ser deslocado.

Como isso poderia ser feito?

O mecanismo destas reações é análogo ao de hidrólise.

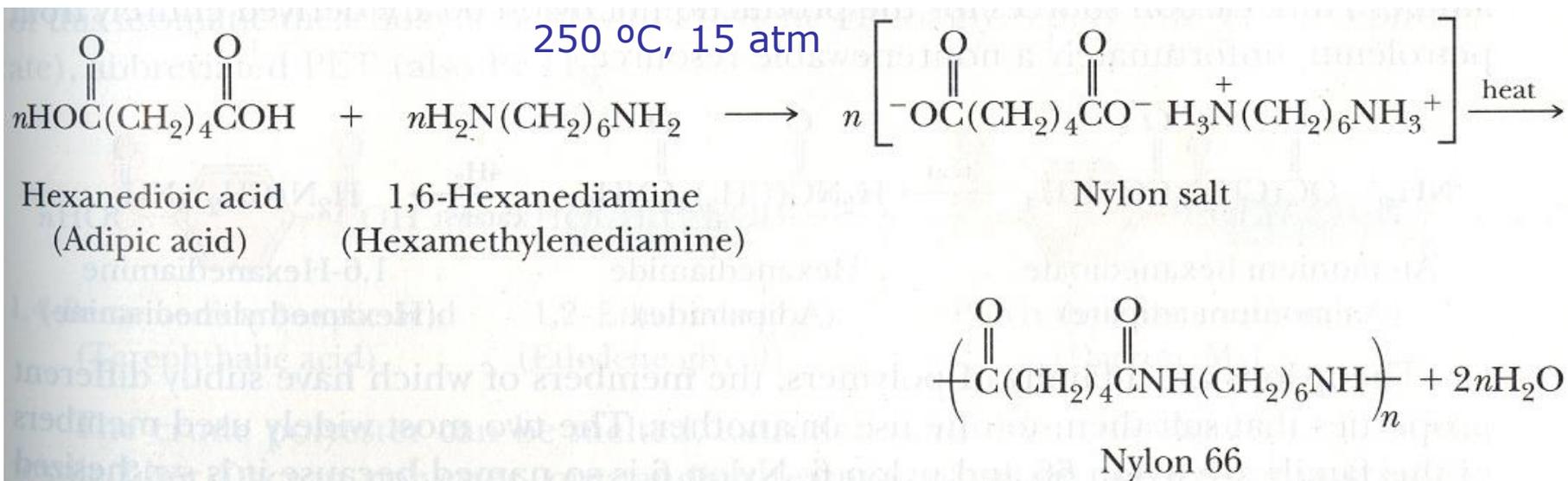
6.8. Formação e Reações de Amidas

Formação a partir de ácidos carboxílicos:

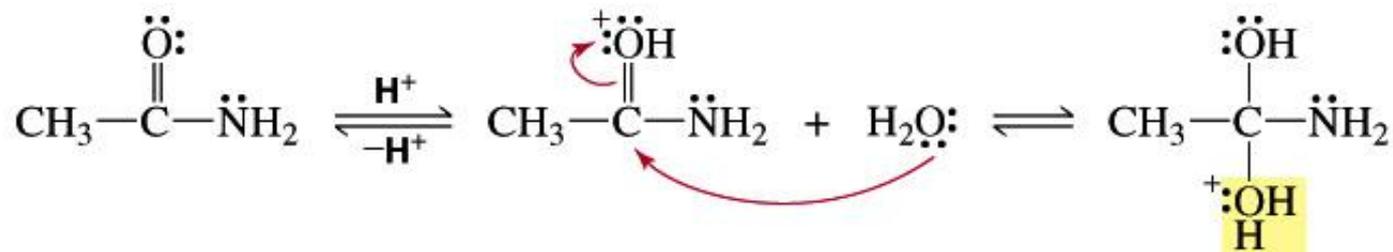


Ácidos carboxílicos não sofrem reações de substituição acílica **direta** com aminas. Reação ocorre via sal de amônio.

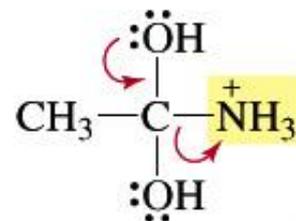
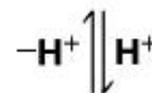
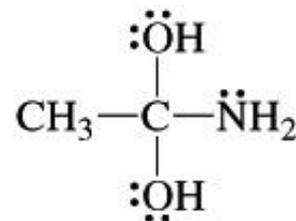
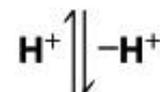
Preparação de Amidas a partir de Ácidos Carboxílicos: Aplicação



Mecanismo da Hidrólise de Amidas

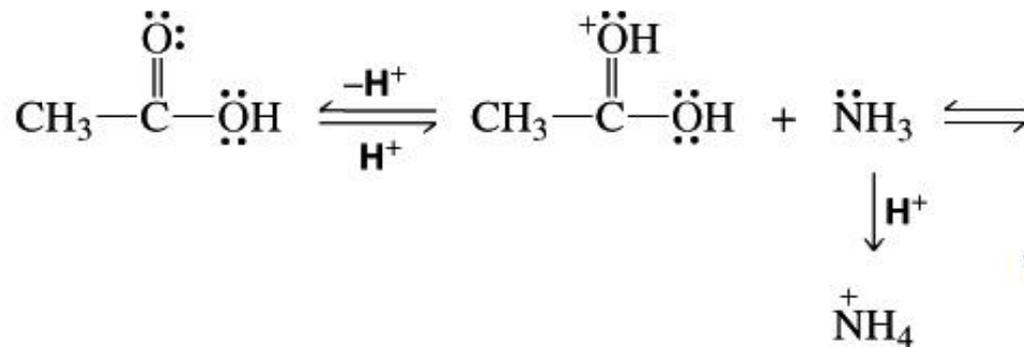


tetrahedral intermediate I

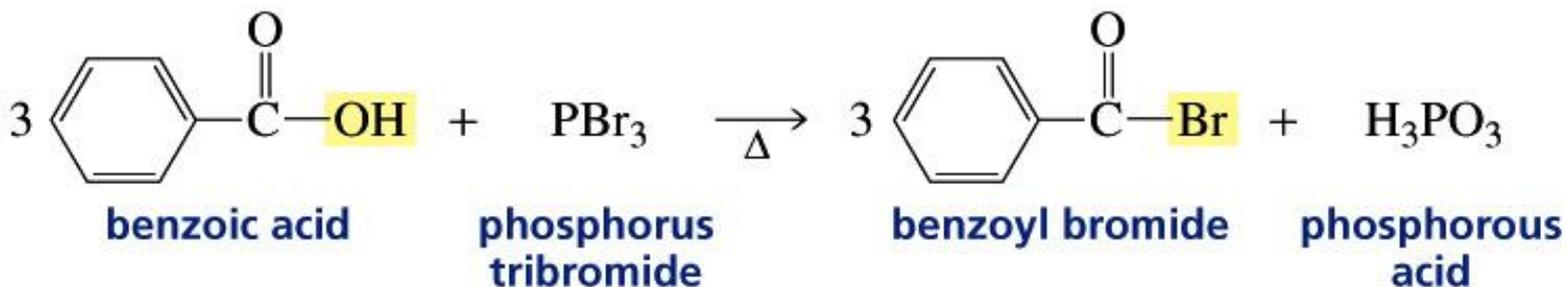
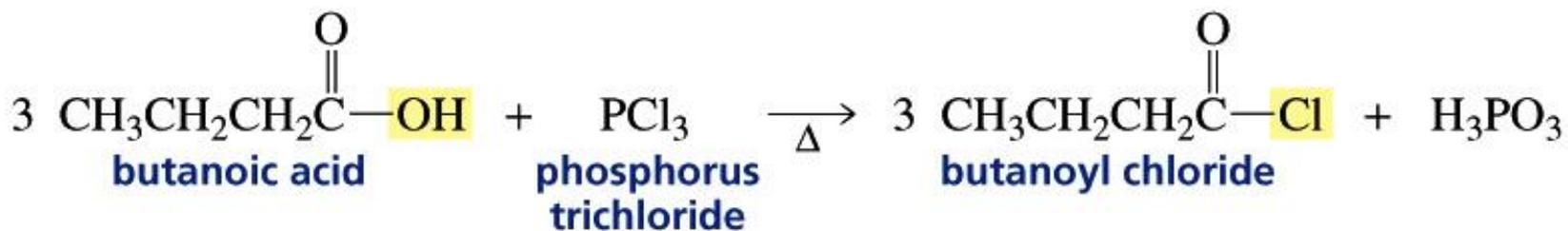
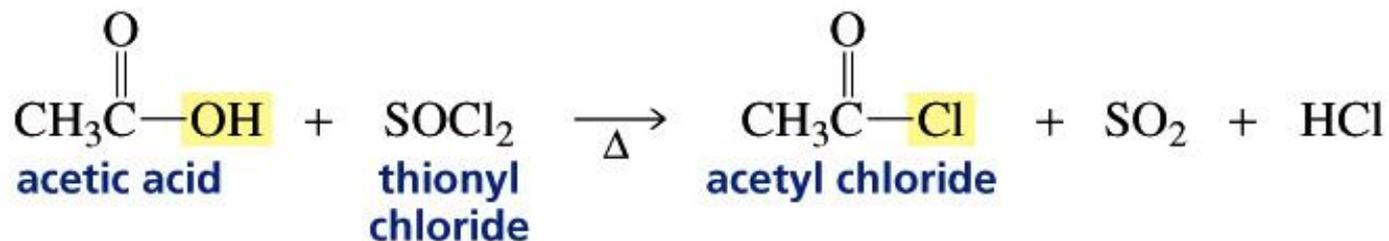


tetrahedral intermediate II

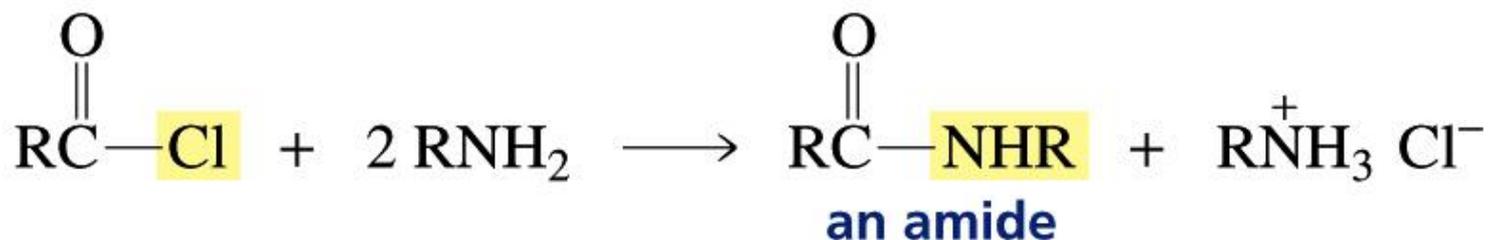
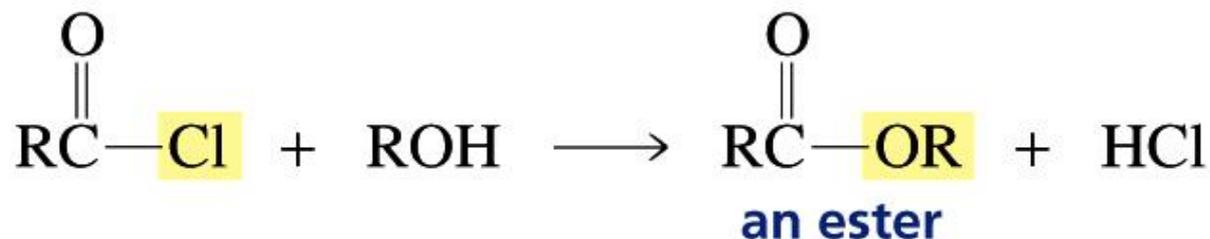
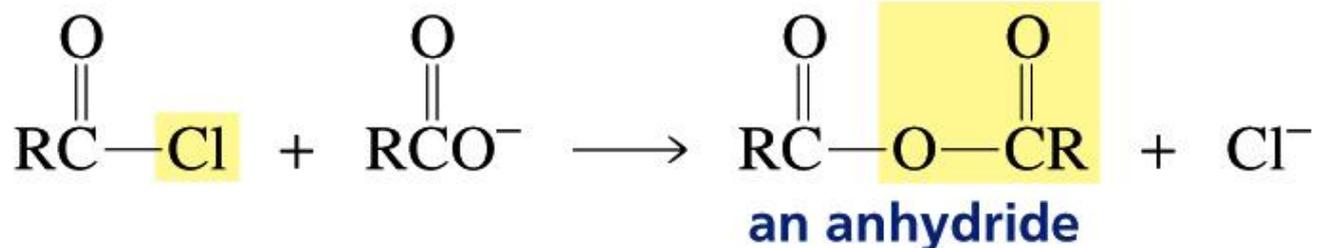
A reação ocorre melhor por catálise ácida:
Grupo de partida amônia é boa; amideto não é bom grupo de partida.



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

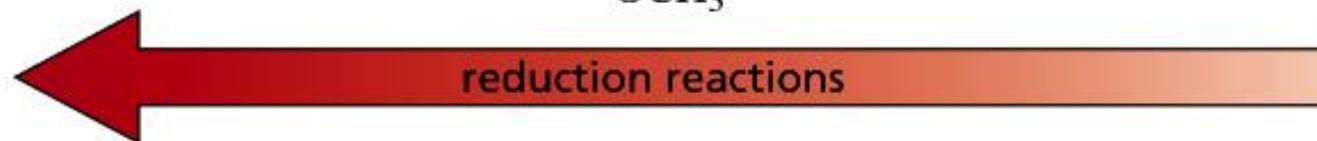
Número de Oxidação 'Formal' de Compostos Orgânicos



OXIDATION STATE

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

OXIDATION STATE	0	1	2	3	4
number of C-Z bonds (Z = O, N, or halogen)					
	CH ₄	CH ₃ OH	$\begin{array}{c} \text{O} \\ \\ \text{HCH} \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{HCOH} \end{array}$	O=C=O
		CH ₃ OCH ₃	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CCH}_3 \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{COCH}_3 \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{OCOCH}_3 \end{array}$
			$\begin{array}{c} \text{NCH}_3 \\ \\ \text{CH}_3\text{CCH}_3 \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CNH}_2 \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{OCNHCH}_3 \end{array}$
			$\begin{array}{c} \text{OCH}_3 \\ \\ \text{CH}_3\text{CCH}_3(\text{H}) \\ \\ \text{OCH}_3 \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CCl} \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{ClCCl} \end{array}$



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

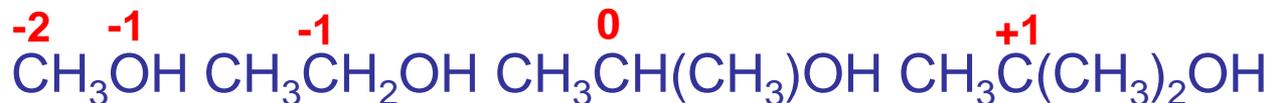
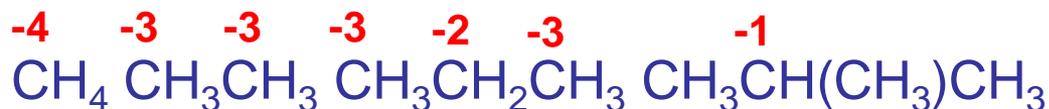
Número de Oxidação 'Formal' de Compostos Orgânicos

Escala alternativa:

C-C: C 0; C-H: H +1, C -1;

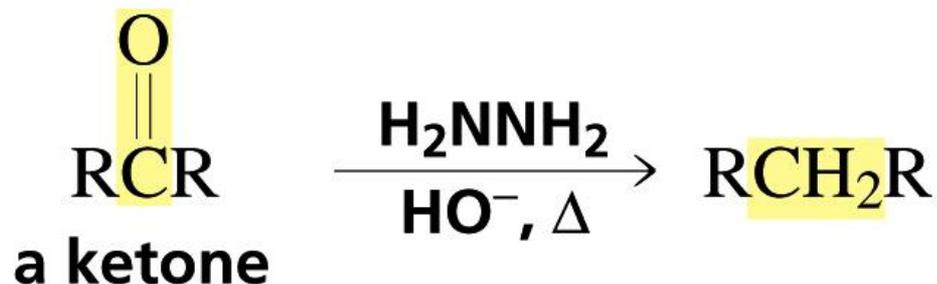
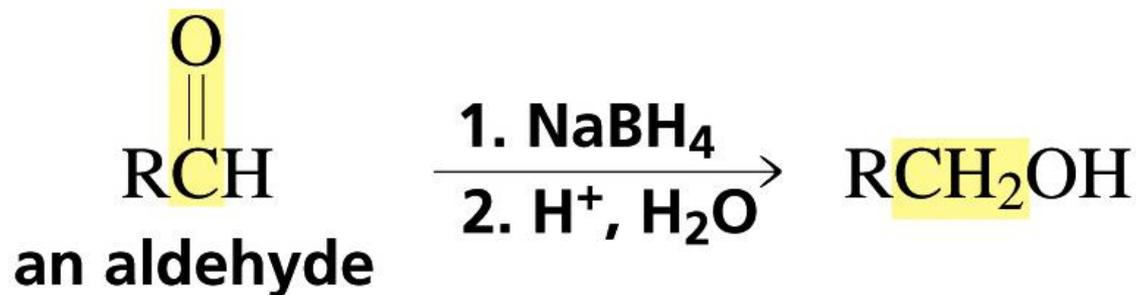
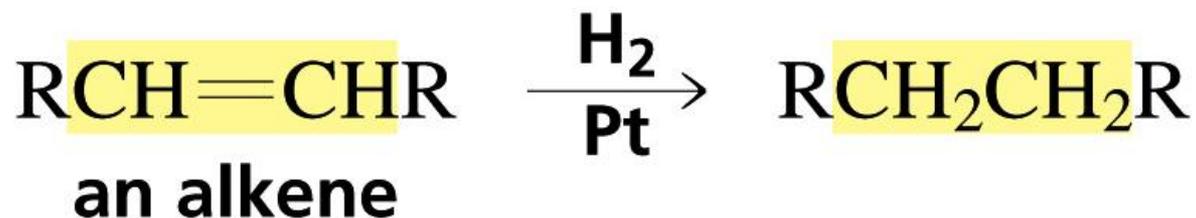
C-Z: C +1, Z -1; C=Z: C +2, Z -2; C≡Z: C +3; Z -3;

-Z: -OH, -OR, -NH₂, -NR₂, Hal; =Z: =O; =NH; ≡Z: C≡N



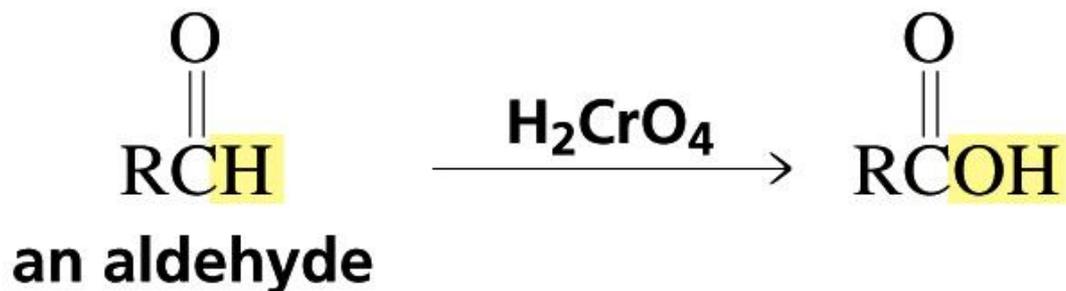
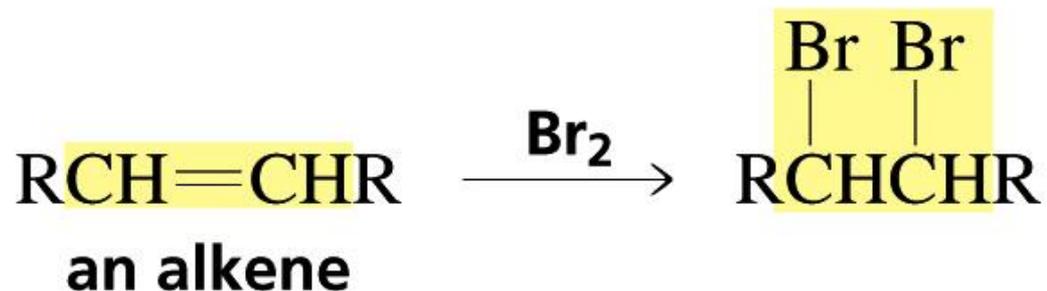
Redução de Compostos Orgânicos:

Hidrogenação catalítica, hidretos complexos, Wolff-Kishner

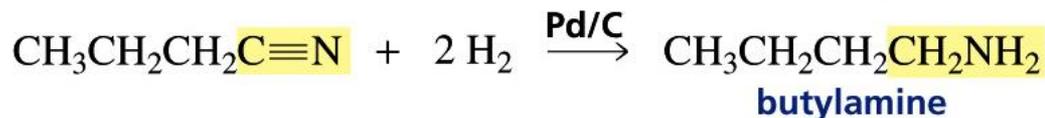
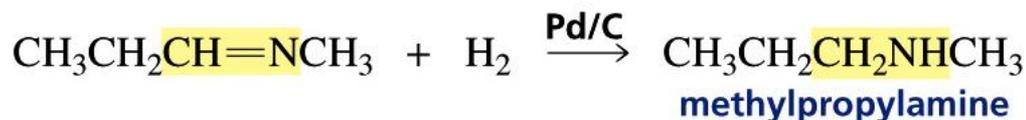
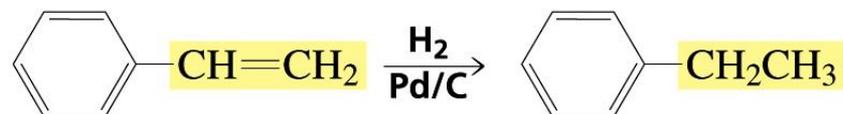
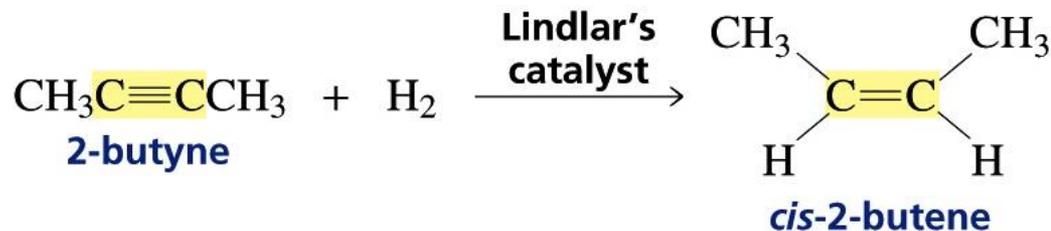
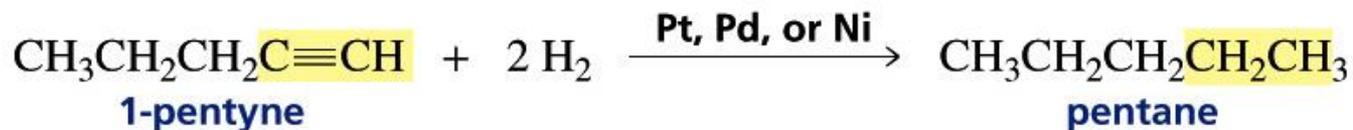
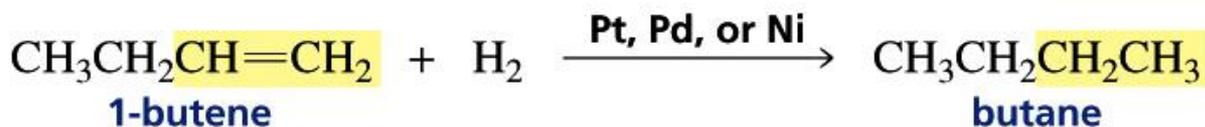


Oxidação de Compostos Orgânicos:

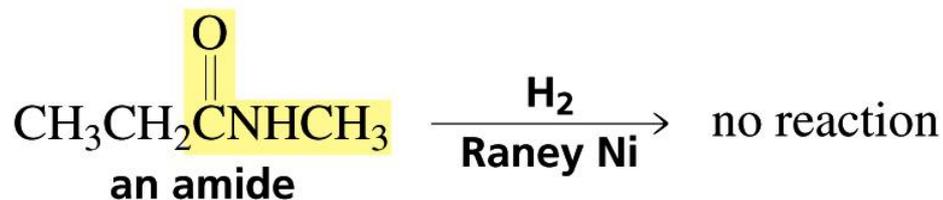
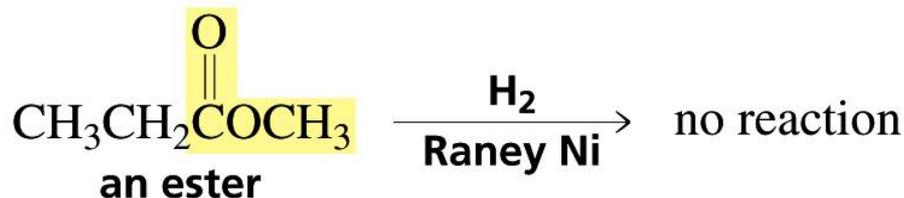
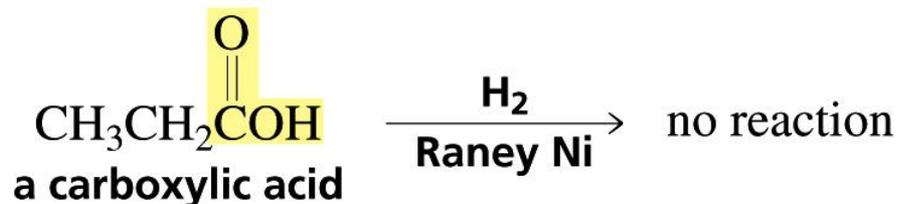
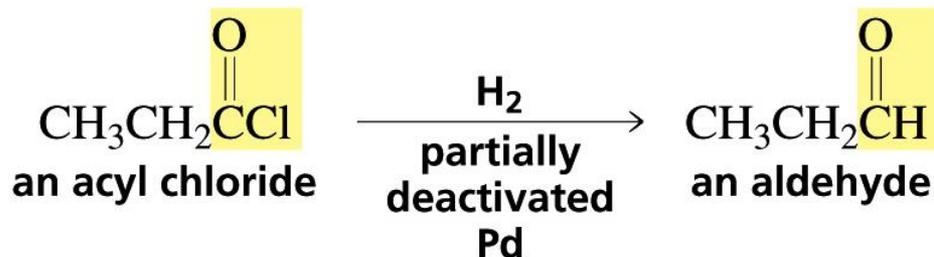
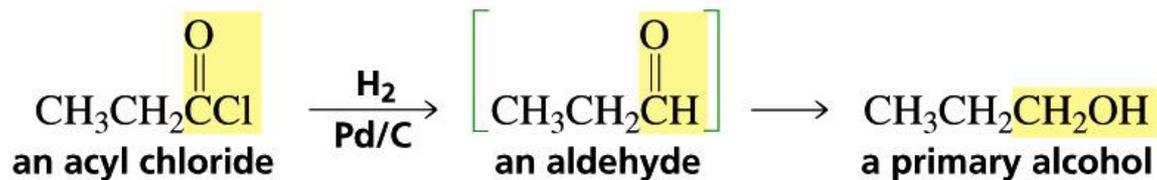
Bromo, ácido crômico



Redução por Hidrogenação Catalítica

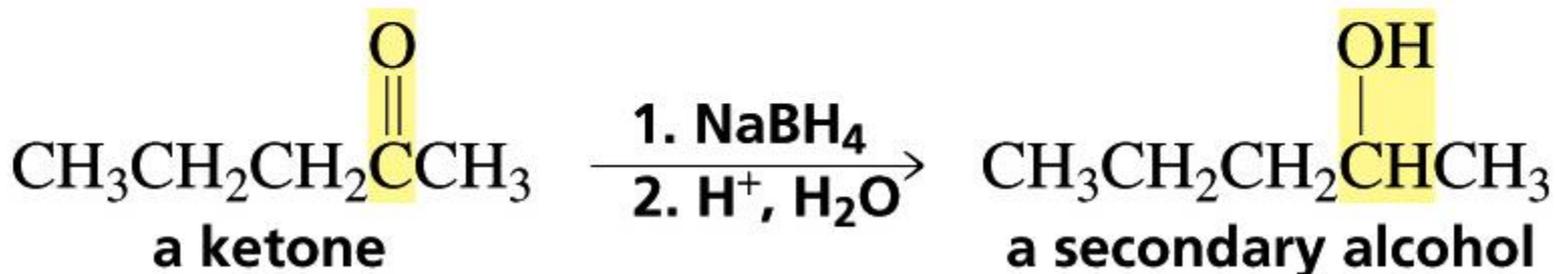
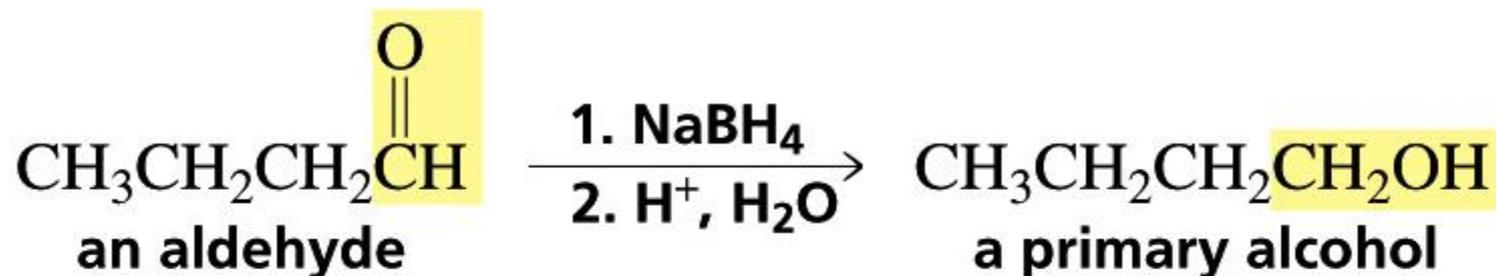


Redução por Hidrogenação Catalítica



Redução de Compostos Carbonílicos:

Adição de Íon Hidreto, seguido de protonação

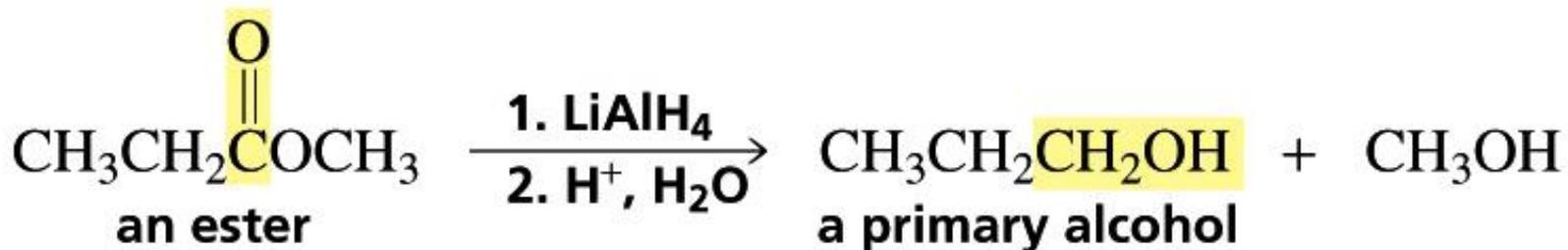
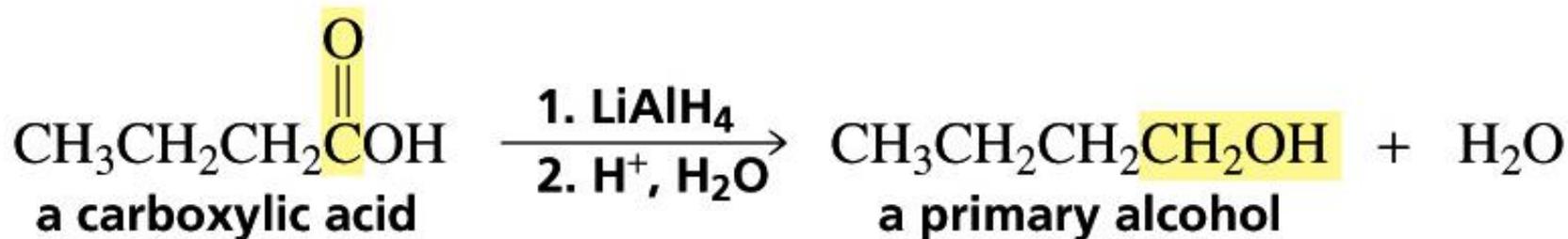


NaBH₄; é capaz de reduzir aldeídos e cetonas;

Mas ele não é redutor forte o suficiente para reduzir derivados de ácidos carboxílicos (reatividade de compostos carbonílicos e carboxílicos);

Redução de Compostos Carboxílicos:

Utilizando-se Hidreto de Lítio Alumínio



LiAlH_4 é agente redutor mais forte do que NaBH_4 ;

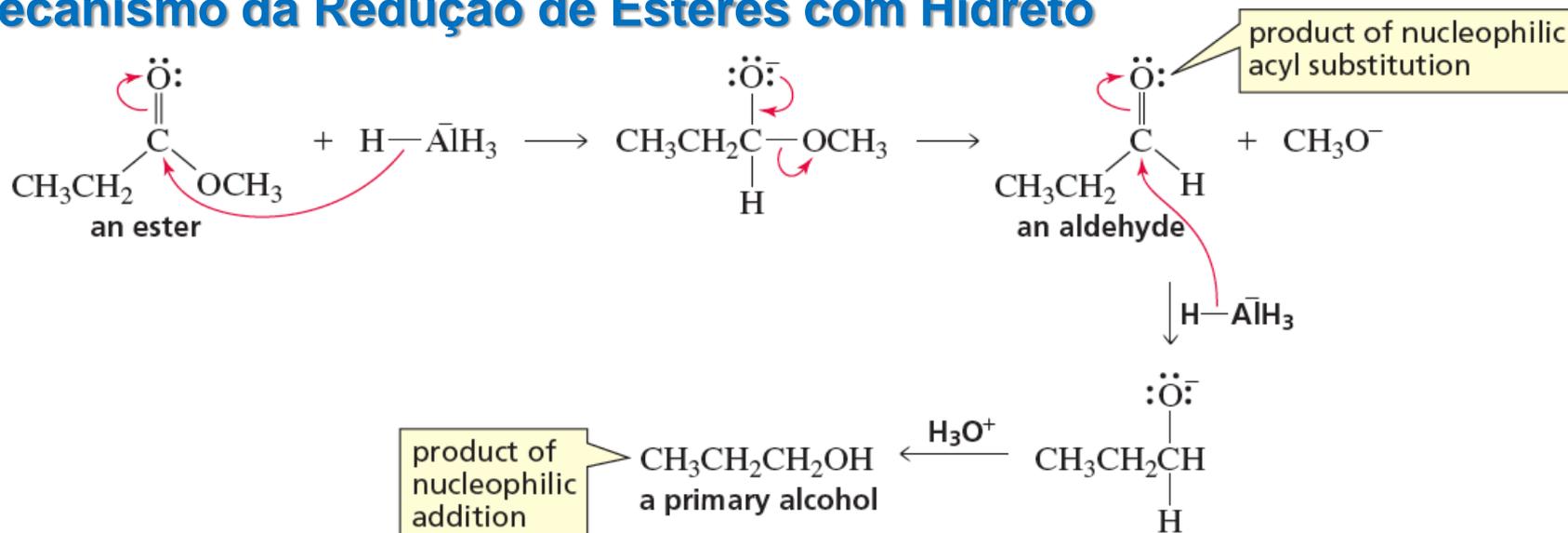
EN: H: 2,2; B 2,0; Al: 1,5 / $\Delta\text{EN}(\text{B}/\text{H})$ 0,2; $\Delta\text{EN}(\text{Al}/\text{H})$ 0,7

ligação Al-H mais polarizada que a ligação B-H

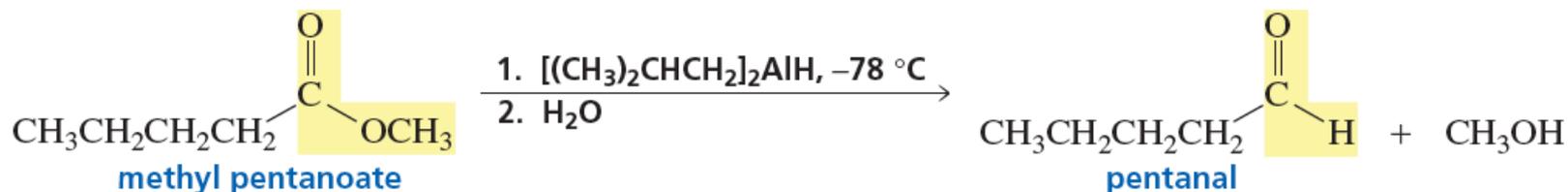
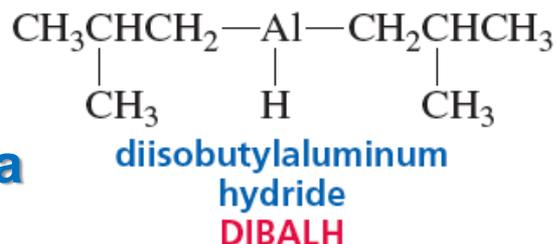
LiAlH_4 é usado para reduzir composto que não reagem com NaBH_4 como ácidos carboxílicos.

Redução de Derivados de Ácidos Carboxílicos

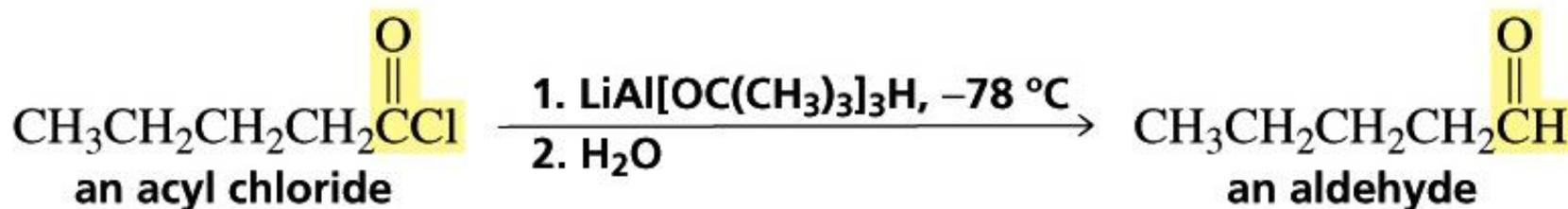
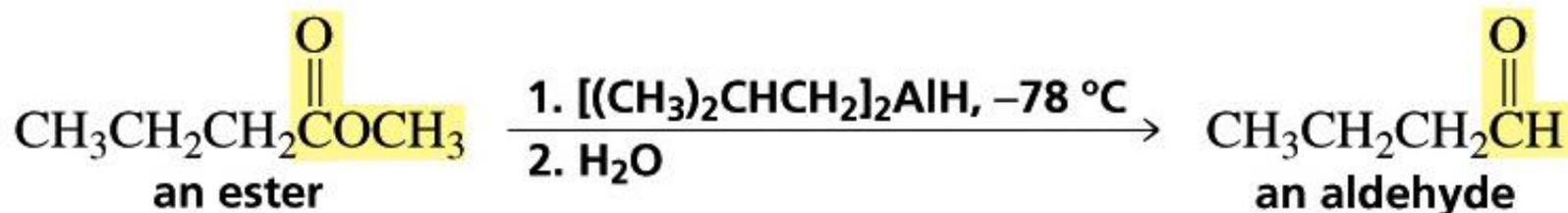
Mecanismo da Redução de Ésteres com Hidreto



Redução de Ésteres para Aldeídos: DIBALH



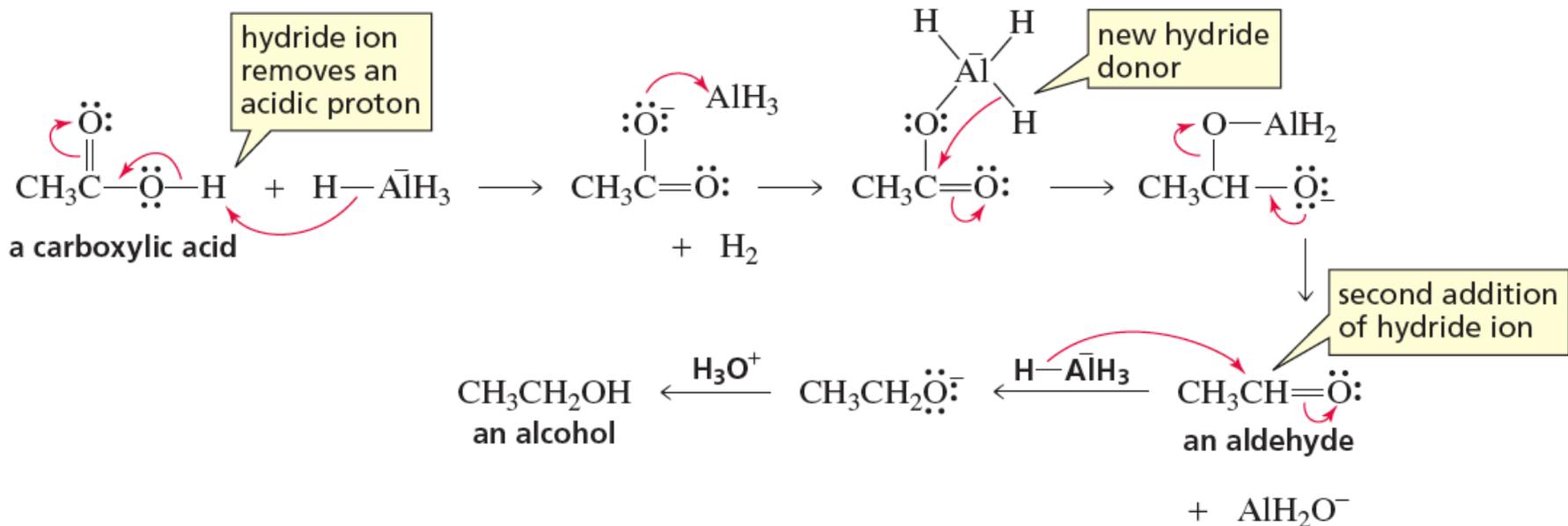
Redução de Ésteres e Cloretos de Ácido para o Aldeído Correspondente com DIBAL



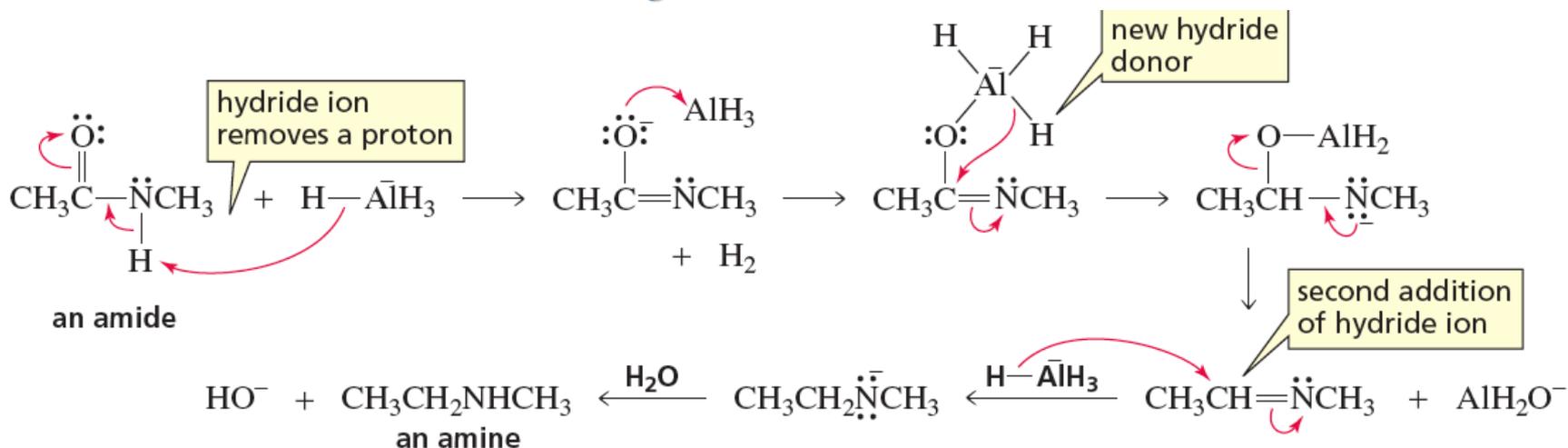
DIBAL permite a adição de somente um hidreto ao éster.

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

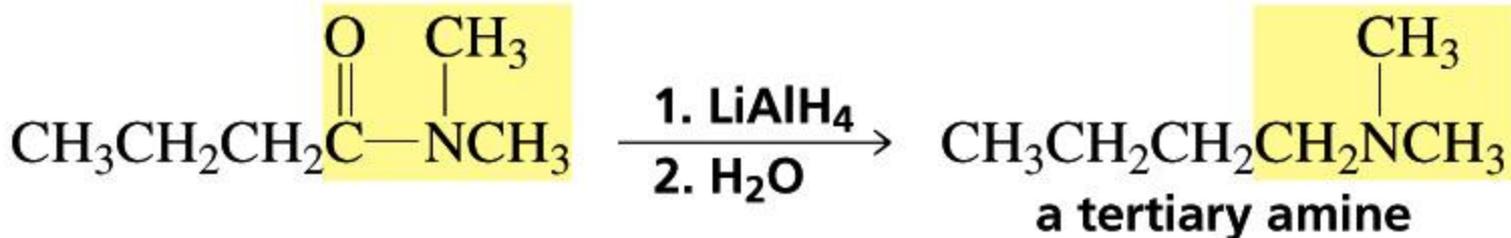
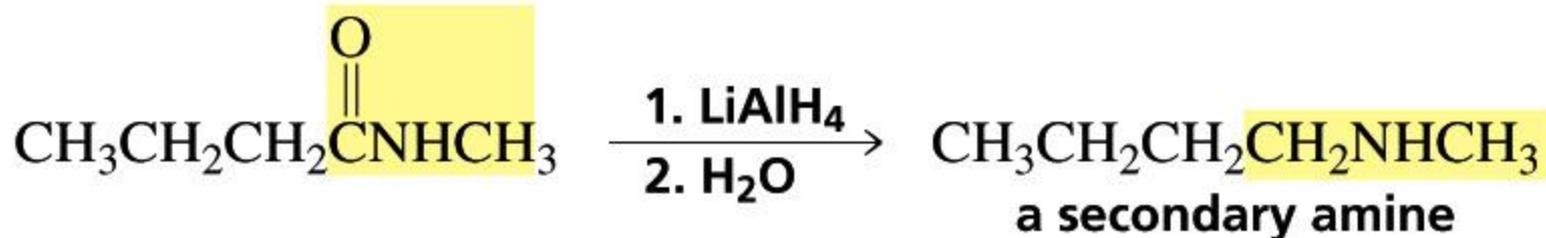
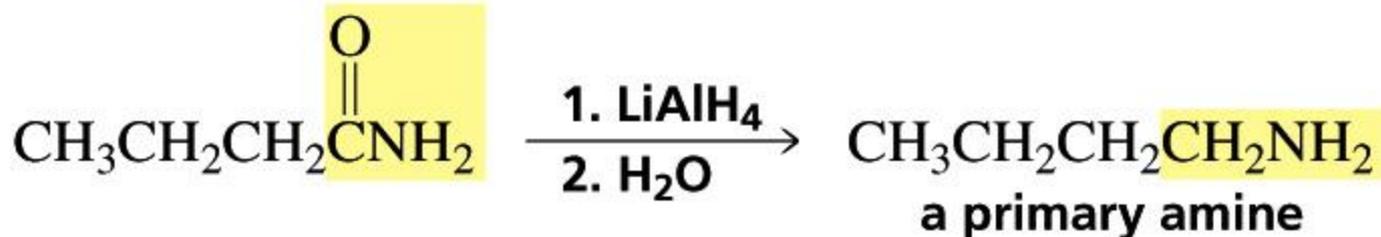
Mecanismo da Redução de Ácidos Carboxílicos com Hidreto



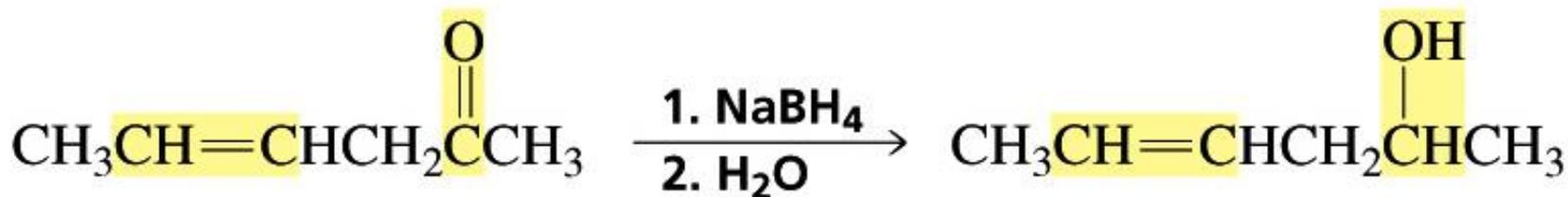
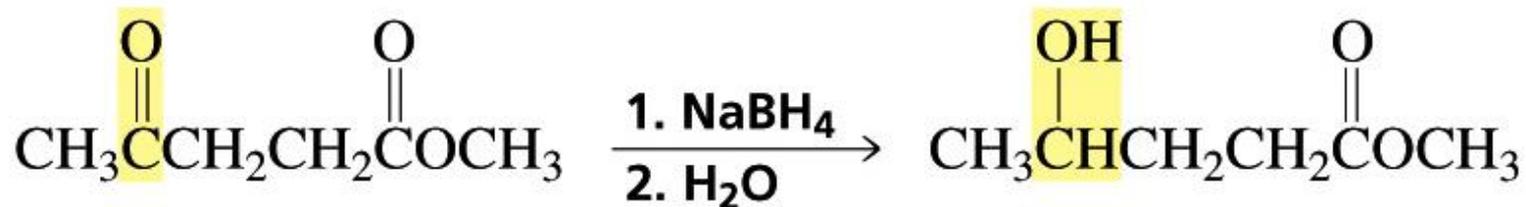
Mecanismo da Redução de Amidas com Hidreto



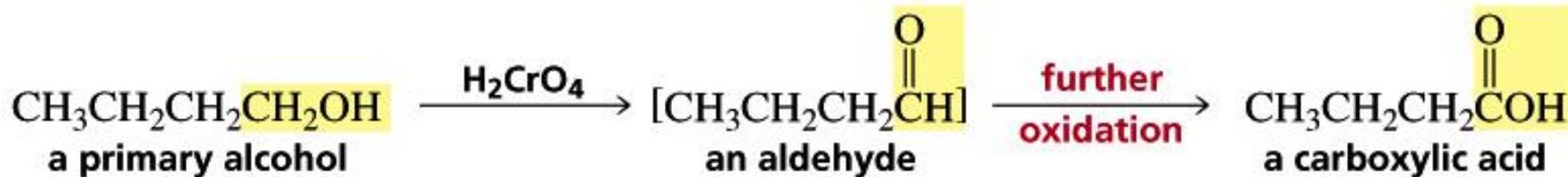
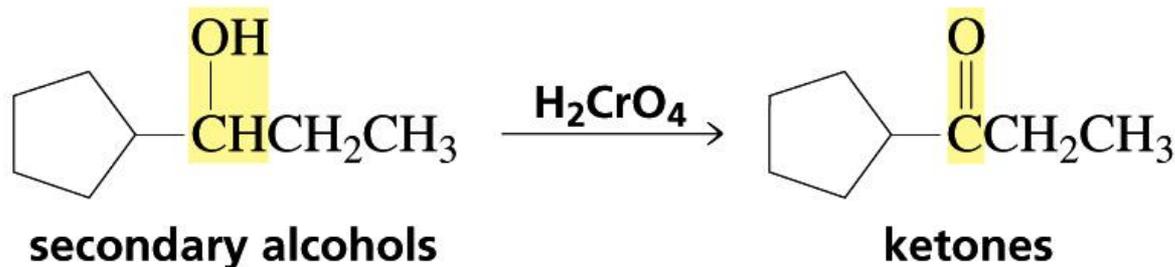
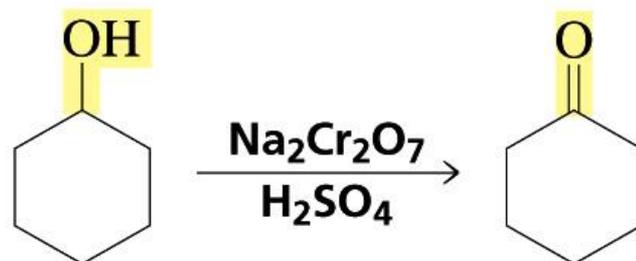
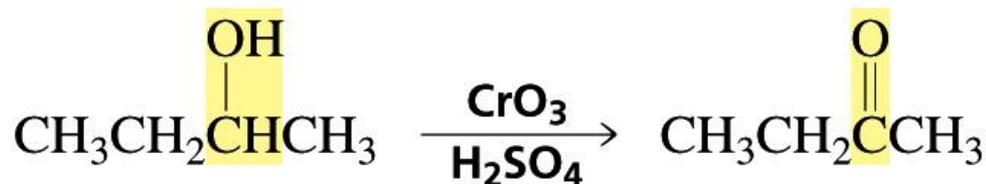
Formação de Aminas por Redução



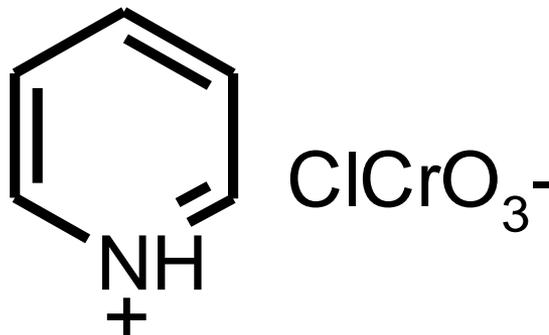
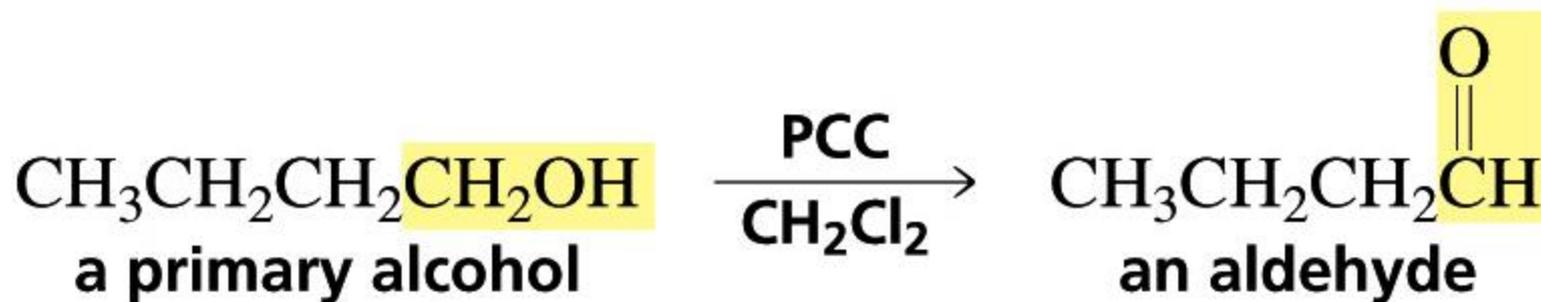
Redução Seletiva de Aldeídos e Cetonas com NaBH₄



Oxidação de Alcóois com Óxidos de Cromo

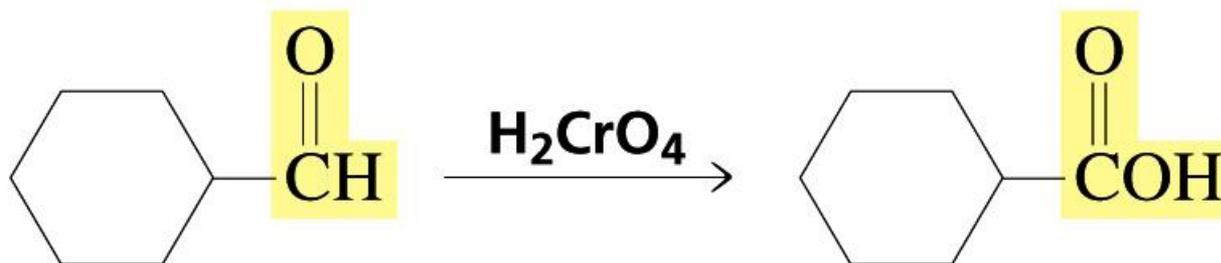
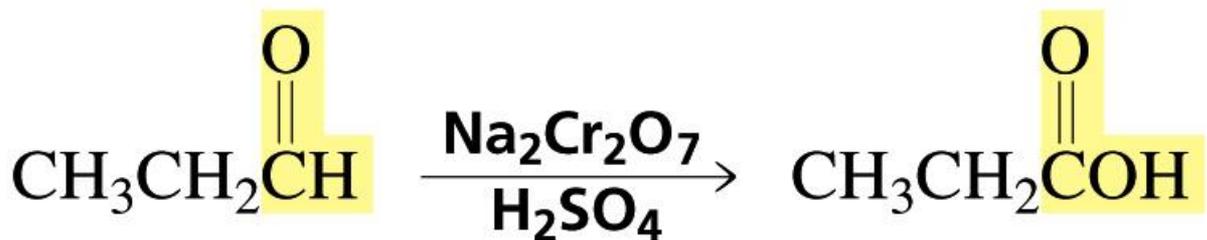


Oxidação Seletiva de Alcóois Primários para Aldeídos com PCC



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

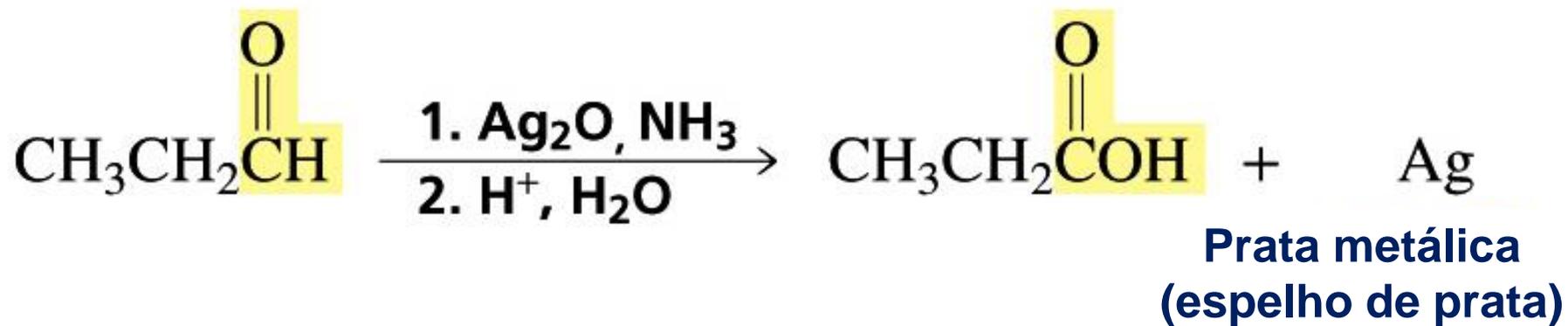
Oxidação de Aldeídos



aldehydes

carboxylic acids

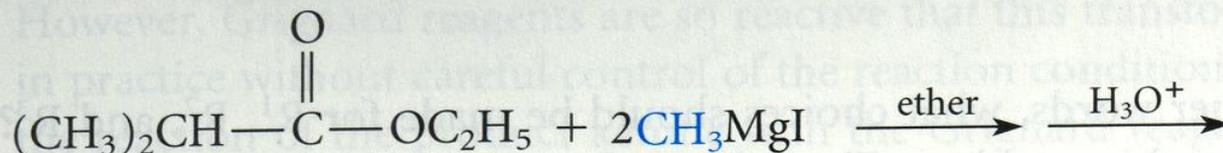
Oxidação de Aldeídos



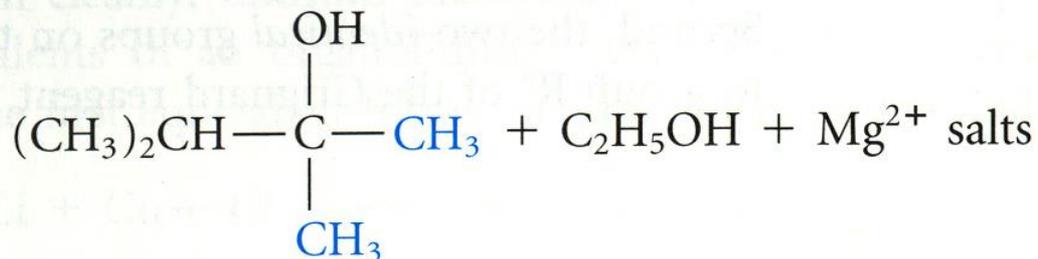
O Reagente de Tollens é seletivo para a oxidação de aldeídos e usado como teste qualitativo para presença destes compostos.

6.12. Reações com Organometálicos

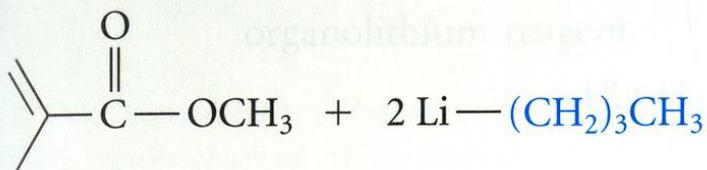
Reação de Ésteres com Organometálicos de Magnésio e de Lítio:



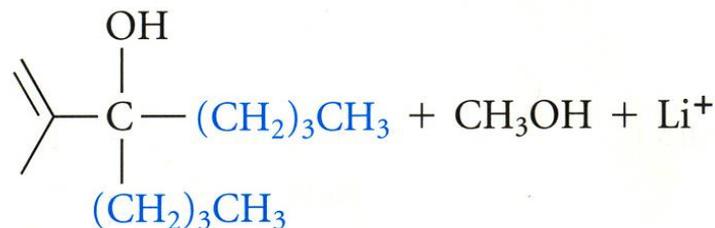
ethyl 2-methylpropanoate



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



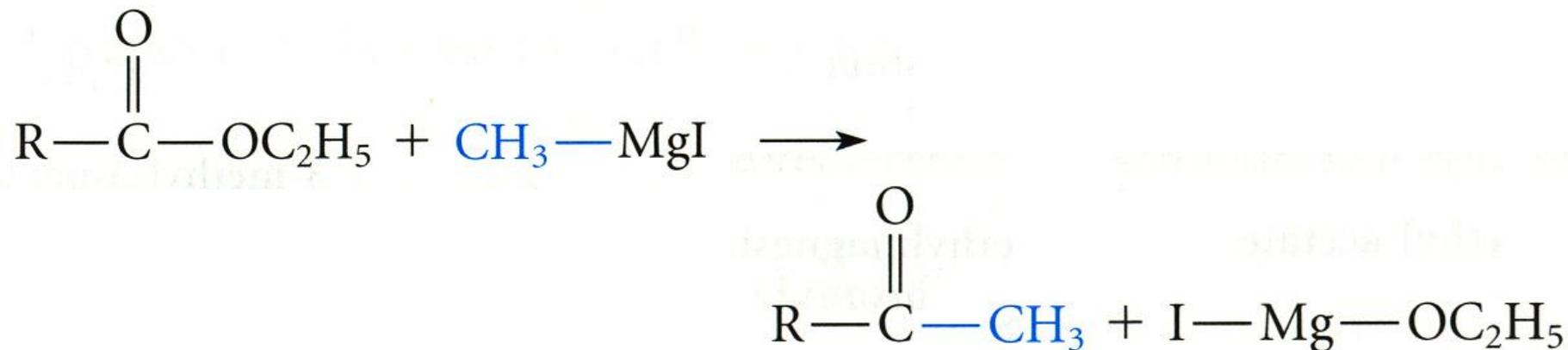
methyl
2-methylpropenoate



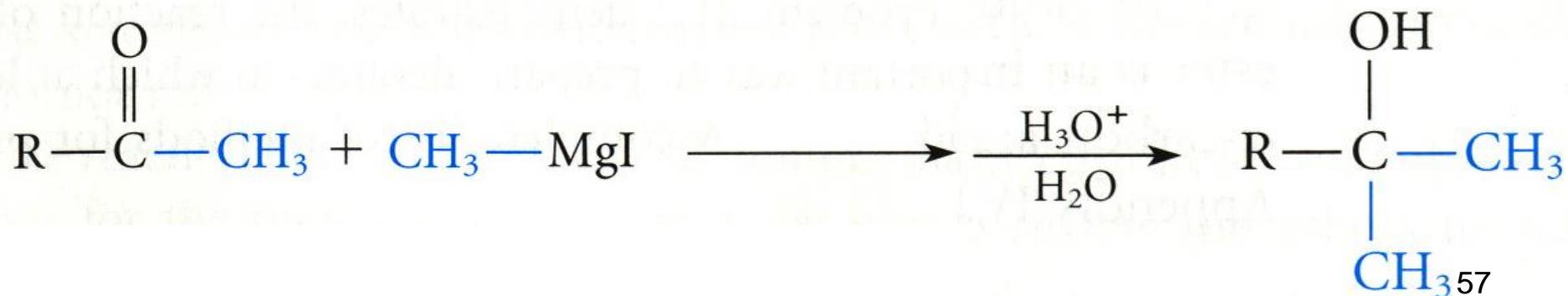
3-butyl-2-methyl-1-hepten-3-ol

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

Etapa 1: Substituição Nucleofílica Acílica:



Etapa 2: Adição Nucleofílica:



Preparação de Cetonas: Reação de Carboxilatos com Organolítio

