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Ácidos Carboxílicos

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Ácidos carboxílicos e seus derivados. Preparação de ácidos carboxílicos. Mecanismo da adição nucleofílica-eliminação no carbono acílico. Descarboxilação dos ácidos carboxílicos. Cloretos de acila. Anidridos de ácidos carboxílicos. Ésteres. Amidas. Condensação de Claisen. Síntese do éster acetoacético. Síntese do éster malônico. Adições de Michael. Reação de Mannich.

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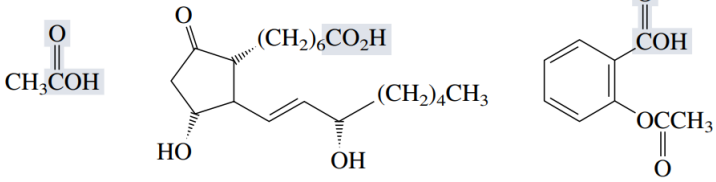

Acetic acid (present in vinegar)

PGE_1 (a prostaglandin; a small amount of PGE_1 lowers blood pressure significantly)

Aspirin

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Ionization of ethanol

$$\underset{\text{Ethanol}}{CH_3CH_2OH} \rightleftharpoons H^+ + \underset{\text{Ethoxide ion}}{CH_3CH_2O^-} \qquad K_a = \frac{[H^+][CH_3CH_2O^-]}{[CH_3CH_2OH]} = 10^{-16}$$

Ionization of acetic acid

$$\underset{\text{Acetic acid}}{CH_3COH} \rightleftharpoons H^+ + \underset{\text{Acetate ion}}{CH_3CO^-} \qquad K_a = \frac{[H^+][CH_3CO_2^-]}{[CH_3CO_2H]} = 1.8 \times 10^{-5}$$

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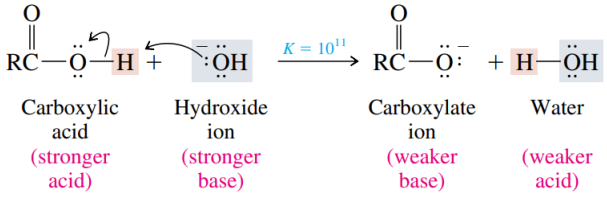

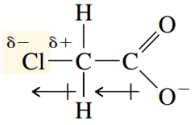

Chloroacetate anion is stabilized by electron-withdrawing effect of chlorine.

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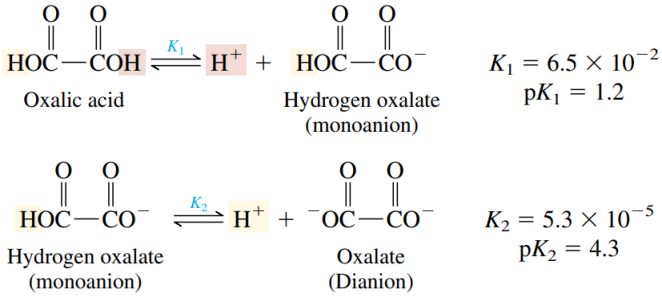
Ácidos dicarboxílicos



$K_1 = 6.5 \times 10^{-2}$
$pK_1 = 1.2$

$K_2 = 5.3 \times 10^{-5}$
$pK_2 = 4.3$

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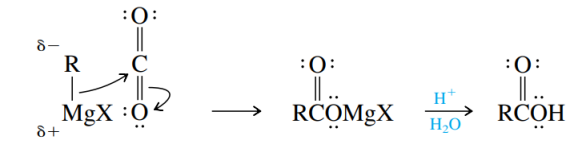
Preparação de ácidos carboxílicos



Grignard reagent acts as a nucleophile toward carbon dioxide

Halomagnesium carboxylate

Carboxylic acid

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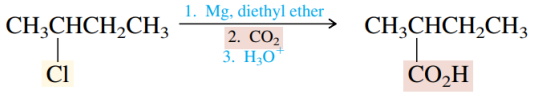
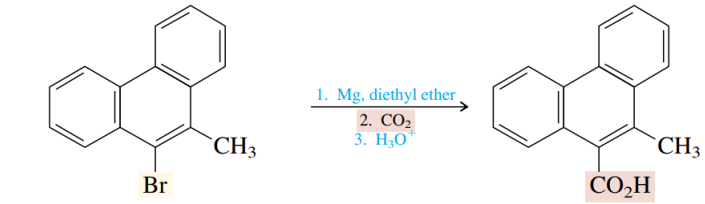
Preparação de ácidos carboxílicos



2-Chlorobutane

2-Methylbutanoic acid (76–86%)



9-Bromo-10-methylphenanthrene

10-Methylphenanthrene-9-carboxylic acid (82%)

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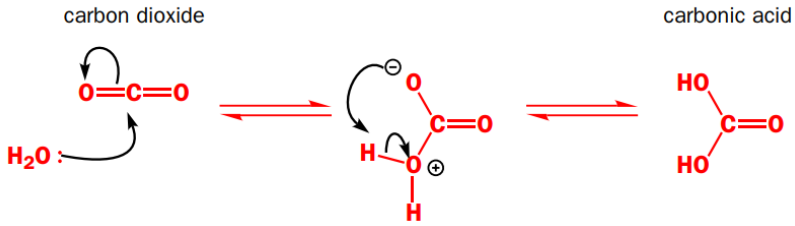
Preparação de ácidos carboxílicos



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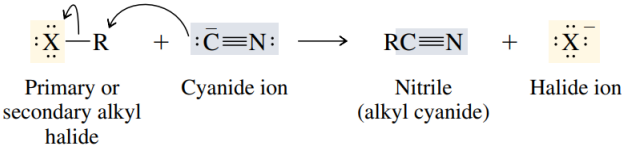
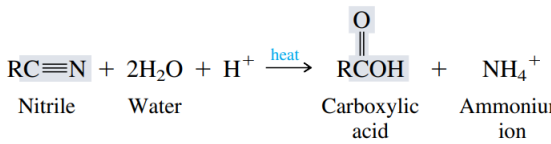
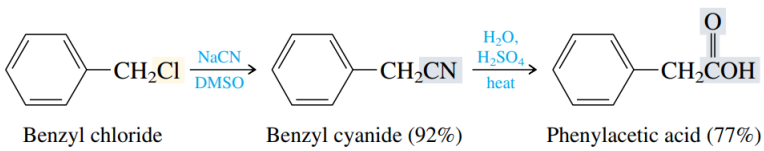
Preparação de ácidos carboxílicos: hidrólise de nitrilas







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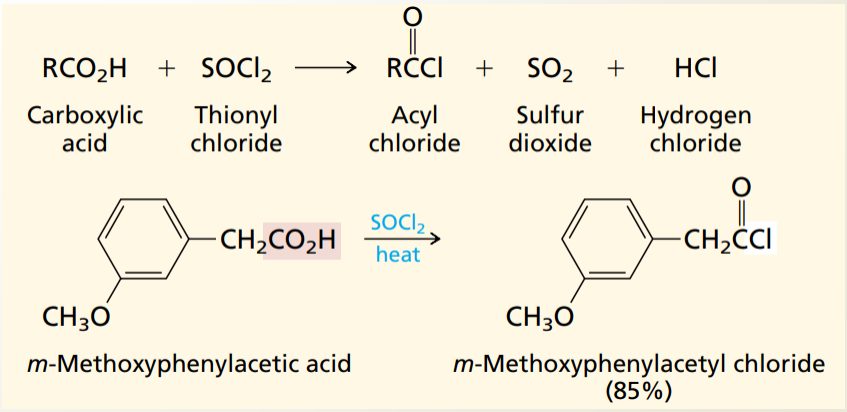
Cloretos de ácidos



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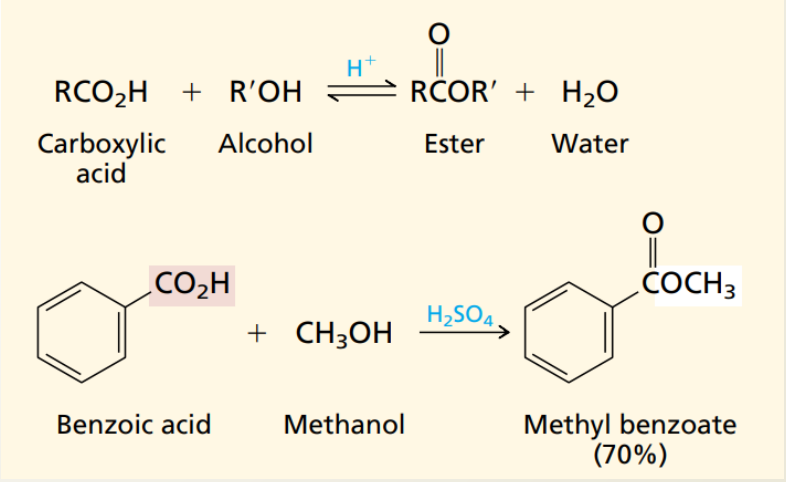
Esterificação



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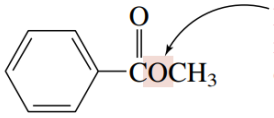
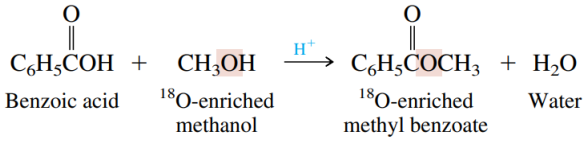
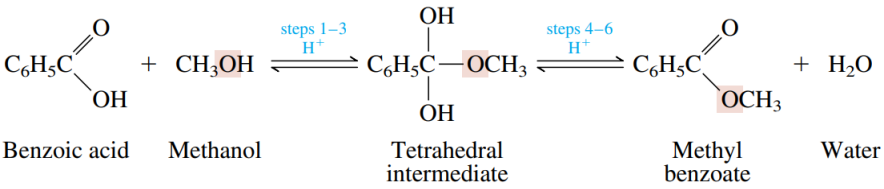
Esterificação



Is this the oxygen originally present in benzoic acid, or is it the oxygen of methanol?





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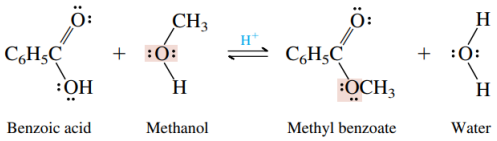
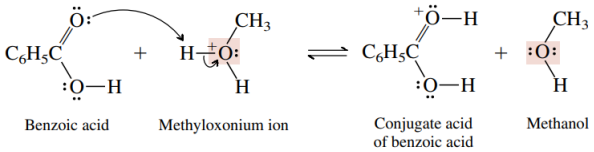
Esterificação

The overall reaction:



Step 1: The carboxylic acid is protonated on its carbonyl oxygen. The proton donor shown in the equation for this step is an alkyloxonium ion formed by proton transfer from the acid catalyst to the alcohol.



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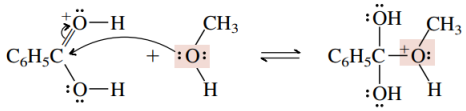
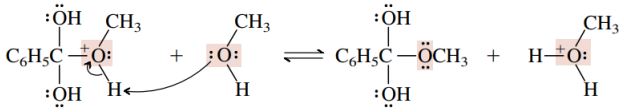
Esterificação

Step 2: Protonation of the carboxylic acid increases the positive character of its carbonyl group. A molecule of the alcohol acts as a nucleophile and attacks the carbonyl carbon.



Conjugate acid of benzoic acid | Methanol | Protonated form of tetrahedral intermediate

Step 3: The oxonium ion formed in step 2 loses a proton to give the tetrahedral intermediate in its neutral form. This step concludes the first stage in the mechanism.



Protonated form of tetrahedral intermediate | Methanol | Tetrahedral intermediate | Methyloxonium ion

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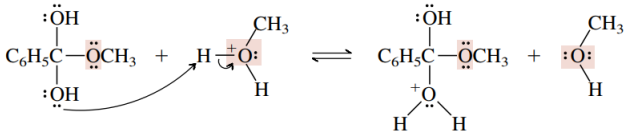
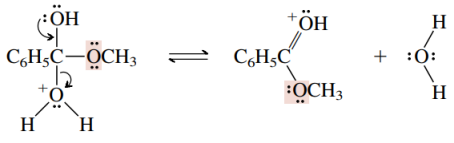
Esterificação

Step 4: The second stage begins with protonation of the tetrahedral intermediate on one of its hydroxyl oxygens.



Tetrahedral intermediate | Methyloxonium ion | Hydroxyl-protonated tetrahedral intermediate | Methanol

Step 5: This intermediate loses a molecule of water to give the protonated form of the ester.



Hydroxyl-protonated tetrahedral intermediate | Conjugate acid of methyl benzoate | Water

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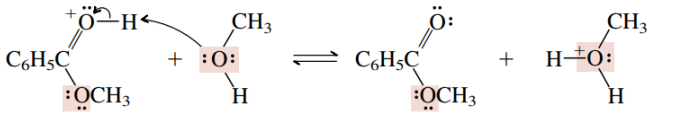
Esterificação

Step 6: Deprotonation of the species formed in step 5 gives the neutral form of the ester product.



Conjugate acid of methyl benzoate | Methanol | Methyl benzoate | Methyloxonium ion

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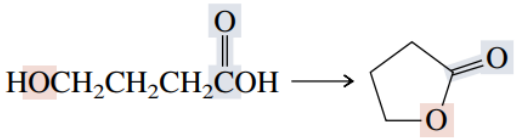
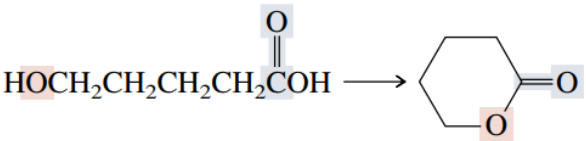
Esterificação: Lactonas



4-Hydroxybutanoic acid | 4-Butanolide



5-Hydroxypentanoic acid | 5-Pentanolide

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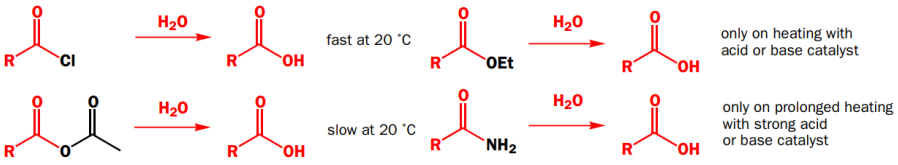
Hidrólise de derivados de ácidos carboxílicos



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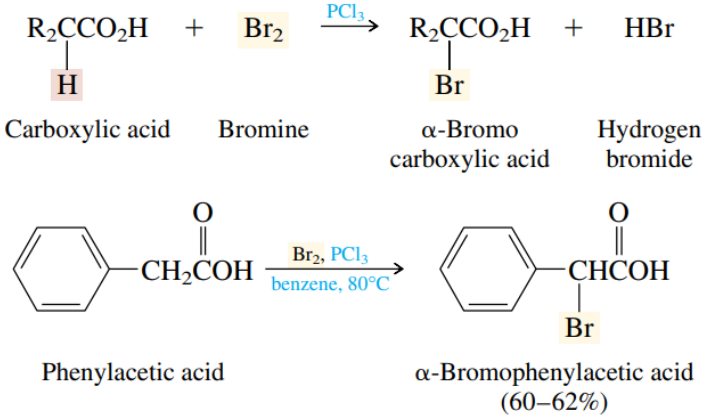
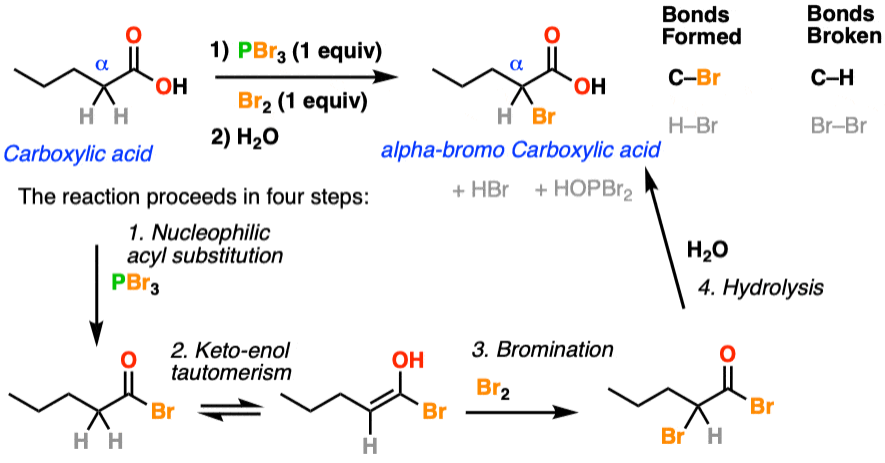
The Hell-Volhard-Zelinsky reaction



The Hell-Volhard-Zelinsky (HVZ) Reaction

The HVZ reaction replaces a C-H bond on the alpha-carbon of a carboxylic acid with a C-Br bond.



The resulting products can be converted into amino acids, alpha-bromo amides and esters.

https://www.masterorganicchemistry.com/

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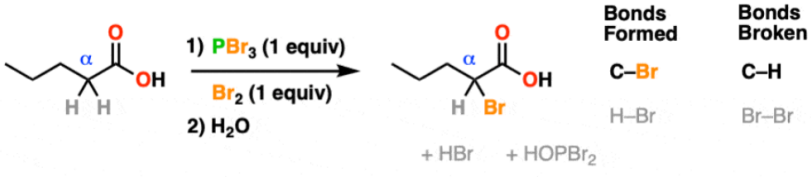
1. The Hell-Volhard-Zelinsky Reaction



Carboxylic acid *alpha-bromo Carboxylic acid*

- The function of PBr_3 is to convert the carboxylic acid to an acyl bromide
- The function of Br_2 is to convert the acyl bromide to an alpha-halo acyl bromide
- The quench with H_2O (step 2) converts the acyl bromide back to a carboxylic acid.

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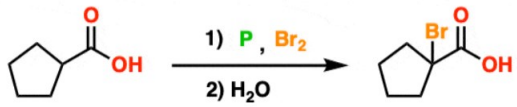
2. Red Phosphorus (P) And Bromine: The Reactants From "Hell"

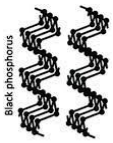
"P, Br_2 " Alternate Way Of Showing Reagents In A Hell-Volhard-Zelinsky Reaction:

(this actually ends up being the same thing as PBr_3 + Br_2)



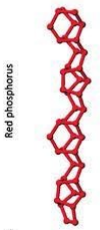
P/Br_2 really just means the same as PBr_3 / Br_2.

2. **Red Phosphorus (P)** and **Bromine**: The Reactants From "Hell"



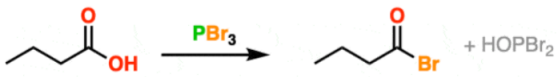
The Reactants From "Hell" - P + Br_2

- The "P" here is **red** phosphorus (not to be confused with the black or white phosphorus allotropes)
- Red phosphorus combined with bromine (Br_2) gives **PBr_3**



2 P + 3 Br_2 → 2 PBr_3

- PBr_3 will convert carboxylic acids to acid bromides:



Carboxylic acid *Acid bromide*

- Bromine (Br_2) will form C-Br bonds on the alpha carbons of acid bromides *(via the enol)*

So long as there is 1 equiv of Br_2 left over after Br_2 reacts with phosphorus to give PBr_3, the reaction will go to completion:

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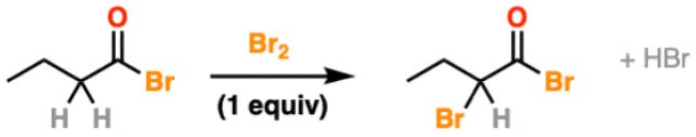
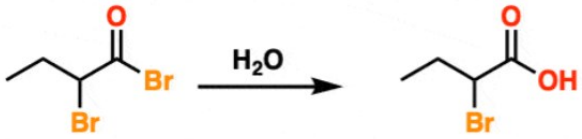


The final step is hydrolysis of the acid bromide with water
(or sometimes, other nucleophiles)



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3. A Guided Tour Through Hell. Stage 1: PBr3

Step 1 of the Hell-Volhard-Zelinsky: Conversion of A Carboxylic Acid To An Acid Halide

Bonds Formed	Bonds Broken
C–Br	C–OH

+ HO-PBr_2

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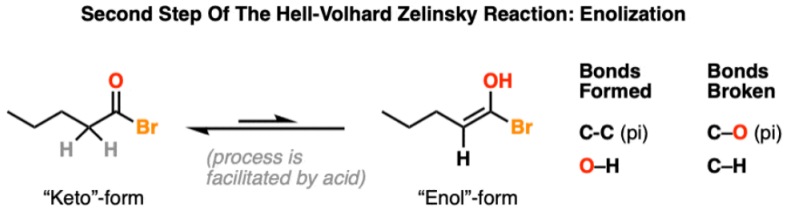
4. Highway To Hell: Enolization



AC/DC - Highway to Hell (Official Video)

The Rube Goldberg machines

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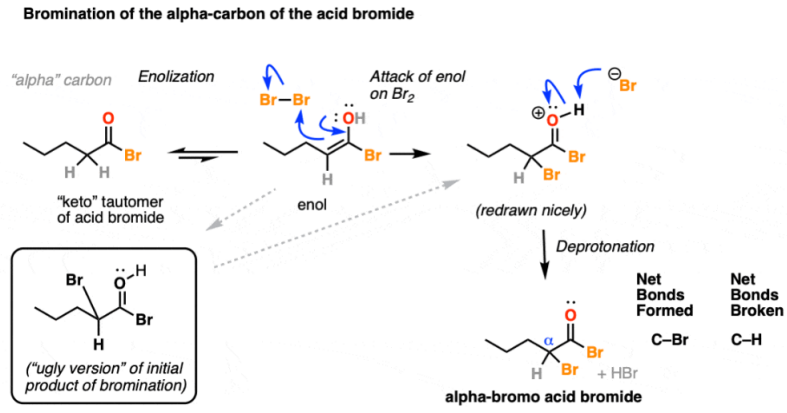
5. Hell's Kitchen: Bromination Of The Enol



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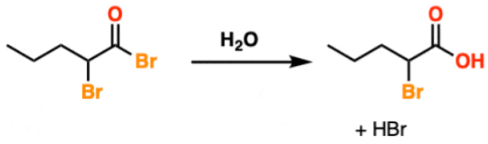
6. Hellish Waters: Hydrolysis of the Acid Bromide

Final Step: Quenching The Reaction With Water Gives A Carboxylic Acid



Bonds Formed	Bonds Broken
C–OH	C–Br
H-Br	O–H

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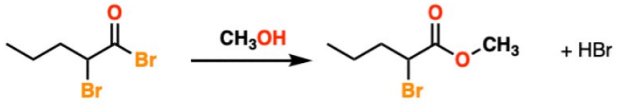
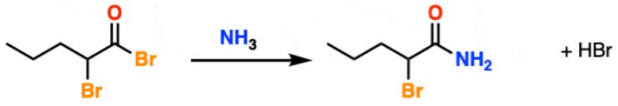
"Quenches" With Alcohols And Amines Can Give Esters And Amides

Quenching with alcohols provides esters



Quenching with NH_3 (or other amines) gives amides:



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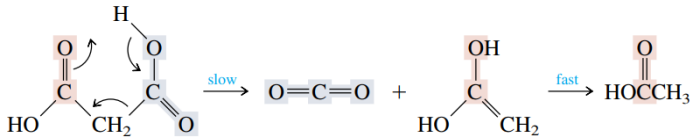
Decarboxylation of malonic acid

$$RCO_2H \longrightarrow RH + CO_2$$

Carboxylic acid — Alkane — Carbon dioxide

$$HO_2CCH_2CO_2H \xrightarrow{150°C} CH_3CO_2H + CO_2$$

Malonic acid (propanedioic acid) — Acetic acid (ethanoic acid) — Carbon dioxide



Carbon dioxide — Enol form of acetic acid — Acetic acid

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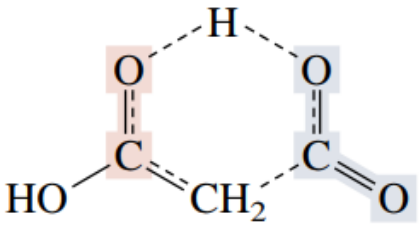
Decarboxylation of malonic acid



Representation of transition state in thermal decarboxylation of malonic acid

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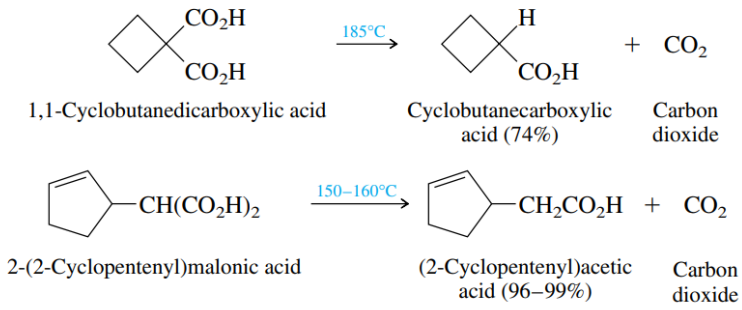
Decarboxylation



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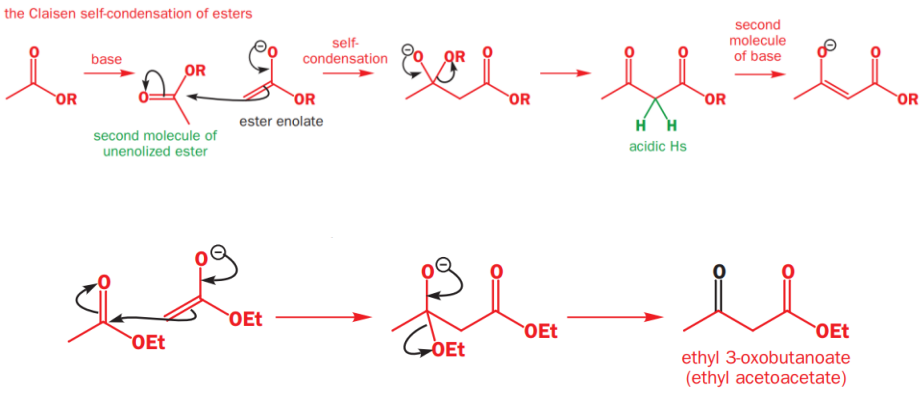
Condensação de Claisen



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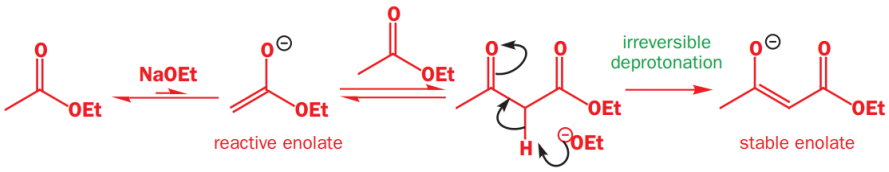
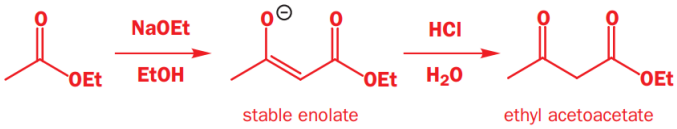
Condensação de Claisen



the complete Claisen ester condensation



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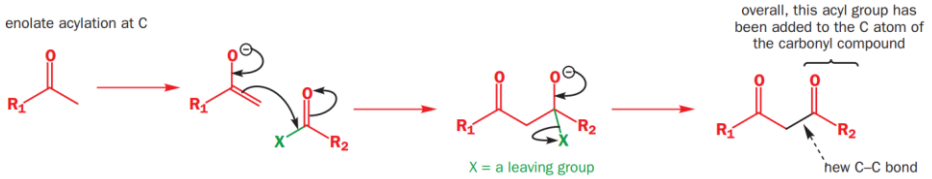
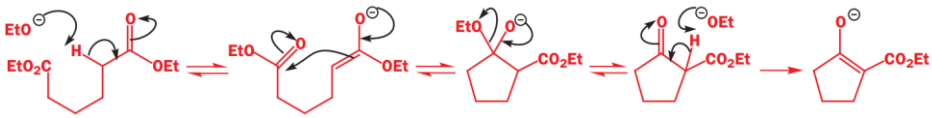
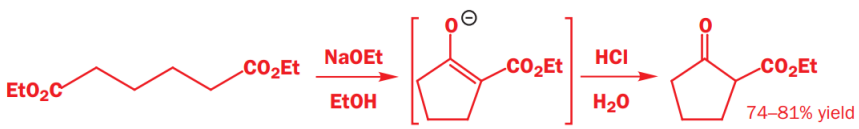
Condensação de Claisen







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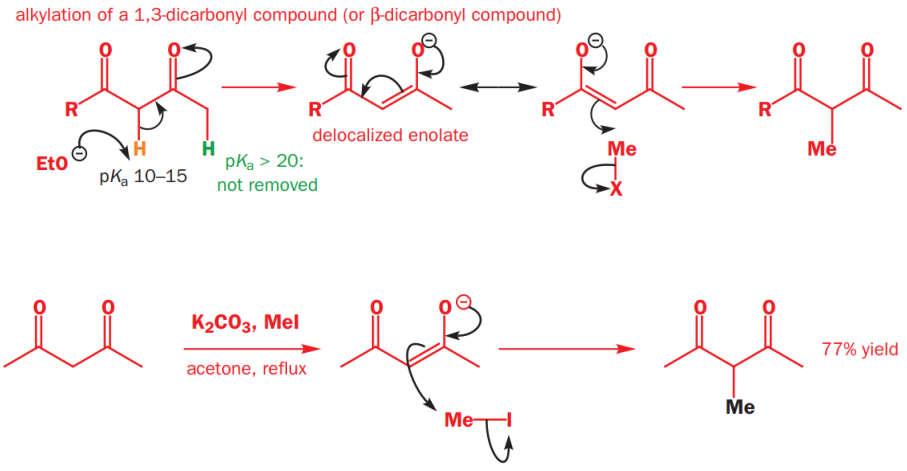
Síntese do éster acetoacético



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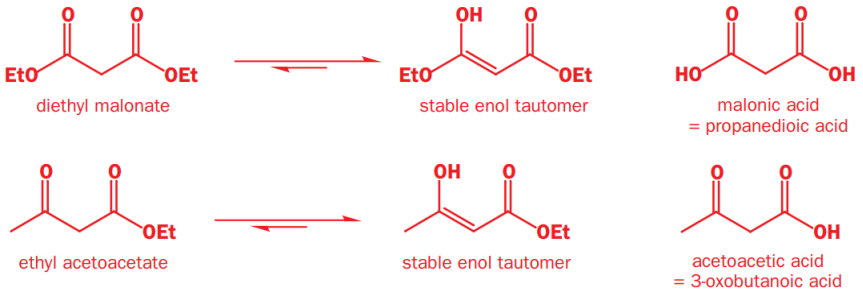
Síntese do éster acetoacético



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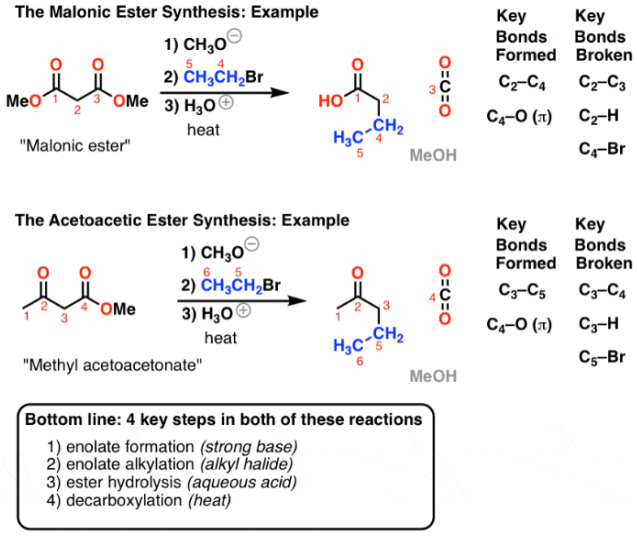
Síntese do éster malônico



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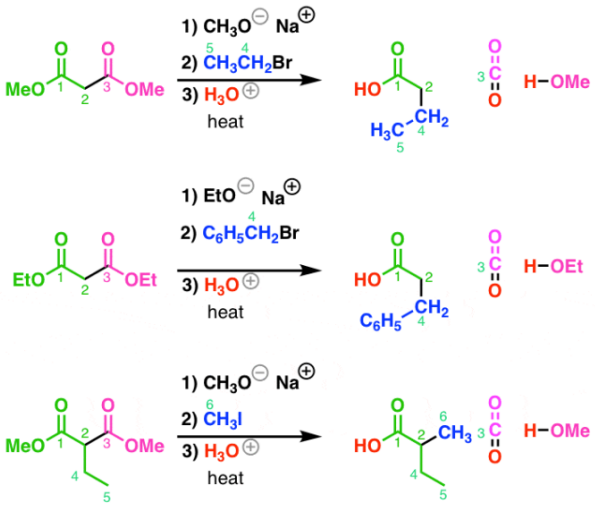
Síntese do éster malônico



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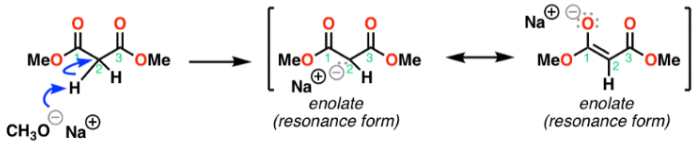
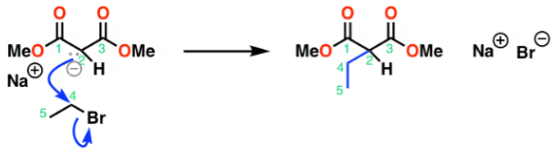
Síntese do éster malônico

The Malonic Ester Synthesis: Mechanism

In step 1, the CH_3O^- acts as a base to remove the most acidic proton (on C_2) to make an enolate



In **step 2**, the enolate acts as a nucleophile to attack an alkyl halide in an S_N2 reaction



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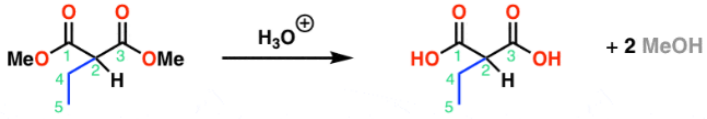
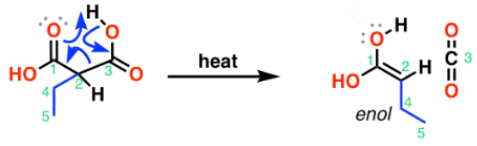
Síntese do éster malônico

In **step 3**, the addition of aqueous acid leads to **hydrolysis of the esters** into carboxylic acids



Then, **decarboxylation** can occur to form an **enol** and **carbon dioxide**



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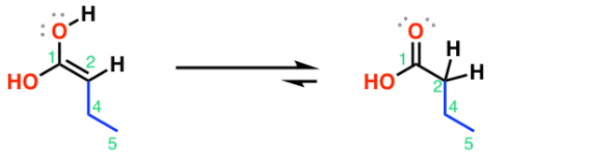
Síntese do éster malônico

Finally, the enol **tautomerizes** back to the carboxylic acid



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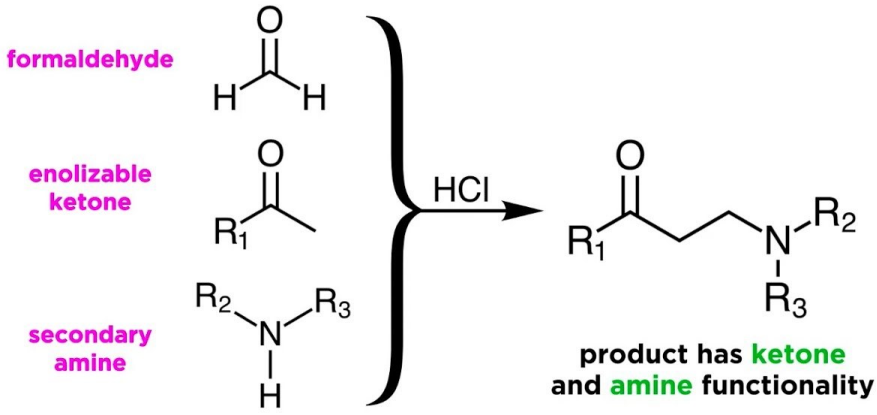
Reação de Mannich

Mannich Reaction



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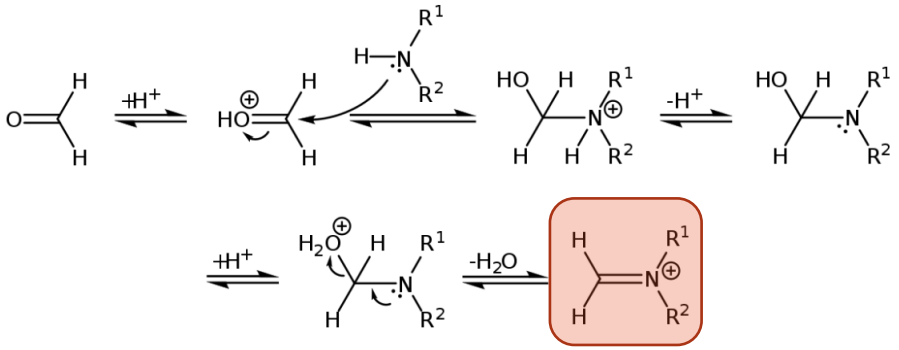
Reação de Mannich Mechanism



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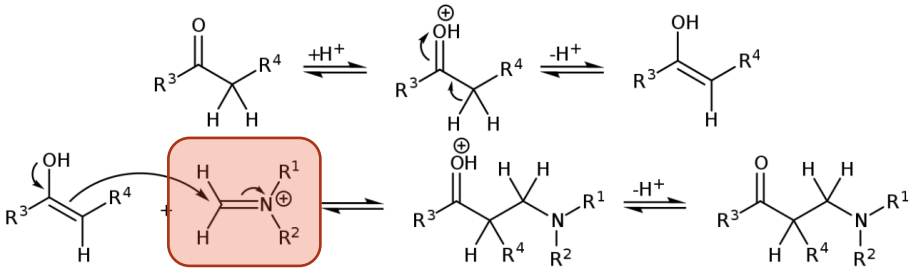
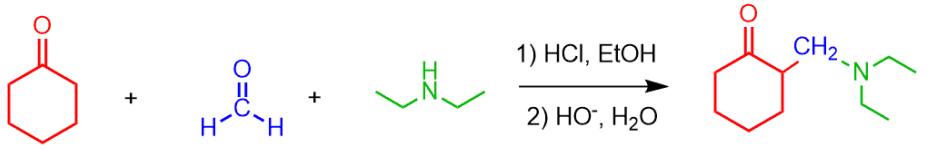
Reação de Mannich Mechanism...



The **Mannich reaction** is a condensation of an aldehyde or ketone in form of an enol with an iminium ion producing β - aminoalkyl carbonyl compounds.



ketone **aldehyde -** **2° amine** **β - aminoalkyl carbonyl**

more reactive than the ketone

- *Formaldehyde is used most often due to its higher reactivity.*
- *Works only with primary and secondary aliphatic amines.*
- *Aromatic amines tend not to react.*