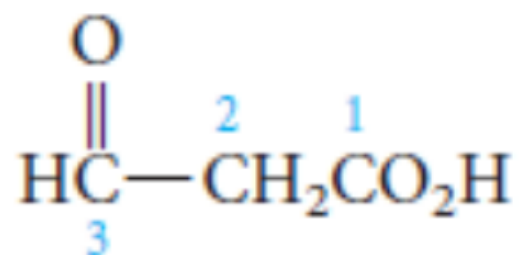


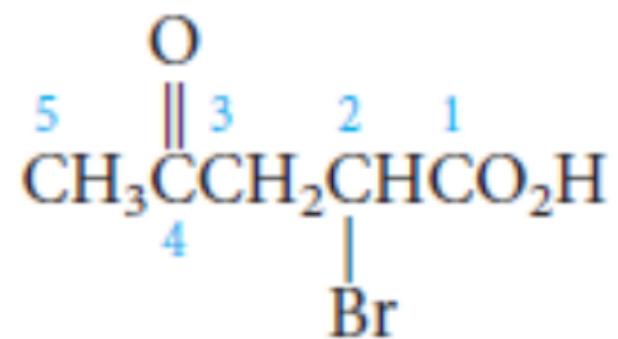
Organic chemistry of
nonmajor students
Chem233

10 Carboxylic Acids
and
Their Derivatives



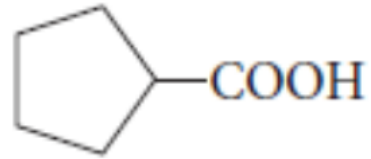


3-oxopropanoic acid

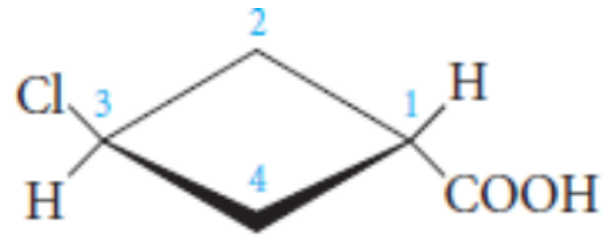


2-bromo-4-oxopentanoic acid

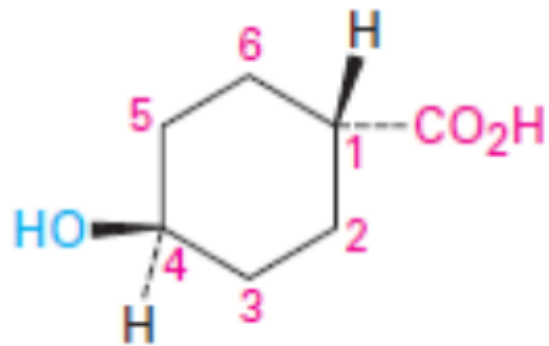




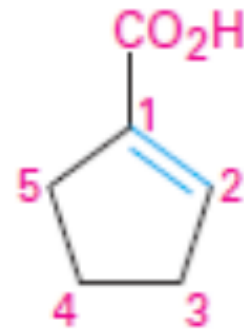
cyclopentanecarboxylic acid



trans-3-chlorocyclobutanecarboxylic acid

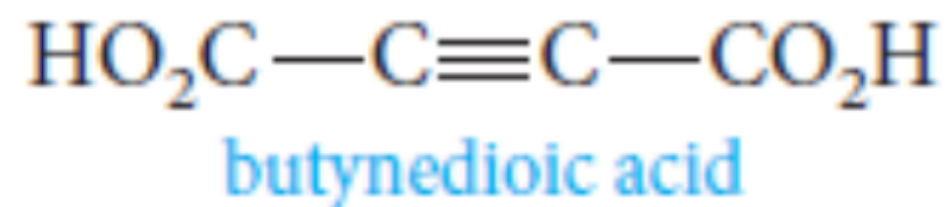
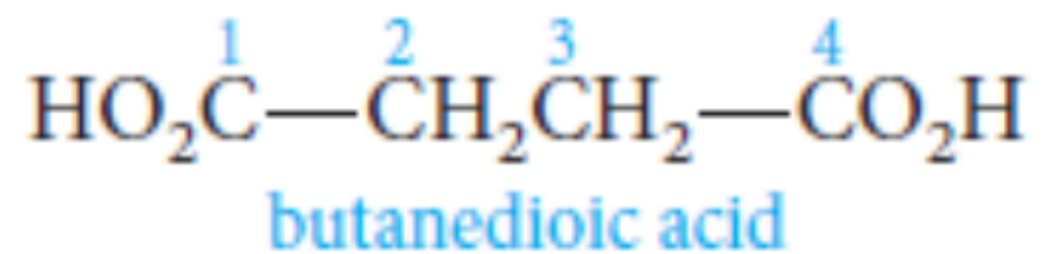


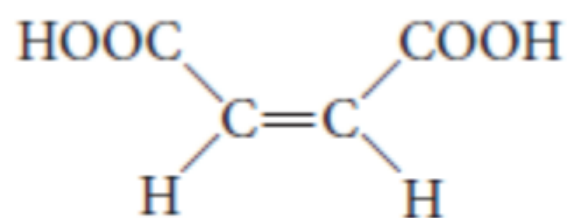
trans-4-Hydroxycyclohexanecarboxylic acid



1-Cyclopentene-1-carboxylic acid



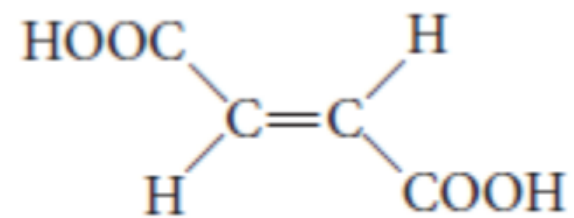




maleic acid

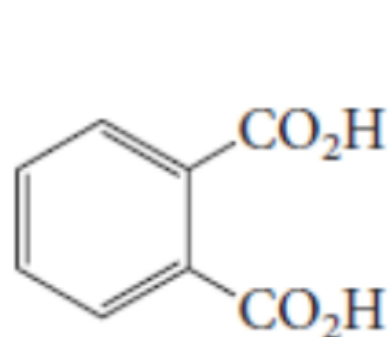
(*cis*-2-butenedioic acid)

and

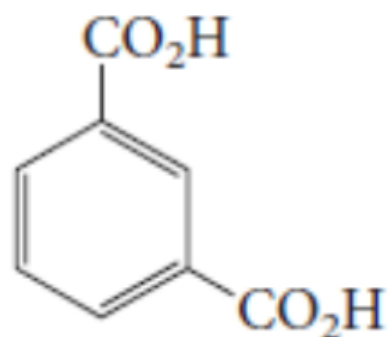


fumaric acid

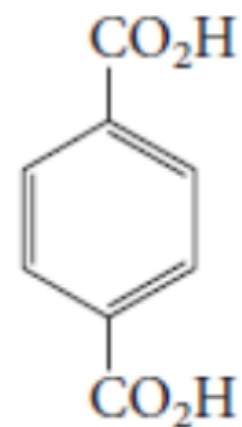
(*trans*-2-butenedioic acid)



phthalic acid



isophthalic acid



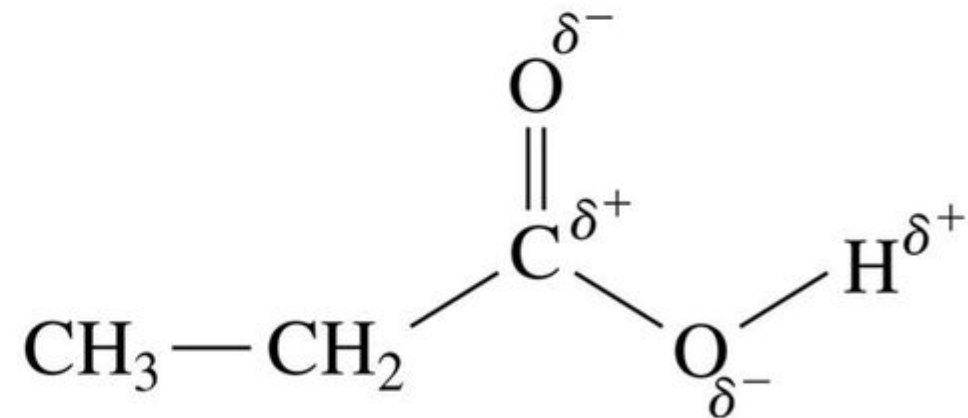
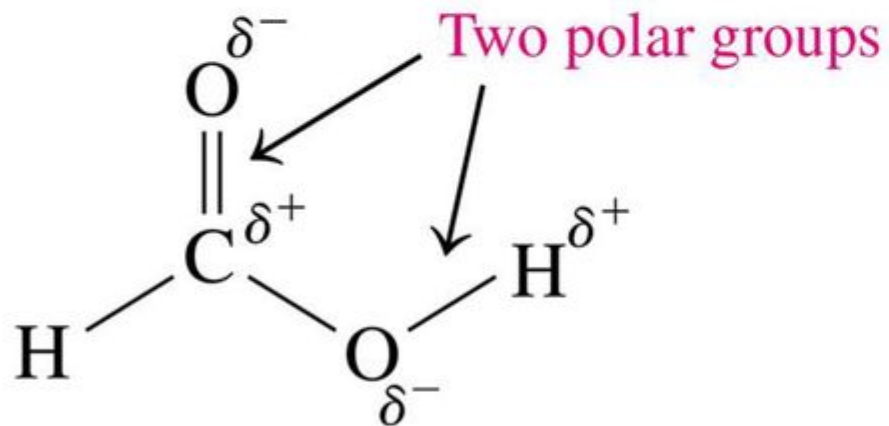
terephthalic acid



10.2 Physical Properties of Acids

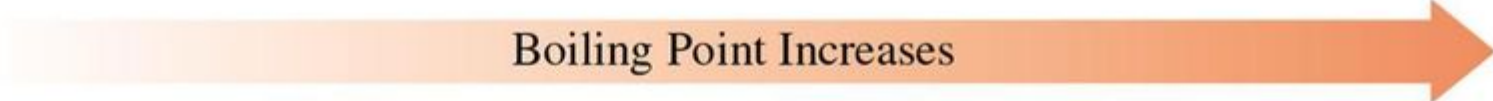
Carboxylic acids are strongly polar because they have two polar groups:

- a hydroxyl group (—OH) and
- a carbonyl group ($\text{C} = \text{O}$).



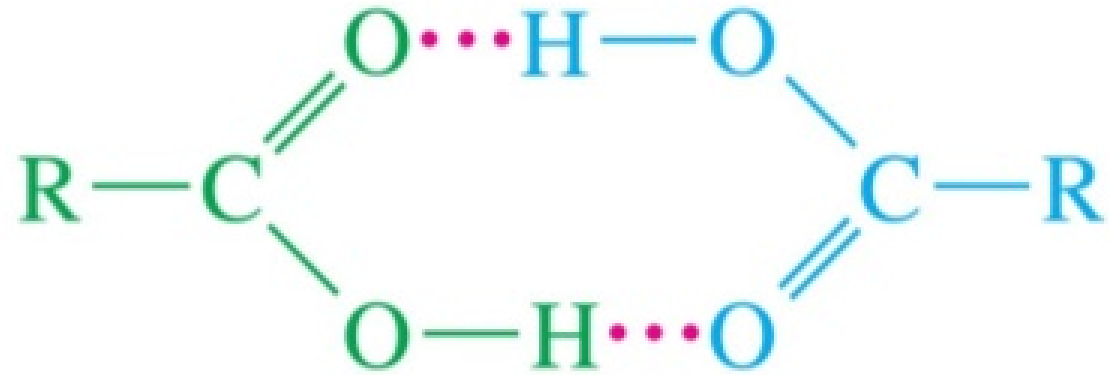
Boiling Points

	$\text{CH}_3-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{H}$	$\text{CH}_3-\text{CH}_2-\text{CH}_2-\text{OH}$	$\text{CH}_3-\overset{\text{O}}{\parallel}{\text{C}}-\text{OH}$
Name	Propanal	1-Propanol	Ethanoic acid
Molar Mass	58	60	60
Family	Aldehyde	Alcohol	Carboxylic acid
bp	49 °C	97 °C	118 °C

Boiling Point Increases 



Boiling Points



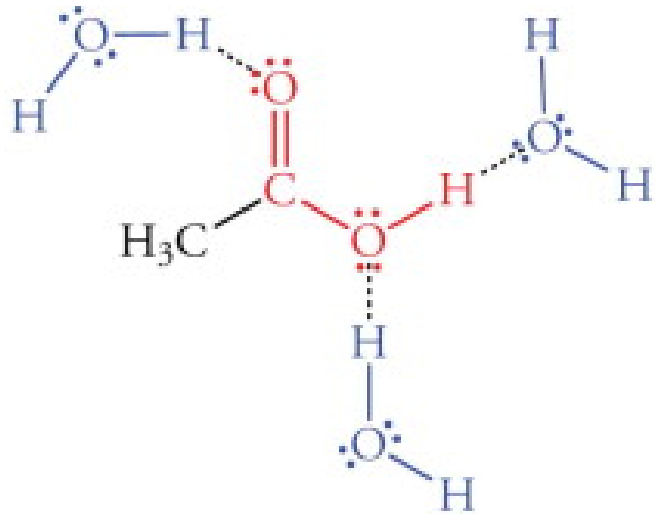
hydrogen-bonded acid dimer

Higher boiling points than similar alcohols, due to the formation of a hydrogen-bonded dimer.

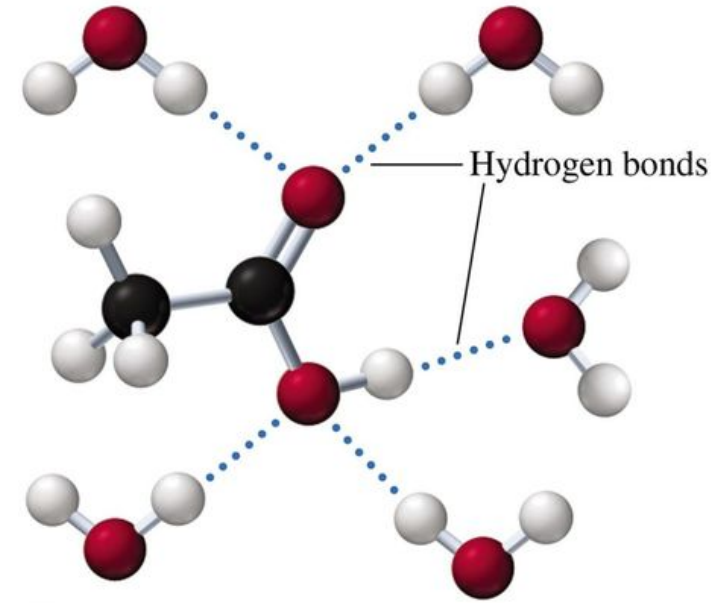


Name	bp, °C	mp, °C	Solubility, g/100 g H ₂ O at 25°C
formic acid	101	8	miscible (∞)
acetic acid	118	17	
propanoic acid	141	-22	
butanoic acid	164	-8	
hexanoic acid	205	-1.5	1.0
octanoic acid	240	17	0.06
decanoic acid	270	31	0.01
benzoic acid	249	122	0.4 (but 6.8 at 95°C)





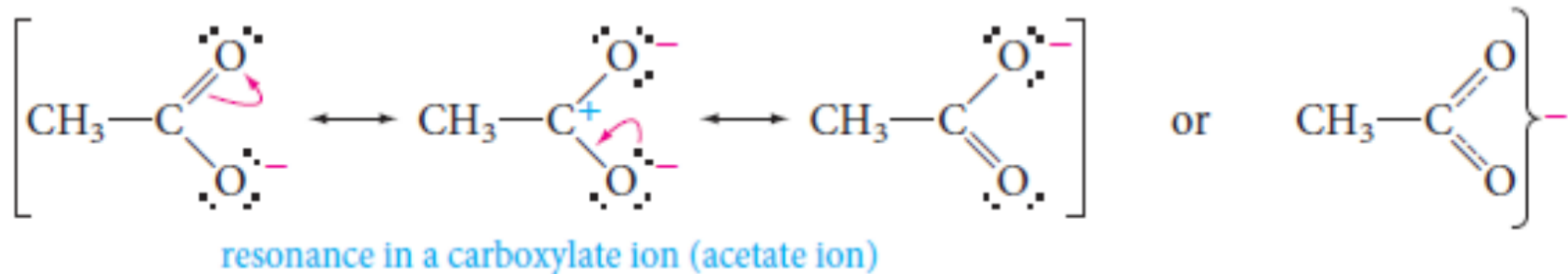
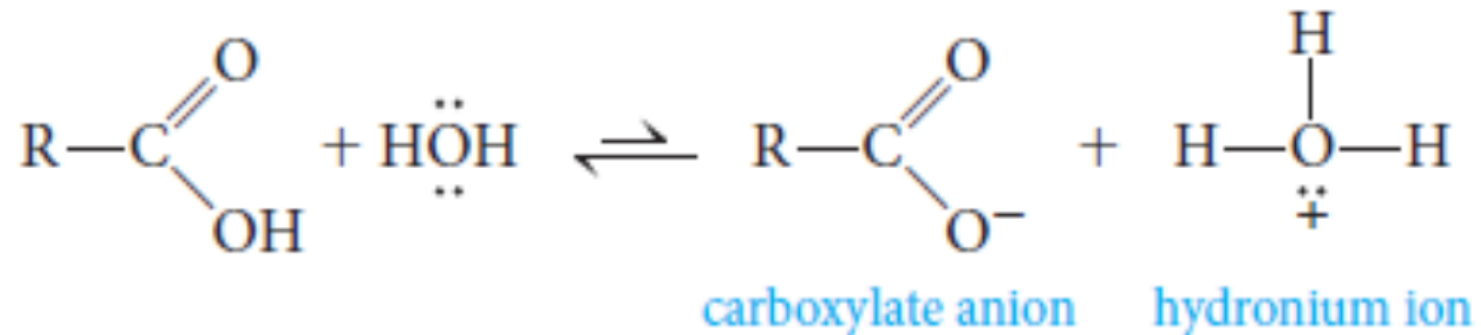
hydrogen bonds between acetic acid and water in aqueous solution

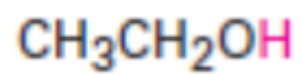


Acetic acid forms hydrogen bonds with water molecules.

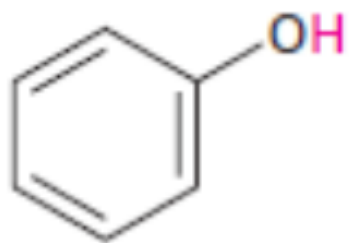


10.3 Acidity and Acidity Constants

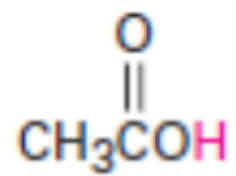




$\text{p}K_{\text{a}} = 16$



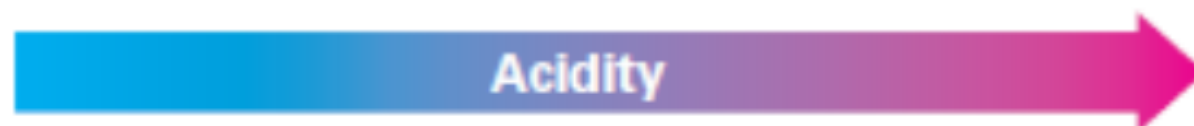
$\text{p}K_{\text{a}} = 9.89$



$\text{p}K_{\text{a}} = 4.76$



$\text{p}K_{\text{a}} = -7$



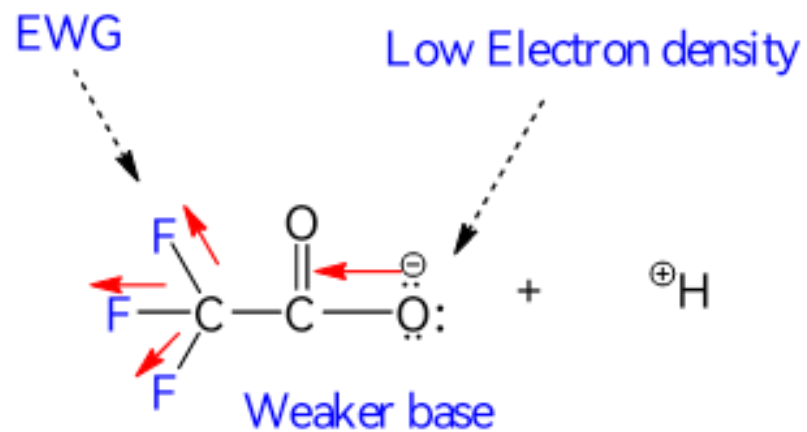
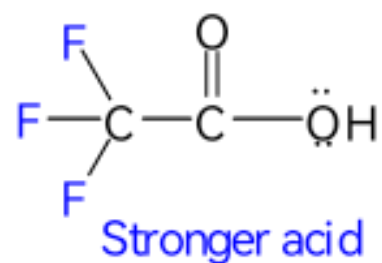
Name	Formula	K_a	pK_a
formic acid	HCOOH	2.1×10^{-4}	3.68
acetic acid	CH ₃ COOH	1.8×10^{-5}	4.74
propanoic acid	CH ₃ CH ₂ COOH	1.4×10^{-5}	4.85
butanoic acid	CH ₃ CH ₂ CH ₂ COOH	1.6×10^{-5}	4.80
chloroacetic acid	ClCH ₂ COOH	1.5×10^{-3}	2.82
dichloroacetic acid	Cl ₂ CHCOOH	5.0×10^{-2}	1.30
trichloroacetic acid	Cl ₃ CCOOH	2.0×10^{-1}	0.70
2-chlorobutanoic acid	CH ₃ CH ₂ CHClCOOH	1.4×10^{-3}	2.85
3-chlorobutanoic acid	CH ₃ CHClCH ₂ COOH	8.9×10^{-5}	4.05
benzoic acid	C ₆ H ₅ COOH	6.6×10^{-5}	4.18
<i>o</i> -chlorobenzoic acid	<i>o</i> -Cl—C ₆ H ₄ COOH	12.5×10^{-4}	2.90
<i>m</i> -chlorobenzoic acid	<i>m</i> -Cl—C ₆ H ₄ COOH	1.6×10^{-4}	3.80
<i>p</i> -chlorobenzoic acid	<i>p</i> -Cl—C ₆ H ₄ COOH	1.0×10^{-4}	4.00
<i>p</i> -nitrobenzoic acid	<i>p</i> -NO ₂ —C ₆ H ₄ COOH	4.0×10^{-4}	3.40



Inductive Effect

PKa

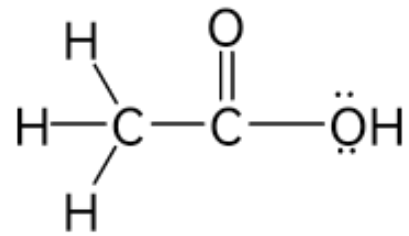
0.23



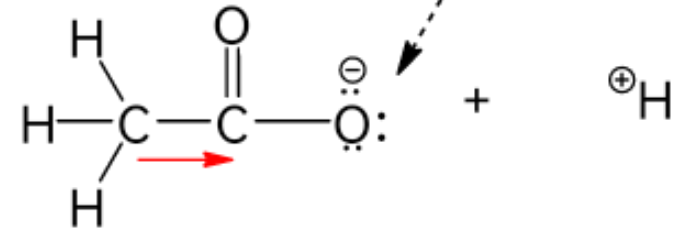
Fluorine is high electronegative atom so it is EWG



pK_a = 4.78



Weaker base



Stronger base

Higher Electron density

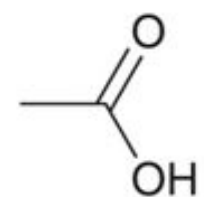


Acidity of Substituted Carboxylic acid

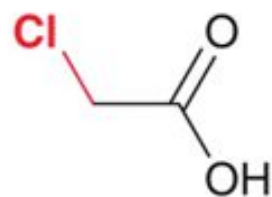
* The strength of the EWG



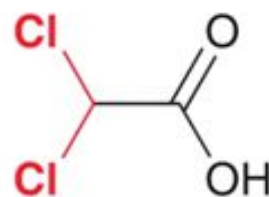
* Number of EWG



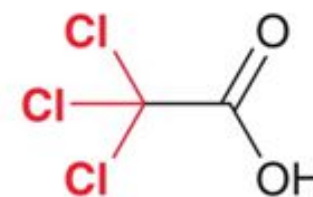
$\text{p}K_a = 4.8$



$\text{p}K_a = 2.9$

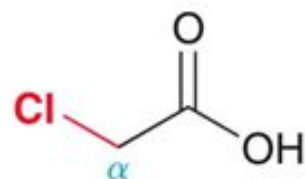


$\text{p}K_a = 1.3$

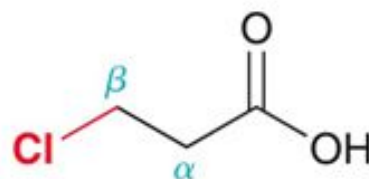


$\text{p}K_a = 0.9$

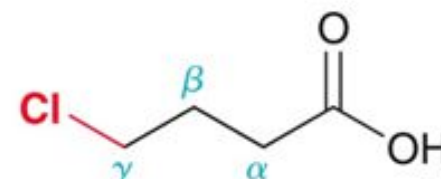
* Position of EWG



$\text{p}K_a = 2.9$



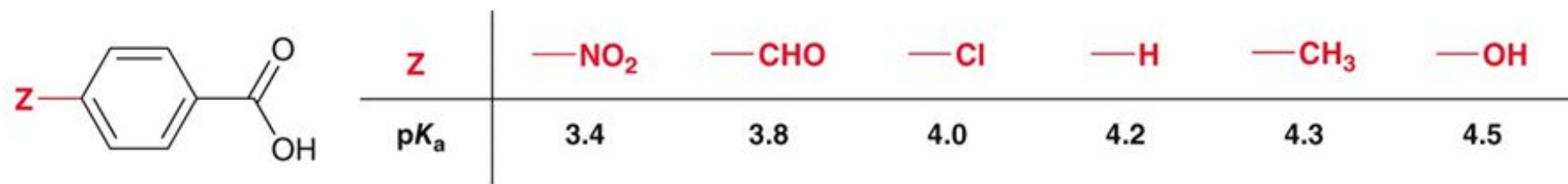
$\text{p}K_a = 4.1$



$\text{p}K_a = 4.5$

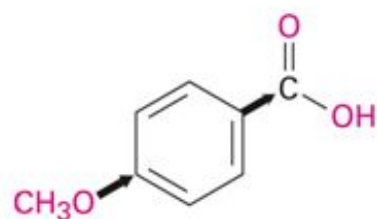


- Substituted benzoic acids

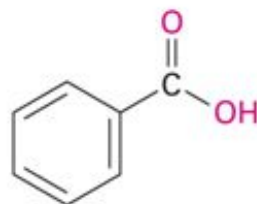


→ If Z = electron-donating group, acid is weaker

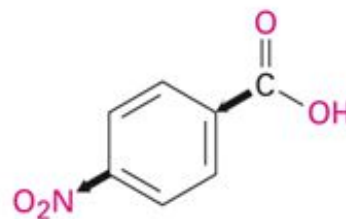
→ If Z = electron-withdrawing group, acid is stronger



p-Methoxybenzoic acid
(pK_a = 4.46)



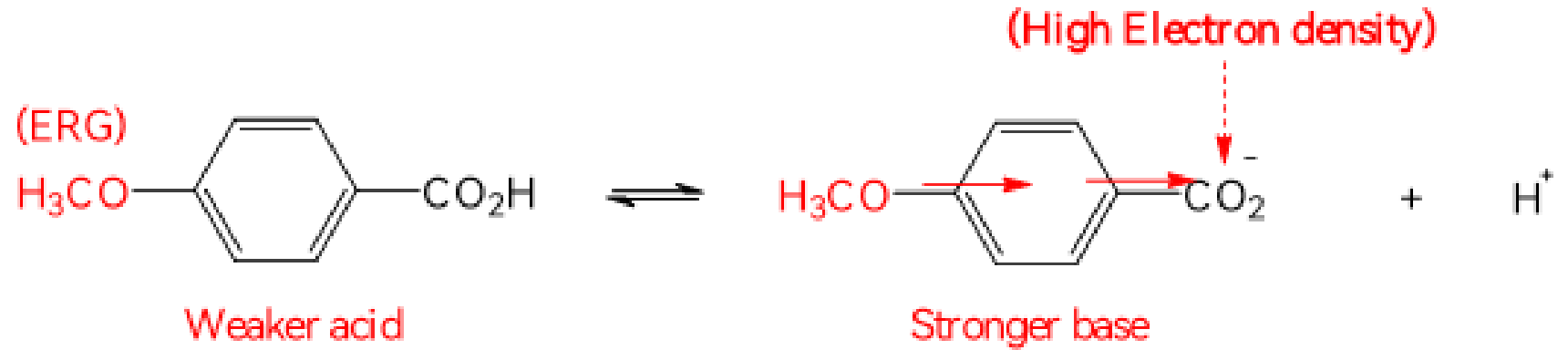
Benzoic acid
(pK_a = 4.19)



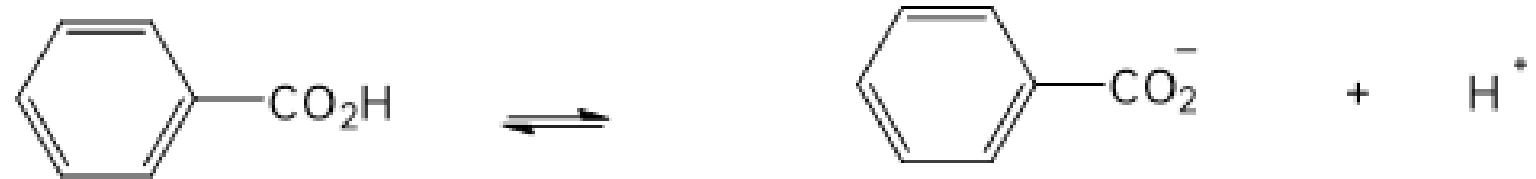
p-Nitrobenzoic acid
(pK_a = 3.41)



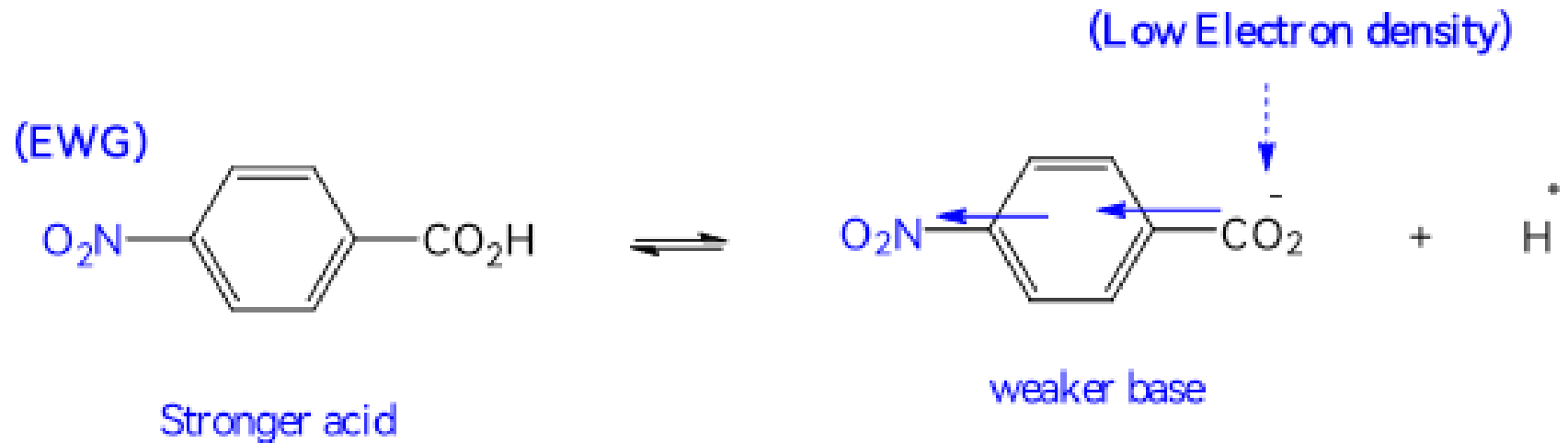
pKa = 4.46



pKa = 4.19

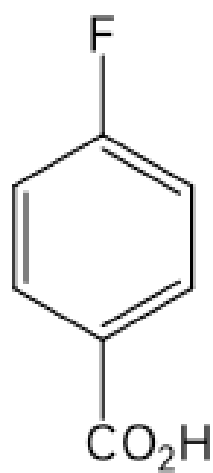


pKa = 3.41

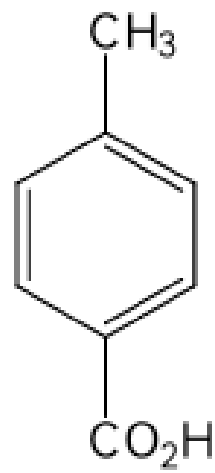


Acidity of different substituted Aromatic carboxylic acids

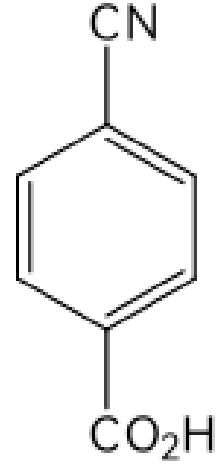
Rank the following compounds according to their acidities



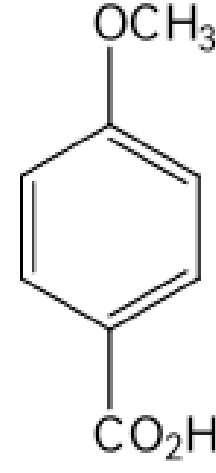
I



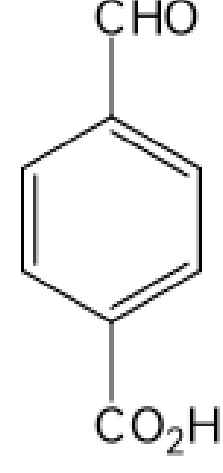
II



III



IV

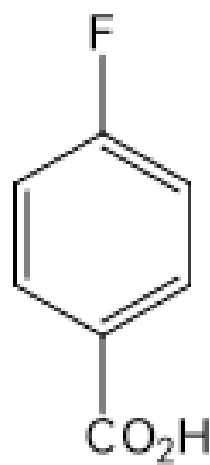


V

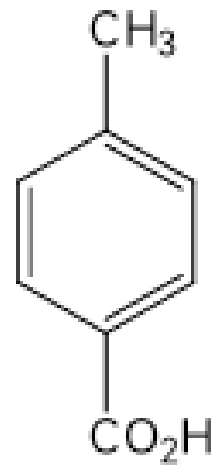


Acidity of different substituted Aromatic carboxylic acid

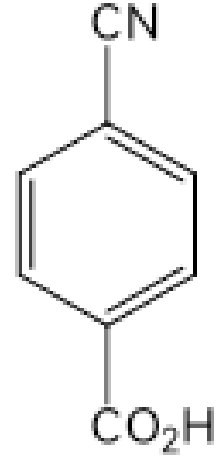
Rank the following compounds according to their acidities



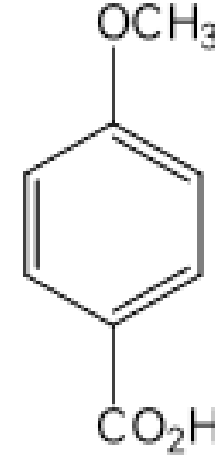
I
De



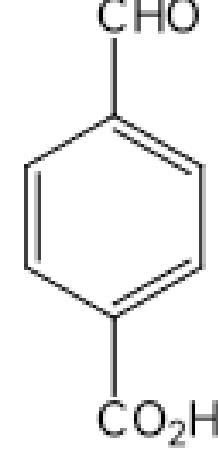
II
Ac



III
De



IV
Ac



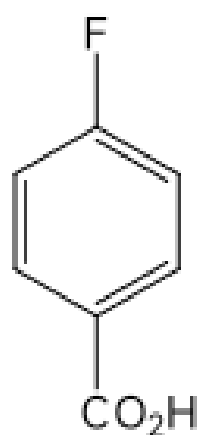
V
De

Classify each group substituted on benzene wither is it
A ctivation or D eactivation

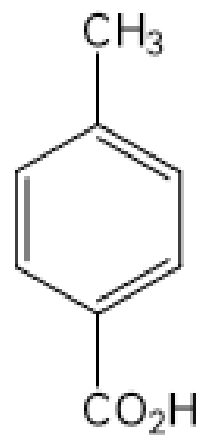


Acidity of different substituted Aromatic carboxylic acid

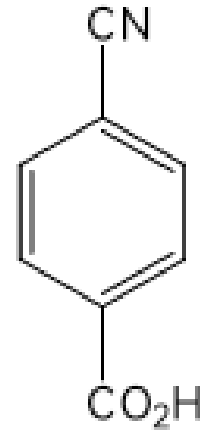
Rank the following compounds according to their acidities



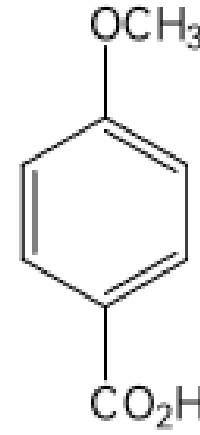
I
De



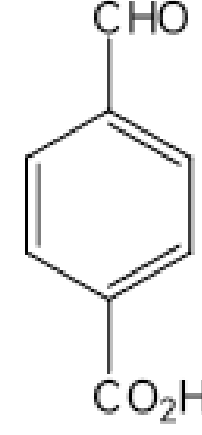
II
Ac



III
De



IV
Ac



V
De

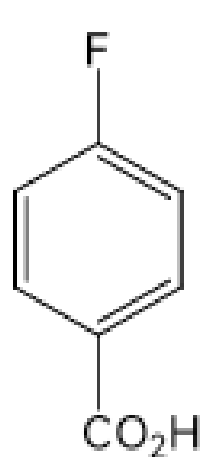
Stronger deactivating group stronger acid

III

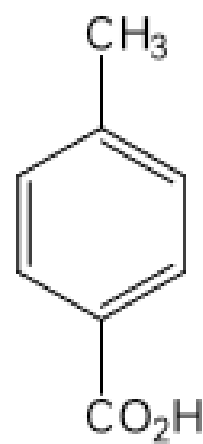


Acidity of different substituted Aromatic carboxylic acids

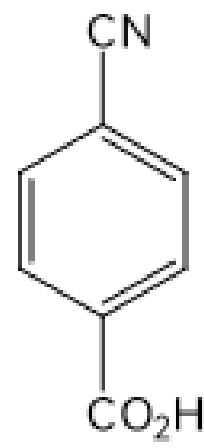
Rank the following compounds according to their acidities



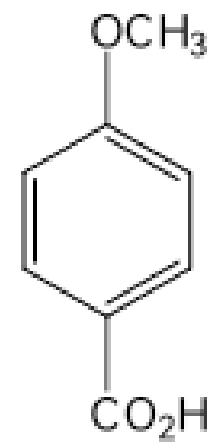
I
De



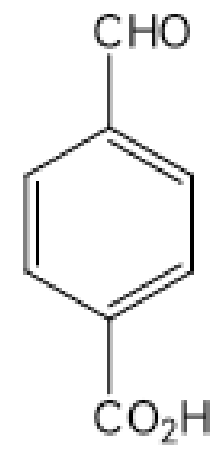
II
Ac



III
De



IV
Ac



V
De

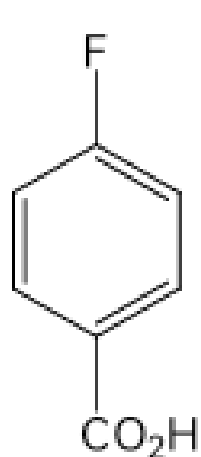
Stronger deactivating group stronger acid

III > V

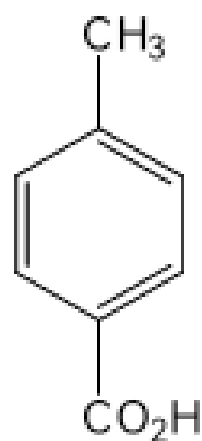


Acidity of different substituted Aromatic carboxylic acids

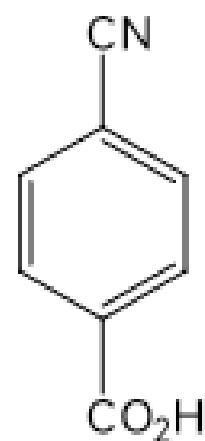
Rank the following compounds according to their acidities



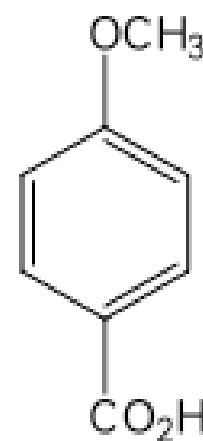
I
De



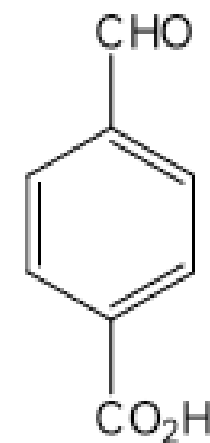
II
Ac



III
De



IV
Ac



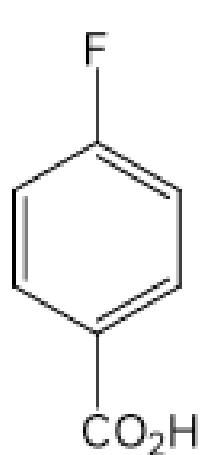
V
De

Stronger deactivating group stronger acid

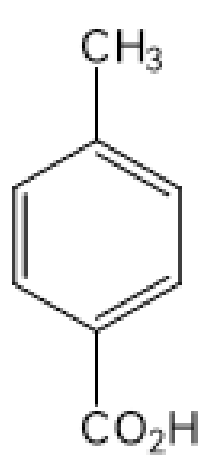


Acidity of different substituted Aromatic carboxylic acids

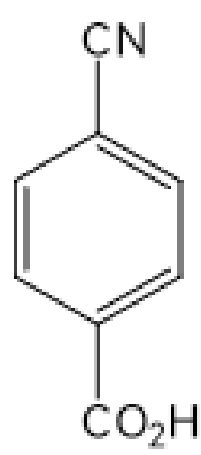
Rank the following compounds according to their acidities



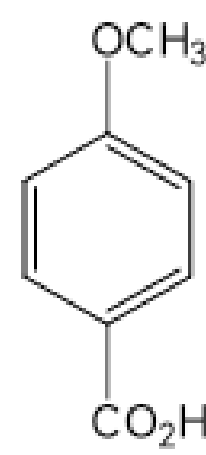
I
De



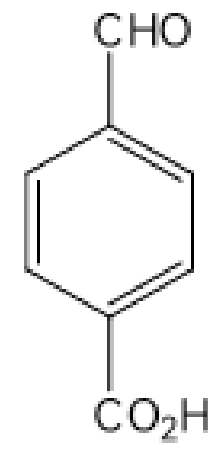
II
Ac



III
De



IV
Ac



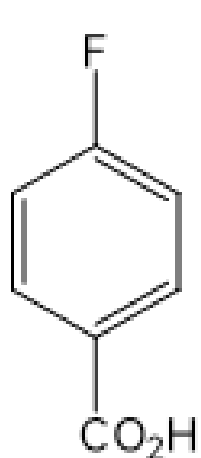
V
De

Weaker activating group stronger acid

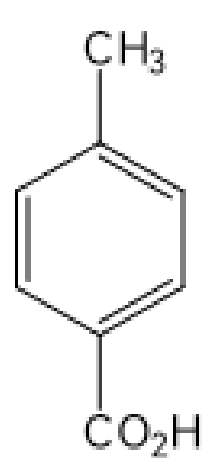


Acidity of different substituted Aromatic carboxylic acids

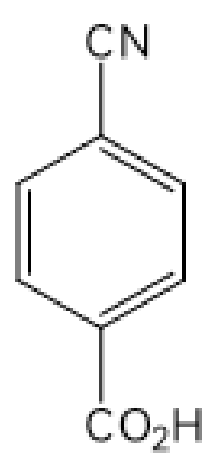
Rank the following compounds according to their acidities



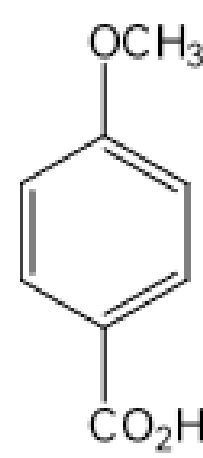
I
De



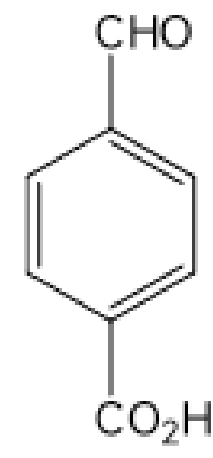
II
Ac



III
De



IV
Ac



V
De

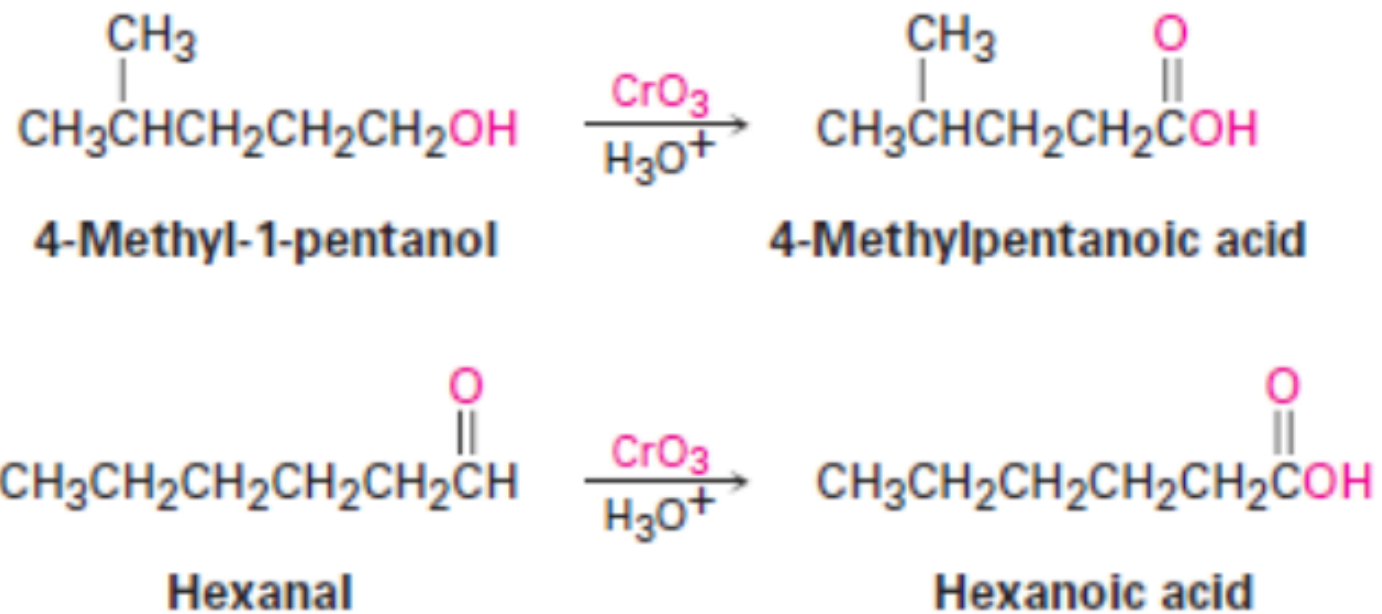
Weaker activating group stronger acid



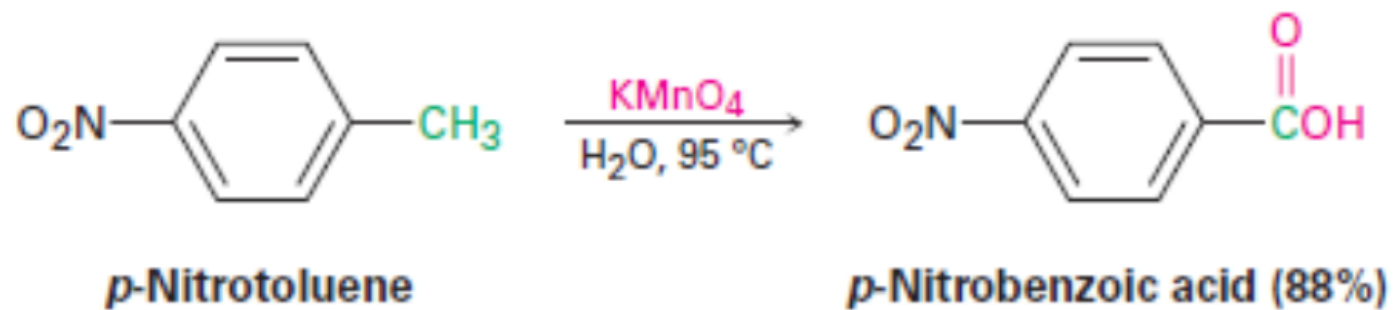
10.7 Preparation of Acids



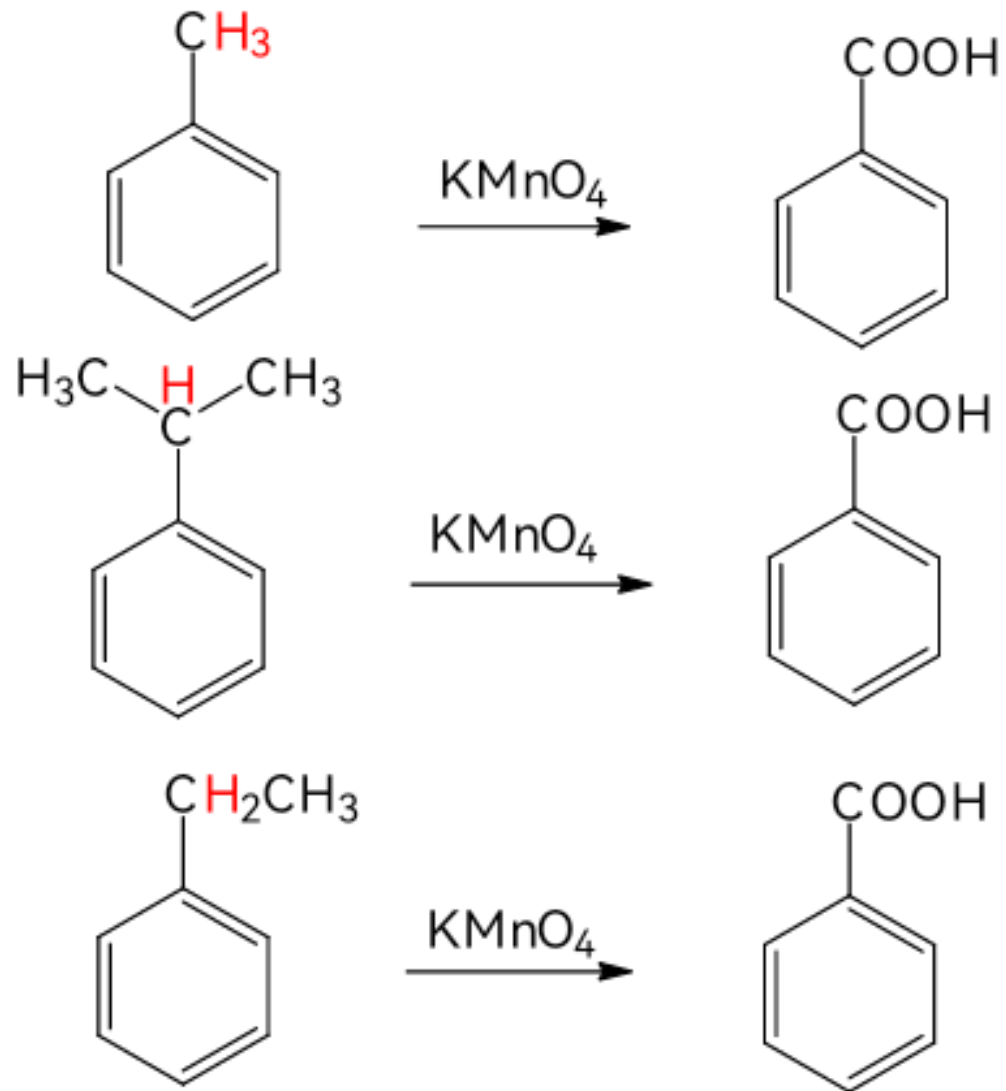
Oxidation of a primary alcohol or an aldehyde



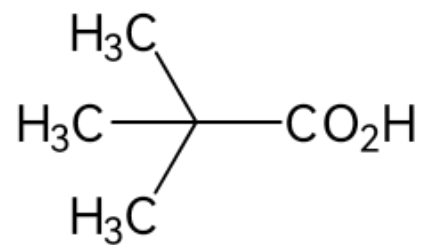
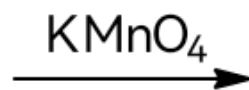
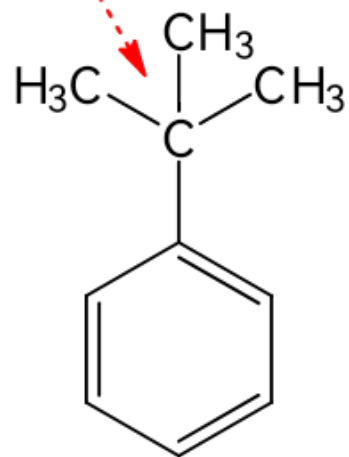
Oxidation of a substituted alkylbenzene with KMnO_4



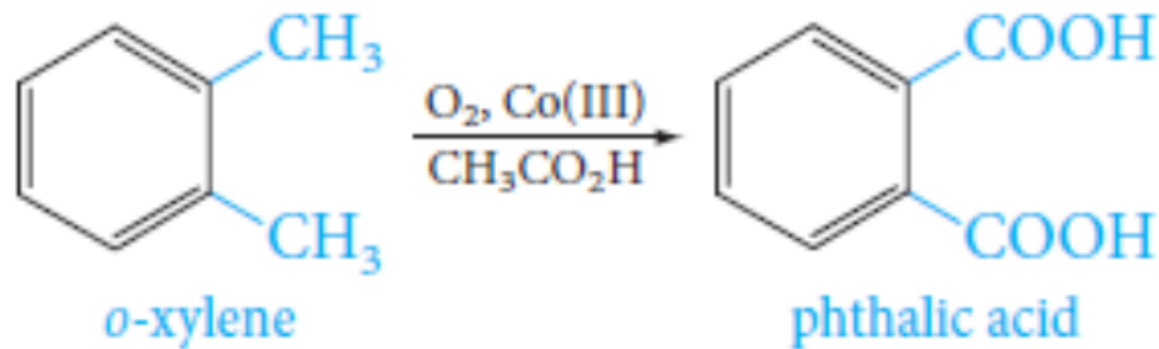
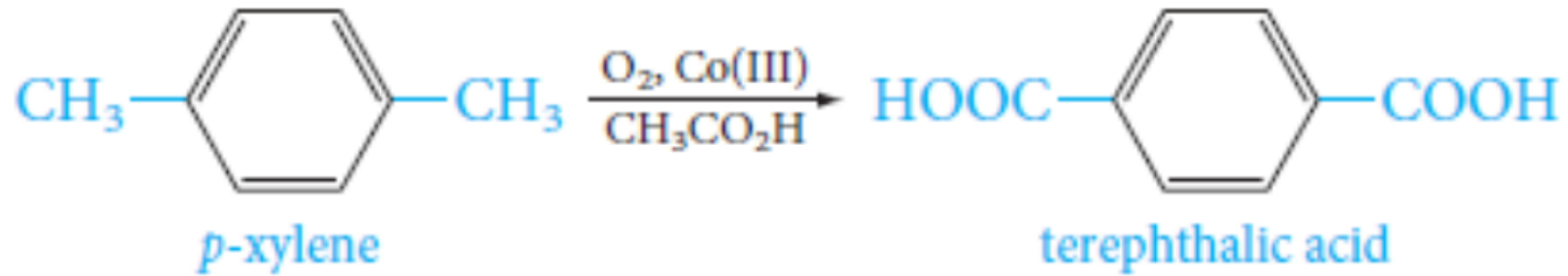
Oxidation of Alkyl-substituted benzene



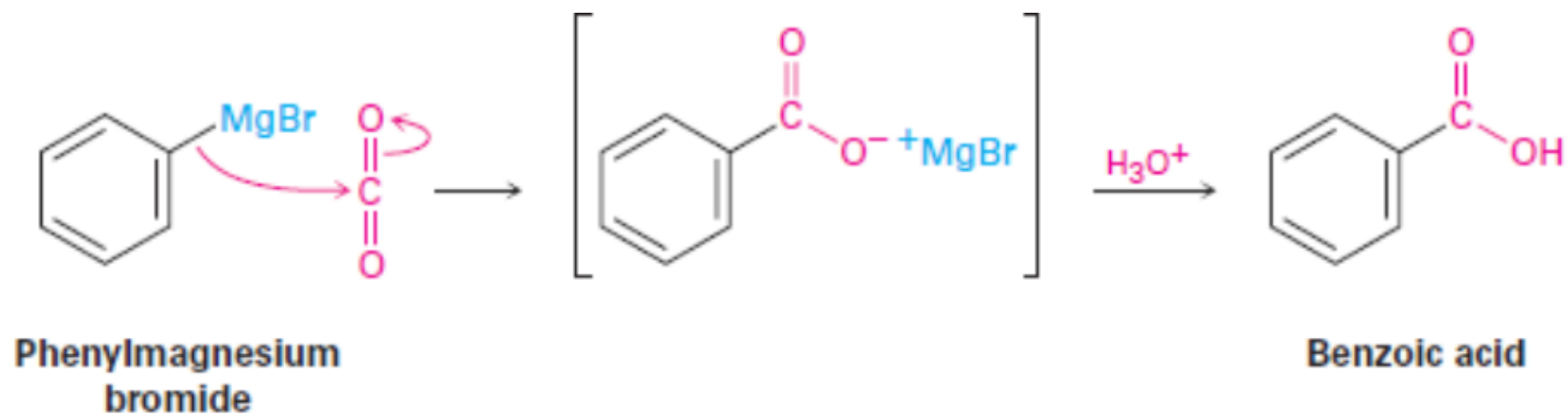
No Hydrogen atom



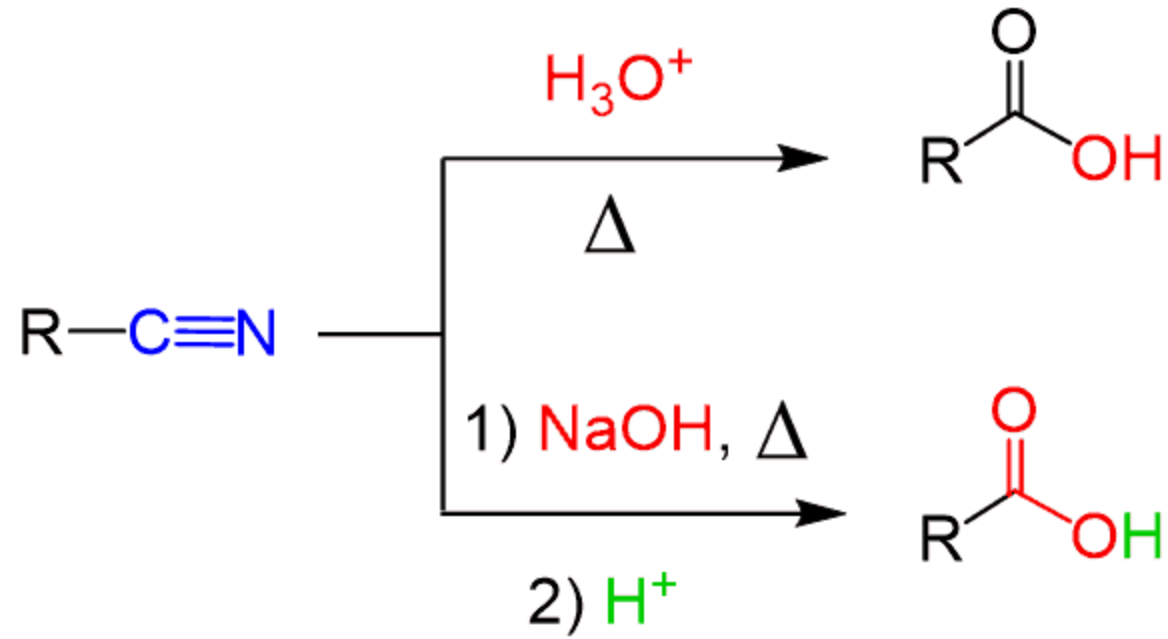
Preparation of commercially important terephthalic acid

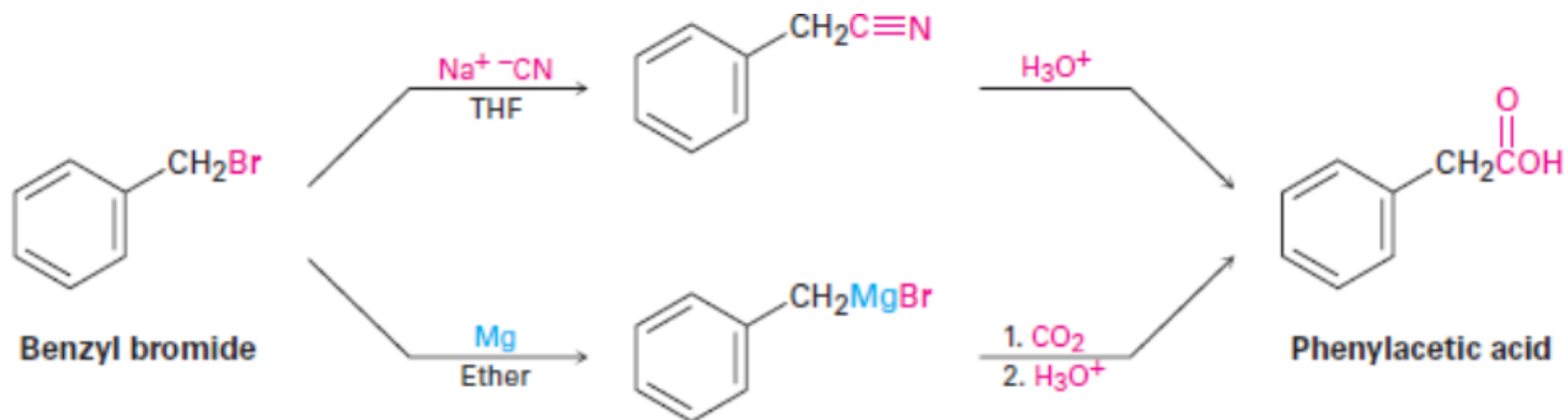
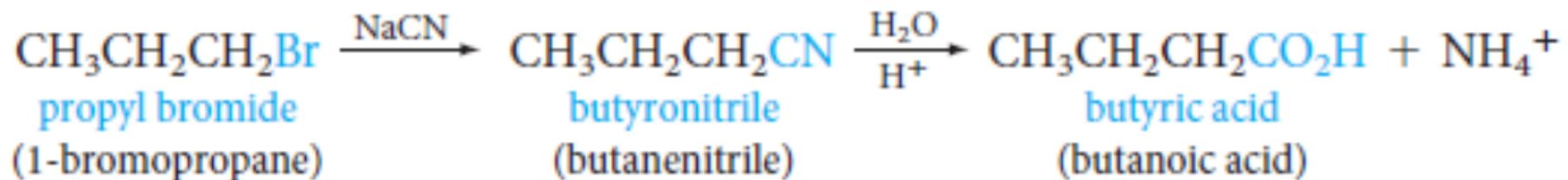


Reaction of Grignard Reagents with Carbon Dioxide



Hydrolysis of Nitriles





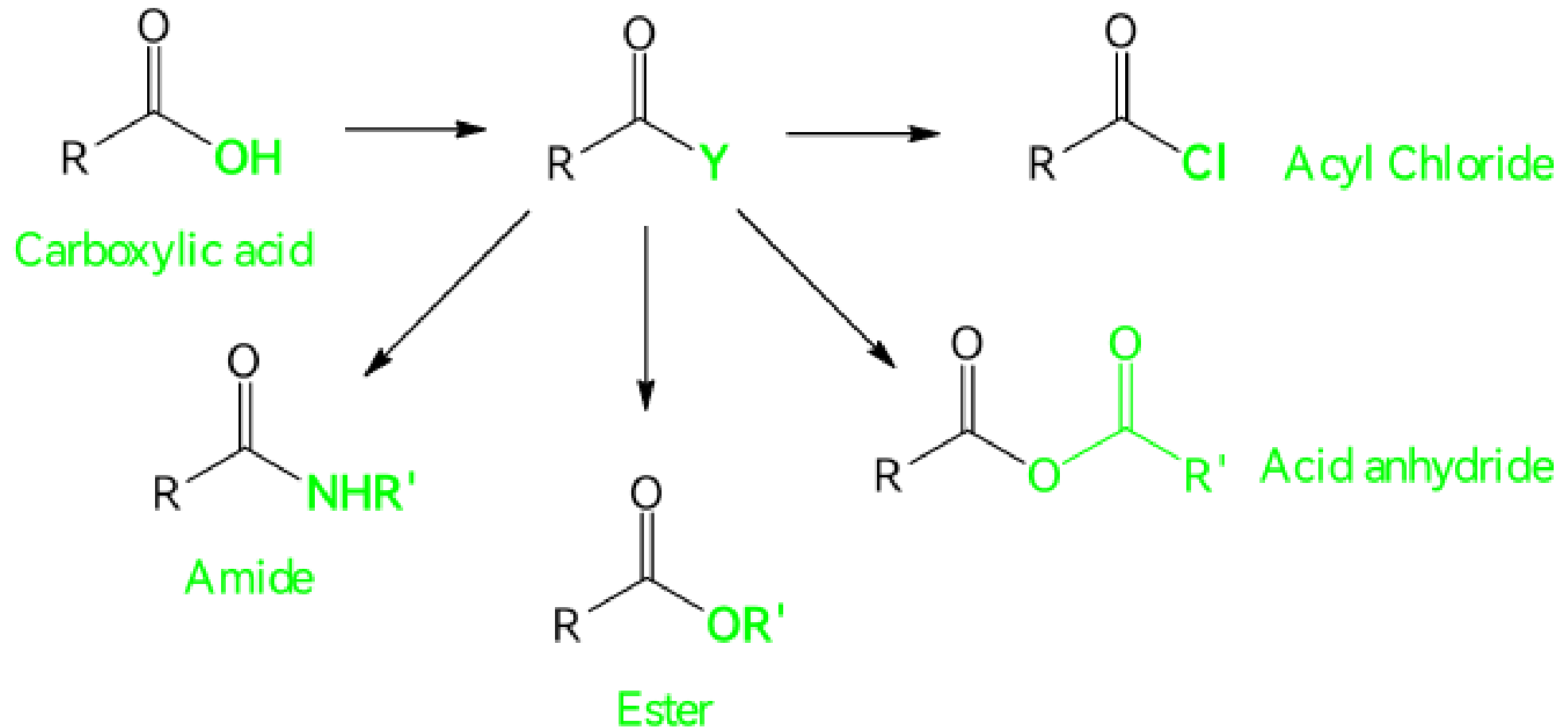
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10.8 Carboxylic Acid Derivatives

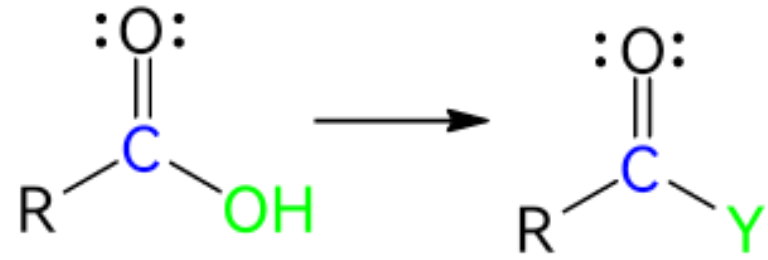
10.21 Carboxylic Acid Derivatives summery



Acid Derivatives



Carboxylic Acid derivatives



Y = Cl Acid chloride

OAc Acid anhydride

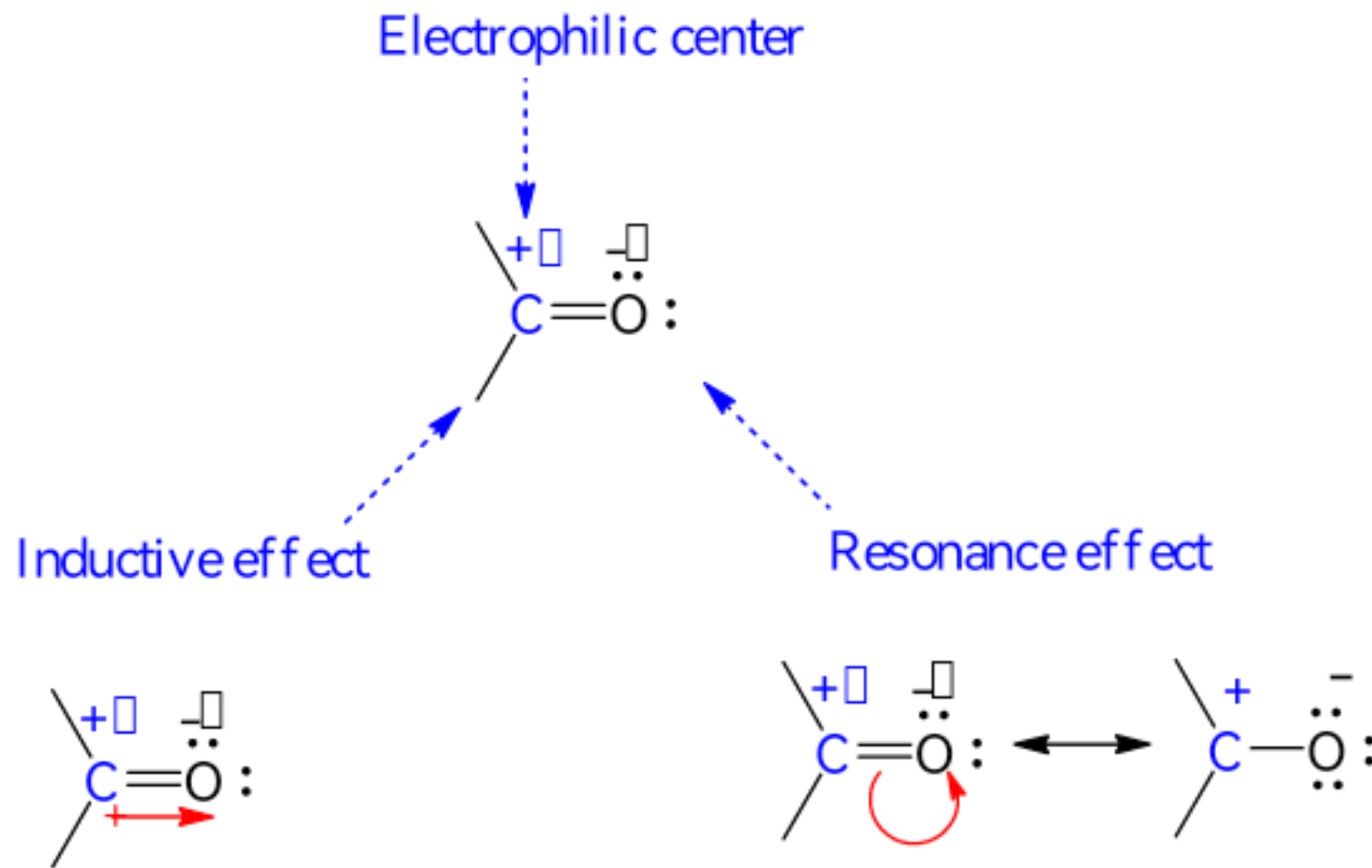
OCH₃ Ester

NH₂ Amide

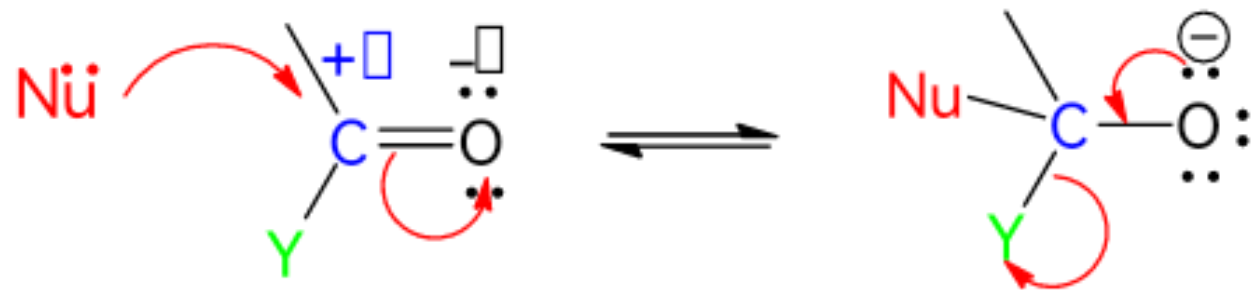


Preparation of Carboxylic Acid Derivatives from carboxylic acid





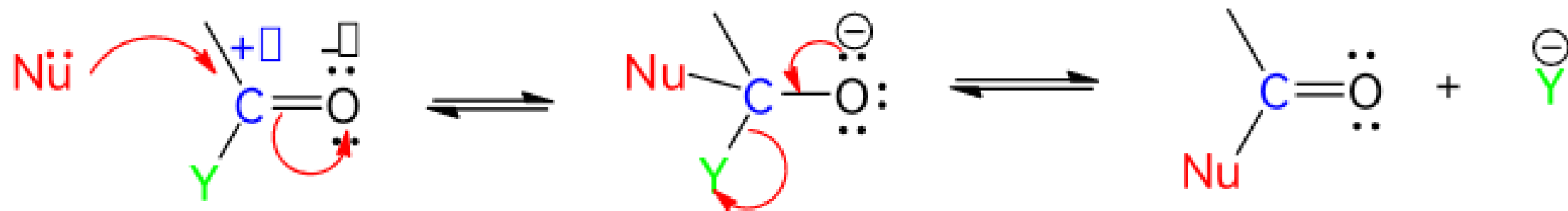
Nucleophilic Substitution in Acid derivatives



Y = Cl
OCH₃
OAc
NH₂

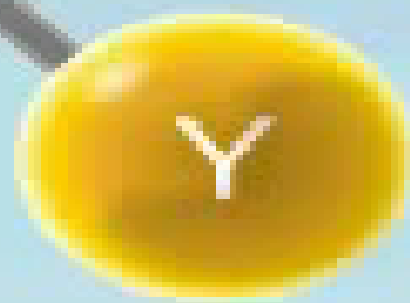


Nucleophilic Substitution in Acid derivatives



Y = Cl
OCH₃
OAc
NH₂



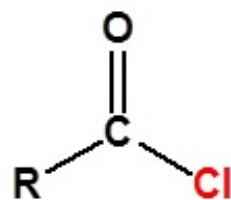


Reactivity

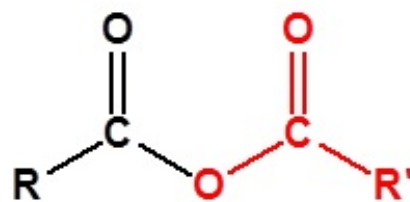


Functional Group

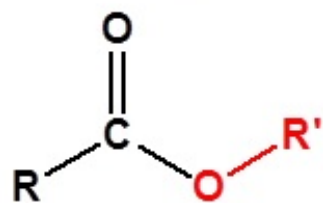
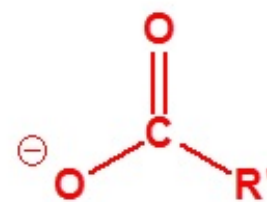
Leaving Group



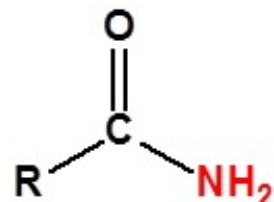
Acid Chloride



Acid anhydride



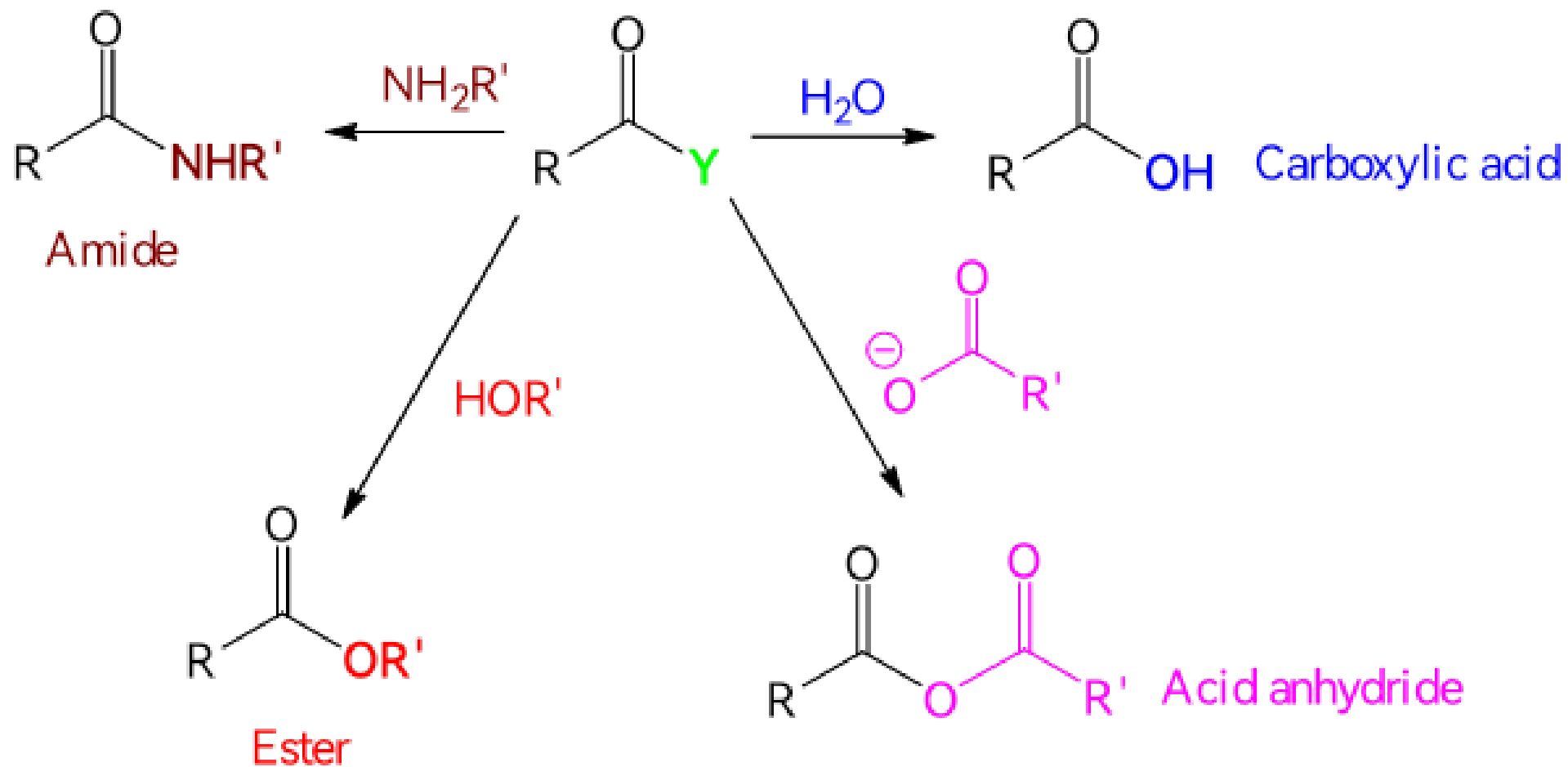
Ester



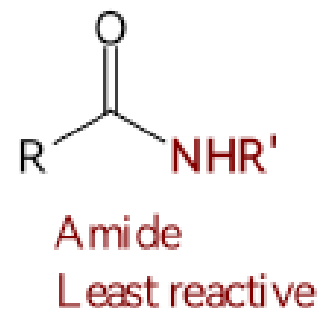
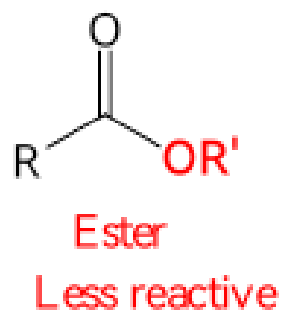
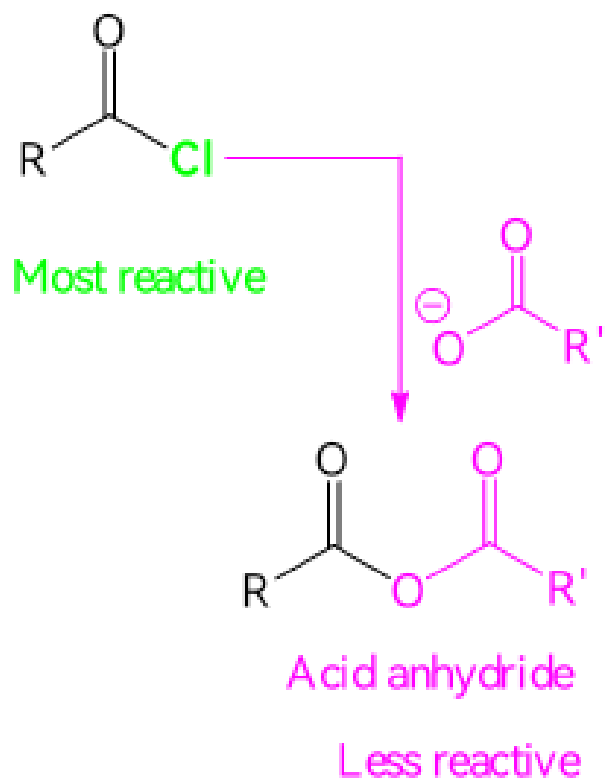
Amide



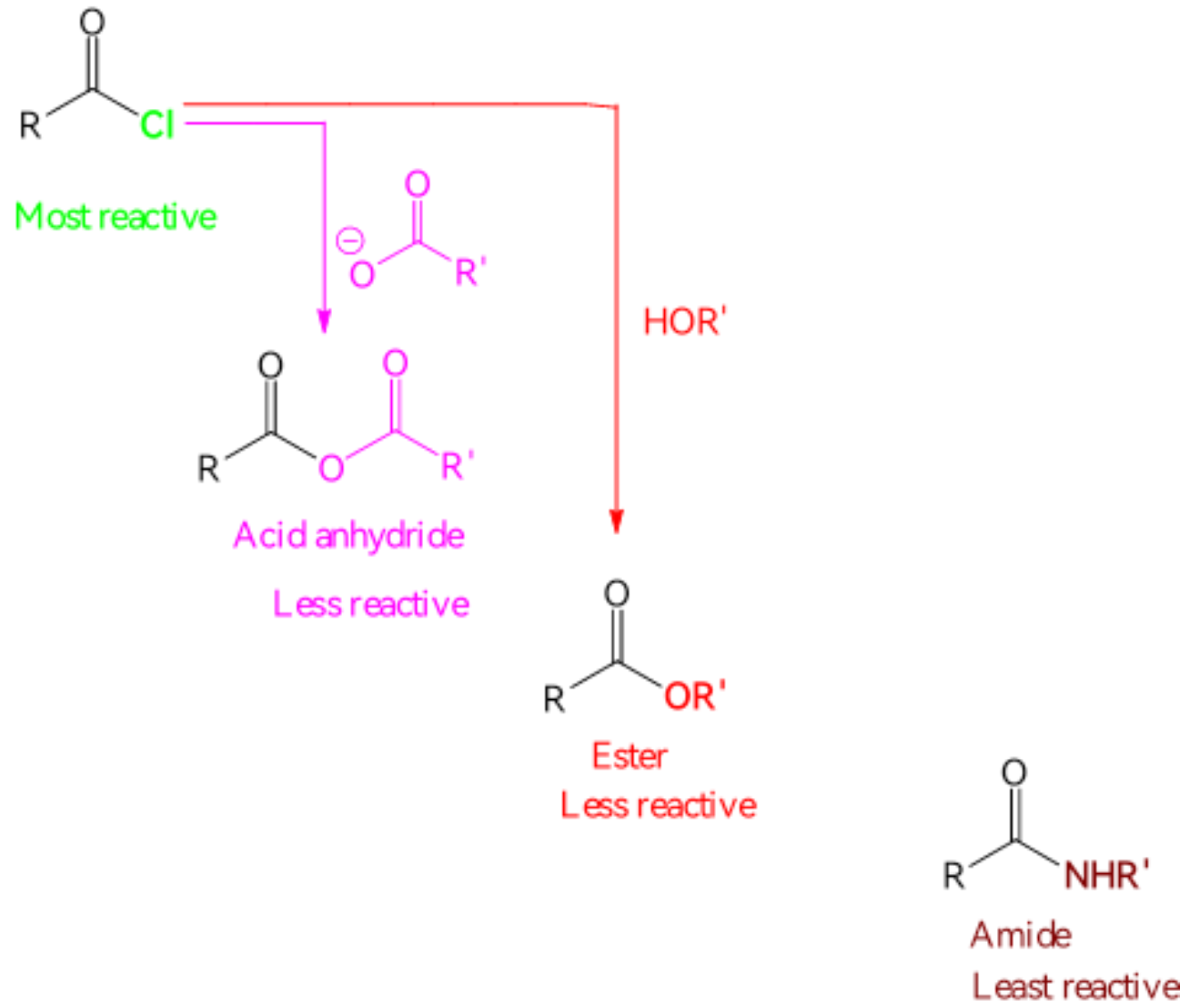
Acid Derivatives



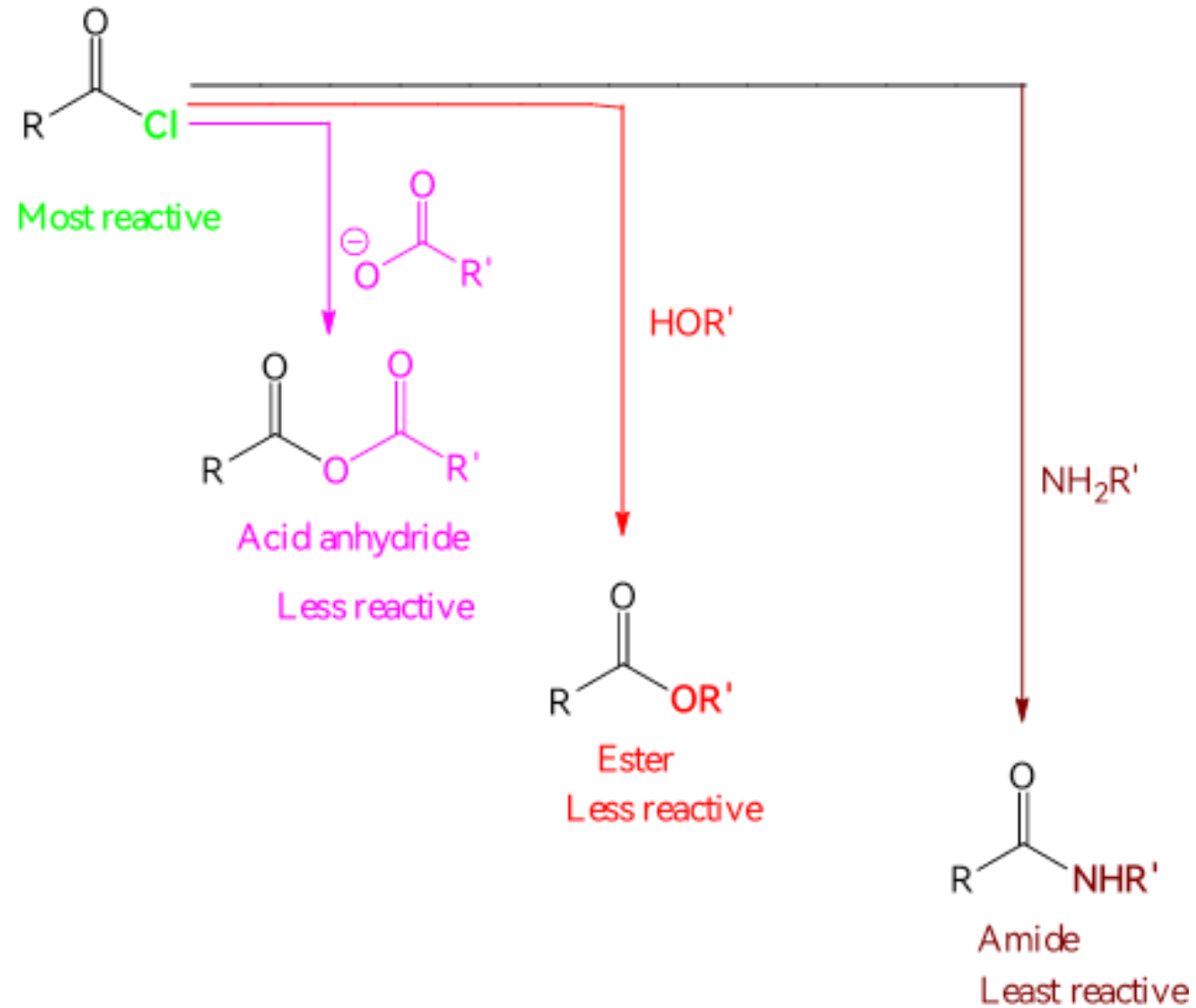
Preparation of Acid Derivatives from each other



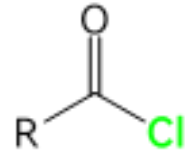
Preparation of Acid Derivatives from each other



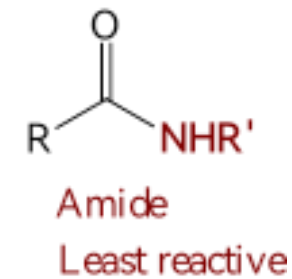
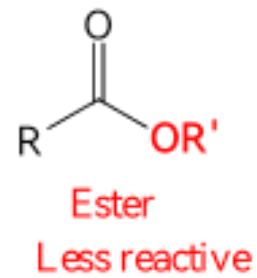
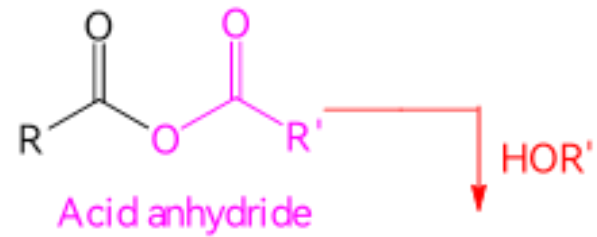
Preparation of Acid Derivatives from each other



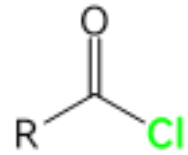
Preparation of Acid Derivatives from each other



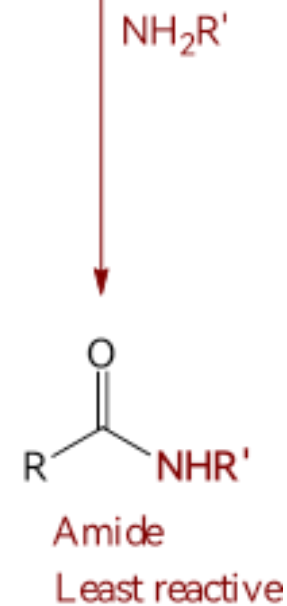
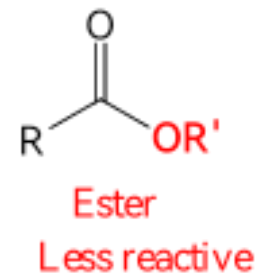
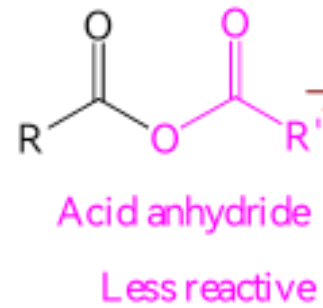
Most reactive



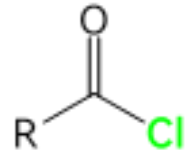
Preparation of Acid Derivatives from each other



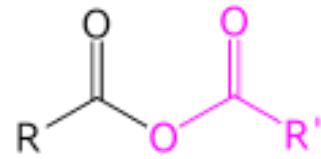
Most reactive



Preparation of Acid Derivatives from each other

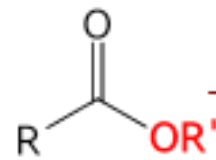


Most reactive

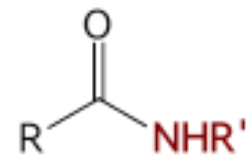


Acid anhydride

Less reactive



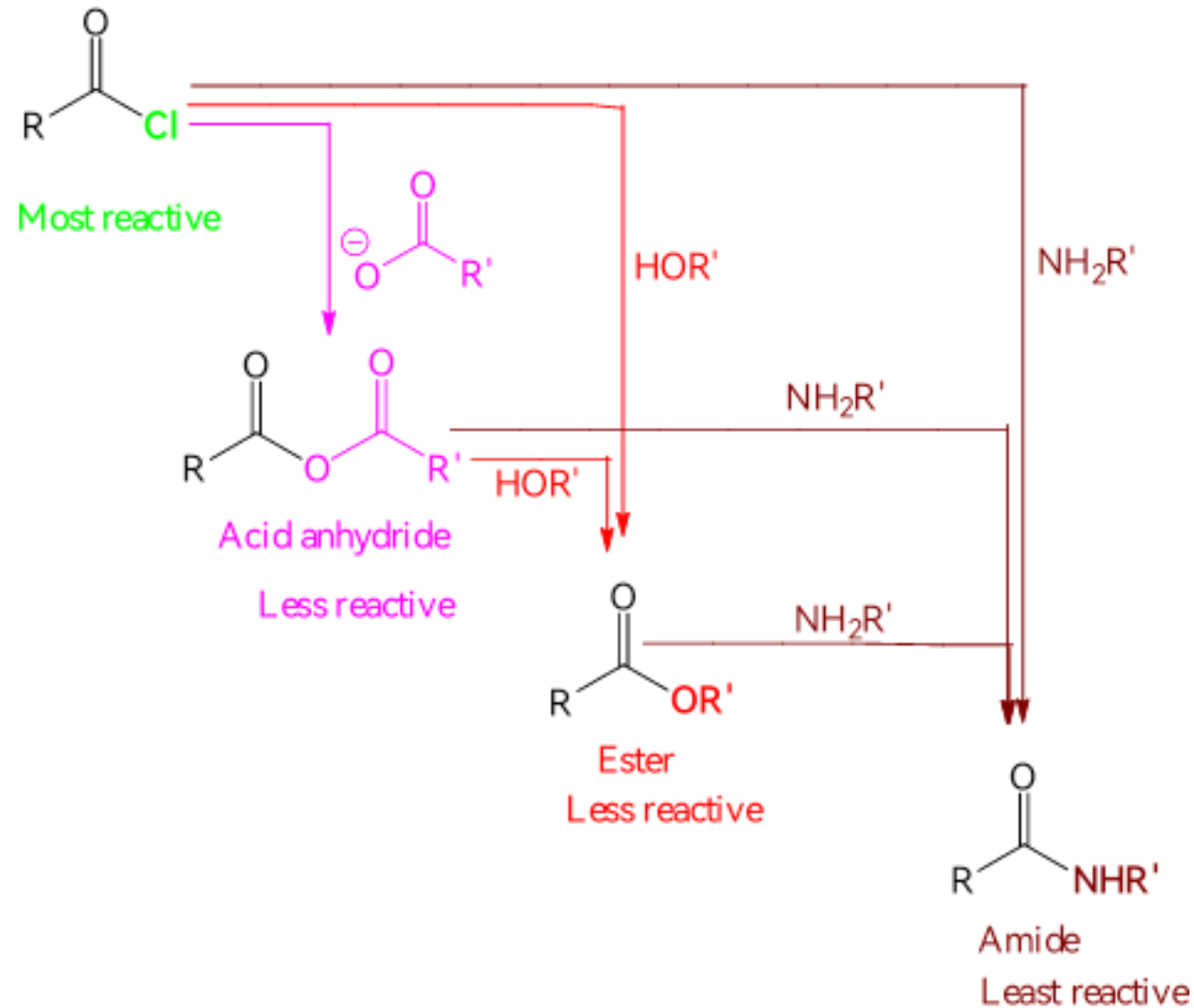
Ester
Less reactive



Amide
Least reactive



Preparation of Acid Derivatives from each other

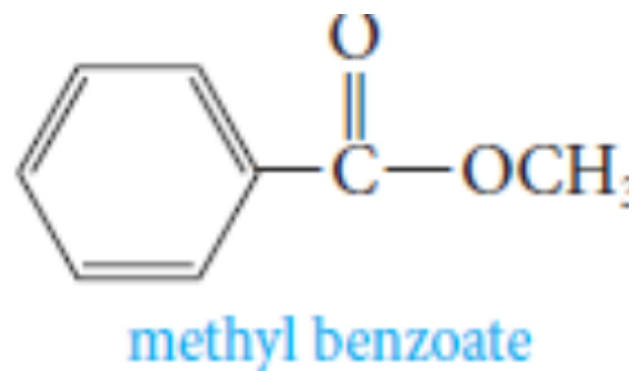
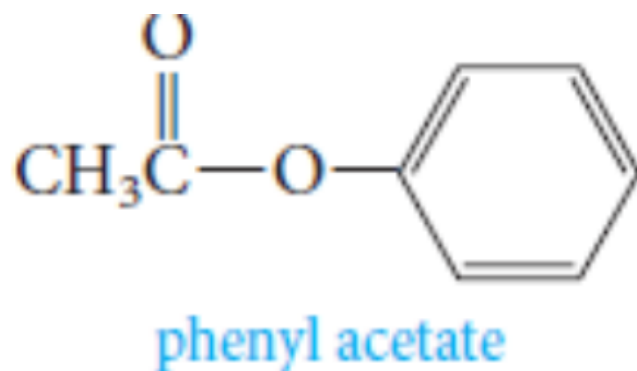
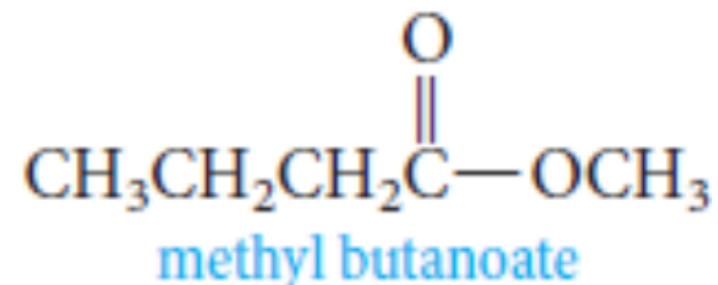
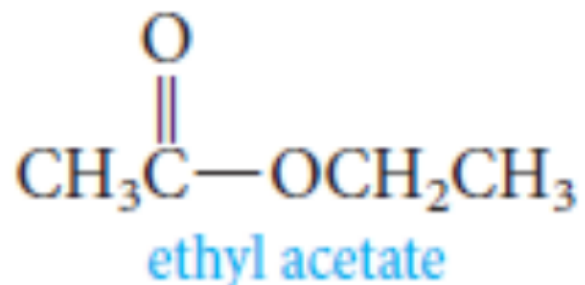
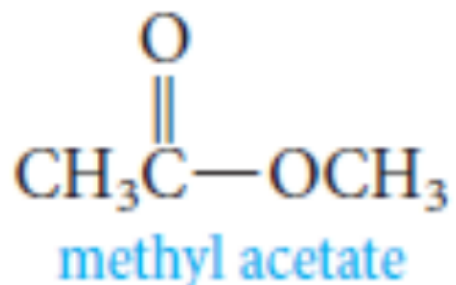


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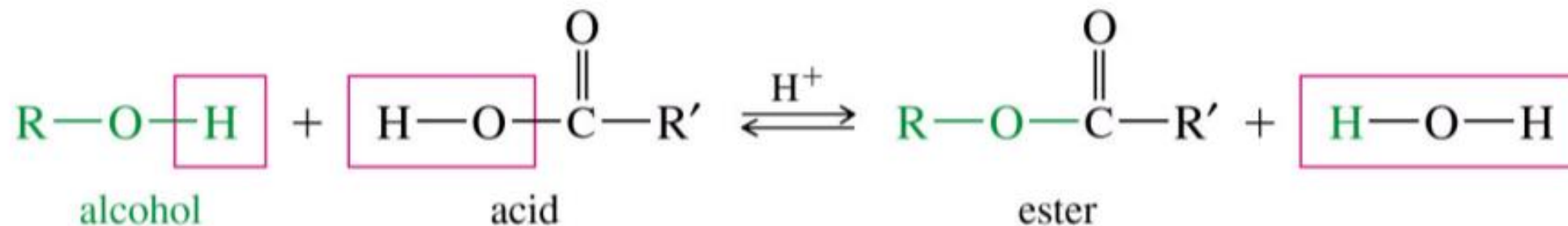
10.9-16 Esters



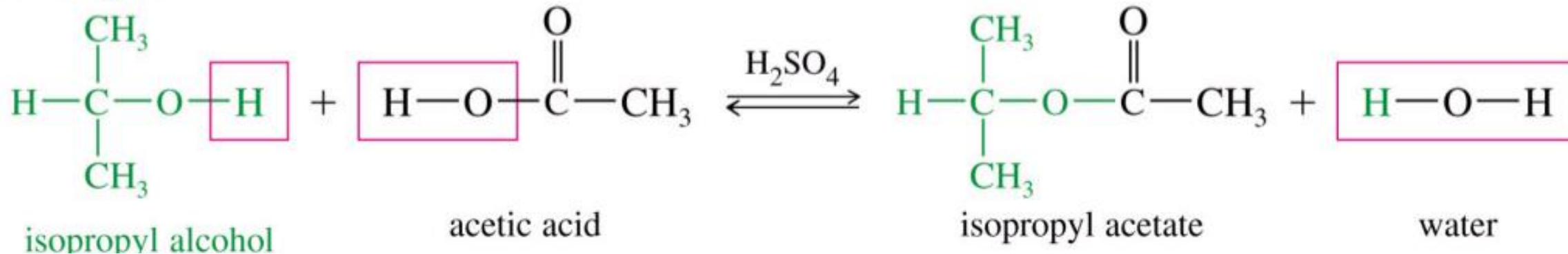
Esters



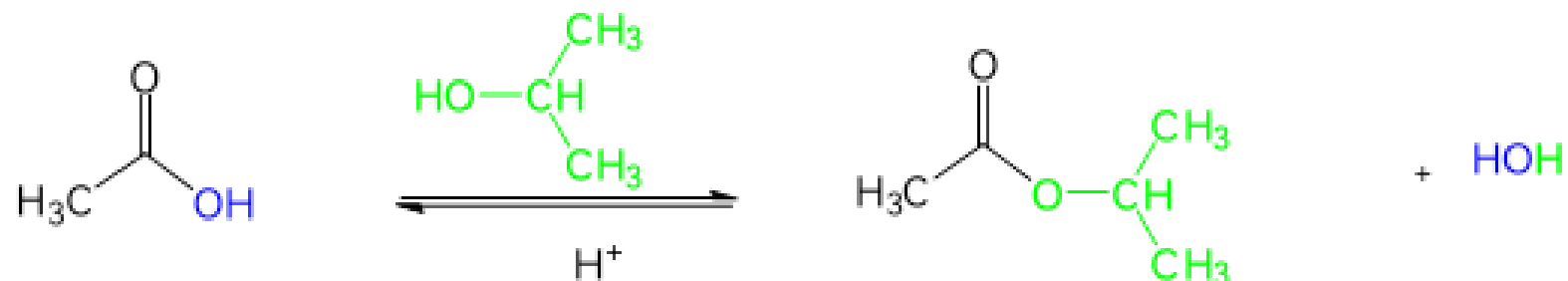
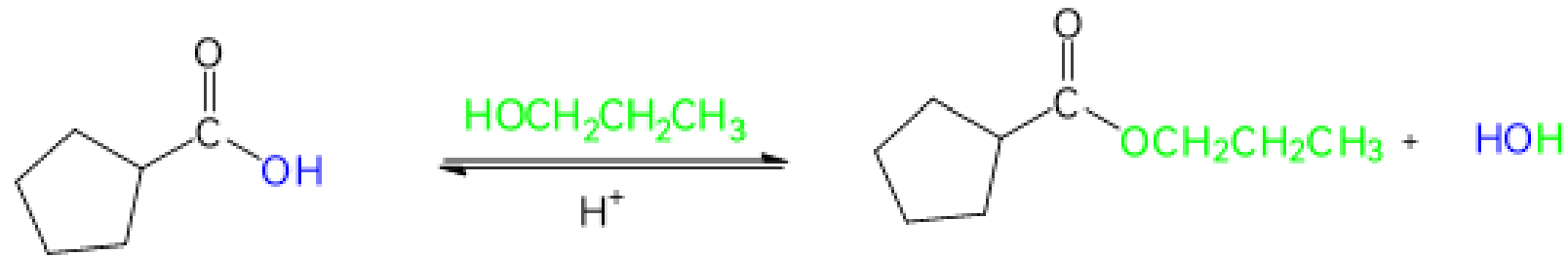
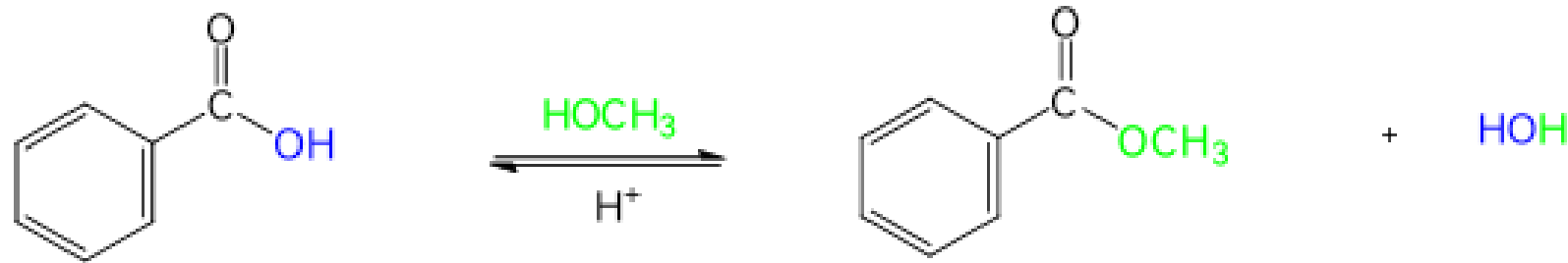
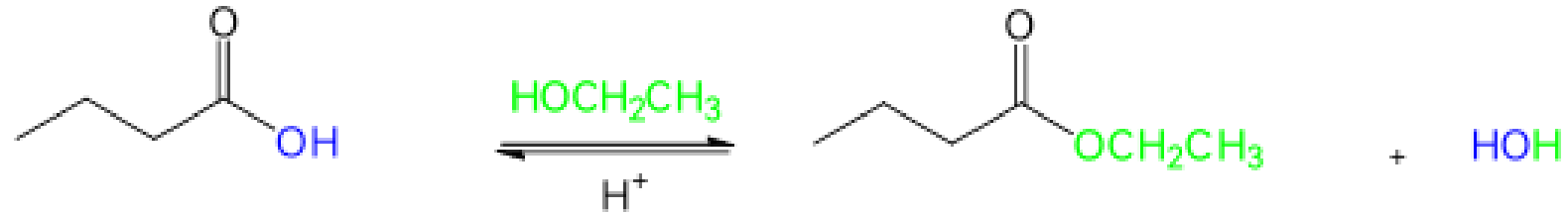
10.10 Preparation of Esters; Fischer Esterification



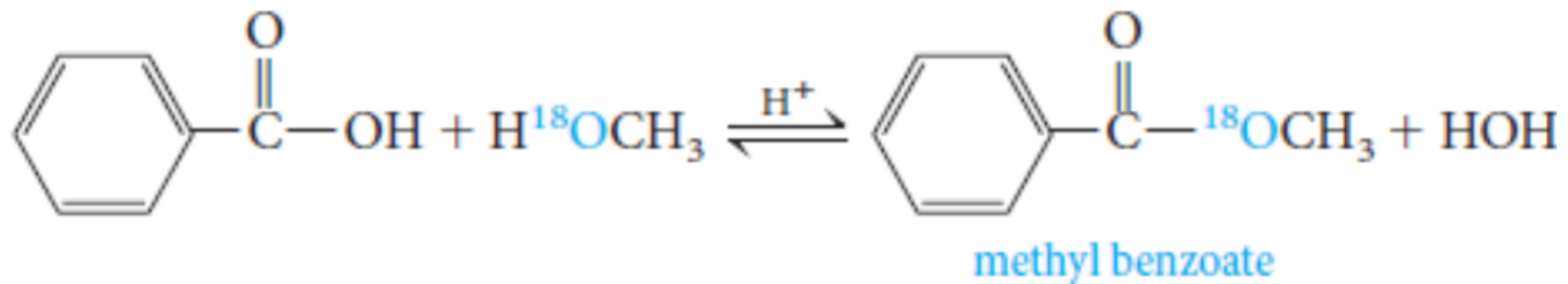
Example



Preparation of Esters; Fischer Esterification

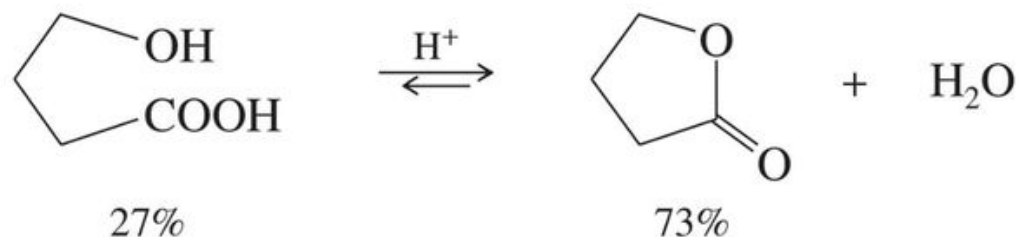


10.11 The Mechanism of Acid-Catalyzed Esterification



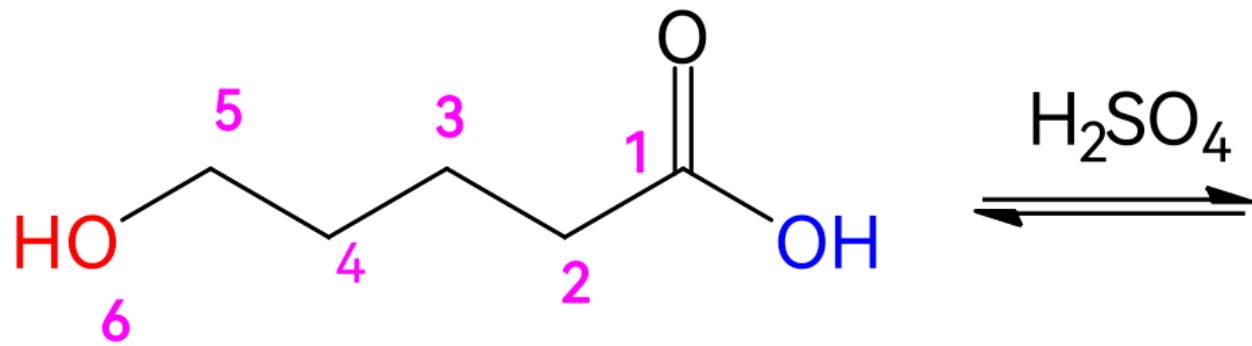
10.12 Lactones

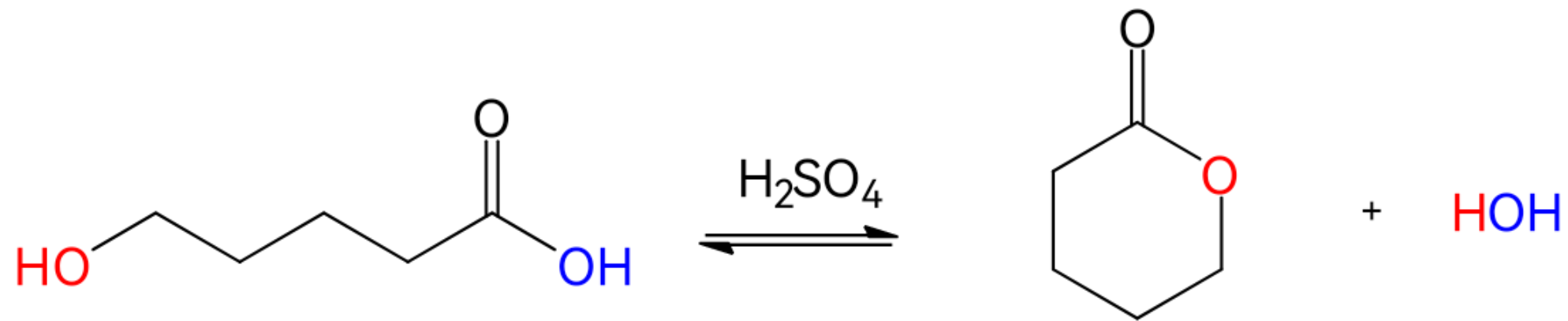
- Formation is favored for five- and six-membered rings.



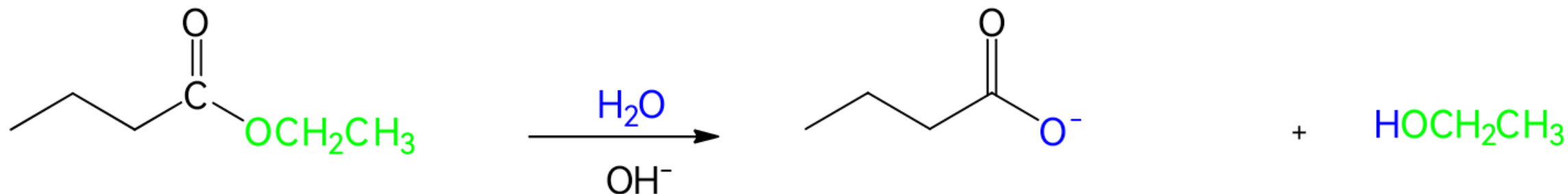
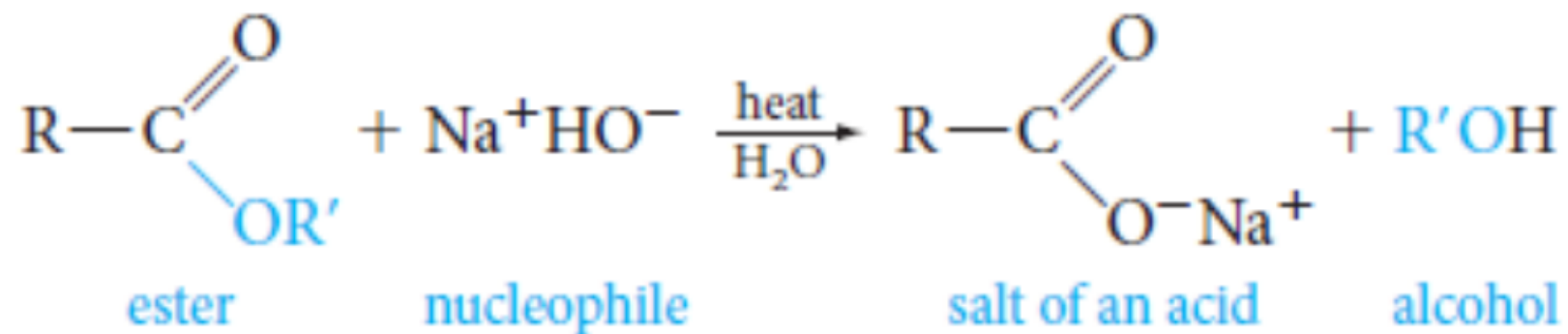
- For larger rings, remove water to shift equilibrium toward products.



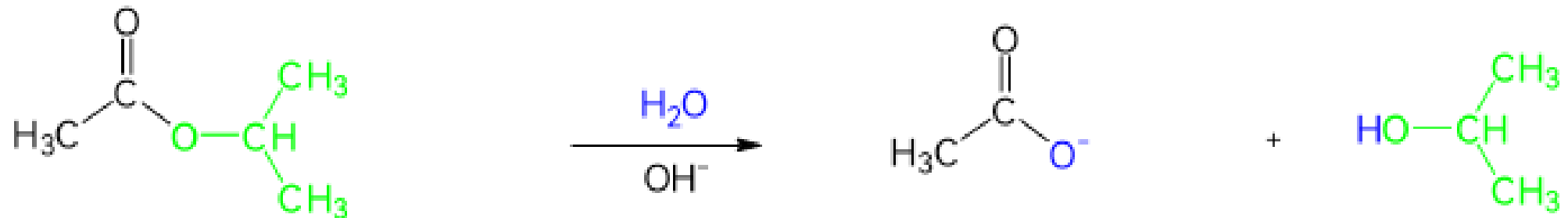
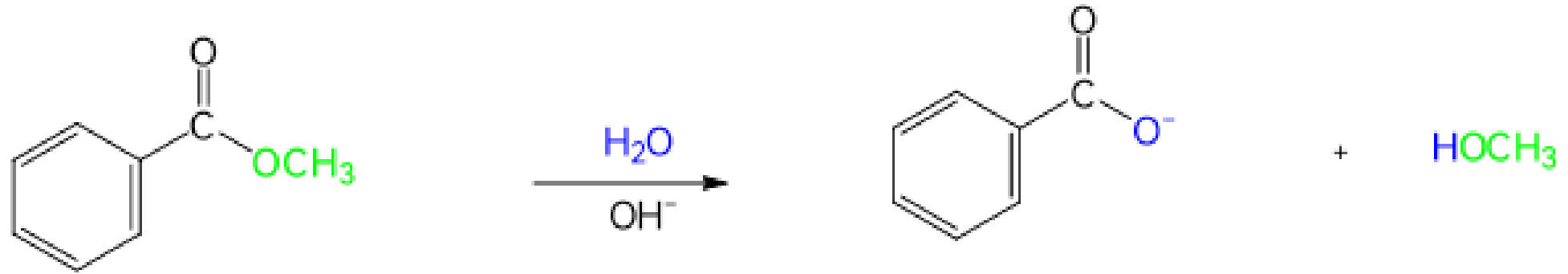




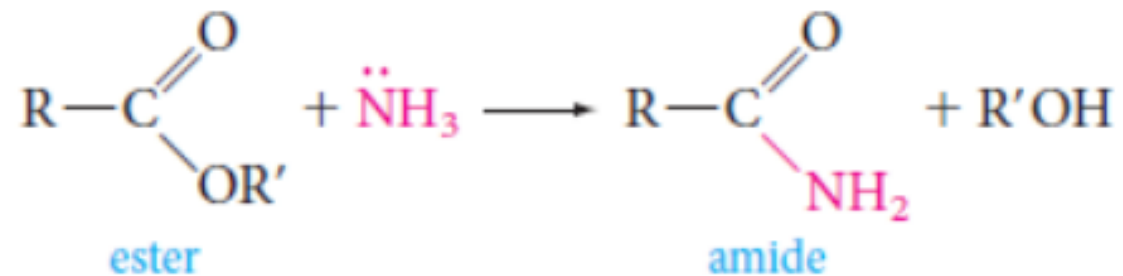
10.13 Saponification of Esters



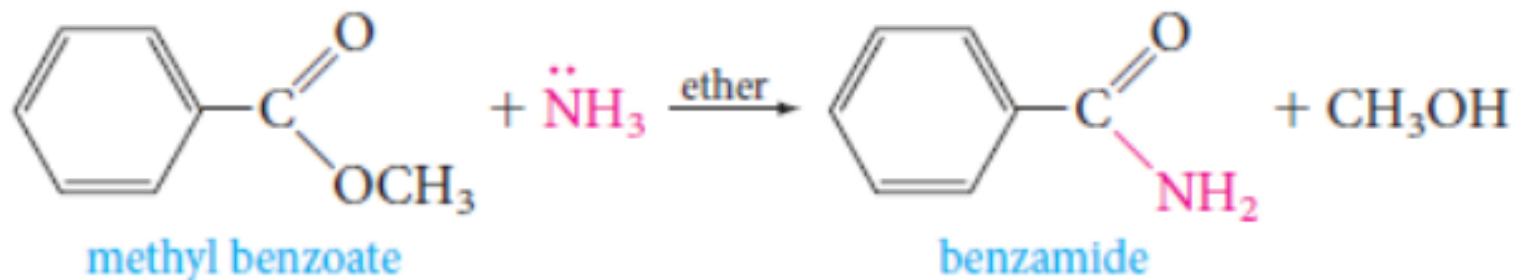
Saponification of Esters



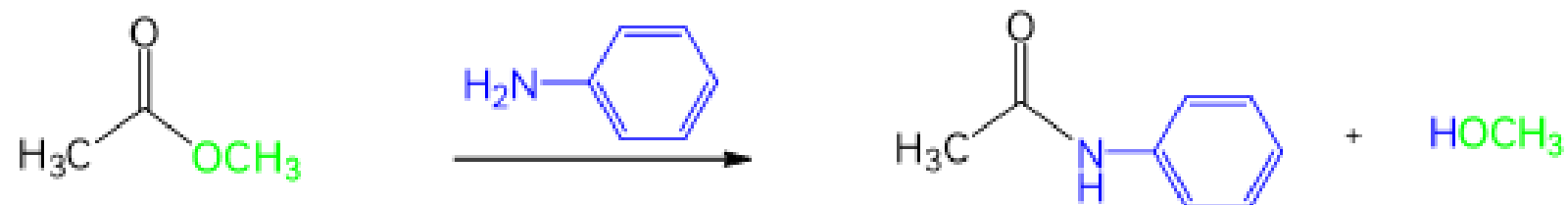
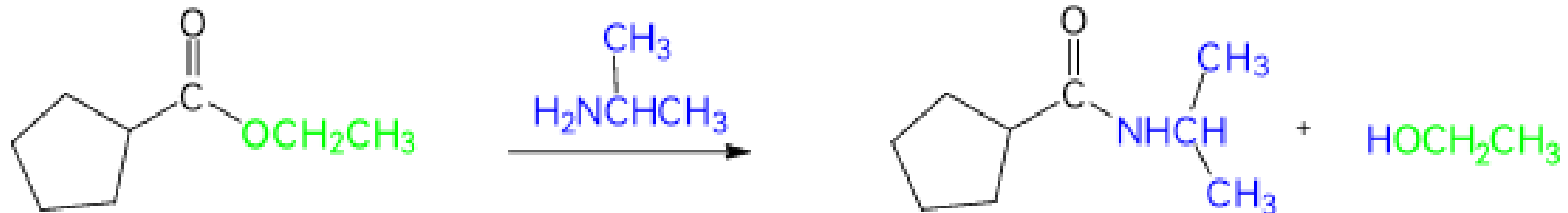
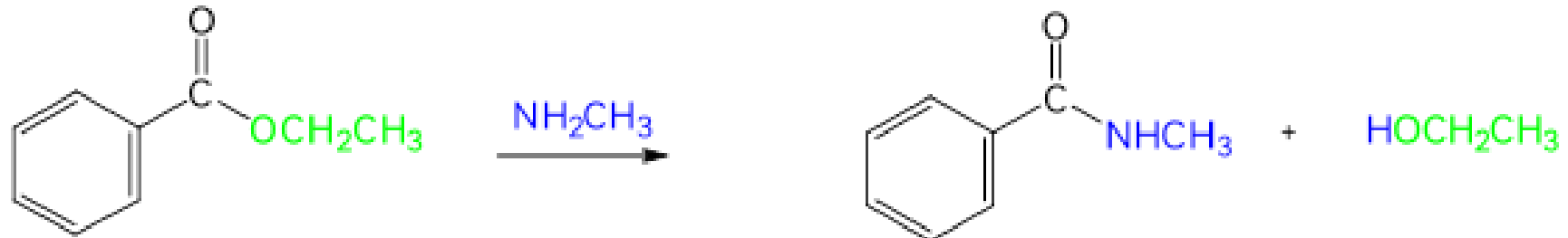
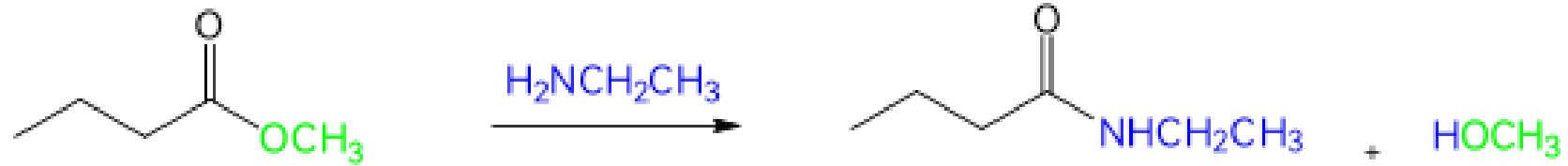
10.14 Ammonolysis of Esters



For example,

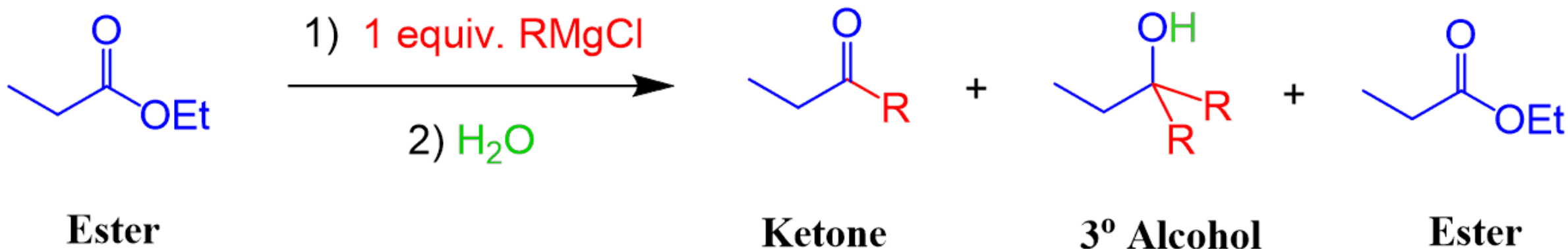


Ammonolysis of Esters

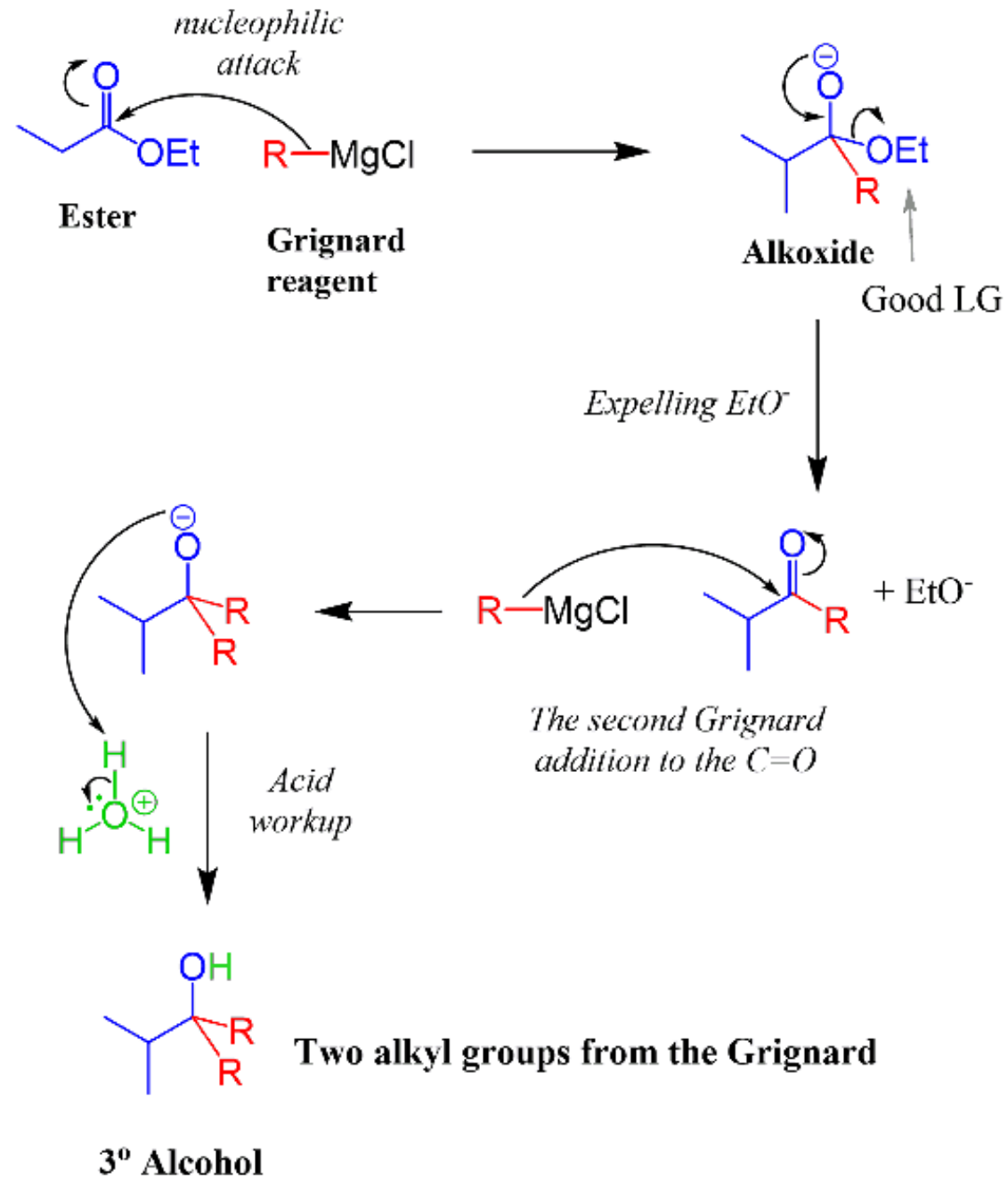


10.15 Reaction of Esters with Grignard Reagents

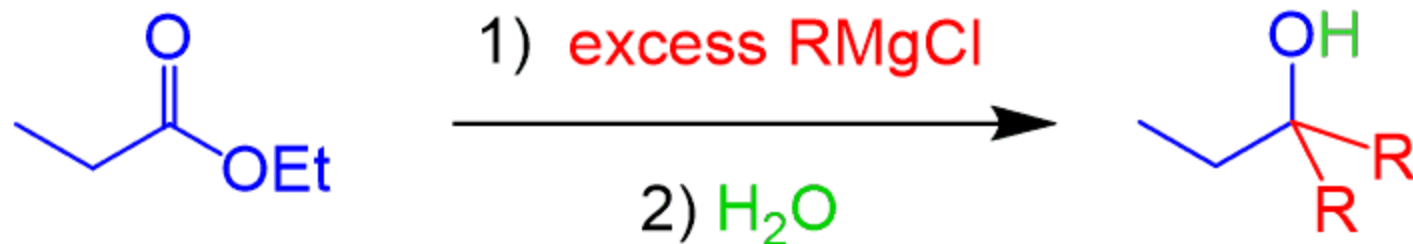
Esters will give a mixture if reacted with equivalent of Grignard reagent



The Mechanism of Grignard reaction with Esters



Reaction of Esters with Excess of Grignard Reagents



Ester

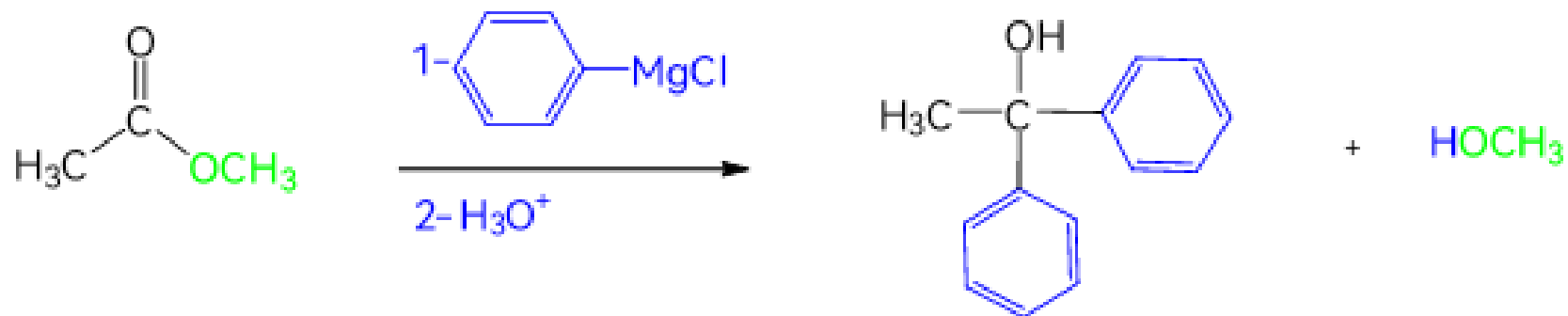
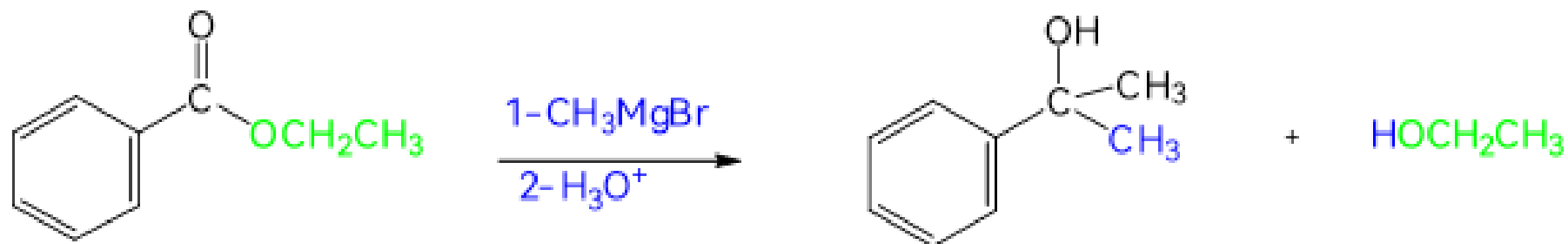
3° Alcohol

2 Alkyls from the Grignard reagent

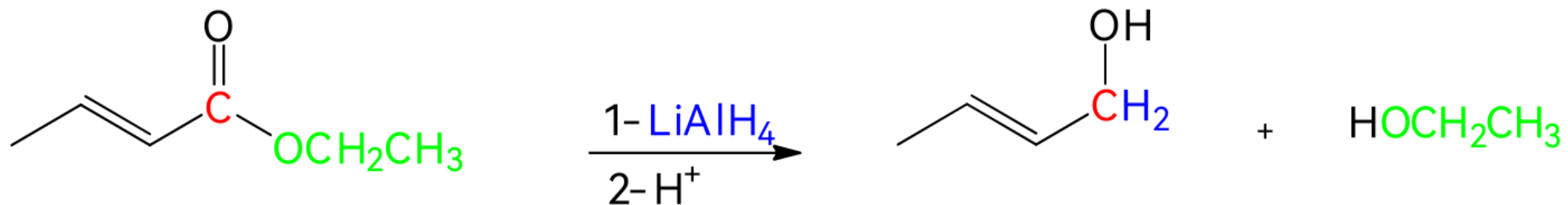
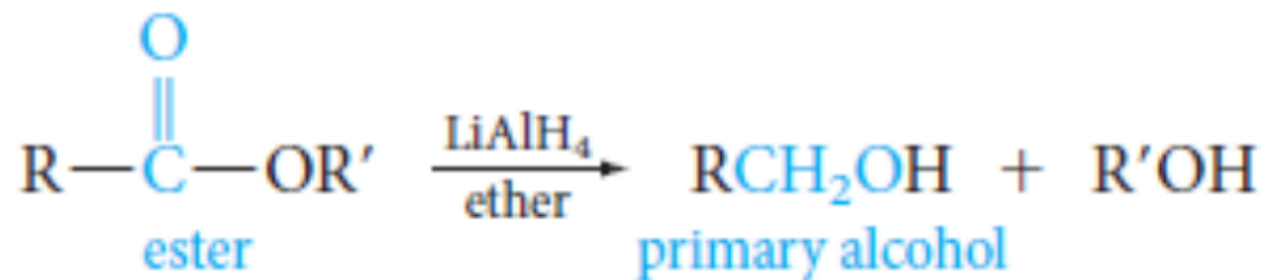
Yields tertiary alcohols in which *two* of the substituents carbon come from the Grignard reagent



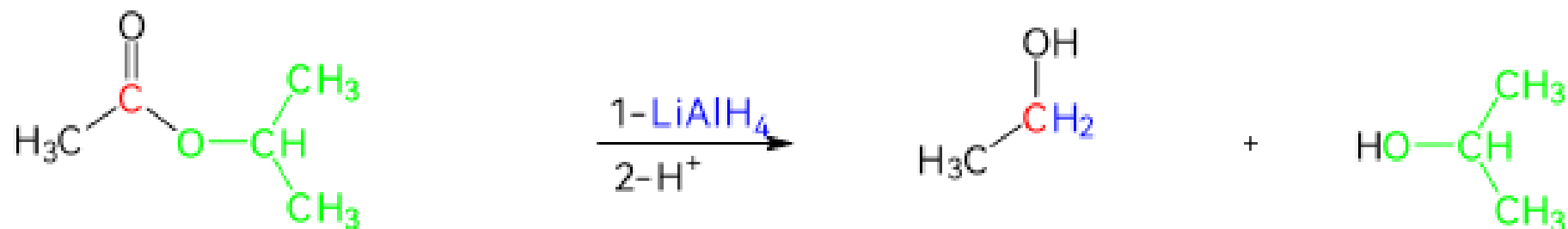
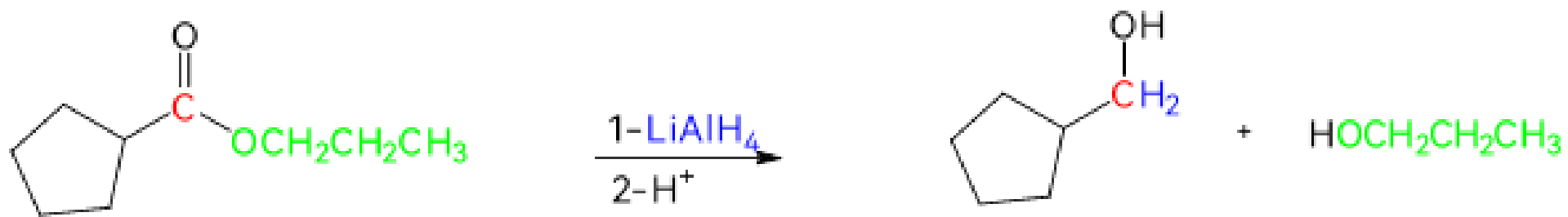
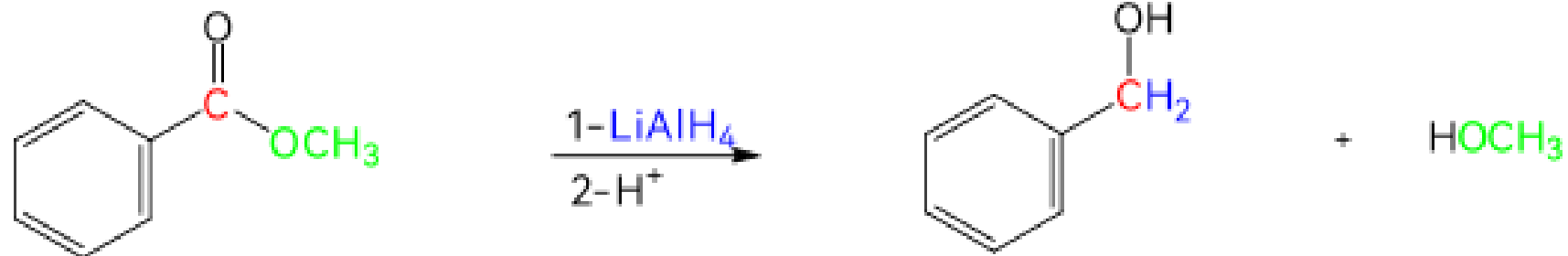
Reaction of Esters with excess Grignard reagents



10.16 Reduction of Esters



Reduction of Esters



Thanks to [chemistrysteps.com](https://www.chemistrysteps.com) for their valued schemes



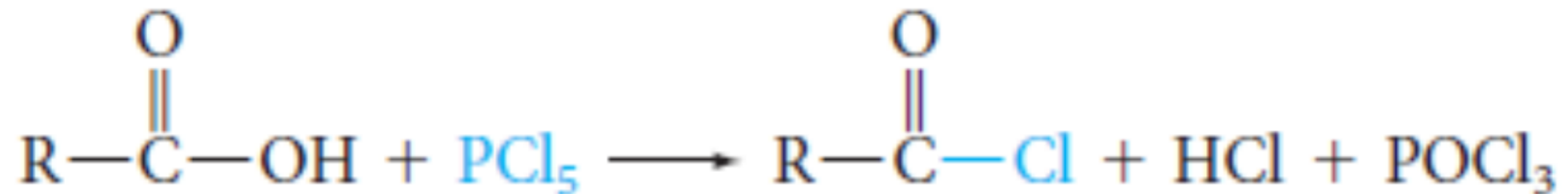
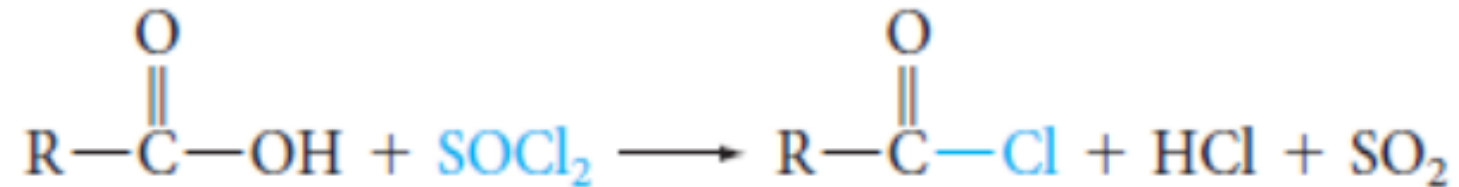
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10.18 Acyl Halides

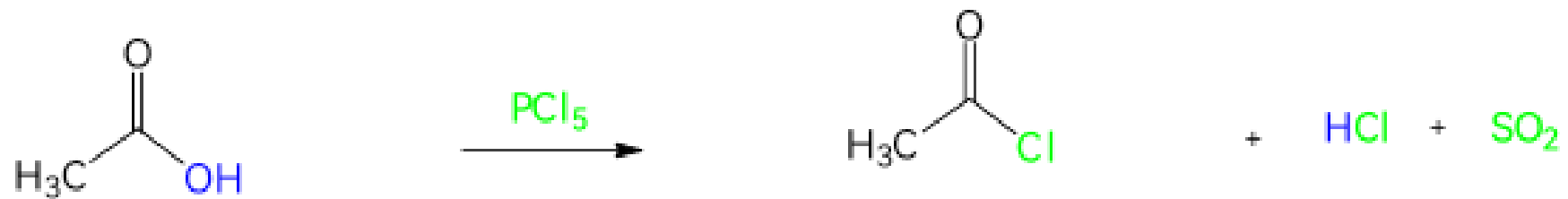
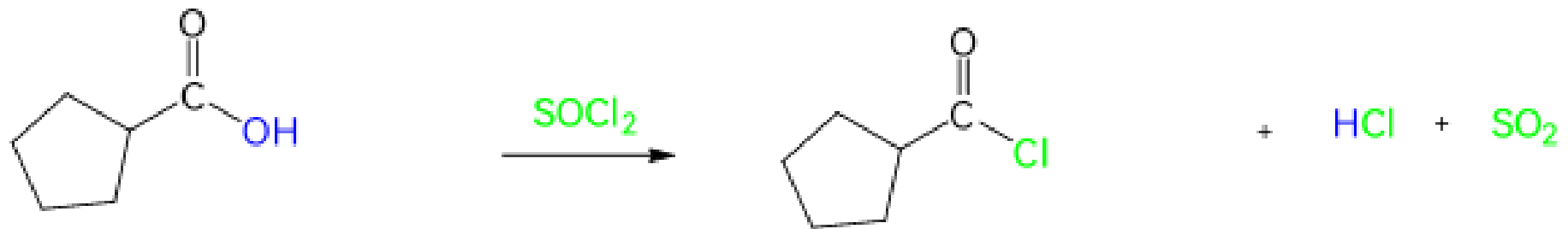
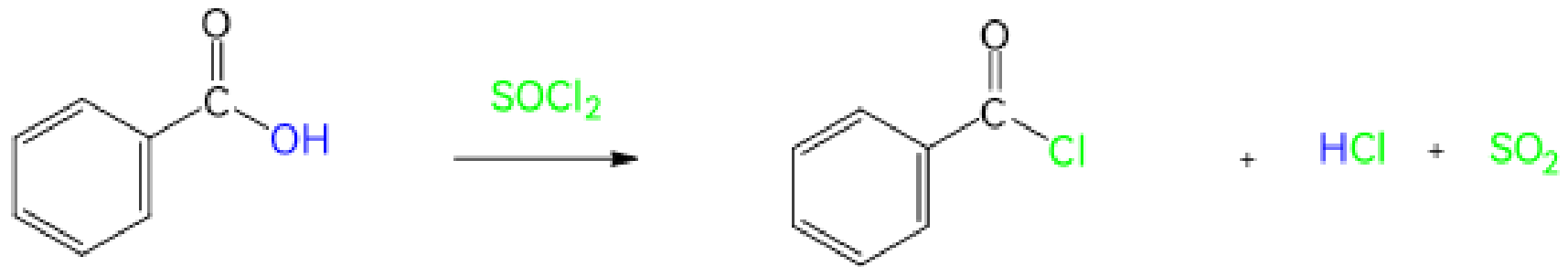
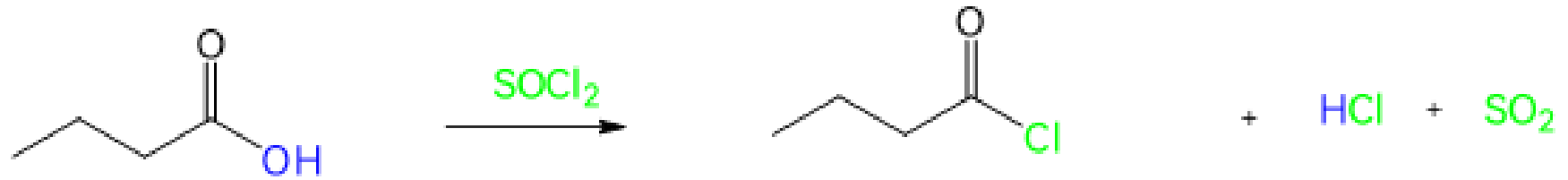


Preparation of Acyl chlorides

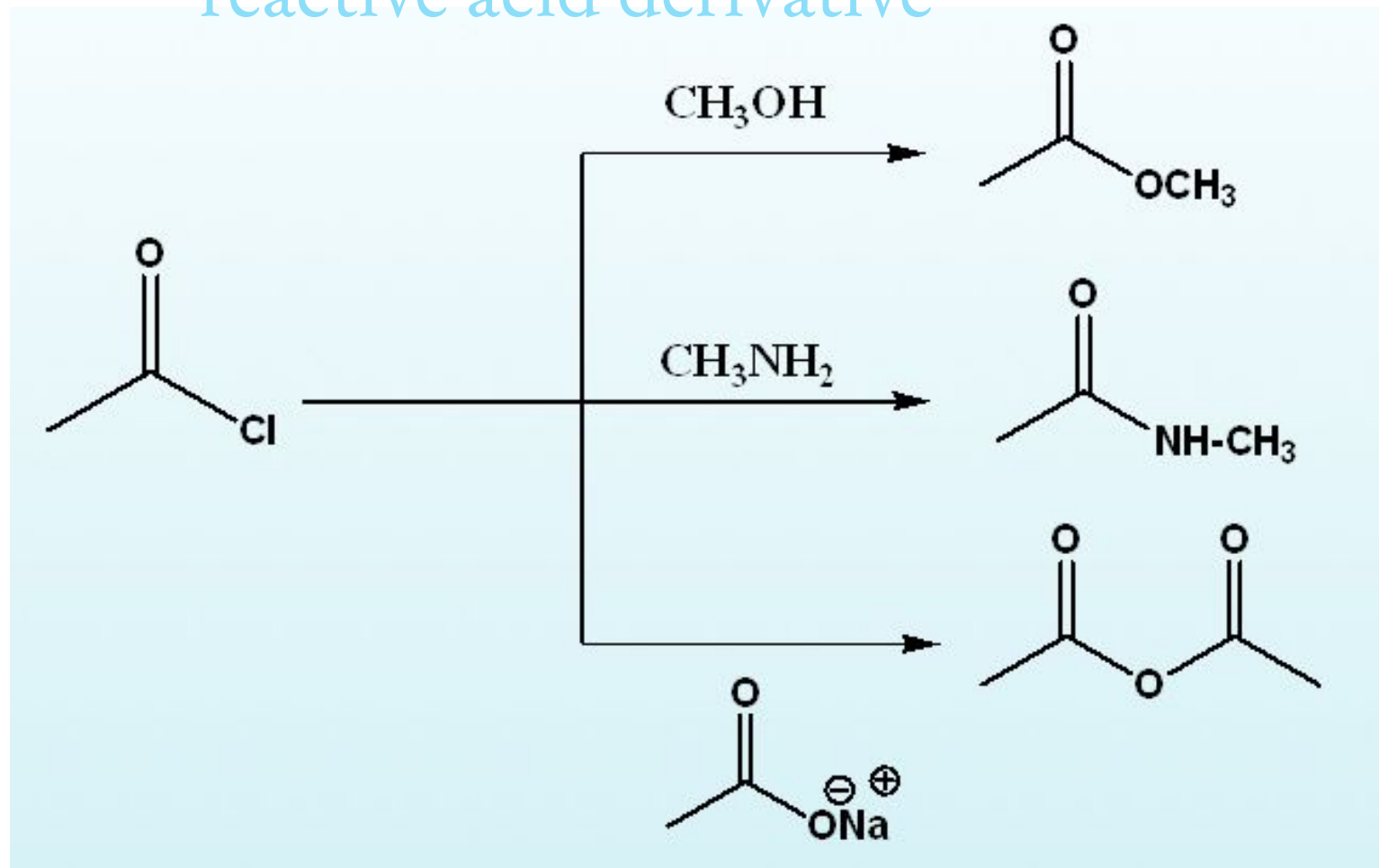
Acyl chlorides are prepared by the reactions of carboxylic acids with thionyl chloride, or with Phosphorus pentachloride



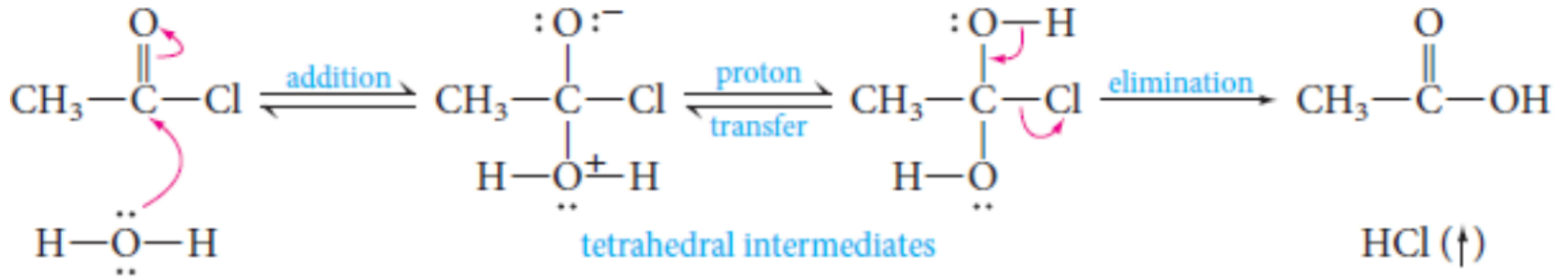
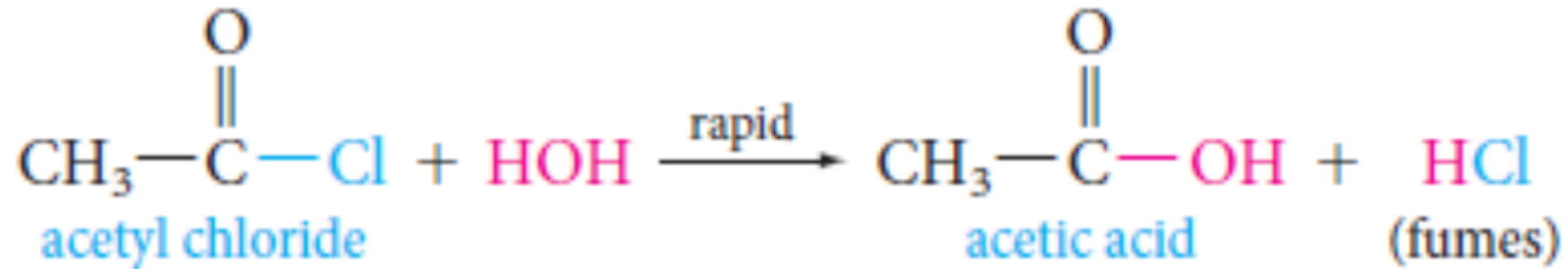
Preparation of Acyl chlorides



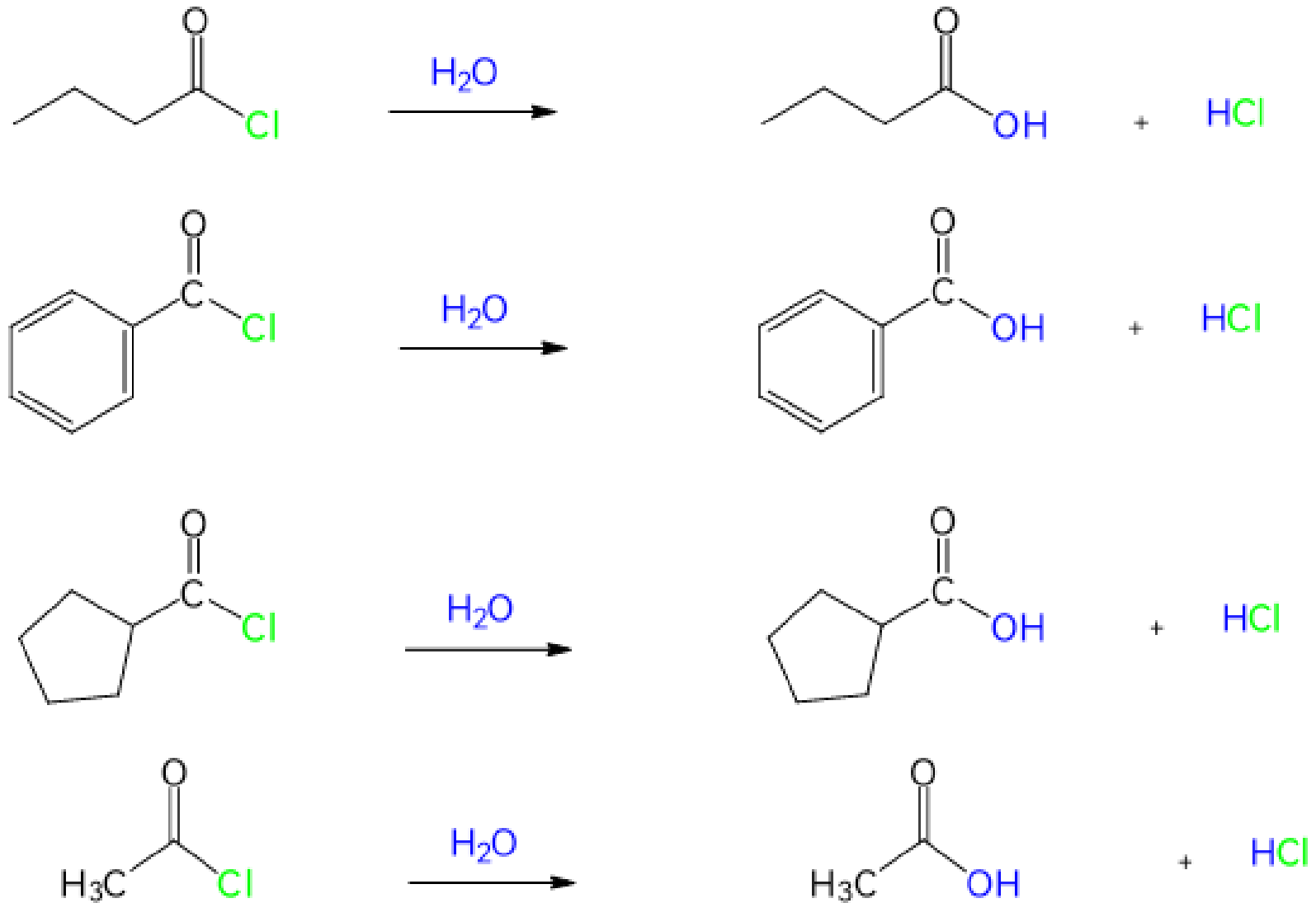
Acyl chlorides is the most reactive acid derivative



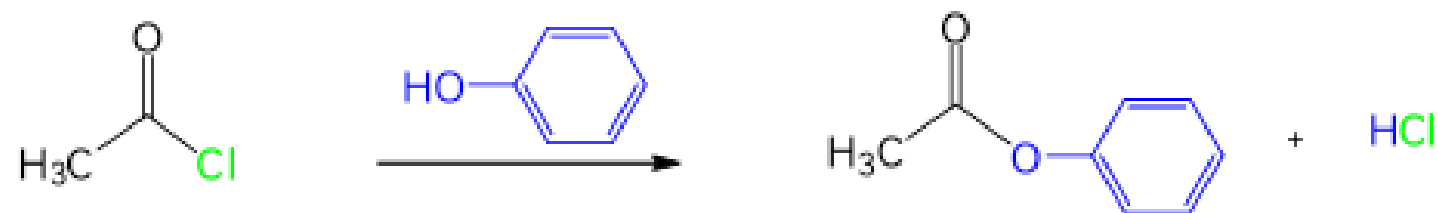
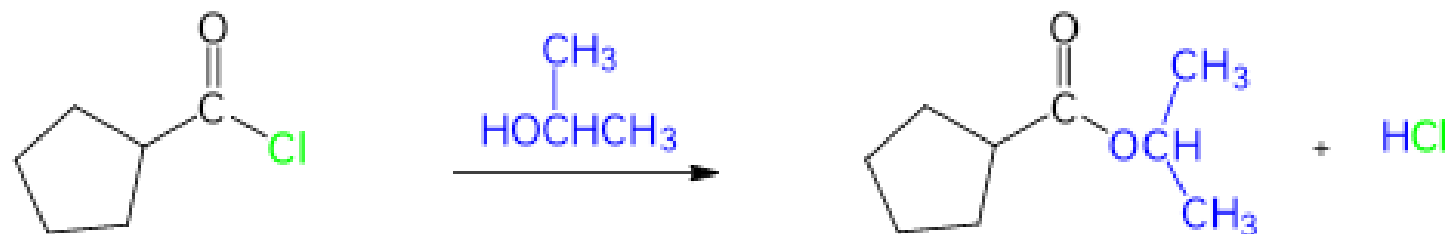
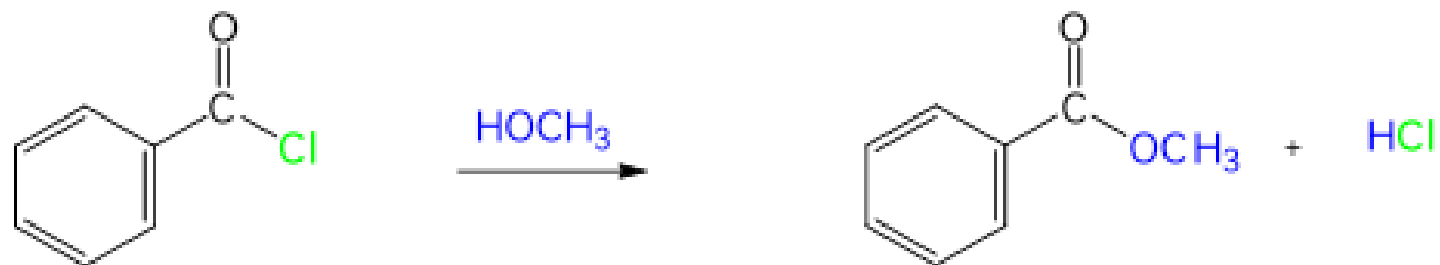
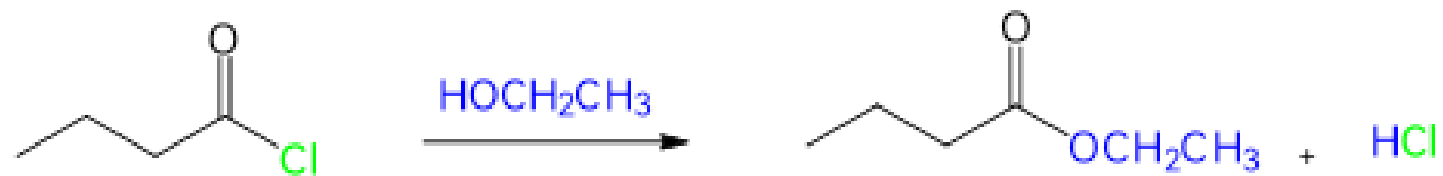
Hydrolysis of Acyl chlorides



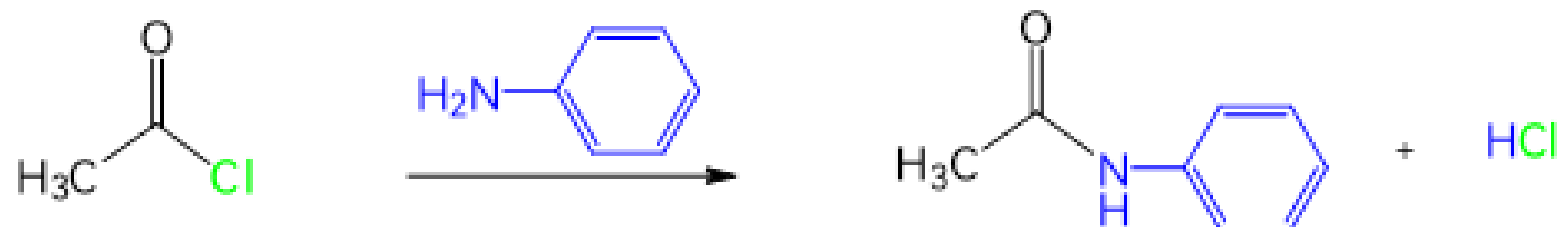
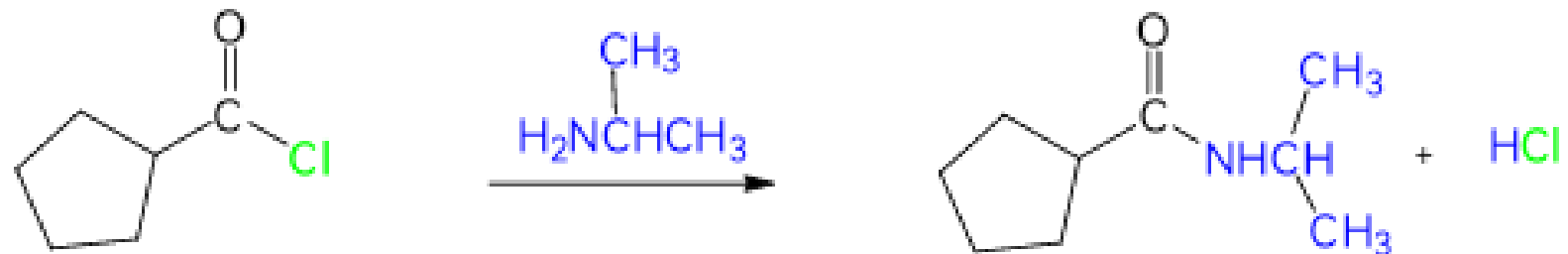
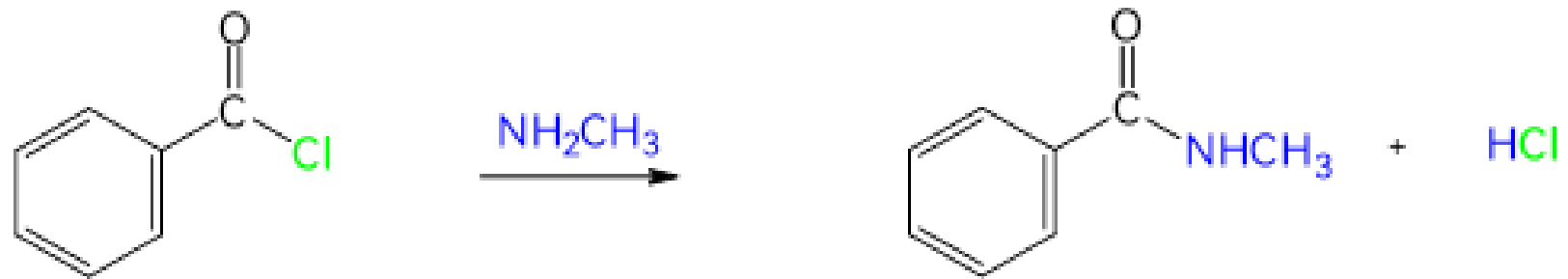
Hydrolysis of Acyl chlorides



Reaction of Acyl chlorides with alcohols to form esters



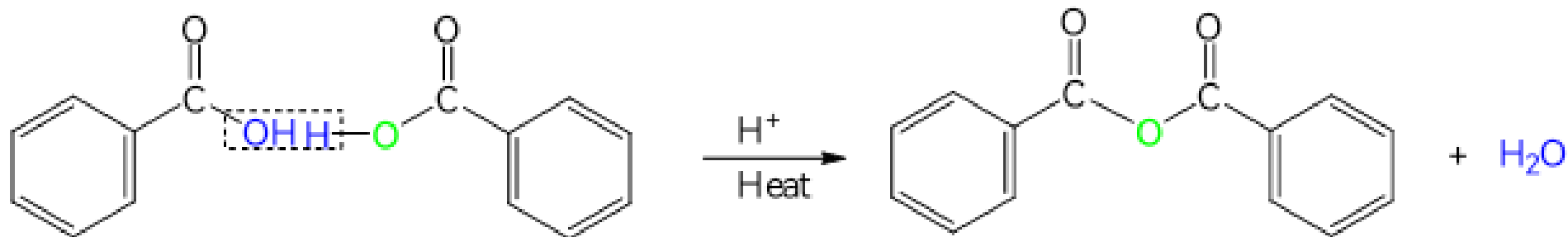
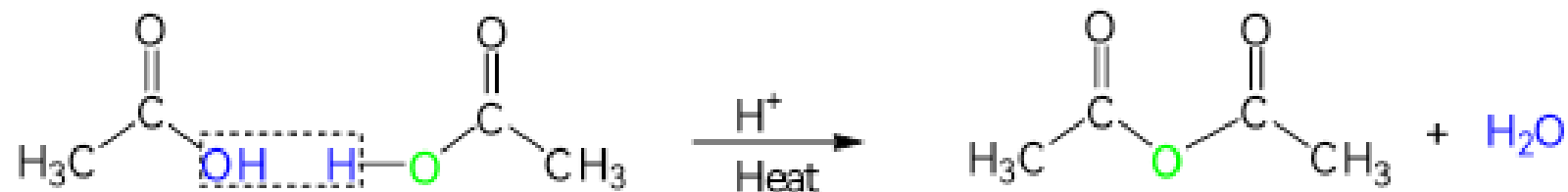
Reaction of Acyl chlorides with amines to form Amides



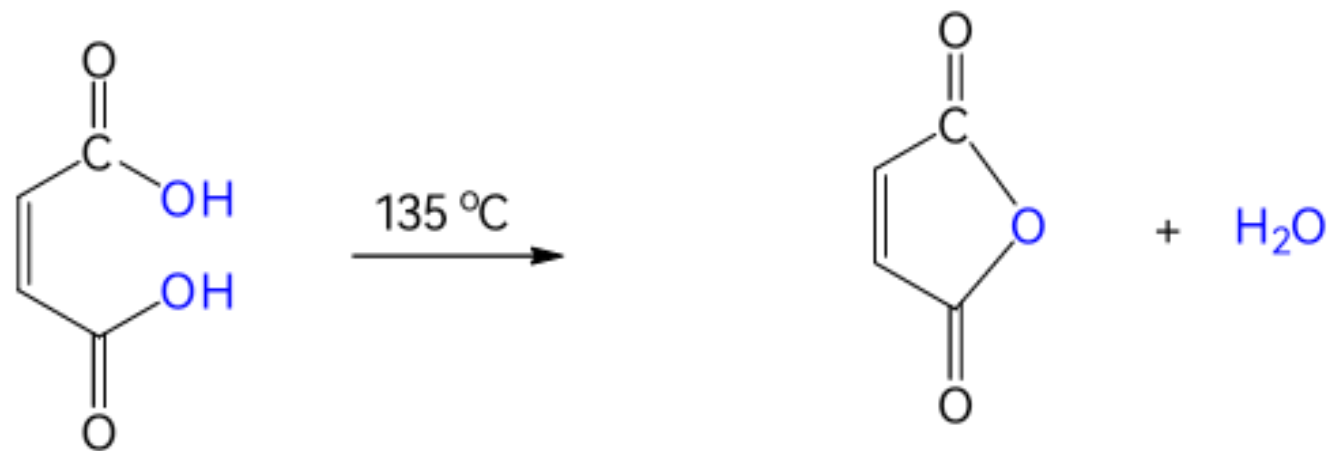
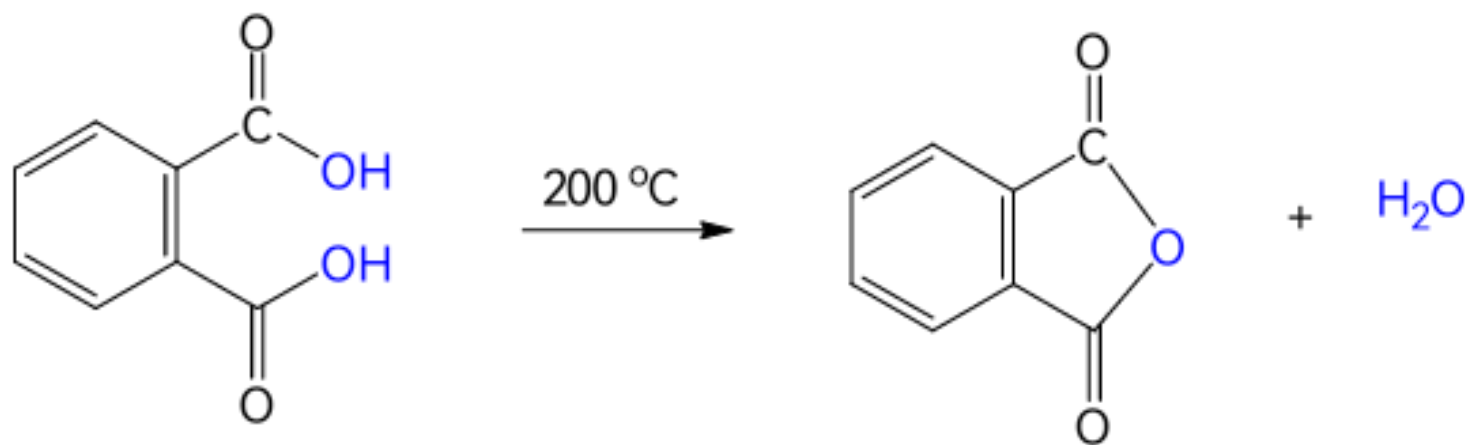
10.19 Acid Anhydrides

Acid anhydride is less reactive acid derivative than acyl chloride

Acid anhydride is prepared by heating of carboxylic acid



Intramolecular acid anhydride



Acid anhydride is more reactive
than ester and amide



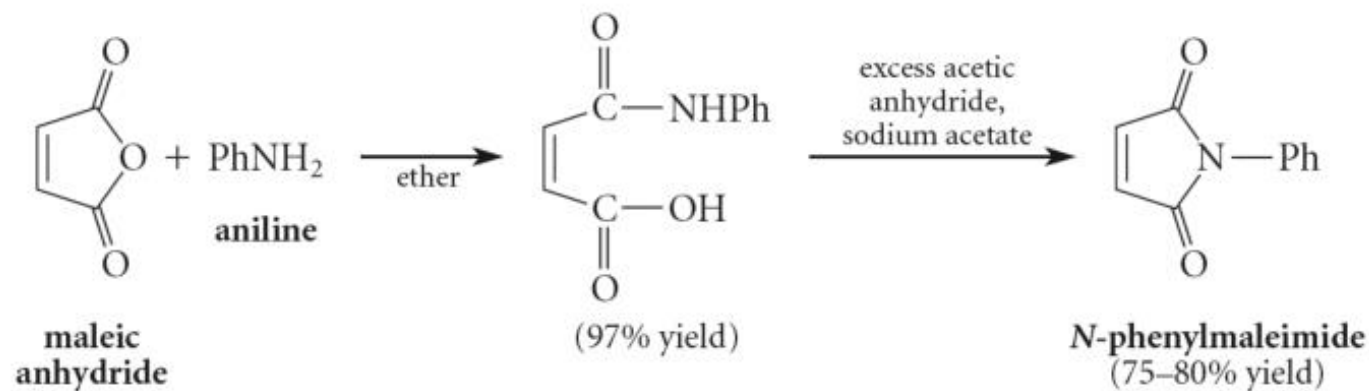
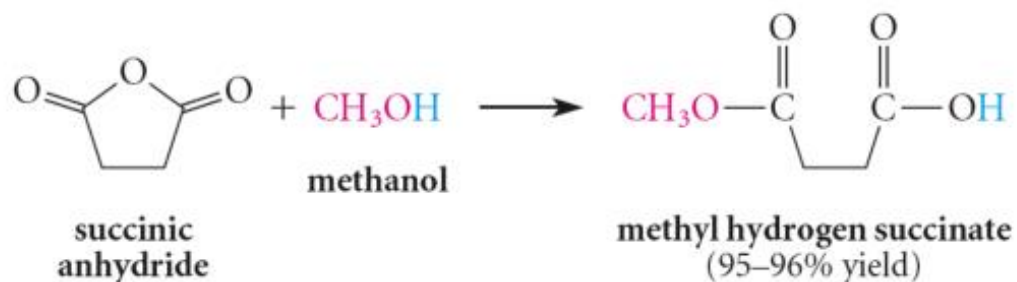
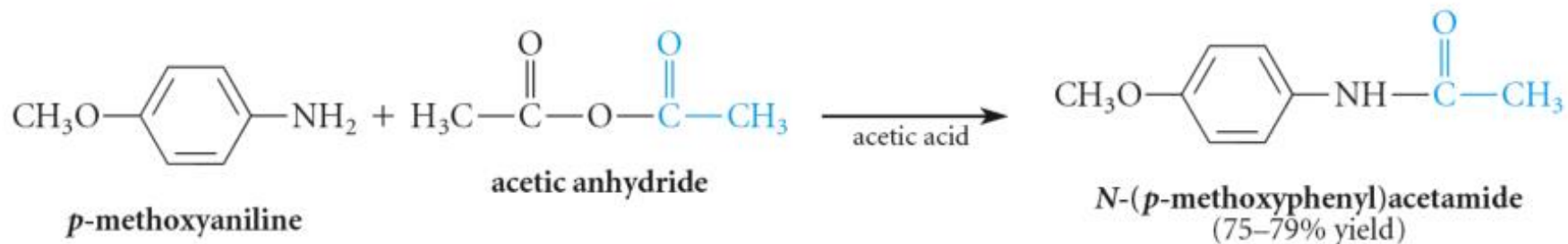
Synthesis of Aspirin



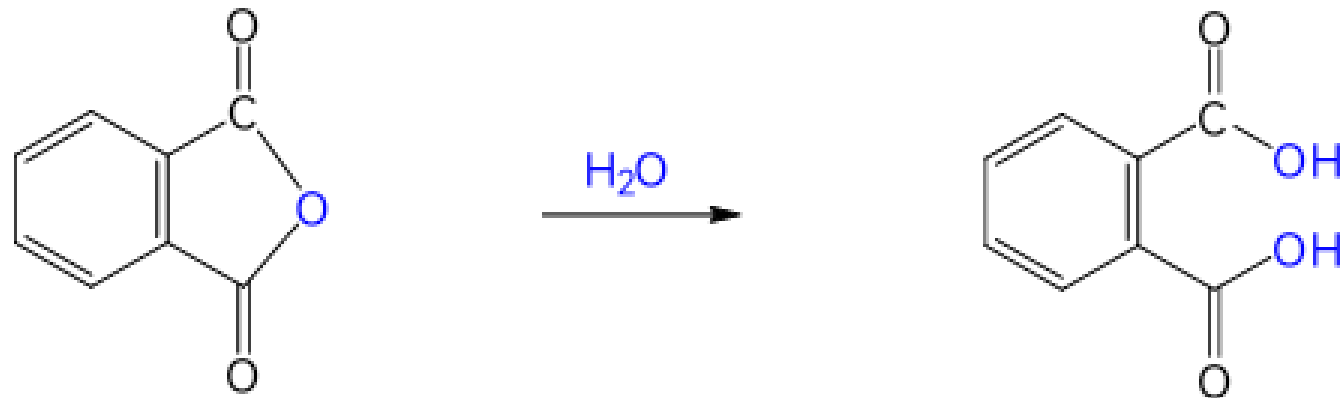
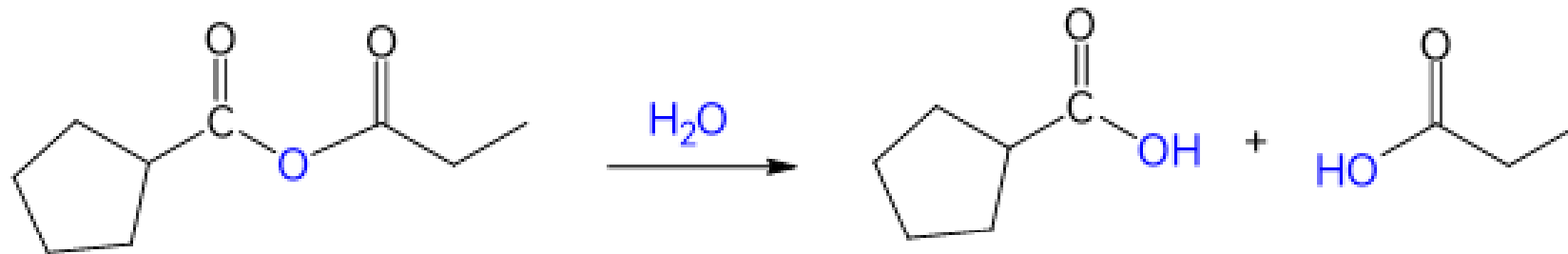
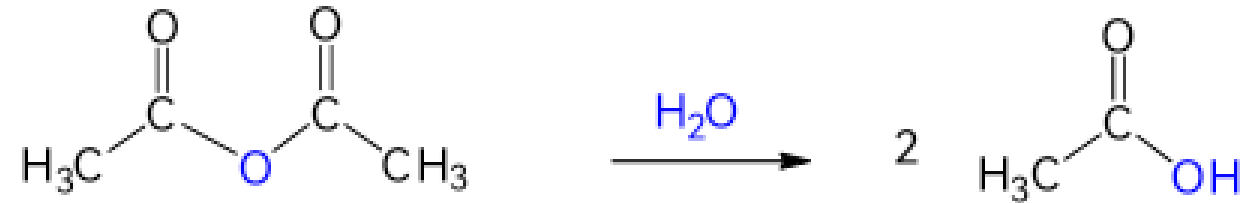
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Reactions of Anhydrides with Nucleophiles



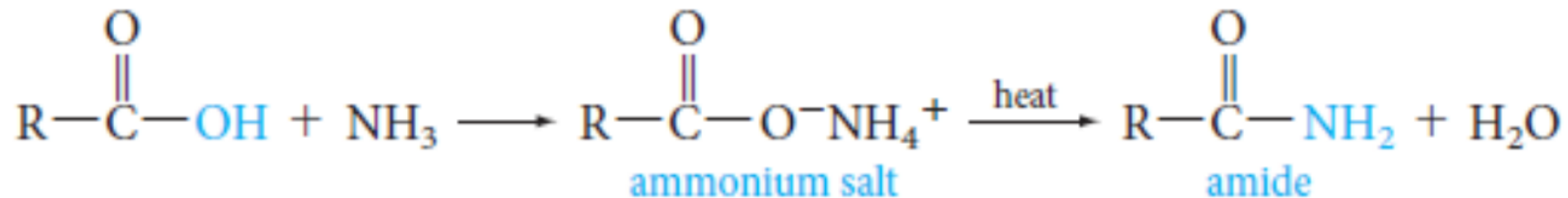
Hydrolysis of Acid Anhydride



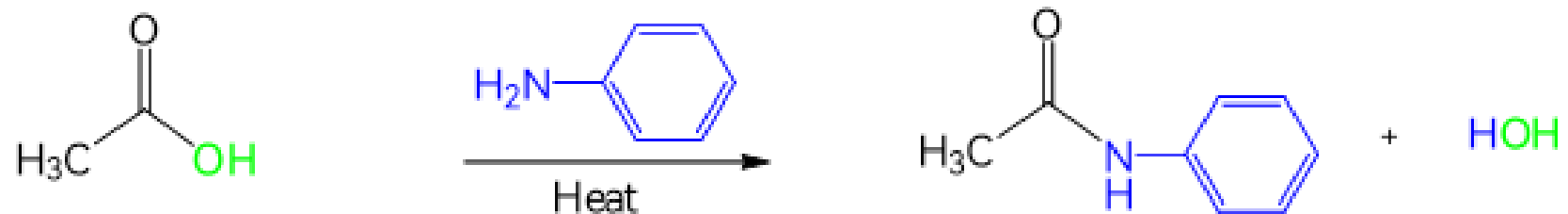
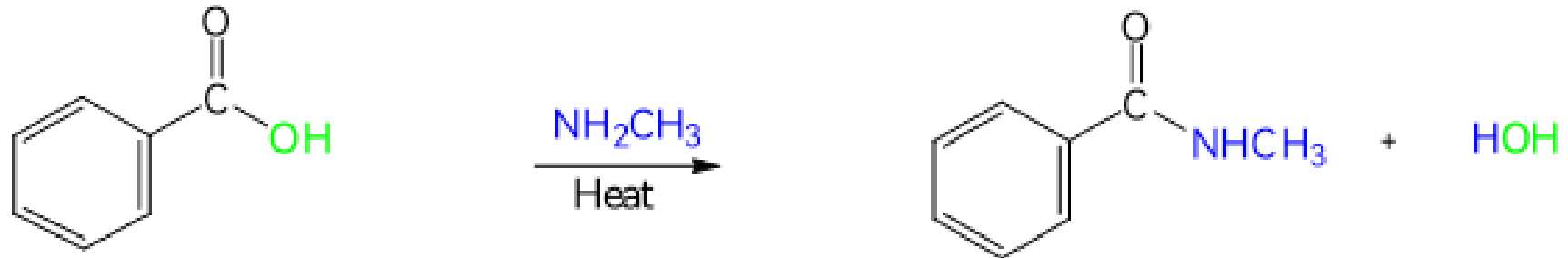
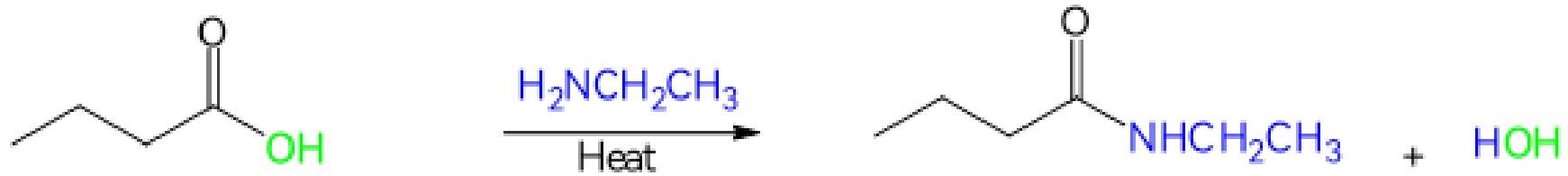
10.20 Amides

Amides are the least reactive of the common carboxylic acid derivatives.

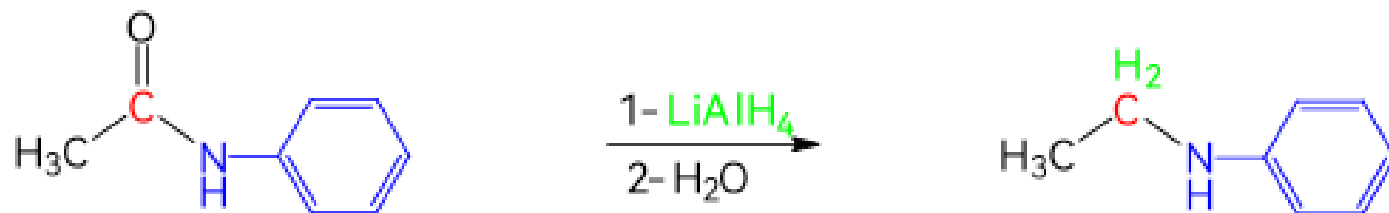
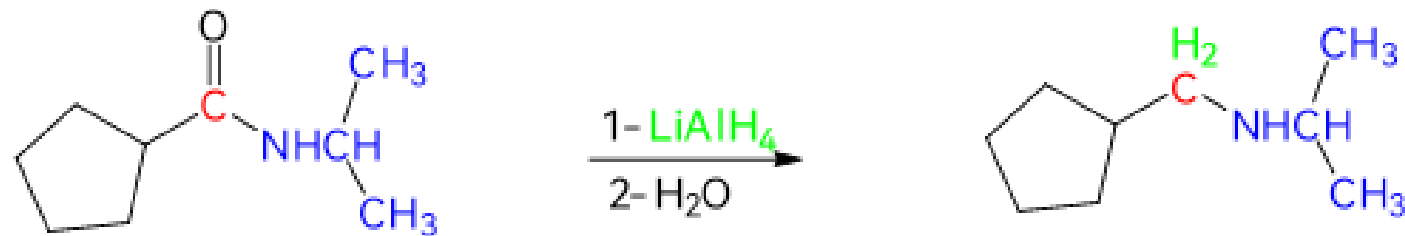
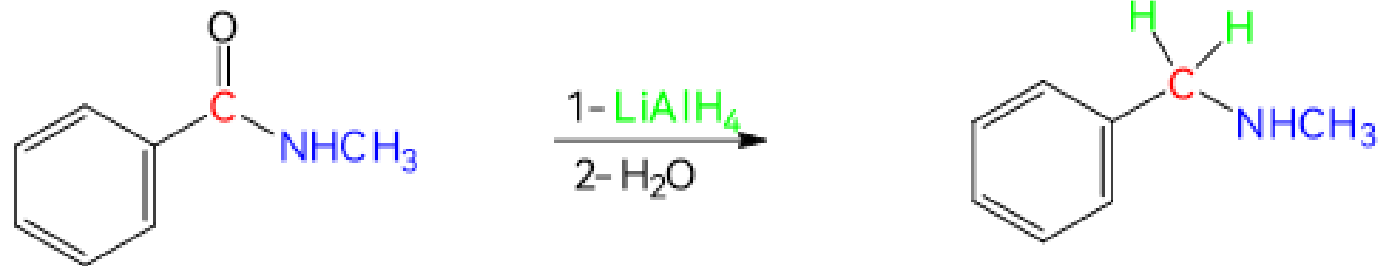
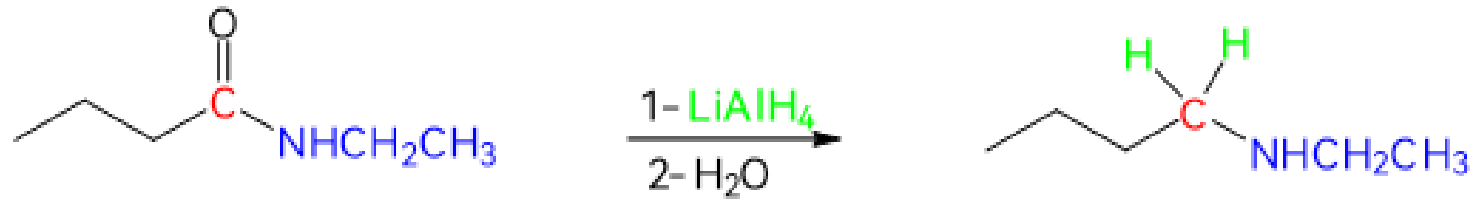
Amides are prepared from all acid derivatives



Preparation of Amide from Carboxylic acid



Reduction of Amides



Hydrolysis of Amide

