

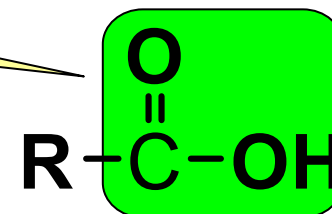


Chapter 13: Carboxylic Acids

Based on
McGraw Hill's *Organic Chemistry*, 5th edition, Chapters 12,
15, 19, and 20

Carboxylic Acids (R-COOH)

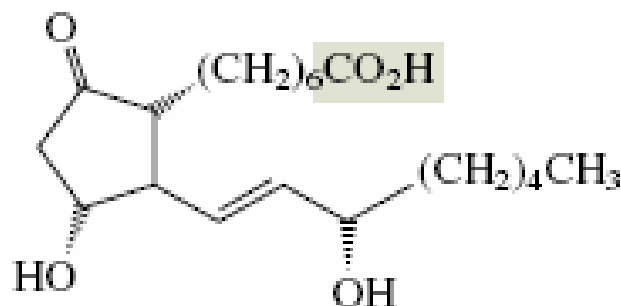
Carboxyl group



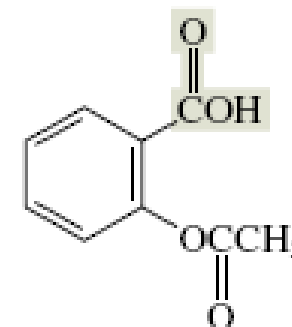
- Carboxylic acids, compounds of the type R-COOH
- Countless natural products are carboxylic acids or are derived from them.



Acetic acid
(present in vinegar)



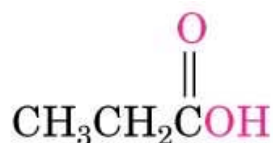
PGE1
(a prostaglandin; a small amount
of PGE1 lowers blood pressure
significantly)



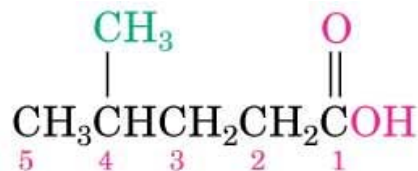
Aspirin

13.1 Naming Carboxylic Acids

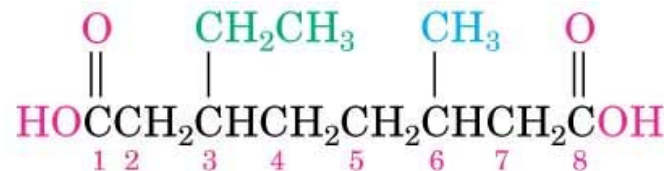
- Carboxylic Acids, RCO_2H
- If derived from open-chain alkanes, replace the terminal -e of the alkane name with -oic acid
- The carboxyl carbon atom is C1



Propanoic acid
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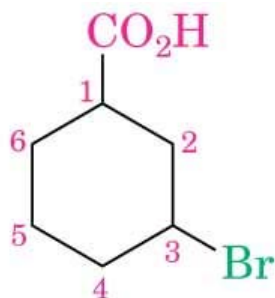
4-Methylpentanoic acid



3-Ethyl-6-methyloctanedioic acid

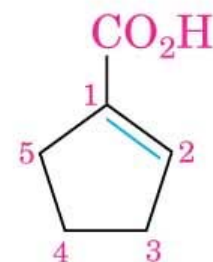
Alternative Names

- Compounds with $\text{—CO}_2\text{H}$ bonded to a ring are named using the suffix *-carboxylic acid*
- The CO_2H carbon is not itself numbered in this system
- Use common names for formic acid (HCOOH) and acetic acid (CH_3COOH)

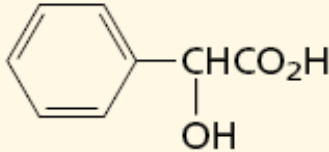
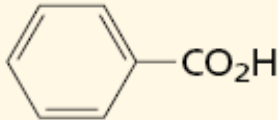
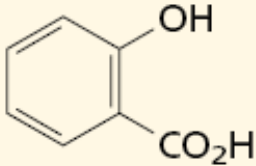
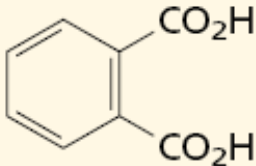


3-Bromocyclohexanecarboxylic acid

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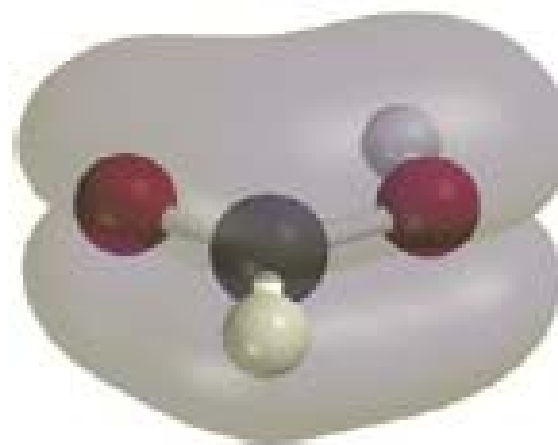
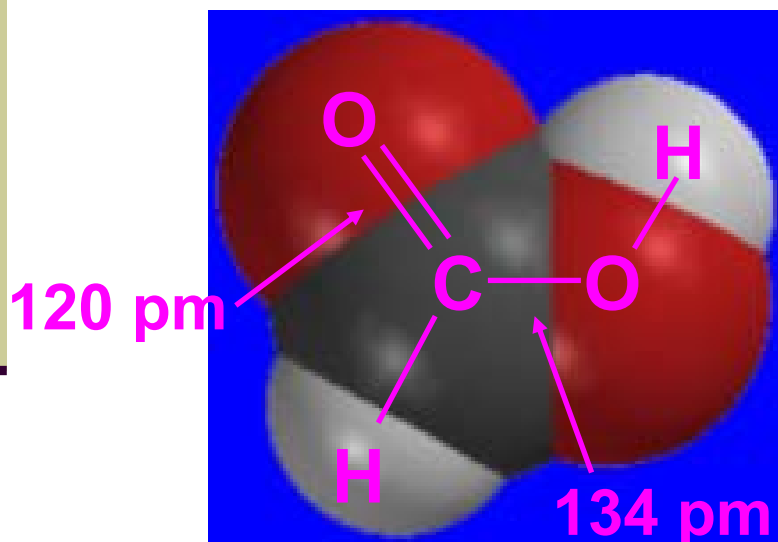


1-Cyclopentene-1-carboxylic acid

Structural formula	Systematic name	Common name
HCO ₂ H	Methanoic acid	Formic acid
CH ₃ CO ₂ H	Ethanoic acid	Acetic acid
CH ₃ (CH ₂) ₁₆ CO ₂ H	Octadecanoic acid	Stearic acid
$\begin{array}{c} \text{CH}_3\text{CHCO}_2\text{H} \\ \\ \text{OH} \end{array}$	2-Hydroxypropanoic acid	Lactic acid
	2-Hydroxy-2-phenylethanoic acid	Mandelic acid
CH ₂ =CHCO ₂ H	Propenoic acid	Acrylic acid
$\begin{array}{c} \text{CH}_3(\text{CH}_2)_7 \quad (\text{CH}_2)_7\text{CO}_2\text{H} \\ \quad \quad \quad \diagdown \quad \diagup \\ \quad \quad \quad \text{C}=\text{C} \\ \quad \quad \quad \diagup \quad \diagdown \\ \quad \quad \quad \text{H} \quad \quad \quad \text{H} \end{array}$	(Z)-9-Octadecenoic acid	Oleic acid
	Benzenecarboxylic acid	Benzoic acid
	o-Hydroxybenzenecarboxylic acid	Salicylic acid
HO ₂ CCH ₂ CO ₂ H	Propanedioic acid	Malonic acid
HO ₂ CCH ₂ CH ₂ CO ₂ H	Butanedioic acid	Succinic acid
	1,2-Benzenedicarboxylic acid	Phthalic acid

13.2 Structure and Bonding

- Carboxyl carbon sp^2 hybridized: carboxylic acid groups are planar with C–C=O and O=C–O bond angles of approximately 120°

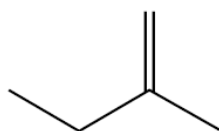
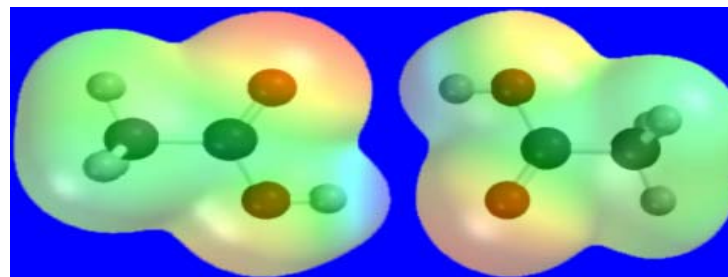
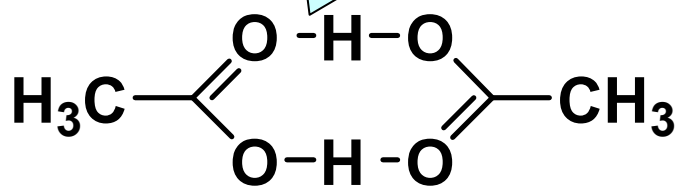


Formic acid is planar

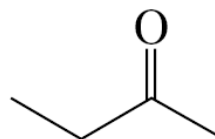
13.3 Physical Properties: Hydrogen bond

- Carboxylic acids form hydrogen bonds, existing as cyclic dimers held together by two hydrogen bonds
- Strong hydrogen bonding causes much higher boiling points than the corresponding alcohols

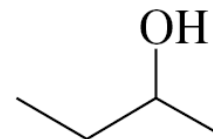
Hydrogen bond



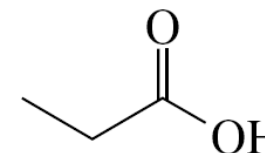
2-Methyl-1-butene
31°C



2-Butanone
80°C



2-Butanol
99°C

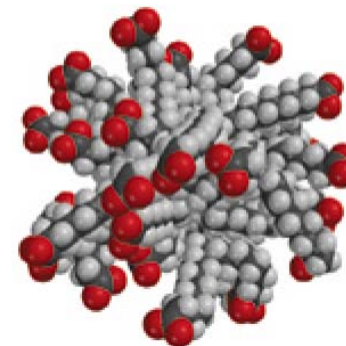
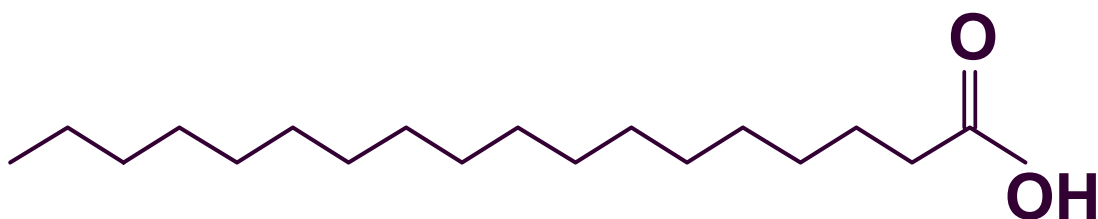


Propanoic acid
141°C

bp (1 atm):

Solubility in Water

- The solubility properties of carboxylic acids are similar to those of alcohols.
- Carboxylic acids of four carbon atoms or fewer are miscible with water in all proportions.



nonpolar

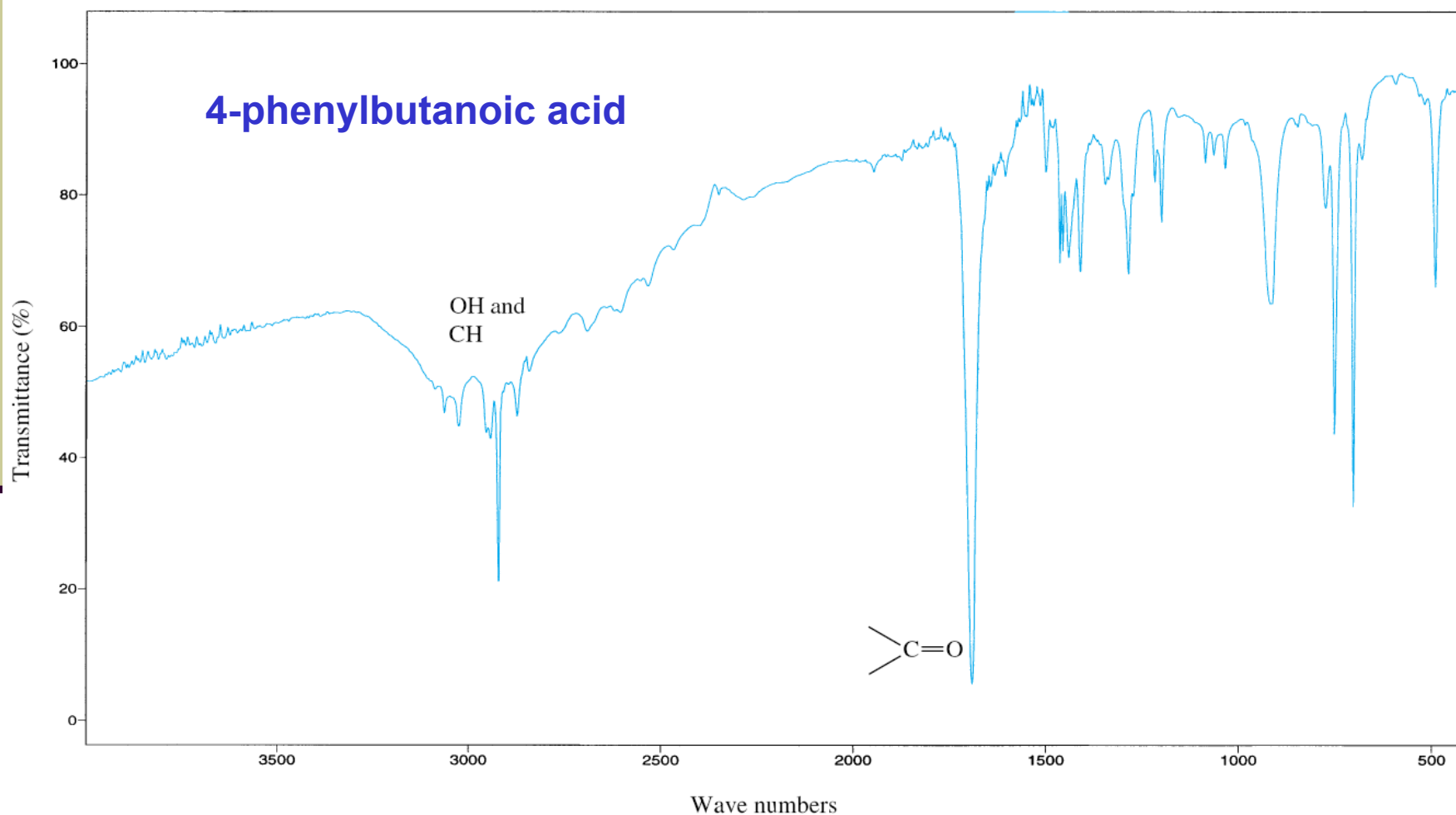
polar

water-hating" or hydrophobic

water-loving" or hydrophilic

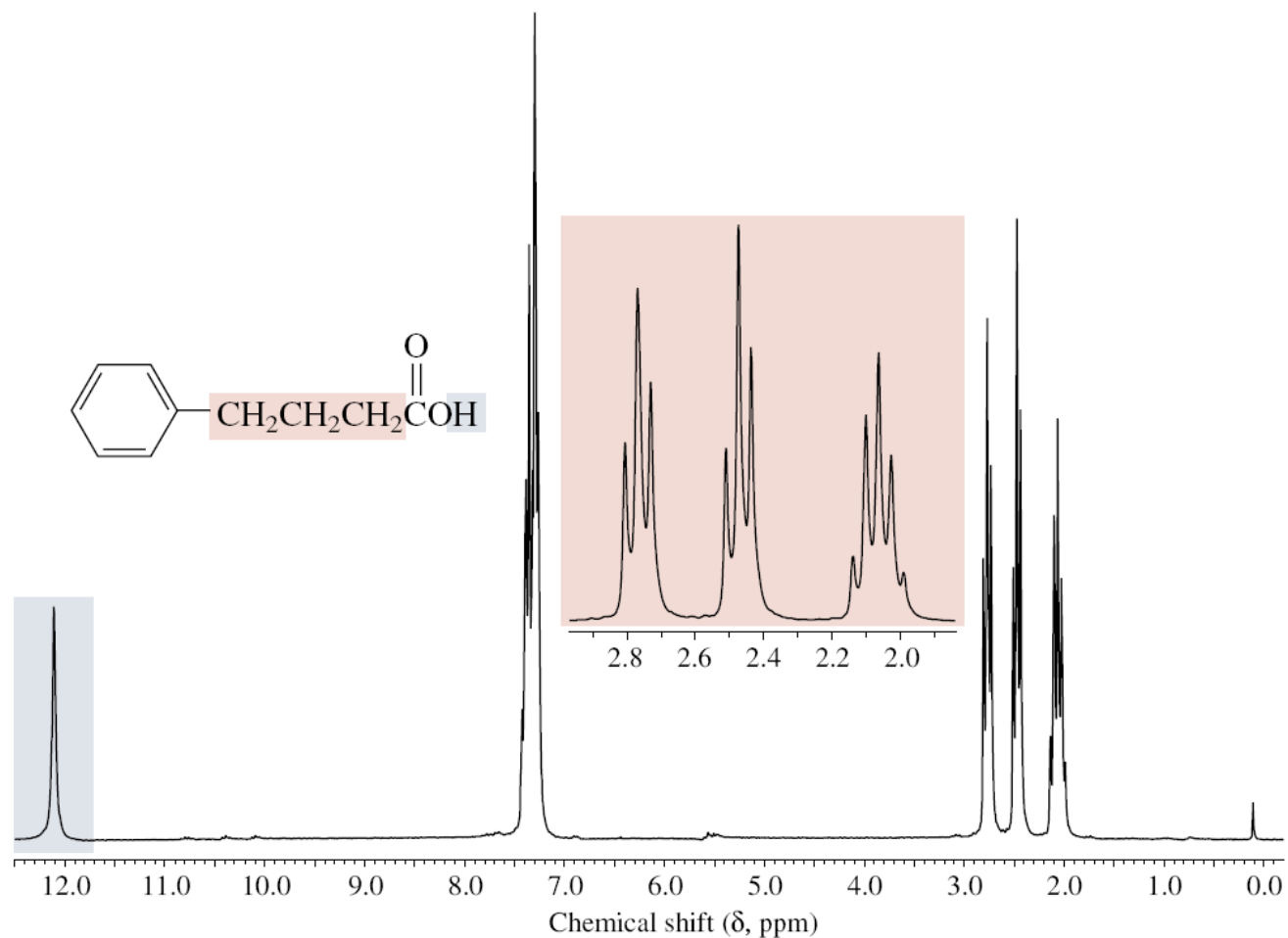
13.4 Spectroscopic Analysis of Carboxylic Acids

- Infrared: C=O, 1700–1720 cm^{-1} ; -OH: 2500~3000 cm^{-1}



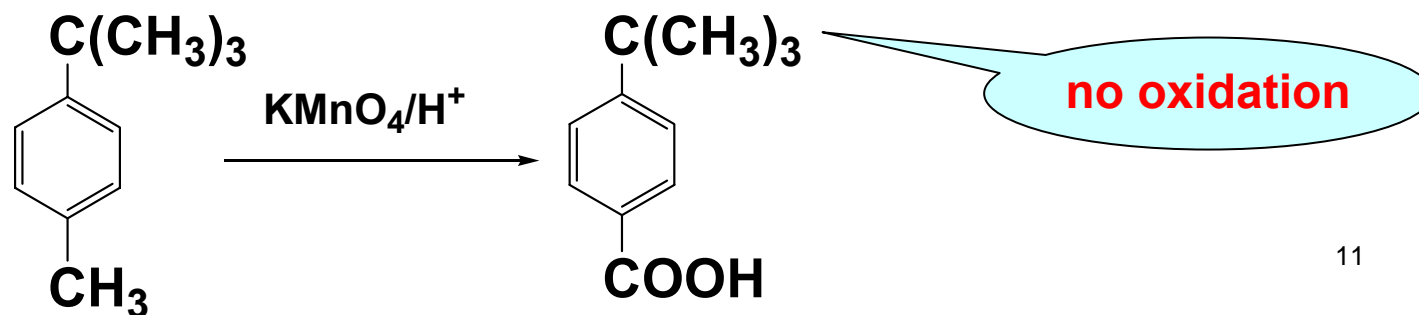
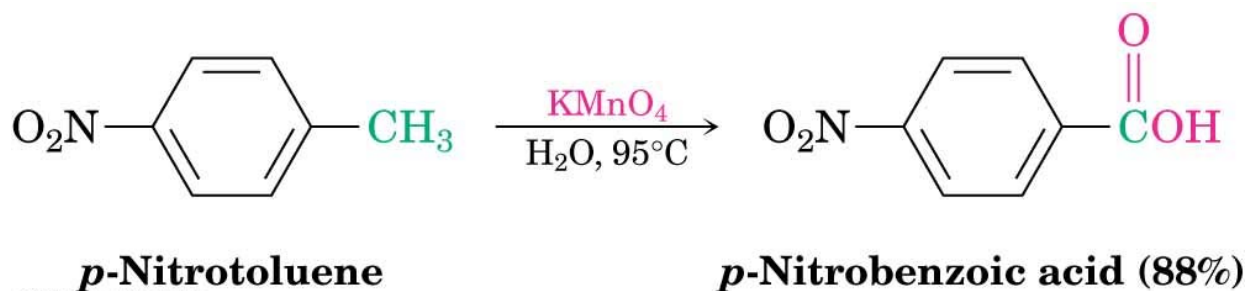
Spectroscopic Analysis of Carboxylic Acids

- $^1\text{H-NMR}$: δ_{COOH} : 10.5~12 ppm



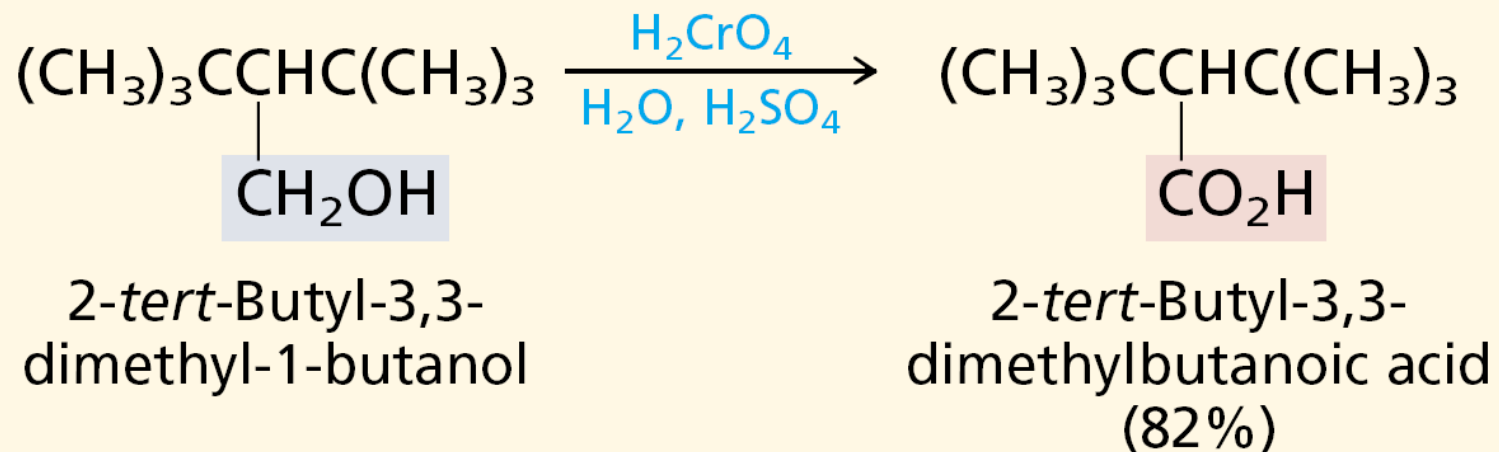
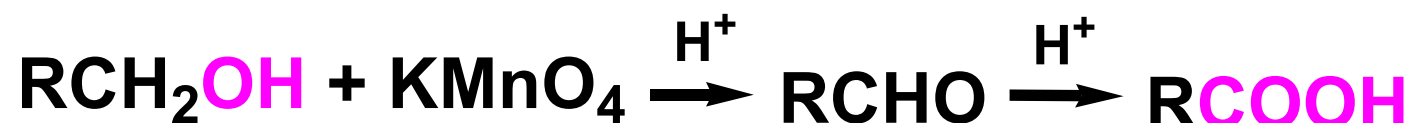
13.5 Preparation of Carboxylic Acids

- Side-chain oxidation of alkylbenzenes with KMnO_4 or $\text{Na}_2\text{Cr}_2\text{O}_7$
- 1° and 2° alkyl groups can be oxidized, but tertiary groups are not



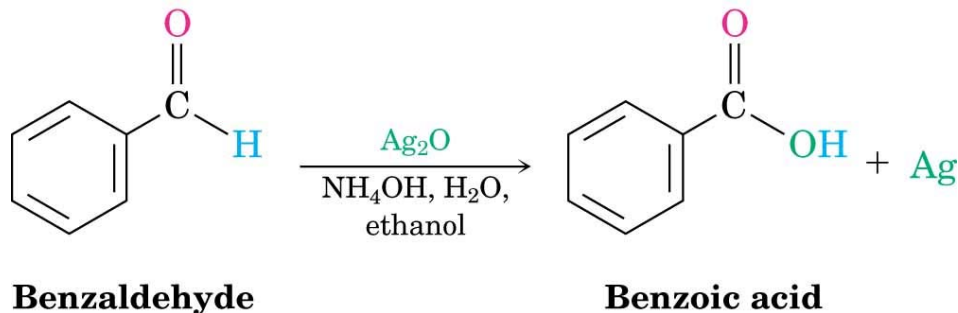
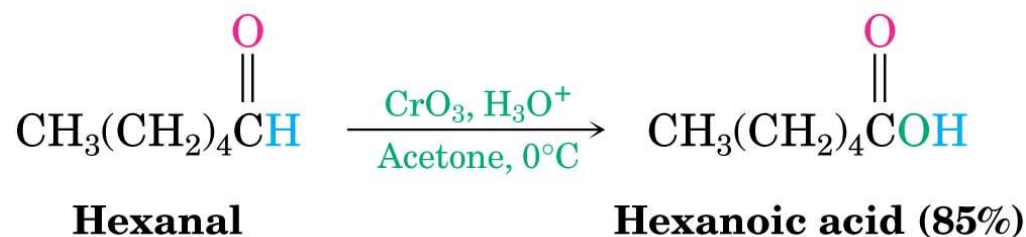
Preparation of Carboxylic Acids

- Oxidation of a primary alcohol with KMnO_4 , CrO_3 in aqueous acid.

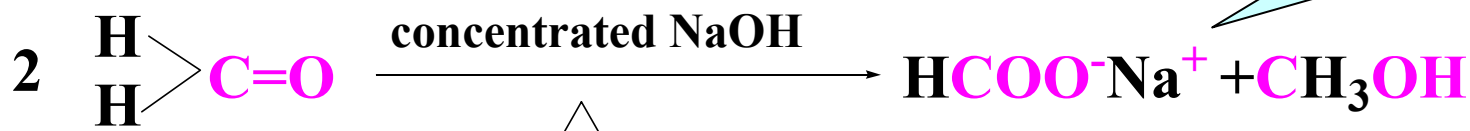


Preparation of Carboxylic Acids

- Oxidation of aldehydes by a number of oxidizing agents.

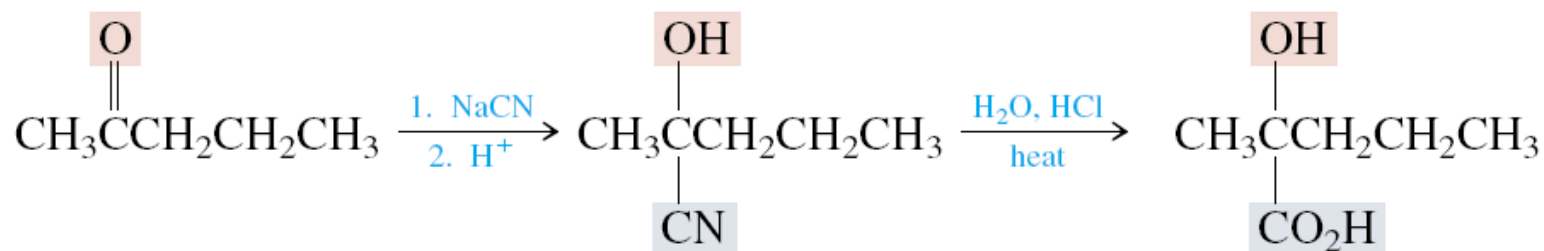
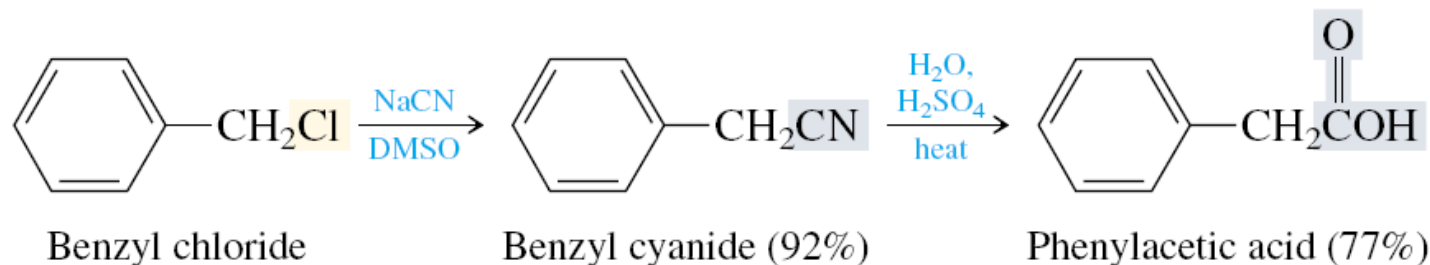
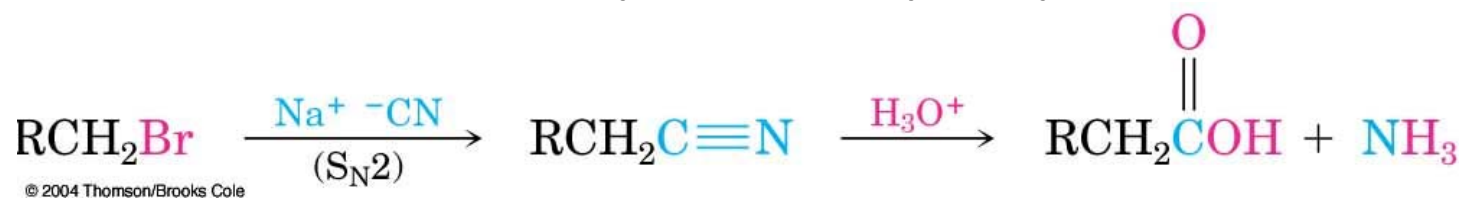


Cannizzaro reaction



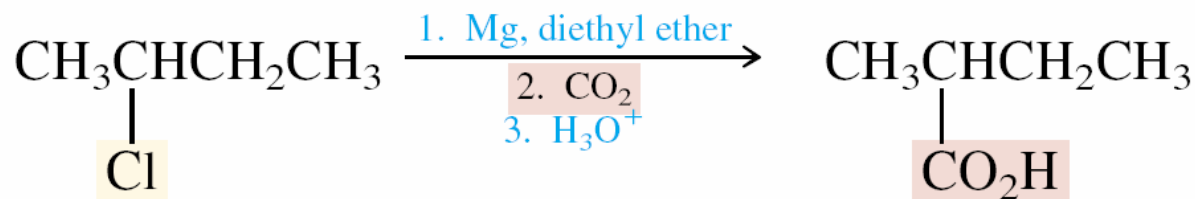
Preparation of Carboxylic Acids

- Hydrolysis of nitriles in hot acid.
- Best with primary halides because elimination reactions occur with secondary or tertiary alkyl halides.



Preparation of Carboxylic Acids

- Grignard reagents react with dry CO_2 to yield a metal carboxylate.



2-Chlorobutane

2-Methylbutanoic acid
(76–86%)

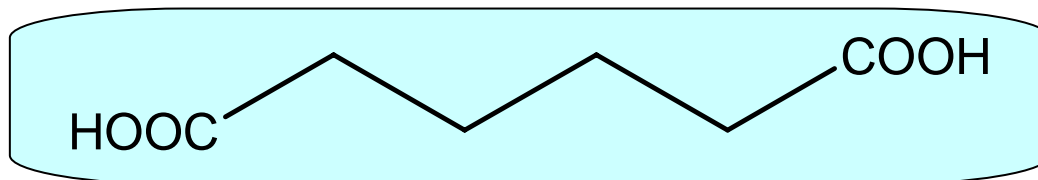
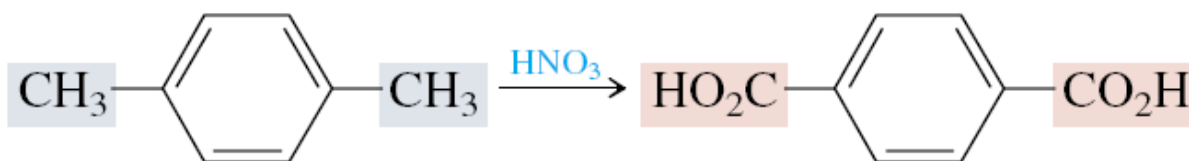
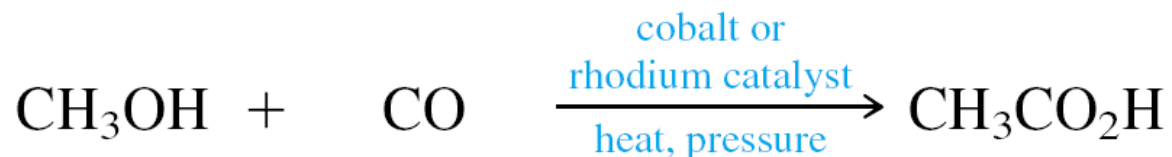


1-Bromo-2,4,6-trimethyl-
benzene

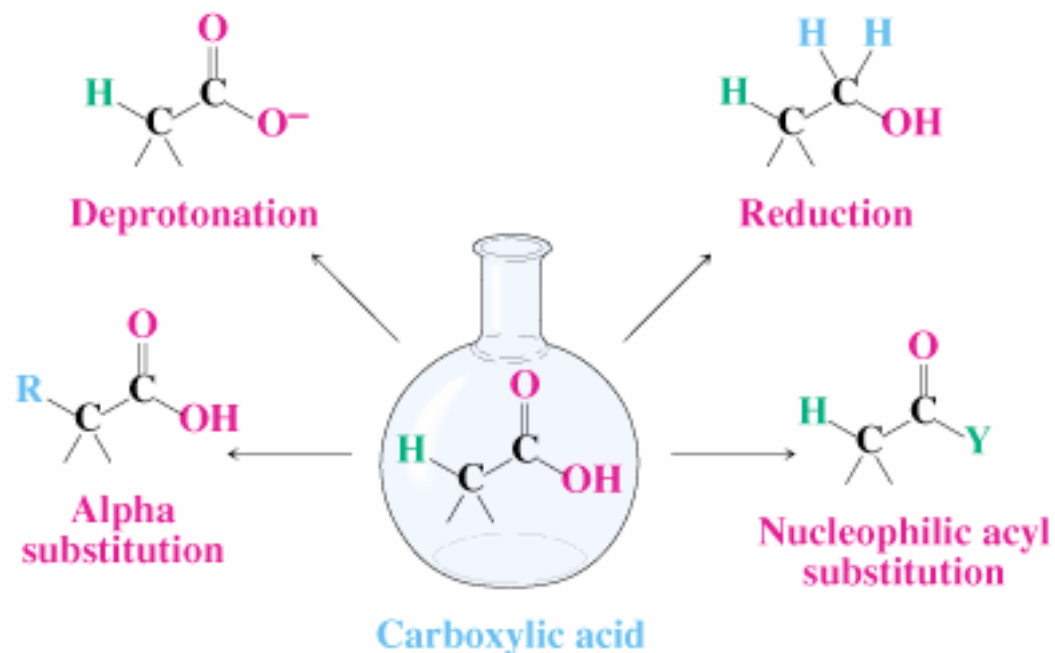
2,4,6-Trimethylbenzoic acid
(87%)

Preparation of Carboxylic Acids

■ 羧酸的工业合成



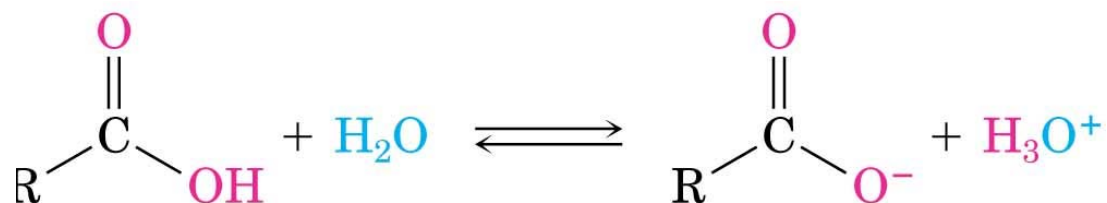
13.6 Chemical Properties



- Acidity of carboxylic acids
- Substitution of -OH group
- Nucleophilic addition of -C=O group
- Chemical properties of -COOH group
- Acidity of β - hydrogen

13.6.1 Acidity of carboxylic Acids

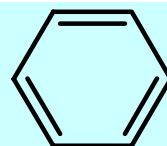
- Carboxylic acids are the most acidic class of compounds that contain only carbon, hydrogen, and oxygen.
- The acidity constant, K_a , is about 10^{-5} for a typical carboxylic acid ($pK_a \sim 5$)



$$K_a = \frac{[\text{RCO}_2^-][\text{H}_3\text{O}^+]}{[\text{RCO}_2\text{H}]} \quad \text{and} \quad pK_a = -\log K_a$$

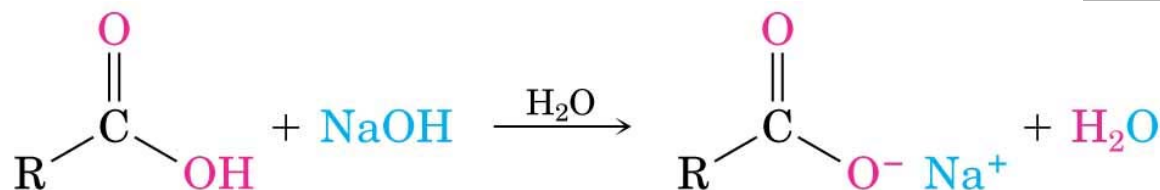
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H_2CO_3 , $pK_a = 7$,



OH , $pK_a = 10$

Salts of Carboxylic Acids



A carboxylic acid
(water-insoluble)

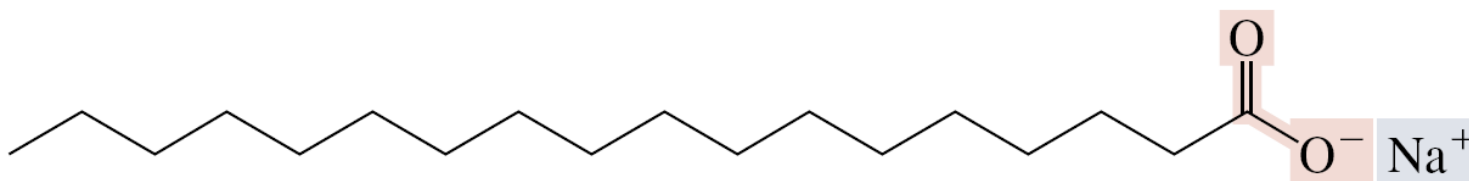
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A carboxylic acid salt
(water-soluble)

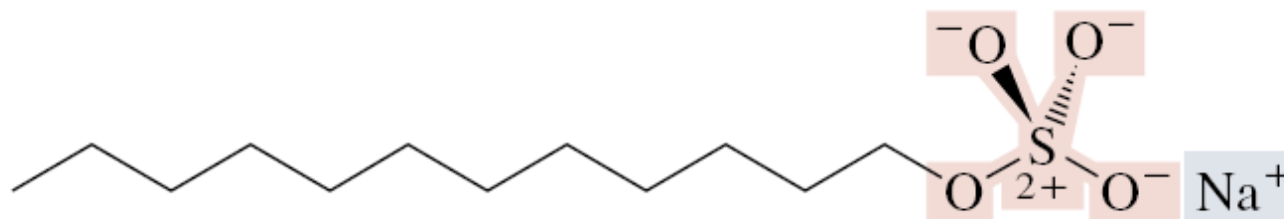
- In the presence of strong bases such as sodium hydroxide, carboxylic acids are neutralized rapidly and quantitatively.
- Carboxylic acids with more than six carbons are only slightly soluble in water, but their conjugate base salts are water-soluble.

Salts of Carboxylic Acids

- sodium and potassium salts of C_{12} – C_{18} unbranched carboxylic acids are designed to be effective detergents



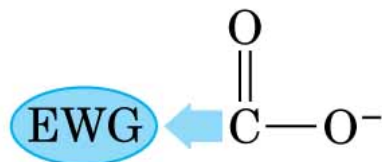
Sodium stearate



Sodium lauryl sulfate

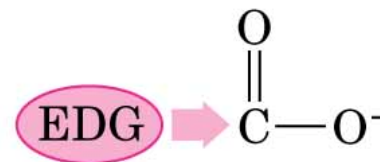
13.6.1.1 Substituent Effects on Acidity

- An electronegative group will drive the ionization equilibrium toward dissociation, increasing acidity
- An electron-*donating* group destabilizes the carboxylate anion and decreases acidity



Electron-withdrawing group
stabilizes carboxylate
and strengthens acid

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Electron-donating group
destabilizes carboxylate
and weakens acid

Examples of Inductive Effects on Acidity

- Fluoroacetic, chloroacetic, bromoacetic, and iodoacetic acids are stronger acids than acetic acid
- Multiple electronegative substituents have synergistic effects on acidity

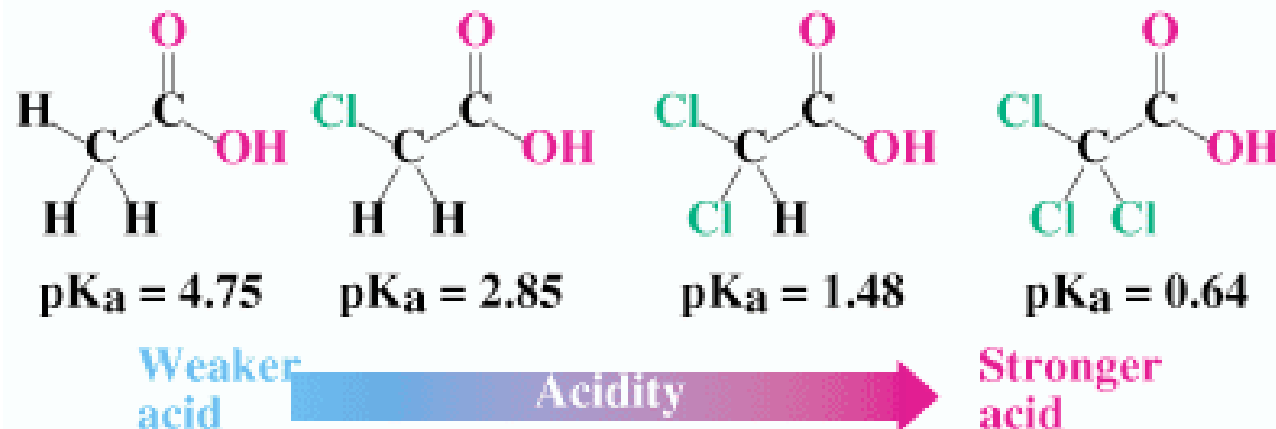



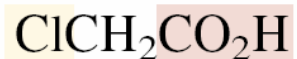
TABLE 20.4 Acidity of Some Carboxylic Acids

Structure	K_a	pK_a
F_3CCO_2H	0.59	0.23
FCH_2CO_2H	2.6×10^{-3}	2.59
$ClCH_2CO_2H$	1.4×10^{-3}	2.85
$BrCH_2CO_2H$	2.1×10^{-3}	2.68
ICH_2CO_2H	7.5×10^{-4}	3.12
HCO_2H	1.77×10^{-4}	3.75
$HOCH_2CO_2H$	1.5×10^{-4}	3.83
$C_6H_5CO_2H$	6.46×10^{-5}	4.19
$H_2C=CHCO_2H$	5.6×10^{-5}	4.25
CH_3CO_2H	1.76×10^{-5}	4.75
$CH_3CH_2CO_2H$	1.34×10^{-5}	4.87
CH_3CH_2OH (ethanol) ^a	(10^{-16})	(16)

^aValue for ethanol is shown for reference.



Effect of Substituents on Acidity of Carboxylic Acids



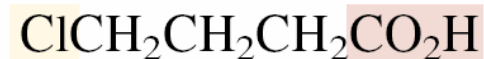
Chloroacetic acid

$$pK_a = 2.9$$



3-Chloropropanoic acid

$$pK_a = 4.0$$



4-Chlorobutanoic acid

$$pK_a = 4.5$$



Weaker acid

$$K_a = 5 \times 10^{-6}$$
$$(pK_a = 5.3)$$



Stronger acid

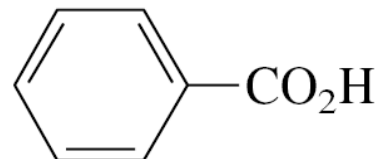
$$K_a = 1.5 \times 10^{-2}$$
$$(pK_a = 1.8)$$



$$(pK_a 4.8)$$



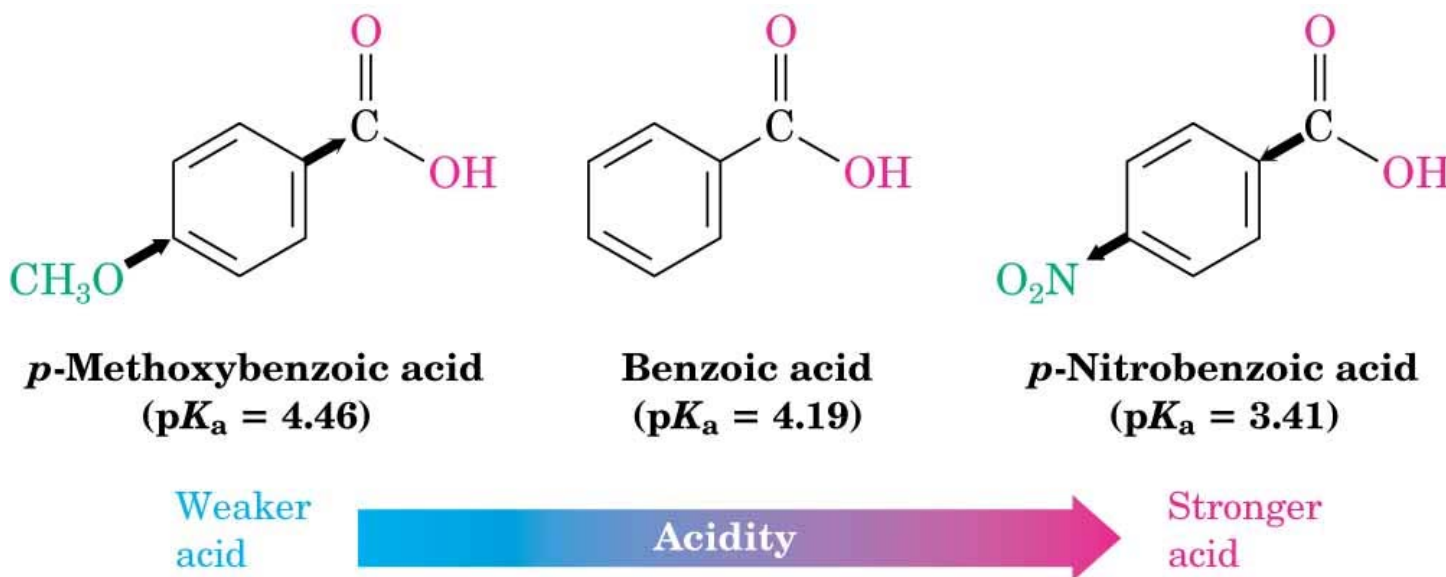
$$(pK_a 4.3)$$



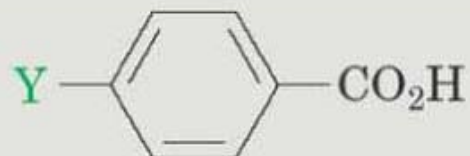
$$(pK_a 4.2)$$

13.6.1.2 Aromatic Substituent Effects

- An electron-withdrawing group ($-\text{NO}_2$) increases acidity by stabilizing the carboxylate anion, and an electron-donating (activating) group (OCH_3) decreases acidity by destabilizing the carboxylate anion



Substituent Effects in Substituted Benzoic Acids

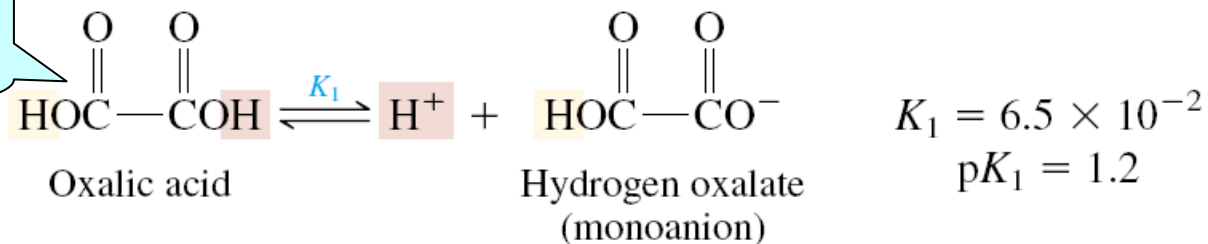


	Y	K_a	pK_a		
<p>Weaker acid</p> <p>Stronger acid</p>	—OH	3.3×10^{-5}	4.48	} Activating groups	
	—OCH ₃	3.5×10^{-5}	4.46		
	—CH ₃	4.3×10^{-5}	4.34		
		—H	6.46×10^{-5}	4.19	
		—Cl	1.0×10^{-4}	4.0	} Deactivating groups
		—Br	1.1×10^{-4}	3.96	
		—CHO	1.8×10^{-4}	3.75	
		—CN	2.8×10^{-4}	3.55	
		—NO ₂	3.9×10^{-4}	3.41	

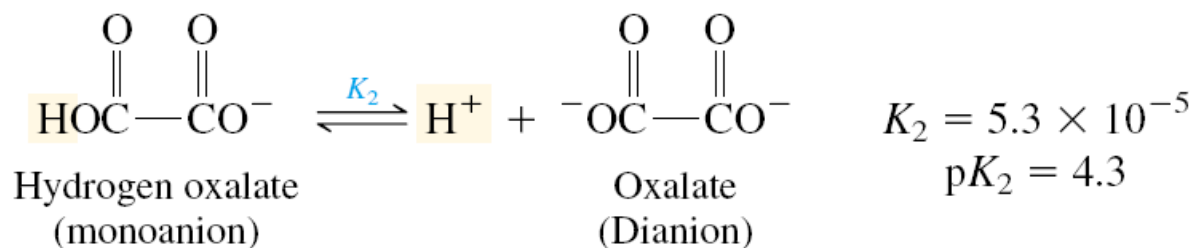
Dicarboxylic Acids

- The first ionization constant of dicarboxylic acids is larger than K_a for monocarboxylic analogs.

electron-withdrawing group



$k_1 > k_2$



$K_1 6.5 \times 10^{-2}$
($\text{p}K_1 1.2$)

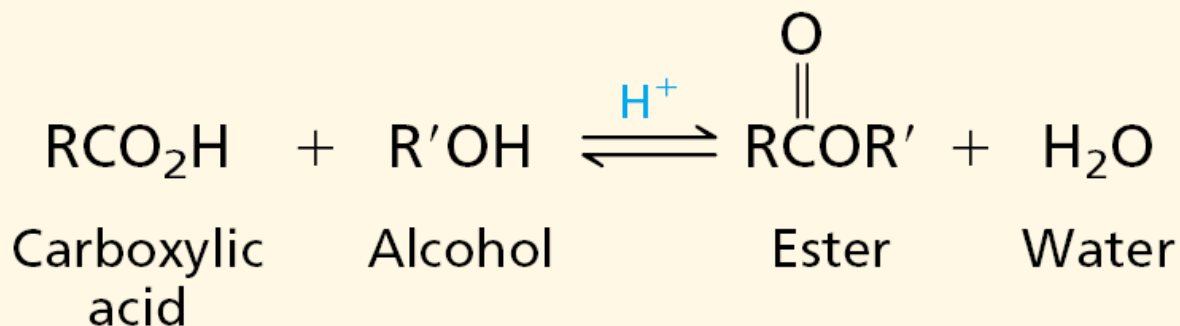


$K_1 1.4 \times 10^{-3}$
($\text{p}K_1 2.8$)

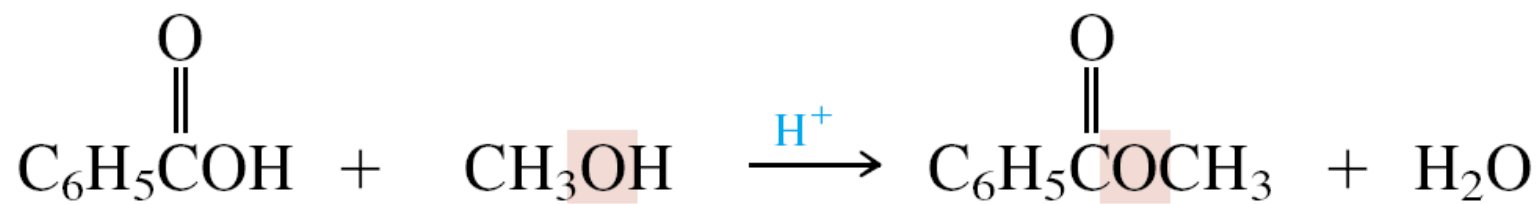
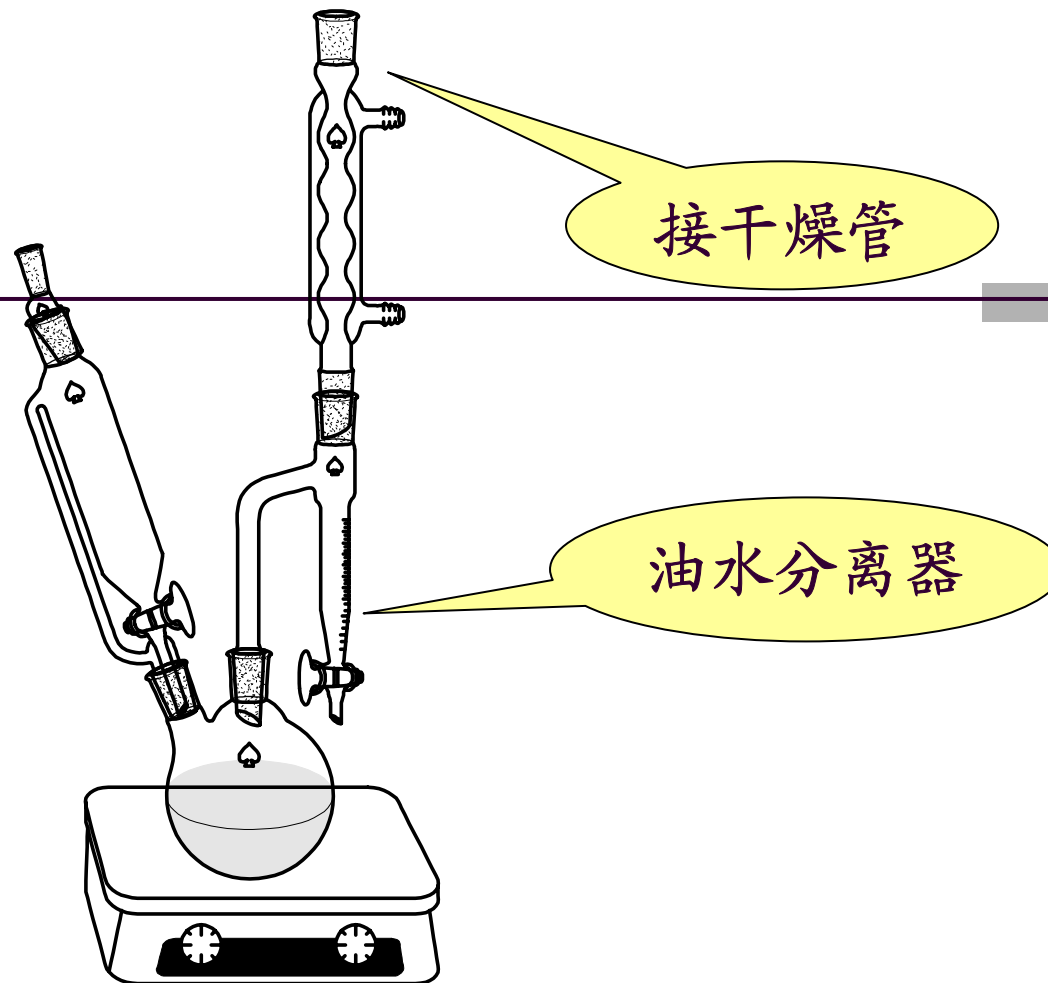


$K_1 3.1 \times 10^{-5}$
($\text{p}K_1 4.3$)

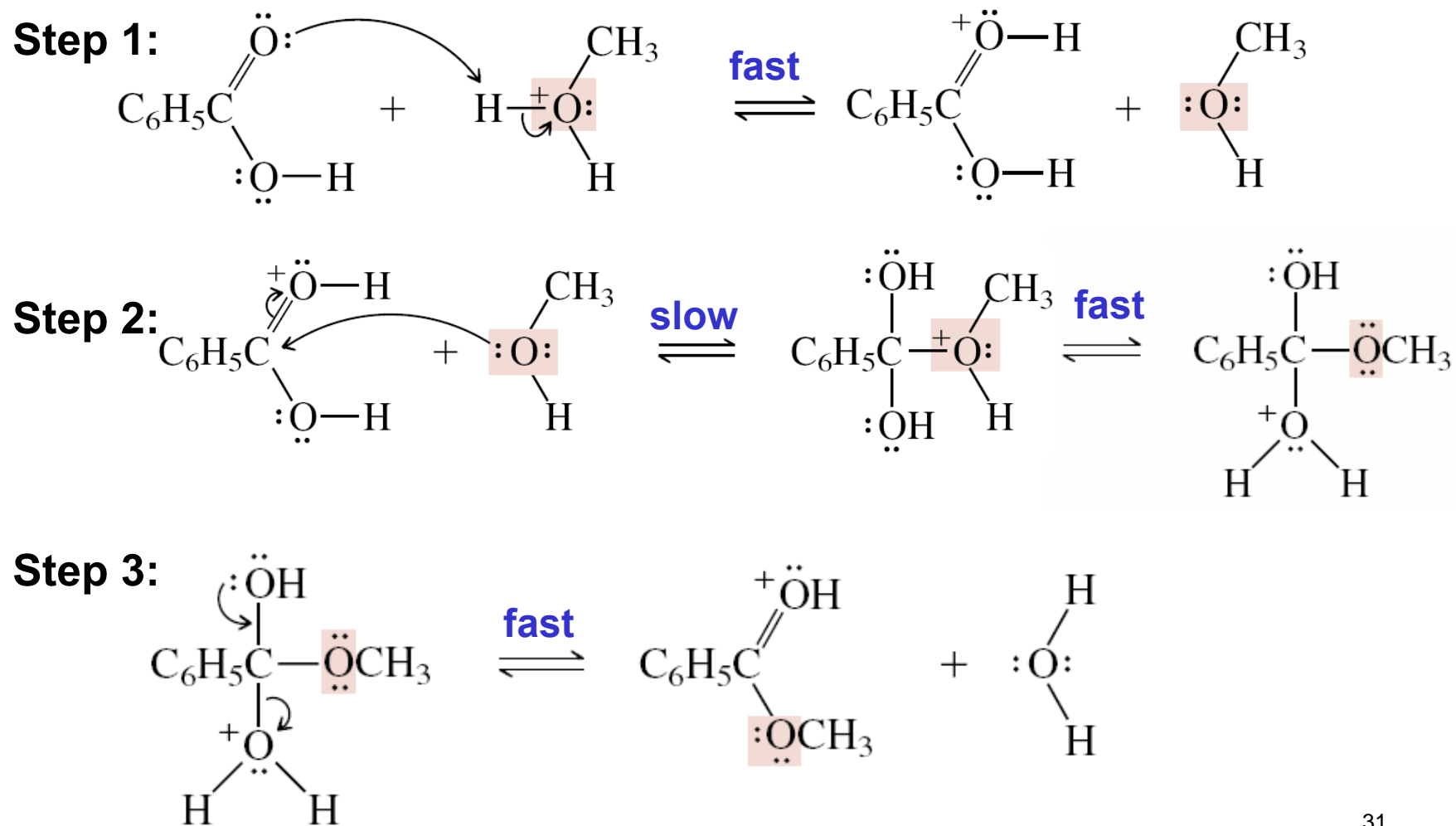
13.6.2 Acid-Catalyzed Esterification



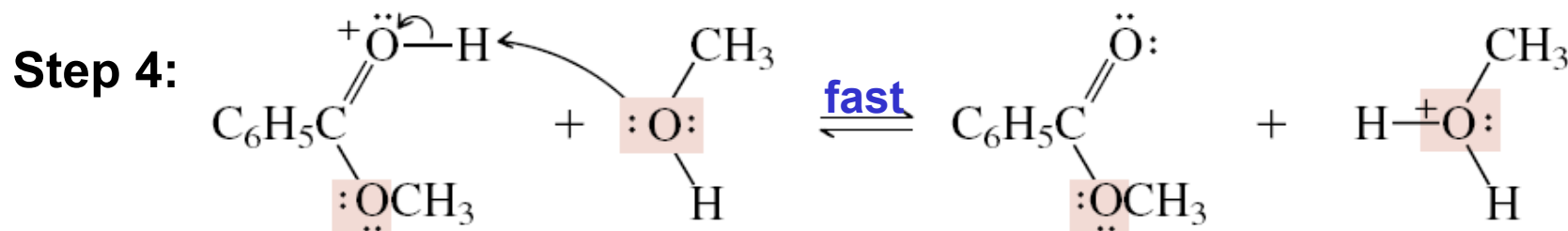
- Acid-catalyzed condensation of an alcohol and a carboxylic acid yields an ester and water and is known as the **Fischer esterification**
- Fischer esterification is reversible
- Two ways to shift the position of equilibrium to favor the formation of ester: (1) using either the alcohol or the carboxylic acid in excess; (2) removing water from the reaction mixture.
- For steric reasons, the order of alcohol reactivity in the Fischer esterification is $\text{CH}_3\text{OH} > \text{primary} > \text{secondary} > \text{tertiary}$.



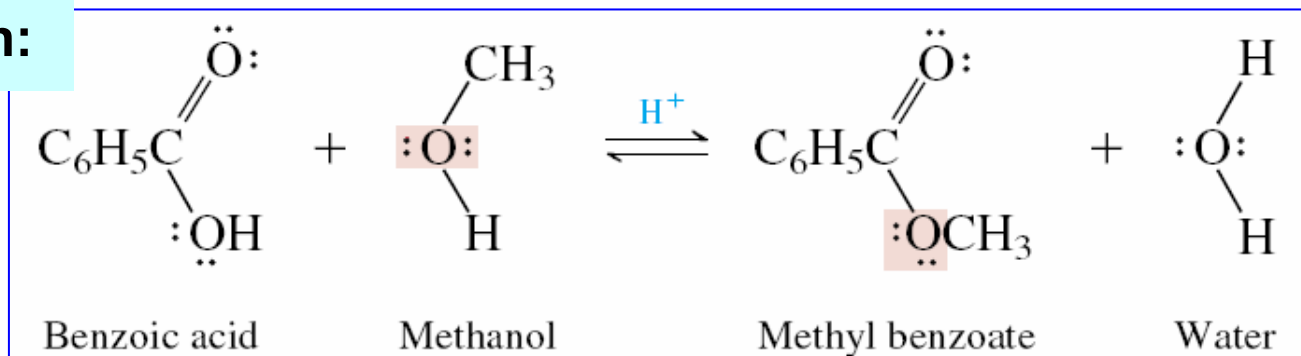
Mechanism of Esterification



Mechanism of Esterification



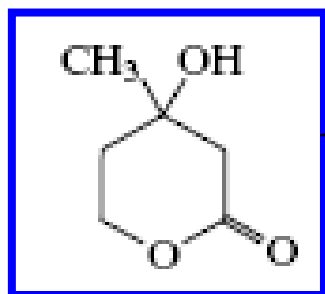
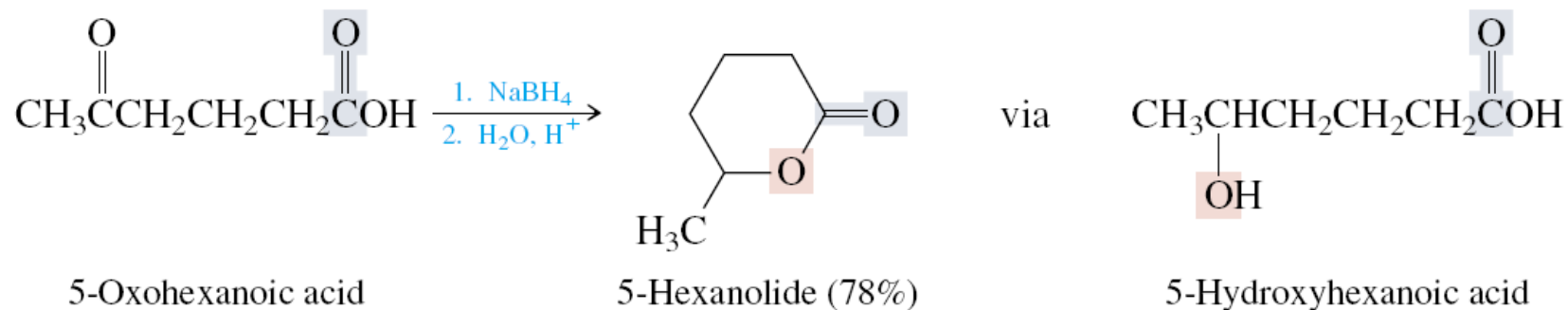
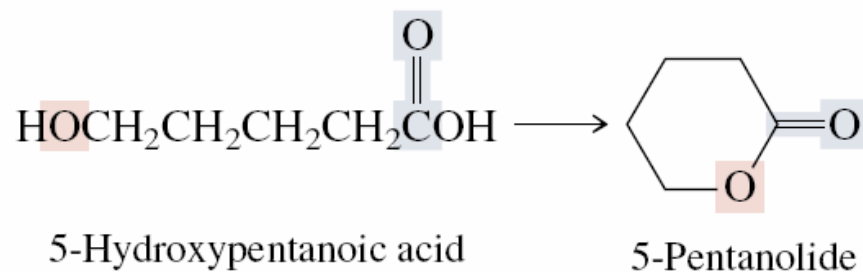
Overall reaction:



- Activation of the carbonyl group by protonation of the carbonyl oxygen
- Nucleophilic addition to the protonated carbonyl to form a tetrahedral intermediate
- Elimination from the tetrahedral intermediate to restore the carbonyl group

Lactones

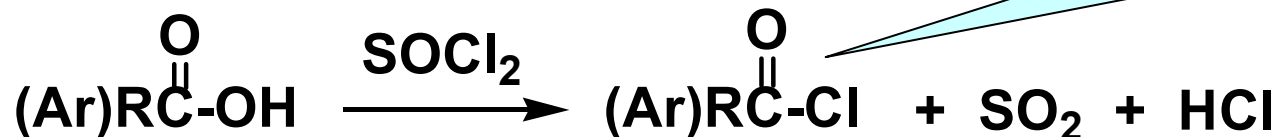
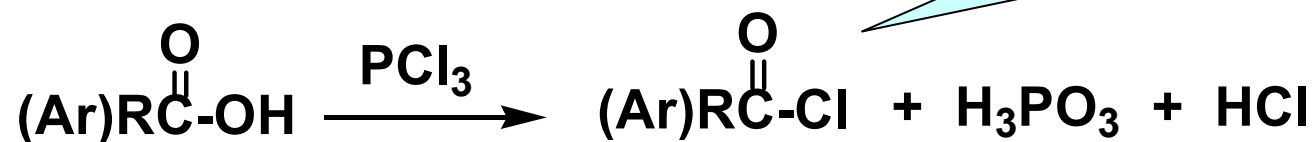
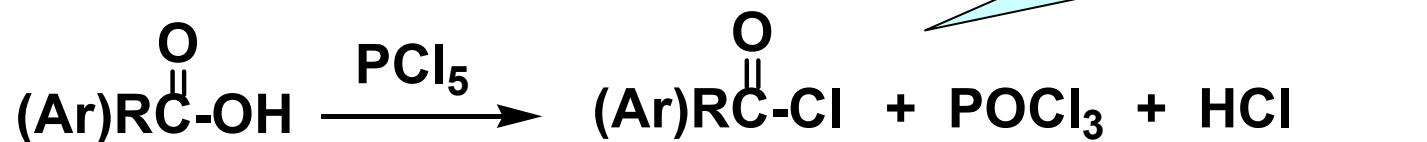
- Intermolecular ester form cyclic esters, called lactones.



an intermediate in the biosynthesis of terpenes and steroids

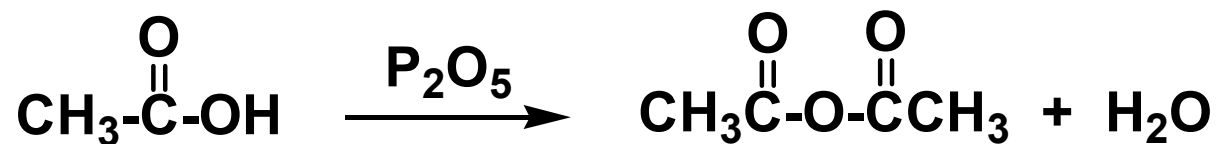
13.6.3 Other substitution of -OH

- Formation of chlorides.

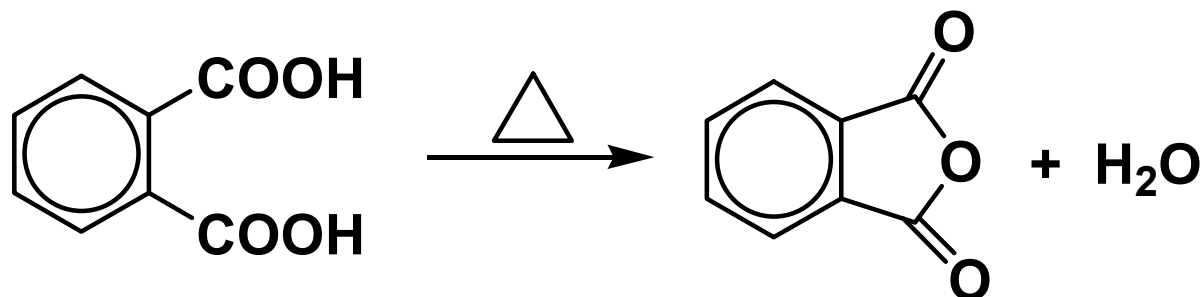
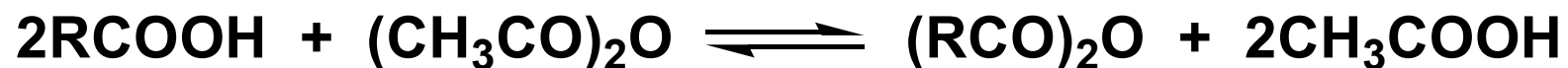


Other substitution of -OH

- Formation of carboxylic acid anhydrides.

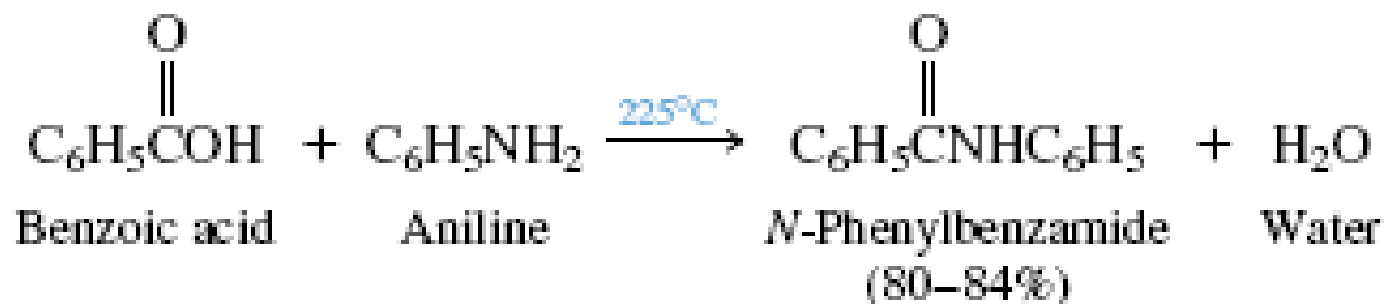
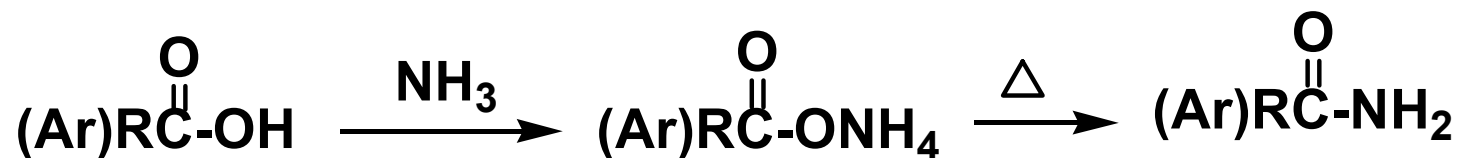


low yield



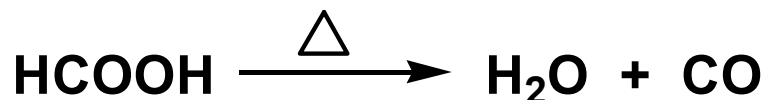
Other substitution of -OH

- Formation of amides—the most stabilized derivatives



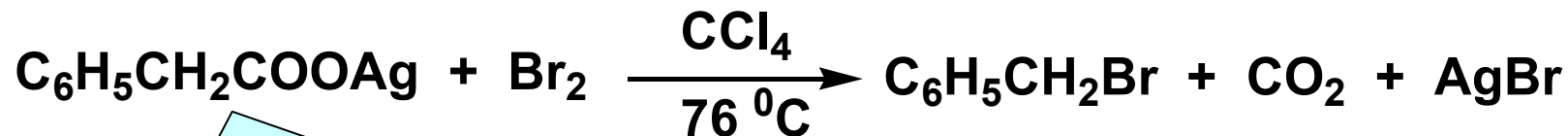
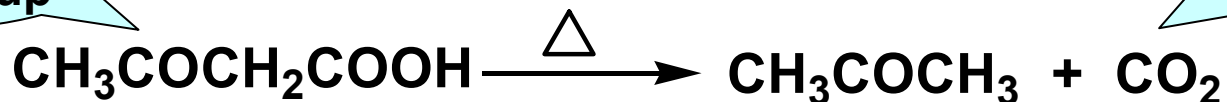
These thermal methods for preparing amides are limited in their generality.

13.6.4 Decarboxylation



electron-
draw group

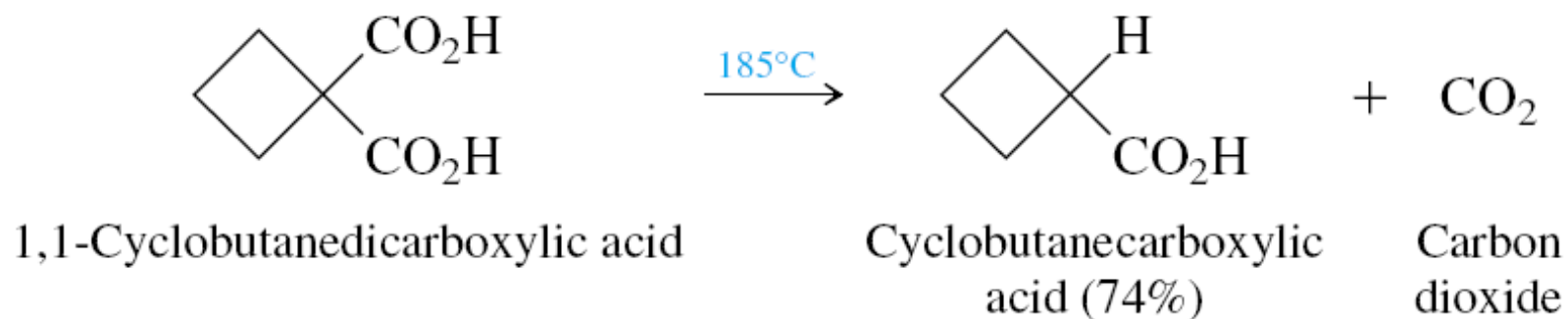
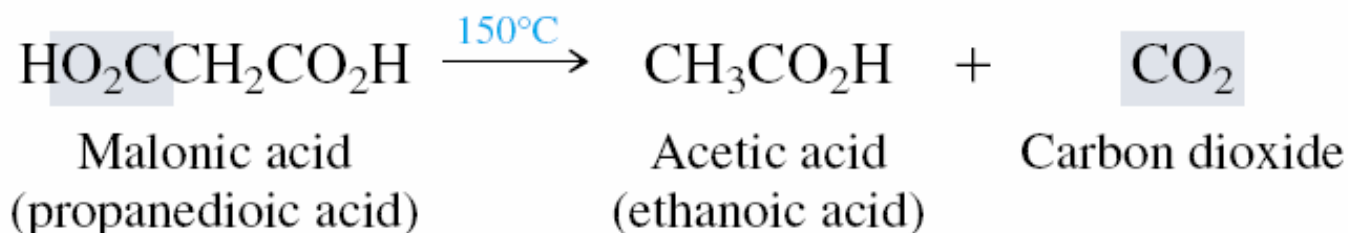
easy reaction



Hunsdiecker reaction

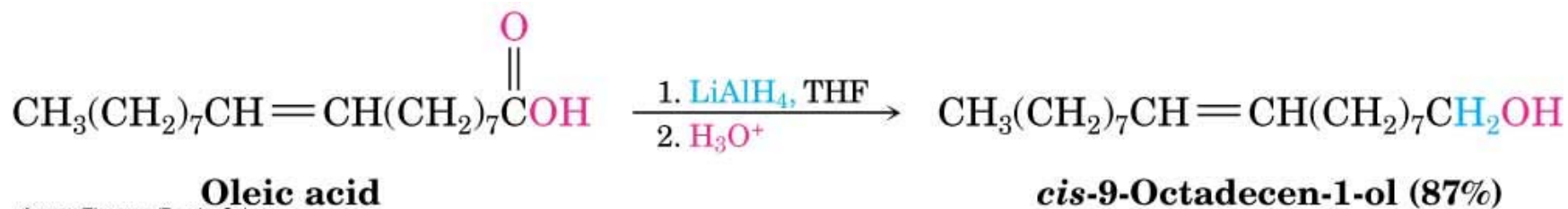
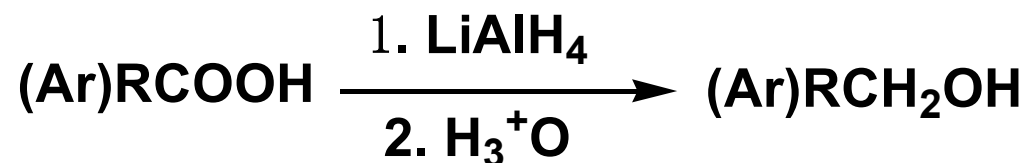
Decarboxylation

- Compounds that readily undergo thermal decarboxylation include those related to malonic acid.



13.6.5 Reduction with Lithium Aluminum Hydride

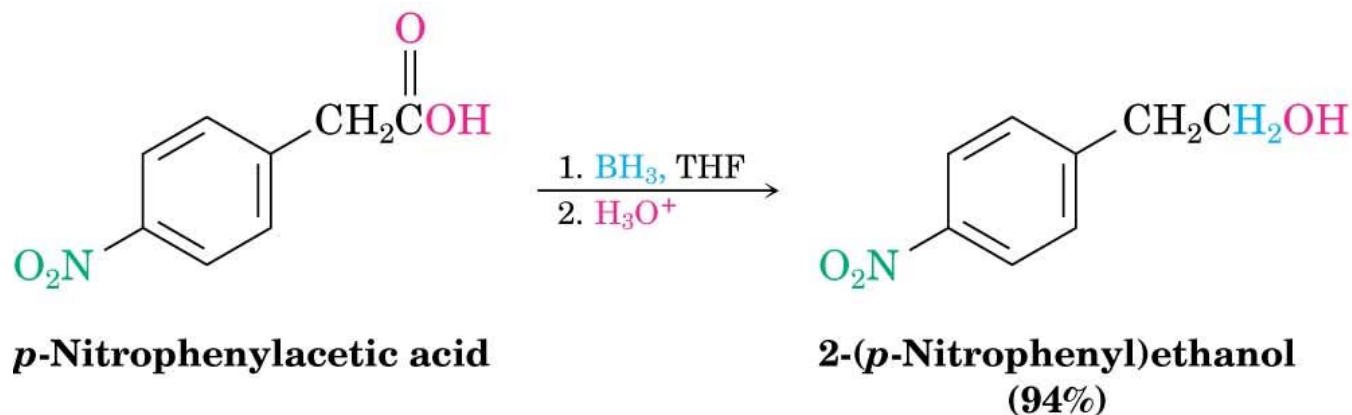
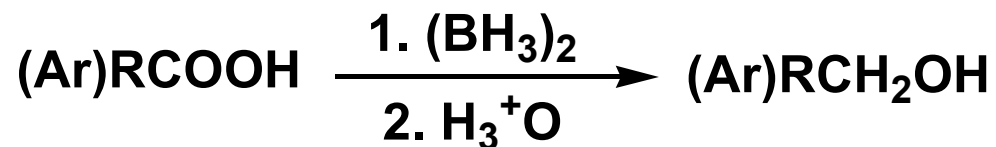
- Reduced by LiAlH_4 to yield primary alcohols.
- The reaction is difficult and often requires heating in tetrahydrofuran solvent to go to completion.



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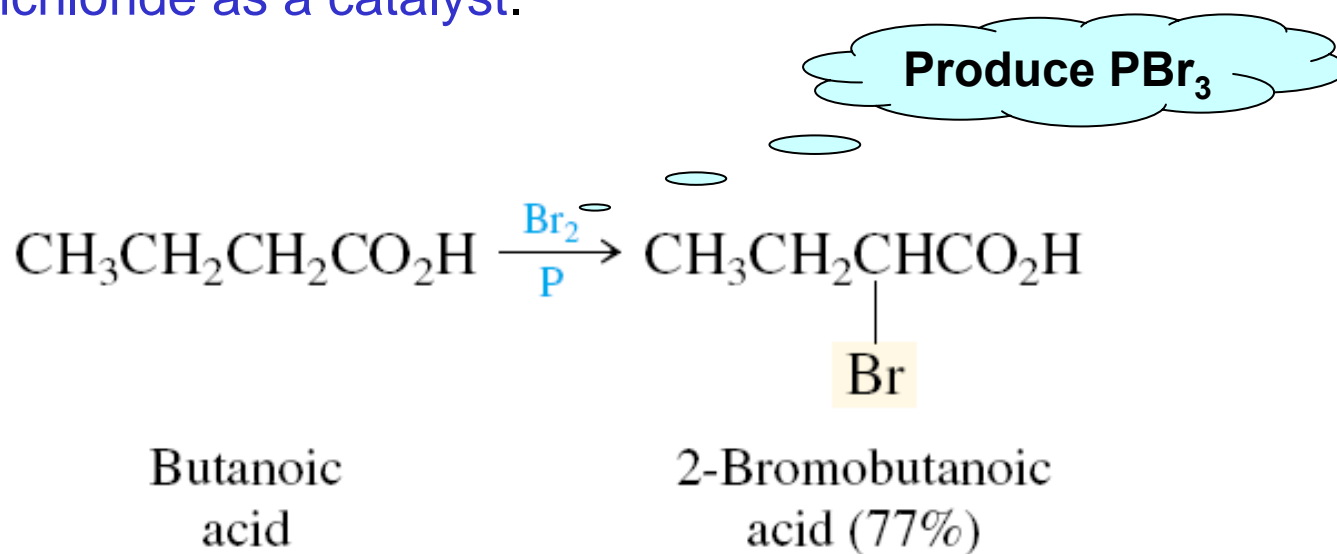
13.6.6 Reduction with Borane

- Borane in tetrahydrofuran (BH₃/THF) converts carboxylic acids to primary alcohols selectively.
- Preferable to LiAlH₄ because of its relative ease, safety, and specificity.
- Borane reacts faster with COOH than it does with NO₂.



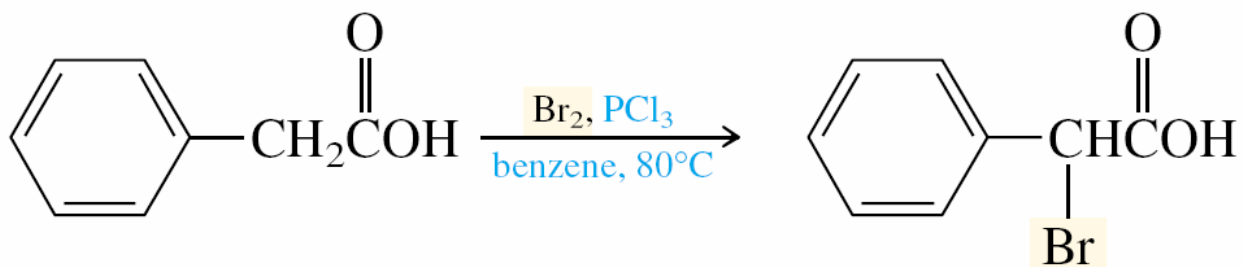
13.7 Substituted Carboxylic Acids

- **α-Halogenation:** treatment of the carboxylic acid with bromine in the presence of a small amount of phosphorus trichloride as a catalyst.



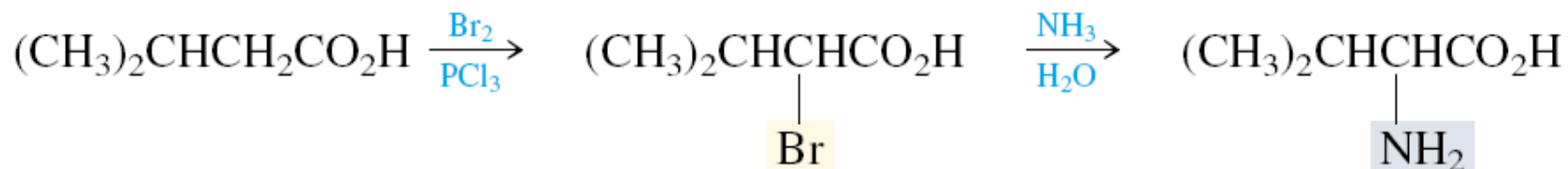
Hell-Volhard-Zelinsky Reaction

α -Halogenation to other α -substitution



Phenylacetic acid

α -Bromophenylacetic acid
(60–62%)

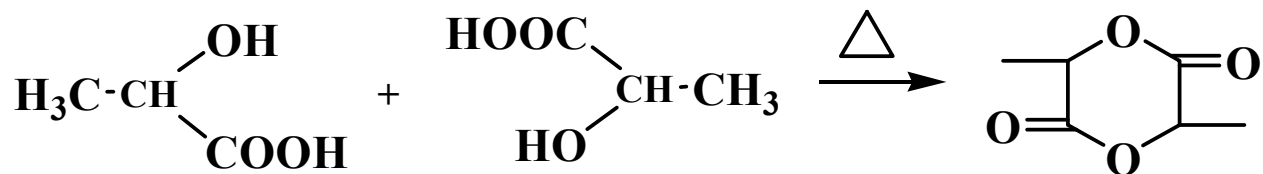
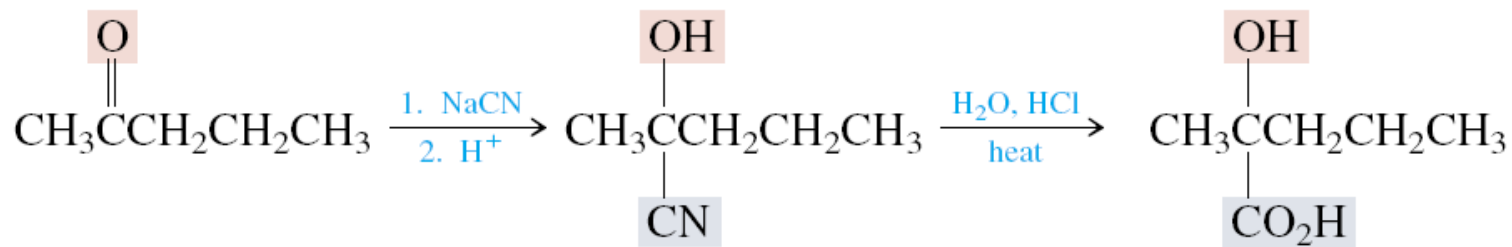
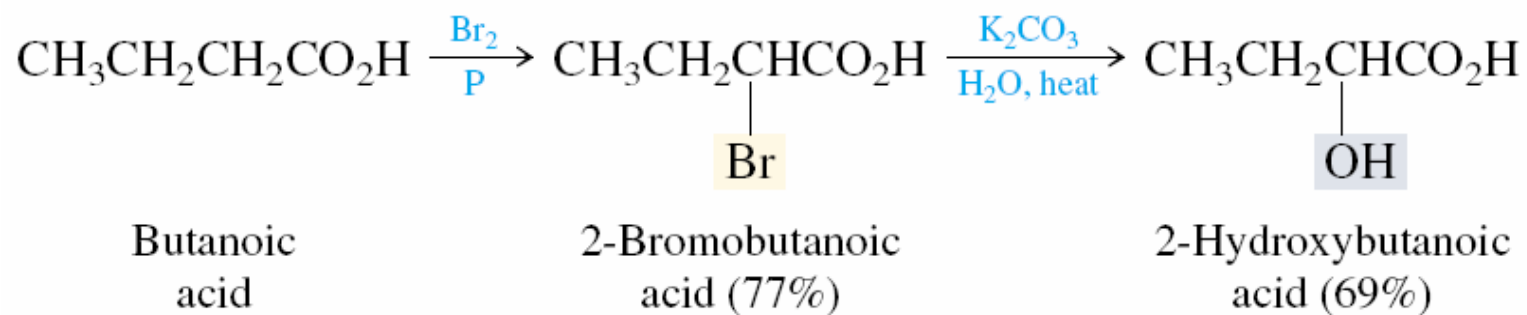


3-Methylbutanoic acid

2-Bromo-3-methylbutanoic acid (88%)

2-Amino-3-methylbutanoic acid (48%)

■ α -hydroxylation



■ β -hydroxylation: Reformatsky reaction

