Chapter 19: Carboxylic Acids
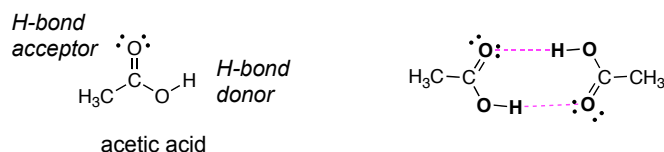
19.1: Carboxylic Acid Nomenclature (please read)

19.2: Structure and Bonding (please read)

19.3: Physical Properties. The carboxylic acid functional group contains both a hydrogen bond donor (-OH) and a hydrogen bond acceptor (C=O).
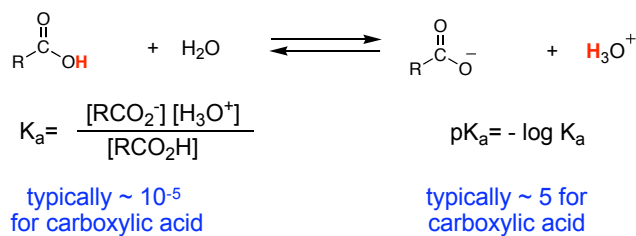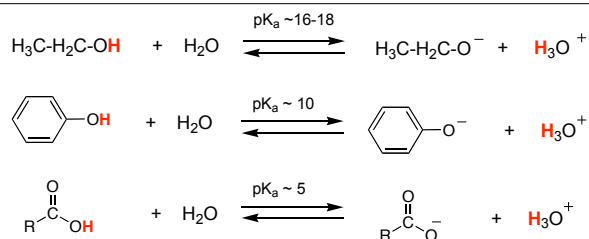Carboxylic acids exist as hydrogen bonded dimers.

H-bond acceptor   *H-bond donor*

acetic acid

19.4: Acidity of Carboxylic Acids. The pK_a of carboxylic acids typically ~ 5. They are significantly more acidic than water or alcohols.

Bronsted Acidity (Ch. 1.13): Carboxylic acids transfer a proton to water to give H_3O^+ and carboxylate anions, RCO_2^-

$$K_a = \frac{[RCO_2^-]\,[H_3O^+]}{[RCO_2H]}$$

$$pK_a = -\log K_a$$

typically ~ 10^{-5} for carboxylic acid

typically ~ 5 for carboxylic acid

	CH_3CH_3	CH_3CH_2OH	PhOH	CH_3CO_2H	HCl
pK_a	~50-60	16	10	4.7	-7

Increasing acidity

$$H_3C\text{-}H_2C\text{-O}\textbf{H} \quad + \quad H_2O \quad \xrightleftharpoons{\quad pK_a \sim 16\text{-}18 \quad} \quad H_3C\text{-}H_2C\text{-O}^- \quad + \quad \textbf{H}_3O^+$$

(phenol) $\text{OH} \quad + \quad H_2O \quad \xrightleftharpoons{\quad pK_a \sim 10 \quad} \quad$ (phenolate) $\text{O}^- \quad + \quad \textbf{H}_3O^+$

$$R\text{-C(=O)-O}\textbf{H} \quad + \quad H_2O \quad \xrightleftharpoons{\quad pK_a \sim 5 \quad} \quad R\text{-C(=O)-O}^- \quad + \quad \textbf{H}_3O^+$$
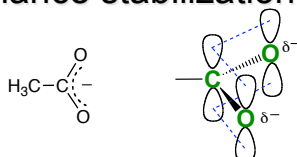
The greater acidity of carboxylic acids is attributed to greater stabilization of carboxylate ion by:

a. Inductive effect of the C=O group

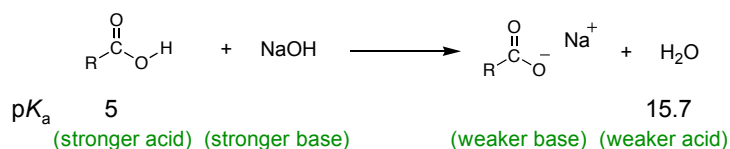b. Resonance stabilization of the carboxylate ion
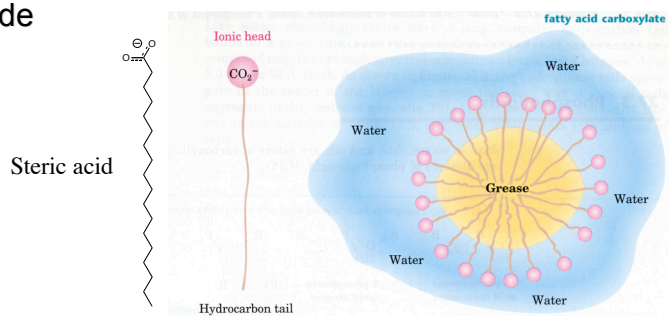
4 π-electrons delocalized over three p-prbitals

C-O bond length of a carboxylates are the same

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19.5: Salts of Carboxylic Acids. Carboxylic acids react with base to give carboxylate salts.

$$R\text{-C(=O)-O-H} \quad + \quad NaOH \quad \longrightarrow \quad R\text{-C(=O)-O}^- \ Na^+ \quad + \quad H_2O$$

pK_a 5   15.7

   (stronger acid) (stronger base)   (weaker base) (weaker acid)

Detergents and Micelles: substances with polar (hydrophilic) head groups and hydrophobic tail groups form aggregates in Water with the carboxylate groups on the outside and nonpolar tails on the inside

Steric acid

Ionic head

CO_2^-

Water

Water

Grease

Water

Water

Water

fatty acid carboxylate

Hydrocarbon tail

19.6: Substituents and Acid Strength. Substituents on the α-carbon influence the pK_a of carboxylic acids largely through inductive effects. Electron-withdrawing groups increase the acidity (lower pK_a) and electron-donating groups decrease the acidity (higher pK_a). (see table 19.2, p. 800)
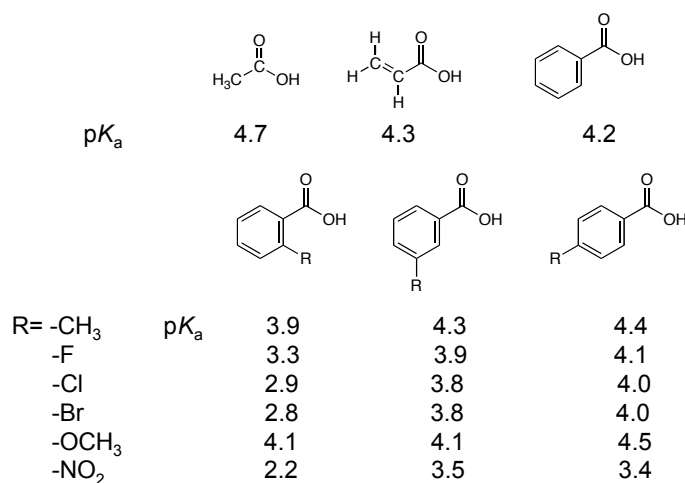

pK_a	4.7	2.9	1.3	0.9

pK_a	4.9	5.1	4.8	4.9	4.7
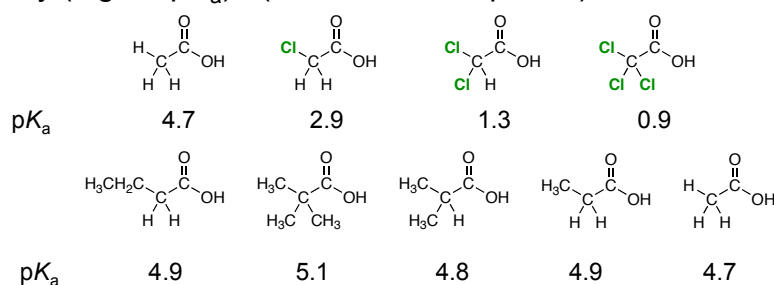
Inductive effects work through σ-bonds, and the effect falls off dramatically with distance

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|			
pK_a	4.9	4.5	4.1	2.8
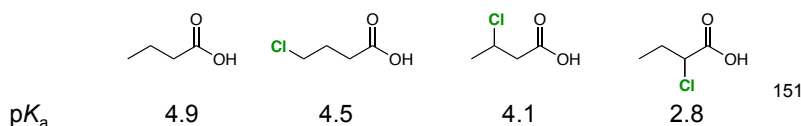
19.7: Ionization of Substituted Benzoic Acids. The charge of the carboxylate ion cannot be delocalize into the aromatic ring. Electron-donating groups decrease the acidity. Electron-withdrawing groups increase the acidity. (Table 19.3, p. 802)


pK_a	4.7	4.3	4.2

R=	pK_a			
-CH$_3$		3.9	4.3	4.4
-F		3.3	3.9	4.1
-Cl		2.9	3.8	4.0
-Br		2.8	3.8	4.0
-OCH$_3$		4.1	4.1	4.5
-NO$_2$		2.2	3.5	3.4

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19.8: Dicarboxylic Acids. one carboxyl group acts as an electron-withdrawing group toward the other and lowers its pKa; effect decreases with increasing separation
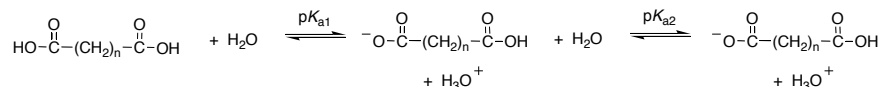
|	pK_{a1}	pK_{a2}
Oxalic acid (n= 0)	1.2	4.2
Malonic acid (n= 1)	2.8	5.7
Succinic acid (n=2)	4.2	5.6
Glutaric acid (n=3)	4.3	5.7
Adipic acid (n=4)	4.4	5.4
Pimelic acid (n=5)	4.7	5.6

19.9: Carbonic Acid (please read)

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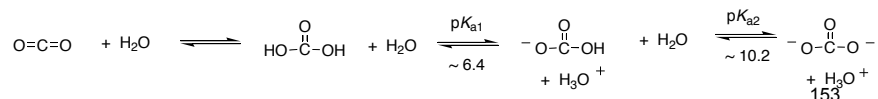
19.10: Sources of Carboxylic Acids. Summary of reaction from previous chapters that yield carboxylic acids (Table 19.4, p. 805)

a. Side-chain oxidation of alkylbenzene to give benzoic acid derivatives (Ch. 11.13): reagent: $KMnO_4$

b. Oxidation of primary alcohols (Ch. 15.10)
   reagent: $H_2CrO_4/H_2Cr_2O_7$

c. Oxidation of aldehydes (Ch. 17.15)
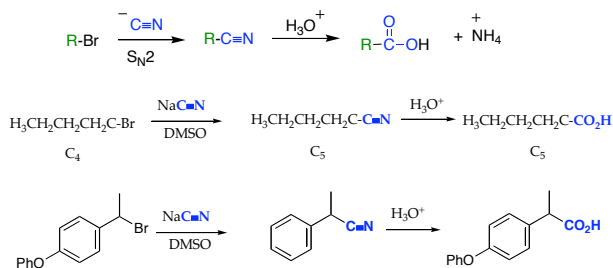   reagent: $H_2CrO_4/H_2Cr_2O_7$

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19.11: Synthesis of Carboxylic Acids by the Carboxylation of Grignard Reagents. Conversion of an alkyl or aryl Grignard reagent to a carboxylic acid with an addition carbon (the CO_2H group). The CO_2H group is derived from CO_2.

R-Br $\xrightarrow{\text{Mg(0)}}$ R-MgBr $\xrightarrow{CO_2}$ R–C(=O)–O⁻ + MgBr $\xrightarrow{H_3O^+}$ R–C(=O)–OH
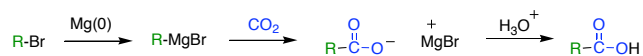
Grignard reagents are strong bases and strong nucleophiles and Are incompatible with acidic (alcoholc, thiols, amines, carboxlic acid, amides,) or electrophilic (aldehydes, ketones, esters, nitrile, halides) groups.

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19.12: Synthesis of Carboxylic Acids by the Preparation and Hydrolysis of Nitriles. Cyanide ion is an excellent nucleophile and will react with 1° and 2° alkyl halides and tosylates to give nitriles. This reaction add one carbon. The nitrile Can be hydrolyzed to a carboxylic acid
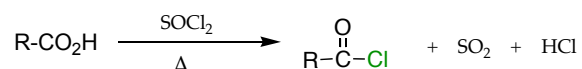
R-Br $\xrightarrow[\text{S}_N2]{^-C\equiv N}$ R-C≡N $\xrightarrow{H_3O^+}$ R–C(=O)–OH + NH₄⁺

$H_3CH_2CH_2CH_2C$-Br $\xrightarrow[\text{DMSO}]{\text{NaC}\equiv\text{N}}$ $H_3CH_2CH_2CH_2C$-C≡N $\xrightarrow{H_3O^+}$ $H_3CH_2CH_2CH_2C$-CO_2H
C₄   C₅   C₅

PhO— (CH(CH₃)Br) $\xrightarrow[\text{DMSO}]{\text{NaC}\equiv\text{N}}$ C≡N $\xrightarrow{H_3O^+}$ PhO— CO_2H

Cyanohydrins (Ch. 17.7) are hydrolyzed to α-hydroxy-carboxylic acids.

$\xrightarrow{\text{NaC}\equiv\text{N}}$ HO CN $\xrightarrow{H_3O^+}$ HO CO_2H
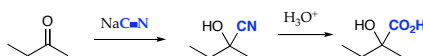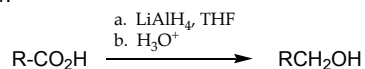
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19.13: Reactions of Carboxylic Acids: A Review and Preview.

a. Conversion to acid chlorides (Ch. 12.7). Reagent: $SOCl_2$

$$R\text{-}CO_2H \xrightarrow[\Delta]{SOCl_2} R-\overset{\overset{\displaystyle O}{\|}}{C}-Cl \quad + \quad SO_2 \quad + \quad HCl$$

b. Reduction to a 1° alcohol (Ch. 15.3). Reagent: $LiAlH_4$
   Carboxylic acids are reduced to 1° alcohols by LAH, but not $NaBH_4$.

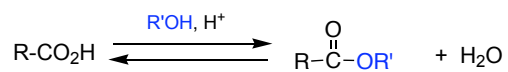$$R\text{-}CO_2H \xrightarrow[\text{b. } H_3O^+]{\text{a. } LiAlH_4,\ THF} RCH_2OH$$

c. Acid-catalyzed esterification (Ch. 15.8)
   Reagent: R'OH, H+ ($-H_2O$)

$$R\text{-}CO_2H \underset{}{\overset{R'OH,\ H^+\ (-H_2O)}{\rightleftarrows}} R-\overset{\overset{\displaystyle O}{\|}}{C}-OR'$$
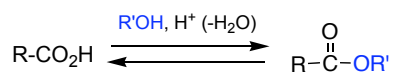
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19.14: Mechanism of Acid-Catalyzed Esterification.
Fischer Esterification (Fig. 19.1, p. 809-810)

$$R\text{-}CO_2H \underset{}{\overset{R'OH,\ H^+}{\rightleftarrows}} R-\overset{\overset{\displaystyle O}{\|}}{C}-OR' \quad + \quad H_2O$$
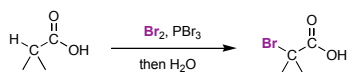
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19.15: Intramolecular Ester Formation: Lactones. Lactones are cyclic esters derived from the intramolecular esterification of hydroxy-carboxylic acids. 4-Hydroxy and 5-hydroxy acids cyclize readily to form 5- and 6-membered ring (γ and δ) lactones.
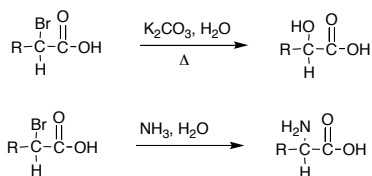
HO-CH$_2$-CH$_2$-CH$_2$-C-OH $\longrightarrow$ [structure] + H$_2$O

γ-butyrolactone

HO-CH$_2$-CH$_2$-CH$_2$CH$_2$-C-OH $\longrightarrow$ [structure] + H$_2$O

γ-valerolactone
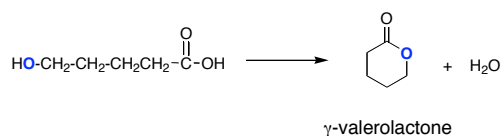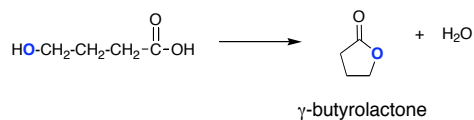
19.16: α-Halogenation of Carboxylic Acids: The Hell-Volhard-Zelinsky Reaction.

[structure] $\xrightarrow[\text{then } H_2O]{\text{Br}_2, \text{PBr}_3}$ [structure]

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Mechanism of α-halogenation goes through an acid bromide intermediate. The acid bromide enolizes more readily than the carboxylic acid. Mechanism is analogous to the α-halogenation of aldehydes and ketones

The α-halo carboxylic acid can undergo substitution to give α-hydroxy and α -amino acids.

R-C-C-OH $\xrightarrow[\Delta]{\text{K}_2\text{CO}_3, \text{H}_2\text{O}}$ R-C-C-OH

R-C-C-OH $\xrightarrow{\text{NH}_3, \text{H}_2\text{O}}$ R-C-C-OH

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19.17: Decarboxylation of Malonic Acid and Related Compounds. Carboxylic acids with a carbonyl or nitrile group at the β-position will decarboxylate (lose CO_2) upon heating

malonic acid

β-keto-acid
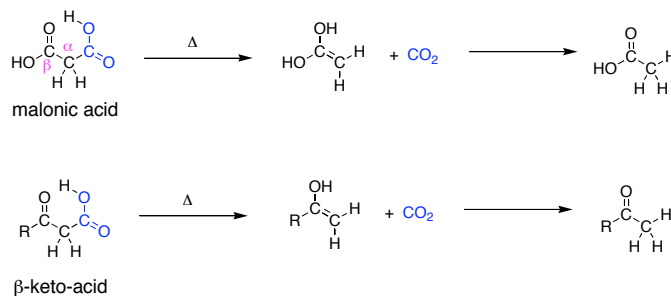
Decarboxylation initially leads to an enol of the β-carbonyl group. This is a key step in the *malonic acid synthesis* (Ch. 21.8) and the *acetoacetic ester synthesis* (Ch. 21.7).

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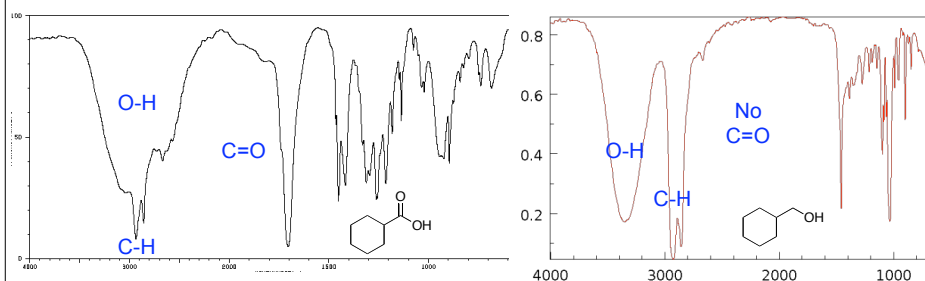**19.18: Spectroscopic Analysis of Carboxylic Acids**
Infrared Spectroscopy
Carboxylic acids:
> Very broad O-H absorption between 2500 - 3300 cm^{-1}
>> usually broader than that of an alcohol
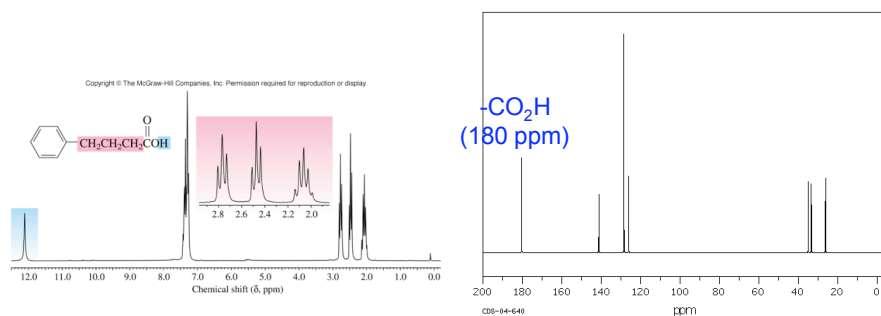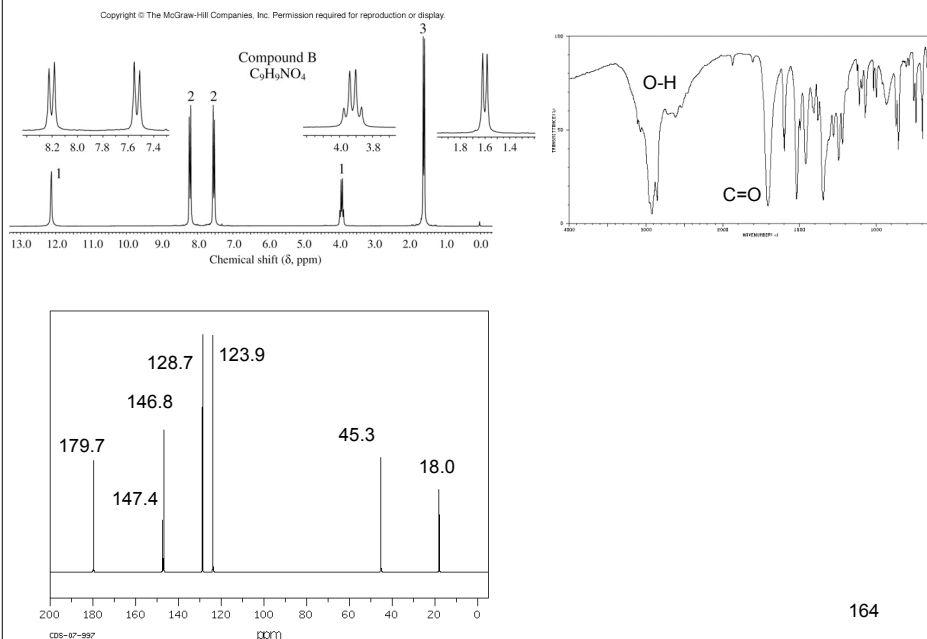> Strong C=O absorption bond between 1700 - 1730 cm^{-1}

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¹H NMR: The -CO₂**H** proton is a broad singlet near δ ~12. When D₂O is added to the sample the -CO₂**H** proton is replaced by D causing the resonance to disappear (same for alcohols). The -CO₂**H** proton is often not observed.

¹³C NMR: The chemical shift of the carbonyl carbon in the ¹³C spectrum is in the range of ~165-185. This range is distinct from the aldehyde and ketone range (~190 - 220)

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problem 19.34b

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