

Organic Chemistry, *Fourth Edition*

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Chapter 19 Lecture Outline

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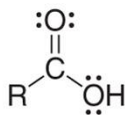
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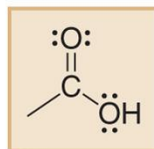
Carboxylic Acid Structure

- **Carboxylic acids** are compounds containing a carboxy group (COOH).
- The structure of carboxylic acids is often abbreviated as RCOOH or RCO₂H, but keep in mind that the central carbon atom of the functional group is doubly bonded to one oxygen atom and singly bonded to another.

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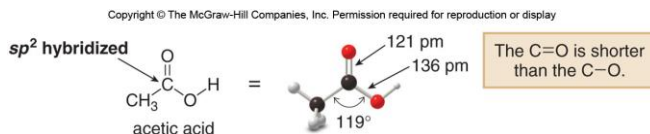
carboxylic acid



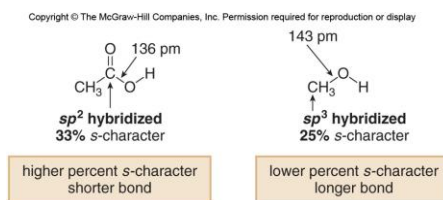
carboxy group

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Bonds in Carboxylic Acids



- The C–O single bond of a carboxylic acid is shorter than the C–O bond of an alcohol.
- This can be explained by looking at the hybridization of the respective carbon atoms.



- Because oxygen is more electronegative than either carbon or hydrogen, the C–O and O–H bonds are polar.

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Naming Carboxylic Acids

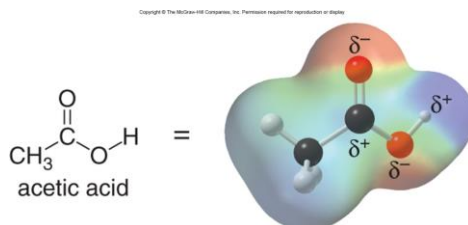
- In the IUPAC system, carboxylic acids are identified by a suffix added to the parent name of the longest chain with different endings being used depending on whether the carboxy group is bonded to a chain or a ring.
 - If the COOH is bonded to a chain, find the longest chain containing the COOH, and change the “e” ending of the parent alkane to the suffix “oic acid”.
 - If the COOH is bonded to a ring, name the ring and add the words “carboxylic acid”.
 - Number the carbon chain or ring to put the COOH group at C1, but omit this number from the name.
 - Apply all the other usual rules of nomenclature.

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Electrostatic Potential Plot of Acetic Acid

- Acetic acid contains two electron-rich oxygen atoms.
- Its carbonyl carbon and hydroxy hydrogen are both electron deficient.

Figure 19.1



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Table 19.1 Common Names for Some Simple Carboxylic Acids

Number of C atoms	Structure	Parent name	Common name
1		form-	formic acid
2		acet-	acetic acid
3		propion-	propionic acid
4		butyr-	butyric acid
5		valer-	valeric acid
6		capro-	caproic acid
		benzo-	benzoic acid

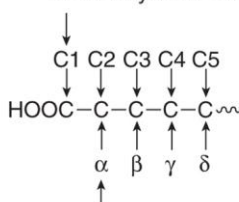
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Common Naming for Carboxylic Acids

- Greek letters are used to designate the location of substituents in common names.
- The carbon adjacent to the COOH is called the α carbon, followed by the β carbon, followed by the γ carbon, the δ carbon and so forth down the chain.
- The last carbon in the chain is sometimes called the Ω carbon.
- The α carbon in the common system is numbered C2 in the IUPAC system.

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IUPAC system: Start numbering here.



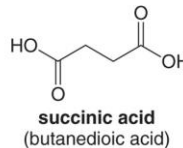
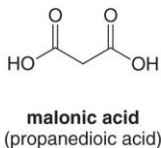
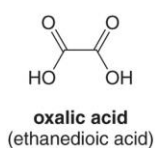
Common system: Start lettering here.

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Naming Diacids and Salts

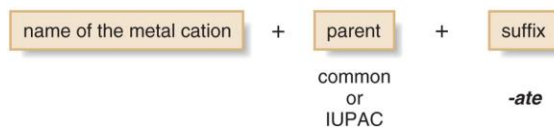
- Compounds containing two carboxy groups are called **diacids**.
- Diacids are named using the suffix **-dioic acid**.

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- Metal salts of carboxylate anions are formed from carboxylic acids in many reactions.
- To name the metal salt of a carboxylate anion, put three parts together:

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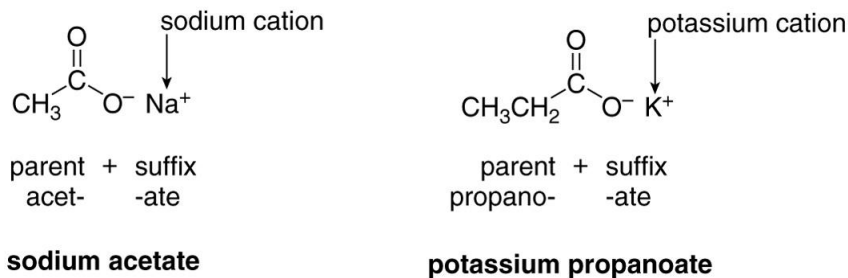


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Naming Metal Salts of Carboxylate Anions

Figure 19.2

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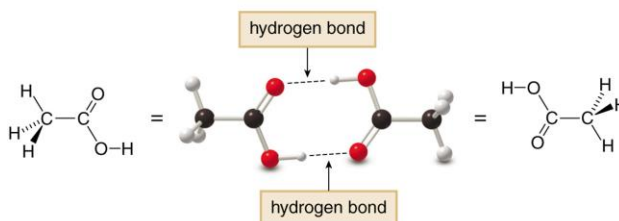
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Hydrogen Bonds Cause Dimers

- Carboxylic acids exhibit dipole–dipole interactions because they have polar C–O and O–H bonds.
- They also exhibit intermolecular hydrogen bonding.
- Carboxylic acids often exist as dimers held together by two intermolecular hydrogen bonds.

Figure 19.3

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Table 19.2 Physical Properties of Carboxylic Acids

Property	Observation
Boiling point and melting point	Carboxylic acids have higher boiling points and melting points than other compounds of comparable molecular weight. $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$ VDW MW = 58 bp 0 °C $\text{CH}_3\text{CH}_2\text{CHO}$ VDW, DD MW = 58 bp 48 °C $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ VDW, DD, HB MW = 60 bp 97 °C CH_3COOH VDW, DD, two HB MW = 60 bp 118 °C  Increasing strength of intermolecular forces Increasing boiling point
Solubility	- Carboxylic acids are soluble in organic solvents regardless of size. - Carboxylic acids having ≤ 5 C's are water soluble because they can hydrogen bond with H_2O (Section 3.4C). - Carboxylic acids having > 5 C's are water insoluble because the nonpolar alkyl portion is too large to dissolve in the polar H_2O solvent. These "fatty" acids dissolve in a nonpolar fat-like environment but do not dissolve in water.

Key: VDW = van der Waals, DD = dipole-dipole, HB = hydrogen bonding, MW = molecular weight

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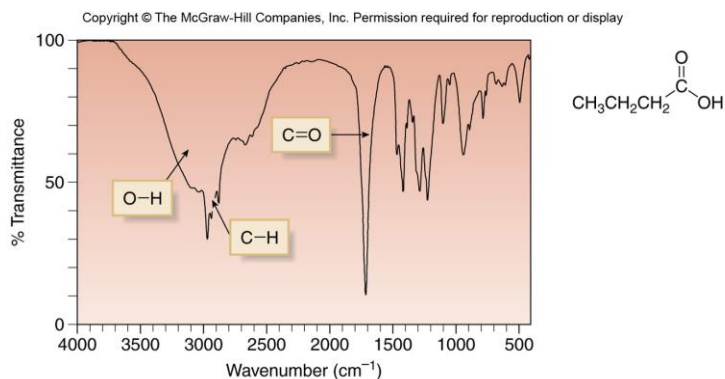
Spectroscopy of Carboxylic Acids

- Carboxylic acids have very characteristic IR and NMR absorptions.
- In the IR:
 - The C=O group absorbs at $\sim 1710\text{ cm}^{-1}$.
 - The O–H absorption occurs from $2500\text{--}3500\text{ cm}^{-1}$.
- In the ^1H NMR:
 - The O–H proton absorbs between $10\text{--}12\text{ ppm}$.
 - The α protons absorb between $2\text{--}2.5\text{ ppm}$.
- In the ^{13}C NMR: the C=O appears at $170\text{--}210\text{ ppm}$.

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IR Spectrum of Butanoic Acid

Figure 19.4

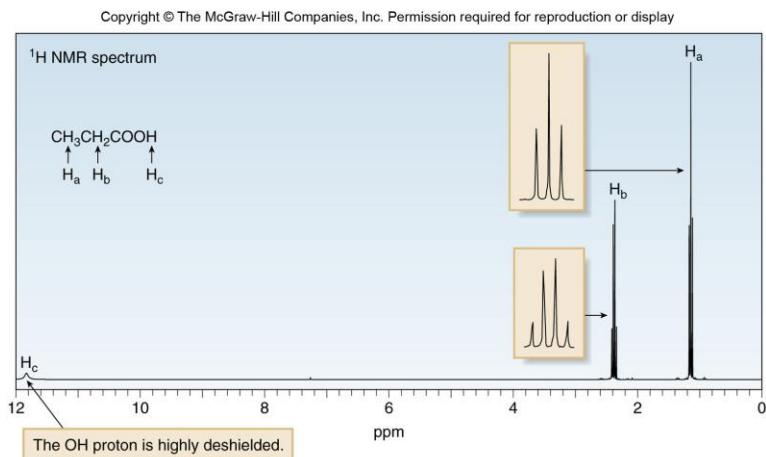


- A strong C=O absorption occurs at 1712 cm^{-1} .
- The broad O-H absorption (2500–3500 cm^{-1}) nearly obscures the C-H peak at ~3000 cm^{-1} .

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^1H NMR Spectra of Propanoic Acid

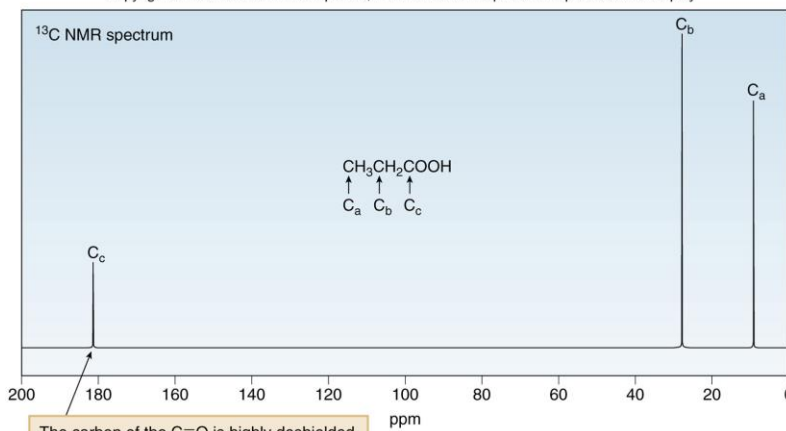
Figure 19.5



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^{13}C NMR Spectra of Propanoic Acid

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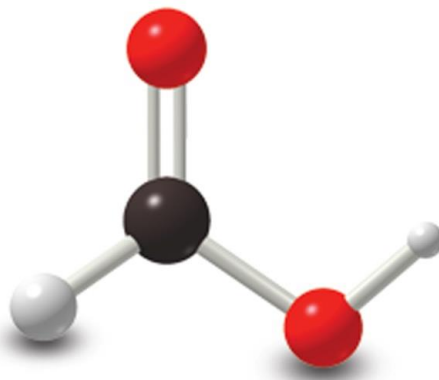
- **^1H NMR spectrum:** There are three signals due to three different kinds of H atoms. The H_a and H_b signals are split into a triplet and quartet, respectively, but the H_c signal is a singlet.
- **^{13}C NMR spectrum:** There are three signals due to three different kinds of carbon atoms.

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Formic Acid

- **Formic acid** is responsible for the sting of some types of ants.
- The name is derived from the Latin word formica, meaning “ant.”

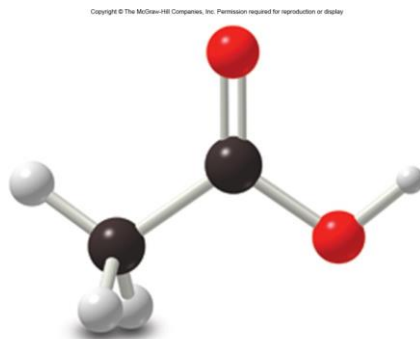
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Acetic Acid

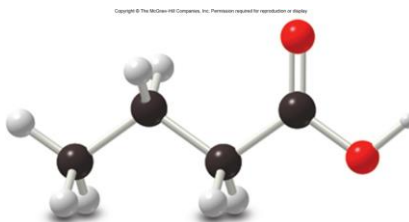
- **Acetic acid** is the sour component of vinegar.
- The air oxidation of ethanol to acetic acid is the process that makes “bad” wine taste sour.
- Acetic acid is an industrial starting material for polymers used in paints and adhesives.



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Butanoic Acid

- **Butanoic acid** is an oxidation product that contributes to the disagreeable smell of body odor.
- Its common name, butyric acid, is derived from the Latin word butyrum, meaning “butter,” because butyric acid gives rancid butter its peculiar odor and taste.



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Carboxylic Acids in Nature

- Oxalic acid and lactic acid are simple carboxylic acids that are quite prevalent in nature.
- **Oxalic acid** occurs naturally in spinach and rhubarb.
- **Lactic acid** gives sour milk its distinctive taste.

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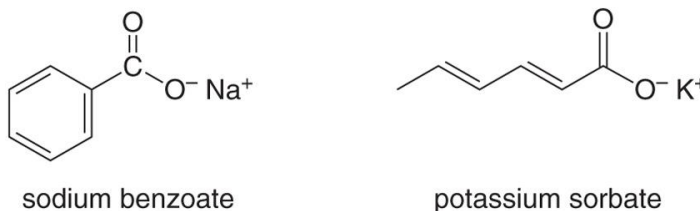


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Interesting Salts of Carboxylic Acids

- Salts of carboxylic acids are commonly used as preservatives.
- **Sodium benzoate** is a fungal growth inhibitor and is also used as a preservative in soft drinks.
- **Potassium sorbate** is an additive that prolongs the shelf-life of baked goods and other foods.

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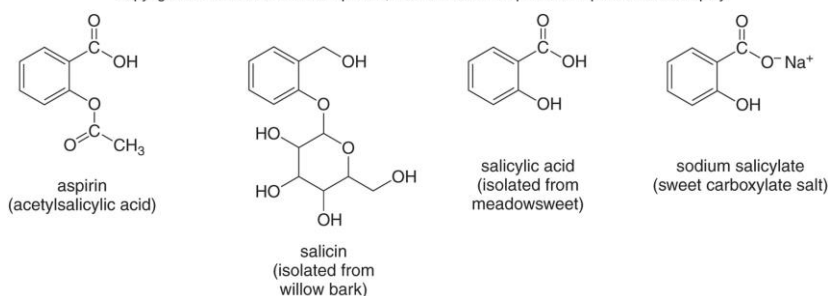


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Aspirin and Related Compounds

- **Aspirin** (acetylsalicylic acid) is a synthetic carboxylic acid, similar in structure to salicin and salicylic acid.
- **Salicin** is a naturally occurring compound isolated from willow bark.
- **Salicylic acid** is found in meadowsweet.

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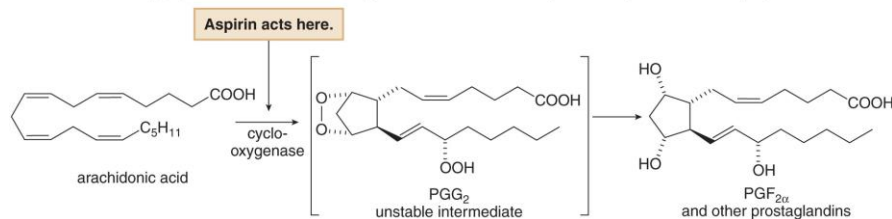


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Arachidonic Acid and Prostaglandins

- Aspirin lessens pain and decreases inflammation because it prevents the synthesis of prostaglandins, the compounds responsible for both of these physiological responses.
- Aspirin inactivates cyclooxygenase, an enzyme that converts **arachidonic acid** to PGG₂, an unstable precursor of PGF_{2α} and other prostaglandins.

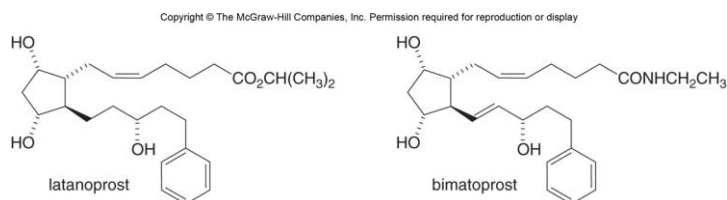
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Prostaglandin Analogues

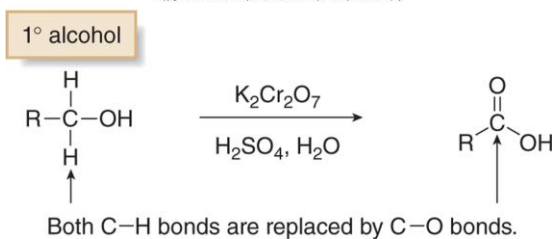
- Prostaglandins have a wide range of biological activity, however their inherent instability often limits their usefulness as drugs.
- More stable analogues with useful medicinal properties have been synthesized.
- **Latanoprost** and **bimatoprost** are prostaglandin analogues used to reduce eye pressure in individuals with glaucoma.



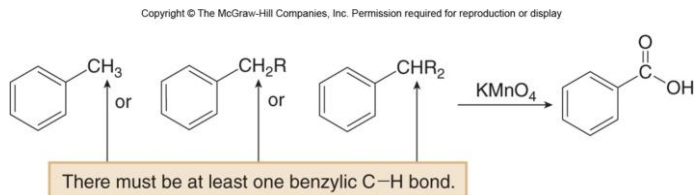
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Preparation of Carboxylic Acids

[1] Oxidation of 1° alcohols



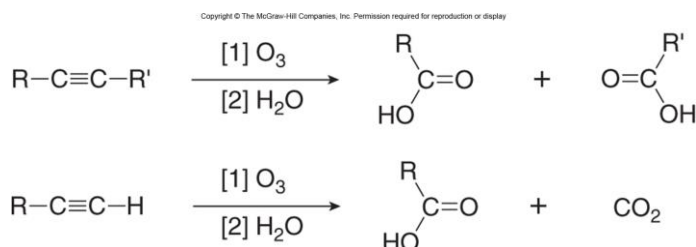
[2] Oxidation of alkyl benzenes



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Preparation of Carboxylic Acids

[3] Oxidative cleavage of alkynes



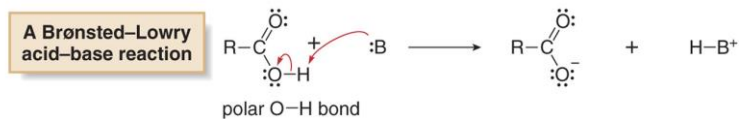
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Acid-Base Reactions of Carboxylic Acids

- The most important reactive feature of a carboxylic acid is its polar O–H bond, which is readily cleaved with base.

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- Carboxylic acids react as Brønsted–Lowry acids—that is, as proton donors.

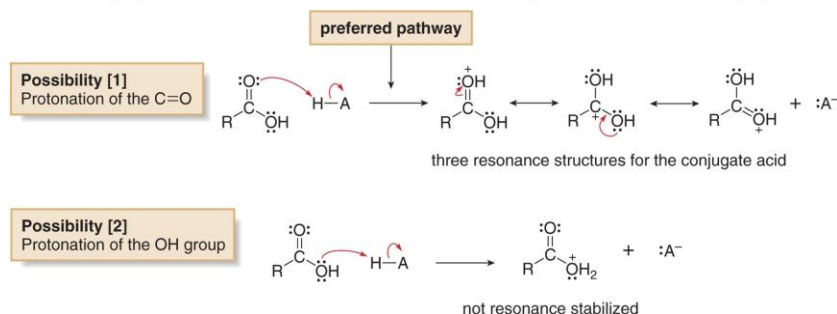


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Protonation of Carboxylic Acids

- The nonbonded electron pairs on oxygen create electron-rich sites that can be protonated by strong acids (H-A).
- Protonation occurs at the carbonyl oxygen because the resulting conjugate acid is resonance stabilized (Possibility [1]).
- The product of protonation at the OH group (Possibility [2]) cannot be resonance stabilized.

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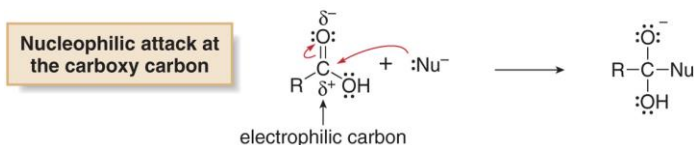


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Reaction with Nucleophiles and Bases

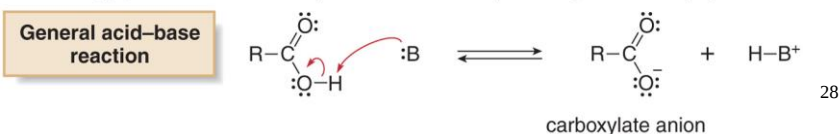
- The polar C–O bonds make the carboxy carbon electrophilic.
- Thus, carboxylic acids react with nucleophiles.
- Nucleophilic attack occurs at an sp^2 hybridized carbon atom, so it results in the cleavage of the π bond as well.

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- Carboxylic acids are strong organic acids, and as such, readily react with Brønsted–Lowry bases to form carboxylate anions.

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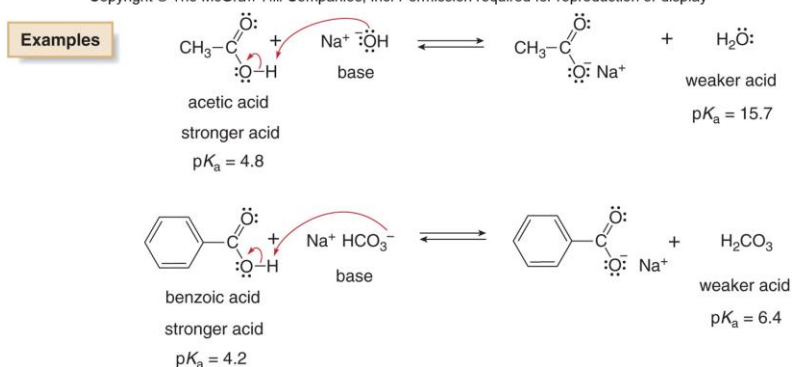


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Deprotonation of Carboxylic Acids

- An acid can be deprotonated by a base that has a conjugate acid with a higher pK_a .
- Because the pK_a values of many carboxylic acids are ~ 5 , bases that have conjugate acids with pK_a values higher than 5 are strong enough to deprotonate them.

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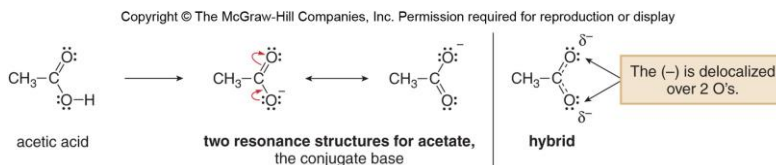
Table 19.3 Common Bases Used to Deprotonate Carboxylic Acids

	Base	Conjugate acid (pK_a)
	$\text{Na}^+ \text{HCO}_3^-$	H_2CO_3 (6.4)
	NH_3	NH_4^+ (9.4)
	Na_2CO_3	HCO_3^- (10.2)
	$\text{Na}^+ ^-\text{OCH}_3$	CH_3OH (15.5)
	$\text{Na}^+ ^-\text{OH}$	H_2O (15.7)
	$\text{Na}^+ ^-\text{OCH}_2\text{CH}_3$	$\text{CH}_3\text{CH}_2\text{OH}$ (16)
	$\text{Na}^+ \text{H}^-$	H_2 (35)

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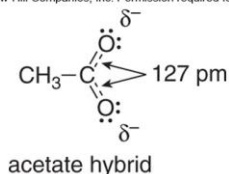
Resonance of Carboxylate Anions

- Carboxylic acids are relatively strong acids because deprotonation forms a resonance-stabilized conjugate base—a carboxylate anion.



- The **acetate** anion has two C–O bonds of equal length (1.27 Å) and intermediate between the length of a C–O single bond (1.36 Å) and C=O (1.21 Å).

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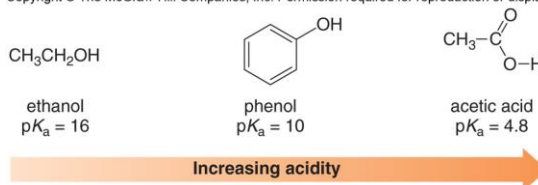


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Acidity of Common Organic Acids

- Resonance stabilization accounts for why carboxylic acids are more acidic than other compounds with O–H bonds—namely alcohols and phenols.

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- To understand the relative acidity of ethanol, phenol, and acetic acid, we must compare the stability of their conjugate bases and use the following rule:
 - Anything that stabilizes a conjugate base A^- makes the starting acid $\text{H}-\text{A}$ more acidic.

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Acidity of Ethanol

- **Ethoxide**, the conjugate base of ethanol, bears a negative charge on the O atom, but there are no additional factors to further stabilize the anion.
- Because ethoxide is less stable than acetate, ethanol is a weaker acid than acetic acid.

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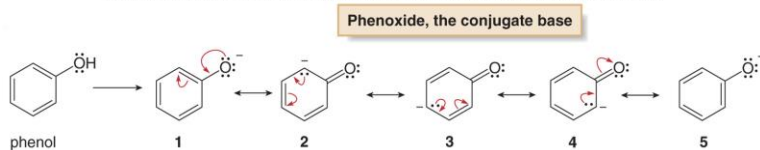


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Acidity of Phenol

- **Phenoxide**, the conjugate base of phenol, is more stable than ethoxide, but less stable than acetate because acetate has two electronegative O atoms upon which to delocalize the negative charge, whereas phenoxide has only one.

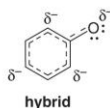
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Five resonance structures delocalize the negative charge over four atoms.

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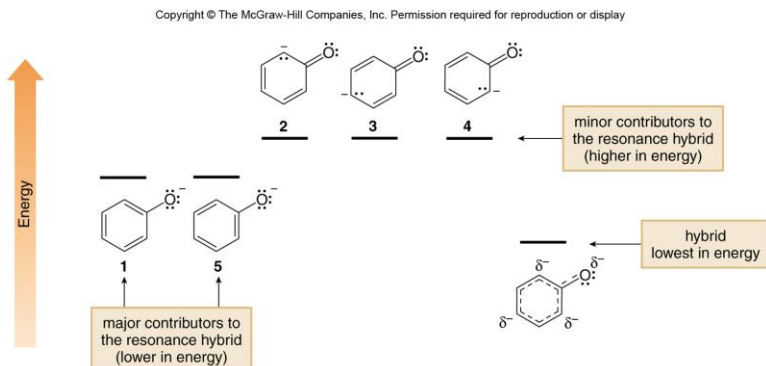
The resonance hybrid of phenoxide illustrates that its negative charge is dispersed over four atoms—three C atoms and one O atom.



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Energies of Resonance Structures for Phenoxide

Figure 19.6

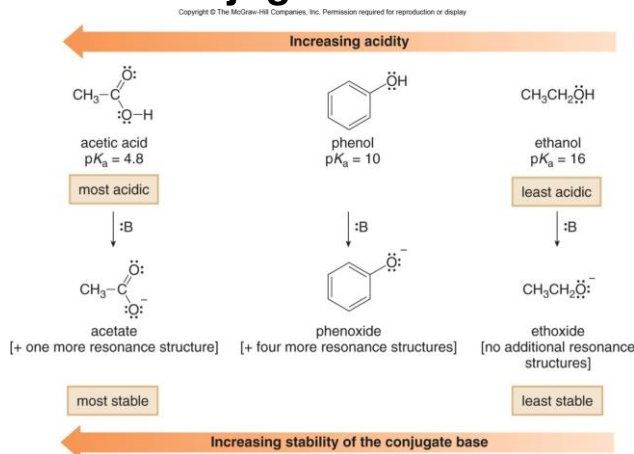


- Structures 2–4 have the negative charge on a C atom, a less electronegative element than O, making them less stable than structures 1 and 5.
- Structures 1 and 5 have intact aromatic rings, whereas structures 2–4 do not, making structures 1 and 5 more stable.

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Relationship Between Acidity and Stability of Conjugate Base

Figure 19.7



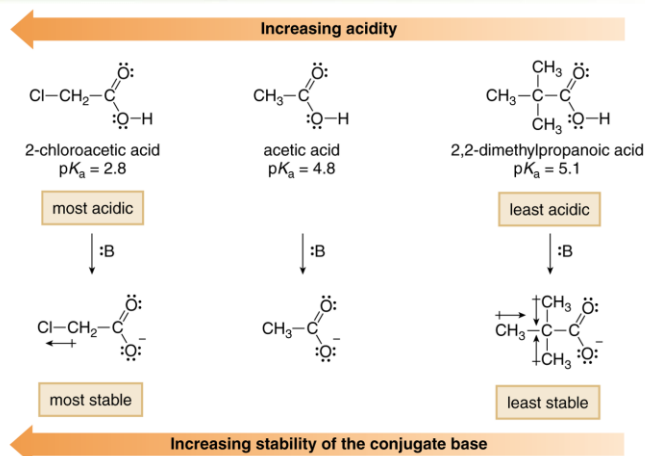
- Resonance stabilization of the conjugate base is important in determining acidity, the absolute number of resonance structures alone is not what is important!

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Inductive Effects in Carboxylic Acids

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- Electron-withdrawing groups stabilize a conjugate base, making a carboxylic acid more acidic.
- Electron-donating groups destabilize the conjugate base, making a carboxylic acid less acidic.

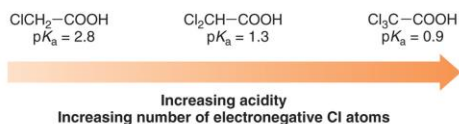


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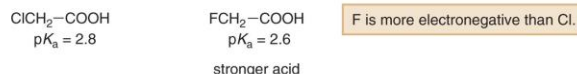
Inductive Effects in Carboxylic Acids

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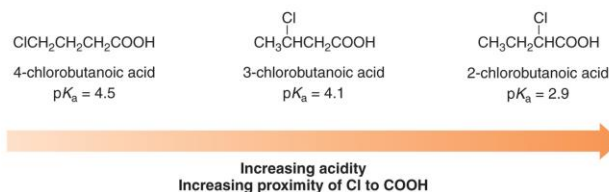
- The larger the number of electronegative substituents, the stronger the acid.



- The more electronegative the substituent, the stronger the acid.



- The closer the electron-withdrawing group to the COOH, the stronger the acid.



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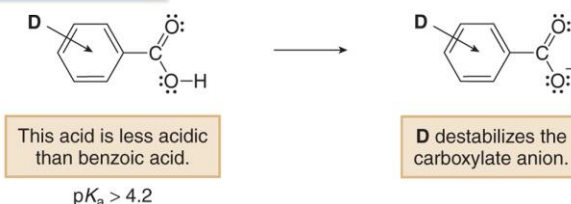
Substituent Effects in Aromatic Carboxylic Acids

- Substituents on a benzene ring either donate or withdraw electron density, depending on the balance of their inductive and resonance effects.
- These same effects also determine the acidity of substituted benzoic acids.

[1] **Electron-donor** groups destabilize a conjugate base, making an acid less acidic—the conjugate base is destabilized because electron density is being donated to a negatively charged carboxylate anion.

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D = Electron-donor group



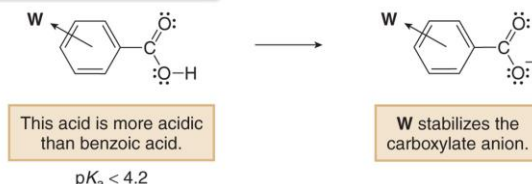
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Substituent Effects in Aromatic Carboxylic Acids

[2] **Electron-withdrawing** groups stabilize a conjugate base, making an acid more acidic. The conjugate base is stabilized because electron density is removed from the negatively charged carboxylate anion.

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W = Electron-withdrawing group



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Electron-donor groups
D

- activate benzene to electrophilic attack
- make a benzoic acid less acidic

Electron-withdrawing groups
W

- deactivate benzene to electrophilic attack
- make a benzoic acid more acidic

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Common Substituent Effects

Figure 19.8
How common substituents affect the reactivity of a benzene ring towards electrophiles and the acidity of substituted benzoic acids

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Substituent	Effect in electrophilic substitution	Effect on acidity of substituted benzoic acids
electron-donating groups -NH_2 (NHR , NR_2) -OH -OR -NHCOR -R	activating groups	These groups make a benzoic acid less acidic.
electron-withdrawing groups -X: ($\text{X} = \text{F}, \text{Cl}, \text{Br}, \text{I}$) -CHO -COR -COOR -COOH -CN $\text{-SO}_3\text{H}$ -NO_2 -NR_3	deactivating groups	These groups make a benzoic acid more acidic.

Increasing acidity

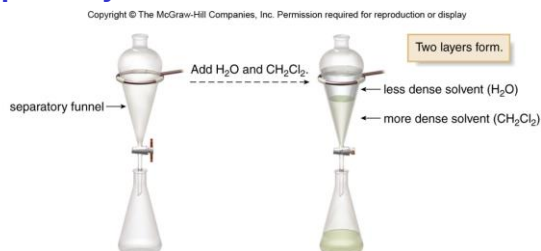
- Groups that donate electron density activate a benzene ring towards electrophilic attack and make a benzoic acid *less* acidic. Common electron-donating groups are R groups, or groups that have an N or O atom (with a lone pair) bonded to the benzene ring.
- Groups that withdraw electron density deactivate a benzene ring towards electrophilic attack, and make a benzoic acid *more* acidic. Common electron-withdrawing groups are the halogens, or groups with an atom Y (with a full or partial positive charge) bonded to the benzene ring.

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Organic Extraction

- Extraction** is a technique that permits the separation of mixtures of compounds based on acid–base principles, and solubility differences.
- When two immiscible liquids come into contact, two layers are formed.
- The two layers can be separated using a piece of glassware called a **separatory funnel**.

Figure 19.9



- When two insoluble liquids are added to a separatory funnel, two layers are visible, and the less dense liquid forms the upper layer.
- To separate the layers, the lower layer can be drained from the bottom of the separatory funnel by opening the stopcock. The top layer can then be poured out the top neck of the funnel.

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Separating Benzoic Acid and Salt

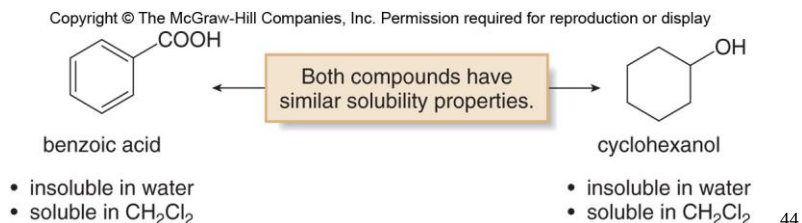
- Suppose you had a mixture of benzoic acid and NaCl.
 - Benzoic acid will be soluble in an organic solvent such as CH_2Cl_2 , and NaCl will dissolve in water.
 - Since CH_2Cl_2 and H_2O are immiscible, you now have two layers.
 - The more dense bottom layer (CH_2Cl_2) will contain the benzoic acid, and the less dense top layer (H_2O) will contain the NaCl.
 - If the mixture of liquids is transferred to a separatory funnel, the two layers can be separated by simply draining away the bottom layer.
 - Once the two layers are separated, the solvents can be evaporated away, leaving behind pure benzoic acid and NaCl.

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Separating Benzoic Acid and Cyclohexanol

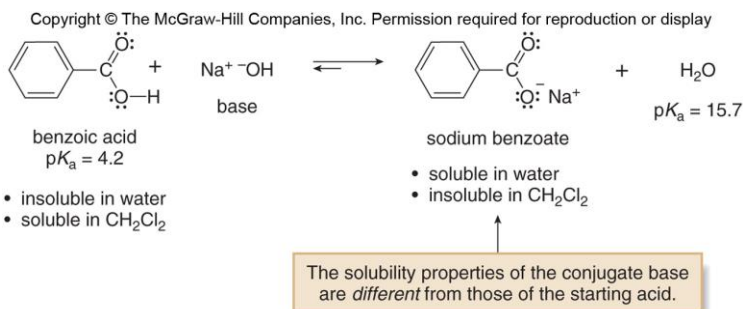
How could a mixture of benzoic acid and cyclohexanol be separated?

- Both compounds are organic, and as a result, both are soluble in an organic solvent such as CH_2Cl_2 , and insoluble in H_2O .
- If a mixture of benzoic acid and cyclohexanol was added to a separatory funnel with CH_2Cl_2 and water, both would dissolve in the CH_2Cl_2 layer, and the two compounds would not be separated from one another.



Separating Benzoic Acid and Cyclohexanol

- Since there is a significant enough difference in acidity between benzoic acid and cyclohexanol, extraction can be used to separate the two compounds.
- When benzoic acid is treated with NaOH, it is deprotonated, forming sodium benzoate, an ionic, water soluble salt.
- The much weaker acid, cyclohexanol, does not react with NaOH and remains in the organic solvent.



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Separation of Benzoic Acid and Cyclohexanol

Figure 19.10

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Step [1] Dissolve benzoic acid and cyclohexanol in CH_2Cl_2 .

Step [2] Add 10% NaOH solution to form two layers.

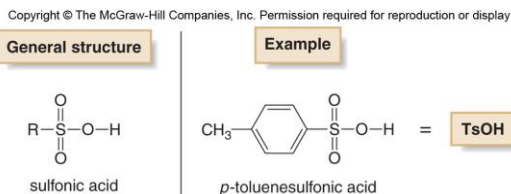
Step [3] Separate the layers.

- Both compounds dissolve in the organic solvent CH_2Cl_2 .
- Adding 10% aqueous NaOH solution forms two layers. When the two layers are mixed, the NaOH deprotonates $\text{C}_6\text{H}_5\text{COOH}$ to form $\text{C}_6\text{H}_5\text{COO}^-\text{Na}^+$, which dissolves in the aqueous layer.
- The cyclohexanol remains in the CH_2Cl_2 layer.
- Draining the lower layer out the bottom stopcock separates the two layers, and the separation process is complete.
- Cyclohexanol (dissolved in CH_2Cl_2) is in one flask. The sodium salt of benzoic acid, $\text{C}_6\text{H}_5\text{COO}^-\text{Na}^+$ (dissolved in water) is in another flask.

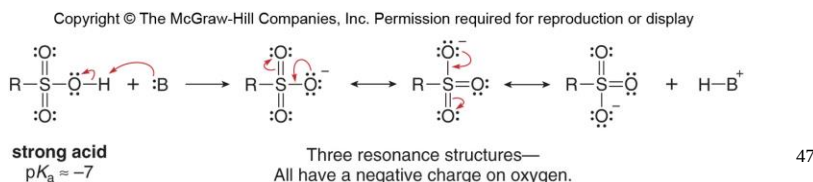
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Sulfonic Acids

- **Sulfonic acids** have the general structure RSO_3H .
- The most widely used sulfonic acid is ***p*-toluenesulfonic acid (TsOH)**.

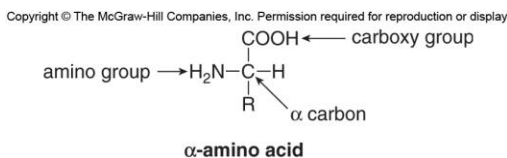


- Sulfonic acids are very strong acids because their conjugate bases (sulfonate anions) are resonance stabilized, and all the resonance structures delocalize negative charge on oxygen.



Amino Acids

- **Amino acids** contain two functional groups—an amine group (NH_2) and a carboxy group (COOH).
- Amino acids are the building blocks of proteins.



- The simplest amino acid, glycine, has $\text{R}=\text{H}$. When R is any other group, the α carbon is a stereogenic center.

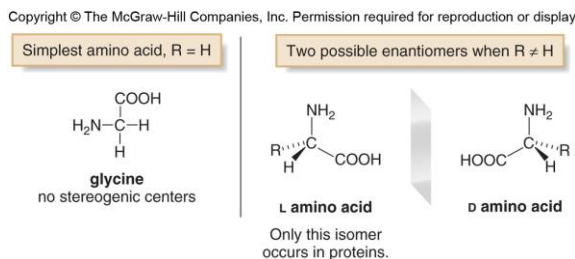


Table 19.4 Representative Amino Acids

General structure: $\begin{array}{c} \text{COOH} \\ \\ \text{H}_2\text{N}-\text{C}-\text{H} \\ \\ \text{R} \end{array}$			
R group	Name	Three-letter abbreviation	One-letter abbreviation
H	glycine	Gly	G
CH ₃	alanine	Ala	A
CH ₂ C ₆ H ₅	phenylalanine	Phe	F
CH ₂ OH	serine	Ser	S
CH ₂ SH	cysteine	Cys	C
CH ₂ CH ₂ SCH ₃	methionine	Met	M
CH ₂ CH ₂ COOH	glutamic acid	Glu	E
(CH ₂) ₄ NH ₂	lysine	Lys	K

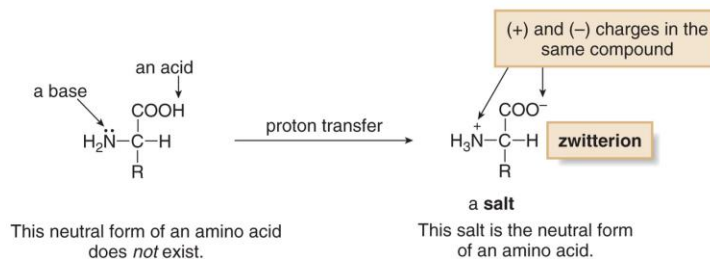
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Zwitterion Character of Amino Acids

- An amino acid is both an acid and a base.
- Amino acids are never uncharged neutral molecules, they exist as salts, so they have very high melting points and are very water soluble.

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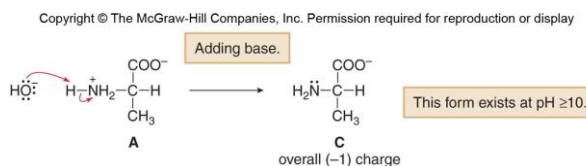
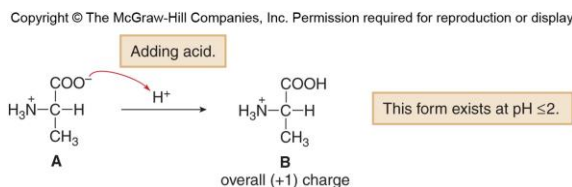
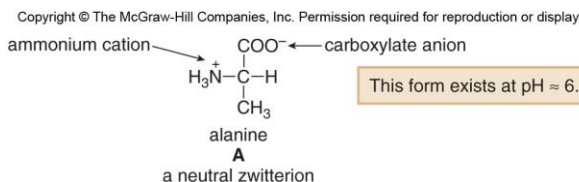
- Proton transfer from the acidic carboxy group to the basic amino group forms a salt called a **zwitterion**, which contains both a positive and a negative charge.



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pH and Amino Acid Structure

- An amino acid can exist in three different forms depending on pH.



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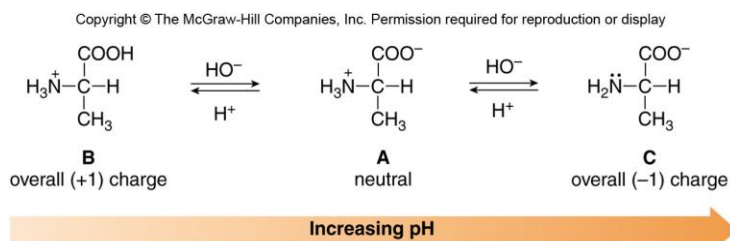
Summary of Acid-Base Reactions

- Alanine exists in three different forms depending on the pH of the solution in which it is dissolved.
- As the pH of a solution is gradually increased from 2 to 10, the following process occurs:

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- At low pH alanine has a net (+) charge (form B).
- As the pH is increased to $\sim$ 6, the carboxy group is deprotonated, and the amino acid exists as a zwitterion with no overall charge (form A).
- At high pH, the ammonium cation is deprotonated, and the amino acid has a net (-) charge (form C).

Figure 19.11



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Isoelectric Point

- Because a protonated amino acid has at least two different protons that can be removed, a pK_a value is reported for each of these protons.
- The pH at which the amino acid exists primarily in its neutral form is called its **isoelectric point**, abbreviate as pI .
- Generally, the isoelectric point is the average of both pK_a values of an amino acid:

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$$\text{Isoelectric point} = pI = \frac{pK_a(\text{COOH}) + pK_a(\text{NH}_3^+)}{2}$$

$$\text{For alanine: } pI = \frac{2.35 + 9.87}{2} = 6.12 \text{ } pI(\text{alanine})$$

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