Teacher: DR. SUBHANKAR SARDAR
Class : Semester-2
Paper: C4T: Organic Chemistry
Topic : General Treatment of Reaction Mechanism II
(Concept of Organic acids and bases)

Comments: Read whole the notes thoroughly. This part is very important for final examination.

References:

1)   Part-2: Organic Chemistry by T.W. Graham Solomons, Craig B. Fryhle

AN INTRODUCTION TO ORGANIC REACTIONS: ACIDS AND BASES

SHUTTLING THE PROTONS

1. **Carbonic anhydrase** regulates the acidity of blood and the physiological conditions relating to blood pH.

$$HCO_3^- + H^+ \rightleftarrows H_2CO_3 \xrightarrow{\text{Carbonic anhydrase}} H_2O + CO_2$$

2. The breath rate is influenced by one's relative blood acidity.

3. **Diamox** (acetazolamide) **inhibits** carbonic anhydrase, and this, in turn, **increases the blood acidity**. The increased blood acidity **stimulates breathing** and thereby decreases the likelihood of **altitude sickness**.
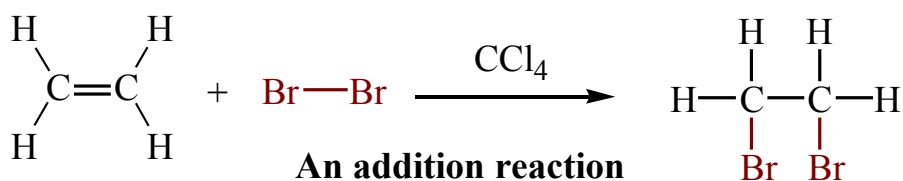

Diamox (acetazolamide)
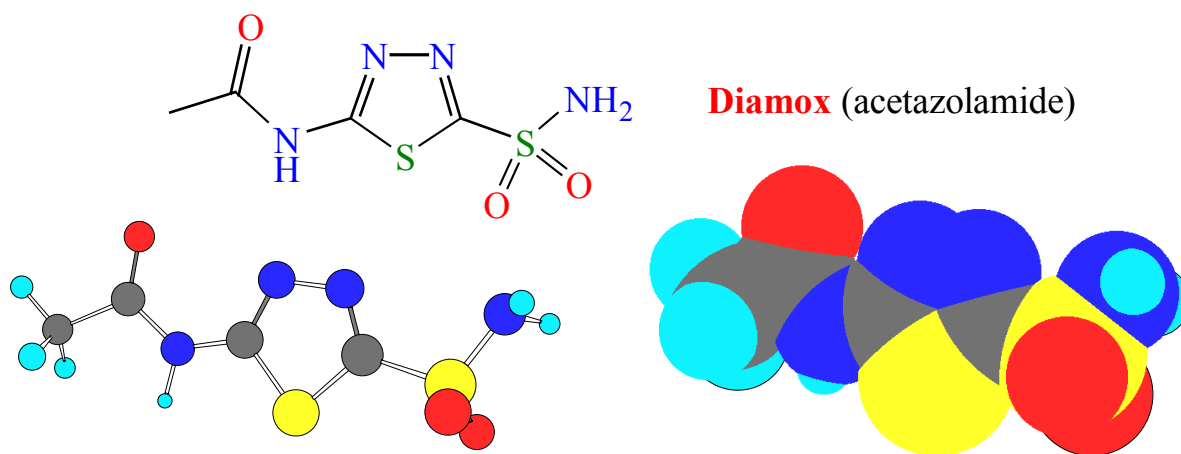
3.1   REACTIONS AND THEIR MECHANISMS

3.1A   CATEGORIES OF REACTIONS

1. **Substitution Reactions:**

$$H_3C{-}Cl + Na^+\,OH^- \xrightarrow{H_2O} H_3C{-}OH + Na^+\,Cl^-$$
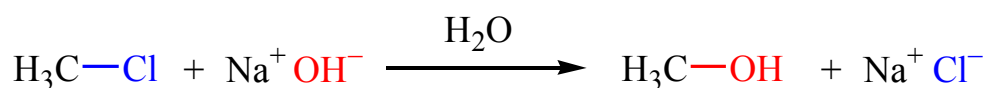
A substitution reaction

2. **Addition Reactions:**

An addition reaction

3. **Elimination Reactions:**

An elimination reaction (Dehydrohalogenation)
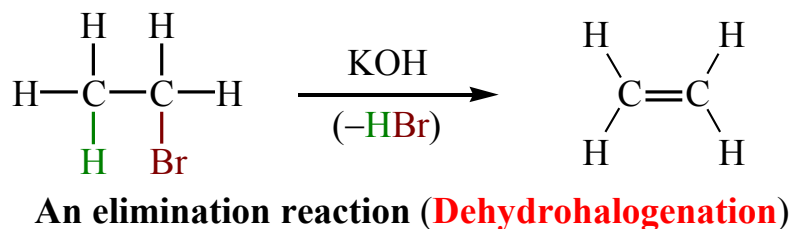
4. **Rearrangement Reactions:**

An rearrangement
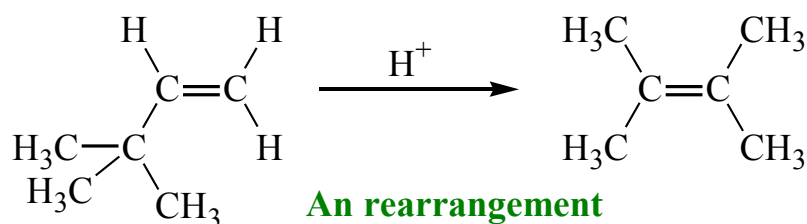
3.1B MECHANISMS OF REACTIONS

1. **Mechanism** explains, on a molecular level, how the reactants become products.

2. **Intermediates** are the chemical species generated between each step in a multistep reaction.

3. A proposed mechanism must be **consistent** with all the **facts** about the reaction and with the **reactivity** of organic compounds.

4. Mechanism helps us organize the seemingly an overwhelmingly complex body of knowledge into an understandable form.
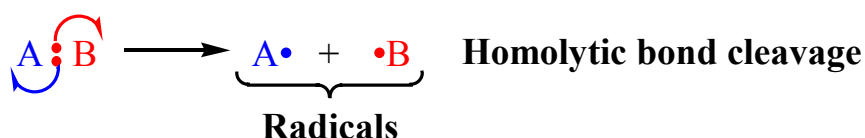
3.1C HOMOLYSIS AND HETEROLYSIS OF COVALENT BONDS

1. **Heterolytic bond dissociation** (**heterolysis**):   electronically *unsymmetrical* bond
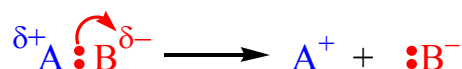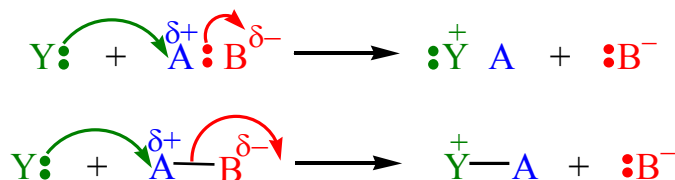
breaking $\Rightarrow$ produces **ions**.

$$A \overset{\curvearrowright}{:} B \longrightarrow \underbrace{A^+ + :B^-}_{\textbf{Ions}} \quad \textbf{Hydrolytic bond cleavage}$$
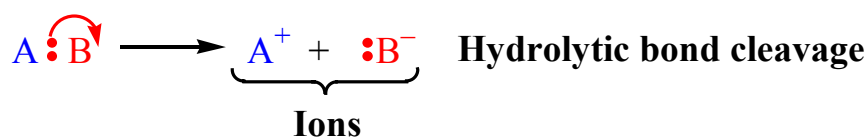
2. **Homolytic** bond dissociation (**homolysis**): electronically *symmetrical* bond breaking $\Rightarrow$ produces **radicals**.

$$A \overset{\curvearrowright}{:} B \longrightarrow \underbrace{A\bullet + \bullet B}_{\textbf{Radicals}} \quad \textbf{Homolytic bond cleavage}$$

3. **Heterolysis** requires the bond to be **polarized**. *Heterolysis requires separation of oppositely charged ions*.

$$\overset{\delta+}{A} \overset{\curvearrowright}{:} \overset{\delta-}{B} \longrightarrow A^+ + :B^-$$

4. **Heterolysis** is assisted by a molecule with an **unshared pair**:

$$Y: + \overset{\delta+}{A} : \overset{\delta-}{B} \longrightarrow :\overset{+}{Y} A + :B^-$$

$$Y: + \overset{\delta+}{A} - \overset{\delta-}{B} \longrightarrow \overset{+}{Y} - A + :B^-$$
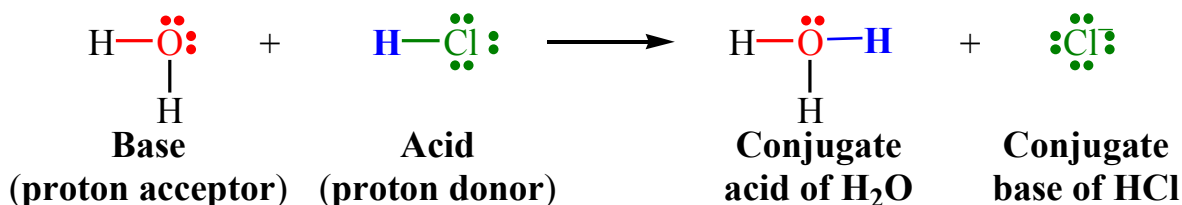
Formation of the new bond furnishes some of the energy required for the heterolysis.
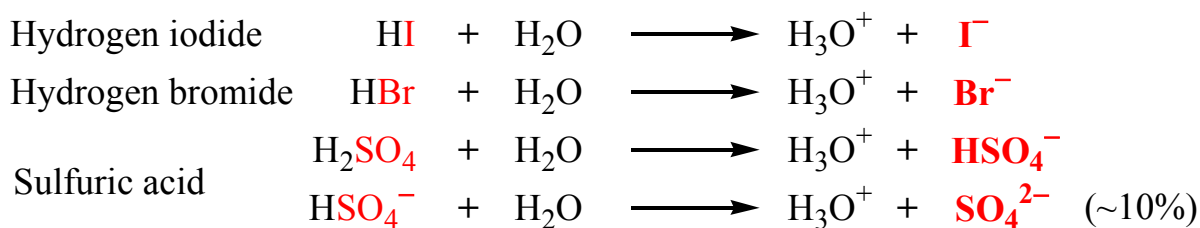

3.2 ACID-BASE REACTIONS

3.2A THE BRØNSTED-LOWRY DEFINITION OF ACIDS AND BASES

1. **Acid** is a substance that can donate (or lose) a **proton**; **Base** is a substance that can accept (or remove) a **proton**.

	H—Ö:	+	H—Cl:	⟶	H—Ö—H	+	:Cl:

Base **Acid** **Conjugate** **Conjugate**
(proton acceptor) (proton donor) **acid of H₂O** **base of HCl**

1) Hydrogen chloride, a very strong acid, transfer its proton to water.

2) Water acts as a base and accepts the proton.

2. **Conjugate acid:** the molecule or ion that forms when a base accepts a proton.

3. **Conjugate base:** the molecule or ion that forms when an acid loses its proton.

4. Other strong acids:

Hydrogen iodide $\quad$ HI + H_2O ⟶ H_3O^+ + I^-

Hydrogen bromide $\quad$ HBr + H_2O ⟶ H_3O^+ + Br^-

$\qquad\qquad\qquad H_2SO_4$ + H_2O ⟶ H_3O^+ + HSO_4^-

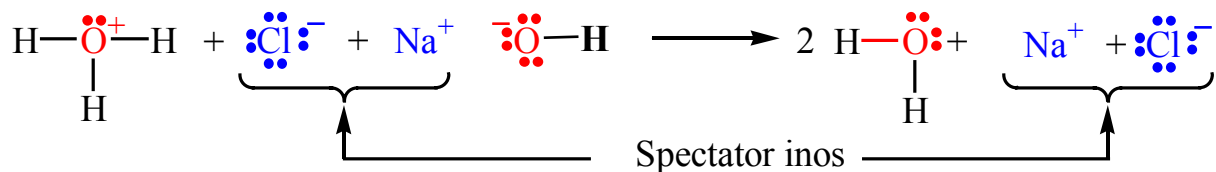Sulfuric acid $\qquad HSO_4^-$ + H_2O ⟶ H_3O^+ + SO_4^{2-} (~10%)

5. **Hydronium** ions and **hydroxide** ions are the strongest acid and base that can exist in aqueous solution in significant amounts.

6. When sodium hydroxide dissolves in water, the result is a solution containing solvated sodium ions and solvated hydroxide ions.

$$Na^+ OH^-_{(solid)} \longrightarrow Na^+_{(aq)} + HO^-_{(aq)}$$

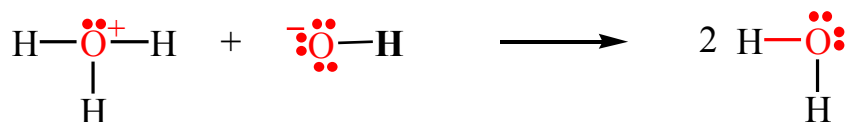**Solvated sodium ion** $\qquad\qquad$ **Solvated hydroxide ion**
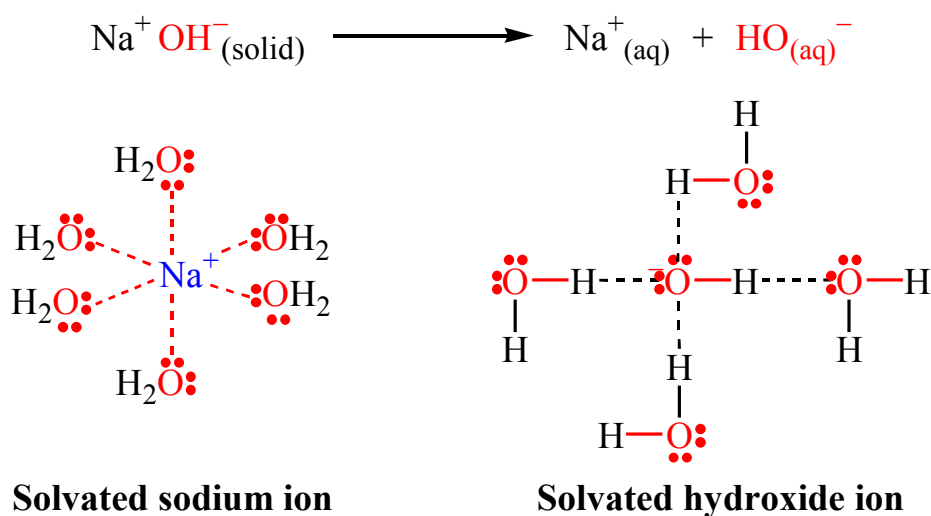
7. An aqueous **sodium hydroxide** solution is mixed with an aqueous **hydrogen chloride** (hydrochloric acid) solution:
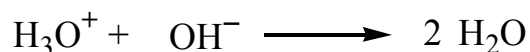
1) ***Total Ionic Reaction***

$$H-\overset{+}{\underset{H}{\overset{\cdot\cdot}{O}}}-H \ + \ :\overset{\cdot\cdot}{\underset{\cdot\cdot}{Cl}}:^- \ + \ Na^+ \quad ^-:\overset{\cdot\cdot}{\underset{\cdot\cdot}{O}}-H \ \longrightarrow \ 2 \ H-\overset{\cdot\cdot}{\underset{H}{O}}:+ \ Na^+ \ +:\overset{\cdot\cdot}{\underset{\cdot\cdot}{Cl}}:^-$$

Spectator inos

2) ***Net Reaction***

$$H-\overset{+}{\underset{H}{\overset{\cdot\cdot}{O}}}-H \ + \ ^-:\overset{\cdot\cdot}{\underset{\cdot\cdot}{O}}-H \ \longrightarrow \ 2 \ H-\overset{\cdot\cdot}{\underset{H}{\overset{\cdot\cdot}{O}}}:$$

3) The ***Net Reaction*** of solutions of all aqueous strong acids and bases are mixed:
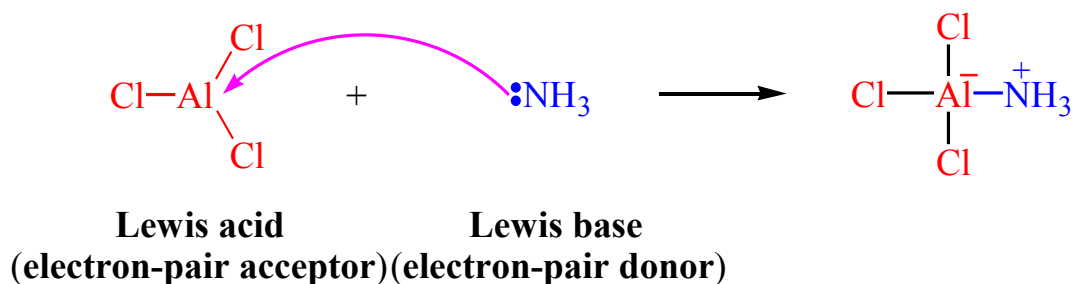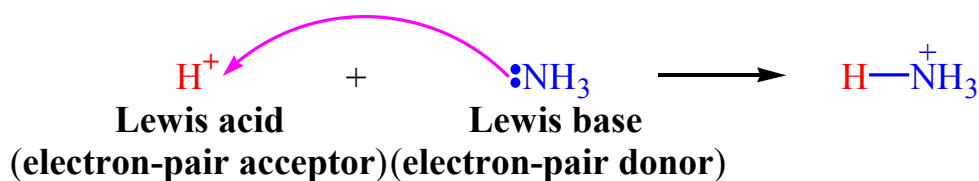
$$H_3O^+ + \ OH^- \longrightarrow \ 2 \ H_2O$$

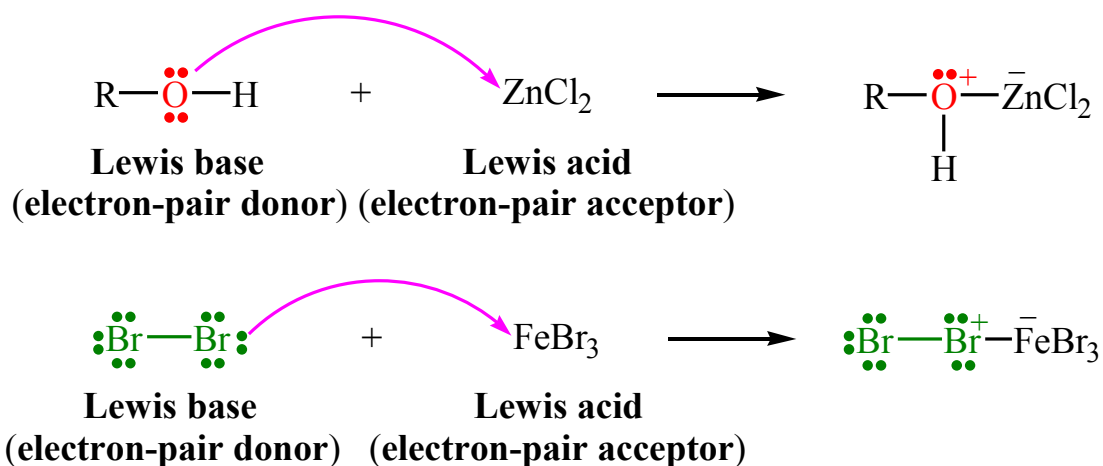## 3.2B   THE LEWIS DEFINITION OF ACIDS AND BASES

1. **Lewis acid-base** theory: in 1923 proposed by G. N. Lewis (1875~1946; Ph. D. Harvard, 1899; professor, Massachusetts Institute of Technology, 1905-1912; professor, University of California, Berkeley, 1912-1946).

1) **Acid: electron-pair acceptor**

2) **Base: electron-pair donor**

$$H^+ \qquad + \qquad :NH_3 \qquad \longrightarrow \qquad H-\overset{+}{N}H_3$$

Lewis acid   **Lewis base**
(electron-pair acceptor)(electron-pair donor)

curved arrow shows the donation of the electron-pair of ammonia

$$Cl-\overset{\overset{\displaystyle Cl}{|}}{\underset{\underset{\displaystyle Cl}{|}}{Al}} \qquad + \qquad :NH_3 \qquad \longrightarrow \qquad Cl-\overset{\overset{\displaystyle Cl}{|}}{\underset{\underset{\displaystyle Cl}{|}}{\bar{Al}}}-\overset{+}{N}H_3$$

Lewis acid   **Lewis base**
**(electron-pair acceptor)(electron-pair donor)**

3) The central aluminum atom in aluminum chloride is **electron-deficient** because it has only a **sextet** of electrons. Group 3A elements (B, Al, Ga, In, Tl) have only a **sextet** of electrons in their valence shell.

4) Compounds that have atoms with vacant orbitals also can act as Lewis acids.

R—Ö—H   +   ZnCl$_2$ ⟶   R—Ö$^+$—ZnCl$_2$
                                                 |
                                                 H

Lewis base   **Lewis acid**
(electron-pair donor) (electron-pair acceptor)

:Br—Br: +   FeBr$_3$ ⟶   :Br—Br$^+$—FeBr$_3$

Lewis base   **Lewis acid**
(electron-pair donor)   **(electron-pair acceptor)**

3.2C   OPPOSITE CHARGES ATTRACT

1. Reaction of boron trifluoride with ammonia:

   **BF$_3$**   **NH$_3$**   **F$_3$B̄—$\overset{+}{N}$H$_3$**
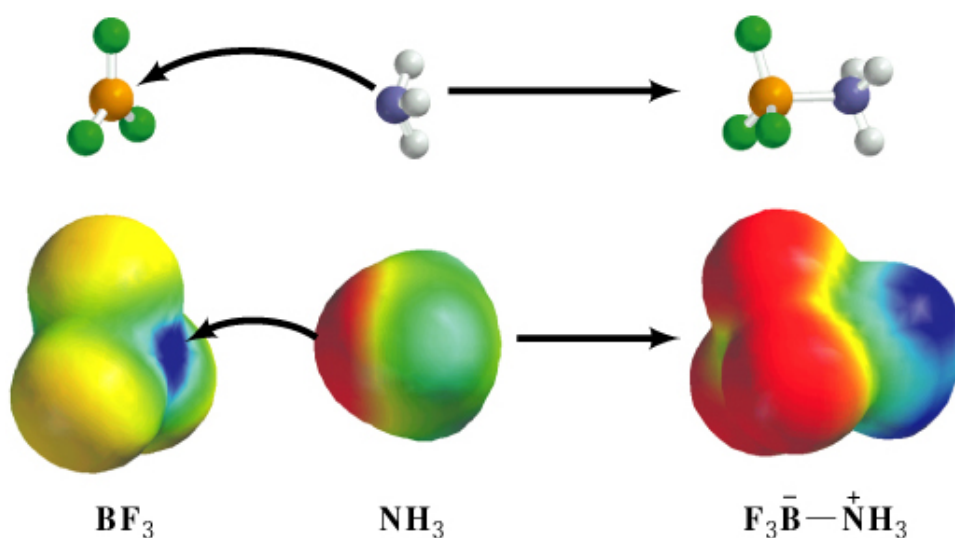
Figure 3.1   **Electrostatic potential maps for BF$_3$, NH$_3$, and the product that results from reaction between them. Attraction between the strongly positive region of BF$_3$ and the negative region of NH$_3$ causes them to react. The electrostatic potential map for the product for the product shows that the fluorine atoms draw in the electron density of the formal negative charge, and the nitrogen atom, with its hydrogens, carries the formal positive charge.**

2. BF$_3$ has substantial **positive charge** centered on the **boron** atom and **negative charge** located on the three **fluorine** atoms.

3. NH$_3$ has substantial **negative charge** localized in the region of its **nonbonding electron** pair.

4. The **nonbonding electron** of ammonia attacks the boron atom of boron trifluoride, filling boron's **valence shell**.

5. **HOMOs** and **LUMOs** in Reactions:

   1) **HOMO:**   highest occupied molecular orbital

   2) **LUMO:**   lowest unoccupied molecular orbital
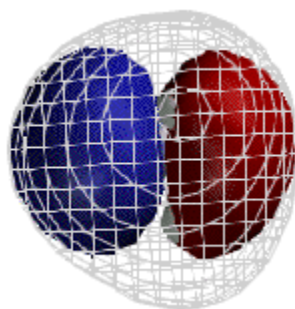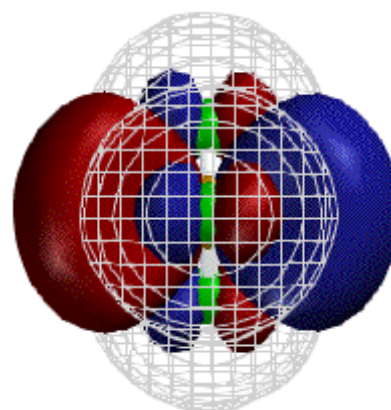
HOMO of NH$_3$ **LUMO of BF$_3$**

   3) The nonbonding electron pair occupies the **HOMO** of NH$_3$.

   4) Most of the volume represented by the **LUMO** corresponds to the empty p orbital in the sp^2-hybridized state of BF$_3$.

   5) The **HOMO** of one molecule interacts with the **LUMO** of another in a reaction.

3.3   HETEROLYSIS OF BONDS TO CARBON: CARBOCATIONS AND CARBANIONS

3.3A   CARBOCATIONS AND CARBANIONS
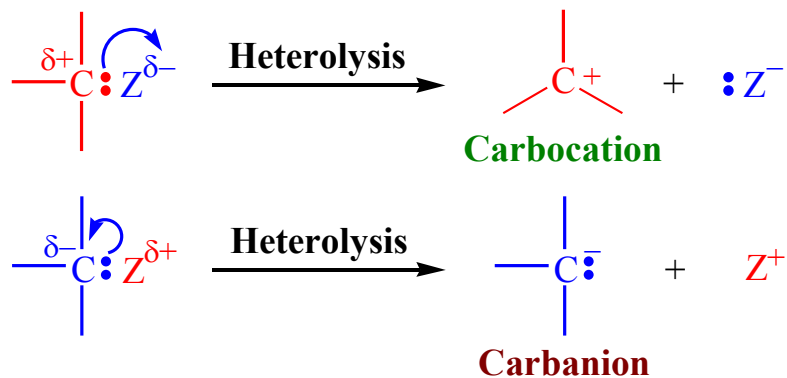
1. **Carbocations have six electrons in their valence shell, and are electron deficient. $\Rightarrow$ Carbocations are Lewis acids.**

   1) Most carbocations are **short-lived** and **highly reactive**.

   2) Carbonium ion (R^+) $\Leftrightarrow$ Ammonium ion (R_4N^+)

2. Carbocations react rapidly with Lewis bases (molecules or ions that can donate electron pair) to achieve a stable octet of electrons.
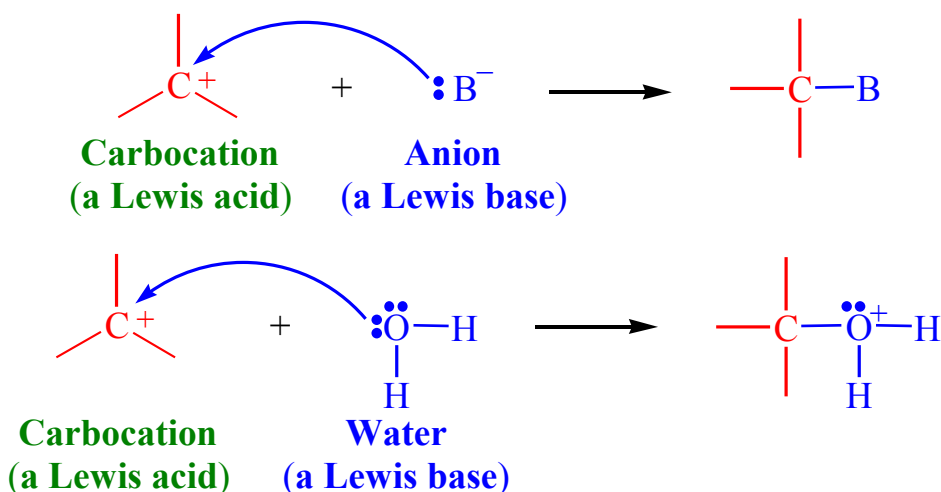
3. **Electrophile:** "electron-loving" reagent

   1) Electrophiles seek the extra electrons that will give them a stable valence shell of electrons.

   2) A proton achieves the valence shell configuration of helium; carbocations achieve the valence shell configuration of neon.

4. **Carbanions are Lewis bases.**

   1) Carbanions donate their electron pair to a proton or some other positive center to neutralize their negative charge.
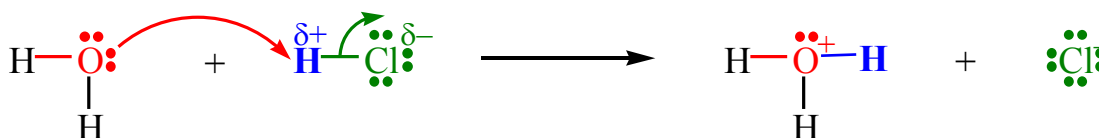
5. **Nucleophile:** "nucleus-loving" reagent

Carbanion   **Lewis acid**

Carbanion   **Lewis acid**
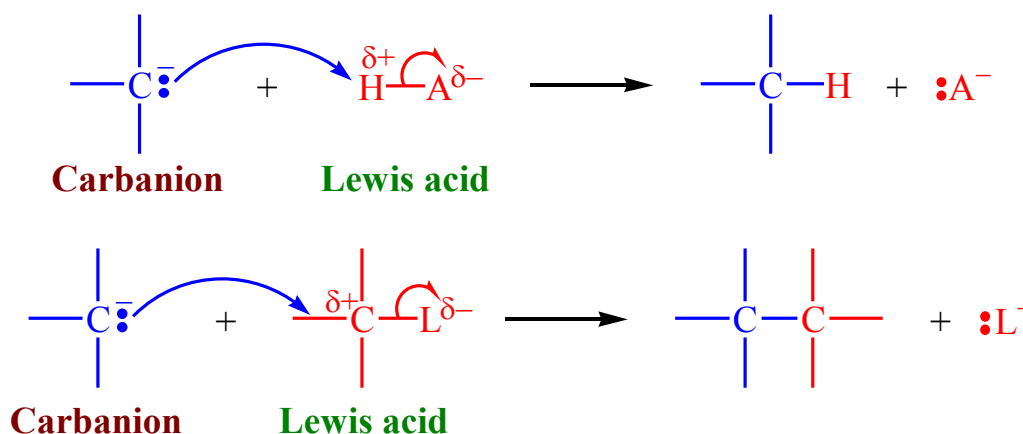
3.4   THE USE OF CURVED ARROWS IN ILLUSTRATING REACTIONS

3.4A   A Mechanism for the Reaction

Reaction:

$$H_2O \; + \; HCl \longrightarrow H_3O^+ \; + \; Cl^-$$

Mechanism:

A water molecule uses one of the electron pairs to form a bond to a proton of HCl. The bond between the hydrogen and chlorine breaks with the electron pair going to the chlorine atom

**This leads to the formation of a hydronium ion and a chloride ion.**

Curved arrows point from electrons to the atom receiving the electrons.

1. **Curved arrow:**

   1) The curved arrow begins with a covalent bond or unshared electron pair (a site of higher electron density) and points toward a site of electron deficiency.
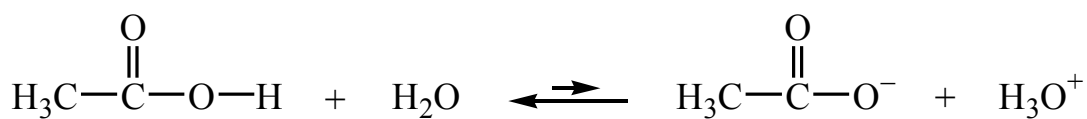
2) The negatively charged electrons of the oxygen atom are attracted to the positively charged proton.

2. Other examples:
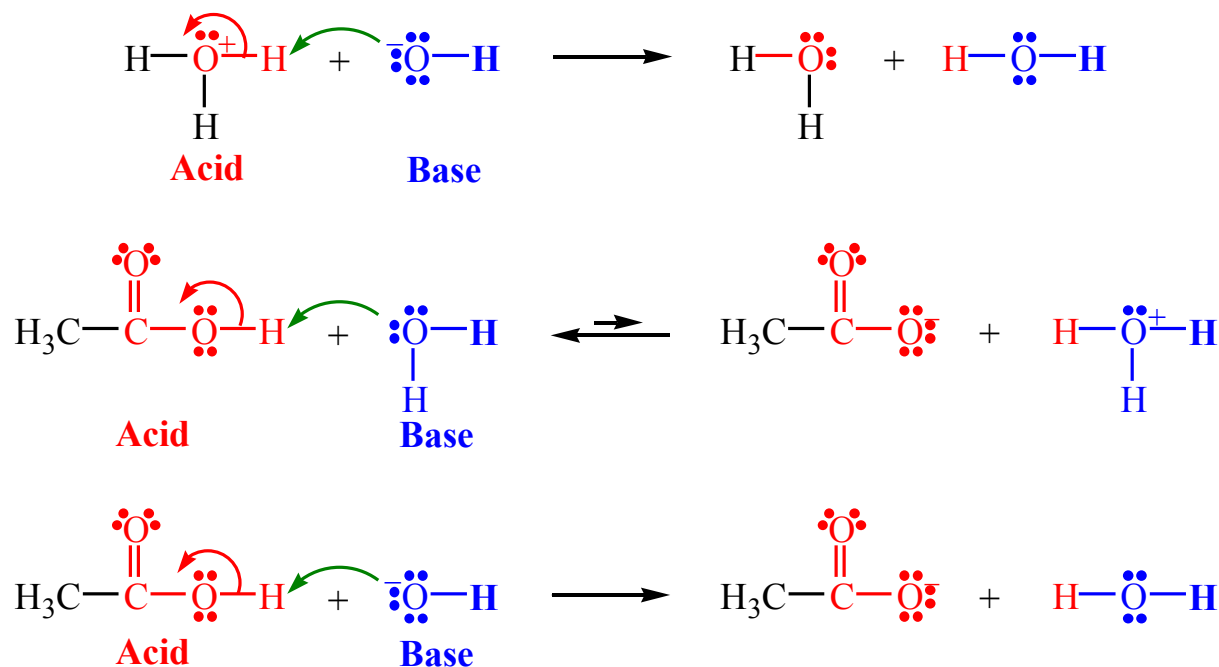
3.5 THE STRENGTH OF ACIDS AND BASES: K_a AND pK_a

1. In a 0.1 *M* solution of acetic acid at 25 °C only 1% of the acetic acid molecules ionize by transferring their protons to water.

3.5A THE ACIDITY CONSTANT, K_a
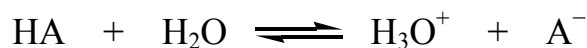
1. An aqueous solution of acetic acid is an equilibrium:

$$K_{eq} = \frac{[H_3O^+][CH_3CO_2^-]}{[CH_3CO_2H][H_2O]}$$

2. **The acidity constant:**

1) For dilute aqueous solution: water concentration is essentially constant (~ 55.5 *M*)

$$K_a = K_{eq}[H_2O] = \frac{[H_3O^+][CH_3CO_2^-]}{[CH_3CO_2H]}$$

2) At 25 °C, the acidity constant for acetic aicd is 1.76×10^{-5}.

3) General expression for any acid:

$$HA + H_2O \rightleftharpoons H_3O^+ + A^-$$

$$K_a = \frac{[H_3O^+][A^-]}{[HA]}$$

4) A **large value of K_a** means the acid is a **strong acid**, and a **smaller value of K_a** means the acid is a **weak acid**.

5) If the **K_a** is greater than 10, the acid will be completely dissociated in water.

3.5B ACIDITY AND pK_a

1. **pK_a:** $\qquad\qquad\qquad$ $pK_a = -\log K_a$

2. pH: $\qquad\qquad\qquad\qquad$ $pH = -\log[H_3O^+]$

3. The **pK_a** for acetic acid is 4.75:

$$pK_a = -\log(1.76 \times 10^{-5}) = -(-4.75) = 4.75$$

4. The **larger the value of the pK_a, the weaker is the acid**.

$$\textbf{CH}_3\textbf{CO}_2\textbf{H} \qquad \textbf{CF}_3\textbf{CO}_2\textbf{H} \qquad \textbf{HCl}$$

$$\textbf{p}K_a = \textbf{4.75} \qquad \textbf{p}K_a = \textbf{0.18} \qquad \textbf{p}K_a = \textbf{-7}$$

Acidity increases ⟹

1) For dilute aqueous solution: water concentration is essentially constant (~ 55.5 *M*)

Table 3.1 Relative Strength of Selected Acids and their Conjugate Bases

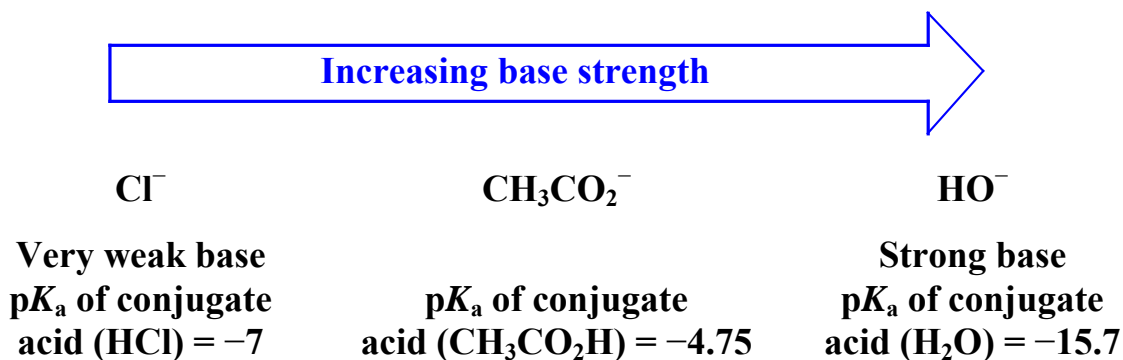|	Acid	Approximate pK_a	Conjugate Base	
Strongest Acid	$HSbF_6$ (a super acid)	< -12	SbF_6^-	Weakest Base
	HI	-10	I^-	
	H_2SO_4	-9	HSO_4^-	
	HBr	-9	Br^-	
	HCl	-7	Cl^-	
	$C_6H_5SO_3H$	-6.5	$C_6H_5SO_3^-$	
	$(CH_3)_2O^+H$	-3.8	$(CH_3)_2O$	
	$(CH_3)_2C=O^+H$	-2.9	$(CH_3)_2C=O$	
	$CH_3O^+H_2$	-2.5	CH_3OH	
	H_3O^+	-1.74	H_3O	
	HNO_3	-1.4	HNO_3^-	
	CF_3CO_2H	0.18	$CF_3CO_2^-$	
	HF	3.2	F^-	
	H_2CO_3	3.7	HCO_3^-	
	CH_3CO_2H	4.75	$CH_3CO_2^-$	
	$CH_3COCH_2COCH_3$	9.0	$CH_3COCH^-COCH_3$	
	NH_4^+	9.2	NH_4^+	
	C_6H_5OH	9.9	$C_6H_5O^-$	
	HCO_3^-	10.2	HCO_3^{2-}	
	$CH_3NH_3^+$	10.6	CH_3NH_3	
	H_2O	15.74	HO^-	
	CH_3CH_2OH	16	$CH_3CH_2O^-$	
	$(CH_3)_3COH$	18	$(CH_3)_3CO^-$	
	CH_3COCH_3	19.2	$^-CH_2COCH_3$	
	$HC\equiv CH$	25	$HC\equiv C^-$	
	H_2	35	H^-	
	NH_3	38	NH_2^-	
	$CH_2=CH_2$	44	$CH_2=CH^-$	
Weakest Acid	CH_3CH_3	50	$CH_3CH_2^-$	Strongest Base

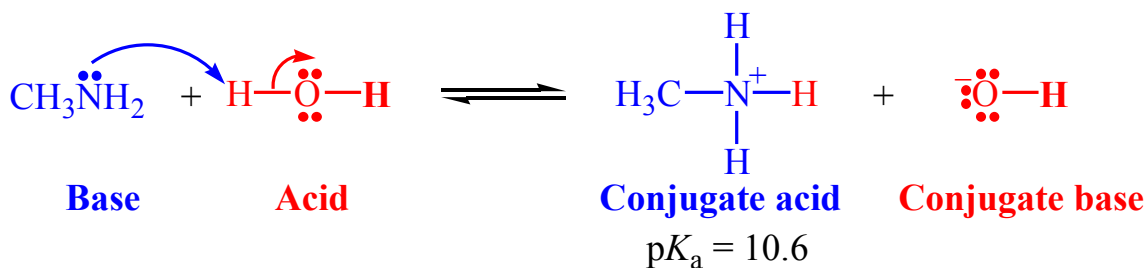*Increasing acid strength* (left arrow) *Increasing base strength* (right arrow)

3.5C PREDICTING THE STRENGTH OF BASES

1. **The stronger the acid, the weaker will be its conjugate base.**

2. **The larger the pK_a of the conjugate acid, the stronger is the base.**

Cl^-	$CH_3CO_2^-$	HO^-
Very weak base pK_a of conjugate acid (HCl) = −7	pK_a of conjugate acid (CH_3CO_2H) = −4.75	Strong base pK_a of conjugate acid (H_2O) = −15.7

3. **Amines are weak bases:**

$$\overset{\cdot\cdot}{N}H_3 \;+\; H-\overset{\cdot\cdot}{\underset{\cdot\cdot}{O}}-H \;\rightleftharpoons\; H-\overset{H}{\underset{H}{\overset{+}{N}}}-H \;+\; \overset{\cdot\cdot}{\underset{\cdot\cdot}{:O}}-H$$

Base	Acid	Conjugate acid	Conjugate base

$$pK_a = 9.2$$

$$CH_3\overset{\cdot\cdot}{N}H_2 \;+\; H-\overset{\cdot\cdot}{\underset{\cdot\cdot}{O}}-H \;\rightleftharpoons\; H_3C-\overset{H}{\underset{H}{\overset{+}{N}}}-H \;+\; \overset{\cdot\cdot}{\underset{\cdot\cdot}{:O}}-H$$

Base	Acid	Conjugate acid	Conjugate base
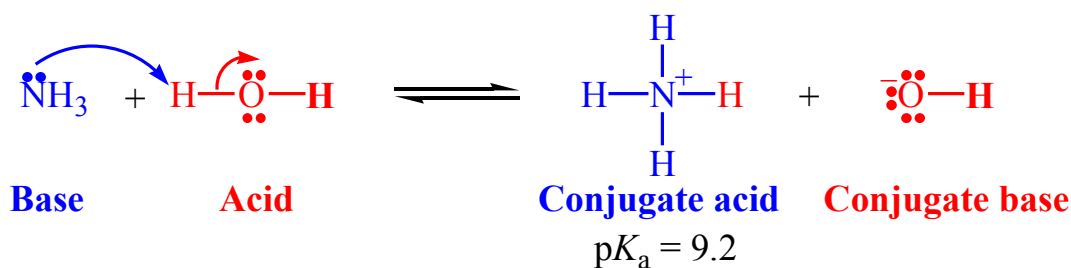
$$pK_a = 10.6$$

1) The conjugate acids of ammonia and methylamine are the ammonium ion, NH_4^+ (pK_a = 9.2) and the methylammonium ion, $CH_3NH_3^+$ (pK_a = 10.6) respectively. Since methylammonium ion is a weaker acid than ammonium ion, methylamine is a stronger base than ammonia.

3.6   PREDICTING THE OUTCOME OF ACID-BASE REACTIONS

3.6A   General order of acidity and basicity:

1. **Acid-base reactions always favor the formation of the weaker acid and the weaker base.**

   1) **Equilibrium control:** the outcome of an acid-base reaction is determined by the position of an equilibrium.

Stronger acid   **Stronger base**   **Weaker base**   **Weaker acid**

$pK_a = 3\text{-}5$ $pK_a = 15.7$
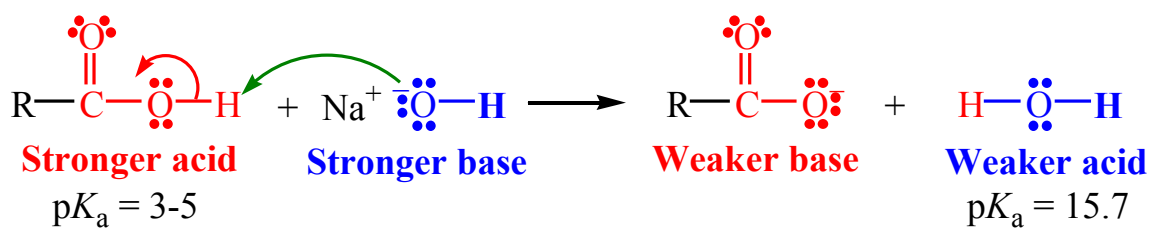
Large difference in pK_a value $\Rightarrow$ the position of equilibrium will greatly favor the formation of the products (one-way arrow is used)

2. **Water-insoluble carboxylic acids dissolve in aqueous sodium hydroxide:**

      Insoluble in water   **Soluble in water**
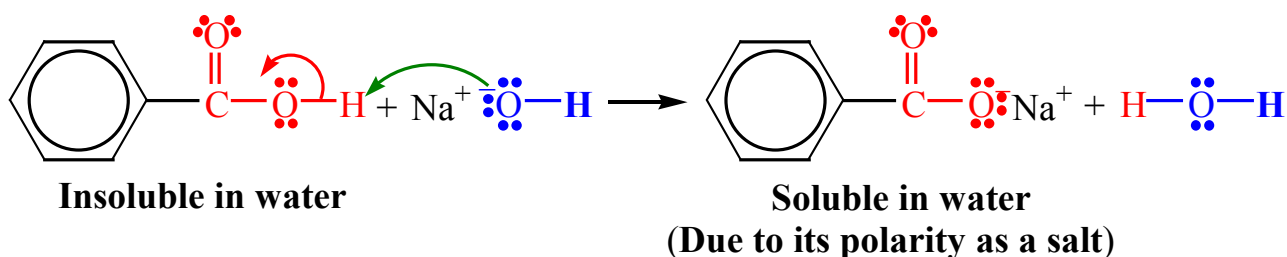
                                           (Due to its polarity as a salt)

1) Carboxylic acids containing fewer than five carbon atoms are soluble in water.

3. **Amines react with hydrochloric acid:**

Stronger base   **Stronger acid**   **Weaker acid**   **Weaker base**

                 $pK_a = -1.74$ $pK_a = 9\text{-}10$
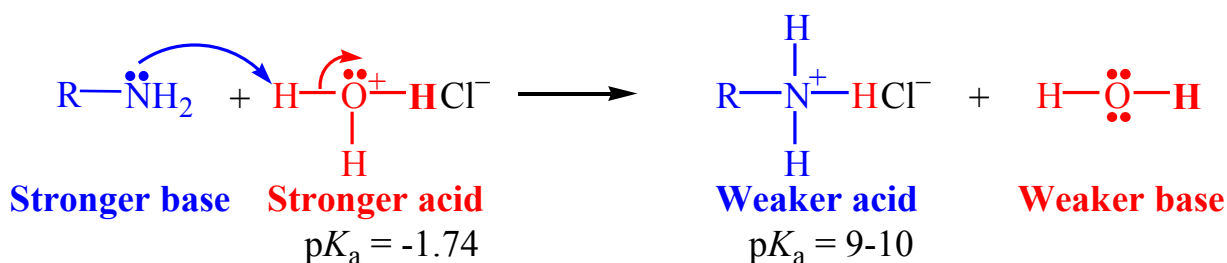
4. **Water-insoluble amines dissolve readily in hydrochloric acid:**

Water-insoluble   **Water-soluble salt**
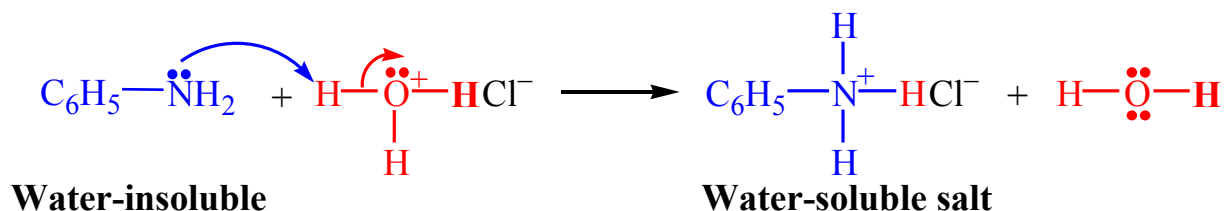
1) Amines of lower molecular weight are very soluble in water.

3.7 THE RELATIONSHIP BETWEEN STRUCTURE AND ACIDITY

1. The strength of an acid depends on the extent to which a proton can be separated from it and transferred to a base.

    1) Breaking a bond to the proton ⇒ **the strength of the bond to the proton is the dominating effect**.

    2) Making the conjugate base more electrically negative.

    3) **Acidity increases as we descend a vertical column:**

Acidity increases →

H–F	H–Cl	H–Br	H–I
$pK_a = 3.2$	$pK_a = -7$	$pK_a = -9$	$pK_a = -10$

← The strength of H−X bond increases
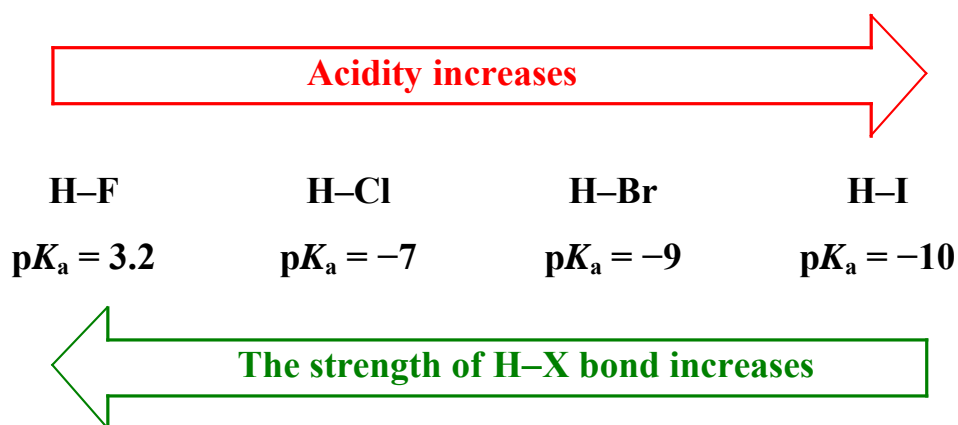
    4) **The conjugate bases of strong acids are very weak bases:**

← Basicity increases

F^- Cl^- Br^- I^-
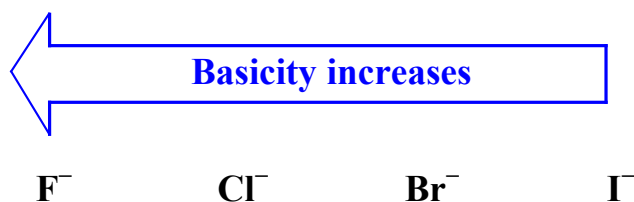
2. Same trend for H_2O, H_2S, and H_2Se:

Acidity increases →

H_2O H_2S H_2Se

← Basicity increases

HO^- HS^- HSe^-
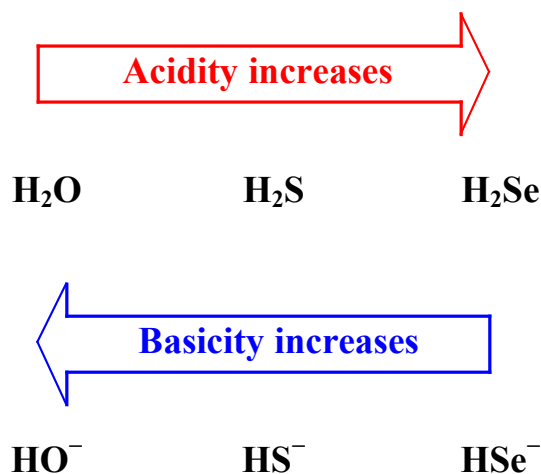
3. **Acidity increases from left to right when we compare compounds in the same horizontal row of the periodic table.**

   1) **Bond strengths are roughly the same, the dominant factor becomes the electronegativity of the atom bonded to the hydrogen.**

   2) The electronegativity of this atom affects **the polarity of the bond to the proton**, and it affects **the relative stability of the anion** (conjugate base).

4. If **A** is more electronegative than **B** for **H—A** and **H—B**:

$$\overset{\delta+\ \ \delta-}{H—A} \quad \text{and} \quad \overset{\delta+\ \ \delta-}{H—B}$$
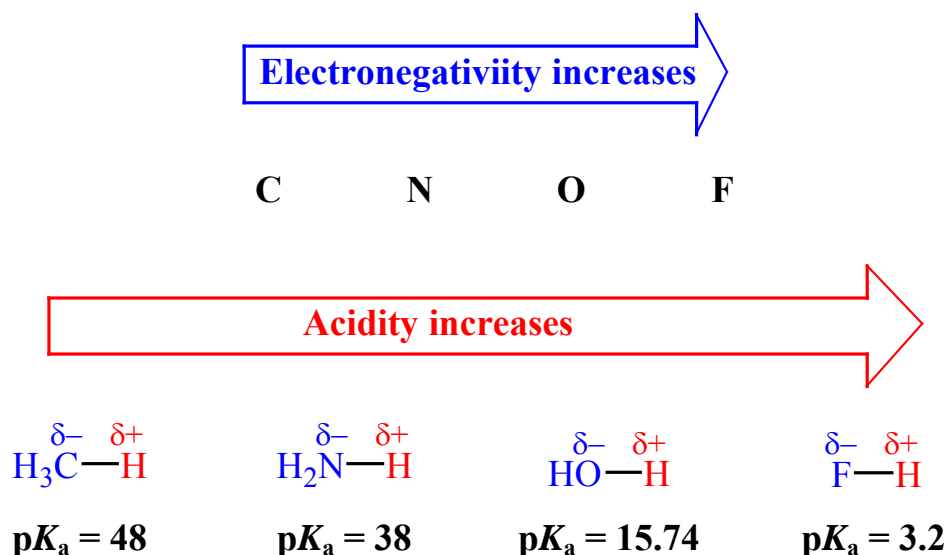
   1) Atom **A** is more **negative** than atom **B** $\Rightarrow$ the proton of **H—A** is more **positive** than that of **H—B** $\Rightarrow$ the proton of **H—A** will **be held less strongly** $\Rightarrow$ the proton of **H—A** will **separate and be transferred to a base more readily**.

   2) **A** will **acquire a negative charge more readily** than **B** $\Rightarrow$ **A**⁻.anion will be **more stable** than **B**⁻.anion

5. The acidity of CH_4, NH_3, H_2O, and HF:

   Electronegativiity increases →

   C   N   O   F

   Acidity increases →

$$\overset{\delta-\ \ \delta+}{H_3C—H} \qquad \overset{\delta-\ \ \delta+}{H_2N—H} \qquad \overset{\delta-\ \ \delta+}{HO—H} \qquad \overset{\delta-\ \ \delta+}{F—H}$$

   $pK_a = 48$ $pK_a = 38$ $pK_a = 15.74$ $pK_a = 3.2$

6. Electrostatic potential maps for CH_4, NH_3, H_2O, and HF:

   1) Almost no positive charge is evident at the hydrogens of methane ($pK_a = 48$).

   2) Very little positive charge is present at the hydrogens of ammonia ($pK_a = 38$).

   3) Significant positive charge at the hydrogens of water ($pK_a = 15.74$).

4) Highest amount of positive charge at the hydrogen of hydrogen fluoride (pK_a = 3.2).
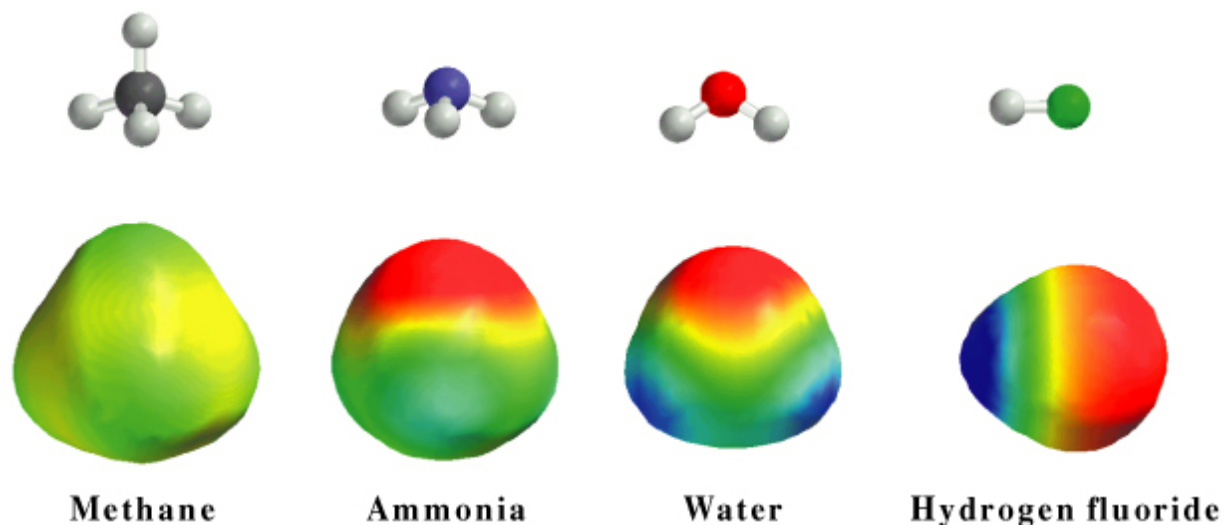
Figure 3.2 **The effect of increasing electronegativity among elements from left to right in the first row of the periodic table is evident in these electrostatic potential maps for methane, ammonia, water, and hydrogen fluoride.**

$$CH_3^- \qquad H_2N^- \qquad HO^- \qquad F^-$$
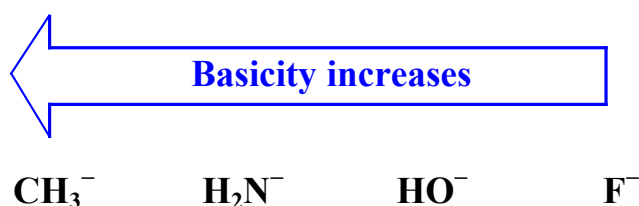
3.7A   THE EFFECT OF HYBRIDIZATION

1. The acidity of ethyne, ethane, and ethane:
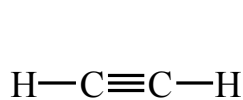
Ethyne	Ethene	Ethane
$pK_a = 25$	$pK_a = 44$	$pK_a = 50$
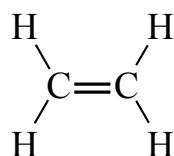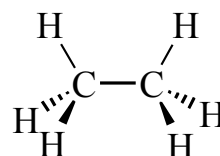
1) Electrons of $2s$ orbitals have lower energy than those of $2p$ orbitals because *electrons in 2s orbitals tend, on the average, to be much closer to the nucleous than electrons in 2p orbitals*.

2) **Hybrid orbitals having more *s* character means that the electrons of the anion will, on the average, be lower in energy, and the anion will be more stable**.

2. **Electrostatic potential maps for ethyne, ethene, and ethane:**
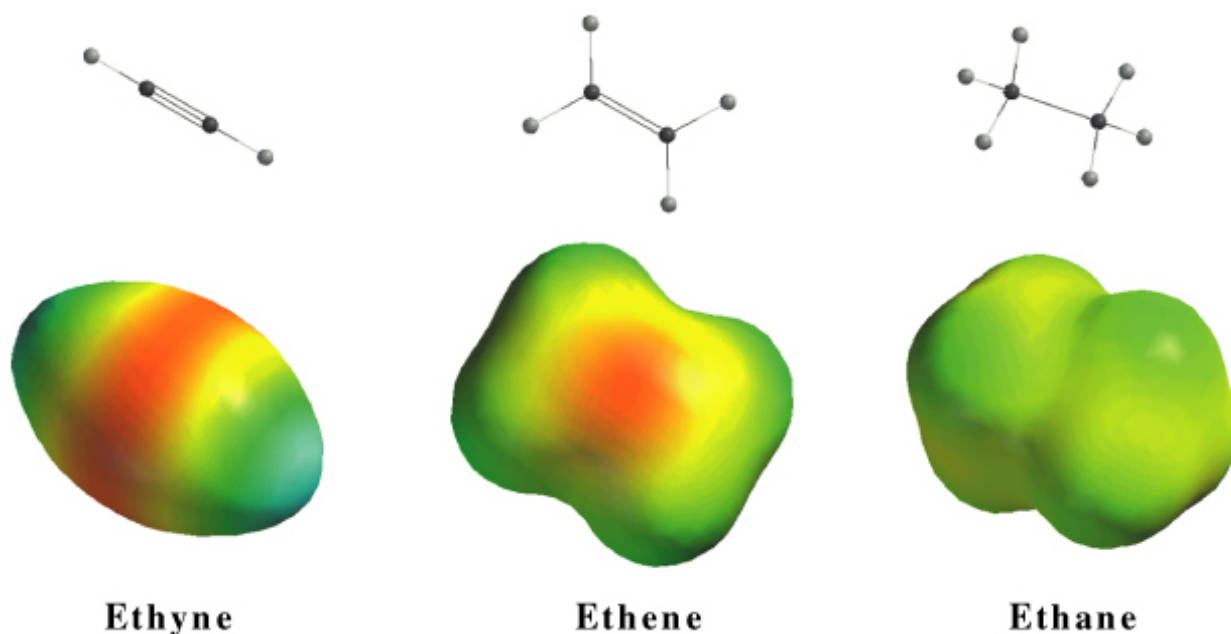
Figure 3.3   Electrostatic potential maps for ethyne, ethene, and ethane.

1) Some positive charge is clearly evident on the hydrogens of ethyne.
2) Almost no positive charge is present on the hydrogens of ethene and ethane.
3) Negative charge resulting from electron density in the π bonds of ethyne and ethene is evident in **Figure 3.3**.
4) The π electron density in the triple bond of ethyne is cylindrically symmetric.

3. *Relative Acidity of the Hydrocarbon*:

$$HC{\equiv}CH \quad > \quad H_2C{=}CH_2 \quad > \quad H_3C{-}CH_3$$
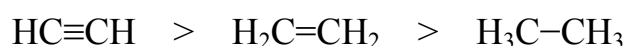
4. *Relative Basicity of the Carbanions*:

$$H_3C{-}CH_2{:}^- \quad > \quad H_2C{=}CH{:}^- \quad > \quad HC{\equiv}C{:}^-$$
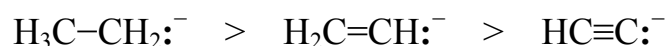
3.7B INDUCTIVE EFFECTS

1. The C—C bond of ethane is completely nonpolar:

<div align="center">

$H_3C{-}CH_3$ **Ethane**
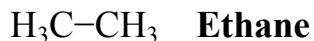
The C−C bond is nonpolar.

</div>

2. The C—C bond of ethyl fluoride is polarized:

<div align="center">

$\overset{\delta+}{H_3C}{\rightarrow}{-}\overset{\delta+}{CH_2}{\rightarrow}{-}\overset{\delta-}{F}$

2   1

</div>
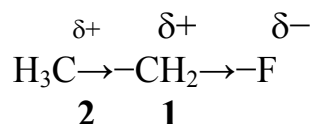
1) **C1** is more positive than **C2** as a result of the electron-attracting ability of the fluorine.

3. **Inductive effect:**
   1) **Electron attracting** (or **electron withdrawing**) **inductive effect**
   2) **Electron donating** (or **electron releasing**) **inductive effect**

4. **Electrostatic potential map:**
   1) **The distribution of negative charge around the electronegative fluorine is evident.**
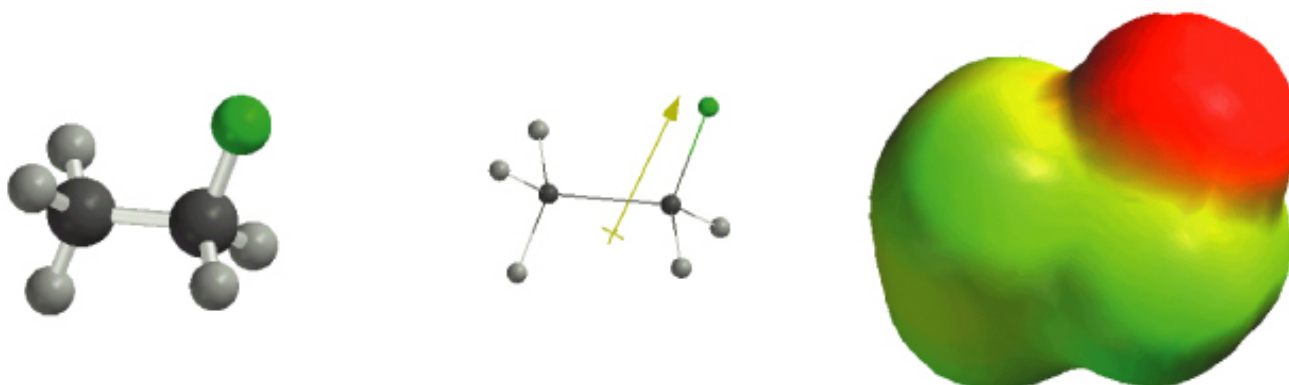
Figure 3.4   Ethyl fluoride (fluoroethane): structure, dipole moment, and charge distribution.

3.8   ENERGY CHANGES

1.   **Kinetic energy** and **potential energy**:

   1)   **Kinetic energy** is the energy an object has because of its motion.

$$K.E. = \frac{mv^2}{2}$$

   2)   **Potential energy** is stored energy.
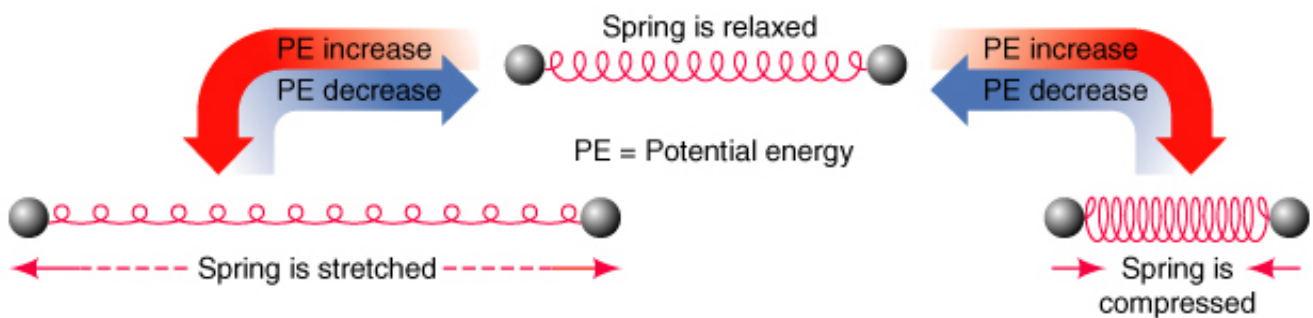
Figure 3.5   Potential energy (PE) exists between objects that either attract or repel each other.   When the spring is either stretched or compressed, the PE of the two balls increases.

2.   **Chemical energy** is a form of potential energy.

   1)   It exists because attractive and repulsive electrical forces exist between different pieces of the molecule.

   2)   Nuclei attract electrons, nuclei repel each other, and electrons repel each other.

3.   **Relative potential energy**:

   1)   The **relative stability** of a system is inversely related to its relative potential energy.

   2)   The **more potential energy** an object has, the **less stable** it is.

3.8A POTENTIAL ENERGY AND COVALENT BONDS

1. **Formation of covalent bonds:**

$$H\bullet \;+\; H\bullet \longrightarrow H-H \qquad \Delta H° = -435 \text{ kJ mol}^{-1}$$

   1) The **potential energy** of the atoms decreases by 435 kJ mol^{-1} as the covalent bond forms.
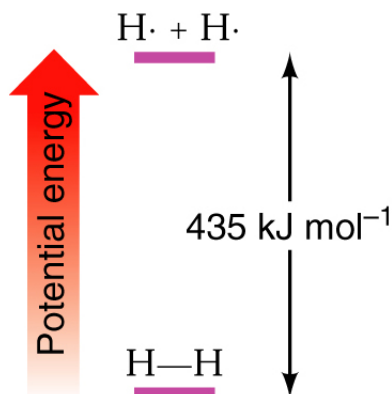
Figure 3.6 **The relative potential energies of hydrogen atoms and a hydrogen molecule.**

2. **Enthalpies** (**heat contents**), *H*: (***Enthalpy*** comes from *en* + Gk: *thalpein* to heat)

3. **Enthalpy change, ΔH°:** the difference in relative enthalpies of reactants and products in a chemical change.

   1) **Exothermic** reactions have ***negative*** ΔH°.

   2) **Endothermic** reactions have ***positive*** ΔH°.

3.9 THE RELATIONSHIP BETWEEN THE EQUILIBRIUM CONSTANT AND THE STANDARD FREE-ENERGY CHANGE, *ΔG°*

3.9A Gibbs Free-energy

1. **Standard free-energy change (*ΔG°*):**

$$\Delta G° = -2.303 \; RT \log K_{\text{eq}}$$

   1) The unit of energy in SI units is the joule, J, and 1 cal = 4.184 J.

   2) A kcal is the amount of energy in the form of heat required to raise the

temperature of 1 Kg of water at 15 °C by 1 °C.

3) The reactants and products are in their standard states: 1 atm pressure for a gas, and 1 *M* for a solution.

2. **Negative value of $\Delta G°$**: **favor the formation of products** when equilibrium is reached.

   1) The K_{eq} is larger than 1.

   2) Reactions with a $\Delta G°$ more negative than about 13 kJ mol^{-1} (3.11 kcal mol^{-1}) are said to *go to completion*, meaning that almost all (>99%) of the reactants are converted into products when equilibrium is reached.

3. **Positive value of $\Delta G°$**: **unfavor the formation of products** when equilibrium is reached.

   1) The K_{eq} is less than 1.

4. $\Delta G° = \Delta H° - T\Delta S°$

   1) $\Delta S°$: changes in the relative order of a system.

   i) A positive entropy change $(+\Delta S°)$: a change from a more ordered system to a less ordered one.

   ii) A negative entropy change $(-\Delta S°)$: a change from a less ordered system to a more ordered one.

   iii) A **positive entropy change** (from order to disorder) makes a **negative contribution to $\Delta G°$** and is energetically **favorable** for the **formation of products**.

   2) For many reactions in which the number of molecules of products equals the number of molecules of reactants $\Rightarrow$ **the entropy change is small $\Rightarrow \Delta G°$ will be determined by $\Delta H°$** except at high temperatures.

3.10 THE ACIDITY OF CARBOXYLIC ACIDS

1. **Carboxylic acids are much more acidic than the corresponding alcohols:**

   1) pK_as for R–COOH are in the range of 3-5;.pK_as for R–OH are in the range of 15-18.

$$
\begin{matrix}
& O \\
& \| \\
H_3C-&C-OH \\
\end{matrix}
\qquad\qquad
H_3C-CH_2-OH
$$

Acetic acid	**Ethanol**
$pK_a = 4.75$	$pK_a = 16$
$\Delta G^\circ = 27$ kJ mol^{-1}	$\Delta G^\circ = 90.8$ kJ mol^{-1}
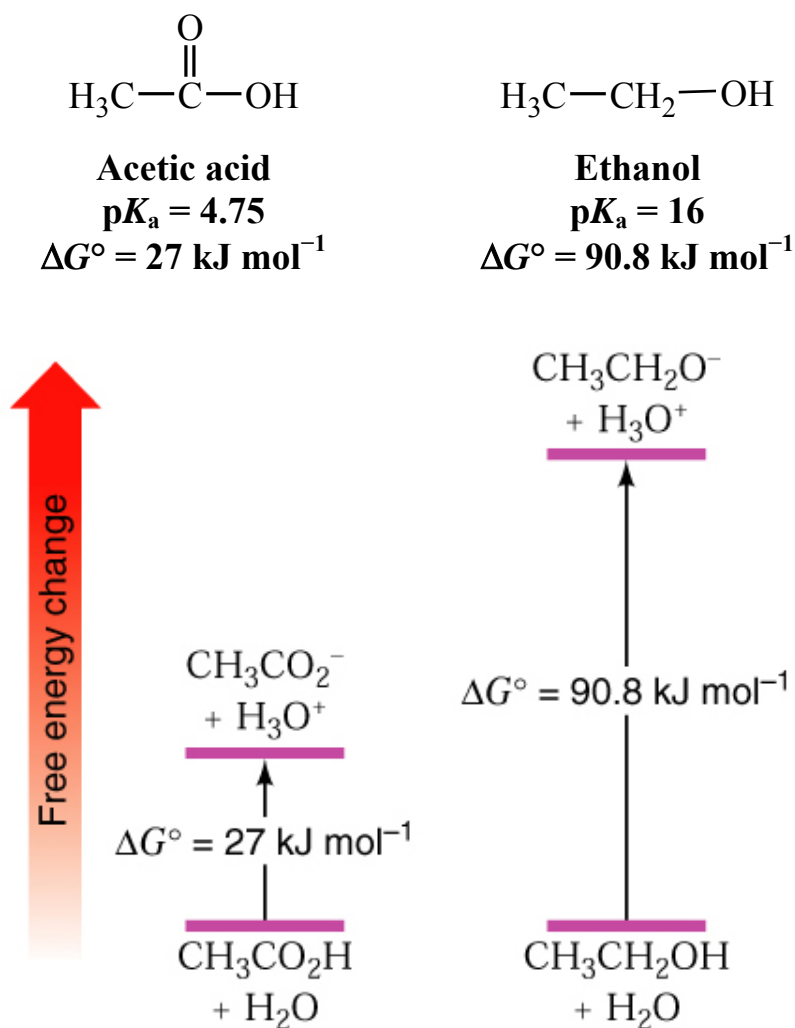
Figure 3.7 A diagram comparing the free-energy changes that accompany ionization of acetic acid and ethanol. Ethanol has a larger positive free-energy change and is a weaker acid because its ionization is more unfavorable.

3.10A   AN EXPLANATION BASED ON RESONANCE EFFECTS

1. **Resonance stabilized acetate anion:**

Acetic Acid   Aceate Ion

Small resonance stabilization   **Largeresonance stabilization**

(The structures are not equivalent   *(The structures are equivalent*
and the lower structure requires   *and there is no requirement for*
charge separation.)   *charge separation.)*
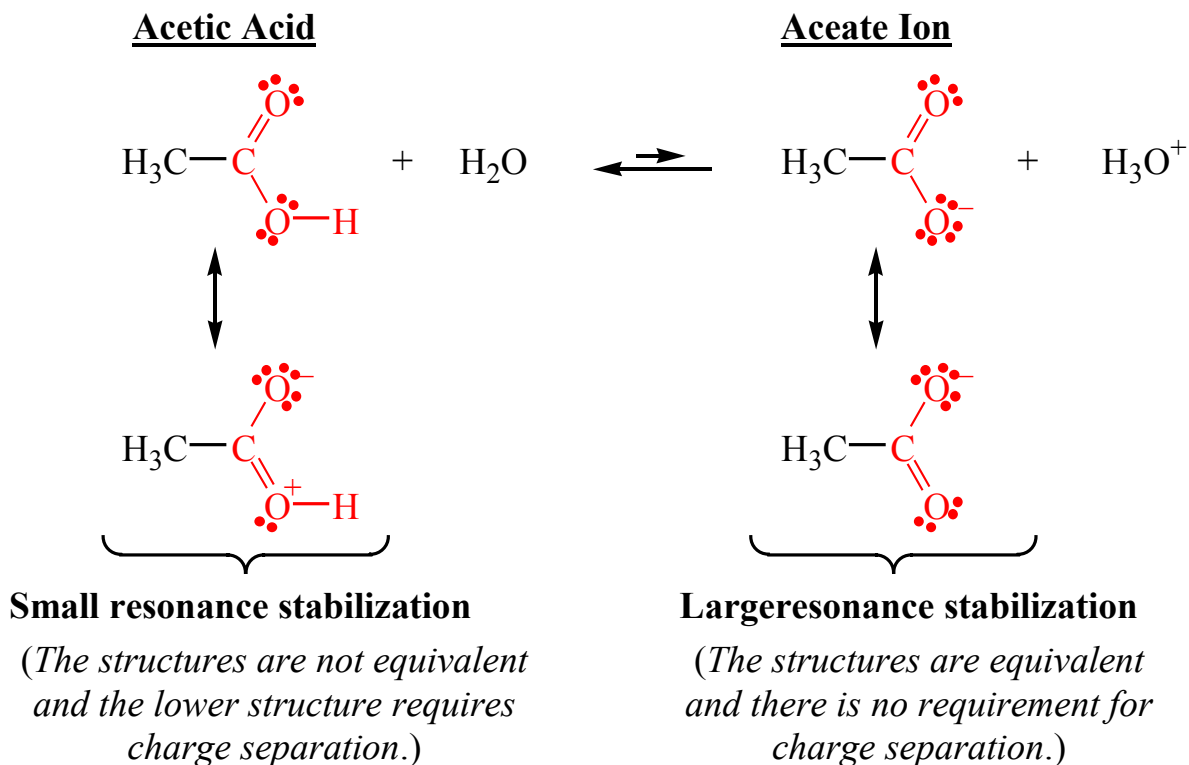
Figure 3.8   **Two resonance structures that can be written for acetic acid and two that can be written for acetate ion. According to a resonance explanation of the greater acidity of acetic acid, the equivalent resonance structures for the acetate ion provide it greater resonance stabilization and reduce the positive free-energy change for the ionization.**

1)   The greater stabilization of the carboxylate anion (relative to the acid) lowers the free energy of the anion and thereby decreases the positive free-energy change required for the ionization.

2)   **Any factor that makes the free-energy change for the ionization of an acid less positive (or more negative) makes the acid stronger.**

2. **No resonance stabilization for an alcohol and its alkoxide anion:**

$$H_3C-CH_2-\overset{..}{\underset{..}{O}}-H \;+\; H_2O \;\rightleftharpoons\; H_3C-CH_2-\overset{..}{\underset{..}{O}}\!:^{-} \;+\; H_3O^{+}$$
No resonance stabilization   **No resonance stabilization**
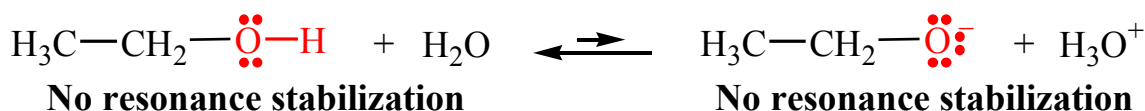
3.10B AN EXPLANATION BASED ON INDUCTIVE EFFECTS

1. **The inductive effect of the carbonyl group** (C=O group) is responsible for the acidity of carboxylic acids.

$$H_3C-\overset{\overset{\displaystyle O}{\parallel}}{C}\!\leftarrow\!O\!\leftarrow\!H \qquad\qquad H_3C-CH_2-O\!\leftarrow\!H$$

<div align="center">

Acetic acid
(Stronger acid)   **Ethanol**
(Weaker acid)

</div>
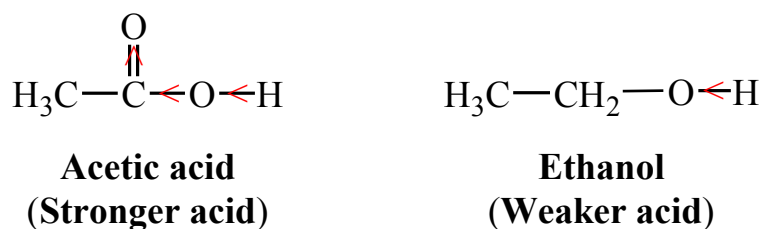
1) In both compounds the O—H bond is highly polarized by the greater electronegativity of the oxygen atom.

2) The carbonyl group has a more powerful electron-attracting inductive effect than the CH_2 group.

3) The carbonyl group has two resonance structures:

<div align="center">
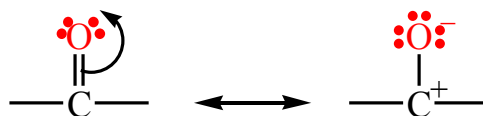
Resonance structures for the carbonyl group

</div>

4) *The second resonance structure above is an important contributor to the overall resonance hybrid.*

5) The carbon atom of the carbonyl group of acetic acid bears **a large positive charge**, it adds its electron-withdrawing inductive effect to that of the oxygen atom of the hydroxyl group attached to it.

6) **These combined effects make the hydroxyl proton much more positive than the proton of the alcohol.**

2. The electron-withdrawing inductive effect of the carbonyl group also stabilizes the acetate ion, and therefore **the acetate ion is a weaker base than the ethoxide ion**.

$$H_3C-\overset{\overset{\displaystyle O\delta-}{\parallel}}{C}\!\leftarrow\!O^{\delta-} \qquad\qquad H_3C-CH_2\!\leftarrow\!O^-$$

3. The electrostatic potential maps for the acetate and the ethoxide ions:

Acetate ion   Ethoxide ion
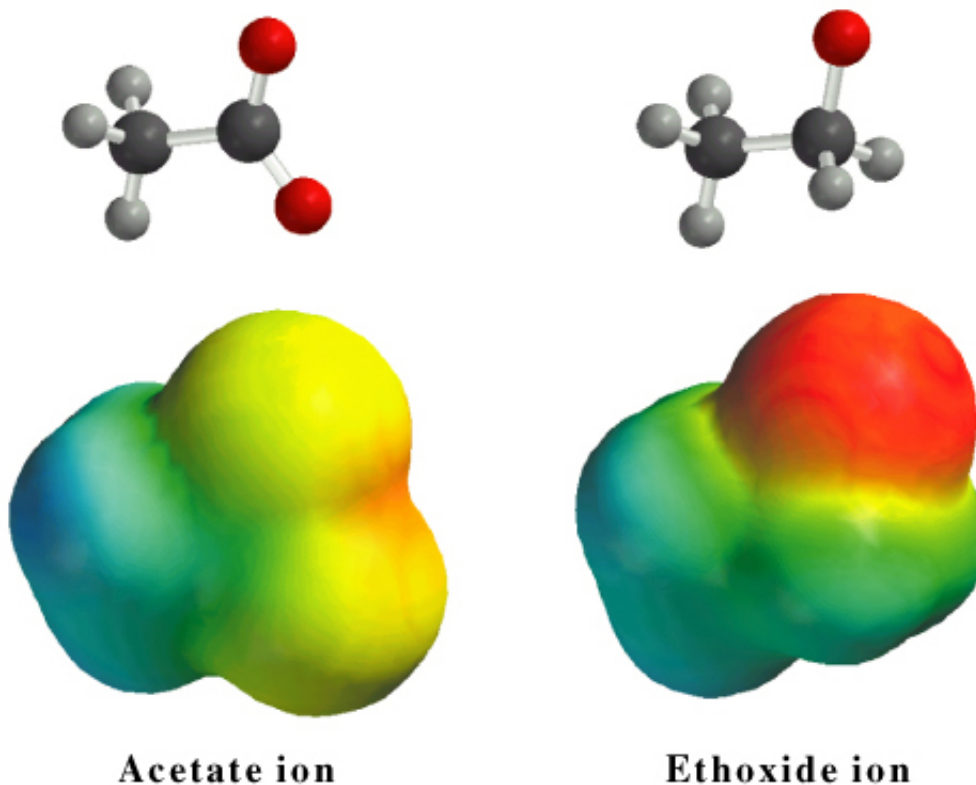
Figure 3.9   Calculated electrostatic potential maps for acetate anion and ethoxide anion.   Although both molecules carry the same –1 net charge, acetate stabilizes the charge better by dispersing it over both oxygens.

1) The negative charge in acetate anion is evenly distributed over the two oxygens.

2) The negative charge is localized on its oxygen in ethoxide anion.

3) The ability to better stabilize the negative charge makes the acetate a weaker base than ethoxide (and hence its conjugate acid stronger than ethanol)..

3.10C INDUCTIVE EFFECTS OF OTHER GROUPS

1. Acetic acid and chloroacetic acid:

$$H_3C-\overset{\overset{O}{\|}}{C}\leftarrow O\leftarrow H \qquad\qquad Cl\leftarrow CH_2\leftarrow\overset{\overset{O}{\|}}{C}\leftarrow O\leftarrow H$$

$$\text{p}K_a = 4.75 \qquad\qquad \text{p}K_a = 2.86$$

1) The extra electron-withdrawing inductive effect of the electronegative **chlorine atom** is responsible for the greater acidity of chloroacetic acid by making the hydroxyl proton of chloroacetic acid even **more positive** than that of acetic acid.

2) It stabilizes the chloroacetate ion by **dispersing its negative charge**.
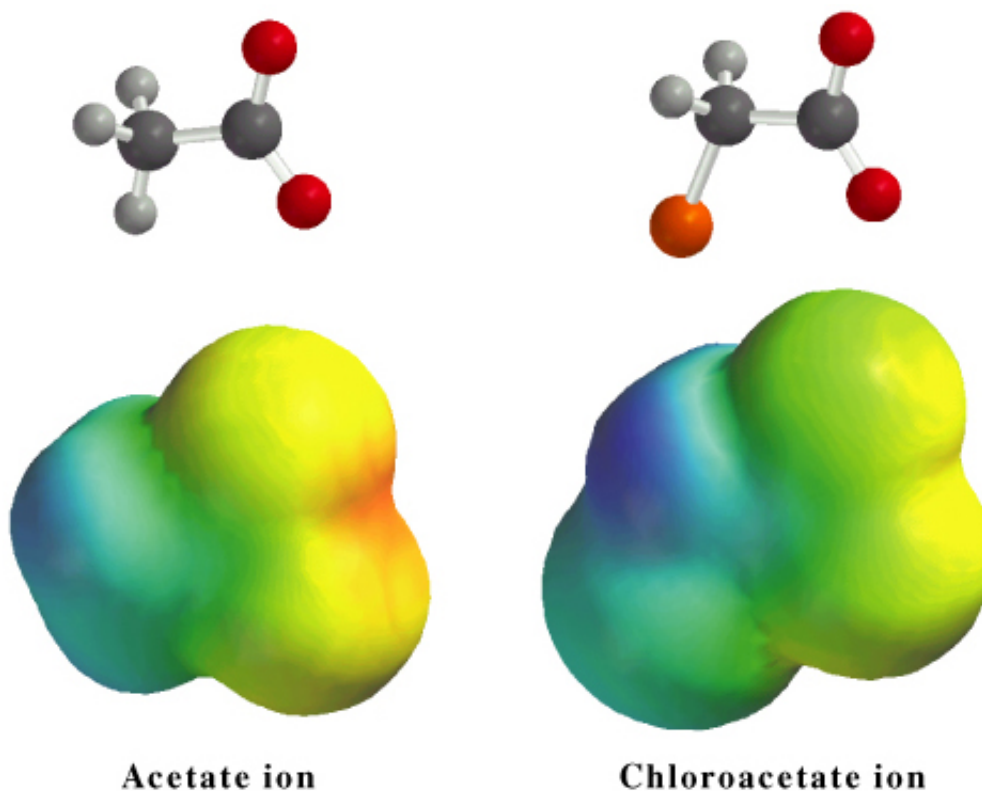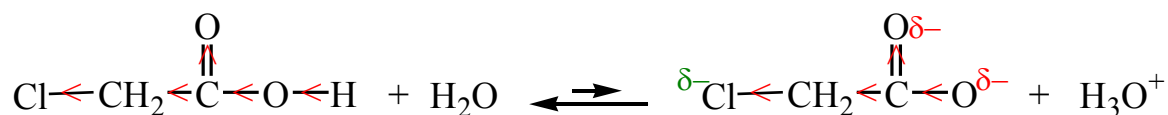
Figure 3.10 The electrostatic potential maps for acetate and chloroacetate ions show the relatively greater ability of chloroacetate to disperse the negative charge.

3) **Dispersal of charge always makes a species more stable.**

4) **Any factor that stabilizes the conjugate base of an acid increases the strength of the acid.**

3.11 THE EFFECT OF THE SOLVENT ON ACIDITY

1. In the absence of a solvent (i.e., in the gas phase), most acids are far weaker than they are in solution.   For example, acetic acid is estimated to have a pK_a of about 130 in the gas phase.

$$H_3C-\overset{\overset{\textstyle O}{\|}}{C}-O-H \quad + \quad H_2O \quad \rightleftharpoons \quad H_3C-\overset{\overset{\textstyle O}{\|}}{C}-O^- \quad + \quad H_3O^+$$

> 1) **In the absence of a solvent, separation of the ions is difficult.**
>
> 2) **In solution, solvent molecules surround the ions, insulating them from one another, stabilizing them, and making it far easier to separate them than in the gas phase.**

3.11A Protic and Aprotic solvents

1. **Protic solvent:** a solvent that has a **hydrogen atom attached to a strongly electronegative element** such as oxygen or nitrogen.

2. **Aprotic solvent:**

3. Solvation by hydrogen bonding is important in protic solvent:

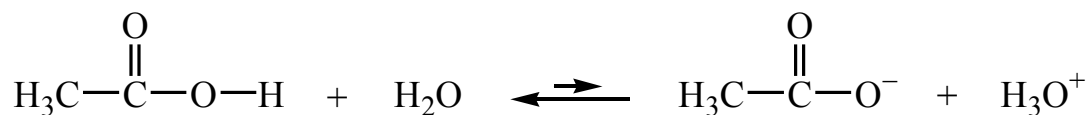   1) Molecules of a protic solvent can form **hydrogen bonds** to the unshared electron pairs of oxygen atoms of an acid and its conjugate base, but **they may not stabilize both equally**.

    2) Hydrogen bonding to $CH_3CO_2^-$ is much stronger than to CH_3CO_2H because the water molecules are more attracted by the negative charge.

4. Solvation of any species decreases the entropy of the solvent because the solvent molecules become much more ordered as they surround molecules of the solute.

    1) Solvation of $CH_3CO_2^-$ is stronger $\Rightarrow$ the the solvent molecules become more orderly around it $\Rightarrow$ the entropy change ($\Delta S°$) for the ionization of acetic acid is negative $\Rightarrow$ the $-T\Delta S°$ makes a positive contribution to $\Delta G°$ $\Rightarrow$ weaker acid.

2) **Table 3.2** shows, the $-T\Delta S°$ term contributes more to $\Delta G°$ than $\Delta H°$ does $\Rightarrow$ the free-energy change for the ionization of acetic acid is positive (unfavorable).

3) Both $\Delta H°$ and $-T\Delta S°$ are more favorable for the ionization of chloroacetic acid. The larger contribution is in the entropy term.

4) Stabilization of the chloroacetate anion by the chlorine atom makes the chloroacetate ion less prone to cause an ordering of the solvent because it requires less stabilization through solvation.

Table 3.2   Thermodynamic Values for the Dissociation of Acetic and Chloroacetic Acids in H$_2$O at 25 °C

Acid	pK_a	$\Delta G°$ (kJ mol^{-1})	$\Delta H°$ (kJ mol^{-1})	$-T\Delta S°$ (kJ mol^{-1})
CH$_3$CO$_2$H	4.75	+27	–0.4	+28
ClCH$_2$CO$_2$H	2.86	+16	–4.6	+21

Table   Explanation of thermodynamic quantities: $\Delta G° = \Delta H° - T\Delta S°$

Term	Name	Explanation
$\Delta G°$	Gibbs free-energy change (*kcal*/*mol*)	Overall energy difference between reactants and products. When $\Delta G°$ is negative, a reaction can occur spontaneously. $\Delta G°$ is related to the equilibrium constant by the equation: $\Delta G° = -RT\ln K_{eq}$
$\Delta H°$	Enthalpy change (*kcal*/*mol*)	Heat of reaction; the energy difference between strengths of bonds broken in a reaction and bonds formed
$\Delta S°$	Entropy change (*cal*/*degree*×*mol*)	Overall change in freedom of motion or "disorder" resulting from reaction; usually much smaller than $\Delta H°$

3.12 ORGANIC COMPOUNDS AS BASES

3.12A Organic Bases

1. An organic compound contains an atom with an unshared electron pair is a potential base.

1)

$$H_3C-\overset{\cdot\cdot}{\underset{|}{O}}: \quad + \quad H-\overset{\cdot\cdot}{\underset{\cdot\cdot}{Cl}}: \quad \longrightarrow \quad H_3C-\overset{\cdot\cdot}{\underset{|}{O}}{}^{+}-H \quad + \quad :\overset{\cdot\cdot}{\underset{\cdot\cdot}{Cl}}:$$

Methanol   **Methyloxonium ion**
           (a protonated alcohol)
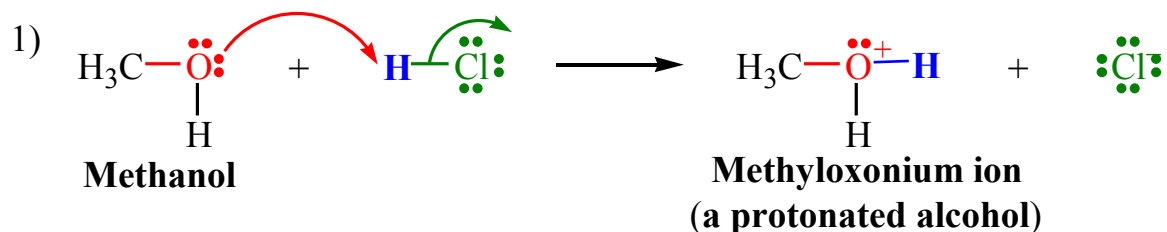
  i) The conjugate acid of the alcohol is called a **protonated alcohol** (more formally, **alkyloxonium ion**).

2)

$$R-\overset{\cdot\cdot}{\underset{|}{O}}: \quad + \quad H-A \quad \longrightarrow \quad R-\overset{\cdot\cdot}{\underset{|}{O}}{}^{+}-H \quad + \quad :A^-$$

Alcohol   **Strong acid**   **Alkyloxonium ion**   **Weak base**

3)

$$R-\overset{\cdot\cdot}{\underset{|}{O}}: \quad + \quad H-A \quad \longrightarrow \quad R-\overset{\cdot\cdot}{\underset{|}{O}}{}^{+}-H \quad + \quad :A^-$$

Alcohol   **Strong acid**   **Dialkyloxonium ion**   **Weak base**

4)

$$\underset{R}{\overset{R}{\diagdown}}C=\overset{\cdot\cdot}{\underset{\cdot\cdot}{O}}: \quad + \quad H-A \quad \longrightarrow \quad \underset{R}{\overset{R}{\diagdown}}C=\overset{\cdot\cdot}{O}{}^{+}-H \quad + \quad :A^-$$

Ketone   **Strong acid**   **Protonated ketone**   **Weak base**
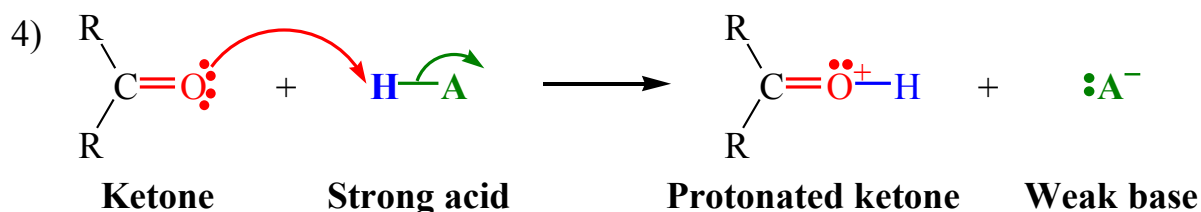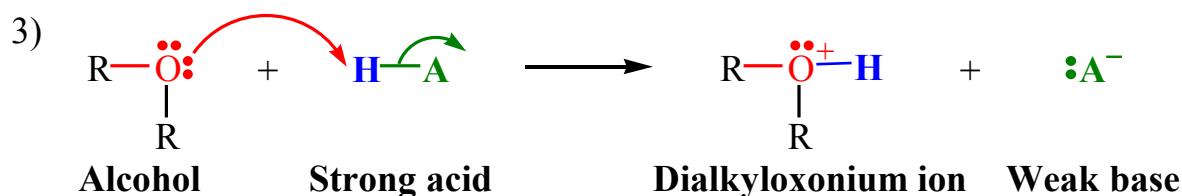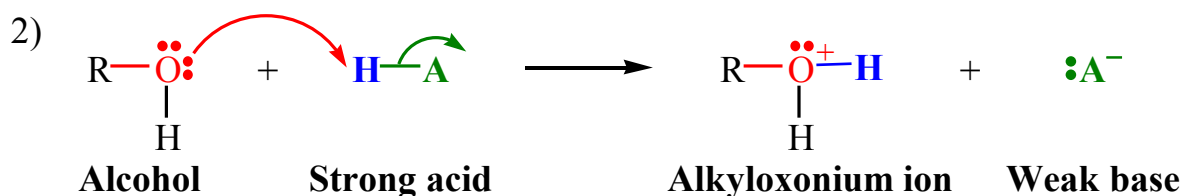
5) **Proton transfer reactions are often the first step in many reactions that alcohols, ethers, aldehydes, ketones, esters, amides, and carboxylic acids undergo.**

6) The π bond of an alkene can act as a base:

The π bond breaks

This bond breaks

This bond is formed

C=C + H—A → C—C—H + :A⁻

Alkene   **Strong acid**   **Carbocation**   **Weak base**
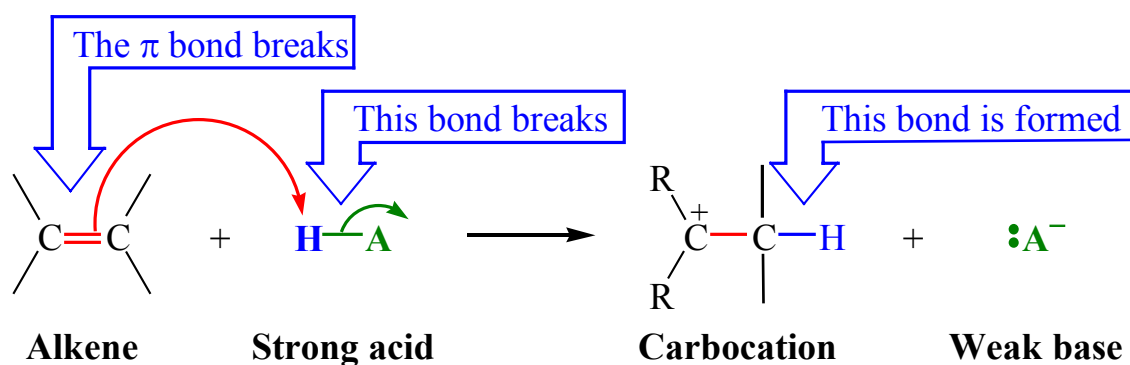
i)   The π bond of the double bond and the bond between the proton of the acid and its conjugate base are broken; a bond between a carbon of the alkene and the proton is formed.

ii) A **carbocation** is formed.

3.13 A MECHANISM FOR AN ORGANIC REACTION

1.

$$H_3C-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-OH \quad + \quad H-\overset{+}{\underset{H}{O}}-H \quad + \quad :\ddot{Cl}:^- \quad \xrightarrow{H_2O} \quad H_3C-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-\ddot{Cl}: \quad + \quad 2\,H_2O$$

tert-Butyl alcohol
(**soluble in H₂O**)

Conc. HCl

tert-Butyl chloride
(**insoluble in H₂O**)
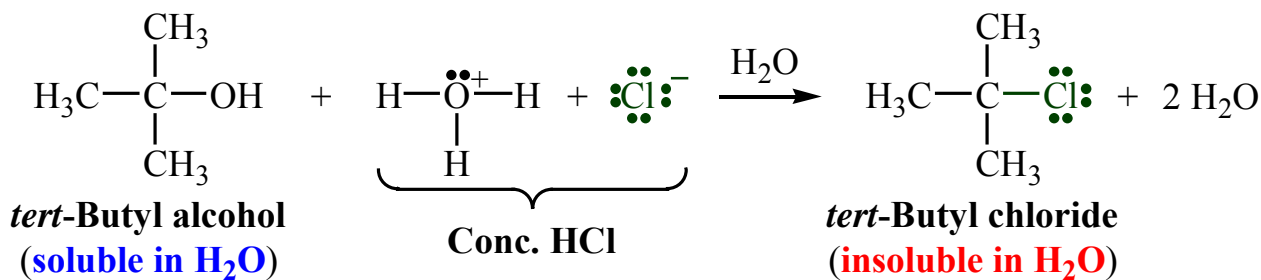
A Mechanism for the Reaction

Reaction of *tert*-Butyl Alcohol with Concentrated Aqueous HCl:

Step 1

***tert*-Butyloxonium ion**
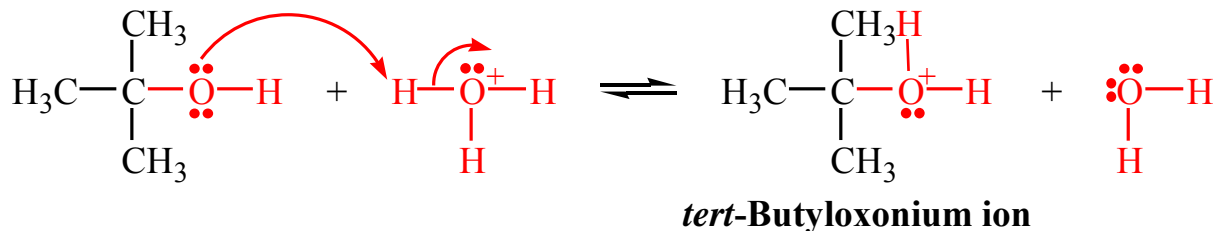
***tert*-Butyl alcohol acts as a base and accepts a proton from the hydronium ion.** **The product is a protonated alcohol and water (the conjugate acid and base).**

Step 2
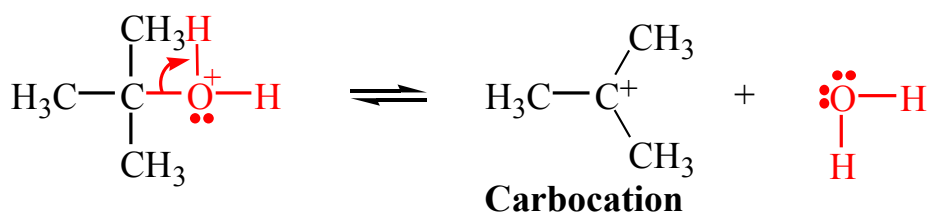
Carbocation

The bond between the carbon and oxygen of the *tert*-butyloxonium ion breaks heterolytically, leading to the formation of a carbocation and a molecule of water.

Step 3

***tert*-Butyl chloride**
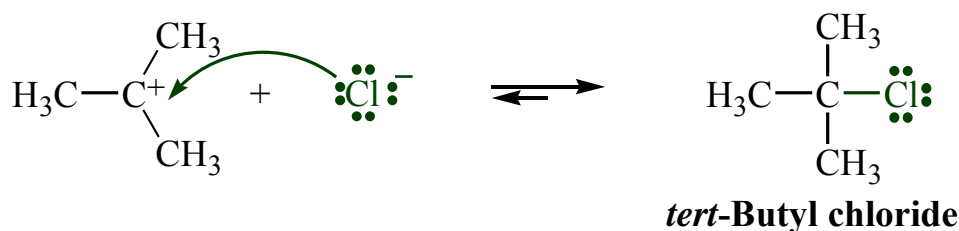
The carbocation, acting as a Lewis acid, accepts an electron pair from a chloride ion to become the product.

2. Step 1 is a straightforward Brønsted acid-base reaction.

3. Step 2 is the reverse of a Lewis acid-base reaction. (The presence of a formal positive charge on the oxygen of the protonated alcohol weakens the

carbon-oxygen by drawing the electrons in the direction of the positive oxygen.)

4. Step 3 is a Lewis acid-base reaction.

3.14 ACIDS AND BASES IN NONAQUEOUS SOLUTIONS

1. The amide ion (NH_2^-) of sodium amide ($NaNH_2$) is a very powerful base:

$$\text{H}-\overset{..}{\underset{..}{\text{O}}}-\text{H} \quad + \quad :\!\overset{..}{\text{N}}\text{H}_2^- \quad \xrightarrow[\text{NH}_3]{\text{liquid}} \quad \text{H}-\overset{..}{\underset{..}{\text{O}}}:^- \quad + \quad :\text{NH}_3$$

Stronger acid   **Stronger base**   **Weaker base**   **Weaker acid**
$pK_a = 15.74$ $pK_a = 38$
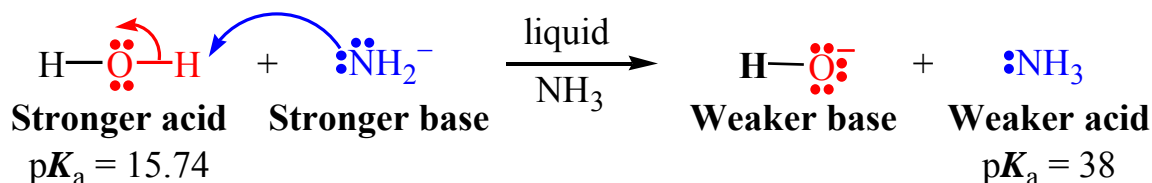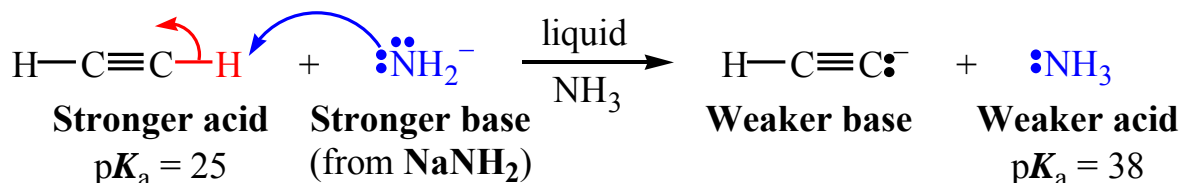
1) **Leveling effect**: the **strongest base** that can exist in aqueous solution in significant amounts is the **hydroxide** ion.

2. In solvents other than water such as hexane, diethyl ether, or liquid ammonia (b.p. –33 °C), bases stronger than hydroxide ion can be used. All of these solvents are **very weak acids**.

$$\text{H}-\text{C}\equiv\text{C}-\text{H} \quad + \quad :\!\overset{..}{\text{N}}\text{H}_2^- \quad \xrightarrow[\text{NH}_3]{\text{liquid}} \quad \text{H}-\text{C}\equiv\text{C}:^- \quad + \quad :\text{NH}_3$$

Stronger acid   **Stronger base**   **Weaker base**   **Weaker acid**
$pK_a = 25$ **(from NaNH$_2$)** $pK_a = 38$

1) **Terminal alkynes**:

$$\text{R}-\text{C}\equiv\text{C}-\text{H} \quad + \quad :\!\overset{..}{\text{N}}\text{H}_2^- \quad \xrightarrow[\text{NH}_3]{\text{liquid}} \quad \text{R}-\text{C}\equiv\text{C}:^- \quad + \quad :\text{NH}_3$$

Stronger acid   **Stronger base**   **Weaker base**   **Weaker acid**
$pK_a \cong 25$ $pK_a = 38$
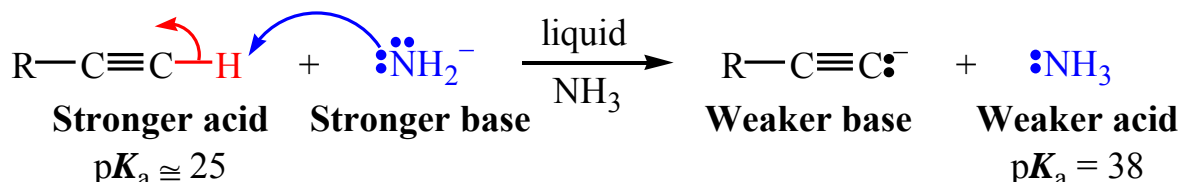
3. **Alkoxide ions** (RO^-) are the conjugate bases when alcohols are utilized as solvents.

1) Alkoxide ions are somewhat **stronger bases** than hydroxide ions because alcohols are weaker acids than water.

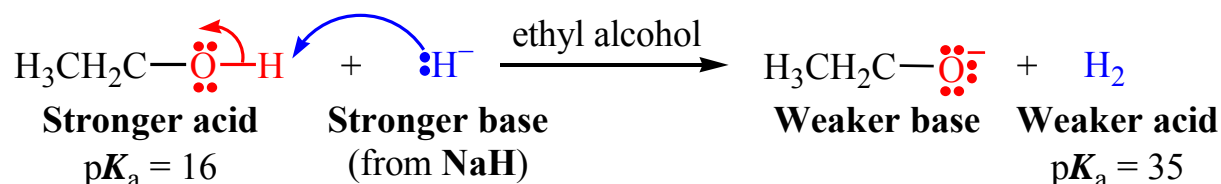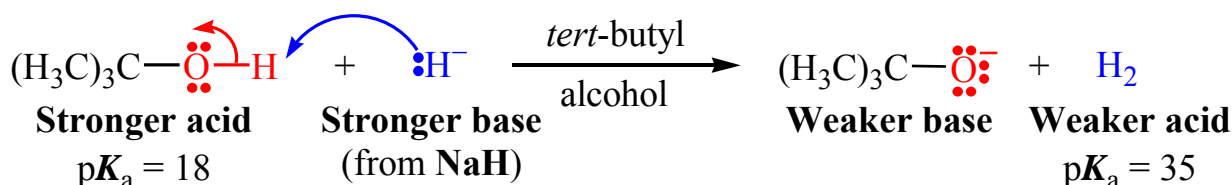2) Addition of sodium hydride (NaH) to ethanol produces a solution of sodium ethoxide (CH_3CH_2ONa) in ethanol.

$$H_3CH_2C\!-\!\ddot{O}\!-\!H \quad + \quad :H^- \xrightarrow{\text{ethyl alcohol}} H_3CH_2C\!-\!\ddot{O}:^- \quad + \quad H_2$$

Stronger acid   **Stronger base**   **Weaker base**   **Weaker acid**

$pK_a = 16$ (from **NaH**) $pK_a = 35$

3) Potassium *tert*-butoxide ions, $(CH_3)_3COK$, can be generated similarily.

$$(H_3C)_3C\!-\!\ddot{O}\!-\!H \quad + \quad :H^- \xrightarrow[\text{alcohol}]{\textit{tert}\text{-butyl}} (H_3C)_3C\!-\!\ddot{O}:^- \quad + \quad H_2$$

Stronger acid   **Stronger base**   **Weaker base**   **Weaker acid**

$pK_a = 18$ (from **NaH**) $pK_a = 35$
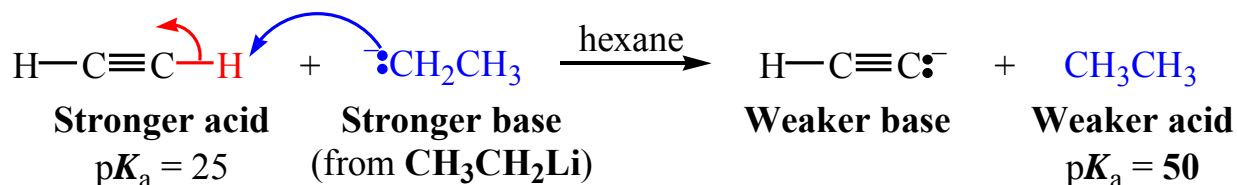
4. **Alkyllithium (RLi):**

1) The C—Li bond has covalent character but is highly polarized to make the carbon negative.

$$\overset{\delta-}{R}\!\!\longleftarrow\!\!\overset{\delta+}{Li}$$
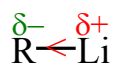
2) Alkyllithium react as though they contain alkanide (**R:⁻**) ions (or alkyl carbanions), the conjugate base of alkanes.

$$H\!-\!C\!\equiv\!C\!-\!H \quad + \quad :CH_2CH_3 \xrightarrow{\text{hexane}} H\!-\!C\!\equiv\!C:^- \quad + \quad CH_3CH_3$$

Stronger acid   **Stronger base**   **Weaker base**   **Weaker acid**

$pK_a = 25$ (from **CH_3CH_2Li**) $pK_a = 50$

3) Alkyllithium can be easily prepared by reacting an alkyl halide with lithium metal in an ether solvent.

3.15 ACIDS-BASE REACTIONS AND THE SYNTHESIS OF

DEUTERIUM- AND TRITIUM-LABELED COMPOUNDS

1. Deuterium (^{2}H) and tritium (^{3}H) label:

   1) For most chemical purposes, deuterium and tritium atoms in a molecule behave in much the same way that ordinary hydrogen atoms behave.

   2) The extra mass and additional neutrons of a deuterium or tritium atom make its position in a molecule easy to locate.

   3) Tritium is radioactive which makes it very easy to locate.

2. **Isotope effect**:

   1) The extra mass associated with these labeled atoms may cause compounds containing deuterium or tritium atoms to react more slowly than compounds with ordinary hydrogen atoms.

   2) Isotope effect has been useful in studying the mechanisms of many reactions.

3. Introduction of deuterium or tritium atom into a specific location in a molecule:

$$\underset{\substack{\textbf{Isopropyl lithium} \\ (\textit{stronger base})}}{H_3C-\overset{\overset{\displaystyle CH_3}{|}}{CH\!:^-}} \quad + \quad \underset{(\textit{stronger acid})}{D_2O} \quad \xrightarrow{\text{hexane}} \quad \underset{\substack{\textbf{2-Deuteriopropane} \\ (\textit{weaker acid})}}{H_3C-\overset{\overset{\displaystyle CH_3}{|}}{CH}-D} \quad + \quad \underset{(\textit{weaker base})}{OD^-}$$