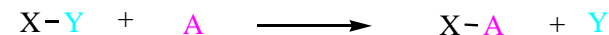# Chapter 3
An Introduction to Organic Reactions:
Acids and Bases

There are 4 types of Organic Reactions
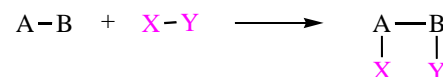
SUBSTITUTION:

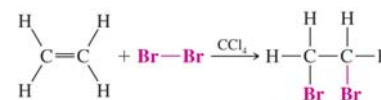$$X-Y \ + \ A \longrightarrow X-A \ + \ Y$$

Example

$$H_3C-Cl + Na^+OH^- \xrightarrow{H_2O} H_3C-OH + Na^+Cl^-$$

ADDITION:

$$A-B \ + \ X-Y \longrightarrow A-B \ (with \ X, Y \ below)$$
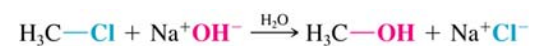
Example

There are 4 Types of Organic Reactions

ELIMINATION

$$\begin{array}{c} A-B \\ |\ \ | \\ X\ \ Y \end{array} \longrightarrow A=B \ + \ X-Y$$
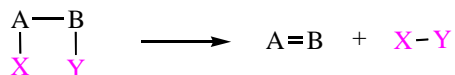
Example

REARRANGEMENT

$$X-A-B \longrightarrow A-B-X$$
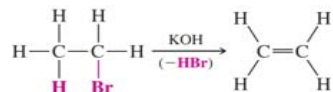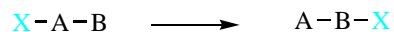
Example
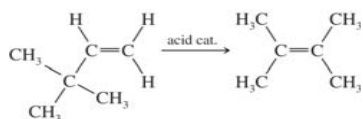
Intermediates In Organic Reactions

Reaction mechanisms are detailed descriptions of changes at the molecular level as reactants become products. Often the reactions involve a sequence of steps with one or more chemical species called **intermediates** that are formed and consumed.

$$A \longrightarrow X$$
Overall Reaction

$$A \longrightarrow [B \longrightarrow C \longrightarrow D] \longrightarrow X$$
Intermediates
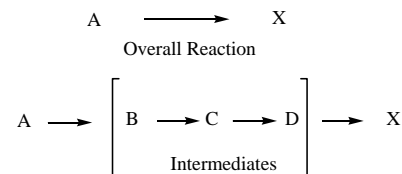
Chemical intermediates typically are not stable structures that can be put in a bottle. Many exist for very short times (10^{-6} - 10^{-9} seconds).

How do bonds break – two options

• **Homolysis**

A : B ⟶ A· + ·B   Homolytic bond cleavage

{ Radicals }

• **Heterolysis**

A : B ⟶ A$^+$ + :B$^-$ Heterolytic bond cleavage

{ Ions }

Heterolytic reactions almost always occur at polar bonds
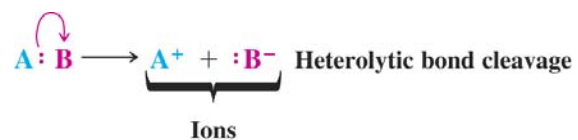
$$^{\delta+}A : B^{\delta-} \longrightarrow A^+ + :B^-$$

• **The reaction is often assisted by formation of a new bond to another molecule**

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

Heterolysis of Bonds to Carbons

Can give a carbocation or carbanion depending on the nature of leaving group Z

$$^{\delta+}C - Z^{\delta-} \xrightarrow{\text{heterolysis}} -C^+ + :Z^-$$

Carbocation

$$^{\delta-}C - Z^{\delta+} \xrightarrow{\text{heterolysis}} -C:^- + Z^+$$

Carbanion
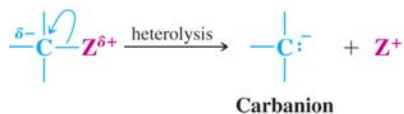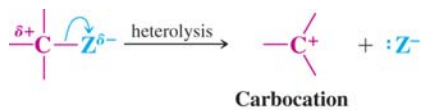
Carbocation has a formal charge on the carbon

$-\overset{|}{\underset{}{C}}{}^+$
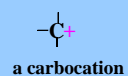
a carbocation

In a carbocation, only **3** of the 6 bonding electrons "belong" to the carbon. There are no nonbonding electrons.

Recall the process for calculating formal charge

Formal Charge = Group # - 1/2 shared - unshared

Formal Charge = 4 - 0 - 1/2 (6) = +1

Carbocation is an Example of a Reactive Intermediate

Carbocation

Reacts quickly with something that has electrons to form a stable C with no + charge.

Carbanion has 8 valence electrons and a negative charge

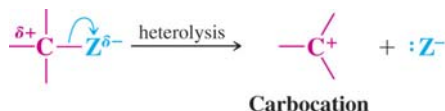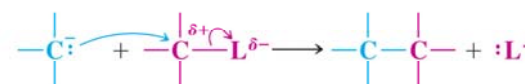It will react with something that is electron-deficient in order to lose its negative charge.

Acids and Bases

Brønsted-Lowry Acids and Bases
- **A Brønsted-Lowry acid is a proton donor.**
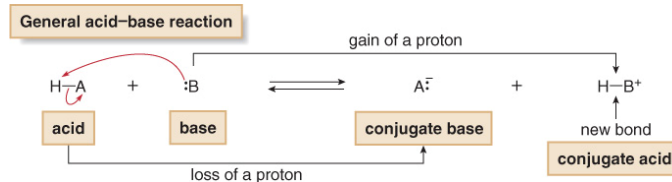- **A Brønsted-Lowry base is a proton acceptor.**
- **H$^+$ = proton**

Figure 2.1 Examples of Brønsted–Lowry acids and bases

Brønsted–Lowry acids [H – A]		Brønsted–Lowry bases [B:]	
Inorganic	Organic	Inorganic	Organic
HCl	CH$_3$CO$_2$H		CH$_3$NH$_2$ CH$_3$O:$^-$
H$_2$SO$_4$	acetic acid	H$_2$O: :NH$_3$	methylamine methoxide
HSO$_4^-$			CH$_3$
H$_2$O	OH		C=O
H$_3$O$^+$	HO$_2$CCH$_2$–C–CH$_2$CO$_2$H	:OH :NH$_2$	CH$_3$
	COOH		acetone CH$_2$=CH$_2$
	citric acid		ethylene

- All Brønsted–Lowry acids contain a proton.
- The net charge may be zero, (+), or (–).
- All Brønsted–Lowry bases contain a lone pair of electrons or a π bond.
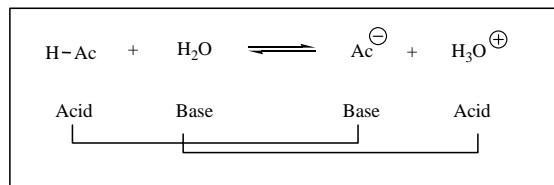- The net charge may be zero or (–).

Acids and Bases

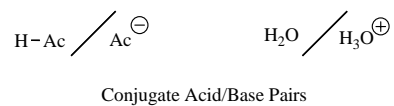**Reactions of Brønsted-Lowry Acids and Bases**

- **A Brønsted-Lowry acid base reaction results in the transfer of a proton from an acid to a base.**
- **In an acid-base reaction, the electron pair of the base B: forms a new bond to the proton of the acid.**
- **The acid H—A loses a proton, leaving the electron pair in the H—A bond on A.**

3

Acids and Bases

$$H-Ac \quad + \quad H_2O \quad \rightleftharpoons \quad Ac^{\ominus} \quad + \quad H_3O^{\oplus}$$

Acid   Base   Base   Acid

Every acid/base reaction has two acids and two bases.

$$H-Ac \diagup Ac^{\ominus} \qquad H_2O \diagup H_3O^{\oplus}$$

Conjugate Acid/Base Pairs

Acids and Bases

There are two kinds of acids:

Strong Acids (completely dissociated in water)

Example:

$$H-Cl \quad + \quad H_2O \quad \longrightarrow \quad Cl^{\ominus} \quad + \quad H_3O^{\oplus}$$
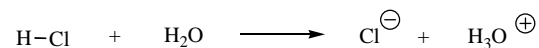
Weak Acids (partly dissociated in water)

Example:

$$H-Ac \quad + \quad H_2O \quad \rightleftharpoons \quad Ac^{\ominus} \quad + \quad H_3O^{\oplus}$$
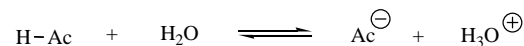
Acids and Bases

There are only about 6 "STRONG ACIDS":

$$HCl, HBr, HI, H_2SO_4, HNO_3, HClO_4$$

ALL other acids are "WEAK ACIDS"

For Weak (most) Acids

Acid Strength and pK_a
- **Acid strength is the tendency of an acid to donate a proton.**
- **The more readily a compound donates a proton, the stronger an acid it is.**
- **Acidity is measured by an equilibrium constant**
- **When a Brønsted-Lowry acid H—A is dissolved in water, an acid-base reaction occurs, and an equilibrium constant can be written for the reaction.**

Dissolving an acid in water

$$H-A \quad + \quad H-\ddot{O}-H \quad \rightleftharpoons \quad A:^- \quad + \quad H-\overset{H}{\underset{+}{O}}-H$$
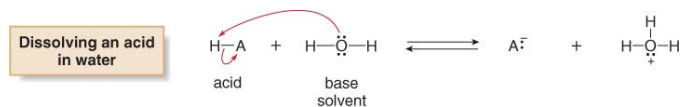
acid   base solvent

Equilibrium constant

$$K_{eq} = \frac{[products]}{[starting\ materials]} = \frac{[H_3O^+][A:^-]}{[H-A][H_2O]}$$

Acids and Bases

Acid Strength and pK_a

Because the concentration of the solvent H_2O is essentially constant, the equation can be rearranged and a new equilibrium constant, called the acidity constant, K_a, can be defined.

$$\text{Acidity constant} = K_a = [H_2O]K_{eq} = \frac{[H_3O^+][A:^-]}{[H-A]}$$

$$H-A \quad + \quad H_2O \quad \underset{}{\overset{K_a}{\rightleftharpoons}} \quad A^{\ominus} \quad + \quad H_3O^{\oplus}$$

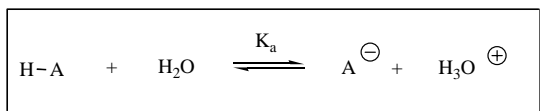Larger K_a, the further to the right, the stronger acid

Smaller K_a, the further to the left, the weaker the acid.

Therefore, the value of Ka is a measure of acid strength

Acids and Bases

Acid Strength and pK_a

It is generally more convenient when describing acid strength to use "pK_a" values than K_a values.

Definition: $pK_a = -\log K_a$

K_a	$pK_a = -\log K_a$
K_a values of typical organic acids	pK_a values of typical organic acids
10^{-5} to 10^{-50}	+5 to +50
larger number — stronger acid / smaller number — weaker acid	smaller number — stronger acid / larger number — weaker acid

Larger K_a = stronger acid/Smaller pK_a = stronger acid
Smaller K_a = weaker acid/Larger pK_a = weaker acid

Acids and Bases

	Acid	Approximate pK_a	Conjugate Base	
Strongest acid	HSbF$_6$	< −12	SbF$_6$$^-$	Weakest base
	HI	−10	I$^-$	
	H$_2$SO$_4$	−9	HSO$_4$$^-$	
	HBr	−9	Br$^-$	
	HCl	−7	Cl$^-$	
	C$_6$H$_5$SO$_3$H	−6.5	C$_6$H$_5$SO$_3$$^-$	
	(CH$_3$)$_2$OH	−3.8	(CH$_3$)$_2$O	
	(CH$_3$)$_2$C=ÖH	−2.9	(CH$_3$)$_2$C=O	
	CH$_3$ÖH$_2$	−2.5	CH$_3$OH	
	H$_3$O$^+$	−1.74	H$_2$O	
	HNO$_3$	−1.4	NO$_3$$^-$	
	CF$_3$CO$_2$H	0.18	CF$_3$CO$_2$$^-$	
	HF	3.2	F$^-$	
	CH$_3$CO$_2$H	4.75	CH$_3$CO$_2$$^-$	
	H$_2$CO$_3$	6.35	HCO$_3$$^-$	
	CH$_3$COCH$_2$COCH$_3$	9.0	CH$_3$COCHCOCH$_3$	
	NH$_4$$^+$	9.2	NH$_3$	
	C$_6$H$_5$OH	9.9	C$_6$H$_5$O−	
	HCO$_3$$^-$	10.2	CO$_3$$^{2-}$	
	CH$_3$NH$_3$$^+$	10.6	CH$_3$NH$_2$	
	H$_2$O	15.7	OH$^-$	
	CH$_3$CH$_2$OH	16	CH$_3$CH$_2$O$^-$	
	(CH$_3$)$_3$COH	18	(CH$_3$)$_3$CO$^-$	
	CH$_3$COCH$_3$	19.2	$^-$CH$_2$COCH$_3$	
	HC≡CH	25	HC≡C$^-$	
	H$_2$	35	H$^-$	
	NH$_3$	38	NH$_2$$^-$	
	CH$_2$=CH$_2$	44	CH$_2$=CH$^-$	
Weakest acid	CH$_3$CH$_3$	50	CH$_3$CH$_2$$^-$	Strongest base

Increasing pKa value (left arrow) / Increasing base strength (right arrow)

Acids and Bases

Amphoteric or Amphiprotic Substances

Substances which can be either acids or bases.

For example: H_2O

Such compounds exist as two, independent conjugate acid/base pairs with two different pK_a values.

H_2O as an acid: H_2O / HO^- ($pk_a = 15.7$)

H_2O as a base: H_3O^+/ H_2O ($pK_a = -1.74$)

Acids and Bases

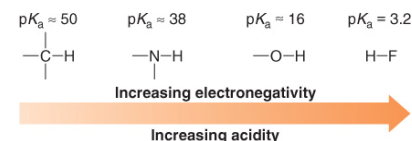**Factors that Determine Acid Strength**

❑ **Anything that stabilizes a conjugate base A:⁻ makes the starting acid H—A more acidic.**

❑ **Four factors affect the acidity of H—A. These are:**

  o **Element effects**

  o **Inductive effects**

  o **Resonance effects**

  o **Hybridization effects**

❑ **No matter which factor is discussed, the same procedure is always followed. To compare the acidity of any two acids:**

  o **Always draw the conjugate bases.**

  o **Determine which conjugate base is more stable.**

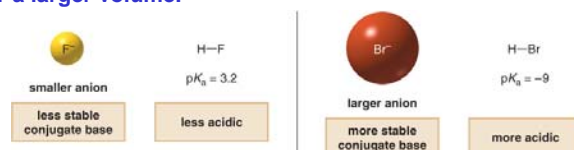 o **The more stable the conjugate base, the more acidic the acid.**

Acids and Bases

Factors that Determine Acid Strength

Element Effects—Trends in the Periodic Table.

Across a row of the periodic table, the acidity of H—A increases as the electronegativity of A increases.

$pK_a \approx 50$	$pK_a \approx 38$	$pK_a \approx 16$	$pK_a = 3.2$
—C—H	—N—H	—O—H	H—F

Increasing electronegativity

Increasing acidity

Positive or negative charge is stabilized when it is spread over a larger volume.

F⁻	H—F	Br⁻	H—Br
smaller anion	$pK_a = 3.2$	larger anion	$pK_a = -9$
less stable conjugate base	less acidic	more stable conjugate base	more acidic

Acids and Bases

Factors that Determine Acid Strength—Inductive Effects

• **An inductive effect is the pull of electron density through σ bonds caused by electronegativity differences in atoms.**

• **In the example below, when we compare the acidities of ethanol and 2,2,2-trifluoroethanol, we note that the latter is more acidic than the former.**

CH_3CH_2O—H	CF_3CH_2O—H
ethanol	2,2,2-trifluoroethanol
$pK_a = 16$	$pK_a = 12.4$ ← **stronger acid**

Acids and Bases

Factors that Determine Acid Strength—Inductive Effects

• **The reason for the increased acidity of 2,2,2-trifluoroethanol is that the three electronegative fluorine atoms stabilize the negatively charged conjugate base.**

$CH_3CH_2O^-$

No additional electronegative atoms stabilize the conjugate base.

CF₃ withdraws electron density, stabilizing the conjugate base.

Acids and Bases

Factors that Determine Acid Strength—Inductive Effects

- When electron density is pulled away from the negative charge through σ bonds by very electronegative atoms, it is referred to as an **electron withdrawing inductive effect**.
- More electronegative atoms stabilize regions of high electron density by an electron withdrawing inductive effect.
- The more electronegative the atom and the closer it is to the site of the negative charge, the greater the effect.
- The acidity of H—A increases with the presence of electron withdrawing groups in A.
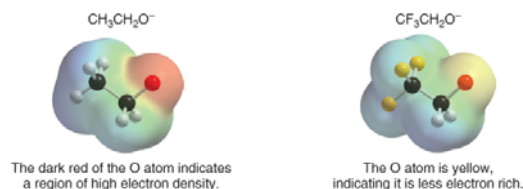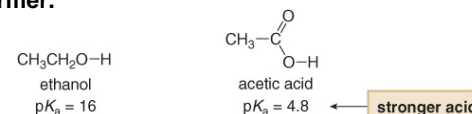
$CH_3CH_2O^-$ $CF_3CH_2O^-$

The dark red of the O atom indicates a region of high electron density.

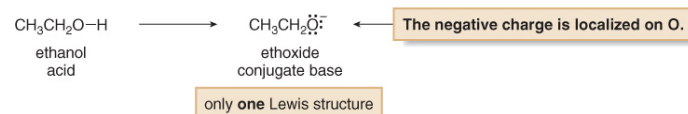The O atom is yellow, indicating it is less electron rich.

Acids and Bases

Factors that Determine Acid Strength—Resonance Effects

- Resonance is a third factor that influences acidity.
- In the example below, when we compare the acidities of ethanol and acetic acid, we note that the latter is more acidic than the former.

CH_3CH_2O-H
ethanol
$pK_a = 16$

CH_3-C ... $O-H$
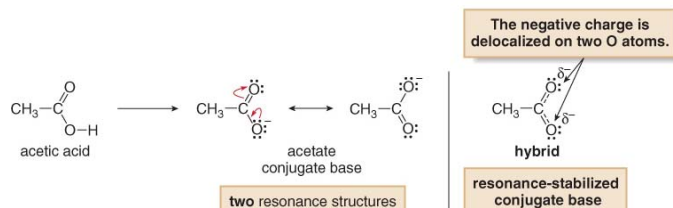acetic acid
$pK_a = 4.8$ ←   stronger acid

- When the conjugate bases of the two species are compared, it is evident that the conjugate base of acetic acid enjoys resonance stabilization, whereas that of ethanol does not.

CH_3CH_2O-H → $CH_3CH_2\ddot{O}{:}^-$ ←   The negative charge is localized on O.
ethanol
acid

ethoxide
conjugate base

only **one** Lewis structure

Acids and Bases

Factors that Determine Acid Strength—Resonance Effects

- Resonance delocalization makes CH_3COO^- more stable than $CH_3CH_2O^-$, so CH_3COOH is a stronger acid than CH_3CH_2OH.

The negative charge is delocalized on two O atoms.

CH_3-C ... $O-H$
acetic acid

CH_3-C ... $\ddot{O}{:}$
acetate
conjugate base

CH_3-C ... $\ddot{O}{:}^-$

CH_3-C ... $O{:}^{\delta-}$
hybrid

two resonance structures

resonance-stabilized conjugate base

- The acidity of H—A increases when the conjugate base A:⁻ is resonance stabilized.

Acids and Bases

Factors that Determine Acid Strength—Resonance Effects

- Electrostatic potential plots of $CH_3CH_2O^-$ and CH_3COO^- below indicate that the negative charge is concentrated on a single O in $CH_3CH_2O^-$, but delocalized over both of the O atoms in CH_3COO^-.

$CH_3CH_2O^-$

CH_3COO^-

The negative charge is concentrated on the single oxygen atom, making this anion *less stable*.

The negative charge is delocalized over both oxygen atoms, making this anion *more stable*.

Acids and Bases

Factors that Determine Acid Strength—Hybridization Effects

- **The final factor affecting the acidity of H—A is the hybridization of A.**

Let us consider the relative acidities of three different compounds containing C—H bonds.

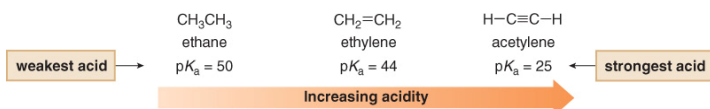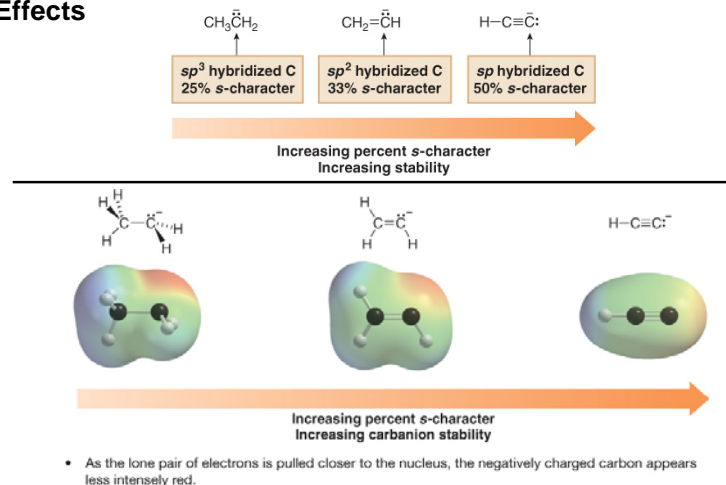|		
CH_3CH_3	$CH_2=CH_2$	$H-C\equiv C-H$
ethane	ethylene	acetylene
$pK_a = 50$	$pK_a = 44$	$pK_a = 25$

weakest acid → Increasing acidity ← strongest acid

- **The higher the percent of *s*-character of the hybrid orbital, the closer the lone pair is held to the nucleus, and the more stable the conjugate base.**

Acids and Bases

Factors that Determine Acid Strength—Hybridization Effects

$CH_3\ddot{C}H_2$	$CH_2=\ddot{C}H$	$H-C\equiv\ddot{C}:$
sp^3 hybridized C 25% *s*-character	sp^2 hybridized C 33% *s*-character	sp hybridized C 50% *s*-character

Increasing percent *s*-character
Increasing stability

Increasing percent *s*-character
Increasing carbanion stability

- As the lone pair of electrons is pulled closer to the nucleus, the negatively charged carbon appears less intensely red.
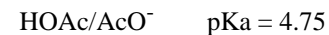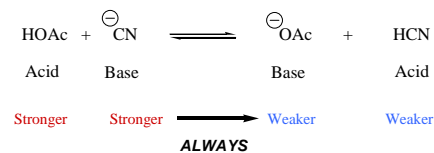

Acids and Bases

Summary of Factors that Determine Acid Strength—Hybridization Effects

Factor	Example

1. **Element effect:** The acidity of H–A increases both left-to-right across a row and down a column of the periodic table.	Increasing acidity
	—C–H —N–H —O–H H–F
	                       —S–H H–Cl
	                                    H–Br
	                                    H–I
	Increasing acidity (down)

2. **Inductive effects:** The acidity of H–A increases with the presence of electron-withdrawing groups in A.	CH_3CH_2O-H CF_3CH_2O-H more acidic
3. **Resonance effects:** The acidity of H–A increases when the conjugate base A:⁻ is resonance stabilized.	CH_3CH_2O-H CH_3COO-H more acidic
4. **Hybridization effects:** The acidity of H–A increases as the percent *s*-character of A:⁻ increases.	CH_3CH_3 $CH_2=CH_2$ $H-C\equiv C-H$ Increasing acidity

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Acids and Bases
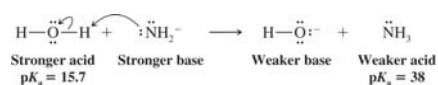
Acid/base equilibria always favor the side of the weaker acid and the weaker base

For Example:

$$HOAc + \overset{\ominus}{CN} \rightleftharpoons \overset{\ominus}{OAc} + HCN$$

HOAc	CN	OAc	HCN
Acid	Base	Base	Acid
Stronger	Stronger	Weaker	Weaker

ALWAYS

HOAc/AcO⁻   pKa = 4.75
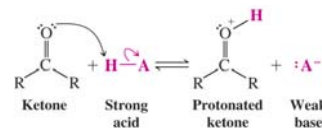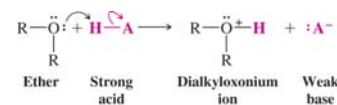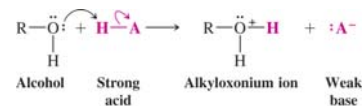
HCN/CN⁻   pKa = 9.22

ANOTHER CONSEQUENCE: Any base stronger than hydroxide will be converted to hydroxide in water

(Again, that's because acid/base reactions always favor the side of the weaker acid and the weaker base)
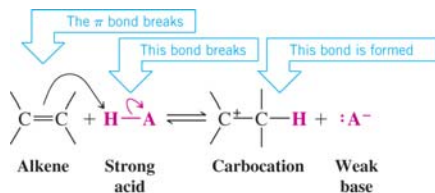

H—O—H + :NH₂⁻ ⟶ H—O:⁻ + NH₃

Stronger acid   Stronger base   Weaker base   Weaker acid
$pK_a = 15.7$ $pK_a = 38$

♦ **What Makes a Compound Behave as a Base?**

→ Any organic compound containing an atom with a lone pair (O,N) can act as a base

Alcohol   Strong acid   Alkyloxonium ion   Weak base

Ether   Strong acid   Dialkyloxonium ion   Weak base

Ketone   Strong acid   Protonated ketone   Weak base

→ π Electrons can also act as bases

 ♦ π Electrons are loosely held and available for reaction with strong acids

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

Acids and Bases

Lewis Acids and Bases

• **The Lewis definition of acids and bases is more general than the Brønsted-Lowry definition.**

• **A Lewis acid is an electron pair acceptor.**

• **A Lewis base is an electron pair donor.**

• **Lewis bases are structurally the same as Brønsted-Lowry bases. Both have an available electron pair—a lone pair or an electron pair in a π bond.**

• **A Brønsted -Lowry base always donates this electron pair to a proton, but a Lewis base donates this electron pair to anything that is electron deficient.**

Examples of Lewis bases

:Ö—H   CH₃—Ö—H   C=C

available electron pair

Acids and Bases

Lewis Acids and Bases

- **A Lewis acid must be able to accept an electron pair, but there are many ways for this to occur.**
- **All Brønsted-Lowry acids are also Lewis acids, but the reverse is not necessarily true.**
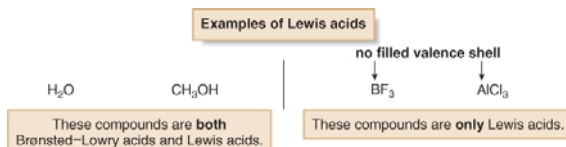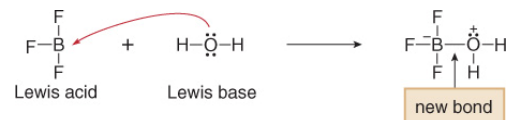 - o **Any species that is electron deficient and capable of accepting an electron pair is also a Lewis acid.**
- **Common examples of Lewis acids (which are not Brønsted-Lowry acids) include BF_3 and $AlCl_3$. These compounds contain elements in group 3A of the periodic table that can accept an electron pair because they do not have filled valence shells of electrons.**

Examples of Lewis acids

no filled valence shell

H_2O CH_3OH | BF_3 $AlCl_3$

These compounds are **both** Brønsted−Lowry acids and Lewis acids.

These compounds are **only** Lewis acids.

Acids and Bases

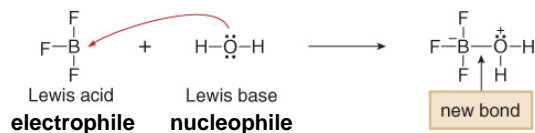**Lewis Acids and Bases**

- **Any reaction in which one species donates an electron pair to another species is a Lewis acid-base reaction.**
- **In a Lewis acid-base reaction, a Lewis base donates an electron pair to a Lewis acid.**
- **Lewis acid-base reactions illustrate a general pattern in organic chemistry. Electron-rich species react with electron-poor species.**
- **In the simplest Lewis acid-base reaction one bond is formed and no bonds are broken. This is illustrated in the reaction of BF_3 with H_2O. H_2O donates an electron pair to BF_3 to form a new bond.**

Lewis acid   Lewis base   new bond

Acids and Bases

Lewis Acids and Bases

- **A Lewis acid is also called an electrophile.**
- **When a Lewis base reacts with an electrophile (other than a proton), the Lewis base is also called a nucleophile. In this example, BF_3 is the electrophile and H_2O is the nucleophile.**

Lewis acid   Lewis base

electrophile   nucleophile

new bond

Nucleophiles and Electrophiles

The Organic chemistry terms for Lewis acids and bases

Electrophiles ("electron-loving" reagents): seek electrons to obtain a stable valence shell of electrons
  ➔ **Are electron-deficient themselves**

Some Examples are: $H^{\oplus}$ $Cl-Al-Cl$ with Cl below $H-C^{\oplus}$ with H above and H below

NOTE:

An electrophile can either be neutral or have a positive charge.

The important thing is that they have "room" for
a pair of electrons.

Nucleophiles and Electrophiles

Nucleophiles ("nucleus-loving" reagents): seek a proton or some other positively charged center
→ Are electron-rich themselves

Some Examples are:

NOTE:

A nucleophile can either be neutral or have a negative charge.

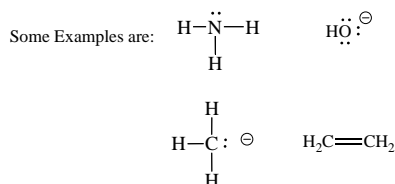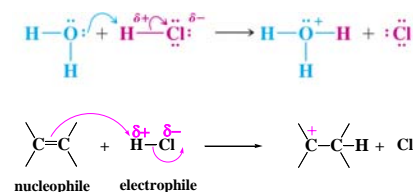The important thing is that it be able to donate a pair of electrons (either from a lone pair or from a pi-bond)

Use of Curved Arrows in Illustrating Reactions

♦ **Curved arrows show the movement of electrons in a reaction**
♦ **An arrow starts at site of higher electron density (a covalent bond or unshared electron pair) and points to site of electron deficiency**
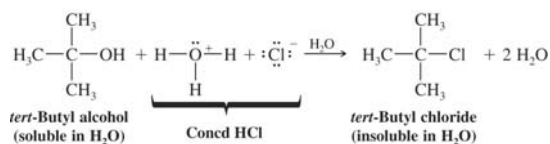♦ **Examples:**

nucleophile   electrophile

NOTE: Electron pairs move from the nucleophile to the electrophile

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A Mechanism for an Organic Reaction
(The First Example of Many)

The Substitution Reaction of *tert*-Butyl Alcohol

This is the overall reaction:

tert-Butyl alcohol   *tert*-Butyl chloride
(soluble in H_2O)   (insoluble in H_2O)

Concd HCl

You will be doing this exact reaction in the lab this semester

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The Mechanism Has Three Steps

→ All steps are actually acid-base reactions

Step 1:

tert-Butyloxonium ion
tert-Butyl alcohol acts as a base and accepts a proton from the hydronium ion. (Chloride anions are spectators in this step of the reaction.)
The products are 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.

Acids and Bases in Nonaqueous Solutions

Sodium amide (NaNH$_2$) can be used as a strong base in solvents such as liquid NH$_3$

$$\text{H}-\text{C}\equiv\text{C}-\text{H} + :\ddot{\text{N}}\text{H}_2^- \xrightarrow{\text{liquid NH}_3} \text{H}-\text{C}\equiv\text{C}:^- + :\text{NH}_3$$

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

♦ **Alkyl lithium reagents in hexane are extremely strong bases**

$$\text{H}-\text{C}\equiv\text{C}-\text{H} + :\text{CH}_2\text{CH}_3 \xrightarrow{\text{hexane}} \text{H}-\text{C}\equiv\text{C}:^- + \text{CH}_3\text{CH}_3$$
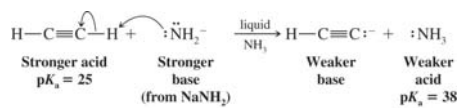
Stronger acid   Stronger   Weaker   Weaker
pK_a = 25   base   base   acid
              (from CH$_3$CH$_2$Li)   pK_a = 50