

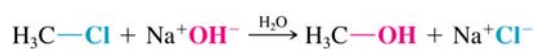
Chapter 3

An Introduction to Organic Reactions: Acids and Bases

◆ Reactions and Their Mechanisms

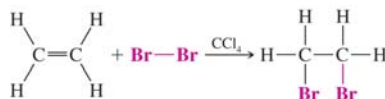
- There are four general types of organic reactions

→ Substitutions



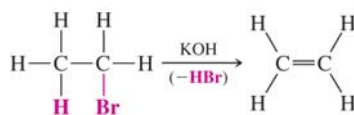
A substitution reaction

→ Additions



An addition reaction

→ Eliminations

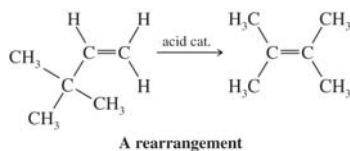


An elimination reaction

Chapter 3

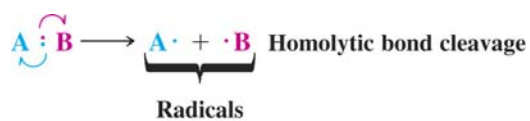
2

→ Rearrangements

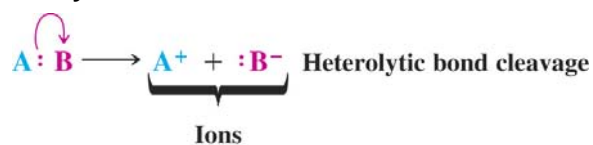


◆ Cleavage of Covalent Bonds

● Homolysis



● Heterolysis



Chapter 3

3

● Heterolytic reactions almost always occur at polar bonds

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



Chapter 3

4

◆ Introduction to Acid-Base Chemistry

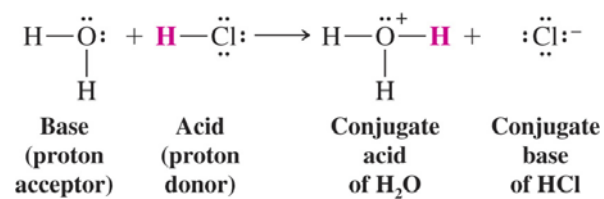
- Brønsted-Lowry Definition of Acids and Bases

→ Acid: a substance that can donate a proton

→ Base: a substance that can accept a proton

→ Example

⚡ Hydrogen chloride is a very strong acid and essentially all hydrogen chloride molecules transfer their proton to water



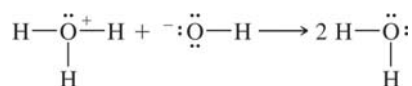
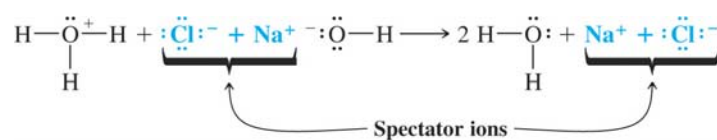
Chapter 3

5

- Example

→ Aqueous hydrogen chloride and aqueous sodium hydroxide are mixed

→ The actual reaction is between hydronium and hydroxide ions



Chapter 3

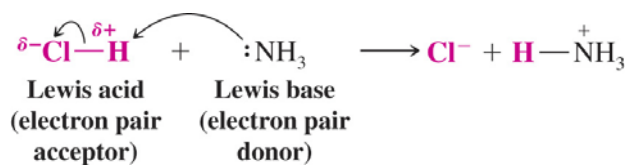
6

- **Lewis Definition of Acids and Bases**

- Lewis Acid: electron pair acceptor

- Lewis Base: electron pair donor

- Curved arrows show movement of electrons to form and break bonds



Chapter 3

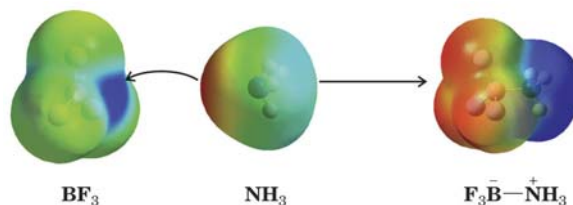
7

- ◆ **Opposite Charges Attract and React**

- **BF₃ and NH₃ react based on their relative electron densities**

- BF₃ has substantial positive charge on the boron

- NH₃ has substantial negative charge localized at the lone pair

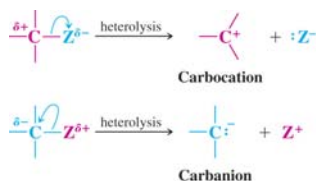


Chapter 3

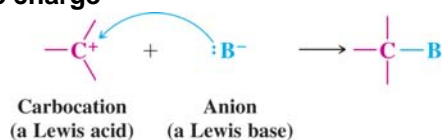
8

◆ Heterolysis of Bonds to Carbons: Carbanions and Carbocations

- Reaction can occur to give a carbocation or carbanion depending on the nature of Z



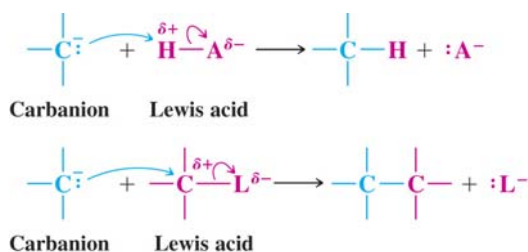
- Carbocations have only 6 valence electrons and a positive charge



Chapter 3

9

- Carbanions have 8 valence electrons and a negative charge



- 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 e.g. carbocations

→ Nucleophiles (“nucleus-loving” reagents): seek a proton or some other positively charged center

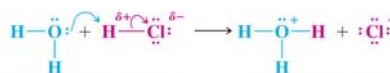
⌘ Are electron-rich themselves e.g. carbanions

Chapter 3

10

◆ The Use of Curved Arrows in Illustrating Reactions

- Curved arrows show the flow of electrons in a reaction
- An arrow starts at a site of higher electron density (a covalent bond or unshared electron pair) and points to a site of electron deficiency
- Example: Mechanism of reaction of HCl and water



A water molecule uses one of the nonbonding 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.

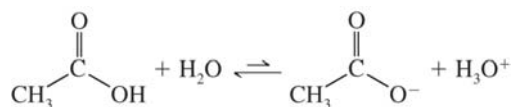
Chapter 3

11

◆ Strengths of Acids and Bases

• K_a and pK_a

- Acetic acid is a relatively weak acid and a 0.1M solution is only able to protonate water to the extent of about 1%



- The equilibrium equation for this reaction is:

$$K_{\text{eq}} = \frac{[\text{H}_3\text{O}^+][\text{CH}_3\text{CO}_2^-]}{[\text{CH}_3\text{CO}_2\text{H}][\text{H}_2\text{O}]}$$

Chapter 3

12

→ Dilute acids have a constant concentration of water (about 55.5 M) and so the concentration of water can be factored out to obtain the acidity constant (K_a)

⌘ K_a for acetic acid is 1.76×10^{-5}

$$K_a = K_{eq} [\text{H}_2\text{O}] = \frac{[\text{H}_3\text{O}^+][\text{CH}_3\text{CO}_2^-]}{[\text{CH}_3\text{CO}_2\text{H}]}$$

→ Any weak acid (HA) dissolved in water fits the general K_a expression

⌘ The stronger the acid, the larger the K_a

$$K_a = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]}$$

→ Acidity is usually expressed in terms of $\text{p}K_a$

⌘ $\text{p}K_a$ is the negative log of K_a

⌘ The $\text{p}K_a$ for acetic acid is 4.75

$$\text{p}K_a = -\log K_a$$

→ The larger the $\text{p}K_a$, the weaker the acid

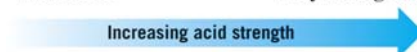


$$\text{p}K_a = 4.75 \quad \text{p}K_a = 0 \quad \text{p}K_a = -7$$

Weak acid

Very strong acid

Increasing acid strength



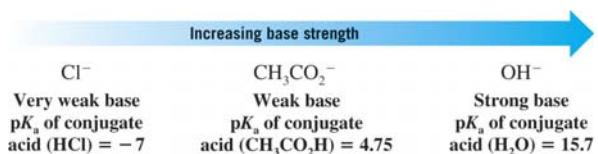
	Acid	Approximate pK_a	Conjugate Base	
Strongest acid	HSbF ₆	< -12	SbF ₆ ⁻	Weakest base
	HI	-10	I ⁻	
	H ₂ SO ₄	-9	HSO ₄ ⁻	
	HBr	-9	Br ⁻	
	HCl	-7	Cl ⁻	
	C ₆ H ₅ SO ₃ H	-6.5	C ₆ H ₅ SO ₃ ⁻	
	(CH ₃) ₂ OH	-3.8	(CH ₃) ₂ O	
	(CH ₃) ₂ C=OH	-2.9	(CH ₃) ₂ C=O	
	CH ₃ OH ₂	-2.5	CH ₃ OH	
	H ₂ O ⁺	-1.74	H ₂ O	
	HNO 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) ₂ COH	18	(CH ₃) ₂ 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 ⁻	
Weakest acid	CH ₂ =CH ₂	44	CH ₂ =CH ⁻	Strongest base
	CH ₂ CH ₃	50	CH ₂ CH ₂ ⁻	

Chapter 3

15

◆ Predicting the Strengths of Bases

- The stronger the acid, the weaker its conjugate base will be
 - An acid with a low pK_a will have a weak conjugate base
 - Chloride is a very weak base because its conjugate acid HCl is a very strong acid

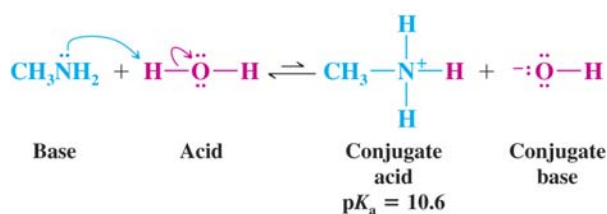
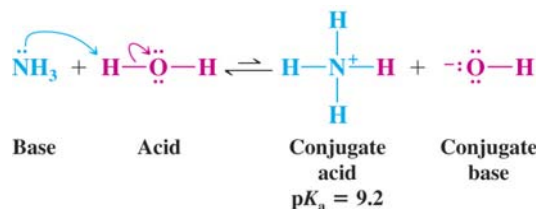


Chapter 3

16

- **Methylamine is a stronger base than ammonia**

→ The conjugate acid of methylamine is weaker than the conjugate acid of ammonia



Chapter 3

17

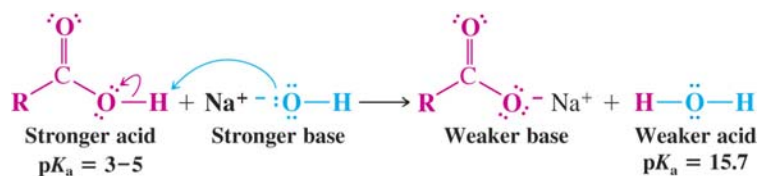
- ◆ **Predicting the Outcome of Acid-Base Reactions**

- Acid-base reaction always favor the formation of the weaker acid/weaker base pair

→ The weaker acid/weaker base are always on the same side of the equation

- **Example**

→ Acetic acid reacts with sodium hydroxide to greatly favor products



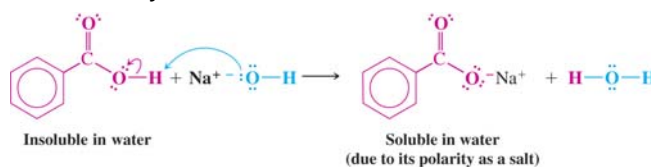
Chapter 3

18

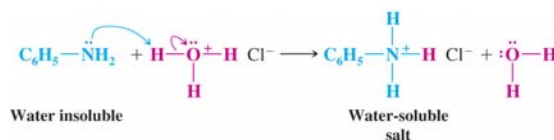
- **Water Solubility as a Result of Salt Formation**

→ Organic compounds which are water insoluble can sometimes be made soluble by turning them into salts

→ Water insoluble carboxylic acids can become soluble in aqueous sodium hydroxide



→ Water insoluble amines can become soluble in aqueous hydrogen chloride



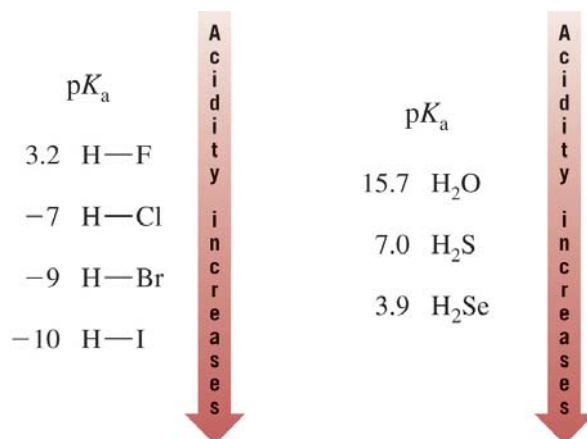
Chapter 3

19

- ◆ **The Relationship Between Structure and Acidity**

→ Acidity increases going down a row of the periodic table

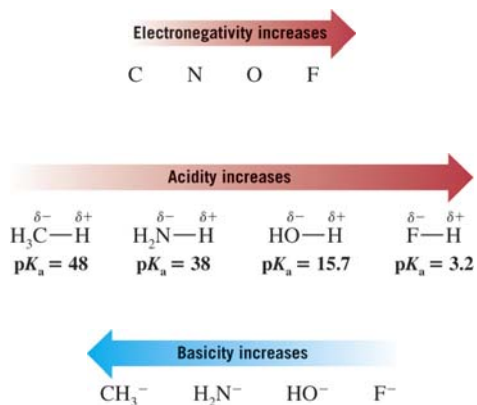
→ Bond strength to hydrogen decreases going down the row and therefore acidity increases



Chapter 3

20

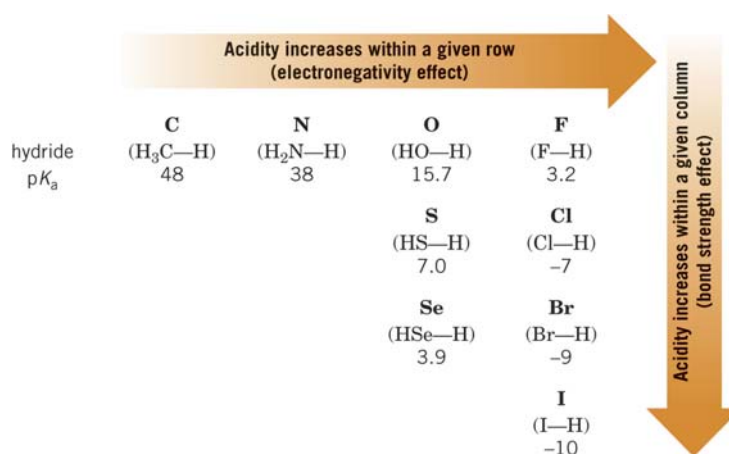
- Acidity increases from left to right in a row of the periodic table
- Increasingly electronegative atoms polarize the bond to hydrogen and also stabilize the conjugate base better



Chapter 3

21

● Overview of Acidity Trends



Chapter 3

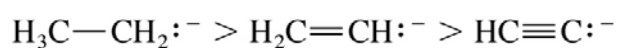
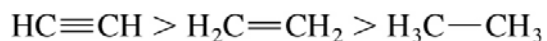
22

◆ The Effect of Hybridization on Acidity

- Hydrogens connected to orbitals with more *s* character will be more acidic

→ *s* orbitals are smaller and closer to the nucleus than *p* orbitals

→ Anions in hybrid orbitals with more *s* character will be held more closely to the nucleus and be more stabilized



Chapter 3

23

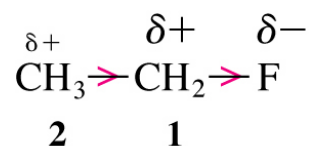
◆ Inductive Effects

→ Electronic effects that are transmitted through space and through the bonds of a molecule

→ In ethyl fluoride the electronegative fluorine is drawing electron density away from the carbons

⌘ Fluorine is an electron withdrawing group (EWG)

⌘ The effect gets weaker with increasing distance

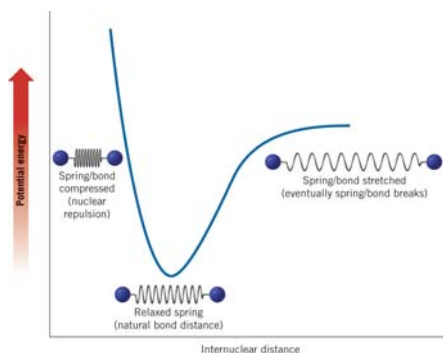


Chapter 3

24

◆ Energy Changes in Reactions

- Kinetic energy is the energy an object has because of its motion
- Potential energy is stored energy
 - ⌘ The higher the potential energy of an object the less stable it is
- Potential energy can be converted to kinetic energy (e.g. energy of motion)



Chapter 3

25

● Potential Energy and Covalent Bonds

- Potential energy in molecules is stored in the form of chemical bond energy
- Enthalpy ΔH° is a measure of the change in bond energies in a reaction
- Exothermic reactions
 - ⌘ ΔH° is negative and heat is evolved
 - ⌘ Potential energy in the bonds of reactants is more than that of products
- Endothermic reactions
 - ⌘ ΔH° is positive and heat is absorbed
 - ⌘ Potential energy in the bonds of reactants is less than that of products

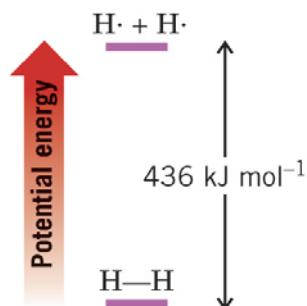
Chapter 3

26

- **Example : Formation of H₂ from H atoms**

- Formation of bonds from atoms is always exothermic

- The hydrogen molecule is more stable than hydrogen atoms



Chapter 3

27

- ◆ **The Relationship Between the Equilibrium Constant and ΔG°**

- ΔG° is the standard free energy change in a reaction

- This is the overall energy change of a reaction

- It is directly related to the equilibrium constant of a reaction

* R is the gas constant (8.314 J K⁻¹ mol⁻¹) and T is measured in kelvin (K)

$$\Delta G^\circ = -RT \ln K_{\text{eq}}$$

- If ΔG° is negative, products are favored at equilibrium ($K_{\text{eq}} > 1$)

- If ΔG° is positive, reactants are favored at equilibrium ($K_{\text{eq}} < 1$)

- If ΔG° is zero, products and reactants are equally favored ($K_{\text{eq}} = 1$)

Chapter 3

28

→ ΔG° encompasses both enthalpy changes (ΔH°) and entropy changes (ΔS°)

$$\Delta G^\circ = \Delta H^\circ - T \Delta S^\circ$$

→ ΔH° is associated with changes in bonding energy

‣ If ΔH° is negative (exothermic) this makes a negative contribution to ΔG° (products favored)

→ ΔS° is associated with the relative order of a system

‣ More disorder means greater entropy

‣ A positive ΔS° means a system which is going from more ordered to less ordered

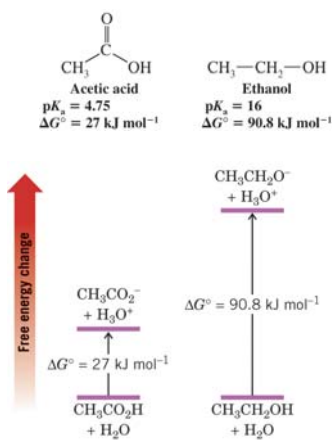
‣ A positive ΔS° makes a negative contribution to ΔG° (products favored)

→ In many cases ΔS° is small and ΔG° is approximately equal to ΔH°

◆ The Acidity of Carboxylic Acids

● Carboxylic acids are much more acidic than alcohols

→ Deprotonation is unfavorable in both cases but much less favorable for ethanol

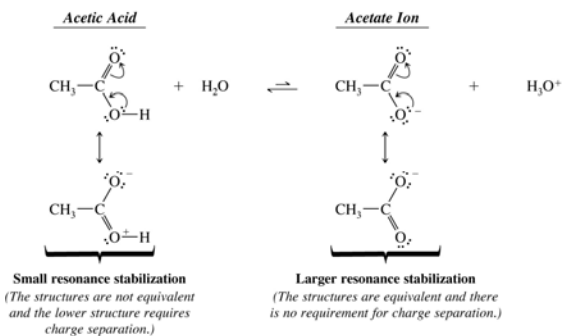


● **Explanation based on resonance effects**

→ Both acetic acid and acetate are stabilized by resonance

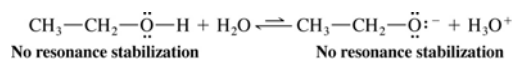
⌘ Acetate is more stabilized by resonance than acetic acid

⌘ This decreases ΔG° for the deprotonation



→ Neither ethanol nor its anion is stabilized by resonance

⌘ There is no decrease in ΔG° for the deprotonation

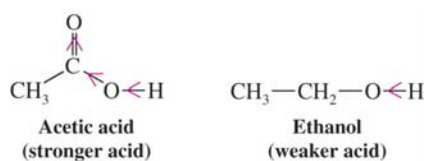


Chapter 3

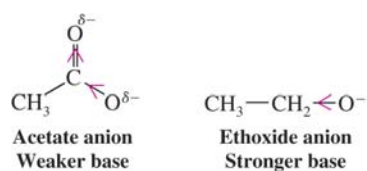
31

● **Explanation based on inductive effect**

→ In acetic acid the highly polarized carbonyl group draws electron density away from the acidic hydrogen



→ Also the conjugate base of acetic acid is more stabilized by the carbonyl group



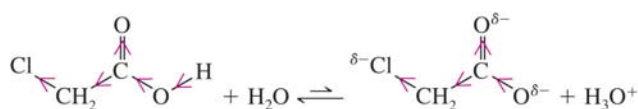
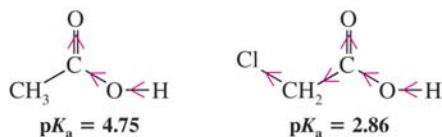
Chapter 3

32

◆ Inductive Effects of Other Groups

→ The electron withdrawing chloro group makes chloroacetic acid more acidic than acetic acid

- ⌘ The hydroxyl proton is more polarized and more acidic
- ⌘ The conjugate base is more stabilized



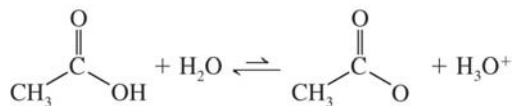
Chapter 3

33

◆ The Effect of Solvent on Acidity

→ Acidity values in gas phase are generally very low

- ⌘ It is difficult to separate the product ions without solvent molecules to stabilize them
- ⌘ Acetic acid has pK_a of 130 in the gas phase



→ A protic solvent is one in which hydrogen is attached to a highly electronegative atom such as oxygen or nitrogen e.g. water

→ Solvation of both acetic acid and acetate ion occurs in water although the acetate is more stabilized by this solvation

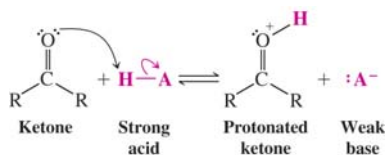
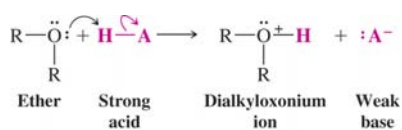
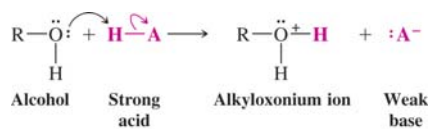
- ⌘ This solvation allows acetic acid to be much more acidic in water than in the gas phase

Chapter 3

34

◆ Organic Compounds as Bases

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

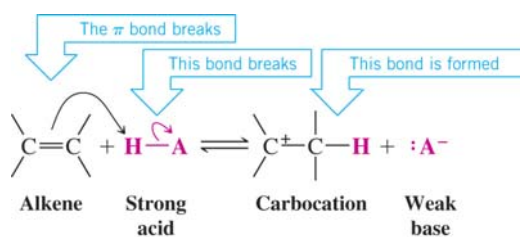


Chapter 3

35

→ π Electrons can also act as bases

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

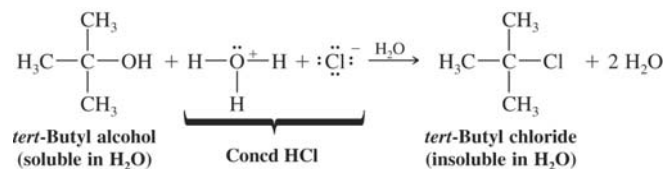


Chapter 3

36

◆ A Mechanism for an Organic Reaction

● The Substitution Reaction of *tert*-Butyl Alcohol

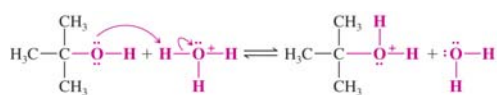


→ All steps are acid-base reactions

- ⌘ Step 1 is a Brønsted acid-base reaction
- ⌘ Step 2 is a Lewis acid-base reaction in reverse with heterolytic cleavage of a bond
- ⌘ Step 3 is a Lewis acid-base reaction with chloride acting as a Lewis base and the carbocation acting as Lewis acid

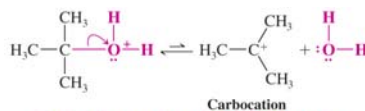
Chapter 3

37



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.)

tert-Butyloxonium ion
The products are a protonated alcohol and water (the conjugate acid and base).



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.



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

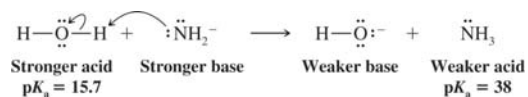
Chapter 3

38

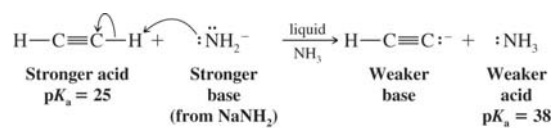
◆ Acids and Bases in Nonaqueous Solutions

→ Water has a leveling effect on strong acids and bases

→ Any base stronger than hydroxide will be converted to hydroxide in water



→ Sodium amide can be used as a strong base in solvents such as liquid NH_3

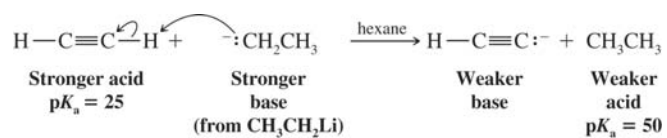


Chapter 3

39

→ Alkyl lithium reagents in hexane are very strong bases

† The alkyl lithium is made from the alkyl bromide and lithium metal



Chapter 3

40

◆ Synthesis of Deuterium- and Tritium-Labeled Compounds

- Deuterium (^2H) and tritium (^3H) are isotopes of hydrogen
- They are used for labeling organic compounds to be able to track where these compounds go (e.g. in biological systems)
- An alkyne can be labeled by deprotonating with a suitable base and then titrating with T_2O

