Chapter 3

An Introduction to Organic Reactions and Their Mechanisms
Acids and Bases

Created by
Professor William Tam & Dr. Phillis Chang

About The Authors

These Powerpoint Lecture Slides were created and prepared by Professor William Tam and his wife Dr. Phillis Chang.

Professor William Tam received his B.Sc. at the University of Hong Kong in 1990 and his Ph.D. at the University of Toronto (Canada) in 1995. He was an NSERC postdoctoral fellow at the Imperial College (UK) and at Harvard University (USA). He joined the Department of Chemistry at the University of Guelph (Ontario, Canada) in 1998 and is currently a Full Professor and Associate Chair in the department. Professor Tam has received several awards in research and teaching, and according to *Essential Science Indicators*, he is currently ranked as the Top 1% most cited Chemists worldwide. He has published four books and over 80 scientific papers in top international journals such as *J. Am. Chem. Soc., Angew. Chem., Org. Lett.,* and *J. Org. Chem.*

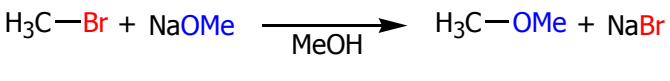
Dr. Phillis Chang received her B.Sc. at New York University (USA) in 1994, her M.Sc. and Ph.D. in 1997 and 2001 at the University of Guelph (Canada). She lives in Guelph with her husband, William, and their son, Matthew.

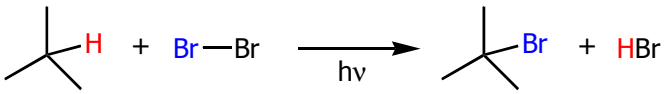
1. Reactions and Their Mechanisms

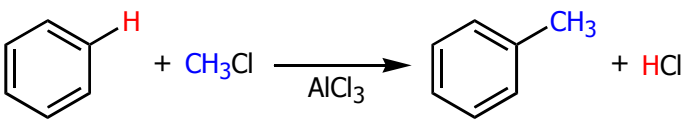
- Almost all organic reactions fall into one of four categories:
  - Substitutions
  - Additions
  - Eliminations
  - Rearrangements

- Substitutions
  - Characteristic reactions of saturated compounds such as alkanes and alkyl halides and of aromatic compounds (even though they are unsaturated)
  - In a substitution, *one group replaces another*

- Examples

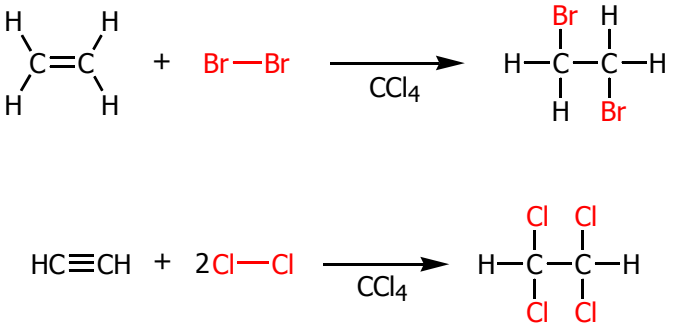






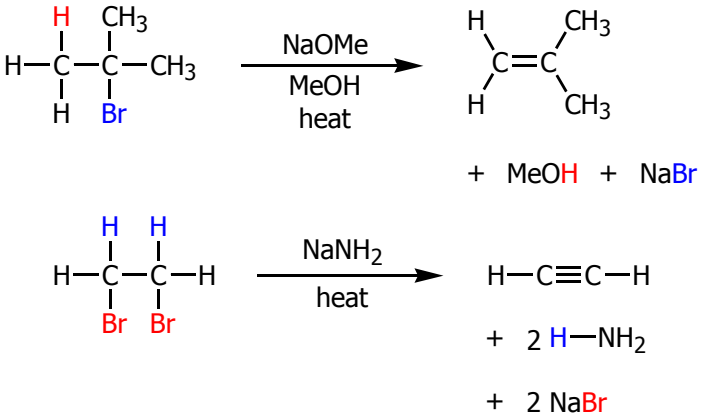
- Additions
  - Characteristic of compounds with multiple bonds
  - In an addition *all parts of the adding reagent appear in the product; two molecules become one*

❖ Examples



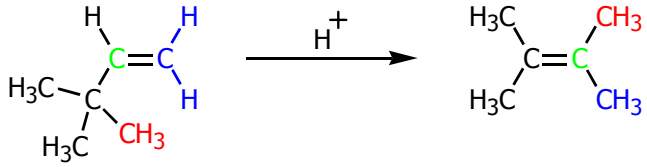
- Eliminations
  - ♦ In an elimination *one molecule loses the elements of another small molecule*
  - ♦ Elimination reactions give us a method for preparing compounds with double and triple bonds

❖ Examples



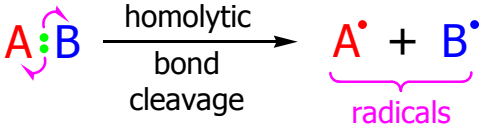
❖ Rearrangements

- In a rearrangement *a molecule undergoes a reorganization of its constituent parts*
- Examples

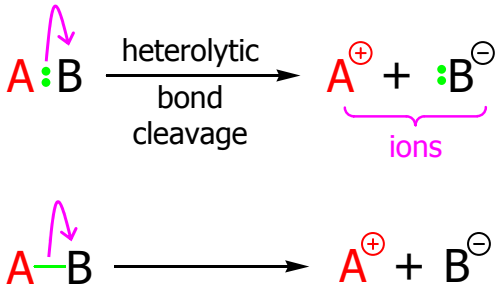


1A. Homolysis and Heterolysis of Covalent Bonds

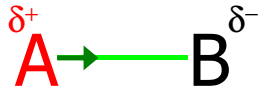
❖ Homolysis



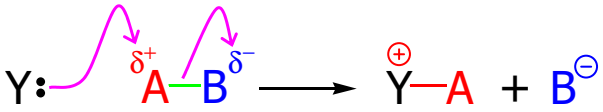
❖ Heterolysis



- Normally requires the bond to be polarized



- Usually occurs with assistance



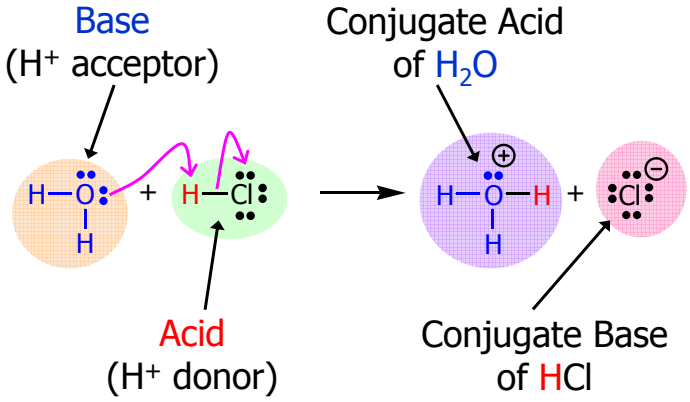
2. Acid–Base Reactions

- Many of the reactions that occur in organic chemistry are either acid–base reactions themselves or they involve an acid–base reaction at some stage
- Two classes of acid–base reactions are fundamental in organic chemistry
  - Brønsted–Lowry
  - Lewis acid–base reactions

2A. Brønsted–Lowry Acids and Bases

- Brønsted–Lowry acid–base reactions involve the transfer of protons
- A **Brønsted–Lowry acid** is a substance that can donate (or lose) a proton
- A **Brønsted–Lowry base** is a substance that can accept (or remove) a proton

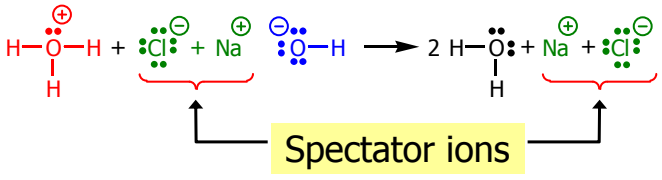
- Example



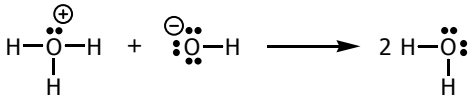
2B. Acids and Bases in Water

- Hydronium ion (H_3O^+) is the strongest acid that can exist in water to any significant extent: Any stronger acid will simply transfer its proton to a water molecule to form hydronium ions
- Hydroxide ion (HO^-) is the strongest base that can exist in water to any significant extent: Any base stronger than hydroxide will remove a proton from water to form hydroxide ions

- Total ionic reaction

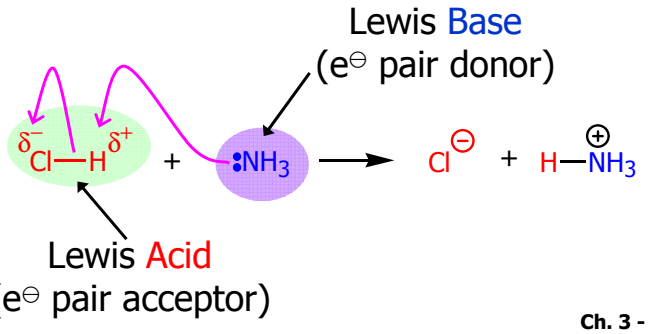


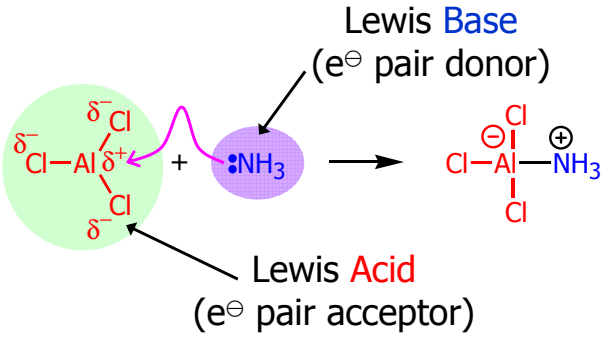
- Net reaction



3. Lewis Acids and Bases

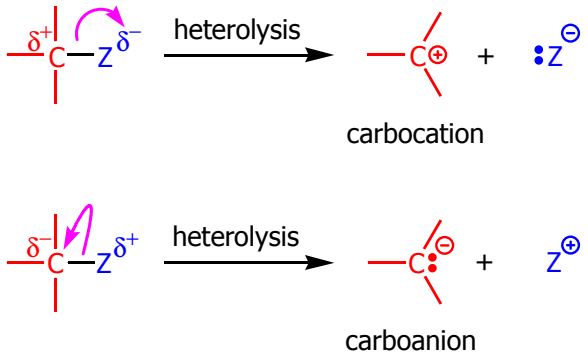
- Lewis Acids are electron pair acceptors
- Lewis Bases are electron pair donors



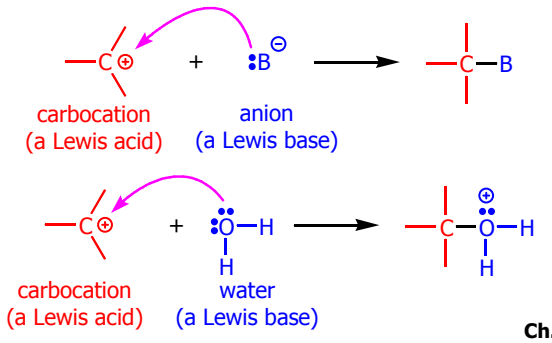


- In Lewis acid–base theory, the attraction of oppositely charged species is fundamental to reactivity

4. Heterolysis of Bonds to Carbon: Carbocations and Carbanions



- Carbocations are electron deficient. They have only six electrons in their valence shell, and because of this, carbocations are Lewis acids

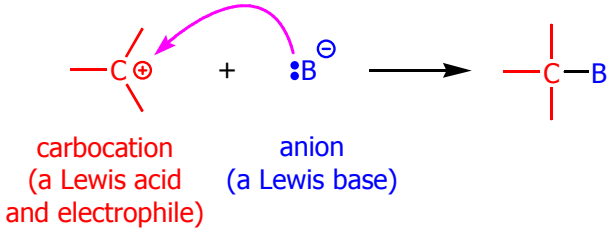


4A. Electrophiles and Nucleophiles

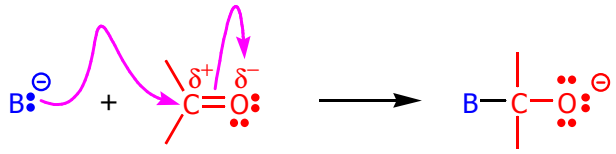
- *Because carbocations are electron-seeking reagents,* chemists call them **electrophiles** (meaning electron-loving)

- **Electrophiles** are reagents that seek electrons so as to achieve a stable shell of electrons like that of a noble gas

- **All Lewis acids are electrophiles.** By accepting an electron pair from a Lewis base, a carbocation fills its valence shell

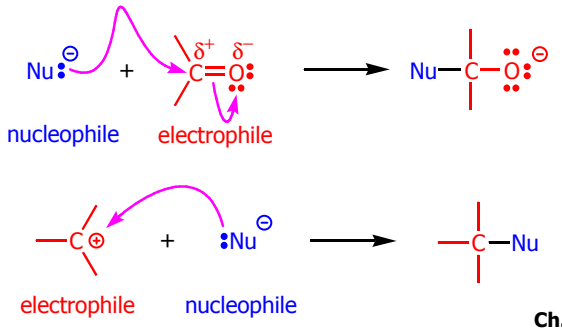


- Carbon atoms that are electron poor because of bond polarity, but are not carbocations, can also be electrophiles



Lewis base Lewis acid electrophile

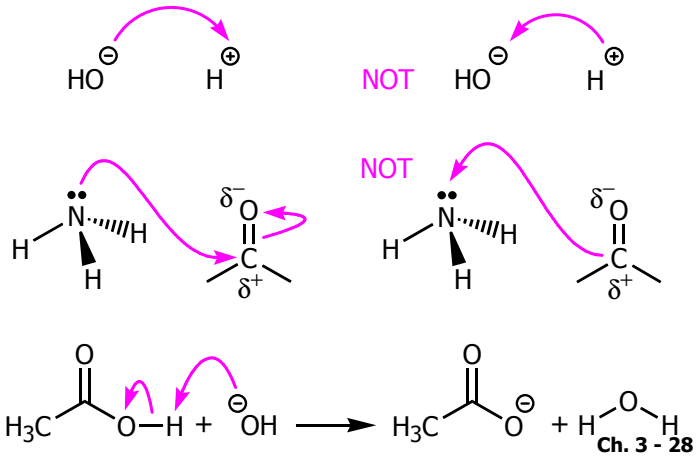
- Carbanions are Lewis bases
- A **nucleophile** is a Lewis base that seeks a positive center such as a positively charged carbon atom



5. How to Use Curved Arrows in Illustrating Reactions

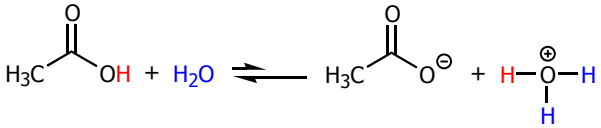
- Curved arrows
  - show the direction of electron flow in a reaction mechanism
  - point from the source of an electron pair to the atom receiving the pair
  - always show the flow of electrons from a site of higher electron density to a site of lower electron density
  - never show the movement of atoms. Atoms are assumed to follow the flow of the electron

- Examples



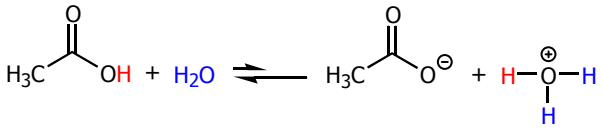
6. The Strength of Brønsted–Lowry Acids and Bases: K_a and pK_a

- In contrast to strong acids such as HCl and H_2SO_4, acetic acid is a much weaker acid



  - At 25°C, in a 0.1 M acetic acid solution, only about 1% of the acetic acid molecules ionize

6A. The Acidity Constant, K_a



- Equilibrium constant (K_{eq})

$$K_{eq} = \frac{[CH_3CO_2^{\ominus}]\,[H_3O^{\oplus}]}{[CH_3CO_2H][H_2O]}$$

- For dilute aqueous solutions, the concentration of water is essentially constant (~55.5*M*); and the K_{eq} expression can be written in terms of the acidity constant (K_a)

$$K_a = K_{eq}[H_2O] = \frac{[CH_3CO_2^{\ominus}]\,[H_3O^{\oplus}]}{[CH_3CO_2H]}$$

- At 25°C, the acidity constant for acetic acid is 1.76×10^{-5}

- For any weak acid dissolved in water

$$HA + H_2O \rightleftharpoons H_3O^{\oplus} + A^{\ominus}$$

$$K_a = \frac{[H_3O^{\oplus}]\,[A^{\ominus}]}{[HA]}$$

- An acid with a large value of K_a
  - a strong acid
- An acid with a small value of K_a
  - a weak acid

6B. Acidity and pK_a

$$pK_a = -\log K_a$$

$$pH = -\log [H_3O^{\oplus}]$$

- For acetic acid the pK_a is 4.75

$$pK_a = -\log [1.76 \times 10^{-5}]$$
$$= -[-4.75]$$
$$= 4.75$$

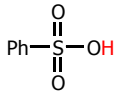
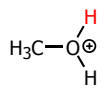
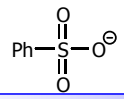
- The larger the value of the pK_a, the weaker the acid

Increasing acid strength

CH_3CO_2H	>	CF_3CO_2H	>	HCl
pK_a = 4.75		pK_a = 0		pK_a = –7
Weak acid				Very strong acid

- Relative Strength of Selected Acids & Their Conjugate Bases

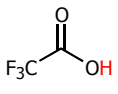
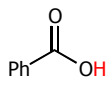
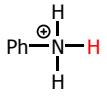
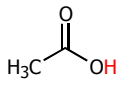
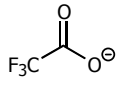
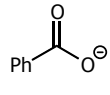
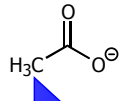
Increasing acid strength

Acid	HCl					HNO_3
pK_a	-7	-6.5	-2.9	-2.5	-1.74	-1.4
Conjugate Base	$Cl^{\ominus}$			CH_3OH	H_2O	$NO_3^{\ominus}$

Increasing base strength

- (Cont'd)

Increasing acid strength

Acid		HF			
pK_a	0.18	3.2	4.21	4.63	4.75
Conjugate Base		$F^{\ominus}$		$Ph-NH_2$	

Increasing base strength

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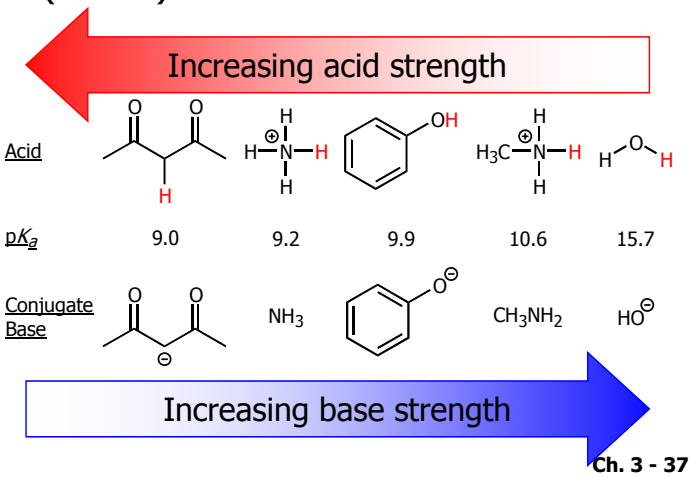

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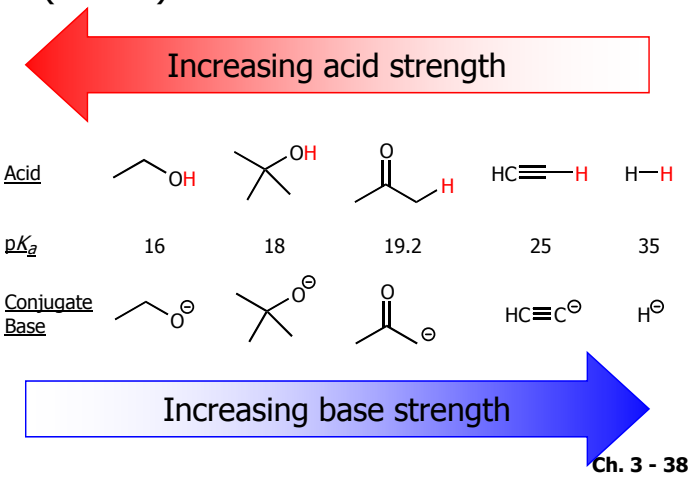

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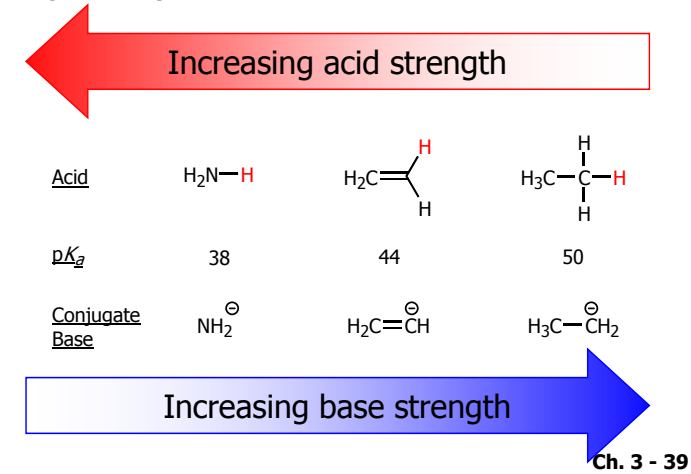


6C. Predicting the Strength of Bases

- The stronger the acid, the weaker its conjugate base
- The larger the pK_a of the conjugate acid, the stronger the base

Increasing base strength

$Cl^{\ominus}$	$CH_3CO_2^{\ominus}$	$HO^{\ominus}$
Very weak base	Weak base	Strong base
pK_a (HCl) = –7	pK_a (CH_3CO_2H) = 4.75	pK_a (H_2O) = 15.7

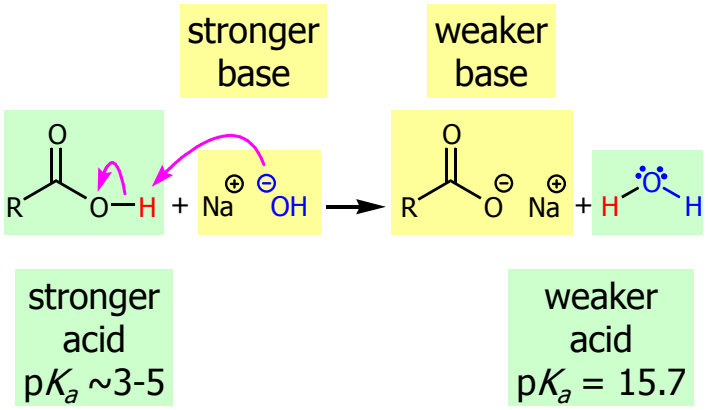
❖ Example

Base	$CH_3\ddot{O}H$	$H_2\ddot{O}$
Conjugate Acid	$H_3C-\overset{\oplus}{O}(H)-H$	$H-\overset{\oplus}{O}(H)-H$
pK_a	-2.5	-1.74

- Since $CH_3O\overset{\oplus}{H}_2$ is a stronger acid than $H_3O\overset{\oplus}{H}$, H_2O is a stronger base than CH_3OH

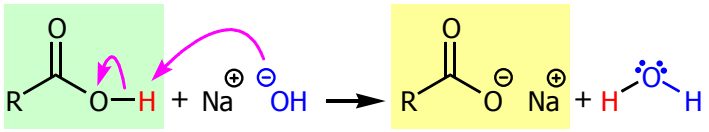
7. How to Predict the Outcome of Acid–Base Reactions

- Acid–base reactions always favor the formation of the weaker acid and the weaker base
- Acid–base reactions are **under equilibrium control**
- Reactions under equilibrium control always favour the formation of the most stable (lowest potential energy) species



7A. Water Solubility as the Result of Salt Formation

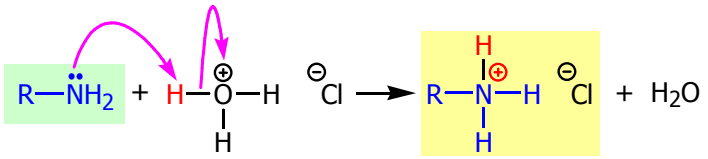
- Most carboxylic acids containing more than 5 carbons are insoluble in water
- However, due to their acidity, they are soluble in aq. NaOH



(R>5 carbons)
Insoluble
in water

Soluble in water
(due to its polarity
As a salt)

- Similarly, amines with high molecular weights are insoluble in water
- However, due to their basicity, they are soluble in aqueous acids



Water
Insoluble

Water
Soluble
(salt)

8. Relationships between Structure and Acidity

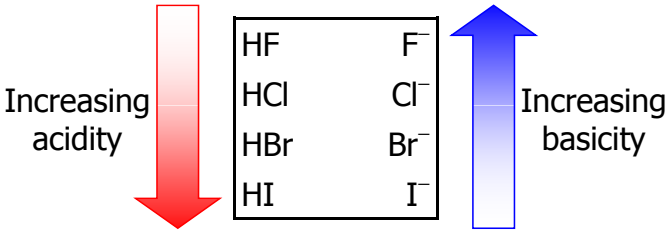
	H–F	H–Cl	H–Br	H–I
Bond Length (Å)	0.92	1.28	1.41	1.60
pK_a	3.2	-7	-9	-10

Increasing acidity

- The strength of H–X bond
  - H–F > H–Cl > H–Br > H–I

The stronger the H–X bond, the weaker the acid.

- Thus acidity increases as we descend a vertical column in a group in the Periodic Table

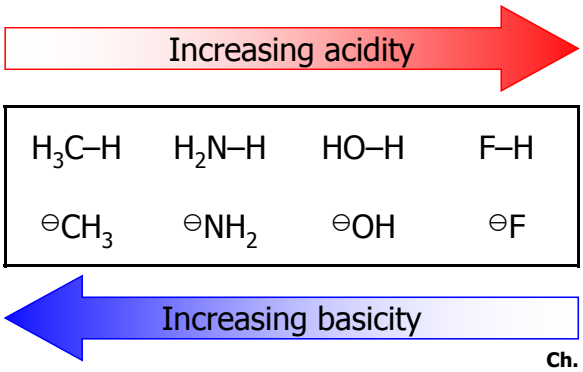


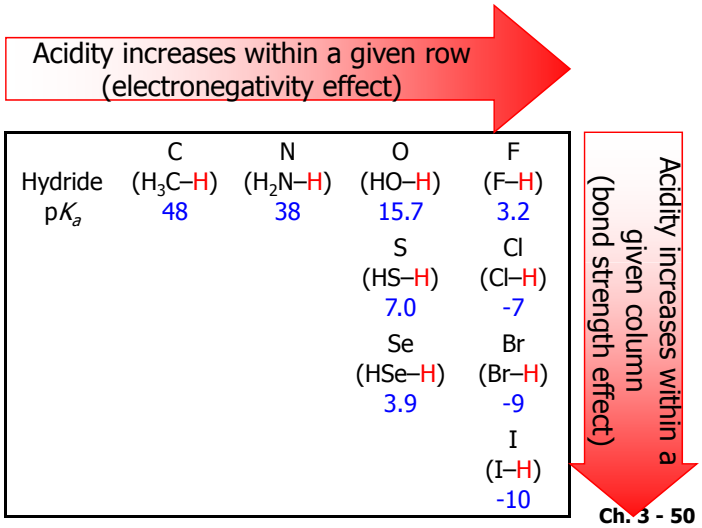
The stronger the acid, the weaker the conjugate base.

	δ^- δ^+ H_3C—H		δ^- δ^+ H_3N—H		δ^- δ^+ HO—H		δ^- δ^+ F—H	
Electro-negativity	2.5	2.1	3.0	2.1	3.5	2.1	4.0	2.1
pK_a	48		38		15.7		3.2	

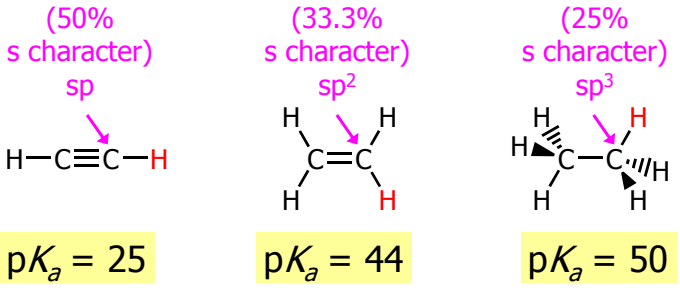
The higher the electronegativity of an atom, the easier it will acquire a negative charge.

- Thus acidity increases from left to right when we compare compounds in the same row of the Periodic Table



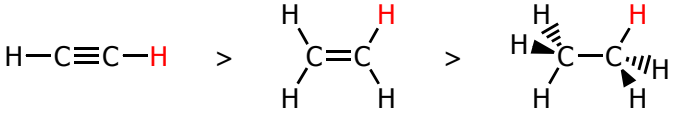


8A. The Effect of Hybridization

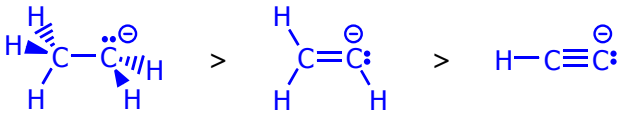


- Having more s character means that the electrons of the anion will, on the average, be lower in energy, and the anion will be more stable

- Relative Acidity of the Hydrocarbons

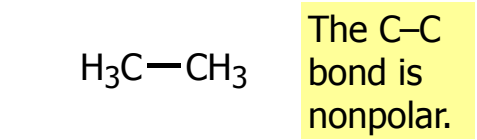


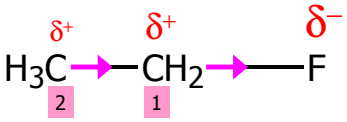
- Relative Basicity of the Carbanions



8B. Inductive Effects

- Inductive effects are electronic effects transmitted through bonds
- The inductive effect of a group can be *electron donating* or *electron withdrawing*
- Inductive effects weaken as the distance from the group increases



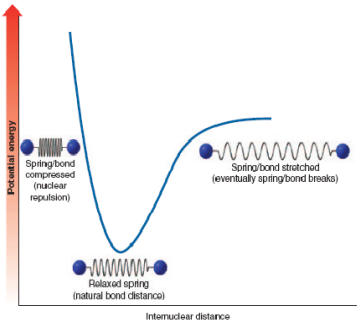


- The positive charge that the fluorine imparts to C1 is greater than that imparted to C2 because the fluorine is closer to C1

9. Energy Changes

- The two fundamental types of energy are kinetic energy and potential energy
- Kinetic energy is the energy an object has because of its motion; it equals one-half the object's mass multiplied by the square of its velocity
  - KE = $\frac{1}{2}mv^2$

- Potential energy is stored energy. It exists only when an attractive or repulsive force exists between objects
- Chemical energy is a form of potential energy
- The *more* potential energy an object has, the *less stable* it is



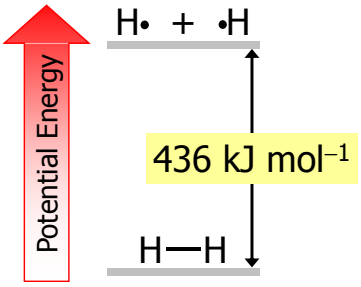
Potential energy exists between objects that either attract or repel each other. In the case of atoms joined by a covalent bond, the lowest potential energy state occurs when atoms are at their ideal internuclear distance (bond length). Lengthening or shortening the bond distance raises the potential energy.

9A. Potential Energy and Covalent Bonds

- Atoms and molecules possess potential energy – often called **chemical energy** – that can be released as heat when they react
- Because heat is associated with molecular motion, this release of heat results from a change from potential energy to kinetic energy

$\Delta H^o = -436$ kJ mol^{-1}

- The relative potential energies of hydrogen atoms and a hydrogen molecule



10. The Relationship between K_{eq} and ΔG^o

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

R is the gas constant = 8.314 J K^{-1}
T is the absolute temperature in kelvins (K)

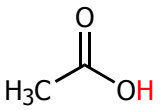
- For a reaction to favor the formation of products when equilibrium is reached it must have a negative value for ΔG^o
- For reactions with a positive ΔG^o, the formation of products at equilibrium is unfavorable

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

ΔH^o is the enthalpy energy
ΔS^o is the entropy energy

- A negative value for ΔH^o will contribute to making ΔG^o negative and will consequently favour the formation of products
- The more random a system is, the greater is its ΔS^o
- A positive entropy change (from order to disorder) makes a negative contribution to ΔG^o and is energetically favourable for the formation of products

11. The Acidity of Carboxylic Acids



Acetic acid

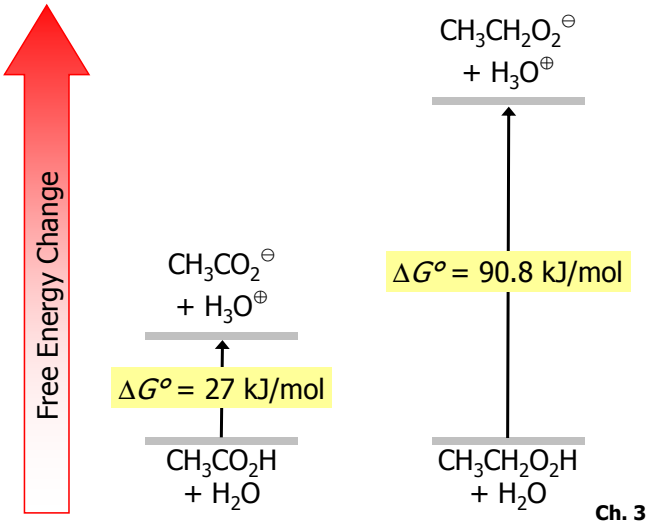
$CH_3CH_2—OH$

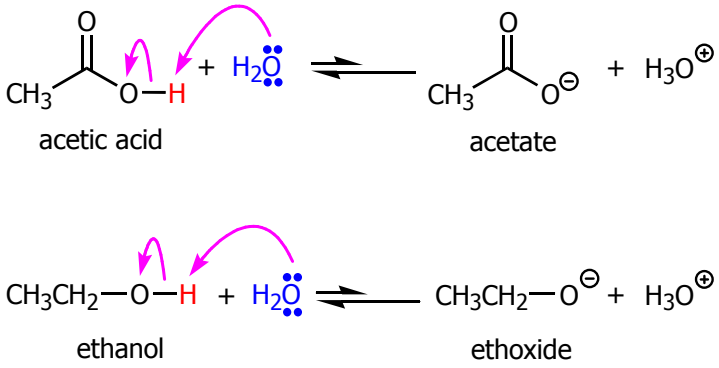
Ethanol

$pK_a = 4.75$
$\Delta G^o = 27$ kJ/mol

$pK_a = 16$
$\Delta G^o = 90.8$ kJ/mol

ΔG^o values are for OH proton ionization



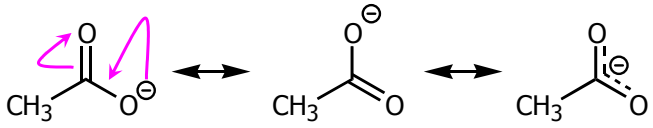


- When comparing acidity of organic compounds, we compare the stability of their conjugate base. The more stable the conjugate base, the stronger the acid

	CH_3COOH	CH_3CH_2OH
pK_a	4.75	16

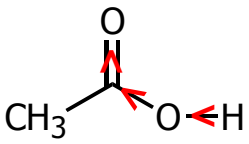
11A. The Effect of Delocalization

- The conjugate base acetate is more stable (the anion is more delocalized) than ethoxide due to resonance stabilization

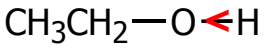


- Thus, acetic acid is a stronger acid than ethanol

11B. The Inductive Effect



Acetic acid



Ethanol

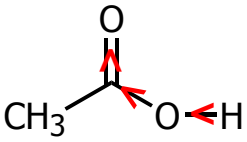
Stronger acid

Weaker acid

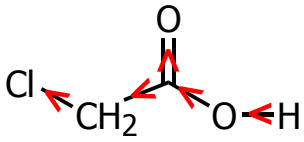
11C. Summary and a Comparison of Conjugate Acid–Base Strengths

- The greater acidity of a carboxylic acid is predominantly due to the ability of its conjugate base (a carboxylate ion) to stabilize a negative charge better than an alkoxide ion, the conjugate base of an alcohol
- The conjugate base of a carboxylic acid is a weaker base than the conjugate base of an alcohol

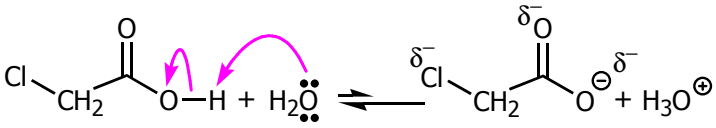
11D. Inductive Effects of Other Groups

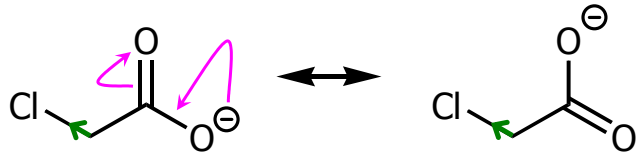


$pK_a = 4.75$



$pK_a = 2.86$

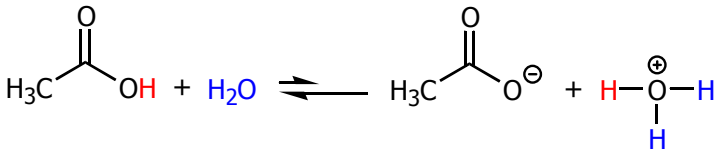




- The Cl further stabilizes the carboxylate anion due to negative inductive effect of the Cl

12. The Effect of the Solvent on Acidity

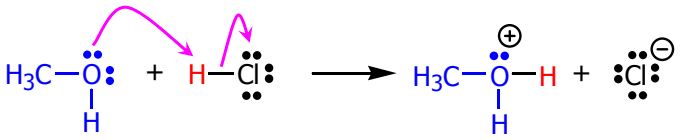
- In the absence of a solvent (i.e., in the gas phase), most acids are far weaker than they are in solution
- In solution, solvent molecules surround the ions, insulating them from one another, stabilizing them, and making it far easier to separate them than in the gas phase
- Solvation of any species decreases the entropy of the solvent because the solvent molecules become much more ordered as they surround molecules of the solute



- Water molecules solvate both the undissociated acid (CH_3CO_2H) and its anion (CH_3CO_2) by forming hydrogen bonds to them
- However, hydrogen bonding to $CH_3CO_2^{\ominus}$ is much stronger than to CH_3CO_2H because the water molecules are more attracted by the negative charge

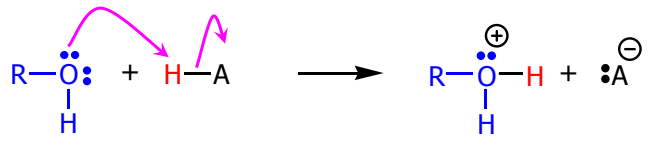
13. Organic Compounds as Bases

- If an organic compound contains an atom with an unshared electron pair, it is a potential base



Methanol

Methyloxonium ion
(a protonated alcohol)

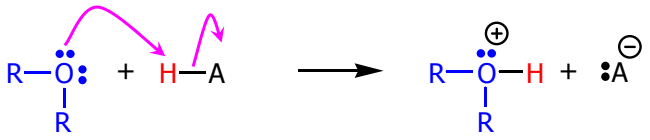


Alcohol

Strong acid

Alkyloxonium ion

Weak base



Ether

Strong acid

Dialkyloxonium ion

Weak base

Ketone

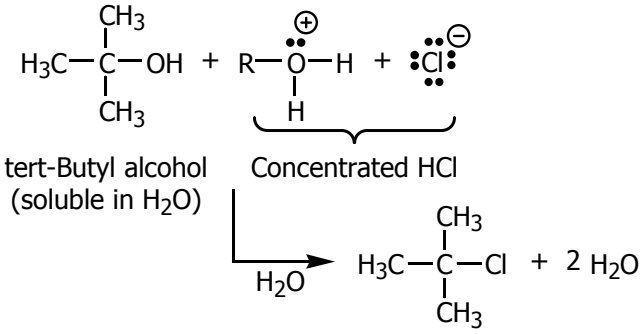
Strong acid

Protonated ketone

Weak base

- Proton transfer reactions like these are often the first step in many reactions that alcohols, ethers, aldehydes, ketones, esters, amides, and carboxylic acids undergo

14. A Mechanism for an Organic Reaction

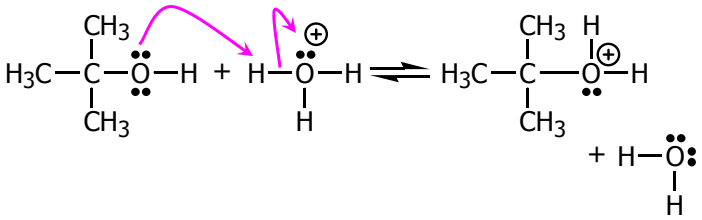


tert-Butyl alcohol
(soluble in H_2O)

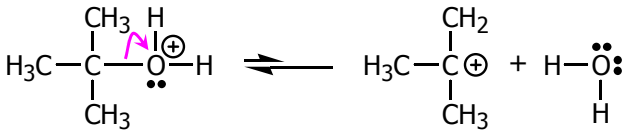
Concentrated HCl

tert-Butyl chloride
(insoluble in H_2O)

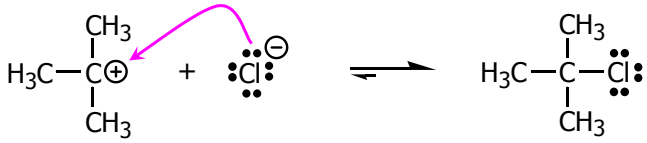
- Step 1



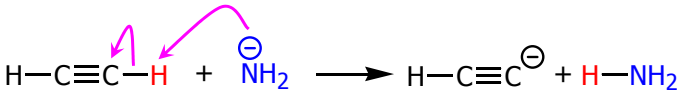
- Step 2



- Step 3

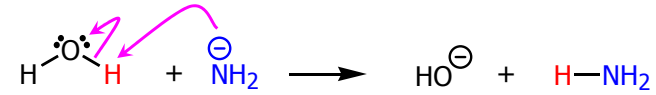


15. Acids and Bases in Nonaqueous Solutions



pK_a = 25 (stronger base) (weaker base) pK_a = 38

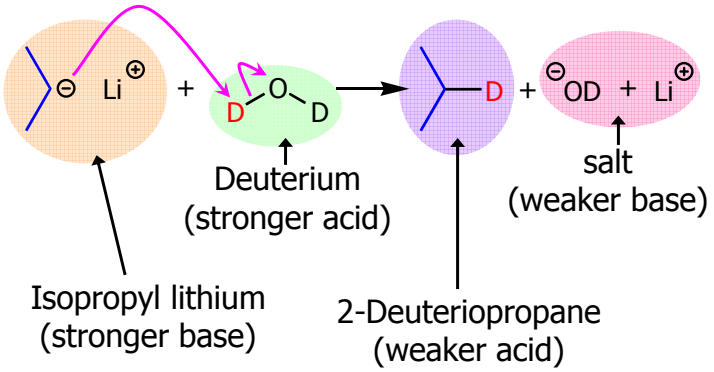
- This reaction cannot be carried using water as solvent



pK_a = 15.7 pK_a = 38

- Since water is a stronger acid than ethyne, $NH_2^{\ominus}$ will react with water first instead of ethyne
- When $NaNH_2$ is used, solvent such as hexane, Et_2O or liquid NH_3 can be used instead of water

16. Acid–Base Reactions & The Synthesis of ^2H- & ^3H-Labeled Compounds



END OF CHAPTER 3