Chapter 3

An Introduction to Organic Reactions: Acids and Bases

NEPHAR 109 Organic Chemistry
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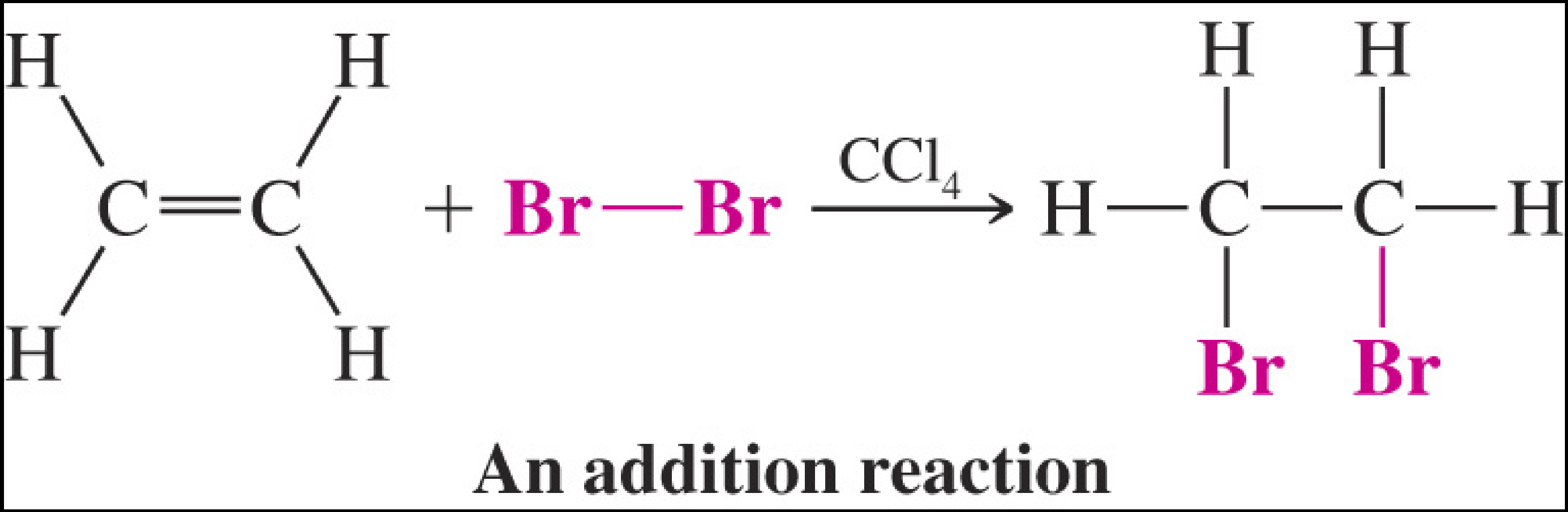
3.1 Reactions and Their Mechanisms

There are four general types of organic reactions

- **Addition Reactions**

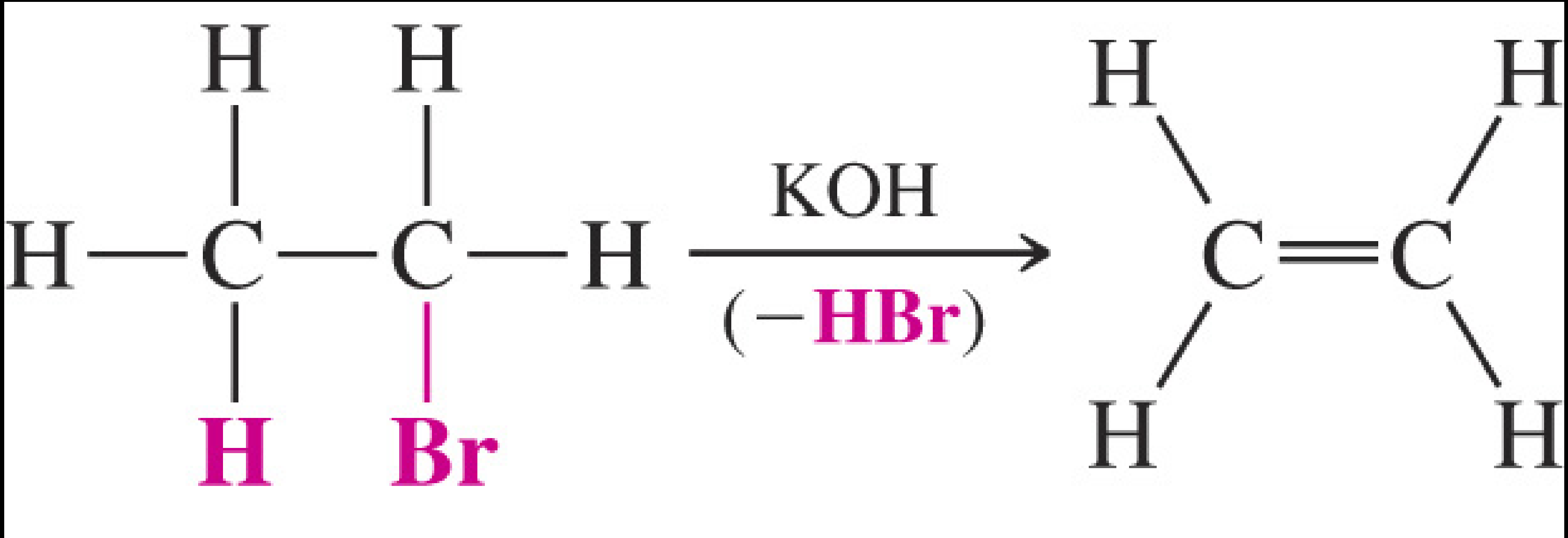
  Two reactants add together to form a single new product with no atoms "left over"



An addition reaction

- **Elimination Reactions**

Single reactant splits into two products



An elimination reaction

- **Substitution Reactions**

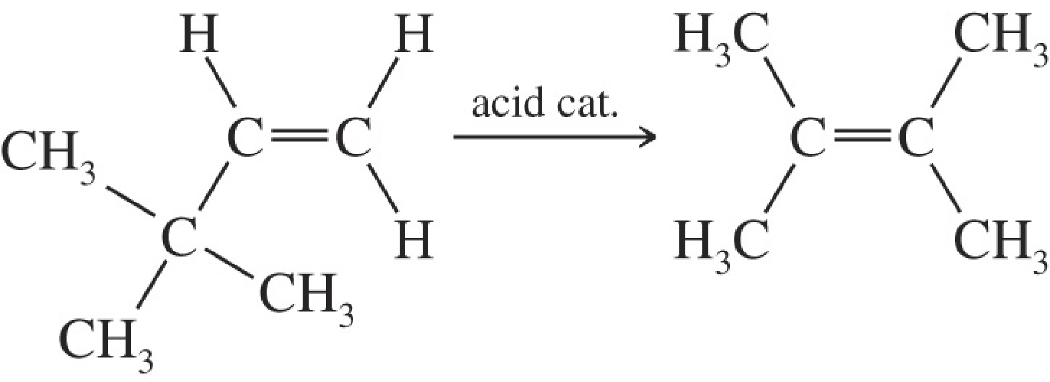
Two reactants exchange parts to give two new products

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

A substitution reaction

- **Rearrangement Reactions**

Single reactant undergoes a reorganization of bonds and atoms to yield an isomeric product



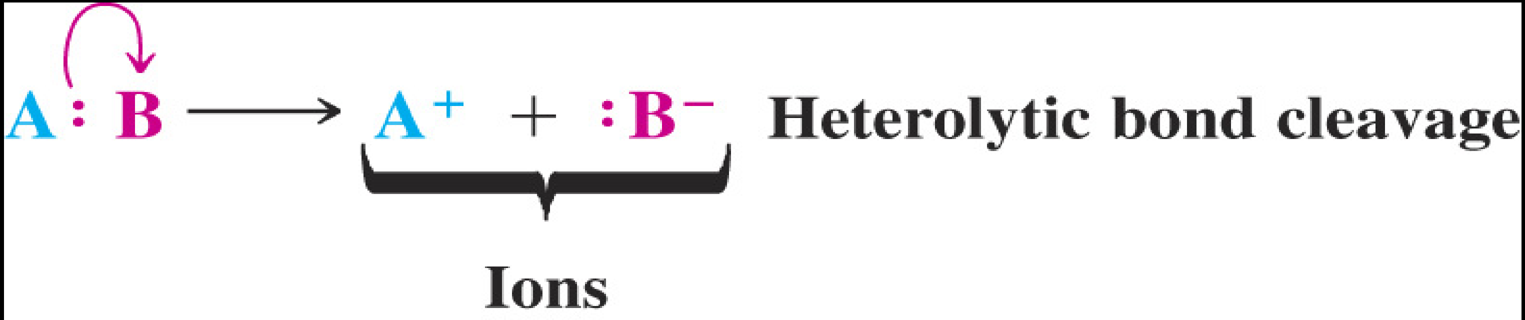
A rearrangement

3.3 Cleavage of Covalent Bonds

Homolysis

- Symmetrical bond breaking leading to radical reactions

Heterolysis

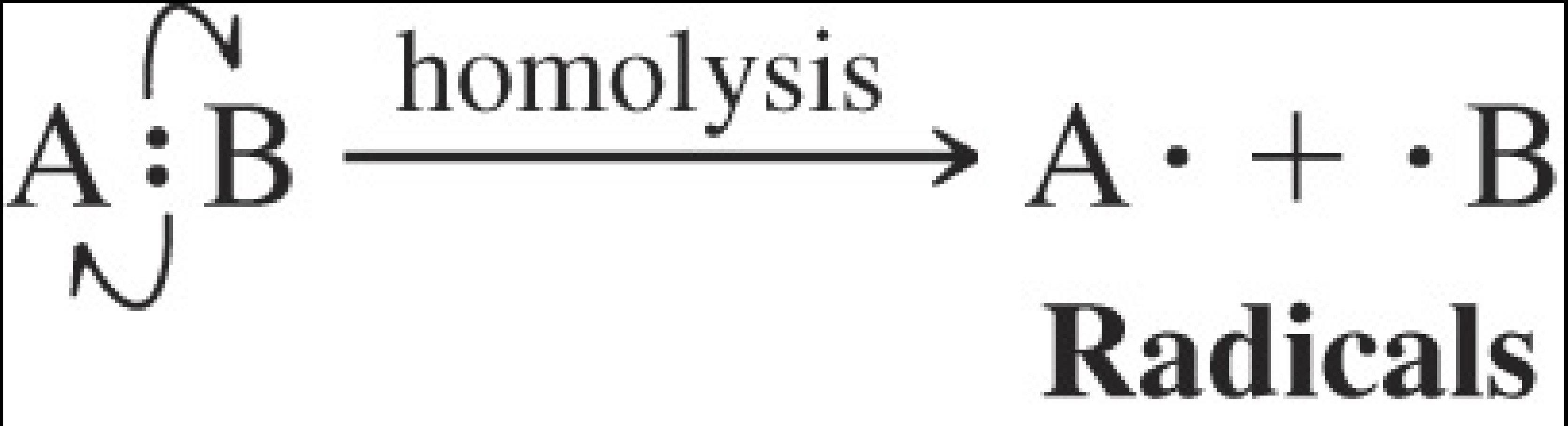


- Unsymmetrical bond breaking leading to polar reactions

Radical Reactions

- ➔Homolytic bond cleavage of relatively weak bonds such as O-O or X-X bonds can occur with addition of energy in the form of heat or light leading to the formation of radicals (also called free radicals)

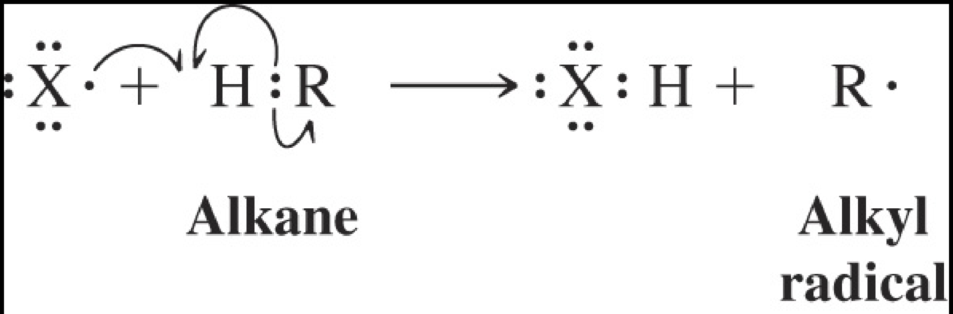
- ➔Radicals are highly reactive, short-lived species
  - Single-barbed arrows are used to show the movement of single electrons



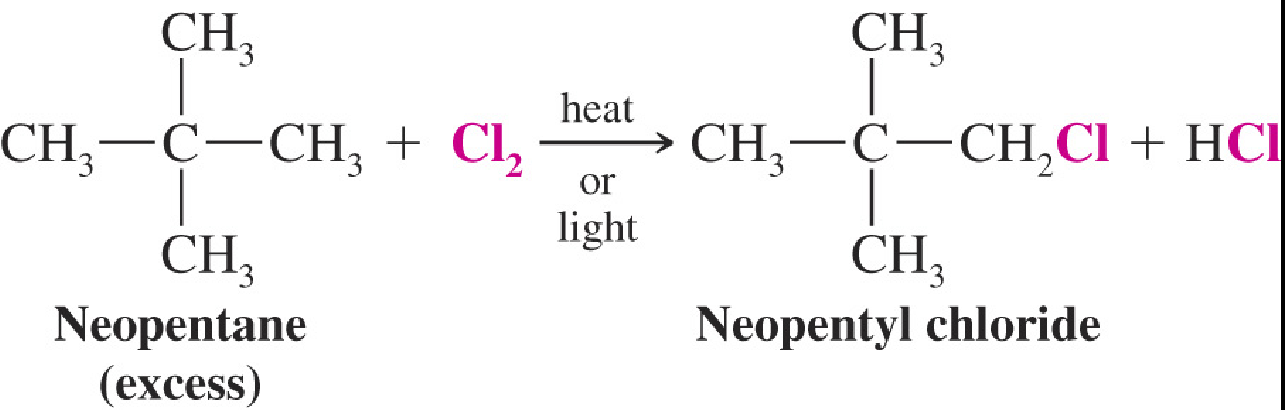
Reactions of Radicals

➔Radicals tend to react in ways that lead to pairing of their unpaired electron

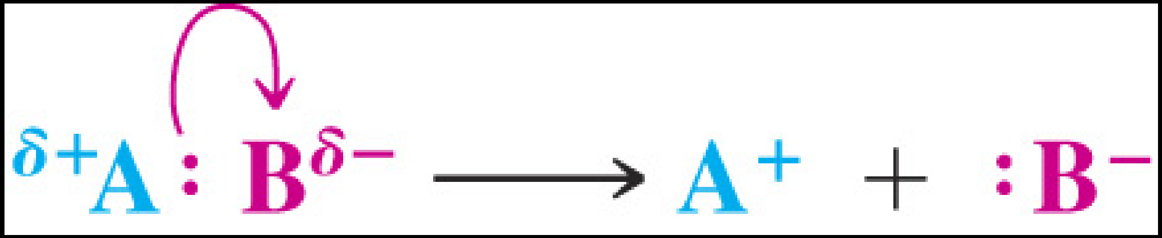
- Hydrogen abstraction is one way a halogen radical can react to pair its unshared electron



Example of a Radical Reaction



- **Heterolytic reactions almost always occur at polar bonds**
  - ➔The reaction is often assisted by formation of a new bond to another molecule



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

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

Introduction to Acid-Base Chemistry

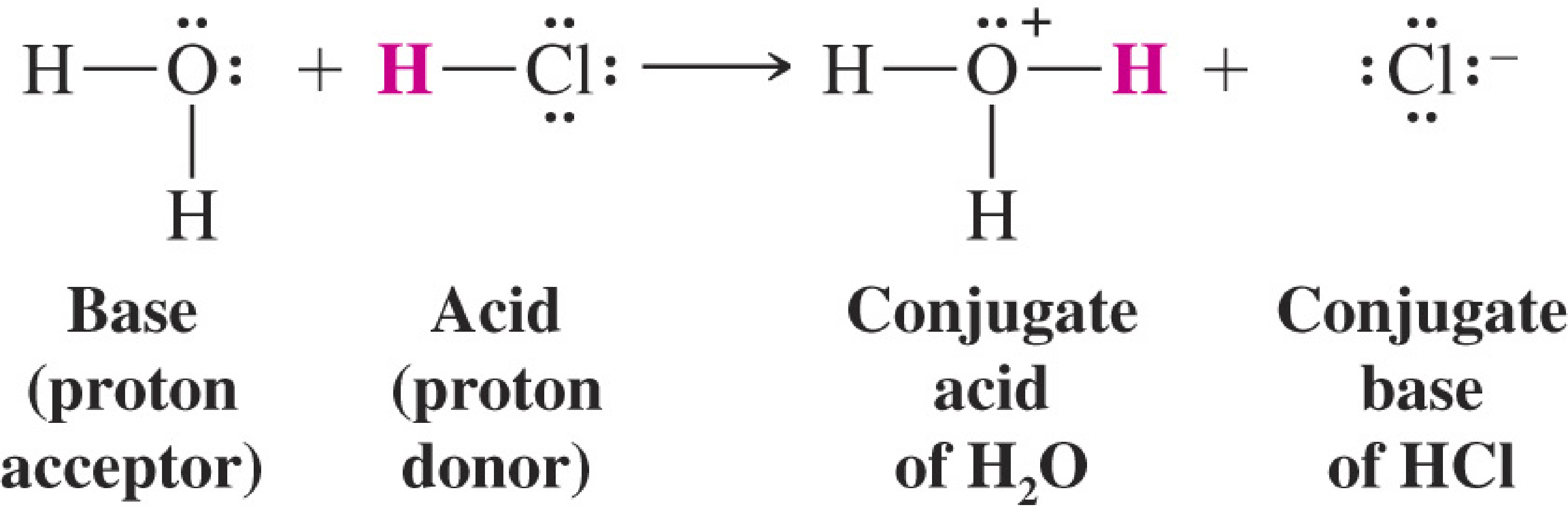
- **Brønsted-Lowry Definition of Acids and Bases**

  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

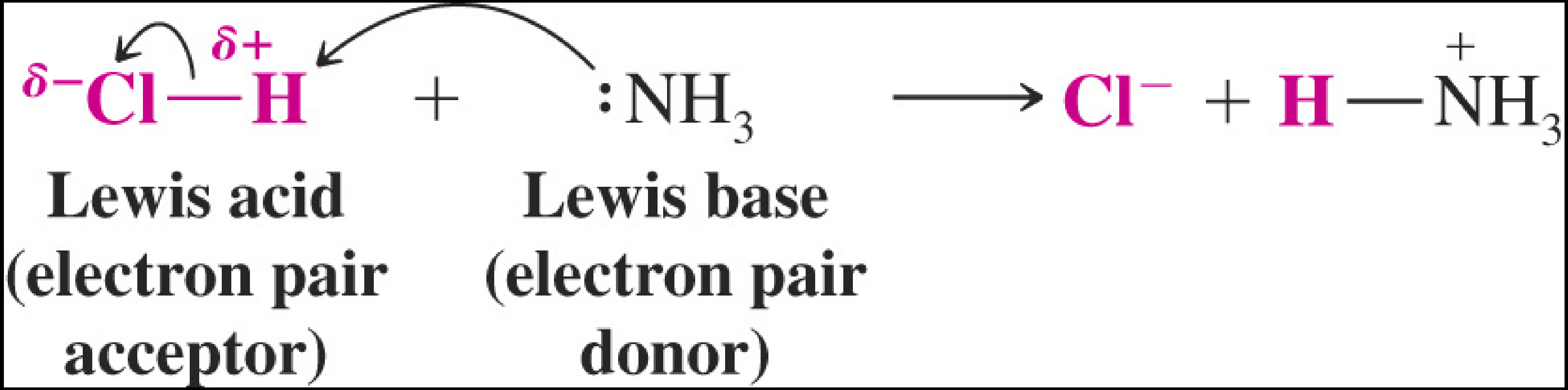


Lewis Definition of Acids and Bases

Lewis Acid: electron pair acceptor

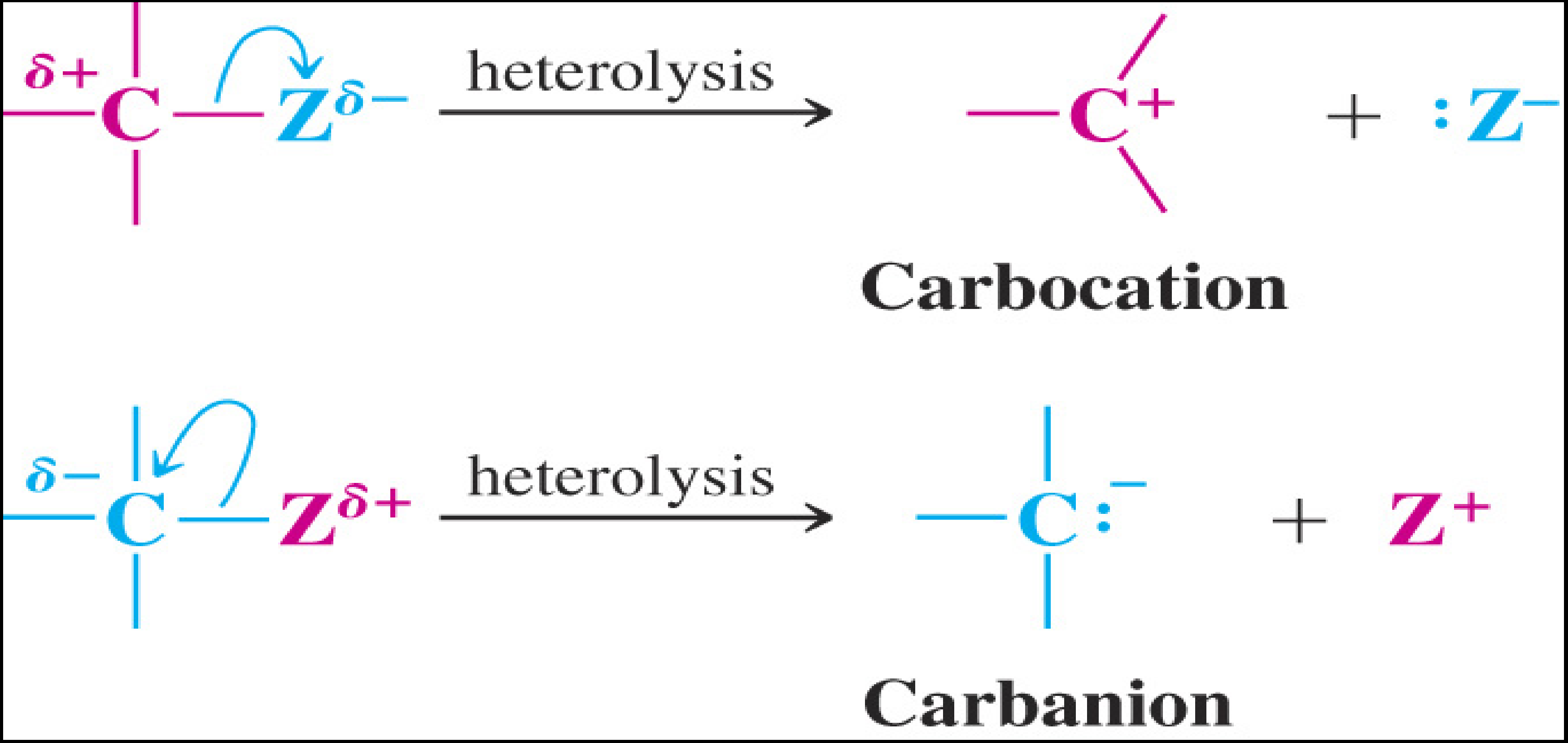
Lewis Base: electron pair donor

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

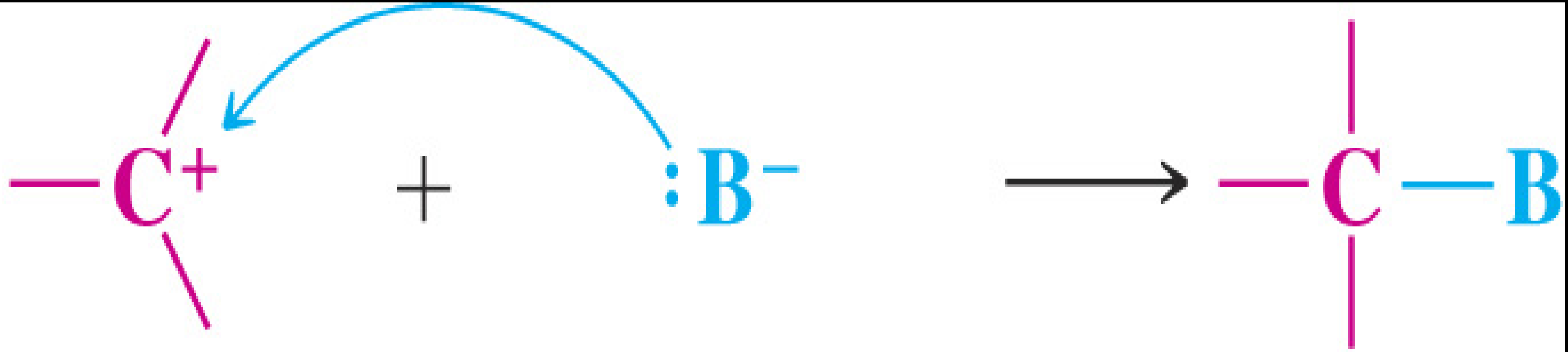


Heterolysis of Bonds to Carbons: Carbanions and Carbocations

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



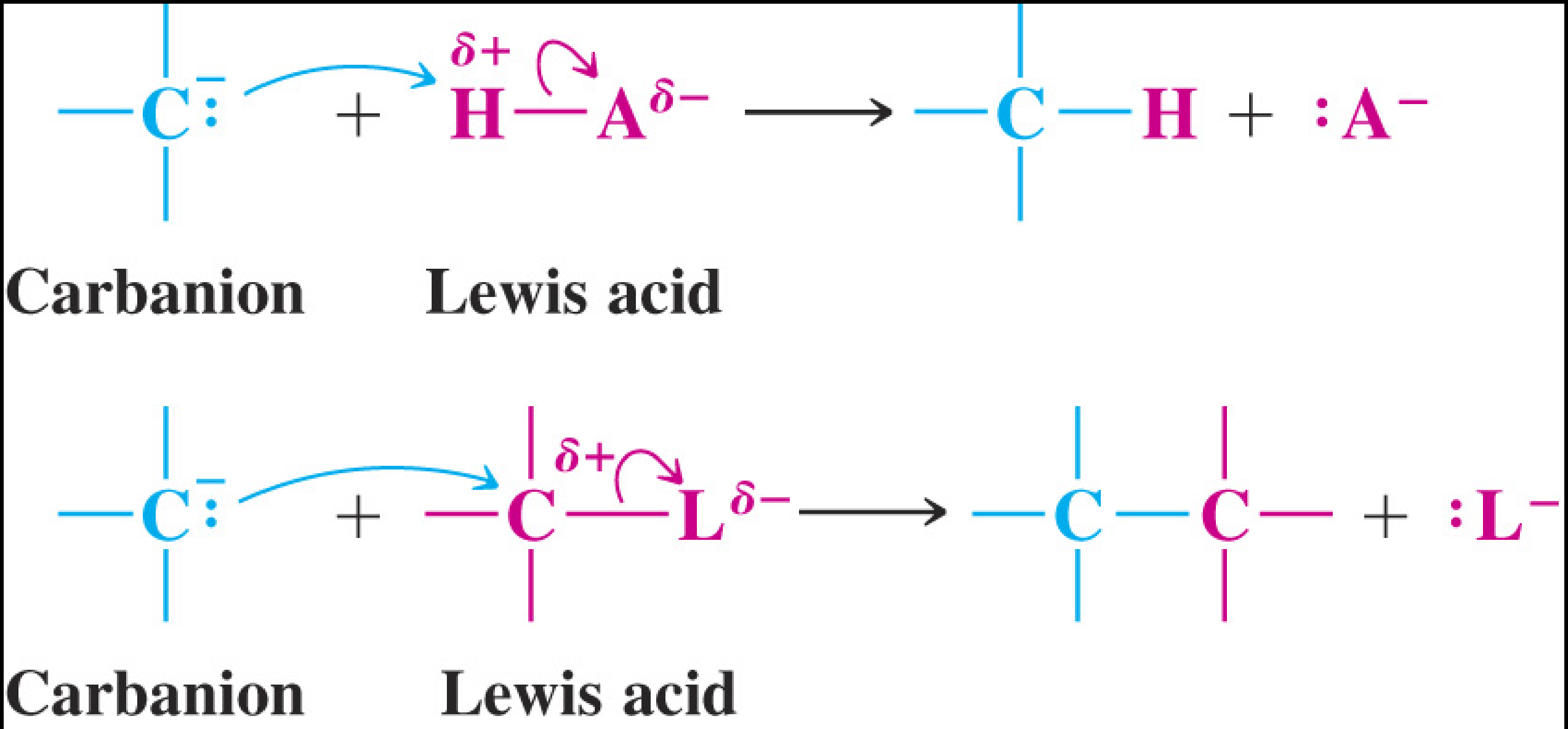
- Carbocations have only 6 valence electrons and a positive charge



Carbocation (a Lewis acid)

Anion (a Lewis base)

- 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

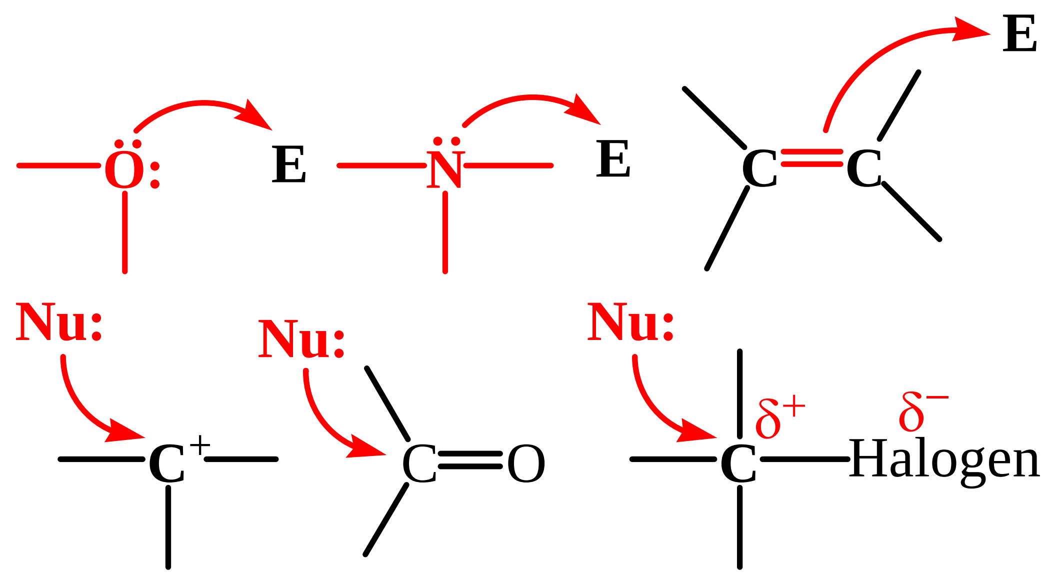
- Are electron-deficient themselves e.g. carbocations

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

- Are electron-rich themselves e.g. carbanions

Rules for Use of Curved Arrows

- Electrons move from a nucleophilic source (Nu:) to an electrophilic sink (E)



- The nucleophile can be either negatively charged or neutral

(e.g. H_2O, NH_3, OH^-, Cl^-, Br^-, CN^-)

- The electrophile can be positively charged or neutral

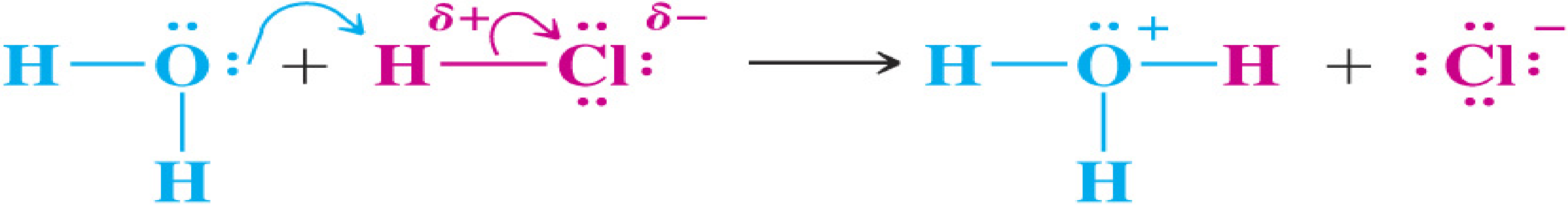
(e.g. H^+, Cl^+, Br^+, I^+, NO_2^+, CH_3^+, alkylhalides)

3.4 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

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



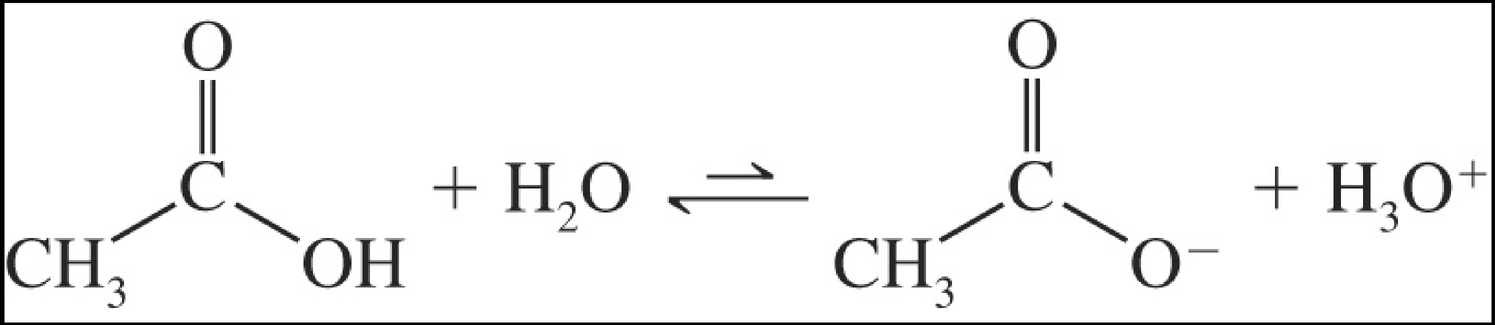
A water molecule uses one of the nonbonding electron pairs to form a bond to a proton of HCl. The bond between the hydrogen and chlorine breaks with the electron pair going to the chlorine atom.

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

3.5. Strengths of Acids and Bases

- ***K*$_a$ and p*K*$_a$**

➔**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:**

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

- ➔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 X 10^{-5}

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

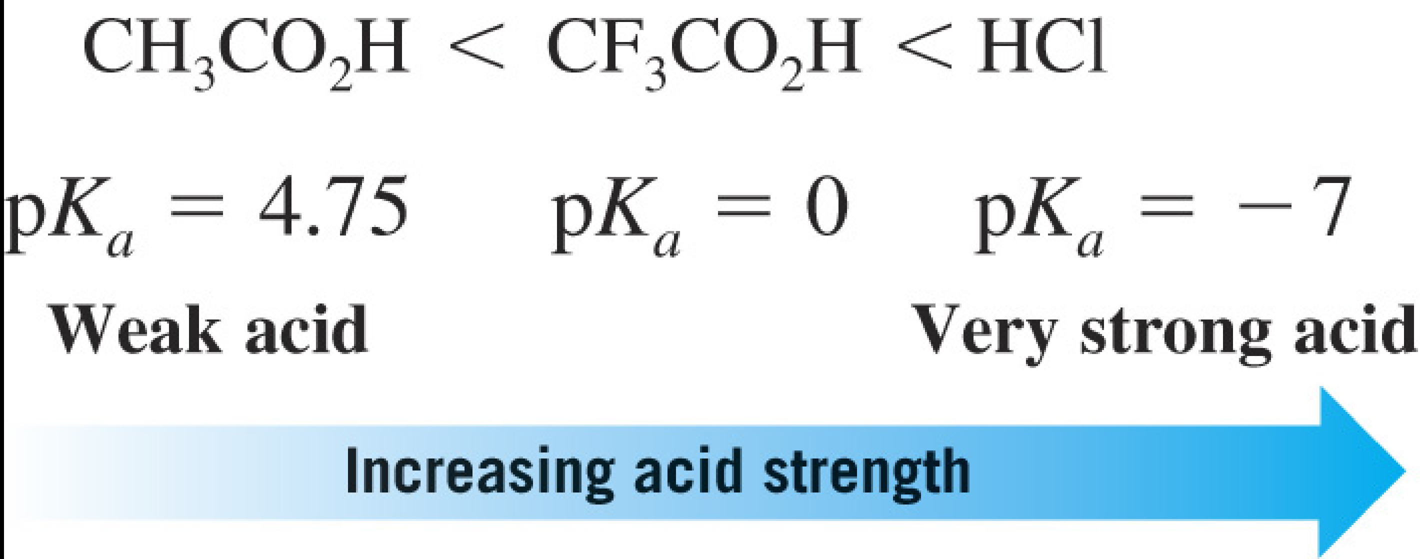
- ➔Any weak acid (HA) dissolved in water fits the general K_a expression
  - The stronger the acid, the larger the K_a

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

- Acidity is usually expressed in terms of pK_a
  - pK_a is the negative log of K_a
  - The pK_a for acetic acid is 4.75

$$\mathrm{p}K_\mathrm{a} = -\log K_\mathrm{a}$$

- The larger the pK_a, the weaker the acid



$CH_3CO_2H < CF_3CO_2H < HCl$

$\mathrm{p}K_a = 4.75$ $\mathrm{p}K_a = 0$ $\mathrm{p}K_a = -7$

Weak acid **Very strong acid**

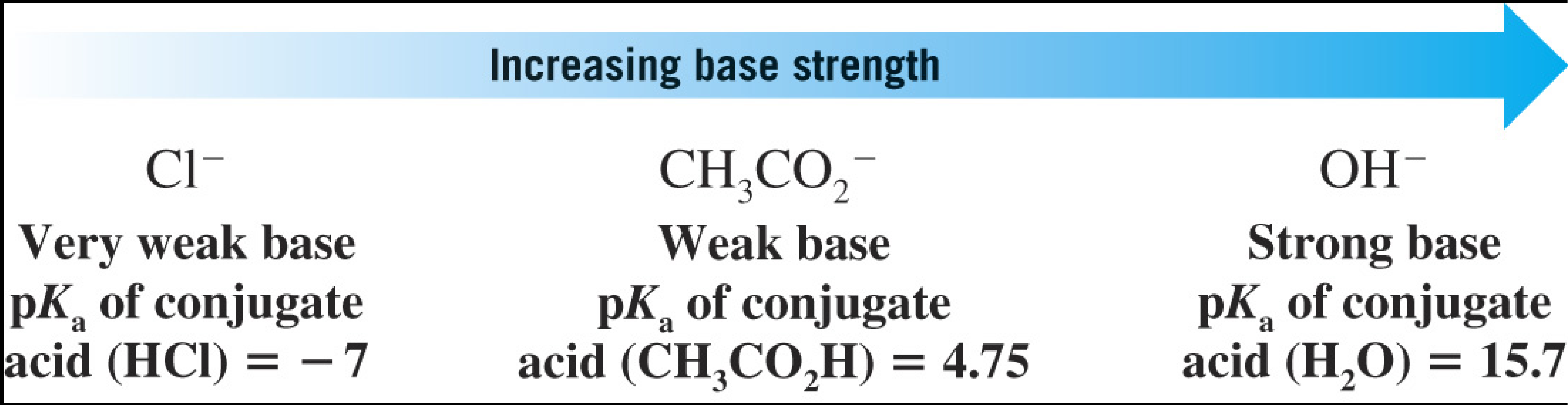
	Acid	Approximate pK_a	Conjugate Base	
Strongest acid	$HSbF_6$	< -12	SbF_6^-	Weakest base
	HI	-10	I^-	
	H_2SO_4	-9	HSO_4^-	
	HBr	-9	Br^-	
	HCl	-7	Cl^-	
	$C_6H_5SO_3H$	-6.5	$C_6H_5SO_3^-$	
	$(CH_3)_2\overset{+}{O}H$	-3.8	$(CH_3)_2O$	
	$(CH_3)_2C{=}\overset{+}{O}H$	-2.9	$(CH_3)_2C{=}O$	
	$CH_3\overset{+}{O}H_2$	-2.5	CH_3OH	
	H_3O^+	-1.74	H_2O	
	HNO_3	-1.4	NO_3^-	
	CF_3CO_2H	0.18	$CF_3CO_2^-$	
	HF	3.2	F^-	
	CH_3CO_2H	4.75	$CH_3CO_2^-$	
	H_2CO_3	6.35	HCO_3^-	
	$CH_3COCH_2COCH_3$	9.0	$CH_3CO\overset{-}{C}HCOCH_3$	
	NH_4^+	9.2	NH_3	
	C_6H_5OH	9.9	C_6H_5O-	
	HCO_3^-	10.2	CO_3^{2-}	
	$CH_3NH_3^+$	10.6	CH_3NH_2	
	H_2O	15.7	OH^-	
	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

Increasing base strength

Predicting the Strengths of Bases

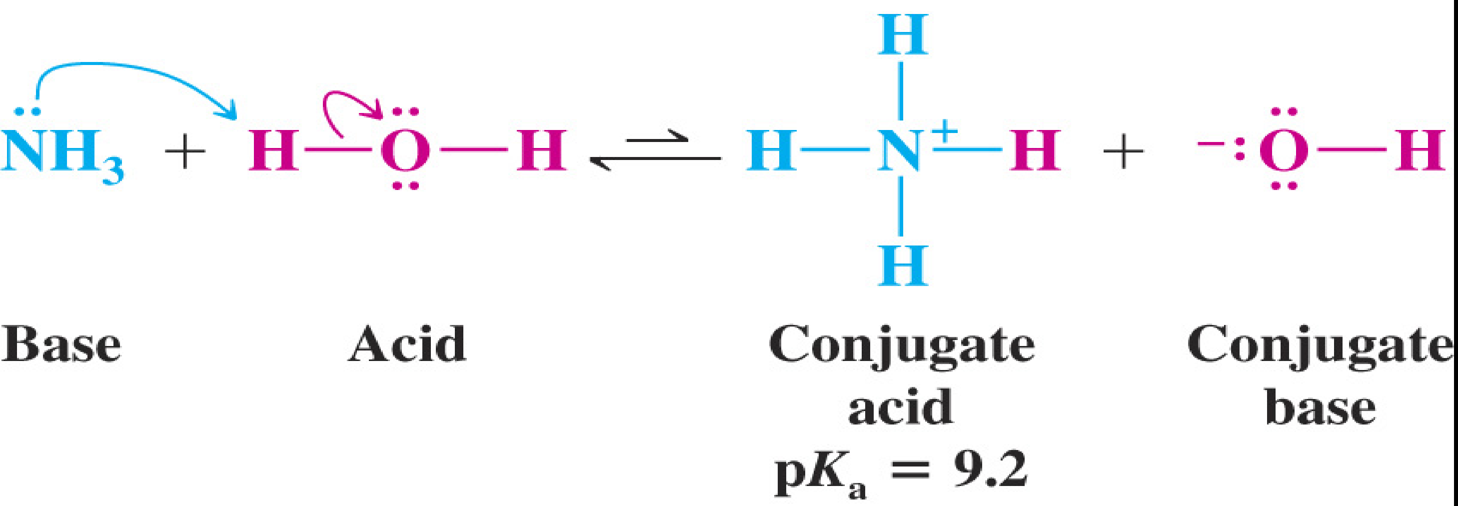
- The stronger the acid, the weaker its conjugate base will be
  - An acid with a low pK_a will have a weak conjugate base
  - Chloride is a very weak base because its conjugate acid HCl is a very strong acid

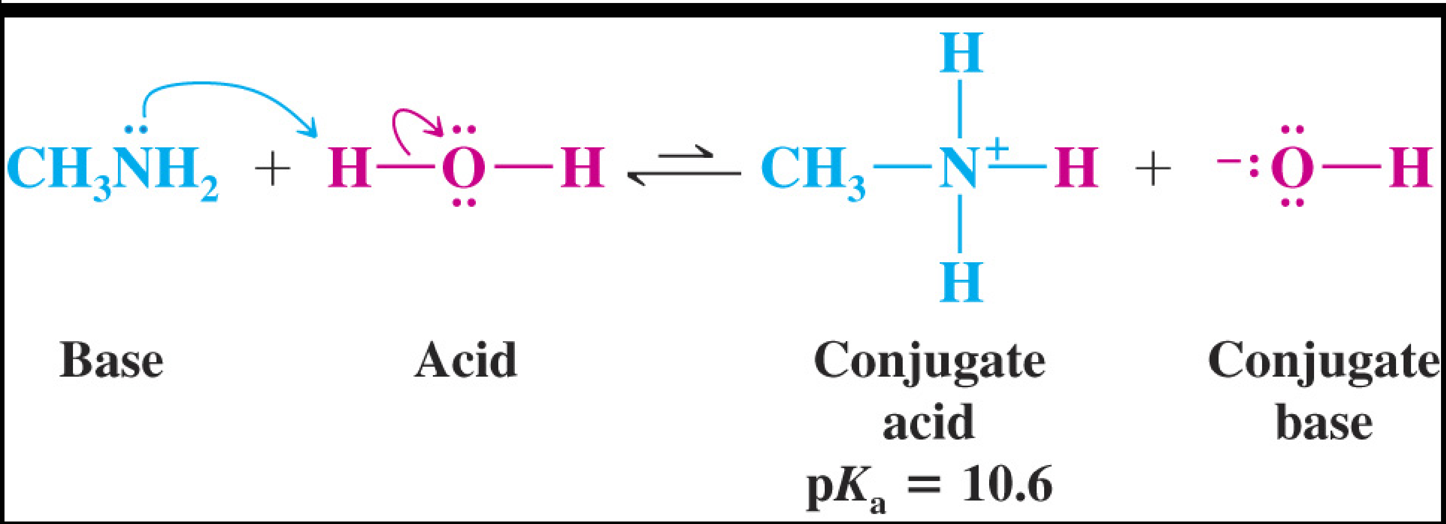


Increasing base strength

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

- **Methylamine is a stronger base than ammonia**
  - →The conjugate acid of methylamine is weaker than the conjugate acid of ammonia



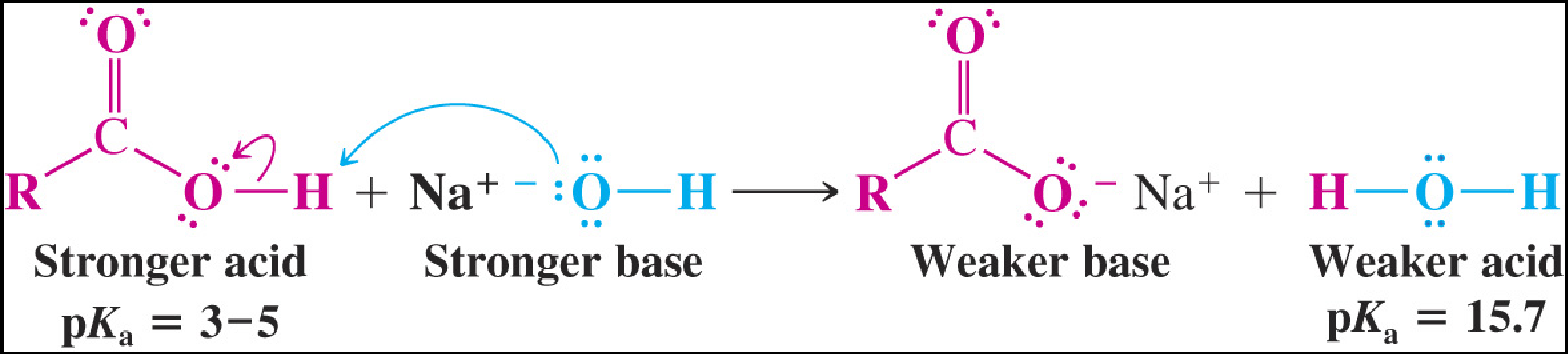


3.6 Predicting the Outcome of Acid-Base Reactions

- 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

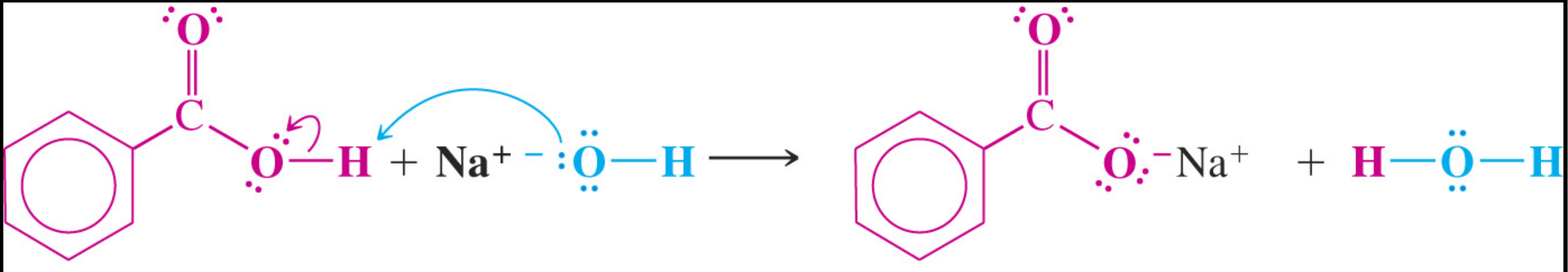
Example

Acetic acid reacts with sodium hydroxide to greatly favor products



Water Solubility as a Result of Salt Formation

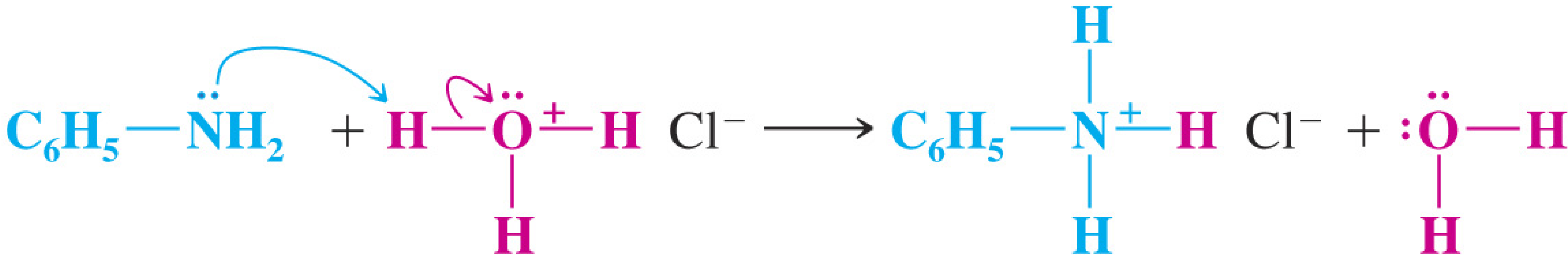
- Organic compounds which are water insoluble can sometimes be made soluble by turning them into salts
- Water insoluble carboxylic acids can become soluble in aqueous sodium hydroxide



Insoluble in water

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

- **Water insoluble amines can become soluble in aqueous hydrogen chloride**



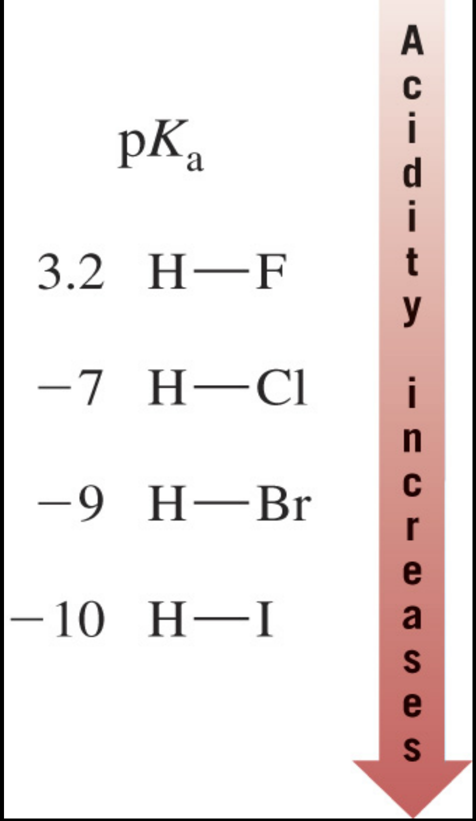
$$C_6H_5-\ddot{N}H_2 + H-\overset{+}{\ddot{O}}(H)-H\ Cl^- \longrightarrow C_6H_5-\overset{+}{N}H_3\ Cl^- + :\ddot{O}(H)-H$$

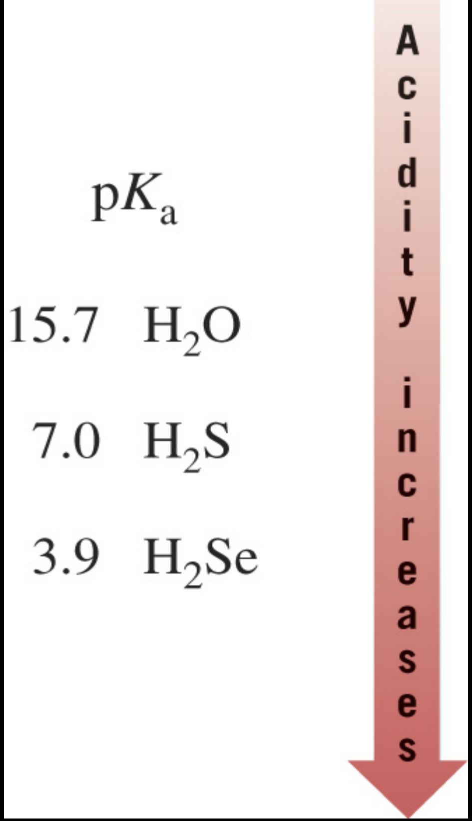
Water insoluble

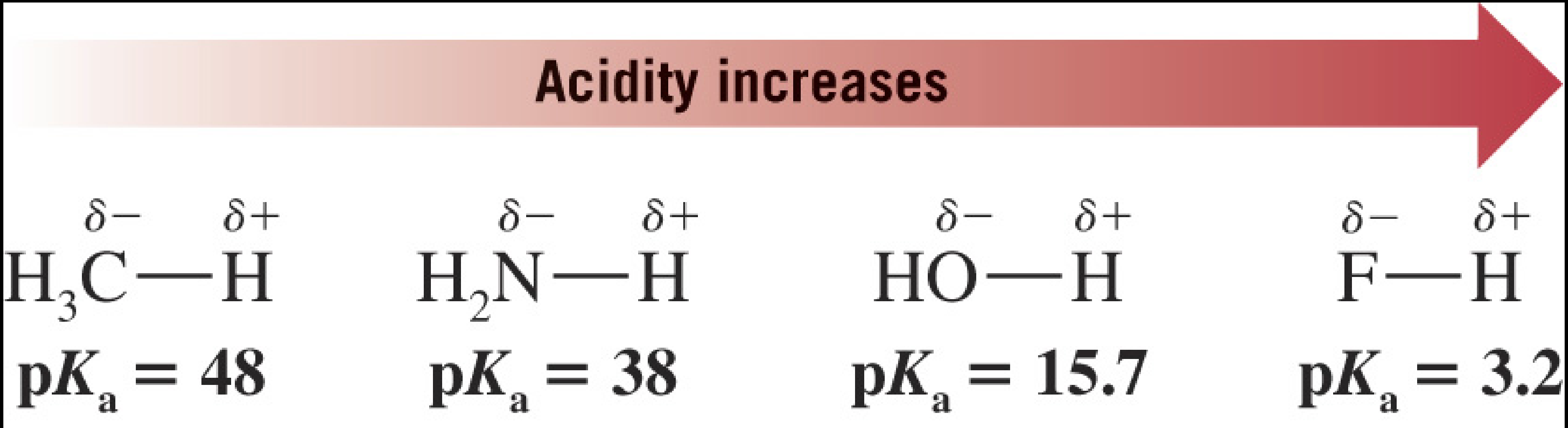
Water-soluble salt

3.7 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



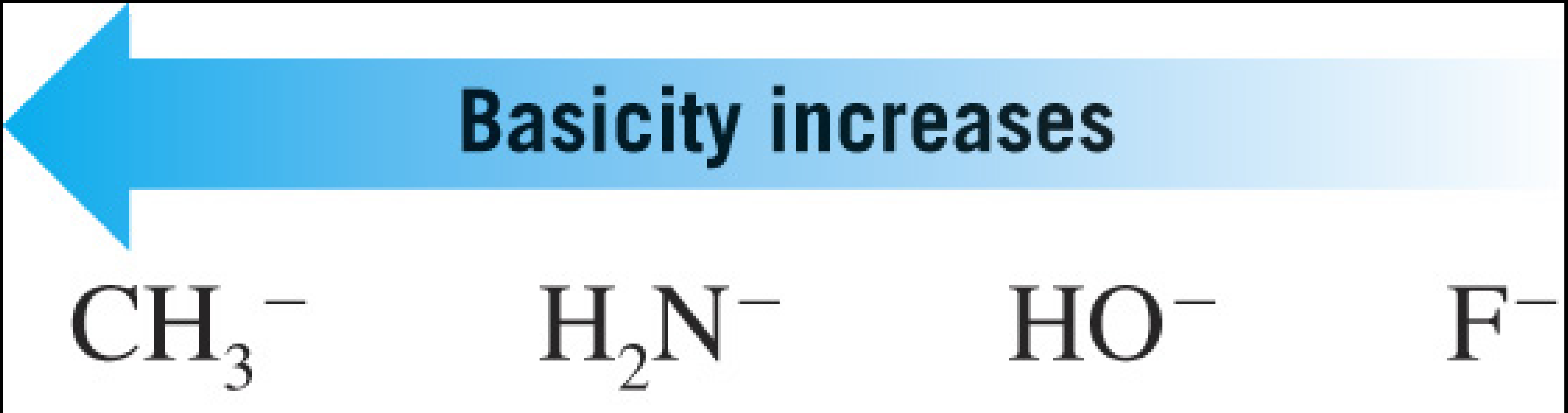




Acidity increases

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

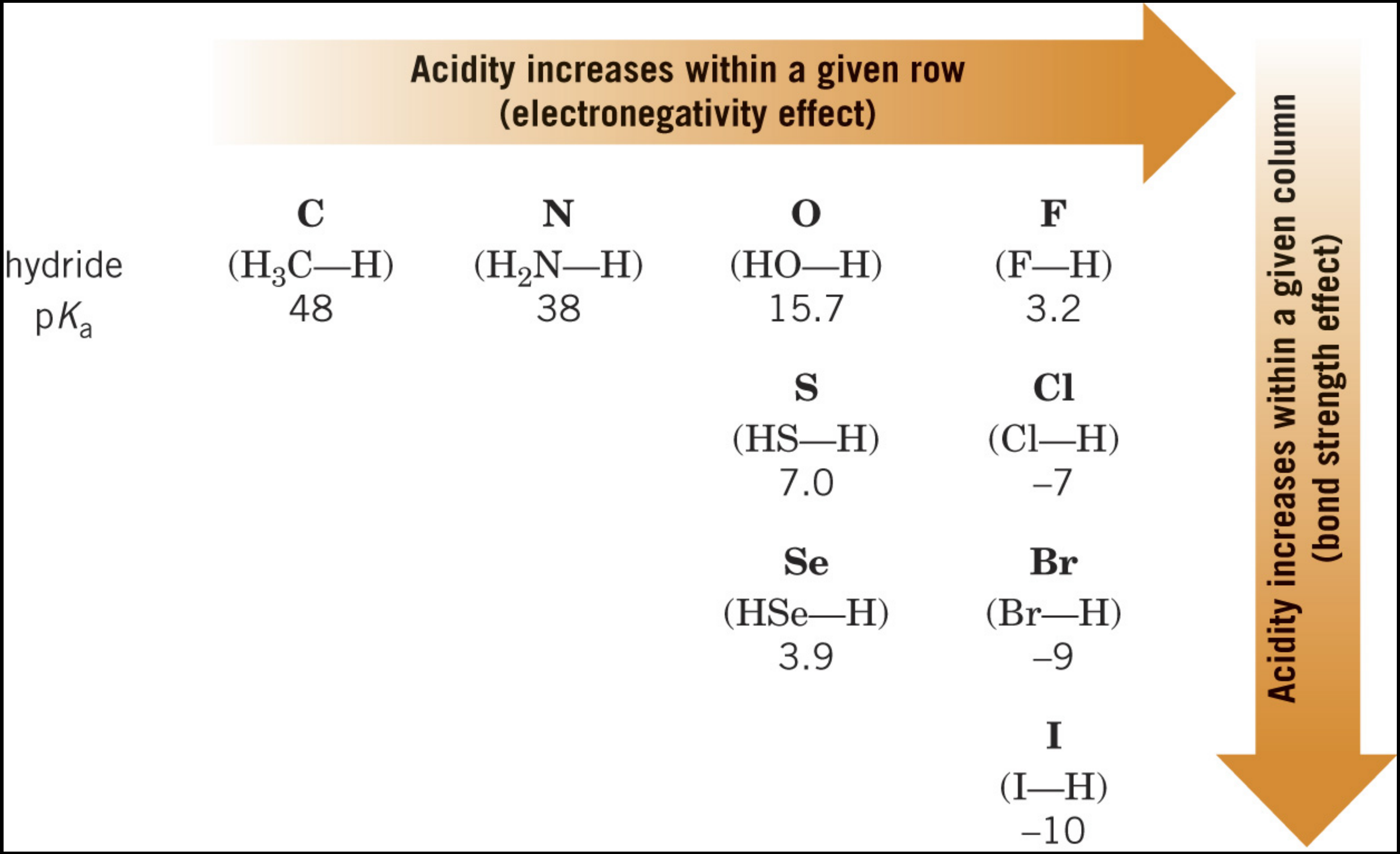
$pK_a = 48$ $\quad$ $pK_a = 38$ $\quad$ $pK_a = 15.7$ $\quad$ $pK_a = 3.2$



Basicity increases

CH_3^- $\quad$ H_2N^- $\quad$ HO^- $\quad$ F^-

Overview of Acidity Trends



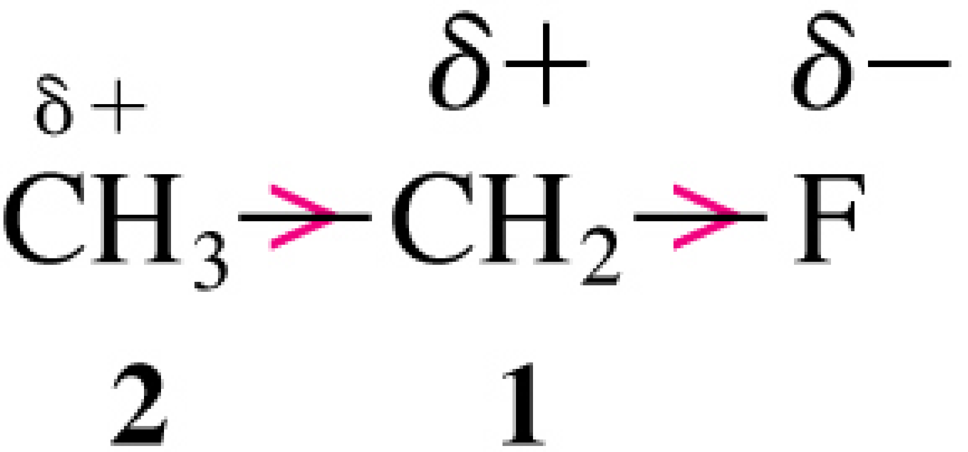
Acidity increases within a given row
(electronegativity effect)

Acidity increases within a given column
(bond strength effect)

	C	**N**	**O**	**F**
hydride pK_a	(H_3C—H) 48	(H_2N—H) 38	(HO—H) 15.7	(F—H) 3.2
			S (HS—H) 7.0	**Cl** (Cl—H) –7
			Se (HSe—H) 3.9	**Br** (Br—H) –9
				I (I—H) –10

Inductive Effects

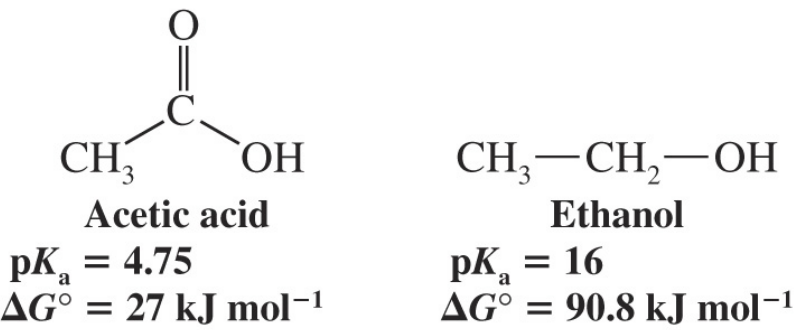
- Electronic effects that are transmitted through space and through the bonds of a molecule
- In ethyl fluoride the electronegative fluorine is drawing electron density away from the carbons
    - Fluorine is an electron withdrawing group (EWG)
    - The effect gets weaker with increasing distance

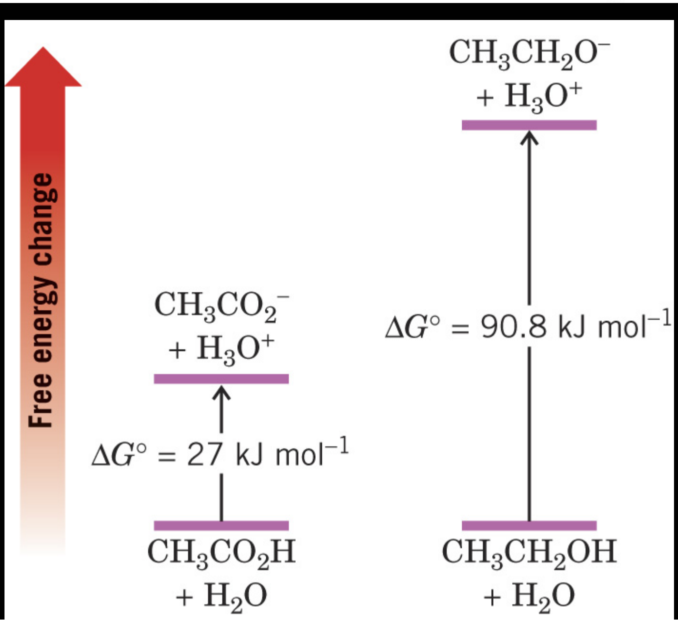


$$\underset{2}{\overset{\delta+}{CH_3}} \rightarrow \underset{1}{\overset{\delta+}{CH_2}} \rightarrow \overset{\delta-}{F}$$

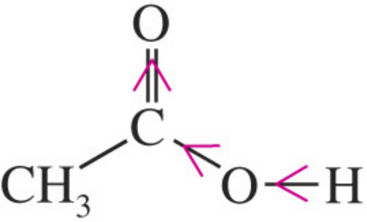
3.10 The Acidity of Carboxylic Acids

- Carboxylic acids are much more acidic than alcohols
  - ➔Deprotonation is unfavorable in both cases but much less favorable for ethanol





- **Explanation based on inductive effect**
  - ➔In acetic acid the highly polarized carbonyl group draws electron density away from the acidic hydrogen

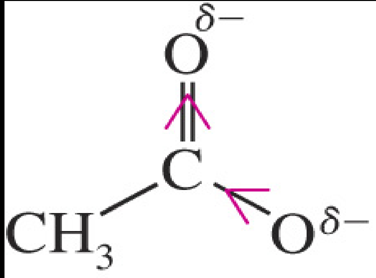


Acetic acid
(stronger acid)

$CH_3-CH_2-O \leftarrow H$

Ethanol
(weaker acid)

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



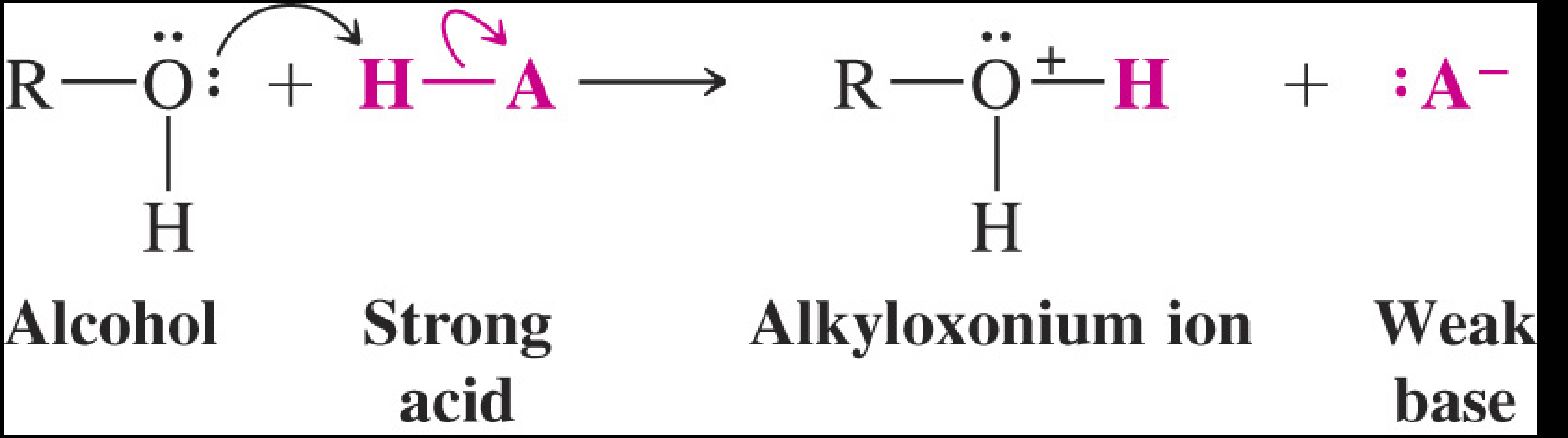
Acetate anion
Weaker base

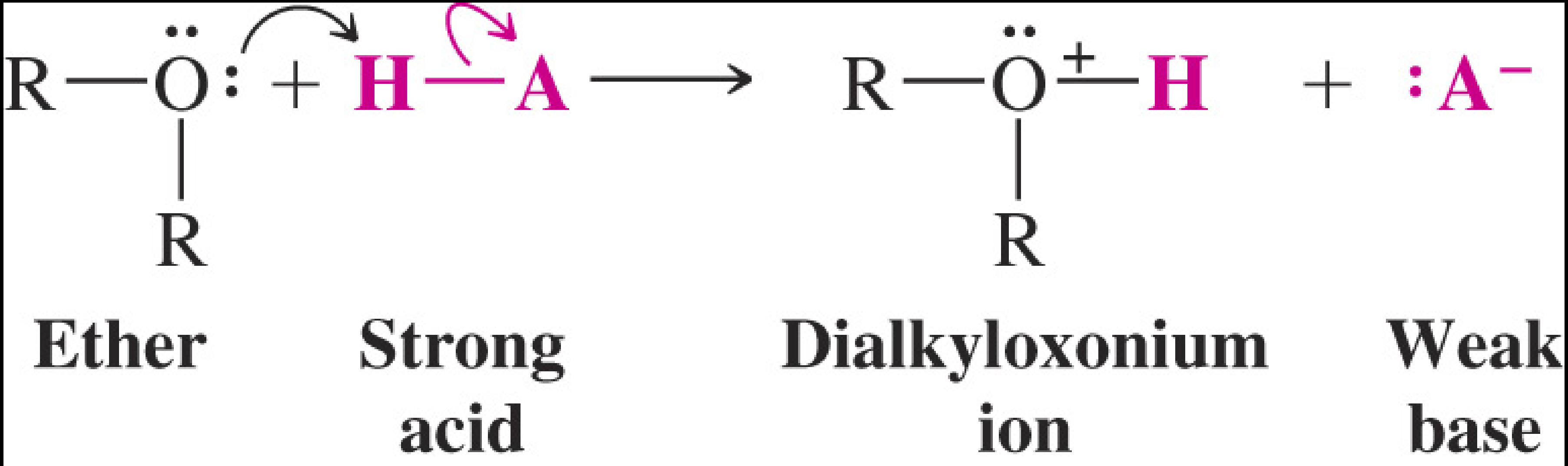
$CH_3-CH_2 \leftarrow O^-$

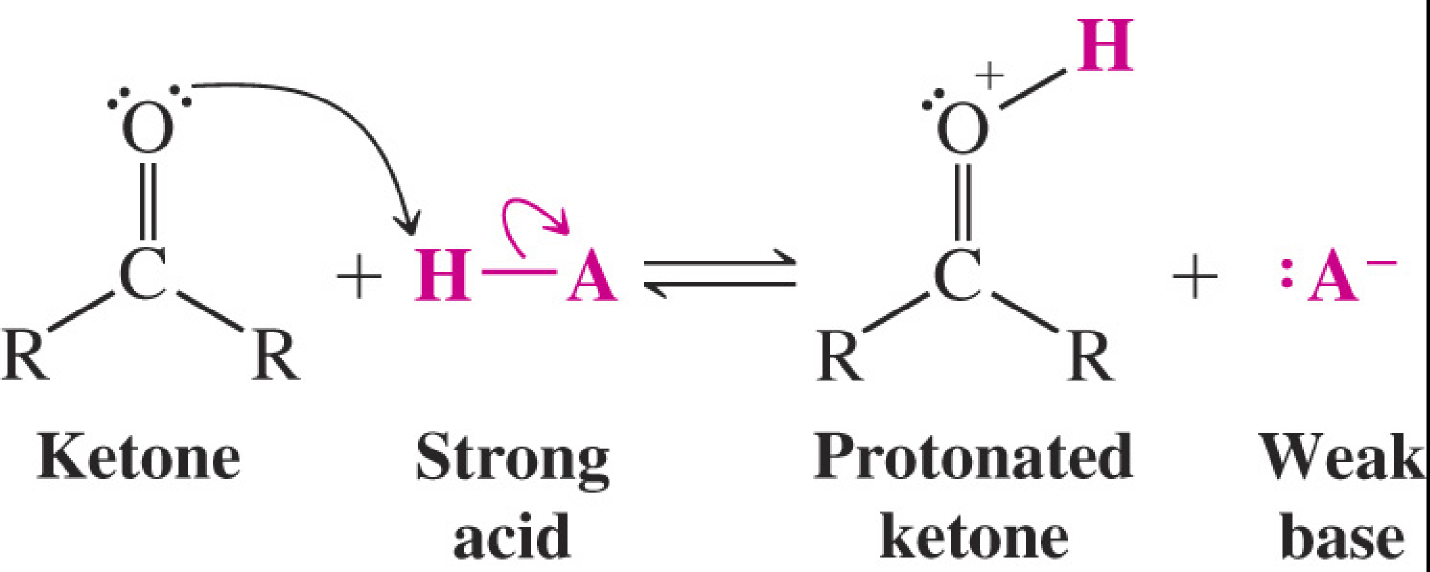
Ethoxide anion
Stronger base

3.12 Organic Compounds as Bases

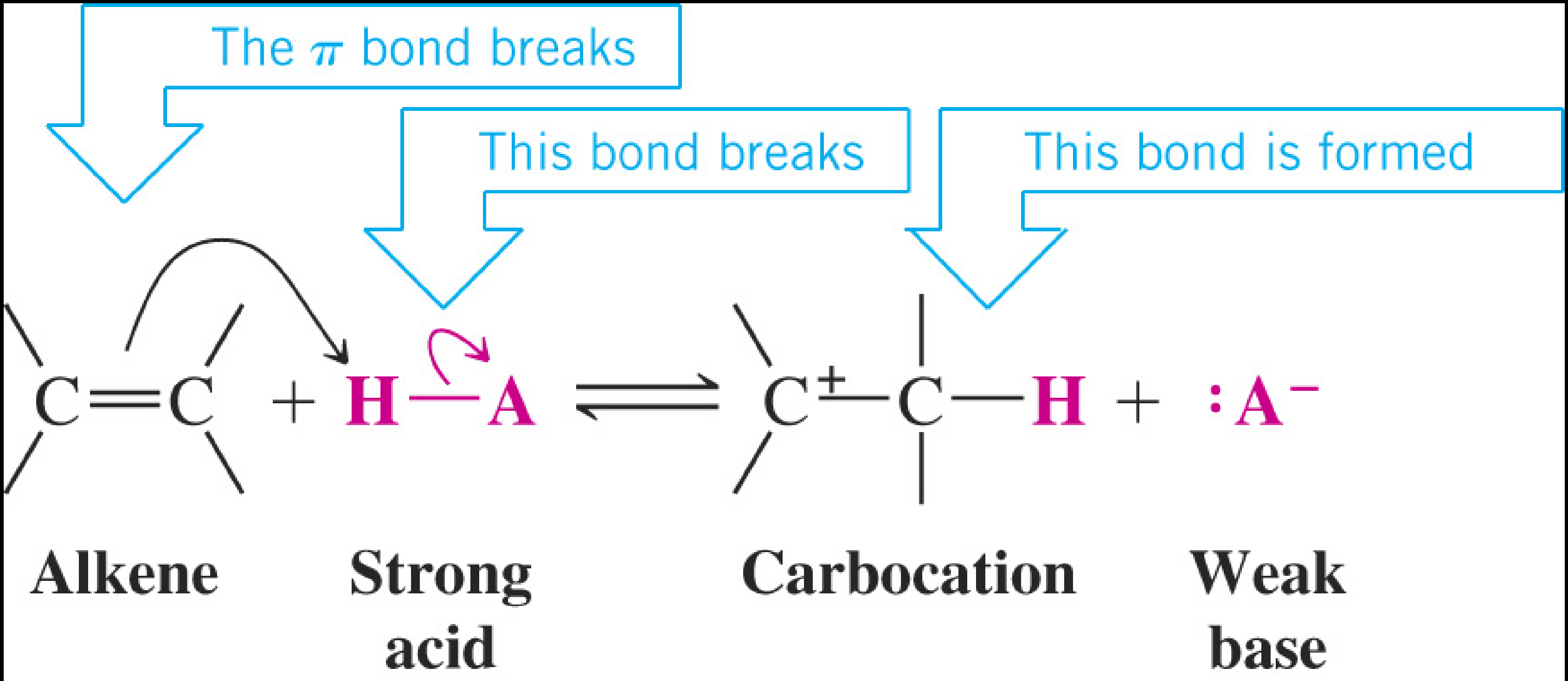
➔Any organic compound containing an atom with a lone pair (O,N) can act as a base




Ether
Strong acid
Dialkyloxonium ion
Weak base

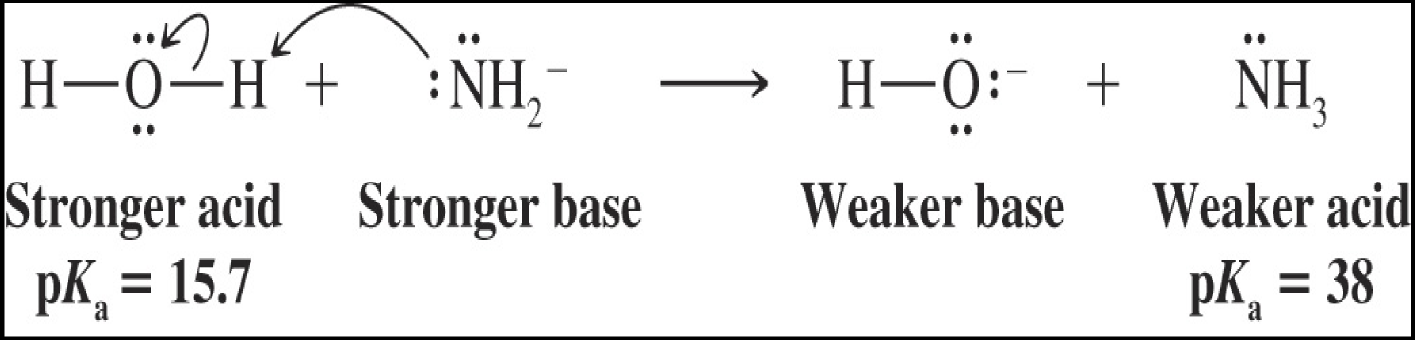

Ketone
Strong acid
Protonated ketone
Weak base

- π electrons can also act as bases
  - π electrons are loosely held and available for reaction with strong acids

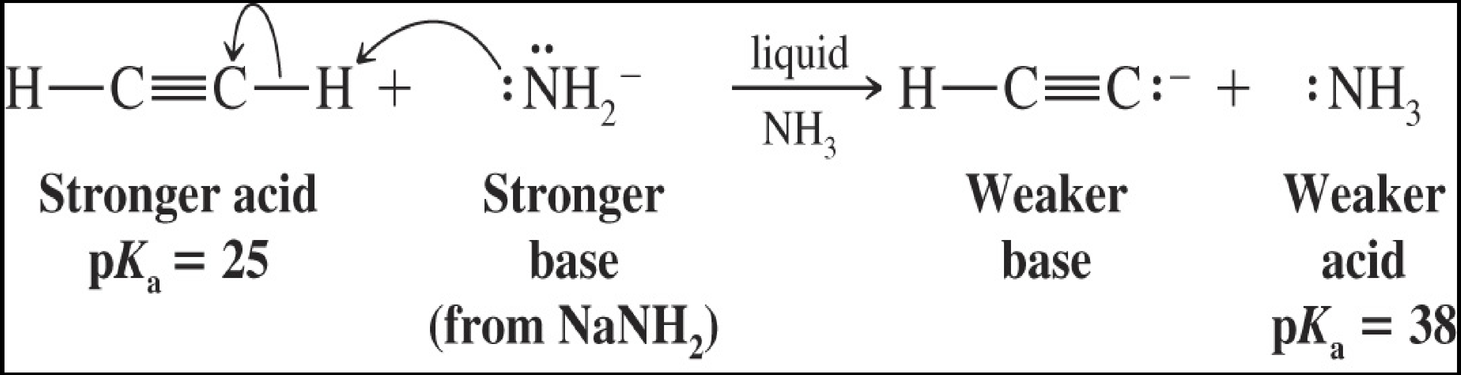


3.14 Acids and Bases in Nonaqueous Solutions

- 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



- Alkyl lithium reagents in hexane are very strong bases
  - The alkyl lithium is made from the alkyl bromide and lithium metal