Organic Acids and Bases

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Carpenter ant

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Opium poppy cultivated in Afghanistan (the world's largest source of opium, around 80% of the world's supply, UNODC).

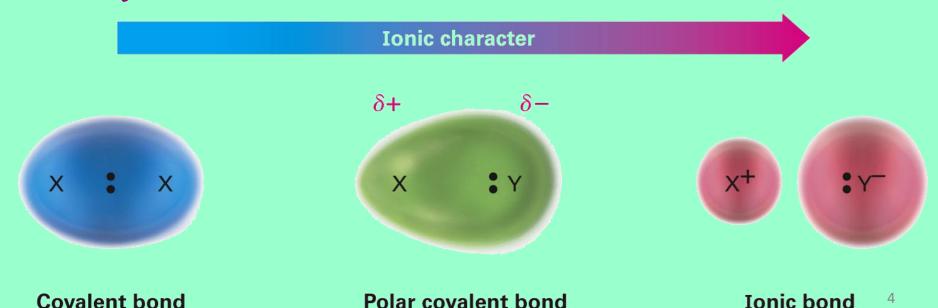
(Source of morphine – used as a pain killer, and some other regulated drugs like codeine, heroin, etc.). One of the first "vegetable alkali", or alkaloids to be isolated.

A Short Review on Previous Lecture

- In our previous lectures 1 & 2, we learned how covalent bonds between atoms are formed with their corresponding molecular geometry due to hybridization.
- We've learned that *hybrid orbitals* (*like sp, sp*², *sp*³) can be formed by mixing *s-* & *p*-orbitals. In some cases, *d*-orbitals are also involved in the like of sulphur & phosphorous atoms.
- Today, we're going to explore the consequences of these covalent bonds when bonding electrons are not shared equally between the two atoms.
- What type of covalent bond will it form?

Examine the type of bonds below:

- Covalent bonds can have ionic character also
 - <u>Bonding electrons attracted more strongly by one</u> <u>atom</u> than by the other
 - Electron distribution between atoms is <u>not</u> <u>symmetrical</u>



- Such unsymmetrical electron distribution in the bond results in neither fully ionic nor fully covalent but are somewhere between the two extremes
- > Such bonds are called *polar covalent bonds*
- This bond polarity is due to the differences in electronegativity of the bonded atoms
- As a loose guide, bonds between atoms whose electronegativities differ by <u>less than 0.5 are nonpolar covalent</u>

- ▶ Bonds between atoms whose electronegativities differ by 0.5 – 2 are polar covalent
- And bonds between atoms whose electronegativities differ by more than 2 are largely ionic
- The value of electronegativities shown in the chart on the next slides are based on an arbitrary scale (in measurements, the absolute value can't be obtained)
- \succ Fluorine is the most electronegative (EN = 4.0)

- Cesium the least (EN = 0.7)
- Red blocks are the most electronegative, yellow are medium and dark greens are the least electronegative

H 2.1													Не				
Li 1.0	Be 1.6											B 2.0	C 2.5	N 3.0	O 3.5	F 4.0	Ne
Na 0.9	Mg 1.2											AI 1.5	Si 1.8	P 2.1	S 2.5	CI 3.0	Ar
K 0.8	Ca 1.0	Sc 1.3	Ti 1.5	V 1.6	Cr 1.6	Mn 1.5	Fe 1.8	Co 1.9	Ni 1.9	Cu 1.9	Zn 1.6	Ga 1.6	Ge 1.8	As 2.0	Se 2.4	Br 2.8	Kr
Rb 0.8	Sr 1.0	Y 1.2	Zr 1.4	Nb 1.6	Mo 1.8	Tc 1.9	Ru 2.2	Rh 2.2	Pd 2.2	Ag 1.9	Cd 1.7	In 1.7	Sn 1.8	Sb 1.9	Te 2.1	I 2.5	Xe
Cs 0.7	Ba 0.9	La 1.0	Hf 1.3	Ta 1.5	W 1.7	Re 1.9	Os 2.2	Ir 2.2	Pt 2.2	Au 2.4	Hg 1.9	TI 1.8	Pb 1.9	Bi 1.9	Po 2.0	At 2.1	Rn

- We use the lower case Greek letter delta (δ) to indicate partial charges
- Note also the representation of crossed arrow to indicate the direction of bond polarity



Methanol



Consequences of Bond Polarity

- When we talk about the atom's ability to polarize a bond, we often use the term *inductive* effect which is simply the shifting of electrons in σ bond in response to the electronegativity of nearby atoms
- Since electronegativities affect bond polarity, this will also affect the substance's acidity or basicity.
- Now let's take a look at the concept of acidity and basicity as applied to organic chemistry

Acids and Bases: The Brønsted–Lowry Definition

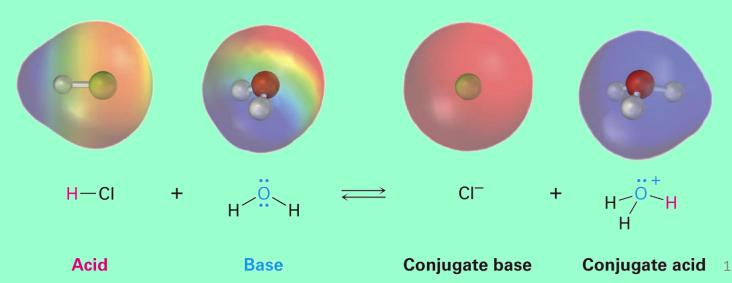
- The terms "acid" and "base" can have different meanings in different contexts
- For that reason, we specify the usage with more complete terminology
- The idea that acids are solutions containing a lot of "H+" and bases are solutions containing a lot of "OH-" is not very useful in organic chemistry
- ► Instead, Brønsted–Lowry theory defines acids and bases by their role in reactions *that transfer* protons (H⁺) between donors and acceptors

Brønsted Acids and Bases

- "Brønsted-Lowry" is usually shortened to "Brønsted"
- A Brønsted acid is a substance that <u>donates</u> a hydrogen ion (H+)
- A Brønsted base is a substance that <u>accepts</u> the H⁺
 - "proton" is a synonym for H+ (loss of an electron from H leaving the bare nucleus) a proton

The Reaction of HCI with H₂O

- When HCl gas dissolves in water, a Brønsted acid-base reaction occurs
- ➤ HCl donates a proton to a water molecule, yielding hydronium ion (H₃O+) and Cl⁻
- This acid-base reaction is reversible, so we can write them with double, forward-and-backward arrows.



H₂O acting as an Acid/Base

- Notice that water can act either as an acid or a base, depending on the circumstances
- ➤ In its reaction with HCI, water is a base that accepts a proton to give the hydronium ion, H₃O⁺
- In its reaction with ammonia (NH₃), water act as an acid that donates a proton to give ammonium ion (NH₄⁺) and hydroxide ion, HO⁻

- In general, acids differ in their ability to donate a proton, H+
- Organic acids are not that strong as mineral acids such as HCl that react completely with water
- Organic acids such as acetic acid (CH₃CO₂H), react only slightly with water
- The exact strength of a certain acid (we denote acid as HA) in water solution is described using the acidity constant (K_a) for the acidity dissociation equilibrium (K_{eq})

- Below is our equilibrium expression, we usually ignored the concentration of the solvent
- The brackets around the substance refer to the concentration of the enclosed species in moles per liter.

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

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

- Stronger acids have their equilibria toward the right and thus have larger K_a , whereas weaker acids have their equilibria toward the left and have smaller K_a
- \triangleright Because of this, the range of K_a for different acids is enormous, running from 10^{15} for the strongest acids to about 10^{-60} for the weakest one
- To aid our understanding and have a rough feeling of which acids are "strong" and which are "weak", it is practical to express this value in terms of pK_a (the negative logarithm of the K_a)

pKa = -log Ka

- > A stronger acid (larger K_a) has a smaller pK_a
- \triangleright A weaker acid (smaller K_a) has a larger p K_a

	Acid	Name	pK _a	Conjugate base	Name	
Weaker acid	CH ₃ CH ₂ OH	Ethanol	16.00	CH ₃ CH ₂ O ⁻	Ethoxide ion	Stronger
acid .	H ₂ O	Water	15.74	HO-	Hydroxide ion	A
	HCN	Hydrocyanic acid	9.31	CN-	Cyanide ion	
	H ₂ PO ₄ ⁻	Dihydrogen phosphate ion	7.21	HPO ₄ ²⁻	Hydrogen phosphate ion	
	CH ₃ CO ₂ H	Acetic acid	4.76	CH ₃ CO ₂ -	Acetate ion	
	H ₃ PO ₄	Phosphoric acid	2.16	H ₂ PO ₄ ⁻	Dihydrogen phosphate ion	
	HNO ₃	Nitric acid	-1.3	NO ₃ -	Nitrate ion	
	HCI	Hydrochloric acid	-7.0	CI-	Chloride ion	
tronger acid						Weaker base

Notice that the pKa value of water is 15.74 because water is both the acid and the solvent

$$H_2O + H_2O \longrightarrow OH^- + H_3O^+$$
(acid) (solvent)
$$K_a = \frac{[H_3O^+][A^-]}{[HA]} = \frac{[H_3O^+][OH^-]}{[H_2O]} = \frac{[1.0 \times 10^{-7}][1.0 \times 10^{-7}]}{[55.4]} = 1.8 \times 10^{-16}$$

$$pK_a = -\log \text{ of } 1.8 \times 10^{-16}$$

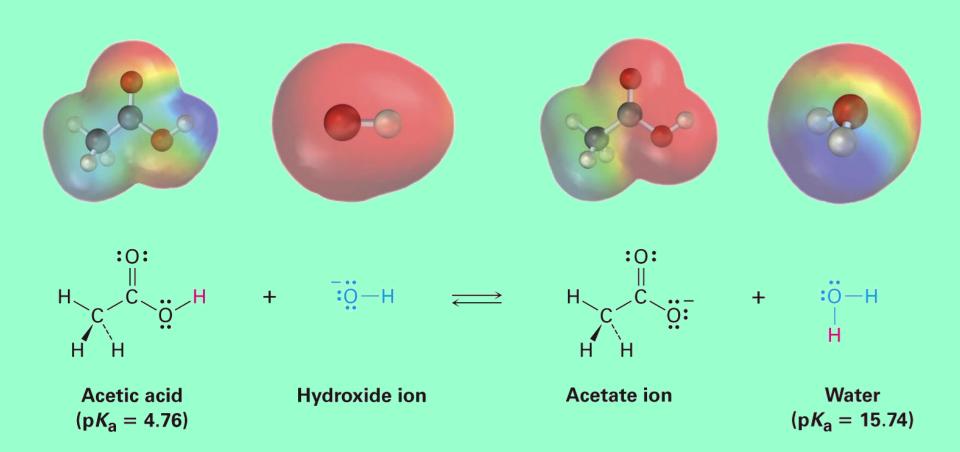
$$pK_a = 15.74$$

The numerator is the ion-product constant for water, $Kw = [H_3O^+][OH^-] = 1.00 \times 10^{-14}$ and the denominator is the molar concentration of pure water, $[H_2O] = 55.4$ M at 25 °C

Predicting Acid–Base Reactions from pK_a Values

- With the pKa values given or calculated, it is now easy for us to predict whether a given acid-base reaction will take place
- How? Always remember that proton (H+) will always transfer from the stronger acid to the stronger base
- The stronger base always holds the proton more tightly
- Now let us take a look at the reaction of acetic acid and hydroxide ion on the next slide, will the reaction be significant?

Predicting Acid–Base Reactions from pK_a Values



Predicting Acid–Base Reactions from pK_a Values

- Some very important concepts to remember in predicting acid-base reaction:
- To predict acid-base reactivity is to remember that the products of an acid-base reaction must be more stable than the reactants
- In other words, the product acid must be weaker and less reactive than the starting acid, and the product base must be weaker and less reactive than the starting base.

Compound	pK _a	Compound	pK _a	Compound	рК _а
CH₃SO₃H	-1.8	CO ₂ H		CH ₂ BrCH ₂ CO ₂ H	4.0
CH(NO ₂) ₃	0.1		3.0	O_2N NO_2	
O_2 N— O_2 OH	0.3	CO ₂ H	3.0	OH CO ₂ H	4.1
NO ₂		OH CH ₂ ICO ₂ H	3.2		4.2
CCl₃CO₂H	0.5	CHOCO ₂ H	3.2	H ₂ C=CHCO ₂ H	4.2
CF ₃ CO₂H	0.5	€11000 <u>2</u> 11	5.2	HO ₂ CCH ₂ CH ₂ CO ₂ H	4.2; 5.7
CBr ₃ CO ₂ H	0.7	$O_2N \bigcirc$ \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc	3.4	HO ₂ CCH ₂ CH ₂ CH ₂ CO ₂ H	4.3; 5.4
HO ₂ CC≡CCO ₂ H	1.2; 2.5	_/		CĮ CI	
HO₂CCO₂H	1.2; 3.7	O ₂ N		<u> </u>	
CHCI ₂ CO ₂ H	1.3	O_2N — CO_2H	3.5	СІ—()—ОН	4.5
CH ₂ (NO ₂)CO ₂ H	1.3			CI CI	
HC≡CCO ₂ H	1.9	HSCH ₂ CO ₂ H	3.5; 10.2	$H_2C = C(CH_3)CO_2H$	4.7
(Z) HO ₂ CCH=CHCO ₂ H	1.9; 6.3	$CH_2(NO_2)_2$	3.6	CH ₃ CO ₂ H	4.8
CO ₂ H		CH ₃ OCH ₂ CO ₂ H	3.6	CH ₃ CH ₂ CO ₂ H	4.8
NO ₂	2.4	CH ₃ COCH ₂ CO ₂ H	3.6	(CH ₃) ₃ CCO ₂ H	5.0
_		HOCH ₂ CO ₂ H	3.7	CH ₃ COCH ₂ NO ₂	5.1
CH ₃ COCO ₂ H	2.4	HCO₂H	3.7	,0	
NCCH ₂ CO ₂ H	2.5	CI		<i></i>	
CH ₃ C≡CCO ₂ H	2.6	√ CO₂H	3.8		5.3
CH ₂ FCO ₂ H	2.7				
CH₂CICO₂H	2.8	CI (CO II	4.0	O ₂ NCH ₂ CO ₂ CH ₃	5.8
HO ₂ CCH ₂ CO ₂ H	2.8; 5.6	CI———————CO ₂ H	4.0	-2	
CH ₂ BrCO ₂ H	2.9				

Compound	pK _a	Compound	pK _a	Compound	pK _a
<u></u>		CH ₂ SH		H ₂ C=CHCH ₂ OH	15.5
\(5.8		9.4	CH ₃ CH ₂ OH	16.0
сно				CH ₃ CH ₂ CH ₂ OH	16.1
CI		ОН		CH ₃ COCH ₂ Br	16.1
сі—Он	6.2	но	9.9; 11.5		16.7
CI			9.9	CH ₃ CHO	17
/ - \				(CH ₃) ₂ CHCHO	17
⟨	6.6	CH ₃ COCH ₂ SOCH ₃	10.0	(CH ₃) ₂ CHOH	17.1
\		OH		(CH ₃) ₃ COH	18.0
HCO ₃ H	7.1		10.3	CH₃COCH₃	19.3
NO ₂	7.2	CH ₃ NO ₂	10.3		23
(CH ₃) ₂ CHNO ₂	7.7	CH ₃ SH	10.3	CH ₃ CO ₂ CH ₂ CH ₃	25
/=\		CH ₃ COCH ₂ CO ₂ CH ₃	10.6	HC≕CH	25
сі—(7.8	CH3COCHO	11.0	CH ₃ CN	25
CI	7.0	CH ₂ (CN) ₂	11.2	CH ₃ SO ₂ CH ₃	28
G.	0.0	CCI ₃ CH ₂ OH	12.2	(C ₆ H ₅) ₃ CH	32
CH ₃ CO ₃ H	8.2	Glucose	12.3	(C ₆ H ₅) ₂ CH ₂	34
ОН	0.5	(CH ₃) ₂ C=NOH	12.4	CH ₃ SOCH ₃	35
CI	8.5	CH ₂ (CO ₂ CH ₃) ₂	12.9	NH ₃	36
	0.5	CHCI ₂ CH ₂ OH	12.9	CH ₃ CH ₂ NH ₂	36
CH ₃ CH ₂ NO ₂	8.5	CH ₂ (OH) ₂	13.3	(CH ₃ CH ₂) ₂ NH	40
F ₃ C-(\)—OH	8.7	HOCH ₂ CH(OH)CH ₂ OH	14.1	CH ₃	
		CH ₂ CICH ₂ OH	14.3		41
CH₃COCH₂COCH₃	9.0		15.0		
но	9.3; 11.1	сн₂он	15.4		43
OH		CH₃OH	15.5	H ₂ C=CH ₂	44
он	9.3; 12.6	CH3OH	13.3	CH ₄	~60

An acidity list covering more than 5000 organic compounds has been published: E.P. Serjeant and B. Dempsey (eds.), "Ionization Constants of Organic Acids in Aqueous Solution," IUPAC Chemical Data Series No. 23, Pergamon Press, Oxford, 1979.

➤ Water has pKa = 15.74, and acetylene has pKa = 25. Which is the stronger acid? Will hydroxide ions react to a significant extent with acetylene?

$$H-C \equiv C-H + OH^- \longrightarrow H-C \equiv C^-: + H_2O$$
acetylene hydroxide acetylide ion

In comparing two acids, the one with the lower pKa is the stronger acid. Thus, water is a stronger acid than acetylene and gives up H⁺ more easily.

$$H-C \equiv C-H + OH^- \longrightarrow H-C \equiv C^-: + H_2O$$
acetylene hydroxide acetylide ion

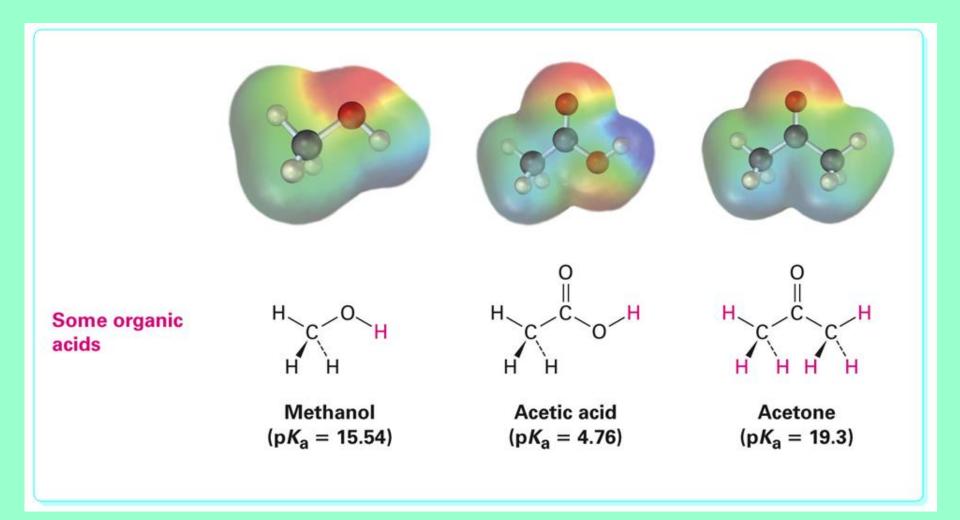
Analysis: Because water is stronger acid and gives up H⁺ more easily than acetylene does, the HO⁻ ion must have less affinity for H⁺ than the HC≡C: ion has.

In other words, the anion of acetylene is a stronger base than the hydroxide ion, and the reaction will not proceed significantly.

What are Organic Acids and Bases

- ➤ The reaction patterns of organic compounds often are acid-base combinations
- The transfer of a proton from strong Brønsted acid to a Brønsted base, for example, is a very fast process and will always occur along with other reactions
- Organic acids are characterized by the presence of a positively polarized hydrogen atom (blue in electrostatic potential maps) and are of two main kinds:

What are Organic Acids and Bases



Organic Acids

Those that lose a proton (H+) from O-H, such as methanol and acetic acid

Anion is stabilized by having negative charge on a highly electronegative atom.

Anion is stabilized both by having negative charge on a highly electronegative atom and by resonance.

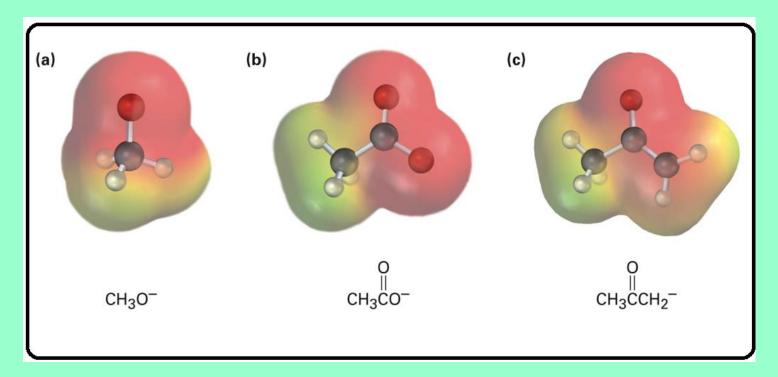
Organic Acids

➤ Those that lose a proton (H+) from C-H, usually from a carbon atom next to a C=O double bond (O=C-C-H)

Anion is stabilized both by resonance and by having a negative charge on a highly electronegative atom.

Organic Acids

- Below are the electrostatic potential maps of the conjugate bases from methanol, acetic acid, and acetone
- All three shows a substantial amount of negative charge (red) on oxygen

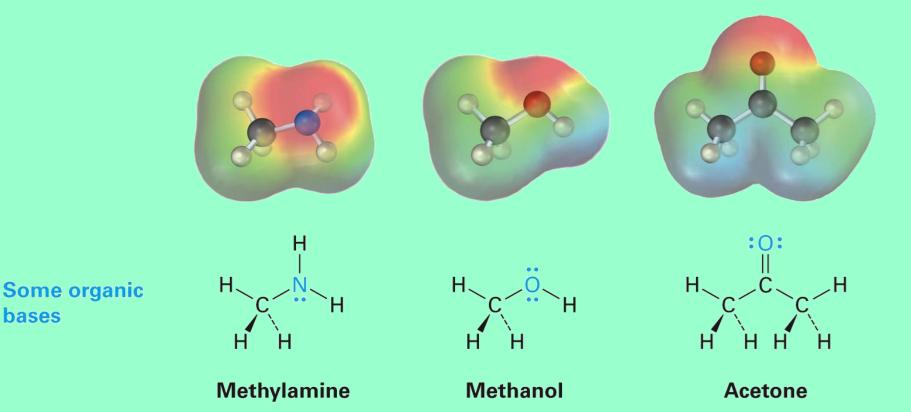


Organic Bases

- Organic bases are characterized by the presence of an atom (reddish in electrostatic potential maps) with a lone pair of electrons that can bond to a proton (H+)
- Nitrogen-containing compounds derived from ammonia are the most common organic bases
- Oxygen-containing compounds can react as bases depending on the circumstances just like water
- Methanol, and acetone act as an acid when they <u>donate</u> a proton but as bases when their oxygen atom <u>accepts</u> a proton (H+)

Organic Bases

bases



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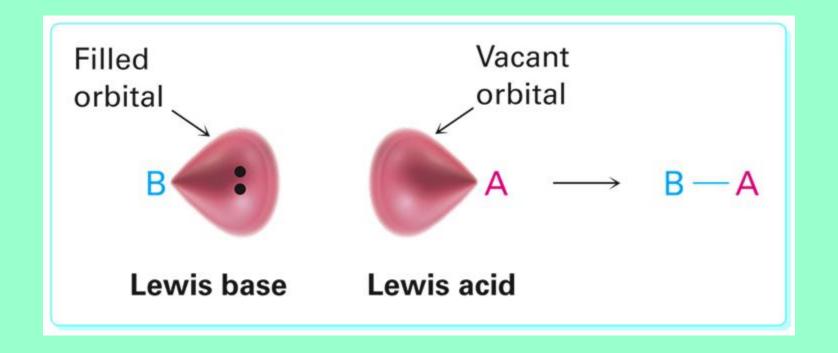
Organic Bases

- Alanine, an amino acid and one of the building blocks of protein exist primarily in a doubly charged form called zwitterion rather than in the uncharged form
- The zwitterion form arises because alanine have both acidic and basic sites within the same molecule and therefore undergo an internal acid-base reaction

Acids and Bases: The Lewis Definition

- Lewis definition of acids and bases is much more broader and encompassing since it is not limited to substances that donate or accept protons (H+)
- A Lewis acid is a substance that accepts an electron pair, while a Lewis base is a substance that donates an electron pair
- This donated electron pair is shared between the acid and the base in a covalent bond
- Now let us explore the mechanism of the Lewis acid –base reaction

Acids and Bases: The Lewis Definition



Since Lewis acid is able to accept an electron pair, means that it must have either a vacant, low-energy orbital or a polar bond to hydrogen so that it can donate a proton (H+, having an empty 1s orbital)

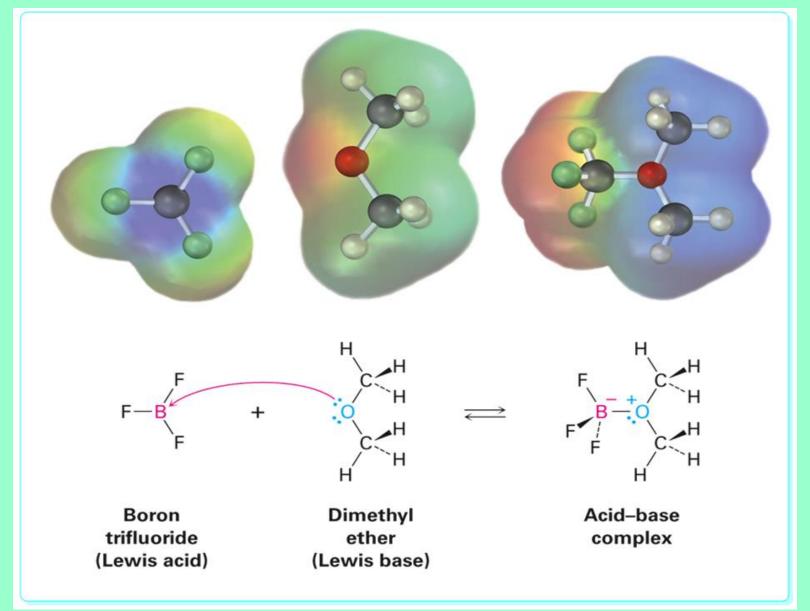
Acids and Bases: The Lewis Definition

➤ The Lewis acid definition may now include metal cations, such as Mg²+ since they accept a pair of electrons when they form a bond to a base

Acids and Bases: The Lewis Definition

- ▶ Group 3A elements, such as BF₃ and AICI₃, are Lewis acids because they have unfilled valence orbitals and can accept electron pairs from Lewis bases
- Transition-metal compounds, such as TiCl₄, FeCl₃, ZnCl₂, and SnCl₄, are Lewis acids
- Organic compounds that undergo addition reactions with Lewis bases (discussed later) are called electrophiles and therefore Lewis Acids

Acids and Bases: The Lewis Definition



Acids and Bases: The Lewis Definition

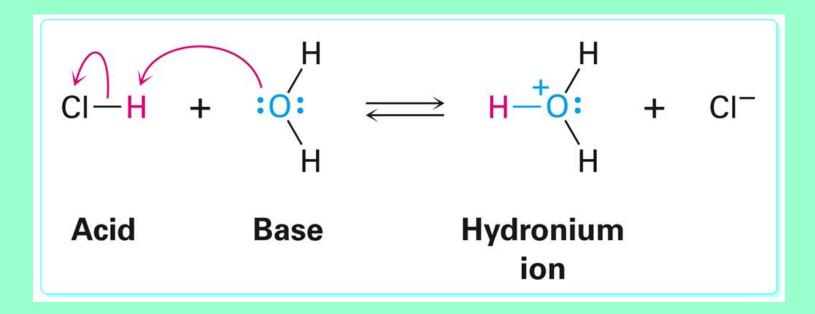
Some neutral proton donors: H_2O HNO_3 HCI HBr H_2SO_4 CH₃CH₂OH An alcohol A carboxylic acid A phenol Some cations: Mg²⁺ Some metal compounds: TiCl₄ FeCl₃ AICI₃ ZnCl₂

Some

Lewis

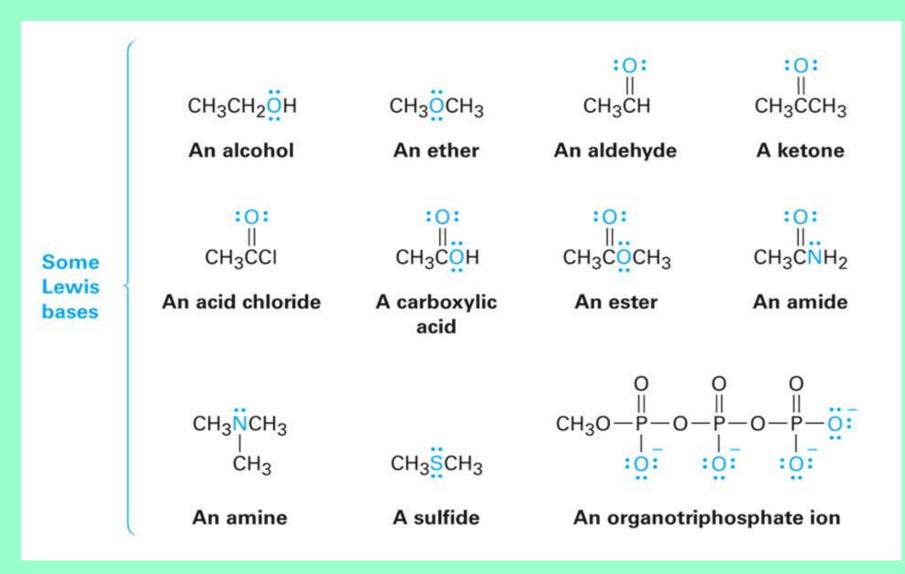
acids

- Lewis definition of a base (a compound with a pair of nonbonding electrons that it can use to bond to a Lewis acid – similar to the Brønsted-Lowry definition
- Water, can be a good example in this case:



- Lewis bases can accept protons as well as Lewis acids, therefore the definition encompasses that for Brønsted bases
- Most oxygen- and nitrogen-containing organic compounds are Lewis bases because they have lone pairs of electrons
- Some compounds can act as both acids and bases, depending on the reaction and circumstances, just in the case of alcohol and carboxylic acid which can act also as bases when their oxygen atom accepts a proton (H+)

In the case of acetic acid, protonation can happen either on the *doubly bonded* oxygen atom or on the *singly bonded* oxygen atom, and the more stable of the two protonation products is formed

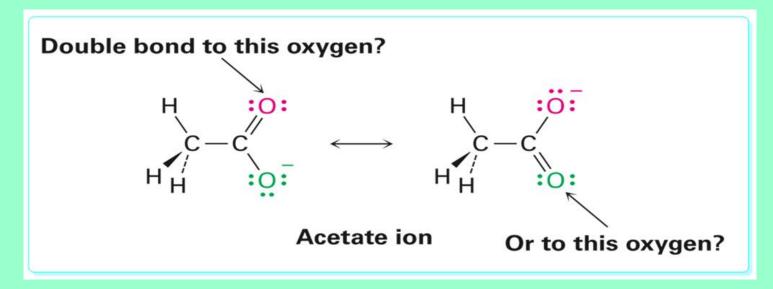


Resonance

- There are some molecules that have structures that cannot be shown with a single representation
- In these cases we draw structures that contribute to the final structure but which differ in the position of the π bond(s) or lone pair(s)
- Such a structure is delocalized and is represented by <u>resonance forms</u>

Resonance

The resonance forms are connected by a double-headed arrow

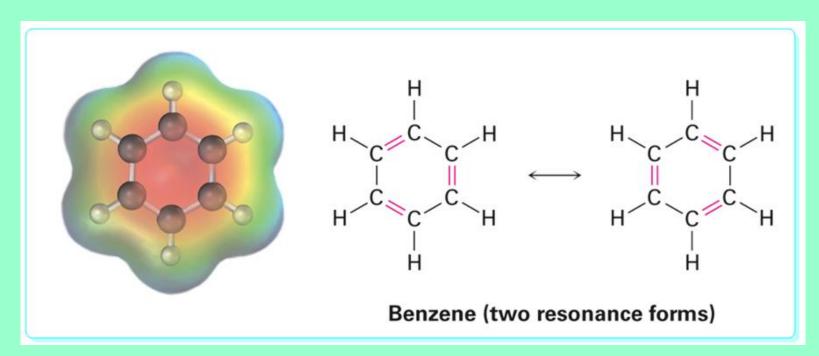


- A structure with resonance forms does not alternate between the forms
- Instead, it is a hybrid of the two resonance forms, so the structure is called a resonance hybrid

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Resonance Hybrids

- ➤ For example, benzene (C₆H₆) has two resonance forms with alternating double and single bonds
- In the resonance hybrid, the actual structure, all its C-C bonds equivalent, midway between double and single

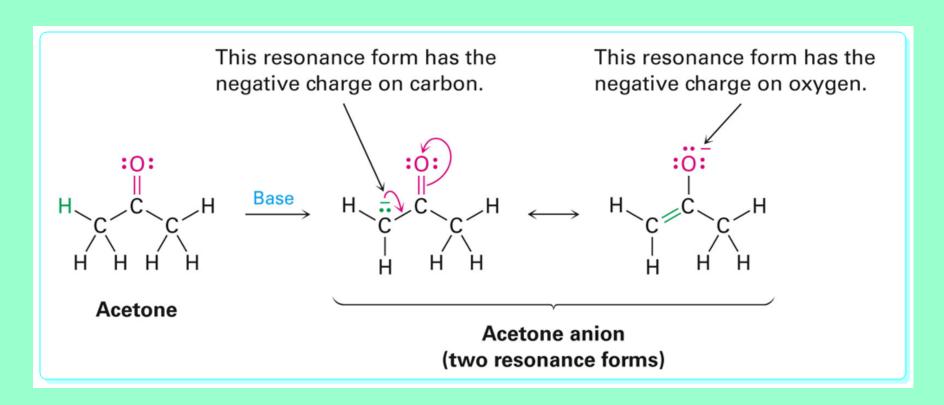


Rules for Resonance Forms

- 1. Individual resonance forms are <u>imaginary</u> the real structure is a hybrid (only by knowing the contributors you can visualize the actual structure)
- 2. Resonance forms differ only in the placement of their π or nonbonding electrons

Rules for Resonance Forms

3. Different resonance forms of a substance don't have to be equivalent



Rules for Resonance Forms

4) Resonance forms must be valid Lewis structures and obey normal rules of valency: the octet rule applies

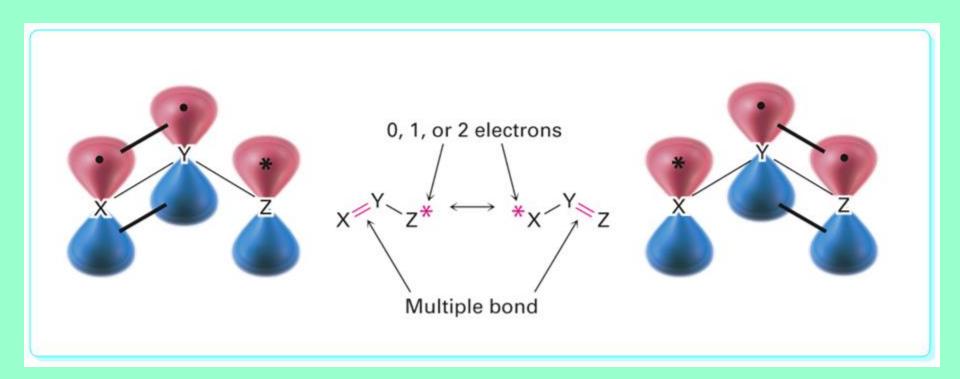
5) The resonance hybrid is more stable than any individual resonance form

Drawing Resonance Forms

- Generally, any three-atom grouping with multiple bonds or with a p orbital on each atom has two resonance forms
- Sometimes resonance forms involve different atom types as well as locations
- We can imagine that electrons move in pairs to convert from one resonance form to another

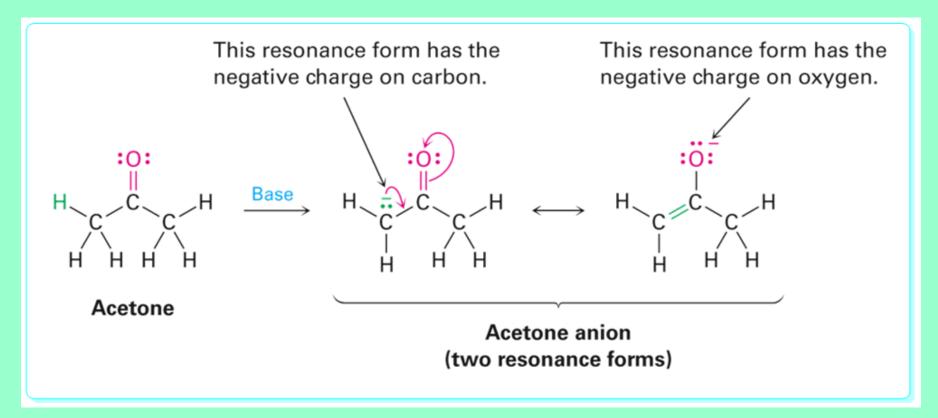
Drawing Resonance Forms

In the illustration below, the asterisk (*) might mean that the p orbital on atom Z is vacant, or that it contains a single electron, or that it contains a lone pair of electrons.



Drawing Resonance Forms

Here in the case of acetone, the "enolate" derived is a good illustration, with delocalization between carbon and oxygen



In the case of 2,4-Pentanedione

- The anion derived from 2,4-pentanedione
 - Lone pair of electrons and a formal negative charge on the central carbon atom, next to a C=O bond on the left and on the right
 - -Three resonance structures result