

Physical pharmacy I 2nd stage Ionic equilibria

2025-2026



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Outlines

- Objectives
- Theories
- Acid-base equilibria
- Calculation of pH, acidity constants
- The effect of ionic strength.



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Objectives

- Define of acids and bases
- Concept of Sörensen's pH scale.
- Understanding different terminology such as Ampholytes, Aprotic , etc
- Ionization of Polyprotic electrolytes.
- pKa and pH calculation of aqueous solutions with different composition



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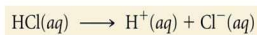
Theories

- **Arrhenius Theory**
- Arrhenius defined
 - an **acid** as a substance that liberates hydrogen ions
 - and a **base** as a substance that supplies hydroxyl ions on dissociation in aqueous media.

Arrhenius Theory

Arrhenius Acid

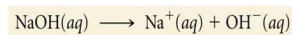
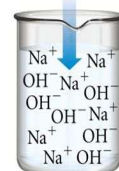
HCl



HCl ionizes in water,
producing H⁺ and Cl⁻ ions

Arrhenius Base

NaOH



NaOH dissociates in water,
producing Na⁺ and OH⁻ ions

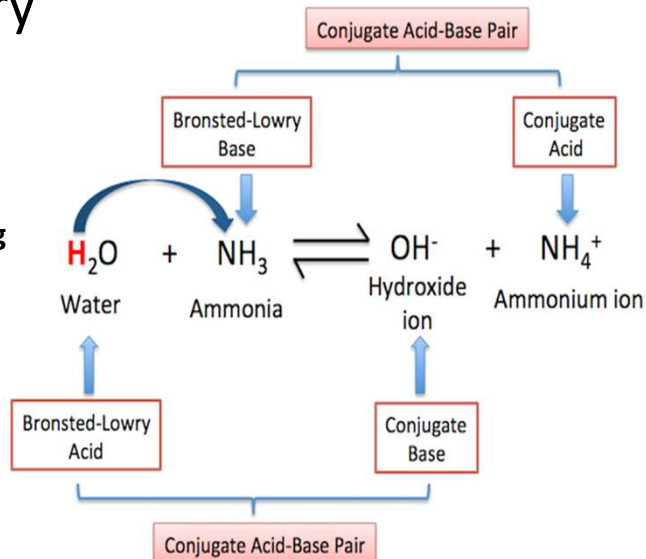


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Brönsted–Lowry theory

- According to the Brönsted–Lowry theory,
 - an acid is a substance, charged or uncharged, that is capable of **donating** a proton,
 - and a base is a substance, charged or uncharged, that is capable of **accepting** a proton from an acid.



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- The strength of an acid or a base varies with the **solvent**.
- HCl is a **strong** acid but it is a **weak** acid in glacial acetic acid.
- Acetic acid, which is a **weak** acid, is a **strong** acid in liquid ammonia.
- Consequently, the **strength** of an acid depends:
 - not only on its ability to give up a proton
 - but also on the ability of the **solvent** to accept the proton from the acid.
This is called ***the basic strength of the solvent***.

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In the Brönsted–Lowry classification, **acids** and **bases** may be

- anions such as HSO_4^- and CH_3COO^- ,
- cations such as NH_4^+ and H_3O^+ ,
- or neutral molecules such as HCl and NH_3 .
- Water can act as either an acid or a base and thus is **amphiprotic**.



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Solvent classification

1. **A protophilic or basic solvent**

- ✓ is one that is capable of **accepting** protons from the solute. Eg. acetone, ether, and liquid ammonia.

2. **A protogenic solvent**

- ✓ is a **proton-donating** compound and is represented by acids such as formic acid, acetic acid, sulfuric acid, liquid HCl , and liquid HF .

3. **Amphiprotic solvents**

- ✓ act as both proton acceptors and proton donors, and this class includes water and alcohols.

4. **Aprotic solvents,**

- ✓ such as the hydrocarbons, neither accept nor donate protons, and, being neutral in this sense, they are useful for studying the reactions of acids and bases free of solvent effects.

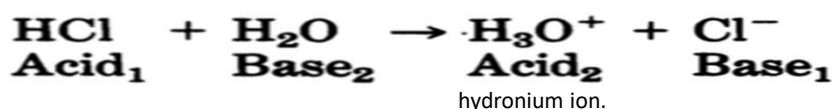


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Proteolytic reactions or protolysis.

- Acid-base reactions occur when an **acid** reacts with a **base** to form a new **acid** and a new **base**, called conjugates. So it is the reaction that involve a transfer of a **proton**, and are known as **protolytic** reactions or **protolysis**. Proton transfer reactions are also known as **protonation–deprotonation reactions**.



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Several examples illustrate these types of reactions, as shown in Table 7-1.

TABLE 7–1. Examples of Acid–Base Reactions

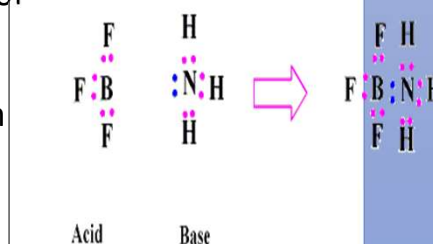
	Acid ₁		Base ₂		Acid ₂		Base ₁
Neutralization	NH ₄ ⁺	+	OH [−]	=	H ₂ O	+	NH ₃
Neutralization	H ₃ O ⁺	+	OH [−]	=	H ₂ O	+	H ₂ O
Neutralization	HCl	+	NH ₃	=	NH ₄ ⁺	+	Cl [−]
Hydrolysis	H ₂ O	+	CH ₃ COO [−]	=	CH ₃ COOH	+	OH [−]
Hydrolysis	NH ₄ ⁺	+	H ₂ O	=	H ₃ O ⁺	+	NH ₃
Displacement	HCl	+	CH ₃ COO [−]	=	CH ₃ COOH	+	Cl [−]

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Lewis Electronic Theory.

- According to the Lewis theory, an acid is a molecule or an ion that **accepts an electron pair** to form a covalent bond.
- A base is a substance that **provides** the pair of **unshared electrons** by which the base coordinates with an acid.
- Lewis acid eg boron trifluoride and aluminum chloride,
- Lewis base eg amines, ethers, and carboxylic acid anhydrides, are classified as bases according to the Lewis definition.

BF_3 can act as a Lewis acid:



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- The Lewis acid theory is widely used for describing the mechanism of many organic and inorganic reactions.
- It is referred to simply as a form of electron sharing rather than as acid–base reactions.
- It will be important in **solubility** and **complexation**.
- *The Brønsted–Lowry nomenclature is **particularly useful** for describing ionic equilibria and is used extensively in this chapter*

Sörensen's pH

- H ion concentration of a solution varies from approximately 1 in a 1 M solution of a strong acid to about 1×10^{-14} in a 1 M solution of a strong base
- The pH of a solution can be considered in terms of a numeric scale having values from 0 to 14, which expresses in a quantitative way the degree of acidity (7 to 0) and alkalinity (7-14).
- The value 7 at which the hydrogen and hydroxyl ion concentrations are about equal at room temperature is referred to as the neutral point, or neutrality. The neutral pH at 0°C is 7.47, and at 100°C it is 6.15.



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Ionic Equilibria

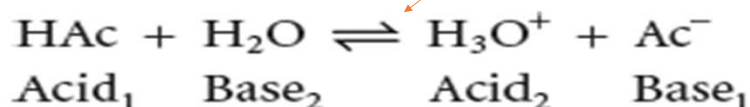
- Equilibrium can be defined as a balance between two opposing forces or actions. TRUE or FALSE?
- This statement **does not imply** cessation of the opposing reactions. Rather, it suggests a dynamic equality between the velocities of the two reactions. **T or F?**
- Equilibrium is the condition where the standard free energy difference between the two sides of reaction equation (7-4) is zero ($\Delta G^\circ = 0$). **T or F ?**



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Ionic Equilibria

The arrows pointing in the forward and reverse directions indicate that reactions are proceeding to the right and left simultaneously



(7-4)

$$\text{Rate of forward} = k_1 \times [\text{HAc}]^1 \times [\text{H}_2\text{O}]^1$$

$$\text{Rate of backward} = k_2 \times [\text{H}_3\text{O}^+]^1 \times [\text{Ac}^-]^1$$

At equilibrium

$$k_1 \times [\text{HAc}] \times [\text{H}_2\text{O}] = k_2 \times [\text{H}_3\text{O}^+] \times [\text{Ac}^-]$$



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$$k = \frac{k_1}{k_2} = \frac{[\text{H}_3\text{O}^+][\text{Ac}^-]}{[\text{HAc}][\text{H}_2\text{O}]}$$

- Mwt of H₂O=18.02g/L
- In dilute solutions of acetic acid, water is in sufficient excess to be regarded as constant .
- 1 L of H₂O at 25°C weighs 997.07 g,
- Thus, the conc. Of H₂O= 997.07/18.02 = 55.3 M).
- **[H₂O]=55.3 M**

$$K_a = 55.3k = \frac{[\text{H}_3\text{O}^+][\text{Ac}^-]}{[\text{HAc}]}$$

K_a : ionization constant or the dissociation constant of acetic acid

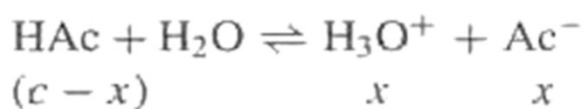
At large conc. Of water (diluent)



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$$K_a = 55.3k = \frac{[H_3O^+][Ac^-]}{[HAc]}$$



$$K_a = \frac{x^2}{c - x}$$

where c is large in comparison with x. The term c - x can be replaced by c without appreciable error, giving the equation



$$K_a \cong \frac{x^2}{c}$$

$$\begin{aligned} x^2 &= K_a c \\ x &= [H_3O^+] = \sqrt{K_a c} \end{aligned}$$



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EXAMPLE 7-1

- In a liter of a 0.1 M solution, acetic acid was found by conductivity analysis to dissociate into 1.32×10^{-3} moles each of hydronium and acetate ions at 25°C. What is the acidity (or dissociation) constant K_a for acetic acid?
- H.W



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Relationship Between K_a and K_b

A simple relationship exists between the dissociation constant of a weak acid HB and that of its conjugate base B^- , or between BH^+ and B, when the solvent is **amphiprotic**. This can be obtained by multiplying the following equations:

$$K_a = \frac{[H_3O^+][B^-]}{[HB]} \quad \times \quad K_b = \frac{[OH^-][HB]}{[B^-]}$$

$$K_a K_b = \frac{[H_3O^+][B^-]}{[HB]} \cdot \frac{[OH^-][HB]}{[B^-]} = [H_3O^+][OH^-] = K_w$$

$$K_a = K_w / K_b$$

$$K_b = K_w / K_a$$

K_w known as the *autoprotolysis constant*, or the *ion product* of water

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EXAMPLE 7-4 Calculate K_a

- Ammonia has $K_b = 1.74 \times 10^{-5}$ at 25°C . Calculate K_a for its conjugate acid, NH_4^+ . We have

$$\begin{aligned} K_a &= \frac{K_w}{K_b} = \frac{1.00 \times 10^{-14}}{1.74 \times 10^{-5}} \\ &= 5.75 \times 10^{-10} \end{aligned}$$

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Ionization of Polyprotic Electrolytes.

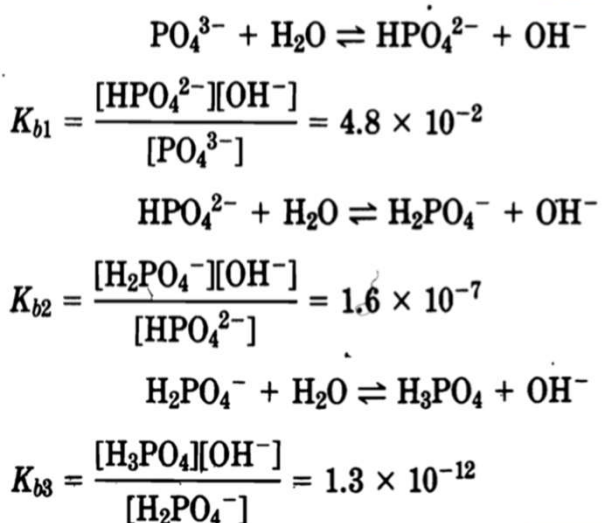
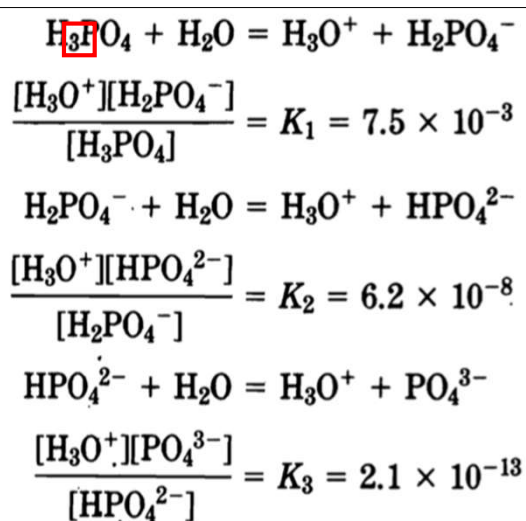
- Acids that donate a **single** proton and bases that accept a single proton are called **monoprotic** electrolytes.
- A polyprotic (polybasic) acid is one that is capable of donating two or more protons, and a polyprotic base is capable of accepting two or more protons.
- A diprotic (dibasic) acid, such as carbonic acid, ionizes in **two** stages, and a triprotic (tribasic) acid, such as phosphoric acid, ionizes in **three** stages.
- In any polyprotic electrolyte, the primary protolysis is greatest, and succeeding stages become less complete at any given acid concentration.



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Ionization of Polyprotic Electrolytes.

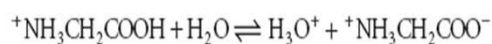


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Ampholytes

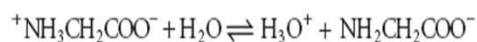
Zwitterion

- A species that can function either as an acid or as a base is called an ampholyte and is said to be amphoteric in nature. Amino acids and proteins are ampholytes of particular interest in pharmacy.
- glycine hydrochloride is dissolved in water,:

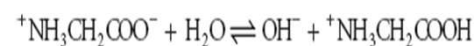


Amphoteric
compound

react as acid
with H₂O



react as base
with H₂O



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- The amphoteric species $^+\text{NH}_3\text{CH}_2\text{COO}^-$ is also called a zwitterion because?
- Ans.: it carries both negative and positive charge; the whole molecule is electrically neutral



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Isoelectric point (IEP)

- It is pH at which zwitterion concentration at maximum
- It has been used for determination of protein and amino acids.
- The molecules have ----- solubility at IEP.
- The net charge of a molecule at its IEP is -----.
- Charge of a molecule at pH above its IEP is ----- and below is -----.

e.g. pH of milk 6.6 (casein IEP=4.6)



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Solutions containing Strong acids

- **Strong acid** concentration of H is equal to initial concentration of acid. Thus, they are considered to ionize fully in aqueous solutions.



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Solutions containing Only a Weak Acid

- Conc. of base (Cb) is zero.
- $[H_3O^+]$ is generally much greater than $[OH^-]$

$$[H_3O^+] = \frac{-K_a + \sqrt{K_a^2 + 4K_a C_a}}{2}$$

In many instances, C_a is much greater than $[H_3O^+]$, and the eq simplifies further to :

$$[H_3O^+] = \sqrt{K_a C_a}$$

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EXAMPLE 7-12 calculate the pH

- Calculate the pH of a 0.01 M solution of salicylic acid, which has $K_a = 1.06 \times 10^{-3}$ at 25°C.

(a) Using equation (7-102),

$$[H_3O^+] = \sqrt{K_a C_a}$$

$$[H_3O^+] = \sqrt{(1.06 \times 10^{-3}) \times (1.0 \times 10^{-2})}$$

$$= 3.26 \times 10^{-3} \text{ M} = 0.00326 \text{ M}$$

Compare to the conc of acid, The approximation that $C_a \gg [H_3O^+]$ is not valid.

(b) Using equation (7-101), we find

$$[H_3O^+] = \frac{-K_a + \sqrt{K_a^2 + 4K_a C_a}}{2}$$

$$[H_3O^+] = \frac{-(1.06 \times 10^{-3}) + \sqrt{(1.06 \times 10^{-3})^2 + 4(1.06 \times 10^{-3})(1.0 \times 10^{-2})}}{2}$$

$$= 2.77 \times 10^{-3} \text{ M}$$

$$\text{pH} = -\log(2.77 \times 10^{-3}) = 2.56$$

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EXAMPLE 7-13

Calculate pH

- Calculate the pH of a 1 g/100 mL solution of ephedrine sulfate. The molecular weight of the salt is 428.5 g/mol, and K_b for ephedrine base is 2.3×10^{-5} .
- (a) The ephedrine sulfate, $(BH^+)_2SO_4$, dissociates completely into two BH^+ cations and one SO_4^{2-} anion. Thus, the concentration of the weak acid (ephedrine cation) is twice the concentration, C_s , of the salt added.

$$[H_3O^+] = \sqrt{K_a C_a}$$

$$K_a = K_w / K_b$$

$$C_a = 2C_s = \frac{2 \times 10 \text{ g/L}}{428.5 \text{ g/mole}} = 4.67 \times 10^{-2} \text{ M}$$

$$(b) \quad K_a = \frac{1.00 \times 10^{-14}}{2.3 \times 10^{-5}} = 4.35 \times 10^{-10}$$

$$(c) \quad [H_3O^+] = \sqrt{(4.35 \times 10^{-10}) \times (4.67 \times 10^{-2})} = 4.51 \times 10^{-6} \text{ M}$$

All assumptions are valid. We have

$$pH = -\log(4.51 \times 10^{-6}) = 5.35$$

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Solutions Containing Only a Weak Base

- Conc. Of acid (C_a) is zero,
- and $[OH^-]$ is generally much greater than $[H_3O^+]$.

$$[OH^-] = \frac{-K_b + \sqrt{K_b^2 + 4K_b C_b}}{2}$$

and if C_b is much greater than $[OH^-]$, which is generally true for solutions of weak bases,

$$[OH^-] = \sqrt{K_b C_b}$$

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EXAMPLE 7-14

Calculate pH

What is the pH of a 0.0033 M solution of cocaine base, which has $K_b = 2.6 \times 10^{-6}$? We have $[OH] = \sqrt{K_b C_b}$

$$[OH^-] = \sqrt{(2.6 \times 10^{-6}) \times (3.3 \times 10^{-3})}$$

$$= 9.26 \times 10^{-5} \text{ M}$$

All assumptions are valid. Thus,

$$pOH = -\log(9.26 \times 10^{-5}) = 4.03$$

$$pH = 14.00 - 4.03 = 9.97$$



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Solutions Containing a Single Conjugate Acid–Base Pair

- In a solution composed of a weak acid and a salt (conjugate base) of that acid (e.g., acetic acid and sodium acetate)
- or a weak base and a salt (conjugate acid) of that base (e.g., ephedrine and ephedrine hydrochloride),
- C_a and C_b are generally **much greater** than either $[H_3O^+]$ or $[OH^-]$.

$$[H_3O^+] = \frac{K_a C_a}{C_b}$$



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EXAMPLE 7-16

Calculate pH

What is the pH of a solution containing acetic acid 0.3 M and sodium acetate 0.05 M? We write

$$[\text{H}_3\text{O}^+] = \frac{K_a C_a}{C_b} \quad [\text{H}_3\text{O}^+] = \frac{(1.75 \times 10^{-5}) \times (0.3)}{5.0 \times 10^{-2}} \\ = 1.05 \times 10^{-4} \text{ M}$$

All assumptions are valid. Thus,

$$\text{pH} = -\log(1.05 \times 10^{-4}) = 3.98$$

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EXAMPLE 7-17

Calculate pH

What is the pH of a solution containing ephedrine 0.1 M and ephedrine hydrochloride 0.01 M? Ephedrine has $K_b = 2.3 \times 10^{-5}$; thus, K_a for its conjugate acid is 4.35×10^{-10} .

$$[\text{H}_3\text{O}^+] = \frac{K_a C_a}{C_b} \quad [\text{H}_3\text{O}^+] = \frac{(4.35 \times 10^{-10}) \times (1.0 \times 10^{-2})}{1.0 \times 10^{-1}} \\ = 4.35 \times 10^{-11}$$

All assumptions are valid. Thus,

$$\text{pH} = -\log(4.35 \times 10^{-11}) = 10.36$$

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Solutions Containing Two Weak Acids

- In systems containing two weak acids, C_{b1} and C_{b2} are zero,
- For all systems of practical importance, C_{a1} and C_{a2} are much greater than K_1 and K_2 , so the equation simplifies to

$$[H_3O^+]^2 + [H_3O^+](K_1 + K_2) - (K_1C_{a1} + K_2C_{a2}) = 0 \quad (7-126)$$

If $C_{a1} \gg [H_3O^+]$ and $C_{a2} \gg [H_3O^+]$, the equation simplifies to

$$[H_3O^+] = \sqrt{K_1C_{a1} + K_2C_{a2}} \quad (7-127)$$

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EXAMPLE 7-21

Calculate pH

What is the pH of a solution containing acetic acid, 0.01 mole/L, and formic acid, 0.001 mole/L? We have

$$[H_3O^+] = \sqrt{K_1C_{a1} + K_2C_{a2}}$$

$$\begin{aligned} [H_3O^+] &= \sqrt{(1.75 \times 10^{-5})(1.0 \times 10^{-2}) + (1.77 \times 10^{-4})(1.0 \times 10^{-3})} \\ &= 5.93 \times 10^{-4} \text{ M} \\ \text{pH} &= -\log(5.93 \times 10^{-4}) = 3.23 \end{aligned}$$

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Solutions Containing a Salt of a Weak Acid and a Weak Base

- The salt of a weak acid and a weak base, such as ammonium acetate, dissociates almost completely in aqueous solution to yield NH_4^+ and Ac^- , the NH_4^+ is an acid and can be designated as HB_1 , and the base Ac^- can be designated as B_2^- in equations .
- *In most instances, however, $C_s \gg [\text{H}_3\text{O}^+]$,*

$$[\text{H}_3\text{O}^+] = \sqrt{K_1 K_2}$$

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EXAMPLE 7-22

Calculate pH

Calculate the pH of a 0.01 M solution of ammonium acetate. The acidity constant for acetic acid is $K_2 = K_a = 1.75 \times 10^{-5}$, and the basicity constant for ammonia is $K_b = 1.74 \times 10^{-5}$. (a) K_1 can be found by dividing K_b for ammonia into K_w :

$$[\text{H}_3\text{O}^+] = \sqrt{K_1 K_2}$$

$$K_1 = \frac{1.00 \times 10^{-14}}{1.74 \times 10^{-5}} = 5.75 \times 10^{-10}$$

$$[\text{H}_3\text{O}^+] = \sqrt{(5.75 \times 10^{-10}) \times (1.75 \times 10^{-5})}$$

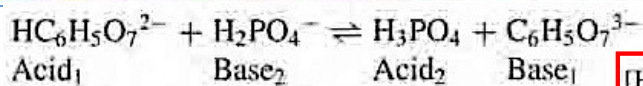
$$= 1.00 \times 10^{-7} \text{ M}$$

Note that all of the assumptions are valid. We have

$$\text{pH} = -\log(1.00 \times 10^{-7}) = 7.00$$

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Solutions Containing a Weak Acid and a Weak Base



$$[\text{H}_3\text{O}^+] = \sqrt{K_1 K_2}$$

EXAMPLE 7-24

Calculate pH

What is the pH of a solution containing NaH_2PO_4 and disodium citrate (disodium hydrogen citrate) $\text{Na}_2\text{HC}_6\text{H}_5\text{O}_7$, both in a concentration of 0.01 M? The third acidity constant for $\text{HC}_6\text{H}_5\text{O}_7^{2-}$ is 4.0×10^{-7} , whereas the first acidity constant for phosphoric acid is 7.5×10^{-3} . We have

$$\begin{aligned} [\text{H}_3\text{O}^+] &= \sqrt{(4.0 \times 10^{-7}) \times (7.5 \times 10^{-3})} \\ &= 5.48 \times 10^{-5} \text{ M} \end{aligned}$$

All assumptions are valid. We find

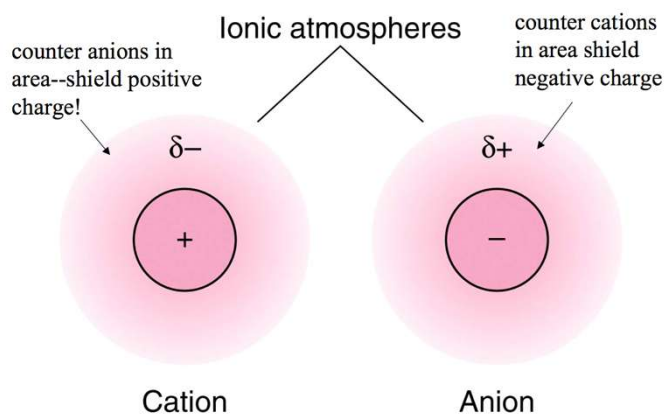
$$\text{pH} = -\log(5.48 \times 10^{-5}) = 4.26$$



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Ionic strength



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Ionic strength

- ionic strength---I or μ ---a measure of the total ion concentration in solution---but ions with more charge are counted more due to stronger electrostatic interactions with other ions (I.e., can influence the increase "ionic atmosphere" greater than singly charged ions)

$$\mu = \frac{1}{2} \sum_i c_i z_i^2$$

where c_i is conc. of i^{th} species
and z_i is the charge on i^{th} species

What is ionic strength of 0.01 M NaCl solution?

$$\mu = 1/2 ([\text{Na}^+]z_{\text{Na}}^2 + [\text{Cl}^-]z_{\text{Cl}}^2) = 1/2 (0.01 (1)^2 + 0.01(-1)^2) = 0.01 \text{ M}$$

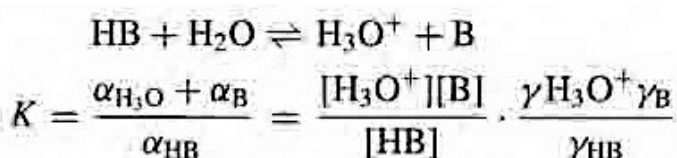
What is ionic strength of 0.01 M Na_2SO_4 solution?

$$\mu = 1/2([\text{Na}^+]z_{\text{Na}}^2 + [\text{SO}_4^{2-}]z_{\text{SO}_4}^2) = 1/2(0.02 (1)^2 + 0.01 (-2)^2) = 0.03 \text{ M}$$

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Effect of Ionic Strength on Acidity Constants



For monotropic molecule

$$\text{p}K' = \text{p}K + \frac{0.51(2Z - 1)\sqrt{\mu}}{1 + \sqrt{\mu}}$$

For zwitterion molecule

$$\text{p}K'_1 = \text{p}K_1 + \frac{0.51\sqrt{\mu}}{1 + \sqrt{\mu}} - K_t\mu$$

$$\text{p}K'_2 = \text{p}K_2 - \frac{0.51\sqrt{\mu}}{1 + \sqrt{\mu}} + K_t\mu$$

K_t =Salting in constant=0.32 for amino acid in water

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EXAMPLE 7-27

Calculate pH

Calculate the pH of a 0.01 M solution of acetic acid to which enough KCl had been added to give an ionic strength of 0.1 M at 25°C. The pK_a for acetic acid is 4.76.

$$(a) \quad pK' = pK + \frac{0.51(2Z - 1)\sqrt{\mu}}{1 + \sqrt{\mu}} \quad pK'_a = 4.76 - \frac{0.51\sqrt{0.10}}{1 + \sqrt{0.10}} \\ = 4.76 - 0.12 = 4.64$$

(b) Taking logarithms of equation (7-99) gives $[H_3O^+] = K_a \frac{(C_a - [H_3O^+] + [OH^-])}{(C_b + [H_3O^+] - [OH^-])}$

$$pH = \frac{1}{2}(pK'_a - \log C_a)$$

in which we now write pK_a as pK'_a :

$$pH = \frac{1}{2}(4.64 + 2.00) = 3.32$$

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EXAMPLE 7-28

Calculate pH

Calculate the pH of a 10^{-3} M solution of glycine at an ionic strength of 0.10 at 25°C. The pK_a values for glycine are $pK_1 = 2.35$ and $pK_2 = 9.78$.

$$(a) \quad pK'_1 = 2.35 + \frac{0.51\sqrt{0.10}}{1 + \sqrt{0.10}} - 0.32(0.10) \\ = 2.35 + 0.12 - 0.03 = 2.44$$

$$(b) \quad pK'_2 = 9.78 - \frac{0.51\sqrt{0.10}}{1 + \sqrt{0.10}} + 0.32(0.10) \\ = 9.78 - 0.12 + 0.03 = 9.69$$

(c) Taking logarithms of equation (7-118) gives

$$pH = \frac{1}{2}(pK_1 + pK_2) \\ = \frac{1}{2}(2.44 + 9.69) = 6.07$$

$$[H_3O^+] = \sqrt{K_1 K_2}$$

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Thanks for your attention

