UNIT II

Chapter ... 2

ACID BASE TITRATIONS

◆ LEARNING OBJECTIVES ◆

- *To describe, by using chemical equations and equilibrium constants, the chemical change(s) that occur during a strong acid/strong base titration.*
- *To identify the equivalence point in an acid-base titration from the pH titration curve.*
- *To describe why the pH at the equivalence point for a strong acid/strong base titration is generally equal to 7.*
- *To describe why the pH at the equivalence point for a weak acid/strong base (or strong acid/weak base) titration is generally not equal to 7.*

OUTCOMES

On satisfying the requirements of this course, students will have the knowledge and skills to:

- Sufficient indepth knowledge of acid base concepts is acquired, so that the theory of acid base titrations can be developed, understood and applied. They should be able to differentiate between acid and base; identify their strength.
- Quantitative analysis of the concentration of an unknown acid or base solution. It makes use of the neutralization reaction that occurs between acids and bases.

2.1 INTRODUCTION

An acid-base titration (or neutralization titration) is based upon the chemical reaction between an acid and a base. Various theories have been proposed to explain or classify acidity and basic properties of substances. Most familiar theory is the Arrhenius theory, but it is applicable only to water as solvent. Rest other theories are more generalized and there applicability was better. Mainly five theories are proposed for acid base titrations i.e.

1. Arrhenius theory
2. Bronsted Lowry theory
3. Lewis theory
4. Usanovich theory
5. Lux flood theory

2.2 THEORIES OF ACID BASE TITRATIONS

1. Arrhenius Theory (H^+ and OH^-):

Arrhenius, as a graduate student, introduced a radical theory in 1894 (for which he received the Nobel prize). According to him an acid is any substance that ionizes (partially or completely) in water to give hydrogen ions (which associates with the solvent to give hydronium ions, H_3O^+).

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

A Base ionizes in water to give hydroxyl ions. Weak (partially ionized) bases generally ionize as follows:

$$B + H_2O \longleftrightarrow BH^+ + OH^-$$

While strong bases such as metal hydroxide (NaOH) dissociate as

$$M(OH)_n \longleftrightarrow M^{n+} + nOH^-$$

This theory is restricted to water as solvent; because hydrogen and hydroxide ion are compulsory to define this theory.

2. Bronsted-Lowry Theory (Taking and giving protons):

In 1923, Bronsted and Lowry separately described a theory known as the Bronsted-Lowry theory. This theory states that an acid is any substance that can donate a proton, and a base is any substance that can accept a proton. Thus, we can write a "half reaction".

$$\text{Acid} = H^+ + \text{Base}$$

The acid and base of a half reaction are called conjugate pairs. Free protons do not exist in solution and there must be a proton acceptor (base) before a proton donor (acid) will release its proton.

3. Lewis Theory (Taking and giving electrons):

In 1923, G. N. Lewis also introduced the electronic theory of acids and bases. In the Lewis theory, a base is a substance that can donate an electron pair and acid is a substance that can accept an electron pair. Base, frequently contains oxygen or nitrogen as the electron donor. Thus, non-hydrogen containing substances are introduced as acids.

$$AlCl_3 + :O\text{-}R_2 \rightarrow Cl_3Al : OR_2$$

Here, Aluminium Chloride is an acid and ether a base. This theory is useful to describe the indicator colour change in non-protonic systems exhibiting acid-base reaction.

4. Usanovich Theory (Cation and anion donor acceptor):

In the year 1934, Usanovich modified the Lewis concept of acid and base by removing the limitation of either acceptance or donation of the electron pair in a more acceptable way. According to this theory "*Acid* is a chemical species that reacts with a base and gives cations or accepts anions or electrons".

"*Base* is a chemical species that reacts with an acid and gives anions or electrons or combines with cations".

$$Fe^{2+}_{(Base)} \longleftrightarrow Fe^{3+}(Acid) + e^-$$

$$Fe^{3+}_{(Acid)} + e^- \longleftrightarrow Fe^{2+}_{(Base)}$$

5. Lux Flood Concept (Oxide-ion acceptor-donor)

Lux (1929) and supported by Flood (1947) first introduced the concept of acid-base reactions with respect to the oxide ion. According to this theory, an acid is the oxide-ion acceptor and a base is the oxide-ion donor.

$$MgO\ (Base) + SiO_2\ (acid) \longleftrightarrow MgSiO_3$$

$$CaO\ (Base) + SO_3\ (acid) \longleftrightarrow CaSO_4$$

Summary of Acid-Base Theories:

Name of Theory	Acid	Base
Arrhenius Theory	Hydrogen ion donor	Hydroxide ion donor
Bronsted-Lowry Theory	Proton donor	Proton acceptor
Lewis Theory	Electron pair acceptor	Electron pair donor
Usanovich Theory	Cation donor and anion acceptor	Cation acceptor and anion donor
Lux-Flood Theory	Oxide-ion acceptor	Oxide-ion donor

2.3 LAW OF MASS ACTION

This law was first proposed by Goldberg and Wage in 1867 and can be defined as:

"The rate of a chemical reaction is proportional to the active masses of the reacting substances".

Active masses may be represented by the concentration of the reacting substances in dilute solutions where conditions approach the ideal state. The constant of proportionality is known as '**velocity constant**'.

Now,

Let us consider a homogeneous, reversible reaction,

$$A + B \longleftrightarrow C + D$$

According to the law of mass action,

$$V_f = K_1 [A][B]$$

$$V_b = K_2 [C][D]$$

Where,

V_f = Velocity of the forward reaction

V_b = Velocity of backward reaction

[A], [B], [C], [D] = Molar concentration of A, B, C and D respectively.

K_1 and K_2 are constants.

At the equilibrium of the reaction,

$$V_f = V_b$$

$$\therefore \quad K_1 [A][B] = K_2[C][D]$$

$$\therefore \quad \frac{K_1}{K_2} = \frac{[C]\,[D]}{[A]\,[B]}$$

Since, K_1 and K_2 are constants, K_1 fraction must also be a constant.

This result may be generalized as:

When equilibrium is reached in a reversible reaction, at constant temperature, the produc of the molecular concentration of the resultants (RHS) is divided by the product of th molecular concentration of reactants (LHS).

Each concentration being raised to a power equal to the number of molecules of th substances taking part in the reaction, is constant.

Hence,

K = Equilibrium constant of the reaction

In extension, the equilibrium constant for the general reversible reactions is,

$$aA + bB + cC \longleftrightarrow pP + qQ + rR$$

$$\therefore \quad K = \frac{[P]^p[Q]^q[R]^r}{[A]^a[B]^b[C]^c}$$

Where a, b, c and p, q, r are number of molecules of reacting species.

It is a mathematical model that explains and predicts behaviour of solution in dynamic equilibrium.

2.4 ROLE OF SOLVENTS

Water is the only solvent used in aqueous acid base titration and shows amphiprotic properties (it can act either as an acid or as a base depending upon experimental conditions). The solvent selected for acidimetric titrations should be either neutral or acidic in nature.

Neutral solvent: Neutral solvent do not enhance dissociation to a great extent.

Examples: Acetonitrile, alcohols, chloroform, benzene, dioxane ethyl acetate.

Acidic solvent: Acidic solvents are protogenic in nature and can be utilised for weak bases.

Examples: Formic acid, acetic acid, propionic acid, acedic anhydrides, sulphonyl chloride.

The solvent should be non-toxic for its wide use in analysis. It should be liquid at the time of analysis. The organic solvents are used but it is mainly dependent on their properties such as –

(i) Self dissociation
(ii) Dielectric constant
(iii) Acid base character of solvent

(i) Self Dissociation

Solvents can be classified as dissociating and non-dissociating solvents.

Dissociating solvents such as 'Ethanol' dissociates to give ethoxide ion.

$$C_2H_5OH \longleftrightarrow C_2H_5O^- + H^+$$

Acetic acid gives acetate ion.

$$CH_3COOH \longleftrightarrow CH_3COO^- + H^+$$

Hydrogen ion represents solvated protons and its range varies with the solvent (Solvated proton means proton bound with solvent). Some solvents dissociates without the production of solvated protons.

Example: Acetic anhydride

$$\underset{\text{Acetic anhydride}}{[CH_3CO]_2O} \longleftrightarrow \underset{\text{Acetate ion}}{CH_3COO^-} + \underset{\text{Acetylium ion}}{CH_3CO^+}$$

A non-dissociating solvent includes ethers, hydrocarbons. These solvents may dissociate but it is not usually detectable. It is always possible to define ion product of dissociating solvent. Here, the solvent is represented by "AB".

$$AB \longleftrightarrow A^+ + B^-$$

Ion-product (K_s) can be written as,

$$K_s = [A^+]\,[B^-]$$

The smaller is the value of K_s of a solvent, the greater is the range available for titration.

(ii) Dielectric Constant

If analysts assume the solvents as a homogenous medium and the ions present as point charges, these expressions can be applied for this system also. It can be concluded that higher the D value of the solvent, smaller amount of energy will separate the ions. It will be easy to dissolve the ionic solute. In a solvent of high dielectric constant, complete dissociation of polar ionic solute occurs easily.

Dielectric constants for some solvents are given below:

• Cyclohexane	2.02
• Chloroform	4.81
• Methanol	32.6
• Water	78.5

Acid-base character:

The non-aqueous solvents can be classified based on their proton donor–acceptor properties. The solvent exerts an influence on the acid-base properties of the solute. They are classified into four categories.

- Protogenic
- Protophilic
- Aprotic
- Amphiprotic

The dissociating solvent AB dissociates to give the cation A^+ [Lyonium ion] and the anions [Lyate ion].

The lyonium ion is reponsible for acidic characteristics of solvent and lyate ion is responsible for basic characteristics of solvents.

(a) **Protogenic solvents:** They are acidic in properties. These solvents have relatively high dielectric constant, they are ionized.

Examples: Acetic acid, formic acid and propionic acid.

(b) **Protophilic solvents:** They are basic in nature and reacts with acid to form the solvated proton. These solvents have high dielectric constant. They are ionized.

Examples: Pyridine, Dimethylformamide, ethylenediamine.

(c) **Aprotic solvents:** These are the solvents which cannot be able to donate hydrogen. In this solvent both acidic and basic properties are entirely absent.

Examples: Hexane and carbon tetra chloride.

(d) **Amphiprotic solvents:** These solvents have both protogenic and protophilic properties.

Examples: Water, Ethanol.

2.5 IONIZATION

Strong acid or strong base is one in which solute (acid or base) reacts fully with solvent whereas, a weak acid or weak base solution is one in which only partial or insignificant reaction with solvent occurs. One can also relate the strength of acid or base with the extent of ionization.

Example: HCl is a strong acid in water because it is completely ionized whereas acetic acid is a weak acid in water because it is slightly ionized. So, the strength of an acid is related to the concentration of H^+ ions that are produced on ionization and at any given concentration will depend upon the value of degree of dissociation.

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

$$H_2O + CH_3COOH \longleftrightarrow H_3O^+ + CH_3COO^-$$

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2.6 RELATIVE STRENGTH OF ACID AND BASES

According to the Bronsted-Lowry theory at equilibrium, the free proton cannot exist in solution in measurable concentration and reaction does not take place unless a base is added to accept the proton from the acid.

By contributing the equations –

$$A_1 \longleftrightarrow B_1 + H^+ \quad \text{... (2.1)}$$

$$B_2 + H^+ \longleftrightarrow A_2 \quad \text{... (2.2)}$$

We obtain,

$$A_1 + B_2 + H^+ \longleftrightarrow B_1 + H^+ + A_2$$

$$A_2 + B_1 + H^+ \longleftrightarrow B_1 + H^+ + A_2$$

$$A_1 + B_2 \longleftrightarrow B_1 + A_2 \quad \text{... (2.3)}$$

According to the law of mass action

$$K = \frac{[B_1][A_2]}{[A_1][B_2]} \quad \text{... (2.4)}$$

Where;

The constant 'K' depends on the temperature and the nature of the solvent.

This expression is strictly valid for the extremely dilute solutions and by using the above expression for measuring the strength of an acid, a standard acid-base pair, say $A_2 - B_2$, must be chosen, and it is usually convenient to refer acid-base strength of the solvent.

In water, the acid-base pair (H_3O^+-H_2O) is taken as standard. The equilibrium reaction of acid is therefore.

$$A + H_2O \longleftrightarrow B + H_3O^+ \quad \text{... (2.5)}$$

So, the constant,

$$K' = \frac{[B]\,[H_3O^+]}{[A]\,[H_2O]} \quad \text{... (2.6)}$$

Equation (2.5) represents dissociation of the acid A in water and constant 'K' is closely related to the dissociation constant A in water. When dealing with dilute solutions, the value of $[H_2O]$ may be regarded as constant and equation (2.6) may be expressed as:

$$K_a = \frac{[B]\,[H^+]}{[A]} \quad \text{... (2.7)}$$

This equation defines the strength of acid A.

Example: Ammonium ion, interacts with water as shown by the equation

$$NH_4^+ + H_2O \longleftrightarrow NH_3 + H_3O^+$$

The acid strength is given by,

$$K_a = \frac{[NH_3][H^+]}{[NH_4^+]}$$

So,

$$[NH_4^+] = \frac{[NH_3][H^+]}{K_a}$$

Since, any protolytic reaction involving an acid must also involve its conjugate base.

$$NH_3 + H_2O \longleftrightarrow NH_4 + OH^-$$

So,

$$K_b = \frac{[NH_4^+][OH^-]}{[NH_3]}$$

Since $[H^+][OH^-] = K_w$ (the ionic product of water)

We have

$$K_b = \frac{K_w}{K_a}$$

The value of K_a and K_b for different acids and bases vary through many powers of ten. It often convenient to use the dissociation constant exponent pK, which is defined as,

$$pK = \log_{10}\left(\frac{1}{k}\right) = -\log_{10}k$$

The larger the pK_a value is, the weaker is the acid and the stronger is the base.

Common Ion Effect:

A weak electrolyte AB, when dissolved in water will dissociate to a small extent into A and B^- ions. If, in this solution, we add a strong electrolyte CB, it will dissociate into C^+ and B ions. So both the electrolytes will give B^- which is called the common ion effect.

$$AB \longleftrightarrow A^+ + B^- \text{ (Poorly Dissociated)}$$

$$CB \longleftrightarrow C^+ + B^- \text{ (Strongly Dissociated)}$$

The effect of addition of CB to solution of AB will thus increase the concentration of B ions. This will push equilibrium to backward direction as per the law of mass action.

$$AB \longleftrightarrow A^+ + B^-$$

So, the poor dissociation of AB will further decrease. Thus, when to a solution of a wea electrolyte a strong electrolyte with common ion is added, the dissociation of the wea electrolyte is suppressed, this is known as the common ion effect.

2.7 pH AND pOH

pH:

pH is a numeric scale used to indicate the acidity or alkalinity (basicity) of any solution. is the negative of the logarithm to base 10 of the hydrogen ion. Solutions with a pH under are acidic and pH more than 7 are alkaline. Pure water has a pH of 7 and is neutral. pH defined as 'the decimal logarithm of the reciprocal of the hydrogen ion activity, H^+ in solution'.

$$pH = -\log 10\,[H^+]$$

$$pH = \log 10\left[\frac{1}{H^+}\right]$$

pOH:

pOH is important for measurement of concentration of hydroxide ions (OH^-) or basicity. Values for pOH are derived from pH measurements. The concentration of hydroxide ions in water is related to the concentration of hydrogen ions by

$$[OH^-] = \frac{K_w}{[H^+]}$$

Where,

K_w = Self-ionization constant of water.

Taking negative logarithms ($-\log_{10}$) on both side,

$$-\log_{10}[OH^-] = -\log_{10}\frac{K_w}{[H^+]}$$

$$pOH = pK_w - pH$$

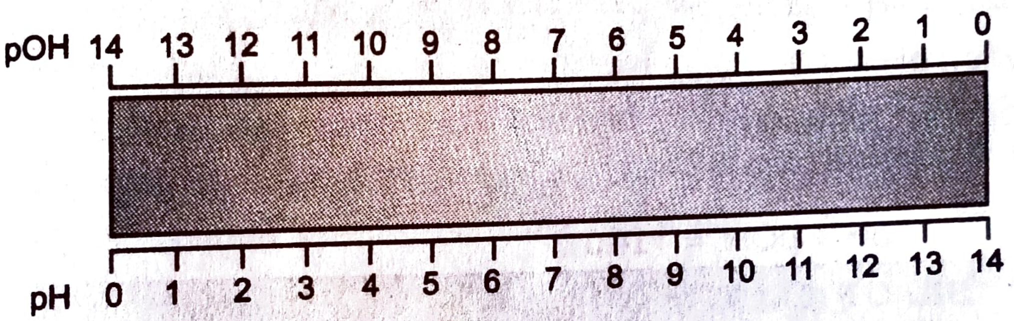


Fig. 2.1

2.8 IONIC PRODUCT OF WATER

Water is auto ionized into $H_3O^+_{(aq)}$ and $OH^-_{(aq)}$ ions although to a very small extent.

$$H_2O + H_2O \longleftrightarrow H_3O^+ + OH^-$$

The Equilibrium constant for this reaction 'K_w' is called the ionic product for water.

$$K_w = [H_3O^+] \times [OH^-]$$

At 25°C

$$K_w = 1 \times 10^{-14}$$

For pure, neutral water

$$[H_3O^+] = [OH^-] = 1.0 \times 10^{-7} \text{ mol/litre}$$

So pH of neutral water is 7 because

$$\begin{aligned} pH &= -\log[H^+] \\ &= -\log[H_3O^+] \\ &= -\log 1.0 \times 10^{-7} \\ &= 7 \end{aligned}$$

Anything added to water which raises $[H_3O^+]$ above 1.0×10^{-7} mol/litre, causes $[OH^-]$ to immediately drop below 1.0×10^{-7} mol/litre.

So, keeping K_w constant at 1.0×10^{-14} mol/litre.

Reaction with Strong Acid and Bases:

Strong acid react completely with water to form $[H_3O^+]$

Example:

$$\underset{\text{(ACID 1)}}{HCl} + \underset{\text{(BASE 1)}}{H_2O} \longleftrightarrow \underset{\text{(ACID 2)}}{H_3O^+} + \underset{\text{(BASE 2)}}{Cl^-}$$

Strong bases also completely react with water and form $[OH^-]$.

Example:

$$\underset{\text{(ACID 1)}}{H_2O} + \underset{\text{(BASE 1)}}{H^-} \longleftrightarrow \underset{\text{(ACID 2)}}{H_2} + \underset{\text{(BASE 2)}}{OH^-}$$

Calculating concentration of H^+ and OH^- in solutions of strong acids and bases i.e. 0.50 mol HCl dissolved in 1.0 litre H_2O, then $[H_3O] = 0.50$ mol/litre.

$$pH = -\log_{10} [H_3O^+]$$

In Neutral solution $pH = 7.0$

In Acidic solution $pH < 7.0$

In Basic solution $pH > 7.0$

From Ionic product for water

$$pK_w = pH + pOH$$

So, $$pH + pOH = 14.0$$

2.9 HYDROLYSIS OF SALTS

A **salt** is formed between the reaction of an acid and a base. Usually, a neutral salt is formed when a strong acid and a strong base is reacted in the reaction:

$$H^+ + OH^- = H_2O$$

Most of the neutral salts consist of cations and anions. These ions have slight tendency to react with water. So, salts consisting ions are neutral.

Example: KNO_3, $NaCl$, $CaBr_2$, $CsClO_4$ are neutral salts.

Cations of the neutral salts: K^+, Na^+, Cs^+, Rb^+, Ca^+, Mg^+, Ba^+, Sr^+

Anions of the neutral salts: Br^-, Cl^-, I^-, BrO_4^-, ClO_3^-, NO_3^-, ClO_4^-.

When weak acids and bases react, the relative strength of the conjugated acid-base pair in the salt determines the pH of its solution. The salt, or its solution, so formed can be acidic, neutral or basic. A salt formed between a strong acid and a weak base is an **acid salt**, for example NH_4Cl. A salt formed between a weak acid and a strong base is a **basic salt**, for example $NaCH_3COO$.

Hydrolysis of Acidic Salts:

A salt formed between a strong acid and a weak base is an **acidic salt**. Ammonia is a weak base, and its salt with any strong acid gives a solution with a pH lower than 7.

Example: $$HCl + NH_4OH = NH_4^+ + Cl^- + H_2O$$

2.10 HENDERSON HESSELBACH EQUATION

$$HA \longleftrightarrow H^+ + A^-$$

Here,

$$HA = \text{Weak acid}$$

HA (Weak acid) is ionized as H^+ and A^- has some pK_a. So, it is frequently helpful to have the capacity to relate the pH of a solution of a weak acid to the pK_a of the acid and the degree of ionization.

The K_a (acid dissociation constant) for the reaction can be expressed by:

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

Rearrangement of equation

$$\frac{1}{[H^+]} = \frac{1}{[K_a]\,[HA]}$$

Taking log on both sides,

$$\log\frac{1}{[H^+]} = pH$$

$$\log\frac{1}{K_a} = pK_a$$

So, final equation will be

$$pH = pK_a + \log\frac{[A^-]}{[HA]}$$

This is the well-known Henderson-Hasselbach equation and utilized for calculations required in preparation of buffers or other applications. Notice several interesting facts about this equation.

Specific conditions;

Condition 1: If pH = pK_a; The log value of dissociated and un-dissociated acid will be zero. So, the concentrations of both the species will be equal. In other terminology, when the pK_a and pH equals, the acid will be half dissociated.

Condition 2: When pH increases or decreases by one unit relative to the pK_a, the proportion of dissociated and un-associated form of the acid will be 10 folds. So, if the pH of a solution is 6 and the pK_a is 7, the proportion of $[A^-]/[HA]$ will be 0.1, if the pH was 5, the ratio would be 0.01 and if the pH was 7, the ratio would be 1.

Condition 3: If pH < pK_a, the proportion will be < 1, while if the pH > pK_a, the ratio will be >1. Henderson-Hasselbach equation contains a lot of information.

2.11 BUFFER SOLUTION

Buffers are solutions which by definition resist a change in pH when a small amount of acid, base or water is added to it.

An acidic buffer solution can be made by mixing a weak acid with the salt of its conjugate base. For example, acetic acid with sodium acetate would make a buffer solution with a pH of less than 7. The way this is usually done is to take a solution of acetic (acetic acid) and add sodium hydroxide as a limiting reagent to it. Once, all the sodium hydroxide has reacted with the acid, some acid will be left along with the salt, sodium acetate.

$$\underset{\text{(excess)}}{NaOH + CH_3COOH} \longrightarrow CH_3COONa_{(aq)} + H_2O + \underset{\text{(left over)}}{CH_3COOH}$$

The solution acts as a buffer and the acid is weakly dissociated, but the salt is fully dissociated; so there is a lot of acetate in solution.

$$CH_3COONa_{(aq)} \longrightarrow Na^+ + CH_3COO^-$$

$$CH_3COOH \longrightarrow CH_3COO^- + H^+$$

If a small amount of acid is added, the extra H^+ initially decreases the pH but then combines with acetate shifting the second equilibrium to the left so the concentration of H^+ remains unchanged. If a small amount of base is added, the pH initially increases but then the OH^- ions react with the H^+ ions to make water, and the acid dissociates more anion and once again the concentration of H^+ remains constant.

$$OH^- + H^+ \longrightarrow H_2O\text{, then}$$

$$CH_3COOH \longrightarrow CH_3COO^- + H^+$$

A basic buffer solution can be made by mixing a weak base with the salt of its conjugate acid. For example, ammonia with ammonium chloride would make a buffer solution with a pH of more than 7. We can also add HCl as a limiting reagent to a solution of ammonia, so both ammonia and ammonium ion are present in the solution.

$$NH_4Cl \longrightarrow \overset{+}{NH_4} + Cl^-$$

$$NH_3 + H_2O \longrightarrow \overset{+}{NH_4} + OH^-$$

If a small amount of H^+ ions are added, the pH initially decreases and then the weak base, ammonia, reacts with the H^+ and causes the pH to increase to its original value.

$$NH_3 + H^+ \longrightarrow \overset{+}{NH_4}$$

If a small amount of base is added, the pH initially increases and then

$$OH^- + H^+ \longrightarrow H_2O$$

Water is formed and then NH_4^+ dissociates to form more H^+ ions restoring the solution to its original pH.

Blood is an example of a buffered solution. The bicarbonate ion plays a very important role in maintaining blood pH. The transport of oxygen in the blood is very pH dependent.

$$HHb^+ + O_2 \longrightarrow H^+ + HbO_2$$

This binding produces hydrogen ions making the process pH sensitive.

$$CO_{2(aq)} + H_2O_{(l)} \longrightarrow H_2CO_{3(aq)} \longrightarrow H^+_{(aq)} + HCO^-_{3(aq)}$$

$4.760 - 0.602 = 4.158$

2.12 CLASSIFICATION OF ACID BASE TITRATIONS

Acid base titrations are classified in four categories according to the titration curves.

1. Strong acid vs Strong base.
2. Weak acid vs Strong base.
3. Strong acid vs Weak base
4. Weak acid vs Weak base.

Strong acid or Base:

A strong acid is completely dissociated into its' component ions in dilute aqueous solution. Strong base is also completely dissociated into its' component ions.

Examples: HCl, H_2SO_4, NaOH, KOH etc.

Weak acid:

A weak acid is one which is incompletely dissociated. The extent to which it dissociates is characterized by K_a.

Example: CH_3COOH.

Weak base:

A weak base does not ionised fully in an aqueous solution. The extent of dissociation of dissociates is characterized by K_b.

Example: NH_4OH.

Buffer solution:

It is a solution of substance or a mixture of substances which helps in maintaining and establishing pH.

If we study the changes in the hydrogen ion concentration during the course of titration we get a clear idea about the mechanism of neutralization process. The pH value of greatest importance is the one near the equivalence point as it helps us in selecting an indicator which will give the smallest titration error. The curve obtained by plotting pH as ordinate against the percentage of acid remaining during titration is known as neutralization curve or more generally titration curve.

Classification of Acid-base titration is described below:

1. Strong Acid with Strong Base Titration:

When a strong acid and a strong base are mixed together, as in titration one by other, the reaction can be represented as:

$$H^+ + OH^- \longleftrightarrow H_2O$$

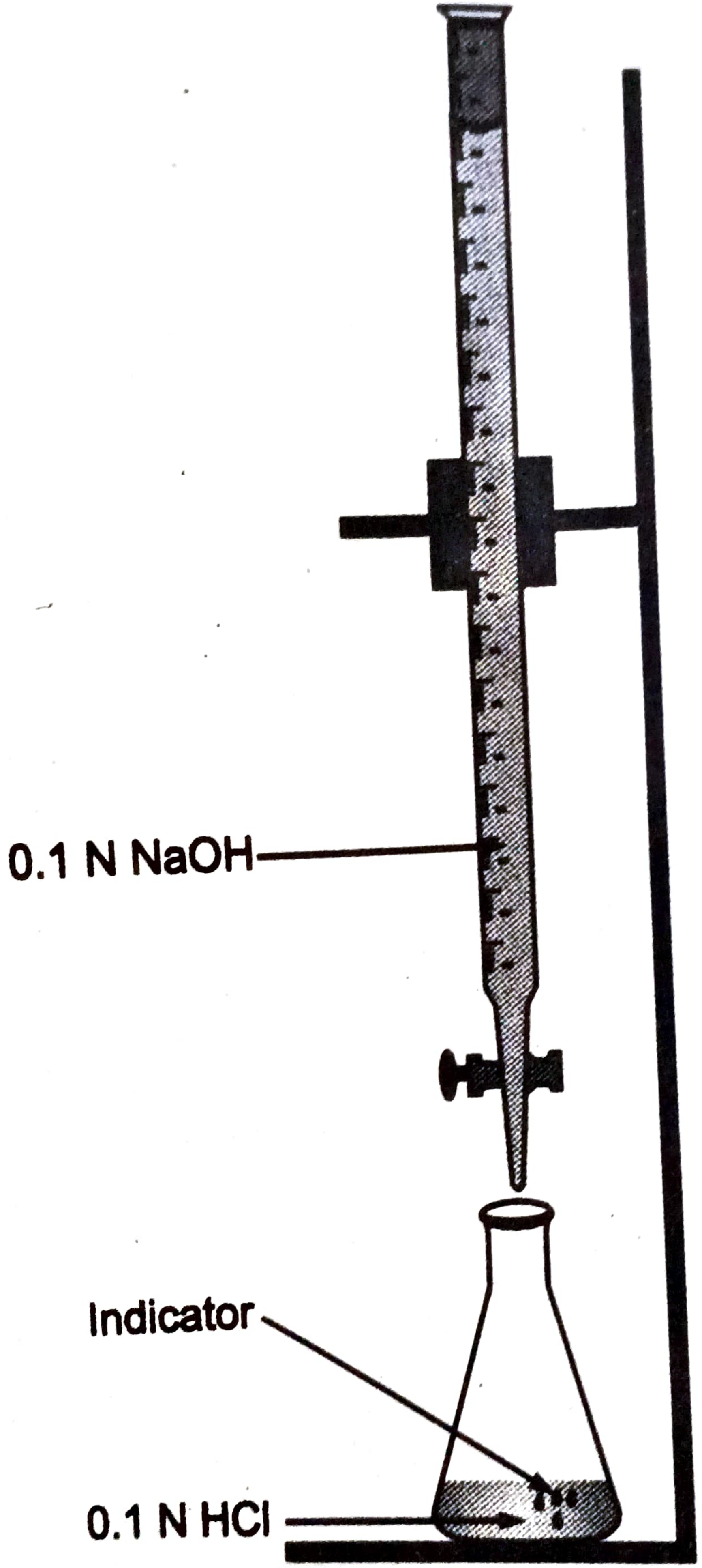


Fig. 2.2: Strong acid vs. Strong base titrations

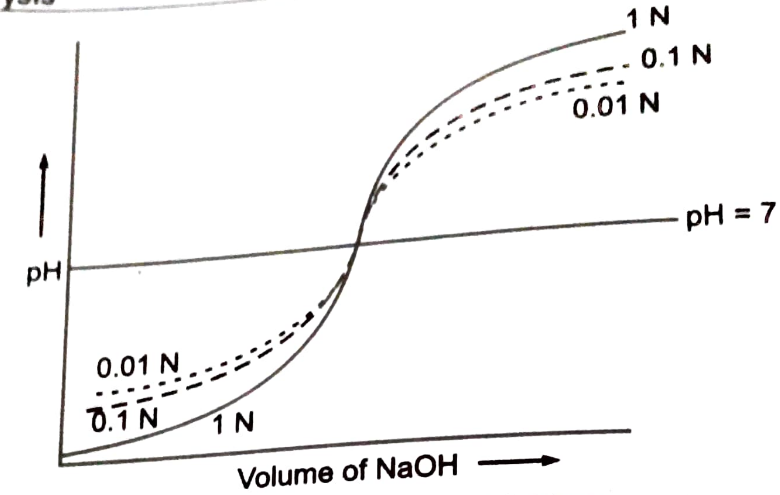


Fig. 2.3: The pH titration curve of strong acid (HCl) vs strong base (NaOH)

2. Weak Acid with Strong Base Titration:

This type of titration may be represented as

$$HA + OH = H_2O + A$$

HA represents a weak acid that is why it is written in the un-dissociated form. There are three important differences between this titration and a strong acid and a strong base titration.

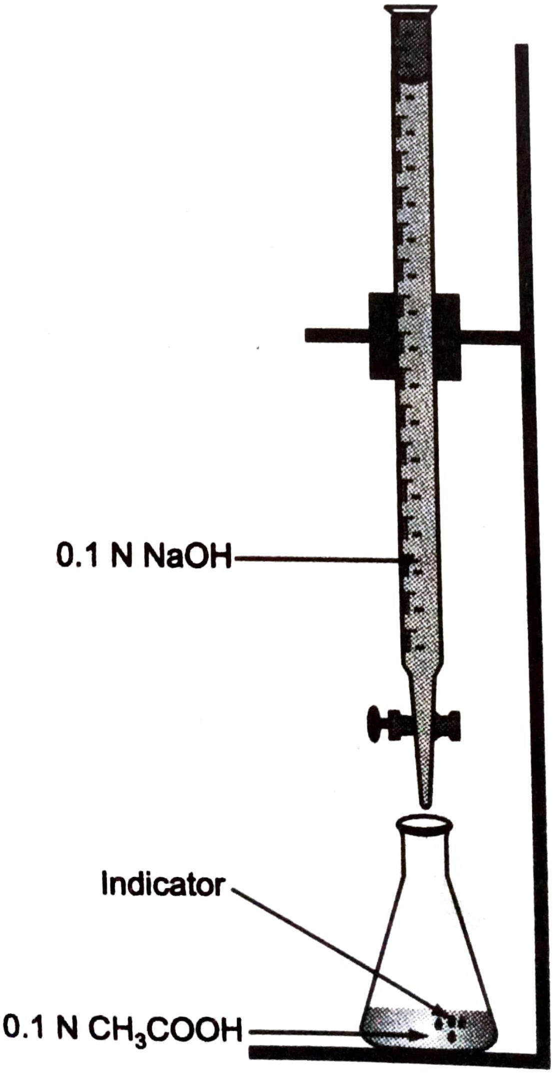


Fig. 2.4: Weak acid vs. Strong base titrations

The above discussion can be summarized by stating that,

- The initial pH is higher.
- The rate of increase of pH during the titration is greater.
- The pH at the equivalence point is higher.

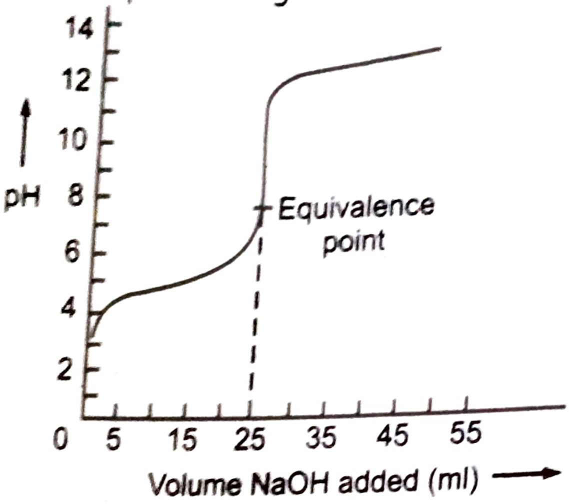


Fig. 2.5: The pH titration curve of weak acid (CH_3COOH) and strong base (NaOH)

3. Weak Base with Strong Acid Titration:

Consider the titration of 0.1 M and 0.1 N aqueous ammonia solution with 0.1 M and 0.1 N HCl solution.

The reaction involved is,

$$NH_4OH + HCl \longrightarrow NH_4Cl + H_2O$$

The salt NH_4Cl undergoes hydrolysis.

$$\therefore \quad NH_4 + H_2O \longrightarrow NH_4OH + H^+$$

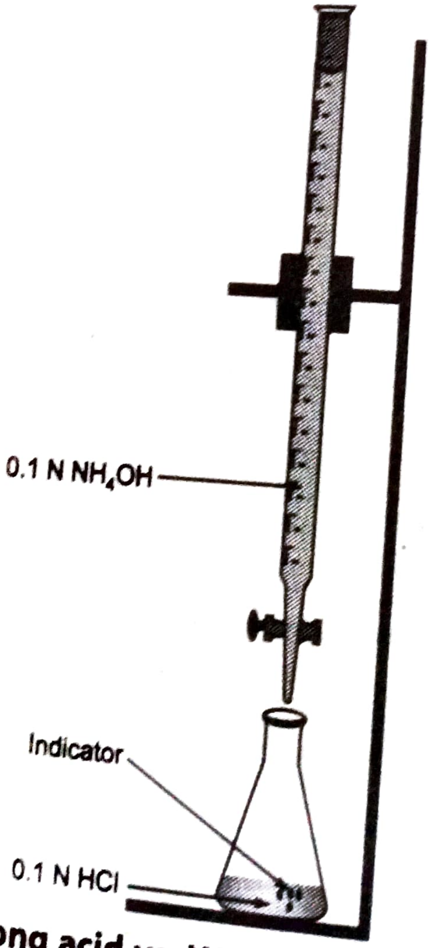


Fig. 2.6: Strong acid vs. Weak base titrations

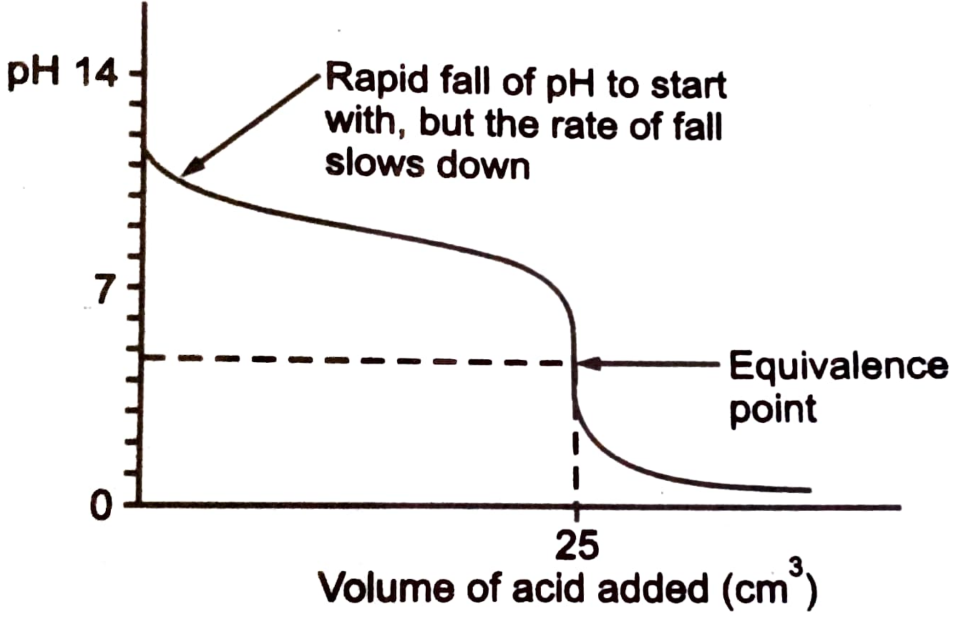


Fig. 2.7: The pH titration curve of strong acid (HCl) vs weak base (NH_4OH)

4. Weak Acid with Weak Base Titration:

Consider the titration of 0.1 M CH_3COOH with 0.1 N NO_4OH.

$$CH_3COOH + NH_4OH \longrightarrow CH_3COONH_4 + H_2O$$

The salt formed, CH_3COONH_4, undergoes hydrolysis,

$$CH_3COONH_4 + H_2O \longrightarrow CH_3COOH + NH_4OH$$

The disadvantage in such titrations is that, the inflection on the pH neutralization curve is very small near the equivalence point.

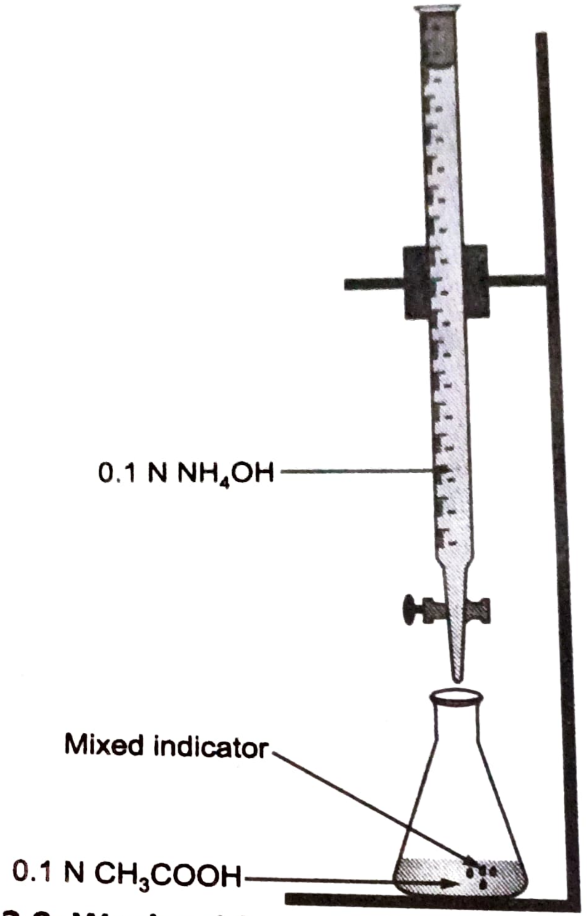


Fig. 2.8: Weak acid vs. weak base titrations

For example:

In the titration of 0.1 N CH_3COOH with 0.1 N NH_4OH the pH near the equivalence point slowly raises from 6 to 8. With more dilute solutions the rise in pH is smaller. It should be noted that, if the pH change at the equivalence point is smaller than 2 pH units, it is very difficult to judge the colour change and accurate result cannot be achieved. In this type of titration, equivalence depends on the relative values of dissociation constant.

If $K_a = K_b$ then pH = 7

If $K_a > K_b$ then pH > 7

If $K_a < K_b$ then pH < 7

Generally, mixed indicator is used for these titrations.

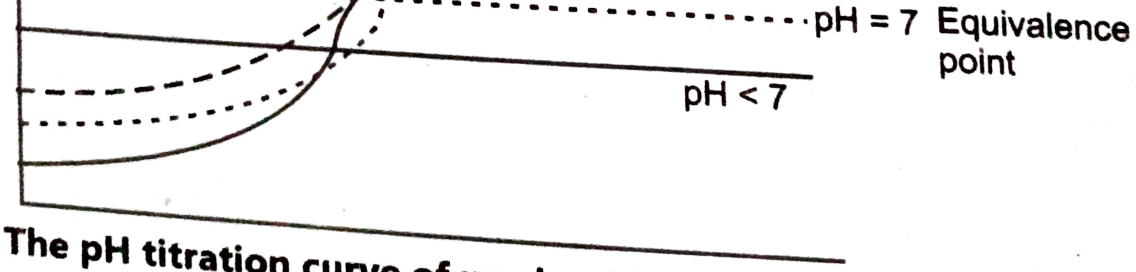


Fig. 2.9: The pH titration curve of weak acid (CH_3COOH) vs. weak base (NH_4OH)

2.13 THEORIES OF INDICATORS

"Indicator is a substance which exhibits colour change at a particular stage of a chemical reaction". These are the substances which exhibits different colours at various values of pH. Indicators are weak acids or weak bases which have different colours in their conjugate base and acid forms. Most indicators are used in dilute solution form. For an acid base titration we select an indicator which will show a distinct colour change at pH close to the equivalence point. Two theories of indicators are proposed.

Ostwald Theory:

The first theory which explained the behaviour of indicators was given by W. Ostwald. According to this theory "The undissociated indicator acid (HIn) or a base (InOH) has a colour different than its ions". For an acid indicator equivalence can be written as

$$\text{HIn} \longrightarrow \text{H}^+ + \text{In}^-$$

In an acid solution, there is a depression of ionization of indicator due to common ion effect. In alkali solution ionization increases and solution acquires ionized form.

$$\text{HIn} \longleftrightarrow \text{H}^+ + \text{In}^-$$

By applying law of mass action,

$$\text{KIn}_a = \frac{[\text{H}^+][\text{In}^-]}{[\text{HIn}]}$$

$$\therefore \quad [\text{H}^+] = \text{KIn}_a \times \frac{[\text{HIn}]}{[\text{In}^-]}$$

Taking log on both sides

$$\log [\text{H}^+] = \log \text{KIn}_a + \log \frac{[\text{HIn}]}{[\text{In}^-]}$$

Taking negative log

$$-\log [\text{H}^+] = -\log \text{KIn}_a - \log \frac{[\text{HIn}]}{[\text{In}^-]}$$

$$\therefore \quad \text{pH} = -\log \text{KIn}_a + \log \frac{[\text{In}^-]}{[\text{HIn}]}$$

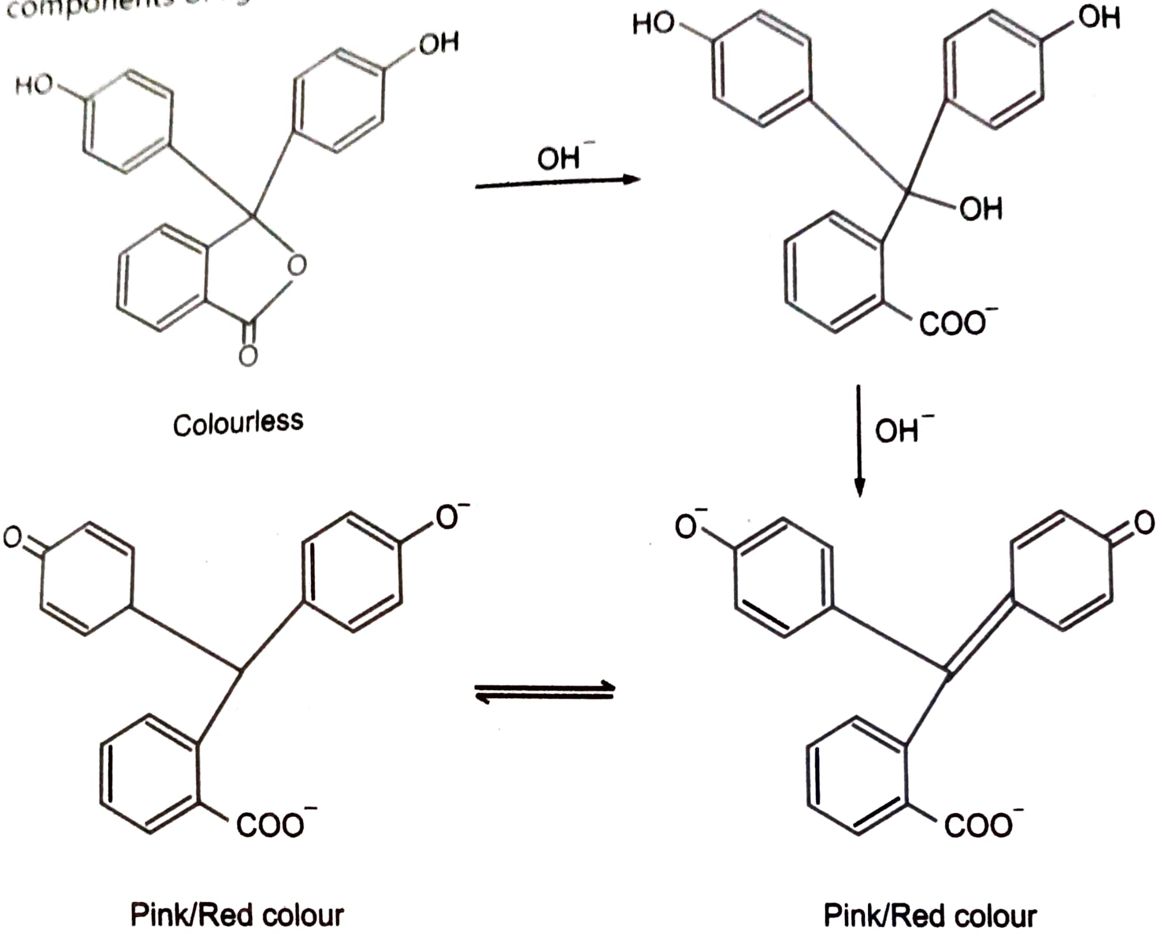
$$\therefore \quad \text{pH} = \text{pKIn}_a + \log \frac{[\text{In}^-]}{[\text{HIn}]}$$

KIn_a is dissociation constant of indicator. The colour of the indicator depends upon the ratio of concentration of ionized and unionized form and hence directly proportional to pH.

The indicator should be such that the pH at equivalence point false within the transition interval of the indicator.

Resonance Theory:

All the acid base indicators, which are commonly used are organic compounds. The difference in colour of some compound in acid and base medium is apparently due to difference in structure of two forms. Colour shown by the compound is associated with the capability of the compound to absorb the visible light and this capability is related to the electronic structure. Change in the electronic features will result in the absorption of different colour components of light with a resultant colour change.



The Pink/Red colour in alkaline solution is due to increased possibility of resonance between various ionic forms.

2.14 INDICATORS OF ACID BASE TITRATIONS

Strong acid strong base titrations:

Example: Methyl orange, Methyl red, Phenolphthalein Bromothymol Blue, Phenol Red.

Weak acid strong base titrations:

Example: Phenolphthalein, Thymolphthalin, Thymol Blue.

Strong acid weak base titrations:

Example: Methyl orange, Methyl red, bromophenol, Bromocresol green.

Weak acid weak base titrations:

Example: Mixed Indicators.

Table 2.1: List of commonly used indicator in acid base titrations

Sr. No.	Indicator name	pH range	Acidic medium	Alkaline medium
1.	Thymol blue	1.2 - 2.8	Blue	Yellow
2.	Bromophenol blue	3.0 - 4.6	Yellow	Blue
3.	Methyl orange	3.1 - 4.4	Red	Orange
4.	Bromocresol green	3.8 - 5.4	Yellow	Blue
5.	Methyl red	4.2 - 6.3	Red	Yellow
6.	Phenol red	6.8 - 8.4	Yellow	Red
7.	Phenolpthalein	8.3 - 11.0	Colourless	Pink/Red

According to the type of titration, we choose the appropriate indicator which gives colour change at defined pH range.

Mixed Indicators

When weak acid and base is involved in titration, the pH range is very narrow at the end point, so sharp colour change is required to identify the end point. Ordinary acid base titration indicators are not able to show sharp colour change at the end point when pH change is less than two units. Mixed indicator is used to overcome the problem which is the combination of more than one indicator with close pK_a values. Colour changes are complementary colours after overlapping of different colours at various pH ranges.

Example 1:

Neutral red (0.1% solution in alcohol) and methylene blue (0.1% in alcohol) gives a sharp colour change from violet blue to green from acidic to basic solution at pH 7.

Example 2:

Methyl green (2 parts of 0.1% solution in ethanol) and phenolphthalein (1 part of 0.1% solution in ethanol) gives colour change from gray to pale blue at the pH range 8.4 - 8.8.

Example 3:

Thymol blue (3 parts of 0.1% aqueous solution) and cresol red (1 part of 0.1% aqueous solution) gives colour change from yellow to violet at the pH 8.3.

QUESTIONS

Non aqueous titration

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NONAQUEOUS ACID–BASE TITRATION.

Titration in water solutions is limited by factors:

- **It is impossible** to titrate for a mix of acids or the bases
- **It is impossible** to titrate for a mix of strong and weak acids (bases)
- **It is impossible** to titrate separately for a mix of acids (bases) with near constants of dissociation
- **It is impossible** to define substances which are insoluble in water.

Non- aqueous titrations have the following advantages

- Organic acids and bases that are insoluble in water are soluble in non- aqueous solvent.
- A non-aqueous solvent may help two are more acids in mixture. The individual acid can give separate end point in different solvent.
- Enlargement of solubility range: many substances that are not soluble in water can be easily titrated in water-free media (e.g. fats and oils) Enlargement of application range: weak bases and acids can be easily titrated
- Substance compositions that cannot be separately determined in aqueous media can often be titrated in non-aqueous media
- Non-aqueous solvents are useful for the titration of very weak acids or bases that cannot be titrated in water
- Non aqueous titrations are simple and accurate, examples of non aqueous titration are :
- Ephedrine preparations, codeine phosphate in APC, tetracycline, teramycin, Anti- histamines and various piprazine preparations.

What is non-aqueous solvent & it's types

- Solvent which are used in non aqueous titration are called non aqueous solvent.
- They are following types:-

1. Aprotic Solvent
2. Protogenic Solvent
3. Protophillic Solvent
4. Amphiprotic Solvent

1.Aprotic solvent

- **Aprotic solvent are most important solvent in this titration. This solvent are chemically inert and they work as a catalyst. Like this solvent are increase the rate of speed in reaction and also decrease the rate of speed in reaction during the chemical process or reaction it will depend on condition.**
- **Neither acidic nor basic (inert solvent),**

  The most important examples of aprotic solvent are
- **Chloroform**
- **Benzene**

2. Protogenic solvent

- Protogenic solvent are acidic in nature. And they can donate the proton, and they enhance the strength of weak bases. Examples of Protogenic solvent are
- HCL
- H_2so_4

3.Protophillic solvent

- **Protophillic solvent are basic in nature. Which possess a high affinity for proton.**

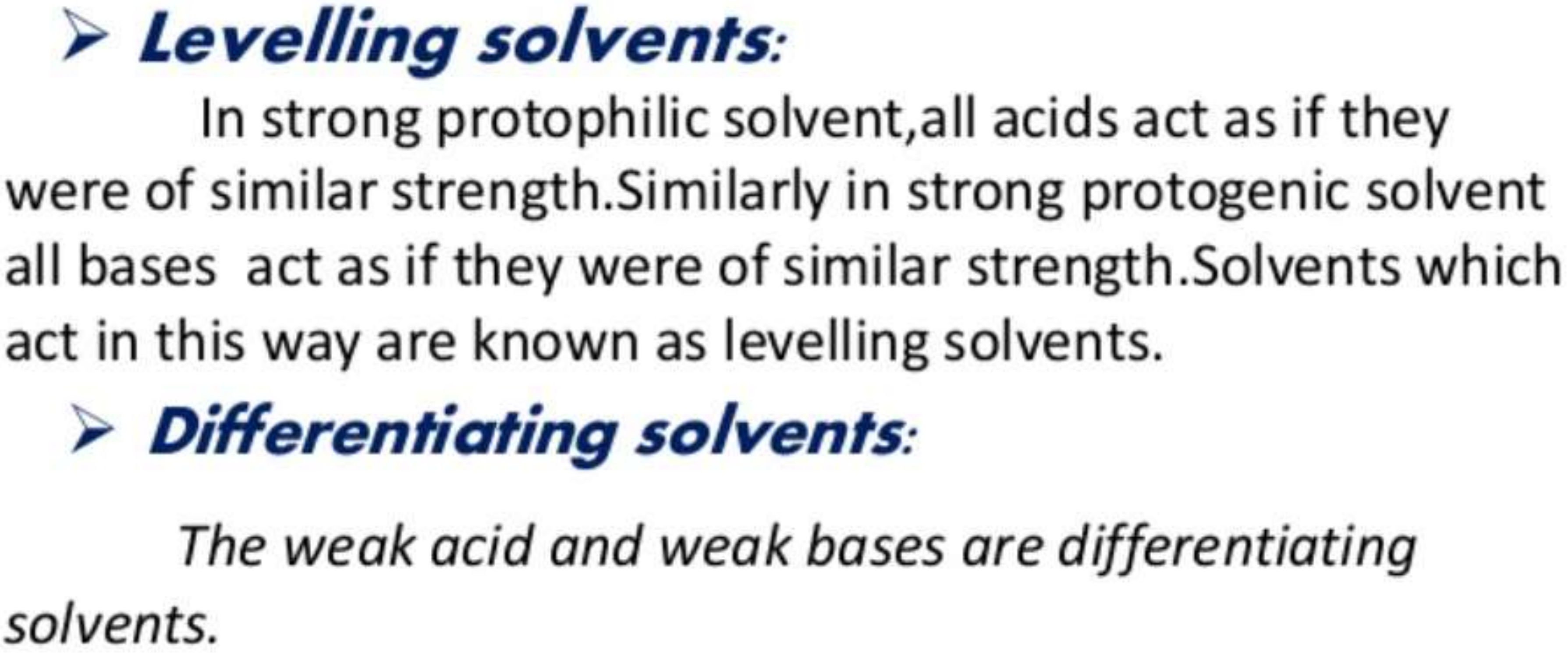
  Examples:-Liquid ammonia, amines and ketone.

4.Amphiprotic Solvent

- Amphiprotic solvent are those solvent they work as a both mean Protogenic or Protophillic. It means Amphiprotic solvent are acidic and basic in nature. And they are accept the proton and donate the proton.

  For examples:- Water, Alcohols and weak organic acids

Effect of solvents



- ***Levelling solvents:***

In strong protophilic solvent,all acids act as if they were of similar strength.Similarly in strong protogenic solvent all bases act as if they were of similar strength.Solvents which act in this way are known as levelling solvents.

- ***Differentiating solvents:***

The weak acid and weak bases are differentiating solvents.

Detection of end point

- **Visual indicator are formed to the most suitable for the detection of end point in non-aqueous titration.**
- **The important indicator used for non-aqueous titration are follow:-**

1. **Crystal voilet:-** **It is used as 0.5% solution in glacial acetic acid, it gives voilet colour in basic medium and yellowish green in acidic medium.**

- **It is most widely use for the titration of pyridine with prechloride acid.**

2. **Oracet Blue B Indicator:-** **It is prepared o.5% glacial acetic acid. It gives blue colour in basic medium while pink colour in acidic medium.**

Selection of Solvents for NAT

Acetic acid used for titration of weak bases, Nitrogen containing compounds

Acetonitrile / with ACOH: Metal ethanoates

Alcohols (IPA, nBA) : Soaps and salts of organic acids,

DMF: Benzoic acid, amides etc

Titrants for NAT

- **Perchloric acid in acetic acid**
  - **Amines, amine salts, amino acids, salts of acids**

- **Potassium Methoxide in Toluene-Methanol**
- **Quan ammonium hydroxide in Acetonitrile-pyridine**
  - **Acids, enols, imides &sulphonamides**

ASSAY BY NON-AQUEOUS TITRATIONS

- Acidimetry in Non-aqueous Titrations— **It can be further sub-divided into** *two* **heads, namely :**

  (i)Titration of primary, secondary and tertiary amines, and

  (ii) Titration of halogen acid salts of bases.

- Alkalimetry in Non-aqueous Titrations— **titration of acidic substances**

ACIDIMETRY IN NON AQUEOUS TITRATIONS

Example : Primary amines

METHODOLOGY: **four steps**

- (*i*) **Preparation of 0.1 N Perchloric acid,**
- (*ii*) **Standardization of 0.1 N Perchloric Acid,**
- (*iii*) **Choice of Indicators, and**
- (*iv*) **Effect of Temperature on Assays**

PREPARATION OF 0.1 N PERCHLORIC ACID

- Materials Required : **8.5 ml of perchloric acid (70.0 to 72.0%) ; 1 Litre of glacial acetic acid ; 30ml of acetic anhydride.**

- Procedure : **Gradually mix 8.5 ml of perchloric acid to 900 ml of glacial acetic acid with vigorous and continuous stirring. Now add 30 ml acetic anhydride and make up the volume to 1 litre with glacialacetic acid and allow to stand for 24 hours before use.**

- **The acetic anhydride reacts with the water (approx. 30%) in perchloric acid and some traces in glacialacetic acid thereby making the resulting mixture practically anhydrous. Thus, we have :**

$$H_2O + (CH_3CO)_2O \rightarrow 2CH_3COOH$$

Acetic anhydride Acetic acid

STANDARDIZATION OF 0.1 N PERCHLORIC ACID

- Weigh accurately about 0.5 g of potassium hydrogen phthalate in a 100 ml conical flask.
- Add 25 ml of glacial acetic acid and attach a reflux condenser fitted with a silica-gel drying tube. Warm until the salt gets dissolved completely. Cool and titrate with 0.1 N perchloric acid by making use of either of the following *two* indicators :
- (*a*) acetous crystal violet-2 drops, end point Blue to Blue-Green (0.5% w/v)
- (*b*) acetous oracet blue B-2 drops, end point Blue to Pink.

CHOICE OF INDICATORS

S.No.	Name of Indicator	Colorchange	Observed	Acidic
		Basic	Neutral	
1	Crystal violet (0.5% w/v in glacial acetic acid)	Violet	Bluish green	Yellowish green
2	Oracet Blue B(0.5% in glacial acetic acid)	Blue	Purple	Pink
3	α-Naphtholbenzein (0.2% in glacial acetic acid	Blue	Orange	Dark-green
4	Quinalidine Red (0.1% in methanol	Magenta	—	Almost colourless

PRECAUTIONS

(*a*) Perchloric acid is usually available as a 70 to 72% mixture with water .It usually undergoes a spontaneous explosive decomposition and, therefore, it is available always in the form of a solution.

(*b*) Conversion of acetic anhydride to acetic acid requires 40-45 minutes for its completion. It being an exothermic reaction, the solution must be allowed to cool to room temperature before adding glacial acetic acid to volume,

(*c*) Avoid adding an excess of acetic anhydride especially when primary and secondary amines are to be assayed, because these may be converted rapidly to their corresponding acetylated non-basic products :

$$\mathrm{R{—}NH2 + (CH3CO)_2O \rightarrow R.NH.(CH3CO) + CH3COOH}$$

Primary amine   Acetylated product

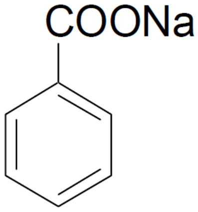
(*d*) Perchloric acid is not only a powerful oxidising agent but also a strong acid. Hence, it must be handled very carefully.

THANK YOU

Estimation of Sodium Benzoate by NAT :-

Sodium Benzoate :

Formula : $C_7H_5NaO_2$
Mol. Wt. 144.1



Sodium Benzoate contains not less than 99.0 per cent and not more than 100.5 per cent of $C_7H_5NaO_2$, calculated on the dried basis.

Description : A white, crystalline or granular powder or flakes; odourless or with a faint odour; hygroscopic.

For the Estimation of Sodium Benzoate :

Preparation of 0.1N solution of $HClO_4$ and its standardization: Dissolve 8.5 ml of 72% $HClO_4$ in about 900 ml glacial acetic acid with constant stirring, add about 30 ml acetic anhydride and make up the volume (1000 ml) with glacial acetic acid and keep the mixture for 24 hour. Acetic anhydride absorbed all the water from $HClO_4$ and glacial acetic acid and renders the solution virtually anhydrous. $HClO_4$ must be well diluted with glacial acetic acid before adding acetic anhydride because reaction between $HClO_4$ and acetic anhydride is explosive.

Standardisation of $HClO_4$: To 500 mg of potassium acid phthalate add 25 ml of glacial acetic acid and add few drops of 5% w/v crystal violet in glacial acetic acid as indicator. This solution is titrated with 0.1 $HClO_4$. The colour changes from blue to blue green.

Assay Procedure : Weigh accurately about 0.25 g of Sodium Benzoate, dissolve in 20 ml of anhydrous glacial acetic acid, warming to 50° if necessary, cool. Titrate with 0.1 M perchloric acid, using 0.05 ml of 1-naphtholbenzein solution as indicator. Carry out a blank titration.

Equivalent or I.P factor : 1 ml of 0.1 M perchloric acid is equivalent to 0.01441 g of $C_7H_5NaO_2$.

Calculations :

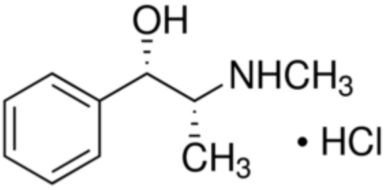
$$\% \text{ Sodium Benzoate} = \frac{\text{X ml} \times \text{Normality (Calculated)} \times 0.01441 \times 100}{\text{N(Given)} \times \text{Wt. of sample(in gm)}}$$

Where,
X ml = Volume of titrant consumed at end point
Normality Calculated = Normality of Perchloric acid after standardisation
Normality Given = 0.1 N (theoretically)

Estimation of Ephedrine Hydrochloride by NAT :-

Ephedrine Hydrochloride :

Formula : $C_{10}H_{15}NO,HCl$
Mol. Wt. 201.7



Ephedrine Hydrochloride contains not less than 99.0 per cent and not more than 101.0 per cent of C10H15NO,HCl calculated on the dried basis.

Description : Colourless crystals or a white, crystalline powder; odourless. It is affected by light.

For the Estimation of Ephedrine Hydrochloride :

Preparation of 0.1N solution of $HClO_4$ and its standardization: Dissolve 8.5 ml of 72% $HClO_4$ in about 900 ml glacial acetic acid with constant stirring, add about 30 ml acetic anhydride and make up the volume (1000 ml) with glacial acetic acid and keep the mixture for 24 hour. Acetic anhydride absorbed all the water from $HClO_4$ and glacial acetic acid and renders the solution virtually anhydrous. $HClO_4$ must be well diluted with glacial acetic acid before adding acetic anhydride because reaction between $HClO_4$ and acetic anhydride is explosive.

Standardisation of $HClO_4$: To 500 mg of potassium acid phthalate add 25 ml of glacial acetic acid and add few drops of 5% w/v crystal violet in glacial acetic acid as indicator. This solution is titrated with 0.1 $HClO_4$. The colour changes from blue to blue green.

Assay Procedure : Weigh accurately about 0.17 g of Ephedrine Hydrochloride, dissolve in 10 ml of mercuric acetate solution, warming gently, add 50 ml of acetone and mix. Titrate with 0.1 M perchloric acid, using 1 ml of a saturated solution of methyl orange in acetone as indicator, until a red colour is obtained. Carry out a blank titration.

Equivalent or I.P factor : 1 ml of 0.1 M perchloric acid is equivalent to 0.02017 g of $C_{10}H_{15}NO,HCl$.

Calculations :

$$\%\ \text{Ephedrine Hydrochloride} = \frac{\text{X ml} \times \text{Normality (Calculated)} \times 0.02017 \times 100}{\text{N(Given)} \times \text{Wt. of sample(in gm)}}$$

Where,
X ml = Volume of titrant consumed at end point
Normality Calculated = Normality of Perchloric acid after standardisation
Normality Given = 0.1 N (theoretically)

3.

Chapter ... 3

NON-AQUEOUS TITRATIONS

◆ LEARNING OBJECTIVES ◆

- *To describe the necessity of the non-aqueous titrations.*
- *To identify the solvents applicable for non-aqueous titrations.*
- *To describe why the non-aqueous titrations are highly useful for weak acids and bases.*

OUTCOMES

On satisfying the requirements of this course, students will have the knowledge and skills to:

- Requirement of non-aqueous titrations, levelling effects of solvents and nature of the solvents.
- Quantitative analysis of the weak acids and bases by non-aqueous titrations.

3.1 SOLVENTS

Most of the titrations are performed in the aqueous media, means water is used as solvent. There may be difficulty if reactant is insoluble in water or reactant is reactive with water or the analyte (sample) is either too weak acid or too weak base.

Those too weak acids or bases can not be titrated in aqueous solution due to the amphiprotic behaviour of water (i.e. water can react as an acid on titration with a base and act as a base on titration with acid). So water will compete with the sample if it is weak acid or weak base.

The simple solution for this problem is to replace water as solvent with another non-aqueous solvent. So this type of titration is named *"Non-Aqueous Titration"*.

Reasons for Non-aqueous Titrations:

The reactant is insoluble in water: If the reactant compound is insoluble in water, then non-aqueous solvent is mandatory to dissolve the compound.

The reactant is reactive with water: If the reactant is reactive with water and converts its chemical composition when dissolved in water, then also non-aqueous titration method is used.

The sample is too weak acid or too weak base: If the reactant compound is very weak acid or base, then dissociation of the compound will be very less and enough concentration of the ion cannot be achieved and non-aqueous titration is preferred method.

3.2 TYPES OF SOLVENTS IN NON-AQUEOUS TITRATIONS

Protogenic solvents:

These are acidic solvents and used to enhance the basicity of weak bases.

Examples: Glacial acetic acid. (Anhydrous acetic acid is called glacial acetic acid, it is free from water content and solidifies at 16.7°C).

Protophilic solvents:

These are basic solvents and used to enhance the acidity of weak acids.

Examples: Pyridine, Ethylenediamine and Dimethylformamide (DMF).

Amphoteric solvents:

These solvents behave as acid as well as base depending on the substance dissolved in it. They can accept or donate protons.

Examples: Alcohols, Ethanol, Methanol.

Aprotic solvents:

These solvents neither accept proton nor donate proton. They are used in dissolving the drugs especially those are insoluble in water.

Examples: Benzene, Carbon tetrachloride.

Selection of solvent:

The selection of solvent in non-aqueous titration is based on:

***Solubility of drug*:** The weak acidic or basic drug should be soluble in the solvent which at the same time must be miscible with the titrant.

Nature of drug: The solvent is used according to the nature of drug, whether it is weak acid or weak base.

Unreactivity: The solvent should be unreacted with the drug.

Selected Examples of Non-Aqueous Solvents:

Many inorganic solvents are used in non-aqueous titrations, but most commonly used solvents are listed below:

1. *Glacial acetic acid (CH_3COOOH):*

It is also known as Glacial ethanoic acid and is most commonly used non-aqueous solvent. Before using glacial acetic acid, water content should be checked and permitted within the range of 0.1% and 1.0%.

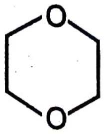
2. *Acetonitrile (CH_3CN):*

It is used with other solvents (chloroform, acetic acid) and enables sharp end points to be obtained in the titration of metal ethanoates when titrated against perchloric acid.

3. *Alcohols (CH_3OH, C_2H_5OH, C_3H_7OH, C_4H_9OH, $HOCH_2CH_2OH$):*

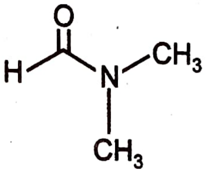
Methanol, ethanol, propanol, butanol and ethylene glycols are used as solvents for both polar and non-polar reactants in non-aqueous titration. All the solvents should be free from water content.

4. *Dioxane:*



Dioxane is also used in non-aqueous titration as a replacement of glacial acetic acid. Dioxane is not a levelling solvent.

5. *Dimethylformamid* (DMF):



DMF is a protophillic solvent and commonly used for titration of amides and benzoic acid in non-aqueous titrations.

3.3 LEVELLING EFFECT

The acidity of weak acids can be enhanced in presence of a basic solvent. This is because basic solvent has a higher affinity to take up protons from the acid. So acetic acid behaves as a strong acid in ammonia solution (basic solvent). Also the basicity of weak bases can be enhanced in presence of acidic solvent. This is called the **levelling effect** of the solvent. By using this concept, the strength of weak acidic or weak basic drugs can be enhanced by dissolving it in the appropriate solvent to enhance its strength and then can be titrated by acid-base titration (non-aqueous titration).

Moisture should be avoided in non-aqueous titration to increase the sharpness of the end point; also temperature should be kept constant during titration due to higher coefficients of expansion of organic solvents.

Differentiating Solvents: Degree of dissociation varies for different acids or basis in differentiating solvents; means these types of solvents do not gives levelling effect.

Example: A strong acid acts as a levelling solvent for bases, but a weak acid acts as a differentiating solvent for the acids, because complete dissociation not occurs. Same rule is applicable for strong basic and weak basic solvents.

3.4 ACIDIMETRY AND ALKALIMETRY TITRATION

Acidimetry:

It involves the quantitative determination of weak bases by non-aqueous titration.

Alkalimetry:

It involves the quantitative determination of weak acids by non-aqueous titration.

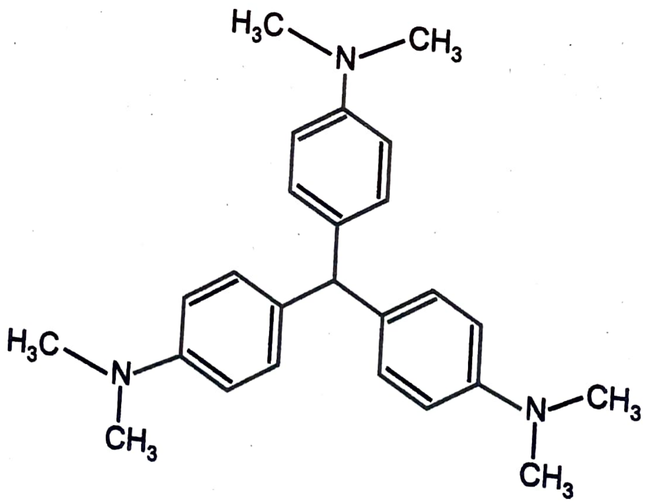
Details	Acidimetry	Alkalimetry
Samples:	Basic drugs such as: Ephedrine, Adrenaline, Caffeine, Acyclovir.	Acidic drugs such as: Nalidixic acid, Flurouracil.
Solvent:	Protogenic solvents such as: glacial acetic acid	Protophilic solvents such as: DMF
Titrant:	Perchloric acid $HClO_4$	Sodium methoxide.
Indicator:	Crystal violet (0.5% in glacial acetic acid) Colour change from violet to yellowish green.	Thymol blue (0.5% in methanol) Colour change from pink to blue.

3.5 INDICATORS

The ionized and non-ionized indicators are used for non-aqueous titrations, but colour changes during the end point vary for different titration, because it is dependent on the nature of the titrant. The resultant colour at the correct end point can be determined by carrying out a potentiometric titration and at the same time observing the colour change of the indicator.

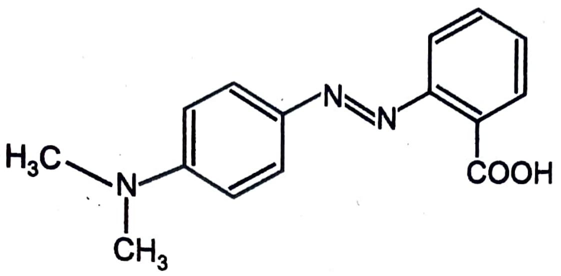
List of commonly used indicators in non-aqueous titrations are given below:

1. *Crystal Violet* (0.5% w/v solution in glacial acetic acid)



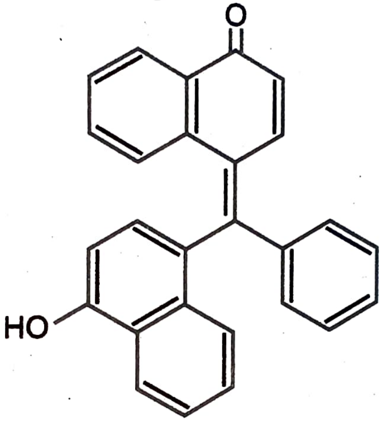
Colour change: Violet through blue followed by green, then to greenish yellow, in reactions in which bases such as pyridine are titrated with perchloric acid.

2. *Methyl Red* (0.2% w/v solution in dioxane)



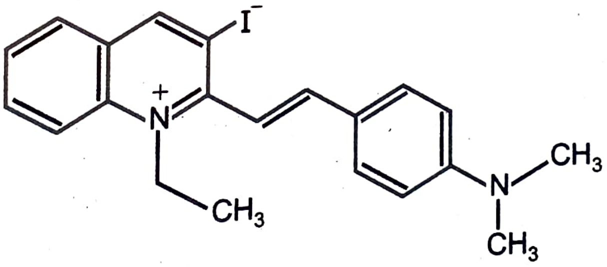
Colour change: Yellow to red colour.

3. *Naphthol Benzein* (0.2% w/v solution in glacial acetic acid)



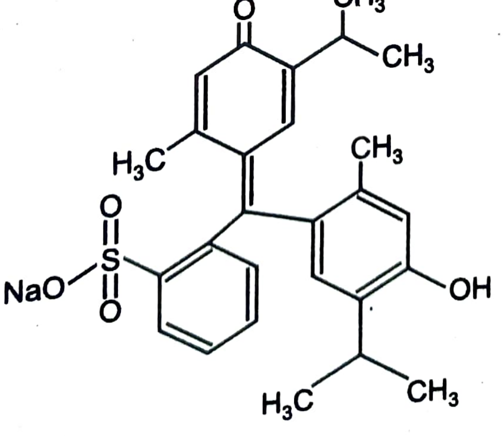
Colour change: Yellow to green colour change. It gives sharp end points in nitro methane containing acetic anhydride for titration of weak bases against $HClO_4$.

4. *Quenaldine Red* (0.1% w/v solution in ethanol)



Colour change: Purple red to pale green.

5. *Thymol Blue* (0.2% w/v solution in methanol)



Colour change: Yellow to blue at the end point.

Table 3.1 enlists the various cognate determinations using different indicators but employing the same titrant i.e. 0.1 N perchloric acid.

Table 3.1: Acidimetric indicators for non-aqueous titrations

Sr. No.	Name of Substance	Indicator Employed
1.	Amantadine hydrochloride	Crystal violet
2.	Cyproheptadiene HCl	Crystal violet
3.	Dehydroemetine HCl	Crystal violet
4.	Ephedrine hydrochloride	Crystal violet
5.	Imipramine hydrochloride	Crystal violet
6.	Isoprenaline hydrochloride	Crystal violet
7.	Lignocaine hydrochloride	Crystal violet
8.	Morphine hydrochloride	Crystal violet
9.	Morphine sulphate	Crystal violet
10.	Phenylephrine hydrochloride	Crystal violet
11.	Thiabendazole	Crystal violet
12.	Chlorpromazine hydrochloride	Methyl orange
13.	Promethazine hydrochloride	Methyl orange
14.	Clonidine hydrochloride	α-Naphthol benzene
15.	Phenytoin sodium	α-Naphthol benzene

Table 3.2: Alkalimetric indicators for non-aqueous titrations

Sr. No.	Name of Substance	Indicator Employed
1.	Bendrofluazide	Azo violet
2.	Acetazolamide	Potentiometric determination
3.	Amylobarbitone	Quinaldine red
4.	Allopurinol	Thymol blue
5.	Mercaptopurine	Thymol blue
6.	Nalidixic acid	Thymolphthalein

3.6 ESTIMATION OF SODIUM BENZOATE

Principle:

Assay of sodium benzoate is based on non-aqueous acid base titration method.

$$C_7H_5NaO_2 + HClO_4 \longrightarrow C_7H_6O_2 + NaClO_4$$

Preparation of Reagents:

Preparation of 0.1 N $HClO_4$:

Gradually mix 8.5 ml of perchloric acid to 900 ml of glacial acetic acid with vigorous and continuous stirring. Now, add 30 ml acetic anhydride and make up the volume to 1 litre with glacial acetic acid and allow to stand for 24 hours before use.

Experimental Methodology:

1. Weigh accurately about 0.5 g of potassium hydrogen phthalate in a 100 ml conical flask and add 25 ml of glacial acetic acid and attach a reflux condenser attached with a silica-gel drying tube.
2. Warm the conical flask until the salt gets dissolved completely.
3. Cool and titrate with 0.1 N perchloric acid by using acetous crystal violet indicator (2 drops).
4. Colour at the end point will be blue to bluish-green.
5. Accurately weigh about 0.25 g of sodium benzoate and dissolve in 20 ml of glacial acetic acid, heat the solution at 50°C if required and cool.
6. Titrate the above solution with 0.1 M perchloric acid, using acetous crystal violet indicator (2 drops) solution as indicator.
7. Colour at the end point will be blue to bluish-green.

Calculation:

$$\text{Each ml of 0.1 N } HClO_4 \equiv 0.01441 \text{ g of } C_7H_5NaO_2$$

$$\% \text{ purity of } C_7H_5NaO_2 = \frac{\text{Vol. of } HClO_4 \times \text{Actual normality of } HClO_4 \times 0.01441 \times 100}{\text{Weight of } C_7H_5NaO_2 \text{ (in g)} \times 0.1 \text{ (Expected normality of } HClO_4)}$$

Results:

Percentage purity of the given sample of sodium benzoate was found to be x %.

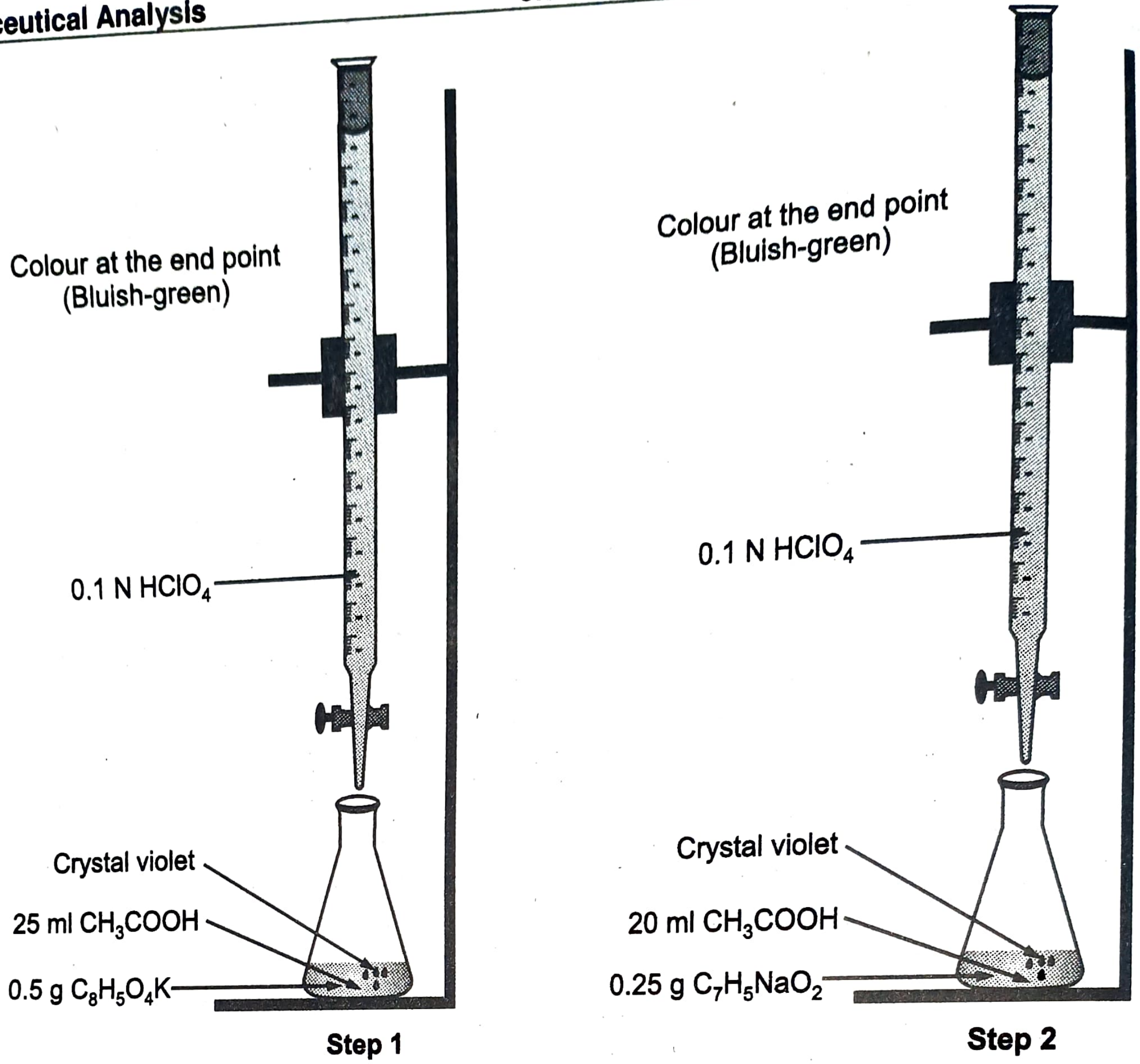


Fig. 3.1: Assay of $C_7H_5NaO_2$

3.7 ESTIMATION OF EPHEDRINE HCl

Principle:

Assay of ephedrine HCl is based on non-aqueous acid base titration method.

$$HClO_4 + CH_3COOH \longleftrightarrow CH_3COOH_2^+ + ClO_4^-$$

Onium ion

$$C_{10}H_{15}NO + CH_3COOH \longleftrightarrow C_{10}H_{15}N + HO + CH_3COO^-$$

Ephedrine Protonated ephedrine

$$CH_3COOH_2^+ + CH_3COO^- \longleftrightarrow 2CH_3COOH$$

Preparation of Reagents:

Preparation of 0.1 N $HClO_4$:

Gradually mix 8.5 ml of perchloric acid to 900 ml of glacial acetic acid with vigorous and continuous stirring. Now, add 30 ml acetic anhydride and make up the volume to 1 litre with glacial acetic acid and allow standing for 24 hours before use.

Experimental Methodology:

1. Weigh accurately about 0.5 g of potassium hydrogen phthalate in a 100 ml conical flask and add 25 ml of glacial acetic acid and attach a reflux condenser attached with a silica-gel drying tube.
2. Warm the conical flask until the salt gets dissolved completely.
3. Cool and titrate with 0.1 N perchloric acid by using acetous crystal violet indicator (2 drops).
4. Colour at the end point will be blue to bluish-green.
5. Dissolve 0.5 g ephedrine hydrochloride in glacial acetic acid, add few drops of crystal violet indicator and titrate with standard perchloric acid till the appearance of blue to bluish green.
6. Glacial acetic accepts the proton from perchloric acid to form the onium ions which is the actual titrating species. The onium ions react with acetate ions liberated after protonation of ephedrine hydrochloride.

Calculation:

$$\text{Each ml of 0.1 N } HClO_4 \equiv 0.02017 \text{ g of } C_{10}H_{15}NO.HCl$$

$$\%\text{ purity of } C_{10}H_{15}NO.HCl = \frac{\text{Volume of } HClO_4 \times \text{Actual normality of } HClO_4 \times 0.02017 \times 100}{\text{Weight of } C_7H_5NaO_2 \text{ (in g)} \times 0.1 \text{ (Expected normality of } HClO_4)}$$

Result:

Percentage purity of the given sample of ephedrine hydrochloride was found to be x %.

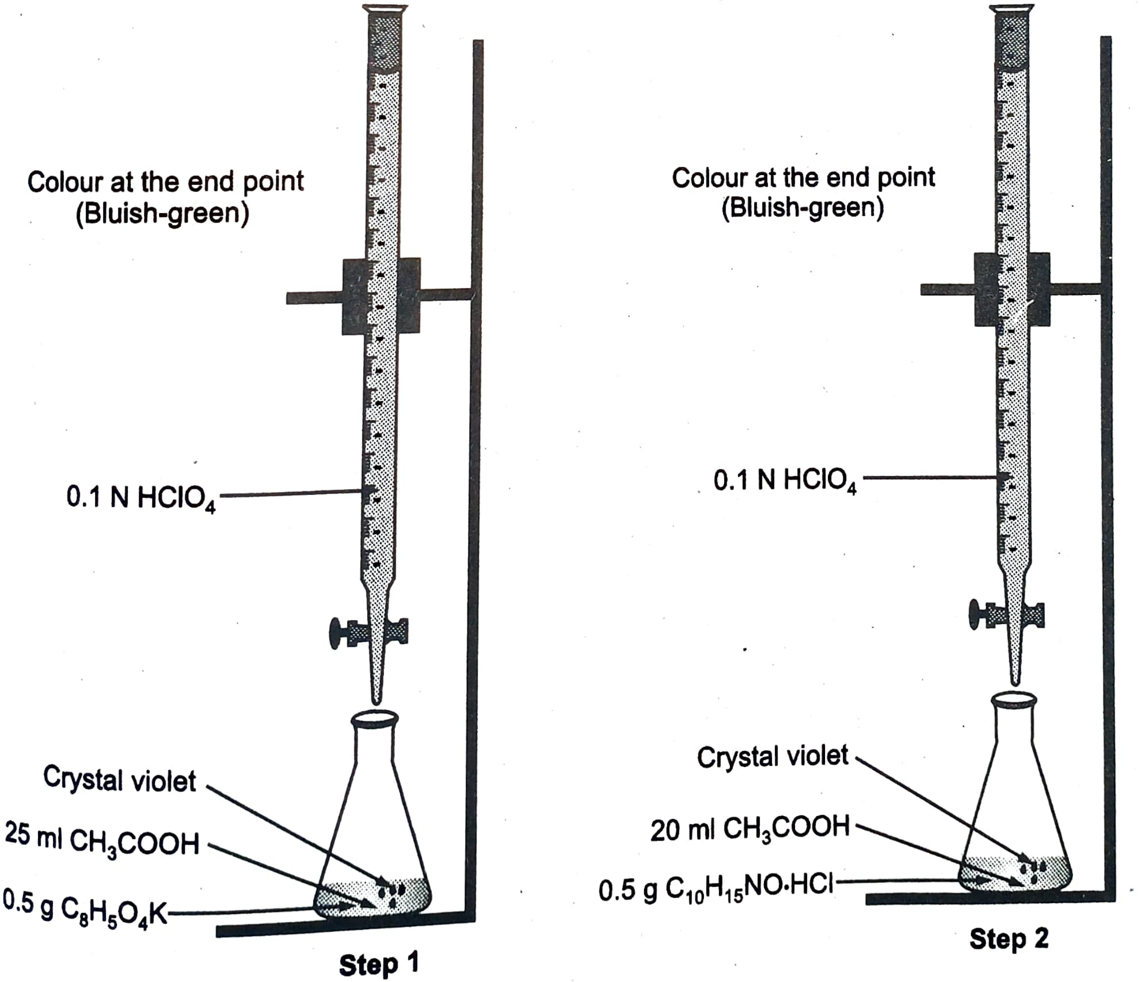


Fig. 3.2: Assay of $C_{10}H_{15}NO.HCl$

QUESTIONS

1. Define non-aqueous titrations?
2. Enlist types of drugs analyzed by non-aqueous titrations.
3. Enlist types of solvents used in non-aqueous titrations.
4. Explain differentiating solvents.
5. Give details about acidimetric and alkalimetric titrations.
6. Give the preparation and standardization method of 0.1 N perchloric acid.
7. What do you understand by levelling effect of solvent?
8. What are the indicators used in non-aqueous titrations?
9. Write a note on estimation of Ephedrine HCl by non-aqueous titrations.
10. Write a note on estimation of sodium benzoate by non-aqueous titrations.

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