DIAZOTISATION TITRATION

INTRODCTION

The process of forming diazonium compounds or salts is called *diazotation*, *diazoniation*, or *diazotization*

Diazonium compounds or **diazonium salts** are a group of organic compounds sharing a common functional group with the characteristic structure of $R\text{-}N_2^+ X^-$ where R can be any organic residue such alkyl or aryl and X is an inorganic or organic anion such as a halogen.

The reaction was discovered by **Peter Griess** in 1858, who subsequently discovered several reactions of the new compound. This method is first used in the determination of dyes.

Diazonium salts have been developed as important intermediates in the organic synthesis of dyes

Diazotization titrations are carried out for the estimation of drugs containing primary aromatic amino group.

Several drugs contain either primary aromatic amino group or they can be converted to have such groups by simple reaction like hydrolysis orreduction.

An primary aromatic amine reacts with nitrous acid produced by the reaction of sodium nitrite in acidic medium to form diazonium salt.

The reaction is quantitative under the controlled conditions of temp. (approx 15^0C) and the end point can be detected when a small quantity of excess nitrous acid present at the end point gives colour change with indicator or by electromerically.

It uses the titrant- Sodium Nitrite hence method is *Sodium Nitrite Titration / Nitrite Titration*

CONDITIONFOR DIAZOTIZATION

RATE OF TITRATION

Different amino compound react with HONO atdifferent rates

$NaNO_2$ added from the burette needs time to react with amino group accumulating in the solution

Amines are classified as rapidly, slowly diazotisable depending on the rate of conversion into azo compounds.

TEMPERATURE

The diazonium compounds formed are unstable and readily decompose at elevated temperature

This can lead to side reaction and give wrong result .

To eliminate this problem, this titration is carried out at lowtemperature ($0\text{-}5^0$C).

Optimum temperature for most amine is $10\text{-}15^0$ C, when they form relatively stable diazocompounds.

PRINCIPLE

The first involved is addition of sodium nitrite to hydrochloric acid cause formation of nitrous acid

$$NaNO_2 + HCl \longrightarrow HONO + NaCl$$

This nitrous acid diazotises the aromatic amino group

$$R - NH_2 + NaNO_2 + HCl \longrightarrow R - N^+ \equiv N - Cl^- + NaCl$$

After the end point , excess nitrous acid formed is shown by instant formation of blue colour with starch iodide paper.

$$KI + HCl \longrightarrow HI + KCl$$

$$NaNO2 + HCl \longrightarrow HNO2 + NaCl$$

$$2HI + 2HONO \longrightarrow I_2\uparrow + 2NO + 2H_2O$$

Starch iodide paper is prepared by immersing a filter paper in starch mucilage and potassium iodide solution

The iodine formed reacts with starch mucilage to give the blue colour.

$$I_2 + \text{Starch} \longrightarrow \text{blue color (end point)}$$

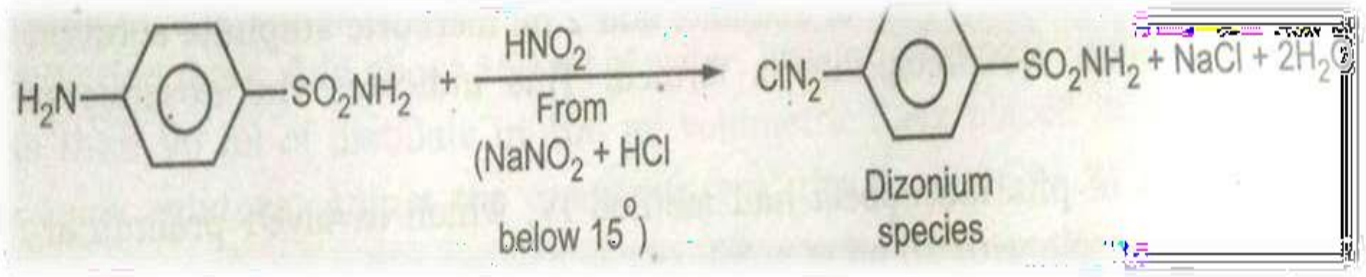
The end point can also be end point and potentiometric technique.

Method:

Weigh accurately 0.5 g sulphonamide add to it 20 ml of hydrochloric acid and 50 ml water, stirr, dissolve and cool to 15^0c. Immerse the electrode in the solution and apply the voltage of about 50 mV. Place burette tip just below the solution to eliminate oxidation of sodium nitrite. Stirr it gently & maintain the temp below 15^0c.

This method is suitable for most of the pharmacopoeial sulphonamides & its preparations as well as the drugs which contains primary aromatic amines.

The reaction with sulphonamide can be shown as,



Slow diazotisable compounds include compounds that contain sulpha groups, nitrous oxide group, or carboxylic group in aromatic ring or besides aromatic ring

Eg: isomeric nitro aniline, sulphanilic acid and anthranilic acid

Fast diazotisable compounds do not contain any substituent group other than amino group but some times they may contain $-CH_3$ or –OH group along with NH_2 group.

Eg : aniline, toluidine and aminophenol

Adding KBr to the solution can increase the rate of titration.

TYPESOFDIAZOTISATIONTITRATIONS

DIRECT TITRATIONS

These are carried out by treating 1 mole of the drug with 3 moles of acid solution.

Ice can be used to lower the temperature to about 0-5°c. 0.1M sodium nitrite is added in small amounts and titration is carried out.

The end point is determined by any one of the techniques as said before.

REVERSE METHOD

In this method a solution of amine and sodium nitrite are run into a solution ofacid.

This method is used when the diazonium salts are insoluble.

Eg: naphtylamine sulphonic acids form insolublediaonium salts due to formation of zwitterions.

SPECIAL METHOD

Aminophenol are readily oxidized by nitrous acid to quinones

For such substances , the titration is carried out in the presence of copper sulphate which formsdiazo-oxide

These diazo-oxides are more stable and undergo coupling reaction.

APPLICATIONS

The first use of diazonium salts was to produce water-fast dyed fabrics.

A more common process uses a paper coated with diazo.

It is also applicable in nanotechnology.

It is also used in the preparation of hydrocarbons, aryl halide, aryl cyanide and aryl hydrazines.

It is used in the assay of sulpha drugs like dapsone, sulphonamides, sulphacetamide sodium, sulphadiazine, sulphamethazole, sulphadoxine, sulphamethoxazole & sulphaphenazone etc.

It is also used in the assay of various drugs like benzocaine, procainamide, procaine, suramin, sodium amino salicylate, primaquine sulphate etc.,