

Diazotization titration

(Nitrite Titration)



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INTRODCTION

- The process of forming diazonium compounds or salts is called *diazotation*, *diazonation*, or *diazotization*
- **Diazonium compounds** or **diazonium salts** are a group of organic compounds sharing a common functional group with the characteristic structure of $R-N_2^+ X^-$ 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.



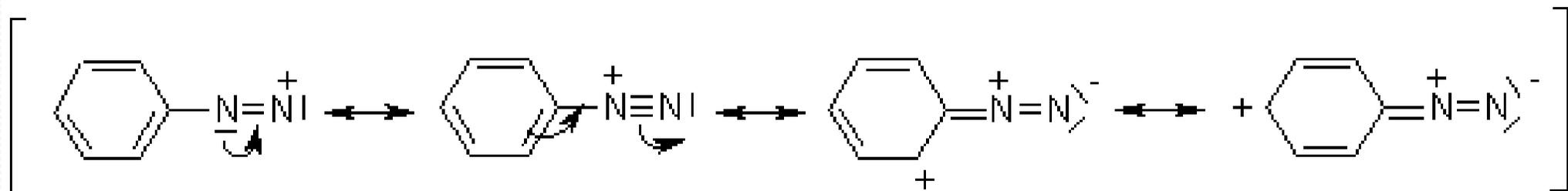
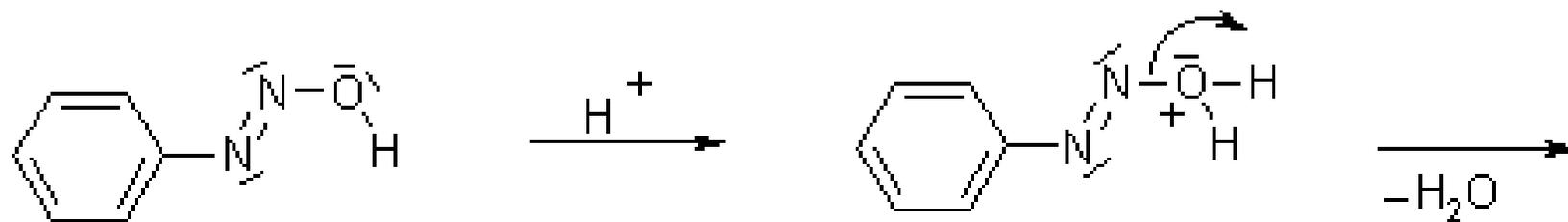
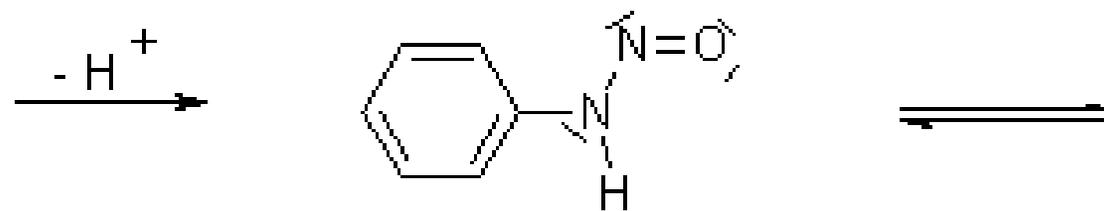
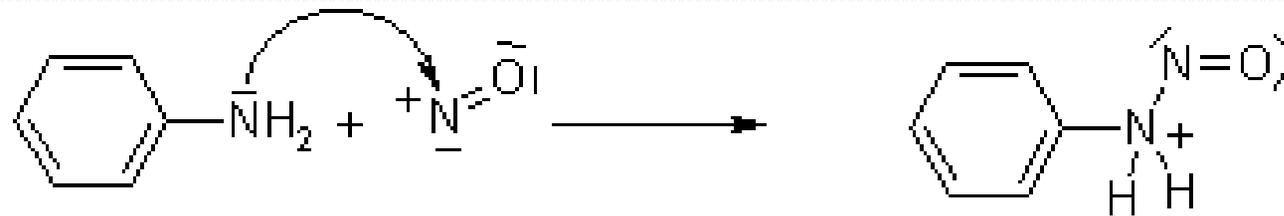
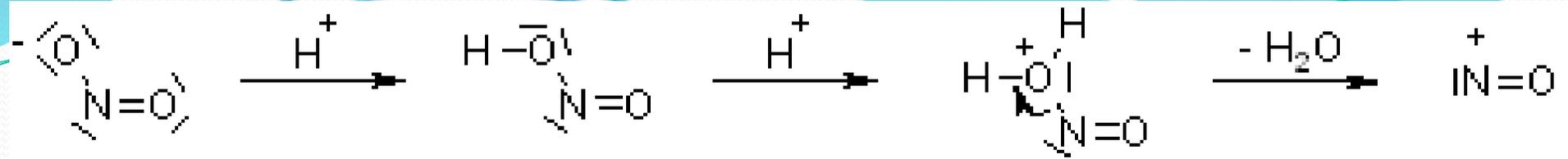
P. Griess

- 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 or reduction.

- 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°C) 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

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Mechanism of Diazotisation



CONDITION FOR DIAZOTIZATION

➤ RATE OF TITRATION

- Different amino compound react with HONO at different 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.

- 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 $-\text{CH}_3$ or $-\text{OH}$ group along with NH_2 group.
- Eg : aniline, toluidine and aminophenol
- Adding KBr to the solution can increase the rate of titration.

➤ TEMPERATURE

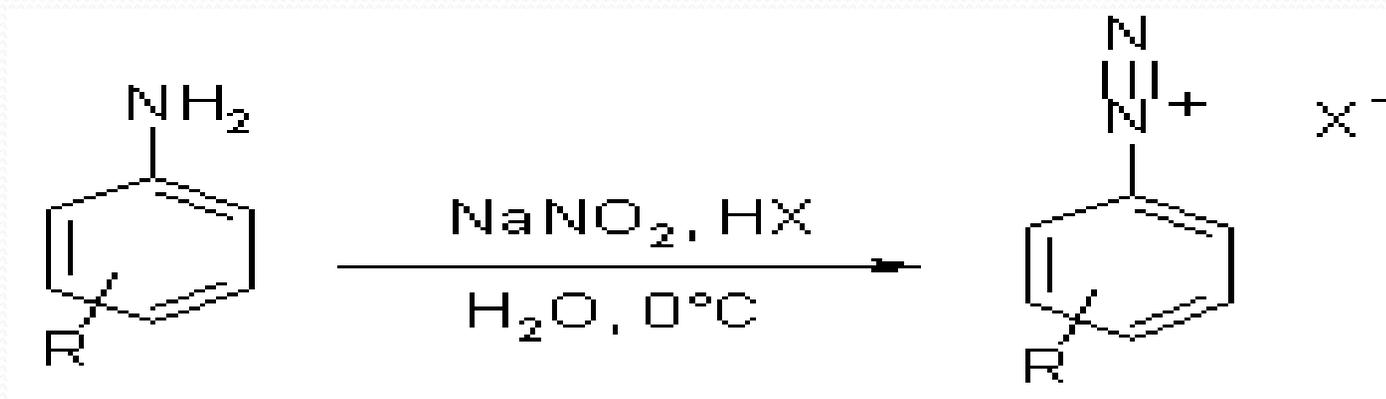
- The diazonium compounds formed are unstable and readily decompose at elevated temperature
- This can lead to side reaction and give wrong result .
- To eliminate this problem, this titration is carried out at low temperature ($0-5^{\circ}\text{C}$).
- Optimum temperature for most amine is $10-15^{\circ}\text{C}$, when they form relatively stable diazo compounds.

PRINCIPLE

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



- This nitrous acid diazotises the aromatic amino group



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



- 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.

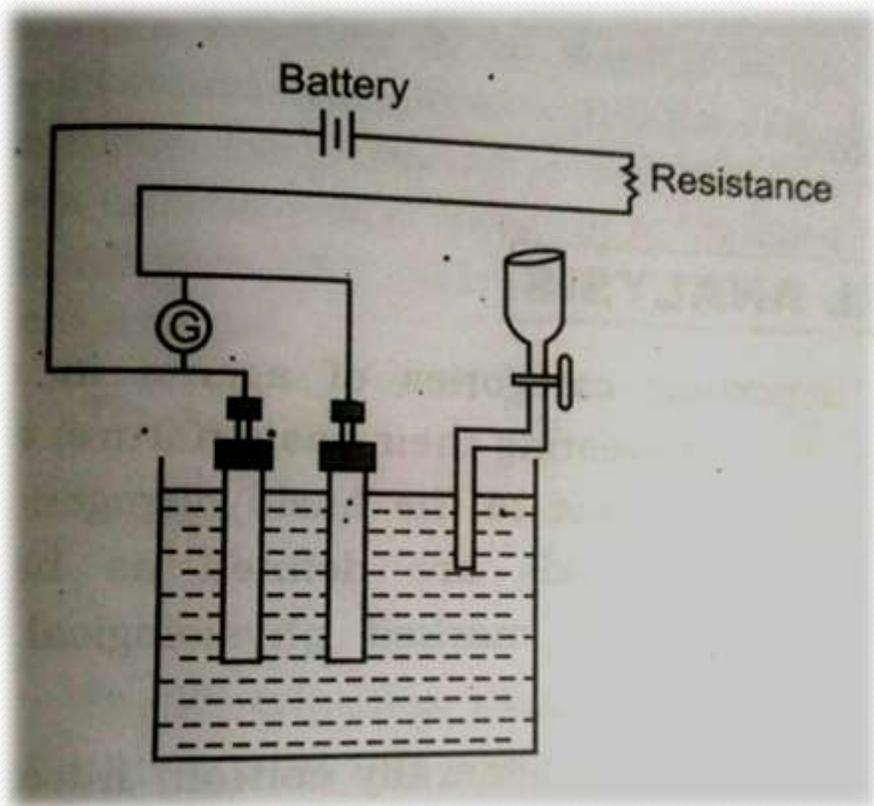


- The end point can also be determined by dead stop end point and potentiometric technique.

- ***IMPORTANT NOTE***

It is important to check the acidity at the end of the titration. If there is no excess of acid present in the solution, starch-iodide paper will not detect excess HNO_2 and so will not indicate the end point.

■ Potentiometric method for determination of end point (Electrometric method) :

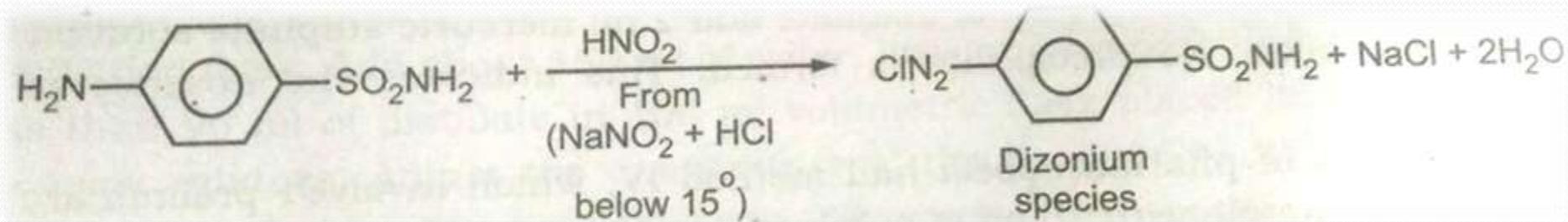


- Apparatus consists of a beaker (200 ml) capacity with two similar platinum electrode having 0.5 to 1.0 sq.cm surface area & placed 1.5 cm apart fitted with magnetic stirrer.
- 1.5 volt dry cell battery
- variable potentiometer with sensitive galvanometer.
- Surface of electrode cleaned by immersing boiling nitric acid with small amount of ferric chloride followed by washing with water.

Method:

- Weigh accurately 0.5 g sulphonamide add to it 20 ml of hydrochloric acid and 50 ml water, stir, dissolve and cool to 15°C. 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. Stir it gently & maintain the temp below 15°C.

- 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,



TYPES OF DIAZOTISATION TITRATIONS

- **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 of acid.
- ✓ This method is used when the diazonium salts are insoluble.
- ✓ Eg: naphthylamine sulphonic acids form insoluble diaonium salts due to formation of zwitter ions.

● 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 forms diazo-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 nano technology.
- 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 dapson, 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.

**Thank You for
Your Attention...!!!**

