Diazotization – Titrations

BY:RANJEET RANJAN

Diazotization Titration or Nitrite Titration:

Diazotization is used in the analysis of aromatic compounds containing an amino group in the molecules. This analysis is based on the reaction between aromatic primary amine ($–NH_2$), HONO, in presence of excess mineral or inorganic acids.

$NaNO_2$ is generally used in direct method of diazotization. It gives HNO_2 in acidic solution. Many aromatic primary amine with free $–NH_2$ group can be analyzed quantitatively by measuring the volume of $NaNO_2$ solution required to convert them into diazonium salts. The typical reaction of diazotization reaction in presence of HCl is given as:

$$NaNO_2 + HCl \longrightarrow HONO + NaCl$$
$$ArNH_2 + HONO + HCl \longrightarrow ArN_2Cl + 2H_2O$$

When all the aromatic amine has reacted with $NaNO_2$ then next portion (excess) of $NaNO_2$ added to the solution under test, converted to HONO that remain in the solution and can be detected by the starch paper or paste as an external indicator. This appearance of free HNO_2 in solution indicates that diazotization reaction is complete and equivalence point is attained.

Starch iodide paper or paste is the starch solution plus equal volume of 5% KI solution in H_2O. Starch iodide paste with reaction mixture is as follows-

$$KI + HCl \longrightarrow HI + KCl$$
$$2HI + 2HONO \longrightarrow I_2 + 2NO + 2H_2O$$
(excess)
$$I_2 + Starch \longrightarrow \text{blue color (end point)}$$

The liberated I_2 reacts with starch to give blue colour. The diazotization proceeds quantitatively only in presence of inorganic acid. It is important to check the acidity at the end of the titration. If there is no excess of acid present, starch – iodide paper will not detect excess HNO_2 and so will not indicate the end point.

Condition for diazotization:

(1) Rate of titration

(2) Temperature of the solution

(1) **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 besides aromatic ring.
Example: - 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.
Example: - aniline, toluidine and aminophenol.

Adding KBr to the solution can increase the rate of titration. In case of slowly diazotisable compound sufficient time (5-10 min) should be given to the solution under test. So, that last portion of nitrous acid could fully react with amine.

If the test for end point determination is carried out immediately after addition of the sodium nitrite, the nitrous acid so formed has not yet entered into the reaction with amine will be taken as excess nitrous acid, indicate the end point has reached. By sufficient stirring and slow addition of $NaNO_2$ and keeping in view the time factor, a large excess of $NaNO_2$ is not allowed to build up. It is also suggested that the burette tip is placed below the surface of reaction mixture to prevent the loss of HNO_2.

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

End point determination: - is done by two methods.

a. Visual end point determination method
b. Electrometric end point determination method.

(a) Visual end point determination method:

Principle: - aromatic primary amine reacts with sodium nitrite in acid solution (i.e, nitrous acid) to form diazonium salts.

$$C_6H_5NH_2 + NaNO_2 + HCl \longrightarrow C_6H_5N_2Cl + NaCl + 2H_2O$$

Under controlled condition reaction is quantitative and can be used for the determination of most substance containing a free primary amino group as in sulphanilamide and other sulpha drugs. Observation of end point depends upon the detection of small excess of nitrous acid, which is then present. This can be demonstrated visually by using starch iodide paste as external indicator.

$$KI + HCl \longrightarrow HI + KCl$$
$$2HI + 2HNO_2 \longrightarrow I_2 + 2NO + 2H_2O$$

The liberated iodine (I_2) reacts with starch to give blue colours.

Method: - weigh 2.5 gm of sample; transfer it into a 250 ml flask. Add 50 ml of concentrated HCl and 5 gm of KBr, adjust the final volume to 250 ml. pipette out 50 ml of this solution into a conical flask cool the solution so that the temperature is maintained between 10 to15 ^{0}C. Titrate the solution with N/10 $NaNO_2$ and shaking continuously until distinct blue color is produced on a small piece of starch iodide paper. The reaction is slow initially but behaves normal as the reaction proceeds.

(b) Electrometric End Point determination method:

Principle- End point may be detected electrometrically using a pair of bright platinum electrodes immersed in the titration liquid. Electrode polarization occurs in the titration liquid. Electrode polarization occurs when a small voltage (30-50 mμ) is applied across the electrodes and no

current flows through the sensitive galvanometer included in the circuit, during the course of titration. Liberation of excess of nitrous acid at the end point depolarizes the electrode, current flows and full deflection in galvanometer needle is observed. This is known as the dead stop end point.

The electrode must be clean other wise the end point is sluggish cleaning can be accomplished by immersing the electrodes in boiling nitric acid containing a little ferric chloride for about 30 sec and then washing with water. The blank determination is necessary, the difference between the two titrations represent the volume of sodium nitrite solution equivalent to the aromatic amine.

Method : Weigh accurately the sample (about 0.5 gm) and transfer into a 250 ml beaker and dissolve in the HCl 10 ml and water 75 ml. insert a pair of bright platinum electrodes into the solution, connected through a sensitive galvanometer and suitable potentiometer at a 2V battery in such a way as to produce a potential drop between 30-50 mμ across the electrodes.

Titrate slowly with N/10 $NaNO_2$ with continuous stirring until a permanent deflection of the galvanometer is observed at the end point.

Application of diazotization titration: An important pharmaceutical application of sodium nitrite titration is the analysis of sulphonamides by diazotization of primary aromatic amino group usually present in this class of drugs. Several sulphonamides require the formation of primary amine prior to diazotization step.

Example – phthalylsulphathiazole and succinyl sulphathiazole are first hydrolyzed to give primary aromatic amine and determined by $NaNO_2$ titration method.

List of compounds assayed by sodium nitrite titration:

(1) Dapsone
(2) Benzocaine
(3) Procaine hydrochloride
(4) Calcium amino salicylate
(5) Sodium amino salicylate
(6) Sulphacetamide tablet
(7) Sulphadoxine
(8) All sulpha drugs