Lab.10

Assay of sulfa drugs by diazotitration

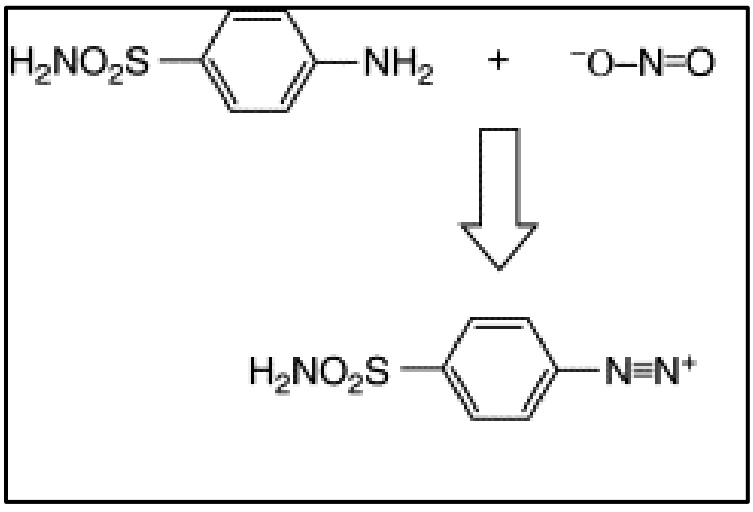
Diazotization Titrations

INTRODUCTION

The diazotization titration represents the conversion of the primary aromatic amine to a diazonium compound. This process was first discovered in 1853 and was applied to the synthetic dye industry. In this method, the primary aromatic amine is reacted with the sodium nitrite in acidic medium to form a diazonium salt. This method is first used in the determination of dyes.

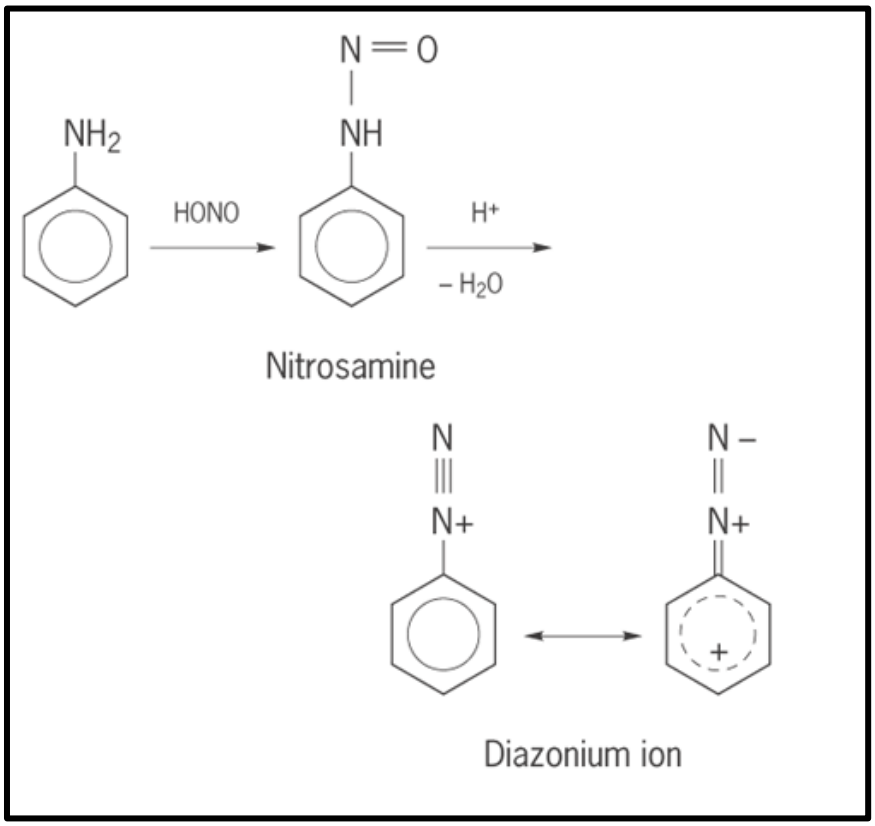
PRINCIPLE

The principle involved in this method is that the primary aromatic amine present in the sample reacts with the sodium nitrite in the presence of acid such as hydrochloric acid to obtain a diazonium salt.



Mechanism of the reaction

Sodium nitrite is added to the solution of sulfa drug in the presence of acid at 0–5 °C. it reacts with the nitrous acid to form nitrosamine, which is followed by the tautomerisation and the water molecule is lost to form the diazonium ion. This diazonium ion is stabilized by the displacement of the positive charge at the ortho and para positions of the ring.



The end point is detected by the formation of the blue colour with starch iodide paper. This is prepared by immersing the filter paper in the starch mucilage and potassium iodide solution.

$KI + HCl \rightarrow KCl + HI$
$2HI + 2HNO_2 \rightarrow I_2 + 2NO = 2H_2O$
I_2 + starch mucilage $\rightarrow$ blue colour end point

PROCEDURE

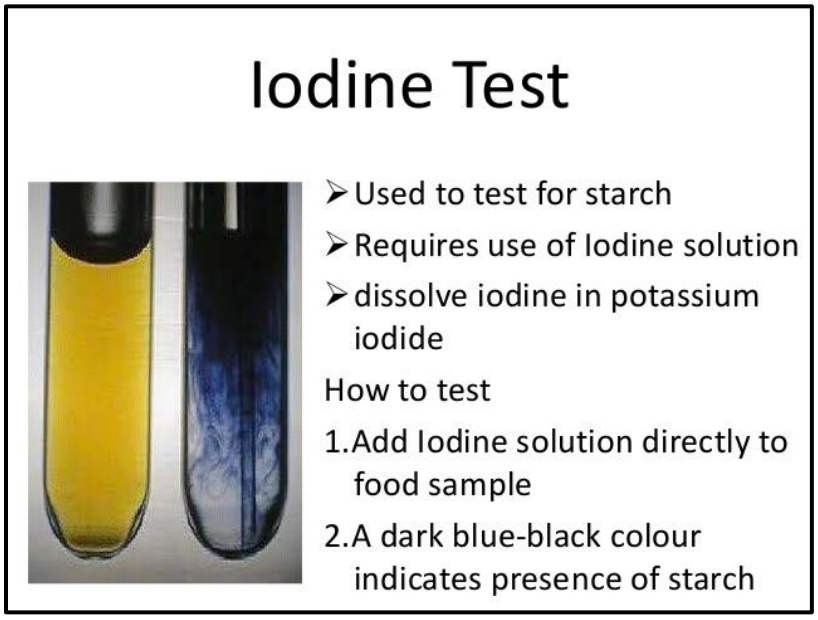
1- Weighing 0.4 g of the sulfa drug sample and transfer it into the standard flask.
2- Dissolve the sample in 100 ml distilled water
3- Then 5 ml of concentrated hydrochloric acid is added
4- The temperature is maintained at 0-5 °C.
5- Then the solution is titrated with the sodium nitrite solution until the starch iodide paper turns into blue colour.

END POINT DETECTION

The end point in diazotization titration is detected by the following procedure:

- The excess of nitrous acid is determined by the addition of the starch iodide as an external indicator. After diazotization, one drop of the resulting solution is placed on the starch iodide paper which changes into dark colour.

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



FACTORS AFFECTING THE DIAZOTIZATION

1- Acid concentration.
2- pH of the $NaNO_2$.
3- Temperature of the reaction (should be maintained at 0–5 °C): the diazonium compounds are decomposed at elevated temperatures.
4- Reaction time (it takes 10–15 min): the compounds react with nitrous acid at different rates based on the nature of the compound.
5- Slow diazotizable groups: sulpha groups, carboxylic groups and nitrogen oxide group.
6- Fast diazotizing groups: anilide, toluidine and aminophenol.

CONDITIONS FOR THE DIAZOTIZATION TITRATION

The following conditions are required for the diazotization titration of the amino group containing samples. They are as follows:

1- Rate of titration: Addition of sodium nitrite to the sample solution takes time to react with the amino group present in the sample solution. Different amino compounds react with the nitrous acid at different rates. Based on this, the amino compounds are classified into two main groups. They are as follows:

a- Slow diazotizable compounds

Example: Sulphanilic acid and anthranilic acid

b- Fast diazotizable compounds

Example: Aniline, aminophenol, and toluidine

c- The reaction rate is increased by the addition of the potassium bromide solution.

2- Temperature: Maintenance of the temperature is the main condition for the diazotization titration. The diazonium salts formed are not stable at elevated temperatures. They are readily decomposable at elevated temperatures, therefore, the temperature should be maintained at 0–5 °C.

ADVANTAGES

- Selective for the all types of sulphonamides.
- Sensitive
- Reproducibility

DISADVANTAGES

- Applicable for a very less variety of samples.
- Relatively slow when compared to other methods.
- Temperature conditions to be properly maintained throughout the reaction.
- The end point detection is very difficult.
- The colour produced is not stable.
- Lack of specificity.