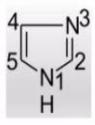
Characteristic Reactions of Imidazole



1. Electrophilic substitution

Imidazole is more susceptible to electrophilic attack than pyrazole. Electrophilic aromatic substitution of Imidazole involves through the intermediate formation of arenium ion.

Electrophilic substitution at 4 or 5 position in Imidazole is favoured due to the formation of highly stable resonance hybrid.

$$E^{+} + \bigvee_{H}^{N} \longrightarrow E^{+} \longrightarrow E^{+} \bigvee_{H}^{N} \longrightarrow E^{+} \longrightarrow E^{+$$

The attack at 2-position involves a canonical form with highly unfavoured nitrogen at 3-position. In case, positions 4 & 5 are blocked, substitution takes place in position-2.

a. Nitration: Imidazole undergoes nitration with nitric acid in sulphuric acid.

$$N$$
 + HNO $_3$ + H $_2$ SO $_4$ \longrightarrow O_2N N + O_2N N H O_2N N H O_2N O_2N

b. Sulphonation: Sulphonated with disulfuric acid at 100°C

c. Halogenation

i) Bromination: Brominated with bromine in chloroform

2, 4, 5- tribromoimidazole

ii) Iodination: Imidazole is iodinated with iodine in alkaline condition

2, 4, 5- triiodoimidazole

2. Alkylation

The imino hydrogen atom of Imidazole can be replaced by alkyl groups on reaction with alkyl halide. N-alkylimidazoles isomerise on passing through red-hot tube to 2-alkylimidazole.

3. Coupling reaction

Coupling of Imidazole with diazonium salts takes place in the 2-position.

$$\begin{array}{c|c} N & C_6H_5N_2CI & N \\ N & CH_3COONa & N=N-C 6H_5 \\ H & 2- (phenylazo)imidazole \\ \end{array}$$

4. Ring opening reaction

Benzoyl chloride in the presence of sodium hydroxide opens the Imidazole ring.

5. Oxidation and Reduction

Imidazole is extremely stable to oxidising and reducing agents, but hydrogen peroxide opens the nucleus to form oxamide.

Medicinal uses of Imidazole



Metronidazole

Metronidazole is used in the treatment of bacterial infections and parasitic infections. It is used in infections of the brain, reproductive system, gastrointestinal tract, vagina, skin and other areas of the body.

$$O_2N$$
 N
 CH_3
 CH_2CH_2OH

Metronidazole

Tolazoline

Tolazoline is a non-selective competitive α -adrenergic receptor antagonist. It is a vasodilator that is used to treat spasms of peripheral blood vessels.

$$\mathbb{I}_{N}$$

Tolazoline

Methimazole

Methimazole is used to treat hyperthyroidism, a condition that occurs when the thyroid gland produces too much thyroid hormone.

Methimazole (Thiamazole)

Tolazoline

Tolazoline is a non-selective competitive α -adrenergic receptor antagonist. It is a vasodilator that is used to treat spasms of peripheral blood vessels.

$$\mathbb{I}_{N}$$

Tolazoline