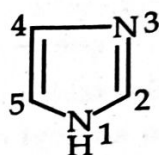


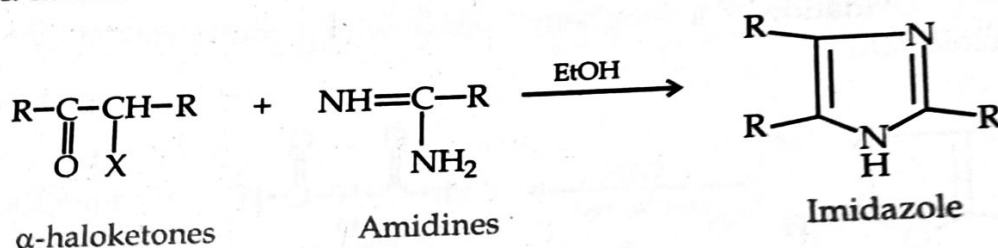
IMIDAZOLE



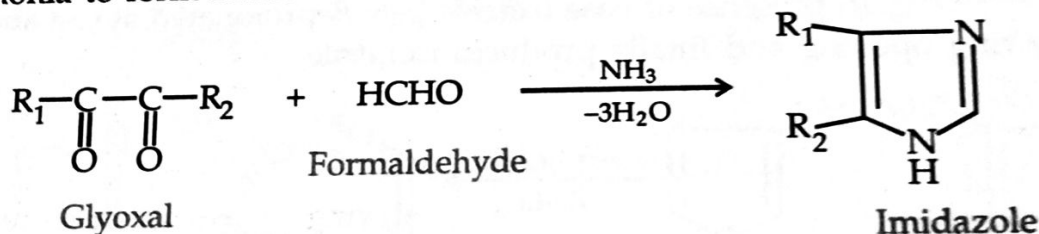
Imidazole is an aromatic heterocycle with the formulae $C_3N_2H_4$. It is a white or colourless solid that is soluble in water and produce alkaline solution. Most of naturally occurring alkaloids contain the imidazole ring. Many drugs such as antifungal drugs, antibiotics, sedative also contains imidazole ring.

Methods of Preparation :

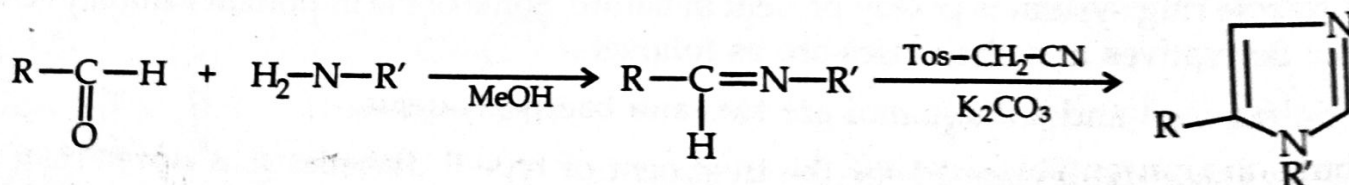
1. **From α -haloketones :** α -haloketones reacts with amidines to form imidazole.



2. **Debus method :** It involves reaction between glyoxal with formaldehyde in presence of ammonia to form Imidazole.

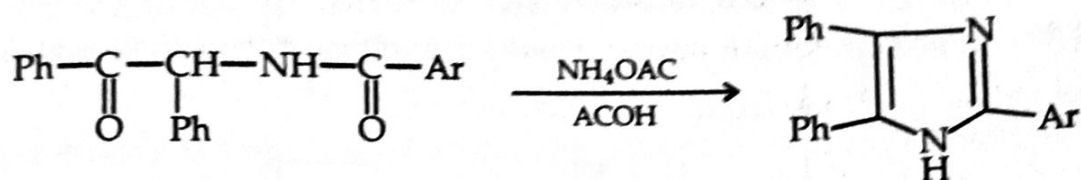


3. **Van-Leusen Synthesis :** This method involves the preparation of imidazoles from aldimines by reaction with tosylmethyl isocyanide. In this aldimine is first generated in situ by reaction of aldehyde and amine.

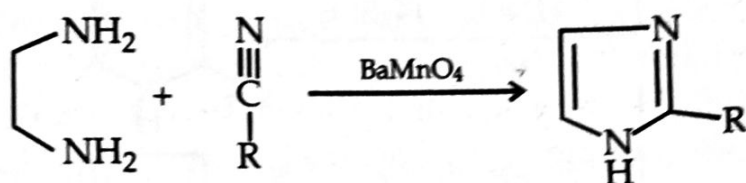


4. **Robinson-Gabriel Synthesis :** Acylamino ketones on reaction with ammonium ac-

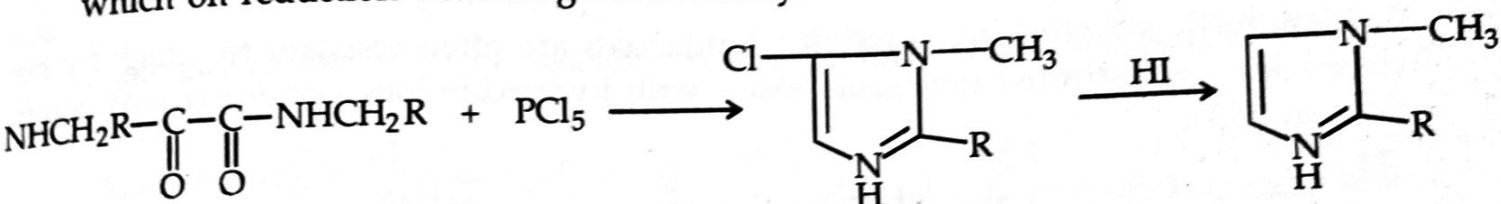
etate in presence of acetic acid forms imidazole.



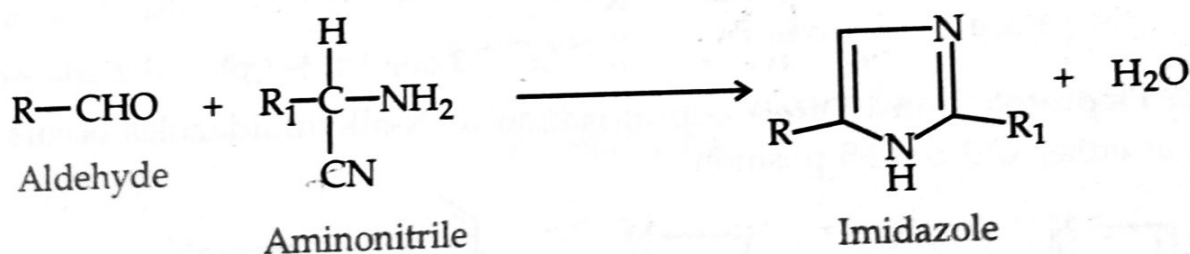
5. **Dehydrogenation of Imidazoline** : Barium managnate convert imidazolines into imidazole in the presence of sulphur. Imidazolines itself obtained from 1,2 ethenediamine and alkyl nitriles.



6. **Wallach Synthesis** : N,N-dimethyloxamide on reaction with PCl_5 gives a product which on reduction with HI gives N-methyl imidazole.

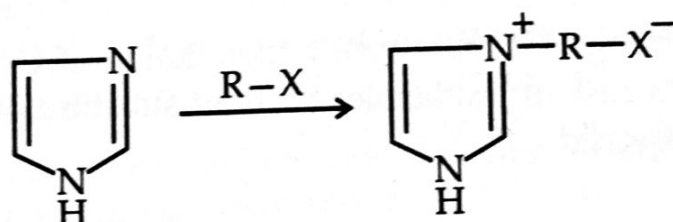


7. **From Aminonitrile and Aldehyde** : Mixture of an aldehyde and aminonitrile on condensation under suitable conditions gives substituted imidazoles.

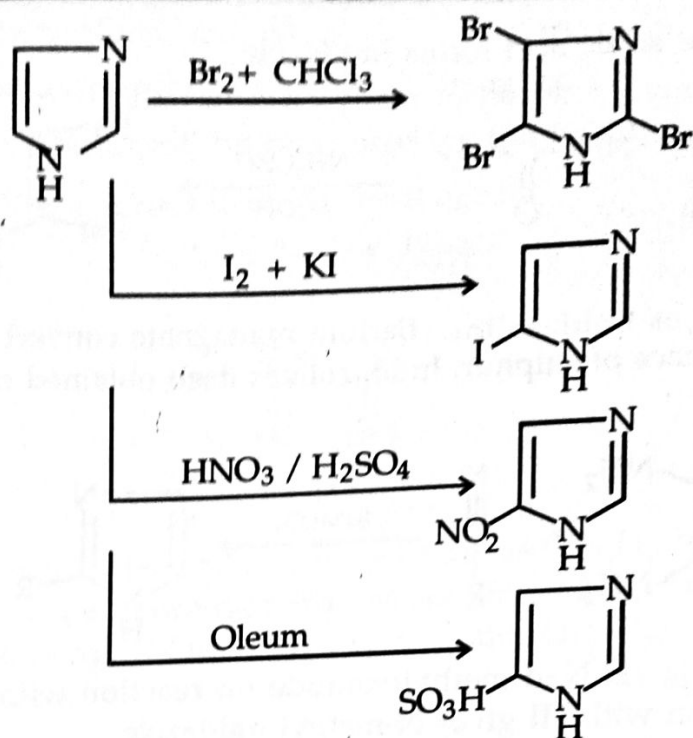


Chemical Reactions of Imidazoles

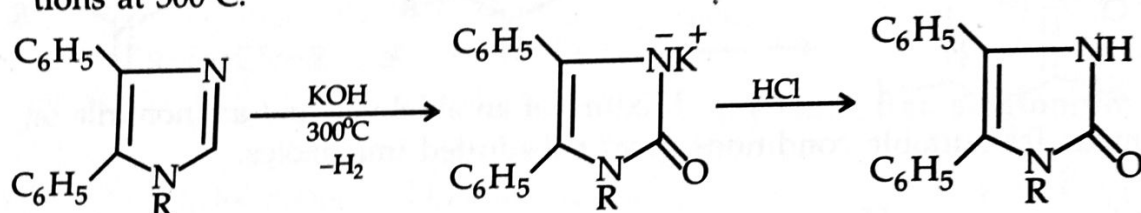
1. **Formation of Quaternary salts** : Imidazoles carrying a substituent on nitrogen on reaction with alkyl halides forms quaternary salts.



2. **Electrophillic substitution reaction** : Electrophillic substitution occurs at C-2 and C-5 but substitution at C-2 would be unfavourable as compared to C-5 because the charge in the intermediate cation has to be delocalized through the imine nitrogen.

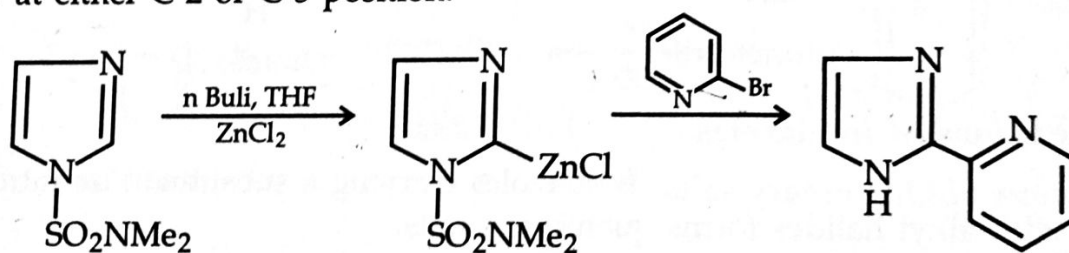


3. **Nucleophilic substitution reaction** : Imidazoles are often resistant to attack by nucleophiles. 1-substituted imidazole reacts with hydroxide ions under extreme conditions at 300°C.

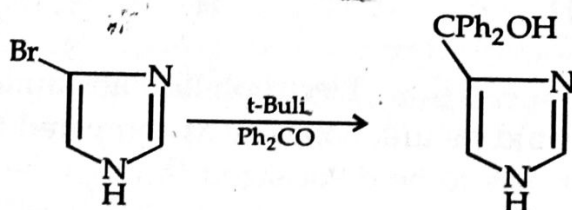


3-alkyl-4, 5-diphenyl-2-imidazolinone

4. **Direct Deprotonation** : Direct deprotonation of N-alkylimidazoles occurs preferentially at either C-2 or C-5 position.



5. **Metal-Halogen Exchange (Metallation)** : Metallation at C-4 position occurs by metal-halogen exchange. In case of imidazoles without substitution at 1-position, two equivalents of base are required.



MEDICINAL USES OF IMIDZOLE

Imidazoles are an important part of many pharmaceuticals. Synthetic imidazoles are a part of many fungicides and antifungal drugs, antiprotozoal & various antihypertensive agents.

Imidazole moiety is present in theophylline molecule which is present in tea and coffee leaves and which helps in stimulating CNS.

Mercaptopurine, an anticancer drug also contains imidazole ring and helps in the treatment of leukemia by causing interference with DNA activities.

Substituted imidazoles are also useful as antiinflammatory. For example, clotrimazole acts as selective inhibitors of nitric oxide synthase. Various imidazole derivatives are also useful as they causes down regulation of intracellular Ca^{+2} and K^{+2} fluxes and also causes interference with translation initiation.

Various azole antifungals includes Ketoconazole, Miconazole and Clotrimazole. Some imidazole derivatives are insecticidal also. For example, Sulconazole nitrate has a strong anti-feeding effect on the carpet beetle larvae. Econazole nitrate also has same effect and use.

Some, nitroimidazoles like metronidazole are active against intestinal infections to control amoebic dysentary.

Imidazole ring occurs in a number of naturally occurring compounds. For example, L-histidine which is an essential amino acid contains imidazole moiety. Histidine gets decarboxylated into histamine which causes stimulation of glands and smooth muscles and dilation of capillaries. It also causes allergies and gastric ulcers.

Imidazole ring is present in many H_2 receptor antagonists to control gastric acidity and to treat peptic ulcer. For example Cimetidine has been used as antiulcer drug.