CHB-401: Heterocyclic Compounds (Section B)

PYRIDINE

Organic Chemistry III

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INTRODUCTION

Pyridine is a basic heterocyclic organic compound with the chemical formula C_5H_5N . It is structurally related to benzene, with one methine group (=CH–) replaced by a nitrogen atom. It is a highly flammable, weakly alkaline, water-miscible liquid with a distinctive, unpleasant fish-like smell. Pyridine is colorless, but older or impure samples can appear yellow. The pyridine ring occurs in many important compounds, including agrochemicals, pharmaceuticals, and vitamins. Historically, pyridine was produced from coal tar.



AROMATICITY

Pyridine have 5 Carbon and 1 Nitrogen, all are sp^2 hybridised, sp^2 hybridization is planar, it makes a planar pyridine ring structure. Each ring atoms containes one electron in unhybridized p orbital that is perpendicular to the plane of sigma bonds (plane of ring). p orbitals are parallel to each other, thus overlapping between p orbital is possible. The total numbers of non bonding electrons are 6 (5 of five carbons, and 1 from N). The resonance of 6 electrons follows the Huckel rule which makes pyridine an aromatic system.

BASICITY

Pyridine is more basic than pyrrole because in Pyridine the non bonding electrons on N atom is in the same plane of pyridine hybridized orbitals plane, so it is not participating in resonance phenomenon, due to this the lone pair of electrons on Nitrogen are readily available for acid-base reaction.

Nitrogen atom of pyrrole has lone pair of electrons perpendicular to pyrrole hybridized orbitals plane, here the lone pair of electron participate in resonance phenomenon, due to this the lone pair of electron on N is not readily available for acid-base reaction. Pyridine is less basic than aliphatic amines

RESONANCE STRUCTURE



Resonance energy of pyridine is about 125 KJ mol⁻¹

Hydrogen bonding in pyridine. Pyridine is soluble in water



HANTZSCH SYNTHESIS OF PYRIDINE



MECHANISM





FROM 1, 5 DICARBONYL COMPOUNDS



FROM PENTAMETHYLENEDIAMINE



Pyridine can also be prepared by 2-furyl ketone and ammonia



Electrophilic substitution reaction in pyridine occurs at position 3



N is electronegative atom positive charge on N destabilize the ring, here attack at position 2 and position 4 generates N with positively charged intermediate, thus are less favorable for attack. Only attack at position 3 is favourable as it positively charged N intermediate is not formed

REACTIVITY

Pyridine has a high resonance energy and its structure resembles that of benzene quite closely. The presence of the nitrogen atom in the ring does, of course, represent a major pertubation of the benzene structure. The lone pair orthogonal to the π - system provides a site for alkylation and protonation which has no analogy in benzene. Many of the properties of pyridine are thus those of a tertiary amine and the aromatic sextet is not involved in these reactions. The other major influence of the nitrogen atom is to distort the electron distribution both in the π -system and in the sigmabonds (by an inductive effect). This confers on the system some of the properties which are associated with conjugated imines or conjugated carbonyl compounds.

Electrophilic addition to N

Protonation



FORMATION OF ANHYDRO-BASE

Pyridine forms quarternary salts when heated with alkyl halides. Pyridine when reacts with methyl iodide forms methiodide or 1-methylpyridinium iodide which on heating at 300°C gives 2- and 4-methyl pyridine (Hoffmann Martius rearrangement)

When quarternary hydroxides are heated water is eliminated with the formation of anhydro-base. This is possible only when there is a suitable alkyl group in 2- or 4- position



ELECTROPHILLIC SUBSTITUTION REACTIONS IN PYRIDINE



NUCLEOPHILIC SUBSTITUTION REACTION

Pyridine undergoes nucleophilic substitution reaction at postion 2.



CHICHIBABIN REACTION



Mechanism



PYRIDINE-1-OXIDE

Pyridine is oxidised by per acids (m-chloroperbenzoic acid, perbenzoic acid etc.) to pyridine oxide



The canonical structures of pyridine shows that low and high charge densities occur at position 2 and 4. Thus pyridine N-oxide is more reactive than pyridine. Since Oxygen atom of pyridine can be easily removed, it becomes a powerful method for the preparation of pyridine derivatives that are difficult to prepare by any other route Preparation of pyridine derivatives that are difficult to prepare by any other route



HOFMANN EXHAUSTIVE METHYLATION OR DEGRADATION

Hofmann exhaustive methylation or degradation It is a most important method of opening heterocyclic rings. Hexahydro pyridine (piperidine) is repetedly methylated to form quarternary salt. Anion is replaced by hydroxide using silverhydroxide. On elimination alkenes are formed

