Review Article

A Review on Pyridine Derivatives Having Appropriate Remedies for Extreme Diseases

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ABSTRACT

A large and emergent demand for the pyridine derivatives exists because of their many medicinal, pharmaceutical and agricultural uses. The pyridine derivatives have several considerable biological applications such as anticonvulsant, antimicrobial, anticancer, antidiabetic agents. This created interest in researchers to synthesize verity of pyridine derivatives. In this review we have summarized the biological uses of number of pyridine derivatives.

Keywords: Pyridine, Synthesis, derivatives, Biological use.

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INTRODUCTION

Pyridine is a heterocyclic organic compound with the chemical formula C5H5N. It is structurally related to benzene where the one CH group in aromatic six membered ring is replaced by nitrogen atom. Pyridine has a conjugated system of six π-electrons exactly as benzene, that are delocalized over the heterocyclic ring. Pyridine was industrially produced by extraction from coal tar. It is currently synthesized from formaldehyde, ammonia and acetaldehyde.

$$CH2O + NH3 + 2CH3CHO \rightarrow C5H5N + 3H2O$$

Pyridine is an important solvent and reagent in organic synthesis. It is used as solvent in Knoevenagel condensations. Pyridine is widely used polar and aprotic solvent. It is miscible with broad range of solvents including hexane and water[1].

Structural Characteristics

Pyridine is an aromatic compound have five carbon atoms and one nitrogen atom. However, the nitrogen's lone pair of electrons is a sp2 orbital orthogonal to the *p* orbitals of the ring. Therefor it is not involved in maintain aromaticity, but it is available to react with ptrotons thus pyridine is basic.

Figure: 1

Pyridine can be represented as a resonance hybrid of the following structures.

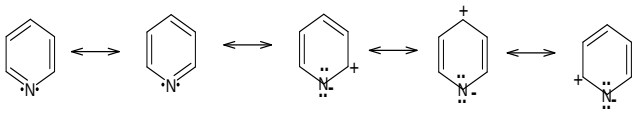

Figure: 2

Due to the greater electronegativity of nitrogen (relative to carbons) it tends to withdraw the electron density from carbon atoms at positions 2,4 and 6 which therefore acquire partial positive charges while the N atom acquires partial negative charge while the carbons at positions 3and 5 remains neutral. Nitrogen containing six membered aromatic pyridine and its derivatives abundantly exist in nature and they play a vital role in the field of heterocyclic chemistry.

Properties

Physical properties[3]

- Pyridine is a colourless refractive liquid.
- Its boiling point is 115.5^{o}C and melting point -41.6^{o}C.
- It has characteristic unpleasant odour.
- It is soluble in water and most organic solvents.
- Pyridine is conventionally detected by the gas chromatography and mass spectrometer.

Chemical properties

1. Reaction which followings with participation of heteroatom.

   i. Reaction with oxide of sulphur.

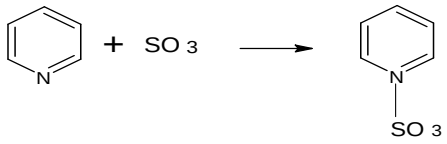

Figure: 3

2. Reaction of substituting for the hydrogen atoms of pyridine ring.

   i. Reaction of electrophilic substitution.

The reactions of nitration and sulfonation pass slowly drastic and with low exists. Thus, an electrophilic reagent is direct in position 3.

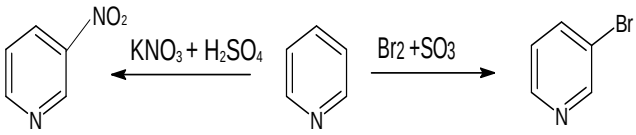

Figure: 4

   ii. Reactions of nucleophilic substitution.

The substitution goes on positions 2,4,6 most easy of nucleophilic reagent is entered in position of 2,6 (α-position). The prime example of reaction of this type is an amination of pyridine with sodium of amide on chychybabyne. The reaction follows to the mechanism SN2.

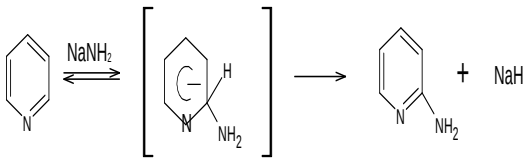

Figure: 5

3. Reactions of oxidation & reduction.

   i. Reduction.

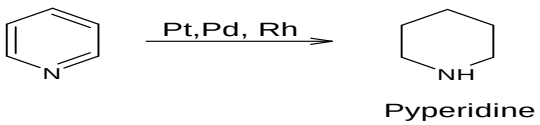

Figure: 6

   ii. Oxidation.

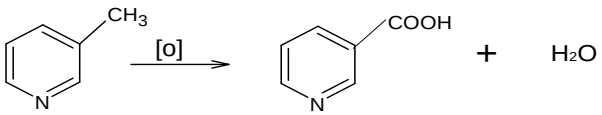

Figure: 7

Synthesis of Pyridine and Its Derivatives

Pyridine was first synthesized by Wiliam Ramsay in 1876, by combining acetylene and hydrogen cyanide, a red hot iron-tube furnace was used to carry out the reaction. It was the ever first synthesis of hetero aromatic compound. Nitrogen containing six membered aromatic pyridine and its derivatives abundantly exist in nature and they play a vital role in the field of heterocyclic chemistry.

Now-a-days several methods are available for the synthesis of pyridine and its derivatives, some of these are given below in scheme 1-5.

1) Synthesis of DMAP[4-(N,N-dimethylamino) Pyridine] Derivative[4] .

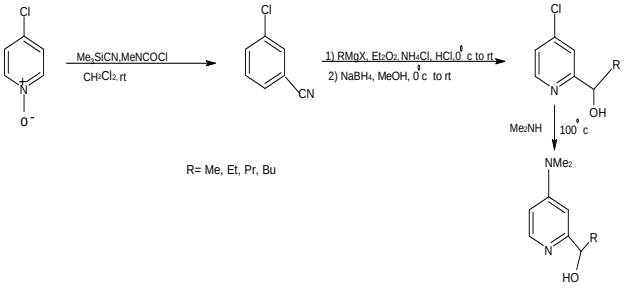

Figure: 8

2) Synthesis of novel Series of Imidazo Pyridine Derivatives[5].

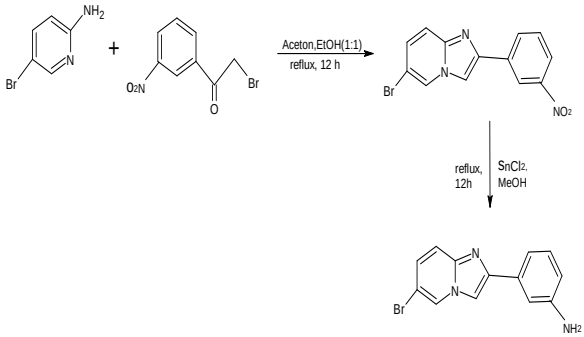

Figure: 9

3) Oxidative Polycondensation Reaction of 3-Aminopyridine[6].

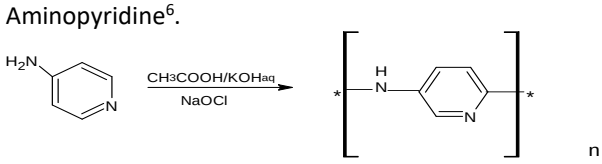

Figure: 10

4) Synthesis of Pyridine-Quinoline hybrid[7].

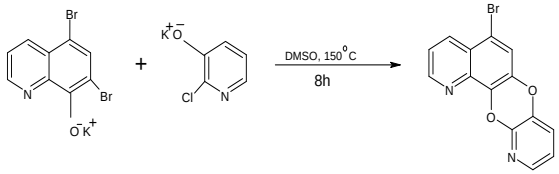

Figure: 11

5) Hantzsh pyridine synthesis[8].

It is a multi-component organic reaction between an aldehyde ,2 equalents of a β-keto ester and a nitrogen donor. The initial reaction product is a dihydropyridine which can be oxidized in a subsequent step to a pyridine.

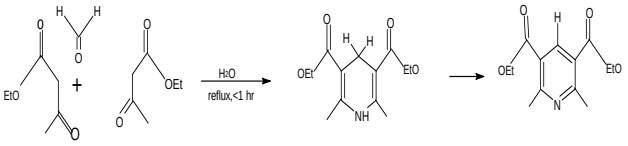

Figure: 12

Pharmacological Activities:

Anti-Convulsant Activity

Huang et al 6 carried out structure-activity relationship studies on 3-(5-pyridin-2-yl-2H-tetrazol-2-yl)benzonitrile that led to the discovery of 2-{2-[3-(pyridin-3-yloxy)phenyl]-2H-tetrazol-5-yl}pyridine, a highly potent and selective mGlu5 receptor antagonist with good brain penetration and in vivo receptor occupancy in rat and cross-species oral bioavailability[9].

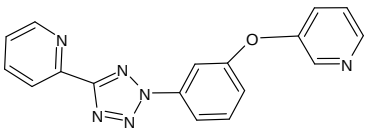

Figure: 13

Antimicrobial Activity

Starr et al synthesized 5-(2-pyrimidinyl)-imidazo[1,2-a]pyridine, which is found to be dual inhibitors of bacterial gyrB and parE and exhibited excellent performance against important Gram–positive pathogens including wild type and methicillin-resistant staphylococcus and wild type and FQR streptococcus and possess desirable in-vivo pharmacokinetic and efficacy properties[10].

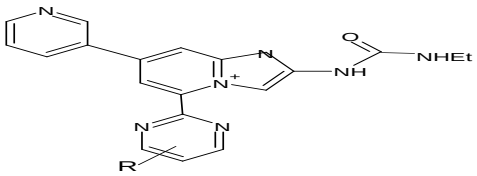

Figure: 14

Anticancer Activity

Basnet et al synthesized a series of 2,6-dithienyl-4-furyl pyridine derivatives and evaluated for the topoisomerase I and II inhibitory activity as well as cytotoxicity against several human cancer cell lines. Compound showed strong topoisomerase-I inhibitory activity[11].

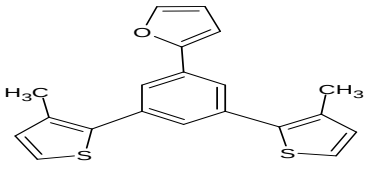

Figure: 15

Antiviral Activity

Vrencken et al reported that 5-[(4-bromophenyl)methyl]-2-phenyl-5H-imidazo[4,5-c]pyridine (BPIP) to be highly potent inhibitor of the in vitro replication of CSFV(classical swine fever virus) thus having the potential to control the spread of infection in an epidemic situation. This compound resulted in a dose-dependent antiviral effect in PK15 cells with a 50% effective concentration (EC50) for the inhibition of CSFV Alfort187 and for CSFV Wingene[12].

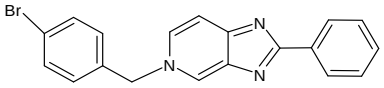

Figure: 16

Antidiabetic Activity

A novel class of 1H-(benzimidazol-2-yl)-1H-pyridin-2-one inhibitors of insulin-like growth factor I (IGF-1R) kinase was described by Wittman et al. 27 They discussed the SAR of 4-(2-hydroxy-2-phenylethylamino)-substituted pyridones with improved IGF-1R potency[13].

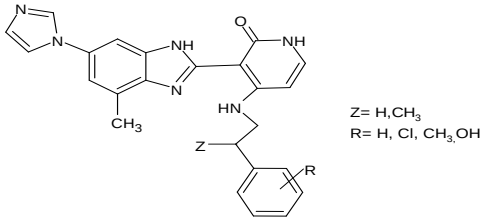

Figure: 17

Marketed Formulations

1) ETORICOXIB
   1. Chemical formula: $C_{18}H_{15}ClN_2O_2S$
   2. Selective COX2 inhibitor
   3. Trade name of etoricoxib is Arcoxia

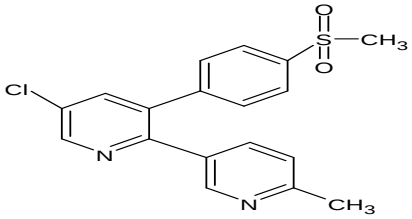

Figure: 18

2) PERAMPANEL
   - Chemical formula: $C_{23}H_{15}N_3O$
   - Antiepileptic drug used to treat partial seizures and generalized tonic- clonic seizures.
   - Other names: E2007, Fycompa.

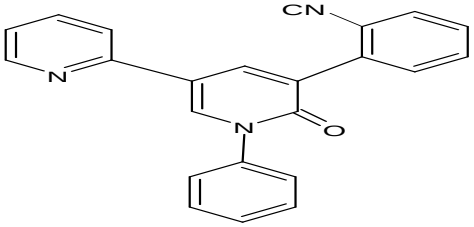

Figure: 19

CONCLUSION

Drugs containing pyridine nucleus have wide spectrum of applications in heterocyclic as well as in pharmaceutical field which are pharmacologically and physiologically active and it is used in the treatment of various diseases. On the basis of various literature surveys pyridine derivatives show various activities like anti-cancer, anti-convulsant, anti-microbial, anti-diabetic, anti-viral.the possible improvements in the activity can be further achieved by slight modification in the substitution the basic pyridine nucleus. Thus, pyridine has been long focused for research interest in the field of medicine, due to excellent activities exhibited by its derivatives.

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