



**REVIEW ON VARIOUS MOLECULE ACTIVITY, BIOLOGICAL ACTIVITY &  
CHEMICAL ACTIVITY OF PYRIDINE**

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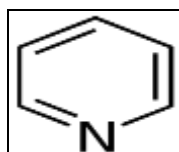
**ABSTRACT**

Derivatives of pyridine and pyridine are the important chemical compounds with lots of application in the various fields. In this review we have summarized the physical, chemical, molecular property, synthesis & biological activity of pyridine molecule for various different type of diseases. Pyridine derivatives have been reported for variety of biological activities like microbial, arrhythmic, ameobic, antioxidant, cancer, malaria, viral, diabetic, hypertensive, bacterial and numbers of the compounds are in clinical uses. Pyridine derivative also have some medicinal imporants in medicinal chemistry.

**KEYWORDS:** Pyridine, Biological Activity, Physical Property, Chemical Property, Synthesis.

**INTRODUCTION**

Pyridine is a basic heterocyclic organic compound with formula C<sub>5</sub>H<sub>5</sub>N. It is structurally related to benzene, with one CH group replaced by a nitrogen atom it is used as a precursor to agrochemicals and pharmaceuticals and is also important solvent and reagent. Pyridine was 1<sup>st</sup> isolated and characterized by Anderson in 1846. The cyclic nature of pyridine was recognized by KORNER and DEWAR in 1869. It was obtained from bone oil and from coal tar, its principle source before e development of a synthesis based on acetaldehyde and ammonia. The pure substance is a colorless, flammable, weakly alkaline, water- soluble liquid with an unpleasant odour; it boils at 115.5°C (234°F). It play a key role in many enzymes of living organisms as a prostatic group (NADP) involved in redox reaction in the living system. Pyridine It naturally present in vitamins like niacin pyridoxine and also in toxic alkaloid nicotine. Most importantly it form the nucleus of around 7000 existing drug pyridine derivative are used in different biological activities namely antiasthmatic, anticonvulsant, antibacterial, antimalarial, antimuscarinic, anticancer, antidibetic, anti-inflammatory, antiprotozoale.<sup>[1]</sup>



**History**

pyridine was undoubtedly prepared by early alchemists by heating animal bones and other organic matter<sup>[7]</sup> but the earliest documented reference is attributed to the Scottish scientist Thomas Anderson<sup>[8-9]</sup> examined the contents of the oil obtained through high-temperature heating of animals bone<sup>[10]</sup> he separated from the oil a colorless liquid with unpleasant odor, from which he isolated pure pyridine two years later. He described it as highly soluble in water, readily soluble in concentrated acids and salts upon heating, and only slightly soluble in oils.<sup>[6]</sup> Owing to its flammability. The suffix idine was added in compliance with the chemical nomenclature, as in toluidine, to indicate a carbon cycle containing a nitrogen atom.<sup>[11]</sup> The chemical structure of pyridine was determined decades after its discovery. Wilhelm Körner and James Dewar suggested that, in analogy between quinoline and naphthalene, the structure of pyridine is derived from benzene by substituting one C–H unit with a nitrogenation by Körner and Dewar was later confirmed in an experiment where pyridine was reduced to piperidine with sodium in ethanol. William Ramsay combined acetylene and hydrogen cyanide into pyridine in a red-hot iron-tube furnace in 1876. This was the first synthesis of a heteroaromatic compound.<sup>[15-16]</sup> the contemporary methods of pyridine production had a low yield, and the increasing demand for the new compound urged to search for more efficient routes. A breakthrough came in 1924 when the Russian chemist Aleksei Chichibabin invented a pyridine synthesis reaction<sup>[5]</sup>, which was based on inexpensive reagents.<sup>[17]</sup> This method is still used for the industrial production of Pyridine.<sup>[18]</sup>

### Physical Property

Pyridine is liquid in nature, colourless that boils at 115.2°C and freezes at -41.6°C. Its density, 0.9819 g/cm<sup>3</sup>, is close to that of water, and its refractive index is 1.5093 at a wavelength of 589 nm and a temperature of 20°C.<sup>[19]</sup> Addition of up to 40 mol% of water to pyridine gradually lowers its melting point from -41.6°C to -65.0°C.<sup>[20]</sup> The molecular electric dipole moment is 2.2 debyes.<sup>[21]</sup> Pyridine is diamagnetic and has a diamagnetic susceptibility of  $-48.7 \times 10^{-6} \text{ cm}^3 \cdot \text{mol}^{-1}$ .<sup>[22]</sup> The standard enthalpy of formation is 100.2 kJ·mol<sup>-1</sup> in the liquid phase<sup>[23]</sup> and 140.4 kJ·mol<sup>-1</sup> in the gas phase. At 25°C pyridine has a viscosity of 0.88 mPa/s<sup>[24]</sup> and thermal conductivity of 0.166 W·m<sup>-1</sup>·K<sup>-1</sup>.<sup>[25,26]</sup> The enthalpy of vaporization is 35.09 kJ·mol<sup>-1</sup> at the boiling point and normal pressure.<sup>[27]</sup> The enthalpy of fusion is 8.28 kJ·mol<sup>-1</sup> at the melting point.<sup>[28]</sup> Pyridine crystallizes in an orthorhombic crystal system with space group Pna21 and lattice parameters a is equal to 1752 pm, b is equal to 897 pm, c is equal to 1135 pm, and 16 formula units per unit cell (measured at 153 K). Comparison of study, crystalline benzene is also orthorhombic, with space group Pbca, a = 729.2 pm, b = 947.1 pm, c = 674.2 pm (at 78 K), but the number of molecules per cell is only 4.<sup>[29]</sup> this difference is partly related to the lower symmetry of the individual pyridine molecule (C<sub>2v</sub> vs. D<sub>6h</sub> for benzene). A trihydrate (pyridine·3H<sub>2</sub>O) is known; it also crystallizes in an orthorhombic system in the space group Pbca, lattice parameters a = 1244 pm, b = 1783 pm, c = 679 pm and eight formula units per unit cell (measured at 223 K).<sup>[30]</sup> The critical parameters of pyridine are pressure 6.70 MPa, temperature 620 K and volume 229 cm<sup>3</sup>·mol<sup>-1</sup>.<sup>[31]</sup> In the temperature ranges from 340–426°C its vapor pressure p can be described with the Antoine equation where T is temperature, A = 4.16272, B = 1371.358 K and C = -58.496 K.<sup>[32]</sup> The optical absorption spectrum of pyridine in hexane contains three bands at the wavelengths of 195 nm ( $\pi \rightarrow \pi^*$  transition, molar absorptivity  $\epsilon = 7500 \text{ L} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$ ), 251 nm ( $\pi \rightarrow \pi^*$  transition,  $\epsilon = 2000 \text{ L} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$ ) and 270 nm ( $n \rightarrow \pi^*$  transition,  $\epsilon = 450 \text{ L} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$ ).<sup>[33]</sup> The <sup>1</sup>H nuclear magnetic resonance (NMR) spectrum of pyridine contains three signals with the integral intensity ratio of 2:1:2 that correspond to the three chemically different protons in the molecule. These signals originate from the  $\alpha$ -protons (positions 2 and 6, chemical shift 8.5 ppm),  $\gamma$ -proton (position 4, 7.5 ppm) and  $\beta$ -protons (positions 3 and 5, 7.1 ppm). Pyridine carbon analog, benzene, has only one proton signal at 7.27 ppm. The larger chemical shifts of the alpha and gamma protons in comparison to benzene result from the lower electron density in the alpha and gamma positions, which can be derived from the resonance structures. The situation is rather similar for the <sup>13</sup>C NMR spectra of pyridine and benzene: pyridine shows a triplet at  $\delta(\alpha\text{-C}) = 150 \text{ ppm}$ ,  $\delta(\beta\text{-C}) = 124 \text{ ppm}$  and  $\delta(\gamma\text{-C}) = 136 \text{ ppm}$ , whereas benzene has a single line at 129 ppm. All shifts are quoted for the solvent-free substances.<sup>[33]</sup> Pyridine is conventionally

detected by the gas chromatography and mass spectrometry methods.<sup>[34]</sup>

### Chemical Property

Pyridine is a weakly basic heteroaromatic compound. It is miscible with water and virtually all organic solvents.<sup>[36]</sup> With hydrochloric acid it forms a crystalline hydrochloride salt that melts at 145–147°C.<sup>[37]</sup> In organic reactions, pyridine behaves both as a tertiary amine, undergoing protonation, alkylation, acylation, and as an aromatic compound N-oxidation at the nitrogen atom, undergoing nucleophilic substitutions. because of electronegativity of nitrogen which is present in pyridine ring, the molecule become electron deficient. Therefore, characteristic of benzene derivatives, enters less readily electrophilic aromatic substitution reactions even more so if the reaction mix doesn't scavenge protons released by the reaction (protonated pyridine is even more electron-deficient). Benzene and its derivatives, pyridine is more prone to nucleophilic substitution and methylation of the ring by strong organometallic bases.<sup>[38,39]</sup> The reactivity of pyridine can be distinguished for three chemical groups. Electrophilic substitution takes place where pyridine expresses aromatic properties. Pyridine reacts at positions 2 and 4 and thus behaves similar to imines and carbonyls with nucleophilic. The reaction with many Lewis acids results in the addition to the nitrogen atom of pyridine, which is similar to the reactivity of tertiary amines.<sup>[40]</sup> The ability of pyridine and its derivatives to oxidize, forming amine oxides (N-oxides), is also a feature of tertiary amines.

### 1, 10-Phenanthroline

Center of pyridine features, the nitrogen basic lone pair of electrons. Due to this lone pair of electron it is not a part of the aromatic ring, pyridine is a base, having chemical properties similar to those of tertiary amines. The pK<sub>a</sub> value for the conjugate acid (the pyridinium cation) is 5.25. Pyridine is protonated by reaction with acids and forms a positively charged aromatic polyatomic ion called pyridinium. The bond angles and bond lengths in pyridine and pyridinium are almost identical. The Pyridinium cation is isoelectronic with benzene. Pyridinium p-toluene sulfonate (PPTS) is an illustrative pyridinium salt; it is produced by treating pyridine with p-toluene sulfonic acid. Pyridine donating its pair of electrons to a Lewis acid as in the sulphur trioxide pyridine complex and act as Lewis bases. Pyridine itself is a relatively weak ligand in forming complexes with transition metal ions. For example, it forms a 1:1 complexes with nickel (II), Ni<sup>2+</sup>, and copper(II), Cu<sup>2+</sup>, with log K<sub>1</sub> values of around 1.9 and 2.6, respectively. Substituted derivative of pyridine, Picolinic acid forms strong complexes due to the chelate effect; 2,2'-bipyridine and 1,10-phenanthroline, which can also be viewed as substituted derivatives of pyridine, also form strong complexes, such as in ferroin, which can be used as a redox indicator in the quantitative analysis of iron.

### Molecular Property

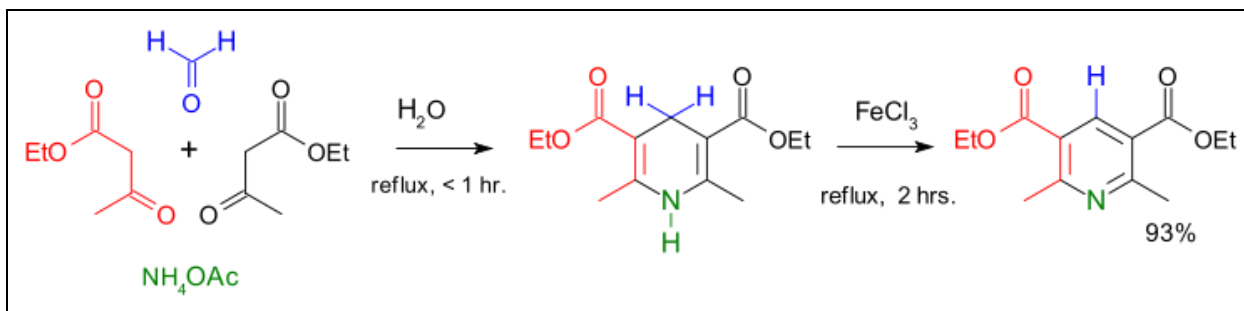
Pyridine present with its free electron pair it has conjugated system of six  $\pi$  electrons that are delocalized over the ring. The molecule is planar in shape and thus, follows the huckel criteria for aromatic system. Benzene in contrast, the electron density is not distributed evenly over the ring, reflecting the negative inductive effect of the nitrogen atom. Because of this reason, pyridine has a dipole moment & a weaker resonant stabilization than benzene (resonance energy 117 kJ·mol<sup>-1</sup> in pyridine vs. 150 kJ·mol<sup>-1</sup> in benzene). Electron localization in pyridine is also reflected in the shorter C–N ring bond (137 pm for the C–N bond in pyridine vs. 139 pm for C–C bond in benzene),<sup>[41]</sup> Whereas the carbon–carbon bonds in the pyridine ring have the same 139 pm length as in benzene. These bond lengths lie between the values for the single and double bonds and are typical of aromatic compounds. All the ring atom in the pyridine molecule are sp<sup>2</sup>-hybridized. The nitrogen involved in the  $\pi$ -bonding aromatic system using unhybridized p orbital. The lone pair is in an sp<sup>2</sup> orbital, projecting outward from the ring in the same plane as the  $\sigma$  bonds. As a result, the lone pair does not contribute to the aromatic system but importantly influences the chemical properties of pyridine, as it easily supports bond formation via an electrophonic attack. Because of the separation of the lone pair from the aromatic system of the ring affects, the nitrogen atom cannot exhibit a

positive mesomeric effect. Many analogues of pyridine are known where N is replaced by other heteroatoms (see figure below). Substitution of one C–H in pyridine with a second N gives rise to the diazine heterocyclic (C<sub>4</sub>H<sub>4</sub>N<sub>2</sub>), with the names pyridazine, pyrimiding, and pyrazine.

### Synthesis of Different Derivatives of Pyridine

#### 1. Hantzsch pyridine synthesis

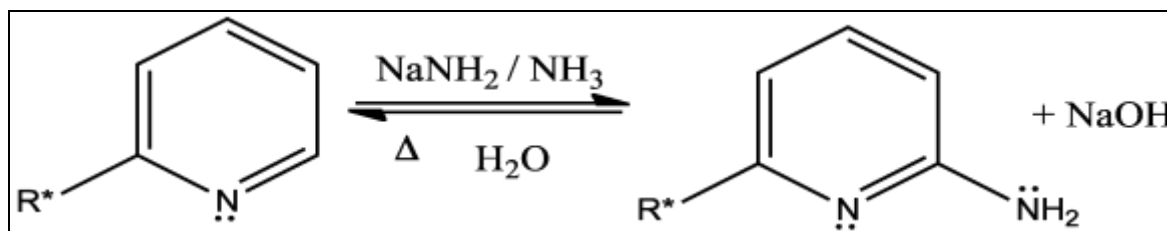
The Hantzsch dihydropyridine synthesis or hantzsch pyridine synthesis is component organic reaction between an aldehyde such as formaldehyde, 2 equivalents of a  $\beta$ -keto ester such as ethyl acetoacetate & a nitrogen donor such as ammonia or ammonium acetate. Initial reaction product is dihydropyridine which can be oxidized in a subsequent step to a pyridine. Aromatization driving force used for this second reaction. This reaction reported Arthur Rudolf Hantzsch in 1881. A 1, 4-dihydropyridine dicarboxylate is also called a 1,4-DHP compound or a Hantzsch compound. These compounds are an important class of calcium channel blockers and as such commercialized in for the instance in for instance nifedipine, amlodipine or nimodipine. The reaction has been demonstrated to proceed in water as reaction solvent and with direct aromatization by ferric chloride, Manganese Dioxide or potassium permanganate in a one-pot synthesis.<sup>[4]</sup>



#### 2. Chichibabin pyridine synthesis

The Chichibabin pyridine synthesis is a method for synthesizing pyridine rings. In its general form, the reaction can be described as a condensation reaction of aldehyde, ketones,  $\alpha,\beta$ -Unsaturated carbonyl compounds,

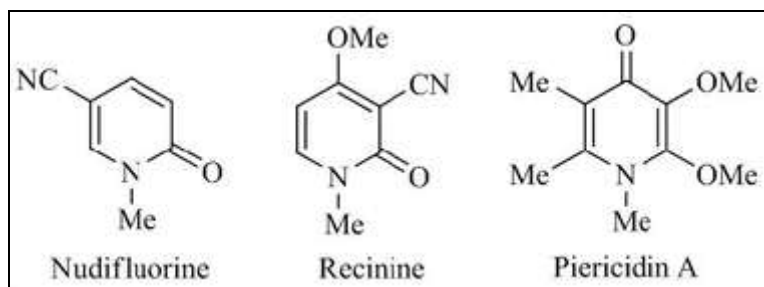
or any combination of the above, in ammonia or ammonia derivatives. It was reported by Aleksei Chichibabin in 1924 The following is the overall form of the general reaction:<sup>[5]</sup>



#### 3 Synthesis of New Isolated and Fused Tri- and Tetracyclic Pyridine Derivatives

A number of functionalized pyridine derivatives in which the pyridine ring is linked to triazole, thiadiazole, thiazole, and tetrazole moieties were synthesized by cyclization with carbon disulfide, phenyl

isothiocyanate, and sodium azide. Benzylation of the synthesized tetrazolyl methylpyridone derivative afforded the *N*(1)-benzylated product; its crystal structure is reported. The substituted fused tetracyclic pyrido furo pyrimidine was synthesized by sequential reactions starting from the 2-pyridone derivative.<sup>[3]</sup>



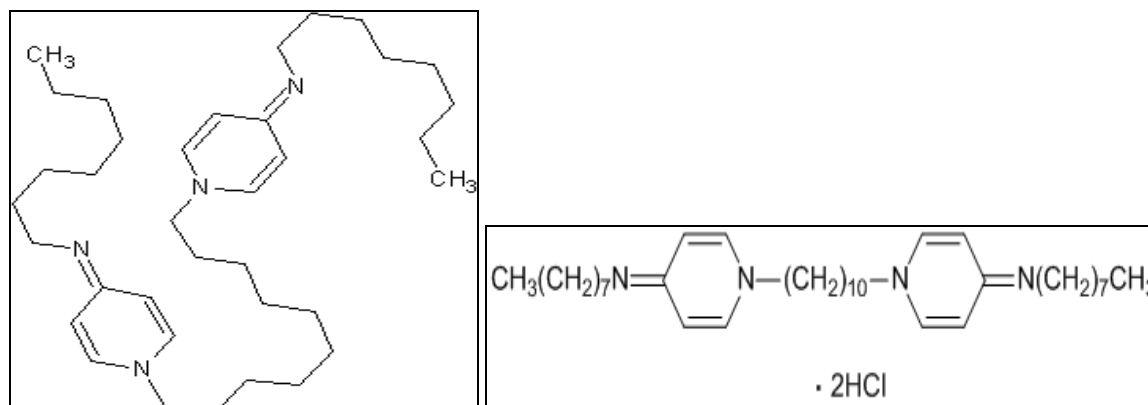
### Biological Activity of Pyridine

Pyridine derivatives have been reported for variety of biological activities and number of the compounds are in clinical uses. Pyridine has conjugated system  $\pi$ -electrons exactly as benzene has, that are delocalized over the heterocyclic ring.

#### 1. Antibacterial

Series of oxazolidine derivatives, which morpholino group of linezolid was replaced with heteroaromatic ring

substituted pyridine moiety, were newly synthesized, and their substituted effects on in vitro and in vivo antibacterial activities were evaluated against four problematic gram positive strains and two gram negative strains including drug resistant strains and two gram-negative strains. Most compounds exhibited the enhanced in vitro activities with 4–16-fold and three compounds exerted more than 2-fold increased in vivo efficacies than linezolid.<sup>[42]</sup>

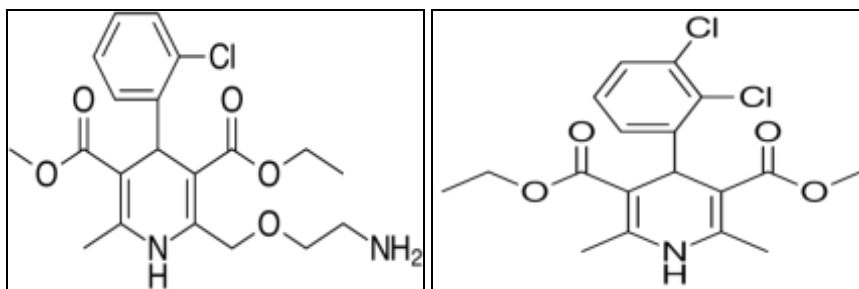


Octenidiene Octenide dihydrochloride

#### 2. Antihypertensive

- The effects on contractile activity of two series of nifedipine derivatives were investigated in isolated, isotonically contracting cat papillary muscles.
- For structure-activity studies the lipophilicity of all compounds was determined by means of reversed phase thin-layer chromatography.
- Neither the ortho-NO<sub>2</sub> group in a series of aryl derivatives nor the methyl-esters in a series of ester derivatives were found to be essential for the typical effect of the nifedipine molecule on myocardial contractility.
- Generally ortho-substituted derivatives induce a greater negative inotropic activity than meta-substituted derivatives. Para-substituted derivatives are the least active compounds.
- In the group of ester-derivatives activity decreases when lipophilicity and/or volume of the substituent increases.

- The quantitative analysis (Hansch analysis) revealed significant correlations between the negative inotropic effect and steric substituent parameters.<sup>[43]</sup>

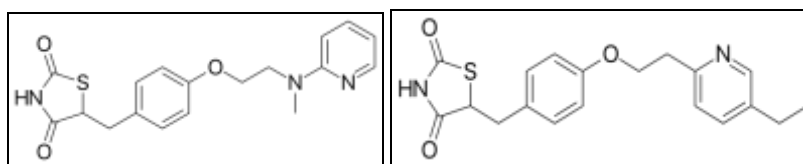


Amlodipine Felodipine

### 3. Antidiabetic

Thiazolidinedione also known as “Glitazones” and they binds to PPAR  $\gamma$ , a type of nuclear regulatory protein involved in transcription of genes regulating glucose and fat metabolism. These PPARs act on peroxysome

proliferator responsive elements (PPRE).<sup>[6]</sup> The PPREs influence insulin-sensitive genes, which enhance production of mRNAs of insulin-dependent enzymes. The final result is better use of glucose by the cells.

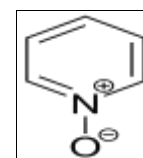


Rosiglitazone Pioglitazone

### 4. Antiviral

Up to 19 different drugs have been approved for the treatment of HIV-infected individuals, including seven nucleoside reverse transcriptase (RT) inhibitors (NRTIs), one nucleotide RT inhibitor (NtRTI), three nonnucleoside RT inhibitors (NNRTIs), seven protease inhibitors (PIs) and one fusion inhibitor. Nevertheless, long-term side effects and virus–drug resistance emergence, together with compliance problems in accurately adhering to the often complicated time schedules of drug uptake, have made it imperative to develop additional drugs, preferably acting at a novel target in the replication cycle of the virus. The pyridine N-oxide derivatives represent a peculiar class of antiviral compound that qualify as promising novel drugs for exploration as potential anti-HIV agents. They have an entirely new mechanism of antiviral action and the capacity to retain antiviral activity against virus strains that have gained resistance to clinically used drugs, such as NRTIs, NtRTIs, NNRTIs (depending on the particular structure of the pyridine N-oxide derivative) and PIs. Indeed, it is clear that, whereas several members of this class of compounds functionally interact with HIV-1 RT as NNRTIs, other distinct members inhibit HIV replication. They do this by interacting, additionally or alternatively, with a target in the HIV replication cycle that is situated, following proviral DNA integration in the host cell chromosome(s). An extensive study on the anti-HIV activity of a wide variety of pyridine N-oxide derivatives has been performed and revealed that several functional subclasses of compound derivatives within the pyridine N-oxides seem to exist. Indeed, whereas a number of pyridine N-oxides are specifically and exclusively inhibitory towards HIV-1 strains targeting HIV-1 RT, but not HIV-2 RT, other closely related compounds are inhibitory to both HIV-1 and HIV-2

strains as well as the simian immuno-deficiency virus (SIV) strain SIVMAC251. Other pyridine N-oxides are also active against human cytomegalovirus (but not other DNA viruses, such as herpes simplex virus or vaccinia virus). Intriguingly, there is no clear structure–antiviral activity relationship between the functionally distinct subgroups within the pyridine N-oxide derivatives.<sup>[44]</sup>

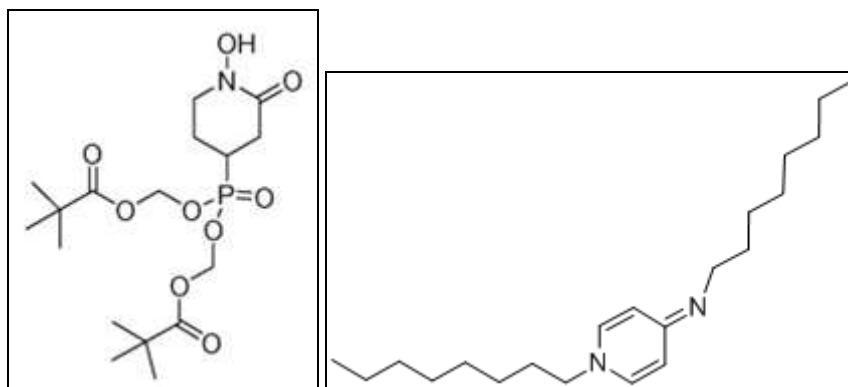


N oxide

### 5. Antimalarial

1-Deoxy-d-xylulose-5-phosphate reductoisomerase (DXR) in the nonmevalonate isoprene biosynthesis pathway is a target for developing antimalarial drugs. Fosmidomycin, a potent DXR inhibitor, showed safety as well as efficacy against *Plasmodium falciparum* malaria in clinical trials. On the basis of our previous quantitative structure–activity relationship (QSAR) and crystallographic studies, several novel pyridine-containing fosmidomycin derivatives were designed, synthesized, and found to be highly potent inhibitors of *P. falciparum* DXR (PfDXR) having  $K_i$  values of 1.9–13 nM, with the best one being  $\sim 11\times$  more active than fosmidomycin. These compounds also potently block the proliferation of multidrug resistant *P. falciparum* with  $EC_{50}$  value as low as 170 nM. A 2.3 Å crystal structure of PfDXR in complex with one of the inhibitors is reported, showing that the flexible loop of the protein undergoes conformational changes upon ligand binding and a hydrogen bond and favorable hydrophobic

interactions between the pyridine group and the PfDXR account for the enhanced activity.<sup>[45]</sup>



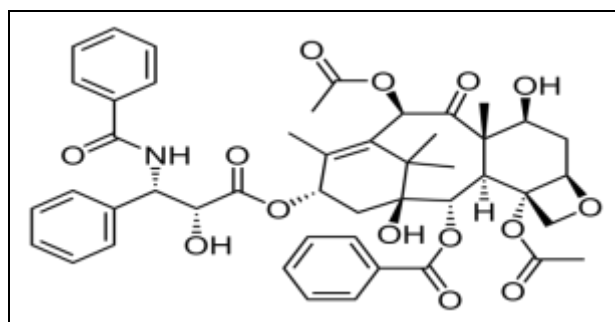
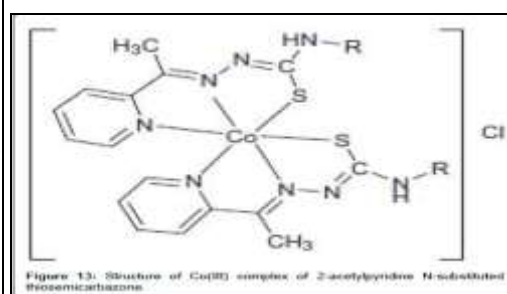
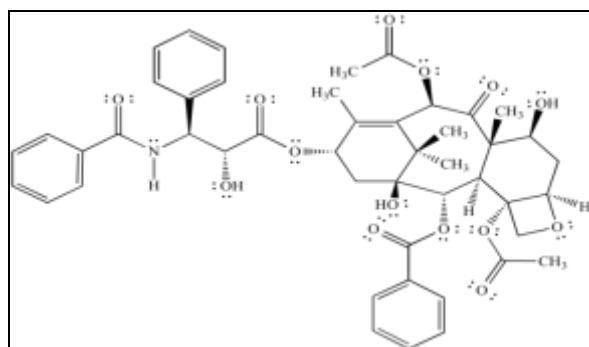
**Fosmidomycin Phosphomycin Sodium**

## 6. Anticancer Activity of Pyridine

Nicolaou et al synthesized pyridine epothilones exhibiting cytotoxic properties against a number of human cancer cell lines. The compounds showed the importance of nitrogen atom at ortho position with the effect of methyl substitution on pyridine ring at 4- or 5-positions. Jong-Keun Son et al synthesized 2, 6-diaryl-substituted pyridines having cytotoxicity against several human cancer cell lines. It has the cytotoxicity and topoisomerase I inhibitory activity also. Hayakawa synthesized imidazo[1,2-a]pyridine derivatives. In a series of imidazo[1,2-a]pyridine compounds the thiazole derivative showed potent p110a inhibitory activity and strong selectivity for p110a over other PI3K isoforms. Compound also inhibited tumor cell growth both in vitro

and in vivo, suggesting that PI3K p110a is a potential target in cancer treatment.

Romagnoli et al synthesized 2-amino-3-(3',4',5'-trimethoxybenzoyl)-6-substituted-4,5,6,7-tetrahydrothieno [2,3-c]pyridine derivatives and evaluated against a panel of four cancer cell lines, and interacts strongly with tubulin by binding to the colchicine site. The compound showed promising antiproliferative activity, inhibition of tubulin polymerization & cell cycle effect. Liou et al synthesized a novel oral indoline-sulfonamide agent, exhibiting potent activity against human cancer cells in vitro and in vivo through the disruption of taxol.

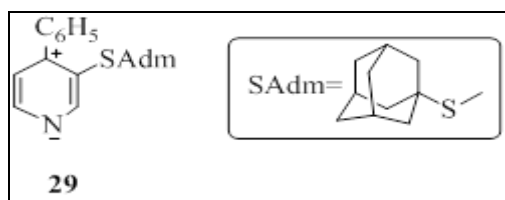


## 7. Antioxidant activity

Some of the thiopyridine derivatives are antioxidant(SOD) in addition to their cytotoxic (DPPH)

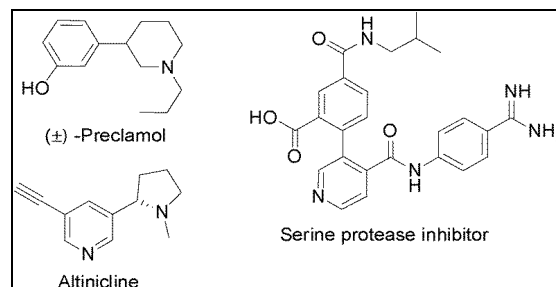
activities, these activities are quite attractive, particularly compounds twenty nine shown highest SOD and DPPH activities. The SOD and DPPH activities are strongly

related to the structure of the compounds. QSAR studies show that dipole moment and electrophilic molecule Index were the most significant descriptors for correlating the molecular structure of Compounds with their respective SOD activities. Results indicated that molecule with high dipole Movement and electrophilic index values also had SOD activity. Those compounds which have lowest atomic polarizability (MATS4p) have highest DPPH activity.<sup>[48]</sup> Representative example of antioxidant.



### 7. Anti-Amoebic Agents

Some ligands which is derived from acetyl pyridine have Anti-amoebic activity, however, when this ligands is coupled With ruthenium (II) to afford a complex, the anti-amoebic Activity drastically increase. The complex 41 show high anti-amoebic activities compared with commercially available standard drug, metronidazole. Below figure shows Ruthenium complex as anti-amoebic agent. Bi-nuclear complex of vanadium containing 2-acetylpyridine exhibit excellent ameobocidal activity with IC50 value 1.68-0.40 then commercial drugs metromidazole with IC50 value 1.81 but ligand itself have no activity against amoeba.<sup>[46]</sup>



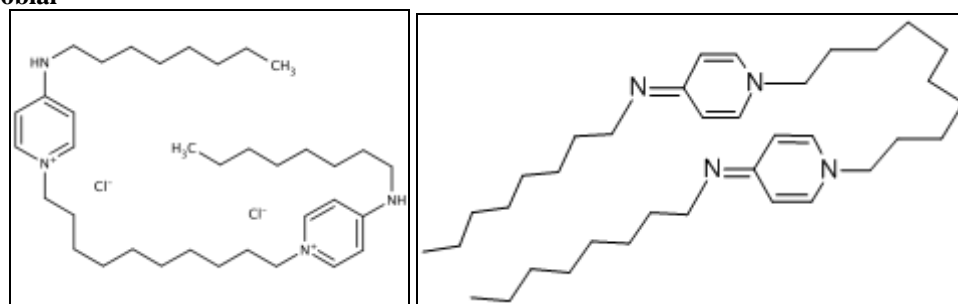
### 8. Anti-arrhythmic activity

The pyridine and pyrimidine derivative can easily be fused with thiophine moiety. When the resultant compounds were further tested for antiarrhythmic activites, results revealed that they have antiarrhythmic activity better than Procaine amide and Lidocaine as standard antiarrhythmic agents.<sup>[64]</sup> Anti-staphylococcal agents; 3-aminopyridine a derivatives of pyridine undergo polymerization and the resulted polymer show anti staphylococcal activity. Results obtained show that the 3-amino pyridine when applied in free state was inactive. Its polymer has anti staphylococcal activity small oligomers were found more efficient. It showed that the antibacterial activity of the polymer is molecular weight dependent.

### 9. Iron Overload Disease

The pyridine derivative, pyridine-2-carboxaldehydeisonicotinoylhydrazone (PCIH) make considerably stable complex with iron, the resulted compounds is a chelator. The ligands derivatives independently are used as medicine in iron overload disease. Ligands equivalent activities as standard drug, desferrioxamine (DFO).<sup>[47]</sup>

### 10. Antimicrobial



Octenidine dihydrochloride Octenidine

### REFERENCES

- Ataf Ali Altaf, Adnan Shahzad, Zarif Gal, Nasir Rasool, Amin Badshah, Bhajan Lal, Ezzat Khan. A Review on the Medicinal Importance of Pyridine Derivatives, Journal of Drug Design and Medicinal Chemistry, 2015; 1(1): PP1-11, doi:10.11648/j.Jddmc.20150101-11.
- <http://en.m.wikipedia.org/wiki/pyridine>.
- The Synthesis and used of certain Pyridine Derivatives as Modulator of the G-protein Couple Receptor mGlu5 and P2Y12. PETER Batch Department of Chemistry and Molecular Biology University of Gothenburg, 2012, ISBN-978-91-628-8579-3.
- [www.chemtube3d.com](http://www.chemtube3d.com)>Hantzsch Synthesis.
- <https://m.wikipedia.org/wiki/cjichibabin> pyridine synthesis.
- "Iodine Solution (0.02 M in THF/pyridine/H<sub>2</sub>O 70:20:10)". Sigma-Aldrich. Retrieved 28 November 2011.
- Weissberger.A, Klingberg. A., Barnes.R. A., Brody. F, Ruby, P.R. (1960). Pyridine and its Derivatives. 1. New York: Interscience.

8. Anderson, T. (1849). Transactions of the Royal Society of Edinburgh, 16: 123.
9. Anderson, T. (1849). "Producte der trocknen Destillation thierischer Materien" [Products of the dry distillation of animal matter]. Annalen der Chemie und Pharmacie, 70: 32. doi:10.1002/jlac.18490700105.
10. Anderson, T. (1851). "Ueber die Producte der trocknen Destillation thierischer Materien" [On the products of dry distillation of animal matter]. Annalen der Chemie und Pharmacie, 80: 44. doi:10.1002/jlac.18510800104.
11. Körner, W. (1869). Giornale academico di Palermo, 5.
12. Dewar, J. (1871). Chemical News., 23:
13. Rocke, Alan J. (1988). "Koerner, Dewar and the Structure of Pyridine". Bulletin for the History of Chemistry, 2: 4. Ladenburg, Albert. Lectures on the history of the development of chemistry since the time of Lavoisier. (PDF). pp. 283–287.
14. Bansal, Raj K. (1999). Heterocyclic Chemistry. p. 216. ISBN 81-224-1212-2.
15. "Pyridine" (PDF). IARC Monographs 77. Washington DC: OSHA. 1985.
16. "A. Henninger, aus Paris. 12. April 1877". Berichte der deutschen chemischen Gesellschaft (Correspondence), 10: 727.
17. Chichibabin, A. E. (1924). "Über Kondensation der Aldehyde mit Ammoniak zu Pyridinebasen" [On condensation of aldehydes with ammonia to make pyridines]. Journal für Praktische Chemie, 107: 122. doi:10.1002/prac.19241070110.
18. Shimizu, S.; Watanabe, N.; Kataoka, T.; Shoji, T.; Abe, N.; Morishita, S.; Ichimura, H., "Pyridine and Pyridine Derivatives", Ullmann's Encyclopedia of Industrial Chemistry, Weinheim: Wiley-VCH, doi:10.1002/14356007.a22\_399.properties
19. Lide, D. R., ed. (2009). Handbook of Chemistry and Physics (90<sup>th</sup> ed.). Boca Raton: CRC Press. ISBN 978-1-4200-9084-0.
20. Mootz, D. (1981). "Crystal structures of pyridine and pyridine trihydrate". The Journal of Chemical Physics, 75(3): 1517. Bibcode:1981JChPh..75.1517M. doi:10.1063/1.442204.
21. RÖMPP Online – Version 3.5. Thieme Chemistry. Stuttgart: Georg Thieme, 2009.
22. Lide, D. R., ed. (2009). Handbook of Chemistry and Physics (90<sup>th</sup> ed.). Boca Raton: CRC Press. ISBN 978-1-4200-9084-0. P-3-673
23. Lide, D. R., ed. (2009). Handbook of Chemistry and Physics (90<sup>th</sup> ed.). Boca Raton: CRC Press. ISBN 978-1-4200-9084-0. P. 5-28
24. Lide, D. R., ed. (2009). Handbook of Chemistry and Physics (90<sup>th</sup> ed.). Boca Raton: CRC Press. ISBN 978-1-4200-9084-0. p. 6-211
25. Lide, D. R., ed. (2009). Handbook of Chemistry and Physics (90<sup>th</sup> ed.). Boca Raton: CRC Press. ISBN 978-1-4200-9084-0., p. 6-221.
26. Lide, D. R., ed. (2009). Handbook of Chemistry and Physics (90<sup>th</sup> ed.). Boca Raton: CRC Press. ISBN 978-1-4200-9084-0. p. 6-221
27. Majer, V.; Svoboda, V. (1985). Enthalpies of Vaporization of Organic Compounds: A Critical Review and Data Compilation. Oxford: Blackwell Scientific Publications. ISBN 0-632-01529-2.
28. Domalski, Eugene S.; Hearing, Elizabeth D. (1996). "Heat Capacities and Entropies of Organic Compounds in the Condensed Phase". Journal of Physical and Chemical Reference Data., 25: 1. Bibcode:1996JPCRD..25....1D.
29. Cox, E. (1958). "Crystal Structure of Benzene". Reviews of Modern Physics, 30: 159. Bibcode:1958RvMP...30..159C. doi:10.1103/RevModPhys.30.159.
30. Mootz, D. (1981). "Crystal structures of pyridine and pyridine trihydrate". The Journal of Chemical Physics., 75(3): 1517. Bibcode:1981JChPh..75.1517M. doi:10.1063/1.442204.
31. Lide, D. R., ed. (2009). Handbook of Chemistry and Physics (90<sup>th</sup> ed.). Boca Raton: CRC Press. ISBN 978-1-4200-9084-0. p. 6-67
32. McCullough, J. P.; Douslin, D. R.; Messerly, J. F.; Hossenlopp, I. A.; Kincheloe, T. C.; Waddington, Guy (1957). "Pyridine: Experimental and Calculated Chemical Thermodynamic Properties between 0 and 1500 °K.; a Revised Vibrational Assignment". Journal of the American Chemical Society, 79(16): 4289. doi:10.1021/ja01573a014.
33. Joule, J. A.; Mills, K. (2010). Heterocyclic Chemistry (5<sup>th</sup> ed.). Chichester: Blackwell Publishing. ISBN 1-4051-3300-7, p. 14.
34. Joule, J. A.; Mills, K. (2010). Heterocyclic Chemistry (5<sup>th</sup> ed.). Chichester: Blackwell Publishing. ISBN 1-4051-3300-7, p. 16.
35. "Pyridine" (PDF). IARC Monographs 77. Washington DC: OSHA. 1985. Chemical prop.
36. Lide, D. R., ed. (2009). Handbook of Chemistry and Physics (90<sup>th</sup> ed.). Boca Raton: CRC Press. ISBN 978-1-4200-9084-0. p. 3-448.
37. "Pyridine hydrochloride MSDS" (PDF). Alfa Aesar. Retrieved, 26 June 2010.
38. Joule, J. A.; Mills, K. (2010). Heterocyclic Chemistry (5<sup>th</sup> ed.). Chichester: Blackwell Publishing. ISBN 1-4051-3300-7, p. 125–141.
39. Davies, D. T. (1992). Aromatic Heterocyclic Chemistry. Oxford University Press. ISBN 0-19-855660-8.
40. Milcent, R.; Chau, F. (2002). Chimie organique hétérocyclique: Structures fondamentales. EDP Sciences. pp. 241–282. ISBN 2-86883-583-X, Mol prop
41. Joule, J. A.; Mills, K. (2010). Heterocyclic Chemistry (5<sup>th</sup> ed.). Chichester: Blackwell Publishing. ISBN 1-4051-3300-7, p. 7.
42. Yeong Woo Ja, Weon Bin Im, Jae Keol Rhee, Mi Ja Shim, Won Bae Kim, Eung Chill Choi, Biorganic and Medicinal Chemistry, 2004; 12(22): 5909-5915.



43. Nathan B Mantlo, Prasun K.Chakravarty Debra L.Ondevka Peter Ks Sieal Ravmonds, *Journal of Medicinal Chemistry*, 34(9): 2919-2922.
44. Jan Balzarini, Miguel Stevens, Erik De Clercy, Dominique Schols and Christophe Pannecouque. Rega Institute for Medicinal Research K.U.Leuven, B-3000 Leuven Belgium *Journal of Antimicrobial chemistry*, 2005; 55: 135-138. doi:10.10933/Jac/dkh 530.
45. Jain, Xue, Jiasheng, Diao, Guobin Cai, Lisheng Dong, Baisong Zheng, Yuan Yao, and Yongcheng Song, *ACS Med. Chem Lett.*, 2013 Feb 14; 2(4): 278-282. Published by 2012 Dec 11.
46. Worachartcheewan, A.; Prachayasittikul, S.; Pingaew, R.; Nantasenamat, C.; Tantimongcolwat, T.; Ruchirawat, S.; Prachayasittikul, V. *Medicinal Chemistry Research*, 2011; 1-9.
47. Bharti, N.; Maurya, M. R.; Naqvi, F.; Azam, A. *Bioorganic & Medicinal Chemistry letters*, 2000; 10: 2243-2245.
48. Chaston, T. B.; Richardson, D. R. *Journal of Biological Inorganic Chemistry*, 2003; 8: 427-438.