Synopsis

This thesis reports the single crystal X-ray diffraction studies on few novel pyridine derivatives:

1. 3-cyano-2-ethoxy-4,6-diphenyl pyridine
2. 1,3-dimethyl-2-oxo-4,6-diphenyl-1,2,3,4-tetrahydropyridine-3-carbonitrile
3. 1,3-diethyl-2-oxo-4,6-diphenyl-1,2,3,4-tetrahydropyridine-3-carbonitrile
4. 1,3-dibenzyl-2-oxo-4,6-diphenyl-1,2,3,4-tetrahydropyridine-3-carbonitrile
5. 2-(2,3-isoprophyledeno dioxy-propyloxy)-3-cyano-4,6-diphenyl pyridine
6. 5,7-diphenyl tetrazolo [1,5-a] pyridine –8-carbonitrile
7. 2-carbethoxy-3-amino-4-(4-methylphenyl)-6-phenyl furo-[2,3-b]pyridine
8. 2-carbethoxy-3-amino-4-(4-methylphenyl)-6-phenyl thieno [2,3-b] pyridine.

Compounds are obtained from Dave C.G. and the group, Organic syntheses Lab, M.G.Science College, Ahmedabad. Single crystals suitable for X-ray study are grown by slow evaporation method. Preliminary structural characterizations of the as grown crystals are carried out using Weissenberg, Precission goniometers. Intensity Data of the single crystals are collected on CAD-4 diffractometer. Direct method, SHELX-97 programme package is used to solve and refine the structures. All the structures have been refined to an highest degree of accuracy. Stability of the structure is due to van der Waal forces in all these heterocycles.

A brief report on the pyridine derivatives highlighting its Chemistry and the pharmaceutical importance are presented in CHAPTER ONE. At this context, the role of X-ray crystallography in drug design is discussed briefly. Crystallographic informations on pyridine derivatives are reviewed at the end of this chapter.

The crystal growth technique, employed for growing single crystal and the relevant theory described in CHAPTER TWO. Experimental techniques- Weissenberg, Precession (for preliminary structural characterization) and CAD-4 diffractometer (for intensity data collection) are discussed in brief. Methods to calculate the two physical parameters- density and mass absorption coefficients are mentioned here. This chapter ends with a brief note on the basic principle of direct method.
The **THIRD CHAPTER** is on the X-ray crystallographic investigations of 3-cyano-2-ethoxy-4,6-diphenyl pyridine. The title compound is an active member of 2-pyridine-3-cyano system which are found to possess antimicrobial, antiviral properties. It crystallizes in monoclinic space group P2\(_1\)/c with Z=8. Unit cell parameters are: \(a=8.554(1)\), \(b=32.027(3)\), \(c=12.391(7)\) Å, \(\beta=104.493(3)^\circ\), \(V = 3286.6\) Å\(^3\), \(\rho_m = 1.204\) Mg m\(^{-3}\) and \(\mu = 0.598\) mm\(^{-1}\). Final residual index is 0.0514 for 5612 unique reflections. Molecular dimension of molecule A is normal but ethoxy carbon of molecule B is disordered at two positions. Dihedral angles between the best plane of pyridine and the two phenyl rings are 35.4(1) and 25.7(2)\(^\circ\) respectively. Cyano moiety is coplanar with pyridine ring plane.

The crystal and molecular structure of 1,3-dimethyl-2-oxo-4, 6-diphenyl-1,2,3,4-tetrahydropyridine-3-carbonitrile is featured on the **FOURTH CHAPTER**. Title compound belongs to Tetrahydropyridine (THP) family exhibiting a large spectrum of biological activity. Crystals are obtained by recrystallization from ethanol. Unit cell parameters are: \(a=13.738(3)\), \(b=7.475(2)\), \(c=17.157(2)\) Å, \(\beta = 110.12(2)^\circ\), \(V = 1654.4(5)\) Å\(^3\), \(\rho_m = 1.205\) Mg m\(^{-3}\), and \(\mu = 0.595\) mm\(^{-1}\). Lorentz-polarization and absorption corrections are applied. Structure is refined to an R-value of 0.046 for 3010 unique reflections. Structure reveals a distorted half-chair conformation of the tetrahydropyridine ring. Oxygen at ortho position is disordered and occupied two positions. Steric interactions force both the phenyl rings out of the THP plane by 49.21(9) and 65.76(5)\(^\circ\) respectively.

The **FIFTH CHAPTER** deals with the X-ray diffraction studies on 1,3-diethyl-2-oxo-4,6-diphenyl-1,2,3,4-tetrahydropyridine-3-carbonitrile. Title compound belongs to tetrahydropryidine (THP) family. This family of compounds shows wide spectrum of biological activity e.g. anthelmintic, cathartic, antihistaminic. It crystallizes in monoclinic space group P2\(_1\)/c with Z = 4. Crystal parameters are: \(a = 8.392(6)\), \(b = 22.475(7)\), \(c = 9.330(1)\) Å, \(\beta = 97.17(3)^\circ\), \(V = 1746.0 (1)\) Å\(^3\), \(\rho_c = 1.257\) Mg m\(^{-3}\), and \(\mu = 0.078\) mm\(^{-1}\). Structure is refined to an R-value of 0.063 for 2223 unique reflections. THP ring has a distorted half-chair conformation. Dihedral angle between the best plane of THP ring
with that of phenyl rings are 89.8(1)° and 55.9(2)° respectively. One of the ethyl group is normal to THP ring plane whereas the other one is coplanar to it.

**CHAPTER SIX** presents the crystal and molecular structure of 1,3-dibenzyl-2-oxo-4,6-diphenyl-1,2,3,4-tetrahydropyridine-3-carbonitrile. Title compound is another potent member of THP family. Besides their pharmaceutical importance, it is also observed that these group of compounds adopt an interesting stereochemistry. Tiny platelike crystals are grown from chloroform-ethanol solution. It crystallizes in monoclinic system in space group P2₁/n with Z = 4, have the unit cell parameters as a = 9.146(1), b = 11.463(3), c = 23.423(5) Å, β = 95.49(2)°, V = 2444.5 (9) Å³, ρₚ = 1.235 Mg m⁻³, and μ = 0.580 mm¹. Structure is refined to an R-value of 0.0380 for 4441 unique reflections. THP ring is in distorted half-chair position. Both the phenyl rings and benzyl groups are planar. Cyano moiety is coplanar with THP ring plane.

X-ray diffraction study on crystal and molecular structure of 2-(2,3-isopropyledene dioxy-propyloxy)-3-cyano-4,6-diphenyl pyridine is included in **CHAPTER SEVEN**. Rectangular transparent crystals are obtained from the mixture of chloroform-ethanol solution. Crystals belong to monoclinic system with space group C2/c and Z = 4. Unit cell parameters are a = 15.462(4), b = 11.445(2), c = 23.005(4) Å, β = 94.20(2)°, V = 4060.5(2) Å³, ρₚ = 1.264 Mg m⁻³, and μ = 0.676 mm¹. Structure is refined to an R-value of 0.067 for 3841 unique reflections and 524 parameters. There are two molecules in the asymmetric unit. Phenyl rings are inclined at 40.32(4) and 24.48(9)° (mol A) and 39.63(22) and 24.11(18)° (mol B) respectively to the Pyridine ring plane. Isoprophyledene moiety of both the molecules are highly distorted and oriented at 65.4(3) and 68.2(3)° respectively to pyridine ring plane. Molecule (A and B both) adopts a trans conformation with respect to O1-C19 bond. Cyano moiety is coplanar to pyridine ring.

Crystal and molecular structure of 5,7-diphenyl tetrazolo [1,5-a] pyridine-8-carbonitrile is presented in **CHAPTER EIGHT**. Title compound belongs to tetrazolo pyridine family which have found use in agrochemical and pharmaceutical industries. Thin needle shaped crystals of the compound are grown from hot-methanol solution. It crystallizes in
monoclinic system with space group $P2_1/c$, unit cell parameters are: $a = 13.386(1)$, $b = 7.522(2)$, $c = 15.109(3) \, \text{Å}$, $\beta = 102.12(2)^\circ$, $V = 1487.4 \, (5) \, \text{Å}^3$, $\rho_c = 1.328 \, \text{Mg m}^{-3}$, and $\mu = 0.084 \, \text{mm}^{-1}$. Final residual index is 0.06 for 2600 unique reflections. Tetrazolo moiety is coplanar with the best plane of pyridine ring. Cyano moiety is slightly deviated from linearity.

CHAPTER NINE contents the crystal and molecular structure of 2-carbethoxy-3-amino-4-(4-methylphenyl)-6-phenyl furo[2,3-b]pyridine. Furopyridine consists of $\pi$-excessive and $\pi$-deficient rings and these group of compounds also play an important role in many biologically active substances. Crystals are orthorhombic having space group $Pbca$ with $Z = 8$. Crystal parameters are: $a = 7.755(3)$, $b = 21.231(6)$, $c = 23.020(7) \, \text{Å}$, $V = 3790(2) \, \text{Å}^3$, $\rho_m = 1.303 \, \text{Mg m}^{-3}$, and $\mu = 0.087 \, \text{mm}^{-1}$. Final residual index is 0.045 for 2466 unique reflections. Furan ring is non-planar and the best plane of it is almost coplanar (dihedral angle 2.42(2)$^\circ$) with pyridine ring plane. Steric interaction forces the phenyl ring away from pyridine ring plane by 45.3(1)$^\circ$ and 18.5(1)$^\circ$ respectively.

Crystallographic studies on 2-carbethoxy-3-amino-4-(4-methylphenyl)-6-phenyl thieno[2,3-b]pyridine has been discussed in CHAPTER TEN. Thieno[2,3-b] pyridines are isostere of isoquinoxaline. It shows important biological properties such as antibacterial, antihypertensive. The title compound crystallizes in monoclinic space group $P2_1/c$ with $Z = 4$. Preliminary crystal parameters are: $a = 9.200(3)$, $b = 22.465(9)$, $c = 9.708(3) \, \text{Å}$, $\beta = 94.06(3)^\circ$, $V = 2001.4(10) \, \text{Å}^3$, $\rho_c = 1.289 \, \text{Mg m}^{-3}$, and $\mu = 0.183 \, \text{mm}^{-1}$. Final residual index R is 0.058 for 3513 unique reflections. Thiophene is coplanar with pyridine ring plane, one of the phenyl rings is almost coplanar 5.2(2)$^\circ$ to pyridine ring whereas the other one is inclined at 69.9(1)$^\circ$ to pyridine ring plane.

In the ELEVENTH CHAPTER, a comprehensive view has been presented of the results obtained by X-ray crystallographic studies carried out by Author and others. Furan and thiophene derivatives are tested for their biological activities. X-ray results are tried to correlate with pharma-chemical studies. At the end, future scope of these kind of work have been mentioned.