PREFACE

The thesis entitled “X-RAY CRYSTALLOGRAPHIC STUDIES OF SOME ORGANOPHOSPHORUS COMPOUNDS OF BIOLOGICAL IMPORTANCE” is a report on the research work carried out by the candidate in the Department of Physics, Sri Venkateswara University, Tirupati-517502, under the guidance of Prof. M. Krishnaiah. The thesis consists of three units with 12 chapters. Unit I, (1-6 chapters) contains introduction and structures of four derivatives of 1,3,2-dioxaphosphorin rings and the comparison among the four structures dealt in Unit I. In Unit II, (Chapter 7) has the structure of ten membered derivative of cyclodecene ring. Unit III, (Chapters 8-11) possesses elucidation of four derivatives of diethyl esters, and the comparative study among the four diethyl ester structures, with last chapter (Chapter 12) as conclusion.

Organophosphorus chemistry has become popular now-a-days due to the versatile nature of phosphorus and its electronic configuration \[\text{[Ne]} \ 3s^2 \ 3p^3 \ 3d^0\]. This unique distribution of electrons in phosphorus and the geometry associated with its various orbitals led to the existence of several classes of multivalent phosphorus compounds from P(II1) to P(V).

Organophosphorus compounds originated in the nineteenth century with the pioneer work of Karl Arnold August Michaelis in Germany and Aleksandr Erminingel’ dovich Arbusov in Russia. Their methods of synthesis and characterization of some compounds with major organophosphorus functional groups are still being used (Quin, 2000). The field acquires international reputation on the foundations laid by them, since then several thousands of organophosphorus compounds have been made and studied.

Most of the organophosphorus compounds have been synthesized to be used as insecticides, herbicides, fungicides, plant growth regulators, flame retardants, lubricants in oil industry and drugs for the anti cancer disease. In view of the wide applications of
organophosphorus derivatives, the structural investigations have become important to understand the effect of substituents on the conformation of the heterocyclic rings and molecular geometry of bonding at Phosphorus. This stimulates us to determine the structures of some organophosphorus compounds and to establish crystallographic database elucidating the following structures of some new organophosphorus compounds.

CHAPTER-2 presents the crystal structure and molecular conformation of 6-Bromo-2(4-nitrophenoxy)-3(1-phenylethyl)-3,4-dihydro-1,3,2-benzoxazaphosphinine 2-oxide

\[
\begin{array}{c}
\text{Br} \\
\text{CH-CH}_3 \\
N \\
\text{O-P-O} \\
\text{NO}_2
\end{array}
\]

In this structure, C\textsubscript{21}H\textsubscript{18}BrN\textsubscript{2}O\textsubscript{5}P, the six-membered oxazaphosphinine ring is in a twist-boat conformation. One of the phosphoryl O atoms is in an equatorial configuration while the other is axial with respect to the oxazaphosphinine ring. The mean plane of the benzene ring to which the nitro group is attached and the phenyl ring form a dihedral angle of 83.5(1)°. In the crystal structure, weak intermolecular C-H…O hydrogen bonds link the molecules into chains to form graph set descriptor \( R^1_1(8) \) along [100] direction. The structure was solved by direct methods with final R-factor 0.034.

CHAPTER-3 deals with the crystal structure and molecular conformation of 3-(6-methyl-2-pyridyl)-2-phenoxy-3,4-dihydro-1,3,2-benzoxazaphosphirine 2-oxide

\[
\begin{array}{c}
\text{O-P-O} \\
\text{N} \\
\text{H}_3\text{C} \\
\text{N} \\
\text{O} \\
\text{O}
\end{array}
\]

In this structure, C\textsubscript{19}H\textsubscript{17}N\textsubscript{2}O\textsubscript{3}P, the six-membered 1,3,2-oxazaphosphorine ring adopts a twist-boat conformation with the phosphoryl O atom in an equatorial position,
In the structure, \( \text{C}_{19}\text{H}_{18}\text{NO}_2\text{P} \), the oxazaphosphinine ring exhibits a boat conformation. The phosphoryl \( \text{O} \) atom is in equatorial position. The dihedral angle between the two phenyl rings is 75.5(1)°. These phenyls are making a dihedral angle of 57.3(1)° and 74.6(1)° respectively, with respect to the heterocyclic ring. In this structure, the phosphoryl \( \text{O}5 \) atom acts as an acceptor participates in intermolecular \( \text{C}(17)-\text{H}(17)\ldots\text{O}(5) \) hydrogen bond with the neighboring molecule to form centrosymmetric \( R_{2}^{1}(14) \) dimmers. The same phosphoryl \( \text{O}5 \) atom also participates in intermolecular \( \text{C}(21)-\text{H}(21)\ldots\text{O}(5) \) hydrogen bonding. These two hydrogen bonds are extended to adjacent atoms of molecules to form \( R_{4}^{1}(28) \) rings. Parallel sheet of rings are viewed along the bc plane and in addition, the crystal structure is stabilized by \( \text{C}(18)-\text{H}(18)\ldots\text{O}(4) \) intramolecular hydrogen bonding. The structure was solved by direct methods with final R-factor 0.055.

**CHAPTER-6**

A comparative study among the four 1,3,2 benzoazaphosphinine derivatives presented in the chapters 2,3,4 & 5 are mentioned in this chapter.

**CHAPTER-7** deals with the crystal structure and molecular conformation of 2,4,8,10,13-pentamethyl-6-phenyl-13,14-dihydro-12H-6\( \chi \)-dibenzo-[d,i][1,3,7,2] dioxazaphosphecin-6-thione

In this structure, \( \text{C}_{25}\text{H}_{28}\text{NO}_2\text{PS} \), the cyclodecene ring assumes a crown conformation. The phosphoryl sulfur and the methyl substituted at N are equatorially oriented to the mean plane of ten membered ring. The phenyl ring substituted at P to the...
while the other in axial position w.r.t the oxazaphosphorine ring. 6-methyl-2-pyridyl and phenoxy groups are almost in the same plane with the dihedral angle of 12.3(1)° and they are oriented at angles of 42.4(1)° and 54.6(1)° respectively with respect to the six membered ring. The crystal structure is stabilized by C–H...O intermolecular hydrogen bond C(19)–H(19)...O(5) which forms zig zag chains along C-axis and also by C–H...π interactions. The structure was solved by direct methods with final R-factor 0.055.

CHAPTER-4 describes the crystal structure and molecular conformation of 3-(6-methyl-2-pyridyl)-2-phenyl-3,4-dihydro-1,3,2-benzoxazaphosphinine 2-oxide

In this structure, C_{19}H_{17}N_{2}O_{2}P, the six-membered 1,3,2-oxazaphosphinine ring possesses a boat conformation with the phosphoryl O atom in equatorial position. The dihedral angle between the 6-methyl-2-pyridyl and phenyl groups is 75.5(1)°. These substituents are trans to each other, and oriented at angles of 57.2(1)° and 74.8(1)°, respectively, to the benzene ring. The crystal structure is stabilized by intra and intermolecular hydrogen bonds. The phosphoryl O atom participates in intermolecular C–H...O interactions with the neighbouring molecules, forming centrosymmetric \( R_1^2(14) \) dimers. The structure was solved by direct methods with final R-factor 0.052.

CHAPTER-5 consists of crystal structure and molecular conformation of 2-phenyl-3-m-tolyl-3,4-dihydro-benzo[e][1,3,2] oxazaphosphinine 2-oxide
ten membered ring is perpendicular with a dihedral angle of 88.4(1)°. The two dimethyl benzenes, which are fused on either side of ten membered ring are at dihedral angles of 20.2(1)° and 18.0(1)°, show they their orientation is nearly symmetrical with respect to ten membered ring. The intramolecular hydrogen bond C(23)−H(23A)⋯O(3) stabilizes the crystal structure. The structure was solved by direct methods with final R-factor 0.049.

CHAPTER-8 describes the crystal structure and molecular conformation of Diethyl [(5-chloro-2-hydroxyanilino)(4-florophenyl)methyl] phosphonate

In the structure, C_{17}H_{20}ClFNO_{4}P, the phosphorus atom has distorted tetrahedral configuration. The crystal structure is stabilized by N−H⋯O, O−H⋯O, C−H⋯N, C−H⋯O type hydrogen bonds, along with C−H⋯F, C−H⋯Cl weak halogen interactions. In this structure, the hydroxyl oxygen, which acts as an acceptor in the N(4)−H(4)⋯O(8) intramolecular bonding, is linked to O(8)−H(8)⋯O(5) intermolecular bonding, where the same hydroxyl oxygen behaves as a donor, to form $R^2_3(14)$ centrosymmetric dimers along C-axis. C(21)−H(21)⋯N(4) and C(24)−H(24B)⋯O(5) intermolecular hydrogen bondings are also present. Additionally, the molecular structure is stabilized by weak C(23)−H(23C)⋯Cl(3) and C(15)−H(15)⋯F(2) halogen interactions. The two benzenes rings are perpendicular to each other with dihedral angle of 88.0(1)°. The structure was solved by direct methods with final R-factor 0.069.
CHAPTER-9 presents the crystal structure and molecular conformation of Diethyl [(5-chloro-2-hydroxyanilino)(4-chlorophenyl)methyl] phosphonate

![Chemical Structure](image)

In the structure, C_{17}H_{20}Cl_{2}NO_{4}P, the P atom is bonded in a distorted tetrahedral environment. The dihedral angle between the two benzene rings is 80.5(1)°. In the structure, C-H...O and N-H...O intermolecular hydrogen bonds, C(24)-H(24B)...O(5) and N(4)-H(4)...O(8) form centrosymmetric $R_{1}^{2}(10)$ linked through O-H...O intermolecular hydrogen bond which form centrosymmetric $R_{1}^{2}(16)$ dimmers. These hydrogen bonds form one-dimensional chains along [010]. Additional stabilization is provided by very weak C-H...Cl interactions. The structure was solved by direct methods with final R-factor 0.053.

CHAPTER-10 consists of the crystal structure and molecular conformation of Diethyl [(5-chloro-2-hydroxyanilino)(4-bromophenyl)methyl] phosphonate

![Chemical Structure](image)

In this structure, C_{17}H_{20}BrClNO_{4}P, intermolecular C-H...O and N-H...O hydrogen bonds form centrosymmetric $R_{1}^{2}(10)$ dimmers linked through O-H...O intermolecular hydrogen bonds, which form centrosymmetric $R_{1}^{2}(16)$ dimmers. All
these hydrogen bonds form chains along [010] plane. Here the phosphonate double bonded oxygen atom, which behaves as an acceptor participates in C-H...O intermolecular hydrogen bonding, where as, the hydroxyl oxygen, which acts as both donor and acceptor, participates in the N-H...O intra and intermolecular hydrogen bonding. The very weak intramolecular N-H...O interaction forms a five-membered ring. In addition, the crystal structure is stabilized by weak C-H...Br hydrogen bonds. The structure was solved by direct methods with final R-factor 0.056.

CHAPTER-11 deals with the crystal structure and molecular conformation of Diethyl [(5-chloro-2-hydroxyanilino)(4-methyl-phenyl)-methyl] phosphonate

\[
\text{In this structure, } \text{C}_{18}\text{H}_{23}\text{ClNO}_4\text{P, the phosphonate double bonded oxygen atom which behaves as an acceptor is linked to hydroxyl oxygen which acts as donor to form } \text{O(8)-H(8)...O(5) hydrogen bonds. These will form centrosymmetric dimers with graph set descriptor } R_1^2(16) \text{ along [101] plane. The structure was solved by direct methods with final R-factor 0.058.}
\]

CHAPTER-12

A comparative study among the four diethyl phosphonate derivatives presented in the chapters 8,9,10 & 11 are mentioned here.

CHAPTER-13

The conclusion of the thesis was represented in this chapter.
The overall details pertaining to crystallization, crystal data, data collection, data reduction, corrections to be applied, structure solution, structure refinement, the formulae used in calculating the geometrical parameters and conformation are explained at the beginning of the thesis itself while the specific details for individual crystal are presented in tabular form in the respective chapters.

All computations involved in this thesis were carried out by using Pentium-III PC available in the department.

The figures and tables are numbered serially chapter wise. The figures are given at the appropriate places in the text while the tables are given collectively at the end of each chapter. The references cited in the text are given in alphabetical order at the end of the thesis.

The structure factor tables (h, k, l, $|F_o|^2$, $|F_c|^2$) for all the structures are given in the compact disc (CD) as a zip file enclosed in a pouch at the back cover of the thesis.
Based upon the above studies, the following papers have been published

6-Bromo-2(4-nitrophenoxy)-3(1-phenylethyl)-3,4-dihydro-1,3,2-benoxazaphosphinine 2-oxide
V.H.H. Surendra Babu, M. Krishnaiah, K. Srinivasulu, C. Naga Raju and B. Sreedhar

3-(6-methyl-2-pyridyl)-2-phenoxy-3,4-dihydro-1,3,2-benoxazaphosphirine 2-oxide
Rajni Kant, Sabeta Kohli, Lovely Sarmal, M. Krishnaiah and V.H.H. Surendra Babu.

3-(6-methyl-2-pyridyl)-2-phenyl-3,4-dihydro-1,3,2-benoxazaphosphinine 2-oxide
V.H.H. Surendra Babu, M. Krishnaiah, M. Anil Kumar, C. Suresh Reddy and Rajni Kant.

2,4,8,10,13-Pentamethyl-6-phenyl-13,14-dihydro-12H-6\alpha^2-dibenzo[d,ij][1,3,7,2]
dioxazaphosphocene-6-thione
M. Krishnaiah, V.H.H. Surendra Babu, A. Uma Ravi Sankar, C. Naga Raju and Rajni Kant.

Diethyl [(5-chloro-2-hydroxyanilino)-(4-chlorophenyl)methyl]phosphonate
M. Krishnaiah, V.H.H. Surendra Babu, G. Syam Prasad, C. Suresh Reddy and

Diethyl [(4-bromophenyl)-(5-chloro-2-hydroxyanilino)methyl]phosphonate

6-(2,4-Dichlorophenoxy) dibenzo[d,f][1,3,2] dioxaphosphepine 6-sulfide
M. Krishnaiah, V.H.H. Surendra Babu, J. Radha Krishna, K. Ananda Kumar, C. Suresh
not related to this thesis work)
List of Papers presented in National and International conferences

A paper entitled “Crystal structure and molecular conformation of 6-bromo-2(4-nitrophenoxy)-3(1-phenylethyl)-2,4-dihydro-1,3,2-benzoazaphosphinine 2-oxide”, with Authors: M. Krishnaiah, V.H.H. Surendra Babu, K. Syam Kumar, K. Srinivasulu, C. Naga Raju and B. Sreedhar, had received the Best Poster Award in 37th National Seminar on Crystallography (NSC-37) conducted by Department of Physics, Jadavpur University, Kolkata during February, 06-08, 2008.

A paper entitled “Structures of Bioactive compounds: Substituted 1,3,2-Benzoazaphosphinine Derivatives” was presented as a poster by my Professor, with Authors: M. Krishnaiah V.H.H. Surendra Babu and Vedavathi G. Puranik at AScA’09, jointly conducted by Asian Crystallography Association & Chinese Crystallographic Society held at Beijing, China, during October, 22-25, 2009.

List of Seminars/Conference Attended

37th National Seminar on Crystallography (NSC-37) conducted by Department of Physics, Jadavpur University, Kolkata during February, 06-08, 2008.

36th National Seminar on Crystallography (NSC-36) conducted by Department of Crystallography and Biophysics, University of Madras, Chennai during January 22-24, 2007.