CHAPTER 1

Introduction
# Chapter 1

## Introduction

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X-ray crystallography is the most comprehensive technique available to determine the structure of any molecule at atomic resolution. Results from X-ray crystallographic studies provide unambiguous, accurate, and reliable 3-dimensional structural parameters at times even before complete chemical characterization is available. There are in total 29 Nobel Prizes (Chemistry, Physics, Physiology and Medicine) are awarded, so far in the field of Crystallography from 1956 to 2014 and almost one in four Chemistry prizes since 1956 have been for molecular structure work [1]. Crystallography can reliably provide the answer of many structure related questions, from global folds to atomic details of bonding. It is the only method for determining the "absolute" configuration of a molecule. Accurate knowledge of molecular structure is a prerequisite for rational drug design and structure-based functional studies. Structure and function are intimately related. As it is well recognized fact that pharmaceutical action of a drug molecule is an involved function of its structure, a small change in the structure can alter its pharmaceutical action drastically and it is therefore, very essential to acquire the knowledge of the structure of the molecule to modify the drug molecule in terms of its efficacy, selectivity and mode of action leading to predict a safer and more effective drug. Absolute configuration is a critical property in biological systems as changes in this may alter the response of the biologic system. Wealth of informations so obtained can not only help to understand the structure-function relationship, but also provide the basis to design a perfect drug without or with fewer side effects.

It is in this context author has attempted to determine the structures of few interesting heterocyclic compounds especially of novel N-heterocycles and chalcone derivatives by X-ray diffraction technique and Ab-initio MO calculations have been carried out using Gaussian-09 software to compare experimental results (by X-ray) with theoretically predicted optimized structure. To correlate the structure-
function relationship, antimicrobial activities of all these compounds have been studied against a panel of different organisms.

1.2 Introduction to Heterocyclic Compounds

Heterocyclic compounds are a class of organic compounds whose molecules contain one or more rings with at least one heteroatom being an element other than carbon in the rings, most frequently oxygen, nitrogen or sulfur. Heterocyclic compounds probably constitute the largest and most varied family of organic compounds. Every first step of life starts with hetero-cyclic compounds. Every man’s potential to think, intelligence, behavior, character depends on his gene. The basic skeleton of the genetic material (DNA) is made up of hetro-cycles like adenine, guanine, cytosine and thymine (Figure 1.1) [2-4]. Thus the knowledge of heterocyclic compounds and its application is part of venturing human life.

![Example of few eminent heterocyclic compounds](image)

Figure 1.1 Example of few eminent heterocyclic compounds

Figure 1.2 shows few five and six membered ring structures. Five membered ring, with one of the hetero-atoms as N is known as Pyrrole (aromatic), O as Furan (aromatic) and S as Thiophene (aromatic)[5-6]. Five membered heterocyclic ring is present in chlorophyll, hemoglobin, indigo, tryptophate etc. and its polymers such as melanin and cumarone. Whereas pyričine, pyrido:xne (vitamin B6), vitamin E, quinine and the pyran nucleus are the heterocyclic compounds with six membered ring which are found in sugar and the anthrocyanin pigments. Nicotine and morphin are the compounds both have five and six membered heterocyclic rings. Purine and pyrimidine are the
parent compounds of nucleic acid and also found in barbiturates, caffines and antibiotics etc. Additionally, heterocyclic compounds are important components in dye chemistry, organic electronic materials, and as chelating agents [7-11]. Looking towards the importance of these groups of heterocycles, Author has picked up few pyrazoline, pyrimidine, quinazoline, benzoimidazol and chalcone derivatives for X-ray crystallographic investigations.

<table>
<thead>
<tr>
<th>Heteroatom</th>
<th>Nitrogen</th>
<th>Oxygen</th>
<th>Sulfur</th>
<th>Nitrogen</th>
<th>Oxygen</th>
<th>Sulfur</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Pyrrolidine</td>
<td>Oxolane</td>
<td>Thiolane</td>
<td>Pyrrole</td>
<td>Furan</td>
<td>Thiophene</td>
</tr>
<tr>
<td>Structure</td>
<td><img src="image" alt="Structure of Pyrrolidine" /></td>
<td><img src="image" alt="Structure of Oxolane" /></td>
<td><img src="image" alt="Structure of Thiolane" /></td>
<td><img src="image" alt="Structure of Pyrrole" /></td>
<td><img src="image" alt="Structure of Furan" /></td>
<td><img src="image" alt="Structure of Thiophene" /></td>
</tr>
<tr>
<td>Name</td>
<td>Piperidine</td>
<td>Oxane</td>
<td>Thiane</td>
<td>Pyridine</td>
<td>Pyran</td>
<td>Thiopyran</td>
</tr>
<tr>
<td>Structure</td>
<td><img src="image" alt="Structure of Piperidine" /></td>
<td><img src="image" alt="Structure of Oxane" /></td>
<td><img src="image" alt="Structure of Thiane" /></td>
<td><img src="image" alt="Structure of Pyridine" /></td>
<td><img src="image" alt="Structure of Pyran" /></td>
<td><img src="image" alt="Structure of Thiopyran" /></td>
</tr>
</tbody>
</table>

Figure 1.2 Few five and six membered ring structures

### 1.2.1 Pyrazoline and Pyrimidine

**Pyrazoline**

Pyrazoline is a prominent nitrogen-containing heterocyclic chemical compound with the molecular formula C_3H_6N_2. It is a heterocycle characterized by a 5-membered ring of three carbon atoms and two adjacent nitrogen centers [4, 7]. Table 1.1 shows the chemical structures of pyrazoline along with few of its physical properties.

<table>
<thead>
<tr>
<th>Table 1.1 Chemical structures and Physical Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="1-Pyrazoline" /></td>
</tr>
<tr>
<td>1-Pyrazoline</td>
</tr>
</tbody>
</table>
Physical Properties

Molecular Formula \( \text{C}_3\text{H}_6\text{N}_2 \)
Molecular weight 70.09 g mol\(^{-1}\)
Boiling point 144°C
Density 1.02 g/cm\(^3\)

**Synthesis of pyrazoline**

Various procedures have been worked out for its synthesis. A one-pot synthesis of nitrogen-containing heterocycles from alkyl dihalides and primary amines and hydrazines occurs under microwave irradiation via a simple and efficient cyclo condensation in an alkaline aqueous medium (Figure 1.3) [12].

![Figure 1.3 Reaction scheme of the pyrazoline derivative](image)

Pyrazoline derivatives found to possess antiamoebic [13], antidepressant [14], antioxidant [15], anti-inflammatory [16-17], anticonvulsant [18], antimicrobial [19], analgesic [20] antiviral [21], antioxidant [22], monoamine oxidase (MAO-A and MAO-B) inhibitors [23] and anticancer [24] activities. Pyrazoline derivatives with a phenyl group at the 5-position possesse good film-forming properties and exhibit excellent characteristics of blue photoluminescence, fluorescence and electroluminescence properties [25-26]. In view of importance of pyrazoline derivatives, three novel \( N \)-substituted pyrazoline derivatives are picked up for systematic X-ray crystallographic investigations and the details of it are reported in Chapters 3, 4 and 5.

**Pyrimidine**

Pyrimidine, one of the members of diazine family is an aromatic heterocyclic organic compound containing two nitrogen atoms at
positions 1 and 3 of the six-membered ring. The other diazines are pyrazine (nitrogen at 1 and 4) and pyridazine (nitrogen at 1 and 2) shown in Figure 1.4 [4, 7].

Figure 1.4 Chemical structures of diazine

The systematic study of pyrimidines began in 1884 with Pinner, who synthesized derivatives by condensing ethyl acetoacetate with amidines and first proposed the name “pyrimidin” [27]. The chemical, ball stick and space field structures with physical properties of pyrimidine are shown in Table 1.2.

Table 1.2 The chemical, ball stick and space field structures with physical properties of pyrimidine

<table>
<thead>
<tr>
<th>Physical Properties</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular formula</td>
<td>C₄H₄N₂</td>
</tr>
<tr>
<td>Molar mass</td>
<td>80.088 g mol⁻¹</td>
</tr>
<tr>
<td>Density</td>
<td>1.016 g cm⁻³</td>
</tr>
<tr>
<td>Melting point</td>
<td>20-22 °C, 293-295 K, 68-72 °F</td>
</tr>
<tr>
<td>Boiling point</td>
<td>123-124 °C, 396-397 K, 253-255 °F</td>
</tr>
<tr>
<td>Acidity (pKₐ)</td>
<td>1.10 (protonated pyrimidine)</td>
</tr>
</tbody>
</table>

The derivatives of pyrimidine play a vital role in many biological processes and are present in nature including substituted and fused
ring derivatives like nucleotides, alloxan, thiamine, nucleic acid, several vitamins, co-enzymes, uric acid and in other purines nucleic acid [28]. Pyrimidine and purine are bound at the sugar moieties. In addition, the synthetic members containing these derivatives are also important as pharmaceutical and biological fields. Some substituted pyrimidines and their derivatives have been reported to possess antimicrobial and antifungal activities [29]. It has also minor antiviral activity against herpes and vaccinia infections [30]. Several pyrimidine non-nucleoside derivatives are known to exhibit anti-cancer [31] and anti-viral [32, 33] properties. In view of the biological importance of pyrimidine derivatives, X-ray crystallographic investigations of pyrimidine derivatives are worked out and reported in Chapters 6 and 7 of the Thesis.

1.2.2 Quinazoline and Benzimidazole

Quinazoline

Quinazoline, another significant member of heterocyclic compound, made up of two fused six-membered aromatic rings; a benzene ring and a pyrimidine ring. Its chemical formula is C8H6N2. Quinazoline is yellow solid. The chemical, ball stick and space field structures of quinazoline with its physical properties are shown in Table 1.3. [4, 7].

<table>
<thead>
<tr>
<th>Physical Properties</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular formula</td>
<td>C8H6N2</td>
</tr>
<tr>
<td>Molar mass</td>
<td>130.15 g mol⁻¹</td>
</tr>
<tr>
<td>Acidity (pKₐ)</td>
<td>3.51</td>
</tr>
</tbody>
</table>

Table 1.3 The chemical, ball stick and space field structures with physical properties of quinazoline
It is first prepared by Gabriel in 1903 and first isolated from the Chinese plant aseru. The development of research on biological activity of quinazoline compounds started when the compound 2-methyl-1, 3-aryl-4 quinazoline derivative is synthesized. This compound has soporific & sedative action. In 1968 only two derivatives are used, soporific & anticonvulsant- methaqualone and diuretic quinathazone. By 1980, about 50 kinds of derivatives of this class are included in medicine with different biological actions like soporific, sedative, tranquilizing, analgesic, anticonvulsant, antitussive, myorelexant, antirheumatic, hypotensive, antiallergic, bronchodilating, antidiabetic, cholagogue, diuretic, cystatic, antimalarial, spermicidal etc [34]. In the literature, the couple of reviews are cited a broad perspective of the pharmacological activities of Quinazoline derivatives [35-36]. The derivatives of quinazoline exhibit anticancer [37], anti-inflammatory [38], anti-HIV [39], antibacterial and anti-fungal activities [40]. In viewing the biological significance of the quinazoline derivatives, author has worked out crystal structure of a quinazoline derivative and reported in Chapter 8 of Thesis.

**Benzimidazole**

Benzimidazole, a class of heterocyclic aromatic chemical compound, which share a fundamental structural characteristic of six-membered benzene fused to a five-membered imidazole ring. The benzimidazole nucleus does not occur widespread in nature. However, the 5, 6-dimethyl benzimidazole moiety has been shown to be part of the structure of vitamin B12. Benzimidazole is relatively nontoxic and has little effect on the blood pressure. The chemical, ball stick and space field structure with physical properties of benzimidazole are shown in Table 1.4. [4,7].
Table 1.4 The chemical, ball stick and space field structure with physical properties of benzimidazoles

![Molecular structure of benzimidazole]

<table>
<thead>
<tr>
<th>Physical Properties</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular formula</td>
<td>C₇H₆N₂</td>
</tr>
<tr>
<td>Molar mass</td>
<td>118.14 g mol⁻¹</td>
</tr>
<tr>
<td>Melting point</td>
<td>170–172 °C</td>
</tr>
<tr>
<td>Acidity (pKₐ)</td>
<td>12.8</td>
</tr>
</tbody>
</table>

Benzimidazole is a commercially available compound. The condensation of O-phenylene diamine with formic acid or the equivalent trimethyl orthoformate gives the benzimidazole, this method is generally able to afford 2-substituted benzimidazoles (Figure 1.5) [41].

**General reaction for synthesis of Benzimidazole**

\[
\text{O-Phenylene diamine + COOH-R} \rightarrow \text{Benzimidazole} \\
\text{C}_6\text{H}_4[\text{NH}_2]_2 + \text{HC(OCH}_3\text{)}_3 \rightarrow \text{C}_6\text{H}_4\text{N(NH)}\text{CH} + 3 \text{CH}_3\text{OH}
\]

**Figure 1.5 Reaction scheme of the Benzimidazole**

The molecular architecture of benzimidazole is such that the imidazole is a precursor to \(N\)-heterocyclic carbenes and the benzene ring provides a convenient scaffold to which additional functionality may be easily added to modify. This combination of a reactive carbene center with a modifiable backbone is without doubt one of the reasons for the recent rise in study and use of benzimidazoles and their \(N\)-heterocyclic carbene derivatives. Benzimidazole moiety are reported to possess a number of interesting biological activities such as antitubercular[42], anticancer[43], anthelmintic[44], antiallergic[45], antioxidant[46], antihistaminic[47] and antimicrobial[48]. 1-Dimethyl amino ethyl benzimidazole and several related compounds containing substituent groups in the 2-position of the benzimidazole ring are
found to possess only slight antihistaminic activity [49]. Benzimidazole derivatives have found many applications as corrosion inhibitor [50-51] and also widely used in dye [52]. Aside from their place in biomedical research, benzimidazoles also have a prominent place in organo-catalysis, organo-metallic [53] and Materials Chemistry [54]. In viewing the biological significance of the benzimidazole derivatives, author has investigated one of the iodo-benzimidazole derivative by X-ray diffraction technique and reported in Chapter 9 of the Thesis.

### 1.2.3 Chalcone

Chalcone is an aromatic ketone and an enone that forms the central core for a variety of important biological compounds, which are known collectively as chalcones or chalconoids. Benzylidene acetophenone is the parent member of the chalcone series. The alternative names given to chalcone are phenyl styryl ketone, benzalacetophenone, β-phenylacrylophenone and α-phenyl-β-benzoylethylene. In the chemical structure, three carbon α – β unsaturated carbonyl system, the backbone of the open chain flavonoid, joins two aromatic rings. The chemical structure with physical properties of chalcone is shown in Table 1.5 [4, 7]. Chalcone can be prepared by an aldol condensation between a benzaldehyde and acetophenone in the presence of sodium hydroxide as a catalyst (Figure 1.6). Kinetic studies have been reported for the base-catalyzed formation of chalcone and its derivatives [55, 56].

**Table 1.5 Chemical structure and physical properties of chalcone**

![Chemical structure of chalcone](image)

<table>
<thead>
<tr>
<th>Physical Properties</th>
<th>Molecular formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>C₁₅H₁₂O</td>
<td></td>
</tr>
</tbody>
</table>
### Synthesis of Chalcone:

![Reaction scheme of the chalcone derivative](image)

The chalcone (1, 3-diaryl-2-propenones), belongs to flavonoid family, and their derivatives are important intermediates in organic synthesis [57]. The derivatives of chalcone, synthesized or the natural one, displayed many interesting properties like anti-inflammatory [58], antifungal [59], antioxidant [60], antimalarial [61], antituberculosis [62], analgesic [63], anti HIV [64] and anticancer [65] activities. These groups of compound constitute an important class of natural products and its derivatives have attracted particular interest in medicine during the last few decades. In view of the pharmacological importance of chalcone, author has determined crystal structures of three novel chalcone derivatives with halogen, hydroxy and methoxy moieties substituted at different sites at (4, 5-dimethoxy-2-methyl-phenyl) prop-2-en-1-one and the details are reported in Chapters 10,11 and 12 of the Thesis.

### 1.3 Introduction to Computational Chemistry

Computational chemistry is simply the application of chemical, mathematical and computing skills to the solution of interesting chemical problems. It uses computers to generate information such as properties of molecules or simulated experimental results [66, 67]. Gaussian, GAMESS, MOPAC, Spartan and SYBYL®-X Suite are some common computer softwares used for computational chemistry.
Computational chemistry has become a useful way to investigate materials those are too difficult to find or too expensive to purchase. It also helps chemists to make predictions before running the actual experiments so that they can be better prepared for making observations. The Schrödinger equation is the basis for most of the computational chemistry. This is because the Schrödinger equation models the atoms and molecules with mathematics. Computational quantum chemistry is primarily concerned with the numerical computation of molecular electronic structures by \textit{ab initio} and semi-empirical techniques.

\textbf{1.3.1 Ab-Initio and DFT Calculations}

Along with single crystal X-ray diffraction study of novel N-Heterocycles and Chalcone derivatives, optimized geometry of all these molecules have been carried out using Gaussian-09 software (ab-initio and DFT calculations). Various methods like single point energy calculation, geometry optimization and frequency calculation have been used. Single point energy is a prediction of the energy and the related properties for a molecule with a specified geometric structure. These calculations are performed to obtain basic informations about a molecule to compute very accurate values for the energy and the other properties, for geometry optimization at a lower level of theory. Total energy of the system, molecular orbitals and orbital energies, charge distribution, dipole and higher multipole moments have been calculated. Geometry optimizations usually attempt to locate minima on the potential energy surface, thereby predicting equilibrium structures of molecular systems. Geometry optimization helped to calculate theoretically bond lengths, bond angles, torsional angles and dihedral angles. Computed bond lengths, bond angles, torsional angles and dihedral angles are compared with the experimental X-ray data.

\textit{Ab-initio calculations}
Ab-initio quantum chemistry methods are computational chemistry methods based on quantum chemistry [68]. The term ab initio was first used in quantum chemistry by Robert Parr and coworkers, in a semi empirical study on the excited states of benzene [69]. In its modern meaning is 'from first principles of quantum mechanics', the term was used by Chen [70]. The simplest or most common type of ab initio electronic structure calculation is called Hartree-Fock calculation. Hartree-Fock method is central starting point for most ab initio quantum chemistry methods. This method offer variety of basis sets of varying complexity as the basis set size increased, the energy and wave function tend towards a limit called Hartree-Fock limit.

In this method, the approximation allows one to treat the Schrödinger equation as a "simple" eigen-value equation of the electronic molecular Hamiltonian, with a discrete set of solutions. Hartree introduced a procedure, which he called the self-consistent field method (SCF) to calculate approximate wave functions and energies for atoms and ions [71-72]. There are two types of Hartree Fock method

1. Restricted Hartree-Fock method (RHF)
2. Unrestricted Hartree-Fock method (UHF)

In Restricted Hartree-Fock, there is no unpaired electron or atom or molecule in a close-cell system. With all orbitals are doubly occupied, while in unrestricted Hartree-Fock method there is an unpaired electron so atom or molecule not in a close-cell but it is open-cell system.

**DFT calculations**

Density functional theory (DFT) is a quantum mechanical modeling method used in Physics and Chemistry to investigate the electronic structure (principally the ground state) of many-body systems, particularly of atoms, molecules and the condensed phases. With this theory, the properties of a many-electron system can be determined by using functionals, i.e. functions
of another function, which in this case is the spatially dependent electron density. Hence the name density functional theory comes from the use of functional of the electron density. DFT is among the most popular and versatile methods available in Condensed Matter Physics, Computational Physics and Computational Chemistry. DFT has been very popular for calculations in Solid State Physics since the 1970s. However, DFT was not considered accurate enough for calculations in quantum chemistry until the 1990s, when the approximations used in the theory are greatly refined to better model three exchange and correlation interactions. In many cases the results of DFT calculations for solid-state systems agree quite satisfactorily with experimental data. Examples of DFT applications include studying the effects of dopants on phase transformation behavior in oxides, magnetic behavior in dilute magnetic semiconductor materials and the study of magnetic and electronic behavior in ferroelectrics and dilute magnetic semiconductors [73-74]. Computational costs are relatively low when compared to traditional methods, such as Hartree–Fock theory and its descendants based on the complex many-electron wave function.

Austin Model (AM1) is a semi-empirical method for the quantum calculation of molecular electronic structure in computational chemistry. It is based on the Neglect of Differential Diatomic Overlap integral approximation. Specifically, it is a generalization of the modified neglect of differential diatomic overlap approximation. AM1 was developed by Michael Dewar and co-workers and published in 1985. AM1 is an attempt to improve the MNDO model by reducing the repulsion of atoms at close separation distances [4,7]. AM1 method is used to calculate optimized geometry parameter of benzimidazole derivatives (chapter 9).

**Applications of computational (ab-initio and DFT) calculations:**

1. Ab initio calculations are used to determine bond lengths and bond angles of molecule by calculating the total energy of a
molecule for different molecular geometries and it finds a conformation having lowest energy.

(2) The good side of ab-initio method is that they eventually converge to exact solution, once all of the approximations are made sufficiently small in magnitudes.

(3) It also calculates the NMR, IR data theoretically, the results are compared with experimental data and one can confirm the structure.

(4) We can calculate dipole moment and higher multi-pole moments.

(5) One can find molecular energies like HOMO (Highest occupied molecular orbitals and LUMO (Lowest Unoccupied Molecular Orbitals).

(6) An electronic structure package is capable of predicting many properties of atoms and molecules, e.g. molecular energies, Vibrational frequencies, electron densities.

1.4 Antimicrobial Activities

The science dealing with the study of the prevention and treatment of diseases caused by micro-organisms is known as medical microbiology. For the treatment of diseases inhibitory chemicals employed to kill micro-organisms or prevent their growth, are called antimicrobial agents. Antibiotics are produced by micro-organisms or they might be fully or partly prepared by chemical synthesis. For an antibiotic to be useful to humans, it must have the ability to destroy pathogens while being relatively non-toxic to the host organism. It should be chemically stable and be able to reach the part of the host organism in which the infection persists. Use of substances with antimicrobial properties is known to have been common practice for at least 2000 years. Ancient Egyptians and ancient Greeks used specific molds and plant extracts to treat infection [75]. Louis Pasteur and Jules Francois Joubert observed antagonism between some bacteria and discussed the merits of controlling these interactions in medicine [76]. Antibiotics are produced by micro-organisms or they might be
fully or partly prepared by chemical synthesis. They inhibit the growth of micro-organisms in minimal concentrations. Antibiotics may be of microbial origin or purely synthetic or semi-synthetic [77]. Various methods have been used from time to time by several workers to evaluate the antimicrobial activity. Most common, Multidisc agar cup method is used to investigate the biological response of these heterocyclic compounds against a panel of different organisms and the percentage potency has been calculated.

It is well established that the function of a molecule is associated with the molecular structure. A small change in the structure is accompanied by the change in its function. To modify the drug molecule in terms of its effectiveness against different bacteria, to correlate the structure-function relationship of a particular molecule, the compound has been tested for its biological response. It is very essential to acquire the information of the structure of a molecule to understand the drug activity of a specific molecule.

1.5 Present Study

The non-covalent interactions responsible for generating supramolecular structure with novel properties are the fundamentals and prime importance for the tuning and prediction of crystal structure of heterocyclic molecules. However, literature survey reveals that systematic studies on N-containing heterocyclic compounds [78-79] are still lacking. Looking towards the importance of X-ray crystallographic investigations, few N-heterocycles: pyrazoline, pyrimidine, quinazoline, benzoimidazol and chalcone derivatives have been investigated by X-ray diffraction technique. The compounds picked up for the present study are

1. 1-[3-(2-benzoyloxy-6-hydroxy-4-methyl-phenyl)-5-phenyl -4, 5-dihydro-pyrazol-1-yl]- propane-1-one
2. 1-[3-(2-benzoyloxy-6-hydroxy-4-methyl-phenyl)-5-(3,5-bis-trifloromethyl - phenyl)-4, 5-dihydro-pyrazol-1-yl]- propane-1-one
3. l-[3-(2-benzyloxy-6-hydroxy-4-methyl-phenyl)-5-(3,4,5-trimethoxy-phenyl)-4, 5-dihydro-pyrazol-1-yl]- propane-1-one
4. 2-Chloro-4-(4-fluro-phenyl) 6-isopropyl-pyrimidine-5-carboxylic acid methyl ester
5. 2-Chloro-4-(4-fluro-phenyl)-5-[2-(4-fluro-phenyl)-vinyl]-6-isopropyl-pyrimidine
6. 3-[2-(3,4-Dimethoxy-phenyl)-ethyl]-2-methyl-3H-quinazoline-4-one
7. 1,3-Dimethyl-3H-benzoimidazol-1-ium; iodide
8. 3-(3-chloro-4,5-dimethoxy-phenyl)-1-(4,5-dimethoxy-2-methyl-phenyl)prop-2-en-1-one
9. 3-(3-chloro-4-methoxy-phenyl)-1-(4,5-dimethoxy-2-methyl-phenyl)prop-2-en-1-one
10. 3-(2-chloro-3-hydroxy-4-methoxy-phenyl)-1-(4,5-dimethoxy-2-methyl-phenyl)prop-2-en-1-one

The different N-heterocyclic compounds are picked up for X-ray crystallographic investigations are tabulated below (Table 1.6).

**Table 1.6** Pyrazoline, pyrimidine, quinazoline, benzoimidazol and chalcone derivates for X-ray crystallographic investigations

<table>
<thead>
<tr>
<th>Pyrazoline derivatives</th>
<th>Pyrimidine derivatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>R&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>Chap-3</td>
<td>H</td>
</tr>
<tr>
<td>Chap-4</td>
<td>CF&lt;sub&gt;3&lt;/sub&gt;</td>
</tr>
</tbody>
</table>
Chapter 1

Sardar Patel University

Department of Physics

Quinoline derivative

Chap-8

Benzimidazole derivative

Chap-9

Chap-10 H Cl oC\textsubscript{3}

Chap-11 H Cl H

Chap-12 Cl OH H

Ph.D. Thesis

Sahaj A. Gandhi

18
Three dimensional structures of these compounds have been worked out with the highest accuracy. Optimized geometry calculations are performed using RHF (Ab-initio) and B3LYP (DFT) methods by Gaussian-09 software. To correlate the structure-function relationship, antimicrobial activities of all these compounds have been studied against a panel of different organisms.

A comprehensive review on the analysis of the results obtained by author and the other reported results have been summarized in Chapter 13. Optimized data and experimental data are compared and the role of intermolecular interactions in the crystal packing has been established. It is attempted to correlate the size and site of the substituents on the conformations of the parent molecule. An attempt has been made by the author to correlate the structure function relationship. Future scope of these kinds of investigations has also been mentioned.