CHAPTER 1

INTRODUCTION

1.1 CRYSTAL STRUCTURE DETERMINATION

X-ray crystallography is a standard technique for solving crystal structures, in which a beam of X-rays whose wavelengths (in the Angstrom range, ~10^{-8} cm) corresponding to interatomic distances, strike a crystal and diffracts into many specific directions. From the angles and intensities of these diffracted beams, a crystallographer can produce a three-dimensional picture of the density of electrons within the crystal. From this electron density, the mean positions of the atoms in the crystal can be determined, as well as their chemical bonds, their disorder and various other details.

The method also revealed the structure and functions of many biological molecules, including vitamins, drugs, proteins and nucleic acids such as DNA. X-ray crystallography is still the chief method for characterizing the atomic structure of new materials and in discerning materials that appear similar by other experiments. X-ray crystal structures can also account for unusual electronic or elastic properties of a material, shed light on chemical interactions and processes, or serve as the basis for designing pharmaceuticals against diseases. Modern X-ray crystallography provides the most powerful and accurate method for determining single crystal structures.
This section provides an overview of the procedures and methods for X-ray crystallographic structure analysis of small organic molecules and hence it is essential to give a brief summary of the crystal structure determination.

1.1.1 Crystal Growth

To perform X-ray crystallography, it is necessary to grow crystals with edges around 0.1-0.3 mm. Crystals are formed, as the conditions in a supersaturated solution slowly change. There are three degrees of saturation in solution; crystallographers take advantage of these when growing crystals:

- Unsaturated - where no crystals will form or grow.
- Low supersaturated - where crystals will grow but no new ones will form.
- High supersaturated - where crystals will both form and grow.

Several techniques are available for crystallization of small molecules such as slow evaporation, slow cooling, diffusion methods etc.

**Slow evaporation** often deposits crystals as a microcrystalline crust on the walls of the container. As the solvent evaporates, the solution recedes leaving the crust, which induces good crystal growth.

In **slow cooling**, the cooling rates from elevated temperatures for solutions contained laboratory vessels of ordinary size and are often too rapid to produce microscopic crystals.

**Vapour diffusion** involves altering the solvent and the methods can often give good single crystals with milligram amounts of solute.

Slow evaporation method was used for all the compounds in this thesis.
1.1.2 Crystal Selection

The crystal for collecting X-ray diffraction data must have two main requirements. One is it must possess uniform internal structure. To fulfill this requirement, a crystal must be pure at the molecular, ionic or atomic level. Secondly, it must be of proper size and shape, means that it should not be twinned or composed of microscopic sub crystals. It should not be grossly fractured, bent or physically distorted [1]. A crystal of good quality for diffraction experiment can be selected using polarizing microscope.

1.1.3 Diffractometer

In general, X-ray diffraction data can be collected using three different diffractometers, namely, Bruker APEX CCD, Enraf-Nonius CAD-4 and SMART CCD area detectors. In the present study, datas were collected using the Kappa APEXII CCD area detector.

1.1.4 Crystal Mounting

A crystal whose structure is to be determined must be a single crystal without defects. The crystal is then attached to the glass fiber and then placed in the goniometer head. The goniometer head is then placed in the correct position of the diffractrometer instrument and gradually rotated while being bombarded with X-rays, producing a diffraction pattern of regularly spaced spots known as reflections. The two-dimensional images taken at different rotations are converted into a three-dimensional model of the density of electrons within the crystal using the mathematical method of Fourier transforms, combined with chemical data known for the sample. Poor resolution or even errors may result if the crystals are too small, or not uniform enough in their internal makeup.
1.1.5 Determination of unit cell parameters and Intensity data collection

The unit cell dimensions (a, b, c, α, β, γ) can be determined from 36 frames measured at three different crystallographic zones and using the method of difference vectors. The intensities of various diffracted beams can be collected by passing the X-ray beam through the crystal. The crystal is rotated at various axes (φ, χ, ω) and the diffracted beam is then recorded with the detectors (2θ). The intensity of each reflection is measured with a quantum detector by any type of scan modes like ω and φ or ω/2θ. The data collection procedure depends on the type of diffractometer used for the experiment. Nowadays, the availability of area detectors allows faster data collection.

1.1.6 Data Reduction

The raw data collected from diffractometer suffers from physical and geometrical factors and hence could not be used for structure elucidation immediately. The collected intensity data is to be corrected for Lorentz and polarization and absorption effects and is given by the equation,

$$ I_{hkl} = \frac{K_{hkl}}{Lp} $$  \hspace{1cm} (1.1)

where p is the Polarization factor, given by

$$ p = \frac{1 + \cos^2 2\theta}{2} $$  \hspace{1cm} (1.2)

L is the Lorentz factor, depends on the measurement technique used and is given by

$$ L = \frac{1}{\sin 2\theta} $$  \hspace{1cm} (1.3)
The absorption of X-rays by the crystal is governed by the relation

\[ I = I_o \exp(-\mu t) \]  \hspace{1cm} (1.4)

where \( \mu \) is the linear absorption coefficient and \( t \) is the average distance travelled by the X-ray beam inside the crystal. Absorption correction becomes vital, when the crystal has more absorbing elements for the incident X-ray wavelength.

1.1.7 Space Group Determination

Space groups describe the symmetry of a unit cell, of which there are 230 variations. The space group of the crystal can be determined from the systematic absences of the hkl reflections. If the space group ambiguity arises, then the content of the unit cell is analysed by measuring the density. In some cases, intensity statistics are used to finalise the space group, particularly, to distinguish between centrosymmetric and non-centrosymmetric cases.

1.1.8 Structure Factor

The X-ray radiation scattered by one unit cell of a structure in any direction in which the diffraction maximum has particular combination of amplitude and phase is known as structure factor.

The general expression for the structure factor is given by

\[ F_{hkl} = \sum_{j=1}^{N} f_j \exp[2\pi i(hx_j + ky_j + lz_j)] \]  \hspace{1cm} (1.5)

where \( f_j \) is the atomic scattering factor for the \( j^{th} \) atom, \( x_j, y_j, z_j \) are the fractional coordinates of the \( j^{th} \) atom and \( N \) denotes the total number of atoms in the unit cell.
Also, $F_{hkl}$ is a complex quantity, written as

$$F_{hkl} = |F_{hkl}| e^{i\phi_{hkl}}$$  \hspace{1cm} (1.6)

$|F_{hkl}|$ is the structure amplitude and $\phi_{hkl}$ is the phase angle of the reflection hkl.

### 1.1.9 Electron Density

The intensities of the diffraction pattern and the arrangement of atoms in the unit cell of the crystal structure are related to each other by Fourier transform. The diffraction pattern is the Fourier transform of the electron density and the electron density itself is the Fourier transform of the diffraction pattern. Thus the atomic positions in the molecular structure is determined by noting the electron density maxima in the unit cell and it is given by the equation,

$$\rho(x,y,z) = \frac{1}{V} \sum_{h} \sum_{k} \sum_{l} F_{hkl} \exp[-2\pi i(hx + ky + lz)]$$  \hspace{1cm} (1.7)

where $\rho(x,y,z)$ is the electron density at position $(x,y,z)$, $V$ is the volume of the unit cell and $F_{hkl}$ is the structure factor for a reflection hkl.

### 1.1.10 The Phase Problem and Structure Solution

The above equation (1.7), requires the exact values of the complex quantity $F_{hkl}$ in terms of magnitude and phases. However, it is possible to obtain only the structure amplitudes $|F|$ directly from the observed intensity as its square root. The phase angles cannot be directly measured from the experimental conditions.
The unavailability of phase angles of the diffracted beams led to the central difficulty in structure determination using X-ray crystallography. This is referred to as the “phase problem”, which arises from the fact that the diffraction data contains information only on the amplitude but not the phases.

Several methods are used to solve the phase problem. Some of them are given below

- Direct methods
- Heavy atom methods
- Anomalous dispersion methods
- Isomorphous replacement method etc.,

The above methods can be successfully used to trace out the approximate positions of all the atoms (trial structure of a molecule) in a unit cell. This process is known as structure solution. If the molecule consists of limited number of light atoms, then direct methods can be used for the structure determination.

1.1.11 Direct Methods

Direct methods are used to calculate the phases directly by simple mathematical means from a single set of X-ray intensities. The basic postulates of direct methods are positivity (i.e., the electron density is positive everywhere) and atomicity (the atoms are spherically symmetric). The structure amplitudes and phases are linked through knowledge of electron density by Fourier transformation. A mathematical constraint on the function \( \rho(x) \) imposes corresponding constraint on the structure factor. This constraint is sufficient to evaluate \( \varphi_{hkl} \) directly.
1.1.12 Structure Refinement

Once all the atoms in a structure are located, the final part of the process is to refine it. Structure refinement is the process of improving the parameters for all atoms in an approximate (trial) structure, until the best fit of calculated structure factor amplitudes to those observed is obtained. Differences between the observed and the calculated values can arise from the random errors (statistical fluctuations) in the observations and defects in the model (systematic errors). The trial structure obtained from the structure solution is refined to get the accurate atomic positions and the associated thermal parameters. This process usually requires many successive stages. Several structure refinement processes are used. Among them, full matrix least-squares refinement technique is the conventional one and widely used in small molecular structure determination.

1.1.13 The R-factor

The agreement between calculated and observed structure factors for the molecule under investigation is usually represented by a residual index called R-factor, which describes the correctness of the model structure, given by

\[ R = \frac{\sum |F_o| - |F_c|}{\sum F_o} \]  

(1.8)

Lower the R-value, greater the accuracy of the molecular model. When R = 0%, there is perfect agreement between observed and calculated intensities. But this cannot be achieved due to the systematic and random errors present in the data collection and refinement procedures. In general, a good structural model will give a final R-value of ~ 5%.
1.1.14 Weighted R-factor

The residual factor used very widely in any computer program for crystal structure determination is weighted R-factor and is given by,

\[ wR^2 = \left[ \frac{\sum w(F_o^2 - F_c^2)^2}{\sum w(F_o^2)^2} \right]^{1/2} \tag{1.9} \]

where each reflection has its own weight \( w \).

\[ w = \frac{1}{\sigma^2 F_o^2 + (K1P)^2 + K2P} \tag{1.10} \]

K1 and K2 are constants and \( P = \frac{F_o^2 + 2F_c^2}{3} \).

Values of \( wR^2 \) and other residual factors based on \( F^2 \) are generally higher than those based on \( F \) values.

1.1.15 Goodness-of-Fit

The Goodness-of-Fit (GOOF), \( S \), is a measure of how good the model is. \( S \) is defined as

\[ S = \left[ \frac{\sum w(F_o^2 - F_c^2)^2}{(n - p)} \right]^{1/2} \tag{1.11} \]

where \( n \) is the number of reflections used in refinement and \( p \) is the total number of parameters refined including the overall scale factor. The goodness of fit is always based on \( F^2 \).
1.1.16 Interpretation of results

The structure thus determined is represented as atoms joined together by chemical bonds. Thus from the atomic coordinates, unit cell geometry and symmetry many geometrical results can be derived. These include

- Bond lengths
- Bond angles
- Torsion angles
- Shapes and conformations of rings
- The planarity (or) otherwise group of atoms
- Degree of association
- Intermolecular geometry such as hydrogen bonding, van der Waals contacts, π-interaction stacking of planar aromatic groups.

1.1.16.1 Bond Length

The important quantities in determining the structure of a molecule are bond lengths and bond angles. The equation by which the bond length is evaluated is given below:

For a triclinic lattice the distance between two points in fractional coordinates \((x_1, y_1, z_1)\) and \((x_2, y_2, z_2)\) is given by the law of cosines in three dimensions,

\[
 l = \sqrt{(\Delta x)^2 + (\Delta y)^2 + (\Delta z)^2 - 2ab\Delta x\Delta y\cos\gamma - 2ac\Delta x\Delta z\cos\beta - 2bc\Delta y\Delta z\cos\alpha}}^{1/2} \tag{1.12}
\]

where \(a, b, c, \alpha, \beta\) and \(\gamma\) are the unit-cell parameters.
The standard deviation in the bond length is given by the equation,

\[
\sigma_l = \left\{ \sqrt{\left(\sigma_{x_1}^2 + \sigma_{x_2}^2\right) \left[ \frac{\Delta x - \Delta y \cos \gamma - \Delta z \cos \beta}{l} \right]^2 + \left(\sigma_{y_1}^2 + \sigma_{y_2}^2\right) \left[ \frac{\Delta y - \Delta x \cos \gamma - \Delta z \cos \alpha}{l} \right]^2 + \left(\sigma_{z_1}^2 + \sigma_{z_2}^2\right) \left[ \frac{\Delta z - \Delta x \cos \beta - \Delta y \cos \alpha}{l} \right]^2} \right\}^{1/2}
\]

(1.13)

where \( \sigma_{x_1} \) and \( \sigma_{x_2} \) are the standard deviations of atoms 1 and 2 in the x direction, with similar meaning for \( \sigma_{y_1}, \sigma_{y_2}, \sigma_{z_1}, \sigma_{z_2} \): \( \Delta x \) is \( x_2 - x_1 \) and so on for y and z and \( l \) is the bond length.

### 1.1.16.2 Bond Angle

If the lengths AB, AC and BC are known, then the law of cosines provides a direct means of computing the angle

\[
\theta = \cos^{-1}\left[ \frac{(AB)^2 + (AC)^2 - (BC)^2}{2(AB)(AC)} \right]
\]

(1.14)

Also the standard deviation in the bond angle is given by the equation,

\[
\sigma_\theta = \sqrt{\left(\frac{\sigma_A^2}{(AB)^2}\right) + \frac{\sigma_B^2}{(AB)^2(AC)^2} + \frac{\sigma_C^2}{(AC)^2}}^{1/2}
\]

(1.15)

where \( \sigma_A, \sigma_B, \sigma_C \) are the standard deviations in the positions of the atoms A, B, C.
1.1.16.3 Torsion Angle

For an arrangement of four atoms 1, 2, 3, 4 the torsion angle $\chi (1, 2, 3, 4)$ is defined by the angle between the planes 1, 2, 3 and 2, 3, 4 and its value lies in the range $-180^\circ < \chi \leq 180^\circ$.

If $\chi = 0^\circ$ the configuration is called cis

$\chi = 180^\circ$ is trans and

$\chi = \pm 60^\circ$ is $\pm$ gauche.

1.1.16.4 Least-Squares Plane

While discussing the results of the crystal structure determination, it is necessary to discuss whether sets of four or more atoms are planar within experimental error or not. The planarity is described in terms of the least-squares plane through the set of atoms, that is, the plane that minimizes $\Sigma m d_m^2$, where $d_m$’s are the perpendicular distances of the $m$ atoms from the plane.

1.1.16.5 Ring Conformation

As far as the closed rings are concerned, the conformations of the ring differ due to the hybridization nature of the atoms. Commonly occurring closed rings are five- and six-membered ones. The six-membered rings possess various conformations namely planar, chair, boat, sofa, twist and half-chair. The five-membered rings adopt planar, envelope, half-chair or twist conformations. The condition for ideal conformations of any type is given by the endo cyclic torsion angles of the ring. Any deviation from the ideal ring conformations is described by the puckering parameters suggested by Cremer and Pople [2].
For a six-membered ring, there are three puckering degrees of freedom. They are described by the single amplitude-phase pair ($q_2$ and $\phi_2$) and a single puckering coordinate $q_3$. These coordinates may be replaced by a “spherical polar set” (Q, $\theta$, $\phi$) where Q is the total puckering amplitude and $\theta$ is an angle ($0 \leq \theta \leq \pi$) such that

$$q_2 = Q \sin \theta \quad (1.16)$$

$$q_3 = Q \cos \theta \quad (1.17)$$

This coordinate system permits the mapping of all types of puckering. The polar coordinate values for the special conformations of the six-membered rings are given below:

- Chair - $\theta = 0.0$
- Half-Chair - $\theta = 50.8$  $\phi = k \times 60 + 30$
- Envelope - $\theta = 54.7$  $\phi = k \times 60$
- Boat - $\theta = 90.0$  $\phi = k \times 60$
- Twist-Boat - $\theta = 90.0$  $\phi = k \times 60 + 30$

where $k = 0, 1, 2, 3, 4, 5$.

The ring conformation can also be calculated from the asymmetry parameters [3, 4]. These parameters are calculated as root mean squares of the sum of mirror-related torsion angles ($\Delta C_s$) or root mean squares of the differences of twofold-axis related torsion angles ($\Delta C_2$). The two equations used to calculate the asymmetry parameters are
\[
\Delta C = \frac{1}{m} \sum_{i=1}^{m} \left( \frac{\phi_i}{m} \right)^{1/2}
\]

(1.18)

\[
\Delta C_2 = \frac{1}{m} \sum_{i=1}^{m} \left( \frac{\phi_i' - \phi_i}{m} \right)^{1/2}
\]

(1.19)

where \( m \) is the number of individual comparisons and \( \phi_i \) and \( \phi_i' \) are the symmetry related torsion angles. The ring conformation may also be defined with the help of symmetry elements. Two types of symmetry that needed to be considered in order to define ring conformation are mirror planes perpendicular to the dominant ring plane and twofold axes lying in the ring plane (Figure 1.1). The six-membered rings possess twelve potential symmetry elements that must be considered in order to determine the ring conformation. The planar ring is highly symmetric and contains all possible symmetry elements (i.e., a mirror plane and a twofold axis of symmetry at each of the six possible locations). The chair possess the next highest symmetry, having three mirror planes of symmetry and three twofold axes of symmetry. The boat and twist-boat conformations each have two mutually perpendicular symmetry elements. The sofa and half-chair conformations each have only a single symmetry element.

### 1.1.16.6 Crystal Packing

A crystal is packed together by non-covalent or weak forces like van der Waals forces, ionic forces, hydrogen bonding and so on. Molecules have the tendency to develop weak interactions that are so important, because they join together and thus generate very strong molecular conformations. For example, the secondary, tertiary and quaternary structure of proteins, the double helix of the DNA, the membrane structures are all maintained by weak interactions. The more the weak interactions, the more stable is the resulting conformation.
Figure 1.1 Possible conformations of the five- and six-membered rings
1.1.16.7 Hydrogen bonds

A hydrogen bond is an attractive force that arises between the donor covalent pair D-H in which a hydrogen atom H is bound to a more electronegative atom D (donor), and other non-covalently bound nearest neighbour electronegative (acceptor) atom A. Hydrogen bonds play a crucial role in determining the structure of water, the folding of proteins and the pairing of base in DNA etc. For this reason, crystal-packing studies are essential to understand the laws governing the intramolecular and intermolecular H-bonding in a molecular crystal. An important feature of hydrogen bond is that they are highly directional. The strongest hydrogen bonds are those in which donor, hydrogen and acceptor atoms are collinear. Strong hydrogen bonds of 20-40 kcal/mol, generally formed between charged donors and acceptors, are nearly as strong as covalent bonds. Weak hydrogen bonds of 1-5 kcal/mol, sometimes formed with carbon as the proton donor, are no stronger than van der Waals interactions. Moderate hydrogen bonds, which are the most common are formed between neutral donors and acceptors, are from 5-15 kcal/mol.

The usual convention for the representation of the hydrogen bond is D-H…A where D is the donor and A is the acceptor. In hydrogen bonds, the distance between the hydrogen and the acceptor atom is shorter than the sum of their van der Waals radii [5].

In general, crystal structures are governed by O-H…O, N-H…O, N-H…N and C-H…O types of hydrogen bonds, in addition to short contacts and halogen atoms involved contacts. An O-H…O interaction is a hydrogen bond, if the H…O distance is significantly less than the sum of their van der Waals radii (2.6 Å) and the angle O-H…O>170° [6]. In N-H…O hydrogen bonds the ideal H…O distance is 2.05 Å and N…O distance is 2.9 Å with an angle of 170°. Regarding N-H…N hydrogen bonds, the distance criteria
is 3.10 Å. The C-H...O hydrogen bond is given as an electrostatic interaction with C...O distance 3.0-4.0 Å and angle 90-180° [7].

In addition to the above hydrogen bonds, there are various other hydrogen bonds like C-H...N, C-H...Cl, C-H...S and N-H...S, which are pronounced in crystal structural chemistry. Apart from them, there is also a possibility of interactions like C-H...π in molecular crystals, where the delocalized electrons in unsaturated terminal alkynes (C≡C) are ready to interact with the C-H group [8]. The π...π interactions are also present in planar molecules, where the planar rings stack one over the other.

1.1.16.8 Graph-set definitions

The graph-set approach to the analysis of hydrogen bond patterns is the fact that even complicated networks can be reduced to combinations of four simple patterns, each specified by a designator: chains (C), rings (R), intramolecular hydrogen bonded patterns (S), and other finite patterns (D). Specification of a pattern is augmented by a subscript designating the number of hydrogen bond donors \( d \) (in the most common case covalently bonded hydrogens, but certainly not limited to them), and a superscript giving the number of hydrogen bond acceptors \( a \). In addition, the number of atoms \( n \) in the pattern is called the degree of the pattern and is specified in parentheses. The graph-set descriptor is then given as \( G_{d}^{a}(n) \), where \( G \) represents one of the four possible designators [9].

1.1.16.9 van der Waals forces

Weak attractive forces between uncharged atoms or molecules are collectively referred to as van der Waals forces. These forces arise from the electrostatic attraction of the nuclei of one molecule by the electrons of a different molecule. The repulsion arising between the electrons of two
molecules as well as the nuclei of two molecules counteract the electrostatic attractions, but there is always a small net attractive force. The van der Waals forces are short range forces i.e., they are significant only when the molecules are very close to one another.

The van der Waals forces are used for non-specific attractions between two atoms that are close to each other. These interactions depend on the distance between the respective atoms (or atom groups or molecules). At too close distances, repulsive forces are dominating (overlapping of electron shells). The energy of van der Waals attractions is only slightly higher than that of thermal molecular movements: -0.7 to -1 kcal/mol (-3 to -4 kJ/mol). Consequently, van der Waals attractions are of importance, if as many atoms of a molecule as possible are engaged. They are strongest, if the involved molecular structures complement each other. van der Waals attractions are additive and have thus a much greater impact on macro than on small molecules.

1.2 HETEROCYCLIC COMPOUNDS

Heterocyclic compounds are organic compounds containing at least one atom being an element other than carbon, such as sulphur, oxygen or nitrogen within a ring structure. These structures may comprise either simple aromatic or non-aromatic rings. Heterocyclic compounds, particularly five- and six-membered ring compounds occupy a prominent place among various classes of organic compounds for their diverse biological activities. At least one heterocyclic ring component is found in about 50% of known organic compounds. They are very widely distributed in nature and are essential to life. The pyrimidine and purine bases of the genetic material DNA; the vitamins and coenzyme precursors thiamin, riboflavin, biotin; the hormone kinetin; together with most of sugars are examples of heterocyclic compounds. There are a vast number of pharmacologically active heterocyclic compounds, many of which
are in regular clinical use. Some of them are natural products like antibiotics such as penicillin, alkaloids such as morphine etc. There are also a large number of synthetic heterocyclic compounds with important practical applications, such as dyestuff, co-polymers, solvents, and photographic sensitizers.

Heterocyclic spiro compounds are of interest in synthetic organic chemistry [10, 11]. Multicomponent 1, 3-dipolar cycloaddition reactions are considered to be one of the most useful processes for the construction of five-membered heterocyclic ring systems [12, 13]. These strategies offer significant advantages over more traditional approaches, allowing the construction of complex molecular architectures from easily available starting materials in a single synthetic operation without the need for isolation of intermediates. Particularly, the chemistry of the azomethine ylide has gained significance in recent years for the construction of nitrogen containing five-membered heterocycles, which are often the central ring systems of numerous natural products [14, 15].

Indole and its derivatives are important heterocyclic nitrogen compounds which display a wide range of biological activities [16]. Indole and its derivatives form a class of toxic recalcitrant N-heterocyclic compounds that are considered as pollutants [17].

Pyridine and pyrrole are both nitrogen heterocycles-their molecules contain nitrogen atoms along with carbon atoms in the rings. The molecules of many biological materials consist part of pyridine and pyrrole rings, and such materials yield small amounts of pyridine and pyrrole upon strong heating. Nowadays, pyridine and pyrrole are prepared by synthetic reactions. The chief commercial interest lies in their conversion to other substances, chiefly dyestuffs and drugs.
Furan is an oxygen-containing heterocycle employed primarily for conversion to other substances (including pyrrole). Furan ring is found in coal tar, and in the chemical structure of some terpenoids such as rose oil. The reduction of furan leads to the heterocyclic ether tetrahydrofuran (THF), which is widely used as an organic solvent.

In view of the importance of the organic compounds, the X-ray crystal structure determination of some of the derivatives of the compounds are studied and the salient conformational features are analysed.

1.3 PRESENT STUDY

In this thesis, the X-ray crystal structure determination of sixteen organic compounds having biological and medicinal interest are carried out to study their conformational details, hydrogen bonding, crystal packing and the motif studies. Out of the sixteen compounds studied, five compounds belong to chromenopyrroles, two indoles, three pyrrolidines, one pyrrolopyrrole, three pyrrolizines, one piperazine and a furan compound. The antibacterial activities of six compounds screened against various human pathogenic bacteria are studied and the results are presented. The induced fit docking studies of four compounds, namely, two chromenopyrrole derivatives and two pyrrolizine derivatives with the protein target are carried out and the results are analysed based on glide score, glide energy and hydrogen bond interactions.

All the compounds were synthesized and supplied by Department of Organic Chemistry, University of Madras, Chennai. Intensity data collection for the above compounds was done at SAIF, IIT Madras, Chennai. The structure factor tables for the compounds are provided in Compact Disc (CD), enclosed at the back cover of the thesis.
1.3.1 Experimental

The research work deals on crystallization, intensity data collection, structure solution, structure refinement and structure analysis. Single crystals of suitable dimension were selected and used for data collection. Bruker Kappa APEXII CCD diffractometer was used for intensity data collection with MoKα radiation (\(λ = 0.71073 \) Å) at room temperature using \(ω\) and \(φ\) scan mode. Accurate unit cell parameters were determined from 36 frames measured at three different crystallographic zones and using the method of difference vectors. Cell refinement and data reduction were carried out using SAINT computer program [18]. The intensities were corrected for Lorentz and polarization effects and multi-scan [19] absorption correction was applied.

1.3.2 Computations

The crystallographic packages SHELX [20], SIR [21] and WINGX suite [22] are used to solve and refine the structures. ORTEP [23] and PLATON [24] are used to draw the thermal ellipsoid plots and packing diagrams. The crystallographic program PARST [4] is used for plane calculation. The commercial software Schrodinger USA [25] is used for docking studies.