CHAPTER I

X-RAY CRYSTALLOGRAPHY

1.1 SINGLE CRYSTAL XRD

A single crystal X-ray study has the unique potential to provide solid knowledge about the three dimensional structure of molecules and complexes in the crystalline state along with their intermolecular interactions. Much of our current knowledge concerning inorganic and metal organic compounds is derived from single crystal studies. This technique was initially used to investigate the structure of minerals, refining and confirming the crystallographic descriptions. Recently, biomedical research has utilized the technique for the investigation of the structure and dynamics of proteins, nucleic acids and other biological molecules. Research into microelectronics and semiconductors, as well as pharmaceutical research, continue to rely on the qualities of X-ray crystallography.

X-rays are electromagnetic radiation with photon energies in the range of 100 eV - 100 keV. Short wavelength X-rays in the range of a few angstroms to 0.1 Å are used in diffraction applications, since the wavelength of X-rays is comparable to the size of atoms. Hence X-rays are ideally suited for probing the structural arrangement of atoms and molecules in a wide range of materials which has brought advances in numerous fields of science and technology.

The energetic X-rays can penetrate deep into the materials and provide information about the bulk structure. Measurement of diffraction pattern therefore allows us to deduce the distribution of atoms in the material. From this electron density, mean positions of the atoms in the crystal, chemical bonds, disorder and various other informations can be determined. In recent years, the advent of
synchrotron radiation sources, area detector based data collection instruments and high speed computers has dramatically enhanced the efficiency of crystallographic structural determination.

1.1.1 Braggs Law

X-rays interact with the electrons present in the atoms and produce diffracted waves. If the atoms are arranged in a periodical fashion as in the case of crystals, the diffracted waves will consist of sharp interference maxima with the same symmetry similar to the distribution of atoms. Therefore, the measurement of the diffraction pattern of the crystal helps us to deduce the distribution of atoms present in it.

W.L.Bragg had described a simple method for obtaining the condition for diffraction. If \( \theta \) be the angle between the primary beam and the family of lattice planes with miller indices \( (h k l) \) and \( \lambda \) be the wavelength of incident beam, then the condition for constructive interference is given by the relation, \( 2d \sin \theta = n \lambda \), where \( n \) is the order of the scattered beam and \( d \) is the spacing between diffracting planes. This is called Braggs Law. In this case, part of the incoming beam is deflected by an angle \( 2\theta \), producing a reflection spot in the diffraction pattern.

1.2 DATA COLLECTION

In X-ray crystallography, the intensities of the diffraction peaks are used in reconstructing the electron density map within the unit cell of the crystal. High accuracy in the reconstruction can be achieved by Fourier transforming the diffraction intensities with appropriate phase assignment, a high degree of completeness and redundancy in diffraction data. This means that all the possible reflections are measured multiple times to reduce systematic and statistical error.

There are two methods available for measuring the intensities of diffracted beams. They are diffractometer or counter method and photographic method. In the counter method, the beams can be detected by a quantum counting device that measures the number of photons directly. In photographic method, the
degree of blackening of spots on diffraction photographs is measured and taken as proportional to the beam intensities. The photographic method of measuring intensities had been used during the initial stage of the growth of crystallography.

During the last two decades, the diffractometers have been used extensively by the researchers throughout the world. The advantages of diffractometers are: high precision, speedy and automatic data collection.

Data collection is done by an area detector which can collect diffraction data in a large solid angle. It can collect diffraction information on an array of positions at once, instead of just one point in space at a time. The most widely used area detector is the multiwire proportional chamber derived from the standard proportional radiation counter.

1.2.1 Diffractometer

Diffractometer is an instrument for measuring the intensity of a diffracted beam by counting the number of X-ray photons arriving at a given time at an appropriately placed detector. The automatic single crystal diffractometer is convenient, since it involves the successive measurements of reflections, one by one, over the whole, on some selected part, of the reciprocal lattice space. The advantage of this method is that, once the parameters of the data collection have been entered into the controlling computer, the collection proceeds continuously without human intervention.

The four circle diffractometer has four arcs which can be used to adjust the orientation of the crystal and counter so as to bring any desired plane into a reflecting position and detect this reflection. These are divided into the crystal orienter which has the phi(φ) and chi(κ) circles, and the base contains omega (ω) and two theta(2θ). The rotations about each of the four angles φ, κ, ω and 2θ leave the crystal within the X-ray beam, but change the crystal orientation. The detector can be slid closer or further away from the crystal, allowing higher resolution data to be taken or better discernment of the Bragg peaks.
The crystal is mounted for measurements so that it may be held in the X-ray beam and rotated. There are several methods of mounting. Although crystals were once loaded into glass capillaries with the crystallization solution, a modern approach is to scoop the crystal up in a tiny loop, made of nylon or plastic and attached to a solid rod that is then flash-frozen with liquid nitrogen. This freezing reduces the radiation damage of the X-rays, as well as the noise in the Bragg peaks due to thermal motion (the Debye-Waller effect). However, untreated crystals often crack if flash-frozen. Therefore, they are generally pre-soaked in a cryoprotectant solution before freezing.

The capillary or loop is mounted on a goniometer, which allows it to be positioned accurately within the X-ray beam and rotated. Since both the crystal and the beam are often very small, the crystal must be centered within the beam to within 25 micrometers accuracy, which is aided by a camera focused on the crystal. The most common type of goniometer is the "kappa goniometer", which offers three angles of rotation, the $\omega$ angle, which rotates about an axis perpendicular to the beam, the $\kappa$ angle, about an axis at 50° to the $\omega$ axis and finally the $\varphi$ angle about the loop/capillary axis. When the $\kappa$ angle is zero, the $\omega$ and $\varphi$ axes are aligned. The $\kappa$ rotation allows for convenient mounting of the crystal, since the arm in which the crystal is mounted may be swung out towards the crystallographer. The oscillations carried out during data collection involve the $\omega$ axis only.

The data for all the compounds discussed in this thesis have been collected using APEX2 CCD area detector equipped with the Mo $k\alpha$ radiation. For data collection, a crystal of suitable size was mounted and accurate values of the unit cell parameters were obtained by least-square analysis of the $\theta$ values for several high Bragg angle reflections. Intensity data were collected at room temperature.

1.3 STRUCTURE SOLUTION

Most of the information about the crystal is contained within the phase of the structure factor. If the structure factor and phase are known, the electron density distribution of the unit cell can be calculated. But the crystallographically available
data consist only the structure factor magnitudes and not their phases. So the resolution of the phase is very important in structure determination by X-ray diffraction. There are various methods for obtaining the phase model and these models are based on two important factors. The first factor involves the direct calculation of initial phases, which allow the deduction of an atomic model from a Fourier map. The second factor involves the direct location of enough atoms in the cell to give approximate phases on an $F_0$ calculation.

Direct method is a widely used X-ray crystallographic technique for the structure determination. Before three decades, the major method of solving the phase problem involved introducing a heavy atom into the molecule of interest. The atom was located by methods involving the Patterson function. This Patterson method is considered as the initial phasing method to solve the entire structure. This method is normally applied to solve centro symmetric space group but there are reports about this method by which a few non centro symmetric structure had also been solved. The direct method has been completely automated so that the raw data is fed in at one end and the solved structure appears at the other end. Almost maximum number of the reported small molecule structures is solved by this direct method. All the compounds that are studied in the present work are also solved using this method.

Although the direct method is the commonly used technique for solving the structures, this method fails with macro molecules. The alternate approach for solving macro molecule is the Patterson method. The publication of a research paper by A.L Patterson in 1935 explored the crystallographic usefulness of the phaseless quantities $|F|^2$ as coefficients. He showed the usual synthesis with F’s as coefficients showed the distribution of atoms in the cell. The map calculated with $|F|^2$ gave peaks corresponding to all the interatomic vectors. The height of a Patterson peak depends on the number of electrons in the atom between which the vector occurs and it is proportional to the products of their atomic numbers. The major importance of this peak height relationship is that the vectors between heavy atoms appear with heights corresponding to the square of their atomic numbers and thus stand out strongly against the background of heavy-light and light-light atoms vector.
In this thesis, the structure solution of all the compounds was carried out using SHELXS program. SHELXS is primarily designed for the solution of small moiety (1-200 atoms in the unit cell) structures from single crystal at atomic resolution. The program is a general one and is efficient for all space groups in all settings, and there are effectively no limits on the number of reflection data, atoms, phases refined in direct methods, scattering factor types etc. The direct method routine of SHELXS is based on the random start multi solution technique. The program is more accurately described as a multiple permutation single solution procedure, since it tries hard to identify the correct solution, which is then improved by the E-Fourier (or) partial structure excitation procedure. The program starts by sorting all reflections with $E > E_{\min}$ into groups. This program uses some selected one phase semivariants with known phase. The initial phase refinement is normally performed using a reflection subset (which includes the fixed phase). The best-set with lowest combined figure of merit is taken as the correct structure.

1.4 STRUCTURE REFINEMENT

The data obtained from an X-ray diffractometer experiment are a set of structure factor magnitudes $|F_0|$ and with the proposal model, the structure factor magnitudes $|F_i|$ should be calculated. The combination is to get the best possible fit between the observed and calculated structure factors. Specifically, it is necessary to find the atomic coordinates $(X_j, Y_j, Z_j)$ and functions that give maximum agreement with the observed structure factor. The ultimate purpose is therefore to refine three positional coordinate and up to six thermal parameters for each atom to give the better fit with the experimental data. The refinement stage of a structure analysis begins with a completed trial structure containing all the atoms. Full matrix least-square refinement techniques are the conventional one which is widely used in small molecular structure refinement. SHELXL-97 were used for full matrix refinement. The least square refinement uses the square of the difference between observed and calculated values and the measure of their disagreement is a minimum. The refinement on $F_o^2$ using all the data provides a good result for weakly diffracting crystals and in particular for pesudosymmetry problems.
For a well refined structure model, the value of \( R \) approaches a small value (about 1% at best), corresponding to the residual errors in both the experimental data and the model. In the early stages of the analysis, however, \( R \) may lie between 0.4 and 0.5.

1.5 GEOMETRICAL PARAMETERS

The determination of molecular geometry is of vital importance to understand the chemical structure and bonding. When the formal structure analysis is complete, we need to express our results in terms of molecular geometry and packing.

1.5.1 Bond Length

The average distance between the centers of the nuclei of two bonded atoms in a molecule is known as bond length. Shorter the bond length, larger is the value of bond energy. Bond length is expressed in Angstrom unit (Å) or picometer (pm). Bond length increases with the increase in the size of the atom. This may be accounted for the increase in the distance of electron from the nucleus with the addition of a new shell.

1.5.2 Bond Angle

Bond angle is the average angle between the orbitals of the central atom containing bonding electron pairs in the molecule. Bond angle can be expressed either in degree or minute or second. Bond angle determine the shape of a molecule. Bond angles are useful to find the type of hybridization of a particular atom.

1.5.3 Torsion Angle

Torsion angle is the angle of inclination between two planes defined as ABC and BCD of sequence of atoms A-B-C-D. Torsion angles are useful conformational parameters which are used to compare different related molecules.
or different conformations of the same molecule. In freely rotating moiety, a torsion angle may be a function of the environment of the molecule.

1.5.4 Ring Conformation

Two types of symmetry (or pseudosymmetry) must be considered in order to define ring conformations namely mirror planes perpendicular to the dominant ring plane and 2-fold axes lying in the ring plane. If there is an odd number (usually 5 or 7) of atoms in the ring, all the symmetry elements pass through one of the ring atoms and bisect the opposite bond. If the rings contain even number (usually 6) of atoms, symmetry elements pass through two ring atoms located directly across the ring, or else bisect two opposite ring bonds.

Five membered ring contains ten symmetry elements. The planar five membered ring possesses five mirror planes and five 2-fold axes. The ideal envelope conformation has only a single plane and it passes through the out-of-plane atom. The ideal half-chair has one 2-fold axis bisecting the bond between two out-of-plane atoms.

Six membered rings possess 12 locations for symmetry elements. The planar ring such as, benzene, has one plane and one 2-fold axis at each of six locations (6/mmm). The chair form of cyclohexane has three planes and three 2-fold axes. The boat and twist-boat have symmetry mm2 and 222 respectively, while the sofa has symmetry m and the half-chair symmetry 2.

1.5.5 Inter and Intra Molecular Interaction

Hydrogen bonding is a donor-acceptor interaction specifically involving hydrogen atoms. Hydrogen bonding is an essential component of the structure and function of biological molecules. The nature of hydrogen bonds depends on the nature of the donor and acceptor group. Very strong hydrogen bond resembles covalent bond, while weak hydrogen bonds are close to van der Wall’s forces. In crystals, hydrogen bonding in hydrates increases the molar volume. In organic compounds, it tends to decrease the volume. It becomes weaker with an increase in
the thermal motion of the atoms involved. Hydrogen bonds can be either intramolecular or intermolecular. Intramolecular hydrogen bonds are formed between donor and acceptor groups in the same molecule when the molecular configuration and conformation brings them with hydrogen bond geometry, whereas the intermolecular hydrogen bonds are formed between the donor and acceptor groups of the different molecules.

1.5.6 Graph Set

Graph sets give information about the donors and acceptors used in a hydrogen bonded pattern and also about the nature of the pattern. The most remarkable feature of the graph set approach in the analysis of hydrogen bond patterns is the fact that even very complicated networks can be reduced to combinations of four simple patterns such as, chain, ring, intramolecular hydrogen patterns and finite patterns.

Specification of a pattern is augmented by a subscript designating the number of hydrogen-bond donors (d) and a superscript giving the number of hydrogen bond acceptor (a). In addition, the number of atoms n in the pattern is called the degree of the pattern and is specified in paranthesis. The graph set descriptor is then given as \( G^a_d(n) \), where G represents one of the four possible designators. The analysis of hydrogen-bonding patterns into these four simple categories can lead to important insights regarding the patterns of recognition between both like and unlike molecules.

1.6 COMPUTATION

In this thesis, all the structures were solved by the procedure of direct method using SHELXS-97 and refined by full matrix least square technique using SHELXL-97 and the graphic plots were obtained using PLATON and ORTEP.