CHAPTER I

A Brief outline of the methods employed in crystal structure analysis.

1.1 Introduction

The aim of science is to understand the observed phenomenon in terms of the known processes and laws of nature that govern a variety of properties of matter. In the understanding of various solid state properties the knowledge of the internal structure of matter is of great importance. X-ray crystallography in this respect occupies a special position in the field of physical science. It unveils the mystery of molecular structure at atomic resolution. It provides information on bond lengths, bond angles, intermolecular interactions, conformations, molecular packing, hydrogen bonding and detail electron density distribution that collectively explain the molecular properties.

Since the subject matter of this thesis is on the crystal structure analysis by X-ray methods a brief outline of the procedures followed in the structure analysis will be presented in this chapter.

1.2 Preliminary data collection

The preliminary data collection requires a very good, tiny, stable single crystals, cylindrical in shape. Such crystals are normally grown from solution by slow evaporation technique. The crystal is mounted on the goniometer head using glass fibre. Depending on the elements present in the crystal Cux or
Moka radiations are used. For organic compounds CuKα radiation is more suitable. The cell dimensions are obtained from the rotation and Weissenberg photographs, since the spacings of the recorded diffraction patterns are reciprocally related to the dimensions of the crystal lattice. The crystal system and the space group are determined from the known cell constants and systematic absences. The density of the crystal is measured by flotation technique. A high quality single crystal (free from defects) is used for intensity data collection.

1.3 Diffraction of X-rays by crystals

The discovery of X-rays by Rontgen in 1895 and the discovery by Von Laue in 1912 that X-rays can be diffracted by crystals are two great events in the history of X-ray crystallography. The mathematical form of Laue’s equations was not convenient and straight forward for the interpretation of experimental results. In 1913 W.L. Bragg showed that Von Laue’s complicated formulation of the diffraction phenomenon could be reduced to reflection phenomenon of X-rays from the planes of crystal lattice and gave the fundamental equation which is known as Bragg’s law which is written as

$$2d_{hkl} \sin \theta_{hkl} = n \lambda$$  \hspace{1cm} (1.1)

Where, \(d_{hkl}\) is the interplanar spacing of a set of \((hkl)\) planes, \(\theta_{hkl}\) is the angle between the incident beam and the crystal plane, \(\lambda\) is the wave length of x-rays
and \( n \) is the order of reflection. Equation (1.1) is the simultaneous fulfillment of the three Laue equations.

Information about the unit cell dimensions and space group are obtained from the rotation and Weissenberg photographs.

X-rays are scattered by electrons associated with each atom in a crystal. Since atoms are arranged periodically, the X-rays scattered by them will have definite phase relations between them. This leads to the interference of the scattered X-rays which will be destructive in most directions and constructive in directions defined by Bragg's equation (1.1) producing a beam of amplitude \( F_{hkl} \) and phase angle \( \theta_{hkl} \) where \( hkl \) are the Miller indices of the diffracting plane.

1.4 Measurement of intensities

The three dimensional X-ray intensities from a single crystal are measured either from the photographs obtained by multi-film equi-inclination Weissenberg technique or from an automatic single crystal diffractometer. Photographically recorded intensities are measured either visually by comparing the intensities with a standard strip or with a densitometer and in either case they are appropriately correlated and averaged. In a diffractometer the intensities are measured using a scintillation or proportional counter. The raw X-ray intensities obtained from different crystal planes are subjected to
various corrections like Lorentz-polarisation effects, absorption correction etc. The process of applying corrections to the observed X-ray intensities is called data reduction.

In crystallography the most extensively used quantity is the structure factor $F_{hkl}$. The structure factor $F_{hkl}$ is related to the intensity by the relation

$$|F_{hkl}| \propto \sqrt{I_{hkl}}$$  \hspace{1cm} (1.2)

Applying corrections

$$|F_{hkl}| = \sqrt{\frac{K I_{hkl}}{L P}}$$  \hspace{1cm} (1.3)

Where $L$ is the Lorentz factor which depends on the precise measurement technique and $p$ is the polarisation factor which is a function of the reflection angle $2\theta$ and $K$ is a constant which depends on the crystal size and beam intensity.

1.4.1 Lorentz correction

The Lorentz factor ($L$) arises due to the variations in time for a reciprocal lattice point to pass through the sphere of reflection. Different reciprocal lattice points will be in contact with the sphere of reflection for different length of time. For zero layer Weissenberg photograph the Lorentz factor is given by
\[ L = \frac{1}{\sin \theta} \]  \hspace{1cm} (1.4)

and for equi-inclination Weissenberg geometry

\[ L = \frac{\sin \theta}{\sin 2\theta \sqrt{\sin^2 \theta - \sin^2 \mu}} \]  \hspace{1cm} (1.5)

where \( \theta \) is the Bragg angle and \( \mu \) is the equi-inclination angle.

1.4.2 Polarisation factor

The polarisation correction arises due to the nature of the X-ray beam and the manner in which its reflection efficiency varies with the reflection angle. The unpolarised incident X-ray beam will be partially polarised on reflection from crystal planes and varies with angle \( 2\theta \). The observed intensities have to be corrected for this effect.

The polarisation factor, \( P \) is given by the relation.

\[ P = \frac{1 + \cos^2 2\theta}{2} \]  \hspace{1cm} (1.6)

For CAD4 diffractometer which uses graphite monochromator, the polarisation factor takes the form

\[ P = \left\{ \frac{P \cos^2 2\theta_m + \cos^2 2\theta_c}{1 + \cos^2 2\theta_m} \right\} + \left( 1 - P \right) \left\{ \frac{\cos^2 2\theta_m + \cos^2 2\theta_c}{1 + \cos^2 2\theta_m} \right\} \]  \hspace{1cm} (1.7)

where \( P = 0 \) for ideally imperfect monochromatic crystal
\( p = 1 \) for a perfect monochromator crystal
\( \theta_m = \text{Bragg angle for (002) reflection of graphite} \)
\( \theta_c = \text{Bragg angle of the reflection being measured} \).

1.4.3 Spot shape correction

This problem arises when the intensity data were obtained from Weissenberg photographs by non-integrating measuring technique. Since
diffractometer data is used for all the structures presented in this thesis, this aspect is not discussed.

1.4.4 Absorption correction

The amount of X-radiation absorbed by the crystal depends upon the matter of which it is made and the disposition of the reflecting planes. A calculation of the absorption coefficient has been suggested by (Palm, 1964). For absorption correction one has to calculate the absorption for the actual path length travelled with in the crystal by the X-ray beam reflected from each infinitesimal portion of the crystal and then to integrate these results over the entire volume of the crystal. In general, this effect can be minimized by choosing small crystal, cylindrical in shape or by using more penetrating radiation like Mokau.

1.5 Structure factor, $F_{hkl}$

$F_{hkl}$ is called the structure factor and is defined as the vector sum of the individual waves scattered by all the atoms in the unit cell and is given by the relation.

$$F_{hkl} = \sum_{j=1}^{N} f_j \exp(2\pi i (hx_j + hy_j + lz_j))$$

(1.8)

where $f_j$ is the scattering factor of the $j^{th}$ atom having coordinates $(x_j, y_j, z_j)$. Therefore, the structure factor is a function of $(h, k, l)$ and the unit cell contents.
The structure factor is a complex quantity and can be expressed as

\[ F_{hkl} = A_{hkl} + i B_{hkl} \]  \hspace{1cm} (1.9)

\[ A_{hkl} = \sum_{j=1}^{N} f_j \cos 2(\mathbf{h} \cdot \mathbf{r}_j + \mathbf{k} \cdot \mathbf{y}_j + \mathbf{l} \cdot \mathbf{z}_j) \]  \hspace{1cm} (1.10)

\[ B_{hkl} = \sum_{j=1}^{N} f_j \sin 2(\mathbf{h} \cdot \mathbf{r}_j + \mathbf{k} \cdot \mathbf{y}_j + \mathbf{l} \cdot \mathbf{z}_j) \]  \hspace{1cm} (1.11)

The phase angle \( \phi_{hkl} \) of the structure factor \( F_{hkl} \) is given by

\[ \phi_{hkl} = \tan^{-1} \left( \frac{B_{hkl}}{A_{hkl}} \right) \]  \hspace{1cm} (1.12)

The phase angle is not a measurable quantity. When x-rays are diffracted, only the intensity of the diffracted beam is recorded and not the phase of the diffracted beam. The intensity of the x-rays scattered from a crystal having large number of unit cells is proportional to

\[ |F_{hkl}|^2 = A_{hkl}^2 + B_{hkl}^2 \]  \hspace{1cm} (1.13)

The structure factor equation (1.8) may be written as

\[ F_{hkl} = \sum_{j=1}^{N} f_j \exp(2\pi i \mathbf{s} \cdot \mathbf{r}_j) \]  \hspace{1cm} (1.14)

Where \( \mathbf{r}_j \) represents the position and \( \mathbf{s} \) is the scattering vector. From equation (1.13) and (1.14) we can write

\[ |F_{hkl}|^2 = \sum_{i=1}^{N} \sum_{j=1}^{N} f_i f_j \cos 2\pi (\mathbf{r}_i \cdot \mathbf{s} - \mathbf{r}_j \cdot \mathbf{s}) \]  \hspace{1cm} (1.15)
Here, the intensity of the scattered beam depends only on the interatomic vectors and hence the choice of the origin has no effect on the symmetry. Where as the value of \( \phi_{hkl} \) generally depends on the choice of the origin. For a centrosymmetric crystal

\[
F_{hkl} = 2 \sum_{j \in I} f_j \cos 2\pi (hx_j + ky_j + lz_j)
\]  

(1.16)

This shows that for a centrosymmetric crystal the phase angle \( \phi_{hkl} \) can be 0 or \( \pi \), whereas for a non-centrosymmetric crystal the phase angle can be anywhere between 0 to \( 2\pi \).

So far we have defined the structure factor \( F_{hkl} \) as the resultant of all the waves scattered from all the atoms in the unit cell in a particular hkl direction. The structure factor can also be defined as the sum of the wavelets scattered from all the infinitesimal electron density in the unit cell. If \( \rho (x,y,z) \) is the electron density at any point \((x,y,z)\) and \( dv \) is the small elemental volume around \((x,y,z)\), then the wavelet scattered by this elemental volume is given by \( \rho (x,y,z) \exp(2\pi i (hx+ky+lz)) dv \). Therefore,

\[
F_{hkl} = \int \rho (x, y, z) \exp 2\pi i (hx + ky + lz) \, dv
\]  

(1.17)

Since \( \rho(x,y,z) \) is a periodic electron density function, \( F_{hkl} \) and \( \rho(x,y,z) \) are Fourier transformations of each other. We can express \( \rho(x,y,z) \) as a summation.

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

(1.18)
Since $F_{hkl}$ is associated with a phase $\phi_{hkl}$, the expression for the electron density becomes:

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

(1.19)

Experimentally one can determine only the structure factor amplitudes $|F_{hkl}|$ and not the phase angle. The computation of the electron density function using $F_{hkl}$ without the associated phase will not lead to any meaningful structure solution. This leads to what is known as phase problem in crystallography. Several methods are employed for determining the phases of the structure factors. Only the methods actually employed in solving the structures will be discussed.

1.6 Absolute scaling and temperature factors

The atoms in the crystal execute oscillations about their mean position due to the thermal energy. The amplitude of vibration varies with temperature. The frequency of oscillation is negligible compared to the frequency of X-rays and hence the atoms appear stationary to X-rays, but little displaced from their mean position. The thermal vibration has the effect of smearing out the electron cloud over a large volume thereby decreasing the scattering factor $f_{oj}$ of any $j$ by a factor

$$\exp\left[-8\pi^2 \hat{u}_j^2 \frac{\sin^2 \theta}{\lambda^2}\right]$$
Where $\bar{u}_j$ is the root mean square displacement of the $j^{th}$ atom. The modified scattering factor for any atom $j$ may be written as

$$f_j = f_{o_j} \exp \left[ -8\pi^2 \bar{u}_j^2 \frac{\sin^2 \theta}{\lambda^2} \right]$$

(1.20)

Where $f_{o_j}$ is the scattering factor of the $j^{th}$ atom.

Substituting $B_j$ for $8\pi^2 \bar{u}_j^2$,

$$f_j = f_{o_j} \exp \left[ -B_j \frac{\sin^2 \theta}{\lambda^2} \right]$$

(1.21)

Where $B_j$ is called the isotropic temperature factor.

The magnitude and mode of vibration of an atom depends on its environment and is generally anisotropic in nature. Therefore, the smeared out shape of the electron density of any atom is an ellipsoid rather than a sphere.

For a reflection only the component of vibration perpendicular to the reflecting plane affects the intensity. For any set of lattice planes (hkl) the temperature factor of an atom is dependent on the magnitude of vibration perpendicular to the plane and interplanar spacing ‘d’. Assuming that the end of the vector $\bar{u}$ lies on the ellipsoid whose centre is at the mean position of the atom, the general temperature factor expression is
\[
\exp \left[ -\frac{1}{4} (B_{11} h^2 a^{*2} + B_{22} k^2 b^{*2} + B_{33} l^2 c^{*2} + 2B_{12} hka^{*} b^{*} + 2B_{13} hla^{*} c^{*} + 2B_{23} klb^{*} c^{*}) \right] 
\]

(1.22)

Where \( B_{ij} \) describes the ellipsoidal electron distribution of an anisotropically vibrating atom. The units of \( B_{ij} \) are same as that of isotropic \( B \).

\( a^{*}, b^{*} \) and \( c^{*} \) are the reciprocal lattice parameters. An equivalent and preferable expression for the general temperature factor is given by

\[
\exp \left[ -\frac{1}{4} (u_{11} h^2 a^{*2} + u_{22} k^2 b^{*2} + u_{33} l^2 c^{*2} + 2u_{12} hka^{*} b^{*} + 2u_{13} hla^{*} c^{*} + 2u_{23} klb^{*} c^{*}) \right] 
\]

(1.23)

\( u_{ij} \)'s are the thermal parameters in terms of the mean square amplitude of vibration. Also,

\[
B_{ij} = 8\pi^2 u_{ij}^2 
\]

(1.24)

Another commonly used expression for temperature factor is

\[
\exp \left[ -(\beta_{11} h^2 + \beta_{22} k^2 + \beta_{33} l^2 + 2\beta_{12} h k + 2\beta_{13} h l + 2\beta_{23} k l) \right] 
\]

(1.25)

Where \( \beta_{11} = (2\pi^2 a^{*2}) u_{11} \), similarly for \( \beta_{22} \) and \( \beta_{33} \).

\( \beta_{12} = (2\pi^2 a^{*} b^{*}) u_{12} \) and similarly for \( \beta_{13} \) and \( \beta_{23} \), where \( \beta_{ij} \) is a dimensionless quantity.

Before the structure solution is undertaken it is necessary to place the observed intensities on an absolute scale. A.J.C. Wilson (1942) evolved a method to determine the scale factor \( K \) to convert the relative intensities to absolute intensities and the temperature factor \( B \). The theoretical average intensity for a randomly distributed \( N \) atoms depends only on the contents of the unit cell and on the distribution of the contents of the unit cell. The average absolute intensity is given by
The average observed intensity corrected for Lorentz-polarisation effects $\langle |F_\alpha|^2 \rangle$ is related to $\langle |F|^2 \rangle$ by a scale factor $K$ such that

$$\frac{\langle |F|^2 \rangle}{|F_\alpha|^2} = K \quad (1.27)$$

$$K \langle |F_\alpha|^2 \rangle = \langle |F|^2 \rangle$$

Where $|F_\alpha|$ is the observed structure factor. Since the atomic scattering factor $\text{f}$ varies with $\sin \theta / \lambda$ and the scale factor becomes complex. To avoid this variation in $\langle |F_\alpha|^2 \rangle$, the entire reciprocal space is divided into concentric annular zones of equal $\sin \theta / \lambda^2$. Each zone is thin enough such that the variation of $\text{f}$ with $\sin \theta / \lambda$ within the shell may be neglected. The average observed intensity $\langle |F_\alpha|^2 \rangle$ for each zone is determined and $\langle |F|^2 \rangle$ for each zone is calculated using the values of $f_j$ appropriate to the zone. The $f$'s required here are the proper scattering factor for real atoms with thermal motion and not for ideal atoms.

$$\sum_{j=1}^{N} f_j^2$$

can be calculated for each zone using the mean value of $\sin^2 \theta / \lambda^2$ of that zone. Combining (1.21) and (1.26), we get
Using equation (1.27), we can write

\[
<|F|^2> = \sum_{j=1}^{N} f_{ij}^2 \exp \left[ -2B \frac{\sin^2 \theta}{\lambda^2} \right]
\]

(1.28)

or

\[
\ln \frac{<|F_0|^2>}{<|F|^2>} = -2B \frac{\sin^2 \theta}{\lambda^2} + \ln K
\]

(1.29)

The LHS is calculated for each annular zone and plotted against \(\sin^2 \theta / \lambda^2\). The plot thus obtained is called Wilson plot. Such a plot should be a straight line. The slope and intercept of the least-squares straight line gives the temperature factor (2B) and the scale factor respectively.

Sometimes there are atomic groups of known geometry present in the structure such as benzene ring and hence the assumption that the atomic distribution is random is grossly violated. In that case the expression given by Debye (1915) is used

\[
<|F_0|^2> = \sum_{k=1}^{a} \sum_{j=1}^{Mk} \sum_{f(ij)} \left[ \frac{\sin 2\pi r_{ij}S}{2\pi r_{ij}S} \right] + \sum f_j^2
\]

(1.30)
Where $S = \sin \theta / \lambda$, $M_k$ is the number of atoms in the group and $G$ is the number of groups in the unit cell. The plot of $\frac{<|F_0|^2>}{<|F|^2>}$ against $\sin^2 \theta / \lambda^2$ in this case is known as Debye plot and gives a better estimation of $B$ and $K$.

1.7 Phase problem

By computing the electron density function one can obtain the precise position of atoms in the unit cell. Computation of the electron density requires structure factor amplitudes and the associated phases. Experimentally one gets only the structure factor amplitude and not the phases. The Fourier map in the absence of phase information will not lead to any meaningful structure solution. This problem is referred to as "Phase Problem" in crystallography.

Several methods have been devised to obtain the relative phases of reflections and the methods employed are

1. Trail and error method.
2. Heavy atom method.
3. Isomorphous replacement method.
4. Direct method.

The first three methods mentioned above are not used in this work and are not discussed. Only direct methods have been employed to obtain the structure solution of the eight compounds reported in this thesis.
1.8 Direct methods

If a structure contains heavy atom then the phases of the structure factor amplitudes can be obtained using Patterson function. However, it can be argued that if a structure can be extracted by way of Patterson, which is the Fourier transform of the intensities, it should also be obtainable from the intensities themselves, since they contain all information normally afforded by X-ray measurements. It is this approach of generating an adequate set of phases by considerations solely of structure amplitudes that constitutes direct methods.

A large number of operating procedures for direct phase determination have been proposed. Most of these are based on the same fundamental principles, but differ in the manner of handling the data and extracting the phases.

In the year 1948 Harker and Kasper arrived at some explicit inequality relationships between the amplitudes and phases based on the impossibility of negative electron density anywhere in the unit cell. Later on these relationships were generalised by Karle and Hauptman in 1950. Further development of direct methods was made by Sayre (1952), Cochran (1952), Zachariasen (1952) and Hauptman and Karle (1953). The real breakthrough in direct methods came with the effective use of symbolic addition procedure (Karle and Karle, 1966) or the multisolution method (Woolfson and Germain, 1968).
Procedure involved in the phase determination by direct method is briefly discussed.

1.9 Unitary and normalised structure factors

One of the difficulties with applying inequalities to ordinary $|F|$'s is that the decline in $|F|$ with $\sin \theta$ will very rapidly lower the $|F|/F_{000}$ ratios below the level at which there is any chance of obtaining phase information by this method. The derivation of the inequalities makes no assumption about the shape of the atoms in the cell, however, they can be applied equally well to the $F_{\text{point}}$'s i.e. the $F$'s which would be found if the real atoms were replaced by point atoms. Thus in practice it is more common to define the unitary and normalised structure factors $U_{hkl}$ and $E_{hkl}$.

The unitary structure factor $U_{hkl}$ is defined as the ratio of $F_{hkl}$ to the maximum value of $F_{hkl}$.

$$U_{hkl} = \frac{F_{hkl}}{\sum_{j=1}^{N} f_j} \quad (1.31)$$

$U_{hkl}$ has the same phase $F_{hkl}$ and its value ranges from -1 to +1. $U_{hkl}$ can also be expressed as

$$U_{hkl} = \sum_{j=1}^{N} n_j \exp 2\pi i (hx_j + ky_j + lz_j) \quad (1.32)$$
Where $n_j$ is called the unitary atomic scattering factor and

$$n_j = \frac{f_j}{\sum_{j=1}^{N} f_j}$$

(1.33)

The normalised structure factor $E_h$ is defined as

$$E_h = \frac{U_{hl}}{\langle |U_{hl}|^2 \rangle^{1/2}}$$

(1.34)

where

$$\langle |U_{hl}|^2 \rangle = \frac{1}{N} \sum |u_{hl}|^2$$

$H$ indicates $hkl$ and $E_h$ has the same phase as that of $F_{hl}$.

The advantage with $E_h$ is that the average value of $|E_{hl}|^2$ is unity and the effects introduced by thermal motion is taken care of by the point atoms. This is true for any space group and the distribution of $E$'s for both centrosymmetric and non-centrosymmetric structures are independent of the complexity of the structure.

The statistical properties of $E_h$ are often used to check whether the distribution of the intensity in the given data is centric or non-centric. The following table gives the expected value of $|E|$ which can be used to resolve the space group ambiguity

<table>
<thead>
<tr>
<th>Centric</th>
<th>non-centric</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\langle</td>
<td>E</td>
</tr>
</tbody>
</table>
These theoretical values are derived for random distribution of atoms and hence any pronounced regularity in the atomic arrangement will result in significant deviation from these theoretical values.

The use of molecular scattering factors for group of atoms of known stereochemistry instead of individual scattering factors \( f_i \), generally give better results. For structures having planar rings, use of molecular scattering factors give better \( E \)-map by reducing spurious peak heights and eliminating peaks frequently observed at the centre of planar ring systems.

1.10 Sayre's equation

The inequalities become ineffective as the structure size becomes large and it is necessary to find another approach to the problem of direct phase determination. Using range of intensities which are too small for inequalities, but still relatively large it is possible to set up equations which are probably true and phase information can be extracted from these equations.

The basis for such a method is considered to be a paper by Sayre (1952) which can be shown with certain restrictions

\[
F_{hk'l} = \phi \ hkl \sum_{h'} \sum_{k'} \sum_{l'} F_{h'k'l'} F_h - h', k - k', j - j' \tag{1.35}
\]
where $\phi_{hkl}$ is simply a calculable scaling term. The implication of this equation is that any structure factor $F_{hkl}$ is determined by the products of all the pairs of structure factors whose indices add to give (hkl). On the surface this equation appears useless, since to determine one $F$ it is necessary to know the magnitude and phase of all others. Sayre pointed out that for the case where $F_{hkl}$ is large, the series must tend strongly in one direction (+ or -) and this direction is generally determined by the agreement in sign among products between large $F$'s. Thus, for the case of all three reflections large

$$S(F_{hk'l'}) \sim S(F_{h'k'1'}). S(F_{h - h', k - k', 1 - l'})$$ \hspace{1cm} (1.36)

$$S(F_{hk'l'}). S(F_{h'k'1'}). S(F_{h - h', k - k', 1 - l'}) \sim + 1$$ \hspace{1cm} (1.37)

Where $S$ means sign of and $\sim$ means "is probably equal to".

The probability of this relationship in terms of $u$'s is given by Cochran and Woolfson (1955) and is given by

$$P_+ = \frac{1}{2} + \frac{1}{2} \tanh \left[ (N^{1/2} |U_H U_k U_H - \kappa|) \right]$$ \hspace{1cm} (1.38)

and in terms of $E$

$$P_+ = \frac{1}{2} + \frac{1}{2} \tanh \left[ (N^{1/2} |E_{H} E_k E_H - \kappa|) \right]$$ \hspace{1cm} (1.39)

The equations (1.38) and (1.39) are based on the assumption that the atomic arrangement is completely random, although these equations give reliable phases they provide a rough estimate as none of the structures satisfy the above assumption.
If Sayre's equation is expressed in terms of $U$ or $E$, then the summation must theoretically be over an infinite number of terms. Since the atoms are considered as point scatterers and the scattering factor is not expected to decreases with the increasing scattering angle. However, in practice, only a few terms of reasonably high magnitude are available.

Hauptman and Karle in a monograph (1953) gave a set of formulae applicable to space group $P1$. These are expressed as

$$\Sigma_1 = S (E_{2H}) \approx S (E_{H}^2 - 1)$$

(1.40)

$$\Sigma_2 = S (E_H) \approx S \sum_k E_k \cdot E_{H-K}$$

(1.41)

$$\Sigma_3 = S (E_H) \approx S \left| \sum_k E_k \left\{ \frac{E_{H-K}^2}{2} - 1 \right\} \right|$$

(1.42)

$$\Sigma_4 = S (E_{2H}) \approx S \left[ \sum_k (E_k^2 - 1) (E_{H=K}^2 - 1) \right]$$

(1.43)

The $\Sigma_4$ relationship is more extensively used in direct methods. The $\Sigma_e$ relationship is basically a modified Sayre's equation with the associated
probability that $E_H$ will be positive is given by the expression (Cochran and Woolfson, 1955).

\[
P + (E_H) = \frac{1}{2} + \frac{1}{2} \tanh \left( \frac{\sigma_2^3}{\sigma_2^3} \right) |E_H| \sum_{K} E_K E_{H-K}
\]

(1.44)

Where $\sigma_n = \sum_{j=1}^{n} Z_j^n$ and $Z_j$ is the atomic number of the $j$th atom. $N$ is the total number of atoms in the unit cell. The quantity

\[
\frac{1}{\sigma_n^2} = \frac{1}{N^{1/2}}
\]

for a crystal with all equal number of atoms.

The larger the values of $E_H$, $E_K$, $E_{H-K}$, the greater will be the probability for the sign assignment.

For non-centrosymmetric crystals Karle and Karle (1966) suggested the formula

\[
\phi_{II} = <\phi_k + \phi_{II-K}> K
\]

(1.45)

$\phi_{II}$ is the phase of the normalised structure factor $E_{II}$ and $K_r$ implies that it ranges over those triplets associated with the largest amplitudes. When there are more than one pair of reflections whose known phases contribute towards determining one unknown phase $\phi_{II}$, then the expectation value of $\phi_{II}$ may be written as

\[
<\phi_H> = \text{phase of } \sum_{K} E_K E_{H-K}
\]

(1.46)

This relation leads to a very important phase determining expression known as Tangent formula. Karle and Hauptman derived from probability
considerations, the tangent formula which can be obtained from Sayre's relation

In equation (1.46) the right hand side can be written as

\[ \sum E_k E_{H-k} = \sum |E_k E_{H-k}| \cos (\phi_k + \phi_{H-k}) + i \sum |E_k E_{H-k}| \sin (\phi_k + \phi_{H-k}) \]  

(1.47)

From this expression we get,

\[ <\phi_H> = \tan^{-1} \left[ \frac{\sum |E_k E_{H-k}| \sin (\phi_k + \phi_{H-k})}{\sum |E_k E_{H-k}| \cos (\phi_k + \phi_{H-k})} \right] \]  

(1.48)

The equation (1.48) is known as tangent formula and may be used to refine the phases and to determine the new phases by iterative process. The terms whose phases are known are incorporated in the summation over K to get an estimation of the phase. This is done for each H in turn and the new phase value thus obtained are used in the next cycle and the process is continued till all the phases attain stable values.

Signs may be assigned to a suitably chosen set of reflections (ODR) so as to define a particular origin from the possible equivalent origins in the unit cell. Normally these linearly independent reflections are chosen as origin defining reflections. The rules for fixing origin in centric and non-centric space groups are given by Hauptman and Karle (1956, 1959), Karle and Hauptman (1961).
It may be possible to arrive at the signs of certain reflections based on inequality relations between structure factors. It must be ensured that the starting set of reflection (SSRs) are associated with large E-values and enter as many TPSRs as possible. The phase propagation is initiated with the SSRs using only those TPSRs with high probability, say 0.95.

However, a point of saturation may be reached when there are no new indications of high probability. In such a situation the symbolic addition method (Zachariasen, 1952; Karle and Karle, 1963 & 1966) may be employed. The SSRs are augmented by adding a few reflections to which symbols are assigned. Generally the signs of the symbols are indicated by interrelationships between the reflections. If any symbol is left undetermined at the end of the phase propagation, it can be assigned both the signs + and -. The structure may be contained in one of the E-maps calculated with $|E_{hkl}|$, as the Fourier coefficients and the signs being determined by phase propagation. In sign correlation method (Buerskens, 1964) a large number of reflections are assigned symbols even to start with and they are expected to be determined during the course of propagation. In multi-solution approach, the two alternatives + and – are tried for the symbolic reflections and the resulting E-maps have to be examined for the best model of the structure.
It may be necessary to extend the sign propagation to low E-values also, because according to Burgi and Dunitz (1971) the exclusive use of large E-values in phase determination procedure may lead to pseudo translational symmetry due to which the recognition of the actual position of the molecule will be rendered difficult.

In non-centric space groups, in addition to ODRs, another reflection which forms a structure invariant with ODRs may be chosen to distinguish between the two possible enantiomorphs. The structure invariant combination which is expected to choose between the enantiomers should not be close to 0 or 180°. However, in centric structures, it is more easy to deal with phase rather than symbols even from the very beginning since, automation of non-centric symbolic addition method is likely to be difficult in practice. In general the reflections whose phases are not known, and are required in the starting set, are assigned four values ± 45°, ± 135°, differing by 90° in the four quadrants and tangent formula is used from the very beginning of the phase determination process.
1.11 Structure refinement and completion

Once a set of phases have been found the remaining task is to calculate the Fourier synthesis using $E$ values. Since $E$'s correspond to completely sharpened atoms, the peaks on the map tend to be very sharp and also, they can be found on a grid with a spacing of about 0.5Å (Karle, Hauptman and Wing, 1958). If only partial structure has been obtained, a difference Fourier synthesis has to be carried out till all the atomic sites are located. A satisfactory trial structure is the one that is chemically plausible and for which there is good agreement between the calculated and observed structure factors. Only after the general correctness of the structure is assured refinement of the structure must be pursued exhaustively. The correctness of the structure is indicated by the reliability factor or simply the R-factor and is given by

$$ R = \frac{\sum_{\text{hkl}} |F_o| - G |F_c|}{\sum_{\text{hkl}} |F_o|} $$

(1.49)

Where $|F_o|$ and $|F_c|$ are the observed and calculated structure factors and $G$ is the reciprocal of the scale factor $K$. The lower the value of $R$ better is the agreement between $F_o$'s and $F_c$'s and closer is the model with the actual structure.

Another index which gives a better indication of the improvement of the model was proposed by Hamilton (1965) and is called the weighted R-factor and is given by
Where $w = 1/\sigma^2(F_o)$ and $\sigma (F_o)$ is the standard deviation of $F_o$.

Huges (1941) first used the method of least-squares for the refinement of the crystal structure. Here, the quantity minimized is $\Sigma w \Delta F^2$ where $\Delta F = |F_o| - |F_c|$. In the final cycles of refinement $\Delta F$ will attain its possible minimum value and hence the R-value as given by the equation (1.49) becomes static. The scale factor, positional and thermal parameters are refined by least-squares methods and the function to be minimized is

$$D = \Sigma W (|F_o| - |F_c|)^2 = W (\Delta F)^2$$  \hspace{1cm} (1.51)

The minimisation is achieved by taking the derivations of the equation (1.51) with respect to each of the parameters and equating it to zero. This leads to $n$ normal equation.

$$\frac{\delta D}{\delta p_j} = 0, \hspace{0.5cm} j = 1, 2, 3, \ldots \ldots n$$  \hspace{1cm} (1.52)

Where there are $n$ parameters $p = p_1, p_2, p_3, \ldots \ldots p_n$. Where

$$\Sigma W_{hkl} (\Delta F) \frac{\delta F_c}{\delta p_j} = 0$$  \hspace{1cm} (1.53)
Where $\Delta F = |F_o| - G |F_d|$ and $w_{hkl}$ is a suitable weight assigned to each observation. The structure factors are non-linear functions of $p$ and therefore, they given rise to a set of non-linear normal equations. This is a very complicated situation. The problem can be solved by approximating the function by a truncated Taylor series. Given a set of trial parameters $p$ which require small shifts $\varepsilon = \varepsilon_1 + \varepsilon_2 + \varepsilon_3 + \ldots \varepsilon_n$ to reach the correct values. We expand $\Delta F (p + \varepsilon)$ by a Taylor series and retain only the first order terms

$$\Delta F (p + \varepsilon) = \Delta F (p) - \sum_{i=1}^{N} \varepsilon_i \frac{\partial \Delta F}{\partial p_i} \tag{1.54}$$

Substituting equation (1.54) to (1.53) we get normal equations.

$$\sum_{i=1}^{N} \left[ \sum_{hkl} W_{hkl} \frac{\partial \Delta F}{\partial p_j} \frac{\partial \Delta F}{\partial p_i} \right] \varepsilon_i = - \sum_{hkl} W_{hkl} \Delta F \frac{\partial \Delta F}{\partial p_j} \quad \tag{1.55}$$

Since, $\frac{\partial \Delta F}{\partial p_j} = -G \frac{\partial |F_c|}{\partial p_j}$, we get,

$$\sum_{hkl} W_{hkl} \frac{\partial |F_c|}{\partial p_j} \gamma \frac{\partial |F_c|}{\partial p_i} = \sum_{hkl} W_{hkl} \Delta F \frac{\partial |F_c|}{\partial p_j} \quad \tag{1.56}$$

$n$ equations correspond to $j = 1, 2, 3, \ldots n$. The required shifts $\varepsilon$ are found out by solving these equations. These values are approximate. Hence, the whole process has to be repeated for several cycles until convergence is reached. One important aspect here is, if the initial set $p$ is significantly different from the correct set of values then the approximation in (1.54) is not justified and hence the above calculations lead to false minimum.
The normal equations can be written in a compact matrix form as

\[ A \varepsilon = V \]  

(1.57)

Where \( n \times n \) matrix has elements

\[ a_{ij} = \sum W_{hkl} \frac{\delta |F_c|}{\delta p_i} \frac{\delta |F_c|}{\delta p_i} \]  

(1.58)

and those of vector \( V \) are

\[ V_i = \sum W_{hkl} \Delta F \frac{\delta |F_c|}{\delta p_i} \]  

(1.59)

the shifts \( \varepsilon \) are given by

\[ \varepsilon = A^{-1} V \]  

(1.60)

The inverse matrix \( A^{-1} \) is a matrix like \( A \) with elements denoted by \( B_{ij} \).

The \( i^{th} \) diagonal element \( b_{ii} \) of the inverse matrix is related to the estimated standard deviation \( \sigma_i \) of the parameter \( p_i \) by the expression

\[ \sigma_i = b_{ii} \left[ \sum W_{hkl} \frac{(\Delta F)^2}{m-n} \right]^{1/2} \]  

(1.61)

Where \( m \) is the number of observations and \( n \) is the number of parameters.

Here we see that for a large number of intensity data, the estimated standard deviations are small.
The non-diagonal element $B_{ij}$ is a measure of the correlation between the parameters $p_i$ and $p_j$ and the correlation coefficient $\delta_{ij}$ is defined by

$$\delta_{ij} = b_{ij} (b_{ii} - b_{jj})^{-1/2}$$  \hspace{1cm} (1.62)

The values of the correlation coefficients can range between 0 and $\pm 1$ and the latter value indicate complete dependence and in such cases one of the two parameters is to be eliminated from the process of refinement. Correlation coefficients from least-squares refinement less than 0.2 cause little difficulty, but for larger correlation coefficients the refinement process is seriously impaired by way of slowing it or by causing the results of the successive cycles to oscillate. Large correlation coefficients generally exist between the scale and the thermal parameters, between positional parameters for an atom if the inter-axial angles of the unit cell are considerably away from $90^0$. They also exist between parameters of atoms which are related through exact or nearly exact symmetry. In such cases a chosen group of parameters are kept fixed during one cycle and varying them in the subsequent cycles while keeping some other groups fixed. The structures reported in this thesis are solved by direct methods using SOLVER and refined by full-matrix least-squares method using NRCVAX the crystal structure system program (Larson et al., 1990). Another structure solved by direct methods using SOLVER and refined by full-matrix least-squares method using SHELXL-93 program (Sheldrick, 1993). Two more structures was solved by direct methods using SHELXS-86 and refined by full-matrix least-squares method using SHELXL-93 program.
(Sheldrick, 1993). Another four structures was solved by direct methods using SHELXS-97 and refined by full-matrix least-squares method using SHELXL-97 program (Sheldrick, 1997).