THE CRYSTAL AND MOLECULAR STRUCTURE OF NAPHTHO[2,1-c] CINNOLINE TOGETHER WITH THE DEVELOPMENT OF THE MINIMUM RESIDUAL TECHNIQUES.

A thesis presented to

the University of Manchester

for the degree of

Doctor of Philosophy

by

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Research experience since first degree

I obtained my M.Sc. degree in Physics from the University of Dacca in 1952. In 1953 I joined the Comilla Victoria College as a lecturer in Physics. Since 1957 I have been working as a Research Physicist in the laboratories of the Pakistan Council of Scientific and Industrial Research, Karachi, where, for a considerable period, I was associated with its X-ray laboratory. In 1960 I was selected for higher studies in U.K. Since October 1960 I have been working at the University of Manchester on the problem which provides the subject matter of this thesis.

Abstract

A study of the X-ray crystal structure of naphtho [2,1-c] cinnoline forms the major part of this thesis. The structure determination, which necessitated the development of new techniques, is described together with the influence of steric hindrance on the configuration of the molecule. The remainder of the thesis is concerned with a brief account of some computer programmes written in the autocode system for crystallographic calculations.

The collection and treatment of the X-ray intensity data are described in Chapter 1. Chapter 2 briefly describes the preliminary investigation and attempted refinement of the [001] projection of the naphthocinnoline. An approximate shape of the molecule in the [001] projection was obtained by the optical transform method. It was originally intended to use the molecular location method (Taylor, 1954) to obtain the position of the molecule in the cell and refine the structure by Fourier and least-squares methods but these methods, however, were unsuccessful.

In Chapter 3 an account of the earlier investigation and refinement of the [010] projection of the naphthocinnoline is given. Although the structure was refined to an R-value of 0.15, the extent of distortion produced in the molecule from its idealised picture was sufficient to cast doubt upon the structure. The structure in this projection is discussed, and attention is drawn to its important features in Section 3.10.

Some further steps in the solution of the [001] projection are described in Chapter 4, where it is pointed out that some difficulties exist

in solving this projection. Neither the minimum function (Buerger, 1951) nor structure factor graphs (Bragg & Lipson, 1936) gave satisfactory results. As such, the shape and orientation of the molecule was re-determined using optical transforms. The molecular location method (Taylor, 1954) was again used to obtain the molecular position in the unit cell, but the structure would not refine from this position. A new method was, therefore, devised in order to fix the molecular position correctly. The beauty of this method is that it provides information whether or not the orientation of the molecule has been correctly determined to start with. The development and application of this method is discussed in Chapters 5 & 6. The position of the molecule so obtained gave a reasonable agreement between observed and calculated structure factors so refinement was carried out by Fourier methods and then by the least-squares method. The results of this refinement are discussed in Chapter 7. Again these methods did not refine the structure below the R-value of 0.34 due to a great deal of overlap in projection. A new method of refinement was, therefore, devised to cope with this difficulty. The development and application of the method are discussed in Chapter 8.

In Chapter 9 the refinement of the [001] projection of the naphthocinnoline using the new method is described. The structure was refined to a final R-value of 0.16, even though there is a great deal of atomic overlap.

Chapter 10 describes the solution of the [010] projection of the naphthocinnoline. The approximate structure in this projection was

obtained with the help of the [001] projection and it was proposed to refine this projection by the new method starting from the trial co-ordinates. When this was done the structure refined to a R-value of 0.12. The new method is particularly useful to deal with overlapped atoms in projection and is capable of refining the structure even when very large co-ordinate changes (>0.5 Å) are necessary.

The final structure is shown diagrammatically and some of its important features are discussed in Chapter 12. Lines of further investigation are indicated.

Details of various programmes, written for the Ferranti Mercury Computer, are given in Chapter 13.

The appendix (1) is concerned with the preliminary X-ray investigation of Strontium Caproate.

I should like to record that none of the work referred to in this thesis has been submitted in support of an application for another degree of this, or any other, University.

Explanatory notes

A word of explanation is perhaps needed on one or two points which arise in this thesis. The axes of the Patterson maps, electron density maps etc., are not all drawn in accordance with the convention adopted in the International Tables for X-ray Crystallography, where ever this occurs it has been done intentionally to aid the lay-out of diagrams and figures and, in some cases, to avoid the necessity and extra work of re-plotting them as this was the way they were received from the Computer.

Contents

Part 1. The crystal and molecular structure of naphtho[2,1-c]cinnoline

Chapter 1

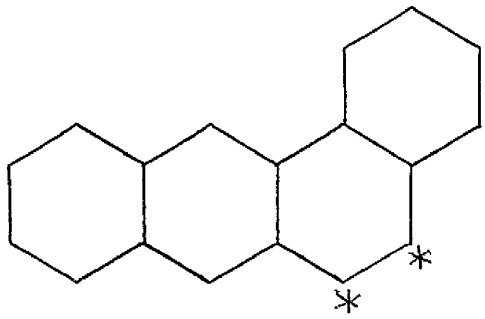
Introductory and Experimental

1.1. Introduction. The structure of naphtho[2,1-c]cinnoline, a potentially carcinogenic compound, is of considerable interest, especially with regard to the molecular configuration and electron distribution in the molecule.

The early history of carcinogenesis began when Sir Percival Pott (1775) described a particular form of cancer occurring in chimney-sweeps due to the contamination of the skin by soot, and there were several other examples of similar disease such as "Mulespinner's" cancer in the Lancashire cotton industry due to lubricating oil and "paraffin" cancer of the refinery workers in oil fields. The next stage was that of systematic enquiry and a major discovery was achieved by Yamagiwa and Ichikawa in 1915, when they produced tumours by application of coal tar to the ears of rabbits. In the early twenties Bruno Bloch and Dreifuss (1921) suggested that the cancer-producing agent might lie in the class of cyclic hydrocarbons. Later on several other workers, Bruno Bloch and Dreifuss (1921-26), Kennaway (1924-25) and Schroeter (1924) successfully demonstrated that certain types of cancer in the body are due to cyclic hydrocarbons. The recognition that cancer can develop as an occupational disease has led to the examination of many hydrocarbons and to the discovery that many of them are specific carcinogenic agents. It was this circumstance which led Cook (1930) to embark on

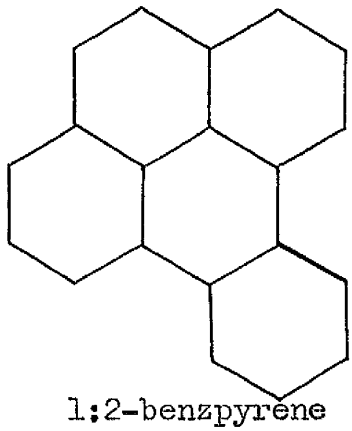
a long series of synthetic studies on homologues of benzanthracene (I) (e.g.

I



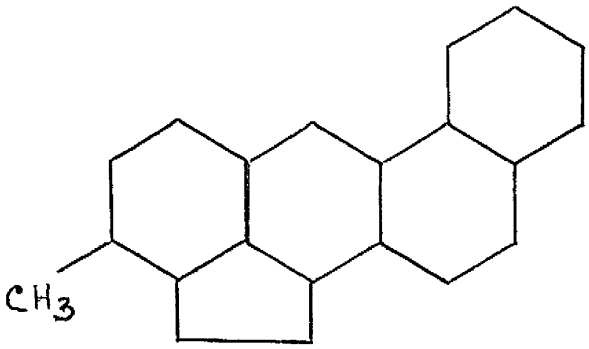
1:2-benzanthracene

II



1:2-benzpyrene

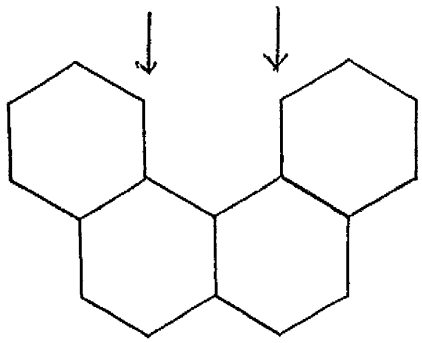
III



methylcholanthrene

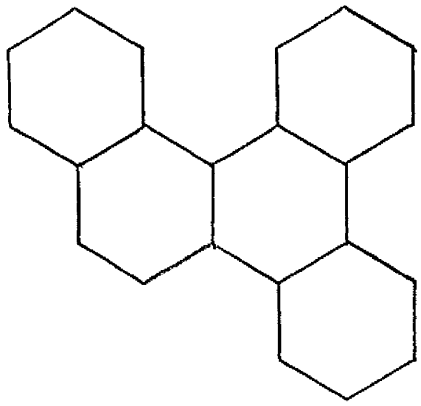
1:2-benzpyrene (II) and methylcholanthrene (III)) which manifested pronounced carcinogenic properties. Hewett (1940) examined several carcinogenic hydrocarbons consisting of 4 condensed aromatic rings

IV



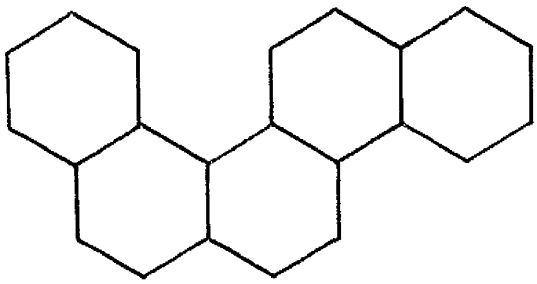
3:4-benzphenanthrene

V



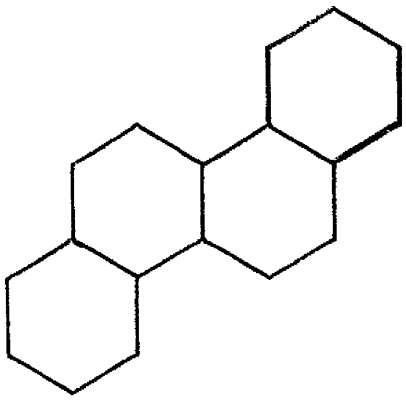
1:2:34-dibenzphenanthrene

VI



1:2:5:6-dibenzphenanthrene

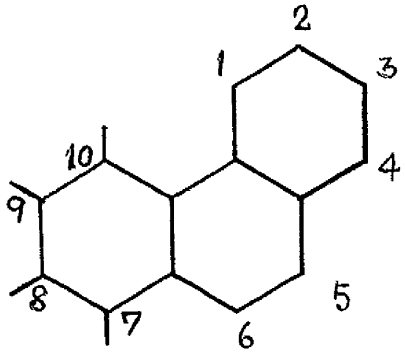
VII



Chrysene

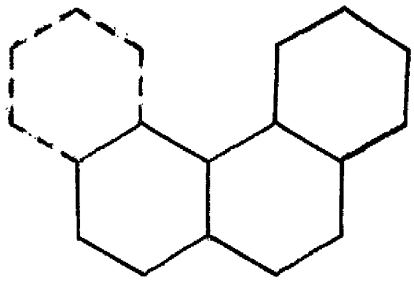
(e.g. 3:4-benzphenanthrene (IV), 1:2:3:4- and 1:2:5:6-dibenzphenanthrene (V and VI), Chrysene (VII) and 1:2-benzanthracene (I)) and derived a fascinating correlation between chemical constitution, molecular disposition and biological action. Each of these hydrocarbons is a derivative of phenanthrene (VIII), substituted in two of the

VIII



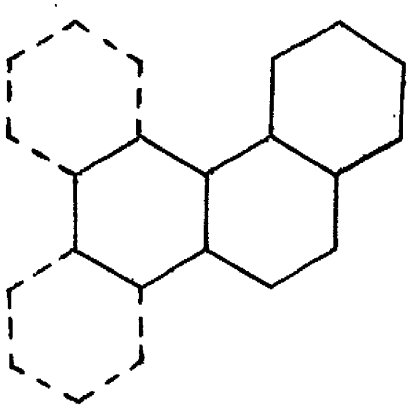
phenanthrene

A



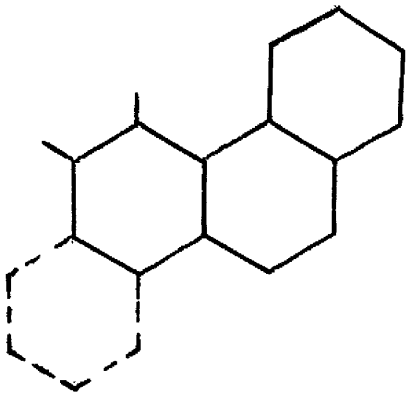
3:4-benzphenanthrene

B



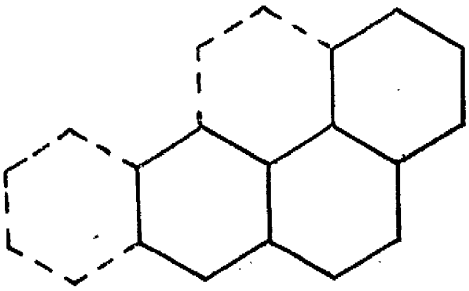
1:2:3:4-dibenzphenanthrene

C



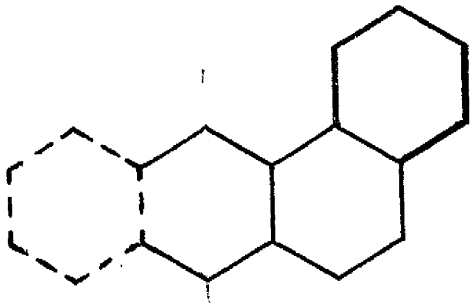
1:2-dimethylchrysene

D



3:4-benzpyrene

E

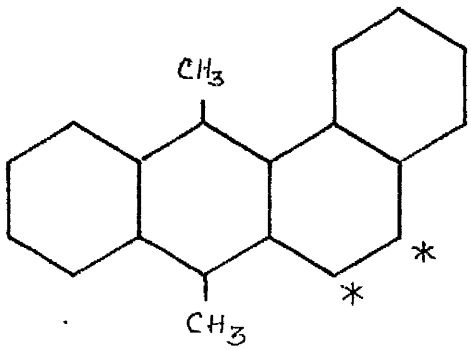


9:10-dimethyl-1:2-benzanthracene

7-, 8-, 9- and 10-positions. Further substitution in either or both of the remaining positions gives rise to highly carcinogenic hydrocarbons.

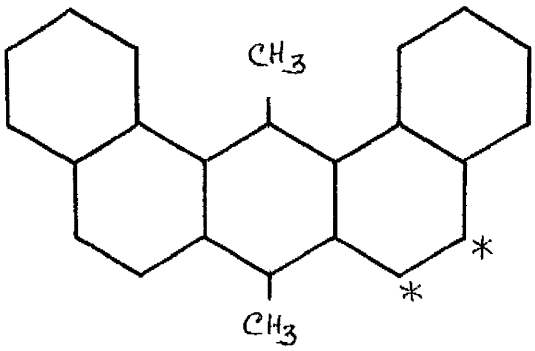
In an attempt to define the essential structural requirement for carcinogenicity, Robinson (1946) examined several polycyclic hydrocarbons (e.g. 9:10-dimethyl-1:2-benzanthracene (IX), 9:10-dimethyl-

IX



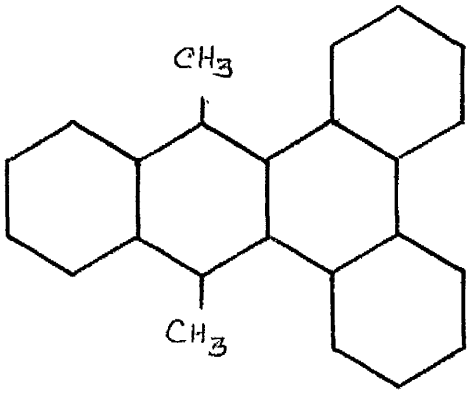
9:10-dimethyl
1:2-benzanthracene

X



9:10-dimethyl
1:2:7:8-dibenzanthracene

XI



9:10-dimethyl
1:2:3:4-dibenzanthracene

1:2:7:8-dibenzanthracene (X) and 9:10-dimethyl-1:2:4-dibenzanthracene (XI)) and suggested that the phenanthrene bridge ("meso" position marked by **) is of great significance for chemical reactivity. These examples are in keeping with the view that an essential requirement may be the phenanthrene double bond, and that the "meso" positions of phenanthrene (shown in IX and X by **) must be unsubstituted. Robinson also suggested that the reactivity of these positions may be enhanced by appropriate substitutions elsewhere, while the activity may be completely reduced if these positions are substituted (e.g. 9:10-dimethyl-1:2:3:4-dibenzanthracene (XI)).

Otto Schmidt (1938, 1939a, 1939b and 1941) was the first to compare the electron density of the "meso" positions of certain carcinogenic substances with that in related non-carcinogens, and on the basis of this comparison he postulated that it is a necessary condition for carcinogenic activity that the density of such regions should exceed $0.44e/\mathring{A}^2$; in particular, he further suggested that the activity of a carcinogen is due to the electro-affinity of its excited state facilitating a quantum change in the neighbouring molecule.

More recently Pullman,A. and Pullman, B. (1946) have theoretically investigated the relationship between electronic structure and carcinogenic activity in aromatic molecules. For the description of the electronic structure of conjugated molecules they have used indexes such as bond orders, free valencies and total charges. These indexes have been very useful for the interpretation of the chemical reactivity of conjugated molecules, so that their application to the study of the relationship between electronic structure and carcinogenic

activity was quite justified.

In recent years a new set of electronic indexes has been introduced by many authors (Pullman, B. and Pullman, A.,(1952); Brown, (1952); Pullman, B.,(1946)) to study of the relationship between the structure and carcinogenic activity. This theory of chemical reactivity, based on a new set of indexes, has been named the localization theory. This set is composed of three main quantities -

(A) carbon-localization energies,

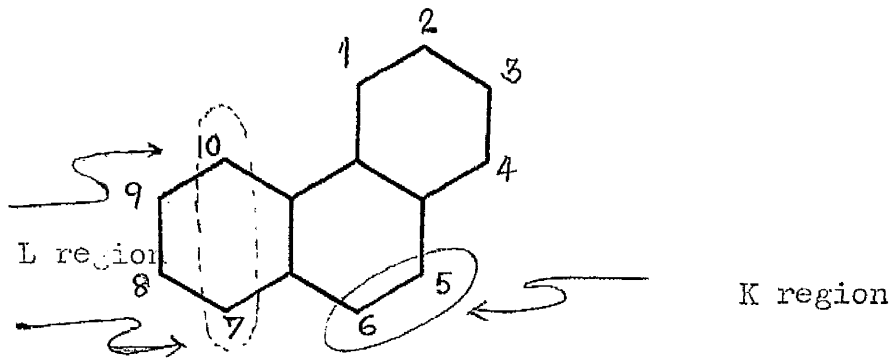
(B) bond-localization energy,

(C) para-localization energy.

It has been shown that the agreement with experiment is greatly improved when these simple basic indexes are replaced by more complex ones, which generally consist of a combination of these simple ones. It has also been shown that the substitution of a methyl group for one of the hydrogens of, say, benzanthracene (I) or the replacement of one of its carbon atoms by nitrogen has practically the same effect on the localization energy of the 5-6 bond (between atoms shown by *) of the molecule.

Quantum-mechanical study (Pullman,A. and Pullman, B., 1946) of the electronic structure of polycyclic aromatic hydrocarbon shows that the majority of these compounds contain two regions which are of particular importance for their chemical and biological behaviour. These are the regions of the type of the 5-6 bond and the 7, 10 positions in phenanthrene which they call respectively the K and L regions.

XII



Phenanthrene

In an isolated molecule, these are the regions which contained, respectively, the bond which had highest mobile order and the carbons which had the highest free valencies. These two types of regions are known to be the principal reactive centres of the polynuclear hydrocarbons. The search for a relationship between the electronic structure and the carcinogenic activity of polynuclear hydrocarbons has led to the two following fundamental propositions (Pullman, A., 1954):-

(1) The appearance of carcinogenic activity in aromatic hydrocarbons is determined by the existence of the K-region, that is the reaction takes place at or through the K-region.

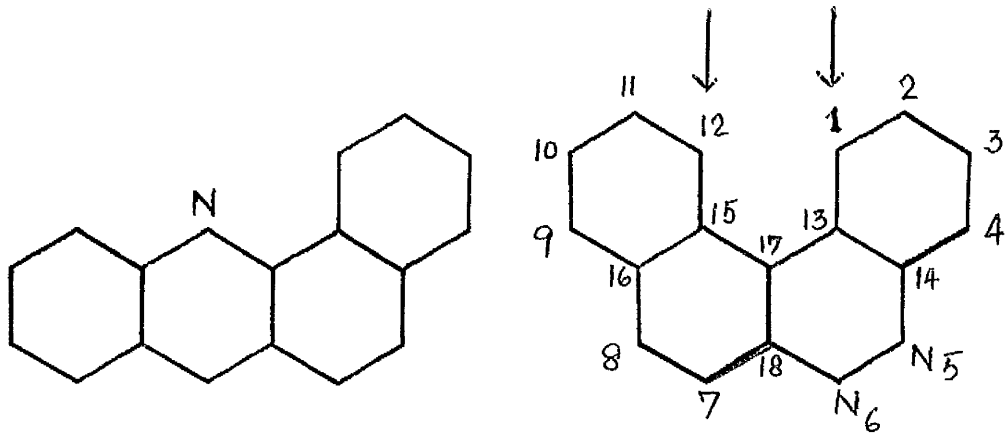
(2) If, however, the molecule contains also the L-region, a supplementary condition requires that these regions should be rather inactive. e.g. [illegible]

3:4-benzphenanthrene (IV) has been shown to possess carcinogenic activity. This case is somewhat special; in contrast to the other compounds which are devoid of steric effects. 3:4-benzphenanthrene has been shown, by X-rays (Herbstein and Schmidt, 1954) and U.V. absorption

spectra (Clar and Stewart, 1952) to be non-planar and to possess a small dipole moment (0.7D) (Bergmann et al., 1951). This phenomenon is due to steric interference between the hydrogen atoms in the positions 1 and 12 shown in the figure by → . Steric interference between these hydrogen atoms in the positions shown in Fig. (IV) creates in the molecule conditions which have not been taken into account in the calculations of the indexes and which may well have the effect of increasing the reactivity of the K-region of this compound beyond the calculated value.

It has also been found in certain nitrogenous analogues of 3:4-benzphenanthrene such as

XIII XIV

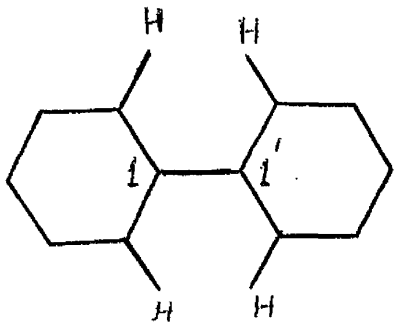


Benzacridine Naphtho[2,1-c]cinnoline

benzacridine XIII possess carcinogenic activity. Naphtho[2,1-c] cinnoline (XIV) is an analogue derived by replacement of the two CH groups in the positions 5-6 by nitrogens and this replacement may have similar effect on the localization energy of the molecule. As the molecule is greatly strained due to steric interactions, its geometrical

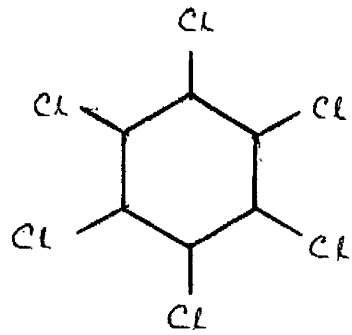
shape is such that the resonance demand for planarity is no longer possible. Such a molecule is said to be overcrowded. These non-planar molecules may be classified into three types (Coulson, 1958a, 1958b) - (a) polyphenyl type, (b) polynuclear type and (c) corrugated ring type. The first type is associated with

XV



Biphenyl

XVI



Hexa-chloro-benzene

biphenyl (XV) and its derivatives. Here if the molecule is planar the four ortho-hydrogens are closer together (about 1.8Å) than the sum of their conventional Van der Waal radii (2.4Å). There are several considerable ways in which this close contact can be reduced and some deformation (either by rotating the molecule around the central 1-1' bond or by rotating C-H bonds around the carbon atoms as pivots) is expected in order to relieve the molecule of the strain. The second type of overcrowding is associated with condensed polynuclear hydrocarbons, such as phenanthrene, dibenzanthracene, 3:4-benzphenanthrene and naphtho[2,1-c]cinnoline. In these molecules the rigidity of the carbon framework no longer permits the rotation of the two rings as in biphenyl. The third type is illustrated (XVI) by hexa-substituted benzene, such as C_6Cl_6.

The steric interactions in naphtho[2,1-c]cinnoline form an interesting subject for study. The present work was, therefore, undertaken in order to determine the extent of deformation produced in the molecule by steric interactions which might affect the chemical reactivity of the hydrocarbons. If the molecule of the naphthocinnoline were planar the separation (2.4Å) between the centres of two carbon atoms at the positions 1 and 12 would be much less than the Van der Waal spheres required to accommodate two hydrogens. The region between the two "legs" of the molecule, which is associated with C_1, C_{12}, H_1 and H_{12} (shown in Fig. (XIV) by →), is grossly overcrowded. It appears that this overcrowding is relieved almost entirely by displacements of various atoms in a direction perpendicular to the mean plane of the molecule. The atoms on one side of the molecule are displaced upwards, the atoms on the other side are displaced downwards. The two hydrogens (1 and 12) are also displaced in opposite directions normal to the plane of the rest of the molecule. In order to investigate quantitatively such deformations the structure of naphtho[2,1-c]cinnoline has been determined by X-ray diffraction techniques and the details of the investigation are described in the subsequent sections of this thesis.

1.2. Collection of crystallographic and X-ray data.

1.2.1. Crystal data. The crystal specimens were provided by Dr. Braithwaite of the Chemistry Department of this College. The crystals of naphtho[2,1-c]cinnoline (R.S.W. Braithwaite and G.K. Robinson, 1962) were large, yellow and blade-like in appearance. The crystals were either badly formed or twinned. As single crystals were not available, from the blades were cut the crystal specimens used for the present study.

As the crystal specimens were blade-like, only one face, (100), could be examined conveniently under a polarising microscope and looking straight down the perpendicular to the plate face nice optic figures suggestive of a biaxial crystal were obtained.

The pyro-electric test was performed with liquid nitrogen. The crystals were observed to exhibit a definite pyro-electric effect, indicating that they were polar and non-centrosymmetric.

The density of the crystal was measured, by a flotation method, in a mixture of a solution of potassium iodide (ρ_0 = 3.13 gm/c.c.) and ethyl alcohol. Different portions of these two liquids were mixed together until the crystal just remained suspended in the resulting liquid, indicating that the liquid and crystal densities were equal. The liquid density was then determined using a specific-gravity bottle. The mean of the three measurements on three crystals gave a value of ρ_0 = 1.25 gm/c.c. The molecular weight is 230, giving the number of molecules per unit cell as 16 (calculated 15.94).

1.2.2. Collection of X-ray data. Oscillation and Weissenberg photographs about the a, b and c axes using CuK_{α} radiation showed the unit cell to be orthorhombic with the following dimensions:-

$$a = 40.80\text{Å}, \quad b = 10.75\text{Å}, \quad c = 10.75\text{Å}.$$

~~The accurate measurement of the cell parameters, using a new technique, is discussed in section 1.3.~~

In an attempt to decide the ~~section 1.3~~ up, with the help of zero-layer Weissenberg photographs taken about the b and c axes, it is observed that reflexions

h00 are present only when $h = 4n$,

0k0 are present only when $k = 4n$,

00ℓ are present only when $\ell = 4n$,

h0ℓ are present only when $(\ell, h = 2n)$, $\ell + h = 4n$,

and hk0 are present only when $(h, k = 2n)$.

The space group therefore has all faces centred, with diagonal-glide planes perpendicular to a and b axes, and the above conditions determine the space group as Fdd2.

The above conditions also demand that a zero-layer Weissenberg photograph about the a-axis should contain 0kℓ reflexions for $k + \ell = 4n$, and $(k, \ell = 2n)$ to satisfy the conditions of the space group Fdd2. In order to confirm this zero-layer Weissenberg photographs about the a-axis were taken. Considerable difficulties were experienced in setting the platy crystals of naphtho[2,1-c]cinnoline to rotate about the 40.8Å a-axis. It was not easy to pick up the layer-lines on the oscillation photographs because there were very few spots in each line

and the layer-lines were very close together. After several attempts a Weissenberg photograph about this axis was taken, but attempts to check the determination of the space group with its help proved inconclusive because of the presence of a few reflexions which were not satisfying the required condition ($k + \ell = 4n$). It was then thought that these might be either occurring from the next higher layer or Renninger (1937) reflexions. In order to eliminate the first suspicion, the crystal setting was checked by taking a zero-layer oscillation photograph for two positions of the crystal 180° apart on the same film. This confirmed that the crystal was correctly set and the ~~0kℓ~~ Weissenberg photograph of the 0kℓ reciprocal lattice layer was therefore taken. All doubtful extra reflexions were found to be present in this Weissenberg photograph also. The next attempt was to take a rotation photograph about this axis with the layer-line screen still in position and a weak reflexion was observed a small distance away from the zero-layer line. From the shape of the spot it appeared that the reflexion had been partially cut off by the screen which suggested that it must belong to the first layer. The zero-layer line photograph was repeated after adjusting the screen and it was found that the spurious reflexion had been eliminated. In the final Weissenberg photograph the doubtful reflexions were absent, i.e. 0kℓ reflexions for $k + \ell = 4n$ and ($k, \ell = 2n$) were present, and the space group was unambiguously decided as Fdd2.

The special projections possess symmetry as follows:-

(001)pgg; $a' = a/2$, $b' = b/2$

(100)cml; $b' = b/2$, $c' = c/2$

(010)clm; $c' = c/2$, $a' = a/2$.

1.3. Measurement and correction of intensities. Multiple-film, zero-layer (normal beam) Weissenberg photographs about the two short axes were used to record the intensities. The X-radiation was filtered by means of nickel foil when it was desired to remove the CuK$_\beta$ radiation. For each projection three packets of five films were used, with exposure time of 130 hours for 1 to 5 films, $1\frac{1}{2}$ hours for films 6 to 10 and 2 minutes for films 11 to 15. In order to determine the intensities of the reflexions, it was necessary to have a series of standards of known relative intensities, with which the observed reflexions could be compared visually. The film ratios between successive films were determined from the ratios of the relative intensities of corresponding reflexions on the two films.

The intensities, thus measured, were corrected for combined L-P factors. The correction was given by,

$$F^2_{(hk\ell)} = \frac{\sin 2\theta}{1 + \cos^2 2\theta} I_{(hk\ell)}.$$

No correction was made for any possible errors due to absorption. The value of the linear absorption coefficient is $\mu = 4{\cdot}7$ cm.$^{-1}$ and since the crystal specimens were small, absorption was kept to a minimum. The crystals of corss-section at right-angles to the oscillation axis having dimensions 0.10 x .40 mm. and 0.10 x 0.35 mm., were used in recording hk0 and h0ℓ reflexions respectively.

No correction for extinction was applied because only a few of the structure factors were at all large. The good agreement obtained in Tables 9.3 and 10.4 for both strong and weak reflexions further indicated that no appreciable correction was required.

Chapter 2

Some earlier attempts to determine and refine the hk0 projection

2.1 The intensities of the reflexions having been accurately determined, the preliminary investigations of the structure of $C_{16}H_{10}N_2$ were carried out by Patterson and Fourier methods. From the dimensions of the unit cell it was obvious that either of the projections down the short axes was going to be of immediate interest. The plane group symmetry of the [001] projection is pgg, and that of the [010] projection is c1m. Owing to the centro-symmetry, the [001] projection was taken up first for investigation. The molecule contains 18 atoms in the asymmetric unit, excluding hydrogen atoms.

2.1.1. Calculation of the hk0 Patterson map

Because the axial lengths along b and c are equal, it was not possible to guess in which projection the atoms of the naphtho [2,1-c] cinnoline molecule would be well resolved. It was hoped that the examination of the Patterson maps would reveal the orientation of the molecule.

The space group being Fdd2, the plane group symmetry of the [001] projection is pgg. The unique area of the cell in projection corresponds to quarter of the new cell. The symmetry of the corresponding Patterson map is pmm, it is sufficient to calculate the Patterson function for the area of the new cell defined by $\frac{a'}{2}$ and $\frac{b'}{2}$. The unique area of the Patterson map of [001] projection is shown in

fig. 2.1 which must contain the peaks corresponding to all the relevant vectors. The magnitudes of the peak heights in Patterson map are proportional to the electron products $(Z_1 Z_2)$. Two Patterson functions P and P_s defined by

$$P_{(x,y)} = \frac{1}{V}\sum_{0}^{\infty}\sum_{0}^{\infty}_{h\ k} F_o^2(hk0) \cos 2\pi(hx+ky) \quad \ldots \quad (1)$$

$$Ps_{(x,y)} = \frac{1}{V}\sum_{0}^{\infty}\sum_{0}^{\infty}_{h\ k} sF_o^2(hk0) \cos 2\pi(hx+ky) \quad \ldots \quad (2)$$

were calculated for the [001] projection, where s is a sharpening function. In figures 2.1 (a & b) are shown the Patterson maps for the hk0 projection, which are calculated using a pmm Fourier summation programme written by Dr. I. G. Edmunds for the Mercury computer. The contours have been drawn at arbitrary intervals. The sharpening function s was obtained by drawing a smooth curve through a plot of $(1/\bar{F}_o^2)$ against sin θ, where $\bar{F}_o^2$ is the average value of F_o^2 taken in zones of sin θ going from 0 to 1.0 in steps of 0.1. The main effect of sharpening was thus to compensate for the falling off with sin θ of the F_o^2 values due to the finite size of the atoms and their thermal vibration, and therefore to give much sharper interatomic peaks, with correspondingly greater resolution. However, by relatively increasing the outer F_o^2 values, series termination errors might become more serious, giving larger diffraction ripples around the sharper peaks giving rise to spurious detail.

Figure 2.1.

The unique area of the hko Patterson functions (a) unsharpened, (b) sharpened. Zero contours are dotted, negative contours broken and positive contours full line.

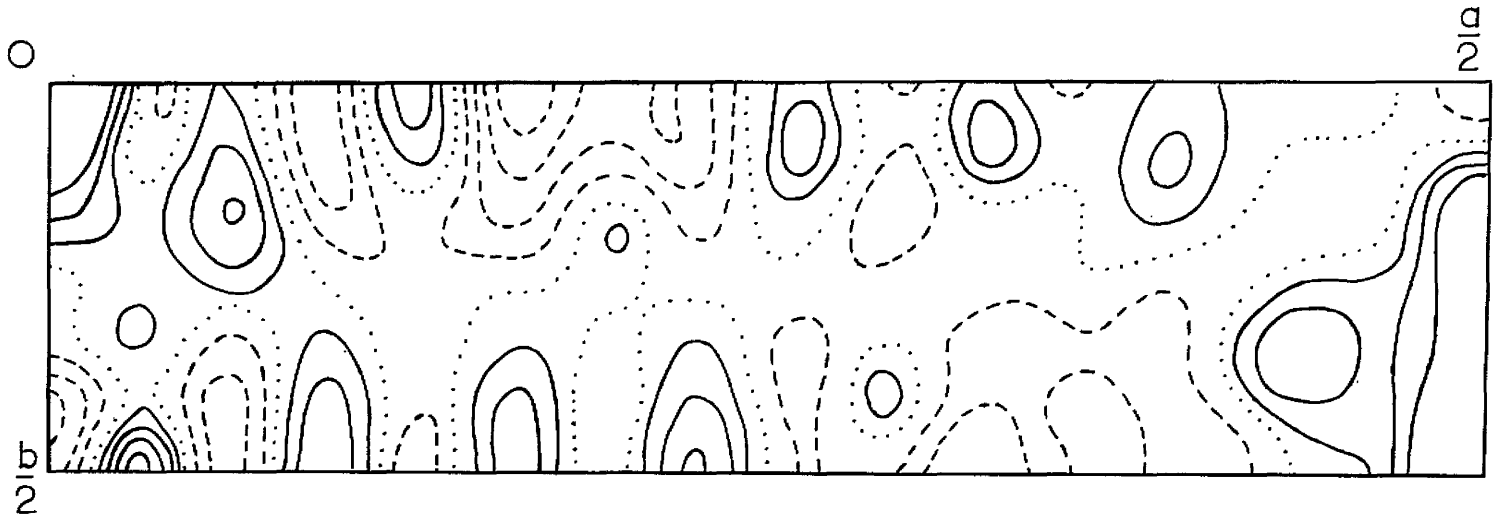


Fig. 2.1(a).

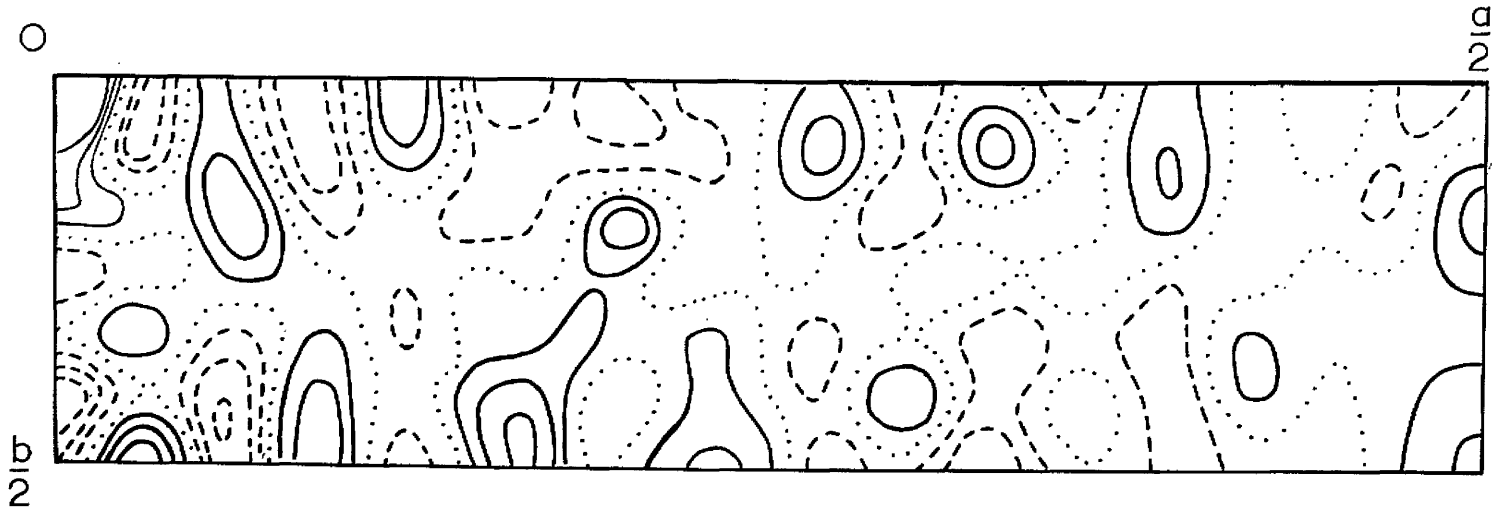


Fig. 2.1(b).

Figure 2.2.

Larger area of the hko sharpened Patterson function, with the interatomic vectors of one molecule marked in with crosses.

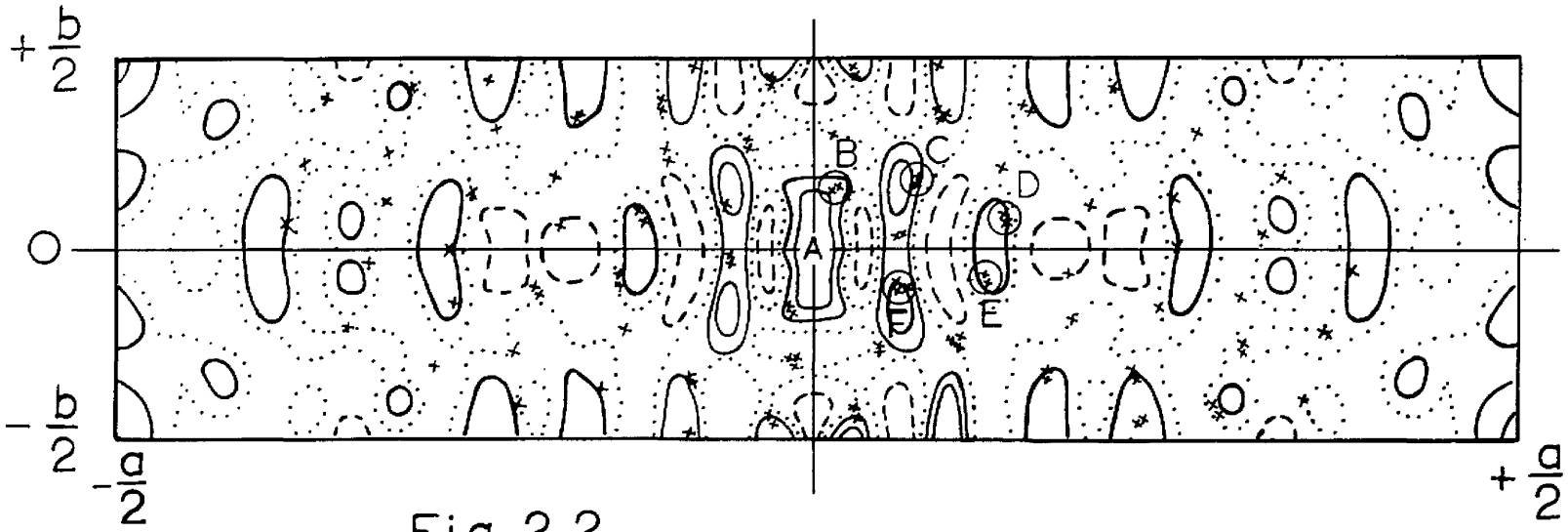


Fig. 2.2.

The peaks in the unsharpened map are broad, with little details, whereas in the sharpened map they are more resolved, with several smaller ones appearing. The heights of corresponding peaks in the two maps are comparable.

2.1.2 Interpretation of the Patterson map

A large area of the sharpened Patterson map about the origin peak (marked A) is shown in figure 2.2 with contours at twice the interval used in fig. 2.1(b). The positions of atoms in one molecule is shown in fig. 2.3.

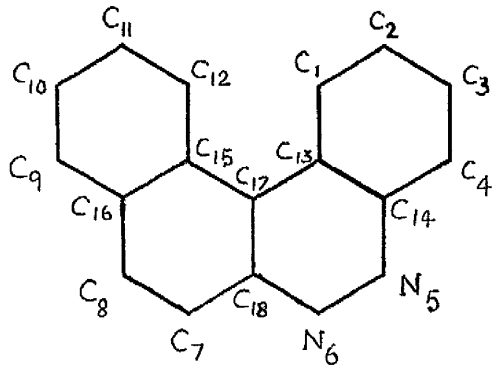


fig. 2.3.

In order to interprete the Patterson map, it is important to realise that the peaks due to the individual C-C, C-N and N-N vectors might not show up prominently but the peaks due to a large number of approximately equal and parallel vectors between the atoms of the benzene rings which might be in parallel orientation should show up in the map. If, however, some of the benzene rings are buckled and twisted in different directions, the assumed group of parallel vectors will not be exactly parallel, and consequently the positions of the

vectors in the Patterson map will be somewhat displaced towards the corresponding direction of the twist. However, at this stage attempts were made to determine the approximate shape and orientation, instead of the exact shape of the different rings, of the molecule.

The Patterson peaks due to the vectors parallel to $C_{13}-C_1$, $C_{13}-C_2$, $C_{13}-C_3$, $C_{13}-C_4$ and $C_{13}-C_{14}$ are first identified in the map and from these the approximate shape and orientation of a single benzene ring is determined. The molecule is then completed by the addition of further benzene rings in parallel orientation.

The peaks due to a large number of approximately equal and parallel (C - C) vectors in the molecule are distributed near the origin of the sharpened Patterson map (fig. 2.2). There are a few large vectors of the type B, C, D, E and F which represent a hexagonal symmetry. These peaks would have defined a regular hexagon if the molecules were perpendicular to the C-axis. The vectors representing the hexagonal symmetry as shown in the map indicate that the rings in the molecule are tilted about the a-axis. However, the configuration of the molecule is not uniquely determined by the orientation of the rings alone, since there are three crystallographically non-equivalent ways of completing the molecule as shown in fig. 2.4 (a, b, c).

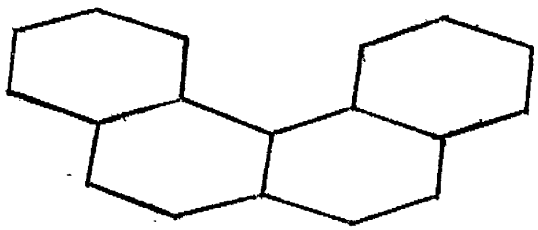


fig.2.4(a)

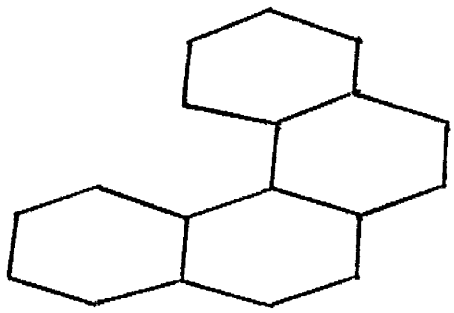


fig.2.4(b)

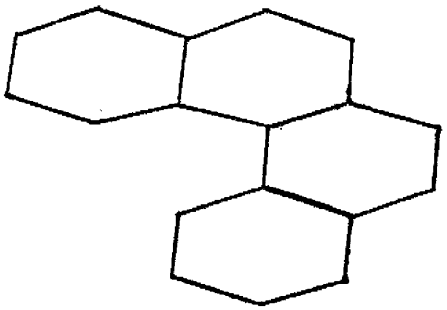


fig. 2.4(c)

The packing considerations suggest that the most probable configuration of the molecule is as shown in 2.4(a) and the length of the molecule should be aligned nearly parallel to the a-axis.

The vector set corresponding to the postulated structure is marked in the sharpened Patterson map (fig. 2.2) by crosses and it is seen that a reasonable fit of the vector set of one molecule is obtained.

The results of the examination of [001] projection by optical transform methods and subsequent calculations of structure factors confirmed the correctness of the configuration of the molecule as shown in fig. 2.4(a).

2.2. Optical Transform methods

It has been shown that there is a direct relationship between a two dimensional section of an x-ray diffraction pattern of a crystal, and the Fraunhofer diffraction pattern of a mask representing the projection of the crystal structure on the appropriate plane. Taylor (1952) has shown mathematically that:-

(a) The Fraunhofer diffraction pattern of a two-dimensional

object is the Fourier transform of its transparency distribution;

(b) there is a complete formal analogy between the two-dimensional optical diffraction patterns and the two-dimensional sections of x-ray diffraction patterns;

(c) a two-dimensional section of the x-ray diffraction pattern of a three-dimensional object is the Fourier transform of the electron density distribution projected on to a plane reciprocal to that of the section.

This relationship formed the basis for the application of physical optics to crystal structure determination. The two dimensional optical diffraction pattern is generally known as the "optical transform" - it expresses the square of the amplitude alone, in contrast with the Fourier transform which has both amplitude and phase. The direct application of this method involves a preparation of the Fraunhofer diffraction pattern by an optical diffractometer (Taylor, Hinde & Lipson, 1951) relating to a proposed crystal structure projection, and its comparison with a suitable representation of the x-ray intensity distribution in the corresponding reciprocal lattice section (Lipson & Taylor, 1951).

The two-dimensional section of the x-ray diffraction data (from the Weissenburg photographs) is represented in the form of a "weighted reciprocal lattice", which is merely a representation of the relative intensities of the reflexions shown in reciprocal lattice points. The unitary structure factors, U's, are usually plotted rather than the intensities, the relative magnitudes of which are represented by

black spots whose areas are proportional to the magnitudes of the U's. The reciprocal lattice section is drawn to a scale 5 cm = 1 $\mathring{A}^{-1}$, the reflexions are arranged into five different groups according to the magnitude of U and each group is represented by spot of appropriate size.

Two factors influence the intensity fall-off in the reciprocal lattice section - temperature effect and the variation of atomic scattering factor with angle. In the optical diffraction pattern, however, there is only one corresponding factor within the mask to effect a diffraction fall-off - the finite size of the holes. To obtain a better comparison between the optical diffraction pattern and the x-ray diffraction section, it is necessary to reduce the intensity fall-off in the latter. In practice it is more convenient to eliminate the variation of the scattering factor with angle, thereby increasing the weight of the high angle reflexions. Consequently the reciprocal lattice section is generally weighted according to the unitary structure amplitudes. Use has been made of the structure amplitudes themselves, but the diameter of the holes in the diffraction mask must then be arranged to simulate the variation of scattering factor with angle (Lipson & Cochran , 1957).

The proposed crystal structure is drawn, in projection, to a scale of 2 cms = 1 $\mathring{A}$. The diffraction mask is then prepared; the holes are punched in opaque film using a pantograph device with a reduction ratio of 12:1 (Hughes & Taylor, 1953). An "optical diffractometer" is then used to record the Fraunhofer diffraction pattern. The

diffraction image, as photographed, is but 1 - 2 mms in size and necessitates enlargement. At this stage the real space and reciprocal space scales are correlated - the magnification being related to the scale 5 cms = 1 $\mathring{A}^{-1}$.

2.3. Determination of the shape of the molecule by Optical Transform methods.

Optical transform methods have proved to be of particular value in the study of compounds containing benzene rings. The optical transform of an untilted benzene ring has six prominent peaks at a distance of 0.8 $\mathring{A}^{-1}$ from the origin. A circle of radius 0.8 $\mathring{A}^{-1}$ units, drawn with its centre at the origin of the weighted reciprocal lattice, is known as the "benzene circle". If the benzene ring is tilted about a given line, its projection contracts in a direction perpendicular to this line; the transform therefore expands in this direction, the factor of expansion being equal to the secant of the angle of tilt. From such considerations, quite often it is possible to determine the shape of the projection of the benzene ring from the positions of the benzene peaks. In this way the orientation of the ring in projection is determined (Hanson, Lipson & Taylor, 1953). Such information has, in fact, been made use of in the present study which is described in the subsequent sections.

In order to compare the optical transform of the naphtho [2,1 - C] cinnoline molecule, the hk0 weighted reciprocal lattice was prepared using a scale of 5 cm = 1$\mathring{A}^{-1}$ (shown in fig. 2.5). The information

Figure 2.5.

Constructing a benzene ring from the evidence of the benzene peaks in the hko reciprocal lattice section.

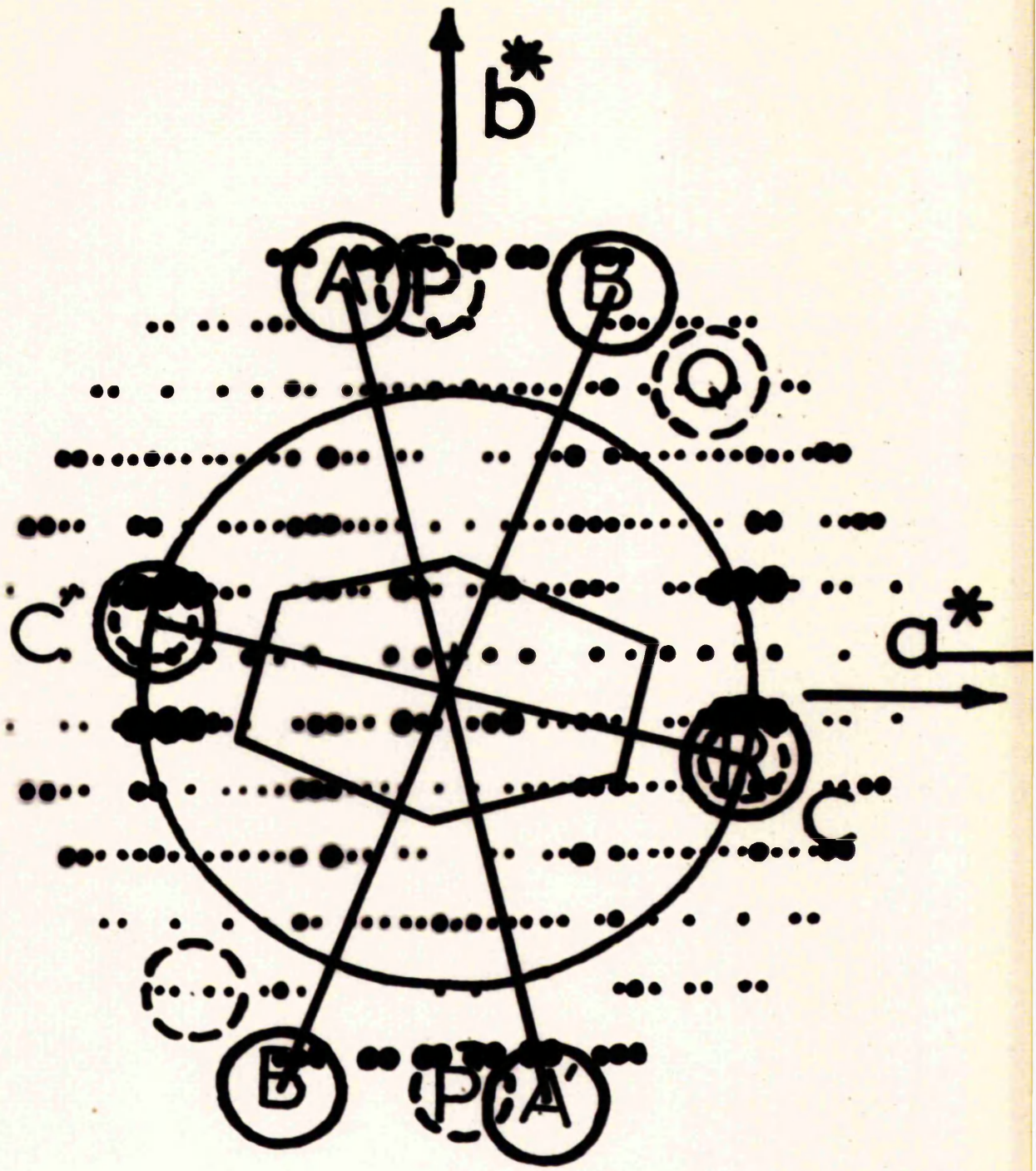


Fig. 2.5.

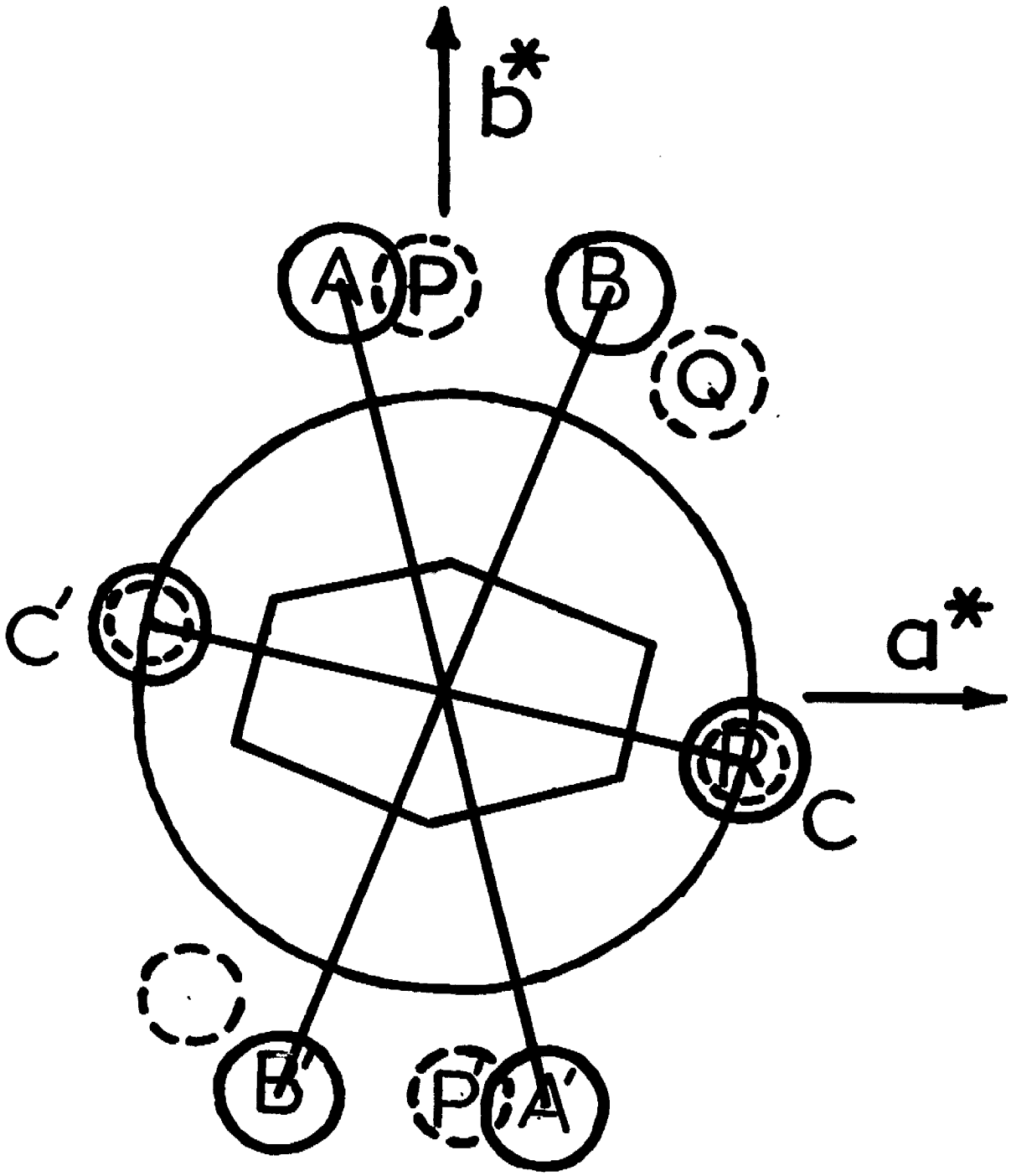


Fig. 2.5.

near the centre of the lattice indicates the general shape of the molecule, whilst the outer regions reveal finer details of the structure.

It will be seen that there are a number of peaks lying outside the "benzene circle" which obviously involved steeply tilted benzene rings. A series of heavy peaks on the b* - axis also suggest that they are produced by different orientations of benzene rings. However, the six largest and most intense peaks (A, B, C, ...) on the weighted reciprocal lattice were located, and the shape and orientation of one benzene ring were found out as shown in fig. 2.5. From this was constructed the molecule as seen in projection and a diffracting mask corresponding to this was punched. The aperture used for carbon was the same as that used for nitrogen. The optical transform corresponding to this orientation of the molecule was compared with the weighted reciprocal lattice (Fig. 2.5(a)); the agreement was poor. The orientation and tilts of the benzene rings were varied, but all efforts to make the optical transform agree with the weighted reciprocal lattice were unsuccessful. The other two possibilities (fig. 2.4 (b & c)) of the configuration of the molecule were also tried out, but showed some serious discrepancies, so it seemed almost certain that these two configurations (fig. 2.4 (b & c)) were not correct.

It was possible that some of the strong peaks lying near the "benzene circle", which were interpreted as benzene peaks, were due to a particular orientation of only some of the benzene rings. A group

Figure 2.5(a).

Optical transform of a molecule with the hko weighted reciprocal lattice section superimposed.

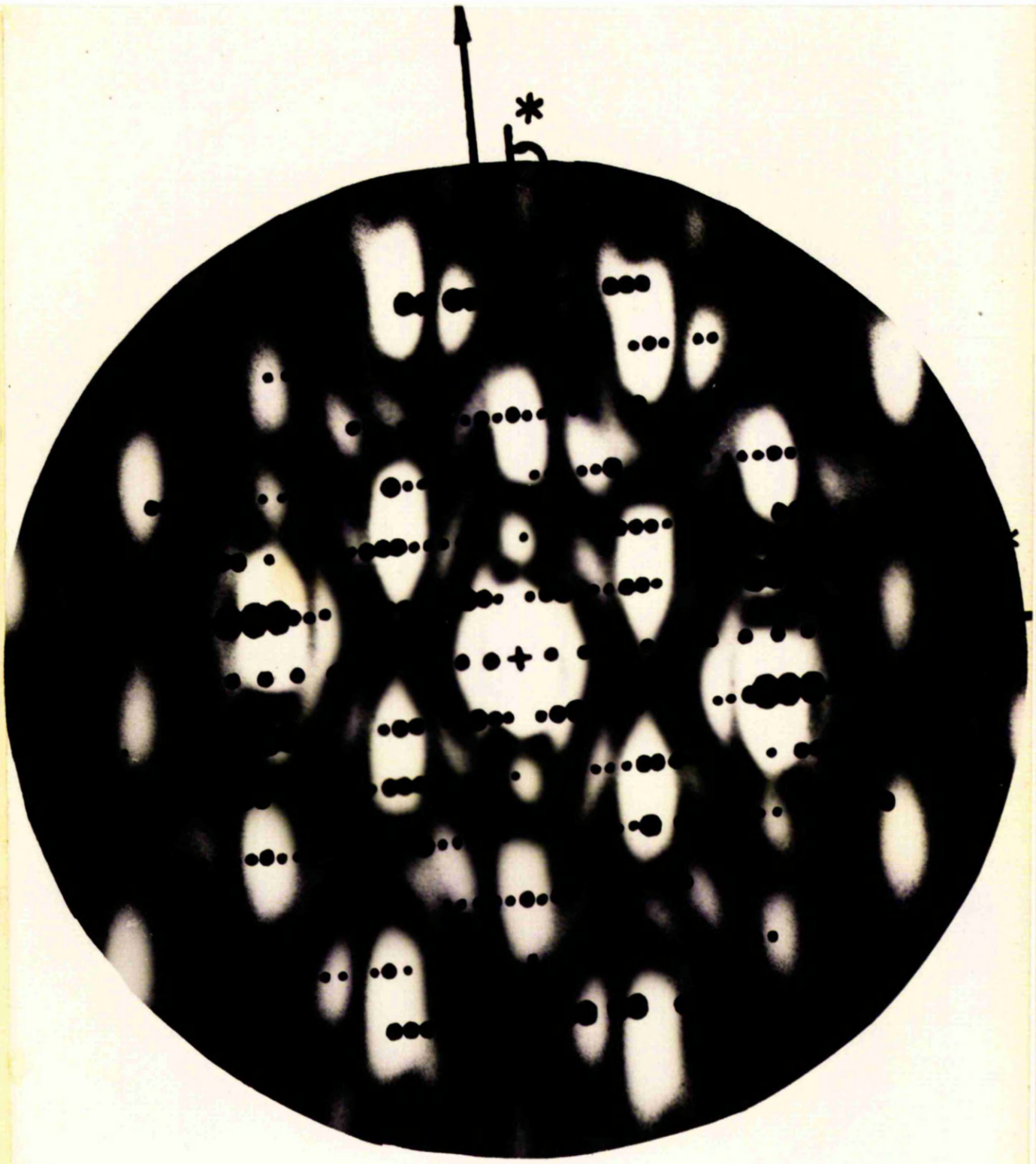


FIG. 2.5(a).

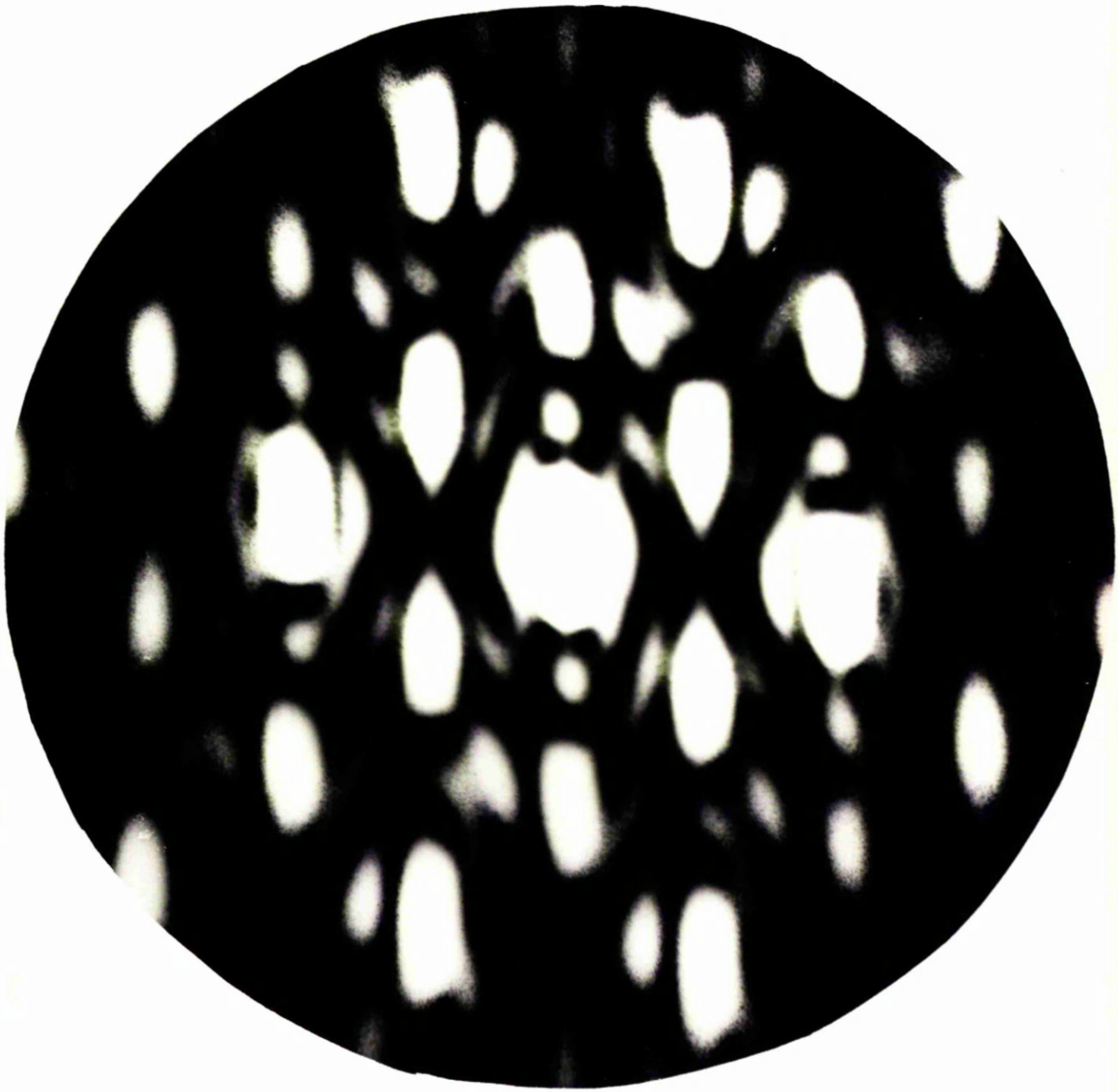


FIG. 2.5(a).

of peaks (P, Q, R, ...) which could not be interpreted by the same orientation of the benzene rings, were selected as being possibly due to a different orientation of some of the benzene rings in the molecule. Thus two possible orientations of the benzene rings were selected from the lattice. The first set of peaks (A, B, C, ...) enabled the benzene ring to be constructed which agree closely with the one previously obtained from the Patterson synthesis. A new molecule was completed by the combination of the benzene rings of two different orientations and an optical transform was prepared and compared with the weighted reciprocal lattice. The agreement was improved but some discrepancies still remained. Even after detailed examination of the optical transform it was not clear how the molecule could be altered to obtain a better fit with the weighted reciprocal lattice and all attempts to improve the agreement further failed. However, it seemed worthwhile to pass on to the next stage of the determination of the structure using this trial molecule.

2.4. The Determination of the relative position of the molecule using Optical Transform Principles.

After an approximation to the shape and orientation of the molecule is obtained, the next step in the methods of structure determination is to find out the molecular position in the unit cell. Optical transform methods have been found to be of great help in such determinations. In general, the principal features of the optical transform are governed by the orientation of a single molecule, but the introduction of the

remaining other symmetry related molecules impresses upon the transform a fringe system which can be used to estimate the positions of the molecules.

In using the optical transform approach, the shape and orientation of the molecule is ascertained by examining the disposition of stronger reflexions; considerations of the weaker and absent reflexions may then give information about the position of the molecule relative to others in the unit cell (Hanson, Lipson & Taylor, 1953). If the shape and orientation of a single molecule is adjusted until agreement between the strongest x-ray intensities and the intensities at the corresponding points of its transform is satisfactory, then the weak intensities occur either because the intensity in the transform of the single molecule is low, or because of the operation of a fringe function. Points of low intensity in the weighted reciprocal lattice which correspond to points of high intensity in the optical transform are selected, and the relative position of the molecules are adjusted until the fringe function has the required effect at these points. Thus the relative molecular positions can be obtained.

2.4.1 Principles of the method

Structure factor graphs (section 4.3)(Bragg & Lipson, 1936) are contour maps which represent the variation with position in the unit cell of the contribution to a certain reflexion by one atom and its plane group related counterparts. If instead of an atom, the projected shape of the molecule or part of a molecule, was known, then a similar

structure factor graph could be prepared. This would show the variation with position in the unit cell of the contribution of that molecule, or part of that molecule, plus its plane group related counterparts, G(h,k), to a particular reflexion. If the reflexion chosen was observed as zero, then the zero contour of $||G(h,k)| - |(F_o(h,k)||$, where G(h,k) is the combined contribution of all the molecules to a reflexion (h,k), would give the locus of possible positions. In practice a few reflexions are chosen and the minimum point of the combined graph specifies the molecular position.

2.4.2 Theory of the Method

The theory is developed for the plane group Pgg, but the development of other plane groups follow the same general principle. If x_i, y_i are the coordinates of the ith atom of a molecule, with respect to an arbitrary chosen origin, and X, Y are the coordinates of this origin, with respect to the true unit cell, (see fig. 2.6), then the combined contribution of all the molecules to a reflexion h, k may be written,

Figure 2.6.

Showing the coordinates x_i, y_i of the ith atom with respect to the arbitrary origin O'. The coordinates of O' with respect to the true origin O are X, Y.

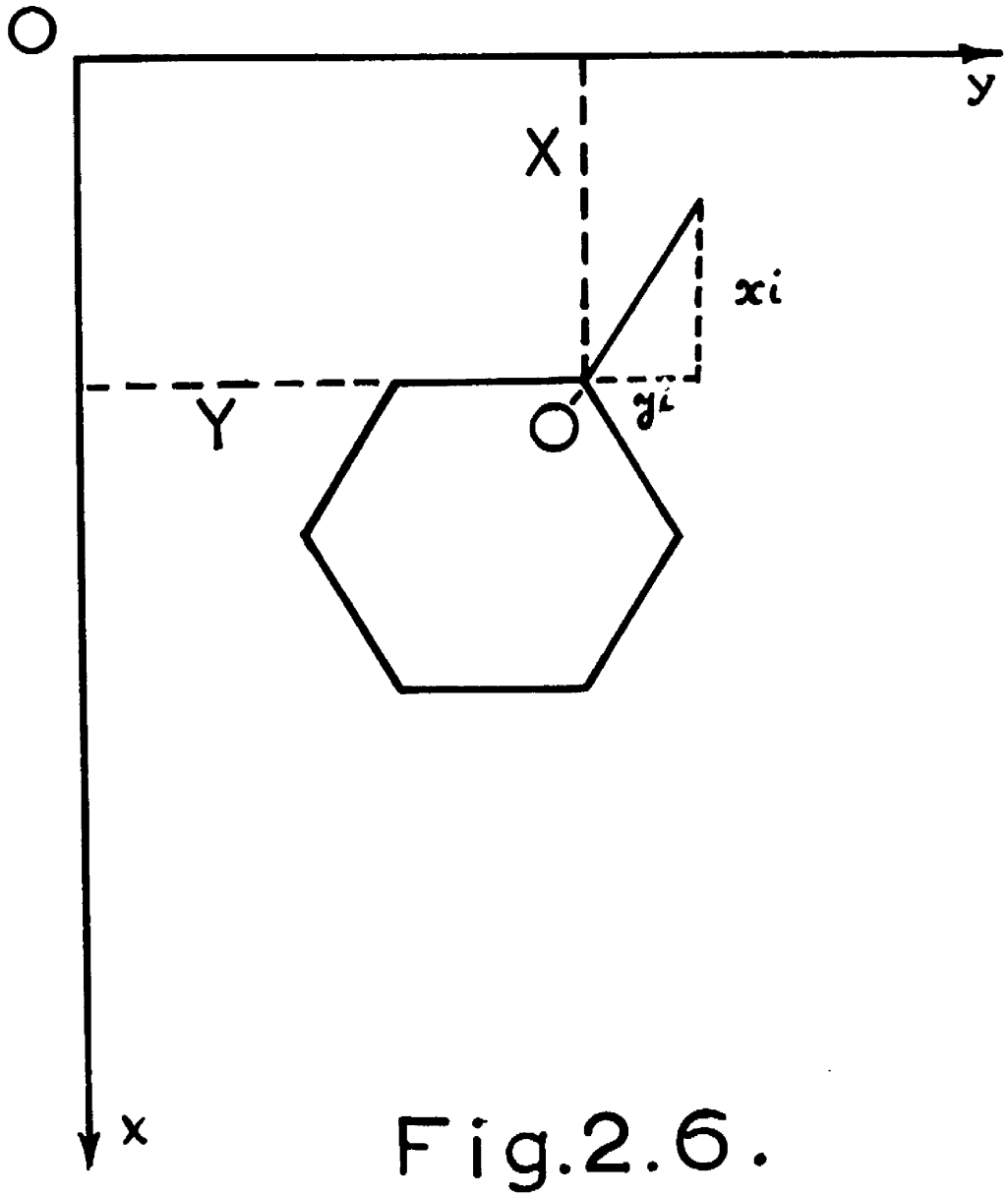


Fig.2.6.

$$G(h,k) = 4 \sum_{i=1}^{N} f_i \cos(2\pi h(X + x_i)) \cos(2\pi k(Y + y_i))$$

if $(h+k)$ is even,

and

$$G(h,k) = -4 \sum_{i=1}^{N} f_i \sin(2\pi h(X + x_i)) \sin(2\pi k(Y + y_i)) \qquad (1)$$

if $(h+k)$ is odd.

These may be rewritten as

$$G(h,k) = 4 \cos 2\pi kY [A(h,k) \cos 2\pi hX - C(h,k) \sin 2\pi hX]$$

$$+ 4 \sin 2\pi kY [-B(h,k) \sin 2\pi hX + D(h,k) \cos 2\pi hX] ,$$

if $(h+k)$ is even, and

$$G(h,k) = 4 \cos 2\pi kY [B(h,k) \cos 2\pi hX + D(h,k) \sin 2\pi hX]$$

$$- 4 \sin 2\pi kY [A(h,k) \sin 2\pi hX + C(h,k) \cos 2\pi hX] \qquad (2)$$

if $(h+k)$ is odd ;

where

$$A(h,k) = \sum_{i=1}^{N} f_i \cos 2\pi hx_i \cos 2\pi ky_i ,$$

$$B(h,k) = -\sum_{i=1}^{N} f_i \sin 2\pi hx_i \sin 2\pi ky_i ,$$

$$C(h,k) = \sum_{i=1}^{N} f_i \sin 2\pi hx_i \cos 2\pi ky_i ,$$

$$D(h,k) = -\sum_{i=1}^{N} f_i \cos 2\pi hx_i \sin 2\pi ky_i .$$

The quantities A(h,k), B(h,k), C(h,k) and D(h,k) depend only on the molecular shape and orientation, and are constant throughout the calculation. The required molecular structure factor graph for a given reflexion is then obtained by computing the values of G(h,k) given by the equation (2) for all possible values of X and Y within the unit cell.

2.4.3 Application of the method

The first step in the molecular location was to compare the transform of the molecule with the weighted reciprocal lattice. There was a good agreement for most, though not all, of the strong parts in the x-ray diffraction pattern. Six reflexions of very weak or zero intensity were selected (see table 2.1) which lie upon strong regions of the transform of one molecule. The six reflexions were of medium Bragg angle. The computation was carried out by using a computer programme for finding the position of a molecule written by Dr. R.A.L. Sullivan. The quantity G(h,k) was then plotted as a function of the position of the molecule in the unit cell. The map obtained from these contained one or two low minima. Another set of six reflexions, of low and medium Bragg angle, were then chosen and the computation was repeated. The map resulting from these had many reasonable sharp minima. From a study of both of these maps, it was possible to deduce a probable position of the molecule. The coordinates of the minimum position were x = 0.267, y = 0.167 with respect to a centre of symmetry of the projection.

TABLE 2.1

Indices		F	Indices		F
h	k	(observed)	h	k	(observed)
8	4	3.3	1	1	5.3
9	5	2.5	13	1	3.3
1	1	5.0	9	1	5.1
0	4	2.0	6	3	4.9
9	1	5.0	9	5	2.5
8	3	2.0	6	6	0

$F_{obs.}$ corrected for scale and temperature factors.

The molecule was then placed in this position and the structure factor calculations with the trial structure showed reasonable agreement between the individual F_o's and F_c's with a residual of 0.56. This suggested that the structure should be refined.

The structure factors were calculated from

$$F_c(hk0) = 4 \sum_{j=1}^{N} f_j \cos 2\pi hx \cos 2\pi ky$$

if h + k is even,

$$F_c(hk0) = -4 \sum_{j=1}^{N} f_j \sin 2\pi hx \sin 2\pi ky$$

if h + k is odd,

utilizing an atomic scattering factor equation suggested by Forsyth and Wells (1959). In order to estimate the overall agreement in terms of the mean discrepancy the so-called "residual" was calculated from

$$R = \sum \left| |F_o| - |F_c| \right| / \sum |F_o|$$

where $|F_o|$ and $|F_c|$ are the moduli of the observed and calculated structure factors respectively.

2.5. Refinement by F_o synthesis

Earlier refinement of the [001] projection was begun by Fourier methods. To each of the observed structure factors was given the signs of the corresponding calculated structure factors and the electron density map of the projection was computed from the relation

$$\rho(x,y) = \frac{1}{A}\Big[F_{(00)} + 2\Big\{\sum_{\substack{h \\ 2}}^{\infty\ h=2n} F(h0)\cos 2\pi hx + \sum_{\substack{k \\ 2}}^{\infty\ k=2n} F(0k)\cos 2\pi ky\Big\}$$
$$+ 4\Big\{\sum_{\substack{h \\ 1}}^{\infty} \sum_{\substack{k \\ 1}}^{\infty\ h+k=2n} F(hk)\cos 2\pi hx \cos 2\pi ky -$$
$$- \sum_{\substack{h \\ 1}}^{\infty} \sum_{\substack{k \\ 1}}^{\infty\ h+k=2n+1} F(hk)\sin 2\pi hx \sin 2\pi ky\Big\}\Big] ,$$

where $\rho(x,y)$ is the electron density at any point (x,y) and A is the area of cross-section. The peaks in the map indicated several large shifts to be applied to the atomic coordinates. From the position of the peaks a new set of atomic coordinates was determined and the set of structure factors calculated. The residual dropped down to 0.48

and the process was continued till there were no major changes in the signs of the structure factors. In three cycles of refinement the residual was brought down to 0.45 only. Further improvement of the atomic positions by this method seemed unlikely because of considerable overlap in this projection both in the atoms of one molecule, and the symmetry related atoms of a different molecule. The possibilities of the other two configurations of the molecule (fig. 2.4 b & c) were also tried with the help of the prominent peaks of the Fourier map and the sets of structure factors were calculated for each of them. Both sets of F_c's showed gross disagreement with the observed F's with very high R-values. It was then felt that these two configurations were most unlikely for this structure and no further attempt to improve them was undertaken. It was, at this stage, decided to pursue the refinement of the structure (fig. 2.4a) by difference Fourier methods.

2.6. Refinement by difference Fourier syntheses

The atomic positions determined from the positions of the peaks in the electron density map are not completely correct as a result of the finite termination of the Fourier series in the F_o synthesis and also partly because of overlapping of several atoms. Corrections to the atomic coordinates can be made by means of difference synthesis which involves a Fourier series whose coefficients are the values $(F_o - F_c)$ and as a result contains no series termination errors (Booth, 1948; Cochran, 1951). In the difference synthesis the terms for which F_o is large and F_c is small should be excluded since errors would

result from an incorrect phase. The synthesis results in a map of the function $D = (\rho_o - \rho_c)$ which can be used to correct the atomic coordinates. Refinement is based on the reduction of the slope of D at the atomic centres and the shift of an individual atom "i" was calculated as described by Lipson and Cochran (1957), by the expression

$$\Delta r_i = \left(\frac{\partial D}{\partial r}\right)_i / 2p(\rho_o)_i$$

where ρ_o is the electron density at the centre of the atom and r denotes a distance from the atomic centre in the direction in which D increases most rapidly, $2p(\rho_o)_i$ gives the central curvature of the ith atom in projection assuming the electron density near the centre of the projection of the atom is closely approximated by the equation

$$\rho = Z(p/\pi)^{3/2} \exp(-pr^2) ,$$

where ρ is the density at a distance r from the centre of the atom. Z is the atomic number (Booth, 1946a). The constant p was taken as 5.0 for all atoms - a value obtained from the preceeding F_o synthesis.

During the process of refinement by $(F_o - F_c)$ synthesis, it was observed that most of the atoms were lying on gradients indicating a major shift in the coordinates. Unfortunately, owing to the tilt of the molecule in this projection, the atoms were never well resolved on the map for calculating proper shifts, and consequently difficulty in refinement was experienced. Moreover, the direction of the movements of the atoms were not always made clear in the difference map because of the large amount of overlap of the two molecules

symmetrically related by glide planes. However, the refinement was continued and after three cycles the residual fell to 0.37. Any attempt to refine it further was unsuccessful. A comparison between the observed and calculated structure amplitudes showed that the individual agreement was fairly satisfactory. This suggested that the structure could possibly refine further. In view of this situation it was decided to refine the structure by the method of least squares.

2.7. Refinement by L.S. method

The method of least-squares used in crystal structure refinement consists basically of a systematic adjustment of structure parameters in order to minimize some function of the observed and calculated structure amplitudes. According to the theory of errors, if the errors in the observed F_o's follow the normal or Gaussian law, then the best atomic parameters are those which minimise the function

$$R = \sum_{hk} w(|F_o| - |F_c|)^2 \qquad (1)$$

where w is the weight factor for a particular term (Lipson & Cochran, 1957).

In view of the fact that the refinement of the structure was sought, the observational equations chosen, were of the form

$$\Delta F = F_o - F_c = \sum_{n=1}^{N}\left(\Delta x_n \frac{\partial F_c}{\partial x_n} + \Delta y_n \frac{\partial F_c}{\partial y_n} + \Delta z_n \frac{\partial F_c}{\partial z_n}\right), \qquad (2)$$

where x_n, ... etc. are the corrections being sought in the positional parameters. The summation is taken over the N atoms of the structure. For each observed reflexion there exists an observational equation like (2).

The criterion that $\sum_{hk} w(\Delta F)^2$ "be a minimum" led to the normal equations for each of the parameters in the form

$$\sum_{hk} w \left\{ \left(\frac{\partial F_c}{\partial x_n} \right)^2 \Delta x_n + \frac{\partial F_c}{\partial x_n} \cdot \frac{\partial F_c}{\partial y_n} \Delta y_n + \frac{\partial F_c}{\partial x_n} \cdot \frac{\partial F_c}{\partial z_n} \Delta z_n \right.$$

$$\left. + \sum_m \frac{\partial F_c}{\partial x_n} \left(\frac{\partial F_c}{\partial x_m} \Delta x_m + \frac{\partial F_c}{\partial y_m} \Delta y_m + \frac{\partial F_c}{\partial z_m} \Delta z_m \right) \right\} = \sum_{hk} w(F_o - F_c) \frac{\partial F_c}{\partial x_n} \qquad (3)$$

where $\sum_m$ denotes a sum over all atoms except the nth.
The number of equations was equal to the number of independent parameters to be refined.

A two-dimensional least-squares programme has been written for a Mercury Computer by Curtis (1959) and uses the full matrix for solving the least squares equations. The present calculations were performed using this programme.

Refinement was continued using all observed reflexions, the residual was brought down to 0.34 and 0.33 in the first and second cycles respectively. The corrections to the positional parameters were quite significant at this stage, but during the third cycle the shifts of the atoms were negligible with no change in the R-value; and it seemed that the structure could be refined no further. A difference map (fig.2.7) was calculated at this stage with the hope that its prominent features should reveal the nature of the deviation from the actual structure and is discussed in the sections 2.8 and 2.9.

Figure 2.7

hko difference map calculated using the coordinates as obtained from least-squares refinement. Contours were drawn at $1e/\mathring{A}^2$, zero contour are dotted, negative contour broken and positive contours full line.

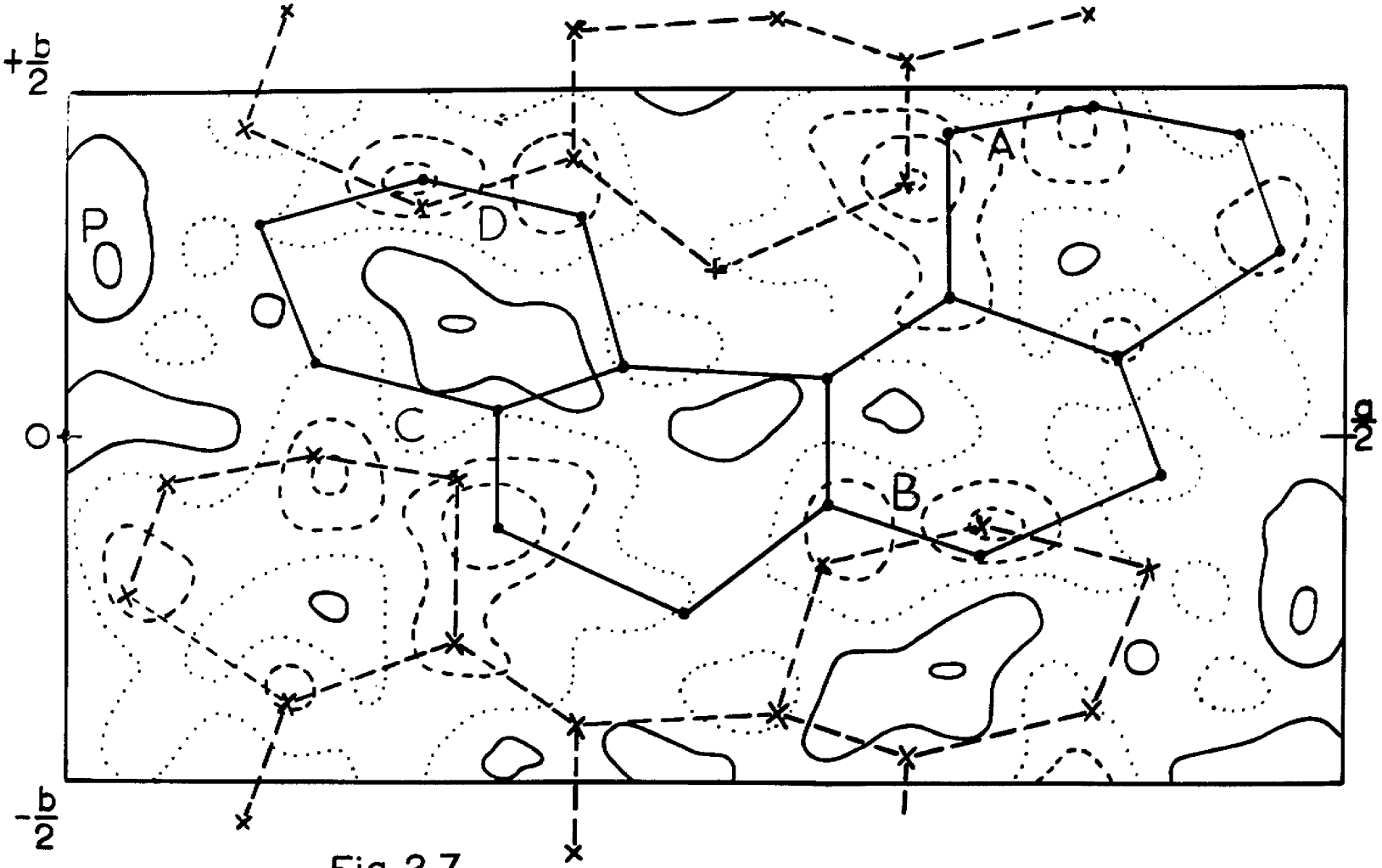


Fig. 2.7.

2.8. Effects of Overlap

Assuming the planar configuration of the molecule, the centre-to-centre distance (2.4 Å) between the overcrowded atoms 1 and 12 is much smaller (as regards the minimum approach distance (3.0 Å) between non-bonded carbon atoms) than would be expected to accommmodate two hydrogens (radius 1.2 Å). In order to achieve the required separation, the molecules are distorted by buckling and twisting the rings A and D (fig. 2.3) in opposite directions. Furthermore, the mean plane of the molecules is inclined at about 60° to ab plane. Consequently there was a great deal of overlap due to the atoms of the same molecule and also symmetry related atoms of a different molecule. The refinement was indeed a difficult task in the regions marked A, B, C & D in fig. 2.7 where atoms, numbers (1 & 2), (6 & 18), (8 & 9) and (11 & 12) and the symmetry related ones overlap. It was difficult to make any shift that would improve the prominent features which were associated with 1, 2, 6 & 8 atoms and also with the region marked P. A few small shifts were, however, tried but none decreased the residual nor improved the striking feature associated with the region P.

2.9. General observations

At this stage of investigation, it seems advisable to make some general observations on the structure which has so far defied all attempts towards solution.

The residual was reduced to 0.33, for the observed reflexions, by Fourier, difference Fourier and least-squares methods, but it could be

reduced no further. The residual for this projection, 0.33, was considered to be unsatisfactory. It was also difficult to see whether any change in the strategy of the refinement would be useful. The scaling of F_o's with F_c's over different ranges of sin θ, corrections to the scaling and temperature factors (many atoms were lying in the negative regions of the difference map) might be useful But at such a high R-value re-scaling did not seem to be appropriate.

Again, the background levels of the difference map in fig. 2.7 are rather high, and the most striking features are the strong negative regions round the positions of the atoms 1, 2, 6 and 8, and a very large peak (marked P) at x = 0.0166, y = 0.25 (which suggests that some atoms must lie near P). The details suggest that the difficulty in solving the structure may be more fundamental than could be attributed to the errors in scaling and temperature factors.

The positional parameters of atoms 1, 2, 6 and 8 were difficult to refine because they almost completely overlapped their symmetry related counterparts.

The molecule in this projection was very distorted and an attempt was made to reduce this distortion. However, this resulted in an immediate rise in the R-value and subsequent difference maps indicated shifts in the atomic coordinates that would bring the structure back to its very distorted form.

In view of this consistent failure to refine the [001] projection, further work on it was postponed for the time being; the [010] projection was then attempted and is discussed in the next chapter.

Chapter 3

Some earlier attempt to determine and refine the h0ℓ projection

3.1. Introduction. The information derived from the investigation of the [001] projection, as described during the last Chapter, was of no help in interpreting the [010] projection. Although it was felt that the atoms of the same molecule overlapped very closely in the [001] projection, they might be well resolved in the [010] projection. The determination of the molecular structure of the naphthocinnoline in the [010] projection was, therefore, undertaken with the hope that this would give considerable aid in interpreting the [001] projection.

The intensities of the reflexions in the [010] projection having been determined and corrected for the combined L-P factors (as described in Section 1.4), the preliminary structure was investigated by the Patterson method. The examination of the Patterson maps, it was hoped, would reveal the orientation of the benzene rings of the molecules in projection.

3.2. Calculation of the h0ℓ Patterson map. The plane group symmetry of the corresponding Patterson map is cmm. It is sufficient to calculate the Patterson function for the area of the cell $\frac{a'}{2}$ and $\frac{c'}{2}$. The unique area of the Patterson map is shown in fig. 3.1 which must contain the peaks corresponding to all revelant vectors. The magnitude of the peak heights in Patterson map is proportional to the

Figure 3.1

Unique area of the hol Patterson function.

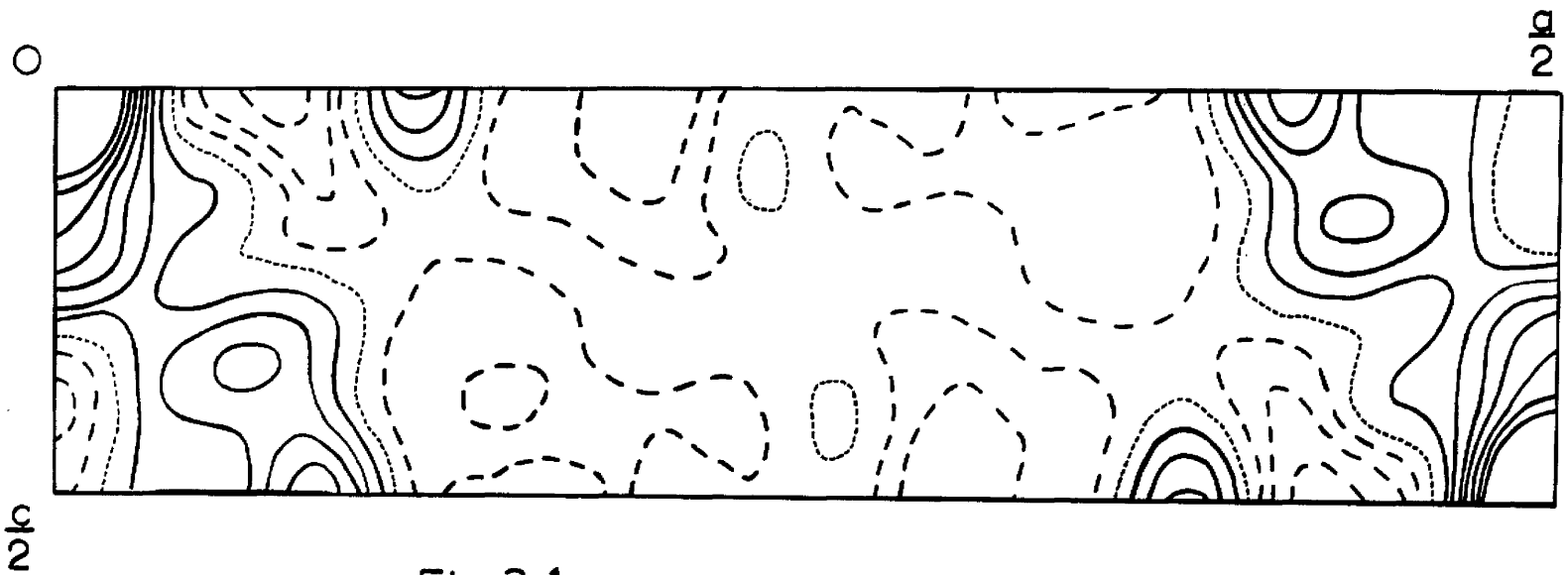


Fig. 3.1.

electron products (Z_1 Z_2). Two Patterson functions P and P_s were calculated, where s is a sharpening function, using cmm Fourier summation programme written by Dr. I. G. Edmunds for the Mercury computer. The contours have been drawn at arbitrary intervals. The sharpening function was obtained by drawing a smooth curve through a plot of ($1/\bar{F}_o^2$) against sin θ, where $\bar{F}_o^2$ is the average value of F_o^2 taken in zones of sin θ, going from 0 to 1.0 in steps of 0.1.

3.3. Interpretation of the Patterson map

Since the information about the intramolecular vectors is almost invariably contained in the near origin peaks, attention was first given to peaks lying within a distance of 1.5 Å from the origin. It can be seen that there were two prominent peaks A and B lying at a distance of about 1.2 Å and 1.4 Å with their peak heights in the ratio 1.4 : 1. This could reasonably be interpreted by assuming a benzene ring to lie at the origin in such a fashion that the view along the b-axis resulted in these positions of atoms in projection. Thus the shape and orientation of a single benzene ring having been obtained, a complete molecule was constructed by the addition of further benzene rings in parallel orientation.

The vector set corresponding to the postulated structure is marked in the sharpened Patterson map (fig. 3.2) by crosses and it is seen that a reasonable fit of the vector set of the molecule to the Patterson peaks is obtained. In view of the peak heights and inter-molecular vector distances, it seemed justifiable to assume that the

Figure 3.2.

Unique area of the hol sharpened Patterson function, with interatomic vectors of one molecule marked in with crosses.

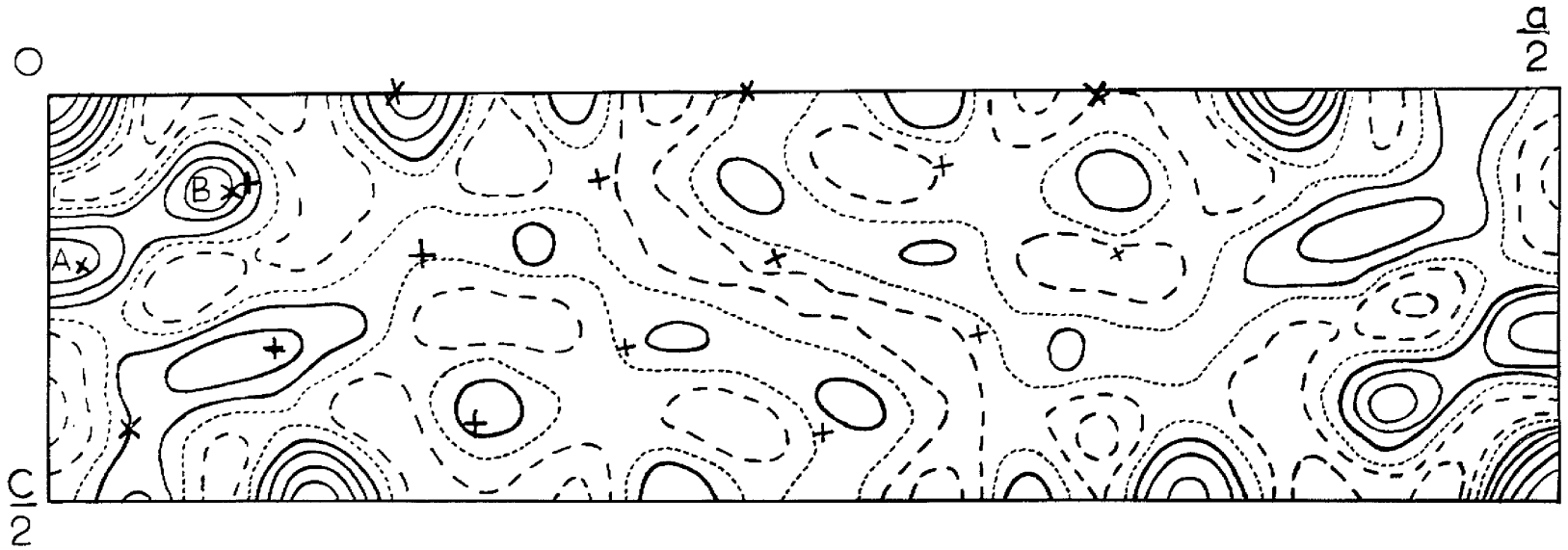


Fig. 3.2.

map gave a fair estimate of the orientation of the molecule.

3.4. Determination of the molecular shape by optical transform method.

With a view to checking the interpretation of the Patterson map and, at the same time, improving the molecular shape and orientation, the optical transform method was employed. The theory and application of the method have been described in Chapter 2 sections (2 & 3).

The x-ray data was represented in the form of a "weighted reciprocal-lattice section" (as described in section 2.3) using a scale 5 cms = 1 $\mathring{A}^{-1}$ and shown in figure 3.3. A benzene circle of radius 0.8 $\mathring{A}^{-1}$ units, drawn within its centre at the origin of the weighted reciprocal-lattice section.

The "benzene peaks" (A, B, C, ...) on the weighted reciprocal lattice were located, and the shape and orientation of one benzene ring were determined as shown in figure 3.3. This orientation of a benzene ring agreed closely with the one previously determined from Patterson synthesis. From this was constructed the molecule in projection, to a scale of 2 cms = 1 $\mathring{A}$. The diffracting mask corresponding to this was punched and the Fraunhofer diffraction pattern was then obtained.

The optical transform corresponding to this orientation of the molecule was compared with the weighted reciprocal lattice; the agreement was fairly good. The orientation and tilt of the benzene rings were varied till the agreement between the optical transform

Figure 3.3

Constructing a benzene ring from the evidence of the benzene peaks.

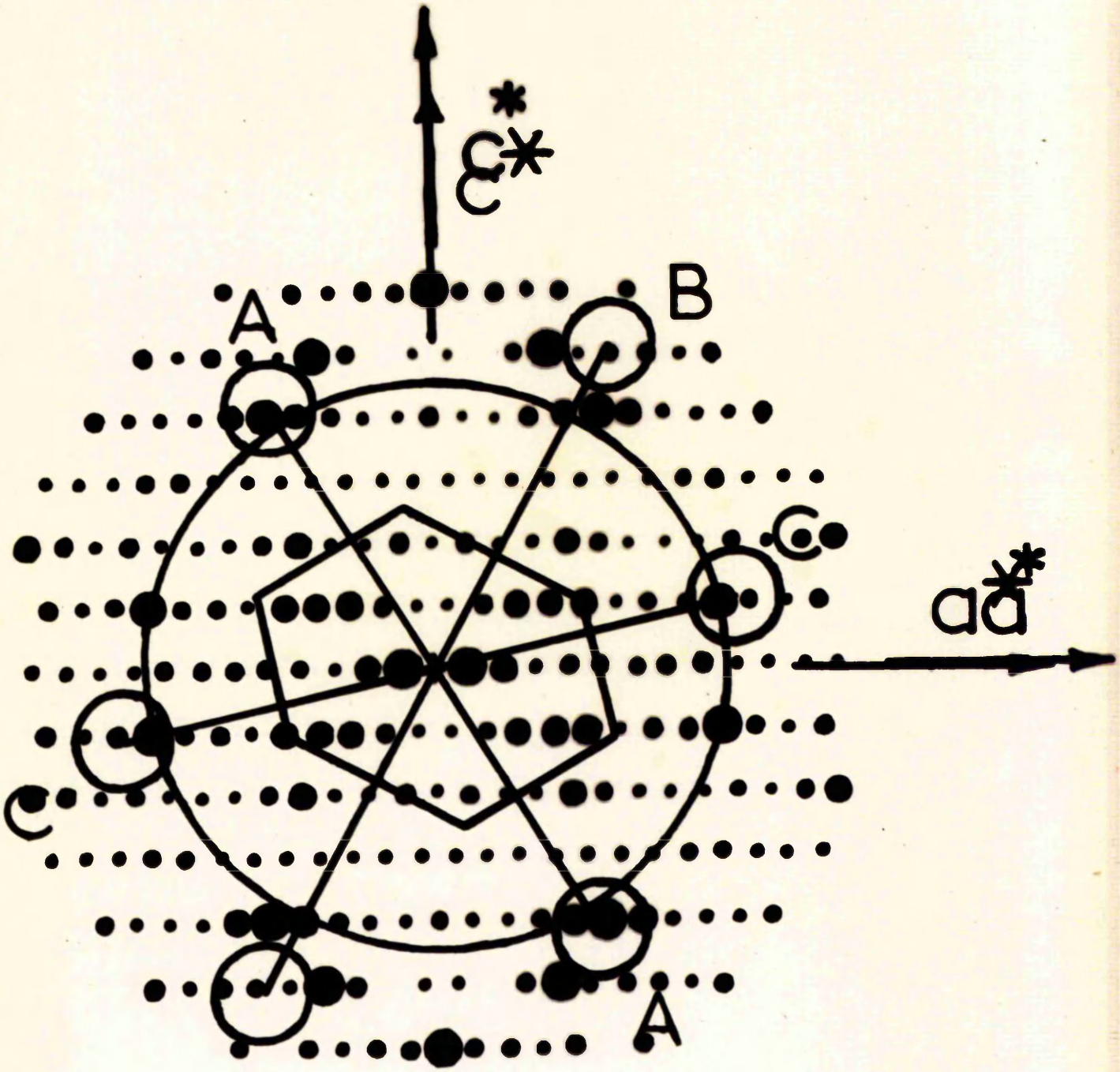


Fig. 3.3.

Fig. 3.3.

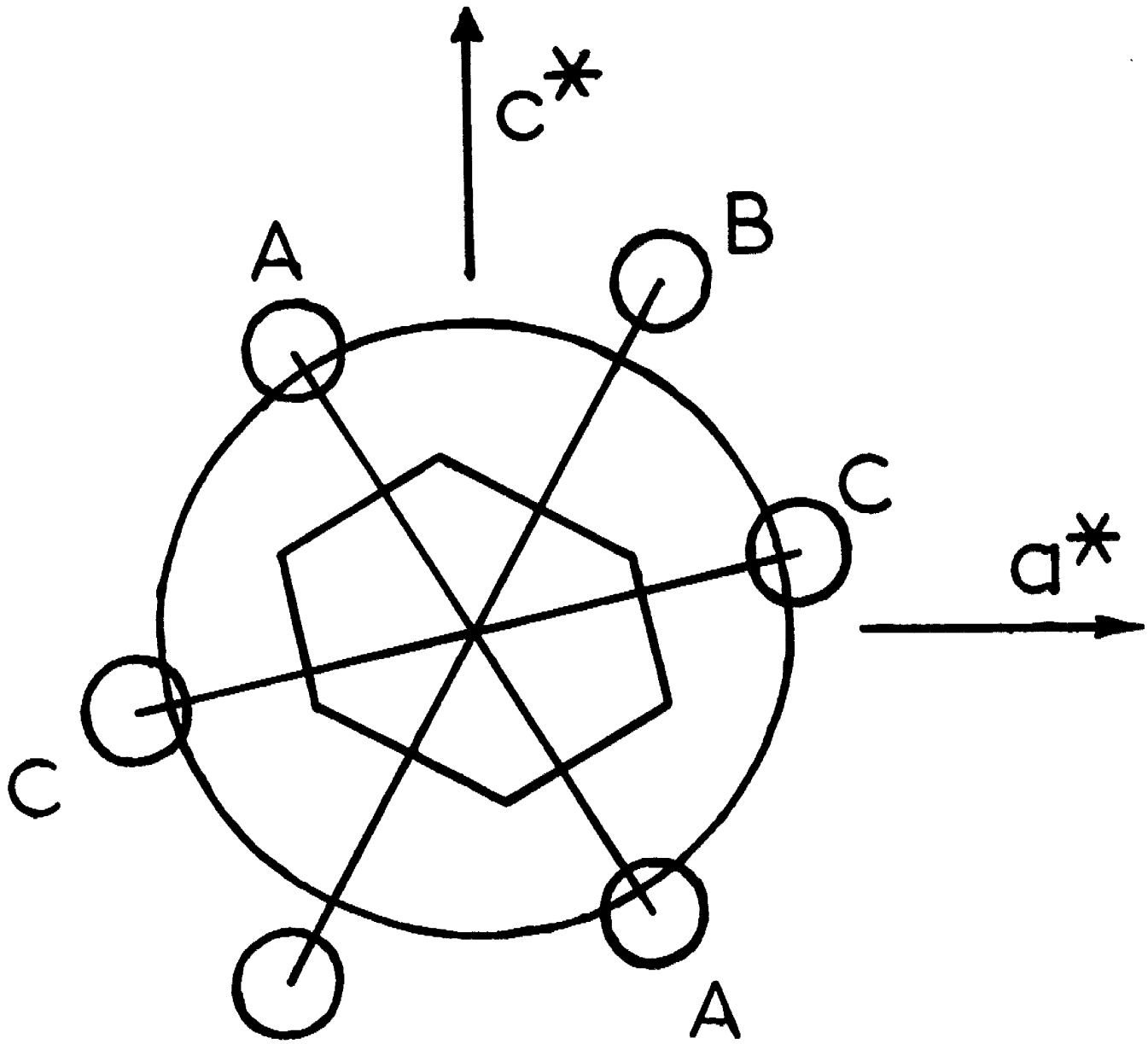


Fig.3.3.

and the weighted reciprocal lattice was quite satisfactory (fig. 3.4). As a further check, the other two probable configurations of the molecule (fig. 2.4 b & c) were tried, but these seemed very unsatisfactory. No attempt was made to improve them further. At this stage it seemed almost certain that the configuration of the molecule as derived by this method in this projection was nearly correct, and it was therefore considered desirable to pursue the structure determination using this trial molecule.

3.5. Determination of the relative positions of the molecules in the cell. When the general shape and orientation of the molecule is known the next step should be to determine the molecular position the cell. For this it is necessary to postulate a likely position of the molecule, and calculate the structure amplitudes which the position would give, and to compare these calculated structure amplitudes with those observed. The prospects of success depend on whether the postulated positions of the atoms are anywhere near the correct positions, giving some measure of agreement with the observed structure amplitudes. If the agreement is good the correct positions can be found by judicious small displacements of some of the atoms from the positions first chosen. If, however, a structure is based on only one variable parameter, all the structure amplitudes can be calculated as a function of this parameter, and it is quite possible to find the value that gives the best agreement with the observed structure amplitudes. The plane group symmetry of the $h0\ell$ projection

Figure 3.4.

Optical Transform of the molecule in the [010] projection compared against its corresponding weighted reciprocal lattice section.

FIG. 3.4.

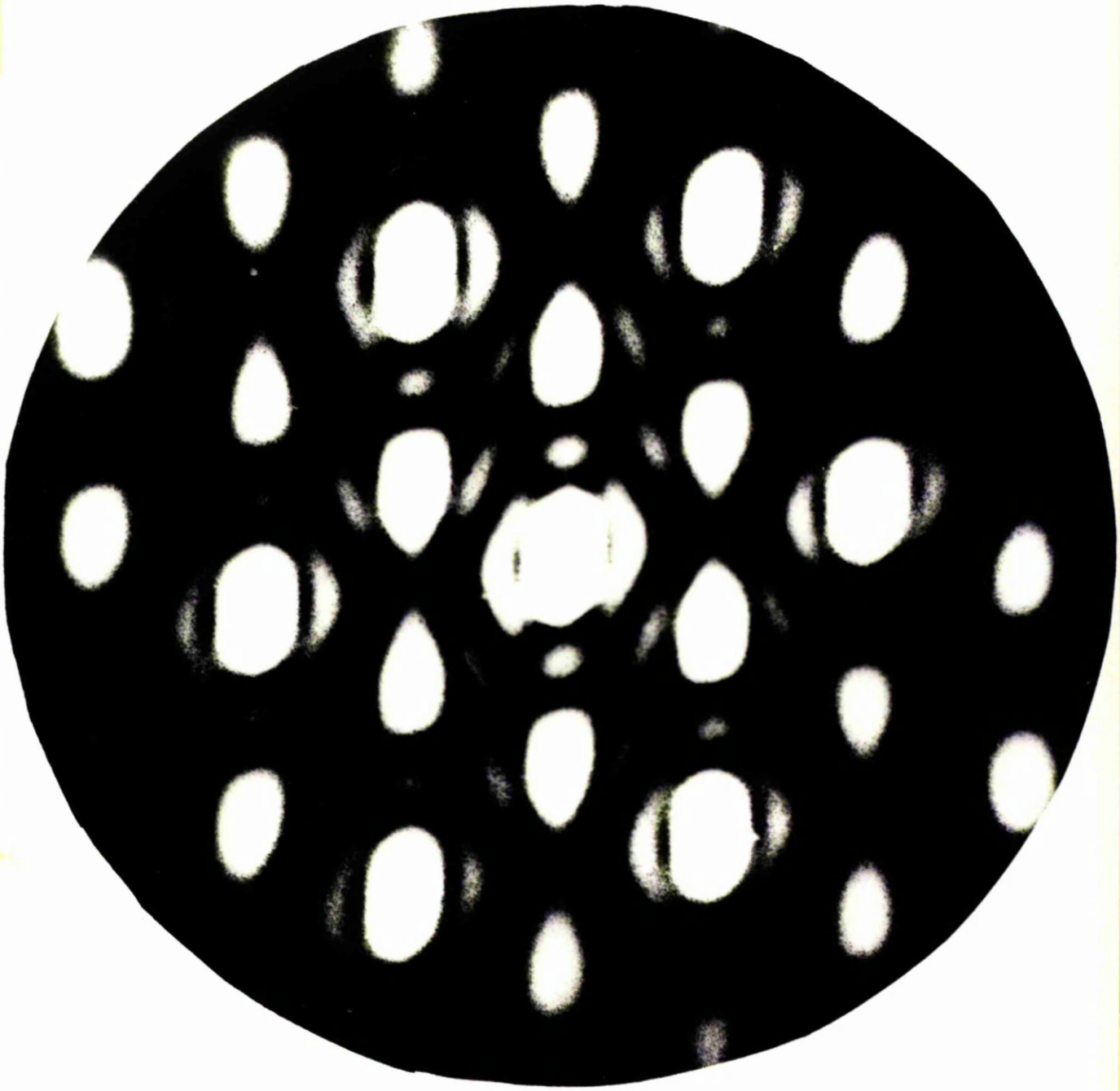


FIG. 3.4.

was cm. Since the origin can lie anywhere along the mirror plane, the structure amplitudes are sensitive only to the changes in the parameter x, and the structure in this projection is based on only one variable parameter.

There were two lines of approach to the problem. In the first place, the optical transform method, which generally gives a convenient way of finding the molecular position in the cell, was considered. The method consists of seeking the region of the (projected) unit cell in which the molecule can lie, giving good agreement between the optical transform of the contents of the unit cell and the reciprocal-lattice section. If the optical transform of one molecule is found to give a reasonably good fit when superimposed upon the weighted reciprocal-lattice section, then the way to produce a perfect fit is to separate the molecules by a distance such that the interference fringes caused by separation improves the agreement. For example, if ~~the~~ a low intensity reflexion is found to lie on a very heavy peak in the transform of one molecule then a fringe must be made to run through this peak.

The crystal structure has four symmetry related molecule per unit cell. The configuration of the molecule as determined by Patterson and optical methods (as described in sections 3.3 & 3.4) was used and the optical transform of a single molecule showed a reasonably good agreement when superimposed upon the weighted reciprocal-lattice section. Six reflexions (101, 602, 905, (11,01), (12,02) & 21,01) of low intensity, which lie on the heavy peaks in

the optical transform of a single molecule, were selected for this purpose. The symmetry related molecules were drawn to a scale of 2 cms to 1 Å (placing the centre of the molecule at a distance of $x = \pm 0.15$ from the origin), and the diffracting mask corresponding to this was punched. The optical transform of this mask showed, when compared with the weighted reciprocal-lattice, that there was no agreement at the regions where the six peaks were lying, and that it was not the correct position of the molecule. The relative separations of the molecules were then increased by a fractional distance 0·01 along x, and the procedure was repeated for ten relative separations of the molecules. A position of the molecule was then found which gave some measure of agreement ~~(fig. 3.5)~~ and attempts to improve it further failed. The coordinate of the centre of gravity of the molecule thus found was $x = 0.22$, ~~which led to the distribution of the molecules as shown in fig. 3.6.~~ The molecule was placed at this position and the calculation of structure factors for all the reflexions showed that the general agreement between the individual F_o's and F_c's was not satisfactory. It was then thought desirable to check the position of the molecule by a different approach which is described in the next paragraph.

The second line of approach to the problem was by the use of a graphical method which provided a possible way of finding the correct solution. The configuration of the molecule, as obtained from the Patterson map and subsequently checked by optical methods, was used, and the position of ~~the centre of gravity of~~ the molecule was

determined by calculating the structure amplitudes of a number of reflexions for a range of parameters.

The work of calculating the structure amplitudes for postulated atomic positions was shortened by selecting only several h00 reflexions. The structure factors of various reflexions (e.g. 200, 400, 600, 800, 10,00 & 12,00) which depended only on values of x, were calculated for a range of values of this parameter (up to 0.5) for the naphthocinnoline from the expression

$$F_{(x00)} = 4 \sum_{j=1}^{N} f_j \cos 2\pi h(X + x_j)$$

when k = 0,

where x_j is the coordinate of the jth atom of a molecule with respect to an arbitrarily chosen origin, and X is the coordinate of this origin with respect to the true unit cell, and the results were presented in the form of curves as shown in fig. 3.7. The curves were shown only for values of x up to 0.5; since they are symmetrical about x = 0.5. The curves also show how the calculated structure amplitudes vary with x. It can be seen that the position (x= 0.265) as shown by → in fig. 3.7, was accepted as the probable position of the arbitrarily chosen origin of the molecule and used for the calculation of the structure amplitudes which agree reasonably with those actually observed (Table 3.1).

The structure factor calculations for all the reflexions with this trial structure showed reasonable agreement between the individual

Figure 3.7.

One-dimensional structure factor graphs showing the position of the arbitrarily chosen origin of the molecule.

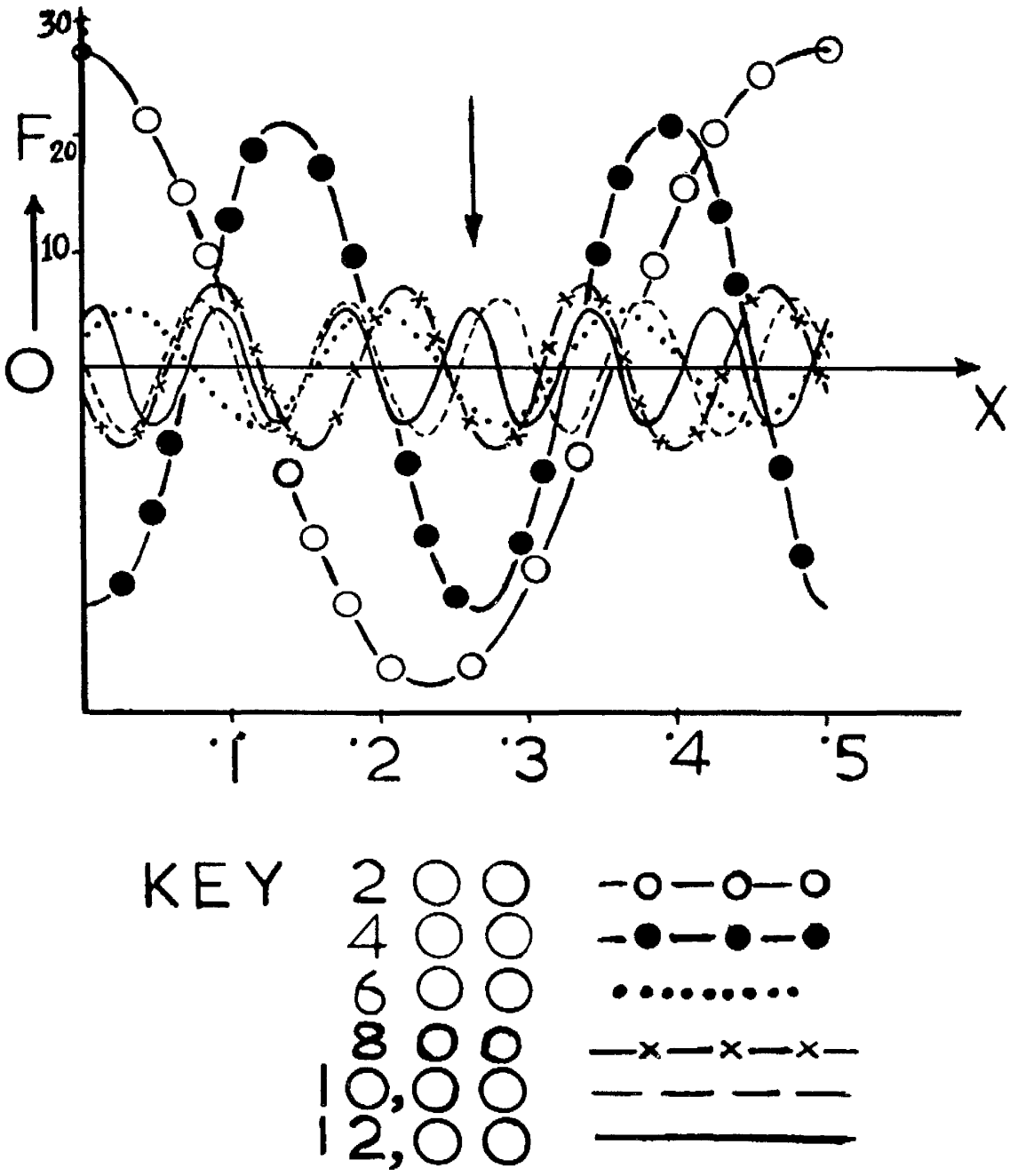


FIG. 3.7.

Table 3.1

indices	F (observed)	F (calculated)
200	28.0	25.0
400	20.8	21.0
600	3.2	3.7
800	10.0	7.0
10,00	8.0	4.5
12,00	8.0	5.0

F_o's and F_c's with a residual of 0.44, which suggested that the trial structure should be refined.

3.6. Earlier refinement by F_o synthesis.

As has been mentioned in section 3.5, a position of the molecule within the unit cell had been found by graphical method and the calculations of structure amplitudes showed a reasonable measure of agreement when compared with the observed structure amplitudes with the R-value of 0.44. The initial refinement was carried out using Fourier methods; the F_o synthesis was completed, using the phases (of 55 out of 75 reflexions) calculated from the trial structure parameters, from the relation

$$\rho_{(x,z)} = \frac{1}{A}\Big[F_{(00)} + 2\Big\{\sum_{2}^{\infty}{}_{h}^{h=2n} |F_{(h0)}| \cos 2\pi hx + \sum_{2}^{\infty}{}_{k}^{k=2n} |F_{(0k)}| \cos [2\pi ky - \alpha(0k)]\Big\}$$

$$+ 4\sum_{1}^{\infty}{}_{h}\sum_{1}^{\infty}{}_{k} |F_{(h,k)}| \cos 2\pi hx \cos[2\pi ky - \alpha(h,k)]\Big]$$

where $\rho_{(x,z)}$ is the electron density at any point (x, z) and A is the area of cross-section. The first Fourier synthesis is shown in fig. 3.8, the contours were drawn at intervals of 2 e/Å^2 ~~arbitrary levels~~. The trial coordinates of the atoms are shown by circles, while the same for the symmetry related atoms by crosses. As has been expected this was also not a very enlightening synthesis. Although the tilt of the molecule was not very much in this projection, the atoms of one molecule completely overlapped the atoms of a different molecule symmetrically related by glide planes, and difficulty was encountered in locating the correct positions of the atoms in the composite peaks of the electron density map - a fundamental limitation of the refinement by F_o synthesis. Only three atoms 9, 10 & 11 out of eighteen were resolved, and the peak heights of the unresolved and well resolved atoms were in the ratio of nearly 2:1 excepting the atom number 17 (in which the ratio was 1.5:1) though it overlapped closely with its symmetry related counterpart. Few atomic shifts were justified, and using the new coordinates the structure factors for all the reflexions were calculated, the residual dropping down to 0.41. Refinement was continued till there were no changes in the signs of structure factors, the residual was brought down to 0.37 only. The peak height of the atom number 17 was improved. At this stage it was

Figure 3.8

Projection of electron density ρ along [010], showing the extent of atomic overlap. Contours are at intervals of $2e/\mathring{A}^2$, zero contours are dotted, ~~negative broken~~ and positive contours full line.

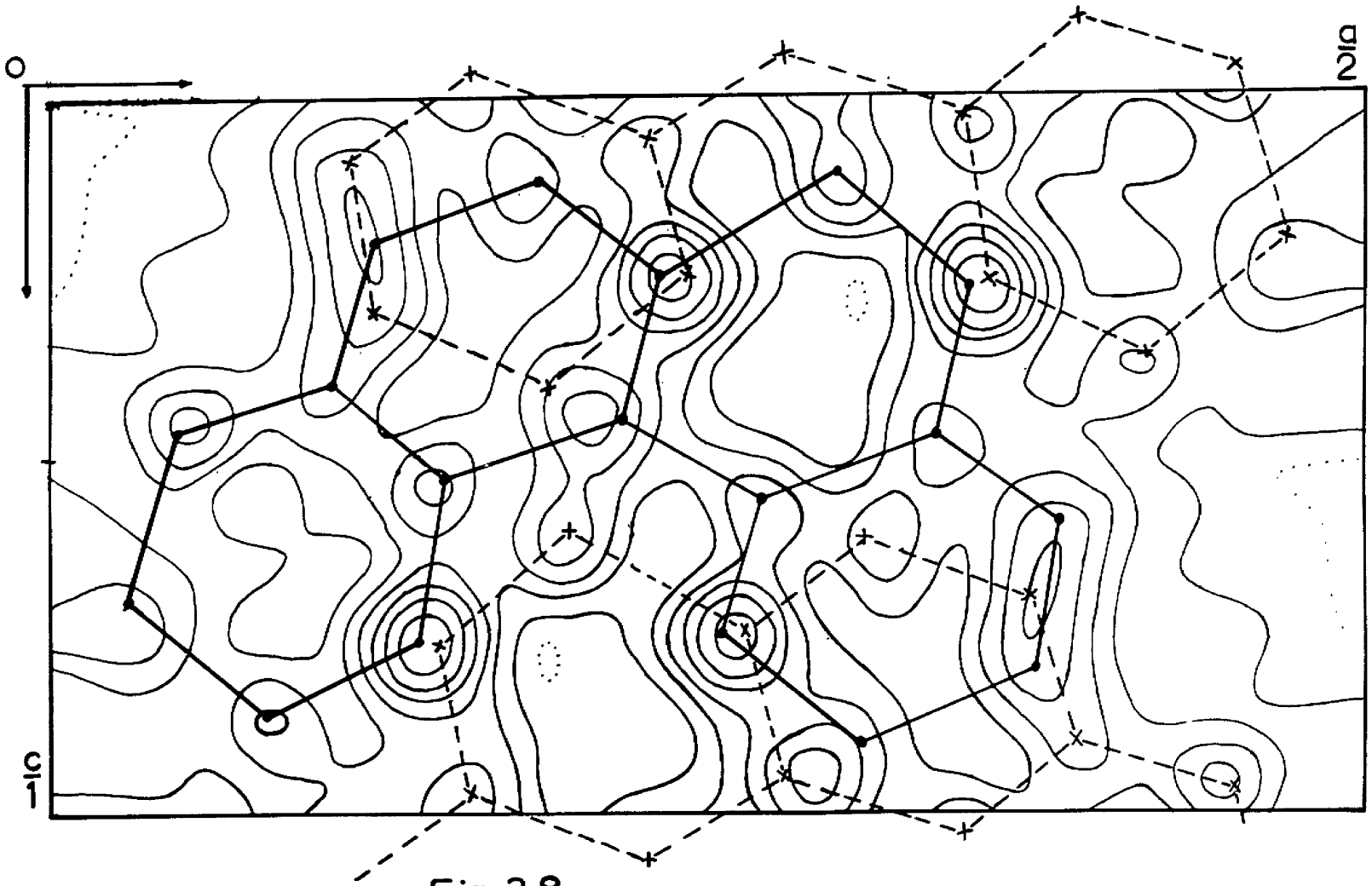


Fig. 3.8.

perceived that the normal Fourier refinement process would not be effective with this projection and other methods would have to be tried.

3.7. Refinement by the $(F_o - F_c)$ syntheses

It has become evident that the usual process of refinement by the continued use of the normal Fourier synthesis would not work with this projection because of the non-resolution of the atoms in each synthesis. It was decided to use a $(F_o - F_c)$ or difference synthesis (Cochran, 1951) to find the movements, if any, of the atoms which would improve the agreement. The synthesis has been discussed at fairly great length in section 2.6. The first $(F_o - F_c)$ synthesis, as shown in fig. 3.9, was calculated using the structure factors which had just been determined ~~and the contours are drawn at arbitrary levels~~. It was found that on plotting it nine atoms 1, 2, 4, 9, 10, 12, 13, 14 & 15 were lying on fairly steep gradients, three atoms 6, 17 & 18 were in positive areas and six atoms 3, 5, 7, 8, 11 & 16 out of eighteen were situated in negative regions. The atoms situated on the steep gradients in the map indicated substantial shifts in their coordinates. The fact that so many atoms were situated in negative regions seems to suggest that something was wrong with the scale of the observed amplitudes and that a further correction was needed. But the re-adjustment of scale seems to be inappropriate at such high R-value. Again, the background level of this map was rather high, and the most important features were two ~~four~~ large peaks (marked P_1 & P_2, ~~P_3 &~~

figure 3.9

Projections of $(\rho_o - \rho_c)$ along [010], showing the extent of atomic overlap and background variations. Contours are at intervals of $0.5e/\mathring{A}^2$, zero contours are dotted, negative broken and positive contours full line.

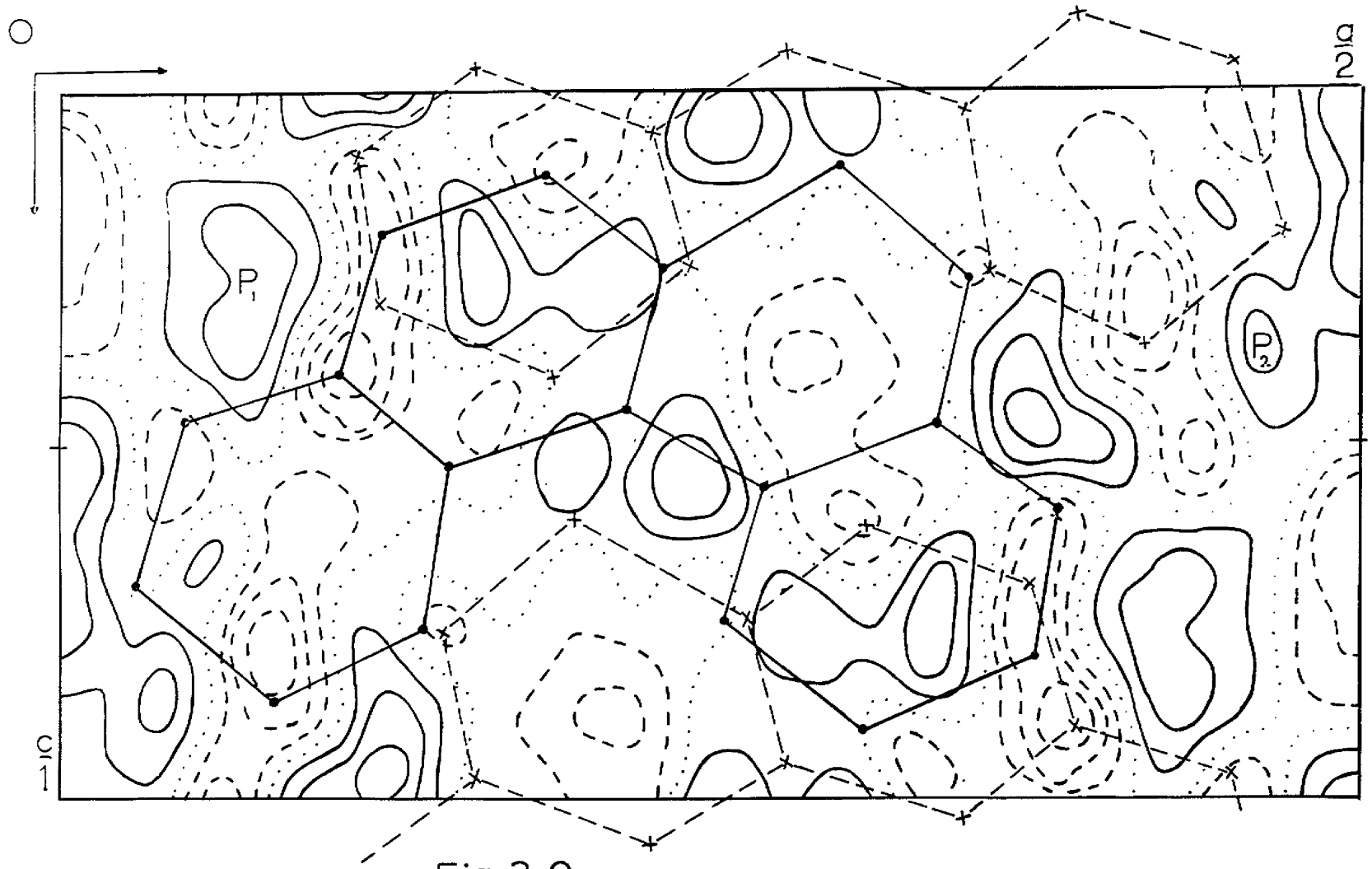


Fig. 3.9.

P_4) which also seemed to suggest that some of the atoms needed large movements. Keeping all these facts in view, the refinement was continued. The new coordinates were used to calculate a further set of the structure factors, which showed a better agreement between the individual F_o's and F_c's with the R-value of 0.35.

A difference synthesis was carried out using the new set of observed structure amplitudes and the general features of the map were found to improve reasonably. This synthesis was used to determine the shifts of the atoms; the new set of coordinates were again used to re-calculate the structure factors which this time gave the R-value of 0.33. Another cycle of refinement was carried out using the new set of observed structure amplitudes, but there was no improvement in the agreement between F_o's and F_c's or in the R-value. During this cycle, most of the atoms showed shifts which were very small. At this stage, as further refinement by this process seemed unlikely a Fourier synthesis was computed using the most recent set of signs with the observed structure amplitudes. The general features of this Fourier map seemed somewhat better in the sense that the shape of the peaks clearly indicated some shifts to be applied to the atomic coordinates. From the shape and position of the peaks a new set of atomic coordinates were determined and the corresponding set of structure factors calculated. The residual dropped down to 0.31. The refinement was then continued using both Fourier and difference Fourier syntheses. The progress of refinement was indeed very slow but it was encouraging, and the general features of the map were improving

gradually. The lowest R-value, as obtained by this process, was 0.27. The $(F_o - F_c)$ synthesis corresponding to this R-value is shown in fig. 3.10. The structure factors calculated using the most recent coordinates showed that the individual agreement between F_o's and F_c's was quite satisfactory. This suggested that the structure may be correct and if so, it ought to refine further. In view of the situation it was decided to refine the structure by the method of least squares.

3.8 Refinement by the method of least squares.

Attempts were then made to continue the refinements by the method of least squares. The method of least squares has been described in section 2.7. As most of the atoms overlapped in this projection, it was decided to refine separately and progressively,

(1) atoms with least overlap,

(2) atoms with considerable overlap,

(3) atoms with almost completely overlap.

It was considered unwise to refine the temperature parameters at this stage an overall constant temperature factor $B = 3.0\ \mathring{A}^2$ was taken for the molecule.

Refinement of the coordinate parameters of the first group of atoms was carried out and continued till indicated shifts were negligible. The refinement of the second group of atoms along with the first was then started and continued till, again, the indicated shifts were insignificant . Similarly, the refinement of all the

Figure 3.10.

Projections of $(\rho_o - \rho_c)$ along [010], showing the extent of atomic overlap and background levels. Contours are at intervals of $0.4 e/Å^2$, zero contours are dotted, negative contours broken and positive contours full line.

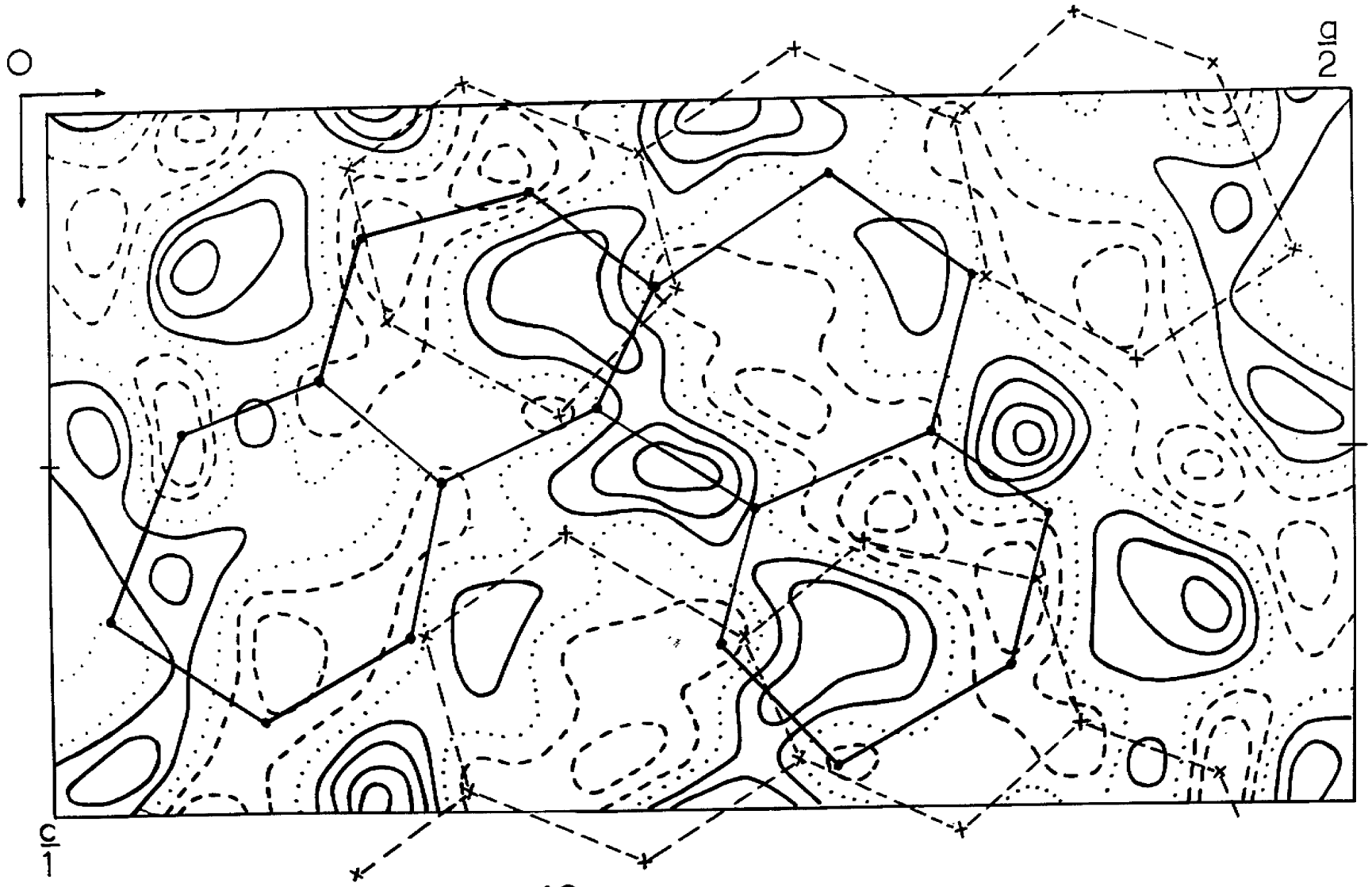


Fig. 3.10.

atoms together was carried out. In two cycles the residual was reduced from 0.27 to 0.23, at this stage the shifts in the coordinates were negligible. The temperature parameters were then refined and the residual was further reduced to 0.21. The Coordinate and temperature parameters were then refined separately till no further refinement took place and the R-value was brought down to 0.18. At this stage it was decided to refine both the positional and temperature parameters together, and in three cycles the residual was further reduced to 0.15. The final atomic coordinates and temperature factors were shown in table 3.2, and the final F_{obs} and $F_{cal.}$ values, for all the observed reflexions used in the refinement are shown in table 3.3. The final difference synthesis (fig. 3.11) was calculated, using the $(F_o - F_c)$ values recorded in table 3.3. The final atomic positions are plotted on the difference Fourier synthesis and some considerable distortion, from the idealised picture of the molecule, may be seen.

~~The initial and final coordinates of the main atoms, with temperature factors, are recorded in table 3.4, the coordinates of the atoms having the largest shift, in one direction (of 0 Å), are marked~~ +.

3.9. Effects of overlap

As can be seen from the map (fig. 3.11) that the atoms 6, 7, 13, 14 & 15 overlapped considerably and the atoms 1, 2, 3, 4, 5, 8, 12, 16, 17

Figure 3.11

Final difference synthesis in the [010] projections showing the distortion produced in the molecule during the least-square refinement. Contour are at intervals of $0.5e/A^2$, zero contours are dotted, negative contours broken and positive contours full line.

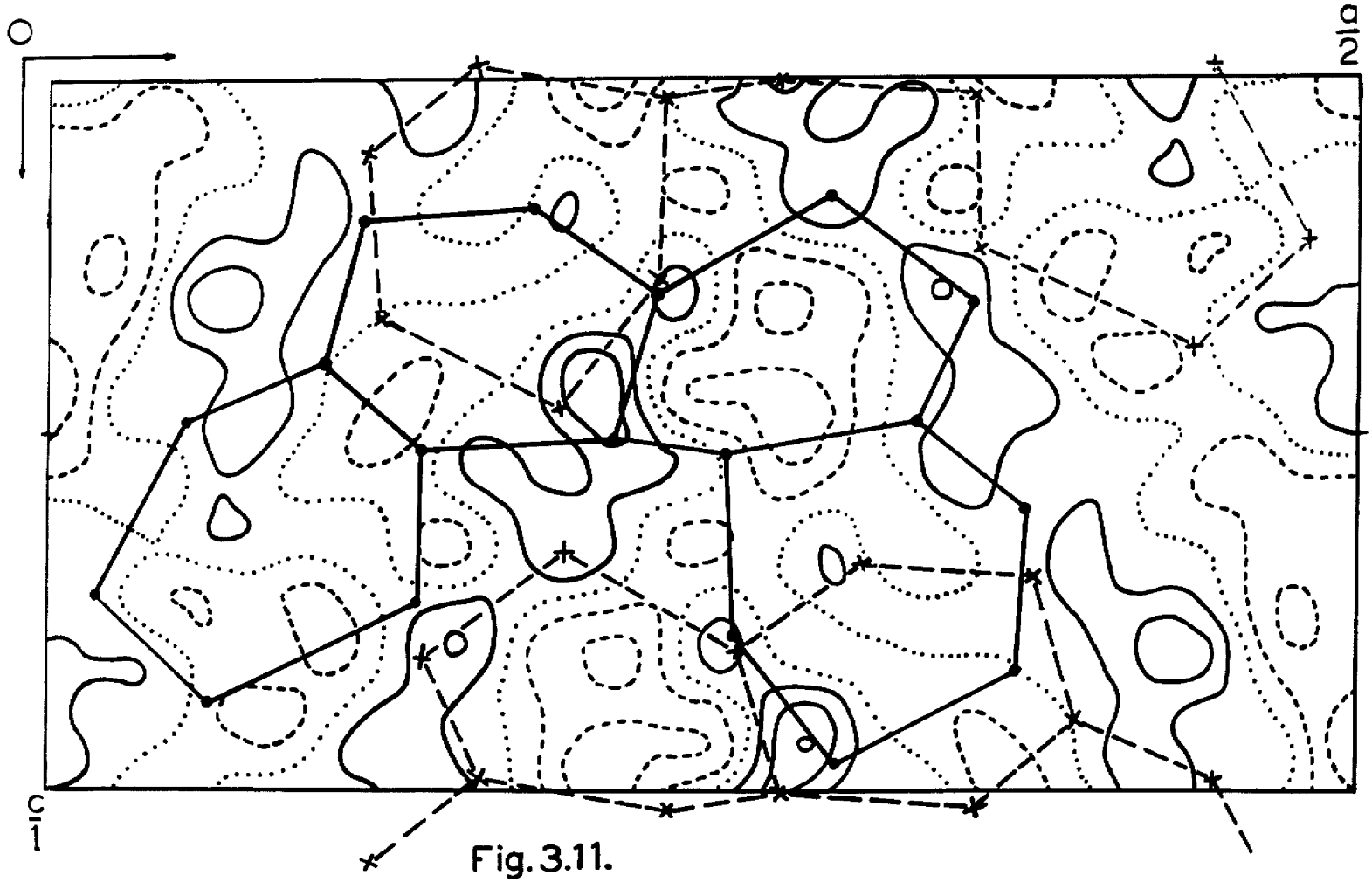


Fig. 3.11.

& 18 overlapped very closely with their symmetry related counterparts. During the refinement by Fourier and difference Fourier syntheses, the directions of the atomic shifts were very difficult to ascertain on account of the overlap of the peaks. Consequently the refinement was slow and involved a great deal of labour. However, with suitable movements of the atoms it was possible to improve some of the features of the map, but not to eliminate them. The refinement serves to emphasize the fact that there may be errors in the coordinates of some atoms which remain undetected because of overlap.

3.10. General observations.

It seems of interest to review the details of the analysis of the structure now that the refinement has been completed. Considerable difficulties were met with both Fourier and least-squares methods of refinement.

Refinement by the Fourier synthesis was discontinued at the R-value of 0.37 only. At this stage, from the shape and position of the peaks, it was very difficult to ascertain any shifts that would improve the agreement.

The first difference map is shown in fig. 3.9. The background level of this map was very high, and the most outstanding features of the map were two ~~four~~ large peaks (P_1 & P_2, ~~P_3 & P_4~~) and the strong negative regions round the positions of the atoms 3, 7, 8, 11 & 16.

The details suggested that something was wrong with the structure, and the difficulty in refining it was obvious. However, the refinement by the $(F_o - F_c)$ synthesis was undertaken and in two cycles the residual was reduced from 0.37 to 0.33, but during the third cycle of refinement the shifts which were estimated from this map failed to improve the overall agreement further. At this stage the agreement between the individual F_o's and F_c's was quite satisfactory excepting two reflexions; the intensity of a low angle reflexion (200) was suspected to be effected by extinction, and the (701) reflexion calculated too high — $F_c = 60$, $F_o = 42$. Few changes in the signs of the structure factors of low intensities were observed, so it was thought that computing a further F_o synthesis using all the reflexions might be of some help at this stage. This F_o synthesis was found to be of great help in determining the shifts of the atoms, and the structure refined further which was evident from a further decrease in the R-value from 0.33 to 0.314 in the next cycle.

One of the difficulties that was experienced in the difference Fourier refinement has been attributed to the incorrect signs of some of the reflexions of small structure amplitudes. It is known that one of the inherent disadvantages of difference Fourier refinement is that there is no obvious way in which one could decrease the influence of inaccurate reflexions (Lipson & Cochran, 1957). Thus the reflexions of small amplitudes, whose signs may change very easily between successive cycles of refinement, may produce some quite disturbing features on the difference map. It is therefore advisable

to make a careful judgment about their signs before they are included in the calculations. However, refinement was continued using both Fourier and difference Fourier maps, and in a further three cycles the residual was decreased by 0.045 (i.e. from 0.315 to 0.27). The sixth difference map (at R-value of 0.27) is shown in fig. 3.10. The temperature factor 3.0 $\mathring{A}^2$ was calculated for the molecule, but the difference maps indicated that different temperature factors for various atoms should be employed. However, this was not done until the coordinates refinement by the method of least squares was completed.

It may be recalled that, by refining the coordinate and thermal parameters simultaneously using least-squares methods, the refinement proceeded on a different course. The reason for this is two-fold - (1) because of the greater number of parameters the least-squares equations are more easily satisfied and a lower residual will result and (2) refining only one set of parameters at a time (i.e. positional or thermal parameters) ignores their interactions on the other set.

In a few cycles of least squares refinement the residual was reduced to 0.15. The final difference map along with the molecules superimposed on it is shown in fig. 3.11. Although the structure refined to such a low R-value, considerable distortion of the molecule from its idealised picture, may be seen (fig. 3.11). The bond length between atoms $C_2 - C_3$, $C_{13} - C_{14}$, $C_{11} - C_{12}$ and $C_{15} - C_{17}$ are longer and the length between $C_{13} - C_{17}$ shorter than expected. The temperature factors of the atoms 2 (suffering from considerable overlap)

and 12 (suffering from complete overlap) were reduced to 0.90 $\mathring{A}^2$ and 0.07 $\mathring{A}^2$ respectively; and the temperature factor of atom 7 (resolved) was increased to 6.5 $\mathring{A}^2$ - the values which have no apparent physical justification.

Having remembered these facts, attempts were made to reduce the distortion, but this resulted in an immediate rise in the R-value and subsequent refinement brought the structure back to its very distorted form.

In a further attempt to find out the correct positions of the atoms 2, 5 & 18, which overlapped very closely, and distorted the molecule greatly, a partial difference synthesis ($\rho_o - \rho_c$) was computed, where ρ_o is the electron density computed using $|F_o|$ and phases from F_c calculations for the 18 atoms, and ρ_c is the electron density computed using F_c values and phases calculated for the 15 atoms, and the resulting map is shown in fig. 3.12. The positions of these atoms indicated by the partial difference map were exactly the same as was obtained by least-squares refinement.

It also needed to be mentioned that hydrogen atoms were not included in the refinement, because their positions were not apparent in the map, and the theoretical positions for all the hydrogens assuming C - H bond length 1.08 $\mathring{A}$ did not seem to be justified. The average hydrogen contribution to the average intensity of the reflexions may be about 8%, and it is quite possible that the hydrogens make a substantial contribution to the individual F_c's. This is important particularly in the case of least-squares refinement where

Figure 3.12

Partial difference Fourier synthesis showing the positions of overlapping atoms which were not included in the calculation of ρ_c. Contours are at intervals of $0.2e/\mathring{A}^2$.

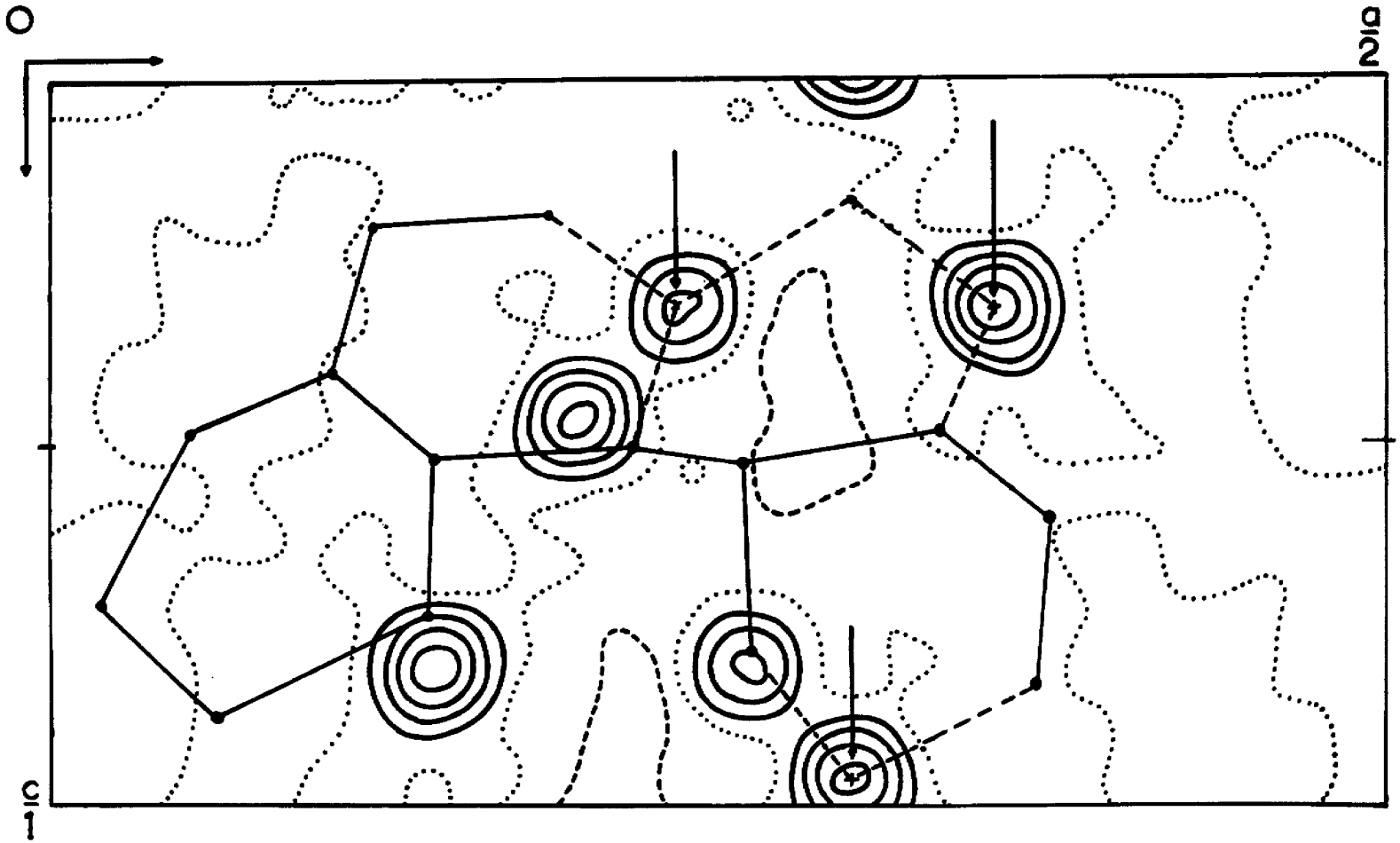


Fig. 3.12.

the difference Δ F (in F_o and F_c) is minimised it would certainly be inadvisable to treat ΔF's as entirely due to errors in the parameters. This argument, of course, would not apply to difference Fourier refinement in general, but in the case of overlapped atoms their positional parameters may be effected by ignoring the presence of hydrogen.

With a molecule as complicated as the naphthocinnoline, however, the details could not be established from one projection alone, and another projection had to be considered, and is discussed in next chapters.

Table 3.2

Atomic coordinates and temperature factors as obtained from the refinement of the [010] projection by the method of least squares.

Atoms	$x/_a$	$y/_b$	B in $Å^2$.
C_1	0.2658	0.2767	2.44
C_2	0.3027	0.4659	0.90
C_3	0.3718	0.3364	1.21
C_4	0.3771	0.1105	4.22
N_5	0.3558	-0.1889	3.51
N_6	0.2997	-0.3424	1.10
C_7	0.1847	-0.3196	6.52
C_8	0.1223	-0.3106	1.56
C_9	0.0568	-0.0259	4.09
C_{10}	0.0172	0.2331	3.43
C_{11}	0.0625	0.3828	4.68
C_{12}	0.1429	0.2408	0.07
C_{13}	0.2595	0.0631	3.95
C_{14}	0.3364	-0.0155	2.22
C_{15}	0.1440	0.0223	4.36
C_{16}	0.1054	-0.1033	4.73
C_{17}	0.2176	0.0181	4.01
C_{18}	0.2370	-0.1953	4.20

Table 3.3

Observed and calculated structure factors for the hol reflexions

h	k	l	$\lvert F_{obs.}\rvert$	$F_{cal.}$	h	k	l	$\lvert F_{obs.}\rvert$	$F_{cal.}$
0	0	2	16.0	-16.7	6	0	2	16.5	-18.5
0	0	4	17.3	16.0	6	0	4	17.1	15.8
0	0	6	16.0	14.4	6	0	6	4.2	6.1
1	0	0	22.2	20.4	7	0	1	61.1	-41.4
1	0	3	20.7	24.0	7	0	3	17.6	18.6
1	0	5	4.4	5.9	7	0	5	20.2	-26.7
2	0	0	75.5	-109.9	8	0	0	38.3	43.7
2	0	2	26.4	-22.0	8	0	2	39.1	-38.6
2	0	4	15.8	-14.0	8	0	4	27.6	25.8
2	0	6	9.4	-12.7	8	0	6	7.5	- 6.9
3	0	1	37.4	-32.4	9	0	1	47.0	44.9
3	0	3	9.0	- 8.5	9	0	3	13.0	-11.7
3	0	5	< 5.9	4.6	9	0	5	6.6	6.6
4	0	0	54.0	-44.2	10	0	0	25.1	-24.7
4	0	2	24.7	12.3	10	0	2	25.1	20.1
4	0	4	10.0	11.2	10	0	4	25.0	-27.1
4	0	6	6.8	- 8.3	10	0	6	< 1.3	2.1
5	0	1	44.1	38.4	11	0	1	9.8	- 8.6
5	0	3	9.0	-11.4	11	0	3	8.5	- 7.4
5	0	5	15.8	15.9	11	0	5	10.8	- 9.1
6	0	0	8.0	9.3	12	0	0	27.1	-29.2

Table 3.3 (continued)

h	k	l	$\lvert F_{obs.}\rvert$	$F_{cal.}$
12,	0	2	12.0	8.5
12,	0	4	12.0	11.6
12,	0	6	4.4	- 8.2
13,	0	1	18.6	-18.5
13,	0	3	8.6	- 8.5
13,	0	5	5.6	5.0
14,	0	0	19.9	16.9
14,	0	2	10.0	- 5.4
14,	0	5	4.4	8.4
15,	0	1	23.3	23.6
15,	0	3	14.8	16.5
15,	0	5	4.2	4.5
16,	0	0	20.7	20.4
16,	0	2	9.2	- 6.3
16,	0	4	10.0	- 9.5
17,	0	1	25.2	-37.0
17,	0	3	14.7	-10.0
17,	0	5	4.6	3.6
18,	0	0	12.4	-11.7
18,	0	2	11.1	10.9
18,	0	4	4.4	- 2.3
19,	0	1	14.2	15.1
19,	0	3	4.7	3.9
20,	0	0	4.4	7.1
20,	0	2	6.5	8.0
20,	0	4	3.7	4.8
21,	0	1	6.5	9.6
21,	0	3	4.0	4.8
22,	0	0	6.2	- 5.0
22,	0	2	8.3	- 8.0
23,	0	1	6.1	- 7.6
23,	0	3	2.4	- 3.8
24,	0	0	3.4	- 5.1
24,	0	2	6.1	7.7

Chapter 4

Further attempts to solve the hko projection

4.1. Introduction. As was stated in Chapter 2, earlier attempts to determine the structure of the naphthocinnoline in the [001] projection were unsuccessful, and the reason for this failure was also given. Attempts were then made (as described in Chapter 3) to solve the structure in the [010] projection; and the structure was refined to the R - value of 0.15. In this Chapter some further attempts (by different lines of approach) to solve the structure in the [001] projection are described.

From the evidence of the shape and orientation of the molecule in the [010] projection, it was possible to deduce a shape and orientation of the molecule in the [001] projection. This was done by orienting a wire model of the molecule so that it satisfied the atomic coordinates of the [010] projection and projecting this model on the (001) plane.

The shape and orientation of the molecule having thus been obtained, it was decided to calculate the structure factors for all the reflexions. The calculated values did not agree very well with the observed values, and the initial value of the residual was 0.58. A cycle of Fourier refinement brought the residual down to 0.51, which seemed satisfactory considering the degree of overlap in this projection. The refinement was then continued by Fourier methods and in a further two cycles the residual was brought down to 0.48 and attempts

to refine it further by this method failed. Refinement by the (Fo-Fc) synthesis was then undertaken and in a few successive cycles the residual was reduced to 0.41 only. Structure factor calculations (using the latest set of coordinates) showed gross disagreement between the Fo's and Fc's of some strong reflexions. Once again a Fourier and a difference Fourier synthesis were computed, but attempts to refine further proved unsuccessful. At this stage refinement of the structure by these methods seemed unlikely to succeed so it was decided to work independently of the known hol projection and determine the shape and position of the molecule in this projection by other approaches.

Buerger's minimum function approach

4.2.1. Introduction. In view of the above situation, attempts were made to solve the structure using the minimum function approach (Buerger, 1950 e). It was hoped that this would reveal an approximate electron density in this projection. The theory and the principles of the method have been described in sufficient detail in literature (see, for example, Buerger, 1959; Lipson & Cochran, 1957).

An early attempt had been made by Wrinch (1939) to relate the Patterson map to the electron density. The problem was simplified by considering a set of discrete points and its Patterson representation, which may be called the vector set. It was shown that there exists a method by which a fundamental set of points may be recovered from its vector set.

Building on Wrinch's fundamental work, Buerger (1951) developed

several general methods for completely analyzing a vector set. These general methods were then extended so that they could be applied to the transformation of a Patterson synthesis to the electron-density map.

A Patterson synthesis is not a set of discrete points, rather it is a continuously variable function. Although such a synthesis can be transformed into a sharpened Patterson and so treated as a set of discrete points, there is an entirely different way of solving the Patterson synthesis i.e., to set up a function (of Patterson values) which will transform the Patterson function into an approximation to the electron density. Such a function is called an image-seeking function. Three such functions have been proposed, a product function, a sum function and a minimum function.

The product and the sum functions are not very suitable for practical purposes because some unfortunate features of these functions are caused by the continuous background of the Patterson synthesis. The minimum function, which is the best of the three is defined as the minimum value of the several Patterson values (weighted, if necessary) which occur at the vertices of the polygon used to search for images of itself.

4.2.2. Principles of the method. A Patterson synthesis can conveniently be transformed to an approximate electron density using this method by first selecting a Patterson peak of single weight (peak due to centrosymmetric "interactions") whose coordinates are uv (say).

Two Patterson syntheses, contoured in different colours, are then placed one over the other so that xy on one sheet coincides with the u + x, v + y on the other. Now the minimum function ${}^{uv}M_{2(xy)}$ can be contoured by tracing on a third sheet those contours from the two underlying Patterson maps which represent the smaller values at all points. The origin of the ${}^{uv}M_{2(xy)}$ map will lie exactly half way between the origins of the two Patterson maps i.e., at $\frac{1}{2}u$, $\frac{1}{2}v$. In principle, the minimum function reduces the n^2 peaks of the Patterson function to the n peaks of the electron density, but in practice a number of other peaks will be present which arise from chance superposition of vectors. However, these extra peaks can be reduced in size and number if two $M_{2(xy)}$ maps are combined to form a minimum function of higher rank, $M_{4(xy)}$. This increased rank of minimum function, so found, provides a new map which is closer to the electron density than either of the original $M_{2(xy)}$ maps.

4.2.3. Application of the method in this case. In solving a Patterson synthesis by the minimum function method, it was necessary to locate peaks of single weight in the Patterson map, but it was not easy to find such a peak. This was so because many Patterson peaks are ordinarily swamped by background and hence are not distinguishable. Again, the regions in the Patterson function of high value are frequently collections of unresolved peaks. However, a few ~~possible~~ positions of probable rotation peaks were determined and marked by crosses (a, b & c shown in fig. 4.1) in the Patterson map. The best position seemed to be the one marked "a". Two Patterson maps each comprising an area of a complete unit cell were drawn on transparent paper, and accepting the

Figure 4.1.

hko Patterson function showing the positions of probable rotation peaks selected for tracing the minimum functions. For each rotation peak at (x,y) there must be other peaks at $(\frac{1}{2}-x,\frac{1}{2})$ and $(\frac{1}{2},\frac{1}{2}-y)$ as shown by "x" for a, $\triangle$ for b and $\odot$ for c.

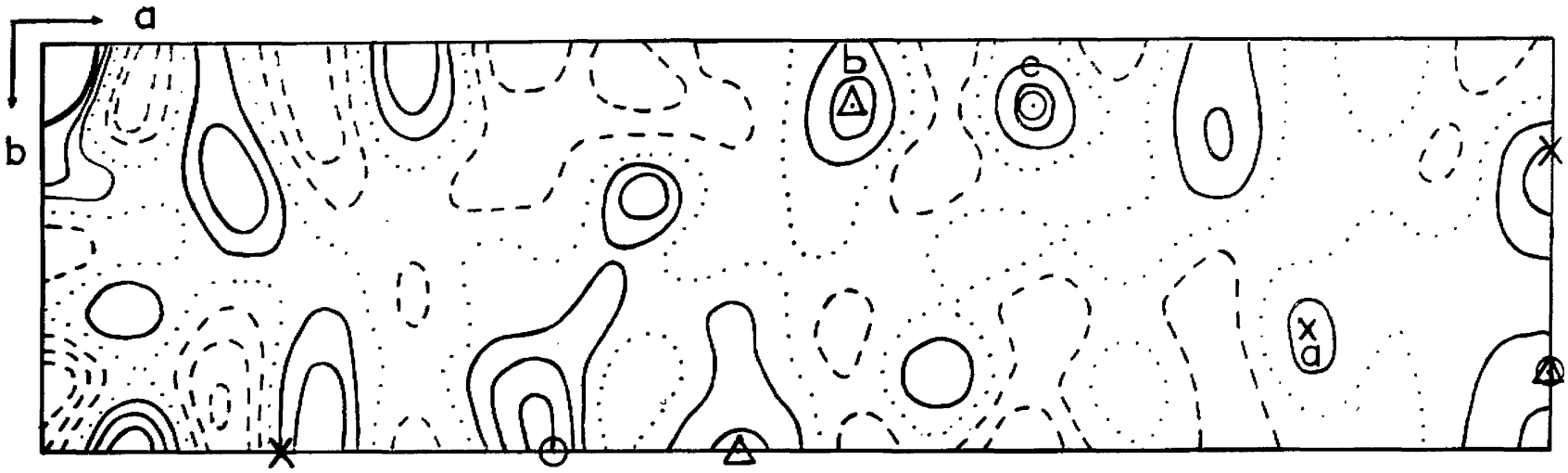


Fig.4.1.

position a as the location of a rotation peak the ${}^{a}M_2(xy)$ minimum function map was traced as described above. The large ${}^{a}M_2(xy)$ map (comprising an area, a/2 x b) thus derived is shown in fig.4.2.

Now in the half cell, each quarter cell (a/2 x b/2) is a glide equivalent of the other. The ${}^{a}M_2(xy)$ map can therefore be divided into two, each half of area a/2 x b/2, and one half placed directly over the other so that the upper quarter cell was in the reverse position (the glide operation). A further minimum function, ${}^{a}M_4(xy)$ was then traced on a separate sheet and this map is shown in fig.4.3.

The most important feature of the ${}^{a}M_2(xy)$ and ${}^{a}M_4(xy)$ maps is that the distribution of atoms in the cell is not very clear from the peaks, although a large number of heavy peaks appear on the maps and the interpretation of the maps proved to be extremely difficult. To facilitate this, a scale model of the molecule was constructed and shadows from a parallel beam of light were used to judge the plausible "fits". Several sets of structure factors were calculated corresponding to different fits but the agreement with the observed structure amplitudes was generally poor. In view of the above results, it was decided to repeat the whole procedure using another peak (marked b). This resulted in the ${}^{b}M_4(xy)$ map as shown in fig.4.4. This also did not seem at all encouraging and attempts to find a reasonable fit of the molecule in the ${}^{b}M_4(xy)$ map were unsuccessful. The next alternative was to use the third peak

Figure 4.2.

Minimum function ($^{a}M_2$) as obtained from the rotation peak marked a.

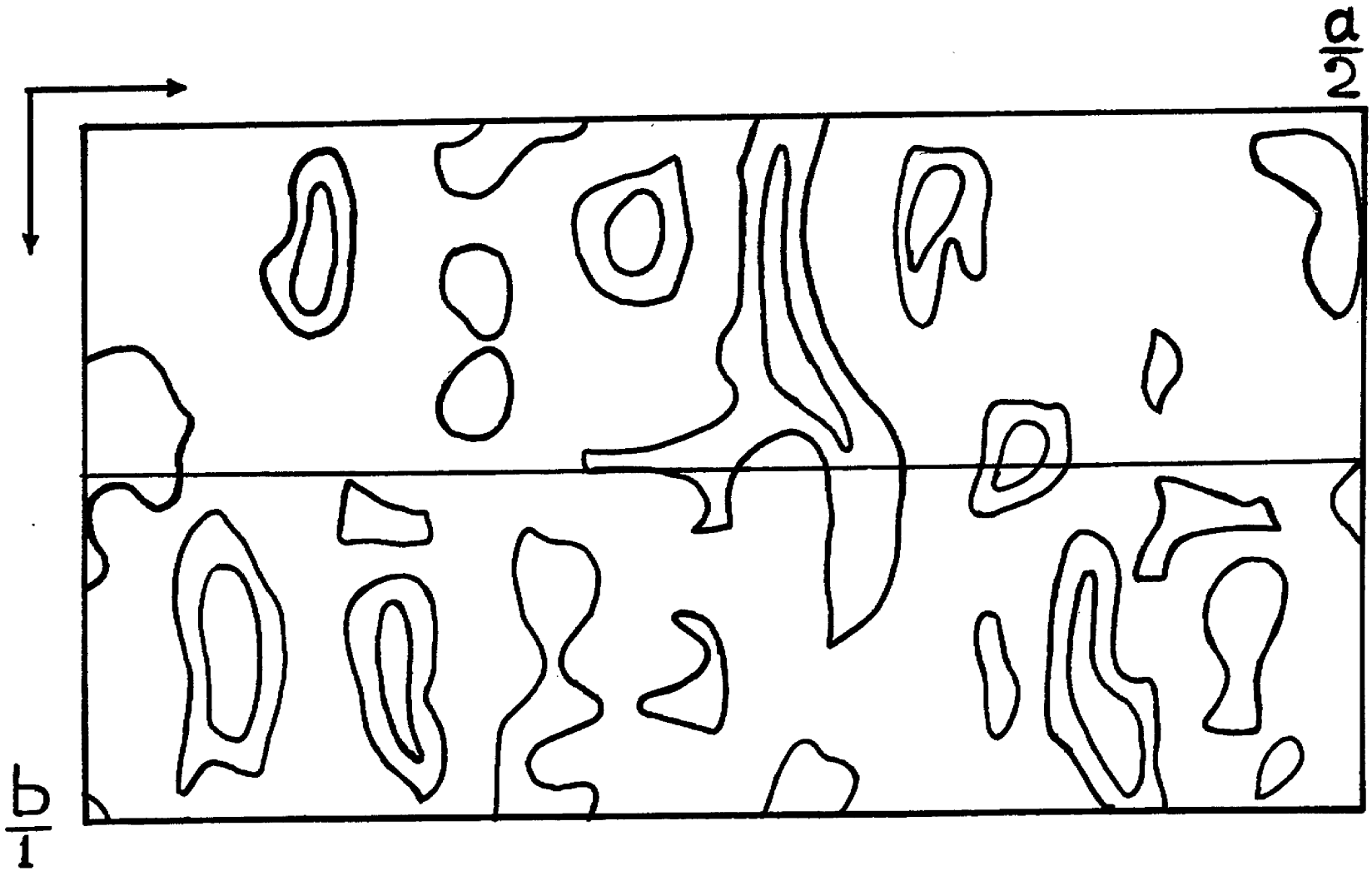


FIG. 4. 2.

Figure 4.3.

Minimum function $({}^{a}M_4)_a$ as obtained from the superposition of two ${}^{a}M_2$ maps.

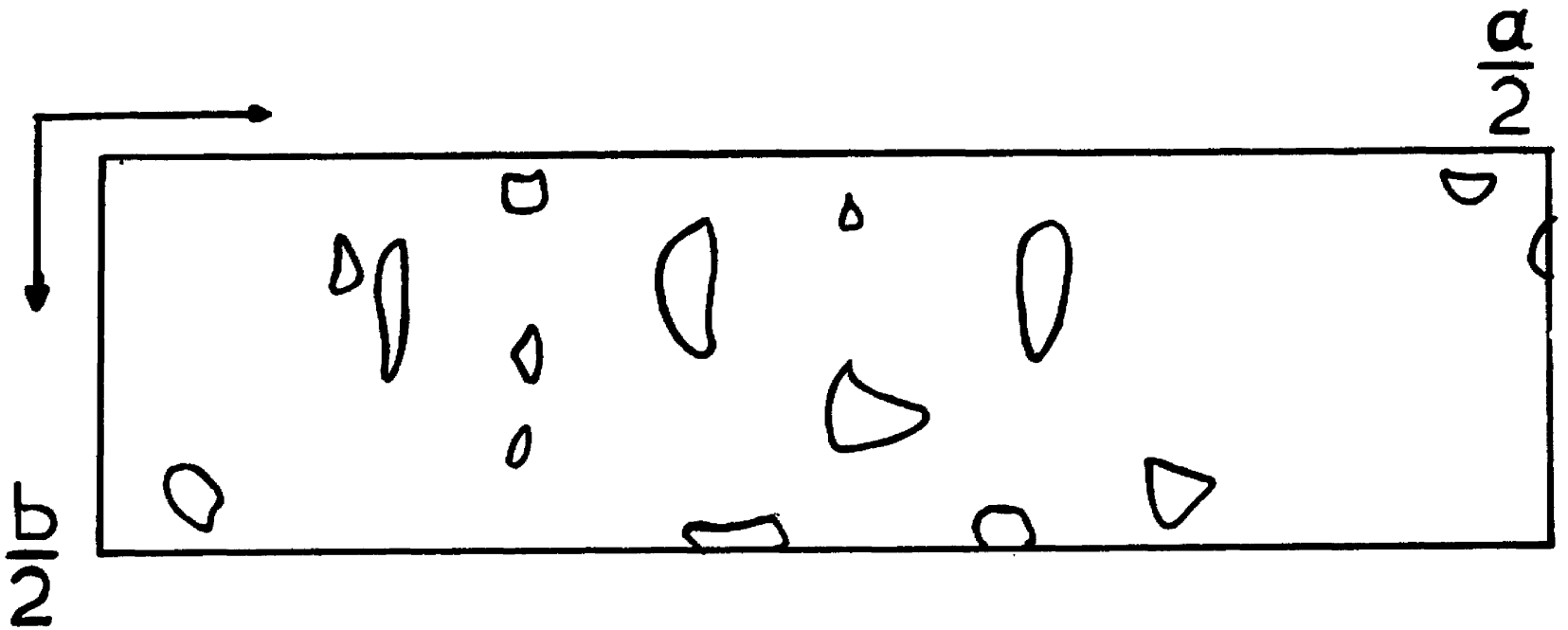


FIG. 4.3.

Figure 4.4.

Minimum functions ($^{b}M_2$ & $^{b}M_4$) as obtained from the rotation peak marked 'b' are shown in figures 4.4(a) & 4.4(b) respectively.

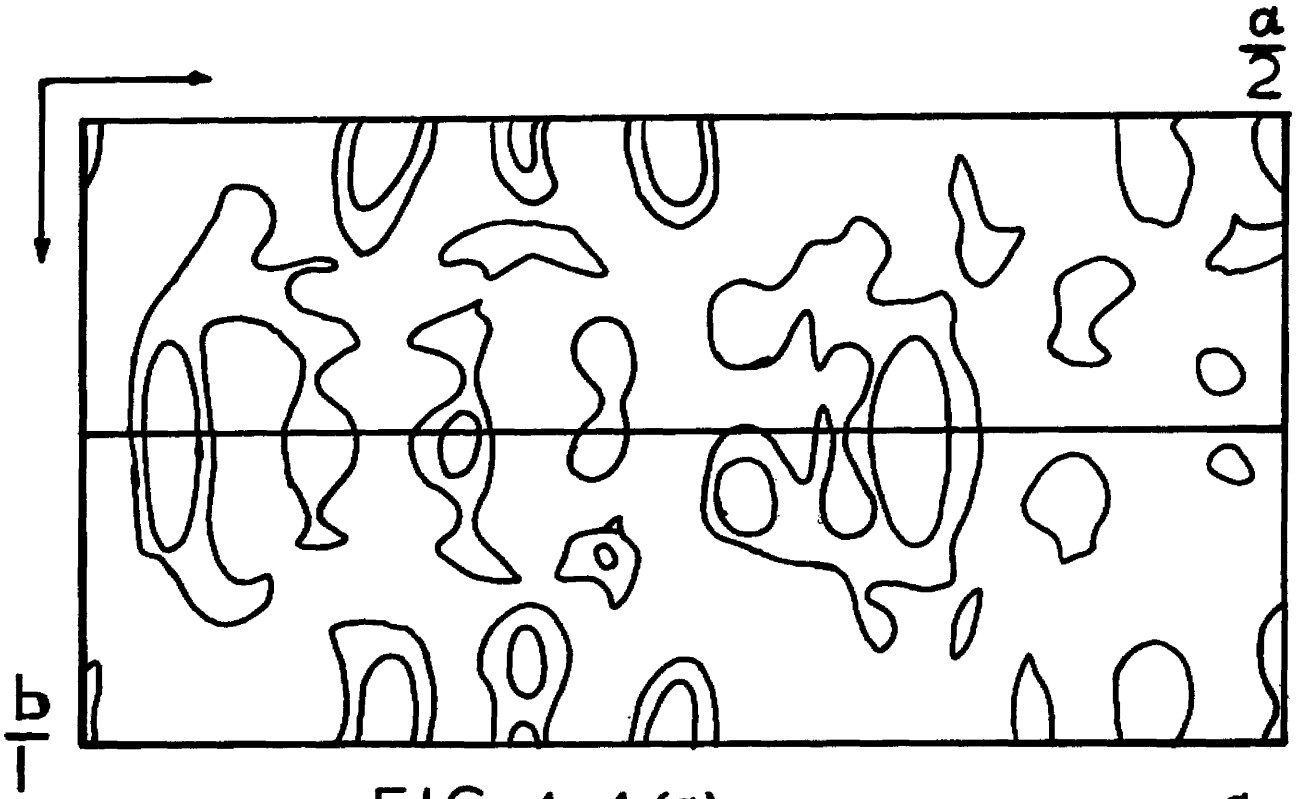


FIG. 4.4 (a).

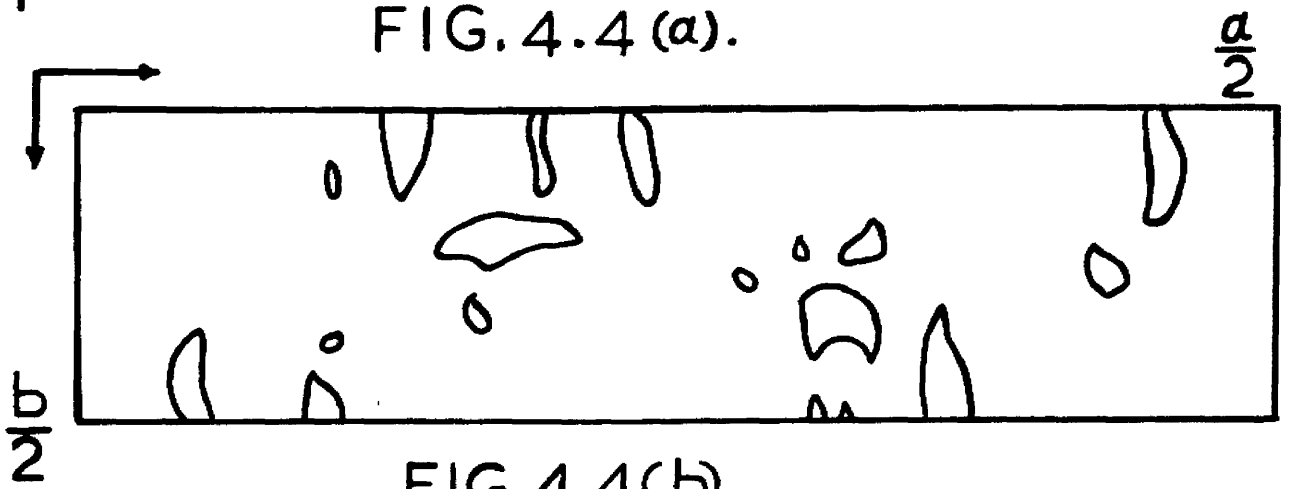


FIG. 4.4 (b).

(marked c). This formed the $^{c}M_{4(xy)}$ map as shown in fig. 4.5. The important feature of this map was that the distribution of atoms in the cell was not clear at all, a few possible "fits" were tried but the structure factor agreement was never encouraging.

4.3. Structure factor graph approach. When it was felt that there was little to be gained by the use of the minimum function method, it was decided to take recourse to the usual structure factor graph approach (Bragg & Lipson, 1936). It is well known that this method is, in general, only used when the postulated atomic coordinates are approximately correct, but still need adjustments. From the structure factor graph it can be seen that some atoms lie in regions where their contribution to the structure factor changes slowly with position, whereas other atoms lie on quite steep gradients where their contribution to the structure factor is very sensitive to changes of position. The graphs can therefore clearly indicate what adjustments of atomic parameters will increase or decrease the structure amplitudes.

As was mentioned in the first section of this chapter, the structure in the hko projection was refined to the R - value of .41 but there were serious discrepancies between the Fo's and Fc's of some reflexions, the most serious of which were the fc's of 310 and 15,10 being too small and that of 420 being too large. The structure factor graphs were employed in an endeavour to obtain atomic movements which would improve the intensity agreement of these reflexions.

Structure factor graphs were drawn for about ten low-angle and one high angle reflexions. The atomic shifts were determined by plotting the coordinates on tracing paper and placing them successively over

Figure 4.5.

Minimum function ($^{c}M_{4}$) as obtained from the rotation peak marked c.

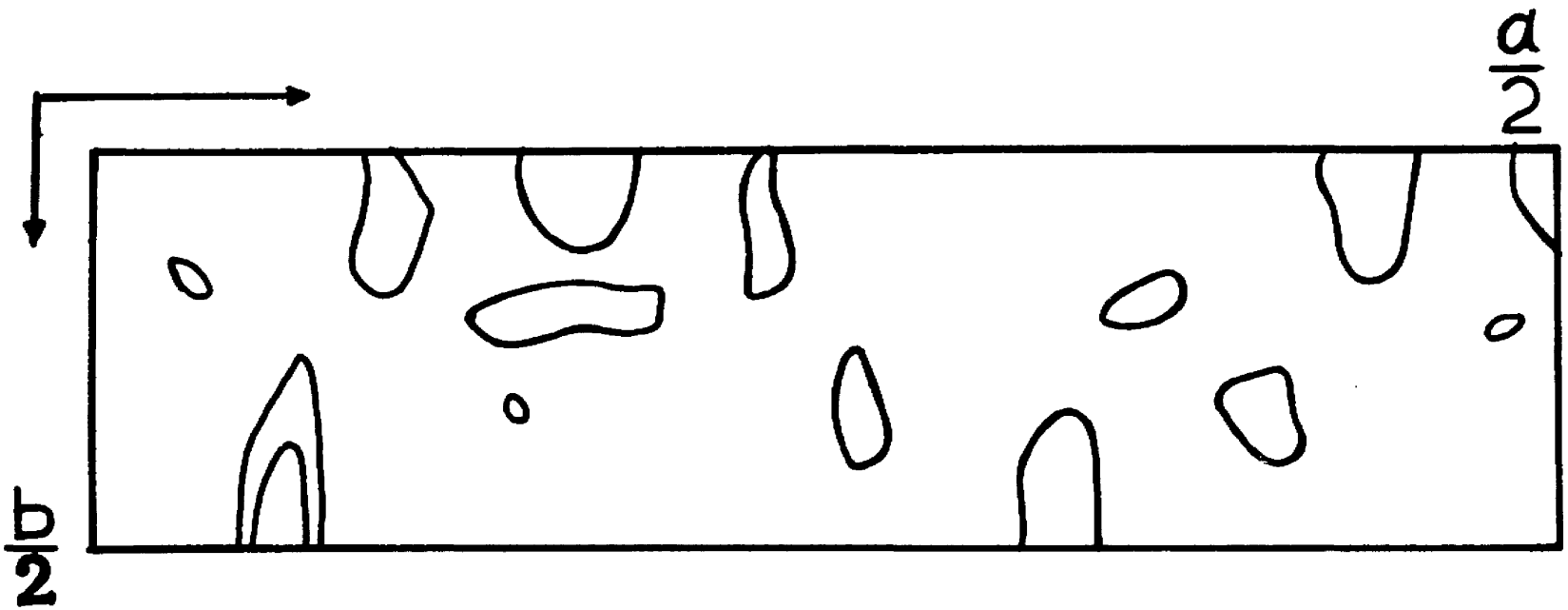


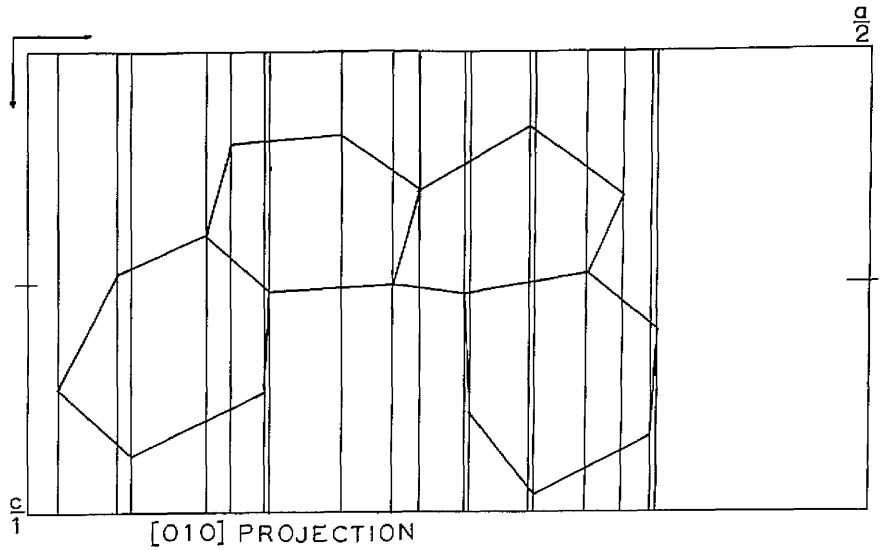
FIG. 4.5.

different graphs, and structure factor calculations showed considerable improvement in the overall intensity agreement with slight decrease in the R - value. In order to improve the intensity agreement of these reflexions further by moving some atoms, it was found that the intensities of some other reflexions were adversely effected; in particular, 710 becomes too strong. However, the graphs were used again and again to determine the atomic shifts and the agreement in the Fo's and Fc's of the above mentioned reflexions was improved considerably, and the final residual was reduced to .38. Although structure factor graphs were used with some success, considerable distortion of the projection of the molecule was produced.

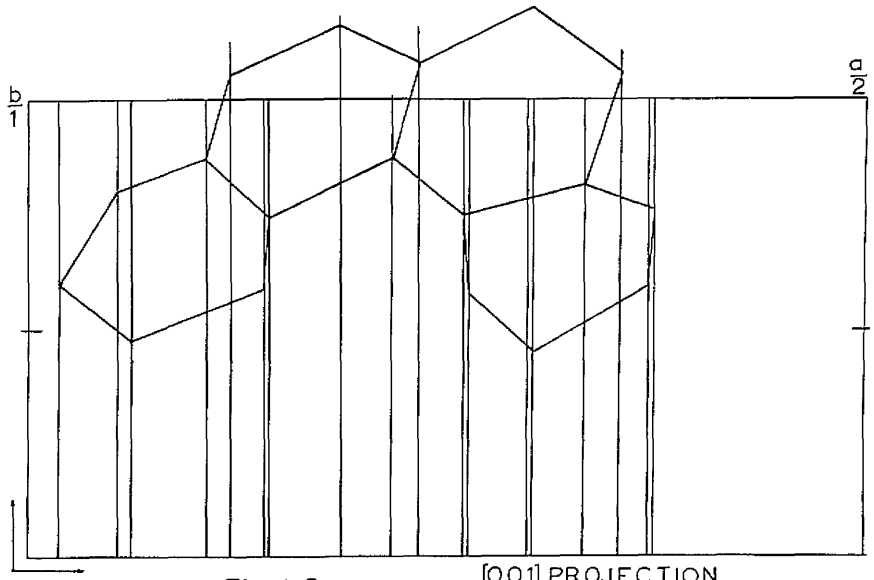
Attempts were then made to derive a better configuration and position of the molecule using structure factor graphs and judging the structure factor agreement of several strong reflexions; a molecule thus obtained is shown in fig. 4.6. Structure factor calculations for all the reflexions with the initial trial coordinates showed reasonable agreement between the Fo's and Fc's with the R - value of .44, which was very encouraging at this stage. There were, of course, discrepancies between the Fo's and Fc's of many reflexions, and it was again hoped that by a further use of the graphs it would be possible to determine the movements of atoms which would rectify the discrepancies. Graphs were then used to improve the structure factor agreement of several reflexions as far as possible. It was found again, at this stage, that the atomic movements indicated by graphs in successive stages brought the molecule back to its distorted form, but the structure factor

Figure 4.6.

A molecule in the [001] projection as derived from the structure factor graph approach.



[010] PROJECTION



[001] PROJECTION

Fig. 4.6.

agreement was improved. This was a very hopeful sign, and so refinement was undertaken by the Fourier and difference Fourier methods. In three cycles, the residual was brought down to 0.34, and attempts to refine it further proved unsuccessful. The final ~~Fourier and~~ difference Fourier map~~s~~ is ~~are~~ presented, showing the molecule by thick lines and the symmetry related one by broken ~~dotted~~ lines, in fig. 4.7 ~~(a & b)~~.

A Review of the work done so far

Figure 4.8(a) shows the deduction of the molecular appearance in the hko projection, from that in the hol projection. Fourier and difference Fourier synthesis were employed for refinement which was terminated at the R - value of .41.

An independent approach to determine the structure in the hko projection, using minimum function method, was attempted. But this failed to yield any fruitful result, because it was difficult to select the appropriate peak for the decomposition.

The next approach was by the use of structure factor graphs. Of all the structures that have been tried so far in this projection, the one shown in fig. 4.8(b) gave the best result. The final refinement was undertaken by Fourier and difference Fourier methods, and the residual was reduced to .34 for the observed reflexions. But it could be reduced no further. The significant features of the difference map were (i) that there were strong positive and negative regions in the map that were difficult to explain, (ii) that some atoms were lying in the deep negative regions as if there were some error in the scaling or temperatures factors. The difference map (fig. 4.7~~.6~~) shows the atoms

Figure 4.7

The extent of deformation of the molecule shown in figure 4.6 after refinement by difference syntheses.

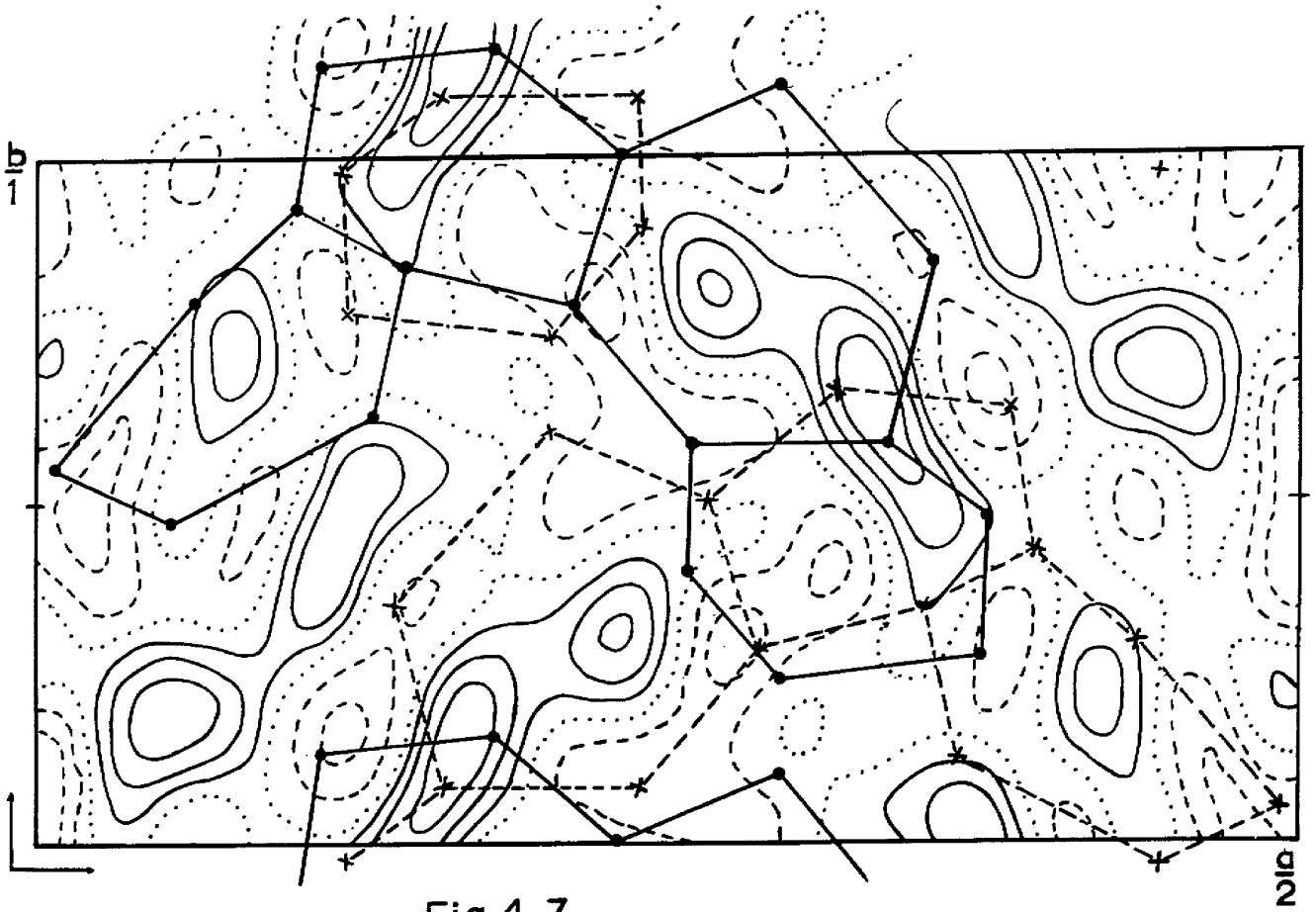


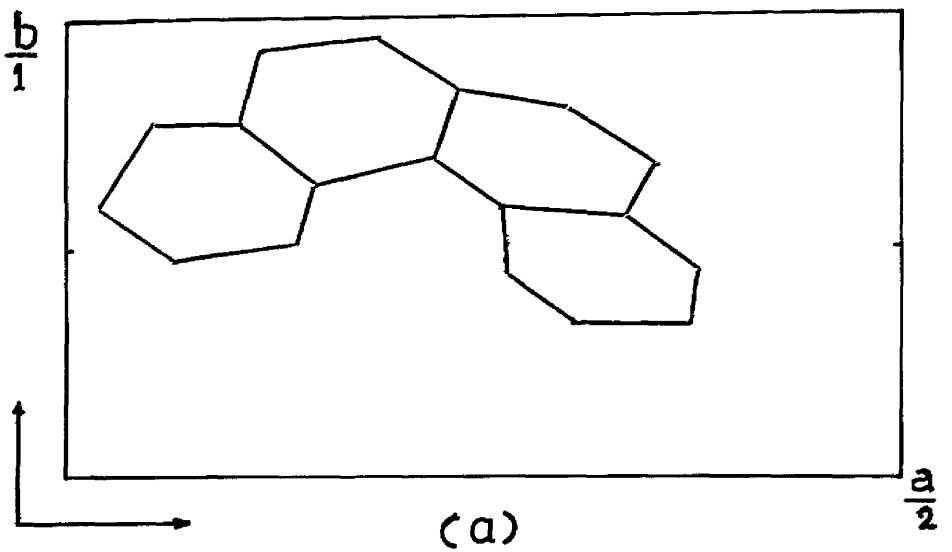
Fig. 4.7.

Figure 4.8.

The molecule in the [001] projection

(a) deduced from the [010] projection

(b) obtained from structure factor graph approach.



(a)

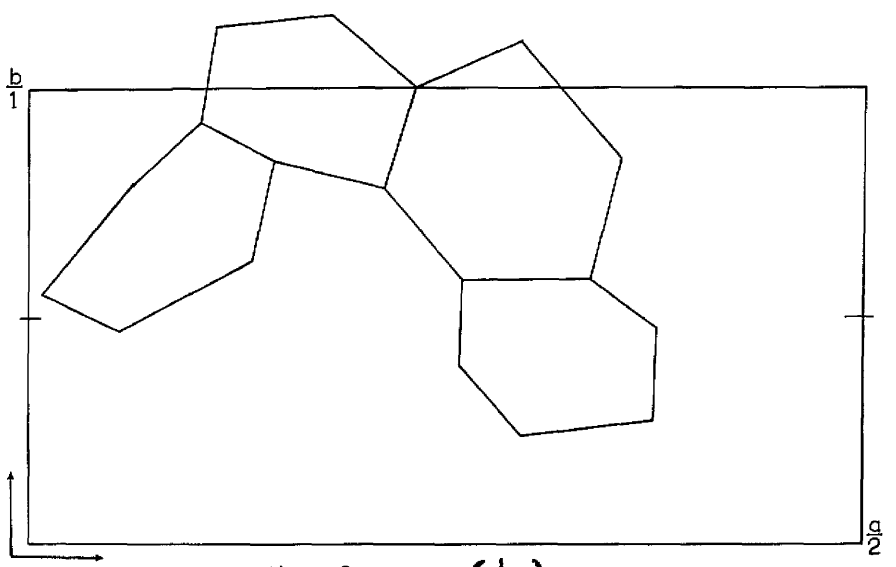


Fig.4.8. (b)

(2, 3, 5, 8, 10, 13, 17 & 18) were lying on gradients, but practically no improvement was obtained in the R - value when corrections for these gradients were made. It was noted that the background peaks (in fig. 4.7, ~~b~~) were as high as $1.9e/\mathring{A}^2$ (negative peaks, ~~and~~ almost equally high, were obtained).

In view of the low residual (.15) for the hol projection, .34 was considered to be unsatisfactory. Again, the difference in the values of the common coordinate (x) of some atoms (9, 10, 11 & 12), obtained from two projections, is as large as $0.23A^{o}$, which is many times the expected standard deviation~~s~~. Furthermore, the bond length between atoms $N_5 - N_6$, $C_9 - C_{10}$ and $C_{11} - C_{12}$ are very long (more than $2A^{o}$), which is unacceptable from a chemical point of view.

Despite the fact that the value of the residual for the hko projection was considerably less than that expected for a randomly incorrect structure (see Wilson, 1950), the poorness of the agreement due to some large discrepancies, the abnormal bond length between some atoms, and the extent of distortion produced in the molecule from its idealised picture are sufficient to cast doubt upon the structure.

In view of these observations it seemed advisable to attempt again the solution of the hko projection, entirely independently of the known hol projection, by optical-transform methods.

4.5. <u>Redetermination of the molecular shape by the optical transform method</u>. As was described in the previous section, it was more than a coincidence that all attempts based on different approaches failed to yield any fruitful result in the [001] projection. It was then decided to work independently of the knowledge of the molecular shape gained

from the previous work and to use once more the evidence available from the weighted reciprocal-lattice section. It was mentioned in section 2.3 that the possible "benzene peaks" on the weighted reciprocal lattice were located and the shape and orientations of the corresponding benzene rings were found as shown in fig. 2.5. From this was constructed the molecule as seen in projection. But the optical transform of this molecule did not show a very nice fit with the weighted reciprocal lattice, and the structure had ceased to refine at the R - value of 0.35.

Detailed examination of the hko weighted reciprocal-lattice section was then undertaken in which some more benzene peaks just outside, the benzene circle, as shown in fig. 4.9 by dotted circles, were considered. A systematic application of the reciprocal-lattice construction (due to Hanson, Lipson & Taylor, 1953 and described in section 2.3) to the full set of peaks resulted in many different sets of orientations of benzene rings for the molecule. These solutions were examined by comparing the weighted reciprocal-lattice section with optical transform of the molecule but no satisfactory fit could be obtained.

As mentioned in section 2.3, every benzene ring gives rise to six principal peaks in its optical transform if the ring is flat or has a reasonable tilt (which for copper radiation is an angle up to 40°). If the ring is tilted through a large angle

Figure 4.9.

The peaks marked by dotted circles on the hko weighted reciprocal lattice section were considered for the determination of the orientation of more benzene rings.

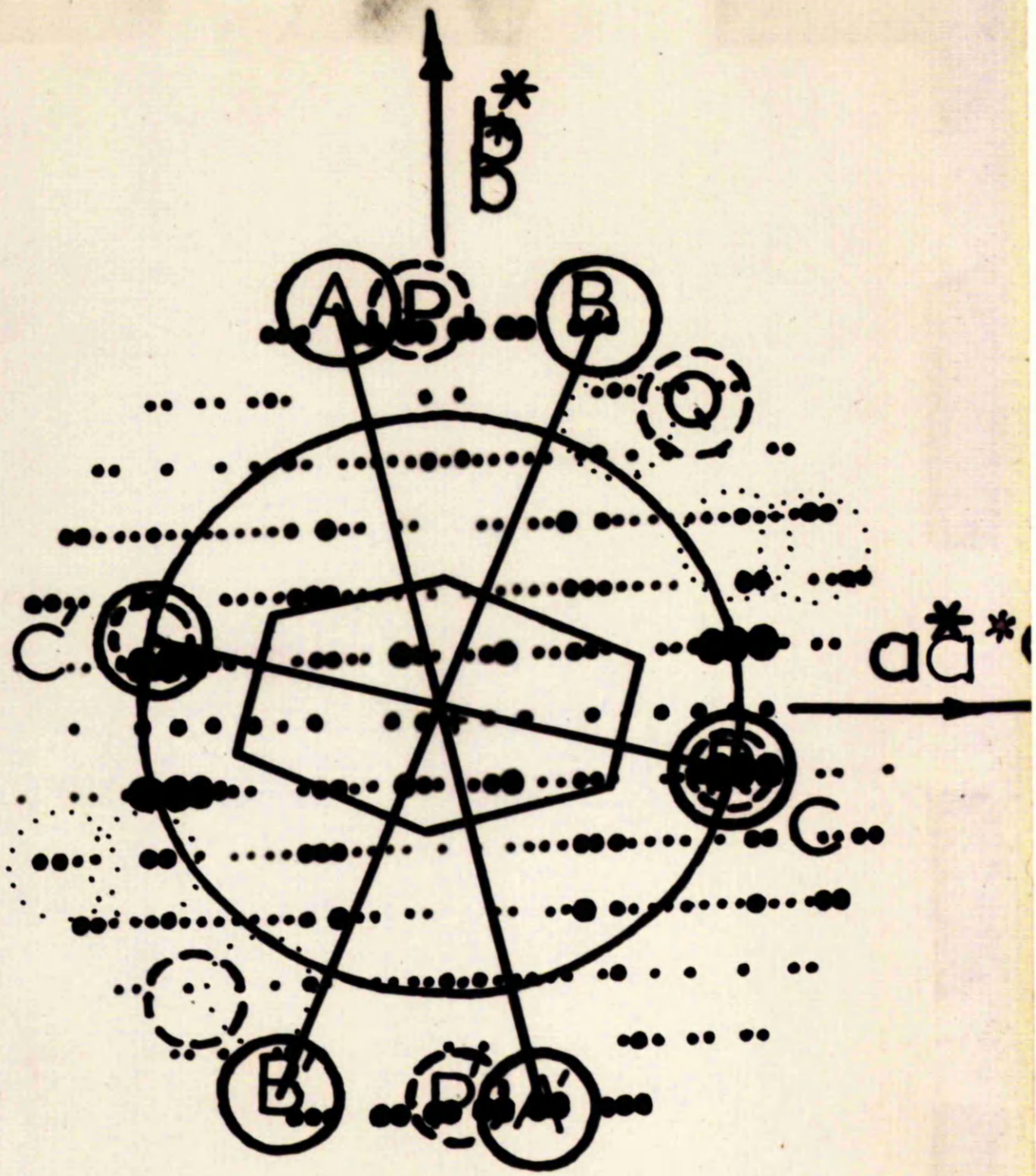


FIG. 4.9.

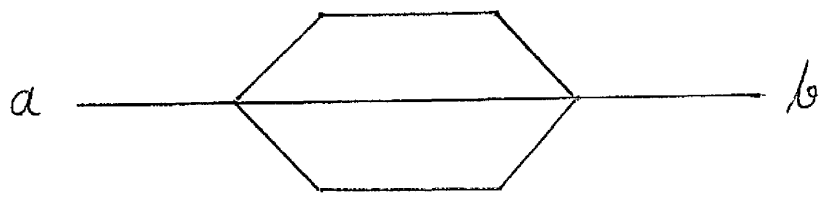


Fig.4.10.

(more than 40° about the axis, say, ab in fig. 4.10) then two of the benzene peaks will be lost (Fig. 11.b) as they will correspond to reflexions which have $\theta > \pi/2$. However, other features of the benzene transform should still be visible, the chief of which are six peaks of smaller amplitude than the principal peaks already mentioned, in the positions shown in fig. 4.11(a). These will be referred to as the "subsidiary peaks".

With these considerations in mind the weighted reciprocal-lattice section was critically examined and the orientations of two other benzene rings were deduced (as shown in fig. 4.12) from the two principal and six subsidiary benzene peaks. These subsidiary peaks were at first difficult to locate and their indentification was mainly achieved by trial and error. The molecule was then built up of the rings as were constructed above, and shown in fig. 4.13. The final agreement obtained between the optical transform of the molecule and the superimposed weighted reciprocal-lattice section (shown in fig. 4.14) suggested that the postulated "naphthocinnoline" orientation was

Figure 4.11(a)

Showing the principal (P) and subsidiary (S) peaks on the optical transform of a benzene ring.

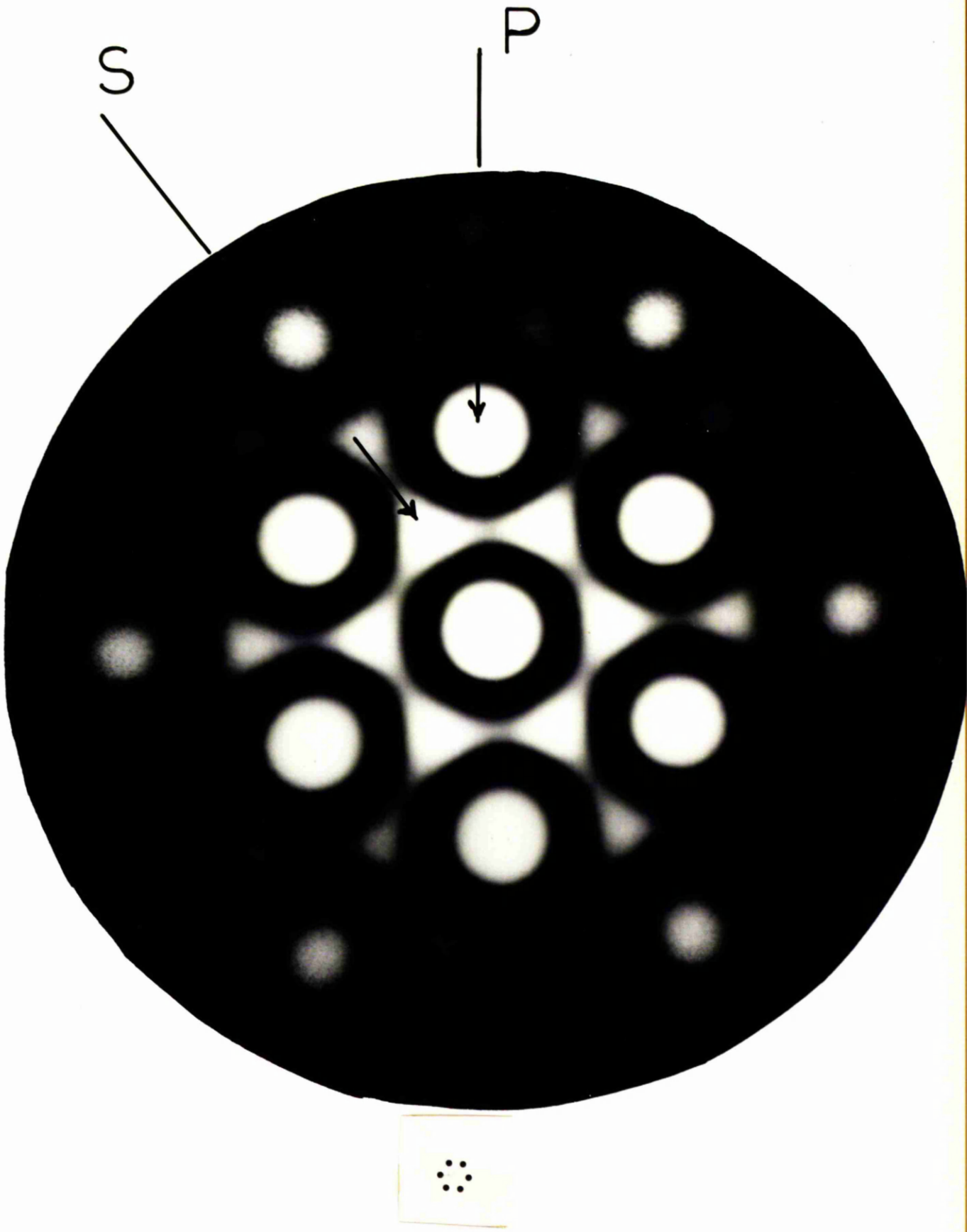


FIG. 4.11(a).

Figure 4.11(b)

Showing the optical transform of a tilted benzene ring in which some of the principal peaks lie outside the reflecting sphere.

FIG. 4.11(b).

Figure 4.12.

Constructing benzene rings from the evidence of subsidiary peaks in the hko reciprocal lattice section.

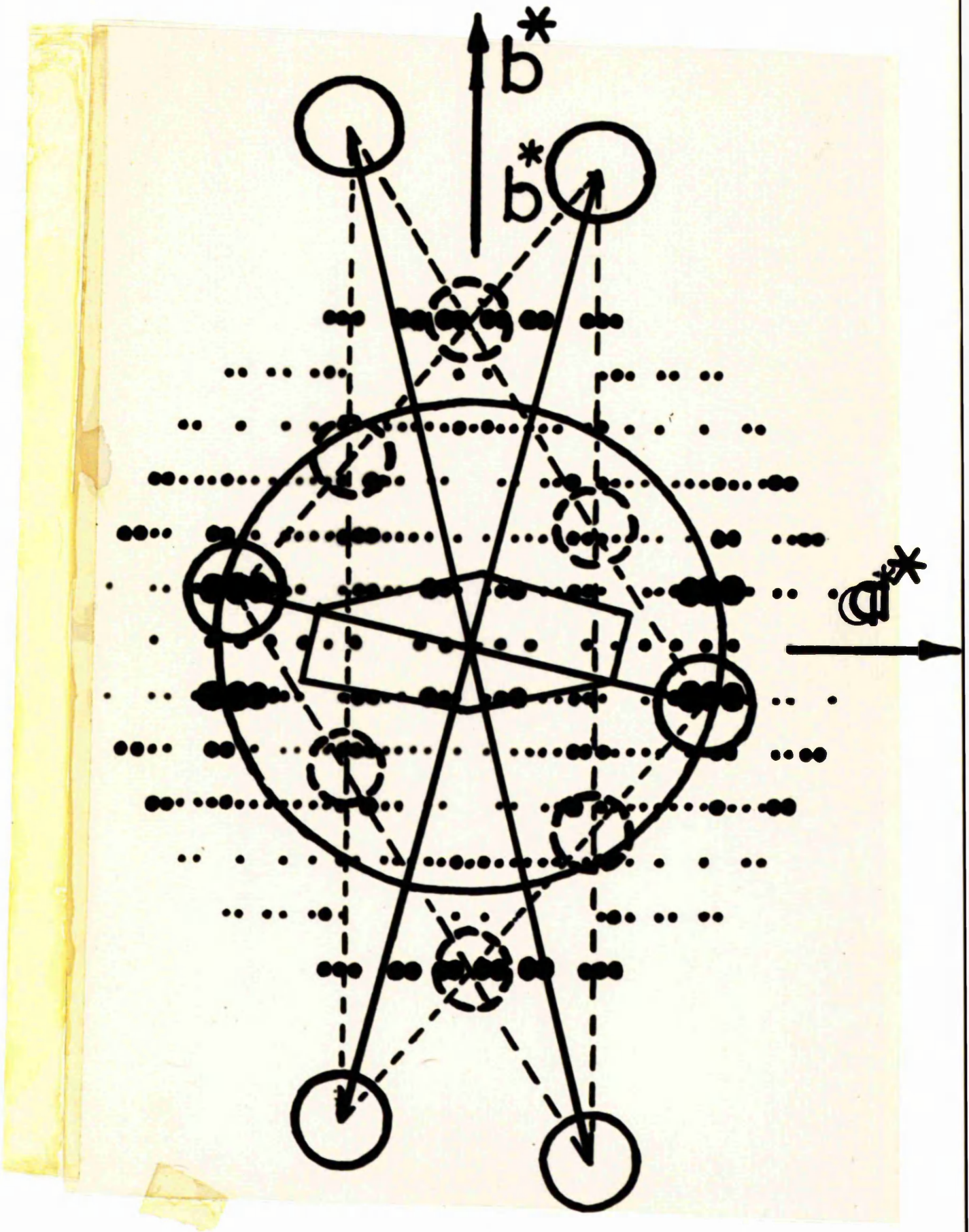


FIG. 4.12.

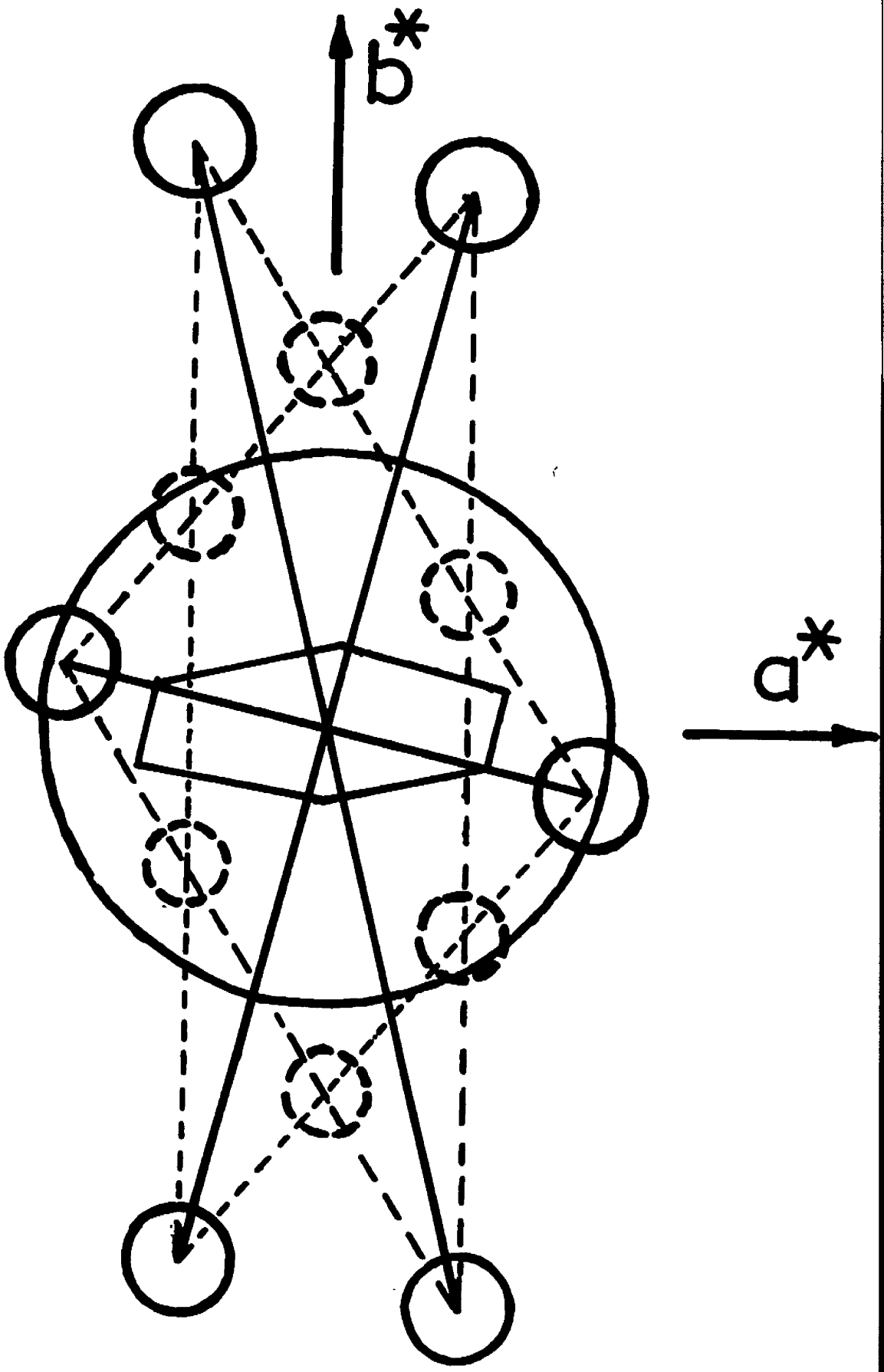


FIG. 4.12.

Figure 4.13.

Final shape of the molecule as obtained from the evidence of both principal and subsidiary peaks.

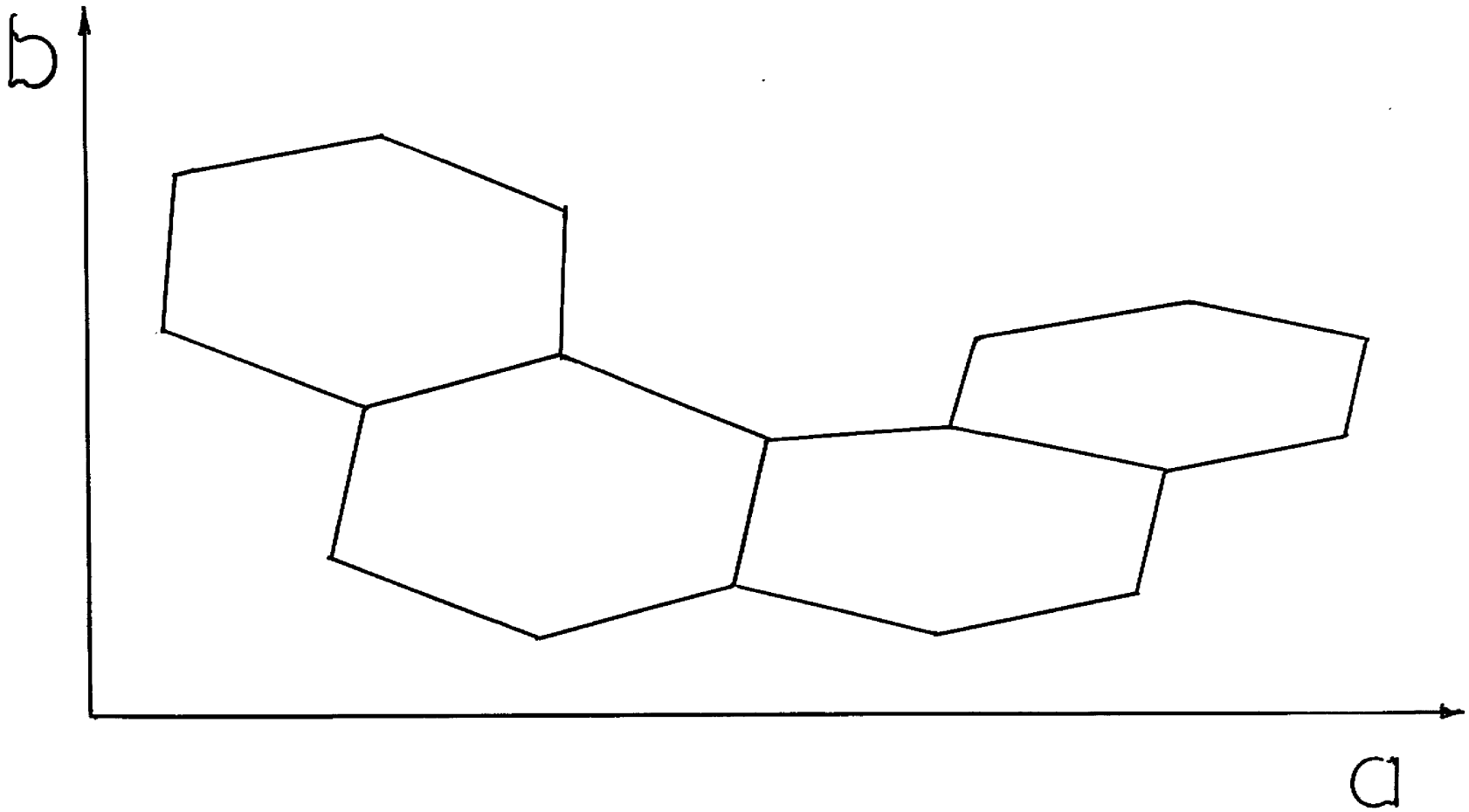


FIG.4.13.

essentially correct and the atoms would refine, by Fourier methods, to their exact positions.

4.6. Attempts to determine the molecular position by Fourier-transform methods and the refinement of the structure. The molecular shape having been established, a molecular location was carried out by the Fourier-transform method described in section 2.4, using a programme written by Dr. R. A. L. Sullivan for a mercury computer. For this, two sets of six weak reflexions of low Bragg angle were selected. The map obtained from these, contained a few minima, the coordinates of the lowest of which were x = 0.2333, y = 0.15 (there was another subsidiary minimum at the positions x = 0.300 & y = 0.217).

The molecule was then placed in this position, and the structure factors for all the reflexions were computed for this trial structure. This showed a reasonable measure of agreement between the Fo's and the Fc's with the R - value of 0.52. The initial refinement was then carried out by Fourier methods using phases calculated from the trial structural parameters. Considerable difficulties were experienced in refining this projection due to a large number of atoms overlapping. However, in three cycles, the R - value was reduced to 0.39. The set of structure factors calculated corresponding to the latest set of atomic coordinates showed a very good measure of agreement with the observed structure factors. This was very encouraging. The fourth Fourier synthesis was computed using the phases calculated from the latest set of coordinates, ~~and is shown in fig. 4.14.~~ The new coordinates derived from the suggested shifts were next used to

Figure 4.14.

Optical Transform of a molecule in the [001] projection with the corresponding weighted reciprocal lattice section superimposed.

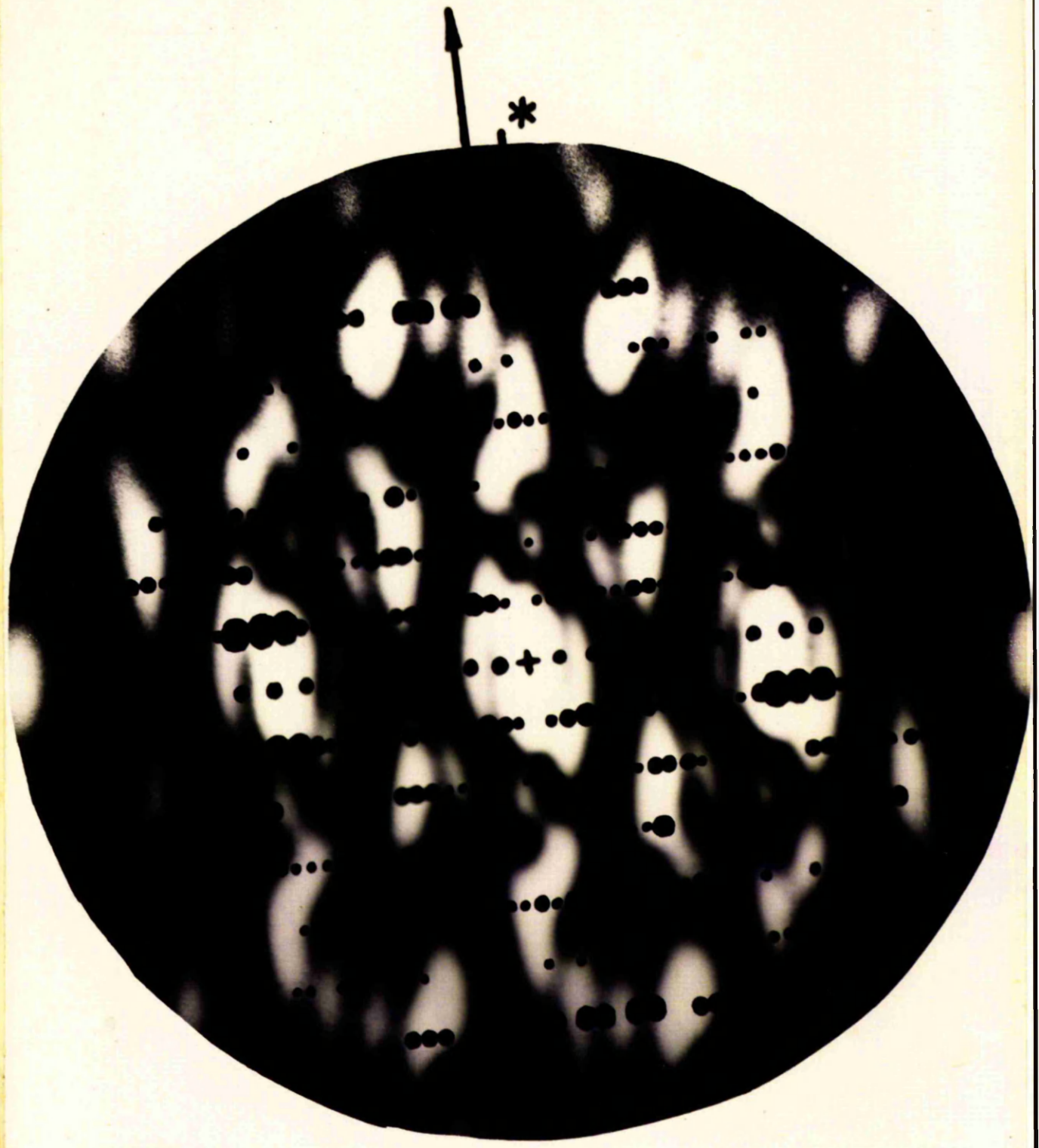


FIG. 4.14.

FIG. 4.14.

re-calculate the structure factors, but these showed no further improvement. Clearly the Fourier refinement had not proceeded as expected. Refinement was then undertaken by the (F_o-F_c) synthesis. In two cycles the R - value reduced to 0.37 after which the structure again ceased to refine. The (F_o-F_c) synthesis calculated at this stage is shown in fig. 4.15. The method of least squares (as described in section 2.7) was then employed, but this produced some shifts (maximum of .15A^o) in one or two atoms, particularly in the y - coordinate of atom N_6, which tended to make one of the benzene rings concave and so were not considered sensible. After two cycles the R - value was 0.33, and it seemed that the refinement had been completed at this stage. But the final molecular shape was unsatisfactory from chemical considerations and, in addition, the R - value was rather high. The structure had not refined properly for this molecular position and it seemed that perhaps this position in the molecular location map did not correspond to the correct position of the molecule in the unit cell. It was, therefore, decided to undertake further refinement by placing the molecule at the second minimum position. In order to do this, a set of structure factors was computed corresponding to the set of trial coordinates, and this gave the R - value of 0.55. The structure factor agreement was, in general, good; as such Fourier synthesis were computed in an effort to refine the structure. After three successive stages of Fourier refinement the R - value fell to 0.45. This method seemed to be ineffective to refine the coordinates further, however, so (F_o-F_c) synthesis were then computed in order to continue the structural

Figure 4.15.

Difference synthesis in the [001] projection prior to the commencement of least squares refinement which tended to make the benzene ring B concave. Contour are at intervals of $0.5e/\AA^2$.

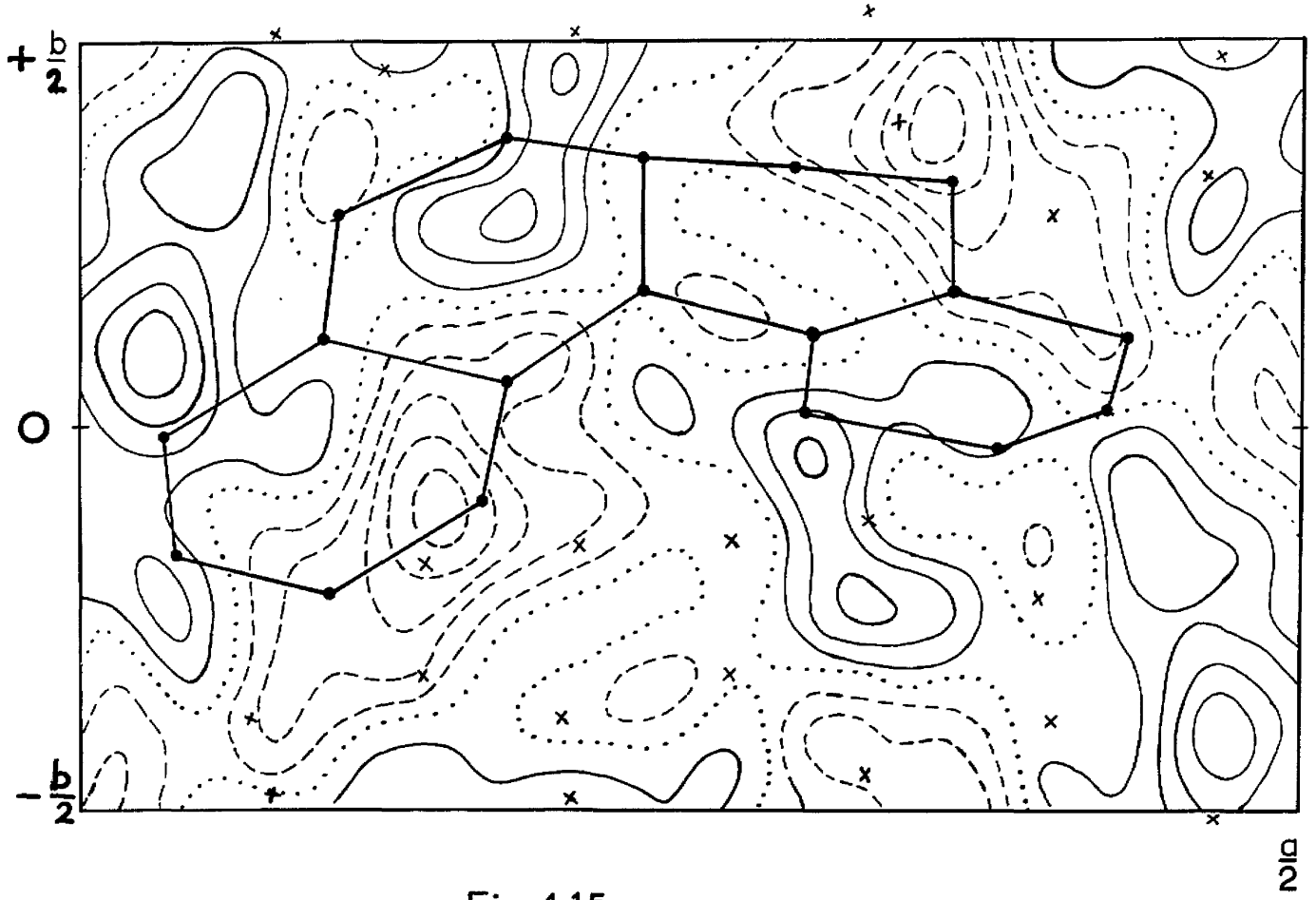


Fig.4.15.

refinement. After three successive stages of difference Fourier refinement the R - value fell to 0.40, but attempts to refine the structure further proved unsuccessful.

4.7. <u>A general survey:- a new approach envisaged.</u> As pointed out in section 4.5. the shape of the molecule in the [001] projection had been determined quite satisfactorily by an optical transform method, and two molecular location calculations were carried out using two sets of reflexions which gave a few possible positions for the molecule. Refinement by the continued use of the Fourier, difference Fourier and least-squares (for one position) methods was stopped at a rather high R - value for each position. The most outstanding features of a typical difference map produced during this refinement (fig. 4.15) were two positive peaks at the positions x = 0.029, y = 0.116 and x = 0.0616, y = 0.396 of peak heights 2.4 $e/\mathring{A}^2$ and 1.4 $e/\mathring{A}^2$ respectively, which were more than 1 $\mathring{A}$ away from the nearest atom and therefore difficult to remove. Furthermore, some atomic shifts indicated by difference Fourier and least-squares methods were not sensible at all.

These were the points which aroused suspicions as to the correctness of the structure. The situation seemed to show some signs similar to the structure of triphenylene published by Klug (1950) where, as has been shown by Pinnock et al.(1956), the molecular orientation was correct but the molecular placings were wrong and a small displacement of the molecule from the correct position resulted in the R - value remaining at a high level. An error of this type showed itself, in abnormally short non-bonding distances between some of the atoms of different molecules.

In view of these observations it seemed advisable to explore other possibilities towards the solution of the structure, particularly, in an endeavour to redetermine the molecular position, a new approach - "molecular location by minimum residual calculations" had been envisaged, which seemed to offer a promising alternative. The theory and the principles of such a method is described in the next chapter.

Chapter 5

Introduction to the minimum residual molecular location method.

5.1. Introduction

In any structure determination where the asymmetric unit is a rigid molecule, as is generally the case in an organic structure, there are two distinct steps in which one can take in its solution. The first consists of an approximate determination of the orientation of the molecule, and the second the location of its position in the unit cell. The first step can be carried out satisfactorily either by optical transform methods or from a study of the Patterson peaks near the origin of the map, and the second step can be achieved using a very useful method for molecular location due to Taylor and Morley (1958), described in section 2.4. The method has been found to be useful in quite a few practical cases, but its application in the case of symmetrical molecules may not give unambiguous results. It is quite likely that in such cases one would get a large number of subsidiary minima, which Taylor calls "pseudo-homometric" structures. Often the position of the minimum is not uniquely determined, and one gets a rather spread-out region instead of a sharp minimum. This is what may be expected if the orientation of the molecule is somewhat incorrect. Moreover, just a small number of weak reflexions (~ 6) which are used to determine the molecular location may not be a sufficiently strong test criterion for distinguishing the correct

position of the molecule unambiguously.

This fact, in particular, makes it important to use as many reflexions as possible to determine the molecular position. With the availability of high speed computing facilities it is quite convenient to calculate the R-values, for a large group of reflexions, for all the positions of the molecule in the unit cell once its orientation and configuration have been determined. The advantages of this method are that (i) it produces a more severe test criterion for obtaining the proper position of the molecule, and (ii) the general features of such calculations may even suggest whether, in the first case, the orientation has been correctly determined. The second advantage, in particular, is quite important.

It is known (Wilson, 1950) that for a random centro-symmetric structure the residual has the probable value of 0.83. Thus if the orientation of the molecule is reasonably well determined the calculation of the residual with the molecule at different points in the cell should give a sharp minimum value (very much less than 0.83) indicative of the correct position of the molecule, and the other minima would be relatively shallow. If the configuration of the molecule has been incorrectly determined, all the positions in the unit cell corresponding to this configuration would represent random structure and so the R-value over the entire area of the cell would be quite large.

5.2. Basic principles of the method.

For a particular orientation of the molecule the best molecular

position in the unit cell will be where the collection of calculated F's are in good agreement with the collection of observed F's. The minimum value of the residual, $R_{(x,y)} = \sum ||F_o| - |F_c|| / \sum |F_o|$, is the familiar criterion which is used to determine the position of the molecule. The position of the molecule in the unit cell is varied systematically and the value of R computed each time. This is an exceedingly time consuming process, and computer techniques have been adopted. The computation has been simplified by calculating the residual relating to an origin fixed in the molecule initially, and then moving the molecule about the unit cell. The quantity $R_{(x,y)}$ is plotted as a function of the position of the molecule in the unit cell and the true molecular position is then given by the minimum of this function. A computer programme has been written to perform the calculations and is described in detail later in section 13.2.

To be strictly correct the F_o's should be rescaled to the F_c's for each molecular position in order to obtain a true value of R. Although this operation can be carried out in a matter of seconds on the computer it takes much longer than the calculations of the F_o's, and so increases the total calculation time by a considerable amount. However, since the calculated scaling factors are not likely to vary a tremendous amount, the F_o's can be scaled using Wilson's statistics and thereafter remain constant. The values of R obtained using these F_o's will be approximate, but as the molecule is also approximate this is not serious.

Usually the molecular model which is used will be inaccurate one,

so the low order reflexions will be most suitable for the calculation, because these are the reflexions which are comparatively insensitive to the errors in the coordinates. Generally in the early stages of a structure determination one tries to get agreement for the strong reflexions, a qualitative sort of agreement is sought and it is considered satisfactory if the strong reflexions calculate strong and weak ones weak. This means that in the early stages the conventional R-value is largely indicative of the agreement for strong reflexions. Thus it is appropriate to make exclusive use of the strong reflexions. However, the experience of some workers (Taylor, 1954; Cochran and Douglas, 1957) in structure determination has been that the weak reflexions provide a better test criterion for determining the correct structure. This suggests that the calculations might be repeated using weak reflexions only, and when the results of the two calculations agree one may feel confident about the correctness of both the model and its position in the cell. This kind of approach in the use of this method seems much more valuable than the indiscriminate use of strong and weak reflexions. One particular advantage in using the strong reflexions exclusively in the first calculation is that the R-values for these reflexions would show the kind of variation which might help to distinguish a reasonable structure from a random one. This certainly would not be the case if only the weak reflexions were used, for in this case the R-values would be higher even for the correct structure. The use of all the strong and weak reflexions in the early calculations will give the result in a form which would lose its discriminating feature that recognises a random structure from the correct one. However, if

one is confident of the orientation and configuration of the molecule to start with, there is no harm in using both strong and weak reflexions simultaneously for calculating the position of the molecule in the cell.

5.3. Applications of the method to known structures

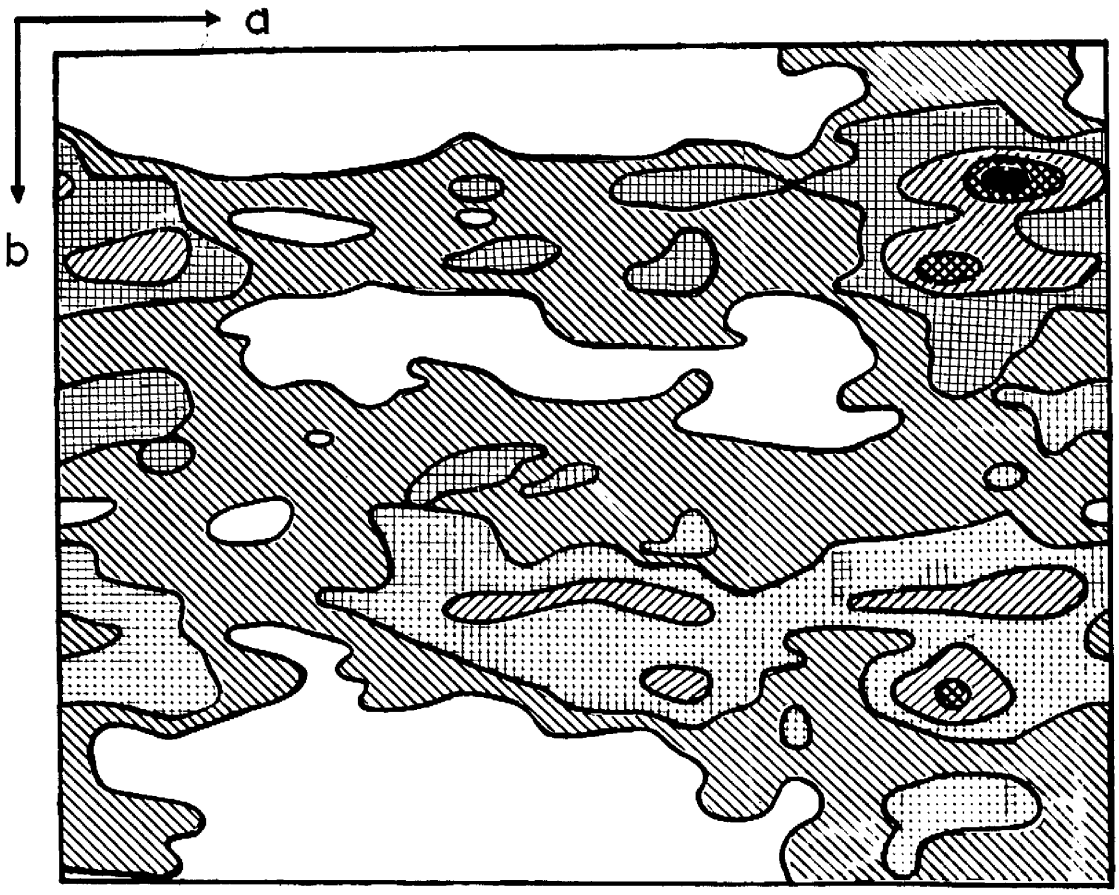
The method has been applied quite successfully to a number of problems, involving both known and unknown structures. In the following are given some examples which provided rigorous tests for the correctness and also the usefulness of this method.

5.3.1. The Structure of triphenylene

This technique was first used in the reinvestigation of the molecular position of triphenylene. The structure was initially investigated by Klug (1950), and was later redetermined by Pinnock, Taylor & Lipson (1956) who found a completely different position for the molecule. The published structures have molecules of the same shape and orientation, using the relative coordinates of the Klug's structure the computation has been carried out by using 40 low order strong reflexions. The result of this calculation is presented in the form of a contoured map (Fig. 5.1) where the lowest minimum is shown by the small black region ($x = 0.4525$, $y = 0.08083$) indicating the position of the molecule. The position of this minimum is exactly the same as that found by Pinnock, Taylor & Lipson (1956). There is also a minor minimum at the position ($x = 0.425$, $y = 0.13083$) found by Klug.

Figure 5.1.

Molecular location map for triphenylene as obtained by the minimum residual method. The black region indicates the position of the molecule, i.e. position of the lowest minimum.



KEY R<22 R<30 R<40 R<50 R<60 R< 80

Fig. 5.1.

5.3.2. The Structure of D-xylose

A structure which has recently been solved in this department is D-xylose, which has the space group $P2_12_12_1$ with four molecules in the unit cell. Data for this structure was therefore readily available and the author is grateful to Miss J.V. Ballard for making it so. This presented a good opportunity to try out the minimum residual molecular location technique to see how well the molecular position so obtained agreed with the position found by Miss Ballard. The calculations were carried out using 40 low order strong reflexions and the original trial molecule (not the refined molecule). The position of the single sharp minimum ($y = 0.16$, $z = 0.315$) on the resultant $R_{(y,z)}$ map agreed within 0.05 Å of the final molecular position in the refined structure.

5.4. Discussion

Of the two applications of the minimum residual molecular location method the first was published with correctly oriented molecules in incorrect positions. One may assume, therefore, that the relative positions of the molecules in this structure were difficult to find using convenitonal methods. In the second, the trial coordinates were used to find the position of the molecule. During these applications it was observed that in both the cases the method offered a more exact way of fixing the positions of the molecules than the conventional methods. In the first map the values of R were generally less than 0.83; while in the second, although some of the R-values were much higher than 0.83, a single sharp minimum was apparent indicating the position of the molecule. In view of the above observations it was felt that this method

was a very useful one, especially at an early stage in the structure determination when there was still considerable doubt about the shape of the molecule. It was therefore considered desirable to apply this method to the structure of the naphthocinnoline which had so far presented an insuperable difficulty.

Chapter 6

Application of the minimum residual molecular location method to the [001] projection of the naphthocinnoline

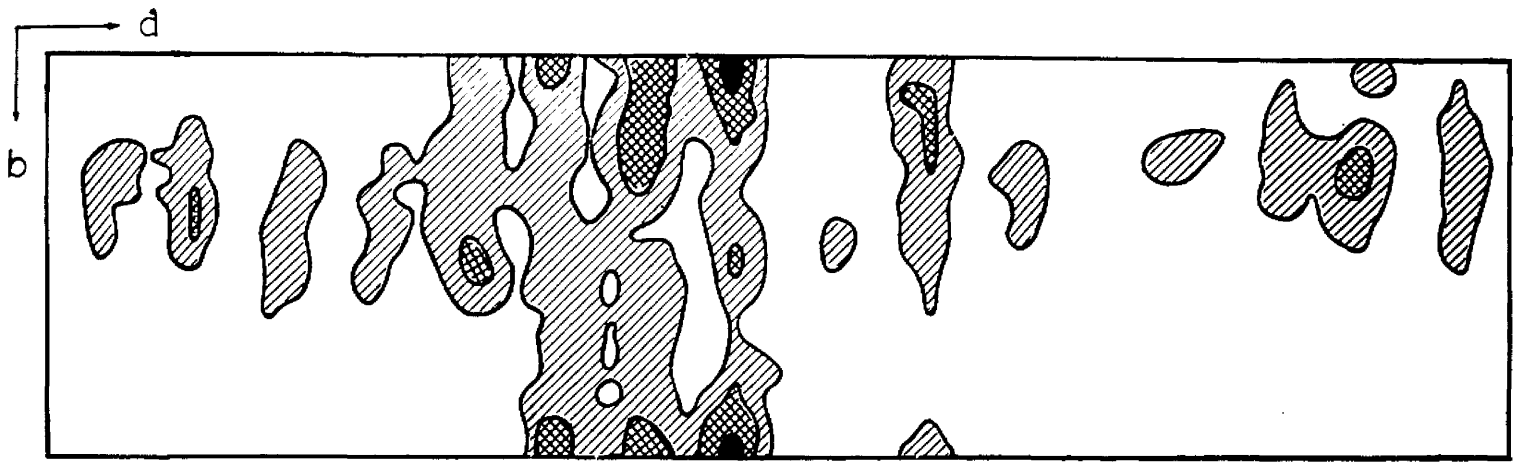
6.1. Determination of the molecular position by this method.

As was described in section 4.6, the orientation of the molecule in the [001] projection was determined by the optical transform method and Taylor's technique was then applied to find the position of the molecule in the unit cell. The maps $G_{(x,y)}$ showed two possible positions but the refinement of both structures stopped at the values of $R \sim 0.35$.

In order to determine the position of the molecule the minimum residual technique as described in chapter 5 was used. It was of interest to see how effective the method would be. 40 low order strong reflexions were used for the computation and the resulting $R_{(x,y)}$ map is presented in fig. 6.1. The lowest value of R is at x = 0.2333, y = 0.[illegible] as shown by the small black region which is different from either of the two positions obtained using Taylor's method (described in section 4.6). The R-value at this position is 0.34, whereas its values at all other points are much higher (but generally less than 0.83, the probable value of the residual for a random structure, Wilson 1950). The calculation was then repeated using 40 low order weak reflexions, and the contoured $R_{(x,y)}$ map is shown in fig. 6.2. The position of one minimum at x = 0.2333, y = 0.[illegible] (shown by the small black region) is exactly the same as that obtained using strong

Figure 6.1.

Molecular location map for the [001] projection of the naphthocinnoline as obtained by the minimum residual method using 40 low-order strong reflexions. The black region indicates the lowest minimum.

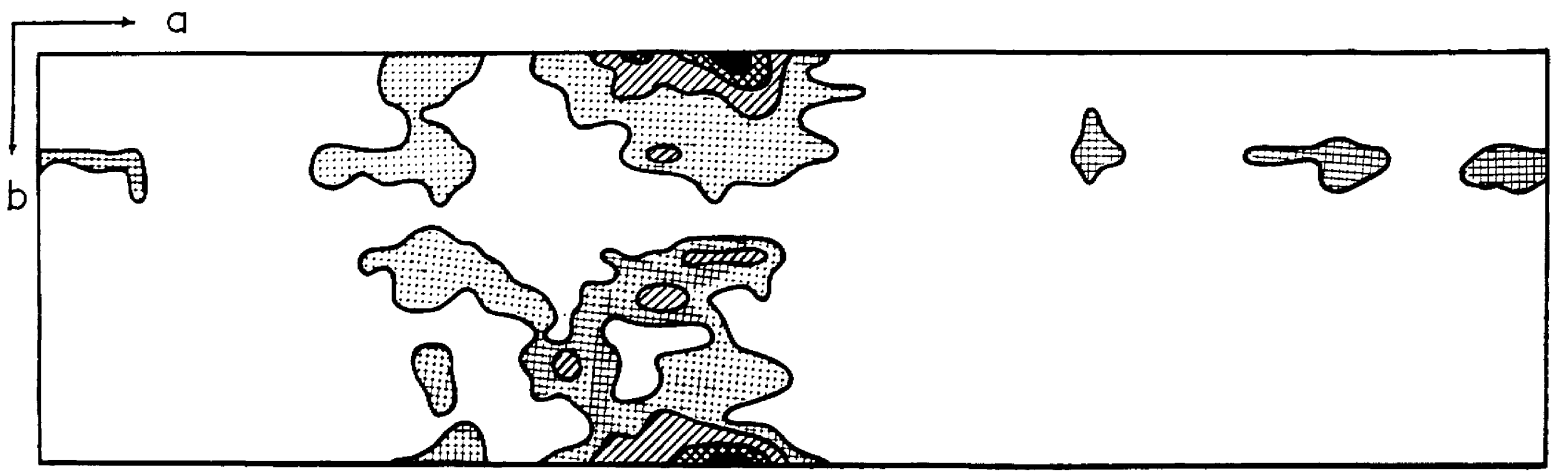


KEY R<40 R<50 R<60 R< 90

Fig. 6.1.

Figure 6.2.

Molecular location map for the [001] projection of the naphthocinnoline as obtained by the minimum residual method using 40 low-order weak reflexions. The black region indicates the lowest minimum.



KEY R<50 R<60 R<70 R<80 R<150

Fig. 6.2.

reflexions although there are other minima as well, and the R-values are generally much higher than 0.83. A further $R_{(x,y)}$ map computed using 40 low order reflexions irrespective of magnitude is given in fig. 6.3. The main minimum is the same as the common minimum of the other two maps, but there were other subsidiary minima as well. In this case, instead of a sharp minimum, an extended region is obtained, which makes the position of the molecule less definite.

The results of the $R_{(x,y)}$ maps, mentioned above, confirmed the theoretical predictions. It seems that the best procedure is to calculate the $R_{(x,y)}$ maps using the low order strong reflexions then, if the map shows only one prominent minimum and the R-values are generally small, to calculate the $R_{(x,y)}$ map using the low order weak reflexions. One of the minima should agree with the principal minimum on the other map if the orientation is correct.

6.2. A subjective application of this method for selecting a reasonable structure.

$R_{(x,y)}$ maps have been computed using different criteria as described in the previous section. It is clear that the chances of interpretation of the map are greatest when strong reflexions are used, in particular, if the orientation of the molecule is wrong then this map tends to have residuals greater than 0.83 and shows several minima. This in itself is a very useful guide to the correctness of the orientation of the molecule.

The coincidence of three main minima at a particular point also indicated the correctness of the molecular shape. Although these gave

Figure 6.3.

Molecular location map for the [001] projection of the naphthocinnoline as obtained by the minimum residual method using 40 low-order strong and weak reflexions.

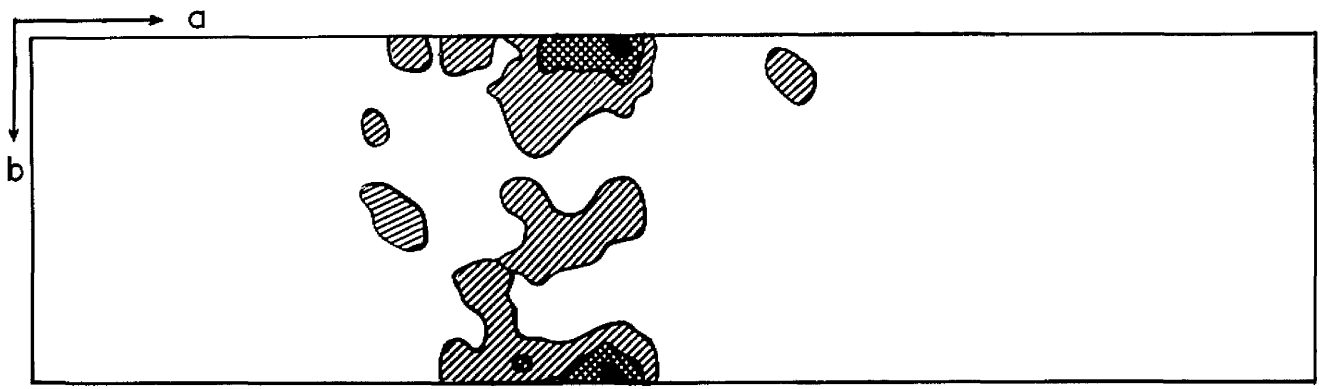
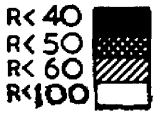


Fig. 6.3. KEY



clear evidence of the approximate position of the molecule, no claim could be made at this stage that it would lead to the correct structure of the naphthocinnoline. However, it is considered justifiable to attach some significance to these results and then use them as a further step in the determination of the structure.

Chapter 7

Refinement of the hko projection by Fourier and least-squares methods

7.1. Refinement by Fourier and difference Fourier methods. As has been mentioned in the previous chapter, that a new position of the molecule in the unit cell had been found by minimum residual technique, and it was considered worthwhile to attempt to refine the structure. The molecule was then placed in this position and the calculation of structure factors for the trial structure showed a reasonable measure of agreement when compared with the observed structure factors with the residual of 0.50. The initial refinement was then carried out using Fourier methods; the Fo syntheses were computed using the phases calculated from the trial structural parameters. In three successive cycles of Fourier refinement the R - value was reduced to 0.40.

It had become evident that the usual process of refinement by the continued use of the Fourier synthesis would not work with this projection because of the non-resolution of the atoms in each synthesis. It was then decided to use a (Fo - Fc) synthesis (Cochran, 1951) to find the shifts, if any, of the atoms which would improve the agreement. The (Fo - Fc) synthesis was carried out using the structure factors which had just been determined and it was found that seven atoms (5, 8, 11, 12, 15, 16 & 17) were lying well inside the negative regions, four atoms (2, 6, 14 & 18) were lying on fairly steep gradients and seven atoms (1, 3, 4, 7, 9, 10 & 13) out of eighteen were situated on positive areas. However, the indicated shifts were determined and the process

of refinement was continued. After three successive cycles the value of the residual was 0.37. Calculation of structure factors using the coordinates derived from the latest synthesis (fig. 7.1)did not show any further improvement, and the most striking feature of the map was a positive peak at the position x = 0.04, y = 0.633 of peak heights about 2.6e/Å^2, which was more than 1Å away from the nearest atom and therefore difficult to remove. Although the map indicated some adjustments in the temperature parameters, no attempt was made to do so at this stage, instead, it was decided to continue the refinement by the method of least squares.

7.2. Refinement by the method of least squares. The refinement of the coordinate parameters was then undertaken by the method of least squares (using the full matrix), an overall constant temperature factor B = 3.0Å^2 being taken for the molecule. After two successive cycles of refinement the residual came down to 0.34, at which stage the coordinate shifts were insignificant. The average shift indicated in the x - coordinates at the end of the second cycle was of the order of 0.002Å and the maximum shift was 0.003Å. For the y - coordinates, the average shift was 0.003Å and the maximum 0.0045Å. The refinement was proceeding very slowly so at this stage it was decided to refine both the positional and temperature parameters together. This reduced the residual to 0.326 after which this method failed to refine the structure further.

7.3. Effects of overlap and the need for a different approach to refine the structure. From the above it can be seen that the refinement by Fourier, difference Fourier and least-squares methods proceeded in the

Figure 7.1.

Projection of $(\rho_0 - \rho_c)$ onto $[00\bar{1}]$, showing the extent of overlap and high background levels. Contours are at intervals of $0{\cdot}5$ e/Å^2.

(The scale of the figure along the a-axis is different from that along b-axis).

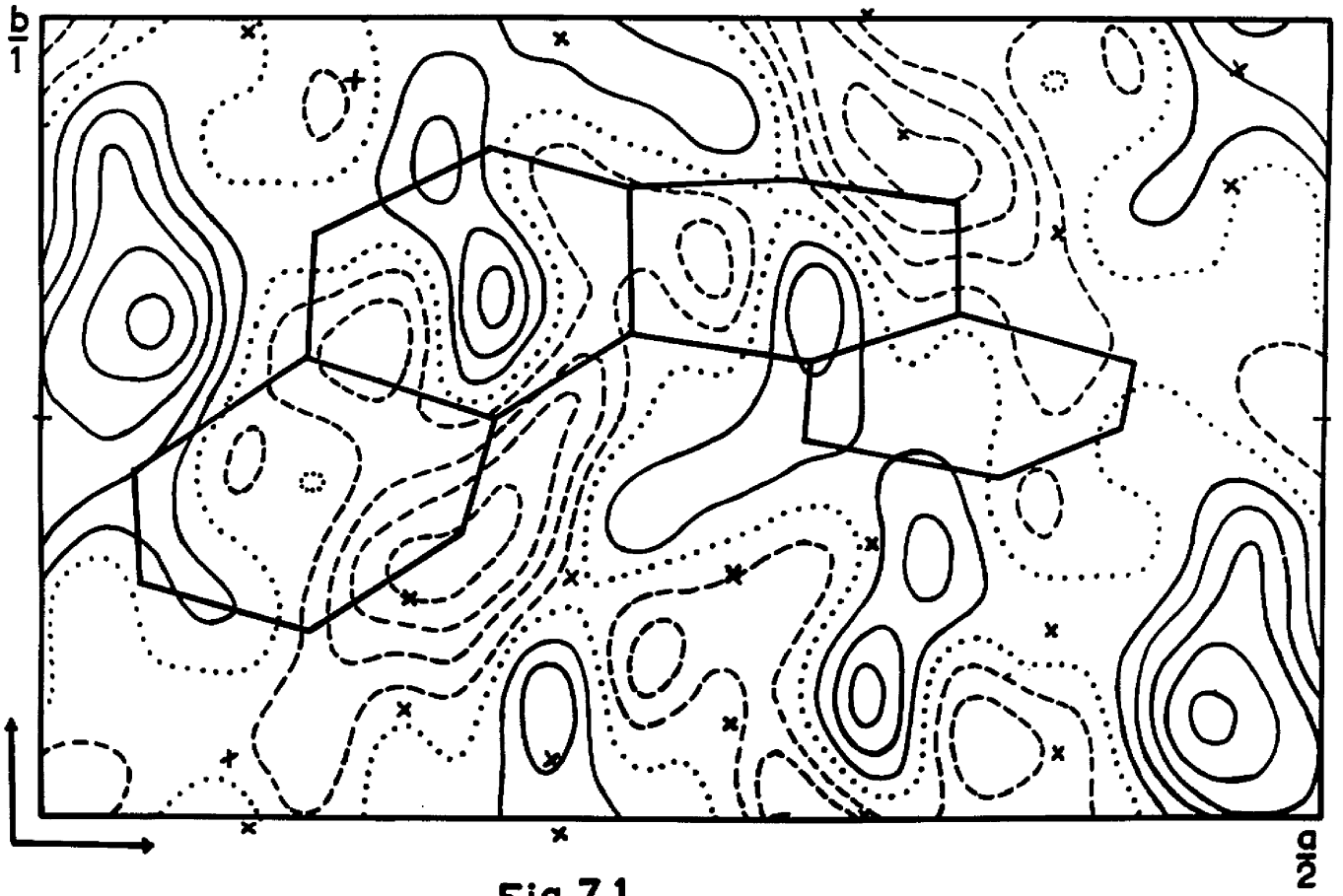


Fig. 7.1.

same manner as described before in sections 2.9 & 4.7. The residual had been reduced from 0.50 to 0.326 which is still rather high. Major difficulties experienced in the process of refinement by these methods were due to a great deal of overlap in projection. Attempts to refine further by these conventional methods failed to yeild any fruitful result.

Since the conventional methods of refining the structure would appear to be impracticable, other types of approach have to be resorted to, and the following chapters contain what is hoped is a reasonably useful summary of these approaches.

Chapter 8

The refinement of atomic parameters by direct calculation of the minimum residual.

8.1. Introduction. After an approximation to the correct structure is obtained, the next important step in the methods of structure determination is the refinement of the structural parameters. As a rule, this is done by Fourier, difference Fourier or least-squares methods. However, the refinement is not always a straight forward process, and quite frequently one may come across structures which, for example, seriously overlap in projection. The difficulties in such cases are that the parameters of the overlapping atoms interact with each other and so cannot be treated independently. In such a case refinement by Fourier synthesis soon reaches its limit since the peak positions no longer correspond to the atomic sites. In principle at least, these difficulties may be overcome by the use of the modified difference Fourier method (Cruickshank, 1952), or in the case of least squares refinement, by including the relevant off-diagonal terms of the matrix in calculating the corrections to the parameters. Nevertheless, there may arise cases of great practical difficulty where these methods may not be very helpful, for instance, the interpretation of difference maps may be ambiguous and the least-squares method will refine the parameters to the correct structure only if small corrections are required (which is tantamount to saying that the phases of almost the entire data are reliably known). Although some successes have been reported (Curtis, 1959; Cruickshank, 1961) where the maximum corrections of ~ 0.5 Å to 0.6 Å to the positional parameters have been made, but

as Cruickshank (1961) points out the success in the particular case he cites was partly because the rest of the atoms needed only small shifts. However, one feels very sceptical if equally happy results would be obtained in cases where the majority of the atoms are (say) 0.2 to 0.4A° away from their correct positions, with one or two atoms being even as far as 0.5A° away. Even the subjective use of the least-squares method, i.e. the use of fudge factors, can hardly bring the atoms to their correct positions. In fact, the calculated corrections to the parameters of these atoms will not only be insensible themselves but will also produce undesirable results on the other atoms because of the strong correlations of the parameters at such an early stage of structure determination (Geller, 1961). Thus the structure may stop refining at a comparatively higher R - value having converged to a secondary minimum. Whenever this occurs and there are good reasons to suppose that the structure is essentially correct, it is common to resort to structure factor graphs (Bragg & Lipson, 1936) in an effort to improve the agreement between the observed and the calculated data. In view of this it is not difficult to see the desirability of a controlled and systematic variation of the structural parameters to get the better agreement between the observed and calculated data. If, for example, the atoms are allowed to systematically scan, or explore, the immediate neighbourhood (say, within a limited circle of radius 0.1Å with its trial position as centre) in order to get a better overall agreement between the observed and calculated data, one may hope to bring even the badly placed atom to its correct position in successive cycles.

Furthermore, the advantage of this approach would be that this would not only stop the atom from moving widely, but that, in general, this would also mean that the chances of getting the atom to its correct position in successive cycles are much brighter. Based essentially on this consideration a refinement method has been worked out which might be called "the refinement of atomic parameters by direct calculation of the minimum residual". A summary of this method has been written and communicated with a view to its publication in Acta Crystallographica.

8.2. Principles of the new methods. In this method the criterion most familiar to the crystallographers, the disagreement residual, $R = \sum\|F_o|-|F_c\|/\sum|F_o|$ is used as a test of the correctness of the structure and it was decided to minimise R in this work.

Booth (1949) investigated the theoretical possibility of a relaxation method of refinement in which the corrections to the parameters are calculated from the incremental relationship,

$$\Delta\phi = \frac{\partial\phi}{\partial u_j}\,\Delta u_j$$

where u_j is any structural parameter and ϕ is some measure of agreement between the observed and calculated structure factors. Equations such as this are correct only if Δu_j is very small. However, if

$$R = \psi(u_1, u_2, \cdots u_j)$$

then the expression, $\Delta R = \psi(u_1, u_2 \cdots u_j \cdots) - \psi(u_1, u_2, \cdots u_j + \Delta u_j, \cdots)$ is always correct whatever may be the magnitude of Δu_j. Δu_j is calculated by trial and error to make ΔR minimum negative.

If it is assumed that all parameters are independent, we may vary each parameter systematically from $u_j - n\Delta u_j$ to $u_j + n\Delta u_j$ in $2n$ steps of Δu_j. The value of R is calculated each time. The value of the parameter, say u_j', which corresponds to the lowest of the $2n+1$ values of R is taken as a better value for this parameter and is used in all subsequent calculations. The same process is repeated for the next parameter u_j+1 and so on. In this way the value of R can be systematically reduced. The values of the increment, Δu_j, can be adjusted to be appropriate to the circumstances - larger increments at the early stages of refinement, small increments at the later stages. The limits of variation of the parameter $\pm n\Delta u_j$ can also be varied by adjusting n so that $n\Delta u_j$ corresponds to the maximum change to be tolerated in any parameter at any stage of refinement.

The individual temperature factors, B_j, can be refined by the same type of process. The value of B_1, the temperature factor of the first atom, is varied from $B_1 - n\Delta B_1$ in 2n steps of B_1. The residuals are calculated and compared as before and the value of B corresponding to the lowest value of R is taken to define the best value of the temperature factor and is used in all subsequent calculations.

With successive refinement of this kind, the uncertainties due to the parameter interactions will be much reduced, assuming that as atoms approach their correct positions, the interaction between the different parameters becomes less significant. This is true when the structure is completely refined, for then a small change in any of the parameters will not affect the value of R. Such an approach has been found to be helpful in a number of structures that have been tried out in this department.

The process is very time consuming and two computer programmes have been written for the calculations to be performed on the Manchester University Mercury Computer and are described later in section 13.3 & 4.

8.3. Applications of the methods. These methods have been applied successfully to four structures of different crystal classes and also various degrees of complexity, the most complex problem having 25 atoms in the asymmetric unit projected along a 12.4A° axis, and the simplest having only 8 atoms in the asymmetric unit and projected along a 6.02A° axis. The largest initial R - value was 0.35 which was refined to 0.12 and the smallest initial R - value was 0.11 which refined to 0.078. Its application to the [001] and the [010] projections of the naphthocinnoline will be described in next chapters.

8.3.1. Application to Triphenyl Phosphate. This structure has been refined by Davies and Stanley (1962) using difference Fourier methods. The space group is $P2_1/a$ and there are 23 atoms of three different types in each of the four asymmetric units. The [100] projection, along a 17A° axis shows a great deal of overlap and the difference Fourier method of refining had reduced the residual to 0.19. Using the coordinates obtained by Davies & Stanley further refinement of the structure has been carried out by the new method. Four stages of coordinate and two stages of temperature coefficient refinement reduced the residual to 0.10. During this refinement the maximum change in a coordinate was 0.17A° and the average change was 0.05A°.

8.3.2. Application to methyl ammonium alum. The structure of a low-temperature form of this salt has been determined by Fletcher & Steeple (to be published). The space group is $Pca2_1$ and there are 25 atoms

in the asymmetric unit, of five different types. The [001] projection has plane-group symmetry pmg and the length of the axis of projection is 12.4A°. There is a great deal of overlap in this projection. The structure - an orthorhombic modification of the cubic, room temperature, form (Fletcher & Steeple, 1960, 1962) - was known to be substantially correct although refinement by difference Fourier and by the full matrix least-squares methods had failed to reduce the residual below 0.24. The present methods of coordinate refinement reduced the residual to 0.13 in three cycles. During refinement the maximum change in any coordinate was 0.24A° and the mean change was 0.06A°.

8.3.3. Application to Di potassium ethylene tetracarboxylic acid. This structure has been determined in detail by Kumra & Darlow (to be published). The space group is Pbca with 8 atoms of 3 different types in the asymmetric unit. At the stage when Fourier and difference Fourier methods had reduced the residuals of the [100] and the [010] projections to 0.13 and 0.11 respectively the new methods were tried. Both projections were further refined by two cycles of coordinate and temperature factor refinement; the residual of the [100] projection, axis of projection 9.75A°, fell to 0.083 and that of the [010] projection, axis of projection 6.42A°, fell to 0.078. During the course of refinement the maximum coordinate change was 0.044A° and the mean change was 0.011A°.

Chapter 9

Refinement of the [001] projection by direct calculation of minimum residual

9.1. Introduction. Since the new methods had been successfully used so far, it was considered worthwhile to attempt to refine the structure of the naphthocinnoline in the [001] projection. The necessary calculations were performed using the computer programmes outlined in chapter 13 sections 3 & 4.

9.2. The strategy of the refinement and experience. The trial structure of the [001] projection, plane group pgg, was obtained by the new molecular location method (described in chapter 5 & 6) and refined using Fourier and difference Fourier methods as described in section 7 to an R - value of 0.37. The projection axis was 10.75Å and there was considerable overlap. Further refinement by full matrix least-squares method only reduced the residual to 0.33 in two cycles after which it would not further refine. Starting from the same initial residual of 0.37 the new method of coordinate refinement described in chapter 8, with a range of scan 0.1Å in steps of 0.02Å, reduced the residual to 0.29 in the first cycle, an initial rate of refinement much greater than that of least-squares. Most of the atoms were shifted significantly, the largest coordinate shift being 0.1Å (which was the maximum shift allowed). The new atomic coordinates were plotted and found to be sensible. When the next cycle was continued the R - value fell by 0.02 and only a few atomic positions were changed during the second cycle. It was then considered desirable to adjust the scaling (A')

and overall temperature (B) factors, which were done using a separate computer programme available in the department. In this, two scaling constants A' and B are fitted by least-squares so that there is an optimum fit between $(A'F_o)$ and $|F_c| \exp(-Bs^2)$ over the whole range of s. It was noticed that the original scaling factors were in error by about 5% and the overall temperature factor by 0.5. (the initial overall temperature factor was increased from 2.5 to 3.0Å). Two further cycles of refinement reduced the residual to 0.24. The refinement, indeed, proceeded quite satisfactorily. A difference synthesis was computed at this stage of refinement in order to confirm that the corrections made to the atomic parameters were physically significant. The general features of this map were obviously improving and the background levels were also reasonable (the highest peak height being 1.4e/Å^2). The observed structure factors were rescaled against the calculated structure factors and in a further two cycles the residual was reduced to 0.18. (The unobserved reflexions were included in the calculations assuming their values to be half that of $F_{min.}$, where $F_{min.}$ is the local minimum value of the observed structure factor.) A difference synthesis computed at this stage ~~is shown in fig. 9.1, which~~ suggested that a different temperature factor for the various atoms should be employed; as such the individual temperature factor refinement was undertaken separately by the new temperature parameter refinement method using the computer programme described in section 13.4. During the first cycle of temperature factor refinement considerable changes in the B - values were observed, the largest being 0.5 (which was the maximum change allowed) and the residual also fell to 0.17. When a further cycle was performed no

appreciable change either in the temperature factors or in the R - value was observed. Using the latest values of the temperature factors one more stage of coordinate parameter refinement reduced the residual to 0.16 after which it would not refine further. At this stage the increment (Δu_j value) was reduced to 0.01Å, i.e. half the previous value. The shifts in the positional parameters were barely significant, the average shift in a coordinate being about 0.01Å and the maximum shift 0.02Å. A Fourier and a difference Fourier synthesis calculated at this stage are presented in fig. 9.2 (a & b) showing the molecule in thick lines and the symmetry related one in broken lines. There was a striking improvement in the difference map. Most of the peaks outside the molecule had disappeared. The background variations were also reasonable. The initial and the final coordinates of the naphthocinnoline in the [001] projection are given in table 9.1 which also shows the total shifts made to the atomic coordinates to bring them to their correct positions. Three atoms, 9, 10 & 16 (marked by crosses) needed shifts $>$ 0.5Å and the majority of the remaining atoms needed shifts of about 0.2 to 0.3Å. The positions of hydrogen atoms were not apparent in these maps. The theoretical positions of all hydrogens were calculated, assuming a C - H bond length of 1.08Å, and it was observed that the positions of six hydrogens along the extension of the diagonals of the ring were lying on the negative regions of the difference map. Structure factors were calculated using the theoretical coordinates of hydrogens, but these did not show any further improvement in the overall agreement. A few other positions (i.e. shorter distances)

Figure 9.2(a)

The final electron density map of the [001] projection after refinement by the minimum residual methods. Contours are at intervals of $2e/\mathring{A}^2$. Zero contours are dotted, negative broken and positive contours full lines.

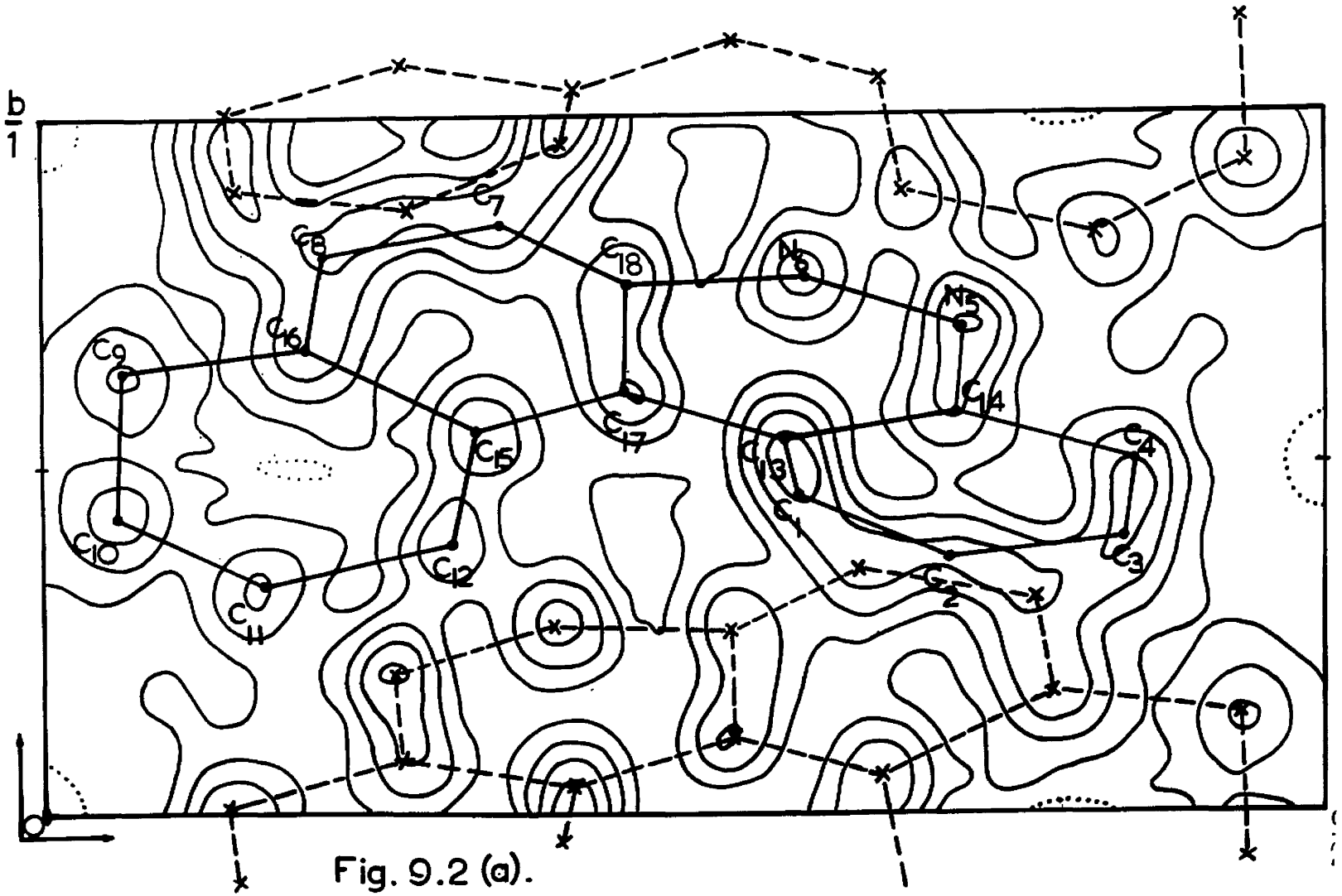


Fig. 9.2 (a).

Figure 9.2(b)

The final difference (F_o-F_c) map of the [001] projection contours are at intervals of 0.3e/Å^2. Zero contours are dotted, negative broken and positive contours full line.

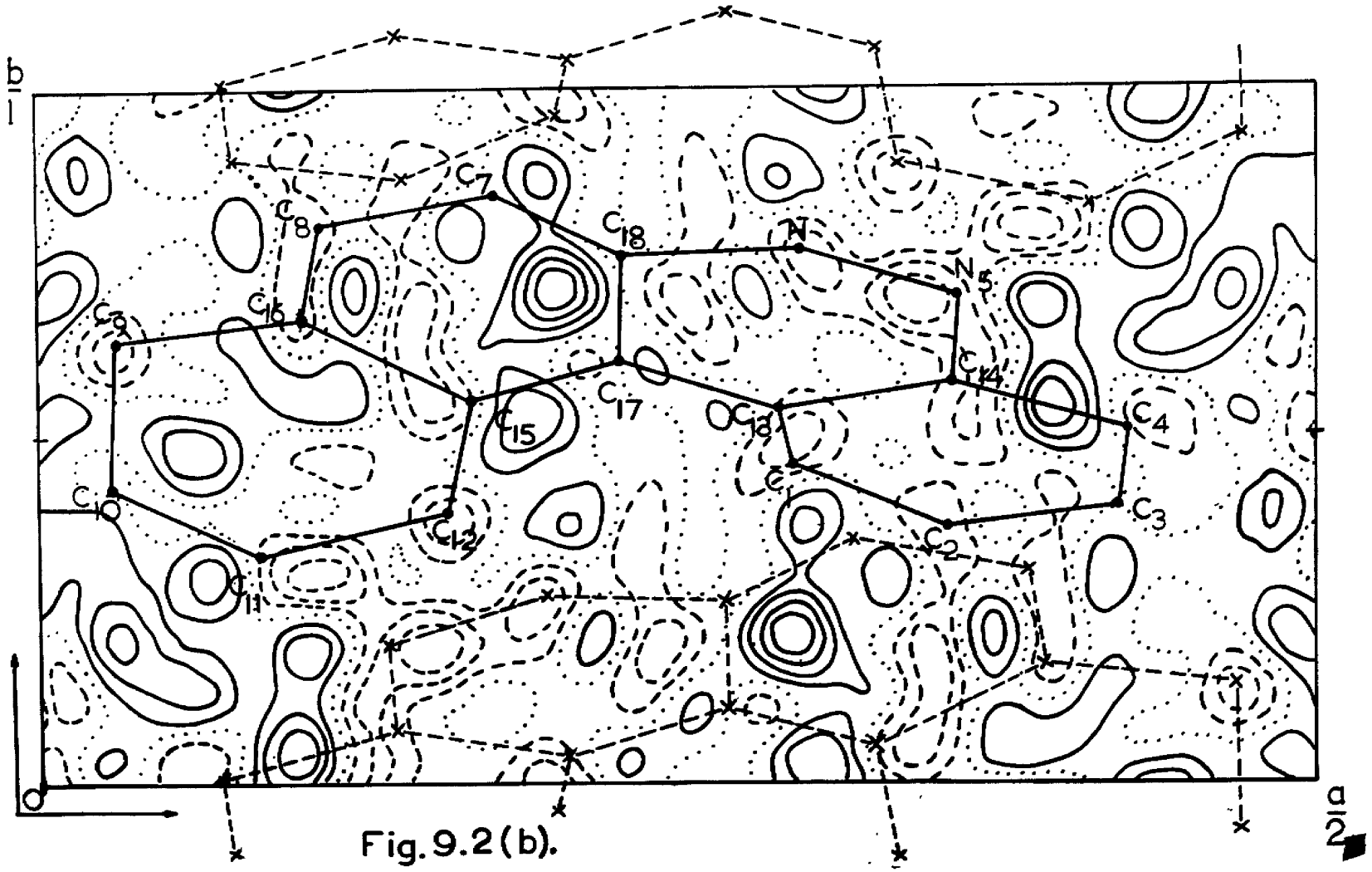


Fig. 9.2 (b).

of the hydrogen atoms were tried but the improvement was not so great. However, it would be surprising if hydrogen atoms could be located from the difference map considering the amount of overlap and the accuracy of the X-ray data available.

9.3. The final coordinates and the structure factor calculations. The fractional coordinates and temperature factors of the carbon and nitrogen atoms as obtained finally by the use of the new methods in the refinement are given in table 9.2. The final structure factors were calculated corresponding to the final coordinates. Table 9.3 shows the final agreement between the observed and calculated structure factors and the agreement is uniformly good. The final residual was 0.16 for the hko reflexions, the unobserved reflexions which calculated less than $F_{min.}$ were omitted from the calculations.

9.4. Discussion. The new methods have provided a means of refining structures at all stages from the relatively rough model of the naphthocinnoline at a residual of > 0.35 to the highly refined dipotassium ethylene tetracarboxylic acid at a residual of 0.11. In all cases further refinement was achieved. The disadvantage that Booth (1949) associated with his relaxation method, of always descending parallel to a unit-cell edge instead of along an axis of the contour ellipse as in the case of steepest-descents or least-squares methods, appears to be much less serious than he suspected.

Athough the methods were originally devised to deal with overlapped atoms in projection it is, in fact, a quite general method of refining any structure. The methods have been shown to work even when very large coordinate changes (> 0.5 Å) are necessary, as in the case of the

naphthocinnoline, and have been shown to work when other methods have failed, as in the case of methyl ammonium alum. It is considered that these methods will be of most use in getting the rough structure into the correct 'hole' for refinement by conventional methods. The final refinement will be most efficiently completed using the full matrix least-squares method.

Intuitively it might be supposed that the order in which the atoms are dealt with is important. In practice it has been found that the method is insensitive to changes in the order even in a single cycle. The assumption that the parameters are all independent is not, of course, true in that more than one cycle is required even when the changes in coordinates are within their permitted range of exploration. The method does, however, converge rapidly with both centro-symmetric and non-centrosymmetric projections (described in chapter 10). In non-orthogonal projections there will be some interaction between the two positional parameters. This should not be serious provided the interaxial angle is not too different from 90°. The method has not yet been applied to such a projection so that the actual effect can be assessed.

The structures so far refined have not involved large variations in the individual temperature factors but in all the cases where the new method has been used the greater part of the refinement of the temperature factor refinement has been completed in a single cycle, provided the overall temperature factor and the scaling factor were correct. It might be expected that the new method would deal more

easily with large variations than the existing least-squares method which tend to overestimate the reductions and underestimate the increase in temperature factors and necessarily need more than one cycle. Provided the coordinate refinement is well advanced there should be no problem in finding the correct 'hole'.

There is no reason why the methods could not be extended to deal with three-dimensional data and anisotropic temperature coefficients except that the existing methods may well be adequate.

It is considered that the methods will be most useful in two-dimensional work where there is a great deal of overlap (which makes it very difficult to get the structure into the right 'hole' to start with) and a danger of refining the structure into a secondary minimum using conventional methods.

Table 9.1

Initial and final coordinates of the atoms and the total shifts made to the coordinates in the [001] projection.

	Atoms	Initial x_1/a	Final x_1/a	Total shift (in Å)	Initial y/b	Final y/b	Total shift (in Å)
	C_1	0.3044	0.2955	0.18	0.4628	0.4592	0.02
	C_2	0.3742	0.3566	0.37	0.4070	0.3681	0.21
	C_3	0.4298	0.4241	0.12	0.4712	0.3916	0.42
	C_4	0.4244	0.4280	0.08	0.5763	0.5070	0.37
	N_5	0.3558	0.3610	0.13	0.7791	0.7000	0.43
	N_6	0.2933	0.2985	0.11	0.8237	0.7663	0.31
	C_7	0.1598	0.1790	0.41	0.8256	0.8482	0.12
	C_8	0.0936	0.1106	0.35	0.7326	0.8056	0.39
×	C_9	0.0397	0.0308	0.18	0.4554	0.6400	0.99
×	C_{10}	0.0403	0.0287	0.24	0.2628	0.4259	0.88
	C_{11}	0.1083	0.0874	0.43	0.2209	0.3222	0.54
	C_{12}	0.1691	0.1601	0.18	0.3140	0.3867	0.39
	C_{13}	0.2946	0.2908	0.08	0.5742	0.5376	0.20
	C_{14}	0.3644	0.3577	0.14	0.6191	0.5759	0.23
	C_{15}	0.1818	0.1703	0.23	0.4860	0.5506	0.35
×	C_{16}	0.1059	0.1038	0.04	0.5484	0.6702	0.65
	C_{17}	0.2345	0.2288	0.13	0.5837	0.6107	0.14
	C_{18}	0.2235	0.2285	0.10	0.7605	0.7593	0.01

Table 9.2

Atomic coordinates and temperature factors for the hko projection

Atoms	$x/_a$	$y/_b$	$B_1 Å^2$
C_1	0.2955	0.4592	3.5
C_2	0.3566	0.3681	3.8
C_3	0.4241	0.3916	3.8
C_4	0.4280	0.5070	3.8
N_5	0.3610	0.7000	3.4
N_6	0.2985	0.7663	3.3
C_7	0.1790	0.8482	3.4
C_8	0.1106	0.8055	3.7
C_9	0.0308	0.6400	3.8
C_{10}	0.0287	0.4259	3.6
C_{11}	0.0874	0.3222	3.7
C_{12}	0.1601	0.3867	3.3
C_{13}	0.2908	0.5376	3.4
C_{14}	0.3577	0.5759	3.3
C_{15}	0.1703	0.5506	3.4
C_{16}	0.1038	0.6702	3.7
C_{17}	0.2288	0.6107	3.1
C_{18}	0.2285	0.7593	3.2

Table 9.3

Observed and calculated structure factors for the hko reflexions.

h	k	l	$\lvert 10\ F_{obs.} \rvert$	$10\ F_{cal.}$	h	k	l	$\lvert 10\ F_{obs.} \rvert$	$10\ F_{cal.}$
0	2	0	73	−70	7	2	0	169	135
0	4	0	75	−80	7	3	0	300	−321
0	6	0	< 26	−13	7	4	0	< 37	16
1	1	0	105	117	7	5	0	< 26	12
1	2	0	96	107	7	6	0	< 19	−38
1	3	0	< 69	80	8	0	0	205	−185
1	4	0	129	−124	8	1	0	227	−210
1	5	0	41	55	8	2	0	227	−240
1	6	0	58	−44	8	3	0	75	−82
2	0	0	600	−660	8	4	0	64	−68
2	1	0	178	154	8	5	0	< 26	−29
2	2	0	66	82	8	6	0	30	−12
2	3	0	90	109	9	1	0	47	48
2	4	0	96	−106	9	2	0	195	−221
2	5	0	94	−98	9	3	0	131	117
2	6	0	67	60	9	4	0	99	105
3	1	0	465	−477	9	5	0	43	21
3	2	0	177	192	9	6	0	26	−23
3	3	0	124	131	10	0	0	134	103
3	4	0	66	66	10	1	0	84	91
3	5	0	< 26	−30	10	2	0	97	−100
3	6	0	41	−45	10	3	0	99	−105
4	0	0	465	−526	10	4	0	112	125
4	1	0	95	125	10	5	0	60	−69
4	2	0	150	176	10	6	0	37	40
4	3	0	84	−106	11	1	0	75	−77
4	4	0	96	93	11	2	0	99	−88
4	5	0	< 26	−13	11	3	0	37	36
4	6	0	64	−69	11	4	0	75	53
5	1	0	197	−168	11	5	0	79	−78
5	2	0	77	−71	11	6	0	< 19	74
5	3	0	51	48	12	0	0	116	−101
5	4	0	60	56	12	1	0	86	75
5	5	0	< 26	60	12	2	0	81	60
5	6	0	112	119	12	3	0	54	15
6	0	0	69	95	12	4	0	90	−94
6	1	0	88	93	12	5	0	28	−41
6	2	0	112	129	12	6	0	< 19	23
6	3	0	92	102	13	1	0	64	61
6	4	0	77	−81	13	2	0	77	86
6	5	0	< 26	−29	13	3	0	39	20
6	6	0	47	−43	13	4	0	31	−20
7	1	0	225	−236	13	5	0	< 22	10

h	k	l	10 $F_{obs.}$	10 $F_{cal.}$
13	6	0	< 19	15
14	o	0	154	165
14	1	0	112	119
14	2	0	< 60	81
14	3	0	66	— 68
14	4	0	< 75	74
14	5	0	22	41
15	1	0	361	401
15	2	0	< 45	16
15	3	0	< 32	— 15
15	4	0	< 24	13
15	5	0	69	— 33
16	0	0	187	— 211
16	1	0	259	— 274
16	2	0	< 37	— 20
16	3	0	54	63
16	4	0	45	65
16	5	0	34	— 50
17	1	0	96	— 86
17	2	0	79	51
17	3	0	112	— 110
17	4	0	< 26	27
17	5	0	28	30
18	0	0	107	— 107
18	1	0	130	116
18	2	0	49	— 14
18	3	0	51	28
18	4	0	< 26	6
18	5	0	< 19	22
19	1	0	37	16
19	2	0	< 26	— 9
19	3	0	62	68
19	4	0	30	— 41
20	0	0	71	— 48
20	1	0	< 26	30
20	2	0	< 26	— 45
20	3	0	49	— 40
20	4	0	< 19	28
21	1	0	24	28
21	2	0	36	29
21	3	0	43	— 41
21	4	0	< 19	11
22	0	0	41	— 32
22	1	0	22	— 4
22	2	0	71	— 76
22	3	0	< 19	— 10
23	1	0	21	— 8
23	2	0	62	— 59
23	3	0	24	— 31
24	0	0	< 26	— 33
24	1	0	19	— 7
24	2	0	32	52
25	1	0	19	— 19
25	2	0	< 19	0

Chapter 10

The determination of the [010] projection and refinement by direct calculation of the minimum residual

10.1. Introduction. As was stated in chapter 4, although the [010] projection was refined by conventional methods to an R - value of 0.15, it was of no help in determining the [001] projection. The [001] projection was finally determined (as described in chapter 9) by the minimum residual methods. Since the x - coordinates were common to two projections, it was expected that there should be good agreement between them; but it was not at all so as can be seen from the table 10.1. The differences in the x - coordinates of atoms 2, 3 & 4 were more ~~were as much as~~ than 1 Å which are too much for a correct structure. In view of this and a few other observations mentioned in section 3.10 it was decided to attempt to redetermine the [010] projection with the help of the information available from the known [001] projection and then apply the new methods for its refinement.

From the evidence of the shape and orientation of the molecule in the [001] projection, it was possible to deduce a shape and orientation of the molecule in the [010] projection. This was done by orienting a wire model of the molecule so that it satisfied the atomic coordinates of the [001] projection and projecting this model on the (010) plane. Structure factor calculations using this (model) trial set of coordinates showed good agreement between the individual F_o's and F_c's with the initial value of the residual of 0.35. This was very encouraging.

10.2. <u>The strategy of the refinement and experience.</u> As it was decided to test the new method of coordinate refinement (described in section 8) using the trial coordinates, no conventional refinement was performed at all and starting from the residual of 0.35 the refinement was undertaken in this projection by the new method with a range of scan of 0.1Å in steps of 0.02Å. The value of the residual was reduced to 0.282 in the first cycle. It was encouraging to note that the major shifts of the atoms were in the y direction (maximum shift 0.1Å), since the x - coordinates had been taken from the previously determined [001] projection. The new atomic coordinates were plotted and found to be sensible. When the next cycle was performed the R - value fell by 0.022 to 0.26 and the difference map computed at this stage indicated that some adjustments in the scaling and temperature factors were necessary. After adjusting the scale and the overall temperature factors (the overall temperature factor B was increased from 2.5 to 3.0Å), a further three cycles of refinement reduced the R - value to 0.19. A difference synthesis computed at this stage indicated that the new coordinates were sensible and the general features of the map were also improving. It was considered desirable to refine individual temperature factors at this stage. Subsequent refinement of the individual temperature factors by the new method and further cycles of coordinate refinement reduced the residual to 0.12. The initial and the final coordinates of the naphthocinnoline in the [010] projection are given in table 10.2 which also shows the total shifts made to the atomic coordinates in bringing them to the correct positions.

During the refinement the maximum change in a coordinate was 0.25Å and the average was 0.10 Å. The final Fourier and difference Fourier synthesis are given in fig. 10.1 (a & b) showing the molecule in thick lines and the symmetry related one in broken lines. The distribution of atoms is much better than in previous difference maps, almost all the atoms lying near the zero contour; the background variation is also reasonable.

Even at this stage of refinement, the positions of the hydrogen atoms were not apparent in the difference map. The theoretical positions of hydrogen atoms were calculated and found that the agreement between F_o's and F_c's was not much improved.

10.3. <u>The final coordinates and the structure factor calculations.</u> The fractional coordinates and the individual temperature factors of the carbon and nitrogen atoms as obtained finally by the use of the new methods in the refinement are given in table 10.3. The calculated structure factors, compared with the observed structure factors are given in table 10.4, the final residual being 0.12. There were only ~~two~~ three unobserved reflexions in this projection, and these had been included in the calculations assuming their values to be half that of the F_{min}. The atomic scattering factors of Berghuis et al. (1955) for carbon and nitrogen and McWeeny (1951) for hydrogen, evaluated by the method of Forsyth and Wells (1959), were used.

Figure 10.1(a)

The final electron density map of the [010] projection. Contours at intervals of $2e/\mathring{A}^2$. Zero contours are dotted, negative broken and positive contours full line.

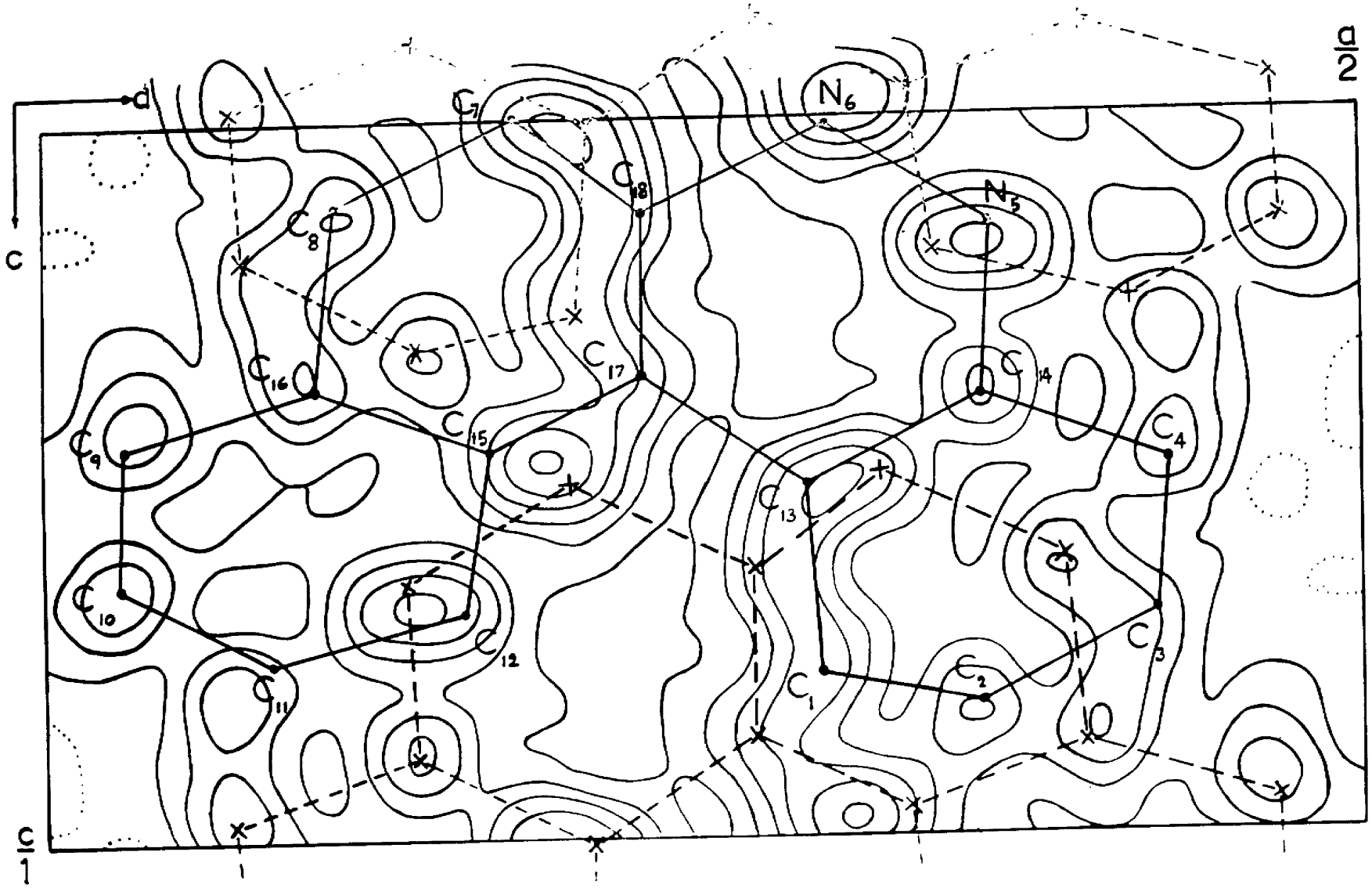

a/2
d
c
c/1
C7
N6
C18
C8
N5
C16
C17
C14
C15
C4
C9
C13
C10
C12
C3
C11
C1
C2

Fig. 10.1 (d).

Figure 10.1(h)

The final difference ($F_o - F_c$) map of the [010] projection. Contours are at intervals of 0.3e/Å^2. Zero contours are dotted, negative broken and positive contours full line.

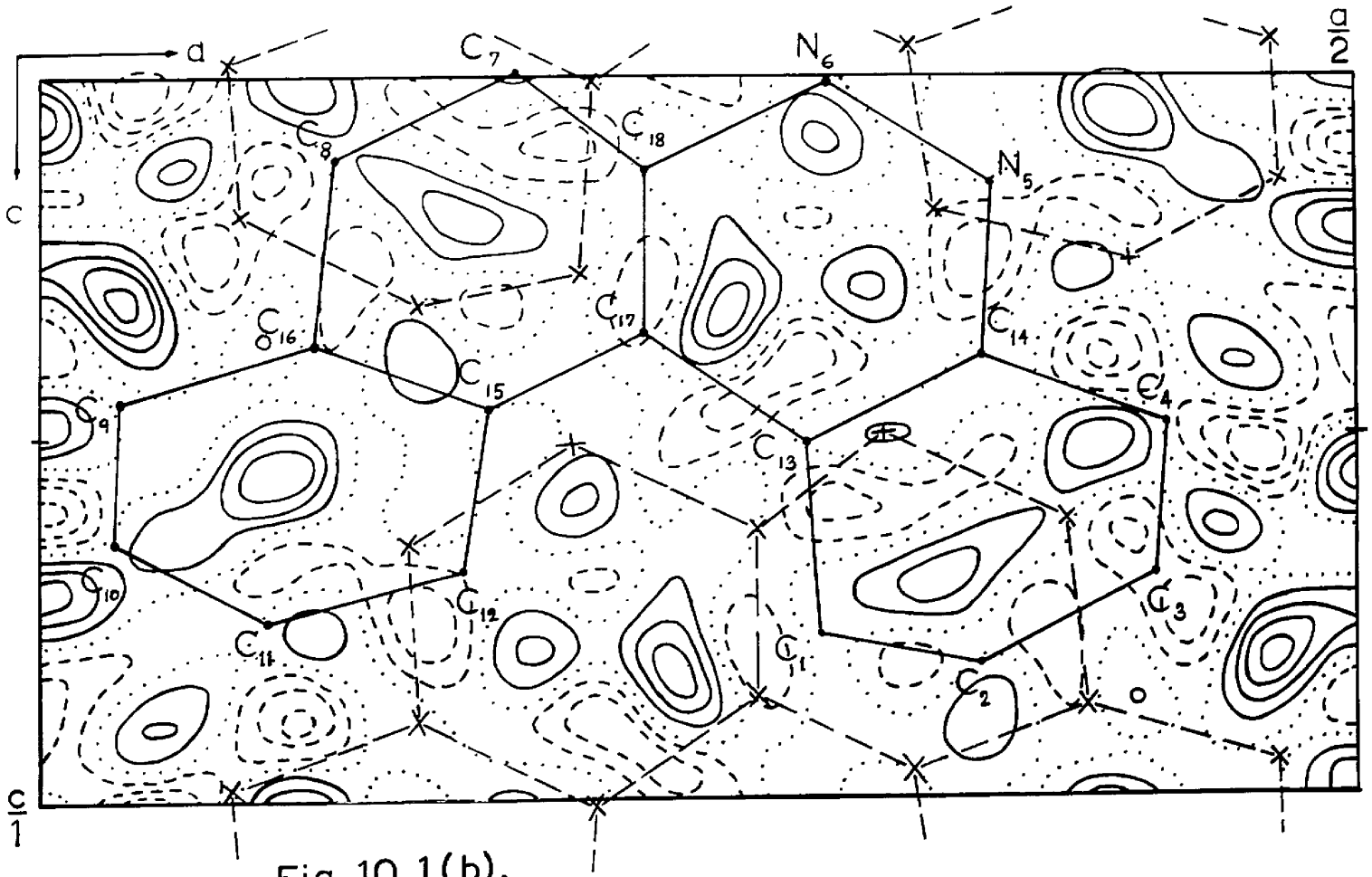

a
c
C7
N6
C18
N5
C8
C17
C14
C16
C15
C4
C9
C13
C10
C12
C3
C11
C1
C2
a/2
c/1

Fig. 10.1(b).

Table 10.1

The x - coordinates and their differences as obtained from the refinement of the [001] and the [010] projections by the methods of minimum residual and least squares respectively

Atoms	x/a for the [001] projection	x/a for the [010] projection	Δx in Å
C_1	0.2955	0.2658	0.61
C_2	0.3566	0.3027	1.10
C_3	0.4241	0.3718	1.07
C_4	0.4280	0.3771	1.04
N_5	0.3610	0.3558	0.11
N_6	0.2985	0.2997	0.02
C_7	0.1790	0.1845	0.10
C_8	0.1106	0.1223	0.24
C_9	0.0308	0.0568	0.53
C_{10}	0.0287	0.0172	0.24
C_{11}	0.0874	0.0625	0.51
C_{12}	0.1601	0.1429	0.35
C_{13}	0.2908	0.2595	0.64
C_{14}	0.3577	0.3364	0.43
C_{15}	0.1703	0.1440	0.54
C_{16}	0.1038	0.1054	0.03
C_{17}	0.2288	0.2176	0.23
C_{18}	0.2285	0.2370	0.17

Table 10.2

Initial and final coordinates of the atoms and the total shifts made to the coordinates in the [010] projection.

Atoms	Initial x_2/a	Final x_2/a	Total Shift (in Å)	Initial z/c	Final z/c	Total Shift (in Å)
C_1	0.3044	0.2957	0.180	0.7300	0.7767	0.251
C_2	0.3742	0.3560	0.365	0.8367	0.8166	0.108
C_3	0.4298	0.4239	0.118	0.7300	0.6967	0.180
C_4	0.4244	0.4286	0.080	0.4983	0.4835	0.080
$N_{5'}$	0.3558	0.3612	0.110	0.1283	0.1467	0.100
N_6	0.2933	0.2987	0.110	0.0200	0.0100	0.054
C_7	0.1598	0.1804	0.405	0.0067	0.0037	0.016
C_8	0.0936	0.1108	0.349	0.1233	0.1167	0.035
C_9	0.0397	0.0312	0.178	0.4700	0.4525	0.094
C_{10}	0.0403	0.0281	0.243	0.6733	0.6480	0.136
C_{11}	0.1083	0.0870	0.428	0.7967	0.7593	0.201
C_{12}	0.1691	0.1590	0.184	0.7133	0.6911	0.120
C_{13}	0.2946	0.2902	0.082	0.4667	0.5100	0.125
C_{14}	0.3644	0.3573	0.141	0.3934	0.3896	0.020
C_{15}	0.1818	0.1704	0.234	0.4567	0.4609	0.223
C_{16}	0.1059	0.1038	0.043	0.3767	0.3730	0.020
C_{17}	0.2345	0.2282	0.126	0.3567	0.3546	0.011
C_{18}	0.2235	0.2281	0.098	0.0967	0.1300	0.180

Table 10.3

Atomic coordinates and temperature factors as obtained from the [010] projection.

Atoms	x_2/a	z/c	B_2, in $Å^2$
C_1	0.2957	0.7767	3.6
C_2	0.3560	0.8166	3.6
C_3	0.4239	0.6967	4.0
C_4	0.4286	0.4835	3.4
N_5	0.3612	0.1467	4.0
N_6	0.2987	0.0100	3.7
C_7	0.1804	0.0037	3.5
C_8	0.1108	0.1167	3.5
C_9	0.0312	0.4525	3.5
C_{10}	0.0281	0.6480	3.5
C_{11}	0.0870	0.7593	3.2
C_{12}	0.1590	0.6911	3.2
C_{13}	0.2902	0.5100	3.5
C_{14}	0.3573	0.3896	3.0
C_{15}	0.1704	0.4609	3.5
C_{16}	0.1038	0.3730	3.5
C_{17}	0.2282	0.3546	3.9
C_{18}	0.2281	0.1300	3.6

Table 10 4.

Observed and calculated structure factors for the hol reflexions

h	k	l	$\lvert 10\ F_{obs.} \rvert$	$10\ F_{cal.}$	h	k	l	$\lvert 10\ F_{obs.} \rvert$	$10\ F_{cal.}$
0	0	2	132	− 145	12	0	2	119	133
0	0	4	142	− 161	12	0	4	98	− 58
0	0	6	132	− 129	12	0	6	36	14
1	0	1	183	− 142	13	0	1	153	155
1	0	3	170	− 162	13	0	3	70	88
1	0	5	36	52	13	0	5	47	− 62
2	0	0	621	− 633	14	0	0	198	223
2	0	2	217	221	14	0	2	98	− 136
2	0	4	130	− 130	14	0	4	68	71
2	0	6	77	69	15	0	1	191	194
3	0	1	308	310	15	0	3	121	− 124
3	0	3	74	− 101	15	0	5	34	27
3	0	5	< 74	− 149	16	0	0	170	− 171
4	0	0	444	− 452	16	0	2	77	− 84
4	0	2	244	308	16	0	4	81	101
4	0	4	83	− 82	17	0	1	149	− 89
4	0	6	55	50	17	0	3	121	73
5	0	1	347	− 334	17	0	5	38	− 59
5	0	3	74	− 74	18	0	0	102	− 82
5	0	5	130	− 111	18	0	2	91	62
6	0	0	66	− 58	18	0	4	36	− 51
6	0	2	136	− 166	19	0	1	117	106
6	0	4	140	90	19	0	3	38	37
6	0	6	34	− 37	20	0	0	36	59
7	0	1	544	− 598	20	0	2	53	− 63
7	0	3	145	141	20	0	4	30	− 31
7	0	5	191	157	21	0	1	53	54
8	0	0	315	317	21	0	3	32	38
8	0	2	321	314	22	0	0	51	56
8	0	4	276	− 290	22	0	2	68	62
8	0	6	62	55	23	0	1	51	42
9	0	1	387	395	23	0	3	19	25
9	0	3	106	67	24	0	0	28	− 30
9	0	5	53	− 56	24	0	2	51	56
10	0	0	206	211	25	0	1	< 19	10
10	0	2	206	176					
10	0	4	204	− 110					
10	0	6	< 19	− 18					
11	0	1	81	− 87					
11	0	3	70	− 93					
11	0	5	89	− 68					
12	0	0	223	233					

Chapter 11

Atomic coordinates and their errors.

11.1. Atomic coordinates and their errors. The final fractional coordinates of the carbon and nitrogen atoms are given in table 11.1. These are the values as obtained from the refinement and given in figs. 9.2 and 10.1. The x-coordinates are common to two projections, so the weighted mean values of x_1 and x_2 corresponding to the [001] and [010] projections respectively are given, the weights given to x_1 and x_2 being inversely proportional to their variances. The individual isotropic temperature factors B_1 and B_2 obtained for the hko and hol reflexions are also given. As the hydrogen atoms could not be accurately located their coordinates are not given.

In order to estimate the standard deviations of the atomic coordinates, the formula

$$\sigma(x_n) = \left\{\overline{\left(\frac{\partial D}{\partial x}\right)^2}\right\}^{\frac{1}{2}} \Big/ C_n \quad \text{- - - - - - - - -} \quad 11(a),$$

was used (Lipson and Cochran 1957), where $D = \rho_o - \rho_c$, and the averages are taken over the whole of the projected area of the unit cell, Cn, the curvature of the nth atom, is equal to $\frac{\partial^2 \rho_c}{\partial x^2}$ which can be replaced by $\frac{\partial^2 \rho_o}{\partial x^2}$ and determined from the shape of the nth atom in the corresponding F_o synthesis. There are two alternative procedures for calculating the numerator of the expression 11(a). In the first procedure the average is taken over all the points in the unit cell (or its projection in two-dimensional cases) for which the difference map has been evaluated, whereas in the second procedure the average is taken over only those points in the map for which the

expected value of $\rho_o - \rho_c$ is zero. The results obtained using the first procedure give a slight overestimate of the error, while the second procedure gives an underestimate.

Using the equation 11(a), the standard deviations in the atomic coordinates $\sigma(x)$, $\sigma(y)$ and $\sigma(z)$ have been caluclated from the [001] and [010] projections respectively. For evaluating $\left\{\overline{\left(\frac{\partial D}{\partial x}\right)^2}\right\}^{\frac{1}{2}}$, etc. The first procedure was adopted and the average was taken over all the points in the cell. $\frac{\partial D}{\partial x}$ was evaluated from the expression

$$\frac{\partial D}{\partial x} = -\frac{1}{A} \cdot \frac{2\pi}{a} \sum_h \sum_k h\, F_{(hk)} \sin 2\pi\,(hx + ky).$$

Since the r.m.s. value of $\frac{\partial D}{\partial x}$ was required the computer programme was modified to calculate and output this as a single number instead of the value of $\frac{\partial D}{\partial x}$ at each point in the unit cell. The curvature C_n was calculated using the expression

$$\frac{\partial^2 \rho}{\partial x^2} = \frac{1}{A} \frac{4\pi^2}{a^2} \sum_h \sum_k h^2 \,(F_{hk}) \cos 2\pi\,(hx + ky) \quad - - - \quad 11(b).$$

This expression after being appropriately modified to take account of the pgg and cm symmetry, was evaluated by doing a Fourier summation over the whole cell in which $h^2(F_{hk})$ were used as Fourier coefficients. The values of C_n could then be determined at the atomic sites. Both the calculations were done using two separate computer programmes written by Mr. P. Main. The factor $\left[\frac{u}{u - v}\right]^{\frac{1}{2}}$, where u is the number of independent F values and v is the number of unknown parameters being refined, was not considered since $u \gg v$ for all projections used. Corresponding procedures were used for determining $\sigma(y)$ and $\sigma(z)$. All values of standard deviations are given in

table 11.2. together with the standard deviation, $\sigma(x)$, in the weighted mean of the x-coordinates. This is given by

$$\frac{1}{\sigma^2 x} = \frac{1}{\sigma^2 x_1} + \frac{1}{\sigma^2 x_2}$$

The formula, 11(a), employed to calculate the standard deviations assumes that the atoms are resolved, which is not the case in this structure. However, because of the method used to calculate them, the values obtained for the atomic curvature will be effected by overlap in such a way that the coordinates of an overlapped atom will have a larger standard deviation. Thus, overlap is taken into account to a certain extent, although the standard deviations calculated in such a way may not be strictly correct.

Table 11.1

Final coordinates and temperature factors of the atoms

Atoms	x_1/a	x_2/a	$\bar{x}/a$ (weighted mean estimate)	y/b	z/c	B_1 ($Å^2$)	B_2 ($Å^2$)
C_1	0.2955	0.2957	0.2956	0.4592	0.7767	3.5	3.6
C_2	0.3566	0.3560	0.3565	0.3681	0.8166	3.8	3.6
C_3	0.4241	0.4239	0.4239	0.3916	0.6967	3.8	4.0
C_4	0.4280	0.4286	0.4283	0.5070	0.4835	3.8	3.4
N_5	0.3610	0.3612	0.3612	0.7000	0.1467	3.4	4.0
N_6	0.2985	0.2987	0.2987	0.7663	0.0100	3.3	3.7
C_7	0.1790	0.1804	0.1800	0.8482	-0.0037	3.4	3.5
C_8	0.1106	0.1108	0.1106	0.8055	0.1167	3.7	3.5
C_9	0.0308	0.0312	0.0310	0.6400	0.4525	3.8	3.5
C_{10}	0.0287	0.0281	0.0285	0.4259	0.6480	3.6	3.5
C_{11}	0.0874	0.0870	0.0872	0.3222	0.7593	3.7	3.2
C_{12}	0.1601	0.1590	0.1592	0.3867	0.6911	3.3	3.2
C_{13}	0.2908	0.2902	0.2903	0.5376	0.5100	3.4	3.5
C_{14}	0.3577	0.3573	0.3576	0.5759	0.3896	3.3	3.0
C_{15}	0.1703	0.1704	0.1704	0.5506	0.4609	3.4	3.5
C_{16}	0.1038	0.1038	0.1038	0.6702	0.3730	3.7	3.5
C_{17}	0.2288	0.2282	0.2283	0.6107	0.3546	3.1	3.9
C_{18}	0.2285	0.2281	0.2282	0.7593	0.1300	3.2	3.6

Table 11.2.

Standard deviations in the atomic coordinates (in Å).

Atoms	$\sigma(x_1)$	$\sigma(x_2)$	$\sigma(\bar{x})$	$\sigma(y)$	$\sigma(z)$
C_1	0.021	0.018	0.014	0.072	0.052
C_2	0.024	0.05	0.022	0.021	0.032
C_3	0.067	0.02	0.019	0.072	0.053
C_4	0.027	0.026	0.019	0.070	0.033
N_5	0.064	0.017	0.016	0.028	0.032
N_6	0.038	0.025	0.021	0.024	0.032
C_7	0.067	0.042	0.036	0.035	0.023
C_8	0.027	0.054	0.024	0.070	0.053
C_9	0.033	0.031	0.023	0.040	0.034
C_{10}	0.021	0.028	0.017	0.031	0.024
C_{11}	0.038	0.035	0.026	0.033	0.050
C_{12}	0.038	0.02	0.018	0.032	0.030
C_{13}	0.048	0.015	0.014	0.040	0.024
C_{14}	0.019	0.026	0.015	0.056	0.023
C_{15}	0.067	0.025	0.023	0.034	0.033
C_{16}	0.033	0.030	0.022	0.040	0.034
C_{17}	0.040	0.022	0.019	0.032	0.040
C_{18}	0.045	0.023	0.021	0.043	0.063

11.2. Bond lengths and angles. When the final coordinates of the atoms had been obtained (table 11.1) the bond lengths and angles within the molecule, with their corresponding estimated standard deviations (e.s.d.), were calculated. This was done using a computer programme written by Dr. R.AL. Sullivan. The standard errors in bond lengths between two atoms, in terms of the errors in coordinates, were calculated from the formula.

$$\sigma^2(\ell) = \{\sigma^2(x_1) + \sigma^2(x_2)\} \cos^2 \alpha + \{\sigma^2(y_1) + \sigma^2(y_2)\} \cos^2 \beta + \{\sigma^2(z_1) + \sigma^2(z_2)\} \cos^2 \gamma ,$$

where $\sigma(x_1)$, $\sigma(y_1)$ and $\sigma(z_1)$ are the standard deviations of the coordinates of the first atom and $\cos\alpha$, $\cos\beta$ and $\cos\gamma$ are the direction cosines of the line joining the atoms (Ahmed and Cruickshank, 1953).

Let the bond between atom 2 and atom 1 have length ℓ_1, and direction cosines $\cos\alpha_1$, $\cos\beta_1$, $\cos\gamma_1$, and the bond between atom 2 and atom 3 have length ℓ_3 and direction cosines $\cos\alpha_3$, $\cos\beta_3$, $\cos\gamma_3$. Then the angle, θ, between the bonds is given by

$$\cos\theta = \cos\alpha_1 \cos\alpha_3 + \cos\beta_1 \cos\beta_3 + \cos\gamma_1 \cos\gamma_3,$$

where $\cos\alpha_1 = (x_2 - x_1)/\ell_1$, $\cos\alpha_3 = (x_2 - x_3)/\ell_3$, with similar expressions for the other direction cosines, and the error in the angle is given by Darlow (1961) as,

$$\sigma(\theta) = \frac{1}{\ell_1 \ell_3 \sin\theta} \left[A_3^2 \sigma^2(x_1) + (A_1 + A_3)^2 \sigma^2(x_2) + A_1^2 \sigma^2(x_3) + \text{similar terms in } y \text{ and } z. \right]^{1/2}$$

where $A_1 = \ell_1 (\cos\alpha_1 - \cos\theta \cos\alpha_3)$,

$A_3 = \ell_3 (\cos\alpha_3 - \cos\theta \cos\alpha_1)$,

with similar terms for β and γ.

The important bond lengths and angles are recorded in table 11.3. and a schematic diagram of the molecule and its environment appears in fig. 11.1.

11.3. The Molecular Symmetry. The molecule as a whole is non-planar. The best planes passing through the various groups of atoms in the molecule and hence the displacements of the individual atoms from these planes were calculated using a computer programme 'Molecular Axes/R. Sparks' by Dr. R. A. Sparks and given in tables 11.4 (a, b, c, d, ... i). The equations for the best planes are as follows:-

(a) for the plane passing through C_1, C_2, C_3, C_4, C_{14}, and C_{13} in ring A,

$$0.12877\, x' + .9039\, y' + 0.40789\, z' = 1.058$$

(b) for the plane passing through N_5, N_6, C_{18}, C_{17}, C_{13} and C_{14} in the ring B,

$$-0.06249\, x' - 0.89246\, y' - 0.44677\, z' = -0.550$$

(c) for the plane passing through C_7, C_8, C_{16}, C_{15}, C_{17} and C_{18} in the ring C,

$$0.10321\, x' + 0.8416\, y' + 0.53014\, z' = 0.552$$

(d) for the plane passing through C_9, C_{10}, C_{11}, C_{12}, C_{15}, C_{16}, in the ring D,

$$0.06056\, x' + 0.73886\, y' + 0.67113\, z' = 0.38$$

(e) for the plane passing through C_1, C_2, C_3 and C_{13},

$$0.17005\, x' + 0.92615\, y' + 0.33664\, z' = 1.244$$

~~(f) for the plane passing through C_3, C_4, C_{14}, C_5, C_{17} and C_{13},~~

~~x' , y' , z' =~~

(g) for the plane passing through C_5, C_6, C_7, C_8, C_{17} and C_{18},

$$0{\cdot}09217\ x' + 0{\cdot}86410\ y' + 0{\cdot}49480\ z' = 0{\cdot}599$$

(h) for the plane passing through C_8, C_{16}, C_9, C_{10}, C_{15} and C_{17},

$$-0{\cdot}07741\ x' - 0{\cdot}78975\ y' - 0{\cdot}60852\ z' = -0{\cdot}350$$

and (i) for the plane passing through C_{10}, C_{11}, C_{12} and C_{15},

$$-0{\cdot}01549\ x' - 0{\cdot}79272\ y' - 0{\cdot}60939\ z' = -0{\cdot}158$$

where x', y', z' define a set of orthogonal axis related to the crystal axes abc in such a way that

$x' \parallel a$,

$y' \perp a$ in the ab plane,

and $z' \parallel c$,

p is evaluated in Å, and the coefficients of x', y' and z' are the direction cosines of the normal to the plane.

In the group (a), the atom C_1 having the greatest departure from the best plane, by a distance of 0.127Å. The angles between the planes of the rings A and B, B and C, C and D are $4^\circ 26'$, $6^\circ 1'$ and $10^\circ 19'$ respectively.

Figure 11.1.

The molecule of naphtho[2,1-c]cinnoline showing :-

(a) the system of numbering of the atoms,

(b) the bond lengths and

(c) the bond angles.

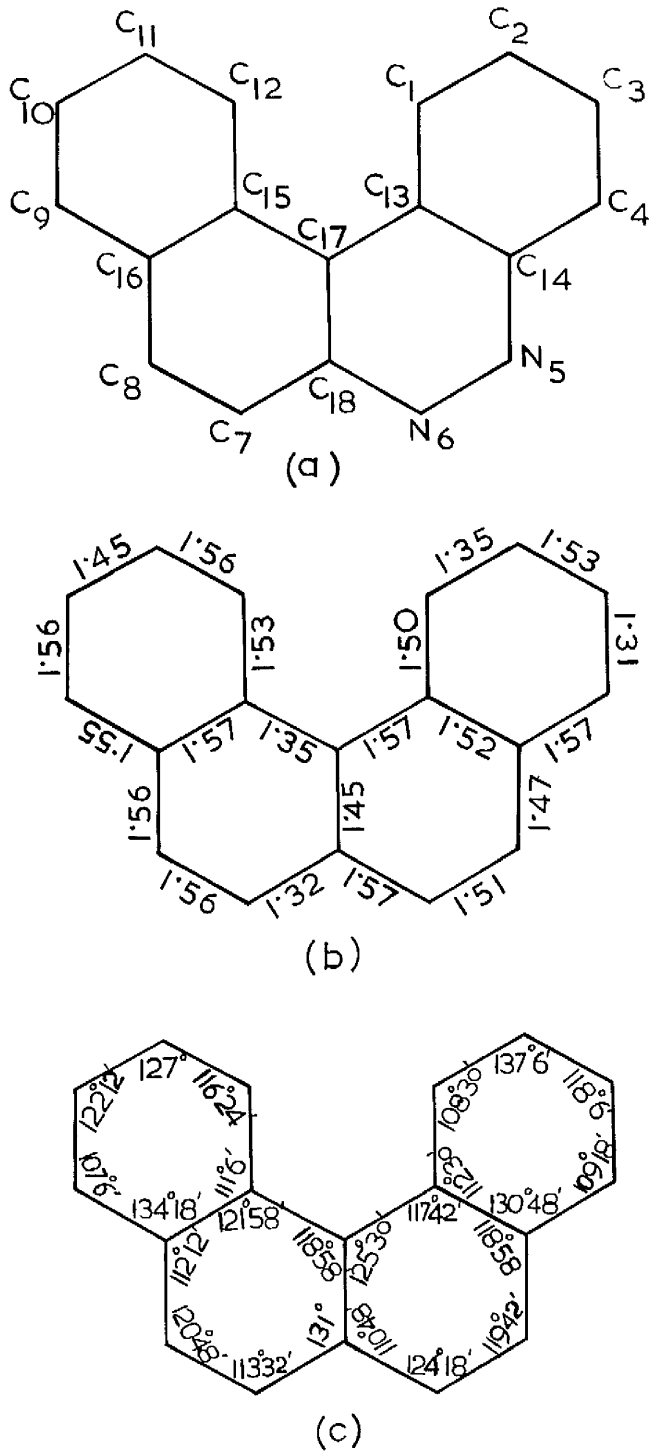

C11
C12
C10
C9
C16
C8
C7
C15
C17
C18
C1
C2
C3
C4
C13
C14
N5
N6
(a)
1·45
1·56
1·56
1·53
1·55
1·57
1·35
1·56
1·45
1·56
1·32
1·57
1·35
1·53
1·50
1·31
1·57
1·52
1·57
1·47
1·51
(b)
127°
116°24'
122°12'
107°6'
111°6'
134°18'
121°58'
118°58'
112°12'
120°48'
113°32'
131°
125°30'
110°48'
124°18'
119°42'
137°6'
118°6'
108°30'
109°6'
112°30'
117°42'
130°48'
118°58'
(c)

Fig.11.1.

Table 11.3

The bond lengths, angles and their corresponding errors

Bond	Bond Lengths (Å)	Standard deviations (Å)
C_1 - C_2	1.35	0.04
C_2 - C_3	1.53	0.04
C_3 - C_4	1.31	0.08
C_4 - C_{14}	1.57	0.03
C_{14} - C_{13}	1.52	0.03
C_{13} - C_1	1.50	0.06
C_{14} - N_5	1.47	0.05
N_5 - N_6	1.51	0.03
N_6 - C_{18}	1.57	0.04
C_{18} - C_{17}	1.45	0.07
C_{17} - C_{13}	1.57	0.03
C_{18} - C_7	1.32	0.05
C_7 - C_8	1.56	0.05
C_8 - C_{16}	1.56	0.07
C_{16} - C_{15}	1.57	0.04
C_{15} - C_{17}	1.35	0.04
C_{16} - C_9	1.55	0.03
C_9 - C_{10}	1.56	0.05
C_{10} - C_{11}	1.45	0.04
C_{11} - C_{12}	1.56	0.03
C_{12} - C_{15}	1.53	0.04

Table 11.3 (continued)

Atoms			Angles	Standard deviations
C_1	C_2	C_3	137° 6'	3° 58'
C_2	C_3	C_4	118° 6'	3° 6'
C_3	C_4	C_{14}	109° 18'	2° 12'
C_4	C_{14}	C_{13}	130° 48'	2° 48'
C_{14}	C_{13}	C_1	112° 30'	1° 36'
C_{13}	C_1	C_2	108° 30'	2° 54'
C_{13}	C_{14}	N_5	118° 58'	1° 58'
C_{14}	N_5	N_6	119° 42'	1° 48'
N_5	N_6	C_{18}	124° 18'	3° 6'
N_6	C_{18}	C_{17}	110° 48'	2° 30'
C_{18}	C_{17}	C_{13}	125° 30'	2°
C_{17}	C_{13}	C_{14}	117° 42'	2° 24'
C_{18}	C_7	C_8	113° 32'	3° 24'
C_7	C_8	C_{16}	120° 48'	2° 54'
C_8	C_{16}	C_{15}	112° 12'	2° 12'
C_{16}	C_{15}	C_{17}	121° 58'	2° 58'
C_{15}	C_{17}	C_{18}	118° 58'	2° 24'
C_{17}	C_{18}	C_7	131°	2° 50'
C_{16}	C_9	C_{10}	107° 6'	2° 18'
C_9	C_{10}	C_{11}	122° 12'	2° 8'
C_{10}	C_{11}	C_{12}	127°	3° 10'
C_{11}	C_{12}	C_{15}	116° 24'	2° 12'
C_{12}	C_{15}	C_{16}	111° 6'	2° 4'
C_{15}	C_{16}	C_9	134° 18'	3°

Table 11.4

Displacements of the atoms from the mean planes.

groups	atoms	displacements in Å
(a)	C_1	0.1267
	C_2	-0.0688
	C_3	-0.0398
	C_4	0.0647
	C_{14}	0.0076
	C_{13}	-0.0904
(b)	N_5	-0.0211
	N_6	0.0688
	C_{18}	-0.0959
	C_{17}	0.0772
	C_{13}	-0.0245
	C_{14}	-0.0044
(c)	C_7	-0.0337
	C_8	-0.0286
	C_{16}	0.074
	C_{15}	-0.0757
	C_{17}	0.0157
	C_{18}	0.0475
(d)	C_9	0.0749
	C_{10}	-0.0732
	C_{11}	-0.0108
	C_{12}	0.089
	C_{15}	-0.0778
	C_{16}	-0.0021

Table 11.4 (continued)

group	atoms	displacements in Å
(e)	C_1	0.0790
	C_2	-0.0915
	C_3	0.04323
	C_{13}	0.03075
~~(f)~~	~~C_3~~	
	~~C_4~~	
	~~C_{14}~~	
	~~C_5~~	
	~~C_{17}~~	
	~~C_{13}~~	
(g)	C_5	0.0696
	C_6	-0.1036
	C_{18}	0.0506
	C_7	0.0164
	C_8	0.0090
	C_{17}	-0.0419
(h)	C_8	0.1323
	C_{16}	-0.1206
	C_9	-0.1375
	C_{10}	0.1358
	C_{15}	-0.0054
	C_{17}	-0.0047
(i)	C_{10}	-0.020
	C_{11}	0.0387
	C_{12}	-0.0355
	C_{15}	0.0169

Chapter 12

Concluding discussion of the structure

As was stated in the previous chapters the minimum residual techniques were used for determining the molecular distribution and the refinement of the structure of the naphthocinnoline in both projections. The reasonably low R-value for the two principal projections and the absence of substantial peaks in the final $(F_o - F_c)$ syntheses (figs. 9.2 (b) and 10.1 (b)) show that the correct structure has been determined. The only aspect of the structure which does not seem satisfactory is the wide variation in the bond lengths (fig. 11.1), the distances between atoms varying from 1.31Å to 1.57Å. The errors in the atomic coordinates reflect the poor quality of the data rather than any mistake in the structure. The atomic arrangement in the [001] and [010] projections (figs. 9.2(b) and 10.1(b)) is not all regular and is essentially due to distortion in the molecule. Although the accuracy of the structure is poor, nevertheless, it has been possible to ascertain most of the important features of the configuration of the naphthocinnoline molecule.

Unfortunately the residual (0.16) for the [001] projection is a little high. Successive refinements did not lead to further improvement in the agreement residual and ended at the stage where the molecule had become greatly distorted but the residual was at its lowest. The intensity values obtained for the hko reflexions are not as reliable as those for the hol reflexions. The high R-value was due to the poor quality of the data and also the serious overlap in

projection; the fact that this projection is centrosymmetric would also make the R-value a little higher than a non-centrosymmetric projection of similar complexity and accuracy of data.

It is quite clear that the molecule of ~~the~~ naphthocinnoline is non-planar. The molecules are arranged in stacks along the short b-axis of the unit cell. Within each stack the molecules are parallel and inclined to this axis at about 60°.

The centre-to-centre distance between C_1 and C_{12} is 2.83Å which is less than the value 3.2Å which is generally supposed to be the normal van der waal separation between two non-bonded carbon atoms (Coulson & Skancke, 1962). The manner in which the molecule is distorted from planarity so as to achieve this separation between C_1 and C_{12} may be seen in fig. 9.2(b). ~~which is a perspective view of a model based on experimental coordinates~~. It is seen that rings A and D are bent in opposite directions out of the mean plane of rings B and C, consequently the distortion of rings A and D is greater than B and C.

Most of the bond lengths between c - c atoms in the molecule are much greater than the usually quoted single bond length 1.477Å (Dewar and Schmeising, 1959; Cruickshank and Sparks, 1960). The distances between $C_4 - C_{14}$, $C_7 - C_8$, $C_8 - C_{16}$, $C_{16} - C_9$, $C_9 - C_{10}$, $C_{11} - C_{12}$, $C_{12} - C_{15}$ and $C_{13} - C_{17}$ are 1.57, 1.56, 1.56, 1.55, 1.56, 1.56, 1.55 and 1.57Å respectively, with estimated standard deviations ·03, ·05, ·07, ·03, ·05, ·03, ·04 & ·03 as shown in table 11.3. These exceed the accepted value of 1.477Å

by $\sim$ 0.08Å which is equal to 2σ and so it is 'possibly significant' (Cruickshank, 1945). Some abnormally long c - c bonds may be expected due to steric interactions between C_1, C_{12}, H_1 and H_{12} which increases the separation between C_1 and C_{12} beyond the value it would have in an unstrained molecule. Coulson and Skancke (1962) suggested, on some theoretical considerations, that some abnormally long c - c bonds may be possible and in their calculations they have assumed the length of the (sp^2) single bond to be equal to 1.517Å. The present values are even significantly larger than this, but the bonds are not as long as the c - c (single) bond length of 1.7Å reported by Grant (1957) in the structure of hydroxydihydroeremophilone. ~~the proposed value of the (sp^2) single bond~~.

The significant differences in the bond lengths between atoms within the benzene ring B (fig.11.1(b)) are observed, particularly the bond C_{18} - N_6 (1.57Å) is much larger than the normal value. Some examples given in the literatures show a wide variation in the C - N bond lengths. The values may vary from 1.32 to 1.45Å (Pauling, 1950). In some examples, such as, 2-2' dichlorobenzidine (Smare, 1948) and m - tolidine (Fowweather, 1952), the values lie between 1.40 and 1.45Å.

The N_5 - N_6 distance is also significantly longer than the normal value, with estimated standard deviation 0.03 Å. There seems to be little point in comparing the bond lengths obtained with the theoretical values except to say that apart from the nine extreme discrepancies the other nine are of correct order.

The most significant feature of this structure is the non-planarity

of the benzene rings. The calculations of the displacements, p, of the individual atoms from the best plane passing through the various groups of atoms as given in tables 11.4 (a, b, c, ...) seemed to indicate that the atoms 1, 2, 3, 4, 14 and 13, constituting ring A, deviate from the best plane passing through these atoms by a root-mean-square of over 0.076Å, and a maximum (C_1 atom) of 0.127Å. The deformation of the ring B is less than A, the root-mean-squares deviation being 0.06Å and C_{18} having the maximum departure from the best plane by a distance of 0.096Å (table 11.4). The distortion of benzene ring C is more or less the same as B, its atoms deviate from the best plane by a root-mean-square distance of 0.05 Å, and a maximum (C_{15} atom) of 0.08 Å. Again the deformation of ring D is much greater than the rings B & C ~~rest~~, the C_{12} atom departing most from the best plane, a distance of about 0.089Å, and the root-mean-square deviation is 0.065Å. It is now clear that the displacements of the atoms of the ring A of one side of the molecule upwards and the ring D on the other side downwards lead to the deformation of the molecule by which the overcrowding associated with C_1, C_{12}, H_1 and H_{12} is relieved almost entirely.

The non-planarity of a few other groups of atoms has been tested and found that the displacements of the atoms 1, 2, 3 and 13 from the best plane passing through them to be significant, the maximum value of p is 0.09 Å and the root-mean-square value 0.07 Å. ~~The group comprising atoms 3, 4, 14, 5, 17 and 13 has been tested in the same manner and was found to be planar to within a root-mean-square deviation of~~

~~0. Å. Again~~, The departures of the individual atoms 5, 6, 18, 7, 8 and 17 from the best plane by 0.04 Å is not very significant. Furthermore, the atoms 10, 11, 12 and 15 also are co-planar to within a root-mean-square deviation of 0.03 Å.

The bending of the rings is reflected in the abnormal bond angles at different atoms. The bond angles at the atoms 1, 4 and 13 in the ring A are 109°, 109° and 112°, while the angles at the atoms 9 and 15 in the ring D are 107° and 111°. It is significant that they all deviate from the expected bond angle of 120°.

Therefore to summarise this work, it has been shown that the structure of the naphthocinnoline as described here is correct. However, the standard deviations in the positional parameters of the atoms are still quite high and it is felt that the only way to improve these is to refine the structure using three-dimensional data.

Part II Programming for the Ferranti Mercury Computer.

Chapter 13

The Mercury Computer and some programming in the Autocode system for crystallographic computations.

13.1. Introduction. With the development and use of electronic digital computers in the past decade has altered many aspects of crystallography. Due to their availability, numerous and often intricate calculations are no longer the prime bottleneck in the solution of crystal structures, as was the case until the late forties.

Several papers have been published, e.g. Bennett & Kendrew (1952), Mayer & Trueblood (1953), and Ahmed & Cruickshank (1953-b) outlining the application of the computer to crystallographic calculations and also dealing with various standard computations necessary in X-ray structure analysis such as the computation of Fourier syntheses and structure factors.

The availability of digital computers has led crystallographers to attempt computations considered out of the question a decade ago; three-dimensional least-squares refinements (Sparks et al., 1956), for example. Altogether, computers have taken much of the tedium from routine crystallographic work, and have provided a means of dealing relatively easily with computations hitherto considered far too formidable. No account of the computer is given here, a full description of this machine has been given by Kilburn and his co-workers (1956).

This chapter deals with three of the programmes written to aid crystallographic computations. They were all written in the Manchester Mercury Autocode System.

13.2. <u>A programme for finding the molecular position by direct calculation of the minimum residual.</u> The principle of the minimum residual molecular location method has been discussed in chapter 5. This programme is designed to calculate the structure factors and residual for the molecule in the plane group pgg, as its position is varied systematically in the unit cell. The flow diagram of the programme is shown in fig. 13.2. For the purposes of the structure factor calculations the formula given in the international tables for X-ray crystallography, Vol. 1, 1952, is rearranged as follows.

If x_i and y_i are the coordinates of the ith atom of the molecule, with respect to some arbitrary origin O^1, and X and Y are the coordinates of this origin with respect to the true unit cell origin (fig. 13.1), then the structure factor expression may be written

$$\left.\begin{aligned} F_{(h,\,k)} &= 4\sum_{i=1}^{N} f_i\, e^{-Bs^2} \cos 2\pi h\,(X + x_i)\, \cos 2\pi k\,(Y + y_i) \\ &\qquad \text{when } h + k = 2n, \text{ and} \\ F_{(h,\,k)} &= -4\sum_{i=1}^{N} f_i\, e^{-Bs^2} \sin 2\pi h\,(X + x_i)\, \sin 2\pi k\,(Y + y_i) \\ &\qquad \text{when } h + k = 2n + 1 \end{aligned}\right] \quad \ldots\ldots(1),$$

where f_i is the atomic scattering factor of the ith atom, B is the temperature factor obtained by the method of Wilson (1944) and s is equal to $\sin\theta/\lambda$ Equation (1) may be rewritten as -

$$
\begin{aligned}
F_{(h,\,k)} = 4 \Big[& \cos 2\pi hX \cos 2\pi kY \sum f_i\, e^{-Bs^2} (\cos 2\pi hx_i \cos 2\pi ky_i) \\
- & \cos 2\pi hX \sin 2\pi kY \sum f_i\, e^{-Bs^2} (\cos 2\pi hx_i \sin 2\pi ky_i) \\
- & \sin 2\pi hX \cos 2\pi kY \sum f_i\, e^{-Bs^2} (\sin 2\pi hx_i \cos 2\pi ky_i) \\
+ & \sin 2\pi hX \sin 2\pi kY \sum f_i\, e^{-Bs^2} (\sin 2\pi hx_i \sin 2\pi ky_i) \Big] \\
& \text{when } h + k = 2n, \text{ and} \qquad \ldots\ldots (2) \\
F_{(h,\,k)} = -4 \Big[& \sin 2\pi hX \sin 2\pi kY \sum f_i\, e^{-Bs^2} (\cos 2\pi hx_i \cos 2\pi ky_i) \\
+ & \sin 2\pi hX \cos 2\pi kY \sum f_i\, e^{-Bs^2} (\cos 2\pi hx_i \sin 2\pi ky_i) \\
+ & \cos 2\pi hX \sin 2\pi kY \sum f_i\, e^{-Bs^2} (\sin 2\pi hx_i \cos 2\pi ky_i) \\
+ & \cos 2\pi hX \cos 2\pi kY \sum f_i\, e^{-Bs^2} (\sin 2\pi hx_i \sin 2\pi ky_i) \Big] \\
& \text{when } h + k = 2n + 1
\end{aligned}
$$

Again let

$$
\left.
\begin{aligned}
\sum f_i\, e^{-Bs^2} (\cos 2\pi hx_i \cos 2\pi ky_i) &= A \\
\sum f_i\, e^{-Bs^2} (\cos 2\pi hx_i \sin 2\pi ky_i) &= B \\
\sum f_i\, e^{-Bs^2} (\sin 2\pi hx_i \cos 2\pi ky_i) &= C \\
\sum f_i\, e^{-Bs^2} (\sin 2\pi hx_i \sin 2\pi ky_i) &= D
\end{aligned}
\right] \quad \text{- - (3)}
$$

$$
\left.
\begin{aligned}
\cos 2\pi hX \cos 2\pi kY &= E \\
\cos 2\pi hX \sin 2\pi kY &= F \\
\sin 2\pi hX \cos 2\pi kY &= G \\
\sin 2\pi hX \sin 2\pi kY &= H
\end{aligned}
\right] \quad \text{- - (4)}
$$

where A, B, C & D in Equations (3) are constants for a particular molecular model and the temperature factors are also constant for any particular model.

The calculation proceeds as follows:- (1) The values of $f_i \exp(-B \sin^2\theta/\lambda^2)$ are calculated for each reflexion and each type of atom using the analytical f values calculated using the constants given by Forsyth and Wells (1959) and the value of B found by the method of Wilson (1942) and are stored temporarily. (2) The values of A, B, C & D are calculated for each reflexion and stored permanently and the value of $\sum|F_o|$ is also calculated and stored permanently. (3) The values of $F_{h,k}$ (X, Y) are calculated for each reflexion for a particular value of X & Y and the corresponding value of R (X, Y) is calculated and printed. The values of X & Y are varied systematically in increments so chosen to be fine enough to make interpolation of the minimum value reasonable and coarse enough to keep the calculation as short as possible. It is only necessary to compute one quarter of the unit cell for the plane group pgg. Using the 'Mercury' computer and only the fast access store it is possible to accommodate a group of 40 reflexions which can be chosen in any way. The time taken to calculate and punch each R - value is about $2\frac{1}{2}$ seconds and the total time for a 900 point calculation including input time is 40 minutes.

The input to the programme consists of the cell sides, temperature factors, total number and types of atoms in the asymmetric unit. These are followed by the Forsyth and Wells' parameters, the number of atoms of each type, the coordinates of the atoms relative to the arbitrary origin O^1, total number of reflexions, the indices of the reflexions (whose structure factors are required) with their corresponding F_o's, and, concluding the data, the increments along both the x & y axes are required.

Flow diagram of the minimum residual molecular location programme.

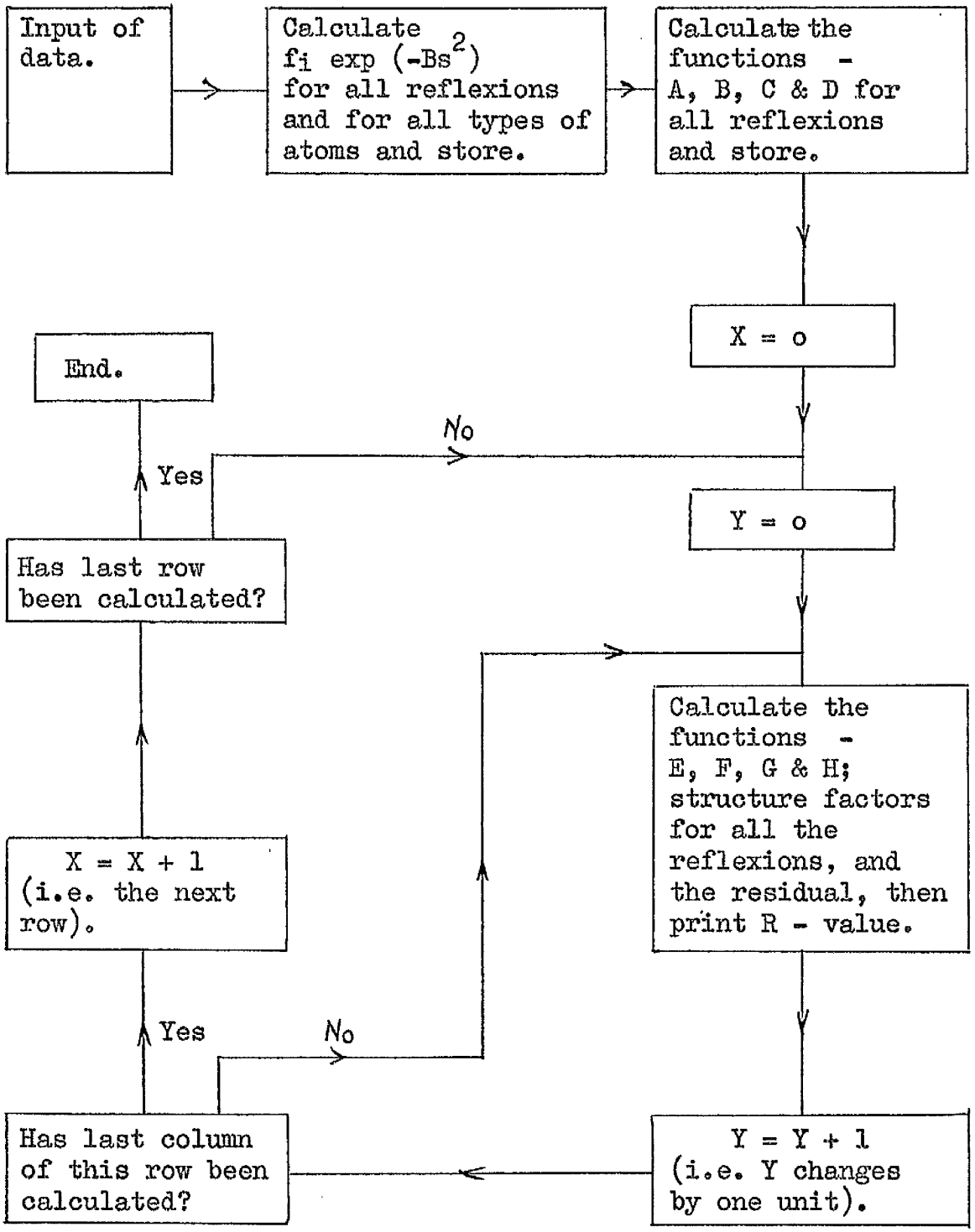


fig. 13.1.

13.3. <u>A programme for the refinement of atomic coordinates by direct calculation of the minimum residual.</u> This programme was designed to refine the coordinates in the plane groups pgg & cm. The flow diagram of the programme is shown in fig. 13.2, and the principle of the method has been discussed in chapter 8.

The programme initially computes and sums the contributions to all the structure factors of all the atoms except the one being refined, and stores these quantities. Suppose x_1 is one coordinate of the first atom to be refined. The coordinate is initially set at $x_1 - n\Delta x_1$ and the contribution to all the structure factors calculated and added to the stored contributions for the remainder of the atoms to give the calculated structure factors of all the reflexions. The corresponding value of R is calculated and stored. The coordinate is then increased to $x_1 - (n-1)\Delta x_1$ and the new R - value calculated in the same way. The latest R - value is compared with the previously stored R - value and the lower of the two values is preserved, together with the corresponding coordinate. The coordinate is then increased to $x_1 - (n-2)\Delta x_1$ and the process continued. In this way the smallest value of R within the range of variation of the coordinate is preserved together with the corresponding value of the coordinate.

When the scan in the x-direction is complete the y-coordinate is similarly treated. When both the x- and y-coordinates of the first atom have been dealt with, the new values of x, y and R are printed. The next atom is then dealt with in the same way, and so on until all the atoms have been included. The corrected parameters of the atoms are

always used in subsequent calculations. After the last atom has been dealt with a second cycle can be started if desired, without any further input of data. The analytical atomic scattering factors of Forsyth and Wells (1959) were used in calculating the structure factors, and individual isotropic temperature coefficients can be included if required. The scaling factor and the overall temperature factor can be adjusted at the end of each cycle using existing programmes. At present, the programme will accommodate up to 180 reflexions and up to 30 atoms of 5 different types. If the number of increments, n, is 5, i.e. the value of R is calculated at 11 points for each positional parameter, the calculation takes 32 minutes for one cycle of refinement involving 25 atoms including 7 minutes for the initial input of the data and for the preliminary calculation and storage of the structure factors. Two cycles can be computed in one hour. A comparable problem using the full matrix least-squares method on the same computer would take about 25 minutes per cycle. The refinement can be terminated at any point within the cycle since the refined coordinates of each atom are printed as they are obtained and are not effected by the refinement of the remaining atoms. The programme has also been modified to perform the necessary calculations for several other plane groups.

The input consists of cell parameters, maximum values of the indices h, k and $\sin\theta/\lambda$, the increment of change of the x and y coordinates, the number of different types of atoms, Forsyth and Wells' constants and the number of atoms of each type, the initial atomic coordinates with individual isotropic temperature factors, and finally,

the $F_{obs.}$ of all the reflexions. The accidentally absent reflexions are also required and these may be included either as 0 or $\frac{1}{2}F_{min.}$

Flow diagram of the programme for the refinement of atomic coordinates by direct calculation of the minimum residual

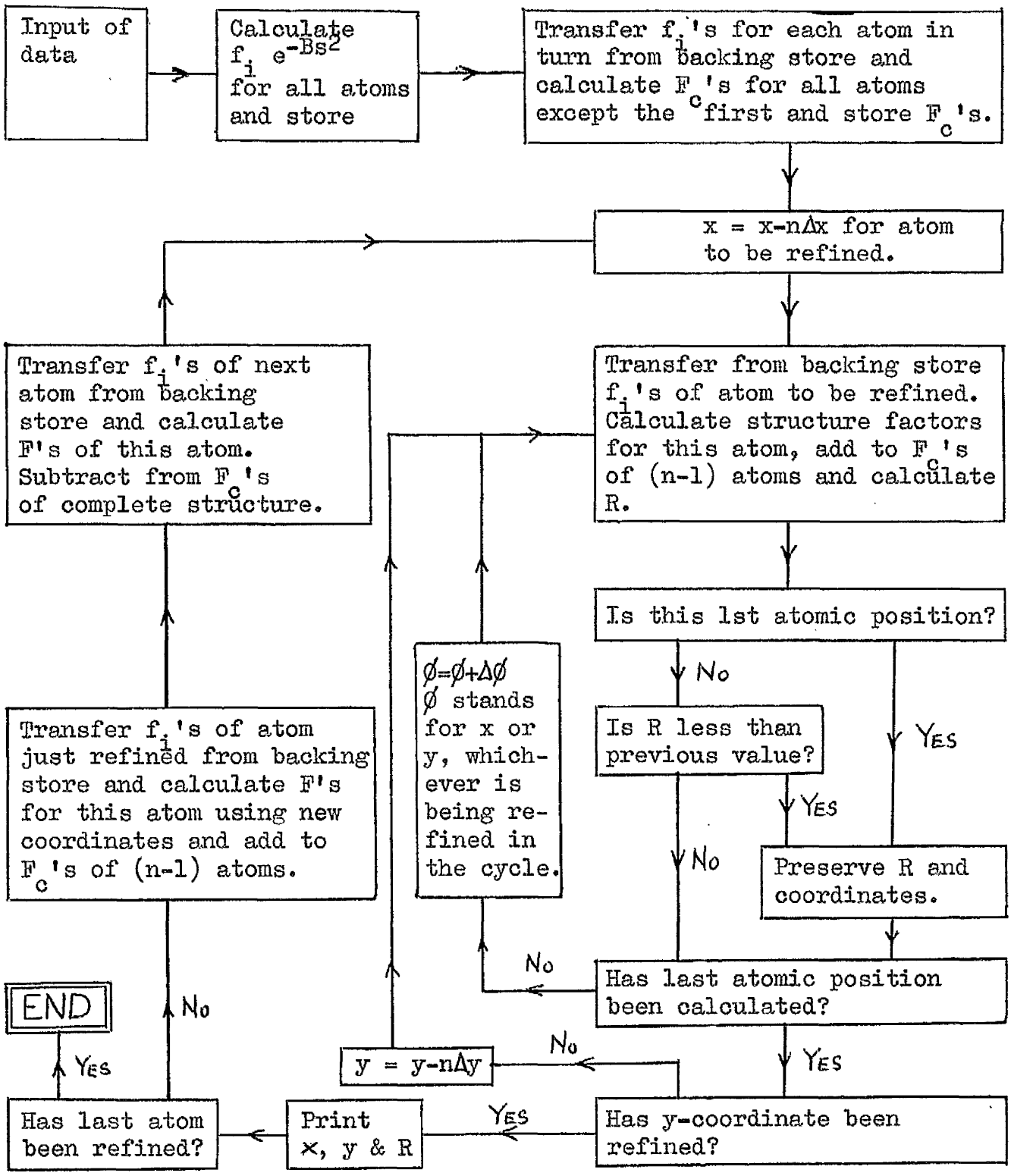


Table 13.2

13.4. <u>A programme for the refinement of isotropic thermal parameters by direct calculation of the minimum residual.</u> This programme was designed to refine the isotropic temperature factors in the plane groups pgg and cm. The principle of the method has been described in chapter 8. The flow diagram of this programme is given in fig. 13.3.

In refining the temperature parameters, this programme initially computes the contribution of each atom without a temperature factor to all structure factors and stores these quantities separately. These quantities are then corrected for individual temperature factors and added to all structure factors of all the atoms except the one being refined. Suppose B_1 is the temperature factor of the first atom to be refined. The value of B_1 is initially set at $B_1-n\Delta B_1$, then the contribution of the first atom to all structure factors is corrected for this value of the temperature factor and added to the contribution of the remainder of the atoms to give the calculated structure factors of all the reflections. The corresponding value of R is calculated and stored. The temperature factor B_1 is then increased to $B_1-(n-1)\Delta B_1$, the new value of R calculated in the same way, is compared with the previous value and the lower of the two is preserved. The value of B_1 is then increased to $B_1-(n-2)\Delta B_1$ and the process continued. In this manner, the value of B_1 corresponding to the lowest value of R within this range of variation of B_1 is taken as the best value of the temperature factor. The lowest value of R together with the corresponding value of B_1 are preserved and also printed. As each atom is dealt with in turn the new values of B_i and R are printed. The corrected parameters of the atoms are

always used in subsequent calculations. After the temperature parameter of the last atom is adjusted in this way, a further cycle can be continued, if desired, without any further input of data. The approximate time required per cycle of 18 atoms with 180 reflexions is about 7 minutes for isotropic refinement. The programme has also been modified to refine temperature parameters for several other plane groups.

The operation of the programme requires the following data:- (i) the unit cell dimensions, (ii) the maximum values of the indices h, k and also $\sin\theta/\lambda$, (iii) the increment of change of temperature parameter, (iv) the number of different types of atoms, (v) Forsyth and Wells' parameters and the number of atoms of each type, (vi) the refined atomic coordinates and individual isotropic vibration parameters, and finally, (vii) the observed structure factors must be included. The accidental absences must also be included either as zero or $\frac{1}{2}F_{min}$.

Flow diagram of the programme for the refinement of isotropic thermal parameters by direct calculation of the minimum residual

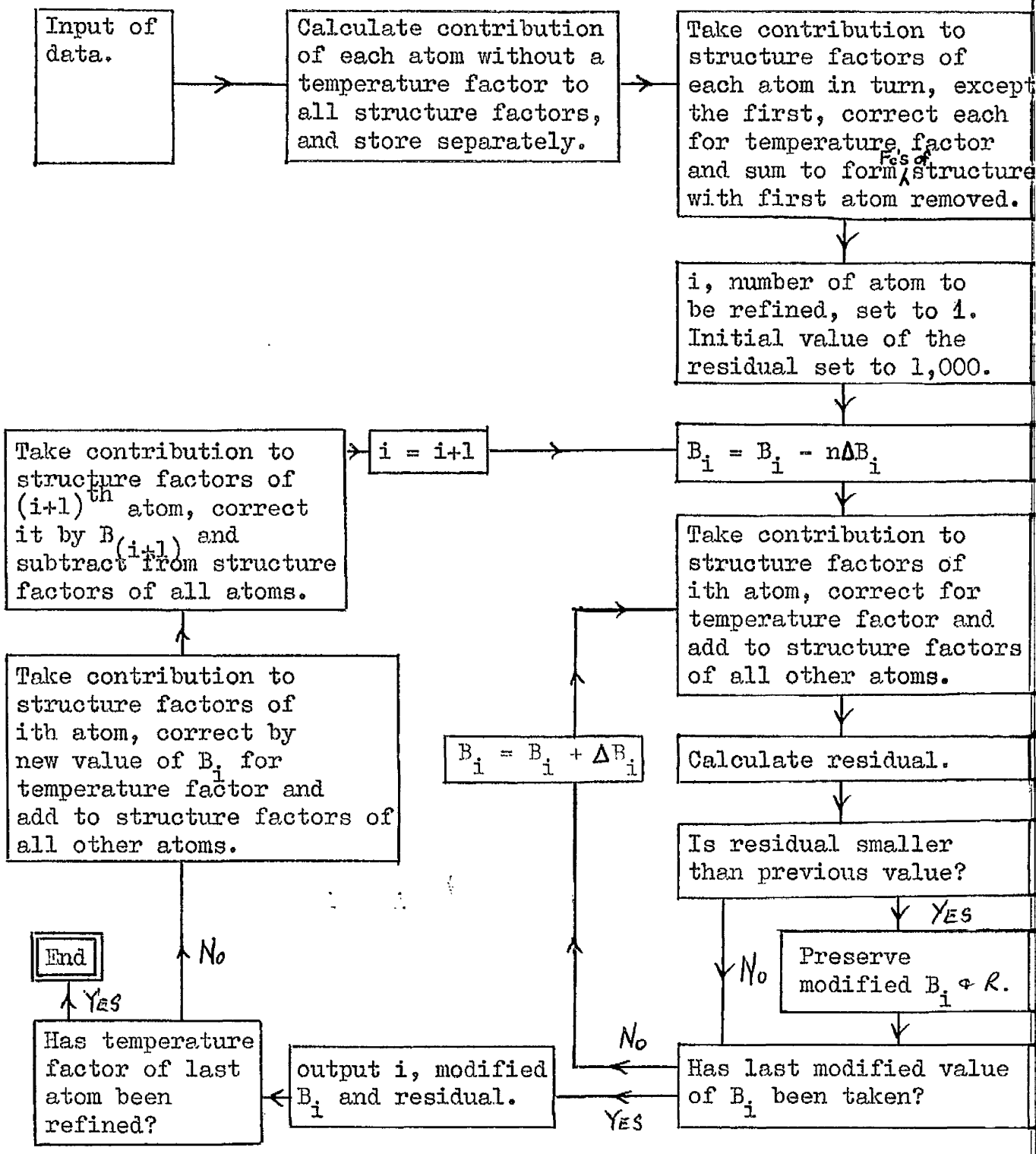


Fig. 13.3.

Appendix 1

Preliminary X-ray investigation of Strontium Caproate

Preparation and properties of crystals. Strontium Caproate crystallises from ethyl alcohol and water in the form of large, very thin, colourless plates. The very platy crystals effloresce rapidly when exposed to the atmosphere; even during a brief exposure to air they turned to powder. Because of this defect, a special technique had to be used for handling the crystals.

Initial attempts to preserve and photograph the crystals were made by covering them with a thin layer of 'vaseline' grease. The crystal was mounted on top of a glass fibre and a few drops of molten vaseline were allowed to run slowly over the crystal. From each drop some grease adhered to the crystal, and a fairly uniform covering was obtained. This method of preserving and photographing the crystals proved to be unsuccessful. The next attempt at preserving the crystals was made by sealing them in Lindemann glass capillary tubes, but even then, they appeared to be quite unstable. They seemed to be stable only in the presence of the mother liquor in the sealed capillary tube, but the placing of the crystals permanently in the tube and the taking of the photographs presented a difficult task. However, after several attempts, using different techniques it was possible to fix the crystal with 'Gloy' (in which the crystal was insoluble) in the presence of the mother liquor in the Lindemann capillary tube. There were practical difficulties in mounting and setting the crystals to any axis, because the long

capillary tubes could not be orientated into the required position.

Crystal data. The crystals are soft and can be cut in any direction in the plate face. When viewed in polarised light the crystals exhibit straight extinction parallel to two directions at right angles to each other in the plate face.

Density of the crystals was reported to be approximately 1.00 gms/cc This value was used for calculating the number of molecules per unit cell.

Collection of X-ray data. X-ray rotation and oscillation photographs taken about the a, b and c axes using cu k_α radiation, and Weissenberg photographs taken with crystals oscillating about the short axis, showed that the crystals of strontium caproate are monoclinic with unit cell dimensions:-

$a = 23.0, \quad b = 8.39 \quad$ and $c = 22.20$ Å.

These gave the number of molecules in the unit cell as .8. The photography was then repeated using a precession camera which was available in the department. The new cell dimensions thus obtained are:-

$a = 23.07, \quad b = 8.42, \quad$ and $c = 22.83$ Å
and $\beta = 97^\circ$.

Examination of the reflexions recorded on the oscillation and Weissenberg photographs showed that the systematic absences were hol for ℓ odd, and oko for k odd. This defined the space group uniquely as $P2_1/c$. The special projections possess symmetry as follows:-

(001) pgm; $a' = a$, $b' = b$,
(100) pgg; $b' = b$, $c' = c$,
(010) p2; $c' = c/2$, $a' = a$.

At this stage the work on the naphthocinnoline was progressing more rapidly, so this work was postponed for the time being.

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