THE CRYSTAL STRUCTURES OF SOME CALABASH-CURARE ALKALOIDS AND OTHER ORGANIC MOLECULES BY X-RAY METHODS

THESIS

for the Degree of
DOCTOR OF PHILOSOPHY
in the
UNIVERSITY OF GLASGOW
submitted
by
ANDREW TENNENT McPHAIL, B.Sc.

Chemistry Department

April, 1963.

ProQuest Number: 13849345

All rights reserved

INFORMATION TO ALL USERS
The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript
and there are missing pages, these will be noted. Also, if material had to be removed,
a note will indicate the deletion.

ProQuest 13849345

Published by ProQuest LLC (2019). Copyright of the Dissertation is held by the Author.

All rights reserved.
This work is protected against unauthorized copying under Title 17, United States Code
Microform Edition © ProQuest LLC.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

PREFACE

I wish to thank particularly Dr. G.A. Sim, and Professor J. Monteath Robertson, C.B.E., F.R.S., for their informative supervision throughout the period of my research.

I am grateful to Drs. J.S. Rollett and J.G. Sime for the use of the numerous programmes devised by them for the DEUCE computer.

I am indebted to the Department of Scientific and Industrial Research for financial support during the first two years of my research and to the University of Glasgow for my appointment to an Assistant Lectureship during which the research was completed.

SUMMARY

The main parts of this thesis describe the determinations of the structures of derivatives of two alkaloids of the calabash-curare series, caracurine-II and macusine-A, by X-ray methods. Another two sections deal with the determination of the crystal structure of a derivative of a naturally-occurring sesquiterpenoid lactone, geigerin, and with that of a monohalogenobenzene derivative, 2-chloro-4-nitroaniline.

A considerable amount of information regarding the major portion of the chemical structure of caracurine-II was available when the analysis of this structure was begun. Nothing was known of the crystal structure or of the absolute position of the atoms in the molecule. Examinations of crystals of the isomorphous dihalide derivatives, the dimethochloride and the dimethobromide, were made but owing to difficulty in ascertaining the locations of the halide ions the work on these was abandoned at an early stage. The elucidation of the structure of caracurine-II resulted from an analysis of the dimethiodide derivative.

Similarly, the greater part of the chemical structure of macusine-A was known when the X-ray analysis of crystals of the iodide derivative of this alkaloid was undertaken. The iodide ion was easily located and the structure was

very readily determined.

In neither the analysis of caracurine-II dimethiodide nor that of macusine-A iodide was great accuracy of the molecular parameters attempted. Consequently, the results have considerable limitations imposed upon them and the finer details of the molecular dimensions are obscured.

A structure and partial stereochemistry of geigerin had been proposed when crystals of bromogeigerin acetate were received from Professor Barton. The X-ray crystal analysis of this derivative of geigerin confirmed the proposed structure. Unfortunately the substitution of the bromine atom into geigerin acetate did not occur at the expected position but at a centre which was of stereochemical interest. The outcome of this was that the relative stereochemistry of the geigerin molecule at that site at which this substitution had taken place could not be inferred from the results of the analysis. The analysis was carried out to a fair degree of accuracy. Some interesting features which can be correlated with those observed in other molecules are evident in the structure. The work on this structure analysis was shared with Miss J.A. Hamilton who performed, as far as possible, alternate series of calculations.

The crystal analysis of 2-chloro-4-nitroaniline was undertaken in order to determine the finer details of the molecule, the gross structure being entirely known. The results clearly establish that, in the solid state, the nitro group of the molecule is twisted out of the plane of the benzene ring by a small amount.

TABLE OF CONTENTS.

Preface

Summary

PART I

Some Methods of X-ray Crystal Structure Analysis

Page

PART II

The Structure of Caracurine II:

X-ray Analysis of Caracurine-II Dimethiodide.

Page

PART III

The Structure of Macusine-A:

X-ray Analysis of Macusine-A Iodide.

Page

PART IV

The Structure of Geigerin:

X-ray Analysis of Bromogeigerin Acetate.

PART V

X-ray Analysis of 2-Chloro-4-nitroaniline.

PART I

Some Methods of X-ray Crystal Structure Analysis.

1.1 INTRODUCTION.

The X-rays produced when high-speed electrons hit atoms have wavelengths of the same order of magnitude as the distances between atoms. The discovery of this fact, due to Laue in 1912, opened the way, not only to the understanding of the nature of X-rays, but also to the determination of the exact arrangement of the atoms in a crystal.

Complex and lengthy calculations are required to build up an image of the pattern of atoms in a crystal. In the early days of crystallography only elements and simple salts could be tackled with any hope of success. However, with the accumulation of knowledge, inorganic structures of ever-increasing complexity were determined. Among organic compounds progress was at first slow but the pace accelerated as soon as the structures of the principal fundamental types of molecules - normal paraffin chain, benzene ring, naphthalene nucleus - were well established and the structures of such complex substances as carbohydrates, sterols, phthalocyanines, strychnine and vitamin B_{12} were determined.

With the advent of the electronic computer the time required for the calculations was greatly reduced, with the result that X-ray analysis now plays an increasingly important part in research and the structures of many complex naturally-occurring organic compounds have been elucidated.

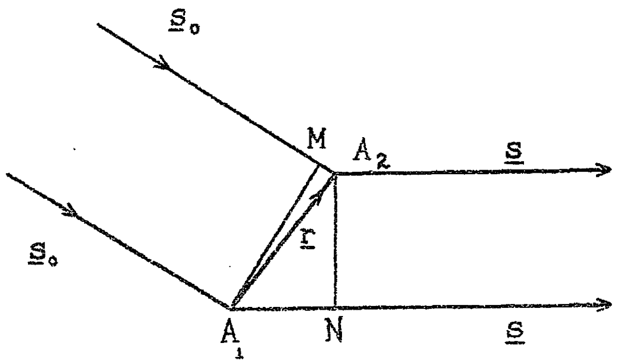
1.2 DIFFRACTION BY A LATTICE.

The simplest kind of three-dimensional pattern is a set of points, each point located at a lattice point. The angles of diffraction produced by a crystal depend only upon the lattice dimensions. Assuming that each lattice point is the site of an electron, the position of the electrons can be specified by the ends of vectors $\underline{r}$ such that

$$\underline{r} = u\underline{a} + v\underline{b} + w\underline{c}$$

where $\underline{a}$, $\underline{b}$, and $\underline{c}$ are the primitive translations of the lattice and u, v, w are integers.

When each electron is located in the path of an X-ray beam, it is forced into oscillation by the electromagnetic field of the X-rays impinging on it, and, due to this, the electron in turn becomes a source of secondary radiation. It is necessary to consider the phase differences between the waves scattered in any particular direction in order to find the total effect of the combination of these secondary waves.



In the diagram A_1 and A_2 are two lattice points separated by a vector distance $\underline{r}$, and A_1M and A_2N are drawn in the incident and diffracted wave front respectively. A parallel beam of X-rays, of wavelength λ, falling on the lattice in a direction defined by the vector $\underline{s}_0$ (modulus $^1/_\lambda$) is scattered in a direction defined by the vector $\underline{s}$ (modulus $^1/_\lambda$).

The path difference between the scattered waves is

$$A_1N - A_2M = \lambda\,(\underline{r}.\underline{s} - \underline{r}.\underline{s}_0) = \lambda\,\underline{r}.\underline{S}.$$

$$\text{where } \underline{S} = \underline{s} - \underline{s}_0$$

The scattered waves interfere with each other except when they happen to be in phase and in order that this condition is satisfied the path difference must be equal to an integral number i.e. $\underline{r}.\underline{S}$ must be an integer.

Thus $(u\underline{a} + r\underline{b} + w\underline{c}).\underline{S}$ must be integral. Since u, v, and w change by integral values each of the products separately must be integral i.e.

$$\left.\begin{aligned} \underline{a}.\underline{S} &= h \\ \underline{b}.\underline{S} &= k \\ \underline{c}.\underline{S} &= \ell \end{aligned}\right)$$

where h, k, ℓ are integers.

These equations are known as the Laue equations and when they are simultaneously satisfied a diffracted beam of maximum intensity will be produced. It was not until W.L. Bragg (1913) identified the integers h, k and ℓ with the Miller indices of the lattice planes that use could be made of these equations to interpret X-ray spectra and to determine the structure of crystals.

Rewriting Laue's equations as

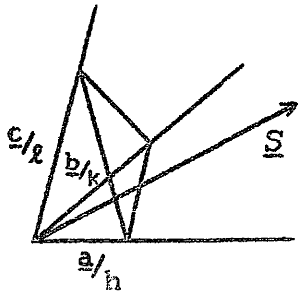
$$\underline{a}/h \cdot \underline{S} = 1$$

$$\underline{b}/k \cdot \underline{S} = 1$$

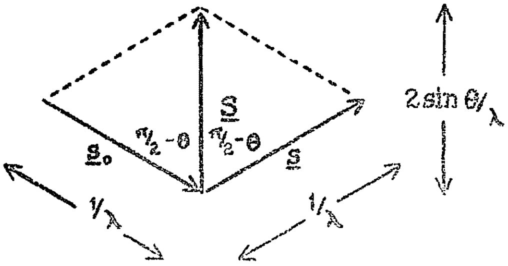
$$\underline{c}/\ell \cdot \underline{S} = 1$$

then, subtraction of these in pairs gives $(\underline{a}/h - \underline{b}/k)\cdot\underline{S} = 0$, $(\underline{a}/h - \underline{c}/\ell)\cdot\underline{S} = 0$. This means that the vector $\underline{S}$ is perpendicular to the vector $\underline{a}/h - \underline{b}/k$ and to the vector $\underline{a}/h - \underline{c}/\ell$. These are vectors in the plane of Miller indices h k ℓ (Fig.I). Thus $\underline{S}$ is perpendicular to this plane.

Since $\underline{S}$ is a vector in the direction of the bisector of the incident and diffracted beam (Fig II), this bisector is identified with the normal to the h k ℓ plane. This justifies the concept of each diffraction as a "reflection" of the rays from lattice planes.



(I)



(II)

The spacing d, the perpendicular distance of the plane from the origin, is the projection of $\underline{a}/h$, $\underline{b}/k$, or $\underline{c}/\ell$ on the vector $\underline{S}$,

$$\text{i.e.} \quad d = \frac{\underline{a}/h \cdot \underline{S}}{|S|} .$$

But, from the Laue equations $\underline{a}/h \cdot \underline{S} = 1$ and from Fig(II), $|S| = \dfrac{2 \sin\theta}{\lambda}$

so,

$$d = \frac{\lambda}{2 \sin\theta} \quad \text{or } \lambda = 2\, d \sin\theta.$$

This is Bragg's Law.

1.3 THE ATOMIC SCATTERING FACTOR.

In the above argument, the scattering units were assumed to be electrons in order that their linear dimensions could be neglected in comparison with both the space-lattice dimensions and the wavelength of X-rays. Atoms in crystals cannot, however, be regarded as scattering points as the diameter of the electron cloud of an atom is of the same order of size as the distance between the centres of adjacent atoms. The consequences of this are that phase differences exist between rays scattered from different points in this volume and so the intensity of the resultant beam is reduced.

The scattering power of an atom, designated f, is expressed in terms of the scattering power of a single, free electron. For small angles of diffraction the above-mentioned phase differences are small and the scattered amplitude will approach Z , the atomic number of the atom. As the angle of diffraction increases the phase differences become larger and thus the scattered beam becomes weaker. From this it can be seen that, for a given wavelength, f is a function of the angle of scattering and of the distribution of electrons in the atom.

For many atoms the scattering powers have been deduced from the measured intensities of reflections from crystals whose structures are firmly established (James and Brindley, 1931) but it is also possible (Hartree, 1928) to calculate the values from the electronic structures of the atoms and these calculated values agree very well with the experimental values.

1.4 THERMAL VIBRATIONS.

In the deduction of the theoretical scattering factors it is assumed that the atoms are at rest. Atoms in crystals vibrate at ordinary temperatures with frequencies much lower than those of X-rays; at any one instant some atoms are displaced from their mean positions in one direction while those in another part of the crystal are displaced in another direction. Consequently, diffracted X-rays which would be exactly in phase if the atoms were at rest are actually not exactly in phase and the intensity of the diffracted beam is thus lower than it would be if all the atoms were at rest.

It is a very complex matter to make an accurate allowance for thermal motion. A fair approximation to this effect on the intensity of the X-ray reflections can be made by using the factor $f = f_o \exp\left(\frac{-B \sin^2 \theta}{\lambda^2}\right)$ where θ is the Bragg angle, f_o is the atomic scattering factor for atoms at rest, and B, the Debye(1914) temperature factor, is a constant.

The value of B is given by $B = 8\pi^2 \bar{u}^2$, where $\bar{u}^2$ is the mean square displacement of the atoms from their mean positions. The use of the above expression for the scattering factor implies that all the atoms vibrate with equal amplitudes. This is not strictly true and, in general, thermal vibrations must be different for every crystallographically independent atom in a unit cell since they depend on the surroundings of the atom as well as on its inertia. Another assumption implied by the expression given above is that the thermal vibrations have the same magnitudes in all directions of the crystal. In some crystals this approximates to the truth but in organic molecules there are many examples in which the vibrations are markedly anisotropic.

Both of these effects are usually ignored at the inception of a structure analysis but allowance can be made for them during the refinement stages.

1.5 THE STRUCTURE FACTOR EXPRESSION.

The crystal lattice described so far consists of atoms of finite size located with their mean positions at lattice points. In most crystals, however, a certain arrangement of atoms exists within each unit cell. Any one set of atoms in different unit cells can be regarded as lying upon a lattice. A crystal with N atoms in the unit cell can be regarded as being based upon N identical interpenetrating lattices, each of which will obey the Laue and Bragg conditions, but the different lattices will, in general, be out of phase. The intensities of the scattered rays will thus depend upon the atomic arrangement within the unit cell.

The position of the $j^{\underline{th}}$ atom situated at the point (x_j, y_j, z_j), where x_j, y_j and z_j are fractions of the lattice dimensions, can be represented by the vector $\underline{r}_j$, where $\underline{r}_j = x_j\underline{a} + y_j\underline{b} + z_j\underline{c}$.

The path difference between the waves scattered by these atoms and those that would be scattered by a set of atoms at the points of the lattice that describes the unit cells is $\lambda\, \underline{r}_j . \underline{S}$. Thus the expression for the complete wave scattered by the $j^{\underline{th}}$ lattice contains a term f_j exp. $2\pi i\, \underline{r}_j . \underline{S}$, where f_j is the scattering factor of the $j^{\underline{th}}$ atom.

A term $F = \sum_{j=1}^{N} f_j \exp 2\pi i.\underline{\underline{r}}_j.\underline{\underline{S}}$ will therefore occur in the expression for a complete wave scattered by the crystal,

$$\text{i.e.}\quad F = \sum_{j=1}^{N} f_j \exp 2\pi i \quad (x_j.\underline{\underline{a}}.\underline{\underline{S}} + y_j.\underline{\underline{b}}.\underline{\underline{S}} + z_j.\underline{\underline{c}}.\underline{\underline{S}})$$

$$= \sum_{j=1}^{N} f_j \exp 2\pi i \quad (hx_j + ky_j + \ell z_j).$$

The quantity F is a function of h, k and ℓ and is called the <u>structure factor</u>. It is a complex resultant, characterised both by an amplitude $|F|$ and a phase constant α. It can be evaluated by means of the expressions:

$$|F(hk\ell)| = \sqrt{A^2 + B^2}$$

$$\alpha(hk\ell) = \tan^{-1} B/A$$

where $A = \sum_{j=1}^{N} f_j \cos 2\pi \quad (hx_j + ky_j + \ell z_j)$

and $B = \sum_{j=1}^{N} f_j \sin 2\pi \quad (hx_j + ky_j + \ell z_j)$.

This is valid for all crystals, whatever their symmetry; but, whenever there is a centre of symmetry at the origin there is no need to calculate the sine terms, since in aggregate they are bound to add up to zero. The resultant therefore can be obtained by summing the cosine terms alone and the possible phase angles are thus limited to 0 or π depending upon whether the expression above for A is positive or negative.

The more general form of the structure factor can be obtained by considering separately each element of volume of the unit cell. If ρ (x, y, z) is the electron-density at the point (x, y, z) the amount of scattering matter in the volume element $V\,dx\,dy\,dz$ is $\rho.V\,dx\,dy\,dz$ and the structure factor equation is

$$F(hk\ell) = \int_{x=0}^{1}\int_{y=0}^{1}\int_{z=0}^{1} V\,\rho\,(x,y,z)\exp 2\pi i(hx + ky + \ell z).\,dx\,dy\,dz,$$

1.6 FOURIER SERIES

It is well-known that a periodic function can be represented by an appropriate sum of the cosine and sine terms known as a Fourier series. Since a crystal is periodic in three-dimensions its electron-density can neatly be represented by such a series in the general form

$$\rho\,(x,y,z) = \sum \sum_{-\infty}^{\infty} \sum A(p,q,r)\ \exp 2\pi i(px + qy + rz)$$

p, q and r being integers and A(p, q, r) the Fourier coefficient of the general form.

In order to evaluate this series and so obtain the electron-density at any point in the crystal it is necessary to calculate the coefficients A(p, q, r).

Substituting this series for ρ (x, y, z) in the general expression for the structure factor gives

$$F(hk\ell) = \int_0^1\!\!\int_0^1\!\!\int_0^1 \sum \sum_{-\infty}^{\infty} \sum VA(p,q,r)\exp 2\pi i(px + qy + rz).\ \exp 2\pi i\,(hx + ky + \ell z).\ dx\ dy\ dz.$$

On integrating, every term is zero except that for which $p = -h$, $q = -k$, and $r = -\ell$, which gives

$$F(hk\ell\,) = \int_0^1\!\!\int_0^1\!\!\int_0^1 VA(\bar{h}\bar{k}\bar{\ell}\,)\ dx\ dy\ dz.$$

Therefore $\quad F(h\ k\ \ell\,) = VA\ (\bar{h}\ \bar{k}\ \bar{\ell}\,).$

This shows that the Fourier coefficients, A, are directly related to the corresponding structure factors and

$$\rho\,(x,y,z) = \sum\sum\sum_{h,k,\ell=-\infty}^{\infty} \frac{F(hk\ell\,)}{V}\ \exp - 2\pi i\ (hx + ky + \ell z).$$

The zero term of the series is a constant

$$F(000) = \int_0^1\int_0^1\int_0^1 V \rho\,(x,y,z)\,dx\,dy\,dz = Z.$$

The Fourier series above is conveniently written

$$\rho\,(x,y,z) = \sum\sum_{-\infty}^{\infty}\sum \frac{|F(hk\ell)|}{V} \cos\left[2\pi hx + 2\pi ky + 2\pi \ell z - \alpha(hk\ell)\right]$$

where $\alpha\,(hk\ell)$ represents the phase constant associated with the amplitude $|F(hk\ell)|$ which can be calculated from the observed intensities.

1.7 RELATION BETWEEN INTENSITY AND STRUCTURE AMPLITUDE.

The total energy reflected by the volume dV in the course of a single pass of the crystal through the region of the Bragg reflection may be written:-

$$E = \left(\frac{I_o \lambda^3 N^2 dV}{\omega}\right)\left(\frac{e^4}{m^2c^4}\right) Lp|F|^2$$

where e = the charge on the electron; m = the mass of the electron; c = the velocity of light; I_o = the intensity of the incident radiation; λ = the wavelength of the X-radiation; N = the number of the unit cells per unit volume; dV = the volume of the crystal; ω = the angular velocity of the crystal; L = the "Lorentz factor"; p = the polarisation factor, $\frac{1 + \cos^2 2\theta}{2}$; F = the factor representing the resultant scattered by a single unit cell.

This expression should only hold for minute crystals but it is found that it is applicable to many comparatively large crystals. It must be inferred that in such crystals perfect continuity of the lattice structure is only maintained over very small regions, and, that some break or slight change in orientation occurs. The crystal, in fact, behaves like a mosaic of small blocks.

In all the usual experimental arrangements the X-ray beam is unpolarised which means that the azimuth of the electric vector assumes all directions with time. The effective amplitude of the radiation after it is reflected at the angle of 2θ consists only of components of these azimuths after reflection. This feature has the effect of reducing the intensity of the X-ray beam by a factor p, the polarisation factor, which is equal to $\frac{1 + \cos^2 2\theta}{2}$ and provides the necessary averaging.

The "Lorentz factor" varies with the type of photograph. For the equatorial reflections on a normal rotation photograph it is $\frac{1}{\sin 2\theta}$. Expressions for rotation photographs taken with the beam not normal to the axis of rotation are given by Tunell (1939) (for equi-inclination Weissenberg photographs).

In addition to these factors of simple geometric origin for which allowance must be made in transforming the measured energies of spectra to the square of the structure amplitude there are some further factors which can arise in a less simple fashion, viz. absorption and extinction.

X-radiation is absorbed by matter. For crystals of a natural shape completely bathed in the X-ray beam it is possible to calculate absorption corrections but the calculations are laborious. Small crystals are generally employed in order to eliminate absorption as much as possible.

In some crystal specimens the region of perfect crystal structure may be too large. In such cases, and particularly for the strong X-ray reflections, extinction of the incident X-ray beam by reflection from the surface layers is an important factor. This effect is called primary extinction and it is very difficult to devise any systematic correction for it.

Secondary extinction occurs even in good mosaic crystals. It is due to the screening of the lower blocks of the crystal by the upper blocks which can reflect away an appreciable amount of the incident radiation in the case of very strong reflections. Systematic corrections for this effect can be applied.

1.8 THE PHASE PROBLEM AND METHODS OF SOLUTION.

It has been shown above that the electron-density of a crystal can be represented by a Fourier series which requires a knowledge of the values of both $|F(hk\ell)|$ and $\alpha(hk\ell)$. Although the value $|F(hk\ell)|$ can be derived from the measured intensities, no experimental means has been found for observing the phases. This constitutes the phase problem in X-ray crystallography.

1.8.1. Trial and Error Method.

In order to try to solve a crystal structure by this method it is necessary to postulate a set of atomic parameters that conforms with the space group symmetry, calculate structure amplitudes and compare these calculated values with those observed. Violent disagreements infer that the postulation is wrong when it is necessary to try another set of parameters. This procedure is continued until the correct result is achieved. In order to simplify the number of possible structures use is made of the distribution of X-ray intensities, experience gained from other crystals and chemical and physical properties of the compound. It will be noted that this method could require many calculations before the correct result is obtained. A way of circumventing these calculations is to make use of the Fourier transform of a set of atoms. Holes representing both the atomic positions in the projection of a unit and the atom type are punched on a mask. The diffraction pattern in parallel light - the Fraunhofer diffraction pattern - represents the required Fourier transform which can be compared with the corresponding weighted reciprocal lattice. This permits the test of various possible trial structures to be performed fairly rapidly.

Whichever of these methods of comparing the results of a trial structure with the experimental results is used, great care has to be taken in their interpretation as a structure which is nearly correct may be discarded when slight shifts in the atomic positions would have achieved success.

1.3.2. Vector Methods.

The vector representation of a crystal structure, developed by Patterson (1934, 1935) does not attempt to determine the phases of the structure factors. Instead of using the structure factors, the squares of the moduli of the structure factors are used as coefficients; these quantities are directly related to the observed intensities.

Patterson defined a function

$$P(u,v,w) = V \int_0^1 \int_0^1 \int_0^1 \rho(x,y,z) \ \rho(x+u,y+v,z+w)dx\ dy\ dz.$$

In this expression ρ (x+u, y+v, z+w) gives the distribution about (x,y,z) as a function of the parameters u,v,w and it represents a distribution similar to ρ (x,y,z) but displaced from the point (x,y,z) through a distance whose components are (u,v,w). This distribution function is weighted by the amount of scattering matter in the volume element at (x,y,z) viz. ρ (x,y,z) dx dy dz.

If the values for the electron-densities given by the Fourier series are substituted in this function then:-

$$P(u,v,w) = \frac{1}{V}\int_0^1\int_0^1\int_0^1 \sum_h \sum_k \sum_{\ell} \sum_{h'} \sum_{k'} \sum_{\ell'=-\infty}^{\infty} F(hk\ell)\exp\{-2\pi i\ (hx+ky+\ell z)\}$$

$$\times\ F(h'k'\ell')\ \exp\left\{-2\pi i(h'x+k'y+\ell' z)\right\}\exp\left\{-2\pi i\ (h'u+k'v+\ell' w)\right\}.dx\ dy\ dz.$$

The right hand side of this equation is zero unless h=h', k=k' and $\ell = \ell'$, when

$$P(u,v,w) = \frac{1}{V} \sum_h \sum_k^{\infty} \sum_{\ell=-\infty} F(hk\ell)\ F(\bar{h}\bar{k}\bar{\ell})\ \exp\left\{-2\pi i\ (h'u+k'v+\ell' w)\right\}$$

and, since $F(hk\ell)$ and $F(\bar{h}\bar{k}\bar{\ell})$ are complex conjugates

$$P(u,v,w) = \frac{1}{V} \sum_h \sum_k^{\infty} \sum_{\ell=-\infty} |F(hk\ell)|^2 \exp 2\pi i\ (hu+kv+\ell w)$$

The Patterson function will be finite only for values of u, v and w that represent vectors joining two atoms. This function will therefore show a superposition of all the interatomic vectors of the crystal. It would perhaps appear that this expression of the results would solve the structural problem but the difficulties of the method are quite considerable.

The number of interatomic vectors for an array of n atoms is $n(n-1)/_2$ and in the general case each of these will give rise to a separate peak in the distribution function. The chance of so many peaks being resolved is extremely small so that large groups of peaks will tend to coalesce. However, if some of the atoms in the cell have much greater scattering powers than the others, the vectors between the "heavier" atoms will stand out and the information thus gained may lead to a knowledge of the co-ordinates of these atoms.

Harker (1936) has shown that provided the crystal has planes or axes of symmetry (or screw axes or glide planes) it is easy to specify on which plane or along which line of the vector cell the most useful information will be found. This provides a useful aid in the solution of the Patterson function.

1.8.3. The Heavy Atom Method.

If a relatively small number of "heavy" atoms are present in the unit cell their positions can be located, in general, fairly easily by Patterson methods. The vectors between light atoms become second order qualities and only the heavy atom - heavy atom and heavy atom - light atom vectors are significant.

The structure factor for a crystal structure with one heavy atom in the unit cell may be written

$$F(hk\ell) = f_H \exp 2\pi i(hx_H+ky_H+\ell z_H) + \sum_n f_n \exp 2\pi i(hx_n+ky_n+\ell z_n)$$

where f_H is the scattering factor of the heavy atom whose parameters are x_H, y_H, z_H. The contributions of the heavy atoms tend to dominate the phases of the structure factors except when their contribution is small or zero. Sim (1957) has performed calculations on the fraction of structure factors whose phases should be determined within specified limits by a selected atom or group of atoms. Those $F(hk\ell)$'s whose phases can be regarded as being approximately correct are used to carry out a first Fourier synthesis which results in a map revealing some, or all, of the features of the structure. If only some of the light atoms are located the work generally proceeds by successive approximations as the positions of the light atoms are revealed and included in the phasing calculations until all the structural features are revealed.

There are unfortunate consequencies in the use of this method. The major portion of the structure amplitude being due to the heavy atom contribution, all information concerning the positions of the light atoms in the structure must be derived from the smaller remaining part. To achieve the same accuracy in determination of atomic positions as in a structure containing light atoms alone, it is therefore necessary to measure the intensities with much greater precision, but, on the other hand, the presence of the heavy atom means a higher absorption coefficient and makes the measurement of intensities more difficult. The isomorphous substitution method minimises this difficulty because after the phase determination has been completed the final analysis can be conducted on the derivative containing the lighter atom.

The determinations of the structures of the phthalocyanines, (Robertson,1935, 1936, Robertson and Woodward,1937, 1940.) present classical cases in the use of both the heavy atom and isomorphous replacement methods of structure determination.

From the foregoing considerations it can be seen that if a heavy atom can be inserted at some point in a structure which does not already contain one then it should be possible to determine the crystal structure employing this technique.

1.9 METHODS OF REFINEMENT.

In order to obtain better agreement between the observed and calculated structure amplitudes and to approximate the calculated to the true phases it is necessary to make adjustments to the positional and thermal parameters of the model of the structure as determined by the foregoing methods.

1.9.1 Fourier Synthesis.

The oldest method of refinement is that of successive Fourier synthesis. The structure factors and phases are calculated on the basis of the structure model. The phases so obtained are attributed to the observed structure amplitudes and, from the resulting Fourier synthesis a new set of improved co-ordinates is obtained. Successive cycles of phasing calculations followed by Fourier synthesis are performed, each cycle taking the structure closer to the correct one.

This method suffers from the serious defect that the number of terms employed in the Fourier series is limited by experimental conditions, particularly by the wave-length used. This results in an artificial termination of the Fourier series which, in turn, causes the diffraction ripple from one atom to add itself to the peaks of other atoms; the resultant disturbance in the peaks is particularly marked on nearest neighbours and is greatest in the vicinity of heavy atoms. As a result of this series-termination effect the co-ordinates of every atom are shifted due to the diffraction ripples of others. The effect is not easy to allow for directly, but may be estimated for by a method due to Booth (1945, 1946). When the process of refinement is complete, the last Fourier synthesis (calculated using F_o as coefficients) is known to have its peak locations displaced by unknown amounts due to series-termination effects. Another Fourier synthesis can be computed, employing the same phases but with F_c as coefficients, and it will be subject to substantially the same series-termination errors. Specific co-ordinates are inserted into this F_c synthesis and the same co-ordinates should be deduced from it but on account of the series-termination errors these two sets are found to differ by Δx_j, Δy_j, Δz_j, for atom j. This error may then be subtracted from the co-ordinates of the atom j as derived from the original F_o synthesis. This correction is known as a "back-shift" correction.

1.9.2 Difference Synthesis.

The difference synthesis method of refinement, using $(F_o - F_c)$ as Fourier coefficients, was first suggested by Booth (1948) and its properties were exploited by Cochran (1951).

When the proposed model exactly matches the crystal structure the difference map is characterised by a flat topography whose only features are minor and random undulations caused by errors of observation. The difference synthesis gives a complete picture of the discrepancies between F_o and F_c and the proposed structure must be modified in such a way as to produce a nearly featureless difference map if any such discrepancies exist. This method of refinement also allows for the series-termination errors which are substantially identical in the proposed and actual structures and therefore will vanish on subtraction.

If the calculated co-ordinates (x_c, y_c, z_c) are marked on the difference Fourier synthesis, the directions of steepest ascent at these points give the directions of the shifts. The magnitude of the shifts (ϵ) can be estimated, with certain assumptions, by computation. Near the centre of the atom the electron-density at a distance r from the centre is given very closely by

$\rho(r) = \rho(o) \exp -pr^2$ where $\rho(o)$ is the maximum density. This may be re-written $\rho(r) = \rho(o)(1-pr^2)$ provided r is small. The gradient $\rho_{obs} - \rho_c$ is the gradient of ρ_{obs} less the gradient of ρ_c, but, at the peak of ρ_c, its gradient is zero, so that

$$\frac{d(\rho_{obs} - \rho_c)}{dr} = \frac{d\rho_{obs}}{dr} = \frac{d(\rho(o)_{obs} - \rho(o)_{obs}\, pr^2)}{dr}$$

$$= 2\,\rho(o)_{obs}\, pr$$

Therefore,

$$\epsilon = r = \frac{d(\rho_{obs} - \rho_c)}{dr} \Big/ 2\rho(o)_{obs}\, p .$$

The value of ρ_{obs} is given approximately by $\rho_{obs} = z(p/\pi)^{3/2}$ where p is about 5.0. This derivation is independent of the scale of ρ_{obs} since ρ_c enters the derivation only in that the gradient at its peak is zero. For this reason the final location of each atom should be at or near zero gradient of the difference map.

If the atom location happens to occur on a hill or depression corrections must be applied to the isotropic thermal parameters. If it appears on a small hill surrounded by a ring-shaped depression then the temperature correction has been overestimated since $\rho_{obs} > \rho_c$ at the peak, but, if it appears in a depression the reverse is the case, $\rho_{obs} < \rho_c$ at the peak.

When the thermal motion is anisotropic the observed electron distribution is drawn out in the direction of maximum vibration and narrowed in a direction at right angles to it giving rise to characteristic saddle points in the difference Fourier synthesis.

1.9.3. The Method of Least-Squares.

Hughes (1941) introduced the "least-squares" refinement of atomic parameters as a supplementary method to that of Fourier synthesis in the final stages of crystal structure analysis. This method introduces a weighting factor to the measured coefficients as a function of their reliability.

The theory of errors predicts that if the errors in the measured F_o's follow the normal or Gaussian law, then the best atomic parameters are those which would result in a minimisation of the quantity

$$R = \sum_{u} w_1 \, (hk\ell) \, (|F_o(hk\ell)| - |F_c(hk\ell)|)^2$$

where w_1, the weight of a particular term, should be taken inversely proportional to the square of the probable error of the corresponding F_o's. $\sum_{u}$ denotes a sum over all independent terms. R depends not only on atomic co-ordinates but also on the temperature factor. When the value of R is close to a minimum, systematic minimisation can be accomplished in the following manner.

The general relation for the computation of each structure factor is

$$F_c = \sum_{r} f_r \exp 2\pi i \, (hx_r + ky_r + \ell z_r).$$

The variables are exponentials in x, y, and z and these do not supply the desired linear equations which can, however, be devised by using the first two terms in Taylor's series. In one-dimension these terms give

$$f(x + \epsilon) = f(x) + \epsilon \frac{df(x)}{dx}$$

where ϵ is the error which, when added to x gives the correct value. In three-dimensions, partial differentials are used. The first two terms in Taylor's series give

$$f(x+\epsilon_x, y+\epsilon_y, z+\epsilon_z) = f(x,y,z) + \epsilon_x \frac{\partial f(x,y,z)}{\partial x} + \epsilon_y \frac{\partial f(x,y,z)}{\partial y} + \epsilon_z \frac{\partial f(x,y,z)}{\partial z} .$$

In this, $f(x+\epsilon_x, y+\epsilon_y, z+\epsilon_z) \longrightarrow F_o$

while $f(x,y,z) \longrightarrow F_c$.

Then $\Delta F = F_o - F_c$

$$= F_c + \sum_{n=1}^{N} \left(\epsilon_x \frac{\partial F_c}{\partial x_n} + \epsilon_y \frac{\partial F_c}{\partial y_n} + \epsilon_z \frac{\partial F_c}{\partial z_n} \right) - F_c$$

and therefore, $\Delta F = \sum_{n=1}^{N} \left(\epsilon_x \frac{\partial F_c}{\partial x_n} + \epsilon_y \frac{\partial F_c}{\partial y_n} + \epsilon_z \frac{\partial F_c}{\partial z_n} \right)$.

For each observed reflection there exists an "observational equation" such as this and the number of these is usually considerably greater than the number of independent co-ordinate corrections to be determined. This set of "observational equations" must be reduced to a set of equations called the "normal equations". The 'n'th of these is formed by multiplying both sides of each equation by $w \frac{\partial F_c}{\partial x_r}$ and then adding the q left-hand sides and the q right-hand sides to produce an equation:

$$\sum_q w\Big\{\left(\frac{\partial F_c}{\partial x_n}\right)^2 \epsilon x_n + \frac{\partial F_c}{\partial x_n}\cdot\frac{\partial F_c}{\partial y_n}\cdot\epsilon y_n + \frac{\partial F_c}{\partial x_n}\cdot\frac{\partial F_c}{\partial z_n}\cdot\epsilon z_n$$

$$+ \sum_m \frac{\partial F_c}{\partial x_n}\Big(\frac{\partial F_c}{\partial x_m}\cdot\epsilon x_m + \frac{\partial F_c}{\partial y_m}\cdot\epsilon y_m + \frac{\partial F_c}{\partial z_m}\cdot\epsilon z_m\Big\} = \sum_q w(F_o - F_c)\frac{\partial F_c}{\partial x_n}$$

where $\sum_m$ denotes a sum over all atoms except the 'n'th. The next "normal equation" is formed by multiplying throughout by $w\,\frac{\partial F_c}{\partial x_{n+1}}$ before adding, and so on. The final result is a set of 3N simultaneous equations which have to be solved for 3N unknowns, ϵx_n, ϵy_n, ϵz_n. Successive applications of this procedure lead to atomic co-ordinates which minimise R.

It has been found in practice, however, that if a large number of equations are used, the off-diagonal terms of the "normal equations" are small and, to a first approximation, can be neglected. If so, the solutions reduce to

$$\epsilon x_n = \frac{\sum_q w(F_o - F_c)\,\frac{\partial F_c}{\partial x_n}}{\sum_q w\left(\frac{\partial F_c}{\partial x_n}\right)^2}$$

(This approximation is not valid if the atoms overlap and is therefore normally only valid for three-dimensional refinement.)

The least-squares refinement method has several advantages over those already mentioned. It is free from the series-termination errors which characterise the

Fourier methods and it is possible to include the temperature factor (isotropic or anisotropic) and scale factor in the refinement process.

In the least-squares program written by Dr. J. S. Rollett each atomic position is evaluated from a 3x3 matrix. The thermal vibrations are computed from a 6x6 matrix for each atomic vibration while a 2x2 matrix is solved for the overall scale factor.

PART II

The Structure of Caracurine II:

X-ray Analysis of Caracurine-II Dimethiodide.

2.1 INTRODUCTION.

The powerful physiological effect - the paralysis of voluntary muscle - of various types of plant extract known as curare has stimulated much interest in their chemical investigation. Since the name curare is a generic term which embraces many types of arrow-head poison prepared in South America, the curares have been conveniently classified (Boehm, 1897) according to the type of container used to pack the final product viz. tube- , pot- and calabash-curare.

The barks of "Strychnos toxifera" and other "Strychnos" species are used in the preparation of calabash-curare which originates in the northern parts of the South American continent and is considerably more active than either tube- or pot- curare. Because of their greater physiological activity the alkaloids of the calabash-curare have been subjected to extensive chemical investigation and an exhaustive survey of work in this field has been published by Bernauer (1959).

An examination of the quaternary alkaloids of the bark of "Strychnos toxifera" obtained from British Guiana was reported by King (1949) who isolated toxiferines I-XII. Toxiferine-I chloride and toxiferine-II had previously been encountered by Wieland et al.(1947) but the remaining ten toxiferines had been isolated for the first time. In 1954, Asmis, Schmid and Karrer isolated caracurine-II, a member of the calabash- curare series, from Venezuelan "Strychnos toxifera". Some time later, Battersby et al.(1960) having re-examined the bark of British Guianian "Strychnos toxifera", isolated caracurine-II dimethochloride which they proved to be identical with toxiferine-IX.

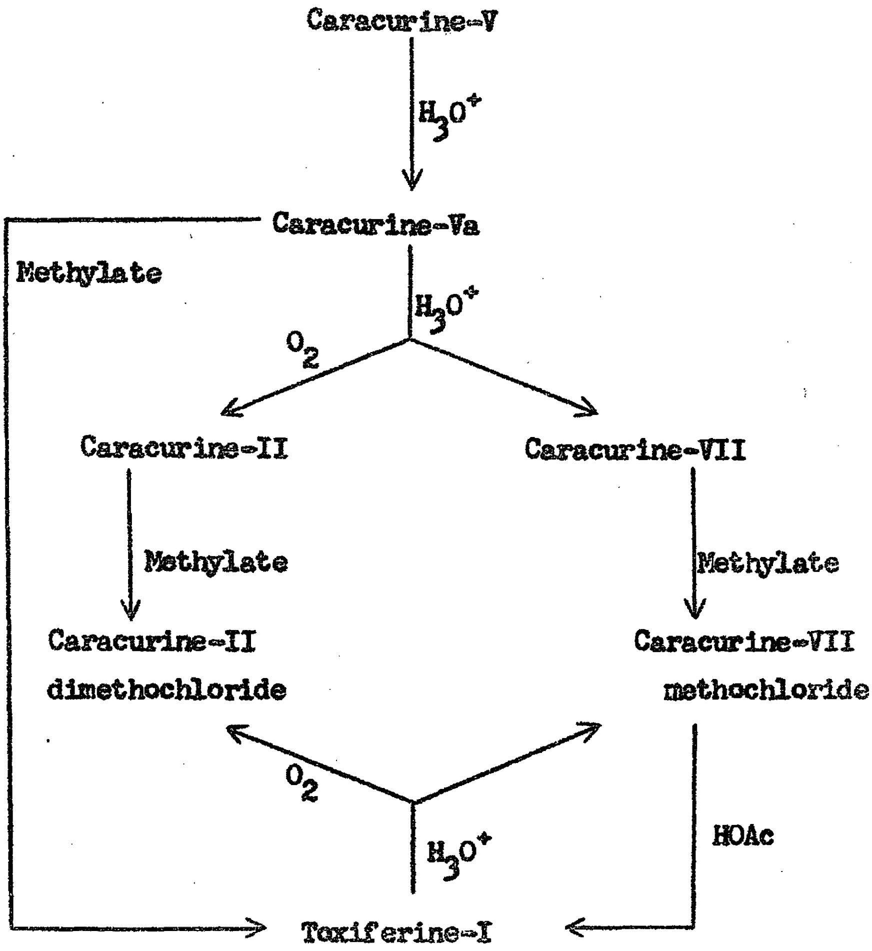
By 1960, the relationship (shown in Table I) between the alkaloids caracurine-V (I), caracurine-VII (II), caracurine VII methochloride (otherwise known as hemitoxiferine-I or Alkaloid A8), caracurine-II and toxiferine-I (III) had been firmly established (Battersby and Hodson, 1960 b). The constitution of caracurine-II was unknown, although it was clear that it must closely resemble those of caracurine-V and toxiferine-I because of the mildness of the reactions required to convert the latter two alkaloids into caracurine-II dimethochloride.

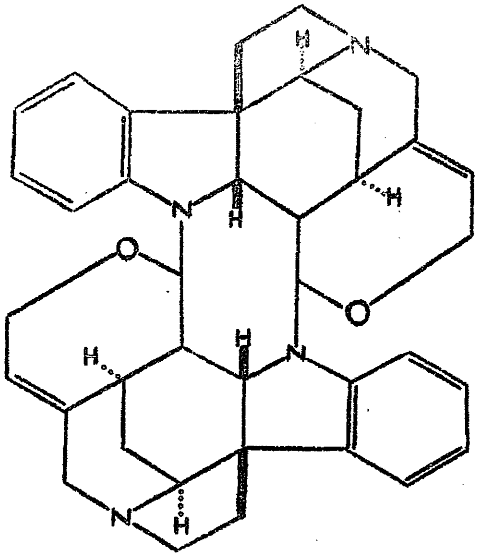
The elucidation of the structure of caracurine-II by X-ray methods has been carried out successfully using the dimethiodide derivative, crystals of which were kindly supplied by Dr. A.R. Battersby, and the results establish structure(IV.) This structure has been independently confirmed by chemical and nuclear magnetic resonance studies (Battersby, Yeowell et al.,1961, Battersby, Hodson et al., 1961)

The nomenclature in the calabash-curare series is confused. The name caracurine-II was assigned when it was believed that all calabash-curare alkaloids were based on

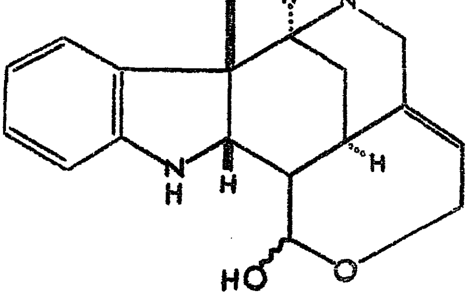
TABLE I

INTERRELATION OF SOME CALABASH-CURARE ALKALIODS

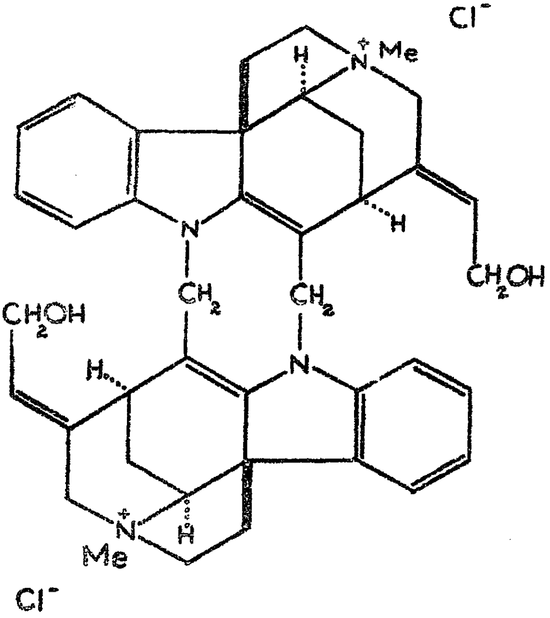



N
O
H
H
H
N
O
H
H
N
N
H

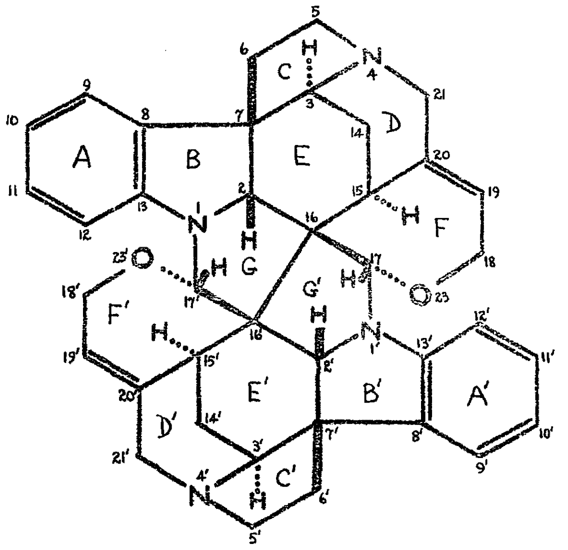
(I)


H
N
N
H
H
H
HO
O

(II)


Cl⁻
N⁺ Me
H
N
H
CH2OH
CH2
CH2
CH2OH
H
N
N⁺
Me
H
Cl⁻

(III)


5
6
H
C
N
4
21
9
10
8
7
3
14
D
A
B
E
20
11
13
2
15
19
12
N
1
16
H
F
H
23′
O
H
G
G′
H
17
O
23
18
18′
17′
F′
H
16′
H
N
1′
12′
13′
11′
19′
H
15′
2′
E′
B′
A′
20′
D′
14′
7′
8′
10′
3′
21′
4′
N
H
C′
6′
9′
5′

(IV)

$C_{19} - C_{21}$ units. In 1956, however, von Philipsborn, Schmid and Karrer demonstrated that in the group of alkaloids possessing high curare activity the molecular formula is based on a $C_{38} - C_{40}$ skeleton with two basic or quaternary nitrogens present in the molecule. In some reports of work in this field since 1956 references to caracurine-II methochloride persist where the dimethochloride is intended. In this thesis the derivatives of caracurine-II will be referred to as the dihalides.

2.2. EXPERIMENTAL.

When this X-ray study was undertaken the molecular formula of caracurine-II was given as $C_{38}H_{40}O_2N_4$ but this was shortly revised to $C_{38}H_{38}O_2N_4$ following a mass spectroscopic molecular weight determination [M.W. = 582] carried out by Dr. R.I.Reed of Glasgow.

Crystal data

	Caracurine-II dimethochloride	Caracurine-II dimethiodide
Molecular formula	$C_{40}H_{44}O_2N_4Cl_2$	$C_{40}H_{44}O_2N_4I_2$
Molecular Weight	683.7	866.6
System	Monoclinic	Orthorhombic
a	12.62 ± 0.03 Å	18.59 ± 0.03 Å
b	7.42 ± 0.02 Å	27.44 ± 0.04 Å
c	21.64 ± 0.04 Å	7.52 ± 0.02 Å
β	96° 54' ± 30'	90°
U	2012 $Å^3$	3836 $Å^3$
d_{obs} (flotation in aqueous $ZnCl_2$ soln)	$<$ 1.5 g./c.c.	1.505 g./c.c.
Z	2	4
d_{calc}	1.129 g./c.c.	1.502 g./c.c.
Absent spectra	0k0 when k=2n+1	h00 when h=2n+1 0k0 when k=2n+1 00ℓ when ℓ=2n+1
Space group	$P2_1$ (C_2^2)	$P2_12_12_1$ (D_2^4)
μ, Absorption coefficient for X-rays (λ=1.542 Å)	17.3cm.$^{-1}$	134.5cm.$^{-1}$
F(000)	724	1736
Total number of independent observed structure amplitudes	2580	1285
$\sum f^2$ "heavy" atoms	648	5832
$\sum f^2$ "light" atoms	1782	1782

Caracurine-II dimethobromide ($C_{40}H_{44}O_2N_4Br_2$), M.W = 722.6, is isomorphous with caracurine-II dimethochloride. The absorption coefficient for X-rays ($\lambda = 1.542$ Å), $\mu = 31.2$ cm.$^{-1}$., F(000) = 796; $\sum f^2$ "heavy" atoms = 2592. The total number of independent observed structure amplitudes = 1414.

Rotation, oscillation, Weissenberg and precession photographs were taken with copper-K_α ($\lambda = 1.542$ Å) and molybdenum -K_α ($\lambda = 0.7107$ Å) radiation. The cell dimensions were obtained from rotation and precession photographs.

Two space groups of the monoclinic system, $P2_1$ and $P2_1/m$, satisfy the condition that the 0k0 reflections will be absent when k is odd. For the space group of caracurine-II dimethochloride to be $P2_1/m$, since there are only two molecules per unit cell but four equivalent positions, a further condition, that the molecule of caracurine-II must possess a mirror plane, is imposed. Since this molecule is laevorotary, $[\alpha]_D^{26} = -232°$ in chloroform (Schroeder et al. 1961), and therefore does not fulfil this condition, the space group of caracurine-II dimethochloride must be $P2_1$.

The orthorhombic space group, $P2_12_12_1$, was determined uniquely from the systematic halvings.

Intensity data were obtained from equatorial and equi-inclination upper layer Weissenberg photographs taken from crystals of the dimethochloride and dimethobromide rotated about the b-axis and from crystals of the dimethiodide rotated about the c-axis; the multiple-film technique (Robertson, 1943) was employed. The intensities were estimated visually by comparison with a calibrated intensity strip and were corrected for Lorentz, polarisation and rotation factors appropriate to the upper layers (Tunell, 1939). No corrections for absorption were applied since small crystals were employed. The various layers were placed on the same scale by comparison of the observed and the calculated structure amplitudes based on the heavy atom alone. Throughout the refinement the scale was adjusted by correlation with the calculated structure amplitudes.

2.3 STRUCTURE DETERMINATION.

The equivalent positions of the space group $P2_1$ (b-axis unique) are x, y, z and $\bar{x}, \frac{1}{2} + y, \bar{z}$. When two heavy atoms are present in the asymmetric unit these equivalent positions give rise to heavy atom- heavy atom vectors in the Patterson function at $2x_1, -\frac{1}{2}, 2z_1$; $2x_2, -\frac{1}{2}, 2z_2$; $x_1 - x_2, y_1 - y_2, z_1 - z_2$; $x_1 + x_2, -\frac{1}{2} + y_1 - y_2, z_1 + z_2$ where x_1, y_1, z_1 and x_2, y_2, z_2 refer to the co-ordinates of the crystallographically non-equivalent heavy atoms. Whatever the values of these co-ordinates, the Patterson projection along the b-axis must contain three heavy atom - heavy atom vector peaks in a straight line and the fourth peak will be at a distance from the origin of this Patterson function corresponding to the projected vector distance between the non-equivalent heavy atoms. These facts should provide a useful aid in the interpretation of this Patterson function.

The Patterson projection and "sharpened" Patterson projection along the b-axis of caracurine-II dimethochloride are shown in Figures 1 and 2, respectively. The function employed for "sharpening" the $h0\ell$ zone data was $M(S) = \left(1/\hat{f}\right)^2 \exp\left(-2.5 \sin^2\theta / \lambda^2\right)$. No unique solution was obtained from these projections for the chloride ion co-ordinates so the three-dimensional "sharpened" Patterson synthesis was computed; the section at $V = \frac{1}{2}$ is shown in Figure 3. The peaks marked A, B in this Figure were chosen as representing the chloride - chloride and chloride'-chloride' vectors. A Buerger (1951) minimum function was deduced employing the complete three-dimensional Patterson vector distribution but it was not possible to visualise any part of a molecular framework which could correspond to the sparse distribution of peaks which resulted. This set of chloride ion co-ordinates was therefore assumed to be incorrect.

There appeared to be little hope of obtaining a satisfactory set of heavy atom co-ordinates for the dimethochloride derivative so the investigation was interrupted at this stage pending the arrival of a supply of the dimethiodide derivative from Dr. Battersby. Some crystals of caracurine-II dimethiodide were soon received but preliminary investigation of these indicated that although this sample was isomorphous with the dimethochloride the crystals were unsuitable for an X-ray structure analysis, long exposures giving only few reflections.

Caracurine-II dimethobromide, prepared in Glasgow from the dimethochloride, proved to be both isomorphous with the latter and suitable for further investigation. The Patterson projection (Figure 4) and "sharpened" Patterson projection (Figure 5) along the b-axis and the three-dimensional Patterson synthesis were computed. The sections at $V = \frac{1}{2}$ of the three-dimensional Patterson function both "unsharpened" and "sharpened" are shown in Figures 6 and 7, respectively. Again it was difficult to decide which set of peaks was that corresponding to the heavy atom - heavy atom vectors. For various sets of bromide ion co-ordinates structure factors were calculated for the $h\,0\,\ell$ zone only but sufficient confidence could not be placed in any one set to make continuation of the analysis appear worthwhile.

A final attempt to locate the heavy atoms was made by computing the difference Patterson (Kartha and Ramachandran, 1955) projection along the b-axis which makes use of the fact that the dimethochloride and dimethobromide derivatives are isomorphous. If $(|F_o|_{Br} - |F_o|_{Cl})^2$ are used as coefficients only the heavy atom - heavy atom vectors should remain in the Patterson distribution function. It is necessary to have the observed structure amplitudes of both derivatives on an approximately absolute scale before subtraction and this was achieved by employing the method of Wilson (1942). The resulting Patterson projection is shown in Figure 8. The peaks in this distribution which were selected as being representative of the heavy atom - heavy atom vectors are indicated by C, D, E and F. More accurate co-ordinates of the bromide ions were obtained by consultation of the three-dimensional Patterson synthesis of the dimethobromide derivative and when structure factors

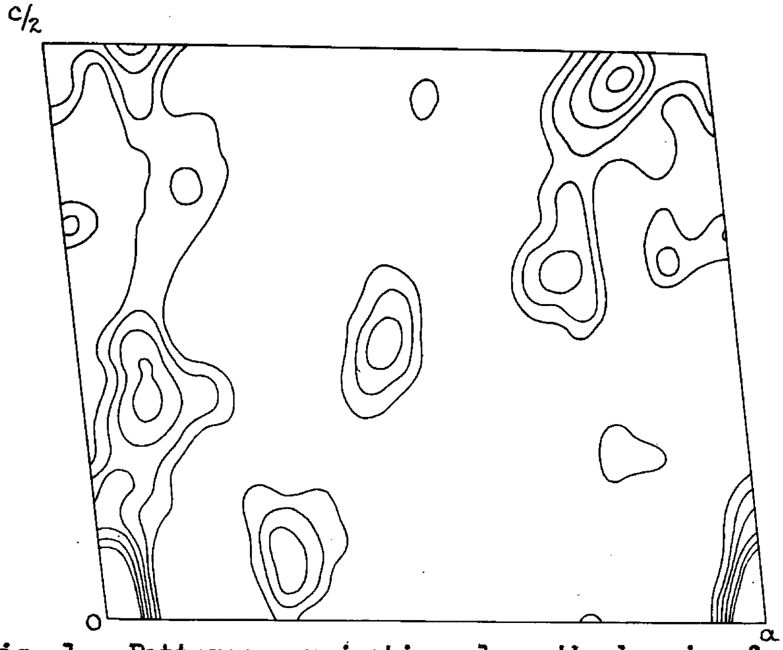


Fig. 1. Patterson projection along the b-axis of caracurine-II dimethochloride. Contour scale arbitrary.

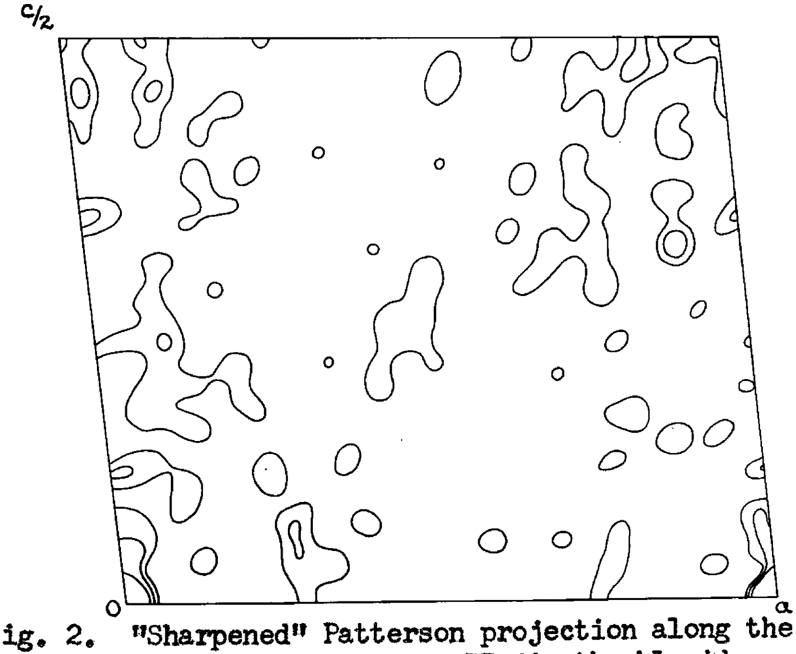


Fig. 2. "Sharpened" Patterson projection along the b-axis of caracurine-II dimethochloride. Contour scale arbitrary.

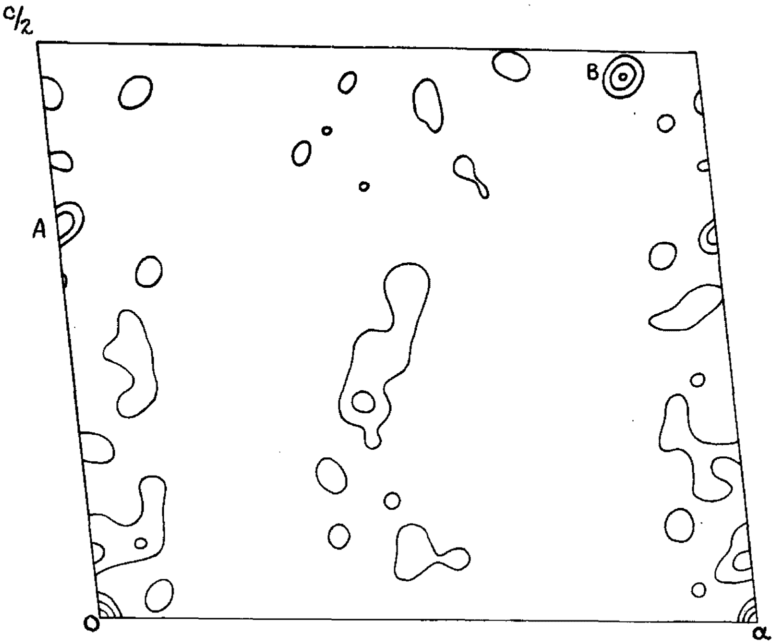


Fig. 3. The three-dimensional "sharpened" Patterson function of caracurine-II dimethochloride; the section at V = $\frac{1}{2}$. A and B denote the vector peaks chosen as representing the chloride-chloride and chloride' - chloride' vectors. (Arbitrary contour scale).

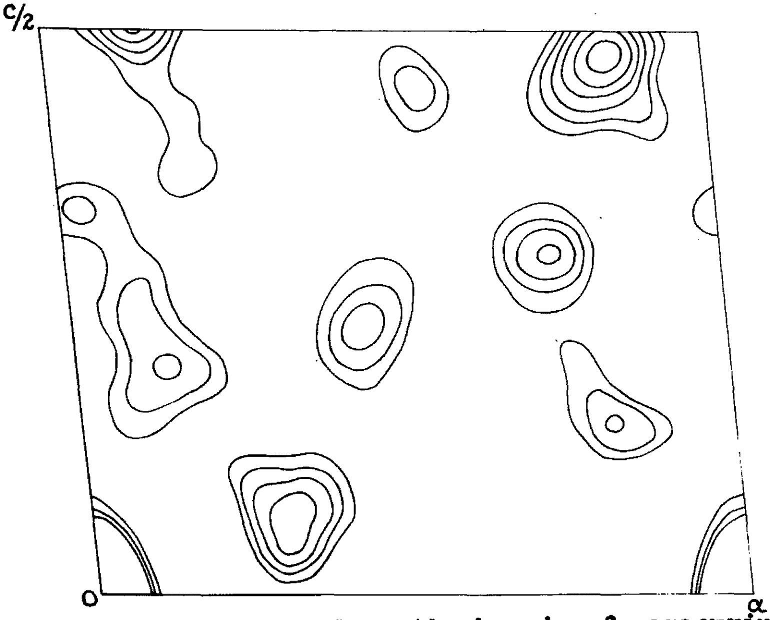


Fig. 4. Patterson projection along the b-axis of caracurine-II dimethobromide. The contour scale is arbitrary.

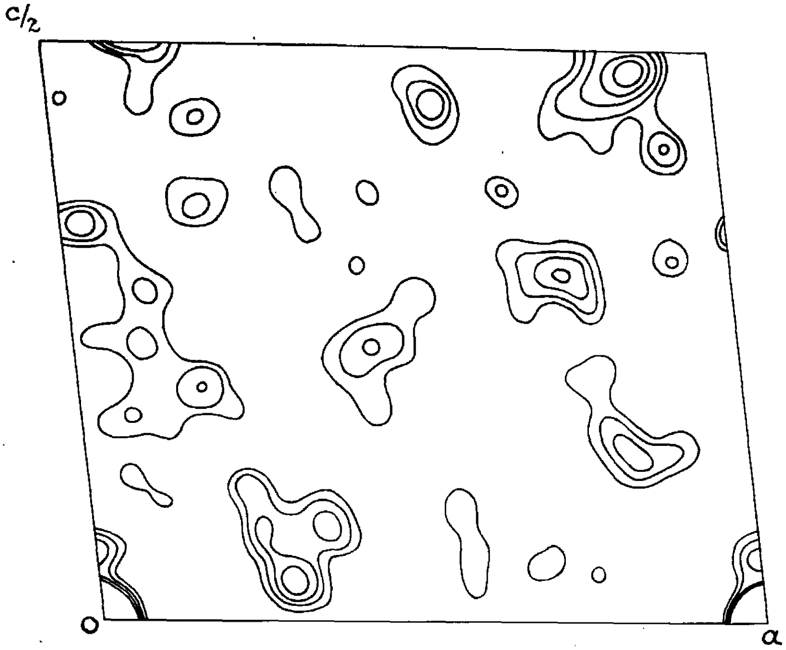


Fig. 5. "Sharpened" Patterson projection along the b-axis of caracurine-II dimethobromide. The contour scale is arbitrary.

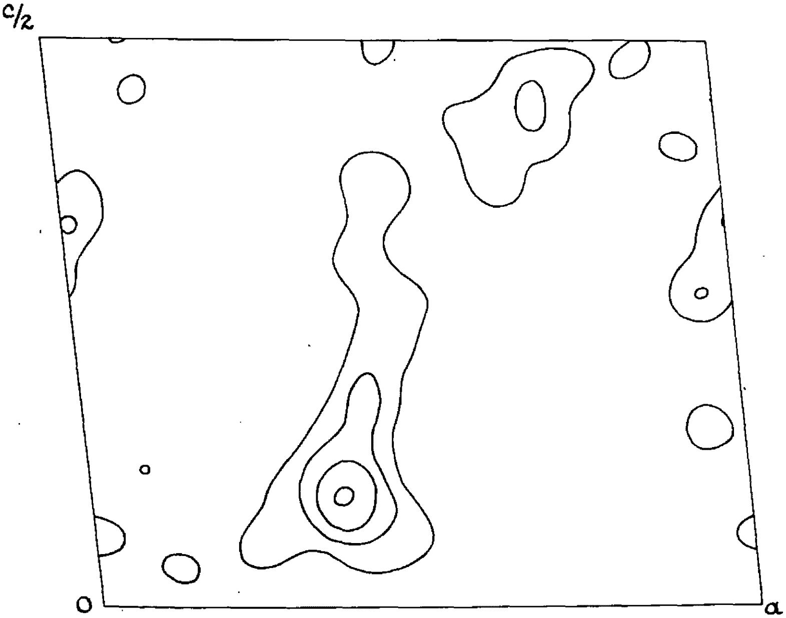


Fig. 6. The three-dimensional Patterson function of caracurine-II dimethobromide; the section at $V = \frac{1}{2}$. The contour scale is arbitrary.

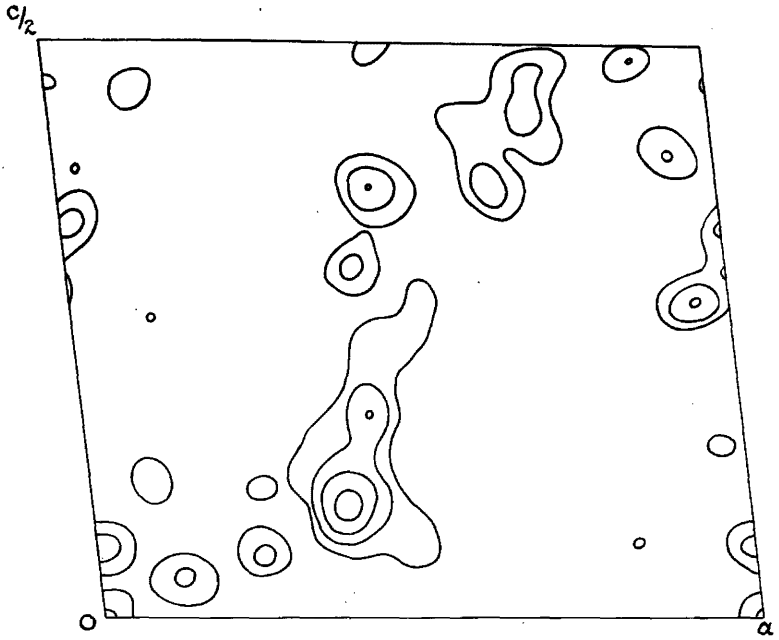


Fig. 7. The "sharpened" three-dimensional Patterson function of caracurine-II dimethobromide; the section at $V = \frac{1}{2}$. The contour scale is arbitrary.

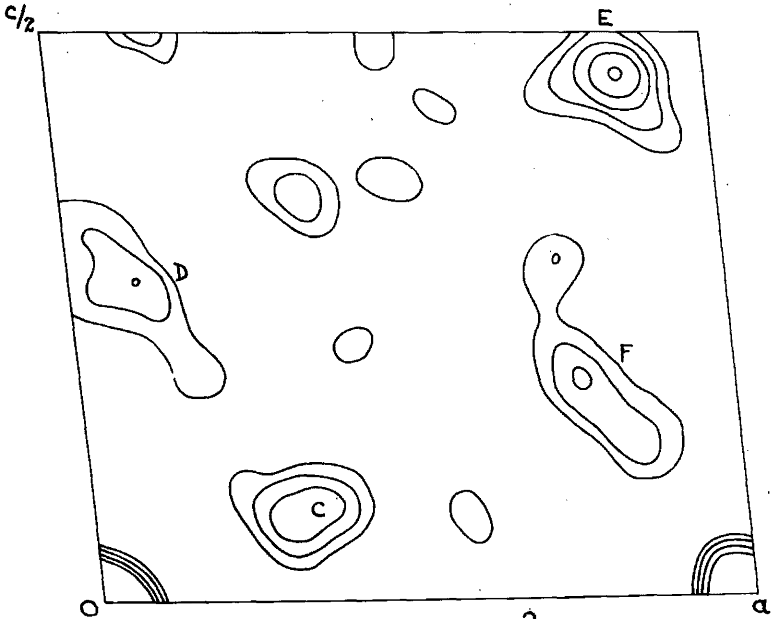


Fig. 8. The difference, $(|F_o|_{Br} - |F_o|_{Cl})^2$, Patterson projection along the b-axis. C, D, E, and F denote the heavy atom - heavy atom vectors. The contour scale is arbitrary.

were calculated on the basis of the bromide ions only, an isotropic temperature factor of $B = 4.0\ \mathring{A}^2$ being employed, the agreement index, R, over all observed structure amplitudes was 0.570. (The agreement index, R, is given by $R = \sum \left| |F_o| - |F_c| \right| / \sum |F_o|$). This result was promising and the correct set of bromide ion co-ordinates had probably been deduced, nevertheless, since a fresh supply of crystals of the dimethiodide derivative had been received from Dr. Battersby it was decided not to pursue this course but to turn attention to the solution of the structure of caracurine-II using the heavier derivative.

The crystals of caracurine-II dimethiodide employed belonged to the orthorhombic system and therefore were not isomorphous with those of the other derivatives which had been subjected to preliminary investigation. Co-ordinates of the iodide ions were determined unambiguously from the three-dimensional Patterson sections at $U = \frac{1}{2}$, $V = \frac{1}{2}$, $W = \frac{1}{2}$, shown in Figures 9, 10 and 11, respectively; the iodide - iodide vectors are designated G,H; J,K; L,M. The co-ordinates of the iodide ions were determined to be

	x/a	y/b	z/c
$I^-(24)$	0.0105	-0.0633	0.1957
$I^-(24')$	0.1857	0.1812	0.3778

and these were confirmed by consultation of the appropriate sections of the three-dimensional Patterson function.

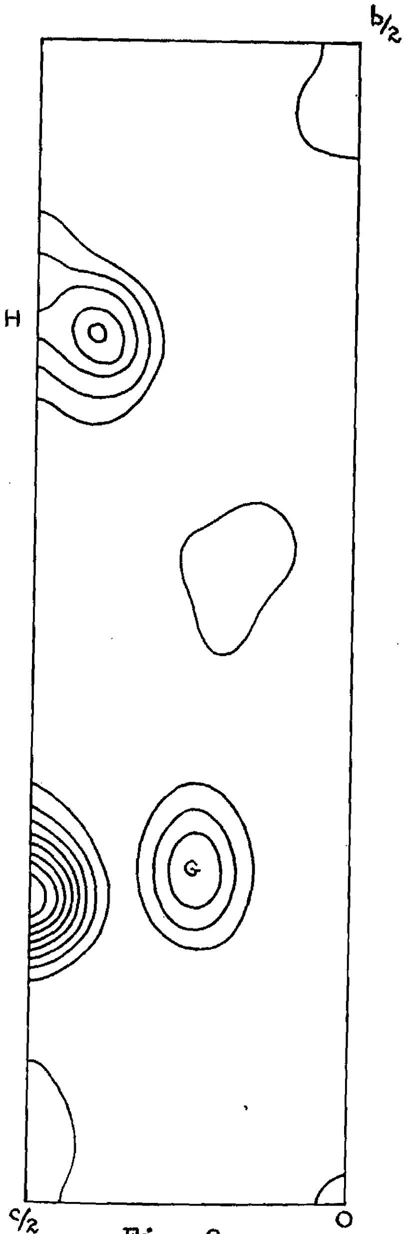


Fig. 9

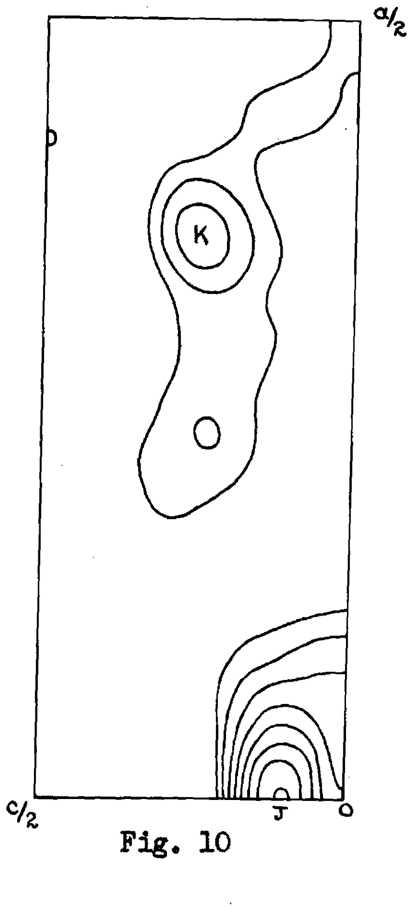


Fig. 10

The three-dimensional Patterson function of caracurine-II dimethiodide.

Fig. 9. The section at U = $\frac{1}{2}$. The iodide-iodide vector peaks are designated G and H.

Fig. 10. The section at V = $\frac{1}{2}$. The iodide-iodide vector peaks are marked J and K.

(The contour scale in both Figures is arbitrary).

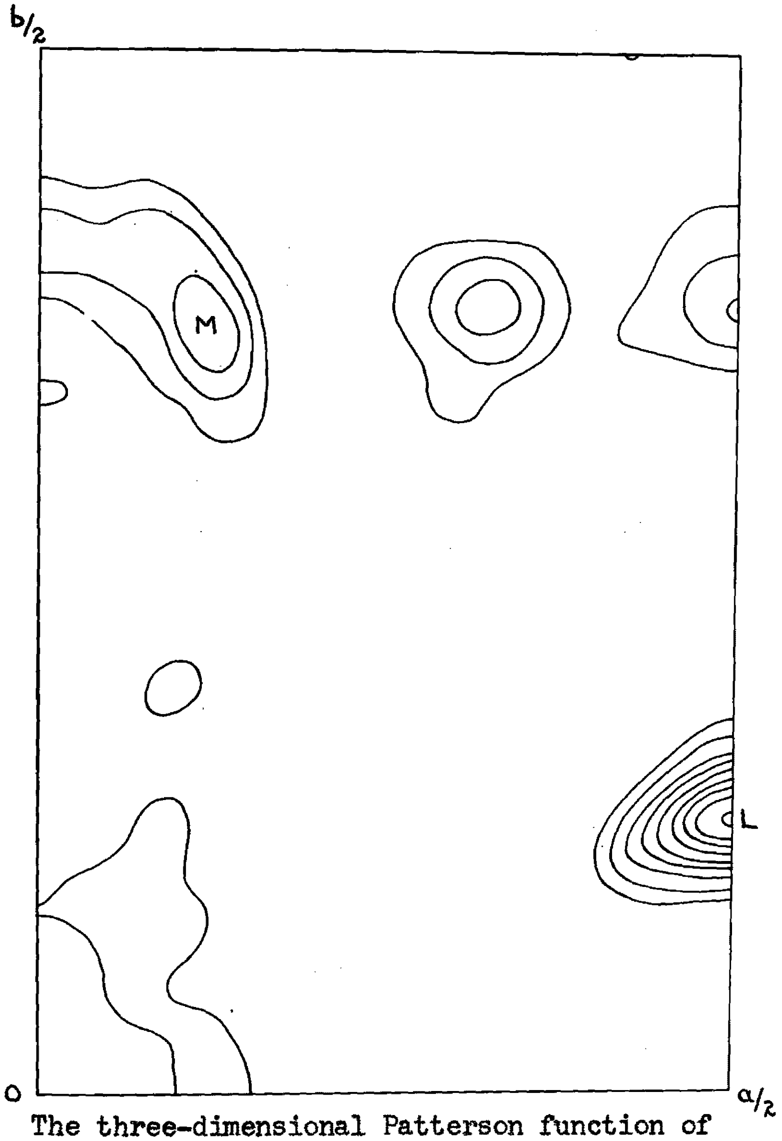
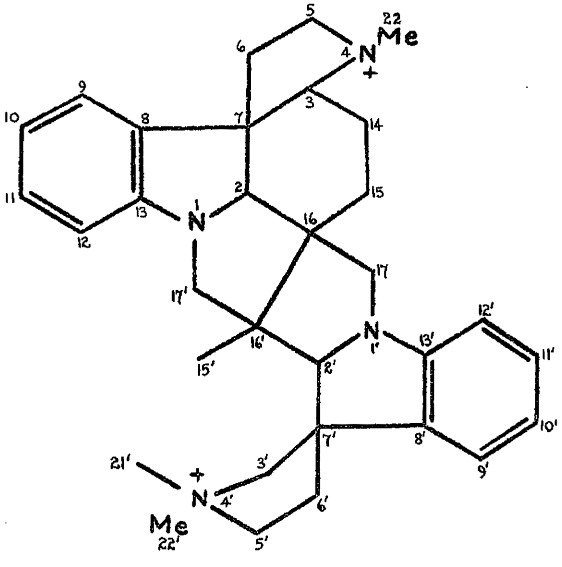


Fig. 11. The three-dimensional Patterson function of caracurine-II dimethiodide; the section at $W = \frac{1}{2}$. The iodide-iodide vector peaks are denoted L and M. Contour scale is arbitrary.

Structure factors calculated using these co-ordinates and employing isotropic temperature factors of $B = 4.0$ Å^2 had an agreement index of $R = 0.402$ with the observed structure amplitudes. The relatively high temperature factor was used because the data faded out rapidly above $\sin\theta = 0.6$.

The first three-dimensional Fourier synthesis, based on the iodide ion phases, resulted in the allocation of approximate co-ordinates to thirty-six of the light atoms - N(1),C(2),C(3),N(4),C(5),C(6),C(7),C(8),C(9),C(10),C(11),C(12),C(13), C(14),C(15),C(16),C(17),C(22),N(1'),C(2'),C(3'),N(4'),C(5'),C(6'),C(7'), C(8'),C(9'),C(10'),C(11'),C(12'),C(13'),C(15'),C(16'),C(17'),C(21'), C(22') - giving rise to the partial skeleton shown (V).



(V)

This partial skeleton conforms to the structures of caracurine-V and toxiferine-I with the exception of the new carbon-carbon bond C(16)-C(16'), the length of which at this stage, 1.77Å, indicated that if the sites selected for these atoms were correct then such a bond was present in caracurine-II.

The thirty-six light atoms were included, all as carbon atoms with B = 3.0Å, in the second phasing calculations when the agreement index dropped to 0.328. The remaining oxygen and carbon atoms, excepting C(18), were located from the second three-dimensional Fourier synthesis calculated employing the improved phase constants. This Fourier synthesis also indicated that the positions which had been assigned to C(11) and C(12) were doubtful as these gave rise to a very odd-shaped ring which, according to the structures of toxiferine-I and caracurine-V, should be the benzene ring of an indoline system. These two atoms were therefore excluded from the next structure factor and phasing calculations.

On the basis of peak heights and knowledge of the structures of other members of this series it was possible to identify the hetero-atoms and, for the third phasing calculations, forty-three light atoms were included as their appropriate chemical type. The isotropic temperature factors employed in this calculation were the same as those of the previous one, viz. $B = 3.0\ \text{Å}^2$ for carbon, nitrogen and oxygen, B = 4.0 Å^2 for iodide ions; the calculated structure factors had an agreement index of R = 0.312. Sections of the third three-dimensional Fourier synthesis were computed around the positions where peaks corresponding to the sites of C(11), C(12) and C(18) were expected to be located.

From the sections around C(8), C(9), C(10), and C(13) one peak having electron-density 1.8 e/Å^3 was in a position which approximated to that expected for C(11) and between this peak and that of C(13) a region of positive electron-density (maximum 0.8 e/Å^3) was present. The maximum of density (maximum 0.8 e/Å^3) was present.o the approximate site of C(12) since an atom located in that position would give rise to a fairly planar six-membered ring which, in turn, would correspond to the expected benzene nucleus. The fact that neither of the peaks corresponding to C(11) or C(12) was well-resolved was not unexpected since they both lie along the lines joining pairs of iodide ions in adjacent unit cells (see Figure 14) and are probably subject to considerable diffraction effects which not only reduce their magnitude but shift them from their true position and cause them to coalesce.

The Fourier sections around C(19) and O(23) showed the presence of two peaks:

		x/a	y/b	z/c	$e/Å^3$
C(18)	peak(i)	0.6769	0.3303	0.0432	2.00
	peak(ii)	0.6688	0.3167	0.2018	1.60
$I^-(24')$		0.6850	0.3200	0.6185	

distances		angle
C(17)-C(18)	C(18)-O(23)	C(17)-C(18)-O(23)
1.57 Å	2.13 Å	84.6°
1.71 Å	2.08 Å	82.8°

These peaks, (i) and (ii), were similarly disposed with respect to the iodide ion $I^-(24')$ at $\frac{1}{2} + x$, $\frac{1}{2} - y$, $\bar{z}$ and probably resulted, to a large extent, from diffraction ripples along the direction of z. From the bond lengths and angles quoted it is apparent that either of these peaks could have corresponded to the site of C(18) but when the disposition of C(18') with respect to C(19'), C(20'), C(21'), and O(23') was considered, peak (i) was obviously the better approximation to the location of C(18).

Co-ordinates were assigned to the three atoms, C(11), C(12), and C(18), and when they were included in the structure factor calculations the agreement index dropped to 0.301. The improved phase constants were employed in the calculation of a fourth three-dimensional electron-density distribution in which all the atoms, except hydrogens, were fairly well resolved.

2.4 STRUCTURE REFINEMENT.

Employing the same phase constants as for the fourth three-dimensional F_o Fourier synthesis an F_c synthesis was computed and corrections for series-termination errors were applied to the co-ordinates deduced from the F_o synthesis. It was apparent that the isotropic thermal parameters of each atom required adjustment and in particular that those of the iodide ions needed to be greatly increased. When structure factors were calculated using the improved co-ordinates and individual thermal parameters the agreement index was reduced to 0.274. Two cycles of further co-ordinate and temperature factor refinement were carried out by three-dimensional difference Fourier syntheses and these lowered the agreement index to 0.249.

In the continuation of the refinement difference Fourier syntheses were used to assign improved co-ordinates and isotropic temperature factors to the carbon, nitrogen and oxygen atoms while least-squares calculations (Rollett, 1961) gave anisotropic temperature factors for the iodide ions; two cycles reduced the agreement index to 0.227.

At first sight this refinement appeared to be progressing smoothly but on closer examination this was not quite the case. The hk0 zone data were refining very slowly as over the last two cycles the agreement index of this zone had dropped by only 0.015, from 0.341 to 0.326.

The value of 0.326 for this zone was also considerably higher than those of the upper layers which ranged from R = 0.176 to R = 0.230 and could not be accounted for entirely by the fact that the hk0 zone is centrosymmetric. During the original visual estimations of the intensities a conservative allowance for variation in the shapes and lengths of the reflections had been made and therefore it was decided that more accurate corrections should be applied. This was achieved by measuring, with a ruler, the lengths and widths of each reflection on the top photograph and multiplying the observed peak intensity of each reflection by the area. When the previous structure factor calculation was repeated the agreement index for the amended hk0 zone data was 0.240. The same kind of correction was then applied to the data of the upper layers and the overall agreement index for the "new" data was 0.211. The two-part refinement was continued for two more cycles using these data.

One cycle of least-squares adjustment of the positional parameters of the light atoms concluded the refinement. It was decided that no further refinement would prove useful as the data are neither of such quantity nor quality to permit the allocation of anisotropic thermal parameters to the light atoms. The course of analysis is provided diagrammatically in Table II.

TABLE II.

Course of analysis.

3-D Patterson synthesis

↓

Iodide ions ($B = 4.0 \text{Å}^2$)

↓

1st Structure factor calculation $R = 0.402$

↓

1st 3-D Fourier synthesis (1244 reflections)

↓

2nd Structure factor calculation [Iodide ions ($B = 4.0 \text{Å}^2$) 36 light atoms ($B = 3.0 \text{Å}^2$)] $R = 0.328$

↓

2nd 3-D Fourier synthesis (1232 reflections)

↓

3rd Structure factor calculation [Iodide ions ($B = 4.0 \text{Å}^2$) 37 carbon, 4 nitrogen, 2 oxygen atoms ($B = 3.0 \text{Å}^2$)] $R = 0.312$

↓

3rd 3-D Fourier synthesis (1285 reflections)

↓

4th Structure factor calculation [inclusion of 3 more carbon atoms ($B = 3.0 \text{Å}^2$)] $R = 0.301$

F_o and F_c 3-D Fourier syntheses

↓

5th Structure factor calculation (All atoms, individual isotropic thermal parameters) $R = 0.274$

$(F_o - F_c)$ 3-D Fourier synthesis

↓

6th Structure factor calculation $R = 0.256$

$(F_o - F_c)$ 3-D Fourier synthesis

↓

7th Structure factor calculation $R = 0.249$

L.S. refinement of iodide ions (anisotropic)

$(F_o - F_c)$ 3-D Fourier synthesis light atom refinement (isotropic)

↓

8th Structure factor calculation $R = 0.233$

L.S. Iodide ions (anisotropic)

$(F_o - F_c)$ 3-D Fourier synthesis (isotropic light atom refinement)

↓

9th Structure factor calculation $R = 0.227$

↓

TABLE II (Contd.).

↓ Improved data

10th Structure factor calculation   R = 0.211

↓ L.S. Iodide ions (anisotropic)
$(F_o - F_c)$ light atoms (isotropic)

11th Structure factor calculation   R = 0.191

↓ L.S. Iodide ions (anisotropic)
$(F_o - F_c)$ light atoms (isotropic)

12th Structure factor calculation   R = 0.186

↓ L.S. light atoms (isotropic)

13th Structure factor calculation   R = 0.181

2.5 RESULTS OF ANALYSIS.

The final atomic co-ordinates and temperature parameters are listed in Table III. The standard deviations of the co-ordinates, Table IV, were derived from the least-squares residuals by application of the equation:

$$\sigma^2(u_j) = \sum w\Delta^2 \Big/ (m-n)\sum w\left(\frac{\partial\Delta}{\partial u_j}\right)^2$$

where m is the number of independent observations and n is the number of parameters to be determined.

Table V lists the observed and calculated structure factors, both rounded off as integers, and the values of the phase constants, α. The final agreement index over 1285 observed structure amplitudes is 0.181. Of the 265 unobserved structure amplitudes also listed in this Table there are 232 for which $|F_c|$ is less than $1\frac{1}{2}$ $|F_o|$ where $|F_o|$ is the minimum observable value of the structure amplitude in question.

The final three-dimensional electron-density distribution over one molecule, calculated from the observed structure amplitudes and the phase constants of Table V, is shown in Figure 12 by means of superimposed contour sections drawn parallel to (001). The atomic arrangement corresponding to this and to the absolute configuration as defined for strychnine by Peerdeman (1956) is shown in Figure 13. It will be noted that in Figure 12 the peaks corresponding to the atoms C(11), C(12), C(18), and C(22) have the lowest electron-density. The reasons for this have been discussed for C(11), C(12), and C(18) in section 2.3. The relatively low electron-density of C(22) is undoubtedly caused by similar effects viz. diffraction ripples from $I^-(24)$ along the direction of z. It was fortuitous that in the early stages of the structure determination the peak corresponding to this atom was not so badly removed from its true location nor sufficiently reduced in density to make interpretation difficult. A few other small peaks were present in the final Fourier synthesis but these are omitted from Figure 12 as they were spurious being diffraction effects of the iodide ions.

The interatomic bond lengths are listed in Table VI while the interbond angles are given in Table VII. The standard deviation σ (AB) of a bond between atoms (A) and (B) is given by the formula

$$\sigma(AB) = \left\{\sigma^2(A) + \sigma^2(B)\right\}^{\frac{1}{2}}$$

where $\sigma(A)$ and $\sigma(B)$ are the standard deviations of the positions of the atoms (A) and (B),

$$\sigma^2(A) = \tfrac{1}{3}\left[\sigma^2(x_A) + \sigma^2(y_A) + \sigma^2(z_A)\right] .$$

The standard deviation, $\sigma(\beta)$ in radians, for an angle formed at (B) between the bonds AB and BC is given by the formula

$$\sigma^2(\beta) = \frac{\sigma^2(A)}{AB^2} + \sigma^2(B)\left[\frac{1}{AB^2} - \frac{2\cos\beta}{AB.BC} + \frac{1}{BC^2}\right] + \frac{\sigma^2(C)}{BC^2} .$$

The average estimated standard deviation for a carbon-carbon single bond is 0.10 Å and for a typical tetrahedral angle is 5°.

Some of the more important intramolecular non-bonded contacts are given in Table VIII

The packing of the molecules as viewed along the c-axis is shown in Figure 14. The shorter intermolecular contacts are listed in Table IX.

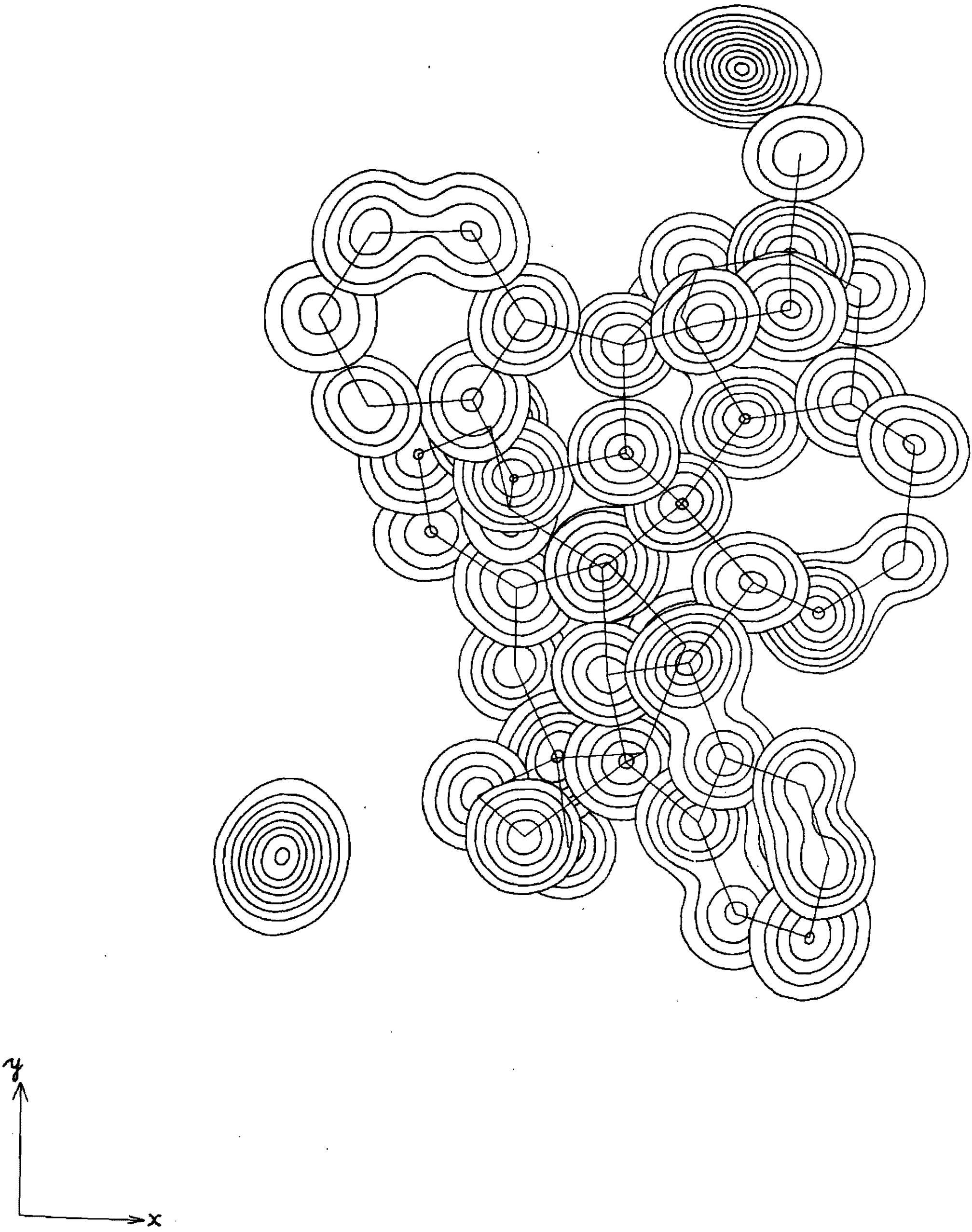


Fig. 12. The final three-dimensional electron-density distribution for caracurine-II dimethiodide shown by means of superimposed contour sections drawn parallel to (001). The contour interval is 1e.Å^{-3} except around the iodide ions where it is 5e.Å^{-3}.

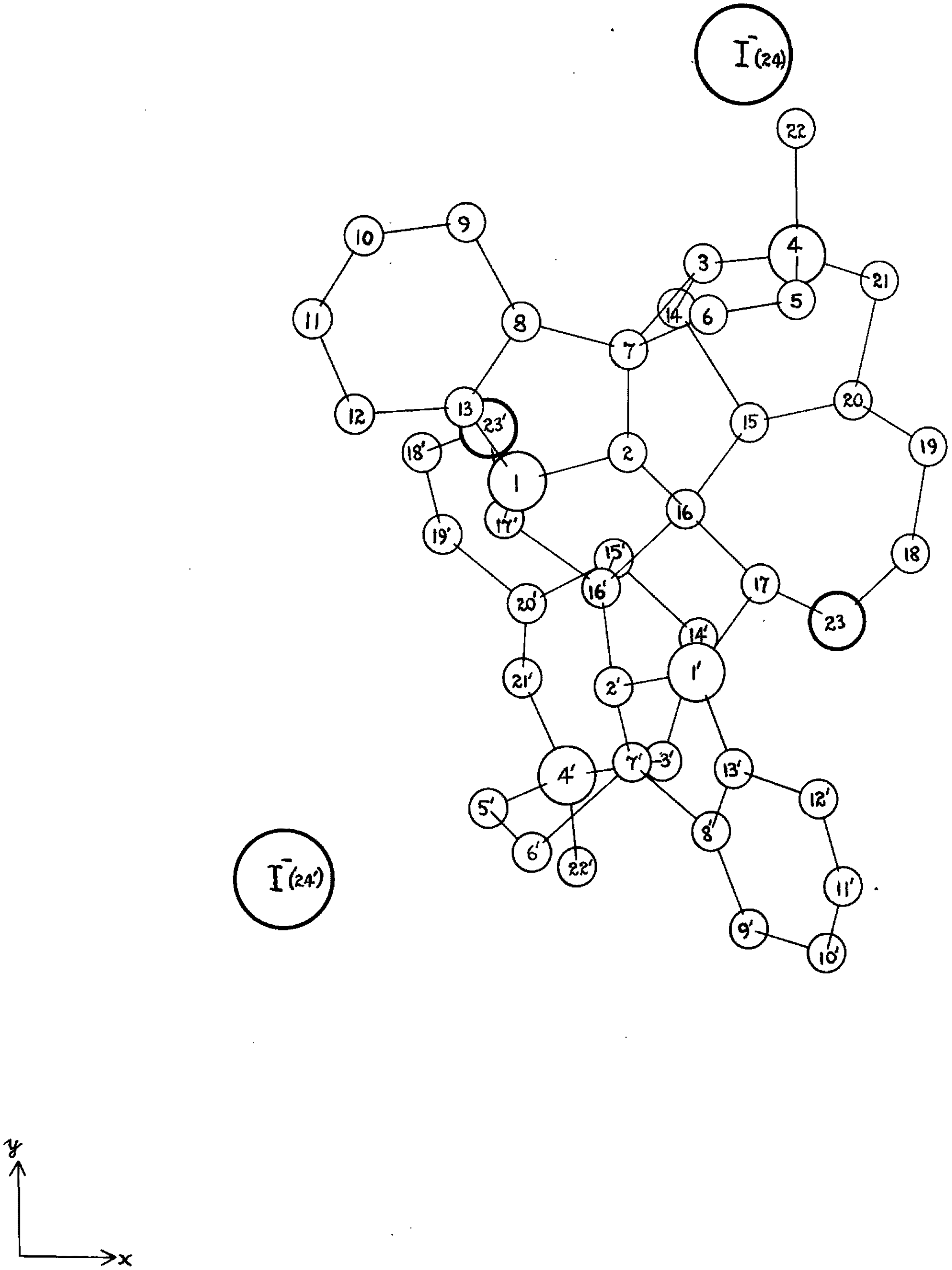


Fig. 13. The atomic arrangement corresponding to Fig. 12.

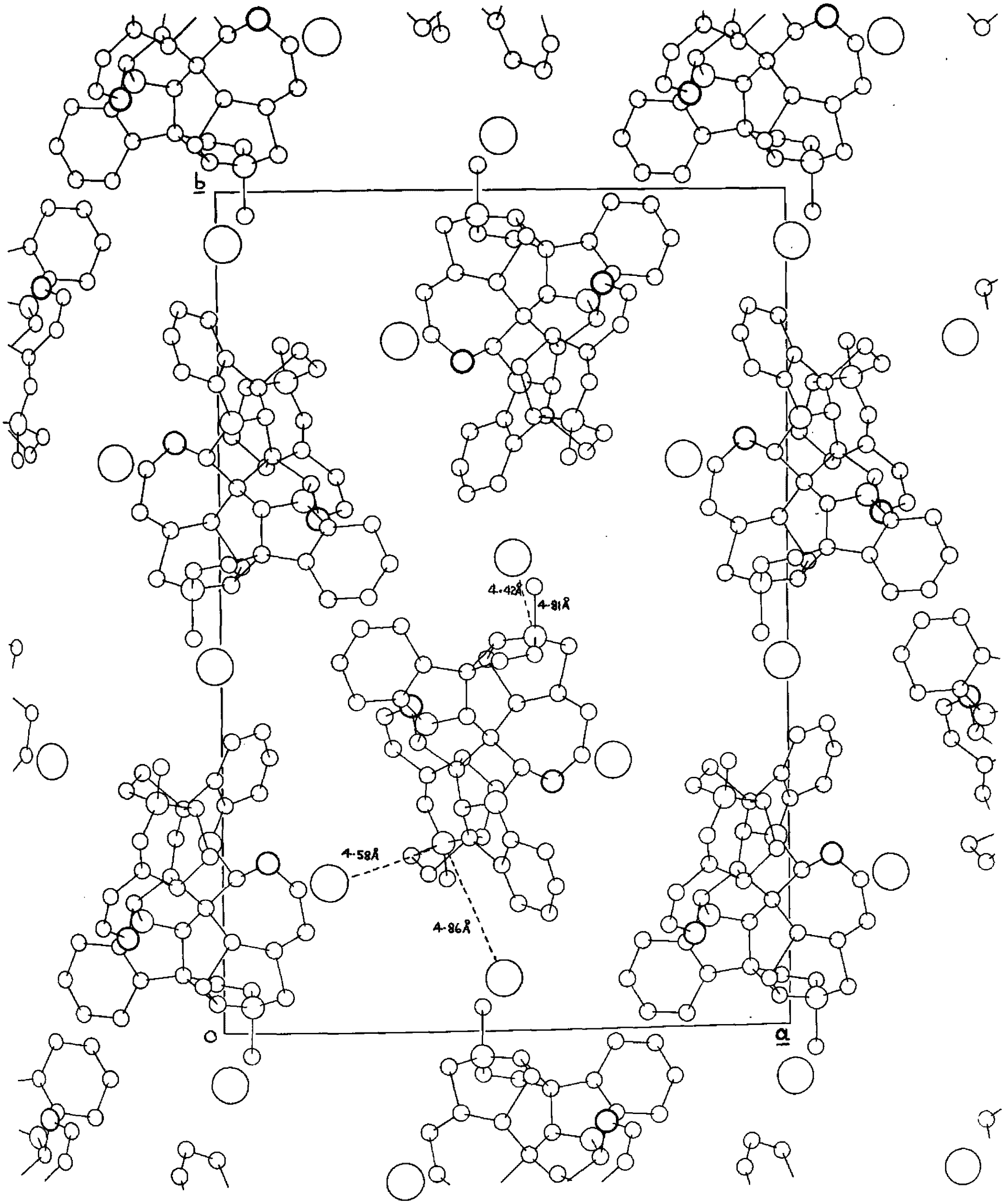


Fig. 14. The molecular arrangement as viewed along the c-axis. The broken lines denote the shorter $N^{+}\ldots\ldots I^{-}$ distances.

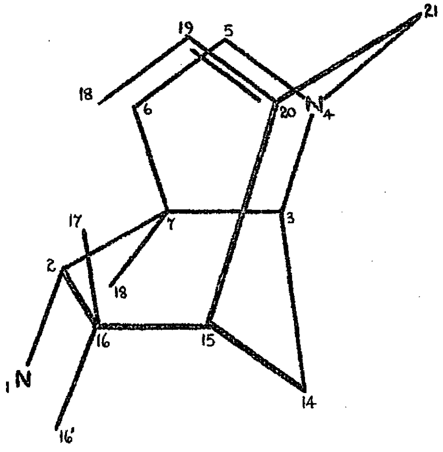
2.6 DISCUSSION OF RESULTS.

The molecule of caracurine-II has a compact three-dimensional structure consisting of 14 rings fused together and as a whole it exhibits almost exact two-fold symmetry.

The bond lengths and interbond angles resulting from this analysis are not sufficiently precise to permit a discussion of apparent differences between chemically equivalent bonds. Table X lists the average bond lengths according to their type. A comparison of these with the accepted values, also listed in this Table, shows no significant differences. A similar conclusion applies to the bond angles. The average bond angle in the benzene ring, 120°, about tetrahedral carbon atoms, 110°, about $N^+(4)$, 109°; N(1), 112°; and O(23), 112°, are not significantly different from the expected values.

Calculations of the best planes through several sets of atoms were carried out employing the method of Schomaker et al. (1959); the results are summarised in Table XI. The following discussion of the molecular conformation refers to one half of the molecule only but it applies equally well to the other half and the quoted deviations from the planes have been averaged over both.

The atoms N(1),C(2),C(7),C(8),C(9),C(10),C(11),C(12), and C(13) of the indoline system are coplanar within the limits of the standard deviations. The cyclohexane ring, E, is cis fused to ring B and is in a "half-chair" conformation, the atoms C(2),C(7),C(3),C(15),C(16), being coplanar while C(14) is displaced by 0.93 Å from the plane. With respect to this cyclohexane ring N(1), C(6), C(17) are equatorial whereas N^+(4), C(20), C(16'), and C(8) are axial.



The piperidine ring is in the "boat" conformation, C(3), N^+(4), C(15), and C(20) are coplanar whereas C(14) is 0.57 Å and C(21) is 0.72 Å from the best plane through these four atoms and on the same side of it; C(5) is axial with respect to this ring.

In the five-membered ring, C, the atoms C(3), N$^+$(4), C(5), and C(7) are approximately coplanar while C(6) is displaced 0.61 Å from the best plane through these four atoms. The atoms of ring G exhibit the same feature, N(1),C(2),C(16),C(16'), being approximately coplanar and the fifth atom, C(17'), is 0.59 Å from the plane. These results are in agreement with the expected "envelope" conformation of saturated five-membered rings.

With respect to the double bond, C(19)-C(20), of the seven-membered ring, F, the atoms C(18) and C(15) are cis. In this ring O(23) is 0.39 Å from the best plane through C(15),C(18),C(19),C(20),C(21), while C(16) and C(17) are 1.30 Å and 1.50 Å, respectively, from this plane and on the same side of it.

The equations of the best planes through the atoms of the indoline ring systems are:

for AB $0.0824X - 0.3171Y + 0.9450Z + 0.5381 = 0$
for A'B' $0.7047X + 0.3745Y - 0.6023Z - 7.833 = 0$

and these planes are mutually inclined at 58°.

There is considerable strain involved in the central rings G and G' of caracurine-II when it assumes this conformation and some idea of the factors effecting this strain can be obtained from the construction of a molecular model on the basis of standard bond lengths and angles. The conformation adopted by this model differs quite markedly from that described above. The piperidine ring assumes a distorted "boat" conformation while, in the cyclohexane ring, C(2),C(3),C(7),C(14), and C(16) are approximately coplanar and C(15) is out of the plane defined by these atoms. The approximate values of some of the intramolecular non-bonded contacts of this model are given in Table XII. Of these, the distances C(14)....C(15'), C(14)....C(14'), C(15)....C(15') are much too short since the hydrogen atoms of C(14) and C(15') lie along the same line, as do those of C(14') and C(15). In order to reduce these interactions both halves of the molecule are rotated away from each other about the C(16)-C(16') bond as axis. This rotation may be accompanied by mutual repulsion of these halves which would cause increases in the angles C(15)-C(16)-C(16') and C(15')-C(16')-C(16) but because of the low accuracy of this analysis it is not possible to say whether this does occur. By performing this rotation the remainder of the molecule assumes approximately its true conformation and all intramolecular non-bonded distances become normal.

It is of interest to note that during the mass spectroscopic studies of Dr.R.I.Reed the caracurine-II molecule readily split into two parts of equal molecular weights thus giving physical evidence of the strain involved in the central ring system.

The molecular packing as viewed along the c-axis is shown in Figure 14 and the intermolecular distances less than 4.0 Å are listed in Table IX. The shortest carbon....iodide ion contacts of 3.66, 3.87, 3.89 and 3.96 Å can be taken as normal and compare favourably with the values 3.81, 3.99 Å reported for (+) des-(oxymethylene) -lycoctonine hydriodide monohydrate (Przybylska, 1961a) and 3.81 Å for N-methylgelsemicine hydriodide (Przybylska, 1962).

The $N^+....I^-$ distances of less than 5 Å are quoted in Table IX and shown in Figure 14 by the broken lines. The shortest of these, 4.42 and 4.58 Å are comparable with the values found in N-methylgelsemicine hydriodide, 4.39 Å, morphine hydriodide, 4.38 Å, (Mackay and Hodgkin, 1955) and macusine-A iodide, (this thesis p.73), 4.52 Å.

The two iodide ions of the asymmetric unit are in different environments and the co-ordination of each appears to account for the anisotropic thermal motion (see Table III). The electrostatic attractions between $I^-(24)$ and the three quaternary nitrogens at distances less than 5 Å are concentrated in the y- and z- directions. Consequently the temperature factors of this ion in these directions are relatively smaller than that in the x-direction. $I^-(24')$ has only one quaternary nitrogen in close proximity and the electrostatic attraction lies mainly in the x- and z- directions. As a result of this the temperature factor in the y-direction is relatively greater than in the x- and z-directions. Since this iodide ion has electrostatic attraction to one side only with respect to the x-direction, the relative reduction in this direction is not so great as in the case of $I^-(24)$. The thermal parameters of both iodide ions are rather large. This effect is possibly correlated with the lack of intensity data above moderate values of sin θ and may be indicative of some disorder in the crystal.

In the highly active toxiferine-I and d-tubocurarine the distance between the two quaternary centres has been estimated as being approximately 14 Å (Battersby and Hodson, 1960c). Caracurine-II possesses relatively low curarising activity and in view of this the distance of 8.5 Å between these centres in this molecule is interesting.

An unfortunate consequence of the fact that caracurine-II dimethiodide was not isomorphous with the other dihalides is that no direct use of the isomorphous replacement method was possible. It is hoped, however, that in the near future the analysis of the dimethochloride and dimethobromide derivatives will be resumed at the point indicated in section 2.3 at which it was presumed that the correct bromide ion co-ordinates had been deduced. If this analysis is successful the refinement of the structure will be carried out using the dimethochloride data and much more accurate positional parameters will be obtainable which, in turn, should permit a more accurate estimation of how the strain is distributed throughout the caracurine-II molecule and the central ring system in particular.

TABLE III.

Atomic co-ordinates and temperature factors.

(Origin of co-ordinates as in "International Tables" Vol. I)

Atom	x/a	y/b	z/c	B.
N(1)	0.3496	0.3632	0.2751	3.1
C(2)	0.4265	0.3765	0.3116	3.0
C(3)	0.4817	0.4650	0.2205	4.1
N(4)	0.5489	0.4694	0.2702	3.6
C(5)	0.5474	0.4488	0.4529	4.2
C(6)	0.4856	0.4416	0.5220	3.9
C(7)	0.4291	0.4293	0.3498	3.1
C(8)	0.3518	0.4380	0.3842	3.4
C(9)	0.3138	0.4834	0.4519	4.6
C(10)	0.2425	0.4813	0.4592	3.8
C(11)	0.2068	0.4411	0.4158	5.8
C(12)	0.2366	0.3952	0.3707	5.5
C(13)	0.3125	0.3983	0.3411	4.5
C(14)	0.4637	0.4440	0.0281	4.6
C(15)	0.5148	0.3914	0.0338	2.4
C(16)	0.4693	0.3503	0.1452	3.7
C(17)	0.5215	0.3149	0.2067	3.7
C(18)	0.6302	0.3284	0.0855	4.3
C(19)	0.6424	0.3795	0.1589	4.5
C(20)	0.5892	0.4011	0.1028	4.1
C(21)	0.6068	0.4571	0.1618	4.3
C(22)	0.5477	0.5249	0.2873	6.3
O(23)	0.5771	0.2966	0.0846	3.4
I(24)	0.5107	0.5633	-0.1980	†
N(1')	0.4765	0.2736	0.2479	3.7
C(2')	0.4175	0.2669	0.1268	3.4
C(3')	0.4466	0.2319	-0.1796	3.3
N(4')	0.3839	0.2254	-0.3014	4.2
C(5')	0.3281	0.2104	-0.1801	4.7
C(6')	0.3589	0.1890	-0.0026	3.2
C(7')	0.4305	0.2312	0.0175	3.8
C(8')	0.4872	0.1979	0.1150	2.5
C(9')	0.5149	0.1518	0.1082	5.8
C(10')	0.5698	0.1396	0.2364	3.8
C(11')	0.5822	0.1712	0.3612	3.0
C(12')	0.5638	0.2135	0.3689	3.3
C(13')	0.5035	0.2274	0.2497	4.9
C(14')	0.4777	0.2858	-0.2093	4.3

TABLE III (contd).

Atom	x/a	y/b	z/c	B.
C(15')	0·4183	0·3222	−0·1699	2·2
C(16')	0·4086	0·3172	0·0454	3·1
C(17')	0·3452	0·3500	0·0823	5·4
C(18')	0·2823	0·3771	−0·1714	2·9
C(19')	0·2967	0·3991	−0·2898	5·2
C(20')	0·3560	0·3066	−0·2646	3·7
C(21')	0·3529	0·2713	−0·3870	3·4
C(22')	0·3910	0·1826	−0·4271	3·7
O(23')	0·3291	0·3878	−0·0320	4·4
I(24')	0·1849	0·1788	−0·6185	†

†Anisotropic temperature factors obtained from the least-squares refinement of the iodide ion parameters are given below. These are the values of b_{ij} in the equation:

$$\exp\left(-B\sin^2\theta/\lambda^2\right) = 2^{-(b_{11}h^2+b_{22}k^2+b_{33}\ell^2+b_{12}hk+b_{23}k\ell+b_{13}h\ell)}$$

Anisotropic temperature factor parameters.
($b_{ij} \times 10^5$)

	b_{11}	b_{22}	b_{33}	b_{12}	b_{23}	b_{13}
I (24)	1089	282	3170	−27	31	−112
I (24')	867	502	3229	−20	73	129

Equivalent anisotropic thermal parameters along the directions of the crystal-axes in the form $\exp(-B_{ii}\sin^2\theta/\lambda^2)$.

	B_{11}	B_{22}	B_{33}
I (24)	10·4	5·9	5·0
I (24')	8·3	10·5	5·1

TABLE IV.

Standard deviations of the final atomic co-ordinates (Å).

Atom	σ (x)	σ (y)	σ (z)
N(1)	0.051	0.049	0.058
C(2)	0.066	0.060	0.075
C(3)	0.073	0.067	0.079
N(4)	0.056	0.052	0.061
C(5)	0.074	0.070	0.079
C(6)	0.072	0.068	0.074
C(7)	0.065	0.061	0.069
C(8)	0.065	0.067	0.075
C(9)	0.082	0.073	0.080
C(10)	0.073	0.065	0.078
C(11)	0.080	0.083	0.090
C(12)	0.084	0.078	0.097
C(13)	0.078	0.068	0.079
C(14)	0.073	0.075	0.084
C(15)	0.065	0.058	0.064
C(16)	0.069	0.066	0.077
C(17)	0.067	0.064	0.077
C(18)	0.074	0.070	0.080
C(19)	0.074	0.070	0.080
C(20)	0.071	0.068	0.085
C(21)	0.074	0.068	0.084
C(22)	0.088	0.083	0.103
O(23)	0.044	0.041	0.050
I(24)	0.008	0.007	0.007
N(1')	0.055	0.051	0.059
C(2')	0.069	0.063	0.076
C(3')	0.067	0.062	0.078
N(4')	0.059	0.053	0.067
C(5')	0.076	0.069	0.090
C(6')	0.066	0.065	0.074
C(7')	0.073	0.066	0.081
C(8')	0.064	0.056	0.066
C(9')	0.081	0.077	0.092
C(10')	0.072	0.065	0.075
C(11')	0.064	0.062	0.069
C(12')	0.068	0.064	0.075
C(13')	0.082	0.070	0.081
C(14')	0.073	0.068	0.084
C(15')	0.059	0.057	0.066
C(16')	0.064	0.066	0.070
C(17')	0.082	0.080	0.093
C(18')	0.064	0.062	0.071

TABLE IV (Contd).

Atom	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$
C(19')	0.078	0.075	0.093
C(20')	0.070	0.063	0.073
C(21')	0.068	0.064	0.078
C(22')	0.069	0.068	0.074
O(23')	0.050	0.047	0.053
I(24')	0.009	0.008	0.008

TABLE V. Measured and calculated values of the structure factors.

h	k	l	$\|F_o\|$	$\|F_c\|$	α
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

TABLE VI.

Intramolecular Bonded Distances (Å).

N(1)	–	C(2)	1.50	N(1')	–	C(2')	1.44
N(1)	–	C(13)	1.28	N(1')	–	C(13')	1.36
N(1)	–	C(17')	1.50	N(1')	–	C(17)	1.44
C(2)	–	C(7)	1.48	C(2')	–	C(7')	1.30
C(2)	–	C(16)	1.65	C(2')	–	C(16')	1.52
C(3)	–	N(4)	1.31	C(3')	–	N(4')	1.49
C(3)	–	C(7)	1.69	C(3')	–	C(7')	1.51
C(3)	–	C(14)	1.59	C(3')	–	C(14')	1.60
N(4)	–	C(5)	1.49	N(4')	–	C(5')	1.44
N(4)	–	C(21)	1.39	N(4')	–	C(21')	1.53
N(4)	–	C(22)	1.53	N(4')	–	C(22')	1.51
C(5)	–	C(6)	1.27	C(5')	–	C(6')	1.57
C(6)	–	C(7)	1.70	C(6')	–	C(7')	1.77
C(7)	–	C(8)	1.48	C(7')	–	C(8')	1.58
C(8)	–	C(9)	1.52	C(8')	–	C(9')	1.37
C(8)	–	C(13)	1.35	C(8')	–	C(13')	1.33
C(9)	–	C(10)	1.33	C(9')	–	C(10')	1.44
C(10)	–	C(11)	1.33	C(10')	–	C(11')	1.30
C(11)	–	C(12)	1.42	C(11')	–	C(12')	1.21
C(12)	–	C(13)	1.43	C(12')	–	C(13')	1.49
C(14)	–	C(15)	1.73	C(14')	–	C(15')	1.52
C(15)	–	C(16)	1.64	C(15')	–	C(16')	1.63
C(15)	–	C(20)	1.50	C(15')	–	C(20')	1.42
C(16)	–	C(17)	1.45	C(16')	–	C(17')	1.51
C(16)	–	C(16')	1.63				
C(17)	–	O(23)	1.47	C(17')	–	O(23')	1.38
C(18)	–	C(19)	1.53	C(18')	–	C(19')	1.40
C(18)	–	O(23)	1.32	C(18')	–	O(23')	1.39
C(19)	–	C(20)	1.24	C(19')	–	C(20')	1.43
C(20)	–	C(21)	1.63	C(20')	–	C(21')	1.34

TABLE VII.

Interbond Angles (°).

C(2) - N(1) - C(13)	105	C(2') - N(1') - C(13')	100
C(2) - N(1) - C(17')	107	C(2') - N(1') - C(17)	114
C(13) - N(1) - C(17')	122	C(13') - N(1') - C(17)	121
N(1) - C(2) - C(7)	108	N(1') - C(2') - C(7')	111
N(1) - C(2) - C(16)	102	N(1') - C(2') - C(16')	103
C(7) - C(2) - C(16)	124	C(7') - C(2') - C(16')	117
N(4) - C(3) - C(7)	116	N(4') - C(3') - C(7')	116
N(4) - C(3) - C(14)	120	N(4') - C(3') - C(14')	108
C(7) - C(3) - C(14)	101	C(7') - C(3') - C(14')	103
C(3) - N(4) - C(5)	102	C(3') - N(4') - C(5')	102
C(3) - N(4) - C(21)	123	C(3') - N(4') - C(21')	117
C(3) - N(4) - C(22)	96	C(3') - N(4') - C(22')	114
C(5) - N(4) - C(21)	118	C(5') - N(4') - C(21')	103
C(5) - N(4) - C(22)	108	C(5') - N(4') - C(22')	104
C(21) - N(4) - C(22)	108	C(21') - N(4') - C(22')	114
N(4) - C(5) - C(6)	117	N(4') - C(5') - C(6')	113
C(5) - C(6) - C(7)	106	C(5') - C(6') - C(7')	96
C(2) - C(7) - C(3)	118	C(2') - C(7') - C(3')	130
C(2) - C(7) - C(6)	111	C(2') - C(7') - C(6')	114
C(2) - C(7) - C(8)	99	C(2') - C(7') - C(8')	105
C(3) - C(7) - C(6)	88	C(3') - C(7') - C(6')	94
C(3) - C(7) - C(8)	125	C(3') - C(7') - C(8')	109
C(6) - C(7) - C(8)	116	C(6') - C(7') - C(8')	100
C(7) - C(8) - C(9)	130	C(7') - C(8') - C(9')	140
C(7) - C(8) - C(13)	111	C(7') - C(8') - C(13')	99
C(9) - C(8) - C(13)	119	C(9') - C(8') - C(13')	120
C(8) - C(9) - C(10)	116	C(8') - C(9') - C(10')	117
C(9) - C(10) - C(11)	122	C(9') - C(10') - C(11')	117
C(10) - C(11) - C(12)	127	C(10') - C(11') - C(12')	129
C(11) - C(12) - C(13)	112	C(11') - C(12') - C(13')	116
N(1) - C(13) - C(8)	114	N(1') - C(13') - C(8')	118
N(1) - C(13) - C(12)	123	N(1') - C(13') - C(12')	122
C(8) - C(13) - C(12)	123	C(8') - C(13') - C(12')	118
C(3) - C(14) - C(15)	99	C(3') - C(14') - C(15')	109
C(14) - C(15) - C(16)	108	C(14') - C(15') - C(16')	103
C(14) - C(15) - C(20)	112	C(14') - C(15') - C(20')	107
C(16) - C(15) - C(20)	115	C(16') - C(15') - C(20')	112
C(2) - C(16) - C(15)	110	C(2') - C(16') - C(15')	118
C(2) - C(16) - C(17)	112	C(2') - C(16') - C(17')	124
C(2) - C(16) - C(16')	105	C(2') - C(16') - C(16)	104
C(15) - C(16) - C(17)	106	C(15') - C(16') - C(17')	103
C(15) - C(16) - C(16')	120	C(15') - C(16') - C(16)	109
C(17) - C(16) - C(16')	104	C(17') - C(16') - C(16)	97
C(16) - C(17) - O(23)	120	C(16') - C(17') - O(23')	120
C(16) - C(17) - N(1')	102	C(16') - C(17') - N(1)	106

TABLE VII (Contd).

O(23) - C(17) - N(1')	106	O(23') - C(17') - N(1)	116
C(19) - C(18) - O(23)	137	C(19') - C(18') - O(23')	121
C(18) - C(19) - C(20)	101	C(18') - C(19') - C(20')	122
C(15) - C(20) - C(19)	141	C(15') - C(20') - C(19')	120
C(15) - C(20) - C(21)	117	C(15') - C(20') - C(21')	127
C(19) - C(20) - C(21)	101	C(19') - C(20') - C(21')	109
N(4) - C(21) - C(20)	104	N(4') - C(21') - C(20')	107
C(17) - O(23) - C(18)	107	C(17') - O(23') - C(18')	116

TABLE VIII.

Some intramolecular non-bonded distances (Å).

N(1)	.....	C(3)	3.74	N(1')	.....	C(3')	3.46
N(1)	.....	C(6)	3.84	N(1')	.....	C(6')	3.70
N(1)	.....	C(9)	3.62	N(1')	.....	C(9')	3.58
N(1)	.....	C(11)	3.57	N(1')	.....	C(11')	3.53
N(1)	.....	C(14)	3.59	N(1')	.....	C(14')	3.45
N(1)	.....	C(15)	3.65	N(1')	.....	C(15')	3.58
N(1)	.....	C(17)	3.50	N(1')	.....	C(17')	3.45
N(1)	.....	N(1')	3.42				
N(1)	.....	C(2')	3.13	N(1')	.....	C(2)	3.01
N(1)	.....	C(15')	3.75	N(1')	.....	C(15)	3.68
N(1)	.....	C(18')	3.60	N(1')	.....	C(18)	3.45
C(2)	.....	N(4)	3.43	C(2')	.....	N(4')	3.47
C(2)	.....	C(5)	3.18	C(2')	.....	C(5')	3.24
C(2)	.....	C(9)	3.76	C(2')	.....	C(9')	3.64
C(2)	.....	C(12)	3.59	C(2')	.....	C(12')	3.59
C(2)	.....	C(20)	3.47	C(2')	.....	C(20')	3.34
C(2)	.....	O(23)	3.95	C(2')	.....	O(23')	3.89
C(2)	.....	C(2')	3.32				
C(2)	.....	C(15')	3.92	C(2')	.....	C(15)	3.93
C(2)	.....	O(23')	3.17	C(2')	.....	O(23)	3.09
C(3)	.....	C(9)	3.61	C(3')	.....	C(9')	3.34
C(3)	.....	C(13)	3.75	C(3')	.....	C(13')	3.40
C(3)	.....	C(19)	3.84	C(3')	.....	C(19')	4.14
C(3)	.....	C(17')	4.18	C(3')	.....	C(17)	3.94
N(4)	.....	C(8)	3.86	N(4')	.....	C(8')	3.75
N(4)	.....	C(16)	3.71	N(4')	.....	C(16')	3.66
N(4)	.....	C(19)	3.14	N(4')	.....	C(19')	3.52
C(5)	.....	C(8)	3.68	C(5')	.....	C(8')	3.71
C(5)	.....	C(14)	3.56	C(5')	.....	C(14')	3.47
C(5)	.....	C(15)	3.58	C(5')	.....	C(15')	3.50
C(5)	.....	C(16)	3.84	C(5')	.....	C(16')	3.70
C(5)	.....	C(19)	3.42	C(5')	.....	C(19')	3.68
C(5)	.....	C(20)	3.04	C(5')	.....	C(20')	2.77
C(6)	.....	C(9)	3.44	C(6')	.....	C(9')	3.19
C(6)	.....	C(13)	3.69	C(6')	.....	C(13')	3.45
C(6)	.....	C(14)	3.74	C(6')	.....	C(14')	3.79
C(6)	.....	C(15)	3.96	C(6')	.....	C(15')	4.02
C(6)	.....	C(16)	3.79	C(6')	.....	C(16')	3.65
C(6)	.....	C(20)	3.86	C(6')	.....	C(20')	3.78
C(6)	.....	C(21)	3.55	C(6')	.....	C(21')	3.67
C(6)	.....	C(22)	3.11	C(6')	.....	C(22')	3.25
C(7)	.....	C(10)	3.84	C(7')	.....	C(10')	3.97
C(7)	.....	C(12)	3.70	C(7')	.....	C(12')	3.66
C(7)	.....	C(17)	3.74	C(7')	.....	C(17')	3.66
C(7)	.....	C(20)	3.59	C(7')	.....	C(20')	3.27
C(7)	.....	C(21)	3.67	C(7')	.....	C(21')	3.54
C(7)	.....	C(22)	3.46	C(7')	.....	C(22')	3.67

TABLE VIII (Contd).

TABLE VIII (Contd).

C(7)	.....	C(16')	3.85	C(7')	....	C(16)	3.48
C(7)	.....	C(17')	3.35	C(7')	....	C(17)	3.19
C(7)	.....	O(23')	3.60	C(7')	....	O(23)	3.30
C(8)	.....	C(14)	3.39	C(8')	....	C(14')	3.44
C(8)	.....	C(16)	3.71	C(8')	....	C(16')	3.62
C(8)	.....	C(17')	3.32	C(8')	....	C(17)	3.34
C(8)	.....	O(23')	3.44	C(8')	....	O(23)	3.19
C(12)	.....	C(17')	3.21	C(12')	....	C(17)	3.14
C(12)	.....	O(23')	3.49	C(12')	....	O(23)	3.13
C(13)	.....	C(14)	3.87	C(13')	....	C(14')	3.84
C(13)	.....	C(16)	3.52	C(13')	....	C(16')	3.40
C(13)	.....	C(16')	3.62	C(13')	....	C(16)	3.52
C(13)	.....	C(18')	3.94	C(13')	....	C(18)	3.84
C(13)	.....	O(23')	2.84	C(13')	....	O(23)	2.65
C(14)	.....	C(17)	3.94	C(14')	....	C(17')	3.74
C(14)	.....	C(19)	3.91	C(14')	....	C(19')	3.72
C(14)	.....	C(22)	3.34	C(14')	....	C(22')	3.65
C(14)	.....	C(15')	3.75	C(14')	....	C(15)	3.49
C(14)	.....	C(16')	3.63	C(14')	....	C(16)	3.20
C(14)	.....	C(17')	3.41	C(14')	....	C(17)	3.33
C(14)	.....	C(18')	4.12	C(14')	....	C(18)	3.78
C(14)	.....	O(23')	2.97	C(14')	....	O(23)	2.90
C(15)	.....	C(15')	3.03				
C(15)	.....	C(17')	3.37	C(15')	....	C(17)	3.43
C(15)	.....	O(23')	3.47	C(15')	....	O(23)	3.59
C(16)	.....	C(21)	3.89	C(16')	....	C(21')	3.64
C(16)	.....	C(20')	3.92	C(16')	....	C(20)	4.09
C(16)	.....	O(23')	3.10	C(16')	....	O(23)	3.20
C(17)	.....	C(17')	3.54				
C(18)	.....	C(21)	3.60	C(18')	....	C(21')	3.58
C(20)	.....	C(22)	3.75	C(20')	....	C(22')	3.67

TABLE IX.

Intermolecular distances ≤ 4.0Å.

I (24')	C (18)$_{\mathrm{V}}$	3.66	C (5')	C (18)$_{\mathrm{III}}$	3.90
C (22)	C (9')$_{\mathrm{II}}$	3.75	C (10)	C (10)$_{\mathrm{I}}$	3.91
O (23')	C (10)$_{\mathrm{I}}$	3.83	C (11')	C (12)$_{\mathrm{VI}}$	3.95
C (22)	C (10')$_{\mathrm{II}}$	3.84	I (24)	C (9')$_{\mathrm{IV}}$	3.96
I (24)	C (22')$_{\mathrm{IV}}$	3.87	C (9)	C (10)$_{\mathrm{I}}$	3.97
I (24')	C (19)$_{\mathrm{III}}$	3.89			

Closest approaches of N^{+} ...... I^{-}

N(4)	I(24)	4.42
N(4')	I(24')	4.58
N(4)	I(24)$_{\mathrm{VII}}$	4.81
N(4')	I(24)$_{\mathrm{IV}}$	4.86

The subscripts refer to the following equivalent positions.

I	$\frac{1}{2} - x$,	$1 - y$,	$-\frac{1}{2} + z$
II	$1 - x$,	$\frac{1}{2} + y$,	$\frac{1}{2} - z$
III	$-\frac{1}{2} + x$,	$\frac{1}{2} - y$,	$\bar{z}$
IV	$1 - x$,	$\frac{1}{2} + y$,	$-\frac{1}{2} - z$
V	$-\frac{1}{2} + x$,	$\frac{1}{2} - y$,	$-1 - z$
VI	$\frac{1}{2} + x$,	$\frac{1}{2} - y$,	$1 - z$
VII	x,	y,	$1 + z$

TABLE X.

Average bond lengths in the molecule.

Bond	No. of Bonds	Mean Value (Å)	Standard Value (Å)	Reference.
Carbon-carbon (aromatic)	12	1.38	1.395	(1)
Carbon-carbon (aliphatic)	19	1.57	1.544	(1)
Carbon-carbon (ethylenic)	2	1.34	1.337	(1)
Carbon (sp^3) - carbon (sp^2)	6	1.47	1.53	(1)
Carbon (sp^3) - aromatic carbon	2	1.53	1.525	(1)
Carbon (sp^3) - $N^+(4)$	8	1.46	1.479	(1)
Carbon (sp^3) - N (1)	4	1.47	1.472	(1)
Aromatic carbon - N (1)	2	1.32	1.37	(2), (3)
Carbon (sp^3) - O	4	1.39	1.43	(1)

References (1) Tables of Interatomic Distances and Configuration in Molecules and Ions. (1958).

(2) K. N. Trueblood, E. Goldish and J. Donohue (1961). Acta Cryst 14, 1009.

(3) G. M. Brown and R. E. Marsh (1960). Acta Cryst. 13, 1037.

TABLE XI.

Deviations from best planes through sets of atoms.

Atoms included	d(Å)	Atoms omitted	d(Å)	Atoms included	d(Å)	Atoms omitted	d(Å)
N(1)	-0.13			N(1')	-0.10		
C(2)	0.13			C(2')	0.19		
C(7)	-0.05			C(7')	-0.10		
C(8)	0.00			C(8')	-0.06		
C(9)	0.02			C(9')	0.02		
C(10)	-0.01			C(10')	0.01		
C(11)	-0.03			C(11')	0.08		
C(12)	0.10			C(12')	-0.07		
C(13)	-0.02			C(13')	0.03		
C(3)	0.00	C(14)	0.73	C(3')	-0.05	C(14')	0.71
N(4)	0.00	C(21)	0.63	N(4')	0.05	C(21')	0.50
C(15)	0.00			C(15')	0.05		
C(20)	0.00			C(20')	-0.05		
C(2)	0.01	C(14)	1.02	C(2')	0.02	C(14')	0.83
C(7)	-0.02			C(7')	-0.05		
C(3)	0.01			C(3')	0.03		
C(15)	-0.01			C(15')	-0.02		
C(16)	0.00			C(16')	0.02		
C(3)	-0.07	C(6)	-0.46	C(3')	-0.05	C(6')	-0.76
N(4)	0.07			N(4')	0.02		
C(5)	-0.04			C(5')	-0.02		
C(7)	0.04			C(7')	0.05		
N(1)	-0.04	C(17')	-0.66	N(1')	-0.01	C(17')	-0.51
C(2)	0.05			C(2')	0.01		
C(16)	-0.05			C(16')	-0.01		
C(16')	0.03			C(16)	0.01		
C(15)	-0.03	C(16)	-1.31	C(15')	0.05	C(16')	-1.28
C(18)	0.06	C(17)	-1.57	C(18')	-0.06	C(17')	-1.43
C(19)	-0.10	O(23)	-0.45	C(19')	0.11	O(23')	-0.33
C(20)	0.04			C(20')	-0.11		
C(21)	0.04			C(21')	0.00		

TABLE XII.

Comparison of some intramolecular non-bonded contacts. (Å)

	Molecular model.	Average calculated from true conformation.
N(1) ...... N(1')	3.7	3.42
N(1) ...... C(2')	3.5	3.07
C(3) ...... C(15)	3.7	4.90
C(7) ...... O(23')	3.8	3.45
C(11) ..... O(23')	2.8	3.31
C(12) ..... C(18')	3.7	4.09
C(13) ..... O(23')	2.5	2.75
C(14) ..... C(15')	2.6	3.61
C(14) ..... C(14')	2.8	4.70
C(14) ..... C(16')	3.0	3.42
C(14) ..... C(17')	3.6	3.37
C(14) ..... O(23')	3.8	2.94
C(15) ..... C(15')	2.8	3.03
C(15) ..... C(17')	3.7	3.40
C(15) ..... O(23')	4.3	3.53
C(15) ..... C(2')	3.6	3.93
C(16) ..... O(23')	3.5	3.15

PART III

The Structure of Macusine-A:

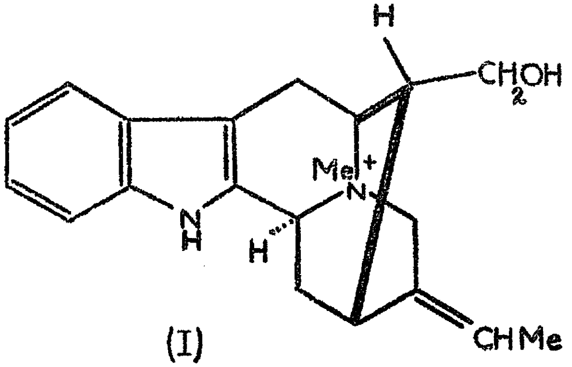
X-ray Analysis of Macusine-A Iodide.

3.1 INTRODUCTION.

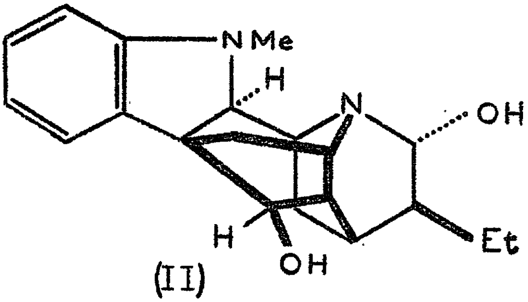
During their researches on the total alkaloid content of the bark of British Guianian "Strychnos toxifera" Schomb. Battersby et al. (1960) isolated, in small quantity, three new quaternary alkaloids, hemitoxiferine-I, macusine-A and macusine-B. The latter two alkaloids were named after the Macusi tribe of Indians who are reported (MacIntyre, 1947) to have carried out the first investigations on "Strychnos toxifera". The isolation of hemitoxiferine-I had been briefly recorded earlier (Battersby and Hodson, 1958) and its structure and stereochemistry had been discussed in a later report (Battersby and Hodson, 1960a) but the structures of the macusines were unknown.

From the infrared and ultraviolet spectra (Battersby et al., 1960) it was apparent that macusine-A and -B were closely related. Both were found to have ultraviolet spectra characteristic of 2,3 - disubstituted indoles; the infrared spectrum of macusine-A showed the presence of hydroxyl, imino and ester groups whereas that of macusine-B showed the presence of hydroxyl and imino groups but no ester group.

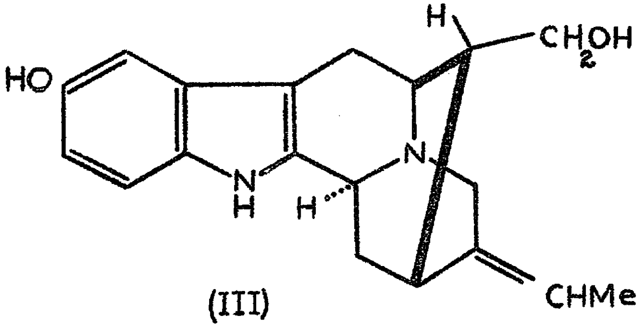
Chemical studies conducted by Battersby and Yeowell (1961) established the constitution of macusine-B (I) and these workers determined its absolute configuration, with the exception of the configuration of the ethylidene system, by independent correlation with ajmaline (II) and


H
CH2OH
Me+
N
N
H
H
CHMe

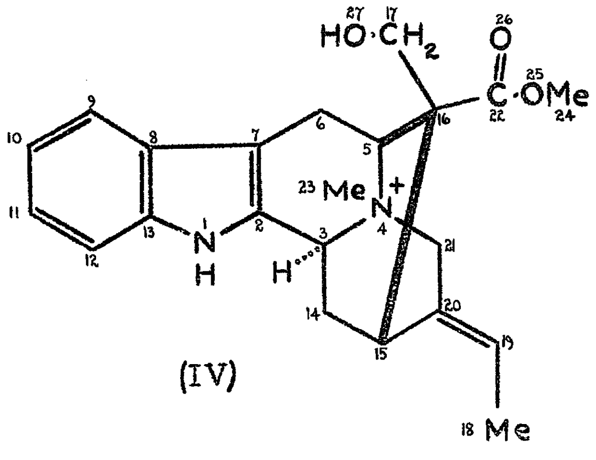
(I)


NMe
H
N
OH
H
OH
Et

(II)


H
CH2OH
HO
N
N
H
H
CHMe

(III)


27 17
HO·CH2
26
O
25
C·OMe
22 24
16
9
10
8
7
6
5
23 Me
N+
4
11
13
1
N
H
2
3
H
21
12
14
20
15
19
18 Me

(IV)

sarpagine (III) for both of which the relative and absolute stereochemistry were known (Bartlett, Schlittler et al., 1960, Bartlett, Sklar and Taylor, 1960, Bartlett et al., 1962). Having this knowledge of the constitution of macusine-B several plausible structures could be postulated for macusine-A from biosynthetic considerations. Since macusine-A had been isolated in smaller yield than macusine-B only limited researches could be carried out to confirm which of the possibilities was correct and so Dr. A.R.Battersby provided crystals of the iodide derivative for an X-ray crystal structure determination.

The results of the X-ray investigation establish the structure (IV) for macusine-A and chemical studies which alone do not establish it (Battersby, Hodson and Yeowell, 1961) are fully consistent with this constitution. The absolute stereochemistry of macusine-A has been determined by correlation with macusine-B (Battersby, 1962) and is represented by (IV).

3.2 EXPERIMENTAL.

Crystal data: Macusine-A iodide, $C_{22}H_{27}N_2O_3I$. M = 494.4. m.p. 274°C(decomp.). Orthorhombic, a = 13.82 ± 0.03, b = 9.06 ± 0.03, c = 17.43 ± 0.04 Å. U = 2182 $Å^3$ $D_{obs.}$(flotation in aqueous $ZnCl_2$ solution) = 1.503 g.cc.$^{-1}$ Z = 4. D_c = 1.505 g.cc^{-1}. Absent spectra: h00 when h = 2n+1, 0k0 when k = 2n+1, 00ℓ when ℓ = 2n+1. Space group $P2_12_12_1$ (D_2^4). Absorption coefficient for X-rays (λ = 1.542 Å), μ = 119.6 cm^{-1}. Total number of electrons per unit cell = F(000) = 1096. Total number of independent observed structure amplitudes = 1145. $\sum f^2$ "heavy" atoms= 2916, $\sum f^2$ "light" atoms = 1096.

Rotation, oscillation and moving-film photographic methods were used and copper-K_α (λ = 1.542 Å) radiation employed. The cell dimensions were determined from rotation and equatorial layer line Weissenberg photographs and the space group was determined uniquely from the systematic halvings. Intensity data were obtained from equatorial and equi-inclination upper-layer multiple-film Weissenberg photographs taken from crystals rotated about the needle axis (a-crystal axis). The intensities were estimated visually and corrected for Lorentz, polarisation and the rotation factors appropriate to the upper layers (Tunell, 1939). The various layers (0kℓ - 8kℓ) were placed on the same scale by comparison of $\sum|F_o|$ and $\sum|F_c|$ based on the iodide ion alone and adjusted throughout the refinement to ensure that $\sum|F_o| = \sum|F_c|$.

3.3 STRUCTURE DETERMINATION AND REFINEMENT.

The co-ordinates of the iodide ion were obtained from the Patterson projection along the a-axis (Figure 1) and that section of the three-dimensional Patterson function at W = ½ (Figure 2). The peaks corresponding to the iodide - iodide vectors are denoted by A, B, C in Figure 1 and by D in Figure 2. The iodide ion co-ordinates were determined from these to be $^{x}/a = 0.4504$, $^{y}/b = 0.6574$, $^{z}/c = 0.5707$.

The first phasing calculations based on these co-ordinates and employing an isotropic temperature factor, B, of 4.0 $\mathring{A}^2$ because of the rapid fall off in data above sin $\theta = 0.6$, led to an agreement index of 0.316. From the first three-dimensional Fourier synthesis, for which the observed structure amplitudes and phase constants appropriate to the iodide ion alone were employed, approximate co-ordinates were assigned to N(1),C(2),C(3),N(4), C(5),C(6),C(7),C(8),C(9),C(10),C(11),C(12),C(13),C(14),C(15),C(16),C(19), C(20),C(21),C(22),C(23),O(25). (Comparison of the complete structure of macusine-A (IV) with that of macusine-B (I) will show that this partial skeleton is common). These twenty-two light atoms were included, all as carbon atoms with an isotropic temperature factor, B, of 3.0 $\mathring{A}^2$, in the next phasing calculations. The value of the agreement index at this stage was 0.274.

The second three-dimensional Fourier synthesis, for which the improved phase constants were used in conjunction

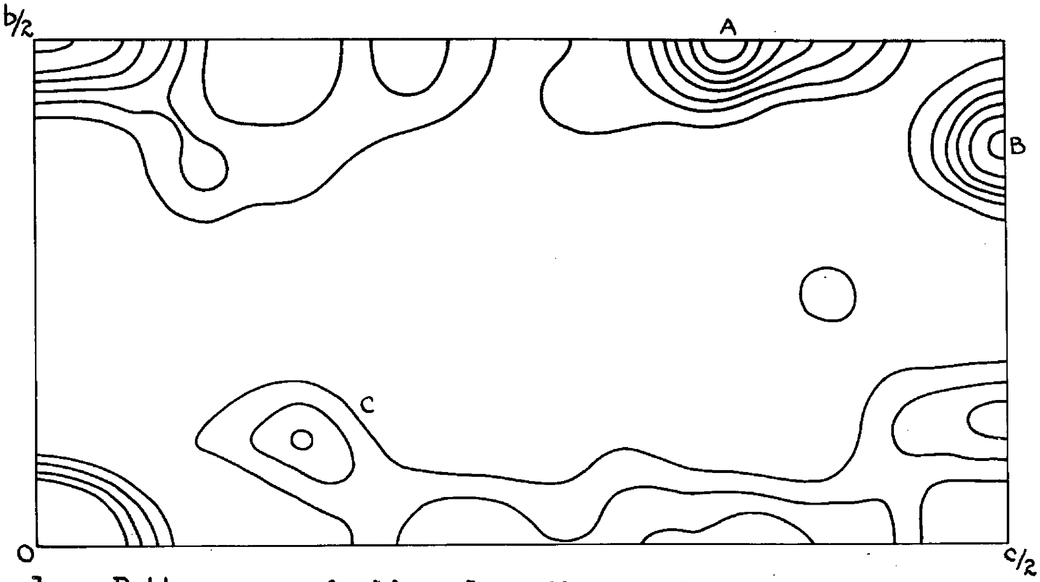


Fig. 1. Patterson projection along the a-axis. The contour scale is arbitrary. The iodide-iodide vector peaks are designated A, B, and C.

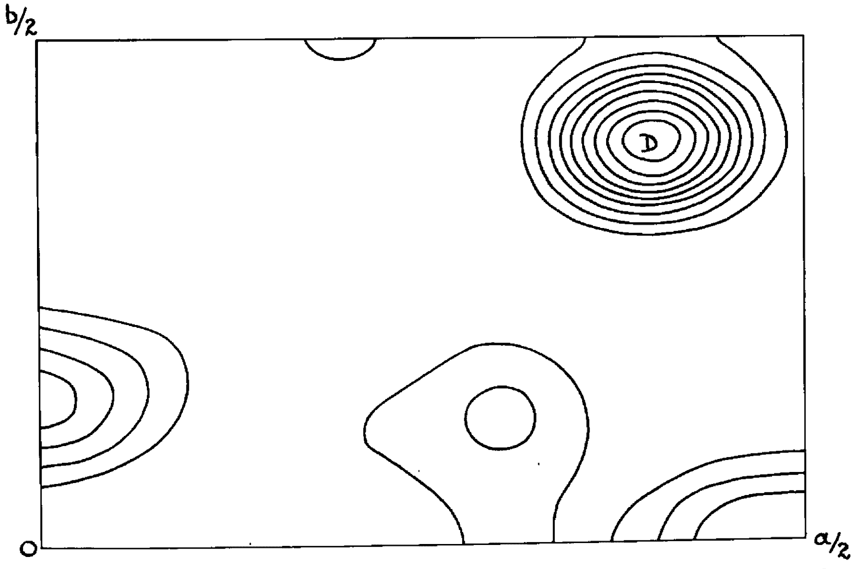


Fig. 2. The three-dimensional Patterson function; the section at $W = \frac{1}{2}$. The iodide-iodide vector peak is marked D. The contour scale is arbitrary.

with the observed structure amplitudes permitted the remaining carbon and oxygen atoms to be located. On the basis of peak heights, interatomic distances and knowledge of the structure of macusine-B, identification of the hetero-atoms was possible. Calculation of a further set of structure factors, with each atom included as its appropriate chemical type and employing isotropic temperature factors of $B = 3.0$ Å^2 for carbon, nitrogen and oxygen, and $B = 4.0$ Å^2 for the iodide ion, reduced the R value to 0.213. The subsequent three-dimensional F_o Fourier synthesis showed all the atoms (except hydrogens) clearly resolved. Corrections for series-termination errors were applied to the atomic co-ordinates by calculating "back-shift" corrections from a three-dimensional F_c Fourier synthesis computed using the same phase constants. By comparison of the peak heights of both of these Fourier syntheses adjustments were made to the individual isotropic thermal parameters. Refinement of the co-ordinates and isotropic thermal parameters was continued by this method for another two cycles and resulted in a reduction of the agreement index to 0.167.

A suitable conclusion of the refinement process was attained following two cycles of anisotropic least-squares (Rollett, 1961) adjustment of the positional and thermal parameters of the atoms. The course of analysis is presented diagrammatically in Table I.

Theoretical scattering factors were employed for the structure factor calculations; those of Berghuis et al. (1955) for carbon, nitrogen and oxygen and the Thomas-Fermi (1935) values for iodine were chosen.

The weighting system used in the least-squares refinement was

$$\text{if} \quad |F_o| \leqslant 40.00 \qquad \sqrt{w}(hk\ell) = 1$$

$$\text{if} \quad |F_o| > 40.00 \qquad \sqrt{w}(hk\ell) = 40.00/|F_o(hk\ell)|.$$

TABLE I.

Course of Analysis.

2-D. and 3-D. Patterson functions

↓

Iodide ions ($B = 4.0$ Å^2)

↓

1st Structure factor calculation $R = 0.316$

↓

1st 3-D Fourier synthesis (all observed reflections)

↓

2nd Structure factor calculation
Iodide ion $B = 4.0$ Å^2)
22 'light' atoms) $R =$
as carbon) 0.274
atoms $B = 3.0$ Å^2)

↓

2nd 3-D Fourier synthesis

↓

3rd Structure factor calculation
Iodide ion $B = 4.0$ Å^2)
22 carbon, 2)
nitrogen, 3) $R =$
oxygen atoms) 0.213
$B = 3.0$ Å^2)

↓

3rd 3-D Fourier syntheses (F_o and F_c)

↓

4th Structure factor calculation (individual isotropic thermal parameters)
$R = 0.187$

↓

3-D F_o and F_c Fourier syntheses

↓

5th Structure factor calculation $R = 0.173$

↓

3-D F_o and F_c Fourier syntheses

↓

6th Structure factor calculation $R = 0.167$

↓

Anisotropic least-squares

↓

7th Structure factor calculation $R = 0.157$

↓

Anisotropic least-squares

↓

8th Structure factor calculation $R = 0.145$

3.4 RESULTS OF ANALYSIS.

The final atomic co-ordinates and anisotropic temperature factor parameters given by the least-squares refinement are listed in Tables II and III, respectively. The standard deviations of the final co-ordinates, Table IV, were derived from the least-squares totals in the normal manner.

The observed and calculated structure amplitudes, both rounded off as integers, and the values of the phase constants, α, are listed in Table V. The final agreement index over 1145 independent observed structure amplitudes is 0.145. Of 266 unobserved reflections also included in Table V there are 254 for which $|F_c(hk\ell)|$ is less than $1\frac{1}{2}$ $|F_o(hk\ell)|$, where $|F_o(hk\ell)|$ is the minimum observable value of the reflection in question.

Employing the observed structure amplitudes and phase constants of Table V a final three-dimensional electron-density distribution was calculated and this is shown in Figure 3 by means of superimposed contour sections drawn parallel to (010). Other peaks which appeared in this three-dimensional Fourier synthesis, but which are not included in this Figure, occurred in the direction of x along the line joining iodide ions of adjacent unit cells. These peaks were spaced at intervals of about 1.6 Å and decreased in magnitude the more distant they were from the iodide ions. They were undoubtedly spurious peaks and were attributed to series-termination effects which would be expected to arise in the direction of x since the data were collected about the a-axis only.

The atomic arrangement corresponding to Figure 3 and to the absolute configuration of macusine-A as determined by Battersby (1962) is shown in Figure 4. The distances of the carbon, nitrogen and oxygen atoms of the macusine-A molecule from the best plane through the atoms of the indole system are also given in this Figure.

The intramolecular bond lengths and interbond angles are listed in Tables VI and VII, respectively. The average estimated standard deviation of a carbon-carbon single bond length is 0.07 Å and of a tetrahedral angle is 4°. Some of the more important intramolecular non-bonded contacts are given in Table VIII.

The arrangement of molecules as viewed along the b-axis is shown in Figure 5 where the system of possible hydrogen bonds is denoted by the broken lines. Table IX lists the shorter intermolecular contacts.

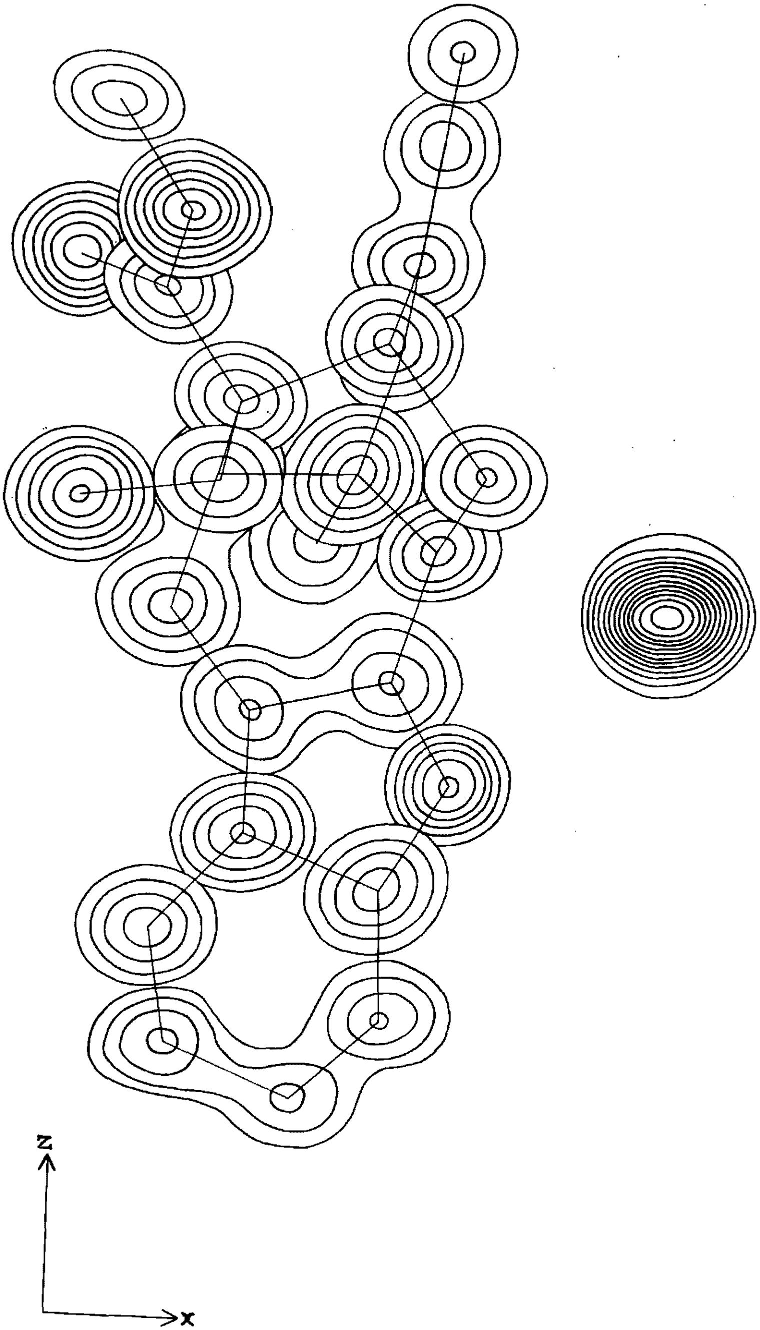


Fig. 3. The final three-dimensional electron-density distribution for macusine-A iodide shown by means of superimposed contour sections drawn parallel to (010). The contour interval is 1e/Å^3 except around the iodide ion where it is 5e/Å^3.

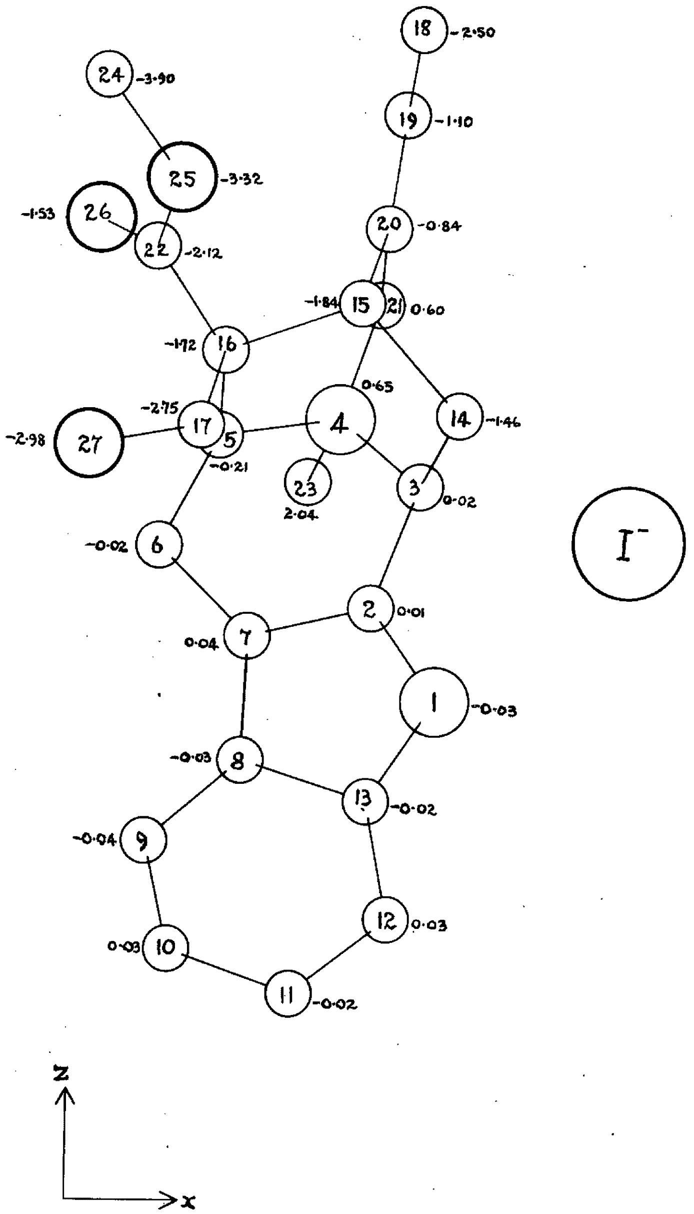


Fig. 4. Atomic arrangement corresponding to Fig. 3. Figures give height in Å above or below the indole plane. A right-handed set of axes has been chosen.

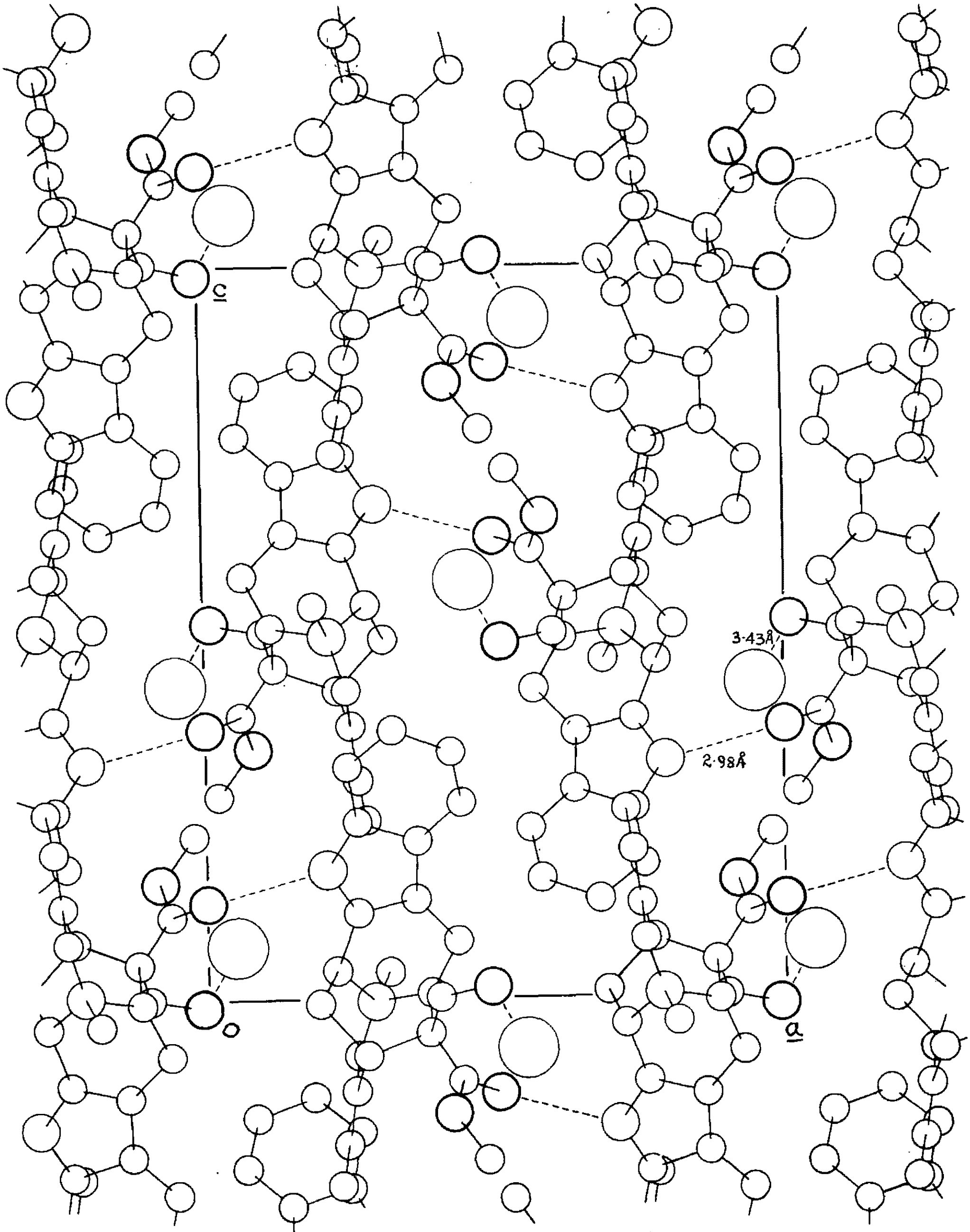


Fig. 5. The arrangement of molecules as viewed along the b-axis. The broken lines denote the system of possible hydrogen bonds.

3.5 DISCUSSION OF RESULTS.

As in the structure determination of caracurine-II (part II of this thesis) the bond lengths and interbond angles are not determined with sufficient precision to permit a discussion of apparent differences between chemically equivalent bonds.

The average carbon-carbon bond length in the indole system, 1.41 Å, is in agreement with the expected value of 1.395 Å for a bond between aromatic carbon atoms. The average of the carbon-carbon single bond lengths between sp^3- hybridised carbon atoms is 1.57 Å and between sp^3- and sp^2- hybridised carbon atoms is 1.51 Å. These do not differ significantly from the accepted values of 1.544 Å and 1.51 Å, respectively. The length of the carbon-carbon double bond of the ethylidene system, C(19)-C(20), 1.31 Å, is comparable with that of 1.33 Å reported for ethylene (Bartell and Bonham, 1957). The values of the sp^3- hybridised carbon-quaternary nitrogen, $N^+(4)$, bond lengths vary from 1.36 to 1.66 Å; the average of these, 1.49 Å, is compatible with the accepted value of 1.49 Å. The accepted values cited for the bond lengths are those given in Tables of Interatomic Distances (1958).

The mean length of the pyrrole carbon-nitrogen, N(1), bonds, 1.33 Å, is not significantly different from the values for aromatic carbon-nitrogen bonds found in p-nitroaniline, 1.37 Å (Trueblood et al., 1961), 2-amino-3-methylbenzoic acid, 1.37 Å (Brown and Marsh, 1960) and 2-chloro-4-nitroaniline, 1.39 Å (this thesis p.109).

The average interbond angle in the benzene ring is 120° and in the pyrrole ring is 108°; both of these agree with the expected values (Tables of Interatomic Distances, 1958). Within the limits of the standard deviations the atoms of the indole rings, N(1),C(2),C(3),C(8),C(9),C(10),C(11), C(12),C(13), and the adjacent substituent atoms, C(3) and C(6), are coplanar. The equation of the best plane through these eleven atoms, calculated by the method of Schomaker et al.(1959), is

$$0.0446\ X + 0.9714\ Y - 0.2312\ Z - 1.6459 = 0$$

and the distances of the carbon, nitrogen and oxygen atoms of the macusine molecule from this plane are given in Figure 4.

About sp^3-hybridised carbon atoms the average bond angle is 110° and about the quaternary nitrogen it is 109°. These results are in agreement with the expected value of $109^\circ 28'$ for the tetrahedral angle.

The dimensions of the methyl ester group are comparable with those found in methyl acetate (O'Gorman et al.,1950), dimethyl oxalate (Dougill and Jeffrey, 1953) and methyl formate (Curl, 1959). The atoms C(24),O(25),C(22),O(26),C(16), are coplanar within the limits of the standard deviations, the equation of the best plane through these atoms being

$$0.6646\ X + 0.5249\ Y + 0.5316\ Z - 11.657 = 0$$

and the individual deviations are given in Table X. The reasons for this preferred planar conformation and the difference in carbon-oxygen single bond lengths are discussed for bromogeigerin acetate in section 4.5 of this thesis.

The quinuclidine system is in the expected "boat" conformation with the bonds C(5)-C(16), C(3)-C(14) and C(20)-C(21) approximately parallel to one another while $N^+(4)$ and C(15) are on the same side of the planes formed by taking these bonds in pairs and the displacements of the atoms from these planes are given in Table XI.

The equation of the best plane through the atoms of the ethylidene system, C(18),C(19),C(20),C(21), and C(15), is

$$0.9819\ X - 0.0395\ Y - 0.1839\ Z - 8.031 = 0$$

The deviations of these five atoms from this plane are given in Table XII; none of these deviations is significant.

The configuration of the ethylidene system in macusine-A, and hence in other related alkaloids, is established unequivocally by this analysis. The absolute stereochemistry at C(15) is the same as that at the corresponding carbon of all α - and β - indole alkaloids (Bose et al., 1956, Wenkert et al., 1957) with the sole exception of ψ - akuammacine (Edwards and Smith, 1960) and, with respect to the C(19)-C(20) double bond, C(18) is cis to C(15). The same configuration of the ethylidene system has recently been found in akuammidine (Silvers and Tulinsky, 1962), the methiodide of which is isomeric with macusine-A iodide and differs only in the sterochemistry at C(16). Moreover, in echitamine (Hamilton et al., 1961, Birch et al., 1961), which possesses features similar to macusine-A, the stereochemistry of the ethylidene system is the same as that in macusine-A.

Intermolecular contacts less than 4.0 Å are listed in Table IX. Although no direct determination of the positions of the hydrogen atoms was attempted because of the presence of the iodide ion, two of these intermolecular contacts strongly suggest the presence of hydrogen bonding in the crystal. The angle C(2)-N(1)-O(26) is 109° and N(1) is only 2.98 Å from the carbonyl oxygen, O(26), of an adjacent macusine molecule. Comparison of this distance with some values reported for N-H....O hydrogen bonds is favourable e.g. 2.85 Å in diketopiperazine (Degeilh and Marsh, 1959), 2.86, 2.89 Å in glycyl-L-tryptophan dihydrate (Pasternak, 1956), 2.86, 2.92, 2.94 Å in L-glutamic acid (Hirokawa, 1955). Another close contact exists between the iodide ion and the oxygen of the hydroxyl group, O(27), of an adjacent molecule. This distance is 3.43 Å, which, when considered along with the value of 107° for the angle C(17)-O(27)-I^-, is indicative of an O-H....I^- hydrogen bond and it is comparable with that of 3.57 Å in muscarine iodide (Jellinek, 1957) and with those of 3.52–3.62 Å in (+)-demethanolaconinone hydriodide trihydrate (Przybylska, 1961b).

The shortest carbon-iodide ion contacts of 3.93, 3.95, 4.00 Å can be taken as normal and compare favourably with those found in DL-isocryptopleurine methiodide, 3.96 Å, (Fridrichsons and Mathieson, 1955) and in (+) des-(oxymethylene)-lycoctonine hydriodide monohydrate, 3.81, 3.99 Å (Przybylska, 1961a).

The closest approach of $N^{+}(4)....I^{-}$ is 4.52 Å, comparable with the reported distances of 4.39 Å in (−)N-methyl-gelsemicine hydriodide (Przybylska, 1962) and 4.42, 4.58 Å in caracurine-II dimethiodide (this thesis p.57).

The system of possible hydrogen bonds is represented by broken lines in Figure 5. Adjacent macusine-A molecules at $-\frac{1}{2}+x$, $\frac{1}{2}-y$, $1-z$ and x, y, z, and at x, y, z and $\frac{1}{2}+x$, $\frac{1}{2}-y$, $1-z$ are joined by N–H....O hydrogen bonds along the direction of x; the molecules at $1-x$, $\frac{1}{2}+y$, $1\frac{1}{2}-z$ and $1\frac{1}{2}-x$, $1-y$, $\frac{1}{2}+z$, and at $1\frac{1}{2}-x$, $1-y$, $\frac{1}{2}+z$ and $2-x$, $\frac{1}{2}+y$, $1\frac{1}{2}-z$ are joined in a similar manner. Macusine-A molecules are also linked by an electrostatic attraction between the iodide ion at x, y, z and the quaternary nitrogen, $N^{+}(4)$, at x, y, z and by an I^{-}....H–O hydrogen bond between this iodide ion and the hydroxyl group of an adjacent molecule at x, $1+y$, z. This iodide ion is further involved in a weaker electrostatic attraction with a quaternary nitrogen of the adjacent molecule at $-\frac{1}{2}+x$, $1\frac{1}{2}-y$, $1-z$; the $N^+(4)....I^-$ distance is 4.90 Å and the nitrogen is on the opposite side of the iodide ion, with respect to the x-direction, from the other quaternary nitrogen mentioned. In the direction of z the molecules are held together by van der Waals forces.

TABLE II.

Atomic co-ordinates.

(Origin of co-ordinates as in "International Tables" Vol. I)

Atom	x/a	y/b	z/c
I	0.4499	0.6976	0.5713
N(1)	0.7927	0.2613	0.3229
C(2)	0.7402	0.2981	0.3830
C(3)	0.7777	0.3322	0.4615
N(4)	0.7120	0.4285	0.5038
C(5)	0.6077	0.3385	0.4993
C(6)	0.5674	0.3277	0.4224
C(7)	0.6399	0.3016	0.3646
C(8)	0.6364	0.2584	0.2852
C(9)	0.5600	0.2436	0.2323
C(10)	0.5774	0.2139	0.1622
C(11)	0.6782	0.1861	0.1342
C(12)	0.7558	0.2075	0.1824
C(13)	0.7394	0.2386	0.2594
C(14)	0.8075	0.1829	0.5081
C(15)	0.7321	0.1785	0.5779
C(16)	0.6190	0.1871	0.5464
C(17)	0.6080	0.0505	0.5001
C(18)	0.7759	0.1809	0.7551
C(19)	0.7633	0.3155	0.7011
C(20)	0.7490	0.3122	0.6269
C(21)	0.7405	0.4539	0.5774
C(22)	0.5622	0.1778	0.6138
C(23)	0.6873	0.5701	0.4638
C(24)	0.5208	0.0288	0.7220
O(25)	0.5808	0.0598	0.6571
O(26)	0.4999	0.2575	0.6303
O(27)	0.5096	0.0256	0.4856

TABLE III.

Anisotropic temperature factor parameters ($b_{ij} \times 10^5$).

Atom	b_{11}	b_{22}	b_{33}	b_{12}	b_{23}	b_{13}
I	814	1964	609	-1	66	-145
N(1)	494	1540	544	114	-1	-9
C(2)	325	1770	586	314	95	37
C(3)	144	2676	935	-688	-356	682
N(4)	996	1549	601	-304	-8	20
C(5)	992	2397	737	271	84	791
C(6)	119	2068	602	-1019	228	379
C(7)	918	2049	699	-460	735	-151
C(8)	1033	1226	504	1026	419	112
C(9)	351	1496	726	-709	3	-935
C(10)	463	1625	524	-293	-82	-68
C(11)	1243	1489	818	-678	60	-263
C(12)	1647	1349	677	132	497	-559
C(13)	528	1243	607	322	188	113
C(14)	707	2673	724	723	617	-313
C(15)	244	2157	680	456	-230	-494
C(16)	1329	1122	744	1411	-356	263
C(17)	341	2307	808	-506	-684	338
C(18)	915	2044	787	46	-63	303
C(19)	406	2424	858	-977	-249	92
C(20)	667	2121	588	114	-358	63
C(21)	1129	2700	651	627	244	290
C(22)	491	1677	744	-1689	-65	165
C(23)	1654	1371	1033	74	1016	-88
C(24)	2465	2033	476	-185	-111	-1226
O(25)	336	2138	625	242	79	149
O(26)	298	1697	889	-370	-22	107
O(27)	398	2081	976	-407	3	120

TABLE IV.

Standard deviations of the final atomic co-ordinates (Å).

Atom	σ (x)	σ (y)	σ (z)
I	0.004	0.004	0.003
N(1)	0.042	0.032	0.034
C(2)	0.045	0.048	0.040
C(3)	0.057	0.053	0.053
N(4)	0.046	0.037	0.037
C(5)	0.061	0.054	0.052
C(6)	0.045	0.040	0.041
C(7)	0.058	0.052	0.044
C(8)	0.058	0.040	0.043
C(9)	0.053	0.037	0.045
C(10)	0.049	0.040	0.037
C(11)	0.055	0.050	0.047
C(12)	0.061	0.045	0.045
C(13)	0.053	0.038	0.043
C(14)	0.056	0.053	0.048
C(15)	0.049	0.047	0.048
C(16)	0.060	0.045	0.046
C(17)	0.069	0.048	0.056
C(18)	0.057	0.048	0.048
C(19)	0.055	0.054	0.050
C(20)	0.053	0.051	0.043
C(21)	0.058	0.049	0.051
C(22)	0.054	0.044	0.042
C(23)	0.069	0.048	0.056
C(24)	0.070	0.051	0.043
O(25)	0.032	0.032	0.030
O(26)	0.033	0.031	0.034
O(27)	0.035	0.033	0.036

TABLE V. Measured and calculated values of the structure factors.

h	k	l	$\lvert F_o \rvert$	$\lvert F_c \rvert$	α
0	0	2	130	164	0
		4	18	1	0
		6	70	78	180
		8	29	46	180
		10	12	18	180
		12	67	54	0
		14	74	68	0
		16	37	35	0
		18	< 8	0	180
		20	24	21	180
		22	9	9	180
0	1	1	46	34	270
		2	29	21	90
		3	31	34	90
		4	58	67	270
		5	80	91	270
		6	16	20	270
		7	106	142	270
		8	28	30	90
		9	92	101	270
		10	31	38	90
		11	26	17	90
		12	8	7	90
		13	61	53	90
		14	< 9	2	90
		15	28	24	90
		16	20	16	270
		17	9	3	90
		18	15	13	270
		19	25	13	270
		20	12	7	270
		21	15	12	270
0	2	0	343	325	180
		1	75	72	0
		2	32	18	0
		3	129	130	0
		4	101	91	0
		5	88	94	0
		6	110	119	0
		7	20	15	180
		8	50	68	0
		9	42	46	180
		10	28	29	0
		11	55	56	180
		12	23	19	180
		13	17	16	180
		14	31	29	180
		15	15	11	0
		16	29	28	180
		17	15	15	0
		18	14	7	0
		19	13	11	0
		20	22	16	0
0	3	1	84	80	270
		2	23	20	90
		3	52	51	270
		4	55	56	90
		5	20	11	90
		6	43	46	90
		7	43	45	90
		8	48	51	270
		9	26	33	90
		10	54	58	270
		11	29	29	270
		12	45	50	270
		13	52	50	270
		14	< 9	2	270
		15	18	19	270
		16	23	18	90
		17	< 8	4	270
		18	18	15	90
		19	< 7	2	90
0	4	0	115	117	0
		1	52	46	180
		2	42	35	180
		3	178	177	180
		4	12	3	180
		5	166	151	180
		6	25	17	180
		7	< 7	4	0
		8	< 7	9	180
		9	52	55	0
		10	< 8	8	180
		11	37	49	0
		12	< 9	9	0
		13	< 9	14	0
		14	13	11	0
		15	15	13	180
		16	< 9	2	0
		17	34	29	180
		18	< 7	0	360
		19	16	14	180
0	5	1	26	17	270
		2	48	39	270
		3	24	22	90
		4	93	91	270
		5	23	18	270
		6	36	38	270
		7	11	12	270
		8	33	33	90
		9	< 8	5	270
		10	49	54	90
		11	< 9	1	90
		12	31	36	90
		13	15	14	270
		14	< 9	0	90
		15	< 8	3	270
		16	29	21	270
		17	< 7	2	270
		18	16	16	270
0	6	0	38	38	0
		1	41	34	0
		2	52	49	0
		3	79	73	0
		4	16	14	180
		5	56	53	0
		6	34	36	180
		7	< 8	7	180
		8	24	20	180
		9	35	36	180
		10	< 9	0	0
		11	31	35	180
		12	< 9	4	0
		13	9	16	180
		14	12	12	0
		15	< 8	12	0
		16	< 7	10	0
		17	15	13	0
0	7	1	12	7	90
		2	22	17	90
		3	12	12	270
		4	53	55	90
		5	24	23	270
		6	15	14	90
		7	31	32	270
		8	24	29	270
		9	20	28	270
		10	22	26	270
		11	< 9	0	90
		12	17	20	270
		13	11	12	90
		14	< 7	0	270
		15	10	9	90
		16	14	13	90
0	8	0	76	74	180
		1	< 9	0	0
		2	45	51	180
		3	24	25	180
		4	19	17	0
		5	13	11	180
		6	20	24	0
		7	< 9	0	180
		8	19	25	0
		9	12	15	0
		10	< 8	8	0
		11	< 8	8	0
		12	13	12	180
		13	< 7	6	0
		14	20	17	180
0	9	1	29	32	270
		2	< 9	8	270
		3	< 9	1	270
		4	12	18	270
		5	< 8	10	90
		6	< 8	1	90
		7	21	29	90
		8	< 8	1	90
		9	11	16	90
		10	< 7	8	90
		11	< 6	4	270
		12	< 6	4	90
		13	15	16	270
0	10	0	19	[illegible]	0
		1	< 8	8	180
		2	13	19	0
		3	< 7	7	180
		4	< 7	14	180
		5	< 7	7	180
		6	18	17	180
		7	< 5	3	0
		8	14	18	180
0	11	1	13	18	90
1	0	[illegible]	[illegible]	[illegible]	[illegible]
1	1	0	23	18	90
1	1	1	56	48	119
		2	104	79	152
		3	73	80	259
		4	157	169	176
		5	92	100	310
		6	56	78	174
		7	43	53	11
		8	65	66	7
		9	36	41	43
		10	77	93	7
		11	23	23	112
		12	48	47	347
		13	14	19	139
		14	<10	9	286
		15	21	21	214
		16	38	36	179
		17	10	13	260
		18	20	24	181
		19	9	7	338
		20	< 8	7	176
		21	< 7	5	327
1	2	0	174	142	270
		1	64	66	357
		2	80	66	306
		3	224	180	260
		4	46	39	46
		5	83	85	263
		6	56	57	77
		7	14	19	212
		8	49	64	112
		9	52	52	88
		10	29	32	134
		11	37	39	86
		12	25	25	227
		13	12	17	67
		14	22	25	288
		15	<10	14	351
		16	<10	10	301
		17	29	28	279
		18	<10	7	357
		19	11	11	245
		20	< 8	9	73
		21	< 6	3	186
1	3	0	63	49	90
		1	221	170	338
		2	65	54	26
		3	51	41	45
		4	71	65	6
		5	51	39	143
		6	66	63	310
		7	61	66	191
		8	38	40	227
		9	27	35	205
		10	41	48	197
		11	15	17	339
		12	40	39	136
		13	56	56	350
		14	13	10	75
		15	30	33	6
		16	16	18	19
		17	<10	8	47
		18	< 9	8	340
		19	< 8	9	181
		20	< 7	6	329
		21	11	11	175
1	4	0	102	86	90
		1	75	62	169
		2	66	63	106
		3	79	67	40
		4	45	42	280
		5	15	11	30
		6	106	100	270
		7	18	12	330
		8	76	82	277
		9	26	23	312
		10	13	20	280
		11	10	17	304
		12	18	22	81
		13	10	8	265
		14	26	27	90
		15	<10	9	165
		16	14	18	88
		17	9	8	102
		18	9	5	225
		19	< 8	6	33
		20	12	11	266
1	5	0	58	50	270
		1	99	91	162
		2	45	41	314
		3	23	29	272
		4	26	22	251
		5	72	61	2
		6	20	21	98
		7	64	66	352
		8	21	19	64
		9	38	45	354
		10	<10	10	124
		11	10	12	186
		12	20	25	240
		13	33	40	176
		14	<10	9	293
		15	22	29	189
		16	< 9	5	269
		17	< 9	3	162
		18	< 8	3	22
		19	10	9	10
1	6	0	113	108	270
		1	36	34	24
		2	51	49	282
		3	29	29	150
		4	13	17	161
		5	42	43	112
		6	45	42	86
		7	14	14	184
		8	37	43	90
		9	10	17	251
		10	10	14	55
		11	11	13	295
		12	17	25	282
		13	10	10	307
		14	25	25	267
		15	< 9	10	12
		16	< 9	9	253
1	7	0	19	11	90
		1	51	53	328
		2	32	31	180
		3	10	6	338
		4	39	39	182
		5	32	34	224
		6	18	15	227
		7	33	34	177
		8	17	17	302
		9	13	18	147
		10	18	25	344
		11	<10	11	80
		12	12	17	36
		13	12	17	4
		14	9	2	100
		15	11	12	352
		16	11	11	172
1	8	0	13	17	90
		1	22	23	247
		2	<10	13	109
		3	33	34	287
		4	17	22	342
		5	33	35	270
		6	18	18	274
		7	10	3	304
		8	16	19	257
		9	12	21	84
		10	<10	7	285
		11	16	22	103
		12	< 9	13	108
		13	8	8	109
1	9	0	<10	4	270
		1	13	14	186
		2	24	27	351
		3	<10	8	89
		4	27	27	349
		5	14	20	80
		6	<10	9	14
		7	< 9	3	47
		8	< 9	15	188
		9	< 9	4	309
		10	13	18	179
		11	11	8	281
		12	< 7	16	184
		13	< 7	7	196
1	10	0	< 9	3	90
		1	< 9	9	86
		2	< 9	4	181
		3	17	20	97
		4	11	13	209
		5	18	26	86
		6	< 8	3	302
		7	< 8	[illegible]	195
		8	< 7	6	301
		9	< 7	15	254
		10	11	5	285
1	11	[illegible]	[illegible]	[illegible]	[illegible]
2	0	[illegible]	[illegible]	[illegible]	[illegible]
2	1	0	272	237	180
		1	224	174	75
		2	76	64	195
		3	62	64	31
		4	82	82	302
		5	42	45	292
		6	66	77	341
		7	93	115	274
		8	38	41	342
		9	37	47	253
		10	24	22	46
		11	28	24	138
		12	22	22	177
		13	46	45	100
		14	39	43	173
		15	29	29	79
		16	13	12	214
		17	<11	11	77
		18	<10	7	274
		19	13	11	285
2	2	0	31	17	180
		1	146	115	303
		2	125	110	186
		3	95	86	342
		4	111	85	48
		5	47	35	6
		6	109	104	22
		7	21	27	81
		8	49	67	345
		9	48	57	141
		10	26	32	301
		11	35	38	209
		12	29	26	198
		13	35	38	240
		14	34	38	178
		15	16	16	307
		16	15	15	138
		17	15	16	342
		18	<10	11	71
		19	11	10	78
2	3	0	68	59	0
		1	85	77	248
		2	109	95	86
		3	103	96	178
		4	100	92	99
		5	61	51	175
		6	79	74	150
		7	53	57	80
		8	38	40	222
		9	43	51	32
		10	50	59	256
		11	25	28	4
		12	35	37	265
		13	29	29	303
		14	11	14	2
		15	11	7	216
		16	15	16	87
		17	15	16	197
		18	17	16	102
2	4	0	55	47	0
		1	53	39	141
		2	38	40	329
		3	85	81	179
		4	41	42	276
		5	50	46	195
		6	28	27	248
		7	< 9	9	273
		8	17	20	74
		9	51	53	347
		10	37	46	94
		11	29	35	16
		12	15	20	86
		13	15	22	22
		14	16	16	338
		15	<11	5	165
		16	10	12	269
		17	23	22	169
		18	< 9	10	274
2	5	0	12	10	180
		1	43	32	324
		2	79	75	286
		3	72	68	355
		4	92	80	258
		5	52	48	1
		6	29	30	246
		7	10	9	230
		8	12	17	134
		9	31	35	176
		10	39	48	92
		11	24	24	161
		12	11	22	98
		13	13	17	160
		14	<11	6	159
		15	<10	9	325
		16	16	18	290
		17	< 9	14	15
		18	17	17	261
2	6	0	27	19	0
		1	38	38	21
		2	38	29	26
		3	56	52	6
		4	57	50	72
		5	37	41	1
		6	30	24	124
		7	10	7	274
		8	20	29	220
		9	33	36	189
		10	19	28	275
		11	21	32	181
		12	<11	16	324
		13	<11	16	152
		14	<10	7	3
		15	<10	10	37
2	7	0	47	41	180
		1	35	35	113
		2	47	46	131
		3	31	31	162
		4	35	37	61
		5	37	37	240
		6	13	18	53
		7	24	23	263
		8	16	20	318
		9	19	20	306
		10	17	21	280
		11	<11	12	18
		12	<10	13	228
		13	<10	10	40
		14	< 9	10	205
		15	10	17	104
2	8	0	17	12	180
		1	<11	8	254
		2	13	17	216
		3	13	14	187
		4	13	18	292
		5	16	23	147
		6	23	26	349
		7	15	22	101
		8	20	31	12
2	9	0	20	23	0
		1	27	32	264
		2	15	20	327
		3	<11	11	263
		4	13	16	181
		5	10	17	82
		6	14	13	179
2	10	0	9	14	0
		1	15	18	104
		2	< 9	14	8
		3	< 9	10	166
		4	< 9	1	63
		5	< 8	6	306
		6	13	18	195
3	0	1	75	109	90
		2	94	100	180
		3	71	86	90
		4	146	161	180
		5	32	36	90
		6	42	51	180
		7	49	40	270
		8	85	74	0
		9	24	22	270
		10	90	67	0
		11	31	33	270
		12	36	35	0
		13	38	34	270
		14	<11	7	0
		15	18	18	90
		16	40	45	180
		17	18	16	90
		18	24	27	180
		19	10	11	90
3	1	0	131	137	270
		1	35	51	106
		[illegible]	[illegible]	[illegible]	[illegible]
3	2	[illegible]	[illegible]	[illegible]	[illegible]
3	2	12	37	38	213
		13	41	41	29
		14	20	23	256
		15	22	22	327
		16	29	33	339
		17	23	20	269
		18	13	12	345
3	3	0	80	71	90
		1	103	75	10
		2	48	43	79
		3	86	79	66
		4	78	61	301
		5	75	62	109
		6	72	68	286
		7	77	74	180
		8	49	59	255
		9	43	51	225
		10	39	46	201
		11	21	22	279
		12	11	14	198
		13	20	23	0
		14	14	15	93
		15	12	10	342
		16	11	11	74
		17	13	18	90
3	4	0	64	55	90
		1	113	107	167
		2	42	39	102
		3	51	46	159
		4	45	37	199
		5	45	37	11
		6	53	47	262
		7	64	60	344
		8	31	35	281
		9	33	39	350
		10	11	16	325
		11	24	29	189
		12	16	17	78
		13	57	66	193
		14	17	20	73
		15	26	20	166
3	5	0	96	83	270
		1	52	48	195
		2	53	48	291
		3	29	25	142
		4	37	35	97
		5	34	33	31
		6	54	56	95
		7	54	54	1
		8	42	48	106
		9	31	36	2
		10	31	12	49
		11	<12	10	149
		12	14	15	206
		13	17	18	202
		14	21	22	269
		15	<11	11	274
3	6	0	54	50	270
		1	32	32	15
		2	42	42	217
		3	25	19	13
		4	15	11	175
		5	34	38	174
		6	31	29	106
		7	48	50	184
		8	18	20	69
		9	25	31	201
		10	17	21	2
		11	12	14	284
		12	14	19	315
		13	18	25	358
		14	19	19	254
		15	19	12	350
3	7	0	57	56	90
		1	26	21	332
		2	39	41	131
		3	33	31	277
		4	32	31	201
		5	23	22	238
		6	23	20	236
		7	25	22	193
		8	12	17	285
		9	<12	17	141
		10	<12	8	334
		11	<11	11	62
		12	15	21	50
		13	10	14	45
		14	17	17	85
3	8	0	<12	8	90
		1	19	22	218
		2	26	29	14
		3	22	22	267
		4	29	27	340
		5	17	17	308
		6	18	19	318
		7	11	15	354
		8	16	20	216
		9	<11	11	46
		10	18	22	185
3	9	0	<11	0	90
		1	11	12	125
		2	16	19	356
		3	26	28	91
		4	17	18	10
		5	17	18	86
		6	15	12	30
		7	<10	2	188
		8	<10	8	163
		9	13	16	276
3	10	0	12	2	270
		1	<10	7	91
		2	15	18	180
4	0	1	70	92	90
		2	9	9	0
		3	34	47	90
		4	12	9	180
		5	83	86	270
		6	73	67	180
		7	119	132	270
		8	< 9	16	180
		9	46	53	270
		10	12	3	180
		11	<11	5	90
		12	14	12	0
		13	54	51	90
		14	<12	4	0
		15	33	29	90
		16	18	19	0
		17	<12	8	90
		18	<11	5	180
		19	15	14	270
		20	< 9	10	180
4	1	0	268	235	180
		1	66	55	0
		2	106	97	205
		3	69	67	40
		4	25	21	283
		5	20	23	29
		6	73	83	356
		7	37	40	266
		8	99	91	353
		9	31	34	236
		10	16	19	21
		11	33	27	165
		12	56	50	178
		13	17	19	116
		14	33	35	181
		15	13	15	49
		16	15	18	205
		17	<12	3	9
		18	<11	3	208
		19	<10	7	15
		20	11	15	353
4	2	0	88	70	180
		1	84	75	267
		2	59	40	60
		3	27	21	28
		4	94	76	55
		5	89	86	55
		6	39	33	30
		7	73	85	97
		8	32	41	286
		9	34	41	106
		10	39	43	288
		11	18	17	177
		12	30	30	[illegible]
		13	45	47	260
		14	<12	8	296
		15	18	19	277
		16	25	24	138
		17	<12	7	311
		18	14	14	73
4	3	0	90	80	0
		1	[illegible]	[illegible]	195
		[illegible]	[illegible]	[illegible]	[illegible]
4	4	[illegible]	[illegible]	[illegible]	[illegible]
4	4	11	17	25	350
		12	36	43	82
		13	<13	14	107
		14	<13	4	123
		15	<12	9	146
		16	23	24	289
		17	<11	6	164
		18	15	14	266
4		0	<10	4	180
		1	48	44	338
		2	37	39	312
		3	95	89	357
		4	31	27	289
		5	60	69	3
		6	19	20	216
		7	<11	9	235
		8	<12	3	347
		9	29	38	188
		10	<12	9	33
		11	25	36	177
		12	<13	16	89
		13	12	14	198
		14	12	7	43
		15	<12	10	358
		16	<11	11	306
		17	20	21	346
4	6	0	11	11	0
		1	<11	1	204
		2	41	39	89
		3	21	16	323
		4	56	62	87
		5	23	24	306
		6	19	21	118
		7	23	23	246
		8	28	30	244
		9	22	28	246
		10	22	32	275
		11	13	13	150
		12	15	23	267
		13	<12	8	117
		14	<11	7	314
		15	<11	6	81
		16	15	17	104
4	7	0	48	47	180
		1	19	17	148
		2	32	36	155
		3	35	36	176
		4	<12	12	86
		5	18	23	195
		6	22	28	12
		7	13	4	30
		8	13	21	359
		9	15	24	332
		10	<12	5	300
		11	15	22	0
		12	<11	17	231
		13	11	6	41
4	8	0	<13	10	180
		1	22	29	275
		2	15	17	257
		3	18	18	226
		4	15	23	272
		5	15	17	95
		6	12	15	331
		7	24	29	91
		8	12	17	45
		9	12	21	80
		10	<11	11	120
		11	<11	8	285
		12	<10	9	96
		13	13	12	270
4	9	0	25	28	0
		1	12	14	245
		2	12	21	2
		3	<12	3	302
		4	<12	6	205
		5	<11	6	27
		6	16	24	182
		7	11	8	90
		8	15	21	178
4	10	0	<10	7	0
		1	19	21	94
5	0	1	11	19	90
		2	34	57	180
		3	5	4	90
		4	152	178	180
		5	20	16	270
		6	47	50	180
		7	< 9	1	90
		8	27	30	0
		9	24	20	270
		10	75	74	0
		11	<11	6	270
		12	39	40	0
		13	<13	7	270
		14	<13	1	0
		15	<13	1	90
		16	20	20	180
		17	<12	2	270
		18	18	25	180
5	1	0	49	57	270
		1	79	72	254
		2	31	32	343
		3	143	137	269
		4	19	8	65
		5	48	64	269
		6	20	24	118
		7	28	26	146
		8	20	24	105
		9	71	65	85
		10	11	12	86
		11	50	51	92
		12	12	12	274
		13	28	38	91
		14	16	13	264
		15	23	23	259
		16	<13	6	339
		17	25	28	267
5	2	0	< 6	8	90
		1	120	98	341
		2	95	73	356
		3	42	35	322
		4	158	183	359
		5	56	44	139
		6	32	38	19
		7	65	77	202
		8	28	28	156
		9	30	34	188
		10	53	60	180
		11	<12	12	18
		12	33	37	165
		13	20	23	356
		14	<13	3	9
		15	21	21	355
		16	18	17	1
		17	<12	7	19
5	3	0	117	91	90
		1	14	8	144
		2	65	57	119
		3	76	71	83
		4	30	26	310
		5	39	40	95
		6	78	82	205
		7	10	7	359
		8	53	58	264
		9	32	34	287
		10	<12	15	289
		11	21	27	238
		12	34	34	91
		13	21	22	246
		14	26	29	87
		15	<13	11	88
		16	12	17	97
		17	18	14	79
5	4	0	18	12	90
		1	126	99	164
		2	25	13	130
		3	9	4	224
		4	39	38	198
		5	48	43	333
		6	13	14	81
		7	70	76	359
		8	<11	3	302
		9	48	46	359
		10	18	14	80
		11	<13	9	141
		12	<13	7	84
		13	23	29	189
		14	<13	10	81
		15	30	22	185
5	5	0	87	61	270
		1	29	21	41
		2	48	40	270
		[illegible]	[illegible]	[illegible]	[illegible]
5	6	[illegible]	[illegible]	[illegible]	[illegible]
5	7	[illegible]	[illegible]	[illegible]	[illegible]
5	7	3	33	33	299
		4	13	11	300
		5	16	24	286
		6	23	28	269
		7	13	14	51
		8	26	33	252
		9	13	13	69
		10	<13	10	260
		11	12	21	94
5	8	0	<13	8	270
		1	21	25	147
		2	21	21	350
		3	<13	2	169
		4	32	34	357
		5	<13	9	328
		6	13	18	351
		7	<12	21	13
		8	<12	15	193
		9	12	8	32
5	9	0	<12	13	270
		1	12	20	69
		2	<12	4	3
		3	24	26	95
		4	<12	7	196
		5	12	21	76
5	10	0	<10	2	270
		1	<10	5	221
		2	<10	17	182
		3	<10	4	170
		4	12	23	194
6	0	1	85	7	90
		2	6	1	0
		3	18	20	90
		4	24	26	0
		5	20	25	270
		6	57	50	0
		7	74	81	270
		8	41	41	0
		9	49	54	270
		10	<11	5	0
		11	12	5	90
		12	32	32	180
		13	33	36	90
		14	<13	10	180
		15	30	31	90
		16	13	7	180
		17	<12	9	90
		18	<11	2	0
		19	<10	9	270
		20	< 8	5	0
6	1	0	77	66	180
		1	21	19	343
		2	67	70	189
		3	30	34	6
		4	57	53	15
		5	24	21	0
		6	112	117	3
		7	19	17	108
		8	60	64	339
		9	31	33	152
		10	14	15	351
		11	17	19	201
		12	37	36	191
		13	16	20	238
		14	33	38	185
		15	13	7	331
		16	12	18	169
		17	<12	4	21
		18	<11	6	33
		19	<10	5	29
		20	10	12	348
6	2	0	80	70	0
		1	142	116	260
		2	61	52	81
		3	70	51	194
		4	97	80	69
		5	23	23	164
		6	59	56	135
		7	59	65	87
		8	22	19	176
		9	27	35	85
		10	29	32	274
		11	15	15	349
		12	23	25	299
		13	30	32	271
		14	<13	3	283
		15	20	24	259
		16	<12	12	69
		17	<12	7	227
6	3	0	44	38	0
		1	66	50	123
		2	46	38	348
		3	107	93	192
		4	21	14	181
		5	55	51	181
		6	65	58	182
		7	13	8	355
		8	24	23	182
		9	46	59	345
		10	12	14	169
		11	35	40	6
		12	20	17	23
		13	16	17	50
		14	16	14	5
		15	13	13	163
		16	<12	15	310
		17	13	19	187
6	4	0	11	8	0
		1	30	23	84
		2	72	60	286
		3	55	51	347
		4	80	70	266
		5	42	40	351
		6	43	41	288
		7	32	37	283
		8	17	15	46
		9	19	25	205
		10	34	44	86
		11	13	14	161
		12	24	34	106
		13	<13	12	116
		14	<13	4	72
		15	<12	5	35
		16	18	14	273
6	5	0	<11	0	180
		1	43	32	329
		2	13	11	101
		3	74	70	6
		4	21	21	154
		5	44	42	1
		6	<12	4	148
		7	<12	9	176
		8	<12	22	214
		9	36	51	192
		10	<13	8	290
		11	24	35	171
		12	<13	14	264
		13	<12	16	163
		14	<12	1	300
		15	11	11	347
6	6	0	25	21	180
		1	34	29	92
		2	48	44	108
		3	49	39	139
		4	54	56	74
		5	12	12	219
		6	30	30	63
		7	<13	6	322
		8	13	12	321
		9	<13	12	296
		10	22	33	265
		11	<13	7	359
		12	15	20	284
6	7	0	31	27	180
		1	13	14	140
		2	16	15	198
		3	34	38	205
		4	29	30	314
		5	20	23	107
		6	24	26	339
		7	<13	6	82
		8	18	29	12
6	8	0	27	28	0
		1	26	28	257
		2	16	20	296
		3	16	15	291
		4	18	19	224
		5	15	17	89
		6	18	10	235
		7	15	21	108
6	9	0	22	25	0
		1	<12	1	232
		2	10	17	7
6	10	0	< 9	6	180
		1	11	20	85
7	0	1	16	24	270
		2	67	94	180
		3	73	86	270
		4	78	87	180
		5	80	85	270
		6	43	51	180
		7	25	24	270
		[illegible]	[illegible]	[illegible]	[illegible]
7	1	[illegible]	[illegible]	[illegible]	[illegible]
7	1	10	32	34	185
		11	39	36	73
		12	20	17	182
		13	17	18	43
		14	<17	14	251
		15	<17	11	321
		16	16	20	343
		17	15	14	288
7	2	0	56	55	90
		1	45	33	4
		2	69	48	13
		3	54	45	71
		4	69	63	324
		5	50	43	134
		6	34	39	327
		7	38	43	177
		8	30	34	237
		9	42	53	232
		10	45	48	193
		11	16	18	278
		12	21	22	171
		13	24	25	339
		14	<17	11	130
		15	<17	12	19
		16	16	14	0
7	3	0	107	81	90
		1	48	36	132
		2	78	58	125
		3	45	38	93
		4	60	51	207
		5	49	42	35
		6	27	28	279
		7	34	37	354
		8	18	18	268
		9	33	37	321
		10	<16	14	351
		11	17	26	245
		12	<17	11	49
		13	21	23	193
		14	21	24	85
		15	16	13	155
		16	22	21	122
7	4	0	89	69	270
		1	56	46	177
		2	48	38	252
		3	23	25	197
		4	20	18	159
		5	55	47	350
		6	37	29	101
		7	69	71	348
		8	20	22	102
		9	35	44	22
		10	17	17	342
		11	<17	5	62
		12	<17	12	275
		13	21	25	183
		14	<16	18	276
7	5	0	81	74	270
		1	39	37	349
		2	50	43	261
		3	24	16	23
		4	19	22	63
		5	19	23	187
		6	34	38	118
		7	31	31	173
		8	17	20	102
		9	17	20	186
		10	<17	10	10
		11	<17	10	382
		12	<17	8	295
		13	16	20	8
		14	19	24	252
7	6	0	43	37	90
		1	43	32	350
		2	<16	14	175
		3	29	29	311
		4	24	27	230
		5	17	19	206
		6	24	23	233
		7	27	31	163
		8	17	25	295
		9	21	22	187
7	7	0	17	19	90
		1	24	20	188
		2	<17	18	65
		3	24	24	235
		4	24	20	295
		5	<17	18	317
		6	27	34	304
		7	<17	16	354
		8	17	19	230
7	8	0	17	19	270
		1	17	15	135
		2	20	21	2
		3	17	23	104
		4	20	21	354
7	9	0	<15	3	270
		1	<15	8	66
		2	<15	14	217
		3	15	23	95
8	0	1	39	68	90
		2	34	43	180
		3	26	29	90
		4	23	25	0
		5	44	45	270
		6	51	53	0
		7	23	33	270
		8	64	63	0
		9	26	20	270
		10	<12	13	0
		11	<13	11	90
		12	35	38	180
		13	33	32	90
		14	23	24	180
		15	18	21	90
8	1	0	54	60	180
		1	103	98	272
		2	11	15	195
		3	10	12	36
		4	23	24	85
		5	48	52	63
		6	30	35	11
		7	54	54	93
		8	43	43	339
		9	17	15	120
		10	12	21	315
		11	18	17	110
		12	<13	12	252
		13	23	30	258
		14	<13	12	197
		15	23	21	272
8	2	0	58	47	0
		1	55	38	220
		2	73	66	32
		3	61	50	210
		4	38	27	70
		5	56	43	123
		6	41	39	167
		7	40	41	86
		8	33	40	196
		9	27	38	17
		10	32	24	278
		11	23	19	5
		12	38	38	338
		13	<13	14	282
		14	19	20	1
8	3	0	63	55	0
		1	63	43	119
		2	64	43	294
		3	39	41	227
		4	74	68	267
		5	43	44	228
		6	22	28	260
		7	23	26	252
		8	17	19	145
		9	<13	7	304
		10	29	37	96
		11	23	26	330
		12	27	25	59
8	4	0	<11	5	0
		1	36	24	0
		2	31	29	348
		3	54	49	11
		4	46	44	272
		5	47	44	339
		6	17	24	190
		7	<12	9	249
		8	29	32	49
		9	26	36	189
		10	<13	26	82
		11	<13	19	105
		12	13	19	118
8	5	0	<12	8	0
		1	30	26	335
		2	42	38	79
		3	30	25	353
		4	50	40	66
		5	18	23	356
		6	23	28	88
		7	<13	2	35
		8	<13	17	287
		9	<13	19	237
		10	23	38	288
8	6	0	18	18	180
		1	23	20	180
		2	23	28	111
		3	33	35	188
		4	27	37	68
		5	23	25	207
		6	19	28	38
8	7	0	<13	13	180
		1	27	27	244
		2	13	18	248
		3	13	19	218
		4	10	25	109
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

TABLE VI.

Intramolecular bonded distances (Å).

N(1) - C(2)	1.32	C(10) - C(11)	1.50
N(1) - C(13)	1.35	C(11) - C(12)	1.38
C(2) - C(3)	1.50	C(12) - C(13)	1.39
C(2) - C(7)	1.42	C(14) - C(15)	1.59
C(3) - N(4)	1.46	C(15) - C(16)	1.66
C(3) - C(14)	1.64	C(15) - C(20)	1.50
N(4) - C(5)	1.66	C(16) - C(17)	1.49
N(4) - C(21)	1.36	C(16) - C(22)	1.42
N(4) - C(23)	1.50	C(17) - O(27)	1.40
C(5) - C(6)	1.46	C(18) - C(19)	1.55
C(5) - C(16)	1.61	C(19) - C(20)	1.31
C(6) - C(7)	1.44	C(20) - C(21)	1.55
C(7) - C(8)	1.44	C(22) - O(25)	1.33
C(8) - C(9)	1.41	C(22) - O(26)	1.16
C(8) - C(13)	1.50	C(24) - O(25)	1.43
C(9) - C(10)	1.28		

TABLE VII.

Interbond angles (°)

C(13) - N(1) - C(2)	113	C(10) - C(11) - C(12)	120
N(1) - C(2) - C(3)	126	C(11) - C(12) - C(13)	119
N(1) - C(2) - C(7)	111	N(1) - C(13) - C(8)	105
C(3) - C(2) - C(7)	123	N(1) - C(13) - C(12)	137
C(2) - C(3) - N(4)	112	C(8) - C(13) - C(12)	118
C(2) - C(3) - C(14)	112	C(3) - C(14) - C(15)	104
N(4) - C(3) - C(14)	113	C(14) - C(15) - C(16)	112
C(3) - N(4) - C(5)	103	C(14) - C(15) - C(20)	108
C(3) - N(4) - C(21)	113	C(16) - C(15) - C(20)	107
C(3) - N(4) - C(23)	115	C(5) - C(16) - C(15)	107
C(5) - N(4) - C(21)	112	C(5) - C(16) - C(17)	115
C(5) - N(4) - C(23)	102	C(5) - C(16) - C(22)	115
C(21) - N(4) - C(23)	111	C(15) - C(16) - C(17)	104
N(4) - C(5) - C(6)	114	C(15) - C(16) - C(22)	104
N(4) - C(5) - C(16)	108	C(17) - C(16) - C(22)	110
C(6) - C(5) - C(16)	117	C(16) - C(17) - O(27)	109
C(5) - C(6) - C(7)	113	C(18) - C(19) - C(20)	127
C(2) - C(7) - C(6)	122	C(15) - C(20) - C(19)	127
C(2) - C(7) - C(8)	104	C(15) - C(20) - C(21)	110
C(6) - C(7) - C(8)	134	C(19) - C(20) - C(21)	123
C(7) - C(8) - C(9)	133	N(4) - C(21) - C(20)	114
C(7) - C(8) - C(13)	107	C(16) - C(22) - O(25)	114
C(9) - C(8) - C(13)	120	C(16) - C(22) - O(26)	125
C(8) - C(9) - C(10)	120	O(25) - C(22) - O(26)	120
C(9) - C(10) - C(11)	122	C(22) - O(25) - C(24)	120

TABLE VIII.

Some intramolecular non-bonded distances (Å).

N(1)	...	N(4)	3.67
N(1)	...	C(6)	3.61
N(1)	...	C(9)	3.59
N(1)	...	C(11)	3.71
N(1)	...	C(14)	3.33
N(1)	...	C(23)	4.00
C(2)	...	C(9)	3.65
C(2)	...	C(12)	3.60
C(2)	...	C(15)	3.57
C(2)	...	C(16)	3.45
C(2)	...	C(17)	3.54
C(2)	...	C(21)	3.67
C(2)	...	C(23)	2.93
C(3)	...	C(8)	3.70
C(3)	...	C(13)	3.66
C(3)	...	C(17)	3.53
N(4)	...	C(17)	3.71
N(4)	...	C(19)	3.66
N(4)	...	C(22)	3.62
N(4)	...	O(26)	3.98
C(5)	...	C(8)	3.82
C(5)	...	O(25)	3.75
C(5)	...	O(26)	2.82
C(5)	...	O(27)	3.15
C(6)	...	C(9)	3.40
C(6)	...	C(13)	3.79
C(6)	...	C(14)	3.87
C(6)	...	C(15)	3.79
C(6)	...	C(17)	2.91
C(6)	...	C(21)	3.79
C(6)	...	C(22)	3.60
C(6)	...	C(23)	2.85
C(6)	...	O(26)	3.80
C(6)	...	O(27)	3.06
C(7)	...	C(10)	3.72
C(7)	...	C(12)	3.66
C(7)	...	C(14)	3.59
C(7)	...	C(16)	3.35
C(7)	...	C(17)	3.31
C(7)	...	C(23)	3.06
C(7)	...	O(27)	3.73
C(14)	...	C(17)	3.01
C(14)	...	C(19)	3.61
C(14)	...	C(22)	3.85
C(14)	...	C(23)	3.96
C(15)	...	C(18)	3.15
C(15)	...	O(25)	2.73
C(15)	...	O(26)	3.41
C(15)	...	O(27)	3.74
C(16)	...	C(19)	3.55
C(16)	...	C(23)	3.87
C(16)	...	C(24)	3.64
C(17)	...	C(20)	3.78
C(17)	...	O(25)	2.76
C(17)	...	O(26)	3.30
C(18)	...	C(21)	3.99
C(18)	...	C(22)	3.85
C(18)	...	C(24)	3.83
C(18)	...	O(25)	3.38
C(19)	...	C(22)	3.40
C(19)	...	O(25)	3.51
C(19)	...	O(26)	3.88
C(20)	...	C(22)	2.86
C(20)	...	C(23)	3.78
C(20)	...	O(25)	3.30
C(20)	...	O(26)	3.48
C(21)	...	C(22)	3.57
C(21)	...	O(26)	3.88
C(22)	...	O(27)	2.72
C(24)	...	O(26)	2.63
O(25)	...	O(27)	3.16
O(26)	...	O(27)	3.28
I	...	C(23)	3.95

TABLE IX.

Intermolecular distances (⩽ 4 Å).

$N(1)$	$O(26)_{I}$	2.98
$O(25)$	$C(12)_{II}$	3.34
I	$O(27)_{V}$	3.43
$C(3)$	$O(26)_{I}$	3.56
$O(26)$	$C(24)_{IV}$	3.57
$C(21)$	$C(12)_{III}$	3.57
$C(3)$	$O(27)_{I}$	3.57
$C(21)$	$C(11)_{III}$	3.59
$C(2)$	$O(26)_{I}$	3.63
$C(14)$	$O(26)_{I}$	3.64
$C(15)$	$C(11)_{II}$	3.66
$N(1)$	$C(24)_{I}$	3.76
$C(18)$	$C(12)_{II}$	3.77
$C(14)$	$C(6)_{I}$	3.79
$C(18)$	$C(13)_{II}$	3.81
$C(24)$	$C(12)_{II}$	3.82
$C(14)$	$O(27)_{I}$	3.85
$C(21)$	$O(27)_{I}$	3.88
$N(1)$	$C(22)_{I}$	3.92
I	$C(24)_{IV}$	3.93
$C(15)$	$C(12)_{II}$	3.95
$C(18)$	$C(11)_{II}$	3.99
$C(18)$	$C(9)_{I}$	3.99
$C(14)$	$C(11)_{II}$	4.00
I	$C(11)_{VI}$	4.00

The subscripts refer to the following equivalent positions:

I	$\frac{1}{2} + x,$	$\frac{1}{2} - y,$	$1 - z$
II	$1\frac{1}{2} - x,$	$\bar{y},$	$\frac{1}{2} + z$
III	$1\frac{1}{2} - x,$	$1 - y,$	$\frac{1}{2} + z$
IV	$1 - x,$	$\frac{1}{2} + y,$	$1\frac{1}{2} - z$
V	$x,$	$1 + y,$	z
VI	$1 - x,$	$\frac{1}{2} + y,$	$\frac{1}{2} - z$

TABLE X.

Deviations (Å) from the best plane through C(16),C(22),C(24),O(25), and O(26).

C(16)	−0.04	C(24)	−0.05	O(26)	0.00
C(22)	0.04	O(25)	0.05		

TABLE XI.

Deviations (Å) from the best planes through sets of atoms of the quinuclidine rings.

Atoms included		Atoms omitted	
C(5)	0.02	N(4)	0.75
C(16)	−0.01	C(15)	0.84
C(3)	−0.02		
C(14)	0.01		
C(3)	−0.06	N(4)	−0.76
C(14)	0.06	C(15)	−0.56
C(20)	−0.06		
C(21)	0.06		
C(5)	−0.02	N(4)	0.65
C(16)	0.02	C(15)	0.77
C(20)	−0.02		
C(21)	0.02		

TABLE XII.

Deviations (Å) from the best plane through C(15),C(18),C(19),C(20), and C(21).

C(15)	−0.01	C(19)	−0.03	C(21)	0.01
C(18)	0.02	C(20)	0.02		

PART IV

The Structure of Geigerin:

X-ray Analysis of Bromogeigerin Acetate.

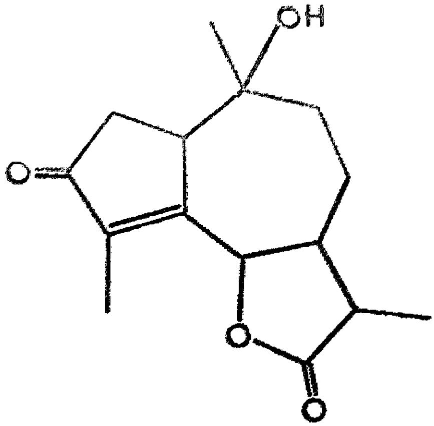
4.1 INTRODUCTION.

The bitter principle geigerin, a sesquiterpenoid lactone, occurs in the vomiting bush which is represented by various "Geigeria aspera" and which grows abundantly in South Africa. Rimington and Roets (1936), who first isolated geigerin, $C_{15}H_{20}O_4$, from "Geigeria aspera" Harv., showed that it was a ketonic lactone and made a preliminary study of its chemistry.

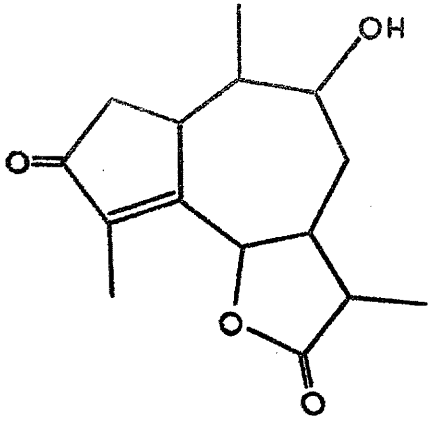
Perold (1955,1957) who made important contributions to the chemistry of geigerin, proved that it was a guanolide (Čekan, Herout and Šorm, 1954) and, on the basis of his researches, proposed structure (I). Having obtained evidence in contradiction of this constitution, viz. that geigerin contained a secondary, not tertiary, hydroxyl group, Barton and Levisalles proposed the alternative structure (II) (see Barton and De Mayo, 1957).

The investigations on the constitution were extended by Barton and Levisalles (1958) who firmly established that structure (III) was representative of geigerin. These workers also elucidated the structure of allogeigeric acid (IV) and, on the basis of the constitution of this acid and other facts, partly defined the stereochemistry of geigerin to be as in (V).

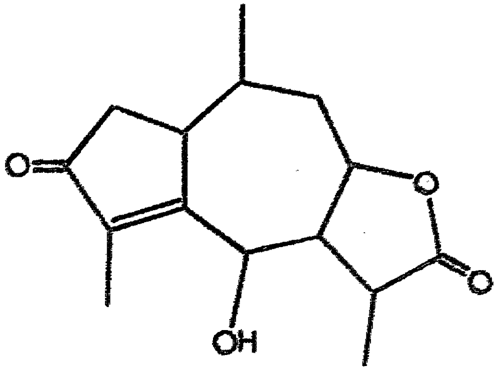
In order to confirm the constitution (III) and extend the stereochemistry (V), a crystal-structure analysis of a bromo-derivative of geigerin acetate was undertaken;


OH
O
O
O

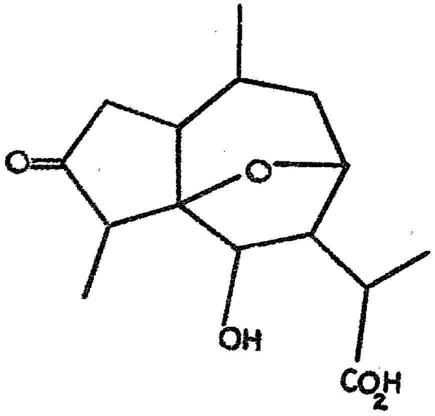
(I)


OH
O
O
O

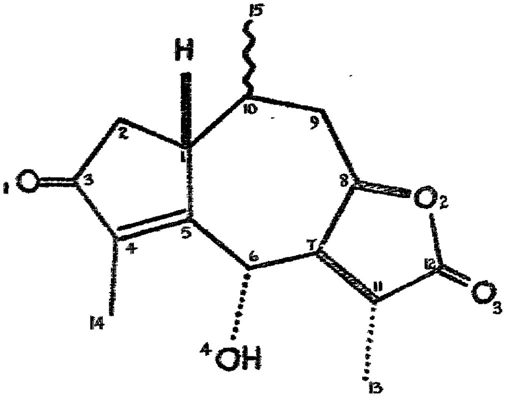
(II)


O
O
O
OH

(III)


O
O
OH
CO2H

(IV)


15
H
10
9
2
1
1O
3
8
O2
4
5
6
7
12
O3
11
14
4OH
13

(V)

Professor Barton and Dr. Pinhey had prepared this derivative by bromination of geigerin acetate with N-bromo-succinimide in carbon tetrachloride.

4.2 EXPERIMENTAL.

Crystal data

Bromogeigerin acetate, $C_{17}H_{21}BrO_5$. M = 385.3, m.p. 147-153°C(decomp). Orthorhombic; a = 8.11 ± 0.02, b = 13.77 ± 0.03, c = 15.24 ± 0.03 Å. U = 1702 $Å^3$. D_{obs} (flotation in $ZnCl_2$ solution) = 1.512 $g.cc.^{-1}$ Z = 4. D_c = 1.505 $g.cc.^{-1}$ Absent spectra: h00 when h = 2n+1, 0k0 when k = 2n+1, 00ℓ when ℓ = 2n+1. Space group $P2_12_12_1(D_2^4)$. Absorption coefficient for X-rays (λ = 1.542 Å), μ = 38.2 cm^{-1}. Total number of electrons per unit cell = F(ooo) = 792. Total number of independent observed structure amplitudes = 1625.

$\sum f^2$ "heavy" atoms= 1225. $\sum f^2$ "light" atoms = 953.

Rotation, oscillation, Weissenberg and precession photographs were taken with copper-K_α (λ = 1.542 Å) and molybdenum-K_α (λ = 0.7107 Å) radiation. From rotation and precession photographs the cell dimensions were obtained and, from the systematically absent reflections the space group was determined uniquely.

The intensity data were obtained from equatorial Weissenberg photographs taken from crystals rotated about the a-and c-crystal axes and from equi-inclination upper-layer Weissenberg photographs taken from a crystal rotated about the a-crystal axis; the multiple film technique with visual estimation was employed. Lorentz, polarisation and Tunell (1939) corrections were applied but no correction was made for absorption. The various layers were put on to the same relative scale by comparison of common reflections on different photographs, the absolute scaling being obtained at a later stage by correlation with the final calculated structure amplitudes, $|F_c|$.

4.3 STRUCTURE DETERMINATION AND REFINEMENT.

The Patterson projections along the a- and c-axes are shown in Figures 1 and 2, respectively. The peaks denoted A, B, C in Figure 1 and D, E, F in Figure 2 correspond to the bromine-bromine vectors. The co-ordinates of the bromine atom determined from these projections were $^{x}/a = 0.4638$, $^{y}/b = -0.0902$, $^{z}/c = 0.7930$, and these were confirmed by a study of the appropriate sections of the three-dimensional Patterson function. Structure factors calculated employing these co-ordinates and an isotropic temperature factor, $B = 3.0\ \mathring{A}^2$, led to an agreement index of 0.350.

The first three-dimensional Fourier synthesis was computed employing the observed structure amplitudes and the phase constants appropriate to the bromine atom alone. From the resulting electron-density distribution it was possible to assign approximate co-ordinates to C(1),C(2), C(3),C(4),C(5),C(6),C(7),C(8),C(9),C(10),C(16),O(1),O(2),O(4),O(5). These atoms were included (all as carbon atoms) in the second structure factor and phasing calculations for which an overall isotropic temperature factor, $B = 3.0\ \mathring{A}^2$, was employed; the resulting agreement index was 0.280.

Employment of the improved phase constants for the calculation of the second three-dimensional Fourier synthesis resulted in the unequivocal location of the remaining carbon and oxygen atoms, other than C(14). Ambiguity in the location of this carbon atom arose because

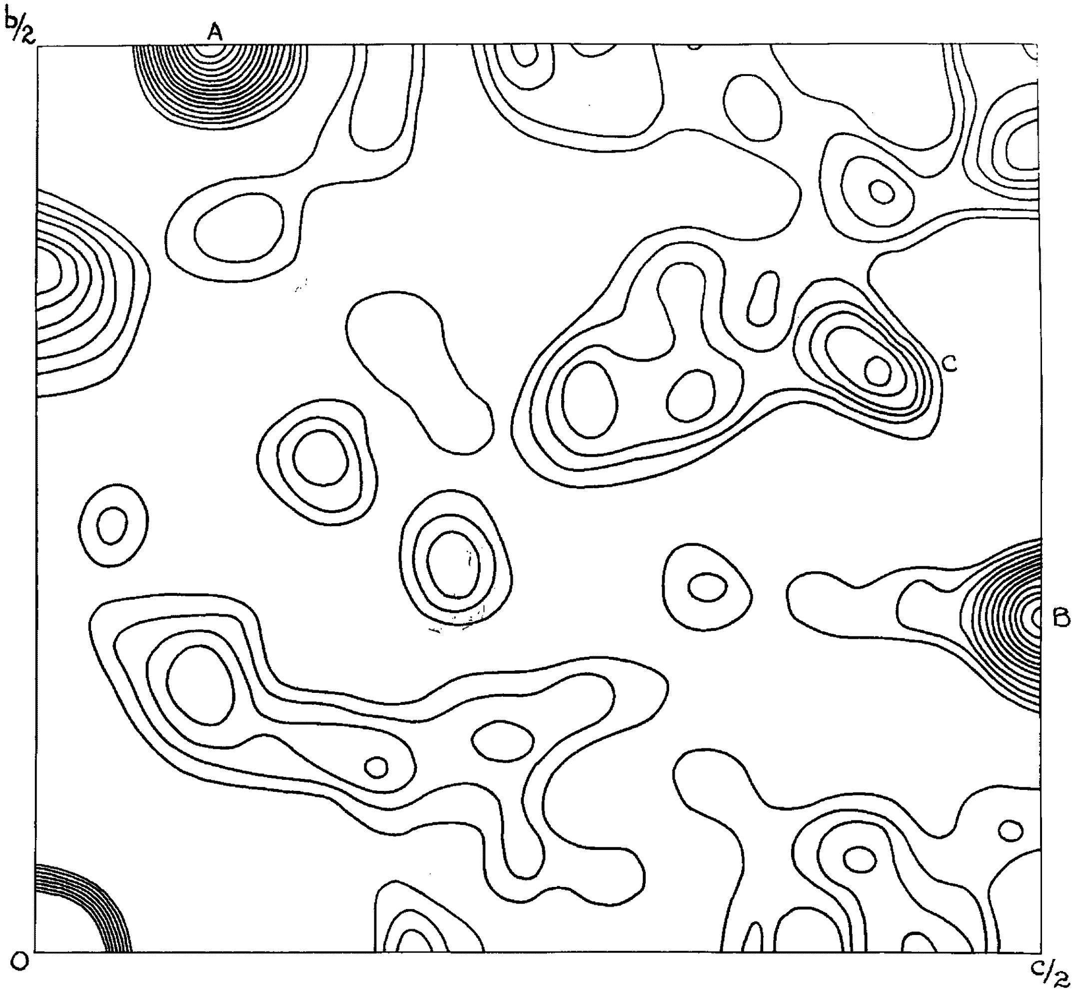


Fig. 1. Patterson projection along the a-axis. Contour scale arbitrary. The bromine-bromine vector peaks are marked A, B and C.

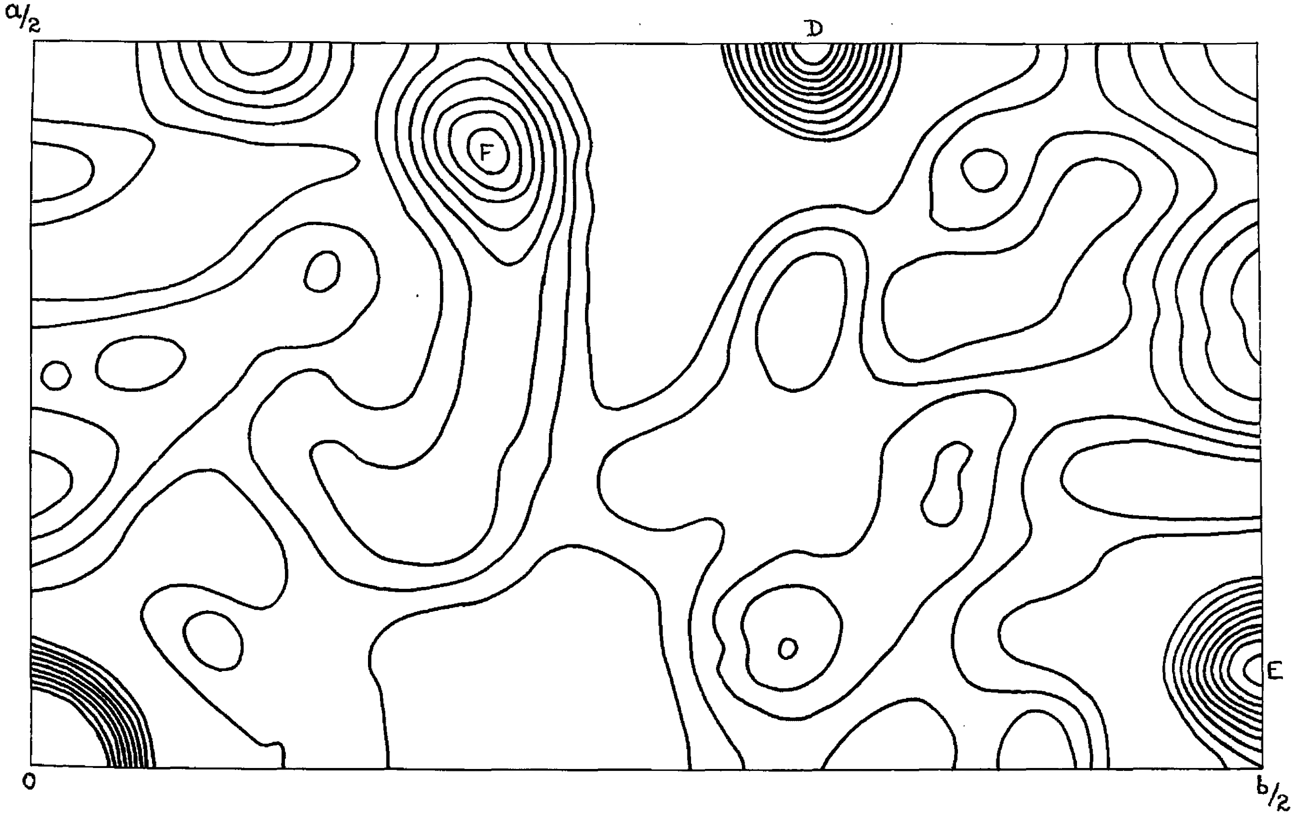


Fig. 2. Patterson projection along the c-axis. Contour scale arbitrary. D, E, and F denote the bromine-bromine vector peaks.

of the presence of two peaks in this electron-density distribution:

	x/a	y/b	z/c	$e/\mathring{A}^3$
peak G	0.450	-0.084	0.516	5.9
peak H	0.798	-0.024	0.529	2.0

Of these, the peak H, being in close proximity to the cyclopentenone ring at C(4), corresponded to the expected position of C(14) from the chemical evidence. Peak G, on the other hand, was situated directly in line with bromine atoms of adjacent unit cells in the direction of z and could have been spurious, nevertheless, an atom located at this site would have been in a reasonable position for attachment to the cycloheptane ring at C(6). Although this would have been contrary to the chemical evidence, this site could not be ignored at this stage in the analysis as a possible location of C(14).

For the third structure factor and phasing calculations the twenty-one light atoms whose approximate locations had been determined unambiguously were included as their appropriate chemical type, with the exception that O(5) which could not be differentiated from C(17) was still included as a carbon atom. The value of the agreement index was 0.230.

The third three-dimensional Fourier synthesis resolved the ambiguity regarding the location of C(14) and permitted, on the basis of peak heights and interatomic distances, differentiation between O(5) and C(17) of the acetate grouping. In this electron-density distribution the peak H had increased in density to 3 e/Å^3 while peak G had decreased to 1 e/Å^3; the former peak therefore corresponded, as expected from the chemical evidence, to the site of C(14) and co-ordinates were assigned accordingly.

All of the atoms, except hydrogens, were included in the fourth structure factor calculation as their appropriate chemical type and, in the subsequent electron-density distribution, calculated employing the observed structure amplitudes and the improved phase constants, all of these atoms were clearly resolved. Using the same phase constants a three-dimensional F_c Fourier synthesis was computed and, by applying "back-shift" corrections, the atomic co-ordinates were corrected for series-termination errors. Comparison of the electron-densities of these F_o and F_c Fourier syntheses confirmed the choice of hetero-atoms and enabled improved isotropic temperature factors to be assigned. The agreement index of the subsequent structure factor calculation was 0.191.

Refinement of the positional and thermal parameters was continued by the method of least-squares, three cycles of which were employed. A diagrammatic representation of the course of analysis is provided in Table I.

(Initial errors in the film-to-film scaling of the intensities corresponding to some of the larger observed structure amplitudes were not discovered until a late stage in the refinement process and were corrected immediately preceding the penultimate refinement cycle. A consequence of this was that, compared with the previous cycle, the final refinement cycle led to a greater reduction in the agreement index.)

The weighting system used in the least-squares refinement was

$$\sqrt{w}(hk\ell) = \frac{|F_o(hk\ell)|}{16.00} \quad \text{if} \quad |F_o(hk\ell)| \leqslant 16.00$$

$$\sqrt{w}(hk\ell) = \frac{16.00}{|F_o(hk\ell)|} \quad \text{if} \quad |F_o(hk\ell)| > 16.00.$$

Theoretical atomic scattering factors were employed for the structure factor calculations; those of Berghuis et al. (1955) for carbon and oxygen and the Thomas-Fermi (1935) values for bromine were chosen.

TABLE I.

Course of Analysis.

2-D and 3-D Patterson syntheses

↓

Bromine atom $(B = 3.0\,\mathring{A}^2)$

↓

1st Structure factor calculation $R = 0.351$

↓

1st 3-D Fourier synthesis (1576 observed structure amplitudes)

↓

2nd Structure factor calculation Bromine + 16 "light" atoms as carbon atoms $(B = 3.0\,\mathring{A}^2)$ $R = 0.280$

↓

2nd 3-D Fourier synthesis (1587 observed structure amplitudes)

↓

3rd Structure factor calculation Bromine + 17 carbon + 4 oxygen atoms $(B = 3.0\,\mathring{A}^2)$ $R = 0.230$

↓

3rd 3-D Fourier synthesis (1597 observed structure amplitudes)

↓

4th Structure factor calculation Bromine + 17 carbon + 5 oxygen atoms $(B = 3.0\,\mathring{A}^2)$ $R = 0.206$

↓

4th 3-D Fourier syntheses (F_o and F_c) (1625 observed structure amplitudes)

↓

5th Structure factor calculation All atoms, individual isotropic thermal parameters $R = 0.191$

↓ Anisotropic least-squares

6th Structure factor calculation $R = 0.168$

↓ Anisotropic least-squares

7th Structure factor calculation $R = 0.155$

↓ Anisotropic least-squares

8th Structure factor calculation $R = 0.135$

4.4 RESULTS OF ANALYSIS.

The final atomic co-ordinates and anisotropic thermal parameters provided by the least-squares refinement are listed in Tables II and III, respectively. The standard deviations of the co-ordinates, Table IV, were derived from the least-squares residuals.

The observed and calculated structure factors , both rounded off as integers, and the values of the phase constants, α, are listed in Table V. The final agreement index over 1625 independent observed structure amplitudes is 0.135. Of 122 unobserved structure amplitudes also listed in Table V there are 105 for which $|F_c(hk\ell)|$ is less than $1\frac{1}{2}$ $|F_o(hk\ell)|$, $|F_o(hk\ell)|$ being the minimum observable value of the structure amplitude in question.

The final three-dimensional electron-density distribution over one molecule, calculated employing the observed structure amplitudes and phase constants of Table IV, is shown in Figure 3 by means of superimposed contour sections drawn parallel to (001). In the final three-dimensional Fourier synthesis, along the line in the direction of x joining bromine atoms of adjacent unit cells, there were several elongated peaks which have been omitted from Figure 3 since they were undoubtedly due, as in the case of macusine-A iodide (section 3.4), to termination-of-series effects. Figure 4 shows the atomic arrangement corresponding to Figure 3.

The intramolecular bonded distances are listed in Table VI; the average estimated standard deviation of a carbon-carbon and of a carbon-oxygen bond is 0.03 Å and of the carbon-bromine bond is 0.02 Å. Table VII lists the interbond angles; the average estimated standard deviation of a valency angle is about 2°.

Some of the more important intramolecular non-bonded distances are listed in Table VIII.

The arrangement of the molecules in the crystal as viewed along the a-axis is shown in Figure 5 while Table IX lists the shorter intermolecular contacts.

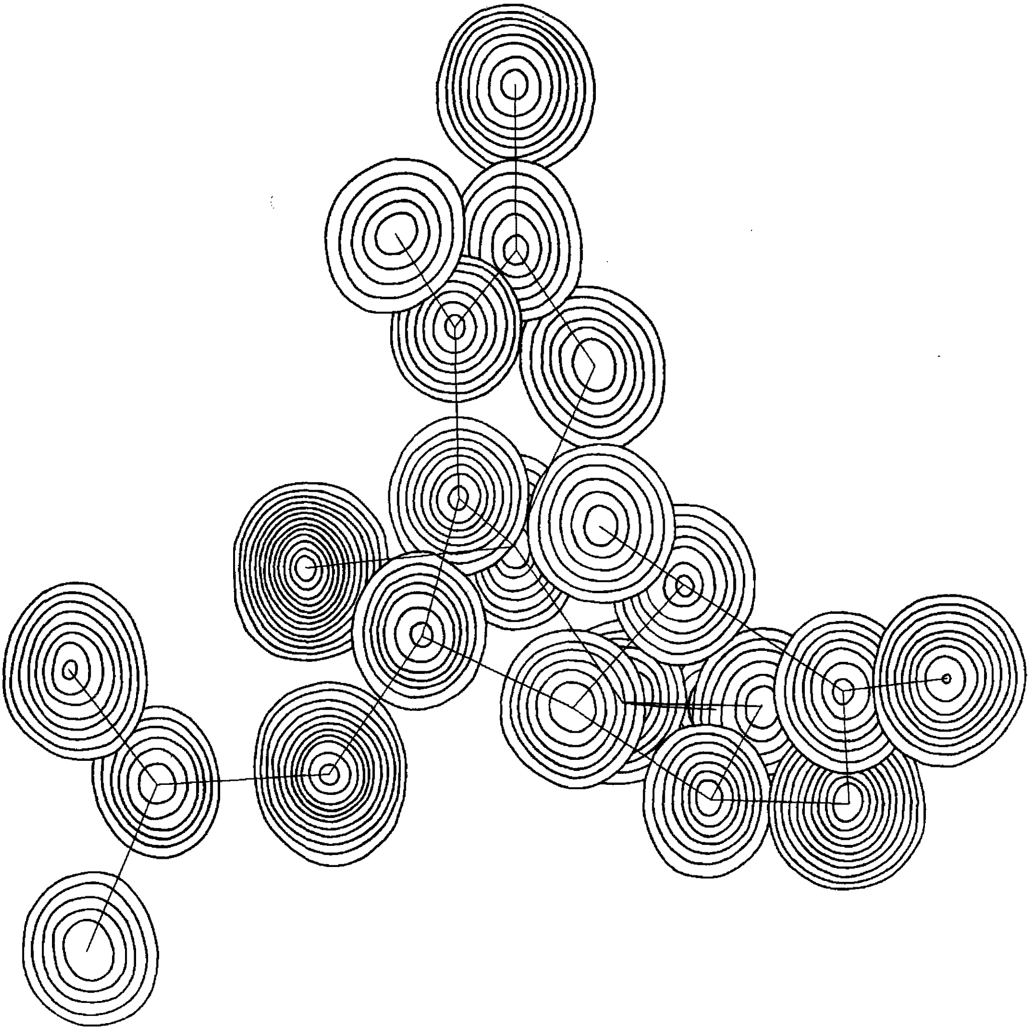


Fig. 3. Final three-dimensional electron-density distribution for bromogeigerin acetate shown by means of superimposed contour sections drawn parallel to (001). The contour interval is 1e/Å^3 except around the bromine atom where it is 5e/Å^3.

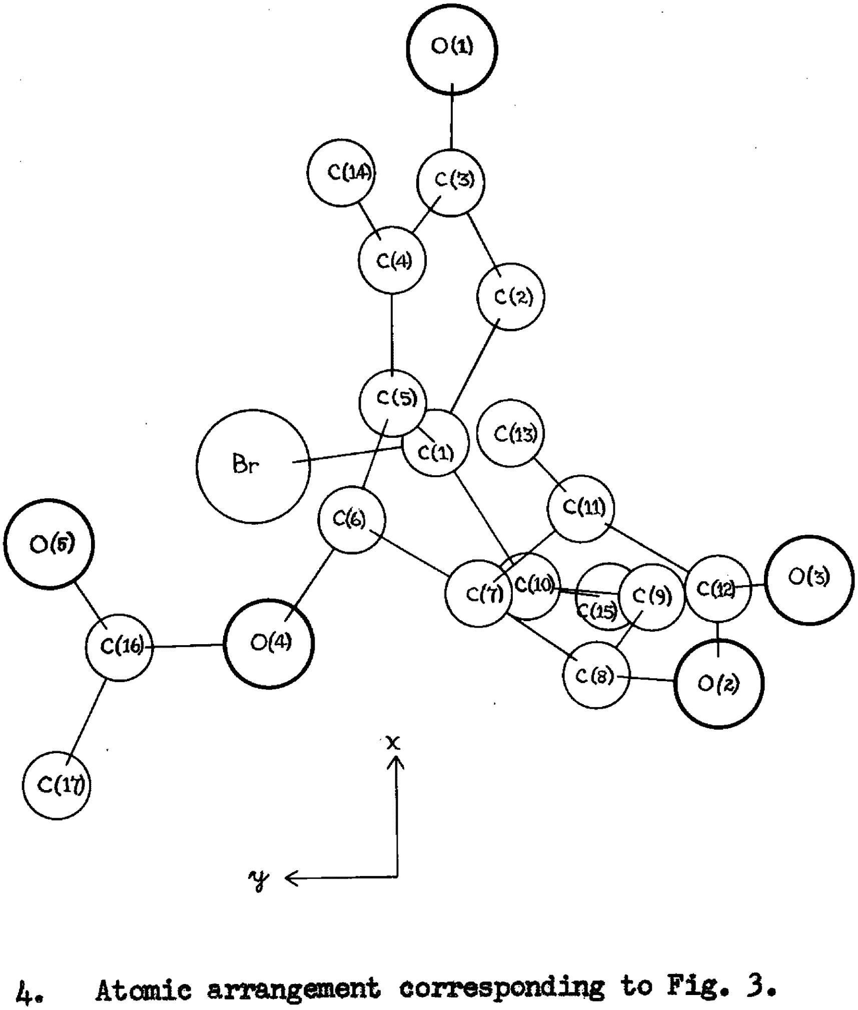


Fig. 4. Atomic arrangement corresponding to Fig. 3.

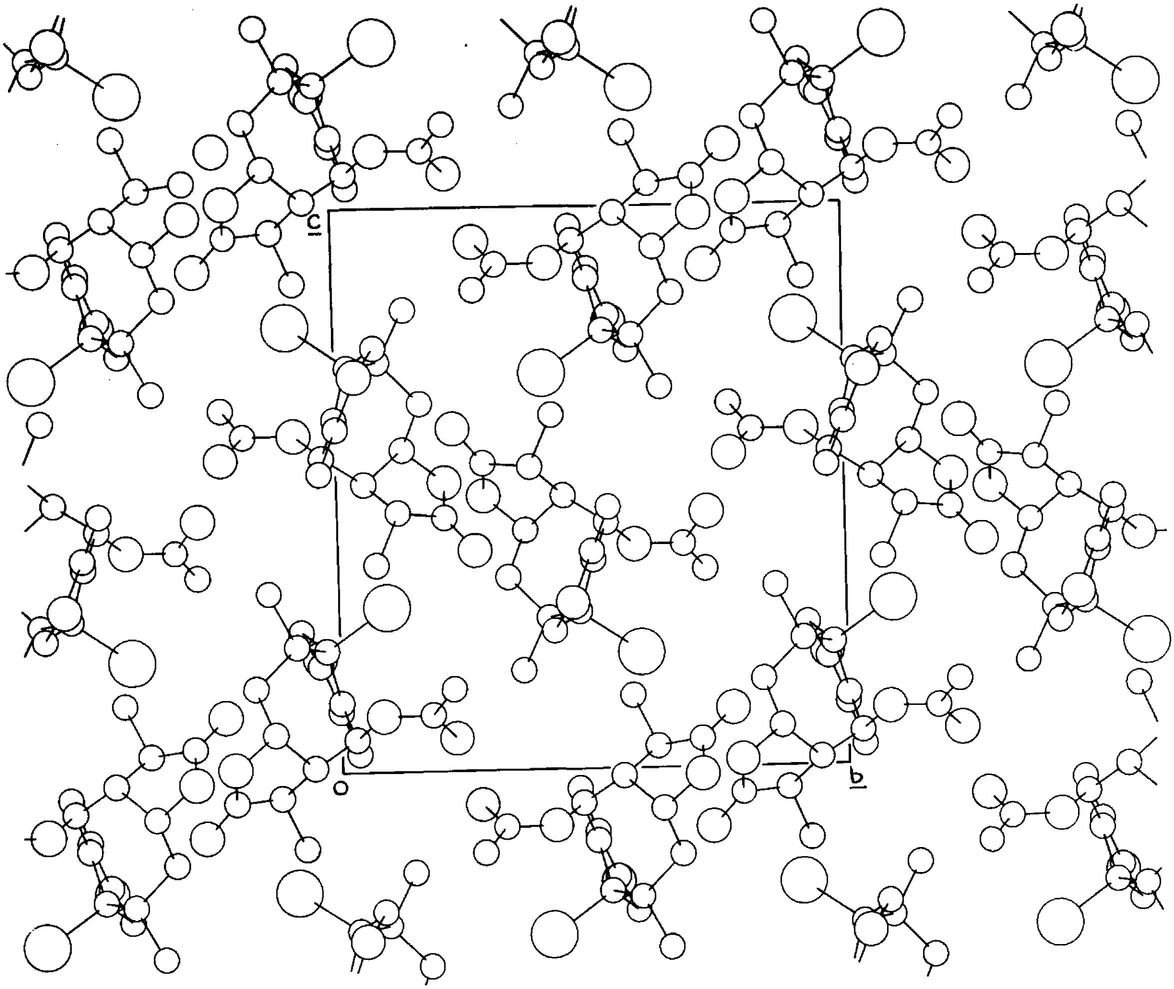
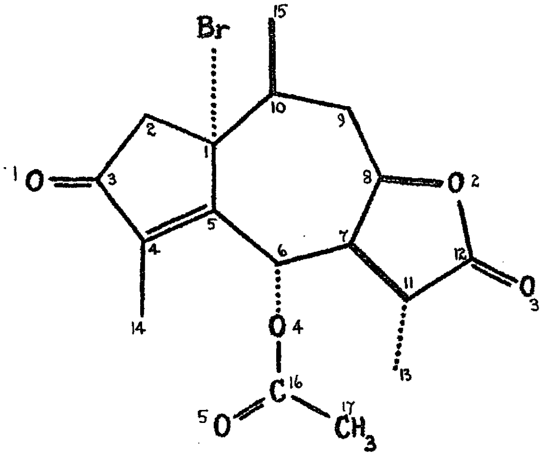


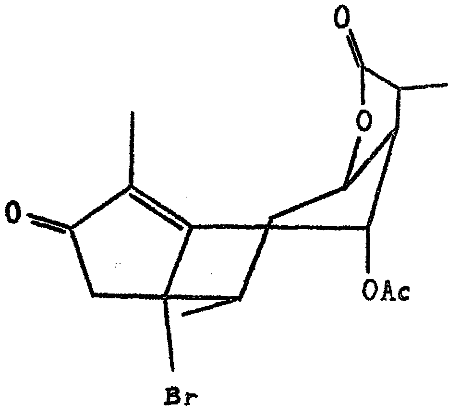
Fig. 5. The arrangement of molecules in the crystal as viewed along the a-axis.

4.5 DISCUSSION OF RESULTS.

The constitution and relative stereochemistry of bromogeigerin acetate as determined by this analysis are shown in (VI). A better representation of the stereochemistry is (VII). This constitution and the relative stereochemistry at positions 6, 7 and 8 are in agreement with those proposed by Barton and Levisalles (1958). The absolute configurations of geigerin and hence of this derivative (VI) have been defined (except at position 1) by a chemical correlation with artemisin (Barton and Pinhey, 1960).



(VI)



(VII)

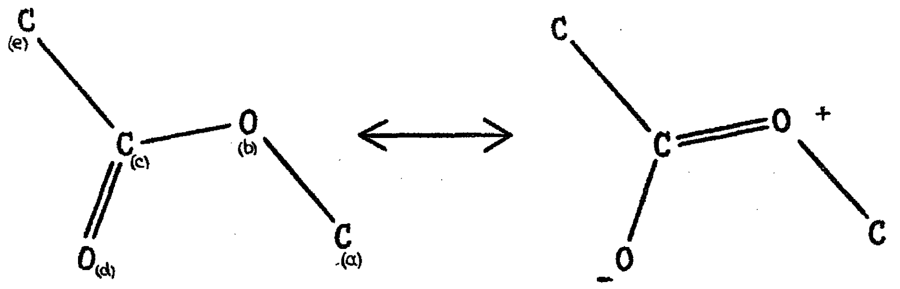
An unfortunate consequence of the fact that substitution of the bromine atom into geigerin acetate occurred at position 1 and not, as had been expected, at position 2, is that the configuration of geigerin at position 1 cannot be inferred from this analysis. Rotary dispersion studies, however, which have been conducted by Djerassi et al. (1957) give evidence of a β-hydrogen configuration at position 1 in geigerin.

The average carbon-carbon single bond length between sp^3- hybridised carbon atoms is 1.56 Å and between sp^3- and sp^2- hybridised carbon atoms is 1.51 Å; neither of these is significantly different from the accepted values of 1.545 Å and 1.53 Å, respectively (Tables of Interatomic Distances, 1958). The length of the carbon-carbon double bond in the cyclopentenone ring, 1.31 Å, is in agreement with that of 1.33 Å reported for ethylene (Bartell and Bonham, 1957).

In the cycloheptane ring, which has a "chair" conformation, the angles are consistently greater than tetrahedral, the average being 116°. These increases in bond angles are comparable with those found in the seven-membered rings of isoclovene hydrochloride (Clunie and Robertson, 1961) and bromodihydroisophoto- α-santonic lactone acetate (Asher and Sim, 1962a, 1963a). Similar increases in bond angles have been reported for the larger carbocyclic rings of cyclononylamine hydrobromide

(Bryan and Dunitz, 1960) and 1,6-trans-diaminocyclodecane dihydrochloride (Huber-Buser and Dunitz, 1960).

In the γ-lactone ring and acetate grouping two classes of carbon-oxygen single bonds are present; those adjacent to a carbon-oxygen double bond have a mean length of 1.29 Å whereas those not adjacent to this bond have a mean length of 1.46 Å. Similar differences in carbon-oxygen single bond lengths have been reported for methyl acetate (O'Gorman et al., 1950), methyl formate (Curl, 1959), dimethyl oxalate (Dougill and Jeffrey, 1953) and indicate that the resonance structure (IX) makes an important contribution in esters just as it does in carboxylic acids (Cochran, 1953, Cox et al., 1952, Ahmed and Cruickshank, 1953).



(VIII) (IX)

The π-character of the C=O carbonyl bond is further exhibited in the planarity of the system C(a),O(b),C(c),O(d),C(e), of these esters and this feature is present in both the acetate and γ-lactone groupings of bromogeigerin acetate.

The equation of the best plane through the atoms C(6),O(4),C(16),O(5),C(17), of the acetate grouping is

$$0.5134\ X - 0.0337\ Y + 0.8576\ Z - 8.9961 = 0.$$

The individual deviations of these atoms are listed in Table XI; no deviation is significant.

The results of the calculations of the best planes through sets of atoms of the γ-lactone ring are summarised in Table X. Application of the χ^2 test (Fisher and Yates, 1957) indicates that for all but one of these planes the atoms cannot be regarded as coplanar; this plane is that through C(8),O(2),C(12),O(3),C(11), the equation being.

$$0.6198\ X + 0.5353\ Y + 0.5738\ Z - 7.1158 = 0.$$

The deviations of these five atoms and of C(7) from this plane are listed in Table X.

The analyses of himbacine hydrobromide (Fridrichsons and Mathieson, 1962) and of 2-bromo-α-santonin (Asher and Sim, 1962b, 1963b,) provide other examples of structures containing γ-lactone rings with which these conclusions may be compared. Employing the results of these analyses, identical mean plane calculations were performed for the atoms of the γ-lactone rings of these structures. The results of these calculations, listed in Table X, compare very favourably with those of the present analysis and indicate that in γ-lactone rings, just as in esters, due to the contribution of the resonance form (IX), the atoms C(a),O(b),C(c),O(d),C(e), can be regarded as being coplanar.

Of the carbonyl carbon-oxygen double bonds C(3)-O(1), 1.21 Å, is shorter than either C(16)-O(5) or C(12)-O(3). This is not unreasonable since the latter two are involved in resonance of the type described above and hence have some single bond character associated with them.

The cyclopentenone ring is non-planar. The equation of the plane through the atoms C(1),C(3),C(4),C(5),C(6), and C(14) is

$$0.6010\ X - 0.9412\ Y + 0.3316\ Z - 3.4432 = 0.$$

The individual displacements of the atoms of the cyclopentenone system from this plane are listed in Table XII. The displacement of C(2), 0.32 Å, is extremely significant. The method employed for the calculations of the best planes was that of Schomaker et al.(1959).

The average value of carbon-bromine bond lengths found in various alkyl bromides is 1.94 Å (Tables of Interatomic Distances, 1958). Application of the Cruickshank and Robertson (1953) criteria to the carbon-bromine bond length of 1.99 Å found from the present analysis indicates that the difference between this length and 1.94 Å lies in the "possibly significant" region. Since there is no analysis of a structure containing a carbon-bromine bond in a similar environment with which to compare this result it would not be pertinent to draw any significant conclusion from the difference in bond length.

The arrangement of bromogeigerin acetate molecules as viewed along the a-axis is shown in Figure 5. In the crystal the molecules are held together by van der Waals forces. The shorter intermolecular contacts, of which none appears to be abnormal, are listed in Table IX.

TABLE II.

Final Atomic Co-ordinates.

(Origin of co-ordinates as in "International Tables" Vol. I.)

Atom	x/a	y/b	z/c
C(1)	0.4872	0.0270	0.7184
C(2)	0.6497	0.0768	0.7521
C(3)	0.7761	0.0384	0.6919
C(4)	0.6912	-0.0003	0.6112
C(5)	0.5324	-0.0008	0.6259
C(6)	0.4028	-0.0286	0.5596
C(7)	0.3199	0.0541	0.5122
C(8)	0.2282	0.1304	0.5715
C(9)	0.3139	0.1670	0.6549
C(10)	0.3270	0.0855	0.7275
C(11)	0.4371	0.1211	0.4602
C(12)	0.3236	0.2107	0.4526
C(13)	0.4978	0.0759	0.3690
C(14)	0.7864	-0.0327	0.5336
C(15)	0.3148	0.1397	0.8209
C(16)	0.2631	-0.1804	0.5999
C(17)	0.1111	-0.2225	0.6449
O(1)	0.9248	0.0396	0.7015
O(2)	0.2166	0.2117	0.5114
O(3)	0.3318	0.2710	0.3928
O(4)	0.2658	-0.0830	0.5994
O(5)	0.3794	-0.2248	0.5587
Br	0.4646	-0.0914	0.7919

TABLE III.

Anisotropic temperature factor parameters.

(b_{ij} x 10^5).

	b_{11}	b_{22}	b_{33}	b_{12}	b_{23}	b_{13}
C(1)	1854	509	505	219	165	638
C(2)	1986	635	401	-461	162	1
C(3)	2206	352	459	274	424	-176
C(4)	864	599	609	637	-55	-215
C(5)	1282	323	496	178	30	-358
C(6)	1067	496	658	242	-191	9
C(7)	2029	557	391	178	212	-132
C(8)	1318	437	600	346	-186	3
C(9)	2177	582	476	310	183	-341
C(10)	1566	461	449	274	223	227
C(11)	1257	499	441	-20	52	-207
C(12)	2280	461	437	-460	-79	-213
C(13)	1417	702	582	42	311	17
C(14)	1617	754	590	512	207	-131
C(15)	1828	766	526	26	26	128
C(16)	1643	430	590	-183	6	32
C(17)	1733	494	766	-243	14	-242
O(1)	1351	821	692	-65	270	-477
O(2)	1215	603	532	278	307	-74
O(3)	2128	705	750	-36	341	-417
O(4)	1954	443	596	-130	354	449
O(5)	2785	552	920	180	-272	490
Br	1594	599	542	4	308	187

TABLE IV.

Standard deviations of the final atomic co-ordinates. (Å)

Atom	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$
C(1)	0.024	0.018	0.019
C(2)	0.025	0.020	0.020
C(3)	0.024	0.017	0.019
C(4)	0.024	0.020	0.020
C(5)	0.025	0.017	0.017
C(6)	0.023	0.020	0.022
C(7)	0.025	0.020	0.020
C(8)	0.024	0.020	0.021
C(9)	0.026	0.020	0.020
C(10)	0.023	0.019	0.017
C(11)	0.024	0.018	0.019
C(12)	0.026	0.020	0.020
C(13)	0.022	0.020	0.020
C(14)	0.027	0.022	0.021
C(15)	0.027	0.023	0.021
C(16)	0.024	0.019	0.021
C(17)	0.026	0.020	0.022
O(1)	0.016	0.014	0.015
O(2)	0.016	0.013	0.013
O(3)	0.018	0.015	0.016
O(4)	0.016	0.013	0.014
O(5)	0.019	0.015	0.017
Br.	0.003	0.002	0.002

TABLE V. Measured and calculated values of the structure factors.

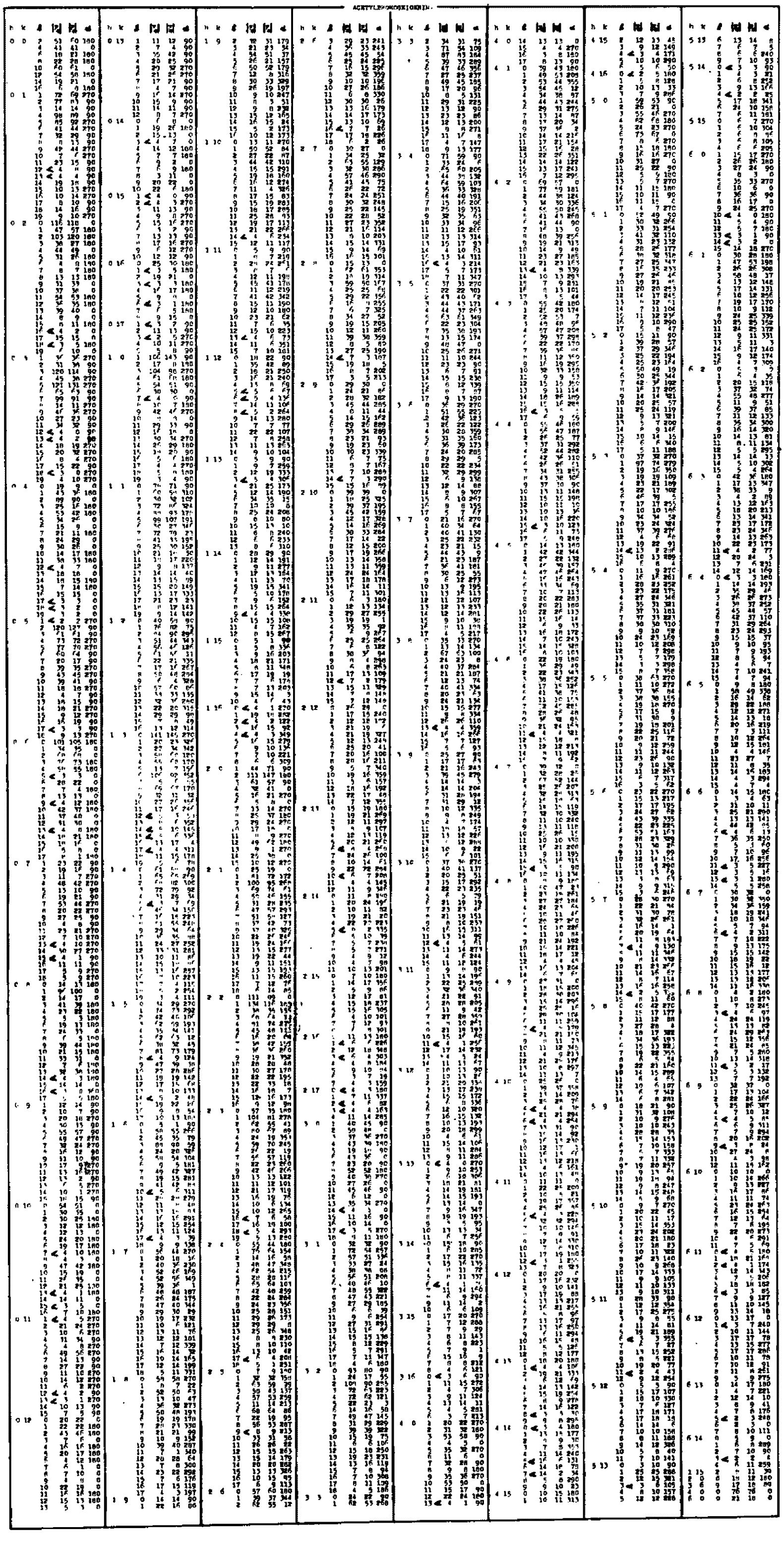


TABLE VI.

Intramolecular bonded distances (Å).

C(1)	-	C(2)	1.57	C(7)	-	C(11)	1.54
C(1)	-	C(5)	1.51	C(8)	-	C(9)	1.53
C(1)	-	C(10)	1.53	C(8)	-	O(2)	1.45
C(1)	-	Br	1.99	C(9)	-	C(10)	1.58
C(2)	-	C(3)	1.47	C(10)	-	C(15)	1.61
C(3)	-	C(4)	1.51	C(11)	-	C(12)	1.54
C(3)	-	O(1)	1.21	C(11)	-	C(13)	1.60
C(4)	-	C(5)	1.31	C(12)	-	O(2)	1.25
C(4)	-	C(14)	1.48	C(12)	-	O(3)	1.24
C(5)	-	C(6)	1.51	C(16)	-	C(17)	1.53
C(6)	-	C(7)	1.51	C(16)	-	O(4)	1.34
C(6)	-	O(4)	1.47	C(16)	-	O(5)	1.29
C(7)	-	C(8)	1.57				

TABLE VII.

Interbond angles ($^{\circ}$).

C(2) - C(1) - C(5)	102	C(6) - C(7) - C(11)	115
C(2) - C(1) - C(10)	117	C(8) - C(7) - C(11)	101
C(2) - C(1) - Br	105	C(7) - C(8) - C(9)	119
C(5) - C(1) - C(10)	115	C(7) - C(8) - O(2)	101
C(5) - C(1) - Br	110	C(9) - C(8) - O(2)	107
C(10) - C(1) - Br	108	C(8) - C(9) - C(10)	112
C(1) - C(2) - C(3)	103	C(1) - C(10) - C(9)	112
C(2) - C(3) - C(4)	108	C(1) - C(10) - C(15)	112
C(2) - C(3) - O(1)	128	C(9) - C(10) - C(15)	107
C(4) - C(3) - O(1)	124	C(7) - C(11) - C(12)	99
C(3) - C(4) - C(5)	108	C(7) - C(11) - C(13)	114
C(3) - C(4) - C(14)	121	C(12) - C(11) - C(13)	115
C(5) - C(4) - C(14)	130	C(11) - C(12) - O(2)	112
C(1) - C(5) - C(4)	114	C(11) - C(12) - O(3)	124
C(1) - C(5) - C(6)	121	O(2) - C(12) - O(3)	124
C(4) - C(5) - C(6)	125	C(17) - C(16) - O(4)	113
C(5) - C(6) - C(7)	116	C(17) - C(16) - O(5)	129
C(5) - C(6) - O(4)	112	O(4) - C(16) - O(5)	117
C(7) - C(6) - O(4)	104	C(8) - O(2) - C(12)	114
C(6) - C(7) - C(8)	116	C(6) - O(4) - C(16)	122

TABLE VIII.

Intramolecular non-bonded distances (≤ 4.0 Å).

C(1)	.....	C(7)	3.44	C(6)	.....	C(17)	3.80
C(1)	.....	C(8)	3.38	C(6)	.....	O(2)	3.71
C(1)	.....	C(14)	3.81	C(6)	.....	O(5)	2.71
C(1)	.....	C(16)	3.84	C(7)	.....	C(10)	3.31
C(1)	.....	O(1)	3.56	C(7)	.....	C(14)	3.98
C(1)	.....	O(4)	2.97	C(7)	.....	C(16)	3.53
C(2)	.....	C(6)	3.84	C(7)	.....	O(3)	3.50
C(2)	.....	C(9)	3.34	C(7)	.....	O(5)	3.93
C(2)	.....	C(14)	3.82	C(8)	.....	C(13)	3.86
C(2)	.....	C(15)	3.04	C(8)	.....	C(15)	3.87
C(3)	.....	C(6)	3.75	C(8)	.....	O(3)	3.45
C(3)	.....	C(10)	3.74	C(8)	.....	O(4)	2.98
C(4)	.....	C(7)	3.45	C(9)	.....	C(11)	3.19
C(4)	.....	C(9)	3.89	C(9)	.....	C(12)	3.14
C(4)	.....	C(10)	3.64	C(9)	.....	O(4)	3.57
C(4)	.....	C(11)	3.51	C(10)	....	O(2)	3.83
C(4)	.....	O(4)	3.64	C(10)	....	O(4)	3.07
C(5)	.....	C(8)	3.17	C(11)	....	C(14)	3.71
C(5)	.....	C(9)	2.95	C(11)	....	O(4)	3.79
C(5)	.....	C(11)	3.13	C(13)	....	O(2)	3.56
C(5)	.....	C(15)	3.96	C(13)	....	O(3)	3.03
C(5)	.....	C(16)	3.32	C(13)	....	C(14)	3.74
C(5)	.....	O(1)	3.43	C(14)	....	O(1)	2.97
C(5)	.....	O(5)	3.48	Br	.....	C(3)	3.45
C(6)	.....	C(9)	3.14	Br	.....	C(4)	3.54
C(6)	.....	C(10)	3.06	Br	.....	C(6)	3.68
C(6)	.....	C(12)	3.73	Br	.....	C(15)	3.43
C(6)	.....	C(13)	3.33	Br	.....	C(16)	3.57
C(6)	.....	C(14)	3.14	Br	.....	O(4)	3.35

TABLE IX.

Intermolecular contacts ($\leq 4\overset{\circ}{A}$).

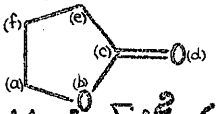
$C(3)$	.....	$O(3)_{I}$	2.96	Br	.....	$C(12)_{III}$	3.76
$O(1)$	.....	$O(3)_{I}$	3.07	Br	.....	$O(3)_{III}$	3.78
$C(11)$	.....	$O(2)_{I}$	3.26	$C(14)$	..	$O(3)_{I}$	3.79
$C(4)$	.....	$O(3)_{I}$	3.36	$C(17)$	..	$O(3)_{III}$	3.86
$C(2)$	.....	$O(3)_{I}$	3.38	$C(13)$	..	$O(2)_{I}$	3.88
$C(12)$	.....	$O(2)_{I}$	3.41	Br	.....	$C(13)_{III}$	3.94
$O(3)$	.....	$O(2)_{I}$	3.45	$C(12)$	..	$C(8)_{I}$	3.96
$C(3)$	.....	$C(8)_{I}$	3.53	$C(15)$	..	$C(13)_{III}$	3.97
$O(5)$	.....	$C(17)_{II}$	3.70	$C(17)$	..	$C(15)_{IV}$	3.98
$C(14)$	.....	$O(5)_{II}$	3.70	$C(5)$	...	$O(3)_{I}$	4.00

The subscripts refer to the following equivalent positions:

I	$\frac{1}{2} + x,$	$\frac{1}{2} - y,$	$1 - z$
II	$\frac{1}{2} + x,$	$-\frac{1}{2} - y,$	$1 - z$
III	$\frac{1}{2} - x,$	$- y,$	$\frac{1}{2} + z$
IV	$- x,$	$-\frac{1}{2} + y,$	$1\frac{1}{2} - z$

TABLE X.

Results of mean plane calculations through the atoms of some γ-lactone rings.



	Atom omitted	$\sum\Delta^2$ $(x\ 10^4)$	χ^2	P% †
Bromogeigerin acetate $(\sigma^2 = 4\ x\ 10^{-4})$	none	1903	476	0.1
	C(a)	1442	356	0.1
	O(b)	1872	468	0.1
	C(c)	1880	470	0.1
	O(d)	1496	370	0.1
	C(e)	445	111	0.1
	C(f)	8.5	2.1	95>P>5 ††
Himbacine hydrobromide $(\sigma^2 = 8\ x\ 10^{-4})$	none	1794	224	0.1
	C(a)	1362	158	0.1
	O(b)	1776	222	0.1
	C(c)	1790	224	0.1
	O(d)	1510	189	0.1
	C(e)	283	35	0.1
	C(f)	33.7	4.2	>5 ††
2-Bromo-α-santonin $(\sigma^2 = 4\ x\ 10^{-4})$	none	1887	472	0.1
	C(a)	1406	352	0.1
	O(b)	1853	463	0.1
	C(c)	1865	466	0.1
	O(d)	1460	365	0.1
	C(e)	538	135	0.1
	C(f)	1.7	0.43	95>P>5 ††

† P gives a numerical value to the probability that the atoms under consideration are coplanar.

†† Displacements (Å) from the best plane.

	Bromogeigerin acetate		Himbacine hydrobromide	2-Bromo-α-santonin
C(a)	-0.010	C(8)	-0.019	-0.007
O(b)	0.005	O(2)	0.035	0.007
C(c)	0.022	C(12)	-0.038	0.006
O(d)	-0.015	O(3)	0.002	-0.007
C(e)	-0.002	C(11)	0.020	0.001
C(f)	-0.630	C(7)	-0.612	-0.622

TABLE XI.

Deviations (Å) of the atoms of the acetate grouping C(6),O(4),C(16),O(5),C(17), from the best plane through these atoms.

C(6)	0.007	O(5)	-0.011
O(4)	-0.017	C(17)	-0.002
C(16)	0.023		

TABLE XII.

Displacements (Å) of the atoms of the cyclopentenone system from the mean plane through C(1),C(3),C(4),C(5),C(6), and C(14).

C(1)	0.076	C(5)	-0.010
C(2)	-0.321	C(6)	-0.048
C(3)	-0.066	C(14)	0.061
C(4)	-0.014	O(1)	0.040

PART V

X-ray Analysis of 2-Chloro-4-nitroaniline.

5.1 INTRODUCTION.

It is a well-established fact that repulsion between non-bonded atoms of aromatic systems can lead to observable deformations from regular forms. Molecules exhibiting such deformations are classed "overcrowded" and descriptions of the structures of a number of these molecules have been published.

In the case of "overcrowded" aromatic hydrocarbons the details of the distortion in the overcrowded regions are difficult to study by means of X-ray analysis because the positions of the hydrogen atoms must be determined. Polyhalogenobenzene derivatives present a similar difficulty since in these molecules the locations of the lighter atoms in the presence of the halogen atoms may not be determined with sufficient accuracy to permit a detailed description of the structure.

In view of these considerations the X-ray structure analyses of monohalogenobenzene derivatives subject to steric effects because of the close proximity of the halogen atom to a neighbouring group offer a more promising prospect in the study of molecular overcrowding since the lighter atoms can be more accurately located than in the polyhalogenobenzene derivatives. Examples of the kind of results that may be obtained from the accurate X-ray analyses of molecules in this class are provided by the series of investigations by

Ferguson and Sim on the structures of some "overcrowded" benzoic acids. These workers have studied o-chloro- (1961) and o-bromobenzoic acids (1962a), 2-chloro-5-nitrobenzoic acid (1962b) and 4-chloro-3-nitrobenzoic acid (Ferguson, 1961). The results of these analyses show that, in the solid state, measurable in-the-benzene-plane and out-of-the-benzene-plane displacements of adjacent substituents occur.

The preliminary results of the analysis of the molecular structure of p-nitroaniline (Donohue and Trueblood, 1956; Abrahams and Robertson, 1948.) having indicated that there were no significant deviations of the substituents from the benzene plane, it appeared that the investigation of a halogen derivative of this aminobenzene would be worthwhile and, in 1959, an investigation of the molecular structure of 2-chloro-4-nitroaniline was undertaken. It seemed possible that, owing to a relayed steric effect in this molecule, the nitro group would be rotated out of the plane of the benzene ring.

A recent account of the results of the more accurate analysis of the structure of p-nitroaniline (Trueblood et al.,1961) has provided evidence that, in the solid state, there are small but significant deviations of the substituents from the benzene plane even in this molecule.

5.2 EXPERIMENTAL.

Crystal data

	2-chloro-4-nitroaniline	2-bromo-4-nitroaniline
M	172.6	217.0
m.p.	105-106°C	103-104°C
System	Orthorhombic	Orthorhombic
a(Å)	11.25 ± 0.03	11.30 ± 0.03
b(Å)	16.85 ± 0.03	16.94 ± 0.03
c(Å)	3.87 ± 0.02	3.97 ± 0.02
U(Å)^3	734.0	760.2
D_{obs}(flotation in $ZnCl_2$ solution)	1.545 g.cc.$^{-1}$	1.908 g.cc.$^{-1}$
Z	4	4
D_c	1.562 g.cc.$^{-1}$	1.896 g.cc^{-1}
F(ooo)	352	424
Systematic absences	h00 when h = 2n+1; 0k0 when k = 2n+1, 00ℓ when ℓ = 2n+1; h0ℓ when h =2n+1, 0kℓ when k+ℓ =2n+1	
Space group	$Pna2_1 - C_{2v}^9$	$Pna2_1 - C_{2v}^9$
Absorption coefficient for X-rays (λ =1.542 Å), μ	42.6 cm.$^{-1}$	77.9 cm.$^{-1}$
Total number of independent observed structure amplitudes	614	245 (hk0 zone only)
$\sum f^2$ "light" atoms	447	447
$\sum f^2$ "heavy" atoms	289	1225

Crystallisation of both derivatives of p-nitroaniline from aqueous ethanol provided crystals in the shape of thin narrow laths elongated along the direction of the c-crystal axis.

Rotation, oscillation, Weissenberg and precession photographs were taken with copper-K_α (λ =1.542 Å) and molybdenum-K_α (λ =0.7107 Å) radiation. The cell dimensions were determined from rotation and equatorial layer-line Weissenberg photographs.

The systematic absences are consistent with two space groups, $Pna2_1$ and Pnam. Since there are only four molecules in the unit cell, the centrosymmetric space group requires two mirror planes ½c apart, each plane containing two molecules flat within it. The c-axis projection has plane group pgg for either space group and examination of this projection clearly indicated that the molecular plane did not coincide with the (001) direction. The space group is therefore $Pna2_1$ and this choice is justified by the results of the analysis.

Intensity data were obtained from equatorial and, for 2-chloro-4-nitroaniline, from equi-inclination multiple-film Weissenberg photographs of the hk1 and hk2 layers. The intensities were estimated visually and were corrected for Lorentz, polarisation and the rotation factors appropriate to the upper layers (Tunell, 1939). No corrections were made for absorption.

Subsequent to refinement of the atomic parameters in two-dimensions, the various layers (hk0-hk2) were placed on approximately the same scale by comparison of the observed and calculated structure amplitudes for a three-dimensional model. The scaling factors were adjusted throughout the three-dimensional refinement to ensure that $\sum |F_o| = \sum |F_c|$ for each layer.

5.3 STRUCTURE DETERMINATION AND REFINEMENT.

5.3.1 The c-axis projection.

Examination of the distribution of the vector peaks present in the Patterson projection along the c-axis of 2-chloro-4-nitroaniline (Figure 1) provided three possible solutions to the location of the chlorine atom. The peaks designated A,B,C; B,D,E; and D,F,G in Figure 1 correspond to the vector sets giving rise to the three different positions. In order to resolve this ambiguity before attempting to utilise the heavy atom method, structure factors were calculated employing, in turn, each of these chlorine co-ordinates and led to agreement factors of 0.64, 0.70 and 0.76, respectively. It was reasonable to assume that the true chlorine co-ordinates were those which gave rise to the best agreement between the observed and calculated structure amplitudes and they were assigned accordingly.

The signs of the structure factors calculated employing the chlorine co-ordinates were attributed to the observed structure amplitudes of which 45% were employed for the calculation of a two-dimensional Fourier synthesis. When it was discovered that this Fourier synthesis did not yield any information about the positions of the light atoms an attempt was made to extract further information concerning the orientation of the benzene ring and its substituents from the vector distribution of the P(U,V)

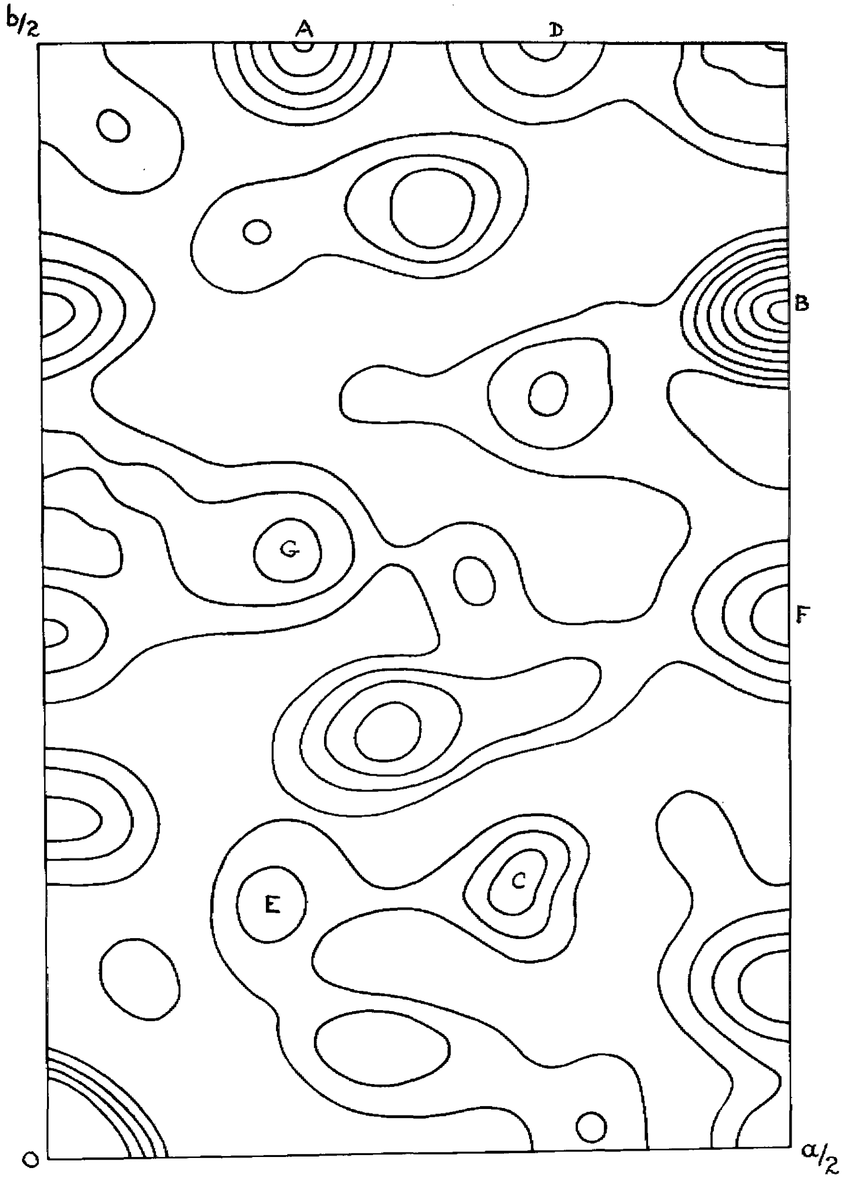


Fig. 1. The Patterson projection along the c-axis of 2-chloro-4-nitroaniline. The contour scale is arbitrary. A, B, C, D, E, F, and G are the vector peaks which give rise to the three vector sets referred to in the text. A, B and C denote the peaks corresponding to the true chlorine-chlorine vectors.

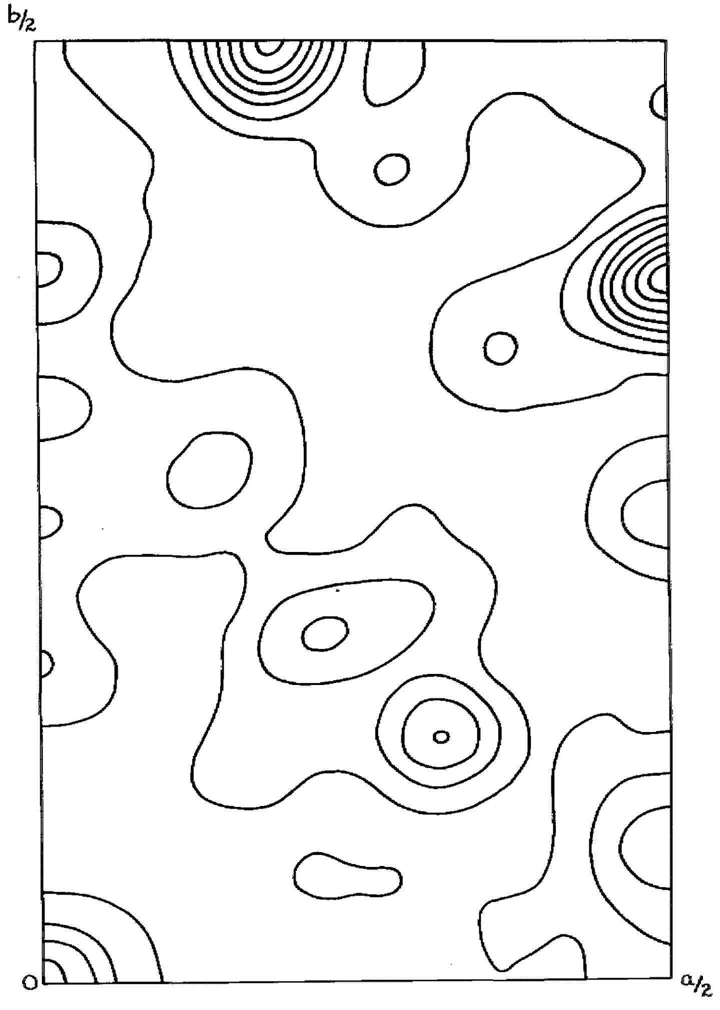


Fig. 2. The Patterson projection along the c-axis of 2-bromo-4-nitroaniline. The contour scale is arbitrary.

Patterson function. That peak which was approximately 1.5 Å from the origin was assumed to correspond to the chlorine-carbon (2) vector and, from this starting point, approximate co-ordinates of the remaining carbon, nitrogen and oxygen atoms were readily determined. Holes corresponding to several unit cells containing this postulated atomic arrangement were punched on a mask which was placed in the optical diffractometer and, when the observed optical transform showed a good agreement with the weighted reciprocal lattice, it appeared that the postulated arrangement was sound. Attempts to refine the atomic co-ordinates by means of conventional two-dimensional Fourier syntheses and structure factor calculations failed, implying that either the Patterson projection had been mis-interpreted in terms of chlorine-light atom vectors or that the orientation of the light atoms with respect to the chlorine atom was correct but the wrong chlorine co-ordinates had been employed.

In order to confirm the choice of chlorine co-ordinates isomorphous 2-bromo-4-nitroaniline was prepared according to the method of Kosolapoff (1953). The co-ordinates of the bromine atom, determined from the Patterson projection along the c-axis (Figure 2), were almost identical with those which had already been assigned to the chlorine atom, indicating that those of the latter were correct but that the deduced orientation of the benzene ring and its substituents with respect to this chlorine was wrong.

Employing 90% of the observed structure amplitudes of 2-bromo-4-nitroaniline and the signs appropriate to the bromine alone, an hk0 Fourier projection was calculated. This Fourier synthesis showed all of the light atoms, excepting hydrogens, clearly resolved. The error in the interpretation of the P(U,V) Patterson function of the 2-chloro derivative was then apparent - full use had not been made of the symmetry of this Patterson function with the result that the chlorine-light atom vectors deduced, although correct in magnitude were wrong in direction. Further, for the calculation of the two-dimensional Fourier synthesis the employment of only 45% of the observed structure amplitudes and the signs appropriate to the chlorine atom alone had been based on much too rigorous a selection rule (only those reflections for which $|F_c(hk\ell)| > |F_o(hk\ell)|$ had been included) and, in retrospect, 74% ought to have been used. Since this was the first structure analysis being attempted by the author and all calculations up to this point had been performed with the aid of a desk calculating machine and Beevers-Lipson strips these elementary errors can be attributed to overcaution and inexperience.

The light atom positions having been thus determined they were included along with those of the chlorine atom in a structure factor calculation for which an overall isotropic temperature factor of $B = 3.0\ \mathring{A}^2$ was assumed; the agreement factor obtained was 0.410. Two cycles of two-dimensional Fourier syntheses and structure factor calculations reduced the agreement factor to 0.276 and subsequent refinement in two-dimensions by means of an anisotropic temperature factor least-squares programme (Rollett, 1961) resulted in a further reduction to 0.142.

5.3.2. Three-dimensional refinement.

There being no fixed origin in the z-direction of the space group $Pna2_1$, the z-co-ordinate of the chlorine atom was arbitrarily chosen and, since the x- and y- co-ordinates of the remaining atoms and the tilt of the molecule were known from the results of the two-dimensional refinement, the z-co-ordinates of the carbon, nitrogen and oxygen atoms were calculated assuming a completely planar structure. These atomic co-ordinates and an overall isotropic temperature factor, B, of 4.0 Å^2 were employed for the calculation of the hk1 and hk2 structure factors and resulted in agreement factors of 0.206 and 0.272, respectively. The agreement factor over the 614 observed structure amplitudes, 0.207, indicated that the co-ordinates were sufficiently accurate to warrant proceeding to a least-squares refinement of both the positional and the anisotropic temperature factors for all of these atoms. After five cycles of calculations the parameter shifts became very small and the values of the agreement factors were reduced to 0.137 for hk0, 0.107 for hk1, and 0.097 for hk2, the overall value being 0.115.

At this stage it was decided to make allowance for the hydrogen atoms of the benzene ring. Co-ordinates for these three hydrogens were calculated assuming that these atoms are located radially at a distance of 1.08 Å from the carbon atoms to which they are covalently bonded. The isotropic temperature factor of the hydrogen atoms was assumed to be 4.2 Å^2. Three further cycles of least-squares refinement of the parameters of all atoms, excepting hydrogens, reduced the overall agreement factor to 0.105 ($\sum w \Delta^2 = 113$).

Calculation of structure factors, $F_{c'}$, omitting the hydrogen atoms resulted in an agreement factor of 0.111 ($\sum w \Delta^2 = 125$). A three-dimensional Fourier synthesis with coefficients ($F_o - F_{c'}$) was then evaluated (see Figure 3). Small peaks of about 0.3-0.4 e/Å^3 appeared in the positions expected for hydrogen atoms of the benzene ring and for one of the hydrogen atoms of the amino group. No peak corresponding to the remaining hydrogen atom was evident in this Fourier synthesis owing to the fact that there was some residual anisotropic thermal motion of the chlorine atom which produced a peak of 0.3 e/Å^3 near to the expected location of this hydrogen atom. Hence, co-ordinates for four of the hydrogen atoms could have been determined using the experimental results but since these would have been extremely inaccurate it was decided that it would be better to calculate positions for all five hydrogen atoms and

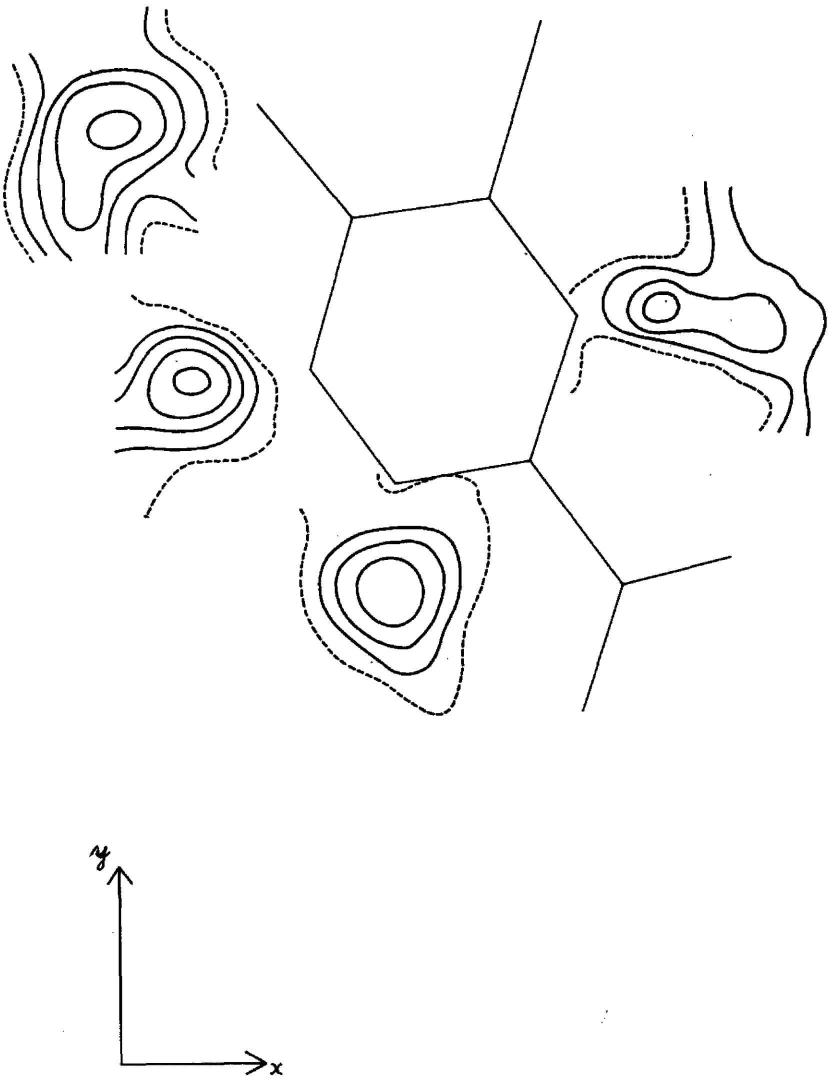


Fig. 3. The three-dimensional $(F_o - F_c)$ Fourier synthesis through the centres of the hydrogen atoms shown by means of contour sections drawn parallel to (001). Contour levels are 0.1e/Å^3. The zero level is given by the broken lines.

include these in a final structure factor calculation.

The assumptions made for the calculation of the co-ordinates of the hydrogen atoms of the benzene ring have already been indicated. The co-ordinates of the hydrogen atoms of the amino group were calculated assuming a completely planar conformation at the nitrogen atom, an N-H bond length of 1.0 Å and, further, that one of the hydrogen atoms lay along the line joining the nitrogen atom, N(1), and the oxygen atom, O(2), of an adjacent molecule in the direction of y. The latter assumption was not unreasonable since the relative positions of these nitrogen and oxygen atoms when considered along with the interatomic distance of 3.05 Å implies the presence of an N-H....O hydrogen bond and the true location of this hydrogen atom will lie close to the presumed direction.

The inclusion of all five hydrogen atoms in the final structure factor calculation reduced the agreement factor over all the observed reflections to 0.103 ($\sum w \Delta^2 = 104$).

For the least-squares refinement the following weighting system was employed:

$$\text{if} \quad |F_o| \leqslant 9.00 \qquad \sqrt{w}(hk\ell) = 1.$$

$$\text{if} \quad |F_o| > 9.00 \qquad \sqrt{w}(hk\ell) = 9.00/|F_o|$$

The theoretical atomic scattering factors used in the structure factor calculations were those of Berghuis et al.

(1955) for carbon, nitrogen and oxygen, those of McWeeny (1951) for hydrogen, and those of Tomiie and Stam (1958) for chlorine.

5.4 RESULTS OF ANALYSIS.

5.4.1 Molecular dimensions.

The final co-ordinates of the carbon, nitrogen, oxygen and chlorine atoms and the final anisotropic temperature factor parameters provided by the least-squares refinement are listed in Tables I and II, respectively. The standard deviations of the positional parameters, derived from the least-squares residuals in the normal manner, are given in Table III.

The final calculated and observed structure amplitudes, both rounded off as integers, and the values of the phase constants, α, are presented in Table IV. 59 unobserved reflections have also been included in this Table and for none of these is the calculated structure amplitude greater than one and a half times the minimum observable value.

Employing the observed structure amplitudes and phase angles of Table IV a three-dimensional Fourier synthesis was calculated. The result is shown in Figure 4 by means of superimposed contour sections drawn parallel to (001) and covering the region of one molecule.

The bond lengths and valency angles of the molecule, calculated from the co-ordinates of Table I, are listed in Tables V and VI, respectively. The estimated standard deviations of the bond lengths are also given in Table V. The estimated standard deviation of a bond angle is about 1^{o}.

The arrangement of molecules as viewed along the c-axis is shown in Figure 5 in which the hydrogen bonds are represented by broken lines. The shorter intermolecular contacts are listed in Table VII.

The atomic co-ordinates of Table I were used for the calculation of the mean planes through various groups of atoms. These planes were evaluated by the method of Schomaker et al.(1959).

The best plane through the chlorine, carbon, nitrogen and oxygen atoms of the molecule has equation

$$0.4573\ X + 0.0503\ Y - 0.8786\ Z - 0.9920 = 0.$$

The displacements of the atoms from this plane (Table VIII) indicate that the molecule cannot be considered planar for $\sum \Delta^2 = 1.23 \times 10^{-2}$ and $\chi^2 = \sum \Delta^2 / \sigma^2 = 59$ (Fisher and Yates, 1957).

When the oxygen atoms are omitted from the calculation of the mean molecular plane, the equation of the resulting plane is

$$0.4641\ X + 0.0495\ Y - 0.8845\ Z - 0.9523 = 0.$$

The individual deviations of the atoms from this plane (Table VIII) are still large, $\sum \Delta^2 = 4.1 \times 10^{-3}$ and $\chi^2 = 20$, and consequently must still be considered significant. Since the nitrogen, N(2), of the nitro group had the greatest deviation from this plane it was omitted along with O(1) and O(2) from a subsequent mean plane calculation through the carbon atoms, Cl and N(1). The equation of the plane through these eight atoms is

$$0.4578\ X + 0.0564\ Y - 0.8874\ Z - 0.9866 = 0.$$

and the deviations of these atoms from this plane (Table VIII) are small enough to be considered insignificant, $\sum \Delta^2 = 1.1 \times 10^{-3}$ and $\chi^2 \approx 5$.

The atoms of the nitro group, N(2), O(1), O(2), and carbon atom C(4) of the benzene ring are coplanar, the equation of the mean plane through these atoms being

$$0.5238\ X + 0.0564\ Y - 0.8500 - 1.2789 = 0.$$

The deviations of these four atoms from this plane are given in Table VIII. The angle between this plane and that through C(1)....C(6), Cl, N(1) is 4°20'

5.4.2. <u>Analysis of thermal motion.</u>

Cruickshank (1956a) has shown that, in terms of rigid-body vibrations, the motion of a molecule may be expressed as two symmetric tensors T and ω, each with six independent components. The first step in the determination of T and ω is the geometrical transformation of the atomic co-ordinates and orthonormal tensor transformation of the U_{ij} from the crystallographic to the molecular axes. The centre of mass, excluding the hydrogen atoms and assuming a completely planar molecule, was chosen as origin. Molecular axes were chosen such that OQ, in the plane of this molecule, corresponded to the direction of minimum inertia of an isolated molecule and OR, chosen parallel to the plane normal corresponded to the direction of maximum inertia. OP was chosen at right angles to both OQ and OR. The direction cosines of these molecular axes, referred to the orthogonal crystal axes are given in Table IX while the axes are shown in Figure 6.

The values of the six independent U_{ij}'s for each atom, derived from the b_{ij} of Table II and referred to the molecular axes are given in Table X in the columns headed "obs". Employing the U tensors of all the atoms, T and ω tensors were determined and from the values of these, U tensors for each atom were calculated; the resulting values of the U_{ij}'s are given in Table X in the columns headed "calc(i)". The signs of the discrepancies between the U_{11}"obs" and U_{11}"calc(i)" of this Table indicated that, retaining the same molecular axes, the centre of oscillation of the molecule required to be moved by an amount ΔQ along the Q-axis towards the amino group. A similar shift of the centre of oscillation away from the centre of mass was required in the interpretation of the thermal motion of monofluoroacetamide (Hughes and Small, 1962) where it was found necessary to consider the molecules not to be vibrating as independent entities but as part of a complex hydrogen bonded arrangement.

Several calculations of the values of T, ω and U_{ij}'s were carried out employing different values of ΔQ. All of the results of these calculations are not reproduced here but those given in Table XI serve to show that a minimum value of $\sum |U_{ij}\text{"obs"} - U_{ij}\text{"calc"}|$ is obtained when the shift, ΔQ, is about 1.2 Å. The T and ω tensors obtained when the origin of the molecular axes was shifted by 1.2 Å, to O', are given in Table XII. The root-mean-square amplitudes of rigid-body translational motion in the directions of the molecular axes O'P, O'Q, O'R, obtained from the square roots of the diagonal elements of T are 0.22, 0.21 and 0.13 Å, respectively. The corresponding root-mean-square amplitudes of rigid-body angular oscillation about the molecular axes are 2.9, 3.7 and 3.5°.

From the T and ω tensors of Table XI the value of the U tensor for each atom was calculated. The values of the U_{ij} so derived are listed in Table X in the columns headed "calc(ii)". The root-mean-square difference between the U_{ij}"obs" and U_{ij}"calc(ii)" values is 0.0066 Å^2, corresponding to an estimated standard deviation for the U_{ij}"obs" of 0.0073 Å^2. The estimated standard deviations of the T_{ij} and ω_{ij} are shown in Table XIII in positions corresponding to those of the elements in Table XII.

The values of the T and ω tensors resulting from this analysis are similar to those obtained for naphthalene

(Cruickshank, 1957) where the corresponding root-mean-square amplitudes of translational vibration in the direction of the molecular axes are 0.20, 0.22, 0.19 Å and the corresponding root-mean-square amplitudes of angular oscillation about the molecular axes are 3.7, 4.4 and 4.2°. For 2-chloro-4-nitroaniline the translational motion in the molecular plane can be considered to be isotropic and is greater than normal to it.

Due to the rotational oscillation of the molecule, errors in the atomic positions are introduced (Cruickshank 1956b, 1961). Approximate corrections ($\Delta P, \Delta Q, \Delta R$) to be applied to the atomic co-ordinates (referred to the molecular axes with centre of oscillation, O', as origin) can be obtained from the relationships

$$-\Delta P = \tfrac{1}{2} P(\omega_{22}^2 + \omega_{33}^2)$$
$$-\Delta Q = \tfrac{1}{2} Q(\omega_{11}^2 + \omega_{33}^2)$$
$$-\Delta R = \tfrac{1}{2} R(\omega_{11}^2 + \omega_{22}^2)$$

where the ω_{ii}^2 values are in (radians)^2.

Using these expressions and the ω values of Table XII the necessary corrections to the atomic co-ordinates were evaluated and the rotation-corrected bond lengths are given in Table V in the column headed "corrected".

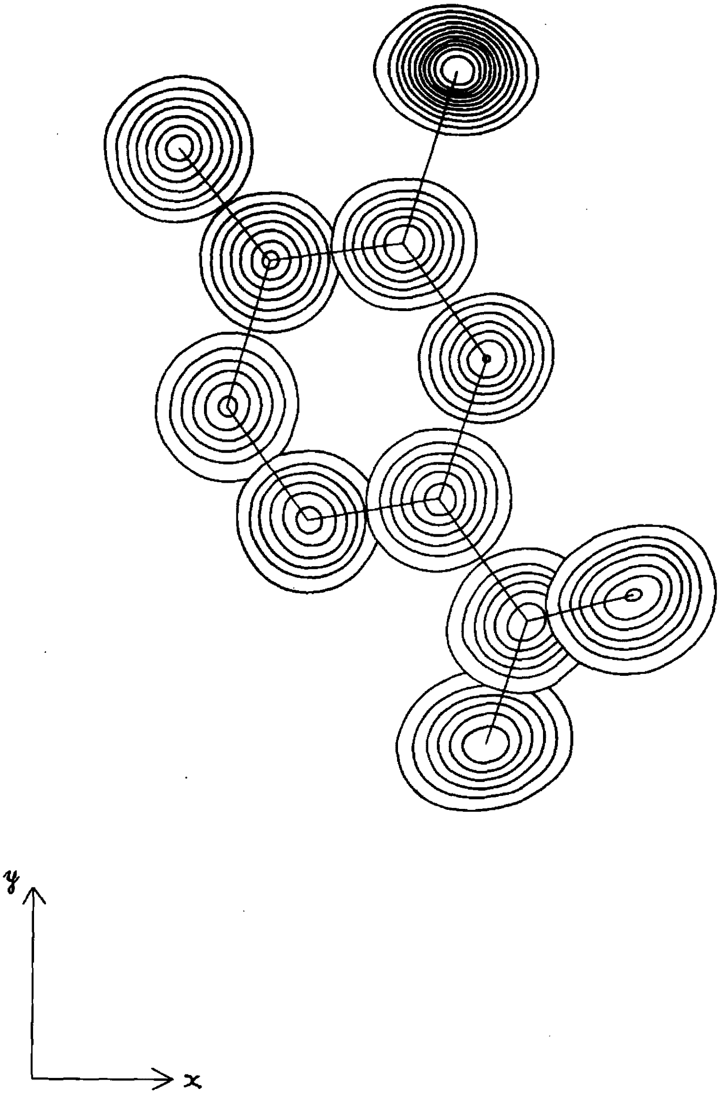


Fig. 4. Final three-dimensional electron-density distribution for 2-chloro-4-nitroaniline shown by means of superimposed contour sections drawn parallel to (001). The contour interval is 1e/Å^3 except around the chlorine atom where it is 2e/Å^3.

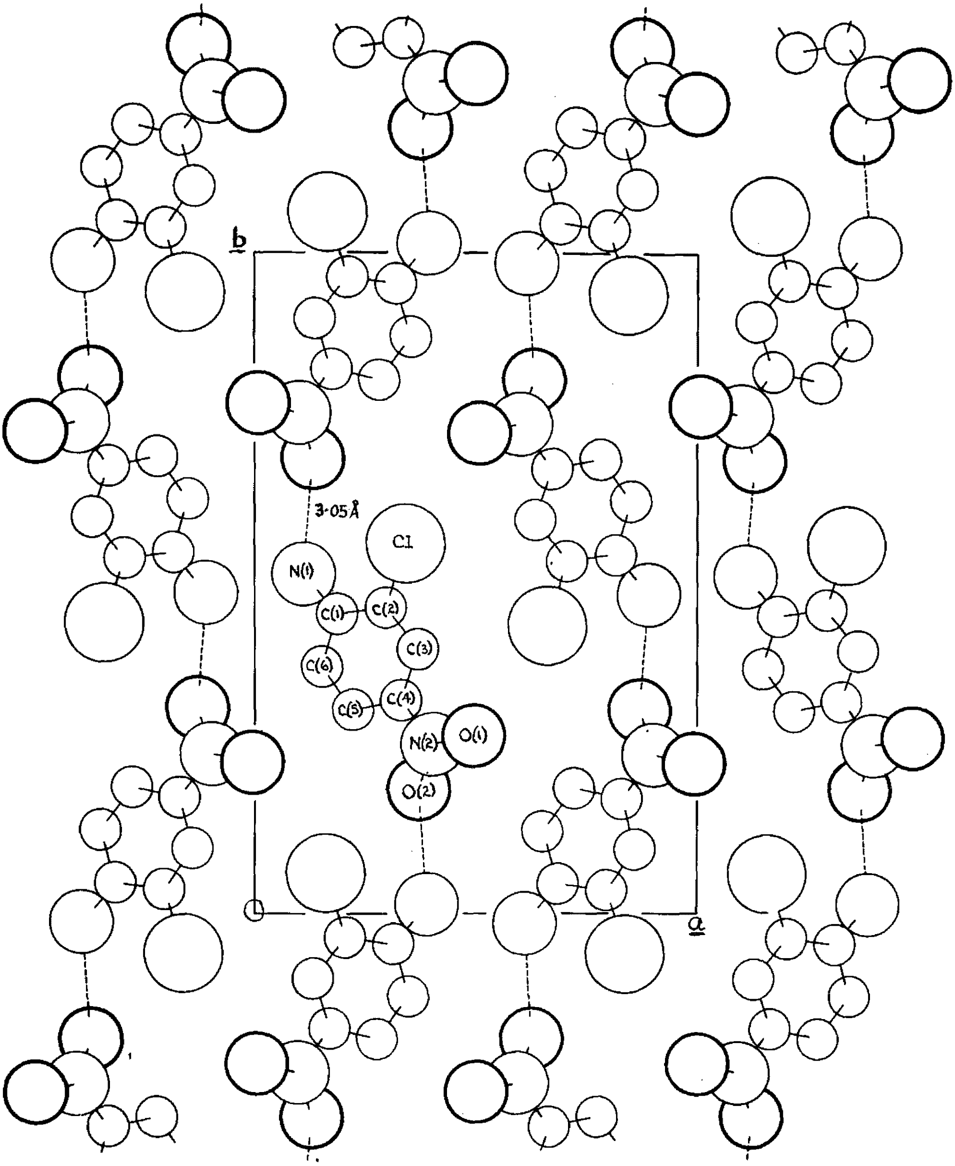


Fig. 5. The arrangement of molecules in the crystal as viewed along the c-axis. The hydrogen bonds are indicated by the broken lines.

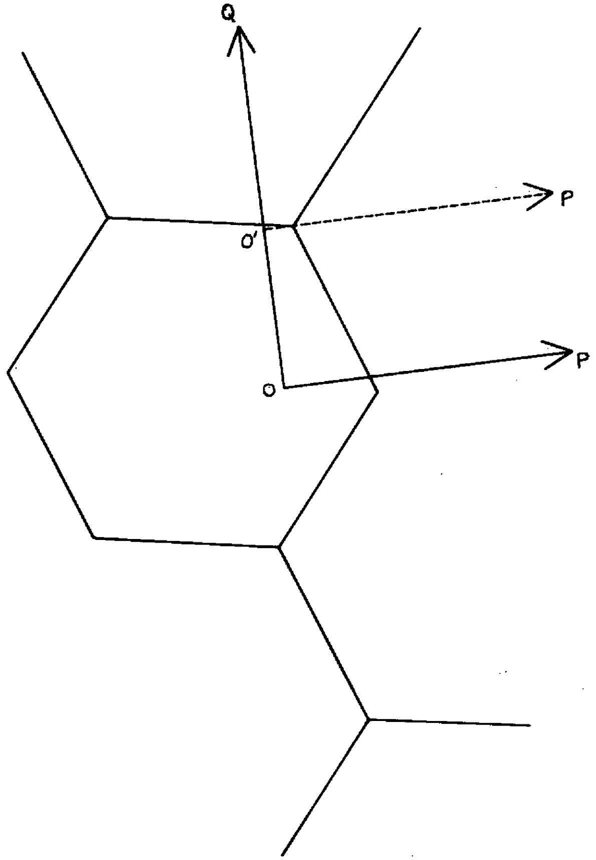


Fig. 6. The molecular axes. OR is perpendicular to OP and OQ.

5.5 DISCUSSION OF RESULTS.

The carbon-carbon bond lengths vary from 1.392 to 1.425 Å, the average being 1.403 Å. This is slightly longer than the average of 1.393 Å reported for the carbon-carbon bond distance in p-nitroaniline (Trueblood et al., 1961) and in crystalline benzene (Cox et al., 1958) but the difference between these average values is probably not significant. In view of the magnitude of the estimated standard deviations in the bond lengths it is not worthwhile attempting an interpretation of the individual carbon-carbon distances in terms of the different valence bond forms which can be written for the 2-chloro-4-nitroaniline molecule.

The carbon-amino nitrogen, N(1), distance of 1.386 Å is in good agreement with the only two precise values of aromatic carbon-nitrogen bond lengths available at present, viz. 1.367 ± 0.003 Å, without correction for librational effects, in 2-amino-3-methylbenzoic acid (Brown and Marsh, 1960) and 1.371 ± 0.007 Å in p-nitroaniline. Truter (1960) has suggested that the distance between a trigonal carbon and a trigonal nitrogen should be 1.32 -1.33 Å. This distance has been found in many amides and related species but that resulting from the present analysis is more comparable with those actually found in the indole rings of many alkaloids and with the trigonal carbon-trigonal nitrogen single bond length of 1.41 ± 0.02 Å as estimated by Trueblood et al. (1961).

The length of the carbon-nitrogen, N(2), bond leading to the nitro group at 1.471 Å is in very good agreement with those found in many nitro-hydrocarbons studied by Trotter (1960), the average of which is 1.48 Å, and is not significantly different from that of 1.460 Å found in p-nitroaniline. In the nitro group the nitrogen-oxygen bond lengths, 1.240 Å, are also in good agreement with those found in the nitro-hydrocarbons studied by Trotter and with those in p-nitroaniline, 1.246 ± 0.007 Å. The angles about the nitrogen atom of this group conform to the expected pattern in that the angle O-N-O exceeds 120° whereas the C-N-O angles are less than 120°. These angular variations are similar to those which are found in carboxyl groups and may be qualitatively interpreted in terms of inter-electron repulsions decreasing in the order non-bond-non-bond pairs, non-bond-bond pairs, and bond-bond pairs.

The nitrogen atom of the nitro group is displaced by 0.077 Å from the mean plane through C(1)....C(6), Cl, N(1) (see Table VIII), implying an out-of-plane deflection of the C(4)-N(2) bond of about 3° while the nitro group is itself twisted 4°20' out of the plane of the benzene ring. The magnitudes of these displacements are only slightly greater than those found in p-nitroaniline for which the reported values are 0.4° and 1.9°, respectively. This result implies that any steric effect on the nitro group due to the chlorine atom must be very small.

The carbon-chlorine distance of 1.766 Å is significantly longer than the value of 1.70 ± 0.01 Å quoted in "Tables of Interatomic Distances and Configuration in Ions and Molecules" (1958) for such a bond, but is more comparable with the more recently reported aromatic carbon-chlorine bond lengths which are given in Table XIV. Nevertheless, since the mean carbon-chlorine distance in halogenated aliphatic compounds is 1.767 Å (Tables of Interatomic Distances, 1958) there appears to be little, if any, double-bond character associated with the carbon-halogen bond of 2-chloro-4-nitroaniline.

The closest intermolecular approach occurs between one of the oxygen atoms of the nitro group, O(2), and the amino nitrogen atom of an adjacent molecule in the direction of y, the distance between these atoms being 3.05 Å. This distance is normal for the type of hydrogen bonding expected and is comparable with those found, for example, in p-nitroaniline of 3.07 Å and 3.14 Å, so that although the hydrogen atom involved in this bond could not be located (section 5.3) from a three-dimensional ($F_o - F_{c'}$) Fourier synthesis there is undoubtedly hydrogen bonding present along the y-direction of the crystal. All other intermolecular approach distances correspond to normal van der Waals interactions.

TABLE I.

Final atomic co-ordinates.

(Origin as in "International Tables" Vol. I)

Atom	x/a	y/b	z/c
C(1)	0.1849	0.4534	0.1159
C(2)	0.2947	0.4641	0.2762
C(3)	0.3676	0.4014	0.3793
C(4)	0.3295	0.3247	0.2942
C(5)	0.2217	0.3095	0.1339
C(6)	0.1513	0.3740	0.0414
N(1)	0.1101	0.5147	0.0218
N(2)	0.4019	0.2573	0.4090
O(1)	0.4937	0.2714	0.5727
O(2)	0.3707	0.1895	0.3287
Cl	0.3396	0.5614	0.3790

TABLE XI.

Anisotropic temperature factors ($b_{ij} \times 10^5$). †

Atom	b_{11}	b_{22}	b_{33}	b_{12}	b_{23}	b_{13}
C(1)	1104	515	4382	6	600	527
C(2)	1258	387	5324	-272	-696	1067
C(3)	1206	492	5743	42	1135	772
C(4)	1477	462	2883	157	768	642
C(5)	1711	443	4047	-201	103	1741
C(6)	1258	520	8623	-175	-93	1524
N(1)	1198	580	8235	151	1129	238
N(2)	1712	531	10475	504	2087	2860
O(1)	2364	844	10260	1109	1027	-218
O(2)	2724	521	17778	470	1112	856
Cl	1487	416	5491	-245	-996	239

† These are the values of b_{ij} in the equation,

$$\exp\left(-B \sin^2\theta/\lambda^2\right) = 2^{-(b_{11}h^2 + b_{22}k^2 + b_{33}\ell^2 + b_{12}hk + b_{23}k\ell + b_{13}h\ell)}$$

TABLE III.

Standard deviations of the final atomic co-ordinates (Å).

Atom	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$
C(1)	0.008	0.009	0.017
C(2)	0.009	0.008	0.013
C(3)	0.009	0.009	0.013
C(4)	0.008	0.008	0.017
C(5)	0.010	0.008	0.016
C(6)	0.008	0.009	0.015
N(1)	0.008	0.008	0.012
N(2)	0.008	0.007	0.016
O(1)	0.009	0.008	0.012
O(2)	0.009	0.007	0.019
Cl	0.002	0.002	0.007

TABLE IV. Measured and calculated values of the structure factors.

h	k	ℓ	$\lvert F_o\rvert$	$\lvert F_c\rvert$	α
0	1	1	53	56	202
0	2	0	14	13	0
		2	19	17	279
0	3	1	65	69	74
0	4	0	49	50	0
		2	14	15	39
0	5	1	25	25	351
0	6	0	22	22	180
		2	31	28	117
0	7	1	36	32	131
0	8	0	41	36	180
		2	36	32	43
0	9	1	9	9	270
0	10	0	20	16	180
		2	13	13	101
0	11	1	27	25	214
0	12	0	5	4	180
		2	12	10	261
0	13	1	42	37	232
0	14	0	7	8	180
		2	9	8	337
0	15	1	18	16	309
0	16	0	18	20	0
		2	13	10	281
0	17	1	2	3	41
0	18	0	3	4	0
		2	9	7	295
0	19	1	14	12	23
0	20	0	1	2	0
0	21	1	6	7	25
1	1	0	9	7	0
		1	82	72	1
		2	35	32	248
1	2	0	25	31	0
		1	19	18	310
		2	25	26	92
1	3	0	5	6	180
		1	22	19	44
		2	15	17	239
1	4	0	33	30	180
		1	24	21	95
		2	20	17	107
1	5	0	23	23	180
		1	33	28	262
		2	17	16	86
1	6	0	22	19	180
		1	30	25	30
		2	37	33	117
1	7	0	45	44	180
		1	37	33	231
		2	17	16	156
1	8	0	5	5	0
		1	18	19	103
		2	15	14	166
1	9	0	7	5	180
		1	27	27	215
		2	14	13	86
1	10	0	20	21	0
		1	17	15	249
		2	15	14	264
1	11	0	15	16	180
		1	10	10	217
		2	6	5	149
1	12	0	21	20	0
		1	10	10	164
		2	19	15	245
1	13	0	13	14	0
		1	13	12	108
		2	3	3	1
1	14	0	7	7	0
		1	13	12	218
		2	22	20	265
1	15	0	6	6	180
		1	<2	1	327
		2	4	3	222
1	16	0	8	9	180
		1	7	6	74
		2	2	3	24
1	17	0	6	7	0
		1	9	9	45
		2	7	6	280
1	18	0	7	8	180
		1	5	4	26
		2	8	7	69
1	19	0	3	3	0
		1	6	5	79
		2	3	3	276
1	20	0	11	12	180
		1	7	6	67
2	0	0	38	52	180
		1	107	141	60
		2	21	25	24
2	1	0	28	37	0
		1	47	52	302
		2	27	26	240
2	2	0	39	45	180
		1	27	23	103
		2	8	8	126
2	3	0	58	63	180
		1	12	12	147
		2	24	23	108
2	4	0	20	22	0
		1	15	13	93
		2	13	13	18
2	5	0	18	14	180
		1	32	31	268
		2	24	22	59
2	6	0	15	14	180
		1	17	18	234
		2	12	11	280
2	7	0	4	4	180
		1	17	18	2
		2	14	14	139
2	8	0	42	42	0
		1	29	27	195
		2	5	4	262
2	9	0	<2	2	0
		1	5	5	337
		2	3	3	321
2	10	0	10	9	0
		1	11	11	246
		2	6	6	261
2	11	0	22	20	0
		1	12	13	22
		2	16	15	266
2	12	0	9	9	0
		1	6	7	350
		2	5	3	58
2	13	0	38	40	0
		1	10	9	47
		2	19	18	283
2	14	0	5	5	0
		1	3	3	204
		2	8	7	123
2	15	0	6	6	0
		1	6	5	127
		2	10	10	16
2	16	0	8	8	180
		1	15	15	55
		2	2	2	168
2	17	0	<2	0	360
		1	4	4	219
		2	5	4	43
2	18	0	<2	0	180
		1	4	5	52
		2	6	5	106
2	19	0	8	9	180
		1	6	5	207
		2	9	9	85
2	20	0	1	0	180
		1	2	3	76
2	21	0	4	5	180
3	1	0	22	26	180
		1	13	9	211
		2	53	50	72
3	2	0	12	15	180
		1	15	14	176
		2	11	10	321
3	3	0	29	31	180
		1	15	14	308
		2	8	7	114
3	4	0	5	5	0
		1	25	22	208
		2	4	4	163
3	5	0	36	37	0
		1	25	24	204
		2	10	10	302
3	6	0	46	42	180
		1	38	34	245
		2	2	3	356
3	7	0	19	19	0
		1	19	18	279
		2	26	27	278
3	8	0	21	21	180
		1	5	4	100
		2	5	4	119
3	9	0	36	35	0
		1	8	7	328
		2	19	18	282
3	10	0	4	4	0
		1	16	16	23
		2	<2	1	280
3	11	0	<2	1	180
		1	5	5	239
		2	12	13	261
3	12	0	13	12	180
		1	21	20	50
		2	4	5	258
3	13	0	7	8	180
		1	8	8	5
		2	2	2	100
3	14	0	10	9	0
		1	15	16	8
		2	4	3	248
3	15	0	4	4	180
		1	5	4	256
		2	6	5	113
3	16	0	4	4	180
		1	4	4	203
		2	3	3	181
3	17	0	7	7	180
		1	3	3	51
		2	10	10	85
3	18	0	<2	0	180
		1	7	8	222
		2	<2	0	315
3	19	0	6	6	180
		1	3	3	4
		2	5	5	129
3	20	0	<1	0	0
		1	9	8	235
4	0	0	56	68	180
		1	52	38	233
		2	50	46	99
4	1	0	22	27	0
		1	23	20	4
		2	16	14	12
4	2	0	26	30	180
		1	26	26	233
		2	18	21	208
4	3	0	19	20	0
		1	25	26	208
		2	9	9	290
4	4	0	12	13	0
		1	12	13	84
4	4	2	7	7	112
4	5	0	40	41	0
		1	15	17	212
		2	15	16	289
4	6	0	5	6	0
		1	6	4	63
		2	16	16	256
4	7	0	6	5	180
		1	14	14	167
		2	11	10	38
4	8	0	10	9	0
		1	29	31	57
		2	17	17	245
4	9	0	2	2	0
		1	5	4	244
		2	9	9	36
4	10	0	3	3	0
		1	11	11	51
		2	2	2	282
4	11	0	16	15	180
		1	10	11	63
		2	12	14	84
4	12	0	4	5	180
		1	9	9	109
		2	6	5	35
4	13	0	14	16	180
		1	19	21	61
		2	9	9	74
4	14	0	<2	1	0
		1	3	3	242
		2	<2	0	269
4	15	0	7	7	180
		1	3	4	95
		2	5	5	194
4	16	0	12	12	180
		1	8	8	249
		2	7	7	87
4	17	0	7	7	0
		1	3	3	113
		2	4	4	253
4	18	0	3	4	180
		1	5	6	233
		2	2	3	73
4	19	0	4	5	0
		1	6	5	243
4	20	0	2	2	180
		1	3	3	349
5	1	0	18	22	0
		1	33	27	205
		2	14	13	262
5	2	0	9	10	0
		1	10	8	319
		2	12	13	254
5	3	0	9	8	0
		1	11	11	213
		2	5	5	348
5	4	0	18	15	0
		1	12	14	48
		2	18	22	269
5	5	0	20	20	0
		1	16	19	24
		2	3	3	287
5	6	0	35	37	0
		1	15	16	275
		2	15	15	287
5	7	0	2	3	180
		1	18	21	61
		2	8	7	53
5	8	0	2	2	0
		1	12	12	218
		2	6	6	303
5	9	0	<2	1	180
		1	16	20	54
		2	18	18	66
5	10	0	13	13	180
		1	7	8	266
		2	6	6	104
5	11	0	<2	1	180
		1	5	6	352
		2	<2	1	342
5	12	0	14	13	180
		1	10	10	221
		2	15	16	91
5	13	0	4	3	0
		1	6	6	208
		2	6	7	55
5	14	0	10	9	180
		1	<2	0	170
		2	10	12	80
5	15	0	3	3	0
		1	5	5	235
		2	7	7	296
5	16	0	2	2	0
		1	<2	1	310
		2	<2	3	172
5	17	0	<2	1	0
		1	7	8	207
		2	3	2	289
5	18	0	6	6	0
		1	<1	2	17
		2	4	4	259
5	19	0	2	1	180
		1	7	6	233
5	20	0	3	4	0
6	0	0	37	45	0
		1	23	22	225
		2	15	13	258
6	1	0	16	17	180
		1	9	8	48
		2	4	4	60
6	2	0	19	17	0
		1	15	14	325
6	2	2	16	15	269
6	3	0	9	8	0
		1	24	24	83
		2	7	7	240
6	4	0	11	11	180
		1	2	1	9
		2	6	7	111
6	5	0	4	2	0
		1	25	27	43
		2	9	9	219
6	6	0	15	14	180
		1	7	5	2
		2	4	6	148
6	7	0	3	2	180
		1	5	6	131
		2	16	17	247
6	8	0	25	25	180
		1	7	8	315
		2	18	21	84
6	9	0	12	11	0
		1	6	7	128
		2	4	4	196
6	10	0	15	15	180
		1	4	5	239
		2	3	4	127
6	11	0	5	6	180
		1	10	12	222
		2	2	3	179
6	12	0	6	6	180
		1	2	3	201
		2	6	7	200
6	13	0	8	9	180
		1	11	13	225
		2	6	7	114
6	14	0	5	5	0
		1	<2	2	331
		2	4	5	286
6	15	0	2	1	180
		1	4	5	275
		2	3	4	140
6	16	0	7	8	0
		1	4	5	192
		2	7	7	273
6	17	0	4	4	180
		1	5	5	37
6	18	0	8	9	0
		1	<1	1	225
6	19	0	2	2	0
		1	3	4	53
7	1	0	11	11	0
		1	21	19	36
		2	12	11	280
7	2	0	2	0	0
		1	7	6	21
		2	12	10	101
7	3	0	<2	0	180
		1	8	8	84
		2	7	8	306
7	4	0	12	11	180
		1	12	12	38
		2	18	20	79
7	5	0	4	4	180
		1	6	6	83
		2	14	15	72
7	6	0	3	2	0
		1	20	19	54
		2	7	7	109
7	7	0	18	19	180
		1	8	9	197
		2	4	5	144
7	8	0	13	13	0
		1	7	8	61
		2	<2	0	326
7	9	0	10	9	180
		1	12	14	199
		2	6	7	116
7	10	0	9	9	0
		1	7	8	281
		2	3	3	337
7	11	0	<2	0	180
		1	3	4	129
		2	<2	3	135
7	12	0	13	11	0
		1	7	8	207
		2	8	9	274
7	13	0	4	5	0
		1	3	3	113
		2	3	3	238
7	14	0	3	3	0
		1	5	7	238
		2	3	3	293
7	15	0	3	4	0
		1	5	6	55
		2	4	4	232
7	16	0	2	2	180
		1	2	1	234
		2	4	4	341
7	17	0	5	5	0
		1	5	5	37
7	18	0	2	2	180
		1	2	2	33
8	0	0	5	6	0
		1	18	14	37
		2	8	7	349
8	1	0	6	5	180
		1	10	8	261
		2	9	9	125
8	2	0	11	10	180
		1	11	9	68
		2	4	4	338
8	3	0	20	19	180
		1	4	3	276
8	3	2	4	4	97
8	4	0	3	3	0
		1	11	11	243
		2	4	3	33
8	5	0	24	22	180
		1	10	10	289
		2	16	16	79
8	6	0	<2	0	180
		1	8	8	263
		2	3	2	35
8	7	0	4	3	180
		1	7	7	350
		2	5	4	97
8	8	0	12	11	0
		1	15	17	209
		2	2	2	331
8	9	0	9	9	180
		1	6	6	2
		2	2	3	256
8	10	0	13	11	0
		1	7	8	271
		2	<2	1	275
8	11	0	6	6	0
		1	<2	1	9
		2	8	9	267
8	12	0	<2	2	0
		1	4	4	304
		2	<2	1	76
8	13	0	10	11	0
		1	<2	1	231
		2	6	6	272
8	14	0	<2	0	180
		1	4	4	39
		2	5	4	106
8	15	0	2	2	0
		1	2	2	219
		2	4	5	293
8	16	0	1	1	180
		1	6	7	36
8	17	0	2	2	180
		1	3	3	190
9	1	0	12	12	180
		1	6	5	99
		2	9	10	103
9	2	0	4	3	180
		1	6	6	223
		2	3	3	4
9	3	0	4	3	180
		1	5	5	100
		2	9	9	163
9	4	0	5	4	180
		1	18	18	195
		2	<2	1	321
9	5	0	5	5	180
		1	7	7	196
		2	5	4	241
9	6	0	18	16	180
		1	7	8	242
		2	3	3	98
9	7	0	8	7	0
		1	3	4	259
		2	7	8	252
9	8	0	9	8	180
		1	6	6	109
		2	2	3	36
9	9	0	13	11	0
		1	5	5	295
		2	7	8	264
9	10	0	2	2	0
		1	5	6	94
		2	2	1	12
9	11	0	7	6	180
		1	<2	2	359
		2	5	5	279
9	12	0	4	4	0
		1	7	9	48
		2	3	4	293
9	13	0	2	2	180
		1	<2	2	356
		2	2	3	71
9	14	0	5	4	0
		1	3	3	54
		2	1	2	252
9	15	0	8	8	180
		1	2	2	348
9	16	0	4	3	0
		1	1	2	104
10	0	0	2	1	180
		1	4	3	203
		2	8	9	89
10	1	0	3	3	0
		1	6	6	254
		2	3	4	290
10	2	0	4	4	180
		1	4	4	292
		2	7	7	110
10	3	0	14	12	0
		1	6	6	210
		2	3	4	278
10	4	0	14	13	0
		1	<2	1	68
		2	2	3	0
10	5	0	13	12	0
		1	11	12	214
		2	2	2	251
10	6	0	5	4	0
		1	3	3	88
		2	2	3	282
10	7	0	<2	0	0
		1	5	5	178
		2	2	2	22
10	8	0	7	7	0
10	8	1	6	7	46
		2	7	8	274
10	9	0	2	2	0
		1	4	5	243
		2	5	6	93
10	10	0	2	2	0
		1	6	6	77
		2	2	3	315
10	11	0	3	2	180
		1	3	4	24
		2	<2	2	116
10	12	0	<2	1	0
		1	3	3	150
		2	4	4	346
10	13	0	2	2	180
		1	4	5	46
10	14	0	4	3	180
		1	3	3	230
11	1	0	-2	2	180
		1	6	7	247
		2	<2	1	238
11	2	0	4	4	0
		1	2	2	66
		2	4	5	257
11	3	0	7	7	180
		1	5	5	290
		2	3	3	269
11	4	0	12	11	0
		1	5	6	5
		2	9	9	252
11	5	0	5	4	0
		1	4	4	308
		2	2	2	211
11	6	0	9	8	0
		1	4	4	261
		2	3	3	260
11	7	0	2	2	180
		1	5	5	47
		2	<2	0	49
11	8	0	<2	0	360
		1	2	2	238
		2	2	2	191
11	9	0	<2	0	0
		1	5	6	55
		2	4	4	55
11	10	0	6	4	180
		1	1	2	314
		2	4	4	163
11	11	0	<2	1	0
		1	<1	0	263
		2	2	3	139
11	12	0	7	6	180
		1	3	3	114
11	13	0	2	1	0
		1	2	3	201
12	0	0	3	4	0
		1	2	2	187
		2	2	3	290
12	1	0	4	4	0
		1	2	2	29
		2	<2	1	339
12	2	0	<2	0	180
		1	3	4	170
		2	<2	2	292
12	3	0	<2	0	180
		1	7	8	56
		2	2	2	297
12	4	0	<2	1	180
		1	4	5	90
		2	2	2	325
12	5	0	2	2	0
		1	5	6	33
		2	4	5	271
12	6	0	5	3	180
		1	2	2	33
		2	1	2	140
12	7	0	2	1	0
		1	1	2	49
		2	2	3	248
12	8	0	5	4	180
		1	2	2	54
		2	3	5	81
12	9	0	3	2	0
		1	<1	1	203
12	10	0	6	4	180
		1	2	2	336
13	1	0	6	5	0
		1	<1	1	331
		2	1	2	306
13	2	0	4	3	180
		1	2	2	15
		2	2	2	106
13	3	0	5	4	0
		1	<1	2	241
		2	2	2	24
13	4	0	5	4	180
		1	4	5	65
		2	2	5	70
13	5	0	<1	1	0
		1	<1	0	26
13	6	0	<1	0	180
		1	3	3	56
13	7	0	<1	3	180
		1	1	2	229
13	8	0	4	1	0
13	9	0	2	3	180
14	0	0	<1	0	180
14	1	0	2	2	180
14	2	0	<1	1	180
14	3	0	1	5	180
14	4	0	5	2	180
14	5	0	2	2	180

TABLE V

Intramolecular bonded distances (Å)

Atoms	Uncorrected	Corrected	E.s.d.
C(1) - C(2)	1.394	1.400	0.014
C(2) - C(3)	1.396	1.401	0.012
C(3) - C(4)	1.401	1.407	0.012
C(4) - C(5)	1.387	1.392	0.015
C(5) - C(6)	1.391	1.395	0.013
C(6) - C(1)	1.420	1.425	0.013
C(1) - N(1)	1.382	1.386	0.012
C(2) - Cl	1.760	1.766	0.009
C(4) - N(2)	1.466	1.471	0.013
N(2) - O(1)	1.235	1.240	0.015
N(2) - O(2)	1.236	1.240	0.011

TABLE VI

Interbond angles (°)

C(1) - C(2) - C(3)	123.3	C(1) - C(2) - Cl	118.4
C(2) - C(3) - C(4)	116.9	C(3) - C(2) - Cl	118.2
C(3) - C(4) - C(5)	122.9	C(3) - C(4) - N(2)	118.3
C(4) - C(5) - C(6)	118.0	C(5) - C(4) - N(2)	118.6
C(5) - C(6) - C(1)	122.2	C(4) - N(2) - O(1)	118.1
C(6) - C(1) - C(2)	116.7	C(4) - N(2) - O(2)	118.9
C(2) - C(1) - N(1)	124.0	O(1) - N(2) - O(2)	123.0
C(6) - C(1) - N(1)	119.3		

TABLE VII.

Intermolecular distances ≤ 3.87 Å.

O(2)	....	$N(1)_{III}$	3.047	C(2)	....	$N(1)_{I}$	3.656
N(1)	....	$N(1)_{V}$	3.182	O(1)	....	Cl_{II}	3.656
O(1)	....	$C(5)_{II}$	3.365	Cl	....	$N(1)_{I}$	3.671
O(1)	....	$N(2)_{I}$	3.406	C(3)	....	$C(5)_{I}$	3.691
O(1)	....	$C(4)_{I}$	3.466	C(2)	....	$C(6)_{I}$	3.699
C(4)	....	$C(5)_{I}$	3.478	N(2)	....	$C(4)_{I}$	3.700
C(2)	....	$C(1)_{I}$	3.481	C(1)	....	$N(1)_{V}$	3.711
O(2)	....	$C(6)_{II}$	3.514	C(3)	....	$C(2)_{I}$	3.720
O(1)	....	$O(2)_{I}$	3.519	C(1)	....	$N(1)_{I}$	3.751
O(1)	....	$C(6)_{IV}$	3.526	N(2)	....	$O(2)_{I}$	3.755
C(3)	....	$C(6)_{I}$	3.564	C(5)	....	$C(6)_{I}$	3.761
N(2)	....	$C(5)_{I}$	3.571	C(3)	....	$C(4)_{I}$	3.794
O(1)	....	Cl_{VII}	3.587	Cl	....	$C(1)_{I}$	3.804
C(4)	....	$C(6)_{I}$	3.615	O(1)	....	$C(5)_{I}$	3.807
C(3)	....	$C(1)_{I}$	3.621	C(1)	....	$C(6)_{I}$	3.842
O(1)	....	$C(5)_{IV}$	3.627	N(2)	....	$C(6)_{II}$	3.846
Cl	....	$O(2)_{VI}$	3.645	O(2)	....	Cl_{III}	3.846

The subscripts refer to the following equivalent positions:

I	$x,$	$y,$	$1 + z$
II	$\frac{1}{2} + x,$	$\frac{1}{2} - y,$	z
III	$\frac{1}{2} - x,$	$-\frac{1}{2} + y,$	$\frac{1}{2} + z$
IV	$\frac{1}{2} + x,$	$\frac{1}{2} - y,$	$1 - z$
V	$\bar{x},$	$1 - y,$	$\frac{1}{2} + z$
VI	$\frac{1}{2} - x,$	$\frac{1}{2} + y,$	$\frac{1}{2} + z$
VII	$1 - x,$	$1 - y,$	$\frac{1}{2} + z$

TABLE VIII.

Deviations (Å) of the atoms from various planes.

(a) Plane through C(1),C(2),C(3),C(4),C(5),C(6),N(1),N(2),O(1),O(2), Cl.
(b) Plane through C(1),C(2),C(3),C(4),C(5),C(6),N(1),N(2), Cl.
(c) Plane through C(1),C(2),C(3),C(4),C(5),C(6),N(1), Cl.
(d) Plane through C(4),N(2),O(1),O(2).

Atom	(a)	(b)	(c)	(d)
C(1)	-0.013	-0.005	-0.001	-
C(2)	0.038	0.028	0.024	-
C(3)	0.023	0.004	-0.015	-
C(4)	0.044	0.032	0.008	0.003
C(5)	0.000	0.005	-0.011	-
C(6)	-0.007	0.008	0.006	-
N(1)	-0.041	-0.023	-0.005	-
N(2)	-0.016	-0.039	-0.077	-0.012
O(1)	-0.070	-0.108	-0.153	0.004
O(2)	0.032	0.016	-0.026	0.004
Cl	0.010	-0.009	-0.006	-

TABLE IX.

Direction cosines of molecular axes (OP, OQ, OR) with respect to orthogonal crystallographic axes.

Axis	a	b	c
OP	0.8255	0.3436	0.4477
OQ	-0.3302	0.9374	-0.1107
OR	0.4577	0.0564	-0.8873

Coordinates of the centre of mass, O, and the centre of oscillation, O'.

	x/a	y/b	z/c
O	0.3082	0.3942	0.2839
O'	0.2730	0.4610	0.2499

TABLE X.

Observed and calculated values of U_{ij} (in units of 10^{-2} Å^2).

Atom		U_{11}			U_{22}	
	Obs.	Calc (i)	Calc (ii)	Obs.	Calc (i)	Calc (ii)
C(1)	4.94	6.22	4.90	4.95	4.83	4.92
C(2)	4.66	5.83	4.86	4.82	4.29	4.50
C(3)	5.75	5.18	5.55	4.63	4.53	4.69
C(4)	6.25	5.85	6.97	4.32	4.26	4.48
C(5)	6.78	5.62	6.60	5.22	5.41	5.37
C(6)	5.83	5.25	5.13	5.68	6.16	5.95
N(1)	6.00	8.84	5.77	5.15	5.48	5.44
N(2)	10.22	8.41	10.21	4.17	4.29	4.50
O(1)	11.57	8.91	10.83	6.06	5.35	5.32
O(2)	12.51	11.08	13.07	4.83	4.39	4.57
Cl	4.89	8.16	5.49	5.15	5.21	5.22

Atom		U_{33}			U_{12}	
	Obs.	Calc (i)	Calc (ii)	Obs.	Calc (i)	Calc (ii)
C(1)	2.46	2.96	2.30	0.38	0.51	0.00
C(2)	2.76	2.42	1.81	-1.52	-0.41	-0.19
C(3)	2.91	1.88	2.52	0.42	-0.21	0.28
C(4)	2.12	2.44	3.28	0.19	-0.37	-0.28
C(5)	2.16	2.61	3.94	-1.47	-0.98	-1.36
C(6)	3.79	2.48	3.59	-0.78	0.09	-0.73
N(1)	4.29	5.69	3.52	0.98	1.84	0.81
N(2)	4.02	4.86	5.56	0.85	0.10	0.30
O(1)	6.67	5.65	6.95	2.50	1.75	2.14
O(2)	9.34	7.52	7.64	-0.73	-1.15	-1.38
Cl	3.60	5.04	3.02	-1.63	-1.95	-0.79

Atom		U_{23}			U_{13}	
	Obs.	Calc (i)	Calc (ii)	Obs.	Calc (i)	Calc (ii)
C(1)	-0.71	-0.55	-0.55	0.64	0.82	0.69
C(2)	0.13	-0.65	-0.68	0.68	0.67	0.65
C(3)	-1.14	-0.60	-0.63	0.27	0.70	0.78
C(4)	-1.00	-0.64	-0.69	1.57	0.69	0.66
C(5)	-0.76	-0.47	-0.48	1.24	0.58	0.36
C(6)	0.00	-0.36	-0.31	-0.29	0.74	0.50
N(1)	-0.91	-0.45	-0.42	0.05	1.00	0.92
N(2)	-1.12	-0.73	-0.75	-0.69	0.74	0.90
O(1)	-0.13	-0.69	-0.58	2.51	1.02	1.48
O(2)	-0.90	-0.66	-0.72	0.58	0.55	0.59
Cl	0.17	-0.49	-0.51	1.49	0.43	0.49

TABLE XI.

The values of $\Delta Q(\mathring{A})$, the shift along OQ of the centre of oscillation from the centre of mass, and the corresponding $\sum|\Delta U_{ij}|$'s(in units of 10^{-2} $\mathring{A}^2$).

ΔQ ($\mathring{A}$)	0.0	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8
$\sum\|\Delta U_{ij}\|$	50.56	45.01	39.26	35.85	34.34	33.39	33.32	33.67	34.30	34.84

TABLE XII.

Values of T_{ij} in 10^{-2} $\mathring{A}^2$ and ω_{ij} in deg.^{2}

$$T = \begin{bmatrix} 4.87 & -0.11 & 0.66 \\ & 4.47 & -0.69 \\ & & 1.78 \end{bmatrix} \qquad \omega = \begin{bmatrix} 8.64 & 0.29 & -0.27 \\ & 13.63 & -3.26 \\ & & 12.23 \end{bmatrix}$$

TABLE XIII.

Values of $\sigma(T_{ij})$ in 10^{-2} $\mathring{A}^2$ and $\sigma(\omega_{ij})$ in deg.^{2}

$$\sigma(T) = \begin{bmatrix} 0.29 & 0.22 & 0.29 \\ & 0.23 & 0.25 \\ & & 0.44 \end{bmatrix} \sigma(\omega) = \begin{bmatrix} 1.08 & 1.49 & 0.97 \\ & 6.03 & 2.62 \\ & & 0.95 \end{bmatrix}$$

TABLE XIV.

Carbon-chlorine bond lengths in some aromatic molecules.

Molecule	C–Cl (Å)	Estimated standard deviation.	Reference.
4:4′-Dichlorodiphenyl-sulphone	1.736	0.007	1
o-Chlorobenzoic acid	1.737	0.007	2
1:4:5:8-Tetra-chloronaphthalene	1.740 (av.)	0.007	3
Chloranil	1.714 (av.)	0.008	4
p-Dichlorobenzene (at -140°C)	1.74	0.01	5
1:3:5 - Trichlorobenzene	1.71 (av.)	0.01	6
Tetrachlorohydro-quinone	1.733 (av.)	0.011	7
Chloranil	1.749 (av.)	0.012	8
5 - Chlorosalicyl-aldoxime	1.777	0.012	9
9:10-Dichloro-anthracene	1.74	0.015	10

1. Sime, J.G. and Abrahams, S.C. (1960). Acta Cryst. 13, 1.
2. Ferguson, G. and Sim, G.A. (1961). Acta Cryst. 14, 1262.
3. Gafner, G. and Herbstein, F.H. (1962). Acta Cryst. 15, 1081.
4. Chu, S.S.C., Jeffrey, G.A. and Sakurai, T. (1962). Acta Cryst. 15, 661.
5. Frasson, E., Garbuglio, C. and Bezzi, S. (1959). Acta Cryst. 12, 126.
6. Milledge, H.J. and Pant, L.M. (1960). Acta Cryst. 13, 285.
7. Sakurai, T. (1962). Acta Cryst. 15, 443.
8. Ueda, I. (1961). J. Phys. Soc. Japan, 16, 1185
9. Simonsen, S.H., Pfleuger, C.E. and Thomson, C.M. (1961). Acta Cryst. 14, 269.
10. Trotter, J. (1959). Acta Cryst. 12, 54.

REFERENCES

Abrahams, S.C. and Robertson, J.M. (1948). Acta Cryst. 1, 252.

Ahmed, F.R. and Cruickshank, D.W.J. (1953). Acta Cryst. 6, 385.

Asher, J.D.M. and Sim, G.A. (1962a). Proc.Chem.Soc. p.111.
(1962b). Proc.Chem.Soc. p.335.
(1963a). Personal communication.
(1963b). Personal communication.

Asmis, H., Schmid, H. and Karrer, P.(1954). Helv.Chim.Acta, 37, 1983.

Bartell, L.S. and Bonham, R.A.(1957). J.Chem. Phys. 27, 1414.

Bartlett, M.F., Schlittler, E., Sklar, R., Taylor, W.I., Amai, R.L.S. and Wenkert, E. (1960). J.Amer.Chem.Soc. 82, 3792.

Bartlett, M.F., Sklar, R. and Taylor, W.I.(1960). J.Amer.Chem. Soc. 82, 3790.

Bartlett, M.F., Sklar, R., Taylor, W.I., Schlittler, E., Amai, R.L.S., Beak, P., Bringi, N.V. and Wenkert, E.(1962). J.Amer.Chem. Soc. 84, 622.

Barton, D.H.R. and De Mayo, P.(1957). Quart.Rev. 11, 189.

Barton, D.H.R. and Levisalles, J.E.D.(1958). J.Chem.Soc.p.4518.

Barton, D.H.R. and Pinhey, J.T.(1960). Proc.Chem.Soc. p.279.

Battersby, A.R.(1962). Personal communication.

Battersby, A.R., Binks, R., Hodson, H.F. and Yeowell, D.A. (1960). J.Chem.Soc. p.1848.

Battersby, A.R. and Hodson, H.F.(1958). Proc.Chem.Soc. p.287.

Battersby, A.R. and Hodson, H.F.(1960a). J.Chem.Soc. p.736.
(1960b). J.Chem.Soc. p.786.
(1960c). Quart. Rev. 14, 77.

Battersby, A. R., Hodson, H. F., Rao, G. V. and Yeowell, D. A. (1961). Proc. Chem. Soc. p. 412.

Battersby, A. R., Hodson, H. F. and Yeowell, D. A. (1961). Proc. Chem. Soc. p. 223.

Battersby, A. R. and Yeowell, D. A. (1961). Proc. Chem. Soc. p. 17.

Battersby, A. R., Yeowell, D. A., Jackman, L. M., Schroeder, H-D., Hesse, M., Hiltebrand, H., von Philipsborn, W., Schmid, H. and Karrer, P. (1961). Proc. Chem. Soc. p. 413.

Berghuis, J., Haanappel, I. M., Potters, M., Loopstra, B. O., MacGillivary, C. H. and Veenendaal, A. L. (1955). Acta Cryst. 8, 478.

Bernauer, K. (1959). Fortschr. Chem. org. Naturstoff, 17, 184.

Birch, A. S., Hodson, H. F., Moore, B. and Smith, G. F. (1961). Proc. Chem. Soc. p. 63.

Boehm, R. (1897). Arch. Pharm. 235, 660.

Booth, A. D. (1945). Nature, 156, 51.
(1946). Proc. Roy. Soc. A 188, 77.
(1948). Nature, 161, 765.

Bose, A. K., Chatterjee, B. G. and Iyer, R. S. (1956). Indian J. Pharm. 18, 185.

Bragg, W. L. (1913). Proc. Camb. Phil. Soc. 17, 43.

Brown, G. M. and Marsh, R. E. (1960). Acta Cryst. 13, 1037.

Bryan, R. F. and Dunitz, J. D. (1960). Helv. Chim. Acta, 43, 3.

Buerger, M. J. (1951). Acta Cryst. 4, 531.

Čekan, Z., Herout, V. and Šorm, F. (1954). Chem. and Ind. p. 604.

Chu, S. S. C., Jeffrey, G. A. and Sakurai, T. (1962). Acta Cryst. 15, 661.

Clunie, J. S. and Robertson, J. M. (1961). J. Chem. Soc. p. 4382.

Cochran, W. (1951). Acta Cryst. 4, 408.
(1953). Acta Cryst. 6, 260.

Cox, E.G., Cruickshank, D.W.J. and Smith, J.A.S. (1958).
Proc. Roy. Soc. A 247, 1.

Cox. E.G., Dougill, M.W. and Jeffrey, G.A. (1952).
J. Chem. Soc. p. 4854.

Cruickshank, D.W.J. (1956a). Acta Cryst. 9, 754.
(1956b). Acta Cryst. 9, 757.
(1957). Acta Cryst. 10, 504.
(1961) . Acta Cryst. 14, 896.

Cruickshank, D.W.J. and Robertson, A.P. (1953). Acta Cryst.
6, 698.

Curl, R.F. (1959). J. Chem. Phys. 30, 1529.

Debye, P. (1914). Ann. Physik, 43, 49.

Degeilh, R. and Marsh, R.E. (1959). Acta Cryst. 12, 1007.

Djerassi, C., Osiecki, J. and Herz, W. (1957). J. Org. Chem.
22, 1361.

Donohue, J. and Trueblood, K.N. (1956). Acta Cryst. 9, 960.

Dougill, M.W. and Jeffrey, G.A. (1953). Acta Cryst. 6, 831.

Edwards, P.N. and Smith, G.F. (1960). Proc. Chem. Soc. p. 215.

Ferguson, G. (1961). Ph.D. Thesis: University of Glasgow.

Ferguson, G. and Sim, G.A. (1961). Acta Cryst. 14, 1262.
(1962a) Acta Cryst. 15, 346.
(1962b) J. Chem. Soc. p. 1767.

Fisher, R.A. and Yates, F. (1957). Statistical Tables,
Oliver and Boyd, Edinburgh.

Frasson, E., Garbuglio, C. and Bezzi, S. (1959). Acta Cryst.
12, 126.

Fridrichsons, J. and Mathieson, A.McL. (1955). Acta Cryst.
8, 761.
(1962). Acta Cryst.
15, 119.

Gafner, G. and Herbstein, F.H. (1962). Acta Cryst. 15, 1081.

Hamilton, J.A., Hamor, T.A., Robertson, J.M. and Sim, G.A.
(1961). Proc. Chem. Soc. p. 63.

Harker, D. (1936). J. Chem. Phys. 4, 381.

Hartree, D. R. (1928). Proc. Camb. Phil. Soc. 24, 89, 111.

Hirokawa, S. (1955). Acta Cryst. 8, 637.

Huber-Buser, E. and Dunitz, J. D. (1960). Helv. Chim. Acta, 43, 760.

Hughes, D. O. and Small, R. W. H. (1962). Acta Cryst. 15, 933.

Hughes, E. W. (1941). J. Amer. Chem. Soc. 63, 1737.

"International Tables for X-ray Crystallography", Vol. 1 (1952). Birmingham: Kynoch Press.

James, R. W. and Brindley, G. W. (1931). Z. Krist. 78, 470.

Jellinek, F. (1957). Acta Cryst. 10, 277.

Kartha, G. and Ramachandran, G. N. (1955). Acta Cryst. 8, 195.

King, H. (1949). J. Chem. Soc. p. 3263.

Kosolapoff, G. (1953). J. Amer. Chem. Soc. 75, 3596.

Laue, M. von (1913). Physik. Z. 14, 1075.

MacIntyre, A. R. (1947). "Curare, Its Natural History and Clinical Use", University of Chicago Press, Chicago.

Mackay, M. and Hodgkin, D. C. (1955). J. Chem. Soc. p. 3261.

McWeeny, R. (1951). Acta Cryst. 4, 513.

Milledge, H. J. and Pant, L. M. (1960). Acta Cryst. 13, 285.

O'Gorman, J. M., Shand, W. and Schomaker, V. (1950). J. Amer. Chem. Soc. 72, 4222.

Pasternak, R. A. (1956). Acta Cryst. 9, 341.

Patterson, A. L. (1934). Phys. Rev. 46, 372.
(1935). Z. Krist. 90, 517.

Peerdeman, A. F. (1956). Acta Cryst. 9, 824.

Przybylska, M. (1961a). Acta Cryst. 14, 424.
(1961b). Acta Cryst. 14, 429.
(1962). Acta Cryst. 15, 301.

Reed, R. I. (1961). Personal communication.

Rimington, C. and Roets, G. C. S. (1936). Onderstepoort J. Vet. Sci. and Animal Ind. 7, 485.

Robertson, J. M. (1935). J. Chem. Soc. p. 615.
(1936). J. Chem. Soc. p. 1195.
(1943). J. Sci. Instr. 20, 175.

Robertson, J. M. and Woodward, I. P. (1937). J. Chem. Soc. p. 219.
(1940). J. Chem. Soc. p. 36.

Rollett, J. S. (1961). "Computing Methods and the Phase Problem in X-ray Crystal Analysis", Paper 7, p. 87. Editors: R. Pepinsky, J. M. Robertson and J. C. Speakman. Oxford: Pergamon Press.

Sakurai, T. (1962). Acta Cryst. 15, 443.

Schomaker, V., Waser, J., Marsh, R. E. and Bergman, G. (1959) Acta Cryst. 12, 600.

Schroeder, H-D., Hiltebrand, H., Schmid, H. and Karrer, P. (1961). Helv. Chim. Acta, 44, 34.

Silvers, S. and Tulinsky, A. (1962). Tetrahedron Letters, 8, 339.

Sim, G. A. (1957). Acta Cryst. 10, 177.

Sime, J. G. and Abrahams, S. C. (1960). Acta Cryst. 13, 1.

Simonsen, S. H., Pfleuger, C. E. and Thomson, C. M. (1961). Acta Cryst. 14, 269.

"Tables of Interatomic Distances and Configuration in Molecules and Ions", (1958). Chem. Soc. Spec. Publ. No. 11.

Thomas, L. H. and Fermi, E. (1935). "International Tabellen zur Bestimmung von Kristallstrukturen" Borntrager, Berlin. Vol. II, p. 572.

Tomiie, Y. and Stam, C. H. (1958). Acta Cryst. 11, 126.

Trotter, J. (1959). Acta Cryst. 12, 54.
(1960). Tetrahedron, 8, 13.

Trueblood, K. N., Goldish, E. and Donohue, J. (1961). Acta Cryst. 14, 1009.

Truter, M. (1960). J. Chem. Soc. p. 997.

Tunell, G. (1939). Amer. Min. 24, 448.

Ueda, I. (1961). J. Phys. Soc. Japan, 16, 1185.

von Philipsborn, W., Schmid, H. and Karrer, P. (1956). Helv. Chim. Acta, 39, 813.

Wenkert, E., Robb, E. W. and Bringi, N. V. (1957). J. Amer. Chem. Soc. 79, 6570.

Wieland, H., Witkop, B. and Bahr, K. (1947). Annalen, 558, 144.

Wilson, A. J. C. (1942). Nature, London, 150, 152.