Acta Cryst. (1964). **17**, 392

Positivity, Point Atoms, and Pattersons

BY J. KARLE AND H. HAUPTMAN
U.S. Naval Research Laboratory, Washington 25, *D.C., U.S.A.*

(*Received* 2 *May* 1963)

A procedure is given for improving the Patterson function on the basis that it is non-negative. In the course of the procedure it has been found possible to include other types of previous knowledge, *e.g.* $|\mathscr{E}_{\mathbf{h}}|^2 \geq 0$, various kinds of statistical information, minimum interatomic distances, *etc.* Preliminary results are presented which show that Patterson maps are obtainable which are essentially non-negative and which show high resolution. A theoretical analysis is included which clarifies the observed results.

Associated with the improvement in the Patterson function is a corresponding extrapolation of the data beyond the observed range.

1. Introduction

Many methods of crystal structure determination are based on analyses of the Patterson function. Clearly then, the problem of obtaining the best possible Patterson function with the data at hand is of great importance. For example, the phase determining formula (2·3·9) of a previous paper (Hauptman & Karle, 1962) is intimately related to the Patterson function and the quality of the latter therefore determines the accuracy with which phases may be computed. The main purpose of this paper is to discuss methods of introducing previous knowledge in order to improve the quality of the Patterson function.

One kind of previous knowledge which has been very useful in various types of structure determination is the positiveness of certain functions associated with the structure. The concept of positivity was first introduced as an aid in structure determination in 1950. Improved electron distributions in atoms were obtained when the experimental scattering data were extrapolated in such a way as to guarantee the positiveness of the electron distribution (Hauptman & Karle, 1950). This procedure was implemented by Bartell & Brockway (1953) in order to obtain the electron distribution in argon from electron diffraction data.

In another application, the determination of molecular structure by electron diffraction was facilitated by making use of the positiveness of the radial distribution curve, related to the probability distribution of interatomic distances in a molecule (Karle & Karle, 1950). This led to increased accuracy in the determination of interatomic distances and the first evaluations of average amplitudes of vibrational motion.

The positiveness of the electron density function in a crystal formed the basis for the derivation of a complete set of inequalities among the structure factors (Karle & Hauptman, 1950). Harker & Kasper (1948) had previously obtained inequalities based on the various symmetries of the space groups. However, in their derivation implicit use was made of the positive electron density. In fact the Harker–Kasper inequalities were shown to be contained in the set obtained subsequently.

Although the inequalities contain all the information derivable from the positiveness of the electron density function, their mathematical formulation is such that they have as yet only been partially implemented. The present development provides a practical alternative for the implementation of the positivity criterion.

There are other kinds of previous knowledge which may be used to improve the quality of the Patterson function. For example, minimal bonded distances are known. Therefore, if the origin peak is removed, the values of the Patterson function in the vicinity of the origin may be set equal to zero. For complex structures, if a sufficiently extensive set of data is not available, the maxima in the Patterson map corresponding to the bonded distances may not actually appear. Should the maxima corresponding to the next larger distances occur, it is conceivable that the nature of the inner maxima may perhaps be inferred from these. This additional information could then, of course, be inserted into the map. Any additional structural information may be confirmed in the Patterson function, or, if missing, may be inserted. In special cases, peak heights and relative orientations may be previously known and used to adjust the Patterson map.

It will be seen that an important aspect of the utilization of previous knowledge to improve the quality of the Patterson function is the extrapolation of the experimental data beyond the observed range. This affords still another opportunity to introduce additional information, *i.e.* the non-negativity of the magnitudes of the structure factors. Clearly the extension of the available data will materially improve the effectiveness of phase determining procedures as well as direct analyses of the Patterson function.

2. Improvement of Patterson functions by use of positivity

A procedure is presented here which makes use of the known positiveness of the Patterson function in order to improve its quality. In the course of the application of the positiveness criterion, additional previous knowledge may be introduced. The procedure to be described does in fact incorporate various kinds of supplementary information.

We start with a set of quasi-normalized structure factors $\mathscr{E}_{\mathbf{h}}$ (Karle & Hauptman, 1959) defined by

$$\mathscr{E}_{\mathbf{h}} = \frac{1}{\sqrt{\sigma_2}} \sum_{j=1}^{N} Z_j \exp(2\pi i \mathbf{h}.\mathbf{r}_j) \qquad (2{\cdot}1)$$

where Z_j is the atomic number of the jth atom in the unit cell containing N atoms, and

$$\sigma_2 = \sum_{j=1}^{N} Z_j^2 \,.$$

The $\mathscr{E}_{\mathbf{h}}$ have the property that

$$\langle |\mathscr{E}_{\mathbf{h}}|^2 \rangle_{\mathbf{h}} = 1 \,, \qquad (2{\cdot}2)$$

where the average is taken over all vectors $\mathbf{h}$, including extinctions. The Patterson function, $P(\mathbf{r})$, corresponding to a point atom structure with origin peak removed, is then computed from

$$P(\mathbf{r}) = \sigma_2 \langle (|\mathscr{E}_{\mathbf{h}}|^2 - 1) \cos 2\pi \mathbf{h}.\mathbf{r} \rangle_{\mathbf{h}} \,. \qquad (2{\cdot}3)$$

We next define an improved Patterson function $P^+(\mathbf{r})$ by means of

$$\begin{aligned} P^+(\mathbf{r}) &= P(\mathbf{r}) \quad \text{if} \quad P(\mathbf{r}) \geq 0 \,, \\ P^+(\mathbf{r}) &= 0 \qquad\ \text{if} \quad P(\mathbf{r}) < 0 \,. \end{aligned} \qquad (2{\cdot}4)$$

Before proceeding to the next step, two other improvements in the Patterson map may be carried out if desired. Equation (2·2) is of course sufficient to insure that $P(0)=0$. However, it is known that $P(\mathbf{r})=0$ also if $|\mathbf{r}|$ is less than the smallest bonded distance, d, which can occur in the crystal. Hence if $|\mathbf{r}|<d$ we may define $P^+(\mathbf{r})$ to be zero. Again, if the atoms constituting the crystal are known, then the minimum non-zero value of $P(\mathbf{r})$ is also known. Therefore, in defining $P^+(\mathbf{r})$, not only would the negative values of $P(\mathbf{r})$ be replaced by zero, but so would those positive values of $P(\mathbf{r})$ which are significantly smaller than the known minimum value.

Assuming then that an improved Patterson map, $P^+(\mathbf{r})$, has been obtained, as described, we may now invert (2·3), replacing $P(\mathbf{r})$ by $P^+(\mathbf{r})$, to obtain

$$|\mathscr{E}_{\mathbf{h}}|^2 - 1 = C(s) \langle P^+(\mathbf{r}) \cos 2\pi \mathbf{h}.\mathbf{r} \rangle_{\mathbf{r}} \qquad (2{\cdot}5)$$

where the scale factor, $C(s)$, is assumed constant for each small s-interval containing some 200 values of $|\mathscr{E}_{\mathbf{h}}|^2-1$. If $\mathscr{E}_{\mathbf{h}}$ is purely real or purely imaginary as a consequence of space group symmetry, it is known that

$$\langle ||\mathscr{E}_{\mathbf{h}}|^2 - 1| \rangle_{\mathbf{h}} = 0{\cdot}968 \,, \qquad (2{\cdot}6)$$

whereas

$$\langle ||\mathscr{E}_{\mathbf{h}}|^2 - 1| \rangle_{\mathbf{h}} = 0{\cdot}736 \qquad (2{\cdot}7)$$

if $\mathscr{E}_{\mathbf{h}}$ is complex. By averaging the second factor on the right side of (2·5) over some 200 values of $\mathbf{h}$ in each small s-interval, (2·6) and (2·7) enable one to evaluate the scale factor $C(s)$ in (2·5) and therefore to compute $|\mathscr{E}_{\mathbf{h}}|^2-1$ on an absolute scale.

It is to be emphasized that in this manner we not only obtain new values for the observed $|\mathscr{E}_{\mathbf{h}}|^2-1$ but, in addition, we obtain values for those $|\mathscr{E}_{\mathbf{h}}|^2-1$ outside the observable range. In this connection, it is important in decomposing the s-range into the small s-intervals for averaging purposes, that the observed $|\mathscr{E}_{\mathbf{h}}|^2-1$'s be isolated from the extrapolated ones. This is a consequence of the fact that the scale factor $C(s)$ in (2·5) is much larger (by a factor of about 4) for the extrapolated $|\mathscr{E}_{\mathbf{h}}|^2-1$ than for the observed ones, since the extrapolated $|\mathscr{E}_{\mathbf{h}}|^2-1$ may be regarded as making zero contributions to the average in (2·3). Naturally the values of $|\mathscr{E}_{\mathbf{h}}|^2-1$ as computed from (2·5) will, in the observable range, differ somewhat from the observed values since $P^+(\mathbf{r})$ used in (2·5) is not identical with $P(\mathbf{r})$ as computed in (2·3).

We now have a set of $|\mathscr{E}_{\mathbf{h}}|^2-1$ values from (2·5) some of which, for various reasons, will be less than -1. We may now make use of the known property of the $|\mathscr{E}_{\mathbf{h}}|^2$, namely,

$$|\mathscr{E}_{\mathbf{h}}|^2 \geq 0 \,, \qquad (2{\cdot}8)$$

and replace by -1 all computed values of $|\mathscr{E}_{\mathbf{h}}|^2-1$ which happen to be less than -1. This will result in increasing slightly the average value of $|\mathscr{E}_{\mathbf{h}}|^2$ which in turn calls for a rescaling of the $|\mathscr{E}_{\mathbf{h}}|^2$ in order to insure that $\langle |\mathscr{E}_{\mathbf{h}}|^2 \rangle_{\mathbf{h}} = 1$. Having carried out these operations we obtain a set of $|\mathscr{E}_{\mathbf{h}}|^2-1$ values. In the observable range we replace these values by their observed values, and retain the computed values in the extrapolated range. We have now an extended set of $|\mathscr{E}_{\mathbf{h}}|^2-1$ values, the observed set plus an extrapolated set, to be used in the next step. We designate this new set of values by $|\mathscr{E}_{\mathbf{h}}^+|^2-1$.

The extended set of $|\mathscr{E}_{\mathbf{h}}^+|^2-1$ is now used in (2·3) to obtain a new Patterson function $P_1(\mathbf{r})$. Because of the way that the extrapolated values, $|\mathscr{E}_{\mathbf{h}}^+|^2-1$, have been obtained, $P_1(\mathbf{r})$ is expected to be an improvement over the first Patterson map $P(\mathbf{r})$, in that the negative excursions should be less prominent. We next treat $P_1(\mathbf{r})$ in the same fashion as $P(\mathbf{r})$ in order to extrapolate the values of $|\mathscr{E}_{\mathbf{h}}|^2-1$ still further, obtain a third Patterson map $P_2(\mathbf{r})$, *etc.* In each successive cycle we have found it expedient to increase the previous range of $|\mathscr{E}_{\mathbf{h}}|^2-1$ values by 10–20%. In this way we finally obtain a Patterson map which is essentially positive and consistent with the observed data. Simultaneously we obtain an extrapolation of the data beyond the observed range. The use of these additional data gives rise to the expectation that the resolution and accuracy of the final Patterson function will be improved.

A program involving the successive cycles described above has been written by Dr J. Holden of the Naval Ordnance Laboratory, White Oaks, Md. The program incorporates provision for printing the number and average of the negative values of successive Patterson maps as well as the scale factors for the $||\mathscr{E}_{\mathbf{h}}|^2-1|$ and $|\mathscr{E}_{\mathbf{h}}|^2$ at each cycle. In addition an R index,

$$R=\frac{\Sigma||\mathscr{E}_o|^2-|\mathscr{E}_c|^2|}{\Sigma|\mathscr{E}_o|^2} \qquad (2\cdot 9)$$

comparing the observed $|\mathscr{E}_o|^2$ with the computed $|\mathscr{E}_c|^2$ at each cycle, is printed. A typical comparison from a test calculation on arginine data is shown in Figs. 1 and 2. Fig. 1 shows a portion of the initial Patterson function calculated from 1406 observed data. Fig. 2 shows the same portion using 2688 data obtained after six iterations of the above outlined procedure. Improvement of the resolution is apparent from inspection and is consistent with the true structure which has been subsequently obtained (I. L. Karle & J. Karle, to be published). We also noted that in the course of the extrapolation of the data, certain of the observed intensities, evidently affected by absorption errors, were corrected by the iterative procedure. Further studies of the details of the procedure are being made and will be reported in due course.

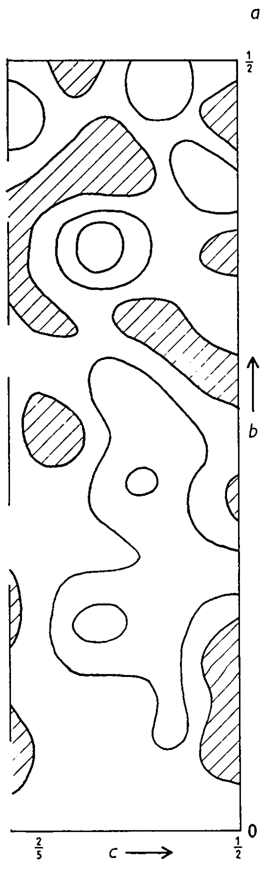

Fig. 1.

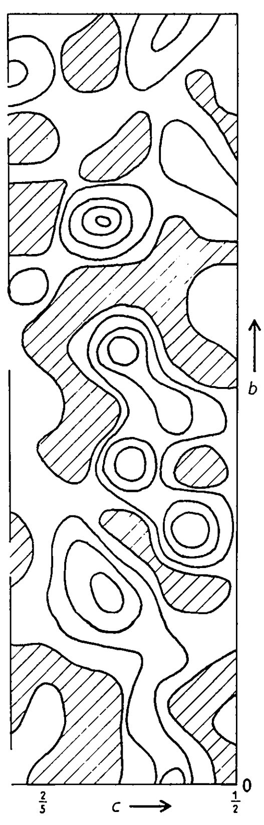

Fig. 2.

Fig. 1. Portion of the original Patterson function for arginine (1406 observed data), computed from (2·3).

Fig. 2. Portion of the Patterson function for arginine after six cycles of iteration (2688 data), computed from (2·3).

3. Improvement of the Patterson function by use of known interatomic vectors

Information concerning interatomic vectors is occasionally known independently of the Patterson calculation. This information may be checked against the computed Patterson function. If necessary, it is evident that the Patterson map may be altered to conform with this *a priori* knowledge.

A case of particular interest occurs in which general structural information is combined with features appearing in the Patterson map to yield additional detail otherwise unobtainable from the limited experimental data. Protein structures constitute an example in which the data are so limited that the shortest interatomic vectors will not appear in the Patterson function. If the 2·4 Å shell is not resolved by the available data, it is possible that the application of the positivity criterion may reveal it. If we assume that the 2·4 Å shell is present in the map, it is possible to utilize additional structural information to infer the nature of the 1·4 Å shell. This affords another basis in addition to positivity, for extending the observed data.

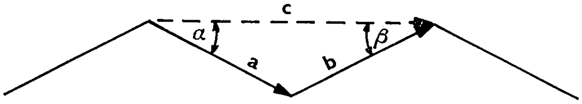

Fig. 3. Portion of an organic structure showing a typical spatial relationship between bonded and skip distances.

We proceed now to describe a method for obtaining the 1·4 Å shell from the 2·4 Å shell. Fig. 3 illustrates a typical detail of the structure. Corresponding to a distance $|\mathbf{c}|$, hereafter referred to as a skip distance, is a pair of adjacent bonded distances $|\mathbf{a}|$ and $|\mathbf{b}|$. We employ the structural information that, in a statistical sense, $|\mathbf{a}|$ and $|\mathbf{b}|$ are in the vicinity of 1·4 Å, $|\mathbf{c}|$ is about 2·4 Å, and the angles α and β are about 35°. In short, corresponding to each skip vector $\mathbf{c}$ are bond vectors $\mathbf{a}$ each lying on the cone having $\mathbf{c}$ as principal axis and semi-vertex angle approximately 35°. Conversely, corresponding to each fixed bond vector $\mathbf{a}$ are skip vectors $\mathbf{c}$ each lying on the cone with principal axis $\mathbf{a}$ and semi-vertex angle about 35°.

Referring to Fig. 4, let $\mathbf{a}$ be any vector of length, for example, 1·4 Å. Construct the cone with vertex at the origin, having $\mathbf{a}$ as the principal axis, and with semi-vertex angle of 35°. In view of the previous discussion, the Patterson value $P(\mathbf{a})$ is obtained by integrating the Patterson function along the circumference of the circle which is the intersection of this cone with the 2·4 Å shell. If the resolution of the

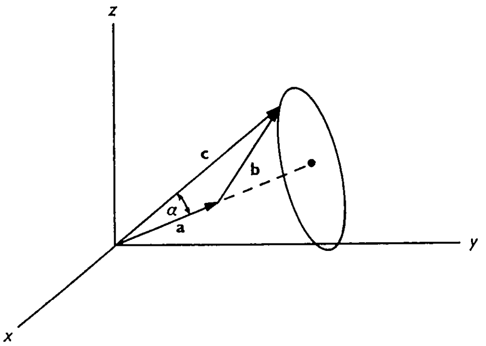

Fig. 4. The density at a specified point on the 1·4 Å shell, represented by the vector **a**, in a complex organic structure is proportional to the density on the circle in the 2·4 Å shell, described by rotating the vector **c** about the axis **a**. The angle α is approximately 35°.

2·4 Å shell is sufficiently good, the magnitude of **a** may range over an interval, *e.g.* 1·2–1·6 Å, with a corresponding range, roughly 2·2–2·6 Å, for the magnitude of **c**.

In this way we obtain the 1·4 Å shell of the Patterson function on a relative scale. It is necessary to put these values on an absolute scale in order to conform with the remainder of the Patterson map. This may be done by observing that the number of bonded distances, and the number of skip distances, are each roughly equal to the number of atoms in the unit cell. Thus the contents of the 1·4 Å and 2·4 Å shells are roughly equal and are given by

$$\int_{1\cdot4} P(\mathbf{r})d\mathbf{r} \simeq \int_{2\cdot4} P(\mathbf{r})d\mathbf{r} \simeq \sum_{\substack{i,j\\ \text{bonded}}} Z_iZ_j \simeq \sum_{\substack{i,j\\ \text{skip}}} Z_iZ_j\,, \qquad (3\cdot1)$$

where the first two integrals are extended over the 1·4 Å and 2·4 Å shells respectively, and the last two sums are over the bonded distances and skip distances respectively.

A process such as this, combined with the positivity criterion, should yield, by an iterative procedure, an improved Patterson function together with a further extrapolation of the observed data.

4. Analysis

We investigate next the procedure for applying the positivity criterion described in § 2. For convenience the analysis is limited to the case of N identical atoms in $P1$. However, the conclusions to be drawn are generally valid.

In view of

$$T(m) = \tfrac{1}{2} + \frac{1}{\pi}\int_0^\infty \frac{\sin mx}{x}\,dx = \left.\begin{aligned} &1, \text{ if } m>0\\ &0, \text{ if } m<0 \end{aligned}\right\}, \qquad (4\cdot01)$$

$P^+(\mathbf{r})$ of equation (2·4) may be defined analytically by means of

$$P^+(\mathbf{r}) = P(\mathbf{r})T(\psi(\mathbf{r})) \qquad (4\cdot02)$$

where, for convenience, we use $\psi(\mathbf{r}) = \sigma_2^{-1}P(\mathbf{r})$, since $T(\psi(\mathbf{r})) = 1$ or 0 depending on whether $P(\mathbf{r}) > 0$ or $P(\mathbf{r}) < 0$.

Employing the Taylor expansion of sin $[x\psi(\mathbf{r})]$ and reversing the order of integration, the average on the right of (2·5) may be written

$$\int P(\mathbf{r}) \exp (2\pi i\mathbf{h}\,.\,\mathbf{r})d\mathbf{r}\left\{\tfrac{1}{2} + \frac{1}{\pi}\int_0^\infty \left[\psi(\mathbf{r}) - \frac{\psi^3(\mathbf{r})}{3\,!}x^2 + \frac{\psi^5(\mathbf{r})}{5\,!}x^4 - \ldots\right]dx\right\}. \qquad (4\cdot03)$$

Denoting by n the number of contributors to the average, (2·3) may be written

$$P(\mathbf{r}) = \frac{\sigma_2}{n}\sum_{\mathbf{k}} (|\mathscr{E}_{\mathbf{k}}|^2 - 1) \exp(-2\pi i\mathbf{k}\,.\,\mathbf{r})\,. \qquad (4\cdot04)$$

We carry out the **r** integration for each of the four terms appearing in (4·03):

$$\tfrac{1}{2}\int P(\mathbf{r}) \exp (2\pi i\mathbf{h}\,.\,\mathbf{r})d\mathbf{r} = \delta_{\mathbf{k}}^{\mathbf{h}}\frac{\sigma_2}{2n}(|\mathscr{E}_{\mathbf{h}}|^2 - 1) \qquad (4\cdot05)$$

where $\delta_{\mathbf{k}}^{\mathbf{h}} = 1$ or 0 depending upon whether or not **h** occurs in the set $\{\mathbf{k}\}$ of (4·04). Next,

$$\frac{1}{\pi}\int P(\mathbf{r})\psi(\mathbf{r}) \exp (2\pi i\mathbf{h}\,.\,\mathbf{r})d\mathbf{r} = \frac{\sigma_2}{\pi n^2}\sum_{\mathbf{k}'}(|\mathscr{E}_{\mathbf{k}'}|^2 - 1)(|\mathscr{E}_{\mathbf{h}-\mathbf{k}'}|^2 - 1) \qquad (4\cdot06)$$

$$\simeq \frac{p\sigma_2}{\pi n^2 N}(|\mathscr{E}_{\mathbf{h}}|^2 - 1) \qquad (4\cdot07)$$

(Hauptman & Karle, 1955), where p is the number of vectors $\mathbf{k}'$ such that both $\mathbf{k}'$ and $\mathbf{h}-\mathbf{k}'$ in (4·06) occur among the vectors **k** of (4·04). Similarly,

$$-\frac{1}{3\,!\,\pi}\int P(\mathbf{r})\psi^3(\mathbf{r}) \exp (2\pi i\mathbf{h}\,.\,\mathbf{r})\,d\mathbf{r} = -\frac{\sigma_2}{3\,!\,\pi}\cdot\frac{p'}{n^4N^3}(|\mathscr{E}_{\mathbf{h}}|^2 - 1)\,, \qquad (4\cdot08)$$

$$\frac{1}{5\,!\,\pi}\int P(\mathbf{r})\psi^5(\mathbf{r}) \exp (2\pi i\mathbf{h}\,.\,\mathbf{r})\,d\mathbf{r} = \frac{\sigma_2}{5\,!\,\pi}\cdot\frac{p''}{n^6N^5}(|\mathscr{E}_{\mathbf{h}}|^2 - 1)\,, \qquad (4\cdot09)$$

where $p'(<n^3)$ and $p''(<n^5)$ depend on **h** and decrease with increasing $|\mathbf{h}|$.

Proceeding as in an earlier paper (Karle & Hauptman, 1953) (4·03) reduces to (4·05) plus

$$\frac{\varrho\sigma_2}{\pi n^2 N}(|\mathscr{E}_{\mathbf{h}}|^2 - 1)\int_0^\infty \exp\left\{\frac{-p'}{6n^2N^2p}x^2\right\} \times \left\{1 - \frac{1}{24n^2N^4}\left(\frac{p'^2}{3n^2p^2} - \frac{p''}{5n^2p}\right)x^4\right\}dx\,. \qquad (4\cdot10)$$

Carrying out this integration we finally obtain, for the average on the right of (2·5),

$$\frac{\sigma_2}{2n}\left\{\delta_{\mathbf{k}}^{\mathbf{h}}+p\left(\frac{6p}{\pi p'}\right)^{\frac{1}{2}}\left[1-\frac{9}{8}\left(\frac{1}{3}-\frac{pp''}{5p'^2}\right)\right]\right\}(|\mathscr{E}_{\mathbf{h}}|^2-1)\,. \quad (4\cdot11)$$

If $|\mathbf{h}|$ is small, then $p \simeq n$, $p' \simeq n^3$, $p'' \simeq n^5$ and both summands in the braces of (4·11) make approximately equal contributions. As $|\mathbf{h}|$ increases the first summand makes a constant contribution (equal to unity) while the contribution of the second summand decreases slowly. As $|\mathbf{h}|$ continues to increase, until finally $\mathbf{h}$ is no longer contained in the set $\{\mathbf{k}\}$, the contribution of the first summand drops suddenly to zero so that the second summand is the only contributor. These results are consistent with the observation that the cycling process yields values of $|\mathscr{E}_{\mathbf{h}}|^2-1$ proportional to the observed data, with slowly increasing scale factor $C(s)$, until at the boundary of the observed range a sharp increase in the scale factor (by a factor of order 4) occurs. This is followed again by a gradual increase in the scale factor.

We wish to express our appreciation to Dr J. Holden for his excellent cooperation in programming and carrying out the calculations and to Peter Gum and Stephen Brenner for carrying out certain auxiliary calculations.

References

Bartell, L. S. & Brockway, L. O. (1953). *Phys. Rev.* **90**, 833.
Harker, D. & Kasper, J. S. (1948). *Acta Cryst.* **1**, 70.
Hauptman, H. & Karle, J. (1950). *Phys. Rev.* **77**, 491.
Hauptman, H. & Karle, J. (1955). *Acta Cryst.* **8**, 355.
Hauptman, H. & Karle, J. (1962). *Acta Cryst.* **15**, 547.
Karle, J. & Hauptman, H. (1950). *Acta Cryst.* **3**, 181.
Karle, J. & Karle, I. (1950). *J. Chem. Phys.* **18**, 957.
Karle, J. & Hauptman, H. (1953). *Acta Cryst.* **6**, 131.
Karle, J. & Hauptman, H. (1959). *Acta Cryst.* **12**, 404.

Acta Cryst. (1964). **17**, 396

The Crystal Structure and Absolute Configuration of α-Bromoisotutin

By B. M. Craven

Crystallography Laboratory, University of Pittsburgh, Pittsburgh 13, *Pa., U.S.A.*

(*Received* 8 *April* 1963)

Crystals of α-bromoisotutin ($C_{15}H_{17}O_6Br$) are trigonal, space group $P3_12$, with lattice parameters $a = 8\cdot449$, $c = 36\cdot61$ Å and six molecules to the unit cell. The crystal structure has been determined by a three-dimensional X-ray analysis and the absolute configuration established by a study of the X-ray dispersion effect of the bromine atoms with Cu K radiation. The molecular structure of α-bromoisotutin has the unusual feature of a cyclopentane ring to which are attached two epoxy rings. One of these is a spiro ring while the other is fused to the cyclopentane ring in a position which is α, β with respect to the spiro ring. The molecular framework and its absolute configuration are the same as in the chemically and pharmacologically related members of the picrotoxinin series.

Introduction

Tutin ($C_{15}H_{18}O_6$) was first isolated by Easterfield & Aston (1901) and identified as the convulsive poison present in the leaves and seeds of the New Zealand species of *Coriaria*, a shrub known to the Maori as 'toi toi'. This poison is a considerable hazard to grazing animals.

Tutin is one of a series of chemically and pharmacologically similar compounds of which picrotoxinin ($C_{15}H_{16}O_6$) has been the most intensively studied. The structure (I) for picrotoxinin was proposed by Conroy (1951, 1957) and this was confirmed by the X-ray crystal structure analysis of α_1-bromopicrotoxinin (Craven, 1962). The absolute configuration of α_1-bromopicrotoxinin (II) was also determined from the X-ray dispersion effect. The structure (III) for tutin was proposed by Karyone & Okuda (1953) on the basis of chemical degradation studies and the picrotoxinin structure. Further chemical and spectral evidence led Johns & Markham (1961) to propose the structure (IV) for tutin.

A detailed account is now given of an X-ray crystal structure analysis of α-bromoisotutin (V) which has already been reported briefly (Craven, 1963) together with the crystal data of three other bromine derivatives of tutin.

In addition to the present work, the crystal structure of α-bromoisotutinone is being studied by Mrs MacKay (University of Melbourne, Australia) and Dr A. L. Mathieson (C.S.I.R.O., Melbourne, Australia). Their results (private communication) show that the molecule of this derivative possesses the same molecular framework as α-bromoisotutin.

Crystal data

The crystals of α-bromoisotutin, which were supplied through the courtesy of Dr Basil Johns (University