

THE ABSOLUTE CONFIGURATION OF ECHITAMINE IODIDE BY THE X-RAY TECHNIQUE

BY H. MANOHAR AND S. RAMASESHAN, F.A.S.C.*

(Department of Physics, Indian Institute of Science, Bangalore-12)

Received May 29, 1963

INTRODUCTION

ECHITAMINE IODIDE, $C_{22}H_{29}O_4N_2I$, crystallizes in the orthorhombic space group $D_2^4 - P2_12_12_1$ with four molecules in the unit cell of dimensions $a = 18.45 \text{ \AA}$, $b = 13.83 \text{ \AA}$, $c = 8.48 \text{ \AA}$. Its X-ray structure was recently solved from $hk0$, $0kl$ and $h0l$ data by Fourier methods (H. Manohar and S. Ramaseshan, 1961; 1962). The absolute configuration of the quaternary echitamine ion was subsequently determined by the Bijvoet technique and the preliminary results have been announced (H. Manohar and S. Ramaseshan, 1961 *a*). Although the absolute configurations of a fair number of optically active substances have been determined by the anomalous scattering technique, the detailed procedures to be followed have seldom appeared. It was therefore thought worthwhile to record the systematic procedures that were followed in this particular case.

ANOMALOUS SCATTERING AND FAILURE OF FRIEDEL'S LAW

The molecule of echitamine iodide has six asymmetric centres, five carbons and one nitrogen and it should therefore have theoretically 2^6 optical-isomers. But in determining the structure by X-ray methods, the relative positions of various atoms have been fixed—in other words, the complete conformation of the molecule is known. Therefore, the problem is only to decide between two enantiomorphous forms. This information cannot be obtained by X-ray methods in the normal course due to the operation of Friedel's law. However, as is well known, the law fails when the frequency of the incident radiation is close to, but slightly greater than the critical absorption edges of an atom in the crystal. Under the circumstances

* Present address: Department of Physics, Indian Institute of Technology, Madras-36. Most of this work was done at Bangalore. The simple method of using the stereographic projection for deriving the "Bijvoet pair" was developed at Madras.

there is not only a decrease in the scattering power of the atom, but the scattering factor undergoes a phase shift as well. The atomic scattering factor is then a complex quantity which can be represented by

$$f = f_0 + \Delta f' + i \Delta f''$$

where f_0 is the normal scattering factor for wavelengths far from the critical absorption wavelengths of the scattering element. $\Delta f'$ and $\Delta f''$ are the two correction terms due to dispersion effects. $\Delta f'$ is usually negative and $\Delta f''$, the imaginary part, is always *ahead* of the real part $f_0 + \Delta f'$ by $\pi/2$. The correction factors can be considered to be independent of scattering angle since these effects are caused by electrons very close to the nucleus.

If we consider the hkl and $\bar{h}\bar{k}\bar{l}$ reflections from an acentric crystal which contains an anomalous scatterer I (Fig. 1), the phases of F_R , the component due to the rest of the atoms which scatter normally and $F_{I'}$, the component due to the real part of the scattering factor of atom I will be equal and opposite in sign for the reflections hkl and $\bar{h}\bar{k}\bar{l}$. However, this will not be true for $F_{I''}$, the component due to the imaginary part of the scattering factor $\Delta f''$, since this "anomalous" part always has the same orientation $+\pi/2$ with respect to the real part. Thus the resultant amplitudes $|F(hkl)|$ and $|F(\bar{h}\bar{k}\bar{l})|$, indicated by F and \bar{F} in Fig. 1—and in consequence the observed intensities—become unequal and, therefore, the two planes could be distinguished.

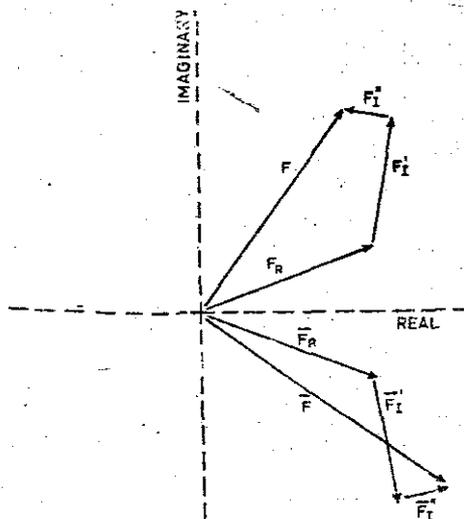


FIG. 1. Illustration of the failure of Friedel's Law for a non-centro-symmetric crystal when the crystal has, apart from the normally scattering atoms R, one set of anomalously scattering atoms I.

THE BIJVOET TECHNIQUE

The principle of anomalous scattering was first employed by Bijvoet and his coworkers (Peerdeman, van Bommel and Bijvoet, 1951) to establish the absolute configuration of sodium rubidium tartrate whose structure had already been determined. They used Zr K_{α} radiation ($\lambda_{\alpha_1} = 0.786 \text{ \AA}$, $\lambda_{\alpha_2} = 0.791 \text{ \AA}$) to excite the Rb atom (K absorption edge: $\lambda = 0.816 \text{ \AA}$) and observed significant intensity differences between hkl and $\bar{h}\bar{k}\bar{l}$ reflections. Knowing the atomic co-ordinates, the amplitudes $F(hkl)$ and $F(\bar{h}\bar{k}\bar{l})$ to be expected for the two enantiomorphs were calculated. Experimentally it was determined whether $I(hkl)$ is greater or less than $I(\bar{h}\bar{k}\bar{l})$. A comparison of the experimentally observed inequality with the computed one uniquely settled the question of the absolute configuration.

Peterson (1955) has observed that the effects of anomalous scattering with phase change are manifested even at wavelengths far from the absorption edges of atoms in a crystal. This is so because even if the incident radiation is on the longer wavelength side of the K absorption edge, and is therefore unable to excite the K electrons, it still has sufficient energy to excite the L and sometimes even the M electrons. This result has also been pointed out by Templeton (1955). Dauben and Templeton (1955) have calculated the values of $\Delta f'$ and $\Delta f''$ due to anomalous scattering of the K_{α} radiations of Mo, Cu and Cr by elements with atomic numbers between 20 and 96.

It is obvious that the intensity differences between hkl and $\bar{h}\bar{k}\bar{l}$ reflections due to anomalous dispersion will be greater the larger the magnitude of the term F'' and this depends on the value of the correction factor $\Delta f''$. The latter is dependent on the choice of suitable radiation and a heavy atom to scatter this anomalously. Okaya and Pepinsky (1961) have given a list of useful radiations and corresponding anomalous scatterers. Values of $\Delta f'$ and $\Delta f''$ are also given in a manner useful for workers in the field. The incident radiation and the scattering atom being fixed, it can be very easily shown that the intensity differences will be a maximum for those reflections for which the resultant of F_R and F_I' (in Fig. 1) is normal to F_I'' , i.e., it lies in a line with F_I'' . In such a case F_I'' will get added on for one reflection and get subtracted for the inverse reflection. A point which has to be stressed is that in order to employ the Bijvoet method, the atomic co-ordinates have to be known to a good degree of accuracy. Spurious differences in observed intensities could sometimes arise due to absorption effects if the shape of the crystal specimen is irregular and this has to be guarded against.

PROCEDURE—INDEXING OF REFLECTIONS

During the course of the structure analysis of echitamine iodide, it was observed in the table of Dauben and Templeton (1955) that for the scattering of CuK_α by the iodine atom $\Delta f''$ was as high as 7.2, $\Delta f'$ being equal to -1.1. It was therefore expected that the anomalous scattering effects could be visually observed. An inspection of higher layer Weissenberg photographs revealed that this was indeed the case. It was then decided to take up the determination of the absolute configuration of the quaternary echitamine ion by the Bijvoet technique.

The first step in the procedure is to assign correct signs to the indices of all the reflections on the film. This has been discussed by Peerdeman and Bijvoet (1956) (see also Vaidya and Ramaseshan, 1963). Since all three projections of the space group $P2_12_12_1$ are centrosymmetric, only the general hkl reflections are useful. The arrangement of the Weissenberg camera to record higher layer $-hkl$ data ($l = 1$ to 6) by the equi-inclination method is shown in Fig. 2(a), as seen by an observer from above. The

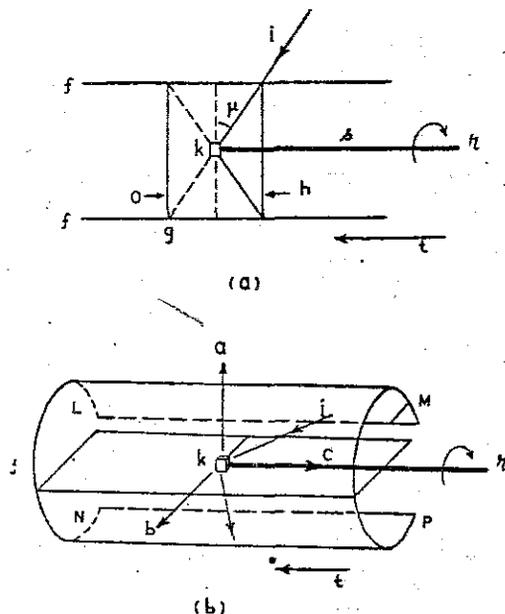


FIG. 2. (a) Schematic diagram of a Weissenberg camera to record higher layer data by the equi-inclination method. i , incident beam; g , beam catcher; k , crystal; s , spindle; f , film; o , zero layer; h , higher layer; r , direction of rotation of the spindle; t , direction of translatory motion of film; μ , equi-inclination angle. (b) Position of the film (LMNP) inside the cassette. abc form an orthogonal coordinate system.

relationship between the direction of rotation of the spindle and the coupled translatory motion of the film in the camera that was used is indicated by arrows r and t . The original position of the film in the cassette has to be known and this is achieved by adopting the convention of cutting the top right-hand corner (in relation to the experimenter standing on the side of the camera away from the X-ray tube) of a film as soon as it is removed for developing. Thus if the position of the film LMNP inside the cassette is as shown in Fig. 2 (b), the same film on which second layer reflections are recorded, when opened out, will appear as in Fig. 3.

Suppose the c axis, about which the crystal is rotated, is chosen as indicated in Fig. 2 (b). Then the orthorhombic a and b axes would be oriented as shown forming a right-handed orthogonal co-ordinate system. The right-handed system has to be chosen so as to conform to the convention adopted in the *International Tables* (1952). The orthogonal co-ordinate system in this position is shown separately in Fig. 4 (i) while the orientation of the reciprocal lattice vectors is indicated in Fig. 4 (ii). In the present experimental arrangement the camera has been turned in such a way that the film has to be shifted to the right (*i.e.*, in the direction of the positive c axis) to record higher layer data. Therefore all the hkl reflections will have their l indices positive.

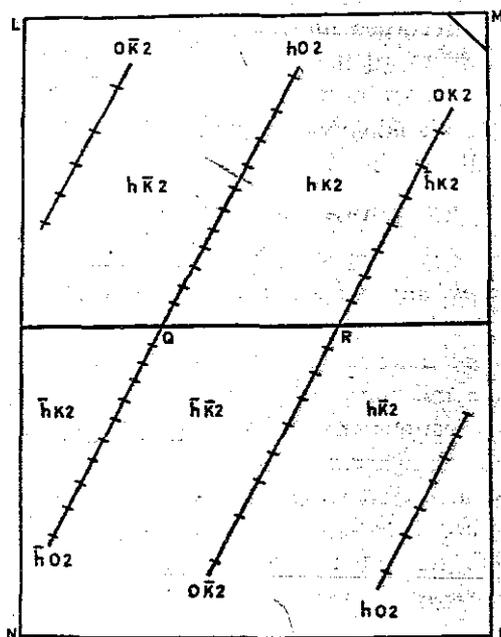


FIG. 3. The appearance of the film shown in Fig. 2 b on being opened out.

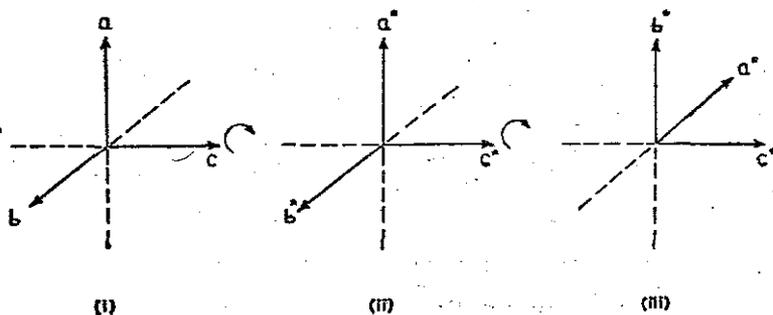


FIG. 4. (i) and (ii). The real and reciprocal co-ordinate axes used for indexing. (iii) Position of the reciprocal co-ordinate axes after a rotation of 90° .

Corresponding to the point Q on the film (Fig. 3) the a axis in the crystal will be vertical and the reciprocal co-ordinate system will be oriented as shown in Fig. 4 (ii). As the crystal rotates in the direction indicated by the arrow r , the reciprocal co-ordinate system will also rotate along with it and axial spots $h02$ would be recorded on the top half of the film. The higher angle spots would be recorded progressively to the right as the film moves to the left. A rotation of 90° will make the b^* axis vertical and this will correspond to the point R on the film. As the crystal rotates further, the $0k2$ reflections will be recorded above R. After a further rotation of 90° the axial spots $\bar{h}02$ will record themselves on the top half of the film. The spots in line with these in the bottom half of the film will have indices $h02$. With the signs of all the axial spots being fixed the rest of the reflections are easily indexed as indicated in Fig. 3.

REFLECTIONS TO BE COMPARED

Due to the symmetry elements possessed by the crystal there may be reflections other than hkl and $\bar{h}\bar{k}\bar{l}$ which may also be compared for the determination of the absolute configuration. It is necessary to know these since the Bijvoet pair $hkl, \bar{h}\bar{k}\bar{l}$ may not record itself in the same photograph, and even if it did both the reflections may not be on the same half of the film. The equivalence of reflections from a crystal when normal scattering takes place is governed by the symmetry elements of the Laue group. On the other hand, the equivalent reflections of the same crystal when anomalous scattering is present are obtained from the symmetry elements of the point group. For any point group it is easy to work out the Bijvoet pairs using the difference in the elements of symmetry between a point group and its Laue group.

For the crystal under study (space group $P2_12_12_1$) when anomalous scattering takes place the X-ray reflections have the point group symmetry 222 . Under normal scattering, however, they have the Laue group symmetry mmm . Figure 5a shows the equivalent reflections under anomalous scattering (222) while Fig. 5b shows the equivalent reflections under normal

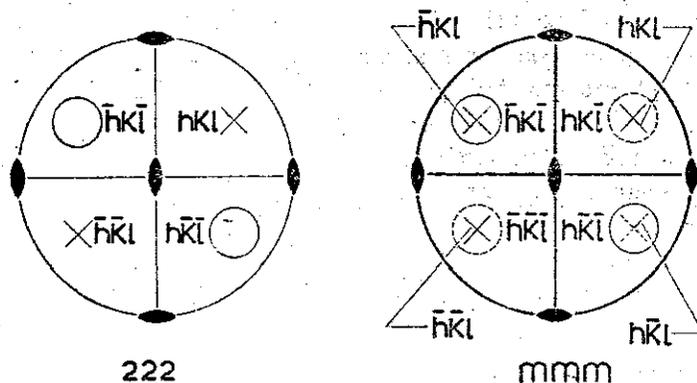


FIG. 5. Stereographic projection for the point group (222) and the Laue group ($mn:m$). Equivalent reflections when anomalous scattering is present are shown by continuous lines in (a). The extra equivalent reflections due to the introduction of a spurious centre of symmetry due to normal scattering are shown by dotted lines. Every reflection represented by continuous lines forms a Bijvoet pair with every one represented by dotted lines.

scattering (mmm). The extra reflections that are made equivalent due to the spurious centre of inversion are marked by dotted lines. It is clear that any reflection marked by full lines forms a Bijvoet pair with any marked by dotted lines. This result is shown in Table I. The same result may be obtained from the relationship between the phases of various reflections,

$$\alpha(hkl) = -\alpha(\bar{h}\bar{k}\bar{l}) = -\alpha(\bar{h}kl) = -\alpha(h\bar{k}l) = -\alpha(hk\bar{l})$$

for the point group 222 .

TABLE I

Bijvoet equality relations for point group 222. Reflections in group A are not equivalent to reflections in Group B and therefore can be compared

Equivalent reflections Group A	Equivalent reflections Group B
$hkl, h\bar{k}\bar{l}, \bar{h}\bar{k}l, \bar{h}kl$	$\bar{h}kl, h\bar{k}l, hkl, \bar{h}\bar{k}\bar{l}$

Okaya and Pepinsky (1961) have tabulated the equivalence relationships for all non-centro-symmetric point groups and Vaidya and Ramaseshan (1963) have listed the reflections that have to be compared and their dispositions on zero and higher layer Weissenberg equi-inclination photographs for various point groups.

It is clear from Table I that the Bijvoet pairs for $P2_12_12_1$ are symmetrically distributed about the axial rows in higher layer Weissenberg equi-inclination photographs. There are, however, no Bijvoet pairs in the zero layer. In the case of echitamine iodide 22 pairs of spots showed significant differences in intensity in the $hk4$ and $hk5$ layers. These were picked out and the intensities approximately estimated using calibrated intensity strips. The L_p corrections are the same for the reflections of each pair and since the crystal is cylindrical (about the c axis) the absorption corrections are also the same. It is therefore not necessary to reduce these intensities to an absolute scale. Each Bijvoet pair in the upper half of the film would have a corresponding pair in the lower half. Reflections in the same half of the film must always be compared since the contraction and elongation of the spots which occur on the different halves of a Weissenberg higher layer photograph would distort the intensity in the two halves of the film. This may cause even a fictitious reversal in the sign of the Bijvoet inequality giving a completely wrong absolute configuration.

THE CALCULATION OF THE STRUCTURE AMPLITUDES

In the normal process of determining the structure one finally obtains the co-ordinates of the various atoms as x_j, y_j, z_j ($j = 1$ to N). The two enantiomorphs x_j, y_j, z_j ($j = 1$ to N) and $\bar{x}_j, \bar{y}_j, \bar{z}_j$ ($j = 1$ to N) give the same values for the magnitude of the structure amplitudes. The problem of the absolute configuration is to determine which of these two enantiomorphs is the actual structure of the molecule under investigation. Using any one of these sets of atomic co-ordinates, the structure amplitudes are calculated for all the Bijvoet pairs making use of the expressions for the space group $P2_12_12_1$ given in the *International Tables*. For example, taking the group of reflections with

$$h + k = 2n + 1, \quad k + l = 2n$$

the expression for the structure factor is

$$F = A' + iB'$$

where

$$A' = \sum f_j (-4 \sin 2\pi h x_j \cos 2\pi k y_j \sin 2\pi l z_j)$$

and

$$B' = \sum f_j (4 \cos 2\pi hx_j \sin 2\pi ky_j \cos 2\pi lz_j).$$

For the iodine atom which scatters anomalously f has to be replaced by

$$f_0 + \Delta f' + i \Delta f''.$$

Thus for one iodine atom in the asymmetric unit, one obtains on separating the real and imaginary terms,

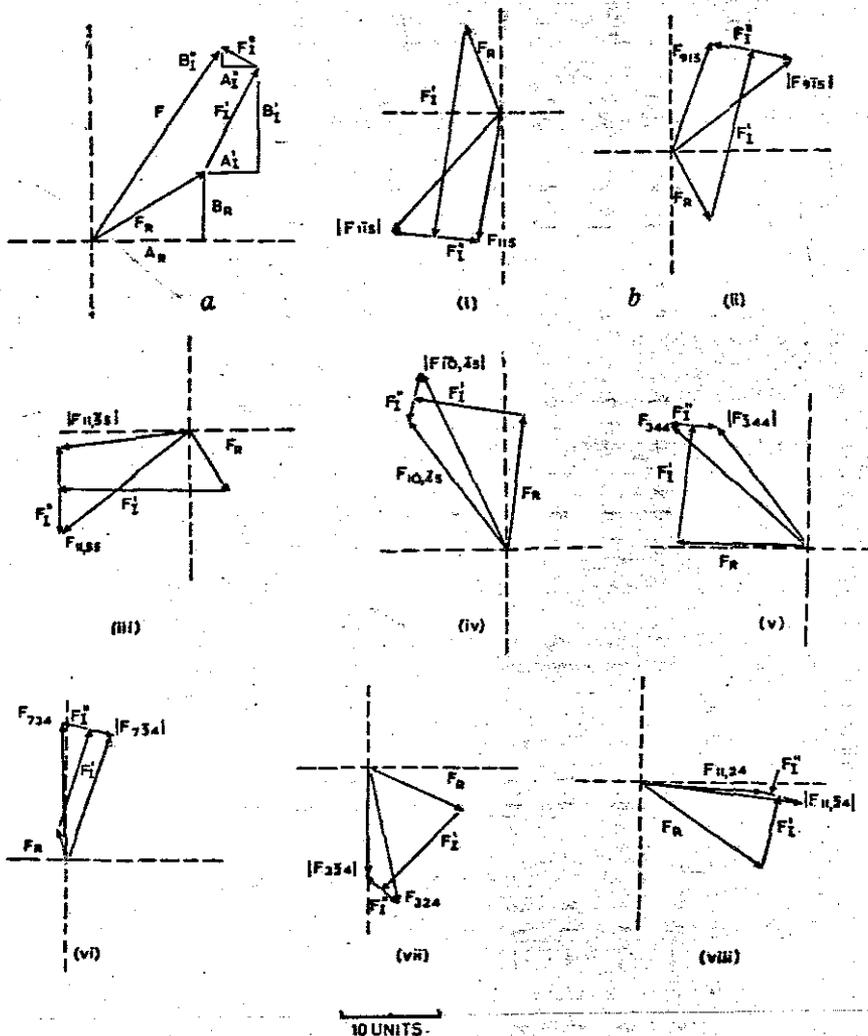


FIG. 6. (a) Graphical method of obtaining F and (b) illustrated for a few representative pairs of reflections.

TABLE II
Comparison of calculated and observed Bijvoet inequalities

hkl	A_r	B_r	A_r'	B_r'	A_r''	B_r''	$F_{\text{cal.}}$	$I_{\text{cal.}}$	Inequality calculated	Inequality observed
115	-3.6	9.5	-3.4	-22.4	-0.7	-4.7	13.8	190		
$\bar{1}\bar{1}\bar{5}$	-3.6	-9.5	-3.4	22.4	-0.7	4.7	16.8	282	$I_{115} < I_{\bar{1}\bar{1}\bar{5}}$	$I_{115} > I_{\bar{1}\bar{1}\bar{5}}$
315	-1.8	4.7	7.5	7.5	1.6	1.6	14.2	202		
$\bar{3}\bar{1}\bar{5}$	-1.8	-4.7	7.5	-7.5	1.6	-1.6	12.9	166	$I_{315} > I_{\bar{3}\bar{1}\bar{5}}$	$I_{315} < I_{\bar{3}\bar{1}\bar{5}}$
915	3.9	-7.4	4.3	17.7	1.0	4.2	12.0	144		
$\bar{9}\bar{1}\bar{5}$	3.9	7.4	4.3	-17.7	1.0	-4.2	15.4	237	$I_{915} < I_{\bar{9}\bar{1}\bar{5}}$	$I_{915} > I_{\bar{9}\bar{1}\bar{5}}$
11, 15	11.4	-1.4	-7.0	-1.5	-1.7	-0.4	13.3	177		
$\bar{1}\bar{1}, \bar{1}\bar{5}$	11.4	1.4	-7.0	1.5	-1.7	0.4	8.2	67	$I_{1115} > I_{\bar{1}\bar{1}\bar{1}\bar{5}}$	$I_{1115} < I_{\bar{1}\bar{1}\bar{1}\bar{5}}$
11, 55	4.0	-6.4	-17.3	0.6	-4.5	0.1	17.0	289		
$\bar{1}\bar{1}, \bar{5}\bar{5}$	4.0	6.4	-17.3	-0.6	-4.5	-0.1	13.4	180	$I_{1155} > I_{\bar{1}\bar{1}\bar{5}\bar{5}}$	$I_{1155} < I_{\bar{1}\bar{1}\bar{5}\bar{5}}$
725	-0.4	-2.3	-13.6	-3.5	-3.1	-0.8	15.9	253		
$\bar{7}\bar{2}\bar{5}$	0.4	-2.3	13.6	-3.5	3.1	-0.8	14.8	219	$I_{725} > I_{\bar{7}\bar{2}\bar{5}}$	$I_{725} < I_{\bar{7}\bar{2}\bar{5}}$
175	1.4	5.1	-19.0	-1.3	-4.2	-0.3	17.0	289		
$\bar{1}\bar{7}\bar{5}$	-1.4	5.1	19.0	-1.3	4.2	-0.3	19.3	372	$I_{175} < I_{\bar{1}\bar{7}\bar{5}}$	$I_{175} > I_{\bar{1}\bar{7}\bar{5}}$

745	1.8	2.0	-19.0	0.6	-4.5	0.1	17.2	296	$I_{745} > I_{746}$
745	-1.8	2.0	19.0	0.6	4.5	0.1	18.6	346	$I_{745} < I_{746}$
165	-14.4	1.9	14.6	-5.9	3.4	-1.4	1.9	3.6	$I_{165} > I_{175}$
165	14.4	1.9	-14.6	5.9	-3.4	-1.4	7.1	50.4	$I_{165} < I_{175}$
365	-3.6	-9.2	-4.9	13.3	-1.2	3.1	11.9	142	$I_{365} < I_{335}$
365	3.6	-9.2	4.9	13.3	1.2	3.1	7.9	62	$I_{365} > I_{335}$
825	-9.3	-4.9	15.8	3.7	3.7	0.9	6.1	37.2	$I_{825} > I_{875}$
825	9.3	-4.9	-15.8	3.7	-3.7	0.9	8.9	78.3	$I_{825} < I_{875}$
10, 75	1.7	14.0	-10.8	2.0	-2.7	0.5	16.4	269	$I_{10,75} < I_{10,85}$
10, 75	1.7	-14.0	10.8	-2.0	2.7	-0.5	20.2	408	$I_{10,75} > I_{10,85}$
265	-2.7	-6.6	13.0	-8.7	3.0	-2.0	17.3	299	$I_{265} > I_{266}$
265	-2.7	6.6	-13.0	8.7	-3.0	2.0	20.0	400	$I_{265} < I_{266}$
485	8.6	2.4	-0.6	-17.6	-0.1	-4.4	19.9	396	$I_{485} > I_{455}$
485	-8.6	2.4	0.6	17.6	0.1	-4.4	15.7	246	$I_{485} < I_{455}$
415	1.7	-7.9	-9.0	-2.7	-1.9	-0.6	14.0	196	$I_{415} > I_{416}$
415	1.7	7.9	9.0	2.7	1.9	0.6	11.8	139	$I_{415} < I_{416}$
264	-6.9	-3.2	5.0	18.2	1.1	4.0	17.0	289	$I_{264} > I_{264}$
									$I_{264} < I_{264}$

TABLE II—(Contd.)

hkl	A_x	B_x	A'_1	B'_1	A''_1	B''_1	$F_{cal.}$	$I_{cal.}$	Inequality calculated	Inequality observed
264	-6.9	3.2	5.0	-18.2	1.1	-4.0	14.0	196		
214	4.9	-10.8	-9.4	-8.7	-1.8	-1.7	21.3	454	$I_{214} > I_{214}$	$I_{214} < I_{214}$
274	-4.9	-10.8	9.4	-8.7	1.8	-1.7	18.4	339		
734	-0.6	3.1	2.7	10.6	0.6	2.3	14.2	202		
734	0.6	3.1	-2.7	10.6	-0.6	2.3	13.9	193	?	$I_{734} < I_{734}$
324	9.3	-4.2	-7.7	-8.8	-1.5	-1.7	15.0	225	$I_{324} > I_{324}$	$I_{324} < I_{324}$
324	9.3	4.2	-7.7	8.8	-1.5	1.7	11.4	130		
11, 24	12.5	-8.9	1.5	7.6	0.4	1.8	12.1	146		
11, 24	12.5	8.9	1.5	-7.6	0.4	-1.8	15.6	243	$I_{1124} < I_{1124}$	$I_{1124} > I_{1124}$
144	-4.6	4.5	-3.6	-5.7	-0.7	-1.2	6.7	44.9	?	$I_{144} > I_{144}$
144	4.6	4.5	3.6	-5.7	0.7	-1.2	6.9	47.6		
344	-13.4	0.4	1.4	12.3	0.3	2.5	19.2	369	$I_{344} > I_{344}$	$I_{344} < I_{344}$
344	13.4	0.4	-1.4	12.3	-0.3	2.5	15.5	240		

$$\begin{aligned}
 F &= (f_0 + \Delta f') (-\sin 2\pi hx \cos 2\pi ky \sin 2\pi lz) \\
 &\quad + i(f_0 + \Delta f') (\cos 2\pi hx \sin 2\pi ky \cos 2\pi lz) \\
 &\quad - \Delta f'' (\cos 2\pi hx \sin 2\pi ky \cos 2\pi lz) \\
 &\quad + i\Delta f'' (-\sin 2\pi hx \cos 2\pi ky \sin 2\pi lz) \\
 &= A_1' + iB_1' - A_1'' + iB_1''
 \end{aligned}$$

A_1' and B_1' give rise to F_1' , and A_1'' and B_1'' to F_1'' in Fig. 1. The values of $\Delta f'$ and $\Delta f''$ being known, these four terms are computed. Again A_R and B_R for the rest of the atoms which scatter normally are calculated, remembering that in this case $\Delta f'$ and $\Delta f''$ are zero. The resultant F is very easily obtained by a graphical method as shown in Fig. 6 (a). Now the same components for the other reflection of the pair are calculated in a similar manner and hence \bar{F} obtained. The graphical method of obtaining F is illustrated in Fig. 6 (b) for a few representative pairs of reflections. For convenience only one diagram is drawn for both the non-equivalent reflections from which $F(hkl)$ and $|F(\bar{h}\bar{k}\bar{l})|$ (magnitude only) could be obtained by measurement. The inequalities in intensities are thus obtained for all the pairs.

The results obtained by computation are now compared with the experimentally observed inequalities. The results obtained are shown in Table II. In 20 cases out of 22 it is seen that the computed results are opposite to those obtained from experiment. In two cases alone the results are ambiguous as the computed values of F and \bar{F} are nearly equal. It therefore follows that the correct configuration of the quaternary echitamine ion in echitamine iodide is not that given by the atomic co-ordinates used in the calculation of the structure factors but its mirror image. The atomic co-ordinates for echitamine iodide in the correct absolute configuration, with reference to a right-handed co-ordinate system are given in Table III. The parameters are referred to the same origin as chosen for the space group $P2_12_12_1$ in the *International Tables*.

DISCUSSION

A view of the quaternary echitamine ion down the c axis in the correct absolute configuration is shown in Fig. 7 while the more conventional representation is given in Fig. 8 a. The dispositions of the various groups in the latter figure are indicated with respect to the substituted cyclo-hexane ring which is actually a 'boat' with carbon atoms (11) and (14) above the plane of the paper. This representation of the cyclohexane ring with the different attached groups is shown separately in Fig. 8 b.

TABLE III

Atomic co-ordinates for echitamine iodide in the correct absolute configuration

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
I	0.317	0.192	0.172	C (15)	0.521	0.425	0.450
C (1)	0.629	0.050	0.367	C (16)	0.550	0.467	0.297
C (2)	0.673	0.012	0.283	C (17)	0.513	0.217	0.588
C (3)	0.725	0.013	0.167	C (18)	0.400	0.217	0.692
C (4)	0.729	0.108	0.117	C (19)	0.642	0.225	0.625
C (5)	0.683	0.171	0.200	C (20)	0.633	0.442	0.075
C (6)	0.629	0.146	0.317	C (21)	0.458	0.467	0.496
C (7)	0.638	0.329	0.275	C (22)	0.433	0.483	0.667
C (8)	0.596	0.246	0.358	N (1)	0.679	0.275	0.154
C (9)	0.525	0.325	0.142	N (2)	0.583	0.392	0.192
C (10)	0.521	0.254	0.283	O (1)	0.500	0.133	0.525
C (11)	0.692	0.383	0.383	O (2)	0.467	0.267	0.700
C (12)	0.658	0.421	0.542	O (3)	0.633	0.229	0.792
C (13)	0.579	0.383	0.558	O (4)	0.742	0.446	0.325
C (14)	0.579	0.271	0.533				

The stereochemistry of the molecule has already been discussed in previous publications. However, it is recapitulated here to make this paper self-contained. The molecule contains two five-membered rings and a cyclohexane ring fused along a common bond. In addition, there are two inter-locking seven-membered rings, one of them in boat form and an eight-membered ring. The CH_2OH group and H attached to C (11) are in the flag-pole positions, while the COOCH_3 and OH groups and H atom linked to C (13) are equatorial in relation to the six-membered ring. The five-membered ring containing the quaternary nitrogen is below while the

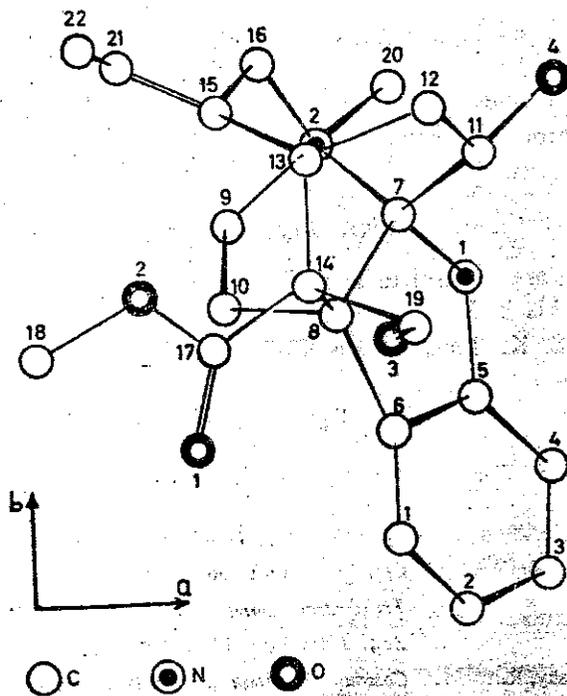


FIG. 7. View of the quaternary echitamine ion down the c axis in the correct absolute configuration.

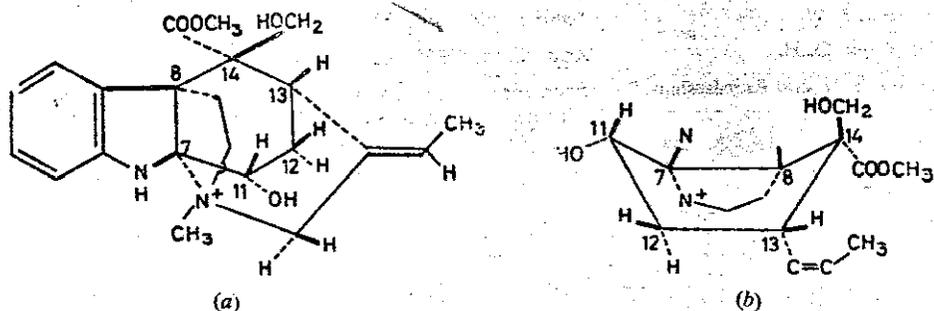


FIG. 8. (a) Molecular formula of the quaternary echitamine ion in the correct absolute configuration. (b) Boat-shaped cyclohexane ring in echitamine iodide with the different attached groups.

five-membered ring of the dihydroindole nucleus is above. The methyl group of $=C-CH_3$ is *cis* to C (13).

SUMMARY

The absolute configuration of echitamine iodide has been determined by the Bijvoet technique, making use of the intensity differences between hkl and $\bar{h}\bar{k}l$ reflections due to the anomalous scattering of CuK_α radiation by the iodine atom. The various steps in the procedure are discussed in detail in this paper.

ACKNOWLEDGEMENT

The authors are grateful to Prof. T. R. Govindachari for samples of the crystal and for his keen interest in this investigation. They also wish to thank Prof. R. S. Krishnan for his kind interest.

REFERENCES

- Dauben, D. H. and Templeton, C. H. *Acta Cryst.*, 1955, **8**, 841.
- International Tables for X-ray Crystallography*, 1952, **1**, Birmingham: Kynoch Press.
- Manohar, H. and Ramaseshan, S. *Curr. Sci.*, 1961, **30**, 5.
- *Tetrahedron Letters*, 1961 *a*, No. 22, 814.
- *Zeit. Kristallogr.*, 1962, **117**, 273.
- Okaya, Y. and Pepinsky, R. *Computing Methods and the Phase Problem in X-ray Crystal Analysis*, Pergamon Press, 1961.
- Peerdeman, A. F., van Bommel, A. J. and Bijvoet, J. M. *Proc. Koninkl. Ned. Akad. Wetenschap.*, 1951, **54 B**, 16.
- and Bijvoet, J. M. *Acta Cryst.*, 1956, **9**, 1012.
- Peterson, S. W. *Nature*, 1955, **176**, 395.
- Templeton, D. H. *Acta Cryst.*, 1955, **8**, 842.
- Vaidya, S. N. and Ramaseshan, S. *International Symposium on Crystallography and Protein Structures*, Academic Press, London, 1963.