

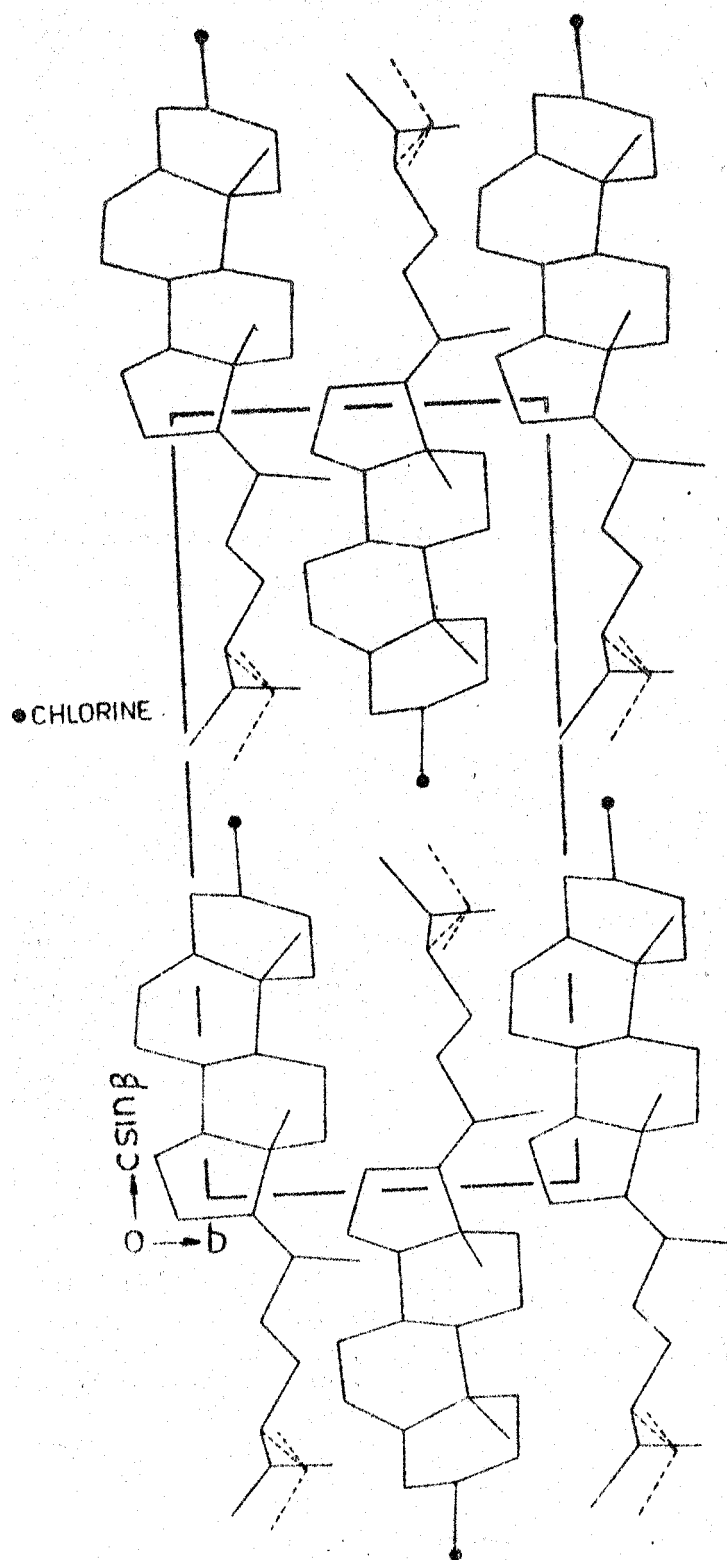


Figure 4.13: Molecular arrangement in the bc-projection.

Here, as given by Duax and Norton [29], the length of the steroid is the direction parallel to the C(10)-C(13) direction, the width is the dimension parallel to the C(12)-C(14) direction and the thickness is the dimension orthogonal to the length and the width. This type of packing arrangement is frequently observed in steroid structures with two molecules per unit cell [29]. The thickness of the molecule makes an angle of 35° with the a-axis. The width of the molecule is at 8° to the b-axis and the length is at 5° to the c-axis. Therefore, the modified Hodgkin notation [29] is $Ma_{35^\circ}b_{8^\circ}c_{5^\circ}$, 211.

The molecules are arranged in clearly separated layers which are parallel to the ab-plane. The adjacent molecules inside a layer are related by the 2_1 screw axis and hence are oriented antiparallel to each other. Within each layer, the molecules are tilted with respect to the plane normal giving rise to a smectic C-type of packing. This type of layered molecular arrangement, with the molecules within the layer oriented antiparallel, is found to occur in many steroid crystal structures consisting of two molecules in the unit cell [29]. Among the cholestane group of steroids, cholesteryl iodide [5], 7-bromocholesteryl chloride [6], 3',3'-dichloro-2 β ,3 β -dihydrocyclobuta(2,3)-5 α -cholestan-4'(3'H)-one [12] and 2 α ,3 β -dichloro- and 2 α ,3 β -dibromo-5 α -cholestane [8] all have a similar molecular arrangement in the crystal. It is interesting to note

that the **molecular structure** for cholesteryl chloride and **bromide** predicted by Bernal et al [2] in 1940, is in broad agreement with the results of the present analysis.

As mentioned in Chapter 1, the cholesteric liquid crystal may be looked upon as a twisted **nematic** and therefore, a **cholesterogenic** crystal **structure** could be expected to have an **imbricated** molecular **arrangement** as in the **case** of a nematogen. The layered arrangement of cholesteryl chloride and cholesteryl bromide **seems** to suggest that these compounds may have a latent smectic C (or twisted smectic C) phase which does not appear before the **compound** transforms from the cholesteric phase to the solid phase. This possibility is also supported by the fact that cholesteryl **myristate** [3], **which** has a similar layered **arrangement** of molecules in the crystalline phase, exhibits a smectic A phase intermediate between its solid and aholesteric phases.

In cholesteryl chloride and bromide, the three-dimensional sCructure is **stabilised** by non-bonded van der Waals forces between the molecules. Table 4.11 lists all the intermolecular **contact distances** less than $4 \text{ \AA}$ for both the structures. There are no **significantly** ehort **intermolecular** contacts. **This** is another common feature, of many **cholestane structures** and **signifies** the rather 'loose' **packing** in the crystal. The only intermolecular

that the molecular structure for cholesteryl chloride and bromide predicted by Bernal et al [2] in 1940, is in broad agreement with the results of the present analysis.

As mentioned in Chapter 1, the cholesteric liquid crystal may be looked upon as a twisted nematic and therefore, a cholesterogenic crystal structure could be expected to have an imbricated molecular arrangement as in the case of a nematogen. The layered arrangement of cholesteryl chloride and cholesteryl bromide seems to suggest that these compounds may have a latent smectic C (or twisted smectic C) phase which does not appear before the compound transforms from the cholesteric phase to the solid phase. This possibility is also supported by the fact that cholesteryl myristate [3], which has a similar layered arrangement of molecules in the crystalline phase, exhibits a smectic A phase intermediate between its solid and cholesteric phases.

In cholesteryl chloride and bromide, the three-dimensional structure is stabilised by non-bonded van der Waals force between the molecules. Table 4.11 lists all the intermolecular contact distances less than 4 Å for both the structures. There are no significantly short intermolecular contacts. This is another common feature, of many cholestane structures and signifies the rather 'loose' packing in the crystal. The only intermolecular

TABLE 4.11

Intermolecular short contacts $< 4 \text{ \AA}$

(i) Cholesteryl Chloride

C(1) ^a - C(22) ^b	3.82 ^o Å
C(2) ^a - C(24) ^b	3.94
C(4) ^a - Cl ^c	3.86
C(6) ^a - C(262) ^d	3.89
C(7) ^a - C(262) ^d	3.40
C(7) ^a - C(26) ^d	3.93
C(8) ^a - C(262) ^d	3.91
C(12) ^a - C(14) ^b	3.96
C(16) ^a - C(21) ^e	3.94
C(19) ^a - C(262) ^f	3.82
C(19) ^a - C(27) ^f	3.97
C(19) ^a - Cl ^g	3.38
C(26) ^a - C(27) ^h	3.83
C(27) ^a - C(272) ⁱ	3.80

(ii) Cholesteryl Bromide

C(1) ^a - C(22) ^b	3.72 ^o Å
C(4) ^a - Br ^c	3.85
C(7) ^a - C(262) ^d	3.44
C(7) ^a - C(11) ^e	3.69
C(7) ^a - C(26) ^d	3.86
C(8) ^a - C(262) ^d	3.70
C(8) ^a - C(26) ^d	3.83
C(19) ^a - C(27) ^f	3.73
C(19) ^a - C(262) ^f	3.99
C(26) ^a - C(27) ^h	3.81
C(26) ^a - C(272) ^h	3.95
C(27) ^a - C(272) ⁱ	3.99

- a : x, y, z
 b : 1-x, $\frac{1}{2}+y$, -z
 c : 2-x, $y-\frac{1}{2}$, 1-z
 d : 2-x, $y-\frac{1}{2}$, -z
 e : x, y-1, z
 f : 2-x, $\frac{1}{2}+y$, -z
 g : 2-x, $\frac{1}{2}+y$, 1-z
 h : 1-x, $\frac{1}{2}+y$, -z-1
 i : 1-x, $y-\frac{1}{2}$, -z-1.

contact distance less than the sum of the van der Waals radii is due to the introduction of disorder in the chain atoms and is between C(7) of one molecule and C(262) of its neighbour related by the 2_1 screw axis. This distance is equal to 3.40 Å in cholesteryl chloride and 3.44 Å in cholesteryl bromide. Each molecule is surrounded by 10 neighbours.

The determination of the absolute configuration of the molecule, using anomalous scattering effects, is under way. The results will be reported elsewhere.

References

1. **Bernal, J.D. and Crowfoot, D.** (1933) Trans. Farad. Soc. 29, 1032.
2. **Bernal, J.D., Crowfoot, D. and Fankuchen, I.** (1940) Phil. Trans. Roy. Soc. A239, 135.
3. **Craven, B.M. and De Titta, G.T.** (1976) J.Chem.Soc. Perkin Trans. If, 814.

Barnard, J. A. and Lydon, J.E. (1974) Mol. Cryst. Liq. Cryst. 26, 285.

Carlisle, C.H. and Crowfoot, D. (1945) Proc. Roy. Soc. A184, 64.
6. **Burki, von H. and Nowacki, W.** (1956) Zeit.für Krist. 108, 206.
7. **Geise, B.J., Romers, C. and Rutten, EWM** (1966) Acta Cryst. , 249.
8. **Geise, H.J. and Homers, C.** (1966) Acta Cryst. 20, 257.
9. **Craven, B.M.** (1976) Nature 260, 727.
10. **Sheldrick, G.M. and Oeser, E.** (1976) Acta Cryst. B32, 1984.
11. **Chandross, K.J. and Bordner, J.** (1977) Acta Cryst. B33, 2934.
12. **Nassimbeni, L.R., Orpen, A.G., Sheldrick, G.M., van Niekerk, J.C. and Cragg, GML** (1977) Acta Cryst. B33, 3326.
13. **Russell, J.C., Nassimbeni, L.R. and Cragg, G.M.L.** (1977) Acta Cryst. B33, 2128.

14. van Niekerk, J.C., Nassimbeni, L.R. and Cragg, G.M.L. (1977) *Acta Cryst.* **B33**, 3582.
15. Gilliland, G.M., Newcomer, M.E., Parish, E.J., Schroepfer, G.J., Jr. and Quirocho, F.A. (1977) *Acta Cryst.* **B33**, 3117.
16. Prelesnik, B., Jeremic, M., Stefanovic, M., Micovic, I. and Herak, R. (1977) IV European Crystallographic Meeting Abstracts. PI.97.
17. Abrahamsson, S. and Dahlen, B. (1977) *Chem. Phys. Lipids* **20**, 43.
18. Pascher, I. and Sundell, S. (1977) *Acta Chem. Scand.* **A31**, 767.
19. Buerger, M.J. (1960) *Crystal Structure Analysis*, New York: John Wiley & Sons, Inc.
20. Phillips, D.C. (1954) *Acta Cryst.* **7**, 746; (1956) *Acta Cryst.* **9**, 819.
21. Palm, J.H. (1964) *Acta Cryst.* **17**, 1326.
22. Busing, W.R. and Levy, H. A. (1957) *Acta Cryst.* **10**, 180.
23. Acton, B.S. (1970) *Numerical Methods that Work*, p. 102. Harper and Row, New York, Evanston & London.
24. Wilson, A.J.C. (1942) *Nature* **150**, 151.
25. Stout, G.H. and Jensen, L.H. (1968) *X-ray Structure Determination*. Collier-Macmillan Ltd., London.
26. Cruickshank, D.WJ. (1965) *Computing Methods in Crystallography*, Ed. Rollett, J.S., Pergamon Press.

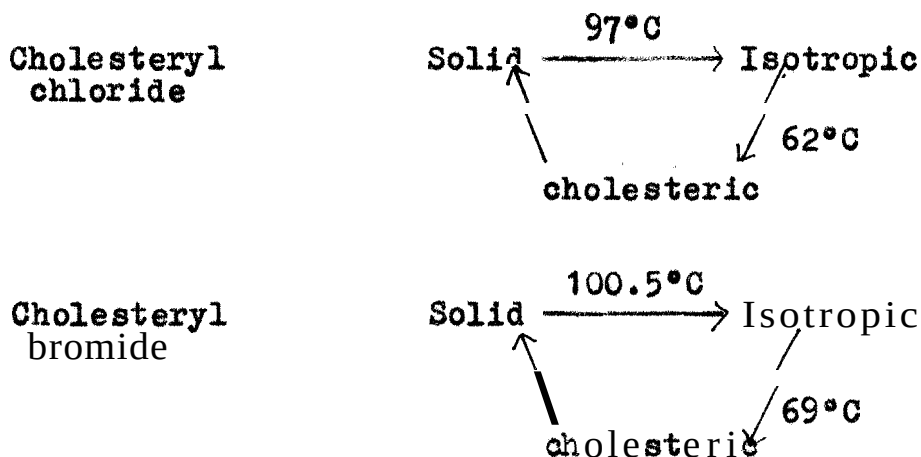
27. Zachariasen, W.H. (1963) Acta Cryst. 16, 1139.
28. Cromer, D.T. and Waber, J.T. (1965) Acta Cryst. 21, 849.
29. Duax, W.L. and Norton, D.A. (1975) Atlas of Steroid Structure. New York: Plenum.
30. Fieser, L.P. and Fieser, M. (1950) Organic Chemistry, D.C. Heath and Company, Boston.

CHAPTER 4

CRYSTAL AND MOLECULAR STRUCTURE OF CHOLESTERYL CHLORIDE AND THE ISOMORPHOUS CHOLESTERYL BROMIDE

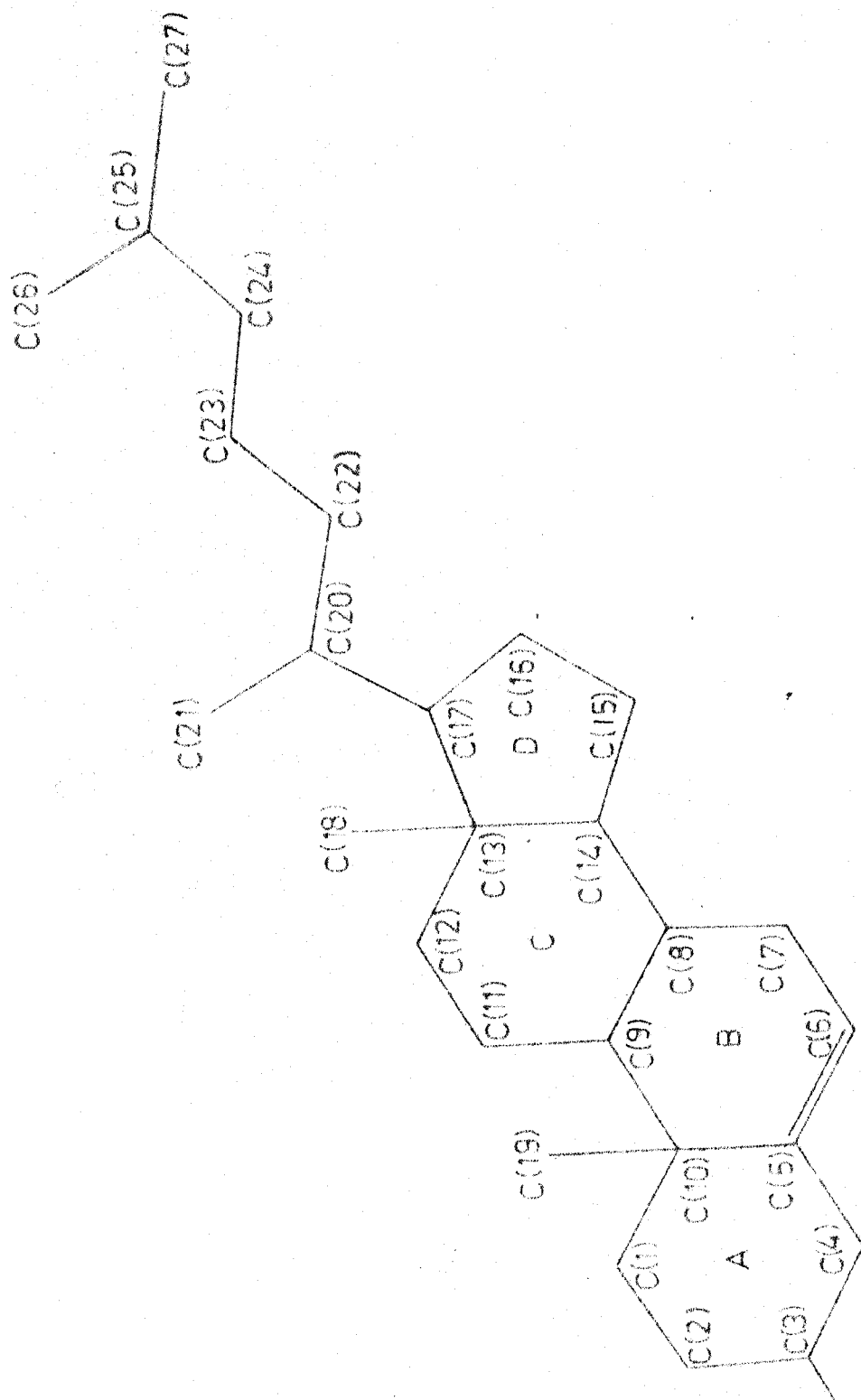
4.1 Introduction

Cholesteryl chloride ($C_{27}H_{45}Cl$) and cholesteryl bromide ($C_{27}H_{45}Br$)(III) are compounds belonging to the cholestane group of steroids. Both the compounds are cholesterogenic and exhibit monotropic mesomorphism, i.e., on heating, they transform directly to the isotropic phase, but, while cooling, pass through an intermediate liquid crystalline phase (see below).



They supercool from the cholesteric phase to the solid phase.

Based on their preliminary X-ray and optical studies in 1933, Bernal and Crowfoot [1] predicted the



R

R = Cl, Br

(III)

orientation of these isomorphous molecules **in** the unit cell. Later, Bernal et al [2] undertook a slightly more detailed X-ray investigation and worked out the approximate molecular structure as derived from the (h o l) projection Patterson synthesis. No further **X-ray** studies on these compounds have been reported in the literature.

Unlike the X-ray data on **nematogenic** and smectogenic compounds, single crystal **X-ray** analyses of **cholesterogens** have been **very** few in number. Apart from the crystal structures of **cholesteryl** chloride and **cholesteryl** bromide reported in this chapter, **cholesteryl** myristate [3] is the only other compound **exhibiting** the cholesteric **mesophase** whose **crystal** structure has been **determined** by single **crystal** X-ray methods. But **cholesteryl** **myristate** shows a **smectic** A phase prior to the cholesteric phase **whereas**, as already pointed out, **cholesteryl** chloride and **cholesteryl** bromide exhibit only the cholesteric phase. **Barnard** and **Lydon** [4] have **determined** the **unit** cell dimensions and space groups of a series of **n-alkyl** esters of **cholesterol** which exhibit cholesteric mesophase.

However, crystal structures of a number of non-mesogenic compounds belonging to the choleotane group of **steroids** have been reported. These include **cholesteryl** iodide [5]; 7-bromo-**cholesteryl** bromide, **chloride** and methyl ether [6]; **2 β ,3 α -dichloro-5 α -cholestane** [7];

2 α ,3 β -dibromo-5 α -cholestane [8]; 2 α ,3 β -dichloro-5 α -cholestane [8]; cholesteryl monohydrate [9]; cholest-4-en-3-one [10]; cholesteryl g-toluene sulphonate [11]; 4',4'-dichloro 2 β ,3 β -dihydrocyclobuta(2,3)-5 α -cholestan-3'(4'H)-one [12]; 3',3'-dichloro-2 β ,3 β '-dihydrocyclobuta(2,3)-5 α -cholestan-4'-(3'H)-one [12]; 4 β ,5 β -epoxycholestan-3-one [13]; 4 β ,5 β -epoxycholestan-6-one [14]; 5 α ,14 β -cholest-7-ene-3 β ,15 β -diol di-p-bromobenzoate [15]; 2,4-dibromocholesta-1,4,6-triene-3-one [16]; cholesteryl 17-bromoheptadecanoate [17]; and sodium cholesteryl sulphate dihydrate [18]. Bernal et al [2] have surveyed a large number of sterol derivatives belonging to the cholesterol series and recorded their unit cell dimensions, space group and data on crystal morphology and optics.

4.2 Experimental

cholesteryl chloride and cholesteryl bromide were crystallised from solutions in acetone. Whereas cholesteryl chloride crystallised easily, the bromide crystals were obtained after repeated trials. Crystals of both the compounds were white, transparent, platy and elongated. The bromide crystals were very small and fragile; the chloride crystals were bigger and easier to handle.

Oscillation and Weissenberg photographs were recorded with the crystals of both the compounds mounted along and perpendicular to the needle axes. The diffraction

patterns showed that both the **crystals belonged** to the monoclinic system and were **isomorphous**. The space group was determined as $P2_1$, based on the systematic extinctions of the type $0k0$, k odd.

The direct cell dimension b was measured **from** the rotation photograph. The values of the reciprocal **cell** dimensions a^* , c^* and β^* were obtained from the b -axis zero level **Weissenberg** photograph and from these the values of a , c and β were calculated. The densities of both the crystals, as measured by flotation in aqueous potassium iodide solution, indicated that there were two molecules per unit **cell**. The crystal data for both the compounds are listed in Table 4.1.

Intensity data

Three-dimensional intensity data were recorded from the reciprocal levels hkl , $k = 0$ to 4 for **cholesteryl** chloride and $k = 0$ to 3 for **cholesteryl** bromide. **Multifilm equi-inclination Weissenberg** technique was used, with nickel-filtered copper radiation ($\lambda = 1.5418 \text{ \AA}$). The **chloride** crystal used for data collection was in the form of an **approximate** cylinder of mean radius 0.018 cm ($\mu r = 0.25$). As mentioned **earlier**, the bromide crystals were very small and **fragile** and hence could not be shaped into cylinders. The **bromide** crystal used for data collection had a

TABLE 4.1

Crystal Data

	Cholesteryl chloride $C_{27}H_{45}Cl$	Cholesteryl bromide $C_{27}H_{45}Br$
Molecular weight	405.92	449.57
a	$10.82 \pm 0.01 \text{ \AA}$	$11.10 \pm 0.01 \text{ \AA}$
b	7.61 ± 0.02	7.56 ± 0.02
c	21.46 ± 0.01	21.83 ± 0.01
β	$131.8 \pm 0.3^\circ$	$133.9 \pm 0.3^\circ$
Space group	$P2_1$	$P2_1$
Z	2	2
ρ_c	1.02 gm. cm^{-3}	1.13 gm. cm^{-3}
ρ_m	1.03 gm.	1.14 gm. cm^{-3}
μ for copper $K\alpha$ radiation	13.41 cm^{-1}	23.99 cm^{-1}

rectangular cross-section of 0.035 x 0.005 cm. Intensity data from the **okl** reciprocal levels were also recorded with a chloride **crystal** of mean radius 0.022 cm ($\mu r = 0.3$) and a bromide **crystal of cross-section** 0.033 x 0.009 cm.

The diffraction **patterns** of both the compounds were **xx weak** and faded away at relatively low **Bragg angles**. The **highest θ** recorded was only 42°52' for **cholesteryl chloride** and 37°35' for oholeeteryl bromide. The total number of independent, observable reflections reasured was 487 and 293 for the **chloride** and the bromide compounds respectively. These are only 8% and 5% of the total number of possible **reflections** in the **respective CuK α** spheres.

The **intensities** were **estimated** visually by comparison with a calibrated strip. Each reflection was measured at least twice and averaged. The measured **intensities** were oorrected for Lorentz-polarisation factors [19] and **spot** shape effect [20].

Since the **chloride crystals** used for **intensity** data collection were nearly cylindrical, the absorption correction for cylindrical specimens, as given by Palm [21], wae applied to the **chloride** data. As **mentioned** earlier, the bromide **crystals used** were platy with a rectangular cross-section. Hence, the **computer programme** **ABSCOR**, written by **Ramesh**

Narayan, based on the method of Busing and Levy [22] was used for correcting the absorption **effects** in the bromide data. This programme **ABSCOR** **calculates** the absorption correction for **monoclinic** crystals of rectangular cross-section mounted **along** the unique axis. For crystals mounted **along** the non-unique axis, the programme is **applicable** only for correcting the equatorial reflections. The principle behind the calculations **in ABSCOR** is briefly described below.

Fig. 4.1(a) shows the rectangular cross-section of a monoclinic **crystal** mounted along its unique axis. A rectangular coordinate system $(\hat{i}, \hat{j}, \hat{k})$ is chosen with $\hat{i}$ and $\hat{j}$ along the reciprocal cell vectors $\vec{a}^*$ and $\vec{b}^*$ so that $\hat{k}$ is perpendicular to $\hat{i}$ in the $a^* c^*$ plane. The cross-section of the **crystal** in the xs -plane is a rectangle of **dimensions** $p \times q$ with the q edge oriented along the direction $h_0 \vec{a}^* + l_0 \vec{c}^*$ and the p -edge being perpendicular to it, i.e., the p -faces of the crystal are **parallel** to the planes $(h_0 \ 0 \ l_0)$.

The equations of the four **lines** bounding the **crystal** cross-section can be written down with respect to the coordinate frame $(\hat{i}, \hat{j}, \hat{k})$ in **terms** of p , q , h_0 , l_0 , etc.

The **Ewald** sphere **construction** is shown in **Fig. 4.2**. For simplicity, the **case** of a **zero** level reflection hol

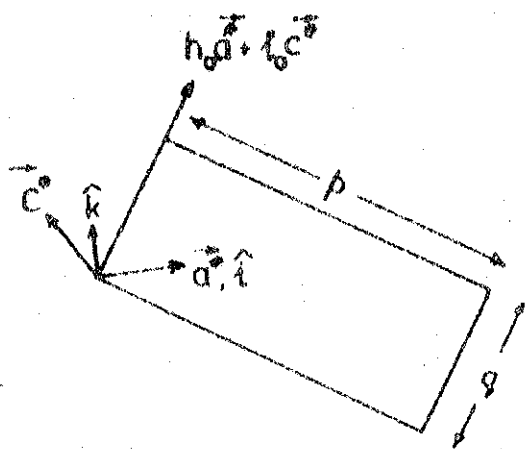


Figure 4.1(a)

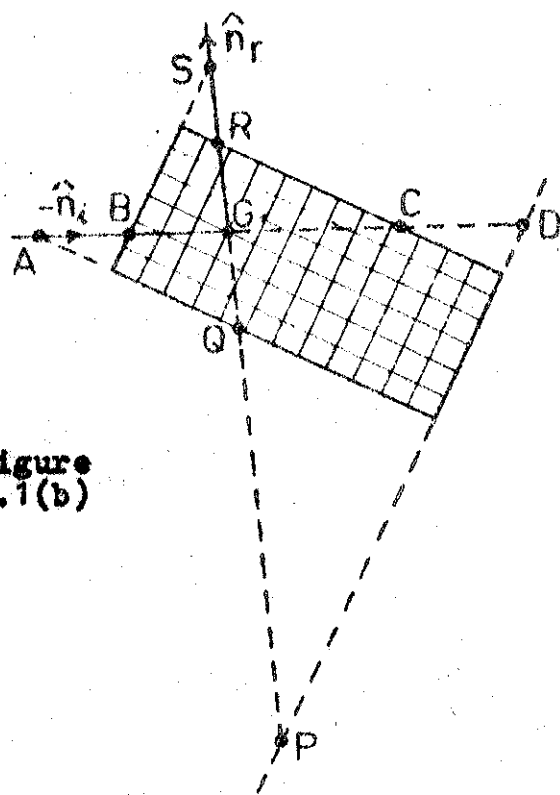


Figure 4.1(b)

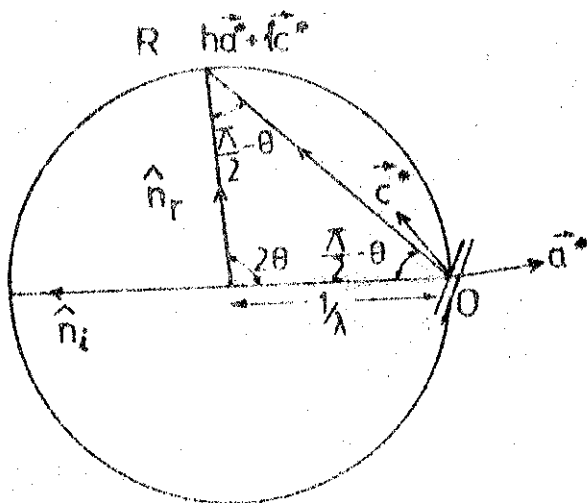


Figure 4.2

will be considered first. $\hat{n}_1$ and $\hat{n}_r$ are the unit vectors along the reverse direction of the primary beam, and the forward direction of the diffracted beam, respectively. θ is the Bragg angle corresponding to the reflection h_0l and $\vec{O} \vec{R}$ is the vector $h\vec{a}^* + l\vec{c}^*$ in the reciprocal space. $\hat{n}_1$ is obtained by rotating $\vec{O} \vec{R}$ in the clockwise direction by an angle $(\theta - \frac{\pi}{2})$ and normalising it. Similarly $\hat{n}_r$ is obtained by rotating $\vec{O} \vec{R}$ by $(\frac{\pi}{2} - \theta)$ and normalising it.

Having obtained expressions for $\hat{n}_1$ and $\hat{n}_r$, and the equations of the four bounding lines of the crystal cross-section, the absorption correction is calculated as follows. The rectangular crystal cross section is divided into a grid of $n \times m$ points (Fig. 4.1 (b)). From any given grid point, the lengths of the intercepts on the four bounding lines of the crystal are calculated along the direction $\hat{n}_1$. The smallest positive intercept value (BG) is the length l_1 traversed in the crystal by the incident beam. Similarly, the length l_r traversed by the diffracted beam is also calculated (GR). The absorption correction for this grid point is then given by $e^{-\mu(l_1+l_r)}$, where μ is the linear absorption coefficient for the crystal. Similar values are calculated for all the $n \times m$ grid points and these are averaged using the Simpson's rule for integration [23]. This integrated value gives the absorption correction

corresponding to the **h0l reflection** considered,

The above discussion **is** for an equatorial reflection of the type **h0l**. **For** the higher level reflections ($k \neq 0$) obtained from a crystal mounted along the **unique** axis, the values of l_i and l_r , as calculated above, **correspond** to the projected path **lengths** in the **xz-plane**. These values **are** scaled up by a factor $\sec \psi_n$, where ψ_n **is** the **equi-inclination** angle **corresponding** to the n^{th} level ($|k| = n$), to account for the deviation from the equatorial plane. **The** scaled values are then used for calculating; the absorption correction.

ABSCOR was also **used** to estimate the absorption correction for the **okl** type of equatorial reflections obtained from a crystal mounted along the a-axis. **Here**, the **values** of the indices h and k, **and** a^* and b^* , were **interchanged** during the **calculations**.

The intensities were **scaled** to an absolute value using Wilson's **statistics** [24]. From the Wilson's graphs, drawn using the **three-dimensional** intensity data, the overall isotropic temperature factors B were estimated as **equal** to $7.1 \text{ \AA}^2$ and $5.9 \text{ \AA}^2$, **which** correspond to $\overline{u^2} = 0.09 \text{ \AA}^2$ and $0.07 \text{ \AA}^2$ **for** the chloride and the bromide structures respectively. These values are slightly high, especially for the chloride structure, and the paucity

of the high angle observed data in these structures could be correlated to the large **overall thermal** parameters.

Structure Determination

Since the cholesteryl bromide molecule contained the heavy bromine atom, the **structure** solution of the isomorphous compounds was attempted by the heavy atom method [25] **using** the data from the bromide derivative. A three-dimensional bromine-sharpened Patterson map was **computed** using the intensity data of cholesteryl bromide. In the **space** group $P2_1$, the equivalent positions in the **unit** cell are x, y, z and $\bar{x}, \frac{1}{2} + y, \bar{z}$. The Patterson **vector** $[u \ v \ w] = [2\bar{x}, \frac{1}{2}, 2\bar{z}]$ **represents** the vectors between the atoms related by the 2, screw **axis** and, **therefore**, the $v = \frac{1}{2}$ section in the Patterson map **corresponds** to the **Harker** plane. **The** vector distribution in the Patterson map **was** highly directional. **The** vector density was found to be in the form of a strip running **parallel** to the c-cell edge. In **addition** to the highly directional character, the very preferential distribution of the Patterson vectors in only a few **sections of** the **map** was very conspicuous. Apart from the **plane** $v = 0$, which included the self-vectors at the origin, the **Barker** plane $v = \frac{1}{2}$ was the only other section where vectors were found to be concentrated. **The** vector

distribution in the other **sections** of the three-dimensional map only corresponded to the gradual fall of the **peak** distribution found in the $v = 0$ and $v = \frac{1}{2}$ **sections**. The vector density distribution in the Harker section **was** in the form of a strip of approximate width $6 \text{ \AA}$ running parallel to the z -axis and centred about the line $u = \frac{1}{2}$. **These** features indicated that the molecules were arranged parallel to the c -axis at $x = \frac{1}{4}$ (and by symmetry at $x = \frac{3}{4}$ also) in the **unit** cell. The length of the **cholesteryl** bromide, molecule is approximately $19 \text{ \AA}$, and is **quite** close to the length of the **c-cell** edge, which is $21.83 \text{ \AA}$. **Fig. 4.3** shows the **vector** distribution in the **Harker** section of the Patterson map. The Br-Br vector, with a peak height nearly 1.5 times greater than the next highest peak could be **easily** identified in the Harker plane. The x and z coordinates **of** the bromine atom were calculated from the position of the Br-Br **vector** in the **Harker** section as $x = \frac{93}{120}$ and $z = \frac{57}{120}$. The three-dimensional chlorine-sharpened Patterson **map was also** computed at this stage, and it was found to contain all the **features** of the bromine-sharpened Patterson map described above.

The x and z **coordinates** of the bromine **atom** obtained from the Patterson map were refined by **block-diagonal** structure factor **least-squares** procedure after

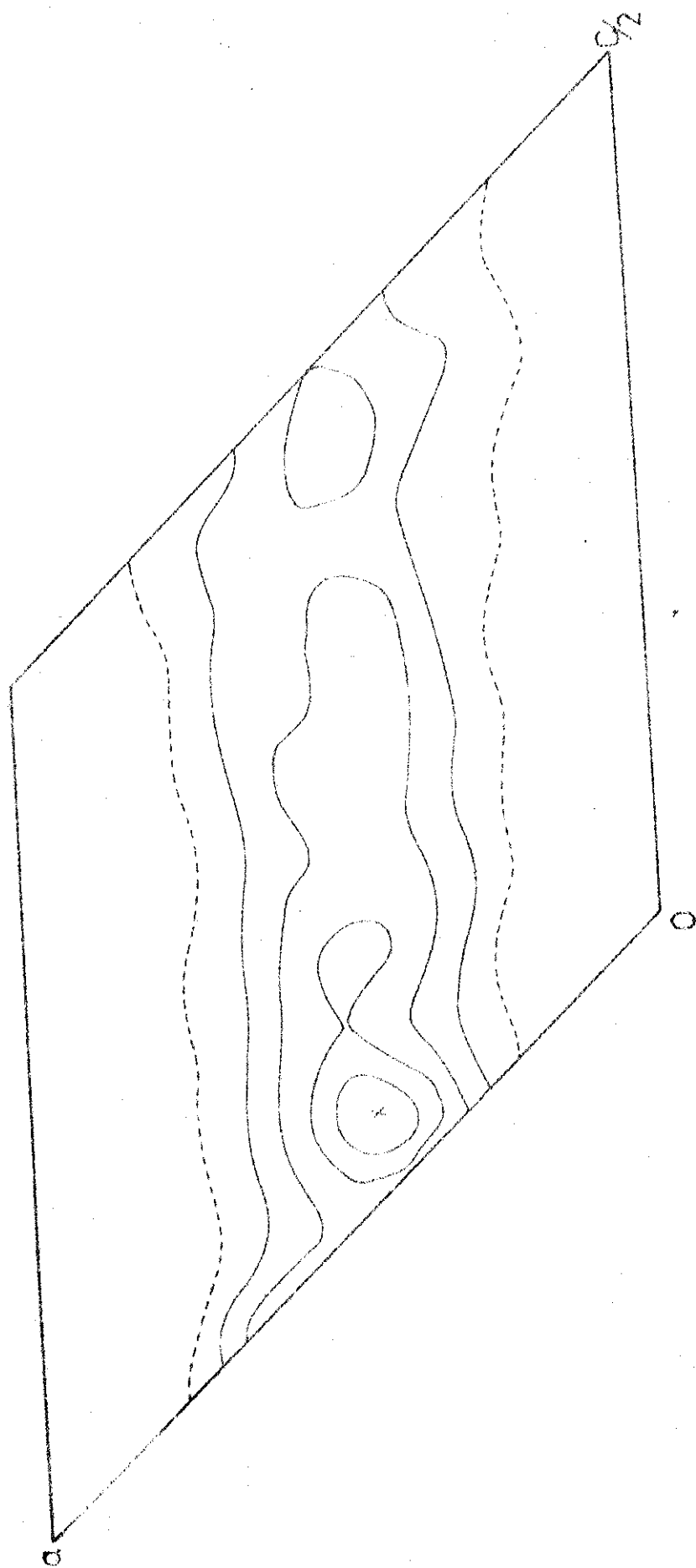


Figure 4.3: The Harker section in the three-dimensional Patterson map of cholesterol bromide. x indicates the Br-Br vector.

assigning the isotropic temperature factor of $5.9 \text{ \AA}^2$ obtained from the Wilson's graph. In the space group $P2_1$, since the origin of the unit cell has to be on the 2_1 screw axis, and since there is no unique origin point along the unique axis, in order to define the origin, the y-coordinate of the bromine atom was assigned arbitrarily and kept fixed. The R-factor at the end of two cycles of refinement was 0.445.

A bromine-phased Fourier map and a difference Fourier map were next computed. The electron density distribution in these maps were running parallel to the c-axis, thus confirming the orientation indicated by the vector density distribution in the Patterson map. However, by placing atoms on the prominent high peaks in the electron density map, no satisfactory molecular model could be fitted. There were many more high peaks than required. This feature was probably due to the use of very limited data, which introduced very strong series termination effects. Hence, as the next step, refinement of the occupancy factors of 49 highest peaks in the Fourier maps was undertaken. (Fig. 4.4 shows the peak distribution in the bromine-phased Fourier map.) Each of these peak positions was assigned a normalised occupancy factor of 0.55 with the scattering factors of carbon, so that the effective number of scatterers in the asymmetric port of the unit cell was approximately equivalent to

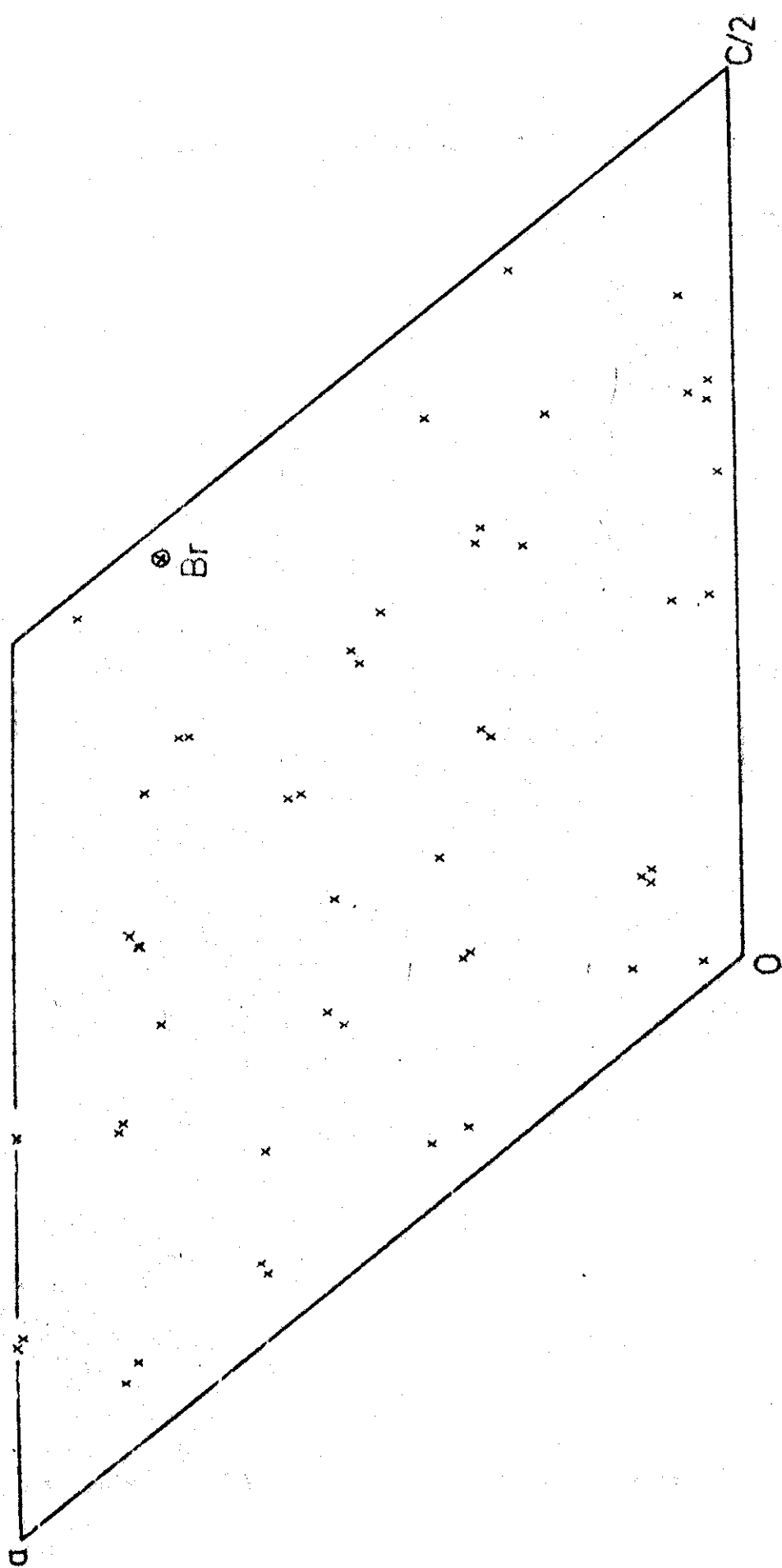


Figure 4.4: Peak distribution in the bromine-phased Fourier map.

27 carbon atoms, which is the total number of carbon atoms per molecule. The contribution of the bromine atom was included in the structure factor calculations. At the end of two cycles of refinement of occupancy factors, 19 positions were found to have occupancy values greater than 0.7, while the others had values much less than 0.4. Occupancy values of 1.0 were assigned to these 19 positions and four cycles of least-squares Calculations refining the isotropic temperature factors and the positional coordinates were carried out, The R-value reduced to 0.314. At the end of the fourth cycle of refinement, 5 among the 19 positions were found to have very high temperature factors ($B \gg 20$) and hence were rejected from further calculations. The remaining 14 atomic positions have been marked in Fig. 4.5. In order to appreciate the departure of this model from the final structure, the Final refined coordinates have also been marked in this diagram. A Fourier map was computed including the contributions from the 14 atoms (carbons) and the bromine atom. The electron density distribution in this map was not sufficiently resolved to enable the identification of the rest of the atomic positions in an unambiguous manner, but a unique molecular model which explained all the major features of the electron density distribution could be fitted on the diffuse density. Subsequent least-squares calculations

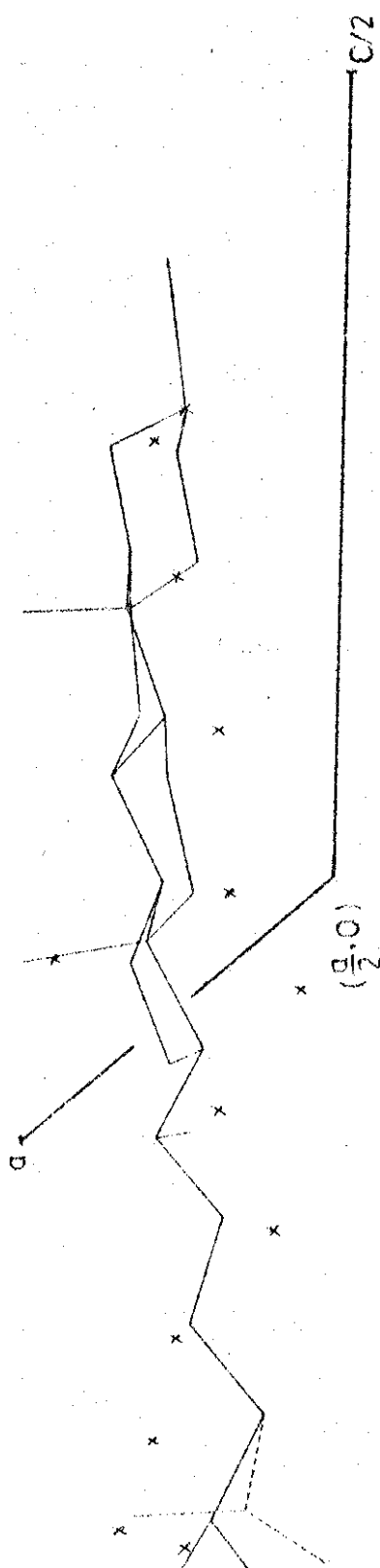


Figure 4.5: The 14 carbon positions obtained from the least-squares refinement of the occupancy factors of the peaks in the bromine-phased Fourier map. The final refined coordinates of cholesteryl bromide have also been marked for comparison.

proved that the trial **molecular** model was correct. The model was **further** refined with both the bromide and the obloride data.

Due to the meagre **amount** of **reflections** data **available**, the presence of 28 non-hydrogen atoms in the asymmetric part of the unit cell leads to a very **poor** reflections to parameters ratio, the value being; ~ 4.1 for the chloride **structure** and ~ 2.6 **for** the bromide **structure**. Hence, **least-squares technique** alone could not be employed for a meaningful refinement of the **structure**; **Fourier and** difference **Fourier** methods were coupled **with** the **least-squares technique** during the refinement of the **structure**. After every two **cycles** of **least-squares** calculations, **Bourier and** difference **Fourier maps** were computed. The maps were computed after removing the **contributions** of 6 to 7 **carbon** atoms at a time (**i.e.**, atoms **belonging** to a ring or the end chain). **This corresponded** to nearly 75-80% of the scattering matter **always** put in $\frac{1}{2}$ ^{to} ensure correct phasing. In general, the **Fourier maps** were **considered** more reliable **and**, whenever the **least-squares** refinement led to bad molecular geomstry, the **atomic** coordinates were adjusted only on the basis of the **maps**. The coordinates derived on the **basis** of these maps were used **in the** subsequent **least-squares** calculations. **Thus, the** **positions** of **all** the atoms **in the molecule** were adjusted

with the help of a series of **Fourier** and **difference Fourier maps** and least-squares refinement. **6 successive** cycles of refinement with the bromide data **employing** this combination of **techniques** reduced the R-value to 0.183. All the atoms were refined **isotropically** and **Cruickshank's** weighting scheme [26] of the form $w = 1/(a + bF_o + cF_o^2)$ with $a = 1.814$, $b = -0.014$ and $c = 0.001$ was used. A similar **refinement** on the trial model using the chloride data and **Cruickshank's** weighting **scheme** with $a = 0.139$, $b = 0.207$ and $c = -0.001$ gave an R-value of 0.22. Since the **number** of reflections for **cholesteryl** chloride was slightly larger than for **cholesteryl** bromide, all further refinement **was** carried out on the chloride **structure**.

At **this** stage, **some** of the atoms of the chain at **C(17)** were found to have **higher** temperature **factors** than the atoms in the sterol **nucleus**. In particular, the **thermal parameters** of **C(25)**, **C(26)** and **C(27)** were found to be significantly large. (**Atom** numbering is shown in Fig. 111). In the chloride **structure**, the **average B value** for the **sterol ring system** was $10.4 \text{ \AA}^2$ and those of **C(25)**, **C(26)** and **C(27)** were $17.8 \text{ \AA}^2$, $15.1 \text{ \AA}^2$ and $18.3 \text{ \AA}^2$ respectively. Also, the **molecular dimensions** involving these **three** atoms were very **different** from the standard values. The bond distances **C(24)-C(25)**, **C(25)-C(26)** and **C(26)-C(27)** were $1.80 \text{ \AA}$, $1.28 \text{ \AA}$ and

1.68 Å respectively. All of them correspond to $C_{sp^3} - C_{sp^3}$ type of bonds. Similar unusual features were found to occur in the bromide structure also. Manual adjustment of these positions was not effective as the least-squares shifts always tended to move the atoms back to the original positions, leading to unsatisfactory molecular dimensions. Phase disconcerting features suggested the presence of disorder in this part of the molecule. Hence, a difference Fourier map was computed using the chloride data, after removing the contributions from the three atoms. The map contained very diffuse areas of positive electron density, the value varying from $1e/\text{\AA}^3$ to $3e/\text{\AA}^3$. On this distribution, two sets of positions could be fixed for each of the three carbon atoms which were not included in the map. Fig. 4.6 shows the composite electron density distribution in this region and the two sets of positions assigned for the three chain atoms. Least-squares refinement of the occupancy factors of these two sets of positions was carried out, starting with an initial value of 0.5 for each of them. The occupancy factors of the two sets refined to the values 0.65 and 0.35 respectively in four cycles. The set with the occupancy value 0.65 corresponds to the original set of positions.

Another striking feature noted from the difference map was regarding the atoms Cl and the covalently bonded carbon atom C(3). The difference electron density distri-

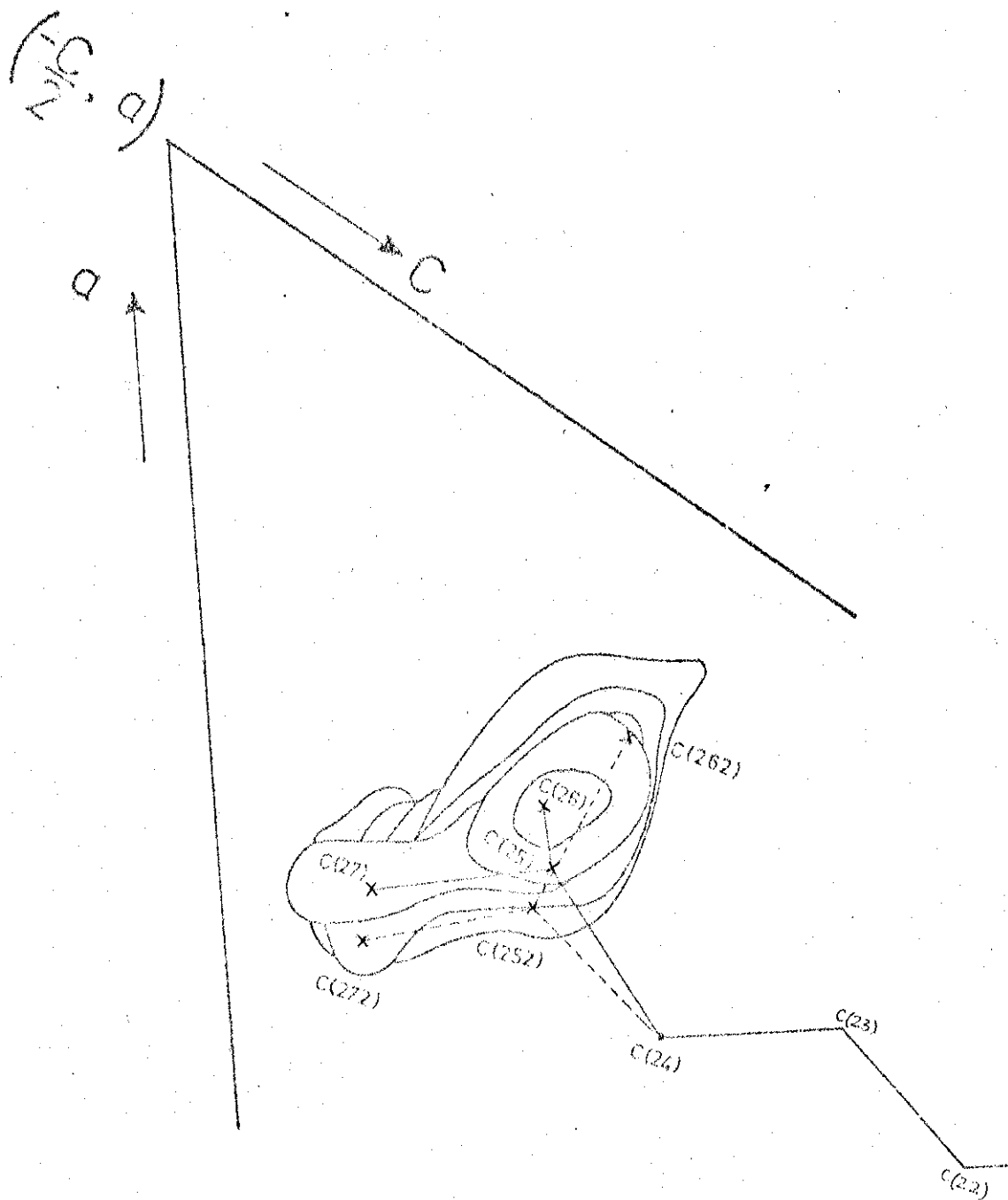


Figure 4. ⁶ Composite electron density distribution in the C(25) ... C(27) region. The two sets of positions fitted for the chain atoms C(25), C(26) and C(27) have been marked.

bution near the C1 and C(3) positions indicated highly anisotropic thermal motions for these atoms and therefore, in the subsequent calculations, C1 and C(3) were assigned anisotropic thermal parameters. Five more cycles of block-diagonal least-squares refinement with anisotropic thermal parameters for C1 and C(3), alternated with Fourier and difference Fourier synthesis, reduced the R-factor to 0.18. The two sets of positions for C(25), C(26) and C(27) were also refined isotropically. The molecular dimensions involving the atoms in the end chain had noticeably improved after including the disorder in the least-squares refinement. In the course of the least-squares refinement, the low angle reflections 110, 200 and 20 $\bar{1}$ had F_o values much greater than their respective, F_c values and hence were corrected for the secondary extinction effect by the method of Zachariasen [27].

The refined coordinates of cholesteryl chloride were used to refine the structure of cholesteryl bromide. Five cycles of least-squares refinement, alternated with Fourier and difference Fourier syntheses, using the bromide data, gave an R-value of 0.155. The atoms Br and C(3) were assigned anisotropic thermal parameters during the refinement. The reflections 110 and 200 were corrected for secondary extinction effects.

The refinement of the anisotropic thermal parameters

for the remaining atoms in the molecule was not undertaken due to %helack of a sufficient number of reflections. The scattering factors given by Cromer and Waber [28] were used in these calculations. Corrections for the anomalous scattering effect have not been included.

4.4 Results and Discussion

The final positional and thermal parameters of cholesteryl chloride and cholesteryl bromide are listed in tables 4.2 and 4.3 respectively. Tables 4.4 and 4.5 give the respective structure factors. The interatomic distances are marked in Figures 4.7 and 4.8 and the valency angles are listed in Tables 4.6 and 4.7 respectively. As mentioned earlier, the number of observed reflections was very small and consequently, the standard deviations of the molecular dimensions are high. However, as the number of observed reflections for the chloride structure was slightly more than that for the bromide structure, the standard deviations for the dimensions in the former are found to be slightly lower than those in the latter. Even though the accuracy of the structure determination is lowered on account of the large standard deviations of the molecular dimensions, the details of the conformation of the molecule and the molecular packing in the crystal are not disputable. The lengths of the unsaturated C-C bonds in the steroid skeleton average to $1.55 \pm 0.08 \text{ \AA}$ and $1.58 \pm 0.17 \text{ \AA}$ in the chloride and the bromide structures

TABLE 4.2

Final fractional positional coordinates ($\times 10^3$) and thermal parameters of cholesteryl chloride.
Estimated standard deviations are given in parentheses.

Atom	x	y	z	$B(\text{\AA}^2)$ or $b_{11}(\times 10^3)$	$b_{22}(\times 10^3)$	$b_{33}(\times 10^3)$	$b_{12}(\times 10^3)$	$b_{13}(\times 10^3)$	$b_{23}(\times 10^3)$
C(1)	727(6)	309(8)	279(3)	12.5(1.5)					
C(2)	760(5)	306(6)	354(3)	9.3(1.1)					
C(3)	759(7)	125(9)	386(4)	58(17)	90(29)	15(4)	-6(21)	21(8)	-3(10)
C(4)	881(6)	-12(8)	392(3)	12.3(1.5)					
C(5)	848(6)	-4(7)	312(3)	10.9(1.3)					
C(6)	832(7)	-155(8)	273(3)	12.8(1.5)					
C(7)	816(6)	-175(8)	196(3)	12.8(1.5)					
C(8)	844(4)	2(6)	170(2)	8.0(1.0)					
C(9)	761(5)	149(7)	184(3)	9.4(1.2)					
C(10)	838(5)	171(6)	275(3)	9.6(1.2)					
C(11)	776(5)	332(6)	161(3)	9.5(1.1)					
C(12)	700(5)	321(7)	65(2)	9.7(1.2)					
C(13)	802(5)	174(6)	59(3)	9.5(1.2)					
C(14)	761(4)	-1(6)	83(2)	7.7(1.0)					
C(15)	823(6)	-133(8)	55(3)	13.1(1.6)					
C(16)	759(5)	-81(7)	-30(3)	10.0(1.3)					
C(17)	715(5)	122(7)	-26(2)	9.2(1.1)					
C(18)	983(5)	227(6)	106(2)	9.3(1.1)					
C(19)	1015(6)	281(7)	333(3)	11.3(1.3)					
C(20)	746(5)	221(6)	-79(2)	8.7(1.1)					

C(21)	702(6)	418(7)	-92(3)	10.7(1.3)				
C(22)	638(5)	128(8)	-168(3)	11.8(1.4)				
C(23)	692(6)	221(8)	-217(3)	13.0(1.6)				
C(24)	588(6)	114(10)	-305(3)	14.3(1.7)				
C(25)	659(9)	130(12)	-350(4)	12.3(2.3)				
C(26)	697(7)	305(9)	-354(3)	8.2(1.6)				
C(27)	558(12)	1(16)	-427(6)	17.4(3.3)				
C(252)	618(18)	236(22)	-357(9)	12.8(4.5)				
C(262)	796(15)	160(18)	-303(7)	10.8(3.6)				
C(272)	501(22)	125(27)	-439(11)	14.9(5.8)				
CL	797(2)	117	480(1)	67(5)	67(6)	15(1)	8(4)	22(2)
								5(2)

TABLE 4.3

Final fractional positional coordinates ($\times 10^3$) and thermal parameters of cholesteryl bromide.
Estimated standard deviations are given in parentheses.

Atom	x	y	z	$B(\text{\AA}^2)$ or $b_{11}(\times 10^3)$	$b_{22}(\times 10^3)$	$b_{33}(\times 10^3)$	$b_{12}(\times 10^3)$	$b_{13}(\times 10^3)$	$b_{23}(\times 10^3)$
C(1)	727(9)	329(12)	273(4)	8.0(2.4)					
C(2)	766(8)	311(12)	355(4)	8.0(2.4)					
C(3)	756(13)	115(44)	375(6)	110(38)	328(151)	18(8)	78(88)	43(17)	28(44)
C(4)	876(9)	-21(11)	392(4)	8.4(2.5)					
C(5)	838(11)	1(14)	314(6)	12.6(3.2)					
C(6)	841(11)	-150(15)	285(5)	11.8(3.0)					
C(7)	815(10)	-180(13)	204(5)	9.7(2.6)					
C(8)	860(7)	-12(9)	181(3)	2.9(1.7)					
C(9)	773(9)	150(18)	188(4)	7.8(2.2)					
C(10)	841(7)	175(14)	279(4)	8.7(1.9)					
C(11)	759(9)	345(12)	152(5)	7.1(2.4)					
C(12)	722(9)	327(13)	65(5)	8.7(2.4)					
C(13)	796(8)	158(13)	59(4)	8.5(2.3)					
C(14)	770(10)	-14(13)	88(5)	11.4(3.0)					
C(15)	819(10)	-151(15)	54(5)	10.9(2.9)					
C(16)	759(10)	-75(14)	-29(5)	9.3(2.6)					
C(17)	702(9)	129(19)	-39(4)	10.7(2.6)					
C(18)	981(8)	205(11)	106(4)	6.8(2.2)					
C(19)	1015(9)	260(12)	333(5)	8.8(2.5)					
C(20)	774(11)	202(14)	-71(6)	12.9(3.1)					
C(21)	713(8)	397(12)	-87(4)	7.0(2.2)					

Tabl 4.3 continued

C(22)	657(10)	100(19)	-159(5)	9.5(2.7)					
C(23)	711(13)	150(17)	-208(7)	12.2(4.0)					
C(24)	579(12)	125(20)	-310(6)	10.2(3.3)					
C(25)	663(15)	122(29)	-351(7)	6.2(4.0)					
C(26)	704(14)	296(18)	-365(7)	6.1(3.7)					
C(27)	597(15)	-39(21)	-406(8)	12.8(4.4)					
C(252)	602(39)	217(50)	-364(20)	13.3(12.6)					
C(262)	796(27)	160(54)	-303(14)	5.9(7.4)					
C(272)	472(19)	97(33)	-439(9)	8.0(4.5)					
Br	787(2)	117	478(1)	79(4)	73(5)	16(1)	10(5)	27(2)	8(3)

TABLE 4.4

The observed and calculated values of structure factors ($\times 10$) and S_{Ha} phase values for all the measured reflections of cholesterol chloride.

H	0	0	-2	162	124	132	0	228	271	31	-4	100	86	153
1	175	108	-1	148	204	109	1	86	71	145	-3	83	81	254
2	133	135	0	265	328	281	2	164	166	220	-2	224	167	326
3	182	195	180	137	189	284	3	70	55	239	0	158	75	175
4	154	225	180	138	224	93	H	3	2		1	128	112	190
5	90	0	0	138	108	48	2				2	61	48	270
							3				3	72	82	8
H	1	0	-5	37	49	327	-5	42	40	283	H	4	3	
1	1328	1451	318	54	67	186	-1	138	146	46	-5	36	48	296
2	407	427	336	58	43	111	-1	181	174	261	-4	17	29	163
3	321	333	171	171	181	344	2	17	93	310	-3	142	124	96
4	206	211	76	185	125	56	H	4	2		0	58	40	23
5	60	73	19	91	95	193	-4	57	68	234	1	68	43	32
				96	99	40	-1	60	32	43	2	27	28	172
H	2	0	-5	39	55	329	-5	115	163	33	H	0	4	
0	270	390	139	-1	57	291	1	113	97	221	-6	46	56	0
1	114	125	346	-4	98	148	2	68	44	134	-5	137	151	0
2	88	103	345	-3	88	93	H	5	2		-4	89	82	180
3	149	173	190	-2	125	270	0	23	28	8	-3	308	462	180
4	134	120	189	-1	123	77	1	21	34	48	-2	183	210	180
				3	22	113	0	6	2		-1	155	152	0
H	3	0	-5	39	55	329	-5	115	163	33	1	192	152	180
1	70	114	77	-1	123	77	H	6	2		2	143	102	180
2	91	50	140	3	22	113	0	34	38	178	3	111	87	180
3	61	23	348	H	5	1	H	0	3		H	1	4	
4	75	60	256	0	30	33	6	134	88	180	-6	59	66	132
				H	6	1	-5	134	121	180	-5	50	63	10
H	4	0	-5	39	55	329	-5	134	121	180	-4	148	136	286
0	124	10	170	-1	123	77	-4	48	54	0	-3	111	302	231
1	124	121	133	0	34	37	-2	168	201	0	-2	192	300	150
2	24	32	29	H	0	2	-1	189	94	180	-1	180	158	91
				7	54	53	2	84	78	180	0	66	61	236
H	6	0	-7	54	53	180	-7	221	202	0	1	209	196	232
0	91	85	323	-6	160	180	H	1	3		2	34	46	148
H	0	1	-7	54	53	180	-7	47	25	304	H	2	4	
1	346	389	0	-6	160	180	-6	60	57	301	-6	66	16	333
2	334	438	0	-5	128	180	-5	117	79	187	-4	34	48	196
3	1264	1187	180	-4	136	180	-4	137	115	140	-3	86	44	90
4	442	571	0	-3	136	180	-3	162	115	140	-2	188	184	5
5	287	356	0	-2	136	180	-2	229	251	313	-1	200	213	310
6	93	69	180	-1	136	180	-1	214	157	143	0	194	170	297
				0	136	180	0	226	228	133	1	206	201	72
H	1	1	-6	43	36	133	-6	171	100	142	-1	145	144	94
1	55	59	46	-5	180	94	-5	134	120	213	0	110	73	246
2	105	88	154	-4	150	24	H	2	3		1	75	67	294
3	207	313	185	-3	180	24	-6	36	28	239	2	31	44	9
4	324	330	276	-2	224	275	-5	68	54	244	H	3	4	
5	216	267	303	-1	268	168	-4	23	26	310	-7	30	17	358
6	164	276	99	0	303	51	-3	105	94	14	-6	44	51	283
7	470	477	130	-1	322	287	-2	208	162	130	-4	221	229	71
8	161	172	337	0	332	338	-1	229	256	232	-3	177	144	246
9	139	111	674	1	332	109	0	227	220	248	-2	295	285	276
	30	50	224	2	132	90	-1	68	78	36	-1	318	202	276
H	2	1	-4	151	154	32	2	66	106	48	0	107	196	30
1	40	64	306	-3	209	304	H	3	3		1	54	139	66
2	28	42	243	-2	214	305	-6	28	58	318	H	4	4	
3	197	174	104	-1	181	86	-5	29	33	214	5			

-5	93	22	20	-3	149	156	160	-1	180	165	19	0	28	22	138
-4	69	65	25	-3	171	122	180	-0	91	169	241	1	56	67	200
-3	196	165	26	-1	178	122	180	-1	175	141	155	H	3	8	
-2	164	164	26	0	125	128	100	2	41	74	18				
-1	159	189	21	1	92	46	100	3	57	80	310				
0	16	18													
1															
H	0	5													
-7	123	107	180	-7	44	61	22	-7	34	69	120	-6	20	49	58
-6	144	107	180	-6	47	49	301	-4	160	134	207	-5	22	12	117
-5	165	62	180	-5	76	89	288	-4	22	30	69	-4	51	46	238
-4	113	81	180	-4	105	110	355	-3	217	154	164	-3	18	13	345
-3	56	73	0	-3	124	99	107	-2	92	95	268	-2	52	113	186
-2	290	303	180	-2	135	128	102	-1	166	119	277	-1	33	24	168
0	197	249	180	0	149	129	146	0	46	43	264	0	31	33	246
1				1	123	134	115	1	65	49	92	-4	47	18	130
H	1	5		2	39	61	180	2				-3	54	40	325
-7	65	65	293	-7	44	52	62	-6	86	82	78	-2	51	56	169
-6	40	64	246	-6	97	97	62	-5	22	31	179	-1			
-5	177	152	75	-5	116	99	275	-4	156	134	235	0			
-4	195	189	69	-4	104	104	199	-3	33	63	36	-7	48	40	0
-3	95	106	320	-3	103	168	166	-2	128	146	43	-6	153	162	180
-2	328	302	309	-2	82	81	294	-1	76	84	155	-4	175	267	0
-1	360	326	15	-1	61	45	356	0	53	51	128	-3	309	337	0
0	47	59	80	0	199	121	91	1	41	8	238	-2	464	355	0
1		37	146	1	105	87	286	H	4	7		-1	39	27	130
H	2	5		2	48	54	244	0				0	174	168	180
-7	39	79	27	-7	29	42	116	-6	74	67	333	H	1	7	
-6	113	101	360	-6	26	22	156	-5	32	54	2	0			
-5	143	139	39	-5	130	91	263	-4	61	57	130	-3	77	179	181
-4	194	174	89	-4	133	99	267	-3	55	77	173	-2	171	169	159
-3	277	277	42	-3	113	82	143	-2	51	63	315	-1	198	147	357
-2	314	290	341	-2	191	160	110	0	45	25	299	0	211	185	390
-1	310	275	317	-1	170	70	178	H	0	3		-1	99	93	228
0	88	28	335	0	59	42	170	-6	114	108	0	2	62	78	144
1	24	64	118	1	73	64	10	-5	85	64	0	0	48	68	79
H	3	5		H	4	6		-4	129	132	180	H	2	9	
-7	42	45	60	-7	64	58	3	-3	122	70	0	-6	55	50	232
-6	43	36	291	-6	20	29	119	-2	48	60	0	-5	65	81	302
-5	193	181	249	-5	72	75	148	-4	80	51	180	-3	146	126	100
-4	117	70	181	-4	50	23	208	-3	184	188	180	-2	146	164	170
-3	349	304	93	-3	95	60	333	-2	45	55	0	-1	65	44	204
-2	187	136	95	-2	44	26	45	H	1	H		0	68	52	274
-1	133	111	272	-1	60	99	136	-5	160	168	354	H	3	9	
0	135	154	243	0	52	30	42	-4	78	73	292	-6	30	40	70
1	68	77	234	1				-3	136	121	250	-5	34	45	205
H	4	5		H	0	7		-2	222	174	37	-4	77	95	271
-7	45	54	59	-7	50	46	0	-1	140	102	394	-3	21	23	10
-6	67	65	175	-6	24	160	0	0	121	97	254	-2	53	68	97
-5	162	155	205	-5	160	151	183	-1	81	90	71	-1	28	21	90
-4	22	34	193	-4	277	233	182	0	54	92	39	0	26	43	225
-3	154	71	34	0	143	159	0	H	2	8		H	4	9	
-2	61	59	340	-2				-7	34	62	143	-6	44	50	321
-1	21	20	121	-1				-6	54	61	369	-5	28	27	5
0	56	65	145	0				-4	49	62	369	-3	19	32	116
1	25	40	255	1				-2	24	45	212	-1	24	42	307
H	0	6		H	1	7		-1	168	118	212	0	31	36	25
-5	112	141	0	-5	151	157	216	-4	116	110	55				
				-3	144	114	305	-2	261	198					

TABLE 4.5

The observed and calculated values of structure factors ($\times 10$) and the phase values for all the measured reflections of cholesteryl bromide.

H	0	0	0	1	155	229	47	-4	257	212	135	0	170	183	182
2	1431	1491	188	H	4	1		-3	235	196	114	H	0	5	
3	284	307	188	0	79	120	287	-2	414	418	307	-6	160	91	180
4	291	281		H	6	1		-1	27	93	299	-5	170	143	180
5	144	118	0	0	78	68	62	1	346	319	136	-4	151	126	180
H	1	0		H	0	2		2	109	131	199	-3	142	180	0
1	1739	1710	315	0	78	68	62	H	2	3		-2	183	221	0
2	493	386	253	H	0	2		-5	180	115	278	-1	183	221	0
3	459	445	188	0	78	68	62	-3	201	209	88	0	573	538	180
4	218	218	87	H	0	2		-2	362	381	101	1	415	392	180
H	2	0		-5	149	111	180	-1	360	399	249	2	81	75	0
0	403	518	111	-4	381	323	180	0	466	433	250	H	1	5	
1	163	118	206	-3	304	278	180	1	65	92	43	-6	72	126	288
2	61	119	286	-2	329	355	180	2	90	200	71	-5	174	160	26
3	121	119	204	0	261	301	1	H	3	3		-4	285	322	107
4	180	151	179	1	113	103	180	-4	79	83	203	-3	205	124	189
H	3	0		2	304	323	180	-3	161	250	240	-2	569	520	311
2	55	104	127	H	1	2		-2	172	175	355	-1	556	473	356
3	76	91	139	0	101	89	10	1	87	51	168	1	68	126	169
H	4	0		-5	188	177	85	H	4	3		H	2	5	
0	414	293	179	-4	337	319	281	0	123	118	357	-5	205	261	254
H	6	0		-3	540	507	150	H	0	4		-4	180	174	102
0	113	133	317	-2	179	270	123	0	259	224	0	-3	412	397	75
H	0	1		-1	475	421	309	H	0	4		-2	207	195	2
1	370	362	0	3	178	194	121	-5	498	429	180	-1	506	425	296
2	525	472	0	H	2	2		-3	309	381	180	0	186	243	306
3	625	582	0	-4	178	195	31	-2	336	377	0	H	3	5	
4	105	555	0	-3	272	304	278	-1	230	140	180	-5	235	198	252
H	1	1		-2	259	267	252	2	235	154	180	-4	101	130	206
1	296	357	184	0	358	354	62	H	1	4		-3	443	343	95
2	273	306	257	1	157	110	173	-6	91	104	118	-2	303	278	66
3	301	285	315	2	222	195	246	-5	66	105	47	0	148	237	224
4	307	195	111	H	3	2		-4	258	240	291	H	0	6	
5	274	248	106	-3	208	205	32	-3	319	319	243	-6	90	20	0
6	886	750	126	-2	199	266	227	-2	484	528	140	-5	253	262	0
H	2	1		0	66	90	336	-1	321	320	120	-4	327	388	180
1	222	192	106	1	85	83	26	1	283	254	258	-3	174	237	180
2	368	265	108	H	4	2		H	2	4		-2	422	398	0
3	161	245	97	0	185	142	199	0	201	125	77	1	307	237	0
4	482	907	257	H	6	2		-5	190	205	356	0	124	141	180
5	337	290	263	0	79	59	184	-4	366	335	364	H	1	6	
H	3	1		H	0	3		-3	326	364	291	-5	73	100	287
1	222	192	106	0	79	59	184	-2	316	346	75	-4	309	297	328
2	368	265	108	0	79	59	184	-1	299	303	92	-3	167	164	305
3	161	245	97	H	0	3		0	134	135	247	-2	346	321	129
4	482	907	257	0	79	59	184	1	88	155	263	-1	280	263	108
5	337	290	263	-6	99	72	180	H	3	4		1	160	218	313
H	3	1		-5	210	181	180	-4	336	306	57	H	2	6	
1	222	192	106	-3	325	338	0	-3	262	190	67	-4	209	207	189
2	368	265	108	-2	63	87	0	-2	563	364	240	-3	228	245	211
3	161	245	97	0	54	12	184	-1	593	440	261	-2	167	153	290
4	482	907	257	2	153	238	0	0	270	220	26	-1	188	170	64
5	337	290	263	H	1	3		1	186	201	55	0	251	242	90
H	3	1		0	77	85	328	H	4	4		1	153	155	270
1	222	192	106	-6	77	85	328	0	77	85	328	H	3	6	
2	368	265	108	-5	66	73	180	-5	66	73	180				

-5	203	142	0	-5	167	154	268	-5	156	167	156
-4	183	185	180	-4	209	233	87	-4	97	104	165
-3	68	94	180	-3	238	218	124	-3	167	161	316
-2	77	39	0	-2	75	107	211	-2	81	63	322
-1	167	134	0	-1	159	125	259	H	2	11	
0	88	144	180	H	3	9		-3	209	146	98
H	1	H		H	3	9		H	3	11	
H	4	6		-4	85	171	233	-4	142	125	236
0	91	73	141	-2	101	130	47	H	0	12	
H	0	7		H	0	10		-6	133	99	0
H	86	51	180	-6	88	107	0	-4	133	103	180
88	88	88	180	-5	237	261	0	H	1	12	
275	305	259	0	-4	383	393	180	-7	111	112	119
313	354	180	0	-3	528	487	180	-5	104	151	294
372	354	180	0	-2	369	274	0	-4	75	95	322
268	337	180	0	-1	300	419	0	-3	84	178	104
65	92	0	0	H	1	10		-2	84	114	153
149	201	0	0	-6	84	109	155	H	0	13	
H	1	7		-5	66	78	299	-6	138	157	160
-6	101	89	333	-4	312	314	302	-4	101	51	0
-5	59	94	73	-3	300	320	136	H	1	13	
-4	212	214	153	-2	391	411	129	-5	109	154	168
-3	163	180	110	H	0	102	293	H	0	14	
-2	344	315	307	-7	97	72	0	-6	104	60	0
-1	260	218	346	-6	101	101	180	-4	113	80	180
0	66	88	134	-5	290	284	180	H	1	14	
158	203	141	0	-4	291	268	0	-5	83	161	284
H	2	7		-3	544	554	0	H	0	15	
-5	243	267	293	-2	941	422	0	-6	108	79	180
-4	98	98	46	-1	226	135	180	-4	122	91	0
-3	376	304	100	0	135	205	180	H	1	15	
-2	140	169	176	-7	75	75	313	-7	135	129	321
-1	107	144	258	-6	149	141	338	-6	70	57	163
0	176	146	320	-5	257	259	113	-4	226	242	0
H	3	7		-4	319	339	142	-2	223	246	180
-4	254	215	224	-1	355	301	338	-1	99	71	180
-3	254	270	34	H	1	9		H	1	11	
-2	104	103	162	-7	160	137	201	-7	135	129	321
H	0	0		-6	91	137	201	-6	70	57	163
-6	198	203	0	H	2	9		-5	88	77	154

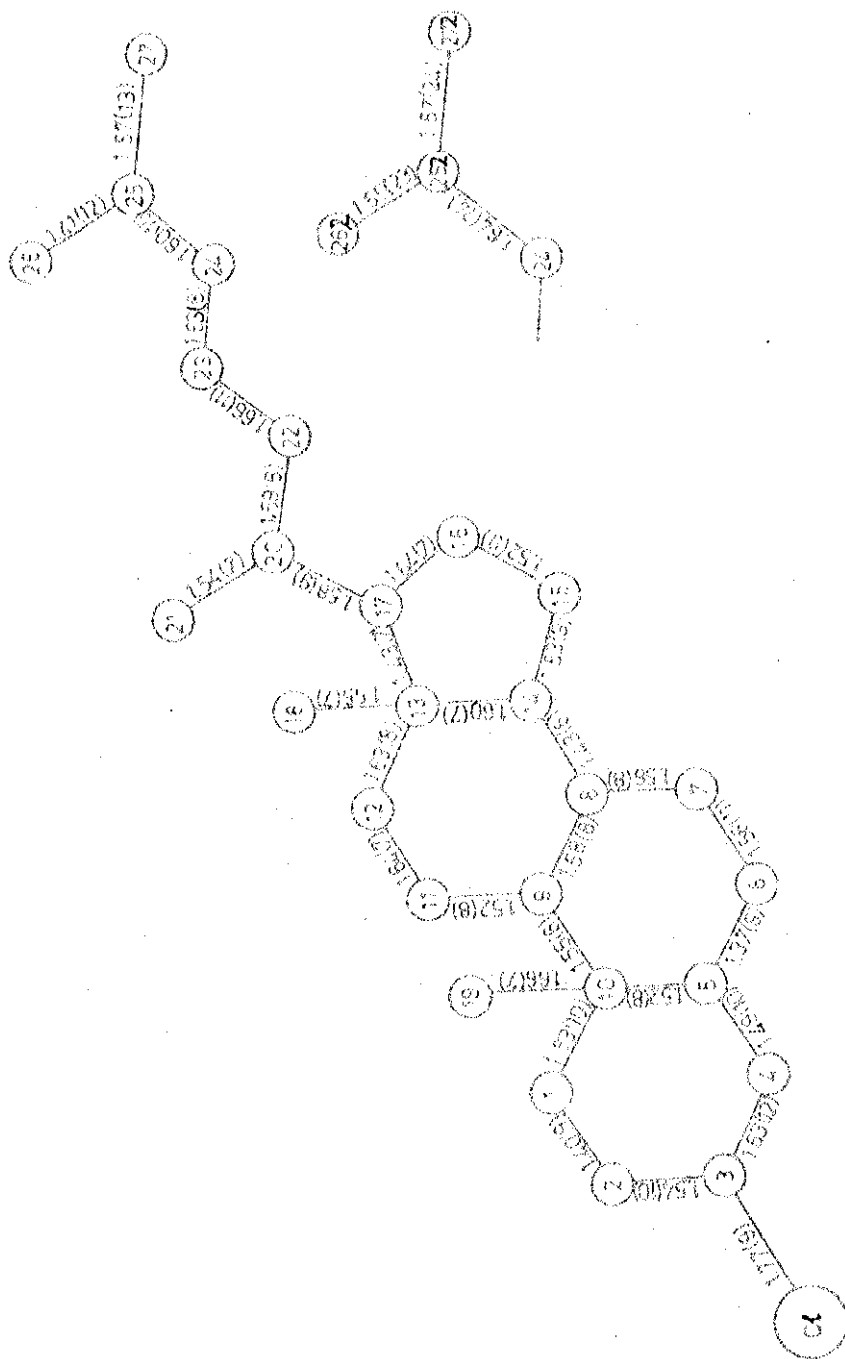


Figure 4.7

Bond lengths - Cholesteryl Chloride

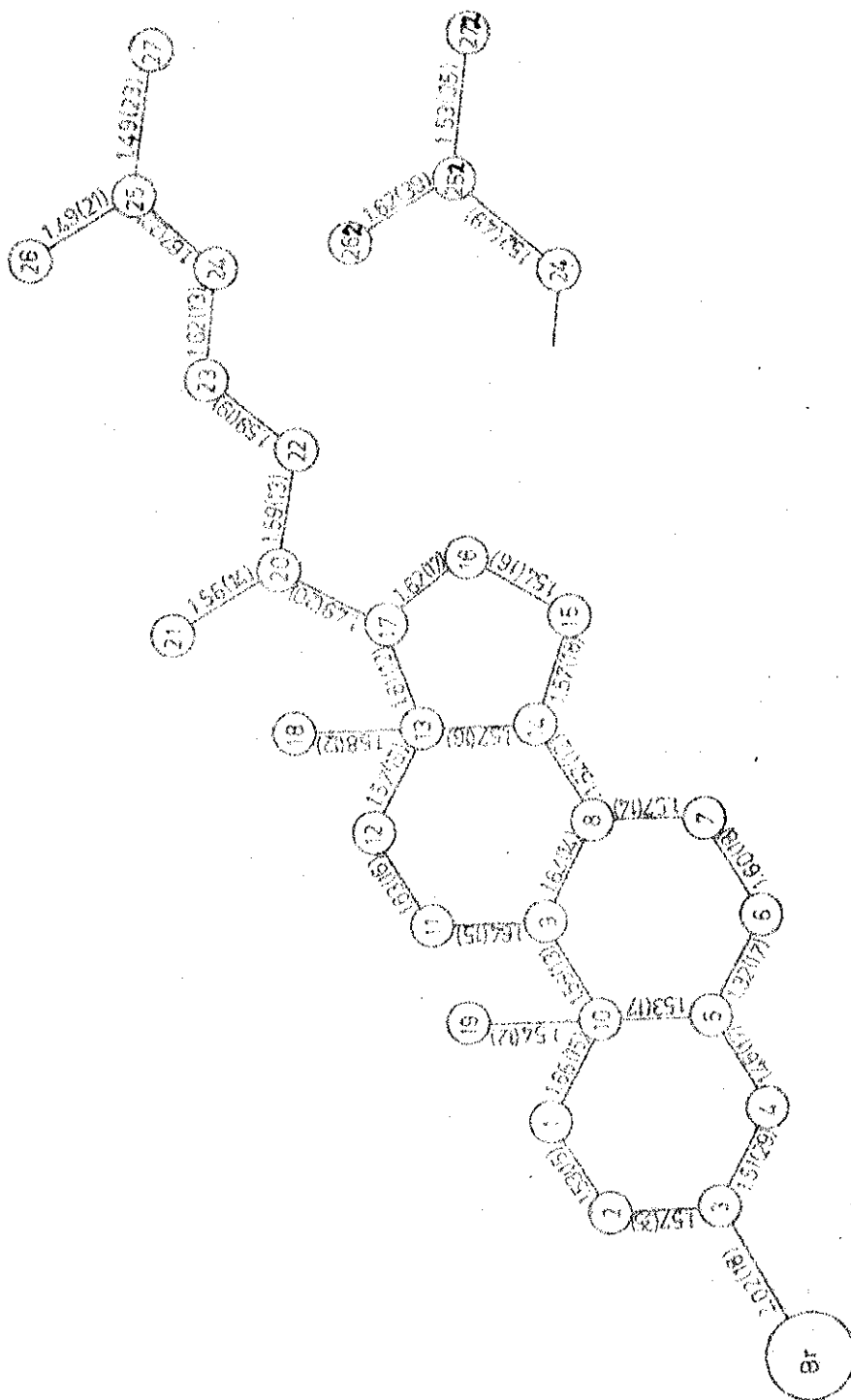


Figure 4.8
Bond lengths - Cholesteryl bromide.

TABLE 4.6

Valency Angles (°)
Cholesteryl Chloride

C1 -C(3)-C(2)	119(5)	C(15)-C(16)-C(17)	95(4)
C1 -C(3)-C(4)	110(5)	C(16)-C(17)-C(13)	111(4)
C(1)-C(2)-C(3)	118(5)	C(17)-C(13)-C(14)	95(4)
C(2)-C(3)-C(4)	111(6)	C(12)-C(13)-C(17)	113(4)
C(3)-C(4)-C(5)	109(5)	C(12)-C(13)-C(18)	113(4)
C(4)-C(5)-C(10)	121(5)	C(17)-C(13)-C(18)	112(4)
C(5)-C(10)-C(1)	110(5)	C(14)-C(13)-C(18)	121(4)
C(10)-C(1)-C(2)	114(5)	C(8)-C(14)-C(15)	118(4)
C(5)-C(6)-C(7)	128(6)	C(7)-C(8)-C(14)	110(4)
C(6)-C(7)-C(8)	113(5)	C(10)-C(9)-C(11)	103(4)
C(7)-C(8)-C(9)	106(4)	C(13)-C(17)-C(20)	120(4)
C(8)-C(9)-C(10)	115(4)	C(16)-C(17)-C(20)	101(4)
C(9)-C(10)-C(5)	111(5)	C(17)-C(20)-C(21)	114(4)
C(10)-C(5)-C(6)	119(5)	C(17)-C(20)-C(22)	109(4)
C(1)-C(10)-C(19)	99(4)	C(21)-C(20)-C(22)	109(4)
C(9)-C(10)-C(19)	112(4)	C(20)-C(22)-C(23)	106(4)
C(1)-C(10)-C(9)	110(4)	C(22)-C(23)-C(24)	105(5)
C(5)-C(10)-C(19)	114(5)	C(23)-C(24)-C(25)	116(6)
C(4)-C(5)-C(6)	120(5)	C(24)-C(25)-C(26)	112(7)
C(8)-C(9)-C(11)	113(4)	C(24)-C(25)-C(27)	108(8)
C(9)-C(11)-C(12)	107(4)	C(26)-C(25)-C(27)	124(8)
C(11)-C(12)-C(13)	110(4)	C(23)-C(24)-C(252)	102(8)
C(12)-C(13)-C(14)	101(4)	C(24)-C(252)-C(262)	90(12)
C(13)-C(14)-C(8)	110(4)	C(24)-C(252)-C(272)	95(13)
C(13)-C(14)-C(15)	97(4)	C(262)-C(252)-C(272)	108(16)
C(14)-C(15)-C(16)	110(5)		

TABLE 4.7

Valency Angles ($^{\circ}$)

Choleeryl Bromide

Br-C(3)-C(2)	108(13)	C(15)-C(16)-C(17)	109(8)
Br-C(3)-C(4)	107(13)	C(16)-C(17)-C(13)	97(8)
C(1)-C(2)-C(3)	113(11)	C(17)-C(13)-C(14)	107(8)
C(2)-C(3)-C(4)	119(16)	C(12)-C(13)-C(17)	110(8)
C(3)-C(4)-C(5)	98(11)	C(12)-C(13)-C(18)	107(7)
C(4)-C(5)-C(10)	127(10)	C(17)-C(13)-C(18)	105(7)
C(5)-C(10)-C(1)	111(8)	C(14)-C(13)-C(18)	116(8)
C(10)-C(1)-C(2)	106(7)	C(8)-C(14)-C(15)	121(8)
C(5)-C(6)-C(7)	127(10)	C(7)-C(8)-C(14)	111(7)
C(6)-C(7)-C(8)	113(8)	C(10)-C(9)-C(11)	108(8)
C(7)-C(8)-C(9)	103(6)	C(13)-C(17)-C(20)	120(9)
C(8)-C(9)-C(10)	115(8)	C(16)-C(17)-C(20)	98(9)
C(9)-C(10)-C(5)	112(9)	C(17)-C(20)-C(21)	100(9)
C(10)-C(5)-C(6)	119(10)	C(17)-C(20)-C(22)	98(9)
C(1)-C(10)-C(19)	104(8)	C(21)-C(20)-C(22)	109(9)
C(9)-C(10)-C(19)	106(8)	C(20)-C(22)-C(23)	109(8)
C(1)-C(10)-C(9)	108(8)	C(22)-C(23)-C(24)	120(9)
C(5)-C(10)-C(19)	115(9)	C(23)-C(24)-C(25)	115(10)
C(4)-C(5)-C(6)	112(10)	C(24)-C(25)-C(26)	117(11)
C(8)-C(9)-C(11)	119(7)	C(24)-C(25)-C(27)	107(12)
C(9)-C(11)-C(12)	111(7)	C(26)-C(25)-C(27)	127(13)
C(11)-C(12)-C(13)	116(8)	C(23)-C(24)-C(252)	122(17)
C(12)-C(13)-C(14)	113(8)	C(24)-C(252)-C(262)	95(23)
C(13)-C(14)-C(8)	113(8)	C(24)-C(252)-C(272)	91(23)
C(13)-C(14)-C(15)	98(8)	C(262)-C(252)-C(272)	117(27)
C(14)-C(15)-C(16)	107(9)		

respectively. The average values of the valency angles involving sp^3 hybridized carbon atoms in the cyclohexane rings of the chloride and the bromide structures are $110 \pm 4^\circ$ and $111 \pm 9^\circ$ respectively. The valency angles in the cyclopentane ring average to $102 \pm 4^\circ$ and $104 \pm 8^\circ$ respectively.

The molecular dimensions of the terminal chain, particularly in the region beyond the atom C(24), are not reliable because of the disorder in this region. Other crystal structures in the choleatane group of steroids exhibiting a similar type of disorder in the same region of the molecule are cholesterol monohydrate [9], cholesteryl myristate [3]; cholesteryl p-toluene sulphonate [11], cholesteryl 17-bromoheptadecanoate [17] and sodium cholesteryl sulphate dihydrate [18]. Chandross and Bordner [11] propose that such a disorder of the molecule could be of significance in the study of biological membrane systems and may be taken as an indication that the 'tail' is in a liquid or semi-liquid state in the membrane system.

The appropriate ring torsion angles for the two crystal structures are listed in Tables 4.8 and 4.9 respectively. The averages of the endocyclic torsion angles of the rings A, B, C and D in the cholesteryl chloride molecule are 48° , 30° , 63° and 36° respectively. The

TABLE 4.8

Torsion Angles (°) - Cholesteryl Chloride

Ring A

C(10)-C(1)-C(2)-C(3)	-50
C(1)-C(2)-C(3)-C(4)	53
C(2)-C(3)-C(4)-C(5)	-47
C(3)-C(4)-C(5)-C(10)	48
C(4)-C(5)-C(10)-C(1)	-44
C(2)-C(1)-C(10)-C(5)	43

Ring B

C(10)-C(5)-C(6)-C(7)	5
C(5)-C(6)-C(7)-C(8)	8
C(6)-C(7)-C(8)-C(9)	-38
C(7)-C(8)-C(9)-C(10)	62
C(8)-C(9)-C(10)-C(5)	-51
C(6)-C(5)-C(10)-C(9)	16

Ring C

C(14)-C(8)-C(9)-C(11)	-62
C(8)-C(9)-C(11)-C(12)	54
C(9)-C(11)-C(12)-C(13)	-58
C(11)-C(12)-C(13)-C(14)	63
C(12)-C(13)-C(14)-C(8)	-70
C(9)-C(8)-C(14)-C(13)	69

Ring D

C(17)-C(13)-C(14)-C(15)	53
C(13)-C(14)-C(15)-C(16)	-46
C(14)-C(15)-C(16)-C(17)	19
C(15)-C(16)-C(17)-C(13)	19
C(14)-C(13)-C(17)-C(16)	-46

TABLE 4.9**Torsion Angles (°) - Cholesteryl Bromide**Ring A

C(10)-C(1)-C(2)-C(3)	-48
C(1)-C(2)-C(3)-C(4)	64
C(2)-C(3)-C(4)-C(5)	-56
C(3)-C(4)-C(5)-C(10)	54
C(4)-C(5)-C(10)-C(1)	-52
C(2)-C(1)-C(10)-C(5)	42

Ring B

C(10)-C(5)-C(6)-C(7)	-12
C(5)-C(6)-C(7)-C(8)	25
C(6)-C(7)-C(8)-C(9)	-45
C(7)-C(8)-C(9)-C(10)	62
C(8)-C(9)-C(10)-C(5)	-52
C(6)-C(5)-C(10)-C(9)	24

Ring C

C(14)-C(8)-C(9)-C(11)	-52
C(8)-C(9)-C(11)-C(12)	37
C(9)-C(11)-C(12)-C(13)	-31
C(11)-C(12)-C(13)-C(14)	44
C(12)-C(13)-C(14)-C(8)	-63
C(9)-C(8)-C(14)-C(13)	64

Ring D

C(17)-C(13)-C(14)-C(15)	48
C(13)-C(14)-C(15)-C(16)	-35
C(14)-C(15)-C(16)-C(17)	11
C(15)-C(16)-C(17)-C(13)	18
C(14)-C(13)-C(17)-C(16)	-41

corresponding values for cholesteryl bromide are 53°, 37°, 49° and 30°. The nomenclature for the rings is as shown in (III). The asymmetry parameters, ΔC_s and ΔC_2 , of Duax and Norton [29], which define the deviation of the conformation of a ring from the ideal conformations, have been calculated for the rings of both the structures. These are listed in Table 4.10. The mirror plane asymmetry parameter ΔC_s given by

$$\Delta C_s = \left[\frac{\sum_{i=1}^m (\phi_i + \phi'_i)^2}{m} \right]^{1/2},$$

is a measure of the deviations from mirror symmetry about a plane perpendicular to the dominant ring plane. The two-fold axis asymmetry parameter ΔC_2 given by

$$\Delta C_2 = \left[\frac{\sum_{i=1}^m (\phi_i - \phi'_i)^2}{m} \right]^{1/2}$$

is a measure of the deviations from two-fold symmetry about an axis lying in the dominant ring plane. The ϕ_i 's and ϕ'_i 's are symmetry related torsion angles and m is the number of such pairs (Fig. 4.9). The nomenclature defining the location of an asymmetry parameter include the symmetry symbol and the lower numbered atom or bond intersected by the symmetry element. For example,

SABLE 4.10

Asymmetry Parameters

(i) For Cholesteryl chloride

Ring A	$\Delta C_s(1) = 6.7$	$\Delta C_2(1-2) = 7.6$
	$\Delta C_s(2) = 3.7$	$\Delta C_2(2-3) = 4.5$
	$\Delta C_s(3) = 3.8$	$\Delta C_2(3-4) = 5.4$
Ring B	$\Delta C_s(5) = 31.4$	$\Delta C_2(5-6) = 11.2$
	$\Delta C_s(6) = 15.9$	$\Delta C_2(6-7) = 44.7$
	$\Delta C_s(7) = 47.3$	$\Delta C_2(7-8) = 55.6$
Ring C	$\Delta C_s(8) = 10.7$	$\Delta C_2(8-9) = 13.8$
	$\Delta C_s(9) = 9.0$	$\Delta C_2(9-11) = 5.3$
	$\Delta C_s(11) = 2.4$	$\Delta C_2(11-12) = 8.6$
Ring D	$\Delta C_s(13) = 19.2$	$\Delta C_2(13-14) = 0.65$
	$\Delta C_s(14) = 20.0$	$\Delta C_2(14-15) = 52$
	$\Delta C_s(15) = 54.5$	$\Delta C_2(15-16) = 83.6$
	$\Delta C_s(16) = 70.1$	$\Delta C_2(16-17) = 83.2$
	$\Delta C_s(17) = 53.7$	$\Delta C_2(17-13) = 51.1$

Table 4.10 (continued)

(11) For Cholesteryl bromide

Ring A	$\Delta C_s(1) = 7.8$	$\Delta C_2(1-2) = 15.7$
	$\Delta C_s(2) = 12.1$	$\Delta C_2(2-3) = 9.8$
	$\Delta C_s(3) = 8.1$	$\Delta C_2(3-4) = 7.8$
Ring B	$\Delta C_s(5) = 19.5$	$\Delta C_2(5-6) = 5.0$
	$\Delta C_s(6) = 15.4$	$\Delta C_2(6-7) = 35.4$
	$\Delta C_s(7) = 34.8$	$\Delta C_2(7-8) = 38.2$
Ring C	$\Delta C_s(8) = 18.2$	$\Delta C_2(8-9) = 29.5$
	$\Delta C_s(9) = 23.5$	$\Delta C_2(9-11) = 20.4$
	$\Delta C_s(11) = 5.8$	$\Delta C_2(11-12) = 9.3$
Ring D	$\Delta C_s(13) = 13.2$	$\Delta C_2(13-14) = 6.5$
	$\Delta C_a(14) = 23.3$	$\Delta C_2(14-15) = 49.0$
	$\Delta C_s(15) = 49.3$	$\Delta C_2(15-16) = 72.9$
	$\Delta C_s(16) = 57.1$	$\Delta C_2(16-17) = 68.9$
	$\Delta C_s(17) = 44.6$	$\Delta C_2(17-13) = 58.7$

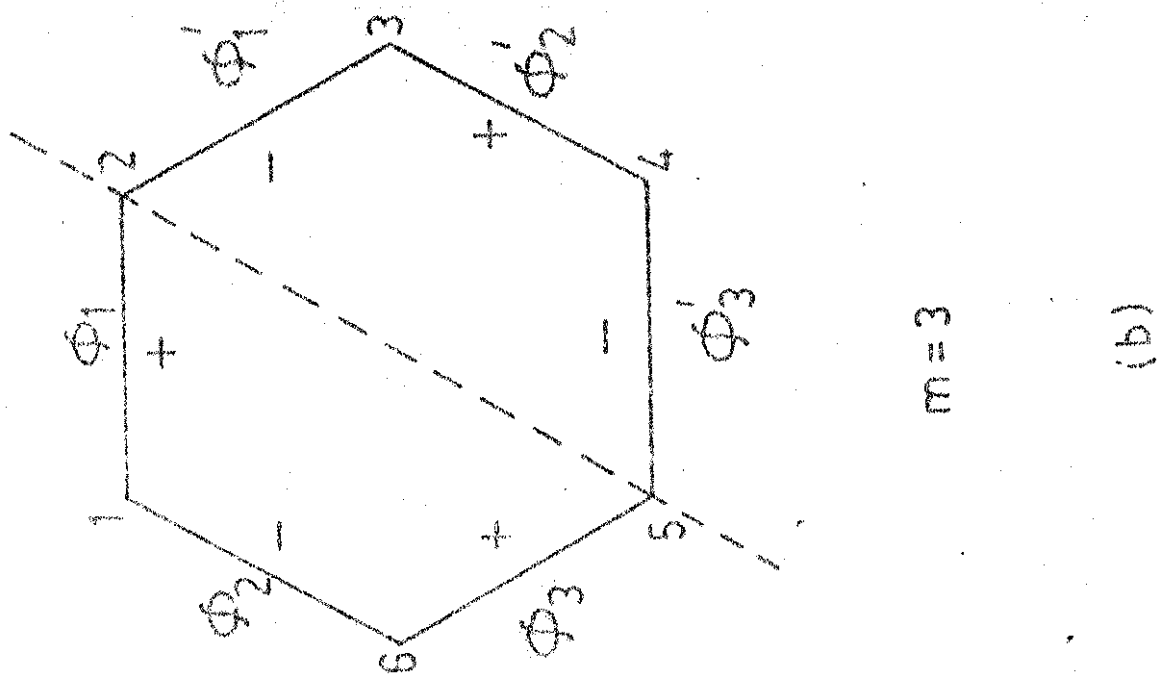
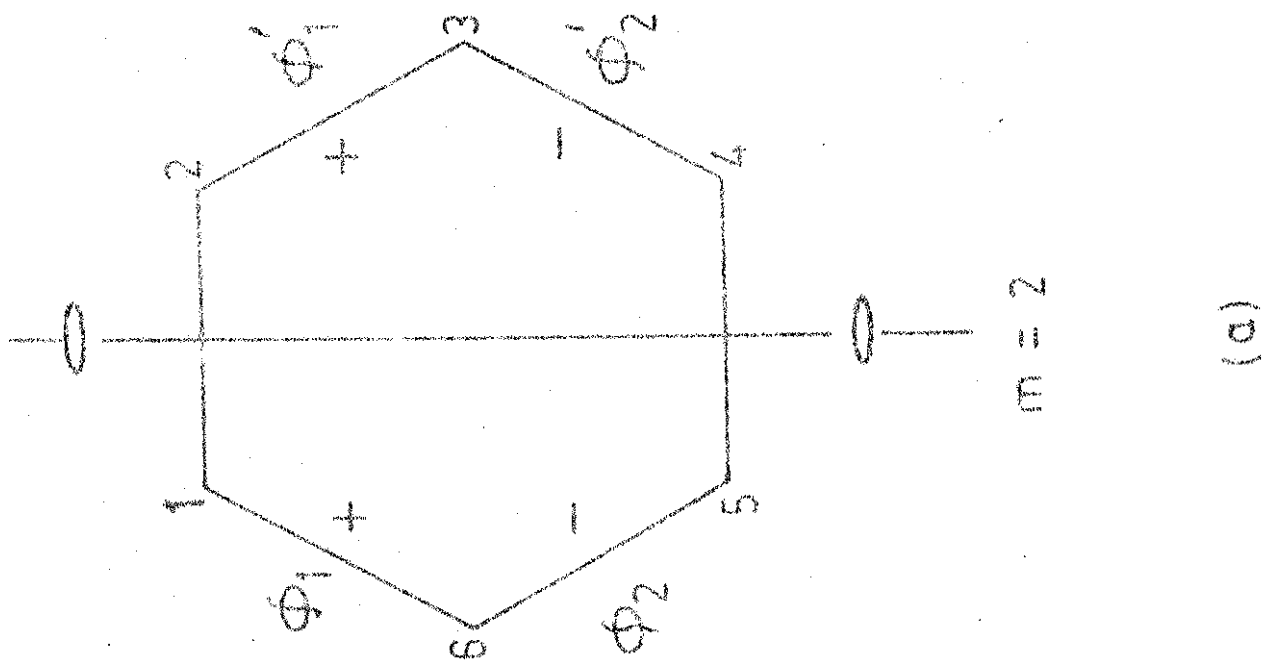


Figure 4.9

in Fig. 4.9(a), the two-fold axis bisects the bonds 1-2 and 4-5, and hence the corresponding asymmetry parameter is represented as $\Delta C_2(1-2)$. Similarly, the asymmetry parameter connected with the mirror plane passing through atoms 2 and 5 (shown in Fig. 4.9(b)) is represented as $\Delta C_s(2)$.

Rings A and C in the molecule are in chair conformation with ring C more distorted than ring A. In ring C, the mirror plane through the atoms C(11)-C(14) is dominant. Ring B has an $8\beta, 9\alpha$ half-chair conformation induced by the double bond between C(5) and C(6). Ring D is in $13\beta, 14\alpha$ half-chair conformation.

A survey of the ring conformations in the various crystal structures belonging to the cholestane group of steroids indicates that cyclohexane rings comprised of sp^3 hybridized carbon atoms tend to have chair conformation. This is found to be true in the case of cholesteryl chloride and cholesteryl bromide. It would be appropriate to compare these isomorphous crystal structures with those of cholesteryl iodide (form B) [5], cholesteryl p-toluene sulfonate [11] and sodium cholesteryl sulphate dihydrate [18] since all these have identical steroid skeletons, with a double bond between C(5) and C(6). It is found that the conformations of rings A, B and C are the same in all these structures. Ring D in cholesteryl iodide

is in $13\beta, 17\alpha$ half-chair conformation, whereas in all the others it is found to have the $13\beta, 14\alpha$ half-chair conformation. The A-B ring junctions in cholesteryl chloride and cholesteryl bromide are quasi-trans. The other two ring junctions, viz., B-C and C-D are trans. This is in conformity with the ring junction geometry required in the **cholestane** group of steroids [30]. The side chain at C(17) is in an extended conformation. The pseudo-torsion angle C(19)-C(10) ... C(13)-C(16) is 15° in the chloride, structure and 11° in the bromide structure. The corresponding value in the crystal. structure of cholesteryl iodide [5] is 7° . Thus, the overall apparent twist of the steroid nucleus in these crystal structures is small.

Fig. 4.10 give the perspective view of the cholesteryl **chloride molecule**. In Fig. 4.11, the final positional coordinates of cholesteryl chloride and cholesteryl bromide have been plotted together to enable a comparison of the **isomorphous structures**.

Fig. 4.12 and 4.13 show the molecular packing in the ac- and bc-planes for cholesteryl chloride. Since the **packing** diagrams for cholesteryl bromide are identical, they are **not** shown separately. The unit cell is two molecules **thick**, one molecule wide and one molecule long.

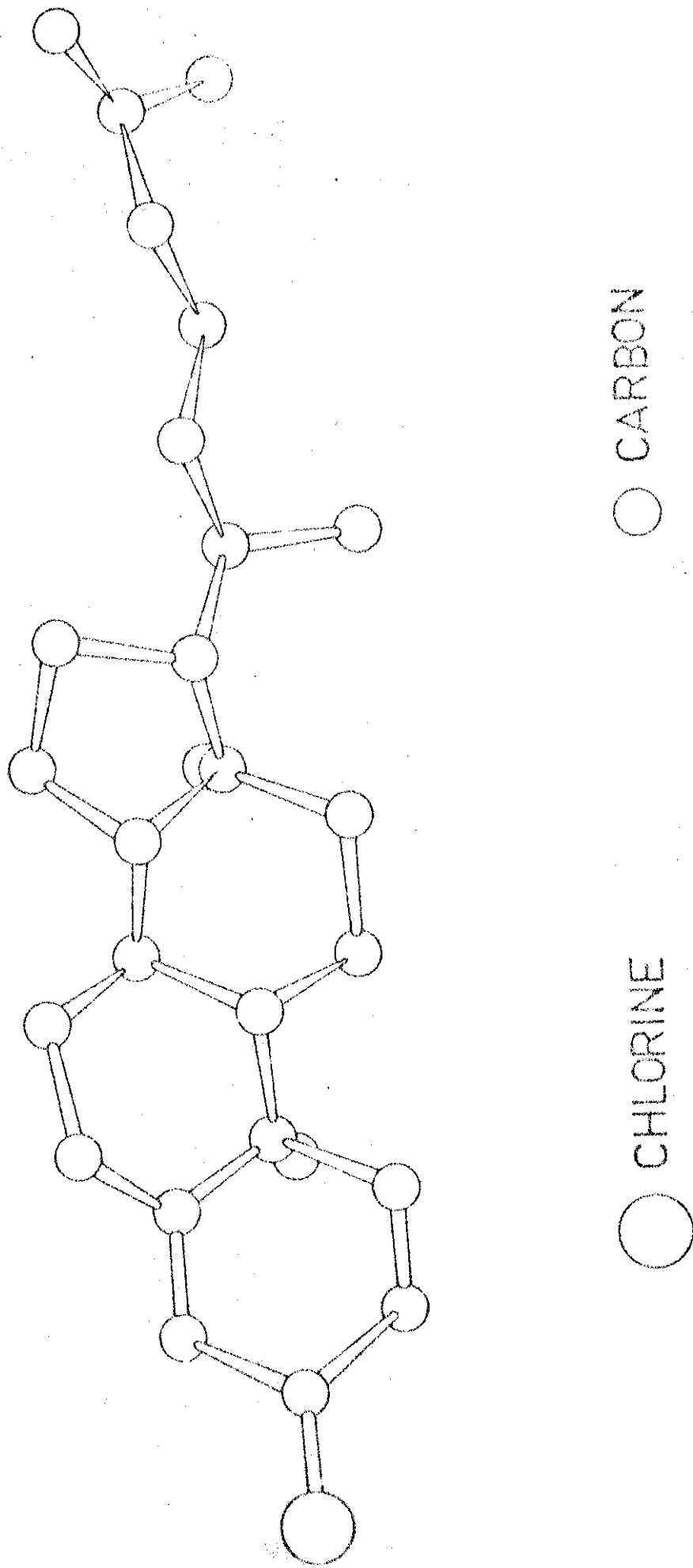


Figure 4.10: A perspective view of the cholesterol chloride molecule.

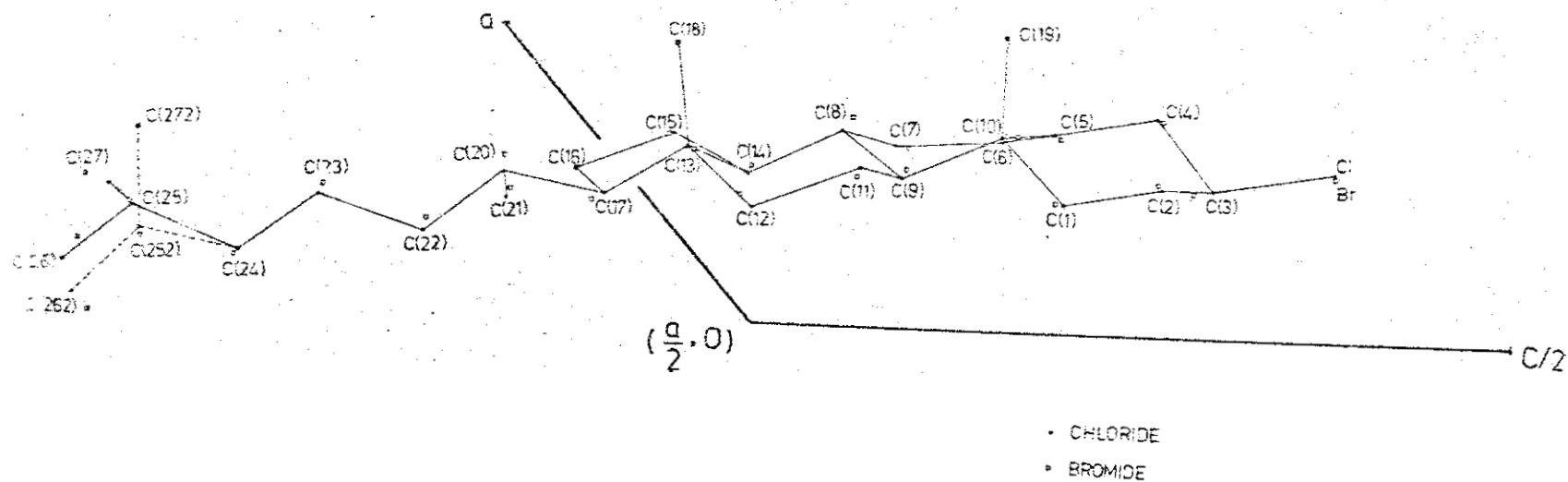
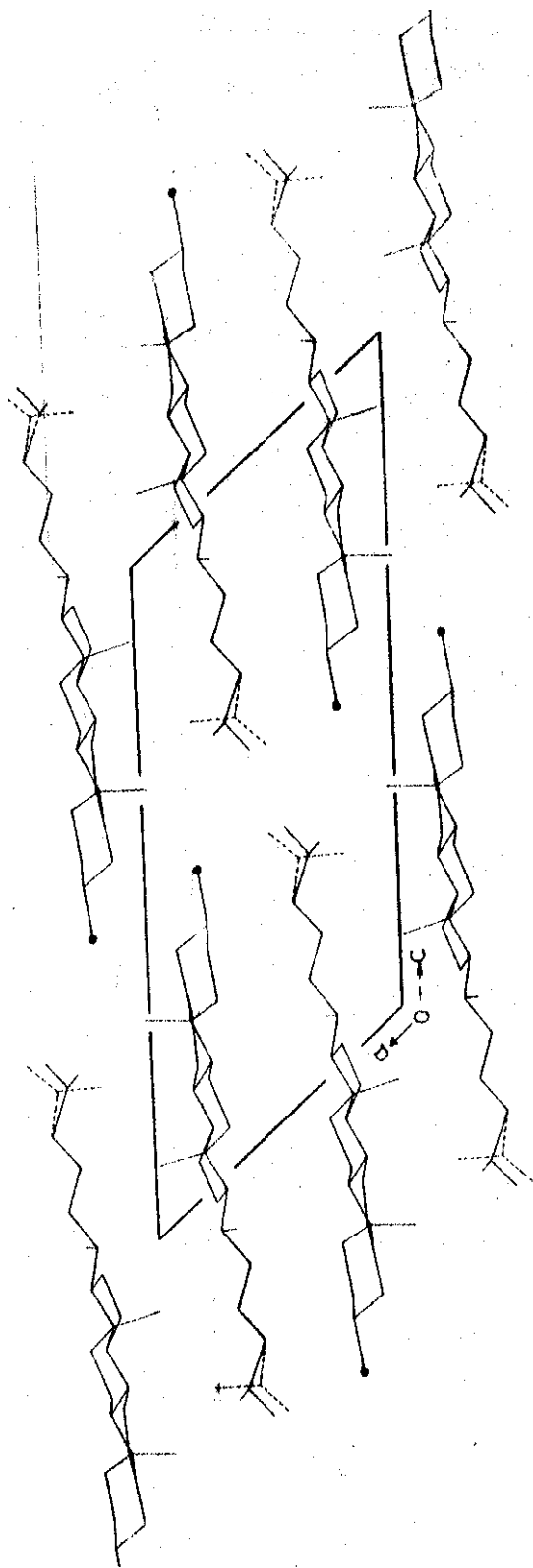


Figure 4.11: Atomic coordinates of cholesteryl chloride and cholesteryl bromide plotted together for comparison.



CHLOROPHYLL

Figure 4.12: Molecular arrangement in the ac-projection.