atoms of overlapping bases are: $O(6) \cdots C(6) = 3 \cdot 323$, $N(1) \cdots O(6) = 3 \cdot 430$, $N(9) \cdots N(8) = 3 \cdot 445$, and $N(8) \cdots C(7) = 3 \cdot 448$ Å; all other contacts are greater than $3 \cdot 500$ Å. The sheets are tilted approximately $32°$ from the bc plane and lie approximately parallel to the $(\bar{1}02)$ plane. Consequently, the largest $|E|$ value was that of the $\bar{1}02$ reflection.

Both of the tautomeric structures shown in Fig. 1 can be proposed for allopurinol. The present X-ray structure analysis has revealed that the keto form (II) is the preferred tautomer in the crystal. It is entirely possible that the molecule might assume the enol form during certain chemical reactions. Allopurinol and hypoxanthine are both substrates for xanthine oxidase. Hypoxanthine is oxidized to xanthine with is further oxidized to uric acid. The latter compound is then released from the active site of the enzyme. However, allopurinol is oxidized to oxoallopurinol which is retained at the active site of the enzyme. The crystalline structure of allopurinol has revealed that in addition to other sites on the base, N(8) is engaged in strong hydrogen bonding. Since N(8) cannot be oxidized by the enzyme, it may be involved in hydrogen bonding to a neighboring amino acid side chain or the main chain at the active site. The latter hydrogen-bonding potential of allopurinol probably makes it a potent inhibitor of xanthine oxidase.

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The Crystal Structure of p-Iodotoluene

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p-Iodotoluene, C_7H_7I, is orthorhombic, space group $P2_12_12_1$, with cell dimensions $a = 7 \cdot 46(1)$, $b = 16 \cdot 50(2)$, and $c = 6 \cdot 11(1)$ Å; $Z = 4$. The structure was determined from precession, Weissenberg, and diffractometer data by means of a Patterson synthesis and least-squares refinement to a final discrepancy index of $R = 0 \cdot 059$. In spite of some disorder, the molecular structure is as expected, with an average C–C distance of $1 \cdot 389$ Å in the benzene ring and C–I $= 2 \cdot 06$ Å. The iodine atoms form a zigzag chain around 2_1 along c, with an $I \cdots I$ distance of $4 \cdot 06$ Å; the arrangement suggests weak bonding between molecules.

Introduction

The existence of short intermolecular contacts in many interhalogen compounds, polyhalide ions, and organic

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molecule–halogen molecule addition compounds is well known. They occur, for example, in IBr (Swink & Carpenter, 1968), CsI₃ (Tasman & Boswijk, 1955), and 2:1 methanol–bromine (Groth & Hassel, 1964). Studies of simple organic halides, such as p-diiodobenzene (Lyan & Struchkov, 1959) and p-dibromobenzene (Bezzi & Croatto, 1942), also show these short

intermolecular contacts between halogen atoms. p-Iodotoluene was chosen for study as another example.

Collection and reduction of the data

A liquid sample of p-iodotoluene (Eastman, m.p. 35 °C) was drawn into a thin-walled capillary of 0·2 mm diameter, allowed to solidify, and sealed off with quick-setting epoxy cement. A single crystal was then grown by a version of the melted-zone technique. The sample-filled capillary was very slowly raised or lowered through a miniature heating coil, which produced a melted region between crystalline material above and below. The progress of crystal growth was observed through crossed Polaroids with the aid of a microscope. It was necessary to reduce drafts by enclosing the heating coil and capillary in a small glass box. Eventually a single crystal was obtained that filled the capillary for a length of about 2 mm. This crystal was used for all diffractometer work.

Precession and Weissenberg photographs prepared at 22 °C with Mo $K\alpha$ radiation ($\lambda = 0\cdot7107$ Å), indicated that the structure is orthorhombic, with cell dimensions $a = 7\cdot46$ (1), $b = 16\cdot50$ (2), and $c = 6\cdot11$ (1) Å. The precession records prepared with a Polaroid cassette were calibrated with single-crystal photographs of lead nitrate (Swink & Carpenter, 1967). Systematic absences indicated the space group to be $P2_12_12_1$, uniquely. The density was found to be $1\cdot918$ g.cm^{-3}, by flotation in a solution of zinc iodide, which was in satisfactory agreement with the value of $1\cdot924$ g.cm^{-3} calculated for four molecules per cell.

Intensity data in one octant of reciprocal space were collected at room temperature with a Picker four-circle automated diffractometer. The a^* axis of the crystal was aligned along the φ axis of the diffractometer; the capillary axis lay in the same direction. The mosaic spread was estimated to be about $0\cdot25°$. Intensities were collected by the θ–2θ scan technique

between values of 2θ of 5 and 50° with Zr-filtered Mo $K\alpha$ radiation. The scan range was $-0\cdot70$ to $+0\cdot70°$ in 2θ and the scanning speed was 1° min^{-1}. A ten-second background count was collected at each end of the scan range. During data collection, the intensities of four standard reflections in different regions of reciprocal space were measured after every 100 reflections. None of the standards deviated more than 4% from its mean value.

After subtraction of the background intensities, reciprocal Lorentz and polarization factors were applied to the observed intensities to yield a set of $|F|_o^2$ values; $|F|_o$ is an observed structure factor amplitude, on a relative scale. The standard deviation of a squared amplitude was estimated by the equation

$$\sigma(|F|_o^2) = (1/\mathrm{Lp})\,[C + 0\cdot5(t_c/t_b)^2(B_1 + B_2) + (0\cdot03I)^2]^{1/2},$$

where Lp is the usual Lorentz–polarization factor, C is the total integrated count obtained in time t_c, B_1 and B_2 are the two background counts each obtained in time t_b, and I is the net integrated count. Of the 819 independent reflections that were measured, 585 had values greater than 2σ, where σ is given by the preceding equation. The error from the combined effects of absorption and varying angle of incidence of the beam into the cylindrical crystal was calculated to be $3\cdot5\%$ of the amplitude in the worst case; hence no corrections were applied.

Solution and refinement of the structure

The three-dimensional Patterson function showed the three large Harker peaks in one octant, as expected for one independent heavy atom in space group $P2_12_12_1$. These peaks implied that the independent iodine atom has fractional coordinates $x = 0\cdot25$, $y = 0\cdot08$, $z = 0\cdot007$ (or at other positions differing by choice of origin or sense of the axes). In addition there were three large

Table 1. *Final atomic coordinates and thermal parameters*

E.s.d.'s in the last digit are given in parentheses.

				$B(\text{Å}^2)$
I(1)	0·21208 (19)	0·07919 (7)	0·02713 (22)	*
C(1)	0·2308 (24)	0·1853 (9)	−0·1474 (25)	4·21 (31)
C(2)	0·3040 (28)	0·1858 (10)	−0·3506 (30)	5·58 (39)
C(3)	0·3359 (25)	0·2584 (11)	−0·4632 (35)	6·45 (45)
C(4)	0·2713 (28)	0·3317 (10)	−0·3685 (29)	5·57 (40)
C(5)	0·2004 (27)	0·3322 (10)	−0·1667 (28)	5·20 (37)
C(6)	0·1755 (20)	0·2572 (9)	−0·0544 (24)	4·48 (33)
C(7)	0·2981	0·4120	−0·4887	6·00
I(2)	0·2961 (11)	0·4212 (4)	−0·5308 (11)	7·87 (17)
C(8)	0·273 (61)	0·159 (6)	−0·180 (32)	⎫
C(9)	0·343 (56)	0·166 (4)	−0·390 (33)	⎪
C(10)	0·350 (38)	0·242 (2)	−0·491 (23)	⎪
C(11)	0·286 (26)	0·310 (2)	−0·382 (14)	⎬ 6·32 (114)
C(12)	0·216 (32)	0·303 (6)	−0·172 (14)	⎪
C(13)	0·210 (50)	0·227 (8)	−0·071 (22)	⎪
C(14)	0·266 (80)	0·076 (8)	−0·069 (42)	⎭

* The anisotropic temperature factor of I(1) is: $\exp[-(0\cdot02655h^2 + 0\cdot00615k^2 + 0\cdot04639l^2 - 2 \times 0\cdot00038hk + 2 \times 0\cdot00017hl + 2 \times 0\cdot00021kl)]$, and the e.s.d.'s of the first three coefficients are between $1\cdot1$ and $1\cdot3\%$ of their values.

non-Harker peaks (in one octant) whose average peak height was nearly 72% that of the two larger Harker peaks, as well as a fourth smaller peak. This indicated a second independent atom of medium size at coordinates 0·296, 0·409, 0·507, a position fortuitously close to $\frac{1}{2}-x$, $\frac{1}{2}-y$, $\frac{1}{2}-z$, where x, y, and z are the coordinates of the iodine atom. Consequently, the new atom yielded Harker peaks almost coinciding with those from the iodine atom. In addition, a difference electron density map, calculated with phases determined from a single iodine atom at 0·25, 0·08, 0·007, revealed the ring carbon atoms, but showed a diffuse peak having three times the number of electrons associated with a ring carbon atom around the methyl carbon position.

The only reasonable explanation for these observations is some kind of disorder that places a fractional iodine atom near the position of the methyl carbon atom of the ordered molecule. The fractional occupancies of the sites of the ordered and disordered iodine atoms, respectively, must be near 0·8 and 0·2 to provide an approximate explanation for the relative heights of all the larger peaks in the Patterson and difference maps. Packing considerations suggested that the disordered molecules are inserted 'backwards' in the crystal, with iodine and methyl ends interchanged.

Initial refinement of the disordered structure included one molecule with 0·8 fractional occupancy and one iodine atom with 0·2 fractional occupancy. To restrict the number of variable parameters, only the 0·8 occupancy iodine was treated as anisotropic. The

Fig. 1. The disorder in *p*-iodotoluene. The higher occupancy molecule is heavily outlined; 16% of it is replaced by the lightly outlined, reversed molecule. The labels for the carbon atoms of the 16% occupancy molecule are omitted for clarity.

Table 2. *Observed and calculated structure factor magnitudes, multiplied by* 10

[Table of structure factor data — columns repeated: H K FOBS FCAL]

refinement converged to $R = 7 \cdot 3$, $R' = 8 \cdot 5\%$.* The other enantiomorph was tested at this point, and it proved to be insignificantly better, with $R = 7 \cdot 2$ and $R' = 8 \cdot 2\%$. The latter enantiomorph was used in further calculations, although the data are not adequate to distinguish between the two possibilities. To locate the rest of the lower-occupancy molecule, a difference electron density map was calculated with phases determined from the refined model above; it revealed five of the carbon atoms, with peak heights in the range $0 \cdot 6$–$0 \cdot 9$ e.Å^{-3}.

Because the methyl carbon atom of the higher-occupancy molecule is close to the iodine atom of the lower-occupancy molecule, it is not possible to carry out a meaningful refinement of the parameters of both atoms (given data of normal accuracy). Accordingly, we chose to fix the smaller scatterer, the methyl carbon atom, at a position lying on the molecular axis at a distance $1 \cdot 53$ Å from the ring carbon atom to which it is bonded, and to assign to it an isotropic temperature factor of $6 \cdot 0$ Å^2 (close to the value of the adjacent ring carbon atom of the higher-occupancy molecule). Furthermore, because the carbon portion of the lower-occupancy molecule contributes such a small fraction of the total scattering, it seemed wise to refine the entire lower-occupancy molecule as a rigid unit with the dimensions of an ideal molecule of p-iodotoluene (planar molecule, ring carbon–carbon distance, $1 \cdot 396$ Å ring-to-methyl carbon distance, $1 \cdot 53$ Å; ring-to-iodine distance, $2 \cdot 05$ Å). Consequently, we gained no information about the dimensions of the lower-occupancy molecule, although its position in the unit cell is reasonably well determined, and no information about the ring-to-methyl carbon distance in the higher-occupancy molecule. In carrying out this refinement, it was necessary to readjust slightly the position of the methyl carbon atom after each cycle so as to keep it on the molecular axis. A separate final refinement of the fractional occupancy of the higher and lower-occupancy molecules, accomplished by calculating structure factors and discrepancy indices for the occupancy factor of the higher-occupancy molecule taken as $0 \cdot 82$, $0 \cdot 84$ and $0 \cdot 86$, gave a minimum discrepancy of $R = 6 \cdot 6$, $R' = 7 \cdot 6\%$ for occupancies of 84 and 16%. (Photographic data previously taken on a different crystal grown from the melt showed approximately the same extent of disorder.)

Finally, an isotropic temperature factor for the lower-occupancy iodine atom and one isotropic factor for all carbon atoms were refined, holding all other parameters fixed, to yield $R = 6 \cdot 6$, $R' = 7 \cdot 5\%$. After omitting six reflections that either appeared to suffer from extinction or were lying on white radiation streaks from nearby strong reflections, the final discrepancy indices fell to $R = 5 \cdot 9$, $R' = 6 \cdot 3\%$. The final

* Throughout, $R \equiv \sum ||F|_o - |F|_c|/ \sum |F|_o$ and $R' \equiv [\sum w(|F_o| - |F_c|)^2/ \sum w|F|_o{}^2]^{1/2}$, where observed reflections only are included in the summations.

parameters are given in Table 1. The physical significance of the temperature factor for the iodine atom of the lower-occupancy molecule is vague, because it depends strongly on the arbitrary choice made for the methyl carbon atom of the higher-occupancy molecule, which nearly coincides with the iodine atom. Observed and final calculated structure factors are listed in Table 2.

The structure thus determined was tested by calculating a final difference map. The largest peak on the map was $1 \cdot 2$ e.Å^{-3} and its position near the iodine atom is not unexpected. The highest noniodine peak was $0 \cdot 71$ e.Å^{-3}, and the deepest hole was $-0 \cdot 79$ e.Å^{-3}.

All least-squares calculations were performed with program *BUGLES*, a local modification of the classic *ORFLS* program (Busing, Martin & Levy, 1962) that allows rigid-group refinement. The function minimized was $\sum w(F_o - F_c)^2$. Weights were taken as $w = 4F_o^2/\sigma(F_o^2)^2$; this is just the reciprocal variance in $|F|_o$. Neutral atom scattering factors were those reported by Cromer & Waber (1965).

Description and discussion of the structure

The presence of disorder renders the determination of molecular dimensions somewhat less accurate than normal, yet the major features of the structure are clear. The nature of this disorder is shown in Fig. 1, in which both the higher- and lower-occupancy molecules are indicated, the latter by light outlines. Only
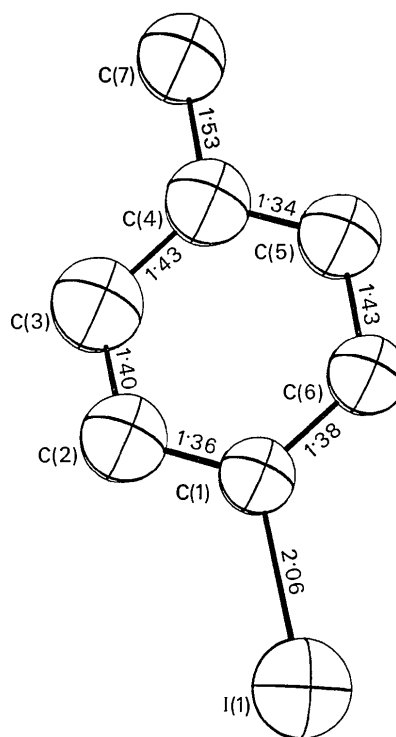

Fig. 2. Atomic labels and bond lengths in p-iodotoluene.
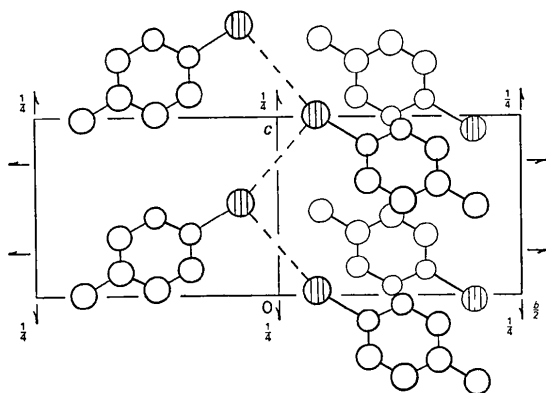
Fig. 3. The crystal structure of *p*-iodotoluene, viewed down the *a* axis and considering only the higher-occupancy molecules. Atoms with *x* coordinates in the range 0 to $\frac{1}{2}$ are shown with heavy outlines; for the $-\frac{1}{2}$ to 0 range (on the right only) they are shown with light outlines. The iodine atoms are shaded. The dashed lines connect iodine atoms 4·06 Å apart around a 2_1 axis.

Table 3. *Bond lengths and angles in p-iodotoluene*

E.s.d.'s in the least significant digit are given in parentheses.

I(1)–C(1)	2·056 (15) Å	I(1)–C(1)–C(2)	120·5 (12)°
C(1)–C(2)	1·356 (24)	C(1)–C(2)–C(3)	121·5 (16)
C(2)–C(3)	1·403 (25)	C(2)–C(3)–C(4)	118·0 (18)
C(3)–C(4)	1·426 (23)	C(3)–C(4)–C(5)	120·8 (16)
C(4)–C(5)	1·341 (24)	C(4)–C(5)–C(6)	119·1 (15)
C(5)–C(6)	1·429 (20)	C(5)–C(6)–C(1)	120·7 (14)
C(6)–C(1)	1·380 (20)	C(6)–C(1)–C(2)	119·5 (14)
C(4)–C(7)	1·530	C(6)–C(1)–I(1)	120·0 (11)
		C(3)–C(4)–C(7)	119·8 (15)
		C(5)–C(4)–C(7)	119·2 (14)

the iodine atom I(2) of the lower-occupancy molecule is labeled. For the higher-occupancy molecule, the thermal motion is indicated by spheres (for carbon atoms) and by an ellipsoid (for the iodine atom) representing the 0·5 probability contour. It is apparent that the position of the methyl carbon atom, C(7), may be adversely affected by the disorder, and that the thermal motion of all atoms is somewhat uncertain. Nevertheless, the thermal motion of the iodine atom is greatest in a direction nearly normal to the C–I bond, as expected.

Another example of disorder between an iodine atom and a methyl group occurs in the structure of IrI(CH₃) (NO) [P(C₆H₅)₃]₂ (Mingos, Robinson & Ibers, 1971). In this case the iodine atom and methyl group are related by a crystallographic twofold axis, so that the disorder is complete. Their similar size (van der Waals radii: iodine, 2·15 Å; methyl, 2·0 Å) allows the two species to interchange places at random without a large energy difference.

One higher-occupancy molecule of *p*-iodotoluene is shown in Fig. 2, which includes bond lengths rounded to two decimal places. Bond lengths and angles are present in Table 3. The best least-squares plane through the benzene ring is given by the equation:

$$6·718x + 1·777y + 2·574z - 1·493 = 0,$$

where x, y, z are in fractional coordinates.

The molecule is essentially planar. The ring atoms deviate from the plane of the ring by less than 0·032 Å, and the iodine atom lies 0·143 Å from this plane. The bond lengths and angles in the benzene ring show rather large variations, apparently random, but the average length, 1·389 Å, is quite normal. The carbon–iodine bond length is 2·06 Å, also reasonable.

The crystal structure of *p*-iodotoluene is shown

schematically in Fig. 3. This structure, in space group $P2_12_12_1$, is isostructural with that of *p*-diiodobenzene (Lyan & Struchkov, 1959) in space group *Pbca* if the appropriate reduction of symmetry is made. To refer the diiodobenzene structure to the axes used here it is necessary to shift the origin to $-\frac{1}{4}$, $-\frac{1}{4}$, $-\frac{1}{4}$, interchange the *a* and *b* axes, and reverse the direction of the *c* axis. If then only the screw axes are retained, the *p*-iodotoluene structure results. The cell dimensions and atomic coordinates differ at most by a few percent.

The structure is also similar to that of *p*-dibromobenzene (Bezzi & Croatto, 1942), monoclinic *p*-dichlorobenzene (Croatto, Bezzi & Bua, 1952; Frasson, Garbuglio & Bezzi, 1959), and disordered *p*-chlorobromobenzene (Klug, 1947), in space group $P2_1/a$. If the origin in $P2_1/a$ is shifted to $\frac{1}{4}, \frac{1}{4}, -\frac{1}{4}$, and *a*, *b*, *c* are changed to $-b$, $-c$, *a*, respectively, then the structure resembles that shown by the heavily outlined atoms in Fig. 3. However, the benzene rings are tilted somewhat more from the plane of the figure and the layers above and below the layer of heavily outlined atoms are related to the latter by lattice translation rather than by screw axes.

The general features of the crystal structure seem, at first sight, to be determined solely by packing considerations; all intermolecular distances involving carbon atoms, and all interatomic distances between molecules of high and low occupancy, are greater than the sum of van der Waals radii. However, the iodine atoms that are related by the twofold screw axis along *c* are moderately close together: I(1)···I(1')=4·06 Å, which is considerably less than the 4·30 Å van der Waals separation. Moreover, the angle C(1)–I(1)···I(1') is 158·3° and the angle I(1)···I(1')–C(1') is 98·6°, which are not far from a straight angle and a right angle, respectively. Thus, a pattern of C–I···I groups, linked into a planar zigzag chain about 2_1 along **c** exist, as shown in Fig. 3. The same pattern also occurs in *p*-diiodobenzene, where the short I···I distance is 4·07 Å, and less conspicuously in dibromo- and *p*-dichlorobenzene. This is reminiscent of the patterns observed in I₂, IBr, and ICl, for example, and suggests a weak bond between iodine atoms.

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The Crystal Structure of D-*iso*-Ascorbic Acid
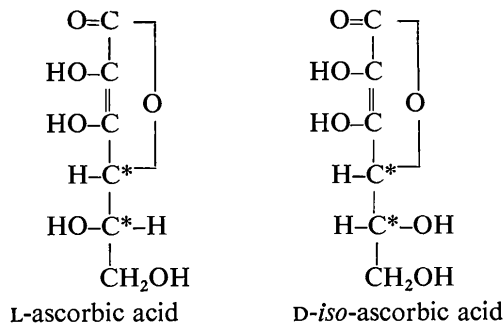
BY NEZHAT AZARNIA, HELEN M. BERMAN* AND R. D. ROSENSTEIN†

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The structure of D-*iso*-ascorbic acid, $C_6H_8O_6$, has been determined from three-dimensional Cu $K\alpha$ ($\lambda = 1.5418$ Å) X-ray data using the noncentrosymmetric direct method. There are two molecules in a unit cell of dimensions $a = 5.165$ (4), $b = 14.504$ (10), $c = 4.724$ (4) Å, and $\beta = 99.50$ (1)°. Space group is $P2_1$, $D_m = 1.654$, $D_x = 1.668$ g.cm^{-3}. The structure was refined by anisotropic full-matrix least-squares methods to an R value of 0.037. As in ascorbic acid, the major acyclic side chain adopts a conformation such that O(5) and C(6) are far from O(3). The molecules, which are arranged head-to-tail along **b**, are linked together by a zigzag chain of hydrogen bonds between hydroxyls; the three repeating links run roughly along **b**, **a**, and **c**, and a single hydrogen bond runs to the carbonyl oxygen atom along **c**. The ring oxygen atom is not hydrogen bonded.

Introduction

D-*iso*-Ascorbic acid, also known as *arabo*-ascorbic acid and erythrobic acid, is a stereoisomer of L-ascorbic acid (vitamin C) with inversion at C(5), one of the two asymmetric carbon atoms.

```
    O=C ┐              O=C ┐
     |  │               |  │
   HO-C │             HO-C │
     ‖  │ O             ‖  │ O
   HO-C │             HO-C │
     |  ┘               |  ┘
   H-C*─┘             H-C*─┘
     |                  |
  HO-C*-H            H-C*-OH
     |                  |
   CH₂OH              CH₂OH

L-ascorbic acid     D-iso-ascorbic acid
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The biosynthesis of L-ascorbic acid is known (Isherwood, Chen & Mapson, 1953) to proceed by two path-

ways involving complete inversion of hexoses. One starts with D-glucose and leads to L-gulono-γ-lactone *via* D-glucuronolactone. The other passes through a series of intermediates from D-galactose to L-galactono-γ-lactone. The crystal structures of most of these compounds are known.

Similarly, D-*iso*-ascorbic acid has been found (Isherwood, Chen & Mapson, 1954) to be synthesized *in vivo* from D-mannono-γ-lactone (rats) or from D-altrono-γ-lactone (cress, mung beans, and peas).

All these precursors share the characteristics that the hydroxyl on C(2) has the L configuration, and the hydroxyl on C(4) has the D configuration. Other lactones that do not comply with these conditions are not converted to ascorbic acids in either the plant or animal.

Ascorbic acid plays a role in several important biochemical processes, such as collagen and serotonin syntheses. In the gross organism, lack of ascorbic acid results in the complex of symptoms known as scurvy. In order for an isomer or homolog of ascorbic acid to have antiscorbutic activity, it must possess: a hydroxyl with a D configuration at C(4), a side chain, a hydroxyl at C(5), and all the hydroxyl groups must be

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