X-RAY STRUCTURAL STUDIES OF SOME BIOLOGICALLY SIGNIFICANT MOLECULES

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by

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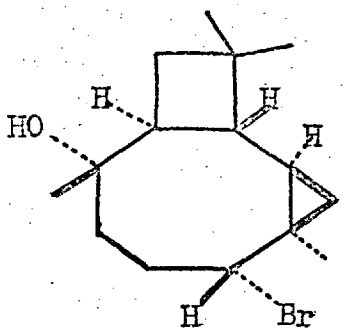
Summary.

The crystal structures of derivatives of four biologically significant molecules have been determined using three-dimensional X-ray diffraction techniques, and the phase-determining heavy-atom method.

The structure of (+)-3-bromocamphor has been re-determined in order to establish unambiguously the absolute configuration of this key terpene. The assignment was made using the X-ray fluorescence technique, and its importance in the stereochemical correlation of the monoterpenes is discussed. The molecular geometry of the molecule is compared with data from other X-ray studies. In connection with this work a list has been prepared of organic molecules whose absolute configurations have been determined by X-ray methods, and the techniques involved have been reviewed.

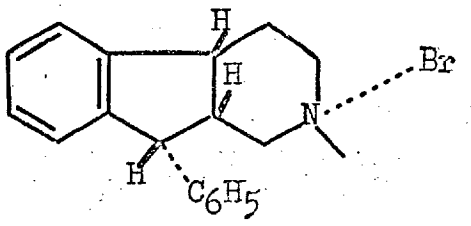
The monocyclic sesquiterpene humulene gives a tricyclic bromohydrin, $C_{15}H_{25}OBr$, which is monoclinic, space-group $P2_1/n$. The structure was elucidated using 1922 visually-estimated intensities, and refined to give a final R of 0.100. The proposed stereochemistry has been corrected to :



The geometry and conformation of the fused-ring system is discussed in some detail.

The biosynthetically important cyclodecatriene sesquiterpene germacratriene has recently been synthesized. The structure of the 1:1 adduct with silver nitrate, $C_{15}H_{24}:AgNO_3$, has been determined from visually-estimated intensity data, and refined to $R = 0.097$. The all-trans stereochemistry has been confirmed. The structure consists of chains of Ag^+ ions and germacratriene units parallel to a, cross-linked by chains of Ag^+ and NO_3^- ions parallel to b. The differences in reactivity between the double bonds is explained in terms of their torsional strain energies.

The synthetic pharmaceutical 2,3,4,4a,9,9a-hexahydro-2-methyl-9-phenyl-1H-indeno [2,1-c] pyridine, a possible antidepressant, has been studied as the hydrobromide $C_{19}H_{22}NBr$. A Siemens automatic single-crystal diffractometer was used to collect the intensity data, which was absorption corrected. The final R-factor was 0.035. The all-cis stereochemistry :



was confirmed. The accuracy of the diffractometer experiment, and the geometry of the fused-ring system, are discussed.

A novel computer procedure, utilizing a 'bonding array', for the calculation of the geometrical characteristics of a molecule, is described.

Acknowledgements.

I should like to thank Professor D. Rogers for his excellent supervision, and for the interest he has shown in this work; his enthusiasm is somewhat contagious. I should also like to thank Dr. J. K. Sutherland for much useful chemical discussion. The crystals were prepared by Dr. J.E. Baldwin, Dr. M. D. Solomon, Mr. E. D. Brown and Dr. P.R. Leeming, all of whom are thanked for their interest and help. Dr Leeming and his colleagues at Pfizer (U.K.) Ltd, Sandwich, Kent, are thanked for their generous hospitality.

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" Fortunately science, like that nature to which it belongs, is neither limited by time nor by space. It belongs to the world, and is of no country and of no age. The more we know, the more we feel our ignorance; and in philosophy.. ..... there are always new worlds to conquer".

Sir Humphrey Davy 1825.

dedicated

to

the memory of my late father.

Contents.

CHAPTER 1.

Crystal Structure Analysis : An Historical Introduction

Robert Bunsen is reported to have said : "Ein Chemiker, der kein Physiker ist, ist gar nichts"; in the present context this could be aptly 'translated' : "A Crystallographer who is not a Physicist, Mathematician, Chemist, Geologist, or even Artist, is worthless". It is the purpose of this chapter to amplify this plagiarism by indicating briefly, and chronologically, the theories and observations from various disciplines which have become coalesced into the theoretical background of the science of crystal structure analysis.

1.1. Early Studies of the Crystalline State.

Crystalline compounds have attracted man's attention since very early times, due to the beautiful facets and light effects exhibited by certain naturally occurring minerals, prized today as gemstones. The treatises of

the Alexandrian Greeks of ca. 250 A.D. contain the first references to practical topics, among them crystallization. The alchemists also knew these techniques, but it was not until the Renaissance brought the learning of the 'Old World' to the 'New' that further progress was made.

Speculation concerning the internal structure of crystals arose from the introduction of the microscope to scientific research by Malpighi (1628-94) and Leuwenhoek (1632-1723). In his 'Micrographia' (1667) Hooke explained their outward regularity as a consequence of the regular stacking of spheres (1). During his work on calcite and its effect on light, Huygens (1629-95) concluded that these spheres could be distorted into 'spheroids', and could be packed in a variety of ways (2). This was, no doubt, an analogy drawn from his explanation of the polarization of light.

Towards the end of the 18th century the Abbe René Haüy proposed (3) that crystals were composed of small cubic blocks, different stacking patterns accounting for observed morphological differences. Studies using the goniometer developed by Wollaston in 1809, put the 'Law of Constancy of Interfacial Angles', first proposed in 1669 by Steno (4), on a firm foundation. Haüy deduced that, if a compound crystallized with constant interfacial

angles, then the structure must consist of stacks of equidistant parallel planes, set at differing angles to each other. Further, each cube centre on his initial hypothesis may be regarded as a point on a lattice, which we may define as an abstraction of points, each having an exactly identical environment in parallel orientation in three dimensions.

W. H. Miller popularized these ideas in his book of 1839 [5], in which he also introduced the term 'unitcell' to define the smallest indivisible unit of structure. His index notation for sets of lattice planes is based on three cell axes, $\underline{a}$, $\underline{b}$, $\underline{c}$, not necessarily orthogonal, but forming a right handed set, with interaxial angles α, β, γ. If the zero'th plane of any stack passes through the origin, then the first plane makes intercepts $\underline{a}/h$, $\underline{b}/k$, $\underline{c}/l$, on the axes. The reciprocals of these intercepts, taken as multiples of $1/\underline{a}$, $1/\underline{b}$, $1/\underline{c}$, are h, k, l, the crystal plane indices. Intercepts on the negative directions of the axes are denoted $\bar{h}$, $\bar{k}$, $\bar{l}$.

The study of external morphology indicated that most crystals exhibited symmetry due to one or more of the following basic operations :

i) centre of symmetry (inversion centre, $\bar{1}$)

ii) axes of rotation (1-,2-,3-,4-, or 6-fold)

iii) mirror planes (m).

Two important propositions arise from this :

i) all crystals belong to one of seven systems, each displaying certain basic symmetry (see Table 1.1).

ii) there are 32 mathematically possible ways of combining symmetry operations acting through a point, these point groups or classes are distributed through the seven systems, each having the basic symmetry of that system, but some having higher symmetry. The class of highest symmetry in any system is designated holosymmetric. The classes are listed in Table 1.1.

In 1848 Bravais [6] deduced the 14 possible lattice types, distributed among the seven systems. The classification is based on the number of lattice points per cell, one denoting a primitive cell (P), and two or more denoting single-face-, body- or all-face-centred cells, (C, I, F). The rhombohedral type (R) is treated as trigonal (Table 1.1).

By 1860 it was obvious that the unitcell must be made up of molecules arranged according to symmetry operations acting throughout three dimensional space. In this case operations involving translation components must be considered :

i) screw axes, n_x : a rotation of $2\pi/n$, followed by a translation, parallel to the axis, of x/n.

ii) glide planes, reflection through a plane, followed by a translation parallel to it.

The complete mathematical analysis of the possible combinations of symmetry elements acting in three dimensions was

System.	Unitcell.	Bravais Lattices.	Crystal Classes.	Laue Symmetry.
(1) TRICLINIC.	$a \neq b \neq c$, $\alpha \neq \beta \neq \gamma \neq 90^\circ$	P.	1, $\bar{1}$.*	$\bar{1}$
(2) MONOCLINIC.	$a \neq b \neq c$, $\alpha = \gamma = 90^\circ \neq \beta$	P, C.	2, m, 2/m.*	2/m
(3) ORTHORHOMBIC.	$a \neq b \neq c$, $\alpha = \beta = \gamma = 90^\circ$	P, C, I, F.	222, mm2, mmm.*	mmm
(4) TETRAGONAL.	$a = b \neq c$, $\alpha = \beta = \gamma = 90^\circ$	P, I.	a) 4, $\bar{4}$, 4/m.* b) 4mm, $\bar{4}$2m, 422, 4/mmm*	4/m 4/mmm
(5) HEXAGONAL.	$a = b \neq c$, $\alpha = \beta = 90^\circ$, $\gamma = 120^\circ$	P.	a) 6, $\bar{6}$, 6/m.* b) 6mm, $\bar{6}$m2, 622, 6/mmm*	6/m 6/mmm
(6) TRIGONAL; (RHOMBOHEDRAL)	As (5)	As (5)	a) 3, $\bar{3}$.*	$\bar{3}$
	($a = b = c$, $\alpha = \beta = \gamma \neq 90^\circ$)	R.	b) 3m, 32, $\bar{3}$m*	$\bar{3}$m
(7) CUBIC.	$a = b = c$, $\alpha = \beta = \gamma = 90^\circ$.	P, I, F.	a) 23, m3.* b) 432, $\bar{4}$3m, m3m.*	m3 m3m

TABLE 1.1. Subdivisions of the Seven Crystal Systems. (Holosymmetric Classes are marked *)

completed, and simultaneously published, by three workers, Fedorov [7], Barlow [8], and Schoenflies [9]. They all deduced the number of possible unique space-groups to be 230.

1.2. Developments in Physics.

The experimental method that was to prove and utilize the foregoing theories was introduced in Munich in 1912. This development was facilitated by the discovery of X-rays by Roentgen, at Wurtzburg, in 1895, and by considerable progress in the theory of wave motion, including diffraction. The latter phenomenon was first noted by Grimaldi (1613-63), and can be expressed in simple mathematical terms for monochromatic light of wavelength (λ) incident upon a grating, with rulings of width (a) separated by a distance (b), as shown in Figure 1.1. Constructive interference of the diffracted wavelets can only occur when the path difference is a whole number (n) of wavelengths :

$$n\lambda = (a + b) \sin\theta \quad \ldots\ldots\ldots\ldots\ldots 1.1$$

where (θ) is the n'th order diffraction angle.

In 1912 Ewald presented his Thesis at Munich on : 'The Optical Properties of an Anisotropic Arrangement of Isotropic Resonators'. Von Laue seized upon an equation developed there, which showed the result of the superposition of all wavelets issuing from the resonators. He speculated on the

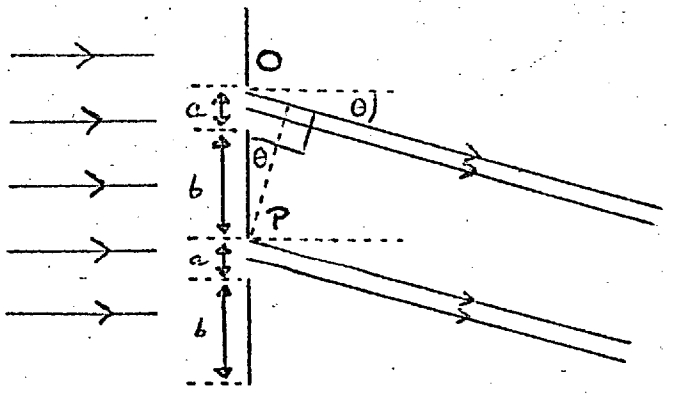


Figure 1.1 : Simple Diffraction Theory.

interaction of a very short wavelength radiation with a crystal lattice, which was thought to be such an arrangement. Sommerfeld [10] had estimated X-ray wavelengths to be of the order of 10^{-8} cm. (1Å), and this radiation was chosen.

Working with Friedrich and Knipping, von Laue produced the first stationary-crystal X-ray diffraction photographs of $CuSO_4$, ZnS, PbS, and NaCl. The results were published together with an analysis of the diffraction theory pertinent to a three-dimensionally repeating unit.[11,12] Von Laue assumed that the pattern obtained was due to the diffraction of certain components of the polychromatic incident radiation, and refuted the idea that the observed

monochromaticity of the diffracted beam was due to a selective action by the crystal.

Late in 1912, W.L.Bragg deduced the first atomic crystal structure from Laue photographs of zinc blende. The paper [13] also contained three important conclusions :

i) the 'Laue spots' could be explained by a reflection of the incident ray by the stacks of crystal planes;

ii) if the incident beam was polychromatic, there was a selective action by the planes, reinforcing only those wavelengths which fitted their repeat distance;

iii) the formulation of his Law concerning reflection from a stack of planes of spacing (d) :

$$n\lambda = 2d \sin\theta \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad 1.2$$

similar to Eq. 1.1, where here :

θ is the glancing angle on the stack,

λ is the wavelength 'selected',

and n is the order of reflection.

Using the X-ray spectrometer, developed with his father, Bragg deduced the alkali halide structures; many other determinations followed in the next decade.

It is interesting to note that the early structure determinations made minimal use of the elegant space-group theory mentioned above. Terada, working in Tokyo in 1913, was one of the first to realize its importance; but it was

not until Niggli [14] showed that the space-group could be determined from the systematic extinction of certain classes of diffracted spectra, that their determination became part of the routine preliminary study of crystals.

1.3. The Diffraction of X-Rays by a Crystal.

With reference to Fig. 1.1, we may note that if the phase of the wave scattered by point (O) is (α), and that of the wave scattered by point (P) is ($\phi + \psi$), then the phase of the wave scattered by the n'th grating point from (O) is ($\phi + n\psi$). Thus we may write the equation for the resultant wave from a one-dimensional grating of (N) similar scattering points as :

$$R = fe^{i\phi} \cdot \sum_{n=0}^{N-1} e^{in\psi} \quad \ldots\ldots\ldots 1.3$$

where (f) is the scattering power of each point.

Let us now consider a more general one-dimensional grating (Figure 1.2 overleaf). Each translation period (a) contains (J) points of differing scattering power (f_j) at distances (X_j) from the origin (O). Further, if we consider (N) such repeats, each of the (J) points is related to a similar point at distances :

$$X_j + a, \quad X_j + 2a, \ldots\ldots X_j + ha, \ldots$$

from the origin. We may represent the resultant wave

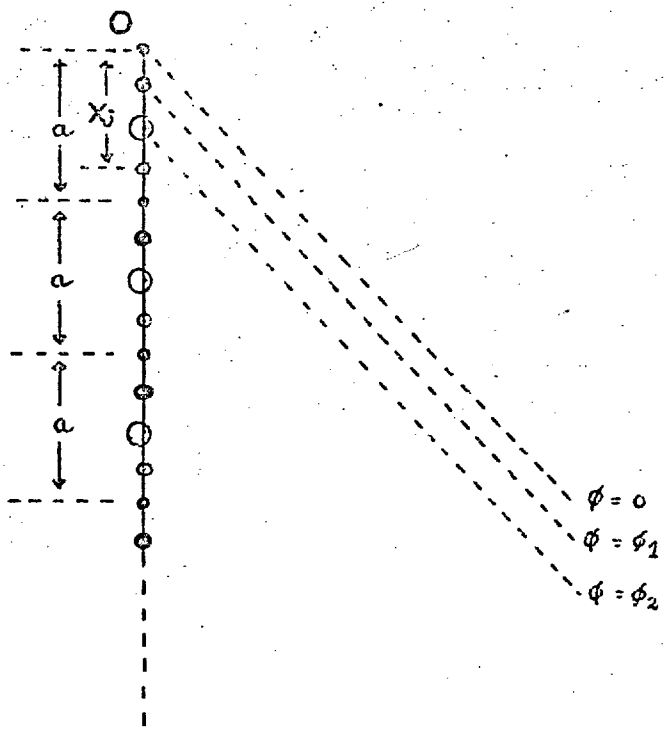


Figure 1.2 : A General One-Dimensional Grating.

from (N) repeats, by an equation analogous to 1.3 above :

$$R = (f_1 e^{i\phi_1} + f_2 e^{i\phi_2} + ... f_j e^{i\phi_j}) \sum_{n=0}^{N-1} e^{in\psi} \quad ..... 1.4$$

The expression in parentheses represents the resultant for one translation period (a). If we represent the h'th order maximum by (F(h)), and since it can be shown that the phase angle can be expressed :

$$\phi_j = h \frac{X_j}{a} 2\pi \quad ..... 1.5,$$

we may write :

$$F(h) = \sum_{j=1}^{J} f_j \, e^{2\pi i h x_j} \quad ..... 1.6$$

where : $\underline{x}_j = X_j/a$ 1.7,

the fractional co-ordinate of the j'th scattering point.

This equation may be extended to treat a general three-dimensional lattice of points, referred to an axial set as previously defined, when the wave of order (hkl) may be represented :

$$F(hkl) = \sum_{j=1}^{J} f_j^o \, e^{2\pi i \, (h\underline{x}_j + k\underline{y}_j + l\underline{z}_j)} \ldots 1.8$$

This equation represents exactly the conditions for the diffraction of X-radiation by a crystal lattice, due to the interference of waves scattered by the electrons of the (J) atoms in the structure. F(hkl) is defined as the 'structure factor' for the plane with Miller indices h, k, l. The factor (f_j^o) is the 'atomic scattering factor', and represents the scattering power of the j'th atom; due to the finite size of the atomic electron cloud it is dependent on (θ) the scattering angle, for any particular wavelength; it is equal to (Z), the atomic number, at $\sin\theta/\lambda = 0$, but falls off rapidly at higher values. The terms $\underline{x}_j$, $\underline{y}_j$, $\underline{z}_j$, are the co-ordinates of the j'th atom as fractions of the unitcell edges $\underline{a}$, $\underline{b}$, $\underline{c}$.

In the above discussion of the interaction of the electric vector ($\vec{E}$) of the incident radiation with the atomic electrons, a static electron cloud has been assumed.

This is only approximately true at the absolute minimum temperature; at all other temperatures a correction term must be applied to the theoretical scattering factors (f_j^o) :

$$f_j = f_j^o \, e^{-(B\sin^2\theta)/\lambda^2} \quad \ldots\ldots\ldots 1.9$$

The factor (B), due to Waller [15], is known as the isotropic temperature factor, with units of $Å^2$. However it is often more realistic to treat the atomic motion as ellipsoidal, rather than spherical, and the anisotropic correction is of the form :

$$f_j = f_j^o \, e^{-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + \beta_{12}hk + \beta_{13}hl + \beta_{23}kl)} \quad \ldots\ldots 1.10.$$

In the discussion which follows these temperature correction terms must be borne in mind, but for simplicity of representation (f_j) will be written for the corrected scattering factor.

1.4. The Reciprocal Lattice and The Sphere of Reflection.

It is pertinent to introduce at this point the concept of the (Gibbs-Ewald) reciprocal lattice [16], which has simplified the interpretation of all types of diffraction techniques based on moving crystals in monochromatic X-ray beams. If we imagine normals to the lattice plane stacks, on which are marked lengths proportional to the inverse of the repeat distance of the stack, then a second lattice is

produced in which a point represents a plane in the real-space lattice. This imaginary lattice is termed the reciprocal of the direct-space lattice, and the constant of proportionality is normally taken as (λ) , the wavelength of the incident radiation. The analogy between the reciprocal lattice and the diffraction pattern is simple, any spot on the pattern represents a reflection from a particular family of planes, which is associated with a specific reciprocal lattice point.

If we now construct a sphere of unit radius (i.e. 1 reciprocal lattice unit), with the incident beam as diameter, and place the origin of the reciprocal lattice at its point of emergence, then as the crystal rotates the reciprocal lattice rotates about a tangential axis. Reflection from a particular direct lattice plane (hkℓ) occurs when the reciprocal point (hkℓ) passes through the 'sphere of reflection'.(Ewald sphere).

The Bragg equation (1.2) sets the limiting value on the interplanar spacing (d) that can be compassed by a wavelength (λ); this is a consequence of the limit on sinθ of unity :

$$d = \frac{n\lambda}{2 \cdot \sin\theta} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad 1.11$$

whence, for a first order reflection :

$$d_{Min} = \frac{\lambda}{2} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad 1.12$$

Thus, no information is obtained about the region of reciprocal space outside a sphere of radius 2 r.l.u., and this is called the limiting sphere.

We may rewrite Eq. 1.8 in vector notation :

$$G = \sum_{j=1}^{J} f_j \exp (2\pi i \vec{r}_j . \vec{H}) \ldots\ldots 1.13$$

where the vector ($\vec{r}_j$) defines the position of the j'th atom, and ($\vec{H}$) defines a point in reciprocal space. (G) is thus the Fourier transform of one unitcell. Thus the structure factors (F) are the values of (G) at the reciprocal lattice points (hkl). We may thus construct a 'weighted' reciprocal lattice, with each point having an area proportional to the value of (F(hkl)). This lattice has the symmetry (Laue symmetry) of the diffraction pattern; this is the point group symmetry of the crystal plus a centre of symmetry*, giving rise to 11 Laue groups listed in Table 1.1.

* This is a consequence of Friedel's Law, which only holds under normal scattering conditions. For further discussion see Chapter 3.

CHAPTER 2.

The Phase Problem and some Methods of Solution.

2.1. Intensity Data and Their Correction.

The only data available to the crystallographer are the relative positions and intensities of the diffracted spectra from the crystal lattice. The latter may be recorded photographically (chapter 4), or measured electronically (chapter 9). Photographic methods must necessarily be used for the former, from which the Laue symmetry, crystal system, and unit cell dimensions may be obtained. In 60 cases the systematically absent spectra define the space-group uniquely, otherwise the choice is reduced to a few; a knowledge of the optical rotatory properties of the crystals or their solutions can further restrict the choice (chapter 3).

A knowledge of the cell dimensions, density (D_m), and approximate molecular weight (M), enables the number

of molecules per cell ($\underline{Z}$) to be calculated; since this must be an integer, back-calculation reveals the accurate value of ($\underline{M}$). Large discrepancies between the calculated and expected values can reveal an inaccurate analysis or the presence of molecules of crystallization. Where ($\underline{Z}$) is lower than expected from a consideration of space-group symmetry, the molecules themselves must posess symmetry, these results are often of chemical significance in themselves.(17)

Once the intensity record has been collected, the data must be corrected for certain geometrical and physical factors, before further progress can be made :

i) The Polarization Factor. The incident X-ray beam (received direct from the X-ray tube) is non-polarized, the electric vector ($\vec{E}$) assuming all directions with time. On reflection the component of ($\vec{E}$) in the plane containing the incident and reflected beams is reduced in amplitude, whereas the component perpendicular to this plane is not; so the resultant is partially polarized. If we designate the measured intensity by ($I^p(hkl)$), and the true value by ($I^o(hkl)$), then :

$$I^o(hkl) = I^p(hkl) \cdot (\tfrac{1}{2} + \tfrac{1}{2}\cos^2\theta)^{-1} = I^p(hkl).p^{-1} \quad \ldots\ldots\ldots 2.1$$

where (θ) is the Bragg angle and (p) is the polarization factor.

ii) The Lorentz Factor (L) is a measure of the rate at which the reciprocal lattice point (hkl) cuts the surface of the sphere of reflection. It is dependent on both (θ) and the radial cylindrical co-ordinate (ζ), and takes the form :

$$L = 1 / \{(\zeta/2)\sqrt{4\cos^2\mu - \zeta^2}\} \quad \ldots\ldots\ldots\ldots 2.2$$

for a Weissenberg photograph recorded at equi-inclination angle (μ). The above expression is usually combined with Eq. 2.1 for computational convenience, the observed intensity being multiplied by (Lp)$^{-1}$ to obtain ($I^o(hkl)$).

iii) The Multiplicity Factor. In some methods of obtaining the intensity record it is impossible to separate certain reflections, $h_1k_1l_1$, $h_2k_2l_2$, ... $h_jk_jl_j$, and the value observed is the summation of the individual values. If the reflections are symmetry equivalent then :

$$I^{total} = m.I(hkl) \quad \ldots\ldots\ldots\ldots 2.3$$

however, for the recording methods used in the work to be described, the factor (m) is unity.

iv) The Renninger Effect.[18] It is possible for X-rays, reflected from a set of planes $h_1k_1l_1$ to be reflected from a second set $h_2k_2l_2$, which are, by chance, in the correct orientation. It can be shown that the doubly reflected ray adds to the intensity of the reflection $h_1 + h_2$, $k_1 + k_2$, $l_1 + l_2$, but obviously no correction

can be applied. The Renninger conditions can, however, be calculated, and the effect avoided by a very slight displacement of the data collection geometry. If large systematic errors can be attributed to this cause, the data so affected can be omitted from refinement; this has not proved necessary in the present work.

v) Absorption. All crystals absorb X-rays to some extent, depending on their size, shape, and the scattering matter present. The equation linking the incident and transmitted intensities (I^{O} & I^{T}), is analogous to the Beer-Lambert law, viz :

$$I^{T} = I^{O}.e^{-\mu t} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad 2.4$$

where (t) is the thickness of the specimen in cm., and (μ) is the linear absorption coefficient in cm^{-1}. This is given by :

$$\mu = \sum_{j=1}^{J} G_j \left\{\frac{\mu}{\rho}\right\}_j \quad \ldots\ldots\ldots\ldots\ldots \quad 2.5$$

for monochromatic radiation. (ρ) is the density in g. $cm.^{-3}$ (D_x ; the experimentally determined density is usually used), and $(\mu/\rho)_j$ is the tabulated[19] mass absorption coefficient for the j'th atom, which comprises mass fraction (G_j) of the total molecular weight.

Correction is only simple for spherical [20] and

cylindrical[21] specimens. The situation is more complex for irregular shapes, but solutions using a three-dimensional grid of sampling points, to obtain the path-length of the ray inside the crystal, give good results. A graphical method[22], based on the work of Albrecht[23], is one of the quickest for hand computation. A computer procedure is mentioned in chapter 9. If the value of (μ) is low, and the crystal dimensions are small, the correction can be ignored in all but the most precise work.

vi) Extinction. Most crystals behave as if they consisted of a number of tiny blocks, whose orientation varies over several minutes of arc, i.e. they are ideally imperfect. Primary extinction results from multiple reflection of rays from a given set of planes within one 'mosaic' block. The incident beam undergoes a phase change of $\pi/2$ on reflection, so a doubly-reflected beam will be π out of phase with the main beam, and so reduces its intensity. The overall effect is that the intensity is now proportional to a power of ($F(hkl)$) between 1 and 2. Secondary extinction is caused by the upper layers of the crystal reflecting an appreciable portion of the primary beam, this reduces the intensity incident on the lower layers (mosaic blocks) of the crystal, which are simultaneously oriented for reflection. Both effects reduce the the observed intensities, and this is

most acute for strong, low-order reflections .

Secondary extinction can be allowed for by defining a new linear absorption coefficient[24] as :

$$\mu' = \mu + gQ \quad \ldots\ldots\ldots\ldots\ldots\ldots 2.6$$

where (Q) is the energy diverted into the reflected beam, and (g) is a constant for a particular specimen. In this work corrections have not been applied, data so affected have simply been omitted from the final stages of refinement.

2.2. The Phase Problem.

The electron density (ρ) at a point with fractional co-ordinates ($\underline{x}$, $\underline{y}$, $\underline{z}$) can be represented by a Fourier series in which the complex coefficients are the structure factors[25] (F(hkl)) given by Eq. 1.8; thus :

$$\rho_{(xyz)} = \frac{1}{V}\sum_{h=-\infty}^{\infty}\sum_{k}\sum_{l} F(hkl)\, \exp\left\{-2\pi i(h\underline{x} + k\underline{y} + l\underline{z})\right\} \quad \ldots\ldots 2.7$$

This formula can be considerably simplified for machine computation by expressing the structure factor in the complex form :

$$F(hkl) = A + iB \quad \ldots\ldots\ldots\ldots\ldots\ldots 2.8$$

where : $$A(hkl) = \sum_j f_j \cos \phi_j = |F(hkl)| \cos \phi(hkl) \quad .2.9$$

and : $$B(hkl) = \sum_j f_j \sin \phi_j = |F(hkl)| \sin \phi(hkl) \quad .2.10$$

and by utilizing the space-group symmetry.

Thus, if the amplitudes and phases of the structure factors are known, a representation of the electron distribution within the crystal can be obtained, with spherically symmetrical peaks occurring at atomic centres. In practice the values of h, k, l, are limited by Eq. 1.12, and the maps suffer from series-termination errors. However the observed intensities are proportional to the square of the structure amplitude (F(hkl)) (for ideally imperfect mosaic crystals) i.e. :

$$I^{o}(hkl) = k.\ F(hkl)^{2} = k\left[A(hkl)^{2} + B(hkl)^{2}\right] \quad \ldots 2.11$$

since (F(hkl)) is normally complex. Thus the experimental data gives no direct information concerning the phases (ϕ(hkl)); this bare statement constitutes the phase problem of crystal structure analysis.

2.3. Patterson's Function and the Heavy Atom Method.

Patterson's function [26] represents a convolution of the electron density with itself, inverted at the origin. The function (P) at a point (u, v, w) in Patterson or vector space, referred to three axes (U,V,W) parallel to the crystallographic axes, is :

$$P(uvw) = \int_{0}^{1}\int_{0}^{1}\int_{0}^{1} \rho(xyz) \cdot \rho\{(x+u),(y+v),(z+w)\}\, V dx dy dz \quad \ldots\ldots 2.12$$

where (V) is the cell volume. It may be represented as

a Fourier series with $|F(hkl)|^2$ as coefficients :

$$P(uvw) = \frac{1}{V} \sum_{h}^{+\infty} \sum_{k}^{+\infty} \sum_{l} |F(hkl)|^2 \exp\{-2\pi i(hu + kv + lw)\} \quad .. \quad 2.13$$

We may rewrite this equation :

$$P(uvw) = \frac{1}{2V} \sum_{h}^{+\infty} \sum_{k}^{+\infty} \sum_{l} \left[|F(hkl)|^2 \exp\{-2\pi i(hu + kv + lw)\} + |F(\overline{hkl})|^2 \exp\{+2\pi i(hu + kv + lw)\} \right] \quad .. \quad 2.14$$

and, assuming that Friedel's Law holds (see chapter 3), we may now write :

$$P(uvw) = \frac{1}{V} \sum_{h}^{+\infty} \sum_{k}^{+\infty} \sum_{l} |F(hkl)|^2 \cos 2\pi (hu + kv + lw) \quad ... \quad 2.15$$

This equation yields a function which is everywhere real, and exhibits a centre of symmetry .

Eq. 2.12 indicates that the Patterson will exhibit peaks when both $\{\rho(xyz)\}$ and $\{\rho(x+u),(y+v),(z+w)\}$ are large, i.e. they represent atomic centres in an electron-density map. Thus a peak will occur for each interatomic vector; if there are (J) atoms in the unit cell there will be (J^2) peaks in the Patterson; of these (J) will coincide at the origin, the remaining (J(J-1)) occurring in two centrosymmetrically related sets of ($\frac{1}{2}$J(J-1)). Theoretically the origin peak should represent $\sum_{j=1}^{J} Z_j^2$ electrons, while a peak representing a vector between the j'th and k'th atoms should contain $Z_j . Z_k$ electrons. In practice frequent overlap of peaks occurs, and the origin peak often obscures those of the second type.

The application of space-group symmetry to the Patterson by Harker [27] led to the first partial deconvolution method. Let us take, for example, a monoclinic crystal, space group P2; the general equivalent positions for the j'th atom are :

1) $\underline{x}_j$; $\underline{y}_j$; $\underline{z}_j$;

2) $-\underline{x}_j$; $\underline{y}_j$; $-\underline{z}_j$;

and a peak of weight (Z_j^2), representing the interatomic vector between two atoms related by the diad, will occur at co-ordinates :

$u = 2\underline{x}_j$; $v = 0$; $w = 2\underline{z}_j$;

obtained by subtraction of (2) from (1). This (uvw) section is referred to as the Harker section (x0z), since the co-ordinates $\underline{x}_j$, $\underline{z}_j$, are directly determined from the position of the peak maximum. Similar expressions can be worked out for other symmetry operations, and solution is sometimes simplified by the presence of atoms in special positions. Unfortunately, however, peaks arising between atoms not related by symmetry can blur the information contained in the Harker lines or sections; solution is facilitated if a small number of atoms in the structure have large (Z_j), when vector peaks between symmetry related atoms will stand out against a low general background.

The determination of 'heavy-atom' co-ordinates in

this way has led to one of the most far-reaching methods of solving the phase problem; the development of the 'heavy-atom' method is largely due to Robertson and his school[28]. We can write the total structure factor ($F(hk\ell)$) as (F^T), and thence as a sum of the heavy- and light-atom contributions (F^H, F^L) :

$$F^T = F^H + F^L \quad \ldots\ldots\ldots\ldots 2.16.$$

In general the contribution (F^H) will be large, usually sufficient to define the phase angles (0 or π) in the centrosymmetric case, for a large number of reflections. In the non-centrosymmetric case there is a similar probability that (ϕ^H) will approximate (ϕ^T) for a great proportion of the data. Thus a Fourier summation based only on the heavy-atom co-ordinates frequently gives a close approximation to the true electron-density distribution; at worst some chemically recognizable features will be shown, which enables the positions of some of the light atoms to be obtained. The use of successive Fourier syntheses then reveals the complete atomic arrangement. Lipson and Cochran [29] have suggested that the method works best when :

$$\sum(Z^H)^2 \doteq \sum(Z^L)^2 = 1 \quad \ldots\ldots\ldots 2.17$$

but, with the advent of more accurate data collection equipment, structures with a ratio greater than unity should be soluble. Cases where the ratio is less than

unity are often soluble by careful iterative Fourier techniques.

In the work to be described the heavy atom method has proved successful. In the initial stages a rejection test has been applied whereby (F(hkl)) has been excluded from the Fourier series if :

$$\left|F^H\right| < x. \left|F^T\right| \quad \text{..... 2.18}$$

where (x) has been reduced from 0.33 in successive summations. Thus reflections of uncertain phase are excluded. A better procedure involves the use of Fourier coefficients of the form (w F(hkl)), where (w) is a weight (from 0 to 1) based on the probability that the phase due to the heavy-atom is correct. Such functions have been described by Woolfson [30] for the centrosymmetric case, and by Sim [31] for the non-centrosymmetric case.

It is pertinent at this point to give a brief review of other methods of surmounting the phase problem. Early structure determinations relied on what are best termed 'trial and error' methods, comparing the observed structure amplitudes with those calculated from a structure model. The advent of the methods discussed above was one of the turning points, giving semi-direct information regarding the phases. A contempory of the heavy-atom method was that of isomorphous replacement of one heavy-atom for another as utilized by Robertson [28] in the centro-

symmetric phthalocyanine derivatives. A method using double replacement was proposed in the acentric case [32]. The method has recently been resurrected in connection with structural work on proteins [33], with remarkable results.

We may conveniently divide other methods of solving the phase problem into two classes :

i) Those which are directly related to the Patterson function, and

ii) Those which work, basically, with the weighted reciprocal lattice.

Each class may be further subdivided into two groups as follows :

(i (a)) Methods which make chemical suppositions. In class (i) this involves the assumption that a fragment of known molecular geometry exists within the molecule. The best known of these are the Patterson searching techniques of Nordmann [34], and the fältmolekul or convolution molecule method of Hoppe [35], which uses a fragment together with others related by symmetry.

(ii (b)) Methods which make no chemical assumptions, but use crystal symmetry and the positions of some known heavier atoms (which, in themselves are not sufficiently heavy to govern the phases of a large proportion of the data). Here we may list superposition methods and their corollaries : minimum functions and implication diagrams,

These methods may be classified as 'image seeking' and have been put on a rigorous theoretical basis by Buerger[36]. A more recent extension of these Patterson deconvolution methods is vector verification [37].

We may also treat class (ii) in the same manner :

(ii (a)) One of the best known methods in this category involves the calculation of the Fourier transform (G) for one unit cell using Eq. 1.13. The transform is the reciprocal of this single unit, just as the reciprocal lattice is the reciprocal of a repeating pattern of many units. From the definition of (F(hkl)) arising from Eq. 1.13, we can compare the calculated transform with the weighted reciprocal lattice. The calculation of (G) is laborious, but can be avoided by the use of optical methods. Both approaches owe much to the work of Lipson and Taylor [38,39].

(ii (b)) This group includes those methods which attempt to derive the phases directly from the observed structure amplitudes, and in which no chemical information is assumed in the derivation. The first major breakthrough was due to Harker and Kasper[40], who applied the inequality relations of Schwartz and Cauchy to the unitary structure factors (U(hkl) $\equiv$ U($\underline{h}$))*. The relationship :

---

* U($\underline{h}$) = F($\underline{h}$)/ $\sum_j f_j$, i.e. the structure factor as a fraction of the maximum possible value : obviously U($\underline{h}$)$^2 \leqslant 1$.

$$U(\underline{h}) \leqslant \tfrac{1}{2} + \tfrac{1}{2}U(2\underline{h}) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad 2.19$$

was derived for a structure containing a symmetry centre, and can be extended to cover other symmetry operations. Karle and Hauptmann [41] showed that restrictions were placed on the structure factors when it was assumed (quite validly) that the electron-density (ρ) was non-negative. They derived some more general inequalities.

The development of relationships between the signs (s) of the structure factors in a centrosymmetric case was initiated by Sayre[42]. His work was extended by Cochran [43], who showed that the relationship :

$$s(\underline{h}) = s(\underline{h}').s(\underline{h} + \underline{h}') \quad \ldots\ldots\ldots\ldots\ldots\ldots 2.20$$

was probably true if the corresponding values of (U) were large. The same result was independently obtained by Zachariasen[44] using a different method. Systematic methods for applying this type of relationship were developed by Grant, Howells and Rogers[45], and by Woolfson [46]. The development of these methods in the last decade is largely due to Hauptmann and Karle and their co-workers. In 1953[47] these authors derived a number of structure factor relationships which they designated ($\Sigma_1 \rightarrow \Sigma_4$) and later obtained formulae assessing the probability that the sign of their sum was the sign of ($U(\underline{h})$). The use of symbols to represent unknown signs has led to the method being called 'sym-

bolic addition'. This type of approach has been extended to cover the non-centrosymmetric case[48], with no mean success. Here, however the number of ambiguous sets of phases produced tends to be large. The theoretical background and practical procedures available in both cases have been reviewed by Karle and Karle[49].

2.4 The Refinement of Atomic Parameters : The Least-Squares Method.

If we have (m) linear equations of condition, involving (n) variables, ($x_1, x_2, \ldots\ldots x_n$), of the form :

$$E_k + q_k = a_k x_1 + b_k x_2 + c_k x_3 + \ldots \qquad \ldots 2.21$$

where each term (q_k) can be determined experimentally with an error (E_k), then if (m) exceeds (n) we may solve for the x's in p (= m!/n!(m-n)!) ways. Since the error terms are all different, (p) different solutions will be obtained. The theorem of Legendre[50] states that the best solution is obtained when $\sum_{k=1}^{n} E_k^2$ is a minimum.

The crystallographic equation of condition is of the form :

$$q_k = f_k (x_1, x_2, x_3, \ldots\ldots x_n) \ldots\ldots\ldots 2.22$$

where the (f_k) terms are the structure factors, which

are functions of the positional and thermal parameters. As can be seen from Eqs. 1.8,9,10, these contain exponential terms, and do not supply the required linear conditions. However, if we assume that approximate solutions (x_i) are known, and that an error (dx_i) is associated with each variable (x_i), we may expand Eq. 2.22 by Taylor's theorem :

$$q_k = f_k x_n + \sum_{i=1}^{n} \frac{\partial f_k}{\partial x_i} dx_i + \frac{1}{2} \sum_{i=1}^{n} \sum_{j=1}^{n} \frac{\partial^2 f_k}{\partial x_i . \partial x_j} . dx_i \, dx_j \quad \ldots\ldots\ldots\ldots 2.23.$$

If terms of order higher than one are ignored, since they involve the product of two small quantities, (m) equations are obtained of the form :

$$\frac{\partial f_k}{\partial x_i} dx_i + \frac{\partial f_k}{\partial x_2} dx_2 + \ldots\ldots \frac{\partial f_k}{\partial x_n} dx_n = q_k - f_k(x_1 \ldots x_n) \quad \ldots\ldots\ldots\ldots 2.24.$$

These may be expressed in matrix form :

$$(A) \, dx = (b) \quad \ldots\ldots\ldots\ldots\ldots\ldots 2.25$$

where any element of (A) may be written :

$$w_k^{\frac{1}{2}} . \partial f_k / \partial x_i \quad \ldots\ldots\ldots\ldots\ldots\ldots 2.26$$

and of (b) :

$$w_k^{\frac{1}{2}} . \left\{ q_k - f_k(x_1, x_2, \ldots\ldots x_n) \right\} \ldots\ldots 2.27$$

The terms (w_k) are weights, expressing the estimated relative accuracy of (q_k).

In this case minimisation of the sum of the squares of the errors involves finding :

$$\min \sum_{k=1}^{m} E_k^2 = \min \sum_{k=1}^{m} w_k \left\{ q_k - f_k(x_1, \ldots x_n) \right\} =$$

$$\min \sum_{k=1}^{m} w_k \left(\left| |F_o| - |F_c| \right| \right)^2 \quad .. \quad 2.28.$$

The process is cyclic, involving successive solution for the parameter shifts (dx_i) , until these are minimal. The value obtained is not a true minimum since higher terms in the expansion (Eq. 2.23) have been ignored. In certain cases when high correlations, say between dx_i, dx_j, occur, the convergence is slow or impossible; it is possible to overcome this by multiplying the shifts by a damping or enhancing factor.

In the work to be described weighting schemes have been used where all (w_k) are unity, or one which makes the final summation of Eq. 2.28 approximately constant over ranges of $|F_o|$. In general the scheme described by Hughes[51], in a paper which introduced the least-squares method to crystallography, has been found satisfactory :

$$w_k^{\frac{1}{2}} = 1 \quad \text{for} \quad F_o \leqslant F^{*}$$

$$\text{and} \quad w_k^{\frac{1}{2}} = F^{*}/F_o \quad \text{for} \quad F_o > F^{*} \qquad \ldots\ldots\ldots \quad 2.29.$$

The constant (F^{*}) is chosen from an analysis of $|F_o|$ & $|F_c|$.

A measure of the accuracy of the structure, and also of the rate of convergence is given by :

$$\underline{R} = \frac{\sum \left| |F_o| - |F_c| \right|}{\sum |F_o|} \quad \ldots\ldots\ldots\ldots 2.30.$$

although changes in the expression minimised (i. e. in $w_k \left(|F_o| - |F_c| \right)^2$) are often more significant. The weighted ($\underline{R}$)-factor ($\underline{R}^w$) will be defined in the next chapter, and its significance discussed in another context .

CHAPTER 3

Molecular Asymmetry :

The Determination of Absolute Configurations by X-Rays.

The study of molecular asymmetry has attracted the attention of chemists since the observations of Biot between 1815 and 1835. He noted that certain natural products, e.g. camphor, turpentine and some sugars, would rotate the plane of polarized light to the left, or to the right. The property was exhibited in solution, showing that it was a molecular, rather than a macroscopic, property. In 1848 Pasteur separated the enantiomorphic forms of tartaric acid by hand; the crystals differed only in the placement of one morphological facet. He noted that solutions of the two ~~two~~ types of crystals rotated the plane of polarization in opposite senses.

The explanation of the phenomenon arose from the proposition of the tetrahedral arrangement of the four bonds formed by carbon (van't Hoff and Le Bel 1874). Previously the four bonds had been assumed coplanar, and

all compounds were their own mirror images. If, however, four different groups are bonded to a single carbon atom, only two tetrahedra are possible, one being the mirror image of the other. The conclusion was reached that all optically active compounds contained one or more of these asymmetric centres.

Although the measurement of the optical rotatory power is simple it does not give unequivocal information regarding the absolute configuration. Degradative chemical work can relate configurations to the arbitrary standards enunciated in the Fischer-Rosanoff convention; this, however, had an exactly evens chance of being correct. It has become increasingly important to know the exact spatial relationships of atoms. Enzymic reaction *in vivo* frequently produces all-dextro or all-laevo products; conversely the *in vivo* system will frequently accept only one form, the other being either completely deleterious or just ignored. If the biochemist is to explain these phenomena, or the drug chemist is to synthesise the correct form, a knowledge of absolute configuration is of paramount importance. The X-ray methods to be described in this chapter have provided the key to the whole problem.

3.1. Normal Scattering : Friedel's Law.

We must first note that optically active compounds can only crystallize in space-groups which do not involve rotation-inversion axes ($\bar{n}$) or mirror planes (m), since these require the presence of the other enantiomorph. Thus all centrosymmetric space-groups are excluded ($\bar{1}$), together with non-centrosymmetric ones involving mirror or glide planes. The only allowed space-groups are those involving pure rotation or screw axes, and there are only 65 possibilities; these are the 'regular point systems' of Sohncke [52].

The formulae derived in chapter 1 only apply under 'normal' scattering conditions : when the incident wavelength is very much less than any natural absorption wavelength of the atomic electrons in the structure. Under these conditions the wave scattered by any atom is $\pi/2$ out of phase with the incident wave. This is true for all atoms, and the phase change can thus be ignored. We may now study the effect of this on the structure factors ($F(hk\bar{l}) \equiv F_N$) and the inverse ($F(\bar{h}\bar{k}\bar{l}) \equiv \bar{F}_N$). Expansion of Eq. 1.5 to three dimensions gives :

$$\phi(hkl) = \sum_j 2\pi(hx_j + ky_j + \bar{l}z_j) \quad \ldots\ldots \quad 3.1$$

therefore : $\phi(hkl) = -\phi(\bar{h}\bar{k}\bar{l})$ ($= -\phi_N$) $\ldots\ldots\ldots\ldots$ 3.2

Combining Eqs. 2.8,9,10, and using the present nomenclature,

we may write : $F_N = |F_N| e^{i\phi_N}$ ..... 3.3.

and : $\overline{F}_N = |F_N| e^{-i\phi_N}$ 3.4

since the Bragg angles (θ) are equal for both reflections. However, Eq. 3.3 is the complex conjugate of Eq. 3.4, and vice versa, so that :

$$|F_N|^2 = |\overline{F}_N|^2 \quad \text{..... 3.5}$$

and : $$I_N = \overline{I}_N \quad \text{..... 3.6}$$

This is Friedel's Law [53], a statement of the centrosymmetric nature of the intensities in reciprocal space. Thus, in the reconstitution of a structural image from the normal X-ray data, it is impossible to distinguish between a structure and its inverse, even though the atomic sequence 'seen' by the incident beam from the sides (hkl), $(\overline{hkl})$ is different.

3.2. Anomalous Scattering : The Bijvoet Technique.

Von Laue [54] was the first to suggest that Friedel's Law should break down if the incident wavelength was slightly shorter than that of an atomic absorption edge (e.g. $\lambda_{K\text{abs}}$) of one or more atoms in the structure. Theoretical calculations by Hönl [55] showed him to be correct; in this case the energy of the incident quanta is sufficient to excite the K-electrons, and the scattered wave from these atoms has a phase lead over those from

the normal scatterers. The scattering factor for the 'anomalous scatterers' is now a complex quantity :

$$f_j^A = f_j^{oA} + f_j'^A + if_j''^A \quad \ldots\ldots\ldots 3.7.$$

If we have a structure containing both normal and anomalous scatterers, we may write an expression analogous to Eq. 2.16 for the total structure factor ($F(hk\ell)$) :

$$F_T = F_N + F_A \quad \ldots\ldots\ldots\ldots\ldots 3.8$$

We may now examine the effect of the presence of anomalous scatterers on the structure factors (F_T) and ($\overline{F}_T$), using the methods and nomenclature of Sect. 3.1, in which the real and imaginary parts of (F_A) will be designated (F_A') and (F_A'') respectively :

$$F_T = |F_N| e^{i\phi_N} + |F_A'| e^{i\phi_A} + i|F_A''| e^{i\phi_A} \quad \ldots\ldots\ldots 3.9$$

$$= |F_N|(\cos\phi_N + i\sin\phi_N) + |F_A'|(\cos\phi_A + i\sin\phi_A) + |F_A''|(i\cos\phi_A - \sin\phi_A) \quad \ldots\ldots\ldots 3.10$$

$$= (|F_N|\cos\phi_N + |F_A'|\cos\phi_A - |F_A''|\sin\phi_A) + i(|F_N|\sin\phi_N + |F_A'|\sin\phi_A + |F_A''|\cos\phi_A) \quad \ldots 3.11$$

We may also derive ($\overline{F}_T$) in a similar manner to be :

$$\overline{F}_T = (|F_N|\cos\phi_N + |F_A'|\cos\phi_A + |F_A''|\sin\phi_A) + i(|F_A''|\cos\phi_A - |F_A'|\sin\phi_A - |F_N|\sin\phi_N) \quad \ldots 3.12$$

We can now obtain ($|F_T|^2$) and ($|\bar{F}_T|^2$) by multiplying Eqs. 3.11, 12, by their complex conjugates. When this is done they are not found equal, the difference being :

$$\Delta I \propto \left\{ |F_T|^2 - |\bar{F}_T|^2 \right\} = 4 |F_N| |F''_A| \sin(\phi_N - \phi_A) \quad \ldots 3.13.$$

Thus Friedel's Law is seen not to hold. The structure factors are best represented on an Argand diagram, such as Figure 3.1, which shows a quite general case. The difference in intensities will be a maximum when :

$$\phi_N = \phi_A \pm \pi/2 \quad \ldots\ldots\ldots\ldots\ldots\ldots 3.14$$

and a minimum when :

$$\phi_N = \phi_A \text{ or } \phi_A + \pi \quad \ldots\ldots\ldots\ldots 3.15$$

the first condition of Eq. 3.15 will always occur if the structure contains one type of anomalous scatterer only.

The effect was noted experimentally as early as 1930[56] when zinc sulphide, which has an asymmetric crystal structure, was irradiated with Au(L_α). The value of (λ_{Kabs}) for Zn is 1.2805 Å, and the unequal intensities of the Au(L_{α_1}) (λ = 1.2738 Å) component scattered from the planes (111) and ($\overline{111}$) was demonstrated. The intensities due to the Au(L_{α_2}) component (λ = 1.2850) were equal.

The further implications of this result were not fully realized until Bijvoet [57] proposed that the absolute configuration could be obtained by comparing the

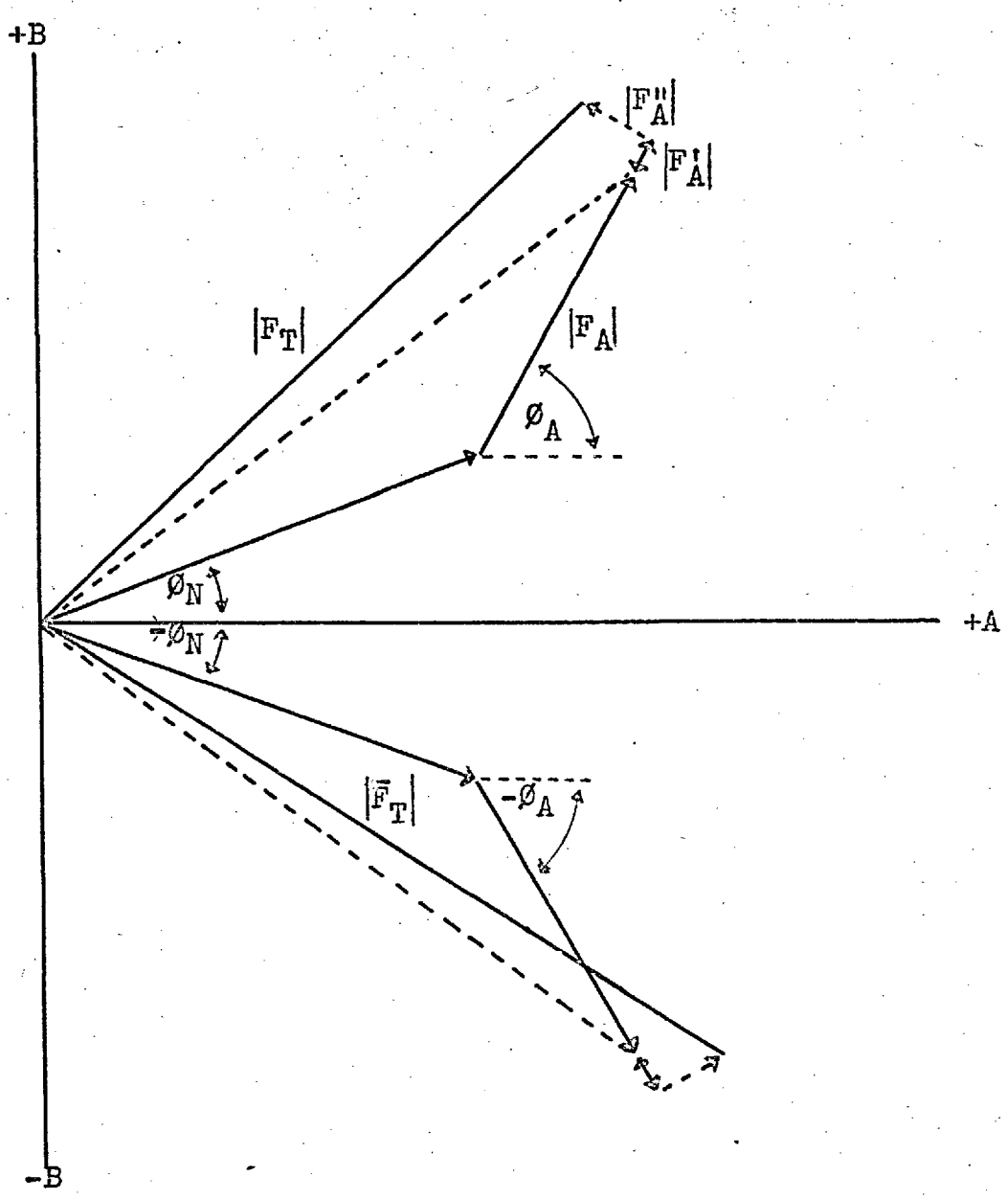


Figure 3.1. Argand Diagram showing the resultant amplitudes of the structure factors $|F_T|$, $|\bar{F}_T|$, after correction for anomalous dispersion. In this perfectly general case $|\bar{F}_T| > |F_T|$.

observed inequalities, with those calculated from the known crystal structure. The intensities compared must be (hkl) ($\overline{hk}\overline{l}$) or their equivalents, and they have become known as 'Bijvoet pairs'. If good (usually $>85\%$) agreement is obtained, the structure, as determined, must represent the true spatial arrangement; a similar level of disagreement indicates that the inverse structure is 'absolutely' correct. For cases where the ' confidence level ' lies between these approximate limits, the experimental method may not have been applied with sufficient care, or the state of the refinement may not have given sufficiently accurate parameters for the calculation (which may be carried out by computer, or using Argand diagrams similar to Fig. 3.1.).

We may now examine the requirements, both chemical and crystallographic, for a successful determination :

i) An anomalous scatterer, or scatterers, must be present in the structure, together with normal scatterers. Atoms of atomic number (Z) $\geqslant$ 16 are required, and the condition is similar to the requirements for the heavy-atom method, which usually facilitates structure solution prior to an absolute configuration determination.

ii) The wavelength of the incident radiation must be sufficient to excite fluorescence, but the choice is not so restrictive as was initially thought. Hönl[55] had

predicted that where $(\lambda_{inc}) > (\lambda_{Kabs})$ the energy was sufficient to excite L- or even M-electrons. This was shown experimentally by Peterson[58], who excited the L-electrons of bromine (λ_{Labs} = 7.989 Å) with Cu(K_α) radiation (λ = 1.54178 Å), and detected an average intensity difference of 8%. Dauben and Templeton[59] have calculated the correction terms (f') and (f") for atoms with $Z \geqslant 20$ for the common wavelengths (K_α lines of Mo, Cu, & Cr).

iii) The Bijvoet pairs must be indexed on a right-handed system of axes (and the corresponding reciprocal lattice) For photographic work the rotational sense of the goniometer axis must be correlated with the translational movement of the camera pot; the order in which the reciprocal lattice points pass through the sphere of reflection may then be analysed. This point has been dealt with by Peerdemann and Bijvoet[60].

iv) Extreme care must be taken in the recording and measurement of the Bijvoet pairs. If photographic methods are used they must be recorded under identical conditions, i.e. on the same film. Usually the space-group symmetry allows pairs other than (hkl), ($\overline{hkl}$) to be compared; This is further discussed in chapter 6. Obviously electronic measurement has advantages, but photographic data may be measured best on a microdensitometer, and gives good results. If the discrepancies are expected to be

small, they will be most apparent among reflections with high (θ); this is because the normal scattering factor (f_j^o) falls off rapidly with increasing (θ), while (f') and (f") are almost independent of (θ), since the electrons involved are confined to a small area close to the nucleus.

v) Care must be taken to avoid absorption errors which could reverse the assignment of absolute configuration in particularly adverse circumstances. For (μ) > $100cm^{-1}$ it is wise to apply a systematic correction.

vi) The initial structure determination must be carried out to a good accuracy; the pitfalls in using inaccurate data will be mentioned in chapter 6.

The first assignment of absolute configuration was that of sodium rubidium-D-(+)-tartrate[61]; the rubidium atom (λ_{Kabs} = 0.81549 Å) was excited by Zr(K_α) radiation ($\lambda_{K\alpha_1}$ = 0.79010, $\lambda_{K\alpha_2}$ = 0.78588 Å). The choice was historically apt : the results showed that " .... Fischer's arbitrary convention corresponds to reality "[62].

3.3. Some Extensions : Anomalous Dispersion Phasing and Hamilton's Method.

Reference to Eq. 3.13 shows that, if the positions of the anomalous scatterers can be found, the value of (ϕ_N) may be obtained, since all other terms in the equation may

be obtained experimentally. This method of solving the phase problem has been developed largely by Pepinsky et. al.[63] and by Ramachandran et. al[64]. If the total structure is solved by this method, the solution automatically shows the absolute stereochemistry.

The use of linear hypothesis tests on the weighted crystallographic R- factor :

$$\underline{R}^{W} = \left[\frac{\sum_{i=1}^{m} w_i \left(|F_i|_o - |F_i|_c \right)^2}{\sum_{i=1}^{m} w_i |F_i|_o^2} \right]^{1/2} \quad \ldots\ldots\ldots 3.16$$

computed for (n) parameters over (m) observations (F_i), was first suggested as a method for the determination of absolute configuration by Hamilton and Ibers[65]. The theory has been extended by Hamilton[66], and he has published tables of the function :

$$\frac{\underline{R}_1^W}{\underline{R}_2^W} = \mathcal{R}_{b,\, m-n,\, \alpha} \quad \ldots\ldots\ldots\ldots\ldots 3.17$$

where (b) is the dimension of the hypothesis, and (α) is the significance level. The terms ($\underline{R}_1^W$) and ($\underline{R}_2^W$) are the weighted R- factors for the structure and its enantiomorph, obtained from parallel refinements using data corrected for dispersion effects. The tables are computed at differing values of (α), and interpolation formulae are derived.

The statement : "the second configuration represents the true absolute stereochemistry", is a one-dimensional hypothesis. It is claimed that its validity may be accepted or rejected on a very small deviation of ($\mathcal{R}$) from unity. However, Hamilton and Ibers have pointed out that the presence of systematic errors will invalidate the procedure. It appears to the present author that the procedure must be considered in the general context of R- factor significance; for instance it is dubious to obtain results in this manner from R^W- values higher than about 15%; it would be better to express the ratio ($\mathcal{R}$) as a percentage of the mean value of R_1^W and R_2^W , this would obviously depend on the value of (f") and this should be quoted. The method has had only limited application, and the results [67,68] are so far unequivocal. The only advantage of the method is that extra photography and measurement is avoided; against this must be set the additional computer time required.

3.4. The Method of Internal Comparison.

Although the techniques discussed above have produced many important results, it is not always possible to satisfy the required conditions. The method of internal comparison employs a known reference asymmetric centre, either within the molecule itself or :

i) introduced in the formation of a simple derivative, or ii) present in the solvent of crystallization. In these cases the determination of the relative stereochemistry automatically leads to the absolute configuration at all other centres.

The method was suggested almost simultaneously by Pepinsky[69], Mathieson[70], and Hine and Rogers[71]. The latter authors gave the first complete example : S-methyl-L-cysteine sulphoxide; the configuration of the L-cysteine was known with reference to the (proven) Fischer convention, and the structure determination established the configuration about optically-active sulphur for the first time.

Mathieson[70] has expounded some of the advantages :

i) no special precautions need be taken with regard to the radiation used;

ii) the method is equally applicable to light-atom structures where Patterson deconvolution or direct phasing techniques have been used;

iii) the addition of the reference centre does not involve extra photography, but requires the positioning and refinement of a few extra atoms.

Additionally we may note that results can be obtained from two-dimensional studies, and, in any case, without recourse to very detailed refinement.

3.5. Conclusion.

The methods outlined above represent the only physical technique by which absolute configurations may be assigned in a completely unambiguous manner. In more complex molecules the detailed degradative chemical work can take much longer than an X-ray arbitration, although these have their limitations. It is pleasing to note that these assignments are being made as a standard part of the sequence of crystal structure analysis. As part of the experimental work on 3-bromo-(+)-camphor, the author performed an extensive literature search to assess the application of the Bijvoet technique; the results[72] showed that, between 1951 and 1966, 54 assignments had been made. The survey was extended to include determinations by other methods, and completed up to the end of 1967; 40 new entries were obtained[73]. Both lists are bound with this thesis as Appendix I.

Although this chapter has dwelt on the absolute configuration of organic molecules, the anomalous dispersion technique is capable of indicating the true absolute spatial atomic arrangement in an asymmetric structure, e.g. zinc sulphide or α-quartz[74]. It is also finding application in the ever expanding field of asymmetric inorganic complexes.

CHAPTER 4.

Data Collection and Treatment : Computer Programs Used.

4.1. Data Collection.

Both photographic and automatic electronic methods of data collection were employed in the work to be described. The Siemens automatic single-crystal diffractometer was used in only one case, and a discussion of its application will be delayed until chapter 9 .

All photographic intensity data were collected using the equi-inclination Weissenberg technique and the multi-film pack method[75]. Two four-film packs were taken for each layer of the reciprocal lattice, with relative exposure times in the approximate ratio of 3:1; in this case, assuming a film-to-film attenuation of ~3.0 for Ilford Industrial 'G' film, the intensities on the bottom film of the first pack approximate to those on the top film of the second.

All films were developed under similar conditions, i.e. immersed for 5 minutes at 60°F in Ilford Phenisol

developer, washed, and then fixed for 7 minutes in Kodak Unifix solution. The treated films were finally washed for about 2 hours.

Before the collection of accurate cell-dimensions and intensity data the camera pot radius was checked; using a suitable powder specimen enclosed in a Lindemann glass capillary tube, sets of powder lines were recorded on the edges of a full film, back calculation from the known d-spacings (listed in the ASTM index) gave the correct radius.

All intensities were measured visually using a graduated step-wedge (except for the Bijvoet pairs (chapter 6) for which a Joyce-Loebl microdensitometer was used). A strong reflection was chosen and exposed for a measured number of traverses of the camera pot, to produce a strip graduated in arbitrary units, usually from 1 to 40. To accomodate changes in spot shape on higher layers several wedges were made, at different equi-inclination angles, for each set of data. The intensities in each layer were then manually scaled-up to the level of the top (most intense) film.

4.2. Data Treatment : Computer Programs Used.

Two distinct sets of crystallographic computer programs were used in this work :

X-RAY '63.

This is a completely homogeneous system, developed by Professor J. M. Stewart of the University of Maryland, and implemented on the Imperial College IBM 7090 in 1966. The program segments are written in FØRTRAN II and stored in a compiled form on magnetic tape (hereinafter magtape), each may be called separately into store, and as many units as required may be used in one run, the linking routines are written in FAP. Intermediate computations are written to magtape ready for the next program, but permanent data, such as the reflection list, scattering factors, atomic positions and temperature factors, and weights, are stored on the user's magnetic tape and saved for future use.

ATSYS.

This is a set of single-program documents, with no linking routines, and does not constitute a system in the above sense. All programs are written in the EXCHLF extension of Mercury Autocode, and, as above, stored in a compiled form on magtape. The user's basic data is similarly stored, and input is cut to a minimum : only a short 'steering tape' indicating the file-number of the program, the locations of stored data, and the operations to be carried out. The formation of ATSYS is largely the

work of Dr. M. G. B. Drew[76], who adapted and integrated programs from a number of different sources. As a 'home-grown' venture it has been amended and added to by a succession of students as the need arose.

The programs in both systems will be referred to only by their names in the text, since these names often give no indication of their function this will be indicated briefly below. There is also considerable overlap between the two systems, programs which cover the same ground will be listed together; programs unique to either system are listed separately . Name(s) of original author(s) are mentioned in as many cases as possible. The present writer is thankful to all those listed; he is more than aware of the frustrations involved !

ATSYS	X-RAY '63
CEDI, P.G.H.Troughton.	PARAM, R.A.Alden, H.L.Ammon.

Least squares refinement of cell parameters from data input as : theta, $n\theta$, $\sin\theta$, or $\sin^2\theta$. Estimated standard deviations are produced for real and reciprocal cell dimensions.

FIFI, R.D.Diamand.	DATRDN, J.M.Stewart, M.A.Jarski, B.Morosin, R.Chastain.

Applies Lp^{-1} correction to raw intensities, and

in both systems is the initial means of magtape storage. All basic data required by X-ray '63 is read in,and stored for future use, at this stage, except, of course, the atomic parameters.

BOSS, M.M.Harding, M.G.B.Drew	FC, J.M.Stewart, R.Braun.
	FOURR, D.F.High et.al.

Both programs will calculate 2D and 3D Patterson and Fourier maps at specified grid intervals. FOURR is completely general and takes precomputed structure factors from FC. BOSS contains its own structure factor routine, and is limited to triclinic, monoclinic, and some orthorhombic space-groups; others can be added as required. BOSS produces an agreement analysis in the form of a list of $|F_o|$, $|F_c|$, and $\underline{R}$, for reflections grouped in layers and by $\sin^2\theta$ intervals, agreement is also assessed over ranges of $|F_o|$ as fractions of $|F_{max}|$; this latter enables a choice of weighting scheme to be made. These functions are covered in X-ray '63 by two programs : RLIST by W.Keefe and J.M.Stewart, and DELSIG by R. V. Chastain.

PAPA, M.G.B.Drew, F.H.Allen, P.Phavanantha.	PEKPIK, D.F.High.

This program, basically the same in both systems, will read a Fourier map stored on magtape, and output fractional and grid co-ordinates of all electron-density maxima which exceed a set maximum. In PAPA Booth's parabolic method (77) is followed

BABA, R.D.Diamand, amended by Drew, Allen, Troughton	ORFLS, BLOKLS, DIAGLS, W.R.Busing, K.O.Martin,H.Levy, adapted by J.M.Stewart et.al.

Structure-factor least-squares refinement programs. BABA uses a block-diagonal approximation, and follows the nethod outlined by Cruickshank[78]. The output parameters and structure-factors are stored on magtape ready for the next run. The agreement analysis from BOSS has recently been added to allow an appraisal of the weighting scheme to be made during refinement. The author has changed the input facilities to allow isotropic-anisotropic temperature factor conversion to be made at the user's discretion; also the scattering factors are now input direct from tables[19], and converted internally to the values required by the program using Rollett's four-point interpolation[79]. Three separate routines are provided in X-ray '63. The standard version of ORFLS[80] has been amended to allow block-diagonal and diagonal-only approximations, as well as the full-matrix method.

ELSI, M.G.B.Drew.	BONDLA, D.F.High, J.M.Stewart, R.V.Chastain.

Interatomic distances and angles programs. ELSI requires input of atomic positions ($\underline{x}_r$) and their variances (V_{rr}), these are converted to estimated standard deviations (σ_{rr}) using Cruickshank's formula[81]:

$$\sigma_{rr}^2 = V_{rr} \sum_{i=1}^{m} w_i (|F_i|_o - |F_i|_c)^2 / (m-n) \quad \ldots.4.1$$

for (m) observations and (n) parameters. Standard deviations of lengths and angles are then computed using the formulae of Ahmed and Cruickshank[82] and Darlow[83]. Symmetry and translation operations are allowed for in both programs to obtain inter-molecular distances. BONDLA will also calculate hydrogen-atom positions, either tetrahedrally, trigonally, or linearly bonded, at a distance set by the user.

DIDO, R.A.Sparkes, D.J.Hunt. | LSQPL, R.W. Chastain.

Calculates the best plane through a set of input atoms, together with their mean distance from the plane. Other atoms may be re-positioned w.r.t. this plane, thus facilitating crystal drawing. DIDO uses the eigenvalue method outlined by Rollett[84], while LSQPL follows the method of Schomaker et.al.[85].

MATT, D.J.Hunt. | DATFIX, J.R. Holden.

Wilson's method[86] is applied to estimate the overall scale and temperature factor from two- or three-dimensional data. The programming method is similar to that outlined by Rogers[87] in the case of MATT. DATFIX also produces unitary structure factors, and is the initial program for application of direct methods via X-ray '63.

SFPO, F.H.Allen.	FCLIST, J.M.Stewart et. al.

Output of structure factor lists in a format suitable for reproduction in Theses and papers. The printing and pageing formats are variable in both programs, and unobserved reflections can be suitably marked.

The following programs are unique to ATSYS :

POLO, M.G.B.Drew.

Reads in sets of data collected by rotation about two or three axes and initially corrected by FIFI. The common reflections are picked out to obtain inter-layer scale-factors, which are then refined by the method of Rollett, Hamilton and Sparkes[88], to obtain the best fit. The final list, on an arbitrary unified scale, is written to magtape for further processing (e.g. MATT). The program also contains routines to sort the data to any order.

MOJO, F.H.Allen.

Produces : i) orthogonalized Ångstrom co-ordinates, ii) bond lengths and direction cosines, iii) bond angles, iv) dihedral angles, for one asymmetric unit in a systematic manner, using a 'bonding array' or 'connectivity chart'. This obviates needless computation of unwanted information incurred in the full interatomic vector search programs. In addition other routines calculate specific

angles, distances, etc.; a specific routine to analyse the molecular geometry of cyclobutane rings was included to give the results listed in chapter 7. The programming scheme, relevant mathematics, and some examples of input and output, are shown in Appendix II.

Computer programs used specifically in connection with the Siemens diffractometer are briefly described in chapter 9.

CHAPTER 5

The Terpenes and Terpenoid Biosynthesis

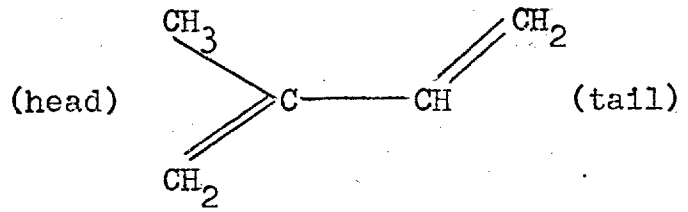
5.1. The Isoprene Rule.

The production of isoprene (5.I) on the thermal decomposition of many naturally occurring hydrocarbons led Wallach[89] to propose that their structures were formed from a number (n) of isoprene units (C_5H_8). The name 'terpene' had originally been used for those hydrocarbons obtained from turpentine oil, but the classification became extended to include those substances which fitted the 'isoprene rule'. The natural diversity of the basic hydrocarbons, and their oxygenated derivatives, mainly from the plant kingdom, led to a sub-classification based on the number (n) (see Table 5.1, over page). The group as a whole became known as the terpenoids, indicating that the molecular formula of the basic carbon skeleton could be written $(C_5H_8)_n$.

Later workers extended the isoprene rule[90], and the

Table 5.1. Sub-Classification of the Terpenoids.

n	class (common name) ; molecular formula of basic hydrocarbon.	
2	Monoterpenes;	$C_{10}H_{16}$
3	Sesquiterpenes;	$C_{15}H_{24}$
4	Diterpenes;	$C_{20}H_{32}$
6	Triterpenes;	$C_{30}H_{48}$
8	Tetraterpenes (carotenoids);	$C_{40}H_{64}$
>10	Polyterpenes (rubbers etc.);	$(C_5H_8)_n$



(5.I)

the basic hydrocarbons were regarded as being formed by :

i) head to tail (regular) fusion,

or ii) head to head or tail to tail (irregular) fusion, followed by :

iii) cross-linking and cyclisation of these isoprene chains to give the observed diversity of carbon skeletons.

Recently the definition of 'terpenoid' has been extended by biosynthetic studies to include all compounds which follow the pathways described briefly in section 5.2. Thus the sterols and their derivatives must be regarded as

true terpenoids, while it has been suggested that other compounds which contain terpenoid elements in their molecules, together with fragments of different biosynthetic origin, should be called 'meroterpenoids'[91].

5.2. The Basic Steps in Terpenoid Biosynthesis.

In the early 1950's Ruzicka and his co-workers[92] recognized that geraniol (5.VII), farnesol (5.IX), and squalene (5.X), were key intermediates in the formation of mono-, sesqui-, and triterpenes respectively. In a series of brilliant rationalizations they derived schemes by which many of the known cyclic terpenoid skeletons could be obtained from these three compounds. This work has been confirmed by intensive biosynthetic studies in which the names of Cornforth, Popják, Bloch, and Lynen are prominent.

The isoprene rule formed a starting point for these studies, and many branched-chain five-carbon anions were used as biosynthetic precursors without total success. The breakthrough came with the discovery of mevalonic acid (5.III)[93], and its rapid incorporation into squalene and cholesterol. The mode of formation of mevalonate from acetate in plant cells, via the intermediacy of coenzyme-A (Co-A), has been studied by many groups, and two schemes appear to hold precedence[94]. The ident-

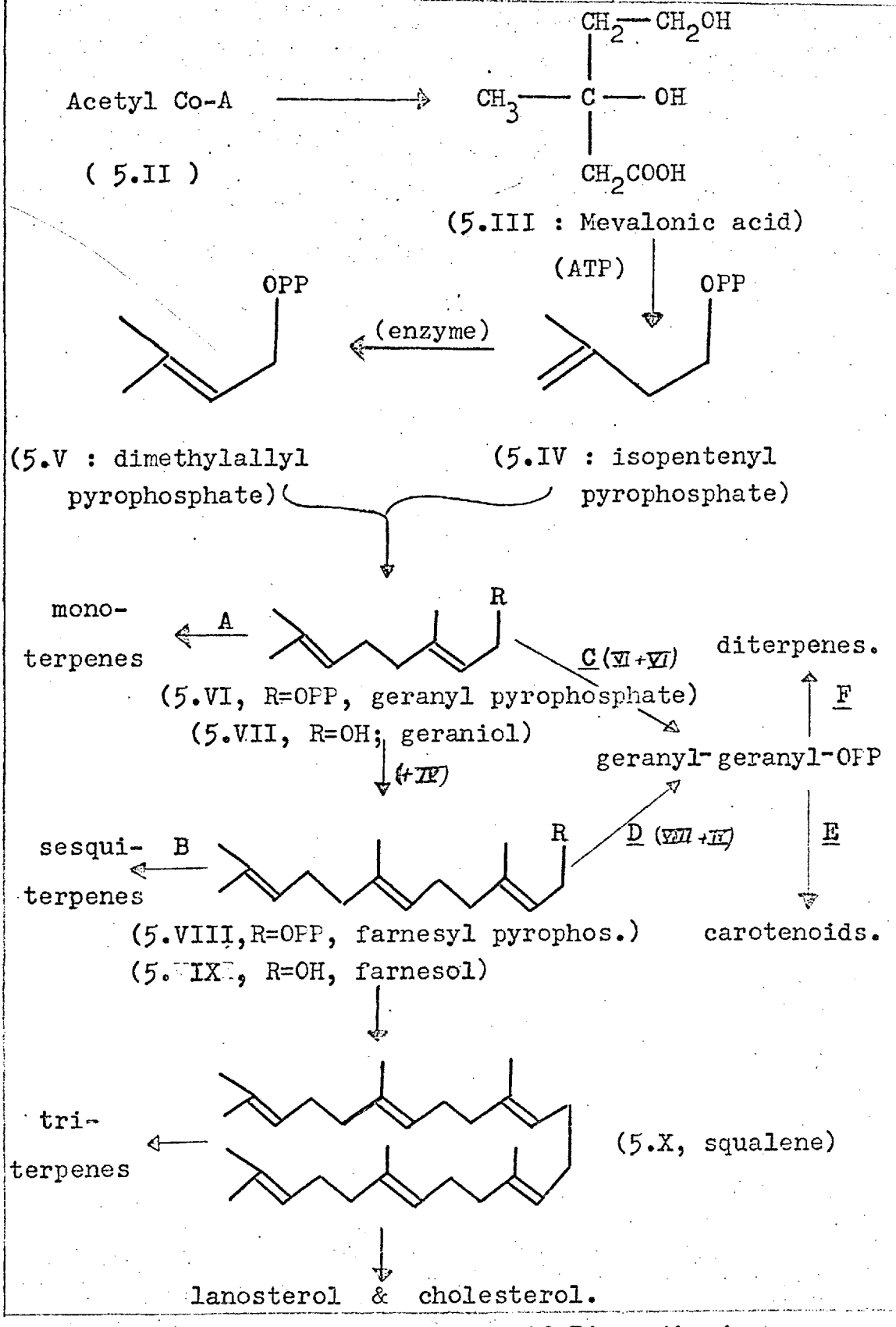


Figure 5.1, Outline of Terpenoid Biosynthesis.

ification of isopentenyl pyrophosphate (5.IV) as the final product of the phosphorylation of mevalonic acid in the presence of adenosine triphosphate (ATP)[95], ended the search for the biological equivalent of isoprene.

The identification of farnesyl pyrophosphate (5.VIII) as a precursor of squalene, by Lynen and his co-workers[96], was the next step in the chain. However they later showed that (5.VIII) was preceded in the biosynthetic sequence by geranyl pyrophosphate (5.VI)[97], and showed that the latter was formed from mevalonate in two steps[98,99] :

i) the enzymic isomerization of (5.IV) to dimethyl-allyl pyrophosphate (5.V), followed by :

ii) the enzymic condensation or 'addition' of (5.IV) and (5.V).

A further 'addition' of (5.IV) to geranyl pyrophosphate gives the farnesyl precursor (5.VIII). We may express the final condensation of two units of (5.VIII) to form squalene (5.X) as being of the 'tail-to-tail' type. Much work has now been done on the biosynthesis of lanosterol and cholesterol from squalene, and this has recently been reviewed[100].

The biosynthesis of the three major precursors suggested by Ruzicka forms the backbone of Fig 5.1. Much work is being conducted to discover the mechanisms of the enzymic condensations or 'additions' which must facilitate

the synthesis of the diterpenes and carotenoids from geraniol or farnesol, via routes C and/or D, and E, in Fig. 5.1. While the Figure only represents the bare bones of present knowledge, it does show how the terpenoids are related on what may be called the 'biogenetic isoprene rule'.

The structure determinations to which a large part of this thesis is devoted, concern derivatives of compounds which belong to the monoterpene ((+)-camphor) and sesquiterpene (humulene and germacratriene) classes. It is pertinent, therefore, to examine more closely the 'arms' A and B of the basic 'skeleton' of Fig. 5.1.

It now seems certain that the acyclic monoterpenes are biosynthesized by :

i) the enzymic condensation of two units of isopentenyl pyrophosphate (5.IV) (or the condensation of this with some isomerization product, or the condensation of two of the latter), in the manner of the original isoprene rule, or ii) the enzymic hydrolysis or rearrangement of the geranyl precursor (5.VI).

The work of Ruzicka et al.[92] showed how some of the common mono- and bicyclic monoterpene skeletons could be formed from geraniol (5.VII). It is perhaps more exact to use the pyrophosphate (5.VI) as the precursor, since the OPP^- anion is a good leaving group, and facilitates

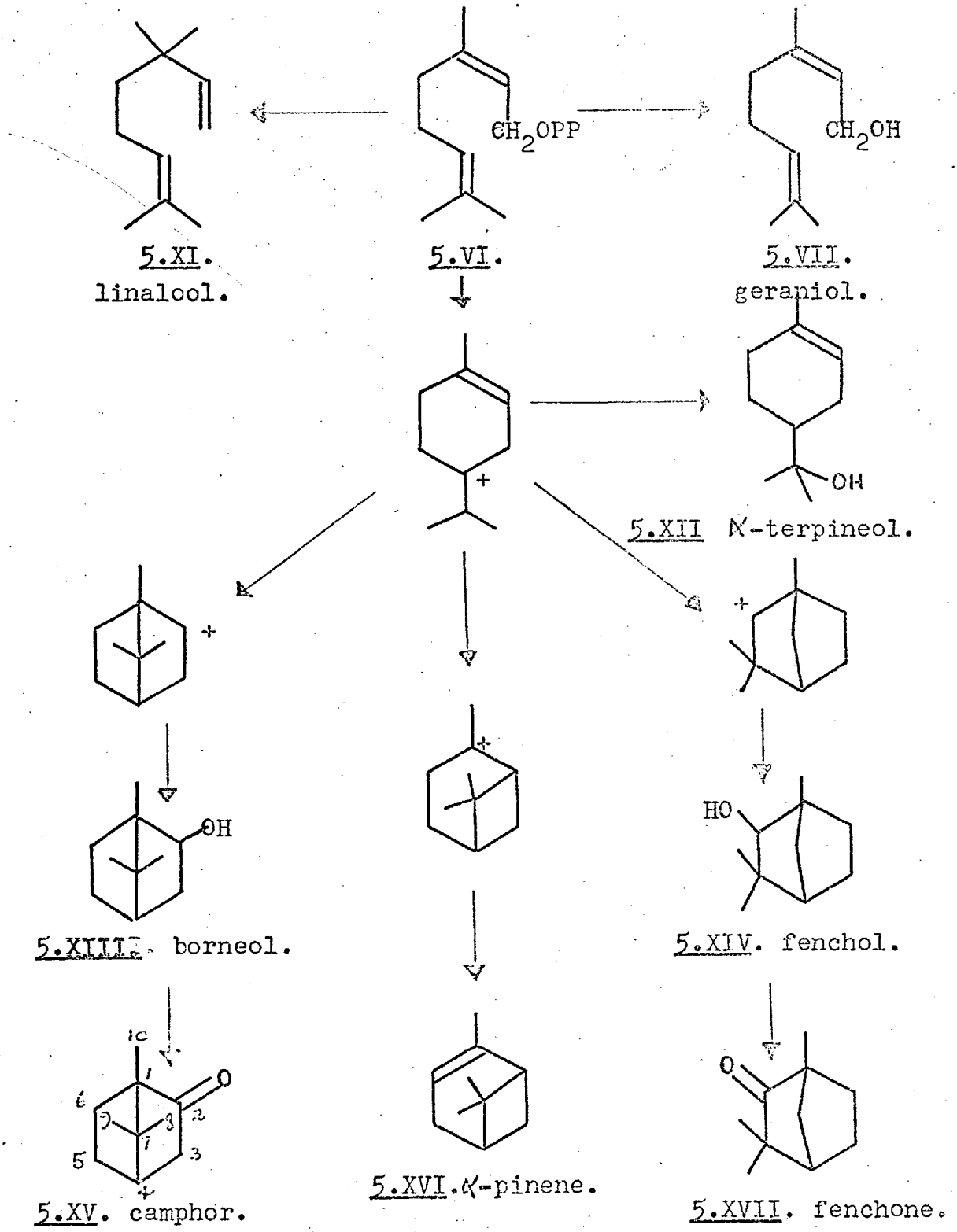


Figure 5.2. Possible Biosynthetic Route to the Cyclic Monoterpenes.

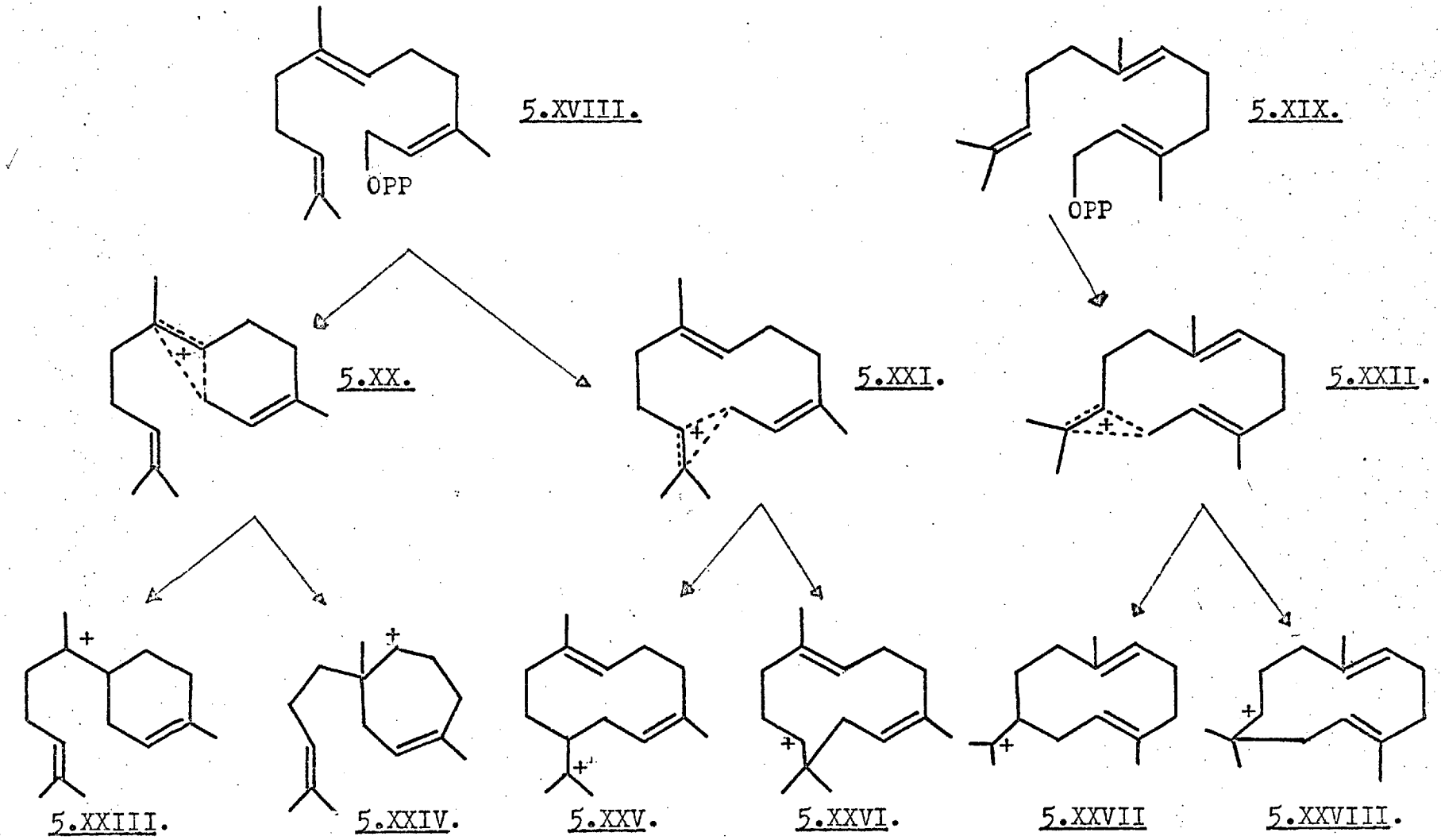


Figure 5.3. Possible cationic intermediates in sesuiterpene biosynthesis[102]

the required ionizations and cyclisations. The scheme shown in Figure 5.2. shows the probable route to camphor, and also indicates its relationship to some other cyclic monoterpenes.

The work of Ruzicka[92] on sesquiterpenes was extended by Hendrickson[101], who showed that the carbon skeletons of virtually all known compounds could be derived by suitable cyclisations of either :

i) cis-farnesyl pyrophosphate (5.XVIII),

or ii) trans- farnesyl pyrophosphate (5.XIX).

Removal of the anion, followed by cyclization, gives rise to the cationic intermediates (5.XXIII-XXVIII), via the intermediacy of the non-classical cations (5.XX-XXII)[102]. The scheme is shown in Figure 5.3. While this scheme is probably not followed directly in nature, its utility as a means of classification cannot be disputed. The derivation of humulene and germacratriene from the farnesyl precursors will be traced in sections 5.4, and 5.5.

5.3. The chemistry of (+)-camphor.

The elucidation of the structure of camphor ($C_{10}H_{16}O$) was one of the most fascinating pieces of early chemical research[103]. It occurs sparingly in nature, predominantly in the dextro-rotatory form, which is extracted from Cinnamonum camphora Nees, found in Southern China, Formosa,

and Japan. Its medicinal properties have been recognized since early times, while it was one of the substances used by Biot in his experiments on optical rotation. The vapour density and molecular weight were determined in 1833 by Dumas[104], who gave the empirical formula shown above. Some thirty structures were suggested for the molecule, before Bredt[105] proposed the bicyclic ketone structure (5.XV) in 1893; this was later confirmed by synthesis[106]. The required cis-arrangement of the $-CO-CH_2-$ bridge means that the two asymmetric centres (C_1 & C_4 in 5.XV) are not independent, a determination of the absolute configuration of (+)-camphor involves determining whether the gem-dimethyl bridge in 5.XV lies above or below the plane of the paper.

The reactions of (+)-camphor are numerous, and are well covered in standard texts[103,107]. Attention should be drawn to the simplicity of heavy-atom incorporation, chlorination and bromination at the 3- (or α-) position being especially facile. The relationship of camphor to other mono-and bicyclic monoterpenes is suggested by Fig. 5.2. (+)-camphor gives (+)-borneol(5.XVIII) on reduction, while it can be prepared from (+)-α-pinene (5.XVI); the latter can also be converted into (+)-α-terpineol (5.XII). The essential similarity between the carbon skeletons of (+)-camphor and (+)-fenchone (5.XVII) has also been shown[108]. The configurational relationships are summarized in an excellent review by Birch[109].

The difficulty of relating mono- and bicyclic monoterpene configurations to the Fischer convention led Hückel[108] to propose a further arbitrary convention for these molecules based on (+)-camphor : if the molecule is drawn as in (5.XV), the gem-dimethyl bridge lies above the plane of the paper. The work of Fredga and Miettinen[110a], and Porath[110b], using the method of 'quasi-racemates'[111], indicated, however, that the convention was incorrect. The experimental method may be summarized as follows[112] : if A and B form a compound, and A and the enantiomer of B form a mixture (or solid solution), then A and B are of the opposite configuration, and the converse. Determinations require the careful study of the melting point diagrams of mixtures of +A/+B, +A/-B (or of +A/+B, -A/+B).

Fredga and Miettinen[110a] applied the method to (+)-fenchone as follows : Wallach[113] had shown that this molecule could be degraded to (-)-X-isopropyl glutaric acid, and Fredga and Miettinen showed that the latter could be oxidised to (+)-isopropyl succinic acid. They went on to show that (-)-isopropyl succinic acid forms a 1:1 compound with (+)-methyl succinic acid, but not with the (-)-form; they therefore concluded that (+)-isopropyl succinic and (+)-methyl succinic acids have the same configuration. The latter has been

related[114] to the Fischer convention via malic acid; the correctness of this assignment has recently been shown[115] by the X-ray method. The stereochemical relationships (which are shown fully in Figure 6.4 on p.116) gave the conclusion that (+)-fenchone, and hence (+)-α-pinene and (+)-camphor were represented by (5.XV-5.XVII) with the gem-dimethyl bridge below the plane of the paper.

The work of Porath[110b] followed a similar pattern; he converted (+)-camphor into (-)-camphoronic acid and thence into (-)-α-methyl-α-isopropyl succinic acid. The quasi-racemate technique was then used to determine the absolute stereochemistry of the latter. Again the gem-dimethyl bridge was shown to be below the plane in the conventional representation (5.XV). The stereochemical relationships involved here are also shown in Fig. 6.4 (p.116); a full discussion of the implications of the above sets of results is deferred until section 6.6.

The method of quasi-racemates has some very serious restrictions however[112] : the compounds compared must be chemically very similar, and both enantiomers of at least one of the compounds must be obtainable. Even then great care must be exercised in the interpretation of the data, a recent example of this was the (incorrect) assignment of absolute configuration to (+)-2-isopropyl-

2-methyl glutaric acid[116], and a consequent wrong assignment to its predecessor in the degradative chain (-)-methyl isopulegone. The correct assignment in the two cases was recently obtained using the X-ray method[117]. Thus the method does not guarantee success, results are best regarded as strong evidence in favour of a certain configuration, but not as absolute proof. If (+)-camphor is to be used as a starting point in stereospecific synthesis (as envisaged by Woodward[118]), or some salt is to be used as an internal reference centre (see sections 3.4, 6.5), the absolute configuration must be known unambiguously. For these reasons, and from its importance as a key terpene in the stereochemical schemes drawn up by Hückel[108] and Birch[109], the X-ray arbitration was undertaken.

A description of this work, and a discussion of its relevance in the general field of terpene stereochemistry, forms the subject matter of chapter 6. It is sufficient to record here that the chemical work described above has been upheld; as has the lengthy stereochemical correlation published by Freudenburg and Lwowski[119]. The latter authors employed a rather complex scheme to arrive at a similar result in 1955; however the very length and complexity of the degradative

scheme used (some 18 compounds were synthesised in all) made the answer (although right) questionable.

5.4. The Chemistry of Humulene.

The monocyclic sesquiterpene humulene was first isolated from oil of hops[120]. Degradative chemical work[121] showed it to be 1,1,4,8,-tetramethylcycloundecatriene ($C_{15}H_{24}$), and this was confirmed by Sorm et. al.[122], who synthesised 1,1,4,8,-tetramethylcycloundecane and showed it identical with hexahydrohumulene. Humulene has also been identified as the α-caryophyllene constituent of clove oil[123]. Another constituent of clove oil, caryophyllene (5.XXIX, Fig.5.4.) (formerly known as β-caryophyllene), whose stereochemistry was elucidated by chemical[124] and X-ray[125] methods, was considered to be derived from the farnesyl precursor (5.XXVI)[101]. It was natural to suggest that its congener humulene had the same precursor, giving the trans-trans-cis-stereochemistry (5.XXX)[101] for humulene. The all-trans-stereochemistry (5.XXXI) was, however, proposed[126,127] on chemical, rather than biogenetic grounds, and has recently been shown correct by two independent X-ray analyses of the adduct $C_{15}H_{24}:2AgNO_3$[128,129]. Thus the farnesyl cation (5.XXVIII) is the probable biogenetic precursor of humulene (5.XXXI).

Recently Sutherland and his co-workers[130] have obtained the tricyclic bromohydrin (5.XXXII) by reaction of (5.XXXI) with N-bromosuccinimide. The relative stereochemistry shown was chemically defined at C(4) and C(5); at other points it was proposed on the basis of an apparrently reasonable reaction mechanism (involving attack by hydroxyl at C(8) of (5.XXXI), followed by a concerted trans-cyclisation). The tricycle can be converted stereospecifically, and with equal facility, into (±)-caryophyllene (5.XXIX) or back to humulene, as shown in Figure 5.4, which sets out the whole series of relationships. Some derivative (probably cationic) analogous to compound (5.XXXII) thus appears to offer a possible alternative biosynthetic pathway from the farnesyl precursors (in this case from (5.XXVIII)) to caryophyllene (5.XXIX).

In view of the possible biosynthetic relevance of humulene bromohydrin, and also to examine the geometry of the fused ring system, a full three-dimensional X-ray study was undertaken to establish the true stereochemistry of (5.XXXII). A description of the analysis[131] forms the subject matter of Chapter 7; it is sufficient to mention here that the results have shown the true relative stereochemistry of humulene bromohydrin to be as in (5.XXXIII), and not as proposed. The implications of this are discussed in Sect. 7.3.

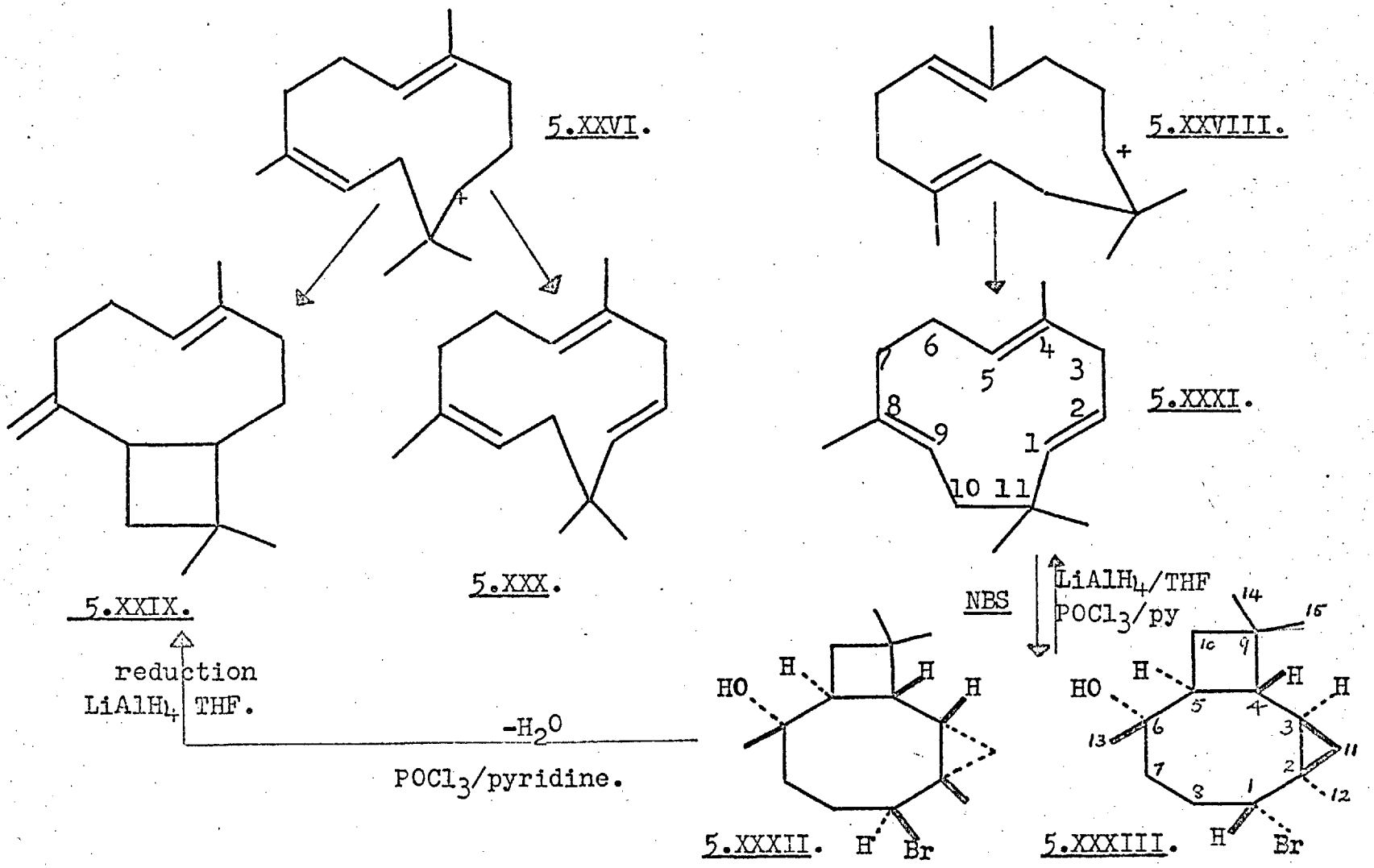


Figure 5.4. Derivation of Humulene from the Farnesyl Precursors: Formation of the Bromohydrin.

5.5 The Chemistry of Germacratriene.

Following the work of Ruzicka et.al.[92], it was suggested by Barton and de Mayo[132] that ten-membered ring compounds could act as biosynthetic intermediates in certain cases. The suggestion was expanded by Hendrickson[101], who used the triene (5.XXXIV, Figs.5.5,6), obtained by deprotonation of the farnesyl cation (5.XXVII), in a scheme for the biosynthesis of sesquiterpenes having the guiane (5.XXXVIII), elemane (5.XXXIX), selinane (5.XLI), and germacrane (cyclodecane) skeletons.

The cyclodecatriene (5.XXXIV) has recently been prepared by Sutherland and his co-workers[133] from the naturally occurring ketone germacrone (5.XXXV, obtained from zdravetz oil); it has been designated 'germacratriene'[134]. The preparation, via the alcohol (5.XXXVI), and the acetate (5.XXXVII), is outlined in Fig. 5.5. The all-trans-stereochemistry was proposed[133] from degradative and spectroscopic evidence, and from the ready (and stereospecific) cyclisation to selinane derivatives (the bromohydrin (5.XLIII), obtained by reaction with N-bromosuccinimide, is typical); the cyclisation probably involves transannular π-π interaction between the two endocyclic double bonds. Germacratriene has also been converted[135] into the diol (5.XLII), having the guiane skeleton, by acid-induced

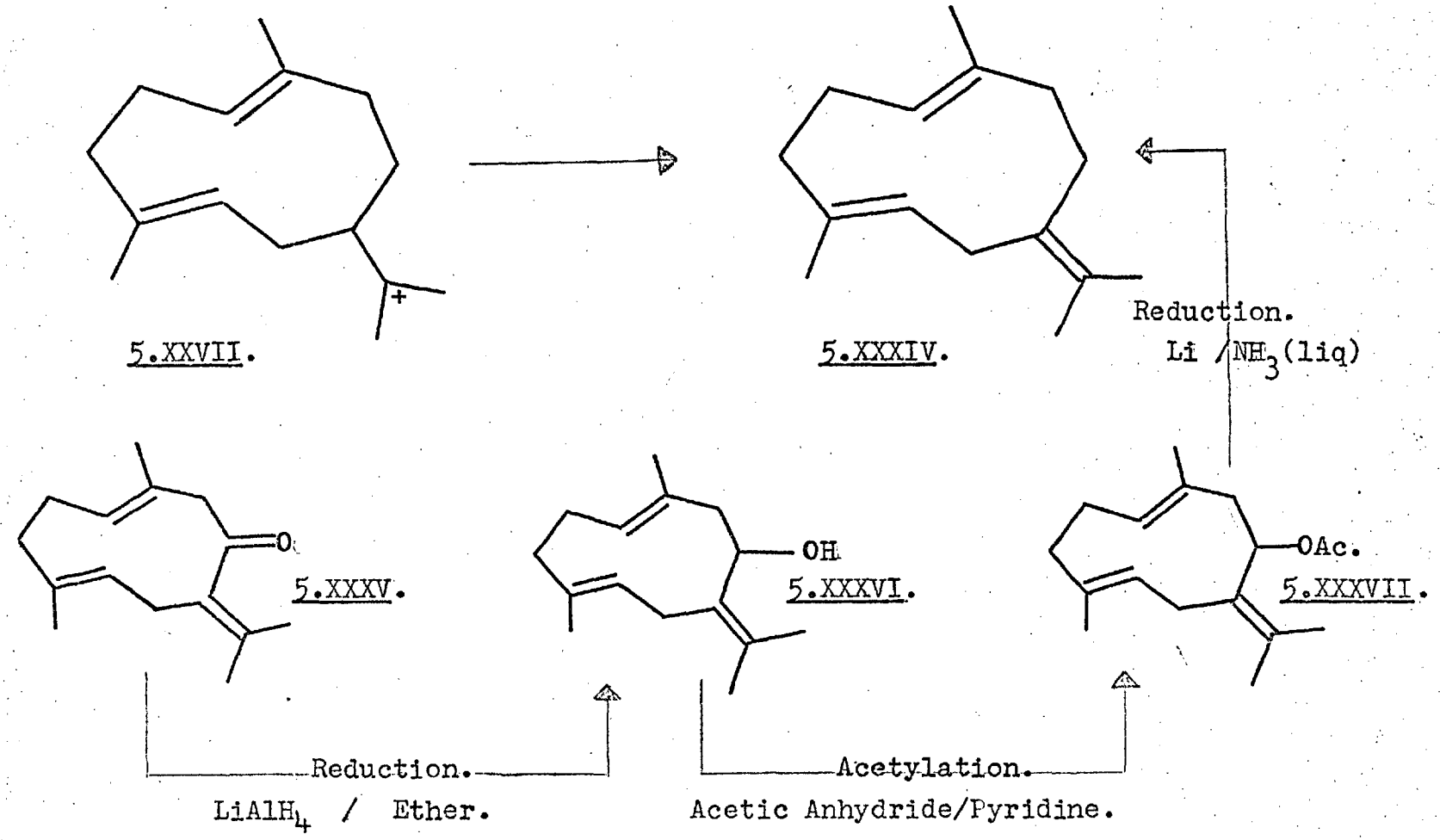


Figure 5.5. Probable Biogenesis of Germacratriene and its Preparation from Germacrone.

cyclisation of the epoxide (5.XLIV); and also into the previously undescribed elemane sesquiterpene γ-elemene (5.XL) via a Cope rearrangement at a temperature in excess of 120°.

A more inexplicable reaction of germacratriene is that with one mole of buffered peracetic acid, this gives a mixture of the three epoxides (5.XLIV-XLVI) with yields in the ratio 65:35: <1[136]. This implies great differences in the reactivities of the three double bonds. This must be a consequence of the geometry adopted just prior to reaction in solution, since π-π transannular interactions should be unimportant in the case of epoxidation.

During the early experimental work it was discovered that germacratriene formed a crystalline adduct $C_{15}H_{24}:AgNO_3$ on standing in a saturated solution of silver nitrate in ethanol[133]. In view of the obvious biosynthetic importance of the compound, a full three-dimensional X-ray study of the silver nitrate adduct was undertaken, both to check the stereochemistry, and to examine the molecular geometry about the double bonds. The X-ray work has confirmed the proposed stereochemistry, and also furnished an explanation[136] of the reactivity differences at the double bonds. A description of the X-ray study, and a discussion of the molecular geometry,

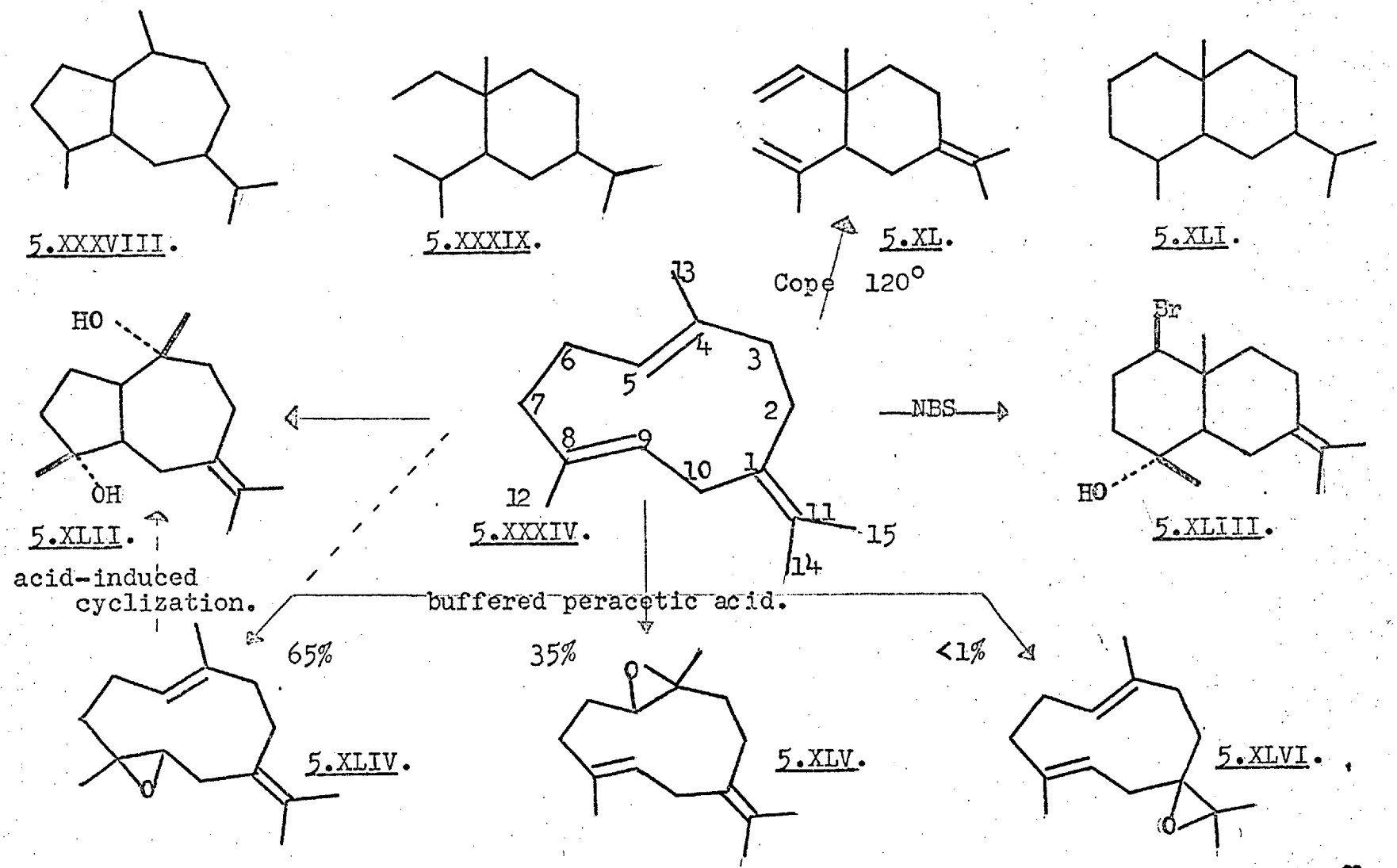


Figure 5.6. Some Reactions of Germacratriene, Showing its Relationship to other Sesquiterpenes

forms the subject matter of Chapter 8.

5.6. Note on Numbering Schemes.

The numbering schemes shown in this chapter, which have been chosen with some 'crystallographic licence', will be adhered to throughout this thesis. For ease of reference they are shown together in the pull-out diagram bound with the end-papers.

CHAPTER 6

The Absolute Configuration of (+)-Camphor : The Crystal and Molecular Structure of (+)-3-Bromocamphor

6.1. Introduction.

The work to be described in this chapter began as a Research Exercise in Physical Chemistry performed by the Author during his final undergraduate year (1964-65) at Imperial College. The results obtained will be summarized below.

Initially attention was focussed on the compound : (-)-2-bromo-2-nitrocamphane; the crystal structure was known with good accuracy (R = 0.125 for visually estimated data)[137], while the identity of its configuration with that of (+)-camphor was known[103]. The compound was prepared by converting (+)-camphor to the oxime[138] which was treated with Br_2/KOH to give a pale yellow solid[139]. Recrystallization from aqueous methanol gave a white

feathery aggregate (m. pt. 218-221°(decomp) lit:220°[139]). Attempts to obtain single crystals suitable for X-ray work were unsuccessful.

Attention was now turned to (+)-3-bromocamphor, a compound first described by Keller[140], which is known to have the same configuration as (+)-camphor[141]. The crystal structure had already been determined by Wiebenga and Krom[142] (hereinafter W & K), who studied the isomorphous series 3-bromo-, 3-chloro-, and 3-cyano-camphor. They determined the x-, z- co-ordinates of all atoms from the [010]-projections and refined them as far as was possible in 1946. The y-co-ordinates for cyanocamphor were estimated from models and refined from the two other principal projections; no y-co-ordinates were found for any atoms in the halides. The crystals were provided by Dr. J. E. Baldwin, then of the Organic Chemistry Dept., Imperial College; they are white prismatic needles, with an extinction direction parallel to the needle axis. The initial sample was too large for X-ray work, and smaller crystals were obtained by rapid cooling of saturated methanolic solutions.

The crystals were found to be unstable to X-irradiation, and numerous methods of protection were tried. It was found that a thin layer of pastel fixative sprayed uniformly, afforded sufficient protection for up to

70 hours exposure. The crystal data given by W & K were checked from oscillation and Weissenberg photographs taken about the a- and b-axes. The cell dimensions found showed good agreement; they were later refined by least-squares and are listed in Sect. 6.2. The crystals are monoclinic, space-group $P2_1$; in this space-group, under normal conditions, the symmetry gives :

$$F(hk\ell) = F(\overline{hk\ell}) = F(h\overline{k}\ell) \neq F(\overline{h}k\ell) \neq F(hk\overline{\ell}) \quad \ldots\ldots\ldots 6.1$$

Thus, to record the Bijvoet pairs photographically, the crystal must be mounted to rotate about either the a- or c-axes. The layers $0k\ell$, $1k\ell$, were therefore recorded, using CuK_α-radiation and the multi-film pack method, and indexed on a rigidly right-handed system.(60) In this case a Stöe Weissenberg goniometer was used, having the geometry shown in Figure 6.1(a) where the goniometer head rotates anti-clockwise (as seen by an observer at the open end of the camera), the translational movement of the pot is away from this observer; the direction chosen for $+\underline{a}^*$ is also shown. The direction of $+\underline{c}^*$ followed from a study of the $1k\ell$-photograph superimposed upon $0k\ell$, and was chosen to make an acute angle with $+\underline{a}^*$. The direction of $+\underline{b}^*$ followed from the requirement that the system be right-handed. The chosen system (Fig. 6.1(b)) was then superimposed upon the crystal, and by utilizing the concept of the sphere of reflection in conjunction with the camera geometry, the correct cyclic sequence of axial rows was determined; the

correct indices were then assigned to all $0k\bar{l}$ reflections.

The sign of the intensity difference $I(0k\bar{l}) - I(0kl)$ was visually estimated for 18 Bijvoet pairs. The calculated differences were obtained using W & K's data for cyanocamphor, their x- and z-co-ordinates for Br, and an estimated y-co-ordinate for this atom. Structure factors (F_N), (F_A) (A=Br) were computed using BABA; isotropic temperature factors (B) of 4.0 $Å^2$ were allotted to C and O, and of 3.0 $Å^2$ to Br. The values were corrected for anomalous dispersion of CuK_α at Br using Argand diagrams (see Fig. 3.1); correction terms[59] :

$$f' = -0.9, \quad f'' = 1.5 \quad \ldots\ldots\ldots\ldots \quad 6.2$$

were employed, and the sign of the difference $F(0k\bar{l}) - F(0kl)$ obtained for all 18 pairs. The agreement between observed and calculated inequalities for this determination (A) is shown in Table 6.8 (p.110). The 77.7% vote obtained indicated that W & K's structure, if drawn on a right-handed set

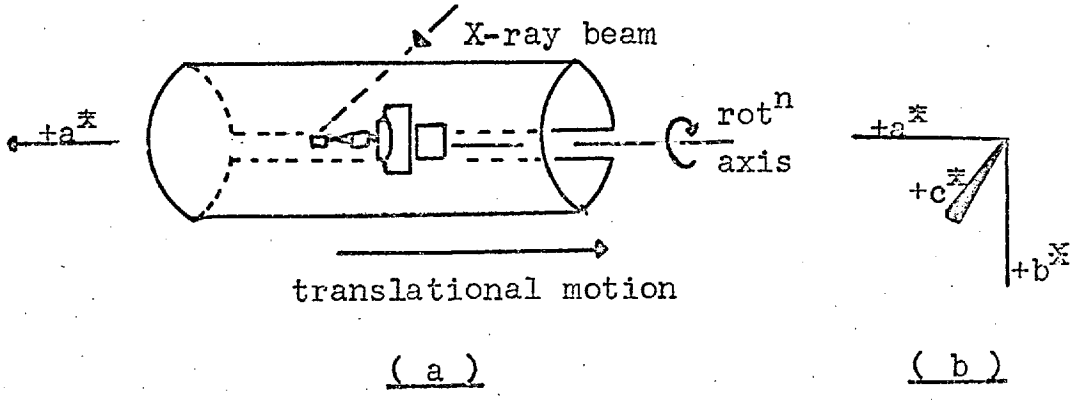


Figure 6.1 (a) Geometry of the Stöe Weissenberg Camera.
(b) The chosen axial system.

of axes, represented the true absolute configuration. (110) This confirmed the chemical work of Fredga and Miettinen, but with only about the same 'level of significance'. It was obvious that the positional data used was not sufficiently accurate to guarantee the result, and a redetermination of the crystal structure was undertaken. Apart from defining the absolute stereochemistry unambiguously, it has provided accurate data on the molecular geometry.

6.2. Data Collection.

The cell dimensions were obtained using CEDI, from some 25 theta values measured from equatorial Weissenberg photographs 0kl, h0l. The values obtained, together with other relevant data, are listed below.

Crystal Data.

(+)-3-bromocamphor: $C_{10}H_{15}OBr$; Monoclinic; Laue symm. 2/m.

a = 7.36 ± 0.01 Å; b = 7.59 ± 0.01 Å;

c = 9.12 ± 0.01 Å; β = 94.1° ± 0.4° ;

V = 508 Å^3 ; D_x = 1.49 ± 0.03 g.cm.$^{-3}$ (by flotation);

D_c = 1.51 g.cm.$^{-3}$; for Z = 2 molecules/cell;

M = 231.03 (taking the standard C^{12} = 12.00);

μ = 56.10 cm.$^{-1}$ for CuKα (λ_{mean} = 1.54178 Å).

Absent spectra (only among 0k0 when k = 2n + 1) defined

the space-group as $P2_1$ (No.4.) or $P2_1/m$ (No.11.)[143]. The known optical activity of the compound ($[\alpha]_D^{30^\circ} = +130^\circ$, in EtOH, c,10)[144] excludes the latter possibility (see sect. 3.1.) and leads to the unique definition as $P2_1$.

The previously described method of protecting the crystals proved unsuccessful over the long periods of X-irradiation required for the collection of the intensity record. A specimen of approximate dimensions : 0.4 x 0.2 x 0.13 mm. was therefore encapsulated in a Lindemann glass capillary tube, and set with the b-axis parallel to the axis of rotation of a Unicam Weissenberg goniometer. Using Ni-filtered CuK_α radiation, the layers h0ℓ - h5ℓ were recorded. The reflections were indexed as described in sect.6.1. and 783 intensities were visually estimated using two graduated step wedges; a further 130 intensities were below the threshold value. No spot-shape correction was applied, but subjective weights were applied during the measurement. A further 50 intensities were similarly measured from the 0kℓ photographs for correlating purposes; the 1kℓ data was not measured, due to the very poor spot-shape.

6.3. Two-Dimensional Work.

A two-dimensional Patterson map for the [010] projection was computed using BOSS. It revealed the x-, z-co-ordinates of the bromine atom to be :

$$x = 0.2628; \qquad z = 0.1663;$$

comparing well with W & K's values of :

$$x = 0.2666; \qquad z = 0.1639.$$

A 2D Fourier map for the same projection, using only the phases given by the bromine atom position, yielded five well defined peaks; R was 0.332. They were identified by comparison with W & K's positional parameters for cyanocamphor; the agreement is shown in Table 6.1. The map also showed that the co-ordinates of the bromine atom in the asymmetric unit were :

$$x = 0.7372; \qquad z = -0.1663;$$

related to that obtained from the Patterson by a centre of

Table 6.1

	W & K.		This Work.	
Atom	x	z	x	z
O	0.403	0.061	0.409	0.068
C(2)	0.567	0.114	0.558	0.117
C(3)	0.728	0.031	0.751	0.039
C(10)	0.506	0.383	0.507	0.395
C(8)	0.933	0.419	0.920	0.406

symmetry in the [010]-projection (plane group P2) at $\underline{x} = \frac{1}{2}$, $\underline{z} = 0$.

From the good agreement shown in Table 6.1, and from the overall similarity of the [010] Fourier projection for bromocamphor obtained here, with that for cyanocamphor obtained by W & K, it appeared that the co-ordinates of the atoms in the camphor framework of both derivatives were very similar[145]. It was felt that a three-dimensional refinement based on W & K's co-ordinates for C and O for cyanocamphor should be successful. A bead model was constructed, and the y-co-ordinate of Br was estimated as 0.354, relative to the origin used by W & K. This value was then fixed as the arbitrary origin in the y-direction in space-group $P2_1$. The co-ordinates used to begin the refinement are shown in Table 6.2 overleaf.

6.4. The Refinement of the Structure.

In this description, and similar ones in chapters 7,8,& 9, refinement runs are designated I, A, or M :

I, indicates least-squares refinement with all atoms having isotropic temperature factors (B's);

A, indicates that all atoms have anisotropic temperature factors (β_{ij}'s);

M, indicates that all non-hydrogen atoms are treated

TABLE 6.2.

(+)-3-Bromocamphor.

Initial Co-ordinates in Least-Squares Refinement.

Atom	x	y	z
C(1)	0.631	0.333	0.267
C(2)	0.564	0.286	0.111
C(3)	0.731	0.214	0.033
C(4)	0.900	0.278	0.150
C(5)	0.894	0.478	0.167
C(6)	0.711	0.508	0.253
C(7)	0.817	0.200	0.278
C(8)	0.936	0.208	0.419
C(9)	0.767	0.014	0.292
C(10)	0.481	0.333	0.369
O	0.403	0.278	0.061
Br	0.7372	0.3540	-0.1663

as for A above, the hydrogen atoms being included in fixed positions, with fixed B-factors; the refinement may be loosely described as Mixed mode.

The main (b-) axis intensity data was Lp^{-1}-corrected using DATRDN and placed on a common arbitrary scale by comparison with intensities common to 0kl. The accidental absences were included at a value of $\frac{2}{3}$ x the minimum observeable intensity in the relevant part of the record.

No absorption correction was applied, since the cross-section of the crystal was fairly small and uniform, and (μ) was not large.

Refinement began with five cycles of unweighted full-matrix least-squares using ORFLS; the positional parameters from Table 6.2 were used, together with B-factors of 4.0 $\AA^2$ for C and O, and 3.0 $\AA^2$ for Br. Due to the paucity of correlating data the inter-layer scale factors were also made parameters in the refinement. The results of this run (I1) and of all subsequent runs will be found in Table 6.3 on page /01/.

Before run I2 an analysis of the agreement between observed and calculated structure factors ($|F_o|$ & $|F_c|$) was made. A weighting scheme of the Hughes [51] type (Eq. 2.29) was devised to give reasonable constancy of $\sum w(|F_o| - |F_c|)^2$ over ranges of $|F_o|$; the constant F^* was 13.0 on the scale of the structure factors in Table 6.7. The scale factors were again refined and R fell to 0.184.

The isotropic temperature factors at the end of run I2 were converted into their anisotropic equivalents (β_{ij}) and the refinement continued with runs A1-A4. During runs designated A or M the inter-layer scale factors were kept fixed, since their high correlations with the vibrational parameters makes this type of refinement formally invalid[146]. The only alterations made during

these runs were : after A1 five small high-order reflections were corrected for mis-indexing, and two others (1,1,0; 1,2,1;) removed for suspected extinction; after A3 a further reflection (0,2,1;) was removed for the same reason.

Molecular geometry calculations were performed,using BONDLA, after A1, A4, during the latter run the positions of the 15 hydrogen atoms were also computed, at bonding distances of 1.025 Å from carbon. In both cases the bond-lengths and angles made good chemical sense. Following run A4 a structure factor calculation was performed using FC to give values of F_N and F_{Br}; the hydrogen atoms being included in their calculated positions. The results were used for an absolute configuration determination[147] which will be discussed in section 6.4.

An examination of the reflection data after A4 showed that some of the accidental absences were greater than the threshold values. A close examination of the photographs indicated that 57 were, in fact, marginally observable; Their intensity values were changed to the threshold value in the relevant part of the record.

It was decided to return to isotropic refinement to re-refine the inter-layer scale factors; no hydrogen atoms were included at this stage, and the weighting

was unchanged. The pertinent results (runs I3,A5, Table 6.3) show the large effect on R of the changes in scale-factors caused by relatively small corrections to the intensity data. It should be noted that this type of refinement has not had its more obvious pitfalls publicised : it appears advisable to return to the isotropic mode,after any change in data, weighting scheme etc., to re-refine the inter-layer scale factors. The experience gained here was used to make the (similar) refinement of germacratriene (chapter 8) a more efficient process.

A difference Fourier, with non-hydrogen atoms 'removed', revealed no spurious peaks; the six non-methyl hydrogens were discernible in positions close to those calculated by BONDLA. The methyl hydrogens were not shown. The final calculated hydrogen positions are shown in table 6.6 compared with those positions obtained from the difference map.

All fifteen hydrogen atoms were now included in structure factor calculations in their calculated positions, with B-factors 0.5 $\AA^2$ greater than the value for the carbon atom to which they were bonded. A review of the weighting scheme was now carried out using DELSIG. Average values of $(\|F_o| - |F_c\|)$ and $|F_o|$ were output over ranges of $|F_o|$; This showed that the bulk of

the data (749 terms) had structure factors in the range 0-20 on the scale of Table 6.7. It was found that a Hughes scheme with F^* set at 6.0 gave the best average of $w(|F_o| - |F_c|)^2$ sums over the ranges chosen. This left 334 reflection intensities with unit weights.

Run I4 was performed to re-refine the scales to allow for the inclusion of hydrogen atoms, and the change in the weighting scheme. The refinement process was concluded with runs M1, M2, in which the scale factors were again fixed. There was no significant change in R, but the standard deviations of the atomic co-ordinates for C, O, Br, improved. The ratio of shift to standard deviation (S/E) on the final cycle was < 0.10 for all parameters refined, and the least-squares process was concluded. The final positional and thermal parameters for C, O, Br, are shown in Tables 6.4 & 6.5 respectively. Final hydrogen atom positions were calculated from this data (Table 6.6) and were included in the final structure factor calculation, which gave an R value of 0.079 for the observed reflections. The final structure factor listing is shown in Table 6.7.

The estimated standard deviations in atomic co-ordinates shown in table 6.4 are significantly poor in the y-direction. This is due to the relatively low data cut-off at k=5. They are probably realistic estimates however, since full-matrix methods were used throughout.

TABLE 6.3.

(+)-3-Bromocamphor.

The Refinement Process*

Run	Cycles	R	Max S/E (scales)	Max S/E (all parameters)	Ave S/E
I1	5	0.256	-	-	-
I2	5	0.184	0.0300	-	-
A1	3	0.121	-	-	-
A2	3	0.102	-	-	-
A3	3	0.099	-	-	-
A4	3	0.098	-	-	-
I3	5	0.144	0.0009	0.0078	0.0020
A5	4	0.079	No ref	0.0538	0.0120
I4	3	0.145	0.0030	0.0100	0.0030
M1	3	0.080	No ref	0.8000	0.2230
M2	2	0.079	No ref	0.1000	0.0210

* The full-matrix least-squares program ORFLS was used throughout.

TABLE 6.4.

(+)-3-Bromocamphor.

Final Positional Parameters* and Their Standard Deviations

Atom	x	σ_x	y	σ_y	z	σ_z
C(1)	0.6404	0.0016	0.3359	0.0031	0.2656	0.0012
C(2)	0.5665	0.0014	0.2949	0.0019	0.1097	0.0012
C(3)	0.7337	0.0016	0.2439	0.0027	0.0280	0.0011
C(4)	0.8838	0.0015	0.2795	0.0024	0.1382	0.0014
C(5)	0.8981	0.0021	0.4856	0.0025	0.1755	0.0015
C(6)	0.7204	0.0024	0.5151	0.0025	0.2555	0.0017
C(7)	0.8097	0.0015	0.2179	0.0029	0.2818	0.0012
C(8)	0.7605	0.0019	0.0174	0.0022	0.2773	0.0015
C(9)	0.9323	0.0020	0.2580	0.0029	0.4225	0.0013
C(10)	0.4928	0.0024	0.3226	0.0042	0.3734	0.0016
O	0.4128	0.0011	0.3090	0.0018	0.0570	0.0010
Br	0.7374	0.0002	0.3540	-	-0.1630	0.0001

Maximum and Average Positional Shifts on the Final Cycle:

	x	y	z
Max shift (Å)	0.00036	0.00140	0.00067
Ave shift (Å)	0.00012	0.00050	0.00024

* Positions are given as fractions of the cell edges (unless otherwise stated) throughout this Thesis.

TABLE 6.5.

(+)-3-Bromocamphor.

Final Anisotropic Thermal Parameters (β_{ij}'s)* for the Non-Hydrogen Atoms

Atom	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	0.02357	0.01211	0.01047	0.00061	-0.00073	0.00162
C(2)	0.01692	0.01164	0.01050	-0.00119	0.00213	0.00009
C(3)	0.02016	0.01715	0.00771	-0.00182	0.00085	0.00401
C(4)	0.01274	0.01704	0.01140	0.00138	-0.00057	0.00595
C(5)	0.02886	0.01148	0.01373	-0.01312	-0.00284	0.00683
C(6)	0.03056	0.00637	0.01606	0.00563	0.00194	-0.00431
C(7)	0.01543	0.02497	0.00873	0.00039	0.00028	0.00252
C(8)	0.02511	0.00273	0.01507	-0.00300	0.00318	0.00339
C(9)	0.02815	0.02288	0.00923	0.00154	-0.00333	0.00048
C(10)	0.03477	0.03606	0.01226	0.00531	0.00651	0.00437
O	0.01881	0.02073	0.01359	-0.00090	0.00067	-0.00100
Br	0.02900	0.02483	0.01037	0.00390	0.00388	0.00383

* The temperature factors in the above table, which are all positive definite, are the parameters (β_{ij}) in :

$$f = f^{o} \exp(-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl))$$

TABLE 6.6.

(+)-3-Bromocamphor.

Observed* and Calculated✓ Hydrogen Positions

H Atom	Bonded to	Calculated x	Calculated y	Calculated z	Observed x	Observed y	Observed z
H(1)	C(3)	0.7003	0.1632	-0.0244	0.723	0.150	-0.079
H(2)	C(4)	0.9657	0.1868	0.1522	0.974	0.187	0.154
H(3)	C(5)	1.0174	0.5148	0.2462	1.090	0.505	0.223
H(4)	C(5)	0.8989	0.5683	0.0772	0.875	0.541	0.082
H(5)	C(6)	0.6288	0.6014	0.1930	0.635	0.609	0.206
H(6)	C(6)	0.7512	0.5696	0.3632	0.775	0.541	0.348
H(7)	C(8)	0.7084	-0.0260	0.3784			
H(8)	C(8)	0.8220	-0.0421	0.1404			
H(9)	C(8)	0.7180	0.0204	0.3069			
H(10)	C(9)	0.8801	0.2146	0.5236			
H(11)	C(9)	1.0315	0.1839	0.4307			
H(12)	C(9)	0.9815	0.4091	0.4108			
H(13)	C(10)	0.4349	0.1931	0.3807			
H(14)	C(10)	0.5051	0.2794	0.4340			
H(15)	C(10)	0.4311	0.4929	0.3858			

* From a difference map following run A5.

✓ Calculated from the final co-ordinates shown in Table 6.4. These parameters were not refined.

TABLE 6.7.

(+)-3-Bromocamphor.

Observed and Calculated Structure Amplitudes after Refinement.

The format of the table is :

h k l $|F_o|$ $|F_c|$ A_c B_c

Accidentally absent reflections are marked (L) (less-than).

The three reflections removed from refinement for suspected extinction were (in the same format) :

1	1	0	66.09	93.67	83.94	41.57
0	2	1	28.70	38.70	-18.10	34.20
1	2	1	42.87	57.48	32.36	42.51

The reflection 0 0 1 was obscured by the backstop.

0	0	2	43.40	43.35	-43.35	-0.01
0	0	3	41.09	43.78	-43.78	0.00
0	0	4	22.26	24.17	-24.17	0.00
0	0	5	11.51	12.51	12.51	-0.00
0	0	6	25.32	21.34	21.34	-0.00
0	0	7	27.09	25.01	25.01	0.00
0	0	8	4.09	3.89	-3.89	-0.00
0	0	9	19.58	21.19	-21.19	0.00
0	0	10	9.46	9.82	-9.82	-0.00
0	0	11	4.21	3.68	3.68	-0.00
1	0	0	16.24	15.49	-15.49	0.00
1	0	1	11.18	10.34	-10.34	-0.00
1	0	2	46.67	52.67	-52.67	0.00
1	0	3	33.97	35.03	-35.03	0.00
1	0	4	35.23	37.98	37.98	0.00
1	0	5	38.34	41.99	41.99	0.00
1	0	6	2.23	1.86	-1.86	0.00
1	0	7	14.65	14.57	-14.57	-0.00
1	0	8	14.23	12.38	-12.38	-0.00
1	0	9	1.78	1.57	1.57	-0.00
1	0	10	8.62	8.47	8.47	-0.00
1	0	11	8.70	7.46	7.46	-0.00
1	0	-1	19.20	16.17	-16.17	0.00
1	0	-2	41.23	44.13	44.13	0.00
1	0	-3	6.96	4.63	4.65	-0.00
1	0	-4	38.47	37.86	-37.88	0.00
1	0	-5	37.52	38.41	-38.41	0.00
1	0	-6	7.14	7.07	7.07	0.00
1	0	-7	27.14	30.19	30.19	-0.00
1	0	-8	10.36	8.98	8.98	-0.00
1	0	-9	3.12	2.37	2.37	0.00
1	0	-10	8.17	7.82	-7.82	-0.00
1	0	-11	14.07	11.81	-11.81	0.00
2	0	1	15.23	16.06	-16.06	0.00
2	0	2	46.60	54.53	54.53	-0.00
2	0	3	39.73	44.81	44.81	-0.00
2	0	4	8.91	8.42	+8.42	-0.00
2	0	5	13.83	13.28	-13.28	-0.00
2	0	6	24.22	23.31	-23.31	0.00
2	0	7	8.44	9.21	-9.21	-0.00
2	0	8	10.86	9.50	9.50	0.00
2	0	9	12.66	11.96	11.96	0.00
2	0	10	5.94	5.32	5.32	0.00
2	0	11	5.91	4.80	-4.80	0.00
2	0	-1	49.16	54.43	-54.43	-0.00
2	0	-2	29.41	25.95	25.95	0.00
2	0	-3	19.08	19.86	19.86	-0.00
2	0	-4	5.96	7.44	7.44	-0.00
2	0	-5 L	1.17	1.40	-1.40	-0.00
2	0	-6	30.47	31.20	-31.20	-0.00
2	0	-7	27.38	29.28	-29.28	-0.00
2	0	-8	1.84	1.44	-1.44	-0.00
2	0	-9	16.62	18.83	18.83	0.00
2	0	-10	10.11	10.78	10.78	0.00
2	0	-11 L	0.95	0.68	-0.68	0.00
3	0	0	6.84	5.34	5.34	0.00
3	0	1	35.46	37.05	37.05	-0.00
3	0	2	34.41	35.98	35.98	-0.00
3	0	3	2.33	2.18	2.58	-0.00
3	0	4	31.98	33.40	-33.40	0.00
3	0	5	26.14	27.50	-27.50	0.00
3	0	6	7.89	7.23	-7.23	0.00
3	0	7	10.39	10.57	10.57	-0.00
3	0	8	8.61	8.04	8.04	-0.00
3	0	9 L	1.31	1.73	-1.73	0.00
3	0	10	8.05	5.54	-5.54	0.00
3	0	-1	28.16	27.37	-27.87	0.00
3	0	-2	45.17	46.84	-46.84	0.00
3	0	-3	18.33	15.63	-15.63	-0.00
3	0	-4	45.64	48.57	48.57	-0.00
3	0	-5	42.46	45.79	45.79	-0.00
3	0	-6	13.99	13.53	13.53	-0.00
3	0	-7	9.22	10.10	-10.10	-0.00
3	0	-8	15.13	16.29	-16.29	-0.00
3	0	-9	3.45	3.03	-3.03	-0.00
3	0	-10	3.87	3.44	3.54	0.00
4	0	0	26.25	28.24	28.24	-0.00
4	0	1	3.38	3.10	3.10	-0.00
4	0	2	19.06	19.25	-19.25	0.00
4	0	3	7.72	8.44	-8.44	-0.00
4	0	4	4.97	4.96	-4.96	0.00
4	0	5	16.07	17.09	17.09	0.00
4	0	6	17.77	18.71	18.71	0.00
4	0	7	5.74	5.44	5.44	-0.00
4	0	8	2.90	2.40	-2.40	0.00
4	0	9	6.86	5.76	-5.76	0.00
4	0	10 L	.76	0.13	-0.13	0.00
4	0	-1	15.67	13.41	13.41	-0.00
4	0	-2	5.04	4.06	-4.06	-0.00
4	0	-3	22.99	22.70	-22.70	0.00
4	0	-4	16.46	15.10	-15.10	-0.00
4	0	-5 L	1.35	1.21	1.51	0.00
4	0	-6	12.66	12.09	12.09	-0.00
4	0	-7	11.34	12.14	12.14	0.00
4	0	-8 L	1.46	0.16	-0.16	0.00
4	0	-9	11.94	11.82	-11.82	0.00
4	0	-10	8.65	8.44	-8.44	-0.00
5	0	0	10.76	9.68	-9.68	0.00
5	0	1	17.75	17.69	-17.69	-0.00
5	0	2	14.33	12.25	-12.55	-0.00
5	0	3	13.32	12.53	12.53	0.00
5	0	4	17.64	17.00	17.00	-0.00
5	0	5	4.11	4.40	4.40	-0.00
5	0	6	4.53	5.56	-5.56	0.00
5	0	7	3.53	4.53	-4.53	-0.00
5	0	8	6.13	5.22	-5.22	-0.00
5	0	9 L	0.86	0.74	-0.74	-0.00
5	0	-1	15.56	15.47	15.47	-0.00
5	0	-2	22.93	22.88	22.88	0.00
5	0	-3	12.86	11.48	11.48	-0.00
5	0	-4	7.19	6.86	-6.86	-0.00
5	0	-5	24.45	26.15	-26.15	-0.00
5	0	-6	10.56	11.27	-11.27	-0.00
5	0	-7	6.24	6.70	6.70	-0.00
5	0	-8	9.41	9.52	9.52	-0.00
5	0	-9	5.46	4.84	4.84	-0.00
6	0	0	19.84	20.25	-20.25	0.00
6	0	1	7.19	7.48	-7.48	-0.00
6	0	2 L	1.49	0.04	-0.04	-0.00
6	0	3	7.58	7.35	7.35	0.00
6	0	4	3.17	3.24	3.24	-0.00
6	0	5	4.33	3.99	-3.99	-0.00
6	0	6	6.73	6.29	-6.29	-0.00
6	0	7	1.99	2.29	-2.29	-0.00
6	0	8	6.78	4.47	4.47	-0.00
6	0	-1	19.19	18.56	-18.56	0.00
6	0	-2	1.80	2.30	2.30	0.00
6	0	-3	16.96	17.15	17.15	-0.00
6	0	-4	10.87	11.62	11.62	0.00
6	0	-5	2.59	0.74	-0.74	-0.00
6	0	-6	7.93	7.96	-7.96	0.00
6	0	-7	8.38	9.44	-9.44	0.00
6	0	-8 L	1.16	0.88	-0.88	-0.00
7	0	0	6.34	6.39	6.39	-0.00
7	0	1	12.49	12.19	12.19	-0.00
7	0	2	5.69	5.27	5.27	-0.00
7	0	3	4.28	3.80	-3.80	-0.00
7	0	4	4.96	5.14	-5.14	0.00
7	0	6	3.10	2.32	2.32	0.00
7	0	7	1.08	1.14	1.14	0.00
7	0	-1	3.17	2.30	2.30	-0.00
7	0	-2	6.05	5.00	-5.00	0.00
7	0	-3	6.76	6.61	-6.61	-0.00
7	0	-4 L	1.44	0.79	0.79	-0.00
7	0	-5	6.28	6.01	6.01	0.00
7	0	-6	5.34	5.22	5.22	0.00
7	0	-7	2.66	2.74	-2.74	-0.00
8	0	0	5.38	4.61	4.61	0.00
8	0	1 L	1.30	1.35	-1.35	0.00
8	0	2	5.89	5.48	-5.48	0.00
8	0	3	3.98	4.08	-4.08	-0.00
8	0	4 L	1.01	0.02	0.02	0.00
8	0	5	4.33	2.98	2.98	0.00
8	0	-1	6.72	7.22	7.22	0.00
8	0	-2 L	1.31	1.43	1.43	0.00
8	0	-3	4.11	4.44	-4.44	-0.00
8	0	-4	4.62	4.79	-4.79	-0.00
8	0	-5 L	1.08	0.46	0.46	-0.00
9	0	0	1.61	1.30	-1.30	0.00
9	0	1	1.51	1.82	-1.82	-0.00
9	0	2 L	0.76	0.85	-0.85	0.00
9	0	3 L	0.45	0.15	-0.15	-0.00
9	0	-1	1.82	1.97	1.97	0.00
9	0	-2	1.76	1.77	1.77	-0.00
9	0	-3 L	0.83	0.04	0.04	0.00
0	1	1	13.42	13.78	-9.55	9.93
0	1	2	37.43	40.79	35.84	19.45
0	1	3	22.67	22.03	-22.03	0.51
0	1	4	41.72	43.35	-39.80	-17.57
0	1	5	35.40	41.27	-35.18	-22.51
0	1	6	8.10	7.22	-0.43	-7.21
0	1	7	21.42	21.50	18.16	11.51
0	1	8	13.42	13.55	7.16	11.27
0	1	9 L	1.41	1.79	-0.65	1.67
0	1	10	8.59	8.74	-7.85	-3.94
0	1	11	10.87	8.31	-7.69	-4.28
1	1	1	37.74	39.45	30.92	24.51
1	1	2	39.84	37.55	-23.41	-29.34
1	1	3	44.61	44.35	-27.84	-35.17
1	1	4	8.77	5.92	3.27	-4.93
1	1	5	19.99	20.32	13.83	14.89
1	1	6	32.16	32.11	27.46	15.65
1	1	7	18.09	17.07	16.18	5.43
1	1	8	8.48	7.34	-6.70	-3.01
1	1	9	13.18	12.64	-10.04	-7.30
1	1	10	8.57	8.62	-6.59	-5.55
1	1	11	5.59	4.41	4.08	1.69
1	1	-1	34.37	35.98	28.37	22.12
1	1	-2	30.11	30.73	-26.36	-15.78
1	1	-3	60.55	60.13	-43.20	-41.83
1	1	-4	44.31	39.40	-30.80	-24.57
1	1	-5	5.95	5.01	3.84	4.09
1	1	-6	24.47	24.39	17.49	17.71
1	1	-7	25.56	27.30	23.47	13.93
1	1	-8 L	1.44	1.05	0.93	-1.37
1	1	-9	16.91	17.94	-15.01	-9.84
1	1	-10	7.91	7.92	-4.48	-6.54
1	1	-11 L	0.94	1.09	1.08	0.11
2	1	0	12.58	11.70	11.63	-1.28
2	1	1	48.18	53.02	-43.63	-30.12
2	1	2	26.18	24.24	-20.78	-12.43
2	1	3	18.41	15.27	-13.10	-7.83
2	1	4	28.42	28.04	24.33	11.02
2	1	5	28.47	31.05	23.35	21.67
2	1	6	7.23	5.08	-2.54	4.99
2	1	7	12.88	13.93	-9.02	-11.39
2	1	8	17.18	16.18	-10.28	-12.49
2	1	9	1.64	1.25	-0.04	-1.25
2	1	10	7.21	6.66	4.74	4.63
2	1	11	5.25	5.66	4.29	2.63
2	1	-1	57.35	56.21	40.75	39.18
2	1	-2	56.64	52.63	41.41	32.48
2	1	-3	27.64	24.74	23.79	6.82
2	1	-4	40.03	39.21	-33.08	-21.04
2	1	-5	34.92	34.55	-29.60	-17.44
2	1	-6	5.18	5.04	-4.65	-1.96
2	1	-7	13.61	13.60	10.53	7.62
2	1	-8	14.68	13.78	8.80	10.60
2	1	-9	1.70	2.93	0.49	2.89
2	1	-10	9.36	9.37	-7.71	-5.33
2	1	-11	11.90	11.16	-9.90	-5.16
3	1	0	39.42	34.42	-30.34	-16.25
3	1	1	18.32	16.66	-11.22	-12.31
3	1	2	16.62	14.65	11.97	8.79
3	1	3	26.16	25.55	12.29	22.41
3	1	4	2.50	2.66	-0.86	2.52
3	1	5	20.31	21.00	-17.83	-12.19
3	1	6	17.95	20.13	-18.83	-7.10
3	1	7	1.77	1.52	-1.38	-0.64
3	1	8	9.25	8.09	7.82	2.09
3	1	9	10.56	10.64	10.02	4.13
3	1	10	4.87	3.99	2.02	3.44
3	1	-1	43.42	40.94	-38.74	-13.23
3	1	-2	1.41	0.99	0.34	-0.93
3	1	-3	15.31	15.04	10.89	10.39
3	1	-4	21.02	18.44	8.20	16.52
3	1	-5	2.61	2.35	-1.36	1.91
3	1	-6	25.51	24.30	-19.39	-14.54
3	1	-7	12.32	11.43	-7.53	-8.73
3	1	-8	5.28	4.98	4.70	1.64
3	1	-9	13.37	14.75	12.92	7.13
3	1	-10	11.92	11.65	9.22	6.61
4	1	0	19.22	18.05	13.11	12.42
4	1	1	36.35	36.13	27.75	23.13
4	1	2	32.29	30.53	28.44	11.12
4	1	3	5.20	5.49	-3.99	-3.77
4	1	4	17.14	17.18	-15.05	-8.27
4	1	5	9.79	8.99	-4.02	-8.04
4	1	6	2.50	2.10	-1.76	-1.15
4	1	7	10.59	10.12	6.01	8.14
4	1	8	7.66	6.27	3.48	5.60
4	1	9	2.96	2.13	-1.30	-1.70
4	1	10	7.61	6.96	-5.66	-4.06
4	1	-1	25.97	24.76	-17.68	-17.31
4	1	-2	33.91	34.05	-22.94	-25.97
4	1	-3	7.31	7.06	-5.54	-4.37
4	1	-4	18.42	17.34	12.55	11.97
4	1	-5	29.32	27.28	24.03	13.54
4	1	-6	14.36	13.12	11.36	6.56
4	1	-7	9.52	9.01	-7.36	-6.19
4	1	-8	16.24	17.00	-13.64	-11.12
4	1	-9	6.84	7.20	-5.00	-5.19
4	1	-10	2.97	3.10	1.96	2.39
5	1	0	21.38	18.27	15.79	9.19
5	1	1	6.26	6.95	1.11	6.86
5	1	2	12.30	10.40	-8.11	-5.86
5	1	3	16.27	16.90	-9.78	-13.79
5	1	4	10.13	10.29	-8.62	-6.14
5	1	5	5.86	6.42	5.21	4.09
5	1	6	9.17	9.49	7.86	5.32
5	1	7	2.78	2.40	2.03	1.45
5	1	8	3.87	4.03	-3.90	-1.04
5	1	9	1.39	1.64	-0.60	-1.74
5	1	-1	19.43	18.26	17.31	5.83
5	1	-2	6.47	5.42	5.30	0.40
5	1	-3	20.58	20.08	-17.49	-9.85
5	1	-4	14.00	13.52	-9.36	-9.75
5	1	-5	6.97	6.63	6.60	1.75
5	1	-6	12.12	13.29	9.80	8.98
5	1	-7	10.90	11.98	9.89	6.76
5	1	-8 L	1.29	0.43	-0.19	-0.39
6	1	-9	7.17	7.20	-6.03	-3.93
6	1	0	6.78	9.66	-5.42	-6.40
6	1	1	15.61	16.96	-14.41	-9.94
6	1	2	3.92	3.65	-3.65	-0.19
6	1	3	12.12	12.90	12.07	4.55
6	1	4	12.77	11.78	10.87	4.54
6	1	5	4.78	5.09	4.78	3.09
6	1	6	3.47	2.68	-2.43	-0.51
6	1	7	3.73	3.40	-2.38	-2.44
6	1	8	3.75	2.90	-2.34	-1.72
6	1	-1	2.98	3.01	-2.07	1.61
6	1	-2	7.75	8.41	2.52	6.02
6	1	-3	4.64	4.47	2.26	3.69
6	1	-4	3.95	5.06	-3.32	-3.81
6	1	-5	12.04	13.19	-11.38	-6.53
6	1	-6	9.30	8.70	-7.62	-4.20
6	1	-7	1.56	2.19	1.97	0.95
6	1	-8	8.70	7.70	5.59	5.29
7	1	0	8.42	7.72	-5.92	-4.94
7	1	1 L	1.43	1.41	0.05	-1.41
7	1	2	4.21	3.45	0.09	3.65
7	1	3	5.53	5.82	2.86	5.06
7	1	4 L	1.28	0.43	-0.36	0.39
7	1	5	4.92	4.42	-3.43	-3.33
7	1	6	6.07	5.44	-4.71	-2.73
7	1	7	1.11	1.47	-1.35	-0.55
7	1	-1	8.95	8.47	-8.22	-4.21
7	1	-2	3.55	3.45	3.15	1.42
7	1	-3	10.93	12.41	10.47	7.43
7	1	-4	10.51	11.20	9.89	4.64
7	1	-5 L	1.31	0.45	-0.45	0.84
7	1	-6	7.01	7.25	-5.95	-4.24
7	1	-7	6.25	6.21	-4.14	-4.05
8	1	0	1.89	1.42	1.47	1.25
8	1	2 L	4.27	4.28	3.80	1.95
8	1	3	1.16	1.15	1.04	1.07
8	1	4	1.65	1.42	-1.29	-0.25
8	1	5 L	2.33	2.15	-1.46	-1.19
8	1	-1	0.72	1.21	0.79	-1.07
8	1	-2	2.45	3.13	-2.44	-2.07
8	1	-3	4.86	5.43	-3.88	3.41
8	1	-4 L	2.55	3.16	-2.79	-1.82
8	1	-5	1.13	1.23	0.56	1.10

8	1	-5	3.72	4.03	3.69	2.26
8	1	0	1.83	2.02	1.88	1.52
8	1	1 L	3.81	0.00	0.06	-3.07
8	1	2	2.38	4.81	-2.46	-1.74
8	1	-1	4.92	4.57	4.18	1.85
8	1	-2	4.02	3.09	3.38	1.21
0	2	2	24.67	27.48	-20.49	18.31
0	2	3	36.68	42.99	4.92	42.70
0	2	4	30.07	32.04	11.38	29.76
0	2	5	11.75	11.96	-3.97	-11.29
0	2	6	23.94	23.92	-4.47	-23.50
0	2	7	15.76	13.91	-4.93	-13.01
0	2	8	5.60	5.00	2.79	4.14
0	2	9	14.62	15.38	3.14	15.05
0	2	10	9.48	9.30	0.96	8.95
0	2	11	2.09	1.72	-0.21	-1.71
1	2	0	23.99	24.89	14.21	20.43
1	2	2	37.17	40.44	7.67	39.71
1	2	3	14.28	10.39	-8.92	5.94
1	2	4	26.80	28.63	-11.23	-26.34
1	2	5	28.43	26.91	-5.67	-26.30
1	2	6	7.09	6.86	5.49	-4.11
1	2	7	16.42	15.43	-0.38	15.42
1	2	8	16.87	15.71	0.69	15.69
1	2	9	3.73	3.91	-2.90	0.15
1	2	10	9.55	9.66	-5.72	-7.09
1	2	11	5.83	5.24	-1.54	-5.32
1	2	-1	32.74	37.41	-1.44	-37.38
1	2	-2	36.82	41.14	-8.55	-40.24
1	2	-3	13.09	10.91	10.85	1.14
1	2	-4	24.38	25.09	7.89	24.66
1	2	-5	25.92	25.59	5.15	25.38
1	2	-6	2.20	1.03	-1.58	0.37
1	2	-7	21.93	21.99	-10.61	-19.32
1	2	-8	16.41	16.06	-1.74	-16.27
1	2	-9	5.37	5.62	0.78	-4.96
1	2	-10	8.30	9.47	6.00	7.33
1	2	-11	10.17	10.18	5.39	8.64
2	2	3	23.85	28.02	-6.01	27.37
2	2	1	18.03	18.24	7.16	17.10
2	2	2	26.62	27.28	1.48	-27.54
2	2	3	45.26	47.36	-13.07	-45.52
2	2	4	12.33	11.54	0.50	-11.53
2	2	5	15.02	15.17	4.87	14.37
2	2	6	21.30	22.01	13.16	18.62
2	2	7	6.33	5.72	1.37	-5.54
2	2	8	9.91	9.59	-6.73	-6.82
2	2	9	10.50	10.66	-3.40	-9.46
2	2	10	7.20	5.62	-0.76	-5.56
2	2	11 L	0.54	3.00	2.53	2.42
2	2	-1	33.39	30.24	19.30	23.28
2	2	-2	10.23	8.29	-2.84	-7.79
2	2	-3	31.90	33.42	-3.59	-33.23
2	2	-4	23.02	23.01	9.35	-23.37
2	2	-5	11.09	11.27	10.18	5.71
2	2	-6	31.29	31.34	13.04	29.04
2	2	-7	20.30	20.02	5.04	19.79
2	2	-8	4.68	4.27	-1.85	-3.85
2	2	-9	12.05	12.04	-4.08	-11.97
2	2	-10	8.28	8.49	-0.44	-8.47
2	2	-11 L	0.80	0.79	0.09	-0.78
3	2	0	9.05	8.02	1.64	-7.85
3	2	1	42.67	42.42	-20.70	-37.03
3	2	2	23.21	19.28	-4.33	-19.19
3	2	3	10.66	9.72	7.28	6.49
3	2	4	21.69	20.93	3.84	18.97
3	2	5	20.89	20.26	0.35	20.24
3	2	6	7.13	7.42	4.93	5.27
3	2	7	11.05	11.37	4.19	-11.12
3	2	8	9.71	9.46	1.17	-9.59
3	2	9 L	1.20	1.00	1.58	0.21
3	2	10	5.83	5.49	0.79	5.23
3	2	-1	34.86	34.09	11.70	32.02
3	2	-2	35.31	37.00	0.01	37.00
3	2	-3	4.32	4.41	0.69	4.36
3	2	-4	29.37	30.83	-11.70	-27.93
3	2	-5	25.67	27.27	-11.26	-24.93
3	2	-6	14.47	15.90	-11.37	-11.12
3	2	-7	7.47	7.43	-3.62	7.05
3	2	-8	16.84	19.09	5.61	17.23
3	2	-9	7.17	7.09	-0.19	7.08
3	2	-10	5.24	5.01	-1.39	-4.81
4	2	3	18.51	19.12	-0.24	-19.12
4	2	1	6.69	5.01	3.51	-4.37
4	2	2	14.40	14.41	1.75	14.30
4	2	3	19.89	20.09	-2.51	19.93
4	2	4	7.53	7.30	0.83	6.95
4	2	5	14.51	18.22	-11.99	-13.85
4	2	6	19.93	17.07	-10.14	-13.72
4	2	7	2.98	3.21	0.98	-3.16
4	2	8	4.69	4.21	3.06	2.90
4	2	9	5.45	4.32	1.23	4.77
4	2	10	2.74	3.01	-2.91	2.14
4	2	-1	19.35	15.57	-9.58	-12.27
4	2	-2	8.69	7.03	-4.83	1.67
4	2	-3	23.22	25.11	10.91	22.62
4	2	-4	23.07	24.07	6.48	24.02
4	2	-5	5.02	4.07	-4.57	-1.70
4	2	-6	16.95	17.07	-5.23	-16.25
4	2	-7	9.51	9.05	1.63	-9.71
4	2	-8	3.75	3.08	3.17	1.87
4	2	-9	8.47	8.99	2.62	8.59
4	2	-10	5.33	5.05	1.93	4.51
5	2	0	7.25	6.23	-0.19	6.12
5	2	1	19.85	17.11	6.13	15.93
5	2	2	9.25	8.07	4.12	7.61
5	2	3	12.03	11.49	-8.97	-7.19
5	2	4	13.49	12.09	-4.48	-12.01
5	2	5	5.86	5.65	1.37	-5.17
5	2	6	5.13	3.32	1.53	3.17
5	2	7	8.39	7.75	2.09	7.46
5	2	8	5.95	5.59	1.89	5.58
5	2	9	2.07	1.40	1.39	-0.16
5	2	-1	19.46	18.02	-9.29	-16.56
5	2	-2	20.63	20.01	-0.11	-20.61
5	2	-3	7.60	7.13	2.93	-6.50
5	2	-4	6.18	6.40	-2.50	5.89
5	2	-5	15.14	15.90	5.83	14.79
5	2	-6	9.50	9.87	5.45	8.22
5	2	-7	5.09	4.61	0.07	-4.61
5	2	-8	9.07	10.56	-2.32	-10.30
5	2	-9	6.30	6.41	-0.11	-6.41
6	2	0	15.20	13.40	3.96	12.80
6	2	1	4.96	4.62	1.34	4.42
6	2	2	8.83	8.91	7.21	-5.24
6	2	3	8.29	8.45	1.69	-8.28
6	2	4	2.13	2.12	-0.30	-2.10
6	2	5	4.68	3.48	0.96	3.34
6	2	6	4.97	4.78	0.17	4.78
6	2	7 L	1.02	1.59	-0.66	1.23
6	2	8 L	0.68	3.61	-2.02	-3.00
6	2	-1	16.72	16.02	9.45	13.67
6	2	-2	3.92	3.82	3.81	-0.18
6	2	-3	14.56	15.09	-6.72	-13.52
6	2	-4	11.60	13.28	-6.10	-11.80
6	2	-5 L	1.42	2.61	1.88	-0.95
6	2	-6	8.31	8.98	2.24	8.70
6	2	-7	6.92	7.70	0.95	7.64
6	2	-8 L	1.04	0.20	-0.11	-0.17
7	2	0	5.77	5.14	-2.98	-4.19
7	2	1	11.19	11.59	-7.93	-8.44
7	2	2	6.10	5.23	-1.39	-5.04
7	2	3	3.99	4.95	4.05	1.83
7	2	4	5.89	5.40	1.93	5.04
7	2	5	1.92	2.48	-0.58	2.41
7	2	6	2.21	2.02	-1.82	-1.89
7	2	7 L	0.37	2.09	-0.14	-2.39
7	2	-1	1.74	2.61	-1.92	1.76
7	2	-2	7.34	7.13	-1.26	7.02
7	2	-3	5.90	5.73	0.06	5.73
7	2	-4	2.38	2.45	1.84	-1.52
7	2	-5	4.65	5.12	0.78	-5.06
7	2	-6	3.96	4.44	-2.92	-3.34
7	2	-7	2.35	2.19	0.46	2.14
8	2	0	4.47	4.10	0.60	-4.05
8	2	1 L	1.19	1.04	0.36	1.80
8	2	2	5.51	5.12	0.41	5.11
8	2	3	2.81	3.47	1.21	2.83
8	2	4 L	0.87	0.26	0.36	0.04
8	2	5	1.99	1.00	-1.03	-1.47
8	2	-1	5.19	5.27	-2.62	-4.57
8	2	-2	2.08	2.48	-2.01	-0.55
8	2	-3	3.16	3.29	1.10	3.42
8	2	-4	3.72	4.20	1.64	3.87
8	2	-5 L	0.95	1.32	-1.52	0.15
9	2	0 L	0.77	1.22	0.58	1.08
9	2	1 L	0.70	1.00	0.44	1.43
9	2	2 L	0.51	1.43	-0.79	1.20
9	2	-1 L	0.79	1.45	-1.07	-0.98
9	2	-2	2.44	2.70	0.66	-2.61
0	3	1	35.41	38.09	29.45	-25.09
0	3	2	43.06	37.92	19.81	-32.33
0	3	3	19.13	18.25	15.19	10.11
0	3	4	37.30	35.35	-4.70	35.04
0	3	5	27.70	26.03	-5.96	25.96
0	3	6	5.15	4.40	-4.72	1.31
0	3	7	19.23	18.05	3.06	-17.79
0	3	8	14.71	15.03	9.27	-12.58
0	3	9	5.23	4.08	4.68	0.20
0	3	10	6.61	6.78	1.51	4.61
0	3	11	5.68	6.35	-2.03	6.23
1	3	0	36.11	37.89	0.68	-37.88
1	3	1	29.68	25.65	4.62	-24.62
1	3	2	23.69	22.09	-12.28	18.36
1	3	3	34.12	31.44	-15.73	27.22
1	3	4	20.62	19.11	-15.28	11.47
1	3	5	11.76	11.01	1.16	-11.46
1	3	6	23.70	22.10	5.84	-21.52
1	3	7	12.30	10.18	2.25	-9.93
1	3	8	5.10	4.46	0.81	4.38
1	3	9	10.43	11.29	-5.36	9.94
1	3	10	6.53	6.74	-2.47	6.27
1	3	11	2.42	2.94	-0.44	-2.91
1	3	-1	3.91	5.69	5.34	-1.98
1	3	-2	24.25	24.32	-1.12	24.30
1	3	-3	40.22	41.06	-17.93	39.28
1	3	-4	25.60	26.71	-6.20	25.98
1	3	-5	3.73	4.27	0.54	-4.24
1	3	-6	20.90	21.05	11.45	-18.01
1	3	-7	17.72	15.47	9.31	-15.04
1	3	-8	3.98	4.06	-3.10	3.49
1	3	-9	10.89	12.13	-3.81	11.51
1	3	-10	5.84	6.09	-4.03	4.25
1	3	-11 L	0.89	1.23	-0.00	-1.23
2	3	0	16.07	13.94	-9.80	9.92
2	3	1	37.10	32.14	-10.65	30.32
2	3	2	23.53	20.95	-13.44	16.09
2	3	3	3.27	4.12	3.23	-2.55
2	3	4	19.56	20.17	6.02	-19.25
2	3	5	18.65	17.94	7.68	-16.21
2	3	6	4.44	4.01	2.65	3.02
2	3	7	16.13	14.74	-8.33	12.40
2	3	8	11.83	11.28	-6.33	9.69
2	3	9	3.42	3.44	-3.44	0.07
2	3	10	5.65	4.86	1.65	-4.35
2	3	-1	40.54	35.49	13.46	-32.84
2	3	-2	40.99	43.61	13.81	-41.58
2	3	-3	16.76	16.07	-1.92	-15.95
2	3	-4	19.74	18.25	-4.67	17.75
2	3	-5	21.19	22.44	-7.24	21.77
2	3	-6	4.33	3.45	-0.37	3.43
2	3	-7	7.13	8.78	3.49	-6.28
2	3	-8	15.13	15.22	9.36	-12.00
2	3	-9	3.96	7.99	6.47	-4.69
2	3	-10	7.02	7.45	-0.37	7.34
3	3	0	32.37	30.17	-11.15	28.03
3	3	1	13.14	11.40	-5.19	10.49
3	3	2	14.74	14.42	4.30	-13.76
3	3	3	29.96	29.02	16.61	-23.80
3	3	4	12.34	11.73	10.82	-4.55
3	3	5	14.99	15.41	2.01	15.46
3	3	6	14.31	14.41	-0.85	14.38
3	3	7	7.23	5.96	-5.69	1.77
3	3	8	8.48	8.00	-0.88	-7.96
3	3	9	10.05	9.38	0.64	-9.36
3	3	10	3.10	3.44	2.39	-1.07
3	3	-1	24.07	22.61	2.99	22.61
3	3	-2	7.38	7.73	6.38	-4.38
3	3	-3	22.37	24.07	14.92	-18.88
3	3	-4	25.16	23.29	14.96	-17.98
3	3	-5	4.71	2.26	0.21	2.25
3	3	-6	21.54	21.22	-7.35	19.91
3	3	-7	12.62	12.15	-9.12	8.02
3	3	-8	7.39	7.23	-1.31	-7.11
3	3	-9	9.53	11.11	1.24	-11.04
3	3	-10	6.18	6.34	1.46	-5.37
4	3	0	10.05	8.28	-3.01	-8.03
4	3	1	25.30	21.48	6.72	-20.61
4	3	2	18.12	17.42	3.25	-17.41
4	3	3	2.87	2.49	-1.79	2.32
4	3	4	11.70	11.24	-4.31	10.38
4	3	5	9.17	8.92	-7.02	5.52
4	3	6	3.24	2.24	2.18	-0.51
4	3	7	7.20	8.48	4.23	-6.83
4	3	8	7.59	6.24	4.57	-4.39
4	3	9L	1.18	1.72	1.27	1.17
4	3	-1	17.96	14.96	-4.22	14.36
4	3	-2	26.70	25.22	-11.32	22.31
4	3	-3	4.95	5.27	-3.84	3.90
4	3	-4	12.06	11.12	3.45	-10.57
4	3	-5	13.06	13.26	1.27	-13.50
4	3	-6	6.91	7.11	0.96	-7.05
4	3	-7	7.87	7.72	-2.72	7.22
4	3	-8	11.91	13.21	-4.01	12.59
4	3	-9	6.18	7.93	-3.93	6.91
5	3	0	15.15	14.44	5.25	-13.35
5	3	1	3.07	3.45	2.93	1.80
5	3	2	16.16	14.79	-5.39	13.99
5	3	3	14.74	13.78	-8.03	11.20
5	3	4	5.65	4.55	-1.43	4.32
5	3	5	3.22	3.26	0.44	-3.53
5	3	6	7.14	6.95	4.06	-5.65
5	3	7	1.91	1.69	1.78	-0.44
5	3	8	4.02	3.72	-0.44	3.69
5	3	-1	15.01	14.79	3.05	-14.47
5	3	-2	6.88	6.23	-3.15	-5.50
5	3	-3	13.10	15.01	-5.24	14.70
5	3	-4	13.48	14.06	-7.47	12.27
5	3	-5	3.25	2.77	-2.16	-1.74
5	3	-6	11.11	11.48	5.83	-7.89
5	3	-7	8.79	10.39	3.80	-9.66
5	3	-8 L	1.59	0.35	0.49	0.29
6	3	0	4.60	4.21	1.29	4.01
6	3	1	9.22	10.04	-1.04	9.98
6	3	2	5.09	6.20	-3.97	4.77
6	3	3	8.22	8.02	-5.25	-4.06
6	3	4	11.04	11.09	0.93	-11.55
6	3	5	4.12	5.00	2.95	-3.31
6	3	6	3.64	3.02	0.78	2.94
6	3	7	3.85	4.04	-1.05	3.93
6	3	-1	7.27	7.40	6.90	-2.72
6	3	-2	9.80	9.02	7.49	-5.89
6	3	-3	6.91	6.13	3.85	-4.77
6	3	-4	6.04	5.03	-2.90	4.47
6	3	-5	9.13	10.14	-2.42	9.86
6	3	-6	3.59	3.00	-0.11	3.00
6	3	-7	4.11	3.17	0.97	-3.01
7	3	0	5.85	5.00	-2.48	5.34
7	3	1	2.18	2.72	1.17	-2.46
7	3	2	6.37	6.96	5.50	-4.27
7	3	3	2.86	2.77	2.50	-1.19
7	3	4L	1.51	1.36	1.19	1.00
7	3	5L	1.31	1.19	-0.40	1.33
7	3	6	2.06	2.43	-0.28	2.41
7	3	-1	6.64	6.11	-1.89	6.81
7	3	-2	4.90	4.49	-1.22	-4.69
7	3	-3	7.10	7.71	0.53	-7.69
7	3	-4	6.15	6.28	0.60	-6.25
7	3	-5 L	1.55	2.02	1.40	-1.46
7	3	-6	5.02	4.63	-1.24	4.75
8	3	0L	1.48	0.99	0.16	-0.87
8	3	1L	1.43	1.79	0.81	-1.59
8	3	2	3.28	3.47	2.54	-2.37
8	3	3L	1.19	0.91	-0.06	0.91
8	3	4L	3.20	4.01	-2.04	3.44
8	3	-1L	1.46	1.27	-0.93	0.86
8	3	-2	5.34	5.08	-2.91	5.09
8	3	-3	4.43	5.05	-1.37	5.28
8	3	-4L	1.24	1.23	1.20	-0.26
9	3	0	2.46	3.16	1.04	-2.93
0	4	1	13.63	17.01	-10.06	14.47
0	4	2	9.63	11.01	6.99	-7.27
0	4	3	24.48	26.04	23.74	-12.54
0	4	4	16.15	17.79	16.28	-7.19

0	4	5	7.22	7.03	-6.64	3.56
0	4	6	18.02	18.35	-17.68	4.92
0	4	7	5.86	4.90	-4.75	1.21
0	4	8	4.04	3.09	2.19	-3.21
0	4	9	9.93	9.57	7.45	-6.03
0	4	10	6.16	5.99	5.42	-2.55
1	4	0	23.71	20.59	10.40	-17.77
1	4	1	39.15	39.07	36.83	-15.27
1	4	2	23.83	25.25	21.96	-12.48
1	4	3	4.93	5.01	-3.50	-3.59
1	4	4	16.79	19.67	-15.91	11.39
1	4	5	11.71	15.06	-10.94	10.35
1	4	6	5.19	4.97	-4.37	-2.37
1	4	7	14.16	15.35	12.66	-8.69
1	4	8	13.20	13.97	12.91	-5.35
1	4	9	4.48	4.52	2.45	3.80
1	4	10	6.11	5.70	-3.37	4.60
1	4	-1	35.65	40.38	-39.96	3.11
1	4	-2	29.39	32.97	-30.12	13.48
1	4	-3	5.97	5.48	-5.16	1.84
1	4	-4	15.31	15.29	12.97	-8.65
1	4	-5	18.18	18.39	17.01	-7.49
1	4	-6	11.24	9.63	6.65	6.12
1	4	-7	13.95	13.40	-6.47	11.73
1	4	-8	16.79	17.19	-16.40	5.14
1	4	-9	6.21	6.20	-6.20	-0.03
1	4	-10	5.98	5.81	3.50	-4.38
2	4	0	20.60	18.28	16.12	-9.24
2	4	1	20.90	17.65	16.61	-3.85
2	4	2	20.46	18.21	-5.78	17.27
2	4	3	32.06	33.52	-26.73	19.90
2	4	4	19.22	19.22	-19.65	-1.58
2	4	5	10.03	11.61	7.33	-8.22
2	4	6	9.48	12.17	11.28	-4.55
2	4	7	5.82	5.98	5.69	1.86
2	4	8	4.95	5.63	-1.96	5.28
2	4	9	7.21	7.00	-5.65	4.12
2	4	10	4.70	4.13	-3.85	1.56
2	4	-1	7.71	6.29	5.68	-3.33
2	4	-2	8.00	8.91	-3.38	8.25
2	4	-3	28.24	29.99	-23.43	9.54
2	4	-4	19.94	19.75	-19.47	3.30
2	4	-5	8.15	7.40	5.92	-4.44
2	4	-6	21.79	22.12	17.67	-13.31
2	4	-7	13.11	11.77	8.21	-8.44
2	4	-8	6.88	6.02	-5.13	4.18
2	4	-9	7.78	7.01	-4.69	5.99
2	4	-10	5.83	5.20	-4.75	2.11
3	4	0	10.80	8.72	-7.61	4.25
3	4	1	25.87	24.04	-22.16	11.22
3	4	2	10.16	8.23	-7.71	2.93
3	4	3	9.93	9.65	9.24	-2.81
3	4	4	7.71	8.30	6.16	-6.29
3	4	5	10.77	11.77	8.24	-8.40
3	4	6	2.39	2.64	-0.92	-2.48
3	4	7	7.64	9.71	-8.69	4.33
3	4	8	7.10	8.20	-8.02	1.73
3	4	9	4.24	3.25	-2.20	-2.40
3	4	-1	23.94	18.22	16.26	-8.22
3	4	-2	27.82	23.67	-19.70	-14.52
3	4	-3 L	1.62	2.09	0.43	-2.04
3	4	-4	15.69	15.09	-3.64	15.27
3	4	-5	12.76	11.44	-6.19	9.63
3	4	-6	5.84	6.44	-5.60	3.18
3	4	-7	3.80	4.01	4.65	-1.32
3	4	-8	13.94	13.37	12.23	-5.41
3	4	-9	7.47	7.38	7.09	-2.35
4	4	0	17.47	14.09	-13.06	5.27
4	4	1	7.32	5.30	-4.79	-2.70
4	4	2	14.19	12.48	6.66	-10.56
4	4	3	22.73	21.09	20.79	-6.85
4	4	4	8.19	8.27	8.18	2.53
4	4	5	10.15	11.24	-5.42	9.85
4	4	6	7.34	9.37	-7.86	5.10
4	4	7 L	1.73	2.33	-1.97	-1.24
4	4	8	3.93	4.14	3.61	-2.02
4	4	9 L	0.88	3.49	3.19	-1.43
4	4	-1	13.49	12.62	-12.61	2.33
4	4	-2 L	1.74	1.83	1.63	0.08
4	4	-3	19.83	18.48	18.09	-5.75
4	4	-4	23.23	23.42	21.17	-10.03
4	4	-5	5.83	3.98	-3.15	-2.43
4	4	-6	17.19	15.33	-14.72	4.97
4	4	-7	9.11	8.81	-8.11	2.59
4	4	-8	2.87	2.45	0.00	-2.45
4	4	-9	6.26	5.99	4.12	-4.34
5	4	0	4.02	3.63	0.11	-3.62
5	4	1	14.03	12.46	11.95	-3.49
5	4	2	7.11	5.77	5.77	0.11
5	4	3	4.14	4.60	-0.03	4.60
5	4	4	7.51	8.06	-5.70	5.70
5	4	5	5.11	4.26	-4.16	0.91
5	4	6	3.63	4.55	-0.46	-4.33
5	4	7	4.35	5.86	2.78	-5.16
5	4	8	3.87	4.96	4.37	-2.36
5	4	-1	17.21	13.44	-11.98	6.07
5	4	-2	16.73	14.36	-10.24	10.07
5	4	-3	4.75	3.78	-1.39	3.51
5	4	-4	6.33	5.36	4.27	-3.25
5	4	-5	8.21	7.64	3.89	-6.46
5	4	-6	4.54	4.17	4.02	-1.07
5	4	-7	4.62	4.29	-3.13	2.93
5	4	-8	9.93	8.72	-8.03	3.43
6	4	0	8.61	8.60	2.28	-6.41
6	4	1	3.36	3.10	-1.78	-2.53
6	4	2	8.15	8.01	-7.94	1.08
6	4	3	6.06	6.19	-6.06	1.27
6	4	4	2.17	1.78	-1.47	-1.00
6	4	5	2.79	2.36	2.84	-0.01
6	4	6	3.33	4.24	4.21	0.55
6	4	7 L	0.89	0.03	0.23	0.59
6	4	-1	10.41	9.05	7.29	-5.36
6	4	-2	3.37	2.73	2.66	0.94
6	4	-3	9.99	7.92	-6.73	4.18
6	4	-4	8.89	8.35	-7.36	3.94
6	4	-5 L	1.78	2.00	-1.07	2.38
6	4	-6	6.88	6.31	5.96	-2.07
6	4	-7	6.53	5.10	3.72	-4.27
7	4	0	4.35	4.32	-0.44	4.50
7	4	1	5.65	5.03	-4.35	3.54
7	4	2	4.11	4.40	-4.44	1.20
7	4	3 L	1.57	1.70	0.69	-1.55
7	4	4	4.18	4.59	3.76	-2.63
7	4	5 L	1.11	2.08	2.07	-0.26
7	4	-1	7.55	7.21	6.29	3.53
7	4	-2	7.75	7.34	6.90	-3.04
7	4	-3	6.24	5.94	2.94	-5.17
7	4	-4	2.77	2.20	-2.45	-0.49
7	4	-5	5.29	5.15	-5.02	1.13
8	4	0	2.85	3.10	-2.28	2.09
8	4	1 L	1.28	1.96	0.76	-1.80
8	4	2	3.16	4.43	1.90	-4.00
8	4	3 L	0.90	1.61	1.34	-1.21
8	4	-1 L	1.35	2.00	-1.42	1.40
8	4	-2 L	1.31	0.73	0.20	-0.70
8	4	-3 L	1.22	2.20	2.15	-0.48
0	5	2	19.75	26.04	-22.35	-13.36
0	5	3	9.74	11.33	-6.28	-7.43
0	5	4	13.52	16.03	15.96	1.51
0	5	5	14.92	17.02	16.50	4.16
0	5	6	4.87	4.04	4.02	1.69
0	5	7	11.93	12.47	-12.41	1.26
0	5	8	13.53	12.13	-12.06	-1.27
0	5	9	4.10	3.07	-0.74	-3.60
0	5	10	2.15	2.76	2.56	-1.04
1	5	0	19.43	18.54	-18.20	-2.29
1	5	1	14.94	13.47	-13.39	1.46
1	5	2	16.46	17.30	17.07	-2.84
1	5	3	18.28	20.50	20.49	-0.85
1	5	4	10.59	11.42	8.62	7.49
1	5	5	8.86	11.40	-8.91	7.10
1	5	6	8.76	10.43	-10.38	-1.02
1	5	7	6.48	6.91	-2.61	-6.47
1	5	9	7.81	6.83	6.56	1.89
1	5	10	0.78	3.98	3.86	0.98
1	5	-1	6.19	5.03	-4.18	-3.77
1	5	-2	12.50	12.35	12.11	-2.40
1	5	-3	20.93	25.41	24.34	-7.39
1	5	-4	10.87	11.49	9.60	-6.32
1	5	-5	3.83	5.28	-5.77	-0.43
1	5	-6	12.14	13.17	-13.15	-0.74
1	5	-7	6.53	6.79	-6.75	-0.75
1	5	-8	3.49	3.93	3.90	-0.48
1	5	-9	8.71	7.57	7.56	0.51
1	5	-10	4.14	4.97	4.73	1.52
2	5	0	12.52	9.91	9.86	1.02
2	5	1	18.67	16.74	16.74	0.34
2	5	2	15.38	12.65	10.73	6.69
2	5	3	3.69	3.40	-2.96	-1.66
2	5	4	10.31	11.45	-9.88	-5.79
2	5	5	9.14	11.48	-11.48	0.12
2	5	6 L	1.79	0.99	0.28	0.95
2	5	7	12.27	13.08	13.03	-1.21
2	5	8	10.33	8.98	8.91	-1.15
2	5	9 L	1.15	1.07	0.14	1.64
2	5	-1	22.37	18.80	-17.76	6.17
2	5	-2	23.45	22.34	-22.24	2.09
2	5	-3	7.55	6.46	-6.36	-1.15
2	5	-4	9.42	7.04	7.62	0.51
2	5	-5	15.97	14.36	13.15	6.25
2	5	-6	5.37	5.12	1.40	4.93
2	5	-7	6.46	6.76	-6.70	-0.89
2	5	-8	11.27	10.90	-10.36	-3.39
2	5	-9	6.19	5.20	-4.01	-3.46
3	5	0	21.76	20.40	15.72	9.13
3	5	1	9.80	7.31	7.04	2.61
3	5	2	10.68	9.17	-9.15	-0.60
3	5	3	20.99	21.56	-21.52	-1.37
3	5	4	10.94	10.91	-6.81	-8.00
3	5	5	10.30	11.19	8.95	-6.71
3	5	6	5.69	6.83	5.60	3.92
3	5	7	7.90	7.05	1.89	7.41
3	5	8	4.04	3.79	-3.28	1.91
3	5	9	3.57	3.47	-3.46	-0.29
3	5	-1	10.10	10.07	9.76	2.47
3	5	-2	11.17	8.55	-3.80	-7.65
3	5	-3	19.84	20.54	-17.63	-10.54
3	5	-4	16.87	17.21	-17.16	-1.23
3	5	-5	4.36	3.08	2.62	2.86
3	5	-6	13.13	13.15	13.11	0.94
3	5	-7	10.00	9.92	8.85	4.47
3	5	-8	4.51	4.19	-1.43	3.94
3	5	-9	5.50	5.77	-5.76	0.35
4	5	0	8.17	7.44	-4.00	6.27
4	5	1	17.69	14.21	-13.82	3.31
4	5	2	7.04	5.66	-5.32	-1.92
4	5	3	3.77	3.49	3.40	-0.80
4	5	4	5.81	5.48	5.02	3.21
4	5	5	6.09	5.96	5.27	2.79
4	5	6	2.03	1.73	-1.63	0.59
4	5	7	6.72	6.68	-6.13	1.77
4	5	8	5.95	5.56	-5.49	-0.88
4	5	-1	12.28	9.72	9.36	-2.59
4	5	-2	16.81	15.45	14.56	-5.16
4	5	-3	3.71	2.58	1.37	2.18
4	5	-4	7.57	6.58	-5.86	3.01
4	5	-5	6.57	5.20	-5.35	
4	5	-6	3.00	2.93	-2.70	
4	5	-7	6.72	6.35	6.91	
4	5	-8	10.54	9.45	8.17	
5	5	0	7.26	4.44	-5.34	
5	5	1 L	1.79	1.15	-0.14	
5	5	2	9.82	8.89	9.99	
5	5	3	11.29	10.03	10.42	
5	5	4	2.10	2.06	2.11	
5	5	5	3.38	3.38	-3.65	
5	5	6	5.12	6.10	-5.18	
5	5	7	3.17	2.14	0.75	
5	5	-1	9.29	9.09	-9.52	
5	5	-2	3.60	3.40	-1.49	
5	5	-3	10.29	9.94	8.29	
5	5	-4	10.61	9.83	9.75	
5	5	-5 L	1.73	0.66	0.36	
5	5	-6	8.41	8.06	-6.65	
5	5	-7	5.54	5.73	-5.53	
6	5	0	6.39	5.82	2.52	
6	5	1	6.99	6.93	6.71	
6	5	2	7.12	7.40	3.24	
6	5	3	4.33	5.01	-1.40	
6	5	4	4.77	5.09	-5.05	
6	5	5	1.55	1.76	-1.67	
6	5	6	1.57	1.92	0.91	
6	5	-1	9.26	8.06	-6.73	
6	5	-2	8.43	7.01	-7.66	
6	5	-3	4.60	4.41	-4.39	
6	5	-4	3.93	3.45	3.38	
6	5	-5	7.02	6.95	6.60	
6	5	-6	2.72	3.08	2.96	
7	5	0	2.56	2.27	2.25	
7	5	1 L	1.44	1.67	-1.52	
7	5	2	3.31	4.39	-4.39	
7	5	3	2.10	2.68	-2.68	
7	5	4	1.18	1.61	-1.62	
7	5	-1	3.14	3.43	2.65	
7	5	-2	2.51	2.26	-2.07	
7	5	-3	3.37	3.24	-3.37	
7	5	-4	3.07	3.21	-2.84	
8	5	0	1.07	1.24	-1.54	
8	5	1	1.56	2.47	-1.54	
8	5	-1 L	0.90	0.88	0.83	

6.5. The Absolute Configuration of (+)-3-Bromocamphor.

It has been noted (Section 6.1) that the Bijvoet method, applied using the data of W & K (Table 6.2), failed to produce a conclusive concensus of anomalies. For the assignment of absolute configuration based on the refined structure the methods of both Bijvoet and Hamilton (see Chapter 3) were used.

i) The Bijvoet Method.

The Bijvoet pairs $0k\bar{1}$, $0k1$, used in the previous determination (A) were remeasured using a Joyce-Loebl integrating microdensitometer; the sign of the intensity difference was noted, and found to agree with the visual estimate in each case. Two additional pairs (035, 044) were included in the list, bringing the total to 20. The signs of the inequalities : $F_T(0k\bar{1}) - F_T(0k1)$ were calculated exactly as described in section 6.1. Two determinations were made, one after refinement run A4 ($\underline{R}$ = 0.098), and the other using the final parameters listed in Tables 6.4-6.6 ($\underline{R}$ = 0.079); the agreement between observed and calculated inequalities is shown in Table 6.8, where the determinations are designated (B) and (C) respectively. Absorption effects were ignored throughout: the very regular shape of the crystal used meant that the correction for reflection and counter-reflection was virtually the same in this case.

TABLE 6.8.

(+)-3-Bromocamphor.

Observed and Calculated Inequalities for the Bijvoet Pairs

hkl	$s[I(0k\bar{l}) - I(0k\bar{\bar{l}})]$	$s[F(0k\bar{l}) - F(0k\bar{\bar{l}})]$		
		A	B	C
011	+	+	+	+
012	-	+	-	-
013	-	+	-	-
014	-	+	-	-
015	-	+	-	-
016	+	+	+	+
017	-	-	-	-
022	+	+	+	+
023	+	+	+	+
024	-	-	-	-
025	+	+	+	+
026	+	+	+	+
027	-	-	-	-
029	+	+	+	+
033	+	+	+	+
034	-	-	-	-
035	-		-	-
036	+	+	+	+
043	+	+	+	+
044	-		-	-
		77.7%	100%	100%

ii) Hamilton's Method.

The data was corrected for anomalous dispersion (FC) using the scattering-factor correction terms given in Eq. 6.2. (p. 91). Four cycles of mixed-mode refinement was carried out using ORFLS; the parameters listed in Tables 6.4-6.6 were used, together with an overall scale-factor; the hydrogen parameters were not refined. The conventional R fell from 7.93% to 7.90%, and the weighted R (R_w^1) was 11.449%; the maximum S/E was less than 0.10. A similar refinement of the enantiomorph (obtained by reversing all y-co-ordinates) was carried out using the corrected data. Convergence was obtained after 5 cycles when the conventional R was 7.963% and the weighted R (R_w^2) was 11.515%.

We may now test the one-dimensional hypothesis :
H : The second absolute configuration represents reality.
The total number of parameters refined (n) was 108, and the number of observations (m) was 908; thus the number of degrees of freedom (m-n) is 800. Thus we have :

$$\mathcal{R}_{1,800,\alpha} = R_w^2/R_w^1 = 0.11515/0.11449 = 1.0057 \quad \ldots\ 6.3$$

From Table 1 of reference 66 we find :

$$\mathcal{R}_{1,120,0.005} = 1.034 \quad \ldots\ 6.4$$

and

$$\mathcal{R}_{1,\infty,0.005} = 1.000 \quad \ldots\ 6.5$$

The required value of $(\mathcal{R})$ may be obtained using the interpolation formulae quoted in the appendix to the paper, whence :

$$\mathcal{R}_{1,800,0.005} = 1.0051 \ldots\ldots\ldots 6.6.$$

The hypothesis therefore has approximately 0.5% significance, and can be rejected.

The exceptionally small difference in weighted R-factors (0.07%) is a consequence of the small value of f" (1.5); nevertheless the application of significance test theory has produced a remarkably high vote of confidence in the correct configuration. However it appears that only very slight systematic errors in the data could lead to erroneous results; assignments obtained solely by this method, and based on a very low R-factor difference, should be treated with caution.

6.6. Discussion of the Absolute Configuration.

The results of both Bijvoet's and Hamilton's techniques show conclusively that the structure as determined, and drawn on a right-handed system of axes, represents the true absolute stereochemistry. Figure 6.2 shows the structure projected down the a-axis, and gives the conventional representation, shown in Figure 6.3 (cf. structural formula 5.XV) with the gem-dimethyl bridge

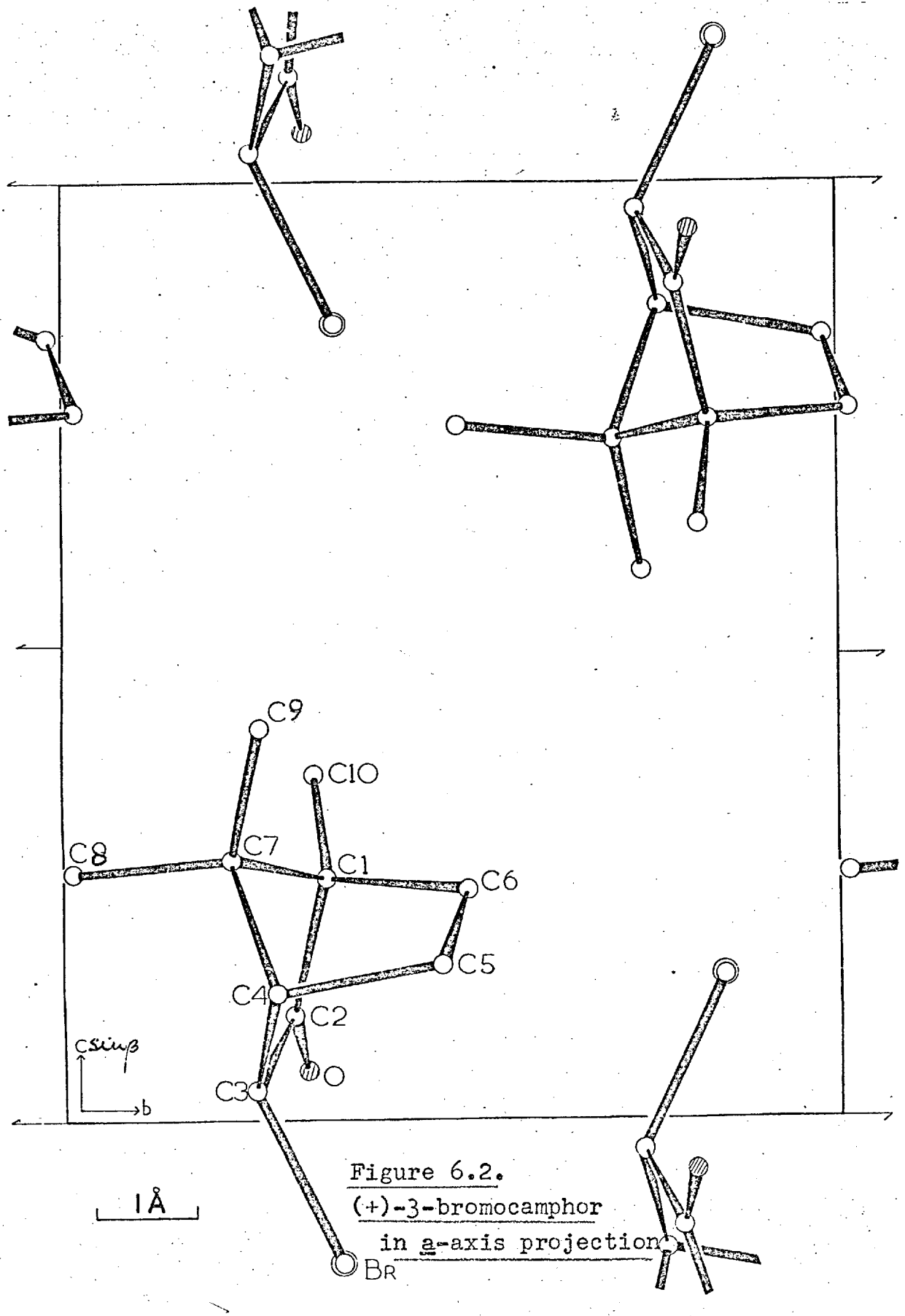


Figure 6.2.
(+)-3-bromocamphor
in a-axis projection

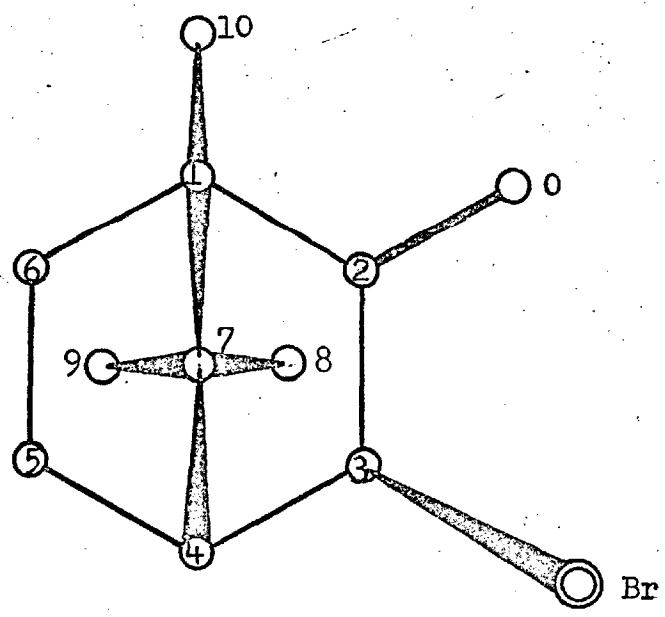
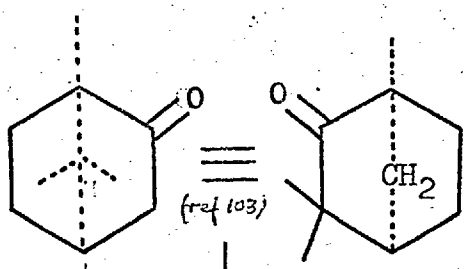


Figure 6.3. Absolute Configuration of (+)-3-Bromocamphor in the Conventional Chemical Representation.

below the plane of the paper. This confirms the degradative work of Fredga and Miettinen[110a], Porath[110b] and Freudenburg and Lwowski[119]. Not only are the absolute configurations of (+)-fenchone (6.II Fig.6.4) and (+)-α-pinene confirmed by this work, but also those of the degradation products mentioned briefly in chapter 5. The next Figure (6.4) shows the stereochemical relationships between (+)-camphor (6.I),(-)-camphoronic acid (6.III), and (-)-α-methyl-α-isopropyl succinic acid (6.IV) after

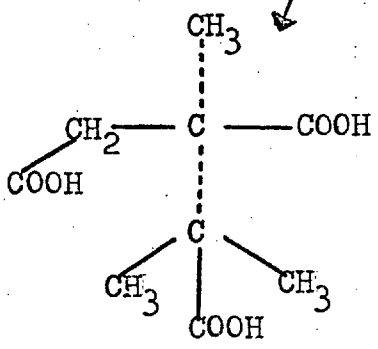
Porath; it also shows the relationships between (+)-fenchone (6.II), (-)-α-isopropyl glutaric acid (6.V) and (+)-isopropyl succinic acid (6.VI) due to Fredga and Miettinen. Since the last mentioned compound occupies a key position in the stereochemical correlation chart for the monoterpenes drawn up by Birch[109], the work described here, together with other X-ray work on substituted succinic acids[115,117], has confirmed the absolute stereochemistry of a wide range of compounds. In particular the unequivocal definition of configuration of (6.IV) from the present work, and by other, more recent X-ray studies[117], has confirmed the configurations assigned by Norin[148] to several members of the thujane group of monoterpenes. The time would seem right for an extensive review of monoterpene correlations, especially in the light of recent X-ray work; the brief outline given here and in chapter 5 does, however, show how the X-ray method, combined with known chemical data, can lead to extensive, and completely unequivocal assignments.

It was gratifying to note that, shortly after the completion of this work, two further determinations of the absolute configuration of (+)-camphor appeared in the literature : both agreed with the work described above. The first of these, by Northolt and Palm[149], followed

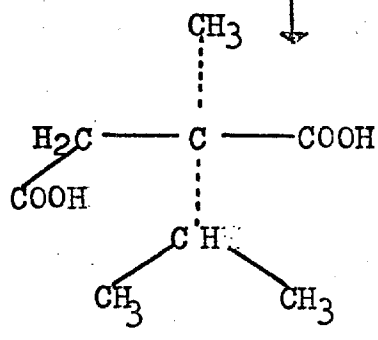


6.I (+)-camphor

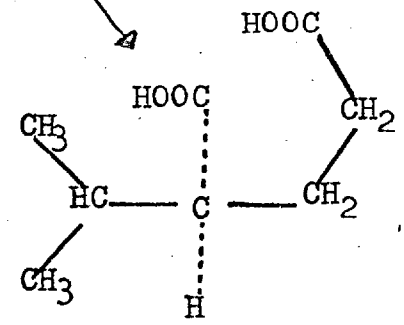
6.II (+)-fenchone



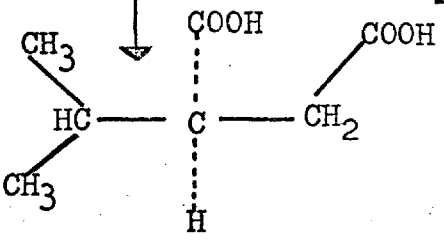
6.III. (-)-camphoronic acid.



6.IV. (-)-α-methyl-α'-isopropyl succinic acid.



6.V. (-)-α-isopropyl glutaric acid.



6.VI. (+)-isopropyl succinic acid.

Stereochemical Correlation Chart due to Birch[109]

Correlations of the thujane group[148] and (-)-methylisopulegone & (-)-menthone[117]

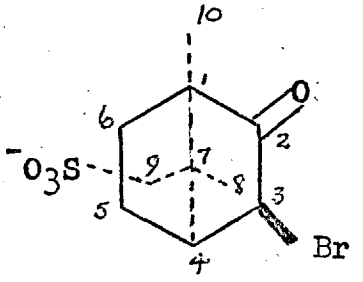
Figure 6.4.

exactly the same scheme as described for determination A (section 6.1). The 3-bromo- compound was studied, and W & K's parameters used to obtain the calculated inequalities for only 9 Bijvoet pairs. We had much earlier rejected this method since it gave an inconclusive concensus of anomalies over 18 pairs. This case shows the danger of resurrecting old structures from the literature, in order to carry out configurational work; the accuracy of the parameters used is frequently not good enough to guarantee the result.

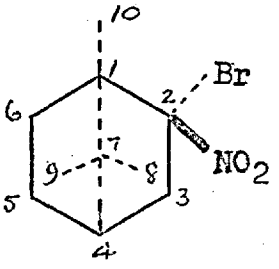
In their paper, Northolt and Palm cite the determination of the structure and absolute configuration of (+)-camphoroxime hydrobromide (H.A.J. Oonk, Ph.D. Thesis, Utrecht 1965). To the author's knowledge this work has not yet appeared in the chemical literature, a surprising omission, considering it's relevance to the monoterpenes.

More recently the crystal structure of retusamine as the (+)-3-bromocamphor-9(π)-sulphonate monohydrate has been published[150]. Using Br excited by CuKα radiation, the absolute configuration of both cation and anion have been established, that of the anion confirming the above assignments. This raises the possibility of using (+)-camphor-π-sulphonate salts (or their derivatives) as internal reference centres, to establish the absolute configuration of a complex organic cation.

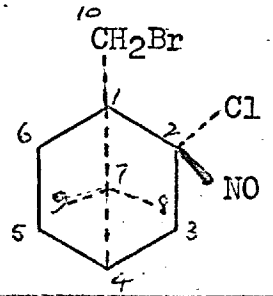
The substitution of bromine at C(3) in (+)-camphor gives rise to a third asymmetric centre. Figure 6.3 shows that the bromine is trans to the gem-dimethyl bridge (endo-configuration). The same configuration is found in the (+)-3-bromocamphor-trans-9(π)-sulphonate anion[150] (BCSO : 6.VII) and in bromo-isofenchone[151]; this contrasts with the cis-position adopted by the bulky halogen atom in (-)-2-bromo-2-nitrocamphane [137] (BNC : 6.VIII), and in (+)-10-bromo-2-chloro-2-nitroso-camphane[152] (BCNC : 6.IX).



6.VII. BCSO.[150]



6.VII. BNC.[137]*



6.IX. BCNC.[152]*

* see footnote [on page 125.

6.7. Discussion of the Structure.

Molecular Geometry.

The bond lengths and valence angles within the asymmetric unit are given in Tables 6.9, 6.10, together with their estimated standard deviations; again these probably represent realistic estimates. The parameters are shown for clarity in Figure 6.5(a) and (b). Comparison with the values obtained by W & K is not significant, due to the lack of refinement in their determination.

The bond lengths are, in general, unremarkable. The short bond C(3)-C(4), and the long bond C(4)-C(5), are the only ones which differ by more than 2.5σ from the accepted C-C single bond length of 1.539 Å[153]. This may not appear significant out of context, but is possibly a result of the strain due to the 'one-sided' substitution pattern. The overall average C-C distance (1.53Å) is close to the accepted average; however the average length on the substituted side of the six-membered ring, C(1)—C(4)[¥] is 1.50Å, while on the unsubstituted side, C(4)—C(1)[¥] it is 1.55Å. Comparable results have been found for BNC (1.52 & 1.58Å), and BCSO (1.53 & 1.56Å); the effect is not marked in BCNC (1.55 & 1.56Å), possibly due to the effect of the bulky Br atom at C(10).

¥ Numbering clockwise.

TABLE 6.9

(+)-3-Bromocamphor.

Intramolecular Bonded Distances (r) and their Estimated Standard Deviations (σ) in Ångstroms

	r	σ		r	σ
C(1) - C(2)	1.52	0.02	C(3) - C(4)	1.47	0.02
C(1) - C(6)	1.49	0.03	C(3) - Br	1.934	0.013
C(1) - C(10)	1.52	0.02	C(4) - C(5)	1.60	0.03
C(1) - C(7)	1.53	0.02	C(4) - C(7)	1.53	0.02
C(2) - C(3)	1.53	0.02	C(5) - C(6)	1.56	0.02
C(2) - O	1.20	0.01	C(7) - C(8)	1.56	0.03
C(7) - C(9)	1.55	0.02			

Average C - C single bond length : 1.53 ± 0.02 Å

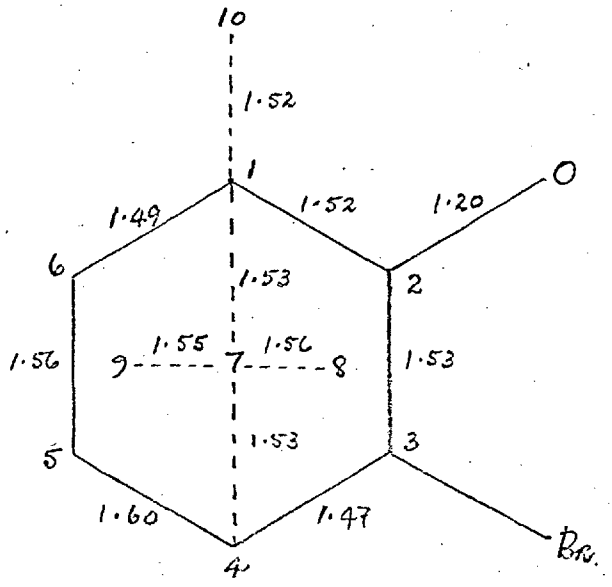


Figure 6.5 (a)

TABLE 6.10.

(+)-3-Bromocamphor.

Valence Angles (θ^{o}) and their Estimated Standard Deviations (σ)

	θ^{o}	σ^{o}		θ^{o}	σ^{o}
C(1)-C(2)-C(3)	105.1	0.8	C(3)-C(2)-O	126.4	1.0
C(1)-C(2)-O	128.4	1.1	C(3)-C(4)-C(5)	111.1	1.3
C(1)-C(6)-C(5)	104.3	1.4	C(3)-C(4)-C(7)	103.5	1.0
C(1)-C(7)-C(4)	94.4	1.2	C(4)-C(3)-Br	118.7	1.1
C(1)-C(7)-C(8)	112.8	1.4	C(4)-C(5)-C(6)	101.2	1.3
C(1)-C(7)-C(9)	112.4	1.2	C(4)-C(7)-C(8)	115.4	1.2
C(2)-C(1)-C(6)	104.3	1.3	C(4)-C(7)-C(9)	111.8	1.3
C(2)-C(1)-C(7)	101.8	1.2	C(5)-C(4)-C(7)	98.0	1.2
C(2)-C(1)-C(10)	111.6	1.1	C(6)-C(1)-C(7)	102.6	1.3
C(2)-C(3)-C(4)	102.2	1.0	C(6)-C(1)-C(10)	113.9	1.8
C(2)-C(3)-Br	113.1	1.0	C(7)-C(1)-C(10)	120.8	1.6
C(8)-C(7)-C(9)	109.5	1.4			

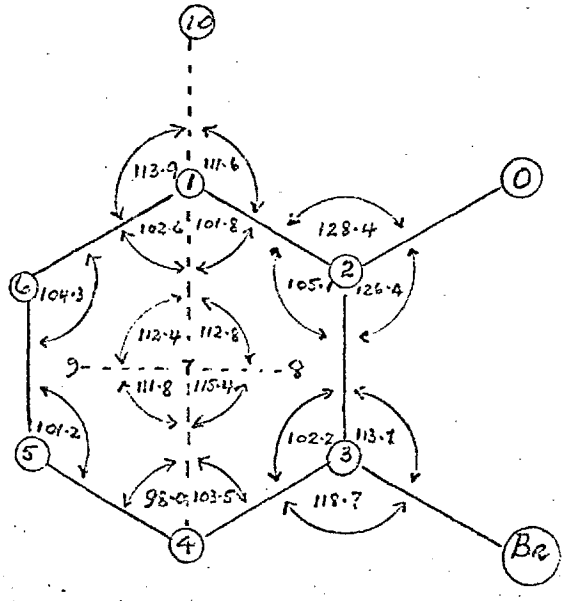


Figure 6.5 (b).

(For additional angles see above)

The C(3)-Br distance of 1.934 Å compares well with the average value for C-Br of 1.94 Å, quoted for the alkyl bromides[153]. The value in BCSO is, however, 0.05Å longer. The C=O distance of 1.20Å is exactly as determined for BCSO, and does not differ significantly from accepted averages[153].

The most interesting feature of Table 6.10 is the negative deviation from the tetrahedral value (109.47°) of the valence angles in the norbornane skeleton, C(1)→C(7), in (+)-3-bromocamphor (BC). Sim[154] has analysed this bicyclo[2,2,1]heptane system in terms of two fused cyclopentane rings having three corners in common, viz: C 2,3,4,7,1; C 5,6,4,7,1; (rings A & B). His theoretical analysis indicates that average values for the endocyclic valence angles should be approximately 100°; Table 6.11 shows the average values for rings A and B obtained here for BC, compared with the values for BCSO, BNC and BCNC. The results support Sim's work very well; in particular they show that the introduction of the ketonic oxygen at C(2) in BC and BCSO has little effect on the ring system.

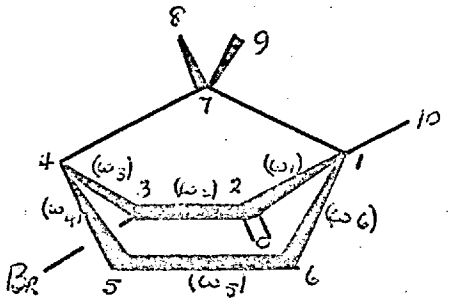
A noticeable feature of all compounds containing the norbornane skeleton is the consistently low value of the 'bridging' angle C(1)-C(7)-C(4). In the present structure it is 94.4°, comparing well with values of

93.1° in BCSO, 93.2° in BNC, and 95.0° & 91.2° in the two crysatllographically independent molecules of BCNC. Sim[154] has ascribed this effect to the eclipsed interactions of groupings at C(2), C(3), C(5), C(6); this would appear reasonable since the interactions are relieved to some extent in anti-7-norbornenyl p-bromobenzoate[155], anti-8-tricyclo-[3,2,1,$0^{2,4}$]octyl p-bromobenzene sulphonate[156], and p-bromobenzyl norbromide[157], and values for the 'bridge' angle of 96°, 97°, and 97°, respectively, are found.

The norbornane skeleton may also be regarded as a bridged cyclohexane ring, where the required <u>cis</u>-fusion of the bridge forces the ring into the boat conformation. This can be seen in Figure 6.2, and also in the perspective view of (+)-3-bromocamphor shown in 6.X below. The ideal conformation of the norbornane unit should consist of four four-atom planes, viz:

1,2,3,4; 1,6,5,4; 2,3,5,6; and 4,7,1,10;

table 6.12 shows the deviations (in Å) of the relevant atoms from the mean planes. The results for BC again compare well



6.X.

TABLE 6.11. Bicyclo[2,2,1]heptane system : average valence angles in the fused cyclopentane rings A & B.

	BC.	BCSO	BCNC		BNC
			1	2	
Ring A	101.4	99.7	101.1	100.4	101.3
Ring B	100.1	102.0	99.8	100.0	99.5

TABLE 6.12. Norbornane Skeleton : Deviations from mean planes (in Angstroms)

	BC.	BCSO	BCNC		BNC
			Mol 1.	Mol 2.	
C(1)	0.0241	-0.0124	-0.0287	0.0096	-0.0253
C(2)	-0.0354	0.0183	0.0421	-0.0139	0.0377
C(3)	0.0359	-0.0182	-0.0413	0.0143	-0.0384
C(4)	-0.0246	0.0123	0.0280	-0.0100	0.0261
C(1)	-0.0195	-0.0128	0.0030	-0.0021	0.0079
C(4)	0.0179	0.0119	-0.0030	0.0020	-0.0079
C(5)	-0.0261	-0.0174	0.0044	-0.0030	0.0113
C(6)	0.0277	0.0183	-0.0044	0.0031	-0.0113
C(2)	-0.0216	0.0105	-0.0259	-0.0234	0.0217
C(3)	0.0202	-0.0100	0.0250	0.0231	-0.0212
C(5)	-0.0199	0.0098	-0.0251	-0.0238	0.0206
C(6)	0.0212	-0.0103	0.0259	0.0241	-0.0211
C(4)	0.0293	-0.0050	0.0269	0.0055	0.0059
C(7)	-0.0140	0.0025	-0.0160	-0.0032	-0.0029
C(1)	-0.0495	0.0083	-0.0408	-0.0086	-0.0103
C(10)	0.0342	-0.0058	0.0299	0.0063	0.0073

with the values for BCSO, BNC, and BCNC; the deviations in all four compounds are small.

The strain-energy minimisation calculations* of Hendrickson[158] have provided theoretical geometrical parameters for the most energetically stable cyclohexane conformations[159]. His optimum values of dihedral angles ($\underline{\omega}$) and valence angles ($\underline{\theta}$) for the boat-form, are compared with the values computed (MOJO)/ for the cyclohexane ring in BC, BCSO, BNC, BCNC, in Table 6.13; The parameters involved are shown in 6.X, on the previous page. The results from the X-ray studies are very close, but differ significantly from the parameters for the minimum-energy form, showing the additional strain introduced by the presence of the gem-dimethyl bridge.

Table 6.14 shows the non-bonded intramolecular distances < 3.0 Å in BC. Robertson and his co-workers[152] cite the slightly longer distances from C(2) to C(7) and C(8) ⌐ (2.41 and 3.03 Å) compared with those from C(6) to C(7) and C(9) ⌐ (2.39 and 2.88 Å) in BCNC as indicative of the distorting effect of the bulky halogen atom cis to the gem-dimethyl bridge; a similar

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* see Appendix III for a brief discussion of this work.

/ see Appendix II. ⌐ the numbering of C(8), C(9), has been reversed from that in the original papers to conform with chemical convention.

TABLE 6.13.

Comparison of Observed Dihedral Angles (ω)° and Valence Angles (θ)° for the Cyclohexane Ring with Values Obtained from Minimum Energy Calculations[159].

Parameter	Theor. (159)	BC	BCSO	BCNC Mol 1	BCNC Mol 2	BNC
ω_1	52.1	77.8	73.8	73.9	67.6	72.7
ω_2	0.0	6.1	3.0	6.9	2.3	6.5
ω_3	52.1	65.1	69.3	65.9	71.5	68.9
ω_4	52.1	68.2	68.7	71.8	71.7	71.2
ω_5	0.0	4.4	2.9	0.7	0.5	1.8
ω_6	52.1	73.1	73.3	67.2	68.5	68.3
θ_1	112.0	104.3	104.2	107.6	108.4	105.2
θ_2	112.5	105.1	104.3	106.9	101.9	105.8
θ_3	112.5	102.2	103.7	100.2	104.4	102.5
θ_4	112.0	111.1	108.4	113.5	112.2	113.9
θ_5	112.5	101.2	100.1	103.7	98.2	100.0
θ_6	112.5	104.3	106.2	104.2	109.6	105.3

TABLE 6.14.

(+)-3-Bromocamphor.

Non-Bonded Intramolecular Distances (in Angstroms) < 3.0Å.

Br ⟶	
C(2)	2.90
C(4)	2.93

C(1) ⟶	
C(3)	2.42
C(4)	2.25
C(5)	2.40
C(8)	2.57
C(9)	2.56
O	2.45

C(2) ⟶	
C(4)	2.33
C(5)	2.86
C(6)	2.37
C(7)	2.37
C(8)	2.91
C(10)	2.51

C(3) ⟶	
C(5)	2.53
C(6)	2.93
C(7)	2.35
C(8)	2.85
O	2.45

C(4) ⟶	
C(6)	2.44
C(8)	2.56
C(9)	2.60

C(5) ⟶	
C(7)	2.36
C(9)	2.84

C(6) ⟶	
C(7)	2.36
C(9)	2.87
C(10)	2.52

C(7) ⟶	
C(10)	2.66

C(8) ⟶	
C(9)	2.54

C(10) ⟶	
O	2.91

pattern was noted for BNC. In the present case this distortion has been relieved due to a trans-substitution of Br at C(3). The table shows that the distances of C(2) and C(3) from C(7) and C(8) do not differ significantly from those of C(5) and C(6) to C(7) and C(9).

Intermolecular distances and Packing.

Figure 6.2 shows that the molecules pack in alternating layers parallel to the screw axes. This system is economical, but still allows clearances to be usually > 3.6 Å, as noted for BNC, and BCNC, which also crystallize in a space-group ($P2_12_12_1$) involving only screw axes. Table 6.15. shows all intermolecular distances less than 4.0 Å. Roman subscripts refer to atoms related to the set given in Table 6.4. by the following operations :

(i) $2-x, \frac{1}{2}+y, 1-z$; (ii) $2-x, \frac{1}{2}+y, -z$; (iii) $x, 1+y, z$;
(iv) $1-x, \frac{1}{2}+y, -z$.

TABLE 6.15. (+)-3-Bromocamphor : Intermolecular Distances

C(9) - $C(8)_i$	3.95 Å	O - $C(8)_{iv}$	3.59 Å
C(5) - Br_{ii}	3.88	Br - $C(8)_{iv}$	3.94
C(5) - $C(3)_{ii}$	3.92	C(5) - O_{iv}	3.88
C(6) - $C(8)_{iii}$	3.83	C(6) - O_{iv}	3.70
O - $C(3)_{iv}$	3.54	Br - O_{iv}	3.77

CHAPTER 7.

The Crystal and Molecular Structure of Humulene Bromohydrin : $C_{15}H_{25}OBr$.

7.1. Preliminary Work.

The crystals were supplied by Dr. J. K. Sutherland and Dr. M. D. Solomon. They are colourless prisms with extinction directions transverse to the needle axis, possibly indicative of a monoclinic crystal with a non-unique axis (a- or c-) parallel to the needle direction. Oscillation and Weissenberg photographs confirmed this (Laue symmetry 2/m), and showed that the crystals were stable to X-irradiation, giving excellent Weissenberg records after only 20 hours.

The photographs were indexed on a cell for which the absent spectra were :

$$h0l, \quad l \neq 2n; \qquad 0k0 \quad k \neq 2n;$$

thus defining the space group uniquely as $P2_1/c$.

Redefining c reduced the β-angle by $\approx 10^{\circ}$, and changed the absence conditions to :

$$h0\ell, \quad h + \ell \neq 2n; \qquad 0k0 \quad k \neq 2n;$$

i.e. the space group was transformed to $P2_1/n^{(160)}$. Cell parameters were obtained by a least-squares procedure (CEDI) applied to some 30 theta values measured from equatorial Weissenberg photographs.

Crystal Data.

Humulene Bromohydrin: $C_{15}H_{25}OBr$; Monoclinic $P2_1/n$: C_{2h}^5: No.14

$a = 6.07 \pm 0.01$ Å; $b = 19.54 \pm 0.02$ Å;

$c = 12.39 \pm 0.01$ Å; $\beta = 93.47^{\circ} \pm 0.25^{\circ}$;

$V = 1647$ Å^3; $D_x = 1.36 \pm 0.03$ g.cm.$^{-3}$ (by flotation)

$D_c = 1.37$ g.cm.$^{-3}$; for $Z = 4$ molecules/cell;

$M = 301.27$ (taking the standard $C^{12} = 12.00$);

$\mu = 38.81$ cm.$^{-1}$ for CuK_α ($\lambda_{mean} = 1.54178$);

$F(000) = 632$ electrons. Needle axis : a.

The layers 0kℓ-5kℓ were photographed using Ni-filtered CuK_α radiation (see Chapter 4), using a crystal of approximate dimensions : 0.5 x 0.25 x 0.20 mm. A total of 1922 reflection intensities were visually estimated, and placed on a common (arbitrary) scale by comparison with 206 common data, from the (similarly recorded) h0ℓ and h1ℓ layers, using the POLO program. A further 529

possible reflections in the Cu-sphere were treated as accidental absences, and included in the data list at a later stage. The absolute scale (K) was obtained during structure solution and refinement by comparing $\sum|F_o|$ and $\sum|F_c|$.

7.2. Structure Solution.

The co-ordinates of the bromine atom were obtained from a 3D Patterson map. The symmetry equivalent positions in $P2_1/n$ are :

$$\begin{array}{llll} 1; & \underline{x}, & \underline{y}, & \underline{z}; \\ 2; & -\underline{x}, & -\underline{y}, & -\underline{z}; \\ 3; & \tfrac{1}{2}-\underline{x}, & \tfrac{1}{2}+\underline{y}, & \tfrac{1}{2}-\underline{z}; \\ 4; & \tfrac{1}{2}+\underline{x}, & \tfrac{1}{2}-\underline{y}, & \tfrac{1}{2}+\underline{z}; \end{array} \qquad \ldots\ldots\ldots\ldots \ 7.1$$

The resultant vector set for the four bromine atoms in the unit cell consists of six pairs of centrosymmetrically related peaks, whose co-ordinates, with respect to the bromine position : $\underline{x}$, $\underline{y}$, $\underline{z}$, are given by :

$$\begin{array}{llll} 1; & \pm\,(& 2\underline{x}, & 2\underline{y}, & 2\underline{z},) \\ 2; & \pm\,(& -\tfrac{1}{2}+2\underline{x}, & -\tfrac{1}{2}, & -\tfrac{1}{2}+2\underline{z},) \\ 3; & \pm\,(& -\tfrac{1}{2}, & -\tfrac{1}{2}+2\underline{y}, & -\tfrac{1}{2},) \\ 4; & \pm\,(& -\tfrac{1}{2}, & -\tfrac{1}{2}-2\underline{y}, & -\tfrac{1}{2},) \\ 5; & \pm\,(& -\tfrac{1}{2}-2\underline{x}, & -\tfrac{1}{2}, & -\tfrac{1}{2}-2\underline{z},) \\ 6; & \pm\,(& -2\underline{x}, & 2\underline{y}, & -2\underline{z},) \end{array} \qquad \ldots\ldots \ 7.2$$

The full Patterson thus exhibits two Harker sections :

1: $\underline{x}$, $\frac{1}{2}$, $\underline{z}$, due to the 2_1 screw;

2: $\frac{1}{2}$, $\underline{y}$, $\frac{1}{2}$, due to the n-glide. .... 7.3.

Use of the Harker sections gave the co-ordinates of bromine as :

$\underline{x}$ = 0.093, $\underline{y}$ = 0.205 $\underline{z}$ = 0.247.

Using the phases given by the heavy atom ($\underline{B}$ = 3.0Å^2) a 3D electron-density map was computed (BOSS); reflections for which $|F_c| \leqslant 0.25|F_o|$ were omitted from the Fourier summation; $\underline{R}$ was 0.427. The nine atoms forming the macrocycle and fused cyclopropane ring* were readily identified, and possible positions for C(9) and C(10) were also given. The resolution was, however, poor at the positions expected for the substituent methyl groups and hydroxyl.

Nine carbon atoms (C(1) → C(8) & C(11)) were added to the structure factor calculation with $\underline{B}$ = 4.0Å^2; $\underline{R}$ fell to 0.338. The same rejection test was applied to the coefficients and the second map computed. This revealed all non-hydrogen atoms, but differentiation between C(13) and O was not possible from the electron-counts.

A third summation was performed to obtain optimum positions for the 17 atoms using Booth's method[161]. No observed structure amplitudes were rejected, and $\underline{R}$ was

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* The numbering scheme is shown in full in the pull-out diagram bound with the end-papers.

0.251. Distinction between C(13) and O was still not possible.

7.3. Refinement of the Structure.

The conventions set up at the beginning of section 6.4, on page 95, will be used here. The progress of the refinement is shown in Table 7.1 on page 135. The block-diagonal least-squares program BABA was used throughout.

Initially the positional parameters and estimated B-factors were allowed to vary for 3 cycles, together with an overall scale factor (K), (run I1). A weighting scheme of the Hughes type (Eq. 2.29) was used, with F^* set at 850 on the scale of the structure factors in Table 7.5, this gave reasonably constant values of $\sum w(|F_o| - |F_c|)^2$ over ranges of $|F_o|$ and $\sin^2\theta$. The R-factor fell to 0.178, but C(13) and O showed anomalous B-factors of 2.5 Å^2 and 7.5 Å^2, respectively lower and higher than the general level ($\approx$4.1 Å^2) for substituent atoms. The designation of the two peaks was interchanged and refinement continued (run I2) to 0.170. A bond-length calculation (ELSI) now showed sensible values for C(6)-C(13) and C(6)-O of 1.57 and 1.44 Å respectively; the B-factor shifts were minimal for the two atoms.

A difference map, with $(F_o - F_c)$ as coefficients in the Fourier series, showed no spurious features, but

revealed some anisotropy in the structure. All B-factors were thus converted into their anisotropic equivalent β_{ij}'s (Eq. 1.10). R fell to 0.122 after runs A1, A2.

The accidental absences were now included in the structure factor calculation at an observed value of $1/\sqrt{2}\,|F_o|_{min}$ in the relevant part of the intensity record. Some misindexing was detected and corrected, and two reflections (2,1,0; 0,0,2;) were omitted for suspected extinction. Two further cycles (run A3) gave an R-value of 0.125 over all reflections.

A second difference map suggested positions for all but three of the non-methyl hydrogen atoms (see Table 7.4). These positions compared well with those calculated using BONDLA. The latter program also showed very sensible geometry at this stage. For the final stages of refinement all 25 hydrogen atoms were included in the structure factor calculations, using the calculated positions, together with a B-factor equal to that of the carbon or oxygen to which they were bonded, plus 0.5Å^2. The hydrogen parameters were not refined. After four further cycles of refinement (runs M1,M2) the ratio S/E (see p. 100) was less than 0.10 for all parameters; the maximum positional shift on the last cycle was 0.0006Å. The final parameters, together with estimated standard deviations where appropriate, are shown in Tables 7.2, 7.3. Hydrogen positions

calculated from the data of Table 7.2, are shown compared with the observed values in Table 7.4. The data from these three tables were used in a final structure factor calculation, with the overall $|F_o|$ scale factor (K) from the final cycle. The overall R-factor was 0.114, but was 0.100 for the 1920 observed reflections not affected by extinction. The list is given in Table 7.5.

TABLE 7.1.

Humulene Bromohydrin : The Refinement Process.

Run.	Cycles.	-R-	Max.shift.Å.	$\sum w(\|F_o\| - \|F_c\|)^2$
I1	3	0.178	0.012	8380
I2	3	0.170	0.004	7725
A1	3	0.131	0.070	3476
A2	3	0.122	0.012	2256
A3	2	0.125*	0.0040	2236
M1	2	0.115*	0.0040	1842
M2	2	0.114*	0.0006	1831

* Overall R-factor (including accidental absences).

Analysis of shifts on the final cycle.

	x	y	z
Max. shift Å.	0.00048	0.00060	0.00036
Ave. shift Å.	0.00025	0.00020	0.00020

TABLE 7.2.

Humulene Bromohydrin.

Final Positional Parameters for the Non-Hydrogen Atoms (in fractional co-ordinates) together with their Estimated Standard Deviations (σ).

	x	σ_x	y	σ_y	z	σ_z
Br	0.08087	0.00015	0.20458	0.00004	0.25105	0.00008
C(1)	-0.10285	0.00134	0.28861	0.00036	0.25998	0.00056
C(2)	-0.17781	0.00127	0.31087	0.00033	0.14718	0.00055
C(3)	-0.19620	0.00125	0.38774	0.00035	0.12942	0.00052
C(4)	-0.15794	0.00111	0.43630	0.00031	0.22137	0.00048
C(5)	-0.35221	0.00124	0.44773	0.00033	0.29540	0.00053
C(6)	-0.38504	0.00111	0.40111	0.00036	0.39043	0.00050
C(7)	-0.45467	0.00115	0.32983	0.00036	0.35070	0.00058
C(8)	-0.28024	0.00130	0.27329	0.00036	0.33670	0.00058
C(9)	-0.27719	0.00118	0.52341	0.00033	0.30842	0.00052
C(10)	-0.15173	0.00113	0.51653	0.00033	0.20302	0.00050
C(11)	-0.00851	0.00139	0.34791	0.00037	0.08455	0.00055
C(12)	-0.34217	0.00156	0.26459	0.00037	0.08688	0.00061
C(13)	-0.19498	0.00140	0.40001	0.00043	0.47589	0.00057
C(14)	0.06909	0.00147	0.54889	0.00045	0.20561	0.00073
C(15)	-0.29349	0.00134	0.54110	0.00039	0.10552	0.00058
O	-0.57628	0.00095	0.43024	0.00030	0.44016	0.00046

TABLE 7.3.

Humulene Bromohydrin.

Final Anisotropic Thermal Parameters (β_{ij}'s) for the Non-Hydrogen Atoms.

Atom	β_{11}	β_{22}	β_{33}	β_{23}	β_{13}	β_{12}
Br	0.03613	0.00227	0.01151	-0.00020	0.00597	0.00254
C(1)	0.03333	0.00217	0.00577	0.00051	0.00181	-0.00137
C(2)	0.02976	0.00177	0.00606	-0.00132	-0.00647	-0.00203
C(3)	0.02973	0.00231	0.00508	-0.00164	0.00378	-0.00036
C(4)	0.02211	0.00205	0.00409	-0.00036	0.00038	-0.00020
C(5)	0.03022	0.00198	0.00514	-0.00013	0.00478	-0.00018
C(6)	0.02006	0.00289	0.00451	0.00136	0.00669	-0.00112
C(7)	0.01869	0.00248	0.00721	-0.00019	0.00344	-0.00372
C(8)	0.03020	0.00214	0.00654	0.00095	0.00422	-0.00007
C(9)	0.02733	0.00203	0.00514	-0.00090	0.00556	-0.00112
C(10)	0.02160	0.00226	0.00473	-0.00025	-0.00092	0.00180
C(11)	0.03841	0.00241	0.00554	-0.00041	0.01171	0.00178
C(12)	0.04194	0.00362	0.00555	-0.00276	-0.00341	-0.00482
C(13)	0.03318	0.00331	0.00519	-0.00095	-0.00097	-0.00063
C(14)	0.03259	0.00319	0.00865	-0.00056	0.00520	-0.00183
C(15)	0.03160	0.00277	0.00594	0.00116	-0.00452	0.00191
O	0.03315	0.00356	0.00850	-0.00048	0.01820	0.00495

The β_{ij}'s are parameters in Eq. 1.10.

TABLE 7.4.

Humulene Bromohydrin.

Observed* and Calculated/ Hydrogen Positions, given as Fractional Co-ordinates.

Atom	Bonded to	Calculated			Observed		
		x	y	z	x	y	z
H(1)	C(1)	-0.0012	0.3287	0.2954	-0.004	0.330	0.286
H(2)	C(3)	-0.3607	0.3973	0.0957	-0.374	0.389	0.053
H(3)	C(4)	-0.0013	0.4227	0.2607	-0.010	0.437	0.285
H(4)	C(5)	-0.5080	0.4490	0.2493	-	-	-
H(5)	C(7)	-0.5670	0.3104	0.4072	-0.510	0.270	0.360
H(6)	C(7)	-0.5407	0.3366	0.2730	-0.531	0.349	0.266
H(7)	C(8)	-0.2002	0.2633	0.4149	-0.165	0.281	0.440
H(8)	C(8)	-0.3660	0.2281	0.3079	-0.359	0.235	0.264
H(9)	C(9)	-0.4100	0.5599	0.3033	-	-	-
H(10)	C(9)	-0.1725	0.5333	0.3798	-0.167	0.534	0.398
H(11)	C(11)	-0.0042	0.3402	-0.0012	-0.017	0.340	-0.002
H(12)	C(11)	0.1569	0.3543	0.1192	0.138	0.356	0.091
H(13)	O	-0.7162	0.4511	0.4766	-	-	-
H(14)	C(12)	-0.3956	0.2805	0.0064	-	-	-
H(15)	C(12)	-0.4305	0.2260	0.1688	-	-	-
H(16)	C(12)	-0.3231	0.2500	0.0459	-	-	-
H(17)	C(13)	-0.1460	0.4501	0.5038	-	-	-
H(18)	C(13)	-0.0695	0.3974	0.4504	-	-	-
H(19)	C(13)	-0.2305	0.3492	0.5356	-	-	-
H(20)	C(14)	0.0733	0.6033	0.1932	-	-	-
H(21)	C(14)	0.1352	0.5415	0.1444	-	-	-
H(22)	C(14)	0.1747	0.5223	0.2826	-	-	-
H(23)	C(15)	-0.2893	0.5955	0.0931	-	-	-
H(24)	C(15)	-0.4685	0.5127	0.1096	-	-	-
H(25)	C(15)	-0.2296	0.5302	0.0413	-	-	-

* From difference map following run A3. / Using BONDLA.

TABLE 7.5.

Humulene Bromohydrin.

Final Observed and Calculated Structure Factors.

The Format of the Table is :

*	h	k
l	50 $\lvert F_o \rvert$	50 F_c
.	.	.

The accidental absences are marked -L- (less-than). The 2,0,0, reflection was partially obscured by the backstop. The two reflections omitted for suspected extinction were (in the same format) :

*	2	1	
0	2010	3429	($\sin^2\theta$ = 0.0663)
*	0	0	
2	7520	-9391	($\sin^2\theta$ = 0.0155)

*	0	0	
4	3591	3625	
6	4887	-4112	
8	2155	1970	
10	791	-654	
12	406	421	
14	194	-170	
*	0	1	
1	847	823	
2	459	520	
3	2292	1919	
4	1719	-1354	
5	925	855	
6	1136	1029	
7	253	209	
8	441	332	
9	910	-818	
10	396	313	
11	167	171	L
12	166	57	L
13	311	-234	
14	137	27	L
15	109	-28	L
*	0	2	
0	2887	-2767	
1	1432	1391	
2	3900	3666	
3	5900	5714	
4	2275	-2410	
5	1713	-1725	
6	3074	2588	
7	1142	1011	
8	2945	-2653	
9	305	-255	
10	2468	2265	
11	529	409	
12	1670	-1598	
13	438	-350	
14	332	304	
15	456	358	
*	0	3	
1	328	244	
2	2455	2265	
3	611	476	
4	2816	2439	
5	784	-703	
6	721	695	
7	129	-129	L
8	449	-278	
9	376	-363	
10	163	-101	L
11	167	202	L
12	659	563	
13	154	72	L
14	134	-119	L
15	257	214	
*	0	4	
0	3955	3924	
1	2545	2671	
2	5870	-5507	
3	4938	-4747	
4	2756	2727	
5	5554	5439	
6	1291	-1207	
7	2404	-2103	
8	144	-81	L
9	1836	1540	
10	164	-122	L
11	530	-407	
12	518	444	
13	215	173	
14	132	-144	L
15	380	-277	
*	0	5	
1	2081	-2042	
2	2547	2517	
3	2142	-1812	
4	538	508	
5	388	342	
6	493	362	
7	382	365	
8	293	-290	
9	222	-189	
10	165	-85	L
11	167	-155	L
12	163	93	L
13	150	155	L
14	128	-169	L
15	97	35	L
*	0	6	
0	1634	-1295	
1	6001	-5416	
2	2082	-1998	
3	3146	3144	
4	107	-57	L
5	3023	-2698	
6	541	462	
7	2968	2577	
8	150	157	L
9	1193	-1154	
10	235	-227	
11	167	-45	L
12	228	199	
13	586	-511	
14	124	145	L
15	496	416	
*	0	7	
1	1886	-1550	
2	882	831	
3	392	-368	
4	276	-335	
5	386	379	
6	132	-76	L
7	404	320	
8	943	-745	
9	323	294	
10	167	142	L
11	166	-98	L
12	159	-158	L
13	143	73	L
14	119	-175	L
15	82	-33	L
*	0	8	
0	5329	-4795	
1	710	854	
2	4583	4070	
3	3863	-3576	
4	3603	-3095	
5	2137	1987	
6	1998	1975	
7	1837	-1619	
8	1252	-1053	
9	1159	977	
10	1207	1030	
11	1190	-1052	
12	311	-222	
13	138	109	L
14	113	-57	L
15	69	41	L
*	0	9	
1	156	119	
2	623	-634	
3	119	35	L
4	1465	-1269	
5	134	182	L
6	451	-365	
7	152	108	L
8	160	188	
9	406	371	
10	167	168	L
11	163	119	L
12	151	-146	L
13	132	60	L
14	105	-95	L
*	0	10	
0	3339	3237	
1	2638	-2599	
2	3520	-3271	
3	1157	1046	
4	3203	2895	
5	1009	-1000	
6	1727	-1666	
7	156	100	L
8	2373	2255	
9	167	35	L
10	1562	-1380	
11	160	-133	L
12	620	429	
13	126	170	L
14	557	-457	
*	0	11	
1	1089	901	
2	366	-299	
3	535	596	
4	395	344	
5	928	-793	
6	376	321	
7	227	-249	
8	907	-877	
9	410	354	
10	329	318	
11	155	208	L
12	140	108	L
13	117	-77	L
*	0	12	
0	3881	-3560	
1	2620	-2088	
2	4392	4043	
3	1764	1400	
4	3195	-2891	
5	1777	-1546	
6	2115	1923	
7	164	167	L
8	1800	-1521	
9	782	730	
10	790	706	
11	424	323	
12	458	-301	
13	107	-46	L
*	0	13	
1	404	344	
2	145	-85	L
3	786	702	
4	306	263	
5	158	129	L
6	163	205	L
7	706	646	
8	167	179	L
9	233	298	
10	221	196	
11	451	-330	
12	123	20	L
*	0	14	
0	2761	1426	
1	1792	1726	
2	2175	-1973	
3	905	-859	
4	2716	2375	
5	1692	1483	
6	1833	-1643	
7	1498	-1369	
8	407	357	
9	908	743	
10	900	-752	
11	734	-590	
12	653	595	
*	0	15	
1	157	-99	L
2	159	60	L
3	644	620	
4	164	-60	L
5	814	-684	
6	410	-305	
7	471	-372	
8	398	334	
9	155	-25	L
10	283	244	
11	175	174	
12	340	-269	
*	0	16	
0	796	-663	
1	3272	-2817	
2	164	99	L
3	2242	1948	
4	236	-186	
5	1253	-1042	
6	408	341	
7	1008	851	
8	157	-175	L
9	775	-661	
10	131	-101	L
11	111	102	L
*	0	17	
1	166	18	L
2	668	-615	
3	167	52	L
4	670	549	
5	166	-48	L
6	164	115	L
7	158	30	L
8	149	-149	L
9	334	-266	
10	119	-179	L
11	231	148	
*	0	18	
0	290	-164	
1	2009	1663	
2	579	445	
3	1415	-1215	
4	810	-507	
5	1171	969	
6	630	503	
7	1038	-857	
8	196	-144	
9	784	660	
*	0	19	
1	165	35	L
2	165	109	L
3	163	41	L
4	160	-77	L
5	155	35	L
6	149	-32	L
7	139	103	L
8	356	324	
*	0	20	
0	1485	1305	
1	598	-533	
2	1246	-994	

3	762	621		13	396	-302		-11	138	-64	L	-3	82	138					
4	1249	1018		14	216	-225		-10	1084	-1144		-2	4059	4026					
5	356	-344		15	435	337		-9	1013	1021		-1	1220	1304					
6	1239	-1011		*	1	2		-8	1320	1213		0	2197	2412					
7	125	134	L	-15	307	309		-7	1085	-1044		1	402	-397					
8	908	684		-14	112	-52	L	-6	1654	-1756		2	3794	3641					
*	0	21		-13	128	-109	L	-5	2111	2228		3	767	-716					
1	151	-194	L	-12	273	258		-4	953	-768		4	2226	-2475					
2	210	-213		-11	757	-761		-3	102	-196		5	702	-740					
3	205	213		-10	502	490		-2	1445	-1471		6	1253	1349					
4	140	-60	L	-9	437	313		-1	2329	-2589		7	1038	948					
5	132	98	L	-8	1117	-1065		0	3918	3916		8	357	-340					
6	299	252		-7	653	-504		1	805	-915		9	327	-426					
*	0	22		-6	1137	1008		2	2080	-2338		10	995	977					
0	1494	-1234		-5	690	-658		3	468	465		11	137	40					
1	195	142		-4	2076	-1988		4	1396	1627		12	738	-685					
2	1381	1168		-3	2579	2555		5	1188	901		13	117	-72					
3	371	284		-2	901	-835		6	707	-872		14	97	-88					
4	1487	-1081		-1	1934	-2213		7	777	799		15	64	-46					
5	116	6	L	0	5770	-5532		8	299	210		*	1	7					
6	103	811	L	1	4248	3876		9	1443	-1378		-15	265	-274					
*	0	23		2	5057	5076		10	864	-728		-14	278	171					
1	122	144	L	3	3555	-3626		11	138	-40	L	-13	440	447					
2	119	106	L	4	218	-208		12	731	642		-12	453	-409					
3	161	-244		5	2643	3000		13	122	-161	L	-11	434	-395					
4	212	-183		6	519	-372		14	327	-276		-10	872	740					
*	1	0		7	2139	-2435		15	75	178	L	-9	134	39					
-15	90	-8	L	8	1315	-1392		*	1	5		-8	803	-686					
-13	128	121	L	9	545	520		-15	80	-128	L	-7	1186	-1192					
-11	1069	-1232		10	507	418		-14	106	-103	L	-6	2742	2802					
-9	731	723		11	438	528		-13	123	266	L	-5	2053	2046					
-7	1609	-1861		12	234	-164		-12	910	967		-4	3012	-3048					
-5	3093	3358		13	124	-86	L	-11	240	-190		-3	722	-740					
-3	5939	-6663		14	107	-12	L	-10	984	-963		-2	1707	1866					
-1	1341	-1344		15	81	-115	L	-9	921	899		-1	1497	1300					
1	7881	7757		*	1	3		-8	1909	1847		0	4461	-4687					
3	488	630		-15	406	431		-7	1318	-1190		1	1191	-1236					
5	1947	-2198		-14	383	377		-6	1994	-2052		2	1672	1822					
7	456	473		-13	127	110	L	-5	373	-248		3	563	503					
9	866	-857		-12	272	-215		-4	3818	4144		4	1321	-1337					
11	938	924		-11	240	114		-3	1102	-989		5	293	-296					
13	307	-201		-10	1061	1046		-2	4074	-4062		6	2230	2276					
15	641	514		-9	1394	-1297		-1	932	744		7	1628	1648					
*	1	1		-8	1817	-1751		0	3671	3788		8	911	-883					
-15	90	37	L	-7	1281	1366		1	680	607		9	662	-631					
-14	276	-241		-6	1542	1573		2	3760	-3887		10	391	349					
-13	748	695		-5	2000	-2074		3	2493	2327		11	386	319					
-12	193	-257		-4	1910	-2360		4	2270	2402		12	573	-553					
-11	1015	-1084		-3	1934	1857		5	573	465		13	321	-394					
-10	423	-383		-2	4027	4348		6	1805	-1967		14	92	188					
-9	1759	1734		-1	5361	-5694		7	115	-30	L	15	52	24					
-8	116	26	L	0	3477	-3377		8	1508	1577		*	1	8					
-7	2711	-3049		1	3318	3342		9	896	-954		-15	158	151					
-6	1611	-1760		2	5459	4624		10	1360	-1085		-14	542	-645					
-5	2847	3315		3	4610	-4613		11	138	187	L	-13	455	-350					
-4	1150	1102		4	3218	-3248		12	296	216		-12	405	347					
-3	4849	-5547		5	3106	3300		13	120	28	L	-11	334	323					
-2	869	852		6	1083	1071		14	284	-245		-10	138	33					
-1	3923	5052		7	1330	-1363		15	71	98	L	-9	136	46					
0	694	1249		8	931	-957		*	1	6		-8	936	922					
1	4362	-4549		9	317	360		-15	75	71	L	-7	829	770					
2	710	-676		10	544	478		-14	102	-131	L	-6	899	-830					
3	4614	4950		11	875	-843		-13	296	487		-5	1303	-1250					
4	-1284	-1011		12	269	-259		-12	420	-468		-4	199	203					
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6	336	-363		14	211	-60		-10	931	955		-2	1994	-2121					
7	2049	2244		15	157	-192		-9	187	168		-1	2061	-2408					
8	784	522		*	1	4		-8	1242	-1236		0	4588	4672					
9	1513	-1488		-15	84	56	L	-7	258	-200		1	67	178					
10	634	-602		-14	109	-73	L	-6	1119	1140		2	1289	-1443					
11	758	669		-13	125	-183	L	-5	337	351		3	189	127					
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5	852	789		•12	282	-194		4	1519	-1371		-2	943	919			
6	972	-1068		•11	868	-795		5	1336	1202		-1	135	-131	L		
7	124	-77	L	•10	271	-169		6	333	225		0	139	-43	L		
8	788	819		-9	1355	1113		7	1381	-1310		1	192	223			
9	335	326		-8	433	383		8	138	•117	L	2	795	640			
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11	135	-57	L	-6	128	-5	L	10	126	111	L	4	586	-573			
12	125	109	L	-5	2233	2305		11	360	•296		5	309	287			
13	109	104	L	-4	1140	-1217		12	304	•235		6	1113	1084			
14	86	-70	L	-3	3278	-3154		13	238	207		7	327	•246			
*	1	9		-2	108	75	L	*	1	14		8	804	-751			
-14	474	-456		-1	2859	3160		-12	259	•232		9	166	157			
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-12	394	349		1	3874	-3655		-10	123	25	L	11	341	-201			
-11	783	732		2	463	-365		-9	295	249		*	1	17			
-10	138	-130	L	3	1928	1863		-8	137	94	L	•10	615	581			
-9	1315	-1171		4	1066	969		-7	959	•933		-9	112	128	L		
-8	593	512		5	2266	-2106		-6	137	28	L	-8	1037	•965			
-7	1511	1429		6	516	-430		-5	331	226		-7	130	20	L		
-6	1528	-1491		7	1849	1805		-4	1106	933		-6	1059	931			
-5	1871	-2056		8	138	-80	L	-3	818	677		-5	137	-130	L		
-4	877	922		9	1634	-1541		-2	1977	-1842		-4	1526	•1372			
-3	4368	4446		10	134	65	L	-1	1400	1428		-3	783	-734			
-2	1905	-1775		11	731	722		0	1483	1423		-2	2077	1895			
-1	3775	-3701		12	294	278		1	1008	•982		-1	1103	1024			
0	1414	1455		13	385	-389		2	1804	-1788		0	1378	•1312			
1	3469	3244		*	1	12		3	318	276		1	138	66	L		
2	1201	-1172		-13	88	-71	L	4	1342	1290		2	1526	1393			
3	3492	-3464		•12	109	-3	L	5	543	•458		3	138	101	L		
4	1520	1538		-11	214	196		6	755	•626		4	1512	•1369			
5	1920	1991		-10	420	362		7	196	191		5	137	182	L		
6	1217	-1264		-9	477	-424		8	385	252		6	944	856			
7	1251	-1250		-8	1015	-1031		9	521	•451		7	314	215			
8	947	900		-7	744	657		10	269	-189		8	449	-582			
9	1136	1037		-6	1101	952		11	104	24	L	9	108	-121	L		
10	138	83	L	-5	1511	-1447		12	84	-161	L	10	93	147	L		
11	296	-200		-4	598	525		13	44	-85	L	*	1	18			
12	420	354		-3	1635	1395		*	1	15		-10	84	-210	L		
13	104	70	L	-2	796	-682		-12	290	202		-9	191	-129	L		
14	79	166	L	-1	554	-641		-11	101	40	L	-8	114	-57	L		
*	1	10		0	275	164		-10	570	-478		-7	325	213			
-14	78	116	L	1	1562	1465		-9	127	104	L	-6	775	-653			
-13	103	-79	L	2	833	-851		-8	1054	902		-5	133	-82	L		
-12	511	-579		3	1292	-1313		-7	952	•847		-4	1360	1162			
-11	186	-252		4	174	195		-6	1089	-967		-3	137	-58	L		
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-9	138	-37	L	6	650	-568		-4	1652	1504		-1	517	-383			
-8	573	-582		7	546	-534		-3	757	-578		0	1016	914			
-7	317	-243		8	705	-728		-2	1295	-1096		1	704	608			
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-4	156	-187		11	481	-315		1	1427	-1339		4	939	904			
-3	1940	-1762		12	104	26	L	2	1856	-1731		5	419	325			
-2	899	819		13	382	330		3	1344	1248		6	404	-309			
-1	912	976		*	1	13		4	2280	2116		7	341	-271			
0	395	-353		•13	363	-370		5	827	-797		8	443	430			
1	1701	-1802		•12	247	-181		6	1553	-1396		9	414	345			
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3	1891	1875		•10	129	86	L	8	325	225		*	1	19			
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5	2006	•2032		-8	1252	-1146		10	619	-530		-8	616	528			
6	125	113	L	-7	1898	1662		11	474	418		-7	380	224			
7	1584	1676		-6	2101	2034		12	204	230		-6	687	-533			
8	304	-249		-5	1609	-1501		*	1	16		-5	1082	-836			
9	138	-27	L	-4	1168	-1098		-10	628	633		-4	765	650			
10	546	559		-3	1779	1704		-9	170	•233		-3	845	739			
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13	392	-334		0	1238	-1161		-6	869	731		0	816	784			
14	69	5	L	1	2385	2388		-5	277	286		1	1343	1103			
*	1	11		2	1879	1880		-4	1499	-1404		2	953	-854			
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	6	379	-283		-2	2843	-3108		1	4486	3458		-5	636	607
	7	521	-416		2	1805	-1182		2	727	*788		-4	810	-733
	8	422	364		4	532	-258		3	1534	-1448		-3	1638	*1842
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	-7	353	-240		12	554	358		7	1698	-1860		1	1644	*1900
	-6	569	452		*	2	1		8	586	721		2	930	779
	-5	119	83	L	-12	313	-304		9	1014	1170		3	2642	2623
	-4	700	-530		-11	944	-1024		10	523	*634		4	251	231
	-3	804	-706		-10	182	172	L	11	183	*248	L	5	1533	*1706
	-2	448	395		-9	914	862		12	173	94	L	6	318	245
	-1	761	687		-8	1302	-1416		*	2	4		7	448	548
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	4	425	-343		-3	1291	-1262		-8	661	747		12	196	182
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	6	464	433		-1	1292	1548		-6	1702	-1736		*12	170	121
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	4	159	-67		-11	185	172	L	9	571	*525		3	3091	*3166
	5	1013	*849		-10	182	-180	L	10	453	*516		4	2552	*2582
	6	193	165		-9	347	403		11	182	*362	L	5	2727	3133
	7	798	648		-8	161	20	L	12	171	-71	L	6	744	744
	*	1	22		-7	933	-860		*	2	5		7	959	*1004
	-7	473	310		-6	565	612		-12	176	*163	L	8	253	219
	-6	83	-46	L	-5	692	735		-11	521	*629		9	1156	1293
	-5	324	-202		-4	1113	-1265		-10	184	142	L	10	369	401
	-4	101	132	L	-3	253	232		-9	1127	1205		11	614	*877
	-3	106	140	L	-2	2378	2618		-8	412	513		12	162	-42
	-2	110	-168	L	-1	836	991		-7	2103	-2215		*	2	8
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	2	109	-53	L	3	4543	4107		-3	3436	-3689		-9	368	-297
	3	235	-255		4	2696	-2404		-2	685	708		-8	435	-415
	4	99	157	L	5	126	-93	L	-1	3714	4288		-7	827	887
	5	532	363		6	1871	1975		0	291	-28		-6	594	738
	6	80	8	L	7	154	-27	L	1	4182	-4358		-5	728	-706
	7	243	-203		8	1590	-1760		2	146	40		-4	1647	*1689
	*	1	23		9	1040	-1193		3	4294	4307		-3	141	-134
	-5	895	-784		10	185	129	L	4	725	563		-2	1417	1389
	-4	293	-254		11	184	116	L	5	1873	-1992		-1	3093	*3340
	-3	990	926		12	174	89	L	6	871	857		0	2455	*2517
	-2	95	58	L	*	2	3		7	2010	2234		1	2257	2240
	-1	1229	-1064		-12	507	621		8	490	*587		2	1279	1242
	0	98	-69	L	-11	740	832		9	772	*878		3	875	-858
	1	389	809		-10	633	-729		10	262	*274		4	643	-645
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	3	879	-686		-8	461	437		12	169	*102	L	6	518	559
	4	571	-402		-7	1036	1098		*	2	6		7	173	-118
	5	588	445		-6	1830	-1864		-12	388	433		8	256	-224
	*	2	0		-5	2446	-2765		-11	580	*694		9	292	296
	-12	626	685		-4	2765	3292		-10	185	213	L	10	183	213
	-10	1310	-1462		-3	4015	4728		-9	510	562		11	174	*46
	-8	932	988		-2	2023	-2143		-8	171	143	L	12	157	-47

	2	9		8	524	-709		7	685	*750		-8	143	-255	L				
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3	2459	2449		-1	388	-281		0	951	-1042		8	270	-325					
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-11	343	-405		11	149	102	L	-10	135	*197	L	1	851	-924					
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-7	435	-402		-9	503	-647		-6	182	43	L	5	597	-733					
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1	400	-367		-1	1224	-1313		2	185	220	L	-4	316	297					
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-9	488	-490		-10	158	-106	L	-5	1142	-1281		-5	462	-556					
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-3	765	-644		-4	511	544		1	1571	1677		1	535	589					
-2	1848	2173		-3	712	700		2	523	490		2	556	882					
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5	243	295		4	258	274		9	262	410		-5	112	-147	L				
6	1157	1415		5	865	1022			2	18		-4	426	-403					
7	183	-274	L	6	370	-368		-9	177	*237		-3	131	18	L				

-2	333	373			3	3		-5	168	*157	L	1	620	-526					
-1	240	246		-10	560	510		-4	3408	-3507		2	419	-246					
0	482	-560		-9	548	-443		-3	1495	-1333		3	357	-328					
1	337	-293		-8	440	-360		-2	3964	4065		4	917	757					
2	268	271		-7	684	-665		-1	259	149		5	519	-438					
3	127	216	L	-6	669	-523		0	4174	-3984		6	204	*57	L				
4	118	-190	L	-5	151	-61	L	1	326	*241		7	210	30	L				
6	228	216		-4	190	-39		2	3667	3249		8	212	-222	L				
*	2	23		-3	577	491		3	569	419		9	207	174	L				
-4	360	457		-2	1084	1011		4	2602	-2544		10	195	408	L				
-3	107	97	L	-1	91	-65		5	562	*458		*	3	10					
-2	360	-440		0	522	-465		6	1572	1615		-10	230	136	L				
-1	262	-328		1	998	839		7	571	567		-9	1026	1074					
0	334	430		2	114	-55	L	8	1148	-1229		-8	367	351					
1	328	434		3	1299	1083		9	212	174	L	-7	1389	*1844					
2	497	-609		4	879	707		10	292	332		-6	353	341					
3	102	-149	L	5	565	411		*	3	7		-5	2222	2571					
4	413	600		6	506	-425		-10	514	455		-4	755	-743					
*	3	0		7	387	-370		-9	590	508		-3	1629	*1894					
-9	918	796		8	502	-516		-8	774	*695		-2	560	451					
-7	1185	-1175		9	211	117	L	-7	198	-84	L	-1	1616	1410					
-5	1411	1669		10	210	216	L	-6	529	430		0	1179	*1019					
-3	332	-570		*	3	4		-5	175	*157	L	1	2466	*2638					
1	2898	-3466		-10	1236	-1372		-4	1202	-1142		2	676	540					
3	4964	4180		-9	589	523		-3	614	*451		3	2523	2461					
5	3538	-3377		-8	487	432		-2	412	*337		4	1402	*1135					
7	1075	1044		-7	455	-447		-1	141	*205	L	5	700	-584					
9	988	-980		-6	2204	-2345		0	141	18	L	6	1443	1348					
*	3	1		-5	582	-503		1	381	296		7	599	586					
-10	992	-963		-4	2756	3025		2	151	19	L	8	557	-525					
-9	1007	-1065		-3	871	-896		3	787	676		9	643	-766					
-8	623	720		-2	1483	-1642		4	172	157	L	10	189	69	L				
-7	670	-640		-1	1776	1763		5	1103	-1087		*	3	11					
-6	1339	1220		0	3059	3048		6	195	141	L	-10	194	123	L				
-5	938	834		1	1924	-1812		7	458	*414		-9	206	93	L				
-4	1337	1117		2	3086	-2838		8	298	245		-8	211	-244	L				
-3	854	728		3	1220	1044		9	211	270	L	-7	473	418					
-2	841	-738		4	2804	2663		10	204	32	L	-6	568	565					
-1	226	266		5	1800	-1462		*	3	8		-5	203	162	L				
0	578	625		6	1858	-1861		-10	465	*449		-4	197	-77	L				
1	557	592		7	678	650		-9	212	*388	L	-3	468	-391					
2	203	140		8	2001	1947		-8	1389	1507		-2	528	-542					
3	121	74	L	9	212	96	L	-7	810	778		-1	451	-349					
4	443	211		10	1109	-1244		-6	1900	-1828		0	1192	1192					
5	223	-217		*	3	5		-5	1804	-1747		1	644	*444					
6	350	-303		-10	212	-214	L	-4	2563	2516		2	190	-51	L				
7	190	-77	L	-9	210	-91	L	-3	1325	1264		3	872	814					
8	203	-21	L	-8	201	-51	L	-2	2804	-2786		4	201	-190	L				
9	632	486		-7	536	448		-1	1805	-1750		5	207	-191	L				
10	211	-69	L	-6	703	-657		0	1610	1372		6	211	*283	L				
*	3	2		-5	1292	-1104		1	1835	1610		7	212	219	L				
-10	599	588		-4	590	-541		2	1643	-1494		8	208	152	L				
-9	1675	-1652		-3	380	-292		3	1178	-1115		9	198	-47	L				
-8	1535	-1403		-2	464	-410		4	1813	1452		10	181	-49	L				
-7	2603	2714		-1	1243	1194		5	1843	1667		*	3	12					
-6	1090	1016		0	466	321		6	1898	-1875		-10	147	57	L				
-5	2132	-2122		1	861	709		7	1176	-1154		-9	852	-874					
-4	2227	-2197		2	1663	-1118		8	1038	1057		-8	219	89	L				
-3	3241	3462		3	576	-532		9	416	446		-7	1405	1425					
-2	3261	3440		4	315	228		10	1059	*593		-6	597	-554					
-1	2236	-2570		5	455	361		*	3	9		-5	1250	*1087					
0	2064	-2379		6	186	238	L	-10	205	249	L	-4	643	603					
1	1561	1760		7	344	-223		-9	211	171	L	-3	1515	1591					
2	2079	2114		8	208	153	L	-8	211	171	L	-2	874	776					
3	2218	-2089		9	212	-106	L	-7	652	588		-1	2048	*2087					
4	669	-519		10	208	90	L	-6	199	112	L	0	947	-916					
-5	1036	957		*	3	6		-5	464	*472		1	2364	2475					
6	1617	1567		-10	845	716		-4	674	*573		2	343	249					
7	271	-295		-9	211	166	L	-3	173	74	L	3	1656	*1670					
8	455	-482		-8	1781	-1714		-2	472	341		4	969	-892					
9	517	451		-7	775	-717		-1	463	294		5	1030	948					
10	211	-163	L	-6	2277	2408		0	163	69	L	6	1038	1040					

7	840	-825		-5	205	-66	L	2	802	757		10	324	-245			
8	203	-116	L	-4	1106	-1118		3	658	731		*	4	3			
9	331	369		-3	596	561		4	570	*561		-10	760	-826			
10	172	354	L	-2	1403	1286		5	490	*498		-9	291	-140			
*	3	13		-1	560	-434		6	211	202		-8	138	10	L		
-10	177	307	L	0	1405	-1327		*	3	21		-7	718	603			
-9	194	-104	L	1	212	-109	L	-2	155	*163	L	-6	1035	*1122			
-8	204	-267	L	2	1765	1736		-1	158	39	L	-5	1796	*1847			
-7	210	-266	L	3	210	-153	L	0	158	*143	L	-4	1462	1516			
-6	212	167	L	4	1306	-1542		1	156	*141	L	-3	2253	2158			
-5	422	355		5	201	-49	L	2	151	187	L	-2	533	-502			
-4	208	256	L	6	771	836		3	143	86	L	-1	1235	*1308			
-3	411	369		7	180	136	L	*	3	22		0	889	908			
-2	703	590		8	765	-796		-1	670	*713		1	1252	1440			
-1	349	-271		*	3	17		0	134	95	L	2	1824	*2018			
0	636	-562		-8	162	-40	L	1	613	697		3	2137	*2043			
1	701	-631		-7	178	-176	L	3	520	*589		4	1335	1201			
2	709	-698		-6	189	-41	L	*	4	0		5	1513	1734			
3	830	779		-5	197	44	L	-10	197	163		6	614	-510			
4	210	214	L	-4	203	-32	L	-8	862	*802		7	953	*1056			
5	212	-266	L	-3	206	-44	L	-6	2108	2140		8	141	114	L		
6	211	57	L	-2	208	-14	L	-4	2172	-2431		9	196	349			
7	206	334	L	-1	209	81	L	-2	2247	2305		10	131	-145	L		
8	197	-43	L	0	209	183	L	0	1410	-1774		*	4	4			
9	182	146	L	1	208	-118	L	2	883	980		-10	138	113	L		
*	3	14		2	207	146	L	4	213	*248		-9	141	-90	L		
-10	521	-523		3	204	257	L	6	445	388		-8	138	-102	L		
-9	451	395		4	398	-365		8	281	*288		-7	839	-849			
-8	791	859		5	383	-348		10	133	-58	L	-6	1140	1093			
-7	583	-472		6	181	-30	L	*	4	1		-5	229	129			
-6	1263	-1165		7	166	94	L	-10	837	912		-4	1353	*1377			
-5	670	605		*	3	18		-9	281	*269		-3	376	-347			
-4	1842	1877		-8	670	708		-8	1851	-2020		-2	825	758			
-3	891	-885		-7	458	-410		-7	365	*343		-1	1516	1882			
-2	2206	-2281		-6	930	-1010		-6	1103	1136		0	693	-770			
-1	1210	1079		-5	455	-437		-5	1749	1819		1	1102	*1119			
0	1606	1460		-4	945	969		-4	1080	-1215		2	651	493			
1	1020	*980		-3	559	554		-3	373	*472		3	722	561			
2	838	-738		-2	1446	-1248		-2	1993	2168		4	162	-130			
3	731	645		-1	571	-564		-1	44	-81	L	5	979	-919			
4	948	917		0	1617	1559		0	1983	-2366		6	133	-34			
5	845	-815		1	636	602		1	434	*567		7	196	245			
6	360	-430		2	1013	-1054		2	1630	1982		8	281	-302			
7	491	473		3	476	-420		3	94	*147	L	9	138	40			
8	188	246	L	4	881	775		4	1468	-1339		10	130	46			
9	417	-406		5	399	404		5	119	114	L	*	4	5			
*	3	15		6	778	-830		6	604	596		-10	137	-190	L		
-10	150	91	L	*	3	19		7	136	267	L	-9	889	914			
-9	172	-184	L	-7	142	184	L	8	688	*801		-8	241	-274			
-8	188	-21	L	-6	159	-129	L	9	130	16		-7	1546	*1409			
-7	346	256		-5	296	-273		10	326	429		-6	742	728			
-6	653	-610		-4	179	252	L	*	4	2		-5	1546	1727			
-5	556	-505		-3	186	213	L	-10	482	-471		-4	941	-939			
-4	423	386		-2	189	-136	L	-9	281	*264		-3	2320	*2698			
-3	599	545		-1	331	-187		-8	274	204		-2	93	72	L		
-2	212	-122	L	0	191	-106	L	-7	130	-68	L	-1	2485	2897			
-1	366	335		1	190	168	L	-6	120	46	L	0	701	609			
0	731	605		2	323	398		-5	576	*538		1	1657	*1657			
1	211	-143	L	3	181	-10	L	-4	747	680		2	225	234			
2	599	-538		4	173	-160	L	-3	203	267		3	1433	1140			
3	367	-343		5	162	83	L	-2	366	-346		4	168	173			
4	211	-260	L	6	147	126	L	-1	90	-24		5	1309	*1482			
5	208	88	L	*	3	20		0	436	602		6	134	80	L		
6	202	-105	L	-7	540	-608		1	413	422		7	1005	992			
7	192	247	L	-6	475	393		2	994	*966		8	344	-346			
8	177	56	L	-5	712	691		3	1010	*712		9	513	-648			
*	3	16		-4	562	-545		4	1065	972		10	128	-138	L		
-10	456	447		-3	830	-780		5	120	-73	L	*	4	6			
-9	158	-158	L	-2	652	566		6	1409	-1439		-10	135	276	L		
-8	558	-559		-1	828	817		7	137	*113	L	-9	560	-570			
-7	190	-44	L	0	707	-572		8	910	901		-8	140	-118			
-6	798	794		1	742	-596		9	278	328		-7	432	449			

-6	521	-504		0	1833	1797		7	131	193	L	2	378	-389			
-5	576	-529		1	950	-881		8	273	379		3	131	-154	L		
-4	324	-216		2	1491	-1516		9	100	-68	L	4	127	120	L		
-3	831	915		3	1194	1116		4	13			5	295	383			
-2	143	-106		4	1292	1406		-10	199	-217		6	273	-236			
-1	259	-202		5	366	-275		-9	115	-45	L	7	242	-303			
0	770	778		6	819	-940		-8	356	456		4	17				
1	960	916		7	140	149	L	-7	652	740		-7	488	579			
2	371	320		8	428	555		-6	892	-951		-6	110	138	L		
3	688	-638		9	310	-357		-5	685	-662		-5	708	-702			
4	347	-335		10	160	-288		-4	844	937		-4	302	-325			
5	368	253		4	10			-3	819	813		-3	823	979			
6	361	-358		-10	122	150	L	-2	840	-827		-2	448	555			
7	443	-264		-9	132	-131	L	-1	484	-487		-1	940	-1024			
8	140	25	L	-8	437	-413		0	593	500		0	226	-169			
9	428	423		-7	562	689		1	594	587		1	984	1220			
10	126	140	L	-6	140	148	L	2	953	-1138		2	402	419			
	4	7		-5	585	-601		3	954	-1088		3	740	-793			
-10	266	282		-4	330	-234		4	816	951		4	118	-141	L		
-9	682	-653		-3	322	268		5	584	655		5	247	285			
-8	562	-546		-2	834	817		6	653	-760		6	100	-25	L		
-7	938	849		-1	649	-577		7	356	-408		7	292	-504			
-6	1033	1050		0	1065	-1104		8	305	441		4	18				
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-4	658	-668		2	347	272		-10	197	276		-4	113	-179	L		
-3	1103	1195		3	503	-504		-9	106	39	L	-3	204	-224			
-2	884	967		4	275	-351		-8	336	-290		-2	121	114	L		
-1	1825	-2006		5	140	-90	L	-7	128	-201	L	-1	299	428			
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1	1940	1846		7	338	396		-5	137	251	L	1	121	-228	L		
2	952	914		8	374	-411		-4	558	-533		2	118	30	L		
3	1348	-1271		9	122	37		-3	140	220	L	3	300	342			
4	127	170	L	10	262	266	L	-2	911	893		4	107	-111	L		
5	1207	1268		4	11			-1	422	-420		5	239	-247			
6	138	-86	L	-10	635	742		0	689	-655		4	19				
7	744	-779		-9	128	-102	L	1	372	-396		-5	321	335			
8	197	-192		-8	741	-763		2	525	453		-4	377	453			
9	422	493		-7	139	-156	L	3	394	377		-3	336	-319			
10	299	415		-6	1071	1242		4	583	-744		-2	438	-518			
	4	8		-5	523	579		5	328	-311		-1	249	328			
-10	130	-179	L	-4	1308	-1616		6	256	221		0	445	618			
-9	515	551		-3	384	-439		7	291	321		1	490	-610			
-8	344	235		-2	1338	1361		8	106	-145	L	2	260	-285			
-7	140	93	L	-1	593	-538		4	15			3	552	677			
-6	817	-834		0	1829	-1977		-9	737	849		4	293	304			
-5	131	-34	L	1	328	349		-8	110	-142	L	4	20				
-4	502	386		2	791	757		-7	511	-585		-3	128	147			
-3	416	-460		3	365	400		-6	338	444		-2	301	321			
-2	971	-926		4	395	-378		-5	704	766		-1	168	-273			
-1	360	362		5	141	-103	L	-4	630	-529		0	257	-333			
0	1018	856		6	558	602		-3	731	-748		1	190	242			
1	614	-553		7	135	-36	L	-2	590	555		2	315	408			
2	700	-589		8	286	-306		-1	882	927		4	21				
3	1473	1456		9	116	141	L	0	140	-45	L	-3	264	287			
4	642	738		4	12			1	736	-911		-2	643	726			
5	577	-587		-10	344	-354		2	138	151	L	-1	189	-230			
6	140	153	L	-9	122	23	L	3	639	758		0	422	-520			
7	141	19	L	-8	294	315		4	461	-539		5	0				
8	138	-53	L	-7	336	324		5	627	-815		-9	162	31	L		
9	130	-106	L	-6	523	-416		6	121	157	L	-7	555	-459			
10	118	-142	L	-5	744	-807		7	270	353		-5	1923	1651			
	4	9		-4	1066	1111		4	16			-3	1234	1692			
-10	537	-564		-3	393	376		-8	198	292		-1	794	1375			
-9	135	221	L	-2	1231	-1257		-7	352	381		1	1334	1605			
-8	685	896		-1	237	-223		-6	294	248		3	511	443			
-7	688	740		0	887	874		-5	438	-418		5	872	761			
-6	518	-516		1	238	-116		-4	321	327		7	518	548			
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-3	1298	1419		4	487	490		-1	360	395		-9	604	491			
-2	1473	1615		5	140	178	L	0	136	-14	L	-8	401	256			
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-6	430	258		6	516	-478		-2	851	*806		-5	390	-325					
-5	1269	-1047		7	163	132	L	-1	840	*751		-4	724	-645					
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-3	1985	2164		9	146	22	L	1	1171	948		-2	612	550					
-2	221	-237		*	5	5		2	370	*259		-1	897	-815					
-1	1507	-1333		-9	446	-364		3	842	*809		0	557	-448					
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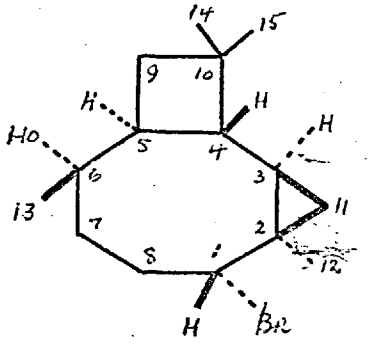
1	874	911		-7	163	175	L	5	518	445		2	231	236					
2	222	137		-6	812	690		6	162	-242	L	3	604	-523					
3	1501	-1233		-5	304	318		7	156	*179	L	4	354	-325					
4	972	-799		-4	1107	-927		8	145	22	L	5	153	149	L				
5	1274	981		-3	133	-109	L	9	128	106	L	6	144	150	L				
6	560	481		-2	750	696		*	5	9		*	5	13					
7	802	-676		-1	120	13	L	-9	285	209		-8	492	520					
8	453	-356		0	541	-410		-8	614	-552		-7	550	-637					
9	475	418		1	439	290		-7	819	*661		-6	147	93	L				
*	5	2		2	1682	1628		-6	231	151		-5	689	672					
-9	558	-450		3	411	-427		-5	1156	1099		-4	158	227					
-8	463	-280		4	1270	-1110		-4	550	*517		-3	737	-738					
-7	683	672		5	454	388		-3	1539	-1453		-2	561	-515					
-6	613	431		6	612	583		-2	494	389		-1	974	908					
-5	402	-367		7	162	-86	L	-1	980	900		0	513	346					
-4	128	-60	L	8	156	-197	L	0	821	*697		1	1022	-954					
-3	665	622		9	143	73	L	1	1064	*837		2	320	-331					
-2	321	340		*	5	6		2	552	448		3	589	582					
-1	561	-658		-9	155	149	L	3	606	570		4	153	81	L				
0	161	-212		-8	688	-611		4	164	*174	L	5	411	-325					
1	274	-220		-7	284	-269		5	326	*229		*	5	14					
2	709	693		-6	559	535		6	504	408		-6	518	-441					
3	131	-81	L	-5	156	-121	L	7	379	345		-5	359	309					
4	542	-465		-4	594	-543		8	449	*456		-4	456	403					
5	582	531		-3	488	-401		*	5	10		-3	440	-317					
6	162	-158	L	-2	737	673		-9	508	484		-2	158	-100	L				
7	518	-535		-1	321	356		-8	149	34	L	-1	501	463					
8	160	-208	L	0	588	-545		-7	545	*557		0	158	99	L				
9	149	162	L	1	815	626		-6	162	189	L	1	314	-220					
*	5	3		2	1009	861		-5	567	426		2	380	-337					
-9	278	238		3	425	368		-4	519	*508		3	370	249					
-8	983	927		4	589	-532		-3	760	*683		4	355	340					
-7	1048	-895		5	162	-134	L	-2	161	34	L	*	5	15					
-6	1278	-1087		6	164	230	L	-1	554	537		-6	358	353					
-5	1003	988		7	161	-65	L	0	224	*205		-4	497	-470					
-4	723	639		8	306	-340		1	720	*633		-3	353	346					
-3	815	*687		9	139	-30	L	2	514	383		-2	769	825					
-2	775	-650		*	5	7		3	164	102	L	-1	568	-500					
-1	1835	2164		-9	430	-419		4	164	*142	L	0	743	-674					
0	1304	1480		-8	507	407		5	161	*219	L	1	637	665					
1	1198	*1171		-7	164	-81	L	6	156	-23	L	2	510	524					
2	1056	-902		-6	977	-863		7	293	275		3	450	-479					
3	270	164		-5	159	-63	L	8	132	23	L	*	5	16					
4	361	237		-4	1020	921		*	5	11		-6	443	484					
5	736	-617		-3	209	177		-9	127	-92	L	-4	528	-574					
6	163	-106	L	-2	949	-938		-8	142	*169	L	-2	631	687					
7	462	432		-1	243	-233		-7	610	611		-1	451	392					
8	159	59	L	0	1227	1053		-6	150	*123	L	0	493	-424					
9	391	*368		1	249	233		-5	974	*966		1	140	-289	L				
*	5	4		2	895	-733		-4	463	389		*	5	17					
-9	159	-32	L	3	410	-273		-3	864	718		-4	404	382					
-8	517	503		4	848	731		-2	163	*119	L	-2	573	-515					
-7	230	-208		5	653	604		-1	977	*796		0	450	446					
-6	666	-622		6	516	-412		0	610	*518									

7.4. Discussion of the Structure.

Stereochemistry.

The structure is shown in a-axis projection in Figure 7.1; this shows that the proposed stereochemistry[130] (5.XXXII in Fig. 5.4) must be revised to 5.XXXIII, which is reproduced below as 7.I. The attack on the C(1)-C(2) double bond of humulene (5.XXXI) is thus revealed as cis-, but is trans- at the other two as proposed[130]. A possible alternative mechanism to the expected all-trans, concerted cyclisation of humulene involves intermediate formation of a bicyclobutonium ion[162], which is attacked by hydroxyl.[163] Although the present study has furnished the complete stereochemistry of humulene bromohydrin, it will require careful biosynthetic studies to establish the pathway from the farnesyl precursor 5.XXVIII (Fig 5.4) to caryophyllene.



7.I. Humulene Bromohydrin : Representation of true Stereochemistry.

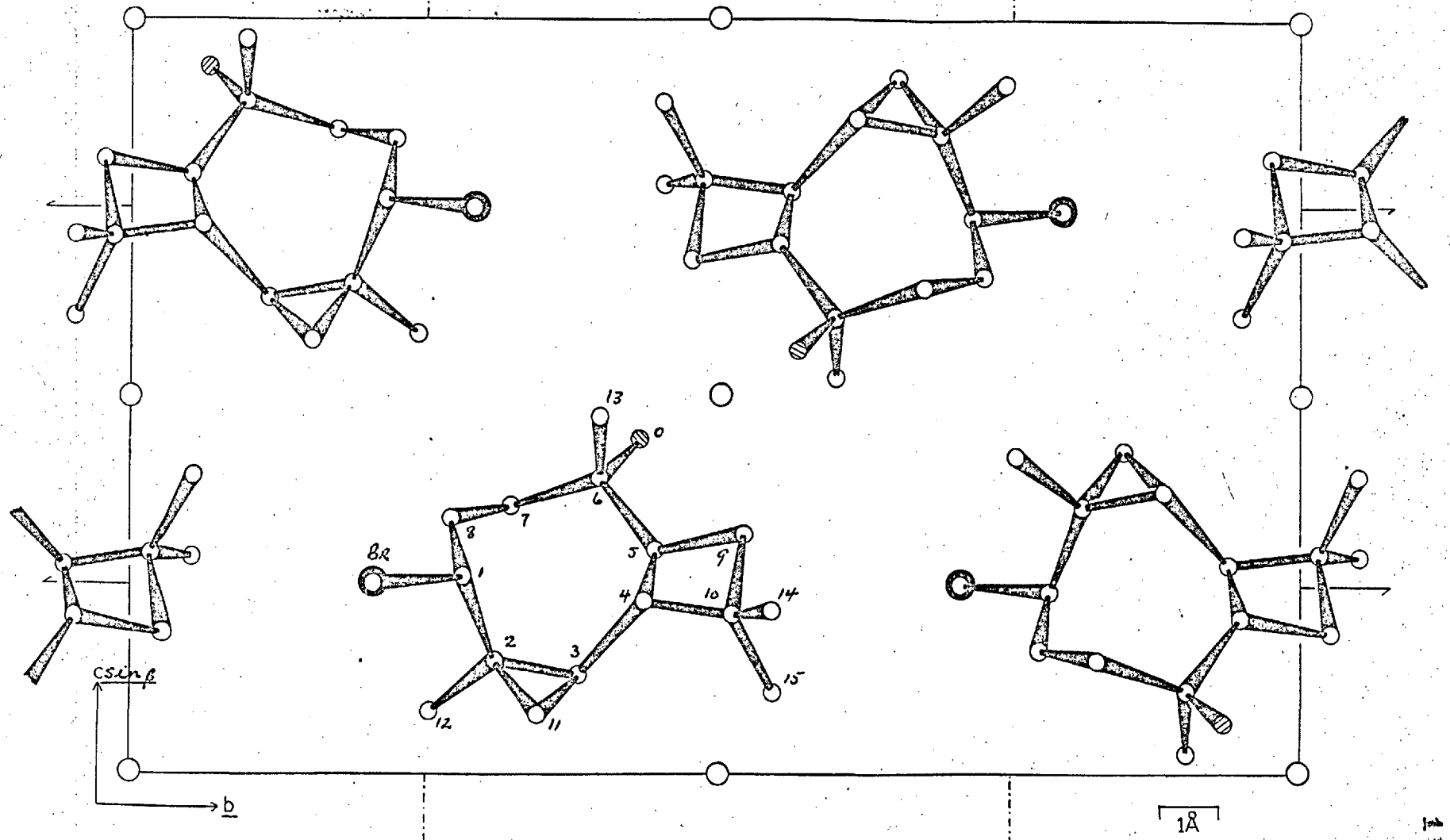
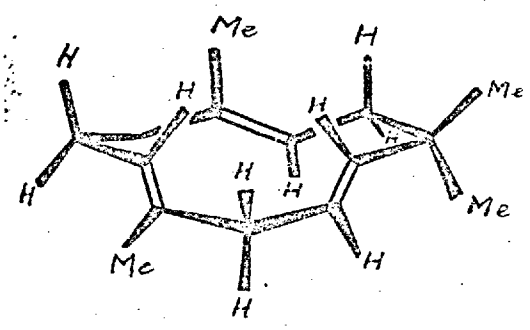


Figure 7.1. Humulene Bromohydrin in a-axis projection.

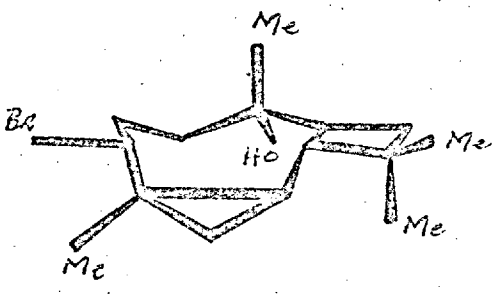
Geometry and Conformation.

In view of the stereospecific reconstitution of the all-trans-triene ring of humulene from the bromohydrin, and the ease with which these reactions proceed in either direction[130] (see Sect. 5.4), it is instructive to note the close similarity between the conformation adopted by humulene in its silver nitrate adduct[128] (7.II, below), and that adopted by the bromohydrin (7.III). The perspective drawing shows that all three double bonds in humulene bis-silver nitrate are nearly perpendicular to the cycloundecatriene ring. This leaves the π-orbitals in 7.II ideally situated for cyclisation to form the cyclobutane ring of 7.III.

One might have expected such a large ring (7.II) to have a very mobile shape, especially in solution, and have ascribed the geometry found to the influence of Ag^+, and to packing requirements. However comparison of 7.II with 7.III indicates that the crystal conformation



7.II



7.III

adopted by humulene is no mere accident, and must have been present in solution immediately prior to cyclisation. Recent n.m.r. studies of the conformational equilibria of humulene in solution[164] have proved inconclusive in establishing 7.II as the preferred conformation. However there is some evidence that the conformations adopted by cyclic olefins in crystalline complexes are an accurate reflection of those adopted prior to reaction in solution : X-ray studies have shown that cis,cis,cis-1,4,7-cyclononatriene has, within experimental error, the same structure in both the free state[165] and in its silver nitrate adduct[166]; the same is also true of trans,trans,trans-1,5,9-cyclododecatriene[167] and germacratriene[136], the latter compound will be discussed in section 8.4.

The interatomic distances and valence angles are shown in Tables 7.6, 7.7, respectively. They are also shown in Figure 7.2 for ease of reference. The standard deviations quoted are probably low estimates, since block-diagonal least-squares approximations were used to optimize the positional parameters.

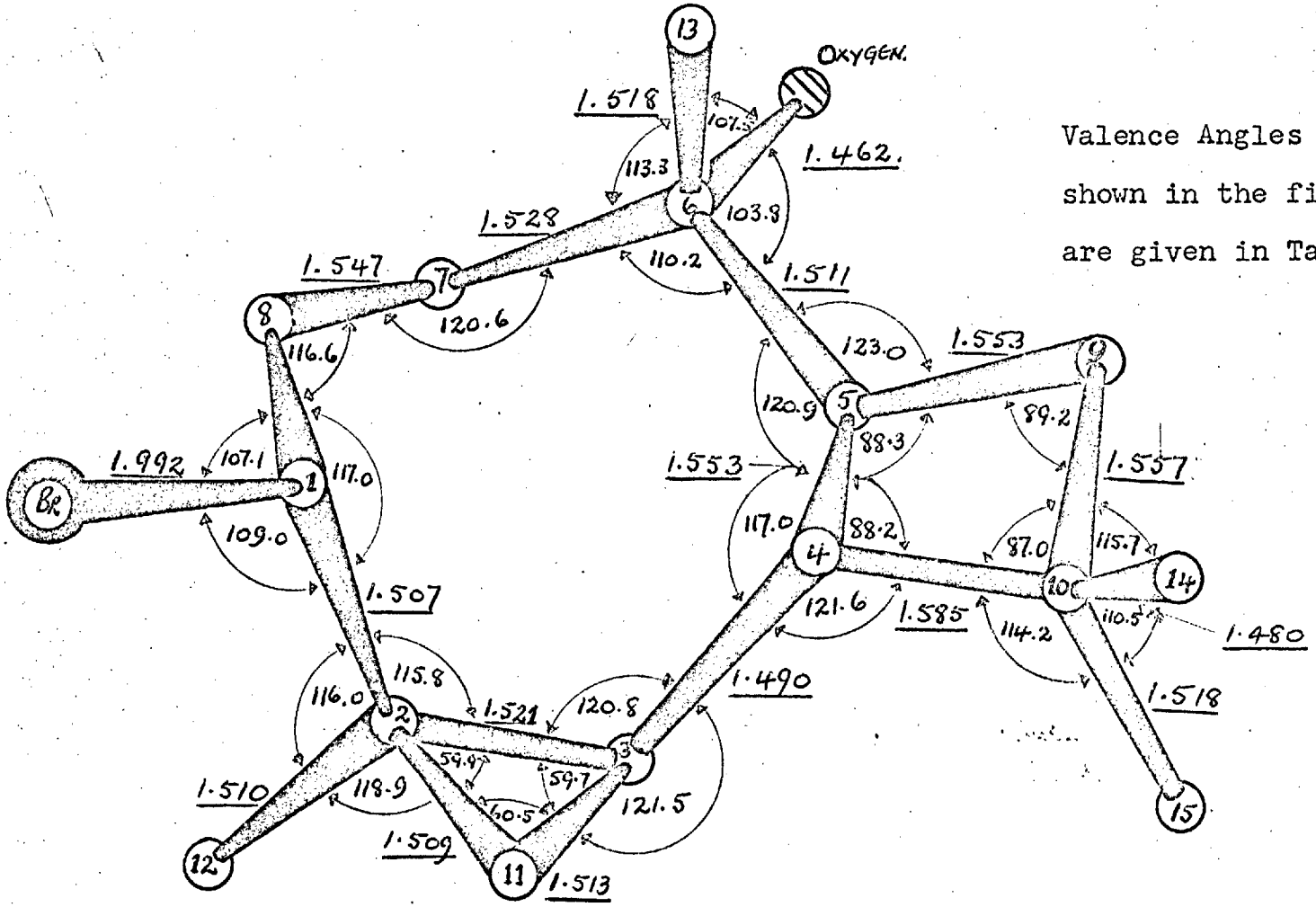
The C(1)-Br distance of 1.992Å is rather longer than the average value quoted for the alkyl bromides (1.94Å [153]), but comparably long distances have been found in retusanine-(+)-3-bromocamphor-9(π)-sulphonate[150]

TABLE 7.6.

Humulene Bromohydrin.

Intramolecular bonded distances (r), in Ångstroms, together with their estimated standard deviations (σ).

Atoms	r	σ	Atoms	r	σ
Br - C(1)	1.992	0.007	C(5) - C(6)	1.511	0.009
C(1) - C(2)	1.507	0.010	C(5) - C(9)	1.553	0.009
C(1) - C(8)	1.509	0.011	C(6) - C(7)	1.528	0.010
C(2) - C(3)	1.521	0.009	C(6) - C(13)	1.518	0.010
C(2) - C(11)	1.509	0.011	C(6) - O	1.462	0.009
C(2) - C(12)	1.510	0.011	C(7) - C(8)	1.547	0.010
C(3) - C(4)	1.490	0.009	C(9) - C(10)	1.557	0.009
C(3) - C(11)	1.513	0.011	C(10)- C(14)	1.480	0.010
C(4) - C(5)	1.553	0.010	C(10)- C(15)	1.518	0.010
C(4) - C(10)	1.585	0.009			



Valence Angles not shown in the figure are given in Table 7.7.

Figure 7.2. a-axis projection showing bondlengths (underlined) and valence angles.

TABLE 7.7.

Humulene Bromohydrin.

Valence Angles (θ)° in the Asymmetric Unit, together with their Estimated Standard Deviations (σ)°.

Atoms	θ°	σ°	Atoms	θ°	σ°
Br-C(1)-C(2)	109.0	0.5	C(4)-C(10)-C(9)	87.0	0.5
Br-C(1)-C(8)	107.1	0.5	C(4)-C(10)-C(14)	116.7	0.6
C(1)-C(2)-C(3)	115.8	0.6	C(4)-C(10)-C(15)	114.2	0.5
C(1)-C(2)-C(11)	116.0	0.6	C(5)-C(4)-C(10)	88.2	0.5
C(1)-C(2)-C(12)	116.0	0.6	C(5)-C(6)-C(7)	110.2	0.5
C(1)-C(8)-C(7)	116.6	0.6	C(5)-C(6)-C(13)	114.9	0.6
C(2)-C(1)-C(8)	117.0	0.6	C(5)-C(6)-O	103.8	0.6
C(2)-C(3)-C(4)	120.8	0.5	C(5)-C(9)-C(10)	89.2	0.5
C(2)-C(3)-C(11)	59.7	0.5	C(6)-C(5)-C(9)	123.0	0.6
C(2)-C(11)-C(3)	60.5	0.5	C(6)-C(7)-C(8)	120.6	0.6
C(3)-C(2)-C(11)	59.9	0.5	C(7)-C(6)-C(13)	113.3	0.6
C(3)-C(2)-C(12)	118.6	0.6	C(7)-C(6)-O	106.2	0.6
C(3)-C(4)-C(5)	117.0	0.6	C(9)-C(10)-C(14)	115.7	0.6
C(3)-C(4)-C(10)	121.6	0.5	C(9)-C(10)-C(15)	111.0	0.6
C(4)-C(3)-C(11)	121.5	0.6	C(11)-C(2)-C(12)	118.9	0.6
C(4)-C(5)-C(6)	120.9	0.6	C(13)-C(6)-O	107.5	0.5
C(4)-C(5)-C(9)	88.3	0.5	C(14)-C(10)-C(15)	110.5	0.6

5'-bromo-5'-deoxythymidine[168], and dibromomenthone[169]. Of the other exocyclic bonds the C(6)-O distance compares favourably with cited values[153], while the C-Me distances, although shorter than the accepted C-C single bond value of 1.539 Å[153], are not significantly so. The fused ring system presents some interesting geometrical and conformational points, and these are discussed separately below.

i) The Cyclo-octane Ring.

The assumption of the distorted crown as the preferred conformation[170], from thermochemical and spectroscopic evidence, has recently been challenged. Hendrickson[158] has calculated the minimum strain-energy (E_{min}) (see Appendix III) for nine symmetrical conformers, as a function of the valence angles (θ), dihedral (torsion) angles (ω), and non-bonded H-H contacts (r). He concluded that, when the valence angles are allowed to vary from the tetrahedral value (109.47°), the conformations with D_2 and C_s symmetry are preferred, the latter being slightly less strained by ca. 0.3 kcal mole^{-1}. In a later calculation[159] C-H and C-C non-bonded interactions were allowed for, and one other conformation included (symmetry S_4). A value of 112° was now taken as that of minimum strain at saturated

carbon, from hybridization studies. In this case the C_s form was preferred by 0.9 kcal $mole^{-1}$ over the S_4, and by 1.7 kcal $mole^{-1}$ over the D_2. Similar calculations by Wiberg[171], and by Bixon and Lifson[172] have given comparable results. The latter workers have lifted the symmetry requirements, and conclude that their are four forms of comparable E_{min}; the boat-chair (Hendrickson C_s form), and the twisted crown (not considered by Hendrickson, since it is not symmetric), have the lowest values.

The occurence of the boat-chair form has recently been shown by several X-ray determinations. Dunitz et.al.[173] have studied the *cis*- and *trans*-cyclooctane dicarboxylic acids, and Groth[174] has studied the cyclooctane peroxide dimer. The structural parameters in both cases have agreed well with the theoretical values. In the structure of taxinol[175] the cyclooctane ring is fused to two cyclohexane rings, but preserves approximate C_s symmetry. Evidence for the distorted crown form, from a study of a salt of azacyclooctane[176] has been shown inconclusive[173] due to structural disorder. More recently 1,2,5,6-tetrabromocyclooctane[177] has been found to exist in this conformation in the crystal, and possibly in solution.

The ring in the present study (C(1)→C(8)) is

boat-chair, but is distorted from $\underline{C}_s$ symmetry by the ring fusion. Figure 7.3 shows the ideal conformation, and the parameters involved; it is numbered as in the present study. Atoms C(2), C(4), C(6), C(8), show an average deviation from planarity (required by $\underline{C}_s$ symmetry) of 0.19Å. Table 7.8(a) shows the values of ($\underline{\omega}$) and ($\underline{\theta}$) obtained in this work, compared with those of Hendrickson[159] and Bixon and Lifson[172]. The latter authors have also predicted the deviation from the mean plane (C(1)-C(8)) of all eight atoms in the ring, these figures are compared with those from the present study in Table 7.8(b). It can be seen that the largest deviations from the theoretical values are caused by the cyclopropane ring fusion, i.e. $\underline{\omega}_2$ differs by $\approx 48^\circ$, and C(2) and C(3) show the largest discrepancies in the comparison of planarity.

The angular strain energy ($\underline{E}_\theta$), involved in the variation of valence angles from 112°, is 7.33 kcal mole^{-1} for the present structure, while the torsional strain ($\underline{E}_\omega$) is 7.8 kcal mole^{-1} *. The non-bonded interactions are difficult to estimate, due to lack of resolution of hydrogen atoms; however the contribution from this source to $\underline{E}_{total}$ is usually small. Comparison with

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* see Appendix III for formulae used.

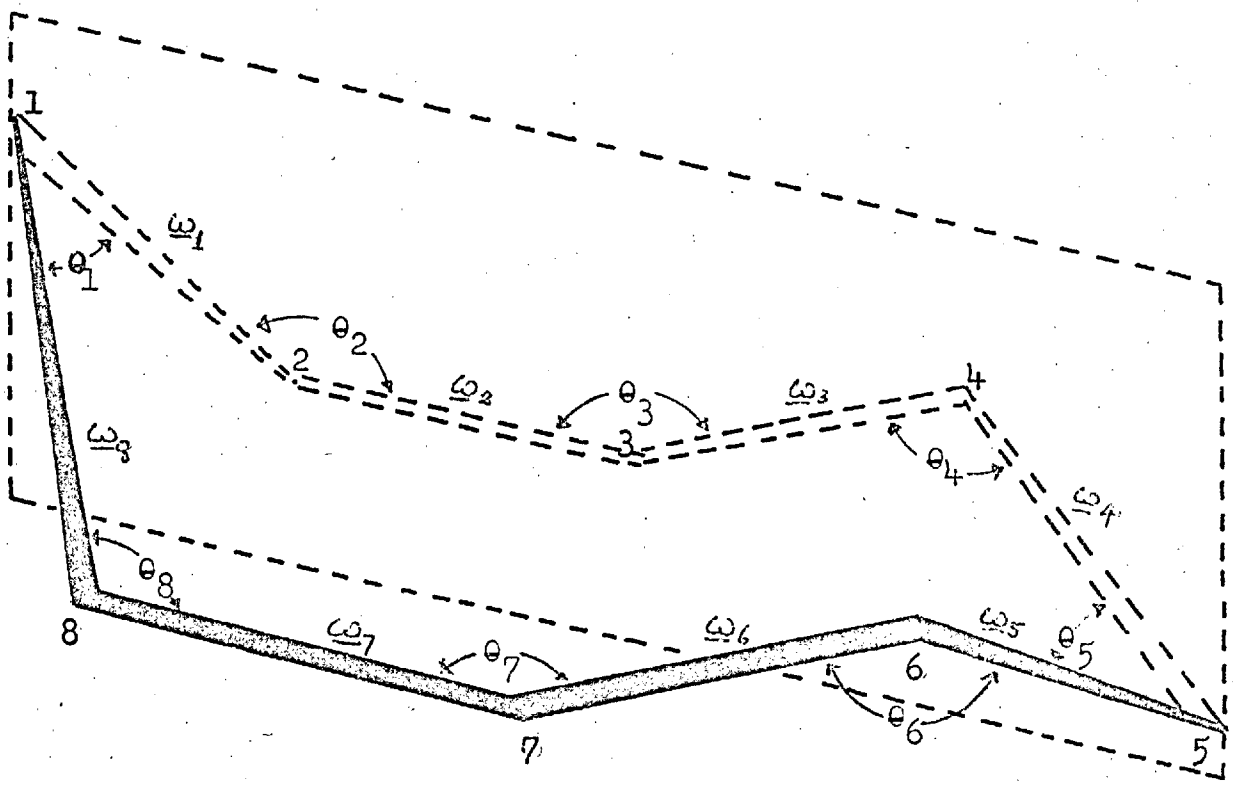


Figure 7.3. Ideal $\underline{C}_s$ (boat-chair) conformation for cyclooctane ring after Hendrickson[158]. The atomic numbering corresponds to the present study. For the minimum-energy form $E_{min} = \underline{E}_\theta + \underline{E}_\omega + \underline{E}_{NB} = 11.1$ kcal/mol

TABLE 7.8(a).

Values of θ_1-θ_8 and ω_1-ω_8^* for Humulene Bromohydrin, in comparison with the theoretical values from minimum-energy calculations[159,172].

Parameter	This work	Bixon & Lifson[172]	Hendrickson[159]
θ_1	117.0°	116°	117°
θ_2	115.7	116	116
θ_3	120.8	114	116
θ_4	117.0	114	116
θ_5	120.9	115	117
θ_6	110.2	113	116
θ_7	120.6	115	116
θ_8	116.6	116	116
ω_1	-92.9°	-64°	-65.0°
ω_2	4.4	-44	-44.7
ω_3	80.7	106	102.2
ω_4	-86.7	-72	-65.0
ω_5	68.6	70	65.0
ω_6	-93.0	-105	-102.2
ω_7	58.7	46	44.7
ω_8	53.3	64	65.0

* Calculated using MOJO (Appendix II).

TABLE 7.8(b).

Displacement (d^{*} in Ångstroms of C(1)-C(8) from the mean plane through the cyclooctane ring of Humulene Bromohydrin, compared with the theoretical values of Bixon and Lifson[172].

Atom	d_{obs}	d_{theor}
C(1)	0.62	0.71
C(2)	-0.37	-0.08
C(3)	-0.38	-0.65
C(4)	0.47	0.35
C(5)	-0.08	0.06
C(6)	0.19	0.34
C(7)	-0.56	-0.65
C(8)	0.11	-0.08

* Calculated using the program DIDO (chapter 4).

Hendrickson's data[159] shows that the value of $E_\theta + E_\omega$ here, exceeds that for the ideal C_s conformation by 6.55 kcal mole^{-1}. This must reflect fairly accurately the additional strain introduced by the fusion with two (highly strained) small rings. It is surprising, therefore, how closely the conformation observed here tallies with that from minimum-energy calculations, despite the effects of what may be termed 'fusion strain'. It would be interesting to perform similar calculations with the parameters of taxinol[175], when the full details are published.

On the limited evidence available it would appear that the X-ray results quoted above support the theoretical concepts. No one conformation appears to be preferred, and although spectroscopic results[177,178] indicate the occurrence of only one conformation in solution, there is no evidence that this is the same one in each case.

The overall average valence angle (θ) in the ring is 117.4° ± 0.6°, and compares well with values for 7-, 9-, and 10-membered saturated carbocycles, viz : 116° in the cycloheptane rings of bromogeigerin acetate[179], and caryophyllene chlorohydrin[180]; 117° in cyclononylamine hydrobromide[181]; 116° in 1,6-cis-diaminocyclodecane[182], and 117° in 1,6-trans-diaminocyclodecane[183]. The

general increase in $\underline{\theta}_{ave}$ over the tetrahedral value obtained from the X-ray results is also borne out by the theoretical minimum-energy calculations.

The average bond length in the cyclooctane ring is 1.521 Å (average e.s.d. 0.010 Å), which does not differ significantly from the accepted average. The short C(3)-C(4) distance is probably a reflection of the 'fusion strain'.

ii) The Cyclobutane Ring.

The proposed trans-fusion[130] has been confirmed, and its feasability on conformational and geometrical grounds has been discussed above. Figure 7.4 shows that the ring is buckled, the average deviation of the atoms from the mean plane is 0.14Å. In Table 7.9 the distortion observed here is compared with results of other studies, by both X-ray and electron diffraction, in terms of :

(a) the average valence angle ($\underline{\theta}^{\circ}$) in the ring,

(b) the average bond-length ($\underline{r}$) in Å,

(c) the perpendicular distance ($\underline{h}$), in Å, between ring diagonals,

and (d) the average dihedral fold about the diagonals,

i.e. $\frac{\underline{\phi}_{13} + \underline{\phi}_{24}}{2}$.

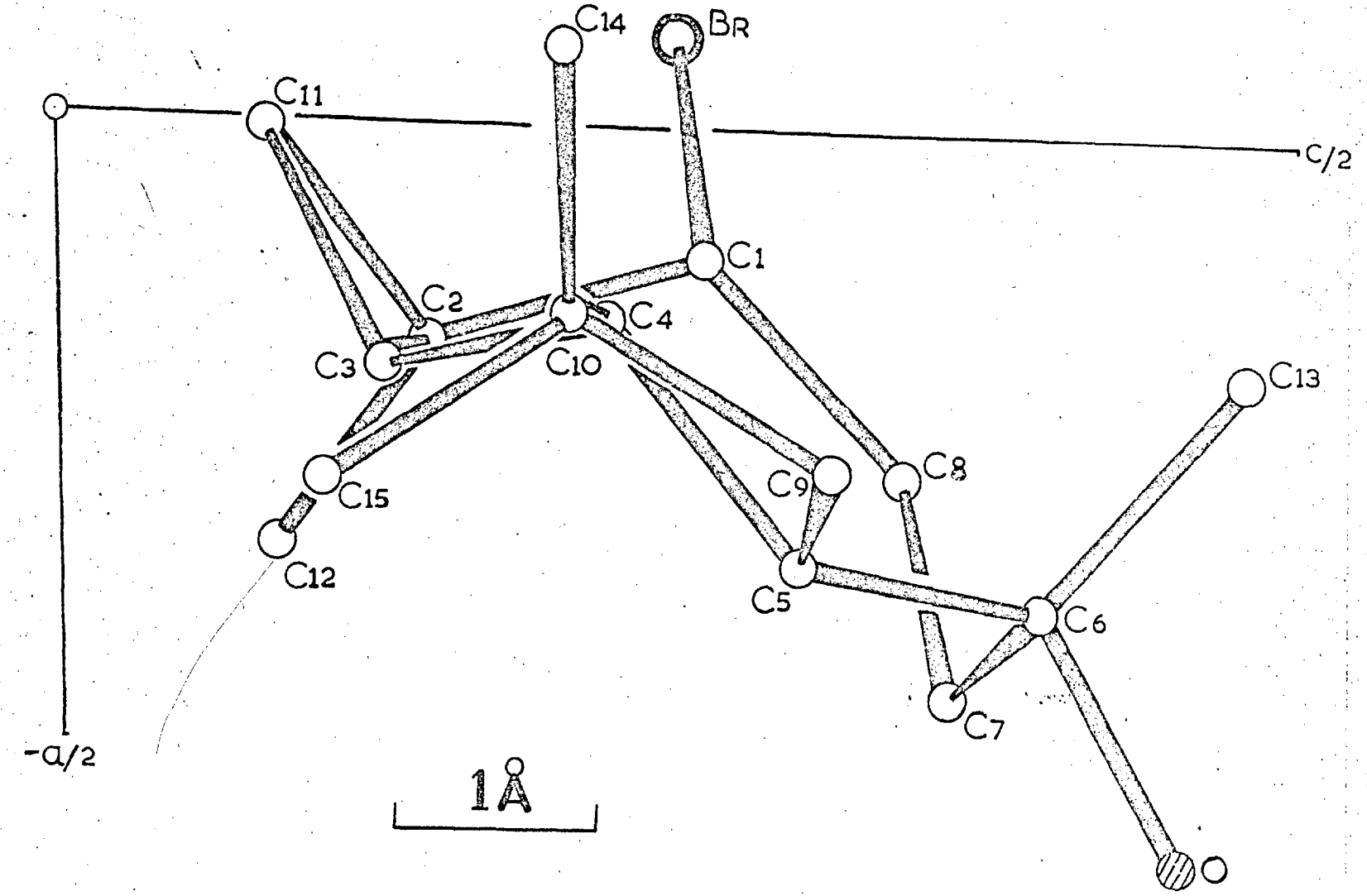


Figure 7.4. Humulene Bromohydrin in 010 projection, showing the buckling of the cyclobutane ring.

Criteria (c) and (d) are illustrated in Figure 7.5 below.

The results show that the ring is generally non-planar, even in cases of simple substitution, as predicted by theoretical work[186,193,194]. The effect is enhanced by trans-fusion to larger ring systems (entries 1,2,3, in Table 7.9). In the former case values of ϕ_{ave} lie between 152° and 160°, but are as low as 139° in the latter. Relatively few idealized planar rings are found; where the X-ray method has been used the centres of such rings coincide with inversion centres ($\bar{1}$).

A notable feature in all cases, except entry 4, is the increase of C-C bondlengths over the accepted value, an average of 1.57Å is given by the X-ray data, agreeing well with the electron-diffraction results. The effect occurs in both buckled and planar rings, and has been

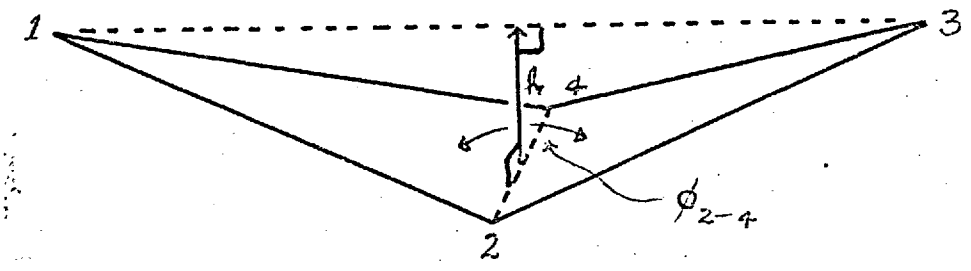


Figure 7.5. Criteria (c) & (d) in cyclobutane ring analysis.

TABLE 7.9.

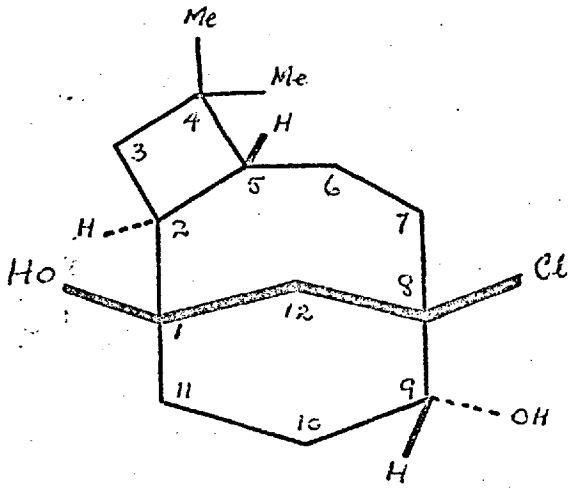
Analysis of Cyclobutane Ring Distortion (Criteria a - d)

Compound & Reference	Ave θ°	Ave r Å	h Å$^{\prime}$	Ave $\phi^{\circ\prime}$
1. Humulene Bromohydrin	88.2	1.562	0.28	151
2. Caryophyllene (180) Chlorohydrin	87.0	1.556	0.36	143
3. Caryophyllene (125) Alcohol Chloride	86.3	1.573	0.40	139
4. Anemonin (184)	88.2	1.537	0.26	152
5. Octachloro-cyclobutane (185)	87.7	1.59	-	158
6. Cyclobutane (186) (*)	-	1.57	-	160
7. Cyclopentanone (187) (photodimer)	90.0	1.57	0.00	Planar
8. Methylene cyclobutane (188) (*)	90.0	1.56	0.00	Planar
9. Methylene cyclobutane (189) (*)	92.5	1.55	-	-
10. Methyl cyclobutane (190) (*)	-	1.56_5	-	-
11. Octafluoro-cyclobutane (190) (*)	89.0	1.60	-	160
12. Dimethyl keten dimer (191) (*)	93.0	1.56	-	-
13. Tetraphenyl cyclobutane (192)	90.0	1.57	0.00	Planar

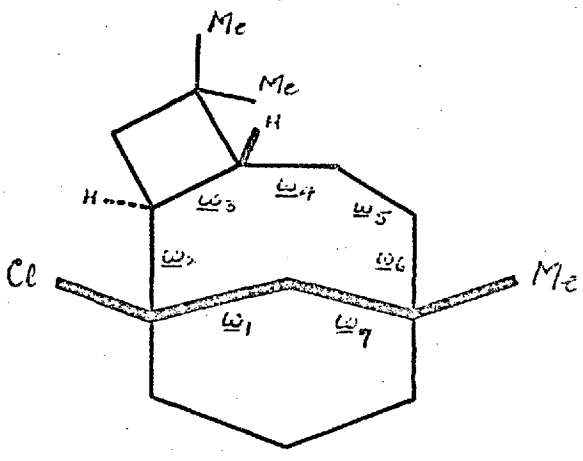
(*) Electron-Diffraction Study. ′ Where values have not been quoted in the cited reference they have been calculated using MOJO (Appendix II).

ascribed[186] to trans annular non-bonded repulsions between carbon atoms. The interactions involved across the diagonals are ca. 2.2 Å; in the present study 2.183 Å for C(5)-C(10), and 2.163 for C(4)-C(9). The C-C bond stretching from this source has been calculated[186] to be of the order of 0.038 Å; this estimate is borne out by the data of Table 7.9.

Caryophyllene chlorohydrin (CC)[180] (entry 2 of Table 7.9) and caryophyllene alcohol chloride (CAC)[125] (entry 3), are the most relevant to the present study; their structural formulae are shown in 7.IV, 7.V. The cyclobutane ring is trans-fused to a seven- (rather than eight-) membered ring, and the distortion is considerably greater. In both cases the cycloheptane ring adopts the boat conformation, which is one of the



7.IV. Caryophyllene Chlorohydrin (CC)



7.V. Caryophyllene Alcohol Chloride (CAC)

TABLE 7.10.

Values of θ°_{ave} and $\omega_1 - \omega_7$ for CC and CAC compared with values from minimum-energy calculations[159]. The values of E_θ and E_ω are also given.*

Parameter	Theoretical	Observed CC[180]	Observed CAC[125]
$\langle\theta\rangle$	115°	116°	112°
ω_1	57.5	62	64
ω_2	30.9	27	34
ω_3	-69.9	-77	-83
ω_4	0.0	13	8
ω_5	69.9	52	70
ω_6	-30.9	-20	-33
ω_7	-57.5	-67	-63
E_θ	1.77	4.07	1.07
E_ω	5.55	6.58	5.90

/ Values calculated using MOJO (Appendix II).

* Values given in kcal mole^{-1}, the method of calculation follows that due to Hendrickson[159] and is set out in Appendix III.

minimum-energy preferred forms[159,195]. The optimum values for $\underline{\theta}_{ave}$ and $\omega_{1\rightarrow7}$ (the latter are shown in 7.IV) for this conformation are given in Table 7.10, together with the corresponding values for CC and CAC. The values of $\underline{E}_{\underline{\theta}}$ and $\underline{E}_{\underline{\omega}}$ are also listed. The agreement is reasonable, considering the strain due to fusion, and is better than in the cyclooctane ring discussed above. Although non-bonded interactions have been omitted it is possible to explain the increased distortion of the cyclobutane rings in CC and CAC in terms of the sums of $\underline{E}_{\underline{\theta}}$ and $\underline{E}_{\underline{\omega}}$ for the cycloheptane rings. The increased distortion of the macrocycles on fusion to smaller rings is reflected in the increase of this sum over that for the minimum-energy form; thus in the cyclooctane ring of humulene bromohydrin it was 6.55 kcal mole^{-1}, in CC it is 3.33 kcal mole^{-1}, while in CAC there is actually a <u>decrease</u> of 0.35 kcal mole^{-1}. Thus it would appear that the <u>trans</u>-fused cyclobutane ring has been able to transfer some of its strain energy to the cyclooctane ring in humulene bromohydrin, and its geometry is approaching that given by non-fused rings (see Table 7.9). This has not happened to such a great extent in CC, and hardly at all in CAC, resulting in increased distortion of the cyclobutane rings. The inability of the cycloheptane rings in CC and CAC to

distort, and thus to relieve the strain in the cyclobutane rings, is almost certainly due to the 'stiffening' effect of the fused chair-form cyclohexane rings, which share the atoms C(1), C(12), C(8),(see 7.IV, 7.V).

The calculations are by no means rigorous, but they do tend to show the distribution of strain energy in the fused-ring systems considered. It is pleasing to note that the extent of distortion exhibited by the cyclobutane rings does follow in the order predicted by the energy calculations, as shown by Table 7.9. Thus the ring in the present study is least distorted, followed by the rings in CC and CAC in that order.

iii) The Cyclopropane Ring.

A noticeable feature here is the slight contraction of the C-C distances (average $\underline{r}$ = 1.514 $\pm$ 0.010 Å), which compares well with the cited average for cyclopropane rings of 1.52 Å [153]. This has been attributed[186,196] to bent-bonding, which brings the atomic nuclei into closer proximity. The distorting effect of the three-membered ring on the cyclooctane ring has been mentioned in (i) above.

TABLE 7.11.

Humulene Bromohydrin.

Non-bonded Intermolecular Contacts less than 4.0 Å.

Roman suffices refer to atoms related to the asymmetric unit given in Table 7.2 by the following symmetry operations :

i) $1 + x, \quad y, \quad z$; ii) $\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$;

iii) $-x, 1 - y, \quad -z$; iv) $-1 - x, 1 - y, 1 - z$;

v) $-1 - x, 1 - y, -z$.

Br	- $C(7)_i$	3.878	O	- $C(6)_{iv}$	3.992
C(13)	- O_i	3.853	O	- $C(9)_{iv}$	3.413
C(14)	- Br_{ii}	3.731	O	- $C(13)_{iv}$	3.767
C(15)	- $C(11)_{iii}$	3.759	O	- O_{iv}	3.213
			C(15)	- $C(15)_v$	3.861.

Intermolecular Distances and Packing.

Figure 7.1 shows the molecular packing projected down the a-axis. The molecules pack in rows parallel to the 2_1 screw axes, but keep well clear of the centres of symmetry ($\bar{1}$). The closest intermolecular contacts < 4.0 Å are shown in Table 7.11; they are all greater than the required van der Waals clearances. The closest contact (3.21 Å) is between two oxygen atoms across a symmetry centre, but the directions of the O-H bonds preclude any possibility of hydrogen bonding.

CHAPTER 8.

The Crystal and Molecular Structure of the 1:1 Adduct of Germacratriene with Silver Nitrate, $C_{15}H_{24}:AgNO_3$.

8.1. Preliminary Work.

The crystals were supplied by Dr. J. K. Sutherland and Mr. E. D. Brown; they were small white prisms. Examination under the polarizing microscope, with the aid of a quartz wedge, showed them to be uniaxial. The The extinction directions, transverse to the needle axis, were indicative of a monoclinic crystal, with a non-unique (a- or c-) axis parallel to the needle direction. Oscillation and Weissenberg photographs exhibited Laue symmetry 2/m, and confirmed the above indication. The conditions for absent spectra were shown to be :

$$h0l, \quad l \neq 2n; \qquad 0k0, \quad k \neq 2n;$$

defining the spacegroup uniquely as $P2_1/c$. The cell parameters were obtained by the least-squares procedure (CEDI), applied to some 20 theta values measured from

the equatorial photographs h0$\bar{l}$, 0k$\bar{l}$. The relevant data is listed below.

Crystal Data.

Germacratriene:$AgNO_3$: $C_{15}H_{24}$:$AgNO_3$; Monoclinic $P2_1/c$ (C_{2h}^5 : No.14)

$\underline{a}$ = 7.530 ± 0.010 Å; $\underline{b}$ = 10.010 ± 0.015 Å;

$\underline{c}$ = 20.905 ± 0.023 Å; β = 102.1 ± 0.3°;

$\underline{V}$ = 1565 Å^3; $\underline{D_x}$ = 1.61 ± 0.03 g.cm.$^{-3}$ (by flotation in KI sol^n)

$\underline{D_c}$ = 1.58 g. cm.$^{-3}$; for $\underline{Z}$ = 4 molecules/cell;

$\underline{M}$ = 374.23 (taking the standard C^{12} = 12.00);

μ = 106.0 cm^{-1} for CuK_α radiation (λ_{mean} = 1.54178Å)

$\underline{F}$(000) = 768 electrons; Needle axis : $\underline{a}$.

The preliminary photography revealed the crystals to be sensitive to both light and X-rays. Similar effects have been reported for other silver complexes : silver perchlorate - benzene[197], silver nitrate - cyclooctatetraene[198], and tris-bullvalene - silver flouroborate[199]. A crystal was encapsulated in a Lindemann glass capillary tube and kept in darkness, as far as was possible, using the layer-line screens and the camera pot. The effect of X-rays, in causing decay and break-up of the crystal lattice, was tested

by taking two equatorial (0kℓ) Weissenberg photographs, two weeks being allowed between each 45hr. exposure. The level of the intensities on the second film was reduced by about 25-30%, but no changes in the relative values could be detected visually. This indicated that no photo-sensitized structural changes were taking place.

A compromise had to be made between the size of crystal required for speedy data collection, and the size required to minimize absorption errors. Several crystals were tried, and one of approximate dimensions : 0.25 x 0.12 x 0.15 mm. was chosen and encapsulated. The layers 0kl - 5kl were recorded as described in section 4.1, using Ni-filtered CuK_{α} radiation. The average exposure time was $\sim$50hr. per layer, and the oscillation range was reduced slightly to obtain as much high-θ data as possible, in order to reduce the Fourier series termination errors. A total of 1198 independent reflection intensities, out of some 2000 in the Cu-sphere, were visually estimated using step-wedges made at 0kℓ, 2kℓ, 4kℓ. The layers h0ℓ, h1ℓ, were similarly recorded and yielded 228 common data for correlation.

The two data lists were corrected for Lorentz and polarization effects (FIFI), and placed on a common, arbitrary scale using the POLO program. The absolute scale-factor (K) was obtained during structure solution

by comparing $\sum|F_o|$ and $\sum|F_c|$. A systematic absorption correction, although desirable, was impossible due to the gradual decay of the crystals.

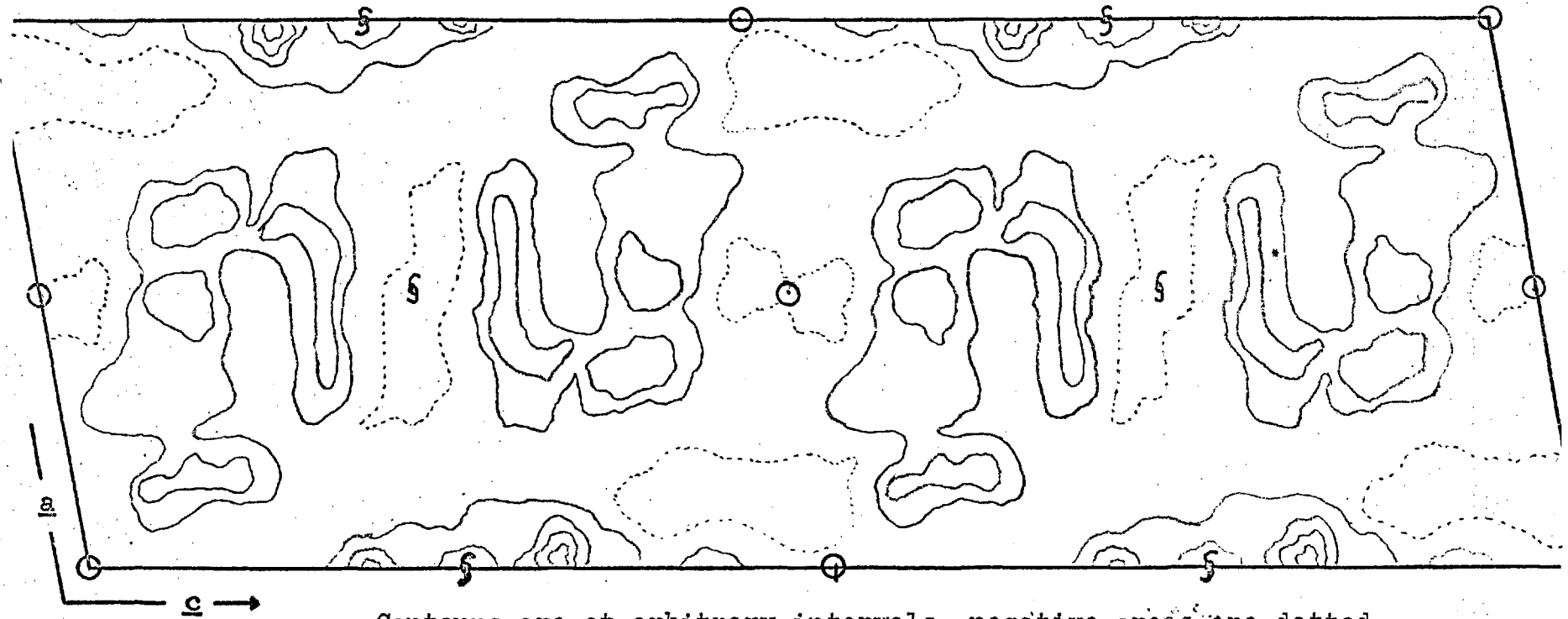
8.2. Structure Solution.

Two-dimensional Patterson maps were computed for the [100]- and [010]-projections, using BOSS. With respect to silver co-ordinates $\underline{x}$, $\underline{y}$, $\underline{z}$, vector peaks between centrosymmetrically related atoms occur at 0, $2\underline{y}$, $2\underline{z}$; and $2\underline{x}$, 0, $2\underline{z}$; respectively in these maps. The silver co-ordinates were given as :

$$\underline{x} = 0.052, \quad \underline{y} = 0.318, \quad \underline{z} = 0.319.$$

A two-dimensional electron-density map (BOSS) for the [010]-projection, using phases given by the above position (together with an estimated $\underline{B}$-factor of 3.0 Å^2), showed the general shape and packing of the molecules; $\underline{R}$ was 0.356. The map is shown in Figure 8.1, which indicates that the molecules lie between symmetry elements at $\underline{z}$ = 0, $\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$, 1. This map may be compared with Figure 8.2 (p.192) which shows the final structure in $\underline{b}$-axis projection.

Using the full, correlated, three-dimensional data list, a 3D Patterson map was computed (BOSS). Equations



Contours are at arbitrary intervals, negative areas are dotted.

Figure 8.1. Germacratriene:$AgNO_3$ [010]-Fourier, which should be compared with Figure 8.2.

similar to 7.1, 7.2, (p. 131) give the Harker sections :

1. x, $\frac{1}{2}$, z; due to the 2_1 screw,
and 2. 0, y, $\frac{1}{2}$; due to the c-glide. ..... 8.1.

The Patterson was solved uniquely for silver, giving the co-ordinates :

$$x = 0.0541, \quad y = 0.3182, \quad z = 0.3177,$$

in excellent agreement with those obtained above.

A structure factor calculation using this position, with estimated B-factor as before, gave $R = 0.346$. These values were then used to compute the first 3D electron-density map; reflections for which $|F_c| \leqslant 0.25|F_o|$ were omitted from the Fourier summation. The nitrate ion was immediately discernible in the $x = 0$ section; nine other peaks appeared to form the basis of the carbon skeleton, but their resolution was not good. Two further maps were computed (using the same rejection test for the structure factors) :

(i) included silver, nitrogen ($B = 4.0$ Å^2), and the three oxygens ($B = 4.0$ Å^2) in the structure-factor calculations, all as neutral atoms; R was 0.327;

(ii) as above, plus the nine possible carbon sites ($B = 4.0$ Å^2), R was 0.284.

The latter map confirmed the nine carbons, and revealed

the positions of all other non-hydrogen atoms. A bead model of the structure at this stage showed chemically sensible geometry.

A fourth map, including all atoms (except hydrogens) in the structure factor calculation ($\underline{R}$ = 0.233), showed no spurious features, but exhibited some series termination ripple; no reflections were rejected. Optimum atomic positions were obtained from the map using Booth's method[161].

8.3. Refinement of the Structure.

The structure was initially refined using the block-diagonal method of BABA. The designation of Run Nos. follows the scheme outlined in Sect. 6.4. (p. 95). Positional parameters, $\underline{B}$-factors, and an overall scale factor (K), were varied for four cycles; no weighting scheme was employed, but scattering factors[19] appropriate to the normal resonance hybrid nitrate ion, i.e. N^{+}, $O^{-\frac{2}{3}}$*, and to Ag^{+}, were used. $\underline{R}$ fell to 0.199 (run I1, see Table 8.1, p. 183).

A weighting scheme of the Hughes type[51] was then introduced, with F^{*} (Eq. 2.29) set to 450 on the scale of the structure factors of Table 8.4; four more cycles reduced $\underline{R}$ by only 0.005 (run I2). An analysis of the

* Obtained by linear interpolation between O^{0} and O^{-1}

agreement within the individual layers showed considerable errors in the inter-layer scales. This was probably due to uncorrected absorption errors (see above), especially in the correlating data. This was collected with the crystal rotating about the b-axis, perpendicular to the needle. The X-ray path-lengths within the crystal were thus more variable in this case, compared with the main axis, where the cross-section presented to the beam was far more uniform.

It was therefore decided to include the inter-layer scale-factors as parameters in the isotropic refinement; as already noted, this procedure is invalid in the anisotropic case[146]. All further refinement was performed using the full-matrix program ORFLS. Four cycles of unweighted refinement, varying the parameters noted above, reduced R to 0.159 (run I3). The value of F^{*} was reset to 45, and a small number of misindexed reflections corrected. Eight strong, low-order, reflections ($10\bar{2}$, 200, $20\bar{2}$, 202, 212, 310, 312, $30\bar{4}$) were removed for suspected extinction, and R fell to 0.104 (runs I4,I5,I6).

An analysis of the observed and calculated structure factors (DELSIG) showed that the average $\left||F_o| - |F_c|\right|$ increased linearly with increasing $|F_o|$, and the Hughes

weighting scheme was no longer applicable. A scheme was devised from the plot to give reasonably constant values of $\sum w(|F_o| - |F_c|)^2$ over ranges of $|F_o|$, it took the form :

$$w = \frac{1}{1 + a|F_o|} \quad \ldots\ldots\ldots\ldots\ldots 8.2.$$

where the constant (a) was derived from the slope and intercept of the plot. Convergence was now slower, and four cycles reduced R to 0.100.

A noticeable feature of these later runs was the oscillatory motion of the nitrogen atom N^+, and O(2). A bond-length calculation showed that the N^+ - O(2) distance was 1.15 Å, compared with N^+ - O(1) and N^+ - O(3) distances of 1.23 and 1.26 Å respectively. The stronger bonding of O(2) indicated that the charge distribution in the nitrate ion should be changed to N^+, $O(3)^{-1}$, $O(1)^{-1}$, and $O(2)^0$. Correction terms were also included to allow for dispersion effects at Ag^+ using the values $\Delta f' = -0.5$, $\Delta f'' = 4.7$ [59]. R fell to 0.099 (run I8), and parameter shifts for the nitrate ion became minimal.

A difference map was now computed using $(F_o - F_c)$ as Fourier coefficients; although it revealed no spurious features, it was not possible to estimate hydrogen atom positions. They were therefore included in the final

stages of refinement in calculated positions (BONDLA), with B-factors equal to that of the carbon to which they were bonded, plus 0.5 Å^2; these parameters were not refined. The refinement was concluded with runs I9, I10; the ratio of shift to standard deviation was less than 0.10 for all parameters on the final cycle, the maximum positional shift was 0.0004 Å.

Some cycles of refinement using anisotropic temperature factors were performed, but these parameters became non-positive-definite for some atoms (i.e. they were physically meaningless), and the process was not pursued. The failure was probably due to :

i) uncorrected absorption effects,

and ii) the paucity of data, in the anisotropic case the ratio of observations to parameters was only 6, hardly high enough to guarantee a valid refinement.

The final parameters from the isotropic refinement (Tables 8.2, 8.3) together with the refined scale-factors, to obtain the structure factors shown in Table 8.4; the hydrogen atoms were included in the calculation in their calculated positions. The final R factor was 0.097, for 1190 reflections not affected by extinction. No attempt was made to assess the accidentally absent data, since the number of such terms was large, and the absorption errors would probably have made a comparison

of $|F_o|$ and $|F_c|$ rather meaningless. It should be noted that the standard deviations quoted in the following tables are probably realistic estimates, since full-matrix methods were used throughout.

TABLE 8.1.

Germacratriene:$AgNO_3$.

The Refinement Process.

Run.	Cycles	R.	$\sum w(\|F_o\| - \|F_c\|)^2$.	Max. Pos^n Shift Å
I1*	4	0.199	50995	0.080
I2*	3	0.194	22595	0.032
I3	4	0.159	76940	0.040
I4	4	0.116	23920	0.021
I5	4	0.110	17630	0.008
I6	4	0.104	15310	0.005
I7	4	0.100	5265	0.0006
I8	4	0.099	5131	0.0006
I9	4	0.097	5065	0.0005
I10	2	0.097	5031	0.0004

* Block-diagonal approximations (BABA), inter-layer scales not refined.

TABLE 8.2.

Germacratriene:$AgNO_3$: Final Positional Parameters as Fractions of the Cell Edges, together with their Estimated Standard Deviations (σ)

Atom	x	σ_x	y	σ_y	z	σ_z
Ag	0.05644	0.00021	0.31799	0.00013	0.31868	0.00007
N	-0.00403	0.00267	0.12024	0.00177	0.20051	0.00098
O(1)	-0.01204	0.00245	0.05989	0.00166	0.25124	0.00091
O(2)	-0.04393	0.00218	0.07619	0.00144	0.14878	0.00081
O(3)	0.04615	0.00200	0.24235	0.00135	0.21058	0.00072
C(1)	0.54685	0.00263	0.02501	0.00160	0.41691	0.00087
C(2)	0.72512	0.00317	0.09135	0.00203	0.45475	0.00115
C(3)	0.86681	0.00303	0.12768	0.00201	0.41241	0.00104
C(4)	0.83943	0.00278	0.27082	0.00166	0.39279	0.00094
C(5)	0.73228	0.00329	0.30357	0.00178	0.33495	0.00109
C(6)	0.65552	0.00318	0.44262	0.00198	0.31070	0.00107
C(7)	0.44453	0.00274	0.42075	0.00160	0.30339	0.00089
C(8)	0.38674	0.00283	0.35095	0.00164	0.35987	0.00098
C(9)	0.37276	0.00281	0.21385	0.00163	0.35561	0.00096
C(10)	0.37644	0.00319	0.12054	0.00213	0.41520	0.00111
C(11)	0.53184	0.00283	-0.09788	0.00169	0.39702	0.00095
C(12)	0.41214	0.00332	0.42417	0.00219	0.42425	0.00121
C(13)	0.88903	0.00311	0.36882	0.00208	0.44878	0.00108
C(14)	0.70867	0.00432	-0.18730	0.00289	0.40367	0.00168
C(15)	0.36347	0.00433	-0.16495	0.00280	0.36365	0.00165

TABLE 8.3.

Germacratriene:$AgNO_3$.

Final Isotropic Thermal Parameters (B), and their Estimated Standard Deviations (σ_B).

Atom	B	σ_B	Atom	B	σ_B
Ag	2.91 Å²	0.05	C(6)	3.55 Å²	0.42
N	3.51	0.36	C(7)	2.34	0.34
O(1)	5.66	0.39	C(8)	2.60	0.36
O(2)	4.27	0.32	C(9)	2.64	0.36
O(3)	3.65	0.29	C(10)	3.83	0.44
			C(11)	2.71	0.36
C(1)	2.37	0.34	C(12)	4.18	0.47
C(2)	3.82	0.45	C(13)	3.62	0.42
C(3)	3.37	0.41	C(14)	6.79	0.71
C(4)	2.42	0.32	C(15)	6.64	0.70
C(5)	3.02	0.39			

TABLE 8.4.

Germacratriene : $AgNO_3$.

Final Observed and Calculated Structure Factors.

The format is :

	h , k	
l	$10\|F_o\|$	$10\ F_c$
.	.	.

The following reflections were omitted for suspected extinction :

h	k	l	$10\|F_o\|$	$10\ F_c$	$\sin\theta/\lambda$
1	0	-2	1268	-1861	0.07512
2	0	0	1376	1981	0.13562
2	0	-2	1002	-1492	0.13451
2	0	2	983	-1342	0.15321
2	1	2	936	1316	0.16117
3	1	0	1042	-1381	0.20949
3	1	2	768	1088	0.22430
3	0	-4	1056	1434	0.20707

	0,0,L	
2	1504	-1493
4	1449	-1321
6	844	794
8	1639	-1605
10	644	554
12	467	509
14	684	-691
16	434	460
18	253	-293
22	372	425

	0,1,L	
1	208	156
2	1790	1764
3	1318	-1356
4	1034	-957
5	1428	1490
6	811	790
8	783	711
9	619	-644
10	1222	-1240
11	317	294
12	793	756
13	324	-339
14	136	-137
15	164	174
16	428	-439
17	249	247
18	466	567
19	201	-178
20	319	-405
24	174	237

	0,2,L	
0	1204	-1089
1	1333	1211
2	886	808
4	604	522
5	1082	-949
6	1189	-1145
7	1226	1103
8	664	603
9	775	-705
10	423	-381
13	524	473
14	432	453
15	665	-717
16	245	-229
17	235	207
19	155	220
20	196	201
21	223	-254
22	223	-223
23	245	289
24	110	145

	0,3,L	
1	593	-489
2	113	-99
3	1310	1283
4	940	819
5	1533	-1371
6	705	614
7	193	134
8	518	-452
9	837	802
10	96	86
11	797	-843
12	227	-240
13	539	518
15	148	110
16	233	224
17	475	-545
18	127	-99
19	332	388
23	153	-158

	0,4,L	
0	719	-627
1	1748	-1506
2	264	-187
3	147	175
4	215	176
5	811	759
7	906	-897
8	269	297
9	378	352
11	254	279
13	654	-676
15	550	603
16	155	-97
18	141	95
21	292	357
22	100	-113
23	189	-241

	0,5,L	
1	408	365
2	427	-453
3	858	-747
4	659	570
5	634	577
6	358	-283
7	186	-126
8	346	-265
9	471	-418
10	326	331
11	741	752
12	239	-164
13	368	-402
15	370	-322
16	156	154
17	446	468
18	174	-171
19	221	-248

	0,6,L	
0	436	391
1	506	516
2	364	-368
4	243	-200
5	367	-300
6	803	718
7	554	527
8	557	-541
9	671	-637
11	150	98
12	365	333
13	410	381
14	422	-414
15	311	-300
16	265	325
20	237	-296
21	169	-160
22	211	292

	0,7,L	
2	628	657
3	241	261
4	1022	-1040
5	116	-84
6	480	464
7	180	135
8	211	162
10	555	-569
11	335	-311
12	459	508
16	168	-186
18	309	337
20	149	-180

	0,8,L	
0	598	-664
1	244	203
2	450	529
4	151	112
5	216	-194
6	549	-662
7	296	290
8	421	483
9	156	109
12	292	-281
14	401	432
16	303	-339

	0,9,L	
1	238	-230
2	270	-255
3	360	384
4	570	601
5	201	-227
6	391	-386
9	232	259
10	258	301
11	279	-300
12	215	-282
14	128	147

	0,10,L	
1	420	-499
5	191	216
6	146	163
7	322	-375
9	419	432
13	171	-223
14	132	-158

	0,11,L	
1	156	109
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9	364	-426
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12	726	718
15	167	-164
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17	249	172
18	526	641
19	192	-125
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-6	545	-416
-9	210	-212
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9	380	-388
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14	506	553
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15	327	297
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-14	215	-123
-15	236	-153

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13	274	293
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-14	432	372
-16	367	-274
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6	177	-202
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-13	306	228
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-6	615	-593
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2	436	466
4	265	279
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6	602	-625
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-1	516	-533
-2	555	584
-4	129	-150
-6	268	-206
-7	496	-421
-8	855	825
-9	455	412
-10	693	-699
	5,2,L	
1	387	-456
2	352	-364
3	513	554
4	243	241
5	445	-521
9	388	420
10	306	359
11	309	-402
-2	173	181
-3	443	401
-5	693	-658
-6	250	207
-7	358	391
-9	234	254
-10	453	-408
-11	605	-532
-12	743	610
-13	618	521
	5,3,L	
0	223	279
1	518	-541
5	446	467
7	534	-538
-1	587	673
-3	324	-271
-5	357	-303
-7	664	656
-9	642	-604
-13	418	337
-14	247	-164
	5,4,L	
1	336	342
3	549	-536
5	334	353
9	357	-384
11	304	329
-2	247	197
-3	669	-723
-5	543	548
-7	239	-181
-9	226	-177
-11	560	524
-13	430	-354
	5,5,L	
0	257	276
1	285	270
5	350	-364
6	306	281
7	252	316
8	309	-198
-1	509	-508
-2	226	-191
-3	277	286
-7	438	-400
-8	314	-213
-9	513	434
-13	309	-278
-14	308	-175
-15	394	311
	5,6,L	
1	276	-289
2	352	309
3	434	380
4	356	-359
-3	345	322
-4	457	392
-5	324	-309
-6	348	-334
-11	437	-385
-12	435	-426
	5,7,L	
0	334	-361
-6	535	-478
-8	471	440
	5,8,L	
-4	551	-497
-6	387	383

8.4. Discussion of the Structure.

i) Accuracy of the Determination.

The final R-factor of 0.097 is one of the lowest so far obtained for a silver adduct, despite the inapplicability of anisotropic temperature factors. In retrospect it may have been better to use a different crystal for the collection of each layer, to obtain a maximum of reflection data. The decay in each crystal would then have been small enough to allow an absorption correction to be made for each layer. The failure of anisotropic refinement would then have been overcome on both counts. The effects of light on the crystal could have been minimized by blackening the tube; however this would be difficult to achieve after setting the crystal on the camera. The additional time required to set the crystal in this case gives little advantage over the method employed, since, with a clear Lindemann tube the crystal could be partially set by eye, and was easily located and realigned when slipping occurred during data collection.

Maximum accuracy with rapidly decaying crystals can only be achieved by a careful appraisal of the photographic method; this gives a time-averaged record

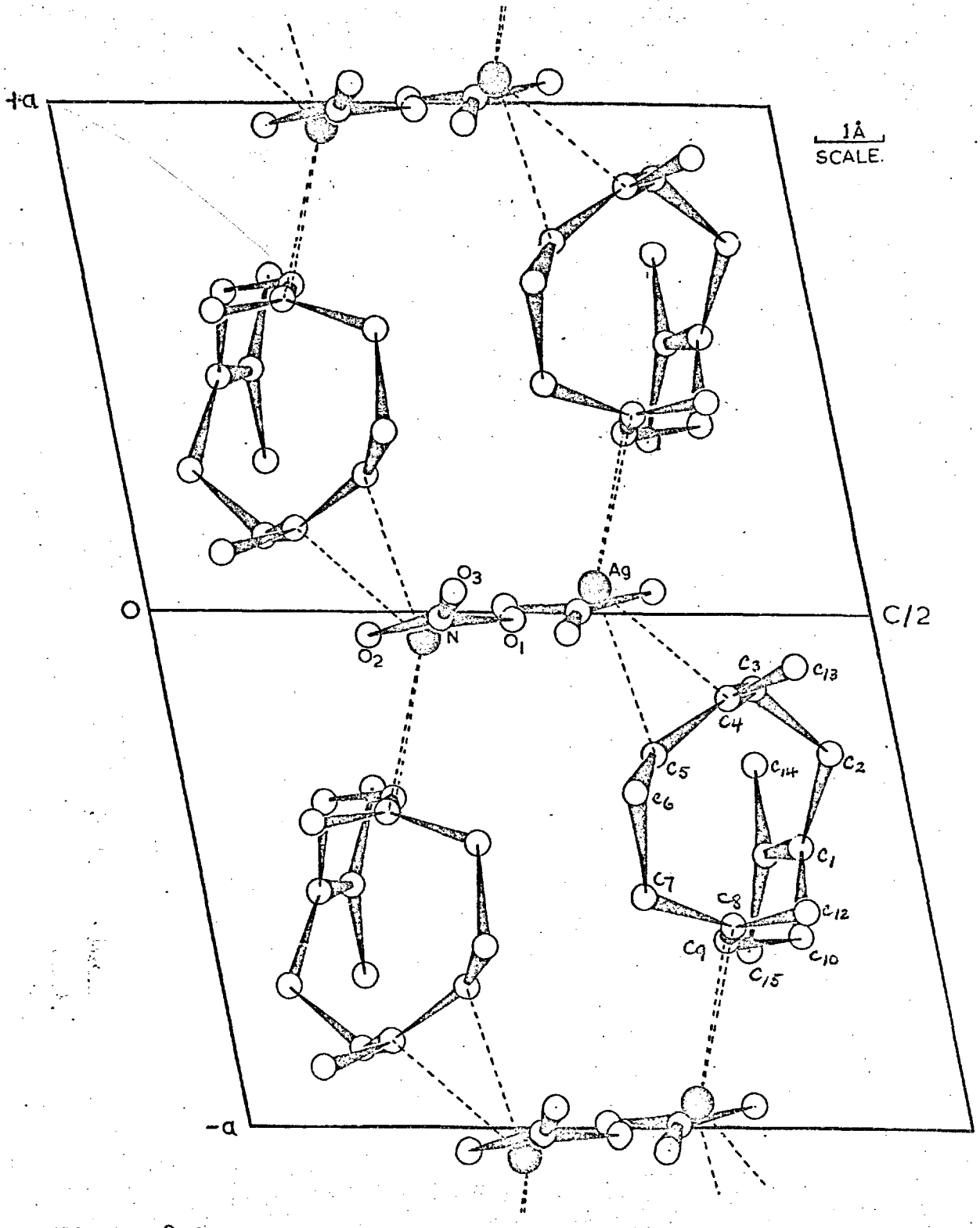


Figure 8.2. Germacratriene in b-axis projection.

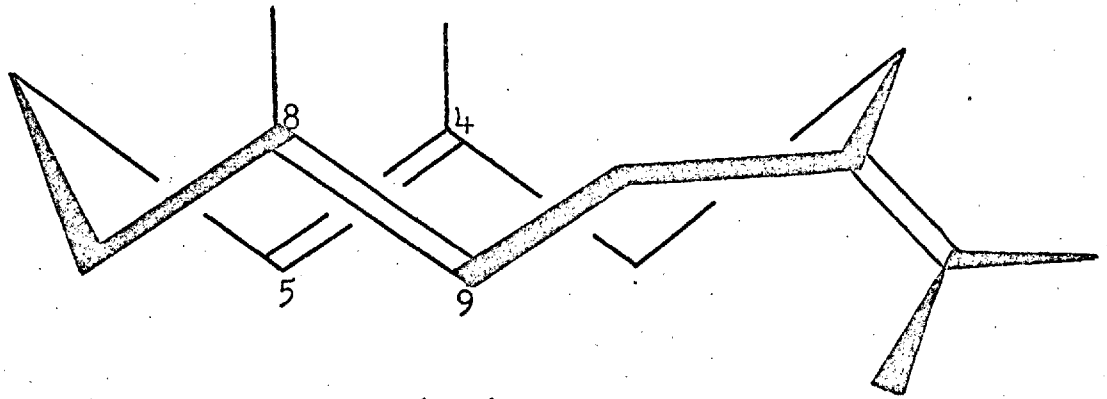
of the individual intensities. The use of an automatic diffractometer, although more accurate in actual measurement, is debatable in these cases; each reflection is measured once only, and the rate of decay governs the precision with which the data can be put on a common scale.

Nevertheless the accuracy obtained certainly warrants the full discussion given below.

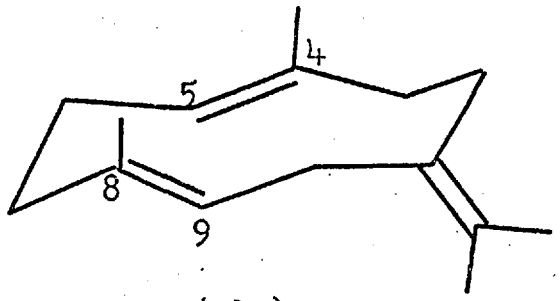
ii) Stereochemistry and Conformation.

The cell contains two L and two D molecules; Figure 8.2 shows the [010]-projection of the structure. The silver and nitrate ions form infinite chains along the screw axes parallel to b (see also Figure 8.4) at $z = \frac{1}{4}, \frac{3}{4}$, and are cross-linked at any one level in z by germacratriene units. Each silver ion is co-ordinated to the C(4)-C(5) double bond of one molecule, and to the C(8)-C(9) double bond of another, giving rise to further chains parallel to a. There are no close contacts (<3.5 Å) between centrosymmetrically related chains, and the packing in the c-direction is relatively loose. The mode of packing is reflected in the elongation of the crystal habit along a.

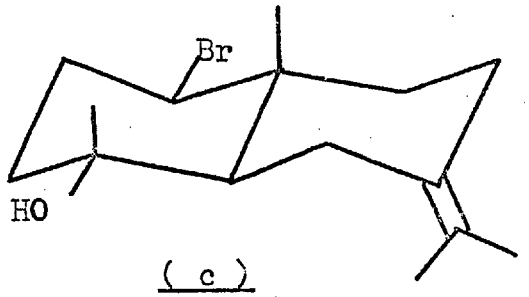
The all-trans stereochemistry proposed[133] for germacratriene has been confirmed. Figure 8.3 (a) and



(a)



(b)



(c)

Figure 8.3. (a) Perspective view of the conformation of germacratriene in the crystals of its $AgNO_3$ adduct. (b) Schematic view of conformation. (c) Schematic view of the conformation of the selinane derivative formed as a cyclisation product of germacratriene.

(b), show two views of the conformation adopted by the molecule in the crystal; as in the case of humulene and its bromohydrin 7.II, 7.III (p.157), there is an obvious chemical similarity between germacratriene and its cyclisation product Figure 8.3 (c). Again the planes of the endocyclic double bonds are roughly perpendicular to the plane of the macrocycle, leaving the π-orbitals ideally situated for the transannular cyclisation to the selinane derivative.

iii) Molecular Geometry.

The bond distances and valence angles are shown in Tables 8.5, 8.6 respectively; the standard deviations given are probably realistic estimates, but have suffered due to the paucity of data. Non-bonded contacts within the ionic layer are shown in Table 8.7, while ionic layer-germacratriene contacts are shown in Table 8.8.

The average C_{sp3}-C_{sp3} and C_{sp3}-C_{sp2} distances are 1.57 ± 0.03 Å and $1.53_5 \pm 0.03_0$ Å respectively, while the average C_{sp2}-C_{sp2} distance is $1.34_0 \pm 0.02_5$ Å. These values do not differ significantly from those found for humulene[128] (1.54, 1.52, and 1.34 Å), or from the accepted averages[153]. The discrepancy between the two C-Me distances in the isopropylidene group is curious, but could be due to crystal-packing forces, since

TABLE 8.5.

Germacratriene:$AgNO_3$.

Intramolecular Bonded Distances (r) in Ångstroms, together with their Estimated Standard Deviations (σ).

Atoms	r	σ	Atoms	r	σ
C(1) - C(2)	1.56	0.03	C(6) - C(7)	1.58	0.03
C(1) - C(10)	1.60	0.03	C(7) - C(8)	1.51	0.03
C(1) - C(11)	1.30	0.02	C(8) - C(9)	1.38	0.02
C(2) - C(3)	1.56	0.03	C(8) - C(12)	1.51	0.03
C(3) - C(4)	1.49	0.03	C(9) - C(10)	1.55	0.03
C(4) - C(5)	1.35	0.03	C(11)- C(14)	1.59	0.04
C(4) - C(13)	1.51	0.03	C(11)- C(15)	1.48	0.04
C(5) - C(6)	1.55	0.03	N - O(1)	1.23	0.03
N - O(2)	1.15	0.03	N - O(3)	1.28	0.02

TABLE 8.6.

Germacratriene:$AgNO_3$.

Valence Angles (θ°) in the Asymmetric Unit, together with their Estimated Standard Deviations (σ°).

Atoms	θ°	σ°	Atoms	θ°	σ°
C(1)-C(2)-C(3)	115.4	1.8	C(5)-C(4)-C(13)	122.9	1.6
C(1)-C(10)-C(9)	105.2	1.8	C(5)-C(6)-C(7)	102.0	1.6
C(1)-C(11)-C(14)	119.4	1.9	C(6)-C(7)-C(8)	115.6	1.5
C(1)-C(11)-C(15)	126.4	2.0	C(7)-C(8)-C(9)	116.1	1.8
C(2)-C(1)-C(10)	111.2	1.5	C(7)-C(8)-C(12)	117.9	1.6
C(2)-C(1)-C(11)	125.2	1.8	C(8)-C(9)-C(10)	124.0	1.8
C(2)-C(3)-C(4)	107.9	1.8	C(9)-C(8)-C(12)	122.4	1.8
C(3)-C(4)-C(5)	120.2	1.6	C(10)-C(1)-C(11)	123.0	1.8
C(3)-C(4)-C(13)	114.3	1.6	C(14)-C(11)-C(15)	114.2	1.9
C(4)-C(5)-C(6)	128.7	1.7	O(1) -N - O(2)	124.9	1.9
O(1)- N - O(3)	113.0	1.8	O(2) -N - O(3)	122.1	1.9

TABLE 8.7.

Germacratriene:$AgNO_3$.

Non-bonded Contacts within the Ionic Layer <4.5Å.

Superscripted atoms (') are related to those in Table 8.2 by the symmetry operation :

$$-\underline{x}, \quad \tfrac{1}{2} + \underline{y}, \quad \tfrac{1}{2} - \underline{z}.$$

Ag - O(1)	2.94 Å	Ag - N'	3.07 Å
Ag - O(2)	4.24	Ag - O(1)'	2.81
Ag - O(3)	2.37	Ag - O(2)'	2.68
Ag - N	3.13	O(3)-N'	4.26
		O(3)-O(1)'	3.30
		O(3)-O(2)'	4.45
		Ag - O(3)'	4.34

TABLE 8.8.

Germacratriene:$AgNO_3$.

Germacratriene - Ionic Layer Contacts <4.5 Å.

Roman subscripts indicate atomic positions related to those in Table 8.2 by the following operations :

(I) $1 + x, \quad y, \quad z;$ (II) $1 + x, \quad \frac{1}{2} - y, \quad \frac{1}{2} + z;$

(III) $1 - x, \quad \frac{1}{2} - y, \quad \frac{1}{2} - z;$ (IV) $1 - x, \quad -\frac{1}{2} + y, \quad \frac{1}{2} - z;$

(V) $-x, \quad \frac{1}{2} + y, \quad \frac{1}{2} - z;$ (VI) $-x, \quad -\frac{1}{2} + y, \quad \frac{1}{2} - z.$

C(7) - Ag	3.18 Å	C(3) - Ag_I	3.26 Å
C(8) - Ag	2.48	C(4) - Ag_I	2.52
C(9) - Ag	2.57	C(5) - Ag_I	2.54
C(10)- Ag	3.44	C(6) - Ag_I	3.24
C(12)- Ag	3.28	C(13)- Ag_I	3.26
C(9) - N	3.96	C(5) - N_I	4.18
C(9) - O(1)	3.60	C(3) - $O(1)_I$	3.73
C(10)- O(1)	4.08	C(4) - $O(1)_I$	3.98
C(15)- O(1)	3.99	C(5) - $O(1)_I$	3.75
C(7) - O(3)	3.69	C(5) - $O(3)_I$	3.90
C(8) - O(3)	3.77	C(6) - $O(3)_I$	4.42
C(9) - O(3)	3.51		
		C(13)- $O(2)_{II}$	4.15

contd.

Table 8.8 Continued :

C(4) - N_{III}	4.31 Å	C(7) - N_V	3.86 Å
C(5) - N_{III}	3.93	C(8) - N_V	3.96
C(6) - N_{III}	3.22	C(12) - N_V	4.10
C(13) - N_{III}	4.23	C(7) - $O(1)_V$	3.51
C(5) - $O(1)_{III}$	3.98	C(8) - $O(1)_V$	3.88
C(6) - $O(1)_{III}$	3.42	C(12) - $O(1)_V$	4.46
C(4) - $O(2)_{III}$	3.61	C(7) - $O(2)_V$	3.71
C(5) - $O(2)_{III}$	3.57	C(8) - $O(2)_V$	3.41
C(6) - $O(2)_{III}$	3.17	C(9) - $O(2)_V$	4.38
C(13) - $O(2)_{III}$	3.29	C(12) - $O(2)_V$	3.26
C(6) - $O(3)_{III}$	3.83	C(7) - $O(3)_V$	4.87
C(14) - N_{IV}	3.92	C(15) - Ag_{VI}	4.43
C(14) - $O(2)_{IV}$	3.78	C(15) - N_{VI}	3.50
C(14) - $O(3)_{IV}$	3.38	C(15) - $O(1)_{VI}$	4.21
		C(15) - $O(2)_{VI}$	3.51
		C(15) - $O(3)_{VI}$	3.29

C(15) is closer to the ionic layer than C(14). The asymmetric position of the isopropylidene group with respect to the ionic layer can be seen in Figure 8.4.

It was noted in Chapter 7 (p.162) that there is appreciable angular strain in medium-sized saturated carbocycles; average C-C_{sp3}-C angles as high as 117° have been found experimentally (refs 179-183), confirming results from minimum-energy calculations[159]. The presence of five C_{sp2} atoms in the cyclodecadiene ring of germacratriene has relieved this strain. Although the C-C_{sp3}-C angles show a fairly wide spread (102° ⟶ 115.6°), the average value in the ring is now 109.2° ± 1.7°, close to the tetrahedral value. The comparable average in humulene is 111° [128].

The germacratriene molecule is distorted much past what can be achieved with a Dreiding model. Most of the distortion is at the endocyclic double bonds, and the two substituent methyl groups C(12), and C(13), are pushed in towards the centre of the ring (see Figure 8.4). Although the average C-C_{sp2}-C angle for these bonds is 120.8°, there is a very wide spread (114.3° ⟶ 128.7°), and substantial out-of-plane twisting (sp_2-sp_2 torsional strain) compared with the exocyclic isopropylidene double bond. The geometry about the double bonds is

further discussed in the next section (8.5), in relation to their observed reactivity differences.

iv) The Ionic Layer.

Figure 8.4 illustrates some interesting features of the ionic layer and its interaction with the organic moiety. It shows that the Ag^+ ion is close to two oxygen atoms (O(1) and O(3)) of one NO_3^- ion, and to two more (O(1)' and O(2)' *) of another, at distances ranging from 2.37 to 2.94 Å (see Table 8.7). The arrangement of the five atoms is nearly planar. The short contact (Ag^+ - O(3)) is significantly shorter than the sum of the ionic radii of Ag^+ and O^- given as 2.46 Å [200], and similar distances have been found in the silver nitrate complexes of cyclooctatetraene[198], humulene[128], and norbornadiene[201]; distances of 2.32 and 2.42 Å have recently been found between Ag^+ and the oxygen atoms of water molecules in the bis-bullvalene : $AgBF_4$:H_2O complex[202]. The mode of chain formation is very similar to that found in the cyclooctatetraene complex[198], and the average Ag^+-O distance there (2.65 Å) compares well with the value of 2.70 Å in the present study.

The atoms of the nitrate ion are, as expected, closely coplanar, but the N^+ is very slightly above the plane

* The superscripts (') are explained in Table 8.7.

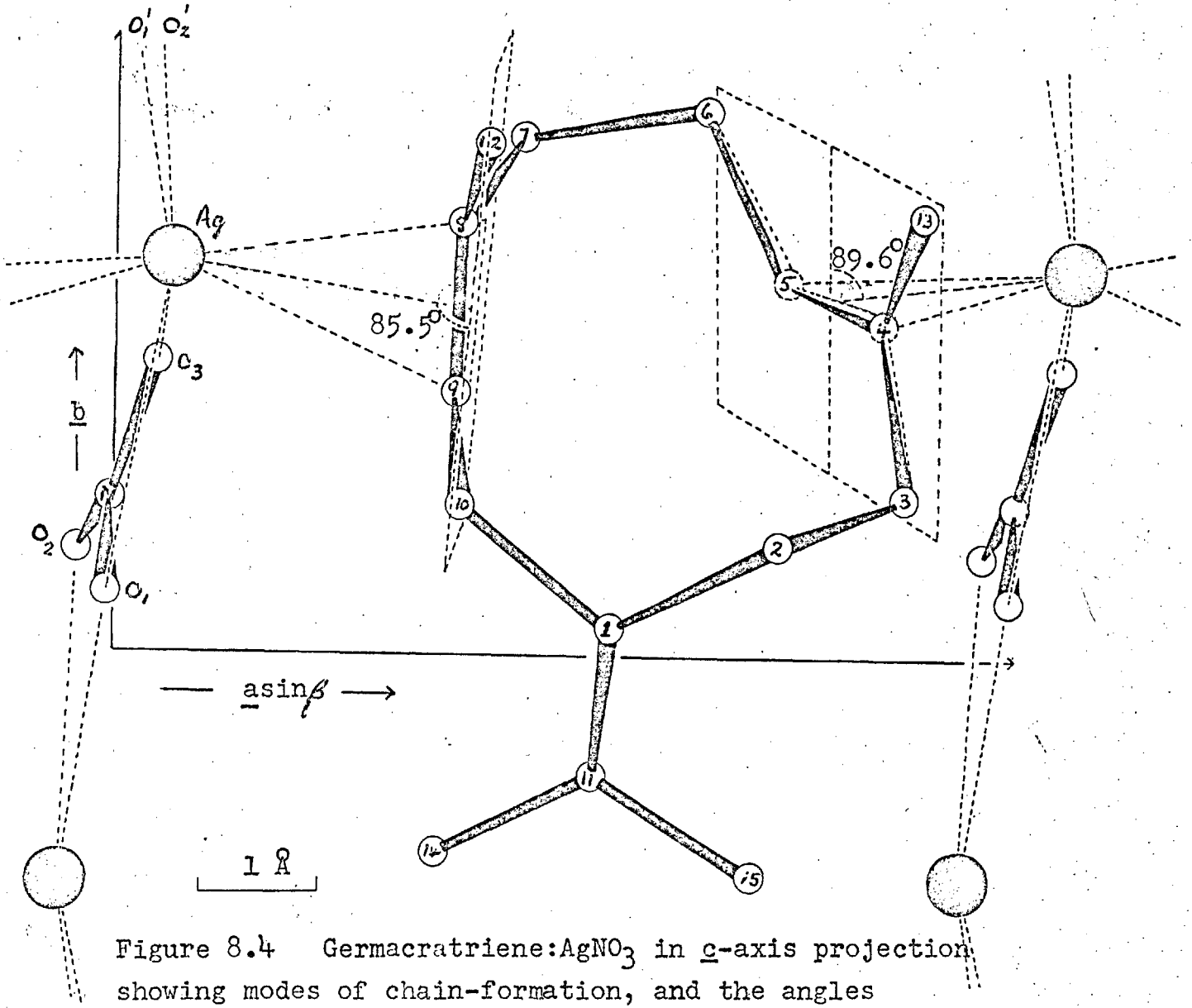


Figure 8.4 Germacratriene:$AgNO_3$ in c-axis projection showing modes of chain-formation, and the angles involved in the silver-ethylenic bond. (mean planes are are dotted, the Ag - C=C planes are lightly shaded).

of the oxygens by ~0.02 Å. The variation of N^+ - O distances, from 1.15 to 1.28 Å, is explicable in terms of the silver ion co-ordination. O(3) is the most strongly co-ordinated to Ag^+ and has the longest N^+ - O distance, O(1) is weakly co-ordinated to two Ag^+ ions and has a slightly stronger (and therefore shorter) bond to nitrogen, while O(2) is co-ordinated only weakly to one Ag^+ and has an N^+ - O distance consistent with double-bond formation[153]. A similar argument could explain the significant deviation of valence angles O-N^+-O, involving O(1), from the expected value of 120°, since this atom has to satisfy the co-ordination requirements of two silver ions.

Figure 8.4 shows that the co-ordination polyhedron of the silver ion consists of eight atoms: the four oxygens noted above, and four C_{sp2} atoms from two germacratriene units. The arrangement may best be described by noting that the vectors from Ag^+ to the midpoints of the double bonds, and to the nitrogen atoms of the nitrate ions, form a distorted tetrahedron. The angles involved are shown in Figure 8.5. The apparently bidentate NO_3^- ligand must be regarded as occupying only one co-ordination position, as in the ionic layer of the humulene adduct[128], where the overall co-ordination is distorted trigonal bipyramidal,

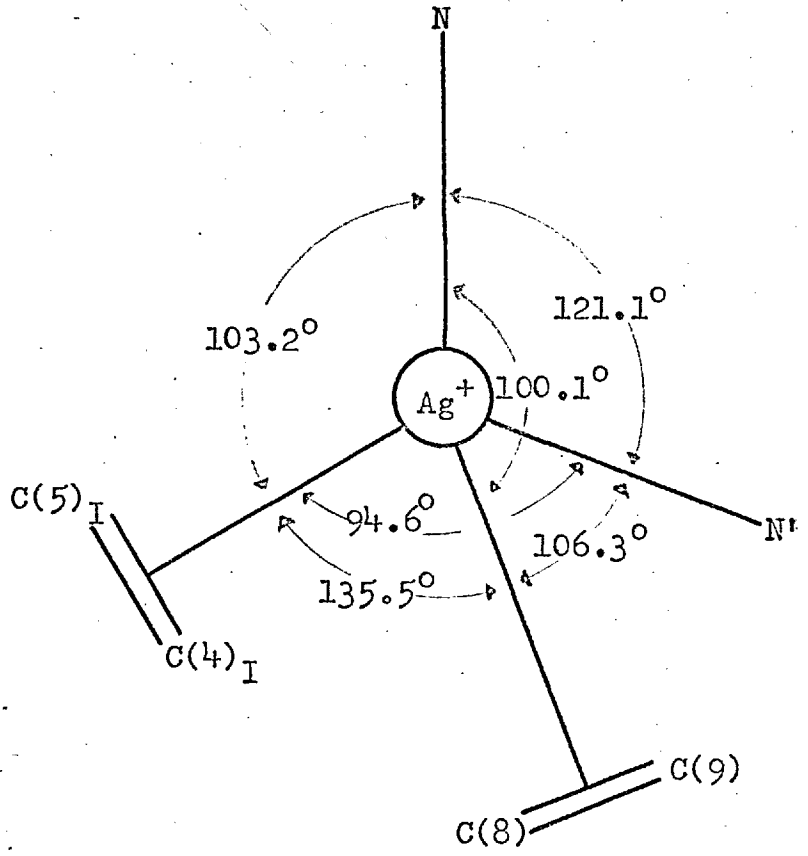


Figure 8.5. The distorted tetrahedral co-ordination of Ag^+ in germacratriene. (The meanings of the subscripts and superscripts (I), (') are given in Tables 8.8, 8.7, respectively).

or in the tetranitritocobaltate(II) ion[203], where the ligand field is effectively tetrahedral. Distorted tetrahedral co-ordination has been found in several mercury complexes[204], where angles range from 92° to 155°.

v) Germacratriene - Ionic Layer Interactions.

The complexes of silver salts with molecules containing ethylenic linkages, studied so far by the X-ray method, show ratios of organic : inorganic moieties rangeing from 3:1 to 1:2. An interesting comparison of the relative bond strengths is afforded by a study of the distances of Ag^+ from the midpoints of the complexed double bonds. The results from this study are shown in Table 8.9, together with the relevant data for five other compounds. In a comparison of the distances given it is more meaningful to describe each compound by the ratio of complexed double bonds to Ag^+ ions; furthermore the Ag^+ - midpoint distances appear to fall into groups by which we may define the Ag^+ - olefin π-bond 'order'. Bonds of the first 'order' occur when a single double-bond is complexed by a single Ag^+ ion, and distances range from 2.26 to 2.29 Å; bonds of the second 'order' are exemplified by the present work, where one Ag^+ ion is complexed to two ethylenic bonds only,

TABLE 8.9.

Silver Salt : Olefin Complexes. Comparison of Ag^+ - C═C midpoint distances (m) in Å.

Compound	Organic : Inorganic.	Complexed double bonds : Ag^+	'Order'	No.	m in Å.
Norbornadiene:$2AgNO_3$ (201)	1 : 2	1 : 1	1	2	2.26, 2.26.
Humulene:$2AgNO_3$ (128)	1 : 2	1 : 1	1	2	2.29, 2.29.
Germacratriene:$AgNO_3$	1 : 1	2 : 1	2	2	2.43, 2.43.
Cyclooctatetraene:$AgNO_3$ (198)	1 : 1	2 : 1	2	1	2.38.
			3(?)	1	2.73.
			-	1	ca. 3.0 Å.
Tris-bullvalene:$AgBF_4$ (199)	3 : 1	4 : 1	2	2	2.42, 2.43.
			3	2	2.63, 2.69.
Bis-bullvalene:$AgBF_4$ * (202)	2 : 1	2 : 1	2	4*	2.36, 2.37, 2.42, 2.46.
			-	4*	ca. 3.0 Å.

* Two crystallographically independent molecules per asymmetric unit.

at midpoint distances of ca. 2.43 Å. By a simple linear extrapolation it would appear that a single Ag^+ ion should be complexed to three equi-distant double bonds (i.e. pure third 'order'), at Ag^+-midpoint separations of ca. 2.6 Å. It is doubtful if the long contacts of ca. 3.0 Å, noted in Table 8.9. represent very strong interactions, but they do have some effect in stabilizing the crystal packing.

Thus, from the arguments above, it has been possible to break down the number of Ag^+-olefin bonds into their respective 'orders'. Although the data at present available is admittedly rather sparse, this break-down appears viable in an attempt at a meaningful classification of these complexes. It is unfortunate that comparison with the silver perchlorate : benzene complex[197], and the complex of silver nitrate with the cyclooctatetraene dimer[205], are not meaningful, due to a disordered Ag^+ position in the former, and lack of definition in the latter. The full details of the structure determination of cis,cis,cis-1,4,7-cyclononatriene:$AgNO_3$[166] have not yet appeared in the literature. Nevertheless, from the information given in the references cited in Table 8.9, it appears that the chemical stability and the number of 'bonds' formed by silver are correlated.

The individual Ag^+-C_{sp2} distances at the C(8)-C(9) double bond are significantly unequal (see Table 8.8), but

this is not true at the C(4)-C(5) bond. The asymmetric orientation of Ag^+ with respect to the complexed double bond has been found in many of the compounds mentioned above, and was initially ascribed to crystal packing forces.[128] A molecular-orbital approach, applied to metal-olefin complexes in general[206,207], has afforded a better explanation. Overlap is required between the symmetrical donor π-orbital of the olefin with a vacant metal orbital (σ-bond), and also between a filled metal orbital and the antibonding π^*-orbital of the olefin (μ-bond). It has been suggested that the asymmetric position adopted affords the best compromise between the two requirements[199].

The strength of the σ-bond in silver-olefin complexes is, however, weak, since the ion does not possess vacant orbitals of the correct symmetry to act as acceptors. This is reflected in the C=C bond lengths, which should be elongated in the case of strong σ-bonding(which reduces the electron-density in the double bond, and thus reduces the bond-order). This has not been found in previous X-ray studies, nor in the present work, where the double-bond lengths (C(4)-C(5), C(8)-C(9)) are not significantly longer than the uncomplexed bond C(1)-C(11). However in the crystal structures of the complexes $K^+(C_2H_4PtCl_3)^-$[208], and $Pt(C_2H_4)(NH(CH_3)_2)Cl_2$[209], the ethylenic bond is elongated to 1.5 Å and 1.47 Å respectively; this is because the

platinous ion possesses a vacant (acceptor) d-orbital. One can only conclude that, in silver-olefin complexes, the μ-bond is predominant; this would not, of course, increase the electron density between the olefinic carbon atoms to any great extent, and no cases of C=C distances less than ca. 1.30 Å have been reported. The lack of asymmetry at the C(4)-C(5) double bond in the present study is probably not explicable on a molecular orbital approach. While this has provided a good general picture of metal-olefin bonding, other factors, such as crystal-packing forces, and the presence of other atoms in the co-ordination polyhedron, must have some effect, and will differ from complex to complex.

In any event maximum overlap should occur when the Ag^{+}-C_{sp2}-C_{sp2} plane is perpendicular to the mean plane through the olefinic linkage. In the present study the angle between the planes Ag,C(4),C(5), and C(3),C(4),C(5), C(6),C(13), is 89.6°, and the angle between the planes Ag,C(8),C(9), and C(7),C(8),C(9),C(10),C(12), is 85.5°. The planes are shown dotted in Figure 8.4. The values agree well with comparable angles in the tris-bullvalene adduct[199] (91.5° & 91.1°),and in the humulene adduct[128] (85° & 87°). Where Ag^{+} is asymmetric to two double bonds (e.g. cyclooctatetraene:$AgNO_3$), or complexed to only one cis-double bond (norbornadiene:$2AgNO_3$), there are substantial

deviations from 90°. Thus the substitution pattern at the complexed double bond also appears to affect the bonding to the metal ion.

On a more empirical scale it is interesting to note that the shortest 'first-order' Ag^+-olefin bond (2.26 Å) is still longer than the sum (2.03 Å) of the Ag^+ ionic radius (1.26 Å[210]) and the covalent radius of carbon (0.77 Å). This indicates that the distance of closest approach of Ag^+ to the olefinic bond is ca. 1.0 Å. A similar result can be obtained for Cu^+ in the complexes norbornadiene:CuCl[211] and catena-μ-chloro-cyclooctatetraene Cu(I)[212]; the Cu^+-midpoint distances are 1.97 and 1.98 Å respectively, and the ionic radius of Cu^+ is 0.96 Å. The comparison is interesting since both Ag^+ and Cu^+ have filled d-orbitals, and do not readily form π-bonds. The value 1.0 Å could thus be termed the 'μ-bonding radius' of carbon. In the case of platinum, which is a ready acceptor of π-electrons (see above), a similar study shows a 'π-bonding radius' of ca. 0.75 Å, indicative of stronger bonding.

A single uniform theory of bonding in metal-olefin complexes is still far from clear. The numerous factors involved make structural predictions difficult, and many further X-ray studies of high precision will be required to clarify the situation. However the very great chemical

interest in these compounds, both from the organic and inorganic points of view, makes them ideal 'targets' for crystallographic investigation.

8.5. The Geometry about the Double Bonds and its Effect on their Reactivity.

i) The Molecular Geometry about the Double Bonds.

The increased distortion of the endocyclic double bonds in germacratriene, compared with that of the exocyclic isopropylidene group, has been mentioned briefly above (see Sect. 8.4 (iii)). The distortion is analysed in Figure 8.6 (for all three bonds) in terms of :

i) Valence Angles (θ^o),
ii) sp^3 - sp^2 torsion angles $(\delta^o)^{\ast}$,

} Fig. 8.6 (a)

and iii) sp^2 - sp^2 torsion angles $(\tau^o)^{\ast}$, shown in Fig. 8.6 (b) in the form of Newman diagrams[/] (213). It can be seen that criteria (i) and (ii) match closely for both endocyclic bonds, and that most of the distortion is due to out-of-plane twisting about the axis of the bond, so that the planes of the pairs of substituents are no

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$\ast$ To preserve clarity in the discussion which follows; the symbol (ω) will be reserved for sp^3-sp^3 torsion angles, as in Chaps. 6 & 7.

/ See also Appendix II, Figure II.2, for further examples.

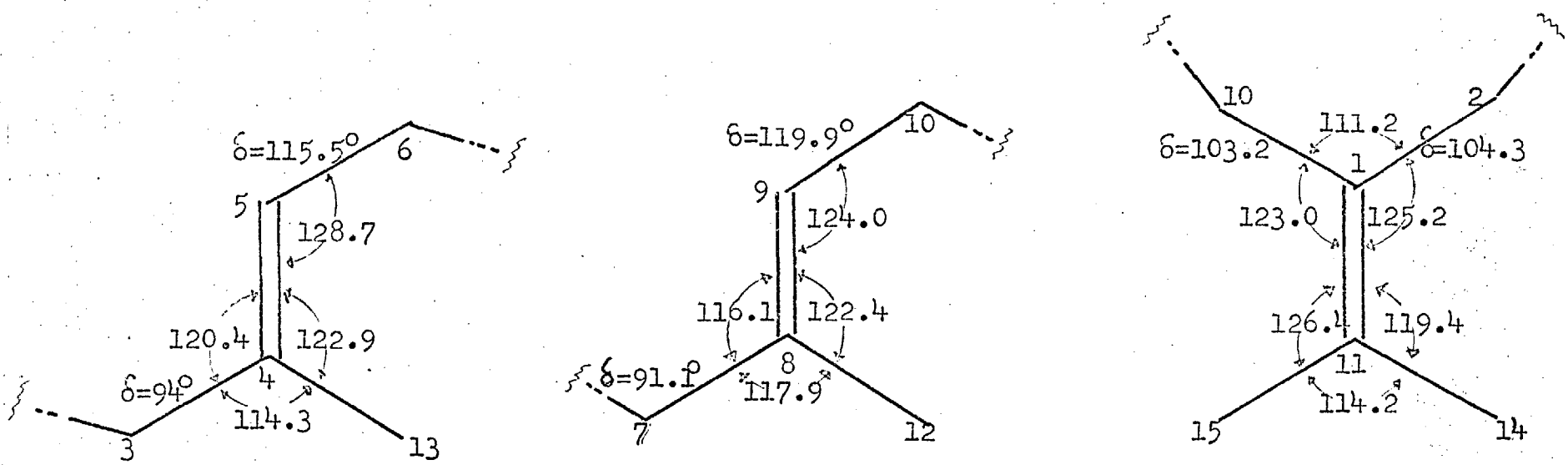


Figure 8.6 (a) Germacratriene:$AgNO_3$, Valence angles and sp^3-sp^2 torsion angles (ζ) about the double bonds.

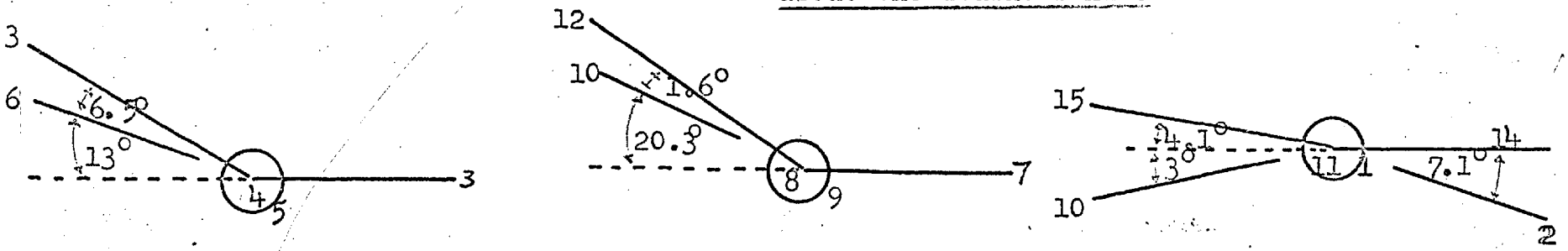
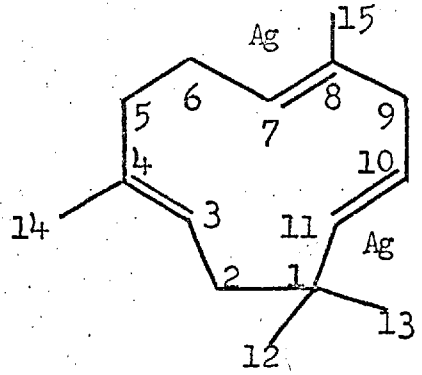
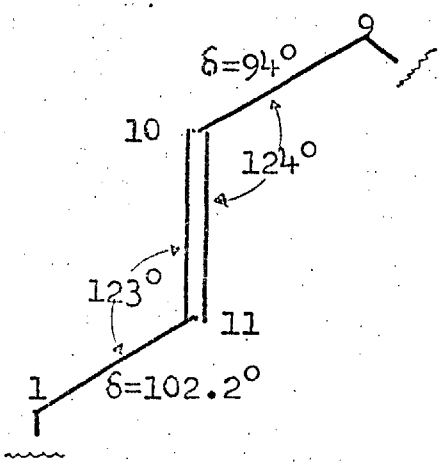
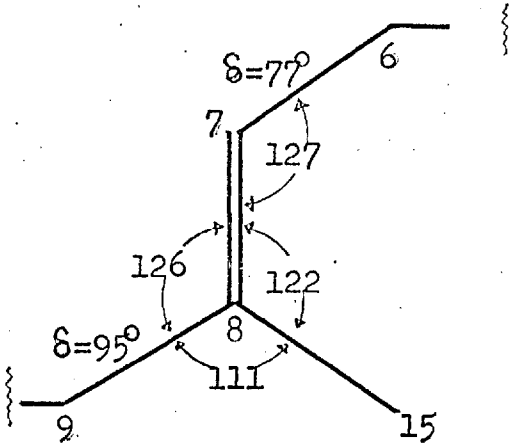


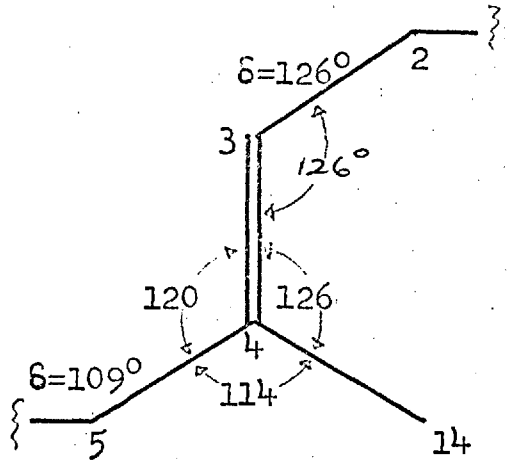
Figure 8.6 (b) Germacratriene:$AgNO_3$, Newman projections down each double bond showing the sp^2-sp^2 torsion angles (τ)



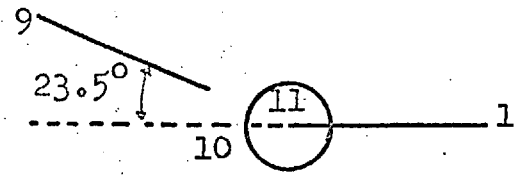
(a)

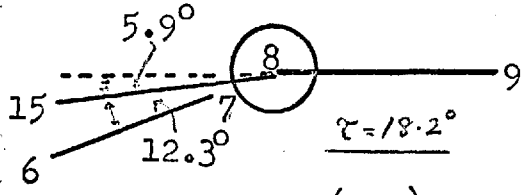


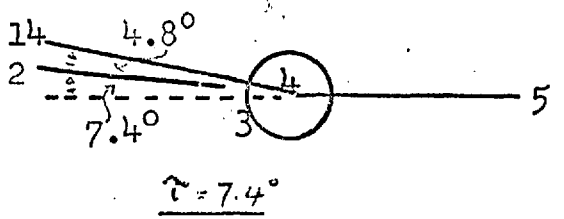




(b)







(c)

Figure 8.7. (a) Structure and numbering scheme for humulene.
(b) Valence angles and sp^3-sp^2 torsion angles (δ) about the three double bonds.
(c) Newman diagrams showing the sp^2-sp^2 torsion angles (τ).

longer parallel (criterion (iii)). This sp^2 - sp^2 torsional strain is greater for the C(8)-C(9) bond than for the C(4)-C(5) bond; it is almost negligible for the C(1)-C(11) bond. The data of Table 8.10, which shows the deviations (d, in Å) of the relevant atoms from the mean plane through each double bond, also reflects this sequence; thus $\langle d \rangle_{8-9} > \langle d \rangle_{4-5} > \langle d \rangle_{1-11}$. The results explain, in a purely qualitative manner, the observed differences in reactivity of the three bonds; however it has been possible to obtain some more quantitative results from strain-energy calculations; these will be discussed below.

It is possible that a small amount of the observed distortion at the endocyclic double bonds is due to Ag^+-C non-bonded repulsions. This may well account for the positions adopted by the two methyls (C(12) & C(13)), pushed in towards the centre of the ring, and towards one another, by angles of 19.5° and 22.0° (Fig. 8.6 (b)). Their distances from Ag^+ (3.26 and 3.28 Å respectively) are almost equal. Even after this deformation the Me-Me separation is still large (3.57 Å), and the positions adopted may be a compromise between Me-Me and Ag^+-Me repulsions.

It is doubtful whether the Ag^+ ion has much effect on the ring geometry and conformation. The distances of Ag^+ from C(3),C(6),C(7),C(10), are all >3.18 Å (Table 8.8), i.e. longer than any distance quoted in Table 8.9, and much

TABLE 8.10.

Germacratriene:$AgNO_3$.

Deviations (d) in Ångstroms of Constituent Atoms from the Mean Plane through each Double Bond *.

Bond	Atom	d	⟨d⟩
C(4)=C(5)	C(3)	-0.080	
	C(4)	0.120	
	C(5)	0.042	0.065.
	C(6)	-0.059	
	C(13)	-0.023	
C(8)=C(9)	C(7)	-0.122	
	C(8)	0.151	
	C(9)	0.098	0.100.
	C(10)	-0.105	
	C(12)	-0.022	
C(1)=C(11)	C(2)	-0.018	
	C(10)	-0.016	
	C(1)	0.053	0.018.
	C(11)	-0.011	
	C(14)	-0.002	
	C(15)	-0.005	

* Calculated using LSQPL.

longer than the sum of the Ag^+ ionic radius and the covalent radius of carbon (2.03 Å, see p. 211). Furthermore none of the atoms in the ring are as mobile as the methyl carbons mentioned above.

In the case of the humulene:$2AgNO_3$ adduct[128] the three double bonds are all endocyclic ; the two complexed bonds C(10)-C(11), C(7)-C(8), (see Fig. 8.7 (a)) show marked, but unequal, distortion; the uncomplexed bond C(3)-C(4) is again almost planar. An analysis of the distortion, similar to that given for germacratriene, is shown in Figure 8.7 (b) & (c). It shows that,while the sp^2 - sp^2 torsional strain is again large for the complexed bonds, the sp^3 - sp^2 torsion angles do not match in this case. Nevertheless it has been possible to perform semi-quantitative strain-energy calculations which explain why epoxidation of humulene gives > 95% of the C(7)-C(8) monoxide[214].

ii) Reactivity in Medium-Ring Olefins.

It is now well established that trans double bonds in medium-ring olefins are more reactive than their acyclic counterparts[215], and this has been ascribed to steric strain. Hitherto it has been difficult to define the types of strain that occur, and to estimate their relative importance, due to the lack of accurate structural data to accompany the experimental results. The X-ray studies of humulene and germacratriene as their silver nitrate adducts,

have provided such data.

Before the parameters discussed above can be used in arguments concerning reactivity two questions must be considered :

1) Are the ring conformations found in the solid silver nitrate adducts an accurate reflection of those adopted in solution just prior to reaction?

2) Does the complexing of a double bond with a silver ion induce changes in hybridisation, with consequent changes in bond-lengths and angles?

The first question has been answered at some length in this Thesis. The obvious chemical similarities between the crystal conformations of both germacratriene and humulene and their respective cyclisation products is shown in Figure 8.3, and in structural formulae 7.II, 7.III. Further evidence is also cited in Chap. 7, as refs. 165-167.

The answer to the second question lies in the discussion given above (Sect. 8.4 (v)), where the bonding of Ag^+ to the olefinic bonds was shown to be weak compared to similar platinum complexes. The bond lengths and valence angles are not significantly altered in comparison with parameters for uncomplexed bonds.

It would seem logical for the silver ion to complex those bonds which have the greatest chemical reactivity;

since the bond formed is weak, the conformation present in solution is then 'frozen' in the crystal structure. This type of argument is not, however, general, and must depend on the type of complex formed, and the strength of the metal-olefin bond.

In an elegant analysis of the reactions of various olefins with diimide Garbisch et. al.[216] have had remarkable success in predicting relative reaction rates by resolving the steric strain (E_s) about each reactive bond into, inter alia, bond-angle and sp^3-sp^2 torsional contributions (E_θ) and (E_δ), and comparing these in starting materials and products. Following this approach the strain-energy differences (ΔE_s) between the C(3)-C(4) and C(7)-C(8) bonds of humulene, and the C(4)-C(5) and C(8)-C(9) bonds of germacratriene, have been estimated. Inclusion of the di- and tetra-substituted double bonds (C(10)-C(11) in humulene, C(1)-C(11) in germacratriene) in the calculation is difficult, due to differences in the inductive effects of substituents, which would make comparison of their strain-energies with those for the trisubstituted bonds rather unreliable.

The data for germacratriene are the simplest to compute, since values of (θ) and (δ) match closely for both double bonds; other factors, such as non-bonded interactions between reagent and substrate, entropies of activation, and nucleo-

philicities should also match closely. Thus only the values of (τ) differ, and while the sp^2-sp^2 torsional strain was thought by Garbisch[216] to make a negligible contribution in the cases he considered, it is obviously of paramount importance here. A reliable estimate of (E_s) for each bond may therefore be obtained by computing (E_τ). The latter is given by :

$$E_\tau = 8\tau^2 \text{ cal mole}^{-1} \ldots\ldots\ldots 8.1;$$

a formula derived for ethylene by Herzberg[217]. Since we are concerned with the strain in the ring, it is correct to use the complements of the angles $\tau_{3(4,5)6}$* (= -167°, whence E_τ = 1.35 kcal mole^{-1}) and $\tau_{7(8,9)10}$ (= -159.7°, E_τ = 3.30 kcal mole^{-1}), in estimating the strain due to the out-of-plane twisting/. Thus ΔE_s (= ΔE_τ) is given as 1.95 kcal mole^{-1}. Any reaction in which this strain can be relieved in the transition state should lead to a higher reactivity for the C(8)-C(9) double bond.

Epoxidation should be a suitable reaction for detecting differences in transition state activation energies ($\Delta\Delta F^*$), since π-π transannular interactions between the double bonds

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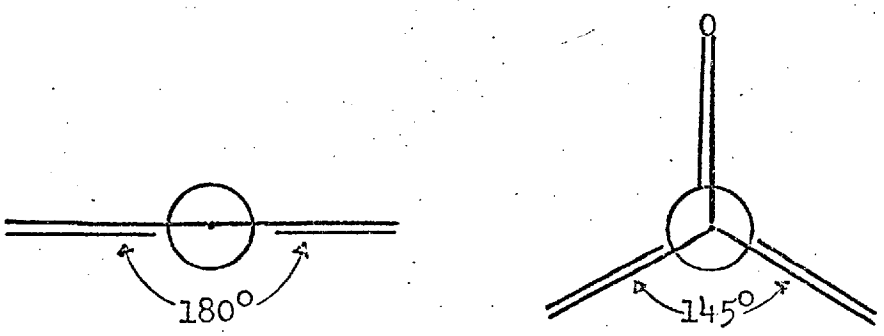
* The meaning of this nomenclature is given in Appendix II.

/ Any bond for which $\tau = \pm 180°$ obviously has $E_\tau = 0$, thus the complements of these angles give the correct E_τ's. The complements are shown in Figure 8.6. (b).

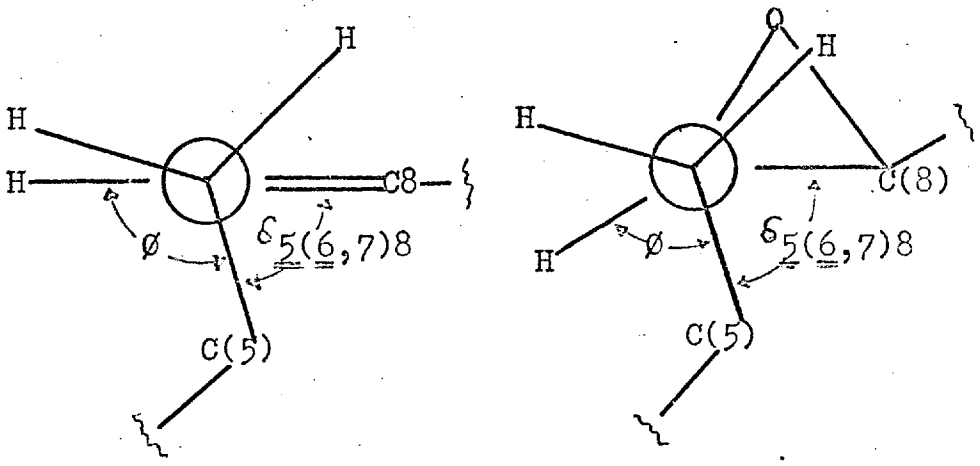
would be expected to be unimportant in the transition state. Further, it involves a minimal geometric change, as shown in Figure 8.8 (a) & (b) (projections down the C=C bond before and after epoxidation), in which the projected angle decreases from 180° to ca. 145°. The epoxidation of germacratriene (Fig. 5.6. p. 86) gave the 8-9 and 4-5 monoxides in the ratio 70:30, implying that the rate of reaction at the bond C(8)-C(9) is more than twice that at the C(4)-C(5) bond. We may therefore use the equation developed by Garbisch[216] :

$$-RT \ln(k_1/k_2) = \Delta\Delta F^{\ddagger} \quad \ldots\ldots\ldots\ldots 8.2,$$

where (R) is the gas constant (1.99 cal deg^{-1} $mole^{-1}$), (T) is the absolute temperature (taken as 298°K), and (k_1/k_2) is the ratio of the reaction rate constants (taken as 70:30). The value of $\Delta\Delta F^{\ddagger}$ given is ca. 0.5 kcal $mole^{-1}$, so that approximately $\frac{1}{4}$ of the torsional strain-energy difference is relieved in the transition state. This result in itself is interesting, since Garbisch[216] only obtained good agreement of observed and calculated rate constants for the diimide reduction of medium ring olefins, by assuming that the transition state occurred somewhat further along the reaction co-ordinate between reactants and products. The high reactivity of the strained trisubstituted double bonds is clear from the isolation of only a trace of the 1-11 oxide.



(a) (b)



(c) (d)

Figure 8.8.

The epoxidation of humulene is reported[214] to give $>95\%$ of the 7-8 monoxide, this corresponds to a $\Delta\Delta F^{\ddagger}$ of $\geqslant 1.7$ kcal mole^{-1}. The relevant sp^2-sp^2 torsion angles are $\tau_{\underline{2}(\underline{3},4)5}$ and $\tau_{\underline{6}(\underline{7},8)9}$, and their complements (see Fig. 8.7 (c)) give $E_\tau = 0.45$ kcal mole^{-1} for bond C(3)-C(4), and $E_\tau = 2.65$ kcal mole^{-1} for C(7)-C(8); thus ΔE_τ is 2.2 kcal mole^{-1}. If we assume that $\frac{1}{4}$ of this energy difference is relieved in the transition state (cf. above), a value of 0.55 kcal mole^{-1} is obtained for $\Delta\Delta F^{\ddagger}$, which is too small to account for the difference in reactivity. However, as noted above, the sp^3-sp^2 torsion angles for the two bonds differ appreciably in humulene. The previous model for epoxidation is extended in Figure 8.8 (c) & (d), which show projections down the C(6)-C(7) bond before and after reaction; the sp^3-sp^2 torsion angle ϕ ($= \delta_{\underline{5}(\underline{6},7)H}$) is effectively reduced by *ca.* 35°. This picture of epoxidation, involving only a twisting about the double bond, with little change in the remainder of the molecule, is reasonable, at least in the early stages of reaction, since C-C-C bond angles are similar in olefins and epoxides, and there are only slight changes in bond lengths. The twisting already present in the double bonds of germacratriene and humulene makes this simple picture even more probable. The description implies that $\delta_{\underline{5}(\underline{6},7)8}$ remains unchanged after reaction; however, this does not mean that

this is the angle to be used in estimating the torsional strain (E_δ) in Fig. 8.8 (d), as it would describe the dihedral angle only if the C-C bond of the oxide were a straight line, rather than the 'bent bond'[196] generally accepted in three-membered rings. Thus Ø, the only angle to change, is a better estimate of torsion angles.

Table 8.11 shows the strain energies ($E_\emptyset$) about the relevant sp^3-sp^2 bonds in humulene, compared with the values estimated for the epoxides, where Ø is reduced by ca. 35°. The results indicate that epoxidation decreases this type of strain by ~1.1 kcal $mole^{-1}$ for bond C(7)-C(8), but increases it by ~1.9 kcal $mole^{-1}$ for bond C(3)-C(4). The combination of sp^3-sp^2 and sp^2-sp^2 torsional strains gives a value of 5.1 kcal $mole^{-1}$ for ΔE_s; if again we assume that $\frac{1}{4}$ of ΔE_s is relieved in the transition state, a value of ca. 1.25 kcal $mole^{-1}$ is obtained for $\Delta\Delta F^{\ddagger}$. This value does not wholly account for the reported disparity in reaction rates, but indicates[216,218] that the proportion of the 7-8 monoxide is at least > 87%.

These energy estimates must be regarded as, at best, semi-quantitative; nevertheless it is gratifying that the results obtained from the X-ray data agree with experiment within an order of magnitude. The errors are due to the assumptions made in the calculations, which may be listed as follows :

TABLE 8.11.

sp^3 - sp^2 Torsional Strain Energies, (E_ϕ)* in kcal $mole^{-1}$, in Humulene and its Monoxides*.

Humulene.			Monoxides.		
Bond	ϕ	E_ϕ	Bond	ϕ	E_ϕ
C(2)-C(3)	54°	0.02	C(2)-C(3)	19°	1.2
C(4)-C(5)	71	0.16	C(4)-C(5)	36	0.9
C(6)-C(7)	103	0.65	C(6)-C(7)	68	0.1
C(8)-C(9)	85	0.74	C(8)-C(9)	50	0.2

* The angle ϕ is defined in Fig. 8.8 (c) & (d); values for humulene were computed from the X-ray results[128] using MOJO, values for the monoxides were estimated from models.

* sp^3 - sp^2 torsional potential functions have the general form : $E\delta = K(1 + \cos 3\delta)$ for angle (δ), if the three substituents on the sp^3 atom are identical. Though this is not true in this work, the function probably yields reasonable estimates, in view of the limited range of ϕ (= δ) achievable. K is the half-height of the potential barrier; values of 2K for relevant compounds are : propene[219] : 2.0 kcal $mole^{-1}$; isobutene[220] : 2.2;

TABLE 8.11 (contd.)

cis-butene[221]: 0.8; propene oxide[222]: 2.6; 2,3-*cis*-butylene oxide[223]: 1.6. As it is well established that the rotational barrier is considerably lower for *cis*-1,2-disubstituted olefins than for the corresponding *trans*-compounds[221], extrapolation to trisubstituted olefins would suggest the use of two different values of K, *viz*: 1.0 kcal $mole^{-1}$ when the alkyl group is *cis* to hydrogen, and 0.4 when *cis* to another alkyl group; the appropriate values for epoxides would be 1.3 and 0.8 respectively. The torsional potential function for sp^3 - sp^3 strain-energy calculations is similar to that described above, it will be discussed in Appendix III.

i) that the relief of strain energy in going from reactants to products follows a straight line graph;

ii) that the relief of sp^2-sp^2 and sp^3-sp^2 torsional strain in humulene follows a graph having the same slope as that for germacratriene;

iii) that the transition state for both types of strain in humulene has the same reaction co-ordinate, i.e. $\frac{1}{4}$, as in germacratriene.

All of the above assumptions have been made, since there is no relevant experimental evidence in the literature. Further, the quality of the X-ray data does not lead to high precision in the energy calculations, for instance a change of $+1^{\circ}$ in $\tau_{3(4,5)6}$ for germacratriene (i.e. from -167° to -166°) gives a value of E_{τ} of 1.57 kcal $mole^{-1}$, a difference of +0.22 kcal $mole^{-1}$. If errors in the estimation of the ratios of the various products are also taken into account (at least $\pm$ 2%), the results obtained must be regarded in a favourable light.

The calculations do give some idea of the order of magnitude of the strain energies about the double bonds, and also of the energetics of the epoxidation reactions. They also illustrate the importance of the contribution made by the sp^2-sp^2 torsional strain to the high reactivity of medium-ring trans-olefins; in certain cases, e.g. germacratriene, this contribution may be much larger than that

of the more familiar sp^3-sp^2 torsional strain. The very basic assumption that the crystal conformations adopted in the silver nitrate adducts are very similar to those adopted just prior to reaction in solution, is, in effect, proven as a corollary to the work described above.

The Author would like to make a special acknowledgement to Dr. J. K. Sutherland at this point, for providing the basic ideas behind this work, and for some lengthy and helpful discussion. He is also grateful for permission to quote experimental results obtained by Dr. Sutherland and Mr. E. D. Brown.

It should be noted that in the original note published on this topic[136], values for the dihedral angles were computed from atomic co-ordinates which were not fully refined. The values used in the discussion above were obtained from the data of Table 8.2, and all strain-energy estimates have been recomputed. The value of the ratio of germacratriene monoxides (8-9 : 4-5) has also recently been obtained to greater precision (70:30) than that quoted in the paper and also in the review, Chapter 5, where the ratio 65:35 was cited.

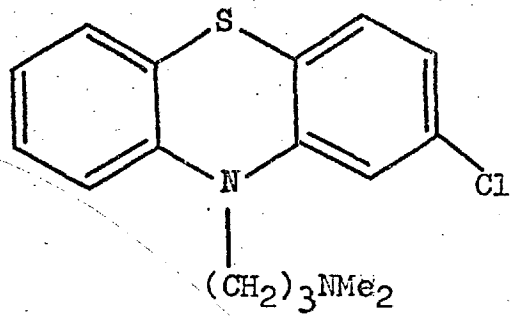
CHAPTER 9.

The Crystal and Molecular Structure of 2,3,4,4a,9,9a-hexahydro-2-methyl-9-phenyl-1H-indeno [2,1-c] pyridine hydrobromide : $C_{19}H_{22}NBr$.

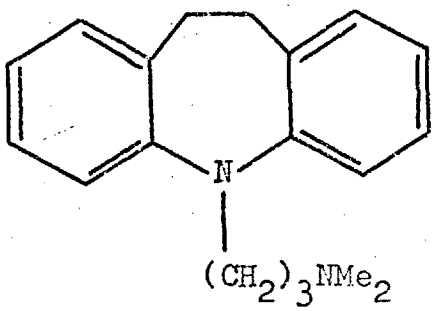
9.1. Chemical Introduction.

The anti-depressant properties of the anti-histamine drugs[224] were noted early in their clinical use. Minor structural modification has led to enhancement of the anti-depressant activity, at the expense of the anti-histamine function, in certain cases. For example chlorpromazine (9.I)[225], a clinical anti-histamine[226], and also the first drug effective in the treatment of schizophrenia[227], can be modified to give imipramine (9.II)[228], which has been found to have strong anti-depressant properties[229], but which is only weakly anti-histaminic.[230]

Following these ideas, Leeming et. al.[231] have effected similar modifications of the well known anti-histamine phenindamine (tetrahydro-indeno-pyridine (9.III)[232],



9.I. Chlorpromazine.
(marketed as the hydrochloride Largactil[226])

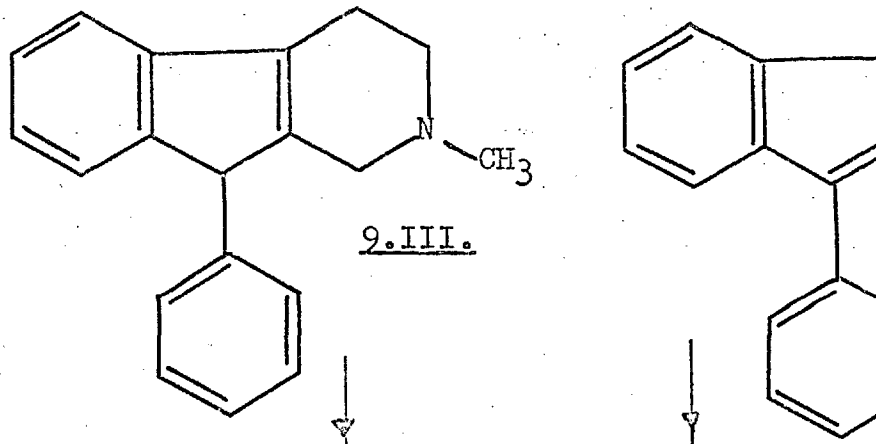


9.II. Imipramine.
(marketed as the hydrochloride Tofranil[230])

marketed as the tartrate dihydrate Thephorin[233]). Catalytic hydrogenation of (9.III), and of the dihydro-1H-indeno [2,1-c] pyridine (9.IV)[234], gives the compound (9.V), which can be irreversibly isomerized to (9.VI) using KOH in butanol. The corresponding demethylated derivatives (9.VII) & (9.VIII) were also obtained.

Correlation of n.m.r. evidence with deuteration studies indicated that, although both (9.V) and (9.VI) contain three asymmetric centres, they are epimeric at C(9) only, the stereochemistry at 9a, 4a, remaining unchanged. The all-cis stereochemistry shown for (9.V) was proposed[231] since :

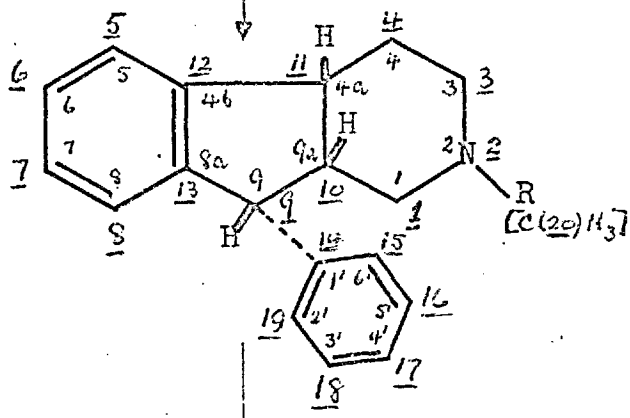
i) It is well established that hydrogenation of double bonds at catalyst surfaces usually gives the product with the incoming hydrogens attached to the same face of the



9.III.

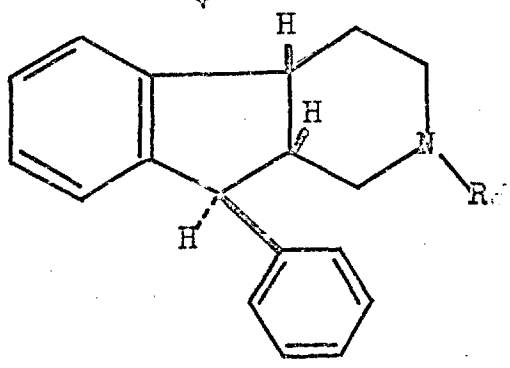
9.IV.

H_2/Pd



9.V* R = CH_3

9.VII R = H



9.VI R = CH_3

9.VIII R = H

* This compound was eventually chosen for a full X-ray study, the numbering shown inside the ring is the chemically correct system, that shown outside is used in this work for computational convenience.

molecule[235];

ii) There is a precedent for such a cis-hydrogenation in the synthesis of the closely related 3:4-cyclopentanopiperidine[236].

Furthermore a study[231] of Dreiding and CPK solid models showed that the all-cis stereochemistry leaves the C(9) proton of (9.V) in a very exposed position; in the thermodynamically more stable epimer (9.VI) this proton is highly hindered. This would explain both the ready epimerization and deuteration at this position in (9.V).

The n.m.r. spectra were, however, somewhat ambiguous, and in parallel with further chemical work (and pharmacological studies to ascertain the anti-depressant properties), all four compounds (9.V → 9.VIII) have been studied by the X-ray method. Samples of the crystalline hydrobromides were supplied by Dr. P. R. Leeming of the Pfizer Co. (U.K.) Ltd. Since all four are related chemically (by the well established epimerization), the crystal structure of any one compound would suffice to establish the stereochemistry of a possibly important new group of pharmaceuticals.

9.2. Preliminary X-ray Studies.

Oscillation and Weissenberg photographs of the hydrobromides were taken using a Unicam X-ray goniometer and Ni-filtered CuK_α-radiation. The crystal data obtained are set out in Table 9.1. The cell dimensions quoted are visual

estimates only, and have not been refined by computer.

All four samples were completely stable to X-irradiation over a period of about four days each, during which the crystal data were obtained. The crystals of the more stable epimer (9.VI), and of its demethylated analogue (9.VIII), were excellent, giving full intensity records of any one layer after ~36 hours. The crystals of the other parent epimer (9.V) were good, but its demethylated analogue was only poorly crystalline, being rather glassy; even the best specimens gave split diffraction spots, indicative of twinning, or more probably split crystals.

Although no measurements of optical rotation had been made the symmetry of the space groups, given in Table 9.1, shows the racemic nature of the compounds as supplied. Thus each cell contains equal numbers of D and L molecules. The only other point of interest is the rough similarity in the cell dimensions of the (9.V) and (9.VII) hydrobromides; the only difference is the doubling-up in the b-direction to accomodate the extra four molecules.

Dreiding models of the proposed stereochemistries of (9.V) and (9.VI) were made up. The former appeared the most interesting, purely on steric grounds, and a full three-dimensional X-ray analysis of this compound (which rejoices under the systematic name: 2,3,4,4a,9,9a-hexahydro-2-methyl-9-phenyl-1H-indeno[2,1-c] pyridine hydrobromide, hereinafter

TABLE 9.1.

Crystal Data for the Hydrobromides.

Compound	9.V:HBr	9.VII:HBr	9.VI:HBr	9.VIII:HBr
Formula	$C_{19}H_{22}NBr$	$C_{18}H_{20}NBr$	$C_{19}H_{22}NBr$	$C_{18}H_{20}NBr$
Habit	Laths.	Laths	Prisms	Rhombs
System	Monoclinic	Orthorhombic	Monoclinic	Monoclinic
M (C^{12}=12.0)	344.3	330.3	344.3	330.3
a (Å)	9.85	8.90	11.05	8.90
b (Å)	15.05	30.40	7.45	10.15
c (Å)	11.60	11.60	19.30	18.35
β °	105.50	90.00	94.00	110.00
V ($Å^3$)	1648	3077	1583	1549
D_x ($g.cm^{-3}$)	1.38	1.39	1.41	1.40
D_c ($g.cm^{-3}$)	1.39	1.42	1.44	1.42
Z	4	8	4	4
μ (cm^{-1})	36.8	37.9	38.2	37.7
Space Group	$P2_1/c$	Pcan	$P2_1/c$	$P2_1/c$
(Int Tab No.)	(14)	(60)	(14)	(14)
Crystallinity	Good	Poor	Excellent	Excellent

called PIPH) was undertaken for three reasons :

i) to check the proposed stereochemistry;

ii) to examine the effect of overcrowding if the all-cis stereochemistry was confirmed;

iii) to study the molecular geometry of the fused-ring heterocyclic system.

A fourth, and non-chemical, reason was to provide a lengthy test, involving the measurement of some 2800 intensities, for the Siemens automatic single-crystal diffractometer, which had recently been installed in the laboratory.

9.3. Experimental : The Siemens Automatic Single-Crystal Diffractometer.

The Siemens Automatische Einkristall Diffraktometer (AED) is a four-circle instrument, designed according to the principles of the Eulerian cradle (see Figure 9.1). The position of any reflection, hkl, is defined by the three Eulerian angles: Θ_{hkl}, ϕ_{hkl}, χ_{hkl}, which can be computed[237] from the lattice parameters, radiation wavelength, and Miller indices. The instrument in use in this laboratory operates in the off-line mode; setting angles, together with other necessary data which will be mentioned below, are input to the machine via five-hole paper tape, the computation and preparation of which is performed by the ATLAS program SEKO (written by P. G. H. Troughton). The tape consists

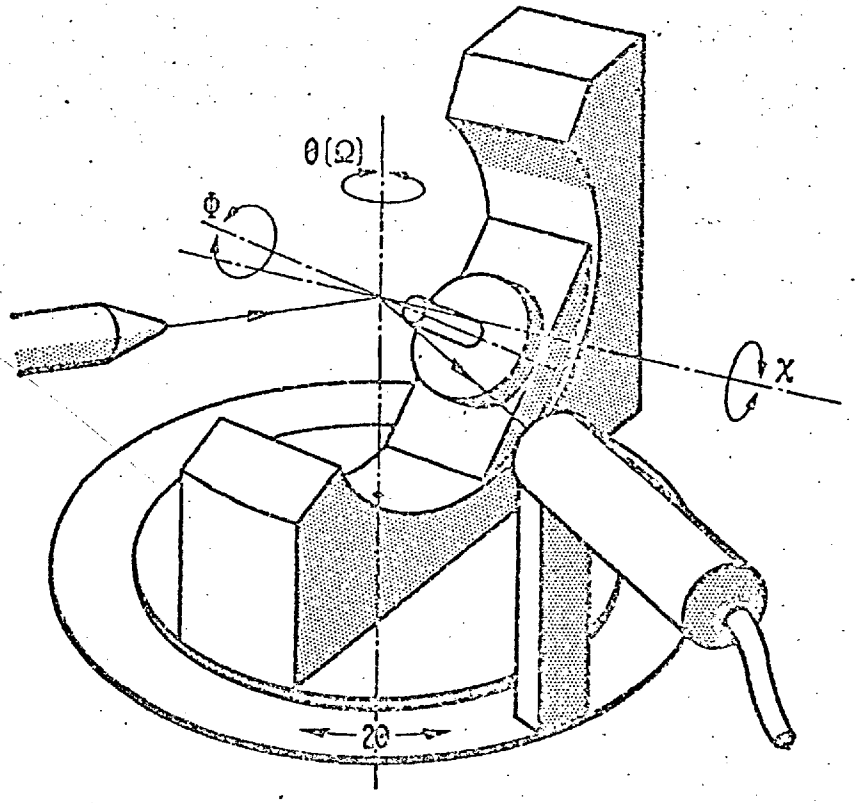


Figure 9.1. The Eulerian Cradle of the AED

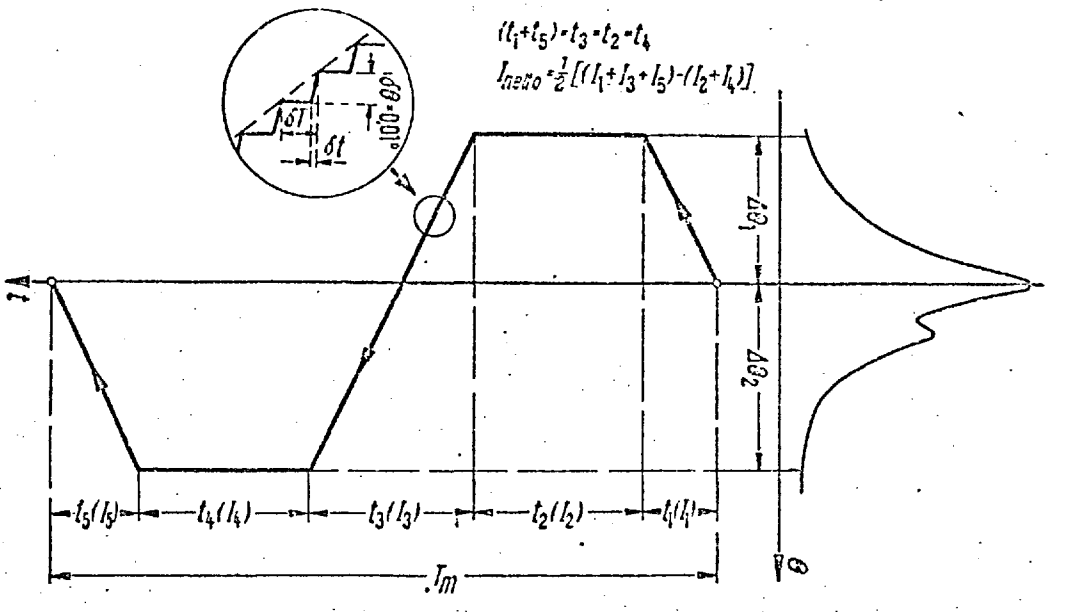


Figure 9.2. Schema of the five-point measurement technique (the values $\Delta\Theta_1$ and $\Delta\Theta_2$ are explained in the text).

basically of a series of commands to the pulse motors, which drive the circles in steps of 0.01°, and a command to start the measuring sequence (or perform various checks). The intensities of the diffracted beams are measured by scintillation counter, mounted on the θ-circle, and kept at a constant temperature using cooling water. The recorded counts are passed, via a photomultiplier and pulse-height analyser, to the output tape. The X-rays are generated by a Siemens KRISTALLOFLEX 4 unit; in this work $CuK\alpha$-radiation was used, and the unit was run at 45 kV. and 16 mA. The mode of use of the machine, and some further instrumental points of interest, are exemplified in the description of the data-collection process for PIPH.

Crystals of PIPH are colourless laths, with [100] prominent, elongated along c. A suitable specimen, of dimensions* 0.61 x 0.20 x 0.14 mm, was mounted on a quartz fibre using Araldite, and set to rotate about the c-axis on a Stöe Weissenberg camera. A photograph of the hk0-layer was taken to check the suitability of the crystal. It was transferred to the diffractometer and, using the visually estimated cell dimensions together with some visually estimated relative intensities, it was possible to locate the reciprocal axes a^*, b^*, c^*; the former was set

* A fuller description of the crystal morphology and dimensions is given in Sect. 9.4, where the application of an absorption correction is described.

to coincide with the $\phi = 0^\circ$ position (thus $\underline{b}^*$ occurred at $\phi = 90^\circ$). The setting angles for some 50 general reflections were then computed (SEKO) using the rough cell data. The values were set manually, and optimum θ-values were obtained for some 30 $CuK\alpha_1$ peaks. The accurate cell parameters are listed below, and were obtained by the least-squares technique (CEDI).

Crystal Data.

2,3,4,4a,9,9a-hexahydro-2-methyl-9-phenyl-1H-indeno[2,1-c] pyridine hydrobromide (PIPH) ..... $C_{19}H_{22}NBr$.
Monoclinic (Laue symmetry 2/m): Space group $P2_1/c$ (C_{2h}^5, No.14)

$\underline{a}$ = 9.853 ± 0.002 Å; $\underline{b}$ = 15.099 ± 0.002 Å;
$\underline{c}$ = 11.682 ± 0.004 Å; β = 105.81° ± 0.030°;
$\underline{V}$ = 1672 Å^3; $\underline{D}_x$ = 1.38 ± 0.03 g. cm.$^{-3}$;
$\underline{D}_c$ = 1.367 g.cm.$^{-3}$ for $\underline{Z}$ = 4 molecules per cell;
μ = 36.220 cm^{-1} for CuK_α-radiation ($\lambda_{K\alpha_1}$ = 1.54051 Å);
$\underline{M}$ = 344.3 (on the standard C^{12} = 12.00);
$\underline{F}(000)$ = 712 electrons.

Using the above data, a steering tape was computed (SEKO) for a quadrant of the Cu-sphere, to a maximum θ-value of 65°; the 0.8 mm diameter collimator was used for data collection to compass the very anisotropic shape of the crystal. A five-point measuring technique was used to obtain the average intensity of each peak above the background

level; the scanning method is illustrated in Figure 9.2, which also shows how the net intensity is obtained from the five measurements. The values of the scanning limits $\Delta\theta_1$, $\Delta\theta_2$, on either side of the peak maxima were obtained by scanning some representative reflections with θ-values in the range $8^\circ \rightarrow 70^\circ$; this information was input to SEKO in the form of a scan table, the correct values for each hkl were then obtained by interpolation.

A coupled ω:2θ scan ($\omega = \theta$) was used throughout; the machine then approximates, as nearly as possible, a constant count per reflection device (as recommended by Killean[238]) except for the weakest intensities. This is effected by the automatic selection of measuring times : a maximum time (τ_{max}) is selected by the user for each step, i.e. 0.01° of scan, and in this experiment 0.6 sec/step was chosen; should any reflection be too strong to fall within the range of maximum counter accuracy (τ) is successively reduced to 0.24, 0.12, and 0.06 sec/step. Reflections which are still too strong to be measured at τ_{min} are further reduced in intensity by the introduction of one of five attenuators, whose permeability to X-rays decrease in the approximate ratios : 100:45:21:9.5:4.5:2. The selection of measuring time, and the introduction of attenuators (if required), is carried out automatically before each five-point measurement; the exact attenuation factors for this machine were determined

soon after its arrival, and were used in the final processing of the output tape.

A check was kept on the stability of the instrument, the setting of the crystal, and the accuracy of the setting angles actually used, in the following manner :

i) A strong reflection (080) was chosen as a 'reference', and measured once in every twenty reflections, i.e. once every two hours. This enabled a 'scale-factor' for each batch to be computed during processing, thus nullifying any instabilities, such as fluctuations in X-ray output or counter efficiency. A plot of the number of counts (N) given by this reflection against time is shown in Figure 9.3. It can be seen that, although most values lie within a band of width $\sim 3\sigma$, there is a gradual decline of $\sim 5\%$ over the two-week period. This was almost certainly due to decreased efficiency of the Cu-target, and deposition of tungsten on the tube windows; the collection of only one other set of data was possible with this particular tube, and following this a complete θ-scan from $0^{\circ} \rightarrow 70^{\circ}$ for the h00 reflections of a glucose monohydrate crystal revealed peaks due to both Fe- and W-radiations. Some of the observed decline could also have been due to radiation damage, but, in the light of the above evidence, the contribution from this source was probably minimal.

ii) A check on the crystal setting was provided by the

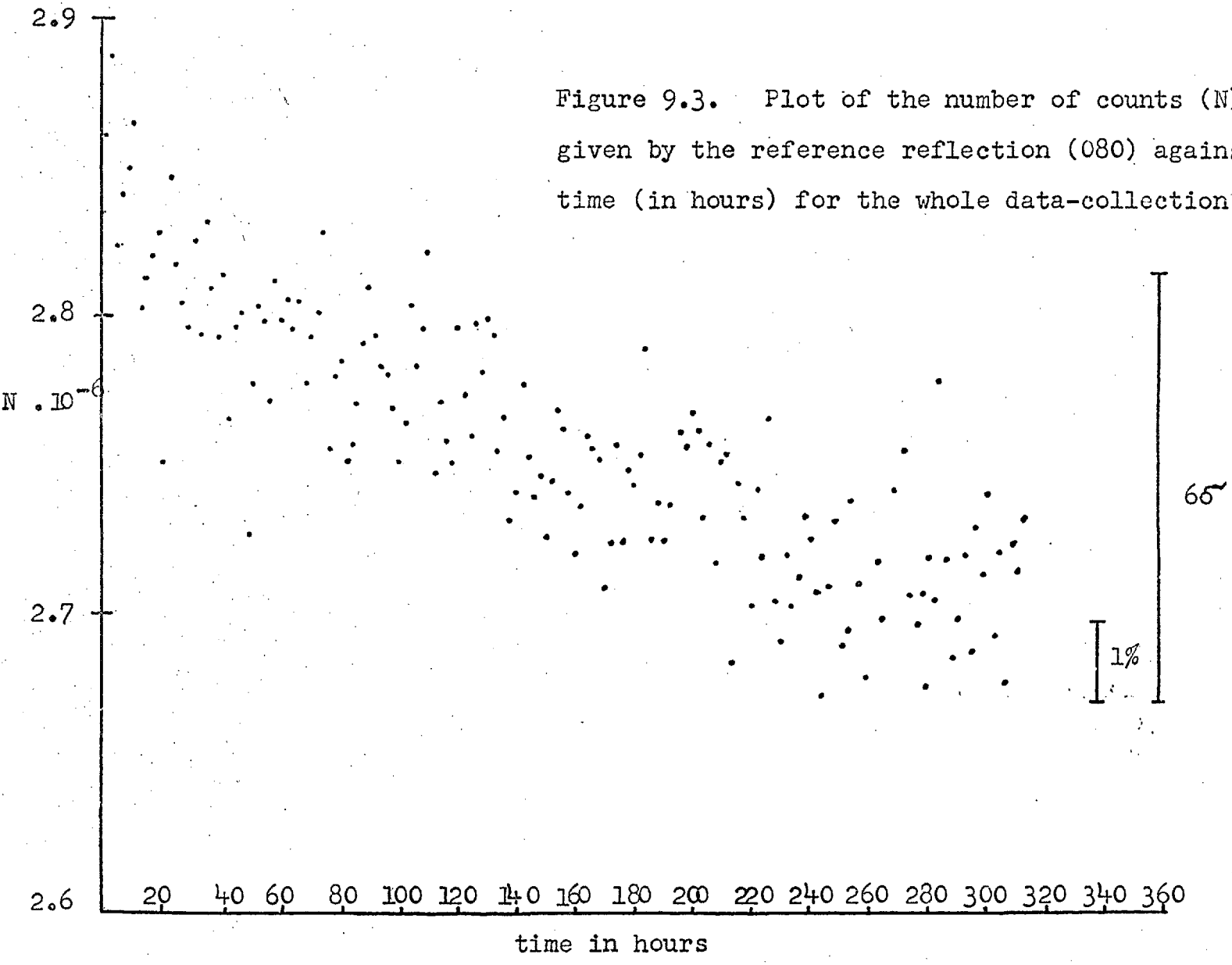


Figure 9.3. Plot of the number of counts (N) given by the reference reflection (080) against time (in hours) for the whole data-collection period.

data from 'kontrol' reflections, obtained after each batch of 100 five-point measurements. The reflections 700, $\bar{7}00$, 0100, $0\bar{1}00$, and 004, were chosen to check both goniometer arcs. The reflections were scanned with :

a) full aperture, i.e. normal setting, (count N_T);

b) insertion of a horizontal half-shutter into the aperture (N_H);

c) insertion of a vertical half-shutter (N_V).

It is experimentally very difficult to keep $N_H = N_V$, and $N_H + N_V = N_T$ for any reflection. However an effective check is obtained by noting the ratio N_H/N_V which should stay reasonably constant for any hkl; also the ratios N_H/N_T, N_V/N_T should remain constant and equal for reflections hkl, $\bar{h}\bar{k}l$, if the crystal remains set. These values were checked periodically and minor adjustments made to the goniometer arcs if neccessary.

iii) After every 40 five-point measurements a check was carried out on the angle circles by moving them by $-\theta_{hkl}$, $-\phi_{hkl}$, and $-\chi_{hkl}$, where hkl was the last reflection measured. Digitizers were then brought into play to check that all circles were then in the zero position; all digitizer checks were successful in this experiment. If a circle is in error by $\leqslant \pm 0.2^{\circ}$ this is automatically corrected, but for larger errors the machine simply stops.

Exactly 3000 reflections were counted, and the five

measurements for each, plus the data for reference and kontrol reflections, were written to the output tape. This was processed using the ATLAS program SODI (P. G. H. Troughton) : the values of the raw intensities were evaluated using the formula quoted in Fig. 9.2, the Lp^{-1} correction applied, and the data (on a common arbitrary scale) written to ATLAS magtape and also output on cards in X-RAY '63 format. Of the possible 2873 independent reflections, 2396 had intensities significantly greater than background. The discrepancy between the number of independent reflections and the total measured is due to the inclusion of the $\bar{h}k0$ reflections (equivalent to the hk0). This was caused by a small programming error, but inadvertently provided a further check on the accuracy of the whole diffractometer experiment, since the data from the hk0 zone were spread evenly over the whole data-collection period. A comparison of $F^2(hk0)$ and $F^2(\bar{h}k0)$ is given in Table 9.2; an 'agreement factor' of the form :

$$R' = \frac{2\sum|F^2(hk0)-F^2(\bar{h}k0)|}{\sum F^2(hk0) + \sum F^2(\bar{h}k0)}$$

had a value of only 0.0116. The low value is a reflection not only of the reproducibility of the machine, but also of the very regular cross-section of the crystal (see Figure 9.3A on page 252); although absorption corrections have been neglected in deriving R', the regularity of the cross-section gives an almost identical correction for any pair of reflections

TABLE 9.2.

PIPH : Comparison of $F^2(hk0)$ and $F^2(\bar{h}k0)$

The format is : * |h| 1

k $F^2(hk0)$ $F^2(\bar{h}k0)$ $F^2(hk0)-F^2(\bar{h}k0)$

* 10 0			
0	429.03	425.82	3.21
1	19.63	15.33	4.60
2	27.33	35.85	-8.52
3	55.02	58.20	-3.18
4	93.42	95.01	-1.59
5	49.30	41.06	8.24
6	65.11	55.88	9.23
* 9 0			
0	61.11	69.08	-7.97
1	229.84	227.53	2.31
2	49.17	47.21	1.96
3	394.97	389.35	5.62
4	155.29	169.48	-14.19
5	154.79	154.85	-0.06
6	94.50	95.31	-0.81
7	95.96	107.48	-11.52
8			
9	111.46	108.06	3.40

* 8 0			
0	289.80	288.36	1.44
1	433.77	427.13	6.64
2	9.53	9.25	0.28
3	124.15	124.24	-0.09
4	10.04	9.70	0.34
5	47.20	49.48	-2.28
6	33.90	35.26	-1.36
7	469.91	472.61	-2.70
8	46.18	55.09	-8.81
9	16.50	24.81	-8.31
10	8.48	8.20	0.28
11	99.51	103.73	-4.22
12	39.47	40.14	-0.67
* 7 0			
0	1283.98	1284.47	-0.49
1	8.33	7.97	0.35
2	8.50	8.18	0.32
3	293.81	300.07	-6.26
4	1215.77	1219.76	-3.99
5	448.61	449.38	-0.77

Table 9.2. (Contd.)

✻	7	0 (contd)	
6	22.85	30.32	-7.47
7	778.60	773.63	4.97
8	204.47	211.70	-7.27
9	10.21	17.20	-6.99
10	21.25	20.25	1.00
11	8.61	8.66	0.05
12	194.42	207.59	-13.17
13	7.18	6.84	0.34
✻	6	0	
0	243.33	235.00	8.33
1	25.39	21.45	4.94
2	47.43	44.22	3.21
3	339.22	338.14	1.08
4	1319.44	1318.12	1.32
5	199.60	197.69	1.91
6	485.18	477.28	7.90
7	8.51	8.29	0.22
8	763.92	794.09	-30.17
9	162.64	172.09	-9.45
10	184.17	187.23	-3.06
11	36.84	38.74	-1.90
12	9.07	14.68	-5.61
13	12.86	14.68	-1.82
14	11.30	9.27	2.03

✻	5	0	
0	228.81	210.30	18.51
1	751.12	737.42	13.70
2	274.13	266.23	7.90
3	1163.53	1165.99	-2.46
4	213.84	217.15	-4.31
5	985.43	993.47	-8.04
6	326.61	330.10	-3.49
7	1385.47	1392.61	-7.14
8	231.33	226.47	4.86
9	163.88	174.63	-10.75
10	226.38	225.08	1.30
11	229.66	229.22	0.44
12	255.84	258.74	-2.90
13	11.15	20.83	-9.68
14			
15	30.60	28.01	2.59
✻	4	0	
0	392.33	373.81	18.52
1	248.59	241.13	7.46
2	195.86	198.94	3.08
3	1999.11	2014.13	-15.02
4	4953.81	4965.52	-11.71
5	663.06	660.19	2.87
6	452.29	443.67	8.62

Table 9.2 (Contd.)

*	4	0	
7	1831.64	1845.33	-13.69
8	753.31	770.06	-16.75
9	8.02	7.99	0.03
10	322.93	330.18	-7.25
11	477.91	481.39	-3.48
12	10.12	9.65	0.47
13	241.97	228.34	13.63
14	228.34	214.56	13.78
15	37.90	36.00	1.90
16	21.29	31.43	-10.14
*	3	0	
0	2756.75	2710.12	46.63
1	1477.96	1470.36	7.60
2	223.91	211.14	12.77
3	1382.12	1341.08	41.04
4	1814.98	1794.73	20.25
5	2444.96	2371.77	73.19
6	5.63	5.38	0.25
7	1598.98	1607.62	-8.64
8	925.47	909.66	15.81
9	82.57	86.53	-3.96
10	1217.32	1233.32	-16.00
11	123.66	111.54	12.12
12	177.23	190.38	-13.15

*	3	0 (Contd.)	
13	32.22	30.09	2.13
14	143.22	147.35	-4.13
15	137.95	137.83	0.12
16	7.66	7.48	0.18
17	6.44	6.15	0.29
*	2	0	
0	1781.08	1790.06	-8.98
1	7068.67	7042.25	26.42
2	4499.66	4397.88	1.78
3	100.78	101.13	-0.35
4	626.23	605.88	20.35
5	1023.48	1039.64	-16.16
6	187.83	192.60	-4.77
7	353.52	344.86	8.66
8	162.26	163.06	-0.80
9	234.70	248.18	13.48
10	38.13	32.08	6.05
11	1325.37	1314.33	11.04
12	12.00	9.93	2.07
13	9.40	9.71	-0.31
14	162.24	161.10	1.14
15	51.12	57.76	-6.64
16	8.21	8.19	0.02
17	6.84	6.66	0.18

Table 9.2 (concluded).

✻	1	0		✻	1	0 (contd.)	
0	52.42	51.26	1.16	9	75.89	74.24	1.65
1	6589.51	6653.58	-64.07	10	40.62	32.80	7.82
2	748.97	739.96	9.01	11	2123.40	2125.14	-1.74
3	17311.76	17279.77	31.99	12	10.01	9.20	0.81
4	77.66	80.02	-2.36	13	215.53	225.84	-10.31
5	522.40	520.06	2.34	14	332.46	335.81	-3.35
6	511.82	508.60	3.22	15	359.90	364.78	-4.88
7	681.28	675.57	5.71	16	22.58	17.77	4.81
8	159.28	164.16	-4.88	17	46.79	51.56	-4.77

9.4. Structure Solution and Refinement.

The position of the bromine ion was obtained from the Harker sections ($\underline{x}$, $\frac{1}{2}$, $\underline{z}$; 0, $\underline{y}$, $\frac{1}{2}$) of a three-dimensional Patterson map, computed using FOURR. Structure factors were calculated (FC) using the phase angles (0 or π) indicated by this position, together with an estimated $\underline{B}$-factor of 3.0 $Å^2$. The data with intensities significantly greater than background were placed on an absolute scale by using the totals $\sum|F_o|$ and $\sum|F_c|$; $\underline{R}$ was 0.437. The first electron-density map (FOURR, in which, inadvertently, no structure factor rejection test was applied) revealed the positions of all 21 non-hydrogen atoms. The co-ordinates were optimized using Booth's method[161], and used to construct a bead model

which showed chemically sensible geometry.

It was gratifying that the complete structure emerged so clearly from this one map, especially since no Fourier coefficients were either rejected or weighted down. The ratio (r) equal to $(\sum Z_H^2/\sum Z_L^2)^{\frac{1}{2}}$ is 1.32 in this case, tolerably close to Lipson and Cochran's suggested optimum value for (r^2) of unity[29] (see Eq. 2.17). The later, and somewhat more precise, analysis of Sim[239] suggests that ca. 83% of the signs predicted by the Br^- position should be correct at this value of (r). This result is compared with similar ones for humulene bromohydrin and germacratriene : $AgNO_3$ in Table 9.3. It would appear that the ease of structure solution is not directly correlated with the value of (r), nor with the value of the initial R-factor obtained.

TABLE 9.3.

Compound	$\sum Z_H^2$	$\sum Z_L^2$	r	No. of maps to give the structure.	R of 1st map	% signs correct Sim(239)
PIPH	1296	742	1.32	1	0.437	83%
Humulene bromohydrin	1225	629	1.40	2	0.427	86½%
Germacratriene:$AgNO_3$	2209	805	1.66	3	0.346	89%

While the presence of a very heavy atom in a general position (e.g. Ag in the germacratriene complex) contributes substantially to all reflections, and thus tends to increase the former (r), and reduce the latter (R), it does require great accuracy in the measurement of the intensity data to avoid the swamping of the light-atom contribution. Itwas this latter factor which made the structure solution so straightforward in the case of PIPH.

For the refinement process the block-diagonal least-squares program BLOKLS was used throughout, except where specifically stated. Only the 'observed' data were used, and no weighting scheme (i.e. w = 1 for all data) was employed the overall scale-factor (k) was varied during all cycles. The designation of run numbers used in previous chapters is adhered to (see p. 95 for definitions), together with the following additional designations :

MR, As for runs of type M, but with the hydrogen atom positional parameters free to refine;

MH, As above, but with non-hydrogen atom parameters fixed.

Runs of type M and MH were alternated during the early stages to reduce the computing time over those of type MR, which required the variation of 256 parameters. The results of all runs are given in Table 9.4 on page 255.

The optimum positional parameters from the electron-

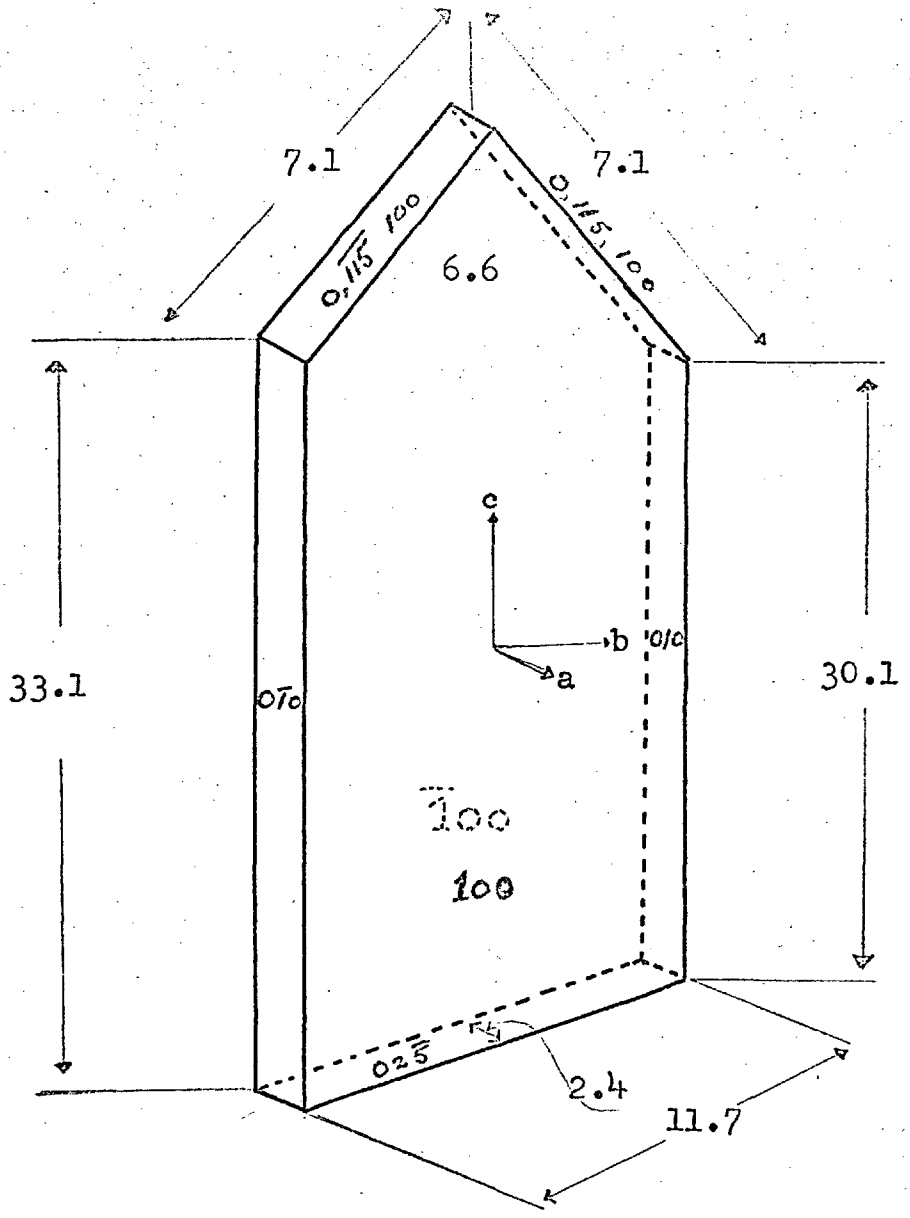
density map, together with estimated B-factors, were initially varied for six cycles (run I1), when R fell to 0.151. Scattering factors[19] appropriate to Br^{-1} and N^{+1} were employed. A difference map, using (F_o-F_c) as Fourier coefficients, showed no spurious features, but indicated some anisotropy, especially for the Br^- ion. The anisotropic thermal parameters were therefore computed (β_{ij}'s in the equation quoted in Table 6.5. p.103), and four cycles (run A1) reduced R to 0.086. Parameter shifts for Br^- and N^+ remained high, and these two atoms only were refined for two cycles of full-matrix least-squares (ORFLS), other parameters being fixed.

A bond-length and valence-angle calculation (BONDLA) following run A3 showed chemically sensible geometry. Hydrogen atom positions calculated at this stage agreed with some tentative values from the difference map. They were included in further refinement at the calculated positions, with B-factors 0.5Å^2 more than the final value for the atom to which they were bonded. An attempt to refine the B-factors (run MR1) failed, and they were fixed for all other runs. Refinement continued slowly (see Table 9.4), and after run M4 all parameter shifts for the non-hydrogen atoms were less than 0.2 of the corresponding estimated standard deviation. An interesting feature of these runs was the movement of H(20) (see the numbering scheme in the pull-out

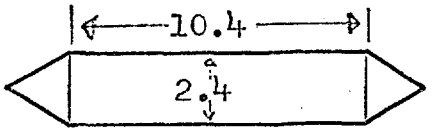
diagram bound with the end-papers) towards the N^+ ion. This effect recurred later and is discussed below and in Sect.9.5; the atom was set back to its calculated position for run M4.

At this stage an absorption correction was applied using a program kindly supplied by Dr. B. J. Brandt of the University of Stockholm. It is modelled on the vector method outlined, and initially programmed, by Coppens et al[240]. The program (ABSO) was amended and altered by P. G. H. Troughton for use on both the IBM 7090 and ATLAS computers. The basic data required are the Miller indices of the crystal faces, and their perpendicular distances from an arbitrary origin within the crystal; this enables the program to set up a three-dimensional grid of sampling points. Figure 9.3(A) shows the relevant data, and also the crystal dimensions, as obtained using the microscope attachment to the AED. The morphology input is slightly idealized, as shown by the inset drawing of the crystal cross-section, but the designation of the boundary planes 010, $0\bar{1}0$, introduces only very minor errors.

A variety of grid sizes were tried using a sample batch of data, and one of 6 x 6 x 6 chosen as the smallest possible without significant loss of accuracy. The correction factors varied by $\sim 1.5\%$ when the size was increased to 10 x 10 x 10. Although the magnitude of (μ) is small (36.22 cm^{-1}), the very anisotropic shape of the crystal gave a wide variation in



(Dimensions are given in AED microscope divisions:



(Inset)

1 div = 0.001714 cm.)

Figure 9.3(A). PIPH : Crystal Morphology and dimensions used in the application of absorption correction. The inset shows the actual cross-section. Both diagrams are exagerated for clarity.

values of (μt), where (t) is the thickness of crystal traversed by the X-ray beam. The 2396 'observed' data were processed in an average time of 1.09 sec/reflection on the IBM machine.

Refinement continued smoothly to $\underline{R}$ = 0.038 (run MR5). Bond-length and valence-angle calculations during this period showed much improved standard deviations, reflecting the improvement in $\sum\left(|F_o| - |F_c|\right)^2$. At this stage the data deck was examined and two reflections (130, 221) were omitted for suspected extinction; two further reflections which had been duplicated were also corrected.

Following run MR6 it was noted that H(20) had again refined towards N^+, to a separation of only 0.476 Å. The N^+, and to a lesser extent Br^-, were showing oscillatory motion which was preventing successful convergence . A difference map was computed, using only non-hydrogen atom contributions to F_c. A rather diffuse peak of height 0.4e^- was noted at $\sim$ 0.6 Å from N^+, but the resolution was very poor compared with other hydrogen peaks. The position adopted by H(20) in the refinement was almost certainly a noda point of electron density due to the lone pair of N^+, and some bonding density directed towards Br^-. These points are more fully discussed in the next section.

The position of the proton was obviously not detectable by the X-ray experiment, and it was decided to try to obtain

convergence by removing H(20) and redefining the valence state of nitrogen as N^{o}. For run M5 the scale-factor (k), Br^{-} and N^{o} only were refined using ORFLS. The scheme was successful and following run MR7 all shifts for non-hydrogen atom parameters were less than 0.15 of their respective estimated standard deviations; some hydrogen parameter shifts were a little higher.

An analysis of the data (DELSIG) showed that $\underline{(|F_o| - |F_c|)^2}_{ave}$ was almost constant over the most populated ranges of $|F_o|$. A weighting scheme of the Hughes[51] type was not, therefore, applicable; some attempts were made to use weights based on the standard deviation of each measurement, but it was not possible to pursue this work due to lack of computer time.

Refinement was, therefore, concluded at run MR7; the final positions and anisotropic temperature factors for the non-hydrogen atoms are shown in Tables 9.5, 9.6, while the refined hydrogen positions are shown in Table 9.7. These values were used to compute the structure factors listed in Table 9.8, for which an R-factor of 0.035 was obtained over the 2392 'observed' reflections not affected by extinction.

A similar structure factor calculation was performed for the 'unobserved' data, and the results (Table 9.9) show that, in general, the calculated values are less than those measured. However the reflections $\bar{2}$,0,10; $\bar{2}$,0,12; $\bar{1}$,0,6; $\bar{1}$,0,8; $\bar{1}$,0,10; $\bar{1}$,0,12; show surprising disagreement. This

was eventually traced to a programming error (now corrected): since χ for these reflections became $> 90°$, a value not attainable on the AED, the equivalent reflections $10\bar{1}$, $20\bar{1}$, should have been studied instead; however this switch was incorrectly programmed, and a value of $180 - \chi°$ was set, leaving the machine to explore a blank area of reciprocal space. It was fortunate that only 6 reflections were so affected!

TABLE 9.4.

PIPH:The Refinement Process.

Run	Cycles	R	$\sum(\lvert F_o\rvert - \lvert F_c\rvert)^2$	max S/E	ave S/E
I1	6	0.151	41860	3.9338	0.2277
A1	4	0.086	18400	5.7896	0.3380
A2[a]	2	0.080	17060	0.3988	0.1220
A3	2	0.077	16410	1.1557	0.1048
M1	3	0.061	9573	0.7817	0.0725
MR1[b]	2	0.058	8082	2.0704	0.2650
MR2[c]	2	0.058	8138	1.6156	0.1232
M2	2	0.057	8026	0.2812	0.0465
MH1	2	0.057	8004	0.2530	0.0421
M3	2	0.057	8002	0.1767	0.0125

Absorption Correction Applied.

Table 9.4 (contd.)

Run	Cycles	R	$\sum(\|F_o\| - \|F_c\|)^2$	max S/E	ave S/E
M4	4	0.050	6198	37.4632[d]	1.4480
MR3[e]	2	0.041	4114	2.4561	0.4062
MR4[f]	2	0.038	3449	1.6586	0.1203
MR5	2	0.038	3391	1.3617	0.0684
MR6	2	0.035	2770	1.7229	0.1272
M5[g]	2	0.035	2808	0.6085	0.1289
MR7[h]	3	0.0353	2792	0.2467	0.0617

a) Scale-factor (k), Br^-, & N^+, only refined using ORFLS.

b) k, C(16), C(17), C(18), & C(20), plus all hydrogen parameters refined.

c) Hydrogen B-factors set back and fixed; hydrogen positions together with k, & C(17) refined.

d) The high shift is due to scale-factor adjustment.

e) All shifts damped by a factor of 0.6 for this run only.

f) Dispersion correction introduced using $f'_{Br} = -0.9$, $f''_{Br} = 1.5$ (ref. 59).

g) k, Br^-, & N^o, only refined using ORFLS, H(20) removed, and all other parameters fixed.

h) H(20) omitted.

TABLE 9.5.

PIPH : Final Atomic Co-ordinates for the Non-Hydrogen Atoms, as Fractions of the Cell Edges, together with their Estimated Standard Deviations.

Atom	x	σ_x	y	σ_y	z	σ_z
Br	0.15327	0.00005	0.38727	0.00003	-0.55468	0.00003
C(1)	0.25447	0.00036	0.29738	0.00023	-0.22910	0.00030
N(2)	0.11316	0.00029	0.31338	0.00019	-0.31627	0.00025
C(3)	0.03116	0.00036	0.37890	0.00028	-0.26531	0.00033
C(4)	0.10613	0.00039	0.46663	0.00026	-0.25155	0.00033
C(5)	0.20427	0.00038	0.48839	0.00025	0.02985	0.00034
C(6)	0.24945	0.00042	0.47413	0.00027	0.15154	0.00035
C(7)	0.36722	0.00044	0.42385	0.00027	0.20009	0.00033
C(8)	0.44327	0.00038	0.38590	0.00024	0.12823	0.00031
C(9)	0.46669	0.00033	0.37161	0.00021	-0.09029	0.00029
C(10)	0.34228	0.00033	0.38194	0.00022	-0.20521	0.00028
C(11)	0.25779	0.00034	0.46072	0.00022	-0.17475	0.00030
C(12)	0.27930	0.00033	0.45007	0.00021	-0.04239	0.00029
C(13)	0.39820	0.00033	0.39916	0.00021	0.00620	0.00028
C(14)	0.54683	0.00034	0.28535	0.00023	-0.07511	0.00031
C(15)	0.51382	0.00043	0.21452	0.00025	-0.01130	0.00038
C(16)	0.59401	0.00052	0.13598	0.00027	0.00262	0.00041
C(17)	0.70561	0.00049	0.12926	0.00032	-0.04910	0.00044
C(18)	0.73644	0.00044	0.19828	0.00032	-0.11364	0.00045
C(19)	0.65845	0.00039	0.27651	0.00028	-0.12677	0.00037
C(20)	0.03511	0.00046	0.22815	0.00029	-0.34909	0.00038

TABLE 9.6.

PIPH : Final Anisotropic Temperature Factors (β_{ij}) for the Non-Hydrogen Atoms.

Atom	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Br	0.01527	0.00569	0.00609	0.00283	0.00285	0.00052
C(1)	0.00848	0.00330	0.00573	0.00053	-0.00034	0.00017
N(2)	0.00834	0.00332	0.00563	0.00026	-0.00096	0.00009
C(3)	0.00704	0.00561	0.00751	0.00079	-0.00023	-0.00015
C(4)	0.00946	0.00429	0.00706	0.00218	-0.00020	0.00025
C(5)	0.00874	0.00370	0.00872	-0.00049	0.00295	-0.00072
C(6)	0.01279	0.00495	0.00790	-0.00218	0.00506	-0.00312
C(7)	0.01444	0.00455	0.00600	-0.00237	0.00241	0.00001
C(8)	0.01026	0.00306	0.00683	-0.00112	0.00005	0.00074
C(9)	0.00631	0.00290	0.00666	-0.00002	0.00088	0.00004
C(10)	0.00761	0.00304	0.00545	0.00053	0.00157	0.00051
C(11)	0.00783	0.00269	0.00641	0.00073	0.00109	0.00070
C(12)	0.00704	0.00262	0.00631	-0.00039	0.00113	-0.00018
C(13)	0.00726	0.00226	0.00604	-0.00057	0.00062	-0.00001
C(14)	0.00644	0.00318	0.00737	0.00064	-0.00073	-0.00073
C(15)	0.01167	0.00332	0.00986	0.00081	-0.00049	-0.00016
C(16)	0.01929	0.00323	0.01085	0.00169	-0.00300	-0.00020
C(17)	0.01425	0.00576	0.01362	0.00470	-0.00567	-0.00375
C(18)	0.00968	0.00662	0.01413	0.00266	-0.00008	-0.00389
C(19)	0.00839	0.00515	0.01012	0.00064	0.00066	-0.00218
C(20)	0.01386	0.00474	0.00888	-0.00172	-0.00297	0.00011

TABLE 9.7.

PIPH : Refined Hydrogen Atom Positions, in Fractional Co-ordinates, with their Estimated Standard Deviations (σ).

The numerical designation of hydrogen atoms is made up of the number of the C or N atom to which they are bonded, together with one other number starting from zero; thus H(202) is the third hydrogen bonded to C(20).

Atom	x	σ_x	y	σ_y	z	σ_z
H(10)	0.2336	0.0043	0.2702	0.0028	-0.1660	0.0037
H(11)	0.2983	0.0043	0.2533	0.0028	-0.2673	0.0036
H(20)	This atom was not accurately definable (see Sect.9.5)					
H(30)	0.0201	0.0047	0.3525	0.0030	-0.1899	0.0039
H(31)	-0.0634	0.0046	0.3842	0.0030	-0.3221	0.0038
H(40)	0.0580	0.0046	0.5054	0.0031	-0.2191	0.0039
H(41)	0.1079	0.0047	0.4879	0.0031	-0.3260	0.0039
H(50)	0.1258	0.0044	0.5249	0.0029	0.0005	0.0038
H(60)	0.1967	0.0046	0.4933	0.0031	0.2058	0.0039
H(70)	0.3976	0.0046	0.4143	0.0030	0.2788	0.0039
H(80)	0.5264	0.0044	0.3497	0.0029	0.1629	0.0037
H(90)	0.5289	0.0043	0.4116	0.0027	-0.0986	0.0036
H(100)	0.3771	0.0042	0.3954	0.0028	-0.2739	0.0036
H(110)	0.3011	0.0043	0.5145	0.0028	-0.1886	0.0036
H(150)	0.4309	0.0047	0.2174	0.0031	0.0172	0.0040
H(160)	0.5703	0.0051	0.0879	0.0033	0.0444	0.0043

Table 9.7 (contd.)

H(170)	0.7650	0.0053	0.0745	0.0034	-0.0415	0.0044
H(180)	0.8148	0.0052	0.1954	0.0034	-0.1552	0.0044
H(190)	0.6762	0.0048	0.3211	0.0031	-0.1706	0.0040
H(200)	0.0908	0.0050	0.1969	0.0032	-0.3890	0.0042
H(201)	-0.0608	0.0050	0.2442	0.0033	-0.4033	0.0042
H(202)	0.0352	0.0050	0.1971	0.0032	-0.2741	0.0043

TABLE 9.8.

PIPH : Final Observed and Calculated Structure Factors for those Reflections with Intensities Significantly Greater Than the Background Level.

The format of the table is :

H, K, L,

L $10|F_o|$ $10F_c$

The reflections omitted for suspected extinction were :

h	k	l	$10\|F_o\|$	$10F_c$	$\sin\theta/\lambda$
1	3	0	152.51	-162.50	0.11248
2	2	0	158.56	-174.70	0.14159

	-11,0,L	
0	45	47
6	186	198
	-11,1,L	
3	85	93
4	43	-50
5	77	83
7	50	60
	-11,2,L	
1	127	-137
3	213	-224
4	69	73
5	31	-19
6	32	43
	-11,3,L	
2	54	-66
3	63	-68
4	60	64
5	74	-73
7	101	-107
	-11,4,L	
1	33	-35
3	51	-51
6	91	-104
	-11,5,L	
2	77	82
3	126	-143
4	69	78
5	149	-163
	-10,0,L	
2	84	92
4	159	172
6	152	172
8	188	204
	-10,1,L	
1	75	-70
2	178	-191
3	276	-278
4	85	-89
5	36	42
6	93	-93
7	58	64
9	61	63
	-10,2,L	
1	36	24
2	56	49
3	159	-177
4	111	111
5	88	-97
6	35	-30
7	99	-104
9	97	102
	-10,3,L	
2	111	-124
3	70	68
4	109	-112
6	157	-162
7	73	-78
8	32	19
9	95	-100
	-10,4,L	
1	75	-81
2	66	65
5	50	-58
6	96	-104
8	99	-104
	-10,5,L	
1	82	94
3	43	46
5	39	-35
6	60	58
7	94	-100
8	49	53
	-10,6,L	
1	57	62
3	128	132
4	78	-84
5	154	-164
6	36	-43
7	90	98
8	73	-84
	-10,7,L	
1	48	-52
2	95	101
3	73	-76
4	110	120
5	43	-44
6	61	71
	-10,8,L	
1	41	41
3	81	82
4	32	31
	-9,0,L	
2	317	-333
4	309	-320
6	179	-187
8	80	84
10	160	169
	-9,1,L	
1	103	-111
2	77	-78
3	133	-142
6	171	-176
8	181	-193
9	54	57
10	50	-59
11	145	155
	-9,2,L	
2	113	-120
3	49	44
5	173	-180
7	172	-182
8	53	58
9	63	-74
11	50	-63
	-9,3,L	
1	94	100
2	67	-74
3	146	153
4	225	-238
6	144	-152
7	59	62
8	212	-226
9	43	-35
	-9,4,L	
1	75	77
2	330	338
3	134	126
4	263	269
5	90	-101
8	44	-38
9	34	30
10	167	-171
	-9,5,L	
1	79	95
2	90	-87
3	48	54
5	144	153
6	85	82
7	39	-42
9	101	-114
	-9,6,L	
1	174	-179
2	63	63
3	42	45
4	100	101
5	88	91
7	181	187
8	57	-65
9	71	82
	-9,7,L	
2	87	-84
3	40	-40
4	95	105
5	100	-96
6	137	149
8	129	134
	-9,8,L	
2	146	-151
3	159	170
4	199	-206
5	114	129
6	108	-109
7	105	115
8	44	45
	-9,9,L	
1	167	-183
2	83	92
3	129	-136
4	53	-54
	-9,10,L	
1	31	45
2	54	-66
3	63	68
4	79	-92
5	76	-74
	-9,11,L	
2	43	-51
4	40	-47
	-8,0,L	
2	350	-359
4	289	-299
6	226	-231
8	243	-258
12	147	156
	-8,1,L	
2	214	220
3	65	-79
4	117	117
5	258	-271
6	72	-76
7	110	-117
9	80	-85
9	63	65
10	131	-133
11	45	59
12	69	-77
	-8,2,L	
1	156	165
2	102	-105
3	142	150
4	126	-135
6	64	-76
7	261	-279
8	86	-97
9	195	-211
11	151	-163
12	52	51
	-8,3,L	
1	81	-80
2	248	261
3	263	269
4	161	166
5	180	130
6	81	-81
7	208	209
8	153	-161
9	52	51
10	230	-242
	-8,4,L	
1	111	117
2	81	-63
3	193	-197
4	138	154
5	89	-91
6	163	173
7	92	-91
8	201	211
9	62	-69
10	87	-89
	-8,5,L	
1	197	208
3	377	392
4	176	-179
5	297	316
6	45	51
7	145	152
10	81	84
	-8,6,L	
1	341	-355
2	66	71
3	117	123
4	120	131
7	164	169
9	181	191
10	84	-88
11	142	150
	-8,7,L	
2	180	-190
3	73	-70
4	72	-79
6	141	147
7	72	-72
8	70	69
10	146	159
	-8,8,L	
1	100	-105
2	38	40
3	56	-54
4	196	-196
5	49	-36
6	90	-92
7	105	110
8	127	-133
9	137	156
10	39	-42
	-8,9,L	
3	186	-195
5	212	-222
6	122	126
7	167	-174
	-8,10,L	
1	104	111
2	131	-135
3	142	138
4	87	-93
6	71	-77
7	87	-81
	-8,11,L	
1	51	-65
2	163	164
3	99	-110
4	52	54
	-8,12,L	
1	69	69
3	48	49
4	50	49
5	76	-81
6	48	51
	-7,0,L	
2	282	272
4	88	-100
6	330	-334
8	291	-311
10	205	-213
	-7,1,L	
1	193	195
2	217	228
4	255	266
5	128	-130
6	131	129
7	333	-349
9	191	-199
10	147	-150
11	59	-53
12	159	-164
	-7,2,L	
1	347	364
3	511	528
4	77	-80
5	350	356
7	93	89
9	83	-86
10	71	-77
11	200	-209
12	71	78

	-7,3,L	
2	328	336
3	59	67
4	326	336
5	42	-45
6	97	102
7	194	200
9	171	171
10	127	-124
11	59	48
12	159	-169
	-7,4,L	
1	125	129
2	197	-199
4	123	116
5	173	187
6	310	311
8	158	161
9	135	-142
10	162	174
12	92	80
	-7,5,L	
1	447	-461
4	192	-188
7	369	391
8	40	-43
9	235	252
10	60	53
12	65	46
	-7,6,L	
1	172	-180
2	186	-184
3	503	-513
4	93	98
5	470	-477
6	162	177
7	245	-261
8	80	81
9	65	57
10	106	120
11	88	93
	-7,7,L	
1	372	394
2	66	46
3	263	265
4	215	-231
5	54	64
6	102	-115
7	127	-120
8	62	69
9	113	-108
10	225	238
11	99	-94
	-7,8,L	
1	222	-223
2	124	133
3	241	-252
6	155	-158
7	47	47
8	107	-106
9	51	-43
10	95	-101
	-7,9,L	
1	226	232
3	49	-44
4	159	156
5	46	-56
6	75	72
7	174	-182
8	115	117
9	206	-216
10	72	89
	-7,10,L	
1	115	119
2	61	-63
3	93	94
4	98	-95
5	137	143
6	179	-189
7	95	102
8	108	-113
9	83	-85

	-7,11,L	
2	149	149
3	45	-52
4	178	187
5	64	-54
	-7,12,L	
1	119	140
2	164	-171
3	136	152
5	78	90
7	38	45
	-7,13,L	
1	43	-30
3	73	-74
5	48	48
6	69	-73
	-7,14,L	
3	57	-64
	-6,0,L	
2	542	578
4	346	363
6	39	41
8	268	-266
10	158	-173
12	264	-276
	-6,1,L	
1	343	348
2	191	175
3	239	253
4	340	342
6	285	282
7	147	-146
8	249	260
9	298	-308
10	45	55
11	256	-263
13	111	-100
	-6,2,L	
1	82	-78
2	190	187
3	234	231
4	178	173
5	319	333
6	51	28
7	440	466
8	50	-56
9	203	212
11	150	-140
13	96	-102
	-6,3,L	
1	181	-186
3	379	-388
4	490	500
5	250	-255
6	427	447
7	60	71
8	180	195
10	135	141
11	164	164
12	137	-145
13	97	70
	-6,4,L	
1	106	103
2	158	-171
3	120	135
4	312	-322
5	107	121
6	52	47
7	59	71
8	424	437
9	80	-79
10	336	359
12	175	193
	-6,5,L	
1	620	-628
3	279	-285
4	141	-134
6	209	-210
8	134	-141
9	132	134
10	54	53

11	177	188
	-6,6,L	
1	199	199
2	145	-152
3	208	-212
4	81	72
5	93	-93
6	47	35
7	164	-178
8	155	164
9	189	-192
10	136	145
11	59	25
	-6,7,L	
1	79	80
2	86	-92
3	142	-139
4	471	-483
5	98	-93
6	433	-456
7	105	98
8	133	-136
10	44	-48
	-6,8,L	
1	87	90
2	230	239
3	157	-171
4	235	234
5	222	-236
6	57	-57
7	193	-204
8	185	-182
9	61	-69
10	168	-178
11	109	102
	-6,9,L	
1	385	392
2	64	-69
3	308	324
5	155	160
6	58	50
7	80	-76
8	51	-44
9	168	-181
11	153	-165
	-6,10,L	
1	116	-124
2	115	121
4	89	100
5	220	233
7	165	167
8	161	-168
9	128	134
10	106	-118
	-6,11,L	
2	181	195
3	49	61
4	215	225
5	64	-66
6	221	232
7	50	-51
8	173	183
9	58	58
	-6,12,L	
1	46	-39
2	143	-144
3	47	42
4	134	-134
5	112	119
7	85	92
8	44	47
	-6,13,L	
1	225	-237
2	167	175
3	101	-118
4	62	64
5	41	-40
6	65	74
	-6,14,L	
1	62	-68
2	93	-88

4	118	-126
5	39	-42
6	59	68
	-6,15,L	
1	100	-117
2	44	43
3	46	-46
	-5,0,L	
2	668	693
4	888	890
6	483	487
8	264	268
10	108	-58
12	304	-320
	-5,1,L	
1	190	203
2	626	-623
3	368	393
4	308	-288
5	485	498
6	146	158
7	182	185
8	436	446
9	107	-104
10	54	66
11	174	-186
12	98	101
13	120	-124
	-5,2,L	
1	688	-702
2	172	173
3	209	-230
5	280	276
6	53	60
7	324	337
9	380	407
10	120	115
11	257	265
12	96	-96
	-5,3,L	
1	97	-105
2	275	-297
3	374	-372
4	159	-162
5	316	-306
6	73	85
8	362	380
9	147	-151
10	183	202
11	166	165
12	112	131
13	78	76
	-5,4,L	
1	99	-101
2	333	-346
3	84	-91
4	583	-602
5	316	307
6	513	-523
7	88	100
8	180	-187
9	315	318
12	162	166
	-5,5,L	
1	281	-291
2	111	123
3	457	-492
5	557	-564
6	60	55
7	223	-245
8	267	-269
9	93	94
10	205	-183
11	232	243
12	64	-88
	-5,6,L	
1	512	527
2	76	-80
3	363	375
4	158	-173
5	202	-198

	-5,6,L	
6	161	-177
7	269	-270
9	227	-239
11	145	-150
12	61	72

	-5,7,L	
1	114	-115
2	344	355
3	135	125
5	251	248
6	89	-104
7	106	101
8	435	-452
10	249	-265

	-5,8,L	
1	139	153
2	325	332
4	212	229
5	74	-80
6	483	501
7	95	-90
8	146	163
11	129	-140

	-5,9,L	
1	84	-63
2	122	-131
3	140	139
4	247	-238
5	247	263
7	42	-16
8	57	-53
9	40	27
10	76	74
11	128	-124

	-5,10,L	
1	351	-354
2	379	389
4	332	339
5	68	47
6	101	116
7	50	-49
9	178	181
10	104	-106

	-5,11,L	
1	98	-105
2	299	-319
4	102	-101
5	71	-78
6	128	132
7	62	-67
8	213	224
9	58	-67
10	61	67

	-5,12,L	
1	108	-107
4	68	-66
5	83	92
6	103	-112
7	172	181
9	137	148

	-5,13,L	
1	70	-71
2	83	94
3	178	-181
5	225	-243
6	119	123
7	59	-71

	-5,14,L	
1	144	147
2	178	-195
3	105	109
4	75	-85
6	83	-86
7	47	-57

	-5,15,L	
2	52	49
3	42	-37
4	57	57

	-5,16,L	
1	103	104
2	36	-38

	-4,0,L	
2	49	48
4	39	58
6	341	375
8	453	474

	-4,1,L	
1	143	-160
2	463	-488
3	337	311
4	145	-174
5	698	690
6	34	8
7	485	490
8	46	-25
9	509	540
10	178	191
11	107	111
12	237	262
13	108	-104

	-4,2,L	
1	594	-618
2	163	-153
3	683	-708
4	124	-104
5	661	-667
6	296	296
7	169	172
8	177	-169
9	396	399
10	92	-98
11	339	358
13	203	226

	-4,3,L	
1	76	55
2	764	-788
4	343	-357
5	264	-261
6	193	-193
7	349	-359
8	174	186
9	87	-99
10	231	243
12	233	239
13	77	88

	-4,4,L	
1	381	-371
2	237	233
3	333	-324
4	480	-482
5	47	-55
6	421	-420
7	190	-175
8	454	-476
9	201	197
10	119	-122

	-4,5,L	
1	104	124
2	309	307
3	170	152
4	95	105
5	668	-670
6	223	217
7	328	-345
8	71	-78
9	327	-341
10	131	-129
11	75	-91
12	73	-68
13	106	111

	-4,6,L	
1	373	392
3	582	607
4	127	-146
5	376	371
6	236	-243
7	98	-83
8	166	-175
9	134	-135
10	48	-42
11	258	-273

	-4,7,L	
1	199	-189
2	796	791
3	184	-165
4	205	231
6	249	257
8	133	-130
9	97	107
10	248	-260
12	156	-174

	-4,8,L	
1	336	346
2	240	-242
3	147	159
4	225	213
5	222	233
6	308	317
7	163	-161
8	199	208
9	133	-140
10	79	84
11	134	-149

	-4,9,L	
1	33	-41
2	238	-224
3	90	87
4	142	138
5	479	499
6	44	-46
7	386	404
8	47	50
9	217	218
10	63	-65
11	81	89

	-4,10,L	
1	70	-85
2	64	-63
3	271	-267
4	180	183
5	251	-264
6	92	104
7	40	38
8	280	290
9	227	235
11	125	148

	-4,11,L	
1	166	173
2	399	-420
3	124	131
4	180	-187
6	169	-181
10	143	156

	-4,12,L	
1	57	-64
2	86	90
3	212	-221
4	69	-62
5	76	-77
6	114	-117
7	72	70
8	110	-113
9	44	34

	-4,13,L	
1	52	46
2	193	-198
3	90	-92
4	151	-161
5	88	-94
6	35	-42
7	183	-190
9	169	-184

	-4,14,L	
1	132	139
2	59	66
3	149	161
4	65	-65
5	155	168
6	195	-204
8	54	-63

	-4,15,L	
2	143	154
3	136	-115
4	52	60
5	64	-66
6	44	51

	-4,16,L	
1	100	109
3	193	203
4	63	55

	-3,0,L	
2	1107	-1176
4	652	-653
6	455	435
8	407	437
10	423	447
12	158	145

	-3,1,L	
1	652	-676
2	334	-341
3	554	-572
4	871	-876
5	300	-292
6	431	-439
7	185	200
8	184	-180
9	432	437
10	100	93
11	168	177
12	136	139
13	152	154

	-3,2,L	
1	261	-251
2	161	-162
3	619	-634
4	196	186
5	778	-794
6	60	56
7	715	-703
8	84	-84
9	361	-374
10	119	122
12	69	100
13	246	253

	-3,3,L	
1	767	758
2	421	-432
3	446	454
4	279	-321
5	407	392
6	705	-725
7	232	-225
8	58	-61
9	50	-73
10	75	88
11	191	-190
12	148	162
13	119	-111

	-3,4,L	
1	135	-135
2	807	817
3	213	-213
4	146	-103
5	242	-255
6	85	-74
7	67	-78
8	378	-405
9	112	-116
10	493	-504
12	177	-184

	-3,5,L	
1	577	607
2	111	-88
3	624	624
4	615	573
5	44	47
6	148	152
7	192	-205
8	249	249
9	315	-317
10	60	64
11	191	-202
12	67	-63
13	107	-112

-3,6,L

2	172	183
3	95	-37
4	66	-55
5	572	595
6	-167	-164
7	378	337
8	215	-210
9	52	61
10	218	-230
11	79	-81

-3,7,L

1	521	487
2	255	258
3	43	-77
4	516	543
5	117	109
6	387	402
7	95	95
8	223	242
9	130	133
11	61	53
12	117	-130

-3,8,L

1	290	280
2	709	-704
3	139	146
4	100	-109
5	394	410
6	121	-107
7	212	228
8	202	208
10	257	269
12	85	109

-3,9,L

1	507	-520
3	310	-320
4	58	65
6	235	-230
7	191	190
9	186	200
11	180	196

-3,10,L

1	102	-101
2	334	-336
3	107	-108
4	133	-134
5	191	-207
6	47	54
7	259	-277
8	122	124
9	119	-127
10	168	178
11	76	-78

-3,11,L

1	55	61
2	68	-67
3	96	100
4	400	-421
6	262	-274
7	234	242
8	58	-64
10	63	59

-3,12,L

1	81	-79
2	177	195
3	290	-294
4	66	65
5	167	-178
6	92	-90
7	158	-162
8	77	-83
9	35	-24
10	55	-72

-3,13,L

1	199	213
3	270	285
4	80	85
5	91	99
7	107	-115
9	127	-132

-3,14,L

2	43	40
4	39	26
6	56	-51
7	107	118
8	138	-147

-3,15,L

1	107	107
3	81	71
4	157	157
5	104	-104
6	80	90

-3,16,L

1	84	89
2	82	-89
3	77	86
5	98	97

-3,17,L

1	49	-66

-2,0,L

2	835	-901
4	1109	-1211
6	471	-473
8	123	138

-2,1,L

1	36	-27
2	74	-59
3	1144	-1226
4	90	90
5	159	-196
6	339	-342
7	270	-264
8	409	-429
9	48	65
10	396	-410
11	158	169
13	189	207

-2,2,L

1	1356	1440
2	499	-489
4	153	146
5	191	-200
6	437	-422
7	529	-557
8	172	157
9	299	-320
10	140	144
11	88	-96

-2,3,L

1	951	959
2	590	600
3	111	137
4	108	-117
5	286	291
6	895	-896
7	60	59
8	463	-490
9	216	-228
10	407	-415
11	163	-160
13	154	-162

-2,4,L

1	356	367
2	917	960
3	336	315
4	883	920
5	117	-133
6	430	438
7	94	-107
8	57	50
9	197	-190
10	194	-192
11	64	-80
12	245	-253

-2,5,L

1	1039	1043
2	424	-412
3	799	825
4	125	-111
5	709	719
6	59	69
7	330	323
8	249	253
9	199	-199
10	127	127
11	281	-302
13	181	-187

-2,6,L

1	736	-747
2	486	472
3	314	-303
4	244	258
5	533	511
6	184	193
7	442	453
8	49	-34
9	264	279
10	55	-49
11	131	140

-2,7,L

1	342	-313
2	522	-516
3	314	-306
4	132	125
5	206	-201
6	372	383
7	67	-60
8	463	479
9	81	74
10	374	387

-2,8,L

1	330	-351
2	542	-539
4	539	-556
5	61	70
6	286	-293
7	252	259
9	39	40
10	137	154
12	140	173

-2,9,L

1	544	-549
2	157	157
3	288	-293
4	214	210
5	290	-307
6	55	-57
7	211	-225
8	37	24
9	232	240
11	138	146

-2,10,L

1	279	293
2	189	-206
3	131	134
4	371	-382
5	253	-254
6	43	-58
7	178	-186
8	90	-90
9	124	-128
10	46	59

-2,11,L

2	135	148
3	61	-61
4	118	116
5	135	-141
6	265	-276
7	63	60
8	210	-224
9	47	-56
10	243	-254

-2,12,L

1	227	230
2	55	54
3	108	-108
4	232	245
5	72	-74
6	103	114
7	186	-190
9	171	-180
10	94	-103

-2,13,L

1	174	178
2	60	-57
3	362	371
4	93	-98
5	122	131
6	58	-56
7	127	136
8	42	-39
9	45	-43

-2,14,L

1	194	-205
2	180	187
3	37	33
4	225	232
6	89	89

-2,15,L

1	42	25
3	102	98
5	81	83
6	151	160
7	61	58

-2,16,L

1	186	-195
2	45	-49
3	127	-135
4	120	-133
5	79	79

-2,17,L

1	106	-103
2	82	91
3	38	-46

-1,0,L

2	507	-514
4	558	-584

-1,1,L

1	871	887
2	649	-569
3	947	-954
4	815	827
5	384	-402
6	41	46
7	595	-611
8	222	-241
9	243	-243
10	200	-205
12	172	-176
13	138	143

-1,2,L

1	60	41
2	42	-33
3	1251	1346
4	121	105
5	193	193
6	206	-201
7	169	-164
9	531	-562
11	351	-361
13	168	-179

-1,3,L

1	699	-673
2	1189	1271
3	550	542
4	387	401
5	440	438
6	67	68
7	444	437
8	144	-159
9	147	159
10	282	-294
11	89	-72
12	237	-254

-1,4,L

1	339	-293
2	358	357
3	392	391
4	455	471
5	187	-149
6	701	707
7	59	49
8	492	509
10	196	207

	-1,4,L	
11	110	-116
	-1,5,L	
1	336	-336
2	387	-386
3	47	74
4	141	-150
5	409	448
6	208	189
7	347	370
8	78	-60
9	54	66
12	142	134
	-1,6,L	
1	633	-657
2	135	119
3	295	-331
4	415	419
5	337	-351
6	356	370
7	56	68
8	232	238
9	433	452
10	95	94
11	270	285
	-1,7,L	
1	33	24
2	740	-775
3	126	-127
4	390	-390
5	211	-214
7	93	-97
8	80	87
9	98	-108
10	152	166
12	161	187
	-1,8,L	
1	652	-651
2	136	-137
3	342	-330
4	38	-64
5	66	-66
6	359	-383
7	84	79
8	145	-155
9	273	282
10	66	-62
11	203	216
	-1,9,L	
1	163	172
3	477	-479
4	136	-136
5	514	-533
7	473	-500
9	170	-181
10	94	-115
	-1,10,L	
1	275	288
2	64	65
3	463	479
4	177	-185
5	44	-41
6	236	-252
8	131	-129
9	205	-220
10	67	-67
11	104	-118
	-1,11,L	
2	221	229
4	348	357
5	42	36
6	54	-53
8	51	-52
9	49	-44
10	156	-163
	-1,12,L	
1	99	106
2	212	219
3	202	213
5	169	172
6	300	317
7	78	-80
8	71	78
9	184	-191
10	70	70
	-1,13,L	
1	367	-374
2	221	220
3	203	213
4	104	96
5	112	125
6	92	91
7	110	115
9	85	91
	-1,14,L	
2	64	68
3	100	-116
4	82	87
5	83	-94
6	225	233
8	141	151
	-1,15,L	
2	170	-184
4	161	-176
6	33	30
7	43	-46
	-1,16,L	
1	143	-147
2	42	34
3	100	-98
5	37	-31
	-1,17,L	
1	54	55
2	122	-117
	0,0,L	
2	742	818
4	550	547
6	101	-137
8	447	-459
10	359	-375
12	127	-134
	0,1,L	
1	101	136
2	829	873
3	871	890
4	1092	1166
5	282	-263
6	499	501
7	405	-410
9	347	-363
10	63	-57
11	206	-214
12	164	-176
	0,2,L	
0	24	46
1	176	-124
2	59	73
3	1266	1372
4	448	416
5	579	617
6	70	41
7	493	493
8	144	-142
9	153	138
10	125	-131
11	155	-154
13	240	-260
	0,3,L	
1	1136	-1180
2	443	460
3	535	-518
4	815	838
5	353	-321
6	683	670
7	131	130
8	258	252
9	338	365
10	214	-226
11	111	103
12	142	-154
	0,4,L	
0	1001	-1049
1	346	328
2	858	-881
3	85	102
4	378	-371
5	142	157
6	408	411
7	179	180
8	453	469
9	80	-76
10	177	178
12	168	159
	0,5,L	
1	819	-862
2	246	-261
3	461	-470
4	287	-285
5	177	162
6	225	-211
7	424	430
9	466	485
10	127	75
11	355	367
12	96	101
	0,6,L	
0	449	-467
1	378	-376
2	352	-352
3	669	-674
4	74	-71
5	687	-701
6	97	97
7	362	-366
8	135	138
9	58	-56
10	108	108
11	210	209
12	104	104
	0,7,L	
1	281	271
2	430	-438
3	34	38
4	577	-594
6	498	-515
7	180	-185
8	135	-131
9	96	-105
10	131	143
11	93	-86
12	112	128
	0,8,L	
0	784	805
1	208	-201
2	586	602
3	212	-228
4	110	114
5	250	-264
6	201	-217
7	234	-246
8	138	-149
9	73	-83
10	185	-201
	0,9,L	
1	353	379
2	71	73
3	452	466
5	45	37
6	135	135
7	283	-292
8	37	-25
9	337	-348
10	120	-125
11	167	-171
	0,10,L	
0	617	614
1	39	-34
2	245	254
3	413	427
4	123	120
5	129	139
6	75	-72
7	264	281
8	93	-92
9	102	105
10	74	-74
	0,11,L	
1	76	70
2	301	317
3	272	-276
4	330	343
5	130	-118
6	338	353
7	68	-69
9	124	-117
10	72	-79
	0,12,L	
0	647	-674
2	145	-153
3	437	439
4	54	-54
5	236	244
6	138	146
7	105	106
8	79	89
9	83	90
	0,13,L	
1	238	-254
2	169	-168
3	119	-122
5	45	51
7	145	152
9	148	159
	0,14,L	
0	227	-233
1	116	112
2	44	-44
3	137	-145
7	45	35
8	121	122
	0,15,L	
1	43	39
2	115	-121
3	42	-38
4	155	-165
5	43	51
6	184	-198
7	146	147
	0,16,L	
3	113	-119
5	95	-96
	0,17,L	
1	52	58
2	80	-82
	1,0,L	
0	100	-45
2	634	-544
4	733	804
6	465	451
8	250	-264
10	483	-515
12	244	-263
	1,1,L	
0	954	-1032
1	675	715
2	215	-190
3	517	563
4	104	-77
5	234	265
6	263	290
7	45	-47
8	449	456
9	77	-82
10	174	183
11	178	-182
	1,2,L	
0	310	305
1	225	-223
2	814	801
3	500	479
4	420	391
5	775	731
6	183	-154
7	535	548
8	117	117

	1,2,L	
9	321	335
10	119	-122
	1,3,L	
1	313	-321
2	243	221
3	140	-174
4	334	345
5	124	-134
6	336	362
7	146	151
8	516	531
9	97	106
10	159	177
11	167	180
	1,4,L	
0	99	48
1	67	-96
2	927	-970
3	160	-161
4	699	-725
5	318	309
6	81	-87
7	320	324
8	164	170
10	268	286
11	131	125
12	189	218
	1,5,L	
0	256	-242
1	1166	-1208
2	99	-95
3	553	-578
4	378	-368
5	533	-544
6	204	-209
7	104	-102
8	219	-223
9	66	84
11	250	255
	1,6,L	
0	254	188
1	517	514
2	462	-460
3	35	-50
4	229	-241
5	426	-443
6	141	-142
7	443	-463
8	76	-65
9	217	-230
10	164	165
11	150	-152
	1,7,L	
0	293	326
1	144	134
2	208	216
3	73	91
4	224	-235
5	54	59
6	473	-492
7	43	46
8	348	-366
9	45	40
10	75	-73
11	72	-76
	1,8,L	
0	142	100
1	227	252
2	402	421
3	30	-19
4	289	302
5	226	-227
6	64	58
7	131	-131
8	176	-185
9	247	-253
10	290	-311
	1,9,L	
0	98	-98
1	536	557
2	29	12
3	625	640
4	166	171
5	181	181
7	43	43
11	174	-185
	1,10,L	
0	71	77
1	74	68
2	91	103
3	110	110
4	207	212
5	236	252
6	110	120
7	306	320
8	180	-182
9	40	-31
10	89	-95
	1,11,L	
0	521	-529
1	123	112
2	75	-78
3	82	70
4	87	92
5	322	329
6	130	144
7	230	235
8	232	246
9	40	50
	1,12,L	
0	35	16
1	233	-240
2	65	-73
3	76	-78
4	130	-143
5	138	147
6	144	-157
7	225	237
8	61	60
9	133	142
	1,13,L	
0	167	-172
1	124	-135
3	229	-240
4	76	79
5	136	-152
	1,14,L	
0	209	-213
2	247	-253
4	221	-224
5	99	-115
6	73	-78
	1,15,L	
0	219	236
1	113	-111
3	192	-188
4	137	-149
5	126	-121
6	42	-46
	1,16,L	
0	55	57
1	84	94
2	75	91
4	66	86
5	79	-75
	1,17,L	
0	81	81
1	122	129
2	69	59
3	57	71
	2,0,L	
0	553	-556
2	499	522
4	922	966
6	374	394
8	443	453
10	130	141
12	71	-58
	2,1,L	
0	1065	-1139
1	158	-138
2	1064	-1156
3	562	592
4	128	87
5	913	947
7	481	484
8	205	213
9	55	46
10	149	162
12	129	129
	2,2,L	
0	793	-769
2	486	-449
3	880	-908
4	194	-169
5	668	-652
6	149	-130
7	341	359
8	169	173
9	315	329
11	243	251
	2,3,L	
0	115	-155
1	636	592
2	781	-803
3	330	-331
4	691	-683
5	694	-688
7	88	-85
8	168	185
9	196	-195
10	349	365
11	93	91
12	71	95
	2,4,L	
0	285	-249
1	553	-558
2	128	-148
3	59	49
4	555	-584
5	57	-62
6	546	-553
7	83	88
8	490	-501
10	59	-29
11	122	121
12	88	106
	2,5,L	
0	365	351
1	163	158
2	335	342
3	258	-285
4	254	251
5	404	-421
6	97	90
7	295	-312
8	246	-254
11	79	68
	2,6,L	
0	155	-125
1	1233	1250
2	379	-340
3	443	449
4	78	-87
5	231	227
6	317	-330
7	85	-93
8	185	-193
9	133	-144
11	211	-223
	2,7,L	
0	212	272
1	230	220
2	816	825
3	124	126
4	176	176
5	105	112
6	142	-142
7	160	161
8	186	-193
9	104	-110
10	222	-236
	2,8,L	
0	144	121
1	193	218
2	130	136
3	368	376
4	327	339
5	261	255
6	212	215
8	271	279
9	173	-171
	2,9,L	
0	173	-170
1	60	-63
2	38	-36
3	242	256
4	152	-155
5	516	522
7	342	351
8	94	-36
9	126	130
	2,10,L	
0	70	-74
1	329	-344
2	175	171
3	359	-372
4	282	286
5	163	-161
6	240	243
7	129	145
8	90	93
9	101	105
10	60	54
	2,11,L	
0	414	-437
1	134	-133
2	319	-341
3	42	-45
4	81	-82
5	61	-66
6	71	77
7	94	-105
8	220	228
9	74	75
	2,12,L	
0	39	28
1	356	-367
2	190	-200
3	150	-146
4	235	-247
5	63	-66
8	142	-153
	2,13,L	
2	39	53
3	93	-94
4	73	-71
5	299	-316
6	60	55
7	105	-115
8	86	94
	2,14,L	
0	147	148
1	172	188
2	37	46
3	45	37
4	194	-202
6	48	-50
7	116	-128
	2,15,L	
0	83	95
2	181	189
3	45	51
4	103	113
5	60	65
6	43	47
	2,16,L	
1	116	112
2	73	-71
	2,17,L	
2	63	53
	3,0,L	
0	667	-700
2	1166	-1190

	3,0,L	
4	409	379
6	259	270
8	399	412
10	209	217

	3,1,L	
0	497	-486
1	526	-534
2	270	-292
3	234	198
4	376	-390
5	54	-32
6	330	-333
7	438	444
9	232	248
10	101	108
11	132	139

	3,2,L	
0	186	-190
1	549	-556
2	127	108
3	305	-356
4	62	60
5	532	-547
6	112	99
8	63	-52
9	101	107
10	113	118
11	192	206

	3,3,L	
0	446	-424
1	185	173
2	380	-411
3	67	-75
4	670	-691
5	49	-49
6	63	-72
8	61	-56
9	261	-280
10	58	71

	3,4,L	
0	499	516
1	65	-62
2	324	332
3	426	-412
4	573	-554
5	202	-198
6	424	-429
7	239	-241
8	295	-301
9	115	111
10	141	-150
11	96	92

	3,5,L	
0	573	523
1	460	491
2	256	265
3	313	305
4	226	229
5	59	-73
6	42	44
7	547	-571
8	148	-152
9	304	-319
10	71	-73
11	148	-157

	3,6,L	
1	74	100
2	473	458
3	356	392
4	106	96
5	253	268
6	170	-165
7	62	56
8	84	-90
9	133	-143
10	68	-74

	3,7,L	
0	459	452
1	70	-61
2	609	618
4	464	491
5	131	129
6	420	425
7	200	209
8	89	96
9	58	65
10	134	-147

	3,8,L	
0	348	-384
1	32	-14
2	209	-216
3	255	257
4	120	123
5	109	114
6	427	440
7	47	-47
8	200	218
9	78	90
10	80	87

	3,9,L	
0	104	94
1	291	-296
3	69	-70
6	326	333
7	83	99
9	172	182

	3,10,L	
0	400	-412
1	307	-320
2	321	-325
3	138	-150
5	169	-173
6	61	57
8	207	216
9	95	101

	3,11,L	
0	128	-130
1	85	-90
2	247	-249
3	135	-143
4	353	-375
6	135	-142
7	47	-66
8	59	-67

	3,12,L	
0	153	143
1	132	-143
2	153	145
3	113	-107
4	96	-105
5	225	-227
6	80	-94
7	98	-104
8	58	-71

	3,13,L	
0	65	-60
1	188	203
4	149	-148
6	86	-91
7	166	-181

	3,14,L	
0	139	146
1	144	155
2	78	87
4	50	-52
5	114	124
6	73	-67

	3,15,L	
0	138	144
1	159	161
2	90	99
4	130	141
5	37	41

	3,16,L	
1	93	36
2	33	20
3	122	130

	4,0,L	
0	243	-265
2	577	-608
4	551	-563
6	105	-110
8	181	187
10	119	122

	4,1,L	
0	196	205
1	1018	-1023
2	389	344
3	352	-378
4	380	-369
5	364	-361
6	175	-181
7	66	-70
8	172	-176
9	165	171
10	61	-71
11	109	120

	4,2,L	
0	178	-181
1	169	179
2	184	149
3	191	-182
4	356	-339
5	526	-542
6	95	88
7	455	-463
9	263	-278
10	65	59

	4,3,L	
0	562	557
1	220	232
2	314	294
3	219	238
4	335	-348
5	141	138
6	331	-351
7	152	-147
8	187	-194
9	146	-151
10	116	-119

	4,4,L	
0	861	849
1	78	-59
2	704	717
3	166	-156
4	698	707
5	112	105
6	473	476
7	268	-274
8	155	-168
9	43	-41
10	167	-183

	4,5,L	
0	309	-296
1	530	553
2	65	-51
3	634	635
4	184	186
5	102	-88
6	336	341
7	60	64
8	104	111
9	43	-47
10	74	71

	4,6,L	
0	251	261
1	121	107
2	244	258
3	236	234
4	174	179
5	164	173
6	90	83
7	196	210
9	198	214

	4,7,L	
0	503	-515
1	402	-397
2	38	37
3	101	-97
4	149	146
5	64	60
6	377	387
7	98	-100
8	169	176
9	74	-73

	4,8,L	
0	321	-324
1	106	-110
2	441	-445
3	84	-86
4	402	-413
5	253	263
7	150	157
8	64	65
9	128	135

	4,9,L	
1	328	-347
2	135	-136
3	302	-314
5	93	-100
6	125	-130
7	42	58
9	141	145

	4,10,L	
0	210	-218
1	39	41
2	186	-195
3	164	-177
4	148	-145
5	166	-176
6	183	-186
7	171	-185
8	103	98

	4,11,L	
0	256	252
1	79	79
2	104	108
3	55	-51
4	163	-171
6	165	-172
8	96	-109

	4,12,L	
0	37	-38
1	119	123
2	132	136
4	75	81
5	116	-125
6	37	-38
7	111	-119

	4,13,L	
0	184	194
1	345	370
2	66	68
3	91	89
5	86	94
6	35	-13

	4,14,L	
0	181	180
2	144	148
4	219	230
5	66	74

	4,15,L	
0	74	-77
2	53	-65
4	139	144

	4,16,L	
0	57	-75
1	98	-101

	5,0,L	
0	191	-140
2	275	-300
4	448	-463
6	139	-153
8	40	-44
10	50	45

	5,1,L	
0	330	331
1	262	-255
2	341	335
3	330	-345
5	474	-485
6	118	-115
7	235	-240

5,1,L		
8	273	-291
10	88	-103
5,2,L		
0	202	193
1	947	963
2	168	175
3	207	221
4	35	30
5	168	-177
6	65	63
7	74	-77
9	257	-268
5,3,L		
0	425	442
1	210	205
2	119	149
3	181	184
4	171	175
5	293	305
6	154	-159
8	173	-178
10	126	-137
5,4,L		
0	-186	-173
1	198	207
2	322	341
3	244	249
4	122	131
5	106	113
6	276	295
8	50	-50
9	78	-82
5,5,L		
0	393	-346
1	39	-26
2	131	-130
3	376	387
4	94	93
5	352	342
6	59	-61
7	238	249
8	62	67
5,6,L		
0	223	-213
1	148	-166
2	173	171
3	430	-442
4	131	129
5	323	334
6	116	113
7	230	252
8	94	102
9	203	219
5,7,L		
0	455	-470
2	231	-247
3	229	-233
4	290	-291
7	41	45
8	216	229
9	135	150
5,8,L		
0	184	176
1	160	-172
2	248	-265
3	174	-182
5	60	61
6	177	-186
7	46	-43
5,9,L		
0	155	-152
1	147	-148
2	117	-120
3	309	-322
4	43	35
5	325	-338
6	140	-151
7	145	-150
5,10,L		
0	182	167
1	320	335
2	115	-106
4	132	-126
5	120	-95
6	146	-152
7	50	-60
5,11,L		
0	183	195
2	225	238
4	51	46
5	81	-83
6	90	-94
7	38	-36
5,12,L		
0	195	217
1	222	237
2	174	171
3	63	61
4	138	152
5	45	43
6	51	61
5,13,L		
0	41	50
1	53	46
2	48	54
3	151	149
4	102	111
5	156	167
5,14,L		
1	83	-95
4	69	71
5,15,L		
0	69	-68
1	63	-60
2	34	-49
6,0,L		
0	183	215
2	189	191
4	120	-130
6	325	-314
8	254	-262
6,1,L		
0	59	66
1	456	456
2	282	286
3	98	88
4	156	162
5	38	-32
6	88	103
9	130	-139
6,2,L		
0	81	-61
1	253	253
2	108	-90
3	309	325
4	44	-45
5	418	441
6	242	-247
7	128	136
8	77	-77
9	80	-83
6,3,L		
0	221	227
2	469	478
3	154	-157
4	131	150
5	212	218
6	112	106
7	119	124
8	41	-31
9	79	91
6,4,L		
0	443	-456
3	240	237
4	139	133
5	75	83
6	310	315
7	44	55
8	133	146
6,5,L		
0	174	-167
1	121	-138
2	259	-258
3	131	-137
4	49	41
5	159	159
6	131	-138
7	113	117
6,6,L		
0	275	-285
3	505	-527
4	47	-56
5	126	-141
6	77	78
7	57	-60
8	89	91
6,7,L		
1	125	-128
2	463	-478
3	67	-69
4	123	-130
5	101	-103
6	108	-118
7	35	-45
6,8,L		
0	350	364
1	91	-100
2	121	-115
3	113	-123
4	78	-74
5	156	-166
6	185	-188
6,9,L		
0	160	167
1	135	142
2	95	103
3	119	123
5	130	-133
6	100	-97
7	103	-113
6,10,L		
0	170	181
1	72	70
2	205	218
3	185	200
4	49	47
5	89	100
6	40	-42
6,11,L		
0	76	79
1	83	96
2	143	150
4	85	82
6,12,L		
1	113	120
2	45	-45
3	162	166
4	55	62
5	158	168
6,13,L		
0	45	-50
1	131	-137
6,14,L		
0	41	-41
2	74	-86
7,0,L		
0	415	424
2	380	390
4	98	113
6	60	-65
8	144	-152
7,1,L		
1	329	347
2	73	56
3	183	179
4	289	307
5	87	94
6	194	207
7	73	-73
7,2,L		
2	150	142
3	138	143
5	129	135
7	96	106
7,3,L		
0	201	-211
1	247	-259
2	88	83
3	112	-114
4	185	196
5	98	97
6	322	335
7	72	72
8	145	161
7,4,L		
0	412	-418
1	121	-119
2	502	-515
4	157	-170
5	58	-69
6	50	-48
7,5,L		
0	252	252
2	80	-78
3	263	-279
4	81	-87
5	42	-60
6	68	-69
7	102	104
7,6,L		
0	57	-68
1	193	-190
2	104	-119
3	88	-87
4	132	-136
5	121	-136
6	83	-83
7	104	-113
7,7,L		
0	337	350
2	146	-145
3	85	91
4	165	-166
6	154	-163
7,8,L		
0	173	174
1	59	63
2	155	156
4	99	103
5	80	-79
7,9,L		
1	215	230
2	45	45
3	212	234
4	39	32
7,10,L		
0	56	58
1	93	99
2	98	109
3	128	131
5	45	50
7,11,L		
2	41	33
3	45	45
4	191	197
7,12,L		
0	168	-182
1	34	-51
2	82	-81
7,13,L		
1	113	-122
8,0,L		
0	195	196
2	84	70

	8,0,L	
4	296	312
6	187	209
	8,1,L	
0	239	-242
1	87	85
2	118	-128
3	132	138
5	46	48
	8,2,L	
1	188	-211
5	104	92
6	40	36
	8,3,L	
0	128	-144
1	169	-170
2	145	-154
3	54	-47
4	75	-85
5	34	-38
	8,4,L	
1	70	-77
2	100	-104
3	50	-46
4	140	-152
	8,5,L	
0	79	-79
2	76	-75
3	193	-202
5	118	-117
6	57	-58
	8,6,L	
0	67	72
1	194	206
2	79	-81
4	157	-165
5	121	-122
	8,7,L	
0	253	265
1	73	72
2	90	99
3	99	104
4	76	85
5	66	72
	8,8,L	
0	79	-79
1	56	56
2	77	81
3	70	79
4	119	129
	8,9,L	
0	47	61
1	126	125
2	113	121
3	119	119
4	80	83
	8,10,L	
1	101	-104
3	40	27
	8,11,L	
0	117	-126
1	33	-45
2	69	-72
	8,12,L	
0	73	-77
	9,0,L	
0	88	-107
2	124	-148
4	43	25
	9,1,L	
0	172	-177
1	118	-133
3	57	56
4	81	-90
5	98	99

	9,2,L	
0	79	-82
1	239	-244
3	220	-237
4	70	70
5	99	-112
	9,3,L	
0	226	-232
1	166	175
2	191	-198
3	78	-76
4	138	-156
5	74	-84
	9,4,L	
0	142	158
4	71	-70
	9,5,L	
0	142	139
1	38	40
2	132	141
3	111	-105
4	60	66
	9,6,L	
0	111	128
1	136	130
2	66	77
3	65	76
4	44	58
	9,7,L	
0	112	120
2	60	71
	9,8,L	
1	80	87
2	59	61
	9,9,L	
0	121	-125
1	157	-178
2	44	-48
	9,10,L	
0	33	-42
	10,0,L	
0	233	-242
2	64	-72
	10,1,L	
0	50	-39
1	86	-94
2	87	-87
3	64	-72
	10,2,L	
0	59	64
1	62	-53
3	69	-66
	10,3,L	
0	83	98
2	59	69
3	35	-29
	10,4,L	
0	109	116
2	42	46
	10,5,L	
0	79	75
1	164	176
	10,6,L	
0	91	90

TABLE 9.9.

PIPH : Observed and Calculated Structure Factors for those Reflections with Intensities not Significantly Greater than the Background Level.

The format is exactly as in the previous table (9.8).

3,3,L
11 57 -31

2,14,L
5 35 -35

1,6,L
12 67 64

-1,10,L
4 32 -2

-3,9,L
5 33 -5

-5,7,L
4 33 32

-6,7,L
9 37 -31

-9,2,L
5 35 -3

-11,9,L
2 29 24
4 30 -35

-11,1,L
0 28 -13
1 29 -16
2 29 -11
6 29 2

-11,2,L
0 27 14
2 29 17
7 28 -0

-11,3,L
1 28 10
6 23 3

-11,4,L
2 28 -16
4 29 11
5 28 -18

-10,1,L
3 31 30

-10,2,L
9 29 -6

-10,3,L
1 32 -9
5 34 -36

-10,4,L
3 33 -36
4 33 16
7 32 32
9 28 -26

-10,5,L
2 32 29
4 32 19

-10,6,L
2 31 -10

-10,7,L
0 28 17
7 28 16

-10,8,L
2 29 -13
5 29 -5
6 28 9

-9,1,L
4 35 -33
5 35 12
7 36 36

-9,2,L
1 35 12
4 35 -10
6 35 -13
10 31 24

-9,3,L
5 35 30
10 31 -28

-9,4,L
6 35 -10
7 34 2

-9,5,L
4 35 -43
8 34 22
10 29 25

-9,6,L
6 35 -11

-9,7,L
1 33 -7
7 33 -25
9 30 -25

-9,8,L
0 32 -0
1 33 18

-9,9,L
5 31 -13
6 31 2
7 30 20

-9,10,L
0 29 -42
6 29 -10

-9,11,L
3 28 15

-8,0,L
10 35 34

-8,1,L
1 34 -48

-8,2,L
0 35 -11

-8,7,L
1 35 -5
5 37 8
9 34 34

-8,9,L
1 35 20
2 35 2
4 35 -4
8 33 -3
9 31 12

-8,10,L
0 33 -37
5 34 35
8 31 5

-8,11,L
5 32 -1

-8,2,L
10 35 -28

-8,3,L
11 43 -17

-3,4,L
0 36 30
11 43 -27

-8,5,L
2 36 2
8 36 29
9 35 2
11 43 11

-8,6,L
5 37 -8
6 37 33
8 36 -11

-8,11,L
6 31 -22
7 30 -10

-8,12,L
2 31 16

-7,0,L
12 56 -45

-7,1,L
0 32 11
3 32 5
8 36 21

-7,2,L
0 33 37
2 32 -7
6 35 10
8 37 -1

-7,3,L
8 38 17

-7,4,L
3 34 15
7 37 9
11 52 -37

-7,5,L
2 35 -22
3 35 7
5 36 16
6 38 29
11 53 26

-7,8,L
4 38 -33
5 38 -33

-7,9,L
2 37 3

-7,11,L
0 35 11
1 36 9
6 36 49
7 34 -20
8 33 3

-7,12,L
4 34 0
6 33 6

-7,13,L
0 31 11
2 32 39
4 32 0

-7,14,L
1 29 12
2 29 -16

-6,1,L
5 31 28
12 64 -21

-6,2,L
10 39 5
12 65 -13

-6,3,L
2 31 14
9 39 -11

-6,4,L
11 59 -34

-6,5,L
2 33 17
5 35 20
7 37 24
12 61 -2

-6,6,L
12 59 59

-6,7,L
0 36 -9
11 54 -37

-6,9,L
4 37 -4
10 37 33

-6,10,L
3 37 -24
6 36 -0

-6,11,L
1 37 28

-6,12,L
0 37 -8
6 36 -32

-6,13,L
7 32 3

-6,14,L
3 33 -19

-5,2,L
4 30 30
8 37 2
13 75 35

-5,3,L
7 34 -16

-5,4,L
10 43 11
11 60 67
13 67 -10

-5,5,L
4 31 49

-5,6,L
8 36 6
10 43 46

-5,7,L
9 36 37
11 56 -29
12 57 -75

-5,8,L
3 33 17
9 36 -16
10 41 -29

-5,9,L
6 36 -37

-5,10,L
3 36 -12
8 36 43

-5,11,L
3 36 -0

-5,12,L
2 37 -39
3 36 -27
8 33 -40

-5,13,L
4 36 48
8 31 19

-5,14,L
0 35 -14
6 33 10

-5,15,L
1 33 11
5 31 0

-4,0,L
10 41 14
12 75 -19

-4,2,L
12 65 -51

-4,3,L
3 26 3
11 60 -4

-4,4,L
11 60 15

	-4,4,L	
12	63	9
13	65	82
	-4,6,L	
2	28	6
12	60	2
	-4,7,L	
5	31	9
7	34	15
11	57	31
	-4,8,L	
12	56	-18
	-4,9,L	
9	33	13
	-4,10,L	
10	40	35
	-4,11,L	
5	35	-33
7	36	21
9	35	4
9	33	-18
	-4,12,L	
9	36	-38
	-4,13,L	
8	32	20
	-4,14,L	
7	31	-4
	-4,15,L	
1	34	-30
	-4,16,L	
2	31	2
	-3,2,L	
11	62	45
	-3,4,L	
11	62	41
13	64	49
	-3,6,L	
0	26	17
12	62	-46
	-3,7,L	
10	47	-12
	-3,8,L	
9	35	3
11	56	-32
	-3,9,L	
2	30	-26
8	35	21
10	44	-25
	-3,11,L	
5	35	22
7	34	18
	-3,13,L	
2	35	5
6	35	-9
8	32	-14
	-3,14,L	
1	35	-17
3	35	-20
5	34	24
	-3,15,L	
2	34	-3
7	30	24
	-3,16,L	
0	32	-18
4	31	-17
	-3,17,L	
2	30	15

	-2,0,L	
10	46	324
12	78	422
	-2,1,L	
12	71	40
	-2,2,L	
3	23	-2
12	70	-3
13	68	-30
	-2,3,L	
12	69	-27
	-2,4,L	
13	64	21
	-2,5,L	
12	66	0
	-2,6,L	
12	64	-72
	-2,7,L	
11	59	7
12	61	31
	-2,8,L	
3	28	-39
8	35	-35
11	57	43
	-2,9,L	
10	46	7
	-2,10,L	
11	52	-44
	-2,11,L	
1	33	-15
	-2,12,L	
8	34	3
	-2,13,L	
0	35	-12
	-2,14,L	
5	34	-3
7	33	34
8	31	-29
	-2,15,L	
2	35	44
4	34	31
	-2,16,L	
0	33	-2
	-2,17,L	
0	30	-5
	-1,0,L	
6	32	-1068
8	38	-450
10	43	-291
12	72	163
	-1,1,L	
11	67	-8
	-1,2,L	
8	32	4
10	51	38
12	73	2
	-1,3,L	
13	69	-65
	-1,4,L	
9	36	1
12	69	-94
13	66	29
	-1,5,L	
10	53	23
11	63	10

	-1,6,L	
12	65	-37
	-1,7,L	
6	31	12
11	60	-5
	-1,8,L	
12	59	18
	-1,9,L	
2	28	4
6	33	-20
8	36	30
11	55	10
	-1,10,L	
7	36	-32
	-1,11,L	
1	32	-1
3	33	-3
7	35	5
	-1,12,L	
0	34	14
4	35	-0
	-1,13,L	
8	33	2
	-1,14,L	
1	36	-20
7	33	-33
	-1,15,L	
1	35	-11
3	35	-22
5	33	6
	-1,17,L	
4	31	-37
	0,1,L	
3	35	2
13	69	-19
	0,2,L	
12	78	-49
	0,3,L	
13	70	69
	0,4,L	
11	65	-16
	0,5,L	
8	34	9
	0,7,L	
5	29	2
	0,8,L	
11	58	39
	0,9,L	
4	30	-8
	0,11,L	
8	35	-14
	0,12,L	
1	34	23
	0,13,L	
4	36	-26
6	35	-33
8	32	5
	0,14,L	
4	34	-27
5	37	-36
6	34	19
	0,16,L	
0	35	56
1	34	-8
2	33	11
4	32	0

	0,17,L	
3	30	24
	1,1,L	
12	68	-9
	1,2,L	
11	67	55
12	69	32
	1,3,L	
12	70	43
	1,4,L	
9	38	-41
	1,5,L	
10	55	-7
12	69	24
	1,8,L	
11	56	9
	1,9,L	
6	36	32
8	36	49
9	36	-15
10	49	24
	1,11,L	
2	35	-49
6	35	-50
7	34	5
8	32	-14
	1,14,L	
1	35	28
3	35	-20
7	31	-14
	1,15,L	
2	35	4
	1,16,L	
3	32	27
	2,1,L	
6	43	27
11	61	-74
	2,2,L	
10	51	17
12	63	-18
	2,3,L	
6	33	-17
	2,4,L	
9	40	-32
	2,5,L	
9	39	-23
10	57	-39
	2,6,L	
10	56	-17
	2,7,L	
11	59	-9
	2,8,L	
7	37	-21
10	52	-24
	2,9,L	
6	35	4
10	49	44
	2,12,L	
6	36	-18
7	35	-19
	2,13,L	
0	35	12
1	35	7
	2,15,L	
1	35	32

2,16,L

3	32	14
4	31	1

2,17,L

0	31	5
1	31	17

3,1,L

8	37	-16

3,2,L

7	36	-20

3,3,L

7	37	-1

3,6,L

0	27	17

3,7,L

3	30	12

3,9,L

2	32	7
4	35	-41
5	36	14
8	38	32

3,10,L

4	36	-5
7	37	-26

3,11,L

5	37	-9

3,13,L

2	30	-11
3	37	17
5	38	-14

3,14,L

3	36	7

3,15,L

3	34	22

3,16,L

0	33	-18

3,17,L

0	31	-34

4,2,L

8	37	-17
11	51	-30

4,6,L

8	38	28
10	45	-5

4,8,L

6	30	-34

4,9,L

0	33	-13
4	37	-35
8	35	-23

4,11,L

5	33	30
7	35	-24

4,12,L

3	38	-36

4,13,L

4	36	41

4,14,L

1	36	29
3	35	41

4,15,L

1	34	3
3	33	-19

4,16,L

1	31	-33

5,1,L

4	33	11
9	34	-8

5,2,L

8	36	-12
10	42	3

5,3,L

7	37	-21
9	33	-4

5,4,L

7	37	-32

5,5,L

9	32	-2

5,7,L

1	34	16
5	38	-22
6	38	26

5,8,L

4	39	-19
8	32	-20

5,9,L

8	30	-28

5,10,L

3	38	14

5,11,L

1	37	-10
3	39	50

5,14,L

0	35	-14
2	35	-19
3	33	-16

6,1,L

7	35	-26
8	33	14

6,3,L

1	32	-5

6,4,L

1	33	31
2	34	20

6,5,L

8	32	41

6,6,L

1	35	-6
2	36	-19

6,7,L

0	36	9
8	29	-2

6,8,L

7	31	-24

6,9,L

4	36	-0

6,11,L

3	36	48
5	31	14

6,12,L

0	38	-3

6,13,L

2	33	-29
3	31	6

6,14,L

1	32	3

7,1,L

0	33	-11

7,2,L

0	34	37
1	34	-41

7,1,L

8	29	16

7,2,L

4	36	50
6	35	32
8	29	6

7,4,L

3	36	9
7	31	-25

7,5,L

1	36	-16

7,7,L

1	37	12
5	33	-0

7,8,L

3	36	11
6	30	-12

7,9,L

0	38	-49
5	31	22

7,10,L

4	32	6

7,11,L

0	35	-11
1	35	17

7,12,L

3	30	19

7,13,L

0	32	-11

8,1,L

4	35	-25
6	31	12

8,2,L

0	35	-11
2	36	-1
3	36	22
4	35	-11

8,3,L

6	30	4

8,4,L

0	36	30
5	33	3
6	29	-12

8,5,L

1	36	-10
4	34	10

8,6,L

3	35	9

8,10,L

0	34	-17
2	31	28

9,1,L

2	34	-14

9,2,L

2	35	20

9,4,L

1	35	19
2	34	-22
3	32	-0

9,7,L

1	33	-30
3	29	21

9,8,L

0	33	-0

10,2,L

2	30	1

10,3,L

1	31	0

10,4,L

1	31	9

10,5,L

2	28	4

10,6,L

1	29	-30

10,7,L

0	29	-17

9.5. Discussion.

i) Accuracy of the Determination.

The standard deviations shown in Tables 9.5, 9.7, are probably low estimates, since they were obtained from block-diagonal least-squares approximations. This is also true of the σ-values obtained for the bond lengths and valence angles shown in Tables 9.10, 9.11. In general the respective $\langle\sigma\rangle$-values obtained here are better, by a factor of two, than those obtained by a similar process for humulene bromohydrin (cf. Tables 7.2, 7.6, 7.7), while the R-factor is better by a factor of three. However a meaningful comparison is difficult, since the weighting schemes used in each case were different, and this plays an important part in determining the magnitude of $\langle\sigma\rangle$. Thus it is not possible to predict the type of relationship to be found between improvements in R and $\langle\sigma\rangle$-values.

The most interesting point to arise from the refinement was the large drop in R ($\sim$2% in 5.7%, an improvement of 35%) due to the absorption correction. As pointed out above, the anisotropic crystal-shape gave wide variations in μt, and the results obtained show the danger of ignoring absorption corrections, even when μ is relatively low, unless the crystal shape is very nearly isotropic. It appears better to apply a rough correction than none at all.

The general accuracy of the data, obtained over a long (~2 weeks) collection period, was encouraging, especially since this was one of the first jobs of any length performed on this machine. It would have been possible to attain higher accuracy in the determination if the crystal had not been so anisotropic in shape, requiring the use of the 0.8mm collimator to encompass the lengths of the needle. A shorter crystal and smaller collimator would have reduced the background scattering, and probably increased the number of 'observed' reflections.

The accuracy of the initial data contributed in no small way to the speed of structure solution, a breakdown of the times is interesting in comparison with the photographic method. The data-collection process took exactly 322 hours (i.e. a rate of 9.32 useful reflections per hour). Data processing and structure solution took a further week, while one more week was required to reduce R to 0.086. Since this experiment formed part of an intensive series of trials of the AED, and was especially chosen because structure solution was expected to be straightforward, it can only be said that the machine gave an excellent response.

ii) Stereochemistry, Conformation and Molecular Geometry.

In the ensuing discussion the numbering adopted in the crystallographic study will be adhered to throughout. The

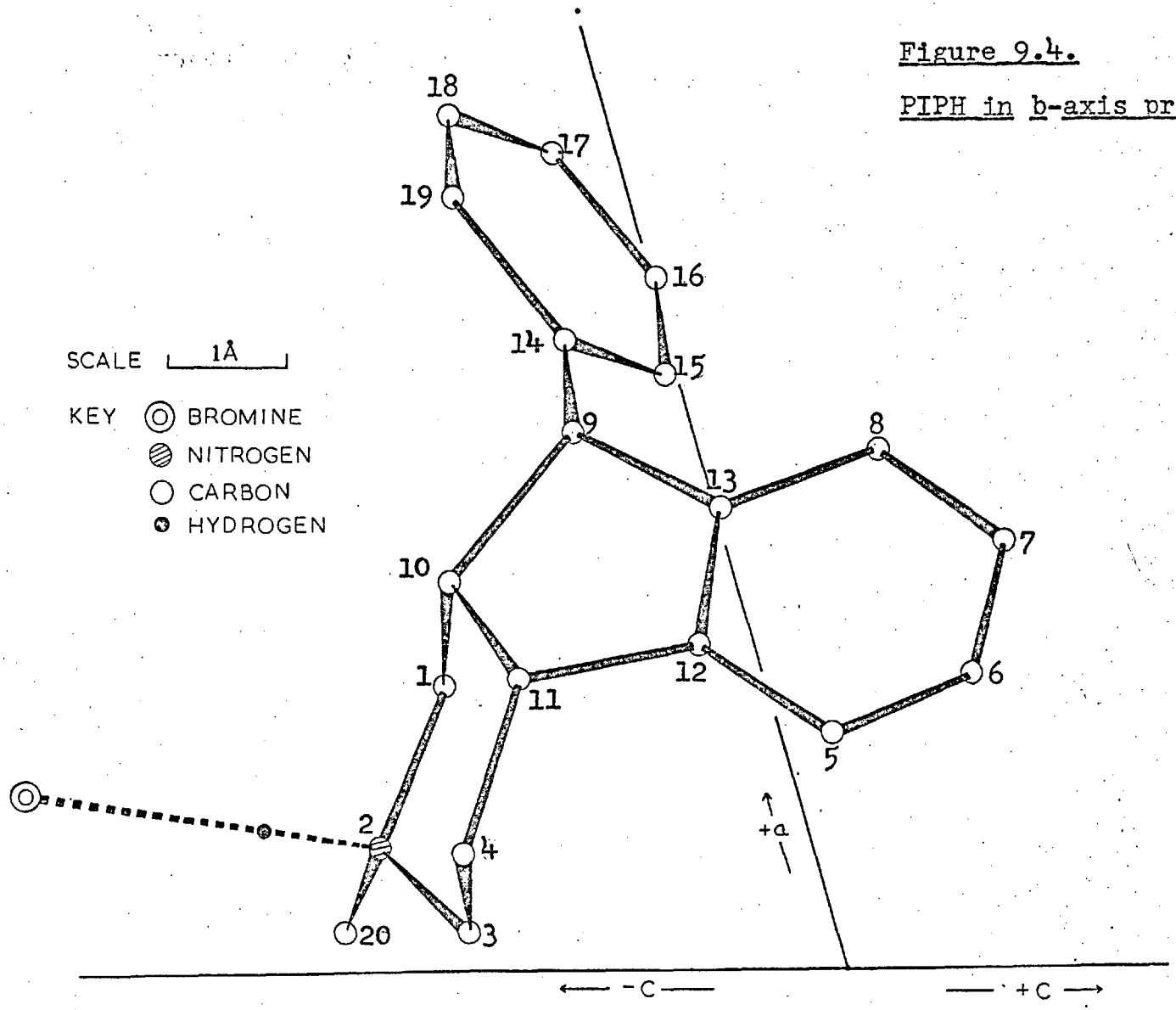


Figure 9.4.

PIPH in b-axis projection.

b-axis projection of one molecule (Figure 9.4) shows that the three protons at C(9), C(10), C(11), are all cis; the proposed stereochemistry[231] is therefore confirmed, and is shown correctly in 9.V (p.237).

The bond lengths and valence angles in Tables 9.10, 9.11, have been subdivided into two groups : those involving only C and N, and those involving hydrogens. The former are shown for clarity in figure 9.5. The average C_{sp3}-C_{sp3} and C-$C_{aromatic}$ distances are 1.531 ± 0.005 and 1.513 ± 0.005Å respectively, not significantly different from the accepted averages of 1.537 and 1.505 Å[153]. The average C-$N_{quaternar}$ distance of 1.499 ± 0.005 Å is a little higher than the cited average (1.479 Å[153]), but comparable averages have been found in the structures of DL-betaprodine hydrobromide and hydrochloride[241,242] (1.495 Å in each case), piperazine hydrochloride[243] (1.50 Å), and also in the piperidine rings of certain alkaloids[244].

The carbon atoms of both benzene rings are closely coplanar, average deviations ($\langle|d|\rangle$) from the mean planes being 0.0022Å for the C(5,6,7,8,12,13) ring, and 0.0043 Å for the phenyl side-chain. The discrepancy is due to the higher thermal motion possible in the latter ring, which also accounts for the increased values of σ_x, σ_y, σ_z, for C(15) → C(19) (see Table 9.5). Inclusion of hydrogen atoms in the calculation of the mean planes increases the

TABLE 9.10.

PIPH : Intramolecular bonded distances (r) in Å, together with their estimated standard deviations (σ_r)

a) Bonds not involving hydrogen atoms.

Atoms	r	σ_r	Atoms	r	σ_r
C(1) - N(2)	1.504	0.004	C(9) - C(13)	1.521	0.005
C(1) - C(10)	1.525	0.005	C(9) - C(14)	1.508	0.005
N(2) - C(3)	1.499	0.005	C(10) - C(11)	1.548	0.005
N(2) - C(20)	1.495	0.005	C(11) - C(12)	1.511	0.005
C(3) - C(4)	1.504	0.006	C(12) - C(13)	1.387	0.004
C(4) - C(11)	1.522	0.005	C(14) - C(15)	1.392	0.006
C(5) - C(6)	1.386	0.005	C(14) - C(19)	1.398	0.006
C(5) - C(12)	1.390	0.006	C(15) - C(16)	1.410	0.006
C(6) - C(7)	1.373	0.006	C(16) - C(17)	1.395	0.008
C(7) - C(8)	1.392	0.006	C(17) - C(18)	1.368	0.007
C(8) - C(13)	1.387	0.005	C(18) - C(19)	1.395	0.006
C(9) - C(10)	1.560	0.004			

Table 9.10 (contd.)

b) Bonds involving hydrogen atoms.

The bond lengths are given in groups, classified according to the degree of substitution of the carbon atom; the average $\underline{r}$ in each group is compared with the spectroscopic average[153].

C(aromatic)-H.

C(5) - H(50)	0.93	0.04
C(6) - H(60)	0.97	0.05
C(7) - H(70)	0.90	0.04
C(8) - H(80)	0.98	0.04
C(15)- H(150)	0.96	0.05
C(16)- H(160)	0.94	0.05
C(17)- H(170)	1.00	0.05
C(18)- H(180)	1.02	0.06
C(19)- H(190)	0.89	0.05

$\langle \underline{r} \rangle$ = 0.99 Å

Spect. Ave. = 1.084 Å

C(methyl)-H.

C(20)- H(200)	0.94	0.05
C(20)- H(201)	1.01	0.04
C(20)- H(202)	0.99	0.05

$\langle \underline{r} \rangle$ = 0.98 Å.

Spect. Ave. = 1.096 Å.

C(disubstituted)-H.

C(1) - H(10)	0.91	0.05
C(1) - H(11)	0.97	0.05
C(3) - H(30)	1.00	0.05
C(3) - H(31)	0.99	0.04
C(4) - H(40)	0.90	0.05
C(4) - H(41)	0.93	0.05

$\langle \underline{r} \rangle$ = 0.95 Å.

Spect. Ave = 1.073 Å.

C(trisubstituted)-H.

C(9) - H(10)	0.88	0.04
C(10)- H(100)	0.98	0.05
C(11)- H(110)	0.95	0.04

$\langle \underline{r} \rangle$ = 0.94 Å

Spect. Ave = 1.070 Å.

TABLE 9.11.

PIPH : Valence angles (θ)° in the asymmetric unit, together with their estimated standard deviations (σ)°

a) Angles not involving hydrogen atoms.

End -Apex -End	θ	σ	End -Apex -End	θ	σ
C(1) -N(2) -C(3)	109.7	0.3	C(1) -N(2) -C(20)	110.6	0.3
C(1) -C(10)-C(9)	110.3	0.3	C(1) -C(10)-C(11)	111.8	0.3
N(2) -C(1) -C(10)	111.3	0.3	N(2) -C(3) -C(4)	108.8	0.3
C(3) -N(2) -C(20)	112.0	0.3	C(3) -C(4) -C(11)	112.7	0.3
C(4) -C(11)-C(10)	114.4	0.3	C(4) -C(11)-C(12)	116.8	0.3
C(5) -C(6) -C(7)	120.6	0.4	C(5) -C(12)-C(11)	128.8	0.3
C(5) -C(12)-C(13)	120.8	0.3	C(6) -C(5) -C(12)	118.9	0.3
C(6) -C(7) -C(8)	120.8	0.4	C(7) -C(8) -C(13)	119.1	0.3
C(8) -C(13)-C(9)	129.8	0.3	C(8) -C(13)-C(12)	119.9	0.3
C(9) -C(10)-C(11)	103.0	0.3	C(9) -C(13)-C(12)	110.1	0.3
C(9) -C(14)-C(15)	122.4	0.4	C(9) -C(14)-C(19)	118.7	0.3
C(10)-C(9) -C(13)	102.0	0.3	C(10)-C(9) -C(14)	116.8	0.3
C(10)-C(11)-C(12)	102.7	0.3	C(11)-C(12)-C(13)	110.2	0.3
C(13)-C(9) -C(14)	118.2	0.3	C(14)-C(15)-C(16)	120.2	0.4
C(14)-C(19)-C(18)	120.5	0.4	C(15)-C(14)-C(19)	119.0	0.4
C(15)-C(16)-C(17)	119.6	0.4	C(16)-C(17)-C(18)	120.2	0.4
C(17)-C(18)-C(19)	120.5	0.5			

Table 9.11 (contd.)

b) Angles involving hydrogen atoms.

C(1) -C(10)-H(100)	109.4	2.4	N(2) -C(1) -H(10)	104.3	2.4
N(2) -C(1) -H(11)	104.2	2.2	N(2) -C(3) -H(30)	106.7	2.7
N(2) -C(3) -H(31)	107.4	2.8	N(2) -C(20)-H(200)	103.4	3.0
N(2) -C(20)-H(201)	106.3	2.8	N(2) -C(20)-H(202)	107.6	2.7
C(3) -C(4) -H(40)	108.5	3.0	C(3) -C(4) -H(41)	109.7	2.7
C(4) -C(3) -H(30)	115.2	2.5	C(4) -C(3) -H(31)	110.3	2.7
C(4) -C(11)-H(110)	105.3	2.2	C(5) -C(6) -H(60)	123.1	2.4
C(6) -C(5) -H(50)	118.1	2.9	C(6) -C(7) -H(70)	121.4	3.1
C(7) -C(6) -H(60)	116.1	2.5	C(7) -C(8) -H(80)	120.6	2.7
C(8) -C(7) -H(70)	117.9	3.1	C(9) -C(10)-H(100)	111.0	2.2
C(10)-C(1) -H(10)	118.0	2.5	C(10)-C(1) -H(11)	111.0	2.6
C(10)-C(9) -H(90)	104.1	2.41	C(10)-C(11)-H(110)	108.8	2.8
C(11)-C(4) -H(40)	109.6	2.5	C(11)-C(4) -H(41)	107.8	2.7
C(11)-C(16)-H(100)	111.1	2.5	C(12)-C(5) -H(50)	123.1	2.9
C(12)-C(11)-H(110)	108.7	2.4	C(13)-C(8) -H(80)	120.4	2.7
C(13)-C(9) -H(90)	110.8	2.9	C(14)-C(9) -H(90)	104.2	2.7
C(14)-C(15)-H(150)	119.7	2.7	C(14)-C(19)-H(190)	118.5	3.2
C(15)-C(16)-H(160)	119.9	3.2	C(16)-C(15)-H(150)	119.9	2.8
C(16)-C(17)-H(170)	122.1	3.3	C(17)-C(16)-H(160)	120.4	3.3
C(17)-C(18)-H(180)	122.8	2.9	C(18)-C(17)-H(170)	117.7	3.3
C(18)-C(19)-H(190)	121.0	3.2	C(19)-C(18)-H(180)	116.8	2.9
H(10)-C(1) -H(11)	106.8	3.8	H(30)-C(3) -H(31)	108.3	3.8

Table 9.11 (contd.)

H(40)-C(4) -H(41)	108.4	4.1	H(200)-C(20)-H(201)	112.5	4.0
H(200)-C(20)-H(202)	109.9	4.2	H(201)-C(20)-H(202)	116.1	4.1

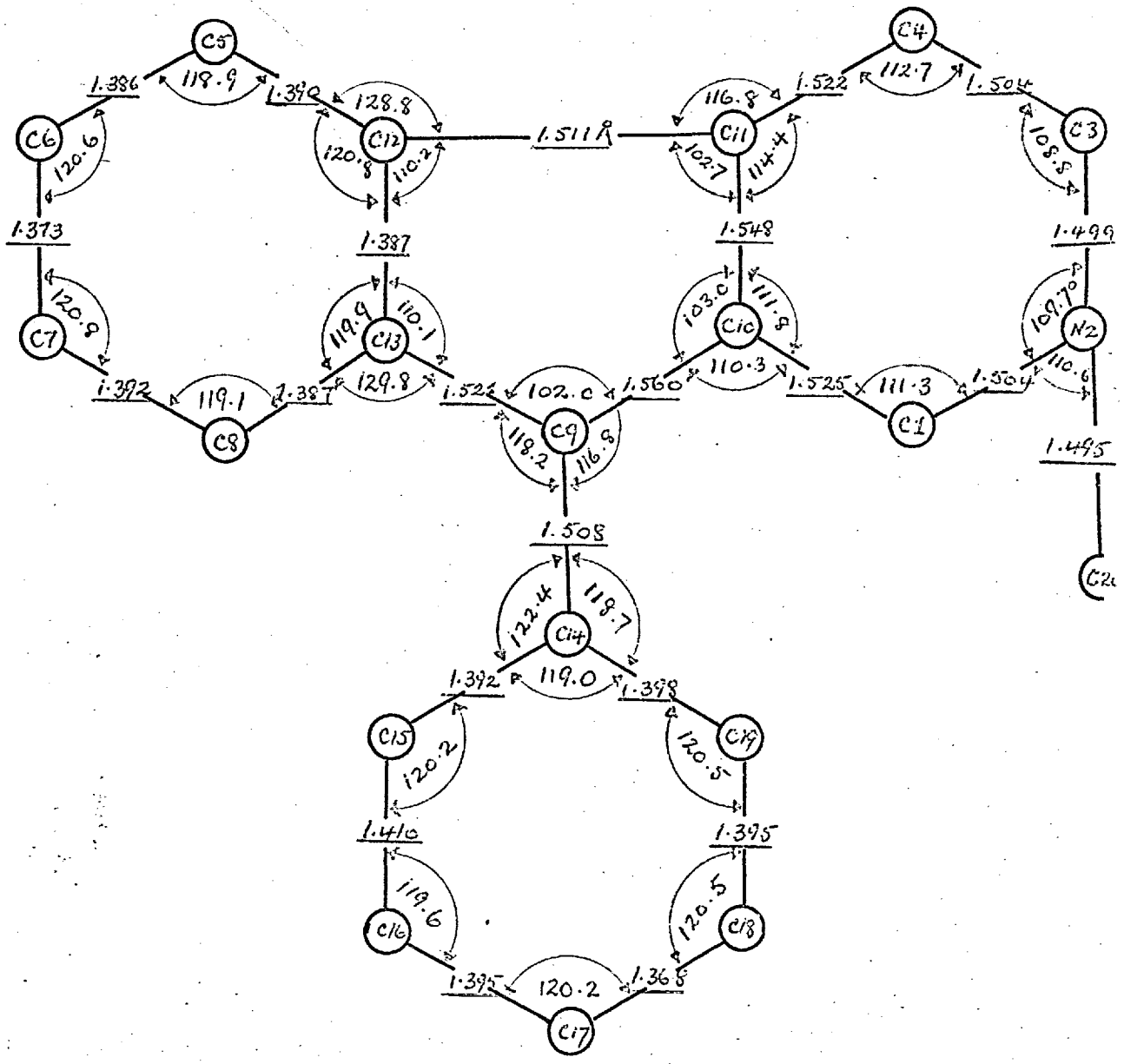


Figure 9.5. Diagramatic representation of bond lengths and valence angles.

$\langle|d|\rangle$-values of 0.021 and 0.024 Å respectively. In both rings the average C-C distances (1.386 Å in the fused ring, 1.393 Å in the phenyl group), and the average C-C-C angles (120.0° in each case), agree well with expected values.

The five-membered ring C(9) → C(13) adopts the envelope conformation[245], frequently found in cyclopentanes*; atoms C(9,11,12,13) are strictly coplanar ($\langle|d|\rangle$ = 0.00068 Å), with C(10) 0.545 Å above the mean plane. This conformation ideally has $\underline{C}_s$ symmetry, and minimum-energy calculations by Pitzer et al[246] and Hendrickson[158,247] have given theoretical optimum values for sp^3-sp^3 torsion angles ($\underline{\omega}$), and valence angles ($\underline{\theta}$). These values are compared with those obtained experimentally in this work in Table 9.12. It can be seen that the ring in this structure deviates surprisingly little from the ideal $\underline{C}_s$-form; the major distortions from the preferred conformation are at $\underline{\omega}_1$, $\underline{\omega}_5$, and at $\underline{\theta}_3$, $\underline{\theta}_4$, due to the fusion of two six-membered rings.

The heterocyclic ring adopts the chair conformation, but is again slightly distorted from the symmetrical minimum-energy form for cyclohexane by the ring fusion, and also by the substitution of nitrogen for carbon at position 2 .

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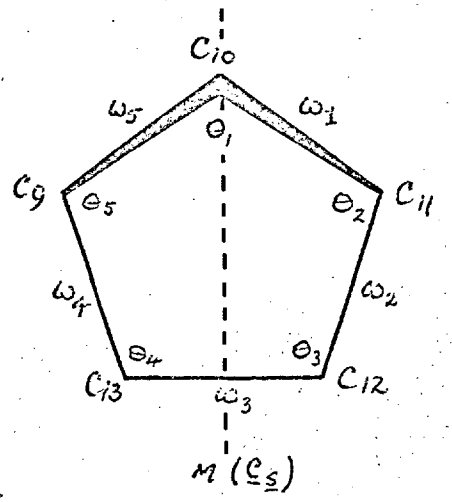
* This ring is not strictly cyclopentanoid, since it contains two atoms, C(12), C(13), common to the benzene ring, which are not true sp^3 hybrids. Nor is it a cyclopentene.

TABLE 9.12.

Comparison of torsion angles (ω) and valence angles (θ) for the five-membered ring in PIPH with values predicted from minimum-energy calculations for the C_s-form of cyclopentane.

Parameter	This work	Pitzer[246]	Hendrickson[158,247]
ω_1	32.82°	46.1°	41.7°
ω_2	-21.02	-28.6	-25.9
ω_3	- 0.16	0.0	0.0
ω_4	21.04	28.6	25.9
ω_5	-32.71	-46.1	-41.7
θ_1	102.99	100.4	101.7
θ_2	102.66	102.4	103.6
θ_3	110.19	105.6	106.0
θ_4	110.13	105.6	106.0
θ_5	101.96	102.4	103.6

The parameters involved are shown below :



Hendrickson[159] predicts all valence angles as 111.6° and all ω-values as 54.4° in cyclohexane. In this work the former vary from 108.75° → 114.38° but average to 111.45°, the latter vary from 41.90° → 65.03° and average to 53.66°.

The high accuracy of the intensity data allowed a complete refinement of all hydrogen atoms (except H(20), the reason for this will be discussed below). The relatively large drop in R-factor and $\sum(|F_o| - |F_c|)^2$ between runs A3 and MR2 can be largely attributed to this factor. The positions obtained are obviously not so well defined as those for C, N, and Br, and have σ-values some 10 times greater than those for the heavier atoms. The successful refinement of the methyl hydrogens, H(200-202), was no doubt due to their proximity to the hydrogens attached to C(1) and C(3), and to some bonding density in the sense N → Br. To minimize the H-H non-bonded repulsions the substituents at N(2) and C(20) have adopted the staggered conformation, as can be seen from the Newman projection[213] (Figure 9.6) down the bond C(20)-N(2). The relevant H-H and C-H non-bonded contacts are also shown.

The C-H bond lengths (Table 9.10(b)) are rather short: the overall average of 0.95 Å is some 0.13 Å less than values obtained spectroscopically, or by electron- and neutron-diffraction studies. This effect has been noted in previous X-ray structure determinations[248] and has been ascribed to

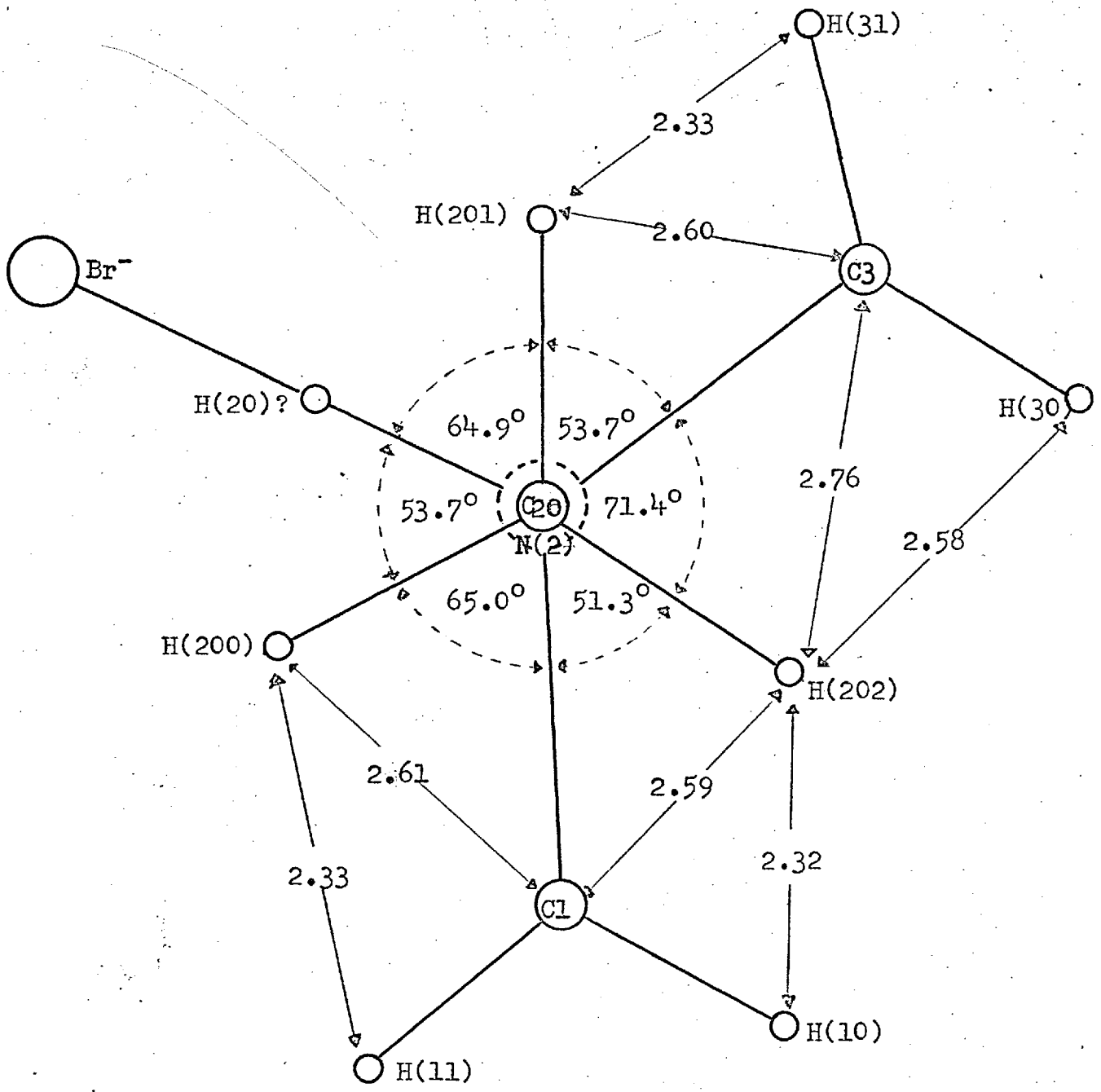


Figure 9.6. PIPH : Newman projection down the bond C(20)→N(2) showing the staggered conformation of the substituents.

'pulling' of the hydrogen K-electron density towards the heavier atom during bond formation. Vainshtein[249] has pointed out that, in a bond A—H, the nuclear position obtained for hydrogen from a difference map represents the centre of gravity of the hydrogen electron density ρ_H, and the bonding density ρ_{AH}; refinement, using scattering factors pertinent to a spherical atom, will simply optimize this position. For such a light atom as hydrogen the resultant foreshortening of r_{AH} is serious; Tomiie[250] has shown that the magnitude of the observed shift in the electron-density maximum (ca. 0.13 Å) is consistent with valence-bond calculations.

In the case of a general bond A—B, where both A and B are of comparable size, and both contain a filled K-shell, the effect is not so serious. However Dawson[251] has predicted a shortening of all terminal bonds, in an X-ray determination, of ca. 0.01 Å, since the distortion of the electron-density about the terminal atom is not counteracted by distortion in other directions, as it would be if the atom were multiply substituted. Nevertheless Coppens and Coulson[252], while agreeing with the general conclusion, have shown that the degree of hybridisation of atoms A and B must be taken into account in certain cases, and predict a slight lengthening in the particular case of an N—O bond in a nitro-group.

Thus, while the C-H distances obtained here are in good agreement with other X-ray results, they do not represent the true inter-nuclear separations. In retrospect it would have been better to have calculated hydrogen positions at a bonding distance of ca. 0.95 Å for the other three structures described in this Thesis; these positions would then have given a better estimate of the electron-density maxima.

The C-H distances shown in the Table have been grouped according to the degree of substitution, and differing hybridisation states, of the carbon atoms. In general the trend of $\langle r_{C-H} \rangle$-values follows that obtained spectroscopically[153] (the comparison can be seen in the Table), but further discussion would be profitless in view of the high σ_r-values obtained in this work. It should be noted that comparison of C-H distances obtained by the X-ray and electron diffraction methods is doubly invalid, since Ibers[253] has estimated that values obtained by the latter method are some 0.03 Å longer than the inter-nuclear distance.

The bond angles involving hydrogen atoms are not significantly different from expected values (see Table 9.11(b)). This is reasonable since, although the r_{C-H}-values are foreshortened, the vector sense of the C-H bond remains unchanged.

In Figure 9.4 it can be seen that a hydrogen bond is postulated between nitrogen and bromine; the valence angles:

$$C(1)\text{-}N(2)\text{-}Br = 110.03^{\circ},$$
$$C(3)\text{-}N(2)\text{-}Br = 109.34^{\circ},$$
$$C(20)\text{-}N(2)\text{-}Br = 105.07^{\circ},$$

show that Br^- is tetrahedrally disposed to N(2), and this supports the proposition. Similar results have been reported for other quaternary amine hydrobromides, and the N-Br distance in the present work (3.124 Å) is somewhat shorter than other values quoted, viz: 3.17 Å in 19-propylthevinol hydrobromide[254] and in strychnine hydrobromide dihydrate[255], 3.26 Å in (+)-hetisine hydrobromide[256], and 3.38 Å in 11-amino-undecanoic acid hydrobromide hexahydrate[257].

The difficulty encountered (p.253) in the refinement of the hydrogen atom of this bond, H(20), is explicable using the type of argument given above. One would expect the K-electron of hydrogen to be more strongly attracted towards N^+, than towards a neutral atom, e.g. carbon. The peak seen in the difference map must have represented the centre of gravity of ρ_H and the electron density due to the lone-pair of nitrogen. The failure to attain convergence using N^+, H°, was almost certainly due to the use of spherically-symmetric scattering factors for these atoms. The relative success obtained by redefining N^+ as N°, and removing H(20), was possibly fortuitous, but probably gave a slightly better estimate of the electron-density distribution about nitrogen. It would have been preferable to employ the aspherical

scattering factors derived by Dawson[258] for quaternary (sp^3) nitrogen, but time did not permit the additional programming and computation involved.

iii) Molecular Overcrowding.

The Dreiding model of the all-cis stereochemistry, made prior to structure solution, showed that the phenyl side-chain must twist about the bond C(9)-C(14) in order to minimize H-H and C-H interactions with the fused indeno-pyridine system. This has been confirmed by the X-ray study (see Figs. 9.4, 9.8): the angle between the mean planes through the phenyl group and the fused ring system being 73°. The closest contacts between the fused ring system and the hydrogens H(150) and H(190), which are bonded to the nearest 'corners' of the phenyl side-chain, are given below :

H(150)-H(10)	2.56 Å	H(190)-H(90)	2.33 Å
H(150)-H(80)	2.63	H(190)-H(100)	3.08
H(150)-C(13)	2.76	H(190)-C(9)	2.62
H(150)-C(9)	2.71		

If we take the van der Waals radii of hydrogen and carbon as 1.2 and 2.0 Å respectively[210], then no distance given above is significantly shorter than the appropriate radial sum. Thus, the position adopted by the phenyl side-chain is completely explicable in terms of the minimization of

non-bonded interactions between the two ring systems.

iv) Molecular Packing.

The molecular packing, projected down the a-axis, is shown in Figure 9.7, in which molecules have been identified by Roman numerals. The 'zig-zag' formation of Br^- ions at any one level in x (e.g. Br_{II}, Br_{III}, Br_{IV}), is important in stabilizing the molecular arrangement. If we take the van der Waals radius of hydrogen as 1.2 Å, and the ionic radius of Br^- as 1.95 Å[210], then their sum (3.15 Å) is comparable with the distances given below :

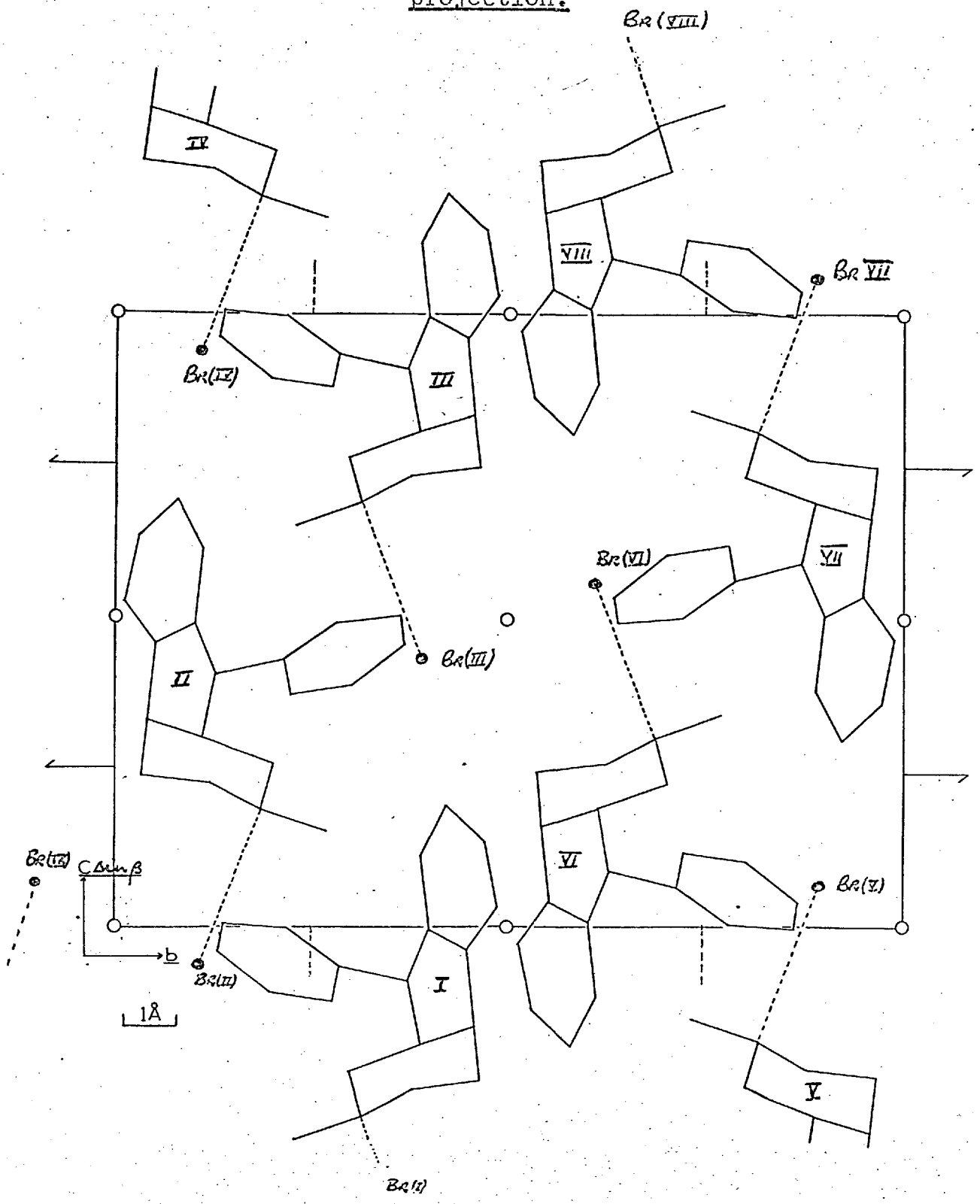
Br_{III}	-	$H(10)_{II}$	2.92 Å
	-	$H(202)_{II}$	2.81
	-	$H(150)_{II}$	3.07
	-	$H(60)_{I}$	3.35
	-	$H(70)_{I}$	3.50
Br_{IX}	-	$H(170)_{I}$	3.07
	-	$H(40)_{IIa}$	3.31
	-	$H(41)_{IIa}$	3.19

N.B. (a) represents the translationally-equivalent molecule to (II) in the cell below, i.e. with co-ordinates : $x_{II}-1$, y_{II}, z_{II}.

The above values, taken together with the strong hydrogen bond (Br_N-$N(2)_N$) in any molecule, shows the effect of Br^- in 'cementing' together the organic moieties.

Additional stability is provided by the close approach of pairs of molecules (e.g. I and VI) across centres of

Figure 9.7. PIPH : The Molecular Packing in a-axis projection.



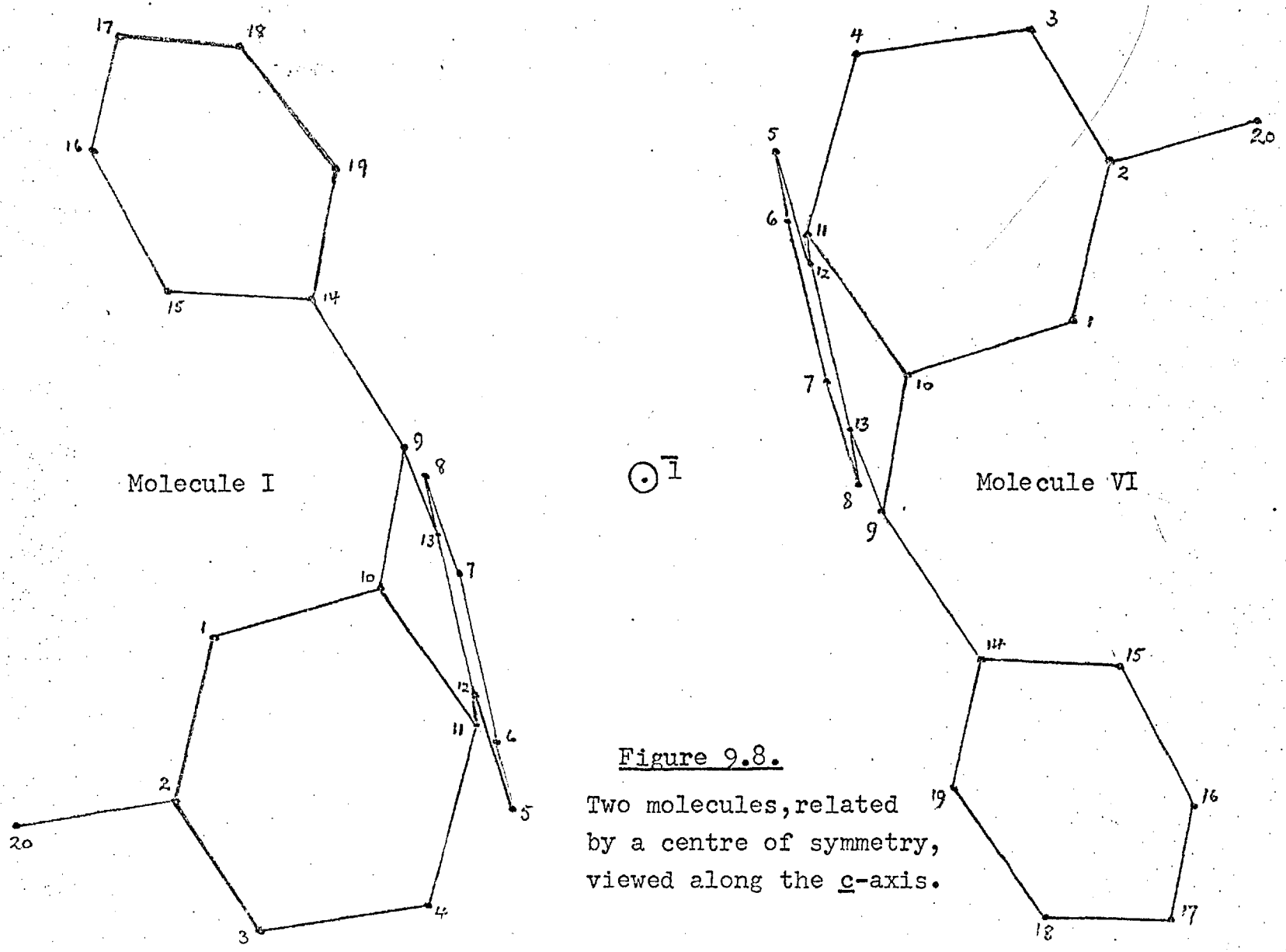


Figure 9.8.

Two molecules, related by a centre of symmetry, viewed along the c-axis.

symmetry. This is shown schematically in Figure 9.8, which shows the arrangement of any two centrosymmetrically related molecules as viewed along c. The planes of the two indene portions are parallel, and the closest C-C contacts are :

$C(9)_{VI}$ - $C(5)_I$	3.773 Å	$C(9)_{VI}$ - $C(8)_I$	3.821 Å
- $C(6)_I$	3.854	- $C(12)_I$	3.715
- $C(7)_I$	3.874	- $C(13)_I$	3.742

The three cis protons of molecule I, i.e. $H(90, 100, 110)_I$, protrude into this gap opposite the fused benzene ring of molecule VI. The closest contact is then between $H(110)_I$ and $H(80)_{VI}$ at 2.62 Å, a distance only slightly greater than twice the van der Waals radius of hydrogen (2.4 Å). Since all contacts occur twice, i.e. $C(5)_I$-$C(9)_{VI}$ = $C(9)_I$-$C(5)_{VI}$, the stability introduced by this interaction is high.

v) Conclusion.

It only remains to report that PIPH was found to be very active as an antagonist of tetrabenazine-induced sedation in rats[259], but its high toxicity (common to all four compounds) precluded its use as a clinical anti-depressant. A suggestion that it be marketed as an exceptionally humane rodent exterminator (happy-rat?) was not well received.

APPENDIX I.

Reference Lists of Organic Structures whose Absolute Configurations have been determined by X-ray Methods.

Reprinted from Chemical Communications 1966, 838; 1968, 308.

APPENDIX II

The Uses of a Connectivity or Bonding Array in Molecular Geometry Calculations.

II.1 Introduction.

The calculation of the various geometrical characteristics of a molecule or crystal structure is lengthy, but mathematically trivial. Computer programs for this task require either the calculation of all possible interatomic distances less than a specified limit[260], a process easy to use but wasteful of computer time (and requiring the user to sift a large volume of output), or the calculation of specified distances, a process wasteful of the user's time and prone to mistakes and omissions. The process to be described here is a compromise, ensuring an exhaustive search over one asymmetric unit (or indeed any portion of the total structure specified by the user). Needless calculations are avoided, and input and output are cut to a minimum.

The process was devised originally for the computation of dihedral angles, but is ideally suited for the quick and efficient checking of bond lengths and valence angles during structure refinement. It utilizes a connectivity or bonding array, an extension of an idea suggested by Mooers[261], and developed by other workers[262] as an important topographical tool. In particular the array in its present form (see Sect. II.2 below) has been employed by Penny[263] in the recognition of certain ring systems in larger chemical units by a computer procedure. The work described below, however, represents the first use of such an array for a purely scientific purpose. Some ideas on the link-up of this work with the topographical studies are set out in Sect. II.6.

The basic theory developed is described in Sections II.2,3,4. The actual program, MOJO, lags a little behind the theory (since both are 'living' entities), and incorporates some adaptations; it will be described in Sect. II.5.

II.2. The Connectivity or Bonding Array.

The fractional co-ordinates, $\underline{x}$, $\underline{y}$, $\underline{z}$, and possibly their standard deviations, $\underline{\sigma}_{\underline{x}}$, $\underline{\sigma}_{\underline{y}}$, $\underline{\sigma}_{\underline{z}}$, for the N atoms in an asymmetric unit are input to the computer, together with an alphanumeric atom identifier (e.g. C24). They may then be referred to by this identifier, or, more simply, by their position (1 ⟶ N) in the input list. An N x N square is

is then cleared to zero in computer store, and the connectivity or bonding information is read in. This requires N lines of input, one for each atom treated, each a string of digits of the form :

$$i \quad j_1 \quad j_2 \quad j_3 \quad j_4 \quad * \quad \ldots\ldots\ldots\ldots \quad \text{II.1}$$

indicating that the atom numbered i in the input list is bonded to those numbered j_1, j_2, j_3, j_4; any convenient non-numeric character may be used to terminate each line.

To set up the array (B), the cells $j_{1,2,3,4}$ on the i'th row have unity added into them; the resultant array should be symmetric (i.e. elements b_{ij} should match b_{ji}), and all cells should contain zero or unity only. Before proceeding these two requirements should be checked : a non-symmetric array indicates incorrect, or incomplete input of bonding information, while entries >1 indicate unwanted duplicates (this is the reason for adding unity to the cells rather than just setting them to 1). Other checks may also be added if required, e.g. the number of entries per row or column for carbon atoms should be $\leqslant 4$. An array (B) made up of single-bit locations is compact, but it is then unsafe to add unity to denote each bond, since duplication would cause errors.

Figure II.1(a) shows the structure of humulene bromohydrin (Chapter 7); both the chemical numbering and atomic designations are given, together with their possible reference numbers in an input positions list. Input of bonding

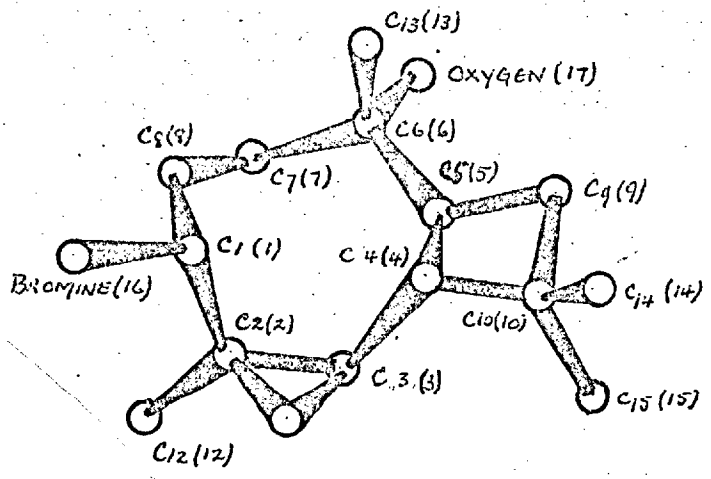


Figure II.1 (a) The structure of humulene bromohydrin, showing the chemical numbering, and the possible reference numbers of the atoms in an input positions list are given in brackets.

i	j_1	j_2	j_3	j_4	
1	2	8	16	*	
2	1	3	12	11	*
3	2	11	4	*	
4	3	5	10	*	
5	4	6	9	*	
6	5	7	13	17	*
7	6	8	*		
8	7	1	*		
9	5	10	*		
10	4	9	14	15	*
11	2	3	*		
12	2	*			
13	6	*			
14	10	*			
15	10	*			
16	1	*			
17	6	*			

Figure II.1(b). Input of bonding information: each atom (i) is bonded to atoms j_1, j_2, j_3, etc.

	values of i, k.		values of j, l.																
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
C(1)		1		1						1								1	
C(2)		2	1		1								1	1					
C(3)		3		1		1							1						
C(4)		4			1		1					1							
C(5)		5				1		1			1								
C(6)		6					1		1						1				1
C(7)		7						1		1									
C(8)		8	1						1										
C(9)		9					1					1							
C(10)		10				1					1					1	1		
C(11)		11		1	1														
C(12)		12		1															
C(13)		13						1											
C(14)		14										1							
C(15)		15										1							
Br		16	1																
O		17						1											

Figure II.1 (c). The bonding array (B) (heavily outlined) for humulene bromohydrin. Both reference numbers and atomic designations are given for clarity.

information is shown in Figure II.1(b), in the form of statements similar to Eq^{n}. II.1 above. Part (c) of the Figure shows the resultant array (B), in which both types of atomic designation are given for clarity.

II.3. The Systematic Calculation of Bond Lengths, Valence Angles, and Direction Cosines.

The position of the i'th atom is defined by the vector :

$$\vec{r}_i = \underline{x}_i\vec{a} + \underline{y}_i\vec{b} + \underline{z}_i\vec{c} \quad \ldots\ldots\ldots\ldots \text{II.2},$$

where $\vec{a}$, $\vec{b}$, $\vec{c}$, are the unit-cell vectors. The vector $\vec{r}_{ij}$ between two atoms is simply the difference between two vectors, $\vec{r}_i$, $\vec{r}_j$, of type II.2 :

$$\vec{r}_{ij} = \Delta\underline{x}_{ij}\vec{a} + \Delta\underline{y}_{ij}\vec{b} + \Delta\underline{z}_{ij}\vec{c} \quad \ldots\ldots\ldots \text{II.3},$$

where Δx_{ij} equals $\underline{x}_i - \underline{x}_j$, with similar expressions for $\underline{y}$ & $\underline{z}$. The square of the magnitude of the bond length $|r_{ij}|$ is given by the scalar product of Eq. II.3 with itself :

$$|r_{ij}|^2 = \vec{r}_{ij}\cdot\vec{r}_{ij} = \underline{x}_{ij}^2\underline{a}^2 + \underline{y}_{ij}^2\underline{b}^2 + \underline{z}_{ij}^2\underline{c}^2 + 2\underline{a}\underline{b}\,\underline{x}_{ij}\,\underline{y}_{ij} + 2\underline{b}\underline{c}\,\underline{y}_{ij}\,\underline{z}_{ij} + 2\underline{a}\underline{c}\,\underline{x}_{ij}\,\underline{z}_{ij} \quad \ldots\ldots \text{II.4}.$$

The direction cosines of the bond, l_{ij}, m_{ij}, n_{ij}, referred to axes a, b, c, are given by :

$$(l, m, n)_{ij} = \frac{(\underline{a}\Delta\underline{x},\ \underline{b}\Delta\underline{y},\ \underline{c}\Delta\underline{z})_{ij}}{|r_{ij}|} \quad \ldots\ldots\ldots \text{II.5}.$$

An ordered and complete sequence of bond lengths and direction cosines can be obtained by working systematically through the bonding array, reading along each row (i) and using equations II.4, II.5, for each cell (j) containing unity. Only the upper right triangular half of the array need be scanned for this purpose: use of the whole array produces each bonded distance twice over. The bond lengths and direction cosines are output, and also stored in similar triangular arrays (R, L, M, N); it should be noted that the full arrays L, M, N, are anti-symmetric (i.e. $m_{ij} = -m_{ji}$); due allowance must be made for this sign reversal when using these half arrays to read the direction cosines of bonds in the lower triangular half (i.e. for vector r_{ji}).

Valence angles, $\underline{\theta}_{ijk}$, are calculated from :

$$\cos\underline{\theta}_{ijk} = \frac{\vec{r}_{ij} \cdot \vec{r}_{jk}}{|r_{ij}|\ |r_{jk}|} \quad \ldots\ldots\ldots\ldots \text{II.6.}$$

All angles occurring at atom (j) can be evaluated together by reading down column (j) to locate the first entry (i), and then reading on down the column to identify the possible values of (k). $\cos\underline{\theta}_{ijk}$ is computed and output for each indicated combination of ijk. The next (i) is selected by moving down the column, and is combined with all (k's) indicated <u>lower down</u> the same column, thus avoiding duplicates $\underline{\theta}_{jki}$. The process is repeated until all permitted combinations (ik) are exhausted for atom (j), scanning is then

transferred to the next column, j + 1. In every case $\cos\underline{\theta}_{ijk}$ is stored, together with the integers i,j,k, for use in the calculation of dihedral angles.

II.4. The Systematic Calculation of Dihedral (Torsion) Angles.

An attempt will first be made to define and generalize the nomenclature for dihedral, or torsion, angles. Reference to Figure II.2(a) shows two groups of atoms, ABC bonded to D, and FGH bonded to E, which is below the plane of the paper. The Newman projection[213] down the bond D→E is shown in Figure II.2(b).

The dihedral or torsion angle ($\underline{\omega}$) is the angle between say, the projections of CD and EF on a plane perpendicular to the bond DE. Thus we may define the angle as :

$$\omega_{\underline{C}(\underline{D},E)F} = x^{o} \quad \ldots\ldots\ldots\ldots\ldots\ldots \text{II.7.}$$

Other more general dihedral angles, of use in certain contexts can be described analogously. Thus the angle between the projections of AD and CD on the plane perpendicular to DE may be written :

$$\omega_{\underline{A}(\underline{D},E)\underline{C}} = x^{o} \quad \ldots\ldots\ldots\ldots\ldots\ldots \text{II.8.}$$

Similarly the angle between proj(GE), proj(EF), as seen from viewing point D is :

$$\omega_{G(\underline{D},E)F} = x^{o} \quad \ldots\ldots\ldots\ldots\ldots\ldots \text{II.9.}$$

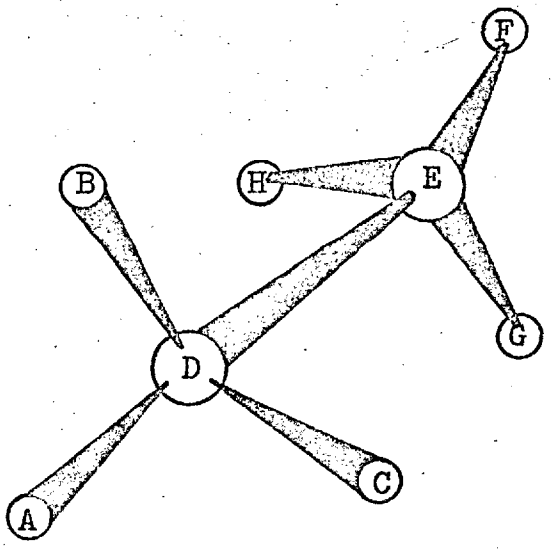


Figure II.2(a)

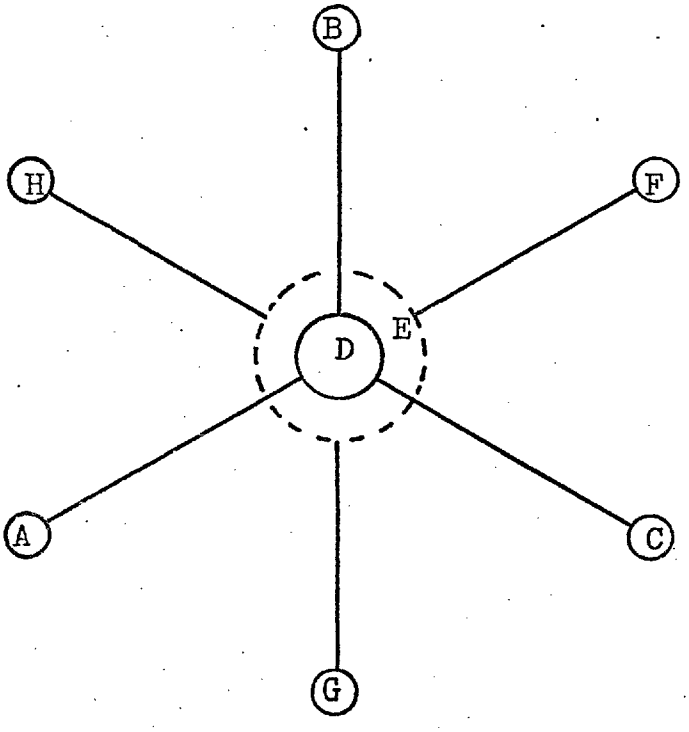


Figure II.2(b)

The atoms in brackets indicate the direction of view down the bond, i.e. from D to E; atoms which are doubly underlined in the above equations should be printed in Clarendon type, they represent atoms of the nearer group in the viewing direction. For ordinary dihedral angles, representing twist or torsion about the bond DE (Eq. II.7) the first quoted atom is a member of the nearer group, and the last of the farther group. For the more general dihedral angles they are both of the nearer group (Eq. II.8), or both of the farther group (Eq. II.9). Furthermore it is often imperative to distinguish between sp^3-sp^3, sp^3-sp^2, and sp^2-sp^2 torsion angles in an organic structure (see Sect. 8.5), where the hybridisation states referred to are those of atoms D and E respectively. This was effected in Section 8.5 by reserving the symbol ($\underline{\omega}$) for the first mentioned, and referring to the other two as ($\underline{\delta}$) and ($\underline{\gamma}$) respectively. General adoption of this type of nomenclature saves the reader from continually referring to the structural formula.

In all cases the sense of rotation is defined in terms of the movement required to rotate the first mentioned bond (CD in Eq. II.7, AD in 8, GE in 9) to overlie the projection of the second bond (EF, DC, EF, respectively). Clockwise rotation of the first-quoted bond is taken as positive, anticlockwise rotation is taken as negative. Thus, with reference to Figure II.2(b), we may write :

$$\omega_{A(D,E)H} = +60^{\circ} \quad \ldots\ldots\ldots\ldots \text{II.7(a)}$$

$$\omega_{A(D,E)G} = -60^{\circ} \quad \ldots\ldots\ldots\ldots \text{II.7(b)}$$

$$\omega_{A(D,E)B} = +120^{\circ} \quad \ldots\ldots\ldots\ldots \text{II.8(a)}$$

$$\omega_{G(D,E)F} = -120^{\circ} \quad \ldots\ldots\ldots\ldots \text{II.9(a)}$$

Figure II.3(a) shows the relationship between the three bond vectors involved, i.e. $\vec{r}_1$, $\vec{r}_2$, $\vec{r}_3$, represent bonds CD, DE, EF, in Eq. II.7, or AD, DE, DC, in 8, or GE, DE, EF, in 9. Figure II.3(b) shows the vectors in relation to a spherical triangle[264, 265], whence we may write :

$$\cos(\omega) = \frac{\cos(\hat{r_1 r_3}) - \cos(\hat{r_1 r_2})\cos(\hat{r_2 r_3})}{\sin(\hat{r_1 r_2})\sin(\hat{r_2 r_3})} \quad \ldots \text{II.10,}$$

where : $\hat{r_1 r_2}$ and $\hat{r_2 r_3}$ are the valence angles :

θ_{CDE} and θ_{DEF} in Eq. II.7,

θ_{ADE} and θ_{CDE} in Eq. II.8,

and θ_{GED} and θ_{FED} in Eq. II.9.

and : $\hat{r_1 r_3}$ is the angle between r_1, r_3 in each case.

The angles $\omega_{i(j,k)l}$ can be evaluated, and systematicall output in a convenient order, using the bonding array as follows. For a given viewing bond DE, identified by unity in cell b_{jk}, look backward and forward along row (k) to identify possible (l's), and up and down column (j) to identify possible (i's). Equation II.10 is then evaluated for all combinations of :

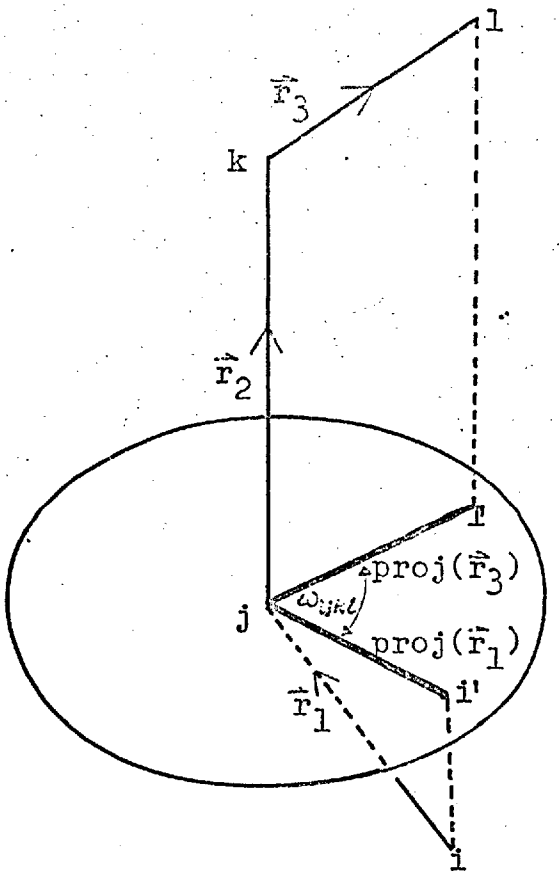


Figure II.3(a) Definition of the dihedral angle ω_{ijkl} where (ijkl) are (for example) ADEF in Eq. II.7.

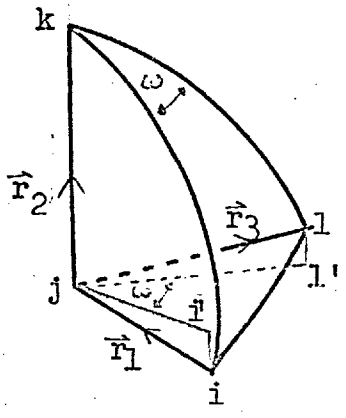


Figure II.3(b) The vectors in relation to a spherical triangle. The angle ω_{ijkl} (=angle $\widehat{i'\,j\,l'}$) is the angle $\widehat{ikl}$ of the triangle i.e. the angle between the planes ijk, ljk; the 'sides' of the triangle are the valence angles $(\widehat{r_1 r_2})$, $(\widehat{r_2 r_3})$, and the angle $(\widehat{r_1 r_3})$, whence Eq. II.10 can be derived from the cosine formulae for spherical triangles.

(i) i, l ($i \neq l$) cf. Eq. II.7,

(ii) i, i' ($i \neq i'$) cf. Eq. II.8,

(iii) l, l' ($l \neq l'$) cf. Eq. II.9,

for any given combination of jk. This process is repeated systematically for all bonds (jk) specified in the upper right triangular half of array (B), this avoids duplication since ω_{ijkl} is equivalent to ω_{lkji} in both magnitude and sign. The sines and cosines of $\hat{r_1 r_2}$, $\hat{r_2 r_3}$, required by Eq. II.10, can be obtained from the previously stored valence angles. $\cos(\hat{r_1 r_3})$ can be obtained using :

$$\cos(\hat{r_1 r_3}) = \cos(\hat{\vec{r}_{ij}\vec{r}_{kl}}) = \frac{\vec{r}_{ij} \cdot \vec{r}_{kl}}{|r_{ij}||r_{kl}|} \quad \ldots\ldots\ldots \text{II.1}$$

The sign of the rotation is given by the sign of the determinant V :

$$V = \begin{vmatrix} l_{ij} & m_{ij} & n_{ij} \\ l_{jk} & m_{jk} & n_{jk} \\ l_{kl} & m_{kl} & n_{kl} \end{vmatrix} \quad \ldots\ldots\ldots\ldots\ldots\ldots \text{II.12,}$$

which gives the volume of the parallelopipedon defined by the vectors $\vec{r}_1$, $\vec{r}_2$, $\vec{r}_3$.

II.5. The Program MOJO.

The theory developed above is given in its most general mathematical form. In the program MOJO, written in 1967 EXCHLF for the University of London ATLAS computer, several adaptations have been made. A brief description of these, and also the input and output, together with a flow chart, forms the subject matter of this section.

Although vector methods afford both mathematical simplicity and generality, the use of orthogonalized Ångstrom coordinates, while being just as general, reduces the geometrical manipulation to simple Cartesian terms. Furthermore they are useful in the preparation of crystal drawings. If we take a perfectly general triclinic lattice, with cell parameters a, b, c, α, β, γ, then we may define three orthogonal unit vectors I, J, K, such that :

I is parallel to a,

J is perpendicular to the a-c plane,

K is perpendicular to a in the a-c plane,

whence, by using spherical triangles[264,265], we may express the lengths of the orthogonal axes as :

$$\begin{aligned} A &= a\mathbf{I} \\ B &= b\cos\gamma\mathbf{I} + b\sin\gamma\mathbf{J} \qquad \text{..... II.13} \\ C &= c\cos\beta\mathbf{I} - c\sin\beta\cos\alpha^{*}\mathbf{J} + c\sin\beta\sin\alpha^{*}\mathbf{K} \end{aligned}$$

or, in matrix notation :

$$(A) = (\beta)(I) \qquad \text{..... II.14,}$$

where the orthogonalization matrix (β) obviously has the form:

$$(\beta) = \begin{pmatrix} \underline{a} & 0 & 0 \\ \underline{b}\cos\gamma & \underline{b}\sin\gamma & 0 \\ \underline{c}\cos\beta & -\underline{c}\sin\beta\cos\alpha^{*} & \underline{c}\sin\beta\sin\alpha^{*} \end{pmatrix} \quad \ldots\ldots\ldots \text{II.15}$$

The determinant of this matrix gives the cell volume (V). The matrix is quite general, and its complexity is obviously reduced for systems of higher symmetry than triclinic.

If the fractional co-ordinates of the atoms in the real cell ($\underline{x}$, $\underline{y}$, $\underline{z}$) are provided, then the orthogonal Ångstrom co-ordinates ($\underline{X}$, $\underline{Y}$, $\underline{Z}$) are given by an expression similar to Eq. II.14, viz :

$$(X) = (\beta)(x) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \text{II.16}$$

We may now rewrite Eqs. II.4,5,6, in terms of $\underline{X}$, $\underline{Y}$, $\underline{Z}$, as follows[266]:

$$R_{ij}^2 = \Delta X_{ij}^2 + \Delta Y_{ij}^2 + \Delta Z_{ij}^2 \quad \ldots\ldots\ldots\ldots \text{II.17}$$

$$(L, M, N)_{ij} = \frac{(\Delta X, \Delta Y, \Delta Z)_{ij}}{|R_{ij}|} \quad \ldots\ldots\ldots\ldots \text{II.18}$$

$$\cos\underline{\theta}_{ijk} = L_{ij}L_{jk} + M_{ij}M_{jk} + N_{ij}N_{jk} \quad \ldots\ldots\ldots \text{II.19}$$

Thus, as can be seen from Figure II.4, the initial operation in MOJO is to read in the cell data, set up the (β)-matrix, and compute (and output) the orthogonal co-ordinates from the input positions list. The bonding information is read in (see Fig. II.1(b)) and the array (B) set up and checked.

The present program does not, at present, incorporate standard deviation formulae; nor does it obtain the valence angles and dihedral angles from the array (B) in quite the same manner as described above. Referring again to Figure II.1(c), the former are obtained by reading across the rows (i) and finding possible values for (j), as in the bond-length calculation; values of (k) are then found by reading down column (j) to avoid duplication. The dihedral angles are found by an extension of this method : once the value of (j) has been found the (k) values are obtained by scanning column (j) completely, but omitting the value k = j; the k'th row is then similarly scanned for values of (l), but omitting l = k. This early method has two drawbacks :

i) All dihedral angles are produced twice over, i.e both ω_{ijkl} and ω_{lkji} are obtained;

ii) The more general dihedral angles, exemplified by Eqs. II.8, II.9, are not obtained.

It is hoped to incorporate the newer theory described in Sections II.3, II.4, in the near future.

Other routines have also been included in the program, using the initial orthogonalized co-ordinate list :

i) Cyclobutane ring analysis : the positions of the four ring atoms in the input positions list are specified (N_{1-4}). The routine then evaluates criteria (c) and (d) of Figure 7.5 (p. 165).

ii) Specified (single) bond lengths, valence angles, or

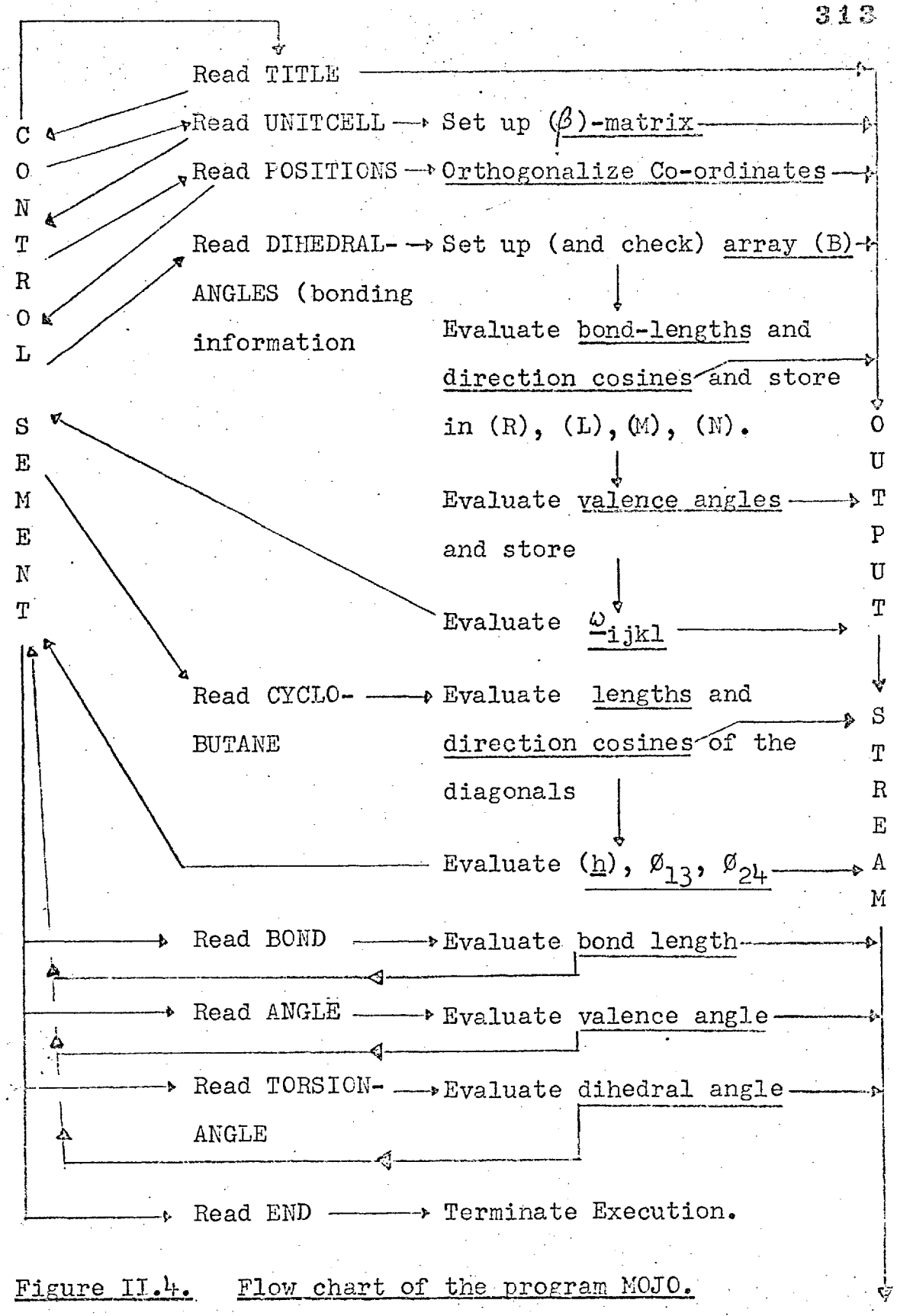


Figure II.4. Flow chart of the program MOJO.

dihedral angles, may be computed by specifying two, three, or four values of N.

All the data required in a particular run are input under one word directives (as in all ATSYS programs); those used here are :

TITLE : followed by one line of information to be output;

UNITCELL : followed by a, b, c, α, β, γ;

POSITIONS : followed by N lines of information of the form:

CA23 x y z

where N is the total number of atoms input, the list is terminated with an asterisk.

DIHEDRALANGLES : followed by a number (n) (which must be $\leq$N) and (n) lines of information similar to Figure II.1(b). This directive turns on the bonding array calculations.

CYCLOBUTANE : followed by four numbers as described above.

Specific functions are requested under the self-explanatory directives : BOND, ANGLE, TORSIONANGLE. A flow chart is given as Figure II.4.

II.6. Further uses of Bonding Array Theory.

The use of the above program, incorporated as a routine in both least-squares and general molecular geometry programs, has possibilities. In the former it would provide a quick and systematic check on the chemical sensibility of the structure being refined, and could be called in automatically at the end of each run. In the latter it would provide an

ordered output listing, for one asymmetric unit, of bond-length and valence angles; a similar ordered list of intra-molecular non-bonded distances can be obtained by reading across rows (i) and avoiding all cells (j) which contain unity, again only the upper right triangular half of (B) need be used.

On a more philosophical plane, the bonding array would appear to have important uses in the field of information storage and retrieval, as applied to crystallographic structural data. At present the information listed under any one compound is limited to the name(s) of author(s) and the literature reference. Inclusion of a list of orthogonalized co-ordinates, and the bonding information, would permit a search program, incorporating the bonding array routine, to provide a complete listing of the basic molecular geometry, in addition to the literature reference, for a specified compound. Far more extensive information could be output by the search program if the bonding array was used to recognize particular ring systems within a larger chemical unit. Thus if a naphthalene nucleus or a cyclobutane ring were found they could be checked for planarity; for larger saturated carbocycles it should be possible to actually define the conformation adopted from the geometry obtained.

This is, however, not the correct place to expand these ideas further. Nevertheless, with the present explosion in

the quantity of structural information appearing in the literature, largely due to the ever increasing use of automatic diffractometers, a satisfactory means of storage and retrieval is of importance to the crystallographer. It is the author's opinion that a computer procedure very similar to the bonding array will provide the ultimate answer, for organic molecules at any rate. The time when one may tell a computer to provide structural data and references for, say, all eight membered carbocycles having the boat-chair conformation, may not be far off. The task of the would-be reference-hunter and/or Thesis-writer will then be considerably less burdensome!

APPENDIX III.

Minimum-Energy Calculations.

Since the work of Pitzer et. al.[267] on ethane, many workers have attempted to predict preferred conformations on the basis of detailed energy calculations. While this is not the place for a full review of the various methods employed, and the results obtained, it is pertinent to give a brief description of the approach for small- and medium-ring saturated carbocycles, since numerous comparisons have been made in this Thesis between parameters obtained crystallographically, and those obtained from minimum-energy calculations. In general the results obtained by various groups of workers are very similar; however since the work of Hendrickson[158,159,247] was chosen for comparison with the X-ray data, mainly due to the completeness of his studies, ranging from simple alkanes to cyclodecanes, his papers have largely been used in the compilation of this Appendix.

A particular n-membered ring conformation may be defined by the (n) values of the C-C-C valence angles (θ), and the (n) sp^3-sp^3 torsion angles (ω). The assumption is made that bond lengths remain invariant, since the energy required to distort a bond from its optimum length is very much more severe than the strain energies mentioned below. A reduction in the number of parameters is effected by the assumption of only symmetrical forms (except in the case of the cyclopentanes[247]); this is reasonable since the calculations of Wiberg[171], which proceed through unsymmetrical forms, result in symmetrical minima only. The strain-energy content of a particular conformation may be subdivided into :

i) Bond angle bending strain ($\underline{E_\theta}$) which is the energy associated with the distortion of a single bond-angle from the optimum. The function used, derived from spectroscopic results, gives :

$$\underline{E_\theta} = K_\theta(\theta - \theta_o)^2 \quad \ldots\ldots\ldots \text{III.1}$$

where, initially[247], the value of θ_o was taken as the tetrahedral value (109.28°). More recent hybridisation studies have shown that θ_o at a methylene carbon is more nearly 112°, and this value was used in later work[159]. the value of K_θ used with the new value of θ_o was 0.0230 kcal $mole^{-1}$.

ii) Torsional Strain ($\underline{E}_\omega$), the function used to calculate the strain-energy, due to twist of substituents about a single bond, has the form :

$$\underline{E}_\omega = \tfrac{1}{2}K_\omega(1 + \cos 3\omega) \quad \ldots\ldots\ldots \text{III.2}$$

in which K_ω is the height of the potential barrier to rotation in ethylene (i.e. the energy difference between staggered and eclipsed conformations). Hendrickson[159] has pointed out that, since non-bonded interactions make up a small, but real, portion of this barrier, K_ω should be less than the quoted value of 2.8 kcal mole^{-1}, and he has derived a value of 2.65 kcal mole^{-1} to exclude the van der Waals forces. Although the general form of the above expression is not well founded theoretically, considerable success has attended its use (see the work of Garbisch[216], who used a similar expression to estimate sp^3-sp^2 torsional strain).

iii) Energy due to non-bonded interactions. Any pair of non-bonded atoms, at inter-nuclear distance (r), possesses a mutual interaction, which is partially repulsive and partially attractive. The form of the expression for E_{NB} is one of the most problematical in this work, it has the general form :

$$\underline{E}_{NB} = Be^{-\mu r} - A/r^6 \quad \ldots\ldots\ldots \text{III.3}$$

and while values of the attractive constant (A) are known the constants B and μ are difficult to evaluate experimentally

Hendrickson has chosen to make them parameters in the minimization procedure (see below) for both H-H and C-C interactions, the geometric mean of the values obtained was used to estimate the C-H interactions.

The energy minimization is carried out by computer : from a given starting conformation each independent angular parameter, plus B and μ, is varied by 1° in turn, and values of $\underline{E}_{\theta}$, $\underline{E}_{\omega}$, and $\underline{E}_{NB}$ (taken over all atoms in the ring), are computed to give the total strain energy $\underline{E}_{T}$. A checking routine is included to ensure that the angles used in each calculation give a closed ring, since this was not the case with some of the cyclopentanes[247].

The comparisons carried out by Hendrickson, using data from X-ray and electron-diffraction work, and from other sources, show that, despite the problematical nature of some of the functions used, the geometrical parameters obtained are in good agreement with experimentally determined values.

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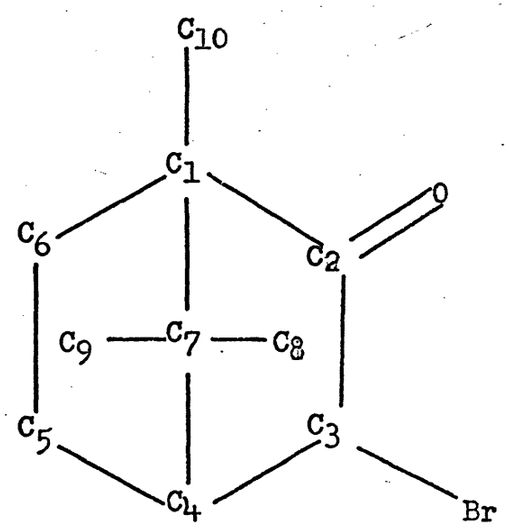
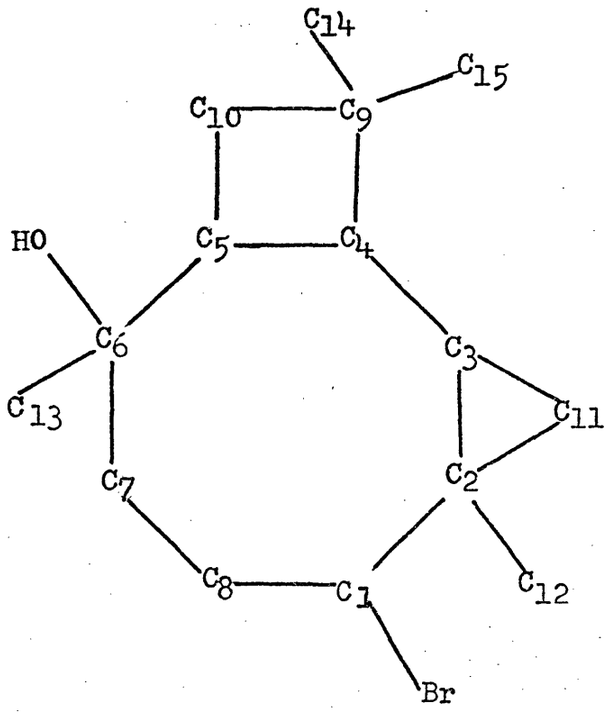
265. J. Blakey, University Mathematics, Blackie, 1966, p.508.

266. Ref. 19, Vol II, p52 et seq.

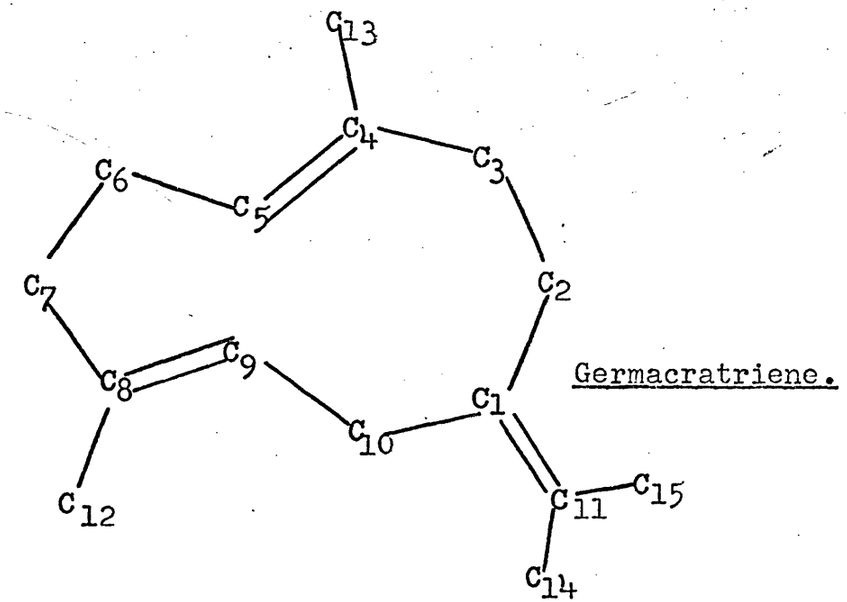
267. J. D. Kemp and K. S. Pitzer, J. Chem Phys., 1936, 4, 749.



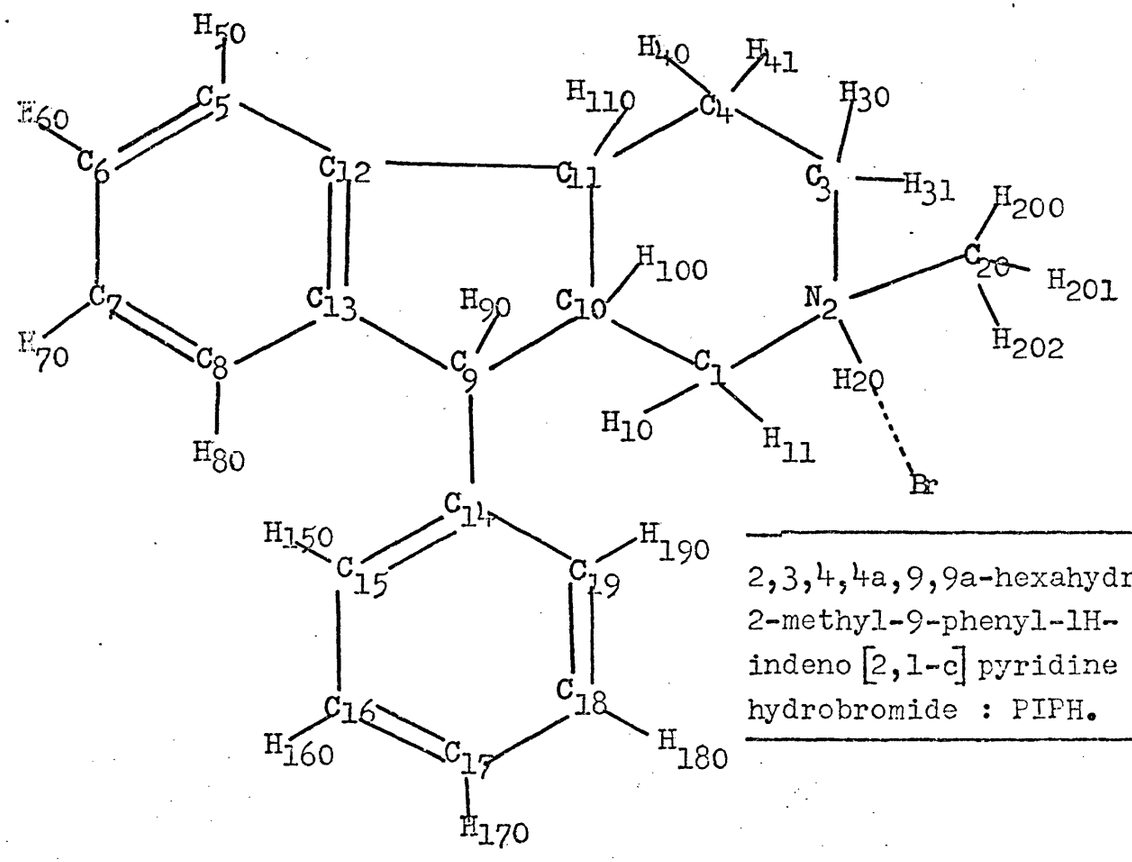
(+)-3-bromocamphor.



Humulene Bromohydrin.



Germacratriene.



2,3,4,4a,9,9a-hexahydro-2-methyl-9-phenyl-1H-indeno [2,1-c] pyridine hydrobromide : PIPH.

A Reference List of Organic Structures whose Absolute Configurations have been determined by *X*-Ray Fluorescence

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A Reference List of Organic Structures whose Absolute Configurations have been determined by *X*-Ray Fluorescence

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DETERMINATIONS of absolute configurations by Bijvoet's *X*-ray fluorescence technique[1] are now appearing frequently in the press, but in rather scattered journals. Most are for organic substances, so the following list has been compiled, and groups them under five headings for the convenience of organic chemists. There are 54 entries, more than half of which have appeared in the last three years. They are confined to determinations based on *X*-ray fluorescence, the fluorescing atom and the radiation being quoted. The list is believed to be comprehensive up to the end of 1965, but we would be grateful if users or crystallographers would advise us of errors or omissions. If the list is found useful we propose to issue supplements and corrigenda, and an attempt will be made in later lists to include assignments involving internal comparisons with reference centres[2,3] if the latter are quite reliable.

It is gratifying to note that more and more authors are determining the absolute configuration whenever possible, but attention is drawn in an accompanying Communication[4] to the possibility of resurrecting old structure determinations from the literature and getting their absolute configurations with comparatively little effort. We hope the list will indicate to crystallographers areas where reference compounds are still needed.

(1) Simple Molecules and Amino-Acids.

Compound	*Fluorescent atom*	*Radiation used*	*Reference*
L-Aspartic acid as cobaltous salt	Co	Cu	T. Doyne, R. Pepinsky, and T. Watanabe, *Acta Cryst.*, 1957, **10**, 438.
D-(+)-Barium uridine-5′-phosphate	Ba and P	Cu	E. Shefter and K. N. Trueblood, *Acta Cryst.*, 1965, **18**, 1067.
Biotin as bis-*p*-bromoanilide of CO_2-biotin	Br	Cu	J. Trotter and J. A. Hamilton, *Biochemistry*, 1966, **5**, 713.
Hirsutic acid as *p*-bromophenacyl ester	Br	Cu	F. W. Comer and J. Trotter, *J. Chem. Soc.* (*B*), 1966, 11.
D-Isocitric acid as (1) Rb salt (2) K salt	Rb K	Mo Cr, Cu	A. L. Patterson, C. K. Johnson, D. Van der Helm, and J. A. Minkin, *J. Amer. Chem. Soc.*, 1962, **84**, 309.
D-(−)-Isoleucine as hydrated hydrobromide	Br	Cu	J. Trommel and J. M. Bijvoet, *Acta Cryst.*, 1954, **7**, 703.
L-Lysine as hydrochloride dihydrate	Cl	Cu	S. Raman, *Z. Krist.*, 1959, **111**, 301.
D-Methadone as hydrobromide	Br	Cu	A. W. Hanson and F. R. Ahmed, *Acta Cryst.*, 1958, **11**, 724.
(+)-Benzylmethylphenylpropylphosphonium bromide	Br	Mo	A. F. Peerdemann, J. P. C. Holst, L. Horner, and H. Winkler, *Tetrahedron Letters*, 1965, 811.
(+)-Methylsuccinic acid	See Section 5 under Ergoflavin.		
(−)-Methyl-α-naphthylphenylsilane	Si	Co, Cu	T. Ashida, R. Pepinsky, and Y. Okaya, *Acta Cryst.*, 1963, **16**, (supplement), A48, abstract 5.8.
Tartaric acid as (1) Na, Rb salt	Rb	Zr	A. F. Peerdemann, A. J. Van Bommel, and J. M. Bijvoet, *Proc., k. ned. Akad. Wetenschap*, 1951, **B54**, 16.
(2) Rb, H salt	Rb	Zr	A. J. Van Bommel, and J. M. Bijvoet, *Acta Cryst.*, 1958, **11**, 61.
L-Tyrosine as hydrochloride	Cl	Cu	R. Parasarathy, *Acta Cryst.*, 1962, **15**, 41.

Compound	*Fluorescent atom*	*Radiation used*	*Reference*
(2) Terpenoids.			
(+)-3-Bromocamphor	Br	Mo	M. G. Northolt and J. H. Palm, *Rec. Trav. chim.*, 1966, **85**, 143.
	Br	Cu	F. H. Allen and D. Rogers, preceding Communication.
(+)-Camphor as oxime hydrobromide	Br	Cu	H. A. J. Oonk, Ph.D. Thesis, Utrecht, 1965.
Cascarillin as deacetylcascarillin acetal iodoacetate	I	Cu	C. E. McEachan, A. T. McPhail, and G. A. Sim, *J. Chem. Soc.* (*B*), 1966, 633.
Clerodin as bromolactone	Br	Cu	I. C. Paul, G. A. Sim, T. A. Hamor, and J. M. Robertson, *J. Chem. Soc.*, 1962, 4133.
Davallol as iodoacetate	I	Cu	Yow-Cam Oh and E. N. Maslen, *Acta Cryst.*, 1966, **20**, 852.
Enmein as acetyl-bromoacetyl dihydro-compound	Br	Cu	M. Natsume and Y. Iitaka, *Acta Cryst.*, 1966, **20**, 197.
Ophiobolin as bromomethoxy-derivative	Br	Cu	S. Nozoe, M. Morisaki, K. Tsuda, Y. Iitaka, S. Tamura, K. Ishibashi, and M. Shirasaka, *J. Amer. Chem. Soc.*, 1965, **87**, 4968.
Picrotoxinin as α_1-bromo-compound	Br	Cu	B. M. Craven, *Acta Cryst.*, 1962, **15**, 387.
Simarolide as *m*-iodobenzoate and 4-iodo-3-nitrobenzoate (both needed)	I	Cu	W. A. C. Brown and G. A. Sim, *Proc. Chem. Soc.*, 1964, 293.
Swietenine as *p*-iodobenzoate of destigloylswietenine	I	Cu	A. T. McPhail and G. A. Sim, *Tetrahedron Letters*, 1964, 2599; *J. Chem. Soc.* (*B*), 1966, 318.
Bromoisotenulin	Br	Cu	D. Rogers and Mazhar-ul-Haque, *Proc. Chem. Soc.*, 1963, 92.
α-Bromoisotutin	Br	Cu	B. M. Craven, *Acta Cryst.*, 1964, **17**, 396.
Verrucarin as *p*-iodobenzoate	I	Cu	A. T. McPhail and G. A. Sim, *Chem. Comm.*, 1965, 350.
(3) Alkaloids.			
Aspidospermine as *N*(a)-acetyl-7-ethyl-5-desethylaspidospermine *N*(b)-methiodide	I	Cu	A. Camerman, N. Camerman, and J. Trotter, *Acta Cryst.*, 1965, **19**, 314.
(+)-Demethanolaconinone as hydriodide trihydrate	I	Cu	M. Przybylska, *Acta Cryst.*, 1961, **14**, 429.
Bulbocapnine as methiodide	I	Cu	T. Ashida, R. Pepinsky, and Y. Okaya, *Acta Cryst.*, 1963, **16**, (supplement) A48, abstract 5.8.
Cleavamine as methiodide	I	Cu	N. Camerman and J. Trotter, *Acta Cryst.*, 1964, **17**, 384.
Codeine as hydrobromide dihydrate	Br	Cu	G. Kartha, F. R. Ahmed, and W. H. Barnes, *Acta Cryst.*, 1962, **15**, 326.
Cucurbitine as perchlorate	Cl	Cu	Hai-Fu Fan and Cheng-Chung Lin, *Wu Li Hsueh Pao*, 1965, **21**, 253.
Echitamine as iodide	I	Cu	H. Manohar and S. Ramaseshan, *Tetrahedron Letters*, 1961, 814.
Ephedrine as hydrochloride	Cl	Cu	G. N. Ramachandran and S. Raman, *Current Sci.*, 1956, **25**, 348.
Erythroidine as hydrobromide of dihydro-compound	Br	Cu	A. W. Hanson, *Proc. Chem. Soc.*, 1963, 52.
Galanthamine as methiodide	I	Cu	D. Rogers and D. J. Williams, *Proc. Chem. Soc.*, 1964, 357.
Gelsemicine as hydriodide of *N*-methyl compound	I	Cu	M. Przybylska, *Acta Cryst.*, 1962, **15**, 326.
Gliotoxin (also establishes sporidesmin in conjunction with circular dichroism data)	S	Cu	A. F. Beecham, J. Fridrichsons, and A. McL. Mathieson, *Tetrahedron Letters*, 1966, 3131.

Compound	*Fluorescent atom*	*Radiation used*	*Reference*
(+)-Hetisine as hydrobromide	Br	Cu	M. Przybylska, *Acta Cryst.*, 1963, **16**, 871.
Himbacine as hydrobromide	Br	Cu	J. Fridrichsons and A. McL. Mathieson, *Acta Cryst.*, 1962, **15**, 119.
Jacobine as bromohydrin	Br	Cu	J. Fridrichsons, A. McL. Mathieson, and D. J. Sutor, *Acta Cryst.*, 1963, **16**, 1075.
Leurocristine (vincristine) as methiodide (also establishes vincaleukoblastine)	I	Cu	J. W. Moncrieff and W. N. Lipscomb, *J. Amer. Chem. Soc.*, 1965, **87**, 4963.
Lucidusculine as hydriodide	I	Cu	A. Yoshino and Y. Iitaka, *Acta Cryst.*, 1966, **21**, 57.
(+)-Des(oxymethylene)lycoctonine as hydriodide monohydrate	I	Cu	M. Przybylska and L. Marion, *Canad. J. Chem.*, 1959, **37**, 1843.
Methyl melaleucate iodoacetate	I	Cu	S. R. Hall and E. N. Maslen, *Acta Cryst.*, 1965, **18**, 265.
Securine as hydrobromide dihydrate	Br	Cu	S. Imado, M. Shiro, and Z. Horii, *Chem. and Ind.*, 1964, 1691.
Strychnine as hydrobromide	Br	Cu	A. F. Peerdemann, *Acta Cryst.*, 1956, **9**, 824.
Thelepogine as methiodide	I	Cu	J. Fridrichsons and A. McL. Mathieson, *Acta Cryst.*, 1963, **16**, 206.
(4) Steroids.			
Lanostane as 3β-acetoxy-7α,11α-dibromolanostane 8α,9α-epoxide	Br	Cu	J. K. Fawcett and J. Trotter, *J. Chem. Soc.* (*B*), 1966, 174.
(5) Miscellaneous large molecules and mould metabolites.			
Duclauxin as monobromo-compound	Br	Cu	Y. Ogihara, Y. Iitaka, and S. Shibata, *Tetrahedron Letters*, 1965, 1289.
Ergoflavin as tetra-*O*-methyl di-*p*-iodobenzoate [also establishes (+)-methylsuccinic acid]	I	Cu	A. T. McPhail, G. A. Sim, J. D. M. Asher, J. M. Robertson, and J. V. Silverton, *J. Chem. Soc.* (*B*), 1966, 18.
Factor VIa, $C_{46}H_{66}O_9N_{11}Co,11H_2O$	Co	Cu	D. Dale, D. C. Hodgkin, and K. Venkatesan. In: "Crystallography and Crystal Imperfection," (ed. G. N. Ramachandran), Academic Press, London, 1963.
Ferrichrome "A", $C_{41}H_{58}N_9O_{20}Fe,4H_2O$	Fe	Cu	A. Zalkin, J. D. Forrester, and D. H. Templeton, *Science*, 1964, **146**, 261.
Dibromoleucodrin	Br	Cu	R. D. Diamand and D. Rogers, *Proc. Chem. Soc.*, 1964, 63.

(*Received, October 7th*, 1966; *Com.* 759.)

[1] J. M. Bijvoet, *Endeavour*, 1955, **14**, 71.
[2] A. McL. Mathieson, *Acta Cryst.*, 1956, **9**, 317.
[3] R. Hine and D. Rogers, *Chem. and Ind.*, 1956, 1428.
[4] F. H. Allen and D. Rogers, preceding Communication.

A Reference List of Organic Structures whose Absolute Configurations have been determined by *X*-ray Methods. Part 2

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A Reference List of Organic Structures whose Absolute Configurations have been determined by *X*-ray Methods. Part 2

By F. H. ALLEN, S. NEIDLE, and D. ROGERS*

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Part 1 of this list (F. H. Allen and D. Rogers, *Chem. Comm.*, 1966, 838) contained 54 entries. This supplement, believed to be complete to the end of 1967, contains 40 new entries.

1. Using the Anomalous Dispersion Method

Compound	*Fluorescent atom*	*Radiation used*	*Reference*
(1) *Amino-acids*			
(+)-2-Benzylglutamic acid as hydrobromide dihydrate	Br	Cu	T. Ashida, Y. Sasada, and M. Kakudo, ***Bull. Chem. Soc. Japan***, **1967**, **40**, 476.
(+)-2-Methyl-2-isopropylglutaric acid (+)-2-Methyl-2-isopropylsuccinic acid as Rb salt	Rb	Cu	M. R. Cox, H. P. Koch, W. B. Whalley, M. B. Hursthouse, and D. Rogers, ***Chem. Comm.***, **1967**, 212.
Cucurbitine as perchlorate (erroneously included under alkaloids in the first list)	Cl	Cu	Fan Hai-Fu and Lin Cheng-Chiung, ***Acta Phys. Sinica***, **1965**, **21**, 253.
(2) *Terpenoids*			
Ginkgolide A as mono-*p*-bromobenzoate	Br	Cu	N. Sakabe, S. Takada, and K. Okabe, ***Chem. Comm.***, **1967**, 259.
Caryophyllene iodonitrosite	I	Mo	D. M. Hawley, J. S. Roberts, G. Ferguson, and A. L. Porte, ***Chem. Comm.***, **1967**, 942.
Pseudoclovene A as mono-*p*-bromobenzene sulphonate ester	Br	Cu	G. Ferguson, D. M. Hawley, T. F. W. McKillop, J. Martin, W. Parker, and P. Doyle, ***Chem. Comm.***, **1967**, 1123.
Laurinterol as acetate (also establishes aplysin)	Br	Mo	A. F. Cameron, G. Ferguson, and J. M. Robertson, ***Chem. Comm.***, **1967**, 271.
Desmotroposantonin as 2-bromo-(−)-β-compound	Br	Cu	A. T. McPhail, B. Rimmer, J. M. Robertson, and G. A. Sims, ***J. Chem. Soc.*** (***B***), **1967**, 101.
Beyerol as monoethylidene iodoacetate derivative	I	Cu	A. M. O'Connell and E. N. Maslen, ***Acta Cryst.***, **1966**, **21**, 744.
Caesalpin as *p*-bromobenzoate	Br	Mo	A. Balmain, K. Bjamer, J. D. Connolly, and G. Ferguson, ***Tetrahedron Letters***, **1967**, 5027.
Gibberellic acid as methyl bromogibberellate	Br	Cu	F. McCapra, A. T. McPhail, A. I. Scott, G. A. Sim, and D. W. Young, ***J. Chem. Soc.*** (***C***), **1966**, 1577.

Compound	*Fluorescent atom*	*Radiation used*	*Reference*
(2) *Terpenoids—continued*			
Taxa-4(16),11-diene-5α,9α,10β,13α-tetraol as dihydro-anhydroisopropylidine derivative	Br	Cu	K. Bjamer, G. Ferguson, and J. M. Robertson, *J. Chem. Soc.* (*B*), 1967, 1272.
(+)-Camphor—see Retusamine below			
(3) *Sugar Derivatives*			
Aristeromycin as hydrobromide	Br	Cu(?)	T. Kishi, M. Muroi, T. Kusaka, M. Nishikawa, K. Kamiya, and K. Mizuno, *Chem. Comm.*, 1967, 852.
Showdomycin as isopropylidine-*N*-methylbisdeoxycycloshowdomycin hydrobromide	Br	Mo(?)	Y. Tsukuda, Y. Nakagawa, H. Kano, T. Sato, M. Shiro, and H. Koyama, *Chem. Comm.*, 1967, 975.
Formycin as monohydrobromide monohydrate	Br	Cu	G. Koyama, K. Maeda, H. Umezawa, and Y. Iitaka, *Tetrahedron Letters*, 1966, 597.
α-D-Glucosamine as hydrochloride	Cl	Cu	G. N. Ramachandran, R. Chandrasekaran and K. S. Chandrasekaran, *Biochim. Biophys. Acta.*, 1967, **148**, 317.
Ethyl 1-thio-α-D-glucofuranoside	S	Cu	R. Parthasarathy and R. E. Davis, *Acta. Cryst.*, 1967, **23**, 1049.
(4) *Alkaloids*			
Tuberostemonine as methobromide dihydrate	Br	Cu	H. Harada, H. Irie, N. Masaki, K. Osaki, and S. Uyeo, *Chem. Comm.*, 1967, 460.
Quinidine as (−)-1,1′-dimethylferrocene-3-carboxylic acid	Fe	Cu	O. L. Carter, A. T. McPhail, and G. A. Sim, *J. Chem. Soc.* (*A*), 1967, 365.
Buxenine-G as dihydroiodide	I	Cu(?)	R. T. Puckett, G. A. Sim, E. Abushanab, and S. M. Kupchan, *Tetrahedron Letters*, 1966, 3815.
Corymine as hydrobromide monohydrate	Br	Cu	C. W. L. Bevan, M. B. Patel, A. H. Rees, D. R. Harris, M. L. Marshak, and H. H. Mills, *Chem. and Ind.*, 1965, 603.
Gliotoxin (also establishes sporidesmin)	S	Cu	J. Fridrichsons and A. McL. Mathieson, *Acta Cryst.*, 1967, **23**, 439.
19-Propylthevinol as hydrobromide (also establishes morphine series)	Br	Cu	J. H. Van den Hende and N. R. Nelson, *J. Amer. Chem. Soc.*, 1967, **89**, 2901.
Mitomycin A as *N*-*p*-bromobenzenesulphonyl compound	Br,S	Cu	A. Tulinsky and J. H. Van den Hende, *J. Amer. Chem. Soc.*, 1967, **89**, 2905.
Haplophytine as dihydrobromide	Br	Cu	I. D. Rae, M. Rosenberger, A. G. Szabo, C. R. Willis, P. Yates, D. E. Zacharias, G. A. Jeffrey, B. Douglas, J. L. Kirkpatrick, and J. A. Weisbach, *J. Amer. Chem. Soc.*, 1967, **89**, 3061.
Retusamine as α′-bromo-D-camphor-*trans*-π-sulphonate monohydrate [also establishes absolute configuration of (+)-camphor]	Br	Cu	J. A. Wunderlich, *Acta Cryst.*, 1967, **23**, 846.
(5) *Steroids*			
Cholestane as 2α,3β-dibromo-5α-compound	Br	Cu	E. Van Heijkoop, H. J. Geise, and C. Romers, *Rec. Trav. chim.*, 1965, **83**, 1626.
17*aβ*-*p*-Bromobenzenesulphonyloxy-17α-methyl-19-nor-9β,10α-D-homoandrost-4-en-3-one	Br,S	Cu	R. T. Puckett, G. A. Sim, A. D. Cross, and J. B. Siddall, *J. Chem. Soc.* (*B*), 1967, 783.
17β-Bromoacetoxy-9β,10α-androst-4-en-3-one	Br	Cu	W. E. Oberhänsli and J. M. Robertson, *Helv. Chim. Acta*, 1967, **50**, 53.
(6) *Miscellaneous large molecules and mould metabolites* (*antibiotics*)			
Erythromycin A as hydriodide dihydrate	I	Cu	D. R. Harris, S. G. McGeachin, and H. H. Mills, *Tetrahedron Letters*, 1965, 679.
Siccanin as *p*-bromobenzene sulphonate	Br	Cu	K. Hirai, S. Nozoe, K. Tsuda, Y. Iitaka, K. Ishibashi, and M. Shirasaka, *Tetrahedron Letters*, 1967, 2177.
Ryridomycin as dihydrobromide	Br	Cu	G. Koyama, Y. Iitaka, K. Maeda, and H. Umezawa, *Tetrahedron Letters*, 1967, 3587.

2. By Internal Comparison with a Reference Centre

Compound	*Internal comparison centre*	*Reference*
(+)-*S*-Methyl-L-cysteine *S*-oxide	L$_8$-Amino-acid	R. Hine and D. Rogers, *Chem. and Ind.*, 1956, 1428; R. Hine, *Acta Cryst.*, 1962, **15**, 635.
(−)-Menthyl (−)-*p*-iodobenzenesulphinate	(−)-Menthyl group	E. B. Fleischer, M. Axelrod, M. Green, and K. Mislow, *J. Amer. Chem. Soc.*, 1964, **86**, 3395.
(−)-Iberin as a thiourea (also establishes all naturally derived sulphoxide mustard oils)	(+)-*R*-Phenylethylamine	K. K. Cheung, A. Kjaer, and G. A. Sim, *Chem. Comm.*, 1965, 100.
Cycloalliin hydrochloride monohydrate	L-Amino acid (from a natural source)	K. J. Palmer and K. S. Leed, *Acta Cryst.*, 1966, **20**, 790.
Monotropein as Rb salt	D-Glucose unit	N. Masaki, M. Hirabayashi, K. Fuji, K. Osaki, and H. Inouye, *Tetrahedron Letters*, 1967, 2367.

3. By External Correlation with a Related Compound

1,2-*O*-Aminoisopropylidene-α-D-glucopyranose hydriodide	Derived from D-glucose	J. Trotter and J. K. Fawcett, *Acta Cryst.*, 1966, **21**, 366.
Triol Q as *p*-iodobenzoate	Correlation with rose-nonolactone	G. Ferguson, J. W. B. Fulke, and R. McCrindle, *Chem. Comm.*, 1966, 691.
Bromoambrosin	Correlation with analogous compound, parthenin	M. T. Emerson, W. Herz, C. N. Caughlan, and R. W. Witters, *Tetrahedron Letters*, 1966, 6151.

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