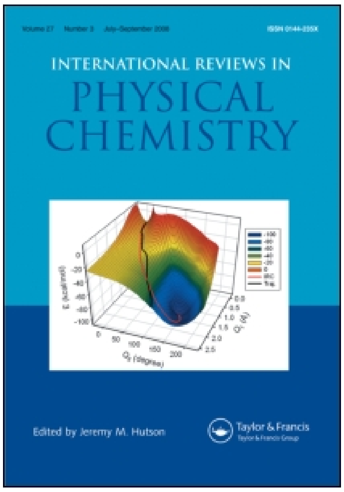

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MOLECULAR HANDEDNESS AND THE ORIGINS OF CHIRAL DISCRIMINATION

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ABSTRACT

The development of the conception of handedness in the physical world is outlined, culminating with the views of Pasteur on the role of chiral structures and dissymmetric forces in nature. The evolution is traced of the general conclusion that steric congruence dominates chiral discrimination in biochemical enantioselection, asymmetric organic synthesis, the crystal structures of enantiomers and racemates, and the distinction between homochiral and heterochiral interactions in the fluid state. The significance of the unification of the electromagnetic with the weak interaction is discussed with reference to the proposed universality of optical activity, and of the particular terrestrial enantioselection observed in natural products.

1. INTRODUCTION

As an anthropic principle, the conception that the physical world has handed properties derives from antiquity, embodied in the theory that man, the microcosm, epitomizes the entire universe, the macrocosm. The Pythagorean school extended the meaning of the word *cosmos* from the perceived social order of ancient Greek society to the organization of the solar and sidereal system, supposing that the universe has a right side and a left side (Conger, 1922). The analogy was prominent in proto-chemistry up to the time of the iatrochemists during the sixteenth and seventeenth centuries, from that of the Greek Alexandrian alchemists, who obtained the microcosm–macrocosm model from the Babylonians, according to Berthelot (1885). Sodium ammonium hydrogen phosphate, isolated by the iatrochemists from urine, was termed the *microcosmic salt*, which Hennig Brand of Hamburg employed *c.* 1675 in the first preparation of elementary phosphorus, with its remarkable sustained chemiluminescence (Partington, 1961).

As a morphological principle, the conception of cosmological handedness arose, with Louis Pasteur (1822–95), from a restricted form of the microscopic–macroscopic epitomization theme, developed by the mineralogists and crystallographers of the eighteenth century. While a given substance might crystallize from the melt or a solution in different crystal habits, cleavage shows that the various secondary forms reduce to a common macroscopic primary form, with a regular polyhedral morphology. Were it possible to continue the cleavage of the primary crystal form down to the ultimate molecular building blocks of the crystal, it would be found that the molecular units have the same morphology as the primary crystalline polyhedron (Bernal, 1953; Burke, 1966). As the crystallographer, René Just Haüy (1743–1822) expressed the principle, the crystal and its constituent molecules are morphologically 'images of each other' (Haüy, 1809).

The principle of Haüy was influential in French stereochemical theory throughout the nineteenth century (Mauskopf, 1976). The principle led Ampère (1814) to an alternative version of Avogadro's hypothesis in which the molecules of the elementary gases were taken

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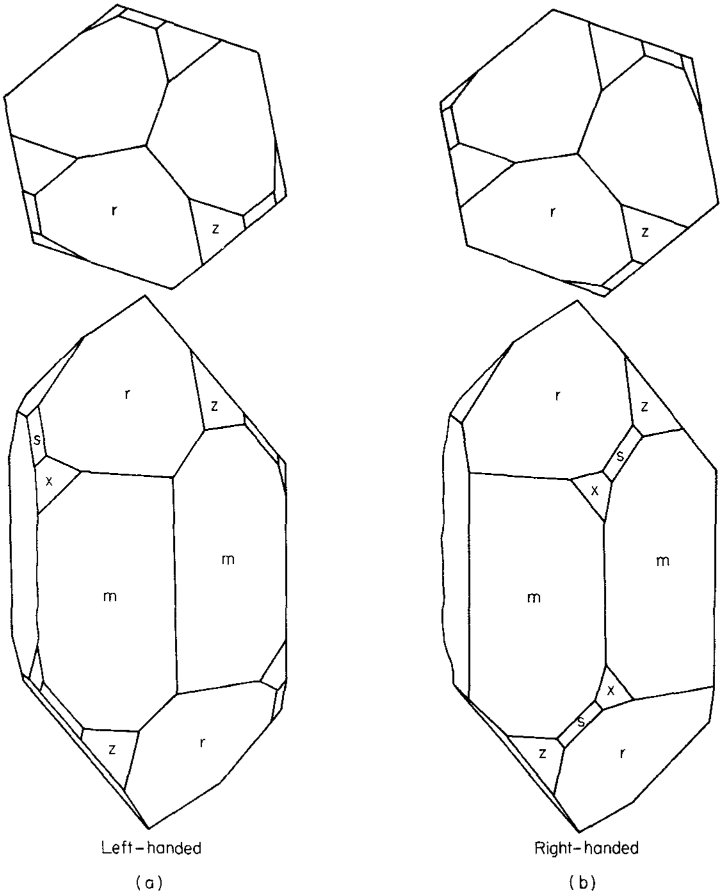
to be tetra-atomic, since the building unit of a crystal must be necessarily three dimensional. At the end of the century, the principle gave Le Bel (1890, 1892) grounds for the view that the valencies of the carbon atom are directed to the apices of a distorted tetrahedron, since the crystals of carbon tetrabromide and carbon tetraiodide are birefringent and do not possess the isotropic cubic form which should result from regular tetrahedral constituent units.

The principle of Haüy was developed by his pupil, Gabriel Delafosse (1796–1878), who taught Pasteur crystallography at the École Normale Supérieure (1843–46). While Haüy recognized that there are two morphological forms of the quartz crystal (*Fig. 1*), he regarded the minor enantiomorphous facets as secondary and inessential, terming them 'plagihedral' faces. The ideal primary form of quartz, Haüy supposed, would be hexagonal rather than the trigonal forms observed, due to the facets. For Delafosse the hemihedral facets of quartz and analogous crystals were not secondary or accidental, since they are associated with singular physical properties, pyroelectricity and optical activity, so that the facets are a macroscopic expression of a polar structural property of the constituent molecules (Mauskopf, 1976). When Pasteur was a student in Paris (1843–46), it was well established, from the correlation made by John Herschel (1822), that quartz crystals of the two morphological sets, left- and right-handed, are optically laevorotatory and dextrorotatory, respectively. Herschel observed of the hemihedral quartz facets, 'these faces are produced by the same cause which determines the displacement of the plane of polarization of a ray traversing the crystal parallel to its axis'.

II. PASTEUR ON DISSYMMETRY IN NATURE

The stimulus which led Pasteur to his concept of dissymmetry was the report by Mitscherlich (1844) of an earlier study of the connection between isomerism and isomorphism, prompted by Berzelius (1831), that the sodium ammonium salt of (+)-tartaric acid and of inactive racemic acid are isomorphous, and identical in density, solubility, and all properties, save optical activity. Working on the salts of (+)-tartaric acid, which all formed hemihedral crystals, Pasteur was astonished by Mitscherlich's report. Repeating the latter's study of sodium ammonium racemate, Pasteur (1848) found that two sets of hemihedral crystals are formed, related morphologically as non-superposable mirror-image forms, like the two sets of quartz crystals. Only one set proved to be truly isomorphous with sodium ammonium (+)-tartrate, and identical in all respects, including specific optical rotation. The other set possessed, in addition to the enantiomorphous crystal facets, a specific optical rotation of opposite sign in aqueous solution. Following Haüy and, more particularly, Delafosse, Pasteur proposed that the individual (+)- and (−)-tartaric acid molecules are stereochemically dissymmetric, related as non-superposable mirror-image forms, like the macroscopic crystals of the corresponding sodium ammonium salts.

Subsequently, at Strasbourg (1849–54), Pasteur (1853) discovered the general method of diastereomer formation for the optical resolution of racemic substances. Here, at Strasbourg, Pasteur came to the view that dissymmetric molecules and hemihedral crystals are the product of universal dissymmetric influences, exemplified by the polar fields of magnetism and electricity, or composite rotations, such as those of the solar system. The discovery by Faraday (1846) of magnetically-induced optical rotation in isotropic transparent media led Pasteur to grow normally holohedral crystals in a magnetic field, with the object of inducing hemihedral crystal forms. Not discouraged by the negative results, Pasteur at Lille (1854–57) attempted to modify the optical activity of natural products by rotating the plants producing them with a large clockwork mechanism or, by means of a



Left-handed
(a)

Right-handed
(b)

FIG. 1. Morphological forms of (a) laevorotatory left-handed and (b) dextrorotatory right-handed quartz crystals viewed in a direction parallel (top view) and perpendicular (lower view) to the trigonal crystal optic axis.

heliostat, presenting to the plants the appearance of the sun rising in the west and setting in the east. These experiments, and their negative outcome, were reported in his later years, in the course of a restatement of his belief in a cosmological dissymmetry, arguing that the solar and sidereal system is dissymmetric, being non-superposable on its mirror-image (Pasteur, 1884a).

Back in Paris, Pasteur (1860) in his lectures on molecular dissymmetry proposed that optical activity provides a demarcation criterion between laboratory synthesis and the biochemical synthesis of living organisms. The latter had become his primary concern already at Lille, where he had found that *Penicillium glaucum* grown on aqueous ammonium racemate containing a small quantity of phosphate preferentially uses the (+)-tartrate as a carbon source, leaving the (−)-isomer (Pasteur, 1858). The distinction between the chemistry of the laboratory and that of living organisms, based upon optical activity, provided the justification for a vitalist school of organic stereochemistry, exemplified by Francis Japp (1898) at Aberdeen.

Pasteur found the vitalist school unattractive but, equally, he took little interest in the contemporary development of mainstream organic stereochemistry, first, the two-dimensional aromatic structural theory of Kekulé, from 1865, and then the aliphatic chemistry in space of van't Hoff and Le Bel, from 1874. Pasteur followed the iatrochemical tradition of Paracelsus and van Helmont with its belief in the chemical autonomy of fermentation and disease, mediated by physico-chemical forces as yet incompletely characterized. The spontaneous optical resolution of sodium ammonium racemate may well be due, Pasteur (1884a) supposed, to dissymmetric influences in the glass of the crystallizing dish. In a subsequent and more general statement of his viewpoint, Pasteur (1884b) wrote, 'Not only have I refrained from posing as absolute the existence of a barrier between the products of the laboratory and those of life, but I was the first to prove that it was merely an artificial barrier, and I indicated the general procedure necessary to remove it, by recourse to those forces of dissymmetry never before employed in the laboratory'.

III. DISSYMMETRIC SYNTHESIS

Forces of dissymmetry, additional to those considered by Pasteur, were proposed by Le Bel (1874) in his pioneer work on the connection between optical activity in the fluid phase and enantiomorphous three-dimensional organic structures. The use of left- or right-handed circularly polarized radiation in photochemical reactions involving racemic mixtures, or of chiral catalysts in the corresponding thermal reaction, would be expected to produce an excess of a particular enantiomeric product.

Following his discovery of the differential absorption of left- and right-circularly polarized light by aqueous solutions of copper(II) and chromium(III) (+)-tartrate (1895), Cotton (1909) investigated the chiral photodiscrimination proposed by Le Bel and, subsequently, van't Hoff, employing solutions of the racemic copper(II) tartrate complex. No optical activity was detected in the photoproducts by Cotton, and the first unambiguous photoresolutions were achieved by Kuhn and Braun (1929) and Kuhn and Knopf (1930), employing circular ultraviolet radiation for the differential photolysis of the enantiomers in a racemic mixture of 1-bromo- and of 1-azido-ethyl-propionate. The optical yields in these and in subsequent photoresolutions and photosyntheses employing circularly polarized radiation and enantiomeric reactants were inevitably low, due to the small dissymmetry ratio (Kuhn, 1930) of the circular dichroism ($\Delta\varepsilon$) to the isotropic light absorption (ε).

The second of the dissymmetric influences on reactivity proposed by Le Bel, chiral catalysis, was implicit in the discovery of diasteromers by Pasteur (1853) where the conclusion was drawn that, 'the absolute identity of the physical and chemical properties of left and right non-superposable substances ceases to exist in the presence of another active substance'. The introduction of a second asymmetric centre into an enantiomer gave a relatively large discrimination between the two diastereomers, as Emil Fischer discovered in the step-wise synthesis of the sugars from glyceraldehyde by the Kilani cyanohydrin procedure. 'There are equal chances for mirror images only', Fischer (1894) noted, 'once a molecule is asymmetric, its extension proceeds also in an asymmetric sense'.

Analogous addition reactions of a carbonyl group in a chiral molecule provided a focus for studies of asymmetric synthesis for the following half-century. McKenzie (1904) initiated the investigation of the enantioselective atrolactic acid synthesis from the esters of benzoyl formic acid with chiral alcohols, employing the recently-discovered methyl magnesium iodide reagent (Grignard, 1901). His student, Ritchie (1933, 1947), found that the chiral esters of benzoyl formic acid undergo mutarotation in ethanol solution, and that the sign of the mutarotation generally correlates with the sign of the optical rotation of the atrolactic acid enantiomer produced in excess by the addition of the Grignard reagent to the benzoyl carbonyl group. From the correlation, Ritchie (1933) concluded that an asymmetric induction from the chiral alcohol group produces enantiomorphous pyramidal conformations of the benzoyl carbonyl group with unequal populations. The pyramidal carbonyl population in excess governs the sign of the mutarotation and the enantiomeric excess of the atrolactic acid produced by the addition of the Grignard reagent to the ester.

Subsequent interpretations of the asymmetric atrolactic acid synthesis, and of enantioselective synthesis generally, became dependent primarily upon the steric constraints imposed upon a reagent attacking a reactive site in a chiral molecule, rather than an asymmetric induction, consisting of a differential bonding interaction deriving from the chiral centre. A steric basis for biochemical enantioselection, implicit in the 'key and lock' hypothesis of Fischer (1894, 1907), had been proposed in the three-point contact model of Easson and Stedman (1933) to account for the differential pharmacological action of enantiomeric miotic benzylamine derivatives, and of Ogston (1948) to explain the retention of the labelled carboxylate carbon atom of L-serine in an enzymatic oxidation to glycine through the achiral intermediate, aminomalonic acid. In an analysis of the series of asymmetric atrolactic acid syntheses investigated by McKenzie and his students, and from his own studies of the synthesis, Prelog (1953) concluded that the Grignard reagent attacks the essentially-planar benzoyl carbonyl group in a chiral ester of benzoyl formic acid from the less-hindered side of the plane, that flanked by the smallest of the three groups bonded to the chiral carbinol centre (*Fig. 2*).

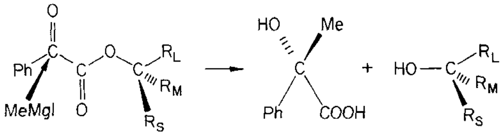


FIG. 2. The steric model of Prelog for the asymmetric synthesis of atrolactic acid from the benzoyl formic ester of a chiral alcohol. A plane is defined by the two carbonyl groups, the ester bonds, and the largest, R_L, of the three groups bonded to the carbinol centre. The Grignard reagent preferentially attacks from the side of the plane flanked by the smallest group, R_S, bonded to the carbinol centre (Prelog, 1953).

More recent studies indicate that the approach of a nucleophile reagent is not orthogonal to the plane of the carbonyl group and the α-carbon atoms. Product analyses, calculations of the reaction coordinate, and X-ray structural studies of carbonyl compounds containing a proximate nucleophilic group suggest that the carbonyl carbon atom is attacked from the rear at an oblique angle of *c.* 109° to the carbonyl bond (Dunitz, 1979; Menger, 1983). The X-ray structure determinations of carbonyl compounds containing a neighbouring oxy- or amino group show that the plane of the carbonyl group and the α-carbon atoms is pyramidally distorted in the solid state (Dunitz, 1979). In the cases where the amino- or oxy-substituted carbonyl compound is chiral, the nucleophilic substituent selectively induces a particular enantiomeric pyramidal distortion of the prochiral carbonyl group plane.

IV. CHIRAL FIELDS

Pasteur viewed the dissymmetric forces of nature as essentially polar fields, expressed in the polarity of magnetism, electricity, and spin and orbital rotation, as in the solar system. None of these in isolation provide a chiral field. Pierre Curie (1894) pointed out that a dissymmetric force field entails collinear axial and polar vector components, such as those provided by the simultaneous application of a magnetic field and a parallel or antiparallel electric field. If the electric and the magnetic field are uniform and constant, their superposed application cannot affect the equilibrium enantiomeric populations in a racemic reaction mixture, since such fields do not lift the one-to-one isoenergetic correspondence between the electronic states of the two enantiomers (de Gennes, 1970; Mead *et al.*, 1977). An exception may be provided by the case where the transition state of a reaction from an achiral or racemic substrate to enantiomeric products involves a change of magnetic moment, due to a transient current density (Rhodes and Dougherty, 1978; Dougherty, 1980).

Similar reservations apply to prochiral chemical reactions carried out in a centrifuge with the spin axis alligned parallel or antiparallel to the gravitation field of the earth (Mead and Moscowitz, 1980; Peres, 1980). Observable enantioselection has been claimed in the alkaline oxidation of isophorone with hydrogen peroxide to the isophorone oxide enantiomers (*Fig. 3*) employing collinear electric and magnetic fields (Gerike, 1975) and in a centrifuge with a vertical spin axis (Edwards *et al.*, 1980), the sign of the optical rotation due to the enantiomer product in excess correlating with a parallel or an antiparallel relative orientation of the axial and the polar vector fields. Order of magnitude calculations indicate that the enantiomeric excess of a reaction attainable in a rotating vessel in the earth's gravitational field would be a few parts in 10^{17} at most (Mead and Moscowitz, 1980), resulting in an optical rotation at least 10^{-12} smaller than the values claimed.

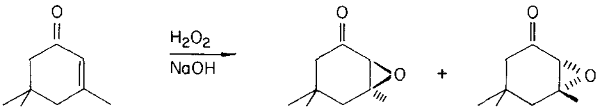


FIG. 3. The reaction of isophorone with alkaline hydrogen peroxide to form the isophorone oxide enantiomers.

The dye, 1,1′-diethyl-2,2′-cyanine, forms a viscous van der Waals polymer in aqueous electrolyte solutions, the dye aggregate being optically active if the electrolyte is chiral, e.g., potassium (+)-tartrate (Mason, 1964). It has been claimed that the enantiomorphs of the dye aggregate are produced in aqueous solutions of achiral electrolytes by stirring uniformly clockwise, or anticlockwise (Honda and Hada, 1976), although the effect reported probably originates from the linear dichroism of the dye polymer orientated by the hydrodynamic shear stress (Norden, 1978). No observable enantioselectivity has been found from the uniform clockwise or counterclockwise stirring of solutions in the crystallization of racemic sodium ammonium tartrate, or the polymerization of racemic γ-benzyl-glutamic-N-carboxyanhydride (Kovács *et al.*, 1981).

A rotating transparent medium becomes optically active for radiation propagated along the rotation axis, the sign of the induced birefringence being dependent upon the clockwise or counterclockwise rotation of the medium relative to the radiation source. The effect, termed rotatory ether drag, has been detected in a rapidly-rotating glass rod with plane polarized light propagated along the rod axis (Jones, 1976). Similarly, an assembly of co-rotating achiral molecules is expected to be optically active for radiation propagated along the common axis of the rotational polarization (Atkins, 1980).

If the assembly of molecules is a fluid racemic mixture and the radiation is circular polarized in the radio frequency region, the molecules rotate by following the chiral radiation field, and the propellor effect leads to a separation of the optical isomers, the two enantiomers moving linearly in opposite directions (Baranova and Zel'dovich, 1978). The application of a static electric field to a solution of ionic chiral molecules produces a coherent linear motion of the ions, and the propellor effect gives rise to a rotation, clockwise for one isomer and counterclockwise for its enantiomer. The field-induced rotation generates an optical activity, additional to the natural optical rotation of the chiral ion, providing an electrical analogue of the Faraday effect (Baranova *et al.*, 1977).

If the applied electric field is oscillatory, an additional source of induced optical activity in an enantiomer arises from the forced oscillations of the electrons in the chiral molecular structure, whether the enantiomer is charged or neutral (Buckingham, 1979). A more general electric analogue of the Faraday effect, applying to achiral molecules and racemates as well as enantiomers, is the differential scattering of right and left circularly polarized light induced by an electrostatic field perpendicular to the plane formed by the excitation and the scattering directions (Buckingham and Shatwell, 1980, 1983).

Another propellor effect, the coupling of the rotation to the translation of chiral molecules in the fluid phase, distinguishes between the molecular diffusion dynamics of an assembly of enantiomers and an assembly composed of the corresponding racemic mixture. The different pair-wise interactions in the two assemblies give a computer-simulated molecular dynamics which predict, in the case of 1, 1-chlorofluoroethane, the absorption of far infrared or radio-frequency radiation by the enantiomer assembly at a longer wavelength than the racemic assembly (Evans, 1983). Differences are reported between the infrared spectra, 50–250 cm^{-1}, of (+)-3-methyl-cyclohexanone and the corresponding racemate in the liquid phase (Evans and Evans, 1983).

The pair-wise interactions between two achiral molecules in the fluid phase differ for co-rotating and counter-rotating molecular pairs. The polarizability of one molecule is sensitive to the rotating field due to its neighbour, and an assembly of co-rotating molecules is expected to have a dispersion energy different from that of the corresponding assembly of counter-rotating pairs (Atkins, 1980). An analogous chiral discrimination is expected between pairs of gaseous atoms containing unpaired electrons, where the role played by rotation in the molecular case is taken over by electron spin. The interaction between a pair of alkali metal atoms is dependent upon the relative spin state of the two unpaired electrons. The atom pair has one doubly-degenerate and two non-degenerate spin orbital states, which are distinguished by the particular value of the dispersion energy between the two atoms. The ratio of the discrimination energy to the average dispersion energy is estimated at *c.* 10^{-4} for a pair of caesium atoms, compared with the value of *c.* 10^{-7} for the corresponding ratio in the case of co-rotating and counter-rotating methane molecules (Buckingham and Joslin, 1981).

Having added in 1874 the chiral field of circularly-polarized light to the array of dissymmetric forces suggested by Pasteur, Le Bel (1925), at a meeting of the Chemical Society of France to celebrate the fiftieth anniversary of his earlier work, and that of van't Hoff, pointed out that views on atomic structure developed during the intervening period implied that the chemical atom is intrinsically chiral. According to the Bohr theory of the atom then prevailing, the electrons of an atom circulate round the nucleus. In some cases the circulation is clockwise and in others anticlockwise, so that a collection of atoms constitutes a racemic mixture, in most cases. Thus sodium chlorate or strontium formate crystallize to give an equal number of laevorotatory and dextrorotatory crystals.

However, potassium silico-tungstate, and the corresponding molybdate, crystallize to give predominantly dextrorotatory crystals, as Wyrouboff (1896) had found and Copaux (1910) had confirmed. Hence the majority of the atoms of silicon belong to one of the two enantiomorphous sets. Similarly the atoms of carbon are enantiomerically enriched, since some of the native petroleums, which Le Bel held to have an inorganic origin, are optically active (Delépine, 1949). Subsequently the results of Wyrouboff (1896) and Copaux (1910) on the predominant or sole formation of dextrorotatory crystals from aqueous solutions of potassium silico-tungstate, where the complex is optically labile, were ascribed to trace impurities of alkaloids, employed in concurrent optical resolutions (Armariglio *et al.*, 1968). Pope (1898) had found that the ratio of (+)- to (−)-crystals of sodium chlorate, while 1 : 1 from aqueous solutions, becomes 1 : 2 from aqueous glucose solutions, containing 200 gℓ^{-1} of the sugar.

V. ENANTIOMER AND RACEMATE CRYSTAL STRUCTURES

The distinctions between an assembly of enantiomers and the corresponding racemic assembly are the most evident in the ordered solid state. It was the enantiomorphous hemihedral crystal facets of sodium ammonium (+)- and (−)-tartrate which had led Pasteur (1848) to the connection between optical activity and molecular dissymmetry, reinforced by the isolation of holohedral crystals of racemic sodium ammonium tartrate on crystallization at temperatures above 27°C, the transition point (Scacchi, 1865). However, the ground upon which Pasteur established the connection, the belief from Haüy and Delafosse that the molecule and the corresponding crystal and morphologically 'images of each other', was undermined by his older contemporary Auguste Bravais.

With Bravais (1850) the crystal was regarded no longer as an assembly of congruent space-filling polyhedra, each an individual molecule, but a reticular array of lattice points, symmetrically related by translational repetition. The external morphological symmetry of a crystal, falling into one of the 32 crystal point groups identified by Hessel (1831) and rediscovered by Bravais (1851), was now related to the lattice symmetry, rather than the molecular morphology. The lattice points represented the centres of gravity of the molecular units, but there appeared to be no necessary connection between the arrangement of the atoms in the molecule and the reticulation of the crystal lattice.

The 14 Bravais lattices accounted for 7 of the 32 crystal point group classes, based on external morphology, since only the translational equivalence of lattice points was taken into account. Sohncke (1879) introduced the screw axis and the glide plane as lattice symmetry operations, extending the number of possible spatial arrangements of crystal lattice points to 65. Finally, Fedorov (1891), Schoenflies (1891) and Barlow (1897), added the rotation–reflection or rotation–inversion lattice symmetry operation, completing the set of 230 space groups.

The problem of the relationship between molecular shape and crystal symmetry in homomolecular crystals was taken up again, notably by the Soviet school of crystallographers descended from Fedorov (Kitaigorodsky, 1973; Vainshtein, 1981; Vainshtein *et al.*, 1982). Surveys of crystal and molecular structure analyses by X-ray diffraction methods indicate a substantial loss of point-group molecular symmetry at a lattice site on crystallization. Only the inversion centre is generally retained. Centrosymmetric molecules are found to occupy a lattice site with inversion symmetry in 92% of the 387 crystals studied (Belsky, 1974). Molecules with dihedral (D_p) point symmetry lose the principal rotation axis C_p and all but one of the p twofold axes at the lattice site in 80% of the crystals investigated, and molecules with C_2 point symmetry occupy a lattice site with the same symmetry only in 43% of the corresponding crystals surveyed. Only 10% of the molecules with C_s mirror-plane point symmetry lie on lattice mirror planes in the corresponding crystal. Molecules with C_{2v} point symmetry retain at the lattice site one of the two mirror planes in 12% of the cases, and the twofold rotation axis in 18%, but the lattice site symmetry corresponds to the full molecular point symmetry in only 5 of the 305 crystals studied (Belsky, 1974).

In a survey of some 5000 X-ray structure determinations of homomolecular crystals carried out up to 1975, Belsky and Zorkii (1977) show that organic molecules crystallize predominantly in the systems of low symmetry, mainly monoclinic and orthorhombic. Of the 219 space groups with non-anomalous distinctive X-ray diffraction patterns, obeying the law of Friedel (1913), only 89 are represented in the collection, and over one-third of all the structures belong to the monoclinic space group $P2_1/c$ (*Table 1*).

TABLE 1. The most common space groups of molecular crystals, based upon a survey of some 5000 crystal structure determinations (from Belsky and Zorkii, 1977). The chiral crystal structure types are, (A), homochiral, (B), heterochiral, and, (C), achiral systems of equivalent molecular positions in the lattice.

Space group	Type	Number	%
$P2_1/c$	B, C	1897	37.9
$P2_12_12_1$	A	839	16.8
$P1$	B, C	449	9.0
$P2_1$	A	418	8.4
$C2/c$	B, C	310	6.2
$Pbca$	B, C	247	4.7

The chirality classification of crystal structures, due to Zorkii *et al.* (1977), distinguishes between (A) homochiral, (B) heterochiral and (C) achiral lattice sites. In the type A structures, the molecules occupy a homochiral system of equivalent lattice positions, or sets of such systems. There are no secondary symmetry relations in the type A lattices, i.e., inversion centres, mirror or glide planes, or the higher-order inversion axes. In the racemic type B lattice, the molecules occupy heterochiral systems of equivalent positions, and the enantiomeric optical isomers are related by secondary lattice symmetry operations. In the type C lattice, the molecules occupy achiral systems of equivalent lattice positions, and each molecule is located on either an inversion centre, or a mirror plane, or a special position of a higher-order inversion axis. The distribution over the 5000 crystal structures studied of the chiral lattices types follows the order: B 55.6%, A 28.4%, C 15.7%, with 0.3% containing two independent sets of lattice positions, one of type B and the other of type C. A large proportion of racemic substances (51.4%) crystallize in the type B structural class, $P2_1/c$, with four molecules in the unit cell ($Z = 4$), and a comparable proportion of enantiomers (56.1%) from the type A lattice, $P2_12_12_1$, again with $Z = 4$ (Belsky and Zorkii, 1977).

The prevalence of low-symmetry space groups among homomolecular crystals is rationalized by Kitaigorodsky (1973) by the principle of maximum space-filling. Kitaigorodsky defines a compacity, or packing coefficient, for molecular crystals given by the ratio of the volume occupied by the molecules in a unit cell to the unit-cell volume. The observed packing coefficient in organic crystals is generally quite large (0.65–0.77), comparable to the corresponding ratio for the close-packing of spheres and ellipsoids.

Close-pack layers of molecules with an arbitrary shape are not feasible in the two-dimensional plane groups which contain mirror symmetry or rotation axes of higher order than two. The stacking of layers with a coordination number of six, to achieve close packing in three dimensions with a coordination number of twelve ($3 + 6 + 3$), or fourteen ($4 + 6 + 4$), requires a translation at an oblique angle to the layer plane, or a twofold screw axis, or a glide plane, or an inversion centre, to relate the neighbouring layers. A mirror plane relation between the layers, like the corresponding relation in a layer, does not allow economic packing. The only molecular point symmetry element preserved in the lattice symmetry of a close-pack structure is an inversion centre. The retention of other elements of molecular symmetry in the crystal space lattice results in a loss of packing efficiency, reducing the compacity ratio by some 0.2 to 0.3. The most prevalent space groups are those allowing the closest packing of racemic substances ($P2_1/c$ and P_1) and of enantiomers ($P2_12_12_1$ and $P2_1$) (*Table 1*).

The principle of maximum space-filling helps to account for the low incidence of the spontaneous optical resolution of racemic substances by crystallization. A survey of the chiral compounds listed in the ten volumes of Beilstein reveals that, at the 95% confidence level, the frequency of the spontaneous formation of homochiral crystals from a neutral racemate is 6.3 ± 1.3%, compared with the corresponding frequency of 15 ± 8% for racemic organic salts (Jacques *et al.,* 1981b). The secondary space group symmetry operations forbidden in homochiral lattices, but allowed for racemic lattices, include the inversion centre and the glide plane, which are conducive to close-packing. The twofold screw axis is the principal crystallographic symmetry element available for a close-packed homochiral lattice, and the addition of the inversion centre and the glide plane allows the corresponding racemate to adopt the more compact structure, in general. The empirical rule of Wallach (1895) states that the combination of two optical isomers to form the corresponding racemate is accompanied by a volume contraction. The rule has many exceptions, and it expresses only a general trend (Jacques *et al.,* 1981a).

VI. FLUID STATE CHIRAL DISCRIMINATION

The thermodynamic and other physical distinctions between a homochiral assembly of enantiomers and the corresponding racemic heterochiral assembly are generally larger for the solid state than the liquid phase. Early studies of the heat of mixing of liquid enantiomers, and measurements of the density, surface tension, viscosity, refractive index, and the dielectric constant of a fluid enantiomer and the corresponding racemic liquid are reviewed by Horeau and Guetté (1974). The authors report an enthalpy of mixing for the liquid enantiomers of *p*-nitrophenyl-2-butane of 1.9 ± 0.4 J mol^{-1} at 298 K. The mixing of aqueous solutions of enantiomeric amino and hydroxy-acids gives enthalpy changes of the same magnitude, e.g., 1.99 ± 0.04 J mol^{-1} for aqueous (+)- and (−)-tartaric acid, 15.6% by weight, at 298 K (Amaya *et al.,* 1968). In contrast, the heat of solution in water of (+)-tartaric acid and the corresponding racemate as crystalline solids at 298.15 K are found to be 16.2 and 25.6 ± 0.1 kJ mol^{-1}, respectively, the difference reflecting the lower lattice energy of the racemate (Matsumoto and Amaya, 1980).

The mixing of the liquid enantiomers of limonene, fenchone, and 1-phenylethylamine to form the corresponding racemic fluid results, at temperatures near 300 K, in a small density increase, the excess molar volume of the mixing having amagnitude of the order -10^{-3} cm^3 mol^{-1} (Atik *et al.,* 1981). The corresponding volume change for the transition from enantiomeric to racemic crystals is more substantial, e.g., − 19.4 cm^3 mol^{-1} for 1,1′-binaphthyl and + 2.56 $cm^3 mol^{-1}$ for mandelic acid (Mason, 1982).

The mutual intermolecular stereochemical compatibility of chiral molecules emerged, from the 'key and lock' hypothesis of Fischer (1894), as the main basis for pharmacological and other biochemical enantioselections, and for the rules governing the course of dissymmetric organic synthesis (Section III). Similarly a wider range of lattice symmetries conducive to close-packing is available for a racemate than for one of the corresponding enantiomers, and intermolecular steric congruity provides the major factor governing chiral discrimination in the solid state (Section V). Recent studies indicate that chiral discrimination in the fluid phase arises in an analogous way, primarily from the more efficient heterochiral contact packing in racemic liquids, relative to the homochiral contact packing of the corresponding fluid enantiomer.

By the use of a hard-core model to simulate the role of the repulsive intermolecular forces, Craig and Elsum (1982) have investigated the orientationally averaged pair distribution function of an enantiomer and the racemic mixture of chlorofluoroacetonitrile in the dense liquid and in the gas phase, employing the integral equation method of Chandler (1978). At the first maximum of the orientationally averaged radial distribution function (500 pm) a racemic molecule pair is found to have a smaller mean separation, by *c.* 1 pm, than the corresponding enantiomer pair. The difference rapidly attenuates, and it becomes negligible outside the nearest-neighbour shell.

Overall the mixing of the enantiomers to form the racemic dense fluid results in a volume contraction, the calculated excess molar volume being -0.1 to $-0.2\ \text{cm}^3\ \text{mol}^{-1}$. In the low-density limit of the gas phase, the orientationally averaged pair distribution function at a given intermolecular separation shows that the racemic pair packs more efficiently than the homochiral pair, but the difference is small, some one part in 10^4 at most.

The mixing of the fluid enantiomers to form the racemic dense liquid gives, by use of the Lennard-Jones potential in the 12–6 form, an enthalpy of mixing of $+12\ \text{J mol}^{-1}$. The apparent anomaly of an endothermic heat of mixing accompanying a volume contraction on mixing the enantiomers is attributed to the dependence of the estimated excess molar volume upon the orientationally averaged radial distribution function at the smaller intermolecular separations, whereas the calculated enthalpy of mixing is the more dependent upon the longer range sections of the distribution function (Craig and Elsum, 1982).

Experimentally a volume contraction on mixing liquid enantiomers to form a fluid racemate may be accompanied by an exothermic or endothermic enthalpy change. The enthalpy of mixing the liquid enantiomers of fenchone and of 1-phenylethylamine at 303.11 K has the value of -4.51 ± 0.07 and $+7.34 \pm 0.06\ \text{J mol}^{-1}$, respectively, whereas the corresponding excess molar volumes of mixing are -0.0069 ± 0.008 and $-0.0018 \pm 0.0004\ \text{cm}^3\ \text{mol}^{-1}$, respectively (Atik, 1982).

The attractive intermolecular potentials provide only a small intrinsic discrimination between a homochiral and the corresponding heterochiral assembly. For the most part, the average attractive potential discriminates passively, by assuming the more negative value for the closer-packed pair. An electromagnetic discrimination in the dispersion energy between a randomly orientated homochiral molecule pair and the corresponding heterochiral pair was first proposed by Mavroyannis and Stephen (1962), dependent upon the rotational strengths, R^A_{on}, of the electronic transitions of molecule A, each with a transition energy, E^A_{on}, and the corresponding quantities for the molecule B, at a separation of R_{AB},

$$\Delta E = -(4/3) \sum_{n(A)} \sum_{m(B)} R^A_{on} R^B_{om} / [(E^A_{on} + E^B_{om}) R^6_{AB}] \qquad (1)$$

Craig *et al.* (1971) extended the treatment to discriminations in the induction energy and the dispersion energy for chiral molecule pairs with a fixed mutual orientation, or semi-locked configurations in which the two molecules rotate around the intermolecular line of centres.

The substitution of the observed rotational strengths and transition energies of the tris-1,10-phenanthroline enantiomer, Δ-(−)-$[\text{Ni(phen)}_3]^{2+}$, and the tris-2,4-pentanedionate, Δ-(−)-$[\text{Cr(pd)}_3]$, in Eq. (1) for the intermolecular contact distance of 1.0 nm provides, however, a discrimination energy between the homochiral and the heterochiral pair of only $5 \times 10^{-7}\ \text{J mol}^{-1}$, whereas a discrimination of $75\ \text{J mol}^{-1}$ is observed at a solution concentration corresponding to a mean separation of 2.4 nm between the chiral species (Kuroda *et al.*, 1978, 1981).

The sum rule for the rotational strengths of a chiral molecule, $\Sigma R_{on} = 0$ (Condon, 1937), limits the magnitude of the electromagnetic dispersion energy discrimination of Eq. (1) and its analogue for fixed or semi-locked mutual orientations of the chiral molecules. Each positive rotational strength has a negative companion of comparable magnitude, often a close neighbour on the energy scale of the circular dichroism spectrum of a chiral molecule. In the sum of Eq. (1), each positive term is largely cancelled by a negative counterpart and the overall sum becomes negligible for both the homochiral and the heterochiral pair.

A similar limitation circumscribes the third-order perturbation theory of chiral dispersion energy discrimination, proportional to R_{AB}^{-9}, dependent upon the signed triple scalar product of the electric dipole transition moments of each of the chiral molecules, A and B (Schipper, 1977, 1982; Schipper and Harrowell, 1983). An extension of the treatment of Condon (1937) shows that the triple scalar product summed over the manifold of the electric dipole moments of the electronic excitations in a chiral molecule necessarily vanishes (Mason, 1979).

A restriction of the dispersion energy estimates to the pairwise Coulombic potential between the transitional charge density on each atom of the chiral molecule A and a corresponding charge density on each atom of the homochiral, or heterochiral, molecule B gives chiral energy discriminations of the magnitude order observed for the liquid phase (Kuroda *et al.,* 1978, 1981). These dispersion energy discriminations between a homochiral and a heterochiral D_3 molecule pair, containing atoms with a hard-sphere boundary at the van der Walls radius, refer principally to contact or near-contact intermolecular separations and to semi-locked mutual molecular orientations in which the molecules rotate about the intermolecular line of centres.

Where the rotations are unaffected by the hard-sphere repulsive potentials, at a separation of 1.0 nm, the discrimination energy has the magnitude order observed for the liquid phase ($\sim$ J mol^{-1}). In the locked mutual orientations at contact intermolecular separations (591 to 758 pm) the dispersion energy discrimination amounts to values typical for the solid state ($\sim$ kJ mol^{-1}). For the locked contact case, the discrimination energy, which may favour the homochiral pair or, more generally, the heterochiral pair, arises principally from a small difference between the two intermolecular separations along a given line of centres conducive to closest packing, collinear C_3 molecular axes, or collinear C_2 axes, in tris-chelate D_3 enantiomers. The smaller discrimination energy of the semi-locked case, where the homochiral pair and the heterochiral pair have the same intermolecular separation, derives wholly from the stereochemically-determined differences in corresponding interatomic separations of the two chiral-pair types, the transitional charge density on a given atom being identical for the two types.

VII. EXTENSIONS OF OPTICAL ROTATION

The criterion of Pasteur (1860) for molecular dissymmetry, circular birefringence in isotropic media appearing as optical rotation over transparent wavelength regions, implied a corresponding circular dichroism at absorption radiation frequencies, an effect discovered by Cotton (1895). Boltzmann (1874) showed that the dipole approximation for the radiation field is inadequate for an analysis of optical activity, as it is an effect dependent upon the ratio of the molecular dimension, d, to the wavelength of light, λ. In the long wavelength limit, where the ratio (d/λ) goes to zero and the dipole approximation becomes strictly valid, the optical rotation is expected to vanish. The analysis of the optical rotation of quartz for c-axis propagation as a function of wavelength by Drude (1893) supported Boltzmann's expectation.

Kuhn (1929) discovered that the optical rotary power of a chiral substance, expressed as the product of the frequency-weighted oscillator strength, f, and the dissymmetry ratio, g, of an electronic transition, vanishes when summed over all transitions of the molecule. The rotatory power, fg/ν, corresponds to the quantum mechanical rotational strength, R_{on}, of the interstate $\psi_0 \rightarrow \psi_n$ electronic transition, due to Rosenfeld (1928), and Kuhn's sum rule is the classical equivalent of the sum rule, $\sum_n R_{on} = 0$, due to Condon (1937). In the formulation of Rosenfeld (1928), the optical rotation, ϕ, in radians cm^{-1}, at the frequency, ν, is given by the expression,

$$\phi = [16\pi^2 N/(3hc)] \sum_n \nu^2 R_{on}/[\nu_{on} - \nu^2] \tag{2}$$

where N is the number of molecules per cm^3. From the classical equivalent of Eq. (2), Kuhn (1929) drew the conclusion that the optical rotation of a chiral substance vanishes, not only in the long wavelength limit, but also at the high frequency limit.

Measurements of the optical rotation of quartz crystals in the infrared region, down to 3.2 μm (Lowry, 1935) and the vacuum ultraviolet region, up to 150 nm (Servant, 1939), provided early support for the expectation of diminishing optical rotation with increasing wavelength and indicated, from single-term analogues of the dispersion Eq. (2), that the optical activity of quartz arises from an electronic transition, or transitions, near 100 nm. The recent development of single-crystal polarizers and analysers for X-ray and neutron beams allows the measurement of the optical rotation of quartz at the X-ray wavelength (154 pm) of the CuK_α line (Hart and Rodrigues, 1981). The magnitude of the optical rotation of quartz in the X-ray region at 154 pm is found to be somewhat smaller than the corresponding rotation in the infrared region at 3.21 μm (*Table 2*), supporting the expectation of Kuhn (1929) that the optical activity of chiral substances vanishes at the high-frequency limit.

TABLE 2. The optical rotation, ϕ (deg. mm^{-1}), of the left-handed quartz crystal (space group $P3_12$) for radiation propagated along the trigonal c-axis as a function of wavelength, λ, and photon energy, E (eV).

λ	E/eV	ϕ/(deg. mm^{-1})	Reference
3.21 μm	0.385	−0.52	Lowry (1935)
152.5 nm	8.13	−776	Servant (1939)
154 pm	8051	−0.35	Hart and Rodrigues (1981)

The optical rotation of a given quartz crystal has the same sign in the X-ray region as in the long-wavelength transparent region (Hart and Rodrigues, 1981). Accordingly the optical activity of quartz originates from two electronic transitions, or two sets of such transitions, with rotational strengths of equal magnitude and opposed signs. Chandrasekhar (1961), using the coupled oscillator theory of Kuhn (1930), showed that the optical rotatory dispersion curve of quartz is better fitted with a two-term dispersion equation, with rotatory power constants of equal magnitude and opposite sign, than the corresponding one-term equation. The rotatory power constants of Chandrasekhar (1961) are equivalent to the rotational strengths of ± 2.28 Debye Bohr magneton per SiO_2 group, centred on 92.6 nm with a splitting of 2.8 nm, employing the radiation field correction of Lorentz (1880).

Chiral molecules are expected to rotate the polarization, not only of the photon, but also of spin-polarized fermions with a non-zero rest mass. When a neutron beam is propagated through a chiral medium, the transverse component of the neutral spin polarization is expected to precess around the beam axis, and the longitudinal component to increase or decrease monotonically. The effects are ascribed to the resonant elastic scattering by the nuclei of the chiral molecule (Kabir *et al.*, 1974), the corresponding inelastic scattering during vibrational excitations (Cox and Richardson, 1977, 1980), and scattering due to interactions of the magnetic moment of the neutron with electronic spin-orbital magnetic fields in the molecule (Harris and Stodolsky, 1979; Gazdy and Ladik, 1982). Similarly a spin-polarized electron beam propagated through a gas-phase assembly of chiral molecules is expected to undergo a spin rotation (Farago, 1980, 1981). Elastic scattering experiments with beams of 25 eV electrons on vapours of (+)-camphor and its (−)-isomer establish that the polarization change is small, less than the error margin of 0.5% (Beerlage *et al.,* 1981). In addition, the spin polarization rotation of neutrons by chiral molecules remains unconfirmed experimentally, as yet.

A spin rotation of a cold neutron beam propagated through a crystalline assembly of formally-achiral tin atoms has been detected, however, the particular isotope ^{117}Sn giving the largest rotation, $(36.7 \pm 2.7) \times 10^{-6}$ radian cm^{-1} (Stodolsky, 1981). The effect here arises from factors other than those proposed for neutron spin rotation by chiral molecules, and it is independent of the neutron energy, lacking the characteristic variation with radiation frequency displayed by optical rotation due to molecular chirality.

An accumulation of anomalies in elementary particle physics was resolved by the proposal of Lee and Yang (1956) that parity, or space-inversion equivalence, is not conserved in the weak nuclear interactions. An immediate consequence, the asymmetric β-decay of radionucleides was verified by Wu *et al.* (1957) in the decay of cobalt-60 to nickel-60 with the emission of an electron (e^-) and an antineutrino ($\bar{\nu}$),

$$^{60}\mathrm{Co} \rightarrow {}^{60}\mathrm{Ni} + e^- + \bar{\nu} \tag{3}$$

The cobalt-60 nuclei, aligned in a magnetic field at liquid He temperature, were found to emit the β-electrons preferentially by 40% in the direction antiparallel to the applied field. In the analogous β-decay of cobalt-58 to iron-58, the positrons (e^+) formed were preferentially emitted in the direction parallel to the field (Rodberg and Weisskopf, 1957). Subsequent experiments on β-decay and other weak nuclear interactions establish generally the bias towards left-chirality, antiparallel momentum and spin vectors, in the electron and right-chirality, parallel momentum and spin vectors, in the positron, proportional to the ratio of the velocity of the particle, or the antiparticle, to the velocity of light.

The weak nuclear interactions initially investigated, such as β-decay, are dependent upon the weak charged currents, involving the charged massive bosons, $W^{\pm}$, recently detected, with good probability, at CERN (Sutton, 1983). The weak charged current has only a minor, high-order, significance for charge-conserving properties. An additional weak neutral current interaction, mediated by the massive neutral boson (Z°), emerged from the unification of the weak and the electromagnetic interaction by Weinberg (1967) and Salam (1968). A consequence of the unified theory is the expectation of a parity-violating interaction of electrons with protons and neutrons, or with other electrons, which is non-vanishing in the non-relativistic limit. In particular, all atoms and achiral molecules, as well as enantiomers, are expected to be optically active to electromagnetic radiation and to polarized matter-waves.

The neutron spin-rotation given by crystals of tin is an expression of the weak neutral current interaction between the neutron and the nucleons making up the tin nucleus. The interaction produces different refractive indices of the tin for left- and right-handed neutrons, corresponding to antiparallel and parallel spin and momentum vectors. The circular birefringence gives rise to a rotation of the neutron spin component perpendicular to the direction of propagation, the angle of rotation ϕ in radians per unit pathlength being approximated by the relation,

$$\phi = \sqrt{2} G_F Q_W N \tag{4}$$

where G_F is the Fermi weak interaction constant, Q_W is the Weinberg parameter, approximately equal to the number of neutrons in the nucleus, and N is the number density of the atoms. Equation (4) contains no reference to the neutron energy. The spin rotations produced by tin were observed, in fact, with low-energy (millivolt) neutrons. The magnitude of the neutron spin rotation observed for ^{117}Sn is, however, some 3000 times larger than the estimate obtained from Eq. (4), due possibly to a resonance enhancement.

A circular birefringence implies a corresponding circular dichroism, and a difference in the rate of transmission of left- and right-handed neutrons through ^{117}Sn is tentatively reported at the level of 9×10^{-6} of the total cross-section (Stodolsky, 1981). The fraction corresponds to the dissymmetry ratio of Kuhn (1930) for optical circular dichroism ($g = \Delta\varepsilon/\varepsilon$) and it is surprisingly large, typical more of an electromagnetic than a weak interaction. An optical g-ratio of 10^{-5} is common in the infrared vibrational circular dichroism spectra of chiral organic molecules (Mason, 1982).

Further support for the unified theory of electromagnetic and weak nuclear interaction is provided by the rotation of polarized electromagnetic radiation by atoms of the heavier metals in the vapour phase (Fortson and Wilets, 1980; Sanders, 1980). The proportionality of the weak neutral current (WNC) rotation to Z^6, where Z is the atomic number, dictates the choice of heavy atoms, the cases of Cs, Tl and Bi being currently investigated.

The WNC interaction has two principal components affecting the extranuclear electrons, the electron–nucleon potential (V_{pv}^{eN}), confined to the nucleus of an atom, and the electron–electron potential (V_{pv}^{ee}), effective in the region of the K-shell of an atom, and generally negligible relative to V_{pv}^{eN}. The parity-violating potential, V_{pv}^{eN}, mixes electronic states of opposite inversion symmetry, and so lifts the mutual exclusion of a magnetic dipole moment and an electric dipole moment in a given atomic electronic transition, according to the rule of Laporte (1924). In particular, the potential V_{pv}^{eN} mixes electronic s-states, where the charge density at the nucleus is non-zero, with p-states, in which the gradient of the wavefunction is non-vanishing at the nucleus. As a consequence, an electronic transition of an atom formally allowed for a magnetic dipole radiation field by Laporte's rule, such as the $^4S_{3/2} \rightarrow {}^2D_{3/2}$ transition within the $6p^3$ ground configuration of the bismuth atom at 875.7 nm, acquires a small electric dipole component by configurational interaction through the V_{pv}^{eN} potential with Laporte-forbidden terms, such as those arising from the excited $6p^27s$ configuration of bismuth.

With a collinear mutual orientation of the parity-violating electric dipole component and the magnetic dipole component, the atomic electronic transition has a rotational strength, accessible experimentally from the circular dichroism or the optical rotatory dispersion. The ratio R of the rotational strength to the corresponding dipole strength for the 875.7 nm transition of the bismuth atom, $^4S_{3/2} \rightarrow {}^2D_{3/2}$, is small. Calculated values ($R/10^{-8}$) lie in the range -8 to -17, compared to corresponding experimental values reported between -0.7 and -12 (Hollister *et al.,* 1981). Comparable agreement between calculated and observed values of the parity-violating atomic rotation ratio R is found for the $^4S_{3/2} \rightarrow {}^2D_{5/2}$ transition within the $6p^3$ ground configuration of the bismuth atom at 647.6 nm, and the interconfiguration transition of atomic thallium, $6p_{1/2} \rightarrow 7p_{1/2}$, at 292.7 nm (Fortson and Wilets, 1980; Sandars, 1980).

VIII. ORIGINS OF MOLECULAR CHIRALITY

A number of classical mechanisms have been proposed for the transition from racemic chemistry to homochiral biochemistry in terrestrial evolution, but none of these account, in principle, for the particular choice of L-amino acids and the D-sugars (Bonner, 1972). The differential photolysis of racemates by solar radiation, circularly polarized by reflection, or the Coriolis forces due to the rotation of the earth, oppositely-signed in the two hemispheres, might generate equally an initial enantiomeric excess of D-amino acids and L-sugars, which were then propagated to dominance by chain-branching enantioselection.

A possible exception might be the initial adsorption of organic materials and the surface catalysis of their reactions by enantiomorphous mineral crystals, notably quartz, since left-handed (−)-quartz crystals are the more abundant in most localities over the surface of the earth (Palache *et al.,* 1962). The enantiomeric excess of (−)-quartz, while small (1%), is general and well-established (*Table 3*). A determination of the absolute configuration of (−)-quartz shows that the crystal belongs to the space group $P3_12$ with a right-handed threefold screw axis (de Vries, 1958), that is, the particular helicity predominantly adopted by the L-polypeptides and by the polynucleotides containing D-sugars in their helical conformations. However, the postulate that biochemical homochirality originated from quartz crystals or, more probably, from layer alumino-silicates, such as kaolinite, which has microcrystalline chirality (Cairns-Smith, 1982), serves only to generalize the problem of the origin of molecular chirality to embrace inorganic as well as organic natural products.

TABLE 3. The relative abundance of left- and right-handed quartz crystals (from Palache *et al.,* 1962)

Number of crystals examined	Twinning	% Left ($P3_12$)	% Right ($P3_22$)	Locality
6404*		50.61	49.39	Soviet Union
4442†	(Brazil)	50.05	49.95	Brazil
2415		50.68	49.32	Brazil, Colombia
1811		50.6	49.4	Switzerland
840‡	(Dauphine)	50.7	49.3	Austria
383‡	(Dauphine)	50.1	49.9	U.S., Alaska
298	(Untwinned)	50.7	49.3	U.S., Alaska
214	(Untwinned)	52.3	47.7	Austria
16 807	Weighted mean	50.5	49.5	

*Number remaining after eliminating 931 crystals from localities differing by more than 5% from the mean. The abundance of left-quartz in the total of 7335 crystals examined, including the 931 eliminated, is 51.15%.

†Data probably of low precision through the failure to recognize the true extent of Brazil twinning, where the inclusions are crystals of opposite chirality.

‡Dauphine twinning, involving reorientations of the *a* crystal axes, leaves unchanged the crystal chirality (a 3_1 or 3_2 screw axis along the *c* crystal axis).

Of the four fundamental interactions, gravitation, electromagnetism and the strong nuclear interaction are indifferent to handed structures, and only the weak interaction provides a possible basis for the physical origin of the minor inorganic chiral bias and the substantial homochirality of organic natural products. Following the discovery of parity non-conservation by Lee and Yang (1956), attention was directed to the chemical consequences of the weak charged current interaction in radioactive β-decay. Ulbricht (1959) and Vester *et al.* (1959) proposed that the circularly polarized γ-ray and X-ray Bremsstrahlung produced by the progressive retardation of the spin polarized electrons in the β-decay of radionucleides should give rise to an enantio-differentiating photolysis or radiolysis of racemates. The radiolysis products of ten different reactions, carried out with a variety of β-emitters, were found to be optically-inactive, however (Ulbricht and Vester, 1962).

Goldhaber *et al.* (1957) showed that, while the high-energy γ-ray Bremsstrahlung from a strontium-90 β-source is almost completely left-circularly polarized, the degree of circular polarization falls off progressively with increasing wavelength to the 0.01% level in the X-ray region, becoming negligible at longer wavelength. The chiral photodiscrimination between enantiomers is expected to be optimum in the visible and ultraviolet wavelength region, where the electromagnetic radiation interacts with the molecular valency electrons, and the optical activity of an enantiomer attains a maximum (*Table 2*).

Subsequent studies of the differential radiolysis of enantiomers have centred upon the amino acids. The self-radiolysis of ^{14}C-labelled amino acids gives no detectable discrimination between the enantiomers. A linear accelerator, providing a choice of electron energy and either a right- or a left-handed spin-polarized electron beam, has been employed for the differential radiolysis of racemic leucine by two different groups. The equivocal results obtained are reviewed by Bonner *et al.* (1981). Low-energy spin-polarized positron beams have been used to investigate radiolytic enantio-selectivity in amino acids (Gidley *et al.,* 1982) and other chiral organic molecules (Jean and Ache, 1977). No definite discrimination between the enantiomers is detected, contrary to some previous reports.

A curious effect ascribed to the parity non-conservation of β-decay is discussed by Kovàcs (1981). The crystallization of racemic sodium ammonium tartrate in the presence of β-radioactive ^{32}P as phosphate is reported to give an enantiomeric excess of the (−)-tartrate salt proportional to the concentration of the β-emitter. In addition, the crystal yield is enhanced in proportion to the β-emitter concentration (*Table 4*).

TABLE 4. Results of the crystallization of racemic sodium ammonium tartrate from aqueous solutions containing β-radioactive ^{32}P as phosphate, recording the mean crystal yield from standardized solutions and the enantiomeric excess of the (−)-(2*S*, 3*S*)-tartrate salt, determined from the positive circular dichroism or ellipticity $< \theta >$ at 215 nm of the (−)-tartrate ion in solution (from Kovàcs, 1981)

Initial ^{32}P radioactivity (mC$_i$/sample)	Number of samples crystallized	Mean yield (g)	Mean CD $<\theta>_{215}$(deg.)	Percent optical purity
0.1	149	0.1964	+ 2.41	3.5
0	149	0.1900	+ 0.47	0.7
1.6	146	0.2331	+ 11.90	17.4
0	149	0.1846	− 0.08	0.1
5.0	137	0.3324	+ 16.07	23.5
0	141	0.2558	+ 0.11	0.2

The unification of the electromagnetic and the weak interaction through the introduction of the weak neutral current by Weinberg (1967) and Salam (1968) implied not only the universality of optical activity in all atoms, whether free or bonded, but also a difference between the electronic binding energy of enantiomeric molecules. The true isoenergetic antimer of a chiral molecule composed of electrons and other particles came to be perceived as the mirror-image structure of positrons and other antiparticles in a counter-world of antimatter (Barron, 1981). The electromagnetic energy degeneracy of enantiomeric molecules is lifted by the WNC coupling of the electromagnetic to the weak nuclear interaction, the parity-violating energy shift, ΔE_{pv}, adding to the electromagnetic energy of one isomer and subtracting from that of its enantiomer.

Approximate order-of-magnitude estimates of the energy shift ΔE_{pv} were made by Rein (1974) and, in more detail, by Zel'dovich *et al.* (1977). The latter workers found that the main contribution to ΔE_{pv} derives from the electron–nucleon component of the WNC interaction, V_{pv}^{eN}, which couples the electron spin to the nuclear charge, involving the spin-orbit interaction, V_{so}. For a closed-shell enantiomer, with the singlet ground state $|O>$, and a manifold of excited triplet states $|T>$, with an energy ΔE_{OT} above the ground state, the parity-violating shift has the form,

$$\Delta E_{pv} = \sum_{T} < O\,|V_{pv}^{eN}|\,T> \, < T\,|V_{so}|\,O > / \Delta E_{OT} \qquad (5)$$

As the spin-orbit interaction is approximately proportional to Z^2, and V_{pv}^{eN} to Z^3, where Z is the atomic number, the energy shift is expected to be appreciable in enantiomers containing heavy atoms. An approximate estimate is afforded by the relation,

$$\Delta E_{pv} \sim (\eta Z^5) 10^{-18} (\mathrm{eV}) \qquad (6)$$

where η is a chirality factor dependent upon the dissymmetric molecular environment of the heavy atom and the WNC mixing of opposite-parity electron functions at the nucleus of that atom. Zel'dovich *et al.* (1977) adopted a crystal-field model for an estimate of the chirality factor, finding that $\Delta E_{pv} \sim 10^{-12}$ eV for heavy-atom molecules with $\eta \sim 10^{-2}$.

The more detailed estimates of ΔE_{pv} by Hegstrom *et al.* (1980) are considerably smaller. These estimates are based upon an expansion of the state functions $|O>$ and $|T>$ in Eq. (5) over the set of molecular spin orbitals, followed by a summation over the magnetic spin components, $M_s = 0, \pm 1$, of the excited triplet configurations. These procedures give the WNC energy shift, ΔE_{pv}, in terms of the parity-violating strengths, P_{jk}, of virtual electronic transitions connecting an occupied MO, ψ_j, to an unoccupied MO, ψ_k, with the energies ε_j and ε_k, respectively,

$$\Delta E_{pv} = [G_F/(m_e c 2\sqrt{2})] \sum_j \sum_k P_{jk}/(\varepsilon_j - \varepsilon_k) \qquad (7)$$

Each parity-violating strength, P_{jk}, is obtained by a summation over the individual atomic centres a and b in the molecule.

$$P_{jk} = \sum_a \sum_b Q_w^a < \psi_j | \{\mathbf{p}, \delta^3(\mathbf{r}_a)\}_+ | \psi_k > < \psi_k | \xi(\mathbf{r}_b) \ell_b | \psi_j > \qquad (8)$$

where $\{\ \}_+$ denotes an anticommutator. In Eq. (8), Q_w^a refers to the weak charge or Weinberg parameter of atom a, **p** is the electronic momentum, and the Dirac delta function represents the electronic charge density at the nucleus a. The orbital angular momentum of an electron round nucleus b, with the spin-orbit coupling parameter, ξ, is denoted by ℓ_b.

The parity-violating strengths, P_{jk}, are signed pseudosoalar quantities, like the rotational strengths governing optical activity, R_{jk}, and they similarly represent the scalar product of an axial and a polar vector transitional quantity. The strengths, P_{jk}, are evaluated by expanding the MOs, ψ_j and ψ_k, over the constituent AOs, and by summing over the two-centre terms of Eq. (8), each term being weighted by the product of the LCAO coefficients, $C_{ja}C_{ka}C_{jb}C_{kb}$. The one-centre terms from Eq. (8), for $a = b$, are smaller by more than an order of magnitude, and they vanish with a pure *sp* basis set, if the three AOs of each *np* subset remain degenerate (Hegstrom *et al.*, 1980).

Applied to the molecular orbitals of a model chiral ethylene molecule, twisted through + 10° to D_2 symmetry (Bouman and Hansen, 1977), and to those of the dialkyl sulphide chromophore, C-S-C, of A-nor-2-thiacholestane (Rosenfeld and Moscowitz, 1972), Eq. (7) gives the (*R*)-isomer of the twisted ethylene an energy higher by 10^{-18} eV than that of the (*S*)-enantiomer, and a ΔE_{pv} stabilization of -6×10^{-21}eV is obtained for the thiacholestane (Hegstrom *et al.*, 1980). The chirality factor, η (Eq. 6), has the value $+3 \times 10^{-4}$ for the (*R*)-twisted ethylene and -2×10^{-8} for the thiachlolestane, values substantially smaller than the magnitude order of 10^{-2}, estimated by Zel'dovich *et al.* (1977).

Subsequent calculations of the parity-violating energy shift (ΔE_{pv}, Eq. 7) have been carried out for a number of small chiral molecules (Tranter, 1983) using the GAUSSIAN 76 computer program (Binkley *et al.*, 1978). Trial runs on hydrogen peroxide (H_2O_2) over a range of conformations showed that the STO–N–31G basis sets, but not the STO–NG sets, give ΔE_{pv} values which converge as the number (N) of Gaussian functions is increased over the standard bound, $4 \leq N \leq 6$, towards the corresponding value obtained with an extended basis set (Mason and Tranter, 1983a). The results obtained, and compared with subsequent runs on hydrogen disulphide (H_2S_2) in *Figure 4,* show not only that ΔE_{pv} is sensitive to molecular conformation, but also that ΔE_{pv} is more nearly proportional to Z^6 than to Z^5 (Eq. 6). The integrated areas of the curves relating ΔE_{pv} to the conformational variable, the dihedral angle, ϕ, for H_2S_2 and H_2O_2 lie in the ratio of 60.8 (*Fig. 4*).

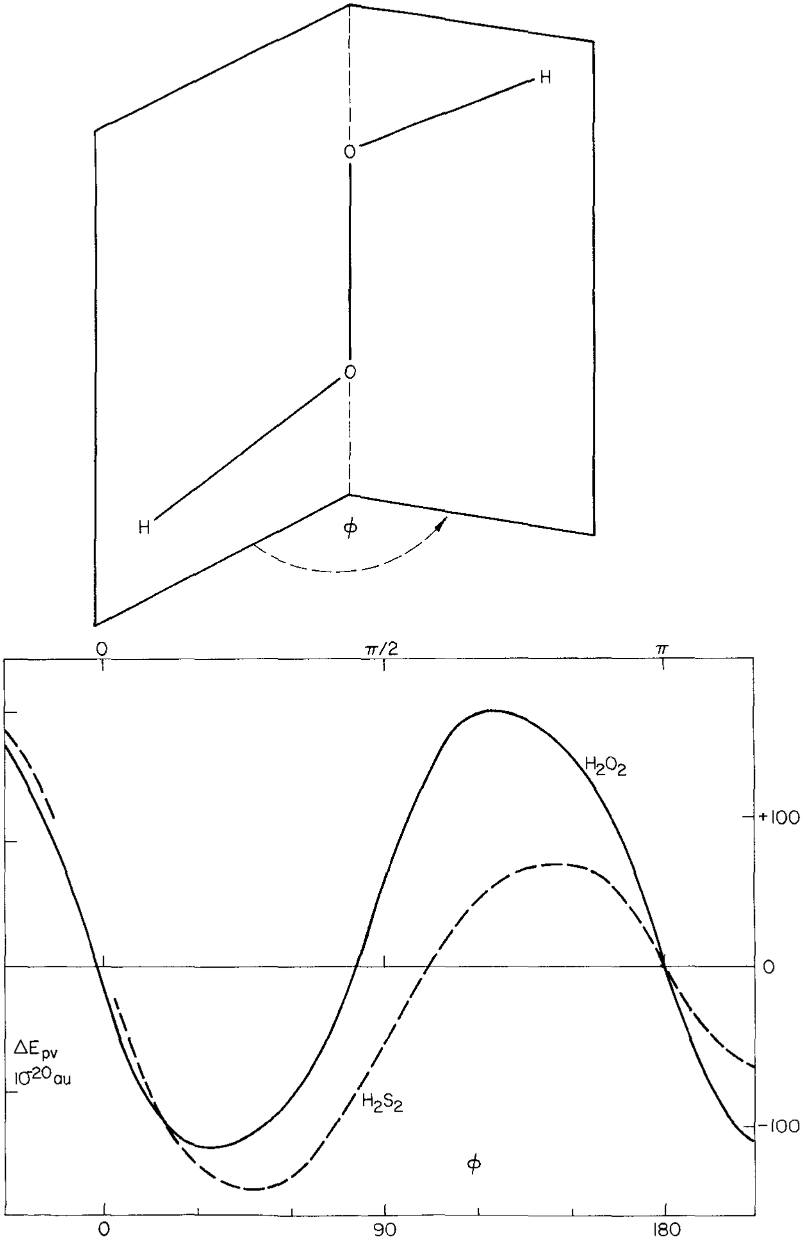


FIG. 4. The variation of the parity-violating energy shift, ΔE_{pv} (10^{-20} a.u.), with the dihedral angle, ϕ, between the HOO planes of hydrogen peroxide, or the corresponding planes of hydrogen disulphide. The left-hand ΔE_{pv} scale refers to H_2O_2 and the corresponding right-hand scale to H_2S_2.

The application of Eq. (7) to L-alanine and the chiral conformations of glycine confirms the sensitivity of ΔE_{pv} to molecular conformation (*Fig. 5*). At the preferred conformation in aqueous solution, where the torsion angle of the carboxylate group around the bond to the α-carbon atom, ϕ, is approximately zero, L-alanine is more stable than the D-enantiomer by *c.* -6×10^{-19} eV (*Fig. 5*). Extended to the peptide unit of a polypeptide in the α-helix or the β-sheet conformation, it is found that polypeptides from the L-amino acids are stabilized relative to the corresponding enantiomers composed of the D-amino acids in both of the conformations by *c.* -9×10^{-20} eV per peptide unit in the polymer (Mason and Tranter, 1983b).

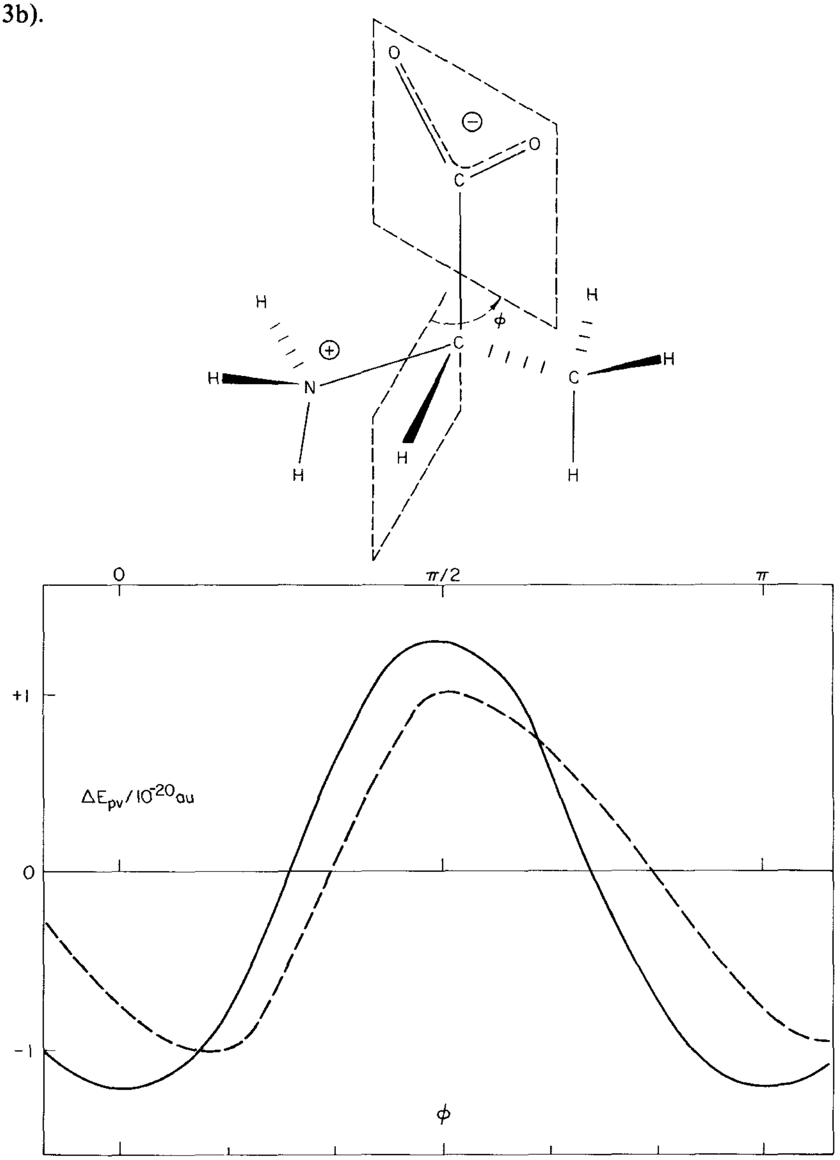


FIG. 5. The relation between the parity-violation energy shift, ΔE_{pv} (10^{-20} a.u.), and the torsion angle, ϕ, of the carboxylate group plane about the bond to the α-carbon atom in L-alanine (full line) and in glycine (broken line).

These parity-violating energy differences between enantiomers amount to no more than *c.* -2×10^{-14} J mol^{-1} per amino acid residue in the polymer, and they correspond to an enantiomeric excess of some 10^6 L-peptide molecules per mole of racemate in thermodynamic equilibrium at ambient temperature. Howsoever small, the enantiomeric excess illustrates a determinate intrinsic bias in organic nature with the particular handedness that in fact evolved into homochiral dominance.

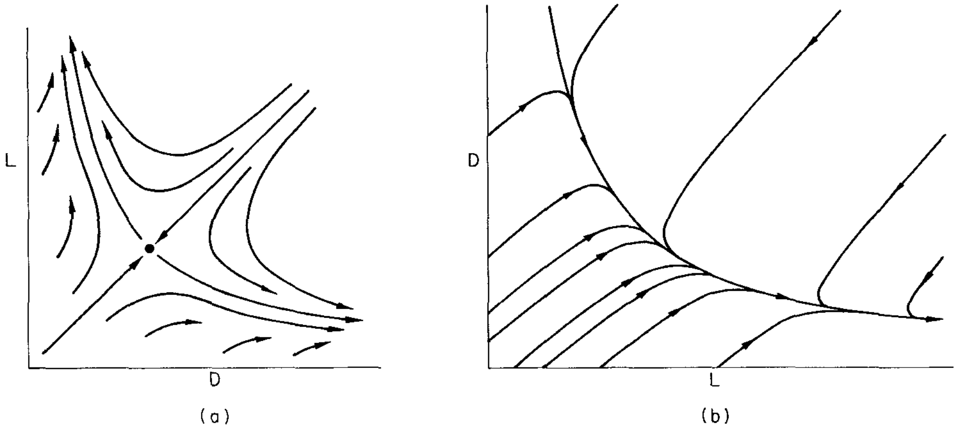
The minor enantiomer excess provides the miniscule perturbation required for a causal resolution of the racemic metastability, otherwise subject to chance events, in kinetic mechanisms for the time-evolution of L-peptide dominance, based upon the catastrophe-theory concepts introduced by Frank (1953). These mechanisms, reviewed by Fajszi and Czégé (1981) envisage the stereospecific autocatalytic production of a chiral molecule with mutual inhibition in the formation of the two enantiomers,

$$d[L]/dt = (k_1 - k_2[D])\,[L] \tag{9a}$$

and,

$$d[D]/dt = (k'_1 - k'_2[L])\,[D] \tag{9b}$$

If each of the rate constants in a pair are equal, $k_1 = k'_1$ and $k_2 = k'_2$, and the substrate is achiral or a racemate, a metastable racemic product evolves continuously in time (*Fig. 6a*). If, however, there is a minor inequality between the two rate constants of one or both pairs, or a minor excess of one enantiomer in the substrate or in the product, the time evolution of the kinetic processes of Eq. (9) drives the system towards homochirality (*Fig. 6b*).



(a) (b)

FIG. 6. The time evolution of L and D enantiomers according to the autocatalytic mechanism, with enantiomeric inhibition, of Eq. (9), (a) with identical values of the paired rate constants, k_1 and k_1', and k_2 and k_2', and equal enantiomer concentrations, and (b) with an inequality between the two rate constants of either pair, or between the enantiomer concentrations.

The application of kinetic bifurcation theory (Prigogine, 1980) to an autocatalytic reaction sequence with a metastable racemic output, as in Eq. (9), provides an estimate of the perturbation required to break the chiral symmetry of the racemic product. A strong chiral selectivity is found to emerge if the difference between the reaction activation energy for the two enantiomers is not smaller than 10^{-14} J mol^{-1} at ambient temperature or, more generally, if $\Delta E/kT \geq 10^{-17}$ (Kondepudi and Nelson, 1983). That is, the parity-violating energy difference found between the D- and the L-amino acid enantiomers, or between the corresponding monomers of the polypeptides in the α-helix or the β-sheet conformation, suffices to account for the evolution of L-peptide predominance.

REFERENCES

AMAYA, K., TAKAGI, S. and FUJISHIRO, R., (1968). *J. Chem. Soc. Chem. Comm.*, 480.

AMPÈRE, A.M. (1814). *Annal. de Chimie, 90,* 43 (Eng. trans. by S.H. Mauskopf, 1969, *Isis, 60,* 61–74).

ARMARIGLIO, A., ARMARIGLIO, H. and DUVAL, X. (1968). *Ann. Chim., 3,* 5.

ATIK, Z. (1982). Ph.D. Thesis, University of London.

ATIK, Z., EWING, M.B. and McGLASHAN, M.L. (1981). *J. Phys. Chem., 85,* 3300.

ATKINS, P.W. (1980). *Chem. Phys. Lett., 74,* 358

BARANOVA, N.B., BOGDANOV, YU. V. and ZEL'DOVICH, B. YA. (1977). *Optics Comm., 22,* 243

BARANOVA, N.B. and ZEL'DOVICH, B. YA. (1978). *Chem. Phys. Lett., 57,* 435.

BARLOW, W. (1897). *Proc. Roy. Dublin Soc.,* n.s., *8,* 527.

BARRON, L.D. (1981). *Chem. Phys. Lett., 79,* 392; *Molec. Phys., 43,* 1395.

BARRON, L.D. (1982). *Molecular Light Scattering and Optical Activity,* Cambridge University Press.

BEERLAGE, M.J.M., FARAGO, P.S. and VAN DER WIEL, M.J. (1981). *J. Phys., B14,* 3245.

BELSKY, V.K. (1974). *J. Struct. Chem., 15,* 631.

BELSKY, V.K. and ZORKII, P.M. (1977). *Acta. Cryst., A33,* 1004.

BERNAL, J.D. (1953). Molecular asymmetry. In *Science and Industry in the Nineteenth Century,* pp. 181–219. London: Routledge and Kegan Paul.

BERTHELOT, M. (1885). *Les Origines de l'Alchemie,* p. 51. Paris: Georges Steinheil.

BERZELIUS, J.J. (1831). *Annal. de Chimie, 46,* 113–147; and letter to Mitscherlich (28 May, 1830) quoted by Mauskopf (1976) and by Bernal (1953).

BINKLEY, J.S., WHITEHEAD, R.A., HARIHARAN, P.C., SEEGER, R., POPLE, J.A., HEHRE, W.J. and NEWTON, M.D. (1978). *Quant. Chem. Prog. Exch., 11,* 368.

BOLTZMANN, L. (1874). *Pogg. Ann. Phys. Chem. Jubelband,* 128.

BONNER, W.A. (1972). Origins of molecular chirality. In *Exobiology* (ed. C. Ponnamperuma) ch. 6, p. 170, Amsterdam: North-Holland.

BONNER, W.A., BLAIR, N.E. and DIRBAS, F.M. (1981). *Origins of Life, 11,* 119.

BOUMAN, T.D. and HANSEN, A.E. (1977). *J. Chem. Phys., 66,* 3460.

BRAVAIS, A. (1850, 1851). *J. École Polytechnique, 19,* 1; and *20,* 101.

BUCKINGHAM, A.D. (1979). *Nonlinear Behaviour of Molecules, Atoms and Ions in Electric, Magnetic or Electromagnetic Fields* (ed. L. Neel), p. 217. Amsterdam: Elsevier.

BUCKINGHAM, A.D. and JOSLIN, C.G. (1981). *Chem. Phys. Letters, 80,* 615.

BUCKINGHAM, A.D. and SHATWELL, R.A. (1980). *Phys. Rev. Lett., 45,* 21.

BUCKINGHAM, A.D. and SHATWELL, R.A. (1983). *J. Chem. Phys., 78,* 3393.

BURKE, J.G. (1966). *Origins of the Science of Crystals.* Berkeley and Los Angeles: University of California Press.

CAIRNS-SMITH, A.G. (1982). *Genetic Takeover and the Mineral Origins of Life.* Cambridge University Press.

CHANDLER, D. (1978). *Ann. Rev. Phys. Chem., 29,* 441.

CHANDRASEKHAR, S. (1961). *Proc. Roy. Soc., A259,* 531.

CONGER, G.P. (1922). *Theories of Macrocosms and Microcosms in the History of Philosophy,* p. 3. New York: Columbia University Press.

CONDON, E.U. (1937). *Rev. Mod. Phys., 9,* 432.

COPAUX, H. (1910). *Bull. Soc. Mineral. France, 33,* 167.

COTTON, A. (1895, 1896). *Compt. Rend. Paris, 120,* 989 and 1044; *Ann. Chim. Phys., 8,* 347.

COTTON, A. (1909). *J. Chim. Physique, 7,* 81.

COX, J.N. and RICHARDSON, F.S. (1977). *J. Chem. Phys., 67,* 5702 and 5714.

COX, J.N. and RICHARDSON, F.S. (1980). *J. Chem. Phys., 73,* 1591.

CRAIG, D.P. and ELSUM, I.R. (1982). *Chem. Phys., 73,* 349.

CRAIG, D.P., POWER, E.A. and THIRUNAMACHANDRAN, T. (1971). *Proc. Roy. Soc. London, A322,* 165.

CURIE, P. (1894). *J. Physique, 3,* 409.

DE GENNES, P.G. (1970). *Compt. Rend. Paris, B270,* 891.

DELÉPINE, M. (1949). *Vie et Oeuvres de Joseph Achille Le Bel.* Paris: Paul Dupont.

DE VRIES, A. (1958). *Nature, 181,* 1193.

DOUGHERTY, R.C. (1980). *J. Am. Chem. Soc., 102,* 380.

DRUDE, P. (1893). *Ann. Physik, 48,* 536; *50,* 595.

DUNITZ, J.D. (1979). *X-ray Analysis and the Structure of Organic Molecules,* p. 366 ff. Ithaca and London: Cornell University Press.

EASSON, L. and STEDMAN, E. (1933). *Biochem. J., 27,* 1257.

EDWARDS, D., COOPER, K. and DOUGHERTY, R.C. (1980). *J. Am. Chem. Soc., 102,* 381.

EVANS, G.J. and EVANS, M. (1983). *Chem. Phys. Lett., 96,* 416.

EVANS, M.W. (1983). *J. Chem. Soc. Chem. Comm.,* 139.

FAJSZI, C. and CZÉGÉ, J. (1981). *Origins of Life, 11,* 143.

FARADAY, M. (1846). *Phil. Mag., 28,* 294.

FARAGO, P.S. (1980). *J. Phys., B13,* L567.

FARAGO, P.S. (1981). *J. Phys., B14,* L743.

FEDOROV, E.S. (1891). *Trans. Mineral. Soc., 28,* 1.

FISCHER, E. (1894). *Chem. Ber., 27,* 2985 and 3231.

FISCHER, E. (1907). *J. Chem. Soc., 91,* 1749.

FORTSON, E.N. and WILETS, L. (1980). *Adv. Atomic Molec. Phys., 16,* 319.

FRANK, F.C. (1953). *Biochem. Biophys. Acta, 11,* 459.

FRIEDEL, G. (1913). *Compt. Rend. Paris, 157,* 1533.

GAZDY, B. and LADIK, J. (1982). *Chem. Phys. Lett., 91,* 158.

GERIKE, P. (1975). *Naturwissenschaften, 62,* 38.

GIDLEY, D.W., RICH, A., VAN HOUSE, J. and ZITZEWITZ, P.W. (1982). *Nature, 297,* 639.

GOLDHABER, M., GRODZINS, L., SUNYAR, A.W. and McVOY, K.W. (1957). *Phys. Rev., 106,* 826 and 828.

GRIGNARD, V. (1901). *Ann. Chim., 24,* 433.

HARRIS, R.A. and STODOLSKY, L. (1979). *J. Chem. Phys., 70,* 2789.

HART, M. and RODRIGUES, A.R.D. (1981). *Phil. Mag., B43,* 321.

HAÜY, R.J. (1809). *Tableau Comparatif des Résultats de la Cristallographie et de l'Analyse Chimique relativement a la Classification des Minèraux,* Paris, p. xvii.

HEGSTROM, R.A., REIN, D.W. and SANDARS, P.G.H. (1980). *J. Chem. Phys., 73,* 2329.

HERSCHEL, J.W.F. (1822). *Trans. Cambridge Phil. Soc., 1,* 43.

HESSEL, J.F.C. (1831). *Krystallometrie, oder Krystallonomie und Krystallographie.* Ostwald's Klassiker der Exakten Wissenschaften, Nos. 88 and 89, Leipzig, 1897.

HOLLISTER, J.H., APPERSON, G.R., LEWIS, L.L., EMMONS, T.P., VOLD, T.G. and FORTSON, E.N. (1981). *Phys. Rev. Lett., 46,* 643.

HONDA, C. and HADA, H. (1976). *Tetrahedron Lett., 16,* 177.

HOREAU, A. and GUETTÉ, J.P. (1974). *Tetrahedron, 30,* 1923.

JACQUES, J., COLLET, A. and WILEN, S.H. (1981a). *Enantiomers, Racemates, and Resolutions.* New York: Wiley.

JACQUES, J., LECLERCQ, M. and BRIENNE, M.-J. (1981b). *Tetrahedron, 37,* 1727.

JAPP, F.R. (1898). *Nature, 58,* 482.

JEAN, Y.-C. and ACHE, H.-J. (1977). *J. Phys. Chem., 81,* 1157.

JONES, R.V. (1976). *Proc. Roy. Soc., A349,* 423.

KABIR, P.K., KARL, G. and OBRYK, E. (1974). *Phys. Rev. D10,* 1471.

KITAIGORODSKY, A.I. (1973). *Molecular Crystals and Molecules.* London: Academic Press.

KONDEPUDI, D.K. and NELSON, G.W. (1983). *Phys. Rev. Lett., 50,* 1023.

KOVÁCS, K.L. (1981). *Origins of Life, 11,* 37.

KOVÁCS, K.L., KESZTHELYI, L. and GOLDANSKII, V.J. (1981). *Origins of Life, 11,* 93.

KUHN, W. (1929). *Z. Phys. Chem., B4,* 14.

KUHN, W. (1930). *Trans. Faraday Soc., 26,* 293.

KUHN, W. and BRAUN, F. (1929). *Naturwissenschaften, 17,* 227.

KUHN, W. and KNOPF, E. (1930). *Z. Phys. Chem., B7,* 292.

KURODA, R., MASON, S.F., RODGER, C.D. and SEAL, R.H. (1978). *Chem. Phys. Lett., 57,* 1; *Molec. Phys., 42,* 33 (1981).

LAPORTE, O. (1924). *Z. Physik, 51,* 512.

LE BEL, J.A. (1874). *Bull. Soc. Chim. France, 22,* 337.

LE BEL, J.A. (1890). *Bull. Soc. Chim. France, 3,* 788; and (1892) *7,* 613.

LE BEL, J.A. (1925). *Bull. Soc. Chim. France, 37,* 353.

LEE, T.D. and YANG, C.N. (1956). *Phys. Rev., 88,* 101.

LORENTZ, H.A. (1880). *Ann. Physik, 9,* 641.

LOWRY, T.M. (1935). *Optical Rotatory Power.* London: Longmans, Green and Co. New York: Dover Reprint (1964).

McKENZIE, A. (1904). *J. Chem. Soc., 85,* 1249.

MASON, S.F. (1964). *Proc. Chem. Soc.,* 119.

MASON, S.F. (ed.) (1979). *Optical Activity and Chiral Discrimination,* NATO ASI Series C, p. 322. Dordrecht: Reidel.

MASON, S.F. (1982). *Molecular Optical Activity and the Chiral Discriminations.* Cambridge University Press.

MASON, S.F. and TRANTER, G.E. (1983a). *Chem. Phys. Letters, 94,* 34.

MASON, S.F. and TRANTER, G.E. (1983b). *J. Chem. Soc. Chem. Comm., 117.*

MATSUMOTO, M. and AMAYA, K. (1980). *Bull. Chem. Soc. Japan, 53,* 3510.

MAUSKOPF, S.H. (1976). *Trans. Amer. Phil. Soc. 66,* Pt. 3, 1–82.

MAVROYANNIS, C. and STEPHEN, M.J. (1962). *Molec. Phys.,* 5, 629.

MEAD, C.A. and MOSCOWITZ, A. (1980). *J. Am. Chem. Soc., 102,* 7301.

MEAD, C.A., MOSCOWITZ, A., WYNBERG, H. and MEUWESE, F. (1977). *Tetrahedron Lett., 17,* 1063.

MENGER, F.M. (1983). *Tetrahedron, 39,* 1013 (Tetrahedron Report No. 145).

MITSCHERLICH, E. (1844). *Compt. Rend. Paris, 19,* 719.

NORDEN, B. (1978). *J. Phys. Chem., 82,* 744.

OGSTON, A.G. (1948). *Nature, 162,* 963.

PALACHE, C., BERMAN, H. and FRONDEL, C. (1962). *Dana's System of Mineralogy,* 7th edn., vol. III, p. 16. New York: J. Wiley.

PARTINGTON, J.R. (1961). *A History of Chemistry,* vol. II, p. 371. London: Macmillan.

PASTEUR, L. (1848). *Compt. Rend. Paris, 26,* 535, *Oeuvres de Pasteur, I,* Dissymétrie Moléculaire (ed. Pasteur Vallery-Radot), pp. 61–64. Paris: Masson et Cie, (1922).

PASTEUR, L. (1853). *Ann. Chim. Phys., 38,* 437, *Oeuvres, I,* 203–241.

PASTEUR, L. (1858). *Compt. Rend. Paris, 46,* 615.

PASTEUR, L. (1860). Recherches sur la Dissymétrie Moléculaire, *Oeuvres, I,* 314–344. Eng. trans., Alembic Club Reprint, No. 14, Livingston, Edinburgh (1948).

PASTEUR, L. (1884a). *Rev. Scientifique, 7,* 2. *Oeuvres, I,* 369–380.

PASTEUR, L. (1884b). *Bull. Soc. Chim. France, 41,* 215. *Oeuvres, I,* p. 385.

PERES, A. (1980). *J. Am. Chem. Soc., 102,* 7389.

POPE, W.J. (1898). *J. Chem. Soc., 73,* 606.

PRELOG, V. (1953). *Helv. Chim. Acta, 36,* 308.

PRIGOGINE, I. (1980). *From Being to Becoming: Time and Complexity in the Physical Sciences,* p. 103 ff. San Francisco: W.H. Freeman and Co.

REIN, D.W. (1974). *J. Mol. Evol., 4,* 15.

RHODES, W. and DOUGHERTY, R.C. (1978). *J. Am. Chem. Soc., 100,* 6247.

RITCHIE, P.D. (1933). *Asymmetric Synthesis and Asymmetric Induction.* London: Oxford University Press.

RITCHIE, P.D. (1947). *Adv. Enzymol, 7,* 65.

RODBERG, L.S. and WEISSKOPF, V.F. (1957). *Science, 125,* 627.

ROSENFELD, J.S. and MOSCOWITZ, A. (1972). *J. Am. Chem. Soc., 94,* 4797.

ROSENFELD, L. (1928). *Z. Physik, 52,* 161.

SALAM, A. (1968). In *Proc. 8th Nobel Symposium; Elementary particle theory* (ed. N. Svartholm). Stockholm: Almquist and Wiksell.

SANDARS, P.G.H. (1980). *Fundamental Interactions and Structure of Matter* (ed. K. Crowe, J. Cuclos, G. Fiorentini and G. Torelli) p. 57. New York: Plenum Press.

SCACCHI, A. (1865). *Atti Accad. Sci. Napoli, 4,* 250.

SCHIPPER, P.E. (1977). *Chem. Phys., 26,* 29.

SCHIPPER, P.E. (1982). *Austral. J. Chem., 35,* 1513.

SCHIPPER, P.E. and HARROWELL, P.R. (1983). *J. Am. Chem. Soc., 105,* 723.

SCHOENFLIES, A. (1891). *Kristallsysteme und Kristallstruktur.* Leipzig.

SERVANT, R. (1939). *Ann. Phys. Paris, 12,* 397.

SOHNCKE, L. (1879). *Die Entwicklung einer Theorie der Kristallstruktur.* Leipzig.

STODOLSKY, L. (1981). *Nature, 290,* 735.

SUTTON, C. (1983). *New Scientist, 97,* 221 and 355.

TRANTER, G.E. (1983). Ph.D. Thesis, University of London.

ULBRICHT, T.L.V. (1959). *Quart. Rev. Chem. Soc., 13,* 48.

ULBRICHT, T.L.V. and VESTER, F. (1962). *Tetrahedron, 18,* 629.

VAINSHTEIN, B.K. (1981). *Modern Crystallography,* vol. I. Berlin: Springer.

VAINSHTEIN, B.K., FRIDKIN, V.M. and INDENBOM, V.L. (1982). *Modern Crystallography,* vol. II. Berlin: Springer.

VAN'T HOFF, J.H. (1874). *Arch. Néeland. Sci. Exact. Nat., 9,* 445.

VESTER, F., ULBRICHT, T.L.V. and KRAUCH, H. (1959). *Naturwissenschaften, 46,* 48.

WALLACH, O. (1895). *Annalen, 286,* 140.

WEINBERG, S. (1967). *Phys. Rev. Lett., 19,* 1264.

WU, C.S., AMBLER, E., HAYWARD, R.W., HOPPES, D.D. and HUDSON, R.P. (1957). *Phys. Rev., 105,* 1413.

WYROUBOFF, G. (1896). *Bull. Soc. Mineral. France, 19,* 219.

ZEL'DOVICH, B. YA, SAAKYAN, D.B. and SOBEL'MAN, I.I. (1977). *JETP Lett., 25,* 94.

ZORKII, P.M., RAZUMAEVA, A.E. and BELSKY, V.K. (1977). *Acta Cryst. A33,* 1001.