

On Chirality and the Universal Asymmetry

Reflections on Image
and Mirror Image

Georges H. Wagnière



Verlag Helvetica Chimica Acta · Zürich



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Preface

This book deals with the ubiquitous phenomenon of chirality and the distinction between image and mirror image. It is neither aimed at being a textbook nor a specialized scientific review. Rather, it is to be considered as an excursion through nature and the universe and an attempt at gaining an overview over the vast fields and expanses where chirality is encountered.

The author being a physical chemist, the focus of the book is essentially molecular. The chapters of the book that deal with elementary particle physics, with astrophysics and cosmology, with biochemistry and biology, are consequently written by a nonspecialist who has also had to rely on secondary literature or on primary sources outside his specialty. If any errors have thereby crept in, they are exclusively the responsibility of the user of these sources.

In general, the choice of scientific references is subjective, sometimes also based on pedagogical considerations and depending on immediate accessibility. An effort has been made to consider references that are as recent as possible. But where a given historic development has appeared particularly interesting and instructive, older references are also included.

It is hoped that this text will be accessible to anyone who has had the equivalent of a first-year university instruction in physics and chemistry. Some elementary knowledge of crystallography will be helpful. On account of the variety of particular subjects, the focus differs from one chapter of the book to the next, as here indicated:

<i>Chapt. 1:</i>	Stereochemical and biochemical
<i>Chapt. 2 and 3:</i>	Physical
<i>Chapt. 4:</i>	Structural and physical; <i>Sect. 4.1</i> and <i>4.2</i> contain some central ideas on symmetry
<i>Chapt. 5:</i>	Astrophysical
<i>Chapt. 6:</i>	Geophysical
<i>Chapt. 7:</i>	Structural, chemical, and physical
<i>Chapt. 8:</i>	Structural, chemical, and physical
<i>Chapt. 9:</i>	Structural and biochemical
<i>Chapt. 10:</i>	Astro- and geophysical; structural and biochemical

This book needs not to be ‘linearly’ read from A to Z. Depending on inclination and taste, the reader may skip certain chapters, while concentrating on others. Mathematical equations may be overlooked. They are not essential to obtain a general view of the phenomenon and its significance. A glossary of scientific terms at the end of the text should be helpful for the nonspecialized

reader. Although all aspects of chirality are related to each other in some way, there is no preset sequence to be followed. For excursions through nature, different trails may be chosen.

The subject of natural optical activity and of chirality, discovered about two centuries ago, is presently as topical as ever. The writing of this book was a long-headed plan. It was stimulated by the possibility to participate in the research initiative ‘Chiral-2’ on enantioselective chemistry of the *Swiss National Science Foundation*. I also much appreciate and herewith gratefully acknowledge the recent hospitality of the *High Magnetic Field Laboratory* in Grenoble, France, and the fruitful collaboration with *Geert L. J. A. Rikken* on the magnetochiral effect and related optical phenomena. I thank *André Dreiding* and *Karl-Heinz Ernst* for drawing my attention to particular aspects of molecular chirality, as well as *Bart van Tiggelen* and *Günther Rasche* for instructive conversations on symmetry laws in physics. Much inspiration was also given me by other colleagues and former students, most recently by *Stanisław Woźniak*, *Peter Kleindienst*, and *Nikolai Kalugin*.

I thank *Barbara Huber* who told me about the detective story of ‘The Documents in the Case’ by *Dorothy L. Sayers*, in which the mystery of a poisoning with muscarine was solved by a polarimetric measurement (*Sect. 1.5*). I am grateful to my wife *Marie-Louise* for her kind patience while I was writing this book, and for pointing out the *Thérèse de Dillmont* reference on lace and embroidery (*Sect. 10.1*).

A book needs not only to be written. To present it to the reader, it must also be edited and printed. I am extremely grateful to *M. Volkan Kisakürek* for having outstandingly carried out this task. My thanks also go to *Richard J. Smith* and *Thomas Kolitzus* for their excellent assistance and counsel, and to *Peter M. Wallimann* for his careful technical support.

Zurich, January 2007

Georges H. Wagnière

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Introduction

'Ah, not in knowledge is happiness, but in the acquisition of knowledge!'

Edgar Allan Poe (1809–1849)

That the world is asymmetric is a trivial observation. How can the world be anything but asymmetric? What would a totally symmetric universe be like? A homogeneous gas? A perfect crystal? Celestial bodies all of the same mass, regularly spaced, coherently moving on perfect circular orbits? The world is asymmetric, because anything else would be unthinkable, including our own human existence.

This asymmetry being a fundamental property of the universe, there is, however, a basic question which, to this day, has not been satisfactorily answered.

According to most laws of physics, any asymmetric object or any asymmetrically moving system could, in principle, exist with equal probability as the corresponding mirror object or mirror system. The laws of *gravitation*, of *electromagnetism*, and the *strong interactions*, governing the structure of atomic nuclei, predict that image and mirror image should have exactly the same energy, and consequently show the same probability of occurring. So then, why would we be living in the world as it is, and not in the mirror world? Or why could not the actual world and the mirror world coexist and be both simultaneously perceptible?

Not before the second half of the 20th century was it discovered that the fourth kind of forces observable in the universe, the so-called *weak interactions*, indeed do distinguish between image and mirror image. But from the point of view of our everyday perception of reality, these weak forces are somewhat esoteric. They govern processes between elementary particles, such as β -decay or the emission of neutrinos, and they act on distances that are almost infinitesimally small. Is the macroscopic asymmetry of the world we live in really the – more or less direct or indirect – consequence of these weak interactions? If yes, how do these interactions, which are operative on such a small scale, then get amplified, so as to shape the whole world we live in, from submicroscopic domains to the dimensions of galaxies?

The scientific endeavor of man aims at a better understanding of his own nature and of the universe he inhabits. One cannot study the one without considering the other. To obtain answers, one must ask questions. Aiming at new answers, one must ask questions deriving from previous answers. We here do not have the ambition to give any new answers, but merely to ask questions based on recently established scientific knowledge.



What we here propose to do is an excursion through nature, in order to observe some of the many ways in which asymmetry manifests itself. We will then immediately realize that our understanding of asymmetry is based on a search for symmetry. This is the way our perception functions. Asymmetry can be understood only as a deviation, or a departure, from what is symmetric, ordered, and clear.

We will start our excursion on Earth, in the chemistry and the physics laboratory. Then we shall venture out into deep space, and back in time. This should broaden our horizon. With an enlarged perspective, we will return to Earth. Our contemplation of the extraordinary richness and complexity of the world, which immediately surrounds us, and which we are part of, is directly connected to our wish and intention to understand it.

1. Image and Mirror Image in Molecules

‘C’est la dissymétrie qui crée le phénomène. Lorsque certains effets révèlent une certaine dissymétrie, cette dissymétrie doit se retrouver dans les causes qui lui ont donné naissance’.

(‘It is the dissymmetry that creates the phenomenon. When certain effects reveal a certain dissymmetry, that dissymmetry must also be found in their causes’.)

Pierre Curie (1859–1906)
(*J. Phys. (Paris) 3ème Série* **1894**, 3, 393)

1.1. The Homochirality of Life

One of our first experiences in life is the observation that our two hands – as well as our two feet – are similar but not identical. If we mirror the left hand, it appears to be identical with the right hand, and *vice versa*. If we take a right glove and turn it inside out, we obtain a left glove. The mirror image of a left shoe is a right shoe. Objects which are distinct from, that is, not superimposable onto their mirror image, such as left hand and right hand (*Fig. 1.1*), are said to be *chiral*. The word ‘*chiral*’ stems from the Greek word for hand, $\chi\epsilon\iota\rho$. A chiral macroscopic object and its mirror image are said to be *enantiomorphous*.

From everyday life, we know of other objects that are chiral, for instance, screws and propellers. A right-handed screw is the mirror image of a left-handed screw and *vice versa*. A right-handed and a left-handed propeller turning in the same sense would make a boat go in opposite directions. However, a right-handed propeller turning clockwise, say, will make a boat go in the same direction as a left-handed propeller turning counterclockwise. What we notice is that both a screw and a propeller combine a turning movement, or *rotation*, with a linear displacement, or *translation*, along the rotation axis. As we shall see in more detail later, the combination of these two kinds of movement is an essential aspect of *dynamic* chirality.

But let us now return to the observation of our hands. Both hands have the same number of bones and muscles, and similar blood vessels. We now imagine that we surgically remove a single muscle cell from our left hand and another one from the corresponding muscle in our right hand. We compare these two cells under a microscope: are they also enantiomorphous? A biologist will immediately say that this can hardly be the case. In fact, it will probably be very hard to discern which cell came from which hand. If we now proceed further down, from the microscopic scale to the submicroscopic and finally to the molecular level, we discover that, in both hands, the conditions are exactly the

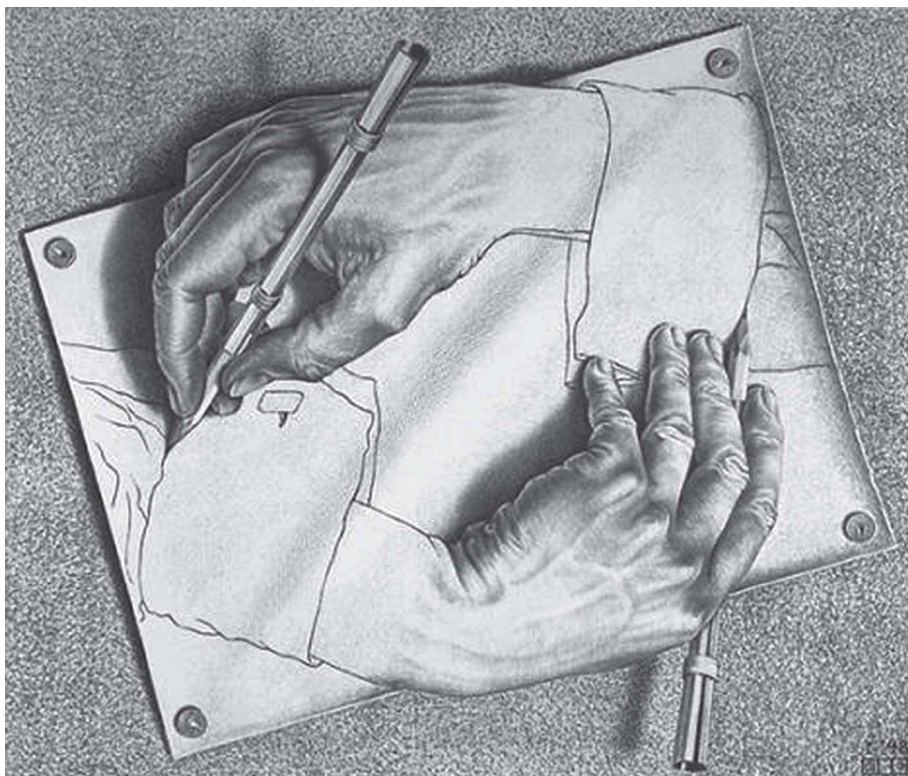


Fig. 1.1. *If the right hand draws the left hand, and the left hand draws the right hand, how then did it start?* By M. C. Escher (Lithograph, 1948; taken from: D. R. Hofstadter, *Gödel, Escher, Bach*, Basic Books, London, 1979; courtesy of M. C. Escher Foundation).

same. Both cells, from our left hand and from our right hand, contain *B*-DNA in the form of a right-handed double helix, all the proteins in these cells consist of *L*-amino acids, and most carbohydrates are derived from *D*-sugars. ‘*L*’ stands for *laevum*, meaning ‘left’ in Latin, and ‘*D*’ signifies *dextrum*, ‘right’.

The very complex molecules that make up living organisms, such as DNA, RNA, proteins, and sugars, are thus all chiral. RNA contains the carbohydrate moiety *D*-ribose and DNA its derivative *D*-2-deoxyribose. One of the most remarkable facts in biology is that the biomolecular chirality, be it in a virus, in a primitive bacterium, or in a human brain cell, is everywhere the same. A chiral molecule and its mirror image are called *enantiomers*. Life based on enantiomeric biomolecules, namely on left-handed *B*-DNA, *D*-amino acids, and *L*-sugars, is nonexistent on Earth. This remarkable selectivity is called *biological homochirality* (Fig. 1.2).

Suppose that in the universe there exists an as yet unknown planet, revolving around an as yet unidentified star, and on which atmospheric and

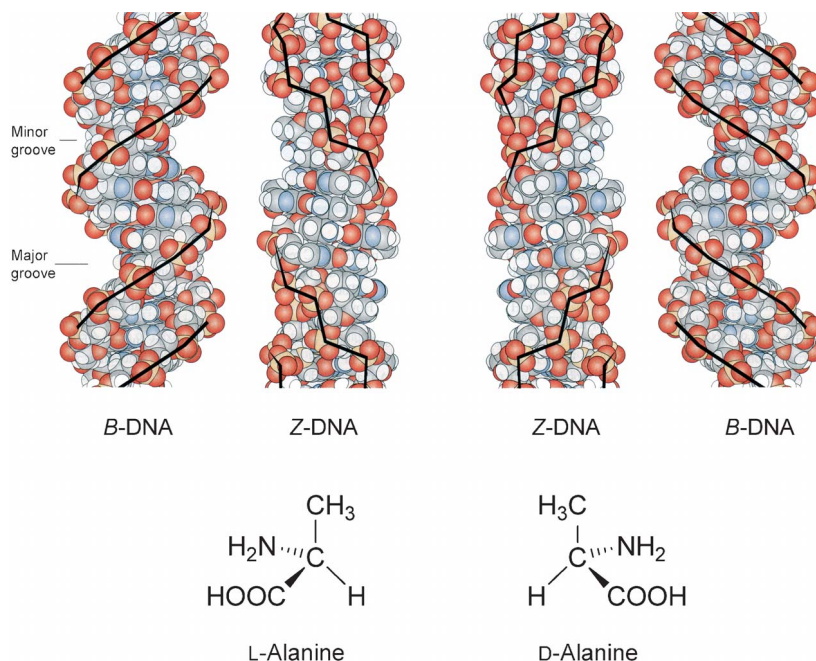


Fig. 1.2. Left: *Forms of biomolecules that occur in nature.* Right-handed B-DNA, left-handed Z-DNA, L-alanine as representative of L-amino acids. Right: *Forms that do not occur in nature.* Left-handed B-DNA, right-handed Z-DNA; very seldom, D-amino acids (adapted from G. L. Zubay, *Biochemistry*, 4th edn., William C. Brown, Boston, 1998, p. 745).

climatic conditions resemble those on Earth. In the course of the history of this planet, life chemically resembling that on Earth has evolved. Will these living organisms be molecularly homochiral to those on Earth? In other words, is the biological homochirality the direct consequence of universal and thus fundamental laws, or is it due to chance – whatever that means – and thus mainly dependent on local conditions? This is indeed one of the first questions to be asked if ever extraterrestrial life is observed.

From a chemical standpoint, a chiral molecule and its enantiomer should, under identical external conditions, have exactly the same energy. In a so-called thermodynamic equilibrium with their surroundings, both enantiomers would consequently have the same probability of existing. If, however, one also takes into account elementary particle interactions called the *parity-violating weak forces*, then one concludes that there must exist a very small energy difference favoring one chiral form with respect to the other. The question then is, do these weak interactions suffice to determine biological homochirality.

In the following chapters, we shall refine our notion of chirality and examine which influences conceivably could be at the origin of the remarkable biological

molecular selectivity. The development of definite homochirality in biopolymers of varying length and monomer sequence, and its maintenance in the course of complex reactions are a fundamental mystery in the origin of living organisms.

1.2. The Discovery of Natural Optical Activity

In a chiral medium, the plane of polarization of linearly polarized light gets rotated. One calls this phenomenon *natural optical rotation* or *natural optical activity*. The angle of rotation is a specific molecular property of the medium and is furthermore proportional to the path length of light inside the probe. In the enantiomorphous – or enantiomeric – medium under the same conditions, the angle of rotation is exactly opposite. This very fundamental effect was discovered by two French scientists in the early 19th century [1].

In 1811, *François Arago* noticed optical rotation in slabs of α -quartz cut perpendicular and irradiated parallel to the optic axis. The observation that optical activity not only is a property of a particular crystal (see *Fig. 1.3*) but that it can also occur in liquids, for instance, in sugar solutions, was demonstrated four years later by *Jean-Baptiste Biot*. He thereby founded the method of saccharimetry and applied it also medically to the research on diabetes.

The angle of rotation is, in general, measured with a so-called *polarimeter*. In principle, this is a simple apparatus consisting of a light source, a polarizer, the probe, a second adjustable polarizer called an analyzer, and a detector. If one measures optical rotation at different wavelengths of light, λ , one observes what is called *optical rotatory dispersion* (abbreviated as ORD). The apparatus then is named a *spectral polarimeter*. While the optical activity of quartz is a consequence of the overall structure of the crystal, that of a sugar solution derives from the individual, randomly distributed molecules. The ORD spectrum

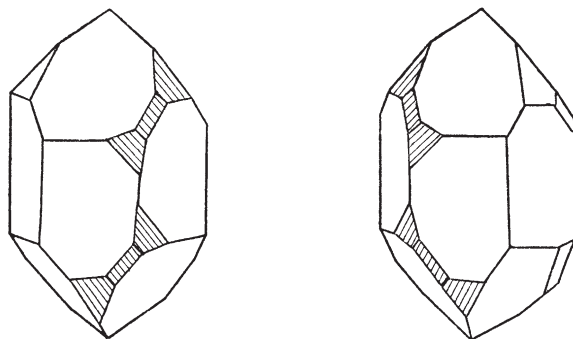


Fig. 1.3. Enantiomorphous left- and right-handed crystals of quartz (adapted from [2])

exhibits the relatively largest, characteristic signals in the wavelength range in which the valence electrons respond most strongly to the incident radiation (ultraviolet/visible light). At wavelengths very short or very long compared to the molecular dimensions (short X-ray and below; far infrared and beyond), the spectrum gradually goes to zero.

The wave theory of light, promoted by *Augustin Jean Fresnel* around 1824, led to the following conclusion: linearly polarized light may be considered as the superposition of *left* and *right circularly polarized* light of same frequency and amplitude. In a chiral medium, the index of refraction for left circularly polarized light n_L is different from that for right circularly polarized light n_R [3]. The rotation of the plane of linearly polarized light at a given wavelength λ' in the optically active medium may thus straightforwardly be shown to be proportional to the difference. For one enantiomer:

$$n_L(\lambda') - n_R(\lambda') = +\Delta n(\lambda') \neq 0,$$

and for the other:

$$n_L(\lambda') - n_R(\lambda') = -\Delta n(\lambda').$$

For any molecule, there are characteristic wavelengths at which it absorbs light, more or less strongly. The strength of such an absorption is measured by the absorption coefficient ε . The absorptions which are most sensitive to the molecular electronic structure, in general, lie in the ultraviolet-visible (UV/VIS) wavelength range. Each absorption corresponds to a so-called *electronic transition*. This means that the molecular electrons are promoted, by light of the corresponding wavelength, from an energetically lower (ground) to a higher (excited) state (a \rightarrow b). The energy difference thereby taken up from the radiation field, $E_b - E_a$, is related to the frequency of the exciting light ν , or the wavelength λ , by the famous *Einstein–Planck* relation:

$$E_b - E_a = h\nu = hc/\lambda$$

where h stands for the very fundamental *Planck's* constant, and c for the light velocity.

In chiral molecules, the nonvanishing difference of the refractive index for left and right circularly polarized light is connected to the fact that, inside absorption bands, the absorption coefficient for left and right circularly polarized light is also different: $\varepsilon_L - \varepsilon_R = \Delta\varepsilon \neq 0$. This phenomenon is called *circular dichroism* (abbreviated as CD).

Every molecule shows a particular absorption spectrum, and every chiral molecule consequently exhibits a corresponding individual CD spectrum. For

enantiomers, the CD spectrum at all wavelengths is equal in magnitude, but opposite in sign. Depending on the molecule, its chirality, and the strength of the absorption, the ratio $\Delta\epsilon/\epsilon = (\epsilon_L - \epsilon_R)/\epsilon$ has an order of magnitude of *ca.* 10^{-2} at best, often only between 10^{-3} to 10^{-5} . CD is thus a relatively small effect. The technology to measure it routinely with a *circular dichrograph* matured relatively late, in the 1960s. Commercial apparatus nowadays can measure $\Delta\epsilon/\epsilon$ values down to *ca.* 10^{-6} .

Molecular optical activity has been widely studied and used as an analytic tool. A central question in the chemistry of chiral compounds is the determination of *absolute configuration*: given an ORD or CD spectrum, which one of the two possible enantiomers lies at its origin? For example, ORD has much contributed to the chemistry of cyclic carbonyl compounds, in particular of steroids [4], the analysis and synthesis of sex hormones, and the development of oral contraceptives. Here, enantioselectivity and the determination of absolute configuration play a decisive role for physiological reasons. The method of CD has the advantage over ORD that, on inspection, its signals can more directly be attributed to particular electronic transitions (see *Sect. 1.4, 3.3, and 8.5*). As already mentioned, in the course of the advancement of optical and electronic technology, CD has become the method of choice in many applications. It is, for instance, very useful in protein chemistry, as it allows to clearly distinguish between secondary polypeptide structures [5]: α -helix, β -pleated sheet, polyproline, random coil (see *Fig. 1.4*).

The relation between the CD and the ORD spectrum has a fundamental basis: if one knows the CD spectrum of a molecule over the whole wavelength range, one may, in principle, directly deduce the ORD spectrum and *vice versa*. Mathematically speaking, CD and ORD are *Kronig–Kramers transforms* of each other. The same kind of relation also exists between the ordinary absorption spectrum and the dispersion spectrum of any molecular system.

1.3. Chirality and the Birth of Stereochemistry

Chirality, as we here understand it, does not exist in two dimensions. In order to occur, chirality needs three spatial dimensions. The projection of a left hand onto a sheet of paper is identical with the projection of a right hand if you cut it out, lift it, and flip it over.

Arago's and *Biot's* discoveries in the early 19th century immediately stimulated much further work on the optical properties of matter. A breakthrough which proved particularly important for the future development of chemistry was achieved in 1848 by *Louis Pasteur* (1822–1895). He investigated solutions of sodium ammonium tartrate that were indifferent to polarized light, that is, not optically active. Letting the solutes crystallize, *Pasteur* discovered,

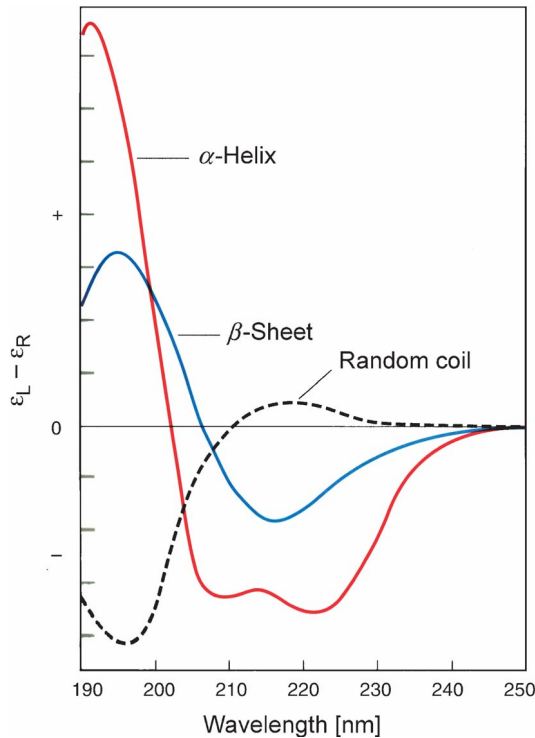


Fig. 1.4. Circular dichroism (CD) spectrum of a polypeptide, like poly-L-alanine, in different, frequently occurring secondary structures. The secondary peptide (protein) structures, the α -helix and the β -pleated sheet, are both stabilized by hydrogen bonds between different amide residues (figure taken from: C. K. Mathews, K. E. van Holde, *Biochemistry*, Benjamin Cummings, Redwood City, 1990). The α -helix, discovered by *Pauling* and *Corey* in 1949, is right-handed, has a pitch of 0.54 nm, and contains 3.6 residues per turn.

however, that the crystals turned out to be hemihedral, indicating that they were chiral. Some crystals were hemihedral to the right, others hemihedral to the left, showing the presence of both enantiomorphous forms. Selectively redissolving the right-handed crystals, *Pasteur* found that the new solutions so obtained rotated the plane of linearly polarized light to one side, while the solutions made from the left-handed crystals rotated the plane of linearly polarized light to the other. The original, optically inactive solutions obviously were *racemic*, containing equal amounts of both enantiomers of the compound. *Pasteur* had, by these experiments, achieved the first resolution of a *racemic mixture* into its chiral components. Unfortunately, only very few racemic mixtures crystallize enantioselectively, and *Pasteur* was fortunate to have found this striking example. Very often, racemic solutions also form racemic crystals [6], and the resolution of the enantiomers has to be carried out by other, often less efficient procedures (see also *Sect. 7.1* and *9.11*).

Pasteur's discovery really started the field of *stereochemistry*. If the two forms of the tartrate had exactly the same atomic composition but showed opposite rotations, then the difference had to be sought in the structure, namely, in the spatial arrangement of the atoms inside the molecule. It gradually became clear that molecules are not just strings of atoms, but that these atoms must have definite relative positions in space. In 1873, *Johannes Wislicenus* wrote: 'If molecules can be structurally identical and yet possess dissimilar properties, this difference can be explained only on the ground that it is due to a different arrangement of the atoms in space' [2].

In 1874, *Jacobus Hendricus van t'Hoff* in Holland and *Joseph Achille Le Bel* in France independently published a theory of the structure of saturated carbon compounds. According to it, the four valences of the carbon atom are directed to the corners of a tetrahedron, at the center of which the carbon atom is situated. If four different atoms, or groups of atoms, are attached at the four corners, then the molecule is asymmetric and capable of existing in two non-superimposable mirror-image forms (see *Fig. 1.5, a* and *b*). For some time, it was believed that the presence of an asymmetric carbon atom – or of several asymmetric carbon atoms connected in such a way that the molecule as a whole and its mirror image are different – was the prerequisite for the occurrence of optical activity.

Lord Kelvin (*William Thomson*, 1824–1907), in his 1884 Baltimore Lectures [7], appears to have been the first to have formulated a general definition of structural chirality: 'I call any geometrical figure, or group of points, chiral, and say that it has chirality, if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself.'

From the point of view of crystallographic point group symmetry, one concludes that all three-dimensional bodies are chiral which lack any rotation–reflection (or improper rotation) axes S_n . This implies, in particular, that they contain no planes of reflection σ , and no point of inversion i (see *Sect. 4.1* for further details). All *totally asymmetric* bodies are, therefore, chiral, and in addition, all bodies that solely contain *pure rotation symmetry axes* C_n , such as a propeller, or a helix.

The extension of three-dimensional structural thinking to inorganic chemistry was largely pioneered by *Alfred Werner* in Zurich in the time period from 1893 to *ca.* 1914. Noticing the existence of different complexes of transition metal ions of same composition but opposite optical rotation, *Werner* recognized that the enantiomerism could be rationalized on geometric grounds. Assuming essentially octahedral ligand arrangement around sixfold coordinated central metal ions, it could be concluded that, depending on the number and types of substituents, chiral forms were conceivable. *Werner* was then able to synthesize and to resolve some of these chiral forms and to prove his structural theory. A striking example is found, when the central metal ion contains

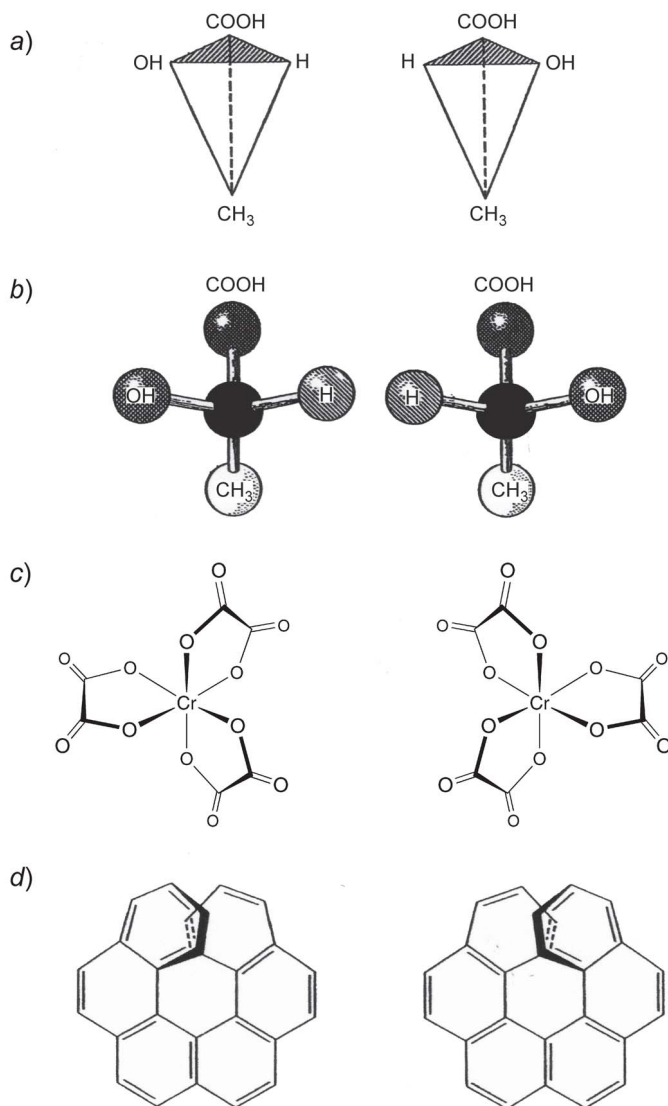


Fig. 1.5. a), b) Different representations of the enantiomers of lactic acid (adapted from [2]). c) The $[\text{Cr}(\text{C}_2\text{O}_4)_3]^{3-}$ complex (adapted from [6]). d) Hexahelicene (from: S. H. Pine, J. B. Hendrickson, D. J. Cram, G. S. Hammond, *Organic Chemistry*, Mc Graw Hill International, London, 1981).

three bidentate ligands, such as in the trisoxalatochromate(III) complex ($[\text{Cr}(\text{C}_2\text{O}_4)_3]^{3-}$). The octahedral ligand arrangement of crystallographic symmetry O_h is here distorted to the lower, chiral symmetry D_3 (see Fig. 1.5, c). O_h is the symmetry of a perfect octahedron, D_3 is the symmetry of a three-bladed propeller.

From what has been mentioned until now, it might appear that optical activity in a molecule is connected to the occurrence of one (or more) asymmetrically substituted atomic center(s). But this needs not be the case: a beautiful example for another type of chiral molecule is to be found in the helicenes, polycyclic *cata*-condensed aromatic hydrocarbons, which, due to steric hindrance, are forced to adopt a nonplanar structure. In a molecule such as hexahelicene [8], there are no asymmetric carbon atoms in the usual sense. Rather, the molecule as a whole is obliged to take on a helical conformation of C_2 -symmetry which can either be right-handed or left-handed (*Fig. 1.5, d*). The molecule thus exhibits *intrinsic chirality*, and the enantiomers show very strong CD signals in the near-UV part of the light spectrum.

The element carbon plays an important role in nature. Until *ca.* 20 years ago, three forms of pure carbon were known to exist under normal conditions, diamond, graphite, and amorphous carbon. The discovery of the fullerenes, stable cage-like molecules of pure carbon [9], opened up vast new fields of investigation in structural chemistry. The molecule C_{60} is of icosahedral holohedral symmetry I_h and thus definitely achiral. However, higher fullerene homologues, such as C_{76} , C_{78} , and C_{84} , exhibit chiral structures and, therefore, may occur in two enantiomeric forms. For instance, C_{84} is of symmetry D_2 . It may in principle transform from one enantiomer to the other *via* an achiral intermediate structure of higher symmetry D_{2d} which, however, also lies so much higher in energy that the chiral forms are thermally stable (see *Fig. 1.6, top*). The molecule C_{84} is of course prepared, by contact-arc vaporization of carbon, as a racemic mixture. The resolution into enantiomers is difficult and has been achieved through a reaction with reagents that also are chiral [10]. The CD spectrum of the enantiomers should, as we have previously stated, at all wavelengths have exactly the same absolute magnitude but the opposite sign. Small deviations therefrom (*Fig. 1.6, bottom*) reflect the difficulty of obtaining the enantiomers in pure form.

1.4. Absolute Configuration

What we call ‘left’ and what we call ‘right’ is a matter of convention. Once we have agreed upon what is what, it is easy to identify a ‘left’ glove or a ‘right’ shoe. But how is it with molecules?

We have seen that enantiomers may be distinguished by their optical activity. It became customary to label chiral compounds by the sign of their optical rotation at a given wavelength, usually the sodium-D line at 589 nm. If (looking towards the light source) the plane of linearly polarized light is rotated *clockwise* by the molecular sample, it is said to be *dextrorotatory* and is designated as (+) or *d*. If the sample rotates the linearly polarized light *counter-*

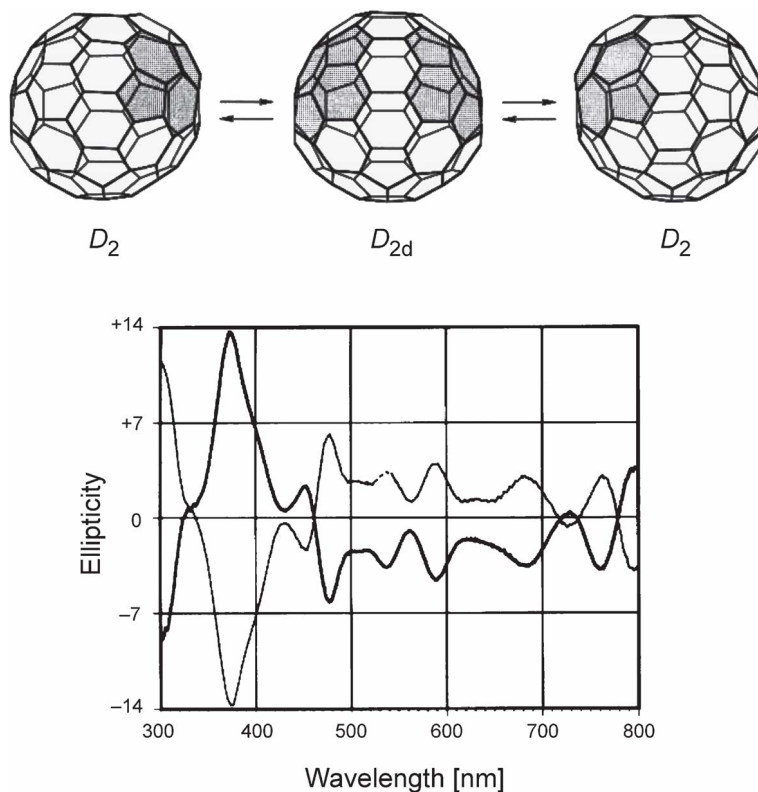


Fig. 1.6. Top: The enantiomers of C_{8H_8} of symmetry D_2 . They are thermally stable, as the achiral intermediate form of symmetry D_{2d} lies significantly higher in energy. Bottom: The CD spectra of the enantiomers. Ideally, the spectra should be exact mirror images with respect to the zero line. The minor inaccuracies reflect the difficulty in quantitatively separating the enantiomers (taken from [10]).

clockwise, it is called *levorotatory* and is designated by $(-)$ or l . This label, of course, says nothing about the exact spatial arrangement of the atoms in the molecule, which is termed the *absolute configuration*. It may well occur that chemically unrelated compounds have similar rotations at the Na-D line, while others that differ by perhaps only one substituent around an asymmetric center may show different magnitudes and sign.

In the course of the evolution of stereochemistry, it became evident that an unambiguous definition and designation of the absolute configuration was needed. A first stage in this development was reached within the chemistry of carbohydrates, amino acids and related compounds. An assumed and later experimentally confirmed absolute configuration attributed to the compound $(+)$ -glyceraldehyde was designated by D . D -Glyceraldehyde was then chosen as the reference basis for the absolute configuration of the naturally occurring