

1

An Introduction to Chirality at the Nanoscale

Laurence D. Barron

1.1

Historical Introduction to Optical Activity and Chirality

Scientists have been fascinated by chirality, meaning right- or left-handedness, in the structure of matter ever since the concept first arose as a result of the discovery, in the early years of the nineteenth century, of natural optical activity in refracting media. The concept of chirality has inspired major advances in physics, chemistry and the life sciences [1, 2]. Even today, chirality continues to catalyze scientific and technological progress in many different areas, nanoscience being a prime example [3–5].

The subject of optical activity and chirality started with the observation by Arago in 1811 of colors in sunlight that had passed along the optic axis of a quartz crystal placed between crossed polarizers. Subsequent experiments by Biot established that the colors originated in the rotation of the plane of polarization of linearly polarized light (optical rotation), the rotation being different for light of different wavelengths (optical rotatory dispersion). The discovery of optical rotation in organic liquids such as turpentine indicated that optical activity could reside in individual molecules and could be observed even when the molecules were oriented randomly, unlike quartz where the optical activity is a property of the crystal structure, because molten quartz is not optically active. After his discovery of circularly polarized light in 1824, Fresnel was able to understand optical rotation in terms of different refractive indices for the coherent right- and left-circularly polarized components of equal amplitude into which a linearly polarized light beam can be resolved. This led him to suggest that optical activity may result from “a helicoidal arrangement of the molecules of the medium, which would present inverse properties according to whether these helices were dextrogyrate or laevogyrate.” This early work culminated in Pasteur’s epoch-making separation in 1848 of crystals of sodium ammonium paratartrate, an optically inactive form of sodium ammonium tartrate, into two sets that, when dissolved in water, gave optical rotations of equal magnitude but opposite sign. This demonstrated that paratartronic acid was a mixture, now known as a *racemic* mixture, of equal numbers of mirror-image molecules. Pasteur was lucky in that his racemic solution crystallized into equal amounts of crystals containing exclusively one or other of the

mirror-image molecules, a process known as *spontaneous resolution*. (Such mixtures of crystals are called conglomerates, as distinct from racemic compounds where each crystal contains equal amounts of the mirror-image molecules.)

Although a system is called “optically active” if it has the power to rotate the plane of polarization of a linearly polarized light beam, optical rotation is in fact just one of a number of optical activity phenomena that can all be reduced to the common origin of a different response to right- and left-circularly polarized light. Substances that are optically active in the absence of external influences are said to exhibit *natural* optical activity.

In 1846, Faraday discovered that optical activity could be induced in an otherwise inactive sample by a magnetic field. He observed optical rotation in a rod of lead borate glass placed between the poles of an electromagnet with holes bored through the pole pieces to enable a linearly polarized light beam to pass through. This effect is quite general: a Faraday rotation is found when linearly polarized light is transmitted through any crystal or fluid in the direction of a magnetic field, the sense of rotation being reversed on reversing the direction of either the light beam or the magnetic field. At the time, the main significance of this discovery was to demonstrate conclusively the intimate connection between electromagnetism and light; but it also became a source of confusion to some scientists (including Pasteur) who failed to appreciate that there is a fundamental distinction between magnetic optical rotation and the natural optical rotation that is associated with handedness in the microstructure. That the two phenomena have fundamentally different symmetry characteristics is intimated by the fact that the magnetic rotation is additive when the light is reflected back through the medium, whereas the natural rotation cancels.

Although he does not provide a formal definition, it can be inferred [6] from his original article that described in detail his experiments with salts of tartaric acid that Pasteur in 1848 introduced the word *dissymmetric* to describe hemihedral crystals of a tartrate “which differ only as an image in a mirror differs in its symmetry of position from the object which produces it” and used this word to describe handed figures and handed molecules generally. The two distinguishable mirror-image crystal forms were subsequently called *enantiomorphs* by Naumann in 1856. Current usage reserves *enantiomorph* for macroscopic objects and *enantiomer* for molecules [7], but because of the ambiguity of scale in general physical systems, these two terms are often used as synonyms [8]. This is especially pertinent in nanoscience that embraces such a large range of scales, from individual small molecules to crystals, polymers and supramolecular assemblies.

The word dissymmetry was eventually replaced by *chirality* (from the Greek *cheir*, meaning hand) in the literature of stereochemistry. This word was first introduced into science by Lord Kelvin [9], Professor of Natural Philosophy in the University of Glasgow, to describe a figure “if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself.” The two mirror-image enantiomers of the small archetypal molecule bromochlorofluoromethane are illustrated in Figure 1.1a, together with the two enantiomers of hexahelicene in Figure 1.1b. The modern system for specifying the absolute configurations of most chiral molecules is based on the *R*

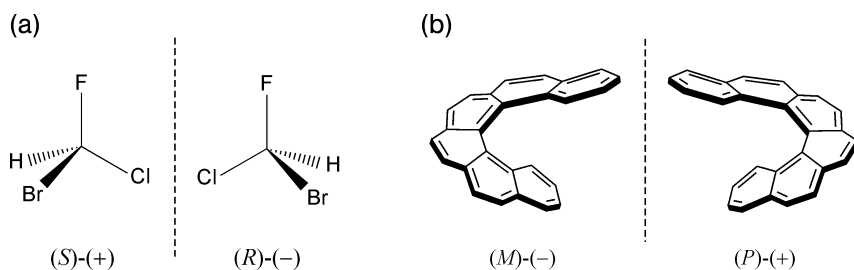


Figure 1.1 The two mirror-image enantiomers of bromochlorofluoromethane (a) and hexahelicene (b).

(for *rectus*) and *S* (for *sinister*) system of Cahn, Ingold and Prelog, supplemented with the *P* (for plus) and *M* (for minus) designation for molecules that have a clear helical structure [7]. The older *D,L* designation, based on Fischer planar projections, is still used for amino acids and carbohydrates. The sense of optical rotation (usually measured at the sodium D-line wavelength of 598 nm) associated with a particular absolute configuration is given in brackets.

Although Lord Kelvin's definition of chiral is essentially the same as that used earlier by Pasteur for dissymmetric, the two words are not strictly synonymous in the broader context of modern chemistry and physics. Dissymmetry means the absence of certain symmetry elements, these being improper rotation axes in Pasteur's usage. Chirality has become a more positive concept in that it refers to the possession of the attribute of handedness, which has a physical content. In molecular physics this is the ability to support time-even pseudoscalar observables; in elementary particle physics chirality is defined as the eigenvalue of the Dirac matrix operator γ_5 .

To facilitate a proper understanding of the structure and properties of chiral molecules and of the factors involved in their synthesis and transformations, this chapter uses some principles of modern physics, especially fundamental symmetry arguments, to provide a description of chirality deeper than that usually encountered in the literature of stereochemistry. A central result is that, although dissymmetry is sufficient to guarantee chirality in a stationary object such as a finite helix, dissymmetric systems are not necessarily chiral when motion is involved. The words "true" and "false" chirality, corresponding to time-invariant and time-noninvariant enantiomorphism, respectively, were introduced by this author to draw attention to this distinction [10], but it was not intended that this would become standard nomenclature. Rather, it was suggested that the word "chiral" be reserved in future for systems that are truly chiral. The terminology of true and false chirality has, however, been taken up by others, especially in the area of absolute enantioselection, so for consistency it will be used in this chapter. We shall see that the combination of linear motion with a rotation, for example, generates true chirality, but that a magnetic field alone does not (in fact it is not even falsely chiral). Examples of systems with false chirality include a stationary rotating cone, and collinear electric and magnetic fields. The term "false" should not be taken to be perjorative in any

sense; indeed, false chirality can generate fascinating new phenomena that are even more subtle than those associated with true chirality.

The triumph of theoretical physics in unifying the weak and electromagnetic forces into a single “electroweak” force by Weinberg, Salam and Glashow in the 1960s provided a new perspective on chirality. Because the weak and electromagnetic forces turned out to be different aspects of the same, but more fundamental, unified force, the absolute parity violation associated with the weak force is now known to infiltrate to a tiny extent into all electromagnetic phenomena so that free atoms, for example, exhibit very small optical rotations, and a tiny energy difference exists between the enantiomers of a chiral molecule.

1.2

Chirality and Life

1.2.1

Homochirality

Since chirality is a *sine qua non* for the amazing structural and functional diversity of biological macromolecules, the chemistry of life provides a paradigm for the potential roles of chirality in supramolecular chemistry and nanoscience [3]. Accordingly, a brief survey is provided of current knowledge on the origin and role of chirality in the chemistry of life.

A hallmark of life’s chemistry is its *homochirality* [1, 11–15], which is well illustrated by the central molecules of life, namely proteins and nucleic acids. Proteins consist of polypeptide chains made from combinations of 20 different amino acids (primary structure), all exclusively the L-enantiomers. This homochirality in the monomeric amino acid building blocks of proteins leads to homochirality in higher-order structures such as the right-handed α -helix (secondary structure), and the fold (tertiary structure) that is unique to each different protein in its native state (Figure 1.2). Nucleic acids consist of chains of deoxyribonucleosides (for DNA) or ribonucleosides (for RNA), connected by phosphodiester links, all based exclusively on the D-deoxyribose or D-ribose sugar ring, respectively (Figure 1.3). This homochirality in the monomeric sugar building blocks of nucleic acids leads to homochirality in their secondary structures such as the right-handed B-type DNA double helix, and tertiary structures such as those found in catalytic and ribosomal RNAs. DNA itself is finding many applications in nanotechnology [5].

Homochirality is essential for an efficient biochemistry, rather like the universal adoption of right-handed screws in engineering. One example is Fischer’s “lock and key” principle [16], which provides a mechanism for stereochemical selection in nature, as in enzyme catalysis. Small amounts of “non-natural” enantiomers such as the D-forms of some amino acids are in fact found in living organisms where they have specific roles [17, 18], but they have not been found in functional proteins (their detection in metabolically inert proteins like those found in lens and bone tissue is attributed to racemization during ageing [17]). Since molecules sufficiently large and

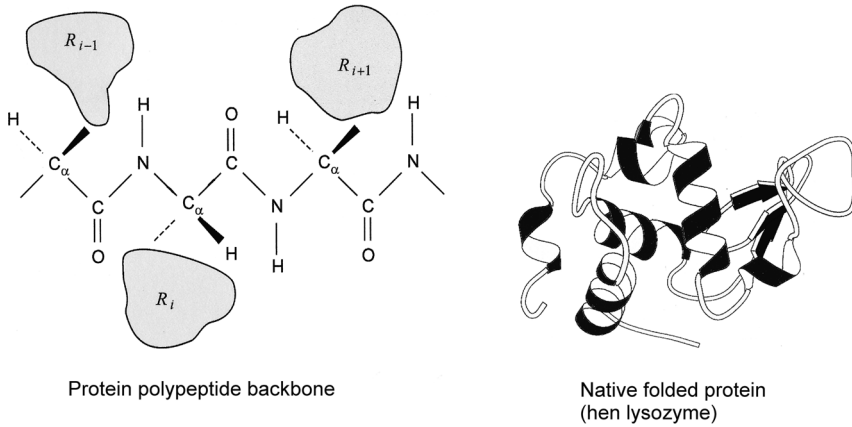


Figure 1.2 The polypeptide backbones of proteins are made exclusively from homochiral amino acids (all L). R_i represents side chains such as CH_3 for alanine. This generates homochiral secondary structures, such as the right-handed α -helix, within the tertiary structures of native folded proteins like hen lysozyme.

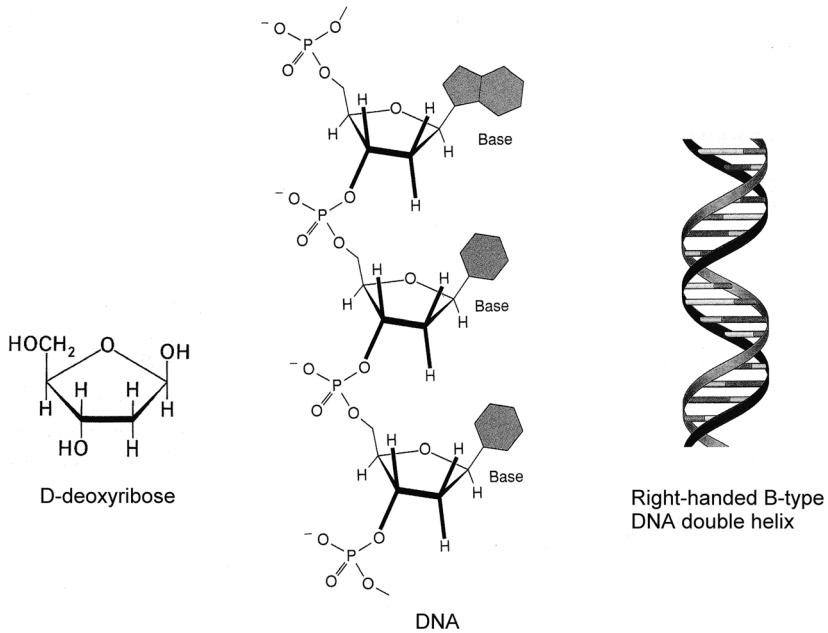


Figure 1.3 Nucleic acids are made exclusively from homochiral sugars (all D) such as D-deoxyribose for DNA. This generates homochiral secondary structures such as the right-handed B-type DNA double helix.

complex to support life are almost certain to exist in two mirror-image chiral forms, homochirality also appears to be essential for any molecule-based life on other worlds. Furthermore, since no element other than carbon forms such a huge variety of compounds, many of them chiral, the chemistry is expected to be organic. Last but not least, the liquid water that is essential for life on Earth is more than simply a medium: it acts as a “lubricant” of key biomolecular processes such as macromolecular folding, unfolding and interaction [19]. No other liquid solvent has the same balance of vital physicochemical properties. Hence homochirality associated with a complex organic chemistry in an aqueous environment would appear to be as essential for life on other worlds as it is on Earth. Nonetheless, the possibility of alternative scenarios based on elements other than carbon and solvents other than water should be kept in mind [20], and could be of interest in the context of synthetic homochiral supramolecular chemistry and nanoscience. Indeed, nanotechnology is already exploiting materials and devices that benefit explicitly from homochirality at the molecular level [5].

A central problem in the origin of life is which came first: homochirality in the prebiotic monomers or in the earliest prebiotic polymers [14, 21]. Homochiral nucleic acid polymers, for example, do not form efficiently in a racemic solution of the monomers [22]. Theoretical analysis suggested that addition of a nucleotide of the wrong handedness halts the polymerization [23], a process called enantiomeric cross-inhibition. However, homochirality in the chiral monomers is not essential for generating homochiral *synthetic* polymers [3]. Although polyisocyanates, for example, constructed from achiral monomers form helical polymers with equal numbers of right- and left-handed forms, the introduction of a chiral bias in the form of a small amount of a chiral version of a monomer can induce a high enantiomeric excess (ee), defined as the percentage excess of the enantiomer over the racemate [7], of one helical sense [24, 25]. This generation of an excess of the helical sense preferred by the small number of chiral units (the sergeants) is called the sergeants-and-soldiers effect. Furthermore, a polyisocyanate constructed from a random copolymerization of chiral monomers containing just a small percentage excess of one enantiomer over the other shows a large excess of the helical form generated from homopolymerization of the corresponding enantiopure monomer. This generation of an excess of the helical sense preferred by the excess enantiomer is called the majority rules effect.

Another example of the dramatic influence a small chiral bias may exert, this time in the generation of homochiral monomers, arises in solid–liquid phase equilibria of amino acids: a few per cent ee of one enantiomer in racemic compounds can lead to very high solution ees, including a virtually enantiopure solution for serine [26]. This is related to the well-known differences in relative solubilities of an enantiopure compound and the corresponding racemate, which forms the basis of enantio-enrichment by crystallization [7]. An important feature of this system is that it is based on an equilibrium mechanism, as distinct from far-from-equilibrium mechanisms as previously invoked in kinetically induced amplification via autocatalytic reactions [27]. Also, sublimation of a near-racemic mixture of serine containing a small percentage ee of one enantiomer was recently found to generate a vapor with up to

98% ee that could be condensed into an almost enantiopure solid [28]. Apparently, clusters of the same enantiomer form preferentially over racemic clusters in the vapor, with those of the majority enantiomer forming faster and selectively plucking more of the majority enantiomer out of the subliming crystals. If all of the serine were allowed to sublime, it would segregate into homochiral clusters with the same overall slight initial ee as in the solid mixture. Similar results for a variety of other amino acids were reported shortly afterwards [29].

Crystal chemistry suggests further possibilities. In addition to spontaneous resolutions in crystallization, or the crystallization of achiral molecules in chiral spacegroups [30], the faces of chiral crystals such as quartz, or the chiral faces of nonchiral crystals such as calcite, could act as enantioselective templates [31]. Related to this is the demonstration that the chiral rims of racemic β -sheets can operate as templates for the generation of long homochiral oligopeptides from racemic monomers in aqueous solution [32].

1.2.2

Pasteur's Conjecture

From the above it is clear that small initial ees in chiral monomers can, in some circumstances, generate large ees in both chiral monomers and polymers. This small ee could be produced by some physical chiral influence. Since in Pasteur's time all substances found to be optically active in solution were natural products, Pasteur himself conjectured that molecular chirality in the living world is the product of some universal chiral force or influence in nature. Accordingly, he attempted to extend the concept of chirality (dissymmetry) to other aspects of the physical world [33]. For example, he thought that the combination of a translational with a rotational motion generated chirality; likewise a magnetic field. Curie [34] suggested that collinear electric and magnetic fields are chiral. However, as explained below, of these only a translating–rotating system exhibits “true chirality.” Pasteur's incorrect belief that a static magnetic field alone is also a source of chirality has been shared by many other scientists. This misconception is based on the fact that a static magnetic field can induce optical rotation (the Faraday effect) in achiral materials (*vide supra*); but as Lord Kelvin [9] emphasized: “the magnetic rotation has no chirality.” In a new twist to the story [35], a magnetic field was recently used in a more subtle fashion than that conceived by Pasteur by exploiting the novel phenomenon of magnetochiral dichroism (*vide infra*) to induce a small ee.

If it were ever proved that parity violation (*vide infra*) was linked in some way to the origin and role of homochirality in the living world, this would provide the ultimate source of a universal chiral force sensed by Pasteur. However, at the time of writing, there is no firm evidence to support the idea [36]. On a cosmic scale, enantioselective mechanisms depending on parity violation are the only ones that could predetermine a particular handedness, such as the L-amino acids and D-sugars found in terrestrial life; in all other mechanisms the ultimate choice would arise purely by chance.

1.3

Symmetry and Chirality

Chirality is an excellent subject for the application of symmetry principles [2, 37]. As well as conventional point group symmetry, the fundamental symmetries of space inversion, time reversal and even charge conjugation have something to say about chirality at all levels: the experiments that show up optical activity observables, the objects generating these observables and the nature of the quantum states that these objects must be able to support. Even the symmetry violations observed in elementary particle physics can infiltrate into the world of chiral molecules, with intriguing implications. These fundamental symmetry aspects, summarized briefly below, are highly relevant to considerations of molecular chirality and absolute enantioselection. They bring intrinsic physical properties of the universe to bear on the problem of the origin of homochirality and its role in the origin and special physicochemical characteristics of life, with important lessons for the generation and exploitation of chirality at the nanoscale.

1.3.1

Spatial Symmetry

A finite cylindrical helix is the archetype for all figures exhibiting chirality. Thus, a helix and its mirror image cannot be superposed since reflection reverses the screw sense. Chiral figures are not necessarily *asymmetric*, that is devoid of all symmetry elements, since they may possess one or more proper rotation axes: for example, a finite cylindrical helix has a twofold rotation axis C_2 through the midpoint of the coil, perpendicular to the long axis (Figure 1.4a). Hexahelicene (Figure 1.1b) provides a molecular example of this. However, chirality excludes improper symmetry elements, namely centers of inversion, reflection planes and rotation–reflection axes. Hence, chirality is supported by the point groups comprising only proper rotations, namely C_n , D_n , O , T and I .

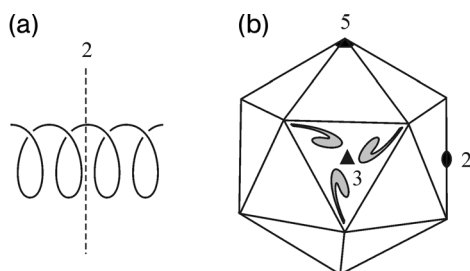


Figure 1.4 (a) A right-handed finite helix illustrating the twofold proper rotation axis. (b) A simple icosahedral virus capsid illustrating one each of the 6 fivefold, 10 threefold and 15 twofold proper rotation axes. Each triangular face contains three asymmetric protein subunits

(only those in one face are shown for simplicity). The chirality of the protein subunits renders the entire capsid chiral but without destroying the proper rotation axes, thereby generating the point group I .

The chiral point group I has high rotational symmetry based on fivefold, threefold and twofold rotation axes (Figure 1.4b). The protein capsids of icosahedral viruses provide an interesting and pertinent example of this point group in the context of chiral supramolecular structures; indeed virus capsids are already widely used in nanotechnology. Although the folds of the many constituent coat protein subunits are intrinsically chiral, being completely asymmetric like the lysozyme fold shown in Figure 1.2, the protein subunits are identical in simple viruses and are tiled over the capsid surface in such a way as to preserve all the rotation axes of the icosahedron. However, their intrinsic chirality destroys any improper symmetry elements of the complete capsid, which renders it chiral overall. This example demonstrates how it is possible to construct a high-symmetry chiral supramolecular structure from the association of low-symmetry chiral macromolecules.

1.3.2

Inversion Symmetry: Parity, Time Reversal and Charge Conjugation

More fundamental than spatial (point group) symmetries are the symmetries in the laws of physics, and these in turn depend on certain uniformities that we perceive in the world around us. In quantum mechanics, the invariance of physical laws under an associated transformation often generates a conservation law or selection rule that follows from the invariance of the Hamiltonian H under the transformation. Three symmetry operations corresponding to distinct “inversions” are especially fundamental, namely parity, time reversal and charge conjugation [38].

Parity, represented by the operator P (not to be confused with the P -helicity specification of absolute configuration) inverts the coordinates of all the particles in a system through the coordinate origin. This is equivalent to a reflection of the physical system in any plane containing the coordinate origin followed by a rotation through 180° about an axis perpendicular to the reflection plane. If replacing the space coordinates (x,y,z) everywhere in equations describing physical laws (e.g., Newton’s equations for mechanics or Maxwell’s equations for electromagnetism) leaves the equations unchanged, all processes determined by such laws are said to conserve parity. Conservation of parity implies that P commutes with H so that, if ψ_k is an eigenfunction of H , then $P\psi_k$ is also an eigenfunction with the same energy.

Time reversal, represented by the operator T , reverses the motions of all the particles in a system. If replacing the time coordinate t by $-t$ everywhere leaves equations describing physical laws unchanged, then all processes determined by such laws are said to conserve time-reversal invariance, or to have reversality. A process will have reversality as long as the process with all the motions reversed is in principle a possible process, however improbable (from the laws of statistics) it may be. Time reversal is therefore best thought of as motion reversal. It does not mean going backward in time! Conservation of time reversal implies that T and H commute so that, if H is time independent, the stationary state ψ_k and its time-reversed state $T\psi_k$ have the same energy.

Charge conjugation, represented by the operator C , interconverts particles and antiparticles. This operation from relativistic quantum field theory has conceptual

value in studies of molecular chirality. It appears in the *CPT* theorem, which states that, even if one or more of *C*, *P*, or *T* are violated, invariance under the combined operation *CPT* will always hold. The *CPT* theorem has three important consequences: the rest mass of a particle and its antiparticle are equal; the particle and antiparticle lifetimes are the same; and the electromagnetic properties such as charge and magnetic moment of particles and antiparticles are equal in magnitude but opposite in sign.

A *scalar* physical quantity such as energy has magnitude but no directional properties; a *vector* quantity such as linear momentum \mathbf{p} has magnitude and an associated direction; and a *tensor* quantity such as electric polarizability has magnitudes associated with two or more directions. Scalars, vectors and tensors are classified according to their behavior under *P* and *T*. A vector whose sign is reversed by *P* is called a *polar* or *true* vector; for example a position vector \mathbf{r} . A vector whose sign is not changed by *P* is called an *axial* or *pseudo* vector; for example the angular momentum $\mathbf{L} = \mathbf{r} \times \mathbf{p}$ (since the polar vectors \mathbf{r} and \mathbf{p} change sign under *P*, their vector product \mathbf{L} does not). A vector such as \mathbf{r} whose sign is not changed by *T* is called *time even*; a vector such as \mathbf{p} or \mathbf{L} whose sign is reversed is called *time odd*.

Pseudoscalar quantities have magnitude with no directional properties, but they change sign under space inversion *P*. An example is the natural optical rotation angle.

1.3.3

True and False Chirality

There is no disagreement when the term “chiral” is applied to a static object displaying distinguishable enantiomers under space inversion *P* (or mirror reflection), like bromochlorofluoromethane or hexahelicene in Figure 1.1. But when the term is applied to less tangible enantiomorphous systems in which motion is an essential ingredient, time-reversal arguments are required to clarify the concept. The hallmark of a chiral system is that it can support time-even pseudoscalar observables, which are only supported by quantum states with mixed parity but that are invariant under time reversal. This leads to the following definition [2, 10].

True chirality is exhibited by systems existing in two distinct enantiomeric states that are interconverted by space inversion, but not by time reversal combined with any proper spatial rotation.

The spatial enantiomorphism shown by a truly chiral system is therefore time invariant. Spatial enantiomorphism that is time *noninvariant* has different characteristics called “false chirality” to emphasize the distinction. Falsely chiral systems have quite different physical properties from truly chiral systems, which is due in part to their inability to support time-even pseudoscalar observables.

Consider an electron, which has a spin quantum number $s = 1/2$, with $m_s = \pm 1/2$ corresponding to the two opposite projections of the spin angular momentum onto a space-fixed axis. A stationary spinning electron is not a chiral object because space inversion *P* does not generate a distinguishable *P*-enantiomer (Figure 1.5a). However, an electron translating with its spin projection parallel or antiparallel to the direction of propagation has true chirality because *P* interconverts distinguishable

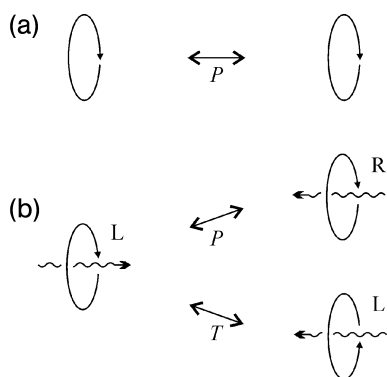


Figure 1.5 The effect of P and T on the motions of (a) a stationary spinning particle and (b) a translating spinning particle. Reprinted from Ref. [2] with permission.

left (L) and right (R) spin-polarized versions by reversing the propagation direction but not the spin sense, whereas time reversal T does not because it reverses both (Figure 1.5b). Similar considerations apply to a circularly polarized photon except that photons, being massless, are always chiral since they always move at the velocity of light in any reference frame.

Now consider a cone spinning about its symmetry axis. Because P generates a version that is not superposable on the original (Figure 1.6a), it might be thought that this is a chiral system. The chirality, however, is false because T followed by a rotation R_π through 180° about an axis perpendicular to the symmetry axis generates the same system as space inversion (Figure 1.6a). If, however, the spinning cone is also translating along the axis of spin, T followed by R_π now generates a system different from that generated by P alone (Figure 1.6b). Hence a *translating* spinning cone has true chirality. It has been argued that a nontranslating spinning cone belongs to the spatial point group C_∞ and so is chiral [39]. More generally, it was suggested that objects that exhibit enantiomorphism, whether T -invariant or not, belong to chiral point groups and hence that motion-dependent chirality is encompassed in the group-theoretical equivalent of Lord Kelvin's definition. However, a nontranslating spinning cone will have quite different physical properties from those of a finite helix. For example, the molecular realization of a spinning cone, namely a rotating symmetric top molecule such as CH_3Cl , does not support time-even pseudoscalar observables such as natural optical rotation (it supports magnetic optical rotation) [2]. To classify it as "chiral" the same as for a completely asymmetric molecule that does support natural optical rotation is therefore misleading as far as the physics is concerned, even though such a classification may be consistent within a particular mathematical description.

It is clear that neither a static uniform electric field \mathbf{E} (a time-even polar vector) nor a static uniform magnetic field \mathbf{B} (a time-odd axial vector) constitutes a chiral system. Likewise for time-dependent uniform electric and magnetic fields. Furthermore, no combination of a static uniform electric and a static uniform magnetic field can

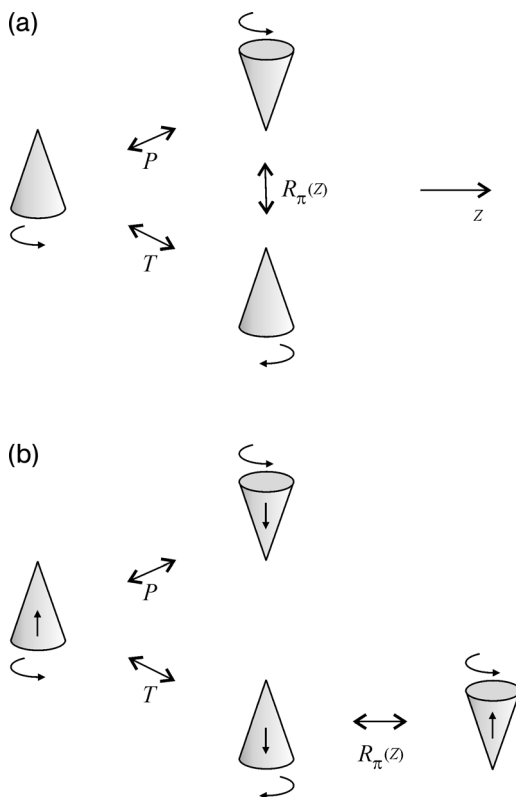


Figure 1.6 The effect of P , T and R_π on (a) a stationary spinning cone, which has false chirality, and on (b) a translating spinning cone, which has true chirality. The systems generated by P and T may be interconverted by a rotation $R_\pi(z)$ about an axis z perpendicular to the symmetry axis of the cone in (a) but not in (b). Adapted from Ref. [2] with permission.

constitute a chiral system. As Curie [34] pointed out, collinear electric and magnetic fields do indeed generate spatial enantiomorphism (dissymmetry). Thus, parallel and antiparallel arrangements are interconverted by space inversion and are not superposable. But they are also interconverted by time reversal combined with a rotation R_π through 180° about an axis perpendicular to the field directions and so the enantiomorphism corresponds to false chirality (Figure 1.7). Zocher and Török [40] also recognized that Curie's spatial enantiomorphism is not the same as that of a chiral molecule: they called the collinear arrangement of electric and magnetic fields a time-asymmetric enantiomorphism and said that it does not support time-symmetric optical activity. Tellegen [41] conceived of a medium with novel electromagnetic properties comprising microscopic electric and magnetic dipoles tied together with their moments either parallel or antiparallel. Such media clearly exhibit enantiomorphism corresponding to false chirality, and are potentially of great interest to nanotechnology. However, although much discussed [42, 43], the fabrica-

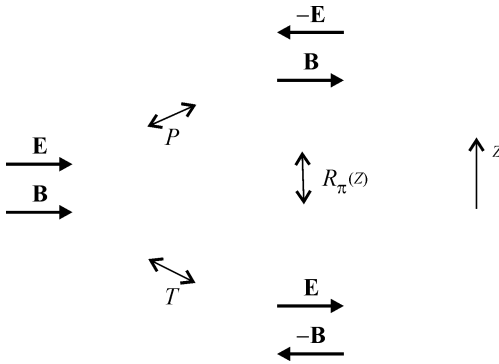


Figure 1.7 The effect of P and T on an arrangement of parallel electric and magnetic fields, which has false chirality. The opposite antiparallel arrangements generated by P and T may be interconverted by a rotation $R_{\pi(z)}$ about an axis z perpendicular to the field directions.

tion of Tellegen media proved elusive until very recently when the construction of particles with coupled electric and magnetic moments was reported for the first time [44]. These particles, made from white titanium oxide and black manganese ferrite suspended in polythene beads, were used to fabricate a switchable room-temperature magnetoelectric material that is isotropic in the absence of any field.

In fact, the basic requirement for two collinear vectorial influences to generate true chirality is that one transforms as a polar vector and the other as an axial vector, with both either time even- or time-odd. The second case is exemplified by magnetochiral phenomena [1, 2, 45] where a birefringence and a dichroism may be induced in an isotropic chiral sample by a uniform magnetic field \mathbf{B} collinear with the propagation vector \mathbf{k} of a light beam of arbitrary polarization, including unpolarized. The birefringence [46] and the dichroism [47] were first observed in the late 1990s. The magnetochiral dichroism experiment is illustrated in Figure 1.8. Here, the parallel

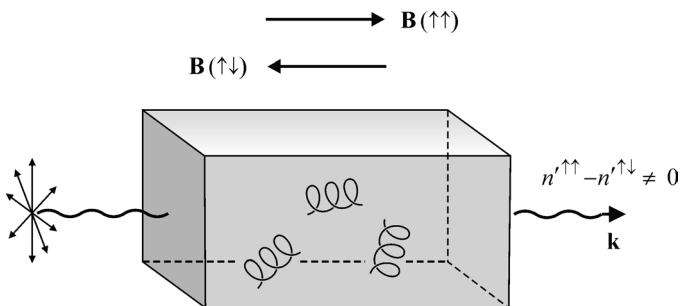


Figure 1.8 The magnetochiral dichroism experiment. The absorption index n' of a medium composed of chiral molecules is slightly different for *unpolarized* light when a static magnetic field is applied parallel ($\uparrow\uparrow$) and antiparallel ($\uparrow\downarrow$) to the direction of propagation of the beam. Reprinted from Ref. [2] with permission.

and antiparallel arrangements of \mathbf{B} and \mathbf{k} , which are interconverted by P , are true chiral enantiomers because they cannot be interconverted by T since \mathbf{B} and \mathbf{k} are both time odd. Magneto-chiral phenomena are not confined to the realm of optics [1]. An important example for nanotechnology is an anisotropy in the electrical resistance through a chiral conductor in directions parallel and antiparallel to a static magnetic field, something that has been observed in both macroscopic chiral conductors in the form of helical bismuth wires [48], and microscopic helical conductors in the form of chiral single-walled nanotubes [49].

1.3.4

Symmetry Violation

Prior to the discovery of parity violation by Lee and Yang in 1956, it seemed self-evident that handedness is not built into the laws of nature. If two objects exist as nonsuperposable mirror images, such as the two enantiomers of a chiral molecule, it did not seem reasonable that nature should prefer one over the other. Any difference was thought to be confined to the sign of pseudoscalar observables: the mirror image of any complete experiment involving one enantiomer should be realizable, with any pseudoscalar observable (such as the natural optical rotation angle) changing sign but retaining exactly the same magnitude. Observations of asymmetries in phenomena such as radioactive β -decay demonstrated that this was not the case for processes involving the weak interactions. It was subsequently realized, however, that symmetry could be recovered by invoking invariance under the combined CP operation in which charge conjugation and space inversion are applied together [50].

The unification of the theory of the weak and electromagnetic interactions into a single electroweak interaction theory [50] revealed that the absolute parity violation associated with the weak interactions could infiltrate to a tiny extent into all electromagnetic phenomena and hence into the world of atoms and molecules. This is brought about by a “weak neutral current” that generates, *inter alia*, the following parity-violating electron–nucleus contact interaction term (in atomic units) in the Hamiltonian of the atom or molecule [36, 51]:

$$V_{eN}^{PV} = \frac{G\alpha}{4\sqrt{2}} Q_W \{ \boldsymbol{\sigma}_e \cdot \mathbf{p}_e, \rho_N(\mathbf{r}_e) \} \quad (1.1)$$

where $\{ \}$ denotes an anticommutator, G is the Fermi weak coupling constant, α is the fine structure constant, $\boldsymbol{\sigma}_e$ and \mathbf{p}_e are the Pauli spin operator and linear momentum operator of the electron, $\rho_N(\mathbf{r}_e)$ is a normalized nuclear density function and Q_W is an effective weak charge. Since $\boldsymbol{\sigma}_e$ and \mathbf{p}_e are axial and polar vectors, respectively, and both are time odd, their scalar product $\boldsymbol{\sigma}_e \cdot \mathbf{p}_e$ and hence V_{eN}^{PV} are time-even pseudoscalars.

One manifestation of parity violation in atomic physics is a tiny natural optical rotation in vapors of free atoms [52]. CP invariance means that the equal and opposite sense of optical rotation would be shown by the corresponding atoms composed of antiparticles. Chiral molecules support a unique manifestation of parity violation in the form of a lifting of the exact degeneracy of the energy levels of mirror-image

enantiomers, known as the parity-violating energy difference (PVED). Although not yet observed experimentally using, for example, ultrahigh resolution spectroscopy, this PVED may be calculated [14, 36, 53]. Since, on account of the PVED, the P -enantiomers of a truly chiral object are not exactly degenerate (isoenergetic), they are not strict enantiomers (because the concept of enantiomers implies the exact opposites). So where is the strict enantiomer of a chiral object to be found? In the antiworld, of course: strict enantiomers are interconverted by CP ! In other words, the molecule with the opposite absolute configuration but composed of antiparticles should have exactly the same energy as the original [2, 37], which means that a chiral molecule is associated with two distinct pairs of strict enantiomers (Figure 1.9).

Violation of time reversal was first observed by Christenson *et al.* in 1964 in decay modes of the neutral K -meson, the K^0 [50]. The effects are very small; nothing like the parity-violating effects in weak processes, which can sometimes be absolute. In fact, T violation itself was not observed directly; rather, the observations showed CP violation from which T violation was implied from the CPT theorem. Direct T violation was observed in 1998 in the form of slightly different rates, and hence a breakdown in microscopic reversibility, for the particle to antiparticle process $K^0 \rightarrow K^{0*}$ and the inverse $K^{0*} \rightarrow K^0$. Since a particle and its antiparticle have the same rest mass if CPT

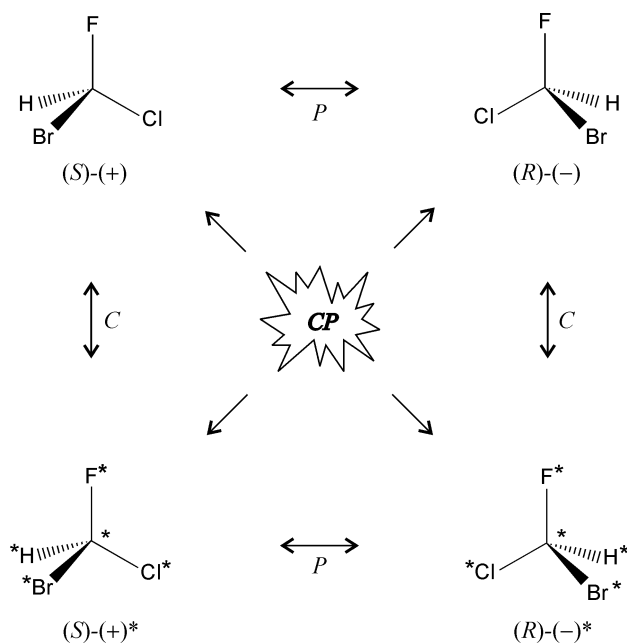


Figure 1.9 The two pairs of strict enantiomers (exactly degenerate) of a chiral molecule that are interconverted by CP . The structures with atoms marked by asterisks are antimolecules built from the antiparticle versions of the constituents of the original molecules. Adapted with corrections from Ref. [2] with permission.

invariance holds, *only the kinetics, but not the thermodynamics, are affected in CP- or T-violating process.* CPT invariance may also be used to show that the CP-enantiomers of a chiral molecule that appear in Figure 1.9 remain strictly degenerate even in the presence of CP violation [54]. Whether or not CP violation could have any direct manifestations in molecular physics is the subject of debate [54].

The concept that a spinning particle translating along the axis of spin possesses true chirality exposes a link between chirality and special relativity. Consider a particle with a right-handed chirality moving away from an observer. If the observer accelerates to a sufficiently high velocity that she starts to catch up with the particle, it will appear to be moving towards her and so takes on a left-handed chirality. The chirality of the particle vanishes in its rest frame. Only for massless particles such as photons and neutrinos is the chirality conserved since they always move at the velocity of light in any reference frame. This relativistic aspect of chirality is a central feature of elementary particle theory, especially in the weak interactions where the parity-violating aspects are velocity dependent [50].

1.3.5

Symmetry Violation *versus* Symmetry Breaking

The appearance of parity-violating phenomena is interpreted in quantum mechanics by saying that, contrary to what had been previously supposed, the Hamiltonian lacks inversion symmetry due to the presence of pseudoscalar terms such as the weak neutral current interaction. Such symmetry *violation*, sometimes called symmetry nonconservation, must be distinguished from symmetry *breaking* that applies when a system displays a lower symmetry than that of its Hamiltonian [2]. Natural optical activity, for example, is a phenomenon arising from parity (or mirror symmetry) breaking because a resolved chiral molecule displays a lower symmetry than its associated Hamiltonian: it lacks inversion symmetry (equivalent to mirror symmetry), whereas all the terms in the molecular Hamiltonian (ignoring tiny parity-violating terms) have inversion symmetry. It has been pointed out that the terms “chiral symmetry” and “chiral symmetry breaking,” which are widely used to describe the appearance of chirality out of achiral precursors, are inappropriate because chirality is not a symmetry at all in molecular science [55, 56]. Rather, chirality is an attribute associated with special types of reduced spatial symmetry that enables an object to exist in two nonsuperposable mirror-image forms. “Mirror-symmetry breaking” is more correct. The term “chiral symmetry breaking” is, however, entirely appropriate in elementary particle physics, which requires relativistic quantum field theory within which chiral symmetry has a rigorous definition [57]. Chiral symmetry is an *internal* symmetry, rather than a geometrical symmetry, of massless particles, with mass associated with broken chiral symmetry.

In spontaneous resolutions such as that of sodium ammonium tartrate studied by Pasteur, mirror-symmetry breaking has not occurred at the bulk level because the sample remains optically inactive overall. However, bulk mirror-symmetry breaking can sometimes be induced to produce a large excess of one or other enantiomer. A famous example is the sodium chlorate (NaClO_3) system [58]. Solutions of this salt in

water are optically inactive because the Na^+ and ClO_3^- ions into which it dissociates are achiral. NaClO_3 crystals, however, are chiral, but in the absence of perturbations a random distribution of the (+) and (-) enantiomeric crystals is obtained. Remarkably, when the evaporating NaClO_3 solution is stirred, mostly either (+) or (-) crystals are obtained; repeating the experiment many times gives equal numbers of (+) and (-) sets of crystals, as it must if parity is to be conserved. Chiral perturbations such as seeding with a small amount of the (+) or (-) crystals, or irradiation with energetic spin-polarized electrons (left-helical) or positrons (right-helical) from radioactive sources [59], can systematically induce bulk mirror-symmetry breaking in the form of a large excess of one or other of the chiral crystal forms. The formation of helical polymers with high ees via the sergeants-and-soldiers or majority rules phenomena (*vide supra*), and analogous phenomena in two dimensions in the context of the supramolecular assembly of molecules into homochiral domains on surfaces [60, 61], are further examples of mirror-symmetry breaking in the bulk induced by chiral perturbations.

1.3.6

Chirality in Two Dimensions

Since surfaces play an important role in nanoscience, a consideration of chirality in two dimensions is pertinent. This arises when there are two distinct enantiomers, confined to a plane or surface, that are interconverted by parity but not by any rotation within the plane about an axis perpendicular to the plane (symmetry operations out of the plane require an inaccessible third dimension). In two dimensions, however, the parity operation is no longer equivalent to an inversion through the coordinate origin as in three dimensions because this would not change the handedness of the two coordinate axes. Instead, an inversion of just one of the two axes is required [62]. For example, if the axes x , y are in the plane with z being perpendicular, then the parity operation could be taken as producing either $-x$, y or x , $-y$, which are equivalent to mirror reflections across lines defined by the y - or x -axes, respectively. Hence, an object such as a scalene triangle (one with three sides of different length), which is achiral in three dimensions, becomes chiral in the two dimensions defined by the plane of the triangle because reflection across any line within the plane generates a triangle that cannot be superposed on the original by any rotation about the z -axis. Notice that a subsequent reflection across a second line, perpendicular to the first, generates a triangle superposable on the original, which demonstrates why an inversion of both axes, so that x , $y \rightarrow -x$, $-y$ is not acceptable as the parity operation in two dimensions.

Arnaut [63] has provided a generalization of the geometrical aspect of chirality to spaces of any dimensions. Essentially, an N -dimensional object is chiral in an N -dimensional space if it cannot be brought into congruence with its enantiomorph through a combination of translation and rotation within the N -dimensional space. As a consequence, an N -dimensional object with N -dimensional chirality loses its chirality in an M -dimensional space where $M > N$ because it can be rotated in the $(M - N)$ -subspace onto its enantiomorph. Arnaut refers to chirality in one, two and

three dimensions as axichirality, planochirality and chirality, respectively, and provides a detailed analysis of planochirality with examples such as a swastika, a logarithmic spiral and a jagged ring. He concludes that, for time-harmonic excitations, axichiral media have no significance, although the concept is significant for static and more general rectified fields. He also concludes that the notion of zero-dimensional chirality would be meaningless based on his view of chirality as a geometrical concept. However, these conclusions based on a strictly geometrical definition of chirality may need to be qualified if motion is an essential ingredient in the generation of the chirality.

One striking optical manifestation of planochirality is a large circular intensity difference in second-harmonic light scattering from chiral molecules on an isotropic surface [64]. Because the mechanism involves pure electric dipole interactions, the effect is three orders of magnitude larger than analogous phenomena observed in the bulk since the latter require interference between electric dipole and magnetic dipole interactions [2]. Other manifestations include rotation of the plane of polarization in light refracted from [65], and transmitted through [66], the surface of artificial chiral planar gratings based on swastika-like chiral surface nanostructures.

The concept of false chirality arises in two dimensions as well as in three. For example, the sense of a spinning electron on a surface with its axis of spin perpendicular to the surface is reversed under the two-dimensional parity operation (unlike in three dimensions). Because electrons with opposite spin sense are nonsuperposable in the plane, a spinning electron on a surface would seem to be chiral. However, the apparent chirality is false because the sense of spin is also reversed by time reversal. The enantiomorphism is therefore time-noninvariant, the system being invariant under the combined PT operation but not under P and T separately.

1.4 Absolute Enantioselection

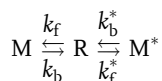
The use of an external physical influence to produce an ee in what would otherwise be a racemic product in a chemical reaction is known as an absolute asymmetric synthesis. The production of an ee in more general situations is often referred to as absolute enantioselection or physical chiral induction. The subject still attracts much interest and controversy [12, 13, 15, 67]. The considerations of Section 1.3.3 above provide a sound foundation for the critical assessment of physical influences capable of inducing ees, however small.

1.4.1 Truly Chiral Influences

If an influence is classified as truly chiral it has the correct symmetry characteristics to induce absolute asymmetric synthesis, or some related process such as preferential asymmetric decomposition, in any conceivable situation, although of course the

influence might be too weak to produce an observable effect. In this respect it is important to remember Jaeger's dictum [68]: "The necessary conditions will be that the externally applied forces are a *conditio sine qua non* for the initiation of the reaction which would be impossible without them."

The ability of a truly chiral influence to induce absolute asymmetric synthesis in a reaction process at equilibrium may be illustrated by a simple symmetry argument applied to the following unimolecular process



in which an achiral molecule R generates a chiral molecule M or its enantiomer M* and the *ks* are appropriate rate constants. In the absence of a chiral influence, M and M* have the same energy, so no ee can exist if the reaction reaches thermodynamic equilibrium. Consider a collection of single enantiomers M in the presence of a right-handed chiral influence (Ch)_R, say. Under parity *P*, the collection of enantiomers M becomes an equivalent collection of mirror-image enantiomers M* and the right-handed chiral influence (Ch)_R becomes the equivalent left-handed chiral influence (Ch)_L. Assuming parity is conserved, this indicates that the energy of M in the presence of (Ch)_R is equal to that of M* in the presence of (Ch)_L. But because parity (or any other symmetry operation) does not provide a relation between the energy of M and M* in the presence of the same influence, be it (Ch)_R or (Ch)_L, they will in general have different energies. Hence, an ee can now exist at equilibrium (due to different Boltzmann populations of M and M*). There will also be kinetic effects because the enantiomeric transition states will also have different energies.

Circularly polarized photons, or longitudinal spin-polarized electrons associated with radioactive β-decay, are obvious examples of truly chiral influences, and their ability to induce absolute enantioselection has been demonstrated in a number of cases [12, 13, 15, 67]. Photochemistry with circularly polarized light is especially favorable because it conforms to Jaeger's dictum above. This photochemistry can occur by photoequilibration of a racemic mixture of molecules, or by selective destruction of one enantiomer over the other. A recent and impressive example, with important implications for astrobiology, was the use of intense circularly polarized synchrotron radiation in the vacuum ultraviolet to induce significant ees in racemic amino acids in the solid state via enantioselective photodecomposition, which models a realistic situation relevant to organic molecules in interstellar or circumstellar dust grains [69].

Vortex motion constitutes a truly chiral influence since it combines rotation with translation perpendicular to the rotation plane. There has been considerable interest in the possibility that vortex motion in a conical swirl might be exploited to induce absolute enantioselection, but until recently no convincing example has been demonstrated experimentally [67]. Then -several years ago reports appeared of mirror-symmetry breaking in homoassociation of achiral diprotonated porphyrins where helical conformations were generated by stirring in a rotary evaporator with the sense of chirality, detected by circular dichroism, being selected by the sense of

stirring [70, 71]. In a later report, the same group claimed to have achieved similar results through magnetic stirring in a small tube, and went on to provide an explanation in terms of hydrodynamic effects of the vortex at the walls of the container [72]. Another recent result illustrates the complexity of such processes and the importance of the conditions. Thus it was found that vortexing an insulin solution at room temperature generated two distinct types of amyloid fibrils with opposite local chiral preferences, the dominance of one or other type of fibrils in a test tube being only stochastically determined; whereas vortexing at 60 °C always generated the same chiral form, presumably under the influence of the chiral bias of the exclusively L-amino acids in the protein [73]. Vortexing in the opposite sense made no difference to these results (W. Dzwolak, private communication). A further recent and highly relevant observation in this context concerns filamentous bacterial viruses: several types form cholesteric liquid crystals under the influence of their chiral protein and DNA constituents, while others form nematic liquid crystals that are apparently “oblivious” to the chirality of their molecular components [74].

Although a magnetic field alone has no chirality and so cannot induce absolute enantioselection, we have seen that a static magnetic field collinear with a light beam of arbitrary polarization (Figure 1.8) is a truly chiral system and hence can induce absolute enantioselection in all circumstances. This has been demonstrated experimentally in the form of small ees observed in an initially racemic solution of a chiral transition-metal complex in the presence of a static magnetic field collinear with an unpolarized light beam at photochemical equilibrium [75].

Being a time-even pseudoscalar, the weak neutral current interaction V_{eN}^{PV} responsible for the tiny PVED is the quintessential truly chiral influence in atomic and molecular physics. It lifts only the degeneracy of the space-inverted (*P*-) enantiomers of a truly chiral system; the *P*-enantiomers of a falsely chiral system such as a nontranslating rotating cone remain strictly degenerate. It has attracted considerable discussion as a possible source of biological homochirality [11, 14, 15, 36, 53, 76]. However, it is still not clear whether or not the PVED preferentially stabilizes the naturally occurring L-amino acids and D-sugars. Measurable differences reported in the physical properties of crystals of D- and L-amino acids and claimed to be due to parity violation have not been corroborated [77]; they have been shown instead to arise from traces of different impurities in the enantiomorphous crystals [78]. So far there is no convincing evidence that the PVED itself has any enantioselective influence on the crystallization of sodium chlorate (*vide supra*) or on that of any other system [30, 59].

1.4.2

Falsely Chiral Influences

It is important to appreciate that, unlike the case of a truly chiral influence, enantiomers *M* and *M** remain strictly isoenergetic in the presence of a falsely chiral influence such as collinear electric and magnetic fields. Again this can be seen from a simple symmetry argument applied to the unimolecular reaction above. Under *P*, the collection of enantiomers *M* becomes the collection *M** and the parallel

arrangement, say, of \mathbf{E} and \mathbf{B} becomes antiparallel. The antiparallel arrangement of \mathbf{E} and \mathbf{B} , however, becomes parallel again under T ; but these last two operations will have no effect on an isotropic collection of chiral molecules, even if paramagnetic. Hence, the energy of the collection M is the same as that of the collection M^* in parallel (or antiparallel) electric and magnetic fields.

When considering the possibility or otherwise of absolute asymmetric synthesis being induced by a falsely chiral influence, a distinction must be made between reactions that have been left to reach thermodynamic equilibrium (*thermodynamic control*) and reactions that have not attained equilibrium (*kinetic control*). The case of thermodynamic control is quite clear: because M and M^* remain strictly isoenergetic in the presence of a falsely chiral influence, such an influence cannot induce absolute asymmetric synthesis in a reaction that has been allowed to reach thermodynamic equilibrium. The case of kinetic control is more subtle. It has been suggested that processes involving chiral molecules in the presence of a falsely chiral influence such as collinear \mathbf{E} and \mathbf{B} may exhibit a breakdown of conventional microscopic reversibility, but preserve a new and deeper principal of *enantiomeric* microscopic reversibility [79]. Since only the kinetics, but not the thermodynamics, of the process are affected, this suggests an analogy with the breakdown in microscopic reversibility associated with CP - and T -violation in particle–antiparticle processes [37, 54, 79]. The force responsible for CP violation may be conceptualized as the quintessential falsely chiral influence in particle physics, being characterized by lack of CP and T invariance separately but possessing CPT invariance overall. This is analogous to a falsely chiral influence in the molecular case, which is characterized by a lack of P and T invariance separately but possessing PT invariance overall.

Since one effect of \mathbf{E} in a falsely chiral influence such as collinear \mathbf{E} and \mathbf{B} is to partially align dipolar molecules [79], it is not required if the molecules are already aligned. Hence, a magnetic field alone might induce absolute enantioselection if the molecules are prealigned, as in a crystal or on a surface, and the process is far from equilibrium [80]. However, to date there has been no unequivocal demonstration of absolute enantioselection induced by this or any other falsely chiral influence [67].

1.5 Spectroscopic Probes of Chirality in Nanosystems

In order to detect chirality in molecular systems, a spectroscopic probe must be sensitive to absolute handedness. This usually means that it must exploit in some way the intrinsic chirality of circularly polarized light. The power of chiroptical spectroscopic techniques for applications to chiral macromolecules and supramolecular structures in general derives in part from their ability to cut through the complexity of conventional spectra (which are “blind” to chirality) to reveal three-dimensional information about the most rigid, twisted chiral parts of the structure, within the backbone in polymers, for example, since these often generate the largest chiroptical signals. Although chiroptical methods do not provide structures at atomic resolution like X-ray crystal and fiber diffraction, and multidimensional NMR, they are usually

easier to apply and a much wider range of samples are accessible. Furthermore, the level of analysis is improving rapidly thanks to current progress in computational chemistry, particularly for the newer vibrational optical activity techniques.

1.5.1

Electronic Optical Activity

To date the most widely used chiroptical spectroscopies to study chiral nanosystems in solution are optical rotatory dispersion (ORD) and circular dichroism (CD), which originate in differential refraction and absorption, respectively, of right- and left-circularly polarized light. Closely related to CD are circular polarization of luminescence, and fluorescence-detected circular dichroism. The principles and applications of CD and other chiroptical spectroscopies, including some applications to supramolecular systems, are reviewed in Refs. [81, 82]. The observable in CD spectroscopy is the following *rotational strength* of the $j \leftarrow n$ electronic transition, which may be related to the area and sign of a corresponding CD spectral band [2, 81, 82]:

$$R(j \leftarrow n) = \text{Im}(\langle n | \boldsymbol{\mu} | j \rangle \cdot \langle j | \mathbf{m} | n \rangle) \quad (1.2)$$

where $\boldsymbol{\mu}$ and \mathbf{m} are the electric and magnetic dipole moment operators, respectively. Since $\boldsymbol{\mu}$ and \mathbf{m} are time-even and time-odd polar and axial vectors, respectively, the imaginary part of their scalar product is a time-even pseudoscalar [2], as befits a chiral observable. Attempts to theoretically simulate observed UV-visible CD spectra focus on quantum-chemical calculations of the rotational strength (1.2) for the corresponding electronic transitions [81, 82]. At present, their use remains significantly limited by the molecular size, conformational flexibility, and difficulties in obtaining sufficiently accurate and reliable descriptions of the corresponding excited electronic states [81–83].

CD is immensely useful in nanoscience, but mainly in its qualitative aspects for monitoring conformation changes, especially inversion of chirality via reversal of CD signals. Theoretical simulations of the rotational strength (1.2) that are sufficiently accurate to provide information about absolute helical sense and conformational parameters from the experimental CD spectra of systems such as helical polyisocyanates [25] and β -peptides [84] have so far proved elusive.

One particularly valuable application of CD in supramolecular chemistry involves the observation of spectral signals arising from different types of intermolecular interactions. Four typical situations are encountered [83]. A chiral “guest” and an achiral chromophoric “host” compound such as a calixarene or a bisporphyrin can form a complex that exhibits an induced CD within the absorption bands of the host. Conversely, a small achiral chromophoric guest compound bound to a chiral host such as a cyclodextrin or an oligonucleotide may show a CD induced by the chiral host. Also, coupling between several achiral guest molecules such as carotenoids bound to different sites of a chiral macromolecular host such as serum albumin may show a diagnostic CD spectrum due to exciton coupling if the guests are held in a chiral orientation relative to each other. Finally, a chiral

nonchromophoric ligand may bind to a metal ion with observable *d*- or *f*-type transitions making them CD-active.

1.5.2

Vibrational Optical Activity

ORD and CD at visible and ultraviolet wavelengths measure natural optical activity in the *electronic* spectrum. It had long been appreciated that extending natural optical activity into the *vibrational* spectrum could provide more detailed and reliable stereochemical information because a vibrational spectrum contains many more bands sensitive to the details of the molecular structure ($3N-6$ fundamentals, where N is the number of atoms) [2]. This was finally achieved in the early 1970s when vibrational optical activity was first observed in small chiral molecules in fluid media using two complementary techniques: a circular polarization dependence of vibrational Raman scattering of visible laser light [85], and circular dichroism of infrared radiation [86]. These are now known as Raman optical activity (ROA) and vibrational circular dichroism (VCD), respectively [2, 81, 82].

Vibrational optical activity is especially powerful for determining the absolute configuration together with conformational details, including relative populations, of smaller chiral molecules by means of *ab initio* quantum-chemical simulations of VCD and ROA spectra [87–89]. These are generally more reliable than the corresponding electronic CD calculations, one reason being that the calculations involve molecules in their ground electronic states that are usually well defined. Attempts to simulate VCD spectra focus on calculations of the rotational strength (1.2), with $j \leftarrow n$ now a fundamental vibrational transition, for all $3N-6$ normal modes of vibration. ROA simulations focus on calculations of products such as $\langle n | \alpha_{\alpha\beta} | j \rangle \langle j | G'_{\alpha\beta} | n \rangle$ and $\langle n | \alpha_{\alpha\beta} | j \rangle \epsilon_{\alpha\gamma\delta} \langle j | A_{\gamma\delta\beta} | n \rangle$, which determine the intensity of an ROA band for the $j \leftarrow n$ fundamental vibrational transition, where $\alpha_{\alpha\beta}$ is an operator corresponding to the electric dipole–electric dipole polarizability tensor and $G'_{\alpha\beta}$ and $A_{\alpha\beta\gamma}$ are electric dipole–magnetic dipole and electric dipole–electric quadrupole optical activity tensor operators, respectively [2]. Like the rotational strength, these ROA intensity terms are again time-even pseudoscalars and so are only supported by chiral molecules.

The recent determination of the solution structure of a supramolecular tetramer of a chiral dimethyl-biphenyl-dicarboxylic acid [90] and of aromatic foldamers [91] from *ab initio* simulations of the observed VCD spectra provide examples of what can currently be achieved. Oligo- and polypeptides, including synthetic β -peptides, in model conformations are also becoming accessible to *ab initio* VCD and ROA simulations [92–94]. All this suggests that, although applications of ROA and VCD in nanoscience are still in their infancy, they appear to have significant potential for characterizing the absolute handedness and conformational details of synthetic chiral macromolecules and supramolecular structures in solution by means of theoretical simulations of observed spectra. ROA is especially promising in this respect because there appears to be no upper size limit to the structures that may be studied: even intact viruses are accessible to ROA measurements from which, *inter alia*, information such as coat protein folds and nucleic acid structure may be deduced [95].

1.6

Conclusion

Chirality is already a burgeoning topic in nanoscience and is expected to stimulate further new and fruitful developments. The homochirality of biological macromolecules and their many diverse structural and functional roles provide important lessons for chiral nanoscience, which is also developing its own themes with regard to synthetic supramolecular systems and nonaqueous solvents not encountered in the chemistry of life. Applications of chiroptical spectroscopies in nanoscience will continue to grow in importance, especially the vibrational optical activity techniques of ROA and VCD. It is hoped that the more fundamental aspects elaborated in this chapter will prove useful for understanding the generation, characterization and functional role of chirality in molecular systems and thereby facilitate the exploitation of its potential in nanoscience.

References

- 1 Wagnière, G.H. (2007) *On Chirality and the Universal Asymmetry*, Verlag Helvetica Chimica Acta, Zürich, and Wiley-VCH, Weinheim.
- 2 Barron, L.D. (2004) *Molecular Light Scattering and Optical Activity*, 2nd edn, Cambridge University Press, Cambridge.
- 3 Cornelissen, J.J.L.M., Rowan, A.E., Nolte, R.J.M. and Sommerdijk, N.A.J.M. (2001) *Chemical Reviews*, **101**, 4039–4070.
- 4 Green, M.M., Nolte, R.J.M. and Meijer, E.W. (eds) (2003) *Topics in Stereochemistry*, Vol. 24, *Materials-Chirality*, Wiley-VCH, New York.
- 5 Zhang, J., Albelda, M.T., Liu, Y. and Canary, J.W. (2005) *Chirality*, **17**, 404–420.
- 6 Lowry, T.M. (1935) *Optical Rotatory Power*, Longmans, Green, London, reprinted by Dover, New York 1964.
- 7 Eliel, E.L. and Wilen, S.H. (1994) *Stereochemistry of Organic Compounds*, John Wiley & Sons, New York.
- 8 Gal, J. (2007) *Chirality*, **19**, 89–98.
- 9 Kelvin, Lord. (1904) *Baltimore Lectures*, C. J. Clay & Sons, London.
- 10 Barron, L.D. (1986) *Journal of the American Chemical Society*, **108**, 5539–5542.
- 11 Mason, S.F. (1988) *Chemical Society Reviews*, **17**, 347–359.
- 12 Bonner, W.A. (1988) *Topics in Stereochemistry*, **18**, 1–96.
- 13 Feringa, B.L. and van Delden, R.A. (1999) *Angewandte Chemie-International Edition*, **38**, 3418–3438.
- 14 MacDermott, A.J. (2002) *Chirality in Natural and Applied Science* (eds. Lough, W.J. and Wainer, I.W.), Blackwell Publishing, Oxford, pp. 23–52.
- 15 Compton, R.N. and Pagni, R.M. (2002) *Advances in Atomic, Molecular, and Optical Physics*, **48**, 219–261.
- 16 Behr, J.-P. (ed.) (1994) *The Lock and Key Principle*, John Wiley & Sons, New York.
- 17 Fujii, N. (2002) *Origins Life*, **32**, 103–127.
- 18 Konno, R., Brückner, H., D’Aniello, A., Fisher, G.H., Fujii, N. and Homma, H. (eds) (2007) *D-Amino Acids: A New Frontier in Amino Acid and Protein Research-Practical Methods and Protocols*, Nova Science Publishers, New York.
- 19 Westhof, E. (ed.) (1993) *Water and Biological Macromolecules*, CRC Press, Boca Raton.
- 20 Ball, P. (2005) *Nature*, **436**, 1084–1085.
- 21 Sandars, P.G.H. (2003) *Origins Life*, **33**, 575–587.
- 22 Joyce, G.F., Visser, G.M., van Boeckel, C.A.A., van Boom, J.H., Orgel, L.E. and van Westresen, J. (1984) *Nature*, **310**, 602–604.

- 23 Avetisov, V.A., Goldanskii, V.I. and Kuz'min, V.V. (1991) *Physics Today*, **44**, 33–41.
- 24 Green, M.M., Peterson, N.C., Sato, T., Teramoto, A., Cook, R. and Lifson, S. (1995) *Science*, **268**, 1860–1866.
- 25 Green, M.M. (2000) *Circular Dichroism: Principles and Applications* (eds. Berova, N., Nakanishi, K. and Woody, R.W.), Wiley-VCH, New York, pp. 491–520.
- 26 Klussman, M., Iwamura, H., Mathew, S.P., Wells, D.H., Jr, Pandya, U., Armstrong, A. and Blackmond, D.G. (2006) *Nature*, **441**, 621–623.
- 27 Plasson, R., Kondepudi, D.K., Bersini, H., Commeyras, A. and Asakura, K. (2007) *Chirality*, **19**, 589–600.
- 28 Perry, R.H., Wu, C., Neffiu, M. and Cooks, R.G. (2007) *Chemical Communications*, 1071.
- 29 Fletcher, S.P., Jagt, R.B.C. and Feringa, B.L. (2007) *Chemical Communications*, 2578–2580.
- 30 Avalos, M., Babiano, R., Cintas, P., Jiménez, J.L. and Palacios, J.C. (2004) *Origins Life*, **34**, 391–405.
- 31 Cintas, P. (2002) *Angewandte Chemie-International Edition*, **41**, 1139–1145.
- 32 Rubinstein, I., Eliash, R., Bolbach, G., Weissbuch, I. and Lahav, M. (2007) *Angewandte Chemie-International Edition*, **46**, 3710–3713.
- 33 Pasteur, L. (1884) *Bulletin de la Société chimique de France*, **41**, 219.
- 34 Curie, P. (1894) *Journal of Physiology, Paris* (3), **3**, 393.
- 35 Barron, L.D. (2000) *Nature*, **405**, 895–896.
- 36 Wesendrup, R., Laerdahl, J.K., Compton, R.N. and Schwerdtfeger, P. (2003) *Journal of Physical Chemistry A*, **107**, 6668–6673.
- 37 Barron, L.D. (2002) *Chirality in Natural and Applied Science* (eds. Lough, W.J. and Wainer, I.W.), Blackwell Publishing, Oxford, pp. 53–86.
- 38 Berestetskii, V.B., Lifshitz, E.M. and Pitaevskii, L.P. (1982) *Quantum Electrodynamics*, Pergamon Press, Oxford.
- 39 Mislow, K. (1999) *Topics in Stereochemistry*, **22**, 1–82.
- 40 Zocher, H. and Török, C. (1953) *Proceedings of the National Academy of Sciences of the United States of America*, **39**, 681–686.
- 41 Tellegen, B.D.H. (1948) *Philips Research Reports*, **3**, 81–101.
- 42 Lindell, I.V., Sihvola, A.H., Tretyakov, S.A. and Viitanen, A.J. (1994) *Electromagnetic Waves in Chiral and Bi-Isotropic Media*, Artech House, Boston.
- 43 Weiglhofer, W.S. and Lakhtakia, A. (1998) *AEU-International Journal of Electronics and Communications*, **52**, 276–279.
- 44 Ghosh, A., Sheridan, N.K. and Fischer, P. (2008) *Small*, **4**, 1956–1958.
- 45 Wagnière, G.H. and Meir, A. (1982) *Chemical Physics Letters*, **93**, 78–81.
- 46 Kleindienst, P. and Wagnière, G. (1998) *Chemical Physics Letters*, **288**, 89–97.
- 47 Rikken, G.L.J.A. and Raupach, E. (1997) *Nature*, **390**, 493–494.
- 48 Rikken, G.L.J.A., Fölling, J. and Wyder, P. (2001) *Physical Review Letters*, **87**, art. No. 236602.
- 49 Krstić, V., Roth, S., Burghard, M., Kern, K. and Rikken, G.L.J.A. (2002) *Journal of Chemical Physics*, **117**, 11315–11319.
- 50 Gottfried, K. and Weisskopf, V.F. (1984) *Concepts of Particle Physics, Vol. 1*, Clarendon Press, Oxford.
- 51 Hegstrom, R.A., Rein, D.W. and Sandars, P.G.H. (1980) *Journal of Chemical Physics*, **73**, 2329–2341.
- 52 Bouchiat, M.A. and Bouchiat, C. (1997) *Reports on Progress in Physics*, **60**, 1351–1396.
- 53 Quack, M. (2002) *Angewandte Chemie-International Edition*, **41**, 4618–4630.
- 54 Barron, L.D. (1994) *Chemical Physics Letters*, **221**, 311–316.
- 55 Walba, D.M. (2003) *Topics in Stereochemistry*, **24**, 457–518.
- 56 Avalos, M., Babiano, R., Cintas, P., Jiménez, J.L. and Palacios, J.C. (2004) *Tetrahedron-Asymmetry*, **15**, 3171–3175.
- 57 Maggiore, M. (2005) *A Modern Introduction to Quantum Field Theory*, Cambridge University Press, Cambridge.
- 58 Kondepudi, D.K., Kaufman, R. and Singh, N. (1990) *Science*, **250**, 975–976.

- 59 Pagni, R.M. and Compton, R.N. (2002) *Crystal Growth and Design*, **2**, 249–253.
- 60 Humbolt, V., Barlow, S.M. and Raval, R. (2004) *Progress in Surface Science*, **76**, 1–19.
- 61 Ernst, K.-H. (2006) *Topics in Current Chemistry*, **265**, 209–252.
- 62 Halperin, B.I., March-Russell, J. and Wilczek, F. (1989) *Physical Review*, **B40**, 8726–8744.
- 63 Arnaut, L.R. (1997) *Journal of Electromagnetic Waves and Applications*, **11**, 1459–1482.
- 64 Hicks, J.M., Petralli-Mallow, T. and Byers, J.D. (1994) *Faraday Discussions*, **99**, 341–357.
- 65 Papakostas, A., Potts, A., Bagnall, D.M., Prosvirnin, S.L., Coles, H.J. and Zheludev, N.I. (2003) *Physical Review Letters*, **90**, art. no. 107404.
- 66 Kuwata-Gonokami, M., Saito, N., Ino, Y., Kauranen, M., Jefimovs, K., Vallius, T., Turunen, J. and Svirko, Y. (2005) *Physical Review Letters*, **95**, art. No. 227401.
- 67 Avalos, M., Babiano, R., Cintas, P., Jiménez, J.L., Palacios, J.C. and Barron, L.D. (1988) *Chemical Reviews*, **98**, 2391–2404.
- 68 Jaeger, F.M. (1930) *Optical Activity and High-Temperature Measurements*, McGraw-Hill, New York.
- 69 Meierhenrich, U.J., Nahon, L., Alcares, C., Bredehöft, J.H., Hoffman, S.V., Barbier, B. and Brack, A. (2005) *Angewandte Chemie-International Edition*, **44**, 5630–5634.
- 70 Ribó, J.M., Crusats, J., Sagués, F., Claret, J. and Rubires, R. (2001) *Science*, **292**, 2063–2066.
- 71 Rubires, R., Farrera, J.-A. and Ribó, J.M. (2001) *Chemistry – A European Journal*, **7**, 436–446.
- 72 Escudero, C., Crusats, J., Díez-Pérez, I., El-Hachemi, Z. and Ribó, J.M. (2006) *Angewandte Chemie-International Edition*, **45**, 8032–8035.
- 73 Dzwolak, W., Lokszejn, A., Galinska-Rakoczy, A., Adachi, R., Goto, Y. and Rupnicki, L. (2007) *Journal of the American Chemical Society*, **129**, 7517–7522.
- 74 Tomar, S., Green, M.M. and Day, L.A. (2007) *Journal of the American Chemical Society*, **129**, 3367–3375.
- 75 Rikken, G.L.J.A. and Raupach, E. (2000) *Nature*, **405**, 932–935.
- 76 Deamer, D.W., Dick, R., Thiemann, W. and Shinitzky, M. (2007) *Chirality*, **19**, 751–763.
- 77 Sullivan, R., Pyda, M., Pak, J., Wunderlich, B., Thompson, J.R., Pagni, R., Pan, H., Barnes, C., Schwerdtfeger, P. and Compton, R.N. (2003) *Journal of Physical Chemistry A*, **107**, 6674–6680.
- 78 Lahav, M., Weissbuch, I., Shavit, E., Reiner, C., Nicholson, G.J. and Schurig, V. (2006) *Origins Life*, **36**, 151–170.
- 79 Barron, L.D. (1987) *Chemical Physics Letters*, **135**, 1–8.
- 80 Barron, L.D. (1994) *Science*, **266**, 1491–1492.
- 81 Berova, N., Nakanishi, K. and Woody, R.W.(eds) (2000) *Circular Dichroism: Principles and Applications*, 2nd edn, Wiley-VCH, New York.
- 82 Urbanová, M. and Maloň, P. (2007) *Analytical Methods in Supramolecular Chemistry* (ed. Schalley, C.A.), Wiley-VCH, New York, pp. 265–304.
- 83 Berova, N., Di Bari, L. and Pescitelli, G. (2007) *Chemical Society Reviews*, **36**, 914–931.
- 84 Glättli, A., Daura, X., Seebach, D. and van Gunsteren, W.F. (2002) *Journal of the American Chemical Society*, **124**, 12972–12978.
- 85 Barron, L.D., Bogaard, M.P. and Buckingham, A.D. (1973) *Journal of the American Chemical Society*, **95**, 603–605.
- 86 Holzwarth, G., Hsu, E.C., Mosher, H.S., Faulkner, T.R. and Moscovitz, A.J. (1974) *Journal of the American Chemical Society*, **96**, 251–252.
- 87 Stephens, P.J. and Devlin, F.J. (2000) *Chirality*, **12**, 172–179.
- 88 Haesler, J., Schindelholz, I., Riguet, E., Bochet, C.G. and Hug, W. (2007) *Nature*, **446**, 526–529.
- 89 Macleod, N.A., Johannessen, C., Hecht, L., Barron, L.D. and Simons, J.P. (2006)

- International Journal of Mass Spectrometry*, **253**, 193–200.
- 90** Urbanová, M., Setnička, V., Devlin, F.J. and Stephens, P.J. (2005) *Journal of the American Chemical Society*, **127**, 6700–6711.
- 91** Ducasse, L., Castet, F., Fritsch, A., Huc, I. and Buffeteau, T. (2007) *Journal of Physical Chemistry A*, **111**, 5092–5098.
- 92** Keiderling, T.A. (2002) *Current Opinion in Chemical Biology*, **6**, 682–688.
- 93** Barron, L.D. (2006) *Current Opinion in Structural Biology*, **16**, 638–643.
- 94** Kapitán, J., Zhu, F., Hecht, L., Gardiner, J., Seebach, D., and Barron, L.D. (2008) *Angewandte Chemie – International Edition*, **47**, 6392–6994.
- 95** Blanch, E.W., Hecht, L., Syme, C.D., Volpetti, V., Lomonosoff, G.P., Nielsen, K. and Barron, L.D. (2002) *The Journal of General Virology*, **83**, 2593–2600.

