CMLS, Cell. Mol. Life Sci. 58 (2001) 44–60
1420-682X/01/010044-17 $ 1.50 + 0.20/0

CMLS Cellular and Molecular Life Sciences

Review

Origin of organic molecules and biomolecular homochirality

J. Podlech

Institut für Organische Chemie der Universität Stuttgart, Pfaffenwaldring 55, D-70569 Stuttgart (Germany),
Fax +49 711 685 4269, e-mail: joachim.podlech@po.uni-stuttgart.de

Received 2 May 2000; received after revision 13 July 2000; accepted 14 July 2000

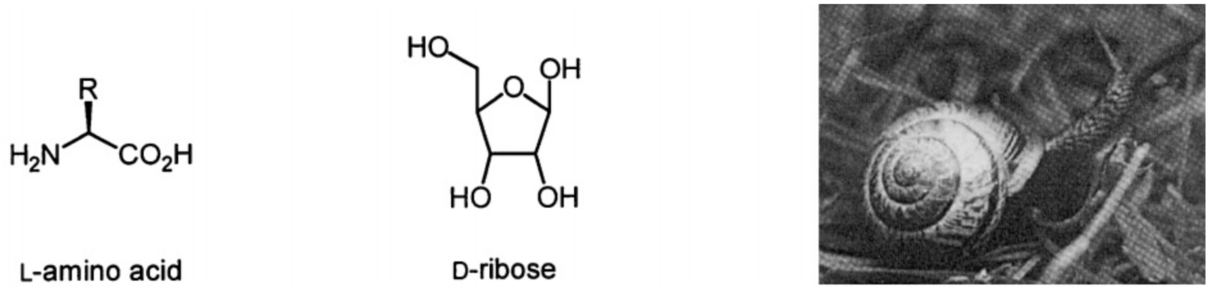
Abstract. Theories about the origin of biomolecular homochirality, which seems to be a prerequisite for the creation of life, are discussed. First, possible terrestrial and extraterrestrial sources of organic molecules are outlined. Then, mechanisms for the formation of enantiomerically enriched compounds and for the amplification of their chirality are described.

Key words. Formation of organic compounds; prebiotic chemistry; molecular evolution; amplification of chirality.

Introduction

Ever since Pasteur discovered that certain molecules can occur in two enantiomeric forms [1], chirality and optical activity have been considered as a principal criterion for life. Essential organic molecules associated with life (e.g., amino acids, nucleic acids, and sugars) are chiral and, with rare exceptions, occur in only one of the two possible enantiomeric forms. Amino acids are usually L-configurated and sugars (such as ribose or 2-deoxyribose) occur almost exclusively in their D-forms (fig. 1). This homochirality can be observed on the macroscopic scale, for example, in the helical chirality of snail shells, the helical winding of plants [2], or in such curious observations as the chewing mode of cows (having an enantiomeric excess of 10%) [3]. The reasons behind these observations are still puzzling, because hard evidence in these fields is difficult to obtain. Nevertheless, the problem can be approached by several methods [4–9], one of which is to investigate remnants that stem from the times when this homochirality evolved. Another approach is to simulate the conditions that might have prevailed during those times, and a final method is to treat this problem by purely theoretical means [10]. Consequently, this topic is of interest to scientists from a wide variety of disciplines. The large number of publications available may be due to the expectation that a solution to this problem could provide hints about the origin of life itself and, consequently, the origin of humankind. That at least enantiomerically enriched, if not (essentially) enantiomerically pure, organic compounds were necessary for the creation of protometabolic life is now widely accepted. Nevertheless, Cairns-Smith [11] suggested that mineral clays might have been the carrier of genetic information before polynucleotide replication took over; consequently, these clays would have been the first kind of protometabolic life present on Earth. However, this theory is not generally accepted, since there is practically no experimental evidence to support it.

When considering the history of Earth, the time scale starts 4.5 billion years (4.5 Gyrs) ago with the formation of the Earth. In the beginning, the Earth was too hot for the evolution of life or even for the persistence of organic molecules. The heat, evaporating all volatile material and sterilizing the surface, was produced by a heavy-impact bombardment and would have stopped all attempts of nature to evolve life. One of these impacts (a Mars-sized body) led to the formation of the terrestrial moon, and craters from this bombardment period can still be observed on the lunar surface. This



L-amino acid

D-ribose

Figure 1. Enantiopure building blocks that are essential for life. A snail with the preferred right-handed shell.

bombardment abated about 4 Gyrs ago and the formation or accumulation of larger amounts of organic molecules became possible. The oldest microfossils that seem to prove the existence of life are as much as 3.5 Gyrs old [12, 13]. However, from isotope distributions (which are known to differ in living organisms) comes the conclusion that biological carbon fixation might have occurred 3.85 Gyrs ago [14]. Calculations based on the similarity of protein sequences in different organisms show that the last common ancestor lived about 3.2–3.8 Gyrs ago, which is of the same order of magnitude [15]. This leaves just a very small window of 100–300 million years (Myrs), in which life could have evolved [16]. In the opinion of some scientists, this period is much too short for the evolution of life; they suggest an extraterrestrial evolution of life and assume the delivery of sperm to Earth via the atmosphere [17]. This panspermia theory, published by its most famous protagonist Arrhenius [18], obviously just shifts the problem from Earth to space and seems to give rise to more problems than it solves; therefore, it is usually neglected.

This review is divided into three parts in which the origin of organic molecules, mechanisms for the formation of enantiomerically enriched compounds, and mechanisms for the amplification of enantiomeric excesses are discussed.

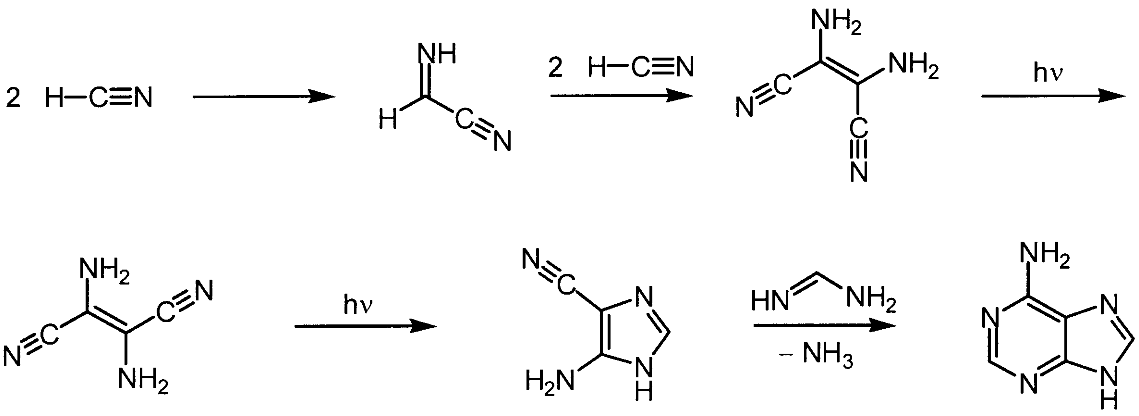
The origin of organic molecules

Before life could evolve, simple organic compounds such as amino acids, sugars, purines, and pyrimidines were needed. These simple organic compounds formed polymers and subsequently might have progressed to the generation of more complex structures and even to the creation of protometabolic organisms. The origin of these organic compounds on early Earth is still not clear and a number of theories have been proposed [8, 19–22]. A very important contribution was made by Stanley Miller (Miller-Urey experiment), who succeeded in synthesizing organic compounds from gaseous precursors under conditions that might have existed on early Earth [23, 24]. Oparin, Urey, and others have proposed that at that time, the Earth was surrounded by a reducing atmosphere consisting of methane, ammonia, water, and hydrogen [20, 25]. Miller passed spark discharges through mixtures of these gases and, after several days, observed a red precipitate, in which he found carboxylic acids, amino acids, hydroxy acids, and other simple organic compounds in a total yield of about 15% (table 1). Similar results were obtained when mixtures of methane, nitrogen, water, and traces of ammonia were treated in the same way [26, 27].

Inspired by these findings, many experiments have been performed to simulate the conditions that might have been present in the primordial broth. A further milestone was set by Oró [28], who synthesized adenine starting from an aqueous solution of ammonium cyanide at 100 °C (scheme 1). Taking the complexicity of the molecule and its synthesis into account, the achieved yield of 0.5% is excellent.

Table 1. Yields (based on carbon) of products following passage of a spark discharge through a mixture of CH_4, NH_3, H_2O, and H_2 (total yield: 15.2% [22]).

Compound	Yield (%)	Compound	Yield (%)
Formic acid	4.0	α-Hydroxybutyric acid	0.34
Glycine	2.1	Succinic acid	0.27
Glycolic acid	1.9	Sarcosine	0.25
Alanine	1.7	Iminoacetic-propionic acid	0.13
Lactic acid	1.6	*N*-Methylalanine	0.07
α-Alanine	0.76	Glutamic acid	0.051
Propionic acid	0.66	*N*-Methyl urea	0.051
Acetic acid	0.51	Urea	0.034
Iminodiacetic acid	0.37	Aspartic acid	0.024
α-Amino-*n*-butyric acid	0.34	α-Aminoisobutyric acid	0.007



Scheme 1. Proposed mechanism for the promordial synthesis of adenine starting from hydrogen cyanide [20, 28].

Further experiments showed that other compounds that are essential in contemporary organisms can be produced under similar conditions [20]. The preparation of cytosine, for example, is possible starting from cyanoacetylene (propynenitrile) and urea (accessible by sparking experiments and by oligomerization of hydrogen cyanide, respectively) [29]. Under special desiccating conditions ('evaporating-pond' or 'drying-lagoon' conditions), a yield of up to 50% is possible (scheme 2) [30].

Nevertheless, some organic compounds that appear to be essential for the evolution of life could not be synthesized under similar conditions. A formose reaction (oligomerization of formaldehyde) led to the formation of ribose, though with very low yields and together with a huge number of other sugars [31]. Therefore, this does not seem to be a suitable source for ribose. Eschenmoser and colleagues created a primordial-type preparation of ribose 2,4-phosphate starting from glycolaldehyde monophosphate and formaldehyde [32]. On the other hand, the existence of phosphate—obviously essential for metabolism—in the primordial broth is not very likely since it was most probably precipitated as calcium phosphate [33].

Although the Miller-Urey experiment is still seen as a breakthrough in prebiotic chemistry, that the conditions used by Miller were actually present on early Earth is currently doubted. Recent results suggest that the atmosphere at that time was composed of oxidative mixtures of gases containing large amounts of nitrogen, carbon dioxide, and water [34, 35]. Spark discharges passed through gas mixtures with these compositions rarely led to any organic compound [20, 36, 37]. It is generally accepted that the atmosphere was formed by volcanic outgassing. (An atmosphere formed together with the Earth would have vanished during the heavy-impact bombardment period.) A controversy arose, because it was not clear what composed the interior of the Earth. About 30 years ago, the assumption was that the Earth did not then have an iron core; the metallic iron included in the mantle would have led to reductive volcanic exhaustions. Now it is assumed that the iron core was already present during the formation of the Earth. This would have led to the exhaustion of oxidative gases [35, 38].

As a consequence of this dilemma, several additional theories on the formation of organic molecules have been proposed. Wächtershäuser claims that simple molecules might have formed on iron-sulfur surfaces [39, 40]. He showed experimentally that iron(II) sulfide acts as a reducing agent for carbon monoxide (or carbon dioxide) leading to the formation of thiocarboxylic acids and pyrites (scheme 3) [41]. Addition of a nitrogen source (e.g., NH_3) led to the formation of amino acid derivatives like glycine, alanine, and glutamic acid [42, 43]. The starting materials and reaction conditions (100 °C, 1 bar CO) needed for these reactions might have been present in the vicinity of hydrothermal vents on the oceans beds. Whether this 'vent theory' will be able to explain the formation of more complex molecules remains to be established.

A major advantage of this mechanism is that it can explain the formation of activated thiocarboxylic acids, which are easily converted to carboxylic acids, amides, or other carboxylic acid derivatives. Therefore, a polymerization to peptides is possible without further activation [44]. The approach or the linkage of organic compounds to the positively charged iron sulfide surface might be favored when phosphate is attached to these compounds. This is a possible explanation for the outstanding role of phosphate in living organisms [45].

The necessity for an appropriate monomer activation for the preparation of biopolymers inspired de Duve [5, 46, 47] to propose a scenario of a thioester world which preceded organisms receiving their energy from oligophosphates (ATP). This theory is additionally supported by the recent finding of thiol-binding sites in several aminoacyl-tRNA synthetases. These sites might, therefore, have originated from ancestral forms that were involved in non-coded thioester-dependent peptide synthesis [48, 49].

Much work has been done on the preparation of more complex molecules (e.g., oligopeptides and nucleosides) under primordial reaction conditions [50]. In this context, reactions catalyzed by clay surfaces (among others, illite and montmorillonite) are worthy of note, even though activated monomeric compounds are sometimes needed as starting materials—species that would have hardly been present at that time [51–55].

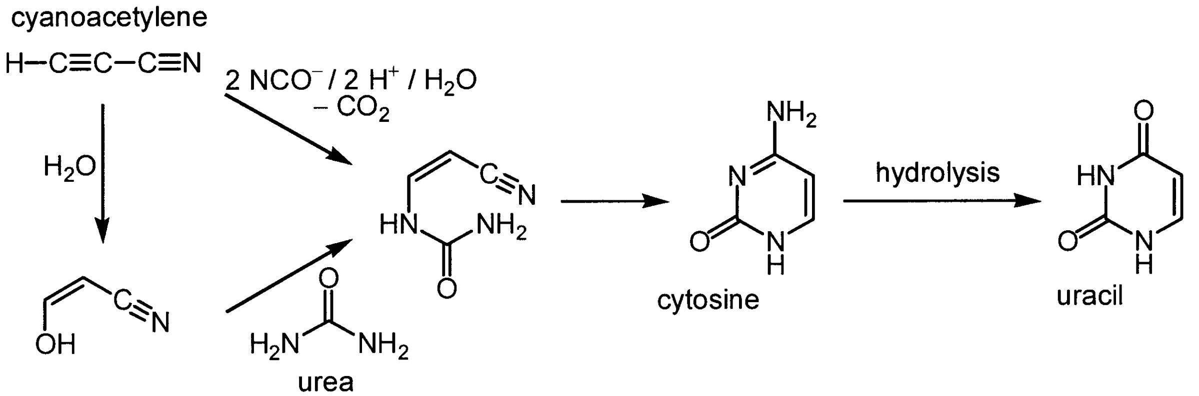
Especially remarkable is the synthesis of pantetheine under reaction conditions that were most probably available in the primordial broth. The starting materials (panthoyl lactone, β-alanine, and cysteamine) are assumed to have been present at that time (scheme 4) [56]. Why coenzyme A (in which ADP is linked to pantetheine via the terminal hydroxy function) has such complexicity when a very simple thiol would also be sufficient for the activation of carboxylic acids has never been totally understood. The availability of pantetheine at the beginning of life might be the reason.

In addition to the formation of organic molecules on Earth, there has been and still is a considerable delivery of organic compounds from space [57]. Most of this material is brought in with interplanetary dust particles, and a smaller fraction is delivered via comets and meteorites [58–60]. Carbonaceous chondrites (carbon-rich meteorites) have been intensely investigated during the last decades [61], especially the meteorite that fell on Australia in 1969 (called the Murchison meteorite) [62, 63]. This meteorite contains about 2% carbon, consisting mostly of macromolecular carbon (70–80%), a smaller fraction of carbonate minerals (2–10%) and 10–20% of low-molecular-weight organic compounds [22]. A plethora of amino (α, β, γ, δ) [64–68], hydroxy [69], phosphonic, and sulfonic acids [70], as well as further organic compounds [21] like purines and pyrimidines (< 7 ppm) [71], has been found in this and other meteorites (table 2, fig. 2). Determination of the isotopic distributions seems to prove that these organic compounds are not of terrestrial origin [72–74]. The similar isotopic distribution in α-amino and α-hydroxy acids suggests their formation in a Strecker-type reaction starting from hydrogen cyanide, ammonia, and carbonyl compounds (all of which are well-known interstellar molecules) [22, 73].

Table 2. Distribution of organic compounds in the Murchison meteorite [22].

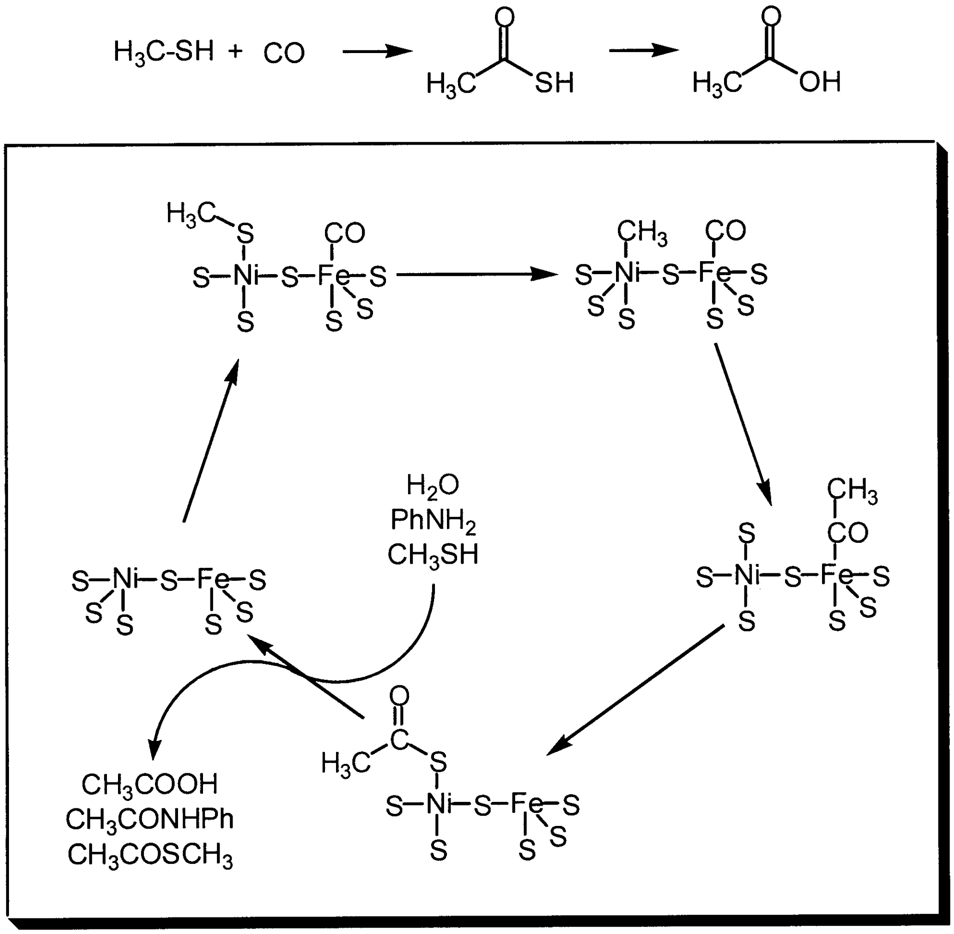
Substance class	Content	Substance class	Content
Polar hydrocarbons	>100 ppm	Carboxamides	>10 ppm
Monocarboxylic acids	>100 ppm	Hydroxy acids	>10 ppm
Sulfonic acids	>100 ppm	Amino acids	>10 ppm
Aliphatic hydrocarbons	>10 ppm	Volatile hydrocarbons	>1 ppm
Aromatic hydrocarbons	>10 ppm	Amines	>1 ppm
Aldehydes and ketones	>10 ppm	Phosphonic acids	>1 ppm
Alcohols	>10 ppm	*N*-heterocycles	>1 ppm
Dicarboxylic acids	>10 ppm	Purines and pyrimidines	>1 ppm

Even today, about 300 tons of organic compounds are delivered from space each year [75], but at the time when life evolved (3.9 Gyrs ago), the input flux was



Scheme 2. Prebiotic synthesis of cytosine and uracil [20].

$$2\ \mathrm{FeS} + 3\,\mathrm{H_2S} + \mathrm{CO} \longrightarrow 2\ \mathrm{FeS_2} + \mathrm{H_2O} + \mathrm{H_3C\text{-}SH}$$



Scheme 3. Formation of simple organic molecules on iron sulfide surfaces (in the presence of catalytic nickel sites) as proposed by Wächtershäuser [43].

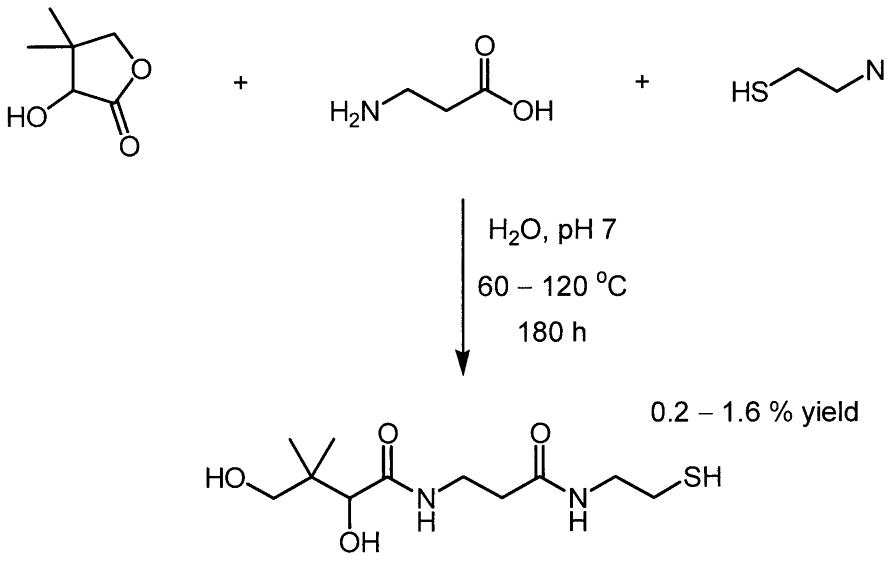
much higher, estimated to have been about 50,000 tons per year [76, 77], which means that one biomass (6×10^{14} kg is the estimated total mass of organic carbon in the biosphere [78, 79]) was delivered within 10 Myrs [38]. Obviously, organic matter was present in sufficient quantity and, at least in 'drying lagoons' [56] where the primordial broth was concentrated, the concentration might have been high enough for the evolution of primitive life.

Mechanisms for the formation of enantiomerically enriched compounds

Several possible mechanisms for the formation of enantiomerically enriched organic compounds have been proposed [80–92]. They can be divided into deterministic and chance mechanisms, whereby the deterministic mechanisms can be subdivided into universal and regional processes.

Universal deterministic mechanisms

In 1957, Lee and Yang [93] proposed a parity violation in the weak nuclear force, which was verified by the experimental discovery of intrinsic dissymmetric β-decay electrons by Wu et al. [94]. With the unification of the weak nuclear force and the electromagnetic forces in the late 1960s came the conclusion that not only these electrons but, in fact, all atoms and molecules are non-symmetric. This means that a pair of enantiomers should indeed behave like diastereoisomers and, conse-



Scheme 4. Synthesis of pantetheine under potentially promordial reaction conditions.

quently, have different energies. This has been calculated for some compounds (fig. 3), including amino acids and carbohydrates [95, 96], but the energy differences turn out to be very small; as yet experimental demonstration of these energy differences has not been possible [88, 97–99].

Almost immediately after the finding of Lee and Yang, Vester et al. [100] proposed a mechanism for an enantioselective reaction originating by the parity-violating effect (Vester-Ulbricht hypothesis). According to this, the longitudinally polarized β-decay electrons would, when decelerated in matter, lead to circularly polarized 'bremsstrahlung' photons (break radiation) which might initiate an enantioselective reaction. Although many experiments have been performed in this direction, most did not support the hypothesis or were not confirmed by other groups [83, 84, 101]. Just two experiments should be mentioned here. The incomplete crystallization of a racemic solution of ammonium sodium tartrate in the presence of β-emitting potassium phosphate (containing the ^{32}P isotope) led to the preferred crystallization of the L-configurated crystals. The enantiomeric excess was very small (0.235%), but was shown to be significant [102]. Thiemann and Darge [103] investigated polymerizations of *N*-carboxyanhydrides (NCAs) of carefully racemized amino acids and observed optical rotations in the resulting polymers ranging from $-0.00025°$ to $-0.00084°$ favoring the polymerization of L- over D-amino acid NCAs.

Regional deterministic mechanisms

In addition, deterministic mechanisms for the formation of enantiomerically enriched compounds have been proposed in which the sense of chirality is dependent on the reaction conditions. Bonner et al. [104, 105] found that amino acids are enantioselectively adsorbed on chiral, enantiopure quartz crystals. D-Alanine is bound selectively to *d*-quartz with an ee of up to 20%. The results of several groups claiming a selective adsorption of amino acids on the surfaces of achiral (!) clays were not confirmed by other groups [104, 105].

The implications of chiral fields and forces on chemical reactions and the difference between 'true and false' chirality were theoretically treated and summarized by Barron and colleagues [92, 106] although early contributions had already been published by Pierre Curie in the 19th century [107]. Circularly polarized light, in particular, was recognized to be a 'truly' chiral field and can be used to induce enantioselectivity in various types of reactions. Kuhn and Knopf [108] investigated the first enantioselective photolytic reactions using circularly polarized light in 1930. Since then, circularly polarized light has repeatedly been used for the enantioselective photolysis of chiral compounds. One enantiomer is occasionally found to be destroyed (photolyzed) faster than the other. When the irradiation is stopped before the degradation is complete, the residue is enantiomerically enriched. Especially noteworthy in this context is the work of Kagan and colleagues who, after 99% photodestruction of racemic camphor, found

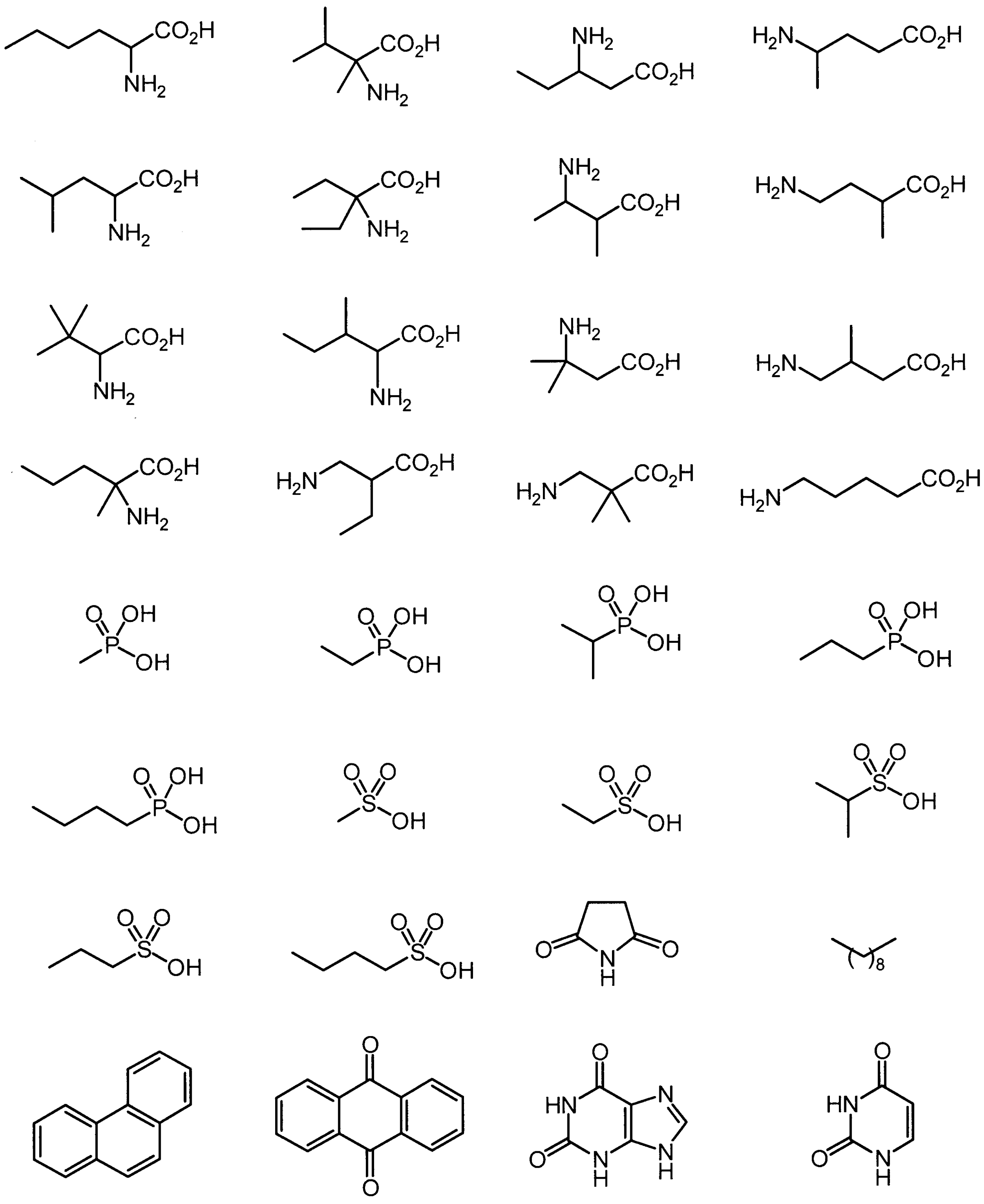


Figure 2. A selection of organic compounds isolated from the Murchison meteorite.

an enantiomeric excess of 20% in the remains; this is as yet the highest value achieved by asymmetric photolysis [109]. Bonner and coworkers studied the photolysis of racemic leucine and found excesses of 1.98 and 2.50% after 59 and 75% photolysis, respectively (scheme 5) [110].

Similar mechanisms may be responsible for the observation of enantiomeric excesses in the amino acids isolated from the Murchison meteorite [62]. The preferential configuration of these amino acids has been under investigation since the early 1970s; nevertheless, the first report of enantiomeric excesses [111] led to a controversial discussion [112, 113] since it could not be clarified whether this finding was due to terrestrial contaminations. Recent work by Cronin and coworkers has been performed taking strict precautions to prevent misinterpretation [114–116]. To avoid enantiomeric enrichment by the analytic methods and to exclude terrestrial contamination, the authors focused on α-branched amino acids that have never been reported in the geosphere (fig. 4). Additionally, one of the amino acids investigated (1) bears two stereogenic centers; therefore, enantiomeric enrichment as an analytical artifact (e.g., by the aqueous processing) is highly unlikely. The analyses were carried out carefully and gave enantiomeric excesses of up to 10% for the amino acids 1–3. α-Aminobutyric acid and norvaline gave no significant ee values.

Even with the above results, the origin of these findings was still elusive! A recent contribution of Bailey et al. [117] has provided new insight into this topic. They reported the observation of circularly polarized infrared light, the source of which is a cloud of dust in the Orion constellation. This cloud, a region of high-mass star formation, quite similar to the region where the solar system was formed, contains many organic molecules. The authors suspect that this polarization may be caused by light scattering on non-spherical grains which are aligned by a magnetic field, but other mechanisms are also possible. According to calculations, the presence of circularly polarized infrared light implies the existence of the correspondingly polarized ultraviolet radiation. Unfortunately, the dust cloud responsible for the polarization obscures ultraviolet radiation and prevents its direct observation.

A simple calculation reveals that 6×10^7 million tons of amino acids (present in a 60 ppm concentration in the carbonaceous chondrites, which are 3% of all meteorites) have reached the Earth during its history, of which 6×10^5 million tons arrived during a period when the conditions on Earth would have allowed the persistence of the amino acids [118]. Therefore, during the development of life, the Earth was possibly covered with matter (dust, meteorites, or comets) stemming from regions that were exposed to circularly polarized irradiation. The thus resulting enantiomeric excess might have tipped the balance toward homochirality in living matter. The global enantiomeric excess on Earth—due to racemization and dilution—was certainly less than that in the meteorites. Bailey et al. [117] estimate that it might have been in the range of 5×10^{-3} to 10^{-7}, possibly with locally higher ee values in the vicinity of meteorite impacts. These enantiomeric excesses are larger by orders of magnitude than those explainable by the parity violation ($10^{-17}\%$) or by stochastic effects (see below). Nevertheless, depending on the polarization of radiation, regions in the universe might exist where molecules with the opposite chirality are more abundant.

New insights into the amounts of enantiomerically enriched material delivered from space and its degree of enrichment are expected from projected missions to comets, such as the ROSETTA mission planned for 2003 by the European Space Agency in collaboration with NASA [119, 120].

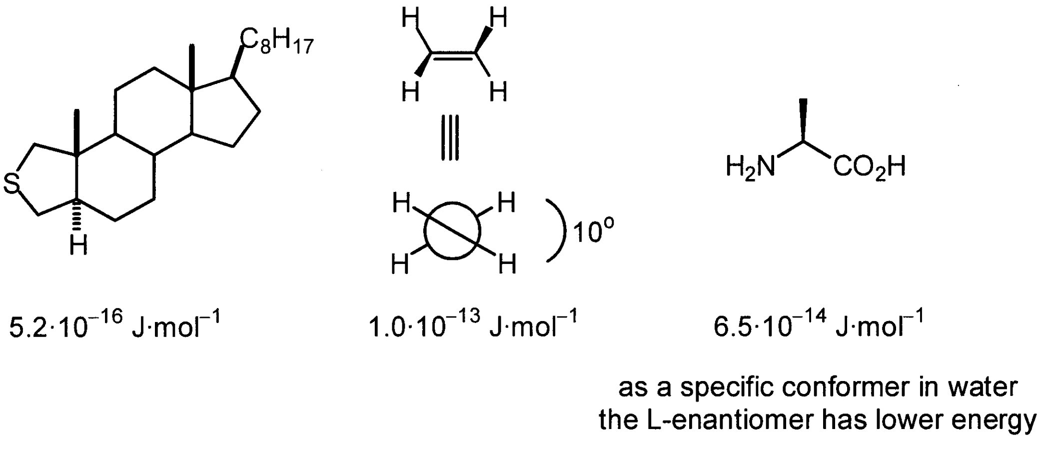
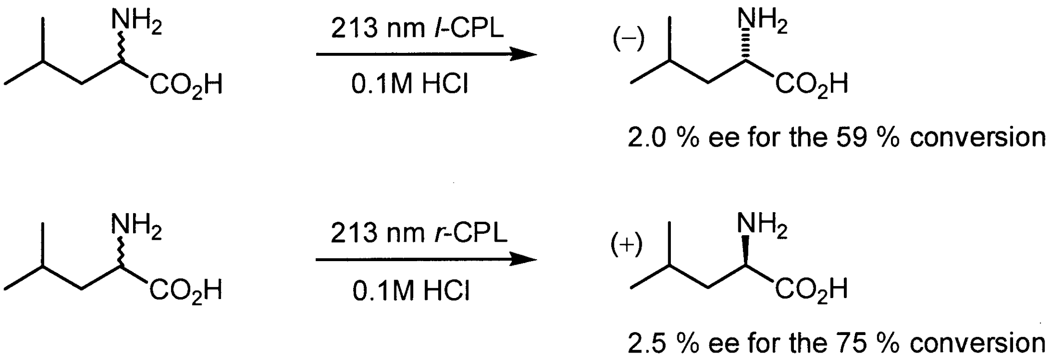


Figure 3. Parity-violating energy differences in organic molecules [88].



Scheme 5. Asymmetric photolysis of amino acids by circularly polarized light.

Chance mechanisms

In general, chance does not play any role in chemistry since chemists deal with ensembles of molecules or atoms usually exceeding numbers of 10^{20}. Nevertheless, when the number of events is dramatically reduced to less than, let us say 10, statistical fluctuations become important. It might be assumed that some of the crucial steps in the evolution of life are not very likely and, in fact, happened just a few times in a given period. If one of these evolutionary steps occurred in an enantiomorphous surrounding (e.g., on a quartz block), this might have led to an enantioselective reaction resulting in enantiomerically enriched compounds. If these compounds were spread over the Earth and initiated further diastereoselective reactions, this might explain the bias in optical enrichment, which, after amplification of chirality (see below), resulted in the homochirality observed in nature. Frank [121] has treated this problem mechanistically and pointed out that 'if the production of living molecules is an infrequent process, compared with the rate of multiplication of living molecules, the whole Earth is likely to be extensively populated with the progeny of the first before another appears.' Naturally, these reflections are rather speculative since chance mechanisms that happened several billion years ago are impossible to reproduce.

Kondepudi and coworkers investigated the spontaneous deracemization during crystallization of sodium chlorate ($NaClO_3$) from stirred solutions [122, 123] and settled the theoretical foundations for this and similar processes [124]. Sodium chlorate, although in solution obviously achiral, forms chiral crystals. From unstirred solutions, both enantiomorphous crystals are usually formed in a 1:1 ratio. When supersaturated solutions of $NaClO_3$ are stirred during crystallization, in all performed experiments, predominantly one enantiomorph is formed (835 crystals are collected in an arbitrarily chosen, typical experiment, all of which show identical enantiomorphism). Obviously, the first formed crystal is crushed to smaller fragments which serve as seed crystals for the further crystallization process. Naturally, which of the two enantiomorphous crystal types predominates in a specific experiment is not foreseeable, although a recent preliminary publication describes an influence on this crystallization direction by irradiation with (left- or right-) spinning electrons. Nevertheless, these findings need further confirmation [125].

Sodium chlorate crystals cannot be expected to have been relevant for primordial processes, but similar scenarios might have occurred with quartz crystals: a single crystal might have been smashed, e.g., during a meteorite impact.

Other mechanisms, in which chance events (statistical fluctuation) are combined with autocatalysis have also been considered [121]. A huge number of, in part rather complex, possible scenarios has been treated theoretically [83, 84, 126]; a fairly simple mechanism is depicted in figure 5 [4, 83]: two rapidly equilibrating enantiomeric reactants are assumed to lead to a pair of non-equilibrating enantiomeric products in a slow reaction. When a statistical fluctuation favors the formation of one enantiomer, this product would immediately catalyze a rapid (autocatalytic) reproduction of itself from its corresponding enantiomeric precursor. Calculations show that this mechanism would lead to the rapid formation of an enantiomerically enriched product. Unfortunately, to date it has not been possible to prove one of these mechanisms by experimental findings. However, similar mechanisms are important for the amplification of chirality (see below).

Amplification of enantiomerical excesses

The mechanisms that have been proposed for the formation of enantiomerically enriched organic molecules lead to enantiomeric excesses reaching from 10^{-17} (theoretically proposed energy difference caused by the parity violation) to 20% (for the asymmetric photolysis of camphor by circularly polarized light). It has been generally accepted that effective mechanisms are required for the amplification of these enantiomeric excesses. Some mechanisms that have been considered in this context are summarized below [83, 84, 86].

Amplification during incomplete diastereoselective reactions

Each incomplete reaction starting from non-racemic material possibly leads to an increased enantiomeric excess in the product. This is because the interaction of a chiral molecule with the (+)-enantiomer differs from the interaction with the (−)-enantiomer which means that the activation barriers for subsequent reactions are different. In the remaining starting material the enantiomeric excesses are thus higher or lower than those of the reacted material. This has been treated theoretically and much experimental work has been done in this field. Horeau defined a principle for the dimerization (or polymerization) of non-racemic mixtures of monomers that can be used for the enhancement of their enantiopurity to virtually 100% [127, 128].

This principle and similar ones have been tested for the hydrolysis of peptides and for the polycondensation of amino acids: an oligopeptide built of leucine moieties adopts a helical conformation that is stable only when the polymer is composed of enantiomerically pure monomers [129, 130]. The stability decreases dramatically when a higher percentage of the ‘wrong’ monomer is incorporated. This stability can be determined by the rate of hydrolysis under well-defined reaction conditions. Some experiments showing that the rate of hydrolysis is essentially higher when DL-oligopeptide is subjected to hydrolysis conditions as summarized in scheme 6. Especially when longer DL-oligopeptide strands are used in this reaction (n = 40), the reaction rate is almost doubled (56% hydrolysis) compared with the hydrolysis of peptidic material composed of enantiomerically pure leucine moieties (30 and 35%) [131, 132].

Interestingly, a similar effect is observed when leucine is subjected to polycondensation under desiccating conditions. Partial polycondensation of leucine (activated as NCA) with an enantiomeric excess of 31% leads to polyleucine composed of leucine with 45% ee [133]. This can be explained by a lower reaction barrier for the attachment of the suitable enantiomer, because this leads to oligopeptides of higher stability.

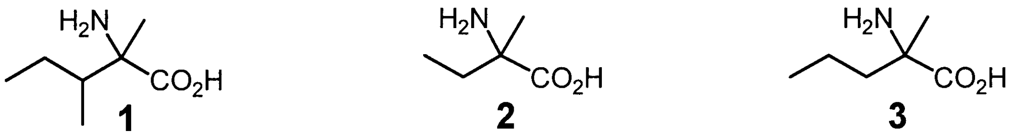
Similar observations have been made by Eschenmoser and colleagues, who found that the rate of oligomerization of homochiral p-RNA tetramers is reduced by orders of magnitude if one of the monomers is replaced by its corresponding enantiomer [134].

If one assumes that repetitive dry (polycondensation) and wet (hydrolysis) periods occurred during the history of early Earth, this might have led over thousands of years to oligopeptide strands composed of essentially enantiomerically pure amino acids.

The majority rule in polymerizations

If achiral or chiral, non-racemic moieties form enantiomorphous aggregates, their chiral properties (i.e., the chiroptical properties or the interaction with other molecules) are not necessarily determined by the monomers but by the chiral system itself. This has been shown for crystals composed of achiral monomers (see above), but it occasionally holds as well for polymers built of (almost) racemic monomers.

Isocyanates (anhydrides of carbamic acids—the mono amides of carbonic acid) polymerize to polyisocyanates. If chiral, enantiopure monomers are used in this reaction, the polymer forms a stable helix, whose helicity is dependent on the configuration of the monomers. The



1 (2*S*,3*S*): 7.6 % ee
(2*S*,3*R*): 10.4 % ee

2 (2*S*): 8.4 % ee

3 (2*S*): 2.8 % ee

Figure 4. Non-racemic amino acids from the Murchison meteorite and the corresponding enantiomeric excesses.

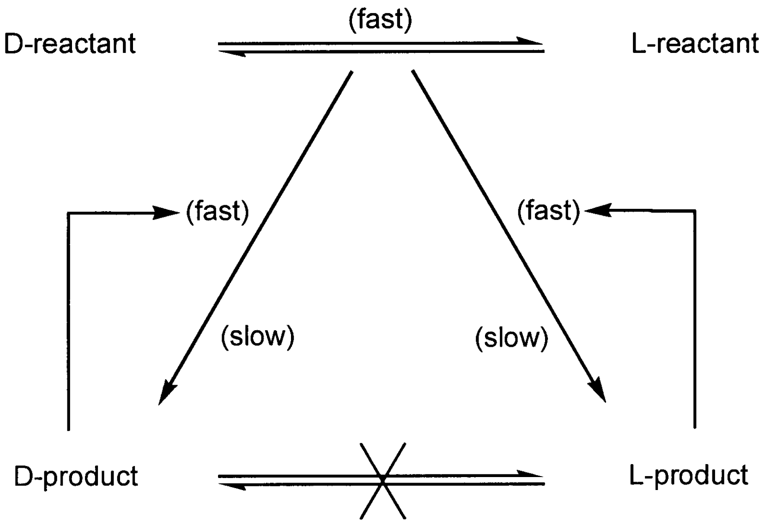
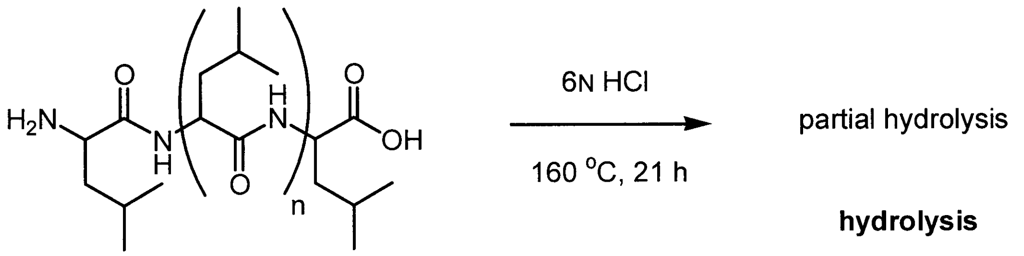


Figure 5. Spontaneous symmetry breaking by stereospecific autocatalysis [4] [adapted from ref. 83].

helicity can be determined by the circular dicroism of the polymeric material (A,B in fig. 6) [135–137]. If racemic isocyanates are used, one would assume that the helicity is not predetermined and non-specific. Nevertheless, if monomeric building blocks with a very small enantiomeric excess are used, the helicity of the polymer is dominated by the enantiomeric monomer which is present in excess. With only 2% ee, the helicity is about 30% of the maximum helicity (C), but with 8% ee, the helicity is not distinguishable from the helicity of the polymer composed of enantiopure material (D). Obviously, in this case, the stability of the helix is high enough (in contrast to peptides) to prevent a frequent reversal of the helicity caused by the incorporation of 'wrong' enantiomers. This means that a slight excess of one enantiomer governs the chirality of these polymers, which might be responsible for the stereochemical outcome in further diastereomeric reactions. One could, for example, think of diastereoselective aggregation of small chiral molecules in the groove of the polymer, which might result in the further promotion of their enantiopurity. This observation of Green et al. [135] is called the majority rule: it might have had great effect on the amplification of enantiopurity in organic compounds, although whether this or similar polymers were actually present in the primordial broth is not clear.

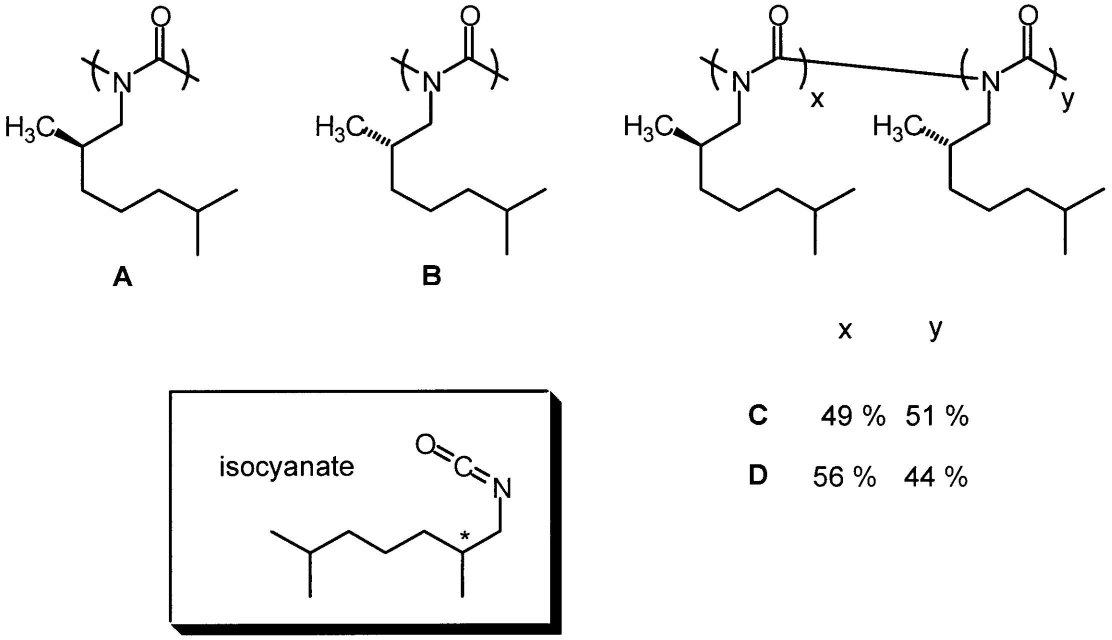
Amplification by stereoselective autocatalysis

Mechanistic models for spontaneous symmetry breaking as depicted in figure 5 are of course equally applicable to the amplification of chirality. Early work in this direction by various groups has not led to a significant amplification of enantiomeric excess values [84]. Recently, Soai and coworkers investigated the addition of dialkylzinc compounds to heteroaromatic aldehydes leading to the corresponding secondary alcohols [138–141]. They found that in the presence of a small amount of product (1%) with a slight enantiomeric excess (6.4 and 0.28%), the reaction yielded the alcohol with an enantiomeric excess of 92 and 87% (scheme 7). However, not only the product can serve as an autocatalyst, even amino acids can be used as catalysts, and again, just a very small enantiomeric excess in the utilized catalyst is necessary to obtain a product with much higher optical purity. When, e.g., 20% of valine with a 1% ee was used, the product was formed with a 51% ee. Addition of 2% of leucine with a 2% ee led to a product with 22% ee. The small bias necessary for the autocatalytic process can be achieved not only by addition of enantiomerically enriched chiral compounds but also by the presence of enantiomorphous crystal faces. Soai and colleagues showed that powdered quartz [142] or sodium chlorate single crystals [143] can be used as initiators in the above-mentioned reaction leading to enantiomeric excesses of up to 98%. Similar results were obtained when *d*- and *l*-quartz were used as a 9:1 mixture. Some of these experiments are of interest in the context of this review, since Bonner and colleagues showed that leucine with the required enantiomeric excess value can be produced by photolysis with circularly polarized light and, of course, quartz was present on Earth at all times. The products in the experiments performed by Soai and colleagues obvi-



	hydrolysis	
	n =16	n = 40
D-polyleucine	45 %	30 %
L-polyleucine	41 %	35 %
DL-leucine	55 %	56 %

Scheme 6. Partial hydrolysis of oligopeptides composed of enantiopure and racemic leucine.



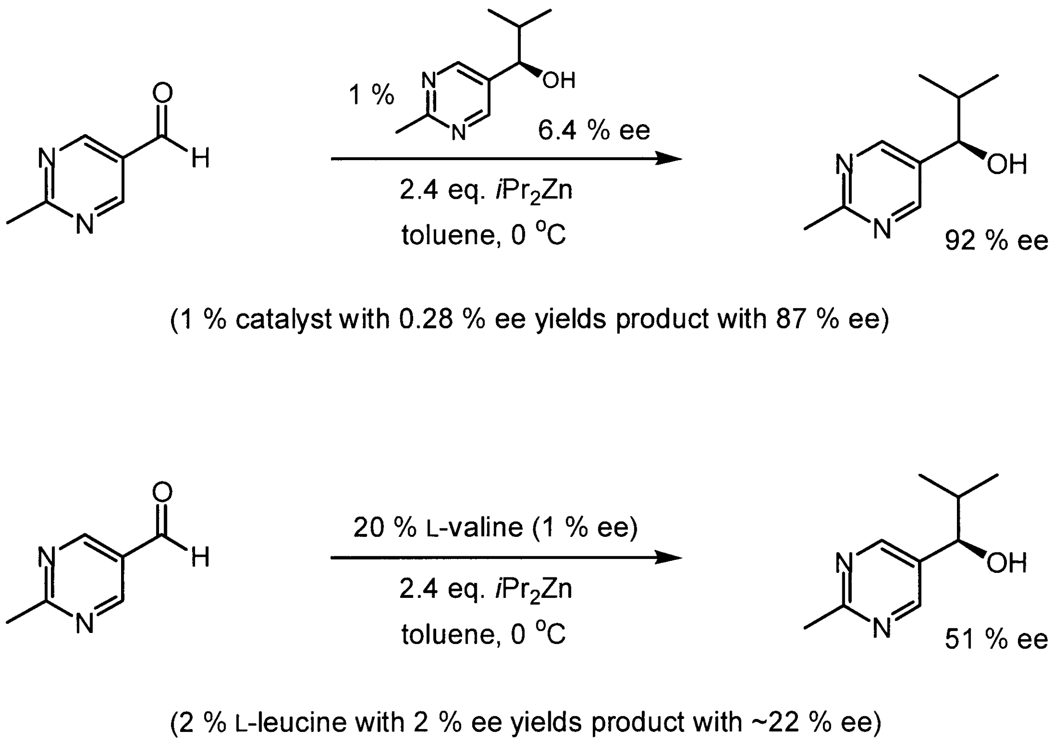
	x	y
C	49 %	51 %
D	56 %	44 %

Figure 6. Polyisocyanates composed of enantiopure and non-racemic isocyanates [135].

ously have no biological relevance since the reaction conditions (utilization of highly hygroscopic organometallic compounds) are not very likely in the prebiotic environment. Nevertheless, these are the first experiments in which such high amplifications of chirality by stereoselective autocatalytic reactions were obtained. One might think of other reactions with higher biological relevance proceeding via similar mechanisms.

Conclusion

The evolution of life can be subdivided into three stages: the appearance of organic molecules on Earth, amplification of whatever enantiomeric excess was present in these compounds, evolution of primordial life. These events, divided into numerous subevents, should have had several impacts on each other, making



(1 % catalyst with 0.28 % ee yields product with 87 % ee)

(2 % L-leucine with 2 % ee yields product with ~22 % ee)

Scheme 7. Stereoselective autocatalysis in the addition of organozinc compounds to aromatic aldehydes by Soai and coworkers [138, 139].

each topic hard to understand without the other. The times when these things happened have long passed and thus these events are hard to investigate. Maybe a full understanding of life and its evolution will never be possible! But this will certainly not prevent scientists from seeking further information that might explain the beginnings and evolution of life. Although the evolution of life might have been very unlikely, many limiting conditions must have been met, and one thing is sure—it worked.

Acknowledgments. Work in the author's laboratory has been supported by the Fonds der Chemischen Industrie, the Deutsche Forschungsgemeinschaft, the Stiftungsfonds Mitsubishi Electric Europe, and the Landesgraduiertenförderung Baden-Württemberg. The continuous help of all members of the Institut für Organische Chemie, especially of Prof. Dr. V. Jäger and Prof. Dr. Dr. h. c. F. Effenberger is gratefully acknowledged. Dr. R. E. Dunmur is thanked for his help in the final preparation of the manuscript.

Glossary

The following terms are explained only as far as they are necessary for understanding this review. Consequently, some of the definitions are incomplete [144].

Autocatalysis: catalytic process in which the product acts as a catalyst for its own formation.

Chiral: if an object is not superimposable with its mirror image it is called chiral. This is usually achieved by *stereogenic centers* or by helical components.

Circular dicroism: the phenomenon whereby circularly polarized light is absorbed to different degrees by a substance, dependent on the sign of the circular polarization of the beam.

Configuration: this term is used in the context of stereochemistry to define the positions of all atoms in space without considering any conformational flexibility.

Diastereoisomers: *stereoisomers* that are not related as mirror images.

Enantiomeric excess: the excess of one enantiomer in a mixture of enantiomers. It can be calculated by the following formula:

$$ee = 100 \times |(F^+ - F^-)|/(F^+ + F^-) \text{ (gives the result in percent)}$$

with F being the molar fraction of the respective enantiomer.

Enantiomers: two stereoisomers that are related as mirror images are called enantiomers. This definition is usually sufficient, but when parity violation effects are discussed it no longer holds (see text). Here one has to consider that every atom is chiral, therefore ensembles of atoms—molecules—behave like diastereoisomers. A real enantiomer would be a mirror image composed of anti-particles. Since the energy differences due to the parity-violating effect are very small, they are usually neglected.

Enantiomorphs: a pair of *chiral* objects that behave like non-superimposable mirror images of each other. This expression is used for objects more complex than molecules—like crystals or surfaces.

Homochirality: describes a sort of similarity, e.g., (roughly) all amino acids present in nature have similar configurations. The expression should not describe the enantiopurity of a specific compound, although it is often used in this way.

Racemate: an equimolar mixture of enantiomers.
Stereogenic center: a grouping of atoms consisting of a central atom and distinguishable ligands, such that the interchange of any two of the ligands leads to another *stereoisomer*.
Stereoisomers: isomers possessing identical connectivity of the atoms but differing in the arrangement of their atoms in space, without regard for conformational changes.
Stereoselectivity: the preferential formation of one *stereoisomer* (enantioselectivity: preferential formation of one *enantiomer*).

1 Pasteur M. L. (1848) Sur les relations qui peuvent exister entre la forme cristalline, la composition chimique et le sens de la polarisation rotatoire. Ann. Chim. Phys. **24:** 442–459
2 Brunner H. (1999) Rechts oder links in der Natur und Anderswo, Wiley-VCH, Weinheim
3 Jordan P. and Kronig R. de L. (1927) Movements of the lower jaw of cattle during mastication. Nature **120:** 807
4 Calvin M. (1969) Chemical Evolution, Oxford, Clarendon
5 Duve C. de (1991) Blueprint for a Cell, Patterson, Burlington, N.C.
6 Mason S. F. (1992) Chemical Evolution – Origin of the Elements, Molecules, and Living Systems, Clarendon, Oxford
7 Brack A. (ed.) (1998) The Molecular Origins of Life: Assembling Pieces of the Puzzle, Cambridge University Press, Cambridge, UK
8 Orgel L. E. (1998) The Origin of Life – A Review of Facts and Speculations. Trends Biochem. Sci. **23:** 491–495
9 Lazcano A. and Miller S. L. (1999) On the origin of metabolic pathways. J. Mol. Evol. **49:** 424–431
10 Pályi G, Zucchi C and Caglioti L (eds) (1999) Advances in BioChirality, Elsevier, Amsterdam
11 Cairns-Smith A. G. (1982) Genetic Takeover and the Mineral Origins of Life, Cambridge University Press, Cambridge, UK
12 Schopf J. W. (1993) Microfossils of the early archean apex chert: new evidence of the antiquity of life. Science **260:** 640–646
13 Schopf J. W. (1998) Tracing the roots of the universal tree of life. In: The Molecular Origins of Life: Assembling Pieces of the Puzzle, pp. 336–362, Brack A. (ed.), Cambridge University Press, Cambridge, UK
14 Holland H. D. (1997) Evidence for life on earth more than 3850 million years ago. Science **275:** 38–39
15 Feng D.-F., Cho G. and Doolittle R. F. (1997) Determining divergence times with a protein clock: update and reevaluation. Proc. Natl. Acad. Sci. USA **94:** 13028–13033
16 Orgel L. E. (1998) The origin of life – how long did it take. Origins Life Evol. Biosphere **28:** 91–96
17 Raulin-Cerceau F., Maurel M.-C. and Schneider J. (1998) From panspermia to bioastronomy, the evolution of the hypothesis of universal life. Origins Life Evol. Biosphere **28:** 597–612
18 Arrhenius S. (1908) Worlds in the Making: The Evolution of the Universe, Harper, New York
19 Oró J., Miller S. L. and Lazcano A. (1990) The origin and early evolution of life on earth. Annu. Rev. Earth Planet Sci. **18:** 317–356
20 Miller S. L. (1998) The endogenous synthesis of organic compounds. In: The Molecular Origins of Life: Assembling Pieces of the Puzzle, pp. 59–85, Brack A. (ed.), Cambridge University Press, Cambridge, UK
21 Cronin J. R. and Chang S. (1993) Organic matter in meteorites: molecular and isotopic analyses of the Murchison meteorite. In: Chemistry of Life's Origins, vol. 416, Greenberg J. M., Mendoza-Gomez C. X. and Pirronello V. (eds), pp. 209–258, Kluwer, Dordrecht
22 Cronin J. R. (1998) Clues from the origin of the solar system: meteorites. In: The Molecular Origins of Life: Assembling Pieces of the Puzzle, pp. 119–146, Brack A. (ed.), Cambridge University Press, Cambridge, UK
23 Miller S. L. (1953) A production of amino acids under possible primitive earth conditions. Science **117:** 528–529
24 Miller S. L. (1955) Production of some organic compounds under possible primitive earth conditions. J. Am. Chem. Soc. **77:** 2351–2361
25 Urey H. C. (1952) On the early chemical history of the earth and the origin of life. Proc. Natl. Acad. Sci. USA **38:** 351–363
26 Ring D., Wolman Y., Friedmann N. and Miller S. L. (1972) Prebiotic synthesis of hydrophobic and protein amino acids. Proc. Natl. Acad. Sci. USA **69:** 765–768
27 Wolman Y., Haverland W. J. and Miller S. L. (1972) Nonprotein amino acids from spark discharges and their comparision with the murchison meteorite amino acids. Proc. Natl. Acad. Sci. USA **69:** 809–811
28 Oró J. (1960) Synthesis of adenine from ammonium cyanide. Biochem. Biophys. Res. Commun. **2:** 407–412
29 Ferris J. P., Sanchez R. A. and Orgel L. E. (1968) Studies in prebiotic synthesis. III. Synthesis of pyrimidines from cyanoacetylene and cyanate. J. Mol. Biol. **33:** 693–704
30 Robertson M. P. and Miller S. L. (1995) An efficient prebiotic synthesis of cytosine and uracil. Nature **375:** 772–774
31 Shapiro R. (1988) Prebiotic ribose synthesis: a critical analysis. Origins Life Evol. Biosphere **18:** 71–85
32 Müller D., Pitsch S., Kittaka A., Wagner E., Wintner C. E. and Eschenmoser A. (1990) Chemie von α-Aminonitrilen. Aldomerisierung von Glycolaldehyd-phosphat zu racemischen Hexose-2,4,6-triphosphaten und (in Gegenwart von Formaldehyd) racemischen Pentose-2,4-diphosphaten: *rac*-Allose-2,4,6-triphosphat und *rac*-Ribose-2,4-diphosphat sind die Reaktionshauptprodukte. Helv. Chim. Acta **73:** 1410–1468
33 Keefe A. D. and Miller S. L. (1995) Are polyphosphates or phosphate esters prebiotic reagents. J. Mol. Evol. **41:** 693–702
34 Kasting J. F. (1993) Early evolution of the atmosphere and ocean. In: Chemistry of Life's Origins, vol. 416, pp. 149–176, Greenberg J. M., Mendoza-Gomez C. X. and Pirronello V. (eds), Kluwer, Dordrecht
35 Kasting J. F. (1993) Earth's early atmosphere. Science **259:** 920–926
36 Schlesinger G. and Miller S. L. (1983) Prebiotic synthesis in atmospheres containing CH_4, CO, and CO_2. I. Amino acids. J. Mol. Evol. **19:** 376–382
37 Schlesinger G. and Miller S. L. (1983) Prebiotic synthesis in atmospheres containing CH_4, CO, and CO_2. II. Hydrogen cyanide, formaldehyde and ammonia. J. Mol. Evol. **19:** 383–390
38 Whittet D. C. B. (1997) Is extraterrestrial organic matter relevant to the origin of life on earth. Origins Life Evol. Biosphere **27:** 249–262
39 Wächtershäuser G. (1992) Groundworks for an evolutionary biochemistry: the iron-sulphur world. Prog. Biophys. Mol. Biol. **58:** 85–201
40 Blöchl E., Keller M., Wächtershäuser G. and Stetter K. O. (1992) Reactions depending on iron sulfide and linking geochemistry with biochemistry. Proc. Natl. Acad. Sci. USA **89:** 8117–8120
41 Huber C. and Wächtershäuser G. (1997) Activated acetic acid by carbon fixation on (Fe,Ni)S under primordial conditions. Science **276:** 245–247
42 Hafenbradl D., Keller M., Wächtershäuser G. and Stetter K. O. (1995) Primordial amino acids by reductive amination of α-oxo acids in conjunction with the oxidative formation of pyrite. Tetrahedron Lett. **36:** 5179–5182
43 Wächtershäuser G. (1998) Origin of life in an iron-sulfur world. In: The Molecular Origins of Life: Assembling Pieces of the Puzzle, pp. 206–218, Brack A. (ed.), Cambridge University Press, Cambridge, UK
44 Huber C. and Wächtershäuser G. (1998) Peptides by activation of amino acids with CO on (Ni, Fe)S surfaces: implications for the origin of life. Science **281:** 670–672

45 Wächtershäuser G. (1988) Before enzymes and templates: theory of surface metabolism. Microbiol. Rev. **52:** 452–484

46 Duve C. de (1995) Vital Dust, Basic Books, New York

47 Duve C. de (1998) Clues from present-day biology: the thioester world. In: The Molecular Origins of Life: Assembling Pieces of the Puzzle, pp. 219–236, Brack A. (ed.), Cambridge University Press, Cambridge, UK

48 Jakubowski H. (1997) Aminoacyl thioester chemistry of class II aminoacyl-tRNA synthetases. Biochemistry **36:** 11077–11085

49 Jakubowski H. (1998) Aminoacylation of coenzyme A and pantetheine by aminoacyl-tRNA synthetases: possible link between noncoded and coded peptide synthesis. Biochemistry **37:** 5147–5153

50 Schwartz A. W. (1996) Did minerals perform prebiotic combinatorial chemistry? Chem. Biol. **3:** 515–518

51 Ferris J. P. and Ertem G. (1992) Oligomerization of ribonucleotides on montmorillonite: reaction of the 5′-phosphorimidazolide of adenosine. Science **257:** 1387–1389

52 Ferris J. P. and Ertem G. (1993) Montmorillonite catalysis of RNA oligomer formation in aqueous solution: a model for the prebiotic formation of RNA. J. Am. Chem. Soc. **115:** 12270–12275

53 Ferris J. P., Hill A. R. Jr, Liu R. and Orgel L. E. (1996) Synthesis of long prebiotic oligomers on mineral surfaces. Nature **381:** 59–61

54 Kawamura K. and Ferris J. P. (1994) Kinetic and mechanistic analysis of dinucleotide and oligonucleotide formation from the 5′-phosphorimidazolide of adenosine on Na^+-montmorillonite. J. Am. Chem. Soc. **116:** 7564–7572

55 Bujdák J. and Rode B. M. (1999) Silica, alumina and clay catalyzed peptide bond formation: enhanced efficiency of alumina catalyst. Origins Life Evol. Biosphere **29:** 451–461

56 Keefe A. D., Newton G. L. and Miller S. L. (1995) A possible prebiotic synthesis of pantetheine, a precursor to coenzyme A. Nature **373:** 683–685

57 Irvine W. M. (1998) Extraterrestrial organic matter: a review. Origins Life Evol. Biosphere **28:** 365–383

58 Greenberg J. M. (1996) Chirality in interstellar dust and in comets: life from dead stars. In: Physical Origin of Homochirality in Life, vol. 379, pp. 185–210, Cline D. B. (ed.), AIP, Woodbury

59 Greenberg J. M. (1997) Prebiotic chiral molecules created in interstellar dust and preserved in comets, comet dust and meteorites: an exogenous source of life's origins. Proc. SPIE-Int. Soc. Opt. Eng. **3111:** 226–237

60 Greenberg J. M. and Li A. (1999) Tracking the organic refractory component from interstellar dust to comets. Adv. Space Res. **24:** 497–504

61 Brack A. and Pillinger C. T. (1998) Life on Mars: chemical arguments and clues from Martian meteorites. Extremophiles **2:** 313–319

62 Podlech J. (1999) New insight into the source of biomolecular homochirality: an extraterrestrial origin for molecules of life? Angew. Chem. Int. Ed. **38:** 477–478

63 Cerf C. and Jorissen A. (2000) Is amino-acid homochirality due to asymmetric photolysis in space? Space Sci. Rev. **92:** 603

64 Kvenvolden K., Lawless J., Pering K., Peterson E., Flores J., Ponnamperuma C. et al. (1970) Evidence for extraterrestrial amino-acids and hydrocarbons in the Murchison meteorite. Nature **228:** 923–926

65 Cronin J. R., Gandy W. E. and Pizzarello S. (1981) Amino acids of the Murchison meteorite: six carbon acyclic primary α-amino alkanoic acids. J. Mol. Evol. **17:** 265–272

66 Cronin J. R., Pizzarello S. and Yuen G. U. (1985) Amino acids of the Murchison meteorite. II. Five carbon acyclic primary β-, γ-, and δ-amino alcanoic acids. Geochim. Cosmochim. Acta **49:** 2259–2265

67 Cronin J. R. and Pizzarello S. (1986) Amino acids of the Murchison meteorite. III. Seven carbon acyclic primary α-amino alkanoic acids. Geochim. Cosmochim. Acta **50:** 2419–2427

68 Engel M. H. and Macko S. A. (1997) Isotopic evidence for extraterrestrial non-racemic amino acids in the Murchison meteorite. Nature **389:** 265–268

69 Cronin J. R., Pizzarello S., Epstein S. and Krishnamurthy R. V. (1993) Molecular and isotopic analyses of the hydroxy acids, dicarboxylic acids, and hydroxydicarboxylic acids of the Murchison meteorite. Geochim. Cosmochim. Acta **57:** 4745–4752

70 Cooper G. W., Onwo W. M. and Cronin J. R. (1992) Alkyl phosphonic acids and sulfonic acids in the Murchison meteorite. Geochim. Cosmochim. Acta **56:** 4109–4115

71 Stoks P. G. and Schwartz A. W. (1982) Basic nitrogen-heterocyclic compounds in the Murchison meteorite. Geochim. Cosmochim. Acta **46:** 309–315

72 Engel M. H., Macko S. A. and Silfer J. A. (1990) Carbon isotope composition of individual amino acids in the Murchison meteorite. Nature **348:** 47–49

73 Pizzarello S., Krishnamurthy R. V., Epstein S. and Cronin J. R. (1991) Isotopic analyses of amino acids from the Murchison meteorite. Geochim. Cosmochim. Acta **55:** 905–910

74 Engel M. H., Macko S. A., Qian Y. and Silfer J. A. (1995) Stable isotope analysis at the molecular level: a new approach for determining the origins of amino acids in the Murchison meteorite. Adv. Space Res. **15:** 99–106

75 Anders E. (1989) Pre-biotic organic matter from comets and asteroids. Nature **342:** 255–257

76 Chyba C. F. (1990) Impact delivery and erosion of planetary oceans in the early inner solar system. Nature **343:** 129–133

77 Chyba C. and Sagan C. (1992) Endogenous production, exogenous delivery and impact-shock synthesis of organic molecules: an inventory for the origins of life. Nature **355:** 125–132

78 Chyba C. F. (1990) Extraterrestrial amino acids and terrestrial life. Nature **348:** 113–114

79 Chyba C. F., Thomas P. J., Brookshaw L. and Sagan C. (1990) Cometary delivery of organic molecules to the early earth. Science **249:** 366–373

80 Bonner W. A. (1972) Origins of molecular chirality. In: Exobiology, vol. 23, pp. 170–234, Ponnamperuma C. (ed.), North-Holland, Amsterdam

81 Bonner W. A. and Liang Y. (1984) β-Decay, Bremsstrahlen, and the origin of molecular chirality. J. Mol. Evol. **21:** 84–89

82 Bonner W. A. and Rubenstein E. (1987) Supernovae, neutron stars and biomolecular chirality. BioSystems **20:** 99–111

83 Bonner W. A. (1988) Origins of chiral homogeneity in nature. Topics Stereochem. **18:** 1–96

84 Bonner W. A. (1991) The origin and amplification of biomolecular chirality. Origins Life Evol. Biosphere **21:** 59–111

85 Bonner W. (1992) Chirality, cosmochemistry and life. Chem. Ind. 640–644

86 Bonner W. A. (1999) Chirality amplification – the accumulation principle revisited. Origins Life Evol. Biosphere **29:** 615–623

87 Mason S. F. (1984) Origins of biomolecular handedness. Nature **311:** 19–23

88 Mason S. F. and Tranter G. E. (1985) The electroweak origin of biomolecular handedness. Proc. R. Soc. Lond. A **397:** 45–65

89 Mason S. F. (1986) Biomolecular handedness from Pasteur to parity non-conservation. Nouv. J. Chim. **10:** 739–747

90 Mason S. (1988) Biomolecular homochirality. Chem. Soc. Rev. **17:** 347–359

91 Feringa B. L. and Delden R. A. van (1999) Absolute asymmetric synthesis: the origin, control, and amplification of chirality. Angew. Chem. Int. Ed. **38:** 3418–3438

92 Avalos M., Babiano R., Cintas P., Jiménez J. L., Palacios J. C. and Barron L. D. (1998) Absolute asymmetric synthesis under physical fields: facts and fictions. Chem. Rev. **98:** 2391–2404

93 Lee T. D. and Yang C. N. (1956) Question of parity conservation in weak interactions. Phys. Rev. **104:** 254–258

94 Wu C. S., Ambler E., Hayward R. W., Hoppes D. D. and Hudson R. P. (1957) Experimental test of parity conservation in beta decay. Phys. Rev. **105:** 1413–1415

95 Tranter G. E. (1985) The parity violating energy differences between the enantiomers of α-amino acids. Mol. Phys. **56:** 825–838

96 Tranter G. E., MacDermott A. J., Overkill R. E. and Speers P. J. (1992) Computational studies of the electroweak origin of biomolecular handedness in natural sugars. Proc. R. Soc. Lond. A **436:** 603–615

97 Bakasov A., Ha T.-K. and Quack M. (1998) Ab initio calculation of molecular energies including parity violating interactions. J. Chem. Phys. **109:** 7263–7285

98 Quack M. (1989) Structure and dynamics of chiral molecules. Angew. Chem. Int. Ed. Engl. **28:** 571

99 Zanasi R., Lazzeretti P., Ligabue A. and Soncini A. (1999) On the stabilization of natural L-α-amino acids and D-sugars via parity-violating effects. In: Advances in BioChirality, pp. 337–385, Pályi G., Zucchi C. and Caglioti L. (eds), Elsevier, Amsterdam

100 Vester F., Ulbricht T. L. V. and Krauch H. (1958) Optische Aktivität und die Paritätsverletzung im β-Zerfall. Naturwissenschaften **46:** 68

101 Szabó-Nagy A. and Keszthelyi L. (1999) Experimental evidences for parity violating energy differences between enantiomers. In: Advances in BioChirality, pp. 367–376, Pályi G., Zucchi C. and Caglioti L. (eds), Elsevier, Amsterdam

102 Kovacs K. L. and Garay A. S. (1975) Primordial origins of chirality. Nature **254:** 538

103 Thiemann W. and Darge W. (1974) Experimental attempts for the study of the origin of optical activity on earth. Origins Life **5:** 263–283

104 Bonner W. A., Kavasmaneck P. R., Martin F. S. and Flores J. J. (1974) Asymmetric adsorption of alanine by quartz. Science **186:** 143–144

105 Bonner W. A. and Kavasmaneck P. R. (1976) Asymmetric adsorption of DL-alanine hydrochloride by quartz. J. Org. Chem. **41:** 2225–2226

106 Barron L. D. (1986) True and false chirality and absolute asymmetric synthesis. J. Am. Chem. Soc. **108:** 5539–5542

107 Curie P. (1894) Sur la symétrie dans les phénomènes physiques, symétrie d'un champ électrique et d'un champ magnétique. J. Phys. (Paris) **3:** 393–415

108 Kuhn W. and Knopf E. (1930) Darstellung optisch aktiver Stoffe mit Hilfe von Licht. Z. Phys. Chem. **7B:** 292–310

109 Balavoine G., Moradpour A. and Kagan H. B. (1974) Preparation of chiral compounds with high optical purity by irradiation with circularly polarized light, a model reaction for the prebiotic generation of optical activity. J. Am. Chem. Soc. **96:** 5152–5158

110 Flores J. J., Bonner W. A. and Massey G. A. (1977) Asymmetric photolysis of (*RS*)-leucine with circularly polarized ultraviolet light. J. Am. Chem. Soc. **99:** 3622–3625

111 Engel M. H. and Nagy B. (1982) Distribution and enantiomeric composition of amino acids in the Murchison meteorite. Nature **296:** 837–840

112 Bada J. L., Cronin J. R., Ho M.-S., Kvenvolden K. A., Lawless J. G., Miller S. L. et al. (1983) On the reported optical activity of amino acids in the Murchison meteorite. Nature **301:** 494–496

113 Engel M. H. and Nagy B. (1983) Reply to On the reported optical activity of amino acids in the Murchison meteorite. Nature **301:** 496–497

114 Cronin J. R. and Pizzarello S. (1997) Enantiomeric excesses in meteoritic amino acids. Science **275:** 951–955

115 Cronin J. R. and Pizzarello S. (1999) Amino acid enantiomer excesses in meteorites: origin and significance. Adv. Space Res. **23:** 293–299

116 Pizzarello S. and Cronin J. R. (2000) Non-racemic amino acids in the Murray and Murchison meteorites. Geochim. Cosmochim. Acta **64:** 329–338

117 Bailey J., Chrysostomou A., Hough J. H., Gledhill T. M., McCall A., Clark S. et al. (1998) Circular polarization in star-formation regions: implications for biomolecular homochirality. Science **281:** 672–674

118 Thomas P. J., Chyba C. F. and McKay C. P. (eds) (1997) Comets and the Origin and Evolution of Life, Springer, New York

119 McKay C. P. (1997) Comets and space missions. In: Comets and the Origin and Evolution of Life, pp. 283–287, Thomas P. J., Chyba C. F., and McKay C. P. (eds), Springer, New York

120 Thomas P. J., Chyba C. F. and McKay C. P. (1997) Introduction: comets and the origin of life. In: Comets and the Origin and Evolution of Life, Thomas P. J., Chyba C. F. and McKay C. P. (eds), pp. 1–2, Springer, New York

121 Frank F. C. (1953) On spontaneous asymmetric synthesis. Biochim. Biophys. Acta **11:** 459–463

122 Kondepudi D. K., Kaufman R. J. and Singh N. (1990) Chiral symmetry breaking in sodium chlorate crystallization. Science **250:** 975–976

123 Kondepudi D. K., Bullock K. L., Digits J. A. and Yarborough P. D. (1995) Stirring rate as a critical parameter in chiral symmetry breaking crystallization. J. Am. Chem. Soc. **117:** 401–404

124 Kondepudi D. K. and Sabanayagam C. (1994) Secondary nucleation that leads to chiral symmetry breaking in stirred crystallization. Chem. Phys. Lett. **217:** 64–68

125 Service R. F. (1999) Does life's handedness come from within? Science **286:** 1282–1283

126 Lippmann D. Z. and Dix J. (1999) Possible mechanisms for spontaneous production of enantiomeric excess. In: Advances in BioChirality, pp. 85–97, Pályi G., Zucchi C. and Caglioti L. (eds), Elsevier, Amsterdam

127 Horeau A. (1975) Method for obtaining an enantiomer containing less than 0.1% of its antipode: determination of its maximum rotatory power. Tetrahedron **31:** 1307–1309

128 Rautenstrauch V. (1994) The two expressions of the Horeau principle, nth-order Horeau amplifications, and scales for the resulting very high enantiopurities. Bull. Soc. Chim. Fr. **131:** 515–524

129 Blout E. R. and Idelson M. (1956) Polypeptides. IX. The kinetics of strong-base initiated polymerizations of amino acid-N-carboxanhydrides. J. Am. Chem. Soc. **78:** 3857–3858

130 Idelson M. and Blout E. R. (1958) Polypeptides. XVIII. A kinetic study of the polymerization of amino acid N-carboxyanhydrides initiated by strong bases. J. Am. Chem. Soc. **80:** 2387–2393

131 Blair N. E. and Bonner W. A. (1981) A model for the enantiomeric enrichment of polypeptides on the primitive earth. Origins Life **11:** 331–335

132 Bonner W. A., Blair N. E. and Dirbas F. M. (1981) Experiments on the abiotic amplification of optical activity. Origins Life **11:** 119–134

133 Blair N. E. and Bonner W. A. (1980) Experiments on the amplification of optical activity. Origins Life **10:** 255–263

134 Bolli M., Micura R. and Eschenmoser A. (1997) Pyranosyl-RNA: chiroselective self-assembly of base sequences by ligative oligomerization of tetranucleotide-2′,3′-cyclophosphates (with a commentary concerning the origin of biomolecular homochirality). Chem. Biol. **4:** 309–320

135 Green M. M., Park J.-W., Sato T., Teramoto A., Lifson S., Selinger R. L. B. et al. (1999) The macromolecular route to chiral amplification. Angew. Chem. Int. Ed. **38:** 3138–3154

136 Green M. M., Garetz B. A., Munoz B., Chang H., Hoke S. and Cooks R. G. (1995) Majority rules in the copolymerization of mirror image isomers. J. Am. Chem. Soc. **117:** 4181–4182

137 Green M. M., Peterson N. C., Sato T., Teramoto A., Cook R. and Lifson S. (1995) A helical polymer with a cooperative response to chiral information. Science **268:** 1860–1866

138 Shibata T., Hayase T., Yamamoto J. and Soai K. (1997) One-pot asymmetric autocatalytic reaction with remarkable amplification of enantiomeric excess. Tetrahedron Asymmetry **8:** 1717–1719

139 Shibata T., Yamamoto J., Matsumoto N., Yonekubo S., Osanai S. and Soai K. (1998) Amplification of a slight enantiomeric imbalance in molecules based on asymmetric autocatalysis: the first correlation between high enantiomeric enrichment in a chiral molecule and circularly polarized light. J. Am. Chem. Soc. **120:** 12157–12158

140 Soai K. and Shibata T. (1999) Asymmetric autocatalysis and biomolecular chirality. In: Advances in BioChirality, pp. 125–136, Pályi G., Zucchi C. and Caglioti L. (eds), Elsevier, Amsterdam

141 Soai K., Shibata T. and Sato I. (2000) Enantioselective automultiplication of chiral molecules by asymmetric autocatalysis. Acc. Chem. Res. **33:** 382–390

142 Soai K., Osanai S., Kadowaki K., Yonekubo S., Shibata T. and Sato I. (1999) *d*- and *l*-Quartz-promoted highly enantioselective synthesis of a chiral organic compound. J. Am. Chem. Soc. **121:** 11235–11236

143 Sato I., Kadowaki K. and Soai K. (2000) Asymmetric synthesis of an organic compound with high enantiomeric excess induced by inorganic ionic sodium chlorate. Angew. Chem. Int. Ed. **39:** 1510–1512

144 IUPAC (1996) Basic terminology of stereochemistry (IUPAC recommendations 1996). Pure Appl. Chem. **68:** 2195–2222