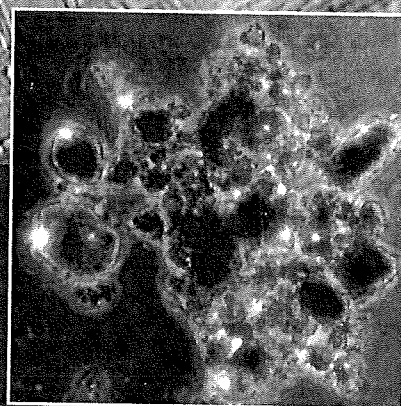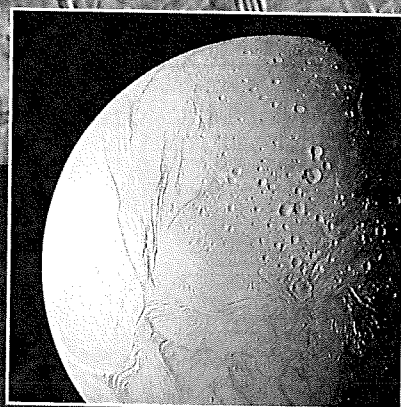# PLANETS AND LIFE

The Emerging Science of Astrobiology

Edited by **Woodruff T. Sullivan III**
and **John A. Baross**

7 The origin of proteins and nucleic acids

Alonso Ricardo, *University of Florida (currently at Massachusetts General Hospital)*
Steven A. Benner, *University of Florida*

Astrobiologists hope to understand the origin, history, extent, and future of life in the Universe. This is a huge task, considering that two of the terms in this mission statement are difficult to define. The definition of "life" is itself worth a chapter in this book (Chapter 5). Here in this chapter, we must not only concern ourselves with a definition of life, but also with the concept of "understanding." What does it mean to say that we "understand life"?

Any attempt to understand life soon engages organic chemistry. Biology today is increasingly focused on the molecular scale. Indeed, it is difficult to find a biologist today who is *not* attempting to put a molecular structure on the phenomenon that they are studying, so much so that biology can be (provocatively!) viewed as the subfield of chemistry dealing with chemical systems capable of Darwinian evolution.

Some illustrations make this point. The human genome is nothing more (and nothing less) than a collection of chemical structures, recording how carbon, oxygen, nitrogen, hydrogen, and phosphorus atoms are bonded in the natural products directly responsible for heritance. Molecular evolution uses organic chemistry to describe the Darwinian evolution of species, the process that drives biology. Neurobiologists are attempting to describe the inventory of molecules, including messenger RNA, that allow neurons to learn and remember.

Nowhere is this more evident than in the segment of astrobiology that investigates the origin of life. At some point, either on Earth or elsewhere in the Cosmos, a collection of inanimate organic molecules found themselves assembled in a way that supported Darwinian evolution. This chemical system must have had three properties. First, it must have been able to direct the synthesis of more of itself, an ability that is uncommon in chemistry, although not unknown.

But simple replication is not sufficient to support Darwinian evolution. To support evolution, the replicates generated by the original Darwinian system must have been imperfect; the replicated chemical structures must have been different from their parents. Lastly, the imperfections themselves must have been heritable. Any system that has these properties (in correct measure) will improve itself via two Darwinian mechanisms: mutation and natural selection.

Unfortunately, we have little idea of what chemical structures support these properties, let alone what structures actually supported them in the first living systems on Earth. No examples are known of Darwinian systems other than the ones that Nature herself presents to us. We do not have an artificial life form working in the laboratory, something that might better define models for the first Darwinian molecular systems. Although many chemists have attempted to create artificial Darwinian molecular systems in the laboratory, they have failed so far because too little is known about chemistry.

These facts create challenges for future astrobiologists, challenges that go far beyond the description of planetary environments or the characterization of unusual forms of life that are found on Earth. The first goal of chemical astrobiology is to define molecular structures that support Darwinian evolution. The second will be to create, in the laboratory, artificial chemical systems that evolve as they exploit these structures. Only by creating life in the laboratory will we demonstrate that we truly understand life.

The purpose of this chapter is to lay the grounds for this future. We begin by describing some general tools for analyzing the reactivity of organic molecules, to allow the non-chemist to better understand the ways that molecules can become other molecules. We then apply these tools to ask simple questions about how

building blocks for proteins and nucleic acids might be created abiologically. Finally, we apply these tools to constrain the historical question about origins: what chemistry might *actually have occurred* four billion years ago that led to the emergence of the life on Earth that we know today.

7.1 Carbon and biochemistry

The carbon produced by stars and the hydrogen that presumably was present near the origin of the Universe can combine to form an unlimited number of organic molecules. Carbon atoms form four bonds. A single bond joining two carbon atoms is strong, on the order of 400 kJ ($\sim$100 kcal) per mole (or $\sim$4 eV per bond). This means that a typical pair of carbon atoms joined by a single bond will remain joined for many thousands of years at the temperatures for which water is a liquid at sea level on Earth.[1] Bonds between carbon and hydrogen, carbon and oxygen, and carbon and nitrogen are similarly strong.

No other element forms so many single bonds that are so strong. Nitrogen–nitrogen single bonds, like oxygen–oxygen single bonds, sulfur–sulfur single bonds, and other single bonds between two identical atoms, are weak enough to easily fall apart at liquid-water temperatures. Nitrogen can use all three of its valences to bond to another nitrogen atom; two nitrogens held together by this triple bond are indeed hard to pull apart ($\sim$800 kJ/mole). But by using all of their three valences simply to hold themselves together, two nitrogen atoms have no valences remaining to form extended chains, or to carry substituents (an atom or group of atoms that can vary in a series of analogous molecules).

As a consequence of their strength, the bonds between two carbon atoms break only when an energetically favorable path exists that allows them to do so. At temperatures accessible to liquid water, such a path generally requires that the carbon form a bond to *another* atom just as, or soon after, the original bond breaks. Understanding ways that a new bond can form as the old bond is breaking is a key to understanding reactivity.

7.2 Reactivity

Reactivity in organic molecules is based on *Structure Theory*, which holds that the behavior of all organic

[1] Liquid water will be regarded here as "standard," even though other solvents might conceivably be used for some type of "weird life" – see Chapter 27 for a discussion of the possibilities.

molecules, including those in living matter, can be understood in terms of the structures of collections of atoms held together by bonds.

Practitioners of Structure Theory sometimes seem to some to have an almost mystical understanding of the relationship between chemical structure and reactivity. In fact, there is nothing mystical to it. Chemists know thousands of reactions that organic molecules undergo, the conditions under which they go, and how forming bonds can rush in and snap up energetic intermediates arising when an old bond breaks. From this, they acquire an intuition as to the plausibility that any given chemical transformation, perhaps one that they have never seen before, might occur. They are similarly able to propose new chemical transformations.

This understanding is critical to evaluate any model relating to the origins of proteins, nucleic acids, fats, or sugars of contemporary *terran* (Earth) life. The difficulty, of course, is that this intuition cannot be gained in a single chapter, or even a semester of study. Thus, we can provide here only the basic skills that are needed to assess the likelihood of chemical pathways that might have led to the components of early life.
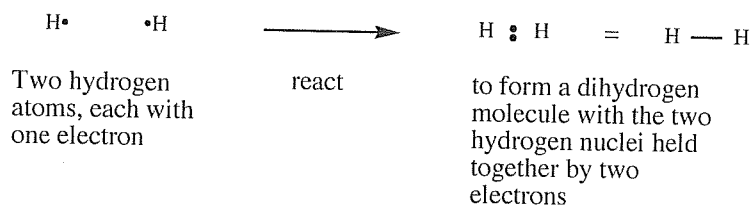
7.2.1 Pairs of electrons form bonds between atoms

We begin by noting that covalent bonds between two atoms are formed by the sharing of a pair of electrons. Thus, in dihydrogen (often written as H-H, or H_2) the line joining the two hydrogen atoms represents a pair of electrons, or a single bond. In water (H-O-H), the lines between the hydrogen atoms and the oxygen atom each represent a pair of electrons that form a single bond holding the hydrogens to the oxygen. In formaldehyde ($H_2C=O$), the double line between the carbon and the oxygen represents two pairs of electrons, four electrons in total (Fig. 7.1).

To simplify the diagrams that represent organic molecules, chemists frequently omit some of the atoms and electrons. Therefore, the first skill that is required in analyzing reactivity in organic chemistry requires that one completes the structure of the organic molecule as it is written on a sheet of paper. This ensures that we know the locations of all of the molecule's electrons.

A completed structure is known as a *Lewis structure*, and must include the electrons present that are *not* involved in bonding. For example, in the Lewis structure of water, oxygen carries two pairs of unshared electrons from the outer valence shell. We represent

H•   •H   ⟶   H **:** H   =   H — H

Two hydrogen atoms, each with one electron

react

to form a dihydrogen molecule with the two hydrogen nuclei held together by two electrons

FIGURE 7.1 Lewis representation of chemical bonds for dihydrogen (H_2), water (H_2O), and formaldehyde (H_2CO).

H **:** O **:** H   =   H — O — H
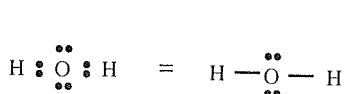
Water molecules are formed by the reaction of two hydrogen nuclei with an oxygen nucleus

H **:** C **:** H   =   H — C — H
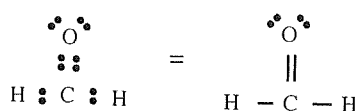
In formaldehyde the bond between the carbon and oxygen is held by four electrons

Nucleophilic center

Nucleophilic center

Electrophilic center

resonance

Electrophilic center

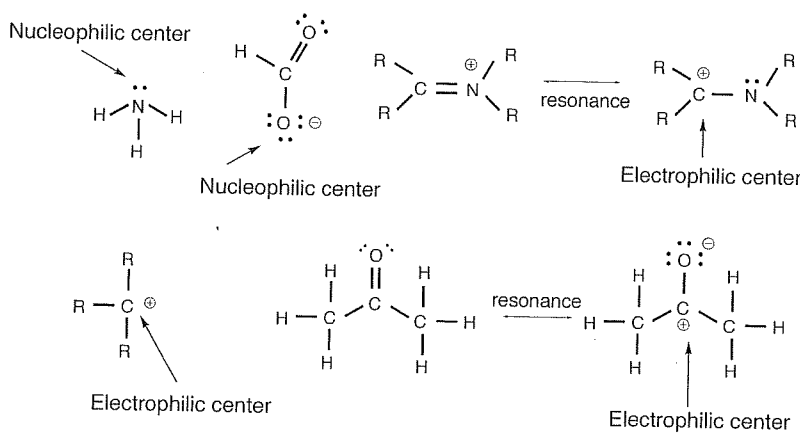Electrophilic center

resonance

Electrophilic center

FIGURE 7.2 Nucleophilic centers have an unshared pair of electrons that can form a new bond, or can get one (via resonance, for example). Electrophilic centers have a vacant orbital (or can get one via resonance, for example) that can accept an unshared pair of electrons from a nucleophilic center to form a new bond. In a *resonance* form a pair of electrons moves between adjacent atoms (electrons are dynamic entities), creating a new representation for the same molecule. The resulting resonance forms are joined by a double headed arrow to indicate equivalence.

each of these valence electrons not involved in a bond by a dot. Hence, the oxygen in the H-O-H structure has four dots, representing electrons on the oxygen that are not involved in bonding. Likewise, the oxygen in formaldehyde carries two pairs of unshared electrons, represented again by four dots on the oxygen.

7.2.2 A nucleophilic center brings a pair of electrons to form a new bond

As a pair of electrons is needed to form a chemical bond, any unshared pair of electrons is available in principle to form a new bond. Atoms that contain pairs of electrons available to form a new bond are called *nucleophilic centers* (Fig. 7.2). To form a bond, the electron pair on the nucleophile must find an atom that lacks a bond, or will soon lack a bond through breakage. This atom is called an *electrophilic center*.

A simple electrophile, for example, is a proton (H^+). H^+ is not bonded to anything, and can intrinsically form one bond. H^+ is therefore looking for a single partner with which to bond. But since H^+ itself has no electrons that it can use to form a bond, it must find a nucleophilic center as that partner.

7.2.3 Curved arrows describe the movement of pairs of electrons in reactions that form and break bonds between atoms

Organic chemists use curved arrows to describe reactions between nucleophilic and electrophilic centers that produce a new bond. The curved arrow begins with an unshared pair of electrons on the nucleophile, the pair that will form the new bond in the product. The arrow is drawn to end at a position (on the structures of the reactants) where the electron pair *will be*
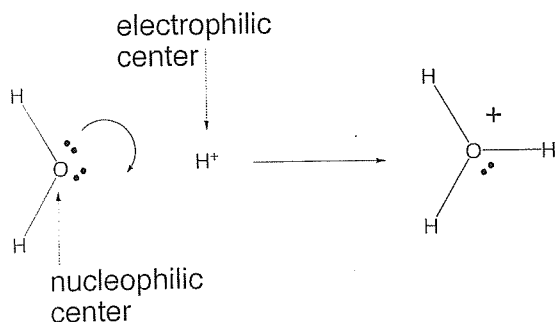
electrophilic
center

nucleophilic
center

FIGURE 7.3 Reaction of the nucleophilic center on the oxygen of water with an electrophilic center, H^+. The movement of a pair of electrons in the reaction is illustrated using a curved arrow. The result is H_3O^+, the hydronium ion.

resonance

vacant
orbital
on this
carbon

formaldehyde

attack of
nucleophile

rapid transfer
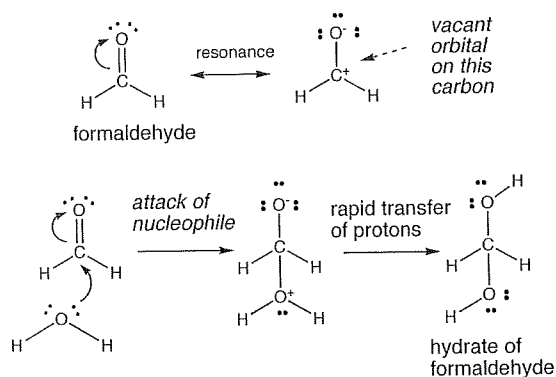of protons

hydrate of
formaldehyde

FIGURE 7.4 Reaction of the nucleophilic center on the oxygen of water with an electrophilic center, the carbon atom of formaldehyde. The movement of a pair of electrons in the reaction is illustrated using a curved arrow.

after the bond is formed. Figure 7.3 shows the reaction of the unshared pair of electrons on the oxygen of water (the nucleophilic center) with H^+ (the electrophilic center) to give H_3O^+ (the hydronium ion).

While nucleophilic centers are often easy to spot (they can bear the relevant electron pair prominently in a correctly drawn Lewis structure), electrophilic centers are frequently less so. This is especially true when the electrophilic center is a carbon atom. For example, the carbon of formaldehyde (H_2CO) has all of its four valences filled. That carbon does not seem to have a valence available to form a new bond with anything.

If, however, one of the two bonds between carbon and oxygen breaks, with the electron pair moving from a position between the carbon and the oxygen to a new position on the oxygen, then the carbon center has a valence free. It then welcomes nucleophilic attack from an oxygen atom, such as from any nearby H_2O molecule.

This process is shown using curved arrows in Fig. 7.4. Here, a bond between carbon and oxygen is broken at the same time as the carbon forms a new bond to an incoming oxygen atom. As the energy in the second C-O bond is lost through breakage, the energy of a new C-O bond is gained. The resulting product is known as the hydrate of formaldehyde (H_4CO_2).

7.3 Curved arrow mechanisms for the synthesis of biological molecules

The curved arrow tool can be used to describe most reactions of organic molecules under standard conditions (water at room temperature). This includes transformations that might have converted formaldehyde, present in a prebiotic world, into molecules that are characteristic of contemporary terran life, as we now show.

7.3.1 Curved arrow mechanisms for the formation of amino acids

Let us use the curved arrow formalism to describe the synthesis from formaldehyde, ammonia, cyanide, and water of a simple amino acid, glycine (NH_2CH_2COOH), one of the basic building blocks of proteins. The following numbered steps are shown in Fig. 7.5.

Ammonia (1) has three hydrogen atoms and one nitrogen atom. A Lewis structure shows that the nitrogen in ammonia also carries an unshared pair of electrons. The nitrogen atom is therefore a nucleophilic center. Ammonia should therefore react with formaldehyde (2) for the same reason that water does. In this reaction, the unshared pair of electrons on ammonia forms a new bond between its nitrogen and the carbon of formaldehyde, just as the pair of electrons forming the second carbon–oxygen bond leaves to form a new bond to H^+. This generates an "amino alcohol" (3).

After the transfer of various hydrogens, the nitrogen of the amino alcohol again has an unshared pair of electrons, and is able to form a second bond with the carbon atom. The resulting compound is known as an imine (4), which contains a (C=N) unit having a carbon atom bonded twice to a nitrogen atom.

The carbon of the C=N unit is also an electrophilic center. This sets the stage for the next reaction, where the carbon of the cyanide anion (5) attacks the imine (4) carbon to form an aminonitrile (6). The nitrile has a C≡N unit, where the nitrogen is bonded three times to the carbon. This carbon is again an electrophilic center. If a pair of electrons forming one of the bonds between
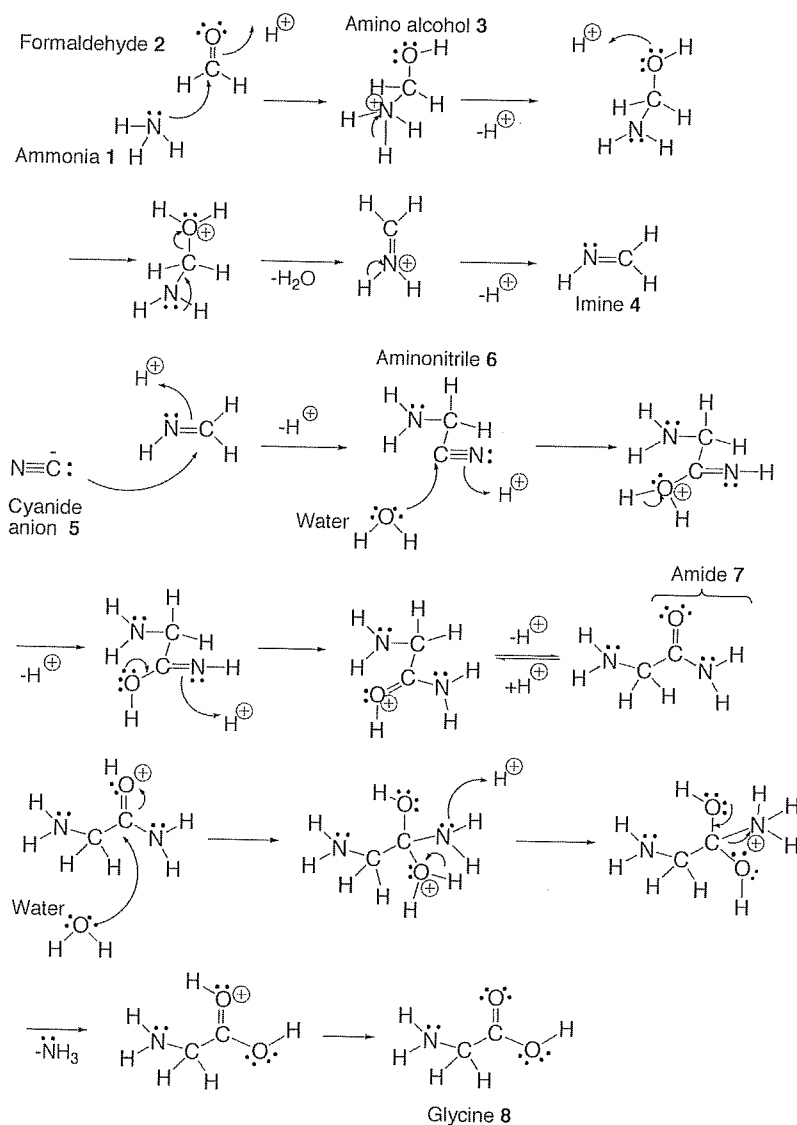
FIGURE 7.5 The Strecker synthesis of glycine. Reaction of the nucleophilic centers on the nitrogen of ammonia, the carbon of the cyanide anion, and the oxygen of water with electrophilic centers on formaldehyde and key intermediates. The movements of pairs of electrons in the reactions are illustrated using curved arrows.

carbon and nitrogen leaves to form a bond with H^+, then the carbon has a free valence. It is therefore available to form a bond with a nucleophilic oxygen atom from water.

The product, again after H^+ atoms are transferred, has another C=O group in a unit known as an *amide* (7). The carbon of the amide is again an electrophilic center, and can therefore now be attacked by the nucleophilic oxygen of another water molecule. This leads to the *hydrolysis* (taking on a water molecule) of the amide and the formation of the amino acid glycine, together with an ammonia molecule.

The net process is the reaction of one molecule of formaldehyde, one molecule of hydrogen cyanide, and one molecule of water to give one molecule of glycine (8). Ammonia is used in the first step, and is released in the last step. Therefore, ammonia is a catalyst for the reaction, being consumed and formed in equal amounts in the reaction cycle.

This sequence of reactions is known as the *Strecker synthesis of amino acids*, named after the chemist who developed it in the 1860s. The Strecker synthesis is driven by the innate reactivity of nucleophiles and electrophiles, and proceeds spontaneously and in reasonable yield. Further, the Strecker synthesis is quite general. It can be used to prepare any amino acid for which the corresponding aldehyde is available, not just formaldehyde; many of these amino acids are among
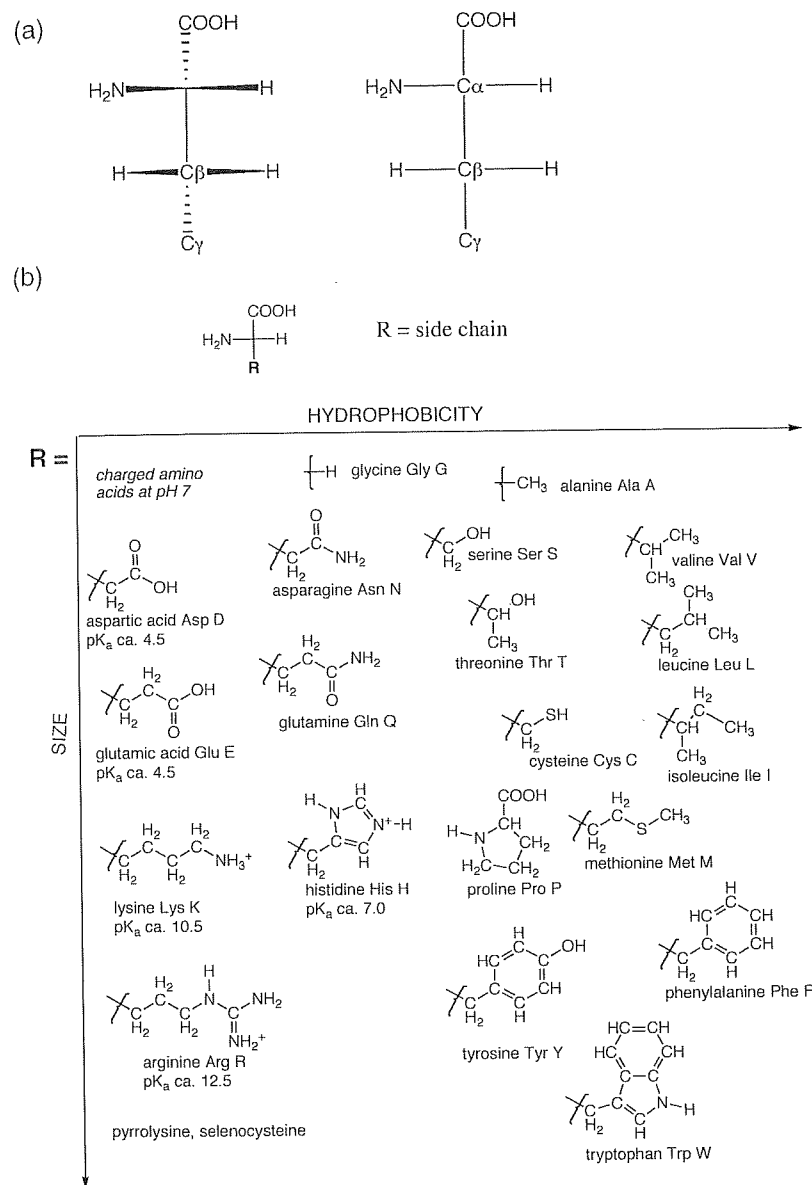
(a)

(b)

R = side chain

HYDROPHOBICITY

R =

FIGURE 7.6 (a) The general structure of an α-amino acid. The α refers to the position on the carbon chain that carries the amino group H₂N; other possibilities are the β and γ carbons. The four atoms attached to each carbon are arranged in space above and below the plane of the paper, as indicated by the wedged lines. On the right is a Fischer projection, which places bonds that project above the paper horizontally, and those below vertically.

(b) The side chains of the 20 predominant amino acids for Earth life. In general, organic chemists do not represent all of the carbon atoms in a molecular structure with the letter "C", or all of the hydrogen atoms in the structure with a letter "H". Rather, carbon atoms are understood to be present at any unlabelled vertex. These carbon atoms are assumed to form four bonds. If four lines are not shown explicitly on the structure, the missing lines are assumed to be bonds to hydrogen atoms, which are not explicitly shown. Recent discoveries have increased the number of encoded amino acids to 22, with the inclusion of the "minor" amino acids selenocysteine and pyrrolysine (Rother et al., 2000; Berry et al., 2001; Hao et al., 2002; Srinivasan, James, and Krzycki, 2002).

those that link together to form the proteins of terran organisms (structures are shown in Fig. 7.6). For example, if we start with acetaldehyde (CH₃CHO) rather than formaldehyde, the amino acid alanine (CH₃CH(NH₂)COOH) is formed (Fig. 7.7).

7.3.2 Curved arrow mechanisms for forming nucleobases for RNA and DNA

Curved arrow mechanisms can be used to generate nonbiological routes for the synthesis of many molecules in biology. For example, the Oró–Orgel synthesis

exploits the reactivity of HCN to make adenine ($C_5H_5N_5$), one of the five *nucleobases* (also called *bases*, symbolized as A, C, T, G, and U) used to store information in DNA and RNA (Fig. 7.8). The cyanide anion again reacts as a nucleophile, this time with HCN, whose carbon atom serves as an electrophilic center.

7.3.3 Curved arrow mechanisms for forming sugars for RNA

Eschenmoser has considered the special reactivity of hydrogen cyanide to generate the sugar ribose, also a
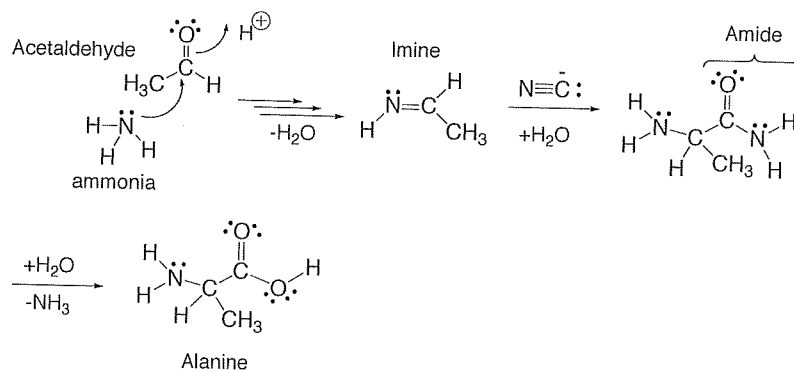
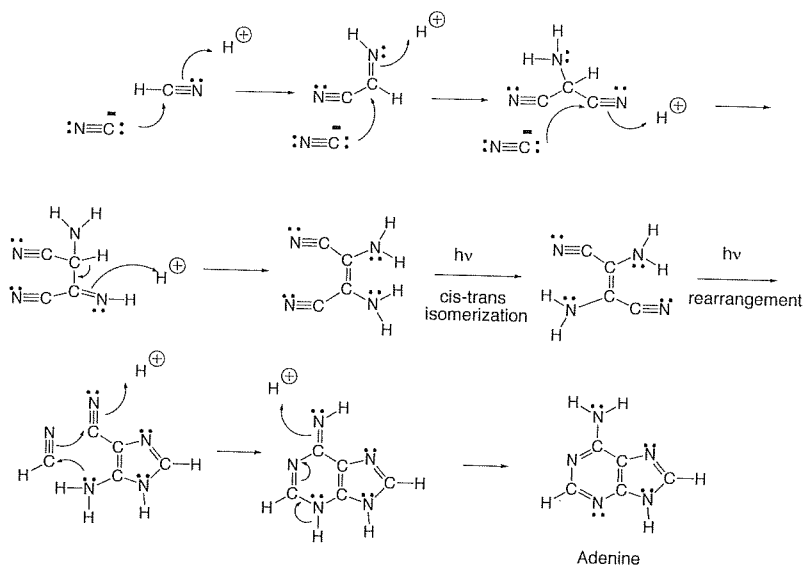FIGURE 7.7 Strecker synthesis of alanine, starting from acetaldehyde.

FIGURE 7.8 HCN yields adenine via the Oró–Orgel synthesis.

part of RNA. An intriguing sequence of reactions from an interesting starting material (derived from HCN) is shown in Fig. 7.9. This process occurs in the laboratory (Mueller *et al.*, 1990). It is not known, however, to occur in nature, and the starting material has not been detected naturally in the cosmos.

7.4 Extraterrestrial sources of organic building blocks

What starting materials might have been available in the cosmos or on Earth to support the origin of life? What kinds of molecules might have been available as precursors for prebiological synthesis? The Cosmos offers several places to look directly. One is the meteorites that fall to Earth continuously. These come in all sizes, including submicron particles that are too small to analyze easily, but may contribute most of the carbon to a forming planet. Another place to look is in the interstellar dust in clouds surrounding stars that are forming.

7.4.1 Organics from meteorites

Many meteorites that fall to Earth are believed to originate in or near the asteroid belt. Asteroids most likely arose as the consequence of a failed planet formation (Section 3.9.2). Particularly interesting are carbonaceous chondrites, which have evidently suffered exposure to water when within their original parent body. These have frequently been reported to contain amino acids, principally glycine and alanine. Early reports may, however, have been partly unreliable, reflecting contamination of the meteorite after it arrived on Earth.

Some of the most reliable work exploited a meteorite that fell in 1969 near Murchison, Australia. This meteorite was quickly recovered, and presumably
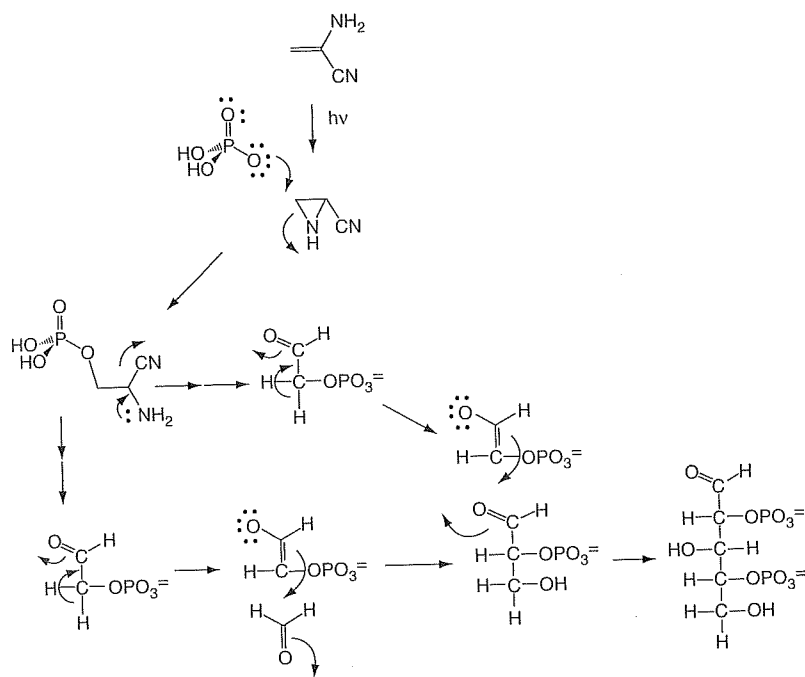
FIGURE 7.9 The Eschenmoser synthesis of ribose-2,4-diphosphate from a proposed starting material derived from HCN.

FIGURE 7.10 A fragment of the carbonaceous chondrite Murchison meteorite.

therefore suffered little contamination (Fig. 7.10). The Murchison meteorite therefore has become the principal sample from which conclusions are drawn about organic molecules that might exist in the Solar System outside of Earth.

Murchison contains a large amount of organic material, summarized in Tables 7.1 and 7.2. The amino acids found in Murchison have been classified into two general groups (Fig. 7.11). Within these groups, some 70 specific amino acids have been reported, some of which are shown in Fig. 7.12. Many of these are not known to occur in contemporary Earth life, diminishing the likelihood that they arose in the meteorite as a result of contamination from a terran source.

Several of these amino acids contain *stereogenic centers*. These are, in these cases, atoms in which carbon atoms are bonded to four different substituents. Compounds having stereogenic centers can give rise to *enantiomers*. A pair of enantiomers have mirror image structures, i.e., related to each other like the left hand is related to the right hand.

Enantiomers are isomers, meaning the left-handed and right-handed forms are different. In natural processes, left- and right-handed molecules are often formed in equal amounts. To form regular structures when these monomers are assembled, however, it is generally more efficient to have the same handedness in all molecules. Thus, 100% of amino acids in terran proteins are left-handed, and all sugars in terran nucleic acids are right-handed. Enantiomeric excess,[2] the predominance of one enantiomer over the other for a given assembly of atoms, is therefore believed to be a

---

[2] This property is often also called *chirality*, or handedness.

TABLE 7.1 Carbon in the Murchison meteorite

Total carbon	2.12% (Jarosevich, 1971), 1.96% (Fuchs, Olsen, and Jensen, 1973)
Carbon as interstellar grains Diamond	400 ppm (Lewis et al., 1987)
Silicon carbide	7 ppm (Tang et al., 1989)
Graphite	<2 ppm (Amari et al., 1990)
Carbonate minerals	2–10 % of total carbon (Grady et al., 1988)
Macromolecular carbon	70–80 % of total carbon

TABLE 7.2 Organic compounds in the Murchison meteorite (Cronin and Pizzarello, 1988)

Amino acids 60 ppm	Purines and pyrimidines 1.3 ppm
Aliphatic hydrocarbons >35 ppm	Basic N-heterocycles 7 ppm
Aromatic hydrocarbons 15–28 ppm	Amines 8 ppm
Carboxylic acids >300 ppm	Amines 55–70 ppm
Dicarboxylic acids >30 ppm	Alcohols 11 ppm
Hydroxycarboxylic acids 15 ppm	Aldehydes and ketones 27 ppm

mono amino alkanoic acids
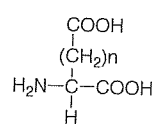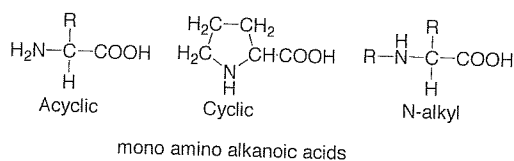
mono amino alkandioic acid

FIGURE 7.11 Typical types of amino acids in the Murchison meteorite. Adapted from Cronin and Pizzarello (1988).

universal feature of chemistry derived from living systems.

In this light, researchers were surprised to find that several of the amino acids found in the Murchison meteorite are in fact slightly enantiomerically enriched (Table 7.3). Especially notable were enantiomeric enrichments of 7–9% in three specific amino acids not known in forms of life presently living on Earth. This makes contamination from terrestrial sources unlikely.

If we assume that the amino acids in Murchison were *not* generated by living processes, this suggests that enantiomeric enrichment can be achieved by processes that are independent of life. Several of these are known in the laboratory, but not in nature. This weighs against the usual thinking that enantiomeric enrichment is a unique signature of life. However, the data available are also consistent with a biotic origin. This would be the case if the Murchison meteorite originated in an asteroid that supported life based on α-methyl amino acids that preferred one enantiomer to the other. While few would argue so, this result is consistent with life having emerged in the asteroid belt.

We do not know the extent to which the Murchison organics reflect what was available on early Earth before life emerged. This rich inventory of amino acids does not appear to be universal in carbonaceous chondrites (although the number of these that have

been examined in detail is very small). For example, only a few amino acids (glycine, alanine, α-aminoisobutyric acid, α-amino-*n*-butyric acid, γ-aminobutyric acid) are found in the meteorite that fell in 2000 on Tagish Lake, Canada (Pizzarello et al., 2001; Table 7.4). The near absence of complex amino acids is significant, as the meteorite was captured in a pristine condition soon after it fell.

Also discouraging is the fact that not even two joined amino acids have ever been found in meteorites. Joining two amino acids is the first step towards the synthesis of proteins, such as those found in contemporary terran life. If the meteorite organics analyzed to date are representative of planetary processing of primitive organic compounds, the problem of assembling amino acids into *polypeptides* (short strings) remains to be solved.

Some of the chemical fragments of DNA and RNA likewise can be found in meteorites. For example, some meteorites have been reported to contain small amounts of adenine, one of the nucleobases found in RNA and DNA. The current view is that Murchison contained adenine, guanine, and their hydrolysis products hypoxanthine and xanthine, as well as uracil. The reported concentration of adenine, however, is low, ~1.3 ppm. Murchison and other meteorites may also contain ribitol and ribonic acid, respectively the reduced and oxidized forms of ribose (Cooper et al., 2001).

TABLE 7.3 Enantiomeric enrichments (EE) for amino acids in two meteorites (Pizzarello and Cronin, 2000). Column 2 refers to the natural abundance of the amino acids in Earth's biosphere

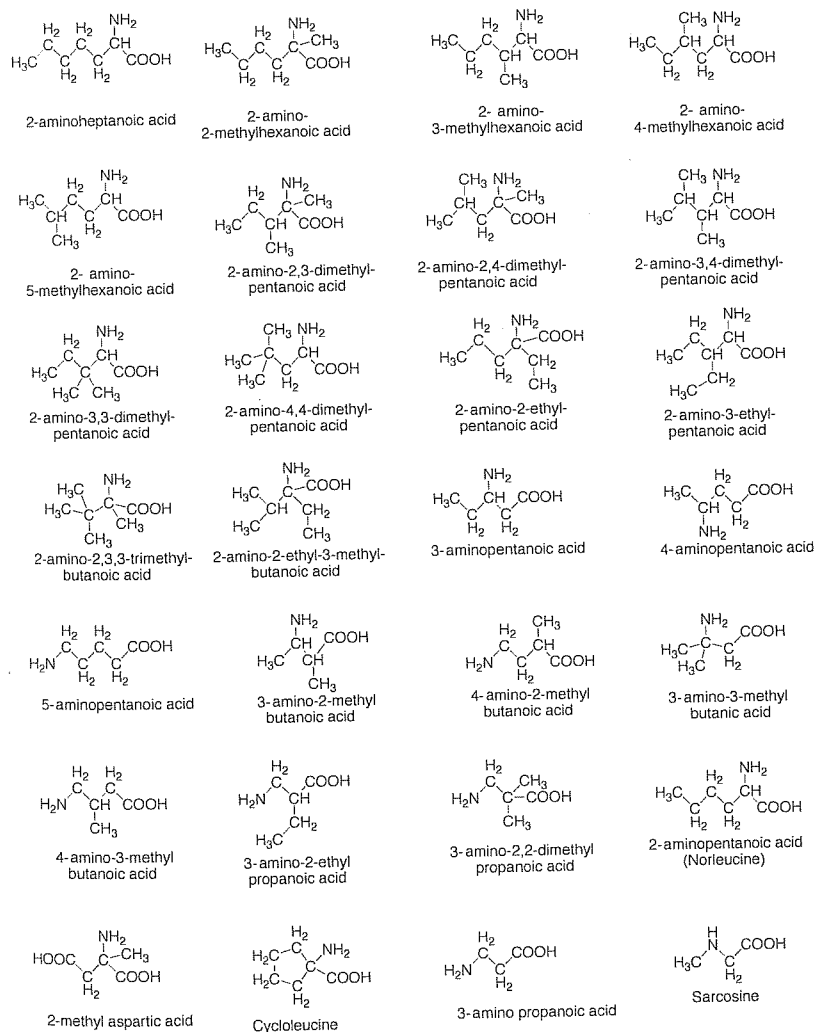| Meteorite sample compound	on Earth	Murchison EE (%)	Murray EE (%)
2-amino-2,3-dimethyl-pentanoic acid			
2 S,3S/2R,3R	unknown	7.6	1.0
2 S,3S/2R,3S	unknown	9.2	2.2
α-methylnorleucine	unknown	4.4	1.8
α-methylnorvaline	unknown	2.8	1.4
α-methylvaline	unknown	2.8	1.0
Isovaline	rare	8.4	6.0
Norvaline	rare	0.4	0.8
α-amino-n-butyric acid	common	0.4	−0.4
Valine	ubiquitous	2.2	−0.4
Alanine	ubiquitous	1.2	0.4

FIGURE 7.12 Some of the 70 amino acids reported in the Murchison meteorite (Kvenvold et al., 1970; Cronin and Moore, 1971; Cronin and Pizzarello, 1986).

TABLE 7.4 The organic content of the Tagish Lake meteorite (Pizzarello et al., 2001)

Aliphatic hydrocarbons 5 ppm	Dicarboximides 5.5 ppm
Aromatic hydrocarbons ≥ 1 ppm	Sulfonic acids ≥ 20.0 ppm
Dicarboxylic acids 17.5 ppm	Amino acids < 0.1 ppm
Carboxylic acids 40 ppm	Amines < 0.1 ppm
Pyridine carboxylic acids 7.5 ppm	Amides < 0.1 ppm

TABLE 7.5 Organic compounds identified in tholin mixtures (Sagan et al., 1978; Sagan and Khare, 1979; Pietrogrande et al., 2001)

Hydrogen sulfide	Hexene	Formamide
Hydrogen cyanide	Heptene	Pyridine
Ammonia	Butadiene	Styrene
Ethane	Benzene	2,3-pentadiene
Propane	Toluene	2-methylpyrimidine
Butane	Thiophene	4-methylpyrimidine
Ethene	2-methyltiophene	3-butenenitrile
Propene	Methylmercaptan	Butyne
Butene	Ethylmercaptan	Acetonitrile
Pentene	Propylmercaptan	Carbon dioxide
Carbon disulfide	Methylisocyanate	Acetamide

Phosphorus is an important component of terran life. It is abundant on the Earth, both as an element (the eleventh most abundant atom in the Earth's crust) and as phosphate. Meteorites hold a variety of phosphate-containing minerals, and some phosphide minerals (Moore, 1971). Unfortunately, a clear prebiotic pathway for the chemical incorporation of phosphate into RNA or DNA has not yet been found.

No *nucleosides* (a nucleobase joined to a sugar), have been reported from meteorites. Nor has evidence been found in any meteorite for the joining of *nucleotides* (a nucleoside attached to a phosphate), as is necessary for RNA or DNA.

7.4.2 Organics from the interstellar medium

The interstellar medium is an alternative source of organic molecules that may have been delivered to the primitive Earth. Organic molecules are assembled from the elements in interstellar space, without the need for a planet (Section 3.8.1 discusses this chemistry). The inventory of organic molecules found in interstellar space is now at 120 species and is illustrated in part in Fig. 7.13. These molecules include formaldehyde, cyanide, acetaldehyde, water, and ammonia, all of which we found useful above when forming amino acids. Glycine, the simplest amino acid, has also been detected in the interstellar medium.

7.4.3 Laboratory simulations

In a number of cases, laboratory environments designed to model conditions on early Earth have generated amino acids and/or components of nucleosides from species known or suspected to be present in the cosmos. For nucleic acids, work by Oró and Orgel showed that the key nucleobase adenine can be prepared from hydrogen cyanide, as discussed above (Fig. 7.8) (Oró, 1960; Sanchez, Ferris, and Orgel, 1967).

Stanley Miller, working in Harold Urey's laboratory in 1953, made the first conscious attempt to model organic synthesis under prebiotic conditions. Amino acids were found to be generated after electrical discharges from electrodes were passed through an atmosphere of hydrogen, methane, and ammonia over water. These amino acids presumably arose from compounds generated in the discharge that later self-assembled in the water (Miller, 1955). The electrical discharge was necessary simply to generate the formaldehyde and cyanide needed as starting materials for the synthesis. Once these precursors were formed, the synthesis of amino acids occurred without the need for any energy at all, presumably via the Strecker synthesis.

The simulated atmosphere chosen by Miller for his laboratory experiments was considered at the time to approximate the atmosphere of early Earth, but today many models hold that the amount of methane on early Earth was much smaller than that used in the Miller experiments. Instead, the carbon inventory of the early Earth is today modeled as being present largely as carbon dioxide (Kasting, 1993; Section 4.4).

Accordingly, much effort has been devoted to seeking nonbiological syntheses of biomolecules under conditions presumed to better fit those of early Earth. Some success has been achieved, reflecting the general reactivity of organic molecules. In general, when simple carbon-containing compounds are treated with energy
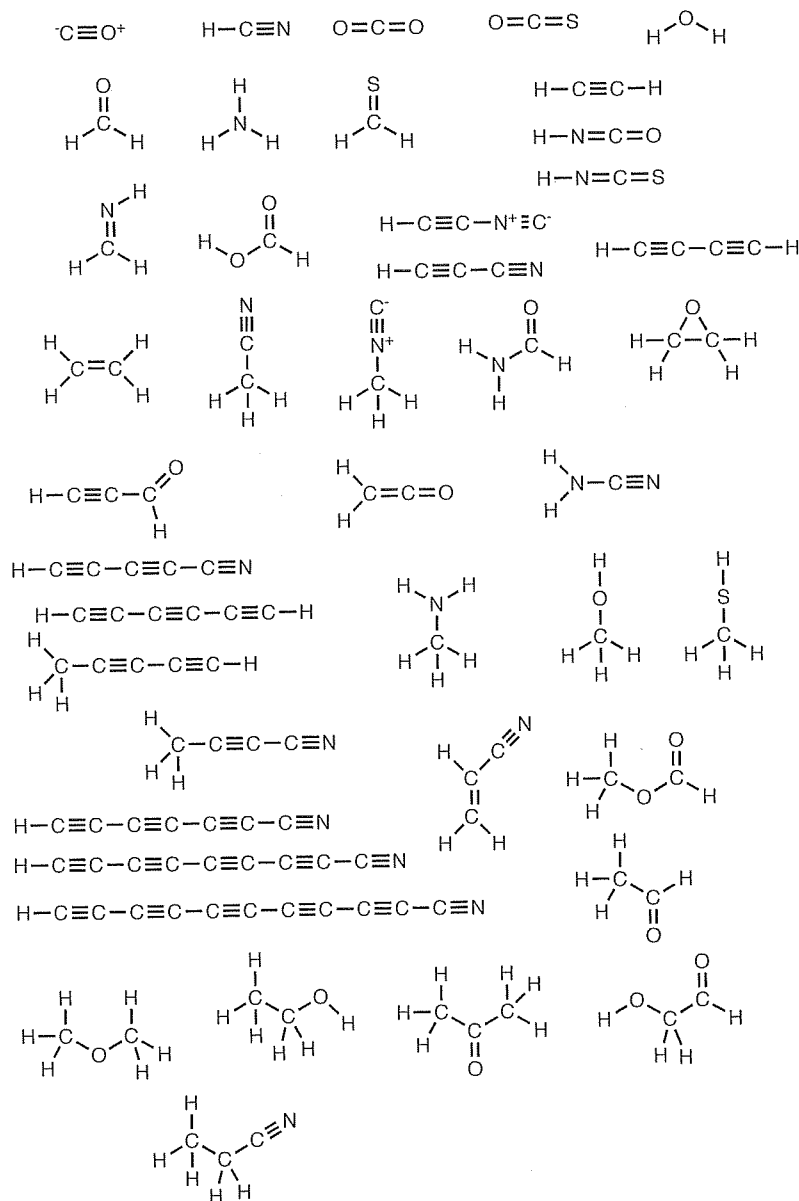
FIGURE 7.13 Some of the 120 organic compounds detected in the interstellar medium, mostly by microwave spectroscopy. (Courtesy Lucy Ziurys.)

sources, they form more complex organic molecules. These energy sources include electrical discharge, ultraviolet light, impact, and ionizing radiation. One example of this is "tholin," a red–brown collection of organic molecules made by irradiating simple molecules (where carbon is present largely as carbon dioxide) (Sagan *et al.*, 1978). A partial inventory of molecules comprising tholins is shown in Table 7.5. Tholins have been proposed as an important part of the atmosphere of Saturn's moon Titan (Chapter 20), and considerable effort is now being made to determine the ratio of carbon to

hydrogen to oxygen in an atmosphere that will optimize the yield of organic species when energy is applied.

Analogous work has been extended to simulate interstellar environments (also see Section 3.8.1). For example, Bernstein, Allamandola, and their colleagues recently synthesized the amino acids glycine, alanine, and serine in their laboratory model of icy interstellar grains irradiated by ultraviolet light as an energy source (Bernstein *et al.*, 2002). This suggests that at least some amino acids may have arrived on early Earth as a product of interstellar photochemistry,

rather than through formation in liquid water on an early Solar System body.

7.5 Thermodynamic equilibria

Given a source of organic precursors, the question remains: which reactions will occur and in what yields? For this, we must consider thermodynamic properties of molecules.

First, we consider the concept of the *reduction/oxidation* (or *redox*) state, frequently used to describe organic and other molecules. The ratio of the number of hydrogen atoms in a molecule to the number of non-hydrogen atoms, excluding carbon, determines the redox state of the molecule.

Carbon dioxide, because its carbon is bonded to two oxygen atoms and no hydrogen atoms, is the most oxidized that a carbon atom can be. Methane, where carbon is bonded only to hydrogen, is the most reduced that a carbon atom can be. Formaldehyde is at the same "oxidation level" as elemental carbon (because it has an equal number of bonds to H and O). Viewed alternatively, the ratio of hydrogen atoms (2) to oxygen atoms (1) in formaldehyde is the same as in water (Fig. 7.14). Thus, compounds of the formula $C_n(H_2O)_n$ can be converted to elemental carbon by heating, which extrudes water without a net change in the redox state of the carbons.

At one level, understanding the thermodynamics of carbon-containing molecules with respect to oxidation or reduction is as simple as asking whether hydrogen or oxygen is more abundant in the environment. In the modern terran atmosphere, which contains abundant dioxygen, essentially all compounds containing reduced carbon are thermodynamically unstable with respect to oxidation to carbon dioxide. From a thermodynamic perspective, virtually all organic matter placed in today's atmosphere will eventually "burn" to give carbon dioxide and water. The *rate* of the burning, however, can be very slow in the 20°–40 °C temperature range and at today's amospheric oxygen partial pressure.

In the absence of oxygen and in the presence of H_2, reduced carbon is thermodynamically preferred. This is certainly true deep in the ocean, near hydrothermal vents for example. Here, the synthesis of reduced organic compounds is thermodynamically favored. Shock, Cody, and others have exploited this fact to propose net synthesis of organic molecules in anoxic environments (Chapter 8).

A reaction that is thermodynamically "uphill" (not energetically favored) in one direction can become
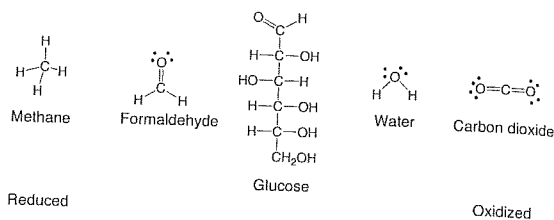

FIGURE 7.14 Redox states. Formaldehyde and glucose have the same oxidation state as elemental carbon, because the ratio of hydrogen to oxygen atoms in both is 2:1, the same as in water. Methane is more reduced (the ratio of hydrogen to oxygen atoms is 4:0). Carbon dioxide is more oxidized (the ratio of hydrogen to oxygen atoms is 0:2).

"downhill" in the same direction if the environmental conditions are changed. If $A + B \Leftrightarrow C + D$, the reaction can be pulled to the right if D is removed, converting all of $A + B$ to C. Conversely, if excess D is added, C will be driven to $A + B$. This behavior of equilibria often appears in textbooks as Le Chatelier's Principle.

It is important to note that no biological compound can ever be said to be universally "high in energy." Students (and sometimes even famous scientists) can easily misunderstand this fact.

Each reaction has a free energy, or ΔG^0, which is defined as $-RT \ln [\text{product}]_{eq}/[\text{reactant}]_{eq}$, where $[\text{product}]_{eq}$ and $[\text{reactant}]_{eq}$ are the concentrations of product and reactant *at equilibrium*, R is the universal gas constant, and T is the absolute temperature. The value for ΔG^0 can be either positive or negative, but this value does *not* determine whether the reaction runs in the forward or reverse direction under any set of conditions.

Nor is it useful to speak of the "energy" of any particular compound. Rather, the free energy ΔG of a system, which makes a statement about whether it can do thermodynamic work, is determined by the degree to which the system is *out of* equilibrium. This, in turn, is defined by the equation: $\Delta G = \Delta G^0 + RT \ln [\text{product}]/[\text{reactant}]$. Systems where ΔG is less than zero will spontaneously yield more product, until the amount of product rises (and the term $RT \ln [\text{product}]/[\text{reactant}]$) rises, ΔG approaches zero, and the net flux ceases. Conversely, systems where ΔG is greater than zero will spontaneously yield more reactant.

In this context, adenosine triphosphate (ATP), the "currency of energy" in all cells (Chapter 10), is viewed as "high energy" only because at equilibrium the reaction: $ATP + \text{water} \Leftrightarrow ADP + \text{inorganic phosphate}$ contains more ADP and inorganic phosphate than ATP. If, however, the initial state contains ADP + inorganic phosphate and *no* ATP, the process spontaneously
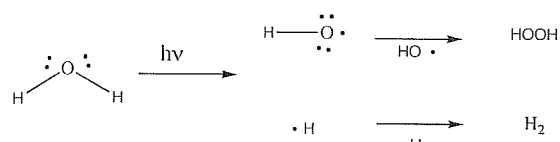
FIGURE 7.15 Possible photodissociation of water on the surface of Mars. Products are hydrogen peroxide (a strong oxidant) and hydrogen gas (which then escapes the planet).

proceeds to the left, i.e., in the direction of the *synthesis* of ATP from ADP and inorganic phosphate. Under these initial conditions, ADP + inorganic phosphate are the "high energy" compounds.

Other generalizations concerning reactivity are based on the principles of thermodynamics. For example, organic molecules contain hydrogen atoms that, given an appropriate catalyst or source of energy (ultraviolet light, for example), might generate H_2. Because H_2 molecules have a low mass compared to other molecules, they move faster on average and therefore preferentially escape from planetary bodies, especially those with low mass and, consequentially, weak gravitational attraction. Although both the formation and loss of H_2 may be slow, cosmic processes have time. A collection of organic molecules thus slowly becomes more oxidized through loss of H_2 (Section 4.2.2 discusses this in detail for the Earth's early atmosphere).

This is presumably what is occurring today on the surface of Mars, whose relatively weak gravity means that the escape of light molecules is easier than on Earth. Above Mars, water is dissociated by ultraviolet light to give H· and ·OH, the hydrogen radical and the hydroxy radical. As illustrated in Fig. 7.15, two H· units can combine to give H_2. The H_2 then escapes from Mars, leaving behind HOOH, hydrogen peroxide. Under typical conditions on Earth, hydrogen peroxide might be viewed as "high energy," but on Mars escape of its reaction partner leads to its formation over time.

For the same reasons, carbon is likely to congeal to high molecular weight polymers as H_2 distills off. In extraterrestrial environments, we thus expect lower hydrocarbons to eventually transform into pure carbon – either diamond (where each carbon is singly bonded to all neighboring carbons), fullerenes and graphite (where each carbon has on average 1.5 bonds to other carbons), or carbon bonded to other elements that cannot be converted to a volatile form.

Polycyclic aromatic hydrocarbons (PAHs) can be viewed as "carbon on the way to forming graphite." These are common in extraterrestrial environments

(Section 3.8.1 and Fig. 3.4). Their central structures are fragments of graphite with bonding to hydrogen atoms at the edges of the structures. These become larger and larger, and more and more like graphite, as more hydrogen distills away.

7.6 Problems in origins and their partial solution

These examples illustrate how concepts of nucleophilicity, electrophilicity, oxidation, and reduction unify processes that might turn prebiotic mixtures into key components of life such as amino acids, nucleobases, and sugars. The Miller experiments are cited in many texts as providing laboratory support to these ideas.

These and other examples over the years have generated a view that the spontaneous emergence of life from inanimate matter in nonbiological environments is easy, in particular in environments that may have been present on the early Earth. In this view, life is a natural consequence of organic chemistry. Organic molecules, if provided with the right kind of energy in the right amounts under the right conditions, will self-organize to give chemical systems capable of Darwinian evolution.

This view, as well as a hint that it might have problems, is reflected by a fictional exchange recorded during a television program between a computer Mnemosyne and the journalist John Hockenberry:[3]

Mnemosyne: Well, chemists think that if you could recreate the conditions of the earth about four and a half billion years ago, you'd see life happen spontaneously. You'd just see DNA ... just pop out of the mix.
John Hockenberry: Can they do that in a laboratory?
Mnemosyne: Well, no. Actually, they've tried, but so far they can't seem to pull it off. In fact chemists have a little joke about that, you know: they say that life is impossible. Experience shows that it can't happen. That we're just imagining it. Ha ha ha ha...
Hockenberry: Right. Those chemists...

As Mnemosyne noted, the chemists' objection to the notion that life is a natural consequence of organic reactivity is simple, and comes from experience that many individuals have had, perhaps in an organic chemistry laboratory, but more commonly in the kitchen. When one bakes a cake too long, it chars, forming a complex mixture of components with the more volatile species lost. With each additional minute

---

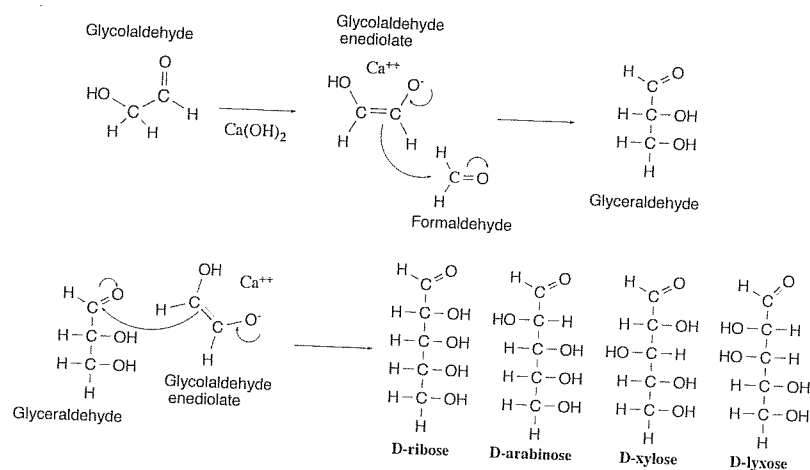[3] *The DNA Files: Astrobiology* (2001).

FIGURE 7.16 The formose reaction yields D, L-pentoses (only D-pentoses shown) by combination of the enediolate of glycolaldehyde and glyceraldehyde.

at 350 °F (175 °C), the material resembles less and less something that we might call "living." Similarly, when one applies random energy to mixtures of organic molecules, one gets *tar*, a complex, ill-defined mixture of organic molecules. Robert Shapiro has provided a thoughtful and detailed discussion of these difficulties (Shapiro, 1987; Chapter 6).

From this perspective, existing prebiotic chemistry experiments are not particularly compelling. In the complex chemical mixtures generated under prebiotic conditions, one may indeed be able to find trace amounts of amino acids and perhaps nucleobases. Some of these might indeed catalyze reactions that might have some utility. But other compounds in these types of mixtures may well inhibit this catalysis, or catalyze undesired reactions. For example, Joyce and Orgel (1999) pointed out that the clay-catalyzed condensation of nucleotides to give small chains must have only one enantiomer; if both are present, the desired reactions are inhibited.

Even crystallization, a well-documented method to obtain order through self-organization, is not a particularly powerful way of separating mixtures of organic chemicals into their constituents. Normally, an organic compound must be relatively pure before crystallization occurs. Salts crystallize better, which may explain why crystals are more common in the mineral world than the organic world. But even organic salts can have problems crystallizing from an impure mixture.

These facts generate the central paradox in prebiotic chemistry. Spontaneous self-organization of organic matter is not known to be an intrinsic property of most organic matter, at least as we observe it in the laboratory. Hockenberry asked the correct question of Mnemosyne. Obtaining the chemical order that is

(presumed to be) necessary for life from complex mixtures of organic compounds (such as those presumed to arise from planetary organic chemistry, the type that is occurring on Titan, for example) seems as unlikely to a chemist as a ball rolling uphill seems to a child. It opposes the apparent natural tendency of organic molecules to become tar.

7.6.1 Nucleophilic and electrophilic reactions can destroy as well as create

The same inherent reactivities that generate organic molecules can also convert them into complex mixtures. This is well exemplified by processes that might have generated the sugar ribose, a key component of RNA and DNA, under prebiotic conditions. A reaction known as the *formose reaction* is known to produce ribose by converting formaldehyde in the presence of calcium hydroxide into several sugars, including ribose (Butlerow, 1861; Breslow, 1959; Zubay, 1998).

The formose reaction exploits the natural electrophilicity of formaldehyde and the natural nucleophilicity of the enediolate of glycolaldehyde,[4] a carbohydrate glycoaldehyde that has been detected in interstellar clouds (Hollis, Lovas, and Jewell, 2000). This species reacts as a nucleophile with formaldehyde (acting as an electrophile) to give glyceraldehyde. Reaction of glyceraldehyde with a second equivalent of the enediolate generates a pentose sugar (ribose, arabinose, xylose, or lyxose, depending on stereochemistry). A curved arrow mechanism describes this process as well (Fig. 7.16).

[4] The enediolate of glycolaldehyde is a closely related molecule to glycolaldehyde, as illustrated in Fig. 7.16.
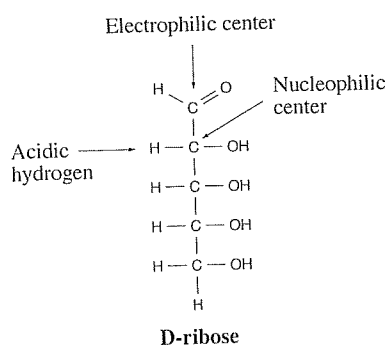
FIGURE 7.17 The open form of ribose contains reactive electrophilic and nucleophilic centers.

FIGURE 7.18 Degradation pathways for nucleosides through the action of water.

Despite this reactivity inherent to glycolaldehyde and formaldehyde, the formose reaction does not offer a compelling source of prebiotic ribose. Under typical formose conditions, ribose not only forms, but also decomposes. In the presence of calcium hydroxide, ribose is rapidly converted to a brown, complex mixture of organic species. This mixture has never been thoroughly characterized, but does not appear to contain much ribose, and is not an auspicious precursor for life.

The further reaction of ribose in the presence of calcium hydroxide arises because ribose itself has both electrophilic and nucleophilic sites, respectively at the aldehyde carbon and at the carbon directly bonded to the aldehyde (following enolization, Fig. 7.17). Molecules having both reactivities are, as expected, prone to polymerization as the nucleophilic sites and electrophilic sites react with each other, or with more formaldehyde, or with water, or with other electrophiles in the increasingly complex mixture.

These reactivities undoubtedly cause the rapid destruction of the ribose formed under formose conditions. Based on this reactivity, Larralde, Robertson, and Miller (1995) concluded that "ribose and other sugars were not components of the first genetic material."

For these reasons, some have suggested that life may have begun with an alternative organic compound as a genetic material, not RNA, but based on molecules that are less fragile (Schöning et al. 2000; Nielsen, 1999). Underlying this concept is the notion of a "genetic takeover," where delicate RNA and/or DNA molecules arose rather late in the development of life, supplanting a hardier genetic molecule that founded life (Cairns-Smith, 1982).

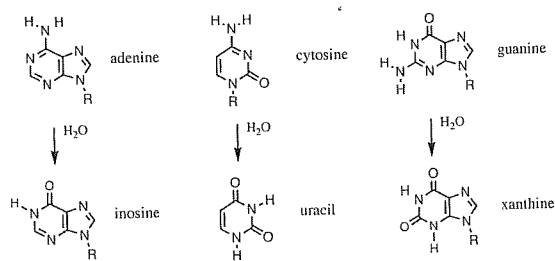In short, the reactivity of nucleophilic and electrophilic centers can convert molecules that were plausibly present on early Earth into biologically interesting products. But these products themselves often have nucleophilic and electrophilic centers, and will therefore further react to give uninteresting products. This is the central paradox associated with the origin of life, even given plausible mechanisms to create its components.

7.6.2 Water as a substance antithetical to life

Water creates its own set of problems for prebiotic synthesis. As noted above, water is an essential ingredient in the formation of amino acids from aldehydes and cyanide. Yet many biological molecules, once they are formed in water, are unstable in the water where they formed. For example, the nucleobase adenine (A in the genetic code) spontaneously hydrolyzes in water to give inosine; cytosine (C) hydrolyzes to give uracil (U); and guanine (G) hydrolyzes to give xanthine (Fig. 7.18).

This is also true for polypeptide chains of amino acids. Two amino acids do not spontaneously join in water. Rather, the opposite reaction is thermodynamically favored at any plausible concentrations: polypeptide chains spontaneously hydrolyze in water, yielding their constituent amino acids.

The same is true for RNA and DNA. Small chains spontaneously hydrolyze in water to generate individual nucleotides. Thus, even if the building blocks for proteins and nucleic acids are obtained, water and environments rich in water mean that their assembly is thermodynamically uphill.

In this regard, it is remarkable that water is viewed as essential for life. We believe that some liquid is needed for life, as a solvent within which to hold chemical reactions. Certainly, in modern terran life, water is a very useful solvent. It is also clear, however, that water is inimical to the stability of many key biological
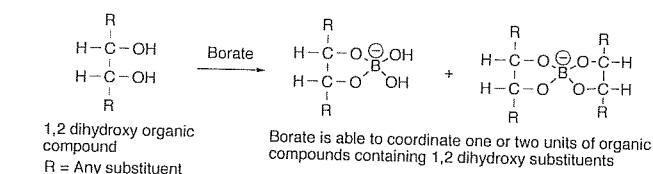
FIGURE 7.19 Borate removes the nucleophilicity of glyceraldehyde (a 1,2-dihydroxy compound) by making an anionic complex. The electrophilic center remains, allowing the addition of the enediol of glycolaldehyde to yield pentoses.
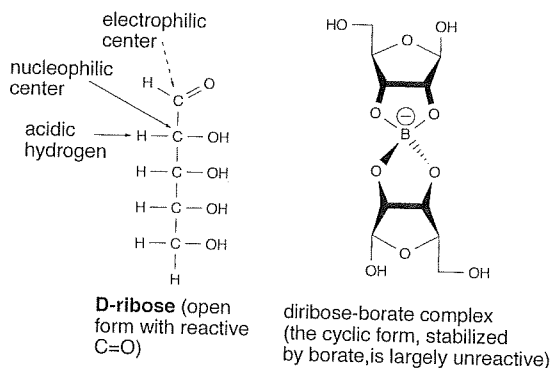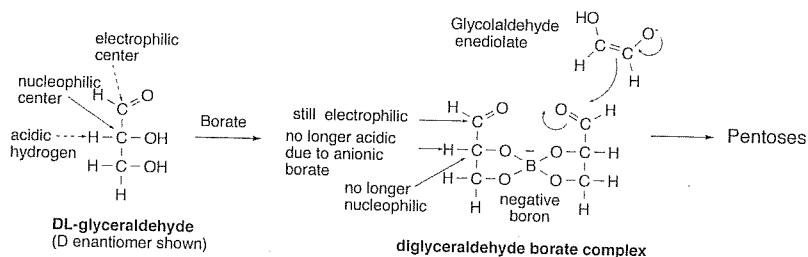

FIGURE 7.20 The cyclic form of ribose forms a stable complex with borate.

polymers. For example, every minute, perhaps ten cytosines in the genome of each human cell suffer spontaneous hydrolysis. These must be repaired to maintain information stored in DNA. It is not easy to see how such repair would occur in the first forms of life.

7.6.3 Minerals as a possible solution to the instability of ribose

To find solutions to individual prebiotic problems, we need to search the full range of chemical reactivity. For example, to make the formose reaction work as a source of ribose that is stable, a prebiotic way is needed to remove the nucleophilicity of glyceraldehyde, and to remove both the nucleophilicity and electrophilicity of ribose.

One promising approach exploits the fact that borate forms complexes with 1,2-dihydroxy units in organic molecules (Fig. 7.19). The borate complex carries a negative charge. This anionic nature of the complex should prevent glyceraldehyde from losing a

proton to create a nucleophilic enolate, but not prevent glyceraldehyde from reacting as an electrophile with the enediolate of glycolaldehyde to generate pentoses.

Further, the 1,2-dihydroxy unit of the cyclic form of ribose should form a stable complex with borate. This will stabilize the cyclic form of ribose at the expense of the aldehyde form. This should render ribose largely unreactive as either a nucleophile or an electrophile, as the cyclic form lacks a C=O carbonyl group, which is the center of this molecule's electrophilicity (Fig. 7.20). Experiments confirm this reasoning. In the presence of $Ca(OH)_2$ under formose conditions at a range of temperatures from 25 to 85 °C, a solution of glycolaldehyde and glyceraldehyde rapidly turns brown, and holds little ribose. However, when the same incubation is done in the presence of the borate-containing mineral colemanite ($Ca_2B_6O_{11} \cdot 5H_2O$), the solution does not turn brown, and one instead finds ribose, together with other five-carbon carbohydrates (Ricardo *et al.*, 2004). Borate has evidently constrained the intrinsic reactivity of glyceraldehyde to form tar, causing it to enter a productive reaction with glycolaldehyde.

Boron is not abundant in the Solar System, although it is known in carbonaceous chondrites, where it is almost certainly present as borate (Zhai and Shaw, 1994). Borate is, however, excluded from many mineral forming processes, appearing mostly in tourmalines, minerals best known as gemstones. Tourmaline weathers to generate borates, which have appreciable solubility in water. As a consequence, colemanite and other borate-containing minerals are delivered to deserts by runoff from the weathering mountains, and then crystallize from water as it evaporates to give *evaporites*. Such conditions are close to what is needed to generate ribose and related sugars.

Curiously, such conditions are also found in the most recent explorations on Mars. Although the instrument package delivered to Mars was not configured to detect either boron or ribose, the ratio of chloride and bromide salts found by the Mars Exploration Rover *Opportunity* is consistent with the formation of evaporite minerals on Mars (Section 18.8). Given the appropriate source rocks, these should contain alkaline borate minerals, analogous to those found in (for example) Death Valley. These are exactly the conditions described above that generate ribose. Indeed, noting that such conditions may not have been present on early Earth, Joe Kirschvink has suggested that terran life originated from ribose formed on Mars.

This synthesis of these carbohydrates in the presence of the mineral colemanite is therefore a plausible prebiotic pathway. Indeed, in the presence of borate, the formation of ribose appears to be a natural consequence of the intrinsic chemical reactivity of compounds available from the interstellar medium under alkaline, calcium-rich conditions.

This example of how minerals can productively control organic reactivity reminds us of the fact that prebiotic chemistry is occurring on a planet, in the context of a larger geology. Minerals must be considered as we constrain models for the origin of life. For example, Orgel and his co-workers have prepared short chains of nucleotides by template-directed polymerization, where clay acts as a catalyst (Ferris *et al.*, 1996). In addition, Szostak and his group have recently shown how clays might have helped the isolation of catalytically interesting biological macromolecules (Hanczyc, Fujikawa, and Szostak, 2003). Going further, Cairns-Smith (1982) has suggested that minerals themselves may have provided the genetic material for early forms of life.

7.6.4 Formamide as a possible solvent

The notion that ribose can be stabilized by minerals found in deserts also suggests an approach to the water problem. Given an activity of water that is sufficiently low, the synthesis of polypeptides from amino acids becomes thermodynamically favorable. But then the absence of water prompts the search for an alternative solvent. Formamide ($HCONH_2$), present in the interstellar medium, is an excellent candidate solvent, being able to dissolve RNA, DNA, and proteins, as well as their precursors. It is created by the reaction of hydrogen cyanide with water following simple rules of nucleophilicity and electrophilicity (Fig. 7.21).
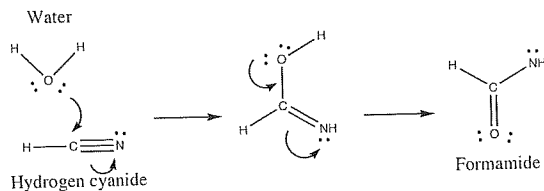

FIGURE 7.21 Formamide is obtained by the hydrolysis of hydrogen cyanide.

In formamide, the synthesis of products through dehydration is thermodynamically favored. Since formamide boils at ~220 °C, a mixture of formamide and water, if placed in the desert, would lose its water over time and end up as a pool of formamide. Within this pool, many syntheses are thermodynamically favorable: polypeptides from amino acids, nucleosides from sugars and bases, nucleotides from nucleosides and inorganic phosphate, and RNA from nucleotides.

7.7 Final thoughts and future directions

The literature contains many theoretical papers that outline possible syntheses of life's organic molecules from possible precursors based on a general knowledge of organic chemical reactivity. A second literature covers experimental work that is presumed to model prebiotic conditions. A third literature objects to the other two because they do not meet a standard of proof that allows one to conclude that such processes actually did generate life, or because such experiments do not generate biological compounds of the correct structure, or chirality, or purity.

This illustrates a defining problem in the field. We are unlikely ever to know the actual events that historically led to the formation of life on Earth. At best, we can simulate conditions in the laboratory believed to have prevailed on early Earth, and try to generate Darwinian molecular systems. Such models will always be open to doubt. There is no reason to insist that the *average* conditions on early Earth were those where life emerged; life could have emerged in a niche with a special, and perhaps unusual, local environment. The environment, or the specific conditions, may have been highly contingent on accident. This has certainly been the case for more recent innovations in the biosphere.

We can, of course, gather more information to constrain such models. The future holds many opportunities to do so. For example, in early 2006 NASA's Stardust mission gathered dust particles from a comet and returned them to Earth for analysis. Comets are believed to contain substantial reservoirs of organic

compounds, and are black in color because of this. Analysis of organics in a comet may generate an "Aha!" experience if discovered compounds clarify issues of origins.

Next, the Cassini–Huygens mission is currently studying Titan. This moon of Saturn contains a large reservoir of organic matter, evidently undergoing chemical transformations on a large scale (Chapter 20). Experiments on board Cassini may generate insight into the fate of organic molecules undergoing transformation on a planetary scale.

In addition to going elsewhere with spacecraft, information from Earth is relevant to the opinion that life is a natural consequence of organic reactivity. If structures in 3.5 Ga rocks from Australia and at least some of the carbon-containing materials in 3.8 Ga rocks from Greenland are indeed biogenic, these would indicate that life emerged on Earth "soon" (that is, within a few hundred million years) after the surface of the Earth cooled (see Chapter 12). Rapid emergence of life is consistent with an easy emergence of life, which in turn suggests that one might see life happen spontaneously if one could only reproduce the conditions on early Earth. If, however, these structures and materials are not biogenic, then this argument is weakened.

Another outcome that may emerge from exploratory missions is a better understanding of the nature of early oceans on Earth. It is not yet clear whether the concentrations of salt in Earth's early oceans was high or low (Knauth, 1998). The activity of water is greatly different at the extremes of salinity (Chapter 15), and this has an impact on the constraints imposed on pre-biotic chemistry by the nature of water.

Further progress is also needed in understanding the potential on the early Earth for mineral catalysis in the transformation of organic molecules. We are far from being able to construct an inventory of the minerals present then, and know very little about what kinds of reactions minerals catalyze. Current models for the accretion of continents speak of an evolving mineralogy, and it may be that life emerged only when the minerals arose that could catalyze key prebiotic reactions.

REFERENCES

Amari, S., Anders, E., Virag, A., and Ziner, E. (1990). Interstellar graphite in meteorites. *Nature*, **345**, 238–240.

Bernstein, M. P., Dworkin, J., Sandford, S. A., Cooper, G. W., and Allamandola, L. J. (2002). Racemic amino acids from the ultraviolet photolysis of interstellar ice analogues. *Nature*, **416**, 401–403.

Berry, M. J., Tujebajeva, R. M., Copeland, P. R., *et al.* (2001). Selenocysteine incorporation directed from the 3′UTR: characterization of eukaryotic EFsec and mechanistic implications. *Biofactors*, **14**, 17.

Breslow, R. (1959). On the mechanism of the formose reaction. *Tetrahedron Lett.*, **21**, 22–26.

Butlerow, A. (1861). Bildung einer zuckerartigen Substanz durch Synthese. *Annalen Chemie*, **120**, 295–298.

Cairns-Smith, Alexander (1982). *Genetic Takeover and the Mineral Origins of Life.* Cambridge: Cambridge University Press.

Cooper, G., Novelle, K., Belisle, W., Sarinana, J., Brabham, K., and Garrel, L. (2001). Carbonaceous meteorites as a source of sugar-related organic compounds for the early earth. *Nature*, **414**, 879–884.

Cronin, J. R. and Moore, C. B. (1971). Amino acid analyses of the Murchison, Murray, and Allende carbonaceous chondrites. *Science*, **172**, 1329.

Cronin, J. R. and Pizzarello S. (1986). Amino-acids of the murchison meteorite. III. Seven carbon acyclic primary alpha-amino alkanoic acids. *Geochim. Cosmochim. Acta*, **50** (11), 2419–27.

Cronin, J. R. and Pizzarello, S. (1988). Organic matter in carbonaceous chondrites, planetary satellites, asteroids and comets. In *Meteorites and the Early Solar System*, eds. J. Kerridge and M. S. Matthews, pp. 819–857. Tucson, AZ: The University of Arizona Press.

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

Fuchs, L. H., Olsen, E., and Jensen, K. J. (1973). Mineralogy, crystal chemistry and composition of the Murchison (C2) meteorite. *Smithsonian Contrib. Earth Sci.*, **10**, 1–39.

Grady, M. M., Wright, I. P., Swart, P. K., and Pillinger, C. T. (1988). The carbon and oxygen isotopic composition of meteorite carbonates. *Geochim. Cosmochim. Acta*, **52**, 2855–2866.

Hanczyc, M. M., Fujikawa, S. M., and Szostak, J. W. (2003). Experimental models of primitive cellular compartments: encapsulation, growth, and division. *Science*, **302**, 618–622.

Hao, B., Gong, W. M., Ferguson, T. K., James, C. M., Krzycki, J. A., and Chan, M. K. (2002). A new UAG-encoded residue in the structure of a methanogen methyltransferase. *Science*, **296**, 1462.

Hollis, J. M., Lovas, F. J., and Jewell, P. R. (2000). Interstellar glycolaldehyde: the first sugar. *Astrophys. J.*, **540**, L107–L110.

Jarosevich E. (1971). Chemical analysis of the Murchison meteorite. *Meteoritics*, **6**, 49–52.

Joyce, G. F. and Orgel, L. E. (1999). Prospects for understanding the origin of the RNA world. In *The RNA World*, second

edn., eds. R. Gestland, J. Atkins, and T. Cech. Cold Spring Harbor, NY: Cold Spring Harbor Press.

Kasting, J. F. (1993). Earth's early atmosphere. *Science*, **259**, 920–925.

Knauth, L. P. (1998). Salinity history of the Earth's early ocean. *Nature*, **395**, 554–555.

Kvenvold, K., Lawless, J., Pering, K., *et al.* (1970). Evidence for extraterrestrial amino-acids and hydrocarbons in Murchison meteorite. *Nature*, **228**, 923.

Larralde, R., Robertson, M. P., and Miller, S. L. (1995). Rates of decomposition of ribose and other sugars. Implications for chemical evolution. *Proc. Natl. Acad. Sci. USA*, **92**, 8158–8160.

Lewis, R. S., Tang, M., Wacker, J. F., Anders, E., and Steel, E. (1987). Interstellar diamonds in meteorites. *Nature*, **326**, 160–162.

Miller, L. Stanley (1955). Production of some organic compounds under possible primitive earth conditions. *J. Am. Chem. Soc.*, **77**(9), 2351.

Moore, B. Carleton. (1971). Phosphorus. In *Handbook of Elemental Abundances in Meteorites*, ed. Mason, Brian, pp. 131–135. New York, NY: Gordon and Breach, Science Publishers, Inc.

Mueller, D., Pitsch, S., Kittaka, A., Wagner, E., Wintner, C. E., and Eschenmoser, A. (1990). Chemistry of a-aminonitriles. Aldomerization of glycolaldehyde phosphate to rac-hexose 2, 4, 6-triphosphates and (in presence of formaldehyde) rac-pentose 2, 4-diphosphates: rac-allose 2, 4, 6-triphosphate and rac-ribose 2, 4-diphosphate are the main reaction products. *Helv. Chim. Acta*, **73**, 1410–68.

Nielsen, P. E. (1999). Peptide nucleic acid. A molecule with two identities. *Acc. Chem. Res.*, **32**, 624 –630.

Oró, J. (1960). Synthesis of adenine from ammonium cyanide. *Biochem. Biophys. Res. Commun.*, **2**, 407–412.

Pietrogrande, M. C., Coll, P., Sternberg, R., Szopa, C., Navarro-Gonzalez, R. Vidal-Madjar, C., and Dondi, F. (2001). Analysis of complex mixtures recovered from space missions. Statistical approach to the study of Titan atmosphere analogues (tholins). *Journal of Chromatography A*, **939**, 69–77.

Pizzarello, S. and Cronin J. R. (2000). Non-racemic amino acids in the Murray and Murchison meteorites. *Geochim. Cosmochim. Acta*, **64** (2), 329–338.

Pizzarello, S., Huang, Y. S., Becker, L., Poreda, R. J., Nieman, R. A., Cooper, G., and Williams, M. (2001). The organic content of the Tagish Lake meteorite. *Science*, **293**, 2236.

Ricardo, A., Carrigan, M. A., Olcott, A. N., and Benner, S. A. (2004). Borate minerals stabilize ribose. *Science*, **303**, 196.

Rother, M., Wilting, R., Commans, S., and Böck, A. (2000). Identification and characterisation of the Selenocysteine-specific Translation Factor SelB from the Archaeon Methanococcus jannaschii. *J. Mol. Biol.*, **299**, 351.

Sagan, C. and Khare, N. B. (1979). Tholins: organic chemistry of interstellar grains and gas. *Nature*, **277**, 102–107.

Sagan, C., Khare, N. B., Bandurski, L. E., and Bartholomew, N. (1978). Ultraviolet-photoproduced organic solids synthesized under simulated jovian conditions: molecular analysis. *Science*, **199**, 1199–1201.

Sanchez, R. A., Ferris, J. P., and Orgel, L. E. (1967). Studies in prebiotic synthesis. II. Synthesis of purine precursors and amino acids from aqueous hydrogen cyanide. *J. Mol. Biol.*, **30**, 223–253.

Schöning, K. U., Scholz, P., Guntha, S., Wu, X., Krishnamurthy, R., and Eschenmoser, A. (2000). Chemical etiology of nucleic acid structure: the α-Threofuranosyl-(3'→2') Oligonucleotide System. *Science*, **290**, 1347–1351.

Shapiro, R. (1987). *Origins: a skeptic's guide to the creation of life on earth*. New York: Bantam Books.

Srinivasan, G., James, C.M., Krzycki, J.A. (2002). Pyrrolysine encoded by UAG in Archaea: charging of a UAG-decoding specialized tRNA. *Science*, **296**, 1459.

Tang, M., Anders, E., Hoppe, P., and Zinner, E. (1989). Meteoritic silicon carbide and its stellar sources: implications for galactical chemical evolution. *Nature*, **339**, 351–354.

Zhai, M. and Shaw, D. M. (1994). Boron cosmochemistry. Part I: Boron in meteorites. *Meteoritics*, **29**, 607–615.

Zubay, G. (1998). Studies on the lead-catalyzed synthesis of aldopentoses. *Orig. Life Evol. Biosphere*, **28**, 13–26.