Chapter 1
Nucleobases on the Primitive Earth: Their Sources and Stabilities

H. James Cleaves II

Abstract Nucleobases are nitrogen heterocycles that are key structural components of biological nucleic acids. Some theories for the origins of life suggest a role for environmentally supplied organic compounds, including nucleobases, as part of a primordial RNA or pre-RNA world. Over the last 65 years, many potentially prebiotic synthetic mechanisms have been experimentally demonstrated for nucleobases, and their presence in extraterrestrial materials has been extensively verified, suggesting some of these are valid explanations for how the environment produces them. However, the abundance of nucleobases in primitive environments would depend on the balance of the rates of their environmental synthesis and decomposition. The literature regarding chemical aspects of these questions is briefly reviewed here.

1.1 Introduction

Nucleobases are components of modern nucleic acids whose role in nucleic acid function is important because they help store the digital information of the genetic code. This role is made possible by the high proportion of their molecular composition that can engage in stacking and hydrogen-bonding interactions (Fig. 1.1).

The chemical properties of the nucleobases are essential for the biological functions of nucleic acids. There are likely a limited number of molecules of any size which have the optimal proportions of such properties and which are also stable under a wide range of conditions and to a wide range of environmental insults, for

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example, radiational excitation (Bertinchamps et al. 2011; Boldissar and de Vries 2018). This chapter will focus on the two topics of the abiotic sources and stabilities of the nucleobases themselves, rather than higher-order derivatives (e.g., nucleosides and nucleotides and their analogues) or alternative "xeno nucleic acids" (XNAs) (Pinheiro et al. 2013; Joyce et al. 1987), consideration of which might suggest other ways to think about some of the issues described here. This chapter is not intended to be an exhaustive review of the nitrogen heterocycle prebiotic synthesis literature; readers interested in this are encouraged to read further elsewhere (Ruiz-Mirazo et al. 2014; Ruiz-Bermejo et al. 2013; Cleaves 2012).

1.1.1 Nomenclature, Structure, and Physical Chemistry

The nucleobases of DNA comprise the purines adenine and guanine and the pyrimidines thymine and cytosine, while those of RNA include adenine, guanine, and cytosine, but the pyrimidine uracil substitutes for thymine (Fig. 1.1). The nucleobases had already been isolated, identified, and synthesized in the laboratory during the nineteenth century and first decade of the twentieth century, well before their role in nucleic acids was understood (Mason 1991). The term *nucleobase* is generally reserved for those compounds found in natural nucleic acids, variants on those structures with similar structures and properties or which allow them to play similar roles in biological systems are typically termed *nucleobase analogues*.

The nucleobases are substituted aromatic N-heterocycles. The pyrimidines are six-membered aromatic rings containing two nitrogen atoms at the 1 and 3 positions of the ring. The purines are fused pyrimidines, containing an additional imidazole ring connected across the C5 and C6 atoms of the pyrimidine ring and containing N atoms in the 1, 3, 7, and 9 positions (see Fig. 1.1). As they contain various exchangeable ring nitrogen-associated protons, these compounds are organic bases. Due to the electronic content of their ring systems, the nucleobases are

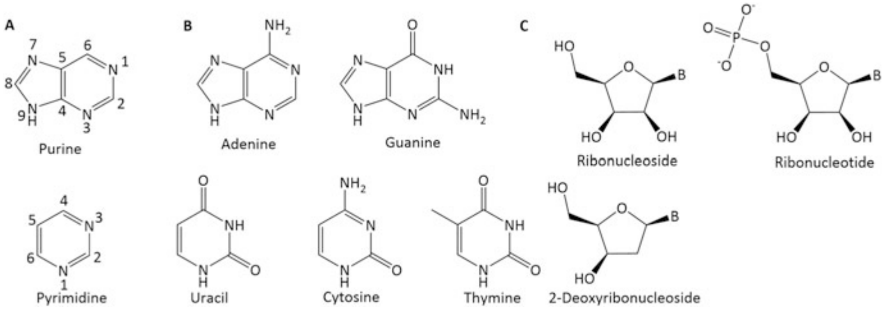

Fig. 1.1 The structures of the nucleobases and nucleic acids that they help constitute. A. The purine and pyrimidine ring systems and their atom numbering. B. The biological purines and pyrimidines. C. The structures of nucleosides and nucleotides containing the nucleobases

aromatic, and this leads to their ring structures being essentially planar. Their ring and exocyclic substitution patterns contain a great deal of structural information that enables them to present highly specific molecular recognition surfaces. The specific hydrogen bonding patterns nucleobases enable are also dependent on the stability of their tautomeric forms.

The nucleobases have attracted great attention in the study of biology since the revelation of the structure of DNA and the elucidation of the genetic code (Woese 1967; Orgel 1968; Crick 1968), which showed that they can be considered the "business end" of the molecules which make up the "alphabet" which specifies biological heredity. Via the spatially oriented presentation of their specific hydrogen bond donor and acceptor functionalities, they serve as a sort of digital information encoding system similar in some ways to that used to store and process information in modern computers. Nevertheless, though information storage and handling can be abstracted greatly, in biology the nucleobases are parts of metabolic chemical systems that operate in aqueous solution, and thus the nuances of their chemical properties, which are a result of their chemical structures, play important and subtle roles in their biological function.

Recent studies have shown that other molecules are able to play the molecular roles that nucleobases do in information storage and transmission (see, e.g., Switzer 1989; Malyshev et al. 2014). Many molecules, given water as a solvent, might also be able to engage in the interactions that enable nucleic acid function. Alternatively, few molecules in the idealized space of molecules may be aromatic, *and* predisposed to self-assembly because of their H-bond donor/acceptor patterns, or be able to do so in the dynamic context of nucleic acid structure (Cleaves and Bada 2012).

The nucleobases have relatively hydrophobic surfaces, though their molar solubility in water ranges over several orders of magnitude at room temperature and neutral pH, depending on their ring substitution. The degree to which the arrangement of H-bond donor and acceptor groups allows for self-pairing is to some degree responsible for their differences in solubility. Nucleobases which are capable of forming stable self-complementary patterns (such as guanine) tend to have very low solubility in water, though hydrophobic properties imparted by the ring systems also contribute, with the purines being generally less soluble than the pyrimidines.

The DNA guanine-cytosine and adenine-thymine pairs, in the context of nucleic acids, engage in H–bond-mediated base pairing, which is due to both the specific arrangement of H-bond donor and acceptor groups and the stacking arrangements of their π-bond systems. The guanine-cytosine and adenine-thymine base pairs engage in bonding involving three and two H-bonds, respectively. As hydrogen bonds require energy to disrupt, these serve as organizing elements for the formation of supramolecular structure. These energetic differences in affinity are exploited by biology at multiple levels: for example, thermophiles appear to preferentially use GC base pairs in their tRNA molecules (Wang et al. 2006), and there is some correlation between genomic DNA and structural RNA GC content and optimal growth temperature in prokaryotes (Musto et al. 2004).

1.1.2 The Relevance of Nucleobase to the Origins of Life

Concurrent with the elucidation of the genetic code and the crystallization of the concept of the central dogma of biology, a paradox was laid bare: if nucleic acids are required to make proteins and proteins to make nucleic acids, which logically would have come first? A cohesive conceptual resolution of this paradox was formulated almost simultaneously by Woese, Crick, and Orgel (Woese 1967; Crick 1968; Orgel 1968), which became known as the "RNA world hypothesis" (Gilbert 1986; Benner and Ellington 1991). Roughly speaking, the fundament of the hypothesis is that since it is possible that RNA could serve as both information storage molecule and catalyst, the modern system of information flow in biology may have grown outward from RNA in two directions: in one to make protein and in another to make DNA. Numerous models and experimental systems have now examined the chemical plausibility of this notion and provide various levels of support for it. Nevertheless, it quickly became clear [and the notion persists to this day (see, e.g., Pearce et al. 2017)] that the central issue in understanding the origins of life is the abiotic synthesis of RNA and thus the abiotic assembly of its components, including nucleobases, as precursors.

It should be made clear that there is no agreed-upon model for the origins of life, and there are competing models to the RNA world. Other models alternatively posit an origin of life based on simpler genetic polymers (Joyce et al. 1987), other types of inheritance (Segré et al. 2000), or chemical systems with only metabolic properties (Wächtershäuser 1988; Morowitz 1999). In addition, various authors have explored methods of building nucleosides directly from simpler components (Sanchez and Orgel 1970; Powner and Sutherland 2008; Powner et al. 2010); thus, the prebiotic synthesis or availability of nucleobases may not be directly relevant to the origin of the RNA world or the origins of life.

Finally, the biosynthesis of the nucleobases in most cases does not mirror the mechanisms of synthesis elucidated in studies of prebiotic chemistry (Zubay 1993). That biological nucleic acids include the nucleobases can be viewed as either predestined by abiotic chemistry or the serendipitous result of biological processes that allowed their discovery during evolution.

1.2 Prebiotic Synthesis of Nucleobases

1.2.1 General Background

Though there are examples of early work that sought to experimentally address the abiological synthesis of biochemicals from the ~100 years which preceded it, it is generally agreed that Miller's 1953 publication on the laboratory generation of amino acids from simulated reducing primitive Earth (Miller 1953) initiated the modern period of experimental origins of life research. This publication appeared within a month of Watson and Crick's proposed structure for the DNA double helix

(Watson and Crick 1953), and it was not long until the notion of the spontaneous "prebiotic" formation of organic compounds was applied to the nucleic acids. At the time of this writing, a simple Google Scholar search for the topic "prebiotic adenine synthesis" returned hundreds of citations. This extensive literature will not be exhaustively reviewed here, rather some of the key advances and open questions will be examined.

Miller's abiotic amino acid synthesis demonstration started an effort to discover methods of generating other components of modern biochemistry, preferably in the fewest steps and in the highest yield from the simplest reactants. This general schema intended to mimic primitive geochemical synthesis environments, where chemistry proceeded undirected. This type of chemistry is generally termed *prebiotic* or *abiotic* chemistry, with the former term stressing the potential role of a process to the origin of life and the latter only that a process occurs in the absence of biology. Both processes include all manner of unknown reaction and the latter all manner of explorable, but poorly understood, reaction.

What exactly constitutes a "plausibly prebiotic" reaction is the subject of some debate among chemists. Roughly speaking, such conditions could include any that produce organic compounds in the absence of biological agents. More restrictively, these are often limited to those that operate under conditions that allow for the existence of liquid water (which can include water above its atmospheric pressure boiling point) and should include only reactants that are themselves justifiable by some similarly environmentally plausible synthetic process. The synthesis should also provide some justification for the concentrations of the reactants and the various parameters that allow reactions to proceed (e.g., the pH, the temperature, the containment of the reactants for the required reaction period, the presence of required catalysts, etc.).

There is little consensus what the conditions on early Earth were at the time life began. It is documented that Earth has swung through several ice ages over the last 2.6 Ga. Earth's surface temperature is a complex function of the output of the Sun coupled with the atmospheric chemistry and dynamics of the Earth system. The Earth almost certainly accreted hot, and there was a period in Earth's earliest history (this could have been as little as 100 million years or as much as almost 1 billion years) during which its surface was too hot to host liquid water. During this period, most organic chemicals would have been rapidly degraded, potentially requiring organic synthesis or delivery to have occurred after that time. Nevertheless, at some point between ~4.4 Ga and 3.5 Ga, Earth cooled enough to allow the condensation of liquid water. There is also uncertainty in the pH of the early oceans once surface conditions allowed for liquid water (Halevy and Bachan 2017; Krissansen-Totton et al. 2018).

There is a great deal of uncertainty regarding the composition of Earth's primitive atmosphere. As will be discussed below in more detail, many prebiotic syntheses depend on reducing conditions for the gas phase (atmospheric) synthesis of precursors such as HCN (Schlesinger and Miller 1983b), and there is little consensus that conditions on the primitive Earth would have supported such reactions for extended periods of time (Rubey 1951; Tian et al. 2005). Extraterrestrially synthesized organic matter (Cronin 1989) delivered to the Earth's surface by infall during the tail end of planetary accretion (Chyba and Sagan 1992) offers one possible solution to this potential problem.

While early research regarding the synthesis of organic compounds on the primitive Earth focused on local planetary environmental conditions, the search for life beyond Earth has extended the range of conditions of interest to chemists. The solar system includes many heterogeneous reaction environments [e.g., ranging from bodies with highly reducing surface environments (e.g., Saturn's moon Titan) to those that have oxidizing surface conditions (e.g., Mars)]. It should be further borne in mind that bodies of various sizes such as asteroids, moons, and planets are themselves heterogeneous across scales and may harbor environmentally variable microenvironments, and both the larger bodies and microenvironments may also change over time.

1.2.2 Retrosynthetic Analysis

Organic chemists commonly employ the approach of "retrosynthetic analysis" when designing molecular syntheses (Corey 1988), which simply attempts to work backward to produce a road map of potential precursors and transformations from which a target molecule could be derived. There is often more than one plausible route, and such routes may be highly branched depending on the complexity of the target and the starting materials.

In prebiotic chemistry, it is generally assumed that the starting materials should be simple environmentally abundant compounds, consisting of a single heavy atom (in addition to hydrogen), for example, water, methane, NH_3, H_2S, etc. Cosmically abundant species containing more than one heavy atom such as N_2 (which makes up some 78% of Earth's present atmosphere and ~98% of Titan's) and CO_2 (which makes up roughly 95% of both Mars' and Venus' atmospheres) are also considered reasonable starting points due to their cosmic abundance.

There is a large body of research exploring how energetic input from various sources including ionizing radiation (Miyakawa et al. 2002b), heat (Yoshino et al. 1971), and electric discharges (Schlesinger and Miller 1983a) can result in the recombination of these simple starting molecules into more complex ones, e.g., those containing more heavy atoms, for example, HCN and HCHO. These are often removed from the site of energetic recombination to lower energy environments where they can undergo still further reactions. For example, Miller's simple experiment showed that NH_3, H_2, H_2O, and CH_4 could be recombined under the action of an electric discharge to give rise to HCN and HCHO (Miller 1955), which diffuse away from the discharge region and irreversibly dissolve into the aqueous phase of the reaction vessel.

1.2.3 Purine Nucleobase Synthesis from One-Carbon Compounds

1.2.3.1 Synthesis from HCN and Formamide

Not long after Miller's experiment, Oró and Kimball (Oró 1961) showed that adenine [which is formally a pentamer of HCN ($C_5H_5N_5$)] could be derived from alkaline aqueous HCN solutions at moderately elevated temperature and proposed a general mechanism, which was elaborated and extended by Orgel and co-workers (Ferris and Orgel 1965; Sanchez et al. 1967) (Fig. 1.2).

The proposed mechanism proceeds through HCN dimerization, trimerization, and tetramerization, giving rise to substituted imidazoles that can react with various simple carbon compounds to yield a suite of purines (including A and G, as well as xanthine, hypoxanthine, 2,6-diaminopurine, and isoguanine; see Fig. 1.2).

Subsequent studies revealed that the pathway to purine formation from HCN likely involves more than one mechanism and that the complex heterogeneous polymer that concentrated HCN produces in solution is itself a major source of adenine and guanine upon hydrolysis (Borquez et al. 2005). This suggests that there are thermally induced rearrangements of this material that produce purines by mechanisms unrelated to those explored by Orgel and Oró. Schwartz showed that adenine-8-carboxamide is also a product of polymerizing HCN, which also gives rise to A upon hydrolysis (Voet and Schwartz 1983) and that this may be simply one example of an 8-substituted precursor that can give rise to that ring system.

HCN is a ubiquitous cosmochemical compound and present in Titan's atmosphere (Gautier et al. 2011), comets (Mumma and Charnley 2011), and

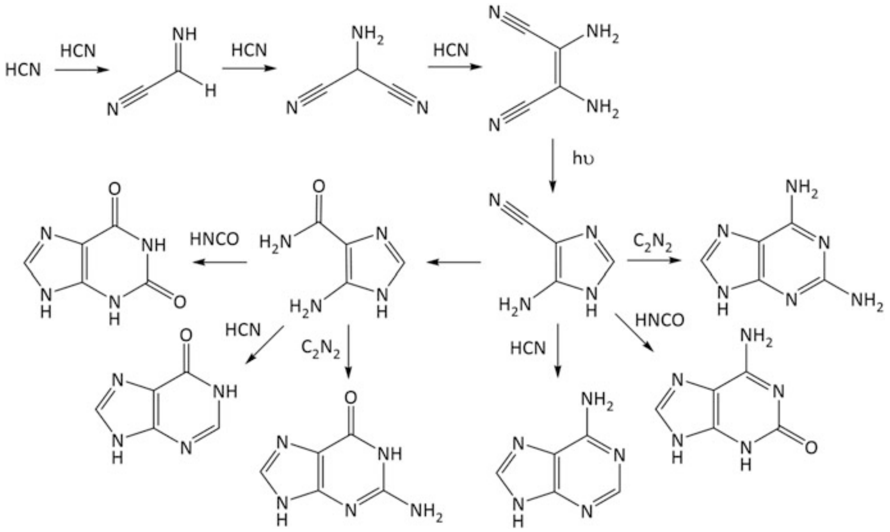

Fig. 1.2 Proposed mechanisms for the synthesis of purines from HCN

carbonaceous meteorites (Pizzarello 2012) and now observed in extrasolar and extragalactic settings as well (http://www.astro.uni-koeln.de/cdms/molecules/). It is reactive and hydrolyzes to give formamide and ultimately the salt ammonium formate (Miyakawa et al. 2002c):

$$HCN + H_2O \rightarrow HCONH_2$$
$$HCONH_2 + H_2O \rightarrow NH_4HCO_2$$

HCN is a gas at standard temperature and pressure. It has a pK_a of ~9.2 at 25 °C and thus readily dissolves in slightly alkaline water but does not concentrate well by evaporation from aqueous solutions below its pK_a. In contrast, formamide is completely miscible in water and has a boiling point above that of water, 210 °C, and thus in principle can be concentrated to purity as it is being produced from HCN hydrolysis by simple evaporation. The environmental and physical chemistry of HCN/formamide/water systems is likely complex enough to warrant more investigation.

Formamide, neat or in concentrated aqueous solution, can also serve as a precursor to various nucleobases, though higher concentrations (close to purity) and temperatures (typically above 110 °C) are required than for HCN condensation. It has been known for some time that $HCONH_2$ can be a starting material for both purine and pyrimidine synthesis (Bredereck et al. 1961), but this has more recently come into greater focus in a prebiotic context (Saladino et al. 2001; Barks et al. 2010; Adam et al. 2018). Formamide and hydrogen cyanide are linked by water-exchange reactions, and their products are similar.

1.2.3.2 One-Pot Purine Synthesis in Electric Discharges and Eutectics

While Oró and Orgel's purine synthesis mechanisms proceed from HCN, for some prebiotic chemists, this represents a purification of reagents too early in the synthetic process, and more heterogeneous syntheses deserve more emphasis. Additionally, few environments likely produce HCN exclusively, and the effects of congeners merit exploration.

The oligomerization of HCN in water is pH, temperature, and concentration dependent. It has been shown that HCN hydrolysis dominates below 0.1 M HCN (depending on pH and temperature), with oligomerization possible above that concentration (Sanchez et al. 1966a). The need for high concentrations of reactants led these authors to suggest that purine synthesis via HCN oligomerization could have more preferably taken place in low-temperature environments where eutectic concentration was possible.

Eutectic freezing of HCN solutions and the products of Miller-Urey type electric discharge reactions can give rise to various purines and pyrimidines (Miyakawa 2002a, b; Levy et al. 2000; Sanchez et al. 1966a; Schwartz et al. 1982). In these cases, it seems plausible that one or more of the previously suggested mechanisms may be at play, and the concentration effects that occur in eutectic brines enable them. Yields are typically not extremely high in such reactions, but they point to the ability of the direct production of these ring systems directly from simple precursors, and in heterogeneous combination, in a single environment.

1.2.4 Pyrimidine Synthesis

Pyrimidines have several possible retrosynthetic disconnects between carbon and nitrogen, though almost all reported prebiotic syntheses begin with a contiguous C3 compound. There are a few examples that start from only 1C compounds, but these depend on C–C bond formation reactions taking place in other contexts.

1.2.4.1 Pyrimidine Synthesis from C3 Precursors

Fox and Harada (1961) performed one of the first deliberate attempts at the prebiotic synthesis of uracil by heating malic acid and urea in polyphosphoric acid at elevated temperature. Oró (1963) later showed that uracil could be derived from the C3 compounds acrylonitrile, β-aminopropionitrile, and β-aminopropionamide reacted with urea in aqueous ammonia at 130 °C (Fig. 1.3). These C3 compounds and urea were all by then demonstrated products of Miller-Urey type syntheses. These reactions involve an oxidation across the nascent C5–C6 pyrimidine bond, which was achieved thermally in that case, though this has also been accomplished photochemically (Chittenden and Schwartz 1976).

Not long after, Orgel and colleagues showed how the biological pyrimidines could be produced from other simple compounds generated in electric discharges, namely, cyanoacetylene (CAA) and cyanate (Sanchez et al. 1966b; Ferris et al. 1968) (Fig. 1.3). This synthesis was later extended to give various pyrimidines including the biological ones (e.g., 2, 4-substituted pyrimidines including uracil, cytosine, isocytosine, 2,4-diaminopyrimidine, and various thio derivatives, depending on the reactants and conditions) when the hydrolysis product of CAA, cyanoacetaldehyde, was reacted with urea derivatives (urea, guanidine, thiourea, etc.) (Robertson and Miller 1995b; Robertson et al. 1996; Nelson et al. 2001).

Various other syntheses have added thymine to the roster of prebiotically accessible pyrimidines (Stephen-Sherwood et al. 1971; Choughuley et al. 1977), making use of the propensity for aldehydes to add to the C5 position of pyrimidines to give 5-hydroxymethyl substituted pyrimidines (Robertson and Miller 1995c), followed by reduction. Biological RNA molecules contain several modifications that allow them to carry out their cytosolic roles (see, e.g., http://mods.rna.albany.edu/), and there are now a number of plausibly prebiotic reactions which allow the introduction of some of these modifications (Robertson and Miller 1995a; Schneider et al. 2018).

1.2.4.2 Pyrimidine Synthesis from C1 Precursors

Voet and Schwartz (1982) showed that uracil could also be derived directly from HCN polymer. Thus, HCN offers a direct route to the nucleobase purines and at least

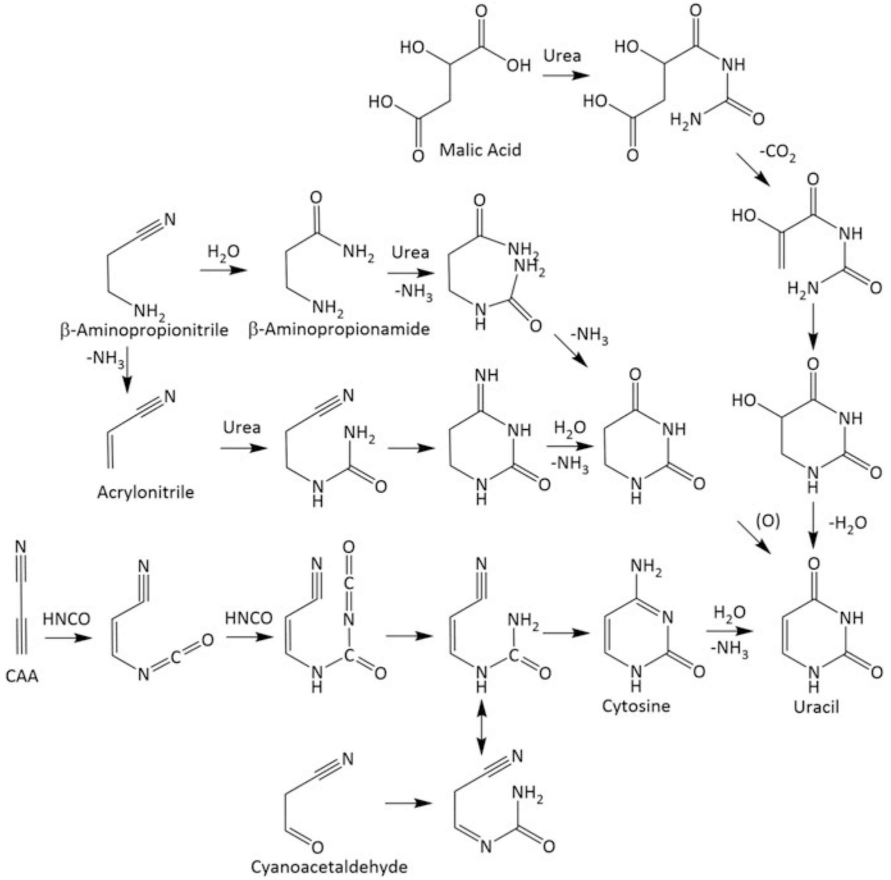

Fig. 1.3 Some proposed mechanisms for the synthesis of pyrimidine nucleobases discussed in the text

one of the pyrimidines. In addition to uracil, it had also been found that other non-biological pyrimidines, including 5-amino and 5-oxo-subsituted pyrimidines (Miyakawa et al. 2002a) as well as the pyrimidine biosynthetic precursor orotic acid, are derivable from HCN (Ferris et al. 1978). Searches for cytosine in such reactions have to date been unsuccessful (Miyakawa et al. 2002a).

1.3 Extraterrestrial Nucleobases

The solar system harbors many environments where organic synthesis evidently occurs. Perhaps the most tangible and compelling examples come from the carbonaceous chondrite meteorites, which are vestiges of the chemistry of the early solar system (Pizzarello and Shock 2010). These meteorites contain a variable though significant fraction (up to ~2% in weight) of organic material (Alexander et al. 2007) which includes a high-molecular weight intractable component (typically constituting 70+ % of the organic material) as well as a variable though often complex (Schmitt-Kopplin et al. 2010) suite of small molecules.

That much of this material is extraterrestrial in origin is now beyond dispute. It was not long after one of the most immediately collected pristine samples, the Murchison meteorite, fell to Earth in 1969 that it was shown fairly conclusively that such materials contain organic compounds of biological relevance, including amino acids (Kvenvolden et al. 1970, 1971). Soon after, it was noted that the types and abundances of amino acids closely corresponded to those produced in some Miller-Urey electric discharge experiments, suggesting common synthesis mechanisms between the two samples (Wolman et al. 1972), e.g., Strecker-like aqueous-phase synthesis from simple precursors including HCN, aldehydes, and ketones, and amines including ammonia. It has also been suggested that Fischer-Tropsch-type synthesis from simple gases such as CO and NH_3 over metal catalysts (as might have been present in the asteroidal parent bodies of carbonaceous chondrites) could be an alternative source of these compounds (Hayatsu et al. 1972), among other proposed mechanisms.

A search for nitrogen heterocycles in carbonaceous chondrites began soon after, with various reports suggesting the presence of nucleobases and other N-heterocycles (Hayatsu et al. 1975; Stoks and Schwartz 1981, 1982). The isotopic composition of nucleobases isolated from carbonaceous chondrites has now been measured, and the data support their being of extraterrestrial origin (Martins et al. 2009). Further, surveys across carbonaceous chondrite petrologic types not only show a wide distribution of these compounds but trends in speciation and abundance which appear to correlate with the degree of aqueous alteration of the meteorites (Callahan et al. 2011). This study also showed the presence of a few purine isomers not typically found in biology including 2,6-diaminopurine and purine itself in low abundance. Pyrimidines were not detected in the same abundance, though this could be attributable to spatial heterogeneity of the samples.

The types and distribution of purines detected were suggested to be concordant with those detected from HCN synthesis, and notably the abundance of purine, which is typically the major purine product of formamide-based syntheses (Bredereck et al. 1961), was very low. However, the 8-hydroxymethyl purine derivatives were not detected, which does not agree well with reports of the dominance of these as products when HCN is polymerized in the presence of HCHO (Schwartz and Bakker 1989). HCHO has now been suggested to be a major organic precursor to carbonaceous chondrite organics (Cody et al. 2011), so there are various data points that do not appear to support a single or simple origin for these compounds in carbonaceous chondrites. There may be still other as-yet-unexplored synthetic pathways that may help explain these discrepancies. Additionally, as there is some correlation of the degree of post-accretional aqueous alteration with the distribution of purines, it is possible that post-synthetic processes skew initial product distributions formed by one of the commonly suggested processes.

1.4 The Stability of the Nucleobases

To have been useful for the origins of life, nucleobases need not only have had a route available for their synthesis, but they must have been stable enough to accumulate for whatever subsequent process enabled the onset of replication. DNA, which is typically more stable than RNA, degrades rapidly under geological conditions, and the kinetics of its decomposition follow predictable Arrhenius kinetics (Allentoft et al. 2012). Even when shielded from biologically mediated degradation under relatively favorable preservational conditions (dry, −5 °C), a maximal survival time for amplifiable and sequenceable DNA fragments using present technologies of 0.4–1.4 Ma has been estimated (Willerslev et al. 2004). However, amplifiable DNA fragments pervade Earth's critical zone even in the most hostile environments (Schulze-Makuch et al. 2018), largely due to the rapidity with which life continuously synthesizes them: they are dynamically stable in the context of living systems. Once the regenerative process of biological reproduction ceases, nucleic acids become yet one more type of compound in the environment subject to degradation.

Nucleic acids tend to degrade by a few principle pathways, including depurination and depyrimidination and backbone strand-scission. The measured concentration of nucleobases liberated from degraded nucleic acids drops off quickly in sediment cores over decadal time scales (Van der Velden and Schwartz 1974). As nitrogen assimilation is an extremely bioenergetically costly process, after nucleobases are liberated from nucleic acids in the environment, they tend to be consumed or degraded by microorganisms. Thus, the rapid production and recycling of nucleobases in the biosphere gives little insight into their abiotic decomposition and preservation in the terrestrial environment.

1.4.1 Thermal Decomposition

Controlled laboratory studies offer a simple means to estimate the survival of nucleobases in abiological environments. Non-biological degradation mechanisms may be slower but are similarly unforgiving for nucleobase survival. Abiological non-catalyzed rates of hydrolysis of the nucleobases and several analogues were measured by Levy and Miller (1998), and decomposition in the dry state was measured by Minton and Rosenberg (1964). Levy and Miller's measurements were made in the context of the surging notions of the origin of life near subsea hydrothermal vents (Baross and Hoffman 1985; Miller and Bada 1988) and underscored the idea that lower temperatures are generally more beneficial to the long-term survival of nucleobases. Their half-lives in neutral water were all found to be less than 100 years at 100 °C (measured $t_{1/2}$ T ~ 56 years, U ~ 12 years, A ~ 1 year, G ~ 0.8 years, and C ~ 19 days), with rates generally increasing under more acidic and more alkaline conditions. At 0 °C, the measured $t_{1/2}$ values were T ~ 2×10^9 years, U ~ 3.8×10^8 years, G ~ 1.3×10^6 years, A ~ 6×10^5 years, and C ~1.7×10^4 years It was pointed out that these rates are comparable to the present rate of seawater circulation through submarine hydrothermal vents (~10^7 years), and thus marine hydrothermal circulation may present an upper bound to the accumulation of nucleobases in the primitive oceans. Importantly, these authors did not study the influence of potential soluble or insoluble catalysts on degradation but noted that some cation-substituted clays markedly increase the rate of deamination of adenine (Strašák and Šeršeň 1991).

In contrast, nucleobases are considerably more stable in the dry state. Minton and Rosenberg (1964), for instance, extrapolated the half-lives of A and C as ~ 10^6 years at 25°, those of G and U as between 10^4 and 10^5 years, and that of T as less than 10^3 years, in contrast with the half-lives measured by Levy and Miller for A and G of ~10^4 years and that of C as 3.4×10^2 years at 25 °C in neutral solution.

The hydrolytic deamination of cytosine presents an interesting example of the importance of considerations of nucleobase stability in astrobiology. The relatively extreme instability of C has been cited variously as a problem for RNA world models (Shapiro 1999), a driver for early evolution (Lewis et al. 2016), and an explanation for the lack of detection of C in carbonaceous meteorites (Levy and Miller 1998).

1.4.2 Decomposition by Ionizing Radiation

In addition to thermally mediated decomposition, radiation presents yet another environmental limitation to nucleobase accumulation. The primitive solar system was undoubtedly a higher-radiation environment, as many primordial radionuclides were still abundant (Draganić et al. 1990). It also seems likely that the early Sun had a greater output in short wavelength regions of the electromagnetic spectrum, and on Earth in particular, UV radiation may have penetrated the atmosphere more efficiently before the advent of a significant ozone layer (Cleaves and Miller 1998).

In most cases, high-energy radiation is significantly more destructive of nucleobases in solution than in the dry state. This is mainly due to the generation of highly reactive species including solvated electrons, hydrogen atoms, hydroxyl radicals, and peroxides (Doane 2017). All of these have a high reactivity with the π electron systems of the nucleobases (Bertinchamps et al. 2011). Interestingly, relative to some other nitrogen heterocycles, the nucleobases appear to be able to especially efficiently eliminate UV-induced electronic excitation by internal conversion (Boldissar and de Vries 2018).

The source of the radiation and relative location of target nucleobases is also important. While UV radiation, galactic cosmic radiation, and solar energetic particles have a low penetrance through various materials including water and minerals, many types of pervasive high-energy particles and waves have significant penetrance or are generable within rock matrices or pore water spaces via the decay of various nuclides. Kminek and Bada (2006) conducted a quantitative study of the stability of amino acids to ionizing radiation under Mars-like conditions. They showed that radiolytic survival is inversely proportional to the molecular weight of the target, likely simply due to larger molecular cross-sectional area, and suggested that it is highly unlikely that there would be much small organic molecule survival in the top 1.5 m of regolith after exposure during the last 3 Ga, despite the prevailing low temperatures. Laboratory studies of unprotected nucleobases irradiated in the gas phase suggest survival times on the order of a few hours in space in Earth's vicinity and at most a few million years in dense molecular clouds (Peeters et al. 2003), the major variable being the energetic flux intensity and degree of shielding.

In contrast, it is evident that carbonaceous chondrites do contain indigenous nucleobases (Stoks and Schwartz 1982; Callahan et al. 2011); thus, it is possible to surmise that these bodies first either inherited these compounds during accretion or harbored conditions conducive to their synthesis and subsequently preserved them over the last 4.5 Ga of solar system history under extremely cold, dry, and radiation-sheltered conditions.

1.5 Conclusions and Future Directions

The nucleobases, and related N-heterocycles, undoubtedly are the products of abiotic synthesis in primitive solar system environments, as evidenced by their presence in carbonaceous meteorites. The molecular mechanism by which they were produced in them is open questions but may include one or more of the routes which have been demonstrated in various laboratories: synthesis from low molecular weight, high-energy compounds such as HCN, formamide, and CAA, either in stepwise fashion or from the degradation of complex heterogeneous polymeric materials derived from similar compounds. The synthesis of these materials can be induced by various energy sources (UV light, electric discharges, heat), provided there is a sufficient abundance of carbon and nitrogen, and the reactive compounds can be concentrated by some environmental process (e.g., eutectic freezing or evaporative drying).

However, the nucleobases also degrade in various geochemical settings by thermal and radiation-induced processes, and their potential roles in the origins of life would depend on the synthetic, depositional, and preservational conditions under which they arose. High carbon-flux, reducing environments appear to be the most amenable to synthesis and cold, dry environments the most conducive to long-term preservation. However, it is possible that the incorporation of nucleobases into higher-order structures and processes that may have led to living systems requires dynamic environments that are not conducive to long-term preservation. Consequently, the origins of life, if dependent on these types of compounds, may be relatively fast in a geological context (Pearce et al. 2017).

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