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Sean J. Hoehn
Case Western Reserve University

Naishka E. Caldero-Rodríguez
Case Western Reserve University

Carlos E. Crespo-Hernández
Case Western Reserve University, cxc302@case.edu

Author(s) ORCID Identifier:

Sean J. Hoehn

Naishka E. Caldero-Rodríguez

Carlos E. Crespo-Hernández

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Photochemistry of RNA, RNA Monomers, and Plausible Prebiotic Precursors[†]

Sean J. Hoehn, Naishka E. Caldero-Rodríguez, and Carlos E. Crespo-Hernández*

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio, USA 44106

* Email: carlos.crespo@case.edu

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Abstract

Sunlight is the primary source of energy to promote change on Earth. In this context, ultraviolet radiation can be thought as a catalyst of chemical change to refine chemical feedstocks and facilitate their transformations into the building blocks of life. To establish reasonable environmental constraints for the chemical origins of life, it is central to understand how the photochemical reactivity or photochemical resistance of prebiotic molecules might have supported the formation of the RNA monomers on the Earth's surface and particularly in aqueous solution. In this chapter, the photochemistry of the RNA monomers and several conceivably important prebiotic precursors are reviewed. The emphasis is on delineating the primary electronic relaxation or photochemical reaction pathways that may have enabled the accumulation and the selection of the RNA monomers as the building blocks of life during prebiotic times. Finally, the moderately investigated photochemistry of RNA is summarized and contrasted to that of DNA. It is surmised that the enhanced structural rigidity and the increased excitation delocalization length in RNA may have conspired during prebiotic times for RNA oligomers to prosper under the otherwise harsh ultraviolet radiation conditions of early Earth.

1.1 Introduction

How nonliving chemicals evolved into molecules capable of life beginning approximately 4 billion years ago is one of the greatest mysteries still captivating scientists. In this context, there are several theories as to the events that sparked the formation of life from chemical evolution. Among them, two important contenders are the RNA World Hypothesis and the Managed-Metabolism Hypothesis.[1–5] In the latter, it is suggested that proto-metabolic molecules emerged and evolved first from a primordial soup of molecules.[1,3,6–8] These proto-metabolic species are thought to have been self-replicating and amplifying because each molecule's formation results from catalysis by another metabolic species. However, there is a cooperation barrier that must be overcome for life to evolve. The RNA and DNA serve as a management system to organize and control the organization of metabolic cycles.

Conversely, the RNA-World Hypothesis suggests that RNA formed on early Earth before DNA, proteins, or higher order metabolic structures.[1,3,4,6,9] Because RNA carries the genetic information of the cell and can catalyze replication of this information, it is plausible that early RNA ancestors could have led to the emergence of life from a chemical feedstock through indigenous synthesis and ultraviolet radiation (UVR) refinement.[10,11] It is then thought that DNA and proteins evolved from patterns of RNA sequences. An important example of the role UVR played in the formation of the RNA nucleobases was the demonstration by Orgel and co-workers[12–14] in the late 1960s of the photochemical formation of adenine and guanine from hydrogen cyanide under plausible primitive Earth conditions. More recently,[15] another example of a photochemical prebiotic route has been provided for the formation of cytidine and uridine starting from the UV-induced photoanomerization of α-2-thiocytidine to β-2-thiocytidine. The idea of an RNA-first approach has been supported by ribonucleotide coenzymes currently used by numerous proteins, considered as "molecular fossils" of an RNA-based metabolism.[5,16,17]

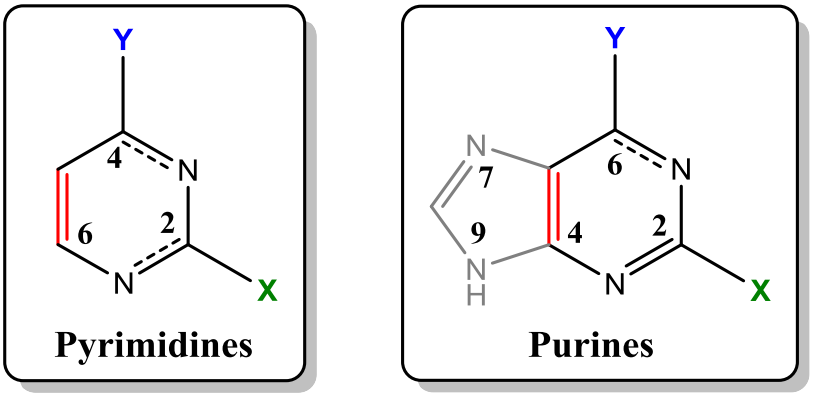
Irrespective of which hypothesis is correct, or whether both occurred in parallel, several considerations should be made when investigating the chemical origins of life. Prebiotic Earth had extremely different environmental conditions than what is known today. The major constituents of the primitive Earth's atmosphere were methane, ammonia, water vapor, CO_2, N_2, H_2, the noble gases, and H_2S, making it a highly reducing environment,[18,19] supported by the Miller and Urey Hypothesis.[20,21] Additionally, the absence of ozone in the stratosphere allowed for the transmission of near-UV radiation (200-400 nm) to the Earth's surface.[11,18,22] Therefore, such considerations include early Earth environment, sources of energy, photochemistry – *defined herein as the photostability of the chemical feedstock or the use of UVR to drive evolutionary chemical change* –, prebiotic chemical synthesis, and molecular cooperation, among others.

Until recently, the synthesis of prebiotic compounds under proposed protobiotic conditions has garnered most of the attention of investigators, rather than an emphasis on their intrinsic photochemistry and the importance of UVR as a selection pressure.[23–32] Some counterarguments posit that protobiotic life was cultivated in secluded UV-free environments, such as in deep-sea hydrothermal vents, within cracks, or in pores of solid surfaces.[10,29,33] It has also been suggested that sufficient quantities of precursor organic absorbers could have accumulated, providing a protective UV shield, thereby allowing prebiotic chemistry to develop at subsurface depths. While chemical evolution segregated in the shadows removes the threat of photodamage, the concern would surround the transition of this chemistry to conditions supporting photoinitiated events. Alternatively, if the chemical synthetic pathways were persistently subjected to UVR exposure, the survival of the photo-fittest would continue the journey to sustain life.[18] Therefore, investigating the photochemistry of prebiotic RNA precursors may hold the key to understand the molecular origins of life.

This chapter is organized as follows. Basic photochemical properties of the canonical RNA monomers and a selected group of plausible candidates that has been investigated as prospective

prebiotic precursors of the RNA monomers are summarized first. Then, whenever documented, the proposed electronic relaxation mechanisms for these molecules are discussed, primarily focusing on the relaxation pathways that are thought to be conducive to chemical resistance or reactivity. Finally, we briefly discuss the photochemistry of RNA oligonucleotides and their primary photoproducts. As is customary in the contemporary scientific literature, the premise "*the faster the electronically excited state population returns to the electronic ground state, the more photostable a molecule would be*" is presumed hereafter to directly correlate with the chemical resistance of a molecule to UVR.

1.2 Photochemical properties and primary electronic relaxation pathways in the canonical RNA monomers



Scheme 1.1 Structure of the RNA nucleic acid bases and ring numbering. **Purines:** ***Adenine*** (Y = NH_2 and X = H); ***Guanine*** (Y = O and X = NH_2). **Pyrimidines:** ***Cytosine*** (Y = NH_2 and X = O); ***Uracil*** (Y = O and X = O).

To understand the effects UVR had on the chemical integrity of RNA monomers and polymers during the prebiotic era, it is essential to identify their photochemical properties and elucidate their electronic relaxation mechanisms. All four nucleic acid monomers that constitute RNA – uracil, cytosine, adenine, and guanine – are comprised of a planar pyrimidine core, where the purine is a heterocyclic pyrimidine that contains a fused imidazole ring about the pyrimidine ethylenic bond (Scheme 1.1). Their conjugated π-system makes them prime candidates for UVR absorption. The electronically excited states populated by absorption of UVR encompass transitions typical within molecular organic photochemistry. These transitions are obtained by optical excitations from π bonding orbitals or lone pair nonbonding orbitals localized on the oxygen or nitrogen heteroatoms, to π* antibonding orbitals, which give rise to more accessible ππ* states or less optically accessible nπ* states, respectively.[34,35] In addition, a third type of excited state is populated by optical excitations from π bonding orbitals to unoccupied σ* orbitals. As shown in Figure 1.1, the lowest energy absorption band of the RNA nucleobases has a

maximum near 260 nm, corresponding to highly allowed ππ* transitions, where the purine's heightened efficiency of absorption compared to the pyrimidine nucleobases can be observed.

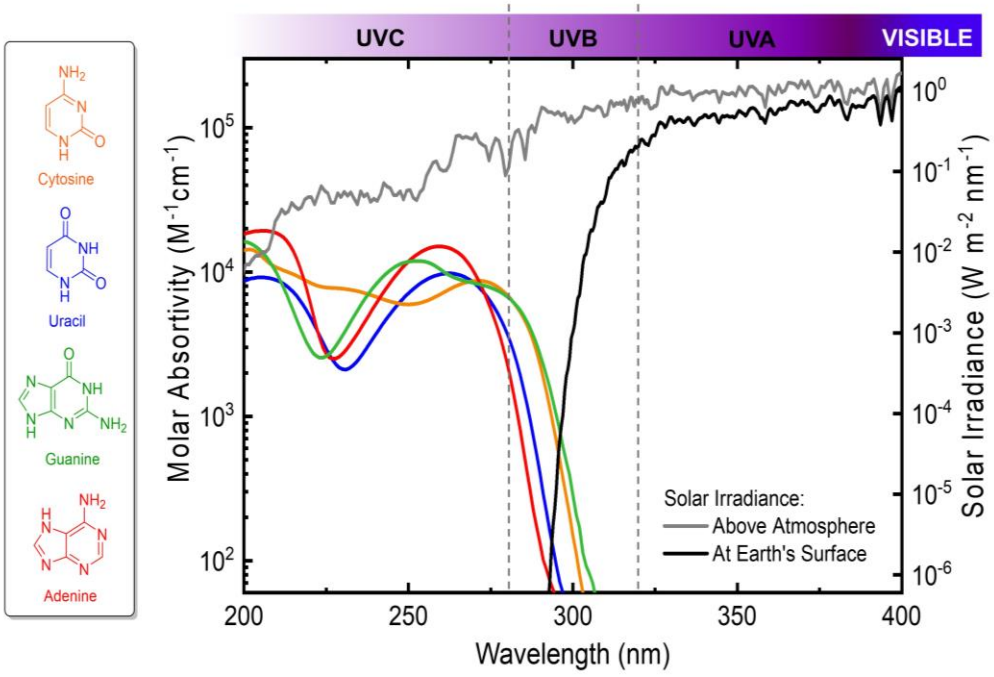


Figure 1.1 UV absorption spectra of the color-coded RNA nucleobases (left vertical axis). Solar irradiance spectra above Earth's atmosphere (air mass zero, ASTM E-490-00) and at Earth's surface (air mass 1.5, ASTM G173-03) are plotted as the gray and black traces, respectively (right vertical axis).[36] Note the logarithmic scale of both the left and right axes. Figure adapted from ref. [10].

In general, initial electronic relaxation events occurring upon UV absorption include nonadiabatic transitions amongst excited electronic states. In cytosine and uracil, Figure 1.1shows that a single ππ* electronic transition is observed in the lowest energy absorption band with a maximum around 267 and 260 nm, respectively. This band shifts bathochromically by ca. 2 to 3 nm going from the nucleobase to the nucleoside. The purine nucleobases exhibit two absorption bands in the spectral region from ca. 220 to 400 nm (Figure 1.1). The maxima of these absorption bands are located at 260 and 270 nm for adenine, whereas they are located at 250 and 275 nm for guanine. These maxima correspond to allowed ππ* singlet state electronic transitions, commonly referred to as ^1L_a and ^1L_b transitions using Platt-Murrell notation, denoting HOMO → LUMO and HOMO-1 → LUMO, respectively.[37] Glycosylation of the purine nucleobase retracts these bands toward one another, where a single absorption band is observed in adenosine or a band with a shoulder in guanosine. Experiment and theory agree that when high energy UV photons are absorbed, dissociative πσ* states can play a role in the electronic relaxation of adenine.[38] Recent experimental and computational results also suggest that a πσ* state with significant

intramolecular charge transfer character could play a considerable role in the relaxation pathways of guanine monomers in solution.[39,40] In addition to the allowed ππ* transitions, the heteroatoms contained within the pyrimidine and purine nucleobases give rise to weak, overlapping nπ* absorption bands. In solution, the ππ* and nπ* transition energies can shift relative to one another depending on the solvent environment, thus fostering or destabilizing one transition relative to another. The ordering and crossing of electronic states have necessary implications on the available avenues for relaxation, including nπ* doorway states of singlet or triplet multiplicity enabling accessibility to the triplet manifold.

The ultrafast decay lifetimes of the natural RNA nucleobases have been associated with electronic relaxation through conical intersections (CIs) seams,[34,35,41,42] which are often accessed through out-of-plane deformations, eventually repopulating the electronic ground state (S_0). Functionalization and the identity of the substituent can modify the topology of the potential energy surfaces, influencing the accessibility of decay pathways available and the outcome of relaxation.[34,35,43,44] A common observation in all the canonical nucleobases is ultrafast non-radiative decay to S_0 following UVR, resulting in exceptionally low fluorescence and photochemical quantum yields.[42]

In aqueous solution, the primary relaxation pathway of the cytosine[45–47] and uracil[45,48–54] monomers is a sub-1 ps decay from the $^1\pi\pi^*$ to the S_0 state. A small fraction of the $^1\pi\pi^*$ population decays to longer-lived $^1n\pi^*$ and $^3\pi\pi^*$ states,[45,48–61] and the sugar and phosphate groups have been shown to increase the fraction of population reaching the $^1n\pi^*$ state upon excitation at 266 nm.[48] The triplet state yield of the uracil monomers varies with solvent but is small (ca. 1 to 2 %) in aqueous solutions.[42,49,62] It should be remarked that a recent study has demonstrated that the detailed electronic relaxation mechanism of the cytosine monomers depends on the excitation wavelength.[56] Lifetimes associated with relaxation pathways of the cytosine and uracil monomers are listed in Table 1.1. Further work is still necessary to quantify the yields of the long-lived excited states as a function of excitation wavelength and to identify their potential participation in the formation of photoproducts.[62–64]

Table 1.1 Lifetimes associated with relaxation pathways of cytosine and uracil monomers.

	Singlet-State Lifetimes (ps)	*Technique, Time Resolution*	*Experimental Conditions* [a]
Cytosine	0.20 ± 0.02, 1.30 ± 0.07[b]	FU [g], 100 fs	H_2O, 2 mM[65]
	0.72	TAS [h], 200 fs	H_2O, pH 6.8[66]
	1.0 ± 0.2	TAS, 320 fs	PBS, pH 6.8[47]
	2.9 ± 0.7[c], 12 ± 3[d]	TAS, 200 fs	PBS, pH 7[48]
	0.251, 3.970	TAS, <10 fs	H_2O[67]
	5.2	TQP [i], 30 ps	H_2O, O_2, pH 6.3, 30 μM[68]
	0.20 ± 0.03, 1.5 ± 0.1, 7.7 ± 0.6	FU, TAS,	PBS, pH 7, 50 mM[61]
Cytidine	0.76 ± 0.12	FU, 360 fs	PBS, pH 7, 3 mM[69]

	0.72 ± 0.04	TAS, 200 fs	H_2O, pH~7, 3-4 mM[70]
	1.0 ± 0.1	TAS, 320 fs	PBS, pH 6.8[47]
	0.95 ± 0.12[e]	FU, 360 fs	PBS, pH 7, 3 mM[69]
	3.7 ± 0.8[c], 34 ± 3[d,e]	TAS, 200 fs	PBS, pH 7[48]
Cytidine 5'-monophosphate	0.20 ± 0.03, 1.8 ± 0.1[c], 34 ± 2[d]	FU, 100 fs TAS,	PBS, pH 7, 50 mM[61]
Uracil	0.096 ± 0.003	FU, 330 fs	H_2O, 2.5 mM[53]
	1.9 ± 0.1[c], 24 ± 2[d]	TAS, 200 fs	PBS, pH 7[48]
	5.2	TQP, 30 ps	H_2O, O_2, pH 6.3, 30 μM[68]
Uridine	0.21 ± 0.03	TAS, 200 fs	buffer[71]
	2.3 ± 0.2[c], 147 ± 7[d,e]	TAS, 200 fs	PBS, pH 7[48]
Uridine 5'-monophosphate	0.20 ± 0.05[c], 0.43 ± 0.05[f], 365 ± 20[d]	TAS, ~200 fs	PBS, pH 7.3[52]

[a] Under air-saturated conditions unless otherwise noted; [b] Lifetimes reported were obtained from a biexponential fit, monoexponential fit values are also reported in the reference; [c] Assigned to direct IC from the initially excited $^1\pi\pi^*$ state to S_0, an additional < 1ps lifetime was observed at 340 nm and assigned to VC in S_0; [d] Assigned to the decay lifetime of the lowest-energy $^1n\pi^*$ state; [e] measured for the nucleotide form; [f] Attributed to VC in S_0; [g] FU = fluorescence up-conversion; [h] TAS = transient absorption spectroscopy; [i] TQP = two quanta photolysis.

Multiexponential decay lifetimes have also been reported for the adenine[45,46,59,69,70,72–79] and guanine monomers[39,40,80–82] upon excitation with UVR in aqueous solution. The decay pathways have been assigned to sub-100 fs internal conversion (IC) from the $^1\pi\pi^*(L_b)$ to the $^1\pi\pi^*(L_a)$ state, relaxation along the ^1L_a state potential energy surface towards a minimum, and access to a CI with the S_0 state from the ^1L_a minimum.[39,40,72,73,79–85] Table 1.2 collects the reported decay lifetimes in aqueous solutions. Most authors have to assigned a 2-3 ps lifetime to vibrational cooling (VC) dynamics in S_0,[39,45,70,73,76,80,81,86–88] or to the decay of a $^1\pi\sigma^*$ state to the S_0 state.[40,84,89] In addition, two recent studies have proposed that a $^1n\pi^*$ state acts as an intermediate state in the electronic relaxation dynamics of adenine monomers.[59,73] According to those studies, the $^1n\pi^*$ state decays to S_0, however, significantly different decay lifetimes were reported in those studies.[59,73] It should be remarked that other time-resolved experiments[40,48,74,76–79,94,95] have not observed the participation of a $^1n\pi^*$ state in the electronic relaxation mechanism of the adenine monomers in aqueous solution. If $^1\pi\sigma^*$ or $^1n\pi^*$ excited state can be accessed in aqueous solution, it is unknown whether its population could lead to a photodissociation event or could explain the photodegradation reported for adenine and guanine monomers upon irradiation at 254 nm in aqueous solution.[90–93] Collectively, there is agreement that ultrafast IC from the $^1\pi\pi^*$ to S_0 state is the primary relaxation mechanism in the adenine and guanine monomers in aqueous solution.

Table 1.2 Lifetimes associated with relaxation pathways of adenine and guanine monomers.

	Singlet-State Lifetimes (ps)	*Technique, Time Resolution*	*Experimental Conditions* [a]
Adenine	0.23 ± 0.05[b], 8.0 ± 0.3[c]	FU, 100 fs	H_2O, 0.5-2 mM[75]
	0.34 ± 0.07[b,d], 8.4 ± 0.8[c]	FU, 200 fs	H_2O, 8 mM[77]
	0.18 ± 0.03[b], 8.8 ± 1.2[c]	TAS, 200 fs	H_2O, pH 6.8[76]

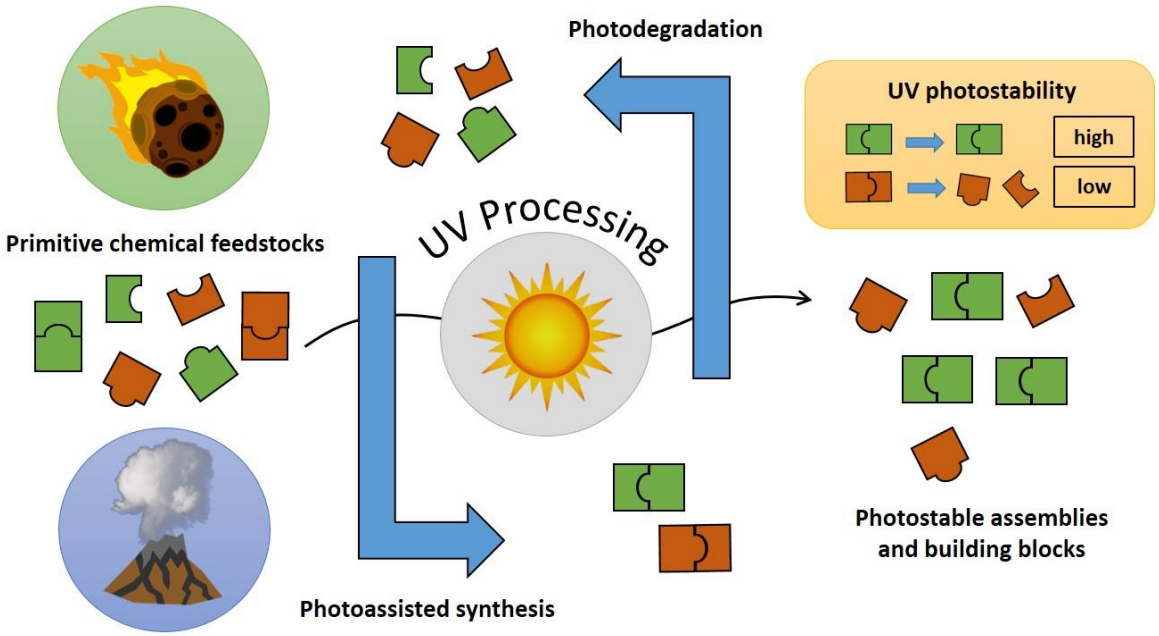
	0.064 ± 0.002[b], 8.5 ± 1.7[c,e]	TRPES[n], 80 fs	TRIS, pH 8, 1 mM[72]
Adenosine	0.31 ± 0.05	FU, 200 fs	H_2O, 1 mM[77]
	0.53 ± 0.12	FU, 360 fs	PBS, pH 7, 3 mM[69]
	0.29 ± 0.04	TAS, 200 fs	H_2O, pH~7, 1 mM[70]
	0.215 ± 0.020[g]	TRPES, 80 fs	TRIS, pH 8, 1 mM[72]
	0.52 ± 0.16[h]	FU, 360 fs	PBS, pH 7, 3 mM[69]
	0.37 ± 0.04[h]	TAS, 200 fs	PBS, pH 6.8[96]
Adenosine 5'-monophosphate	0.39 ± 0.02[i]	TAS, ~250 fs	PBS, pH 6.8, 20 mM[40]
	0.19 ± 0.03[i], 0.45 ± 0.05[m], 2.0 ± 0.2[k]	TAS, ~55 fs	PBS, pH 7.0[97]
Guanine	3.2	TQP, 30 ps	H_2O, O_2, pH 6.3, 30 μM[68]
Guanosine	0.69 ± 0.10	FU, 360 fs	PBS, pH 7, 1.5 mM[69]
	0.46 ± 0.04	TAS, 200 fs	H_2O, pH~7, 3-4 mM[70]
	0.86 ± 0.10[h]	FU, 360 fs	PBS, pH 7, 3 mM[69]
	0.2[i], 0.9[j], 2.5[k,l]	TAS, ~100 fs	PBS, pH 7[80]
Guanosine 5'-monophosphate	0.20 ± 0.04[i], 0.79 ± 0.04[j], 1.98 ± 0.10[l]	FU TAS	PBS, pH 7.0, 50 mM[89]
	0.6 ± 0.1[i], 0.7 ± 0.1[j], 2.7 ± 0.8[l]	TAS, ~250 fs	PBS, pH 6.8, 20 mM[40]

[a] Under air-saturated conditions unless otherwise noted; [b] Attributed to the N9H tautomer; [c] Attributed to the N7H tautomer; [d] Excitation wavelength-dependent; [e] Dependent on probe energy; [f] Limited by time-resolution of the experimental set-up; [g] Independent of probe energy, but higher pump energies decrease this lifetime, which was attributed to greater access to the S_1/S_0 CI; [h] Measured for the nucleotide form; [i] Attributed to the decay lifetime of $^1\pi\pi^*$ (L_a) state; [j] Attributed to relaxation in a plateau-like region of the $^1\pi\pi^*$(L_a') state; [k] Attributed to VC in S_0; [l] Attributed to the decay lifetime of a weakly emissive $\pi\sigma^*$ state; [m] Attributed to the decay lifetime of the $^1n\pi^*$ state; [n] TRPES = time resolved photoelectron spectroscopy.

1.3 Electronic relaxation pathways and photochemistry of plausible RNA prebiotic precursors

For the canonical nucleobases to persist and thrive under intense UVR conditions, there must have been a balance between their production, participation in side reactions, and potential degradation. Thus, as depicted in Scheme 1.2, if photochemistry is to be considered as a prominent evolutionary pressure in the development of life, one must understand the intrinsic photochemistry of the RNA precursors and consider how they may have evolved to form the four nucleobases of RNA. Far more solar radiation would have reached Earth's surface under primitive Earth conditions, notably in the deep UV (ca. 200-280 nm), compared to the present day due to its attenuation by the Earth's atmosphere. Therefore, understanding how plausible precursor molecules managed the excess electronic energy gained from the absorption of UVR is important because of the possibility of transformative photoreactions. It could also help identify the molecules that may have existed in the earliest form of life or were photochemically altered to yield more photofit precursors. Do key structural and electronic elements govern the photostability and the viability of precursors as prospective candidates along the chemical evolutionary assembly line? Research work supports the idea that chemical substitution and its position modulates the photophysics of the nucleobases.[34,35] In building a competitive prebiotic infrastructure, strategic functionalization of the pyrimidine and purine chromophores could have been crucial in supply

chain management, where their photochemistry may have taken center stage in moderating supply chain activities.



Scheme 1.2 Evolutionary refinement through UV radiation of a primitive chemical feedstock of molecules brought to Earth's surface through meteorite infall or indigenous synthesis. Through cycles of photodegradation and photoassisted synthesis, a variety of photofit molecules can be formed. Modified from ref. [10].

Several molecules have been considered as plausible precursors on prebiotic Earth due to their identification in meteorites, interstellar ices, interstellar molecular clouds,[98–101] and model prebiotic reactions. These molecules include pyrimidines, quinolines, isoquinolines, benzoquinolines, hydrocarbons, carboxylic acids, and amino acids,[102,103] which are thought to arise from (indigenous and exogenous sources) smaller molecules such as water, methanol, ammonia, formamide, ammonium cyanide, hydrogen cyanide, cyanoacetylene, and urea. Due to the astrophysical environmental conditions, most reactions of these small molecules to form pyrimidine and purine nucleobase derivatives are proposed to occur in the gas phase, in solids, or ice.[98,104–108] In particular, heterocyclic molecules with similar functionality and base pairing abilities as the canonical bases make for plausible candidates present during chemical evolution. The list of prebiotic precursors candidates includes hypoxanthine, xanthine, 2-aminopurine, 2-pyrimidinone, 4-pyrimidinone, 4-aminopyrimidine, 2,4-diaminopyrimidine, 5-aminouracil, 5-hydroxyuracil, orotic acid, 4,5-dihydroxypyrimidine, nicotinic acid, among others.[23,24,26,105,109–111] Table 1.3 collects the decay lifetimes in aqueous solutions for several pyrimidine and purine nucleobase derivatives that are considered as plausible prebiotic candidates.

Table 1.3 Lifetimes associated with relaxation pathways in aqueous solutions for several pyrimidine and purine nucleobase derivatives that are considered as plausible prebiotic candidates.

	Excited-State Lifetimes (ps)	*Technique, Time Resolution*	*Experimental Conditions* [a]
Purine ǂ	0.20 ± 0.05[b], 8 ± 3[c,d], 645 ± 10[e], >3,000[f]	TAS, ~200 fs	PBS, pH 7.0[44]
9-Methylpurine	0.25 ± 0.05[b], 15 ± 5[c,d], 600 ± 10[e], >3,000[f]	TAS, ~200 fs	PBS, pH 7.0[44]
1-Methyl-2-pyrimidinone	1.1[g], 440[b], >3,000[h]	TAS, ~400 fs	H_2O[112]
(2'-deoxy)-2-Aminopurine	1.0 ± 0.3[g,i], 10,000 ± 1,000[e,i,j], 177,000 ± 30,000[f,i]	TAS, ~200 fs	PBS, pH 7.0[113]
Hypoxanthine	0.13 ± 0.02[b], 2.3 ± 0.3[k]	TAS, 200 fs	H_2O[114]
	<0.1[g], 0.18 ± 0.06[j]	FU, 140 fs	PBS, pH 7.0[115]
	<0.05[l], 0.21 ± 0.08[b], 1.8 ± 0.4[k]	TAS, 50 fs	
Barbituric acid	≤0.18[b], 0.30 ± 0.04[k]	TAS, ~200 fs	PBS, pH 7.4, 50 mM[117]
2,4,6-Triaminopyrimidine	0.66 ± 0.07[b], 2.7 ± 0.4[e]	TAS, ~200 fs	PBS, pH 7.4, 50 mM[117]
Melamine	12.7 ± 0.2[b]	TAS, 480 fs TRIR [n]	H_2O, D_2O pH/pD 7.4[118]
5-Aminouracil	0.15 ± 0.01[m,g], 0.66 ± 0.07[m,g], 2.78 ± 0.05[m,j]	FU, 150 fs	H_2O[119,120]

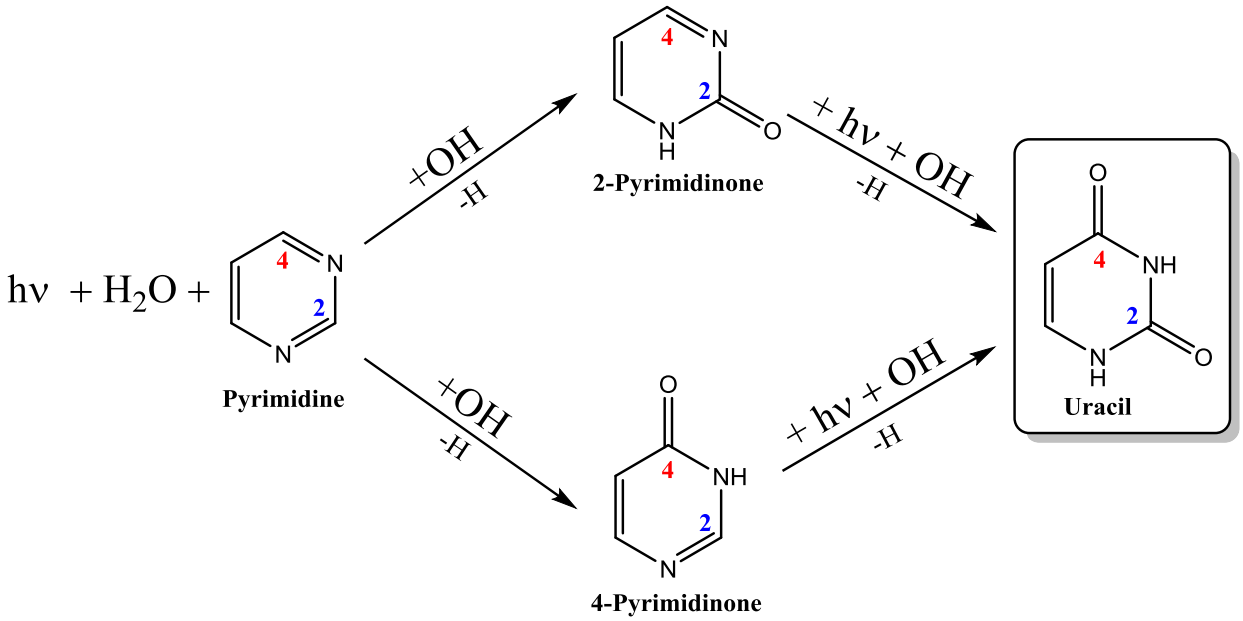
ǂ lifetimes for purine are due to the presence of both N9H and N7H tautomers; [a] Under air-saturated conditions unless otherwise noted; [b] Attributed to the decay lifetime of the $^1\pi\pi^*$ state; [c] Average lifetime from a global fit analysis; its actual value increases in going from the UV to the visible probe wavelengths; [d] Attributed to VC of the $^1n\pi^*$ state; [e] Attributed to the decay lifetime of the $^1n\pi^*$ state; [f] Attributed to the decay lifetime of a $^3\pi\pi^*$ state; [g] Attributed to the lifetime of $^1\pi\pi^*$ near FC region; [h] Attributed to the decay lifetime of a $^3n\pi^*$ state; [i] Measured for the nucleoside form; [j] Attributed to the decay lifetime of non-planar $^1\pi\pi^*$ minimum; [k] Attributed to VC in S_0; [l] Convoluted with the IRF; [m] Dependent on probe energy, becoming slower with decreasing energy; [n] TRIR = time resolved infrared.

At the core of all the canonical nucleobases is the pyrimidine or purine chromophore. The purine chromophore itself being a pyrimidine substituted with an imidazole group (Scheme 1.1). Although these nucleobase chromophores have not been identified in great abundance in meteorites or the interstellar medium, several pyrimidine and purine derivatives have, including the canonical nucleobases.[107,108,121–126] The identification of substituted purine and pyrimidines in meteorites suggests that an abiotic path should exist for their formation in the atmospheric environment.[98,106,121,122,127] Therefore, the pyrimidine and purine core chromophores may be considered ancestors of the nucleobases, and their photochemistry should be investigated. While the pyrimidine chromophore has not been investigated in aqueous solutions, it has been studied in acetonitrile using transient absorption spectroscopy, supported by ab initio calculations.[43] The electronic relaxation pathways of pyrimidine are complex,[43] and only a general relaxation mechanism is discussed herein. Following excitation at 268 nm, the $^1n\pi^*$ excited state population intersystem crosses to the triplet manifold with two different lifetimes. The population reaching the T_1 minimum decays back to S_0 in microseconds or can lead to photochemical transformation.[43] The purine chromophore has been investigated in aqueous solution following excitation at 266 nm.[44] The $S_2(\pi\pi^*)$ state is primarily populated, after which IC to a $^1n\pi^*$ state occurs on an ultrafast

time scale. From the relaxed $^1n\pi^*$ state, intersystem crossing (ISC) to the T_1 state occurs in hundreds of picoseconds,[44] which can relax to S_0 on the microsecond time scale[128] or may undergo chemical transformation to more photofit purine derivatives.[44]

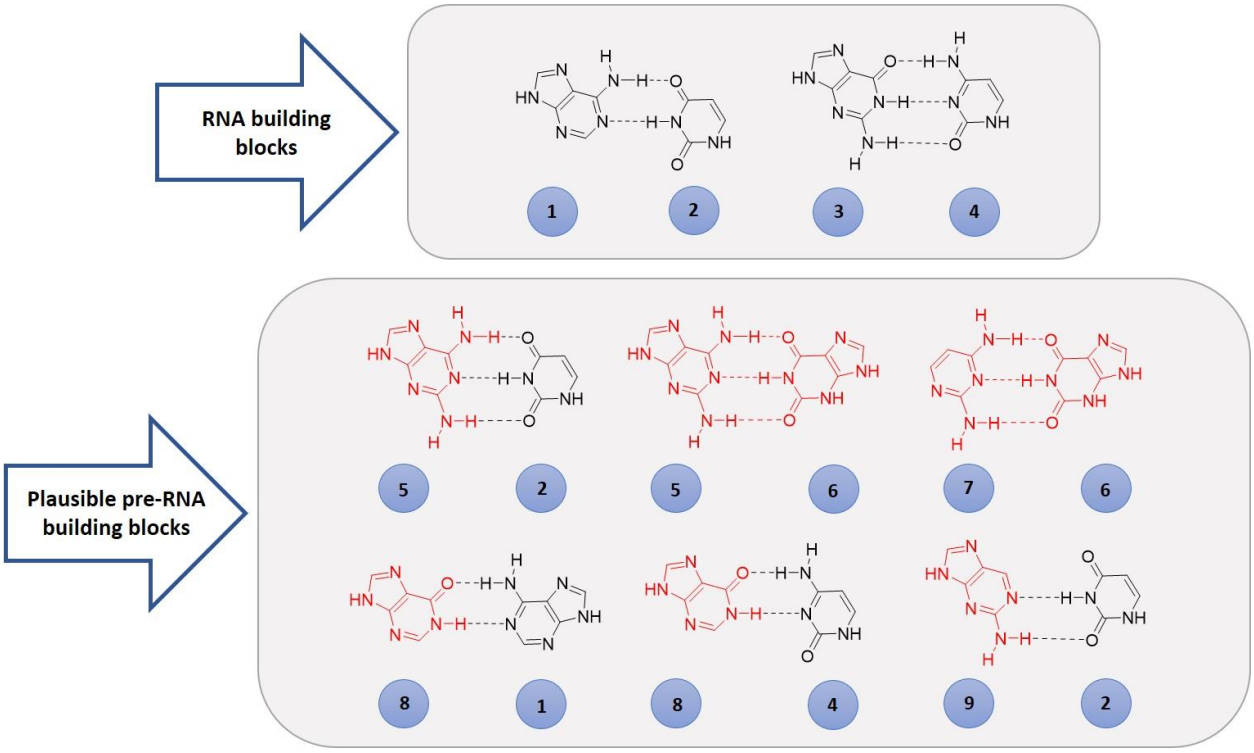
2-Pyrimidinone and 4-pyrimidinone have been experimentally synthesized under prebiotic conditions.[104,121] These nucleobase analogs are plausible candidates as RNA precursors due to their ability to form glycosidic bonds with ribose upon heating and drying.[111,129] To avoid N1H to N3H tautomerization of 2-pyrimidinone in the S_0 state, the photochemistry of 1-methyl-2-pyrimidinone (1MP) has been investigated in solution. Spectroscopic studies demonstrated that relaxation of 1MP consists of both nonradiative and radiative decay pathways, exhibiting significantly longer lifetimes than uracil, which also vary with temperature.[112,130] Given that the temperature of prebiotic Earth also likely varied,[131] the temperature dependence should be remembered because it can affect the relative percentages of the excited state population following each relaxation pathway. The relatively high population of the long-lived triplet state for 1MP is significant because it can increase the potential for photochemical transformation. Indeed, Ryseck et al.[112] determined that the photochemical quantum yield for 1MP is 0.5% following irradiation at 266 nm.

Contrary to 2-pyrimidinone, theoretical studies for 4-pyrimidinone have suggested that a near barrierless path leads to a low energy CI between the S_1 and S_0 states through the twisting of the N1-C2 bond.[132] This result suggests that as uracil, 4-pyrimidinone should dissipate excess electronic energy through ultrafast IC to S_0. This prediction agrees with recent transient absorption experiments that provide evidence for sub-200 fs IC to S_0 of 4-pyrimidinone upon excitation at 266 nm in aqueous solution.[133] While the population of the long-lived triplet state is a minor relaxation pathway in 4-pyrimidinone, the long-lived transient species observed in pyrimidine and 2-pyrimidinone suggest that UVR of these molecules may have resulted in chemical transformation to more photofit molecules like present day nucleobases. In this context, direct UV photoionization of these and other prebiotic precursors in the presence of water is expected to lead to the formation of the nucleobases.[104,134]As an example, a prebiotic reaction mechanism leading to uracil formation is shown in Scheme 1.3.



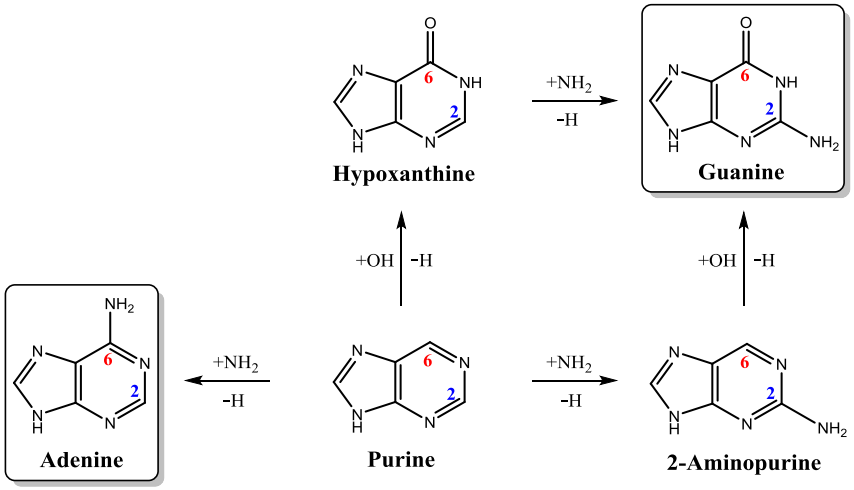
Scheme 1.3 Plausible formation of the uracil nucleobase from the UV photoirradiation of pyrimidine, 2-pyrimidinone, or 4-pyrimidinone prebiotic molecules in the presence of water. Direct UV photoionization of pyrimidine, 2-pyrimidinone, or 4-pyrimidinone is expected to lead to the formation of uracil in the presence of water. Modified from refs.[104,134]

Several amino-substituted purine and pyrimidine derivatives, including 2,6-diaminopurine (26DAPu), 2,4-diaminopyrimidine (24DAPy), and 4-aminopyrimidine have been identified in meteorites, making them plausible proto-RNA molecules.[123,127] As depicted in Scheme 1.4, both 26DAPu and 24DAPy have the potential to form base pairs with a variety of alternative nucleobases, including xanthine and uracil. While little work has been done to study their photochemistry in aqueous solution, their electronic relaxation pathways have been predicted from a computational perspective. Quantum chemical studies using CASSCF/CASPT2 level of theory in vacuum indicated that 24DAPy has an energy barrier along the S_1 potential energy surface to access a S_1/S_0 CI, which allows for the excited state population to be trapped in the S_1 state.[135] 24DAPy may be compared to the natural cytosine nucleobase, which instead has a carbonyl at the C2 position in place of an amino group and exhibits ultrafast IC to S_0. This comparison suggests that 24DAPy should take longer to dissipate the excess electronic energy than cytosine, potentially making it less photostable upon radiation in aqueous solution. This hypothesis can be supported by spectroscopic measurements collected for 24DAPy in the gas phase.[136] Similarly, the 26DAPu purine analog was found to have lifetimes of a few nanoseconds, assigned to the N9H and N7H tautomers, respectively.[136] The lifetimes of these pyrimidine and purine derivatives are significantly longer than those reported for the nucleobases, suggesting an increased probability for photochemical transformations.



Scheme 1.4 Current RNA (black) and plausible pre-RNA (red) building blocks with pairing structures. Structures included are: adenine (**1**), uracil (**2**), guanine (**3**), cytosine (**4**), 2,6-diaminopurine (**5**), xanthine (**6**), 2,4-diaminopyrimidine (**7**), hypoxanthine (**8**), and 2-aminopurine (**9**). Modified from ref.[26].

2-Aminopurine (2AP) has been identified along with 26DAPu in UV-irradiated astrophysical ice analogs, suggesting possible formation in an interstellar environment and subsequently transport to Earth.[104,127] Like adenine, 2AP has also been found to base pair with uracil (Scheme 1.4),[23,24] and may be considered as a plausible prebiotic RNA precursor. In aqueous solution, 2AP was found to decay via both radiative and nonradiative pathways following excitation at 320 nm.[113,137] A percentage of the $^1\pi\pi^*$ excited state population internally converts to a $^1n\pi^*$ state and subsequently ISC to a long-lived $^3\pi\pi^*$ state.[73,113,137,138] Hence, it can be speculated that 2AP may have undergone photochemical transformation to produce a more photostable nucleobase derivative. For example, as depicted in Scheme 1.5, adding a hydroxy group to the C6 position can yield guanine following UV photoionization of 2AP in NH_3:H_2O mixed molecular ice.[127,139] Similarly, the addition of an amino group to the C6 position of purine can yield adenine following the UV photoionization of purine in NH_3:H_2O mixed molecular ice (Scheme 1.5).[127,139]



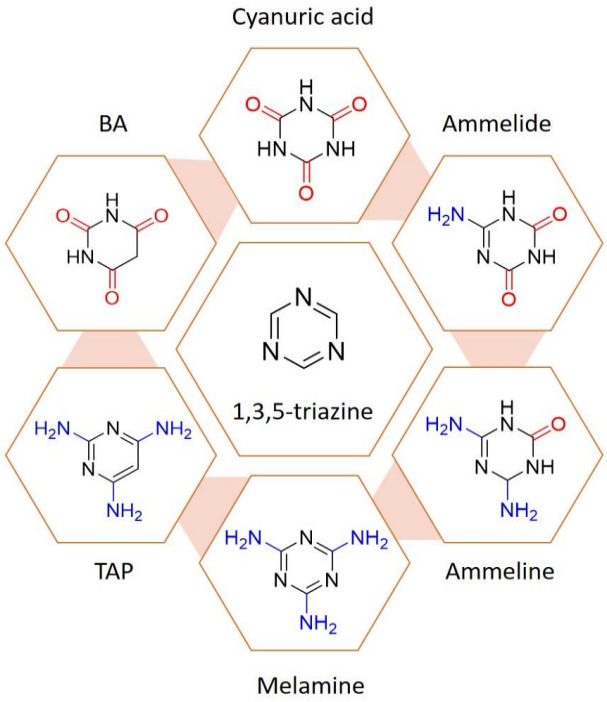
Scheme 1.5 Plausible formation of the canonical purine nucleobases from the initial UV photoirradiation of purine in the presence of water and ammonia. Direct UV photoionization of purine and 2-aminopurine is predicted to lead to the formation of adenine and guanine, respectively, in NH_3:H_2O mixed molecular ice. Vertical arrows indicate hydroxyl group addition, while the horizontal arrows indicate amino group substitutions. Modified from refs.[127,139].

Hypoxanthine (Hyp) and xanthine have also been identified in meteorites and synthesized under prebiotic environmental conditions.[104,123] Both molecules can form alternate base pairs such as hypoxanthine:adenine, xanthine:2,4-diaminopyrimidine, hypoxanthine:cytosine, among others, making them plausible building blocks during abiogenesis (Scheme 1.4). Hyp was found to have a decay lifetime of 0.13 ps, assigned to nonradiative relaxation from the $^1\pi\pi^*$ to the S_0 state, followed by VC in S_0 in approximately 3 ps.[114,140] The ultrafast IC suggests that Hyp is resilient to UVR and could exhibit an increased probability of survival in a prebiotic world. Interestingly, it has been proposed that direct UV photoionization of Hyp in the presence of water and ammonia can lead to guanine formation.[139]

In a separate set of experiments, Cafferty and Hud[24,26,141] subjected a stock of potential ancestral molecules to several criteria, including the ability to base pair, attach a sugar, and self-assemble in aqueous solution, to narrow down proto-RNA nucleobases. Barbituric acid (BA) and 2,4,6-triaminopyrimidine (TAP) emerged as two prospective candidates.[10,117,142] Brister et al. showed that both molecules have efficient nonradiative relaxation pathways after excitation at 266 nm, resulting in ultrafast dissipation of electronic energy. TAP exhibits a sub-picosecond lifetime corresponding to a bifurcation of the $^1\pi\pi^*$ state population to either IC to S_0 or a $^1n\pi^*$ state. The slightly longer picosecond lifetime was assigned to a second bifurcation process in which the population in the $^1n\pi^*$ state either IC to S_0 (primary event) or ISC to a triplet state (minor pathway). For BA, the first lifetime was assigned to IC from the $^1\pi\pi^*$ to the S_0 state, while the second lifetime was assigned to VC in S_0, both occurring in sub-picosecond time scales.[117] Ultimately, the results suggest that the photochemical integrity of both BA and TAP is maintained in aqueous solutions,

at least following excitation at 266 nm, which lends support to the idea[24,26,141] that BA and TAP could be plausible prebiotic precursors of the RNA nucleobases.

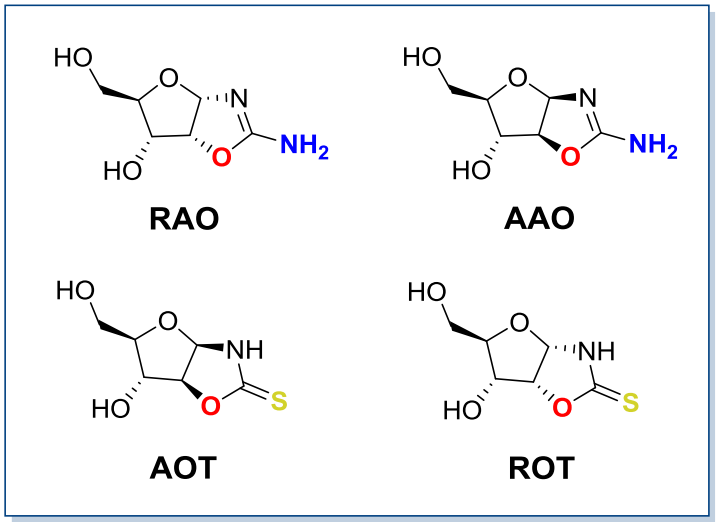
Melamine and cyanuric acid (CA) have been shown to be of particular interest as proto-RNA ancestors. As shown in Scheme 1.6, these molecules are the triazine analogs of TAP and BA, respectively, and self-assemble through hydrogen bonding.[25,26] The excited state dynamics of melamine in aqueous solution were investigated following excitation at 240 nm.[118] A single lifetime was measured and was assigned to the decay of the $^1\pi\pi^*$ to the S_0 state. The photochemistry of CA has yet to be investigated. However, it has been synthesized under prebiotic environmental conditions using urea as a starting compound.[105] Recent time-dependent density functional calculations predict that the triketo neutral form of CA should be photostable in aqueous solution, particularly at radiation wavelengths longer than ca. 210 nm.[143] The calculated vertical excitation energies are in good agreement with the reported absorption spectrum of the triketo neutral form of CA in aqueous solution, which has been reported to have negligible absorption at longer wavelengths than ca. 210 nm.[144]



Scheme 1.6 Triazine-based prebiotic RNA precursors. Adapted from ref.[118].

Like triazines, other six-membered heterocycles have been considered as plausible building blocks of RNA and pre-RNAs. Specifically, 5-hydroxyuracil, 5-aminouracil, and 5-hydroxymethyluracil have been synthesized under prebiotic conditions from simple organic

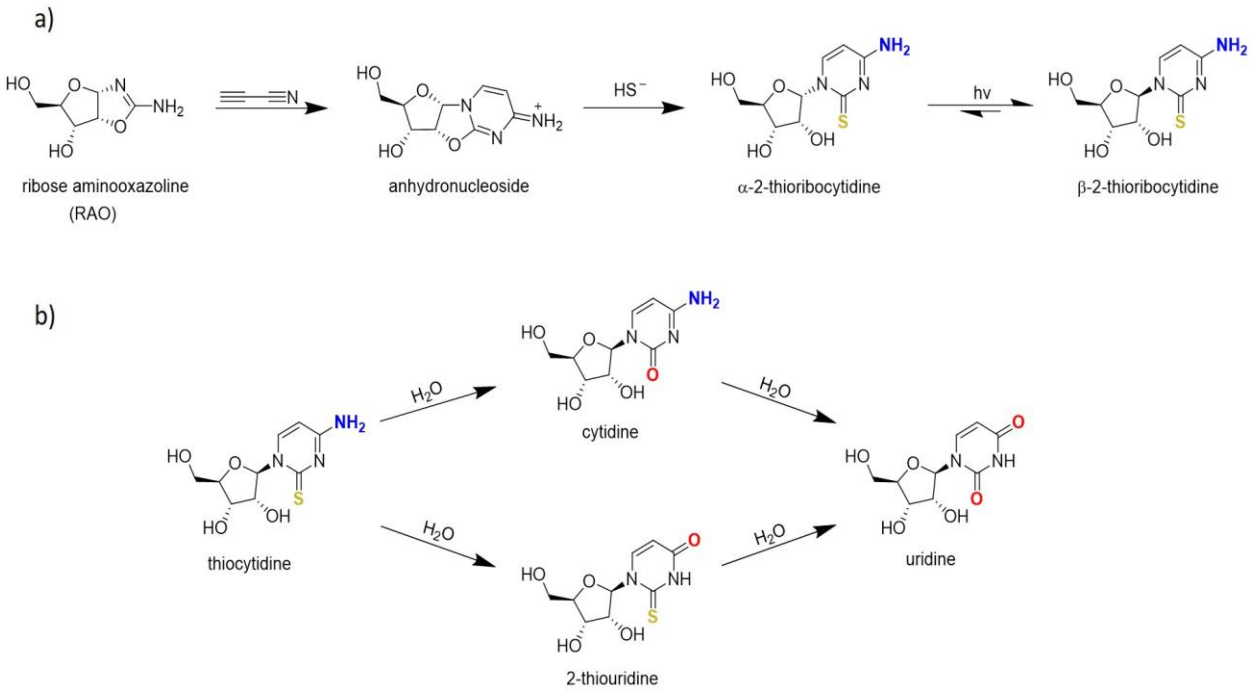
molecules, including hydrogen cyanide, ammonia, and formaldehyde. While the photochemistry of 5-hydroxymethyluracil has not been investigated, the absorption spectra of 5-aminouracil in aqueous solution showed stabilization of the lowest energy $^1\pi\pi^*$ state, resulting in a red shift of approximately 30 nm at the maximum wavelength relative to uracil.[119,145] Time-resolved results demonstrated longer decay lifetimes for the 5-substituted amino- and hydroxyl-uracil derivatives compared to uracil,[119] indicating that the amino and hydroxy substituted derivatives follow slower relaxation pathways than the canonical nucleobase. Although these derivatives do not have ultrafast relaxation dynamics, their ability to be synthesized under prebiotic conditions and hydrogen bond with a base pair could still make them plausible prebiotic candidates. Interestingly, 5-hydroxymethyluracil has been shown to further react with small molecules present in early Earth, resulting in the formation of amino acid analogs.[146]



Scheme 1.7 Structures of ribose aminooxazoline (RAO), arabinose aminooxazoline (AAO), oxazolidinone thione (AOT), and ribose oxazolidinone thione (ROT).

Research by Janicki et al.[147] expanded the investigation of RNA precursors looking into alternative heteroatoms, identifying pentose aminooxazolines and oxazolidinone thiones as key candidates (see, Scheme 1.7). It was suggested that these molecules were chemically evolved into present RNA nucleotides with reactions driven by UVR. A important property of these molecules is that they can overcome the problem of glycosylation of the canonical nucleobase in a harsh prebiotic environment. While there is still some debate on whether D-ribose could efficiently be made under prebiotic conditions, evidence suggest that the direct reaction of ribose with a canonical nucleobase does not occur.[148–150] However, it has been shown that aminooxazoles, such as 2-aminooxazole, can react with glyceraldehyde to yield in high quantity regiospecific glycosylation.[151–153] Arabinose aminooxazoline (AAO) was found to have negligible absorption at longer wavelengths than 200 nm. Therefore, it would have been highly photostable due to early

Earth's atmospheric water and CO_2, shielding radiation below this wavelength.[22,154] Similarly, the derivatives arabinose oxazolidinone thione (AOT) and ribose oxazolidinone thione (ROT) were investigated using UV-irradiation experiments because they are expected to have been under constant UVR exposure given that their absorption spectra are red-shifted relative to that of AAO. After 16 hours of UV irradiation at 254 nm, 68% and 47% of AOT and ROT remained, respectively. To examine the relative photostability of AOT, irradiation of adenine was done simultaneously under 254 nm excitation, revealing that 80% of AOT and 100% of adenine remained following irradiation.[147] These results, along with *ab initio* calculations, support the plausible participation of these oxazolines as precursors of RNA nucleotides.



Scheme 1.8 Plausible synthesis of thio- and canonical nucleobases from precursor molecule RAO. (a) Ribose amionoxazoline (RAO) reacts with cyanoacetylene to yield anhydronucleoside. Upon thiolysis, α-2-thioribocytidine is formed, which can undergo photoanomerization to efficiently produce the more favored beta-enantiomer. (b) Following hydrolysis, β-2-thioribocytidine can form cytidine and 2-thiouridine, which can both be further hydrolyzed to yield uridine. Adapted from ref.[155,156].

Interestingly, ribose aminooxazoline (RAO, Schemes 1.7 and 1.8a) produces 2-thioribocytidine upon reaction with cyanoacetylene followed by thiolysis.[155] 2-Thioribocytidine can then serve as a precursor to canonical nucleosides cytidine and uridine, as well as 2-thiouridine (Scheme 1.8b).[156] These sulfur-substituted nucleosides were also found to phosphorylate under prebiotic conditions via hydrogen sulfide mediated photoreduction to yield nucleotides or initiate the synthesis of deoxynucleosides. Given these observations, and the fact that thiobases are still

found in transfer RNA, the photochemistry of thionucleosides should also be considered. The absorption spectra of substituted thiobases is red shifted compared to that of the canonical nucleobases, thereby stabilizing the lowest-energy $^1\pi\pi^*$ and $^1n\pi^*$ excited states.[157,158] The red shifting results in the absorption of UVR all the way into the UVA region. Derivatives including 6-thioguanine, 2-thiocytosine, 4-thiothymine, 2-thiouracil, and 4-thiouracil have been investigated in aqueous solutions.[157,159,160] These thiobases were found to undergo ultrafast ISC to the triplet manifold in near unity yields.[161] The high triplet yields could have played an important role during prebiotic conditions by leading to the formation of nucleobases[162,163] or by reacting with other molecules to yield more photofit RNA precursors.

Similarly, 2-aminoazole derivatives, such as 2-aminooxazole (AO), 2-aminoimidazole (AI), and 2-aminothiazole (AT), have been implicated as RNA precursors. Using a model prebiotic atmosphere, Sasselov and coworkers estimated relative degradation rates under prebiotic era conditions.[164] The highest relative rate of photodegradation was reported at 225 nm for AO, at 215 nm for AI, and at 265 nm for AT. These relative rates were used to estimate the total rate of destruction and to obtain a half-life for each molecule. A half-life of 7, 26, and 99 hours were estimated for AO, AT, and AI, respectively, suggesting that these molecules could be photostable only below a range of 7 to 100 hours under prebiotic conditions. The experimental results indicate that AO is significantly more photoreactive than AI or AT. However, AO may still have played an important role in prebiotic chemistry because its photoreactivity is expected to depend on its concentration and chemical environment, among other factors.

1.4 Role of temperature on the chemical stability of the canonical nucleobases and some plausible proto-RNA monomers

How the photostability may be affected by temperature is important to consider due to some uncertainty on the environmental conditions of early Earth in the ocean and on land.[131] Interestingly, 24DAPy has been synthesized in good yield under prebiotic conditions, where subsequent hydrolytic deamination can produce cytosine and isocytosine.[156] Both cytosine and isocytosine can then undergo an additional deamination reaction to yield uracil.[165] These reactions are of great interest due to hydrolytic instability of cytosine under prebiotic conditions, having a half-life of just 19 days at 100 °C, 34 years at 25 °C, and 17,000 years at 0 °C.[166] Even though cytosine primarily shows ultrafast S_0 repopulation following UVR, its instability in a prebiotic environment indicates it may not have been present in large quantities. In contrast, uracil could have been present in more significant amounts as an alternative candidate in the early genetic code.

Similarly, the faster electronic relaxation of Hyp to S_0 relative to adenine,[70,140] suggests that it may possess greater photostability to UVR. However, looking at the structural stability, Hyp was found to undergo ring opening with a half-life of 12 days at 100 °C and 5,000 years at 0 °C,[166] while adenine was found to have half-lives of 1 year and 6×10^5 years at 100 °C and 0 °C, respectively. Likewise, xanthine was found to have a half-life of 0.4 years at 100 °C, whereas

guanine is only slightly longer at 0.6 years. Collectively, it is evident that further research is needed to investigate the effect of temperature on the photochemical stability of both the canonical nucleobases and prebiotically plausible molecules.

1.5 Photochemistry of RNA oligomers and RNA damage

π-stacking and hydrogen bonding interactions between nucleobases are essential to stabilize the folded structures in RNA strands. However, the π-stacking and hydrogen bonding architecture complicates the understanding of the excited states of RNA oligomers due to the possible delocalization of the electronic energy over multiple nucleobases and the possibility of hydrogen and proton transfer events upon UVR. As widely discussed for DNA,[10,34,35,167,168] the delocalization energy in RNA oligomers yields longer-lived excited states than monomeric components.[34,94,96,169–172] The short and longer-lived lifetimes are associated with the decay of the excited state population from unstacked and π-stacked complexes, respectively. The relative yield of the longer decay lifetime is reduced at elevated temperatures that disrupt base stacking,[35,96,172] supporting direct association with close nucleobase-nucleobase π-stacking interactions.

Although the excess electronic energy is thought to spread over multiple chromophores within an RNA strand, the spatial extent to which the energy can delocalize is still debatable.[96,173] The additional OH group at the 2'-position of the ribose causes the nucleobases in RNA to arrange in an A-form conformation, differing from the B-form helix found in DNA. Currently, there is no known method to determine the delocalization length within oligomers with certainty. However, some information can be deduced through circular dichroism (CD) and transient absorption. Using a synchrotron radiation source to obtain CD spectra in the vacuum ultraviolet (VUV) region, the intensity of specific bands can be monitored to study the electronic coupling between nucleobases.[173–175] Recent CD spectra focusing on cytosine and adenine homopolymers of varying lengths showed increased delocalization length for RNA polymers than their DNA analogs after excitation at 278 nm. Specifically, intrastrand nucleobase coupling was found up to eleven and five nucleobases for adenine and cytosine ribonucleic homopolymers, respectively. In contrast, coupling was limited to only the nearest neighbor for DNA homopolymers.[173] However, these CD results should be contrasted with transient absorption experiments conducted by Kohler and co-workers[96,171] on DNA and RNA adenine homopolymers after excitation at 260 nm and 266 nm, respectively. In these experiments, the S_0 recovery signals monitored at 250 nm for di, tetra, and poly(A) strands showed the same kinetics. This suggests that excitation energy is delocalized to only the nearest neighbors, regardless of polymer chain length or that the S_0 recovery lifetimes are not sensitive to the delocalization length. Therefore, more work is needed to ascertain the role of delocalization length on the excited state dynamics in RNA polymers.

Regardless of the precise delocalization length, the longer-lived signals observed in RNA oligomers have been assigned to excimer and exciplexes, which can undergo interbase charge transfer, followed by charge recombination and relaxation to S_0.[34,94,96] Alternatively, UVR can

lead to a small but measurable photodegradation in RNA.[176–183] The investigation of RNA photodamage is important because UVR can lead to the formation of photoproducts, including pyrimidine (6-4) pyrimidinone dimers [(6-4)PP],[176] cyclobutane pyrimidine dimers (CPDs), photodimers, and photohydrates.[177–183] Nowadays, many of these photoproduct mutations in DNA are identified and repaired by enzymes within the cell; however, some remain and are precursors to cancer. Consequently, the formation of photoproducts in DNA has been studied to a large extent.[62,184] However, less work has been performed regarding RNA photodamage and possible photoproduct repair processes.[179–183]

Other experiments comparing the photochemistry of single stranded DNA and RNA adenine homopolymers yielded similar results, in which excited state delocalization is greater in RNA.[174,175] Interestingly, however, the CD spectra of poly(dA) following irradiation at 248 nm showed the growth of a new broad band around 290 nm that was absent in the spectrum of poly(A). The change in CD spectra of poly(dA) was also coupled to an increase in the absorbance over the entire absorption spectrum window, out to 350 nm.[185,186] The results suggest that photoproducts are formed in about 10-fold greater yield in poly(dA) than poly(A). Back-to-back irradiation experiments under ambient and nitrogen purged conditions resulted in the same change in spectra for poly(dA), possibly ruling out the involvement of the triplet state in photoproduct formation.[185] However, the exact mechanism of formation is still unknown. Kumar et al. identified the formation of two dimeric adenine photoproducts following irradiation at 254 nm in poly(dA) but not in poly(A).[187] These photoproducts, similar to the pyrimidine photodimers, are formed from covalent unsaturated bonds of nearby adenine monomers. Photoaddition of the N7-C8 double bond of the 5'-adenine across the C5 and C6 positions of the 3'-adenine is proposed to yield an azetidine intermediate species. From this intermediate photoadduct, competing modes of azetidine ring fission yield the two photodimers.[188,189]

The available results suggest that the A-type structure of RNA is more compact and rigid, leading to longer delocalization lengths.[174,175] Similarly, UVC irradiation experiments in tandem with HPLC-MS/MS analysis on RNA hairpins showed a significant decrease in photoproduct formation compared to DNA.[190] While the main chromophores in DNA and RNA are the same, the chromophores stacking arrangement relative to one another are different based on the higher ordered structure adapted by each, respectively. Thus, the more rigid RNA structure may not allow room for the structural rearrangements necessary for the formation of photodimers, making its formation more energetically costly. Alternatively, the larger delocalization length of the excitation energy in RNA oligomers may not lend itself for the favorable formation of photodimers compared to DNA.

In addition to photodimerization reactions, another important photoproduct intrinsic to pyrimidine monomers are the photohydrates.[191–193] The yield of photohydrate formation in aqueous solution depends on pH, excitation wavelength, secondary/tertiary oligomeric structure, and microenvironment, as well as on the identity of the substituted pyrimidine base.[192] The

formation of photohydrates, and their reversal to the monomeric constituents using heat and high concentrations of hydrogen or hydroxyl ion, has been tracked using UV-vis spectroscopy and HPLC.[191,194] Loss of chromophore absorption at approximately 260 nm for uracil derivatives occurs as photohydrate production increases. Both uracil and 3-methyluracil, which are protonated at N1, showed increased photohydrate quantum yields with decreasing pH, whereas N1 substituted uracil derivatives show less pH effect. Conversely, the quantum yield was substantially lowered upon methylation at C5, as in thymine, compared to all analogous uracil derivatives, including 1-methyluracil (1MU), Urd, and UMP. The sugar and phosphate groups were also shown to have an enhancing effect on the formation quantum yield, with poly(U) > poly(dU) > UMP > Urd = dUrd > 1MU > Ura.[191]

Several mechanisms for the formation of pyrimidine photohydrates have been proposed to include the vibrationally excited S_0.[63,179,191,195,196] However, it is important to highlight that all are thought to involve the excited singlet state. This differs from the proposed mechanism of CPDs, which is thought to be formed through an excited triplet state in un-aggregated monomeric constituents in aqueous solution. Evidence of the participation of the excited triplet state in the formation of CPDs was provided from the observation that their quantum yield of formation decreases upon the addition of oxygen.[191] However, investigations of CPD formation in homothymine oligomers have shown that CPDs are primarily formed through the excited singlet state.[167,197–199] While significantly less work has been done to characterize CPD formation in RNA,[200–206] dimer formation was considerably greater in polyU than in a double strand of polyA·polyU where the rate of hydration was suppressed by a factor of 10 in the latter case.[194,207,208] This lends support to the notion that secondary structure (sequence) and its resultant influence on tertiary structure, can have a determining factor on photochemical outcome of polynucleotides. Additionally, photodimer formation for both poly(dU) and polyU was found to decrease with an increase in the irradiation wavelength.[207] Although photodamage can occur in RNA oligomers, a significant knowledge gap remains regarding how RNA secondary and tertiary structures affect photoproduct formation.

1.6 Conclusions

UVR from the sun can be envisioned as a catalytic agent of change in the broader context of the chemical origins of life. Sunlight can promote chemical transformations through which the canonical RNA molecules can be produced. Evidence is growing regarding the important role that UVR may have played in the formation of the canonical nucleobases in aqueous environments at the surface of the young Earth. The high photochemical stability of the RNA monomers is consistent with UVR as a preeminent environmental selection pressure during the prebiotic Era. Of course, there should have been a balance between photochemical formation and photochemical degradation of relevant prebiotic molecules. Invoking a photochemical formation of nucleobases also requires considering plausible mechanisms by which the inventory of prebiotic molecules could have been protected from persistent or excessive UVR. In this context, UV shielding has been proposed as a plausible mechanism to increase the half-time of otherwise photoreactive

precursors. A UV-shielding mechanism can be accomplished by self-shielding (accumulation), by the presence of other UV-absorbing molecules competing for photon absorption and hence acting as molecular sunscreens, or by intermolecular quenching of otherwise reactive excited states.

Todd et al.[209] recently demonstrated that the UV-induced degradation half-live of 2-aminooxazole could be increased two- to threefold by increasing its concentration (self-shielding) or by adding RNA nucleosides into the solution (UV-shielding). This suggests that the formation of moderate amounts of nucleobases may have allowed for the protection of important photoreactive molecules acting as prebiotic intermediates in the synthesis of the canonical nucleobases. If that is the case, sunlight could have allowed for a favorable balance between UV-promoted photochemistry and the accumulation of essential prebiotic molecules. Evidently, the photochemistry of prebiotically plausible molecules needs to be evaluated further. This evaluation should also consider possible UV-shielding or UV-promoting mechanisms such as photosensitization in the presence of complex mixtures of molecules that can affect their intrinsic photochemistry. In particular, the elucidation of the electronic relaxation and the photochemical reaction pathways of prebiotically plausible molecules and their complex mixtures, combined with the measurements of photodegradation rates under controlled experimental conditions, could help to establish reasonable environmental constraints for their conceivable participation in the formation of the RNA monomers (or other relevant biomolecules such as amino acids and lipids) during the prebiotic Era.

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