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PREBIOTIC SYNTHESES OF THE RNA BASES: A CRITICAL ANALYSIS

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In the RNA world scenario (Gilbert, 1986), life began with the spontaneous assembly of a self-replicating RNA molecule. In order to avoid the problems associated with prebiotic ribose synthesis (Shapiro, 1988), some authors have preferred to invoke an RNA-like polymer, which replaces ribose by an alternative backbone, but retains the RNA bases. To explore the viability of this assumption, we have previously assembled data concerning the possible prebiotic availability of adenine (Shapiro, 1995). We will now consider the same arguments with respect to guanine, cytosine and uracil.

In the route commonly cited for prebiotic guanine synthesis (Sanchez, et al, 1968) 4-aminoimidazole-5-carboxamide (AICA) (0.01 M) is allowed to condense with cyanogen (0.2 M) to give guanine in yields of up to 43%. Oligomerization of HCN is suggested as a source for AICN (Oro' and Kimball, 1962). This route has many difficulties, however. The reported yields of AICA from oligomerization of concentrated HCN (2.2 M or higher) have been less than 0.1%. Such HCN concentrations are unrealistic, however, and it is not clear that any AICA would be formed at the much lower concentrations likely to be present in the prebiotic oceans (Stribling and Miller, 1987). It would be necessary, in addition, that formaldehyde concentrations be substantially less than those of cyanide, as formaldehyde sequesters cyanide as glyconitrile (Schlesinger and Miller, 1973). This synthesis also utilized 0.2 M cyanogen. The claim was made that cyanogen can be generated from cyanide, but this was not demonstrated. At 25°, and pH 9 (the usual pH for HCN oligomerization) the half life of cyanogen can be estimated from existing data (Wang, et al, 1987) to be less than 30 seconds. It seems unlikely tht the trace amounts of AICA generated by slow HCN oligomerization would react with cyanogen before it hydrolyzed or reacted with other components of the mixture.

A recent synthesis of cytosine and uracil has been cited in the media as a solution to the problem of the prebiotic origin of these substances

(Browne, 1995). Cyanoacetaldehyde is allowed to react with high concentrations (1-20 M) of urea at 100° C to afford cytosine in good yield (Robertson and Miller,1995). Uracil would be formed by deamination of cytosine. The authors justify the prebiotic significance of their results with a model in which urea would be concentrated from sea water in drying lagoons and on beaches. This model has serious handicaps: The time needed to concentrate urea by evaporation would be very large, compared to the time then available for reaction. During this extended concentration period, both cyanoacetaldehyde (Ferris, et al, 1994) and urea (Kemp and Kohnstam, 1956) would be consumed by hydrolysis.

In addition, the hydrolytic instability of cytosine would appear to preclude *any* role for it in the origin of life. The half life for deamination of cytosine at 25° C is only a few hundred years (extrapolated from data of Garrett and Tsau, (1972), and the reaction would continue after the cytosine had been converted to a substituted cytosine derivative.

The evidence that is available at the present time does not support the idea that RNA, or an alternative replicator using the RNA bases, was present at the start of life. This conclusion could be reversed if a prebiotic simulation were devised that produced all of the bases in good yield under a single set of conditions, using a plausible combination of water, atmospheric components, and minerals. In the absence of such a demonstration, more attention should be given to origin-of-life theories that do not require the RNA bases.

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