SYNTHESIS OF THE COENZYMES, ADPG, GDPG AND CDP-ETHANOLAMINE UNDER PRIMITIVE EARTH CONDITIONS

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Following up on our studies concerning the prebiotic synthesis of phosphorylated metabolic intermediates (Mar et al., 1986, Mar et al., 1987), we report here on the non-enzymatic synthesis of the coenzymes adenosine diphosphate glucose (ADPG), guanosine diphosphate glucose (GDPG) and cytidine diphosphoethanolamine (CDP-ethanolamine) under conditions regarded to have been prevalent on the Archean Earth. These compounds were synthesized by reacting simple precursor molecules under aqueous solutions, at moderate temperatures and short periods of time, using urea and cyanamide as condensing agents. The latter compounds are considered to have been present in significant amounts on the primitive Earth, and have been previously used in our laboratory in the non-enzymatic synthesis of several other important biochemical compounds.

The experimental procedure was as follows, ADPG was obtained by heating G1P, ATP in the presence of cyanamide or urea for 24 hours at 70 °C, the cyanamide mediated reaction of G1P and GTP under the same conditions yielded GDPG, however only traces of GDPG were detected in this reaction when urea was used as the condensing agent. CDP-ethanolamine was synthesized by reacting a mixture of ethanolamine phosphate and CTP for 24 hours at 70 °C in the presence of cyanamide, the use of urea as a condensing agent in this reaction was unsuccessful. The separation and identification of the reaction products was carried out by paper chromatography, thin layer chromatography, high performance thin layer chromatography, high performance liquid chromatography, both normal and reverse phase, UV spectroscopy, enzymatic assays and acid hydrolysis.

The reaction conditions for these syntheses and their respective yields are shown in the following table, and as can be seen the conditions have been designed to simulate a plausible prebiotic Earth environment. The reactions conditions used in these studies include, aqueous solutions, moderate temperatures, mediated by condensing agents and short periods of incubation. Moreover, the best yields of the coenzymes are obtained at slightly

basic pH, which is the accepted pH of the primitive oceans.

Reactants	Conditions	Products	Yields %
ATP + GTP	Cyanamide 70 °C, 24 hrs	ADPG	9.8
	Urea 70 °C, 24 hrs	ADPG	2.1
GTP + G1P	Cyanamide 70 °C, 24 hrs	GDPG	12.5
	Urea 70 °C, 24 hrs	GDPG	traces
CTP + P-ETOHNH$_3^+$	Cyanamide 70 °C, 24 hrs	CDP-ETOHNH$_3^+$	8.6

Due to the the mild conditions employed, and to the relative ease of these reactions, these studies offer a simple system for the non-enzymatic synthesis of phosphorylated high energy metabolic intermediates. Furthermore, these coenzymes, which are essential in metabolic pathways and have not been extensively modified throughout evolution are nucleotide derivatives, and therefore, may be remnants of an early autopoietic system with catalytic and replicating properties based on RNA (White, 1976, White, 1982, Lazcano, et al., 1988). In other words, these nucleotide cofactors may be metabolic fossils of the RNA world (Weiner, 1987).

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