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Interaction between N-Phospho-Amino Acids and Nucleoside in Aqueous Medium

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Abstract: Nucleosides were phosphorylated with different N- (O, O-diisopropyl) phosphoryl amino acids to give nucleoside mono phosphates in aqueous solution. 2', 3', and 5'-isomers had been confirmed by comparison with authentic samples on the basis of HPLC analysis. The conversion percentage of nucleoside indicated that N- (O, O-diisopropyl) phosphoryl aspartic acid reacted with adenosine and guanosine at a much higher rate than other kinds of N- phosphoryl amino acids, while phosphorylation of cytidine and uridine was relatively easy by using N- (O, O-diisopropyl) phosphoryl threonine. The result could give some clue to the prebiotic code origin of nucleic acid and protein.

Keywords: N-Phospho-amino acids, nucleoside mono phosphate, phosphorylation, uridylyl uridine (UpU), origin, chemical evolution.

The biosynthesis of nucleic acid, one of the most important bio-macromolecules, is a highly elegant process, which involves the participation of many enzymes and energy carriers, such as ATP[1], while chemical synthesis of oligonucleotides generally involves complicated protecting and deprotecting processes[2]. In the previous work, nucleotides and oligonucleotides were directly formed by the reaction of N- (O, O-diisopropyl) phosphoryl threonine and uridine in anhydrous pyridine[3]. So N- (O, O- diisopropyl) phospho-amino acid (DIPP-aa) was proposed as a model compound for the common origin for the prebiotic protein and nucleic acid[4-5]. In this letter, the reaction between nucleosides (A, G, C, and U) and different DIPP-aa in aqueous solution was investigated, and the result showed that the reactivity depended on the kind of amino acids and nucleosides.

Different N- (O, O-diisopropyl) phosphoryl amino acids ($\geqslant$98% HPLC purity) were allowed to react with nucleosides, adenosine, guanosine, cytidine and uridine respectively in aqueous medium for six days. The reaction products were subjected to reversed phase HPLC separation, with UV detector set at 260 nm. Comparing the retention time with the authentic sample demonstrated that nucleoside mono phosphates 2'-XMP, 3'-XMP and 5'-XMP (X represents A, G, C, and U) were formed in all the reaction systems. The nucleoside conversion percentage of the reaction, which was calculated by HPLC peak area normalization method (**Table 1**), could reflect the reaction rate between different DIPP-aa and nucleosides.

Table 1 Nucleoside conversion percentage between different DIPP-aa and nucleosides

	A	G	C	U
DIPP-Ala	15.01	10.37	9.85	10.47
DIPP-Leu	15.14	10.13	9.89	8.35
DIPP-Asp	33.42	30.47	9.91	10.63
DIPP-Glu	14.72	17.93	11.95	11.25
DIPP-Arg	11.87	11.05	10.48	8.78
DIPP-Ser	12.85	9.20	9.68	9.23
DIPP-Thr	11.71	12.98	14.76	13.42
DIPP-Cys	11.52	10.95	10.48	9.68
DIPP-Pro	11.85	9.13	10.64	9.42
DIPP-Phe	4.56	7.07	11.69	1.98

From **Table 1**, it can be seen that DIPP-Asp reacted with adenosine and guanosine to a much higher degree (conversion percentage 33.42% and 30.47% respectively) than other kinds of DIPP-aa. Meanwhile, phosphorylation of cytidine and uridine was relatively easy by using DIPP-Thr. The experiments were carried out for three times and HPLC analysis confirmed the consistency and repeatability. The result implies that some inherent relationships might exist between N- (O, O- dialkyl) phosphoryl amino acids and nucleosides.

When the reaction between DIPP-Thr and uridine was carried out at 0°C, oligomerization of nucleosides formed dinucleotide. It was proved by reversed phase and size exclusion HPLC that dimer nucleotide uridylyl uridine (UpU) was formed and the 2'-5' UpU (0.085% RP-HPLC yield) was the major dimer product.

These findings could provide some possible clue to the origin and chemical evolution of genetic code in the prebiotic process.

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