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Stereoselective Prebiotic Nucleotide Synthesis for Threose Nucleic Acid

Hyo-Joong Kim

Firebird Biomolecular Sciences LLC, 13709 Progress Blvd., Alachua, FL 32615

* hkim@firebirdbio.com

The glycosidic bond formation from sugar and nucleic bases is one of the fundamental problems in prebiotic chemistry for the RNA world hypothesis. However, nucleoside synthesis from sugar and nucleobases has not been successful except the marginal success by Orgel and his coworkers.¹ Recently two studies (Sutherland² and Carell³ groups) showed pyrimidine and purine nucleotide and nucleoside can be synthesized in plausible prebiotic condition. In those syntheses, the nucleobases were formed after their precursors were attached to sugar then converted to ribo-nucleotide or nucleoside.

Threose nucleic acid (TNA) is considered to be one of the plausible prebiotic genetic polymers.⁴ In search of the prebiotic pathway of TNA building block (threose nucleoside or nucleotide), the reaction of threose and adenine was investigated. The reaction of threose and adenine gave condensation products in very high yield as an anomeric mixture (more than 70%) but the reaction occurs at the amino-group of the adenine. However the reaction of threose-1,2-cyclic phosphate and adenine provided threose-adenine nucleoside-2'-phosphate stereoselectively (Fig 1). This reaction did not proceed without divalent metal ions (Mg or Ca) which were almost certainly available prebiotically. The prebiotic synthetic pathway of threose-1,2-cyclic phosphate is well known in the literature.⁵ The α -hydroxy aldehyde can be phosphorylated by amidotriphosphate in the presence of magnesium chloride. Threose (one of the α -hydroxy aldehydes) can be easily converted to threose-1,2-cyclic phosphate in high yield. Also, threose can be formed by the dimerization of glycolaldehyde under prebiotic plausible condition in high yield.

In this presentation, the details of the synthesis of threose-adenine nucleotide and structural proof of the compound will be discussed.

References:

[1] Fuller WD, Sanchez RA, Orgel LE (1972) *J Mol Evol* 1:249-257. [2] Powner MW, Gerland B, Sutherland JD (2009) *Nature* 459: 239-242. [3] Becker S, Thoma I, Deutsch A, Gehrke T, Mayer P, Zipse H, Carell T (2016) *Science* 352: 833-836. [4] Schoning K, Scholz P, Guntha S, Wu X, Krishnamurthy R, Eschenmoser A (2000) *Science* 290: 1347-51. [5] Krishnamurthy, R, Guntha, S, Eschenmoser, A (2000) *Angew. Chem.* 39: 2281-2285.

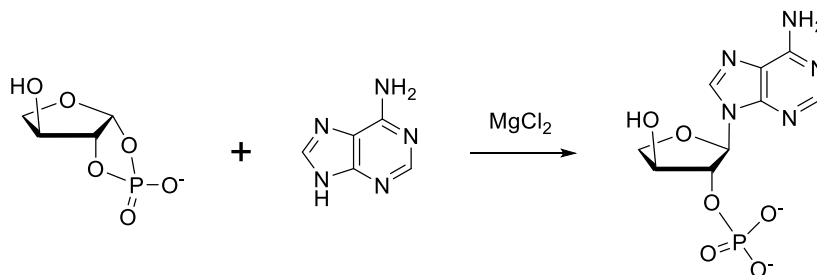


Figure 1 Reaction of threose-1,2-cyclic phosphate and adenine in the presence of magnesium ion provide threose-adenine nucleoside 2'-phosphate