Heterolytic N-N bond formation catalyzed by copper sulfide toward nonenzymatic uracil skeleton synthesis at the origin of life

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Pursuing the origin of nucleotides under early earth environments is significant for understanding the origin of life in the frame of “RNA world” hypothesis. Biosynthesis of pyrimidine ribonucleotides along the *de novo* pathway starts from *N*–carbamoyl aspartic acid (NCA) synthesis with aspartate (Asp), carbamoyl phosphate (CP) and enzyme ATCase. So far chemical experiments under prebiotic conditions nonenzymatically mimicked NCA synthesis using various carbamoyl compounds such as urea and CP. In both reactions, urea and CP are converted into isocyanic acid which is essential for synthesizing NCA. Previous works hypothesized ponds under open atmosphere as the reaction site.
Hydrothermal vents (HVs) have also attracted attention as reaction sites that can continuously supply biomolecular materials. It is proposed that chemical evolution progressed through multi-step chemical reactions in many pores inside the HVs as “natural flow synthesis reactor”. So far, amino acid synthesis catalyzed by metal sulfide minerals has been demonstrated through chemical experiments simulating HVs. However, as far as we know, prebiotic nucleobase synthesis scenario along the *de novo* pathway driven by sulfide mineral surfaces has never been demonstrated.
In this study, we investigated the possibility of isocyanic acid synthesis by utilizing CuS mineral and $^{15}NO_2^-$ as the activator of *N*–methylurea in phosphate-buffered aqueous media at pH 7 at 25˚C. To demonstrate the heterolytic N–N bond formation which occurs simultaneously with the formation of isocyanic acid, hetero-coupled dinitrogen $^{29}N_2$ (^{14}N–^{15}N) was analyzed by gas chromatography-mass spectrometry (GC–MS). The amount of produced $^{29}N_2$ was followed for 16 days. Without *N*–methylurea or CuS, $^{29}N_2$ was not detected even after 16 days passed. On the other hand, as the concentration of *N*–methylurea increased from 100 mM to 400 mM, the produced amount of $^{29}N_2$ also increased at any measured time. This result shows heterolytic N–N bond formation between *N*–methylurea and $^{15}NO_2^-$, which implies simultaneous isocyanic acid formation catalyzed by CuS mineral.

Keywords: The origin of life, Nucleobase, Isocyanic acid, Copper sulfide, Heterolytic N–N bond formation

