

**UREA: A KEY PREBIOTIC REAGENT IN THE ORIGIN OF NUCLEIC ACIDS.** C. Menor-Salvan<sup>1</sup>, D. Fialho<sup>1</sup> and N. V. Hud<sup>1</sup>, <sup>1</sup>School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA 30033 (USA). Cesar.menor@chemsityr.gatech.edu.

**Introduction:** Urea is produced in model prebiotic reactions from one carbon sources, such as cyanide, methane, or carbon oxides [1], as well as in astrochemistry experiments [2]. Previously, the atmospheric formation of reactive species (using methane or acetylene as precursors) over a urea solution subjected to freeze-thaw cycles has been shown to result in the formation of pyrimidines, triazines, and purines [3]. The formation of a eutectic urea solvent in the ice interstices is a key phenomenon, in a complex chemical system not explained by the classic mechanisms of HCN polymerization or cyanoacetylene formation [4]. These results are of renewed interest with the recent discovery of high-yield model prebiotic reactions for the formation of triaminopyrimidine and barbituric acid glycosides; nucleosides that are capable of forming assemblies with each other and with triazines (suggested possible pre-RNA bases). Taken together, these results suggest an early role of urea-derived non-canonical nucleobases in RNA chemical evolution [5].

**Results and Discussion:** A urea and malonic acid solution (0.1M urea and 0.02M acid) was subjected to dry-wet cycles, diluting with pure water in each cycle, at 60°C over the course of two weeks. The analysis by GCMS of the resulting viscous mixture showed the formation of barbituric acid and other pyrimidines. Crystals of intergrown barbituric acid and 2-amino-4,6-dihydroxypyrimidine were separated from solution. Using a urea+guanidine eutectic solvent under the same conditions, 2,4,6-triaminopyrimidine was formed in good yield, together with barbituric acid and other pyrimidines, as well as diaminopurine and 8-hydroxyguanine. These results constitute a prebiotic synthesis of barbituric acid and aminopyrimidines from urea, demonstrating that a variant of Grimaux and Traube's syntheses could be arranged in water-based solvents and mild, prebiotically plausible, conditions and suggests a new mechanism to the prebiotic formation of nucleobases. To test whether the urea concentration is the key factor involved in the formation of bases promoted by environmental cycles, we irradiated (UV 258 nm) an acetylene atmosphere over a concentrated (8M) urea solution at 60°C over the course of one week. The products also reveal the synthesis of pyrimidines, purines, and cyanuric acid (Fig. 1). The formation of purines is favored at pH>8, suggesting a synthesis through formylation at the C5 amine position of aminopyrimidines.

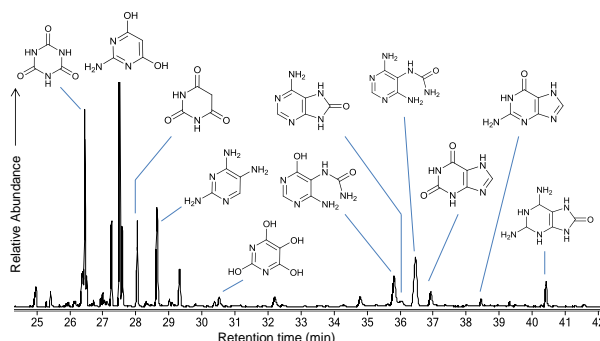
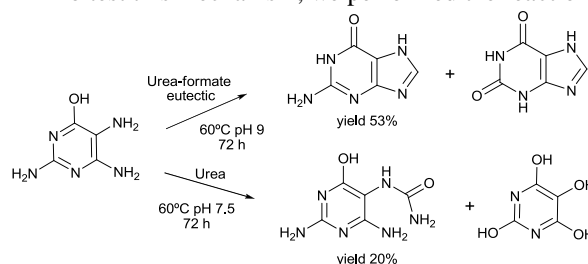


Fig 1. GCMS analysis of nucleobases formed using urea and acetylene as precursors (m/z range 325-460)

To test this mechanism, we performed the reaction:



The exaltation of nucleophilic character of the C5 amine were the basis also of a recently described pathway to the prebiotic formation of adenosine [6] and we showed that could be involved in the origin of purines. The prebiotic formation of urea-based eutectic solvents by gradual concentration in small water reservoirs, promoted by natural environmental cycles could constitute a scenario where robust prebiotic chemistry led to the formation of a relevant nucleobase chemical space for the origin of RNA in a variety of conditions. Furthermore, urea-based eutectic solvents promote the phosphorylation of nucleosides [7]. Thus, model prebiotic reactions are increasingly pointing to urea as a key precursor and catalyst for the origin of nucleic acids.

#### References:

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