SYNTHESIS AND SELF-ASSEMBLY OF MODEL PROTO-NUCLEOSIDES. D. Fialho[1,2], B. J. Cafferty[1,2], I. Gallego[1,2], R. Krishnamurthy[2,3], and Nicholas V. Hud[1,2], [1]School of Chemistry and Biochemistry, [2]NSF-NASA Center for Chemical Evolution, Georgia Institute of Technology, Atlanta, GA 30332, USA, [3]Department of Chemistry, The Scripps Research Institute, La Jolla, CA 92037, USA.

Introduction: The RNA world hypothesis remains one of the most influential theories regarding the origin and early evolution of life. Nevertheless, the prebiotic synthesis of RNA polymers remains a persistent challenge to RNA being accepted as a product of prebiotic chemistry, as opposed to being a product of chemical or biological evolution [1].

In an early attempt to synthesize RNA in model prebiotic reactions, Orgel and co-workers demonstrated that adenosine can be formed by drying and heating adenine with ribose, but the other canonical nucleobases did not exhibit glycosidic bond formation [2,3]. More recently, Powner et al. demonstrated that cytidine can be produced by the concerted synthesis of the cytosine base and the ribose sugar, thereby circumventing the need for glycosidic bond formation [4,5].

Considering the possibility that RNA evolved from an earlier genetic polymer, Miller and co-workers demonstrated that urazole (presented as a potential ancestor of uracil) readily forms nucleosides with ribose in good yield [6]. Subsequently, 2-pyrimidinone, a base that only differs from uracil and cytosine by one exocyclic group, was also shown to form nucleosides when dried and heated with ribose [7]. Thus, it appears that nucleoside formation might not have been such an obstacle in the origin of life if the nucleobases of the earliest ancestral polymers of RNA (or proto-RNA) were different from those found in RNA today.

Results: We are actively investigating the chemical space around the nucleobases of RNA for heterocycles that might also be amenable to glycosidic bond formation in model prebiotic reactions. We have recently discovered the 2,4,6-triaminopyrimidine (**TAP**) will form nucleosides when dried and heated with ribose [8]. Although free ribose exists primarily in its hexose form in aqueous solution, it was found that the major product of **TAP**+ribose reactions is a *C*-nucleoside with ribose in the β-furanose form, which is the same form of ribose found in RNA. This major product was named **TARC**.

The formation of nucleosides by **TAP** was also intriguing because this molecule has long been known to form hydrogen-bonded assemblies with cyanuric acid and barbituric acid [9,10], two plausible prebiotic molecules. Unlike the free bases or mononucleosides of RNA, **TARC** and cyanurinc acid form ordered assemblies in water. For example, AFM images of a **TARC**-cyanuric acid sample in a phosphate-borate buffer reveals fibers that are up to 1 μm in length. Similar fibers are also seen when cyanuric acid is mixed with the *unpurified* products of a **TAP**+ribose reaction (Figure 1).

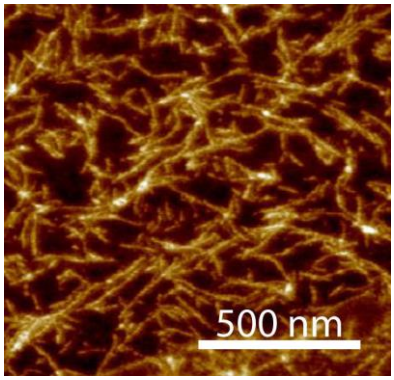

Figure 1: AFM topography image of assemblies formed by a crude **TAP**+ribose reaction mixed with cyanuric acid in a phosphate-borate buffer.

Our most recent studies have identified additional heterocycles that also form nucleosides with ribose in model prebiotic reactions. These model proto-nucleosides self-assemble into fibers that are similar to those shown in Figure 1. The charcterization of these molecules and their assemblies will be discussed. A current goal of this research is to use the preorganization provided by the self-assembly of these model proto-nucleosides to facilitate their polmerization into model proto-RNA polymers. Progress towards this goal will also be discussed.

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