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## Synthesis and characterization of a putative pre-RNA World ribonucleoside precursor

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**Introduction:** Nonenzymatic oligomerization of RNA molecules from non-activated monomers, such as AMP and GMP has been shown to occur under volcanic geothermal conditions. <sup>[1]</sup> This process is however prone to issues mainly due to the propensity of these monomers to undergo depurination when subjected to polymerization under high temperature and low pH conditions prevalent in a volcanic geothermal system. This has further lend credence to a prevailing hypothesis that RNA must have been predated by prebiotically more plausible and stable oligomers made of ‘alternate’ monomers, which might have formed with relative ease on the early Earth. In this regard, our lab has reported the formation of a Barbituric acid (BA) containing ribonucleotide using ribose monophosphate (rMP) and barbituric acid as the starting materials; <sup>[2]</sup> a result that was also demonstrated in a simultaneous study conducted by the Hud group. <sup>[3]</sup> In this study, it was shown that dehydration and rehydration of ribose monophosphate (rMP) and barbituric acid at low pH resulted in the formation of both C- and N-glycoside analogs. Furthermore, it was observed that this product mixture also resulted in oligomerization under acidic condition in which the traditional N-glycosides of purines tend to lose their informational moiety. Therefore, the C- and/or N-glycoside analogs of BA could potentially serve as pre-RNA World candidates for understanding the abiotic oligomerization of RNA like polymers that might have populated such worlds.

In the aforementioned oligomerization it was observed that all possible isomers of the BA nucleotide were formed in the reaction (i.e.  $\alpha/\beta$  anomers of both the C-and N-glycoside). Additionally, the yield of the above reaction was such that the isolation of the desired monomer in substantial quantity was limiting. Therefore, in order to have a suitable starting material to, both, characterize the oligomerization reaction and to demonstrate information transfer potential with extant RNA, chemical synthesis of a BA containing nucleoside is highly desirable. In the present study we report a chemical synthesis scheme for BA containing ribonucleoside (N- and C-linked glycoside) analogs. To achieve this, we have synthesized the ribose donor in a few steps with just D-ribose sugar using sophisticated protection and activation chemistry. <sup>[4]</sup> Subsequent synthesis of BA ribonucleoside will be accomplished by performing glycosylation reaction between the ribose donor and BA, followed by a deprotection step. The resultant product will be used to systematically characterize the oligomerization of the C-and N-glycosides of BA under pertinent prebiotic reaction conditions. Eventually, we also aim to study information transfer capability from such an oligomer with the molecules of a putative RNA World.

**References:** [1] Mungi CV and Rajamani S (2015) *Life (Basel)* 1:65–84. [2] Mungi CV et al. (2016) *Physical Chemistry Chemical Physics* 18:20144–20152. [3] Cafferty BJ et al. (2016) *Nature Communications* 7:11328. [4] Mishra B et al. (2016) *Angewandte Chemie International Edition* 55: 7786–7791.