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Continuous processing approaches for prebiotic syntheses of 2-amino-oxazole and subsequent ribo/arabino furanosyl amino-oxazolines

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Introduction: Glycolaldehyde dimer and cyanamide have been postulated to be the first compounds necessary for the formation of DNA/RNA nucleosides. Under mild conditions, these two molecules can react to form 2-amino-oxazole. Upon exposure to (DL)-glyceraldehyde, 2-amino-oxazole can cyclize to form a precursor to (DL)-ribose/deoxyribose, the backbone of DNA and RNA.[1] However, batch/flask conditions do not offer optimized production of 2-amino oxazole and its derivatives. We report a continuous processing approach towards the synthesis of 2-amino-oxazole under ambient temperatures and pressures using water as solvent produces a mean yield of 68%. Higher temperatures and pressures do not appear to impact yields; however, the presence of base such as NaOH or KH_2PO_4 can have a significant effect: in the presence of 0.25 M NaOH yields are optimized to >80%, with the base promoting the essential elimination. Subsequent reaction of 2-amino-oxazole with (DL)-glyceraldehyde in water under continuous processing conditions provides the ribo/arabino furanosyl amino-oxazolines in yields ranging from 29 to 68 %. An enantioselective approach to furanosyl amino-oxazolines and a telescoped approach to these important RNA precursors will be addressed.

[1] a) Powner, M. W., Gerland, B., and Sutherland, J. D. (2009) *Nature* 459, 239–242; b) Sutherland, J. (2016) *Angew. Chem. Int. Ed.* 55, 104-121.

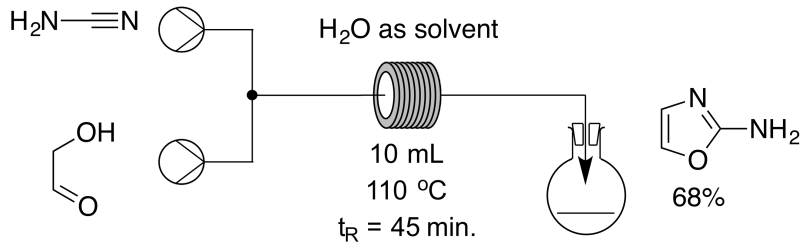

Figure 1 – Continuous processing approach toward the synthesis of 2-amino-oxazole.