Pyrazine Nucleic Acids: From Small Molecules to Proto-Informational Polymers

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Abstract. This project uses organic chemistry principles to identify which small molecules in certain types of conditions would foster the emergence of polymers capable of chemical evolution. The small molecules chosen are alanine amide and pentoses, which are able to undergo cyclocondensation through an amadori rearrangement mechanism to form pyrazine acyclic nucleosides. Pyrazines share features similar to adenine and thymine.

We have synthesized pyrazinone nucleosides and nucleic acids. The acyclic backbone of pyrazine nucleic acids (PzNA) are similar to glycol nucleic acid (GNA), but with minimal gauche interactions (Figure 1). Evaluating the base-pairing capabilities of PzNA with self-strands, RNA, and DNA, enables us to understand the different backbone conformations accessible to PzNA. Current results suggest a pH- and pKa- dependent keto-enol tautomerization in pyrazin-2-one heterocycles, which we hypothesize to compromise base-pairing interactions. The keto-enol tautomerization is believed to play a role in the origin of genetic selection and mutation. While our results show that PzNA is not optimized for base pairing fidelity, PzNA may be considered to be a "starter system" that enables processes that begets chemical evolution.

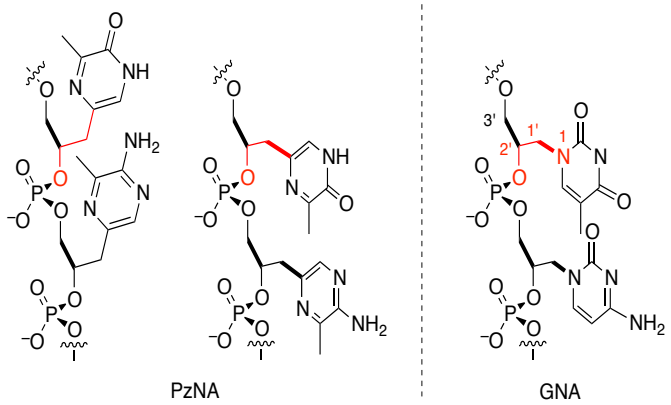

Figure 1. Structural comparisons of pyrazine nucleic acid (PzNA) to glycerol nucleic acid (GNA). The red highlights indicate the interaction between the C–O and the C–N (C–C) bonds in GNA (and PzNA). The gauche effect in GNA restricts the conformation around the C_1'–N_1 bond, while such an effect is absent in PzNA allowing access to both conformations.