

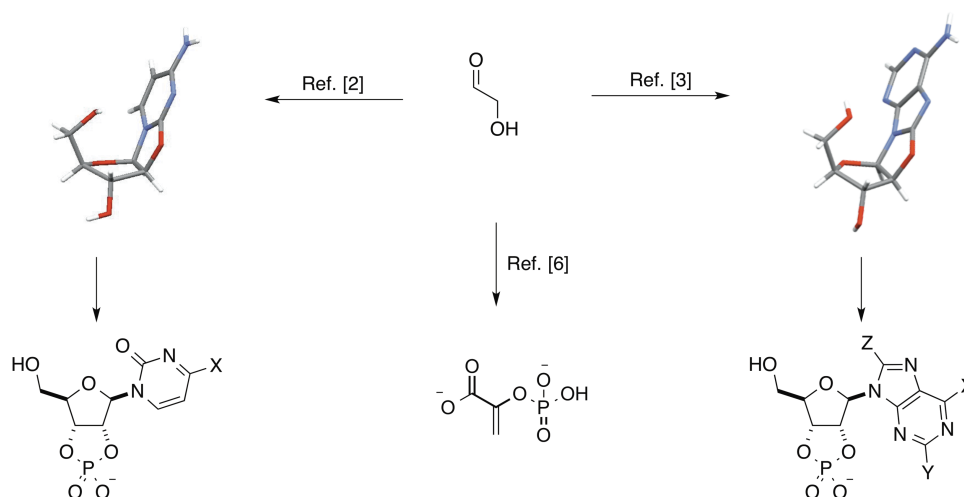
On the Chemical Divergence of Information and Energy

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Introduction: Nucleotides are the cornerstone of all biology and the linchpin of information transfer and inheritance. They are involved in all universally conserved biological processes and RNA genes are ubiquitously used to root phylogenetic trees and define interspecies evolutionary distances. However, the fundamental chemical reactivity that could have led to the “molecular biologist’s dream”—a pool of homochiral nucleotides—at the chemical origins of life remains an unmet scientific challenge.

quently phosphorylation in water has been a highly prized goal for prebiotic chemistry. To address this problem, we have developed a site-specific, chemoselective method for phosphorylation of nucleotide precursors in water as a part of a novel multicomponent reaction.[5] Our reaction avoids the limitations of the more widely investigated electrophilic phosphate activation.



Scheme 1: Divergent synthesis of three key elements of biology; pyrimidine ribonucleotides, purine ribonucleotides and phosphoenol pyruvate. X-ray structures of the key 2'-anhydronucleotide intermediates that control phosphorylation and stereochemical inversion. X=NH₂,OH; Y=H,NH₂,OH; Z=H,OH.

Nucleotide Synthesis: In 2009 and 2010, Powner et al published a prebiotically plausible synthesis of activated pyrimidine ribonucleotides.[1][2] This synthesis was heralded as a major advance in elucidating the chemical origins of life, but left a significant gap for a complementary purine synthesis. We now demonstrate a divergent synthesis of pyrimidine and purine ribonucleotides; our new route develops a novel masked-aldol reaction, exploits sulfide activation with “click-like” efficiency, and allows stereoselective and regiospecific purine glycosylation by construction of the nucleobase on a sugar scaffold in water.[3].

Phosphorylation in water: “Why biology chose phosphates” is a long-standing problem at the heart of elucidating the origins of biochemistry.[4] Conse-

Phosphoenol pyruvate synthesis: Phosphoenol pyruvate is biology’s highest energy phosphate and has a central role in metabolic pathways, including glycolysis and gluconeogenesis, the shikimic acid pathway, carbon fixation in plants and phosphoryl transfer in bacteria. A high-yielding chemoselective synthesis of phosphoenol pyruvate in water will also be demonstrated from the same chemical feedstocks used to synthesise ribonucleotides.[6]

References:

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