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A Non-enzymatic Analog of Pyrimidine Nucleobase Biosynthesis

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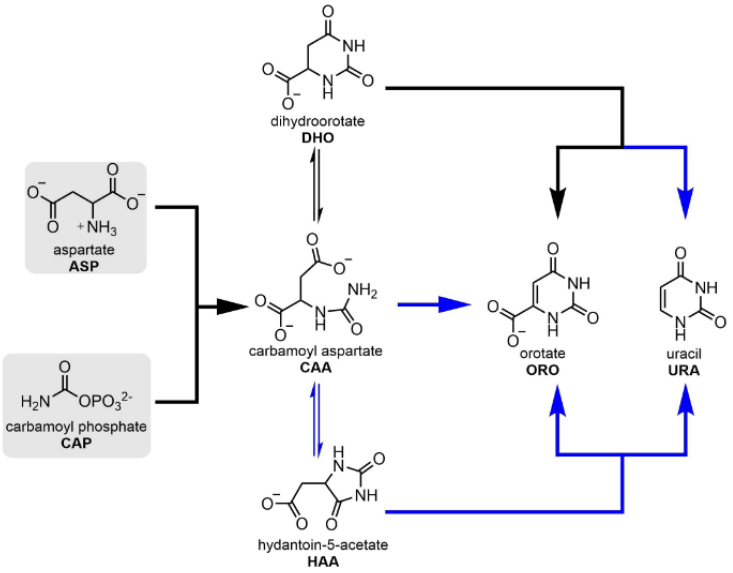

Who are the corresponding authors and what are their research areas?

The corresponding authors are:

1) Joseph Moran

Joseph Moran is professor at University of Strasbourg. He is a synthetic organic chemist interested in catalysis in complex systems and the origin of biological metabolism. His research applies concepts from systems and supramolecular chemistry to catalysis and the chemical origins of life. His work has shed light on how metabolism may have arisen in prebiotic waters before the onset of Darwinian evolution.

What is the main claim of the article?

Main claim: The authors have uncovered a non-enzymatic analog of pyrimidine nucleobase biosynthesis in water at 60 °C without the need for UV light, starting from aspartate and carbamoyl phosphate. Some of the steps are promoted or inhibited by specific transition metals or pH values. Moreover, a one-pot synthesis was successfully carried out, varying pH and adding metals at specific times.

Relevance: The present work can be viewed as a first experimental step toward incorporating genetic molecules into a self-consistent metabolic framework for the origin of life.

How is it demonstrated?

Demonstration: The research is proofed by ^{1}H-NMR and LC-QTOF-MS analyses.

What are the typical experimental conditions?

- To a 2 mL microcentrifuge tube was added 1 mL of starting material (1 equiv., 8.5 µmol) from stock solution, then added other reactants.
  The tube is sealed and stirred at 60 °C (sand bath) for a proper time (e.g. from 6 to 16 h), then the mixture is subjected to work up (vortex and centrifugation)
- NMR sample: prepared by taking 400 µL of the supernatant and adding 200 µL of 6.8 mM solution of internal standard (dimethyl sulfone in D_2O).
- LC-QTOF-MS/MS analysis, 150 µL of the supernatant and 50 µL of 8.6 mM solution of internal standard (maleic acid in MilliQ water)

Which are the key related papers?

Kamila B. Muchowska, Sreejith J. Varma, Joseph Moran, Nonenzymatic Metabolic Reactions and Life's Origins, *Chem. Rev.* 2020, 120, 15, 7708–7744 https://doi.org/10.1021/acs.chemrev.0c00191