

Radical-assisted pathways for the prebiotic formation of nucleobases from plausible precursors

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Abstract

The perplexity of how the building blocks of life formed from simple and abundantly-available precursors on early earth has baffled scientific community for centuries. In order to get a clearer picture, the present study proposes and investigates plausible ammonia-assisted, free radical pathways for nucleobase formation from starting precursors such as cyanoacetaldehyde, urea, cyanoacetylene and cyanamide. Particularly, density functional theory is used to obtain optimized geometries and zero-point vibrational energy corrected electronic energies of reactants, transition states, intermediates and products along the reaction pathways in the gas phase at B3LYP/6-311G(d,p) level, as well as in the water (dielectric constant of 78.3) and ammonia (dielectric constant of 22.4) using the IEFPCM framework. Our proposed mechanisms are characterized by a smaller number of precursors and relatively lower barriers compared to previously reported reactions with other prebiotic precursors [1-3]. Features such as barrier-less formation of imidazole intermediate and favorable contribution of prebiotic enolate chemistry highlight the plausibility of the presently proposed pathways. The pathways are most suitable to environments like prebiotic earth (for purine formation) and present-day Titan (for purine and pyrimidine formation) where radical reactions are rendered feasible by continuous influx of UV and cosmic radiations. Overall, our analysis proposes kinetically accessible routes to nucleobases formation, and will hopefully contribute towards understanding the relevance of these precursors in prebiotic reactions. References: Jeilani, Y. A. Williams, P. N. Walton, S., Nguyen, M. T. (2016) *Phys. Chem. Chem. Phys.*,18, 20177-20188. Jeilani, Y. A. Fearce, C. and Nguyen, M. T. (2015) *Phys. Chem. Chem. Phys.*,17, 24294-24303. Nguyen, H. T. Jeilani, Y. A., Hung, H. M. and Nguyen, M. T. (2015) *J. Phys. Chem. A*, 119, 8871-8883.



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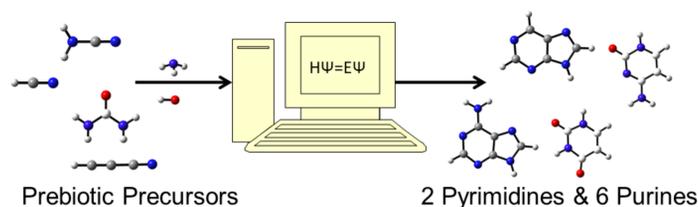
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Introduction

- Canonical nucleobases form an indispensable component of present day genetics.
- Their formation pathways on early earth have attracted attention as well as debate.
- Quantum chemical calculations can complement experimental studies on prebiotic nucleobase formation and provide some insight.
- UV radiations on primitive earth coupled with the detection of radicals in laboratory experiments suggest that nucleobase formation followed radical-based routes
- Thus, our group proposes and investigates plausible free radical pathways for nucleobase formation using quantum chemical tools.



Computational Details

- Geometry optimization and calculation of electronic energies of reactants, transition states, intermediates and products were performed in the gas (B3LYP/6-311G(d,p)) phase.
- Stationery points on the reaction surfaces as minima (reactants, intermediates and products) or saddle points (transition states) were characterized using vibrational frequency calculations.
- IRC scans confirmed the right transition state connecting reactants to products.

Formation of Purines

- Various purines can be formed through radical-assisted pathways from starting precursors *i.e.* cyanamide and cyanoacetylene via five-membered intermediate, 4-cyanoimidazole in the presence of ammonia
- Skeletal components of 4-cyanoimidazole can be solely made from initial precursors.

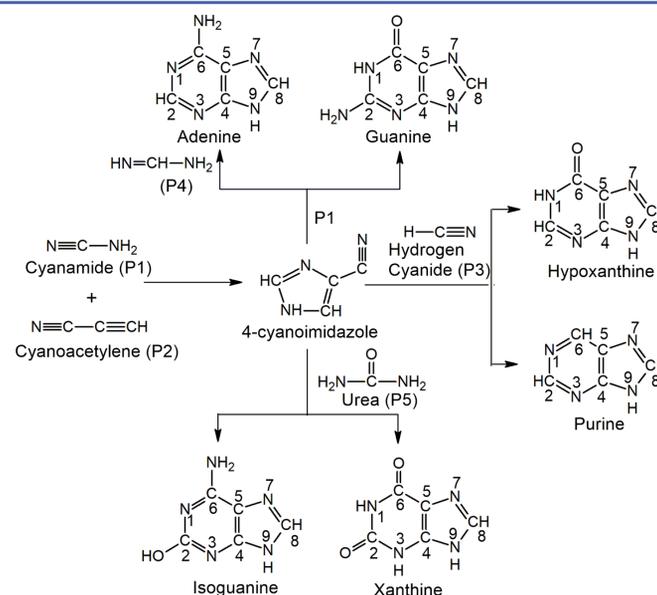


Figure 1. Formation of purines from cyanamide (P1), cyanoacetylene (P2), HCN (P3) and urea (P5).

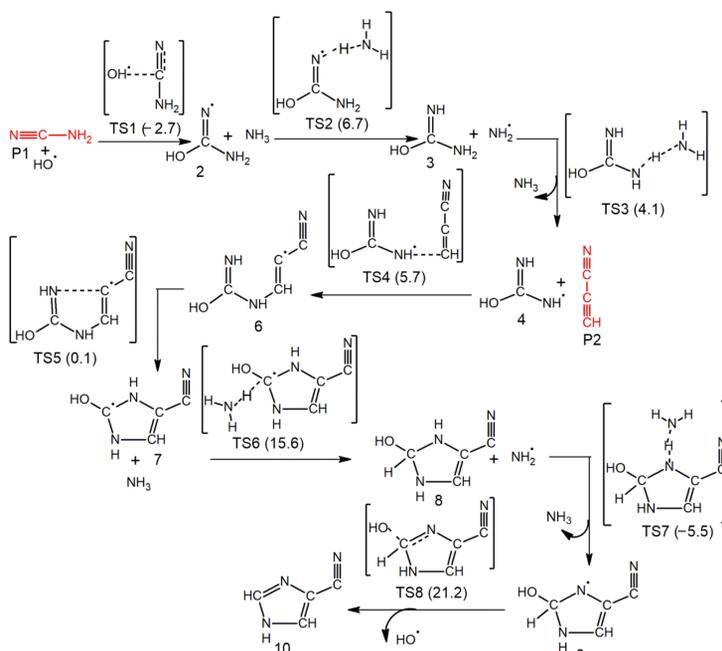


Figure 2. Formation of 4-cyanoimidazole **10** from cyanamide (P1) and cyanoacetylene (P2). Relative energies (in kcal mol⁻¹) of TSs in parenthesis.

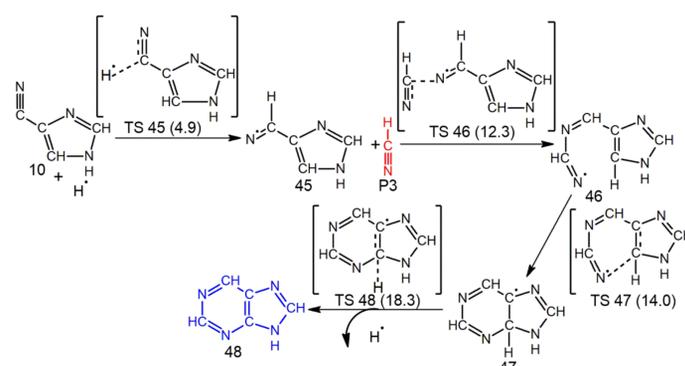


Figure 3. Formation of Purine **48** from 4-cyanoimidazole **10**. Relative energies (in kcal mol⁻¹) of TSs in parenthesis.

Formation of Pyrimidines

- Starting precursors- cyanoacetaldehyde and urea.
- Cyanoacetaldehyde acts as a source of -NH₂ group of cytosine and of the -C=O group of uracil and the NH-CO-NH skeleton of urea converts into N-C-N segment of the pyrimidine ring.

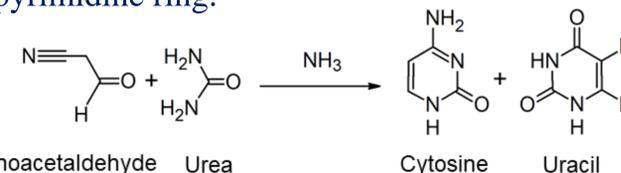


Figure 4. Formation of cytosine and uracil from cyanoacetaldehyde and urea.

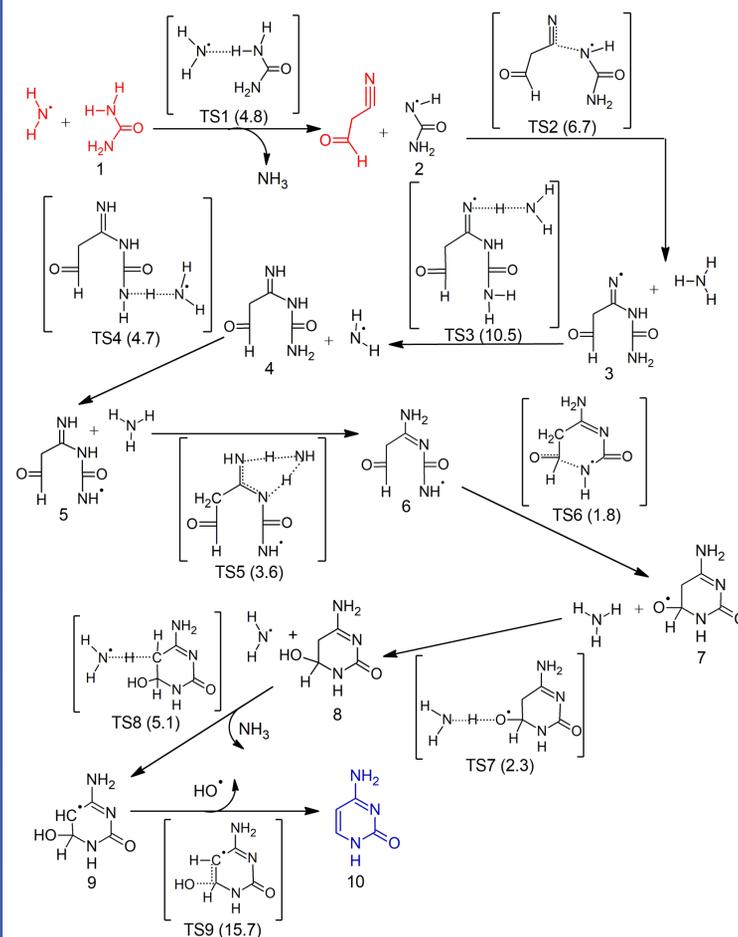


Figure 5. Formation of cytosine **10** from cyanoacetaldehyde and urea. Relative energies (in kcal mol⁻¹) of TSs in parenthesis.

Note: In figures 1–4, reactants are in red and product in blue colour.

Acknowledgements

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