THE ROUTE FROM FORMAMIDE TO SIMPLE RIBOZYMES – STRUCTURES AND MECHANISMS FROM ADVANCED COMPUTATIONAL STUDIES

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The formamide-based synthesis of nucleic acid components offers a new alternative for the origin of informational polymers.[1,2] This chemistry represents an elegant and continuous way from simple prebiotic precursors up to short catalytic oligonucleotides. Since this multistep synthesis proceeds in a very complex reaction mixture, it is very difficult to study its mechanism using purely experimental methods. Our presentation is aimed to illustrate that in such complicated cases computational chemistry might be instrumental to provide an atomic-level insight into the mechanistic details of the reactions. We show that the applicability of theoretical chemistry tools is not restricted to a simple verification of experimentally suggested reaction mechanisms, and, when properly done, computational methods can be used to propose mechanistic models on their own. This is especially important when experimental methods do not allow for obtaining accurate structural information on the reaction complexes under investigation.

In particular, we address the mechanism of the formamide-based nucleobase synthesis,[1] where our quantum chemical model[3] helped to understand the catalytic role of water molecules.

Further, on the example of the high-energy impact chemistry of formamide,[4] we illustrate, how quantum chemical calculations can help interpretation of experimentally measured vibrational spectra and identification of unknown intermediates.

Finally, using a combination of experiments, state-of-the-art quantum chemical calculations and molecular dynamics simulations, we provide a mechanistic proposal for the emergence of a simple ribozyme-like catalytic activity in short oligonucleotide sequences.[5]

References

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