Density Functional Theory for Organic Chemistry: Tackling the Challenges of Small and Large Molecules

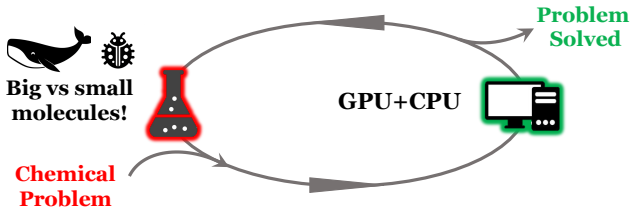
BORIS MARYASIN[1,2], LETICIA GONZÁLEZ[1] and NUNO MAULIDE[2]

[1]*Institute of Theoretical Chemistry, University of Vienna, Vienna, Austria*
[2]*Institute of Organic Chemistry, University of Vienna, Vienna, Austria*
boris.maryasin@univie.ac.at

Recent advancements in quantum chemistry and computational techniques have enhanced our ability to understand and predict organic reactions comprehensively. We showcase the powerful synergy between experimental findings and theoretical understanding, exemplified by current case studies.

For diverse organic transformations, such as novel sulfonium rearrangements [1] or noncanonical Diels-Alder reactions [2], we both elucidate experimental observations and predict more effective reaction pathways by combining density functional theory (DFT) with wave function-based methods. Furthermore, we present an alternative approach for relatively large (ca 250 atoms) molecules, which are challenging for standard DFT structural optimization. For such systems, we integrate several GPU and CPU-based tools in a highly efficient way, enabling us to perform the necessary structural optimization without loss of accuracy.

Overall, we propose a cyclic iterative strategy for refining organic reactions that combines calculations, experiments, and further calculations. Our *in-silico* investigations explain experimental evidence while providing new insights for subsequent experiments and computations.



References

[1] Feng, M.; Mosiagin, I.; Kaiser, D.; Maryasin, B.; Maulide, N. Deployment of sulfinimines in charge-accelerated sulfonium rearrangement enables a surrogate asymmetric Mannich reaction. *J. Am. Chem. Soc.* **2022**, *144*, 13044.

[2] Huang, G.; Guillot, R.; Kouklovsky, C.; Maryasin, B.; de la Torre, A. Diastereo- and Enantioselective Inverse-Electron-Demand Diels- Alder Cycloaddition between 2-Pyrones and Acyclic Enol Ethers. *Angew. Chem. Int. Ed.* **2022**, *61*, e202208185.