

*Computations and Experiments in Synergy: Reaction Development
and the Establishment of Predictive Computational Models*

Owing to tremendous technological advances, computational chemistry has evolved into a powerful tool for the development of reactions used to construct complex molecules. Computational models that allow chemists to predict the selectivity of a reaction are highly sought after because they enable rapid and efficient construction of intricate scaffolds. The first part of the presentation will detail computational studies on the reaction of strained alkynes and arynes with oxadiazinones and the application of this reaction to the synthesis of non-symmetric polycyclic aromatic hydrocarbons. Several mechanistic aspects of the transformation were interrogated using density functional theory (DFT) calculations, including the differing reactivities of non-aromatic strained alkynes versus arynes. Experimental studies also demonstrated the rapid synthesis of polycyclic aromatic hydrocarbons, including tetracene and pentacene scaffolds, using this synthetic platform. The second part of the presentation will center on the development of an asymmetric Ni-catalyzed intramolecular cyclization of lactones to generate spirocyclic scaffolds using a combination of experiments and computations. DFT calculations provide insight on the formation of a Ni-bound lactone enolate that reacts with a pendant aryl nitrile to generate a new spirocyclic quaternary center and β -imino lactone. This work is anticipated to expand the application of Ni-catalyzed nitrile insertion for quaternary center generation and to enable the exploration of new chemical space in drug discovery. Altogether, the establishment of computational models in these two areas of research facilitates 1) the incorporation of arynes and cyclic alkynes in polycyclic aromatic hydrocarbon synthesis and 2) the application of Ni catalysis in the synthesis of spirocyclic scaffolds.