Computational Ligand Design-guided Enantio- and Diastereoselective Cycloisomerization

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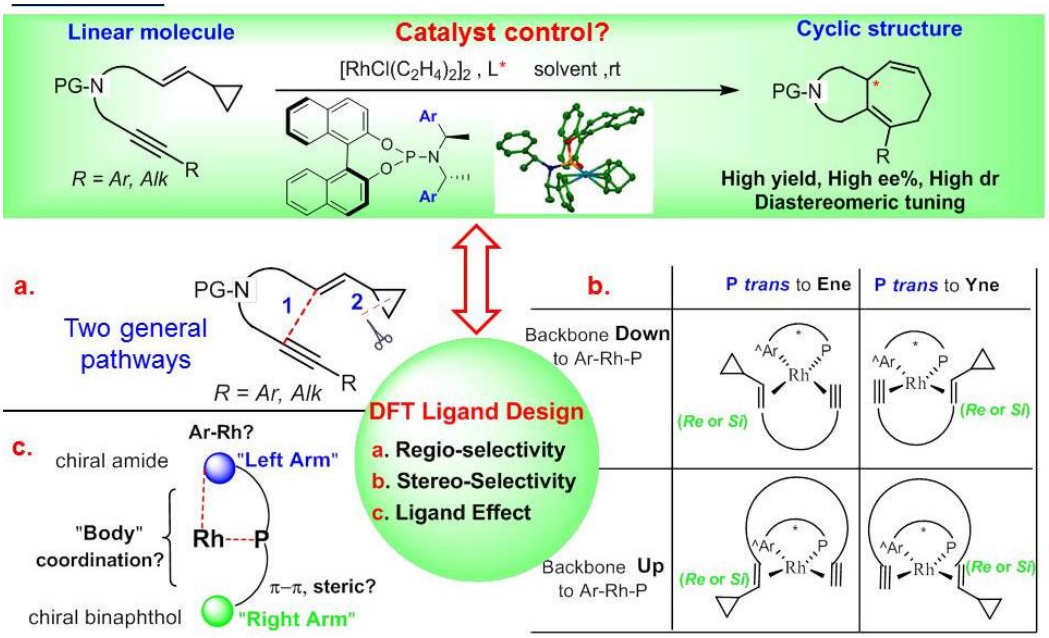
Demand for higher efficiency, economy, and selectivity in the synthesis of novel molecular scaffolds drives organic chemistry. Cycloisomerizations represent ideal methods for the formation of cyclic organic molecules, as they can fulfil all of these criteria. Computational understanding the reaction mechanism of catalyst-control can provide potential ideas to rationalize and guide in the organic synthesis. In collaboration with experimental group (Prof. Edward Anderson in Oxford), we finally realized highly enantio- and diastereoselective catalysed cycloisomerizations of ynamides using new designed chiral phosphoramidite ligands.



Detail mechanism study of Rh-catalyzed cycloaddition has performed to interpret the key factor of reaction selectivity by DFT calculation [1] with solvent correction. Quite noteworthy are the mechanism could be different for the Rh catalysed intermolecular and intramolecular cycloadditions [2]. The results provide a crucial idea for designing new chiral ligands which were tested and proved by our collaborators. These studies set the stage for the development of further computationally-guided enantio- and diastereoselective catalyst systems.

[1] J.-D. Chai, M. Head-Gordon, *Phys. Chem. Chem. Phys* .**2008**, *10*, 6615.
[2]. a) Z.-X. Yu, P. A. Wender, K. N. Houk, *J. Am. Chem. Soc.* **2008**, *126*, 9154. b) Z.-X. Yu, P. H.-Y. Cheong, P. Liu, C. Y. Legault, P.A. Wender, K. N. Houk, *J. Am. Chem. Soc.* **2008**, *130*, 2378.