West Virginia University

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Understanding Conformational Flexibility in Organic Chemistry by Computational Tools

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Analogous to dynamic effects in enzyme catalysis, the conformational flexibility of small molecules might also play a crucial role in organic chemistry. However, the dynamic nature of flexible molecules, exemplified by macrocyclic rings, poses a great challenge for experimental investigations. With advanced conformational sampling tools, we applied computational mechanistic studies to elucidate the effects of conformationally flexible molecules on reaction mechanisms in a) transition metal catalysis and b) peptide macrocyclization. First, in studying the Rh–catalyzed alkene hydroboration reaction, we identified that a conformationally flexible TADDOL-derived phosphite ligand could effectively promote reactivity and control enantioselectivity in different elementary steps. Second, our mechanistic investigation on the intramolecular macrocyclization of peptide aldehydes revealed that conformational flexibility of the macrocyclic peptide ring, along with intramolecular hydrogen bonding, enabled a low energy, stereoselective zwitterionic mechanism. The next challenge in the field is to exploit the conformational flexibility of catalytic peptides, potentially leading to in silico design of new asymmetric peptide catalysts.

Students, meet the speaker after the seminar in a student/postdoc session from 4:45-5:15 pm

Date: Fri, Jan. 20, 2023
Time: 3:30-4:30 pm
Location: Clark Hall 112