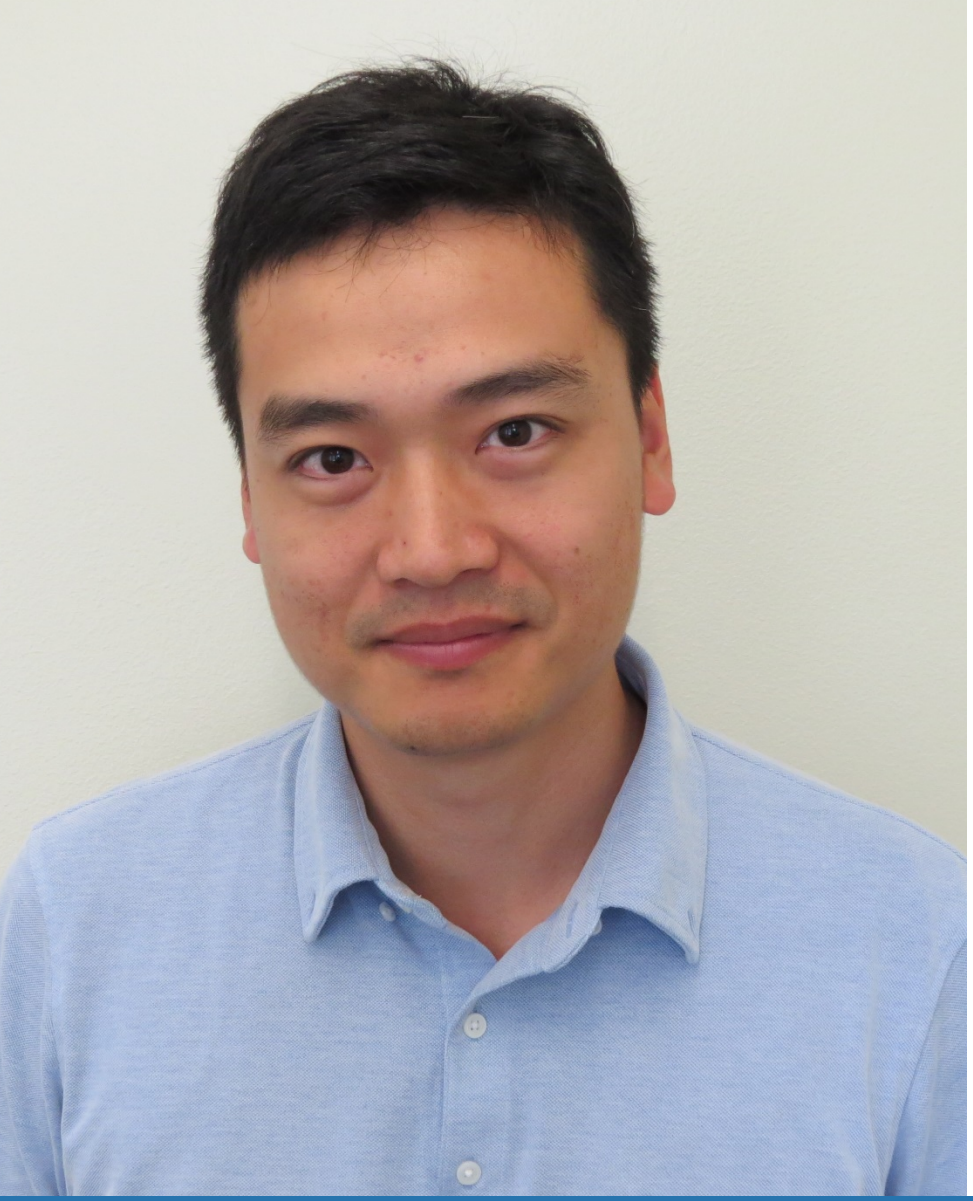

Houk-Jung **Organic Colloquium**

"Strain molecules assist peptide and protein synthesis, a new venue for thiolactones"

Abstract: The broad application of macrocycles has illustrated significant potential as therapeutic agents. 12-membered ring cyclotetrapeptides are particularly attractive entities among all the cyclic peptides. Compared with macrocycles of larger ring size, the characteristic head-to-tail or end-to-end peptidyl backbone provides intrusive structural motif of circular peptides grants distinct biological properties such as resistance to degradation, enhanced conformational stability, and increased epitope interactions with other biomolecules. Ability to acquire a sufficient quantity of high purity of cyclo-tetrapeptide could significantly promote their chemical and biological studies. It is worth noting that the traditional coupling methods to achieve chemical synthesis of macrocycles have been a formidable challenge, requiring fully protected linear precursors and harsh conditions to achieve activation of the C-terminal residue for the cyclization. The harsh activation conditions are required to overcome the entropy barrier during the coupling often lead to epimerization of the C-terminal amino acid residue and peptide oligomerization. The practical strategy to attain macrocycles with a consensus sequence of L-cyclo(Pro-Xxx-Pro-Xxx), where Xxx = Val, Tyr, Leu, Phe, are elusive. There is the urgent need to develop a strategy to prepare circular tetrapeptides. Based on our previously reported β-thiolactone mediated chemistry, iii we were able to construct tetra-cyclic peptides in high yields. The strategy could be applied to produce a broad number of all-L-cyclo-tetrapeptides and the reactions were performed at room temperature in the aqueous buffer. The β-thiolactone furnished cyclization protocol prevented the amino acid epimerization during the cyclization and proved as a powerful general strategy for cyclic peptide synthesis.

Prof. Qiang Zhang
Department of Chemistry
State University of New York, Albany

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Thursday, May 6, 2021
4:00 PM | ZOOM

Questions: jgonzalez@chem.ucla.edu