

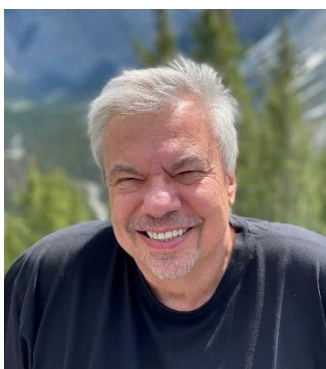
2023-2024

Chemistry Colloquium Series



Friday Sept 15, 1:00pm
SCI 247

Synthesis of Cyclic Bioactive Peptides, Their Analogs and Unusual Amino Acid Building Blocks



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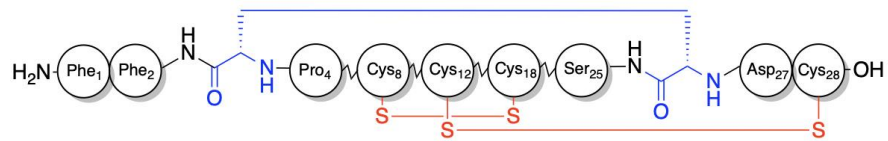
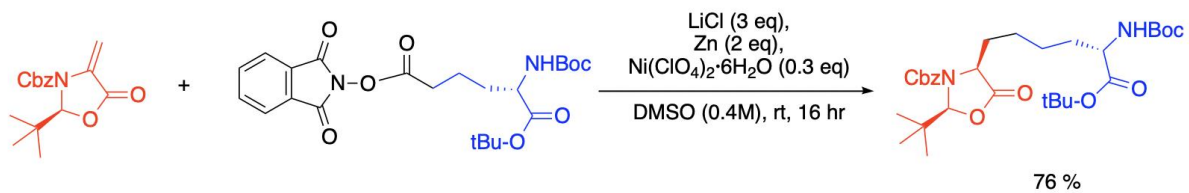
A number of peptides and their analogs have recently been approved as drugs.¹ A recent example includes the orally active Pfizer drug Paxlovid™ (a combination of nirmatrelvir and ritonavir) used to treat COVID19 that had \$18.8 billion in sales in 2022.² Some of our work in this area will be described. There is also interest in new stereospecific syntheses of modified amino acid derivatives as well as of cyclic peptides, which are often more metabolically stable than their linear counterparts. In this regard, substitution of sulfur by methylene (CH₂) in peptide disulfides and in peptide monosulfides (e.g. lantibiotics) can also afford better stability while maintaining activity. One approach to make such compounds involves solid supported peptide synthesis using low loadings of resin to achieve appropriate dilution and incorporation of selectively protected diamino diacids.³ Recent advances in synthesis of natural cyclic bioactive peptides and their analogs with methylene substitutions will be described. One example includes neopetrosiamide, a potential antimetastatic agent, and its carba analogs.⁴

¹ Wang, L. et al. Therapeutic peptides: current applications and future directions. *Signal Transduction & Targeted Therapy*, 7, Article 48 (2022).

² Owen, D.R. et al. An oral SARS-CoV-M^{pro} Clinical Candidate for the Treatment of COVID19. *Science* 10.1126/science.abl4784 (2021).

³ Hsiao, Y.-T. et al. Decarboxylative Radical Addition to Methylideneoxazolidinones for Stereocontrolled Synthesis of Selectively Protected Diamino Diacids. *Org. Lett.* 23, 7270-7273 (2021).

⁴ Pascoe, C.A. et al. Methylene Analogues of Neopetrosiamide as Potential Antimetastatic Agents: Solid Supported Syntheses Using Diamino Diacids for Pre-Stapling of Peptides with Multiple Disulfides. *Org. Lett.* 23, 9216-9220 (2021).



Dicarba Analog of Neopetrosiamide