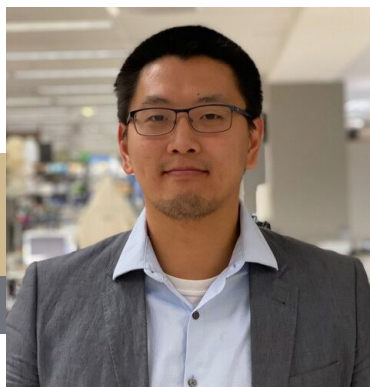


ORGANIC SEMINAR

Chemical and Biocatalytic Synthesis of Amino-Acid Derived Natural Products

Professor Chi Ting

Department of Chemistry
Brandeis University



In this presentation, several chemical and biocatalytic syntheses of amino acid-derived natural products will be discussed. Ribosomally synthesized and post-translationally modified peptides (RiPPs) are a growing class of natural products, many of which possess antimicrobial activity. Sactipeptides are one subclass of RiPPs that are defined by thioaminoketal functional groups. In this presentation, thioaminoketals are assembled through the Markovnikov hydrothiolation of dehydroamino acids using a dithiophosphoric acid catalyst. This method results in the formation of the thioaminoketal directly from peptides containing dehydroamino acids and overrides the inherent reactivity of thiols to undergo conjugate addition. Despite their therapeutic potential, many sactipeptides are stereochemically undefined, preventing their further development into antibiotics. Enteropeptin A is an antimicrobial sactipeptide with a highly unusual thioaminoketal embedded in a thiomorpholine ring. The synthesis of enteropeptin A and its diastereomer enabled the structural elucidation and the determination of the stereochemical configuration of enteropeptin A. In the synthesis, the Markovnikov hydrothiolation reaction was applied in a stereoselective cyclization to form the thiomorpholine ring. These results form a foundation and potential guidelines for the development of stereoselective peptide cyclization.

In the second part of the presentation, a chemoenzymatic synthesis of 13-oxoverruculogen, an anticancer endoperoxide, is achieved using enzymatic C-H peroxidation and transition metal catalyzed C-C bond activation reactions. Biocatalysis is an emerging area of research which incorporates the use of enzymatic reactions to streamline complex molecule synthesis. Central to the synthesis involves the use of a non-heme iron α -ketoglutarate dependent enzyme for C-H oxidation and eight-membered endoperoxide formation. Moreover, the use of a substrate analog for enzymatic endoperoxidation proved essential to accomplish the synthesis of 13-oxoverruculogen.



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James Tarpo Jr. and Margaret Tarpo
Department of Chemistry