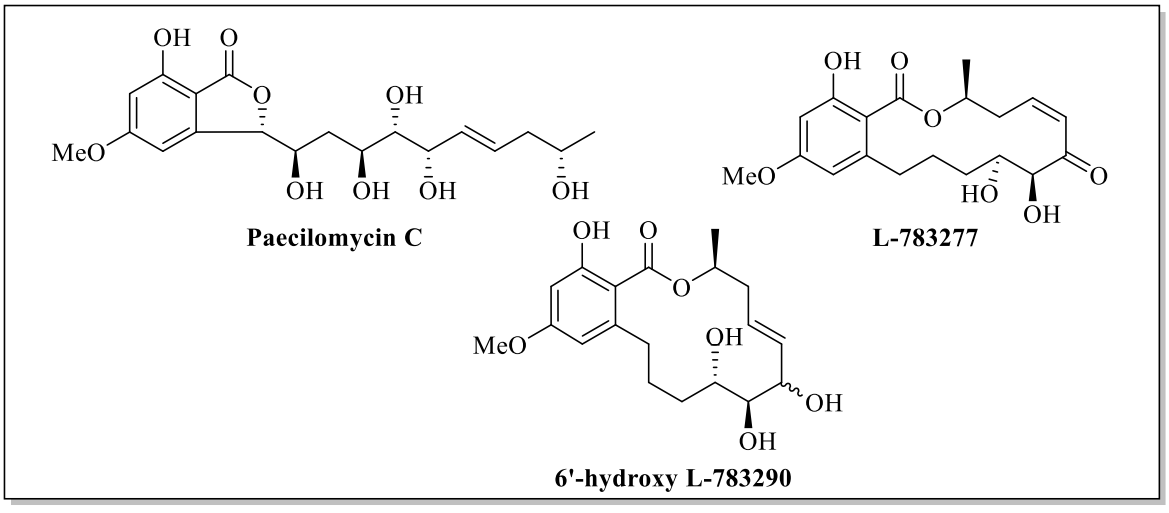
Abstract

Thesis Title: Synthetic Studies Towards Naturally Occurring Resorcylic Acid Lactones Paecilomycin C, L-783277, L-783290 and LL-Z1640-2

Abstract: Resorcylic acid lactones (RALs) are polyketide natural products with a large macrocyclic ring fused to a resorcylic acid residue. The mycotoxins known as resorcylic acid lactones constitute a significant group of 14-membered and benzannulated macrolides that have been isolated from a wide range of microfungi. Some RALs contain an *α*,*β*-unsaturated ketone in the macrocycle unit. RALs containing a *cis*-enone are susceptible to Michael addition reactions with the cysteine residue in the kinase nucleotide-binding site and thus serve as potent inhibitors of several protein kinases. Due to the broad spectrum of bioactivity and the architecturally complex structure of these molecules synthetic organic chemist community have targeted these molecules for total synthesis and biosynthetic study.

The thesis briefly describes successful asymmetric total synthesis of Paecilomycin C and L-783277. Synthetic studies towards the total synthesis of L-783290 and LL-Z1640-2 are also included in this thesis. For the synthesis of the said natural products, we have adopted carboxylate assisted intramolecular nucleophilic ring opening of an epoxide to construct *γ*-lactone framework, Brabander type lactonization to construct 14-membered macrolactone, asymmetric Brown allylation, J-K olefination, Olefin cross-metathesis, and HWE olefination etc.



Key Words: Resorcylic acid lactones, Asymmetric synthesis, Lactonization, Synthetic methods, Total synthesis, Cross metathesis, Natural products etc.