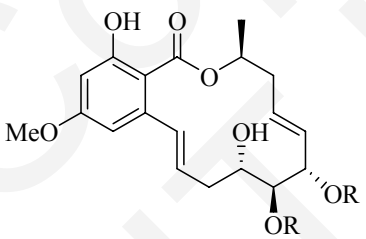
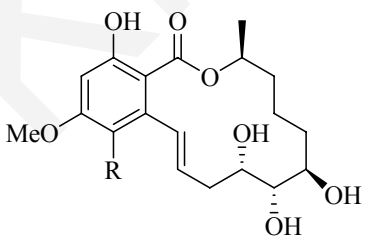
Thesis Title: Synthetic Studies Towards Resorcylic Acid Lactones (RALs) and Stagonolides

Abstract: Resorcylic acid lactones (RALs), a class of mycotoxins, have been known for decades, with the first isolation of radicicol in 1953, more than 30 naturally occurring RALs have been reported which includes recently isolated paecilomycins A-F and cochliomycin A-C. All of these compounds have received considerable attention, due to their potent biological properties, which include antifungal, cytotoxic, antimalarial, antiviral, antiparasitic, estrogenic, nematicidal, protein tyrosine kinase, and ATPase inhibition activities. Stagonolides (A-I) are naturally occurring 10-membered ring lactones isolated in 2008 by and found to have a wide variety of bioactivity. The diverse and important biological functions and curious skeletal features of RALs as well as stagonolides generate interest to synthesize them.

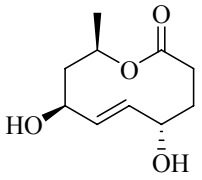
We have focused our attention for the asymmetric total synthesis of recently isolated RALs and stagonolides by adopting lipase catalyzed kinetic resolution (EKR), metal-enzyme combined dynamic kinetic resolution (ME-DKR), various types of asymmetric transformations involving asymmetric allylation, asymmetric alkynylation, asymmetric dihydroxylation, olefination reactions, coupling reactions and cyclization (ring closing metathesis, macrolactonization) methods. The thesis briefly described successful asymmetric synthesis of two RALs cochliomycin A and zeaenol for the first time with successful synthesis of two new RAL analogues 5′-*epi*-peacilomycin F and 5′-*epi*-cochliomycin C. Thesis also described an efficient chemo-enzymatic asymmetric synthesis stagonolide-C and synthetic studies of stagonolide-I.



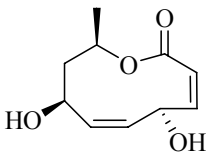
Cochliomycin A, R = -C(CH$_3$)$_2$-
Zeaenol, R = H



5-*epi*-cochliomycin C, R = Cl
5-*epi*-peacilomycin F, R = H



Stagonolide-C



Stagonolide-I

Key Words: Resorcylic acid lactones, 10-membered lactones, Asymmetric synthesis, EKR, ME-DKR, Ring closing metathesis, Macrolactonization, Synthetic methods, Total synthesis.