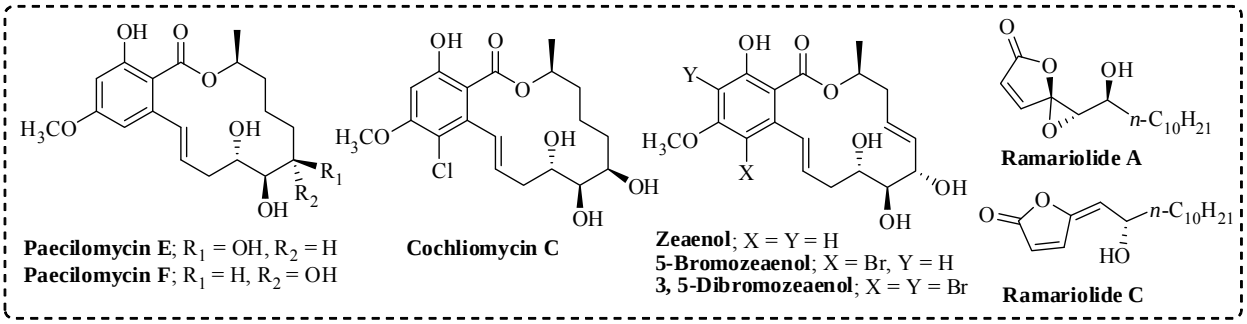
Thesis Title: Asymmetric Total Synthesis of Resorcylic Acid Lactones (RALs) and Ramariolides

Abstract: Resorcylic acid lactones (RALs), a class of polyketide, originate from the fungal metabolites. With the first isolation of radicicol in 1953, more than 40 naturally occurring RALs have been reported which includes 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. Ramariolides A-D, structurally unique butenolides have been recently isolated from the fruiting bodies of coral mushroom *Ramaria cystidiophora* found in the southern British Columbia region. Ramariolide A was found to exhibit significant *in vitro* antimicrobial activity against *Mycobacterium smegmatis* and *Mycobacterium tuberculosis*.

We have focused our attention for the asymmetric total synthesis of RALs and ramariolides by adopting lipase catalyzed kinetic resolution (EKR), metal-enzyme combined dynamic kinetic resolution (ME-DKR), various types of asymmetric transformations involving asymmetric propargylation, asymmetric dihydroxylation, olefination reactions, coupling reactions and lactonization methods. The thesis briefly describes successful asymmetric synthesis paecilomycin E, 10′-*epi*-paecilomycin E, 6′-*epi*-cochliomycin C, paecilomycin F, cochliomycin C, zeaenol and two brominated zeaenols. Synthesis of ramariolides A and C is also described in the thesis.



Key Words: Resorcylic acid lactones, γ-Alkyledene butenolides, Asymmetric synthesis, EKR, ME-DKR, *Z-E* isomerisation, Macrolactonization, Synthetic methods, Total synthesis.