Title of the PhD thesis: Total Synthesis of Cicutoxin and FR252921 via a Unified Pericyclic Approach

The work in this thesis is devoted to the total syntheses of bioactive polyene natural products by using the cyclobutene moiety as a diene linchpin. We demonstrated that the 4π-electrocyclic ring opening of cyclobutene derivatives coupled with other reactions, such as nucleophilic substitution, Suzuki-Miyaura coupling, was a highly reliable and efficient method for the synthesis of polyenes.

In chapter 3, we achieved the divergent and efficient synthesis of polyenols, viz. cicutoxin and virol A, via a tandem nucleophilic substitution/4π-electrocyclic ring opening event.

In chapter 4, we successfully devised a domino Suzuki-Miyaura coupling/4π-electrocyclic ring opening process, and applied it in the total synthesis of deceptively challenging immunosuppressants FR252921, FR252922 and FR256523. Our route was very convergent and allowed us to synthesize a range of analogues. Besides that, molecular probes were designed and synthesized for the identification of its molecular targets of this fascinating family of metabolites.
In chapter 5, we described our efforts towards the total synthesis of cyclamenol A. Our attempted Suzuki-Miyaura coupling/4π-electrocyclic ring opening approach is currently thwarted by our inability to obtain a suitable precursor for the macrocyclization.