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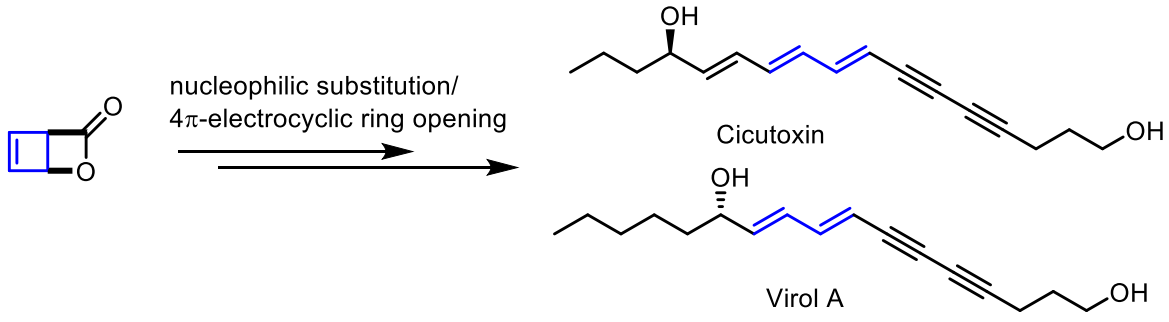
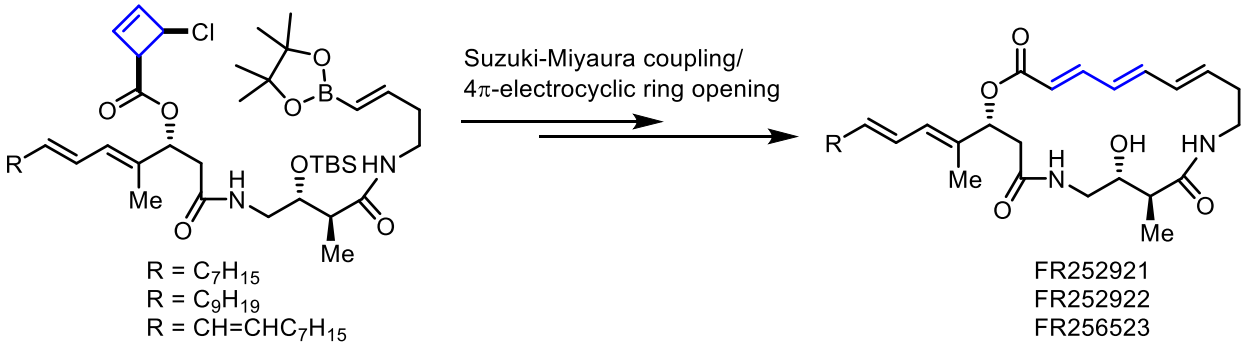
Title of the PhD thesis: Total Synthesis of Cicutoxin and FR252921 via a Unified Pericyclic Approach

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.



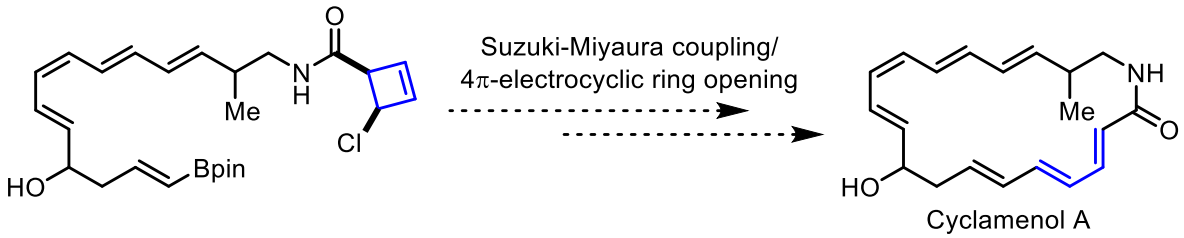
In chapter 4, we successfully devised a domino Suzuki-Miyaura coupling/4π-electrocyclic ring opening process, and applied it in the total synthesis of deceptively challenging immunosuppressants FR252921, FR252922 and FR256523. Our route was very convergent and allowed us to synthesize a range of analogues. Besides that, molecular probes were designed and synthesized for the identification of its molecular targets of this fascinating family of metabolites.



R = C_7H_{15}
R = C_9H_{19}
R = $CH{=}CHC_7H_{15}$

FR252921
FR252922
FR256523

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.



Cyclamenol A