

# Abstract

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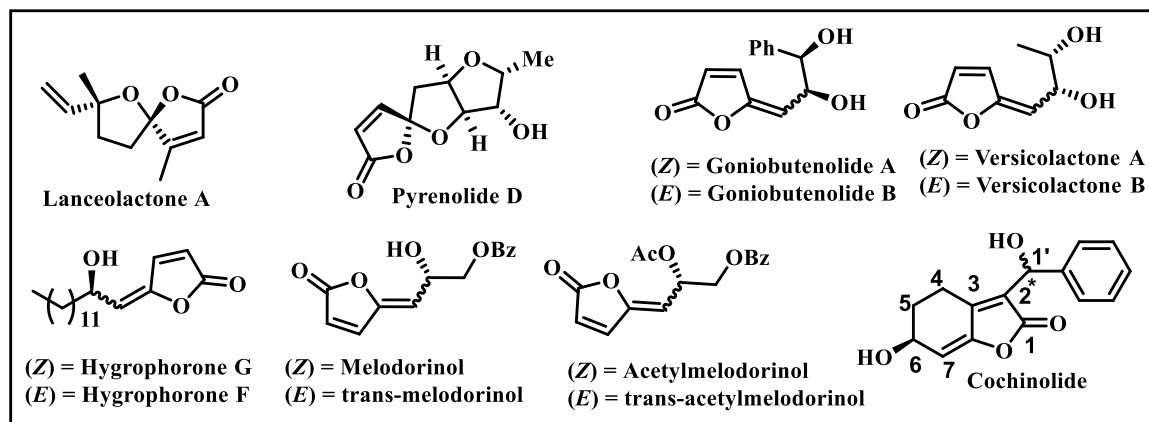
## **Thesis Title: Asymmetric Total Synthesis of Naturally Occurring $\gamma$ -Alkylidenebutenolides and Oxaspirolactones**

**Abstract:**  $\gamma$ -Alkylidene butenolides represent a subclass of butenolides distinguished by the presence of an alkylidene group at the gamma position of the lactone ring. This structural feature imparts unique chemical properties, including enhanced reactivity and potential for further functionalization. The  $\gamma$ -alkylidene substituent can significantly influence the biological activity of these molecules, often enhancing their interaction with biological targets.  $\gamma$ -Alkylidenebutenolide natural products such as xerulene, xerulinic acid, lissoclinolide, versicolactone A & B, pyrenolide D, and cochinelide have been isolated, featuring either  $\gamma$ -(Z)- or  $\gamma$ -(E)-alkylidenebutenolide cores. A new  $\gamma$ -alkylidene bicyclic butenolide, cochinelide, isolated from the root bark of *Homalium cochinchinensis*, demonstrated moderate antiviral activity against HSV-1 and -2. These compounds, noted for their antifungal, cytotoxic, antimalarial, antiviral, antiparasitic, estrogenic, and antibacterial properties, have garnered significant attention. Oxaspirolactones, including [5,5]- and [6,5]-oxaspirolactone scaffolds, are notable for their unique structures and biological activities. Pyrenolide D, distinct for its spiroketal chiral center and highly oxygenated tricyclic spiro- $\gamma$ -lactone, shows significant cytotoxicity against HL-60 cells (IC<sub>50</sub> 4  $\mu$ g mL<sup>-1</sup>). Recently, a methanolic extract of the leaves of *Illicium lanceolactum* A. C. Sm. was used to isolate the [4,4]-spirocyclic tetranorsesquiterpinoid natural product known as Lanceolactone A. When it comes to the periodontal pathogen *Porphyromonas gingivalis*, it has antimicrobial action. Its stunning structural characteristics and biological activity grabbed our attention to its entire synthesis.

The synthesis of  $\gamma$ -E-alkylidenebutenolides is difficult because of the thermodynamic and electrical stability of  $\gamma$ -Z-alkylidenebutenolides. The thesis briefly describes a "visible light-assisted" isomerization process that is proposed to efficiently yield E- $\gamma$ -alkylidenebutenolides in high yield, overcoming previous method difficulties. The thesis contains asymmetric total synthesis of pyrenolide D, lanceolactone A, cochinelide, versicolactone A & B, gonibutenolide A & B, melodorinols, acetylmelodorinols, hygrophorone G & F, ramariolide D and phomopsolidone C & D. For the synthesis of these natural products, we employed lipase-catalyzed kinetic resolution (EKR) and a range of asymmetric transformations. These included asymmetric propargylation, reduction, hydroxylation, olefination reactions, metal-catalyzed lactonizations, visible light-

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induced photoisomerization, Kulinkovich reaction, and palladium-catalyzed carbonylation reactions.



**Key Words:**  $\gamma$ -Alkylidenebutenolides, Oxaspirolactone, Asymmetric synthesis, Isomerisation, Lactonization, Synthetic methods, Total synthesis, Kulinkovich reaction, Palladium catalysed carbonylation