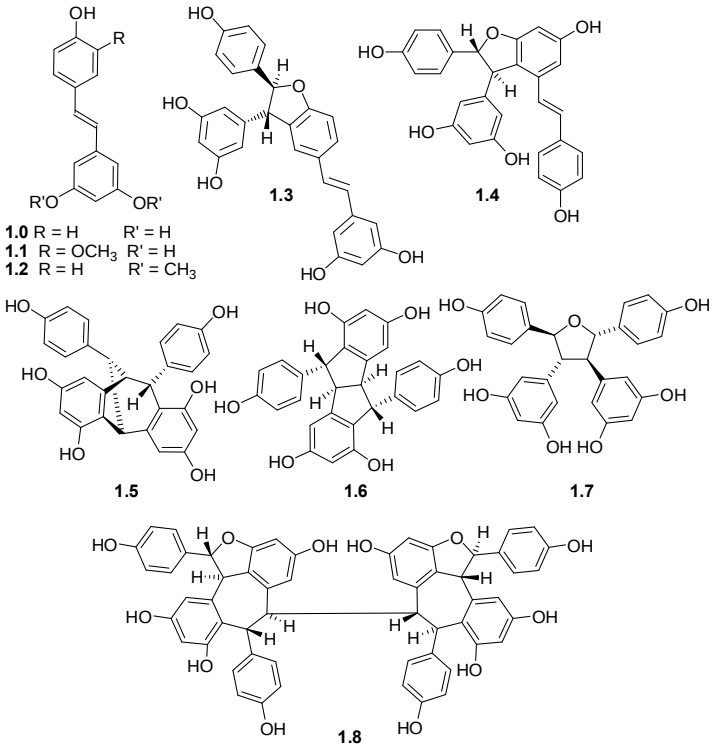
CHAPTER 1. INTRODUCTION

1.1. Background

The naturally occurring oligostilbenoids (*e.g.* dimers, trimers, tetramers, pentamers), such as **1.3**, **1.4**, **1.5**, **1.6**, **1.7** and **1.8**, form a special group of polyphenolic compounds. Their attractiveness originates from their structural diversity that includes rings of unusual sizes, various type of fused rings with or without oxygen atoms as well as numerous stereogenic centers. Biogenetically, oligostilbenoids result from homogenous or heterogeneous coupling between monomeric resveratrol **1.0** or other stilbenoid units like isorhapontigenin **1.1**, pterostilbene **1.2**, etc.



This group of compounds has attracted significant interest due to their diverse biological activities including anti-microbial, antifungal, antioxidant, anti-HIV,

cytotoxic, anti-inflammatory, etc. A literature survey shows that some 15 publications report on oligostilbenoids syntheses *via* biotransformation and enzymatic coupling, while another 20 publications describe biomimetic syntheses of oligostilbenoids (refer to Chapter 4). This project was instigated with the initial intention to synthesize complex tetramers like hopeaphenol **1.8** in a biomimetic manner.

1.2. Problems to be addressed/and or hypothesis

A biosynthesis pathway was proposed for hopeaphenol **1.8** by Sotheeswaran (see Chapter 4). Yet, its inherent flaws would not allow designing a successful biomimetic synthesis of this complex tetrameric species. As stated above, few groups initiated biomimetic syntheses of various stilbene oligomers, starting from resveratrol or its analogues. The stilbene coupling was achieved through microbial biotransformation or with help of chemoenzymatic or mineral catalysts. As it will be fully discussed in Chapter 4, the results did not seem to follow any sort of logics at first sight. Therefore, before any synthesis of hopeaphenol could possibly be undertaken, it was felt that it was necessary to shed some light on this apparently, yet deceptively, simple oxidative coupling. Eventually, attempts to provide comprehensive understanding of the stilbene dimerisation mechanism became the focal point of this work. It was believed that a series of dimerizations of well selected substrates combined with published results would form the basis for a thorough analysis ultimately leading to a theory that would account for all observations and allow predicting stilbene dimerisation outcome.

1.3. General objectives

- To provide detailed insights on the mechanisms that are taking place during the formation of oligostilbenoids.

1.4. Specific objectives

1. To synthesize an array of stilbenoid building blocks using different protecting groups.
2. To perform anodic oxidations on some of the above mentioned stilbene derivatives.
3. To dimerise the above-mentioned protected stilbenoid building blocks using various reagents and conditions as well as comparing the obtained results with the above anodic oxidations products.
4. To infer rules governing the oxidative coupling of stilbene derivatives.
5. To support some of the above presented hypotheses by aid of molecular modeling.

1.5. Scope and limitations

In this study, the synthesized stilbenes were coupled in various chemical and electrochemical oxidative conditions in hope of providing insights into the mechanism of stilbene dimerisation/oligomerisation. The proposed hypotheses were based on the analysis of results obtained herein together with those gathered from the literature. To provide some level of validation, a molecular modeling approach was initiated but does not pretend to be exhaustive. The actual synthesis of hopeaphenol or other

tetramer has been considered as out of scope of this work while biological activities of stilbenoids and oligostilbenoids are not reported here.

1.6. Expected outputs

This biomimetic approach should allow us not only to better understand the biogenesis of oligostilbenoids but also shows direction on how to apply the mechanistic insights obtained from the above study in synthesizing other complex structures of oligostilbenoids (*e.g*. tetramer) in a targeted manner.

1.7. Thesis content

Results are presented in four chapters: i) Stilbene synthesis (Chapter 2); ii) Electrochemical oxidations of stilbene derivatives (Chapter 3); iii) Biomimetic syntheses of oligostilbenoids (Chapter 4); and iv) Molecular modeling on stilbenoids (Chapter 5). Each of these chapters consists of a review of the literature relevant to the topic, a presentation of the results and their full discussion, concluding remarks, spectroscopic evidence (except for Chapter 5), experimental procedures and corresponding list of references. A general conclusion is Chapter 6. An appendix collates all relevant spectra.