ABSTRACT

The aim of this PhD project has been to develop new synthetic strategies in enantioselective preparation of natural products.
In particular my attention has been focused on preparation of some natural metabolite, containing an $\alpha,\beta$-unsaturated dialdehyde in a polycyclic backbone, and their synthetic analogue, in order to better understand structure activity relationship towards TRP receptors ion channels.

The recent discover of the new thermoreceptor TRPA1 and given that these natural metabolites show also a widespread of bioactivities, such as antiproliferative and cytotoxic activity, has increased our interest towards these target ever more.

Our purpose is to assay the bioactivity of synthesized products both as TRP receptor agonists and as antiproliferative compounds.

The first chapter of this work is an introduction to these terpenoidic molecules, with a wide range of described natural occurring metabolite and their classification in drimane, isocopalane, and scalarane dialdehydes.

Thus, the structure of TRP receptor is described with a brief history of these ion channels, starting from the first cloned receptor, the TRPV1 vanilloid.

In the chapter 2 total syntheses of polygodial derivatives, both C-1 and C-3 functionalised, are described.
Polygodial and C-1 functionalised drimanes have been prepared with an approach whose key step is a Diels Alder reaction; Drimane C-3 functionalised have been prepared with a radical chemistry approach.
In the chapter three an approach to the enantioselective syntheses of both diterpenoidic and seserterpenoidic unsaturated dialdehydes, structural analogues of occurring natural product such as ent-isocopalendial, scalaradial and deacethoxyscalaradial, is described.

Chapter four is dedicated to discussion of some bioactivity assays, the receptorial one have been in collaboration with Dott. Luciano De Petrocellis and Dott. Vinenzo Di Marzo, Istituto di Chimica Biomolecolare del CNR (Pozzuoli, Na). The antiproliferative assays have been made in collaboration with Prof. Giuseppina Autore, Dott Giuseppe Bianco, Dipartimento di Farmacia, Università degli Studi di Salerno.

During my PhD studies I have spent six months at The University of York, working in Professor Richard Taylor Research Group.

During these months my research has been focused on developing of a new methodology in synthesis of \(\alpha\)–alkylidene \(\gamma\) butyrolactones.

In the chapter five some natural occurring \(\alpha\)–alkylidene \(\gamma\) butyrolactones. and relevant synthetic routes to prepare these molecules are described, in the chapter six is described a new methodology in synthesis of \(\alpha\)–alkylidene \(\gamma\) butyrolactones motif involving Rh(II) chemistry.