# Contents

# Abstract

The work presented in this Thesis describes several new and novel radical macrocyclisation-transannulation cascade reactions directed towards the single step construction of ring-D aromatic steroid ring systems.

The **Introduction** introduces the steroid class of natural products, their biosynthesis and previous literature strategies towards their construction. The ring-D aromatic steroids, together with their possible total synthesis *via* a novel free-radical cascade strategy, are then discussed.

The **Results and Discussion** Chapter summarises the radical cascade strategies towards ring-D aromatic steroid ring systems that have been investigated. It is divided into two sections:

**Part 1** describes the evolution of our current radical cascade approaches relating to the iododienynone precursors **117a-d** (Schemes 26-29). We proposed that the precursors **117a-d** would lead to the 6,6,6,6 ring-D aromatic steroid ring system (such as that found in the natural product nicandrenone **67**), *via* a cascade of radical ring-forming reactions. However, the proposed radical cascade from the *Z*-iododienynones **117a,c** halted at the macrocyclisation stage producing the macrocycles **137a,b**, whilst a radical cascade from the *E*-iododienynones **117b,d** instead led to the unusual bridged tricyclic structures **148a,b** and **155** (depending on whether benzene or heptane was

used as the solvent), rather than the anticipated linear tetracycles **116a,b**. A rationale for these outcomes is given.

**Part 2** discusses an approach to 6,6,5,6 ring-D aromatic steroids *via* a macrocyclisation-transannulation radical cascade from the vinylcyclopropyl seleno ester precursor **193**. A synthesis of the radical precursor **193** was first examined using a novel aryl-vinylcyclopropane Stille reaction coupling protocol (the development of which is discussed), as well as several alternative routes. A practical, albeit more lengthy, synthesis of the precursor **193**, was then developed. The proposed radical cascade from the vinylcyclopropyl seleno ester **193** led to the desired ring-D aromatic steroid ring system **194a** (with the correct *trans*, *anti*, *trans* stereochemistry) together with the methyl epimer **194b**. Also isolated from the product mixture was the macrocycle **232**, together with the products of reduction and decarbonylation of the acyl radical intermediate **235**, *i.e*. **231** and **230**, and the dioxolane **233**.

The **Experimental** section describes all the procedures used to synthesise the precursor compounds **117a-d** and **193** and the products of their radical mediated cascade cyclisations. Full NMR, and other spectroscopic data, alongside mass spectrometry data are also given.

The **Appendices** include some relevant X-ray and NMR spectroscopic details.