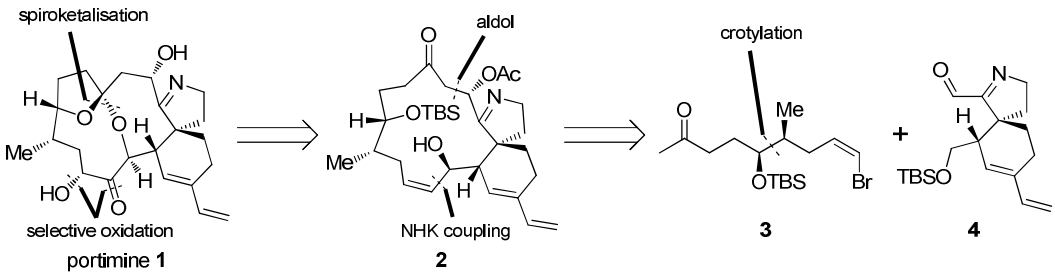
Synthetic Studies Towards the Marine Toxin Portimine

Harry Aitken, Daniel Furkert, Margaret Brimble

University of Auckland, Auckland, New Zealand

Portimine (**1**) is a novel polycyclic marine toxin, containing spiroimine and bridged-spiroketal functionality, isolated from the dinoflagellate *Vulcanodinium rugosum* collected off the coast of Northland, New Zealand. Whilst the spiroimine motif is commonly observed in a number of algae-derived toxins the [4.5]-spiroimine ring system is unique to portimine, thus representing an intriguing synthetic challenge. Portimine is a potent inducer of apoptosis and confers high toxicity against leukaemia cells *in vitro* (P388 cells, EC_{50} = 2.7 nM).



The synthesis of portimine (**1**) has been designed to provide structural analogues of portimine for biological evaluation. The carbon framework of portimine will be accessed by aldol addition of Leighton crotylation-derived polyketide **3** to spiroimine **4**. Subsequent macrocyclisation using a Nozaki-Hiyama-Kishi reaction will provide tricyclic intermediate **2**; finally, spiroketalisation and selective oxidation—to the unusual α,α'-dihydroxyketone moiety—will complete the synthesis of portimine.