2,6-Disubstituted tetrahydropyran (THP) and piperidine rings form key structural motifs in many potent biologically active natural products and pharmaceuticals. In this lecture I will present our recent results into the synthesis of these important structural units.

In the first part of the lecture I will discuss a stereodivergent oxy-Michael approach to the synthesis of 4-hydroxy-2,6-cis- or 2,6-trans-substituted tetrahydropyran rings, which are present in natural products such as phorboxazole B (anti-tumour) and the diospongins (anti-osteoporotic). Experimental and DFT calculations have been used to elucidate the mechanism of the stereodivergence – where a trifluoroacetic acid catalysed formation of 2,6-cis-tetrahydropyrans was mediated by a trifluoroacetate-hydroxonium bridge and proceeded via a chair-like transition state, and a TBAF mediated formation of 2,6-trans-tetrahydropyrans proceeded via a boat-like transition state, where the 4-hydroxyl group formed a crucial hydrogen bond to the cyclizing alkoxide.

The second part of the lecture will detail a new Maitland-Japp inspired route to the synthesis of spirocyclic piperidines, which are suitable for the use as fragments in 3D-compound libraries. 3Dfragments obeying the “rule of 3” are increasingly sought after in medicinal chemistry as they occupy sparsely explored areas of chemical space and can be further elaborated to product lead-like compounds. Our synthesis of spirocyclic piperidines generates these structures in good yields and in in novel areas of chemical space as defined by principle moments of inertia (PMI) analysis.

**CBC SEMINAR ANNOUNCEMENT**

**Professor Paul Clarke**
**University of York**

**New Strategies for the Stereoselective Synthesis of Functionalised Heterocycles**

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**Date:** 27th July 2016 (Wednesday)
**Time:** 11:00am – 12:30pm
**Venue:** SPMS Research & Graduate Studies Office Conference Room
**Host:** Assoc Professor Roderick Bates