Synthesis & Catalysis

Novel Iridium-Based Catalysts for Hydrogen Isotope Exchange of Pharmaceutically Relevant Functionality

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Internship Description:

Transition metal-mediated hydrogen isotope exchange (HIE) is a technique of increasing importance, with a range of applications spanning all aspects of organic synthesis. Importantly for medicinal chemists, such direct and flexible labelling processes now represent a central tool for the fast and efficient incorporation of a tracer into drug candidates, enabling various metabolic, stability, and toxicity studies to be performed earlier in the drug design process. Recent studies from our own laboratory have disclosed a series of highly active iridium(I) catalysts capable of delivering heavy isotopes of hydrogen (deuterium and tritium) to aromatic molecules *via* an *ortho*-directed C-H insertion process.

To date, we have shown that our catalysts are capable of efficiently mediating a range of labelling processes. Labelling of aromatic systems is directed by a broad range of functional groups, including ketones, amides, esters, nitroarenes, sulfonamides, and an array of *N*-heterocycles, all with high levels of D-incorporation under mild conditions. We have recently extended this work to include the labelling of non-aromatic unsaturated systems, as well as the much rarer, and more challenging, hydrogen isotope exchange of sp^3 hybridsed C-H bonds.

In this project, the student will augment our range of catalysts with novel NHC/phosphine-Ir complexes. The design of these complexes will be based on the demands of new, challenging substrates for labelling processes. As part of this programme, the student will gain experience of both organometallic chemistry and organic synthesis through the preparation of the iridium complexes and a spectrum of organic substrates, as well as *via* the central catalysed labelling reactions.