A2-13 Harnessing Non-Covalent Interactions to Address Selectivity Challenges in Catalysis

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This lecture will describe our research program which seeks to develop new catalytic strategies based on attractive non-covalent interactions to tackle outstanding selectivity challenges in modern synthetic methodology. Non-covalent interactions play a crucial role in all manner of chemical and biological processes. In recent times, the incorporation of non-covalent interactions into the design of small molecule catalysts has revolutionised the field of enantioselective catalysis. Our research is centered around applying catalyst designs incorporating non-covalent interactions to tackle foremost selectivity challenges in synthetic chemistry, concerning both positional selectivity and enantioselectivity.

The lecture will briefly describe initial projects focussed on the challenge of site-selectivity which commenced with the development of a bifunctional ligand based on ion-pairing for controlling site-selectivity in iridium-catalysed borylation. We have subsequently applied a bifunctional ligand strategy to control site-selectivity in Suzuki-Miyaura couplings of substrates bearing multiple instances of the same halide, in this case using a sulfonated phosphine. Subsequent investigations will be described which probe the feasibility of using the chiral cation associated with the ligand as the sole source of chirality to achieve an enantioselective remote borylation of a symmetrical substrate and describe how we were able to realise the desymmetrising borylation on two distinct classes of substate, to form both chiral-at-carbon and chiral-at-phosphorous compounds. This approach has been further applied to Rhodium catalysed C-H amination. We synthesised an anionic version of $Rh_2(esp)_2$ and have shown that, when paired with chiral cations, this catalyst gives excellent enantioselectivies for C-H amination of substrates bearing a pendant hydroxy group, which we believe interacts with the catalyst sulfonate group through hydrogen bonding.

A project that was carried out in parallel to the above work originally intended to tackle the long-standing challenge of site-selectivity in Minisci-type reactions and these results may be discussed in the talk. The outcome of this work was that not only were we successful in achieving the original aim of controlling the site-selectivity, but using a chiral phosphoric acid catalyst we were also able to realise an enantioselective Minisci reaction for the first time - a prochiral radical leads to a new stereocentre with excellent control. We have improved our original protocol, which used redox active esters as radical precursors, so that simple amides can undergo hydrogen atom transfer in what is formally a C-H/C-H bond coupling, still with excellent control of enantioselectivity and regioselectivity. This has now been extended to alcohols as coupling partners so that the asymmetric Minisci reaction can be used to form secondary alcohol as well as secondary amine stereocentres.

PROFILE

Dr. Robert J. Phipps（University of Cambridge, Associate Professor）

Robert received his MSci in Chemistry from Imperial College London in 2006. He moved to the University of Cambridge to complete his PhD (2010) with Prof. Matthew Gaunt. In 2011, he moved to the University of California, Berkeley on a Marie Curie Postdoctoral Fellowship with Prof. F. Dean. In 2013 he returned to Cambridge for the return year of the Marie Curie Fellowship and in 2014 he was awarded a Royal Society University Research Fellowship, which allowed him to commence independent research from October 2014. In 2017 was awarded an ERC Starting Grant and in 2019 was a recipient of the RSC Harrison-Meldola Memorial Prize. He was appointed as an Associate Professor at Cambridge in October 2021.