Ion Pair-Directed Meta-Selective C–H Borylation of Aromatic Quaternary **Ammonium Salts UNIVERSITY OF**

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Iridium-catalysed borylation:

- A C-H activation, primarily controlled by steric hinderance excellent for selective borylation of 1,3-disubstituted arenes but generally not mono or 1,2-disubstituted arenes
- Methods exist achieving ortho selectivity through the use of a substrate directing group interacting with the metal¹
- Fewer examples exist of *meta²* or *para³* selective borylation (see right for leading example)

This work – Ion pair directed borylation:

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We envisaged creating a novel bifunctional ligand for iridium containing both the bipyridine moiety, to form the active catalyst complex, as well as an anionic site to ion pair with the cationic substrate and direct borylation to the *meta* position.

Hypothesis for ion pair-directed borylation:

Use of non-covalent interactions to control regioselectivity in catalytic reactions:

Transition metal catalysis is a well established and powerful methodology for many synthetic transformations, however in some cases regioselectivity can be difficult to control.

Hydrogen bonding interactions have been previously exploited to achieve regioselective reactions, in several cases:







Meta-Selective Arene Borylation







Four sulfonate bearing bipyridine ligands were synthesised with varied tether lengths extending from



2-Substituted pyridines typically undergo sterically controlled borylation giving a mixture of C4- and C5-borylation. Additionally, pyridines with an electron withdrawing group in the C2 position can undergo C6-borylation. With our ligand we see exclusively C4,6-diborylation – C4 first then second borylation at C6.

observe a 1:1 mixture of the C2,6- and C2,7-diborylated isomers.



there was a surprising preference for *meta* borylation when the reaction was carried out in cyclohexane with the standard ligand **dtbpy**, albeit in low yields. However, this selectivity diminishes on the introduction of an ortho substituent and L1 is required to restore this.





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PinB

BPin

L1, THF: >20:1, 86%

dtbpy, THF: 1.3:1, 82%

dtbpy, Cyc: 12:1, (74%)

References: (1) For selected examples of *ortho* directed borylation see: Hartwig, J.F., *J. Am. Chem. Soc.* 2008, 130, 7534; Crawford, K. M., Angew. Chem. Int. Ed. 2014, 53, 7589; Ishiyama, T. Chem. Commun. 2010, 46, 159; (2a) Kuninobu, Y., Kanai, M., Nature Chem. 2015, 7, 712; (2b) Bisht, R., Chattopadhyay, B., J. Am. Chem. Soc. 2016, 138, 84; (3) Itami, K., Segawa, Y., J. Am. Chem. Soc. 2015, 137, 5193; (4) Crabtree, R. H., Brudwick, G. W., Science, 2006, 312, 1941; (5) Reek, J. N. H., J. Am. Chem. Soc. 2013, 10817.