



# Visible light activation of boronic esters enables efficient photoredox C(sp<sup>2</sup>)-C(sp<sup>3</sup>) cross-couplings in flow



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❖ Photoredox catalysis emerged as a mild method to trigger single-electron transfers (SETs) in a controllable and selective manner

❖ Previously considered as “wild” intermediates, C(sp<sup>3</sup>) radicals can be tamed by using anionic functional groups susceptible to single-electron oxidation by photoredox catalysts

❖ C(sp<sup>3</sup>) radicals were employed in C(sp<sup>2</sup>)-C(sp<sup>3</sup>) cross-couplings reactions by using them in a dual Ir/Ni catalysed system

❖ Use of anionic groups makes light penetration less efficient and prevents their irradiation in micro flow channels (salts precipitation)

❖ Neutral boronic esters allows intensified couplings in flow

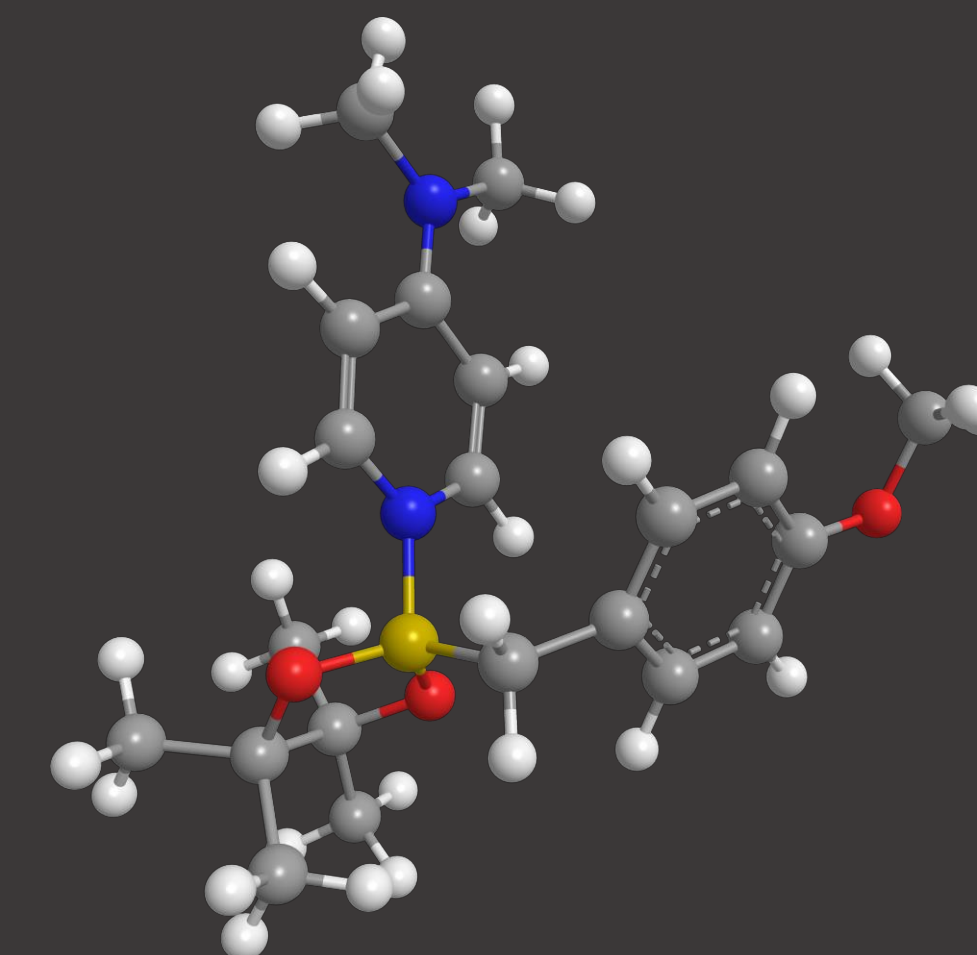
## Lewis base additive effect:

Reaction scheme: MeO-C6H4-CH2-Bpin + LB + Ar-Br <=> [K\_eq] MeO-C6H4-CH2-Ar

Entry	Lewis base (LB)	K <sub>eq</sub>	Yield in 2
1	none	-	0%
2	2,6-lutidine (3.5 equiv.) (used by Molander)	5.1 × 10 <sup>-12</sup>	0%
3	pyridine (3.5 equiv.)	8.1 × 10 <sup>-4</sup>	47%
4	DMAP (3.5 equiv.)	0.30	82%

Ar = 4-CN-Ph [a] Conditions used by Molander<sup>[1]</sup>: 0.5 mmol of Ar-Br, 1.2 equiv. Bn-BF<sub>3</sub>K instead of 1, 3mol% Ni(COD)<sub>2</sub>, 3mol% dtbpy, 2mol% cat(1), 35°C, 24h batch irradiation with CFL (23 W)

DFT calculations → K<sub>eq</sub>

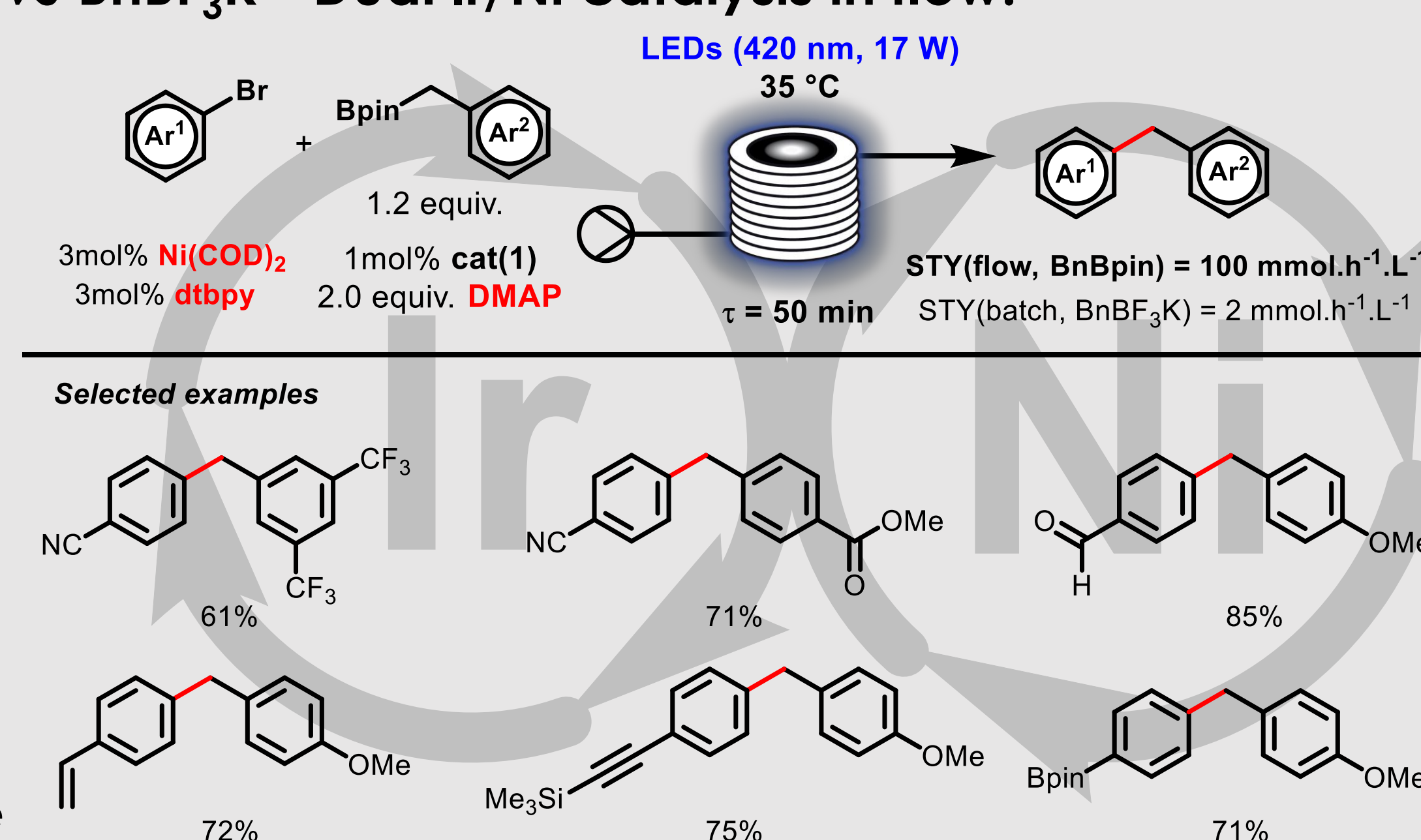


Observed by <sup>1</sup>H-NMR

## Proof of concept - BnBpin vs BnBF<sub>3</sub>K - Dual Ir/Ni catalysis in flow:

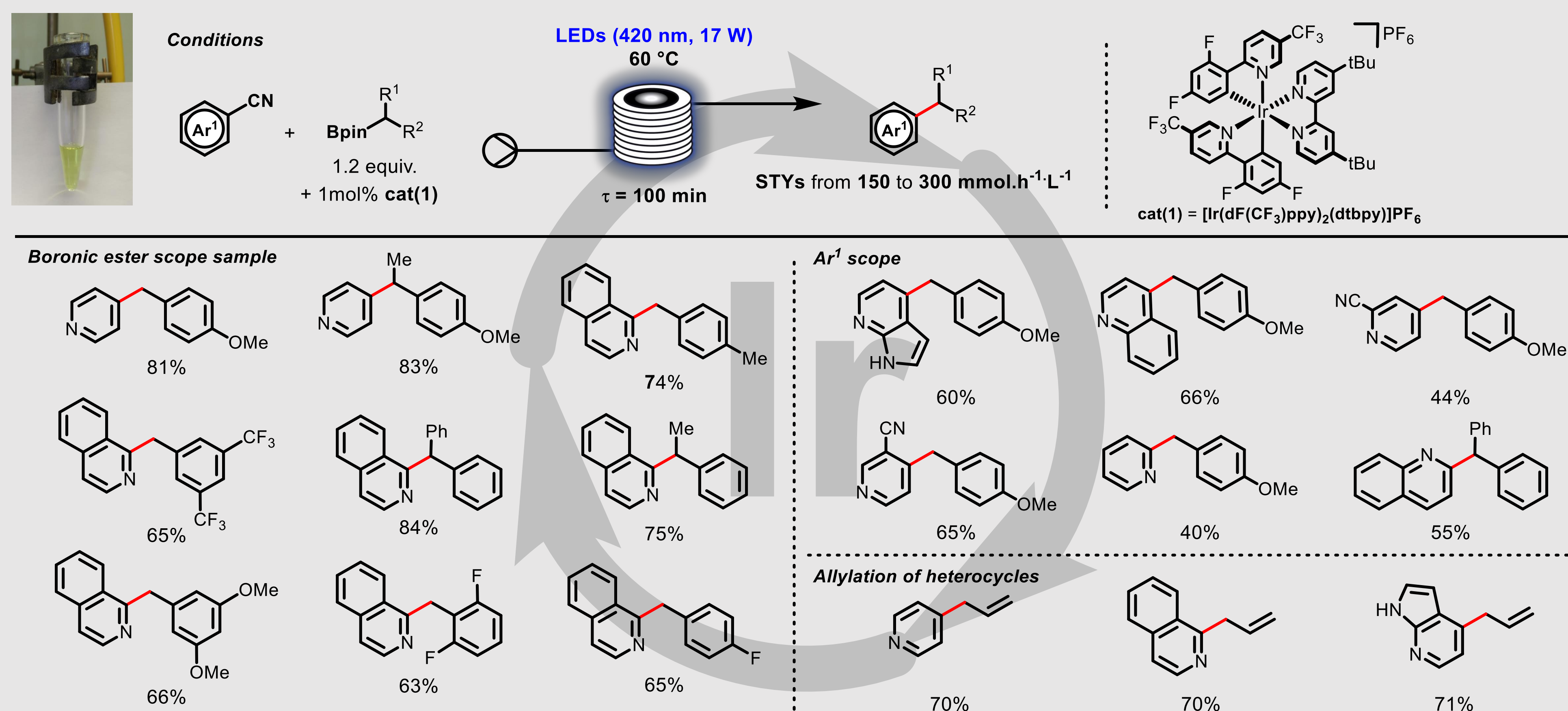


Vapourtec E-series UV-150 module

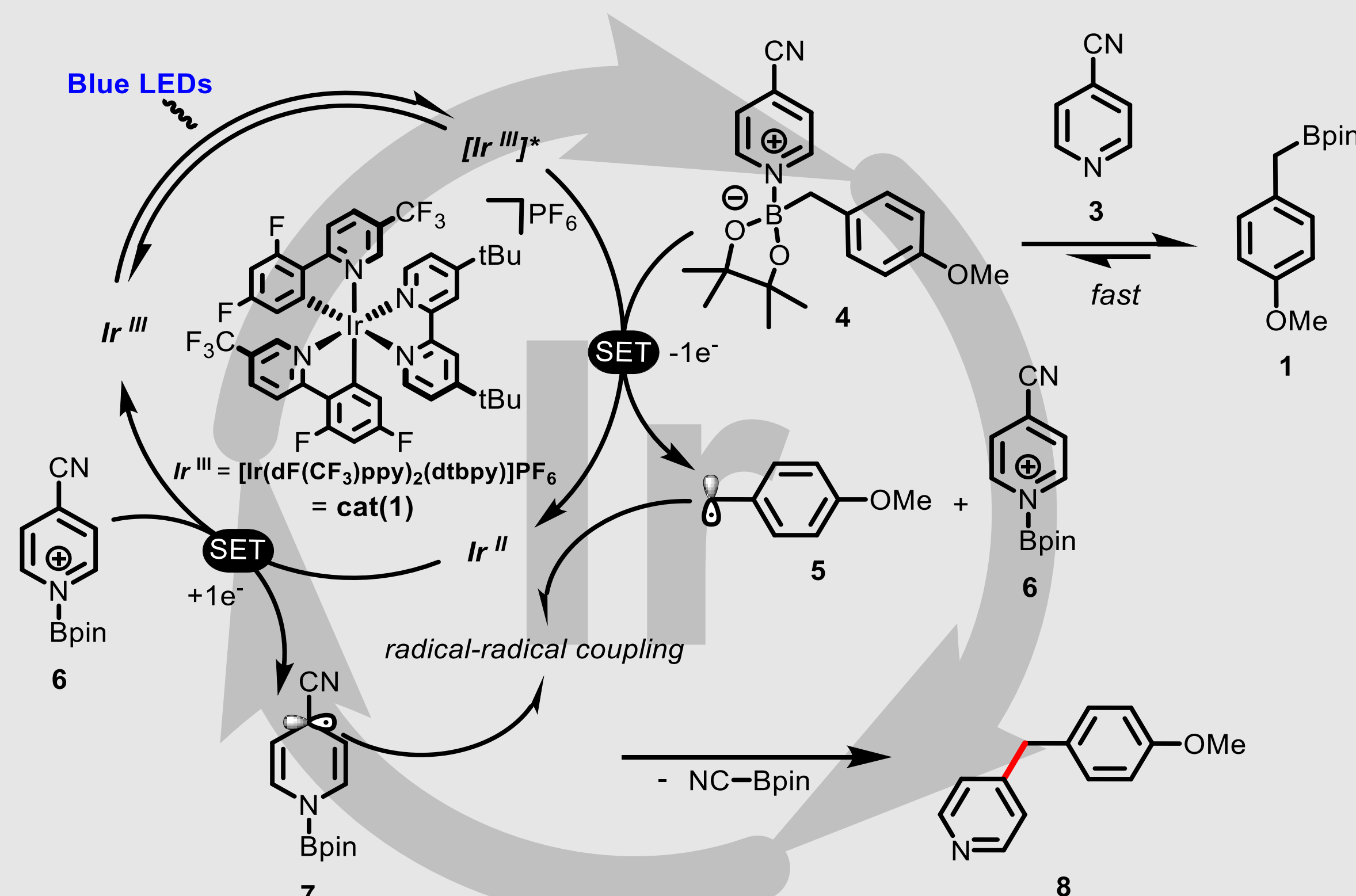


## Lewis base as a substrate:

- Electron-deficient cyanoarenes are known single-electron acceptors<sup>[5]</sup>
- N-containing cyanoarenes can coordinate to boronic esters
- No DMAP additive
- No Ni(COD)<sub>2</sub> (no glovebox) nor dtbpy
- Net neutral photoredox coupling
- Complementary yet simpler method (no additives)
- Good productivity, scalable (1 gram in 5 hours)
- N-heterocycle coupling, no catalyst inhibition
- Extendable for allylation of heterocycles



## Proposed mechanism :



## DFT calculation of catalytic cycle:

- Initial complexation of 1 with various N-heterocycles (such as 3)
- Complex 4 can reductively quench [Ir(III)]\* (reductive quenching cycle)
- Lead to radical 5 and pyridinium 6 (low barrier for C-B bond cleavage)
- Pyridinium 6 is readily reduced by Ir(IV)
- Rapid SET cascade allows selective radical-radical coupling
- Rate-determining step of catalytic cycle is the first SET event

## Conclusion:

- ❖ Unlike free boronic esters, their complexes with a Lewis base are susceptible to single-electron oxidation
- ❖ Boronic esters can replace trifluoroborate salts in an Ir/Ni dual catalysed cross-coupling<sup>[1]</sup> using DMAP additive instead of 2,6-lutidine (50 times intensification of flow process vs batch)
- ❖ N-heteroaromatic nitriles can be used as substrates circumventing the use of DMAP and Ni(COD)<sub>2</sub>
- ❖ This last procedure proceeds as a net-neutral photoredox C(sp<sup>2</sup>)-C(sp<sup>3</sup>) cross-coupling and complements the Ir/Ni dual catalysed method → Towards a photoredox Suzuki coupling?

## Acknowledgements:



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## References:

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