

PHOTO-REDOX FUNCTIONALIZATION OF ARYL BROMIDE DERIVATIVES BY N-HETEROCYCLIC CARBENE (NHC) CATALYSIS

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INTRODUCTION

Research Topic: Utilization of the NHC photocatalyst in Borylation Reactions for greener and more energy and cost efficient Boronate production

- **Rationale:** Metal catalysts cause serious problems like being more costly, energy-soaking, and toxic for the environment. Few techniques have been developed because of the negative reduction potential of the C(sp²)-Br bond in Aryl Bromides (reactants in borylation). This means it is hard for that bond to receive electrons, and without the bond receiving electrons, the reaction will not work. NHCs have the potential to avoid a lot of the negative consequences of metal catalysts and overcome the negative reduction potential because it is a good electron donor under light.

Experimental Question: To what extent can N-Heterocyclic Carbenes (NHCs) sufficiently activate the C(sp²)-Br bond in Aryl Bromides and be used as a photocatalyst for the functionalization of these compounds via Borylation to produce high value Boronate chemicals?

Hypothesis: If N-heterocyclic Carbenes are used as a photocatalyst for borylation, then functionalization of aryl bromides will occur successfully because of NHCs' ability to become powerful electron donors when excited under light that overcome the negative reduction potential of the C(sp²)-Br bond

EXPERIMENTATION

Experimental Design: Factorial Design

Independent Variables:

- Wavelength of light shined
- NHC type
- Type of base
- Type of solvent

Dependent Variable: Yield of Boronate product (mg)

Controlled Variables:

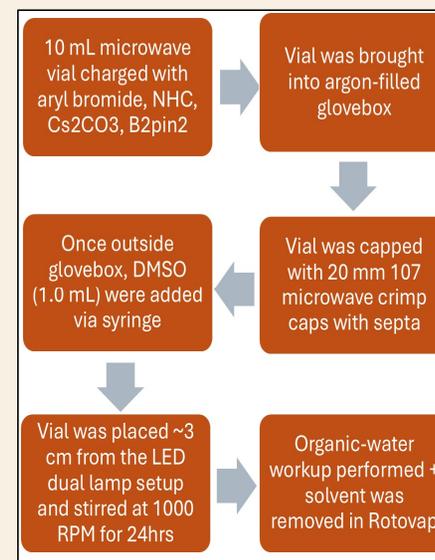
- Temperature (40 degrees Celsius)
- Stir rate (1000 RPM)
- Duration of stirring (24 hours)

EXPERIMENTATION

Experimental Method:

- Occurs after forming general reaction procedure from insight in the literature
- Factorial design was implemented in the form of an optimization framework
- 7 substrates (Aryl Bromides) were tested
- NMR and GC-MS machines were used for characterization of products, amount of yield (mg), and % yield was calculated

General Reaction Procedure



Rotovap Machine for Solvent Removal



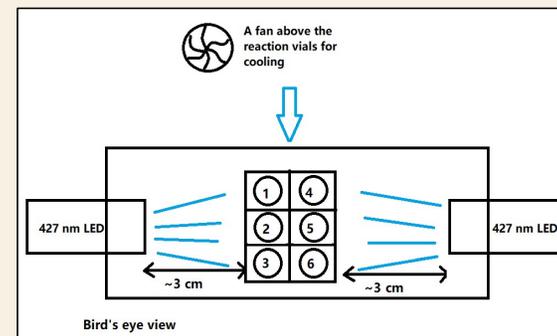
Argon-Filled Glovebox



Dual LED Light Lamp Setup

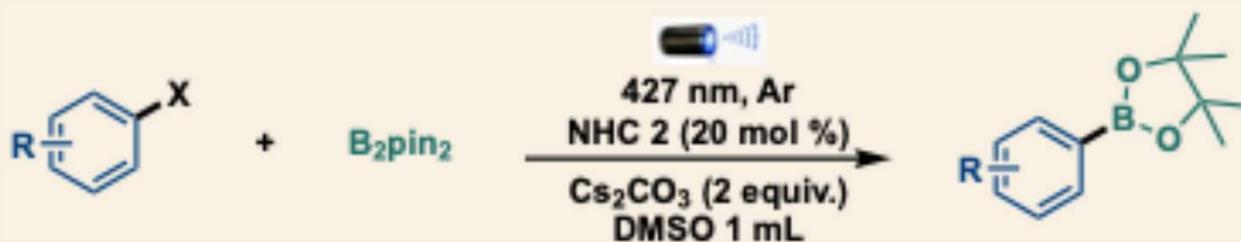


Bird's eye view of Dual LED Light Lamp Schematic



RESULTS

Sample Optimization Table



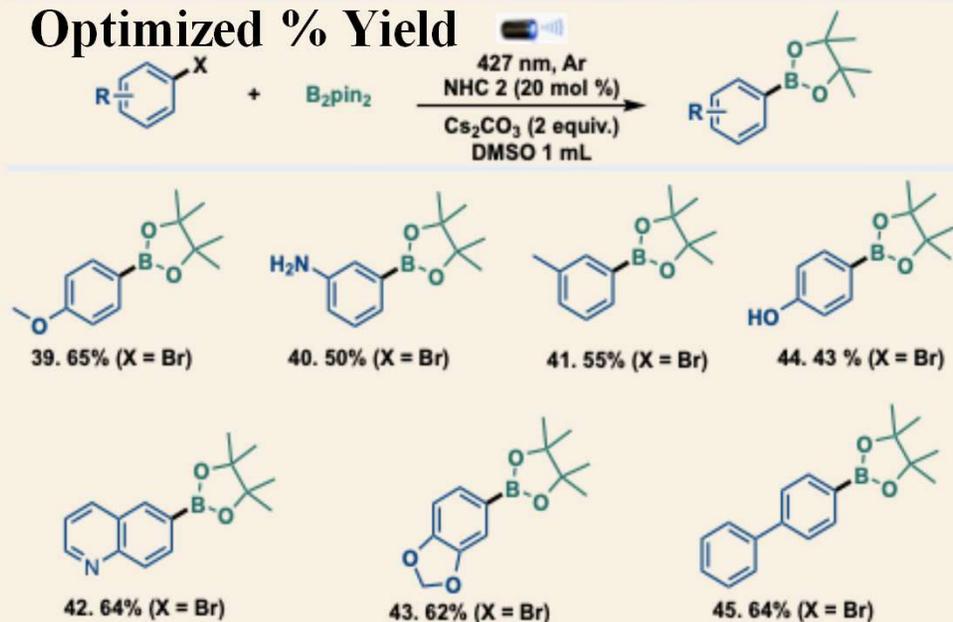
Entry	Deviation	Yield%
1	none	65
2	K ₂ CO ₃ instead of Cs ₂ CO ₃ in MeCN	30
6	MeCN instead of DMSO	21
7	No Photocatalyst	5
8	No Light	0

RESULTS

Post Optimization & Patterns Formed

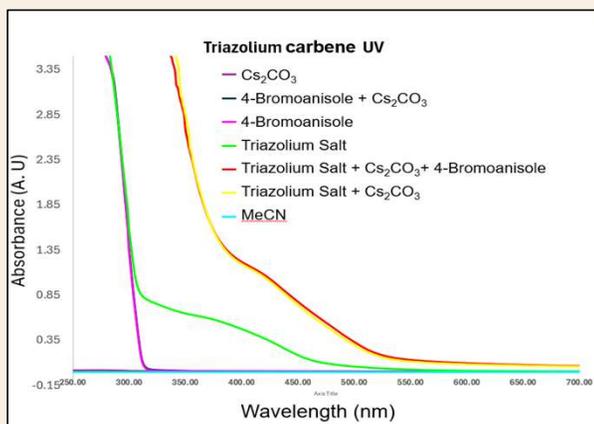
- Best reaction conditions were found to be 425 nm wavelength and Triazolium salt NHC, DMSO solvent, and Cs₂CO₃

Optimized % Yield

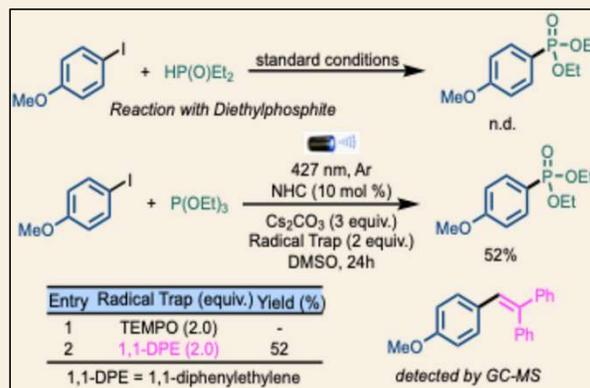


DATA ANALYSIS

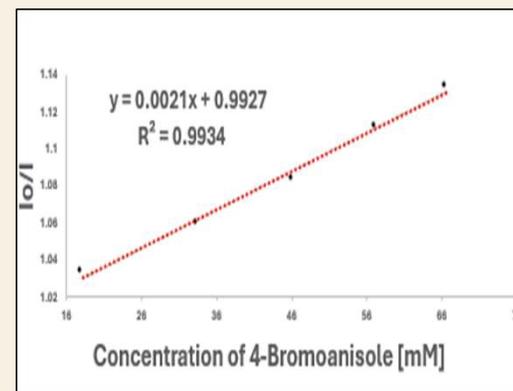
- Various analyses were performed for mechanism formation and to compare the practical data in the lab and match it to the background chemistry to make sure the data matches the theoretical aspect and makes sense



UV-Vis Analysis to confirm NHC is absorbing light shined



Radical Trap Test to confirm electron transfer and radical formation



Stern-Volmer Studies with linear regression model to analyzing quenching constant (slope) for efficiency of quenching (or how well the Aryle Bromides can absorb the electrons)

CONCLUSIONS AND POTENTIAL CHANGES

- The hypothesis is supported by the data because:
 - 65% Boronate molecule yields were reached → showing how high and effective Boronate yields were established with the optimized conditions
 - Theoretical analysis supports NHC is donating electrons and the Aryl Bromides are properly receiving them and culminates in final mechanism
 - Optimized condition at 425 nm (blue light) also means this procedure is mild and not very energy intensive
- Changes to be made if project was repeated:
 - I would start with some pre-analysis before my optimization framework
 - Doing UV-Vis initially would let me know that theoretically optimal NHC absorption of light would occur at ~425 nm light and could build my optimization framework around there instead of going in blindly which would save time

CONCLUSIONS AND FUTURE WORK

- **In summary**, a mild method for functionalization of aryl bromides was effectively developed to improve upon the weaknesses of metal catalysts and make the borylation process more environmentally friendly, energy, and cost efficient
 - This ultimately leads to a better method for production of drugs with boronates like Crisaborole and Vaborbactam
- **Future work** builds towards:
 - Implementing this new process in industry and potentially replacing metal catalysts for this process
 - Increasing the substrate range to other targeted molecules in other high value drugs as well
 - Testing even more optimization conditions to try to increase yield further

REFERENCES

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- (2) Pan, L.; Kelley, A. S.; Cooke, M. V.; Deckert, M. M.; Laulhé, S. *ACS Sustainable Chem. Eng.* **2022**, *10*(2), 691–695.
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