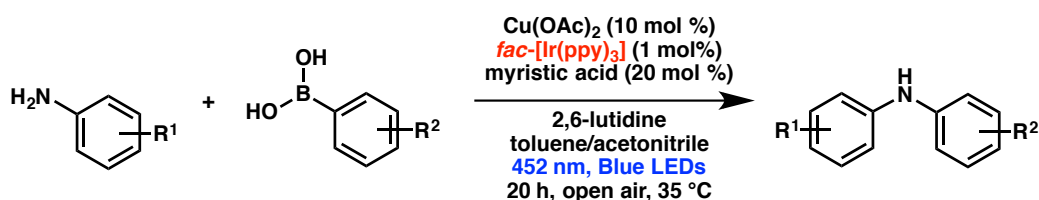


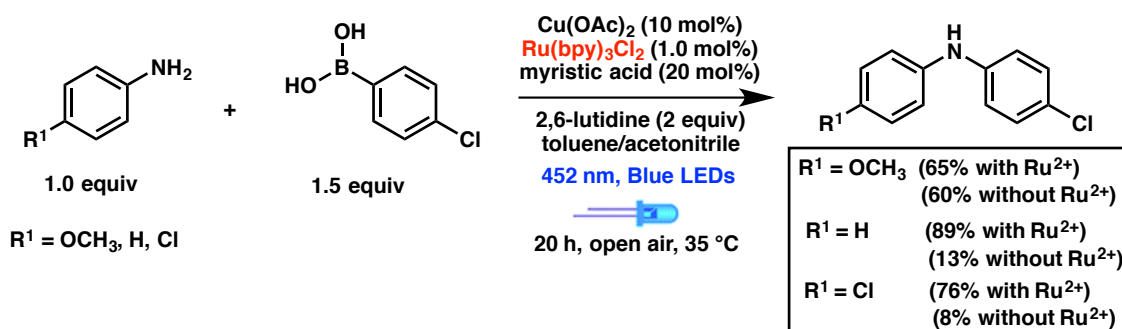
The current ACS PRF UNI Program award has enabled the continued cultivation of scholarly culture in the undergraduate sciences at High Point University. While the shared goals of developing meaningful research experiences for undergraduates have been actively supported by the administration at HPU, this ACS PRF award has added further excitement and motivation for further university investment. This is most profoundly evidenced by the construction of a \$65 million, 128,000-square-foot facility, which supports the undergraduate sciences at HPU. However, the ACS PRF award has also given confidence to the administration to invest not just in physical space but to additionally invest in modern scientific instrumentation to enhance our students' teaching and research experiences (<http://www.highpoint.edu/chemistry/instrumentation/>). In addition to the fundamental science that has been studied through this project to date, the results of this ACS PRF award have been presented by research students at local, regional, and national meetings of the ACS.

A long-standing problem with the Chan-Lam coupling reaction is low and variable yields when using coupling partners of electron-poor character. While other groups have sought to solve this problem with electrochemistry or oxygenated atmospheres, a significant advance was found when using an iridium-based photocatalyst in the copper-catalyzed process, as described by Kobayashi and coworkers (Scheme 1).¹



Scheme 1. The C–N bond forming Chan-Lam coupling reaction showing conditions from the Kobayashi and Lab. Although R¹ and R² are typically electron-rich substituents, the incorporation of the iridium(III) photoredox catalyst facilitates an expanded substrate scope with aryl coupling partners.

As any iridium(III) catalyst is quite expensive, we observed the more economical option of Ru(bpy)₃Cl₂ could provide comparable yields similar reaction conditions. As photoredox methodologies are proving to dramatically affect how the chemist designs and conducts synthesis, we sought to develop this aerobic photoredox process as a teaching experience for our undergraduate science students.² Indeed, this lab has shown a dramatic example of how transition-metal catalysis can be altered by photoredox co-catalysis. As seen in Scheme 2, our undergraduates are given the opportunity to study when a photocatalyst is needed for oxidative copper catalyst turnover and when the substrate choice allows productive union without the ruthenium(II) additive.



Scheme 2. Using alternative aniline derivatives, undergraduates observe a stark contrast in yields with and without ruthenium(II) photocatalyst, which provides clear data as to how putative intermediates in the catalytic cycle could be affected by electron-donating or electron-withdrawing substituents.

During the first ACS PRF budget period, we explored the substrate scope of these reaction conditions during in-semester and summer research opportunities for four talented undergraduate students. The data obtained during our studies into the ruthenium(II) photocatalytic contribution to extending the oxidative copper coupling reaction is shown in abbreviated form in Figure 1, where alkyl amines and aryl boronic acids were productively joined in the C–N bond-forming process.

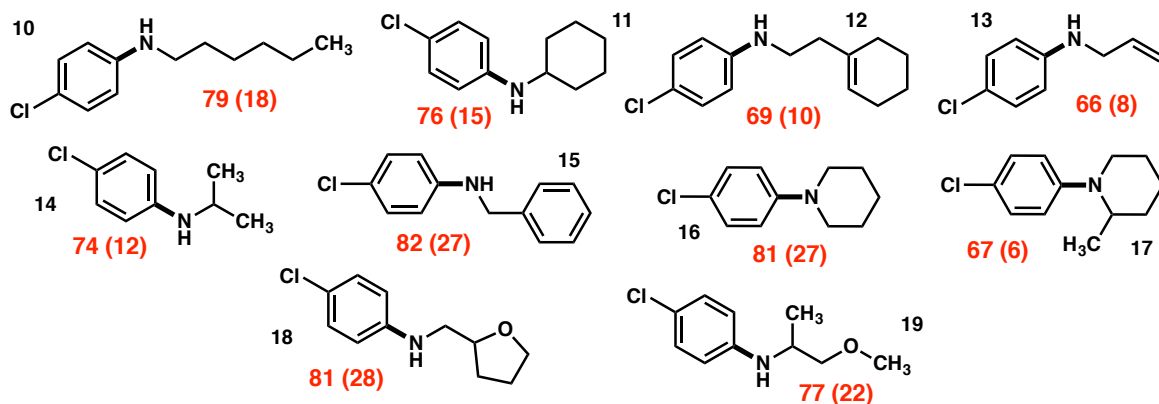
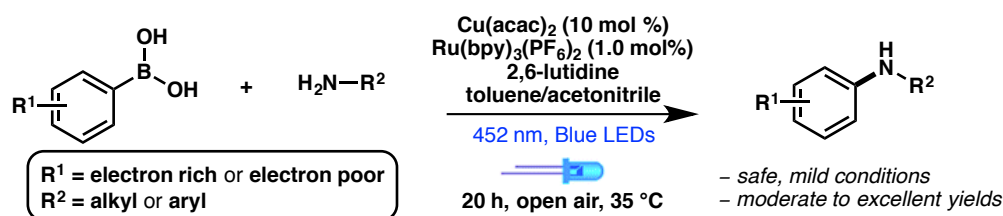


Figure 1. Coupling of alkyl amines with 4-chlorophenylboronic acid allows general access to secondary and tertiary amines products in moderate to high yields. The bolded bond shows the site of the new C–N connection. Yields with photocatalyst are shown in red, where yield without photocatalyst are shown in parentheses.

Our fluorescence quenching studies have shown both copper(II) and copper(I) to powerfully quench the photoexcited state of $\text{Ru}(\text{bpy})_3\text{Cl}_2$ in Ar-degassed solution, which strongly suggests that oxidative turnover of copper-based intermediates is facilitated by the photocatalyst. Prior studies have shown increased byproduct formation, such as protodeboronation, homocoupling, or oxidation, when copper(I) intermediates persist in the reaction media.^{1b}

Following the progress of the first budget period, we were eager to seek new copper and photocatalyst systems to improve the operational simplicity and economic efficiency of the Chan-Lam coupling reaction. Although we had observed some reactivity enhancement with the use of $\text{Ru}(\text{bpy})_3\text{Cl}_2$, we sought to improve the consistency of our results. Careful observation of our reaction media showed solubility issues with the chloride salt and upon switching to the hexafluorophosphate counterion, the reaction yields were extremely dependable. We then turned our attention to a screen of commercially available copper(II) catalysts with different hydrocarbon ligands. These alternative copper(II) sources allowed us to eliminate the addition of the myristic acid reaction component when dealing with $\text{Cu}(\text{OAc})_2$. Shown in Scheme 3 is our current optimized reaction condition that allows successful C–N union even when dealing with electron-poor boronic acids and alkyl amine coupling partners. With these preliminary results, we have submitted our work to the chemistry preprint server, ChemRxiv.³



Scheme 3. With the improved solubility of both the copper(II) and Ru(II) catalysts, the general and mild reaction conditions provide consistent results.

While this summer's research progress was attenuated due to the construction and renovation of buildings on campus, the research project funded by this ACS PRF award will allow undergraduate research engagement during summer 2020. We intend to build on our progress to further investigate non-metal photocatalysts in the promotion of the aerobic Chan-Lam coupling reaction.

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