4-12-2024

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Anna G. Tyshka
Hope College

Tyler J. King
Hope College

Lucas D. Day
Hope College

Timothy R. Welsh
Hope College

Recommended Citation

Repository citation: Tyshka, Anna G.; King, Tyler J.; Day, Lucas D.; and Welsh, Timothy R., "Expanding the Use of Palladium-Catalyzed beta-Aryl Elimination Reactions" (2024). *23rd Annual A. Paul and Carol C. Schaap Celebration of Undergraduate Research and Creative Activity (2024).* Paper 84.
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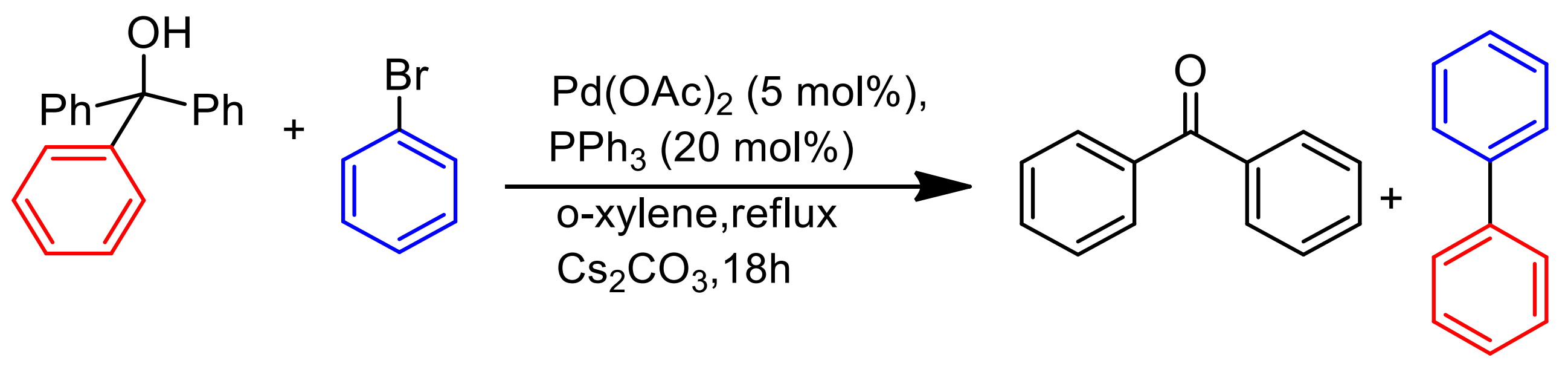
Expanding the Use of Palladium Catalyzed β-Aryl Elimination Reactions

Anna G. Tyshka, Tyler J. King, Lucas D. Day, Timothy R. Welsh, Jeffrey B. Johnson*
Department of Chemistry, Hope College, Holland, MI 49423

For more information, contact:
Dr. Jeff Johnson
Hope College Department of Chemistry
616-395-7083
jjohnson@hope.edu

Background

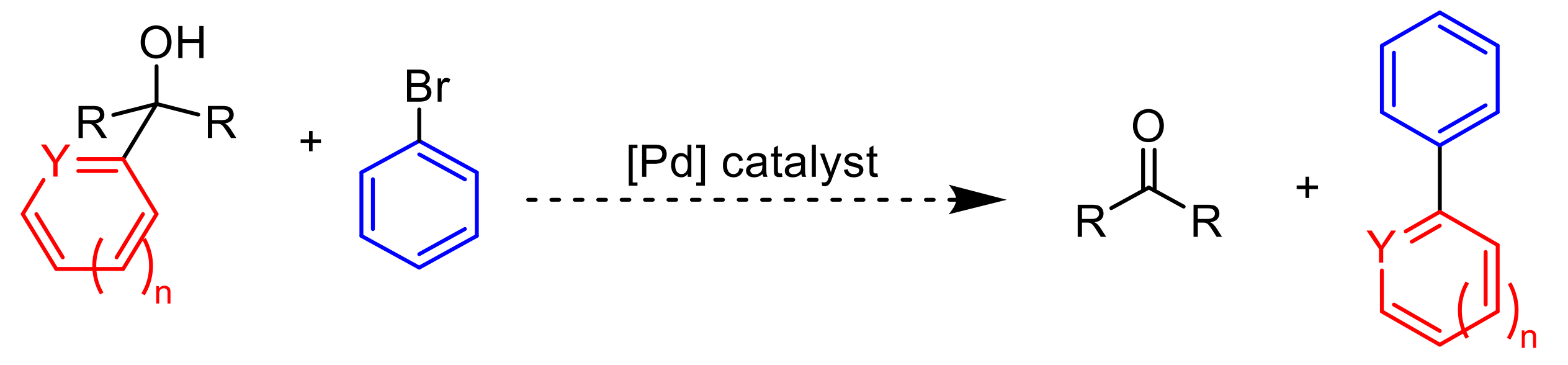
Due to their inert nature, carbon-carbon δ-bonds are typically unutilized in synthetic processes. However, metal catalysts such as palladium have been shown to activate such bonds. One example is the palladium catalyzed β-arylative elimination of triarylmethanols. Previous work has investigated factors affecting the aryl elimination in the aforementioned reaction. Substitution patterns of both the aryl bromide and triarylmethanol allow for insight into aspects affecting the catalytic cycle.



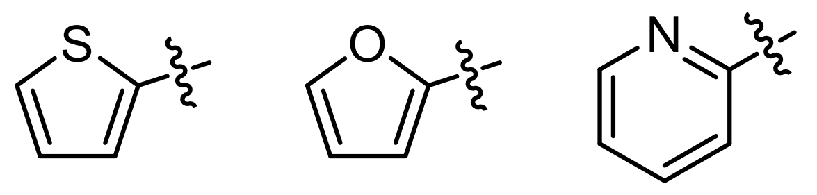
Reference: Bour, Green, Winton, Johnson, *J. Org. Chem.* **2013**, 78, 1665.

Reference: Miura et. al., *J. Org. Chem.* **2003**, 68, 5239.

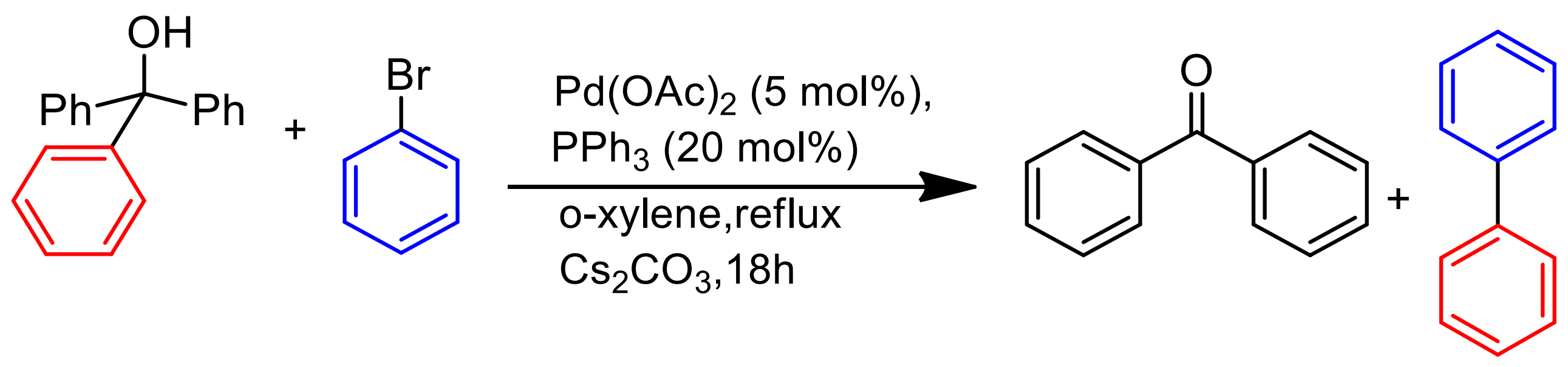
Ongoing efforts are focused on expanding the types of aryl groups that can be transferred via this Suzuki-like methodology. Specific areas of focus including 2-substituted heterocycles, as these compounds are incompatible with a number of related cross coupling methods.

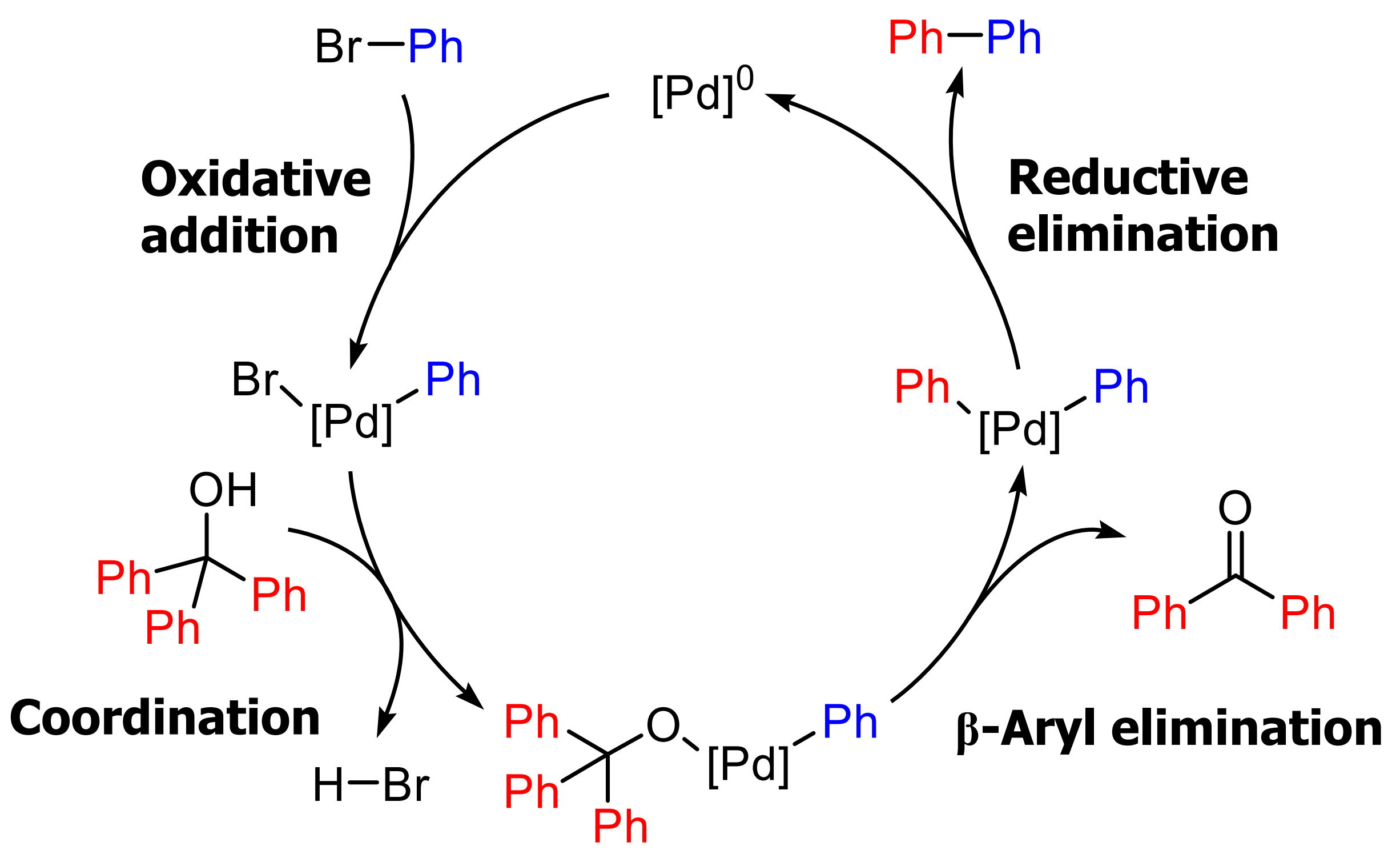


To transfer groups such as:



Catalytic Cycle

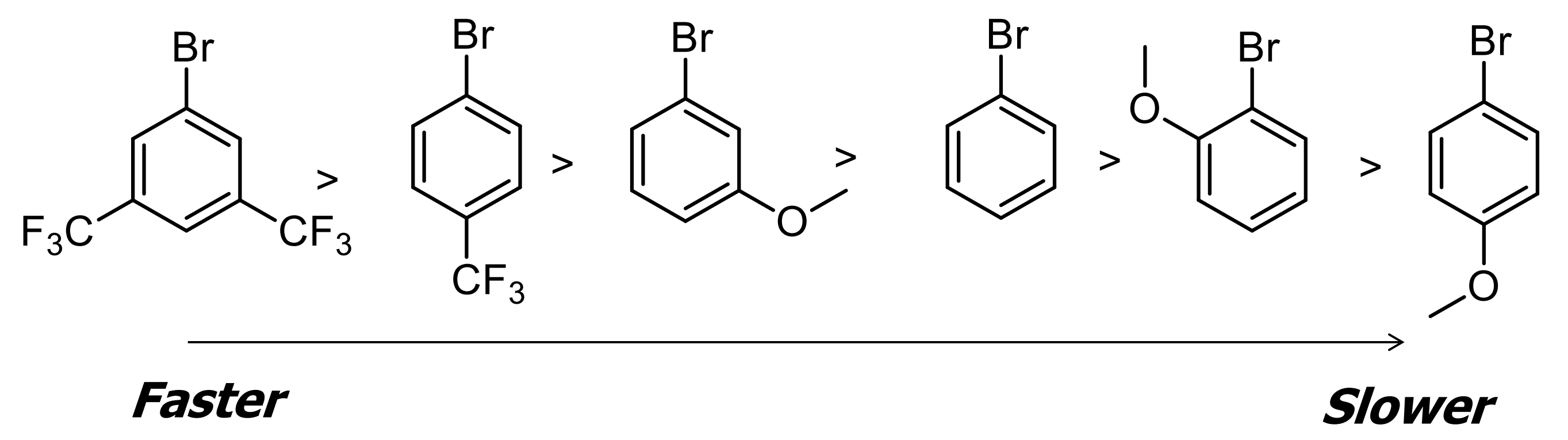




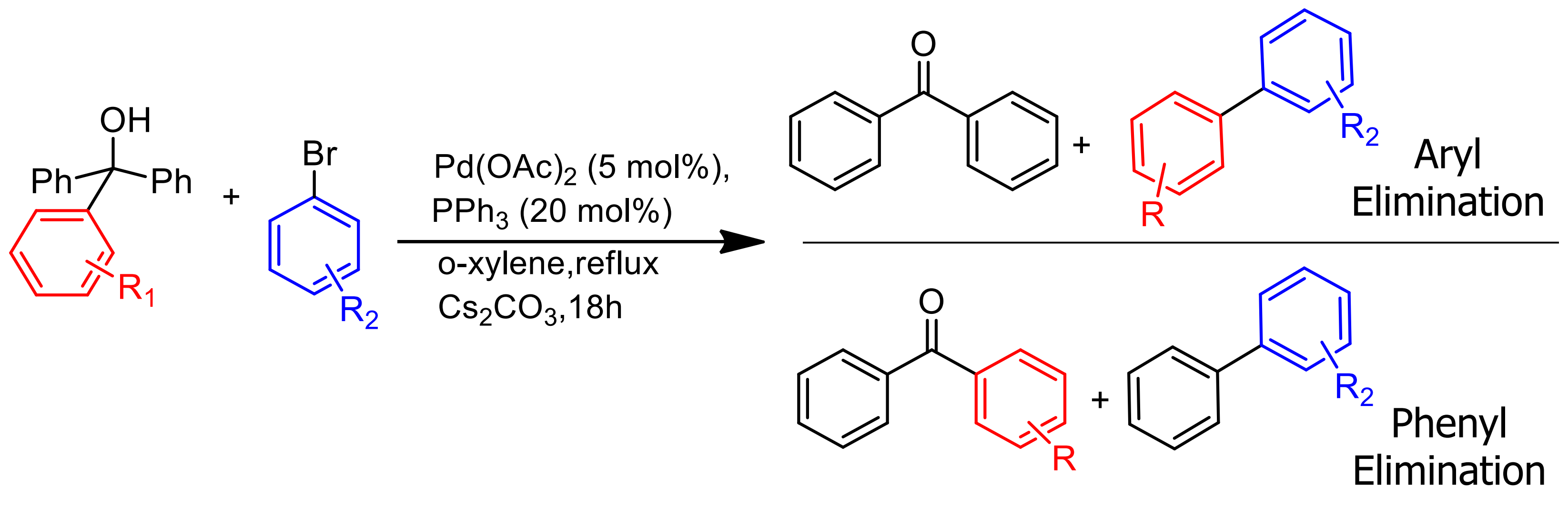
- The catalytic cycle is based upon that proposed by Miura and coworkers
- Palladium(0), the active catalyst, first interacts with the aryl bromide
- Several experiments suggest that the aryl elimination step is the slow step of the cycle, and both it and the reductive elimination are irreversible

Research Methods

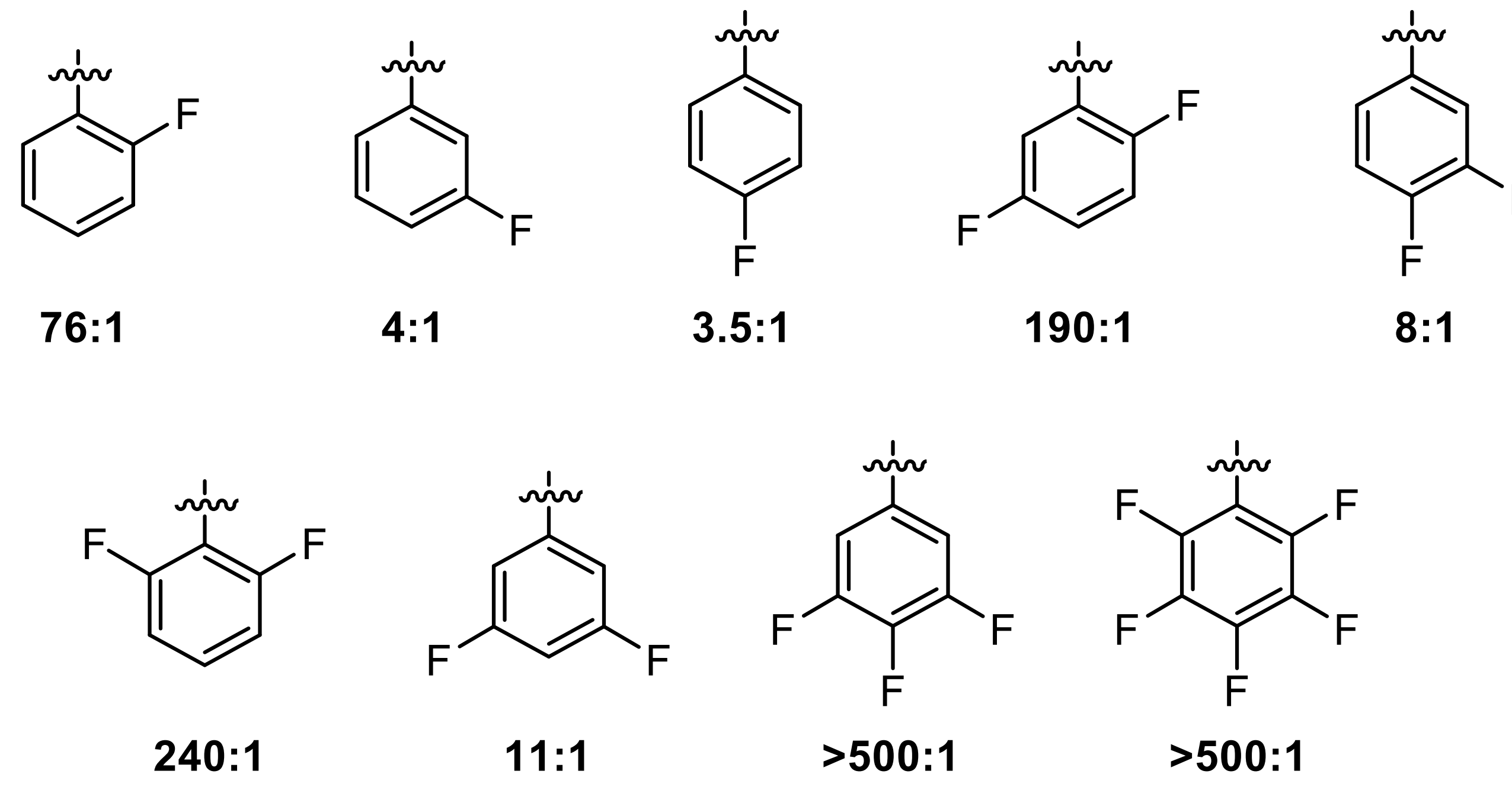
- Previous research established clear trends regarding reactivity of aryl halide
  - Electron deficient groups reacted more quickly than electron rich groups



- For the triarylmethanols, compounds with *ortho*-fluoro substitution reacted much faster and more selectively than other substrates



Sample selectivities *(All ratios are C-Ar elimination vs. C-Ph elimination*

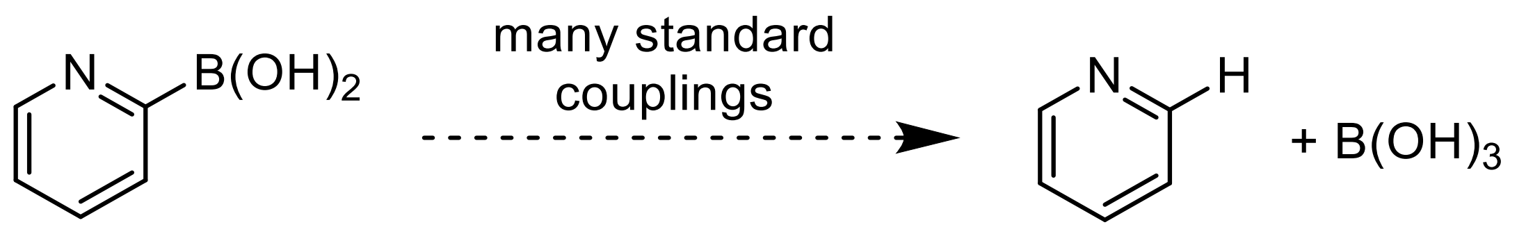


- The effect of triarylmethanol substitution was determined by analysis of product ratios as determined by MS/GC

Extending the Substrate Scope

Boronic acids of 2-heterocycles and 2-fluorophenyl compounds often undergo protodeboronation, making them incompatible with many cross coupling reactions. This methodology promises a means of successfully coupling these groups.

Protodeboronation

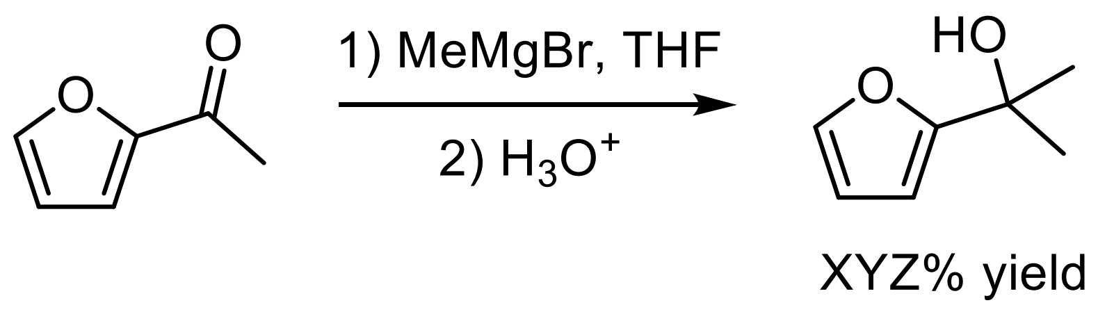


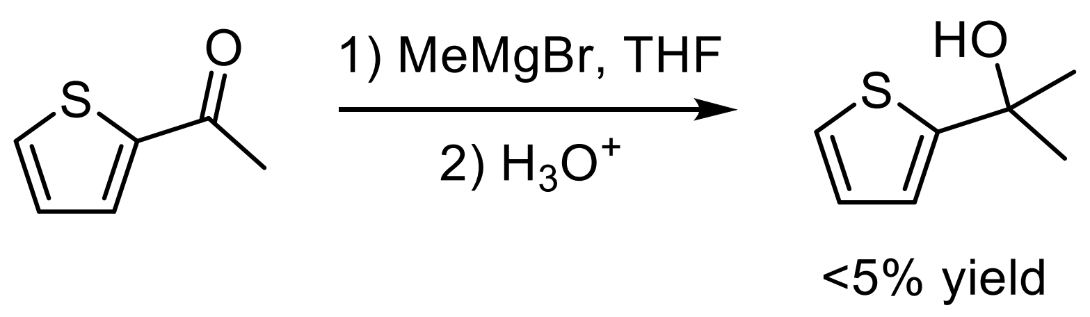
This approach:

available for cross coupling

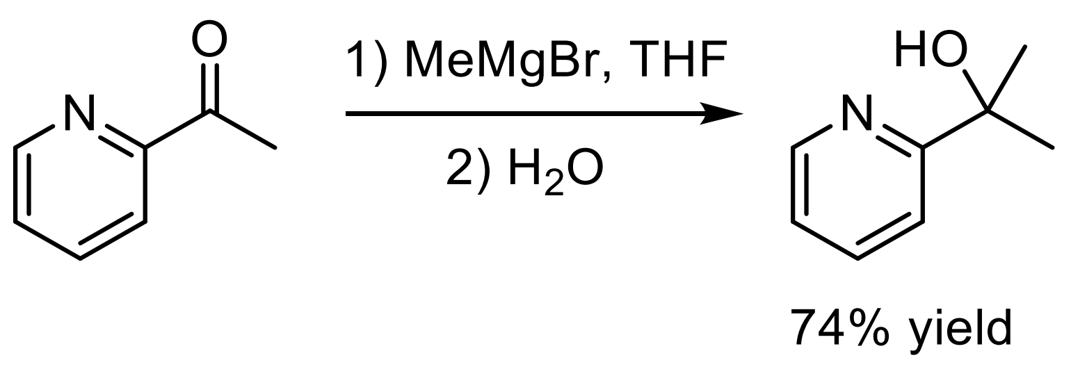
Preparing Potential Substrates

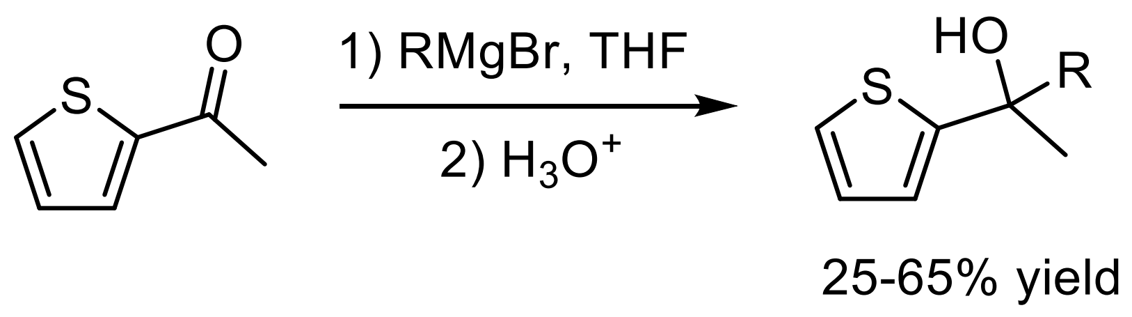
Several substrates have been prepared via Grignard reactions initially producing dimethyl tertiary alcohols.





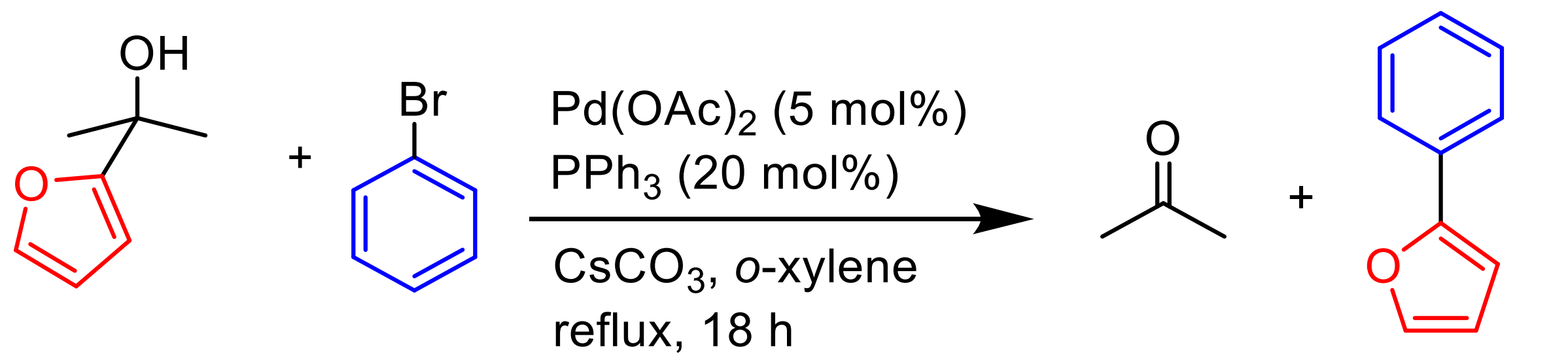
Product successfully formed, but volatile





Have used R = iPr, vinyl, allyl, etc.

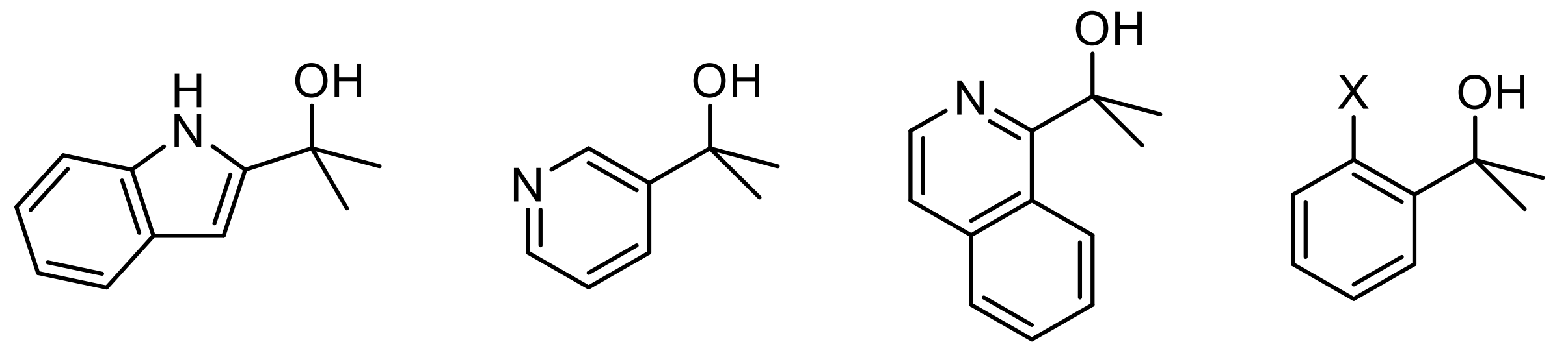
Initial Coupling Efforts



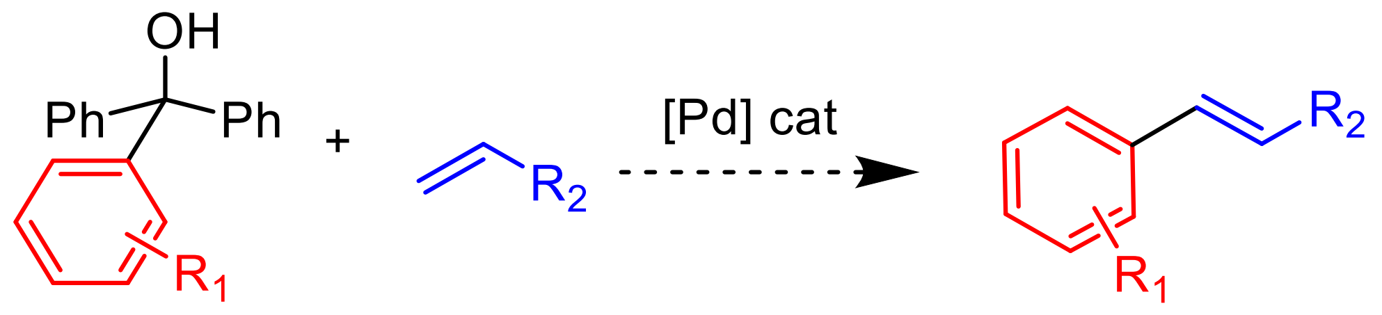
Coupling product observed by GC/MS

Future Work

Substrates Efforts will continue on preparing and testing substrates with a variety of heterocycles.



Extend Nucleophiles to Other Coupling Reactions such as the Heck coupling, the Liebeskind Coupling, and others.



Acknowledgements

- Johnson Group Lab Mates
- National Science Foundation (CHE-17116411)
- Schaap Endowed Fund for Undergraduate Research
- Organic Synthesis, Inc.