Diverse *N*-Heterocyclic Ring Systems via Aza-Heck Cyclizations of *N*-(Pentafluorobenzoyloxy)sulfonamides

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Angew. Chem. Int. Ed. **2016**, 55, p. xxx

Current Literature

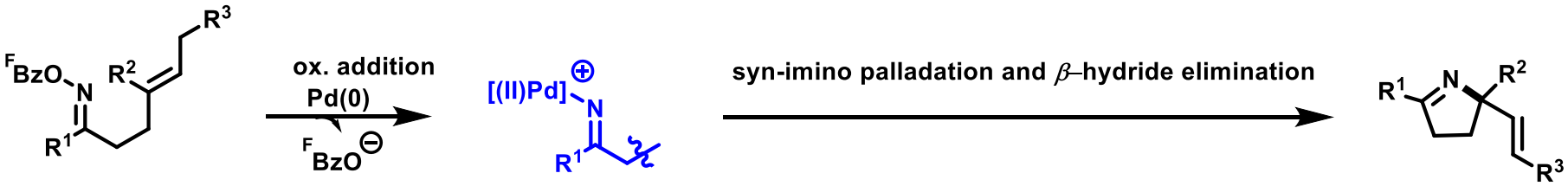
Wipf Group

Leila Terrab

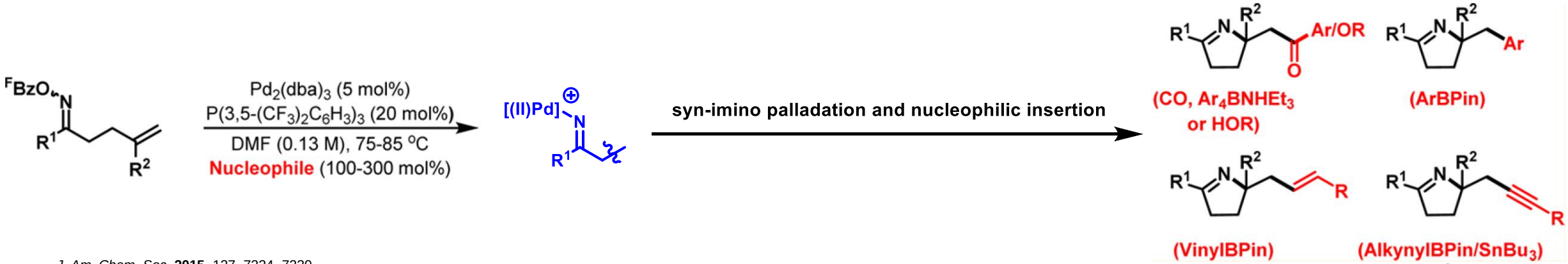
8/6/16

Narasaka-Heck reaction

Limited application via aza-Heck route



More diverse products via non-aza-Heck route



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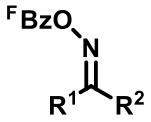
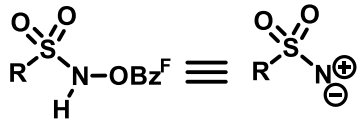
Proposed Aza-Heck cyclization

Narasaka-Heck approach

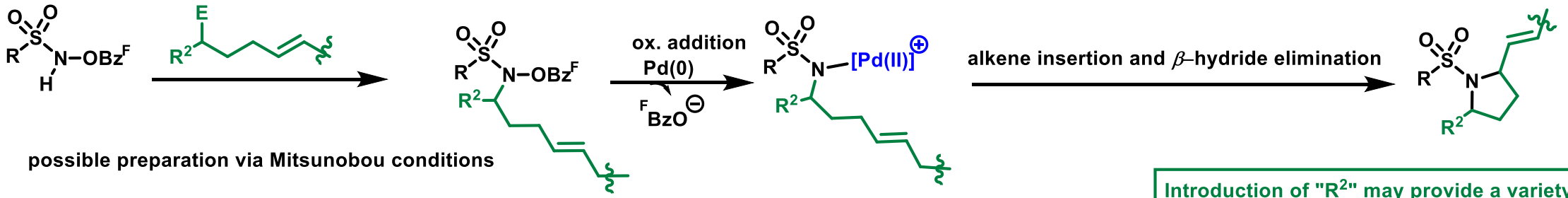


imine derivative

Proposed Approach

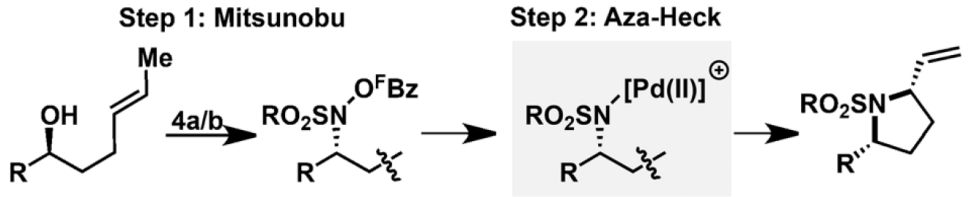


hydroxysulfonamide derivative behaves as a nitrene

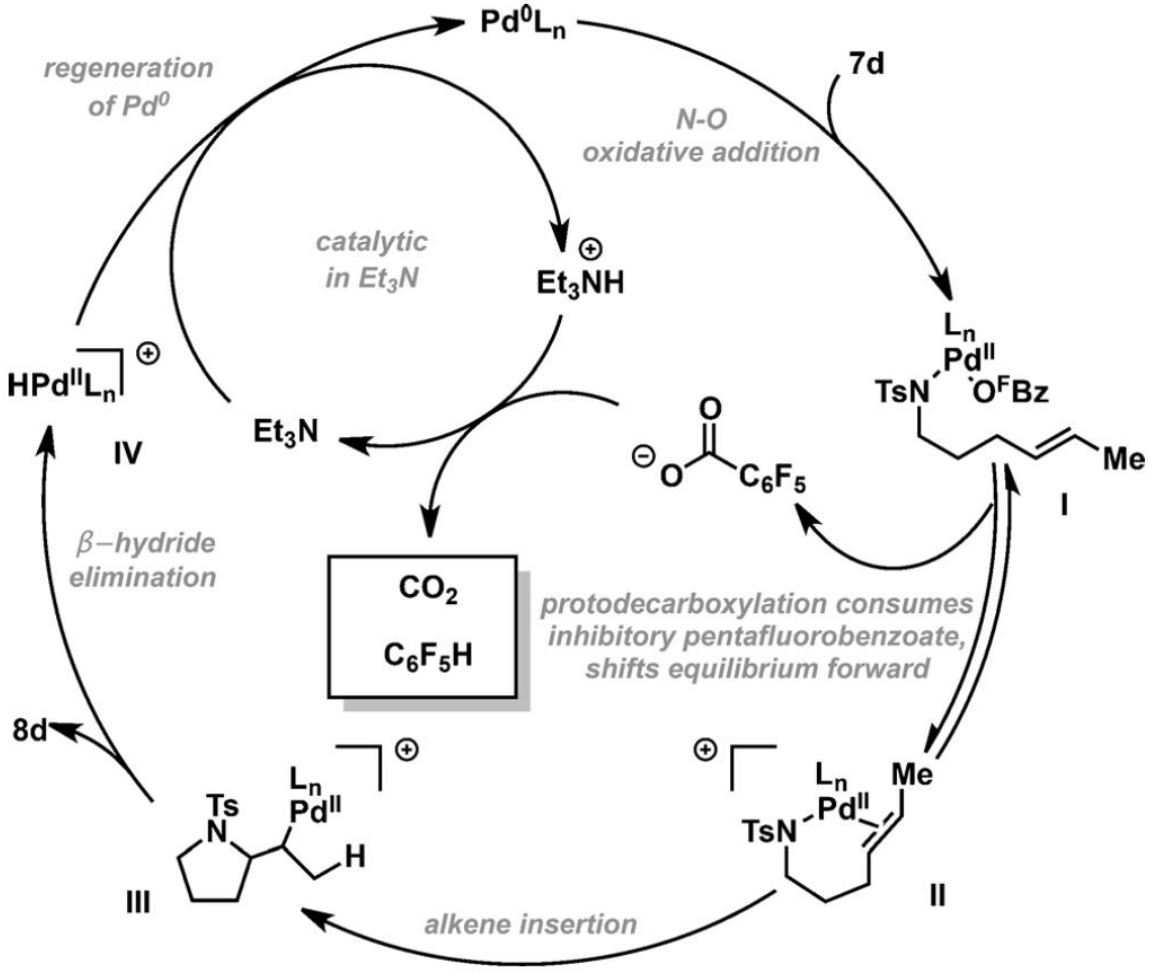


possible preparation via Mitsunobou conditions

Introduction of "R^2" may provide a variety of intermediates

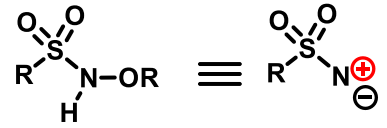


Mechanism



Optimization of oxidative addition:

- Choice of electron withdrawing nature of R

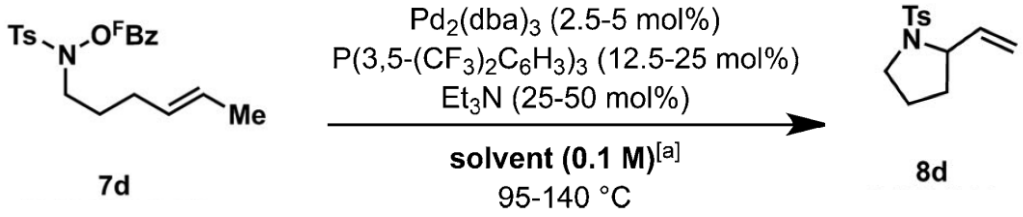


Optimization of alkene insertion:

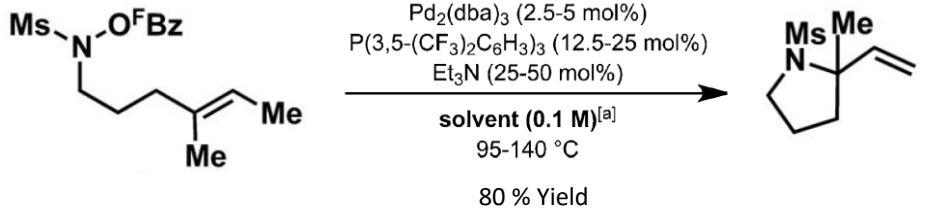
- Addition of NEt_3

Limitation of this aza-Pd II intermediate:

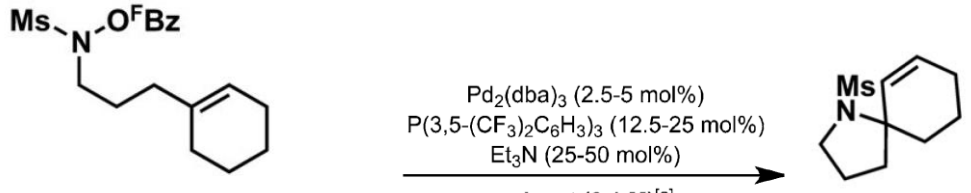
- Protodepalladation
- *B*-hydride elimination



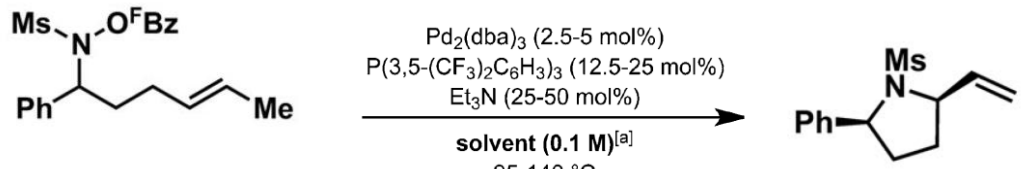
Scope



80 % Yield



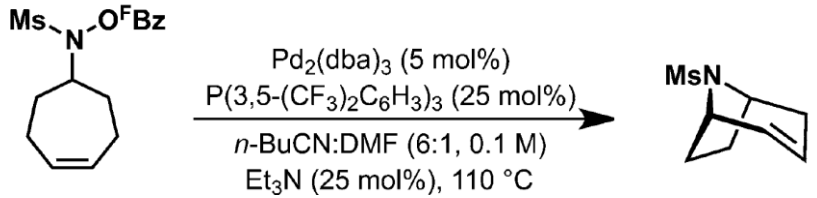
42 % Yield

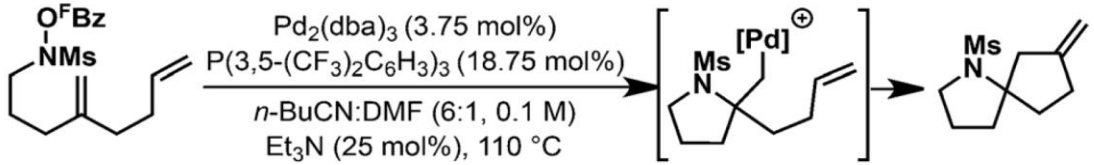


58% Yield
(>10:1 d.r.)

solvent: *n*-BuCN:DMF

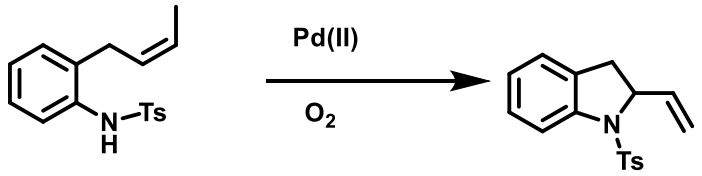
Interesting aza-Heck applications



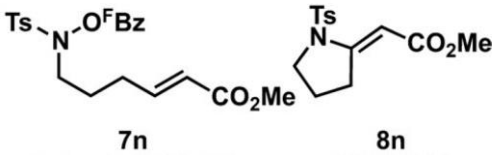


Comparison to aza-Wacker cyclization

aza-Wacker cyclization of alkenyl NH-sulfonamides:



- Alkenyl NH sulfonamides not prepared directly from the alcohol
- Electron-deficient alkenes not used due to possible conjugate addition
- Can not engage in cascade polycyclizations and bridged systems



aza-Heck electron-deficient alkene

Summary

- Expanded the application of aza-Heck cyclizations beyond the previously reported Narasaka-Heck reaction (limited to oximes as SM)

- Used the nitrenoid property of *N*-(pentafluorobenzoyloxy)sulfonamides to install alkene substituents and to undergo the Pd-catalysis cyclization