首届致远学术节
学生科研成果展示

# Palladium-Catalyzed Alkene Carbodiamination Reactions of Ureas for the Synthesis of Heterocycles

Jiaqi Shen,[†] John P. Wolfe,[*]

[†]Chemistry, Zhiyuan Honors Program, Shanghai Jiao Tong University

[*]Department of Chemistry, University of Michigan

---

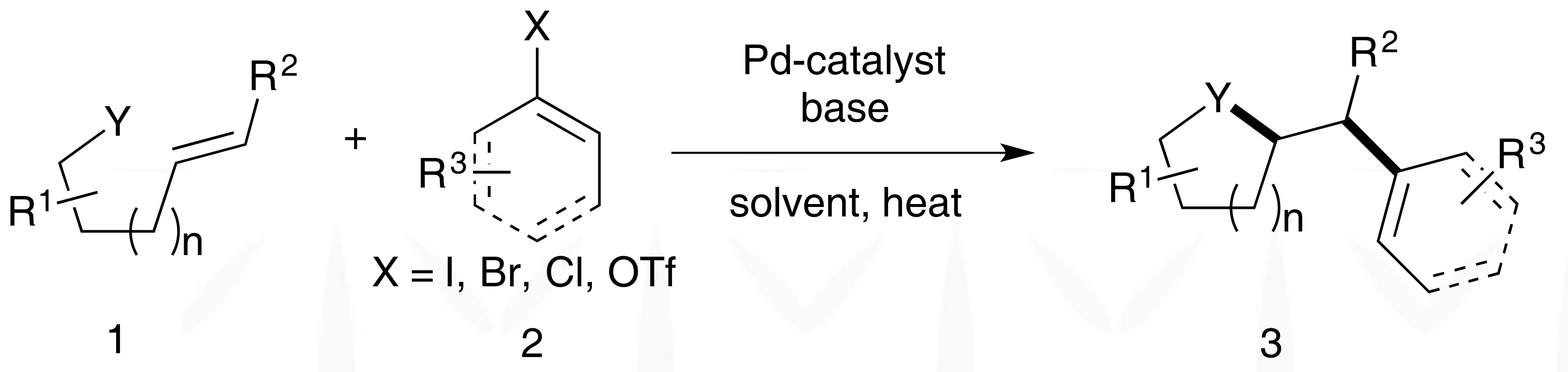
**Abstract:** A Pd-catalyzed difunctionalization reaction between *N*-allylureas and *O*-benzoylhydroxylamines which affords cyclic ureas bearing alkylaminomethyl groups is described. The desired products are obtained in good yield and the mechanism of the reaction appears to involve anti-aminopalladation of the alkene followed by a rare $sp^3C–sp^3N$ bond-forming reductive elimination from a Pd(II) complex with b-hydrogen atoms.

---

**Key words:** Pd-catalyzed difunctionalization, anti-aminopalladation

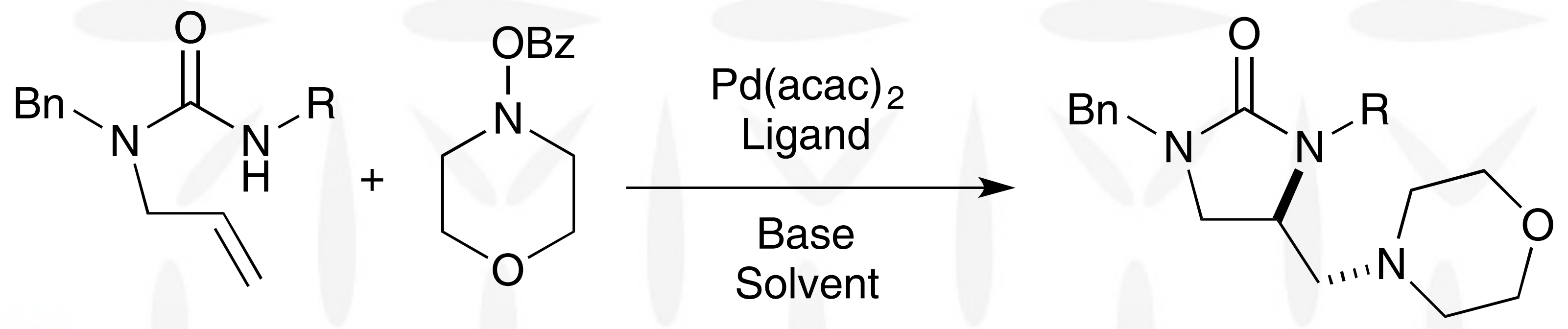
## Introduction

Over the past decade, Pd-catalyzed alkene difunctionalization reactions between aryl or alkenyl halides or triflates and alkenes bearing pendant nucleophiles have been proven to be efficient ways to construct heterocycles. For example, treatment of an alkene bearing a pendant heteroaton(1) with an aryl or alkenyl halide or triflate (2) affords heterocyclic product (3) with good yield and high stereoselectivity (Scheme 1). The majority of Pd-catalyzed aklene carboheterofunctionalization reactions that have been reported undergoes a syn-heteropalladation of the alkene.



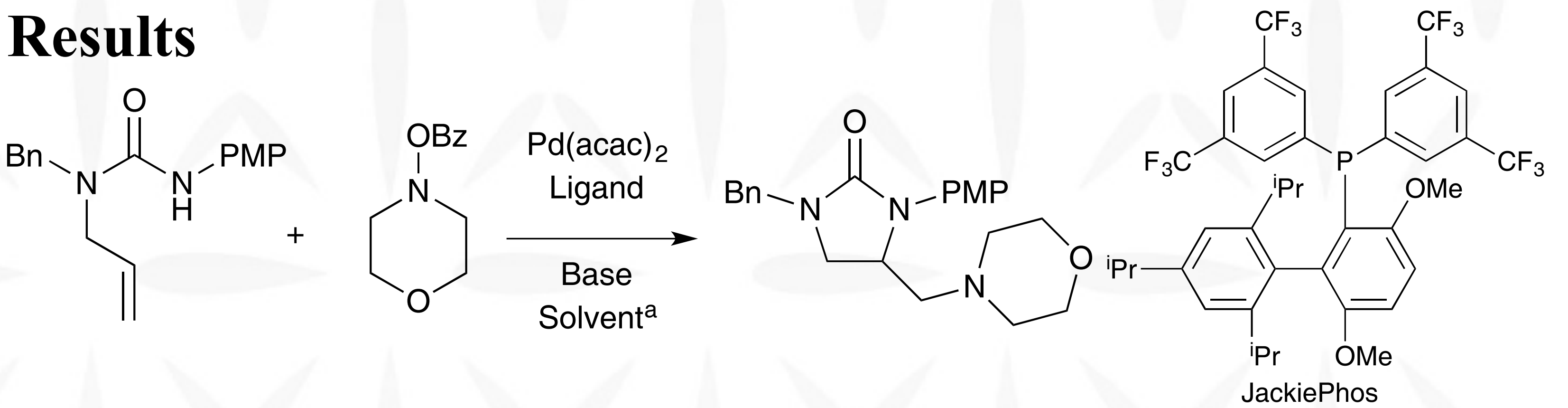
**Scheme 1:** Pd-Catalyzed Alkene Carboheterofunctionalization

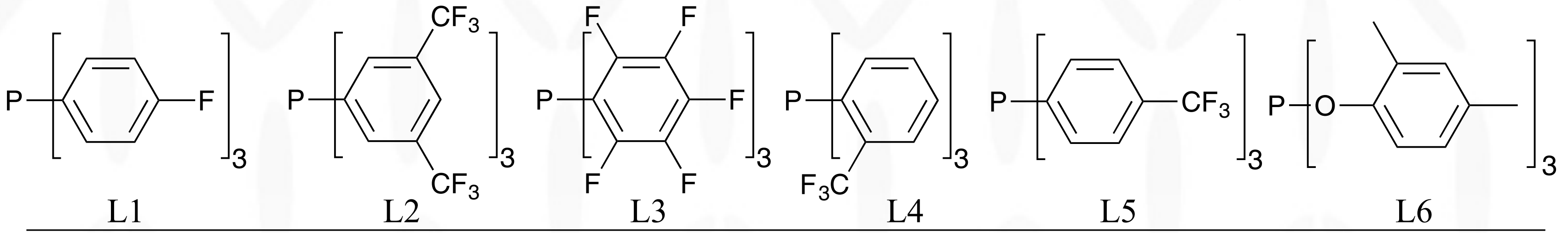
In recent years the use of O-acylated hydroxylamine derivatives as electrophiles in metal-catalyzed reactions has attracted considerable attention. This work is investigating the utility of these electrophiles in alkene diamination reactions (Scheme 2). According to former work, this reaction is believed to undergo *anti*-palladation and the final step in catalytic cycle would be an $sp^3C–sp^3N$ bond-forming reductive elimination, which is a very rare organometallic transformation, and was expected to be challenging.



**Scheme 2:** Pd-Catalyzed Carbodiamination Reaction

## Results





| Entry | Ligand | Ligand/% | Base | Solvent | Yield/%[b] |
|---|---|---|---|---|---|
| 1 | JackiePhos | 6 | $Cs_2CO_3$ | dioxane | 61 |
| 2 | JackiePhos | 8 | $Cs_2CO_3$ | dioxane | 63 |
| 3 | JackiePhos | 12 | $Cs_2CO_3$ | dioxane | 70 |
| 4 | JackiePhos | 16 | $Cs_2CO_3$ | dioxane | Trace |
| 5 | JackiePhos | 6 | $LiO^tBu$ | dioxane | NP |
| 6 | JackiePhos | 6 | $NaO^tBu$ | dioxane | NP |
| 7 | JackiePhos | 6 | $K_3PO_4$ | dioxane | NP |
| 8 | JackiePhos | 12 | $Na_2CO_3$ | dioxane | NP |
| 9 | JackiePhos | 12 | $K_2CO_3$ | dioxane | NP |
| 10 | JackiePhos | 12 | CsF | dioxane | NP |
| 11 | JackiePhos | 12 | $Cs_2CO_3$ | toluene | 34 |
| 12 | JackiePhos | 12 | $Cs_2CO_3$ | trifluorotoluene | 53 |
| 13 | JackiePhos | 12 | $Cs_2CO_3$ | xylene | 42 |
| 14 | L1 | 12 | $Cs_2CO_3$ | dioxane | NP |
| 15 | L2 | 12 | $Cs_2CO_3$ | dioxane | 47 |
| 16 | L3 | 12 | $Cs_2CO_3$ | dioxane | NP |
| 17 | L4 | 12 | $Cs_2CO_3$ | dioxane | NP |
| 18 | L5 | 12 | $Cs_2CO_3$ | dioxane | NP |
| 19 | L6 | 12 | $Cs_2CO_3$ | dioxane | 31 |

[a]Conditions: 1.0 equiv. substrate, 3.0 equiv. nucleophile, 4% Palladium salt, 2 equiv. base, dioxane (0.1M), reflux, 24h. Reactions are conducted on 0.2mmol scale. [b]NMR yield.

## Conclusion

In conclusion, a new class of Pd-catalyzed alkene diamination reactions that involve the coupling of *O*-benzoyl hydroxylamine derived electrophiles with *N*-allylguanidine or urea derivatives is developed. Ether solvent works better than aromatic ones. The amount of ligand and base can effect the results tremendously. More electron-poor and bulky ligand facilitate the reaction. Base plays an important role rather than simply deprotonating but the exact effect of it remains unknown.

个人信息：2014级，化学
邮　　箱：shenjiaqi@sjtu.edu.cn