Literature Report 5

Catalytic Carbo- and Aminoboration of Alkenyl Carbonyl Compounds *via* Five- and Six-Membered Palladacycles

Reporter: **Huan-Ping Xie**

Checker: **Hong-Qiang Shen**

Date: **2018/03/26**

Liu, Z.; Ni, H.-Q.; Zeng, T.; Engle, K. M. *J. Am. Chem. Soc.* **2018**, *140,* 3223.

Contents

Biography

Keary M. Engle

Areas of interest:

- Efficiency, effectiveness of chemical synthesis
- Interface of organometallic chemistry

Research experience:

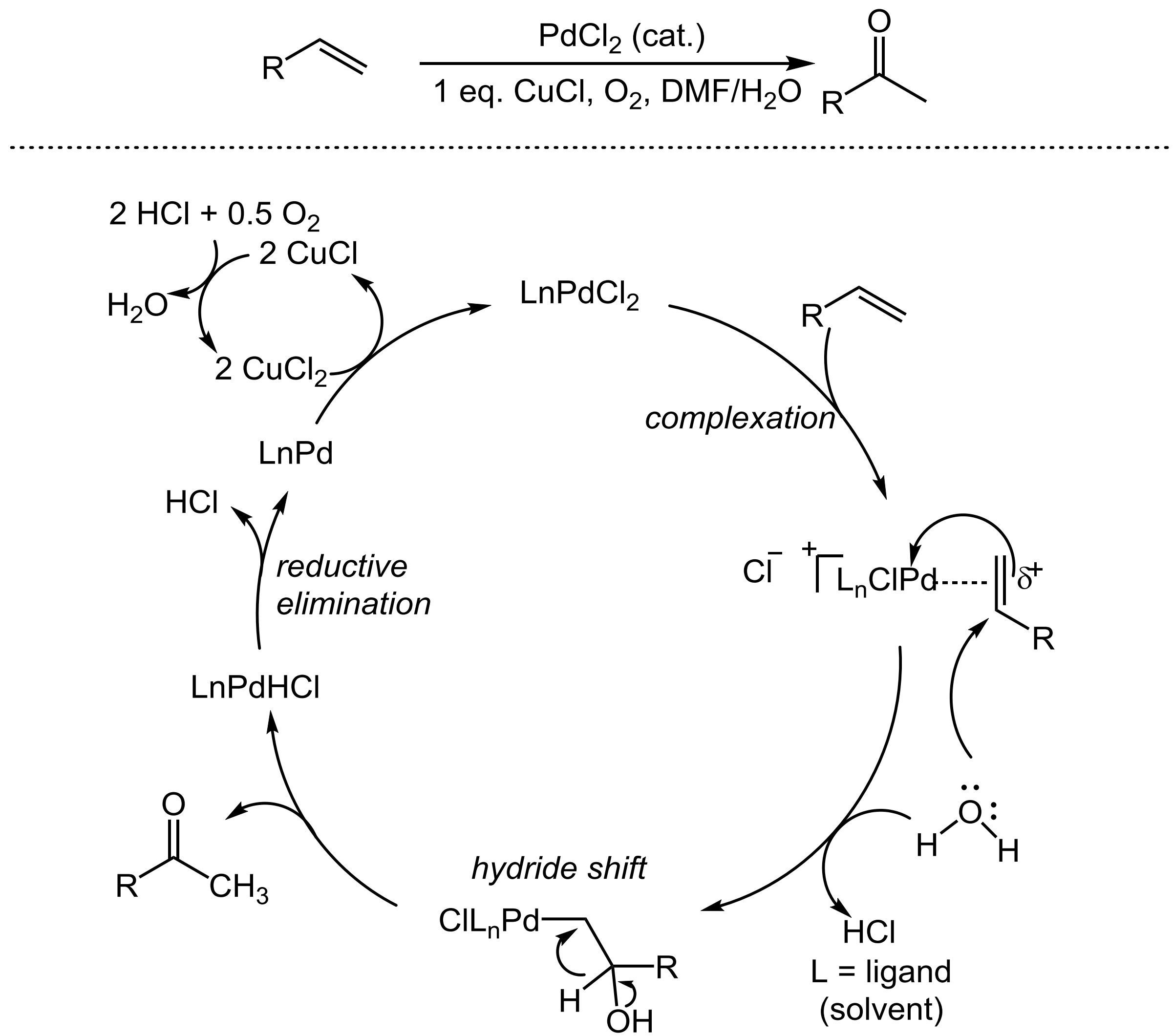
2003-2007 B. S., University of Michigan (Matzger, A. J.);

2008-2013 Ph. D., Scripps Research Institute (Yu, J.-Q.);

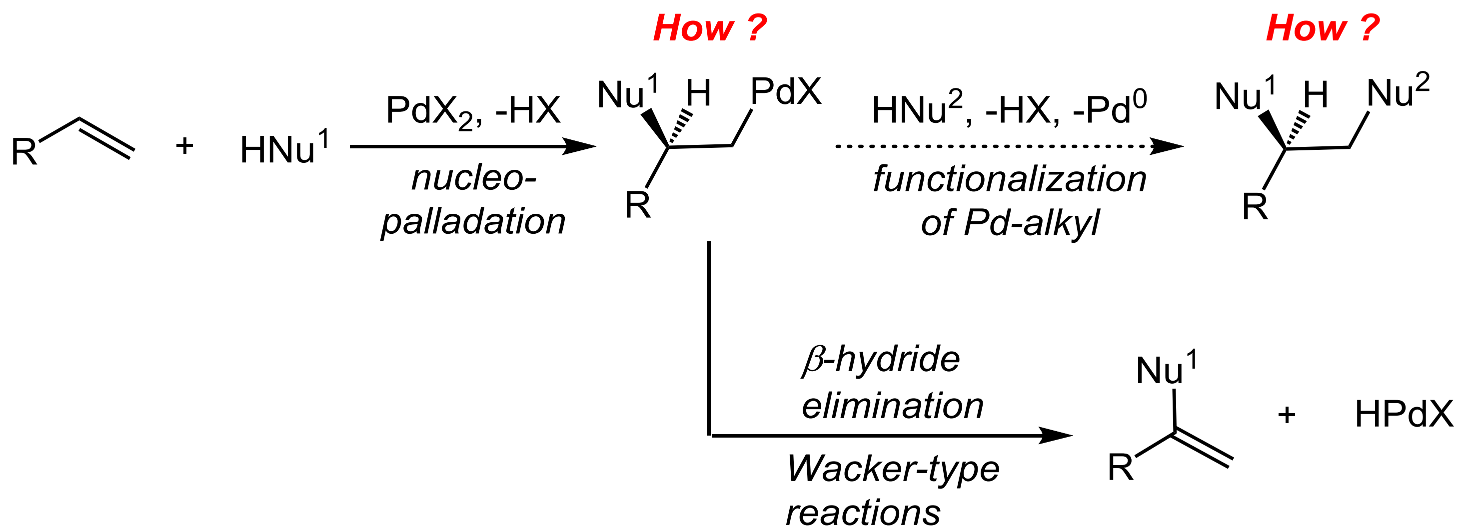
2013-2015 NIH Postdoctoral Fellow, Caltech (Grubbs, R. H.);

2015- Assistant Professor, The Scripps Research Institute.

Wacker reaction



Introduction

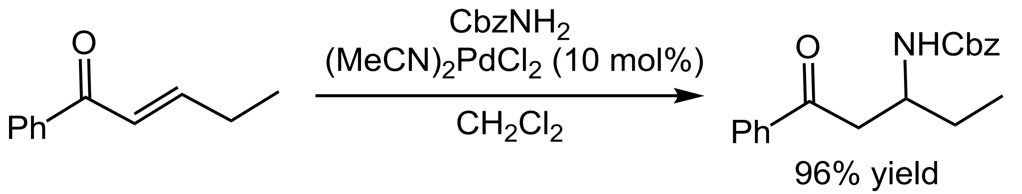


Challenges of nucleopalladation:

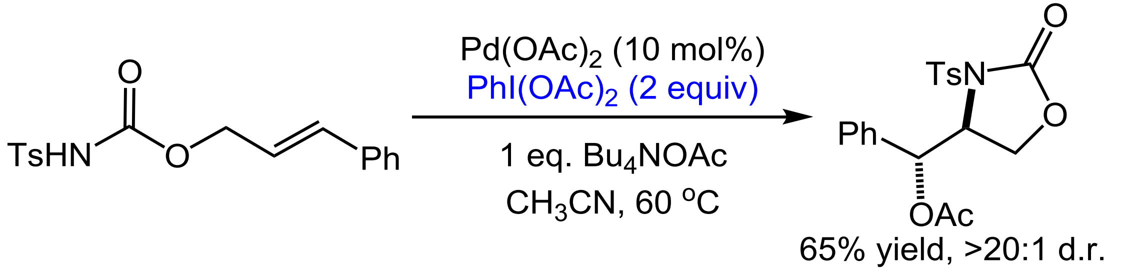
- **The regioselectivity of nucleophilic addition**
- **Supress β-hydride elimination**

Sigman, M. S. *et. al. Org. Biomol. Chem.* **2008**, *6*, 4083.

Introduction

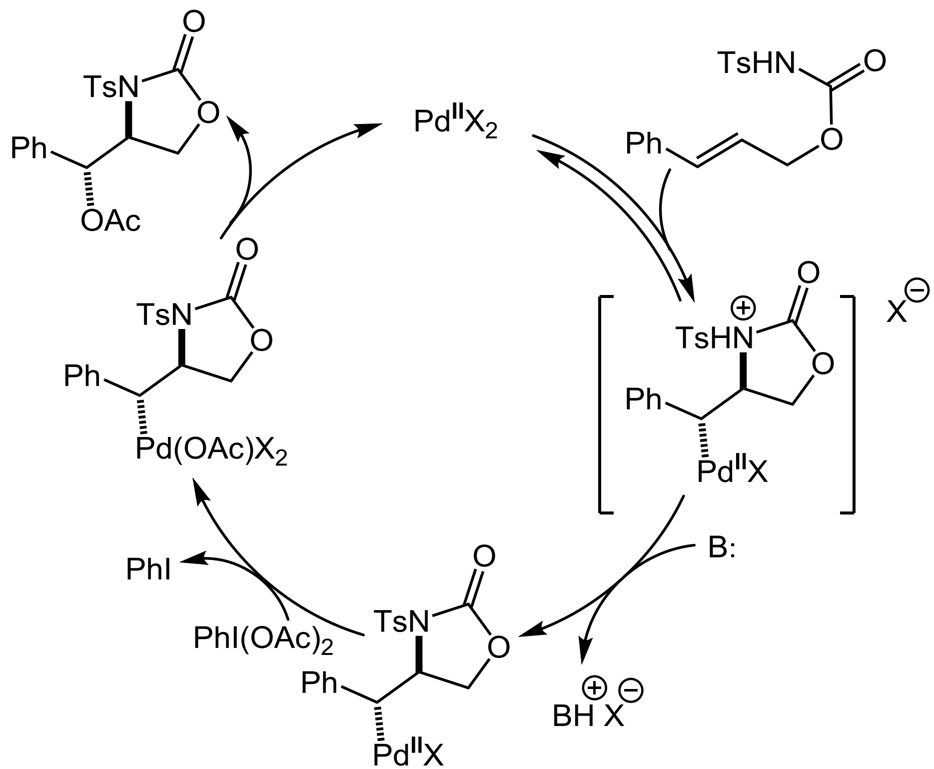


Spencer, J. B. *et al. Org. Lett.* **2001**, *3*, 25.



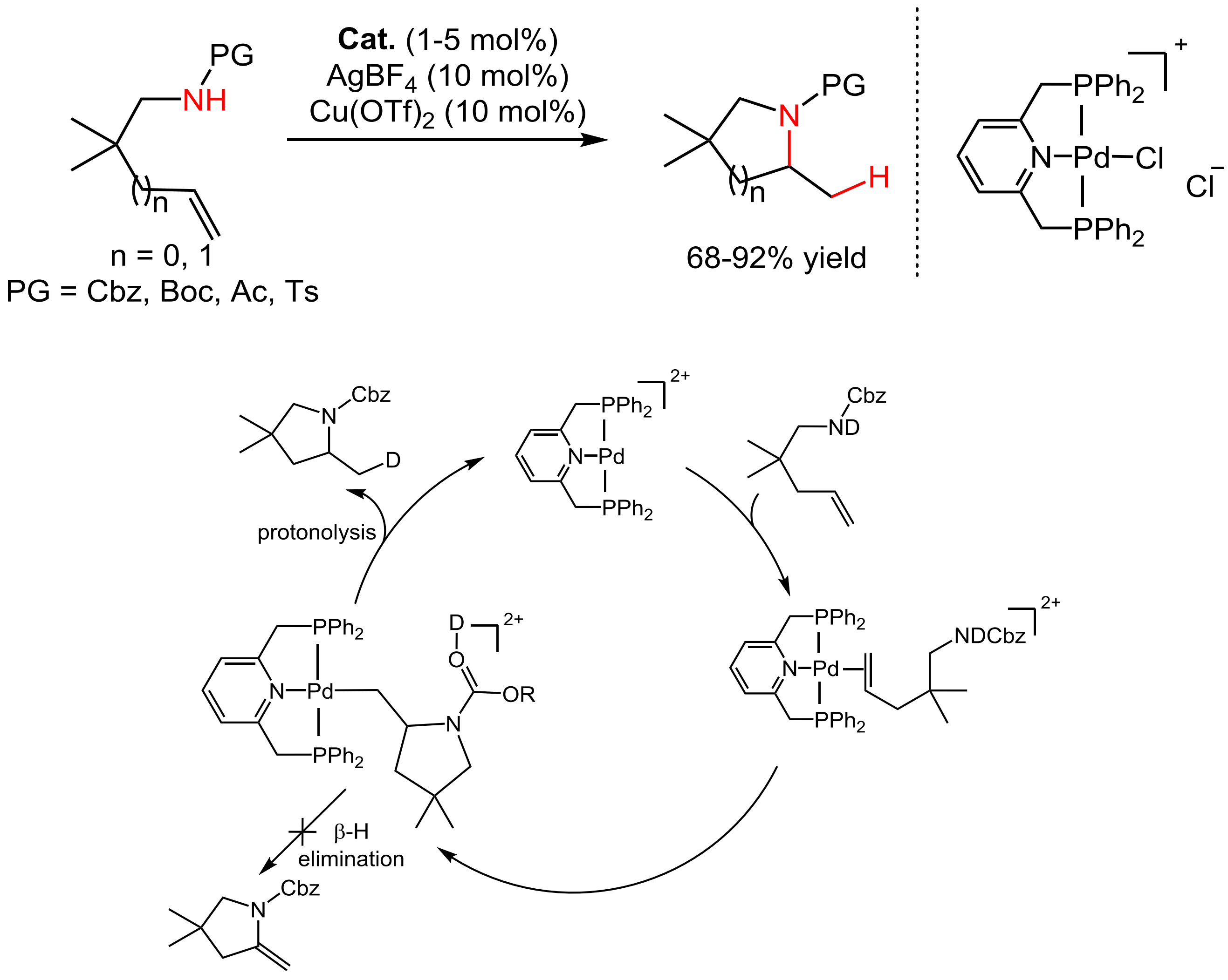
Sorensen, E. J. *et al. J. Am. Chem. Soc.* **2005**, *127*, 7690.

Introduction



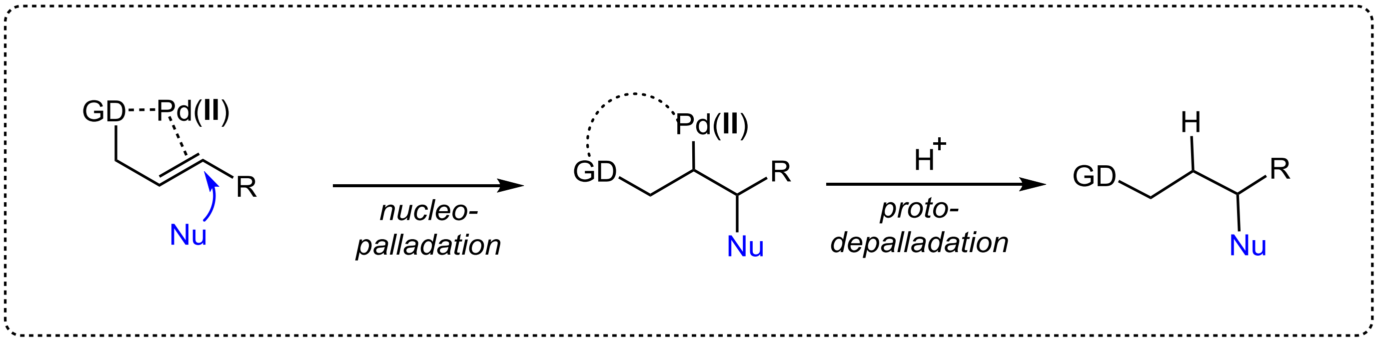
Sorensen, E. J. *et al. J. Am. Chem. Soc.* **2005**, *127*, 7690.

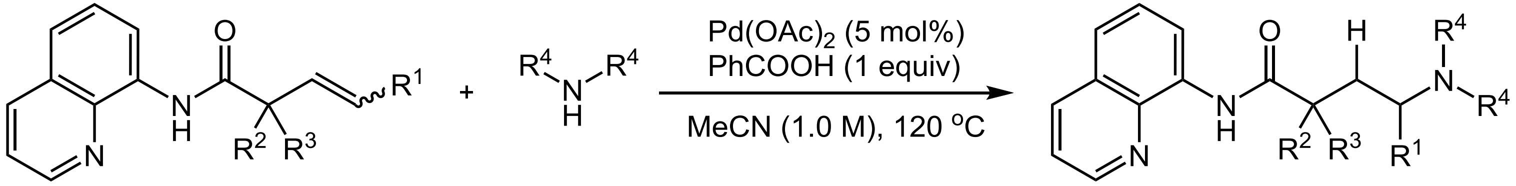
Introduction



Cochran, B. M. *et. al. J. Am. Chem. Soc.* **2006**, *128*, 4246.

Introduction

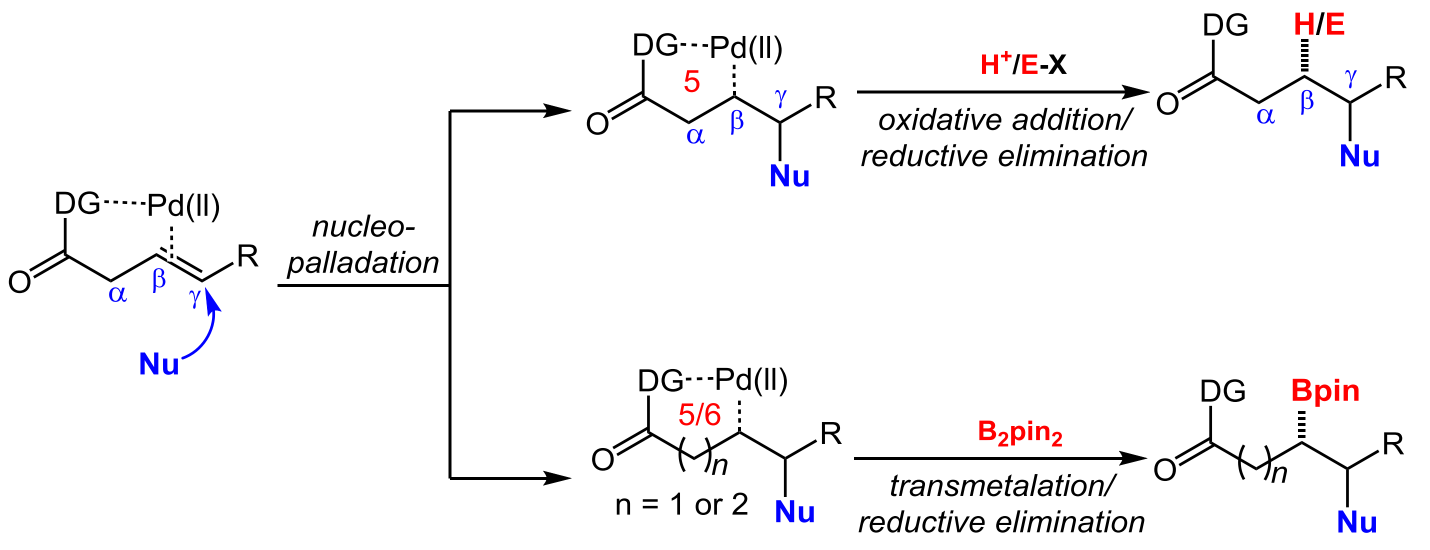




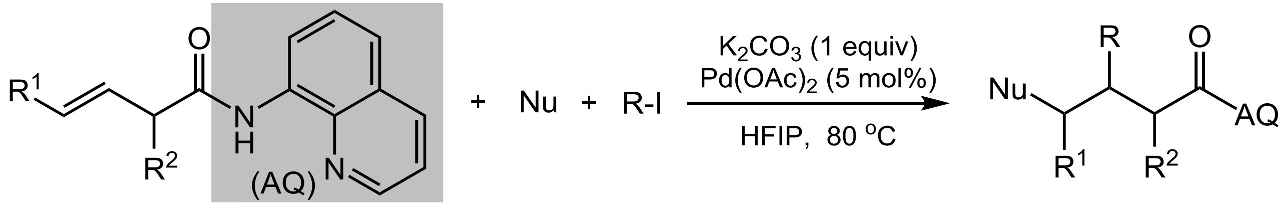
Engle, K. M. *et. al. J. Am. Chem. Soc.* **2016**, *138*, 5805.

Introduction

- **Hydro- and difunctionalization of unactivated, internal alkenes**

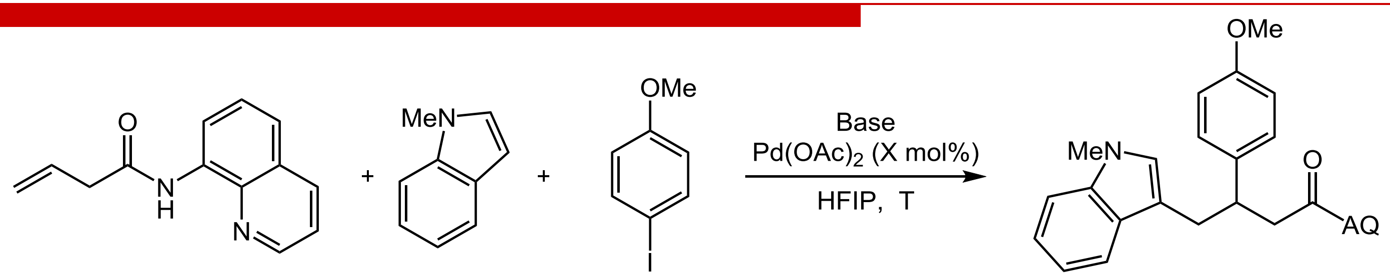


Dicarbofunctionalization of alkenes



Engle, K. M. *et al. J. Am. Chem. Soc.* **2016**, *138*, 15122.

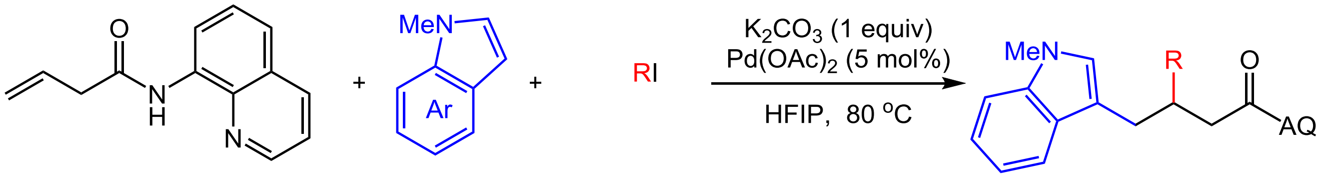
Optimization of the Reaction Conditions



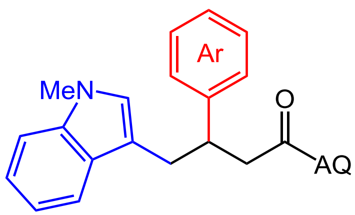
Entry[a]	Additive (equiv)	Base	$Pd(OAc)_2$ (mol%)	Temp (°C)	Yield (%)[b]
1	none	K_2CO_3	10	110	24
2	AgOAc (1)	K_2CO_3	10	110	38
3	AgOAc (2)	K_2CO_3	10	110	28
4	AgOAc (1)	$KHCO_3$	10	110	30
5	AgOAc (1)	K_3PO_3	10	110	45
6	AgOAc (1)	KF	10	110	trace
7	AgOAc (1)	K_2CO_3	10	80	52
8	none	K_2CO_3	10	80	84
9	none	K_2CO_3	5	80	92

[a] Reaction conditions: **1a** (0.10 mmol), **2a** (1.2 equiv), **3a** (4 equiv), $Pd(OAc)_2$ (5-10 mol%), Base (1 equiv), HFIP (0.2 mL), air, 10-12 h. [b] Isolated yield.

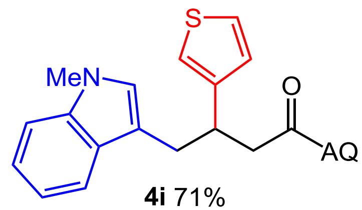
Carbon Electrophile/Nucleophile Scope



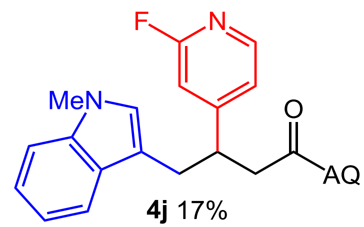
1a **2a-e** **3a-l** **4a-p**



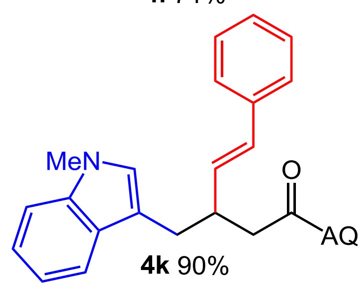
4a Ar = 4-$MeOC_6H_4$, 92%
4b Ar = C_6H_5, 74%
4c Ar = 4-$F_3CC_6H_4$, 74%
4d Ar = 4-ClC_6H_4, 80%
4e Ar = 4-BrC_6H_4, 65%
4f Ar = 3-$MeOC_6H_4$, 75%
4g Ar = 3-$MeO_2CC_6H_4$, 72%
4h Ar = 2-Naphthyl, 92%



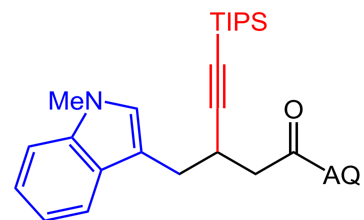
4i 71%



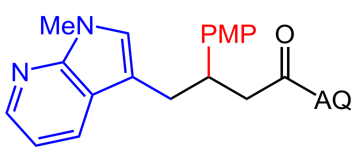
4j 17%



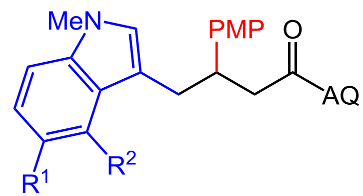
4k 90%



4l 92%

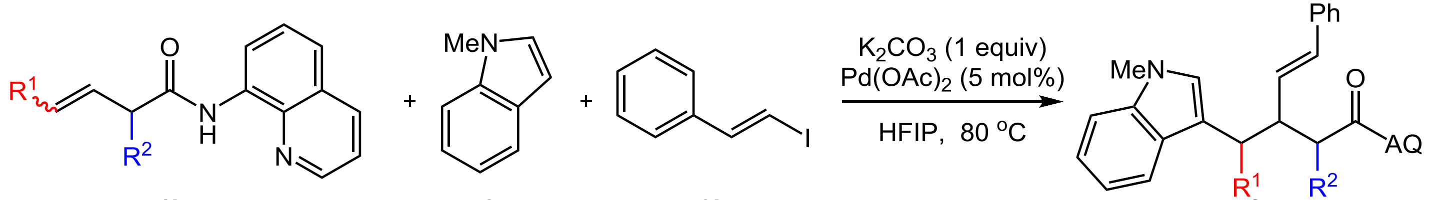


4m 76%

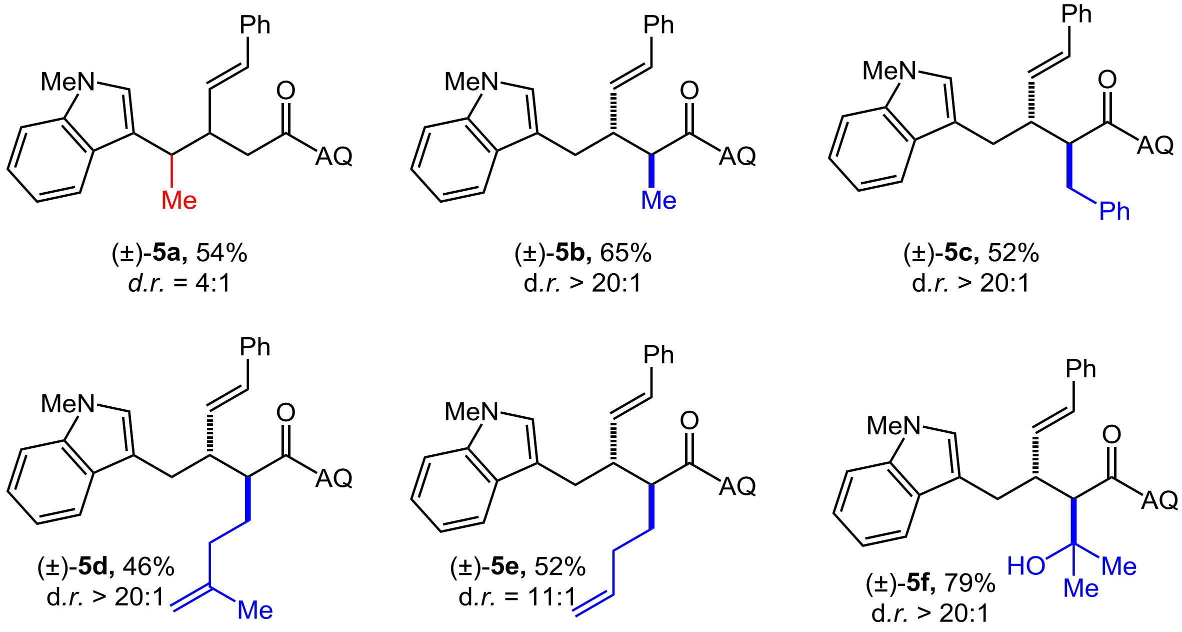


4n R^1 = Br, R^2 = H, 47%
4o R^1 = OMe, R^2 = H, 82%
4p R^1 = H, R^2 = OMe, 96%

Unactivated Alkene Scope



1b-g **2a** **3k** **5a-f**



(±)-**5a,** 54%
d.r. = 4:1

(±)-**5b,** 65%
d.*r.* > 20:1

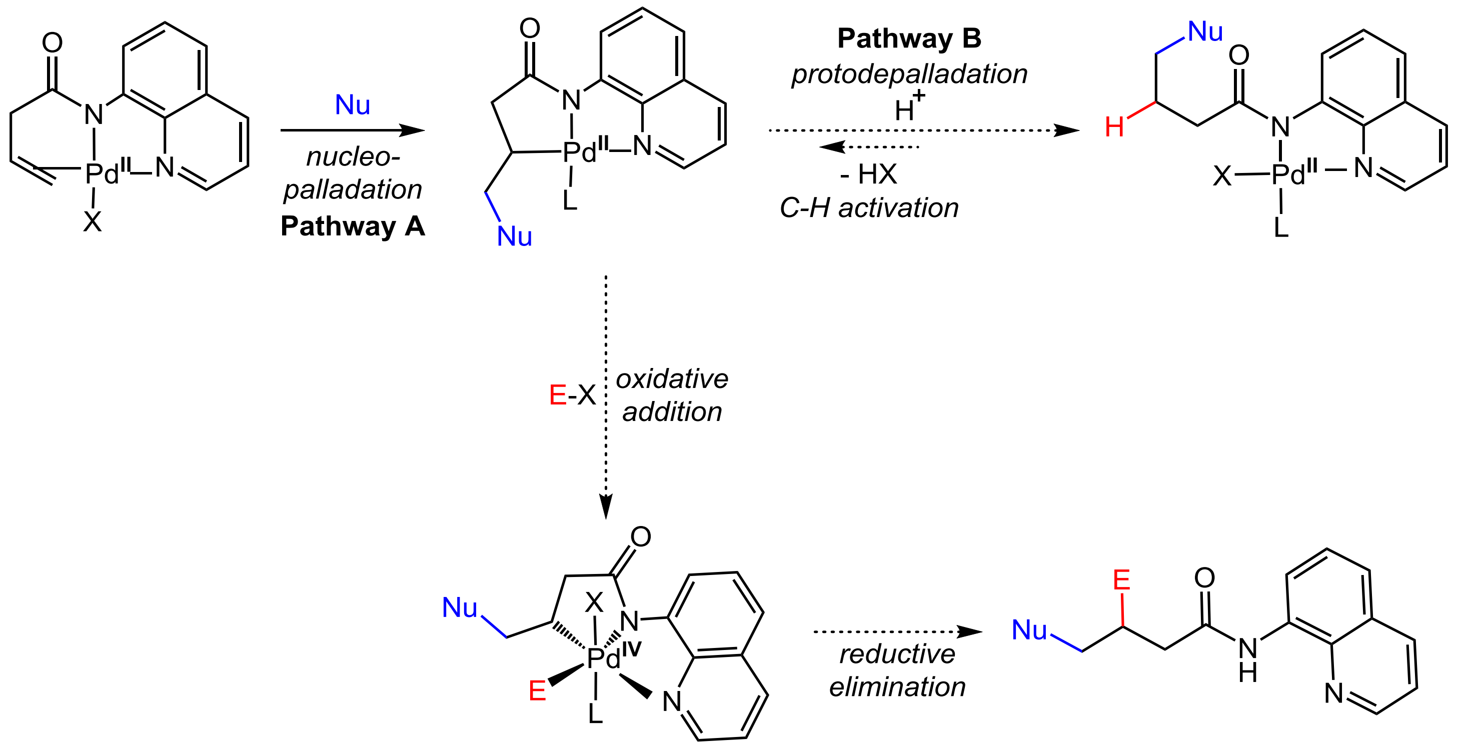
(±)-**5c,** 52%
d.*r.* > 20:1

(±)-**5d,** 46%
d.*r.* > 20:1

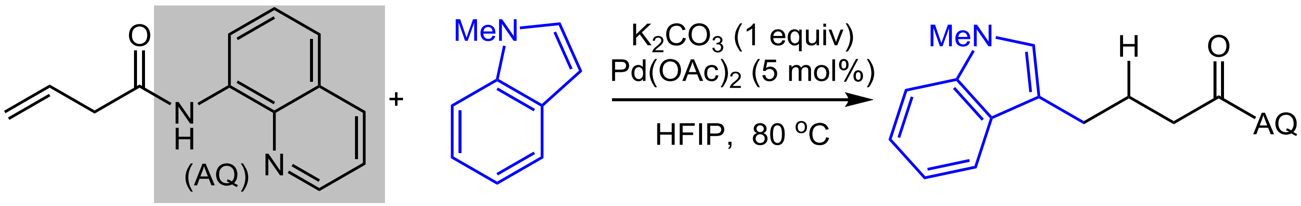
(±)-**5e,** 52%
d.*r.* = 11:1

(±)-**5f,** 79%
d.*r.* > 20:1

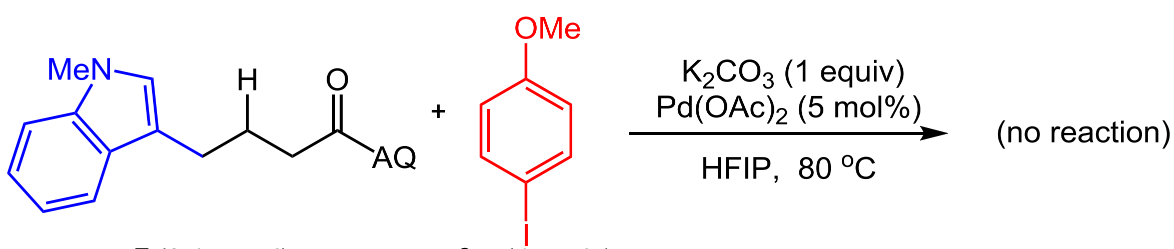
Possible Mechanistic Pathways



Mechanistic Experiments

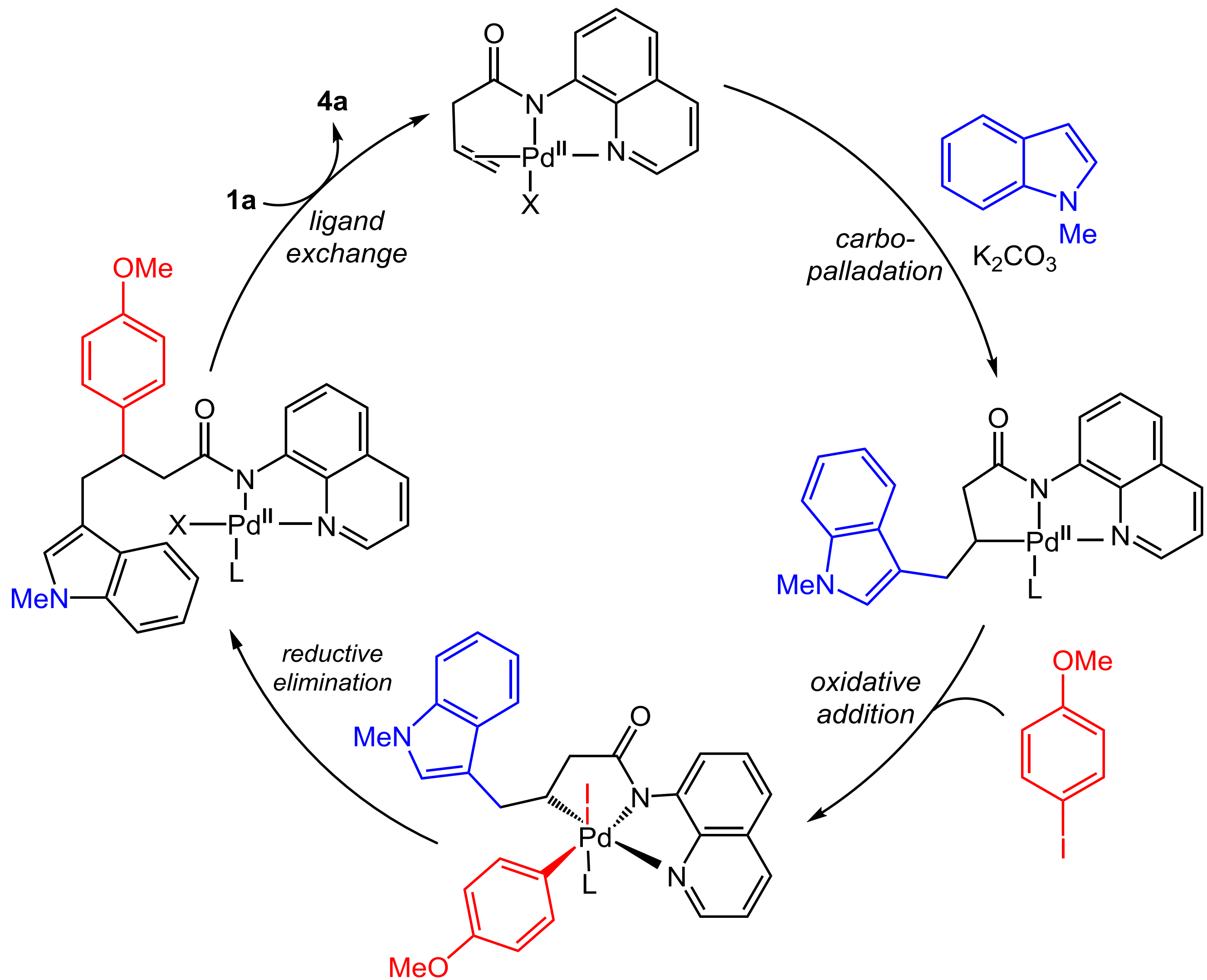


1a (0.1 mmol) **2a** (1.2 equiv) **7** (7%)



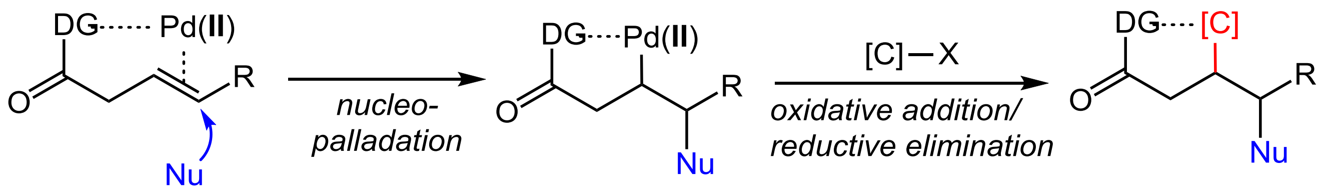
7 (0.1 mmol) **3m** (4 equiv)

Plausible Reaction Mechanism

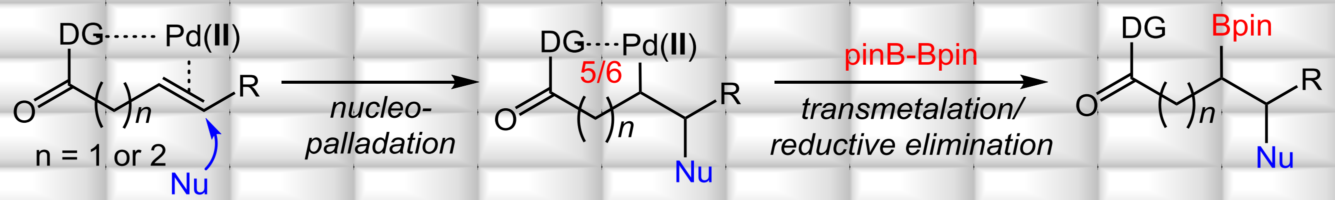


Carbo- and Aminoboration

Previous work: Pd(II)/Pd(IV) cycle, only 5-membered palladacycles



This work: Pd(II)/Pd(0) cycle, 5- and 6-membered palladacycles



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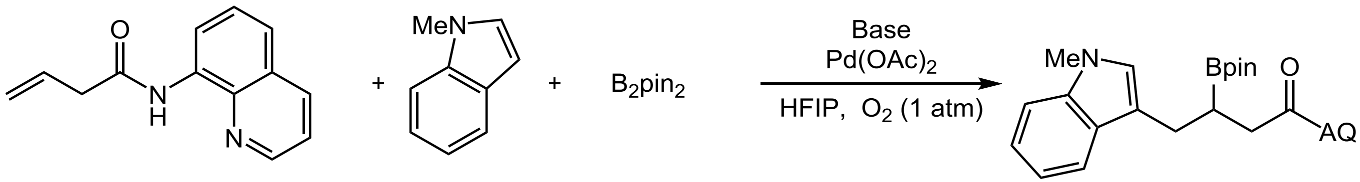
Optimization of the Reaction Conditions

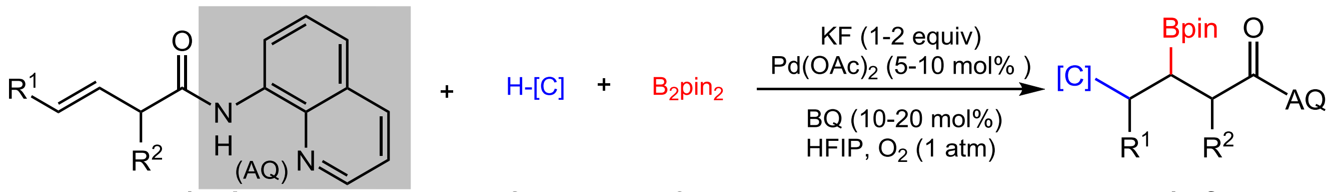


1a **2a** **3a** **4a**

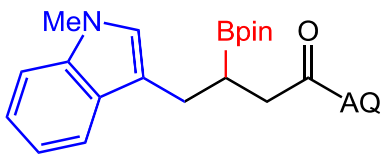
Entry[a]	Additive (equiv)	Base	Temp (°C)	Yield (%)[b]
1	none	KF	80	48
2	none	K_2CO_3	80	10
3	none	NaF	80	35
4	$TEABF_4$ (0.5)	KF	80	40
5	BQ (0.2)	KF	80	70
6	BQ (0.5)	KF	80	58
7	BQ (0.1)	KF	80	52
8	BQ (0.1)	KF	60	86

[a] Reaction conditions: **1a** (0.10 mmol), **2a** (1.5 equiv), **3a** (2 equiv), $Pd(OAc)_2$ (5 mol%)，Base (1 equiv), O_2 (1 atm), 16-20 h. [b] Yield determined by ^1H NMR analysis of CH_2Br_2 as internal standard.

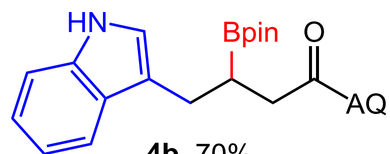
Alkene Carboboration Scope



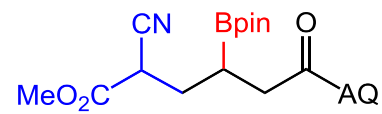
1a-d **2a-c** **3a** **4a-f**



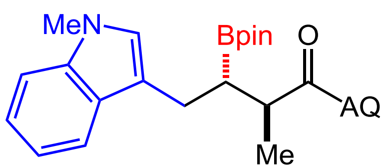
4a, 80%



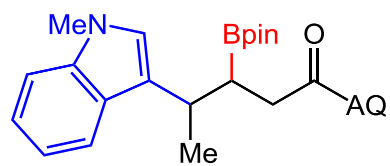
4b, 70%



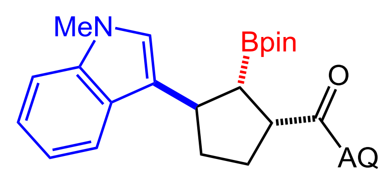
4c, 56%
d.r. = 1.1:1



4d, 84%
>20:1 d.r.

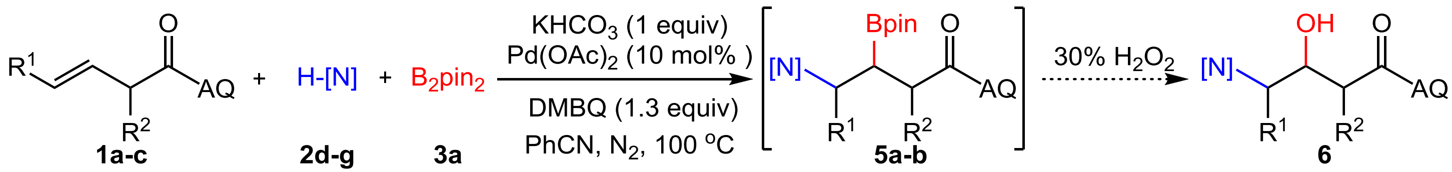


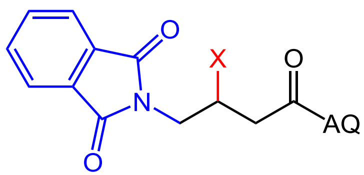
(±)-**4e**, 42%
>20:1 d.r.



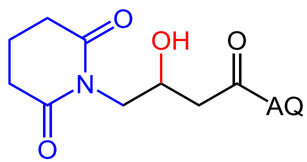
(±)-**4f**, 74%
>20:1 d.r.

Alkene Aminoboration Scope

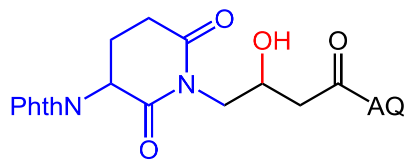




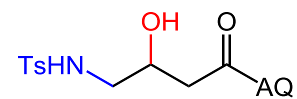
5a, (X = Bpin), 81%
6a, (X = OH), 83%



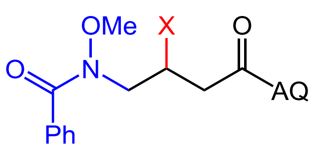
6b, 45%



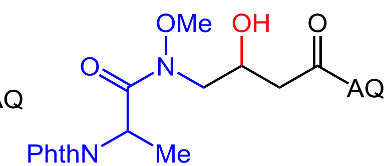
6c, 50%
d.r. = 1.4:1



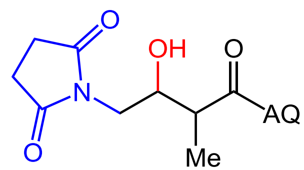
6d, 46%



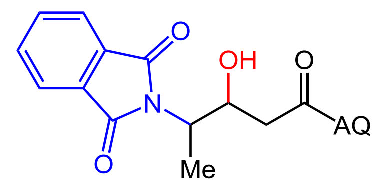
5b, (X = Bpin), 80%
6e, (X = OH), 81%



6f, 82%
d.r. = 1.1:1

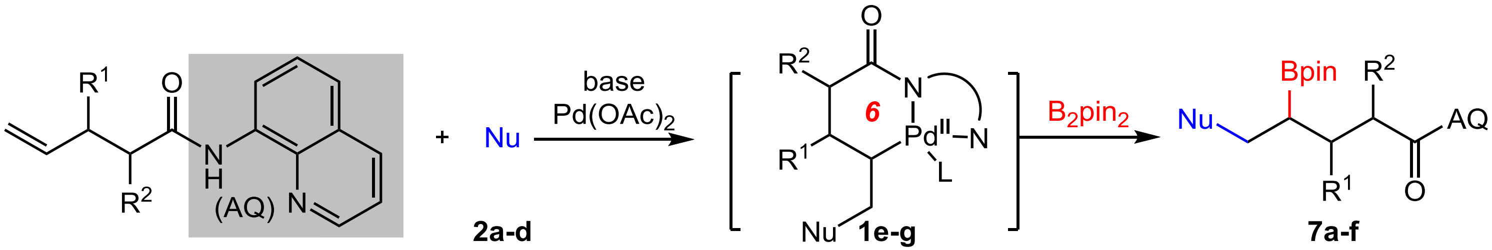


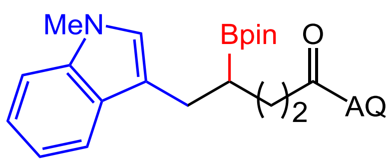
(±)-**6g**, 78%
d.r. = 5.5:1



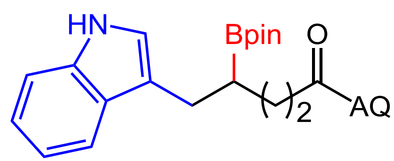
(±)-**6h**, 23%
d.r. = 2:1

γ, δ-Difunctionalization

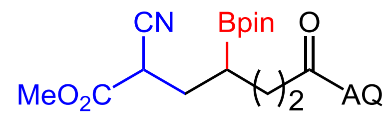




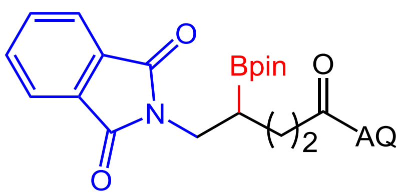
7a, 62%



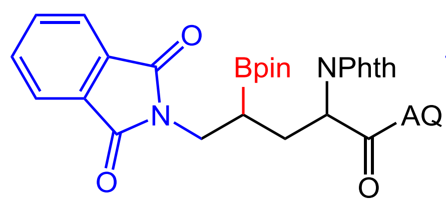
7b, 41%



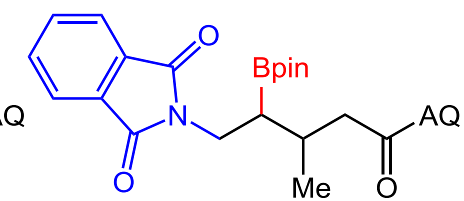
7c, 55%
d.r. = 1.1:1



7d, 66%

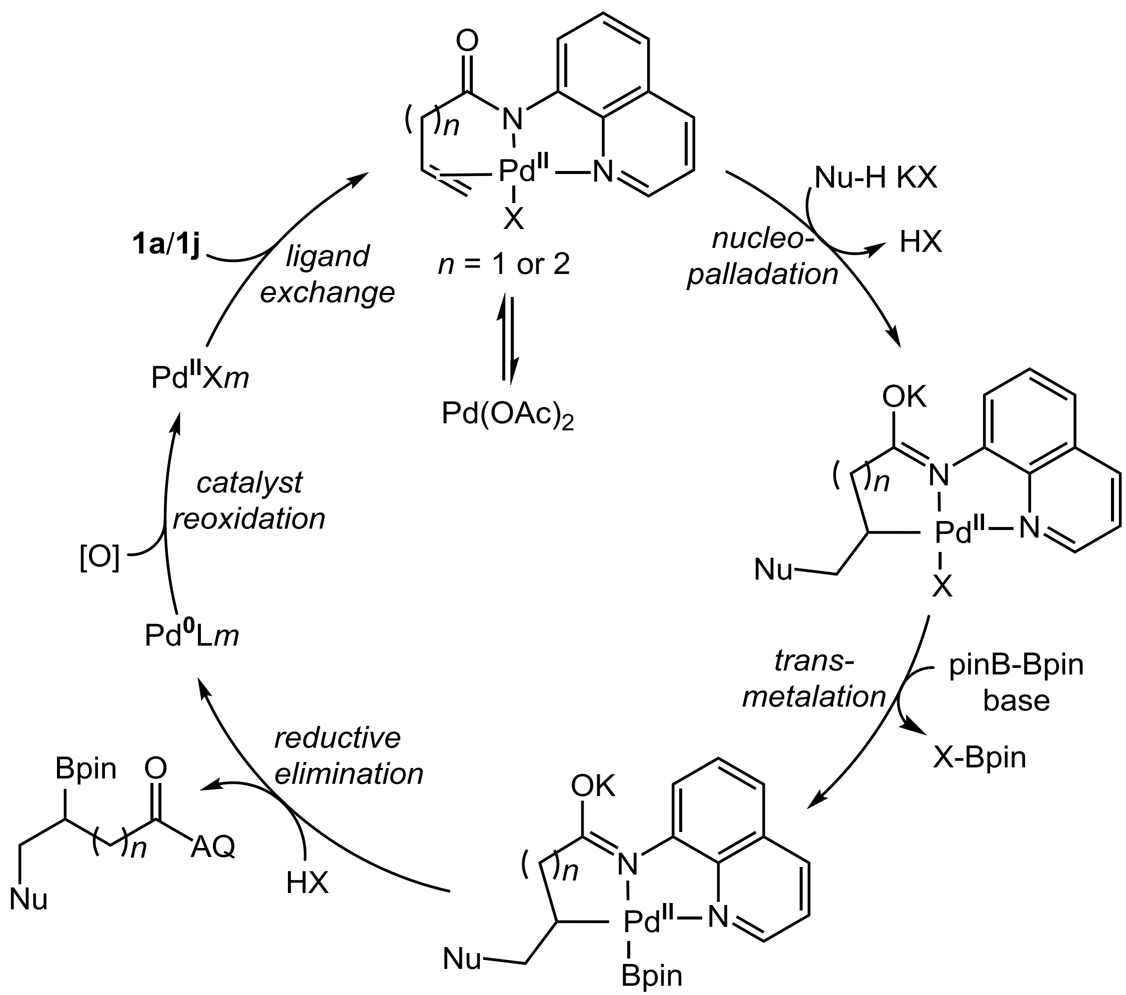


(±)-**7e**, 35%
d.r. = 1.3:1



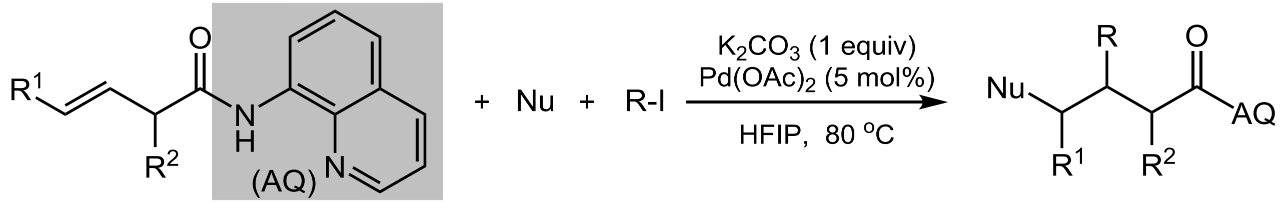
(±)-**7f**, 43%
d.r. = 2.1:1

Plausible Reaction Mechanism



Engle, K. M. *et al. J. Am. Chem. Soc.* **2018**, *140*, 3223.

Summary



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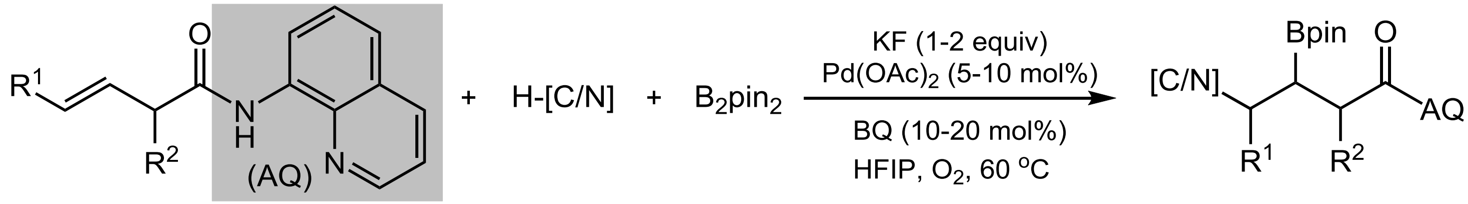

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The First Paragraph

Organoboron compounds are valuable synthetic intermediates and have also been widely used in material science and drug discovery. Alkene difunctionalization reactions involving boron coupling partners are of particular interest because they enable rapid generation of molecular complexity and enable construction of two adjacent stereocenters, including at least one C(sp3)−B stereocenter. Most existing catalytic alkene carbo- and aminoboration reactions involve copper−boryl intermediates that react via syn-1,2-migratory insertion into C−C π-bonds. By contrast, palladium-catalyzed variants remain underdeveloped.

The Last Paragraph

In conclusion, we have developed regiocontrolled carbo- and aminoboration reactions of nonconjugated alkenes using a cleavable 8-aminoquinoline directing group. By using B_2pin_2 as the transmetalating reagent, this methodology enables installation of a boron group at the *β* and *γ* positions of carbonyl compounds through five- and six-membered palladacycle intermediates. To our knowledge, this work represents the first example of intermolecular palladium(II)-catalyzed catalytic alkene 1,2-difunctionalization involving a diboron coupling partner.

The Last Paragraph

The reactions proceeded smoothly with a broad range of carbon and nitrogen nucleophiles as well as sterically hindered internal and α-substituted alkene substrates. The reactions are scalable and operationally simple. Future investigation will focus on elucidating the reaction mechanism and expanding this borylation chemistry to more general alkene substrates. These results will be reported in due course.

Acknowledgement

Thanks for
your kind attention!