

Photoexcited-State Pd Catalysis

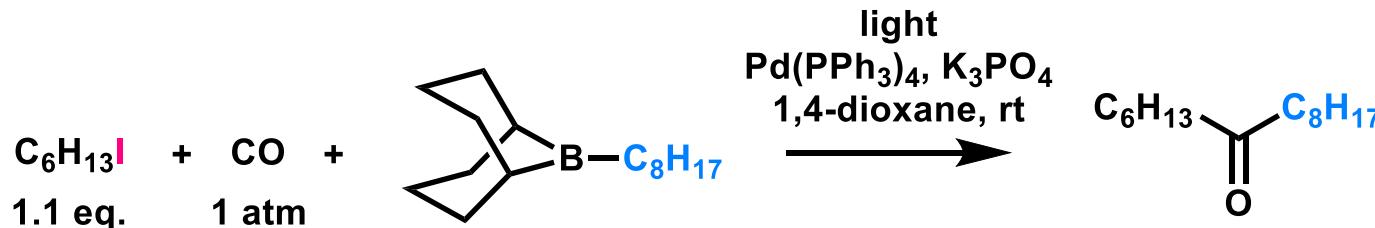
2020/8/1 Takumi Fukuda

Contents

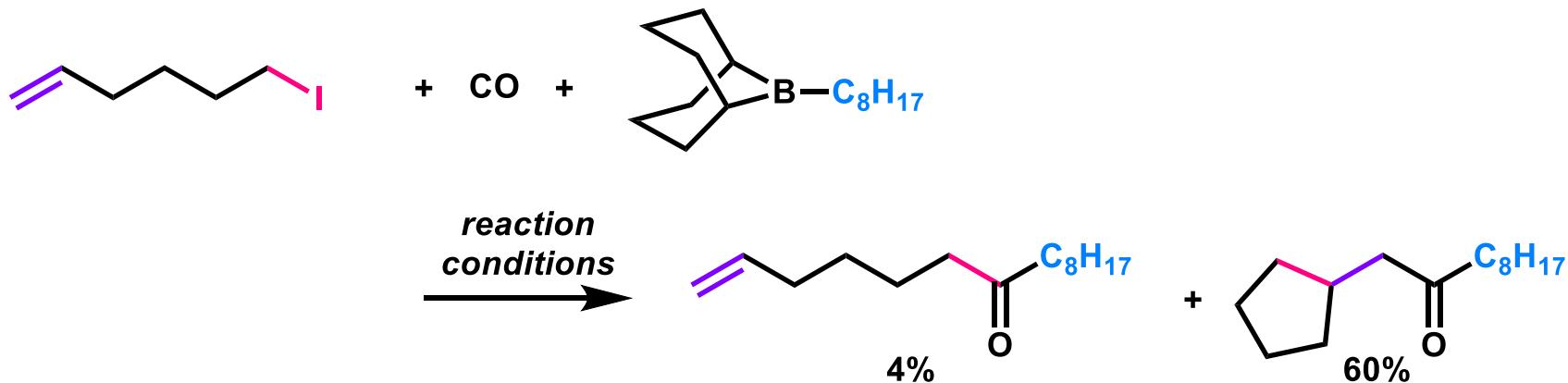
1. Introduction
2. Catalytic Oxidation of Silyl Ethers into Silyl Enol Ethers
(Gevorgyan, 2016)
2. Irradiation-Induced Heck Reaction (Fu, 2017, Main 1)
3. Irradiation-Induced Decarbonylative Desaturation
(Fu, 2018, Main 2)

Effects of Photo-irradiation (1)

(1) Carbonylative Suzuki-Miyaura reaction of alkyl iodide¹⁾



entry	time (h)	light	yield (%)
1	52	dark	18%
2	24	UV	40%
3	5	visible	44%

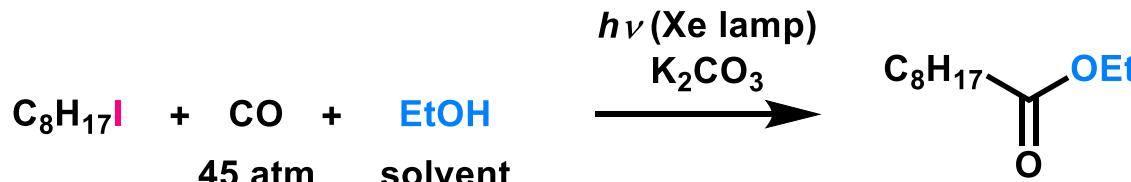


This transformation may be involved a free radical process.

1) Ishiyama, T.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1991**, 32, 6923.

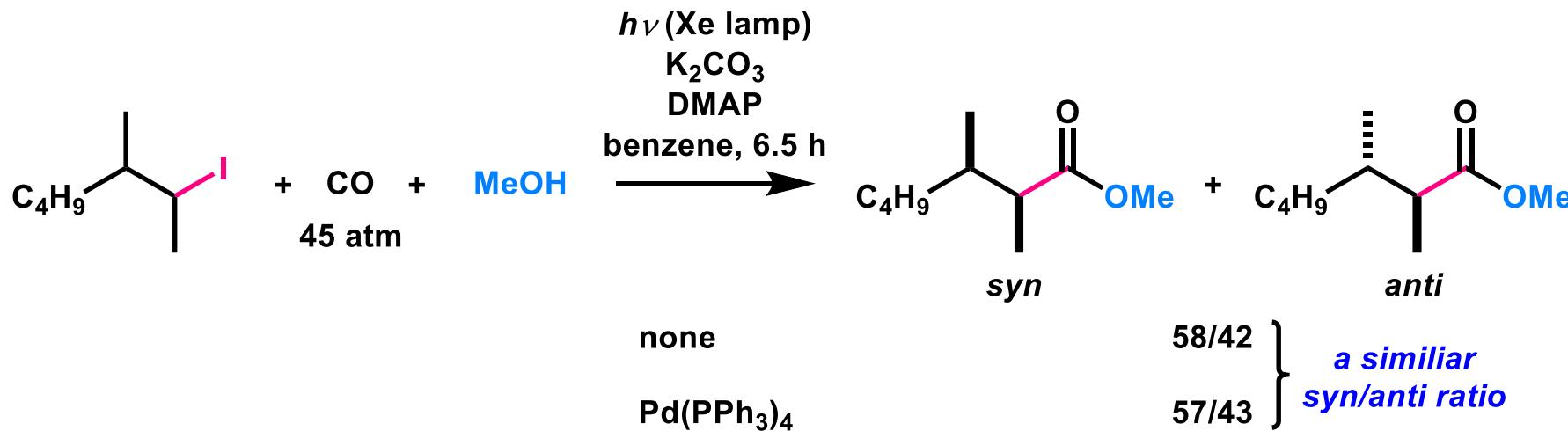
Effects of photo-irradiation (2)

(2) Ester synthesis from alkyl iodide under irradiation conditions¹⁾



none, 50 h 54%

Pd(PPh₃)₄ (5 mol%), 16 h 87%



none

58/42

a similar
syn/anti ratio

Pd(PPh₃)₄

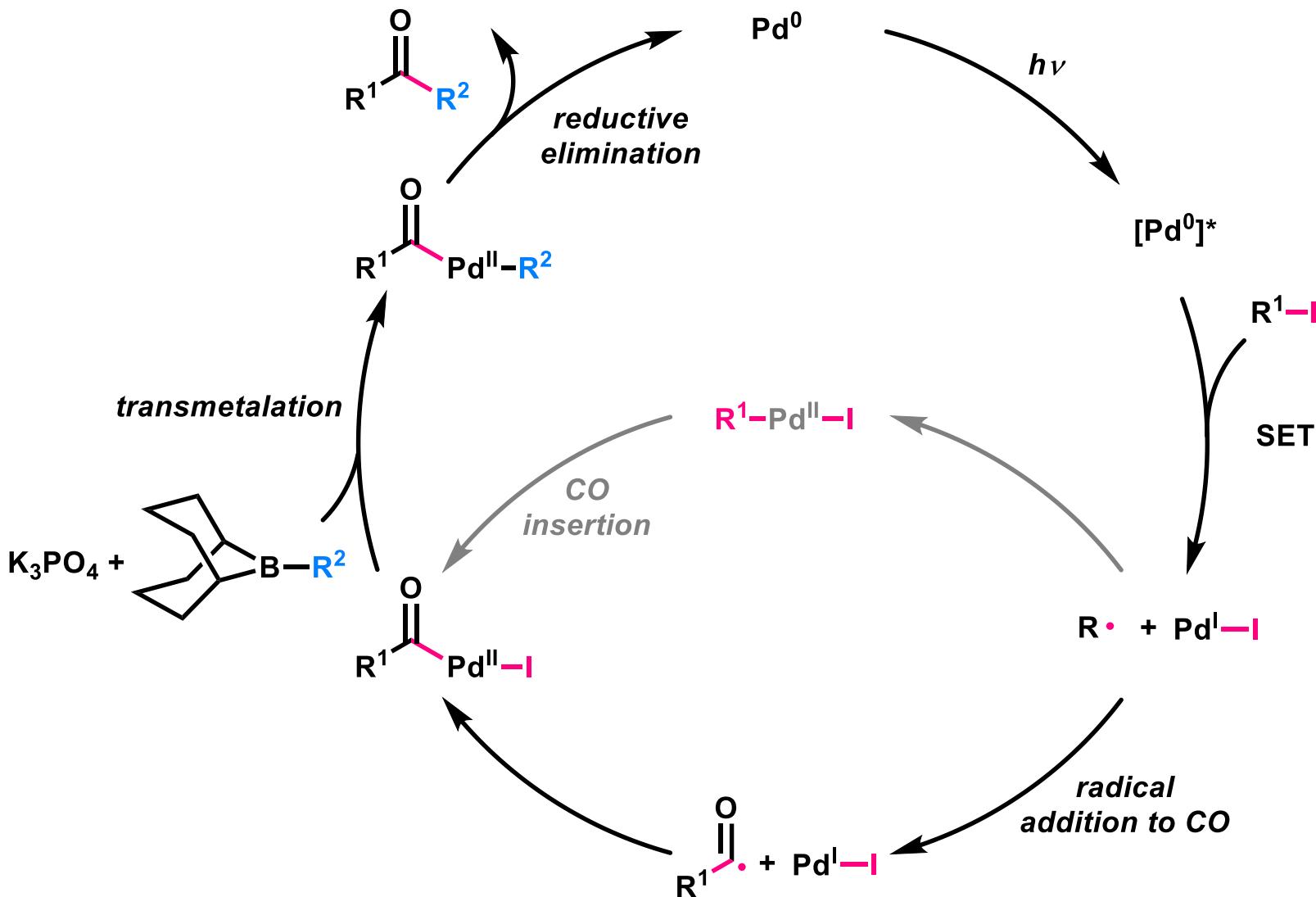
57/43

The products were formed in quite a similar syn/anti ratio with or without palladium catalyst.

The coincidence of the diastereoselectivities strongly suggests that the C-C bond-forming step does proceed via addition of an alkyl radical to CO, which leads to an acylpalladium complex.

1) Sumino, S.; Fusano, A.; Fukuyama, T.; Ryu, I. *Acc. Chem. Res.* **2014**, *47*, 1563.

Proposed Catalytic Cycle of Carbonylative Suzuki-Miyaura Coupling

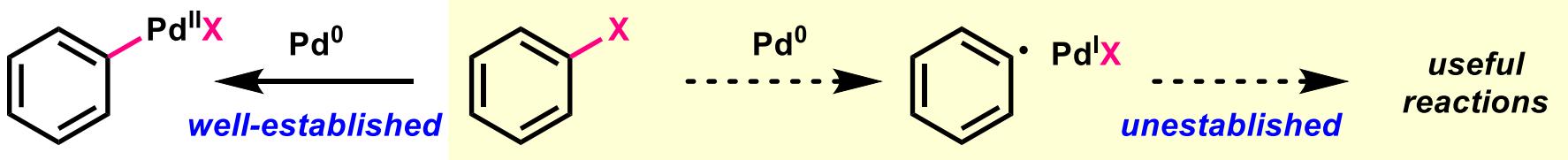


1) Ishiyama, T.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1991**, 32, 6923. 3) Sumino, S.; Fusano, A.; Fukuyama, T.; Ryu, I. *Acc. Chem. Res.* **2014**, 47, 1563.

Contents

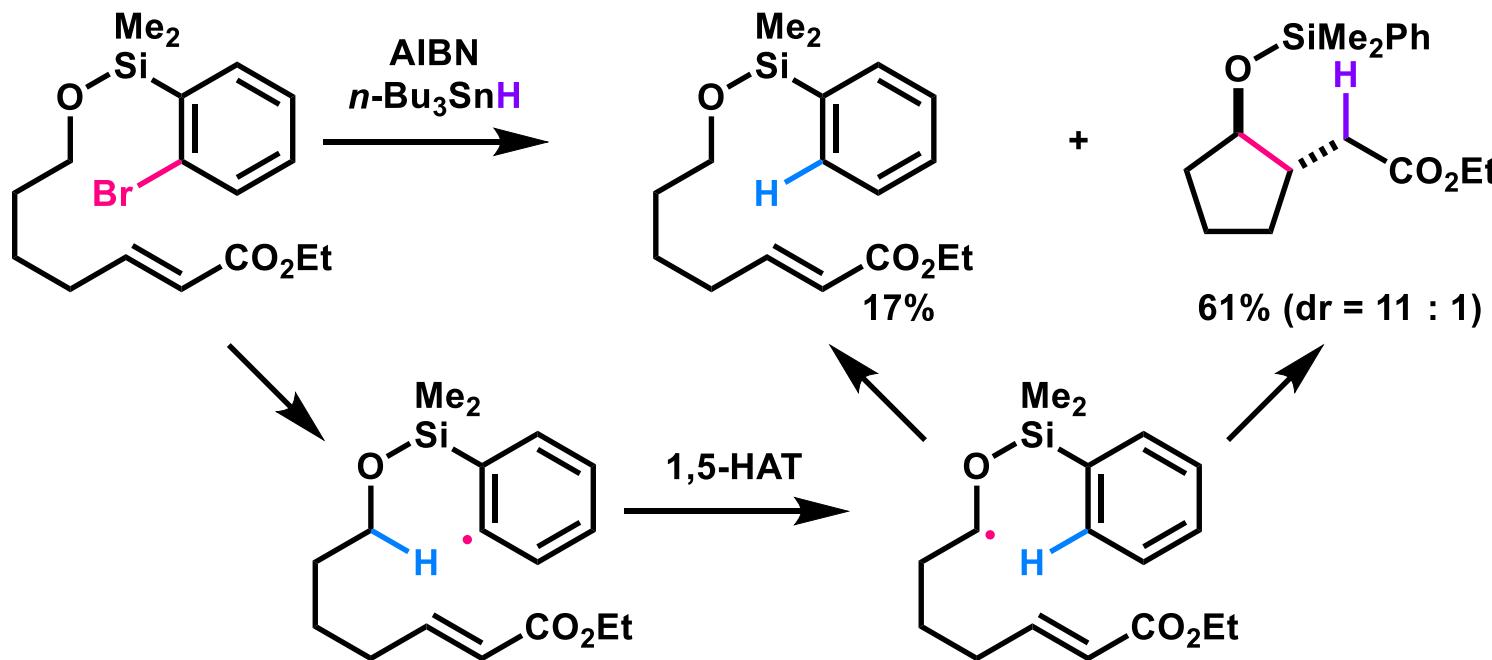
1. Introduction
2. Catalytic Oxidation of Silyl Ethers into Silyl Enol Ethers
(Gevorgyan, 2016)
2. Irradiation-Induced Heck Reaction (Fu, 2017, Main 1)
3. Irradiation-Induced Decarbonylative Desaturation
(Fu, 2018, Main 2)

Working Hypothesis (1)



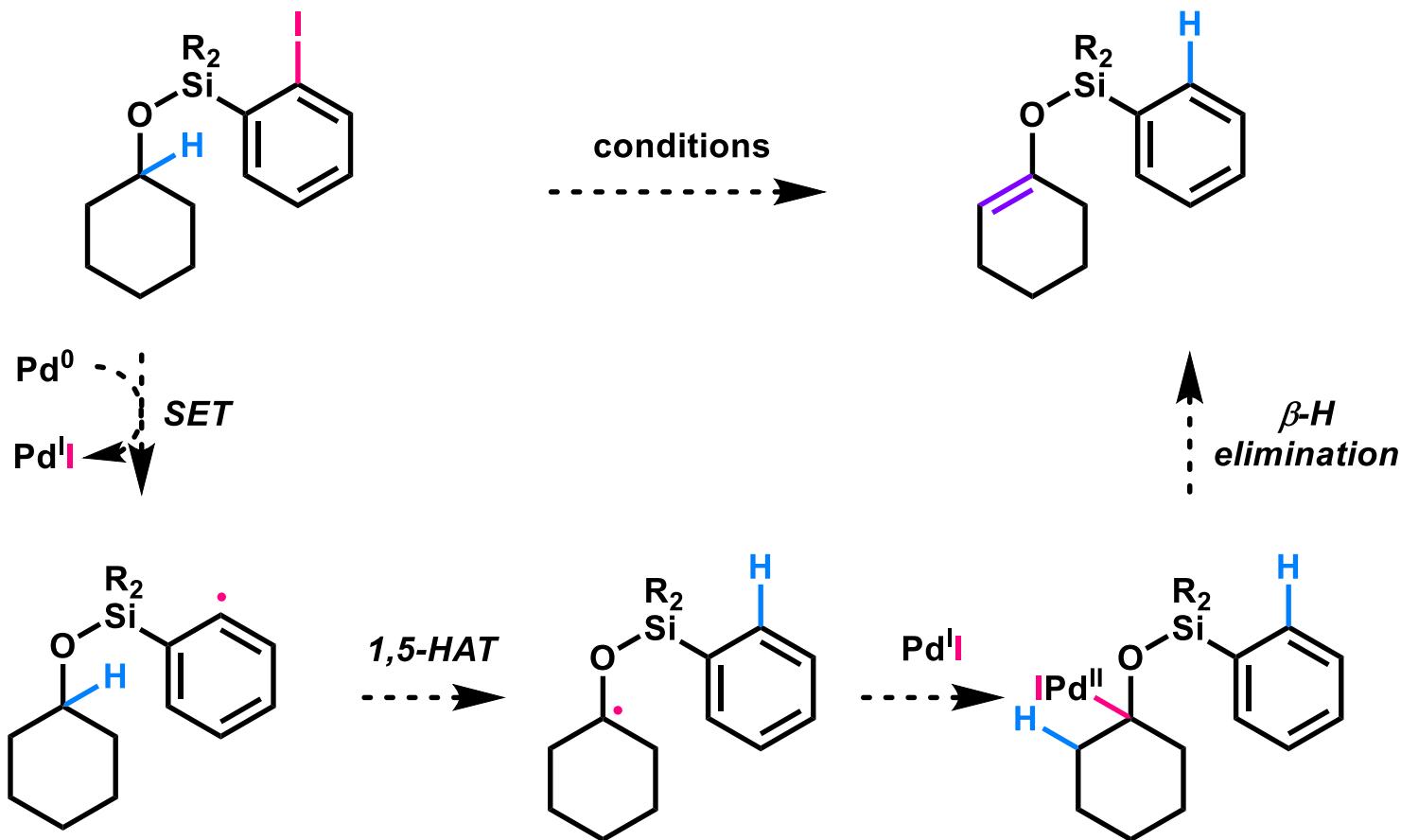
Research Aim

1. How to generate aryl radicals efficiently from aryl halides and palladium catalyst.
→ photo irradiation
2. How to utilize aryl radicals and Pd^IX.
→ inspired by the following Curran's work²⁾



1) Parasram, M.; Chuentragool, P.; Sarkar, D.; Gevorgyan, V. *J. Am. Chem. Soc.* **2016**, *138*, 6340. 2)
Curran, D. P.; Kim, D.; Liu, H. T.; Shen, W. *J. Am. Chem. Soc.* **1988**, *110*, 5900.

Working Hypothesis (2)



Optimization of the Reaction Conditions

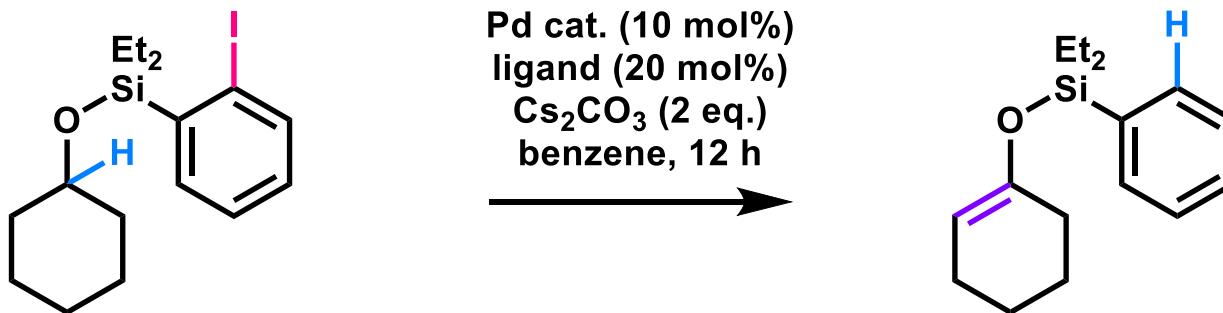
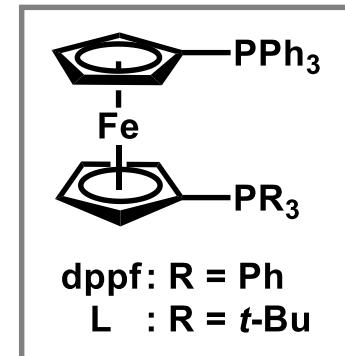


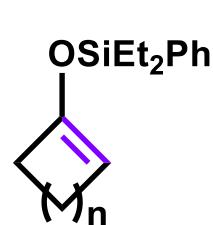
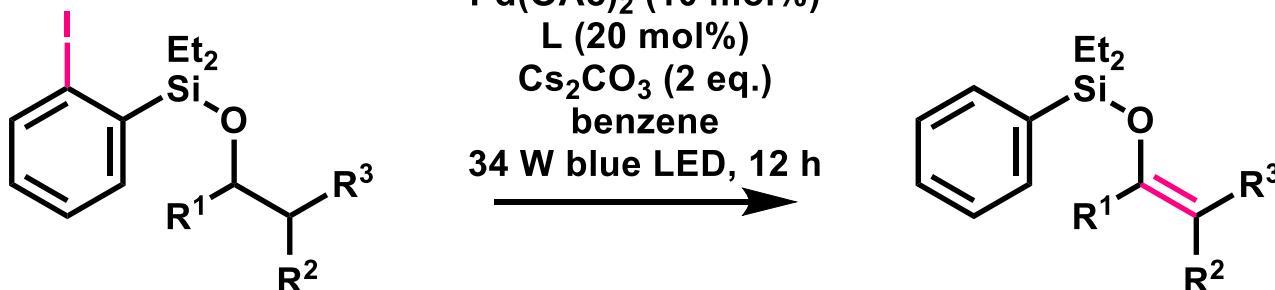
Table. Optimization of the reaction conditions

entry	catalyst	ligand	conditions	yield (%) ^a
1	$\text{Pd}(\text{PPh}_3)_4$	–	120 °C	0%
2	$\text{Pd}(\text{OAc})_2$	dppf	120 °C	0%
3	$\text{Pd}(\text{OAc})_2$	L	120 °C	0%
4	$\text{Pd}(\text{PPh}_3)_4$	–	rt, 34 W blue LED	72%
5	$\text{Pd}(\text{OAc})_2$	dppf	rt, 34 W blue LED	67%
6 ^{a)}	$\text{Pd}(\text{OAc})_2$	L	rt, 34 W blue LED	79% ^{b)}
7 ^{b)}	–	L	rt, 34 W blue LED	0%

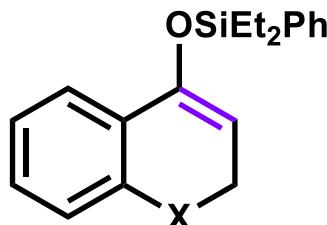


a) NMR yield. b) Isolated yield.

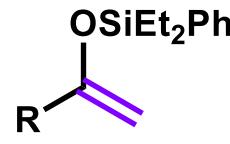
Substrate Scope



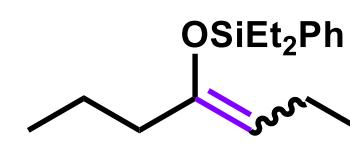
$n = 1$: 43%
 $n = 2$: 65%
 $n = 3$: 79%
 $n = 4$: 61%
 $n = 5$: 72%



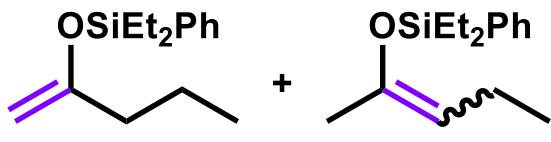
$X = \text{CH}_2$: 86%
 $X = \text{O}$: 75%



$R = \text{Me}$: 79%
 $R = t\text{-Bu}$: 95%
 $R = \text{TMS}$: 97%

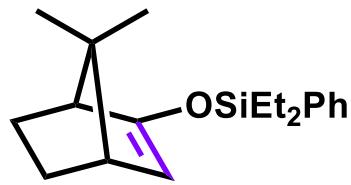


61% ($E/Z = 1 : 3$)

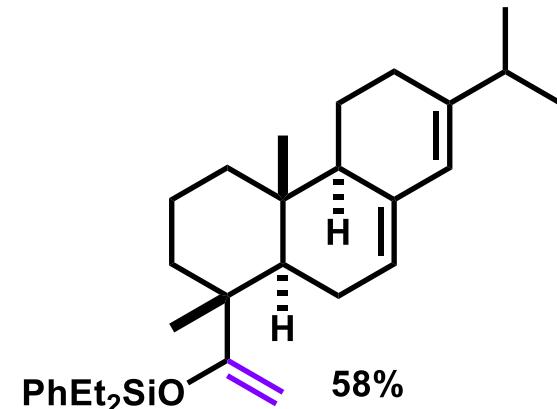


58%

(terminal : $E : Z = 1 : 3 : 7$)



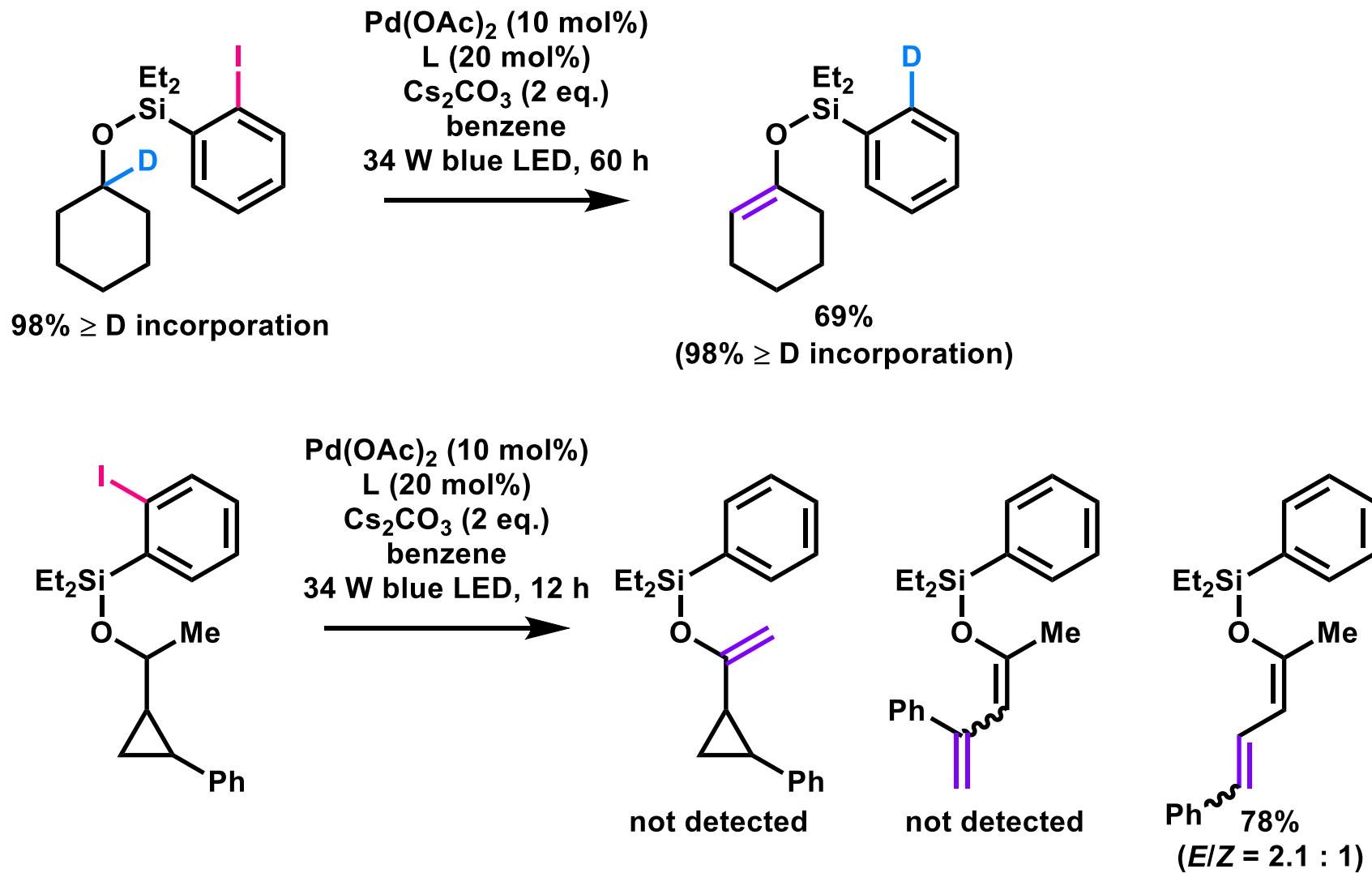
40%



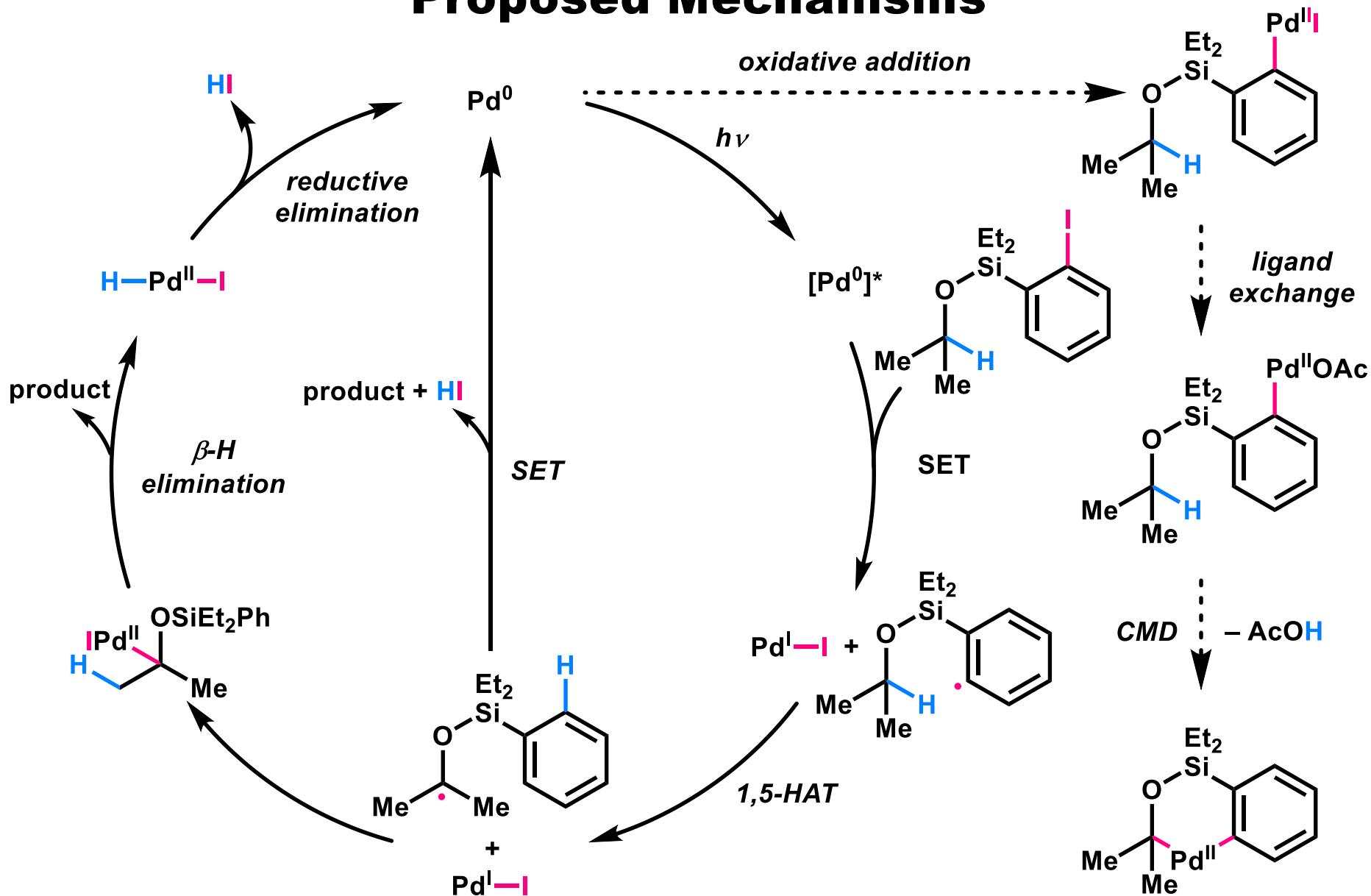
58%

1) Parasram, M.; Chuentragool, P.; Sarkar, D.; Gevorgyan, V. *J. Am. Chem. Soc.* **2016**, *138*, 6340.

Mechanistic Study



Proposed Mechanisms



Contents

1. Introduction
2. Catalytic Oxidation of Silyl Ethers into Silyl Enol Ethers
(Gevorgyan, 2016)
2. Irradiation-Induced Heck Reaction (Fu, 2017, Main 1)
3. Irradiation-Induced Decarbonylative Desaturation
(Fu, 2018, Main 2)

Yao Fu



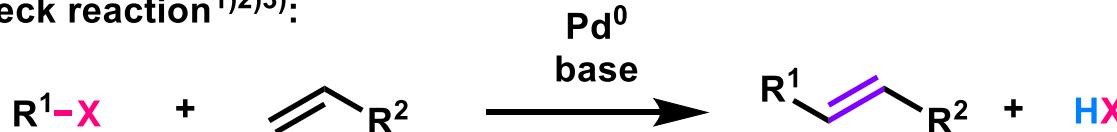
- 2000 : BS at University of Science and Technology of China**
- 2005 : Ph.D. at University of Science and Technology of China (Prof. Qing-Xiang Guo)**
- 2005 - 2010: Associate Professor at University of Science and Technology of China**
- 2010 - : Professor at University of Science and Technology of China and Hefei National Laboratory for Physical Sciences at the Microscale**

Research Topic:

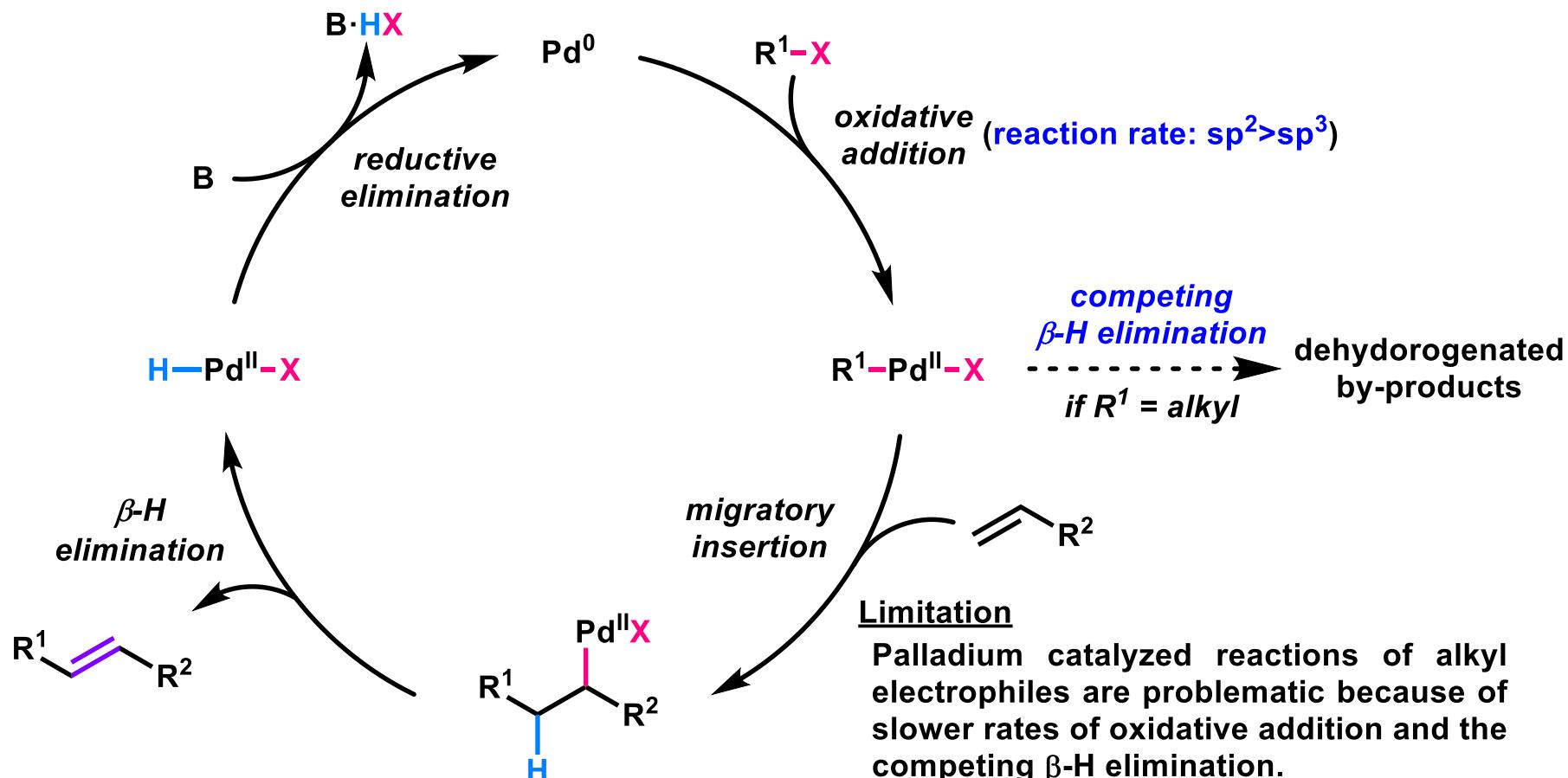
- 1. Physical Organic Chemistry**
- 2. Green Organic Synthesis**
- 3. Biomass Energy and Chemical Industry**

Mizoroki-Heck Reaction

Mizoroki-Heck reaction¹⁾²⁾³⁾:

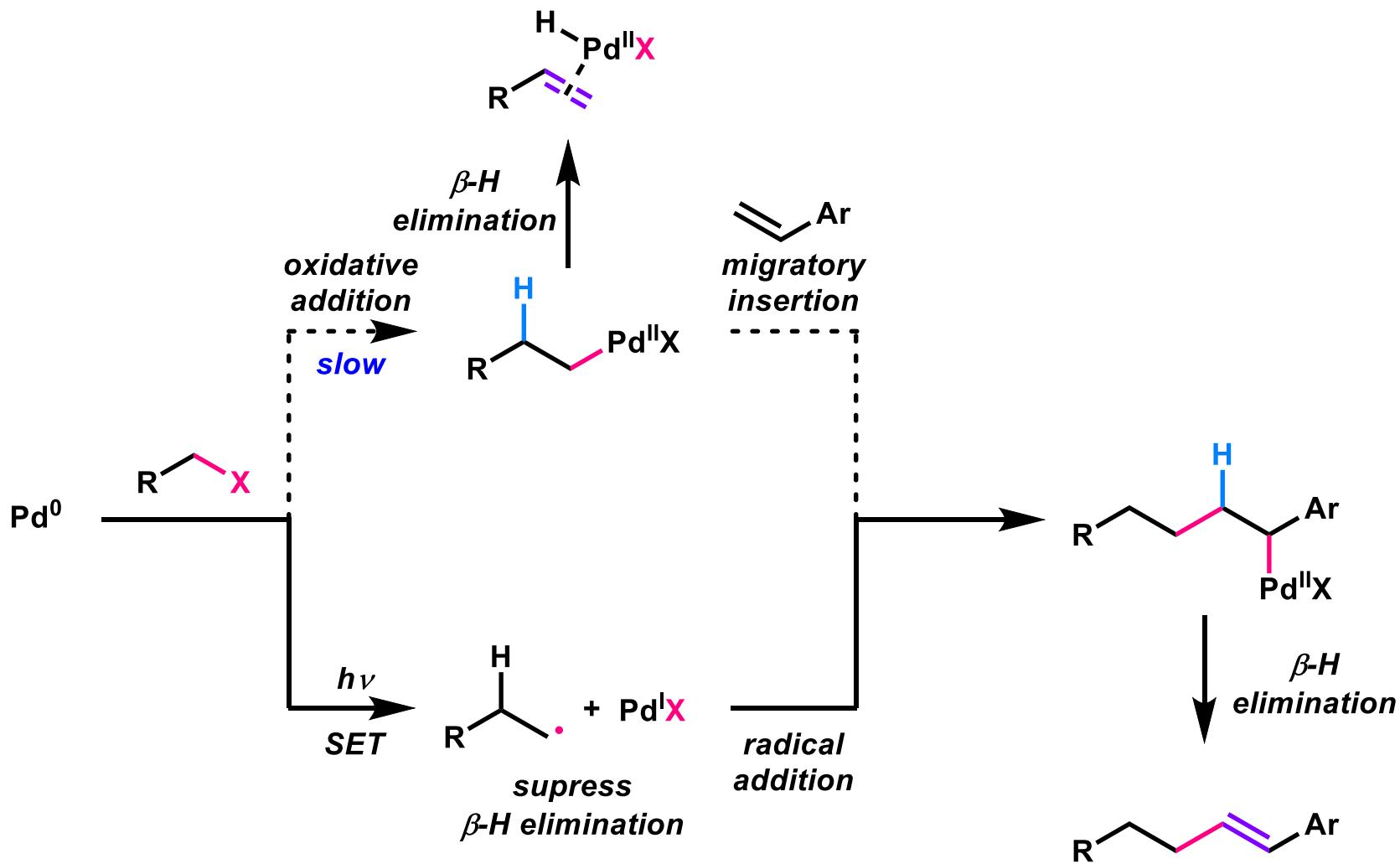


Reaction Mechanisms:



1) Heck, R. F. *J. Am. Chem. Soc.* **1969**, *91*, 6707. 2) Heck, R. F.; Nolley, J. P. *J. Org. Chem.* **1972**, *37*, 2320. 3) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581.

Working Hypothesis



Optimization of the Reaction Conditions (1)

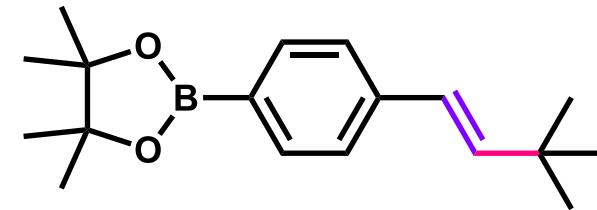
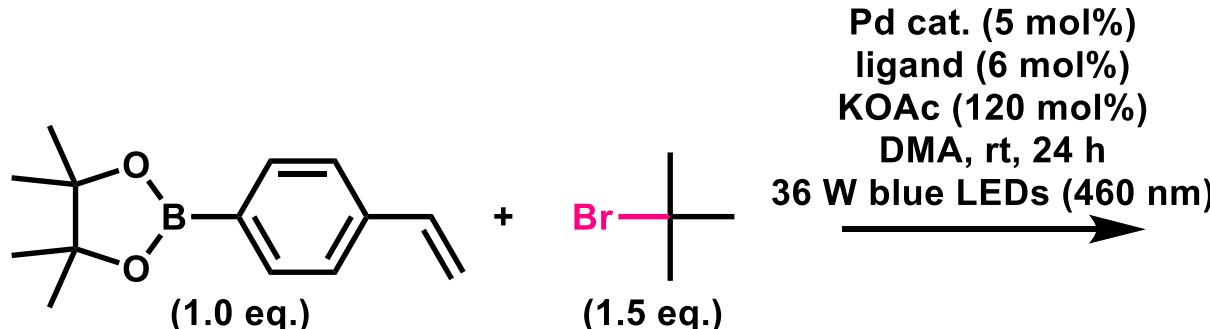
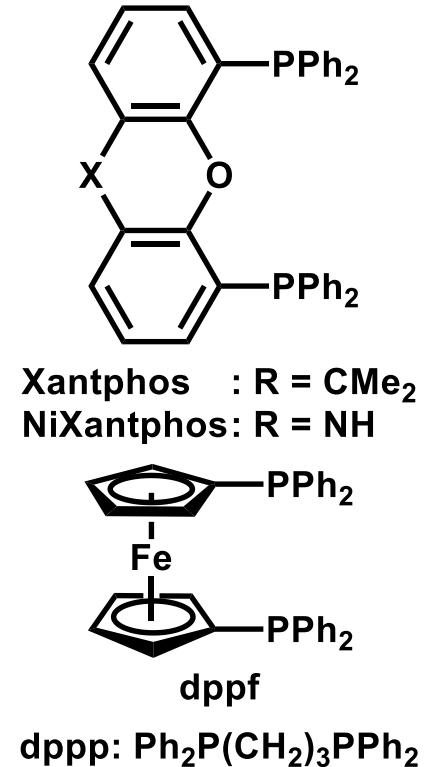


Table. Optimization of the reaction conditions

entry	catalyst	ligand	conversion	yield (%) ^a
1	Pd ₂ (dba) ₃	Xantphos	<5%	0%
2	PdCl ₂	Xantphos	<5%	0%
3	Pd(OAc) ₂	Xantphos	<5%	0%
4	Pd(dppf)Cl ₂	Xantphos	<5%	0%
5	Pd(PPh ₃) ₂ Cl ₂	Xantphos	100%	92%
6	Pd(PPh ₃) ₂ Cl ₂	NiXantphos	90%	81%
7	Pd(PPh ₃) ₂ Cl ₂	Ph ₂ P(CH ₂) ₃ PPh ₂	<10%	<5%
8	Pd(PPh ₃) ₂ Cl ₂	—	<5%	0%



a) GC yield.

Optimization of the Reaction Conditions (2)

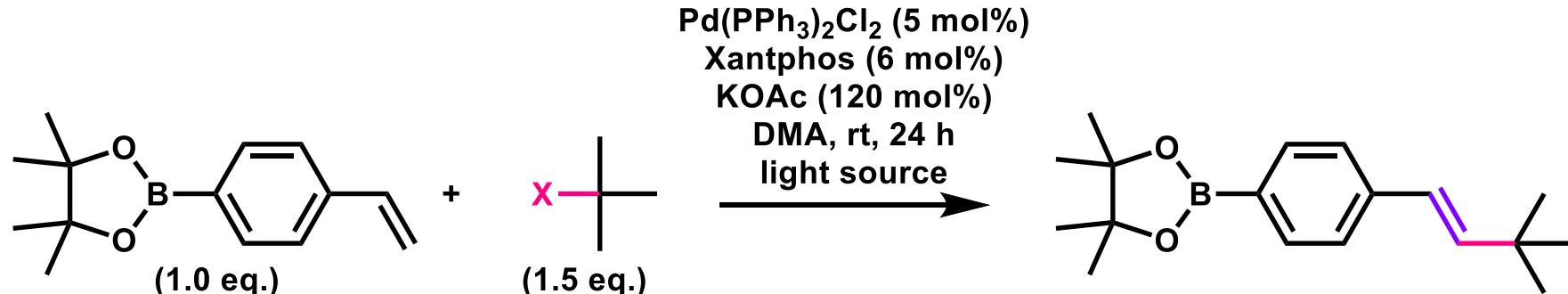
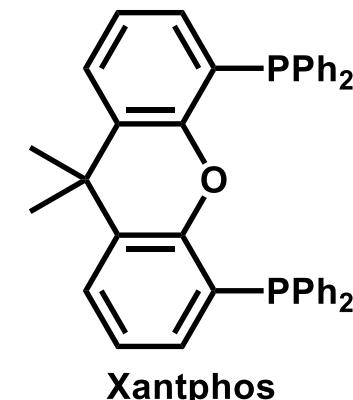


Table. Optimization of the reaction conditions

entry	X	light	conversion	yield (%) ^a
1	Br	36 W blue LEDs	100%	92%
2	Br	100 °C without irradiation	<5%	0%
3	Br	36 W green LEDs	25%	19%
4	Br	36 W white LEDs	30%	21%
5	Br	36 W purple LEDs	87%	82%
6	Br	15 W UV (254 nm)	85%	0%
7	I	36 W blue LEDs	—	26%
8	Cl	36 W blue LEDs	—	0%

a) GC yield.



Substrate Scope of Alkyl Bromide



1.0 eq.



1.5 eq.

$\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (5 mol%)

Xantphos (6 mol%)

K_2CO_3 (120 mol%)

H_2O (100 mol%)

DMA, rt, 24-36 h

36 W blue LEDs

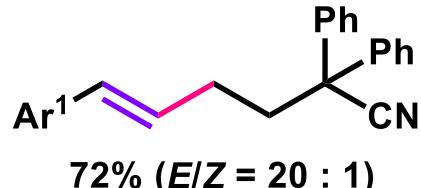
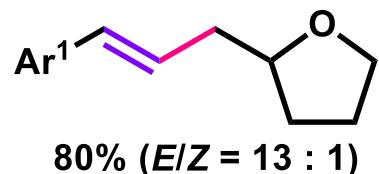


$\text{Ar}^1 = 4\text{-MeO-C}_6\text{H}_4$

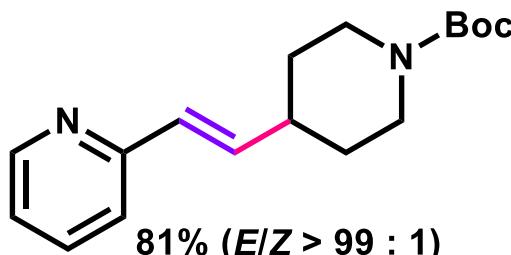
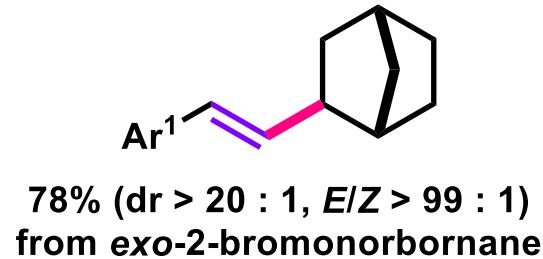
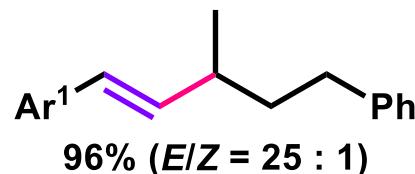
primary alkyl bromide



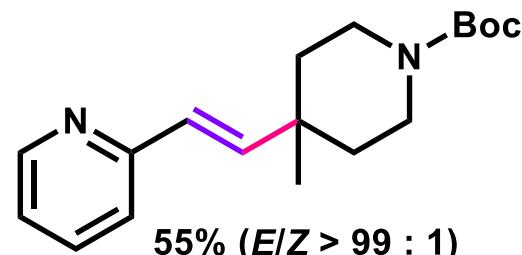
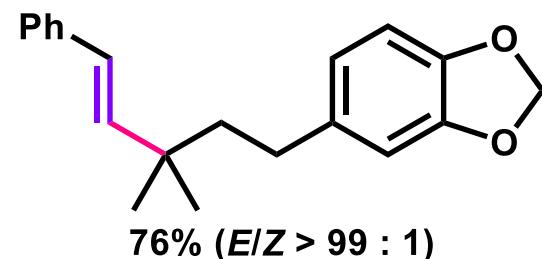
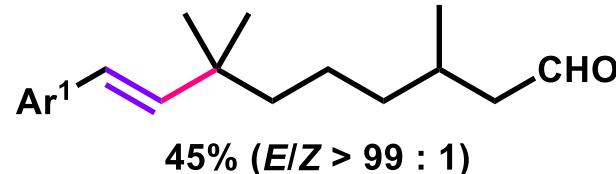
$\text{X} = \text{OTIPS}$: 66% ($E/Z = 15 : 1$)
 $\text{X} = \text{OH}$: 77% ($E/Z = 16 : 1$)
 $\text{X} = \text{Cl}$: 55% ($E/Z = 16 : 1$)



secondary alkyl bromide

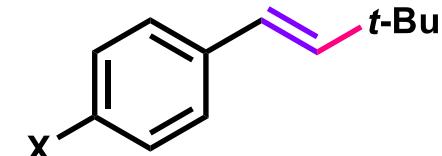
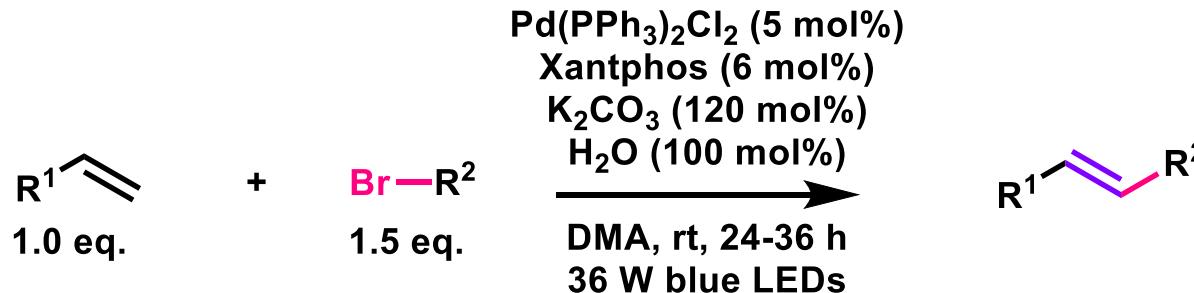


tertiary alkyl bromide

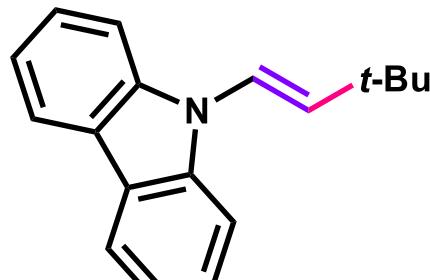
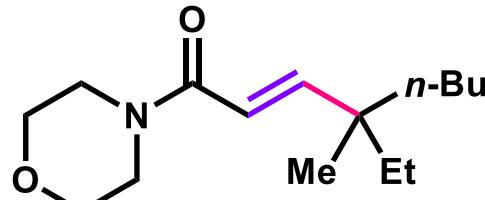
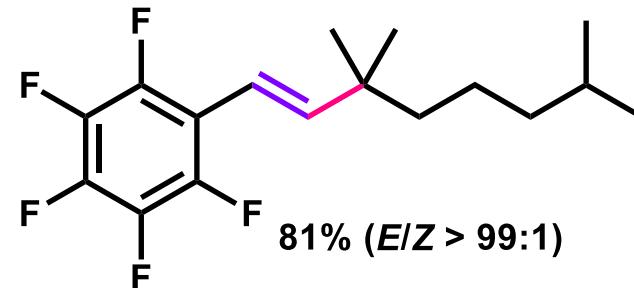
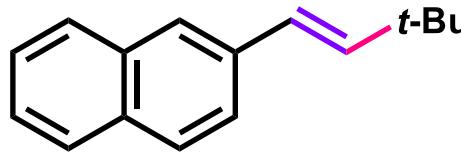


1) Wang, G.-Z.; Shang, R.; Cheng, W.-M.; Yao, F. *J. Am. Chem. Soc.* 2017, 139, 18307.

Substrate Scope of Alkene

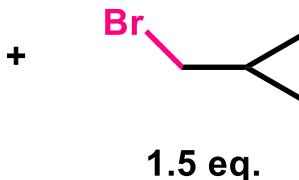
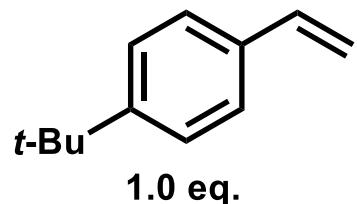


$\text{X} = \text{Bpin}$: 91% ($E/Z > 99:1$)
 $\text{X} = t\text{-Bu}$: 95% ($E/Z > 99:1$)
 $\text{X} = \text{Ph}$: 85% ($E/Z > 99:1$)
 $\text{X} = \text{F}$: 85% ($E/Z > 99:1$)
 $\text{X} = \text{NPh}_2$: 87% ($E/Z > 99:1$)

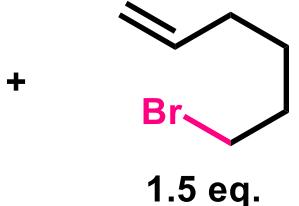
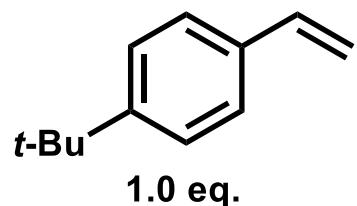
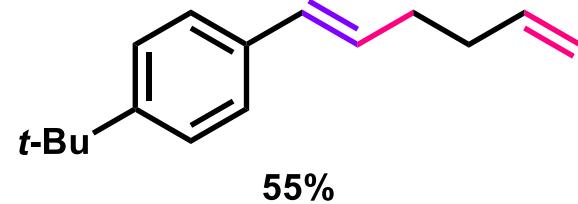


unsuccessful substrates
acrylate ester
internal alkene
1,3-diene

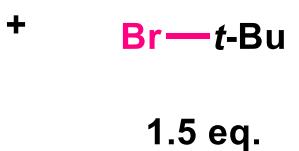
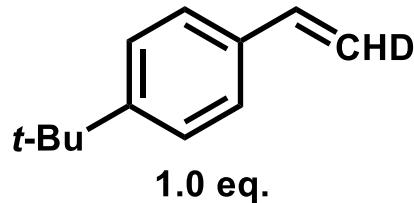
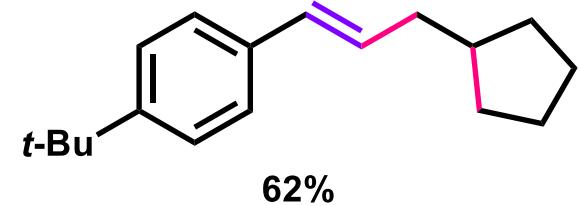
Mechanistic Study



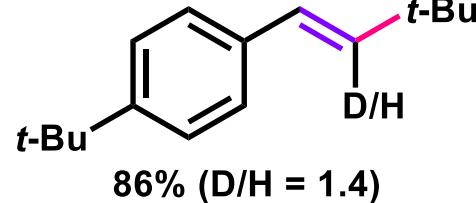
Pd(PPh_3)₂Cl₂ (5 mol%)
Xantphos (6 mol%)
 K_2CO_3 (120 mol%)
 H_2O (100 mol%)
DMA, rt
36 W blue LEDs



Pd(PPh_3)₂Cl₂ (5 mol%)
Xantphos (6 mol%)
 K_2CO_3 (120 mol%)
 H_2O (100 mol%)
DMA, rt
36 W blue LEDs

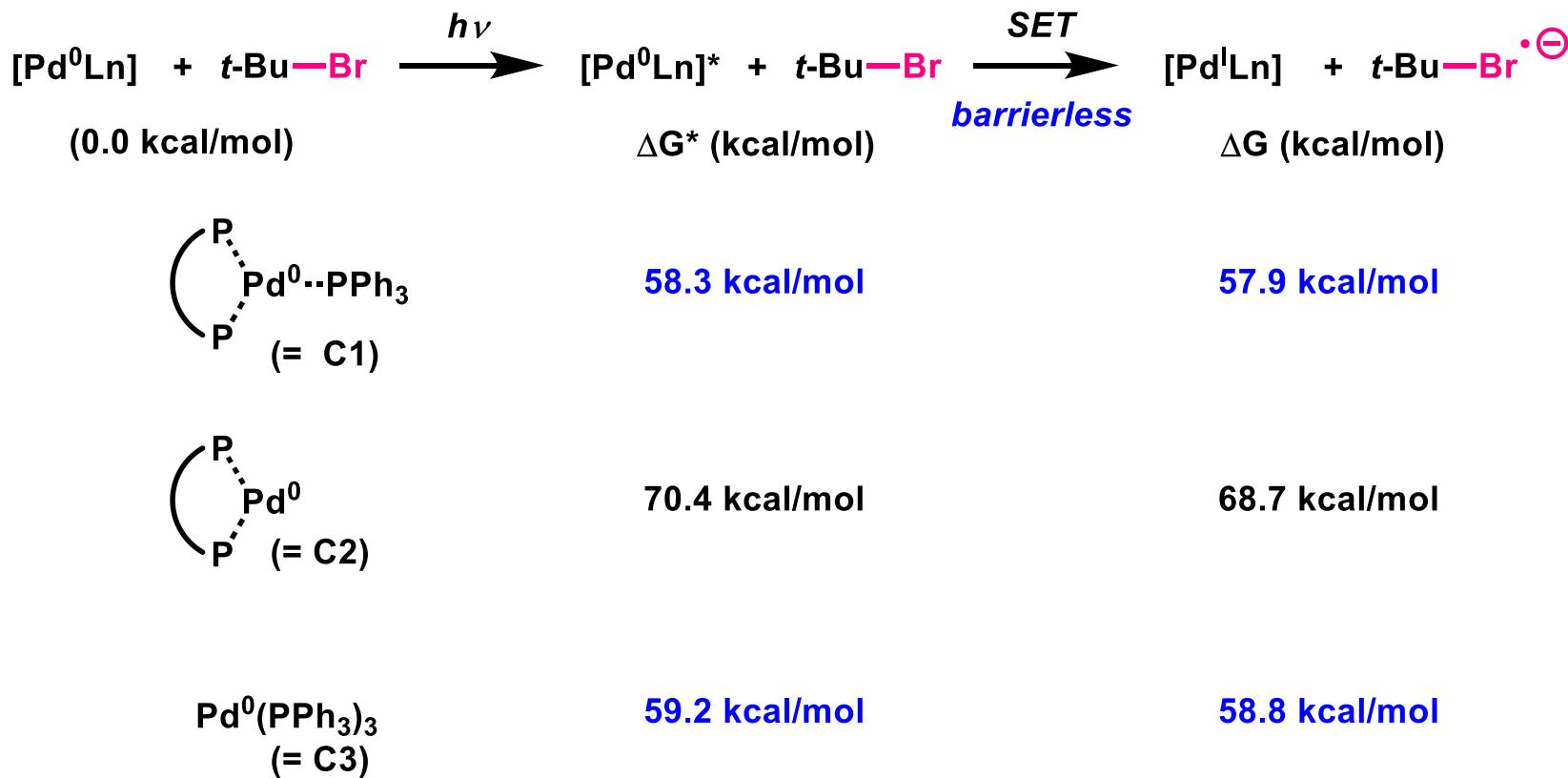


Pd(PPh_3)₂Cl₂ (5 mol%)
Xantphos (6 mol%)
 K_2CO_3 (120 mol%)
 H_2O (100 mol%)
DMA, rt
36 W blue LEDs



1) Wang, G.-Z.; Shang, R.; Cheng, W.-M.; Yao, F. *J. Am. Chem. Soc.* **2017**, *139*, 18307.

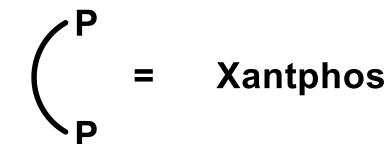
Dual Ligand Effect (1)



Blue LEDs (460 nm) can provide approx. **62 kcal/mol** energy. Therefore, C1 and C3 can be photo-excited under the reaction conditions.

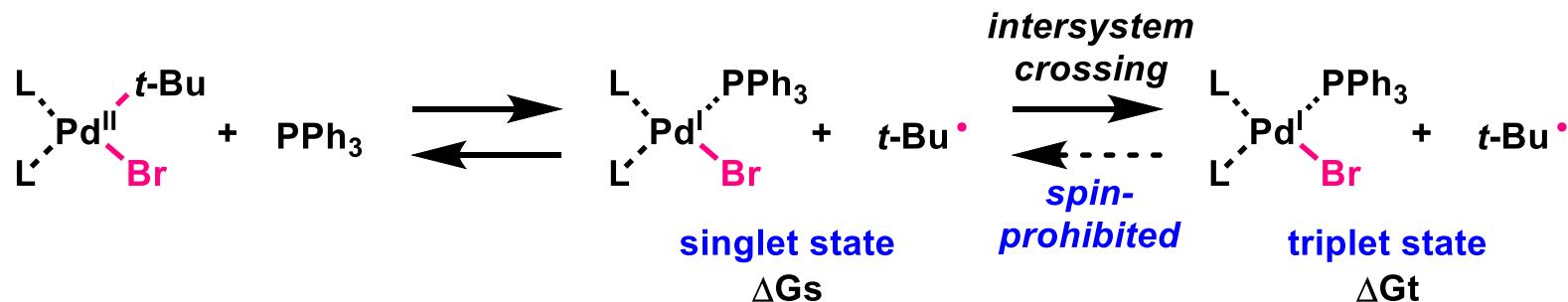
The dual ligand coordinated C1 has the lowest activation energy.

In all cases, barrierless SET from $[Pd^0]^*$ catalysts to alkyl bromides occurs.



Caluculation was conducted at the M06/6-311+G(d,p)-SDD-SMD(dioxane)//B3LYP/6-31G(d)-LANL2DZ level.

Dual Ligand Effect (2)



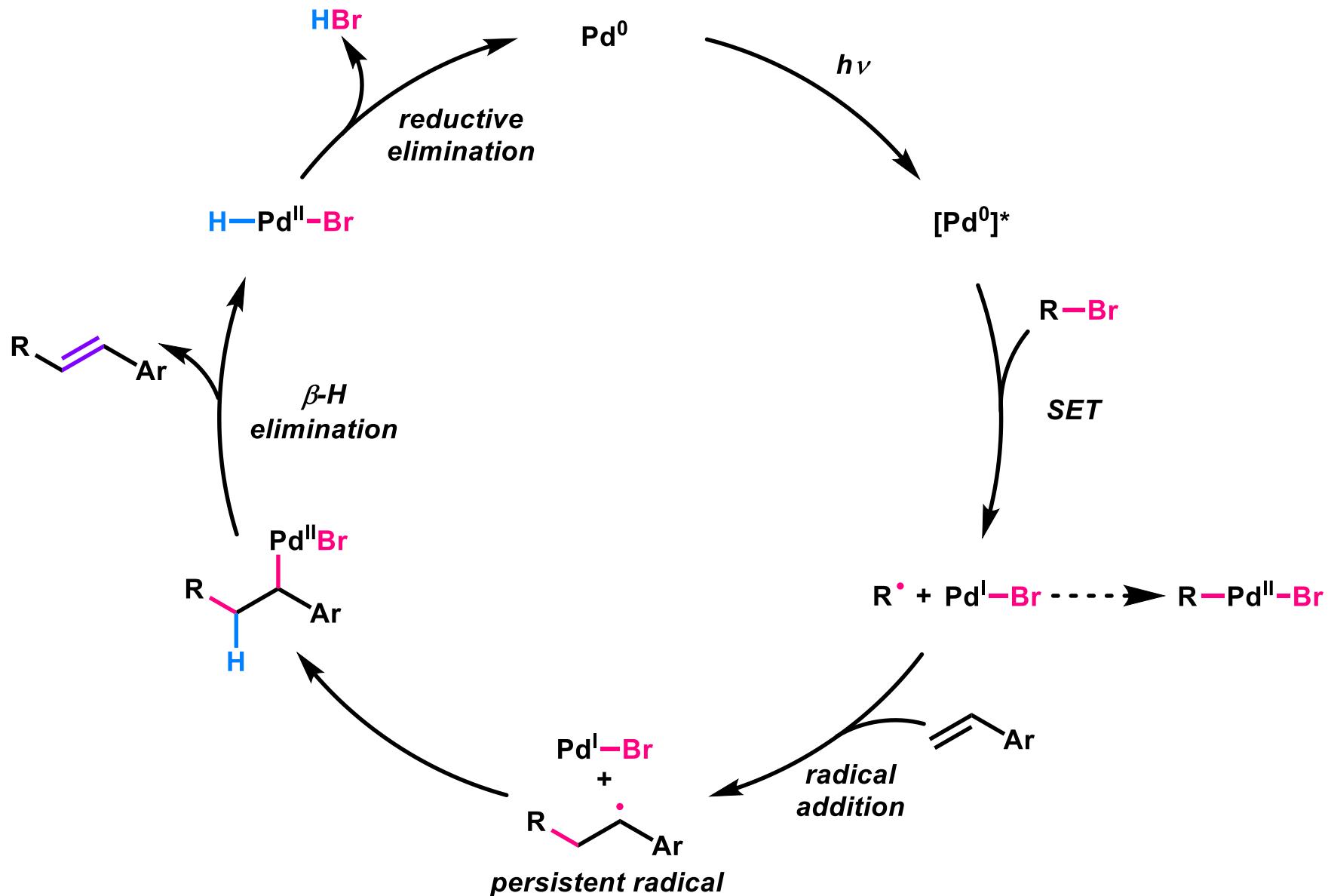
$L = \text{Xantphos}$	$+0.6 \text{ kcal/mol}$	0.0 kcal/mol	-1.4 kcal/mol (most stable)
$L = \text{PPh}_3$	-5.8 kcal/mol (most stable)	0.0 kcal/mol	-0.7 kcal/mol

When Xantphos is used, triplet state Pd^{I} complex is the most stable of the above three intermediates. Therefore, the generation of Pd^{II} complex is suppressed and alkyl radical is considered to be long-lived.

When PPh_3 is used, Pd^{II} complex is the most stable of the above three intermediates. Therefore, the generation of Pd^{II} complex is fast and alkyl radical is considered to be short-lived.

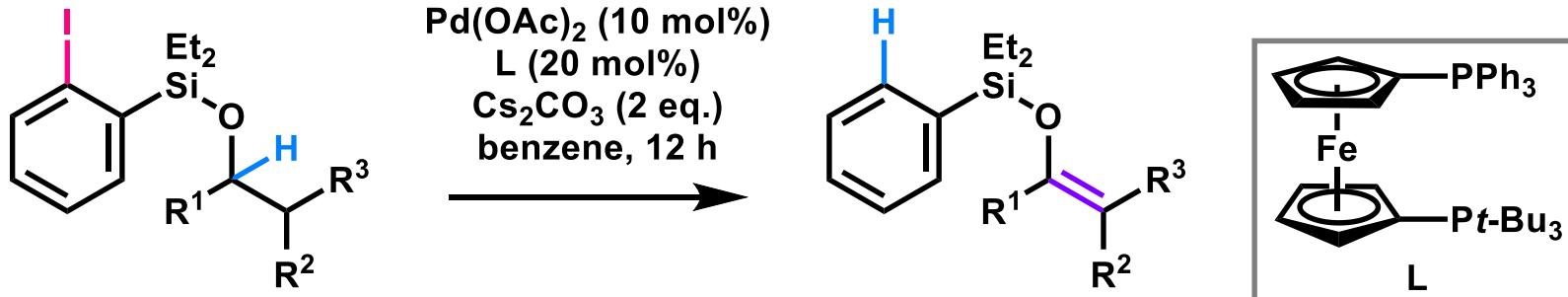
Calculation was conducted at the M06/6-311+G(d,p)-SDD-SMD(dioxane)//B3LYP/6-31G(d)-LANL2DZ level.

Proposed Mechanisms



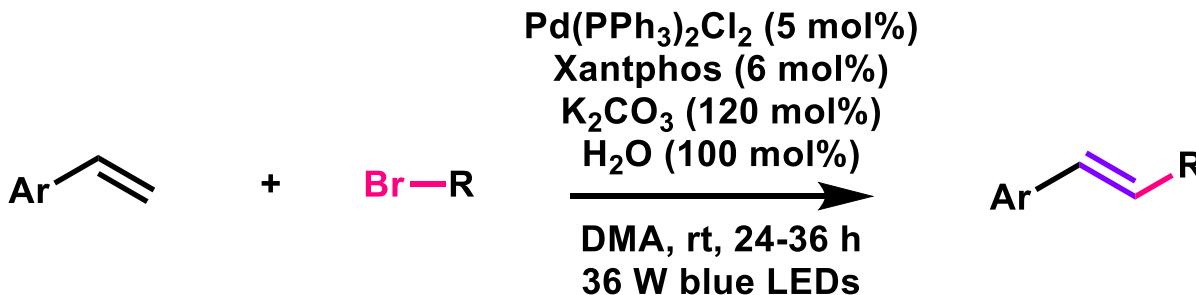
Short Summary

1. Catalytic Oxidation of Silyl Ethers into Silyl Enol Ethers (Gevorgyan, 2016)¹⁾



- Irradiation realizes the novel reactivities of palladium catalyst which possess both traditional organometallic and radical nature.

2. Irradiation-Induced Heck Reaction (Fu, 2017)²⁾



- Primary, secondary and tertiary alkyl bromide can be used in the reaction under the same reaction conditions.
- Photo-excited palladium catalyst with a dual ligand system suppresses β -H elimination and realizes the unprecedented Heck reaction with alkyl bromides.

1) Parasram, M.; Chuentragool, P.; Sarkar, D.; Gevorgyan, V. *J. Am. Chem. Soc.* **2016**, *138*, 6340.

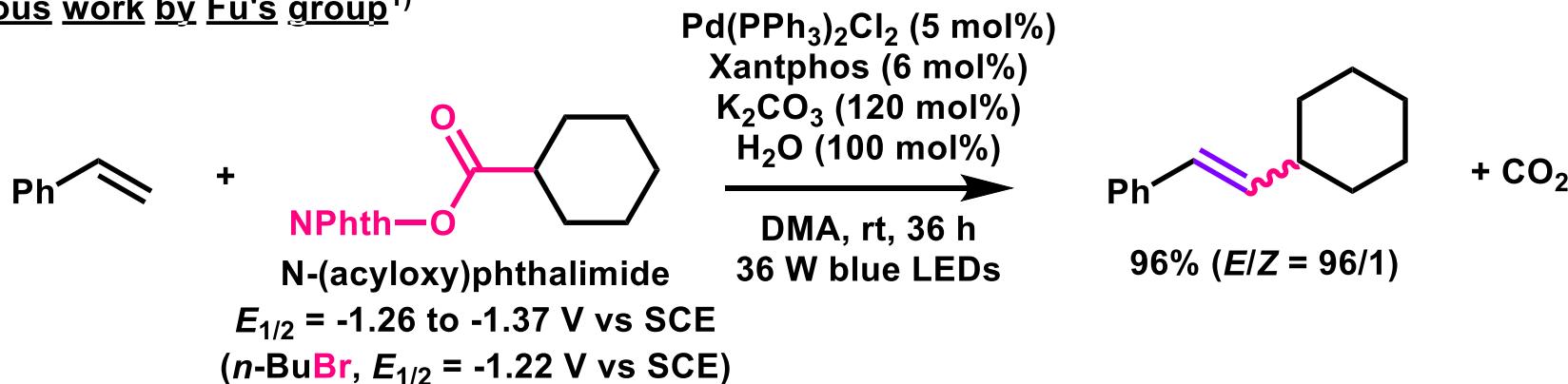
2) Wang, G.-Z.; Shang, R.; Cheng, W.-M.; Yao, F. *J. Am. Chem. Soc.* **2017**, *139*, 18307.

Contents

1. Introduction
2. Catalytic Oxidation of Silyl Ethers into Silyl Enol Ethers
(Gevorgyan, 2016)
2. Irradiation-Induced Heck Reaction (Fu, 2017, Main 1)
3. Irradiation-Induced Decarbonylative Desaturation
(Fu, 2018, Main 2)

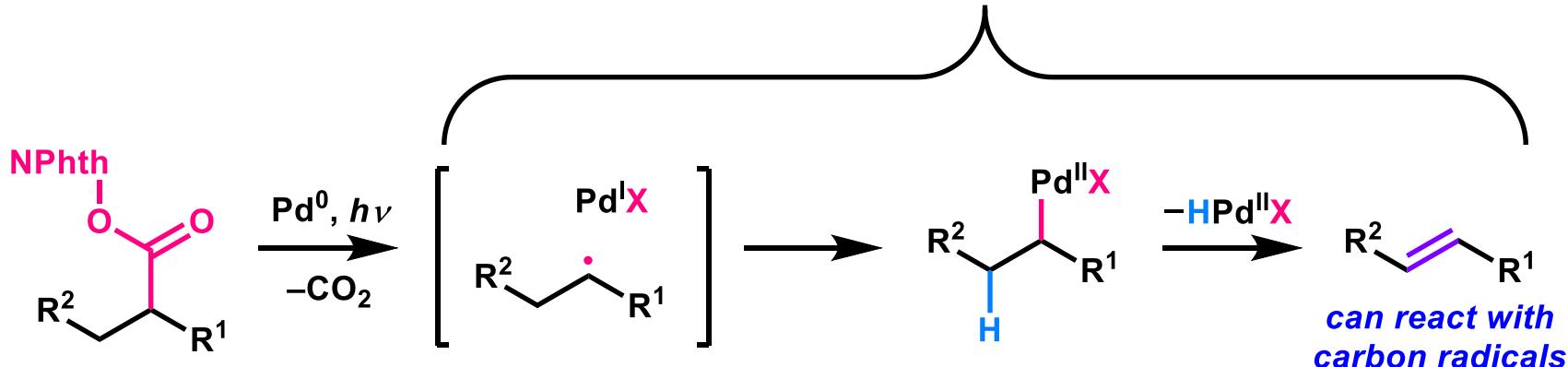
Working Hypothesis

Previous work by Fu's group¹⁾



Working hypothesis of decarboxylative desaturation²⁾

inspired by Gevorgyan's desaturation chemistry³⁾



In contrast to Fu's previous studies, the formation of Pd^{II} complex and β -H elimination must be promoted to realize the above transformation.

1) Wang, G.-Z.; Shang, R.; Fu, Y. *Org. Lett.* **2018**, 20, 888. 2) Cheng, W.-M.; Shang, R.; Fu, Y. *Nat. Commun.* **2018**, 9, 5215. 3) Parasram, M.; Chuentragool, P.; Sarkar, D.; Gevorgyan, V. *J. Am. Chem. Soc.* **2016**, 138, 6340.

Optimization of the Reaction Conditions (1)

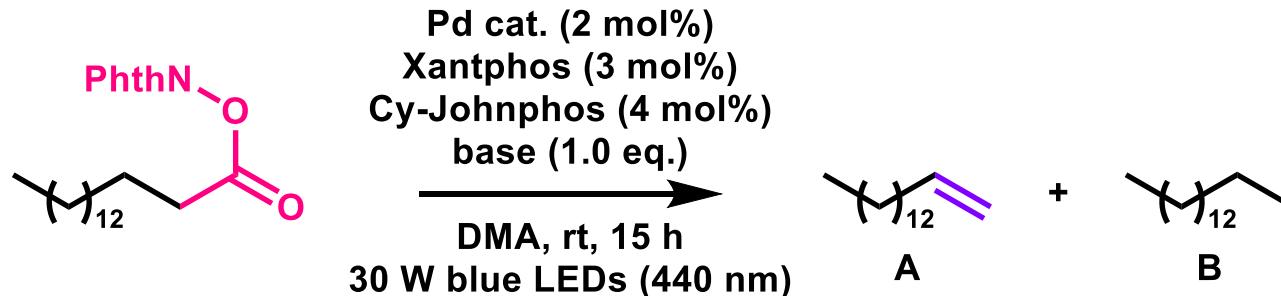
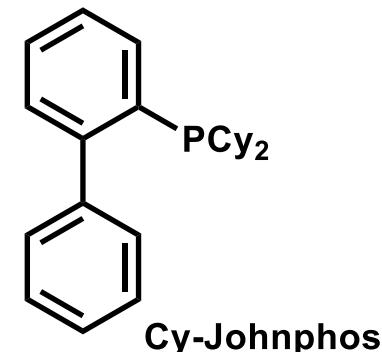
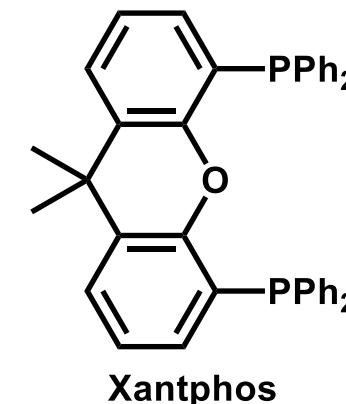


Table. Optimization of the reaction conditions

entry	catalyst	base	yield of A (%) ^a
1	PdCl ₂	without base	51%
2	PdCl ₂	K ₂ CO ₃	30%
3	PdCl ₂	DMAP	43%
4	PdCl ₂	Et ₃ N	40%
5	PdCl ₂	2,4,6-collidine	93% (B: <1%)
6	Pd(OAc) ₂	2,4,6-collidine	10%
7	Pd(TFA) ₂	2,4,6-collidine	<5%
8	Pd ₂ (dba) ₃	2,4,6-collidine	<5%



a) GC yield.

Optimization of the Reaction Conditions (2)

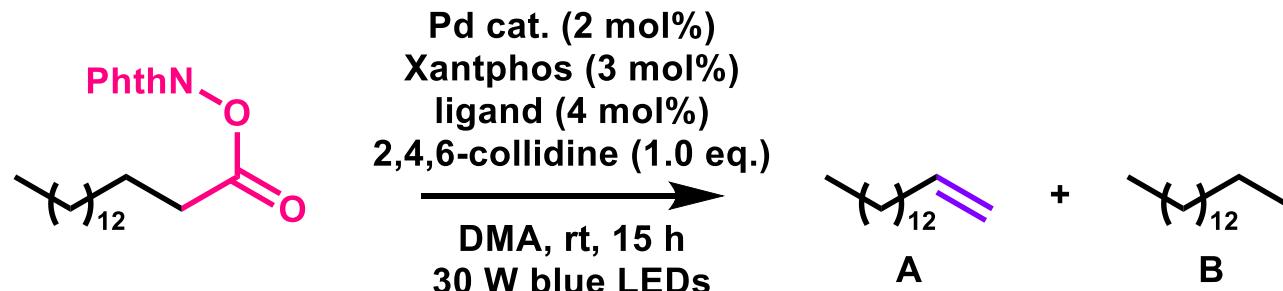
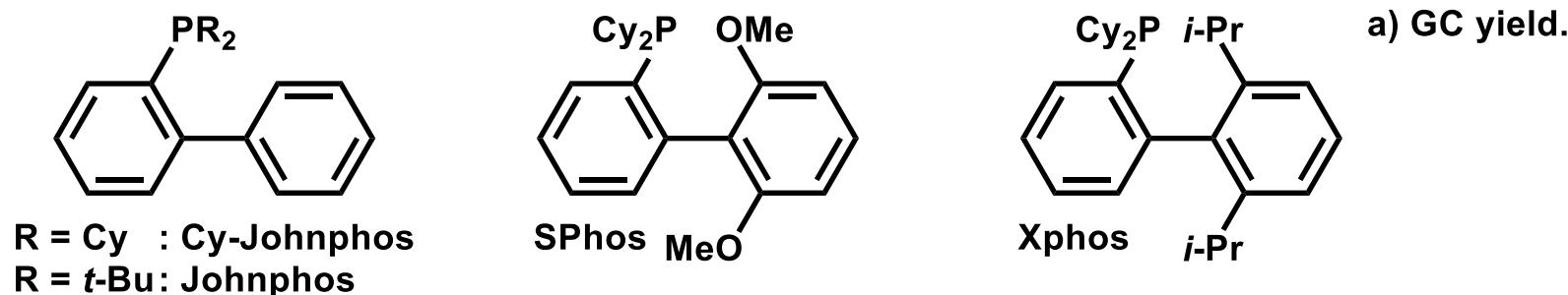
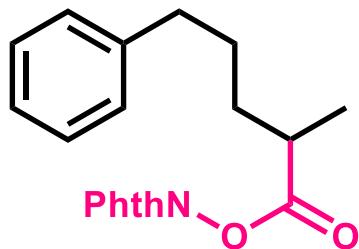


Table. Ligand effect

entry	ligand	yield of A (%)	entry	ligand	yield of A (%)
1	without ligand	44% (B: 6%)	6	P(<i>t</i> -Bu) ₃	54%
2	Cy-Johnphos	93% (B: < 1%)	7	PhPCy ₂	12%
3	PPh ₃	trace	8	Johnphos	64%
4	P(1-Np) ₃	52%	9	Sphos	16%
5	PCy ₃	60%	10	Xphos	19%

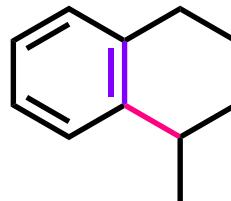


Ligand Effect

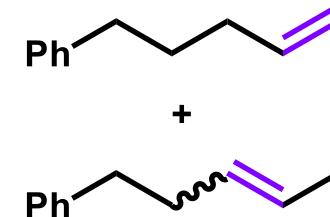


PdCl₂ (2 mol%)
Xantphos (3 mol%)
ligand (4 mol%)
2,4,6-collidine (1.0 eq.)
DMA, rt, 15 h
30 W blue LEDs

Cy-Johnphos



54%



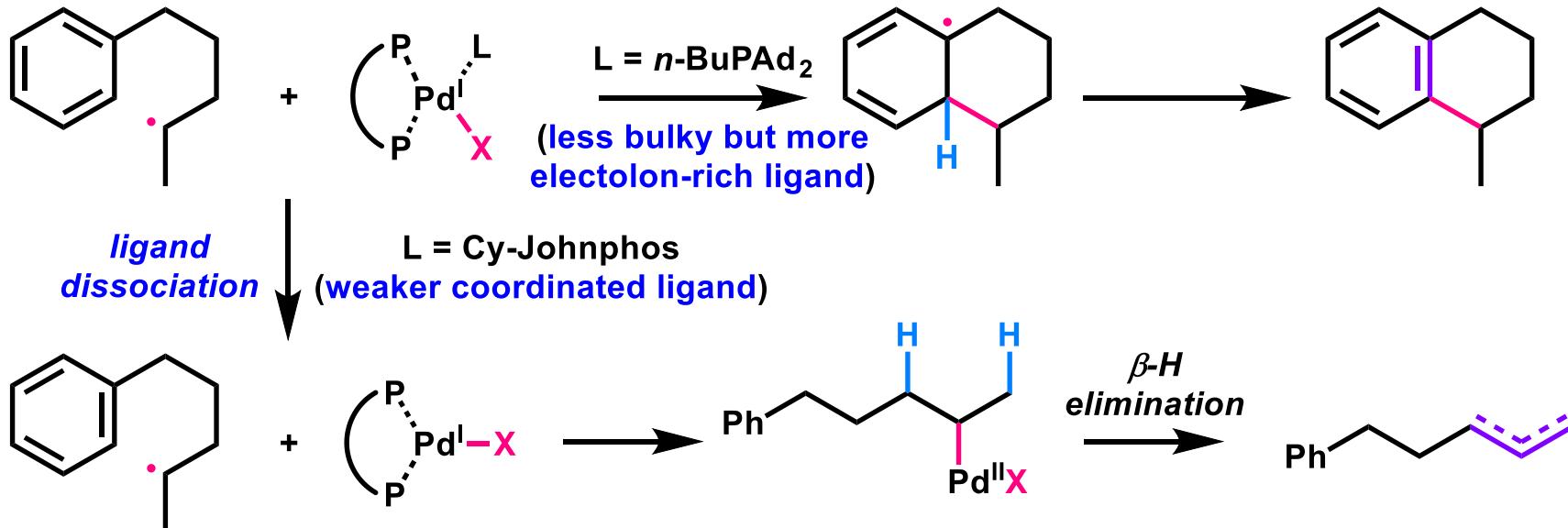
36%
(internal:terminal = 2.6:1)

n-BuPAd₂

65%

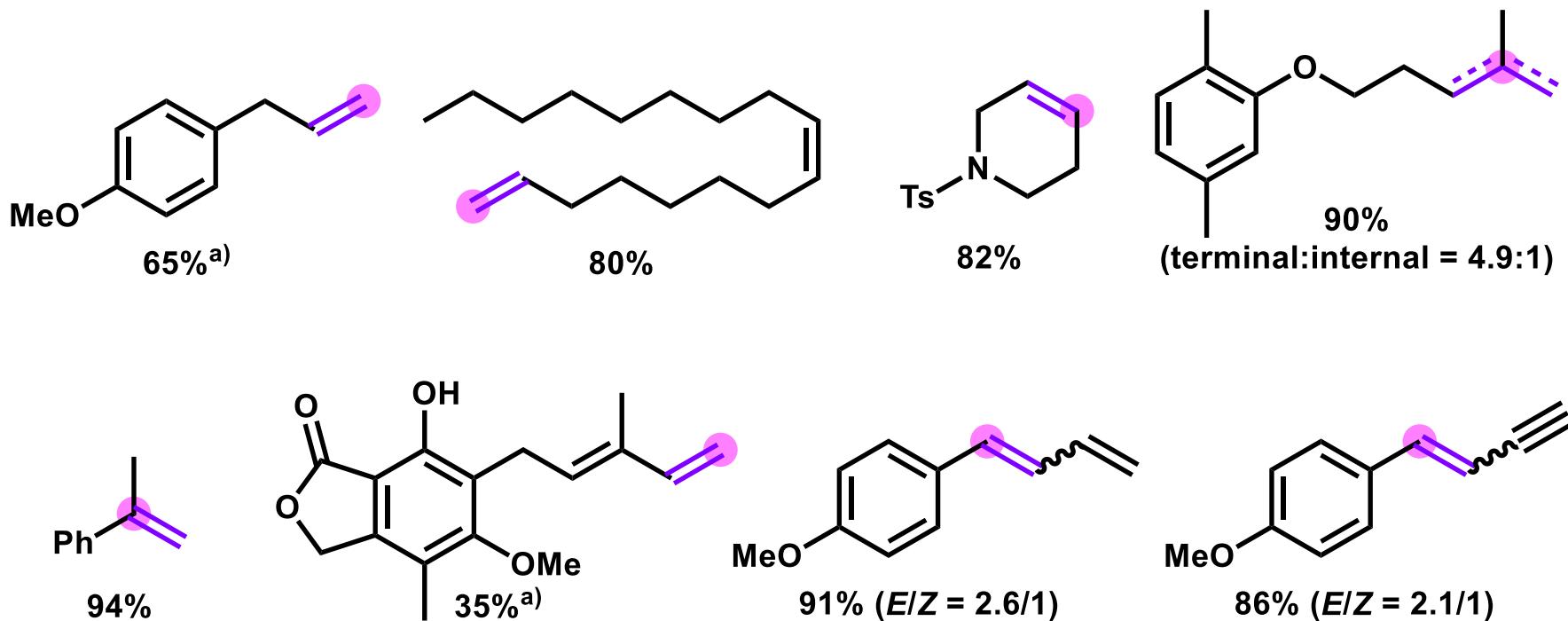
< 5%

Proposed mechanisms:



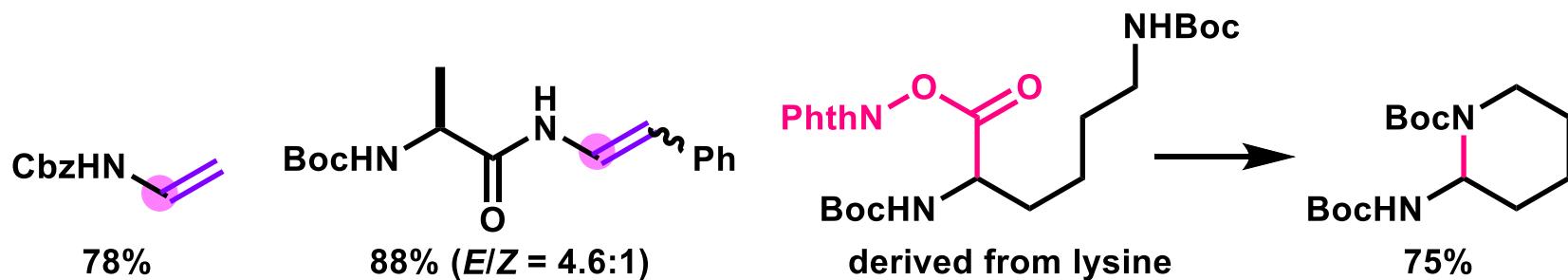
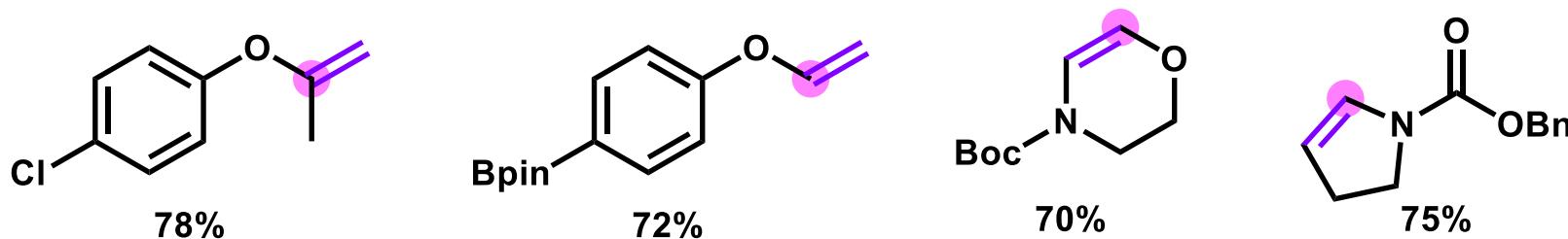
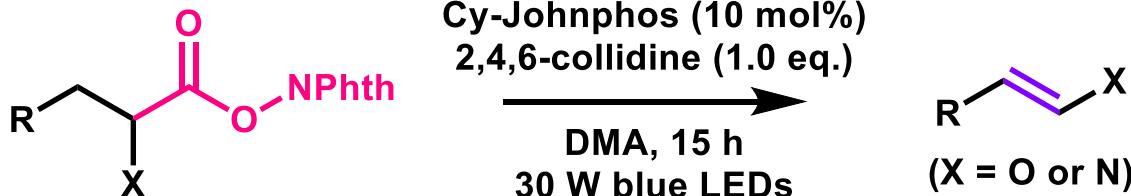
Substrate Scope (1)

PdCl₂ (2 mol%)
Xantphos (3 mol%)
Cy-Johnphos (4 mol%)
2,4,6-collidine (1.0 eq.)
DMA, 15 h
30 W blue LEDs

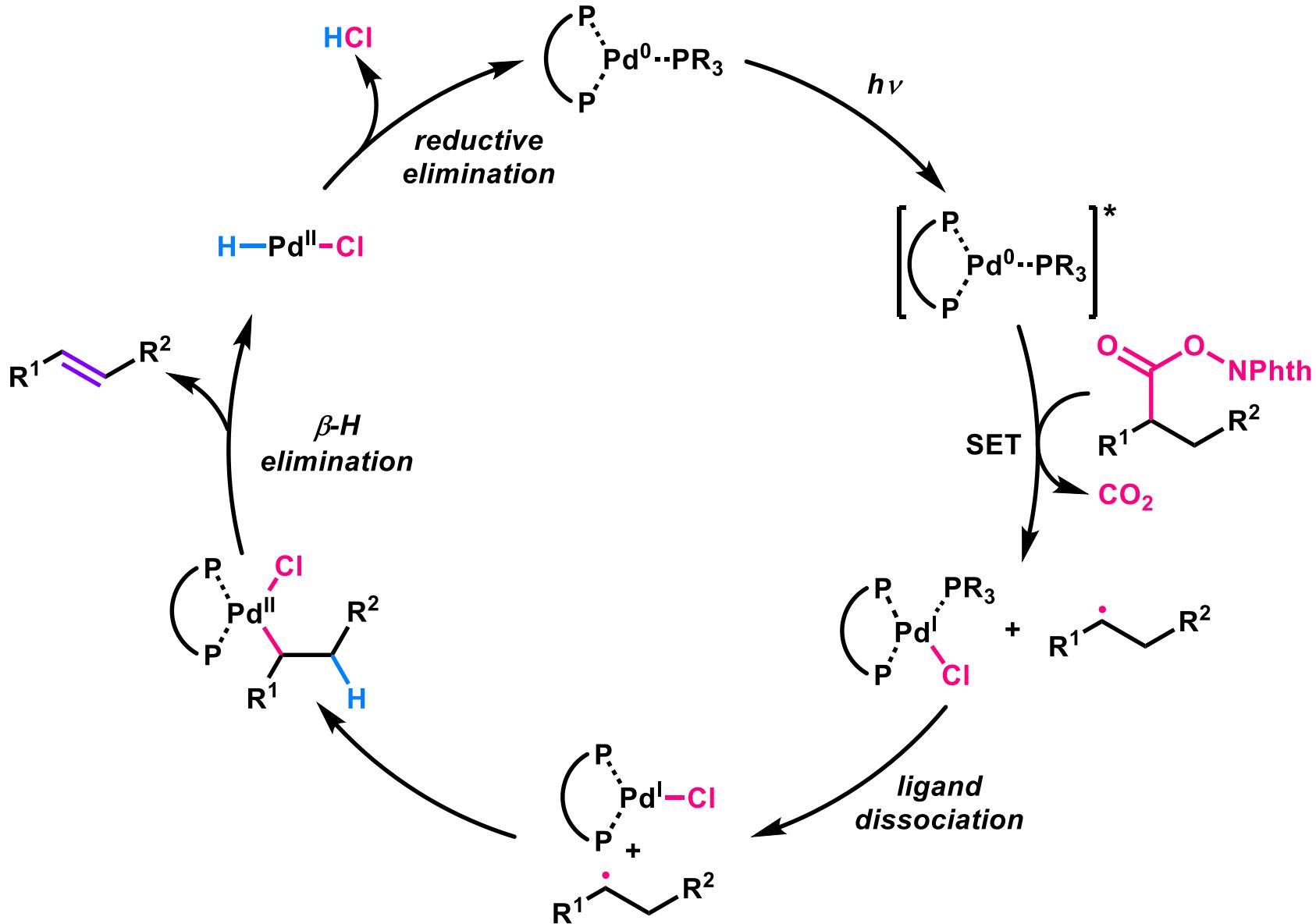


a) PdCl₂ (5 mol%), Xantphos (6mol%) and Cy-Johnphos (10 mol%) were used.

Substrate Scope (2)

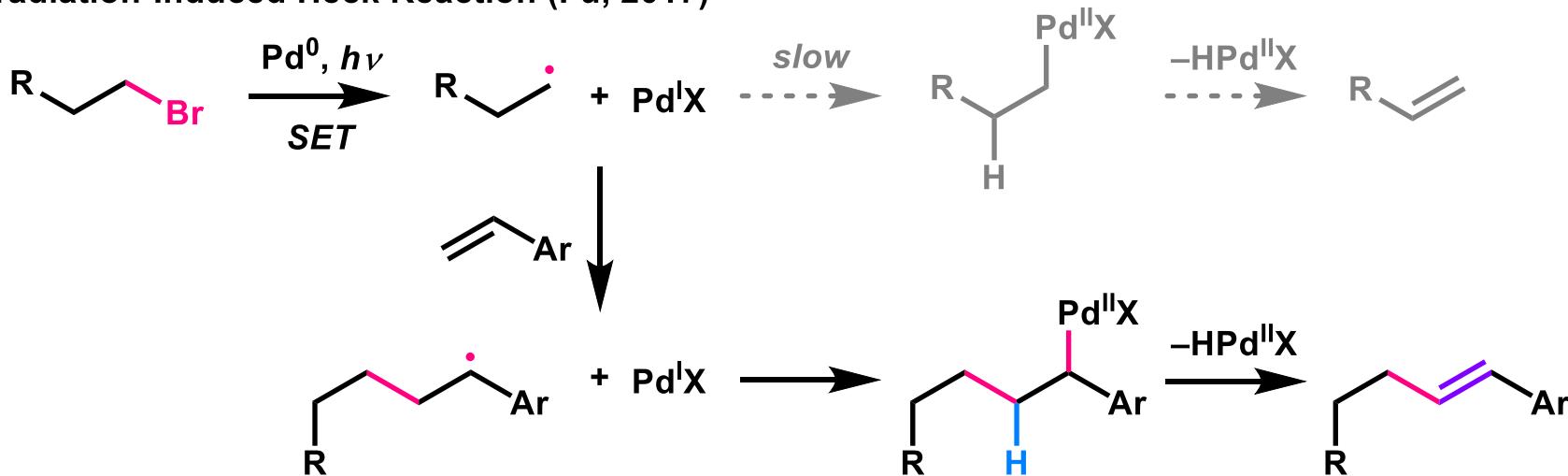


Proposed Mechanisms

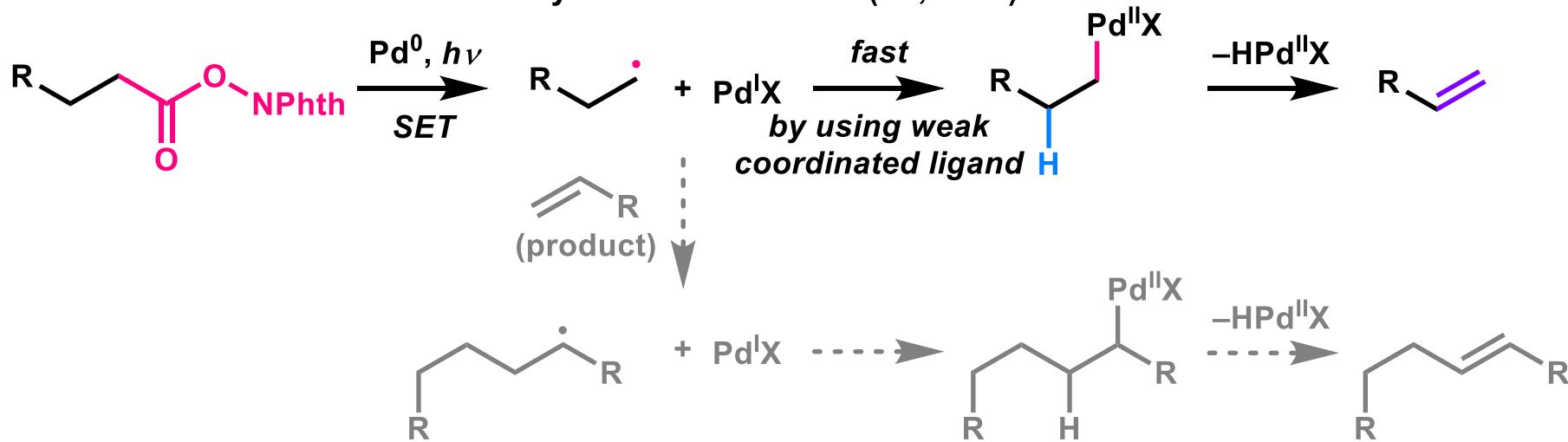


Summary

1. Irradiation-Induced Heck Reaction (Fu, 2017)¹⁾



2. Irradiation-Induced Decarbonylative Desaturation (Fu, 2018)²⁾



1) Wang, G.-Z.; Shang, R.; Cheng, W.-M.; Yao, F. *J. Am. Chem. Soc.* **2017**, 139, 18307. 2) Cheng, W.-M.; Shang, R.; Fu, Y. *Nat. Commun.* **2018**, 9, 5215.