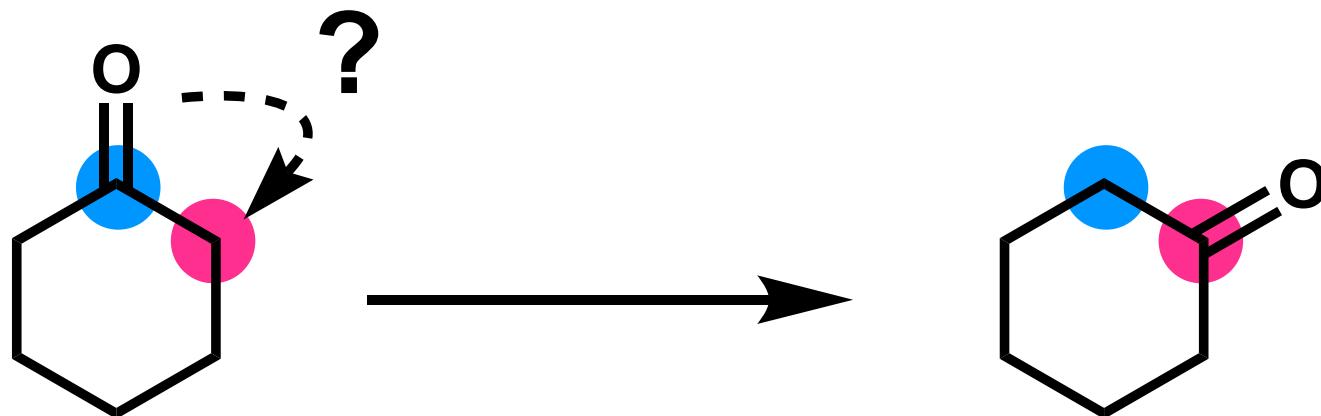


Carbonyl 1,2-transposition through triflate-mediated α -amination



2022. 04.23 Literature seminar
Kyohei Oga

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1. Introduction

2. Alkenyl Catellani reaction

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<https://doi.org/10.1038/s41557-019-0358-y>

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Modular and regioselective synthesis of
all-carbon tetrasubstituted olefins enabled
by an alkenyl Catellani reaction

3. Carbonyl 1,2-transposition (Main)

ORGANIC CHEMISTRY

Carbonyl 1,2-transposition through
triflate-mediated α -amination

Zhao Wu, Xiaolong Xu, Jianchun Wang, Guangbin Dong*

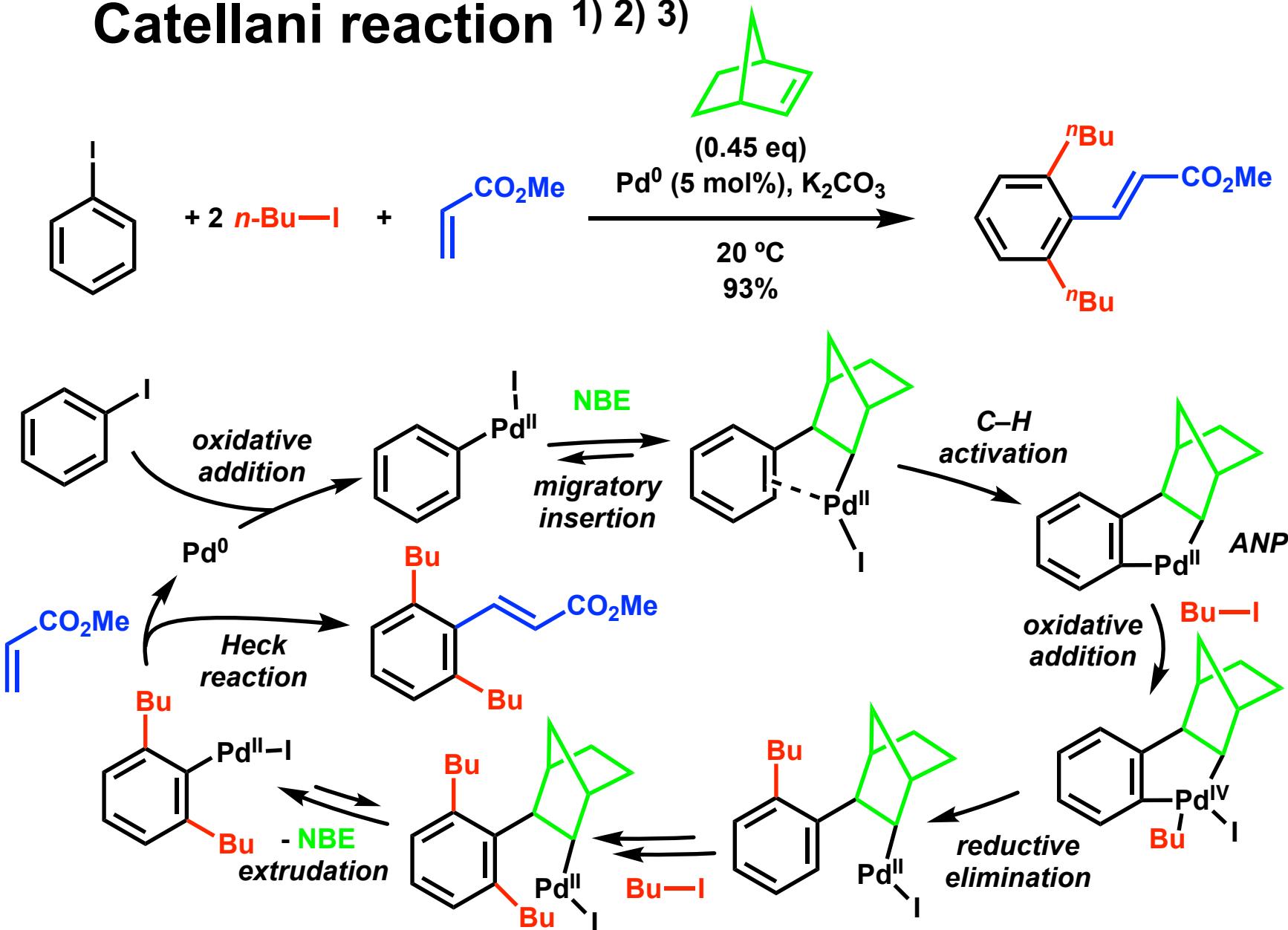
contents

1. Introduction

2. Alkenyl Catellani reaction

3. Carbonyl 1,2-transposition (Main)

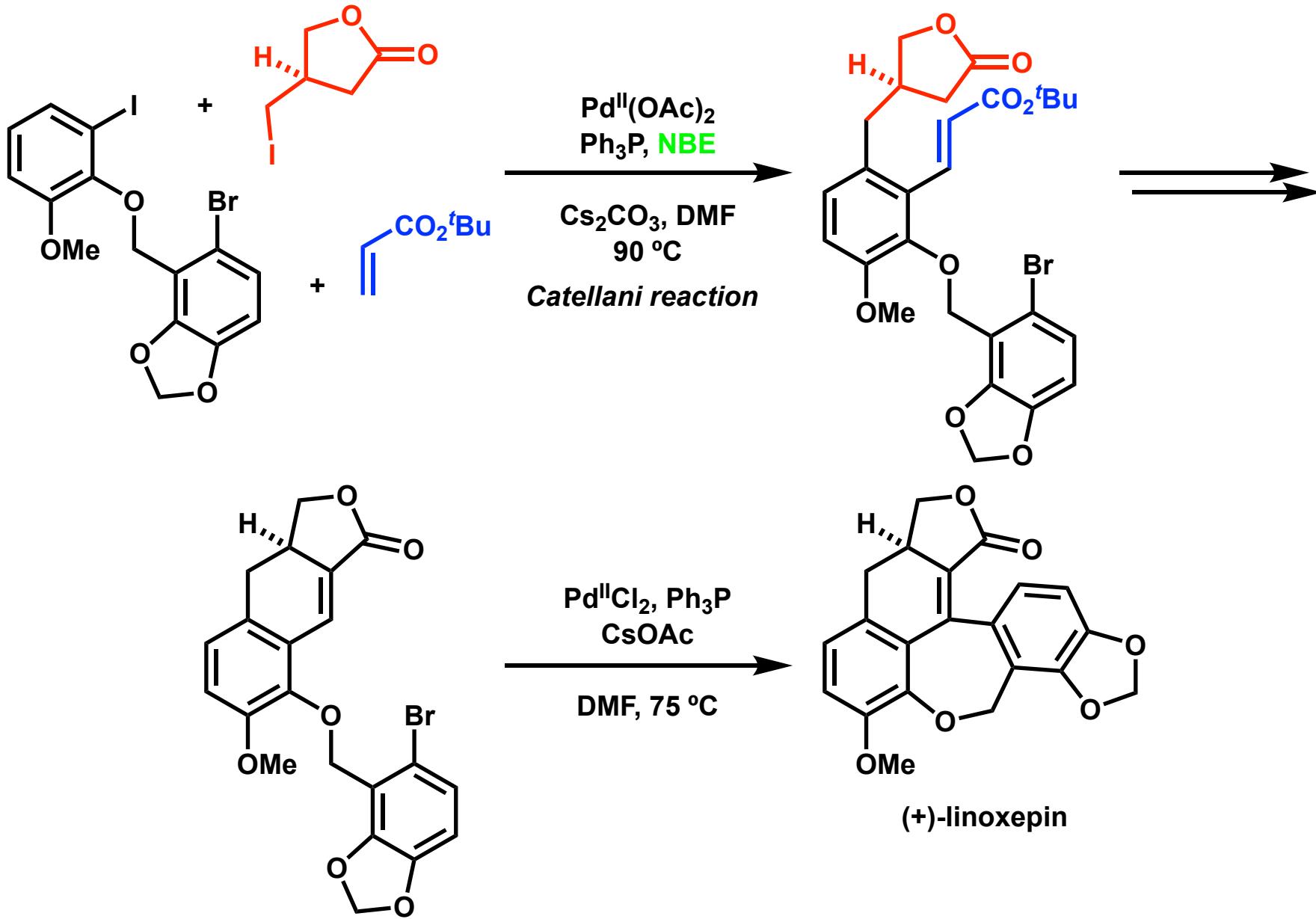
Catellani reaction 1) 2) 3)



1) Catellani, M.; Frignani, F.; Rangoni, A.; *Angew. Chem. Int. Ed.* **1997**, *36*, 119.

2) 181027_LS_Haruka_Fujino 3) 121112_LS_Shunichiro_Katoh

Application for Total synthesis ¹⁾



contents

1. Introduction

2. Alkenyl Catellani reaction

ARTICLES

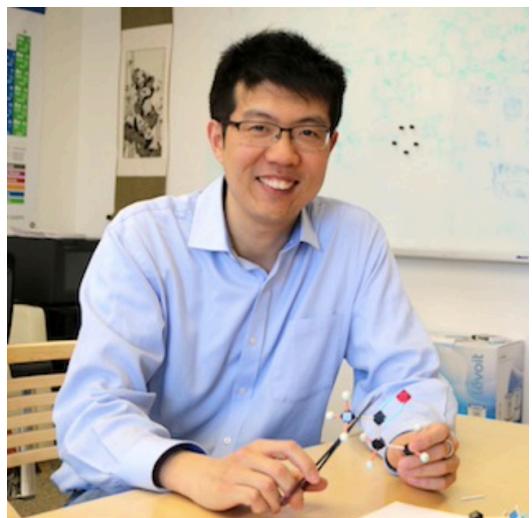
<https://doi.org/10.1038/s41557-019-0358-y>

nature
chemistry

**Modular and regioselective synthesis of
all-carbon tetrasubstituted olefins enabled
by an alkenyl Catellani reaction**

3. Carbonyl 1,2-transposition (Main)

Prof. Guangbin Dong



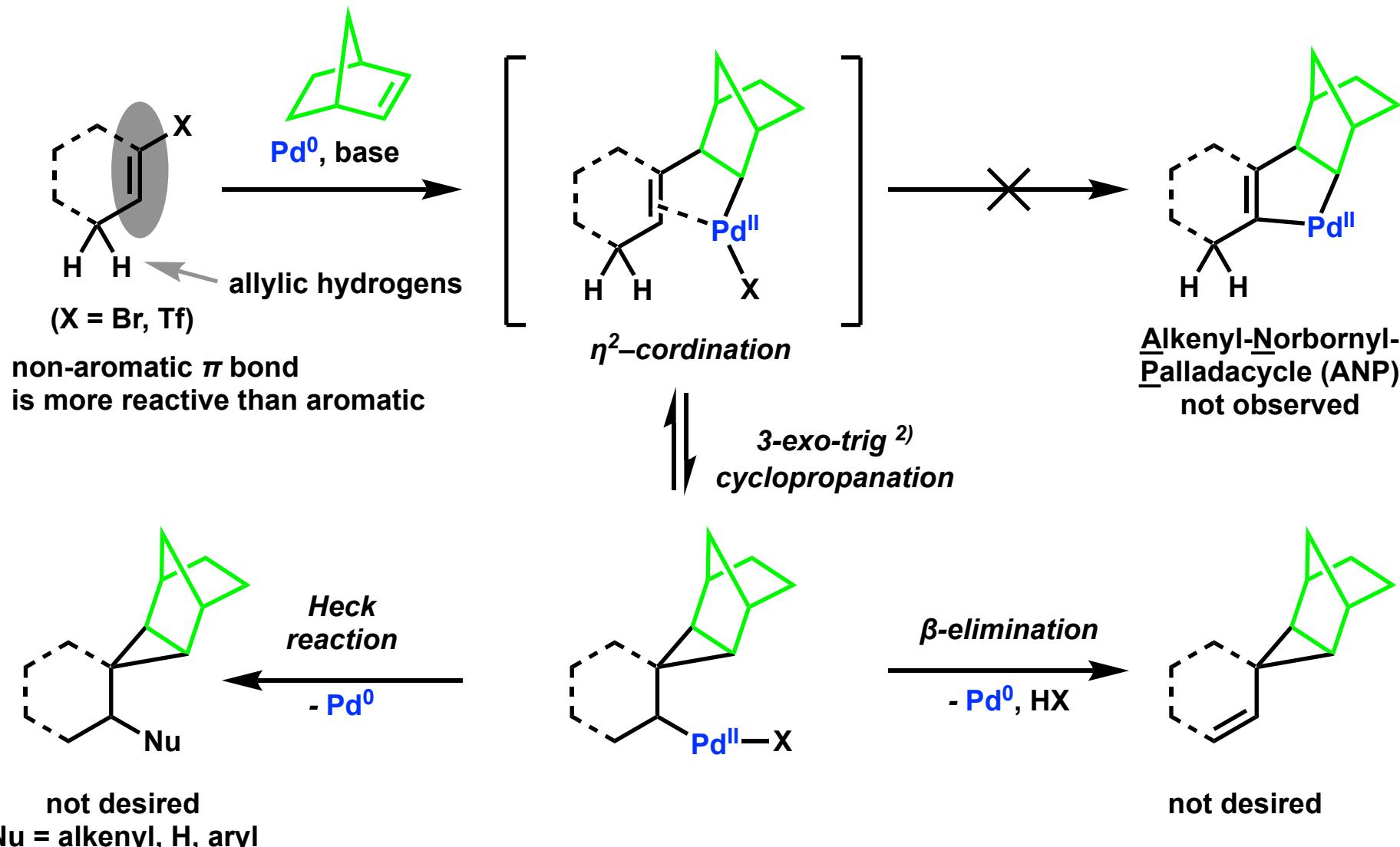
Education and academic career:

2003, B.S., Peking University (Prof. Zhen Yang)
2009, Ph.D. Stanford University (Prof. Barry M. Trost)
2009–2011, Postdoctoral Fellow, California Institute of Technology (Prof. Robert H. Grubbs)
2011–2016, Assistant Professor, University of Texas
2016–Present, Professor, The university of Chicago

Research topics:

1. C–C bond activation (Cut and Sew), C–H bond activation
2. Total synthesis

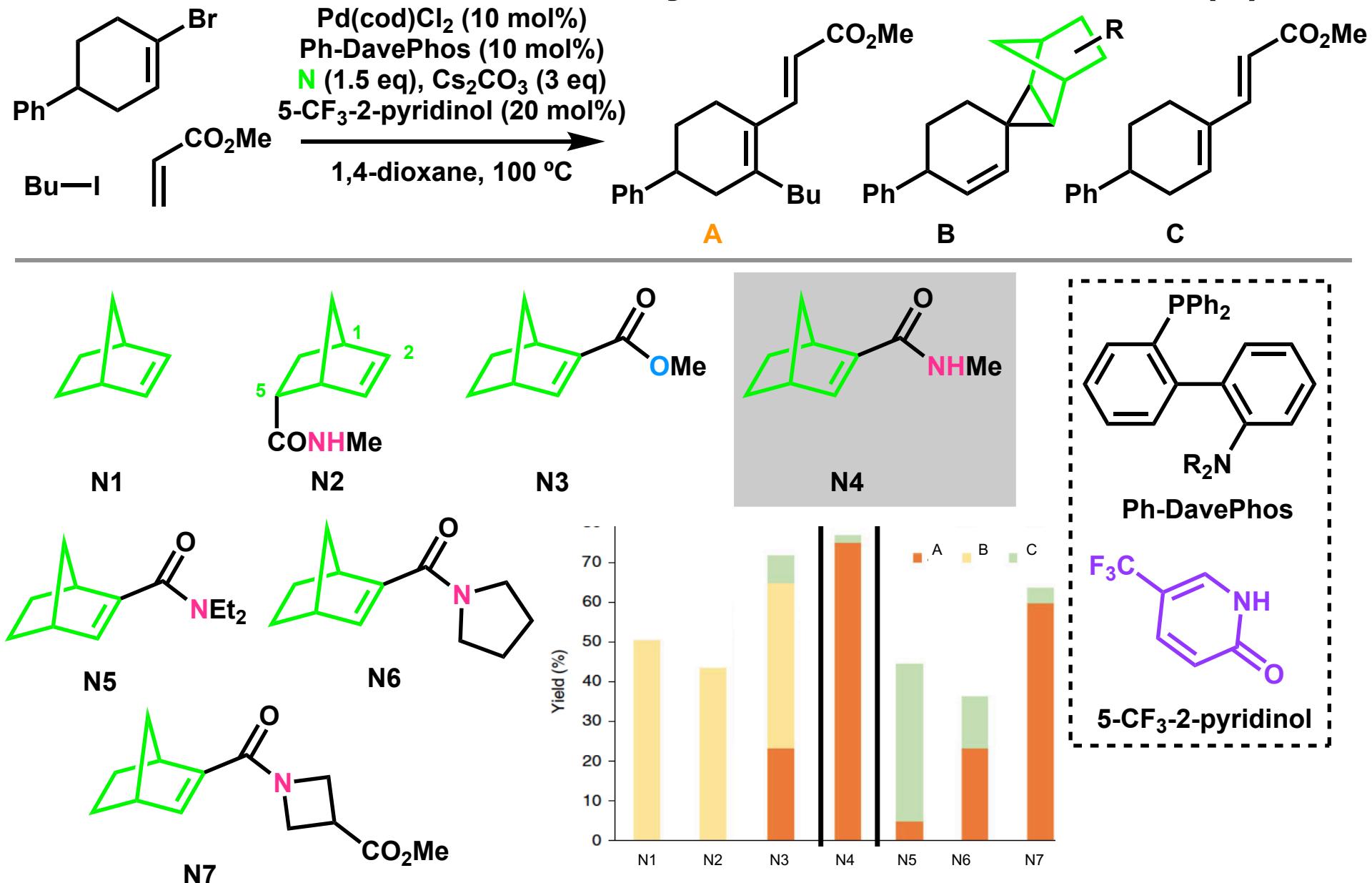
Background and Problematic point ¹⁾



1) Wang, J.; Dong, Z.; Yang, C.; Dong, G. *Nat. Chem.* **2019**, *11*, 1106.

2) Khana, A.; Premachandra, I.; Sung, P.; Vranken, D. *Org. Lett.* **2013**, *12*, 3158.

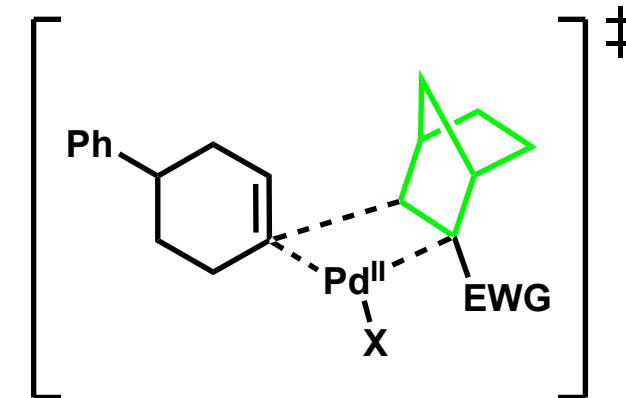
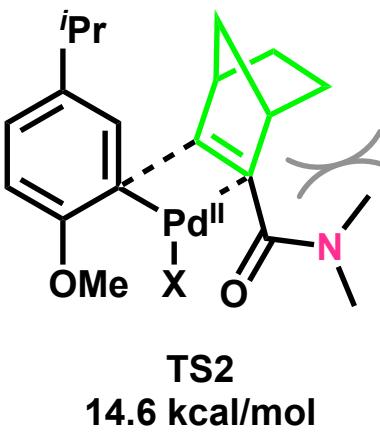
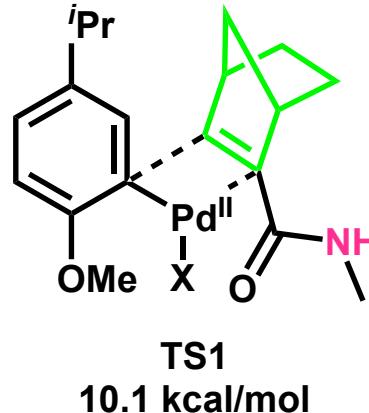
NBE effect for the alkeyl Catellani reaction (1) ¹



NBE effect for the alkeyl Catellani reaction (2)¹

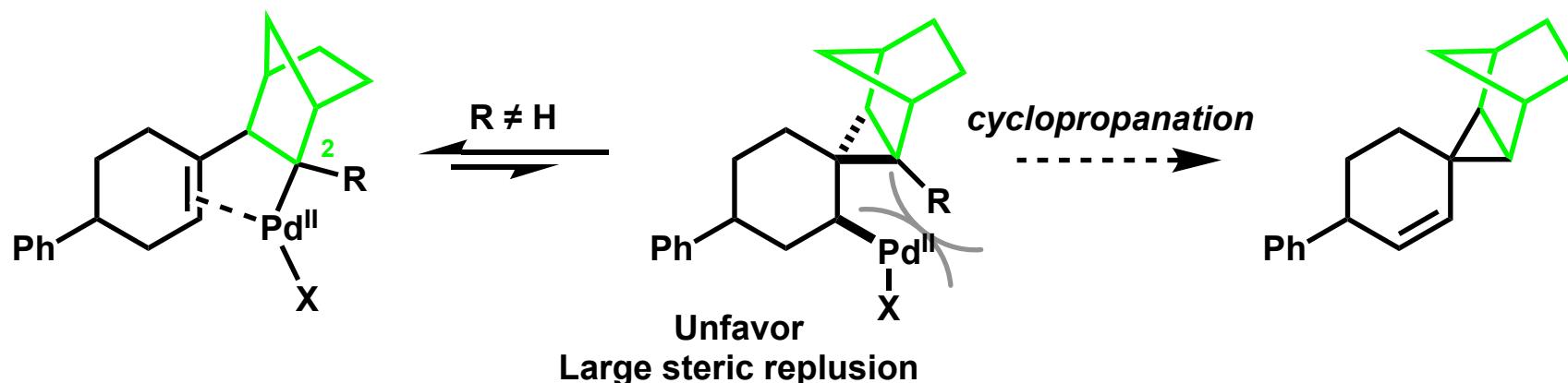
C2 substitution effect

1) NBE insertion step²⁾



The electron-withdrawing C2 substituent can promote migratory insertion

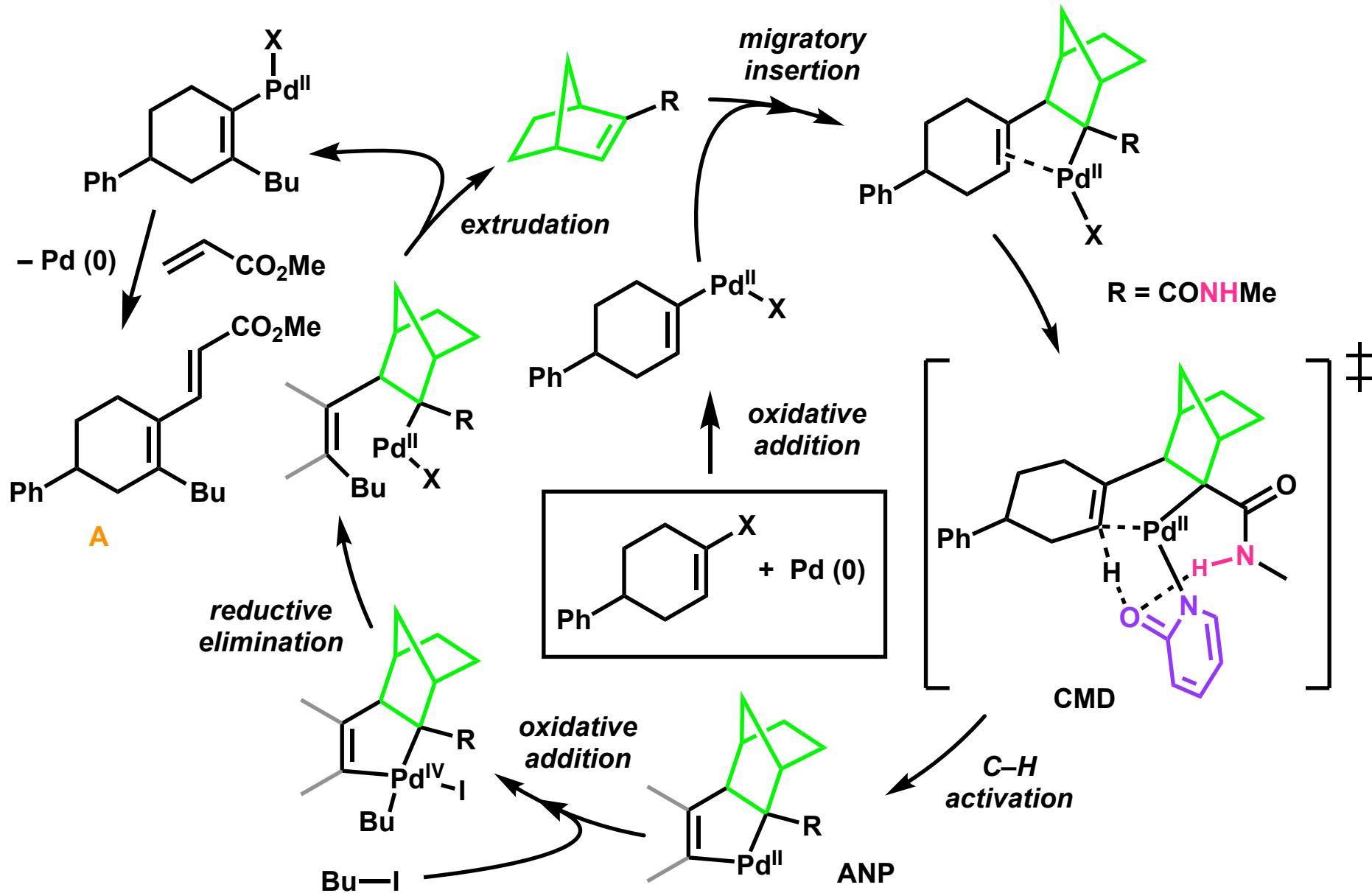
2) prevent from cyclopropanation



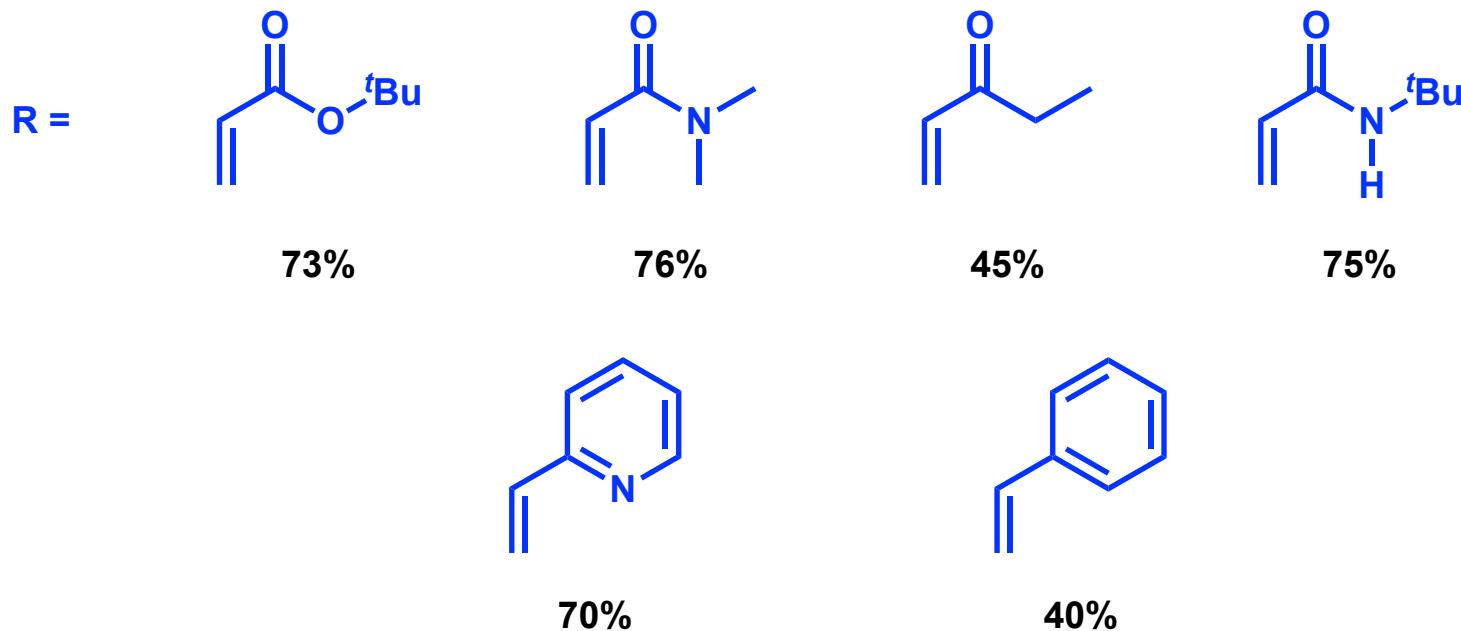
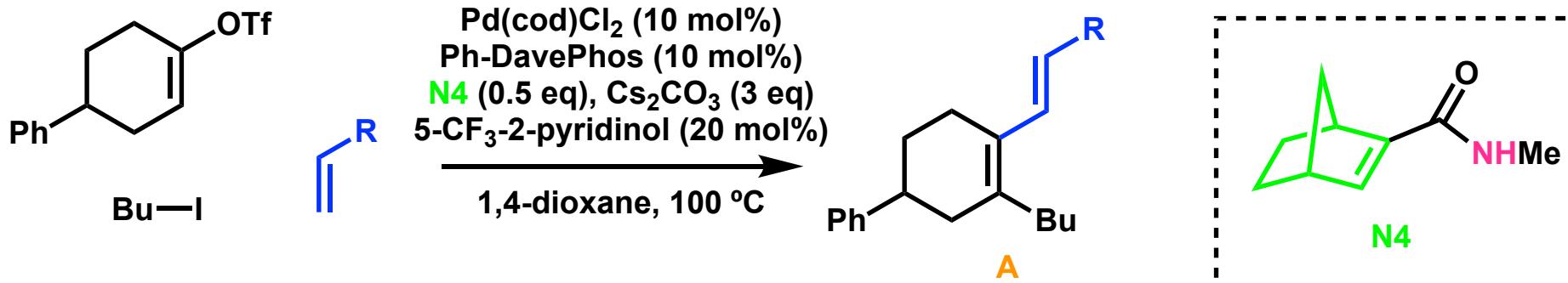
1) Wang, J.; Dong, Z.; Yang, C.; Dong, G. *Nat. Chem.* **2019**, *11*, 1106.

2) Li, R.; Dong, G. *J. Am. Chem. Soc.* **2020**, *142*, 17859.

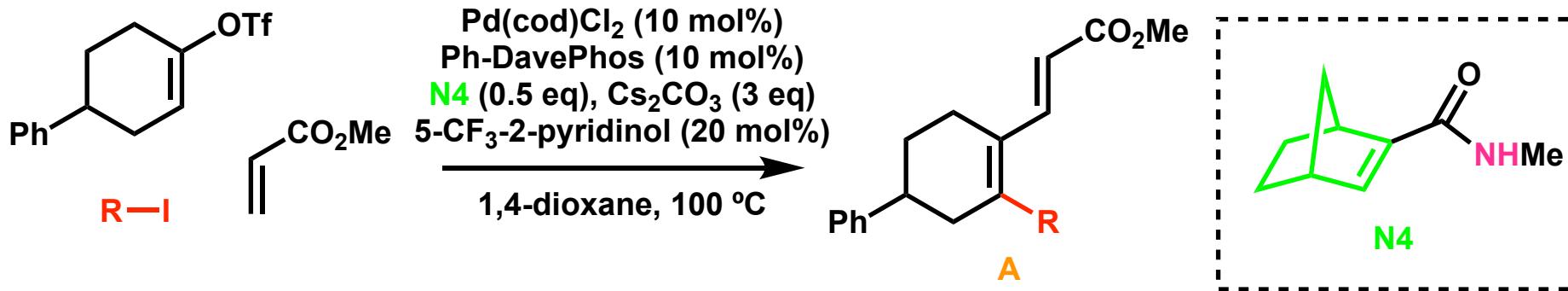
Proposed reaction mechanism



Substrate scope (Olefin)



Substrate scope (Alkyl iodide)



$\text{R} =$	$\text{---C}_{10}\text{H}_{21}$	---OTBS	---CN	---Cl
	76%	73%	68%	56%
	---Ph	$\text{---CO}_2\text{Me}$		
	76%	69%		40%

contents

1. Introduction

2. Alkenyl Catellani reaction

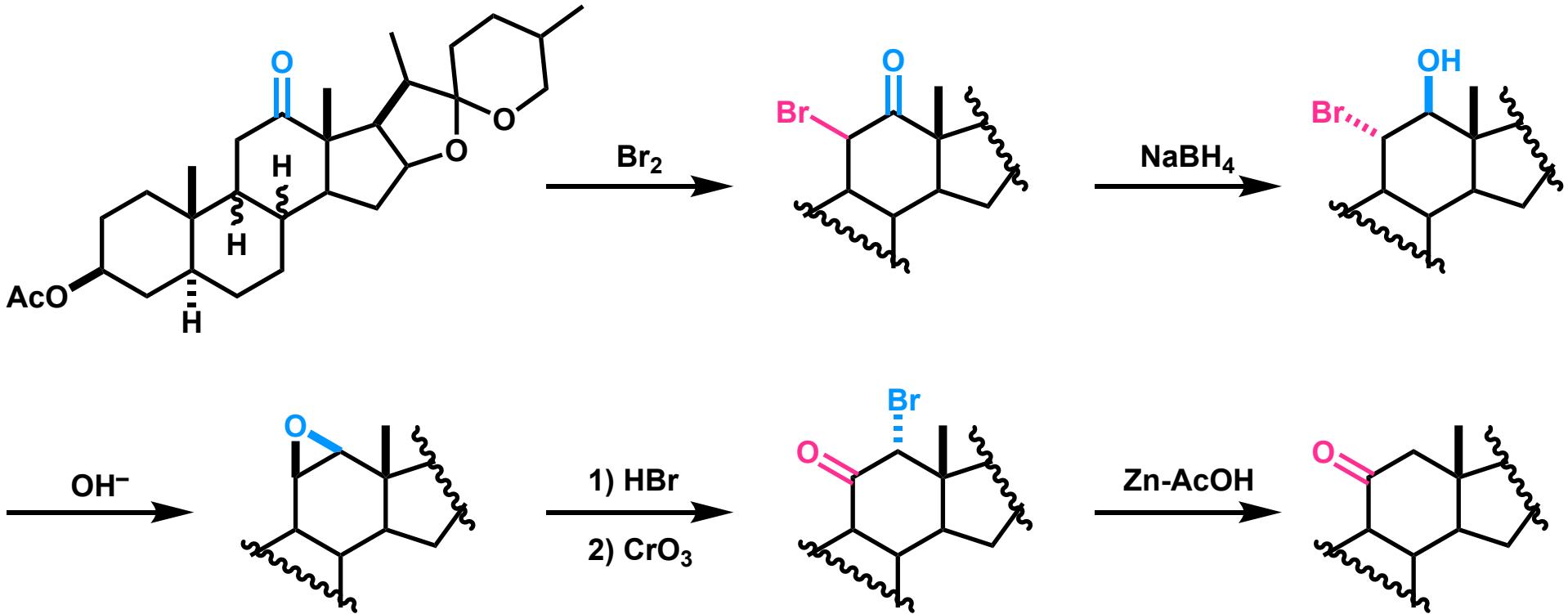
3. Carbonyl 1,2-transposition (Main)

ORGANIC CHEMISTRY

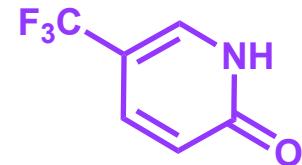
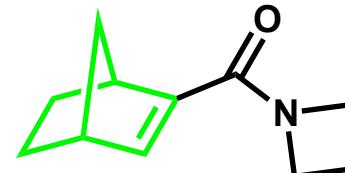
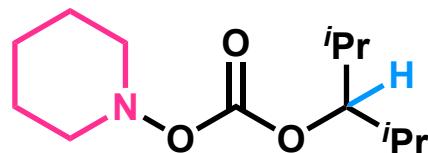
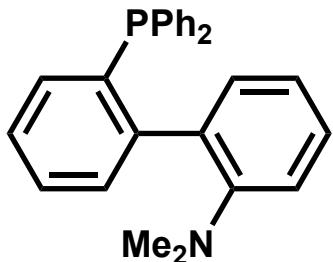
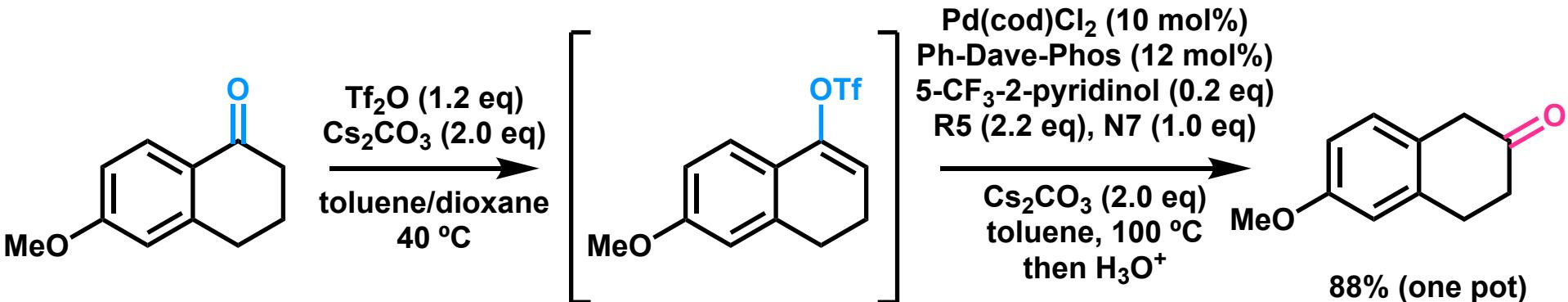
Carbonyl 1,2-transposition through
triflate-mediated α -amination

Zhao Wu, Xiaolong Xu, Jianchun Wang, Guangbin Dong*

Current 1,2-carbonyl transpositions

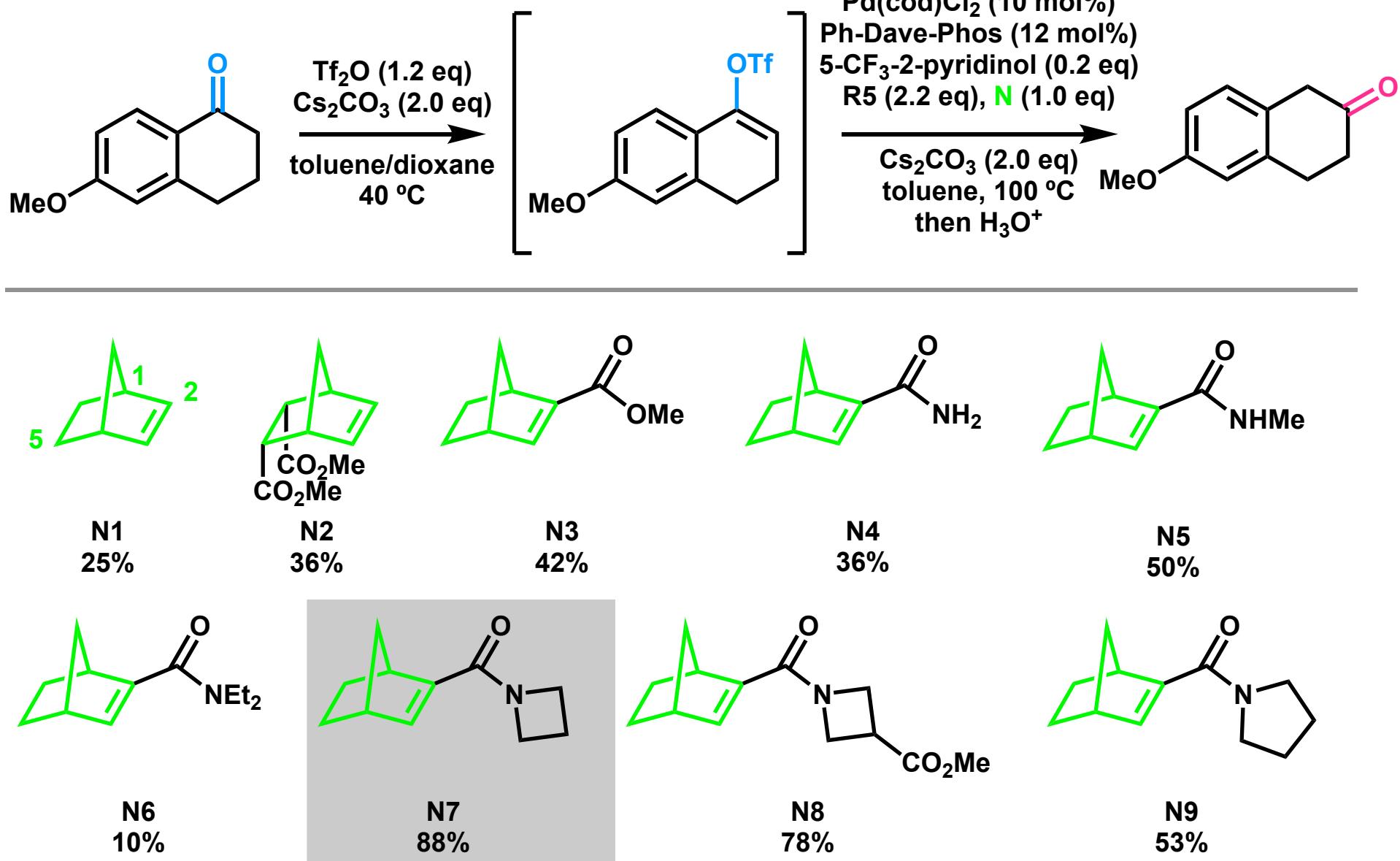


Control experiment

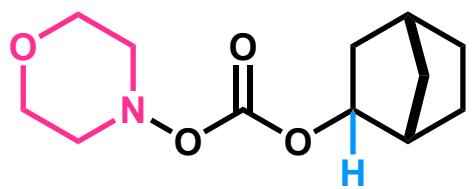
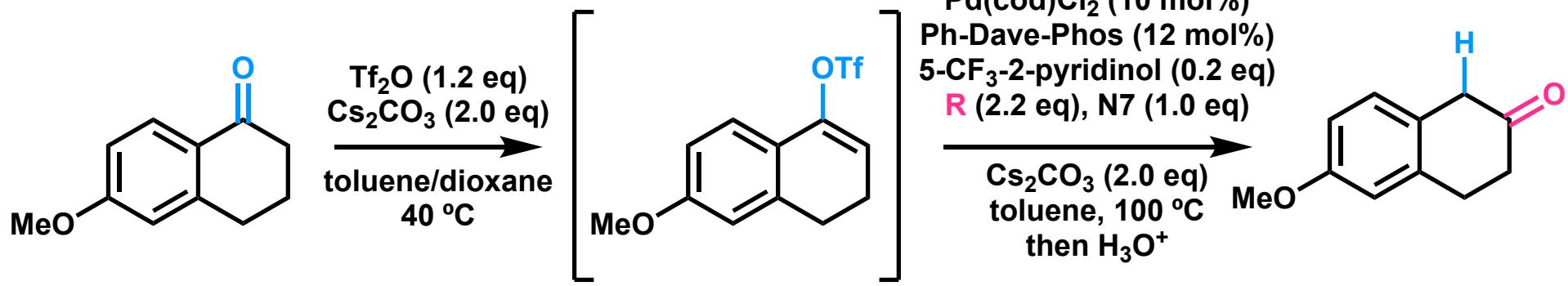


Entry	Variation from second step	Yield
1	w/o Pd(COD)Cl ₂	0%
2	w/o 5-CF ₃ -2-pyridinol	9%
3	w/o N10	0%

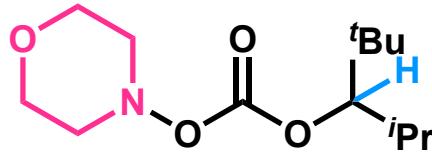
Optimization of NBE



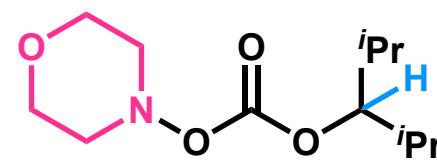
Optimization of bifunctional reagent



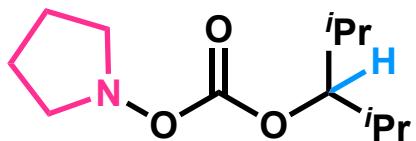
R1
52%



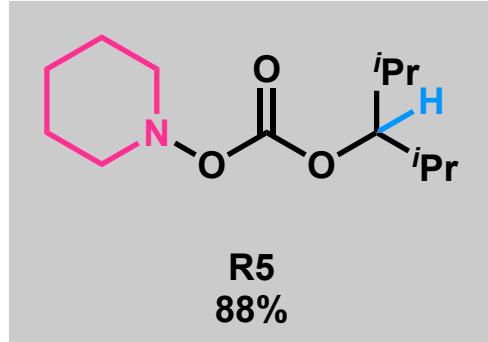
R2
70%



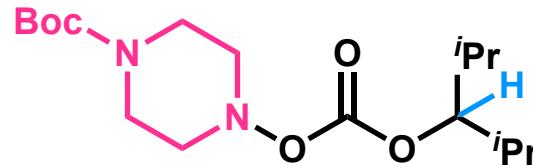
R3
78%



R4
15%

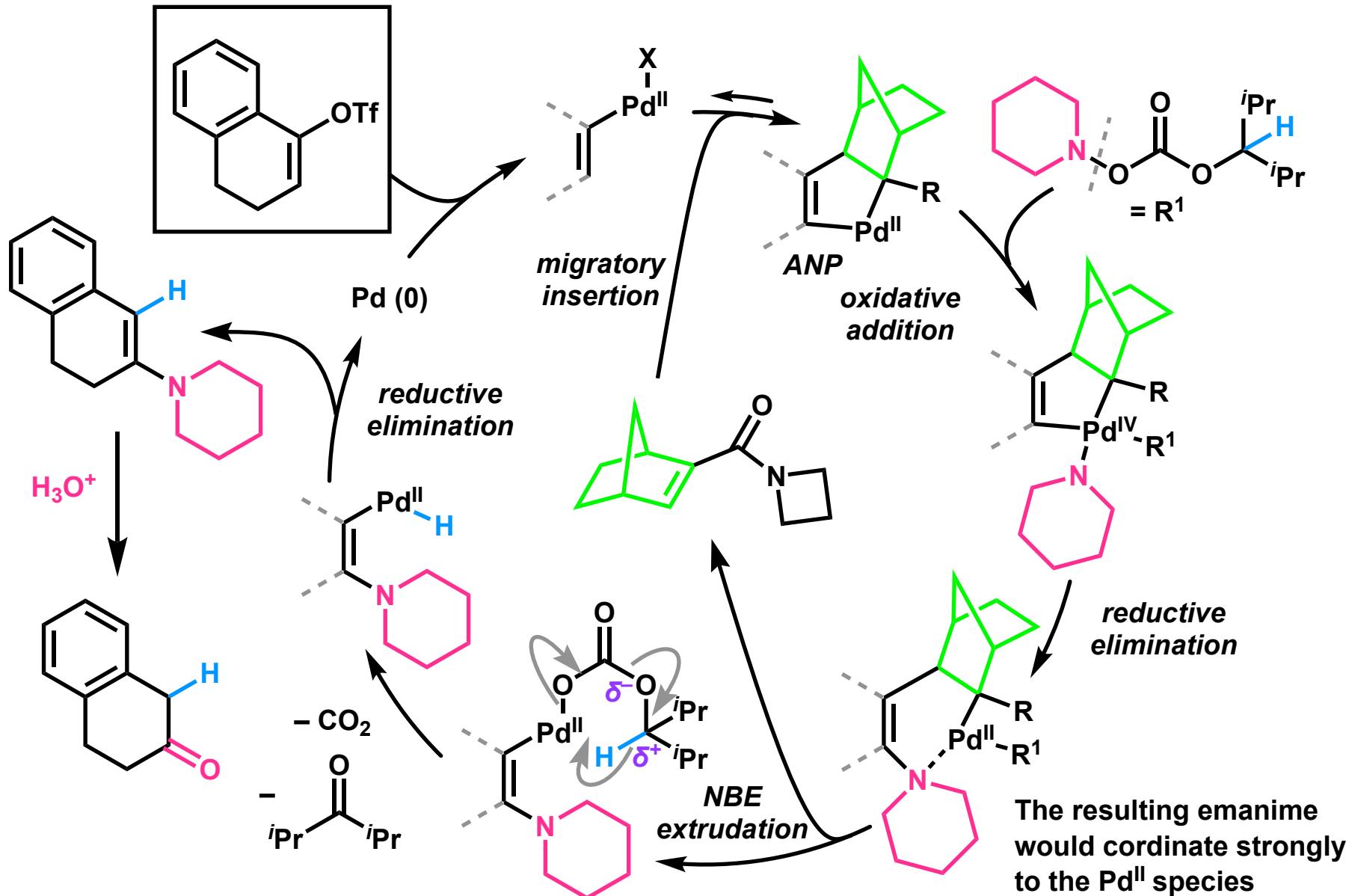


R5
88%

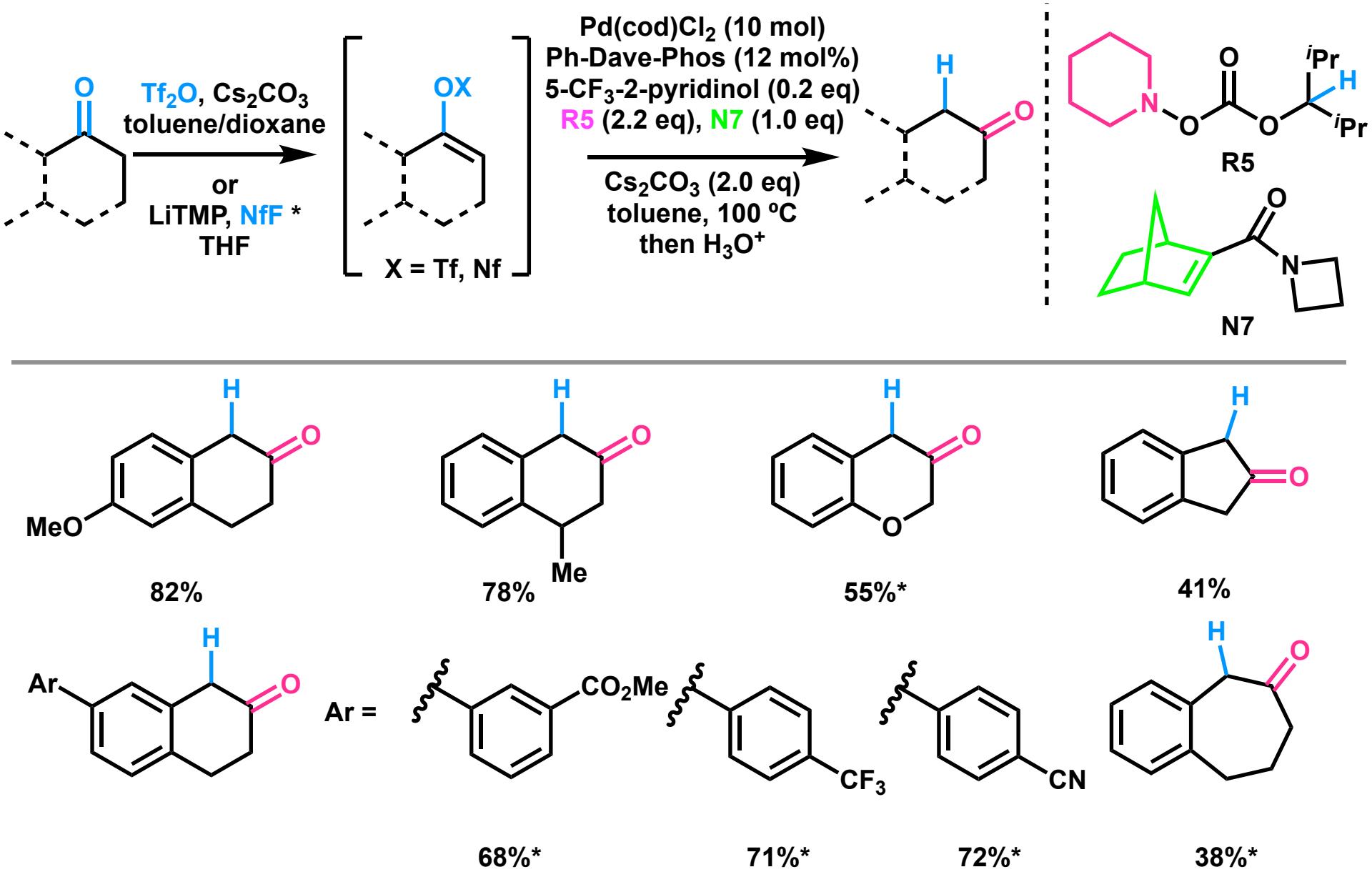


R6
49%

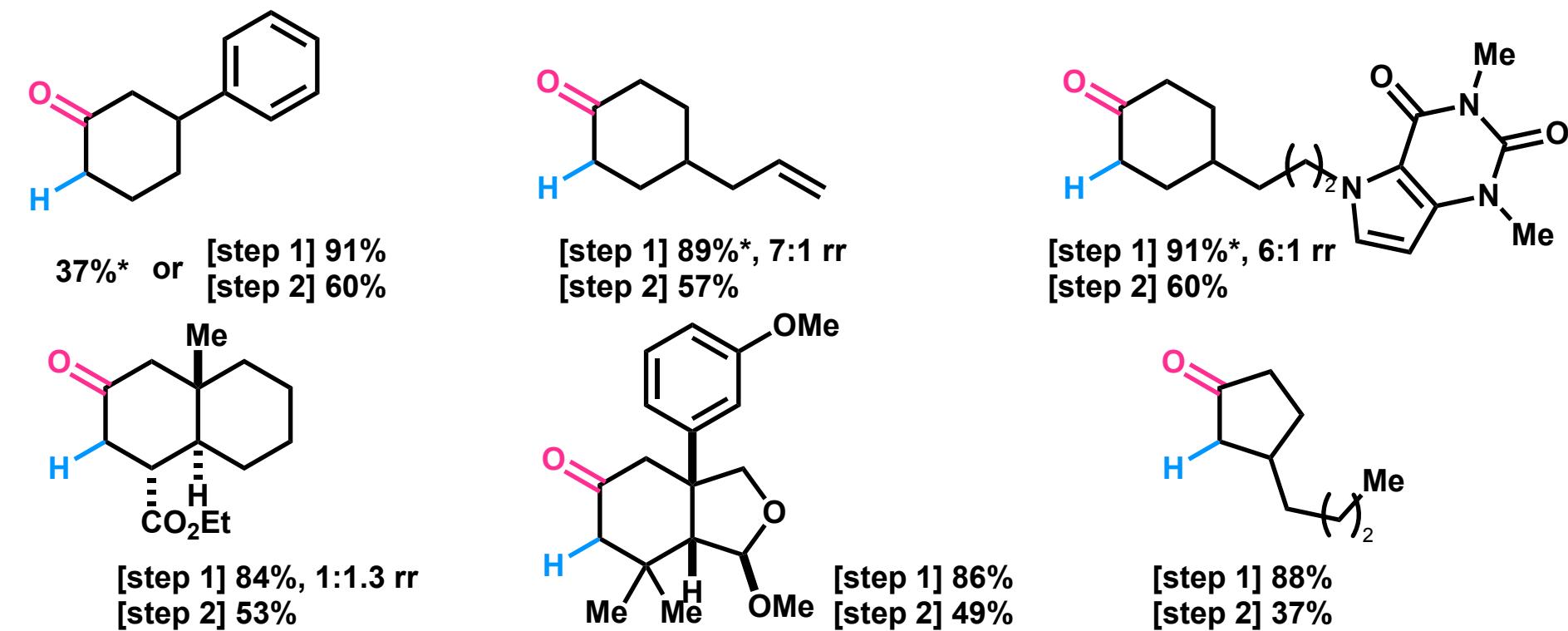
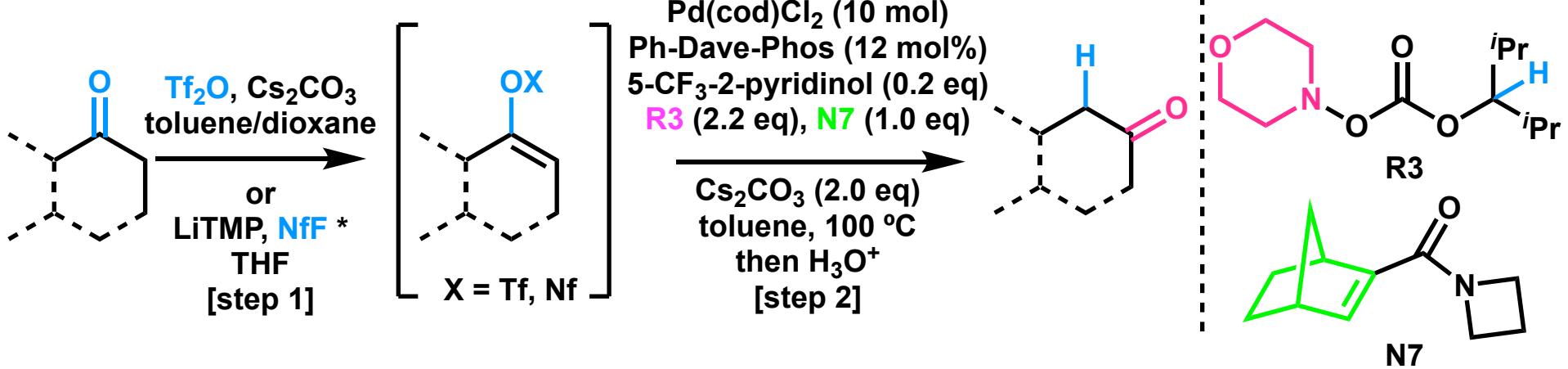
Reaction mechanism (My proposal)



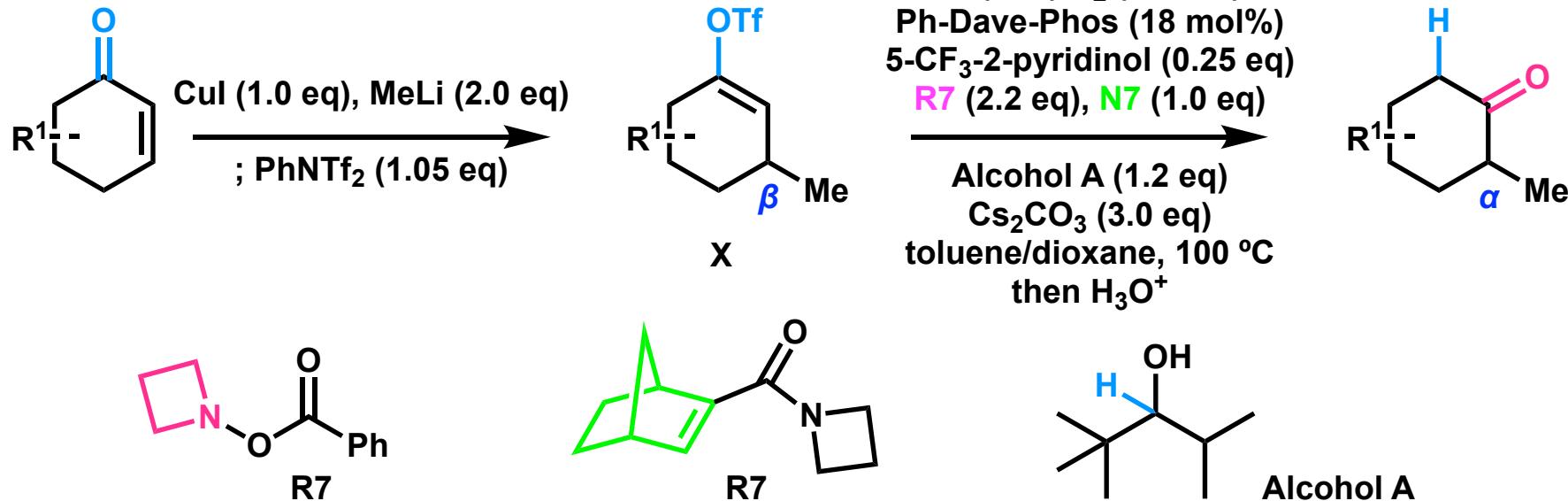
Substrate scope (Conjugate olefin)



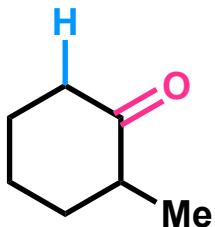
Substrate scope (Non-Conjugate olefin)



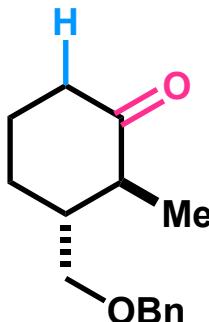
β to α migration protocol



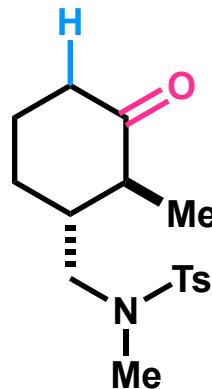
*The yield was calculated from vinyl triflate (X)



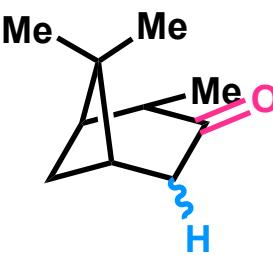
30%*



38%*

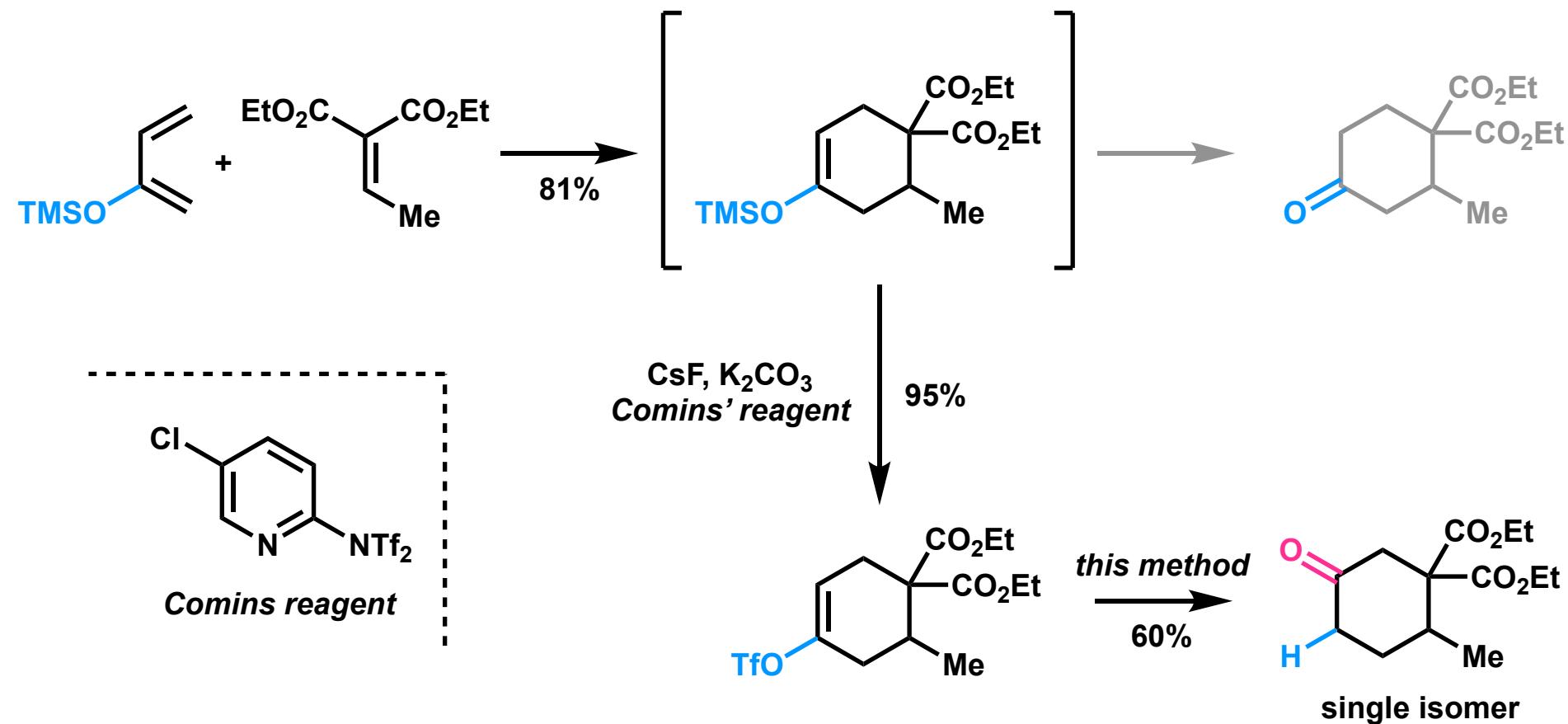


39%*

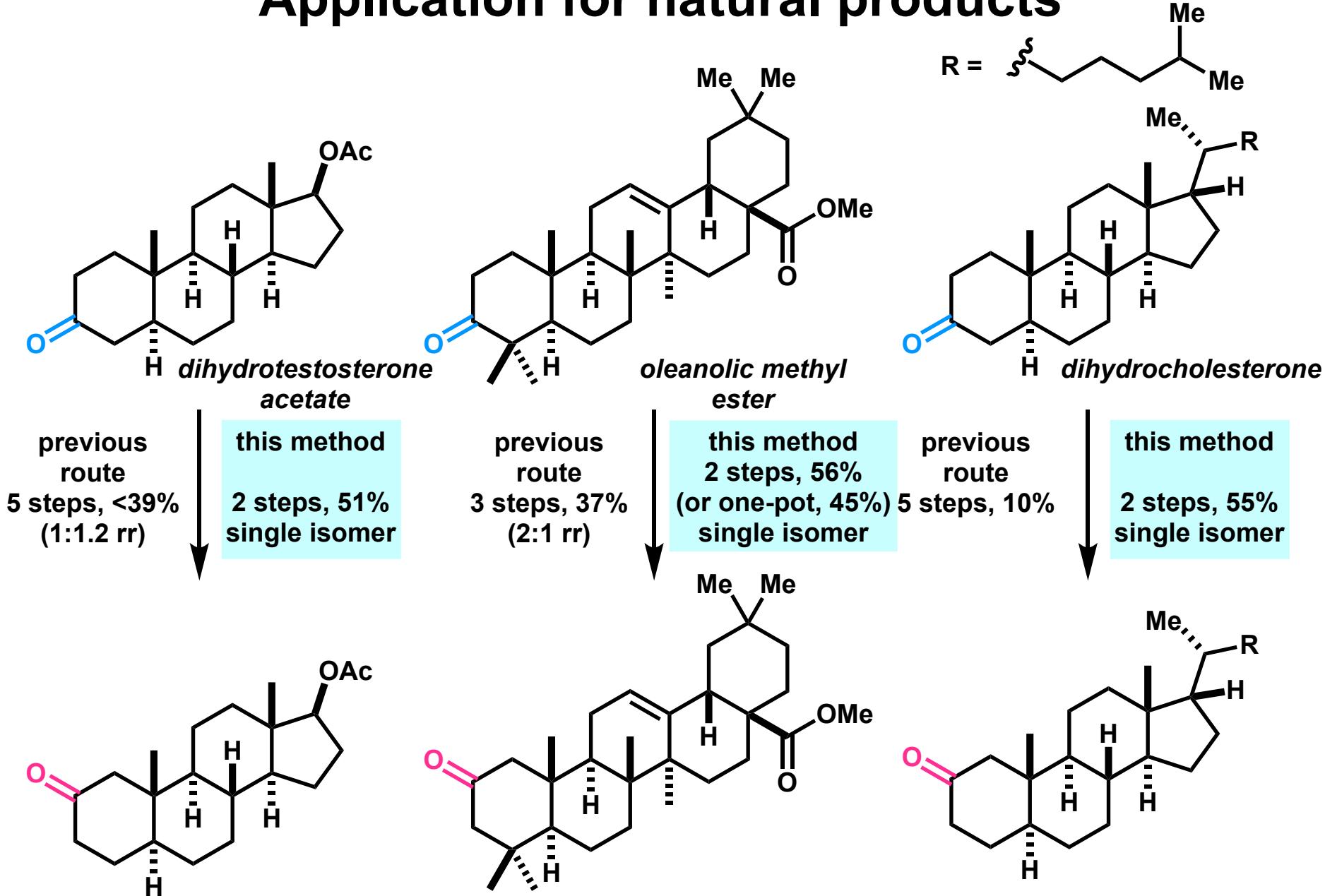


35%*

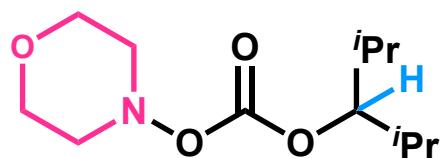
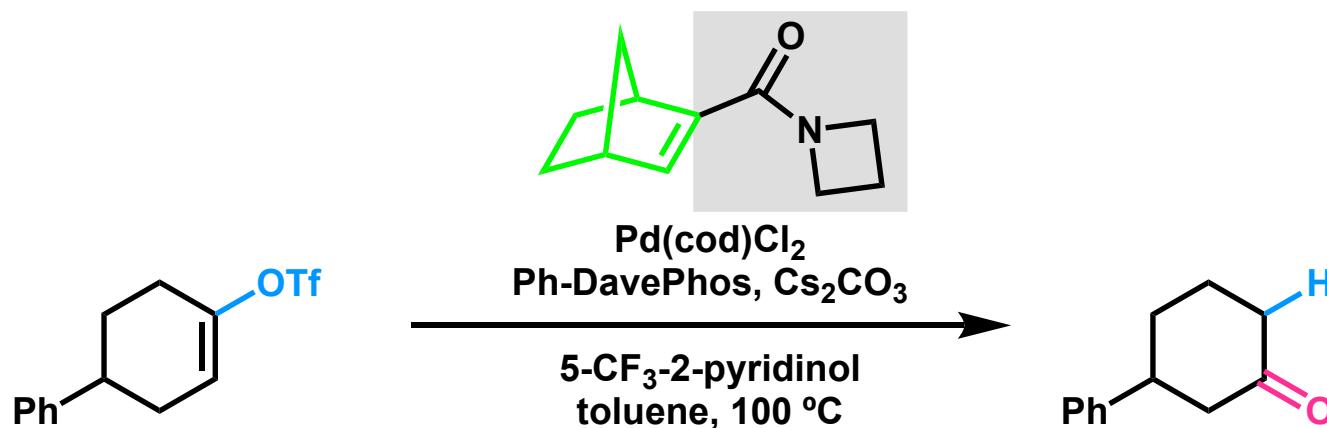
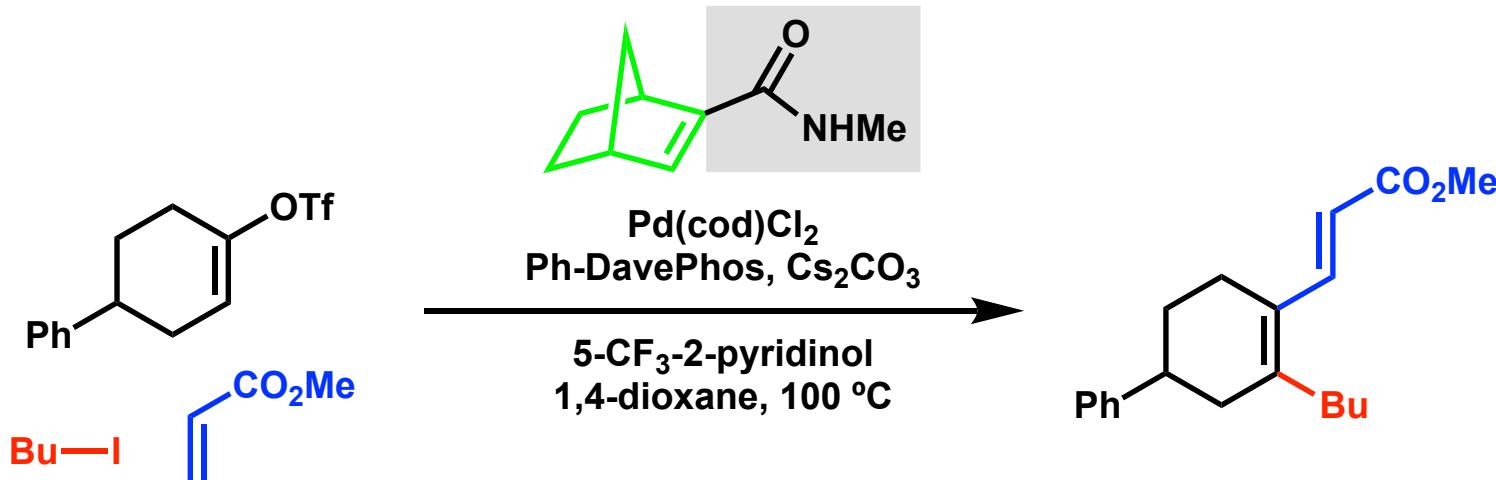
Inverse regioselectivity



Application for natural products

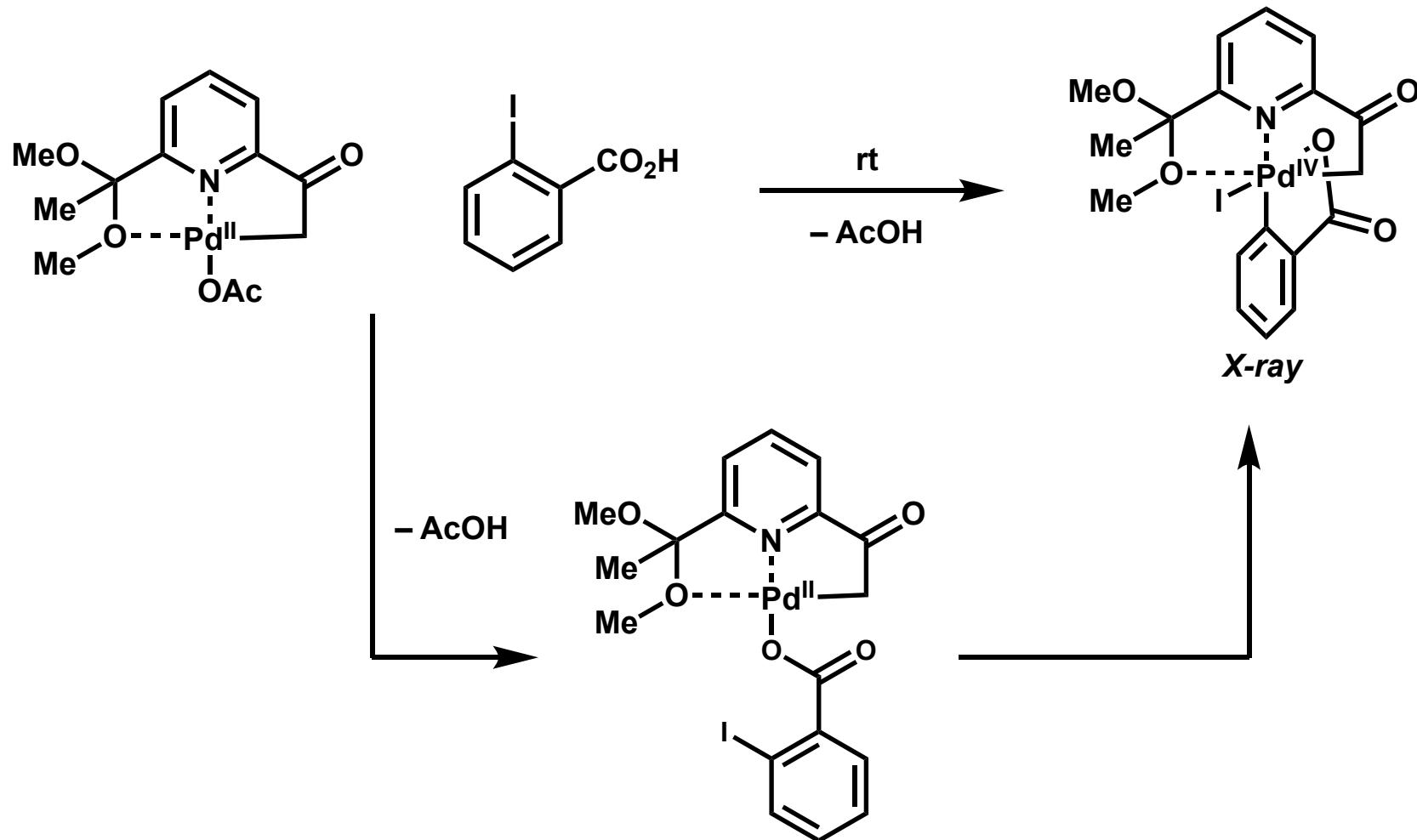


Summary

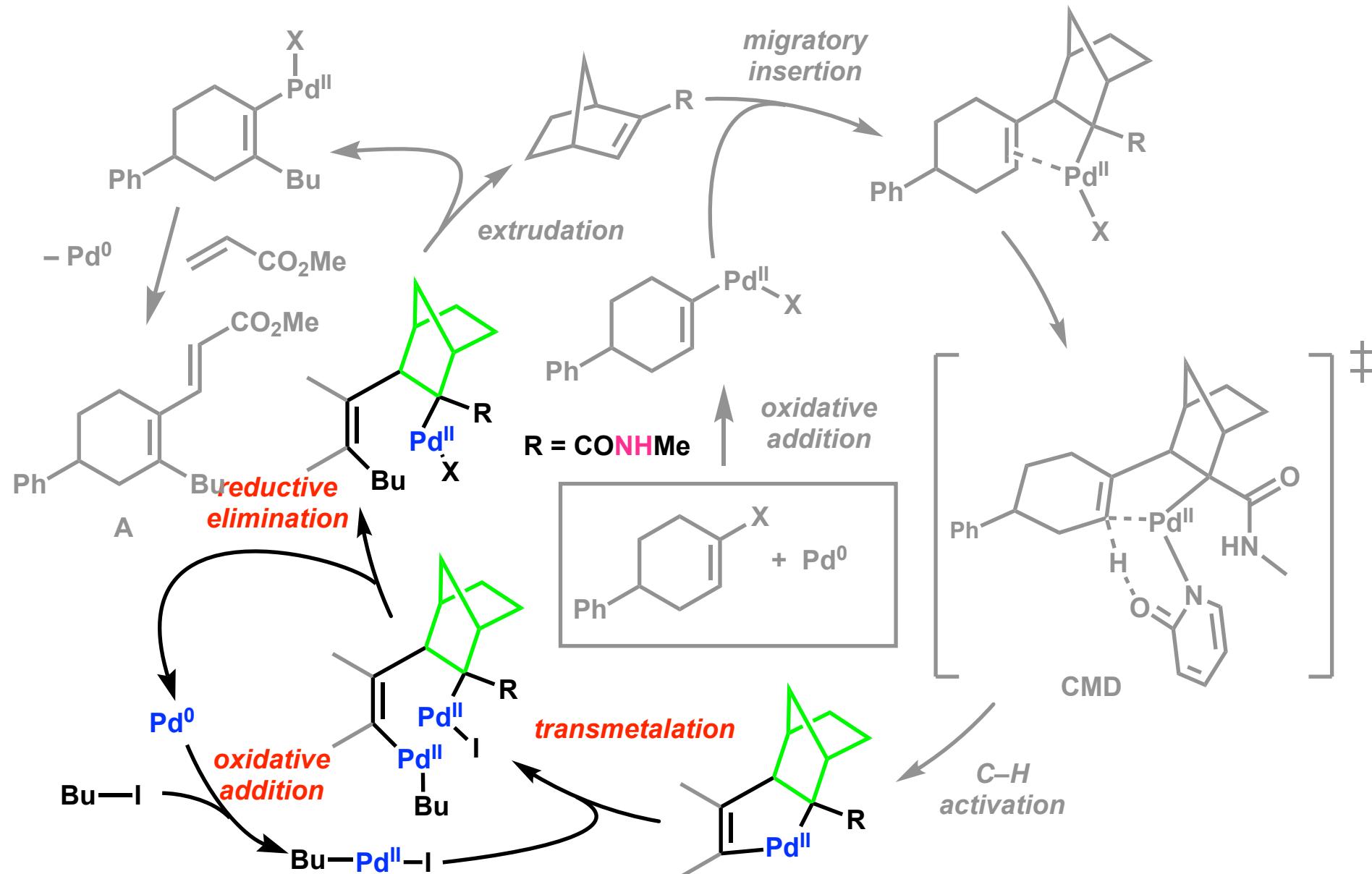


- 1) Wang, J.; Dong, Z.; Yang, C.; Dong, G. *Nat. Chem.* **2019**, *11*, 1106.
2) Wu, Z.; Xu, X.; Wang, J.; Dong, Z.; Dong, G. *Science*. **2021**, *374*, 734.

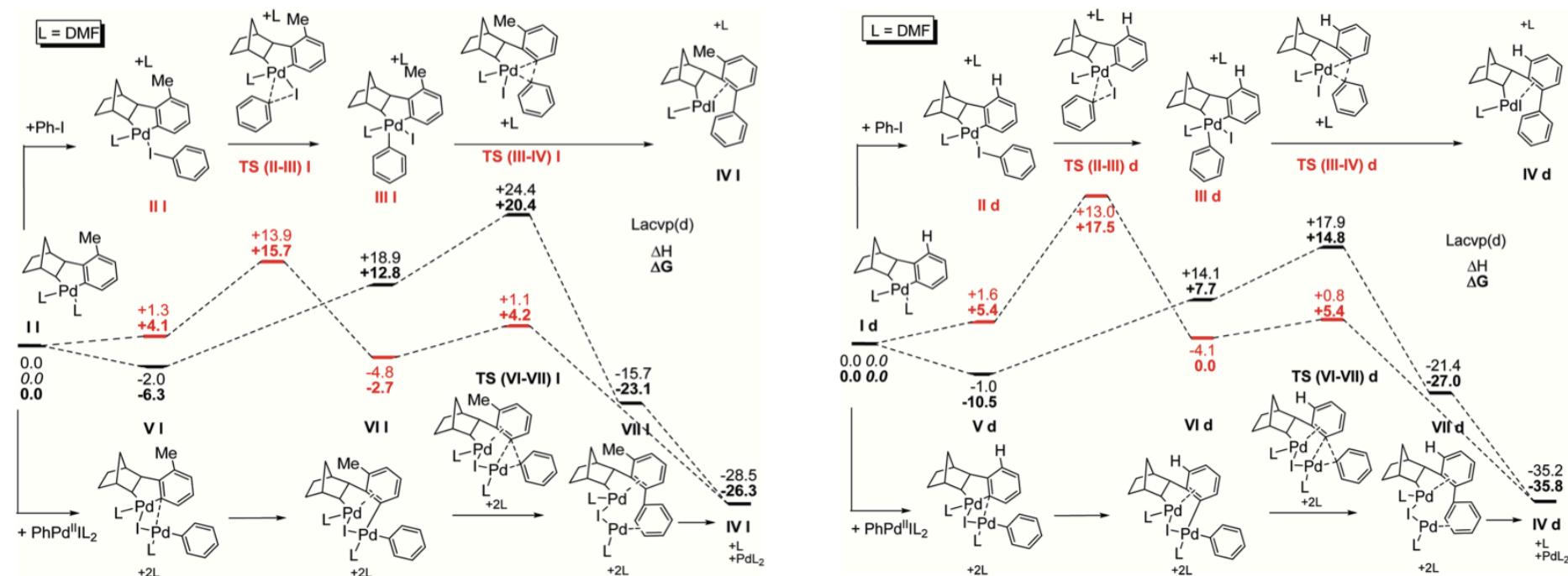
Appendix / Pd (IV) complex



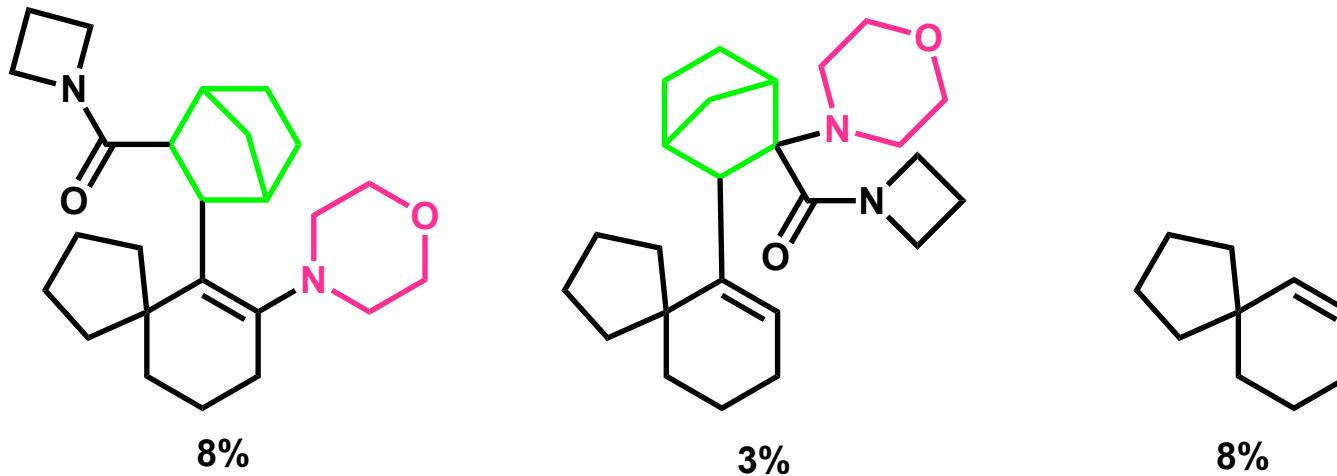
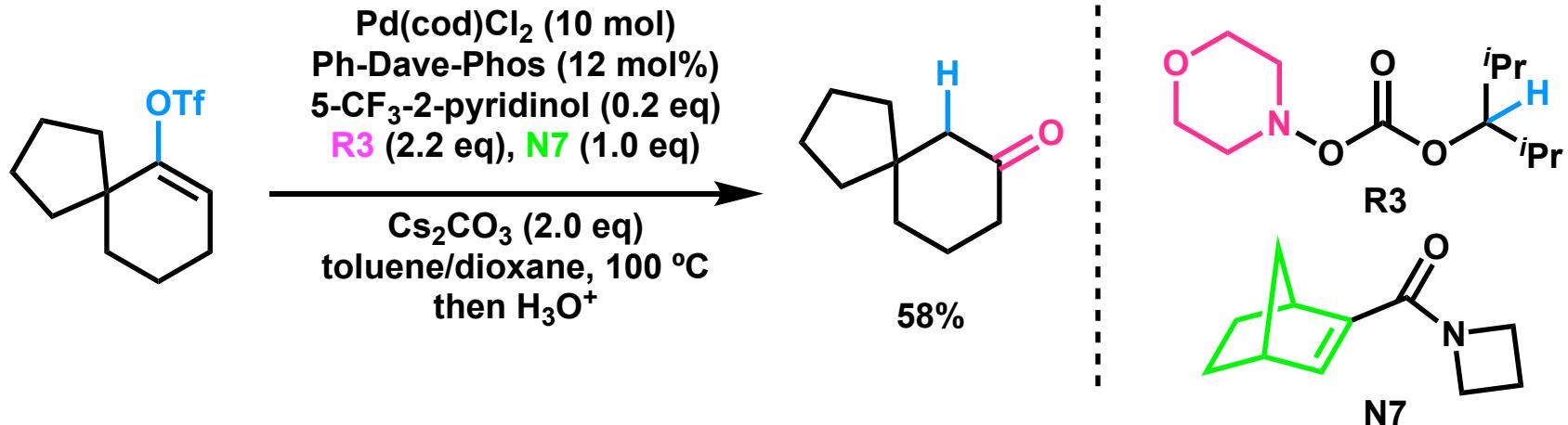
Reaction mechanism (transmetalation pathway)



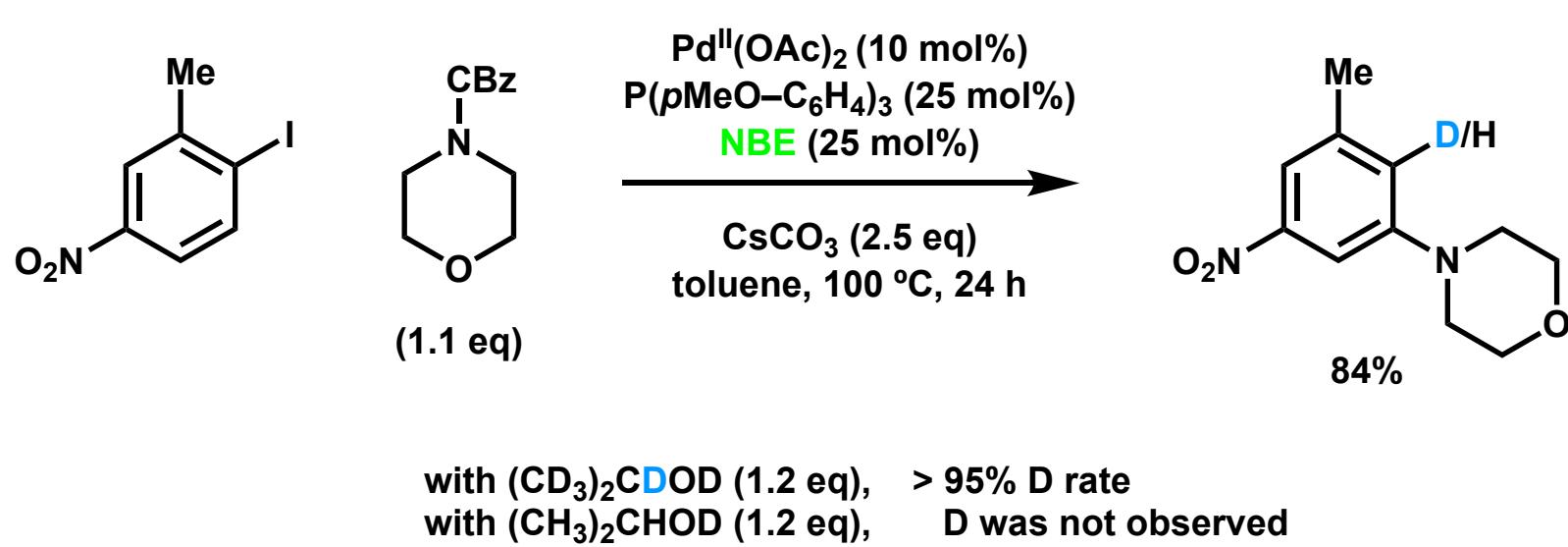
Reaction mechanism study



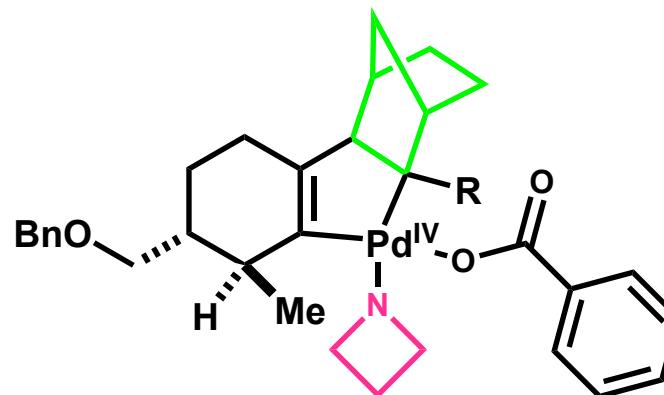
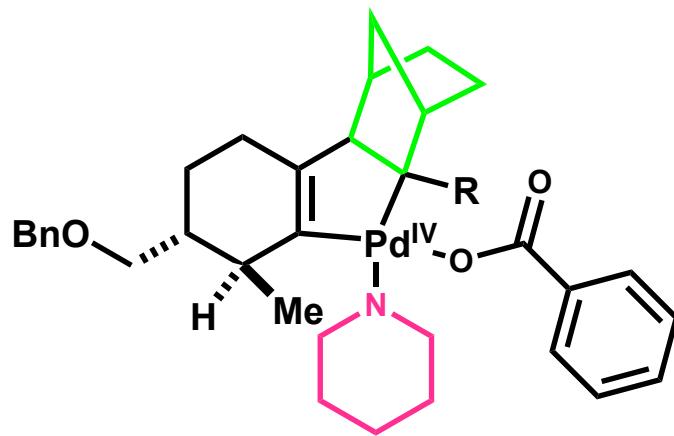
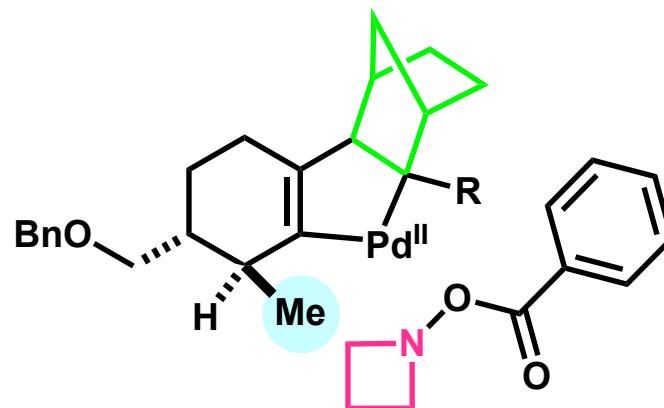
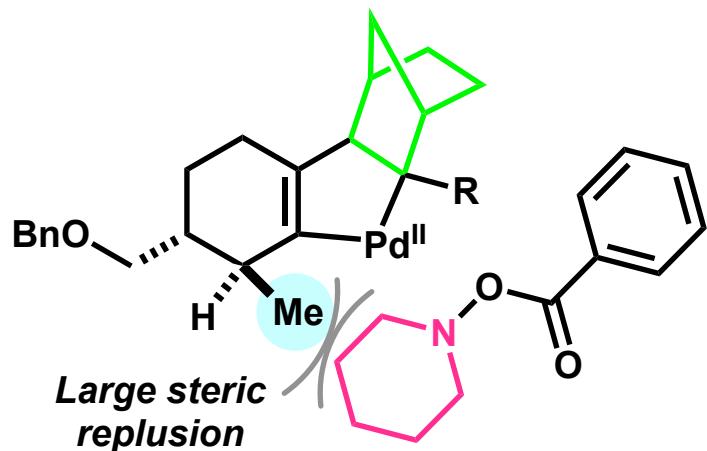
Side products



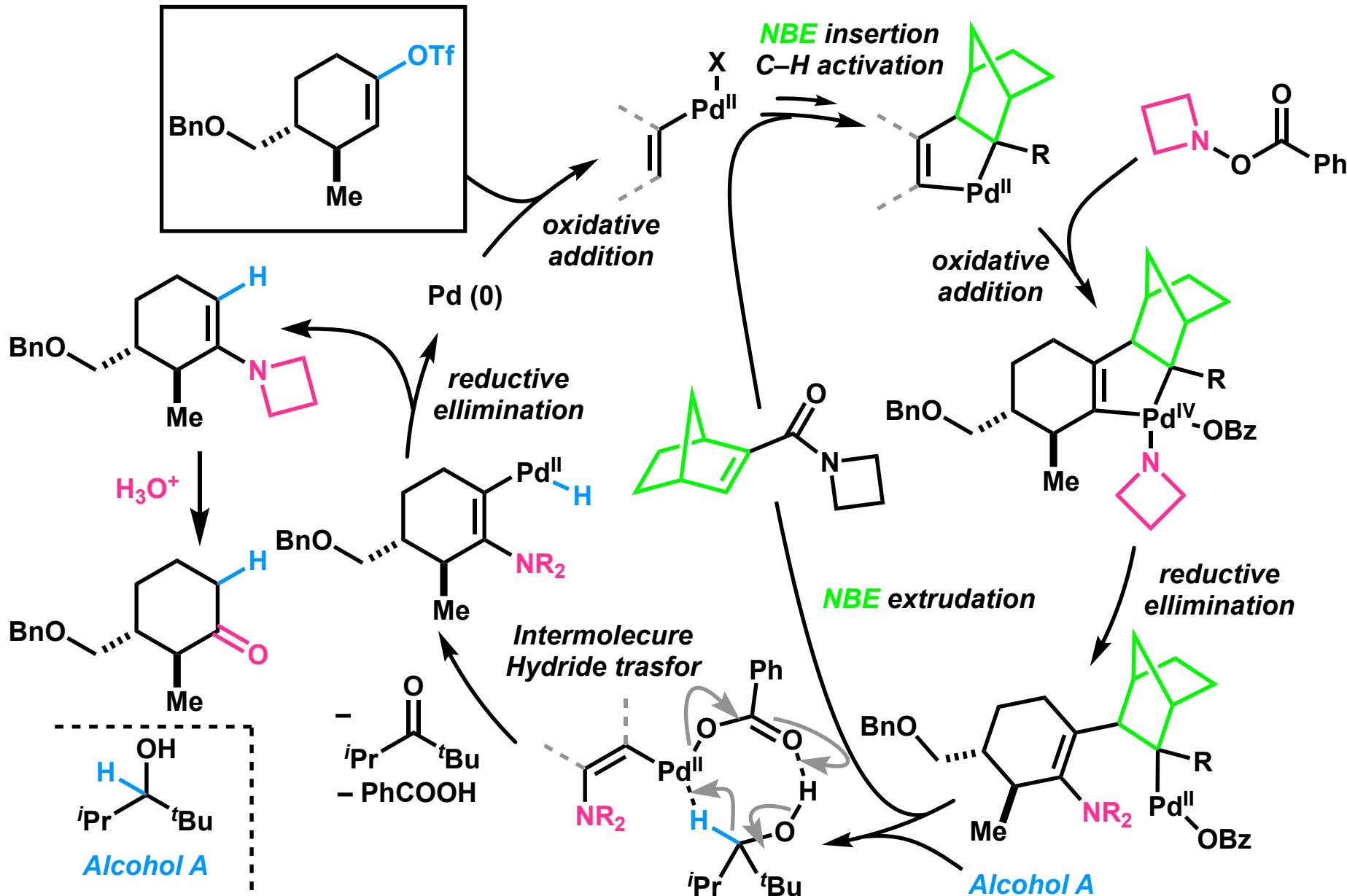
Deuterium-labeling study of hydrogen source



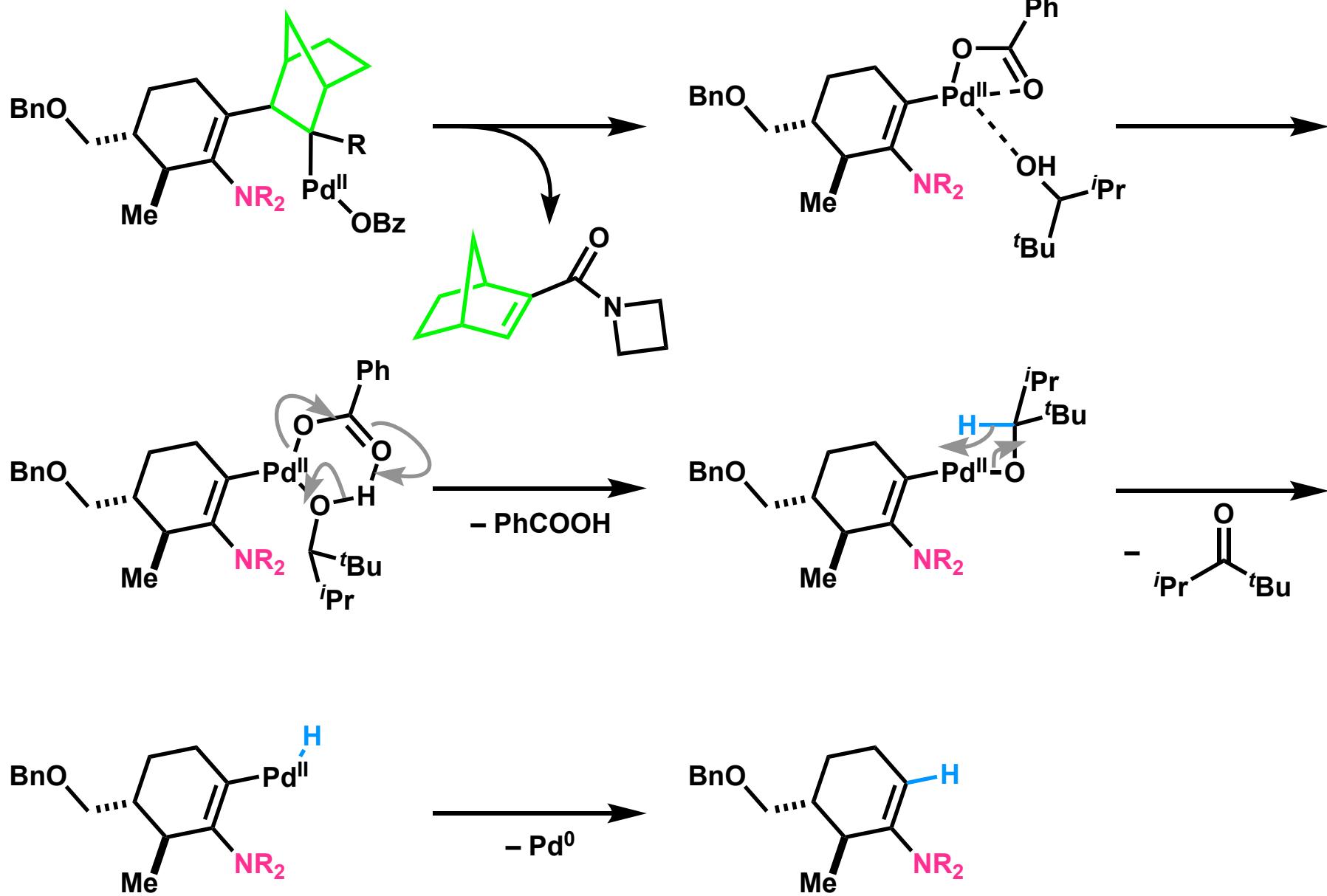
Steric effect at allylic position



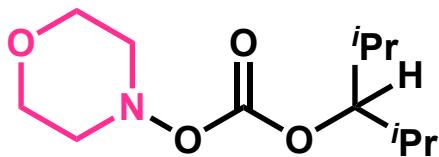
Proposed reaction mechanism (β to α migration)



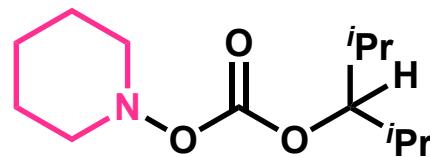
Stepwise path (hydride shift)



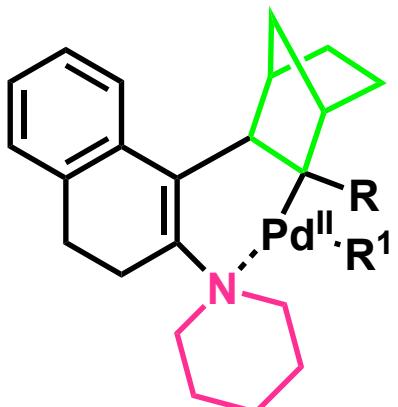
Difference between R3 and R5



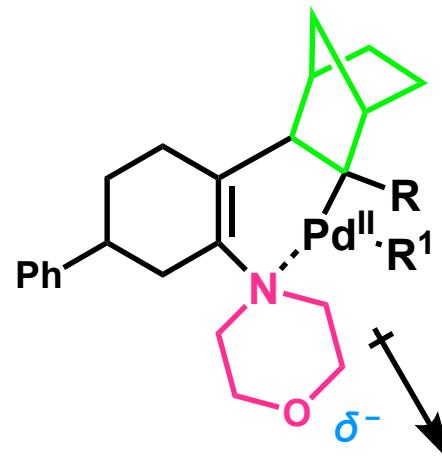
R3
78%



R5
88%



conjugate



non-conjugate

electron donacyc of olefin : conjugate olefin < non-conjugate olefin

electron donacyc of amine : piperidine > morpholine

Total synthesis of Cascarilone

