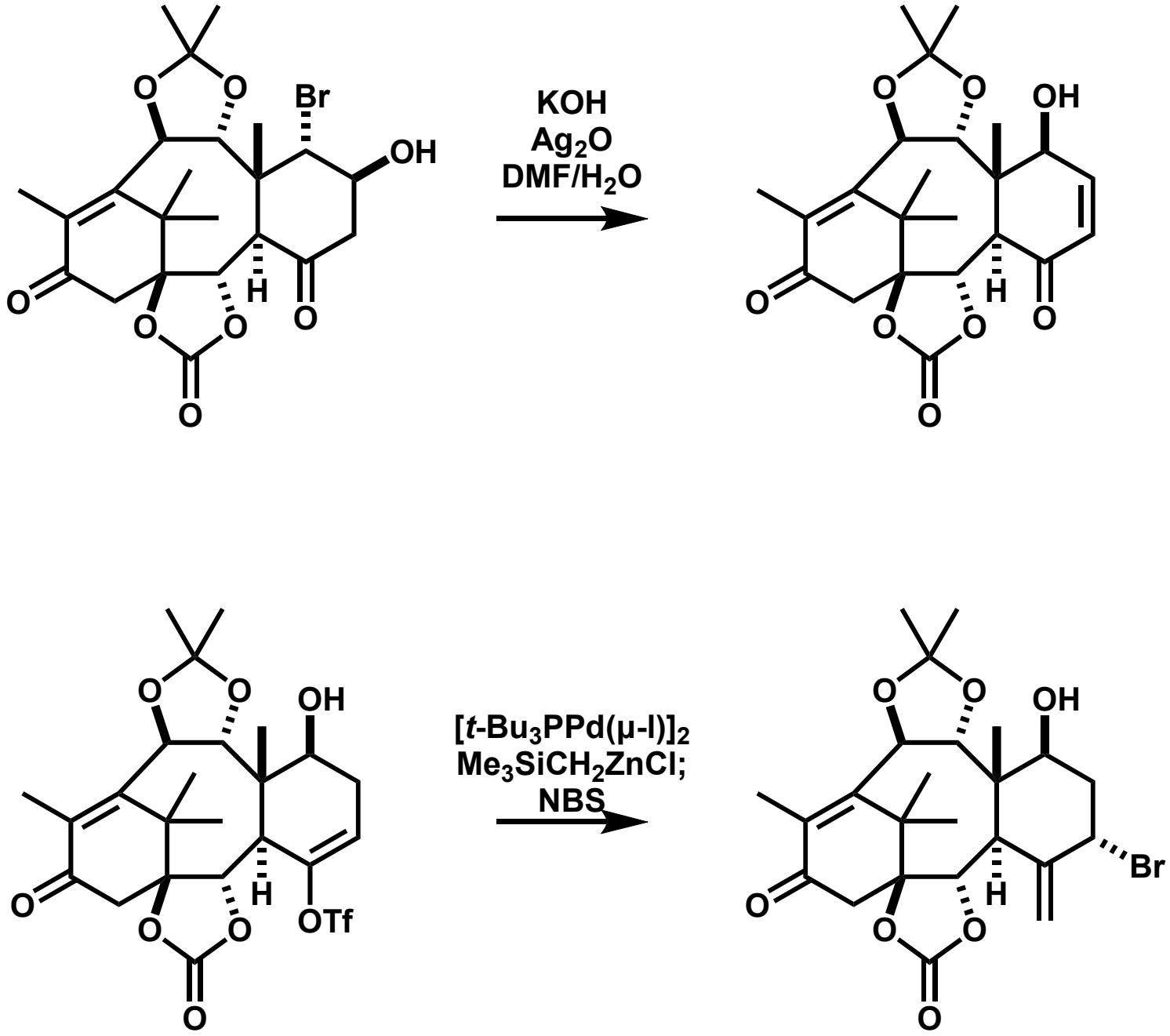
Rhodium Catalyzed Amide Homologation

2024.05.18. Literature Seminar
D3 Yuma Komori

Contents

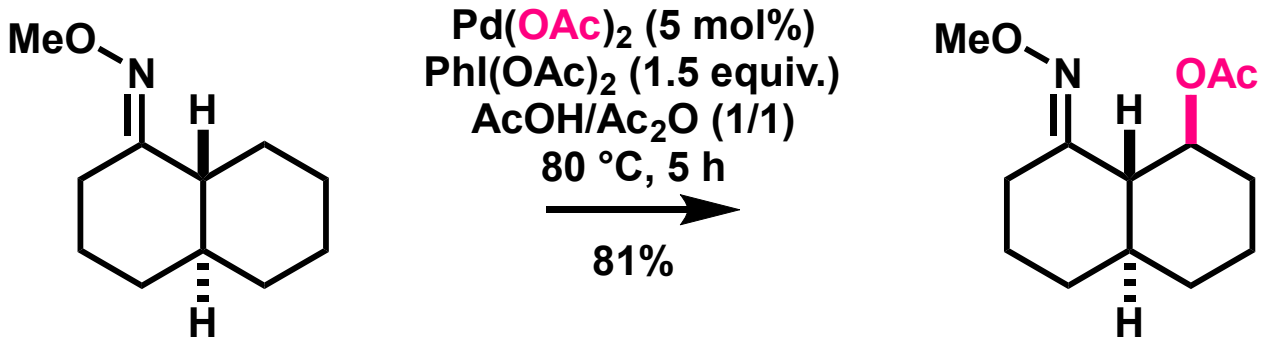
Bond Formation in Organic Chemistry



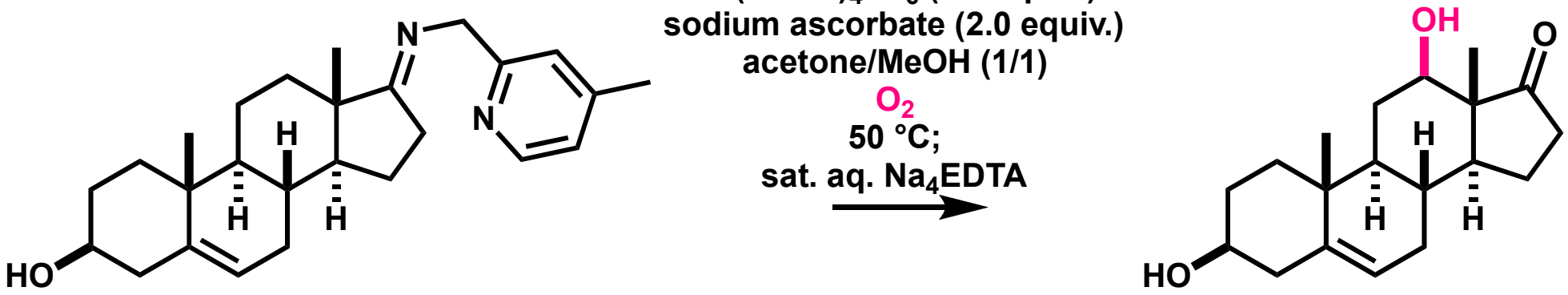
Imamura, Y.; Takaoka, K.; Komori, Y.; Nagatomo, M.; Inoue, M. *Angew. Chem. Int. Ed.* **2023**, *62*, e202219114.

C–H Bond Activation

C–H oxidation with palladium[1)]



C–H oxidation with copper[2)]



1) Desai, L. V.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 9542.
2) See, Y. Y.; Herrmann, A. T.; Aihara, Y.; Baran, P. S. *J. Am. Chem. Soc.* **2015**, *137*, 13776.

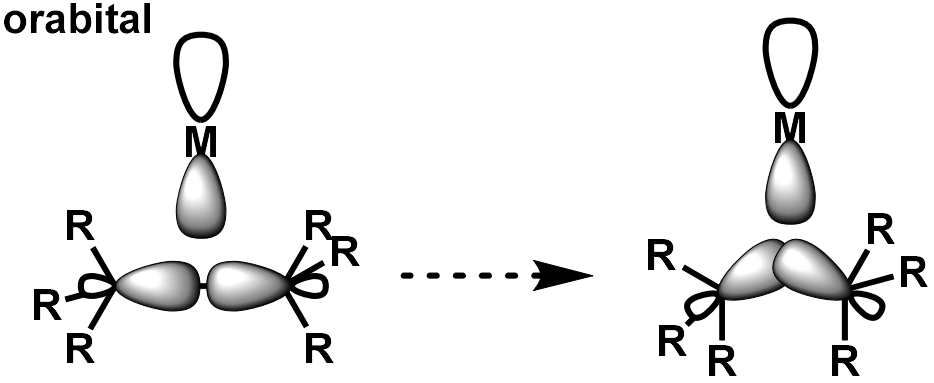
Difficulties in C–C Bond Activation

1. Stability of C–C bond (~90 kcal/mol)

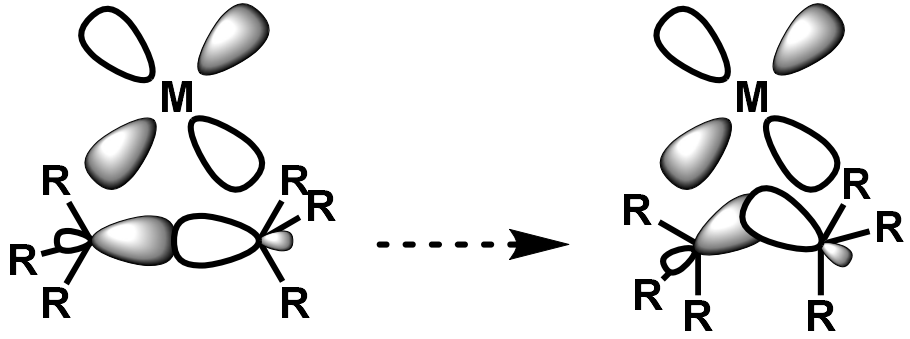
2. Steric hindrance

3. Poor orbital overlap

C–C bonding orabital

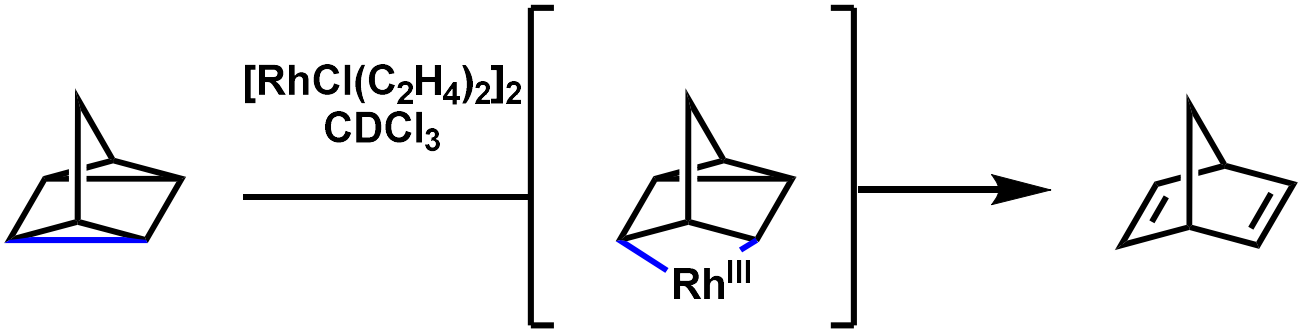


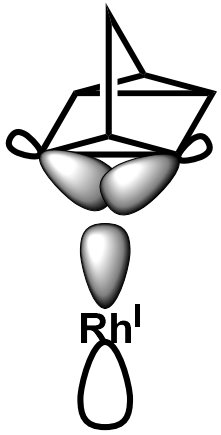
C–C anti-bonding orabital



1) Souillart, L.; Cramer, N. *Chem. Rev.* **2015**, *115*, 9410.
2) Murakami, M.; Ishida, N. *J. Am. Chem. Soc.* **2016**, *138*, 13759.

Strained C–C Bond Activation



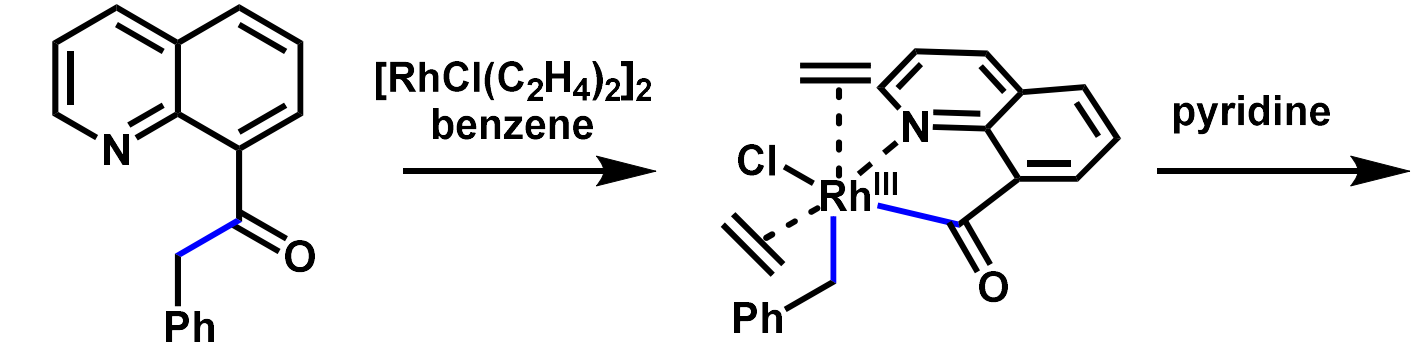


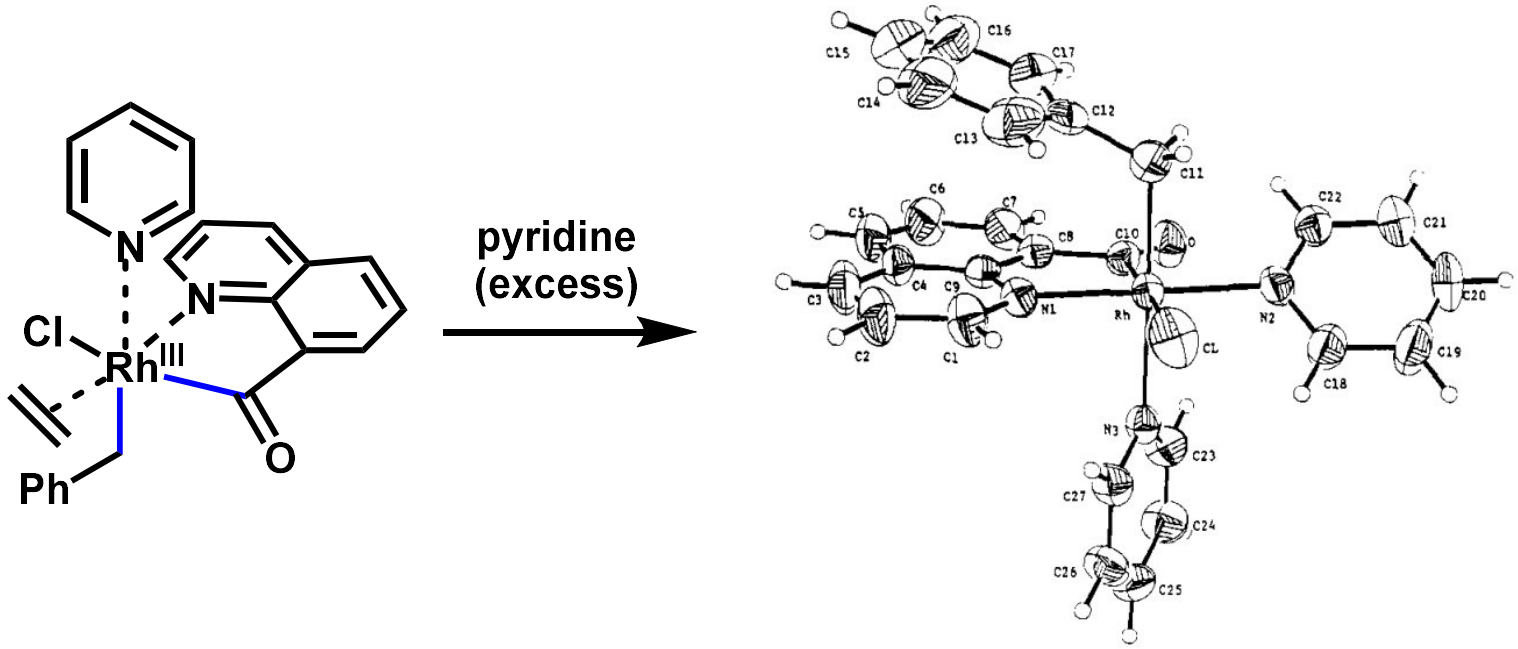
cyclopropane has bent bond "banana bond"

Hogeveen, H.; Volger, H. C. *J. Am. Chem. Soc.* **1967**, *89*, 2486.

Contents

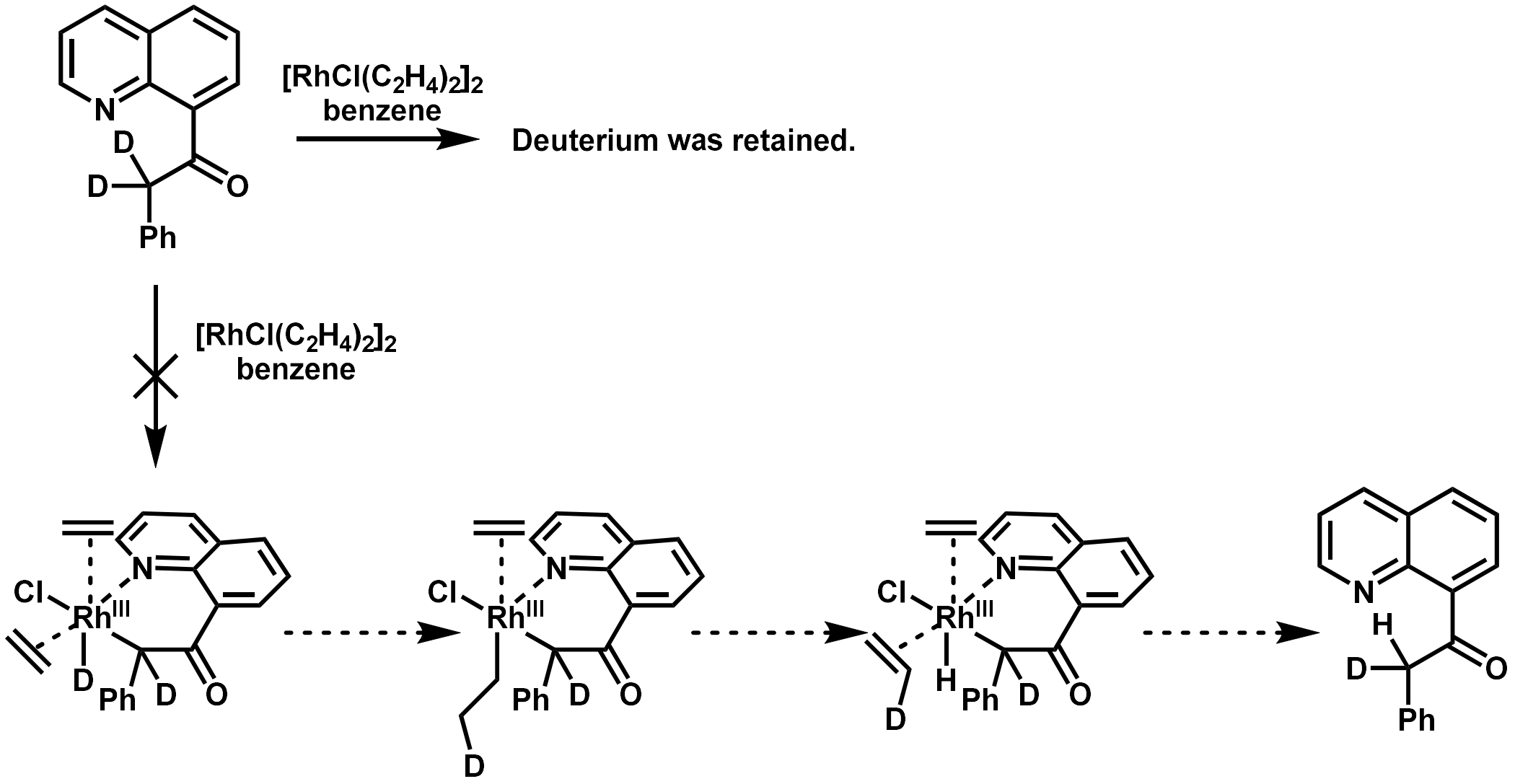
C–C Bond Activation of Unstrained Ketone Using Quinoline





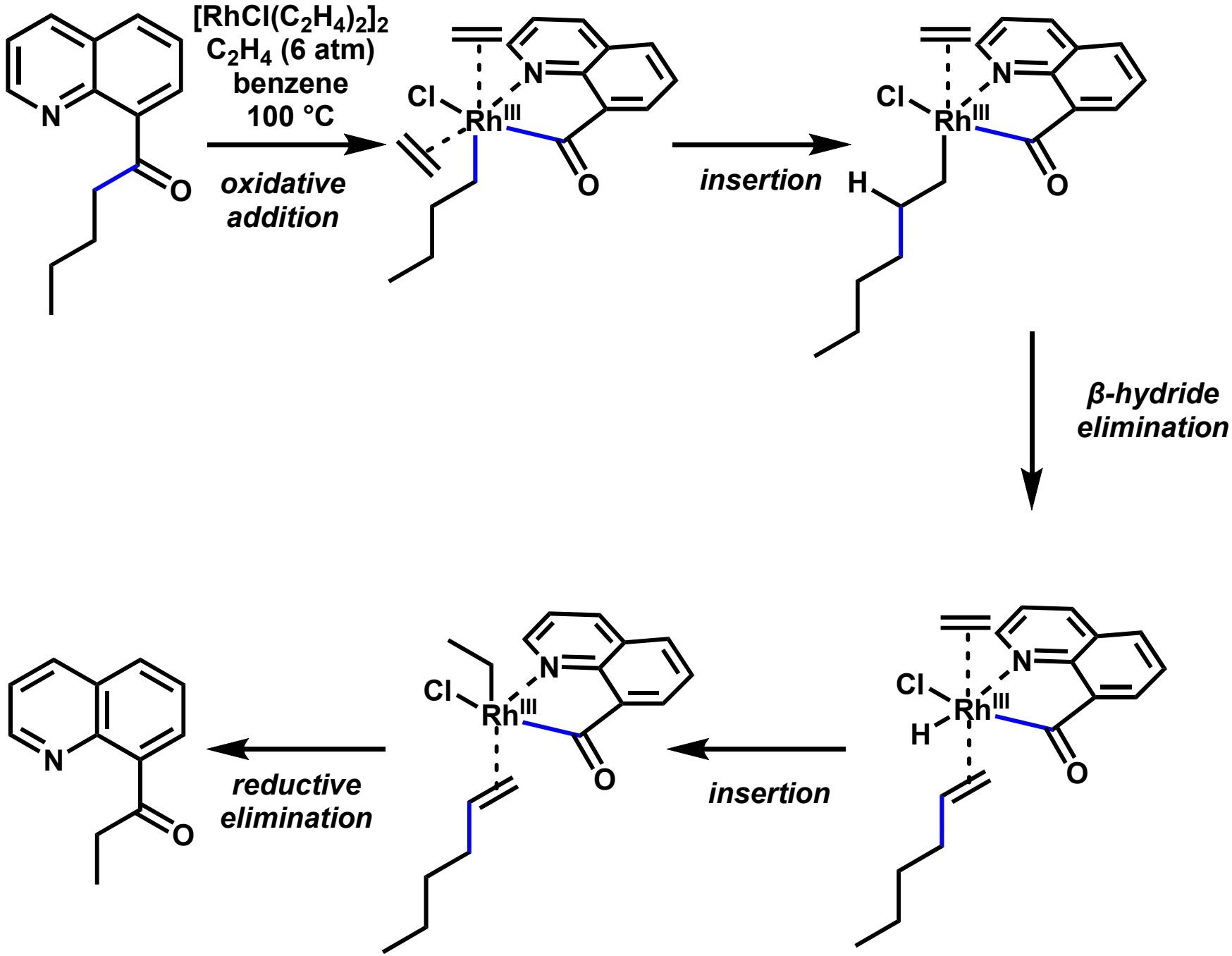
Suggs, J. W.; Jun, C.-H. *J. Am. Chem. Soc.* **1984**, *106*, 3054.

Deuterium Labeling Experiment



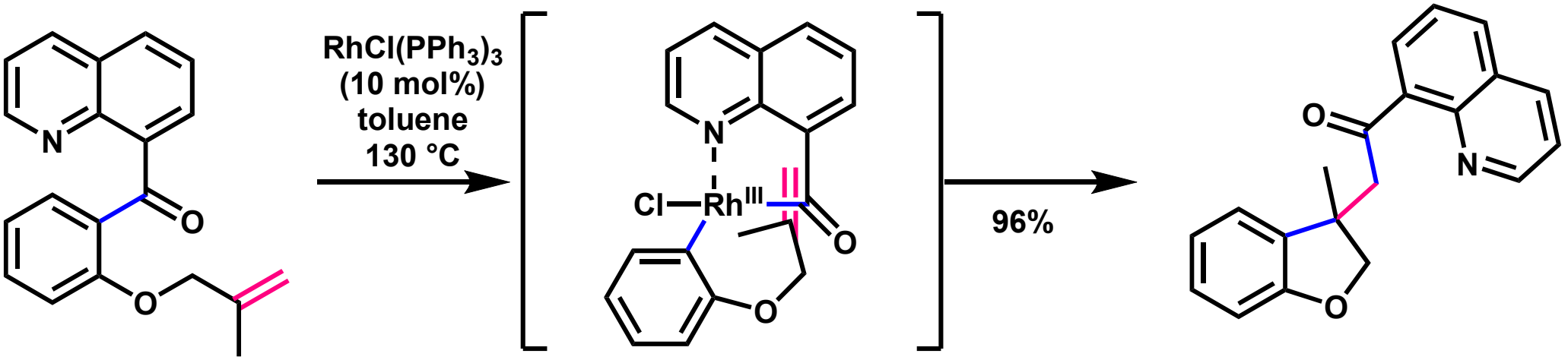
Suggs, J. W.; Jun, C.-H. *J. Am. Chem. Soc.* **1984**, *106*, 3054.

Reductive Elimination from Metalacycle

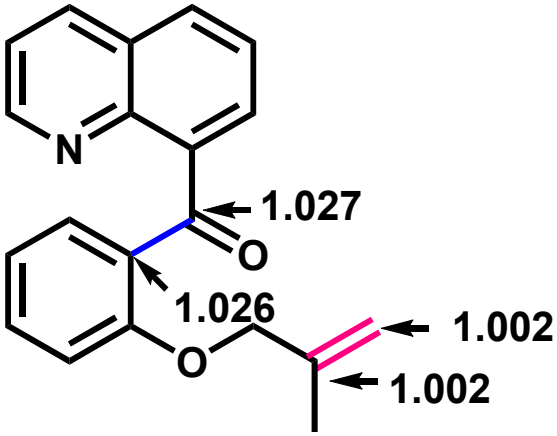


Suggs, J. W.; Jun, C.-H. *J. Chem. Soc., Chem. Commun.* **1985**, 92.

Intramolecular Carbo-Acylation

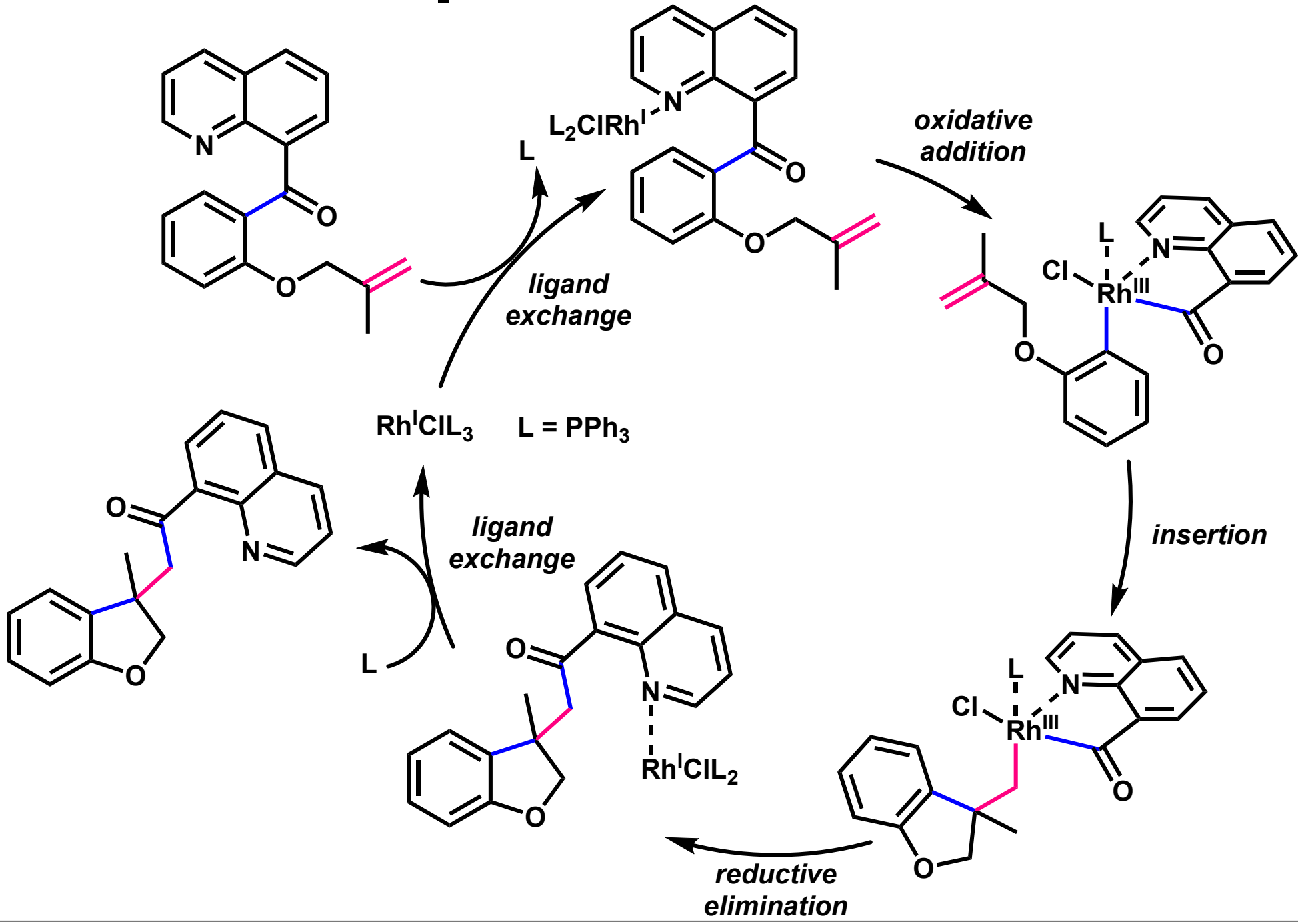


$^{12}C/^{13}C$ kinetic isotope effect[2)]



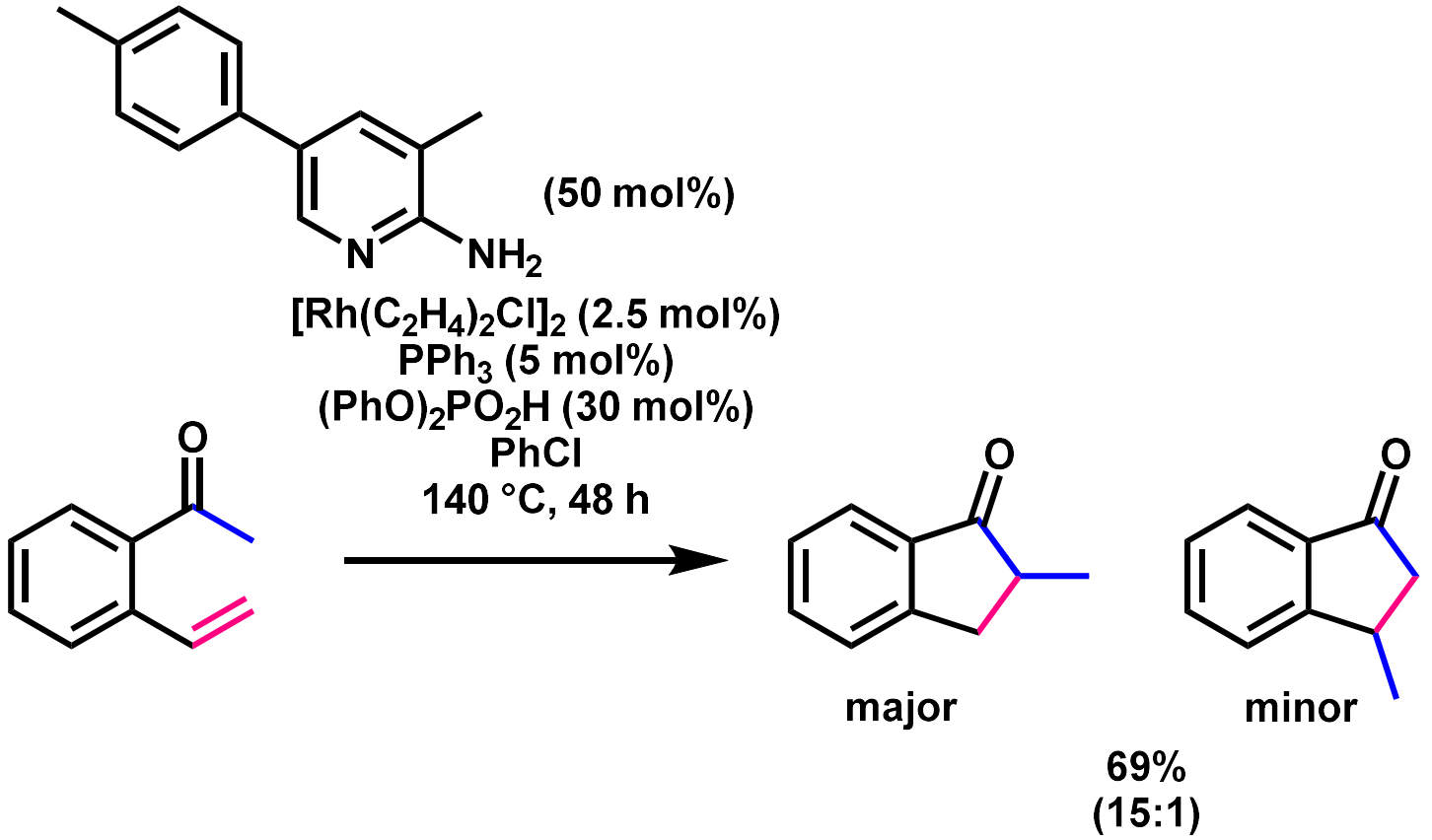
1) Dreis, A. M.; Douglas, C. J. *J. Am. Chem. Soc.* **2009**, *131*, 412.
2) Lutz, J. P.; Rathbun, C. M.; Stevenson, S. M.; Powell, B. M.; Boman, T. S.; Baxter, C. E.; Zona, J. M.; Johnson, J. B. *J. Am. Chem. Soc.* **2012**, *134*, 715.

Proposed Mechanism



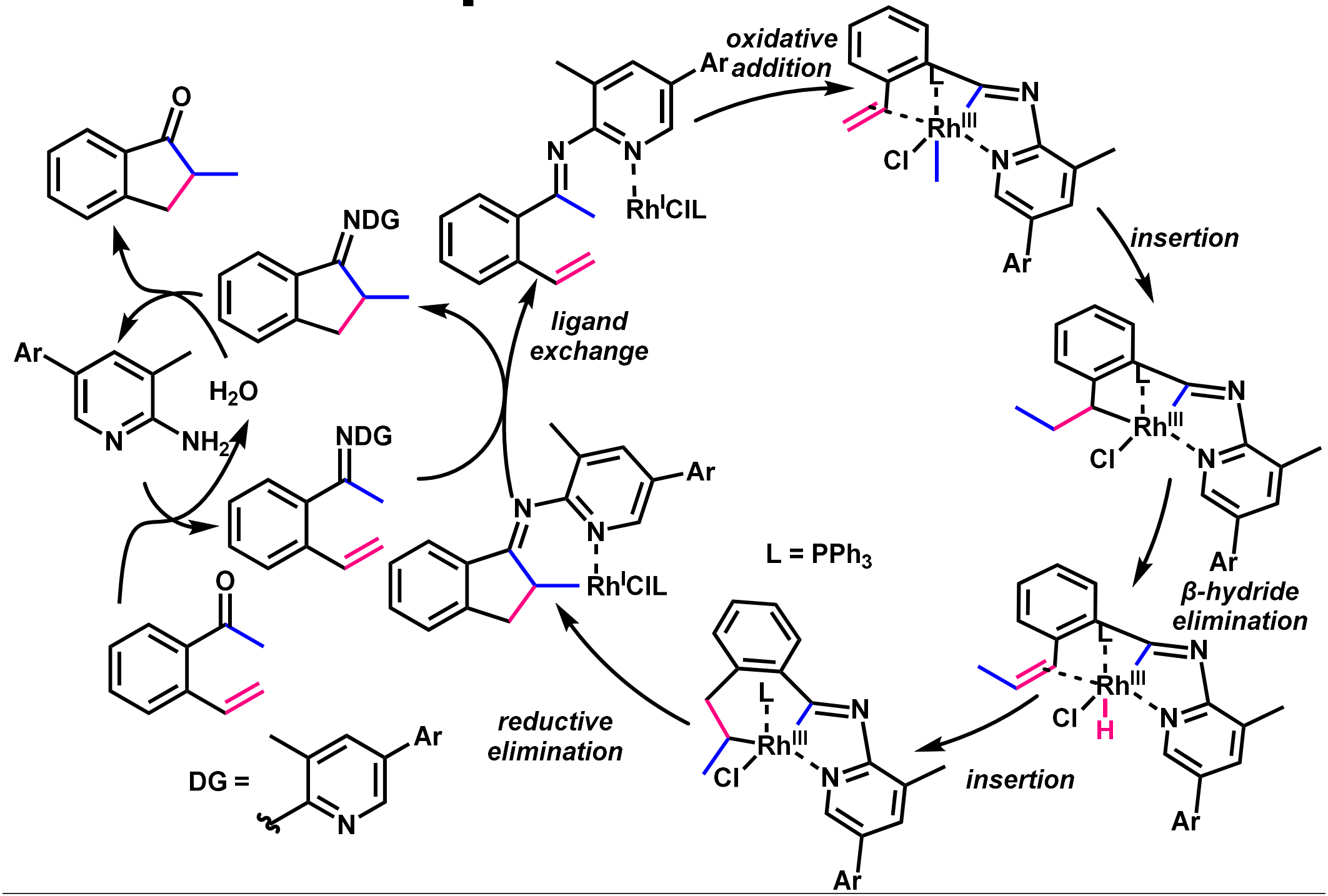
Lutz, J. P.; Rathbun, C. M.; Stevenson, S. M.; Powell, B. M.; Boman, T. S.; Baxter, C. E.; Zona, J. M.; Johnson, J. B. *J. Am. Chem. Soc.* **2012**, *134*, 715.

Intramolecular One-Carbon Homologation of Ketone



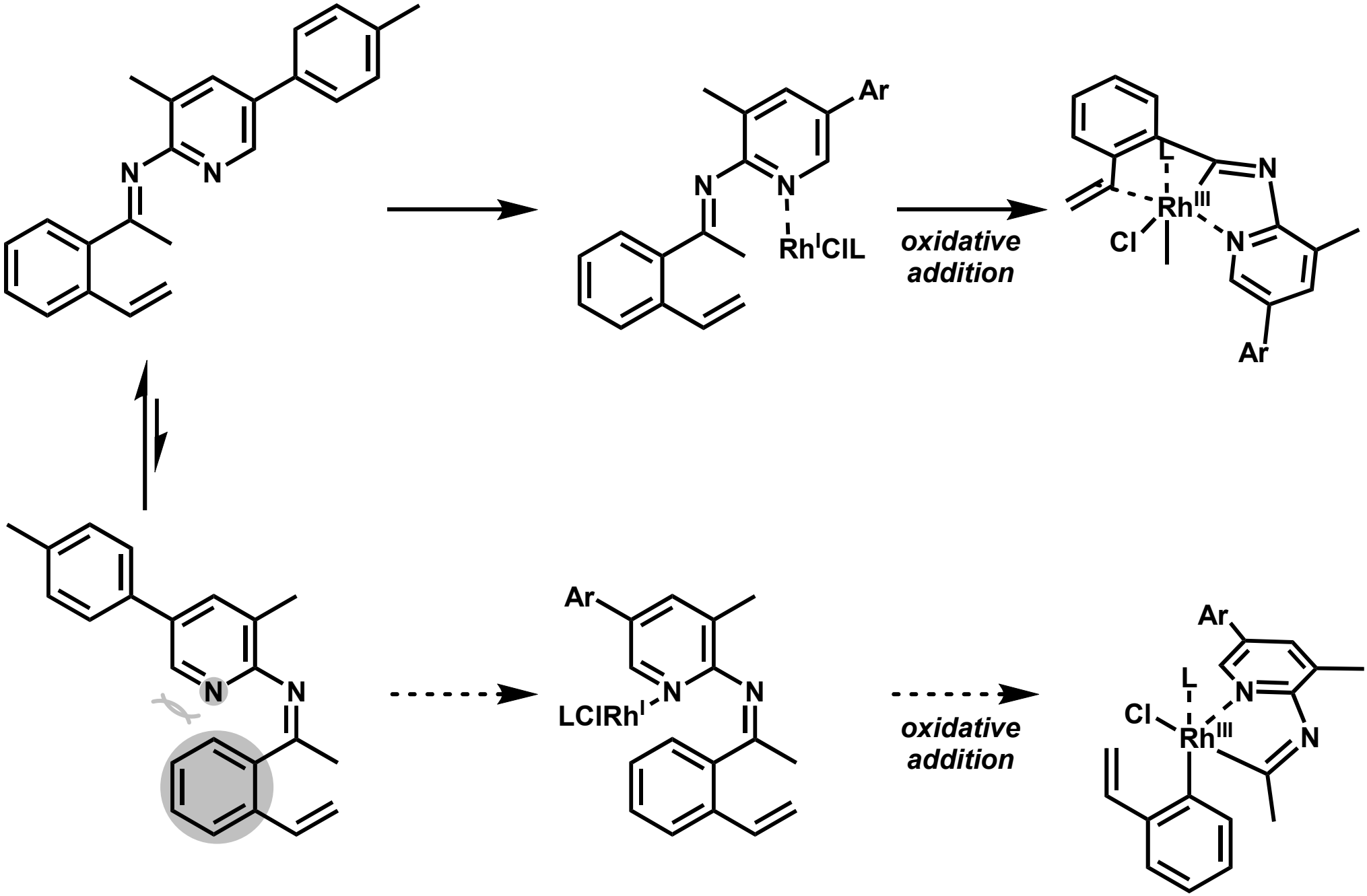
Huang, J.; Zhang, R.; Wu, X.; Dong, G.; Xia, Y. *Org. Lett.* **2022**, *24*, 2436.

Proposed Mechanism

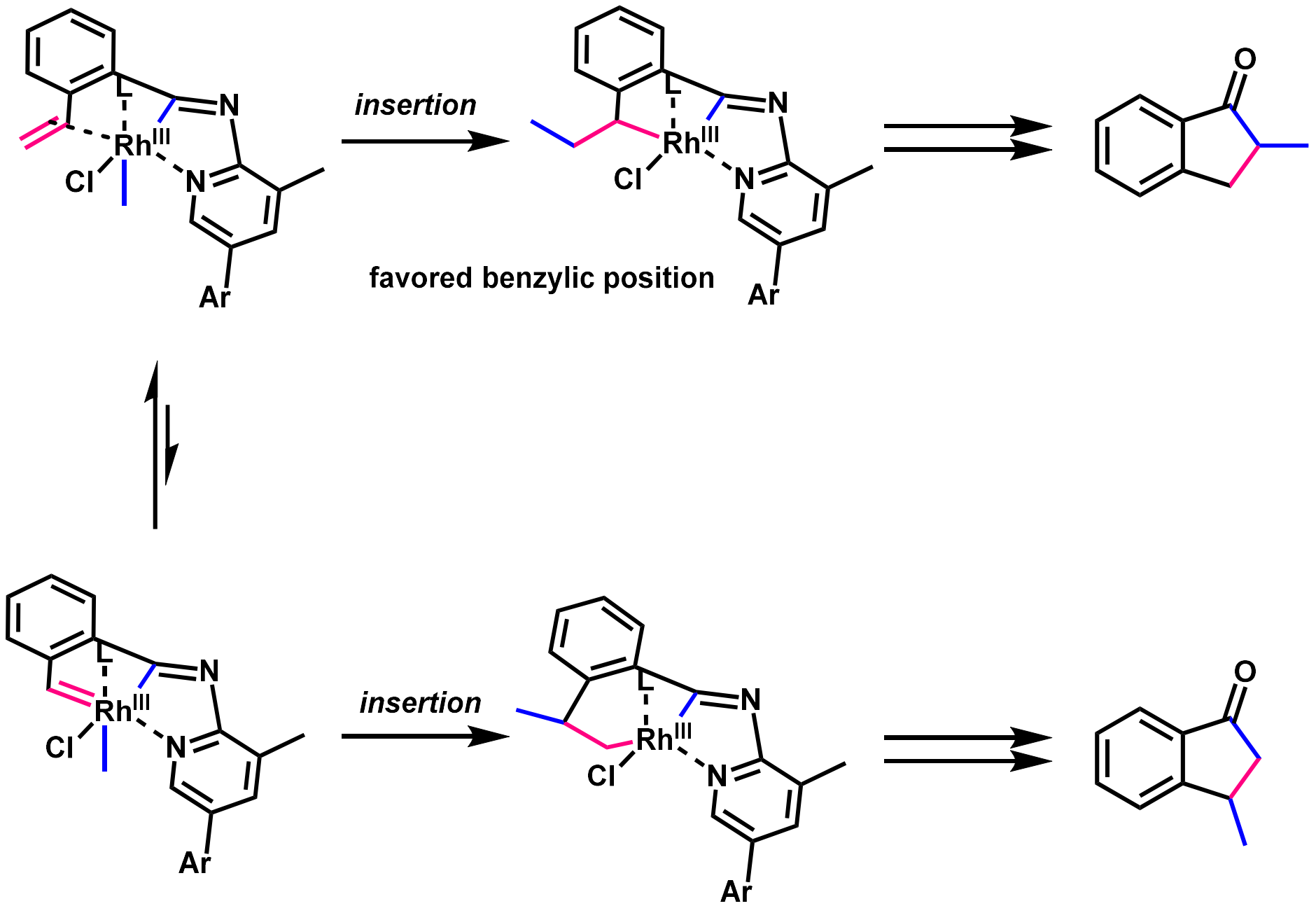


Huang, J.; Zhang, R.; Wu, X.; Dong, G.; Xia, Y. *Org. Lett.* **2022**, *24*, 2436.

Selectivity -C–C(Ar) vs C–C(Me)-



Regioselectivity



Huang, J.; Zhang, R.; Wu, X.; Dong, G.; Xia, Y. *Org. Lett.* **2022**, *24*, 2436.

Contents

1. Introduction

2. C–C Bond Activation of Ketone

3. Rhodium Catalyzed Amide Homologation
(Zhang, R.; Yu, T.; Dong, G. *Science* **2023**, *382*, 951.)

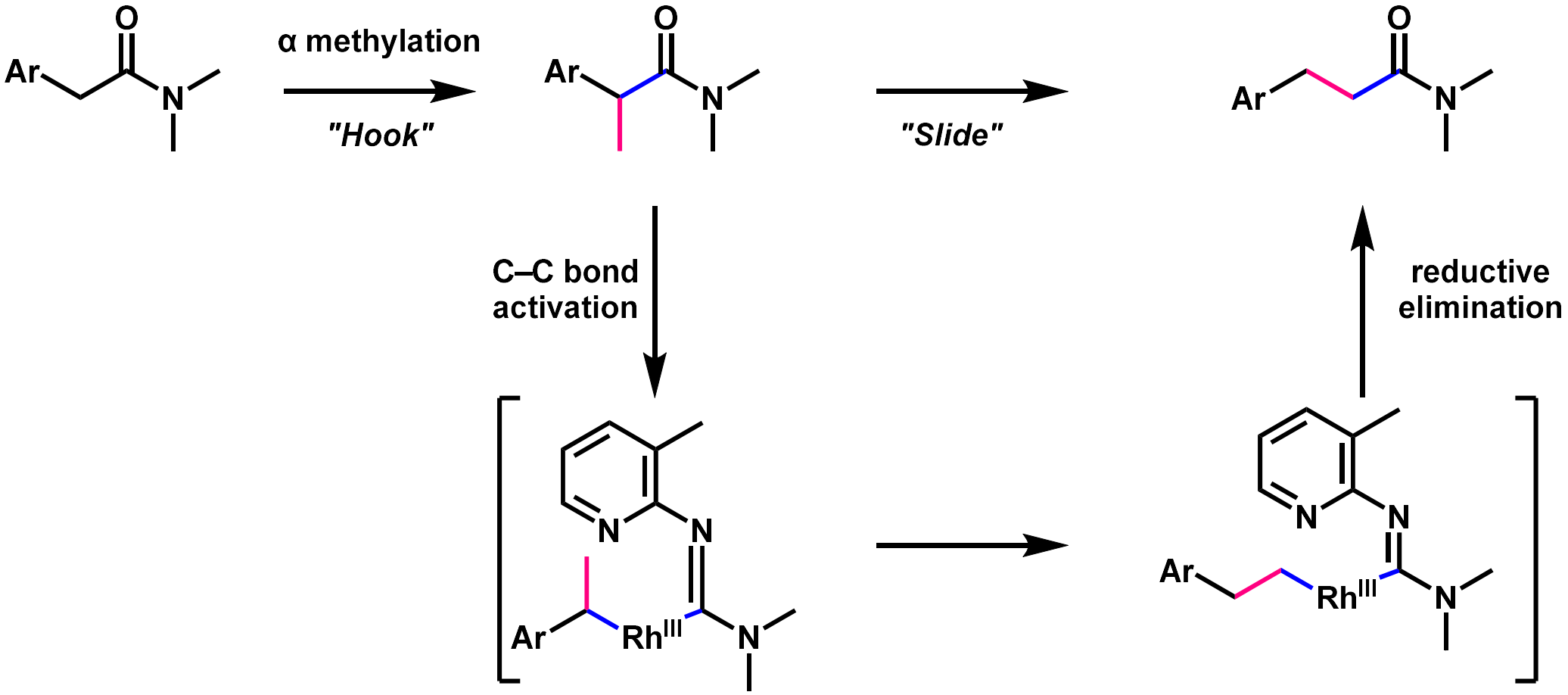
Prof. Guangbin Dong

1999-2003 B.S. @Peking University (Prof. Zhen Yang and Prof. Jiahua Chen)
2004-2009 Ph.D @Stanford University (Prof. Barry M. Trost)
2009-2011 Postdoc. @California Institute of Technology (Prof. Robert H. Grubbs)
2011-2016 Assistant Professor @University of Texas at Austin
2016 Professor @University of Texas at Austin
2016- Professor @University of Chicago

Research topics

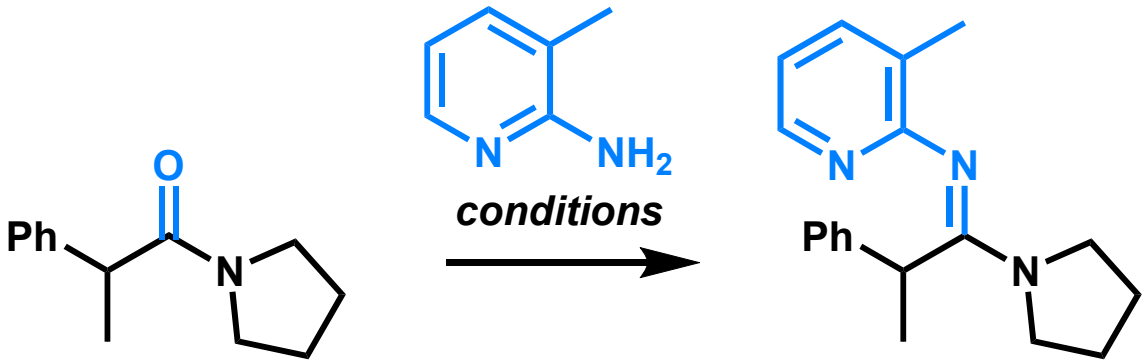
- Developing novel catalytic C–H and C–C bond activation
- Developing new transition-metal catalysts
- Total synthesis
- Synthesis of graphene nanoribbon

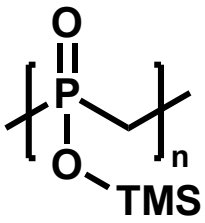
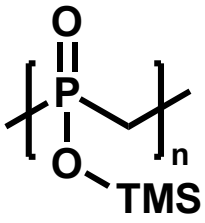
Strategy of Amide Homologation



Zhang, R.; Yu, T.; Dong, G. *Science* **2023**, *382*, 951.

Installation of Directing Group



Tf_2O	<5%
 PPSE 160 °C	51%
 PPSE pyridine 140 °C	97%

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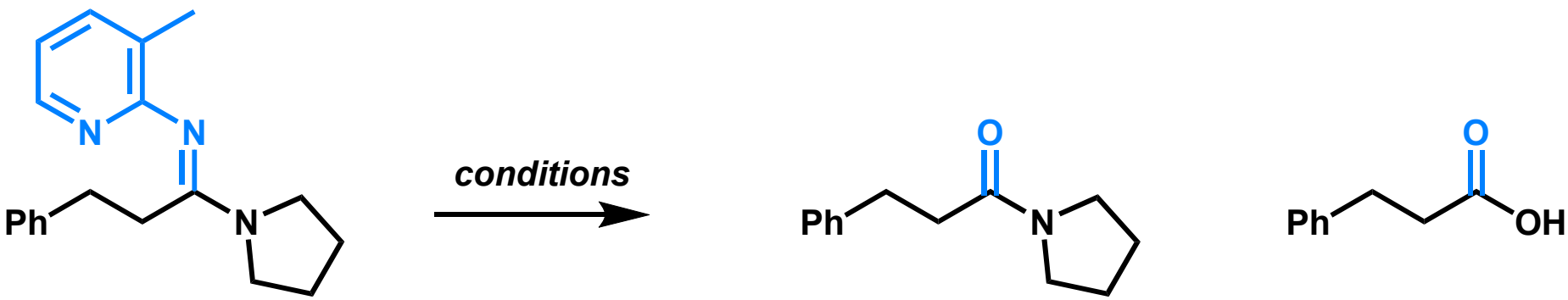
Removal of Directing Group



2 M HCl aq. 100 °C, 12 h	not detected	>95%
2 M NaOH aq./MeOH (1/1) 80 °C, 5 h	21%	31%
i-PrOH/H_2O (1/1) 100 °C, 18 h	88%	not detected
$(Bu_3Sn)_2O$ (1 equiv.) *i*-PrOH/H_2O (1/1) 100 °C, 18 h	>95%	not detected

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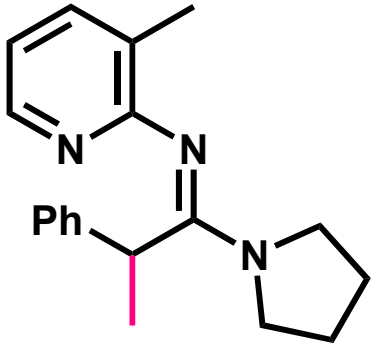
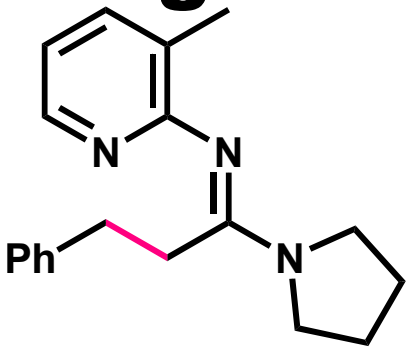
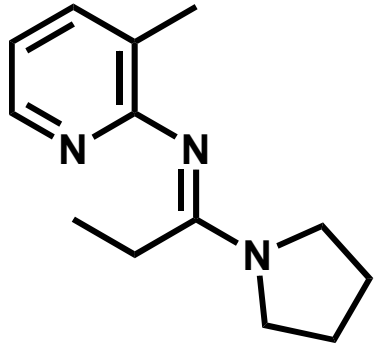
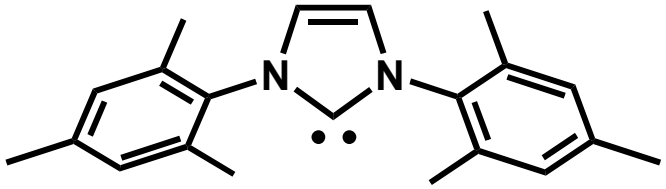
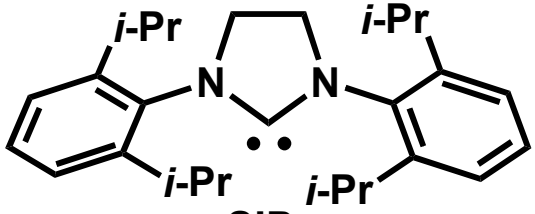
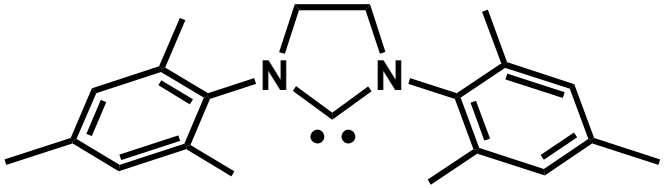
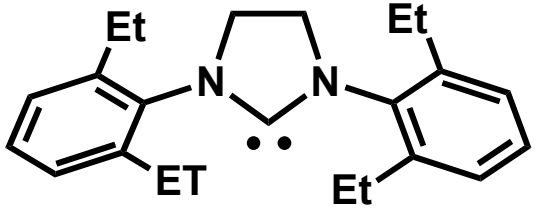
Investigation of Ligand



$[Rh(C_2H_4)_2Cl]_2$ (5 mol%)
ligand (10 mol%)
toluene
60 °C, 24 h





80% (rcv.)	 IMes	4%	obtained*
53% (rcv.)	 SIPr	26%	obtained*
8% (rcv.)	 SIMes	73%	obtained*
2% (rcv.)	 SIDep	82%	obtained*

*Yields were mentioned as 10-15%

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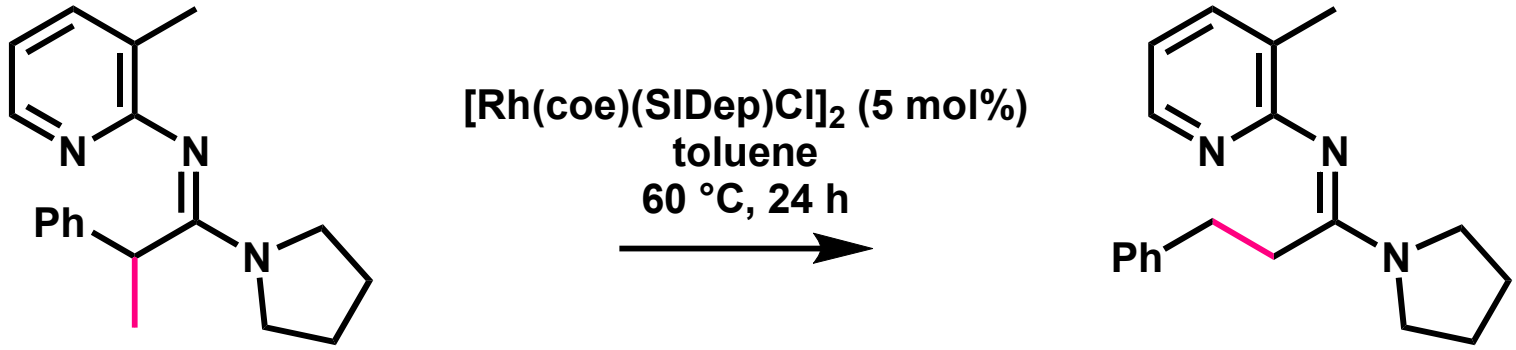
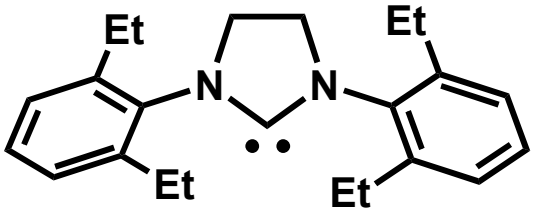
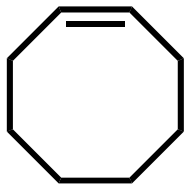
Investigation of Conditions



starting material	variation from condtions above	yield
4% (rcv.)	none	96%
18% (rcv.)	40 °C insted of 60 °C	75%
9% (rcv.)	PhCl insted of toluene	86%
20% (rcv.)	2-MeTHF insted of toluene	69%
14% (rcv.)	[Rh(coe)(SIDep)Cl]$_2$ (2.5 mol%)	82%
36% (rcv.)	[Rh(coe)(SIDep)Cl]$_2$ (1.25 mol%)	64%



SIDep



coe

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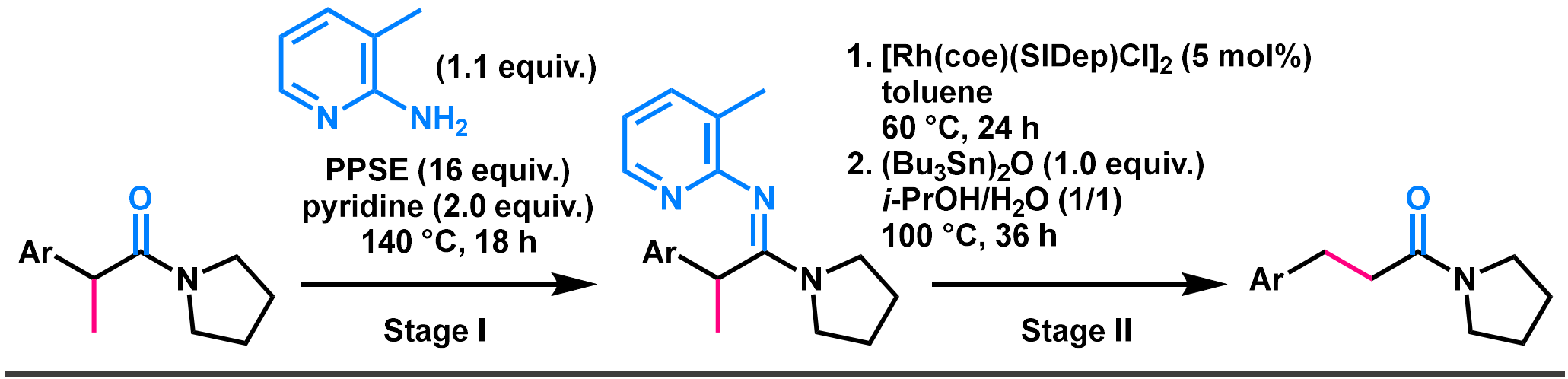
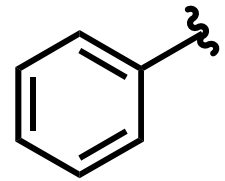
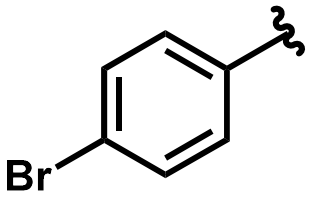
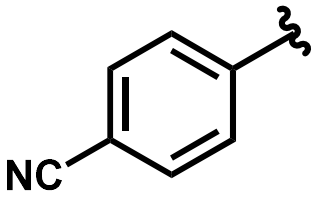
Substrate Scope

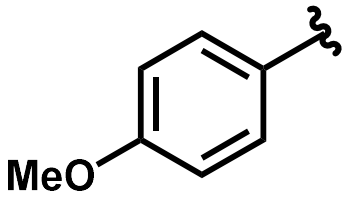


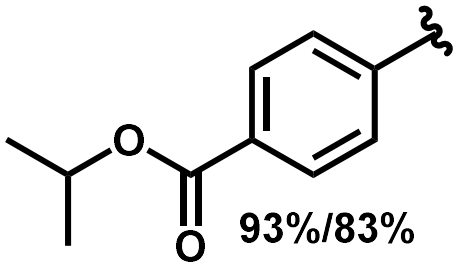
Ar =

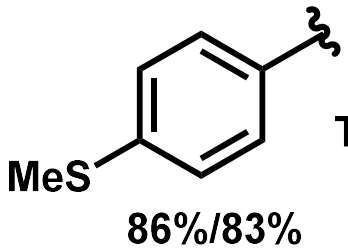

97%/83%

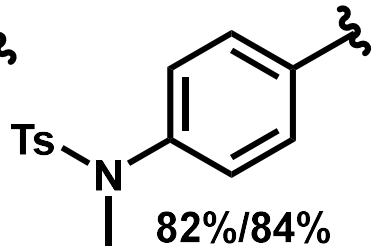

90%/87%

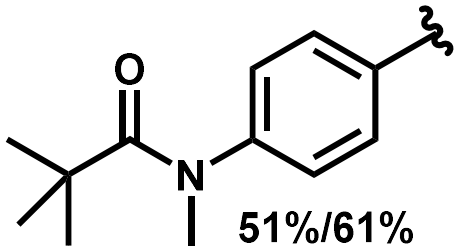

94%/84%

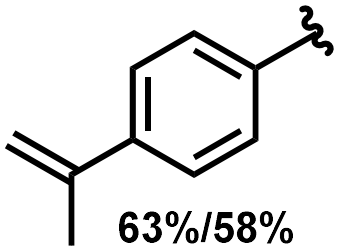

97%/53%

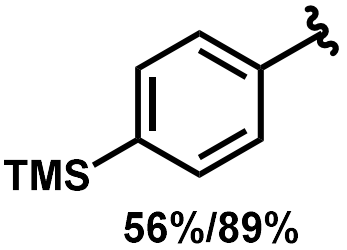

93%/83%


86%/83%


82%/84%


51%/61%


63%/58%


56%/89%

Yield: Stage I/Stage II

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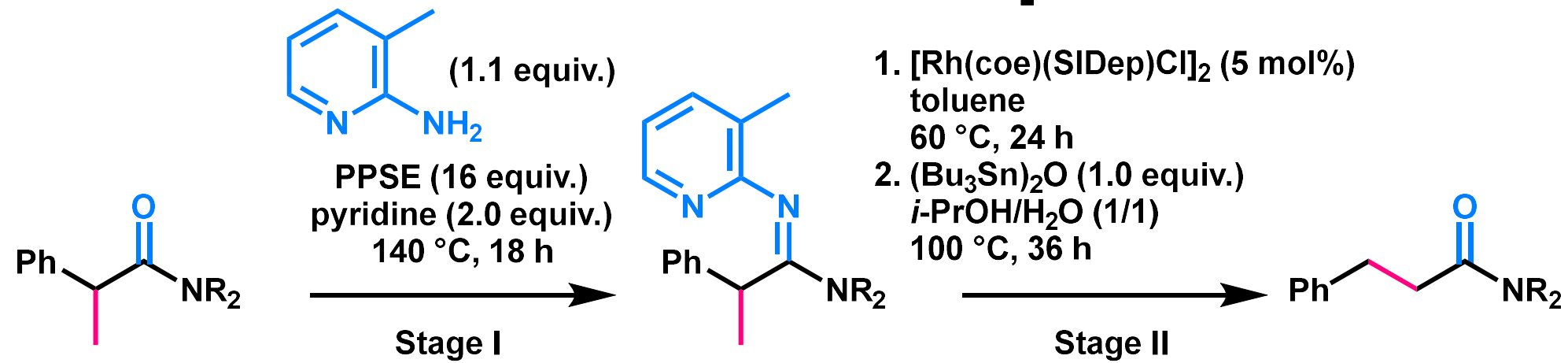
Substrate Scope



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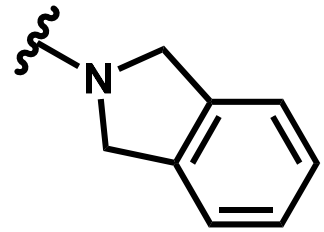
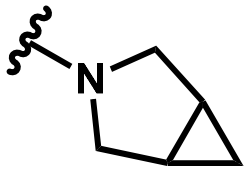
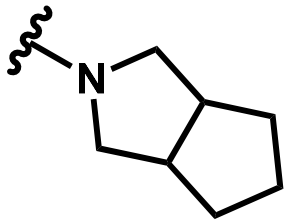


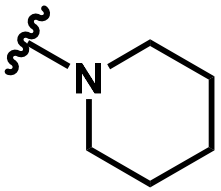
79%*/82%



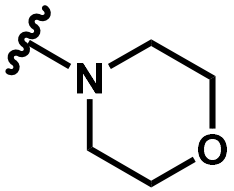
87%*/84%



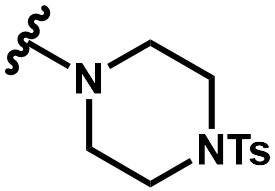
88%*/77%



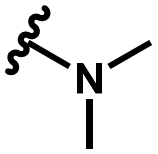
89%/51%



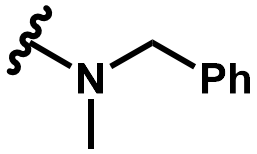
92%/44%



67%*/27%



93%/73%



67%*/42%

Yield: Stage I/Stage II

***Conditions of Stage I: amine (1.5 equiv.), PPSE (12 equiv.), pyridine (3.0 equiv.). 160 °C, 18 h**

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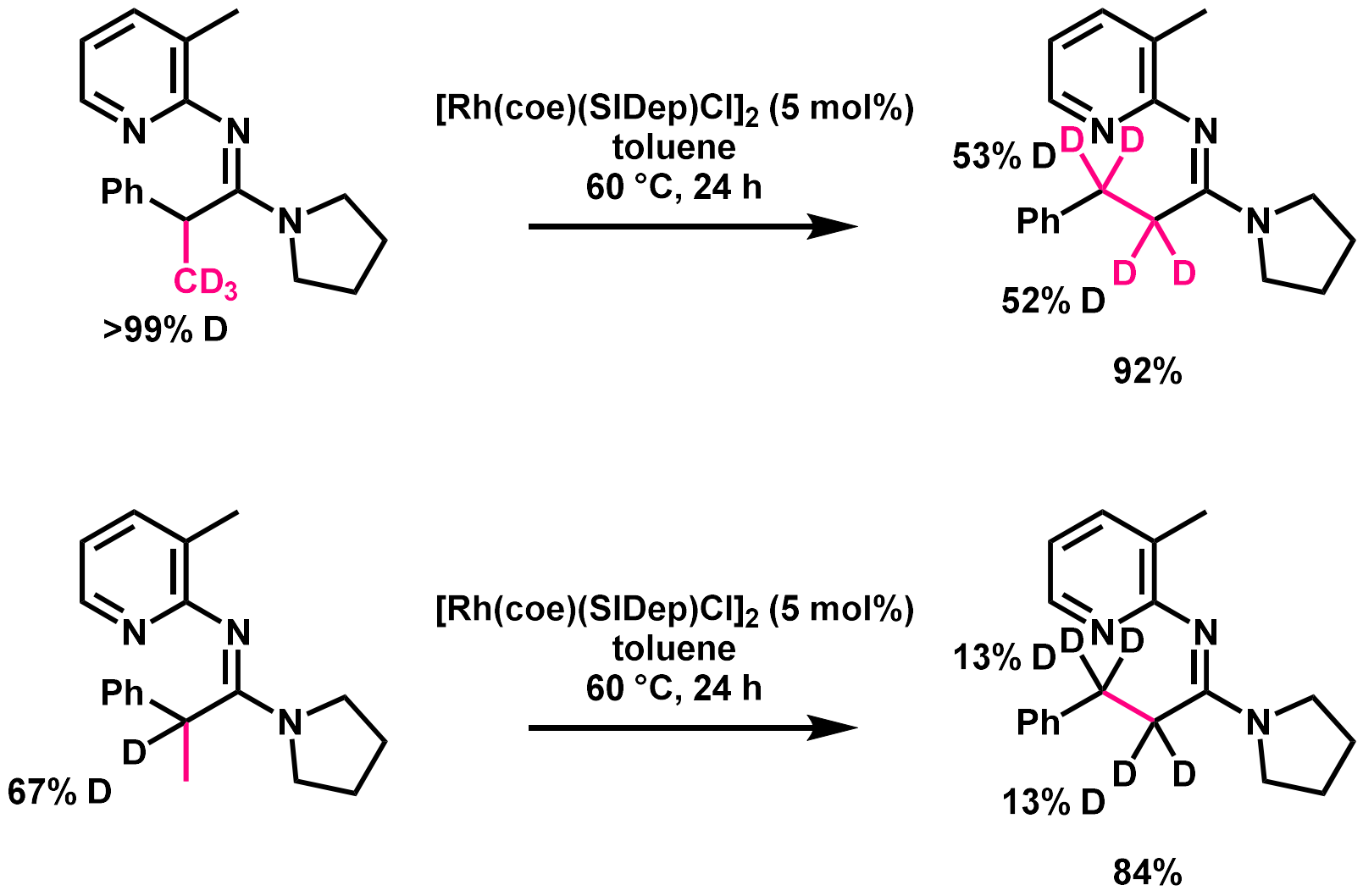
Deuterium Labeling Experiment



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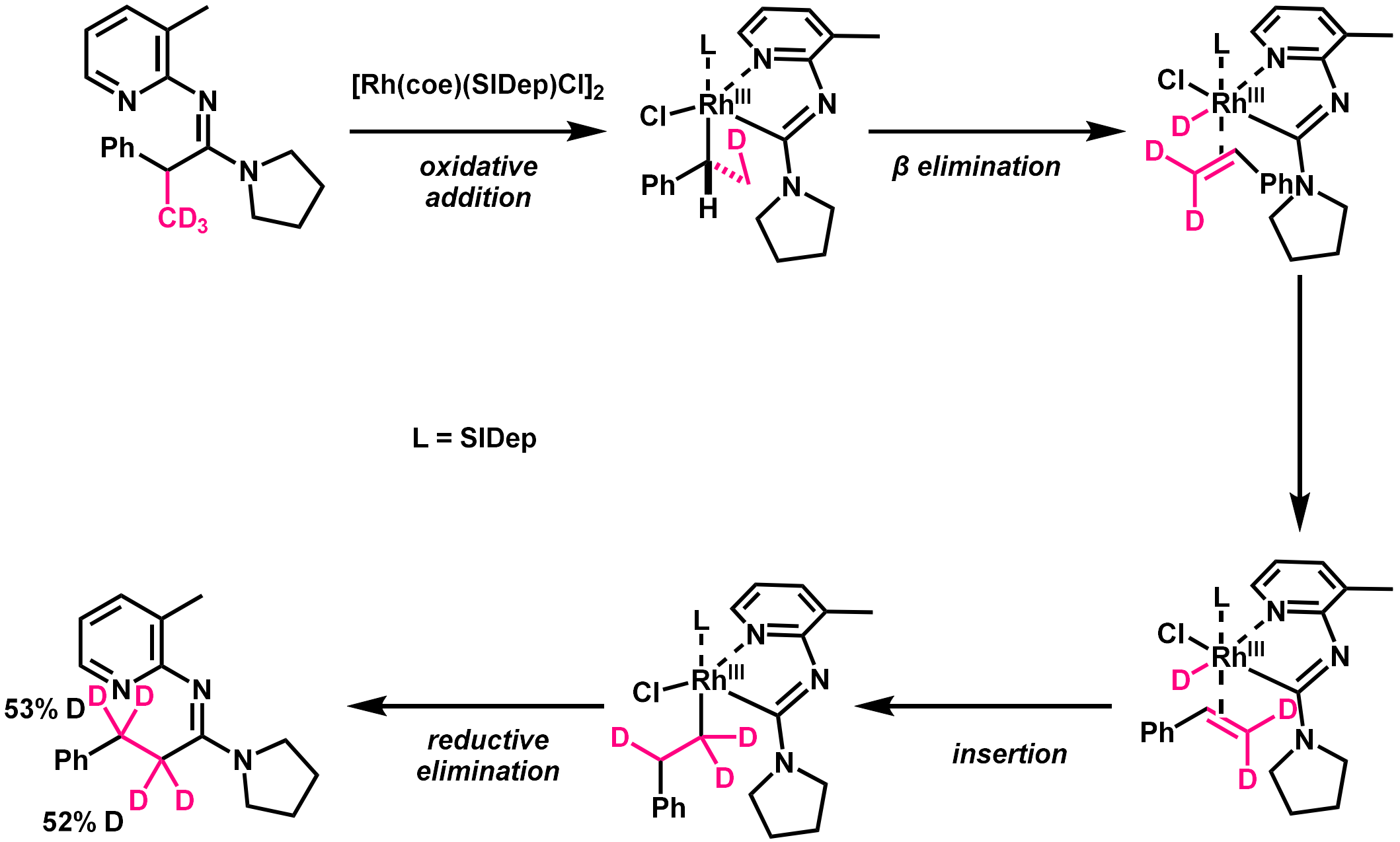
Proposed Mechanism of Deuterium Transfer



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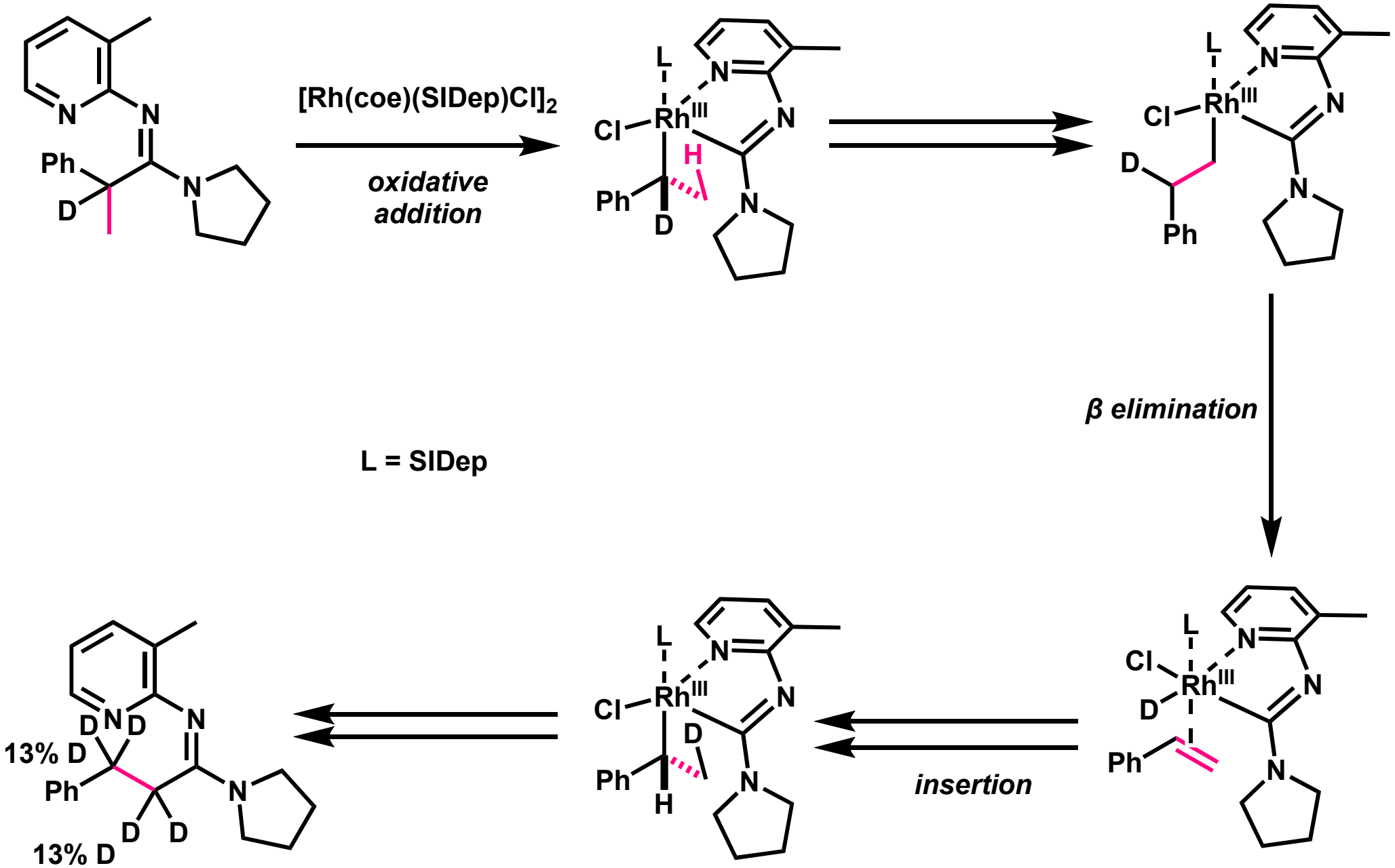
Proposed Mechanism of Deuterium Transfer



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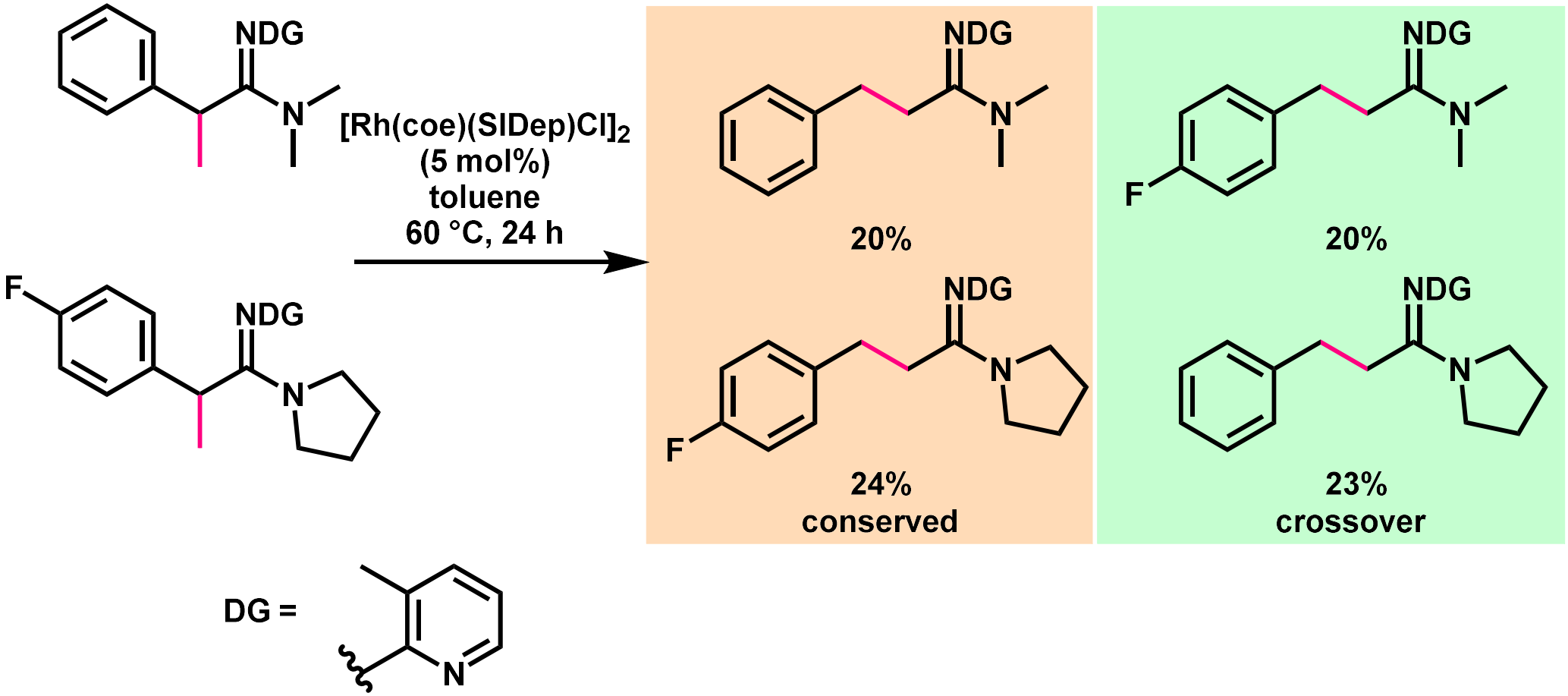
Crossover Experiment



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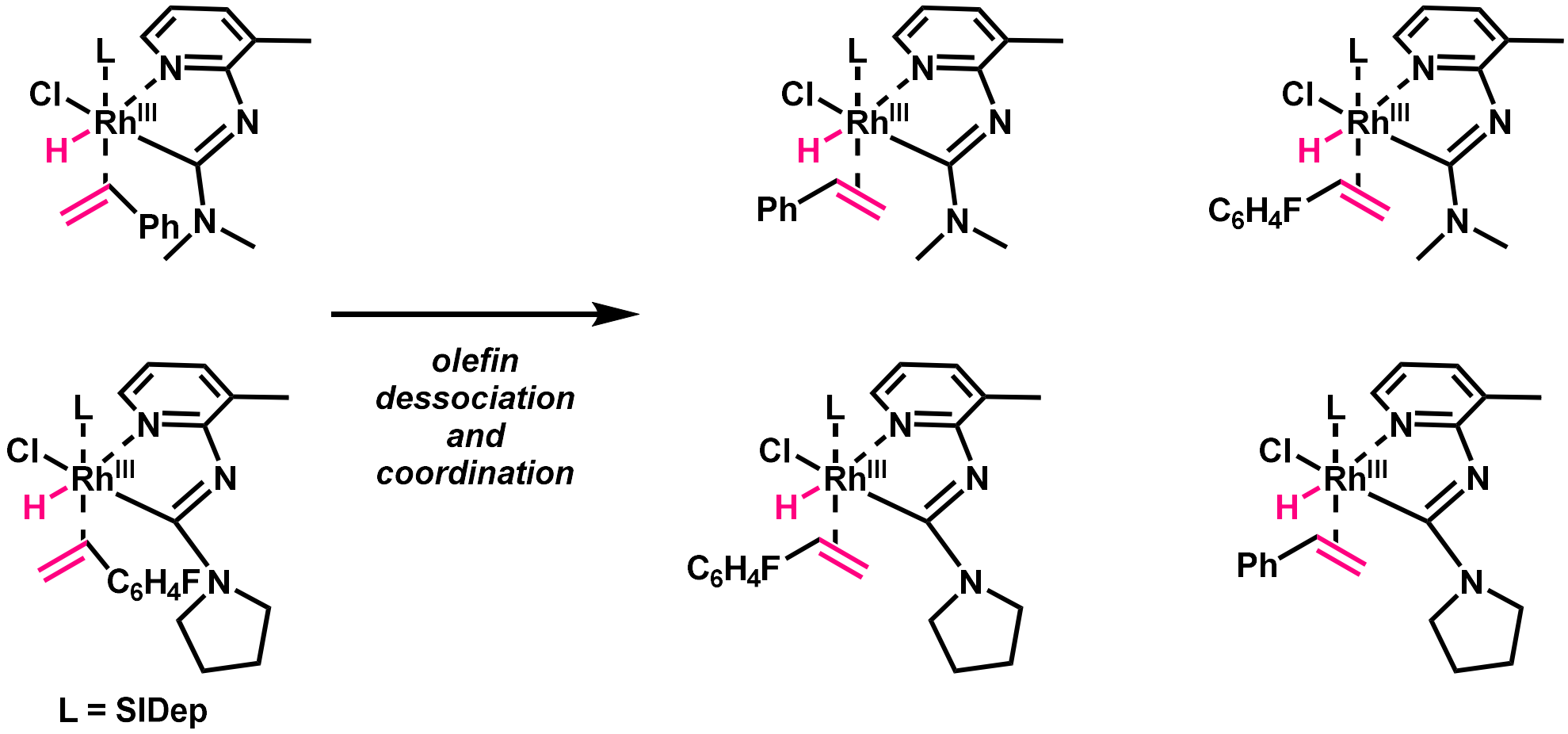
Crossover Experiment

proposed intermediates



L = SIDep

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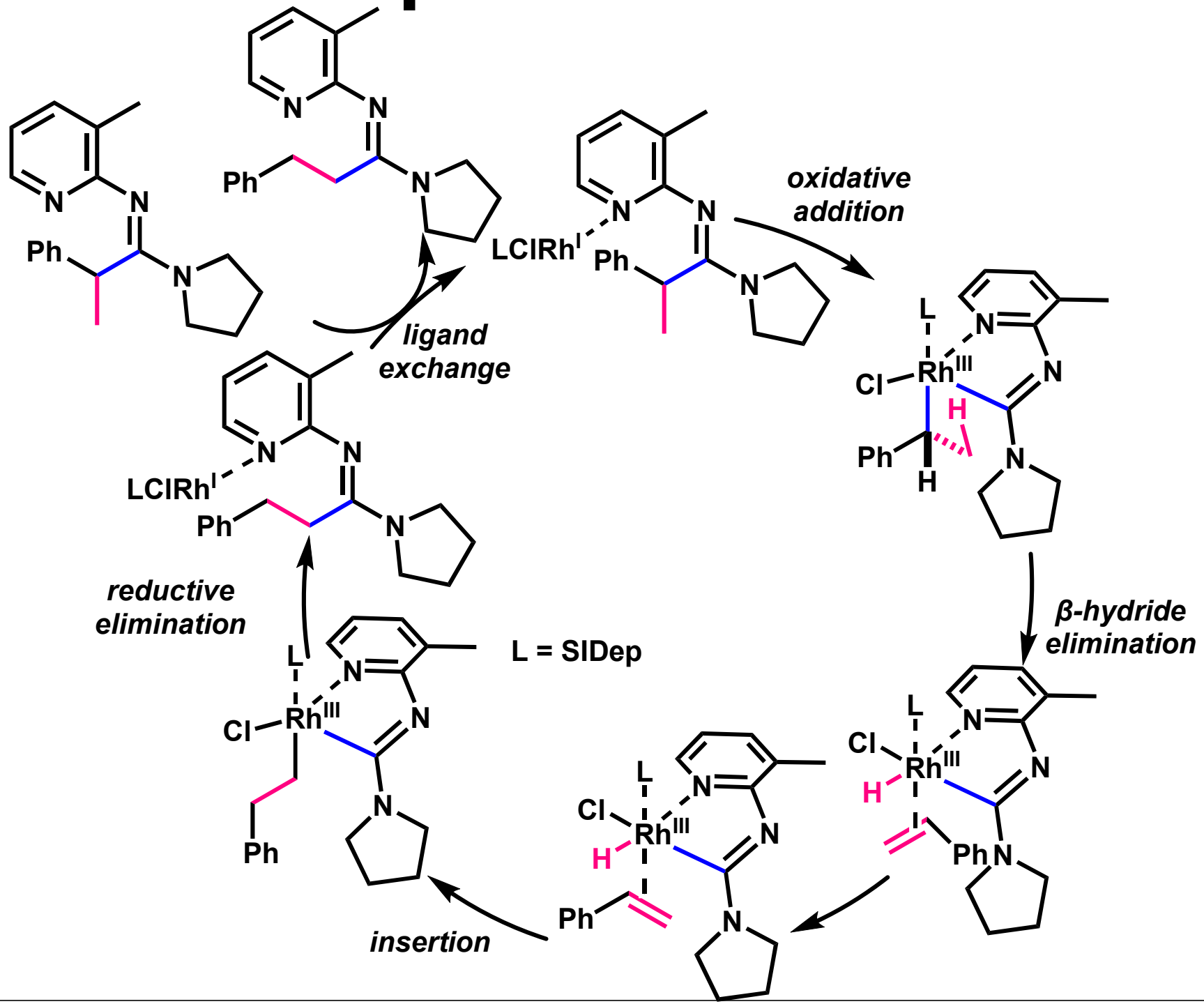
Proposed Mechanism



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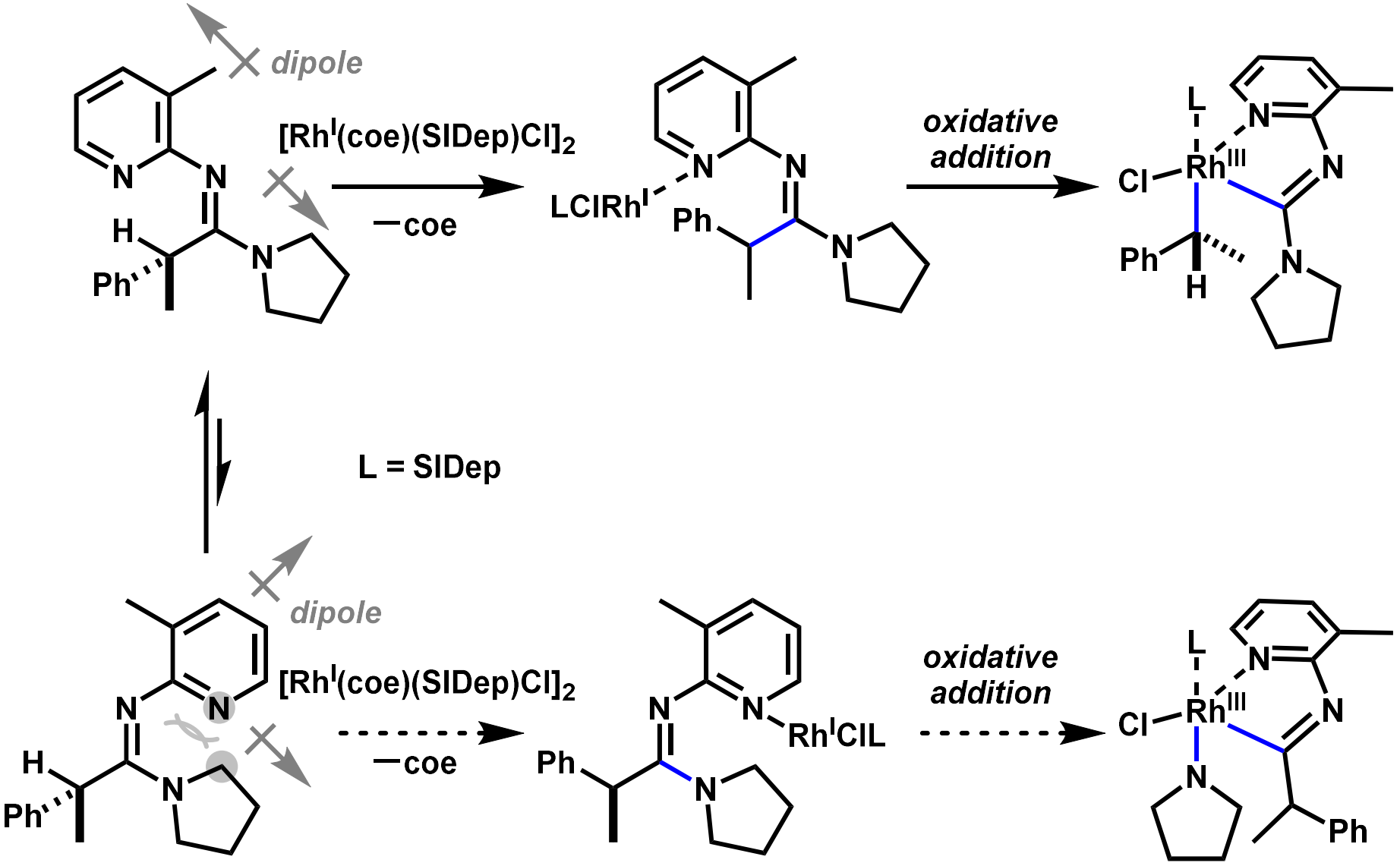
Selectivity -C–C vs C–N-



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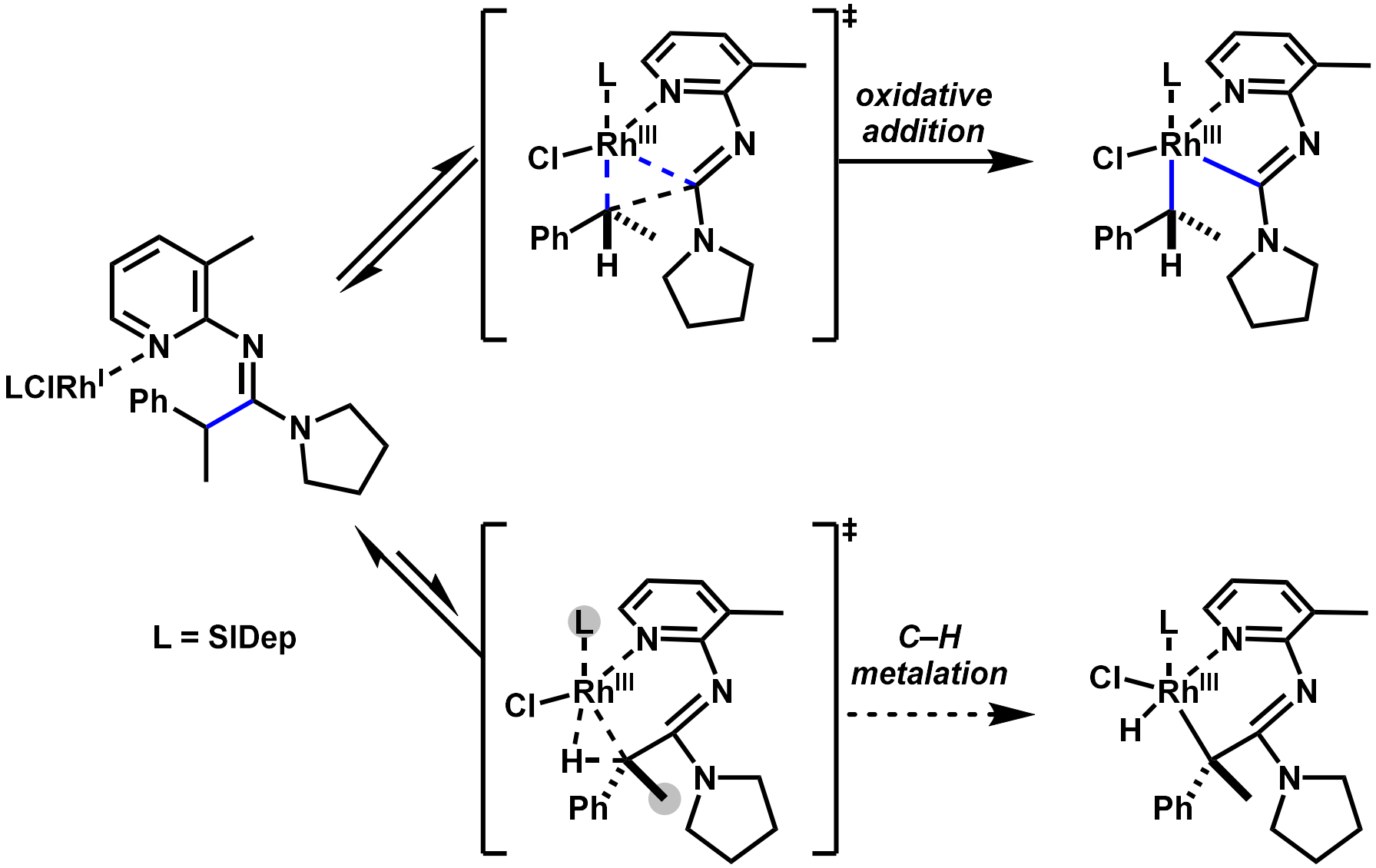
Selectivity -C–C vs C–H-



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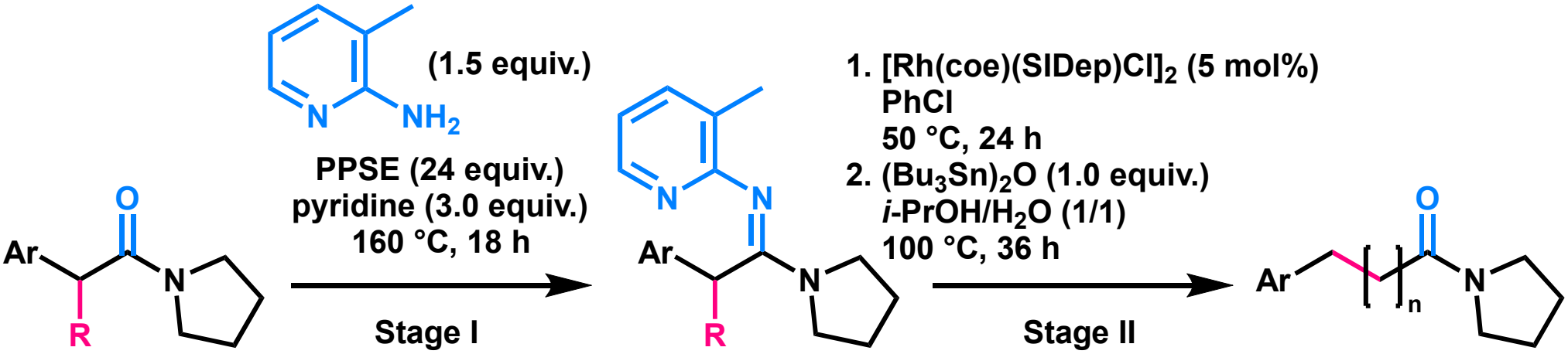
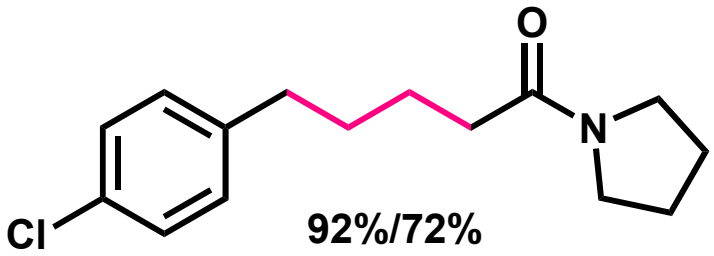
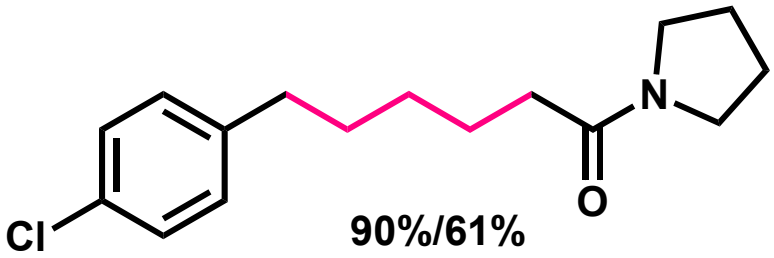
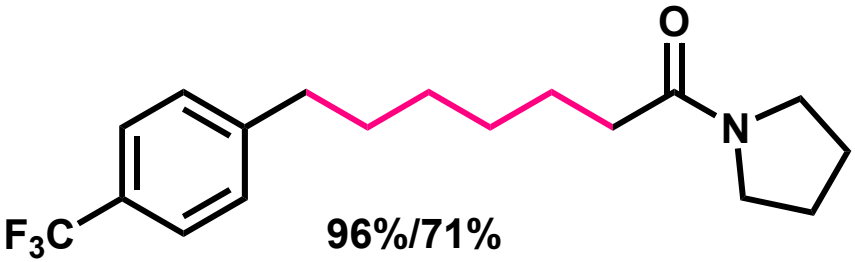
Multiple-Carbon Homologation

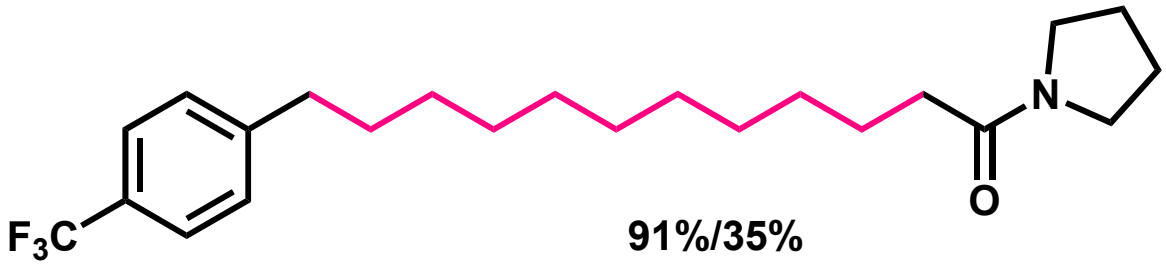


products





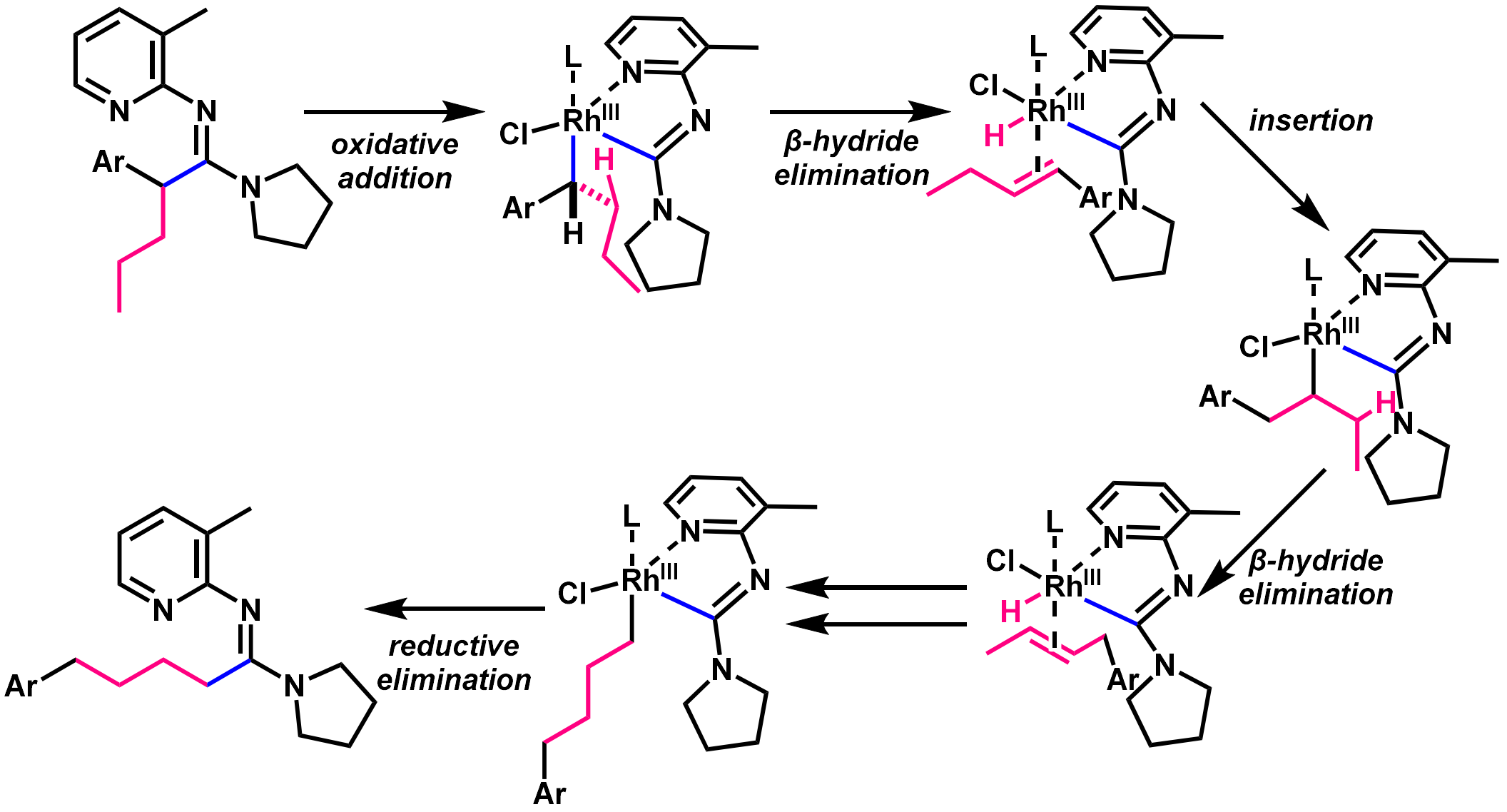




Yield: Stage I/Stage II

Zhang, R.; Yu, T.; Dong, G. *Science* **2023**, *382*, 951.

Proposed Mechanism



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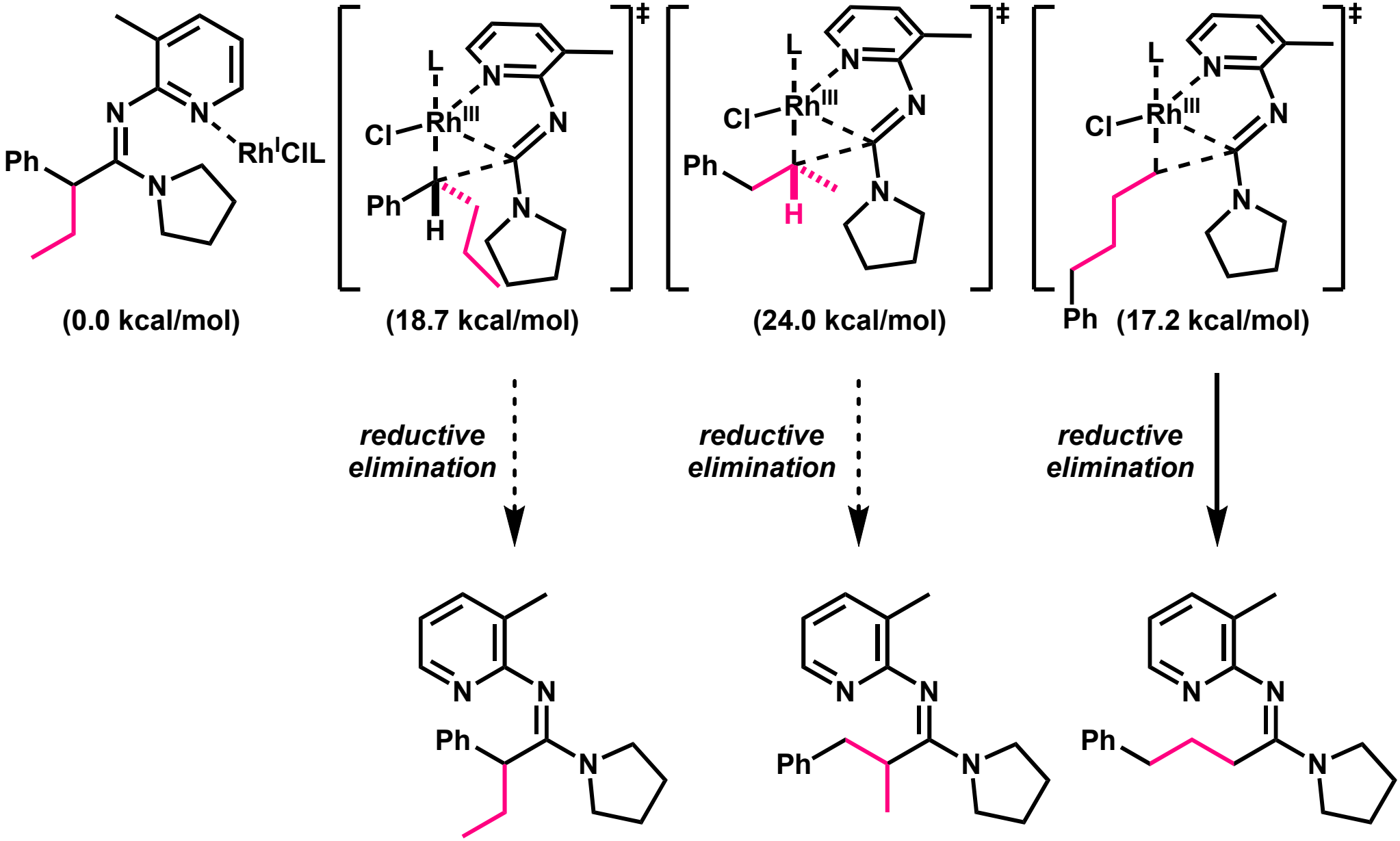
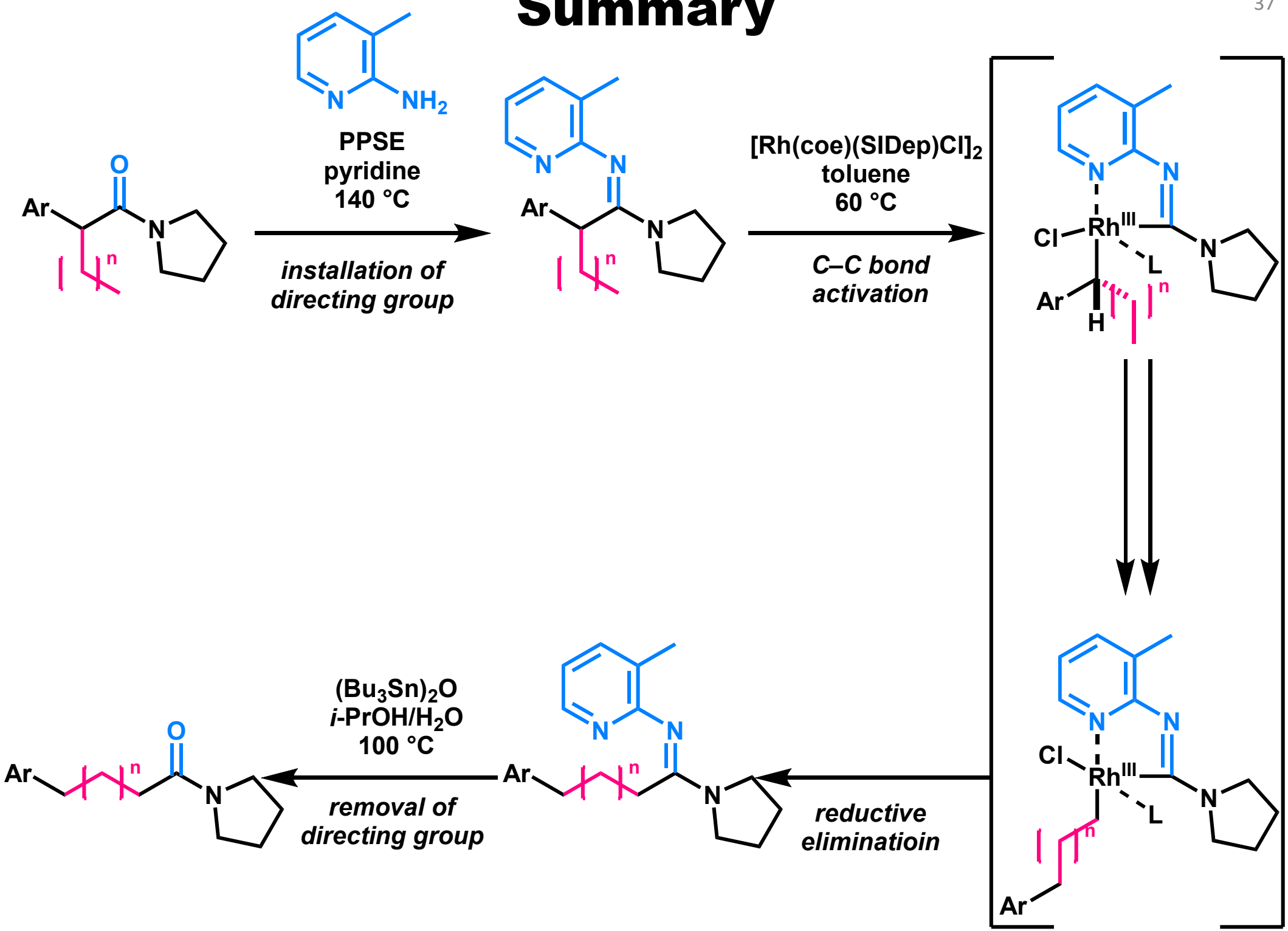
Selectivity in Reductive Elimination



Calculation was conducted at B3LYP-GD3(BJ)/6-31G(d)-SDD level, gas phase.

Zhang, R.; Yu, T.; Dong, G. *Science* **2023**, *382*, 951.

Summary


PPSE
pyridine
140 °C
installation of
directing group
[Rh(coe)(SIDep)Cl]2
toluene
60 °C
C–C bond
activation
reductive
eliminatioin
(Bu3Sn)2O
i-PrOH/H2O
100 °C
removal of
directing group
Ar
n
O
N
NH2
Cl
Rh
III
L
H