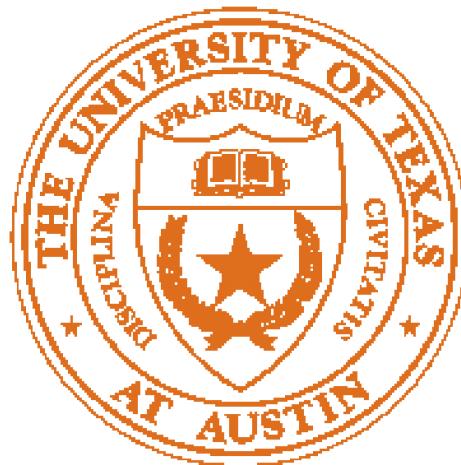


Rh(III)-catalyzed C-H Activation and Annulation *via* Oxidizing Directing Group



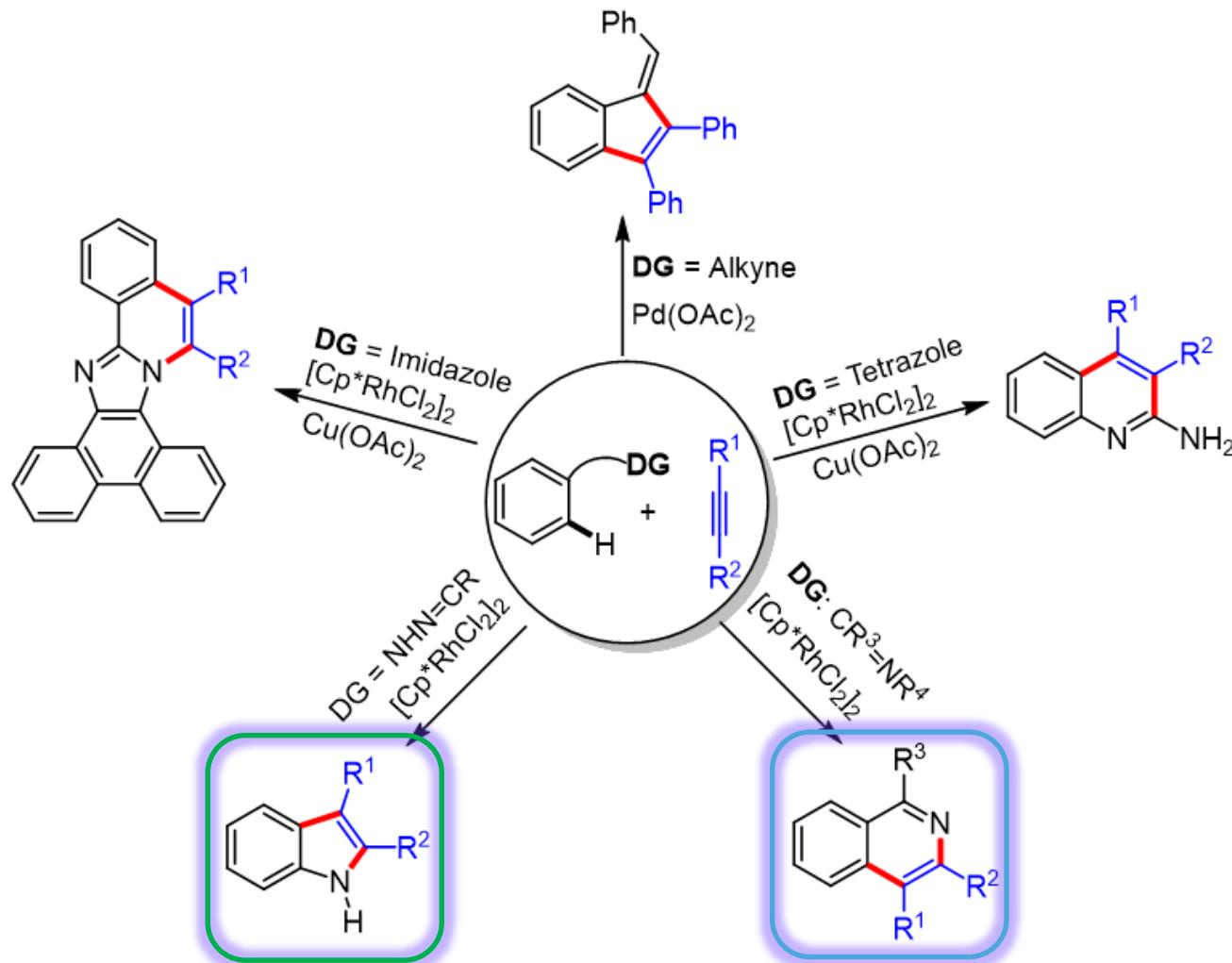
*Lei Zhang
03/23/2016
Dong Group*



Content

- 1** Alkyne involved Annulation in Hua group
- 2** Brief Introduction of Internal Oxidants
- 3** Oxidizing Directing Groups
- 4** Conclusions

Alkyne involved C–H Activation and Annulation in Hua group

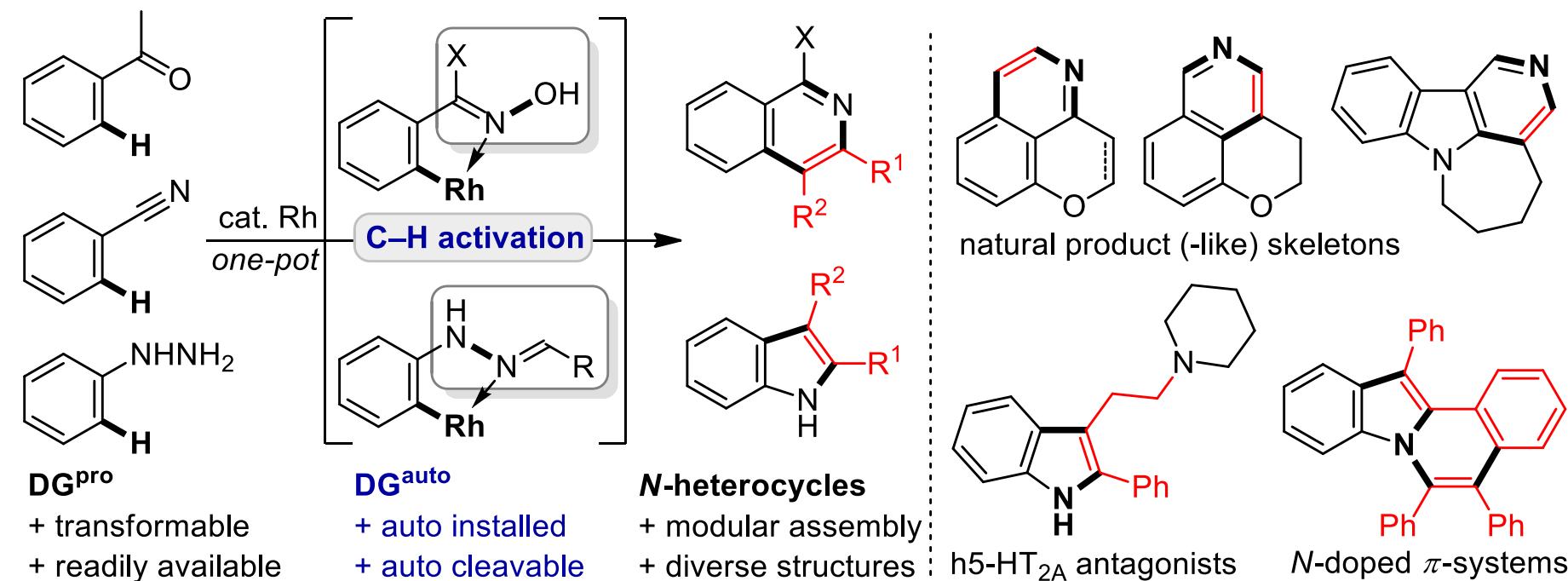


Guo, B.; Hua, R. *J. Org. Chem.* **2015**, 80, 8430.
Zhang, L.; Hua, R. *J. Org. Chem.* **2014**, 79, 11541.
Zheng, L.; Hua, R. *J. Org. Chem.* **2012**, 77, 5794.

Zheng, L.; Hua, R. *Chem. Eur. J.* **2014**, 20, 2352.
Zheng, L.; Hua, R. *J. Org. Chem.* **2014**, 79, 3930.

Indole, Isoquinoline and Heterocycle-Fused Pyridine Synthesis

- Rhodium(III)-Catalyzed C–H Activation *via* an Auto-Formed and Auto-Cleavable Directing Group

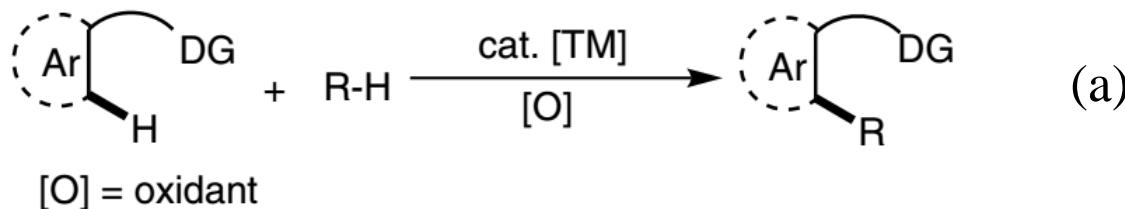


Zheng, L.; Ju, J.; Bin, Y.; Hua, R. *J. Org. Chem.* **2012**, 77, 5794.

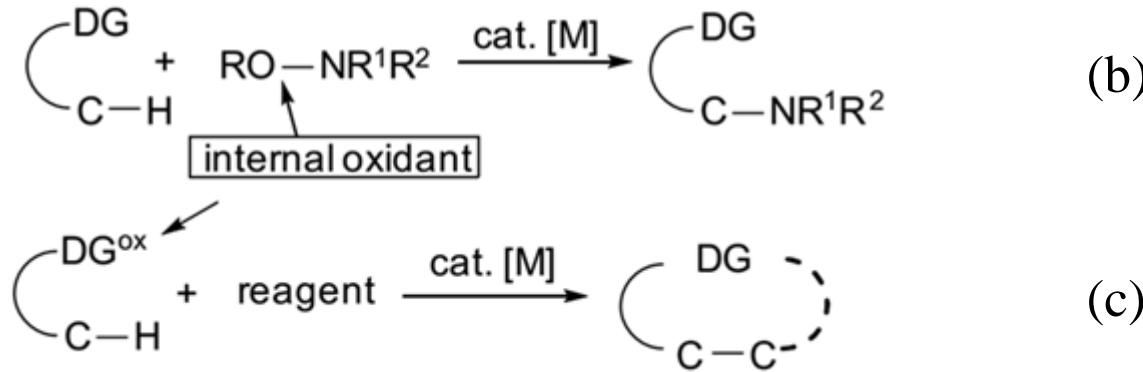
Zheng, L.; Hua, R. *Chem. Eur. J.* **2014**, 20, 2352.

Internal Oxidants

- Strategies for selective C–H functionalization with DGs



- The strategy of internal oxidant used in C–H bond activation



Patureau, F. W.; Glorius, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 1977.

Huang, H.; Ji, X.; Wu, W.; Jiang, H. *Chem. Soc. Rev.* **2015**, *44*, 1155.

Mo, J.; Wang, L.; Liu, Y.; Cui, X. *Synthesis* **2015**, *47*, 439.

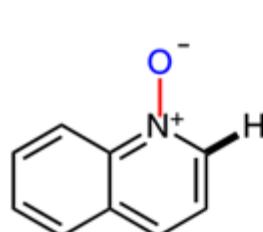


Oxidizing Directing Groups (DG^{ox})

- *The N–O Bond as Internal Oxidant Directing Group*
- *The N–N Bond as Internal Oxidant Directing Group*
- *The N–S Bond as Internal Oxidant Directing Group*
- *The C–N Bond as Internal Oxidant Directing Group*

The N–O Bond as Internal Oxidant Directing Group

❖ *N*-oxides as DG^{ox}

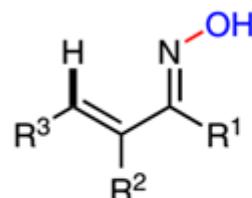


Cui & Wu, 2009

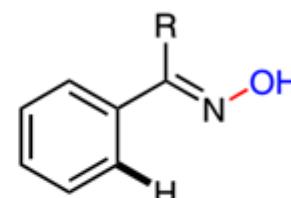


You, 2013

❖ Oximes as DG^{ox}

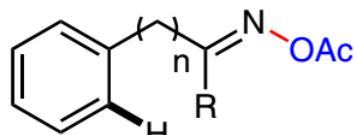


Chiba & Li, 2011
Rovis, 2011



Hua, Ackermann, Rovis, Jia
Jeganmohan 2011–2014

❖ *N*-acyloxy group as DG^{ox}

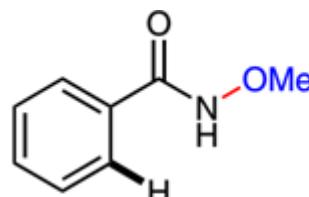


n = 0,1

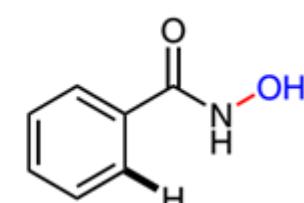
n = 0, Chiba, 2010, 2011

n = 1, Hartwig, 2010

❖ *N*-methoxy/hydroxy group as DG^{ox}



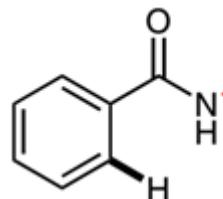
Ackermann, Guimond & Fagnou
Glorius, Wang & Li, 2010–2014



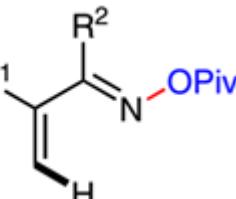
Ackermann 2011, 2014

The N–O Bond as Internal Oxidant Directing Group

❖ *N*-OPiv or *N*-OBoc group

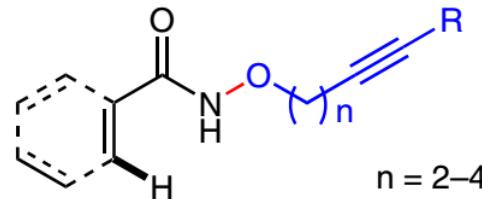


Guimond & Fagnou, Glorius,
Ward & Rovis, Cui,
Huckins & Bercot, Cramer
2011–2014



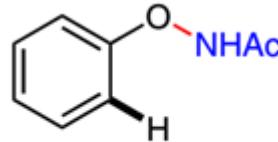
Rovis, 2012

❖ Alkyne-tethered hydroxamic esters as DG^{ox}

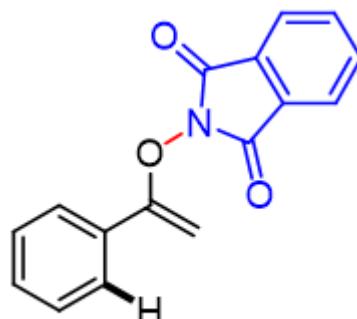


Park, 2012

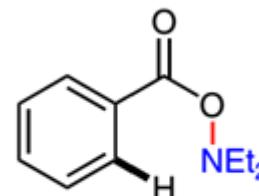
❖ *N*-phenoxyacetamide, *N*-Alkenyloxy amine, *O*-benzoyl-*N,N*-diethylhydroxylamine



Lu & Wang, 2014



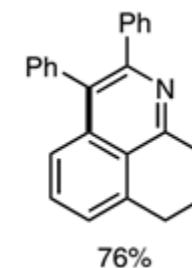
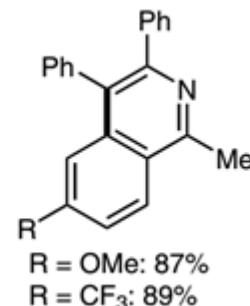
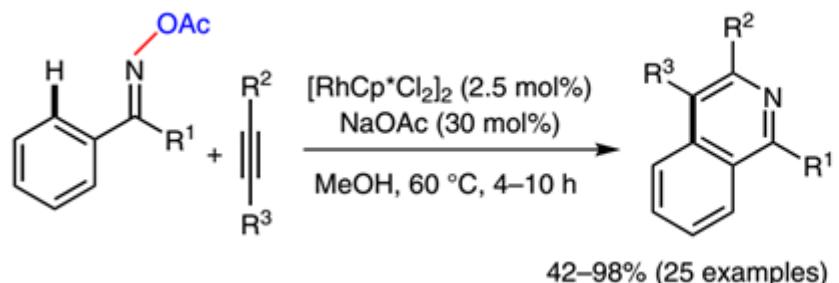
Rovis, 2014



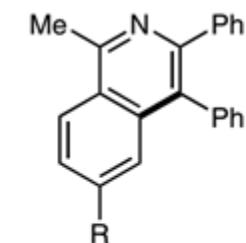
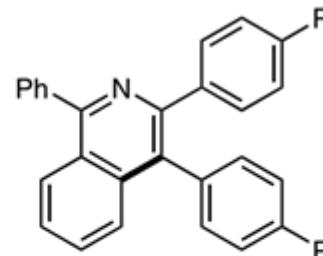
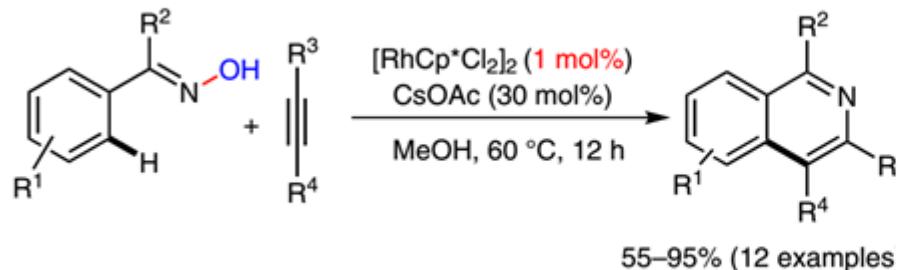
Liu, 2014

Oximes and its derivatives

Chiba



Li



R = OMe: 95%

R = H: 78%
R = OMe: 82%
R = Cl: 78%

Too, P. C.; Wang Y.-F.; Chiba S. *Org. Lett.* **2010**, *12*, 5688.

Zhang, X.; Chen, D.; Zhao, M.; Zhao J.; Jia, A.; Li, X. *Adv. Synth. Catal.* **2011**, *353*, 719.

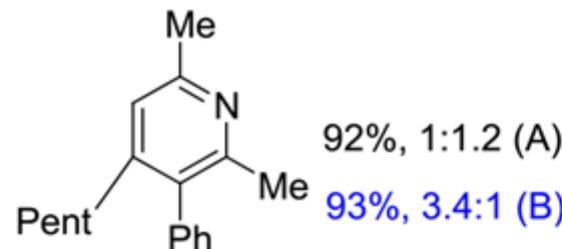
Formation of pyridines by the use of α,β -unsaturated oximines



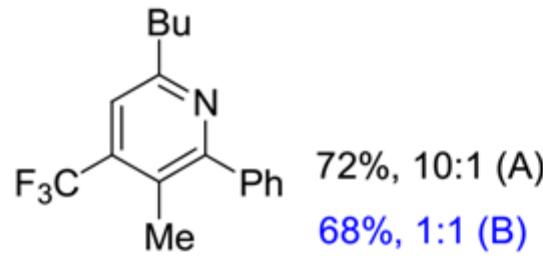
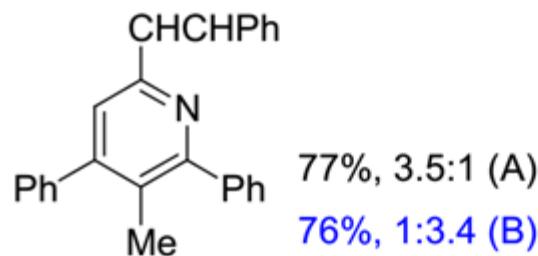
Chiba and Li: $[Cp^*RhCl_2]_2$ (2.5 mol%), CsOPiv (30 mol%), MeOH, 60 °C

Rovis: $[Cp^*RhCl_2]_2$ (2.5 mol%) (A) or $[Cp^tRhCl_2]_2$ (2.5 mol%) (B), K_2CO_3 (2 equiv.), TFE, 45 °C

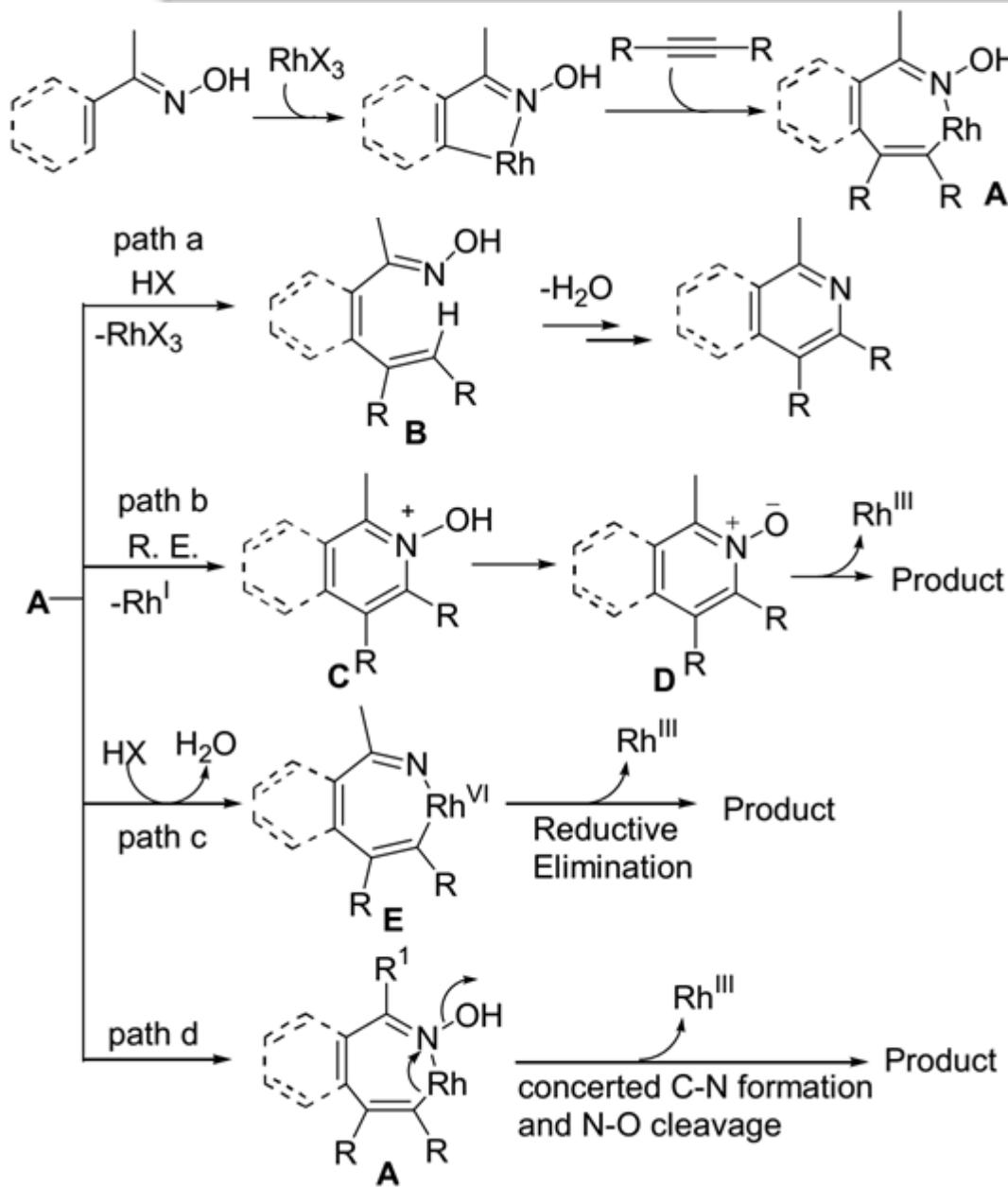
Selected examples (Rovis)



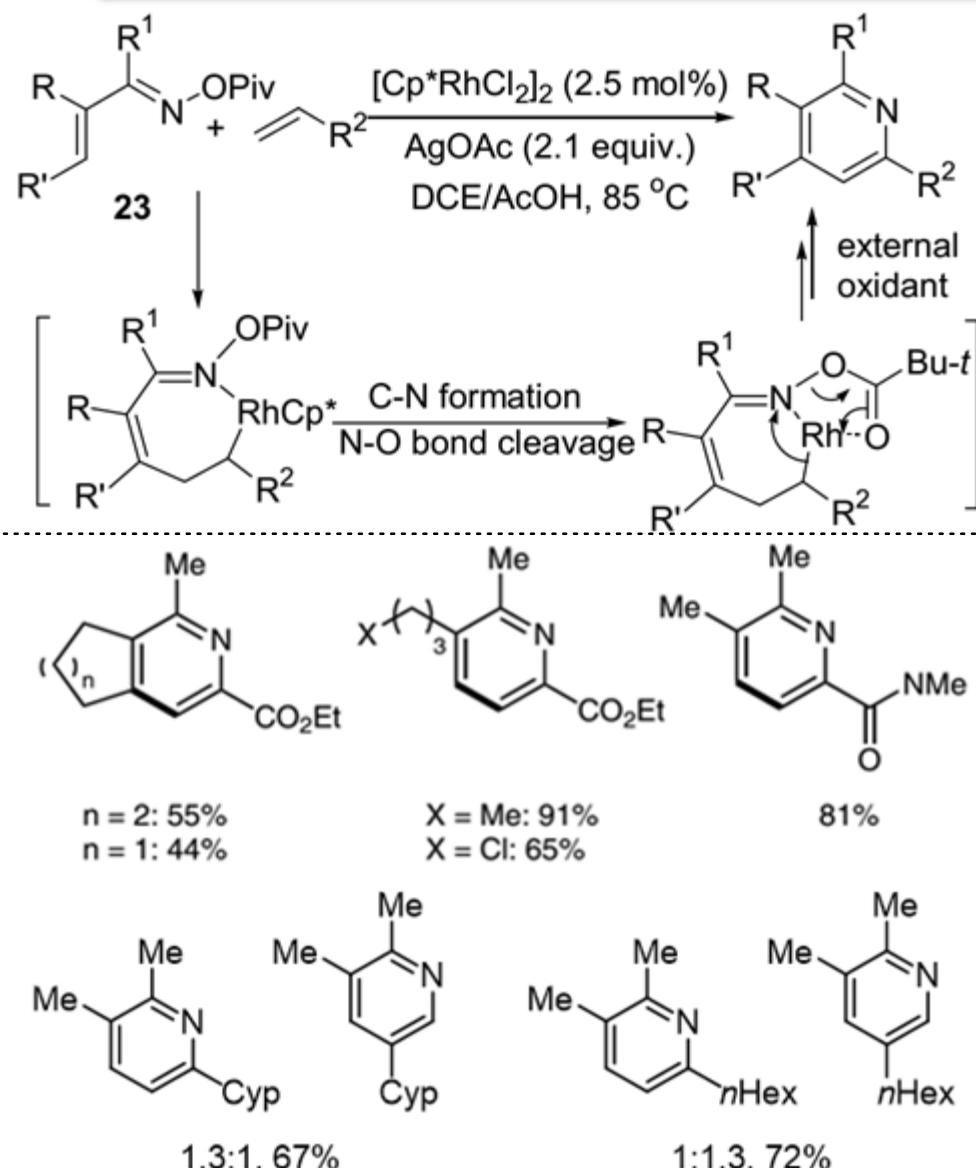
$Cp^t =$



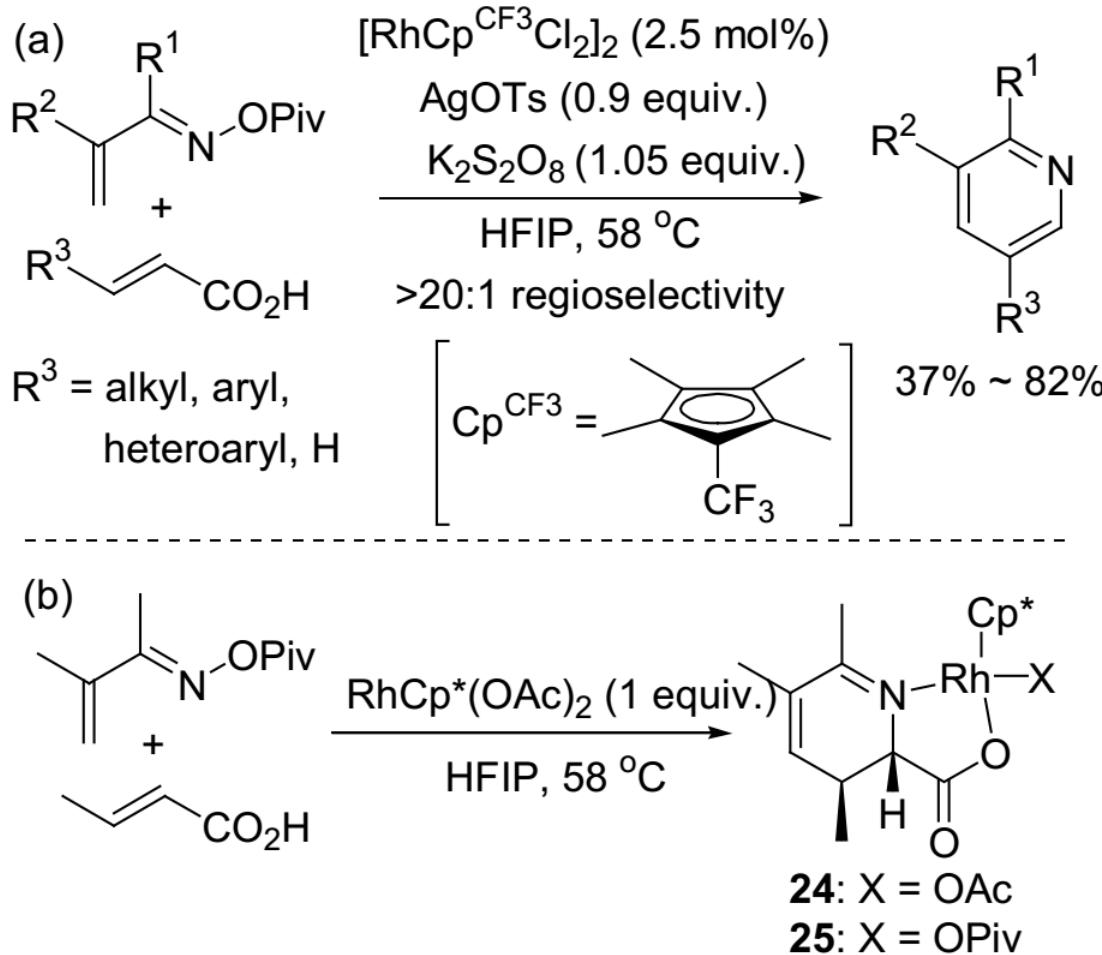
Mechanism discuss on C–H activation of oximines with alkynes



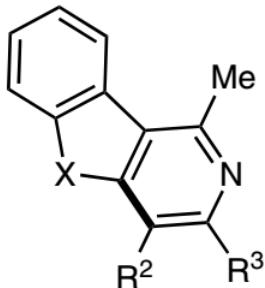
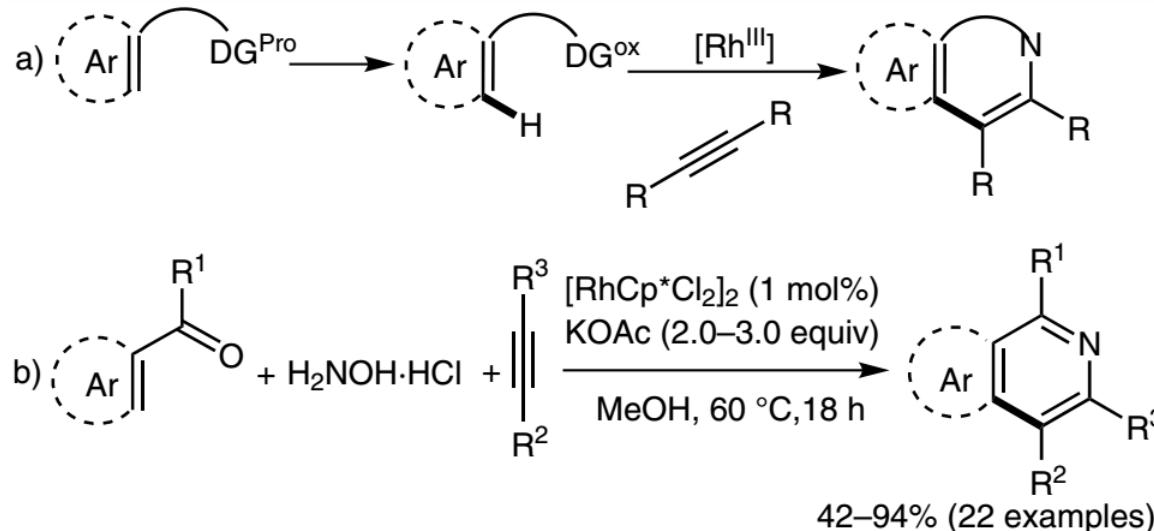
Formation of Pyridines by the Cyclization of α,β -Unsaturated Oximines with Alkenes



Formation of pyridines using acrylic acids



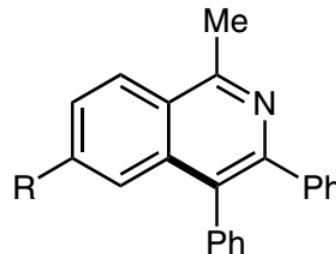
One-pot synthesis of isoquinolines



X = O, R² = R³ = Ph: 65%

X = NH, R² = R³ = H: 90%

X = NH, R² = R³ = n-Pr: 87%

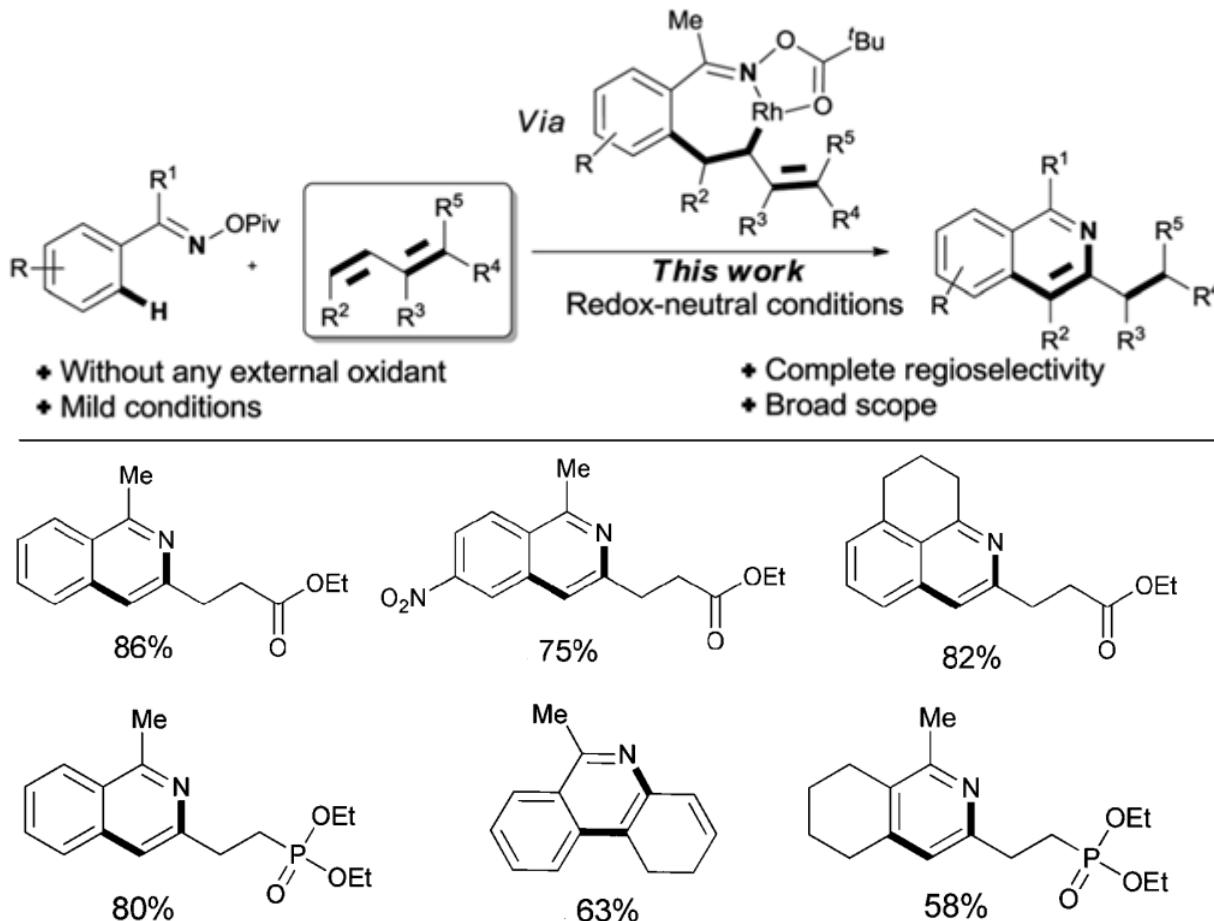


R = Me: 83%

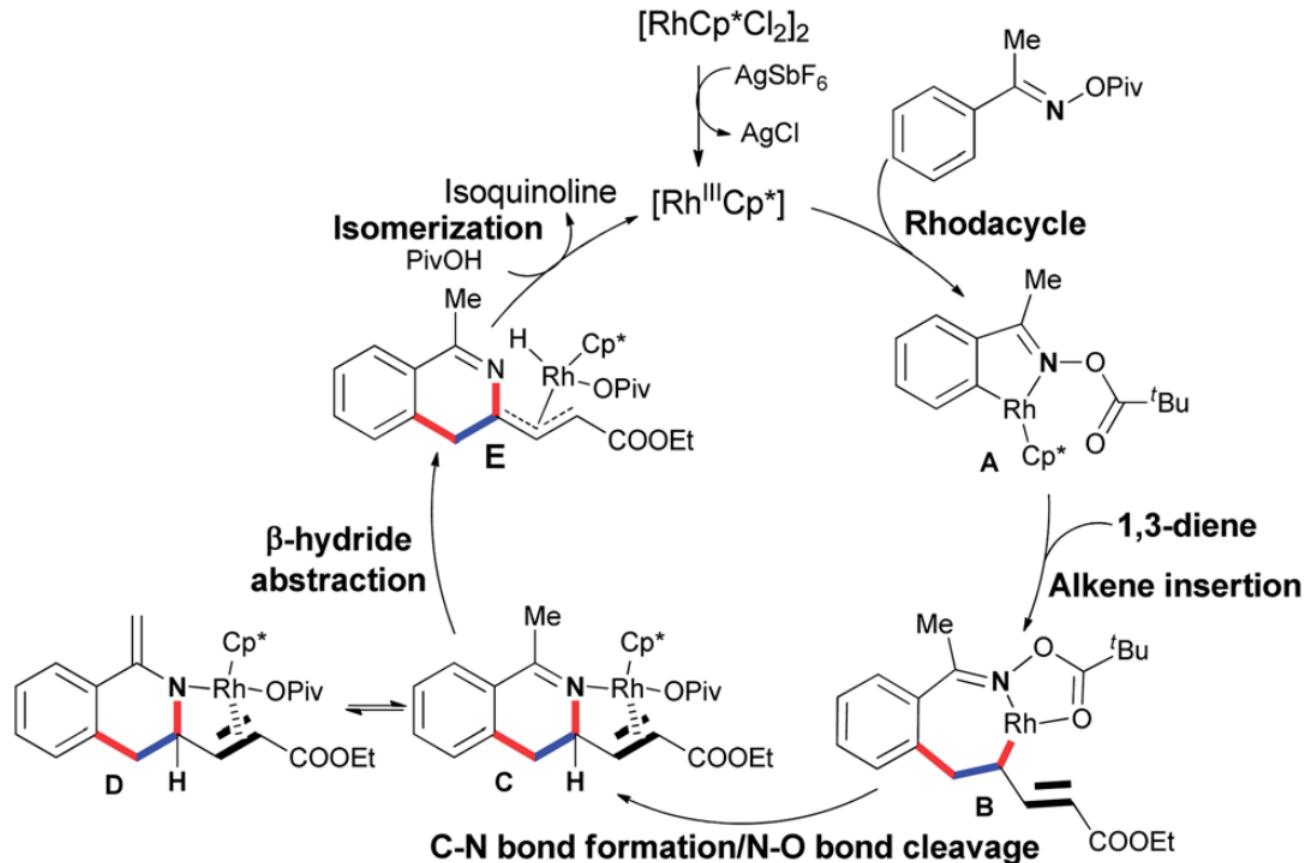
R = OMe: 87%

R = NO₂: 77%

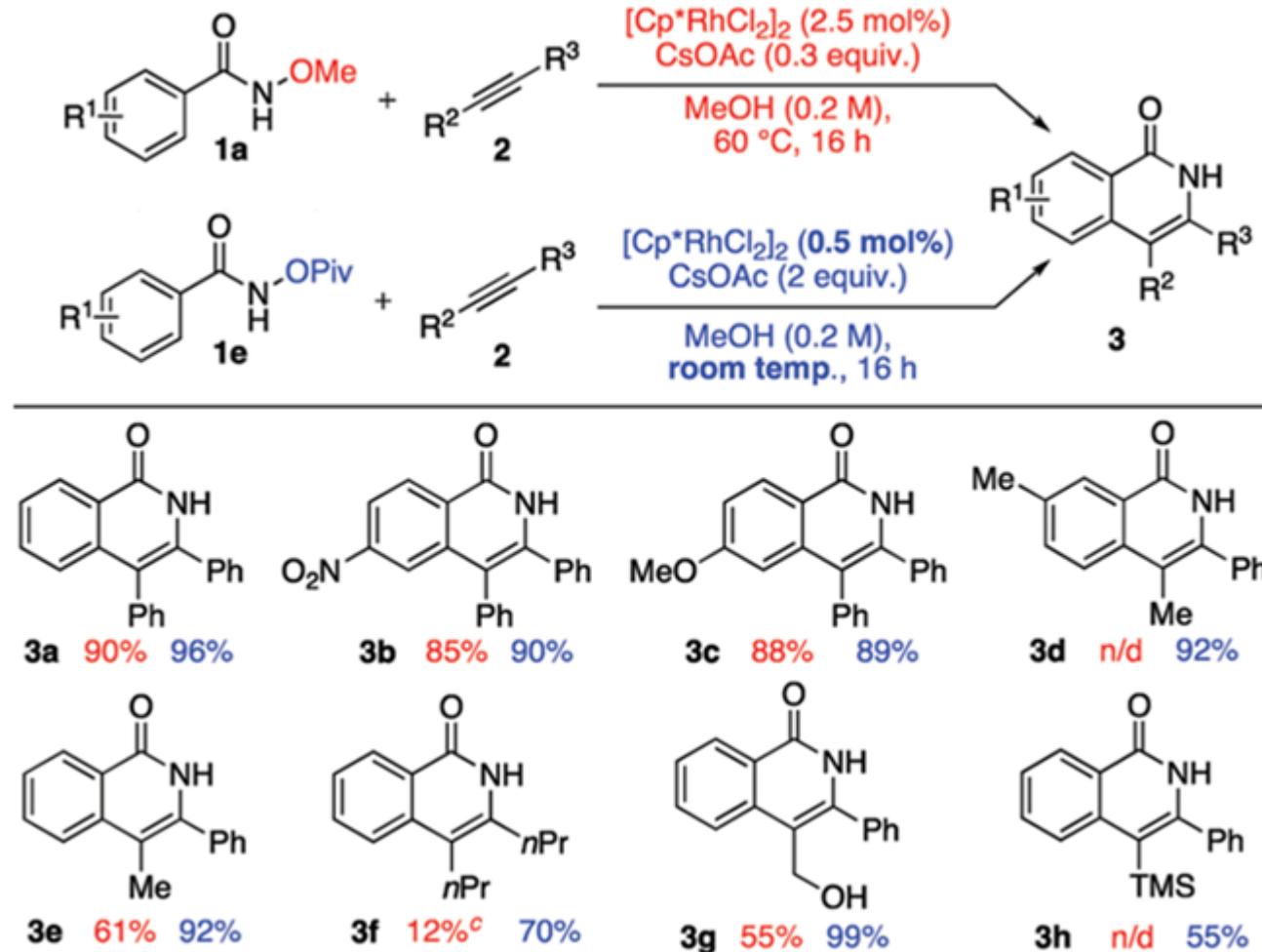
Rhodium catalyzed coupling of oximine esters with 1,3-dienes for the synthesis of isoquinolones



Proposed mechanism



N-hydroxylamine and its derivatives

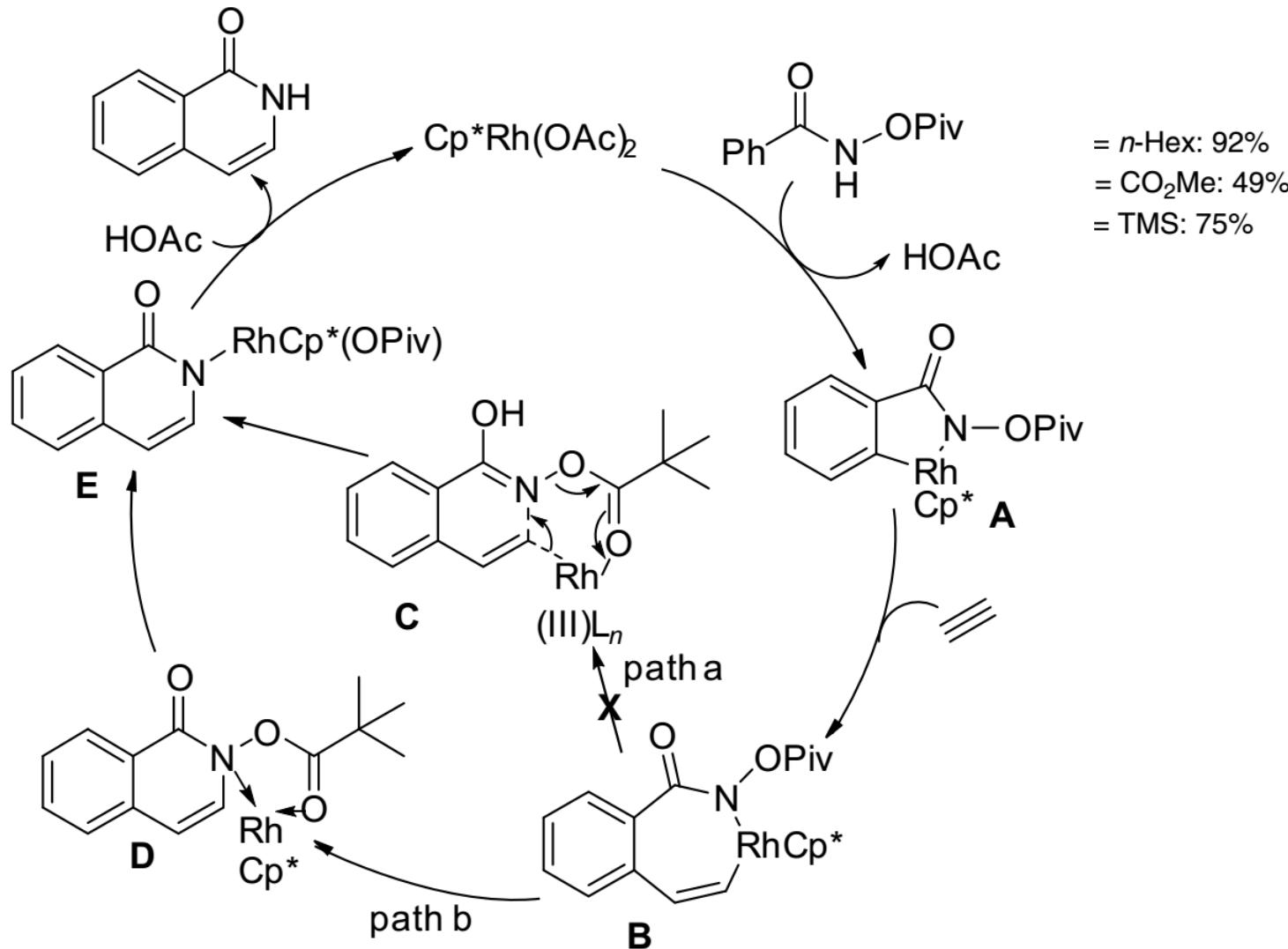


Guimond, N.; Gouliaras, C.; Fagnou, K. *J. Am. Chem. Soc.* **2010**, 132, 6908.

Guimond, N.; Gorelsky, S. I.; Fagnou, K. *J. Am. Chem. Soc.* **2011**, 133, 6449.

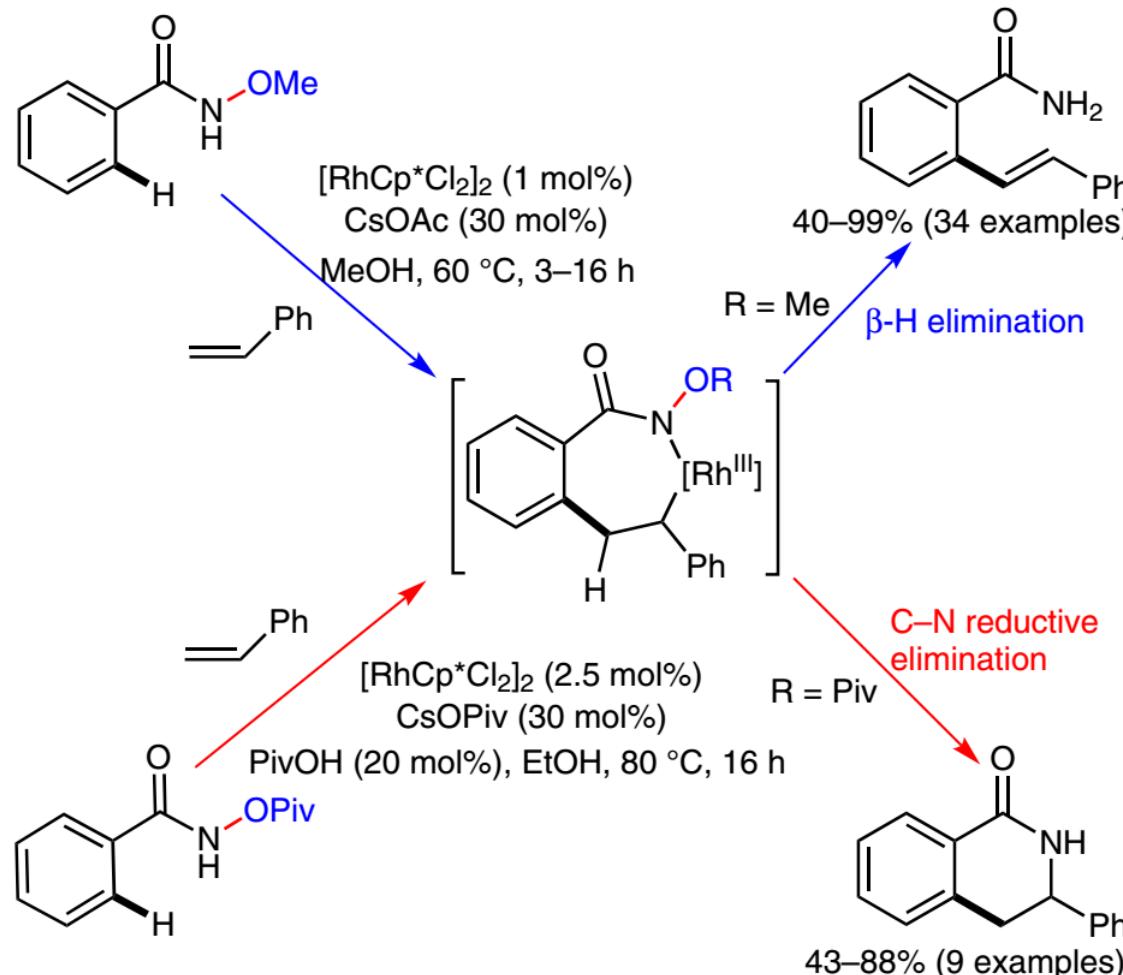
Xu, L.; Zhu, Q.; Huang, G.; Cheng, B.; Xia, Y. *J. Org. Chem.* **2012**, 77, 3017.

Rhodium(III)-Catalyzed Heterocycle Synthesis Using Terminal Alkyne and Alkene

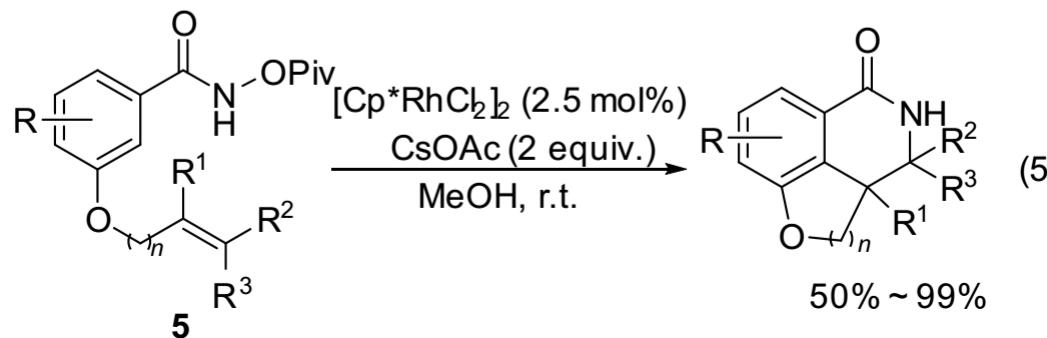
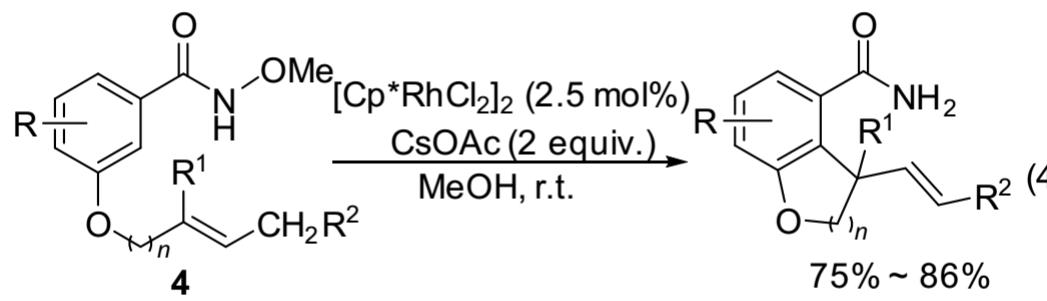
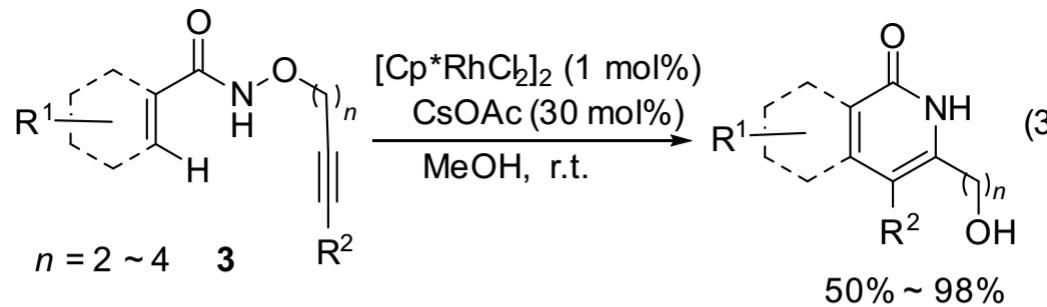


Rhodium catalyzed C–H functionalization between derivatives of N-hydroxybenzamide and alkenes

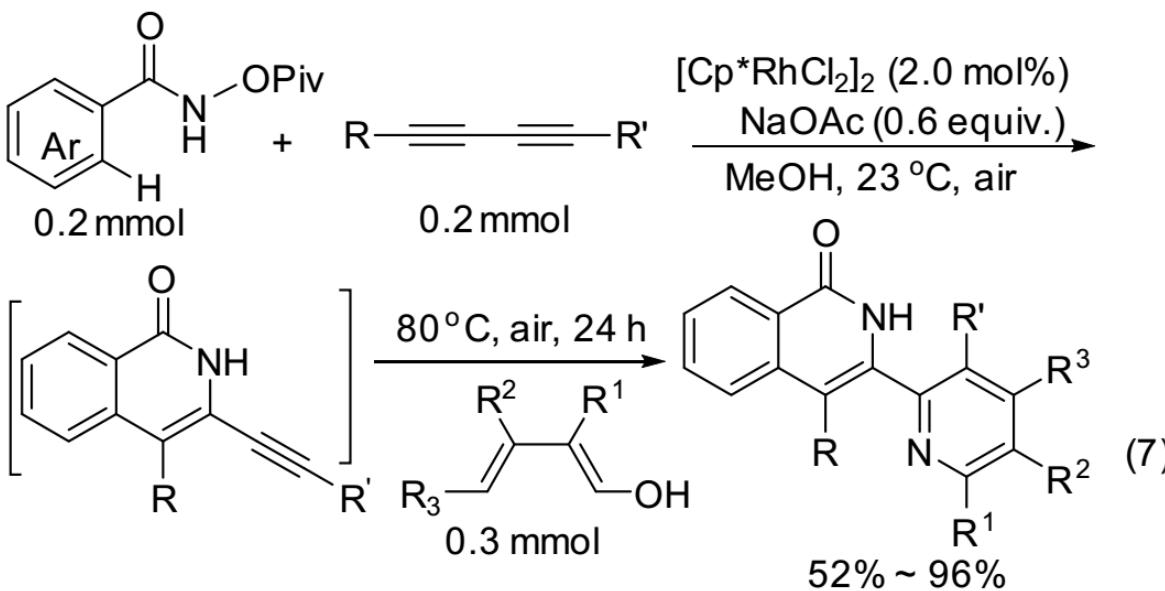
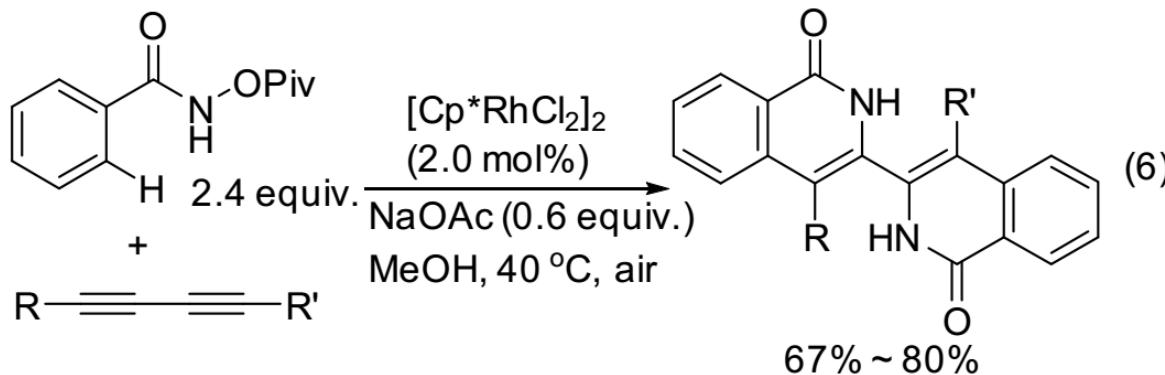
- Switching reaction pathway through different oxidizing directing groups



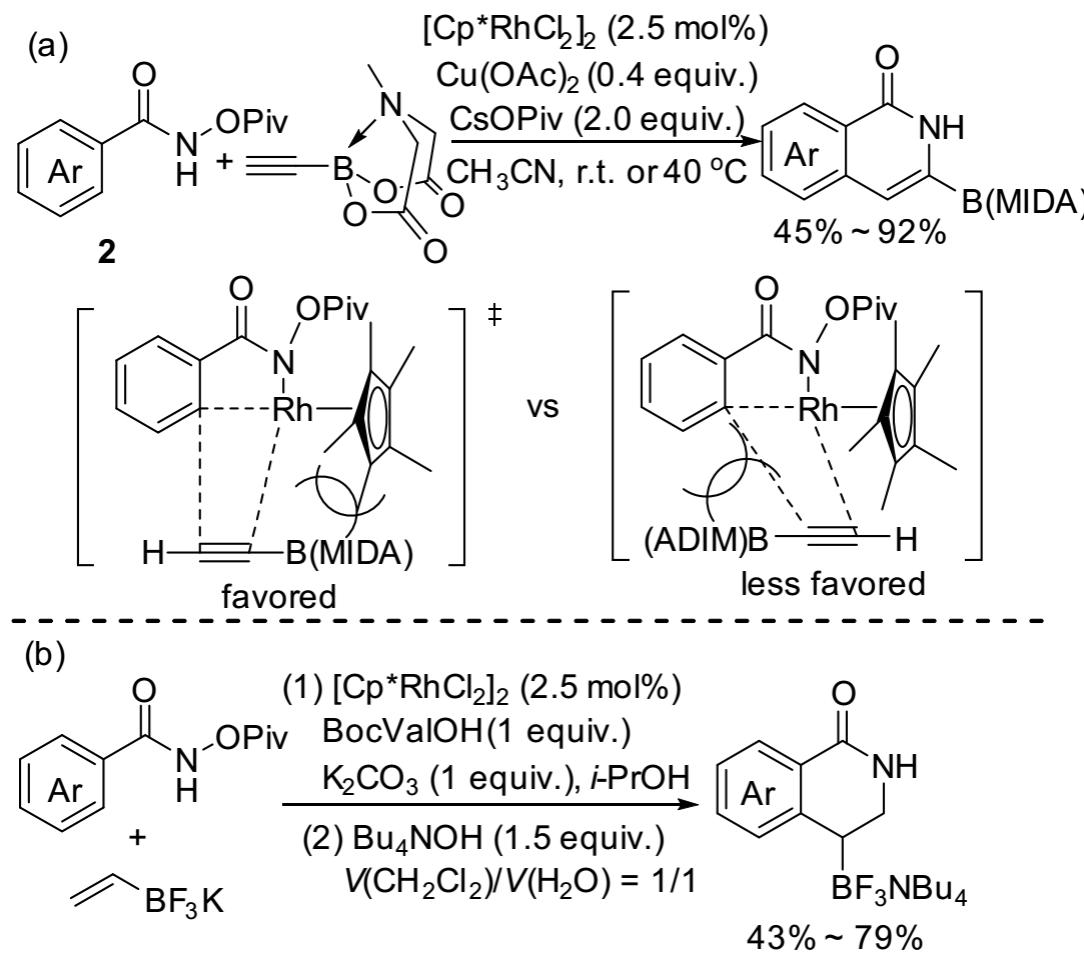
Rhodium(III)-Catalyzed Intramolecular Annulation



Synthesis of Diverse Bisheterocycles of 1,3-Diyne

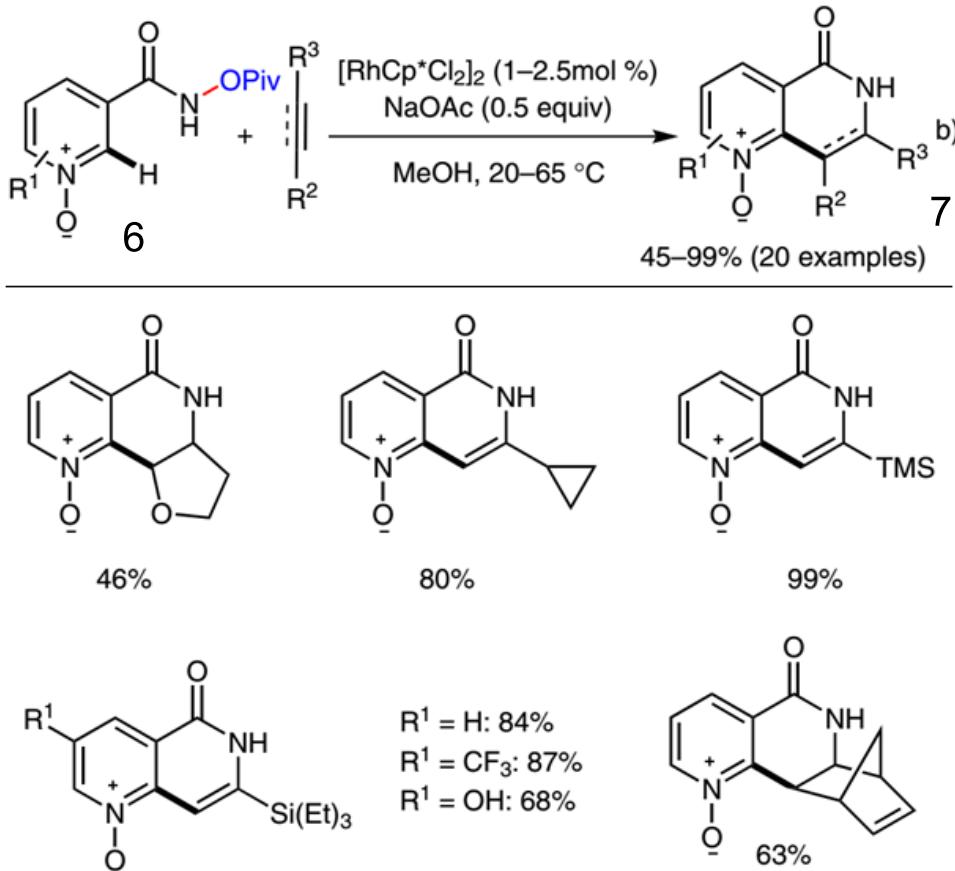


Rh(III)-Catalyzed C–H Activation and Annulation with Alkyne MIDA Boronates

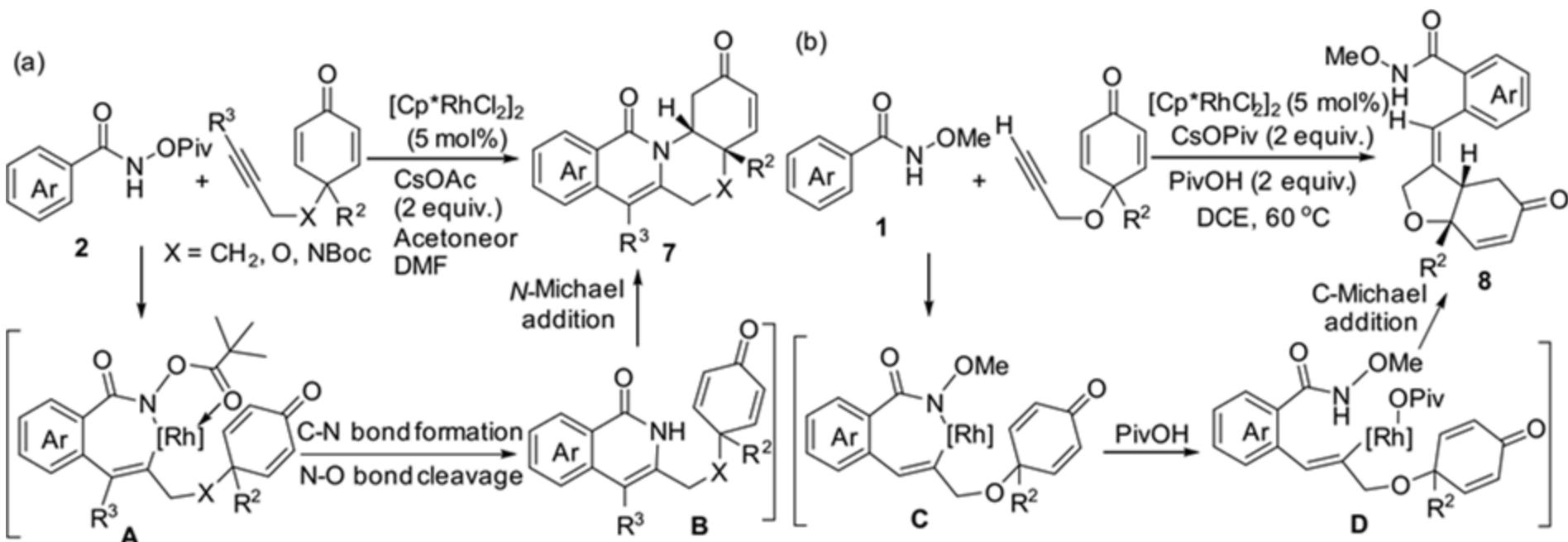


Wang, H.; Glorius, F. *J. Am. Chem. Soc.* **2012**, *134*, 19592.
Presset, M.; Molander, G. A. *Org. Lett.* **2013**, *15*, 1528.

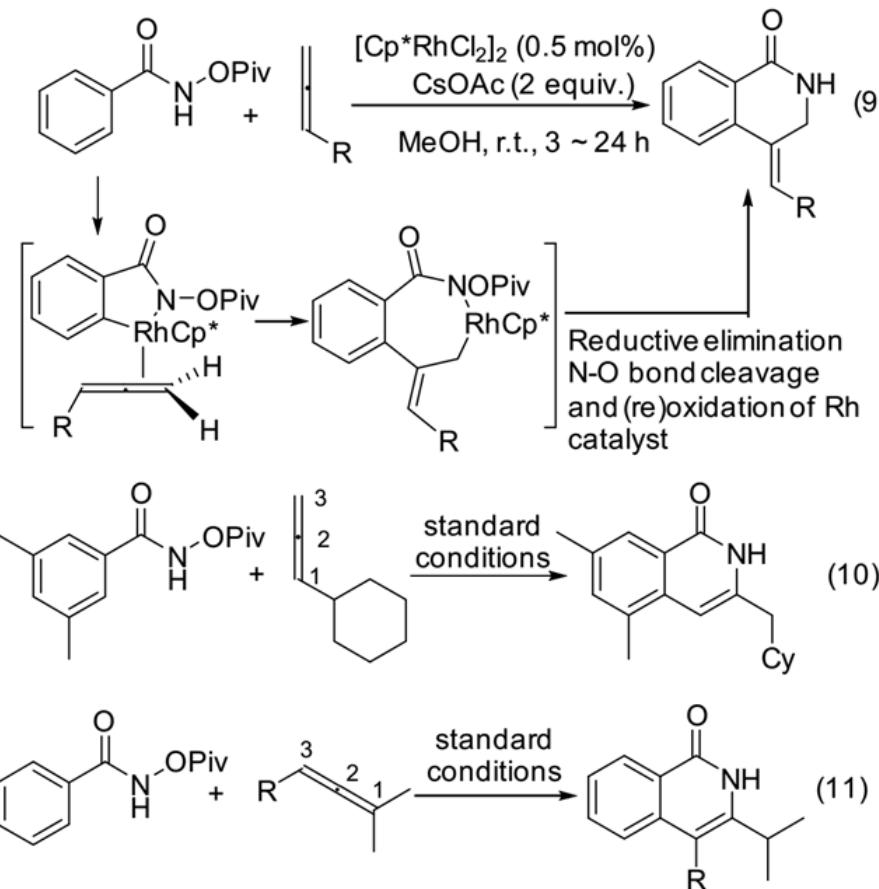
Rh(III)-Catalyzed C–H Activation for the Regioselective Synthesis of Naphthyridinones



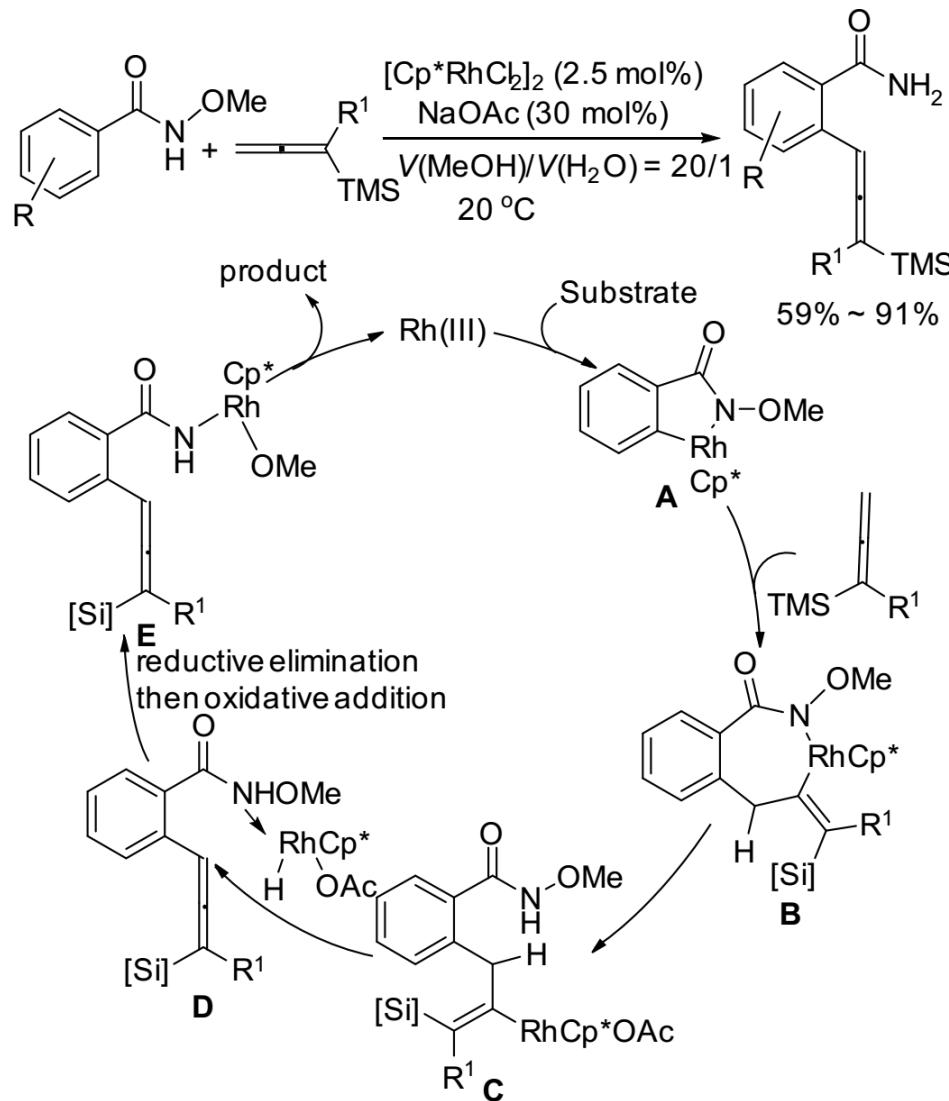
Rh(III)-Catalyzed Cyclization of Benzamides and 1,6-Enynes



Rhodium(III)-Catalyzed C–H Activation and intermolecular Annulation with Allenes

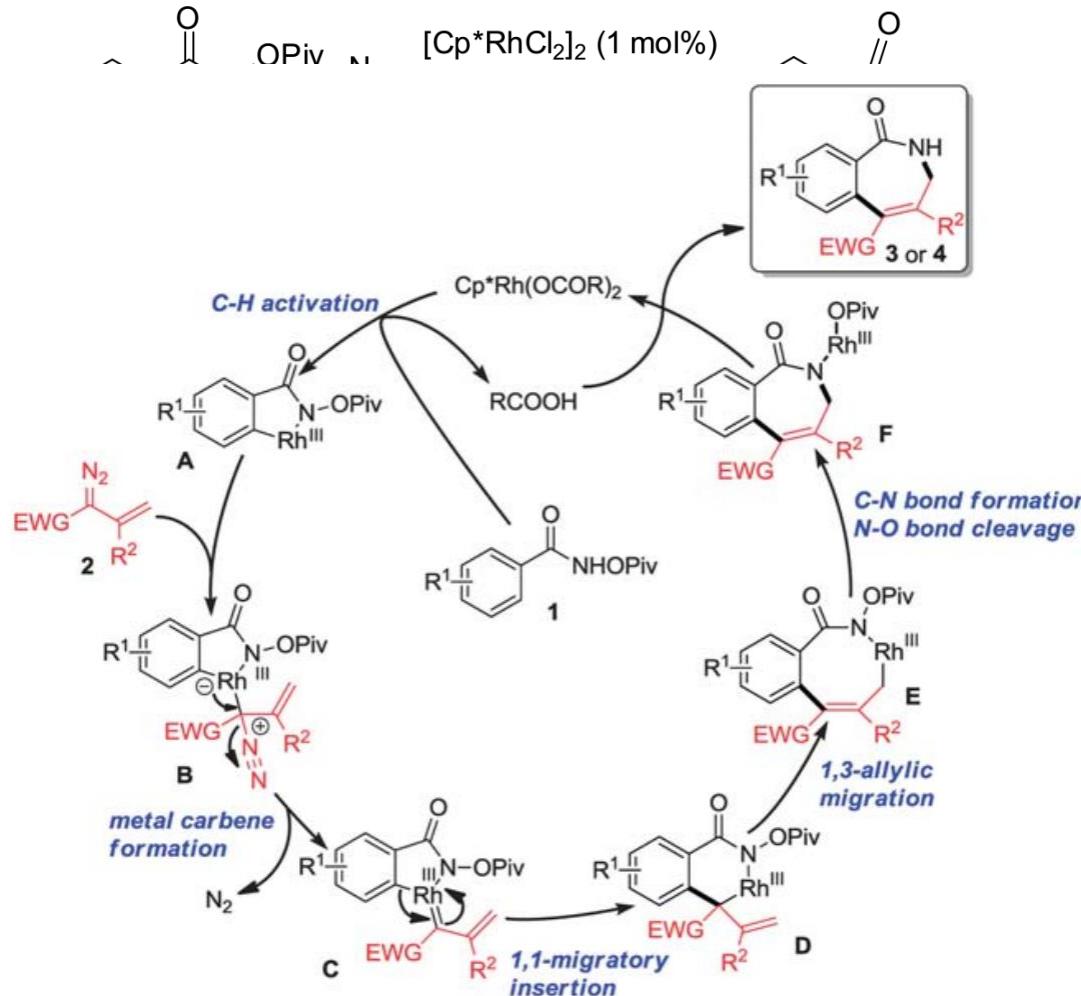


Formation of Trisubstituted Allenes Using Allenylsilanes

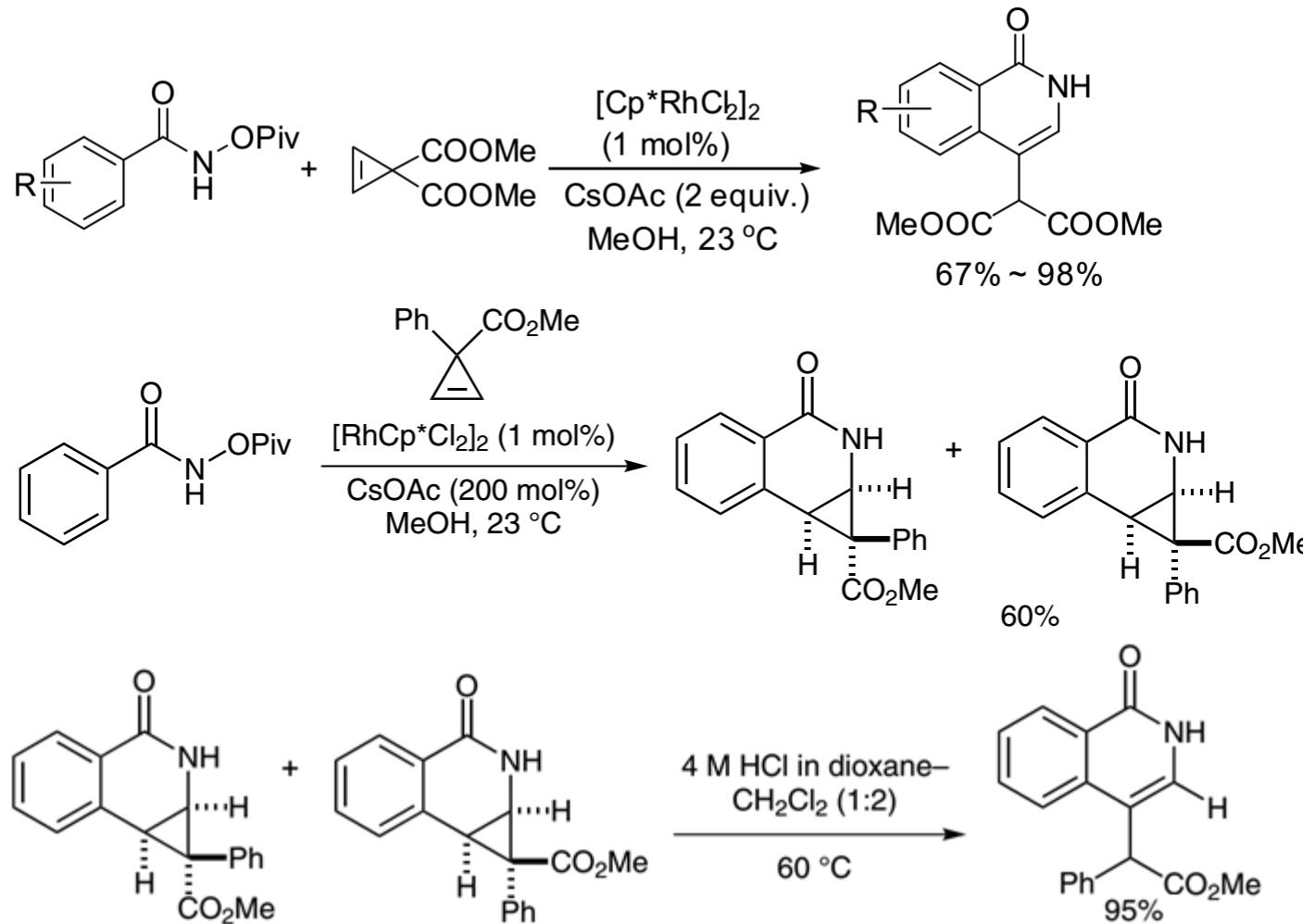


Zeng, R.; Wu, S.; Fu, C. L.; Ma, S. *J. Am. Chem. Soc.* **2013**, 135, 18284.

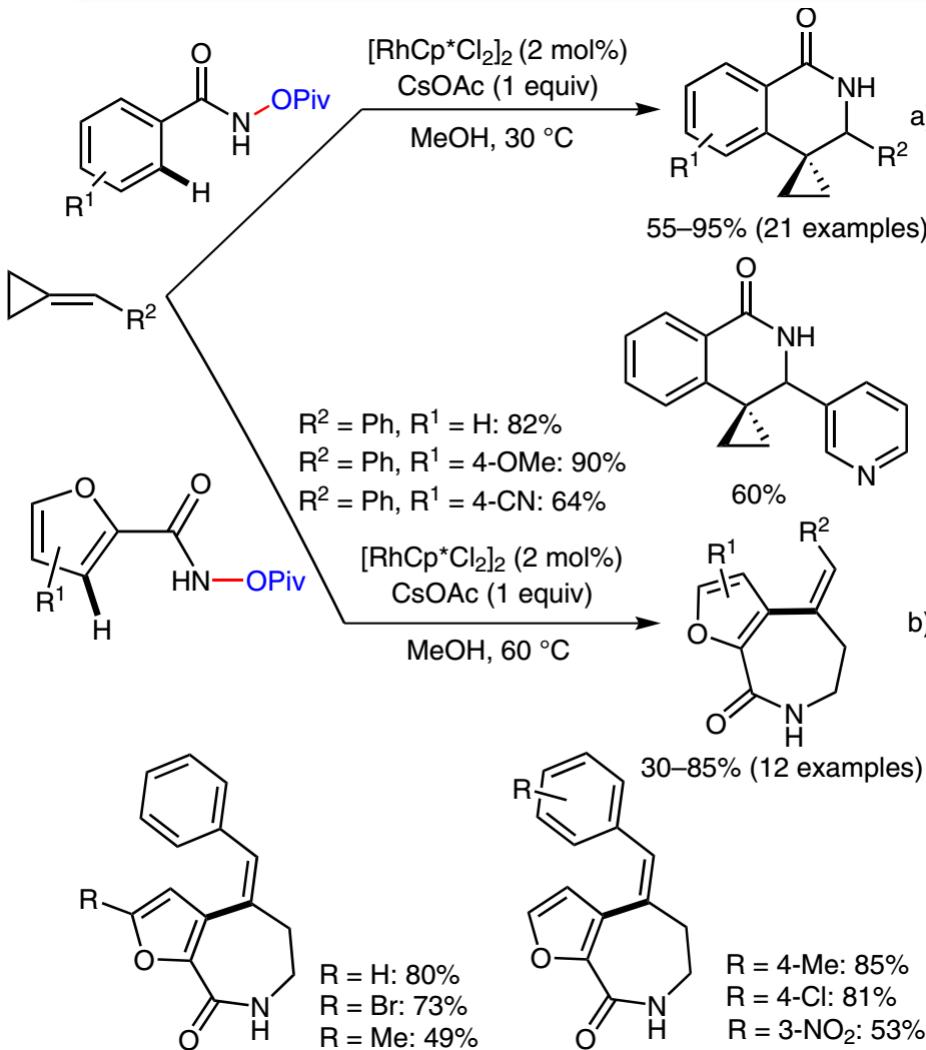
Rh(III)-Catalyzed Coupling of Benzamides and Diazo Compounds



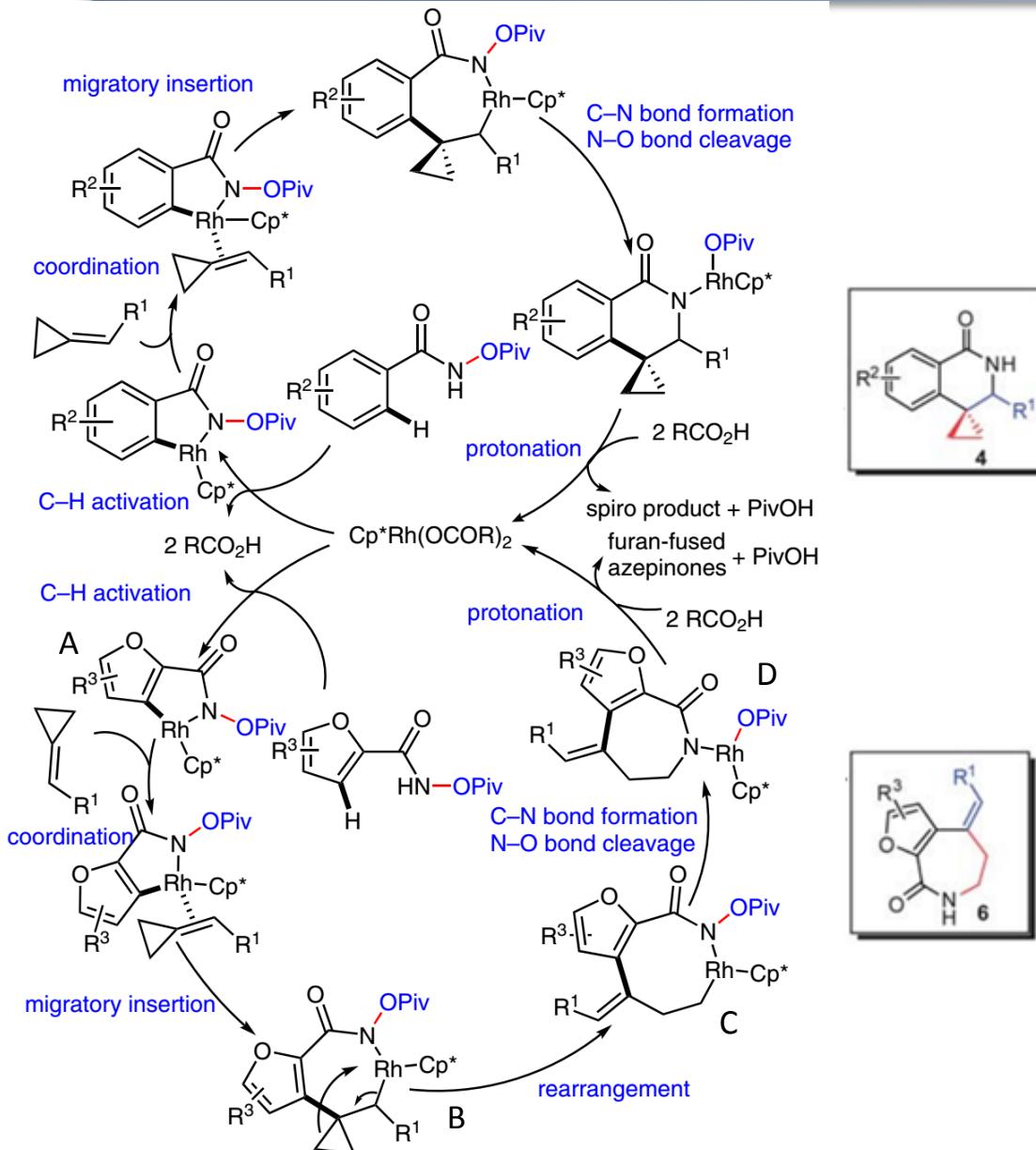
Synthesis of Isoquinolones from Amides and Cyclopropenes



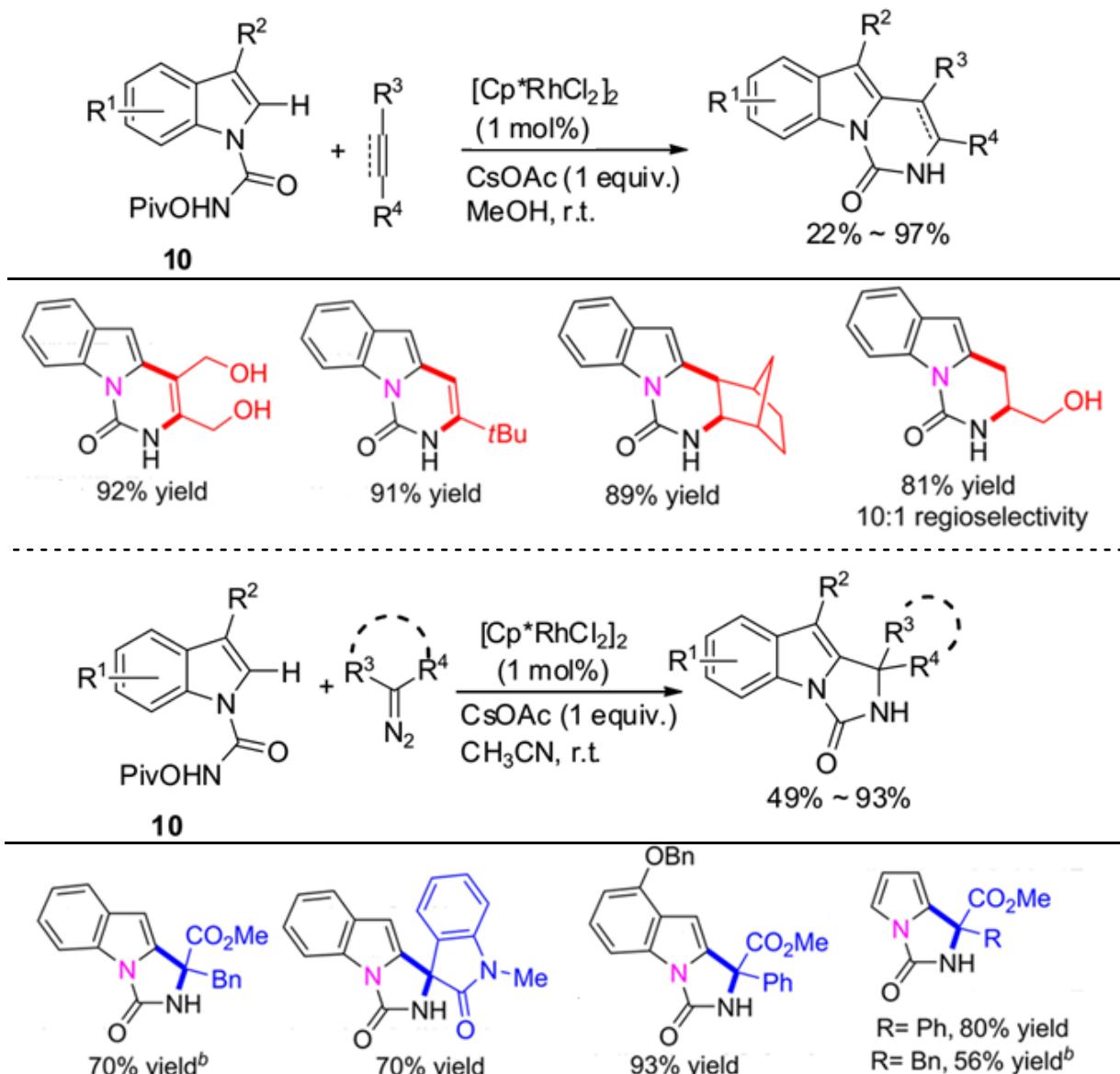
Rh(III)-catalyzed C–H Activation/Cycloaddition of Benzamides and Methylenecyclopropanes



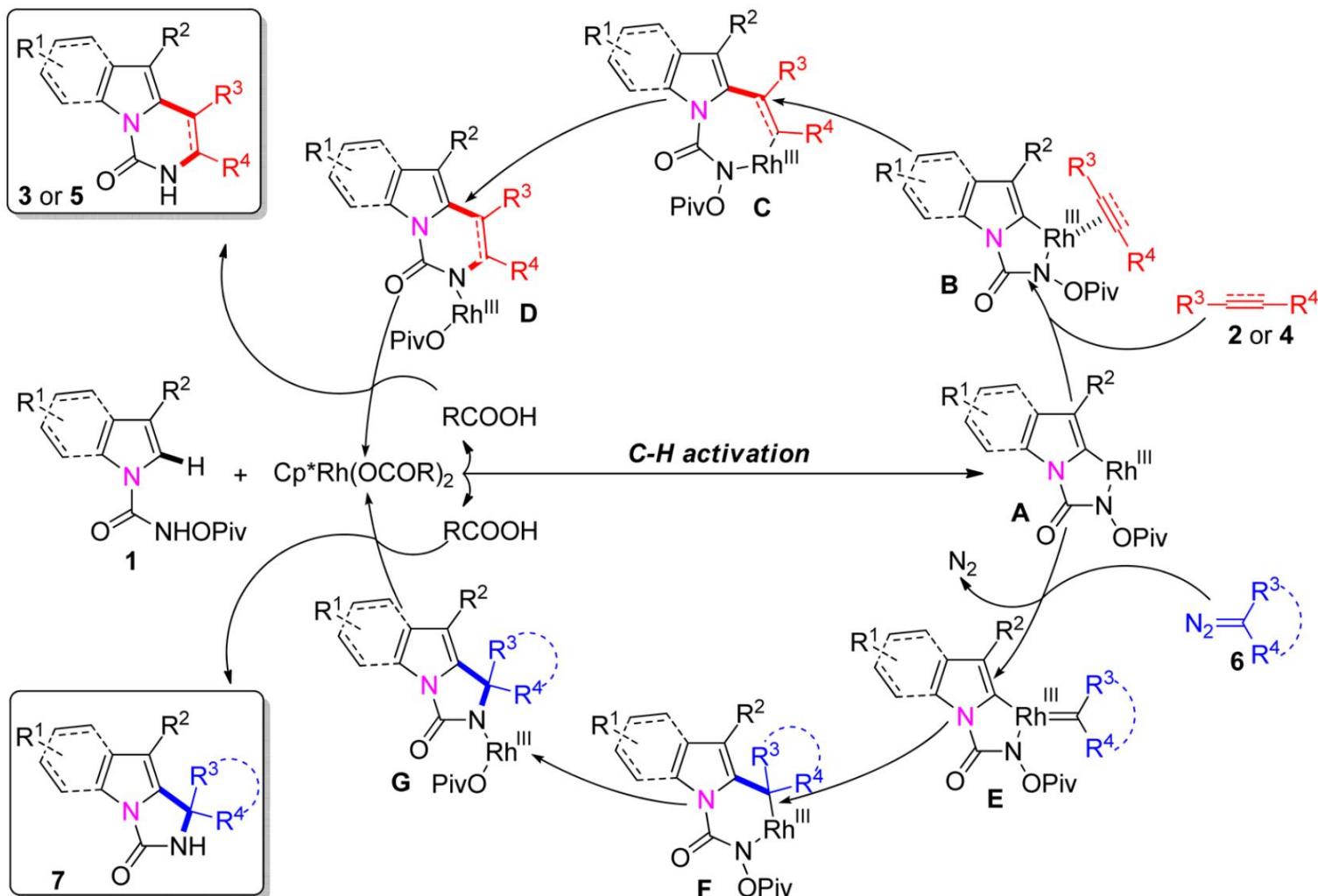
Proposed Mechanism



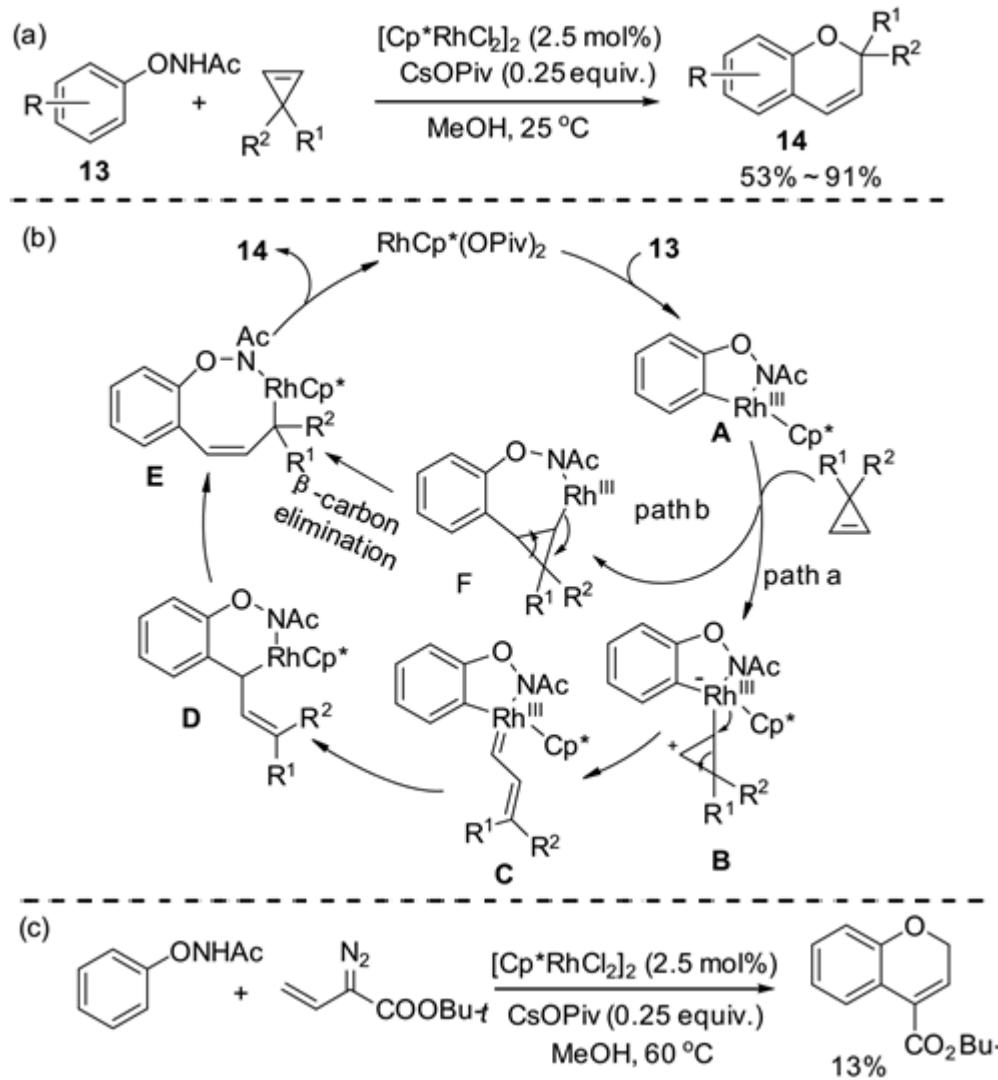
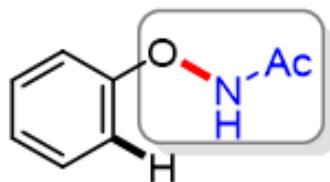
Rh(III)-Catalyzed C–H Activation/Cyclization of Indoles and Pyrroles



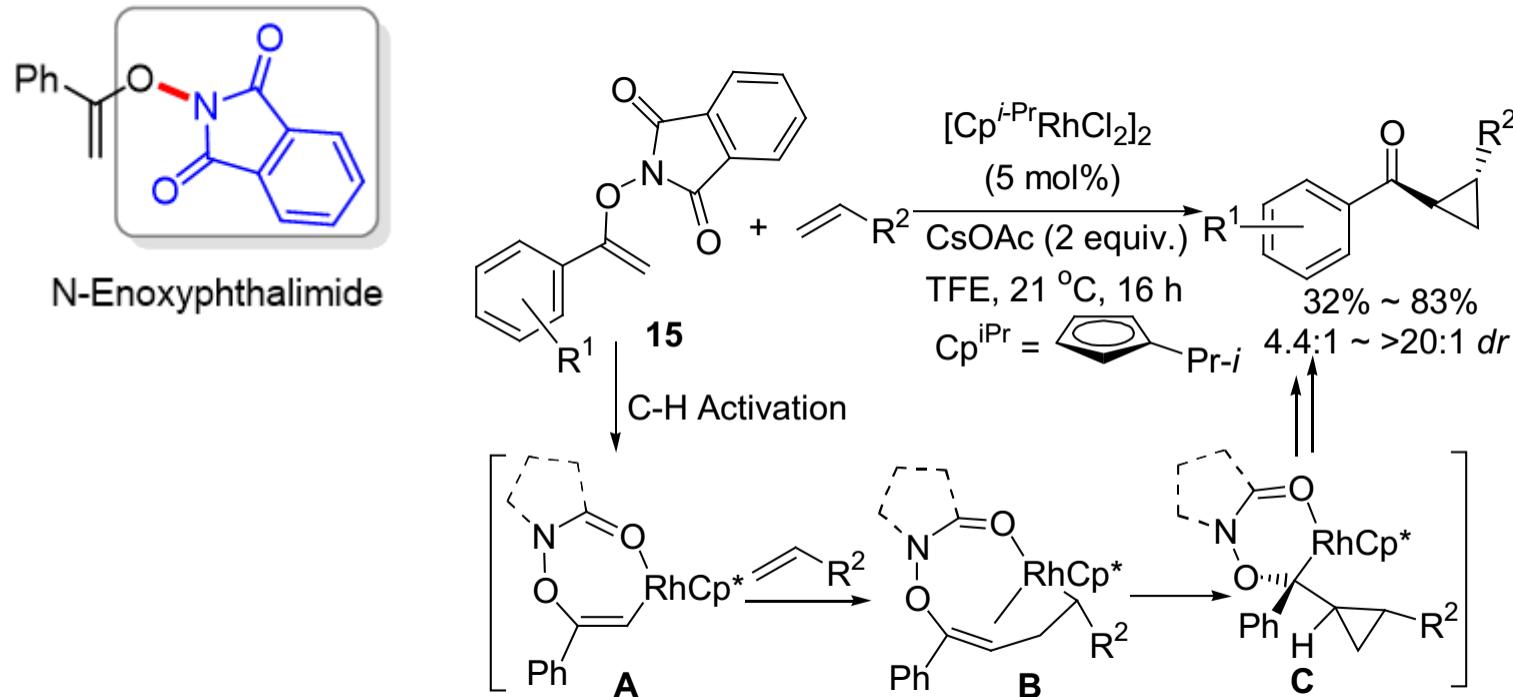
Proposed Mechanism



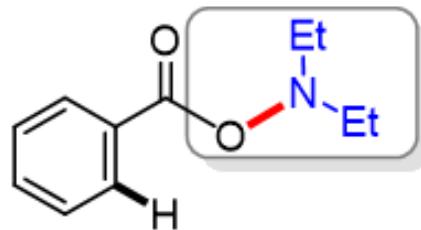
Rhodium catalyzed coupling between *N*-phenoxyamides and cyclopropenes



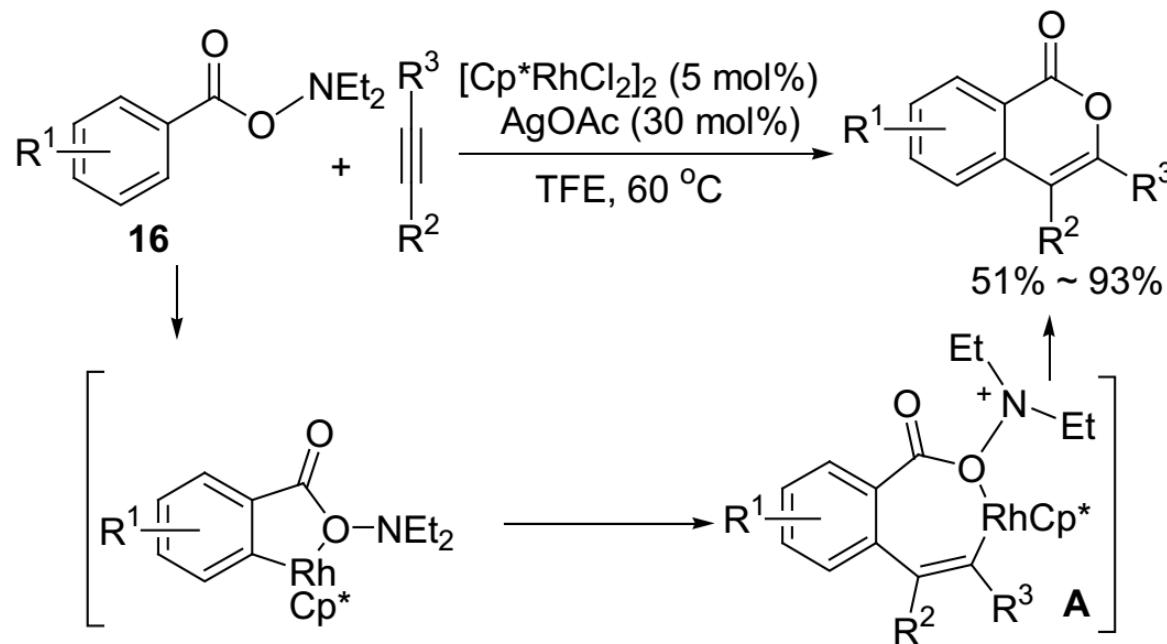
Rh(III)-Catalyzed Cyclopropanation Initiated by C–H Activation



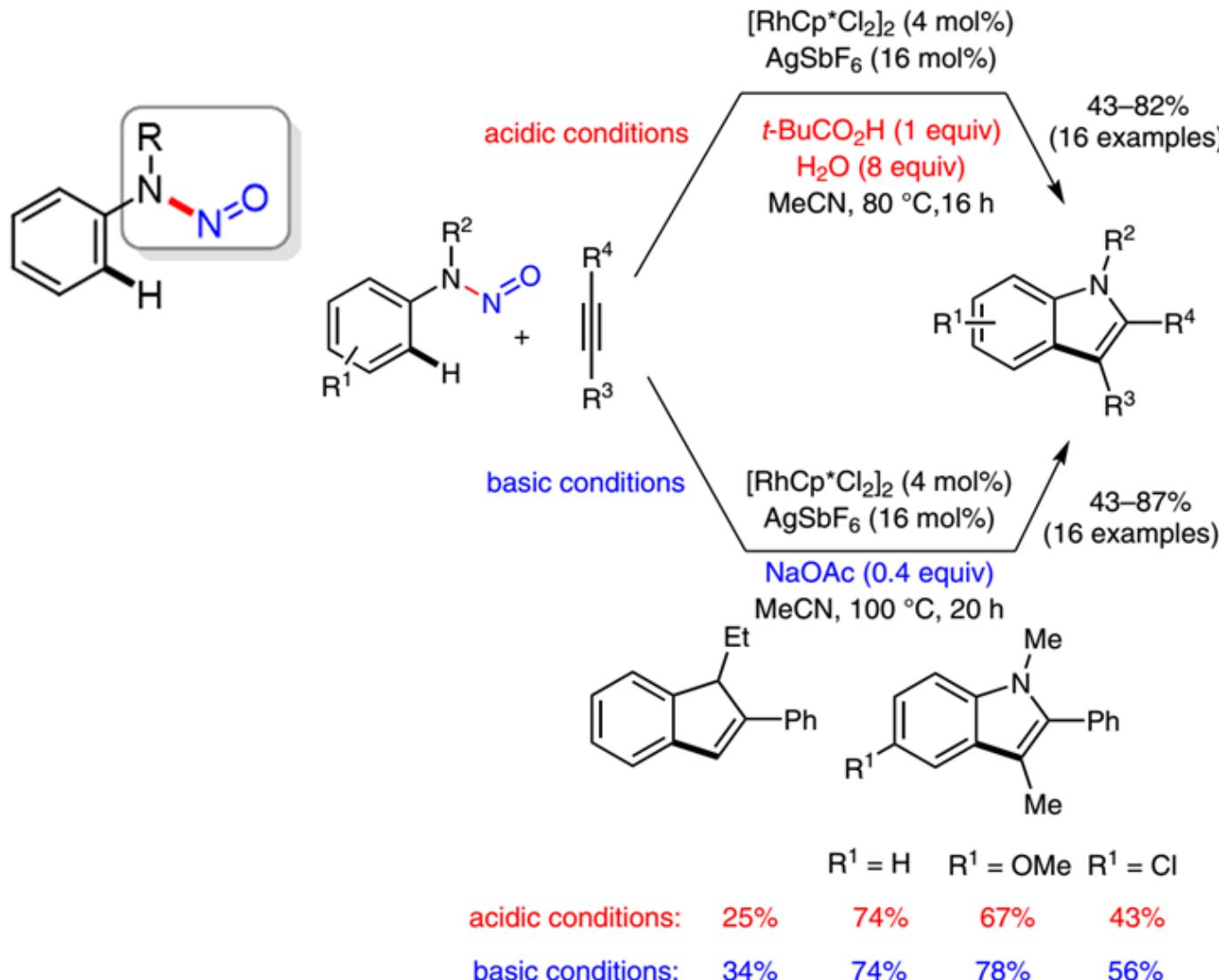
Rhodium catalyzed cyclization of *O*-benzoyl-*N,N*-diethylhydroxylamine with alkynes



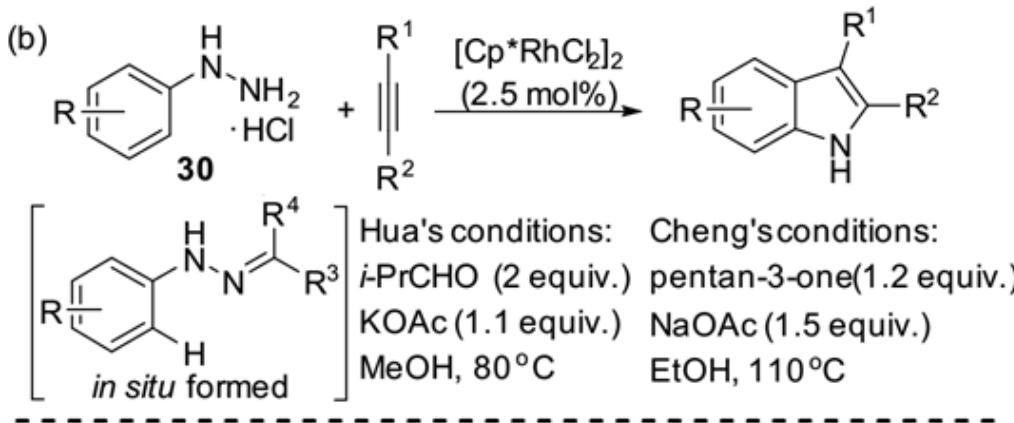
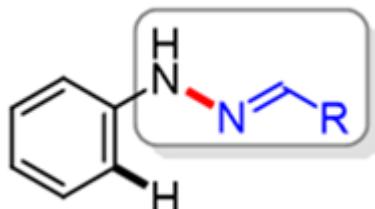
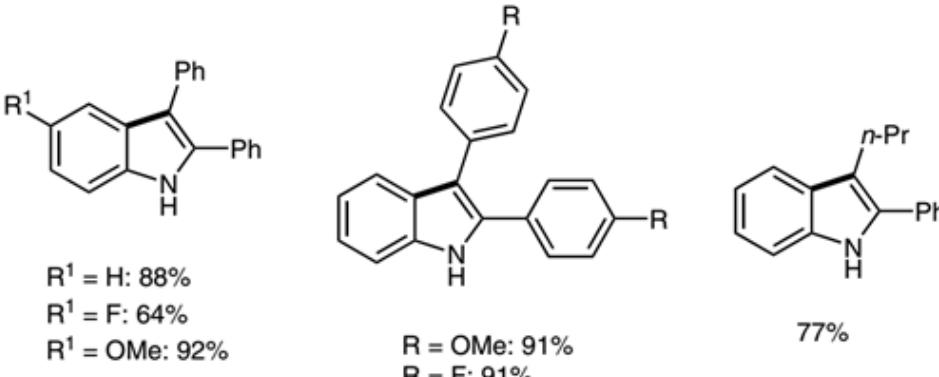
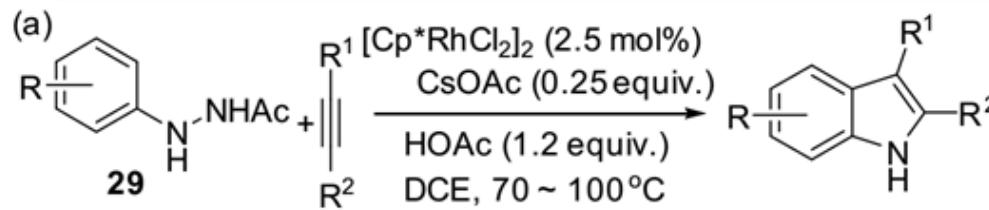
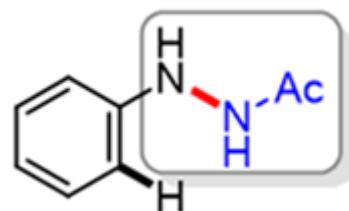
N,N-diethyl-*O*-benzoylhydroxylamine



The N–N Bond as Internal Oxidant Directing Group



Synthesis of Indoles Using N—N Bond as the Internal Oxidant

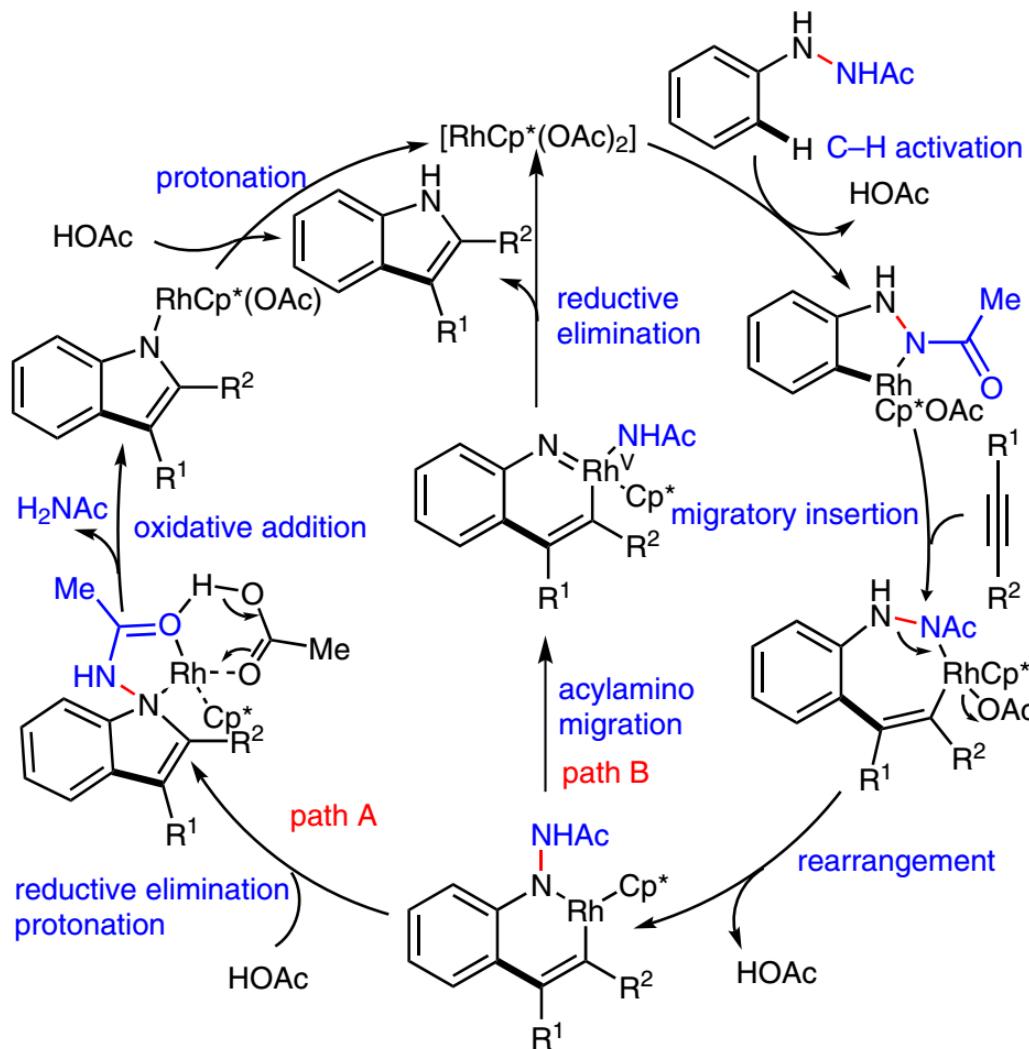


Zhao, D.; Shi, Z.; Glorius, F. *Angew. Chem., Int. Ed.* **2013**, 52, 12426.

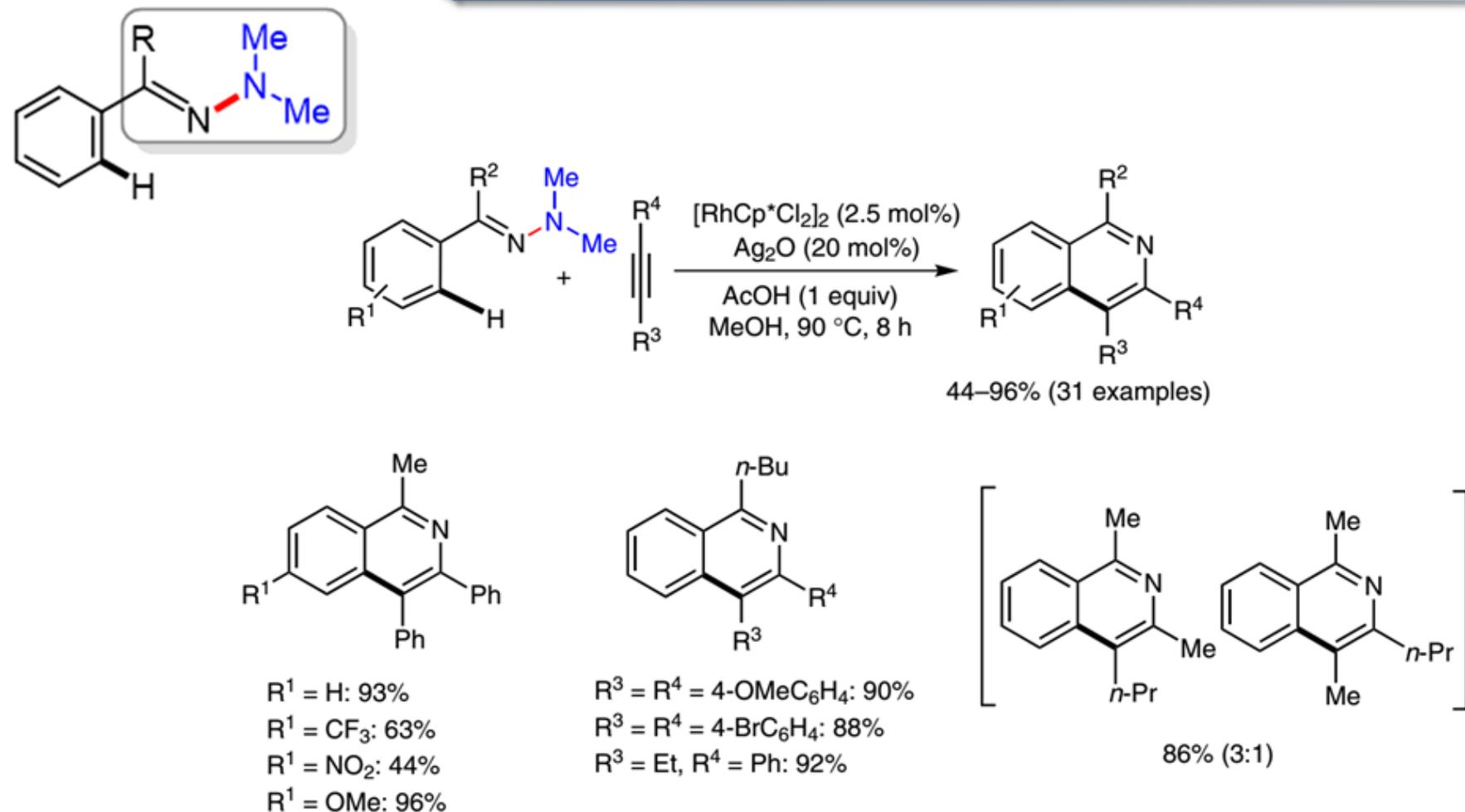
Zheng, L.; Hua, R. *Chem. Eur. J.* **2014**, 20, 2352.

Muralirajana, K.; Cheng, C. H. *Adv. Synth. Catal.* **2014**, 356, 1571.

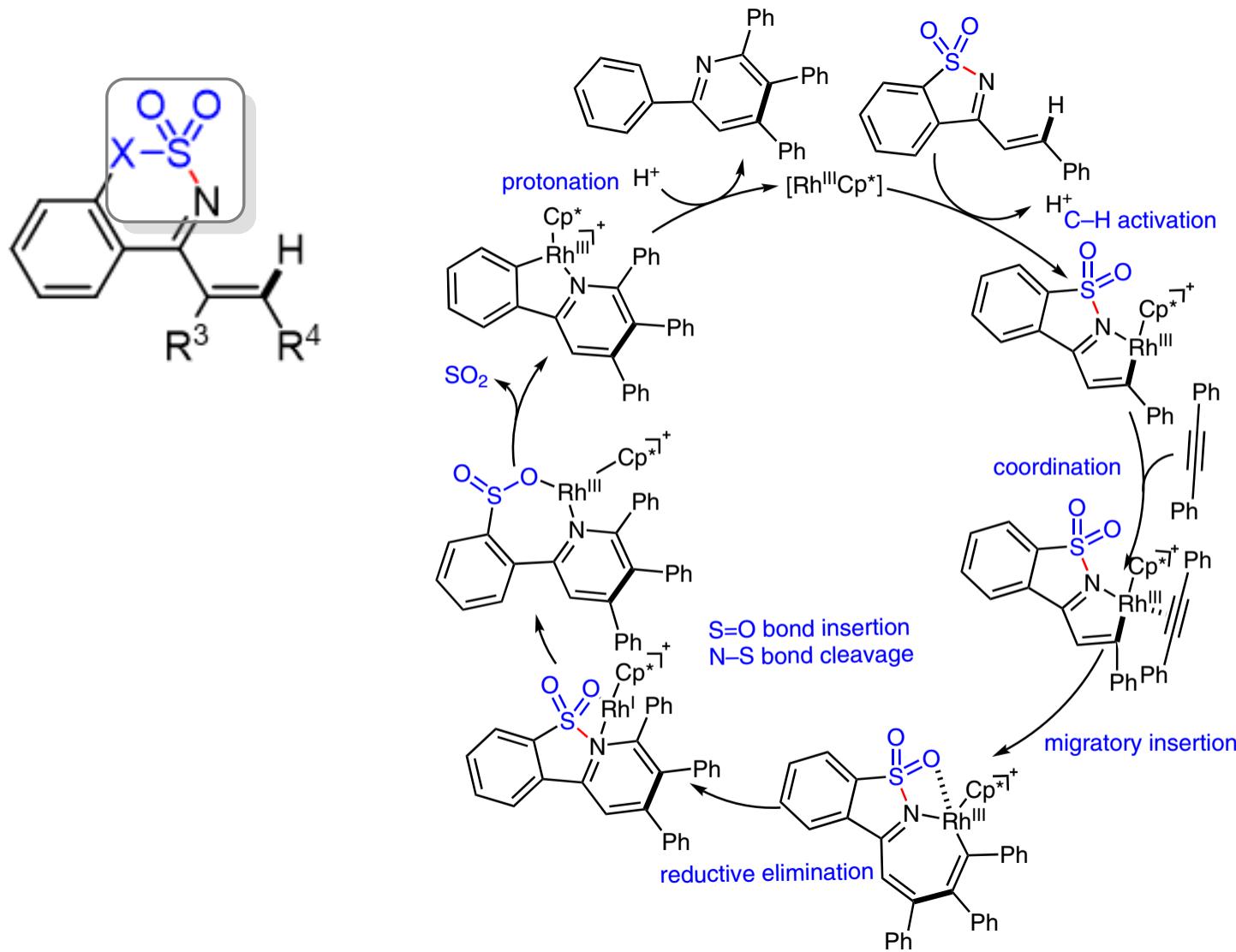
Proposed reaction mechanism for the indole synthesis from hydrazine



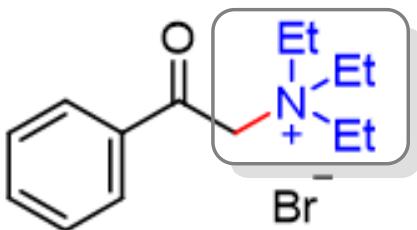
Rhodium(III)-catalyzed the formation of isoquinolines using hydrazine as an oxidizing directing group



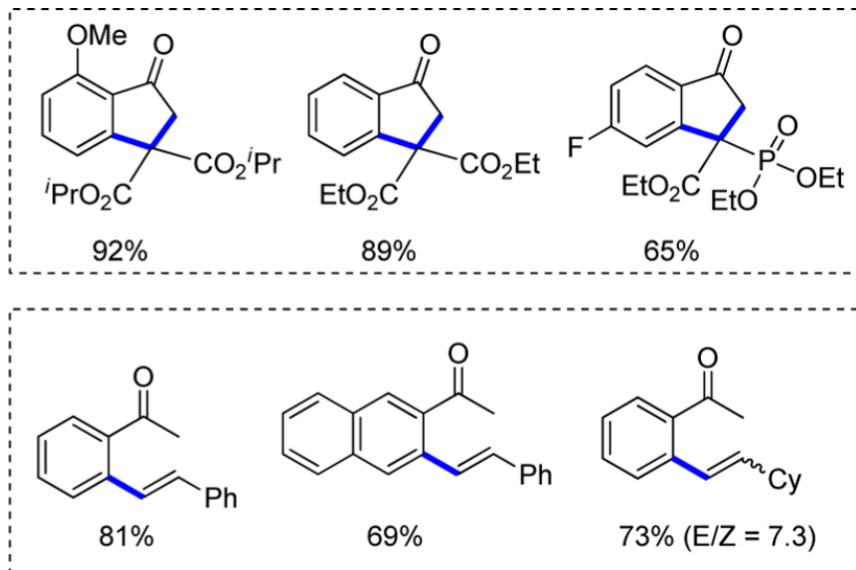
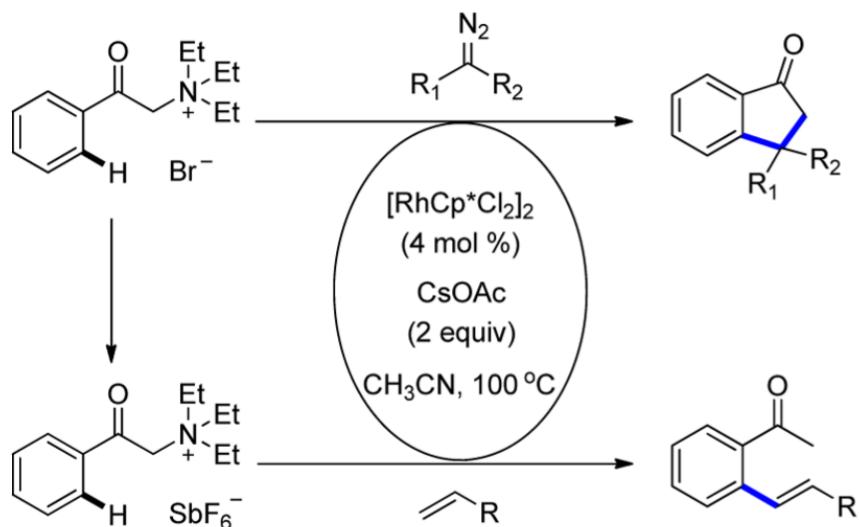
The N–S Bond as Internal Oxidant Directing Group



The C–N Bond as Internal Oxidant Directing Group



► Rhodium-Catalyzed C–H Activation of Phenacyltriethylammonium



Conclusions

- ❖ The ‘internal oxidant’ strategy has emerged as a powerful tool in metal-catalyzed direct C-H activation reactions;
- ❖ As direction group: improve the reactivity and selectivity of C-H functionalization, broaden the substrate scope and decreasing the amount of waste formation;
- ❖ Further development focus on finding new types of internal oxidants and improving the mechanistic understanding.

THANK YOU FOR YOUR ATTENTION!

