



Transition-Metal-Catalyzed C–H Functionalization for the Synthesis of Substituted Pyridines

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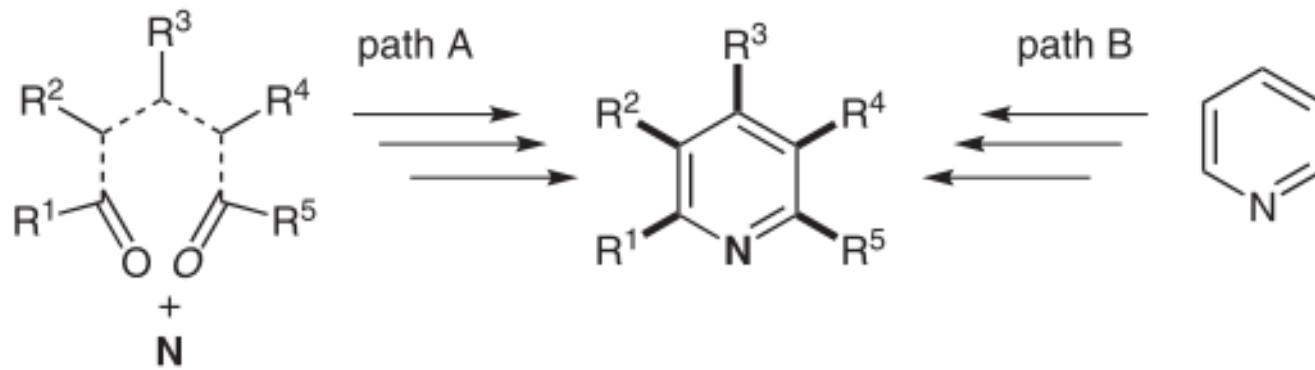


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Background

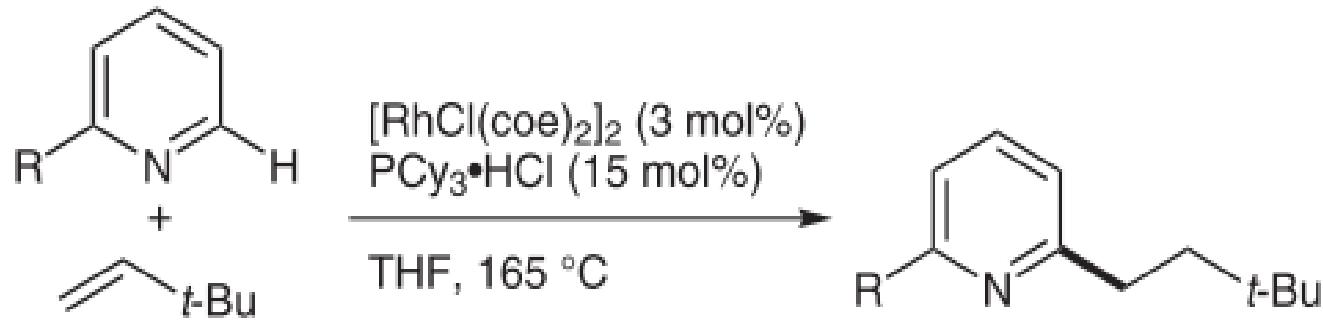


Challenge:

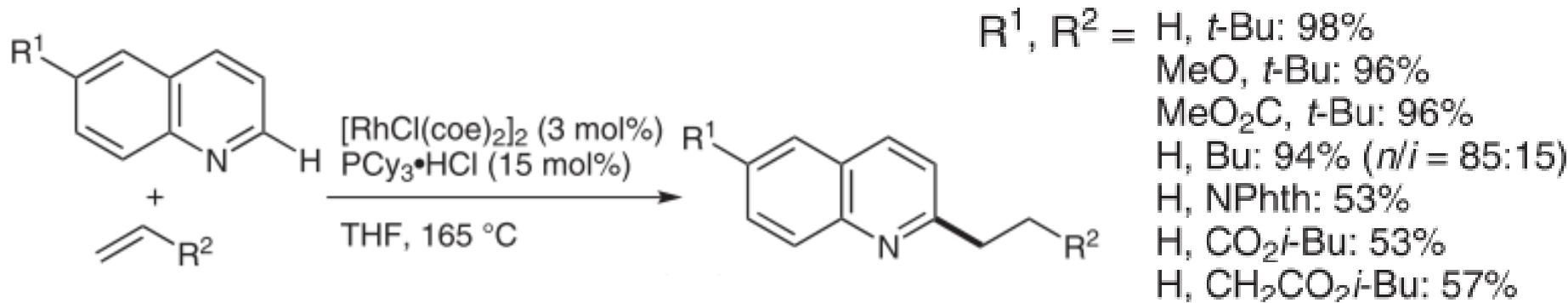
electron-poor;

N-bound coordination mode with metal centers.

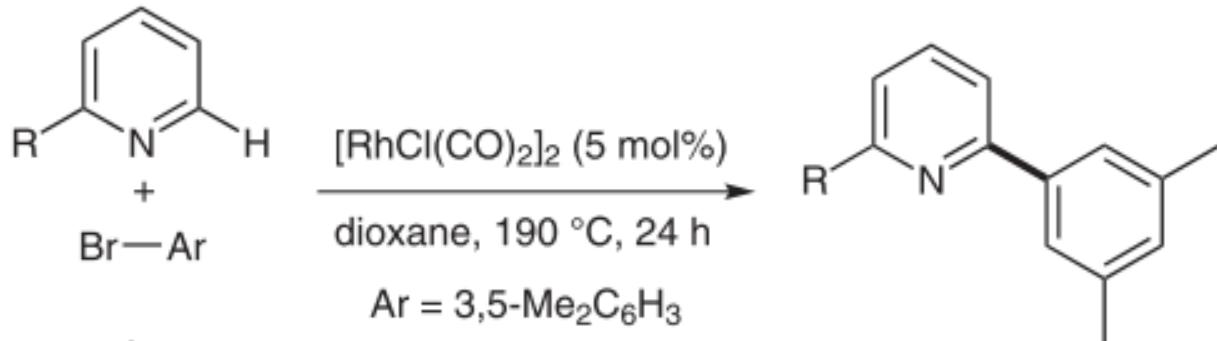
C₂-Selective Functionalization ---alkylation



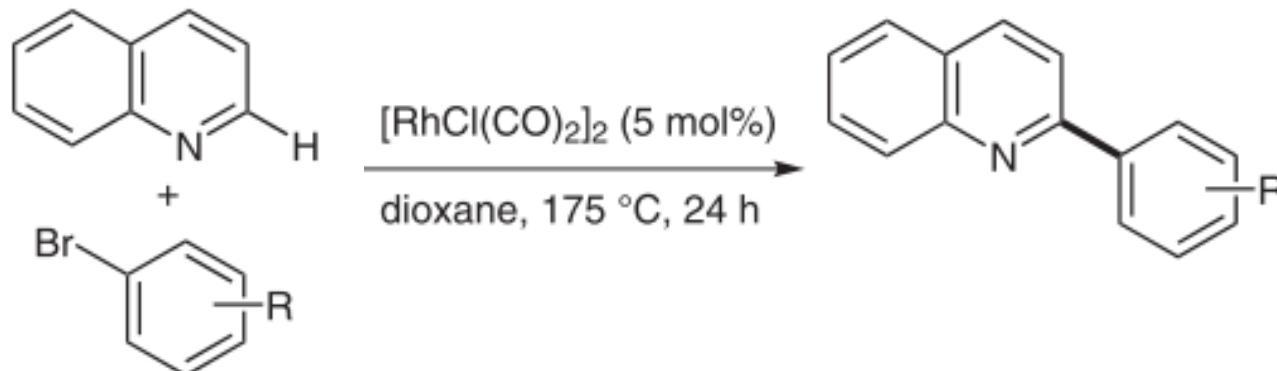
R = H: <5%
Me: 59%
i-Pr: 83%
(*i*-Pr)₃Si: 64%



C₂-Selective Functionalization ---arylation



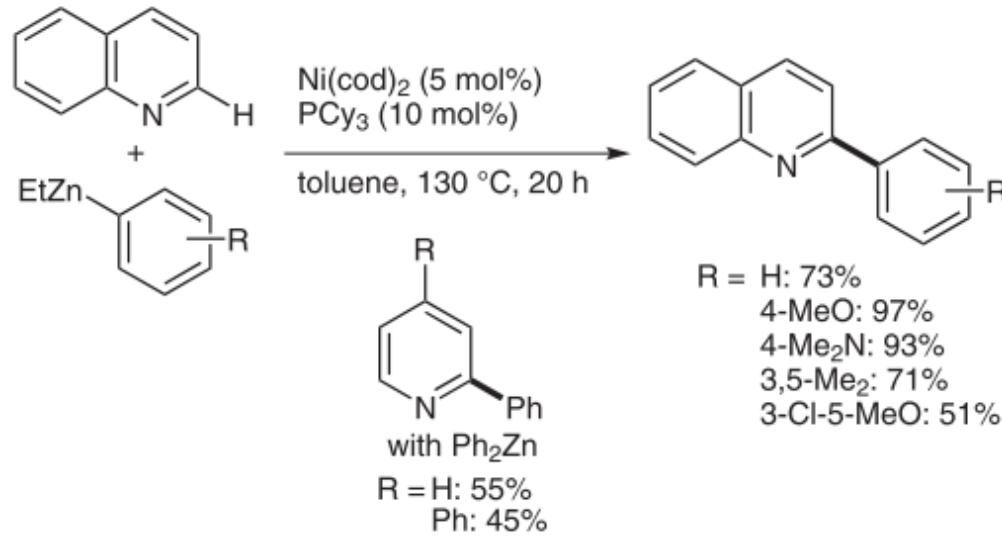
R = H: <5%
Me: 53%
Ph(CH₂)₃: 51%
i-Bu: 78%
Et₂CH: 70%



R = H: 74%
4-PhO: 62%
4-Me: 69%
4-Ph: 77%
4-F: 69%
4-Cl: 68%
4-EtC(O): 70%
4-F₃C: 65%
3-*i*-PrO: 70%
3,5-Me₂: 86%

- a) Berman, A. M.; Lewis, J. C.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 14926.
 b) Wiedemann, S. H.; Lewis, J. C.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 2452.

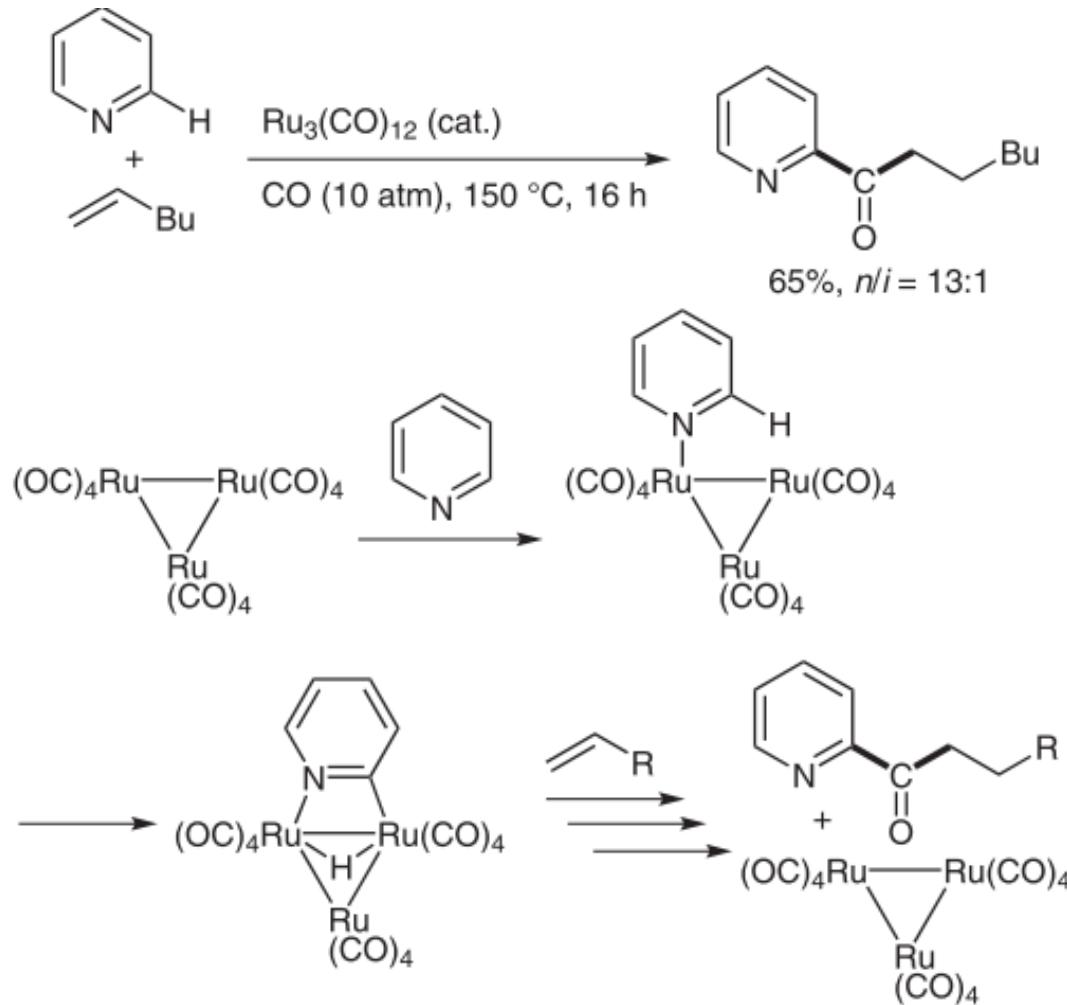
C₂-Selective Functionalization ---arylation



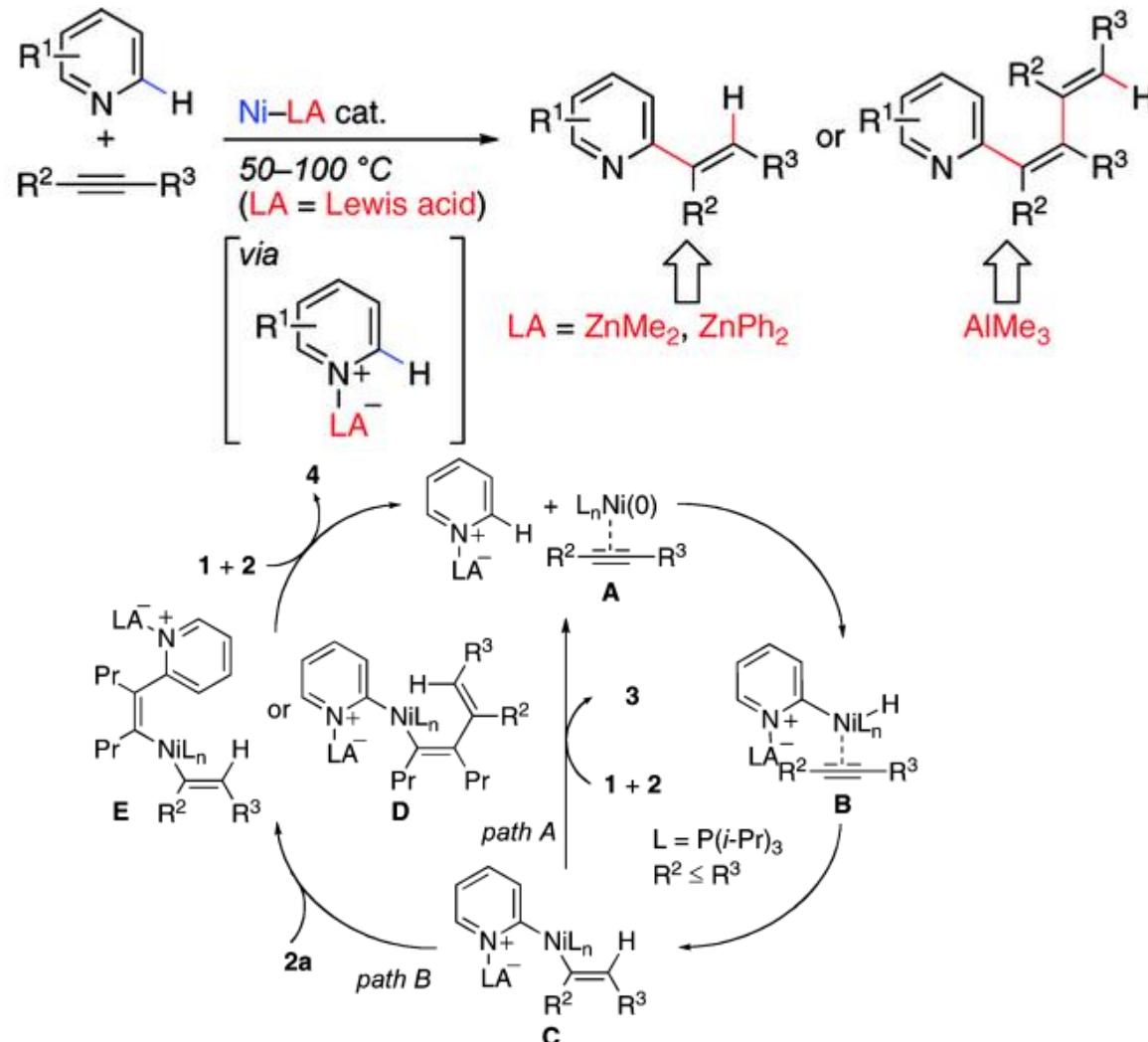
a) Tobisu, M.; Hyodo, N.; Chatani, N. *J. Am. Chem. Soc.* **2009**, *131*, 12070.

b) Colombe, J. R.; Bernhardt, S.; Stathakis, C.; Buchwald, S. L.; Knochel, P. *Org. Lett.* **2013**, *15*, 5754

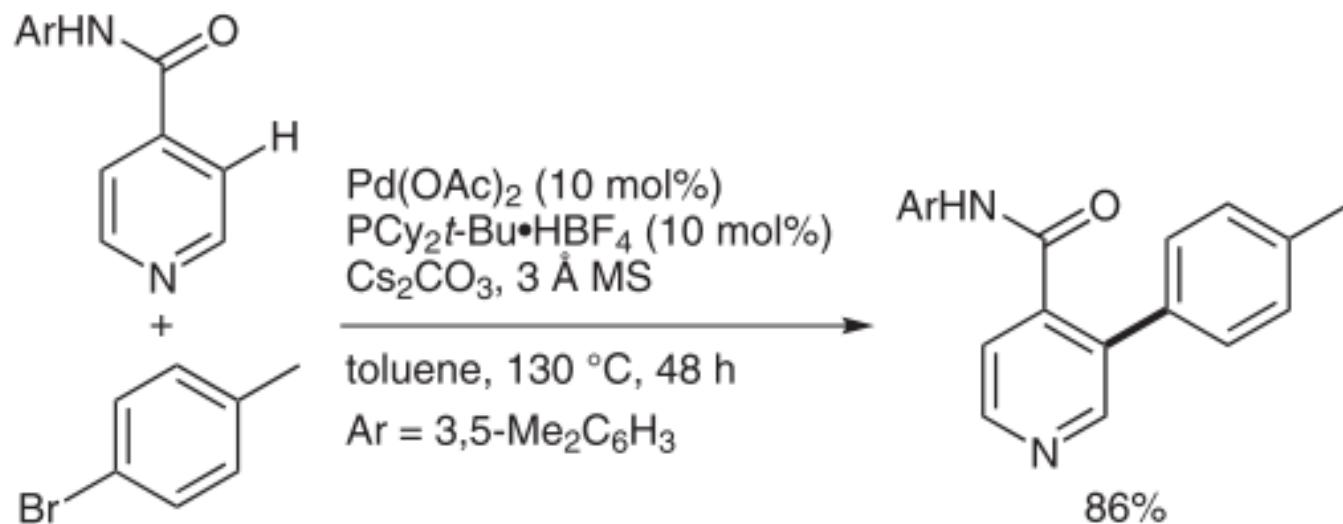
C₂-Selective Functionalization ---acylation



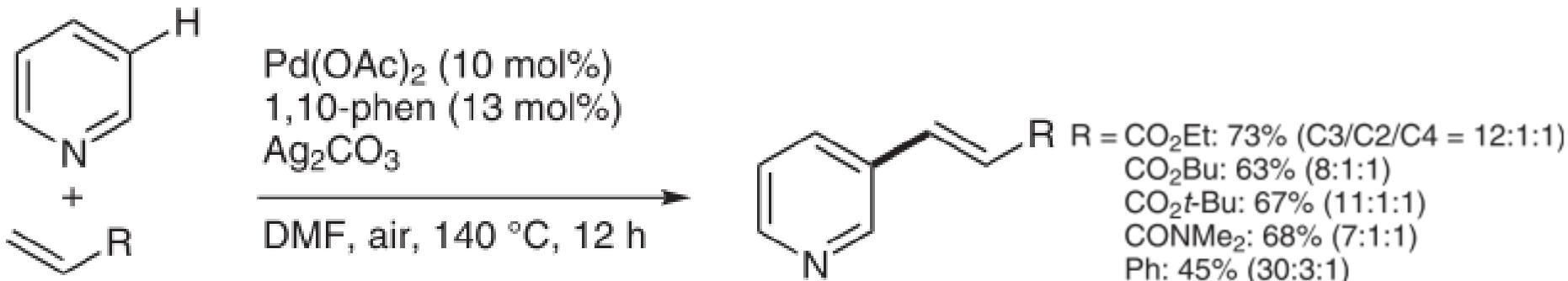
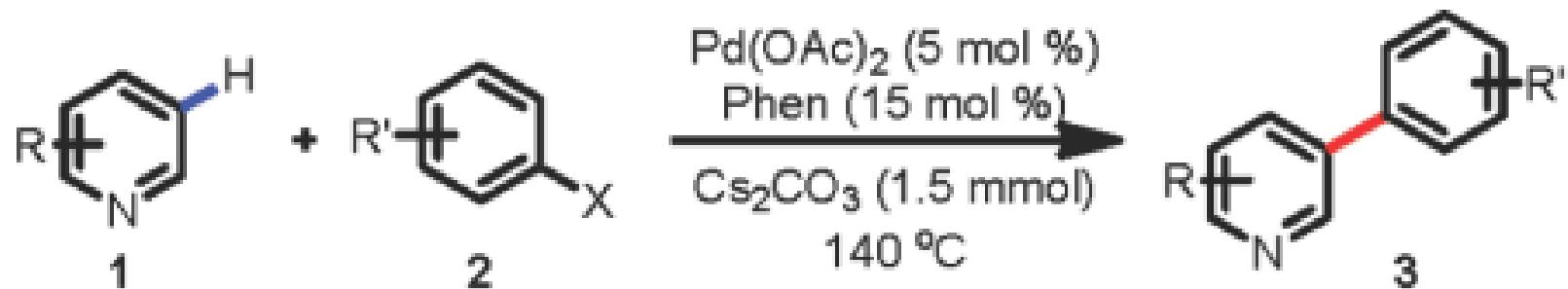
C₂-Selective Functionalization ---alkenylation



C3-Selective Functionalization ---arylation

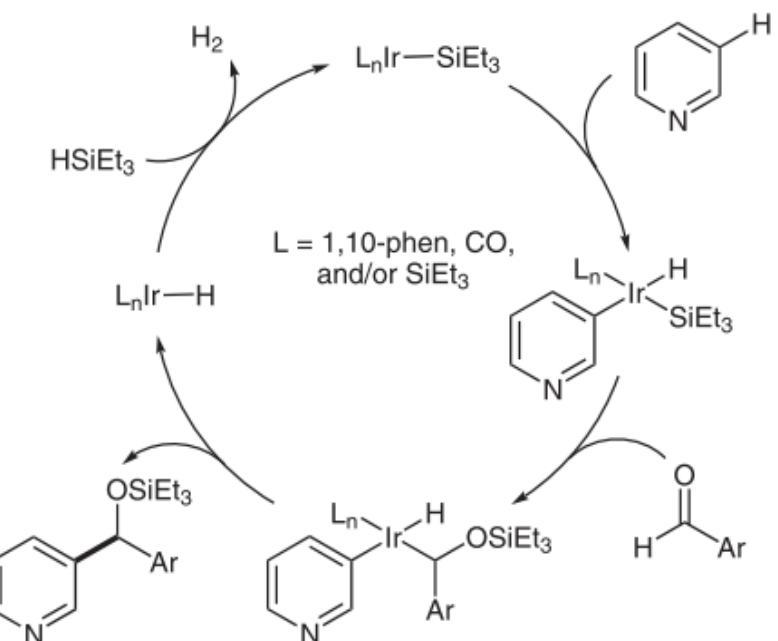
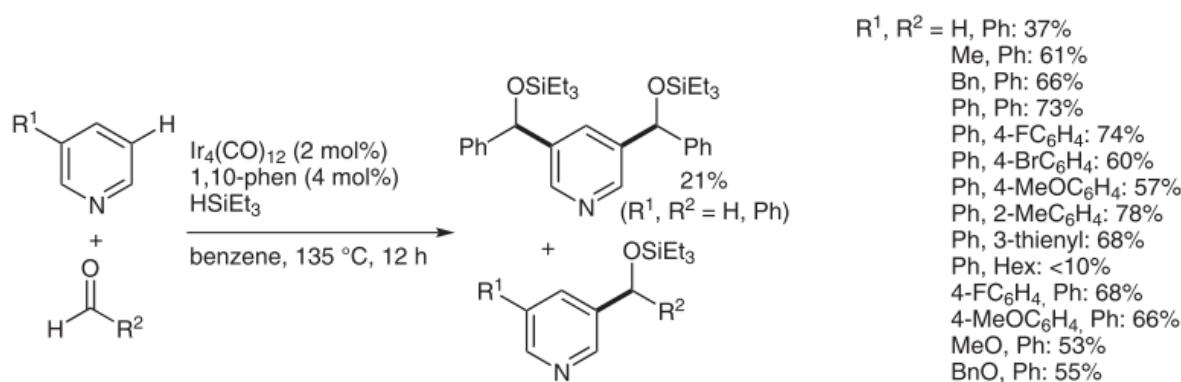


C₃-Selective Functionalization ---arylation and alkenylation



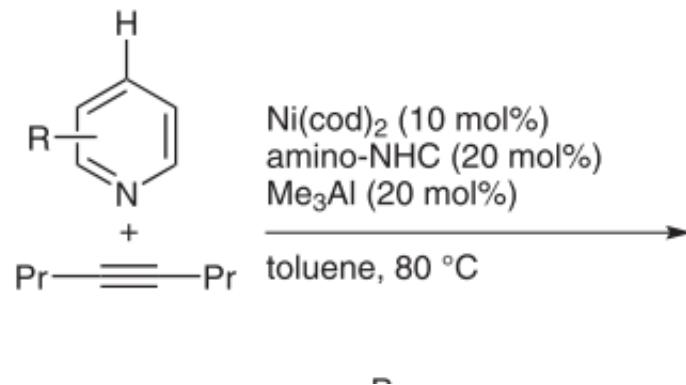
- a) Ye, M.-C.; Gao, G.-L.; Edmunds, A. J. F.; Worthington, P. A.; Morris, J. A.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 19090.
 b) Ye, M.; Gao, G.-L.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 6964.

C₃-Selective Functionalization ---alkylation

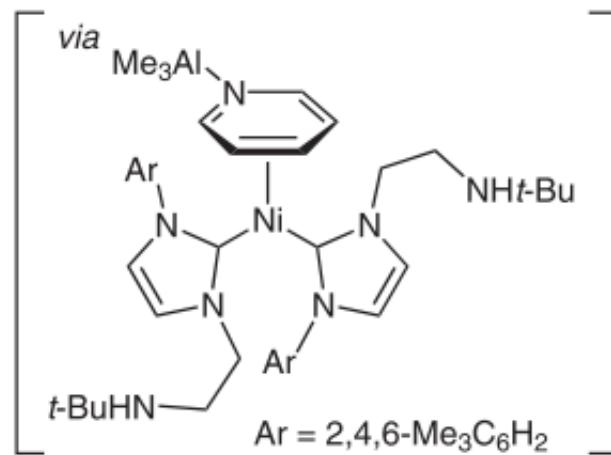


C4-Selective Functionalization

---alkenylation

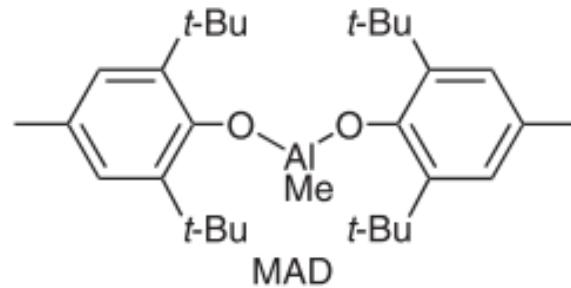
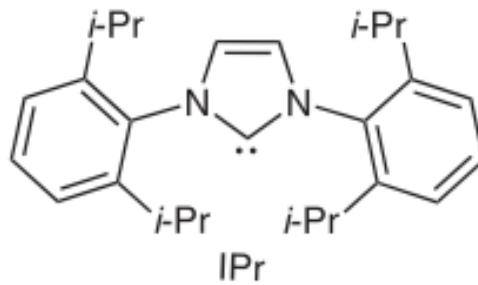
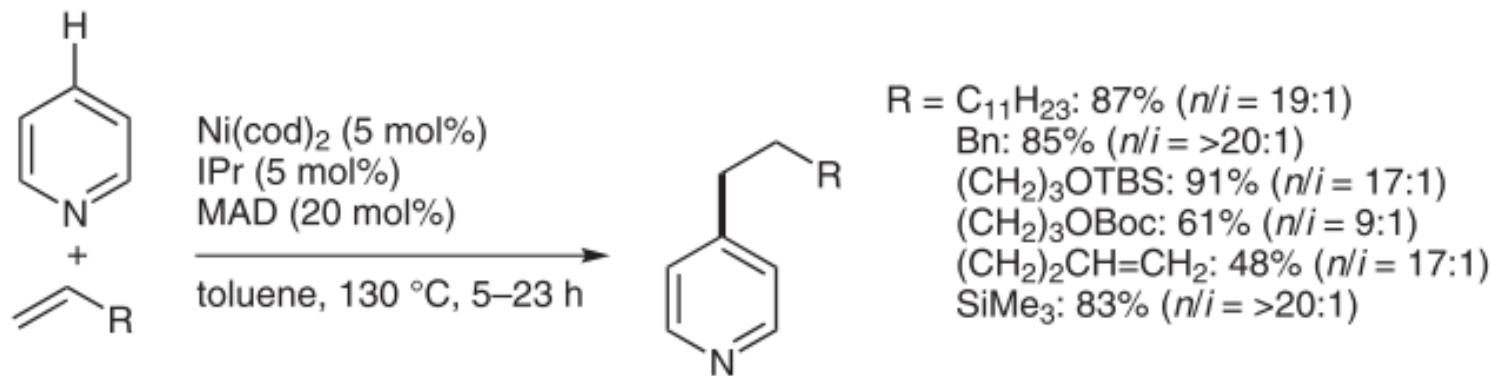


$\text{R} = \text{H}$: 85% (C4/C3 = 3:1)
 2-Me: 56% (C4 only)
 3-Me: 85% (C4/C5 = 2.5:1)
 4-Me: 34% (C3 only)
 2-Ph: 19% (C4/C3 = 1.3:1)
 3-Ph: 71% (C4/C5 = 1:1)
 2-MeO: 49% (C4 only)
 3-MeO: 89% (C4 only)

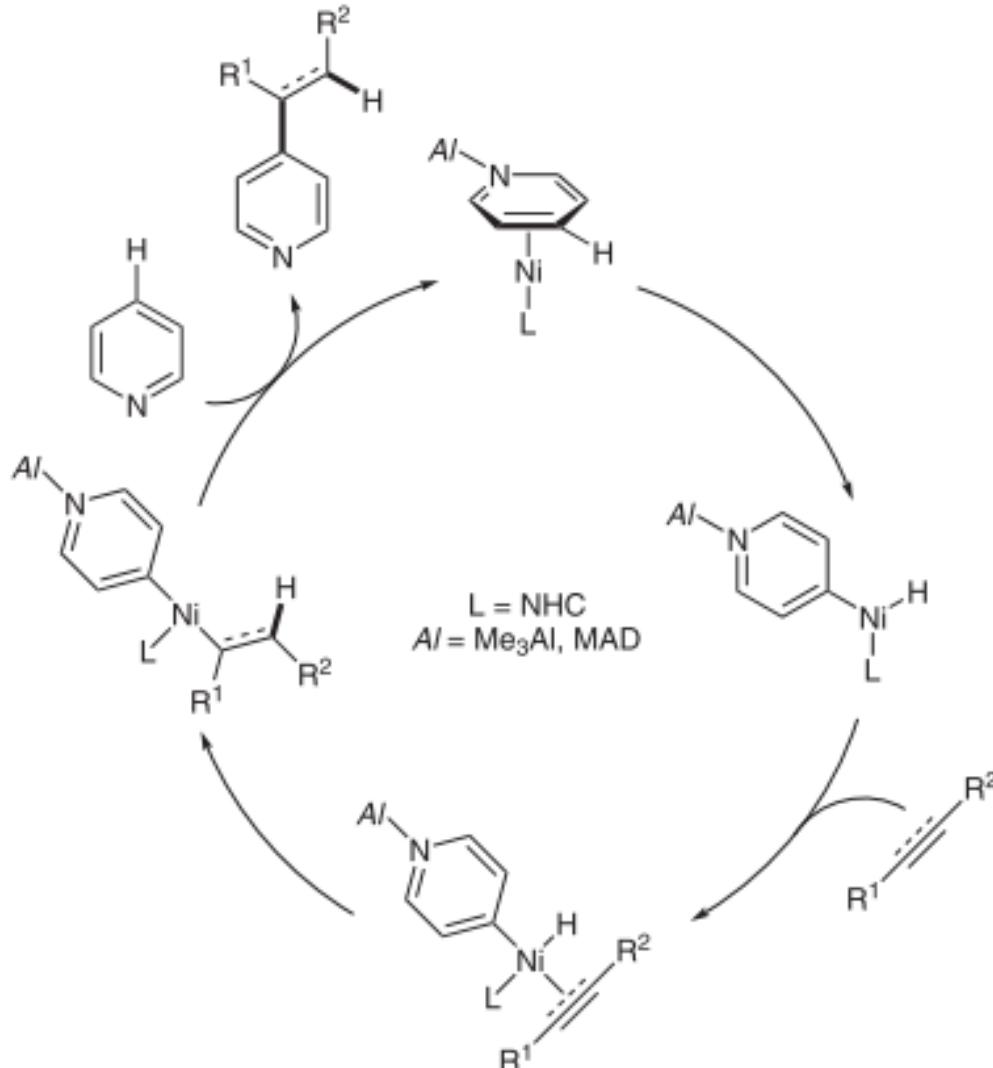




C4-Selective Functionalization ---alkylation



C4-Selective Functionalization ---alkenylation and alkylation





Summary

- *Construct carbon–carbon bonds on pyridine*
 - *alkylation, alkenylation, arylation, acylation*
 - *selectively at C2, C3 or C4*

- *Construct carbon–oxygen and carbon–nitrogen bonds*



Thanks for Your Attentions!

感谢您的关注！