

Catalytic Functionalization of sp^3 C-H Bonds Adjacent to a Nitrogen Atom in Alkylamines

Taku Asaumi

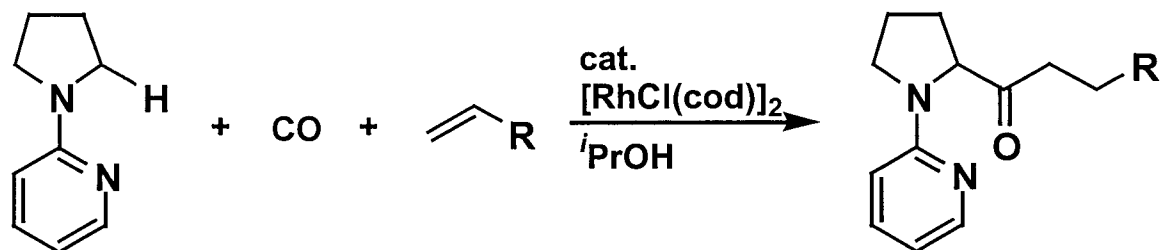
24 JUNE 2003

Murai and Chatani Group

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Faculty of Engineering
Osaka University**

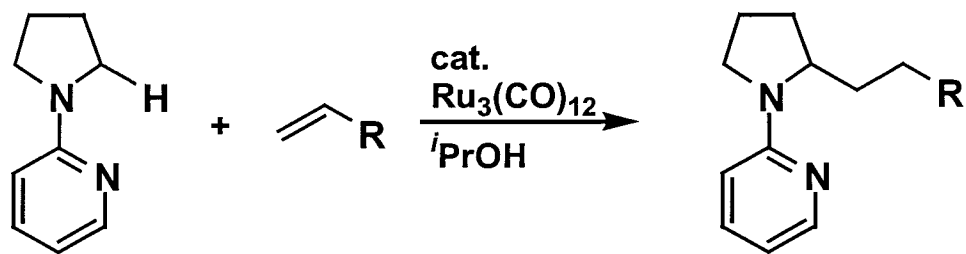
Catalytic Functionalization of sp^3 C-H Bonds Adjacent to a Nitrogen Atom in Alkylamines

carbonylation



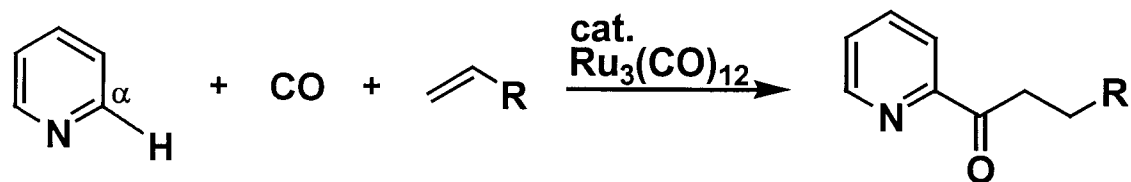
J. Am. Chem. Soc. 2000, 122, 12882.

alkylation

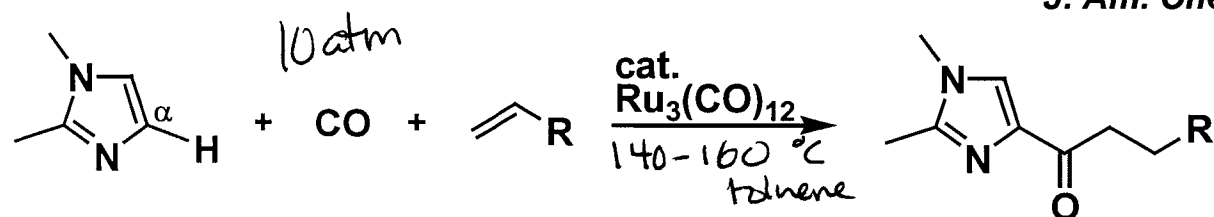


J. Am. Chem. Soc. 2001, 123, 10935.

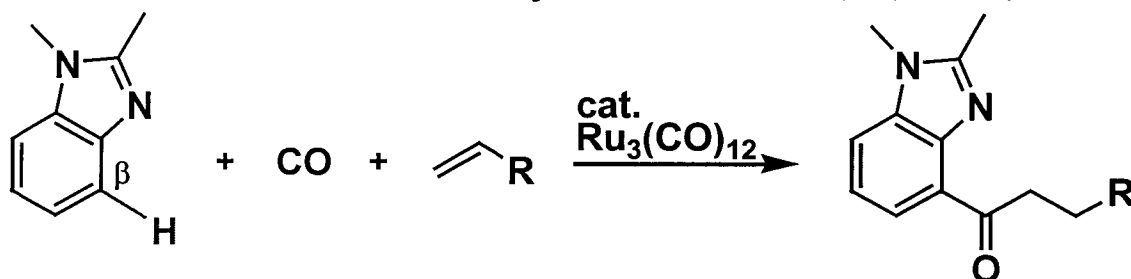
Catalytic Carbonylation at sp^2 C-H Bonds



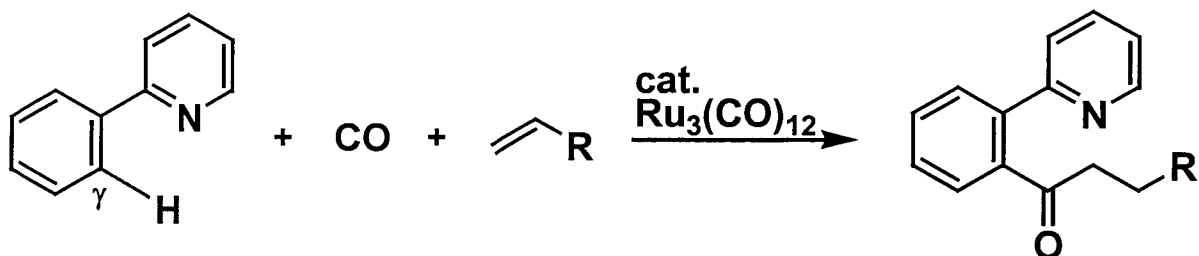
Moore, E. J.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; LaBounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc.* 1992, 114, 5888.



Chatani, N.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* 1996, 118, 493.

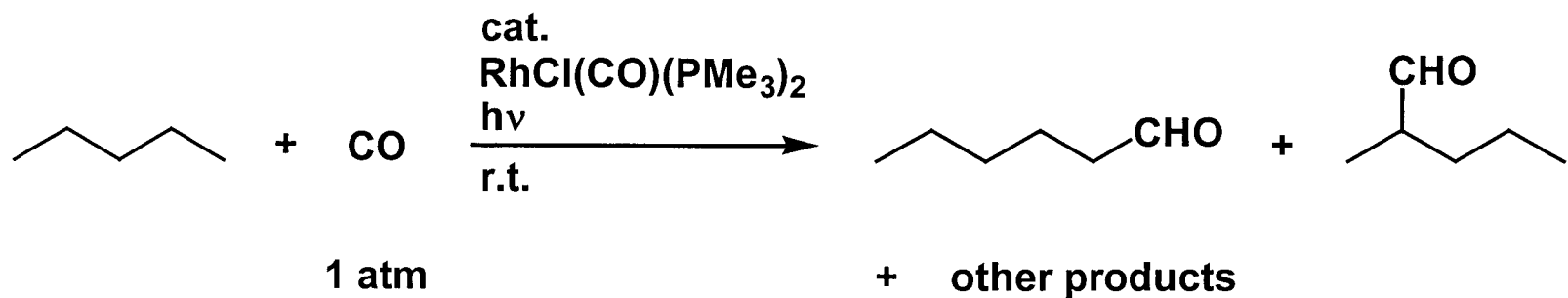


Fukuyama, T.; Chatani, N.; Tatsumi, J.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* 1998, 120, 11522.

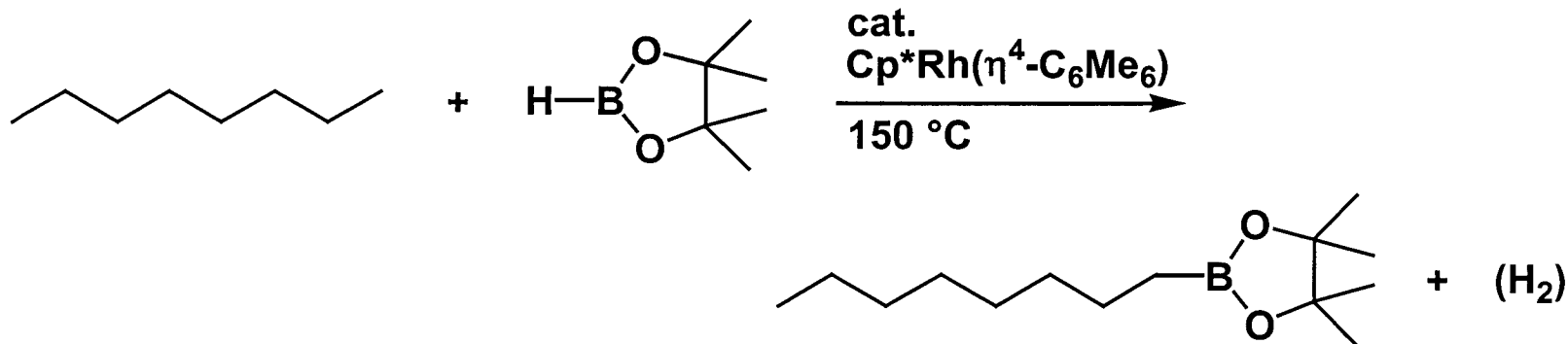


Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* 1997, 62, 2604.

Catalytic Reactions Involving Cleavage of sp^3 C-H Bonds

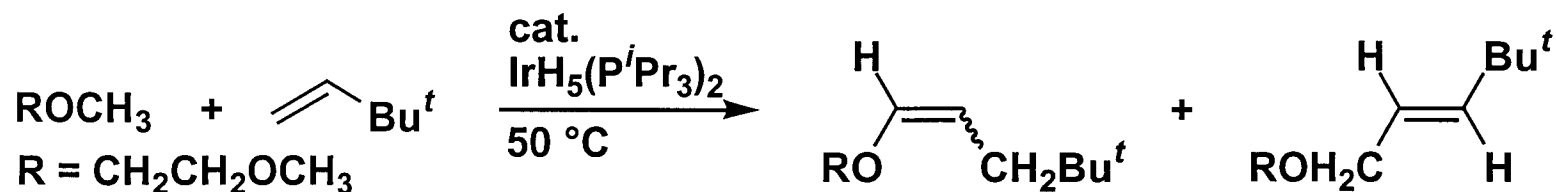


Sakakura, T.; Sodeyama, T.; Sasaki, K.; Wada, K.; Tanaka, M.
J. Am. Chem. Soc. 1990, 112, 7221.

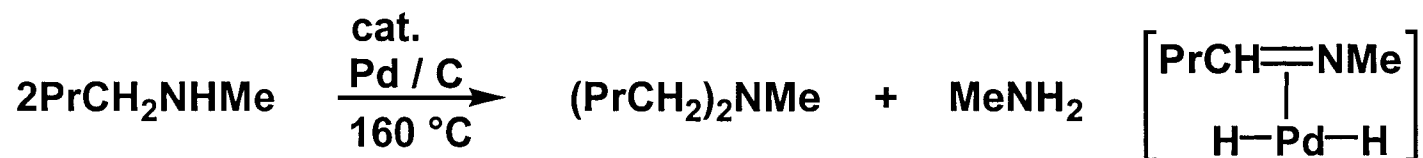


Chen, H.; Schlecht, S.; Semple, T. C.; Hartwig, J. F. *Science* 2000, 287, 1995.

Catalytic Reactions Involving Cleavage of sp^3 C-H Bonds α to Heteroatoms

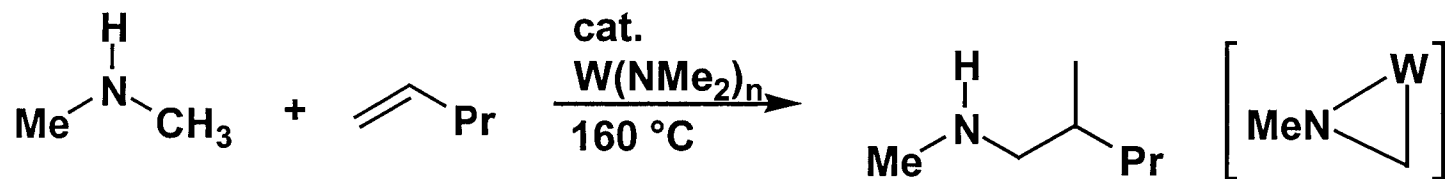


Y, Lin.; D, Ma.; X, Lu. *Tetrahedron Lett.* 1987, 28, 3249.



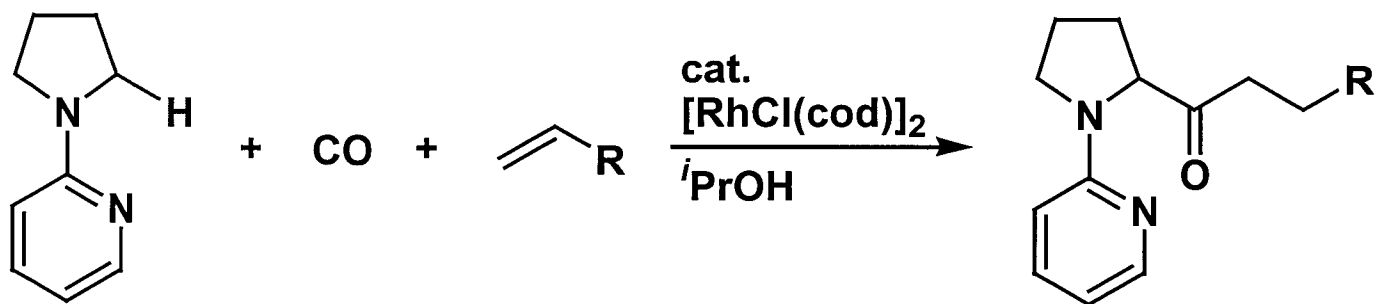
Yoshimura, N.; Moritani, I.; Shimamura, T.; Murahashi, S.-I.
J. Am. Chem. Soc. 1973, 95, 3038.

Shvo, Y.; Laine, R. M. *J. Chem. Soc., Chem. Commun.* 1980, 753.

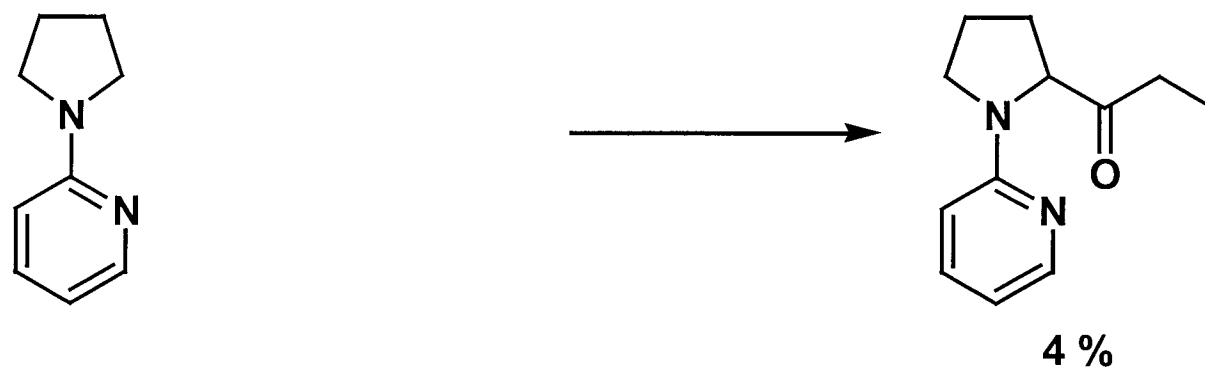
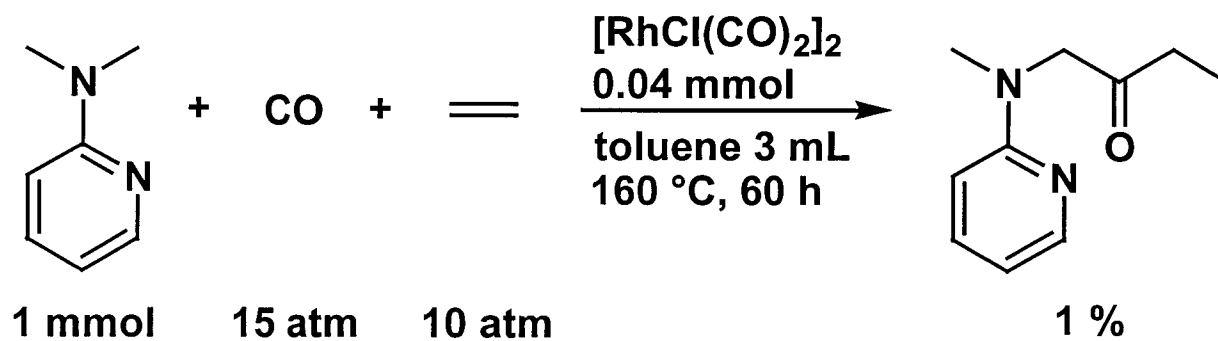


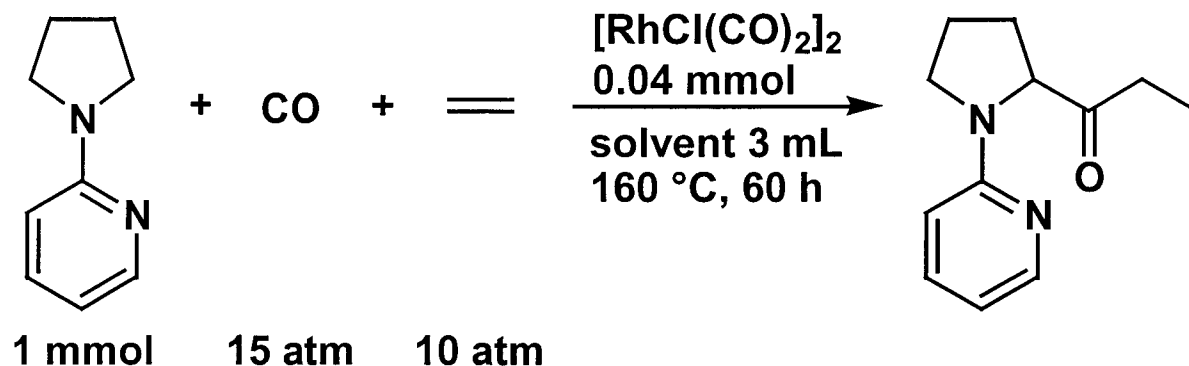
Nugent, W. A.; Ovenall, D. W.; Holmes, S. J. *Organometallics* 1983, 2, 161.

Rhodium-Catalyzed Carbonylation



Initial Attempts





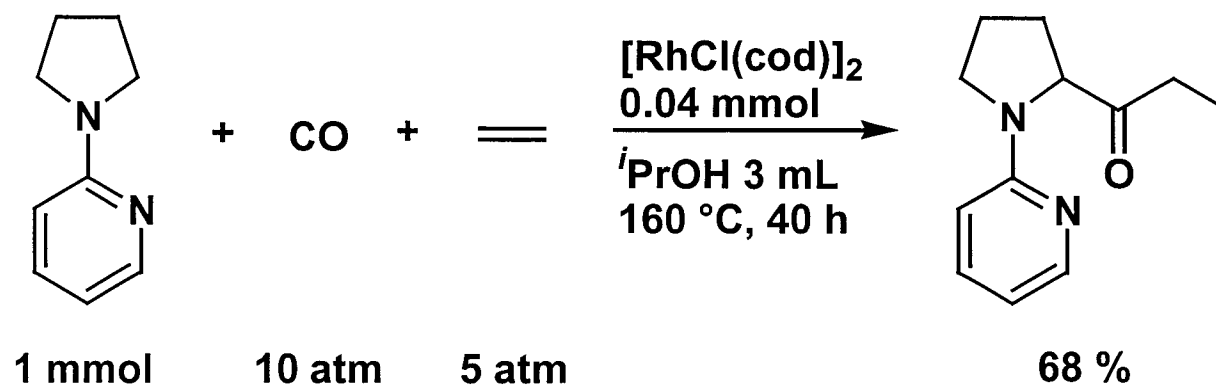
solvent	yield
toluene	4 %
THF	7 %
CH ₃ CN	23 %
<i>i</i> PrOH	70 %
DMF	no reaction

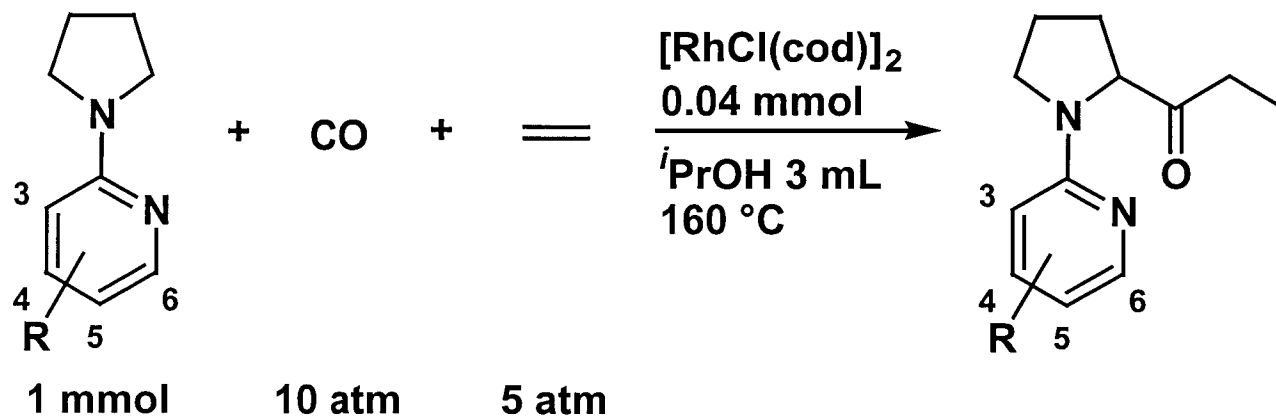
(in *i*PrOH)

ineffective : RhCl₃·3H₂O RhCl(CO)(PPh₃)₂ RhH(CO)(PPh₃)₂
 [RhCl(C₂H₄)]₂ Cp*RhCl(acac)
 Ru₃(CO)₁₂ [RuCl₂(CO)₃]₂ [IrCl(cod)]₂
 [IrCl(CO)₃]_n Mo(CO)₆ W(CO)₆

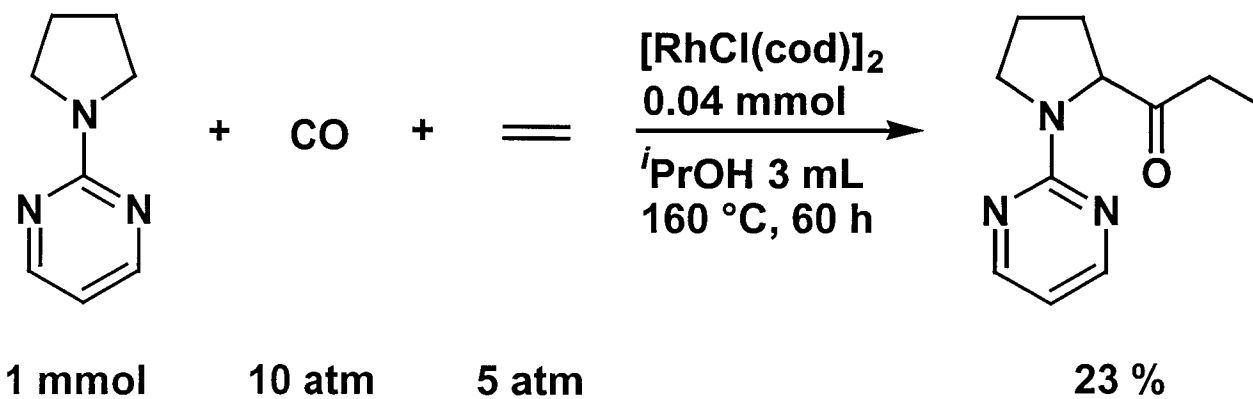
effective : Rh₄(CO)₁₂ Rh₆(CO)₁₆ RhCl(PPh₃)₃
 [Rh(OAc)₂]₂ [RhCl(cod)]₂

Standard Reaction Conditions

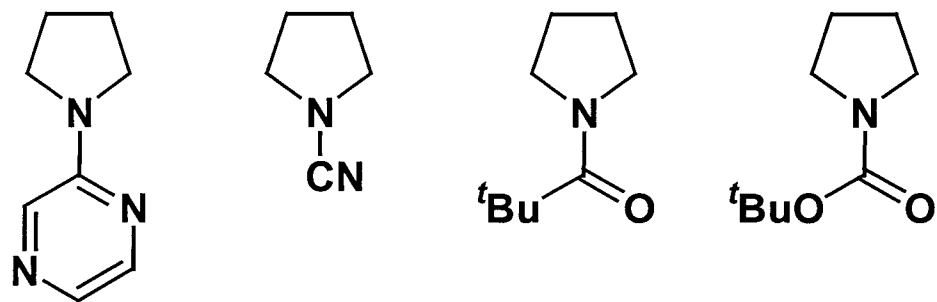




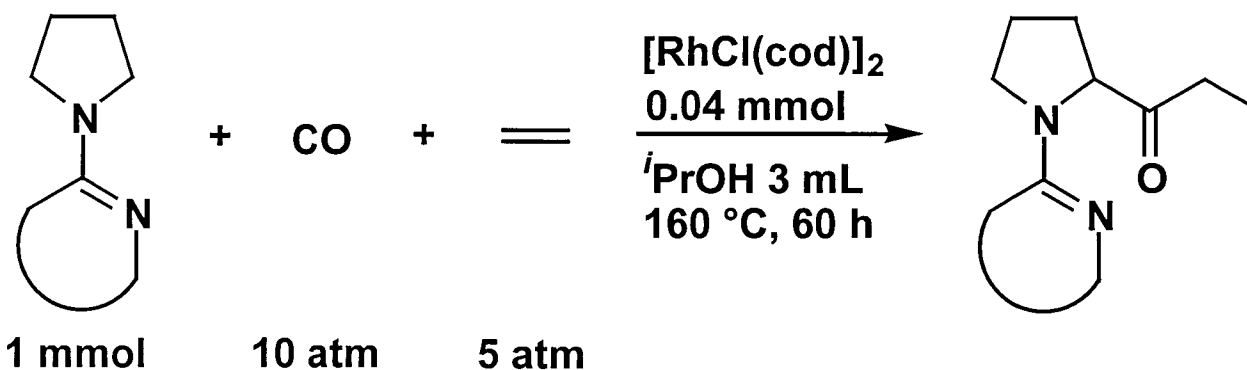
R	reaction time	yield
H	40 h	68 %
3 - Me	60 h	73 %
4 - Me	60 h	73 %
5 - Me	40 h	84 %
6 - Me	60 h	12 %
5 - CF ₃	60 h	15 %



no reaction

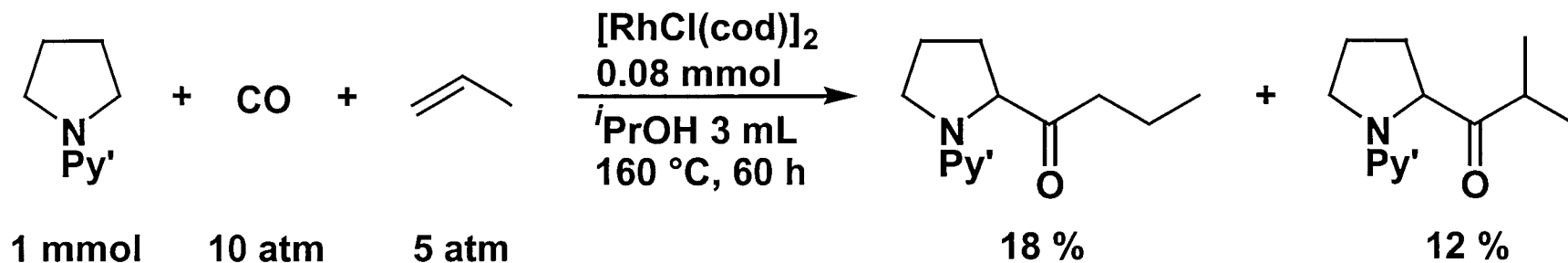


Correlation between pK_a Values and Yields

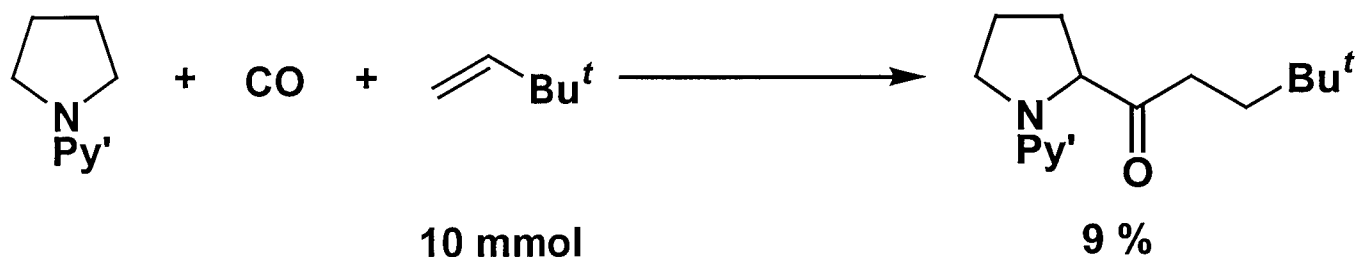


directing group	pK_a^*	yield
	5.23	68 % (40 h)
	1.31	23 %
	0.65	no reaction

* The pK_a values are those of the corresponding conjugate acids of pyridine, pyrimidine, and pyrazine.

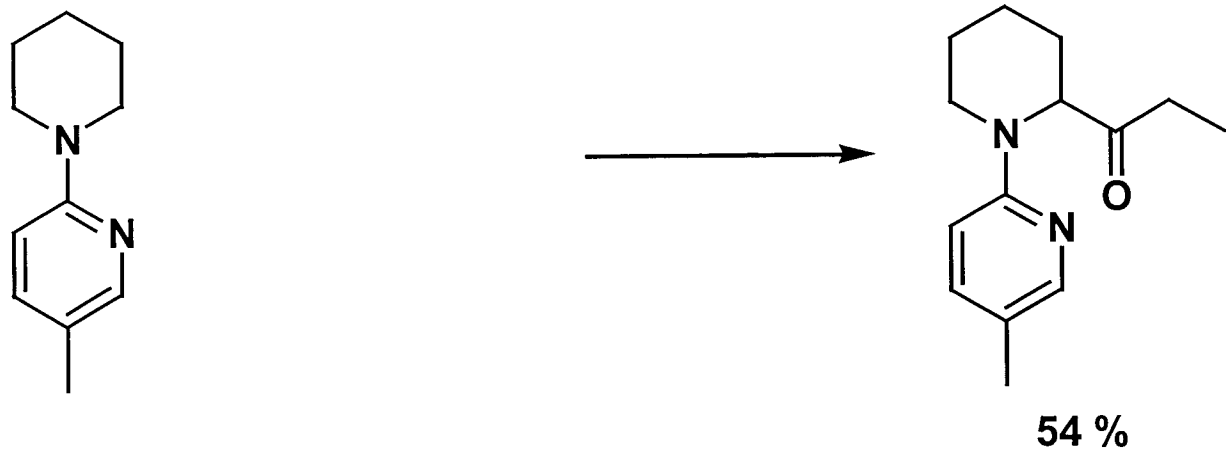
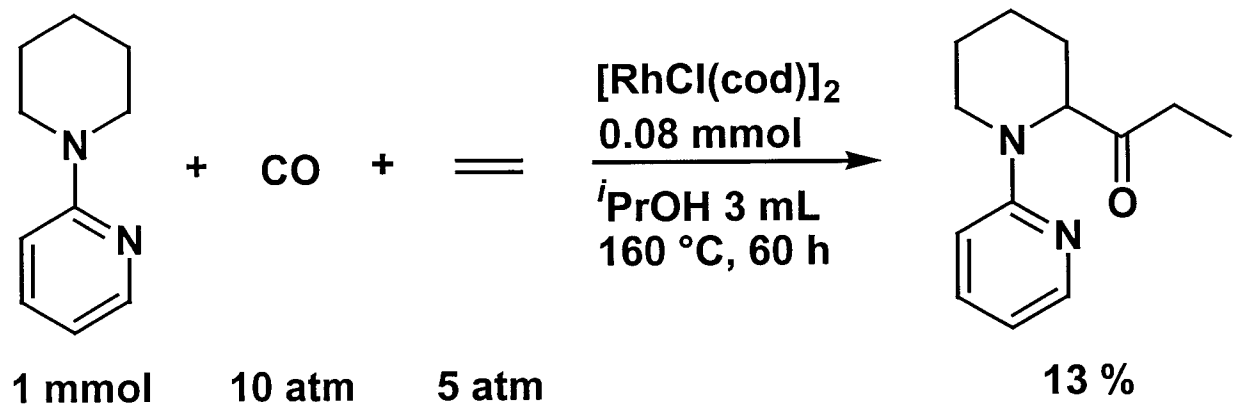


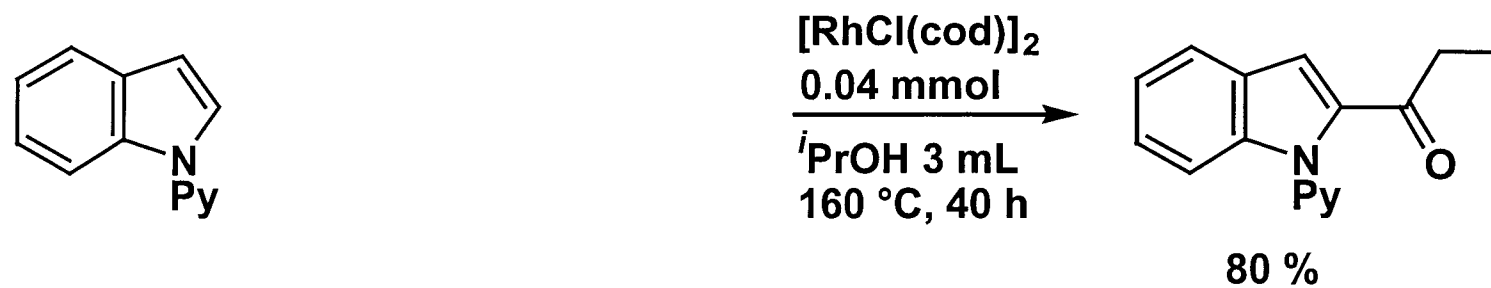
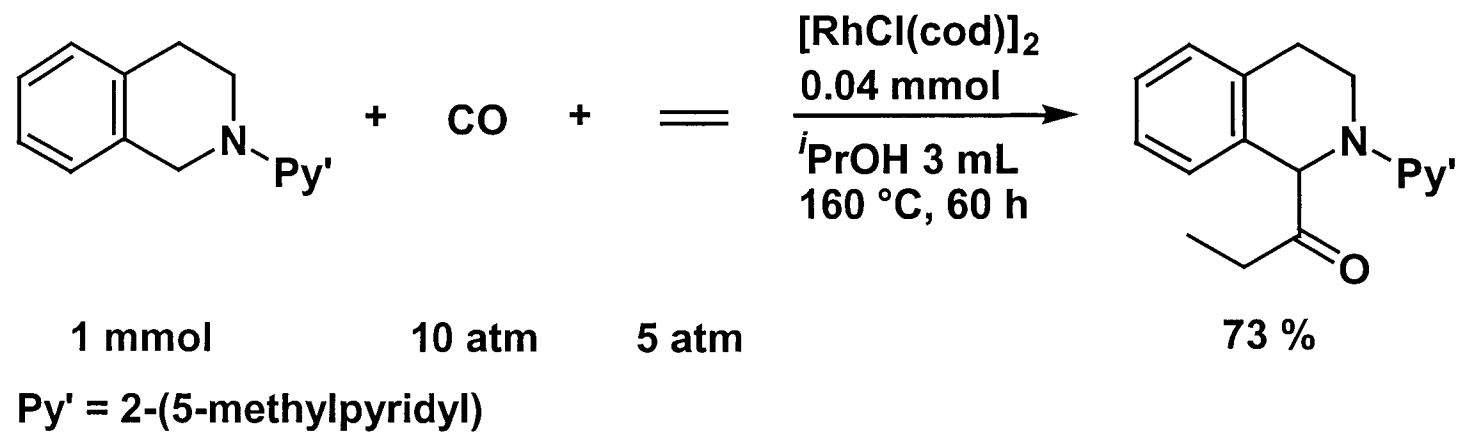
Py' = 2-(5-methylpyridyl)

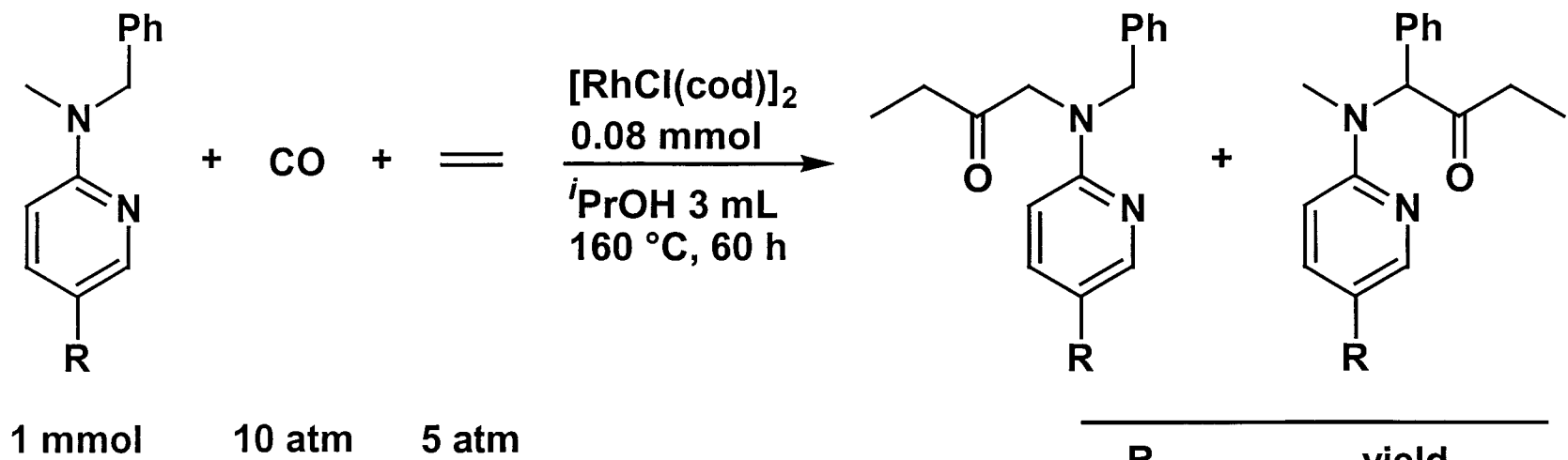


no reaction

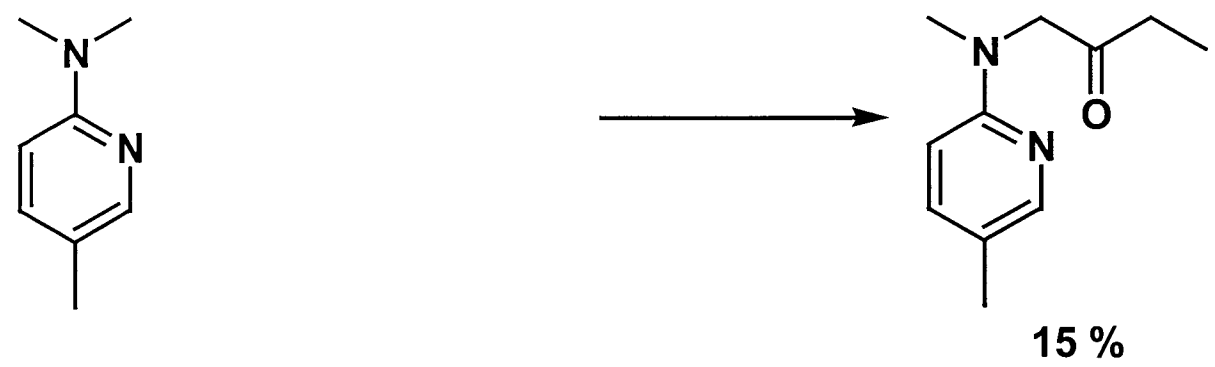




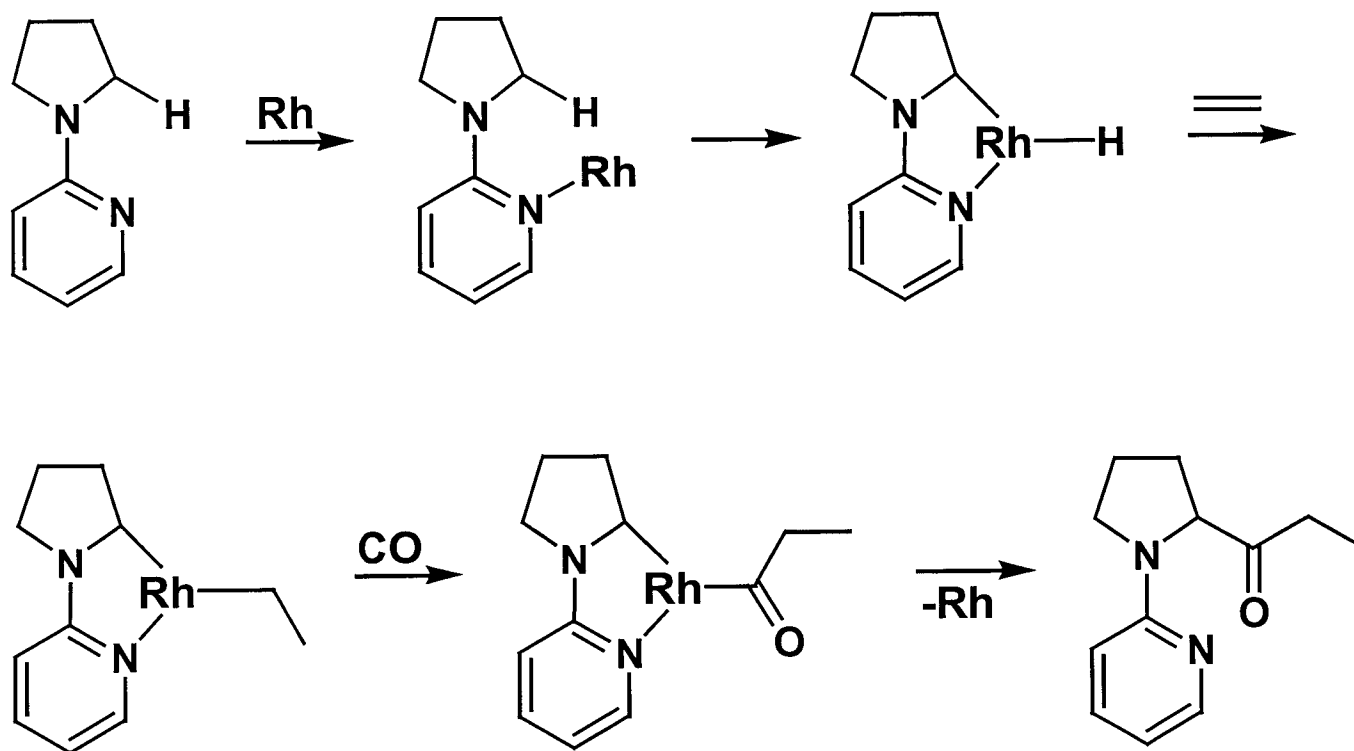




R	yield
H	11 % (>99/1)
Me	18 % (90/10)

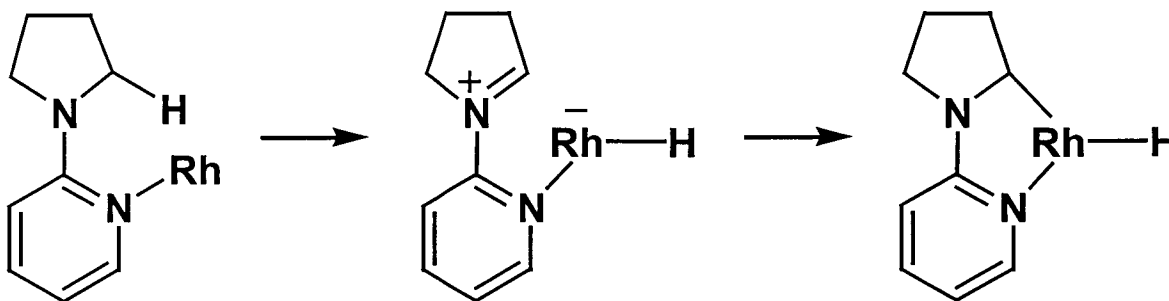


Plausible Mechanism

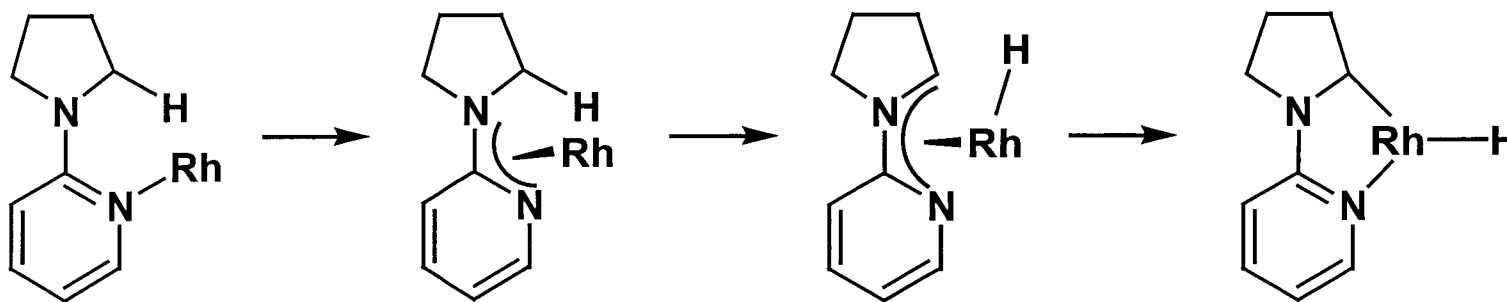


Possible Steps for the Cleavage of C-H Bonds

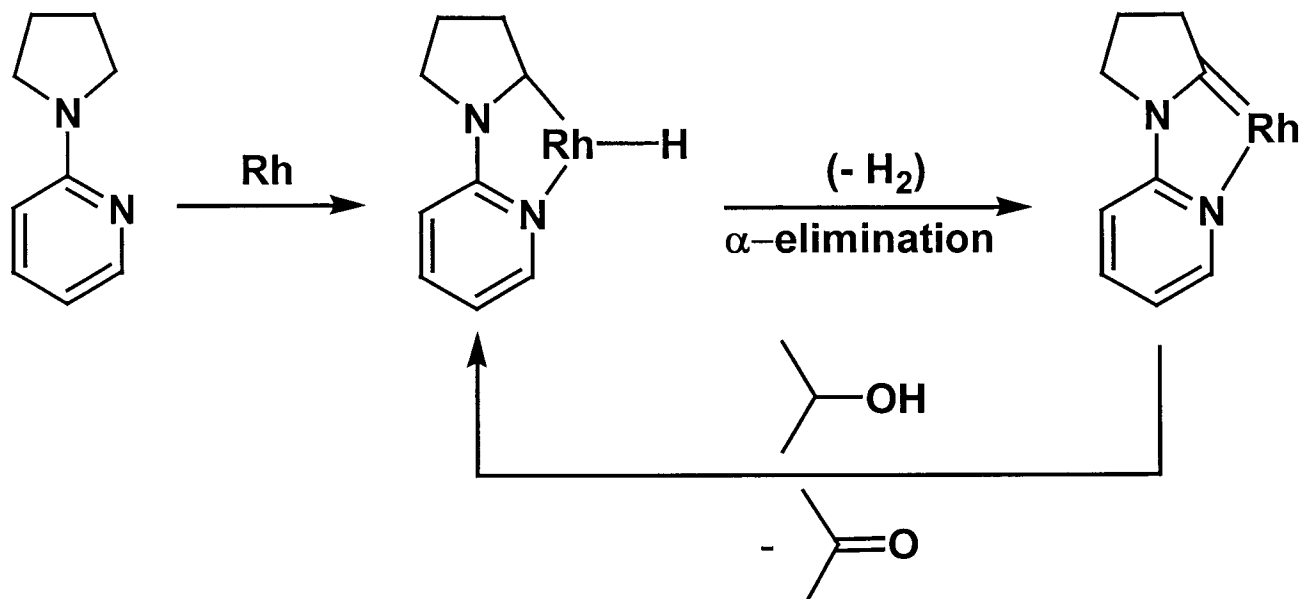
(1) *via an iminium intermediate*



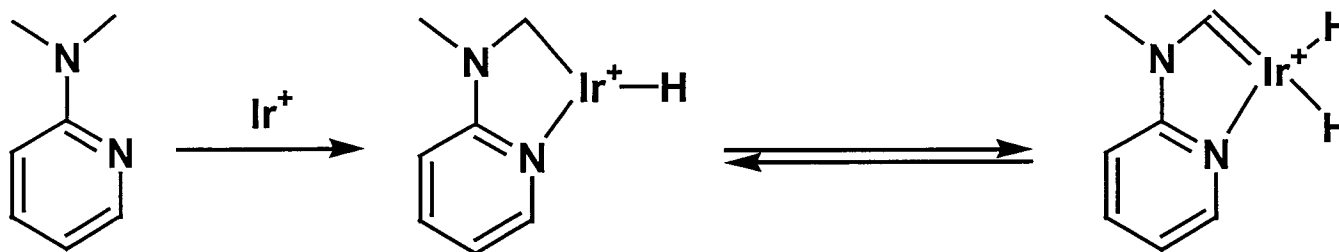
(2) *via a hydride elimination from 1,3-diaza- π -allyl Rh complex*



Our Proposal

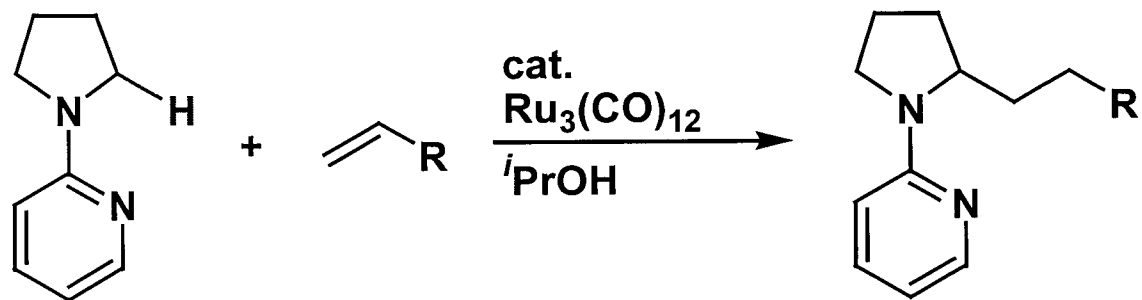


Lee, Faller and Crabtree's Report

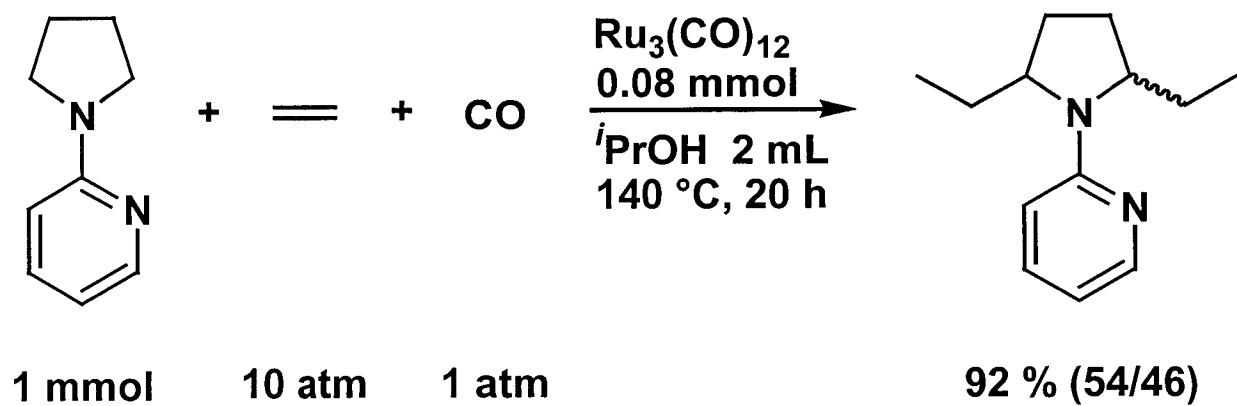


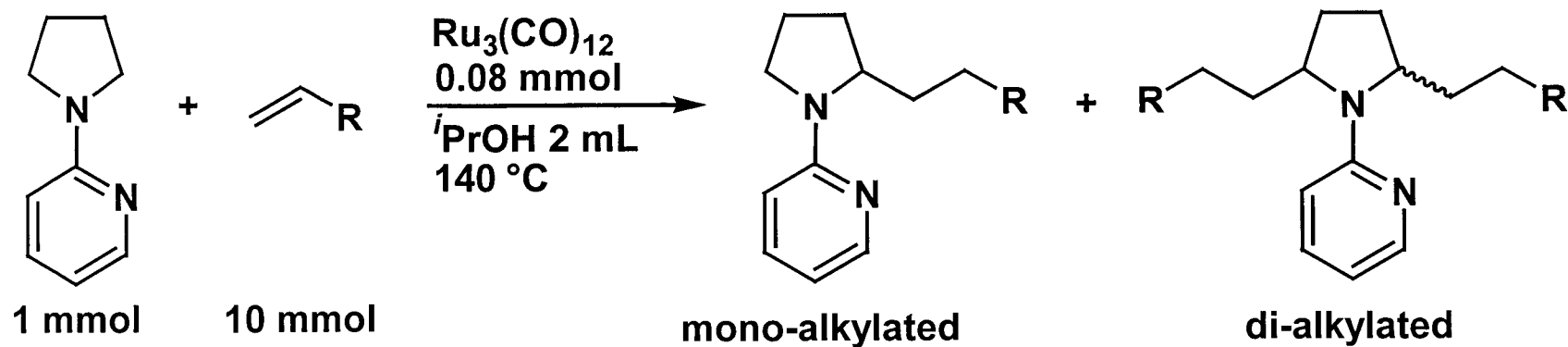
Lee, D.-H.; Chen, J.; Faller, J. W.; Crabtree, R. H. *Chem. Commun.* 2001, 213.

Ruthenium-Catalyzed Alkylation



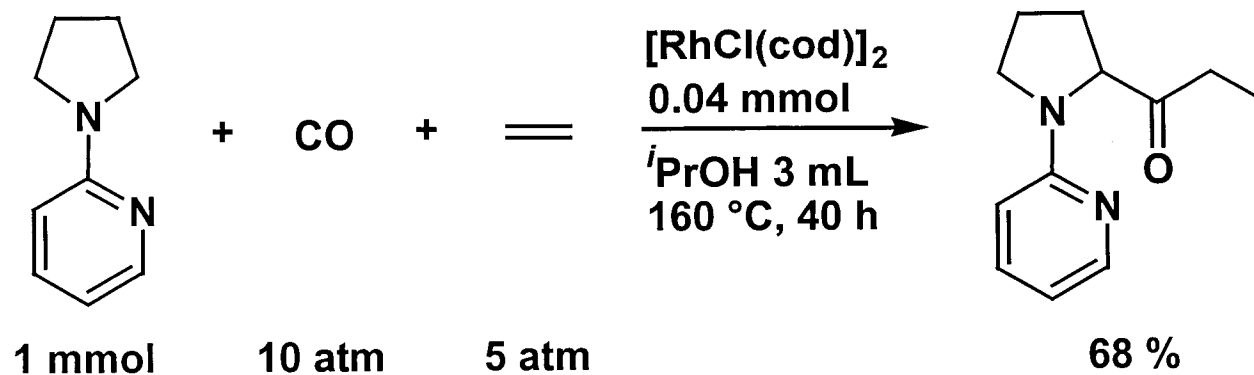
Standard Reaction Conditions



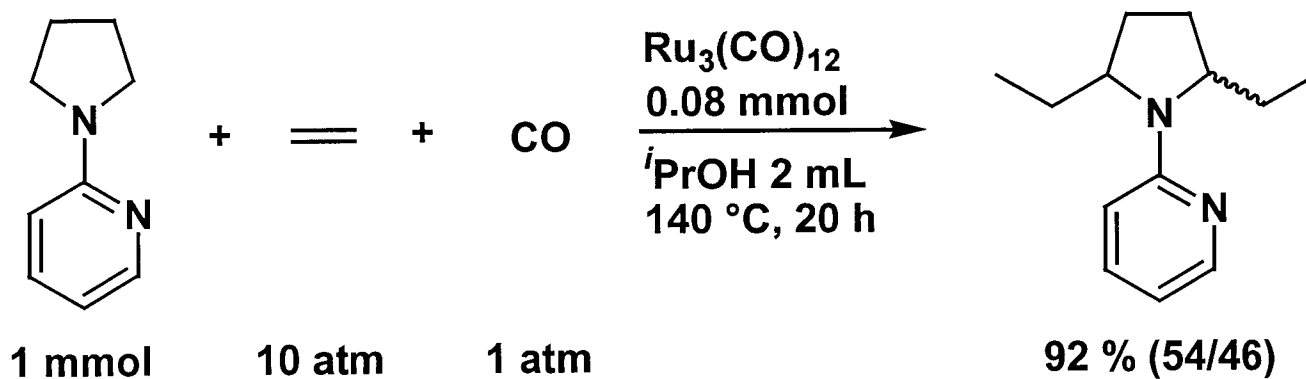


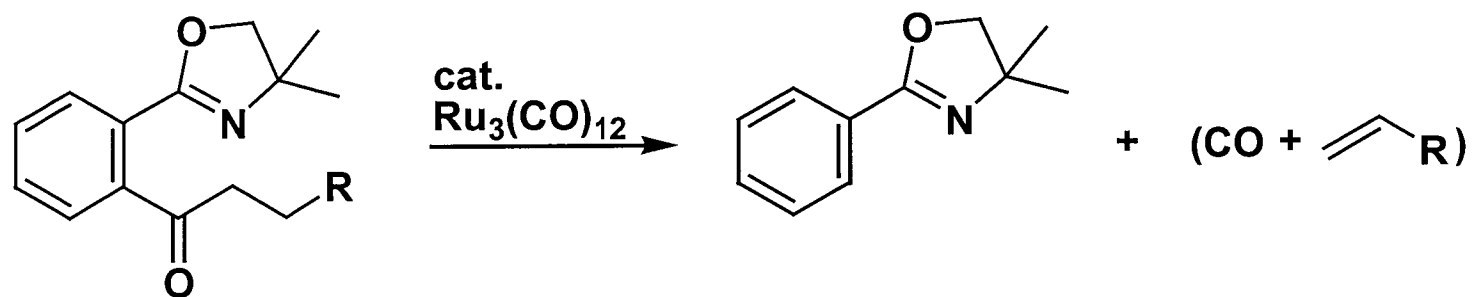
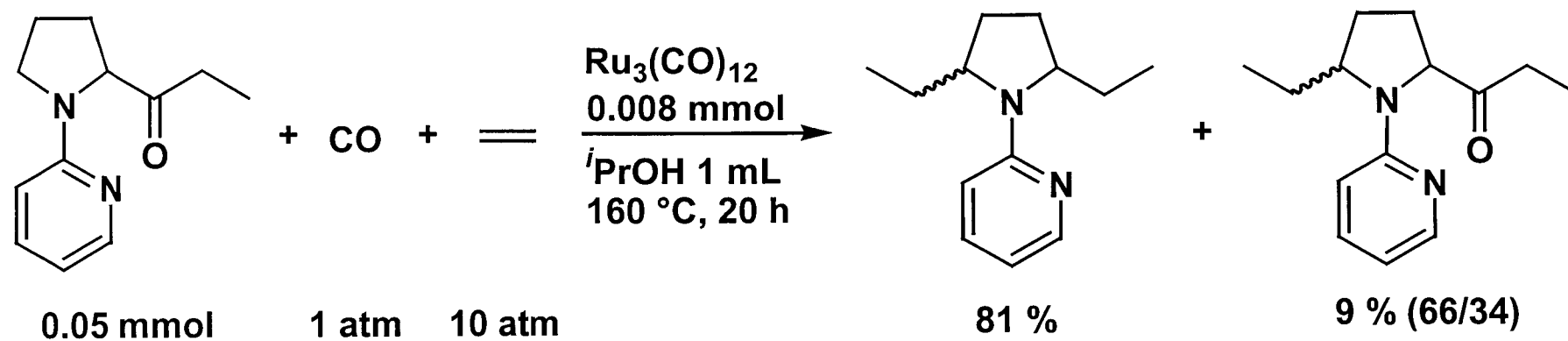
olefin	reaction time	yields	
		mono-alkylated	di-alkylated
Bu	60 h	29 %	53 % (52/48)
Bu ^t	60 h	21 %	73 % (51/49)
Ph	20 h	—	58 % (50/50)
	60 h	33 %	39 % (60/40)

Carbonylation of the C-H Bond



Alkylation of the C-H Bond

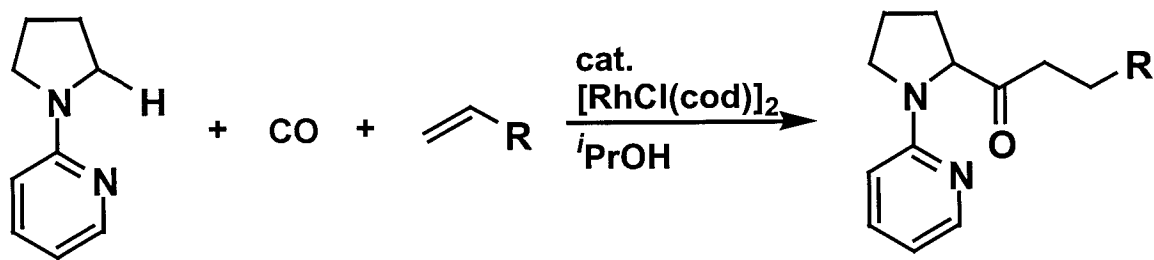




Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* 1999, 121, 8645.

Catalytic Functionalization of sp^3 C-H Bonds Adjacent to a Nitrogen Atom in Alkylamines

carbonylation



alkylation

